触媒的不斉カルベン移動反応を経由する
多官能基性光学活性化合物の合成

（Synthesis of Multi-functionalized Optically Active Compounds via Catalytic Asymmetric Carbene Transfer Reactions）

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論文内容の要旨　(博士)

博士学位論文名	触媒的不斉カルベン移動反応を経由する多官能基性光学活性化合物の合成

(要旨　1,200 字程度)

ジアゾ化合物類と金属触媒による発生する金属カルベン錯体は高い反応活性と特徴的な反応性により，古くから重要な中間体として天然物や医薬品などの生理活性物質の合成に応用され重要な役割を果たしている。しかし，ジアゾ化合物の多くはジアゾエステル系に限られ，また各種結合への不斉カルベン移動反応において，収率，立体選択性，触媒効率にまだ挑戦的な課題が残されている。そこで，本論文では，今までにない様々な官能化されたジアゾ化合物類を新規に合成し，その金属−カルベン錯体の反応性を制御することで B−H 挿入反応，アリル及びビニルシラン類の触媒的不斉シクロプロパン化反応，ジアゾオキシムエーテル類の不斉カルベン移動反応，ナフチルジアゾアセトアミド類の芳香族環へのカルベン移動反応などの各種不斉カルベン移動反応の開発を行った。

第 1 章では，カルベンの発見，その特徴とカルベン前駆体としてのジアゾ化合物の合成法と各結合へのカルベン移動反応などの研究背景についてまとめ，第 2 章では，Ru(II)-Pheox 触媒の開発，その特徴，そして各結合へのカルベン移動反応について概説し研究目的を明示した。

第 3 章では，Ru(II)-Pheox 触媒による B−H 結合への不斉カルベン移動反応の開発についての研究成果についてまとめた。ジアゾ化合物類の置換基効果が本反応系では，重要な要素であることが明らかになった。末端置換基を立体障害の大きい化合物にすることで，立体選択性を高く制御できることが示された(98% ee)。また，α-アリールジアゾエステル類を用いることで，副生成物を防ぎ，高収率で有機ホウ素化合物が得られることを明らかにした(94%収率)。

第 4 章では，Ru(II)-Pheox 触媒によるアリル及びビニルシラン類とジアゾエステル類との光学活性シクロプロパン化反応の開発についてまとめた。アリルシラン類の場合，不斉カルベン移動反応は円滑に進行し，高収率，高立体選択性で目的の不斉シリルシクロプロパン化合物を合成した(99% yield, 95:5 d.r., 99% *trans* ee)。ビニルシラン類の場合，立体障害大きいシラン類は二重結合に直接結合しているため，不斉カルベン移動反応の反応性が低下するが，ジアステレオ選択性とエナンチオ選択性は優れた結果を示した(61% yield, >99:1 d.r., 99% *trans* ee)。さらに，応用として，抗がん剤である Imatinib-7 や抗 HIV 治療薬の重要な鍵化合物を容易に合成できることを示した。

第 5 章では，ジアゾヒドラゾンやジアゾオキシムエーテルのようなイミン型が隣接する金属カルベン錯体を系中で合成し，単結合と二重結合への触媒的不斉カルベン移動反応を開発しその成果をまとめた。さらに Ru(II)-Pheox 触媒によるジアゾヒドラゾンの分子内 C−H 挿入反応を経由するヘテロ環ピラゾール類の新規合成法を見出した(80%収率)。また Ru(II)-Pheox 触媒による α-ジア

ゾオキシムエーテルとオレフィンの初めての触媒的不斉シクロプロパン化反応を開発しその成果をまとめた(99% yield, 80:20 d.r., 98% *trans* ee, 99% *cis* ee)。加えて，本反応の応用として，シクロプロピルオキシムエーテルを出発する有用な生物活性中間体である光学活性シクロプロピルメチルアミン誘導体の合成経路を開発した。

第 6 章では，様々なナフチルジアゾアセトアミド類を新規に合成し，不斉 Ru(II)-Pheox 触媒による芳香族環へのカルベン移動反応を開発した。Buchner 環拡大反応の中間体であるノルカラジエン類を高収率，高エナンチオ選択性で合成した(99% yield, 99% ee)。本反応は，相当するトリエンとの平衡混合物ではなく単独の光学活性ノルカラジエンが生成する系として初めて成果である。

第 7 章では研究結果について総括した。また，第 8 章には，第 3 章から第 6 章までの全ての合成実験の詳細と構造決定に必要な全物理データおよびその解析データをまとめた。

別紙４－１（課程博士（英文））

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Abstract（Doctor）

Title of Thesis	Synthesis of Multi-functionalized Optically Active Compounds via Catalytic Asymmetric Carbene Transfer Reactions

Approx. 800 words

Metal-carbene complexes generated by various diazo compounds and metal catalysts have long been used as important reactants in synthetic organic chemistry due to their high reaction activity and characteristic reactivity. These applied reactions play an important role in the synthesis of bioactive substances such as natural products and pharmaceuticals. However, in the asymmetric carbene transfer reaction of various bonds of functionalized diazo compounds, there are still challenging problems in yield, stereoselectivity and catalytic efficiency.

Recently, we developed a series of Ru(II)-Pheox complex, which is efficient in carbene transfer reactions, in particular, asymmetric intermolecular and intramolecular carbene transfer reactions and C−H, Si−H, N−H insertion reactions in high yields with high enantioselectivities. Thus, I focus on catalytic asymmetric intermolecular and intramolecular carbene transfer reactions, C−H, B−H insertion reactions using Ru(II)-Pheox catalyst and functionalized diazo compounds.

Chapter 1 summarizes the discovery of carbene, its characteristics, the method of synthesizing a diazo compound as a carbene precursor, and the application of the carbene transfer reaction to σ and π bonds.

Chapter 2 outlines the development of Ru (II)-Pheox catalysts, their characteristics, and the carbene transfer reactions to each bonds and presents the research objective of this thesis.

In Chapter 3, we developed the highly enantioselective B−H bond insertion reaction of α-methyl-α-diazoesters and α-aryl-α-diazoesters with phopshine- and amine-borane adducts via a Ru (II)-Pheox-catalyzed carbene transfer reaction to a single bond. It was clarified that the substituent effect of diazo compounds is an important factor in this reaction system. Specifically, it was suggested that the stereoselectivity can be highly controlled by using a compound having a large steric hindrance as the terminal substituent (98% ee). The highest enantioselectivity was achieved in the case of dinaphthylenyl diazopropionate with triphenylphosphine-borane adducts (95% ee, 81% yield). The new α-aryl-α-diazoesters such as dinaphthylenyl diazophenylacetate and dinaphthylenyl diazo(4-chlorophenyl acetate) were synthesized to advance the highly efficient catalytic carbene transfer reactions. Moreover, by using α-aryl diazo esters, by-products were prevented and organoboron compounds were obtained in high yield (94% yield).

In Chapter 4, we developed a Ru(II)-Pheox-catalyzed optically active cyclopropanation reaction between of allyl- and vinylsilanes with diazoesters. In the case of allylsilanes, the asymmetric carbene transfer reaction proceeded smoothly, and the desired asymmetric

silylcyclopropane compounds were successfully synthesized with high yields and high stereoselectivities (99% yield, 95:5 d.r., 99% *trans* ee). In the case of vinyl silanes, silanes with large steric hindrance are directly bound to the double bond, which slows the reactivity of the asymmetric carbene transfer reaction and reduces the yield, but excellent diastereoselectivity and enantioselectivity (61% yield, > 99:1 d.r., 99% *trans* ee). Furthermore, the silylcyclopropane could be applied for the productions of enantioenriched cyclopropylcarbinol derivatives, which are essential building blocks for the synthesis of pharmaceuticals and natural products.

In Chapter 5, Metal carbene complexes from imine forms, such as diazohydrazone and diazo oxime ether were developed and applied to carbene transfer reactions to σ and π bonds. Pyrazoles were obtained via Ru(II)-Pheox-catalyzed intramolecular C−H insertion reaction of diazohydrazone (80% yield, 2% ee). The first catalytic asymmetric cyclopropanation of α-diazo oxime ethers and olefins in the presence of a Ru(II)-Pheox catalyst was developed (99% yield, 80:20 d.r., 98% *trans* ee, 99% *cis* ee). In addition, the catalytic efficiency of Ru(II)-Phoex resulted in a high TON (5500) and TOF (455). As an application, we have developed a synthetic pathway for optically active cyclopropylmethylamine derivatives, which are useful bioactive intermediates starting from the cyclopropyl oxime ethers.

In Chapter 6, various naphthyldiazoacetamides were newly synthesized and applied asymmetric Ru(II)-Pheox-catalyzed carbene transfer reaction to the aromatic ring. The desired product norcaradienes, which are intermediates of the Buchner ring expansion reaction, were synthesized with high yields and high enantioselectivities (99% yield, 99% ee).

Chapter 7 provides the general conclusion for the research outcomes.

Chapter 8 provides the experimental and analytical data for chapters 3 to 6.

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Ar	aryl
Bn	benzoyl
Bu	butyl
Calcd	calculated
d	doublet
dd	doublet of doublet
d.r.	diastereomeric ratio
dt	doublet of triplet
DCM	dichloromethane
ee	enantiomeric excess
EDG	electron-donating group
equiv.	equivalent
EA	ethyl acetate
EWG	electron-withdrawing group
g	gram
h	hour
Hex	hexane
HPLC	high performance liquid chromatography
Hz	hertz
IR	infrared
*i*Pr	isopropyl
m	multilplet

M	molar
Me	methyl
mg	milligram
MHz	megahertz
min	minute
mL	milliter
mmol	millimole
NMR	nuclear magnetic resonance
Np	1-naphthyl
Ph	phenyl
ppm	parts per million
R_f	retention factor (in chromatography)
rt	room temperature
s	singlet
t	triplet
td	triplet of douplet
temp.	temperature
tert	tertiary
THF	tetrahydrofuran
TLC	thin layer chromatography
TON	turnover number
TOF	turnover frequency
tR	retention time
UV	ultra violet

NOTATIONS

α	alpha
$[\alpha]_D$	Specific rotation
^{1}H NMR	proton nuclear magnetic resonance spectroscopy
^{13}C NMR	carbon nuclear magnetic resonance spectroscopy
%	percentage
J	coupling constant
$[M + H]^+$	protonated molecular ion (mass spectrometry)
δ	chemical shift
^{o}C	degree Celsius

第 1 章　序論

1-1 カルベンの発見とその特徴

有機合成反応において，反応機構は主にイオン（カルボカチオン，カルボアニオン），ラジカル，カルベンなどの中間体を経由して進行する。イオンとラジカルは三配位の炭素中間体であり，1 個の空軌道しか持たないため，必然的に電子状態はそれぞれ一つしかない（Figure 1-1）[1]。

一方，カルベンは 1830 年代に Dumas, Regnault によって，P_2O_5 または濃硫酸を用いたメタノールの脱水による CH_2 の発生で初めて報告された[2]。当時はまだ安定な化合物と考えられていたが，20 世紀初めに Staudinger によって行われたジアゾ化合物の分解反応により不安定種として認識され始めてからカルベンの性質とその反応についての研究は多方面にわたり非常に活発に行われるようになった[3]。

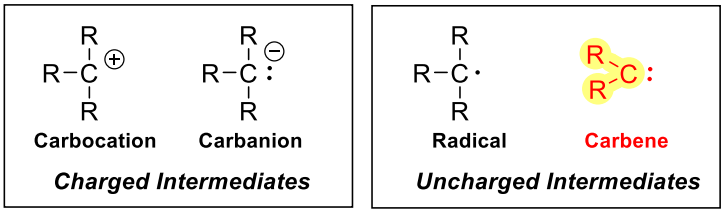


Figure 1-1. 炭素中間体の種類

カルベンは電気的に中性で二配位の炭素中間体である。二配位炭素中間体のカルベンは二つの電子状態を取ることができる。非対電子を持たない一重項状態（singlet）と非対電子を 2 つ持つ三重項状態（triplet）と区別する（Figure 1-2）。この性質を持つために，カルベンの化学は多様であり，複雑となる。この特徴がカルベンの化学を，三配位炭素中間体の化学から際立たせている。そして，どちらの電子状態が安定であるかはカルベンの構造によって変化し，また，それぞれの電子状態での反応性は異なる。一重項状態のカルベンは高エネルギー準位にあるため活発な反応性を示す。一方，三重項状態のカルベンは基底状態にあるため，その反応に選択性がみられる。

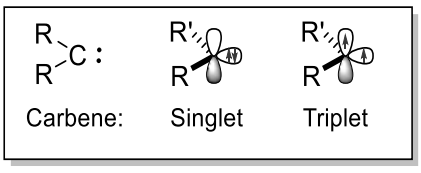


Figure 1-2. カルベンの電子状態

カルベンを発生させるためには前駆体が必要である。基本的には，α 脱離が可能な炭素化合物はカルベンの前駆体になりうる。カルベンの前駆体として代表的な化合物はジアゾ化合物であり，その他にジアジリン，三員環化合物，イリド，ケテンなどが挙げられる。ジアゾ化合物は加熱，光照射，または金属触媒添加によって効率よく窒素を放出してカルベンを発生できる優れた前駆体である。遷移金属触媒とジアゾ化合物との反応により，窒素を放出し，金属カルベン錯体（Metal-Carbene Complex）を形成する。金属カルベンは，過去数十年の間に有機化学における最も重要な反応性中間体の一つである。金属カルベンの多種多様な変換は，さまざまな化学結合を構築するための新しい方法を提供する，または，有機合成方法論への応用として，天然物や医薬品分子の合成にも金属カルベン中間体は広く使用されている。遷移金属カルベン錯体を Fischer と Schrock 型カルベン錯体と 2 つに分離する[4]。Fischer 型カルベンは，正に帯電した炭素の金属へのために，より求電子性を示す。通常は Mo，Cr，W などの低酸化状態の金属で見られる。一方，Schrock 型カルベンは，2 つの分極した共有結合を形成し，炭素原子に負電荷を与えるため，より求核性を示す。Ti や Ta などの高酸化状態の金属によく見られる（Figure 1-3a）。

また，金属カルベンとカルベン炭素に結合する置換基に基づいて acceptor-type carbene (acceptor-acceptor metal carbene, acceptor metal carbene, acceptor-donor metal carbene) と donor-type carbene (donor metal carbene, donor-donor metal carbene) と分離することができる。一般に，acceptor 置換基（EWG = CO_2R, COR, $CONR_2$, CF_3）は金属カルベン種をより求電子性かつより反応性にするのに対し，donor 置換基（EDG = vinyl, aryl, heteroaryl）は金属カルベンをより安定にし，したがって反応においてより選択性をもたらす。近年，有機合成化学において，acceptor-type carbene は容易に入手できる電子吸引基で安定化されたジアゾ化合物から比較的安全な方法で調製することができるため，活発に研究が進み，大きな成果を示した。

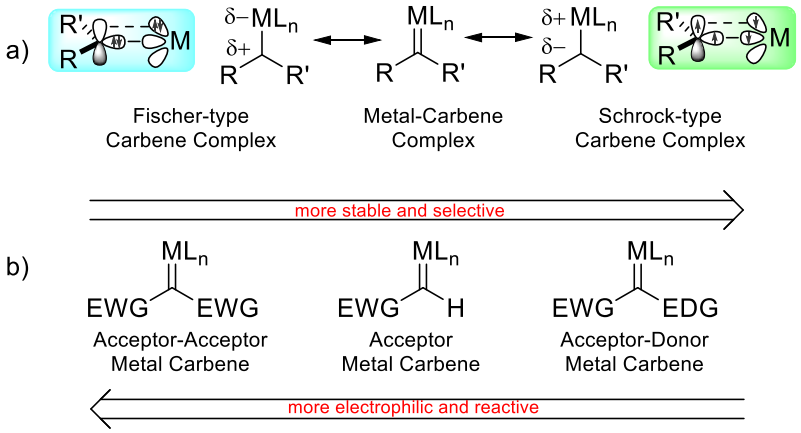
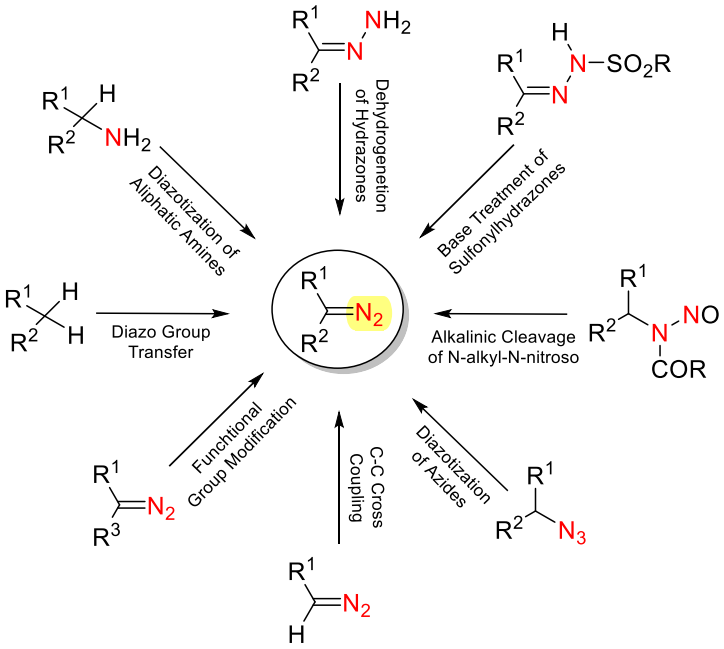


Figure 1-3. 金属カルベンの種類

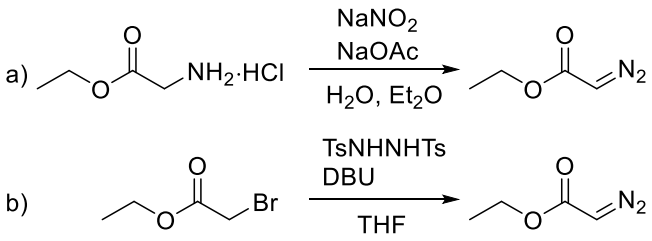
1-2　カルベンの前駆体としてのジアゾ化合物の合成

ジアゾ化合物は最もよく用いられるカルベンの前駆体であるので，その代表的な合成法を以下に示す（Scheme 1-1）。まず，ジアゾ化合物は様々なアミン類の亜硝酸ナトリウムによるジアゾ化反応に合成できる。次に，ヒドラジン類の酸化水銀や酸化銀との酸化反応によって合成できる，トシルヒドラジンのアルカリ分解による合成（Bamford-Stevens 反応），*N*-アルカリ-*N*-ニトロソ化合物のアルカリ分解による合成，様々なアジド類の分解によるジアゾ化合物の合成，トシルアジドによる活性メチレンへのジアゾトランスファーなどの多くの反応が開発されている[5]。いずれの合成方法が適しているかは，構造によって異なる。ジアゾ化合物は金属触媒，熱，光だけではなく，酸にも鋭敏で不安定なものが多いので，取り扱いが難しく，安定に単離して取り扱うことはできないものも多く存在する。このような場合，ジアゾ化合物を“反応系中（*in situ*）”で発生させることもある。



Scheme 1-1. ジアゾ化合物の主な合成法

ジアゾ化合物の中で最もよく使われているのはジアゾ酢酸エチルである（Scheme 1-2）。その合成法は水中でグリシンのエチルエステルを亜硝酸ナトリウム及び酢酸ナトリウムとの反応より得られる[6]。またはブロモ酢酸エチルを DBU 存在下ジトシルヒドラゾンとの反応より合成できる[7]。

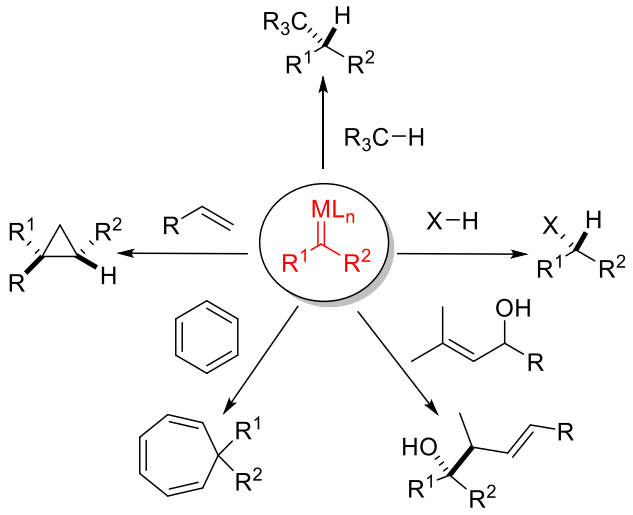


Scheme 1-2. ジアゾ酢酸エチルの合成法

1-3　各種結合への触媒的不斉カルベン移動化反応

現在までに報告されているカルベンの反応には 1) 単結合へのカルベン移動反応 (σ 結合への挿入), 2) 二重結合へのカルベン移動反応 (π 結合への挿入), 3) 独立電子対へのカルベン移動反応 (n 電子挿入) 等が知られている[8]。単結合へのカルベン移動反応には不斉 X–H (X = C, N, O, S, B, P) 結合などのカルベンの挿入反応が報告されている。一方, 二重結合へのカルベン移動反応には触媒的不斉シクロプロパン化反応と芳香族環へのカルベン移動反応による不斉アレンシクロプロパン化反応、さらに電子移動による環拡大反応 Buchner 反応がある (Scheme 1-3)。

触媒的 X–H 結合への不斉カルベン移動反応は, X–C の新規結合を構築できる強力的な方法である。また, シクロプロパン化合物は医薬品や天然物に多くみられる構造である。そのため, それぞれの反応の効率な合成や高い光学活性の合成方法が課題となった。

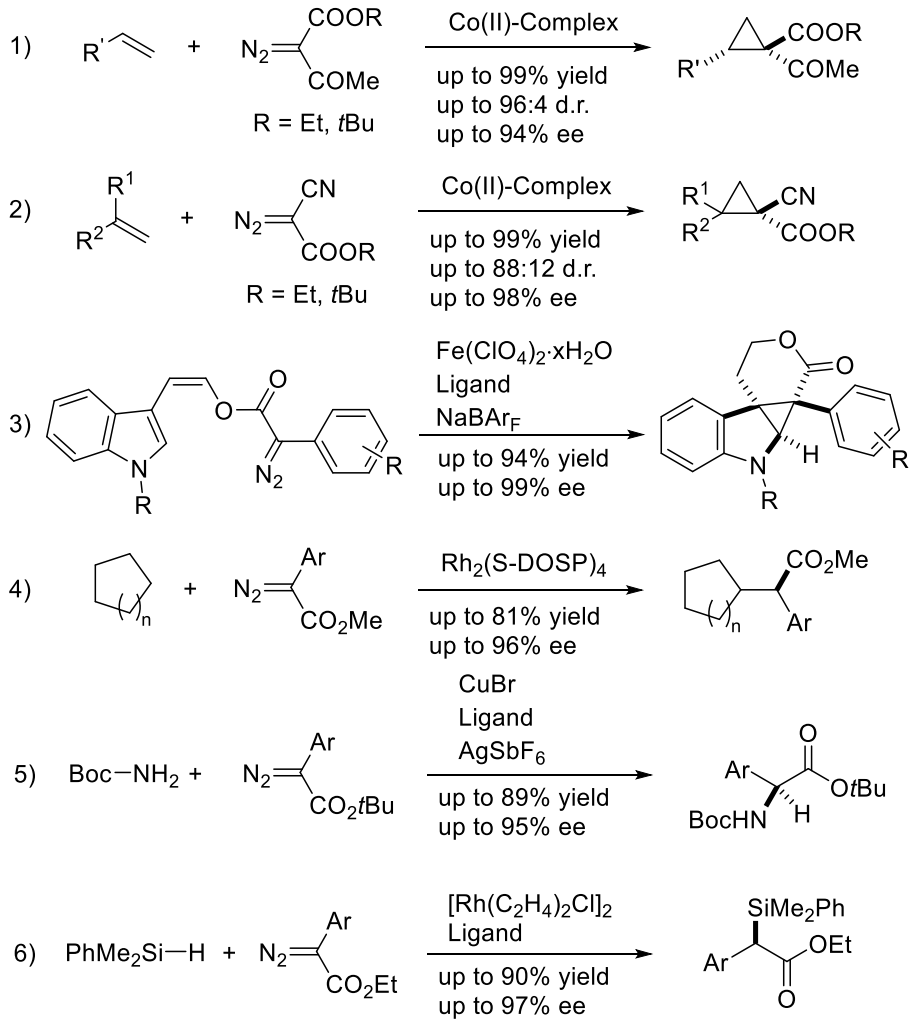


Scheme 1-3. 金属カルベンの反応

様々なジアゾエステル類の触媒的不斉カルベン移動反応の開発の研究は過去数年間にわたって活発に行われてきた(Scheme 1-4)。例えば，二重結合へのカルベン移動反応において，以下の 1)～3)などの反応が報告されている。

1）不斉 Co 触媒存在下, α-ケトジアゾアセテート類とオレフィン類との不斉カルベン移動反応を開発し, 生成物であるエステルやケトンを末端置換基に官能化された不斉シクロプロパン化合物を高収率(up to 99%)，高エナンチオ選択性(up to 94% ee)及び高ジアステレオ選択性(up to 96:4 d.r.)で得ている[9]。

2）Co 触媒存在下，α-シアノジアゾアセテート類と芳香族環とアルキル基を持つオレフィン類の分子間不斉カルベン移動反応が報告されている。生成物である不斉シクロプロパン化合物を高収率(up to 99%)，高立体選択性(up to 98% ee)で得ることに成功している[10]。



Scheme 1-4. ジアゾエステル類の各種結合への触媒的不斉カルベン移動反応

3）Fe 触媒存在下，様々なインドール基を持つジアゾエステル類の分子内カルベン移動反応が開発された。生成物である不斉二環類が高収率（up to 94%），高エナンチオ選択性（up to 99% ee）で得られたことを報告している[11]。

次に，単結合へのカルベン移動反応（X−H）において以下の 4）〜6）などの反応が報告されている。

4）l-プロリンに由来する特権触媒である Rh 錯体 Rh_2(*S*-DOSP)$_4$ によるシクロアルカンとアリールジアゾアセテートの分子間 C−H 挿入反応が開発された（up to 81%, 96% ee）[12]。

5）不斉ビピリジンのリガンドを持つ Cu 触媒によるアミン類とジアゾエステル類の不斉 N−H 挿入反応も開発された。反応は高収率，高エナンチオ選択性で進行することが報告されている（up to 89%, 95% ee）[13]。

6）不斉 Rh 触媒によるシラン類とアゾエステル類の不斉 N−H 挿入反応も開発された。反応は高収率，高エナンチオ選択性で進行することが報告された（up to 90%, 97% ee）[14]。

第 2 章　Ru(II)-Pheox 触媒の開発

2−1 Ru(II)-Pheox 触媒の特徴

本研究では，フェニルオキサゾリン配位子（芳香族オキサゾリン）を有するルテニウム錯体（Ru(II)-Pheox）触媒を 2010 年に独自に開発した[1]。Ru(II)-Pheox 触媒は、遷移金属触媒として働き，様々なアルケン類とジアゾ化合物類の触媒的カルベン移動反応において高い触媒活性及び立体選択性発現することが明らかになっている。また，これまで様々な芳香族オキサゾリンの配位子を待つ Ru(II)-Pheox シリーズの他，様々なアルケニルオキサゾリンを配位子として持つルテニウム錯体である（Ru(II)-Prox）触媒が 2020 年に開発された[2]。第 2 章では，我々の研究室で開発された Ru(II)-Pheox 触媒の特徴とそのカルベン移動反応について概説する。

Ru(II)-Pheox 触媒は，これまで様々なカルベン移動反応において，高い触媒活性と立体選択性を示す理由として以下 Figure 2-1 の 2 点の特徴がある。

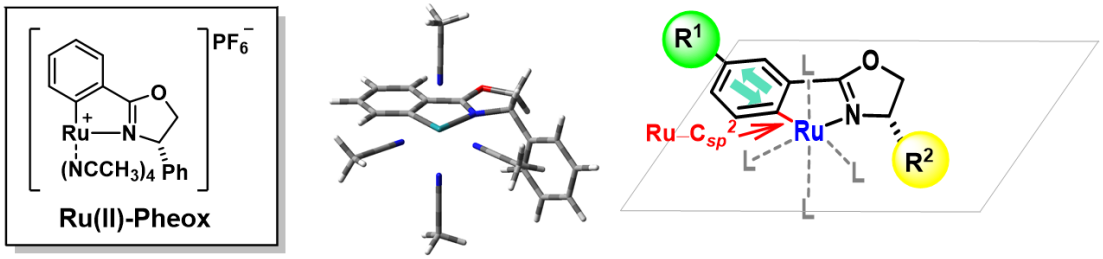


Figure 2-1. Ru(II)-Pheox 触媒とその特徴

1. 不斉環境を容易に微調整できること（R^2）

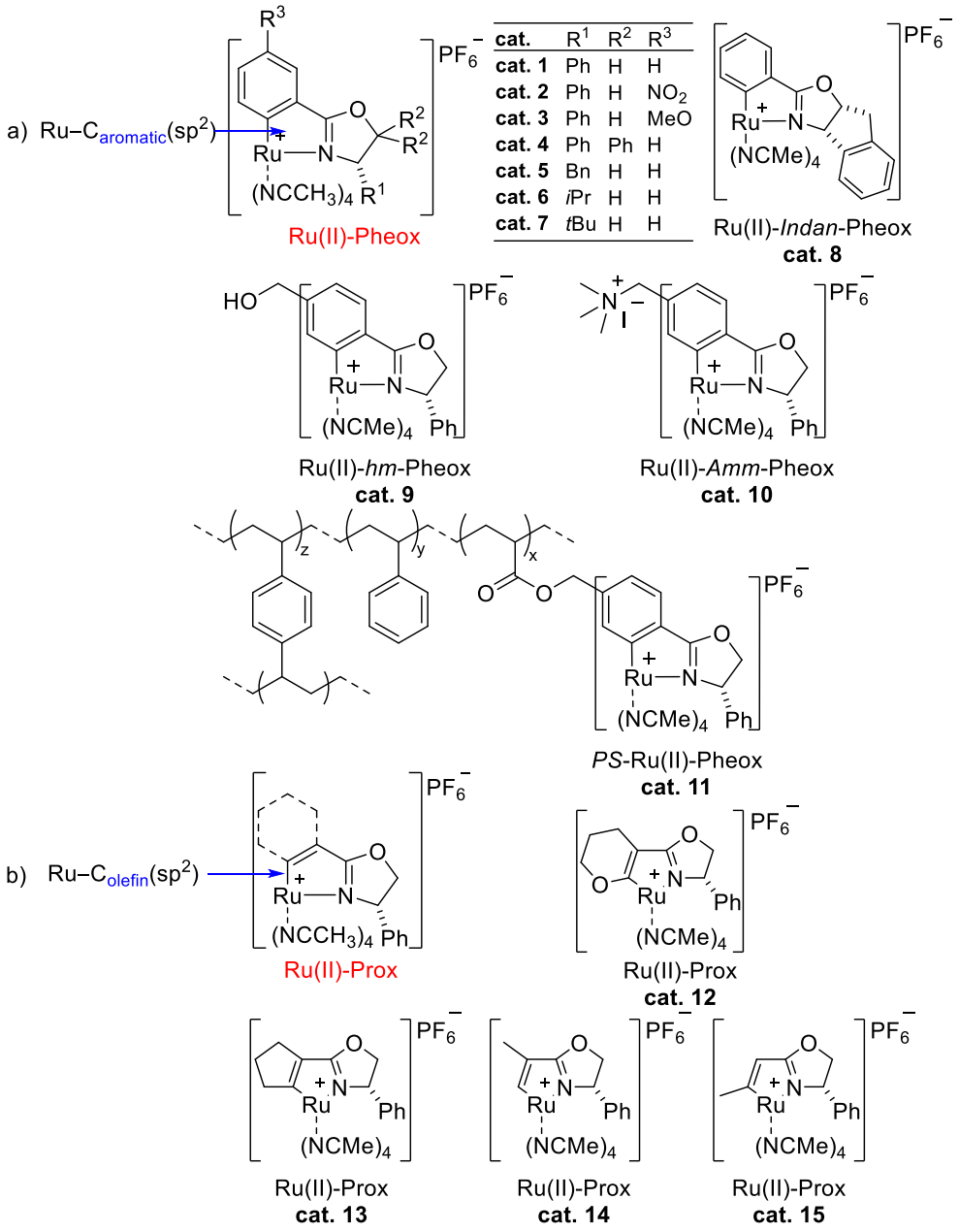
Ru(II)-Pheox 触媒の不斉発現因子はオキサゾリン環上に配位された置換基である。この置換基は入手の容易なアミノ酸由来の光学活性なアミノアルコールによって作られている。また，アミノアルコールは市販されているため，簡単に配位子を合成できるメリットがある。そのため，不斉環境をフェニル基，ベンジル基，インダン基，または嵩高い *tert*-ブチル基などに変えることで，簡単に不斉環境を変化させることができる。

2. 反応中心金属の電子密度を微調整できること（R^1）

Ru(II)-Pheox 触媒の特異性として，Ru−$C_{aromatic}(sp^2)$または Ru−$C_{olefin}(sp^2)$（金属−炭素）結合の存在がある。この結合によって本来電子欠乏性である金属原子に隣接炭素から電子供与が実現し，反応中心金属の電子密度が増大する。また，金属を直結する芳香族環

は容易に入手可能な安息香酸誘導体を利用しているため，その置換基を簡単に変えることで中心金属の電子密度を制御できる。この性質を利用し，金属錯体とカルベン移動反応において律速段階である中心金属へのカルベンの酸化的付加は速やかに進行し，反応性を向上させると考えられる。

また，芳香族環上の置換基を水溶性置換基に変えることで，水溶性触媒（**cat. 9**, **10**）を開発した。本触媒の存在下，水／エーテル系での高立体選択的に不斉カルベン移動反応に成功した。さらに，ポリマー置換基に変えることで，再利用可能なポリマー触媒 Ru(II)-Pheox **cat. 11** も開発した（Figure 2-2）。



cat.	R^1	R^2	R^3
cat. 1	Ph	H	H
cat. 2	Ph	H	NO_2
cat. 3	Ph	H	MeO
cat. 4	Ph	Ph	H
cat. 5	Bn	H	H
cat. 6	*i*Pr	H	H
cat. 7	*t*Bu	H	H

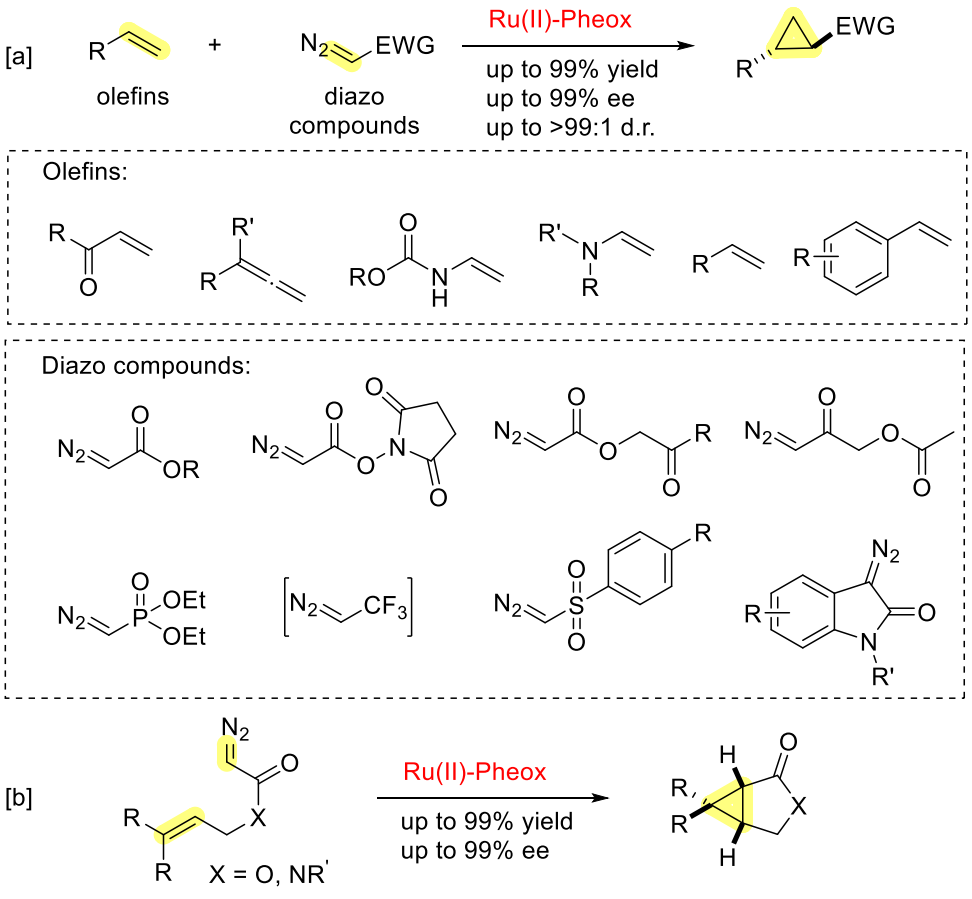
Figure 2-2. 様々な Ru(II)-Pheox, Ru(II)-Prox 触媒

2-2　Ru(II)-Pheox 触媒によるカルベン移動反応

これまでの先行研究より，Ru(II)-Pheox 触媒は様々なカルベン移動反応に有用な知見を示すことが明らかになっている。具体的に 1）二重結合（π 結合）へのカルベン挿入反応，2）単結合（σ 結合）へのカルベン挿入反応において高い触媒活性を示してきた。

1)　二重結合（π 結合）へのカルベン挿入反応

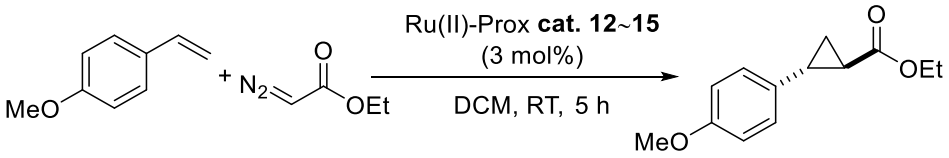
様々な Ru(II)-Pheox シリーズ存在下，アルケン類とジアゾ化合物類のカルベン移動反応を行い，相当する不斉分子間シクロプロパン化合物類を高収率，高立体選択的に得た。Ru(II)-Pheox 触媒はアルケン類との反応においては電子豊富な置換基から電子不足な置換基まで幅広いアルケンでも高い反応性を示した。例えば，電子豊富なスチレン誘導体をはじめとするアルケン類，または、電子不足なアルケン類であるアミド類，アレン類，ケトン類，α, β-不飽和エステルの反応に応用された[3]。また，二重結合への分子内カルベン移動反応においても，Ru(II)-Pheox 触媒が高い収率と立体選択性を示すことが明らかになっている（Scheme 2-1）[4]。

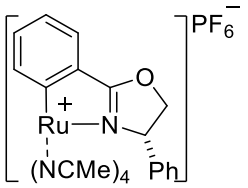


Scheme 2-1. Ru(II)-Pheox 触媒による二重結合へのカルベン移動反応

我々の研究室では，Ru(II)-Pheox 触媒をさらに研究し，Ru−$C_{olefin}sp^2$ 触媒である Ru(II)-Prox 触媒を 2020 年に開発した（**cat. 12**〜**15**）。新たに開発した触媒を用いて様々な二重結合へのカルベン挿入反応に応用した。ジアゾ酢酸エチルとパラメトキシスチレンとの分子間シクロプロパン化反応では，様々な Ru(II)-Prox シリーズを検討した（Table 2-1）。従来の Ru(II)-Pheox **cat. 1** に比較して，新たに合成した Ru(II)-Prox **cat. 13**, **cat. 15** は収率と立体選択性が低下した。一方、**cat. 12**, **cat. 14** が収率と立体選択性が増加した。具体的に，**cat. 14** より収率は 97%，立体選択性は 90:10 d.r., 97% *trans* ee まで向上した。これは反応中心金属と直接結合している置換基がフェニル基に比較して，オレフィンは立体障害による影響が小さくなるためと考えられる。良好な結果を示した **cat. 14** を用いて様々な溶媒と温度の存在下で反応最適化を行った。その結果，ジクロロメタンの他，エーテル溶媒にて高いジアステレオ選択性を示した。さらに，エーテル系の溶媒 MTBE より最も高い収率 98%と高いジアステレオ選択性 97:3 d.r.を示し，低温 −30℃より最も高いエナンチオ選択性 99% ee を示した[2]。

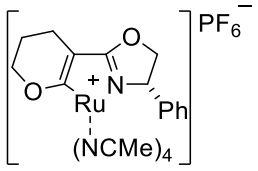
Table 2-1. 様々な Ru(II)-Prox 触媒によるスチレンとの分子間シクロプロパン化反応





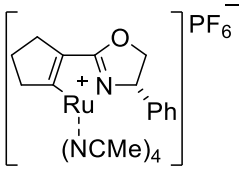
cat. 1

86% yield[a]
88:12 d.r.[b]
96% *trans* ee[c]



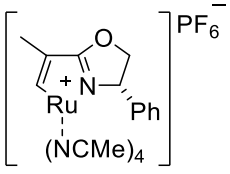
cat. 12

91% yield
88:12 d.r.
97% *trans* ee



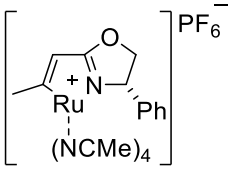
cat. 13

75% yield
88:12 d.r.
78% *trans* ee



cat. 14

97% yield
90:10 d.r.
97% *trans* ee



cat. 15

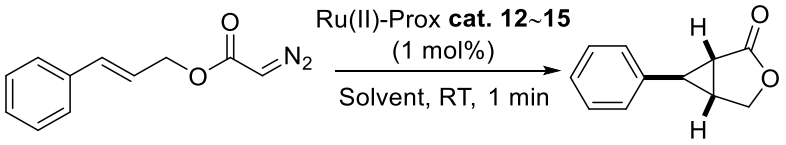
79% yield
89:11 d.r.
90% *trans* ee

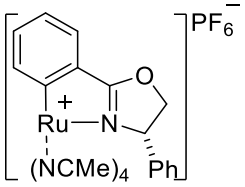
[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.

Ru(II)-Prox 触媒シリーズは分子内不斉シクロプロパン化反応にも用いられた。その結果を Table 2-2 に示す。従来の Ru(II)-Pheox **cat. 1** に比べて, **cat. 12** は若干収率の低下を示した。一方，**cat. 13** は高いエナンチオ選択性 97% ee を示したものの，収率が 87%まで減少した。分子間不斉シクロプロパン化反応において高いエナンチオ選択性と収率を示した **cat. 14** は分子内シクロプロパン化反応においても良好な結果を示した（96% yield, 99% ee）。しかし，**cat. 15** よりエナンチオ選択性は 90% ee まで低下した。

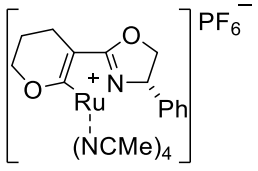
良好な結果を示した **cat. 14** の存在下，溶媒効果を検討した。トルエンより優れた立体選択性を示したが，触媒の溶解性の低下により収率は 69%まで減少した。ジエチルエーテルより優れたエナンチオ選択性 98% ee を示したが，収率は 87%まで減少した。配位性の高い溶媒 THF でも良好な結果を示した。さらに, エーテル系の溶媒である MTBE を用いた場合，最も高い収率 98%と最も高いエナンチオ選択性 98% ee を示すことが明らかとなった[2]。

Table 2-2. 様々な Ru(II)-Prox 触媒による分子内不斉シクロプロパン化反応

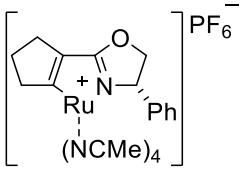




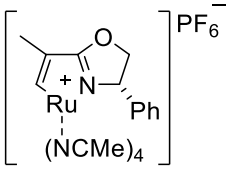
cat. 1
96% yield[a]
96% ee[b]



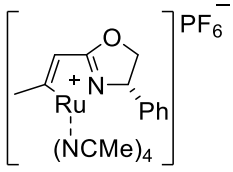
cat. 12
91% yield
96% ee



cat. 13
87% yield
97% ee



cat. 14
96% yield
99% ee



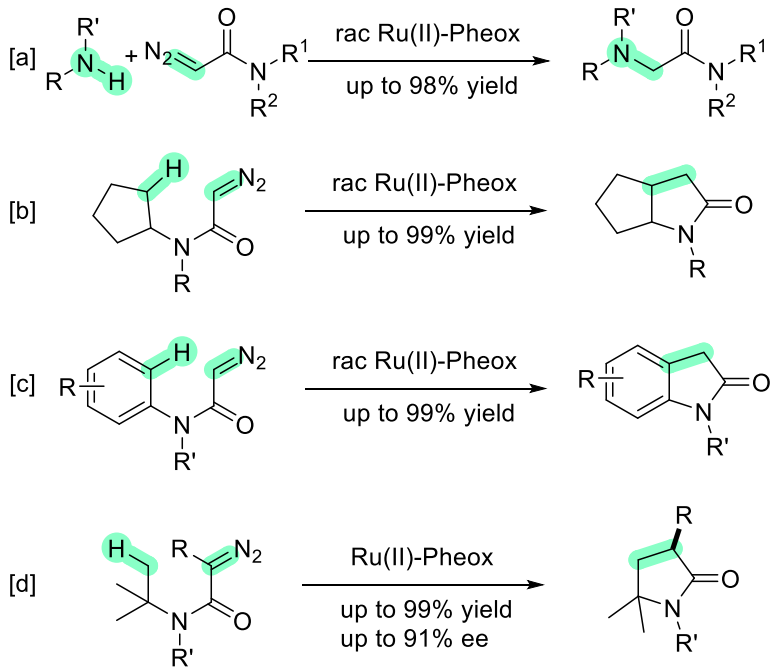
cat. 15
95% yield
90% ee

[a] Isolated yield. [b] Determined by chiral HPLC.

2) 単結合(σ 結合)へのカルベン挿入反応

Ru(II)-Pheox 触媒は単結合へのカルベン移動反応においても高い触媒活性を発現することが先行研究より示された(Scheme 2-2)。まず，N−H 挿入反応については，触媒量は少量(0.5 mol%)で，室温で速やかに進行し，最高 98%収率で目的物が得られた[5]。次に，Ru(II)-Pheox 触媒存在下シクロペンタン骨格を有するジアゾアセトアミド類の分子内カルベン移動反応を検討した結果，シクロペンタンの C−H 結合へカルベンが挿入し，最高 99%収率で γ-ラクタム類が得られた[6]。また，ベンゼン環を有するジアゾアセトアミド類を合成し，Ru(II)-Pheox 触媒との分子内カルベン移動反応を検討した。反応性が高く，室温では 1 分間で反応が終了し，最高 99%収率で様々なオキシインドールの合成に成功した[7]。Ru(II)-Pheox 触媒による *tert*-ブチル基を有するジアゾアセトアミド類の不斉分子内カルベン移動反応を検討した。その結果，分子内 C−H 挿入反応は室温で効率的に進行し，最高 99%収率，91% ee で目的の光学活性 γ-ラクタム類が得られた[8]。本反応はジアゾアセトアミド類の不活性な 1 級 C−H 結合への位置選択的および立体選択的なカルベン挿入反応として，初めての報告例である。

上記ように，Ru(II)-Pheox 触媒は様々な二重結合及び単結合へのカルベン移動反応に対応できる汎用性の高い有機金属触媒であると言える。

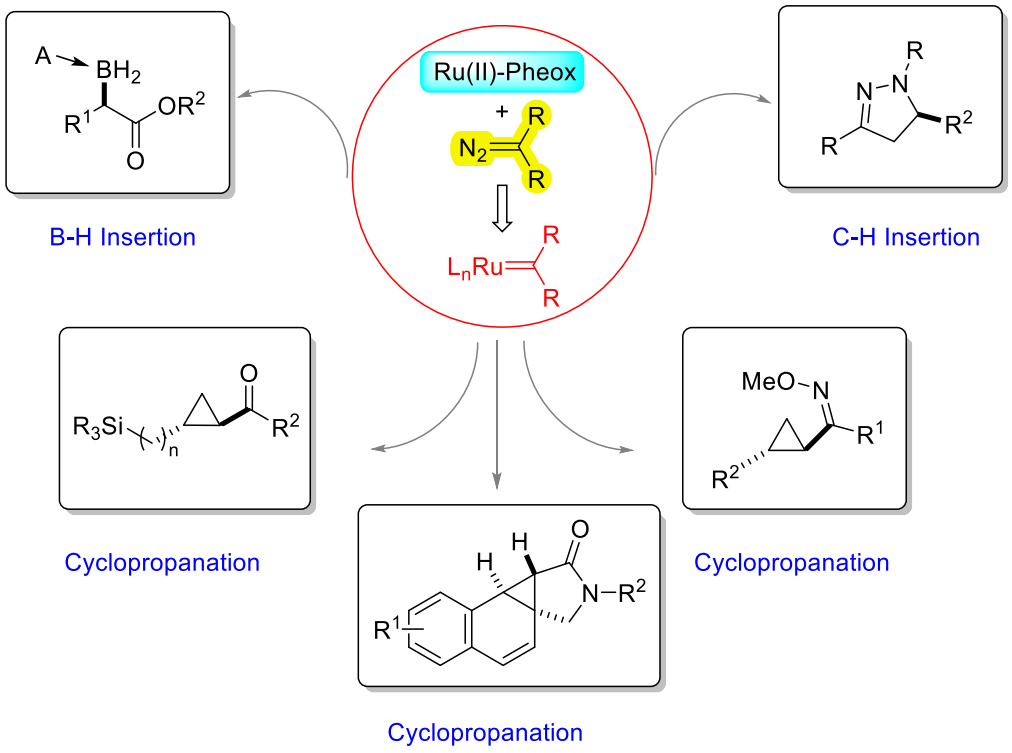


Scheme 2-2. Ru(II)-Pheox 触媒による単結合へのカルベン移動反応

2-3 研究目的

様々なジアゾ化合物類と金属触媒による発生した金属カルベン錯体は高い反応活性と特徴的な反応性により，古くから有機合成化学において重要な反応剤として用いられてきた。これらの応用反応は天然物や医薬品などの生理活性物質の合成に重要な役割を果たしている。しかし，官能化されたジアゾ化合物類の各種結合の不斉カルベン移動反応において，収率，立体選択性，触媒効率にまだ挑戦的な課題が残されている。

そこで，本研究では，第 1 章および第 2 章の前半で述べたようにカルベンの反応性を制御し，今までにない様々な官能化されたジアゾ化合物類を新規に合成し，各種結合への不斉カルベン移動反応の開発を目的とする。具体的に，Ru(II)-Pheox 触媒による不斉 B–H 挿入反応，アリル及びビニルシラン類の触媒的不斉シクロプロパン化反応，ジアゾオキシムエーテル類の不斉カルベン移動反応，ナフチルジアゾアセトアミド類の芳香族環へのカルベン移動反応である。各内容について，以下の各章に記載する。



Scheme 2-3. Ru(II)-Pheox 触媒による不斉カルベン移動反応

第３章　Ru(II)-Pheox による B−H 結合への触媒的不斉カルベン挿入反応とその応用

3−1 有機合成分野における有機ホウ素化合物の重要性

3−1−1 ホウ素の特徴

ホウ素は第 13 族，第 2 周期の元素であり，単体であるとき，金属と非金属元素の中間の性質を示すが，化合物では安定した共有結合形成する。この性質より同じ第 13 族である Al などよりも第 14 族である C，Si に類似している。また，他の金属に比べて電気陰性度が大きい。さらに，炭素−ホウ素結合では，他の金属−炭素結合に比べてイオン性が非常に小さい（Figure 3-1）。これが有機ホウ素化合物は他の有機金属化合物に比して化学的に安定である理由の一つと考えられる[1]。

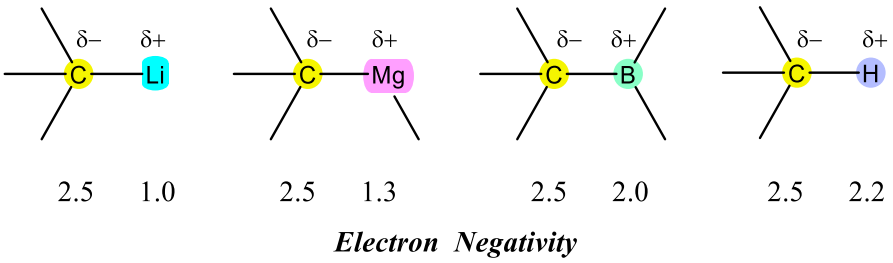


Figure 3-1. 電気陰性度の比較

ホウ素の結合様式は 3 価で，さらに空の p 軌道を持っているため，オクテット則を満たしておらず電子受容体として働く。このような背景から，ホウ素含有化合物は，B−H の不飽和結合への付加反応（ハイドロボレーション），B−H からの H^-による還元反応（ヒドリド還元）、ホウ素元素の電子受容機能としてルイス酸性に基づく多様な有機合成（ホウ素系ルイス酸触媒反応）や錯体形成反応（N，O などの孤立電子対から B への配位）、ホウ素エノラートを利用した求核反応，および Pd 触媒による C−C 結合形成反応（Suzuki-Miyaura クロスカップリング）などの多様な反応形式を生み出し，有機合成化学に広く利用されている。

3-1-2 有機ホウ素化合物の反応

有機ホウ素化合物の合成は，歴史が古く，1 世紀以上前に Frankland によって，有機亜鉛化合物とホウ酸エステルとの反応で初めて開発された[2]。しかし，有機ホウ素化合物そのものを用いた新しい有機合成反応は，ほとんど研究されてなかった。その後，Brown 等によって有機ホウ素化合物をオレフィンとジボランとの反応により効率よく定量的な収率で合成できることが偶然発見された[3]。この簡単で大量に得られる有機ホウ素化合物の合成方法を基に，多くの研究者や技術者が有機ホウ素化合物の化学的性質，反応性，有用性，様々な反応への応用について研究を行い，新しい科学の領域が拓かれた。そして有機ホウ素化合物のユニークな構造特性と多様な反応性を利用して，科学の様々な分野でその役割を拡大し続けている。例えば，有機合成分野においては，有機ホウ素化合物は，官能基合成変換で最も広く使用されている試薬及び中間体の一つであり，また，分子受容体，分子センサー，液晶，有機 EL 材料などの新規材料，生物学的プローブ，医薬品など，他の分野の主要な機能成分としても重要な役割を果たしている[4]。この様に，ボロン酸及びその誘導体などの有機ホウ素化合物は，機能材料や医薬品の主要な原料として，重要性がますます増大している。有機化合物の合成変換の観点から，以下に，有機ホウ素化合物を用いたいくつかの有用な反応を以下に概説する。

① ハイドロボレーション[5]

ハイドロボレーションおよびヒドロホウ素化反応は，1956 年に Brown 等によって報告され，B−H 結合がアルケンまたはアルキンに位置選択的に *syn* 付加する反応である。ホウ素の位置選択制も高く，アルケンへ付加する際にアルキル置換基の数のより少ない炭素にホウ素が結合し，アルキル置換基の数のより多い炭素に水素が付加する。ホウ素が水素よりも電気陰制度が低いということに起因する。つまり，ホウ素 B が δ^+，水素 H が δ^-を帯びているため，求電子剤であるホウ素がよりアルキル置換基の少ない方の炭素に付加する。すなわちカチオンの安定性に依存する。続いて酸化すると C−B 結合は C−OH 結合に変換され *anti*-Markovnikov 型アルコールが合成できる。これらの反応は 2 段階で起こる。まず，ステップ 1 は B−H 結合の付加であり，オルフィンと B 上の空軌道が相互作用し，その後 *syn* 付加機構で進む。次に，ステップ 2 で B−C 結合の酸化的開裂で，B 上の空軌道に過酸化水素の共役塩基が配位する。その後，ヒドロキシル基が脱離する形で転位反応を起こす。炭素原子上の立体化学は保持されている(Scheme 3-1 (a)。

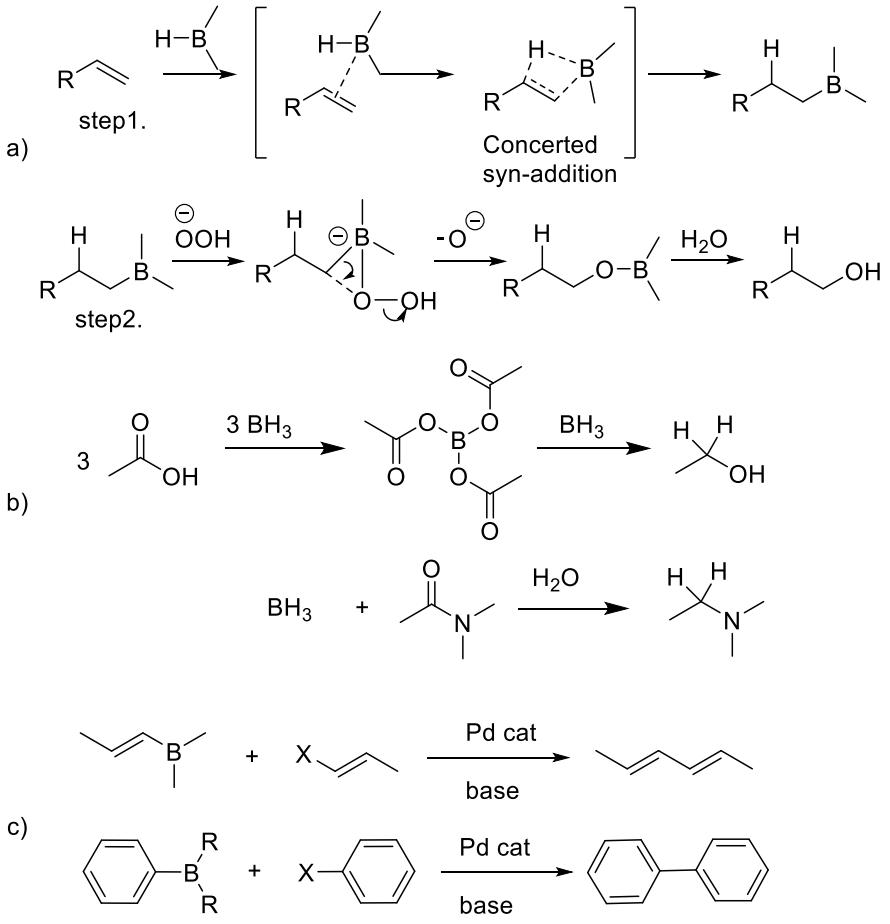
このように，通常のアルケンの HX 型化合物の付加反応では多くの場合 X の方がアルキル置換基の数の多い方へ付加する Markovnikov 則に従う位置選択性を示すのに対し，ヒドロホウ素化はそれとは逆の位置選択を示している。そのため，一旦ヒドロホウ素を導入した後，ホウ素を別の官能基に置換することで通常の付加と相補的な合成法となり極めて有用である。また，酸化反応を行うことで，最終的に様々なアルコールへ変換で，光学活性アルコールは，天然物や生理活性物質や医薬品によく用いられる重要な部分構造である。

② ボランや有機ホウ素化合物の還元反応[6]

ジボランやボラン錯体 L−BH_3（L = アミン、エーテル、有機リン化合物類）が還元剤として働くことができる。これらの還元反応は，ヒドリド（H^-）による還元反応であるためヒドリド還元と呼ぶ。この時，ボラン等の B が空軌道を持っており，電子不足であるためルイス酸として働く。ボランはアルデヒドやケトンをアルコールに還元できるほか，カルボン酸もアルコールに還元する。さらに，アミドの還元にも使われる(Scheme 3-1 (b))。

③ Suzuki-Miyaura カップリング[7]

パラジウム触媒を用い，アリール有機ホウ素化合物とアリールおよびビニル有機ハロゲン化合物をクロスカップリングさせる反応で，1979 年に初めて Suzuki，Miyaura 等によって報告された。反応の特徴は様々な官能基を含む基質に応用でき，立体障害のある基質にも速やかに反応が進行する場合が多い。また，原料である有機ホウ素化合物は，水や空気に安定で取り扱いが容易で含水溶媒中でも反応が進行すること，副生成物が水溶性で除去しやすく，毒性も低いことなど実用上の利点が大きく，実験室から工業生産レベルまで幅広く利用されている。この反応は医薬品合成，精密有機合成はもちろんのこと，化学繊維や液晶分子などの有機材料の合成などにも用いられている。従って，鈴木・宮浦カップリングの進歩は，合成化学における有機ホウ素化合物の価値を高めることにつながった(Scheme 3-1 (c))。



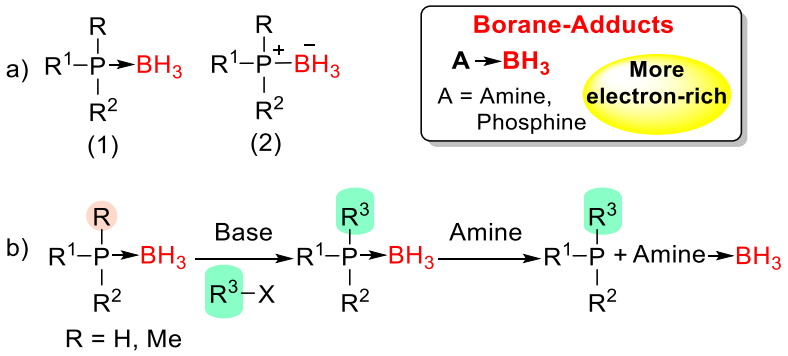
Scheme 3-1. 有機ホウ素化合物の反応

3-1-3 アミンーおよびホスフィンーボラン錯体

上述の様な有機ホウ素化合物の特徴のほかに，ホウ素は，容易にアミンやホスフィンと錯体を形成する。特にモノボランは単独では不安定であり，ルイス塩基と錯体を作らせることによって安定になり，扱いが容易になる。アミンやホスフィンーボラン錯体はN や P 原子上の非共有電子対がボランの空軌道に配位して生成する配位化合物であり，その構造は一般に（1）または（2）で表される(Scheme 3-2 (a))。以下，ホスフィンーボラン錯体を代表として示す。これらの化合物はホウ素アート錯体とも言える。アミンー及びホスフィンーボラン錯体の合成は，ジボランまたはボランーTHF 錯体を用い，THF との配位子交換を経て容易に得られる。これらのアミンーやホスフィンーボラン錯体は化学的にかなり安定である。例えば，三級ホスフィンーボラン錯体は空気，湿気のみならず，強酸や強塩基と接触させても容易に反応しないほど安定である。特に，今本等による 1980 年にホスフィンーボラン錯体の応用研究では，アキラルなホスフィンーボラ

ン錯体の合成法の確立とそれらの誘導体への変換を確立した。その後，光学活性ホスフィンーボラン錯体の合成と反応，さらにボラナート基の有機合成への応用について発展させている。ホスフィンーボラン錯体の原料であるホスフィンそのもの合成は容易ではない。特に，低分子量の脂肪族のホスフィンや二級のホスフィンは，酸化されやすくかつ強い悪臭を有するため，単離するのが困難である。そこで，ボランをホスフィンに配位させることで，隣接基が活性化され，双極子安定化機構を利用して多様な変換が可能になる。そして，アミンと反応させるボランを外すことで様々な有機リン化合物を合成できる。この方法は，不安定な有機リン化合物の合成に大きな貢献した(Scheme 3-2 (b))[8]。

一方，ボラン錯体系での B−H 活性化を利用した研究は非常に少ない。B−H 活性化を利用した反応として遷移金属触媒を用いたカルベンへの B−H 挿入反応法がある。B−H 活性化の研究が多く開発されれば，様々な不斉有機ホウ素化合物が開発されるため，ハイドロボレーションや Suzuki カップリング反応に応用される。アミンやホスフィンをボランに配位させることで，B−H 結合上の電子密度が大きくなり，良好なヒドリド源として働き，カルベン挿入反応が進行できる[9]。



Scheme 3-2. ボラン錯体とその反応

3−1−4 ホウ素を含む生理活性物質

また，有機ホウ素化合物は上記のように様々な反応に利用される以外は，有機ホウ素化合物自身が医薬品にも利用されている。生体分子のほとんどは C, H, N, O, S, P などの元素で構成されており，体内で働く医薬品もこれらの元素で作られたものがほとんどである。これ以外のヘテロ元素を含んだ医薬品は，基本的に少ないが，その中でホウ素を含む医薬品が以下の Tavaborole，Bortezomib，Crisaborole および Diazaborine などが主に抗菌剤として実際に使用されている。Tavaborole は爪真菌症に対する局所投与の抗真菌薬で，Bortezomib は抗悪性腫瘍剤，Crisaborole は湿疹用に薬，そして Diazaborine は抗菌剤である(Figure 3-2)[10]。

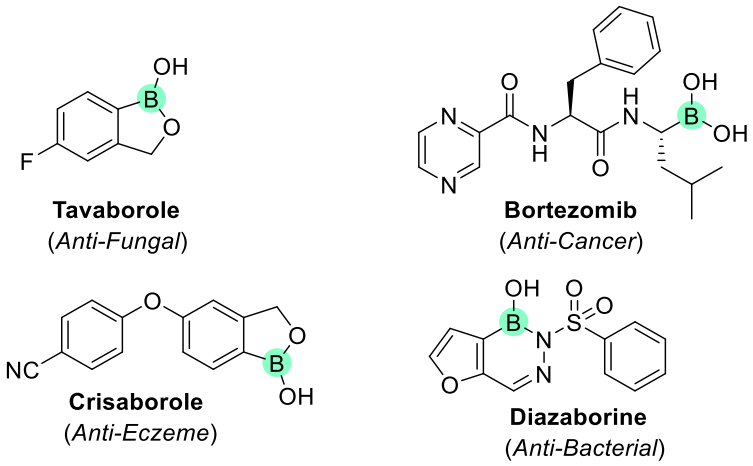
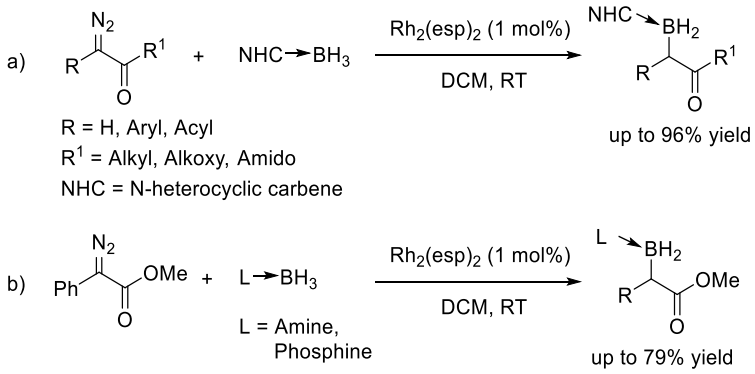


Figure 3-2. ホウ素を含む医薬品

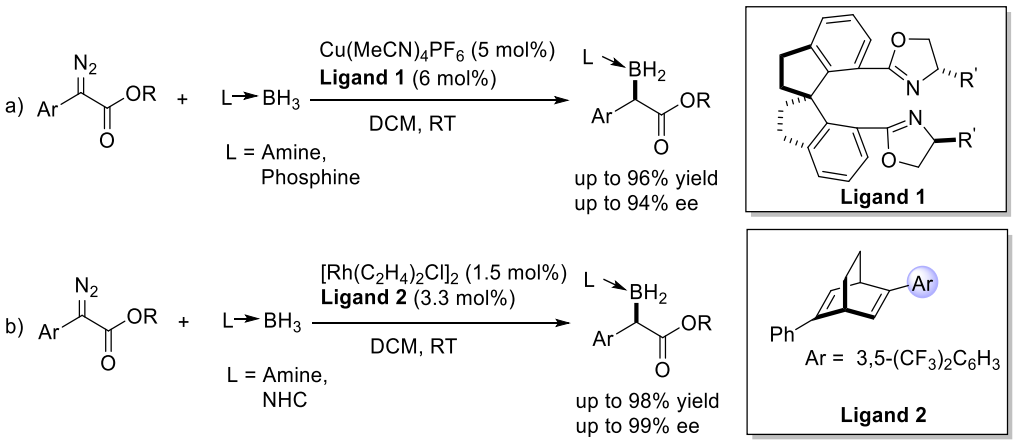
3-2 研究背景　有機ホウ素化合物とジアゾ化合物の反応

近年，有機ホウ素化合物は，様々な分野で有機合成や機能性分子・材料の開発に利用されるようになった。特に，有機合成化学においては重要な中間体として知られている。例えば，酸化分解によるアルコールへの変換，カルボニル化合物のアリルホウ素化，有機ハロゲン化合物とのクロスカップリング反応は生理活性物質や機能性材料などの合成に実用的である。しかし，有機ホウ素化合物の合成法は限られており，ボラン酸やエステル型がほとんどである。一方，アミンやホスフィンをホウ素の空の軌道へ配位させ，ボラン錯体を形成させることで，ボランの B−H 結合の分極が活性化される。その活性化を利用し，金属触媒とカルベンとの錯体，すなわち金属カルベン錯体と単結合 B−H 結合の親和性が増大し，結果として様々な新規有機ホウ素化合物錯体を合成できる。さらに，不斉遷移金属触媒を用いることで，様々な光学活性有機ホウ素化合物錯体を合成し，最終的には，医薬品や生理活性物質天然物によく見られる不斉アルコールへ展開できる。例えば 2013 年に Curran 等によってロジウム触媒によるジアゾカルボニル化合物への B−H 挿入反応の開発を報告した。ボラン錯体には NHC−Borane 錯体を使用している (Scheme 3-3 (a))。次に，Curran 等は 2016 年にボラン錯体の基質適応範囲を拡大し，ボラン錯体 L−BH_3 には，様々なアミン，ピリジン，ホスフィンーボラン錯体を用いた B−H 挿入反応を開発した[1] (Scheme 3-3 (b))。しかし，本先行研究はアキラルな有機ホウ素化合物の合成のみであり，近年，有機ホウ素化合物のホウ素に直結した不斉炭素に関する不斉合成法に注目が集まっている。光学活性有機ホウ素化合物が反応の中間体として非常に重要であるため様々な光学活性有機ホウ素化合物の合成が望まれている。



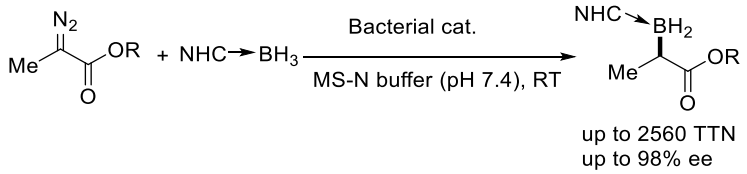
Scheme 3-3. ロジウム触媒によるジアゾ化合物との B−H 挿入反応

そのため, カルベンへの立体選択的 B−H 挿入反応が課題として残されていた。一方, 2013 年に Zhou また，2015 年に Xu 等によって不斉 B−H 挿入反応が開発された。これらの先行研究例を以下(Scheme 3-4)に示す。Zhou 等は遷移金属として銅を用い，不斉配位子には Ligand 1 のスピロ型オキサゾリン系配位子を用いて，室温で最高 96% 収率と 94% ee で目的の光学活性有機ホウ素化合物を合成した。有機ホウ素化合物を高収率，高立体選択的に合成しているが，触媒に 5 mol%, 不斉配位子には 6 mol%を用いて，反応時間は 4 時間から 72 時間かかっている[12]。Xu 等はロジウムを用いて，Ligand 2 を不斉配位子として室温で最高 98%収率, 99% ee で目的化合物を開発した[13]。Zhou 等に比べ, 触媒量が少なく 1.5 mol%, 配位子には 3.3 mol%を用いている。以上の研究では，いずれも高収率かつ高エナンチオ選択的に有機ホウ素化合物が得られているが, 触媒の効率化や基質の適応範囲が α-アリールジアゾ化合物のみに限られているなど課題が多く残されている。



Scheme 3-4. 銅、ロジウム触媒によるジアゾ化合物との不斉 B−H 挿入反応

一方，2017 年に Arnold 等は水中での炭素−ホウ素結合形成に適用できるホウ素試薬を利用して，不斉 B−H 挿入反応を生物学的に開発する方法を報告している[14]。大腸菌 BL21（DE3）細胞グラム陰性の好熱性細菌 Rhodothermusmarinus からの野生型シトクロム c を保有し，N-複素環式カルベンボラン（NHC−ボラン）とインキュベート中性緩衝液（M9-N）中の 2-ジアゾプロパン酸エチル（Me-EDA）との不斉 B−H 挿入反応を検討し，高エナンチオ選択性で有機ホウ素化合物を得た。こちらの先行研究例は生体触媒存在下，α 位にメチル基を持つジアゾ化合物での高エナンチオ選択性を示した初めての報告例である（98% ee, 2560 TTN= Total Turnover Number）（Scheme 3-5）。

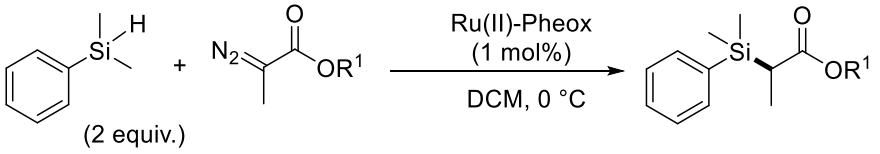


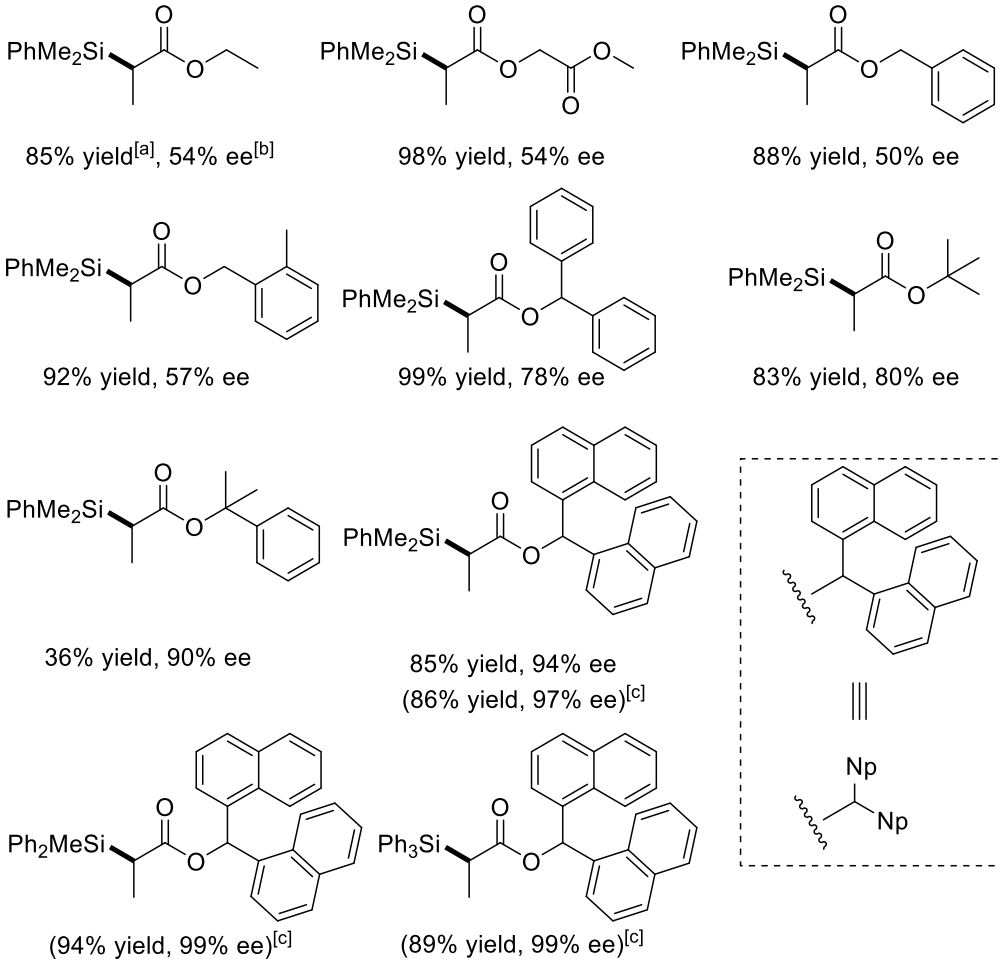
Scheme 3-5. 生体触媒によるジアゾ化合物との不斉 B−H 挿入反応

一方，Nakagawa 等は 2017 年に Ru(II)-Pheox 触媒存在下，α 位にメチル基を持つ様々なジアゾアセテート類の Si−H 挿入反応を高収率・高立体選択的に得ることに成功した[15]（Table 3-1）。まず，立体障害の異なる様々なジアゾ化合物を用いて Si−H 挿入反応の検討を行った。その結果，50%～94% ee で目的の光学活性有機シラン類が得られた。R^1 の立体障害が大きくなるにしたがって立体選択性が上がる傾向がみられ，最も高い立体選択性が発現したのは，ジナフチルメチル骨格（Np）を有するジアゾアセテート類を用いた場合である（85% yield, 94% ee）。最適化な条件検討を行ったところ，−5 ℃が最適化な反応温度であり，ジナフチルメチル骨格（Np）を有するジアゾアセテート類より 86% yield, 97% ee で目的生成物が得られた。さらに，最も高い収率，立体選択性を示したジアゾ化合物と反応条件下でシラン類の基質依存性の検討をさらに行った。その結果，シラン上の置換基が嵩高くなりにつれて，収率とエナンチオ選択性が増加した。

そこで，上記の研究背景を基に，本研究では，基質適応反応の拡大と触媒の効率化を目指し，Ru(II)-Pheox 触媒を用いた新規不斉 B−H 挿入反応の開発を行った。

Table 3-1. Ru(II)-Pheox 触媒による α-メチルジアゾ化合物との不斉 Si–H 挿入反応



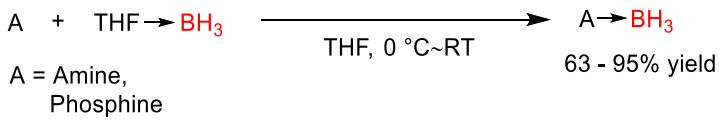


[a] Isolated yield. [b] Determined by chiral HPLC. [c] Reaction carried out at –5 °C.

3-3　原料化合物のボラン錯体およびジアゾエステルの合成

3-3-1 アミン及びホスフィンーボラン錯体の合成

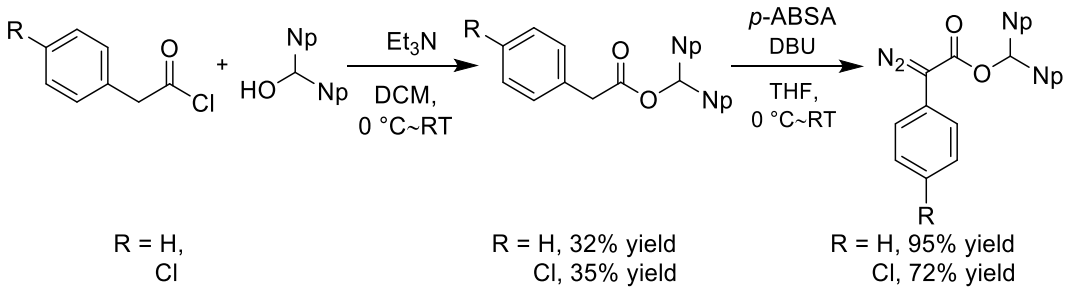
アミンーボラン錯体合成にはアミンとしてメチルピロリジン，トリエチルアミン，トリブチルアミン，ピペリジンおよびピリジンなどのアミンを用いて，1 M テトラヒドロフランーボラン錯体に配位している THF との交換反応を利用して目的のアミンーボラン錯体をそれぞれ合成した。また，ホスフィンーボラン錯体にはトリフェニルホスフィンを上記の方法を用いて 63～95% 収率で合成した。



Scheme 3-6. アミンー及びホスフィンーボラン錯体の合成

3-3-2 ジアゾエステル類の合成

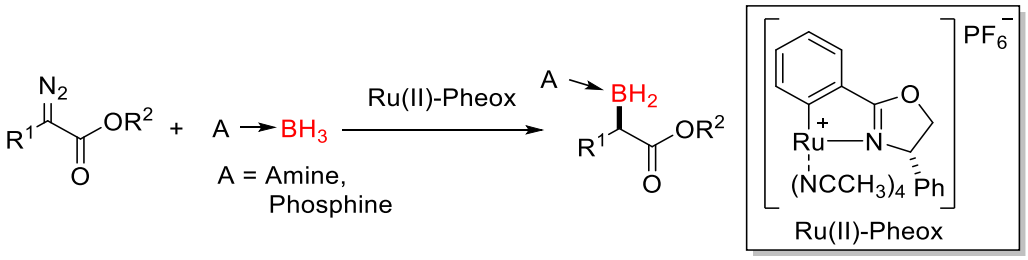
今回, 基質として用いたジアゾエステル類には立体障害の異なる 6 種類のジアゾ化合物を合成した。新規に合成したジアゾエステル類について以下に概説する（Scheme 3-7）。市販されているフェニルアセチルクロリドをトリエチルアミン存在下でアルコールと反応させ、それぞれ 32%、35% 収率で β-ケトエステルを得た。その後，β-ケトエステルとジアザビシクロウンデセン（DBU）強塩基存在下で，4-アセトアミドベンゼンスルホニルアジド（*p*-ABSA）を THF 溶媒中，撹拌し，目的の α-アリールジアゾエステル類を 95%と 72%高収率で得た。ただし，DBU 塩基存在下で，*p*-ABSA との反応でジアゾ化合物を合成する方法は Regitz 移動反応として知られている[16]。



Scheme 3-7. 新規ジアゾエステル類の合成

3−4　Ru(II)-Pheox 触媒による不斉 B−H 挿入反応

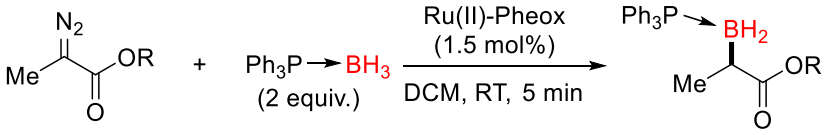
合成したジアゾエステル類を用いて，触媒的不斉 B−H 挿入反応による光学活性有機ホウ素化合物合成について，反応条件の最適化として，基質依存性，触媒効率化，さらに得られた有機ホウ素化合物を用いて応用反応の検討を行った。これまでに遷移金属触媒として Cu，Rh に限られていた不斉 B−H 挿入反応を当研究室の Ru 触媒を用いることと，さらにジアゾ化合物として α-アリールジアゾ化合物を α-メチルジアゾ化合物へ拡大することを本章で目指した。



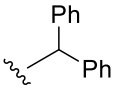
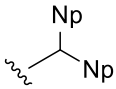
Scheme 3-8. Ru(II)-Pheox 触媒による不斉 B−H 挿入反応の開発

まず，立体障害の異なる様々な α-メチルジアゾエステル類とトリフェニルホスフィンーボラン錯体を用いて，触媒的不斉 B−H 挿入反応を検討した（Table 3-2）。初期条件は，Ru(II)-Pheox 触媒を不斉触媒として 1.5 mol%，ジアゾエステルに対してボラン錯体を 2 当量，溶媒としてジクロロメタン，反応温度は室温の反応条件で行った。反応は速やかに進行し，2-ジアゾプロピオン酸エチル **3-1a** の時，高収率 85%，中程度の立体選択性 40% ee で不斉有機ホウ素化合物 **3-3a** が得られた（entry 1）。続いて，ジアゾエステル類の R 置換基を立体障害の大きい *tert*-ブチル基に変えて検討したところ，58%収率で目的生成物 **3-3b** を得た。しかし，生成物は不安定で，立体選択性を測定できなかったため，次に，立体障害のより大きな置換基であるジフェニル基やジナフチル基を持つジアゾエステル類を用いて触媒的不斉 B−H 挿入反応を行った。その結果，ジナフチル基を持つジアゾエステルを用いた時に，最も高いエナンチオ選択性 87% ee で不斉有機ホウ素化合物 **3-3d** が得られた（entry 4）。この結果より、ジアゾ化合物の末端置換基の立体障害は本反応では高立体選択性を発現するために有用な要素であることが明らかになった。高い収率、立体選択性を示したジアゾ化合物 **3-1d** を用いて、反応の最適化な条件検討を行った。

Table 3-2. α-メチルジアゾ類の不斉 B−H 挿入反応



3-1 **3-2** **3-3**

Entry	R	Product	Yield [%][a]	ee [%][b]
1		**3-3a**	85	40
2		**3-3b**	58	n.d.
3		**3-3c**	74	76
4		**3-3d**	76	87

[a] Isolated yield. [b] Determined by chiral HPLC. n.d. = not determined.
Ph = Phenyl. Np = 1-Naphthyl.

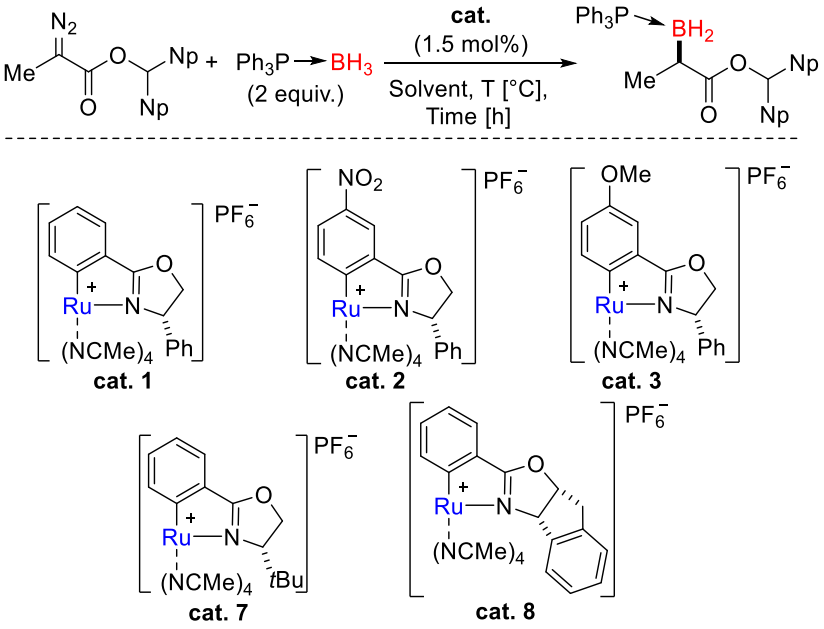
3−5 条件検討

さらに, 不斉有機ホウ素化合物の収率と立体選択性を向上させるために, 触媒, 温度, 溶媒の条件検討をした。結果を以下の Table 3-3 に示す。初めに触媒検討を行った。(entries 1〜5) 反応中心金属 Ru の電子密度を制御できるため，Ru−Ar のベンゼン環のパラ位の置換基を電子吸引基である NO_2 または電子供与基である MeO に設計した触媒 **cat. 2**, **cat. 3** を用いて検討した。電子吸引基を持つ Ru(II)-Pheox 触媒では，収率が若干低下したものの，エナンチオ選択性が増加し，90% ee を示した。一方，電子供与基を持つ触媒では，エナンチオ選択性が若干低下したものの，収率が増加し，77% yield を示した。次に, 触媒の不斉環境を変えた触媒 **cat. 7**, **cat. 8** を用いて検討した。立体障害の大きい *tert*-butyl 基を持つ触媒により，反応性が遅くなり，収率と立体選択性を低下させた結果が観察された(entry 4)。

続いて，温度検討を行った。(entries 6〜9) 低温に伴い，エナンチオ選択性が増加した。温度は，−10 ℃で最も高い収率(81% yield)，立体選択性(95% ee)を与えた。(entry 7) 最適な反応温度を用いて，次に，テトラヒドロフラン，トルエン，クロロホルム，あせとアセトンなどの溶媒を用いて，不斉 B−H 挿入反応の検討を行った。アセトンを溶媒として用いる時，より最も高いエナンチオ選択性 98% ee で有機ホウ素化合物が得られたが，収率は低下した。溶媒によって，生成物の収率が大きく低下することを示し，これは，還元反応によりエステル体と 1, 2-水素移動反応による α, β-不飽和エステル体

が副生成物として得られているからである(Figure 3-3)。また，アセトン溶媒によって，立体選択性が 3%ほど向上した。その理由は，酸素の非共有電子対が影響を与えるではないかと思う。以上，条件検討によって，最適な反応溶媒はジクロロメタン，温度 −10 ℃，触媒 **cat. 1** である。さらに，最も高収率，高立体選択的に得られた有機ホウ素化合物を用いて，再結晶化を行うことで，単結晶を精製し，X 線構造解析によって，生成物の絶対配置を決定することができた(Figure 3-4)。生成物の絶対配置を ***R*** 体であることが分かった。

Table 3-3. 不斉 B−H 挿入反応の条件検討



Entry	cat.	Solvent	T [°C]	Time [h]	Yield [%][a]	ee [%][b]
1	**cat. 1**	DCM	RT	5 min	76	87
2	**cat. 2**	DCM	RT	5 min	70	90
3	**cat. 3**	DCM	RT	5 min	77	85
4	**cat. 7**	DCM	RT	5	23	9
5	**cat. 8**	DCM	RT	30 min	36	29
6	**cat. 1**	DCM	0	1.5	80	90
7[c]	**cat. 1**	DCM	−10	2	81	95
8[c]	**cat. 1**	DCM	−20	7	75	95
9[c]	**cat. 1**	DCM	−30	72	73	92
10[c,d]	**cat. 1**	DCM:Toluene	−10	48	25	94
11[c]	**cat. 1**	THF	−10	1.5	20	94
12[c]	**cat. 1**	$CHCl_3$	−10	10	43	94
13[c]	**cat. 1**	Acetone	−10	2	37	98

[a] Isolated yield. [b] Determined by chiral HPLC. [c] 3 mol% of **cat. 1** was used.
[d] DCM:Toluene = 1:1 was used as a solvent.

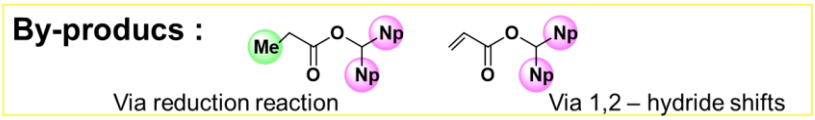


Figure 3-3. 不斉 B−H 挿入反応の副生成物

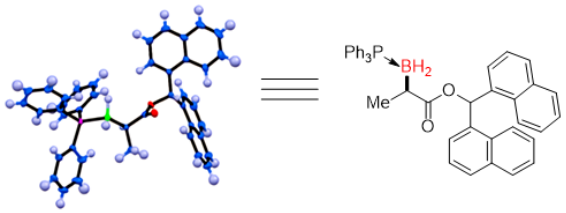


Figure 3-4. 不斉有機ホウ素化合物の X 線構造解析

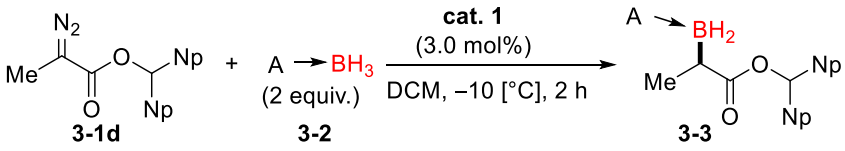
3−6 基質依存性

最適な反応条件を用いて，次にアミン及びホスフィンーボラン錯体の基質依存性の検討を行った。結果を以下の Table 3-4 に示す。トリフェニルホスフィン錯体以外に，ジエチルフェニルホスフィンボラン錯体を用いて，触媒的不斉 B−H 挿入反応を行った。その結果，収率 6%増加し，87% 収率で，有機ホウ素化合物が得られたが，立体選択性が 10%ほど低下した。次に，様々なアミンーボラン錯体での不斉有機ホウ素化合物の検討を行った。まず，線形アルキル置換アミン系であるトリエチルアミン及びトリブチルアミンーボラン錯体を用いた場合，高収率・中程度の立体選択性で生成物が得られた。具体的に，比較的小さい分子であるトリエチルアミンより最も高い収率 91%で有機ホウ素化合物が得られた。一方，トリブチルアミンーボラン錯体よりトリエチルアミンーボラン錯体に比べ，若干増加したエナンチオ選択性 66% ee で生成物が得られた。次に，環状アミン系の基質を用いて，検討を行った。全ての基質に対して高収率，小〜中程度の立体選択性で有機ホウ素化合物を得た。その結果を entries 5〜10 に示す。環状系のアミンーボラン錯体より，最も高い収率 92%を示したのは，ジシクロヘキシルアミンーボラン錯体錯体だった。また，ピリジンーボラン錯体はアミンーボラン錯体の中で最も高い立体選択性 78% ee を示した。

さらに，基質依存性の検討を行うために，α-アリールジアゾエステル類での不斉 B−H 挿入反応を行った（Scheme 3-9)。まず，α 位にフェニル基や *p*-クロロフェニル基を持つジアゾエステル類（**3-1n**，**3-1o**）を新規に合成し，不斉 B−H 挿入反応に応用した。ぞれぞれのジアゾエステル類をトリフェニルホスフィンーボラン錯体と **cat. 1**（10 mol%）存在

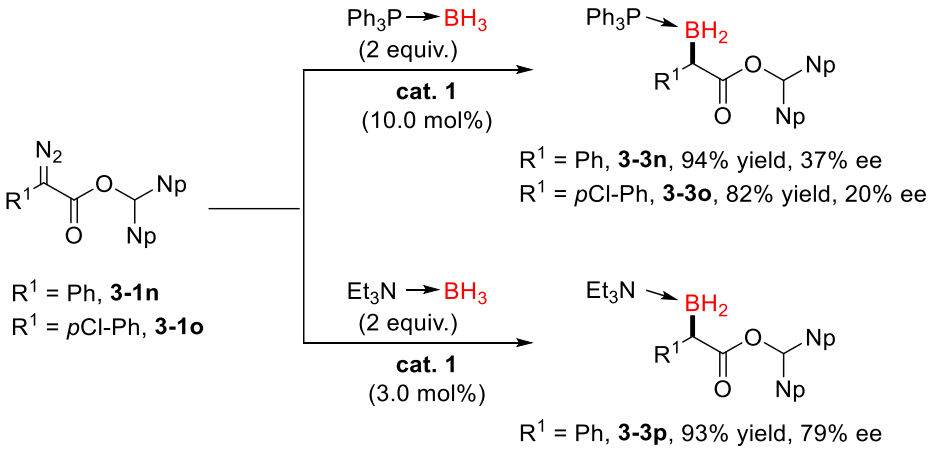
下，触媒的不斉 B–H 挿入反応を検討した。立体障害の大きい分子同士の設計となるため，触媒量を 10 mol%必要とした。α 位に大きな置換基フェニル基を持つため，還元反応によりエステル体と 1, 2-水素移動反応による α, β-不飽和エステル体の副生成物を防ぐことができ，若干収率が増加した。しかし，立体障害の大きい置換基同士の反応になるため，立体制御が困難になり，エナンチオ選択性が低下した。一方，トリエチルアミンーボラン錯体を用いた場合，収率・エナンチオ選択性が増加し，93%収率，79% ee で不斉有機ホウ素化合物が得られた。

Table 3-4. 様々なボラン錯体を用いた不斉 B–H 挿入反応



Entry	A	Product	Yield [%][a]	ee [%][b]
1	Triphenylphosphine	**3-3d**	81	95
2	Diethylphenylphosphine	**3-3e**	87	85
3	*N,N,N*-Triethylamine	**3-3f**	91	60
4	*N,N,N*-Tributhylamine	**3-3g**	86	66
5	Dicyclohexylamine	**3-3h**	92	47
6	Pyrrolidine	**3-3i**	71	37
7	*N*-Methylpyrroline	**3-3j**	89	53
8	Piperidine	**3-3k**	78	50
9	Pyridine	**3-3l**	81	78
10	Morpholine	**3-3m**	73	61

[a] Isolated yield. [b] Determined by chiral HPLC.

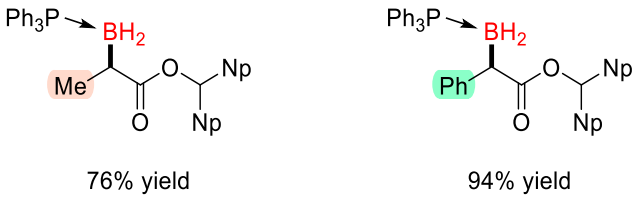


Scheme 3-9. α-アリールジアゾエステル類とボラン錯体との不斉 B–H 挿入反応

以下に，基質検討の結果をまとめて①と②に示す。

① ジアゾエステルの α 位の置換基効果

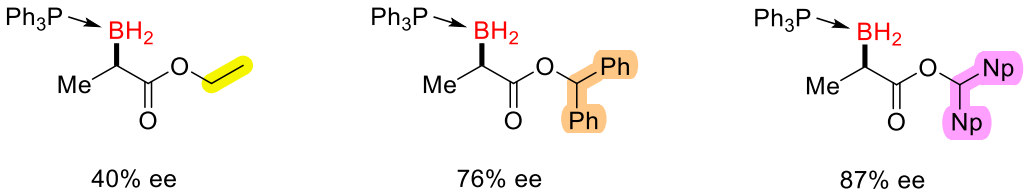
ジアゾエステルの α 位の置換基を立体障害の小さい置換基(メチル基)に変えることで，反応性が早くなり，どの基質に対しても室温では 5 分間で反応が終了している。しかし、副生成物としてエステル体と α, β-不飽和エステル体が得られているため，目的の化合物の収率が低下している。一方，ジアゾエステルの α 位の置換基を立体障害の大きいフェニル基に変えることで，反応性が遅くなり，室温で 1 日間かかることが分かったが，副生成物の合成を防ぐことができ，目的化合物の収率が向上した(Scheme 3-10)。



Scheme 3-10. ジアゾエステルの α 位の影響

② ジアゾエステルの末端置換基効果

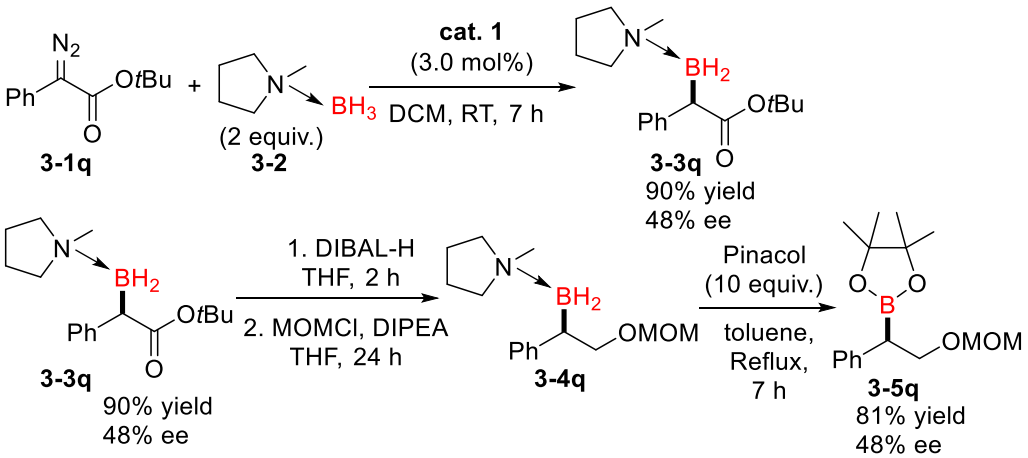
ジアゾエステルの末端置換基は立体選択性に依存していることが分かった。例えば，エチルのような立体障害の小さい置換基を用いることで，40% ee の有機ホウ素化合物を合成した。エチル基に比べ，立体障害の大きいジフェニル基を持つことで，立体選択性が 36%向上し，76% ee で目的化合物が得られた。さらに，立体障害がもっと大きいジナフチルメチル基を用いることで，87% ee まで立体選択性が向上した(Scheme 3-11)。



Scheme 3-11. ジアゾエステルの末端置換基の影響

3-7 不斉有機ホウ素化合物の応用反応

有機ホウ素化合物は有機合成化学においては重要な中間体であり，広い応用が期待できる。例えば，本章の冒頭で述べた様に Ar-B(OR)$_2$ 系では Suzuki-Miyaura カップリング反応に用いられ，有機ホウ素化合物を医薬品や電子材料に利用されるビアリール類を構築できる。また，$R_1R_2R_3NBH_3$ および $R_1R_2R_3PBH_3$ 系ではハイドロボレーション反応に用いることで，アルキンから *anti*-Markovnikov 型の光学活性アルコールが合成可能になる。このように，光学活性な $R_1R_2R_3NBH_3$ および $R_1R_2R_3PBH_3$ 系錯体は，新規有機ホウ素化合物への合成変換も期待される，本研究ではホウ酸エステルへの合成変換を検討した。以下 Scheme 3-12 に，生成した有機ホウ素化合物の応用としてボロン酸エステルへの合成変換をしめす。ジアゾエステル **3-1q** と N-メチルピロリンーボラン錯体を Ru(II)-Pheox (3 mol%) 存在下，不斉有機ホウ素化合物を 90%収率，48% ee で合成した。生成物を用いて応用変換反応を行った。エナンチオ選択性 48% ee の有機ホウ素化合物を用いて，THF 溶媒中，還元剤である水素化ジイソブチルアルミニウム（DIBAL−H）と反応させ，エステル部分の還元反応を行った。得られたアルコールを N, N-ジイソプロピルエチルアミン塩基存在下，アルコールの保護基として使われるクロロメチルメチルエーテル（MOMCl)と 1 日反応させることで，目的化合物が得られた。次に，ピナコールをトルエン中，7 時間還流し，目的の化合物を 2 段階で 81% 収率，48% ee と光学純度を保持したままの不斉アルコールへ変換することができた。不斉アルコールとは生理活性天然物や医薬品によく含まれる重要な部分分子である[17]。こちらの応用変換反応は Xu 等によって報告された先行研究によって行った。



Scheme 3-12. 不斉有機ホウ素化合物の応用

3-8 推定される反応機構

次に，本反応の反応機構を考察した（Figure 3-5）。反応機構の考察を先行研究もとに考察した。まず，ジアゾエステルと Ru(II)-Pheox 触媒が反応して，窒素を放出し，金属カルベン錯体を形成する。その後，触媒の不斉環境の影響で B–H 結合が面選択的に接近し，3 中心の遷移状態を形成し，最終生成物である有機ホウ素化合物が ***R*** 体のエナンチオマーで得られると考えられる。ジアゾエステル類の立体障害によって立体選択性が向上する実験事実から，本反応はジアゾアエステル類の末端置換基を利用した不斉制御がなされていると予想した。ジナフチルメチル基のような嵩高い置換基は，Ru(II)-Pheox 触媒の不斉点のフェニル基との立体反発により，Favorable のように配位すると考えられる。その後，ボラン錯体との反応が進行するが，ジナフチル基により一つ方法のみ反応が選択的に進行し，***R*** 体の有機ホウ素化合物類が立体選択的に得られると考えられる。

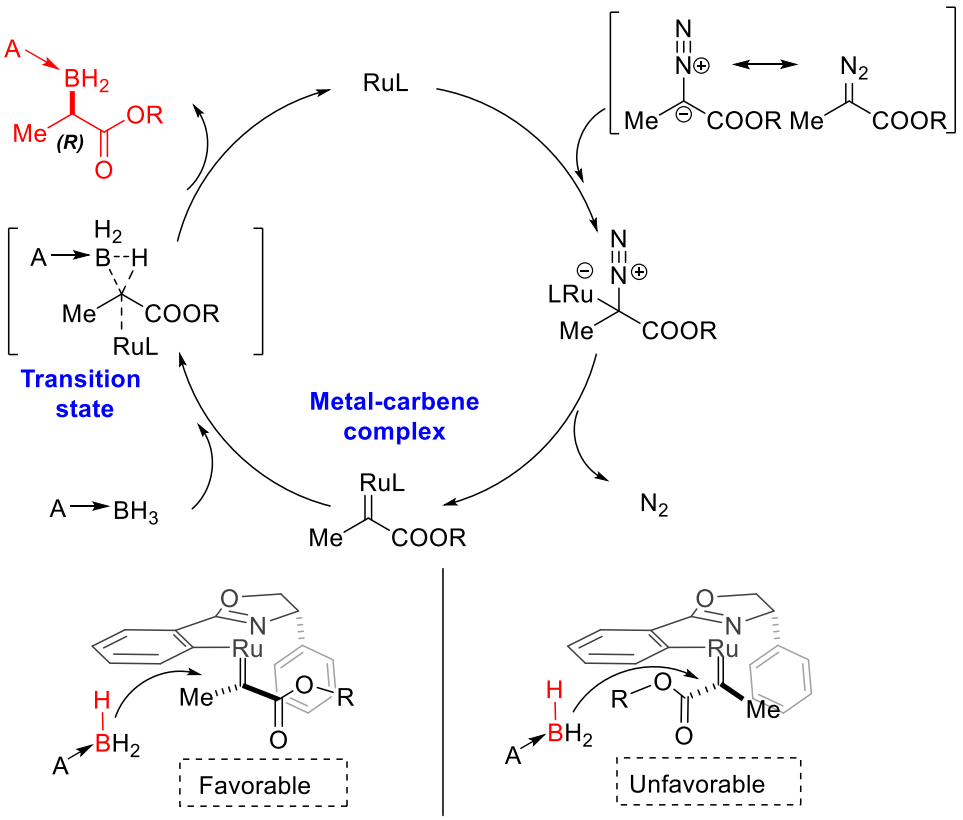
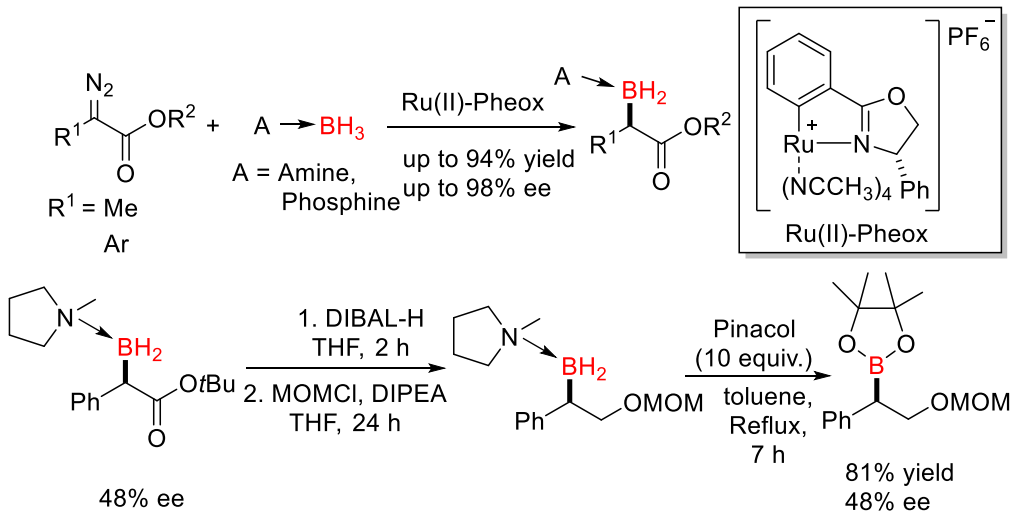


Figure 3-5. 推定される反応機構

3-9 結論

本研究では, カルベン中間体の単結合 σ-結合への挿入反応に着目して，ボラン錯体類とジアゾエステル類から，触媒的 B–H 結合挿入反応を経由する新規光学活性有機ホウ素化合物の開発を行った。不斉触媒は，独自に開発したフェニルオキサゾリン-ルテニウム触媒(Ru(II)-Pheox)を用いた。末端置換基が立体障害の異なる 4 種類の α-メチルジアゾエステル類とトリフェニルホスフィンーボラン錯体を用いて，触媒的不斉 B–H 挿入反応を検討した。その結果，ジアゾエステル類の末端置換基が立体障害の大きいほど高収率，高エナンチオ選択性を示した。続いて，触媒的，温度，溶媒の条件検討を行い，最も高いエナンチオ選択性 98% ee で不斉有機ホウ素化合物を得ることに成功した。さらに，様々なホスフィン及びアミンーボラン錯体の基質依存性の検討を行い高収率，高エナンチオ選択性で様々な有機ホウ素化合物を合成することができた。さらに，立体障害の大きい α-アリルジアゾエステル類を，新たに合成し，不斉有機ホウ素化合物に適用することで，副生成物を防ぎ，高収率で有機ホウ素化合物を得た。さらに本研究によって，これまでロジウムや銅に限られていたホウ素化合物の不斉合成にルテニウム触媒という新たな選択肢を示すことができたと同時に，Ru(II)-Pheox 触媒の新たな適用範囲が示すこともできた。また，α-フェニルジアゾエステル類に限られていた基質の適用範囲に α-メチルジアゾエステルも適用できることを明らかにした。加えて，得られた有機ホウ素化合物は，相当するアルコール類に変換できることを示した。



Scheme 3-13. Ru(II)-Pheox 触媒による不斉 B–H 挿入反応の開発とその応用

第 4 章　アリル及びビニルシラン類の触媒的不斉シクロプロパン化反応とその応用

4-1 有機ケイ素化合物の特徴とその有機合成への応用

有機ケイ素化合物は，ケイ素が地球上に酸素に次いで，2 番目に豊富な元素であること，有機ケイ素化合物の毒性が比較的低いことの 2 つ理由から，最も重要な化合物群である。有機ケイ素化合物の有機合成への応用は，シリコーン工業の発展に伴う安価かつ多様な原料の入手の容易さや，他の有機金属化合物と異なり，一般に安定で種々の変換反応に耐えうること，ケイ素と炭素，水素あるいはハロゲンなどのそれぞれの結合は，適度な反応性を有していること，などに基づいて様々な有機合成反応が数多く開発されてきた。その結果，多種多様な有機ケイ素試薬とともに多様な新反応を生み出してきた[1]。例えば，有機ケイ素化合物の最も一般的な化合物であるアルキルシリルクロリドは，-OH，-NH，-SH，-COOH，-$CONH_2$ などの活性水素の保護基として利用されている[2]。また，有機ケイ素化合物の一つであるシリコーンオイルは無色無臭で，毒性が低く，他の物質との相互作用も少ないため，医療関連や化粧品材料などへ応用されている[3]。

有機ケイ素化合物の中で，アリルシラン類及びビニルシラン類は，オレフィンであるアリル基やビニル基を有する有機ケイ素化合物であり，Si–C 結合の共役によりオレフィンが活性化されている。このため，アリルシラン類及びビニルシラン類のオレフィンは求核剤として，有機合成反応に有用である。以下に，アリルシラン及びビニルシラン類の反応の一般的な特徴と反応について概説する。

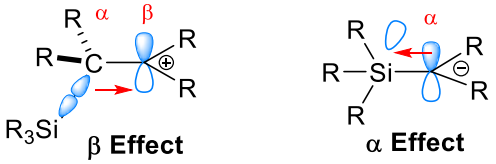
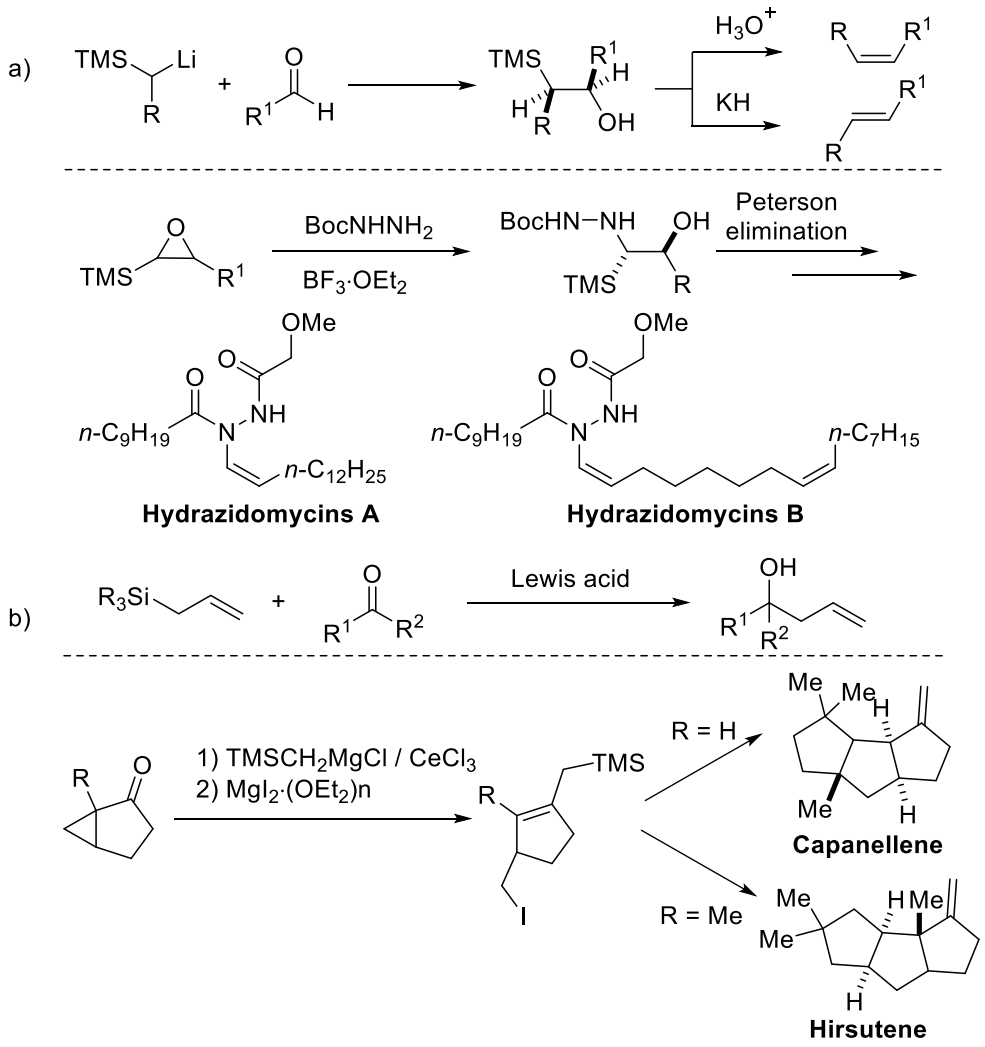


Figure 4-1. ケイ素の置換基効果

有機ケイ素化合物にはシリコーン－共役効果に基づく α 効果と β 効果といわれる特徴がある。α 効果は，ケイ素の電気陰性度が低いため，α 位のカルバニオンが安定しやすい効果である（Figure 4-1）。β 効果は，Si–C 結合の σ 結合と β 位のカルボカチオンの空軌道が共役するため，β 位のカルボカチオンが安定化しやすい。つまり，アリルシラ

ンの二重結合はσ－π結合により求核性を持つ。これらの特徴は，隣接基の関与やLewis酸触媒の存在下でより活性化される。したがって，これらの性質を利用して，様々な反応に応用されてきた[4]。以下に有機ケイ素化合物のいくつかの応用反応の例を示す。

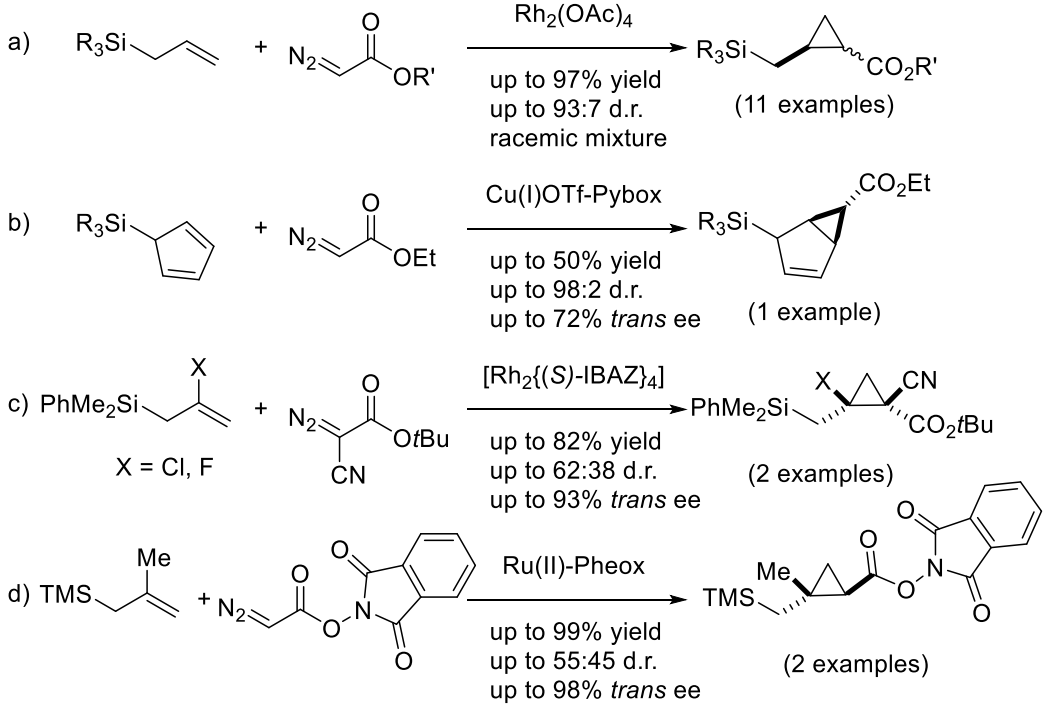


Scheme 4-1. 有機ケイ素化合物の合成的応用

アルデヒドまたはケトンをα位にシリル基を持つカルボニオンと付加反応させ，得られる中間体を酸または塩基条件で処理し，シラノールの脱離反応によって，アルケンを合成する反応であり，Peterson 反応または Peterson olefination と呼ばれている。この Peterson 反応の応用例として，2013 年に Baley らによって報告された論文で，抗腫瘍作用がある天然物 Hydrazidomycins の全合成に初めて成功している[5]（Scheme 4-1a）。また，ルイス酸存在下，求核剤としてアリルシランを用いてケトンとの反応により，炭素−炭素結合を生成する反応は Hosomi-Sakurai 反応と呼ばれている。この反応を用いた応用例として，2013 年に Li らが Capanellene 及び Hirsutene の全合成に成功している[6]（Scheme 4-1b）。

4-2 研究背景 有機ケイ素化合物とジアゾ化合物の反応

一方, アリルシラン及びビニルシラン類への触媒的不斉カルベン移動反応に用いた報告例がいくつか発表されている。2001 年に Turos 等によって，ロジウム触媒存在下，様々なアリルシランとジアゾエステル類との触媒的不斉カルベン移動反応を開発した[7]。高収率でラセミ体のシリルシクロプロパン生成物を得たが，基質によって，ジアステレオ選択性は 55:45 d.r.であり，立体選択性にまだ課題が残された。また，2003 年に Landais 等は，銅触媒と不斉リガンドに Pybox を用いて，環状系のクロスアリルシランであるシクロペンタジエニルシランへのエチルジアゾアセテートの触媒的不斉カルベン移動反応を報告している[8]。



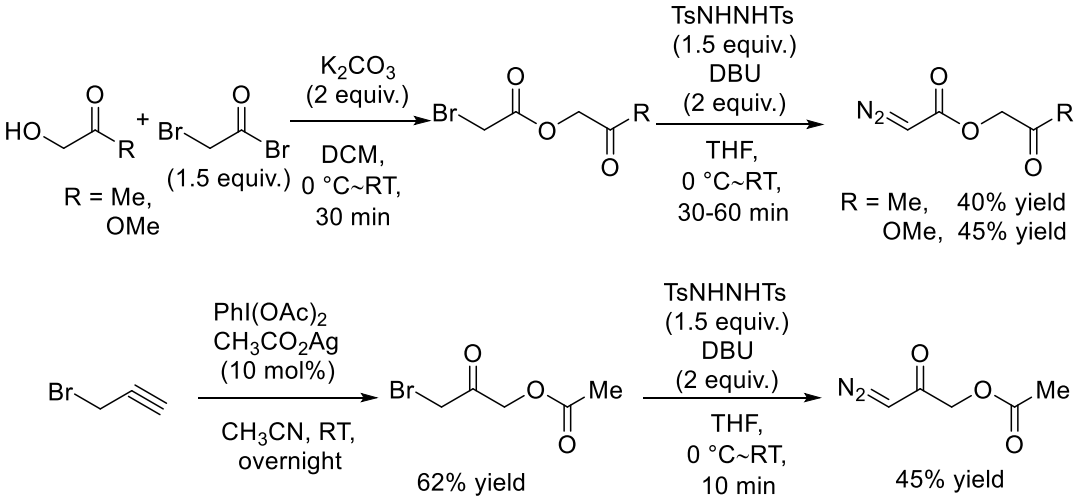
Scheme 4-2. アリルシラン類の触媒的不斉カルベン移動反応

ここでは，高いジアステレオ選択性を示したものの，収率とエナンチオ選択性が中程度だった。また，2016 年に Jubault 等は不斉ロジウム触媒存在下，フロロアリルシランとクロロアリルシランと 2 置換ジアゾエステルとの不斉カルベン移動反応を開発している[9]。生成物であるシクロプロパン化合物は高収率・高エナンチオ選択性で得られたが，ジアステレオ選択性はほぼ 1 対 1 であった。さらに，2019 年に Mendoza 等によって，Ru(II)-Pheox 触媒を用いて，フタルイミジルジアゾアセテートのアリルシランへの不斉カルベン移動反応を高収率・高エナンチオ選択性で報告している[10] (Scheme 4-2)。

以上の様に有機合成化合物において最近特に注目を集めているアリルシランとビニルシランへの触媒的カルベン移動反応では，収率，立体選択性において多くの課題が残されている。したがって本研究では，新規ジアゾ化合物と Ru(II)-Pheox 触媒により，触媒的カルベン移動反応を利用して，高度な立体制御を達成する不斉シクロプロパン化反応の開発を研究課題として行った。

4-3 ジアゾ化合物の基質合成

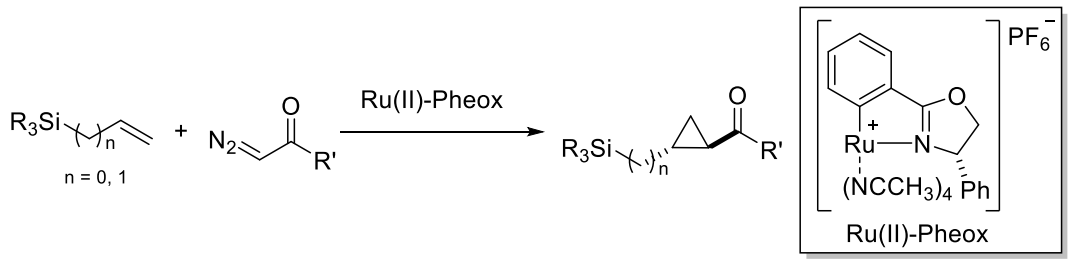
カルベン前駆体としてのジアゾ化合物は，市販されているジアゾ酢酸エチル，*tert*-ブチルジアゾアセテートの他，スクシンイミジルジアゾアセテート，アセトニルジアゾアセテート，メチル(ジアゾアセトキシ)アセテート，ジアゾアセトキシアセトンをカルベン前駆体として[11]，本反応に用いた。また，新たにケトン及びエステル官能化されたジアゾ化合物の合成を行った(Scheme 4-3)。初めに，2 種類のグリコール酸を K_2CO_3 の存在下でブロモアセチルブロマイドと反応させ，ブロモアセチル化合物をそれぞれ得た。その次に，ジトシルヒドラジンと DBU による福山法を用いて，それぞれの官能化されたジアゾ化合物を 40%～45%収率で合成した。ジアゾアセトキシアセトンについて，プロパルギルブロミドを出発物として用いて，銀触媒存在下，ジアセトキシヨードベンゼンとの反応により，ブロモアセチル化合物を 62% 収率で得たのち，福山法にて 45%収率で合成した。



Scheme 4-3. ジアゾ化合物の合成

4-4 アリル及びビニルシラン類の触媒的不斉シクロプロパン化反応

本研究では，Ru(II)-Pheox 触媒存在下，様々なアリル及びビニルシラン類を用いて，新規ジアゾ化合物との不斉カルベン移動反応の検討を行った。さらに，生成物であるシリルシクロプロパン化合物を用いて，生理活性物質への応用変換反応について報告する。



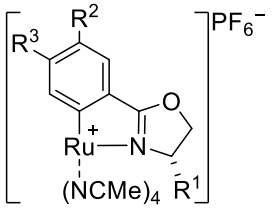
Scheme 4-4. Ru(II)-Pheox 触媒によるシラン類の触媒的不斉カルベン移動反応

4-5 ジアゾ化合物と触媒のスクリーニング

まず，触媒的不斉カルベン移動反応によく用いられているジアゾエステルであるジアゾ酢酸エチルを用いて，アリルトリメチルシランを 5 当量と 1 mol%の Ru(II)-Pheox **cat. 1** 存在下，室温でジアゾ化合物のシリンジポンプによる低速度添加法を行った。更に，1 時間を撹拌し，反応を完結させた（Table 4-1, entry 1）。その結果，触媒的不斉カルベン移動反応が進行し，72% 収率で目的のシクロプロパン化合物が得られた。シス・トランス比（ジアステレオ比）は 85:15 d.r.で *trans* 体のエナンチオ選択性は 98% ee を示し，高度な立体制御が達成された。次に，立体障害の大きい置換基を持つ *tert*-ブチルジアゾアセテートとスクシンイミジルジアゾアセテートを用いて，アリルトリメチルシランへの不斉カルベン移動反応を検討した（entry 2, 3）。その結果，高いエナンチオ選択性を示したものの，収率は 45%まで低下した。ジアゾエステルの末端置換基の立体障害により，ジアゾ化合物の二量体は主な生成物として得られた。続いて，当研究室で，これまでに不斉カルベン移動反応に対して，高い収率と立体選択性を示したカルベン前駆体として報告している官能化されたジアゾ化合物をアリルシランとの不斉カルベン移動反応に応用することにした（Table 4-1, entries 4, 5, 6）。メチル（ジアゾアセトキシ）アセテートより最も高い収率（89% yield），高エナンチオ選択性（96% *trans* ee）で目的の不斉シクロプロパン化合物が得られた。続いて，このジアゾ化合物を最適なカルベン前駆体として用いて，様々な Ru(II)-Pheox と Ru(II)-Prox シリーズでの触媒スクリーニングを行った（Table 4-1, entries 7-15）。まず，様々な Ru−$C_{Ar}(sp^2)$のシリーズの触媒系（**cat. 1**～**cat. 3**, **10**, **7**, **8**），そして，2020 年に開発された Ru−$C_{olefin}(sp^2)$ 触媒系（**cat. 12**～**cat. 15**）を用いて，検討した。

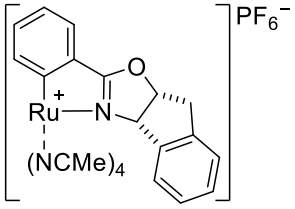
Table 4-1. ジアゾエステル類とアリルシランとの不斉カルベン移動反応

catalysts :

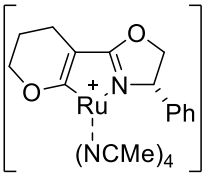


cat.	R^1	R^2	R^3
cat. 1	Ph	H	H
cat. 2	Ph	NO_2	H
cat. 3	Ph	MeO	H
cat. 10	Ph	H	$CH_2N^+(CH_3)_3I^-$
cat. 7	*t*Bu	H	H

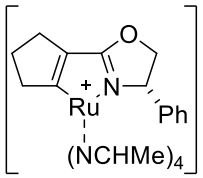
cat.



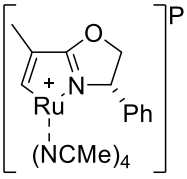
cat. 8



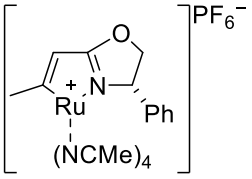
cat. 12



cat. 13

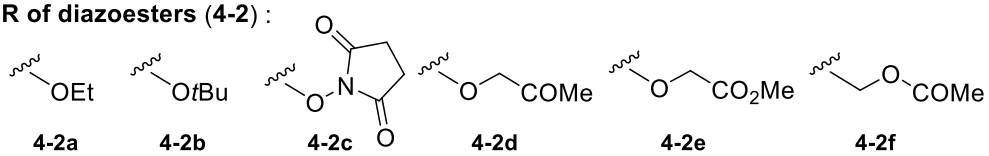


cat. 14

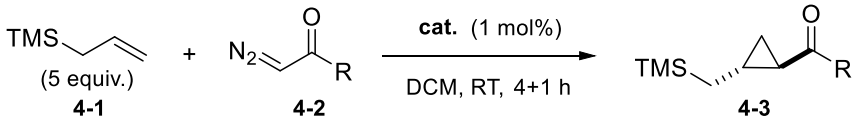


cat. 15

R of diazoesters (**4-2**) :



4-2a **4-2b** **4-2c** **4-2d** **4-2e** **4-2f**



Entry	cat.	4-2	Product	Yield [%][a]	d.r.[b]	*trans* ee [%][c]
1	**cat. 1**	**4-2a**	**4-3a**	72	85:15	98[d]
2	**cat. 1**	**4-2b**	**4-3b**	45	84:16	98
3	**cat. 1**	**4-2c**	**4-3c**	45	85:15	91
4	**cat. 1**	**4-2d**	**4-3d**	77	83:17	98
5	**cat. 1**	**4-2e**	**4-3e**	89	85:15	96
6	**cat. 1**	**4-2f**	**4-3f**	64	82:18	68
7	**cat. 2**	**4-2e**	**4-3e**	86	86:14	97
8	**cat. 3**	**4-2e**	**4-3e**	95	88:12	95
9	**cat. 10**	**4-2e**	**4-3e**	92	85:15	97
10	**cat. 7**	**4-2e**	**4-3e**	76	71:29	86
11	**cat. 8**	**4-2e**	**4-3e**	53	69:31	58
12	**cat. 14**	**4-2e**	**4-3e**	65	84:16	62
13	**cat. 15**	**4-2e**	**4-3e**	66	83:17	83
14	**cat. 13**	**4-2e**	**4-3e**	66	81:19	86
15	**cat. 12**	**4-2e**	**4-3e**	19	75:25	76
16[e]	**cat. 3**	**4-2e**	**4-3e**	77	86:14	95

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.
[d] Determined by GC. [e] 3 equiv. of allylsilane **4-1** was used.

さらに触媒の不斉環境をフェニル基に固定し，反応中心金属であるルテニウムと直結したベンゼン環上の電子密度の変化による反応性，立体選択性への影響について精査した。ルテニウムと結合しているベンゼン環上の置換基を電子吸引（NO_2），電子供与（MeO），$CH_2N^+(CH_3)_3I^-$に変えた触媒を用いて触媒的不斉カルベン移動反応を行った。いずれの触媒にも高い立体選択性を示し，電子供与（MeO）を持つ触媒 **cat. 3** より最も高い収率 95%で反応が進行した（Table 4-1, entry 8）。次に，不斉環境を *tert*-butyl 基や indan 基に変えた触媒 **cat. 7**，**cat. 8** を用いた場合，生成物の収率，ジアステレオ比，エナンチオ選択性が低下した（Table 4-1, entry 10, 11）。したがって，不斉環境のフェニル基が本反応系において，高収率，高立体選択性を及ぼす重要な置換基である。その理由として，ジアゾ化合物のカルボニル基と不斉環境のフェニル基は π–π 結合相互作用によって，安定な金属カルベン錯体を生成し，収率，立体選択性の向上に影響すると考えられる。続いて，Ru–$C_{olefin}(sp^2)$ 触媒系（**cat. 12**～**cat. 15**）での検討を行ったところ，収率，立体選択性が低下した。アリルシランとの不斉カルベン移動反応では，中心金属 Ru の電子密度が収率に大きな影響を及ぼすことが分かった。例えば，電子供与基（MeO）を持つ触媒 **cat. 3**，電子吸引（NO_2）持つ触媒 **cat. 2**，そしてジヒドロピランの酸素は電気陰性度が高いため，電子吸引性質が高い **cat. 12** での収率の結果を比較すると，95%，86%，19%であり，ルテニウムの電子密度が高い方が，触媒的不斉カルベン移動反応を促進すると考えられる。最後に，entry 16 では，アリルシランの当量を 3 まで下げて，検討した。その結果，収率の低下が観察された。生成物の絶対配置をシリルシクロプロパン化合物 **3-3c** の単結晶の X 線構造解析によって，（***1R***, ***2R***）であることが分かった（Figure 4-2）。

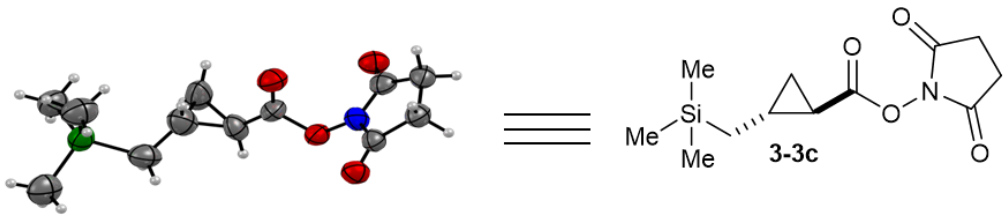


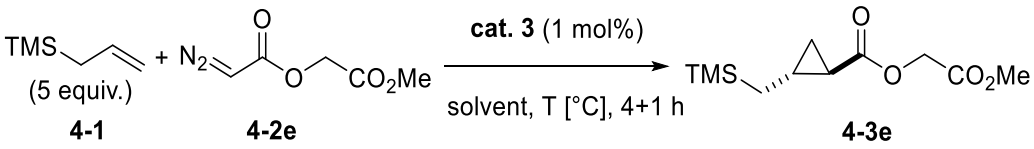
Figure 4-2. 不斉シリルシクロプロパン化合物の X 線構造解析

4−6 溶媒と温度効果

次に，Table 4-2 では溶媒と温度効果について検討した。溶媒にジクロロメタン以外，アセトン，トルエン，テトラヒドロフラン，酢酸エチル，アセトニトリルとジオキサンを用いた。アセトンより高収率 91%，高エナンチオ選択性 94% *trans* ee と若干ジアステレオ選択性が増加し，89:11 d.r.で目的の生成物が得られた。配位性の高い溶媒，テトラヒドロフラン，ジオキサンや配位子として使われているアセトニトリルなどが触媒を安

定化させる効果があり，反応性を遅くさせるため，収率と立体選択性を低下させたと考えられる（Table 4-2, entries 3〜7）。続いて，高い収率と立体選択性を示したジクロロメタンとアセトンを用いて，温度検討を行った。温度を低下するにしたがって，立体選択性が増加した。特に，ジクロロメタンを用いた場合に比べて，アセトンを用いた場合，ジアステレオ選択性が改善される傾向がみられた。具体的に，−50 ℃より，最も高いジアステレオ比 97:3 d.r.，99% *trans* ee を示した Table 4-2, entry 16）。また，温度効果では，反応温度を 0 ℃とした時に，最も高い収率 99% で不斉シリルシクロプロパン化合物が得られた Table 4-2, entry 9）。

Table 4-2. 溶媒と温度効果



Entry	Solvent	T [°C]	Yield [%][a]	d.r.[b]	*trans* ee [%][c]
1	DCM	RT	95	88:12	95
2	Acetone	RT	91	89:11	94
3	Toluene	RT	50	86:14	82
4	THF	RT	84	86:14	85
5[d]	EA	RT	40	91:9	86
6[e]	CH_3CN	RT	25	84:16	88
7[e]	Dioxane	RT	22	88:12	87
8	DCM	0	96	90:10	97
9	Acetone	0	99	90:10	97
10	DCM	−10	95	90:10	97
11	Acetone	−10	89	91:9	97
12	DCM	−20	92	89:11	98
13	Acetone	−20	85	92:8	98
14	DCM	−30	92	88:12	99
15	Acetone	−30	82	93:7	99
16[f]	Acetone	−50	94	97:3	99

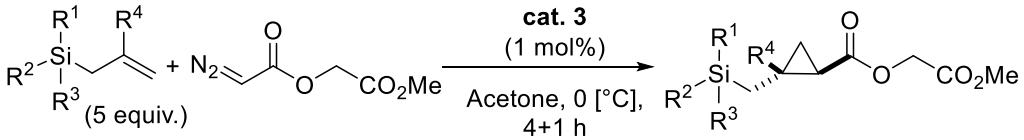
[a] Isolated yield. [b] Determined by crude 1H NMR. [c] Determined by chiral HPLC.
[d] Stirred for 1 day. [e] Stirred for 2 days. [f] 3 mol% of **cat. 1** was used.

4-7 様々なアリルシラン類の基質依存性の検討

続いて，これまでの，条件検討を基に，触媒 **cat. 3**，反応温度を 0 ℃，そして，反応溶媒をアセトンに固定し，様々なアリルシラン類の基質依存性の検討を行った。結果を以下 Table 4-3 に示す。まず，スケールアップの実験を 1 mmol のジアゾ化合物を用いて検討した（Table 4-3, entry 1）。その結果，スケールアップによる収率や立体選択性への影響はなく反応が速やかに進行した（96% yield, 91:9 d.r., 97% *trans* ee）。次に，シラン上の置換基を様々なアルキル基に変えて，置換基効果を検討した。（Table 4-3, entries 3~7）すべての基質において良好な収率とエナンチオ選択性を示した上に，ジアステレオ比に若干改善する傾向が示された。さらに，ケイ素上の置換基をより大きくしたアリルシラン類への不斉カルベン移動反応を検討した（Table 4-3, entries 8~14）。立体障害の大きいフェニル基を持つアリルシラン類でも反応が速やかに進行し，高収率，高立体選択性で目的の不斉シリルシクロプロパン化合物が得られた。ただし，アリルトリフェニルシランの場合，低温でのアセトン溶媒への溶解性が低くなるため，収率の低下が観察された（72% yield, 90:10 d.r., 97% *trans* ee）（Table 4-3, entry 12）。また，もっとも嵩高いアリルシランであるトリス（トリメチルシリル）シランの場合でも，高収率 90%，高ジアステレオ選択性 90:10 d.r.，高エナンチオ選択性 97% ee を示した（Table 4-3, entry 13）。このことは，Si−C 結合が C−C 結合よりも 1.5 倍ほど長く，立体障害の影響をあまり受けないと思われる。

次に, アリルトリエトキシシランを用いた場合, 最も高いジアステレオ選択性 97:3 d.r. を示した（Table 4-3, entry 14）。アルコキシシリル部位はアンカー剤となるのでシリカゲルと反応するためシリカゲルカラムクロマトグラフィーでの生成が困難である。そこで生成物を単離せずに，次の変換反応に用いた。生成物の収率を crude ^{1}H NMR また，エナンチオ選択性水酸基に変換反応にした後，旋光度の比[12]をから決定した。最後に，二置換基アリルシラン類への不斉カルベン移動反応を検討した（Table 4-3, entries 15〜17）。2-ブロモアリルトリメチルシランの場合，高収率（83%），高立体選択性（95:5 d.r., 99% *trans* ee）で目的の不斉シリルシクロプロパン化合物 **4-3s** が生成した。一方，ジメチル 2-メチルアリルフェニルシランと 2-フェニルアリルトリメチルシランよりジアステレオ選択性は 68:31 d.r.，56:44 d.r.だったが，高収率（96%, 98%），高エナンチオ選択性（97% *trans* ee, 98% *cis* ee, 97% *cis* ee）で不斉カルベン移動反応が進行した（Table 4-3, entries 16, 17）。以上, 様々なアリルシラン類への不斉カルベン移動反応が円滑に進行し，高収率，高立体選択性で目的の不斉シリルシクロプロパン化合物が得られることが明らかとなった。

Table 4-3. 様々なアリルシラン類への触媒的不斉カルベン移動反応



4-1 **4-2e** **4-3**

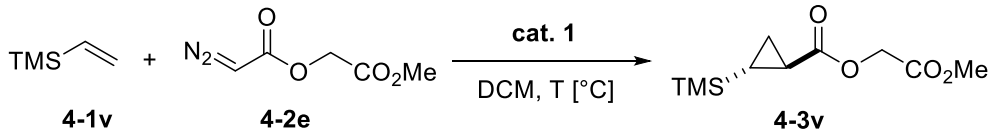
Entry	R^1	R^2	R^3	R^4	Product	Yield [%][a]	d.r.[b]	*trans* ee [%][c]
1	Me	Me	Me	H	**4-3e**	99	90:10	97
2[d]	Me	Me	Me	H	**4-3e**	96	91:9	97
3	Et	Et	Et	H	**4-3g**	84	93:7	98
4	*i*Pr	*i*Pr	*i*Pr	H	**4-3h**	93	92:8	98
5	Me	Me	*i*Pr	H	**4-3i**	85	93:7	97
6	Me	Me	Et	H	**4-3j**	81	94:6	97
7	Me	Me	*n*Bu	H	**4-3k**	80	91:9	96
8	Me	Me	Ph	H	**4-3l**	86	90:10	97
9	Me	Me	Bn	H	**4-3m**	84	91:9	97
10	Me	Ph	Ph	H	**4-3n**	93	92:8	98
11	*t*Bu	Ph	Ph	H	**4-3o**	86	92:8	97
12[e]	Ph	Ph	Ph	H	**4-3p**	72	90:10	97
13	TMS	TMS	TMS	H	**4-3q**	90	90:10	97
14[f]	EtO	EtO	EtO	H	**4-3r**	92[g]	97:3	92
15[i]	Me	Me	Me	Br	**4-3s**	83	95:5	99
16	Me	Me	Ph	Me	**4-3t**	96	68:32	97:98(*cis*)
17	Me	Me	Me	Ph	**4-3u**	98	56:44	97:97(*cis*)

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC. [d] 1.0 mmol scale of **4-2e** was used. [e] Acetone:DCM = 1:1 was used as solvent. [f] 1 mol% **cat. 1** was used at RT. [g] Based on crude material obtained after trituration with Et_2O. [h] Determined by comparison of $[\alpha]_D$ of **4-4r.** [i] 3 mol% of **cat. 1** was used at –50 °C.

4-8 ビニルシラン類の反応条件検討

続いて，Ru(II)-Pheox 触媒存在下，ビニルシラン類を用いて，ジアゾ化合物との不斉カルベン移動反応を検討した。初めに，最適な反応条件検討を以下の Table 4-4 で行った。まず，アリルシラン類の最適な反応条件である 5 当量のトリメチルビニルシランとジアゾ化合物を用いて，1 mol%の **cat. 3** 触媒，反応温度を 0 ℃，溶媒をアセトン，反応時間を低速添加法 4 時間でジアゾ化合物をくわえた。その後，さらに，1 時間撹拌の条件を用いて，反応させたが，生成物の収率はアリルシラン類との結果と比べ大きく低下した。一方，ジアステレオ選択性及びエナンチオ選択性は優れた結果（>99:1 d.r.，98% *trans* ee）を発現した。収率は大きく低下した理由はオレフィンの二重結合に立体障害の大きいトリメチルシランが直接結合しているため，カルベン移動反応が進行しにくくなり，ジアゾ化合物同士が反応しやすくなり，二量体の生成が主に得られたためである。そのため，不斉シリルシクロプロパン化合物の収率を上げるために，ビニルシランの当量，反応時間と触媒量，触媒，溶媒の条件検討を行った。その結果，3 mol% **cat. 1** 反応溶媒はジクロロメタン，反応温度 0 ℃，低速添加法 2 時間，更に，1 時間撹拌し，10 当量のビニルシランを用いたところ，収率は若干改善し，51%で目的物を得た（Table 4-4, entry 6）。どの反応条件でも，ジアステレオ選択性とエナンチオ選択性は優れた結果を示した。続いて，収率が改善した条件を用いて，様々なビニルシラン類との不斉カルベン移動反応の検討を行った。その結果を Table 4-5 に示す。シラン上の置換基をメチル基以外に，嵩高い置換基であるイソプロピル基やブチル基やフェニル基に変えて検討をした。イソプロピルジメチルビニルシランより優れた立体選択性（>99:1 d.r.，99% *trans* ee）と中程度収率 46%で目的物が得られた（Table 4-5, entry 2）。ブチルジメチルビニルシランの場合，若干収率が増加し，61%と優れた立体選択性で不斉シリルシクロプロパン化合物が得られた（Table 4-5, entry 3）。しかし，立体障害の大きいフェニル基を持つフェニルジメチルビニルシランより収率（35%）とエナンチオ選択性（53% *trans* ee）は低下した結果となった（Table 4-5, entry 4）。以上をまとめると，ビニルシランへの触媒的不斉カルベン移動反応においては立体障害の大きさからカルベンの移動反応速度が低下し，その間にジアゾ化合物の二量化が進行する副反応が競合するため収率が中程度に低下するも。しかし，立体選択性は、ほぼ完全なレベルまで制御されることが明らかとなった。

Table 4-4. ビニルシランの最適な反応条件検討

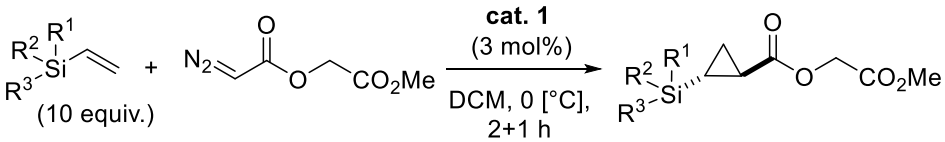


4-1v **4-2e** **4-3v**

Entry	**cat.** [mol%]	**1v** [equiv.]	T [°C]	Time [h]	Yield [%][a]	d.r.[b]	*trans* ee [%][c]
1[d]	1	5	0	4+1	34	>99:1	98
2	1	10	0	4+1	28	>99:1	98
3	2	10	0	4+1	33	>99:1	98
4	3	10	0	4+1	43	>99:1	98
5	5	10	0	4+1	49	>99:1	98
6	3	10	0	2+1	51	>99:1	98
7	3	10	0	1+1	49	>99:1	98
8	3	5	0	2+1	46	>99:1	98
9	3	10	–10	2+1	38	>99:1	99
10	3	10	RT	Dropwise	20	>99:1	98

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC. [d] **cat. 3** was used in acetone.

Table 4-5. ビニルシラン類の基質依存性の検討



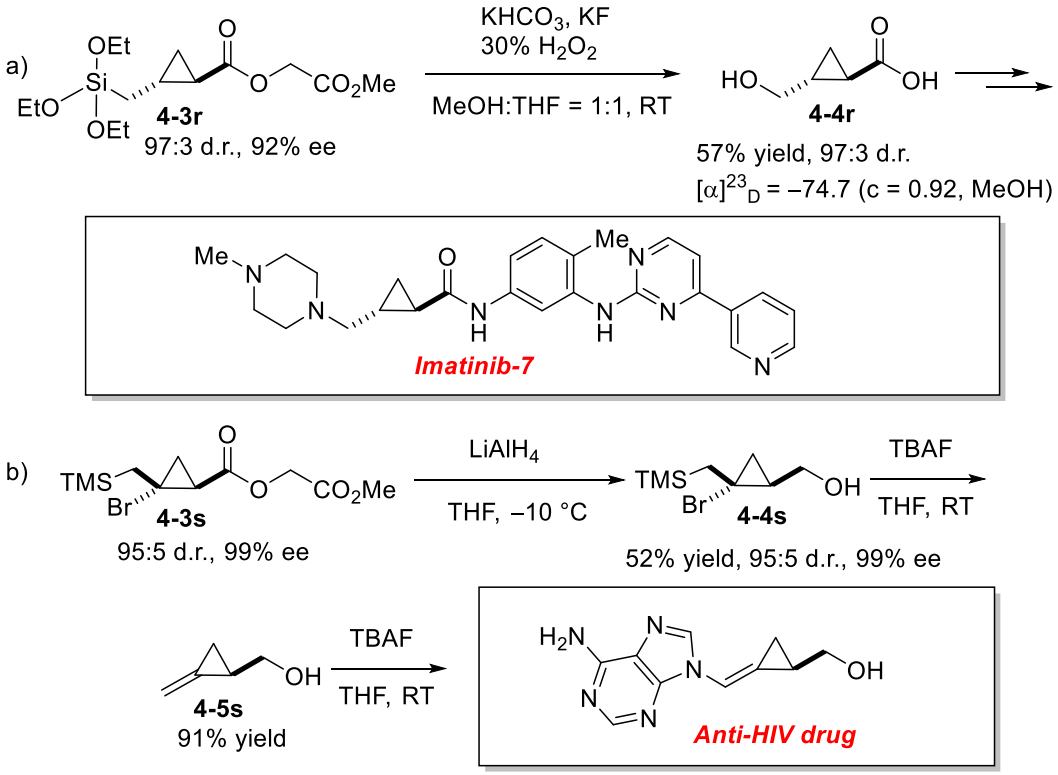
4-1 **4-2e** **4-3**

Entry	R^1	R^2	R^3	Product	Yield [%][a]	d.r.[b]	*trans* ee[c]
1	Me	Me	Me	**4-3v**	51	>99:1	98
2	Me	Me	*i*Pr	**4-3w**	46	>99:1	99
3	Me	Me	*n*Bu	**4-3x**	61	>99:1	99
4	Me	Me	Ph	**4-3y**	35	>99:1	53

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.

4-9 アリルシランへの触媒的不斉反応を利用した生理活性物質合成への応用

最後に，合成した不斉シリルシクロプロパン化合物を用いて，生理活性物質への応用変換反応を行った(Scheme 4-5)。まず，前節 4-6 で得られたトリアルコシキシシリルシクロプロパン化合物を利用した。(Scheme 4-5a)光学活性シリルシクロプロパン化合物を KF と塩基の存在下に過酸化水素を作用させる Tamao 酸化法[13]を用いて，既知化合物であるアルコールへの合成変換を行った。この生成物は Imatinib-7 という抗悪性腫瘍薬として知られている薬の合成中間体[14]であり，型式合成が完成したことになる。従来の合成法よりも格段に工程が短縮されている。次に，光学活性シリルシクロプロパン化合物 **4-3s** を用いて，水素化リチウムアルミニウムによる還元反応を行い，シリルシクロプロパン化合物のエステル部をアルコールへ変換，続いて，TBAF 用いた脱離反応によりメチレンプロパン化合物への合成変換を行った。この生成物は抗 HIV 治療薬の合成中間体[15]であり，型式合成が完成したことになる。(Scheme 4-5b)以上の様に本研究で開発された方法を応用することで効率的に重要な生理活性物質の合成を行うことができる。



Scheme 4-5. 不斉シリルシクロプロパン化合物の応用

4-10 推定される反応機構

Ru(II)-Pheox 触媒によるアリルシラン類とジアゾ化合物との不斉カルベン移動反応の推定される反応機構を Figure 4-3 に示す。推定される反応機構を 2019 年に報告した DFT 計算を用いた Ru(II)-Pheox 触媒による分子内シクロプロパン化反応の反応機構解析[16]を参考に推定した。まず，ジアゾ化合物へ触媒は酸化的付加し，金属カルベン錯体を形成する。金属カルベン錯体は Ru(II)-Pheox 触媒平面に対して真下方向のカルベンの配位になる。この金属カルベン錯体を形成する理由として，1) 触媒のリガンドのフェニル基とジアゾ化合物のカルボニル基との π 電子相互作用，2) ジアゾ化合物の末端のカルボニル基の Ru 原子への配位によって安定化される。

安定した金属カルベン錯体を形成した後，アリルシランは面選択的に接近し，3 員環構造の遷移状態を得て，還元的脱離反応により，高収率，高立体選択性で不斉シリルシクロプロパン化合物を合成すると考えられる。

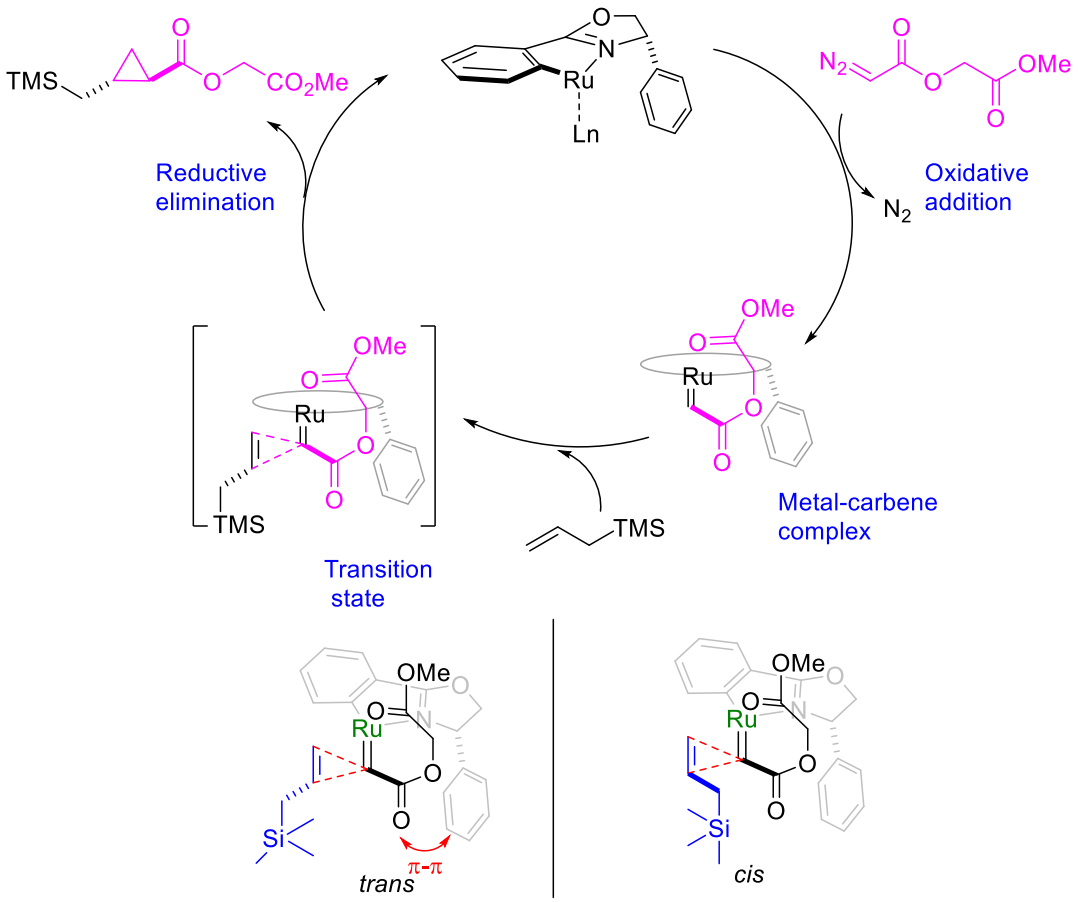
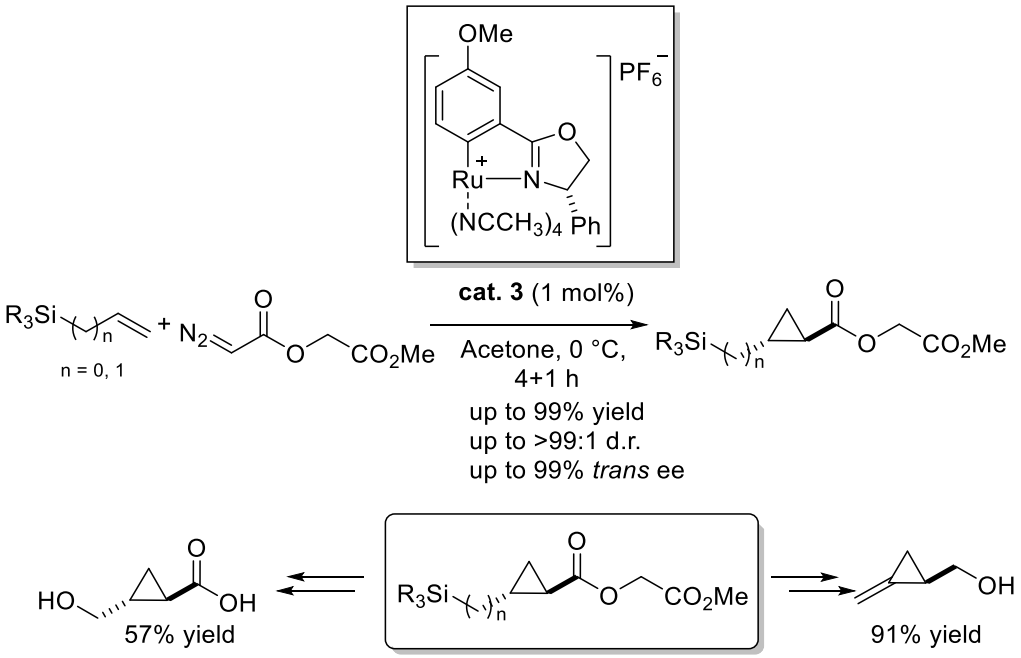


Figure 4-3. 推定反応機構

4-11 結論

本章では，Ru(II)-Pheox 触媒存在下，様々なアリル及びビニルシラン類を用いて，新規ジアゾ化合物との不斉カルベン移動反応の開発を行った。様々な一置換アリルシラン類への不斉カルベン移動反応は円滑に進行し，高収率，高立体選択性で目的の不斉シリルシクロプロパン化合物を合成した。シラン上の置換基を立体障害の大きい置換基に変えることで，ジアステレオ選択性の改善を発現した。二置換基アリルシラン類では，立体障害の影響により，ジアステレオ選択性は低下したものの，収率とエナンチオ選択性は維持し，良好な結果を示した。ビニルシランの場合，立体障害大きいシラン類は二重結合に直接結合しているため，不斉カルベン移動反応の反応性を遅くさせ，収率を大きく低下させるが，ジアステレオ選択性とエナンチオ選択性は優れた結果を発現した。さらに，生成物であるシリルシクロプロパン化合物を用いて，生理活性物質への応用変換反応に成功し，抗がん剤や抗 HIV 治療薬の重要な中間体を簡単に合成できることを示した。



Scheme 4-6. Ru(II)-Pheox 触媒によるシラン類の不斉カルベン移動反応とその応用

第 5 章　ジアゾオキシムエーテル類の触媒的不斉カルベン移動反応とその応用

5-1 オキシム化合物

オキシムやオキシムエーテル類は，実験室レベルだけでなく，工業的な合成においても広く用いられている重要な化合物群の一つである。特に，オキシムエーテル基含有化合物の生理活性は，プラリドキシム（有機リン系の農薬中毒の解毒剤），また，オビドキシム（神経ガスの解毒剤）およびミルベマイシンオキシム（効率的な駆虫物質）などのさまざまな医薬品に応用されている[1]。これらの市販薬に加えて，オキシム類は，抗ウイルス，抗癌，抗凝固，抗菌，抗蠕虫，抗ヒスタミン，抗うつ，ハース抗不整脈，降圧，鎮痛などの幅広い生理活性物質としてもよく知られている[2]。上記のように様々な医薬品だけでなく，食品化学または，材料科学においても，重要な官能基である。例えば，我々の日常生活の中で馴染みの深い物質の一つである甘味料として使われているペリラルチンはオキシム化合物である[2]。また材料分野では，オキシム類の最も重要な用途として，Beckmann 転移によるオキシムからアミドに変換し，産業界で広く使用されているナイロン-6 の原料であるカプロラクタムを合成できる。さらにオキシム類はポリマー改質剤および重金属吸着剤としても使用されている（Figure 5-1）[3]。

オキシムエーテルは上記のような重要な用途の他，有機化学において合成変換され広範な化合物が合成されている。具体的にはオキシムエーテル基よりアミン，アミノアルコール類，ニトリル類，アミノ酸類，ラクタム類，ヘテロ環類などのさまざまな窒素および酸素含有化合物への合成変換反応が報告されている[4]。また，そのオキシム窒素原子の配位子としての高い能力からや触媒配位子として利用されている。以上のように，様々な分野での研究が増加し，過去数十年間，継続してオキシム化学は発展してきている。

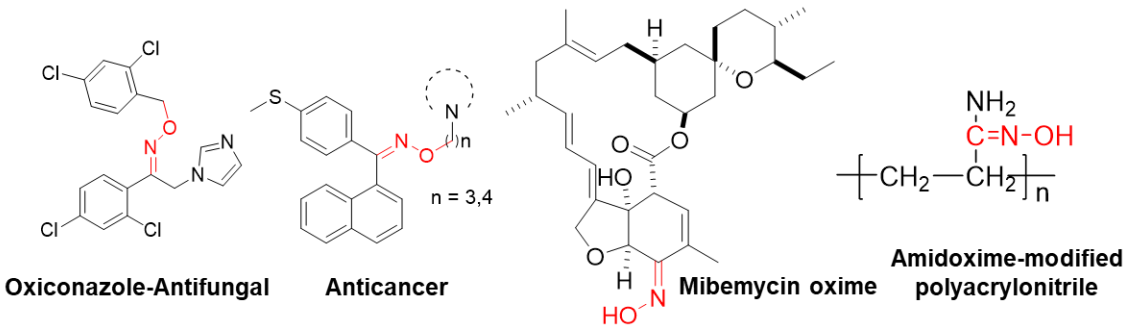


Figure 5-1. オキシ及びそのエーテルを含む生理活性物質

5-2 ジアゾオキシム類の反応

一方，カルベン前駆体としてジアゾカルボニル化合物と同様に α-ジアゾオキシム類は，その安定性と合成の容易さから，広範囲にわたる開発が行われてきた。しかしながら，ジアゾオキシムエーテルの合成に必要な反応条件と α-ジアゾイミンのトリアゾールへの迅速な異性化のために，α-ジアゾオキシムエーテルの合成に関する報告は限られている[5]。近年，前述の欠点を克服することにより，最近，さまざまな α-ジアゾオキシムエーテルが良好から優れた収率で合成することに成功し，α-ジアゾオキシムエーテルを用いた様々な研究が行われるようになった。

金属触媒による α-ジアゾオキシムエーテルの先行研究例を以下に示す(Figure 5-2)。たとえば，Au 触媒または Cu 触媒の存在下でのエナミン類，エノールエーテル類，およびニトリル類とのジアゾオキシムエーテルの付加環化により，対応するピロールおよびオキサゾールが高収率で得られた[6]。また，ジアゾオキシムエーテルと Rh 触媒から発生する金属ルベン錯体は興味深い反応性を示した。R^1=EWG 置換基を持つ場合，C−H 挿入反応が進行し，2-イソキサゾリンを生成するのに対し，R^1=アルキル基を持つ場合，2H-アズリンの形成が観察された[7]。

これらの先行研究よりジアゾオキシムエーテル類は様々な複素環合成のために広範囲で研究されてきた。しかし，不斉カルベン移動反応に応用した報告例がなく未開発である。

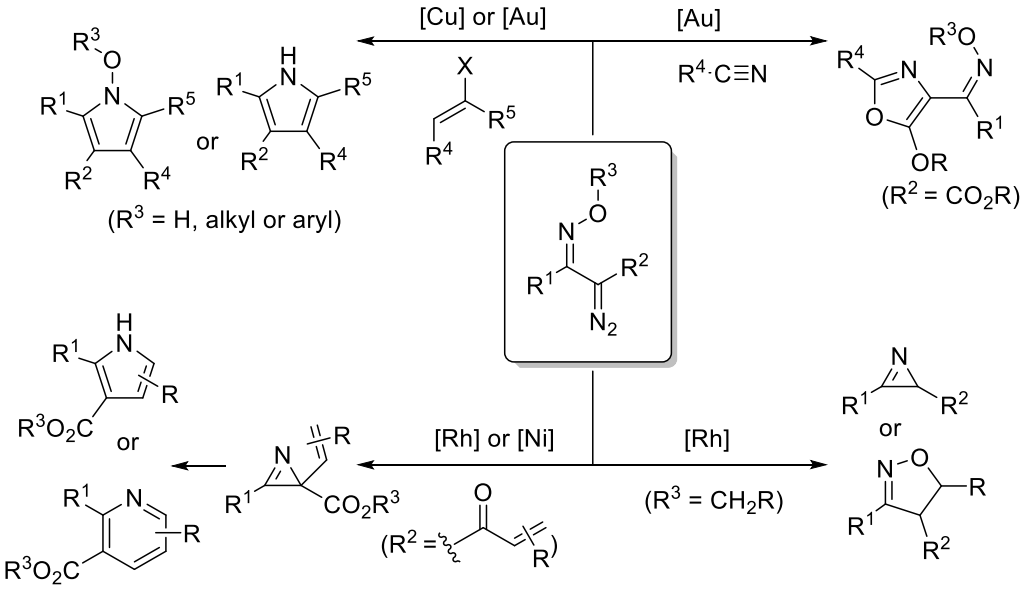


Figure 5-2. これまでのジアゾオキシエーテルの触媒反応

5-3 研究目的

第 1 章で概説したように，カルベン中間体は、その反応性を制御するため配位子を含む金属カルベン錯体形成とカルベンに隣接する電子吸引基によって制御可能な中間体となり有機合成に応用されている。ここで電子吸引基は，ジアゾ化合物の安定性や入手の容易さからエステル類，ケトン類または，アミド類を用いて相当するジアゾ化合物を合成しカルベン前駆体として用いられてきた。これらのジアゾ化合物は金属触媒と反応して，窒素を放出し，カルボニル基を有する金属カルベン錯体 **1** を形成し，様々なカルベン移動反応や双極環化付加反応などに利用されている。一方，オキシムやヒドラジンのようなイミノ基を有する金属カルベン錯体 **2** の先行研究例はほとんどない。そこで，第 5 章では，オキシムやヒドラジン経由の金属カルベン錯体 **2** の形成に基づく様々な新規不斉カルベン移動反応の開発とその応用について研究を行った（Figure 5-3）。

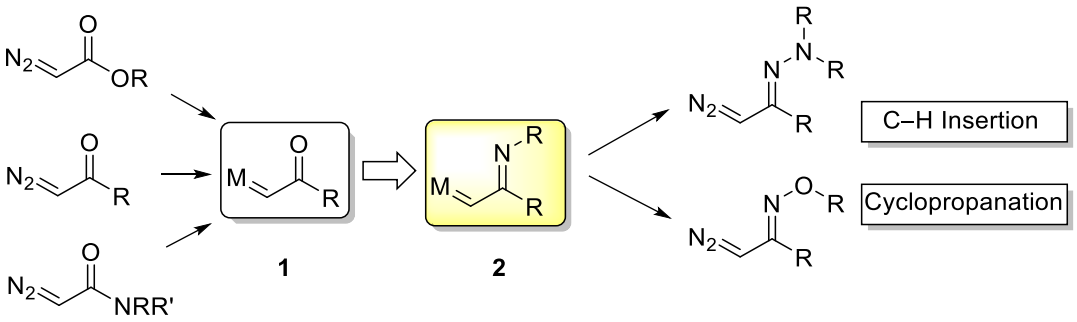
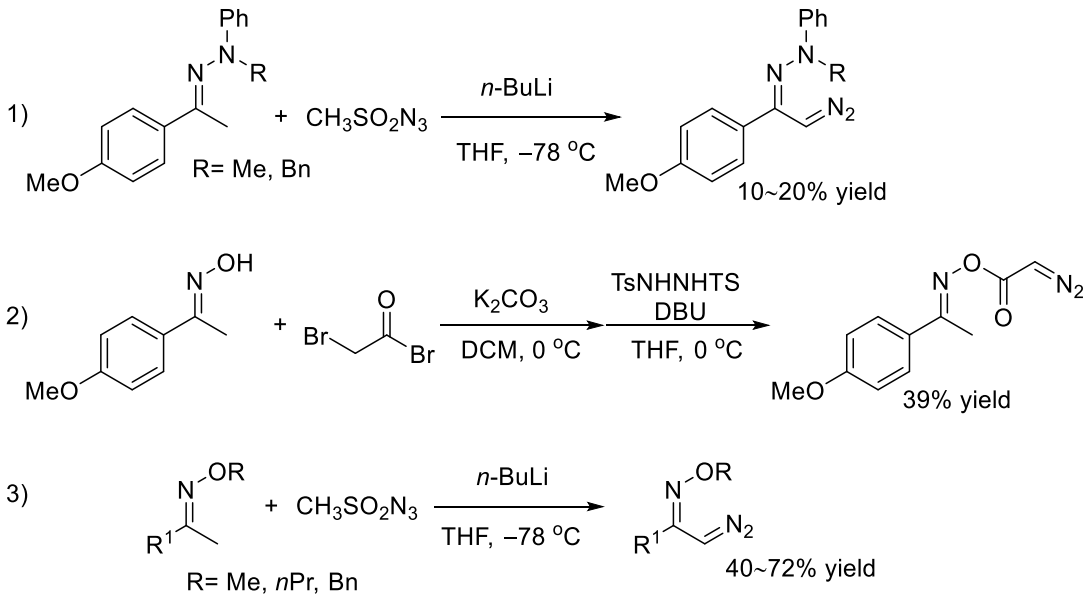


Figure 5-3. 金属カルベン錯体の形成と反応

5-4 基質合成

ジアゾヒドラゾン類とジアゾオキシムエーテル類の合成方法を以下の Scheme 5-1 に示す。ジアゾオキシエーテル類の合成法は 1992 年に Shatzmiller[8]によって開発された方法の一つのみである。したがって，ジアゾヒドラゾン(1)を Shatzmiller 手順に従って合成した。ジアゾヒドラゾンに関しては，合成手順の最適な反応条件はまだ確立されてなく，低収率で合成し，触媒的不斉カルベン移動反応に応用した。オキシムに直接ジアゾを導入する新規ジアゾオキシエーテル類(2)を Fukuyama 等の方法に従って 40%～52%収率で合成した。また，ジアゾオキシムエーテル(3)を Shatzmiller 手順に従って中～良好な収率で合成した。



Scheme 5-1. ジアゾヒドラゾンとジアゾオキシエーテルの合成

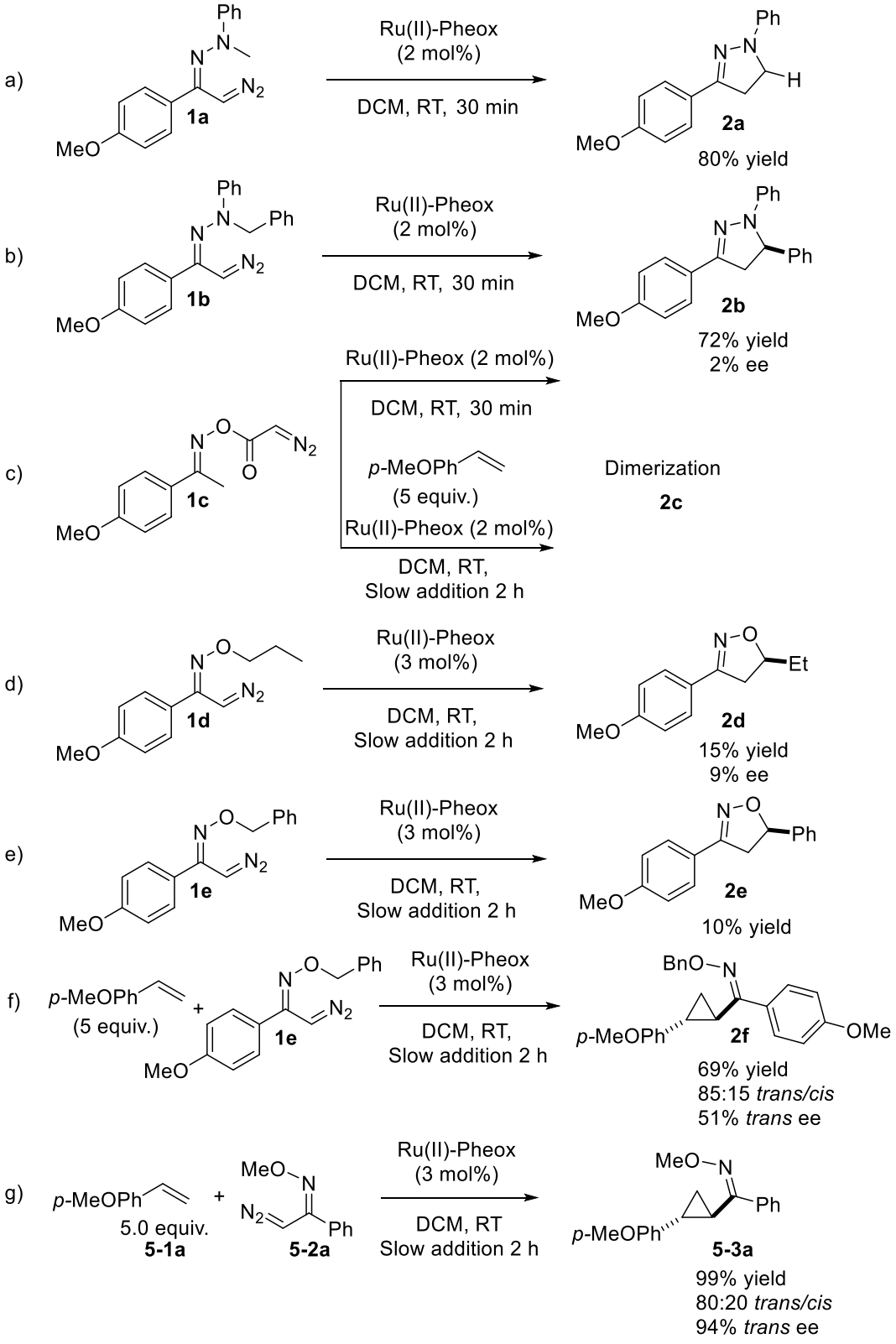
5-5 ジアゾオキシムエーテル類の触媒的不斉カルベン移動反応

ジアゾオキシムエーテルからの複素環の合成に関する広範な研究にもかかわらず，カルベン移動反応による不斉シクロプロパン化反応や不斉 C−H 挿入反応はこれまで報告されていない。そこで，ジアゾヒドラゾンやジアゾオキシエーテル類の官能化されたジアゾ化合物類の触媒的不斉カルベン移動反応を検討した（Scheme 5-2）。

まず，ジアゾヒドラゾン **1a** を用いて，Ru(II)-Pheox 触媒存在下，分子内カルベン移動反応を検討としたところ，メチル基へカルベン挿入反応が進行し，生成物であるピラゾール **2a** を 80%収率で得られた（Scheme 5-2a）。次に，カルベンの触媒的不斉分子内 C−H 挿入反応を検討した。光学活性ピラゾールの合成を目的にジアゾヒドラゾン **1b** を用いて，Ru(II)-Pheox 触媒存在下分子内カルベン移動反応を行った。その結果，目的物 **2b** が 72%収率，2% ee で得られた。このジアゾヒドラゾン系は高い収率で単結合へのカルベン移動反応が進行することが明らかとなった。しかし，エナンチオ選択性は課題として残された。

一方，ジアゾアセトキシオキシム **1c** も容易に合成できることから Ru(II)-Pheox 触媒存在下で分子内カルベン移動反応およびスチレンとの分子間シクロプロパン化反応を検討した。しかし，主生成物は，ジアゾ化合物の二量体であり，アルケンへのカルベン移動反応は観測されなかった。次に，ジアゾオキシムエーテル **1d** を合成し，分子内カルベン移動反応を目指した。C−H 挿入反応を経由する目的物 **2d** が低収率，低立体選択性を示した。そこで，収率，立体選択性の向上をも目的にオキシム基に嵩高い置換基（Bn）を導入したジアゾオキシエーテル **1e** を設計し，分子内カルベン移動反応を行ったが，二量体が主な生成物であると目的物である **2e** が 10%収率で得られた。この場合も二量体が多く生成している。なお分離精製が困難で，立体選択性を確認できなかった。

さらに，このジアゾオキシエーテル **1e** を用いて，スチレン誘導体との分子間不斉シクロプロパン化反応を検討した。その結果，オレフィンの二重結合へのカルベン移動反応が進行し，目的物である不斉シクロプロパン化合物を 69%収率と 85:15 d.r.ジアステレオ選択性，51% *trans* ee で得た。そこで，ジアゾオキシエーテル **5-2a** を設計し，不斉シクロプロパン化反応を検討したところ，高収率，高立体選択性を示した。上記のように，ジアゾヒドラゾンやジアゾオキシムエーテル類の触媒的不斉カルベン移動反応に関し，カルベン金属錯体が形成された後に，ヒドラジゾンやオキシム基の各結合の回転障壁や立体障害が二量化とカルベン移動反応の速度を支配しているものと考えている。これ等の結果から，ジアゾオキシムエーテル類をカルベン前駆体とする本反応について，さらに触媒，反応の最適な条件検討，様々な基質依存性などの反応の精査に取り組んだ。[研究は Linh Da Ho との共同研究である。Linh Da Ho 2019 修士論文][9]



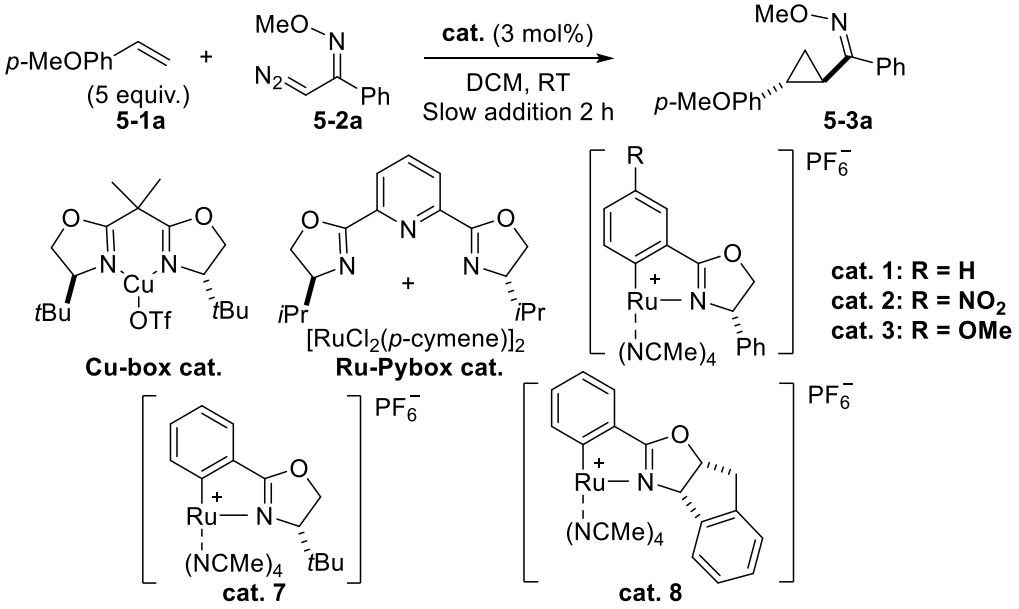
Scheme 5-2. ジアゾヒドラゾンとジアゾオキシエーテルの触媒的カルベン移動反応

5-6 触媒効果

はじめに，α-ジアゾオキシムエーテル **5-2a** と *p*-メトキシスチレン **5-1a** の不斉接触シクロプロパン化において，よく知られている Cu, Ru 触媒と Ru(II)-Pheox 錯体を用いて，触媒の評価を行った。結果を Table 5-1 に示す。Cu-Box または Ru-Pybox 錯体の存在下での **5-1a** とジアゾオキシム **5-2a** の反応により，シクロプロピルオキシム生成物 **5-3a** が低収率と低エナンチオ選択性であり，主に二量体化が進行した（Table 5-1, entries 1, 2）。

一方，**5-2a** は Ru(II)-Pheox 触媒 **cat. 1** の存在下では，二量化が進行するよりも速やかに触媒的不斉反応が進行し，高い ee（94% ee）と定量的収率（99%）で **5-3a** を与えた。そこで，様々な Ru(II)-Pheox 錯体の触媒効率についてさらに評価した。電子吸引性または電子供与性置換基を有する触媒（**cat. 2**, **cat. 3**），及び立体環境を変えた触媒（**cat. 7**, **cat. 8**）は，収率および立体選択性に関してほぼ同じ結果を示した。本カルベン移動反応の場合 Ru(II)-Pheox 錯体の中で，**cat. 1** が反応に最適であることが示された。

Table 5-1. 触媒効果



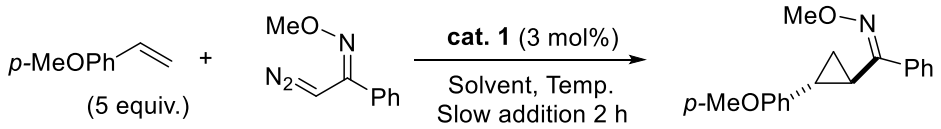
Entry	cat.	Yield [%][a]	d.r.[b]	ee [%][c]
1	**Cu-box**	65	43:57	41:7
2[d]	**Ru-Pybox**	24	76:24	4:-20
3	**cat. 1**	99	80:20	94:86
4	**cat. 2**	92	76:24	93:72
5	**cat. 3**	90	79:21	82:69
6	**cat. 7**	92	78:22	93:95
7	**cat. 8**	89	80:20	93:88

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.
[d] Reaction did not proceed to completion even in 48 h.

5-7 条件検討

次に **cat. 1** 触媒存在下，様々な溶媒と温度で反応条件を最適化した（Table 5-2）。ジクロロメタンはシクロプロパン化に最適な溶媒であり，室温で最高の収率（99%）の生成物が得られた（Table 5-2, entry 1）。一方，Et_2O, THF, CH_3CN を用いたとき，反応性の低下がみられため，生成物の収率がいちじるしく減少した。これらの溶媒が Ru へ配位しカルベンによる反応を妨げているためと考えられる。次に、反応溶媒をジクロロメタンで固定し、反応温度を下げると，エナンチオ選択性はわずかに増加して 95% ee になったが，ジアステレオ選択性と収率は変化しなかった（Table 5-2, entries 7~9）。

Table 5-2. 溶媒と温度効果



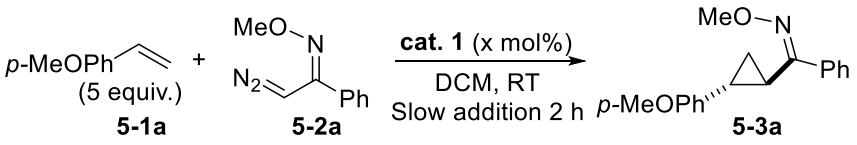
5-1a **5-2a** **5-3a**

Entry	Solvent	Temp. [°C]	Yield [%][a]	d.r.[b]	ee [%][c]
1	DCM	RT	99	80:20	94:86
2	Et_2O	RT	47	69:31	75:33
3	THF	RT	72	78:22	87:63
4	Toluene	RT	48	73:27	73:42
5	Acetone	RT	77	74:26	92:67
6[d]	CH_3CN	RT	37	63:37	83:55
7	DCM	0	99	80:20	94:87
8	DCM	–10	99	80:20	95:87
9	DCM	–20	80	80:20	95:87

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.
[d] Reaction did not proceed to completion even after 24 h of stirring.

続いて，反応を進めていく段階で非常に反応性のいいことが実感していたので、Table 5-3 に示すように，触媒量の影響も調査した。触媒を 0.1 mol%に減らすと，触媒不斉シクロプロパン化がスムーズに進行し，光学活性シクロプロピルオキシム **5-3a** が同じレベルで良好な収率（91%）で得られた（Table 5-3, entry 3）。エナンチオ選択性とジアステレオ選択性も 3 mol%の触媒と同じ高い結果を示した。しかし，触媒量が 0.1 mol%未満になると，エナンチオ選択性と立体選択性の低下が観察された（Table 5-3, entry 4）。高い触媒回転数（TON）は最大 5500 値と触媒回転頻度（TOF）は最大 455 値を示し，本反応系では，Ru(II)-Pheox 触媒は高い触媒活性を示すことが明らかになった。

Table 5-3. 触媒効果



Entry	x [mol%]	Yield [%][a]	d.r.[b]	ee [%][c]	TON[d]	TOF [h^{-1}][e]
1	3	99	80:20	94:86	33	17
2	1	96	80:20	94:86	96	48
3	0.1	91	80:20	94:86	910	455
4[f]	0.01	55	73:27	57:16	5500	115

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC. [d] TON = Product [mol]/cat. [mol]. [e] TOF = TON/time[h]. [f] Reaction did not proceed to completion even after 48 h of stirring.

5-8 基質依存性

検討した最適な反応条件の基に，次に，ジアゾオキシムエーテル **5-2a** と様々なオレフィン類 **5-1a**～**5-1l** との不斉シクロプロパン化反応の基質一般性の検討を行った。結果を Table 5-4 に示す。

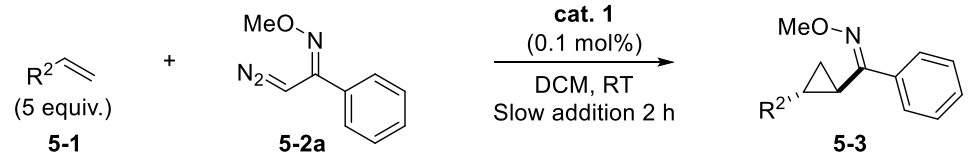
はじめに，シクロプロパン化反応における電子効果について，様々なパラ置換スチレン誘導体について検討した。電子供与基および電子吸引基を持つスチレン誘導体はジアゾオキシエーテルとの不斉シクロプロパン化反応に影響を及ぼした。より電子豊富な置換基をパラ位に置換する場合，生成物の収率が向上した（**5-3a**～**5-3f**）。この現象は，遷移金属によるシクロプロパン化反応の一般的なメカニズムによって説明することができる。電子密度の高いオレフィンは，電子吸引基としてのオキシムエーテル官能基を有する金属カルベン錯体とよりスムーズに反応する。

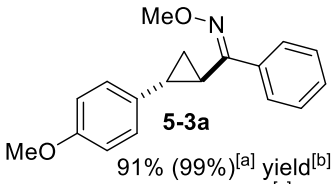
対照的に，パラ-Cl およびパラ-NO_2 置換基（それぞれ 96% ee および 95% ee）などの電子求引性基を含む両方のスチレンでより高いエナンチオ選択性が発現した。最高のエナンチオ選択性は化合物 **5-3e** で観察された（96% *trans* ee，99% *cis* ee）。

また，スチレンのオルト位の電子求引性および電子供与性置換基の両方は，わずかに低いジアステレオ選択性とエナンチオ選択性をもたらした（**5-3g**, **5-3h**）。これはオルト位の置換基はオキシムの置換基との立体反発によるものと考えられる。メタ位に置換基を有するスチレンの場合もジアステレオ選択性とエナンチオ選択は十分に維持されていた（**5-3i**，79:21 *trans*/*cis*，90% *trans* ee, 71% *cis* ee）。**cat. 1** を 3 mol%使用した場合，**5-3a** および **5-3b** は優れた収率で合成され，高い立体選択性とエナンチオ選択性を示した。さらに，α-メチルスチレンは，トランス異性体とシス異性体の両方で高いエナンチオ選択性（92% *trans* ee，93% *cis* ee）と高収率（92%）で **5-3j** を与えた。一方，四置換および内部オレフィンは，ジアゾオキシムエーテルの二量体しか与えなかった。これは立体障害

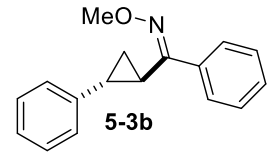
によりカルベン移動反応が遅くなるため二量体が優先して進行したためと思われる。また，α-ジアゾオキシムエーテルのカルベン転移反応は，スチレン以外のオレフィン類も検討した。 ジアゾオキシエーテルと n-ブチルビニルエーテルとの反応により，化合物 **5-3k** が 83%の収率で得られ，トランス異性体では中程度のエナンチオ選択性（74% ee）だが，シス異性体では低いエナンチオ選択性（57% ee）を示した。電子不足のオレフィン **5-1l** は反応性が遅く，多置換シクロプロパン骨格を形成するため立体選択性に低下が見られる（**5-3l**）。

Table 5-4. 様々なオレフィン類の不斉シクロプロパン化合物

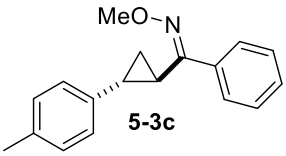




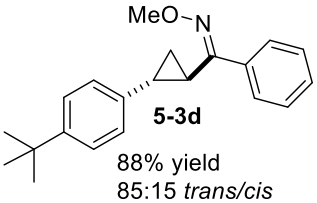
91% (99%)[a] yield[b]
80:20 *trans/cis*[c]
94% *trans* ee[d]
86% *cis* ee[d]



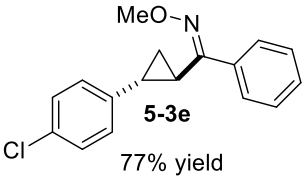
84% (87%) yield
81:19 *trans/cis*
92% *trans* ee
78% *cis* ee



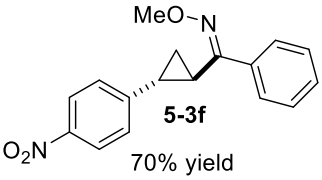
82% yield
80:20 *trans/cis*
94% *trans* ee
76% *cis* ee



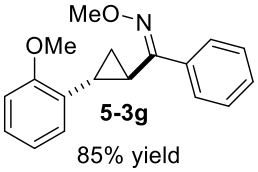
88% yield
85:15 *trans/cis*
92% *trans* ee
84% *cis* ee



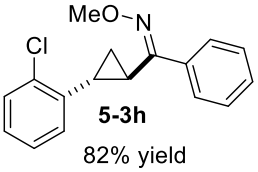
77% yield
80:20 *trans/cis*
96% *trans* ee
99% *cis* ee



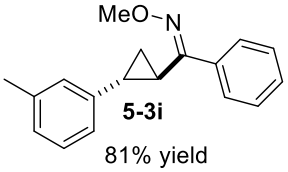
70% yield
75:25 *trans/cis*
95% *trans* ee
70% *cis* ee



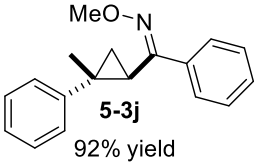
85% yield
68:32 *trans/cis*
90% *trans* ee
66% *cis* ee



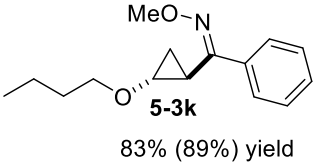
82% yield
65:35 *trans/cis*
93% *trans* ee
73% *cis* ee



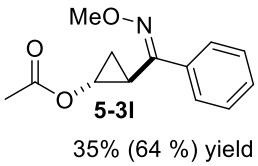
81% yield
79:21 *trans/cis*
90% *trans* ee
71% *cis* ee



92% yield
75:25 *trans/cis*
92% *trans* ee
93% *cis* ee



83% (89%) yield
84:16 *trans/cis*
74% *trans* ee
57% *cis* ee

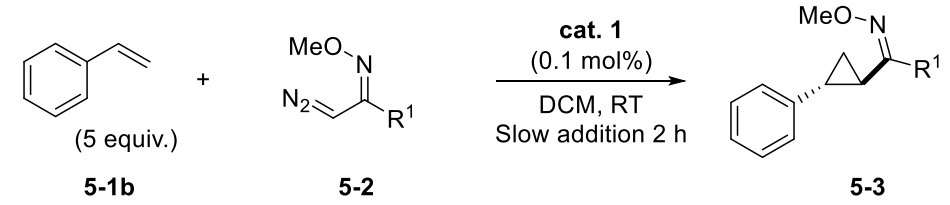


35% (64 %) yield
58:42 *trans/cis*
77% *trans* ee
60% *cis* ee

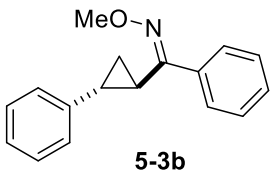
[a] 3 mol% Ru(II)-Pheox was used. [b] Isolated yield. [c] Determined by crude ^{1}H NMR.
[d] Determined by chiral HPLC.

次に，様々な α-ジアゾオキシムエーテルを用いたシクロプロパン化反応の基質一般性を精査するために，**cat. 1** の存在下で，スチレン **5-1b** とともに様々な α-ジアゾオキシムエーテルを用いて検討を進めた。 その結果を Table 5-5 に示す。まず，α-ジアゾオキシムエーテルのベンゼン環への電子効果について検討した。電子供与基であるメトキシ基やメチル基を持つジアゾオキシエーテルの不斉シクロプロパン化反応より高い収率，立体選択性で生成物 **5-3m** と **5-3n** を与えた。ただし，立体障害は立体選択性とエナンチオ選択性に強く影響した。スチレンとのシクロプロパン化反応においては，カルベン前駆体として 1-ナフタルジアゾオキシムエーテル **5-2o** を使用した場合，生成物 **5-3o** が高収率（84%），高いエナンチオ選択性（93% ee），特に高いジアステレオ選択性で得られた（95:5 *trans*/*cis*）。さらに，2-ナフチルジアゾオキシム **5-2p** は，シクロプロピルオキシム **5-3p** を高収率（92%）で，優れたエナンチオ選択性（98% *trans* ee）およびジアステレオ選択性で合成した（85:15 *trans*/*cis*）。

Table 5-5. 様々なジアゾオキシエーテル類の不斉シクロプロパン化合物

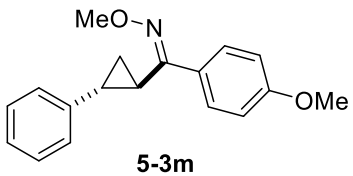


5-1b **5-2** **5-3**



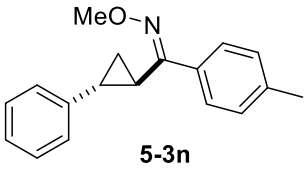
5-3b

84% yield[a]
81:19 *trans*/*cis*[b]
92% *trans* ee[c]
78% *cis* ee[c]



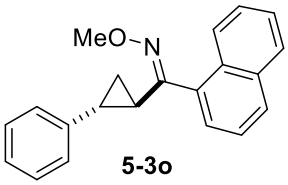
5-3m

85% yield
81:19 *trans*/*cis*
93% *trans* ee
79% *cis* ee



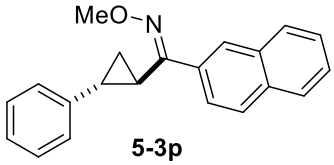
5-3n

86% yield
81:19 *trans*/*cis*
92% *trans* ee
78% *cis* ee



5-3o

84% yield
95:5 *trans*/*cis*
93% *trans* ee

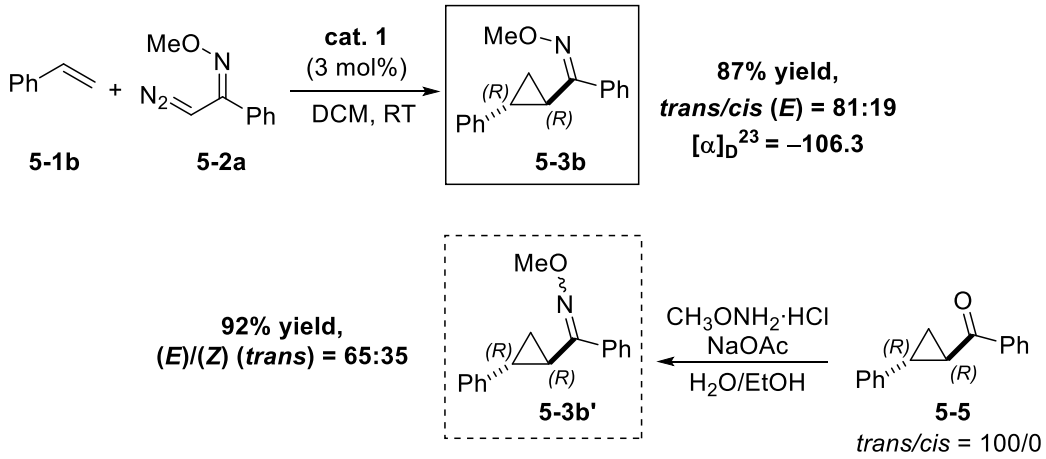


5-3p

92% yield
85:15 *trans*/*cis*
98% *trans* ee
71% *cis* ee

[a] Isolated yield. [b] Determined by crude ^{1}H NMR.[d] Determined by chiral HPLC.

生成物であるシクロプロピルオキシムの構造および絶対配置は，シクロプロピルオキシムをシクロプロピルケトンのシクロプロピルオキシム生成物への合成変換と比較することによって決定した。Scheme 5-3 に示すように，トランス異性体のみを含むジフェニルシクロプロパンケトン **5-5** は，オキシム官能基を有するアンチ異性体とシン異性体 **5-3b'**の混合物に変換され構造を確定することができる。さらに，トランスおよびシスシクロプロピルオキシム生成 **5-3b** は，前述のように，α-ジアゾオキシムエーテル **5-2a** とスチレン **5-1b** との反応によって生成された。**5-3b** 混合物のシン異性体に起因する NMR，および **5-3b'**混合物のシス生成物との比較により，**5-3b** のトランスおよびシスシクロプロピルオキシムの構造を特定した（第 8 章に NMR の比較）。さらに，測定された旋光度の値と先行研究で報告された値[10]との比較によって生成物の絶対配置は（***R***，***R***）であることが明らかとなった。さらに，**5-3f** を再結晶化させることでシクロプロピルオキシムの構造および絶対配置を決定した（Figure 5-4）。



Scheme 5-3. シクロプロピルオキシム生成物の立体構造と絶対配置の決定

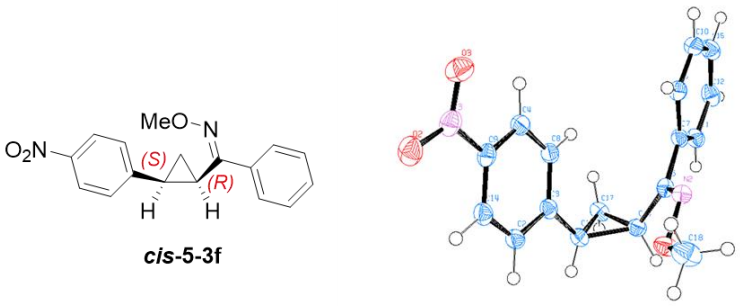
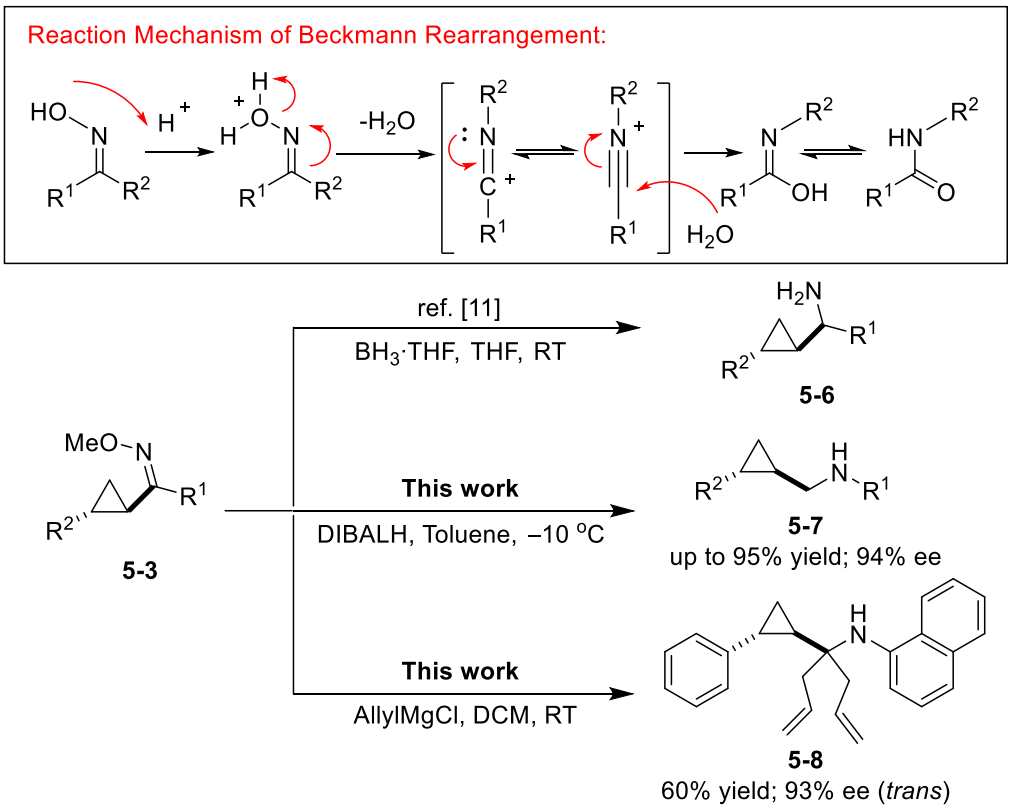


Figure 5-4. X 線再結晶の構造

5-9 応用反応

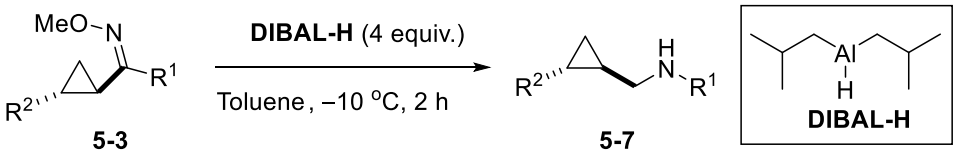
次に，ベックマン転位および金属水素化物還元によるシクロプロピルオキシムエーテルのさらなる合成用途が検討された（Scheme 5-4）。Demir 等は，シクロプロピルオキシムエーテルをホモフェニルアラニン類 **5-6** に変換することに成功している[11]。これ等の反応を元に第一級シクロプロピルアミン **5-6** は，シクロプロピルオキシムエーテル **5-3** の還元反応によって得られる。オキシム骨格を用いた応用反応には Beckmann 転移反応が知られている。本反応の反応機構を以下の Scheme 5-4 に示す。オキシムの酸触媒による転移、引き続く加水分解によりアミドが得られるが、特徴としてオキシの OH 基に対してトランスからの転移が優先的に進行する。そこで、このメカニズムを利用して、合成変換における直接エナンチオ選択的シクロプロピルオキシムエーテルの有用性を示すために，ここでは，最初の DIBAL−H およびグリニャール試薬による Beckmann 転位[12]と生成物 **5-3** より，セロトニン 2C 受容体アゴニストの候補[13]であるシクロプロピルメチルアミン誘導体 **5-7** および **5-8** を合成変換に成功した。生成物を用いて Grignard 試薬による転 Beckmann 移反応を行ったところ、ナフチル基が窒素上に転移し、さらに Grignard が付加することでジアリル化体 **5-8** が 60%収率と立体選択性を維持して得られることが明らかになった。



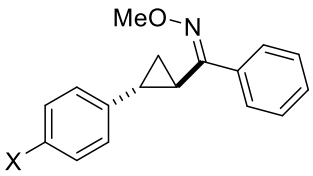
Scheme 5-4. シクロプロピルオキシム生成物の合成変換

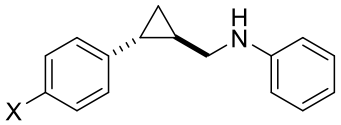
様々なシクロプロピルメチルアミン誘導体 **5-7** は，DIBAL−H を介した還元的 Beckmann 転位反応によって得られた（Table 5-6）。最初，反応条件として室温で DIBAL−H と **5-3o** の反応を行った。その結果，高い収率で目的物を得たが，エナンチオ選択性はわずかに低下した（**5-7o**）。キラル環境を生成物 **5-7** に維持するには，温度効果として低温が不可欠である。−10 ℃では立体選択性は失うことなく，シクロプロピルメチルアミン **5-7** に変換された。**5-3m** は還元的 Beckmann 転位によって高収率 95%で，シクロプロピルメチルアミン **5-7m** へ変換できた。

Table 5-6. DIBALH を介したシクロプロピルオキシムエーテルの還元的 Beckmann 転位



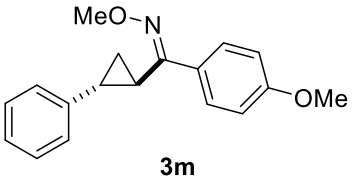
5-3 **5-7**



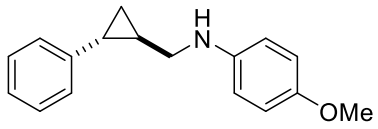


3a (X = OMe): 80:20 d.r; 93%/86% ee
3b (X = H): 81:19 d.r; 92%/78% ee
3c (X = Me): 79:21 d.r; 94%/76% ee
3e (X = Cl): 80:20 d.r; 96%/99% ee

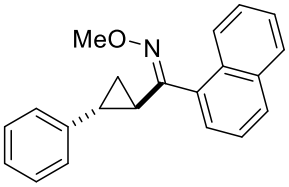
7a (X = OMe): 87% yield[a]; 80:20 d.r.[b]; 93%/78% ee[c]
7b (X = H): 86% yield; 85:15 d.r.; 93%/79% ee
7c (X = Me): 82% yield; 80:20 d.r.; 94%/77% ee
7e (X = Cl): 84% yield; 80:20 d.r.; 94%/98% ee



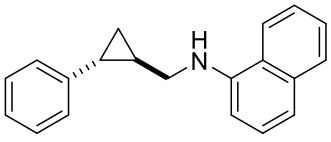
3m
81:19 d.r.; 93%/79% ee



7m
95% yield; 81:19 d.r.; 92%/79% ee



3o
93% ee (trans)



7o
85% yield; 92% ee (trans)
[90% yield; 89% ee (trans)][d]

[a] Isolated yield. [b] Determined by crude ^{1}H NMR. [c] Determined by chiral HPLC.
[d] Reaction was carried out at RT.

5-10 推定される反応機構

Ru(II)-Pheox 触媒によるスチレン類とジアゾオキシムエーテル類との触媒的不斉カルベン移動反応の推定される反応機構を Figure 5-5 に示す。まず，ジアゾオキシムエーテルへ触媒は酸化的付加し，窒素を放出し，金属カルベン錯体を形成する。金属カルベン錯体は Ru(II)-Pheox 触媒平面に対して真横方向のカルベンの配位になると考えられる。

安定した金属カルベン錯体を形成した後，スチレンは面選択的に接近し，3 員環構造の遷移状態を得て，還元的脱離反応により，高収率，高立体選択性で不斉シクロプロパン化合物を合成すると考えられる。

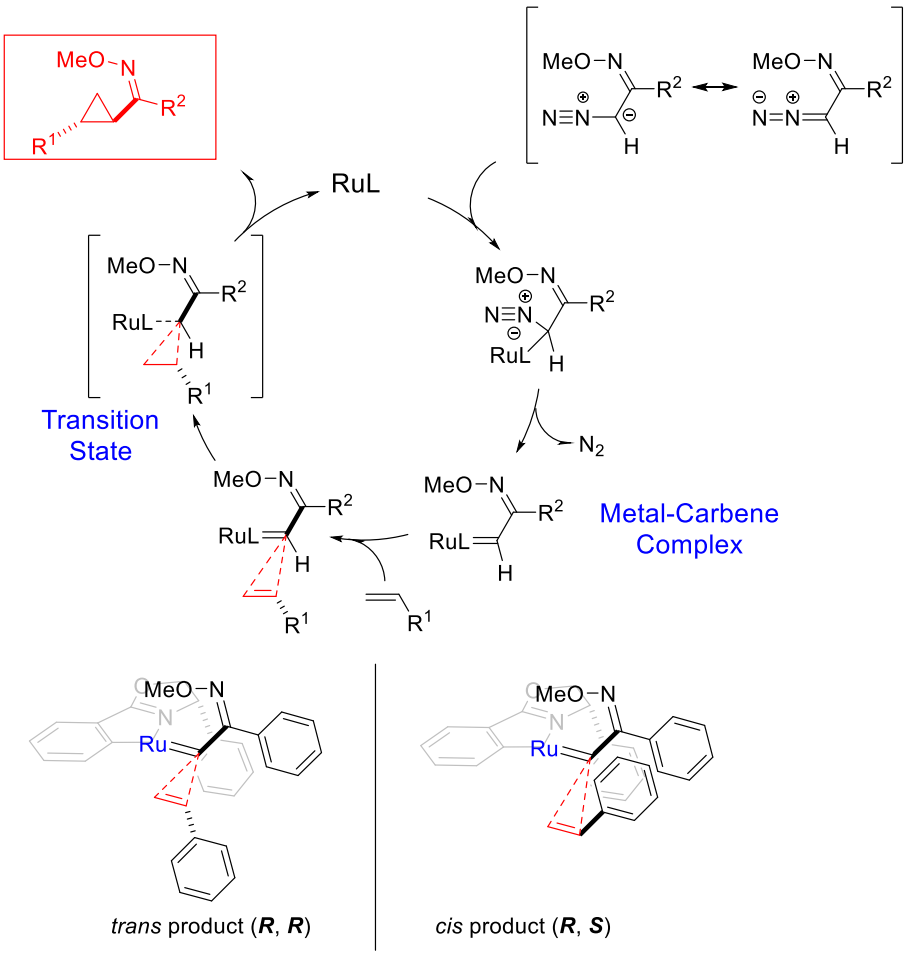


Figure 5-5. 推定される反応機構

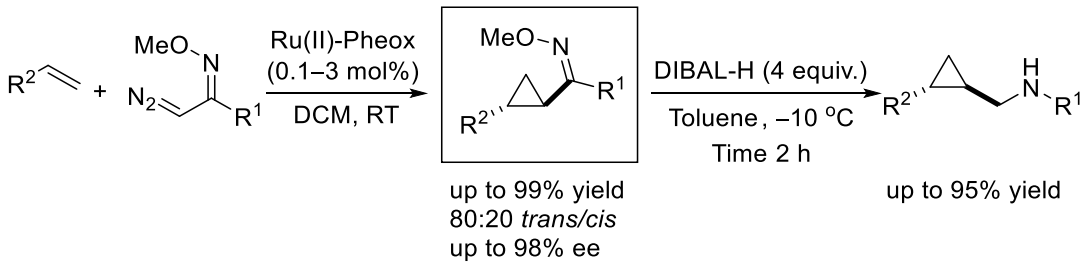
5-11 結論

これまでに金属触媒とジアゾカルボニル類より得られる金属カルベン錯体の様々なカルベン移動反応に限られていた反応をジアゾヒドラゾンやジアゾオキシエーテルのようなイミン型を形成する金属カルベン錯体を合成し，各結合へのカルベン移動反応に応用した。

ジアゾヒドラゾンの触媒的不斉カルベン移動反応は高収率で C−H 挿入反応が進行するものの，原料合成と立体選択性にまだ課題があることが示された。

α-ジアゾオキシムエーテルとオレフィンの初めの接触不斉シクロプロパン化反応を開発し，Ru(II)-Pheox が様々な光学活性シクロプロピルオキシム誘導体を生成するための最良の触媒として発見された。Ru(II)-Pheox 触媒（3 mol%）の存在下で，ジアゾオキシムエーテルはさまざまなオレフィンとスムーズに反応し，高いジアステレオ選択性（最大 95:5）で優れた収率（最大 99%）およびエナンチオ選択性（最大 98% ee）で目的の生成物を生成した。

触媒負荷の減少（0.1 mol%）により，対応する光学活性シクロプロピルオキシム誘導体が良好な収率と同じエナンチオ選択性（> 80% 収率，最大 98% ee）で得られた。さらに，Ru(II)-Pheox の触媒効率は，TON（5500）と TOF（455）であることが示された。最後に，シクロプロピルオキシムエーテルから出発する有用な生物活性中間体として，光学活性シクロプロピルメチルアミン誘導体の合成経路の開発にも成功した。



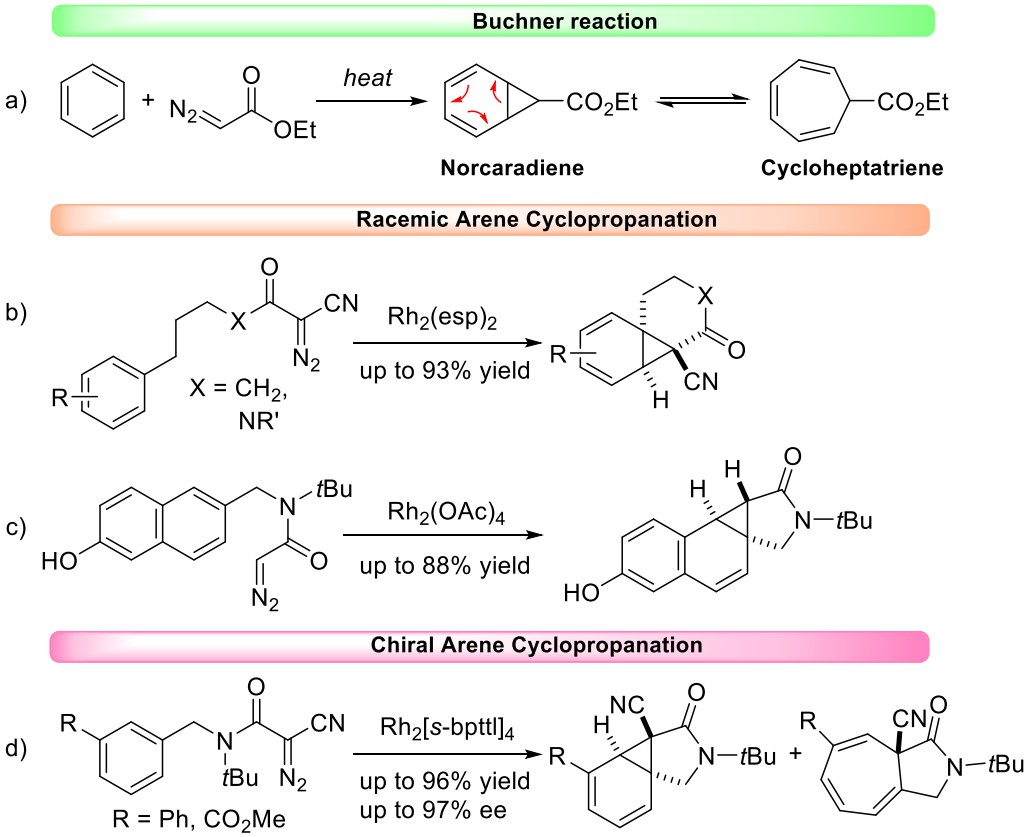
Scheme 5-5. Ru(II)-Pheox 触媒によるジアゾオキシムエーテルの不斉カルベン移動反応

第 6 章　ナフチルジアゾアセトアミド類の芳香環上への触媒的不斉分子内カルベン移動反応の開発

6−1 研究背景　芳香族環へのカルベン挿入反応

芳香族化合物と金属カルベン錯体との反応として，知られているのは 1. Friedel-Crafts 反応，2. 芳香族環 σ 結合への C−H 挿入反応，3. 芳香族環 π 結合へのカルベン前挿入反応によるシクロプロパン反応，さらに，電子移動により，環拡大反応 Buchner 反応などがある[1]。その中で，Buchner 環拡大反応は Buchner によって，19 世紀の終わりに開発された反応で，ジアゾエステルとベンゼン環とのカルベン挿入反応により，シクロプロパンであるノルカラジエンを生成し，電子移動反応により，7 員環化合物であるシクロヘプタトリエン骨格を与える（Scheme 6-1a）[2]。基本的に，ノルカラジエンとトリエンは平衡混合物である。本反応は安定な芳香族化合物をより反応性の高い状態へ変える非常に有用な反応である。近年，Buchner 反応は有機合成化学者に注目されており，遷移金属触媒による分子内 Buchner 反応がいくつか報告されている[3]。しかし，これらの先行研究例は芳香族環へのカルベン移動反応により，シクロプロパン化合物を経由して，7 員環化合物類を最終生成物として合成されている。中間体であるノルカラジエンを最終生成物として合成している報告例は少なく，さらに，不斉合成の反応例はほとんどない。

2013 年 Reisman 等によって，ロジウム触媒存在下，α-ジアゾ-β-ケトニトリルとの分子内芳香族環へのカルベン移動反応を開発し，様々なノルカラジエンの合成に成功した[4]。本反応系では，シアノ基を持つジアゾ化合物は他のカルボニル基を持つジアゾ化合物に比べて，位置選択的にシクロプロパン環形成を優先することが提案されている（Scheme 6-1b）。2020 年に Nemoto 等は銀触媒を用いて，β-ナフトールジアゾアセトアミド類の脱芳香族スピロ環化合物を開発した[5]。様々な遷移金属を用いて触媒検討を行っている最中，ロジウム触媒の場合に高収率で芳香族シクロプロパン化合物を得ることを見出した（Scheme 6-1c）。また，2021 年に Poisson 等は不斉ロジウム触媒を用いて，強力な電子吸引基を持つ α-ジアゾ-β-シアノアセトアミドの分子内不斉 Buchner 反応を高収率，高エナンチオ選択性で開発した[6]。ベンゼン環上の置換基効果を検討しているところ，ベンゼン環上のメタ位に立体障害の大きい置換基 Ph，CO_2Me を持つジアゾ化合物に対して，ノルカラジエンとシクロヘプタトリエンの平衡混合物として得られた（Scheme 6-1d）。いずれにしても二つの電子吸引基が必要であり，安定に合成したノルカラジエンの触媒的不斉反応の開発は少なく，課題として残されている。

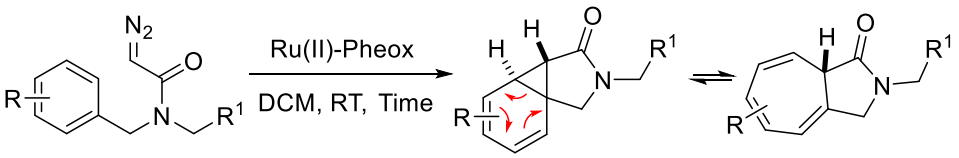


Scheme 6-1. 芳香族環へのカルベン移動反応

一方，2019 年に我々の研究室で，Ru(II)-Pheox 触媒を用いて，様々なジアゾアセトアミド類との不斉分子内 Buchner 反応を高収率，高エナンチオ選択性，高位置選択的に初めて得ることに成功した[7]。本反応系は，ノルカラジエンを経由して，環拡大反応に伴う 7 員環類が最終生成物として得られている。研究の結果を Table 6-1 にまとめる。Table 6-1 に示すように様々なベンジルジアゾアセトアミドを合成し，ベンゼン環上の π 結合への不斉カルベン挿入反応を検討した。まず，ジベンジル基を持つジアゾアセトアミドを用いた時，相当する 7 員環化合物が 69%収率と 78% ee で得られた（Table 6-1, entry 1）。次に，電子供与基であるメトキシ基をパラ位に持つジベンジルジアゾアセトアミドの不斉分子内カルベン移動反応を行った。その結果，目的生成物が優れた収率とエナンチオ選択性で得られた（99% yield, 99% ee）。次に，パラ位の電子密度の影響を調べるために，Me, Cl, Br, F 基を導入したジアゾアセトアミドを用いて検討した。しかし，生成物の収率とエナンチオ選択性が低下した（Table 6-1, entries 3～6）。次に，メタ位にメトキシ基を導入したジベンジルジアゾアセトアミドを用いた場合，収率とエナンチオ選択性は低下した（87% yield, 74% ee）。窒素上の置換基をメチル基に固定し，様々なモノベンジルジアゾアセトアミドを用いて，不斉カルベン移動反応を行った。その結果，パラメトキシベンジルジアゾアセトアミドより高い収率，優れたエナンチオ選択性で目的の 7 員環化

合物が得られた（87% yield, 74% ee）。一方，パラニトロベンジルジアゾアセトアミドより，目的生成物が得られなかった（Table 6-1, entry 15）。この結果より，本反応系では，電子供与基であるメトキシ基がベンジルジアゾアセトアミドのパラに導入されることで，芳香族環へのカルベン移動反応を促進することが明らかになった。また，Buchner 反応の中間体であるシクロプロパン化合物が合成されないことが分かった。さらに，Ru(II)-Pheox 触媒が本反応において優れた触媒活性を示すことが明らかになった。具体的に 0.003 mol%の Ru(II)-Pheox 触媒より高収率，高エナンチオ選択性で目的生成物が得られた（99% yield, 99% ee）（TON = 33000, TOF = 9900）。

Table 6-1. Ru(II)-Pheox 触媒による芳香族環へのカルベン移動反応



Entry	R	R^1	Time [min]	Yield [%][a]	ee [%][b]
1	H	C_6H_5	2	69	78
2	4-OCH_3	4-$CH_3OC_6H_4$	2	99	99
3	4-CH_3	4-$CH_3C_6H_4$	2	96	97
4	4-Cl	4-ClC_6H_4	2	80	96
5	4-Br	4-BrC_6H_4	2	70	95
6	4-F	4-FC_6H_4	2	91	90
7	3-OCH_3	3-$CH_3OC_6H_4$	2	87	74
8	H	H	4 h	40	71
9	4-OCH_3	H	2	76	99
10	4-CH_3	H	2	48	99
11	4-CH_3	H	4 h	67	99
12	4-Cl	H	4 h	61	92
13	4-Br	H	4 h	43	96
14	4-F	H	4 h	55	92
15	4-NO_2	H	4 h	n.o.	-

[a] Isolated yield. [b] Determined by chiral HPLC.

6-2 芳香族環へのカルベン挿入反応の有用性

芳香族環へのカルベン移動反応により得られる生成物であるノルカラジエンまたは，シクロヘプタトリエン骨格は医薬品科学，天然物などの生理活性物質に含有する有用な分子構造である[8]。そのため，近年，Buchner 反応の効率的で新規な合成ルートとして位置付けられる。以下，Figure 6-1 にノルカラジエンを部分構造として含む天然物や生理活性物質を示す。三環縮合系化合物は生理活性物質の基本骨格であり，それらの中で，ベンゾノルカラジエンまたはベンゾノルカレン族の化合物は，抗生物質活性および神経因性疼痛障害，変形性関節症，免疫障害および乳癌に対する薬剤を含む幅広い生物学的活性を示す[9]。

更に，芳香族環へのカルベン移動反応を用いて，実際に天然物の全合成に応用している例もある。2011 年に Reisman 等によって，銅触媒の存在下，α-ジアゾ-β-ケトニトリルとの分子内芳香族環へのカルベン移動反応を合成し，天然物である Salvileucalin B の全合成に成功している（Scheme 6-2）[10]。

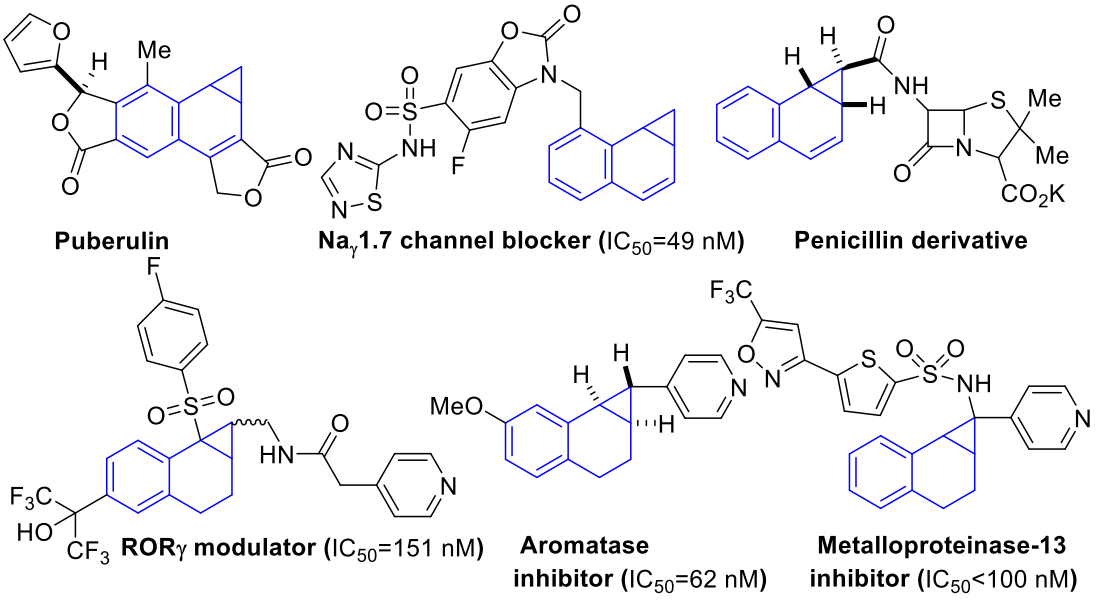
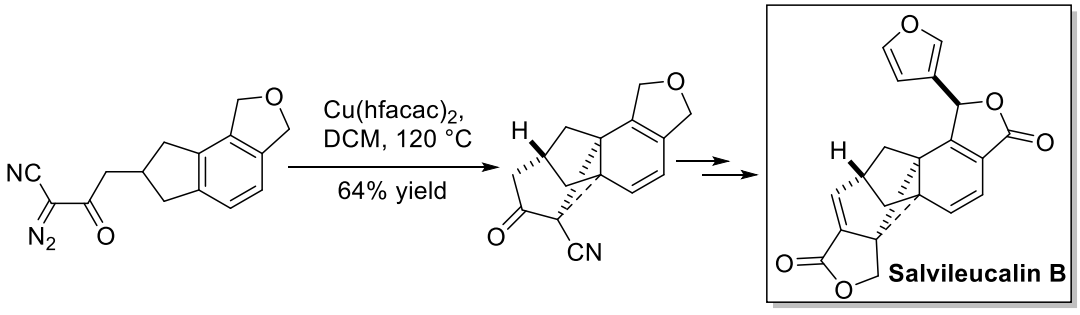


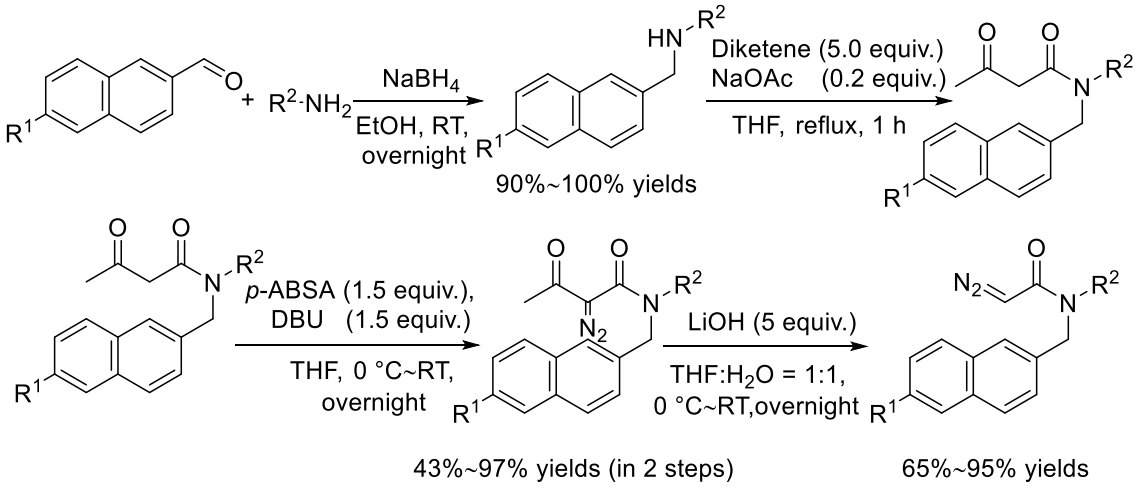
Figure 6-1. ノルカラジエン骨格を有する天然物や生理活性物質



Scheme 6-2. 天然物 Salvileucalin B の全合成

6-3 ナフチルジアゾアセトアミド類の基質合成

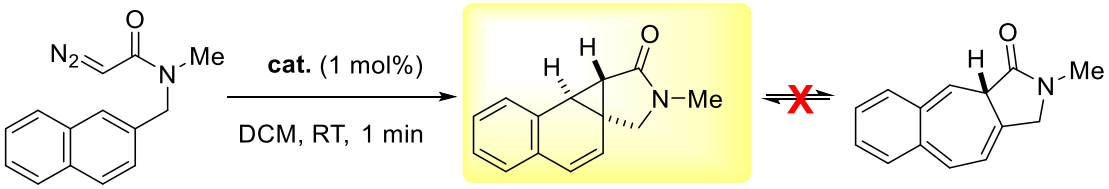
Ru(II)-Pheox 触媒による芳香族環への分子内カルベン移動反応にカルベン前駆体として用いられるジアゾアセトアミドを以下の Scheme 6-3 に示す 4 段階の方法を用いて合成した。まず，様々な 2-ナフトアルデヒド類とアミン類を還元剤である水素化ホウ素ナトリウムとの還元的アミノ化反応を行い，高収率で 2 級アミン類を得た。次に，得られた 2 級アミン類を用いて，酢酸ナトリウムの存在下，ジケテンとの反応を行い，アセト酢酸アミドを合成した。得られた化合物を単離せずに，*p*-ABSA, DBU を用いて，ジアゾ化反応を行い，様々な二置換ジアゾアセトアミドを中～高収率で得た。その後，水酸化リチウムとの脱アセチル化反応を行い，α-ジアゾアセトアミド類を高収率で合成した。



Scheme 6-3. ジアゾアセトアミド類の合成法

6-4　ナフチルジアゾアセトアミド類の芳香環上への触媒的不斉カルベン移動反応

芳香族環へのカルベン移動反応の先行研究例を元に，基質一般性をさらに検討する目的で，ナフチルジアゾアセトアミド類を合成し，不斉 Ru(II)-Pheox 触媒を存在下，芳香族環へのカルベン移動反応を検討した。その結果，興味深いことに，Buchner 環拡大反応の中間体であるノルカラジエン類は最終生成物として安定に単離できた。そこで，本反応系をさらに，触媒，反応条件，基質依存性の検討を行い，高収率，高エナンチオ選択性でノルカラジエンを部分構造として含む不斉合成反応の開発を行った。



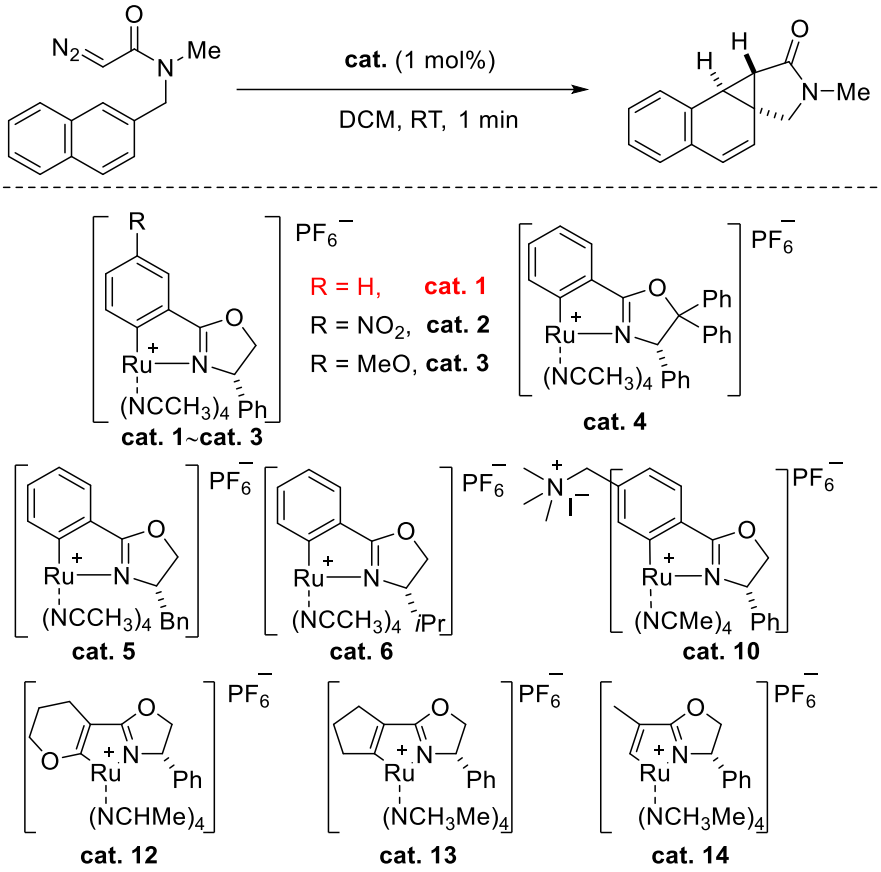
Scheme 6-4. ナフチルジアゾアセトアミドの芳香環上への不斉カルベン移動反応

6-5　触媒効果

ナフチルジアゾアセトアミドを合成し，様々な Ru(II)-Pheox シリーズと Ru(II)-Prox シリーズを用いて，芳香族環へのカルベン移動反応を行った（Table 6-2）。まず，反応中心金属の電子密度の影響を評価するために，ルテニウム金属に直接結合したベンゼン環上の置換基 R を H, NO_2, MeO 基に変えて，検討した（**cat. 1**~**cat. 3**）。電子吸引基である NO_2 基を持つ触媒 **cat. 2** の場合，若干エナンチオ選択性が低下したが，電子供与基である MeO 基を持つ触媒 **cat. 3** と **cat. 1** より高いエナンチオ選択性と収率で反応が進行し，目的の不斉アレンシクロプロパン化合物が得られた。**cat. 4** のような立体障害の大きい置換基を持つ触媒では，エナンチオ選択性が高い 98% ee を示したが，反応性の影響で収率が低下した（71%）。続いて，**cat. 5**，**cat. 6** の不斉環境を R^1=Bn，*i*Pr 基に変えて，検討したところ，収率と立体選択性が低下した。したがって，不斉環境のフェニル基は収率と立体選択性に影響を及ぼすことが分かった。次に水溶性の触媒 **cat. 10** を用いた場合は，高収率，高エナンチオ選択性が発現した。次に，反応中心金属にアルキル基が直接結合した触媒 **cat. 12** と **cat. 13** の存在下で分子内カルベン移動反応を検討した。その結果，高収率，高立体選択性で目的物がそれぞれ得られた。最後に，**cat. 14** の触媒を用いたところ，最も高い収率 99%で反応が進行したものの，エナンチオ選択性は 56% ee まで低下した。こちらは中心金属のメタ位に置換基が持たない場合，金属カルベン錯体は比較的自由に回転できるため，高い立体選択性を示さないと考えられる。以上の結果から，**cat. 1** 触媒が最も有効であることが示された。続いて、触媒活性を評価するために、

0.5 mol%と 0.2 mol%の触媒を用いたところ、比較的高い収率とエナンチオ選択性を示したが、1 mol%の触媒量を最適化な触媒量とした。

Table 6-2. 触媒スクリーニング



Entry	cat.	Yield [%][a]	ee [%][b]
1	**cat. 1**	93	98
2	**cat. 2**	87	95
3	**cat. 3**	82	97
4	**cat. 4**	71	98
5	**cat. 5**	78	75
6	**cat. 6**	71	81
7	**cat. 10**	92	97
8	**cat. 12**	85	96
9	**cat. 13**	96	96
10	**cat. 14**	99	56
11[c]	**cat. 1**	95	97
12[d]	**cat. 1**	80	96

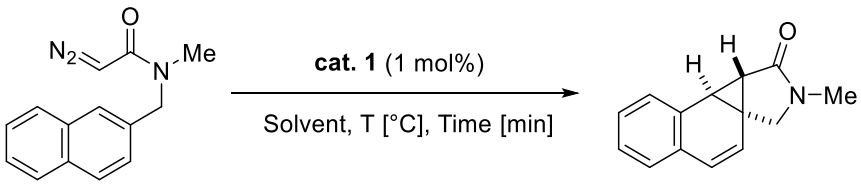
[a] Isolated yield. [b] Determined by chiral HPLC. [c] 0.5 mol% **cat. 1** was used. [d] 0.2 mol% **cat. 1** was used.

6-6 条件検討

次に，高収率と高立体選択性を示した **cat. 1** の触媒を用いて，さらに詳細な反応条件の最適化について検討を行った（Table 6-3）。反応の溶媒にジクロロメタンの他，アセトン，テトラヒドロフラン，トルエン，アセトニトリル，エーテルの有機溶媒を用いた。全ての溶媒に対して，高いエナンチオ選択性で反応が進行した。例えば、アセトンを溶媒に用いた時、高収率 88%、高エナンチオ選択性 97% ee で目的生成物ノルカラジエンが得られた（Table 6-3, entry 2）。テトラヒドロフラン，アセトニトリルなどの配位性の高い溶媒の場合，触媒が安定化されるため，反応時間が遅くなり，収率の低下の原因になったと考えられる（Table 6-3, entries 3, 5）。

そこで良好な結果を示したジクロロメタン溶媒を用いて，次に，反応温度による効果を調査した（Table 6-3, entries 7~9）。反応温度を室温から−10 ℃まで低下させると，反応速度が遅くなり，収率が減少するものの立体選択性が若干増加し，99% ee でほぼ完全なエナンチオ選択制を示す生成物が得られた（Table 6-3, entry 9）。溶媒と温度効果の条件検討より，最適な反応温度を室温，溶媒をジクロロメタンとした。

Table 6-3. 溶媒と温度効果



Entry	Solvent	T [°C]	Time [min]	Yield [%][a]	ee [%][b]
1	DCM	RT	1	93	98
2	Acetone	RT	1	88	97
3	THF	RT	1	62	98
4	Toluene	RT	10	36	96
5	Acetonitrile	RT	60	43	97
6	Diethylether	RT	5	43	97
7	DCM	10	5	86	98
8	DCM	0	10	77	99
9	DCM	−10	30	69	99

[a] Isolated yield. [b] Determined by chiral HPLC.

6-7　基質依存性

次に，ナフチルジアゾアセトアミド類の窒素上の置換基による立体障害や立体選択性に及ぼす影響，さらには他の副反応などについて効果を精査した（Table 6-4）。まず，窒素上の置換基を様々なアルキル基であるイソプロピル基，*tert*-ブチル基、プロピル基に変えて検討をした。その結果，メチル基以外，立体障害の大きい置換基イソプロピル基と *tert*-ブチル基より高収率，高エナンチオ選択性で芳香族環へのカルベン移動反応が速やかに進行することが明らかとなった。一方，プロピル基を持つナフチルジアゾアセトアミドより目的物 **6-2d** が 64% 収率と 96% ee で得られた。収率の低下の原因はプロピル基への C–H 挿入反応が 30% 収率で進行したためである（Figure 6-2, **6-3d**）。次に，ベンジル基やパラ-メトキシ-ベンジル基を持つジアゾアセトアミドの検討を行った（**6-2e**, **6-2f**）。その結果，ベンジル基を持つことで，カルベンはベンゼン環上の π 結合への挿入反応とナフチル環上の π 結合への挿入反応に競争的に進行し，目的生成物の収率が低下した（Figure 6-2, **6-3e**, **6-3f**）。そこで，反応性の高いメトキシ基をナフタレン環の 6 位に導入したジアゾアセトアミドを合成し，触媒的不斉カルベン移動反応に用いた。6-メトキシ-ナフチルジアゾアセトアミドの場合，窒素上の置換基を上記と同じくアルキル基であるイソプロピル基，*tert*-ブチル基，プロピル基に変えて検討も行った（**6-1g~m**）。

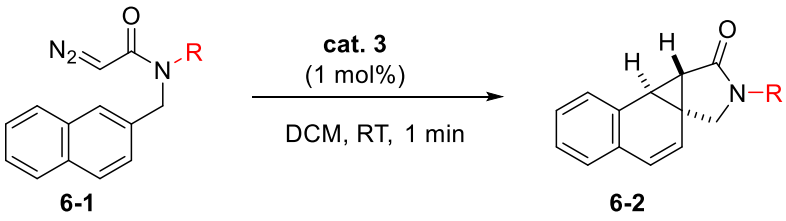
その結果，ジアゾ化合物 **6-1g** と **6-1h** と **6-1i** より高い収率とエナンチオ選択性で目的物が得られた。一方，プロピル基を持つ 6-メトキシ-ナフチルジアゾアセトアミドの場合，目的物 **6-2j** が 66% 収率と 98% ee で得られた。副生成物として同じくプロピル基への C–H 挿入反応の β-ラクタム **6-3j** が 28%収率，31% ee が得られた（Figure 6-2）。

次に，6-メトキシ-ナフチルジアゾアセトアミドを用いて，窒素上の置換基をベンジル基，4-メトキシベンジル基，そして 4-クロロベンジル基に変えて基質依存性の検討を行った。まず，ベンジル基を持つ 6-メトキシ-ナフチルジアゾアセトアミドより，ナフタレン環の π 結合へのカルベン移動反応が優先的に進行し，71% 収率，99% ee で目的物 **6-2k** が得られた。また，ベンジル基のベンゼン環上へのカルベン移動反応が進行し，環拡大反応に伴う 7 員環 **6-3k** が 11% 収率で進行した（Figure 6-2 ）。4-メトキシベンジル基をもつ 6-メトキシ-ナフチルジアゾアセトアミドの場合，主生成物としてベンゼン環上へのカルベン移動反応による 7 員環 **6-3l** が 50% 収率と 97% エナンチオ選択性で得られた（Figure 6-2）。副生成物としてナフタレン環上へのカルベン移動反応によるシクロプロパン化合物 **6-2l** が 46% 収率と 99% ee エナンチオ選択性で得られた。

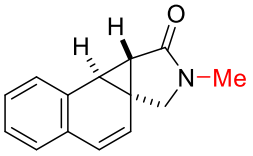
最後に，電子吸引基である 4-クロロベンジル基をもつ 6-メトキシ-ナフチルジアゾアセトアミドの触媒的不斉カルベン移動反応を検討した。その結果，主生成物としてナフタレン環上へのカルベン移動反応によるシクロプロパン化合物 **6-2m** が 81% 収率と 99% ee エナンチオ選択性で得られた。また，副生成物として 18% 収率で 7 員環 **6-3m** が得られた。以上の結果から，窒素上の置換基として Buchner 反応を目的とする場合，

メチル基や *tert*-ブチル基がベストである。その他の置換基では C–H 挿入反応や Buchner 環拡大反応が競争することが明らかとなった。

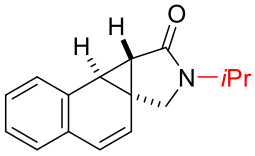
Table 6-4. ジアゾアセトアミドの窒素上の置換基効果



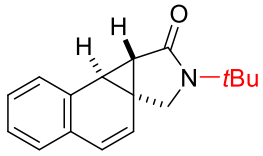
6-1 **6-2**



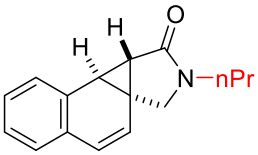
6-2a 93% yield [a]
98% ee [b]



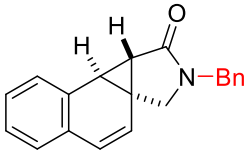
6-2b 93% yield
98% ee



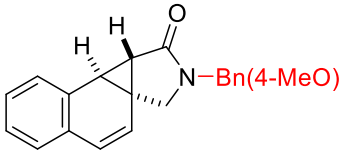
6-2c 94% yield
99% ee



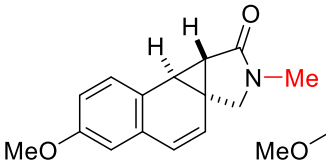
6-2d 64% yield
96% ee



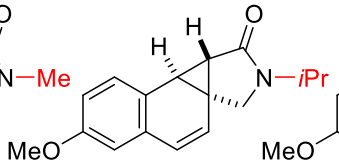
6-2e 83% yield
99% ee



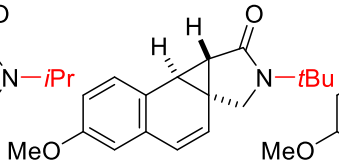
6-2f 46% yield
98% ee



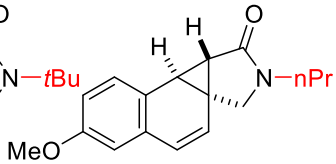
6-2g 98% yield
99% ee



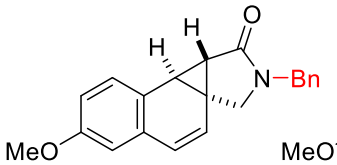
6-2h 95% yield
99% ee



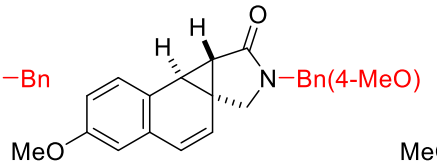
6-2i 98% yield
99% ee



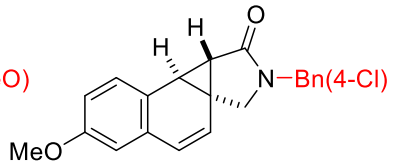
6-2j 66% yield
98% ee



6-2k 71% yield
99% ee



6-2l 46% yield
99% ee



6-2m 81% yield
99% ee

[a] Isolated yield. [b] Determined by chiral HPLC

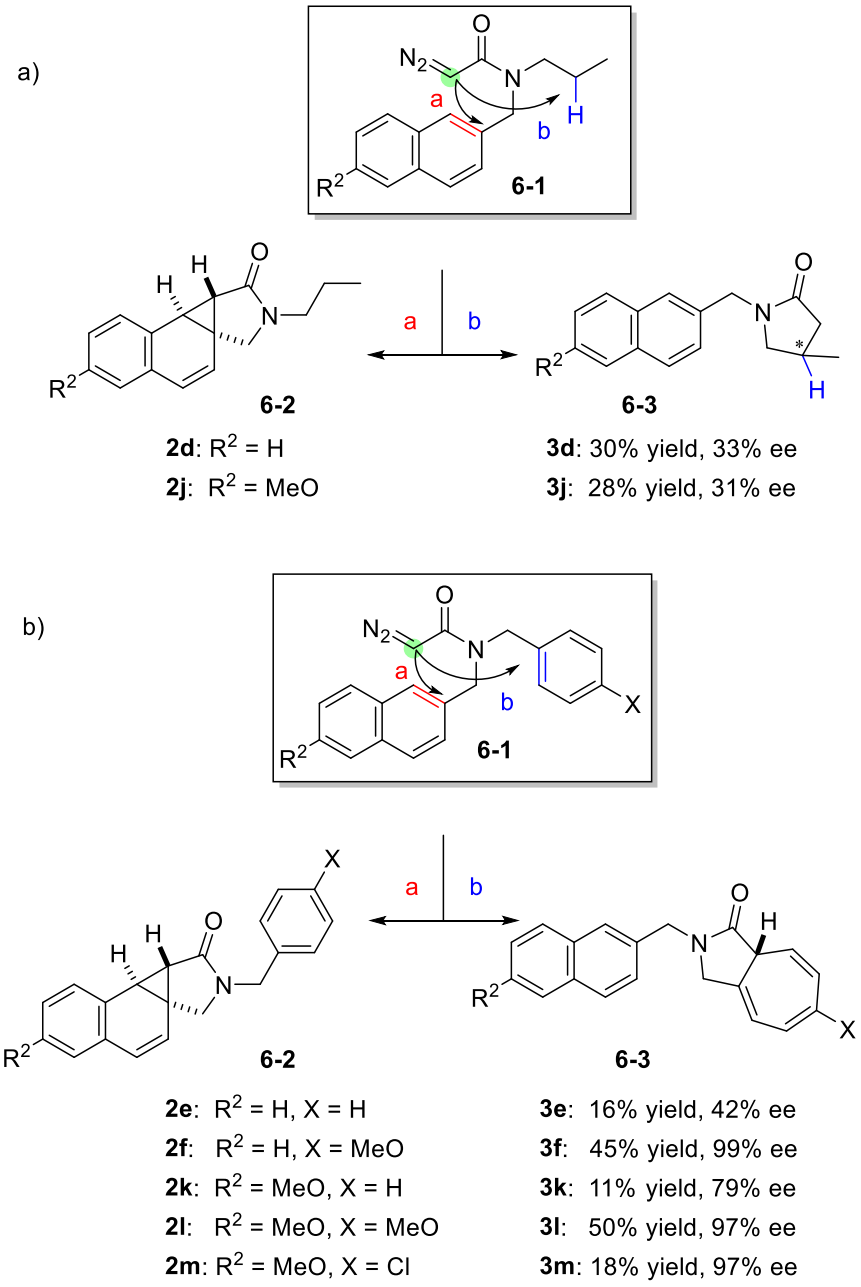
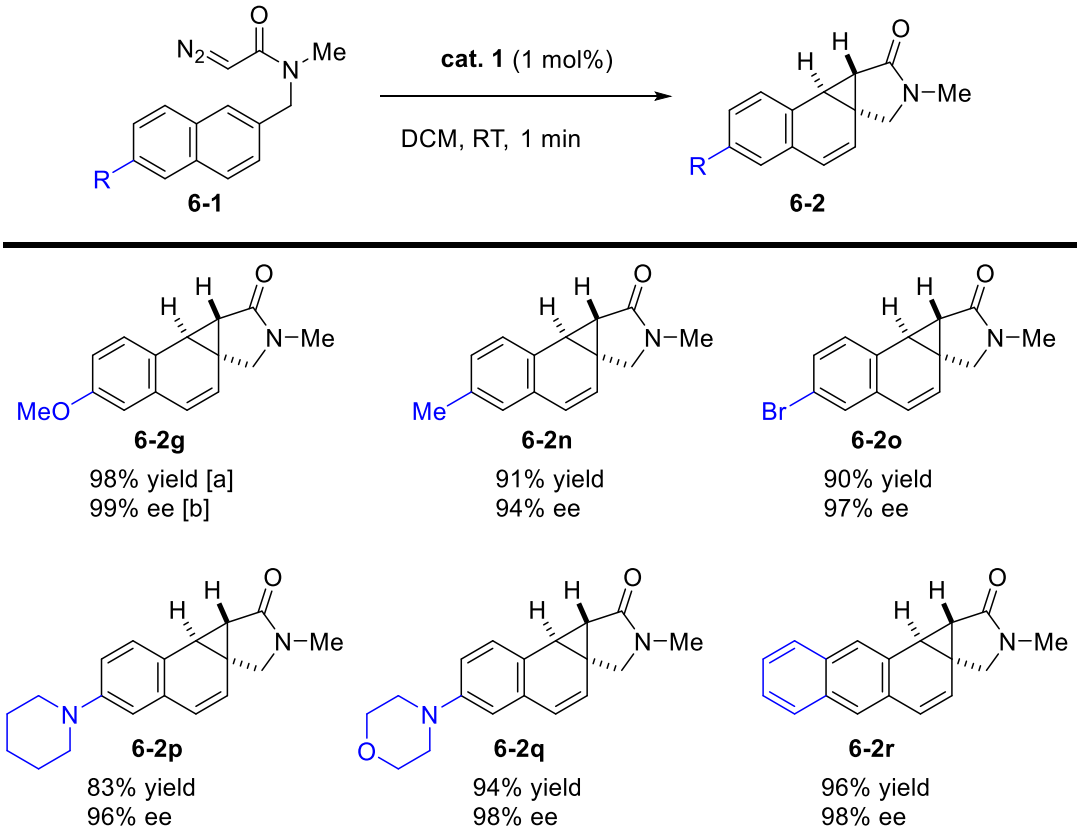


Figure 6-2. 窒素上の置換基の影響による生成物

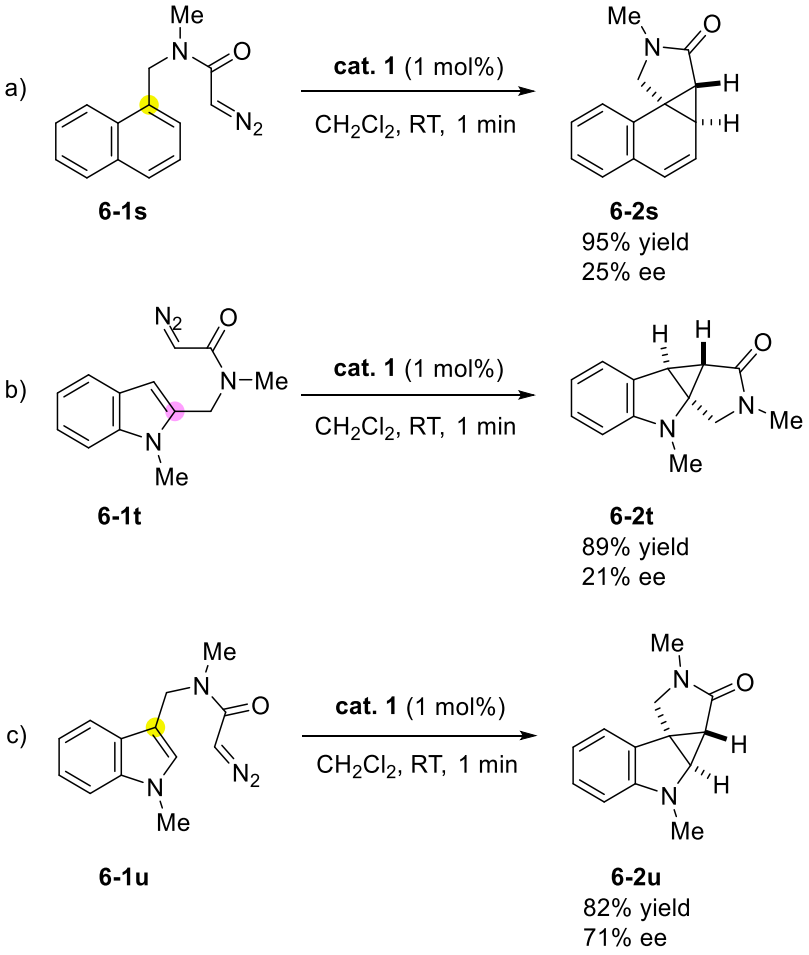
次に，ジアゾアセトアミド類のナフタレン環上の置換基依存性の検討を行った（Table 6-5）。電子供与基であるメチル基を 6 位に持つナフチルジアゾアセトアミドを用いて，芳香族環へのカルベン移動反応を検討した。その結果，高収率 91%，高エナンチオ選択的 94% ee で芳香族環へのカルベン移動反応が速やかに進行し、相当するノルカラジエン **6-2n** が得られた。続いて，電子吸引基であるブロモ基を 6 位に持つナフチルジアゾアセトアミドを用いた時も芳香族環へのカルベン移動反応が速やかに進行し、目的生成物であるノルカラジエン **6-2o** が高収率、高エナンチオ選択性で得られた（90% yield, 97% ee）。また，ピペリジンとモルホリン基をもつジアゾアセトアミドを用いた時も，高収率，高エナンチオ選択性で相当するノルカラジエン類 **6-2p** と **6-2q** が得られた。次に，アントラセンジアゾアセトアミドを合成し，芳香族環へのカルベン移動反応に用いた。その結果、分子内カルベン移動反応が速やかに進行し、目的物 **6-2r** を 96% 高収率，98% ee 高エナンチオ選択性で与えた。この結果より、ジアゾアセトアミドのナフタレン環上の置換基において、電子供与基でも、電子吸引基でも、または嵩高い置換基でも高収率と高立体選択性でシクロプロパン化反応が進行することが明らかになった。

Table 6-5. ジアゾアセトアミドの芳香族環上の置換基効果



[a] Isolated yield. [b] Determined by chiral HPLC

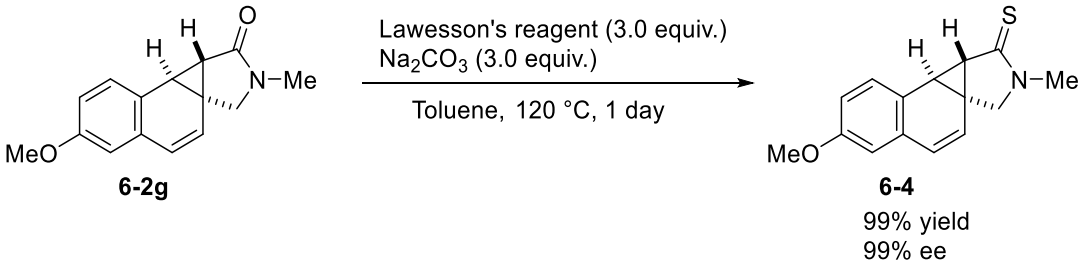
次に，芳香族環のジアゾ化合物の位置を変えたナフチル 1-ジアゾアセトアミドを用いて，不斉カルベン移動反応を行った(Scheme 6-5)。その結果，目的物 **6-2s** が高収率 95%を示したものの，エナンチオ選択性は 25% ee まで低下した。この結果は，本反応の遷移状態を考察する上で重要である。次に，インドール骨格を持つジアゾアセトアミドを合成し，触媒的不斉カルベン移動反応に応用した。インドールジアゾアセトアミド **6-1t** より目的生成物 **6-2t** が 89% yield, 21% ee で得られた。次に，ジアゾアセトアミドの位置が変わったインドールジアゾアセトアミド **6-1u** では立体選択性が増加し，71% ee と 82%収率で不斉カルベン移動反応が進行した。



Scheme 6-5. ジアゾアセトアミドの置換基効果

6-8 絶対配置の決定と合成変換

次に高収率，高エナンチオ選択性で得られた生成物を用いて，変換反応を行った。その結果を Scheme 6-6 に示す。生成物 **6-2g** を用いて，Lawesson 試薬と加熱し，アミド基をチオアミド基へ変換した **6-4** を高収率，完全な立体保持で得た。得られた化合物を再結晶化させ，X 線結晶構造解析よって，絶対配置を決定した（Figure 6-3）。これらの 6-8 で得た生成物と本節での合成変換を併せて，Figure 6-1 ノルカラジエン骨格を有する天然物や生理活性物質を参考に医薬品候補群となることが期待される。



Scheme 6-6. 生成物の応用反応

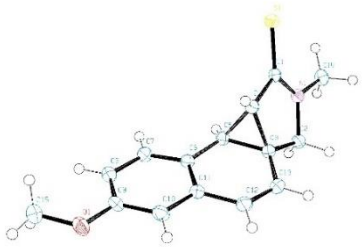


Figure 6-3. 生成物 **6-4** の X 線結晶解析

6-9　推定反応機構

Ru(II)-Pheox 触媒による芳香族環へのカルベン移動反応の考えられる推定反応機構を Figure 6-4 に示す。はじめにルテニウムはジアゾ化合物と反応し，窒素を放出してルテニウムカルベン錯体を形成する。不斉触媒上のフェニル基の不斉環境を不斉源として反応の制御が行われ，最も速やかに進行する立体環境に適合されナフタレン骨格の最も近い芳香族パイ電子と相互作用し，カルベンの挿入反応が起こる。この時ルテニウムカルベン錯体の二重結合と π 電子との相互作用の中で 4 員環遷移状態をとることが示唆される。その後，異性化を経由してシクロプロパン化が進行し相当するノルカラジエン体が精製すると同時にルテニムの還元的脱離が進行し，触媒サイクリが完了するものと考えている。

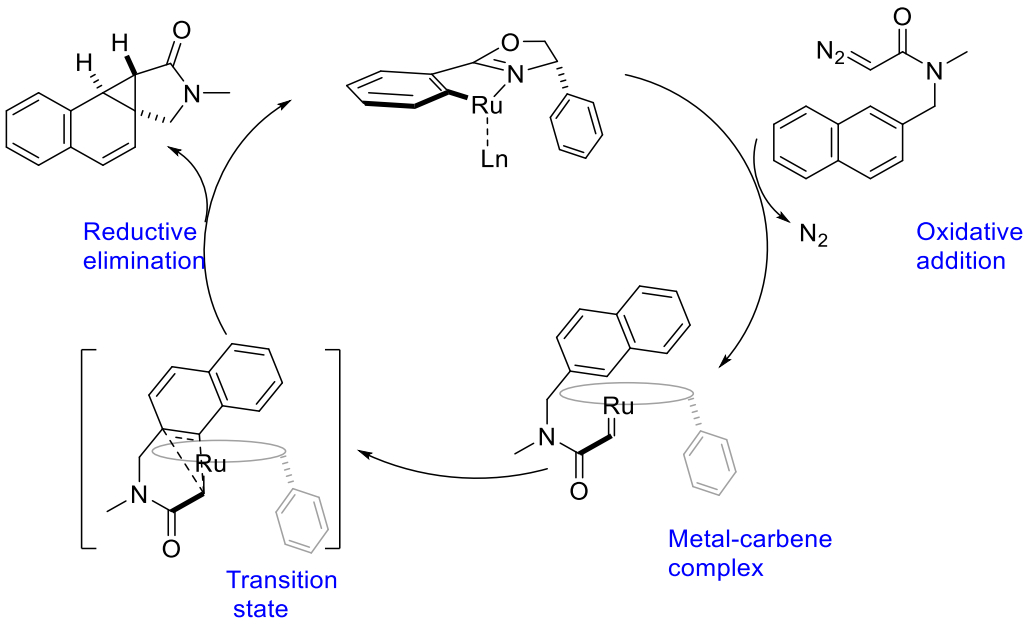
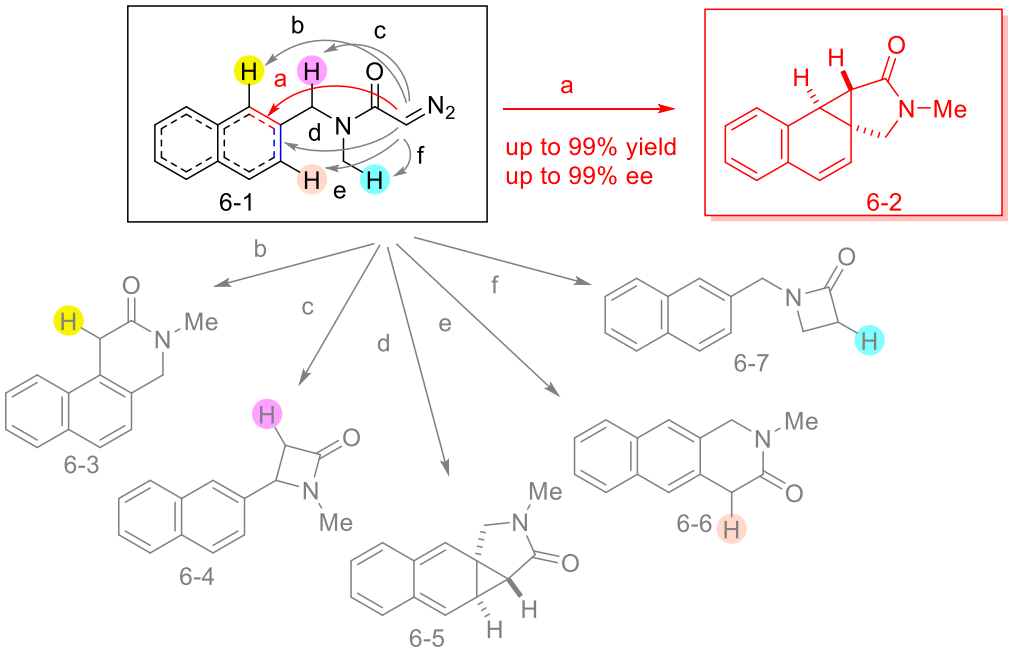


Figure 6-4. 推定される反応機構

6-10　結論

様々なナフチルジアゾアセトアミド類を合成し，不斉 Ru(II)-Pheox 触媒を存在下，芳香族環へのカルベン移動反応を検討した。Buchner 環拡大反応の中間体であるノルカラジエン類を最終生成物として安定に高収率，高エナンチオ選択性で得ることに成功した。ノルカラジエン類は様々な天然物や生理活性物質に用いられる重要な分子構造であるため，本反応は有機合成反応に応用が期待できる。また得られたノルカラジエン体はシクロプロパン骨格の開環反応を伴う骨格転位やアミド基の官能基変換が可能であり，多様な医薬品候補群の提供につながると考えられる。



Scheme 6-7. Ru(II)-Pheox 触媒によるナフチルジアゾアセトアミドへの不斉カルベン移動反応

第 7 章　総括

本研究では，様々な官能化されたジアゾ化合物類を新規に合成し，カルベン前駆体として用い，各結合への不斉カルベン移動反応に応用することを目的に研究を行った。具体的には，独自に開発した Ru(II)-Pheox 触媒による不斉 B−H 挿入反応，アリル及びビニルシラン類の触媒的不斉シクロプロパン化反応，ジアゾオキシムエーテル類の不斉カルベン移動反応，ナフチルジアゾアセトアミド類の芳香族環へのカルベン移動反応の開発を行った。

第 3 章では，カルベン中間体の単結合 σ-結合への挿入反応に焦点を当てボラン錯体類とジアゾエステル類から，触媒的 B−H 結合挿入反応を経由する新規光学活性有機ホウ素化合物を合成することに成功した。ジアゾ化合物類の末端置換基を立体障害の大きな化合物にすることで，高立体選択性を制御できることが示唆された（98% ee）。また，α-アリールジアゾエステル類を新たに合成し，不斉有機ホウ素化合物に適用することで，副生成物を防ぎ，高収率で有機ホウ素化合物を得た（94% yield）。加えて，得られた有機ホウ素化合物は，相当するアルコール類に変換できることを示すことができた。

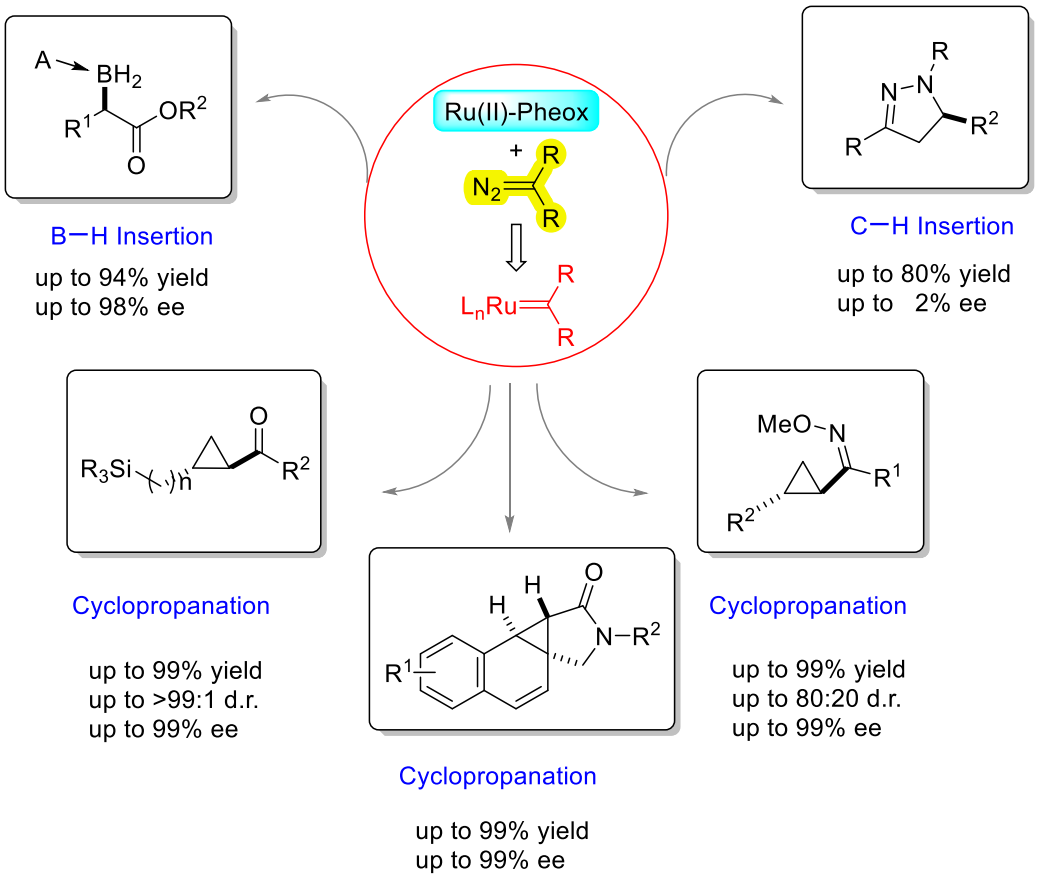
第 4 章では，カルベン中間体の π 結合への挿入反応に焦点を当て，アリル及びビニルシラン類とジアゾエステル類から，触媒的カルベン移動反応を経由する光学活性シクロプロパン化合物を高収率，高立体選択性で合成することに成功した。アリルシラン類の場合，様々なアリルシラン類への不斉カルベン移動反応は円滑に進行し，高収率，高立体選択性で目的の不斉シリルシクロプロパン化合物を合成した（99% yield, 95:5 d.r., 99% *trans* ee）。ビニルシラン類の場合，立体障害大きいシラン類は二重結合に直接結合しているため，不斉カルベン移動反応の反応性を遅くさせ，収率を大きく低下させるが，ジアステレオ選択性とエナンチオ選択性は優れた結果を示した（61% yield, >99:1 d.r., 99% *trans* ee）。さらに，得られたシリルシクロプロパン化合物を用いて，生理活性物質への応用変換反応に成功し，抗がん剤や抗 HIV 治療薬の重要な中間体を簡単に合成できることを示すことができた。

第 5 章では，ジアゾヒドラゾンやジアゾオキシエーテルのようなイミン型を形成する金属カルベン錯体の合成に焦点を当て，各結合へのカルベン移動反応に応用した。Ru(II)-Pheox 触媒によるジアゾヒドラゾンの分子内 C−H 挿入反応を経由して，ピラゾール類が得られた（80% yield, 2% ee）。Ru(II)-Pheox 触媒による α-ジアゾオキシムエーテルとオレフィンの初めの接触不斉シクロプロパン化反応を開発した（99% yield, 80:20 d.r., 98% *trans* ee, 99% *cis* ee）。さらに，Ru(II)-Pheox の触媒効率は，TON（5500）と TOF（455）であることを明らかにした。また，シクロプロピルオキシムエーテルから出発する有用な生物活性中間体として，光学活性シクロプロピルメチルアミン誘導体の合成経路の開

発にも成功した。

第 6 章では, 様々なナフチルジアゾアセトアミド類を新規に合成し, 不斉 Ru(II)-Pheox 触媒による芳香族環へのカルベン移動反応に焦点を当て Buchner 環拡大反応の中間体であるノルカラジエン類を高収率，高エナンチオ選択性で合成することに成功した (99% yield, 99% ee)。ノルカラジエン類は様々な天然物や生理活性物質に用いられる重要な分子構造であるため，本反応は有機合成反応に応用が期待できる。

以上のように，本研究から得られた成果よって，これまでに挑戦的な課題が残されている様々な官能化されたジアゾ化合物類の各結合への不斉カルベン移動反応が可能になり，医・農薬品合成の開発に繋がると期待される。



Scheme 7-1. 官能化されたジアゾ化合物類の各結合への不斉カルベン移動反応

第 8 章　実験項

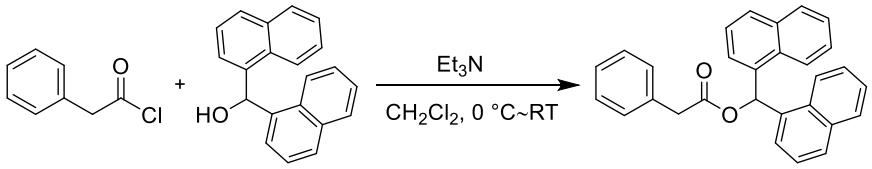
8−1 Experimental Section for Chapter 3

General Information

All reactions were performed under an atmosphere of argon unless otherwise noted. Dichloromethane (CH_2Cl_2) was purchased from Kanto Chemical Co., Inc. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGa A 60 F_{254}, layer thickness 0.2 mm. The products were visualized by irradiation with UV light or by treatment with a solution of *p*-anisaldehyde. Column chromatography was performed using silica gel (Merck, Art. No.7734). ^{1}H NMR (500 MHz, 400 MHz) and ^{13}C NMR (125 MHz, 100 MHz) spectra were recorded on JEOL JNM-ECX500, JEOL JNM-ECS400 spectrometer. Chemical shifts are reported as δ values (ppm) relative to $CDCl_3$ (7.26 ppm), TMS (0.00 ppm) for ^{1}H and $CDCl_3$ (77.0 ppm) for ^{13}C. Optical rotations were performed with a JASCO P-1030 polarimeter at the sodium D line (1.0 mL sample cell). Infrared (IR) spectra were recorded on an FT/IR-4600 instrument (JASCO Co., Ltd., Tokyo, Japan). Enantiomeric excesses were determined by high-performance liquid chromatography (HPLC) analyses with a JASCO GULLIVER using Daicel CHIRALPAK columns. HRMS DART mass (positive mode) analyses were performed on a LC-TOF JMS-T100LP or HRMS (ESI) was recorded on a Bruker micrOTOF II.

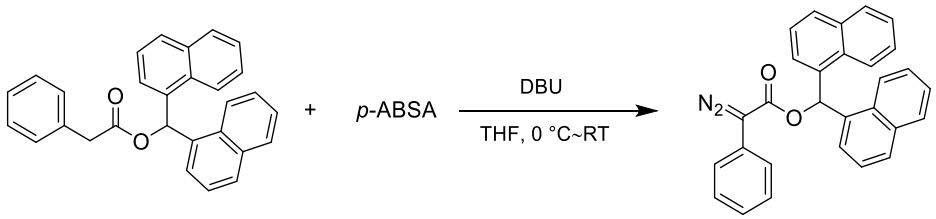
8-1-1 Preparation of Materials

Di(naphthalen-1-yl) methyl 2-phenylacetate:



To an ice cooled solution of di-1-naphthyl methanol (1137.4 mg, 4.0 mmol, 1.0 equiv.) in CH_2Cl_2 (20.0 mL) was added Et_3N (0.83 mL, 6.0 mmol, 1.5 equiv.) under argon atmosphere and then phenylacetyl chloride (0.58 mL, 4.4 mmol, 1.1 equiv.). After 30 min stirring at 0 °C, the reaction mixture was allowed to reach RT and stirred for 1 day. The reaction mixture was washed with $NaHCO_3$ aq. and water. The organic layer was dried over Na_2SO_4 and evaporated to give crude product. Purification was performed by column chromatography with Hex/ CH_2Cl_2=2/1 to give di(naphthalen-1-yl) methyl 2-phenylacetate as white solid (515.2 mg, 32% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.92 (dd, *J* = 12.21, *J* = 4.58 Hz, 4H), 7.84 (d, *J* = 8.24 Hz, 2H), 7.50 (ddd, *J* = 7.78, 6.71, 1.22 Hz, 2H), 7.43 (ddd, *J* = 8.39, 6.71, 1.53 Hz, 2H), 7.33 (dd, *J* = 12.21, 8.54 Hz, 3H), 7.29 (t, *J* = 4.27 Hz, 4H), 7.23 (d, *J* = 7.32 Hz, 2H), 3.77 (s, 2H) ppm.

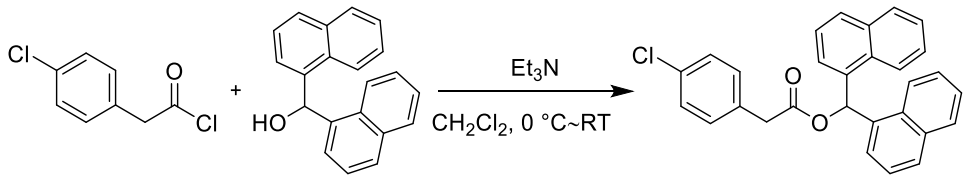
Di(naphthalen-1-yl) methyl 2-diazo-2-phenylacetate :



To a stirred suspension of di(naphthalen-1-yl) methyl 2-phenylacetate (515.2 mg, 1.28 mmol, 1.0 equiv.) in THF (8.0 mL) was added *p*-ABSA (461.3 mg, 1.92 mmol, 1.5 equiv.) under argon atmosphere. The mixture was cooled to 0 °C, and added DBU (0.57 mL, 3.84 mmol, 3.0 equiv.). Then the reaction mixture was stirred at room temperature for 1 day. After water was added, the resulting mixture was extracted with Et_2O 3times. The combined organic layer was washed with brine (10.0 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography with Hex/EA=10/1 to give di(naphthalen-1-yl) methyl 2-diazo-2-phenylacetate as orange solid (521.1 mg, 95% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64

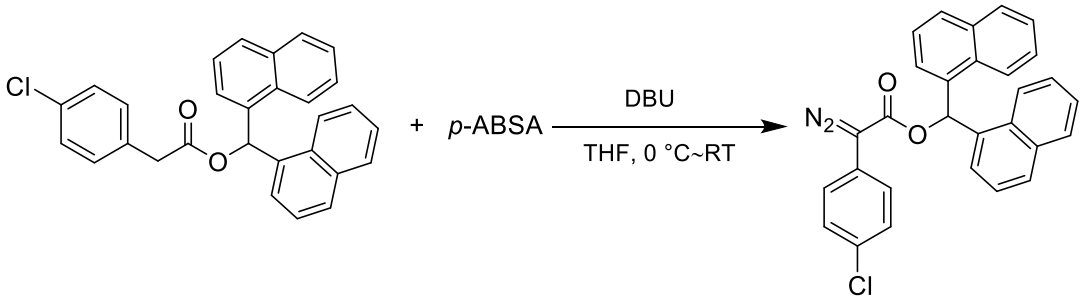
(s, 1H), 8.08 (d, *J* = 7.26 Hz, 2H), 7.93 (dd, *J* = 7.26, 1.91 Hz, 2H), 7.88 (t, *J* = 4.97 Hz, 2H), 7.54–7.49 (m, 6H), 7.43 (d, *J* = 4.59 Hz, 4H), 7.43 (t, *J* = 7.64 Hz, 2H), 7.17 (t, *J* = 7.26 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.34, 134.64, 133.88, 131.06, 129.19, 128.94, 128.88, 126.80, 125.94, 125.90, 125.25, 123.93, 123.47, 71.41 ppm. IR (neat) ν 3057, 2087, 1698, 1354, 800, 755 cm^{-1}. HRMS(ESI) calcd for $C_{29}H_{20}N_2O_2Na$ $[M+Na]^+$: 451.1417 found: 451.1415.

Di(naphthalen-1-yl) methyl 2-(4-chlorophenyl)acetate:



To an ice cooled solution of di-1-naphthyl methanol (1137.4 mg, 4.0 mmol, 1.0 equiv.) in CH_2Cl_2 (20.0 mL) was added Et_3N (0.83 mL, 6.0 mmol, 1.5 equiv.) under argon atmosphere and then 4-chlorophenylacetyl chloride (0.64 mL, 4.4 mmol, 1.1 equiv.). After 30 min stirring at 0 °C, the reaction mixture was allowed to reach RT and stirred for 1 day. The reaction mixture was washed with $NaHCO_3$ aq. and water. The organic layer was dried over Na_2SO_4 and evaporated to give crude product. Purification was performed by column chromatography with Hex/EA=15/1 to give di(naphthalen-1-yl) methyl 2-(4-chlorophenyl)acetate as white solid (611.7 mg, 35% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.90 (d, *J* = 8.79 Hz, 4H), 7.84 (d, *J* = 8.03 Hz, 2H), 7.50 (t, *J* = 8.03 Hz, 2H), 7.41 (t, *J* = 8.03 Hz, 2H), 7.34 (t, *J* = 8.03 Hz, 2H), 7.25 (d, *J* = 8.79 Hz, 4H), 7.17 (d, *J* = 8.41 Hz, 2H), 3.71 (s, 2H) ppm.

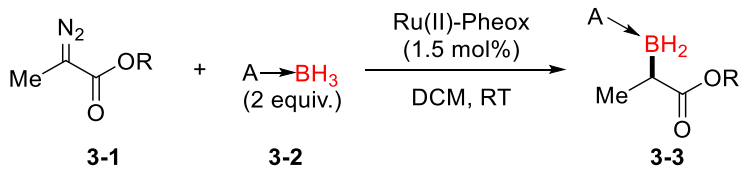
Di(naphthalen-1-yl) methyl 2-diazo-2-(4-chlorophenyl)acetate:



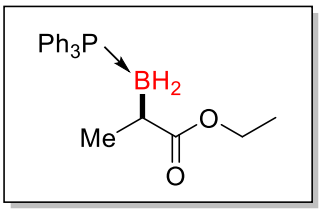
To a stirred suspension of di(naphthalen-1-yl) methyl 2-(4-chlorophenyl)acetate (611.7 mg, 1.40 mmol, 1.0 equiv.) in THF (8.0 mL) was added *p*-ABSA (504.5 mg, 2.1 mmol, 1.5 equiv.) under argon

atmosphere. The mixture was cooled to 0 °C, and added DBU (0.63 mL, 4.20 mmol, 3.0 equiv.). Then the reaction mixture was stirred at room temperature for 7 h. After water was added, the resulting mixture was extracted with Et_2O 3times. The combined organic layer was washed with brine (10.0 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography with Hex/EA=10/1 to give di(naphthalen-1-yl) methyl 2-diazo-2-(4-chlorophenyl)acetate as yellow solid (466.6 mg, 72% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.06 (d, *J* = 8.79 Hz, 2H), 7.90 (dd, *J* = 6.69, 2.30 Hz, 2H), 7.85 (t, *J* = 4.20 Hz, 2H), 7.51–7.46 (m, 4H), 7.40 (d, *J* = 5.73 Hz, 6H), 7.30 (d, *J* = 8.79 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.07, 134.46, 133.87, 131.58, 131.02, 129.26, 129.07, 128.92, 126.84, 125.93, 125.23, 125.07, 123.88, 123.37, 71.60 ppm. IR (neat) ν 3059, 2958, 2095, 1696, 1491, 1147, 775 cm^{-1}. HRMS(ESI) calcd for $C_{29}H_{19}ClN_2O_2Na$ $[M+Na]^+$: 485.1027 found: 485.1023.

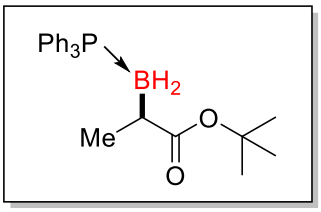
8-1-2 General Procedure for Ru(II)-Pheox catalyzed B−H Insertion Reaction



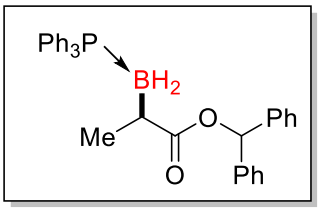
To a solution of Ru(II)-Pheox (0.0015 mmol, 1.5 mol%) and amine- or phosphine-borane adduct **3-2** (0.2 mmol, 2 equiv.) in DCM (1.0 mL) was slowly added a solution of diazoester **1** (0.1 mmol, 1 equiv.) in DCM (1.0 mL) under an argon atmosphere at room temperature. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel (eluted with Hex/EA or Hex/DCM) to give the desired product **3-3**. The enantiomeric excess of the product was determined by chiral HPLC analysis.



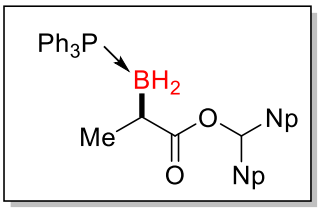
This compound was prepared according to the typical procedure for B–H reaction between ethyl 2-diazopropanoate **3-1a** (12.8 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of Ru(II)-Pheox **cat. 1** (0.9 mg, 0.0015 mmol) for 5 min. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3a** as a white solid (85% yield, 32.1 mg), 40% ee. $[\alpha]^{25}_{D}$ = +24.4 (c 1.5 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 20.62 min (minor product), tR = 22.86 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (t, *J* = 8.79 Hz, 6H), 7.50 (t, *J* = 7.26 Hz, 3H), 7.44 (td, *J* = 7.84, 2.29 Hz, 6H), 3.78 (dq, *J* = 10.70, 7.26 Hz, 1H), 3.29 (dq, *J* = 10.70, 7.26 Hz, 1H), 2.45–1.45 (brs, 2H, BH_2), 2.02 (brs, 1H, CH), 1.12 (d, *J* = 9.17 Hz, 3H), 0.91 (t, *J* = 7.26 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.10 (d, *J* = 6.0 Hz), 133.43 (d, *J* = 9.60 Hz), 131.22, 128.74 (d, *J* = 9.60 Hz), 58.65, 18.87 (d, *J* = 17.99 Hz), 13.99 ppm. IR (neat) ν 3056, 2970, 2920, 1711, 1154, 701 cm^{-1}. HRMS(ESI) calcd for $C_{23}H_{26}BPO_2Na$ $[M+Na]^+$: 399.1660 found: 399.1647.



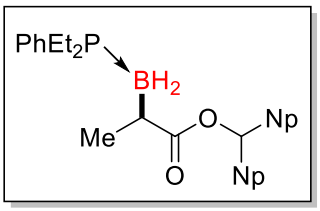
This compound was prepared according to the typical procedure for B–H reaction between *tert*-butyl 2-diazopropanoate **3-1b** (15.6 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of **cat. 1** (0.9 mg, 0.0015 mmol) for 5 min. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3b** as a white solid (58% yield, 24.0 mg), ee % was not determined because of instability of **3-3b**. $[\alpha]^{26}_{D}$ = +54.0 (c 0.9 $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (t, *J* = 8.41 Hz, 5H), 7.50 (t, *J* = 7.64 Hz, 3H), 7.43 (td, *J* = 7.64, 2.29 Hz, 6H), 7.36–7.28 (m, 1H), 2.50–1.45 (brs, 2H, BH_2), 1.89 (brs, 1H, CH), 1.35 (s, 9H), 0.90 (d, *J* = 6.88 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.19 (d, *J* = 12.0 Hz), 133.60 (d, *J* = 8.40 Hz), 131.27, 128.75 (d, *J* = 9.60 Hz), 77.77, 28.24, 18.78 (d, *J* = 10.80 Hz) ppm. IR (neat) ν 3057, 2971, 2924, 1708, 1437, 695 cm^{-1}. HRMS(ESI) calcd for $C_{25}H_{30}BO_2PNa$ $[M+Na]^+$: 427.1973 found: 427.1973.



This compound was prepared according to the typical procedure for B–H reaction between benzhydryl 2-diazopropanoate **3-1c** (26.6 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of **cat. 1** (0.9 mg, 0.0015 mmol) for 5 min. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3c** as a white solid (74% yield, 38.0 mg), 76% ee. $[\alpha]^{25}_{D}$ = +47.8 (c 0.8 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 32.60 min (minor product), tR = 34.91 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (ddd, *J* = 10.42, 8.41, 1.15 Hz, 6H), 7.45 (td, *J* = 7.45, 1.15 Hz, 3H), 7.38 (d, *J* = 7.26 Hz, 2H), 7.34–7.29 (m, 10H), 7.24–21 (m, 3H), 7.18 (t, *J* = 7.26 Hz, 1H), 6.55 (s, 1H), 2.60–1.55 (brs, 2H, BH_2), 2.10 (brs, 1H, CH), 1.10 (d, *J* = 6.50 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.65 (d, *J* = 9.60 Hz), 141.66 (d, *J* = 9.60 Hz), 133.50 (d, *J* = 8.40 Hz), 131.21, 128.71 (d, *J* = 9.60 Hz), 128.24, 128.15, 127.71, 127.21, 127.14, 126.73, 75.19, 18.75 (d, *J* = 13.20 Hz) ppm. IR (neat) ν 3059, 2924, 1696, 1231, 752, 689 cm^{-1}. HRMS(ESI) calcd for $C_{34}H_{32}BPO_2Na$ $[M+Na]^+$: 537.2131 found: 537.2110.

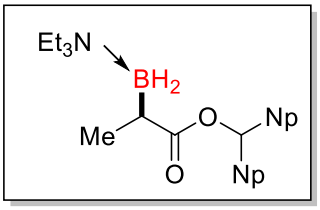


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/DCM = (1/1 v/v) as an eluent to give the desired product **3-3d** as a white solid (81% yield, 50.0 mg), 95% ee. $[\alpha]^{24}_{D}$ = +11.8 (c 1.9 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 46.10 min (major product), tR = 53.47 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.18 (d, *J* = 6.88 Hz, 1H), 7.91 (d, *J* = 8.41 Hz, 1H), 7.86–7.80 (m, 3H), 7.76 (d, *J* = 8.03 Hz, 1H), 7.60 (d, *J* = 6.88 Hz, 1H), 7.49 (ddd, *J* = 9.17, 8.79, 1.53 Hz, 6H), 7.45–7.40 (m, 4H), 7.39–26 (m, 6H), 7.21 (td, *J* = 7.64, 2.29 Hz, 6H), 2.60–1.55 (brs, 2H, BH_2), 2.14 (brs, 1H, CH), 0.98 (d, *J* = 6.88 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.89 (d, *J* = 12.46 Hz), 136.38 (d, *J* = 16.29 Hz), 133.47 (d, *J* = 8.63 Hz), 131.17, 128.68, 128.58, 128.52, 128.45, 128.17, 126.35, 126.18, 125.57, 125.51, 125.47, 125.31, 125.18, 124.31, 69.19, 25.35, 18.67 (d, *J* = 10.20 Hz) ppm. IR (neat) ν 3050, 2954, 1680, 1230, 744, 690 cm^{-1}. HRMS(ESI) calcd for $C_{42}H_{36}BPO_2Na$ $[M+Na]^+$: 637.2438 found: 637.2435.

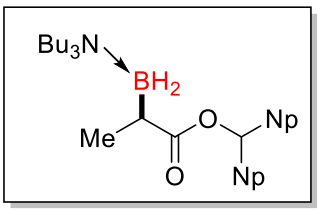


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and diethylphenylphosphine-borane **3-2e** (36.0 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2h. The resulting mixture was purified by silica gel column chromatography with Hex/DCM = (1/1 v/v) as an eluent to give the desired product **3-3e** as a white solid (87% yield, 45.0 mg), 85% ee. $[\alpha]^{25}_{D}$ = –10.5 (c 2.2 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 18.39 min (major product), tR = 22.82 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.20 (dd, *J* = 6.56, 2.75 Hz, 1H), 7.95 (d, *J* = 8.24 Hz, 1H), 7.85 (dd, *J* = 9.46, 5.95 Hz, 2H), 7.79 (dd, *J* = 8.09, 4.88 Hz, 2H), 7.57 (d, *J* = 7.02 Hz, 1H), 7.52–7.24 (m, 12H), 2.03 (brs, 1H, CH), 1.90–1.60 (m, 4H), 1.90–1.20 (brs, 2H, BH_2), 1.14 (d, *J* = 6.71 Hz, 3H), 0.77 (ddt, *J* = 25.33, 15.41, 7.63 Hz, 6H) ppm. ^{13}C NMR (100 MHz,

$CDCl_3$) δ 181.48 (d, J = 5.75 Hz), 136.23 (d, J = 3.83 Hz), 133.75 (d, J = 4.79 Hz), 131.71 (d, J = 7.67 Hz), 131.67, 130.07, 128.64, 128.54, 128.31, 126.46, 126.19, 125.64, 125.51, 125.23, 125.19, 124.07, 69.13, 18.90 (d, J = 15.34 Hz), 15.60 (d, J = 34.50 Hz), 14.50 (d, J = 34.50 Hz), 6.4 ppm. IR (neat) ν 3059, 2966, 1708, 1139, 783, 748 cm^{-1}. HRMS(ESI) calcd for $C_{34}H_{36}BPO_2Na$ $[M+Na]^+$: 541.2468 found: 541.2474.

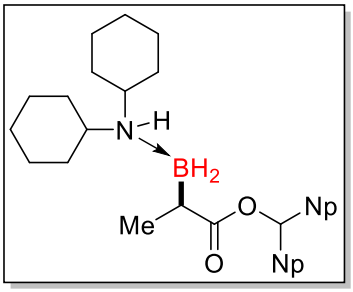


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and triethylamine-borane **3-2f** (23.0 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3f** as a white solid (91% yield, 41.3 mg), 60% ee. $[\alpha]^{23}_D$ = –18.3 (c 1.6 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 26.71 min (major product), tR = 36.51 min (minor product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.31 (d, J = 7.63 Hz, 1H), 7.95 (d, J = 8.54 Hz, 1H), 7.86 (t, J = 8.24 Hz, 2H), 7.79 (t, J = 9.16 Hz, 2H), 7.71 (d, J = 7.02 Hz, 1H), 7.54–7.25 (m, 7H), 2.66–2.47 (m, 6H), 1.91 (brs, 1H, CH), 1.90–1.20 (brs, 2H, BH_2), 1.11 (d, J = 7.02 Hz, 3H), 0.84 (td, J = 7.32, 2.14 Hz, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 182.14, 136.39, 136.28, 133.81, 133.75, 128.56, 128.53, 128.27, 126.60, 126.46, 126.11, 125.65, 125.49, 125.34, 125.22, 125.17, 124.20, 124.08, 68.78, 49.78, 17.48, 7.82 ppm. IR (neat) ν 3051, 2973, 1730, 1169, 782 cm^{-1}. HRMS(ESI) calcd for $C_{30}H_{36}BNO_2Na$ $[M+Na]^+$: 476.2749 found: 476.2746.

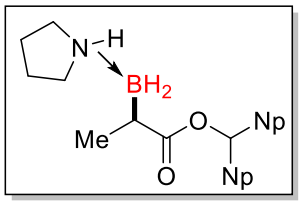


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and tributylamine-borane **3-2g** (39.8 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (50/1 v/v) as an eluent to give the desired product **3-3g** as a white solid (86% yield, 46.4 mg), 66% ee. $[\alpha]^{27}_D$ = –29.6 (c 1.0 $CHCl_3$). The *ee* value

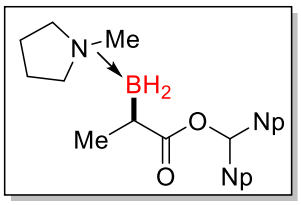
was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 13.84 min (major product), tR = 18.23 min (minor product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.30 (d, *J* = 8.24 Hz, 1H), 7.82 (ddt, *J* = 19.68, 15.56, 7.32 Hz, 5H), 7.71 (d, *J* = 7.32 Hz, 1H), 7.56–7.26 (m, 7H), 2.60 (td, *J* = 12.66, 4.58 Hz, 3H), 2.50 (td, *J* = 12.66, 4.58 Hz, 3H), 1.88 (brs, 1H, CH), 1.88–1.20 (brs, 2H, BH_2), 1.50–1.20 (m, 6H), 1.08 (d, *J* = 7.02 Hz, 3H), 0.99 (sext., *J* = 7.32 Hz, 6H), 0.76 (t, *J* = 7.32 Hz, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.98, 136.36, 133.85, 128.51, 128.23, 126.75, 126.45, 126.08, 125.63, 125.45, 125.32, 125.16, 124.24, 124.16, 69.11, 56.73, 24.35, 20.29, 17.60, 13.72 ppm. IR (neat) ν 3045, 2952, 1705, 1161, 774 cm^{-1}. HRMS(ESI) calcd for $C_{36}H_{48}BNO_2Na$ $[M+Na]^+$: 560.3670 found: 560.3668.



This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and dicyclohexylamine-borane **3-2h** (39.0 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/DCM = (1/1 v/v) as an eluent to give the desired product **3-3h** as a white solid (92% yield, 49.1 mg), 47% ee. $[\alpha]^{25}_{D}$ = –27.0 (c 2.4 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 4.93 min (major product), tR = 5.48 min (minor product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.26 (d, *J* = 8.41 Hz, 1H), 7.83 (ddd, *J* = 30.58, 17.20, 7.26 Hz, 5H), 7.68 (d, *J* = 6.88 Hz, 1H), 7.60–7.35 (m, 4H), 7.32 (td, *J* = 6.88, 1.15 Hz, 1H), 7.28 (t, *J* = 7.26 Hz, 1H), 7.22 (t, *J* = 7.26 Hz, 1H), 4.03 (s, 1H, NH), 2.94 (s, 1H), 2.48 (s, 1H), 2.09 (s, 1H), 1.91 (brs, 1H, CH), 1.90–1.15 (m, 16H), 1.07 (d, *J* = 6.88 Hz, 3H), 1.0–0.80 (m, 4H), 0.62 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.01, 135.75, 133.85, 133.68, 128.87, 128.71 128.54, 128.33, 126.80, 126.68, 126.12, 125.81, 125.54, 125.39, 125.19, 125.18, 124.0, 123.62, 69.38, 59.72, 57.20, 30.73, 30.59, 29.01, 28.60, 25.80, 25.60, 25.51, 25.17, 13.83 ppm. IR (neat) ν 3152, 3050, 2935, 2856, 1662, 1243, 778, 756 cm^{-1}. HRMS(ESI) calcd for $C_{36}H_{44}BNO_2Na$ $[M+Na]^+$: 556.3364 found: 556.3379.

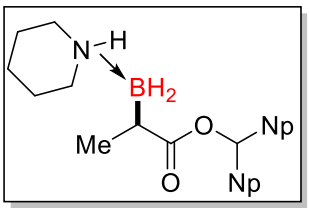


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and pyrrolidine-borane **3-2i** (17.0 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3i** as a white solid (71% yield, 30.0 mg), 37% ee. $[\alpha]^{25}_{D} = -2.7$ (c 1.5 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 16.62 min (major product), tR = 27.42 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.35 (d, *J* = 8.41 Hz, 1H), 7.94 (d, *J* = 8.03 Hz, 1H), 7.87 (dd, *J* = 8.03, 3.44 Hz, 2H), 7.81 (d, *J* = 8.41 Hz, 1H), 7.74–7.67 (m, 2H), 7.65 (d, *J* = 8.41 Hz, 1H), 7.59 (t, *J* = 6.88 Hz, 1H), 7.55 (t, *J* = 7.26 Hz, 1H), 7.42 (t, *J* = 7.26 Hz, 1H), 7.27 (pent., *J* = 7.26 Hz, 2H), 7.03 (d, *J* = 6.50 Hz, 1H), 3.75 (s, 1H, NH), 3.07 (s, 1H), 2.39 (dq, *J* = 15.86, 8.79 Hz, 1H), 2.26 (dq, *J* = 11.66, 9.17 Hz, 1H), 2.01 (brs, 2H), 1.90–1.20 (m, 4H), 1.06 (d, *J* = 6.55 Hz, 3H), 0.90–0.80 (m, 1H), 0.80–0.68 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.82, 136.36, 133.94, 130.87, 130.60, 129.08, 129.01, 128.67, 128.50, 127.58, 127.04, 126.27, 126.19, 125.64, 125.26, 124.23, 123.91, 123.0, 68.85, 51.82, 51.22, 23.74, 23.17, 13.76 ppm. IR (neat) ν 3245, 3040, 2962, 1719, 1158, 775, 760 cm^{-1}. HRMS(ESI) calcd for $C_{28}H_{30}BNO_2Na$ $[M+Na]^+$: 446.2291 found: 446.2293.

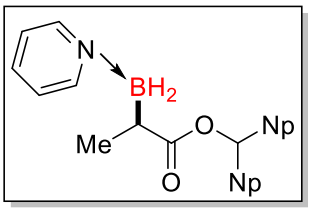


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and methylpyrrolidine-borane **3-2j** (19.8 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **3-3j** as a white solid (89% yield, 38.8 mg), 53% ee. $[\alpha]^{24}_{D} = -32.0$ (c 1.7 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 26.33 min (major product), tR = 38.64 min

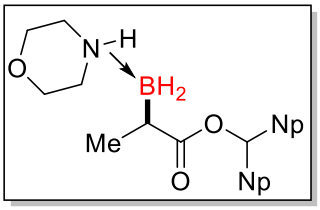
(minor product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.28 (d, *J* = 7.63 Hz, 1H), 7.94 (d, *J* = 8.54 Hz, 1H), 7.85 (t, *J* = 8.54 Hz, 2H), 7.78 (dd, *J* = 12.97, 8.24 Hz, 2H), 7.70 (d, *J* = 7.02 Hz, 1H), 7.53–7.40 (m, 4H), 7.36–7.28 (m, 3H), 3.01 (td, *J* = 11.50, 8.54 Hz, 1H), 2.77 (td, *J* = 11.60, 8.54 Hz, 1H), 2.69–2.55 (m, 1H), 2.50–2.38 (m, 1H), 2.36 (s, 3H), 2.20–1.70 (brs, 2H, BH_2), 2.0 (brs, 1H, CH), 1.80–1.60 (m, 2H), 1.59–1.45 (m, 2H), 1.12 (d, *J* = 7.02 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.0, 136.31, 136.27, 133.77, 133.73, 128.59, 128.55, 128.31, 126.58, 126.45, 126.13, 125.65, 125.51, 125.36, 125.21, 125.16, 124.15, 124.04, 68.95, 62.02, 60.70, 47.48, 22.35, 21.90, 16.99 ppm. IR (neat) ν 3048, 2955, 1711, 1162, 780 cm^{-1}. HRMS (DART) calcd for $C_{29}H_{32}BNO_2$ $[M]^+$: 437.2526 found: 437.2525.



This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and piperidine-borane **3-2k** (19.8 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3k** as a white solid (78% yield, 34.1 mg), 50% ee. $[\alpha]^{25}_{D}$ = –66.1 (c 1.7 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 16.80 min (major product), tR = 31.44 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.34 (d, *J* = 8.41 Hz, 1H), 7.95 (d, *J* = 8.03 Hz, 1H), 7.87 (d, *J* = 8.41 Hz, 2H), 7.81 (d, *J* = 8.03 Hz, 1H), 7.70 (t, *J* = 8.41 Hz, 2H), 7.61 (t, *J* = 8.41 Hz, 2H), 7.56 (dd, *J* = 13.76, 7.26 Hz, 1H), 7.41 (t, *J* = 7.26 Hz, 1H), 7.25 (td, *J* = 21.60, 6.88 Hz, 2H), 6.99 (d, *J* = 6.50 Hz, 1H), 3.33 (d, *J* = 13.0 Hz, 1H), 3.01 (s, 1H), 2.32 (d, *J* = 13.38 Hz, 1H), 2.11 (dd, *J* = 24.85, 10.70 Hz, 2H), 2.04 (brs, 1H, CH), 2.0–1.30 (brs, 2H, BH_2), 1.40 (d, *J* = 14.14 Hz, 1H), 1.24 (d, *J* = 16.05 Hz, 1H), 1.12 (d, *J* = 14.14 Hz, 1H), 1.05 (d, *J* = 6.50 Hz, 3H), 0.98 (dt, *J* = 13.0, 3.82 Hz, 1H), 0.15 (q, *J* = 13.38 Hz, 1H), –0.32 (q, *J* = 13.38 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.65, 136.14, 134.03, 133.73, 129.16, 129.09, 128.63, 128.48, 127.59, 127.30, 126.36, 126.11, 125.62, 125.53, 125.24, 124.10, 123.97, 122.97, 68.88, 51.70, 50.19, 24.61, 24.18, 22.49, 13.54 ppm. IR (neat) ν 3229, 3052, 2947, 1715, 1162, 779, 756 cm^{-1}. HRMS(ESI) calcd for $C_{29}H_{32}BNO_2Na$ $[M+Na]^+$: 460.2423 found: 460.2414.

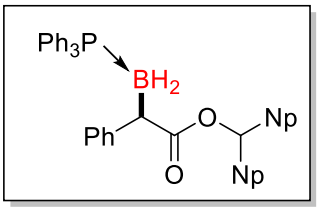


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and pyridine-borane **3-2l** (18.6 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (30/1 v/v) as an eluent to give the desired product **3-3l** as a white solid (81% yield, 35.0 mg), 78% ee. $[\alpha]^{25}_{D}$ = –34.2 (c 0.1 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 27.06 min (major product), tR = 34.15 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.21 (dd, *J* = 6.31, 3.44 Hz, 1H), 8.04 (d, *J* = 5.35 Hz, 2H), 7.90 (dd, *J* = 6.31, 3.44 Hz, 1H), 7.85 (d, *J* = 9.56 Hz, 2H), 7.80 (dd, *J* = 12.23, 8.79 Hz, 2H), 7.57–7.48 (m, 4H), 7.43 (t, *J* = 7.26 Hz, 2H), 7.34 (ddd, *J* = 8.41, 6.88, 1.15 Hz, 1H), 7.30 (d, *J* = 4.20 Hz, 2H), 6.86 (dd, *J* = 7.64, 6.88 Hz, 2H), 3.20–2.25 (brs, 2H, BH_2), 2.21 (brs, 1H, CH), 1.11 (d, *J* = 6.88 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.64, 147,0, 139.08, 128.59, 128.39, 128.37, 126.45, 126.25, 125.81, 125.57, 125.28, 125.21, 125.17, 124.39, 124.05, 68.31, 14.82 ppm. IR (neat) ν 3052, 2923, 1699, 1508, 1457, 1162, 779 cm^{-1}. HRMS(ESI) calcd for $C_{29}H_{26}BNO_2Na$ $[M+Na]^+$: 454.1978 found: 454.1976.

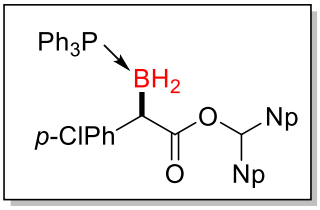


This compound was prepared according to the typical procedure for B–H reaction between dinaphthylenyl 2-diazopropanoate **3-1d** (36.6 mg, 0.1 mmol) and morpholine-borane **3-2m** (20.2 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at –10 °C for 2 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3m** as a white solid (73% yield, 32.0 mg), 61% ee. $[\alpha]^{25}_{D}$ = –64.8 (c 1.5 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 18.34 min (major product), tR = 29.32 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.36 (d, *J* = 8.54 Hz, 1H), 7.98 (d, *J* = 7.93 Hz,

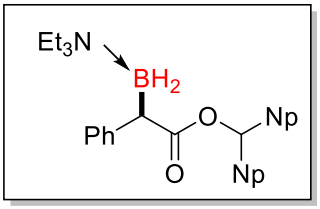
1H), 7.87 (dd, *J* = 12.51, 8.39 Hz, 3H), 7.70 (dd, *J* = 16.33, 7.32 Hz, 2H), 7.58 (pent., *J* = 7.93 Hz, 3H), 7.42 (t, *J* = 7.32 Hz, 1H), 7.27 (t, *J* = 7.63 Hz, 2H), 6.99 (d, *J* = 7.02 Hz, 1H), 3.52 (d, *J* = 12.51 Hz, 1H), 3.39 (s, 1H, NH), 3.26 (d, *J* = 12.82 Hz, 1H), 3.13 (d, *J* = 13.12 Hz, 1H), 2.42 (pent., *J* = 12.82 Hz, 2H), 2.02 (q, *J* = 12.21 Hz, 3H), 1.90–1.20 (brs, 2H, BH_2), 1.62 (t, *J* = 12.51 Hz, 1H), 1.06 (d, *J* = 6.71 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.20, 136.11, 134.93, 133.74, 131.06, 129.38, 128.69, 128.60, 127.78, 127.48, 126.43, 126.21, 125.77, 125.70, 125.22, 123.89, 123.85, 122.86, 68.92, 65.25, 64.91, 50.25, 49.23, 13.33 ppm. IR (neat) ν 3229, 3051, 2962, 1723, 1162, 780, 756 cm^{-1}. HRMS(ESI) calcd for $C_{28}H_{30}BNO_3Na$ $[M+Na]^+$: 462.2216 found: 462.2217.



This compound was prepared according to the typical procedure for B–H reaction between di(naphthalen-1-yl)methyl 2-diazo-2-phenylacetate **3-1n** (42.8 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of **cat. 1** (6.3 mg, 0.01 mmol) at RT for 24 h. The resulting mixture was purified by silica gel column chromatography with Hex/DCM = (2/1 v/v) as an eluent to give the desired product **3-3n** as a white solid (94% yield, 63.5 mg), 37% ee. $[\alpha]^{25}_D$ = +8.3 (c 1.2 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 19.69 min (minor product), tR = 27.25 min (major product). ^1H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.05 (d, *J* = 8.41 Hz, 1H), 7.93 (d, *J* = 8.79 Hz, 1H), 7.83 (d, *J* = 8.03 Hz, 2H), 7.76 (t, *J* = 8.41 Hz, 2H), 7.45–7.25 (m, 17H), 7.19 (td, *J* = 7.84, 1.91 Hz, 6H), 7.14 (d, *J* = 6.50 Hz, 2H), 6.96 (dd, *J* = 14.72, 6.12 Hz, 3H), 3.40 (brd, 1H, CH), 3.20–1.90 (brs, 2H, BH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.63 (d, *J* = 17.99 Hz), 143.59 (d, *J* = 4.80 Hz), 133.37 (d, *J* = 9.60 Hz), 131.11, 129.37, 128.57 (d, *J* = 10.80 Hz), 128.49, 128.37, 127.43, 126.23, 125.71, 125.48, 70.09 ppm. IR (neat) ν 3059, 2924, 1711, 1438, 1116, 756, 693 cm^{-1}. $C_{47}H_{38}BO_2PNa$ $[M+Na]^+$: 699.2603 found: 699.2578.



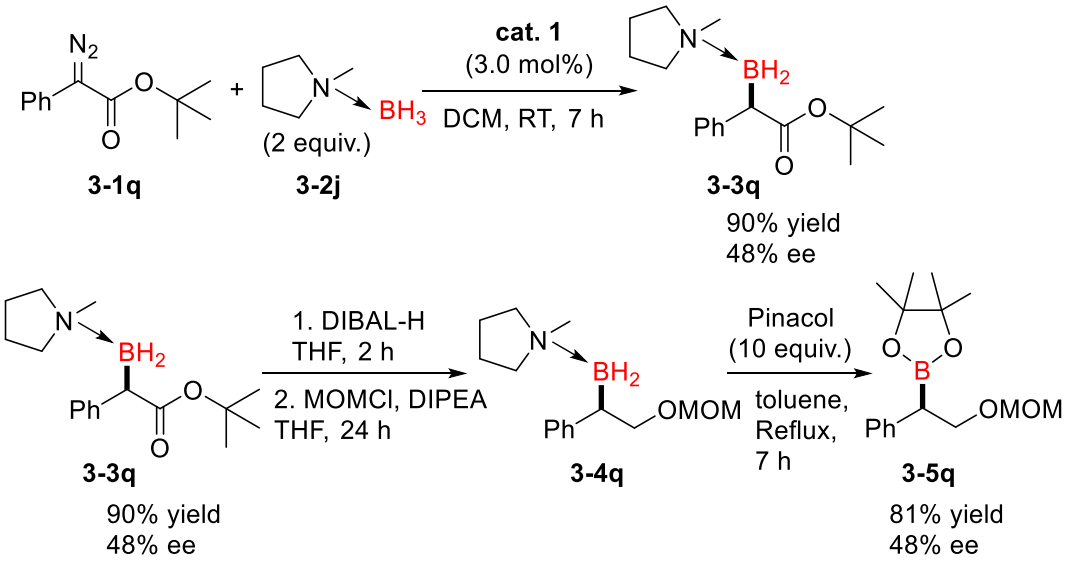
This compound was prepared according to the typical procedure for B–H reaction between di(naphthalen-1-yl)methyl 2-diazo-2-(4-chlorophenyl) acetate **3-1o** (46.3 mg, 0.1 mmol) and triphenylphosphine-borane **3-2a** (55.2 mg, 0.2 mmol) in presence of **cat. 1** (6.3 mg, 0.01 mmol) at RT for 24 h. The resulting mixture was purified by silica gel column chromatography with Hex/DCM = (1/1 v/v) as an eluent to give the desired product **3-3o** as a white solid (82% yield, 58.3 mg), 20% ee. $[\alpha]^{25}_{D}$ = +6.8 (c 2.2 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 14.10 min (minor product), tR = 22.42 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.01 (d, *J* = 8.22 Hz, 1H), 7.94 (d, *J* = 8.41 Hz, 1H), 7.83 (d, *J* = 8.03 Hz, 2H), 7.77 (t, *J* = 8.03 Hz, 2H), 7.55–7.30 (m, 19H), 7.20 (dd, *J* = 7.93, 1.91 Hz, 4H), 7.02 (d, *J* = 8.41 Hz, 2H), 6.86 (d, *J* = 8.79 Hz, 2H), 3.38 (brd, 1H, CH), 3.10–1.95 (brs, 2H, BH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.25 (d, *J* = 17.99 Hz), 142.04 (d, *J* = 3.60 Hz), 135.80, 133.72, 133.29 (d, *J* = 9.60 Hz), 131.19, 130.62, 128.64 (d, *J* = 9.60 Hz), 128.54, 128.48, 128.42, 127.32, 126.29, 125.72, 125.56, 125.53, 125.18, 125.14, 124.17, 123.96, 70.34 ppm. IR (neat) ν 3056, 2924, 1711, 1483, 1119, 760, 689 cm^{-1}. $C_{47}H_{37}ClBO_2PNa$ $[M+Na]^+$: 733.2180 found: 733.2181.



This compound was prepared according to the typical procedure for B–H reaction between di(naphthalen-1-yl)methyl 2-diazo-2-phenylacetate **3-1n** (42.8 mg, 0.1 mmol) and triethylamine-borane **3-2f** (23.0 mg, 0.2 mmol) in presence of **cat. 1** (1.9 mg, 0.003 mmol) at RT for 24 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3p** as a white solid (93% yield, 47.8 mg), 79% ee. $[\alpha]^{27}_{D}$ = +10.2 (c 0.9 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 20.27 min (major product), tR = 23.09 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.14 (d, *J* = 8.41 Hz, 1H),

7.90 (d, *J* = 8.41 Hz, 1H), 7.82 (t, *J* = 8.79 Hz, 2H), 7.75 (t, *J* = 7.64 Hz, 2H), 7.41 (sext., *J* = 7.26 Hz, 6H), 7.32 (td, *J* = 17.58, 6.12 Hz, 4H), 7.18 (t, *J* = 7.64 Hz, 2H), 7.07 (t, *J* = 7.26 Hz, 1H), 3.24 (brs, 1H, CH), 2.52 (q, *J* = 7.26 Hz, 6H), 2.45–1.40 (brs, 2H, BH_2), 0.83 (t, *J* = 7.26 Hz, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.50, 143.91, 135.97, 133.71, 131.24, 131.10, 129.07, 128.49, 128.45, 128.37, 127.62, 126.28, 126.19, 125.52, 125.18, 125.13, 124.71, 124.26, 124.0, 69.99, 49.81, 7.72 ppm. IR (neat) ν 3055, 2941, 1716, 1452, 1108, 778, 735 cm^{-1}. HRMS(ESI) calcd for $C_{35}H_{38}BNO_2Na$ $[M+Na]^+$: 538.2894 found: 538.2904.

8-1-3　不斉有機ホウ素化合物の応用反応



This compound was prepared according to the typical procedure for B–H reaction between diazoester **3-1q** (43.6 mg, 0.2 mmol) and *N*-methylpyrrolidine-borane **3-2f** (59.3 mg, 0.6 mmol) in presence of **cat. 1** (3.8 mg, 0.006 mmol) at RT for 7 h. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **3-3q** as white solid. (52.0 mg, 90% yield), 48% ee, $[\alpha]^{23}_{D}$ = -8.96 (c 1.74 $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 220 nm, eluent: Hex/IPA = 9/1, Flow rate = 1.0 ml/min, tR = 13.04 min (minor product), tR = 16.33 min (major product). ^{1}H NMR (500 MHZ, $CDCl_3$) δ 7.41 (d, *J* = 6.88 Hz, 2H), 7.22 (t, *J* = 7.64 Hz, 2H), 7.07 (t, *J* = 7.64 Hz, 1H), 3.24-3.19 (m, 1H), 3.14-3.07 (m, 1H), 2.99-2.93 (m, 1H), 2.84-2.79 (m, 1H), 2.57-2.53 (m, 1H), 2.52 (s, 3H), 2.40-1.80 (m, 6H), 1.42 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.75, 144.65, 129.14, 127.52, 124.37, 78.38, 61.52, 61.48, 47.75, 28.23, 28.06, 22.31, 22.16 ppm. IR (neat) ν 2969, 2924, 1714, 1144, 703 cm^{-1}. HRMS (DART) calcd for $C_{17}H_{29}BNO_2$ $[M+H]^+$: 290.22906 found : 290.2291.

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Under argon atmosphere to a solution of **3-3q** (0.052 g, 0.18 mmol, 1 equiv.) in THF (4.0 ml) at -78 ℃ was added DIBAL-H 1M in toluene (0.54 ml, 0.54 mmol, 3.0 equiv.) dropwise. The resulting mixture was allowed to room temperature and stirred for another 2 h. The reaction was quenched with 1M HCl solution (4.0 ml) and extracted with EA (3 times), the combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduce pressure and the residue was then dissolved in THF. To this solution in an ice bath was slowly added DIPEA (0.15 ml, 0.90 mmol, 5.0 equiv.) and MOMCl (0.55 ml, 0.72 mmol, 4.0 equiv.). The mixture was then stirred at room temperature for another 24 h. After removing the solvent under reduce pressure, to residue was

purified by silica gel column chromatography to afford to product as colorless oil.

To the above obtained product of first step (0.02 g, 0.075 mmol, 1.0 equiv.) in toluene (2.0 ml) was added pinacol (0.088 g, 0.75 mmol, 10.0 equiv.), the mixture was then heated to reflux for 7 h. The solvent was purified by silica gel flash chromatography to give final product **3-5q** as colorless oil (0.0178 g, 81% yield), 48% ee. The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IC), UV detector 220 nm, eluent: Hex/IPA = 400/1, Flow rate = 0.7 ml/min, tR = 17.64 min (major product), tR = 20.04 min (minor product). ^{1}H NMR (500 MHZ, $CDCl_3$) δ 7.33-7.20 (m, 4H), 7.20-7.08 (m, 1H),4.55 (dd, *J*=26.37, 6.50 Hz, 2H), 3.92 (dd, *J* = 9.4, 7.3 Hz, 1H), 3.84 (t, *J* = 9.0 Hz, 1H), 3.30 (s, 3H), 2.73 (t, *J* = 7.8 Hz, 1H), 1.21 (d, *J* = 11.8 Hz, 12H) ppm.

8-1-4 X-Ray Crystal Structure of B–H Insertion Product

Figure 8-1. X-ray crystal structure of (*R*)-**3-3d**

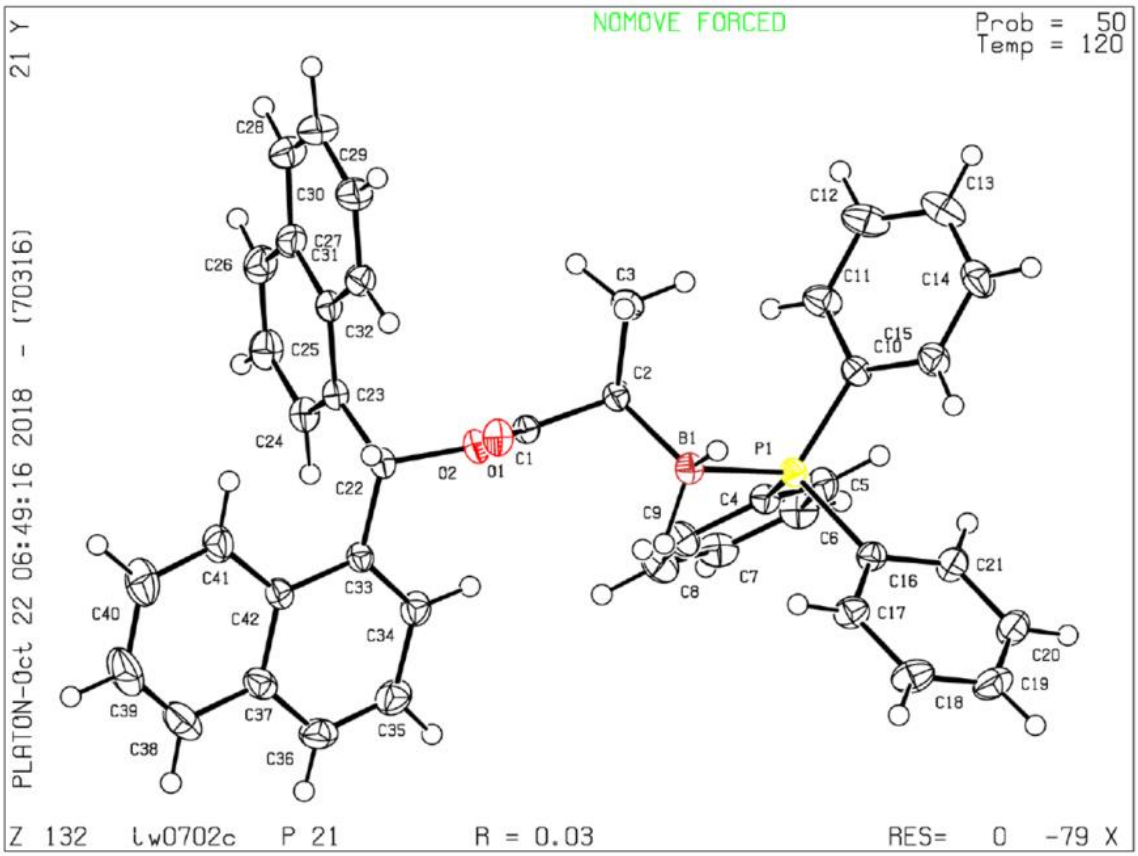
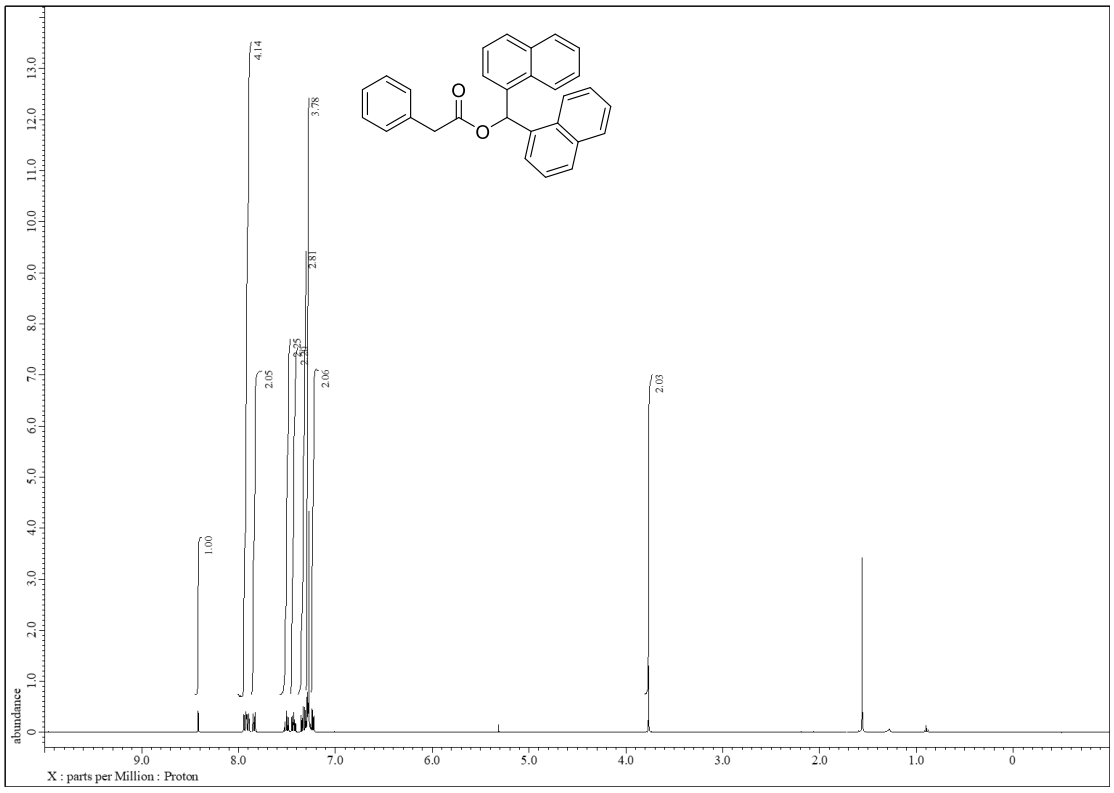
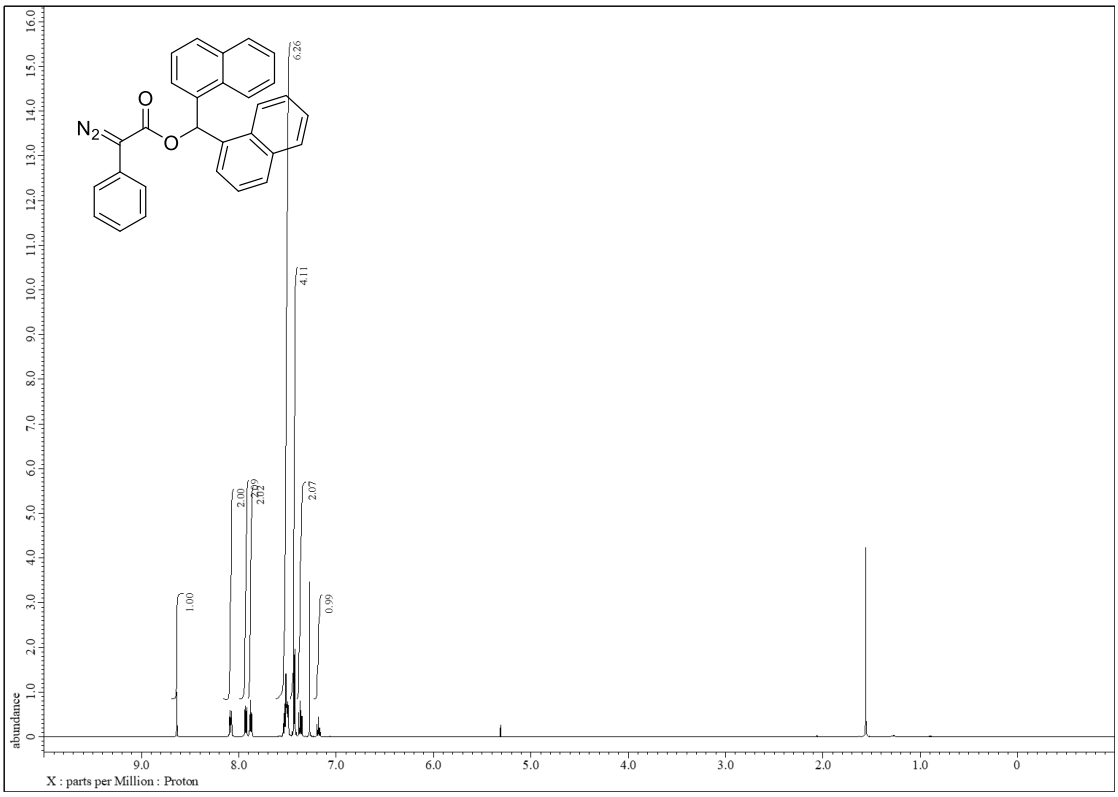


Table 8-1. Crystal data and structure refinement for **iw0702c**.

Identification code	iw0702c
CCDC number	2002858
Empirical formula	$C_{42}H_{36}BO_2P$
Formula weight	614.49
Temperature	120 K
Wavelength	0.71075 Å
Crystal system	Triclinic
Space group	*P*21
Unit cell dimensions	*a* = 9.5398(13) Å α = 90°
	b = 16.937(2) Å β = 107.9238(13)°
	c = 10.5827(16) Å γ = 90°
Volume	1626.9(4) Å^3
Z	2
Density (calculated)	1.254 g/cm^3
Absorption coefficient	0.121 mm^{-1}
F(000)	648
Index ranges	-13<= *h* <=13, -24<= *k* <=24, -15<= *l* <=15
Absorption correction	Numerical
Max. and min. transmission	0.980 to 0.926
R indices (all data)	*R*1 =0.0310(9956) , *wR*2 = 0.0811(10161)

8-1-5 NMR Spectral Data

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O
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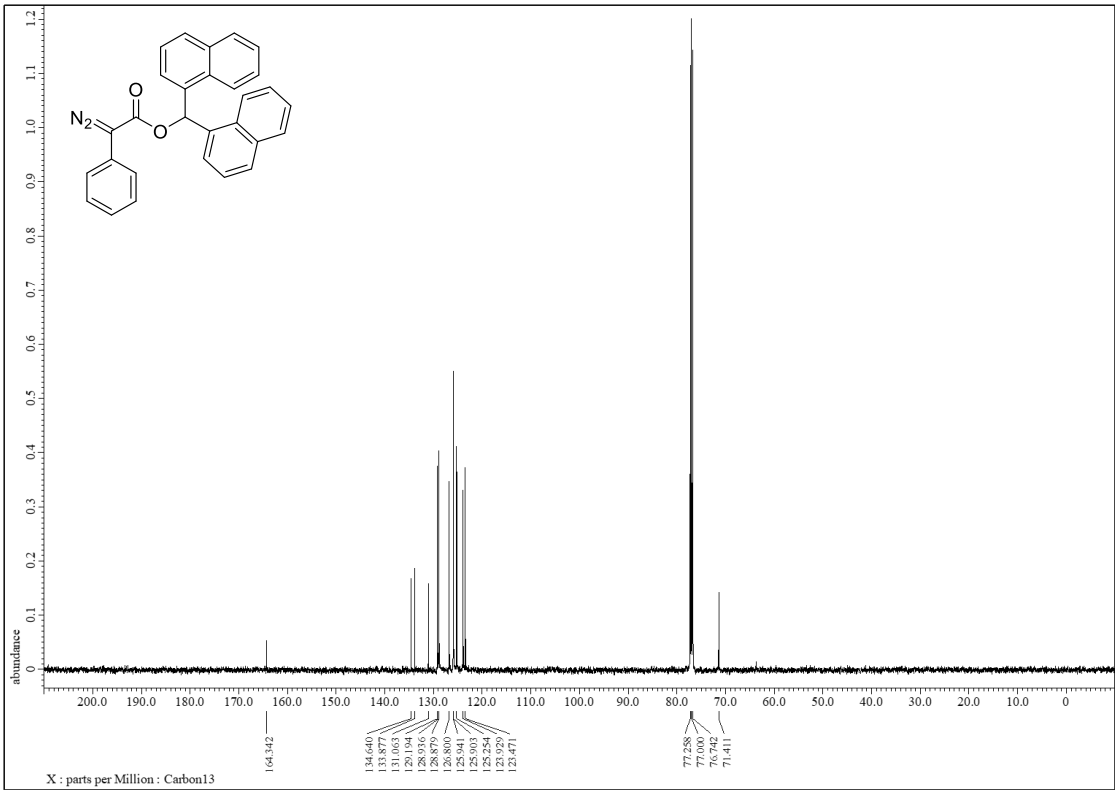
4.11
2.07
2.00
2.02
2.00
1.00
0.99
abundance
X : parts per Million : Proton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O
abundance
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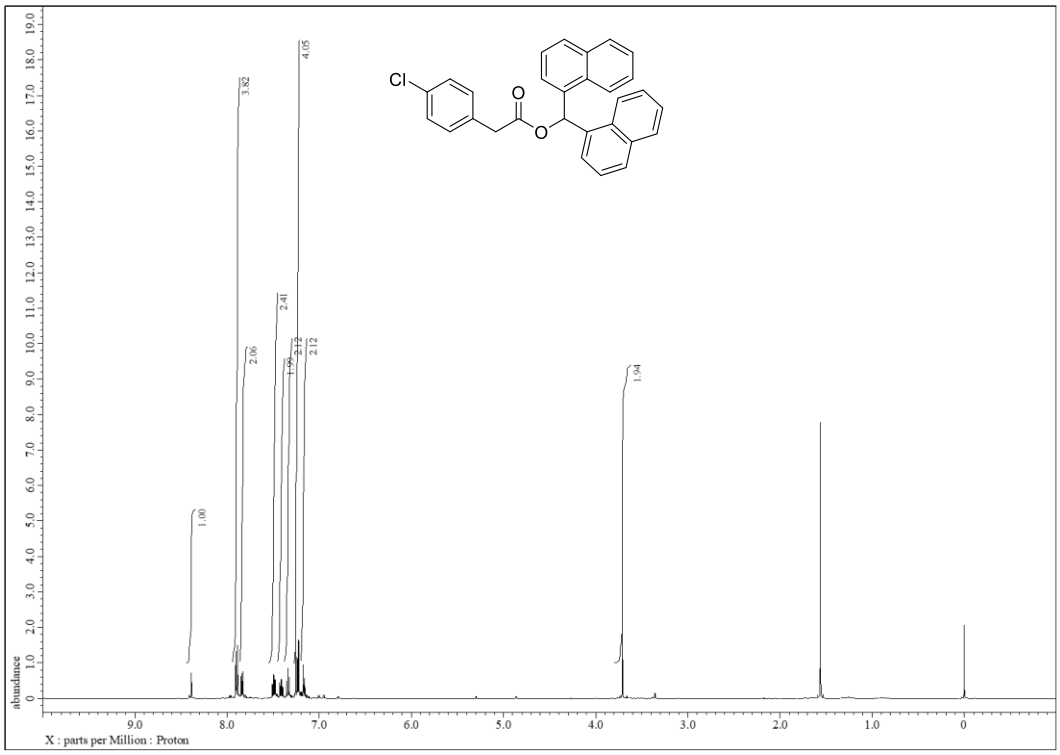
133.877
131.063
129.194
128.936
128.879
126.800
125.941
125.293
125.254
123.929
123.471
77.258
77.000
76.742
71.411
X : parts per Million : Carbon13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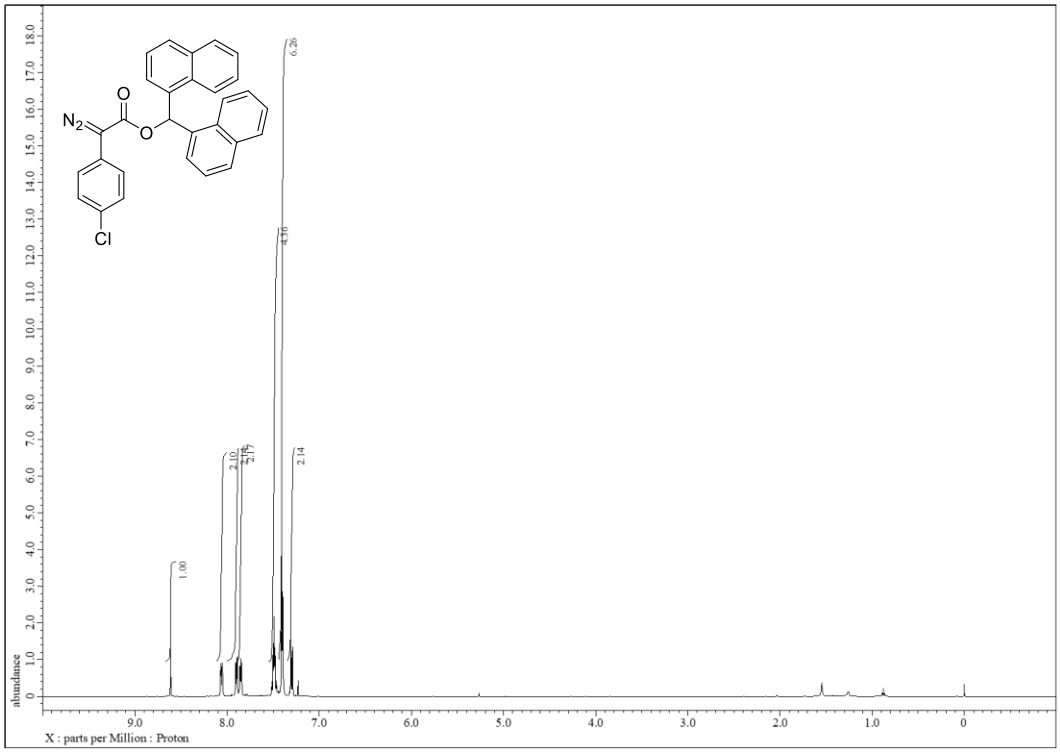
3.82
2.41
2.06
2.12
2.12
1.99
1.94
1.00
abundance
X : parts per Million : Proton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O
Cl
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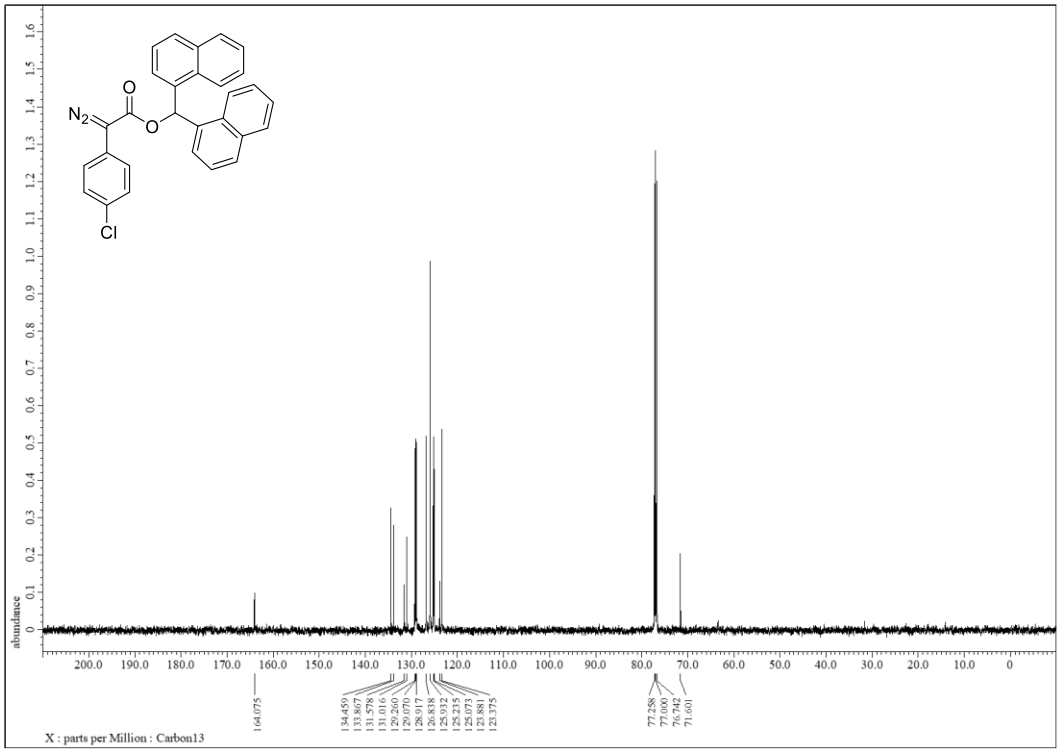
4.36
2.14
2.10
2.07
1.00
abundance
X : parts per Million : Proton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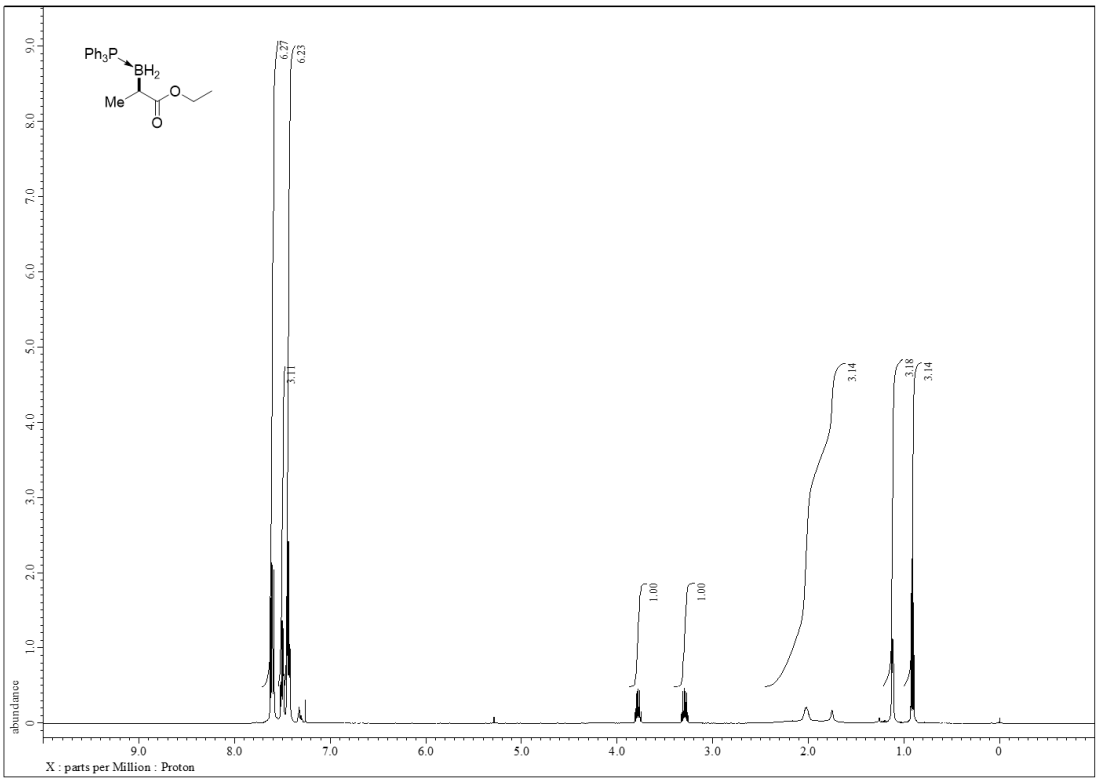
O
O
Cl
abundance
X : parts per Million : Carbon13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BH2
Me
O
O
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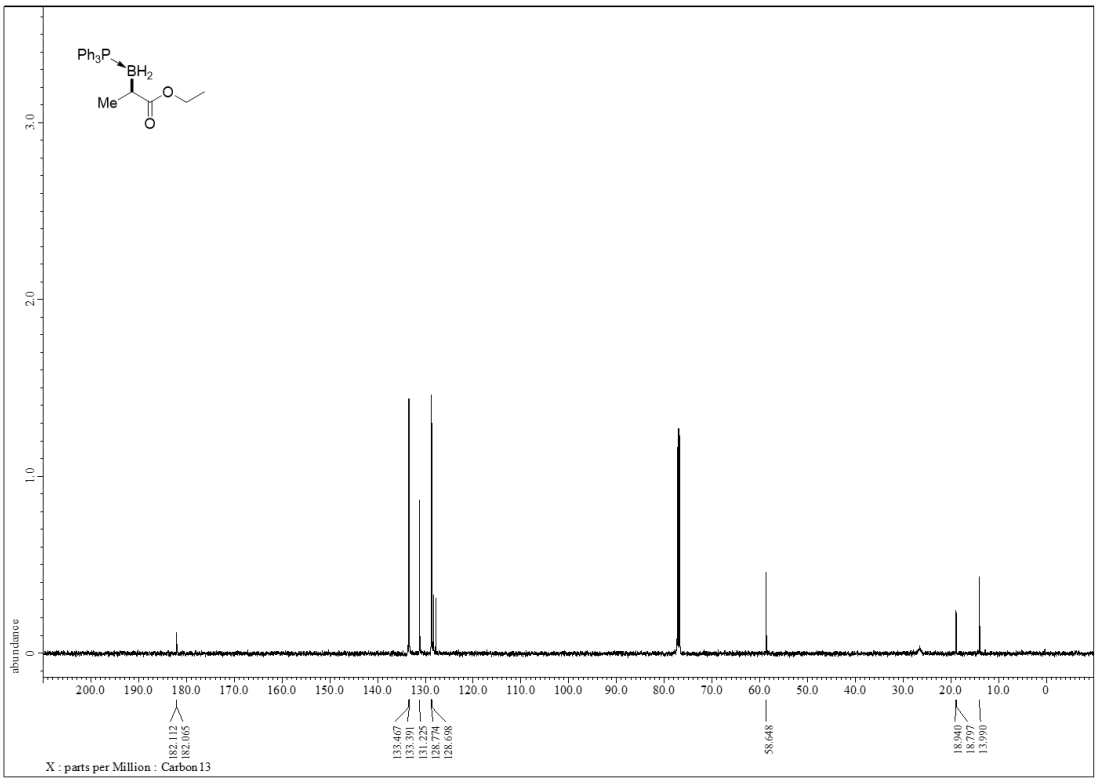
3.11
1.00
1.00
3.14
3.18
3.14
abundance
X : parts per Million : Proton


Ph3P
BH2
Me
O
O
abundance
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133.391
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128.774
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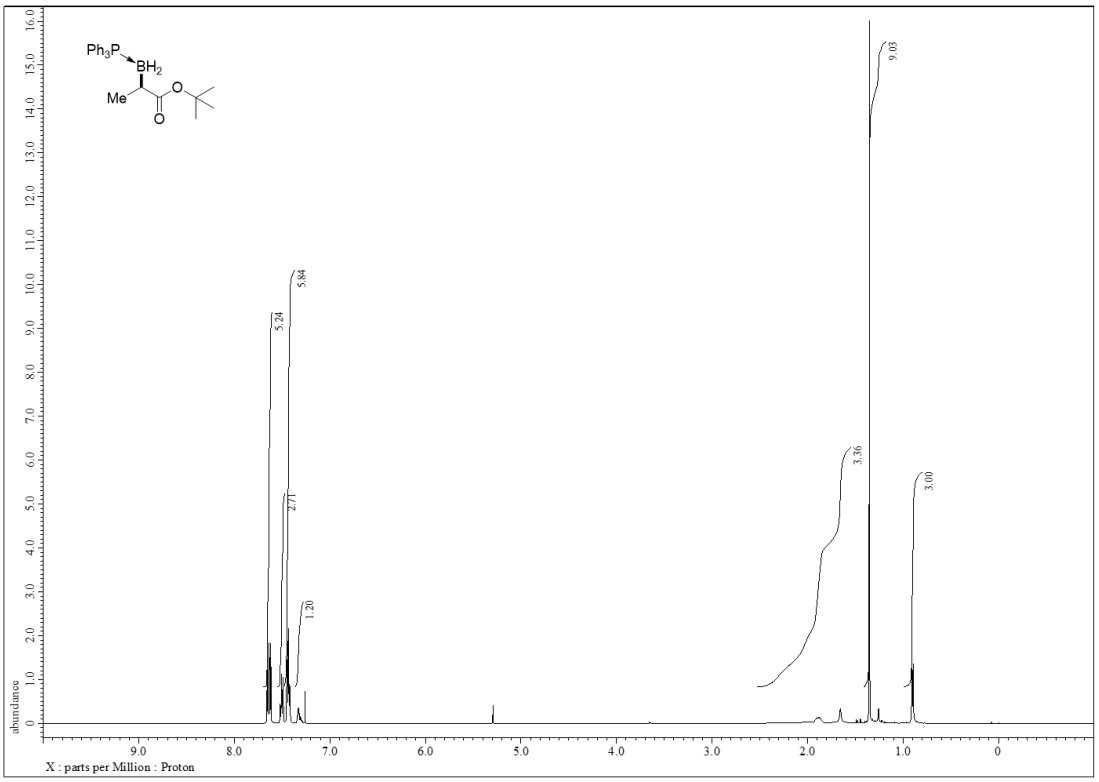
18.940
18.797
13.990
X : parts per Million : Carbon13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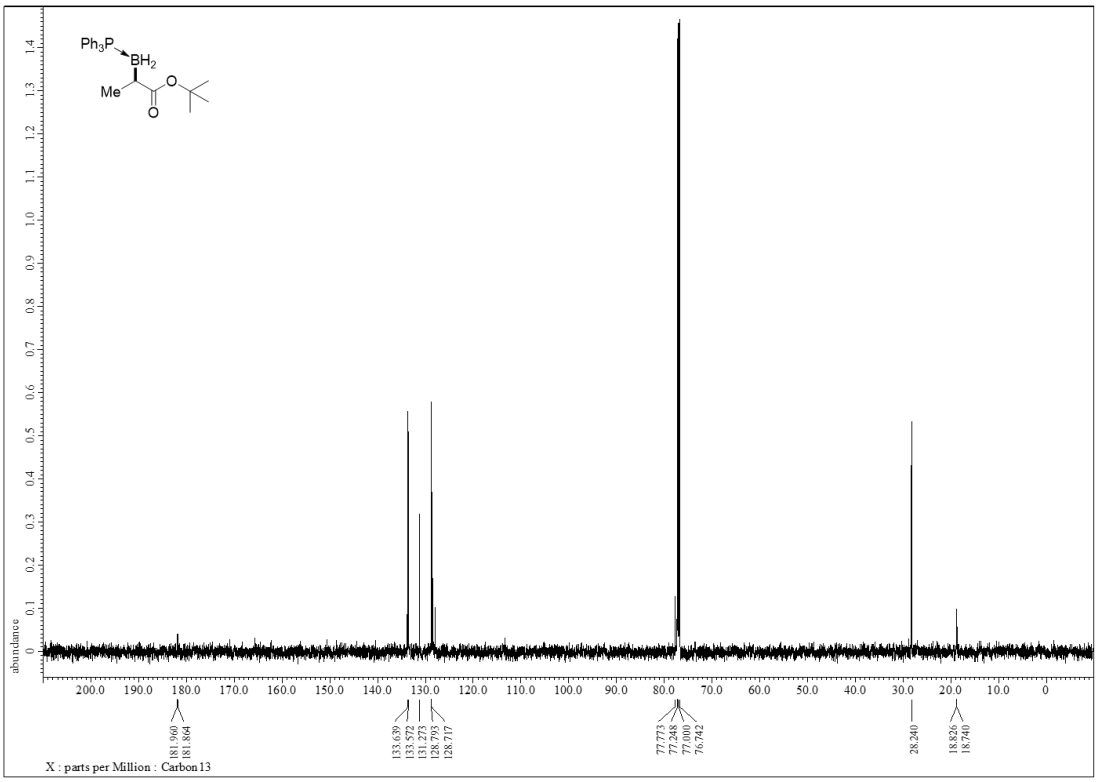
abundance
X : parts per Million : Proton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BH2
Me
O
O
abundance
181.960
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133.572
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77.773
77.248
77.000
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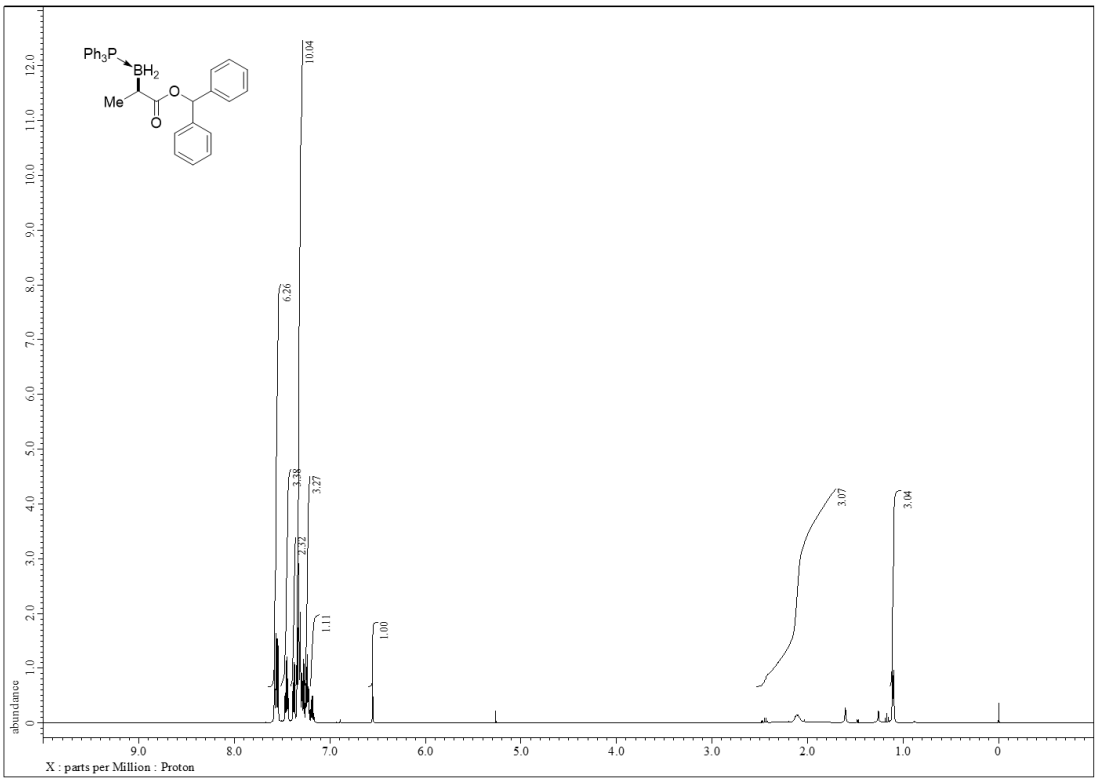
18.826
18.740
X : parts per Million : Carbon13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BH2
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O
O
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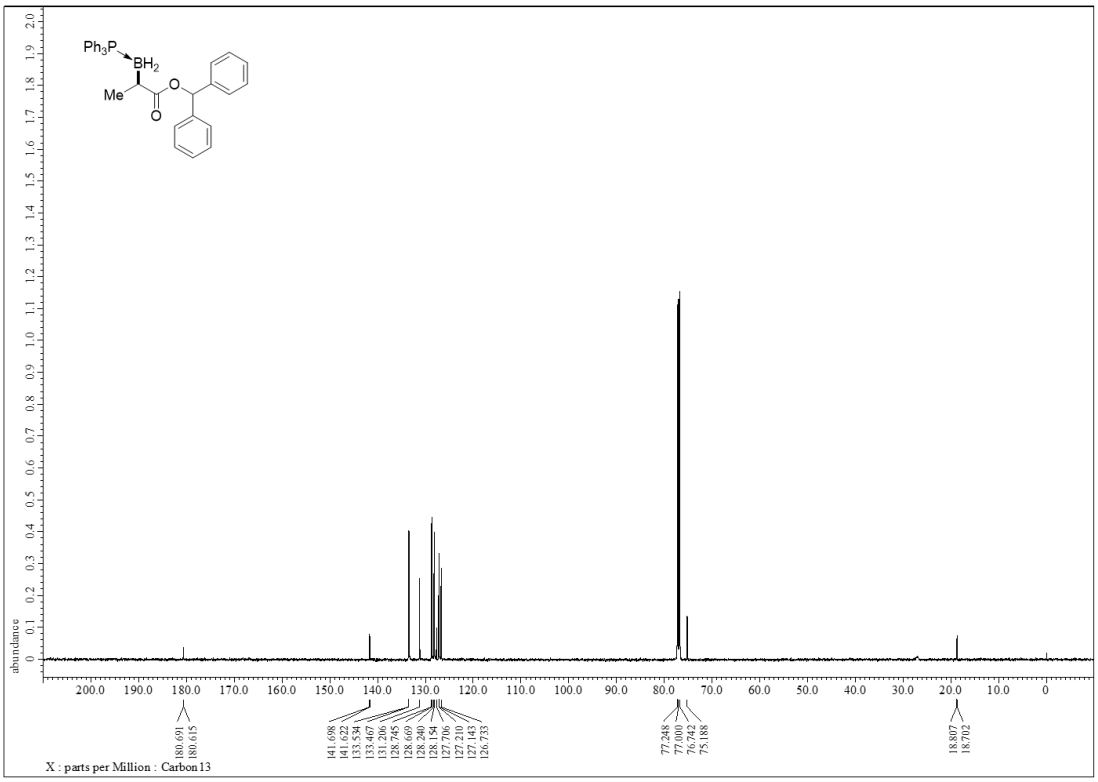
3.27
2.22
1.11
1.00
3.07
3.04
abundance
X : parts per Million : Proton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BH2
Me
O
O
abundance
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141.698
141.622
133.534
133.467
131.206
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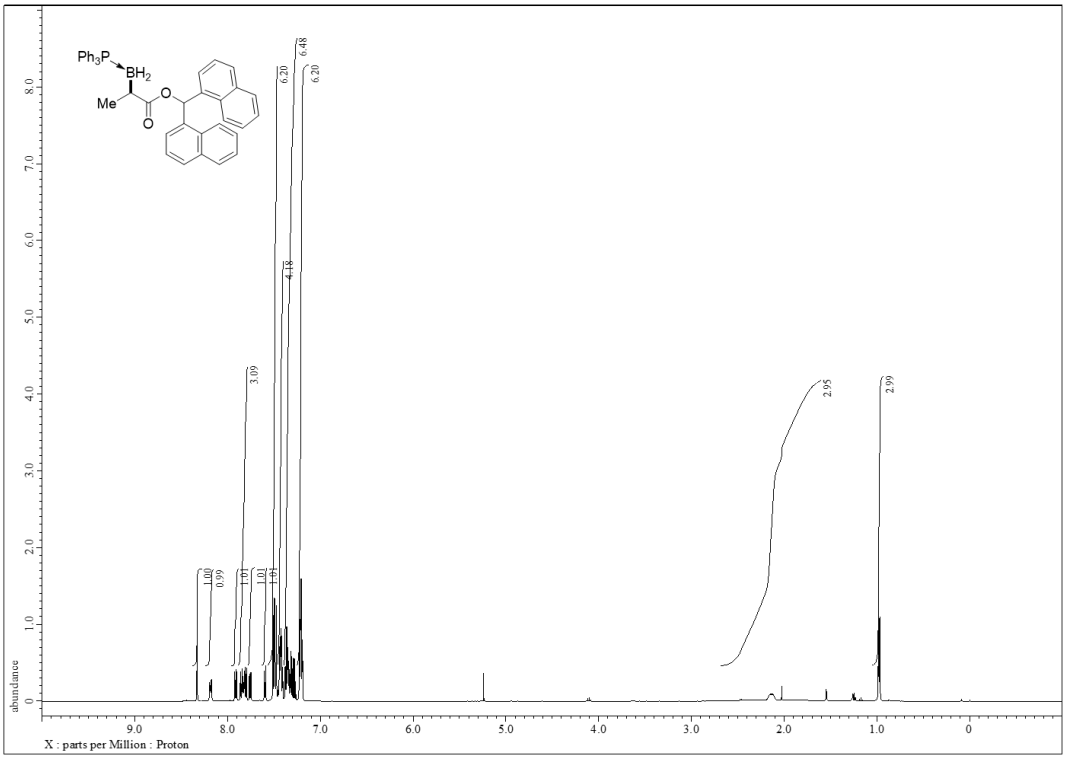
128.669
128.240
128.154
127.706
127.210
127.143
126.733
77.248
77.000
76.742
75.188
18.807
18.702
X : parts per Million : Carbon13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O
6.48
6.20
6.20
4.18
3.09
2.95
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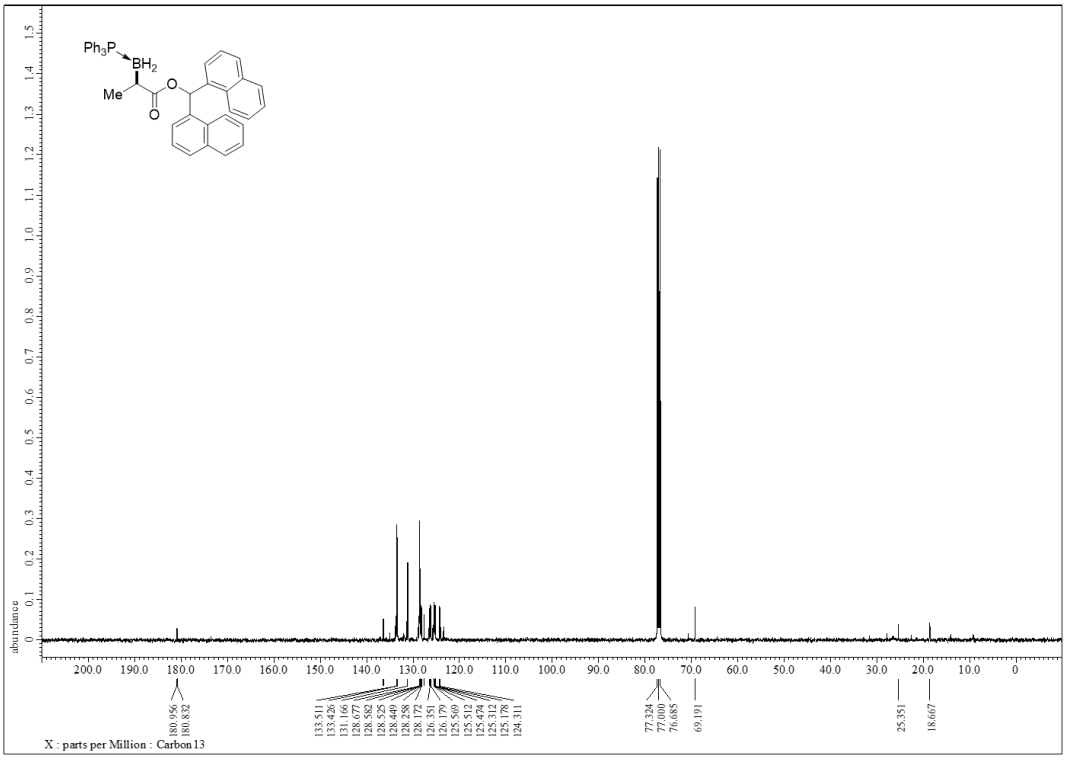
1.00
0.99
1.01
1.01
1.03
abundance
X : parts per Million : Proton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BH2
Me
O
O
abundance
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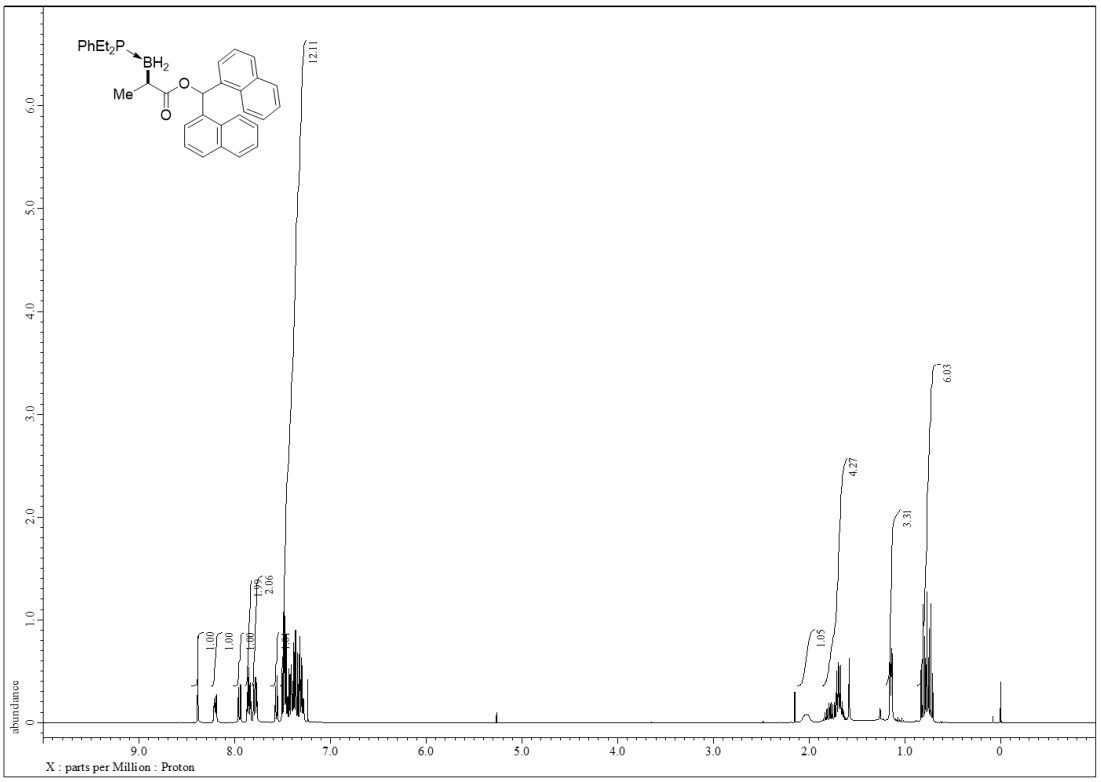
133.426
131.166
128.677
128.582
128.525
128.449
128.258
128.172
126.551
126.370
125.569
125.512
125.474
125.312
125.178
124.311
77.324
77.000
76.685
69.191
25.351
18.667
X : parts per Million : Carbon13


PhEt2P
BH2
Me
O
O
12.11
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4.27
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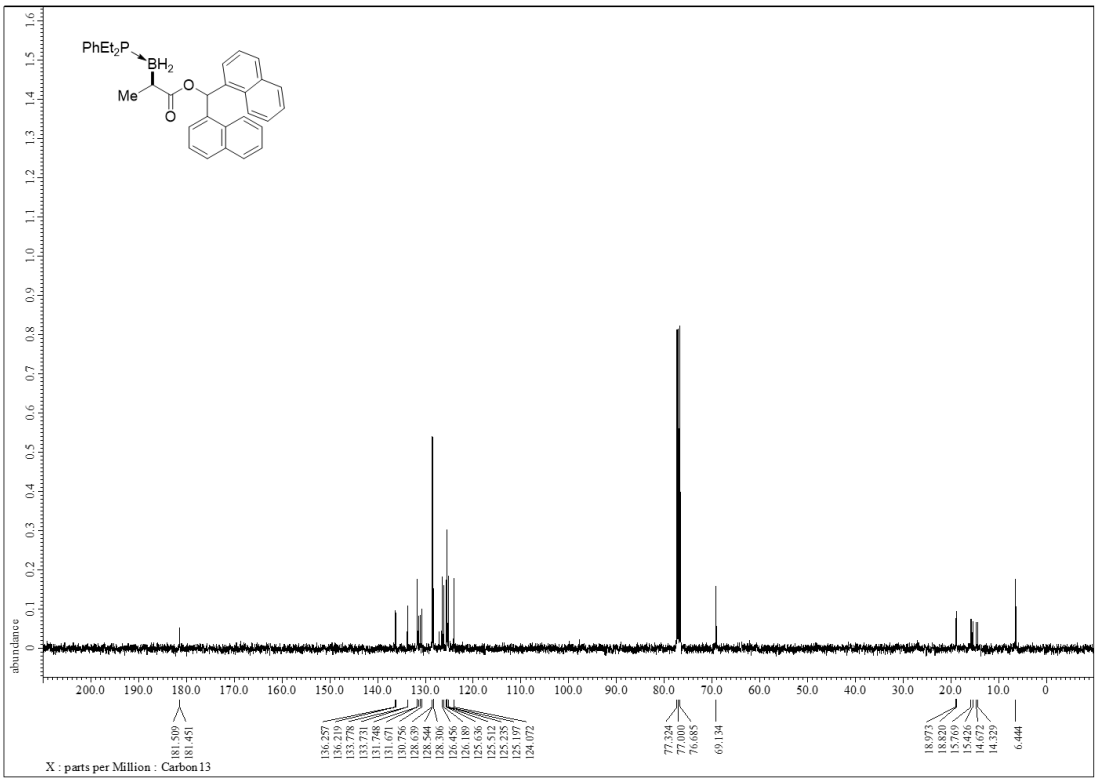
2.06
1.95
1.05
1.00
1.00
1.00
abundance
X : parts per Million : Proton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BH2
Me
O
O
abundance
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133.778
133.731
131.488
131.471
130.756
128.639
128.544
128.306
126.456
126.189
125.636
125.512
125.235
125.197
124.072
77.324
77.000
76.685
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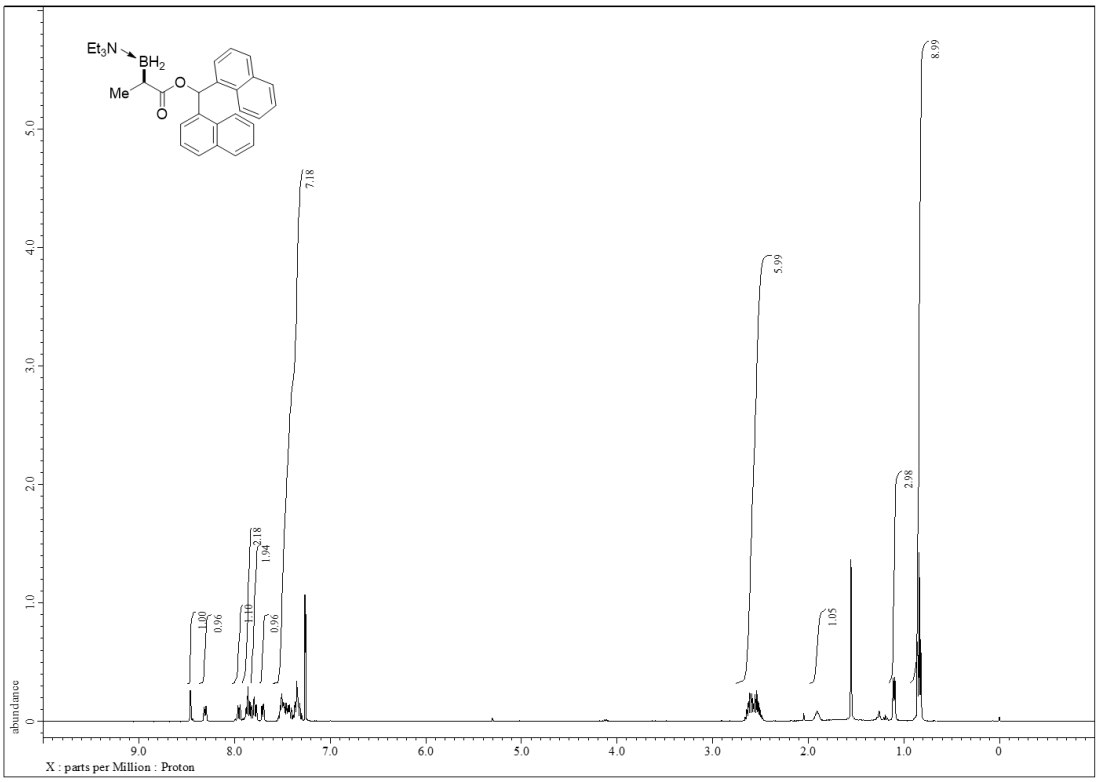
18.820
15.769
15.426
14.672
14.329
6.444
X : parts per Million : Carbon13


Et3N
BH2
Me
O
O
abundance
X : parts per Million : Proton
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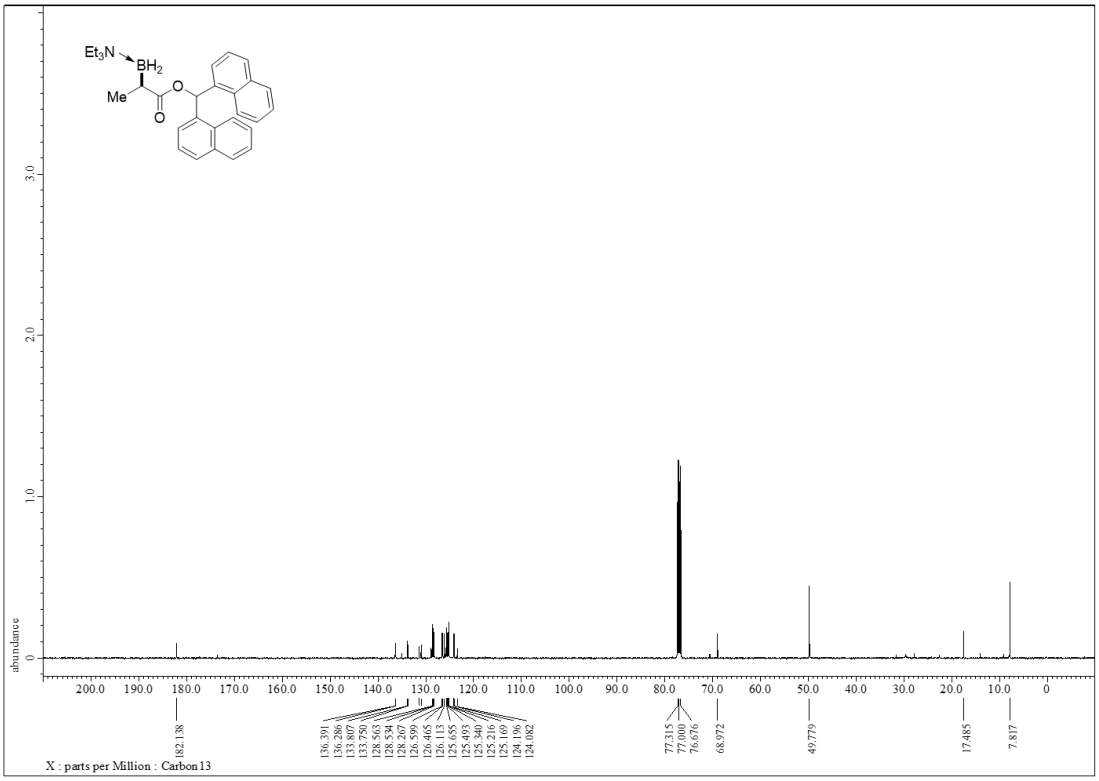
5.99
8.99
2.98
2.18
1.94
1.16
1.00
0.96
0.96
1.05


Et3N
BH2
Me
O
O
abundance
X : parts per Million : Carbon13
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133.750
128.563
128.534
128.254
126.599
126.465
126.113
125.655
125.493
125.340
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124.106
124.062
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77.000
76.676
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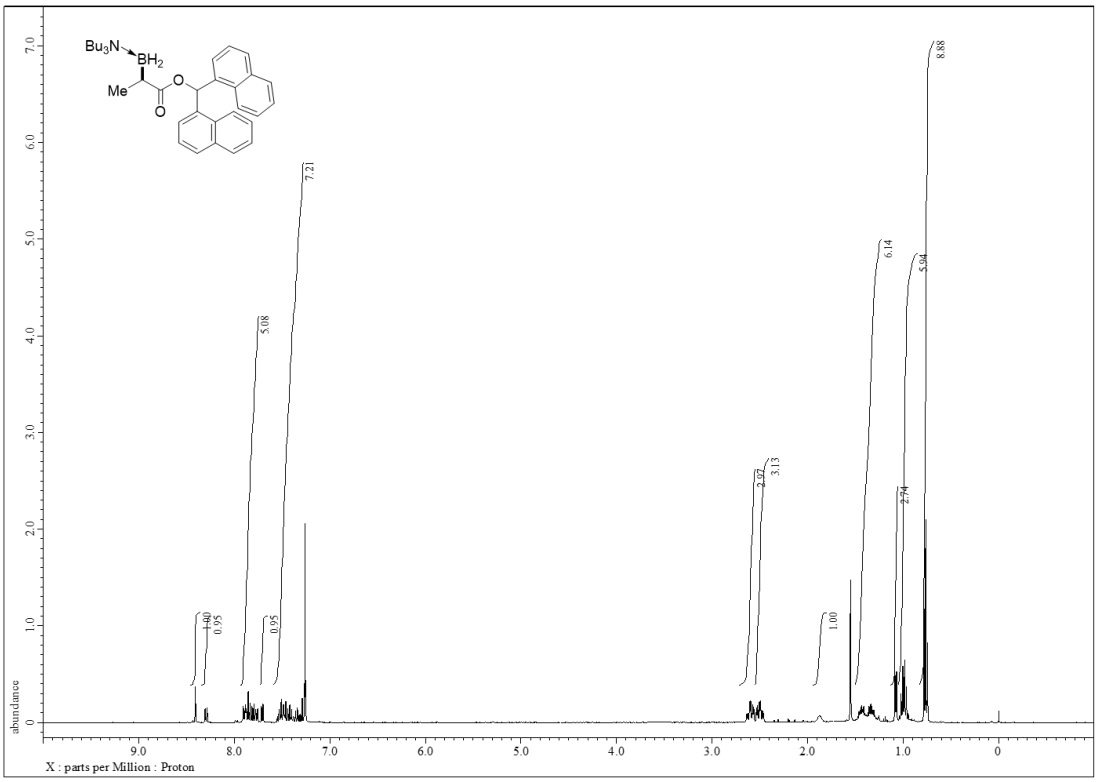
17.485
7.817


Bu3N
BH2
Me
O
O
abundance
X : parts per Million : Proton
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0.95
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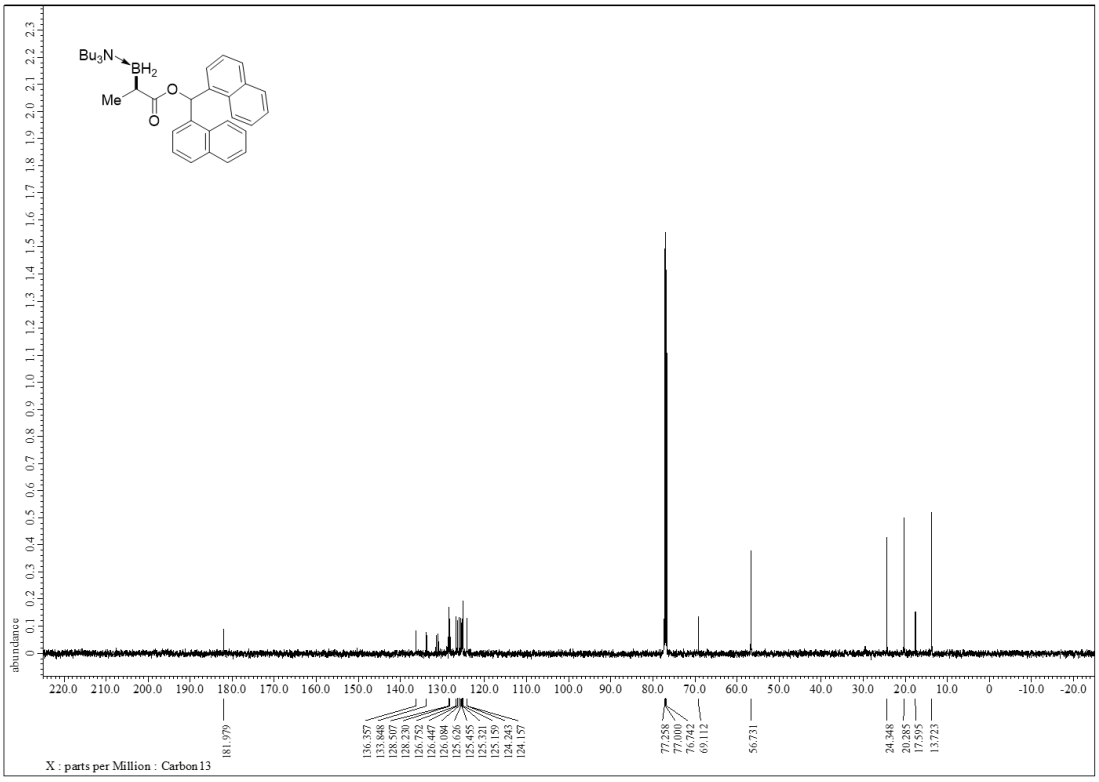
3.13
1.00
6.14
2.74
5.94
8.88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BH2
Me
O
O
abundance
X : parts per Million : Carbon13
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126.447
126.084
125.628
125.455
125.321
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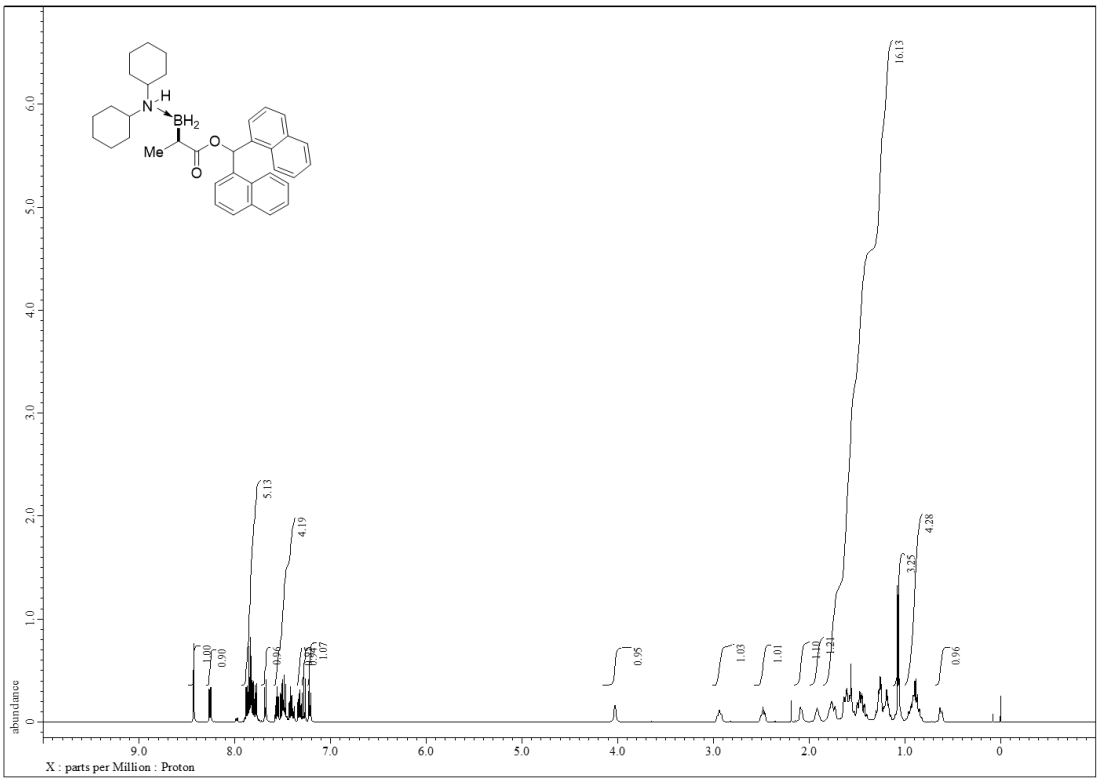
17.595
13.723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H
BH2
Me
O
O
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5.13
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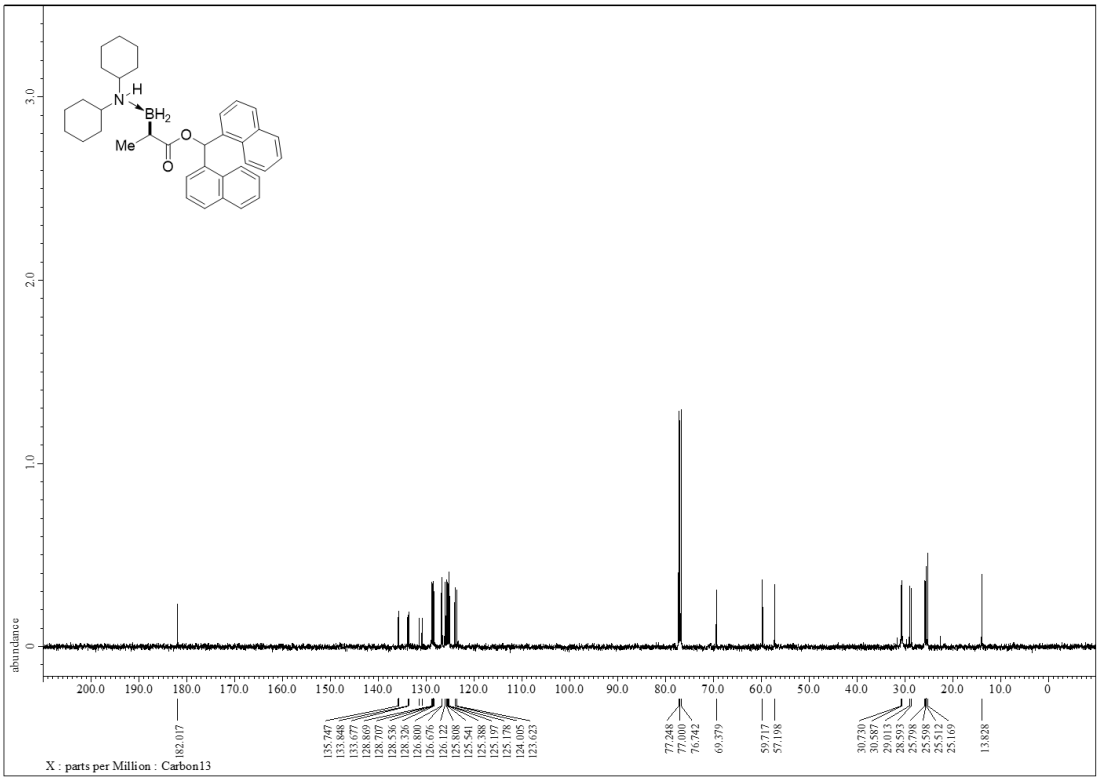
4.28
3.25
1.00
0.90
0.94
0.92
1.07
0.95
1.03
1.01
1.10
1.31
0.96
abundance
X : parts per Million : Proton


N
H
BH2
Me
O
O
abundance
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126.675
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123.623
77.248
77.000
76.742
69.379
59.717
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29.013
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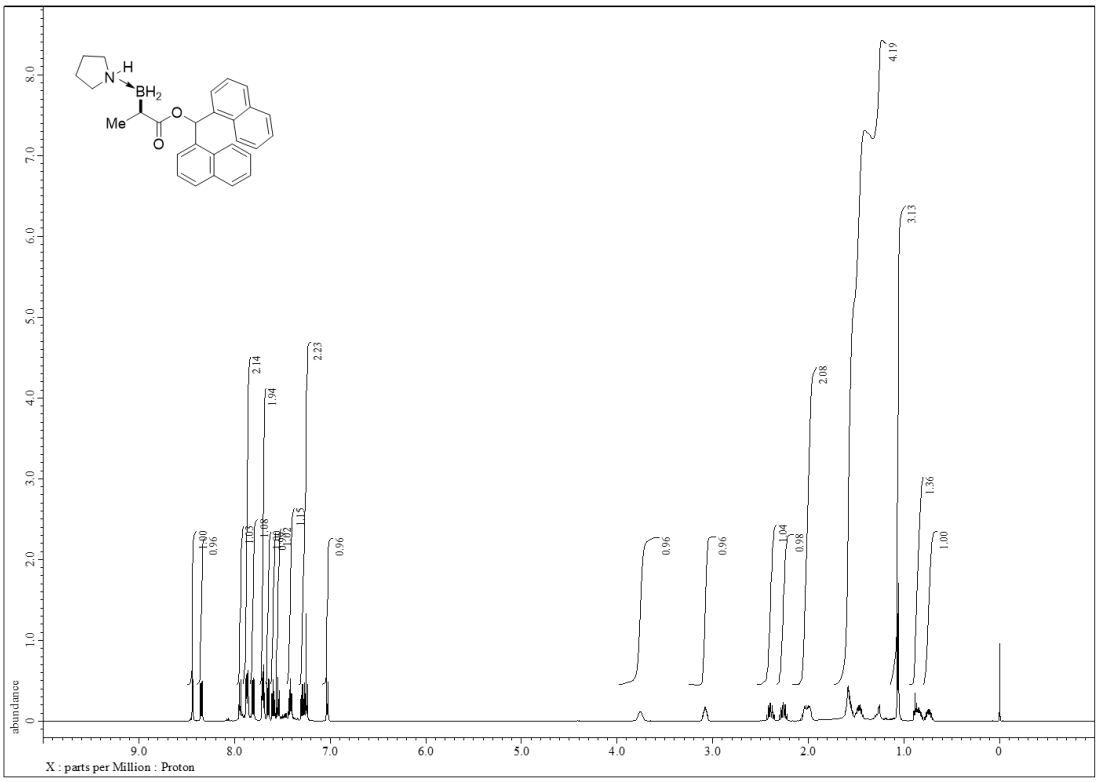
25.798
25.598
25.512
25.169
13.828
X : parts per Million : Carbon13


abundance
X : parts per Million : Proton
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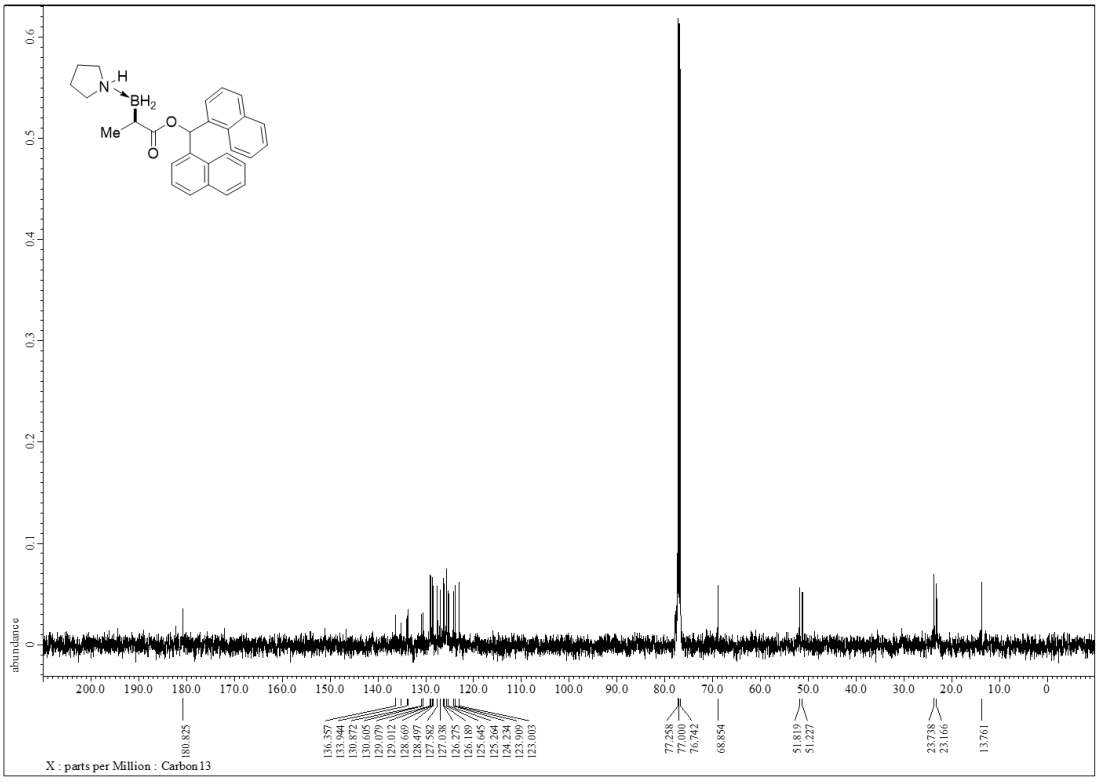
2.08
1.36
1.15
1.00
0.96
0.98
1.04


abundance
X : parts per Million : Carbon13
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133.944
130.872
130.605
129.079
129.012
128.669
128.497
127.582
127.038
126.275
126.189
125.645
125.264
124.234
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23.166
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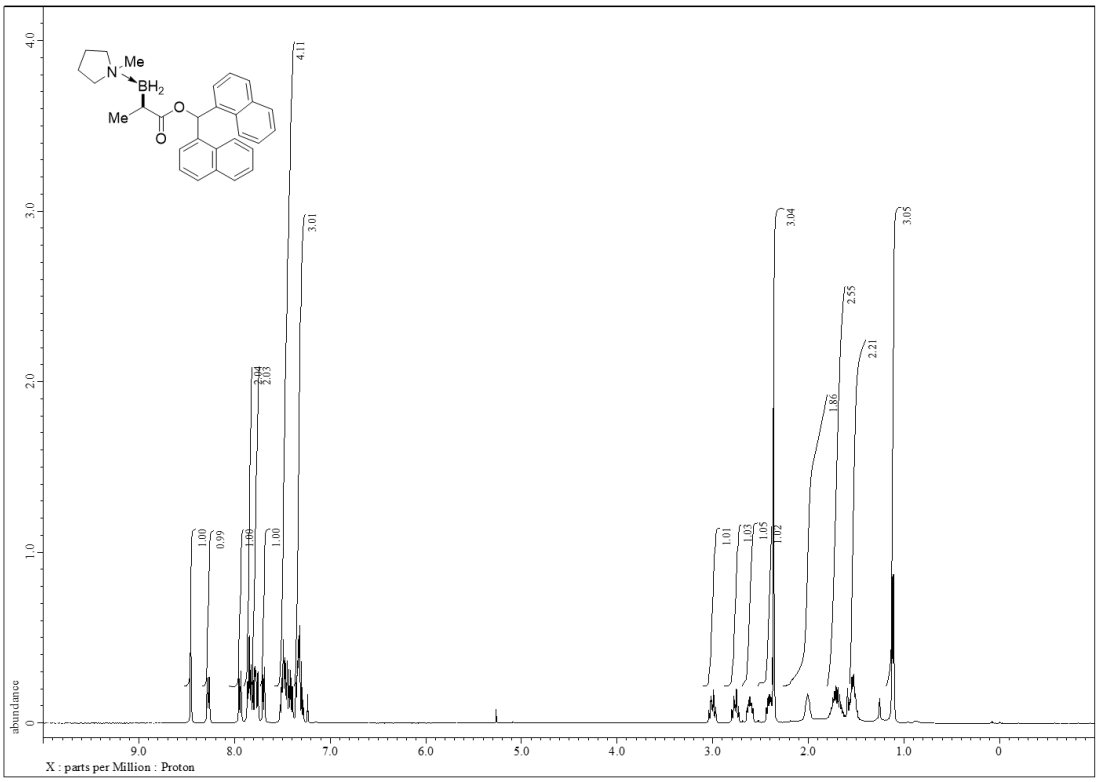
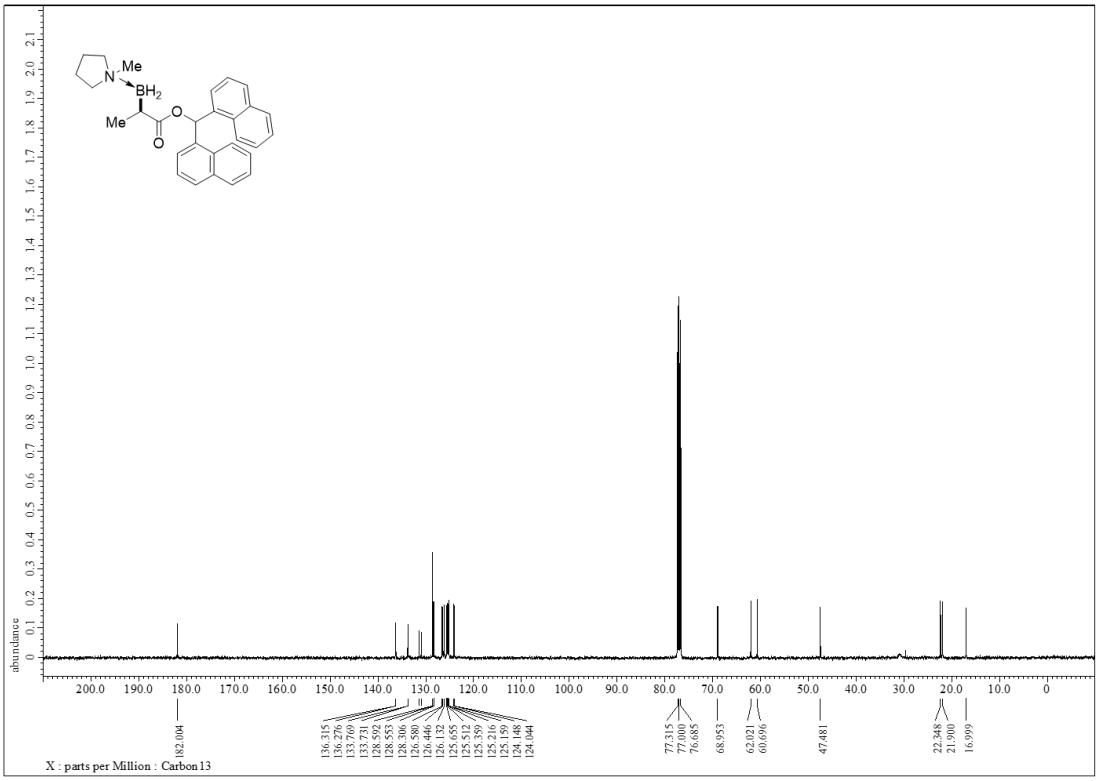
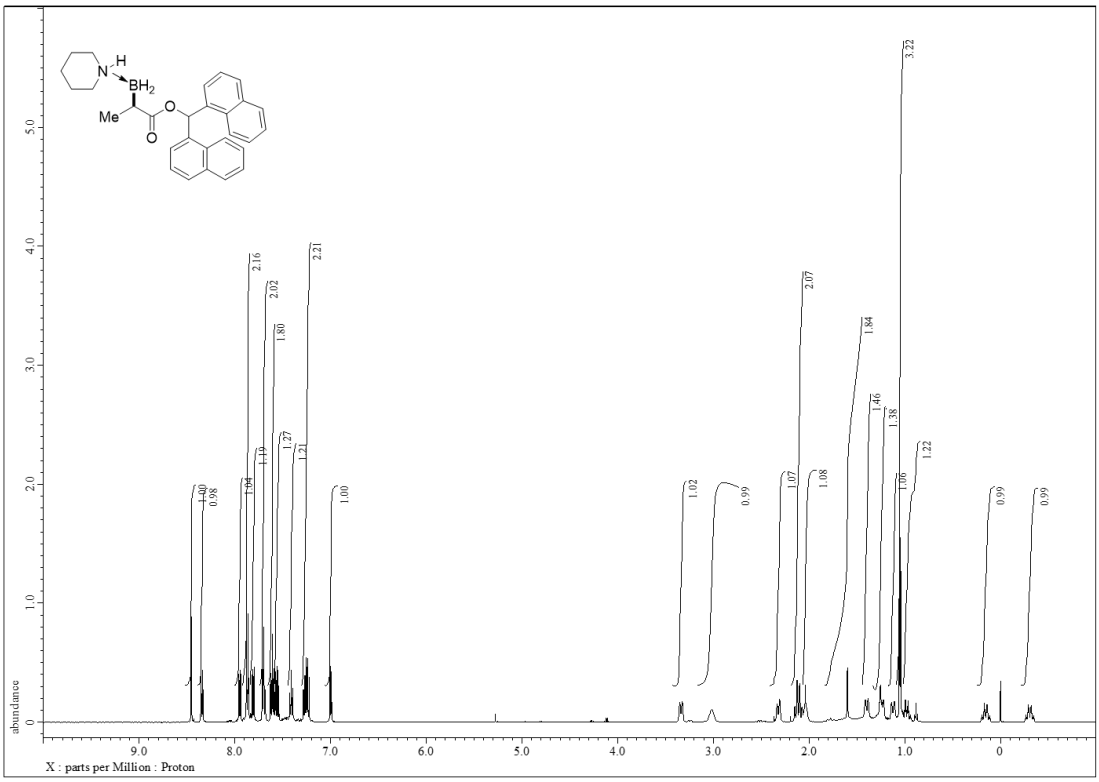
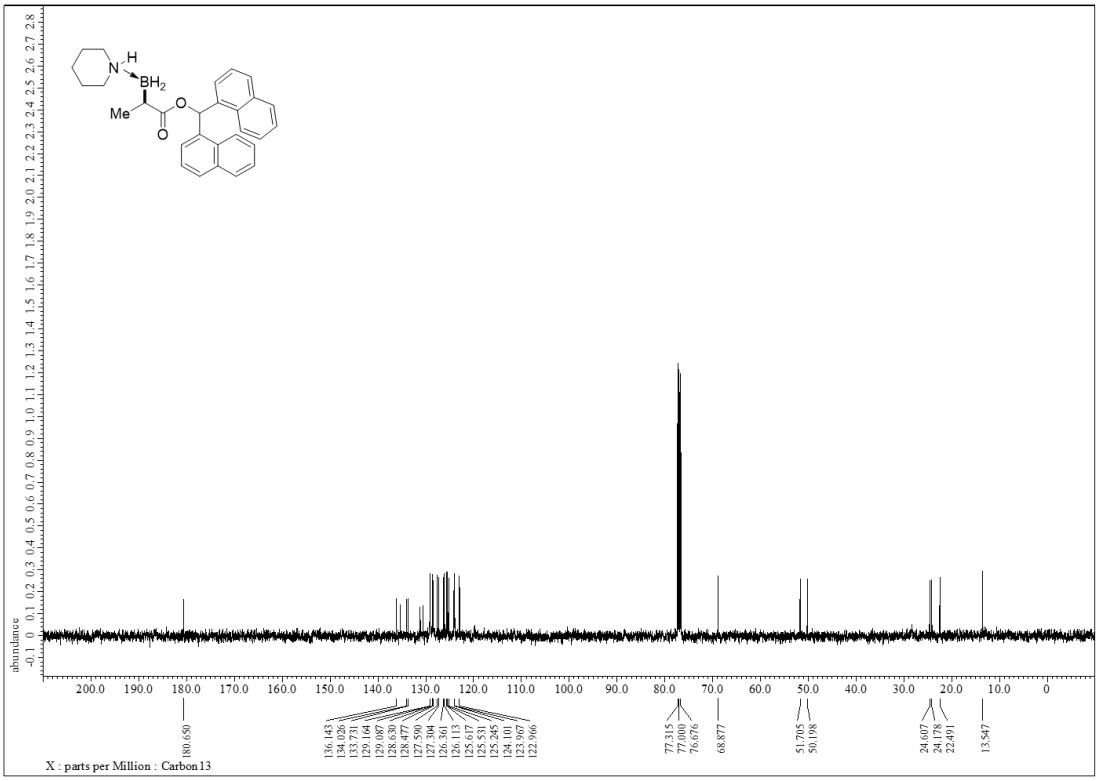
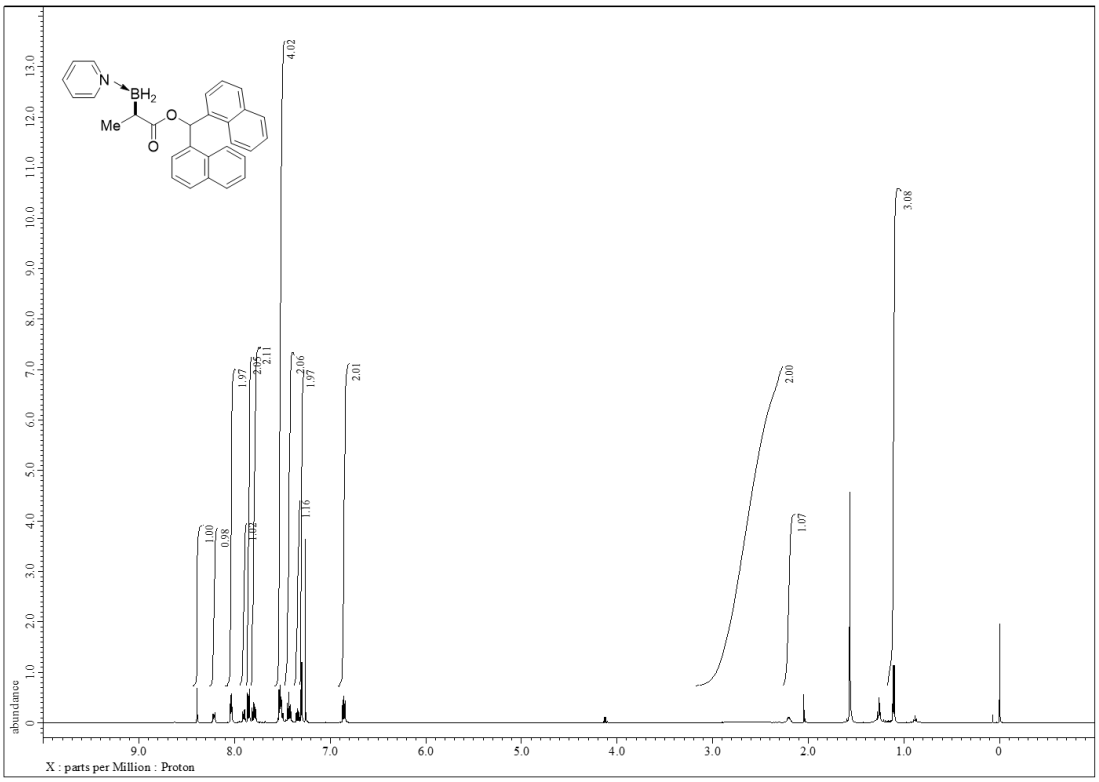
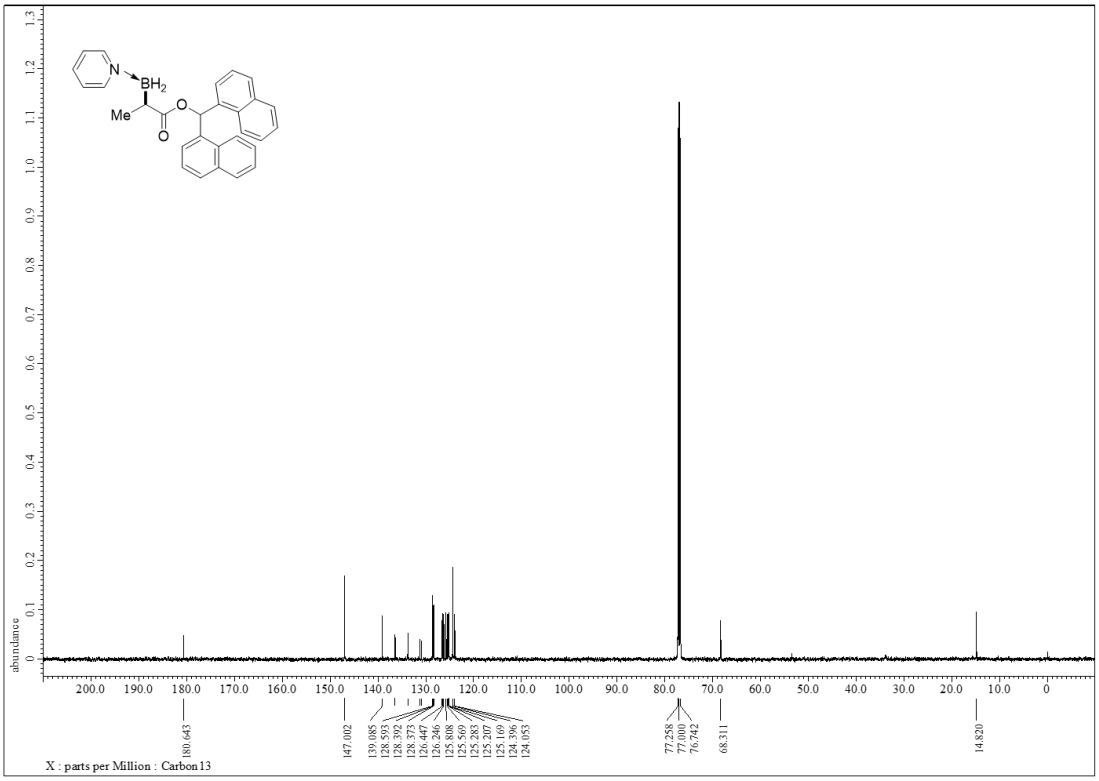

Me
N
BH2
Me
O
O
4.11
3.01
3.04
3.05
2.55
2.21
1.86
2.04
2.03
1.00
0.99
1.00
1.00
1.01
1.03
1.05
1.02
abundance
X : parts per Million : Proton


Me
N
BH2
Me
O
O
abundance
182.004
136.315
136.276
133.769
133.731
128.592
128.555
126.580
126.446
126.132
125.655
125.512
125.359
125.216
125.159
124.148
124.044
77.315
77.000
76.685
68.953
62.021
60.696
47.481
22.348
21.900
16.999
X : parts per Million : Carbon13


N
H
BH2
Me
O
O
abundance
X : parts per Million : Proton


N
H
BH2
Me
O
O
abundance
X : parts per Million : Carbon13


N
BH2
Me
O
O
4.02
3.08
2.00
2.01
2.11
2.05
2.06
1.97
1.97
1.16
1.07
1.00
0.98
1.02
abundance
X : parts per Million : Proton


N
BH2
Me
O
O
abundance
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147.002
139.085
128.593
128.392
128.373
126.447
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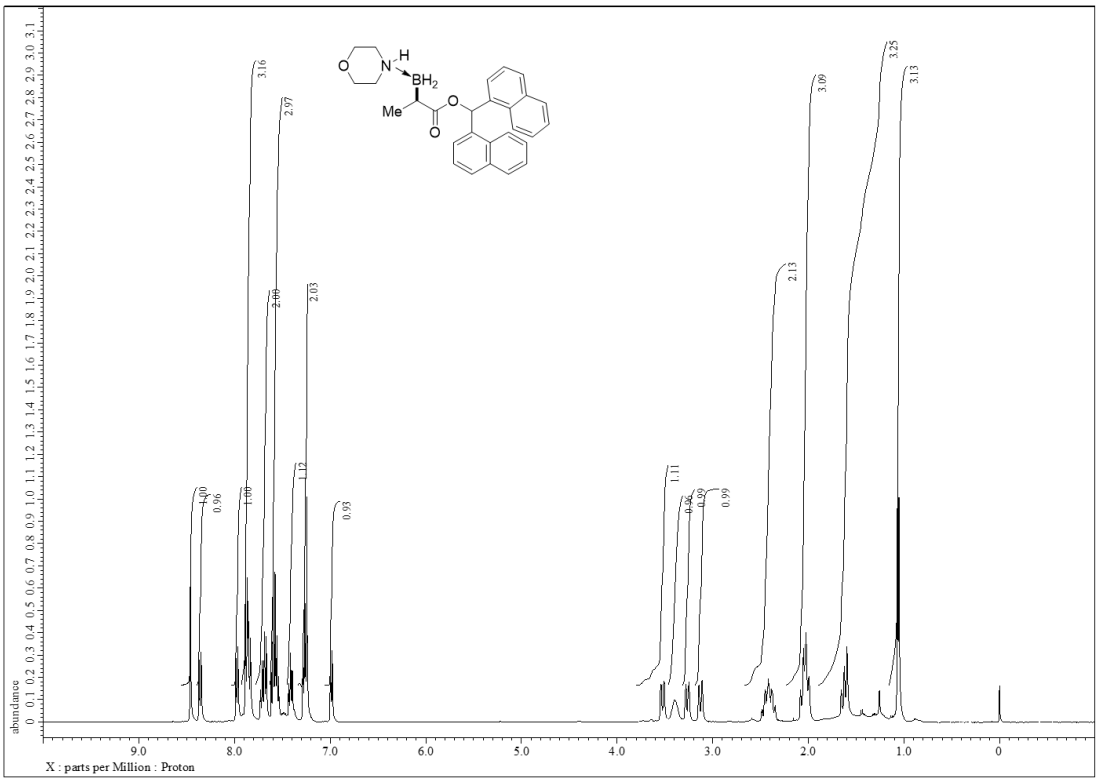
125.808
125.569
125.283
125.207
125.140
124.396
124.053
77.258
77.000
76.742
68.311
14.820
X : parts per Million : Carbon13


abundance
X : parts per Million : Proton
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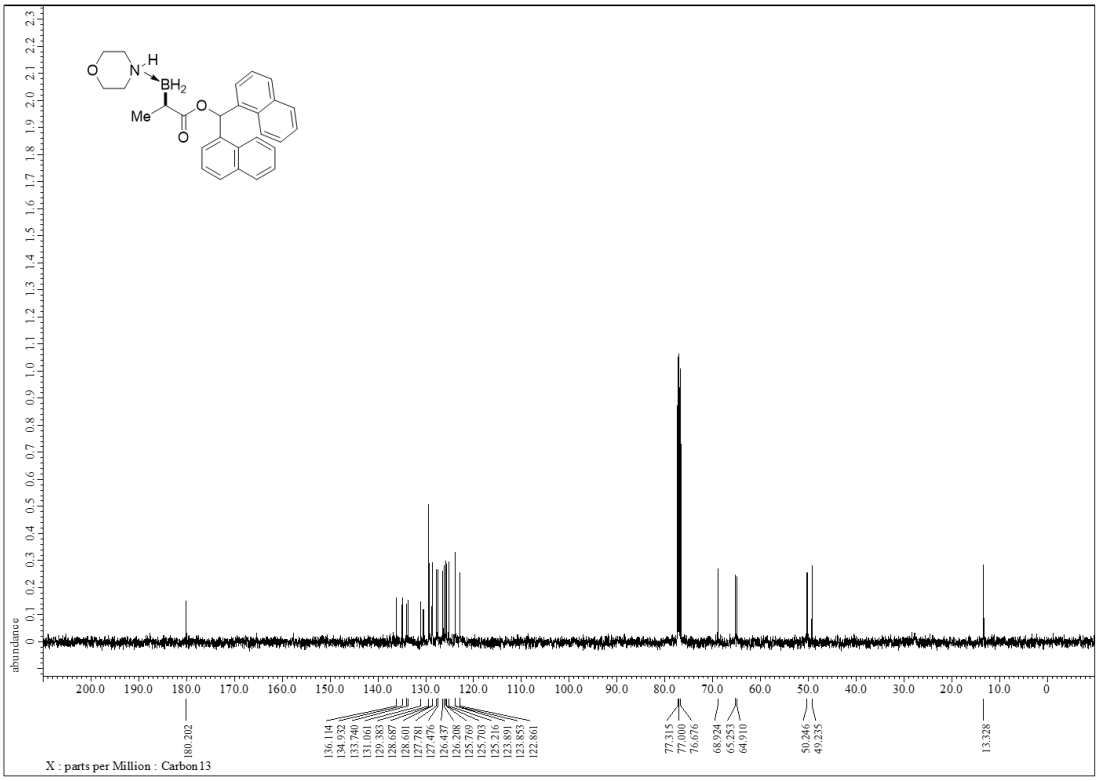
2.97
2.06
2.03
1.12
1.00
0.96
1.00
0.93
1.11
0.98
0.99
0.99
2.13
3.09
3.25
3.13


abundance
X : parts per Million : Carbon13
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134.932
133.740
131.061
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127.479
126.437
126.208
125.769
125.703
125.216
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76.676
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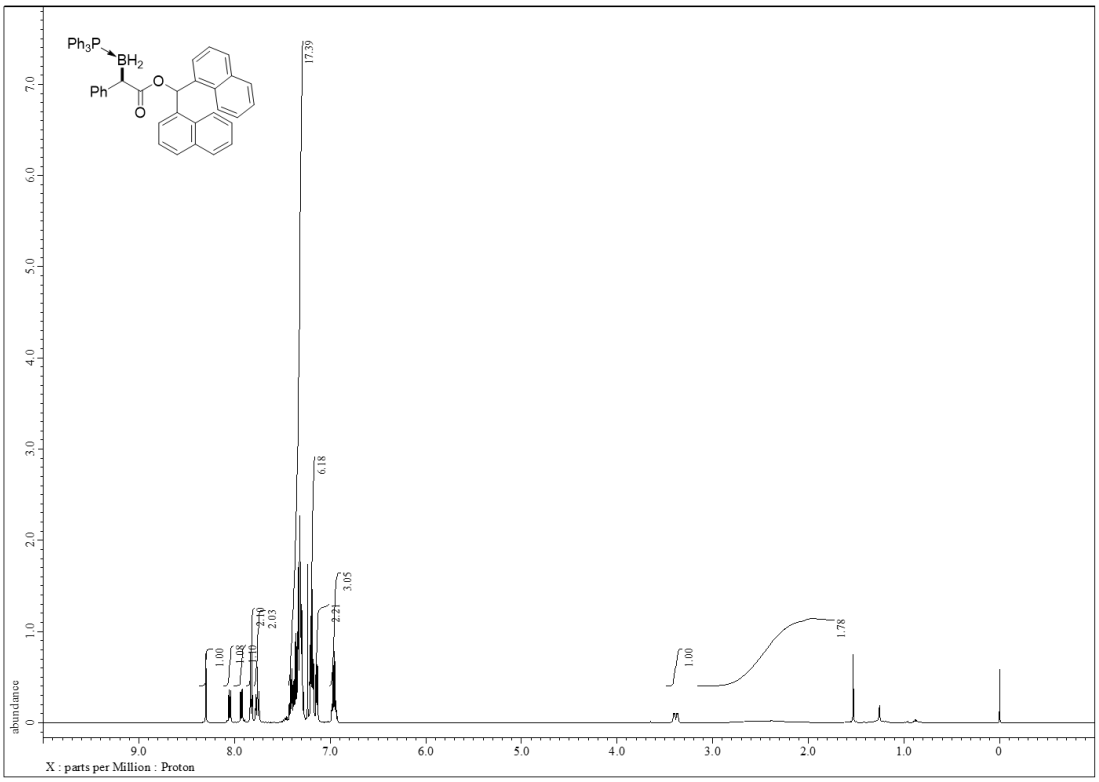
50.246
49.235
13.328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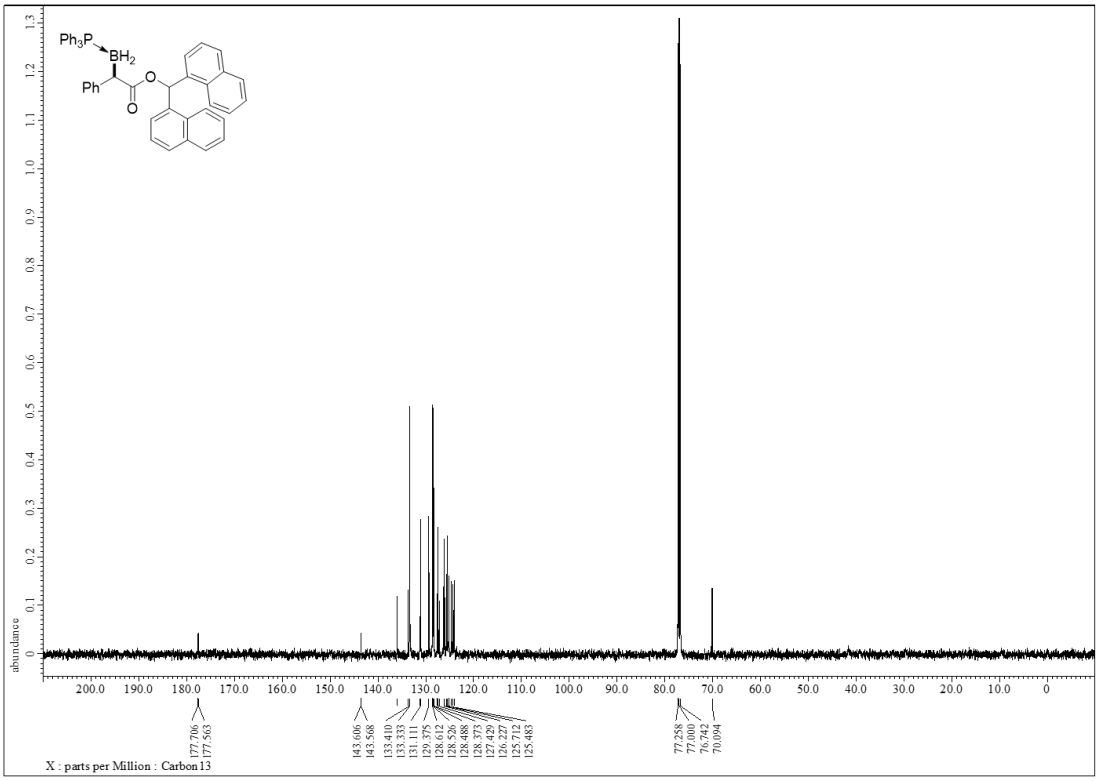
BH2
Ph
O
O
17.39
6.18
3.05
2.21
2.10
2.03
1.08
1.10
1.00
1.00
1.78
abundance
X : parts per Million : Proton


Ph3P
BH2
Ph
O
O
abundance
177.706
177.563
143.606
143.568
133.410
133.333
131.111
129.375
128.612
128.526
128.488
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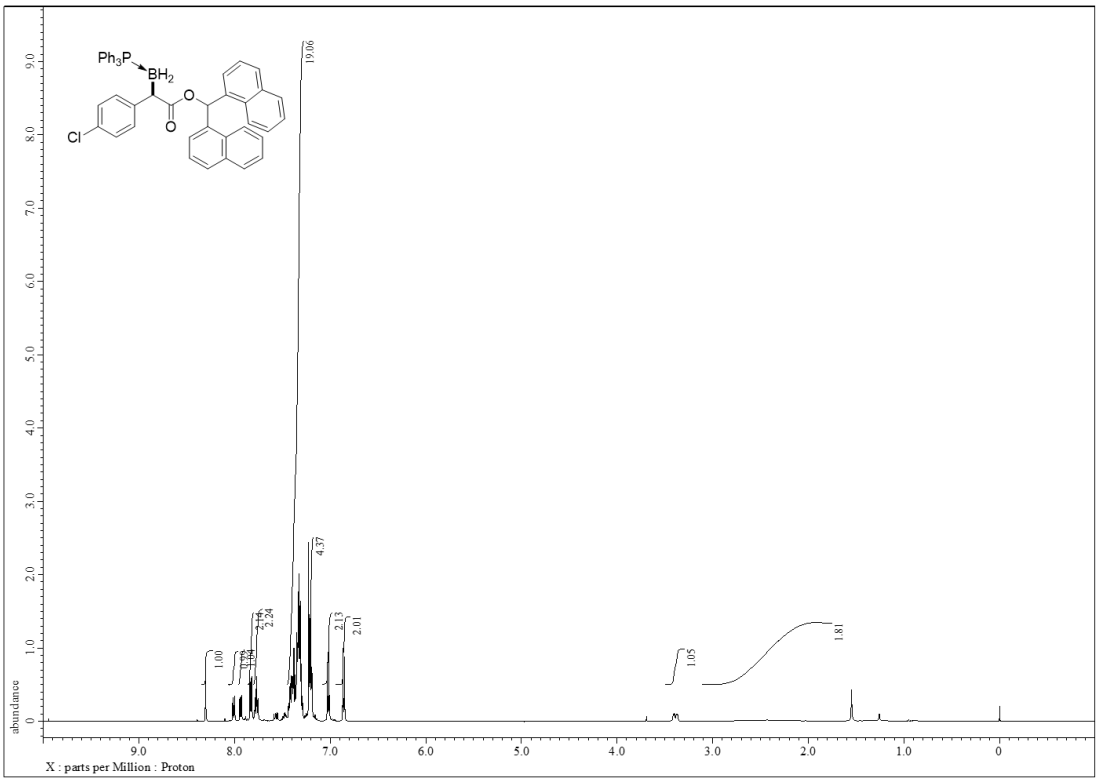
125.712
125.485
77.258
77.000
76.742
70.094
X : parts per Million : Carbon13


Ph3P
BH2
O
O
Cl
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2.13
2.01
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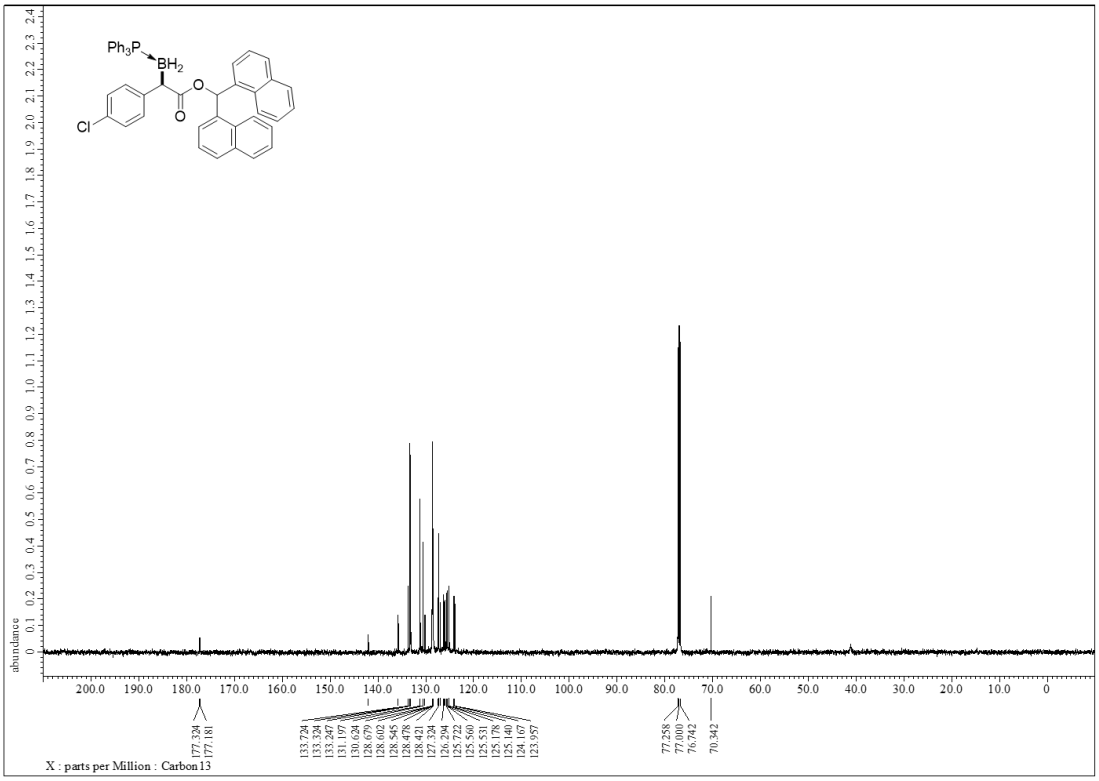
1.05
1.00
abundance
X : parts per Million : Proton


Ph3P
BH2
O
O
Cl
abundance
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177.181
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133.328
133.247
131.197
130.624
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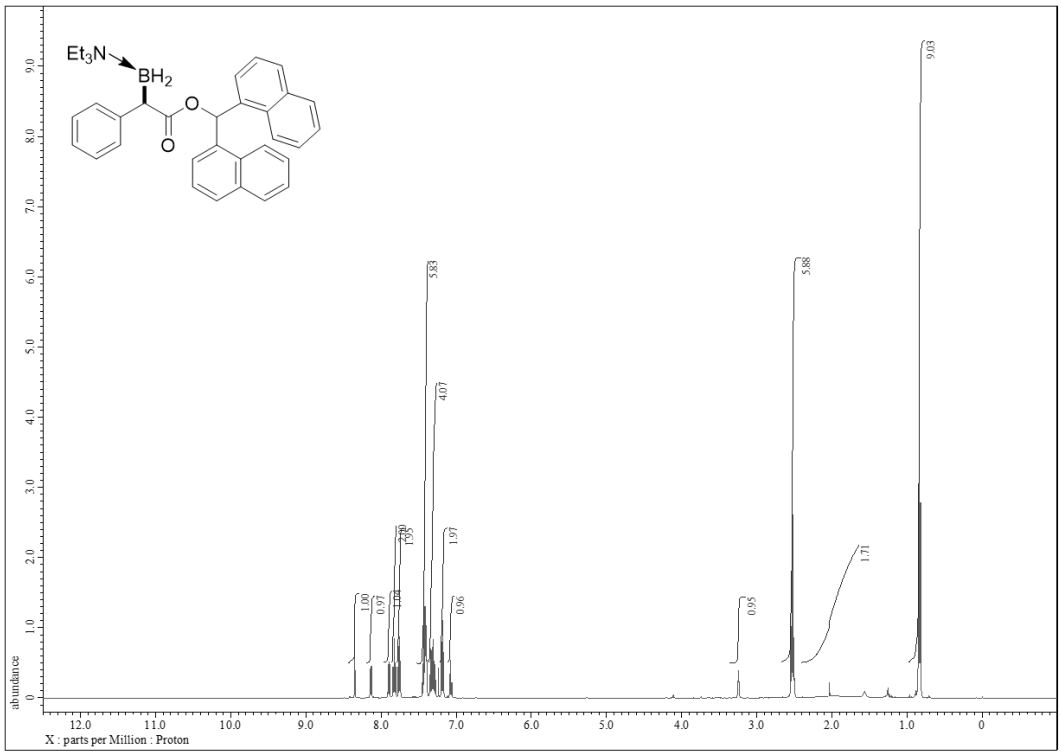
128.602
128.545
128.478
128.421
127.324
126.294
125.722
125.560
125.531
125.178
125.140
124.107
123.957
77.258
77.000
76.742
70.342
X : parts per Million : Carbon13


Et3N
BH2
O
O
abundance
X : parts per Million : Proton
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4.07
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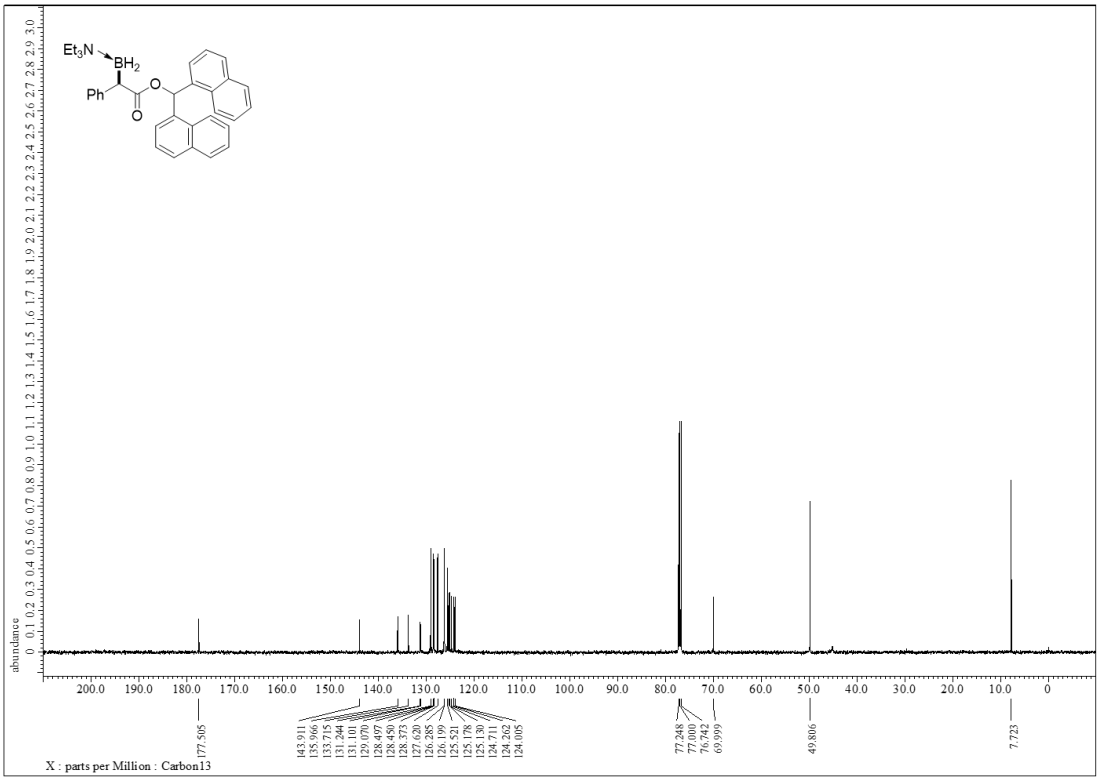
1.71
1.00
0.97
1.04
0.95
0.96


Et3N
BH2
Ph
O
O
abundance
X : parts per Million : Carbon13
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133.715
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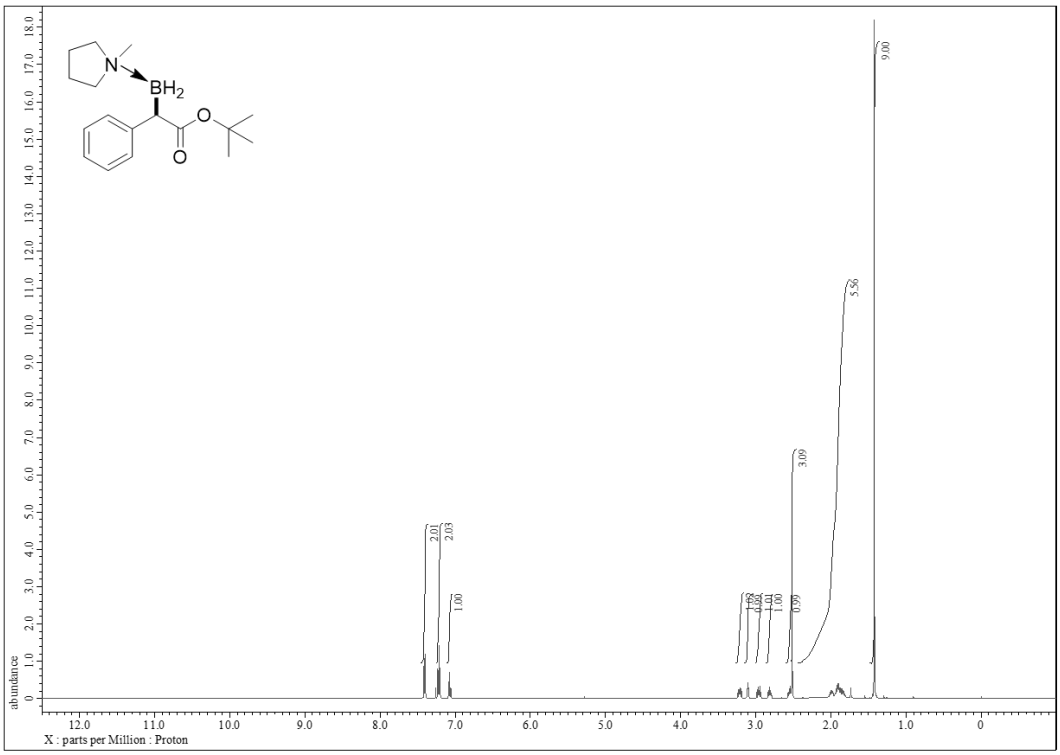
7.723


N
BH2
O
O
abundance
X : parts per Million : Proton
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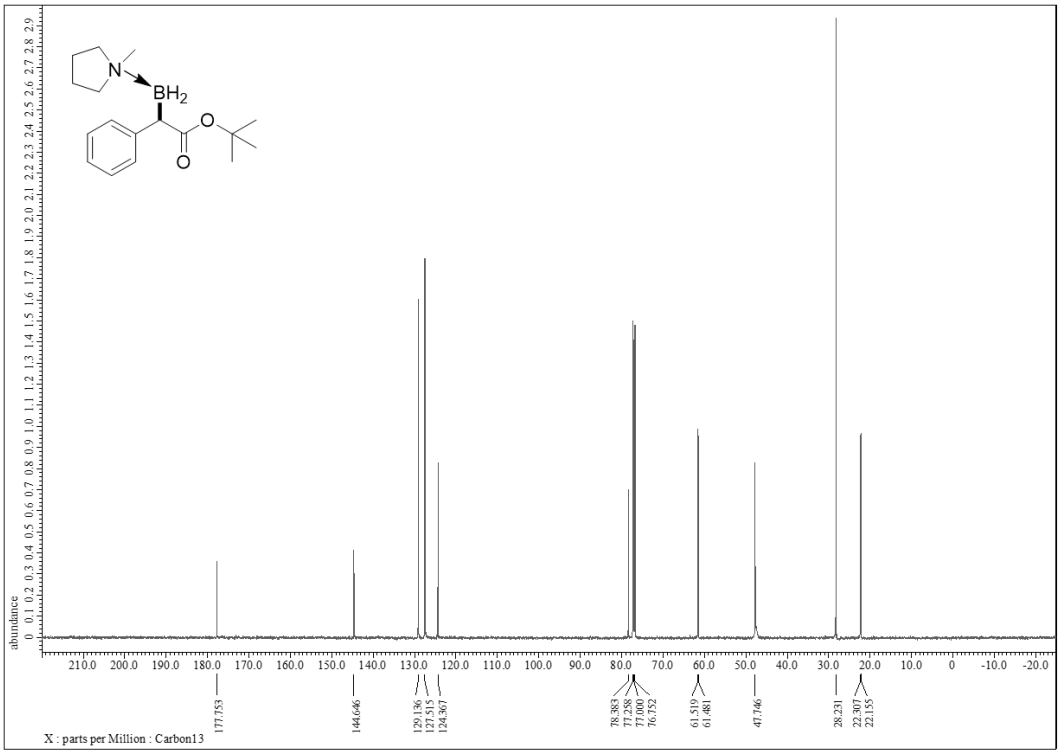
2.01
2.03
1.00
0.98
1.04
1.01
1.00
0.99


N
BH2
O
O
abundance
X : parts per Million : Carbon13
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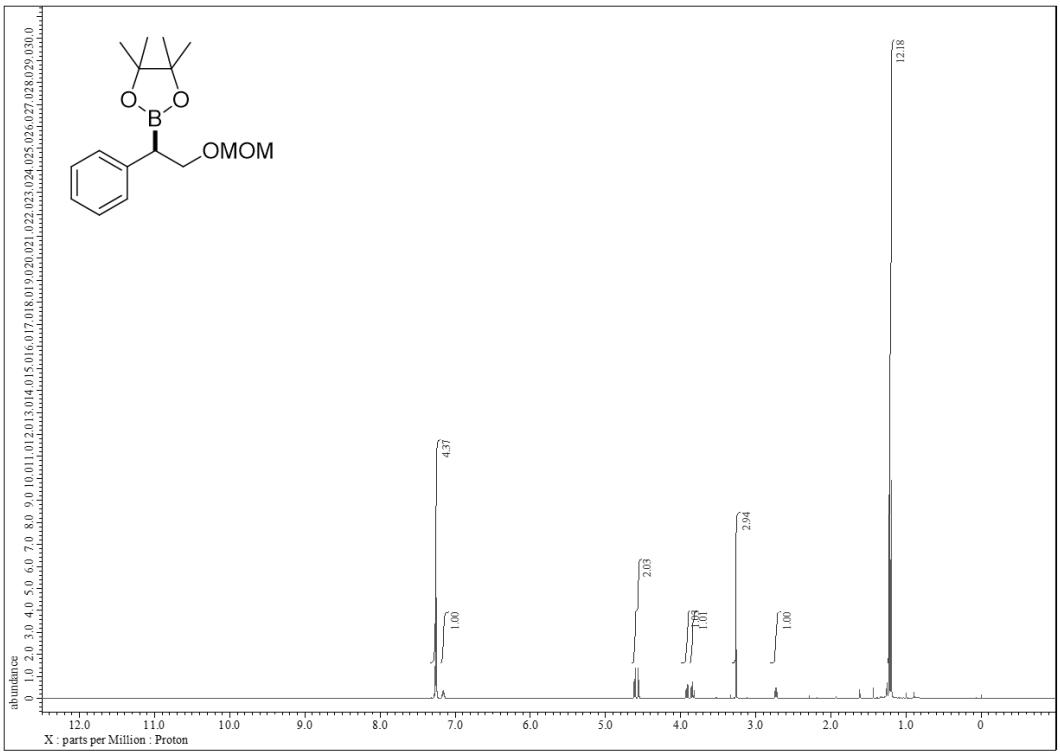
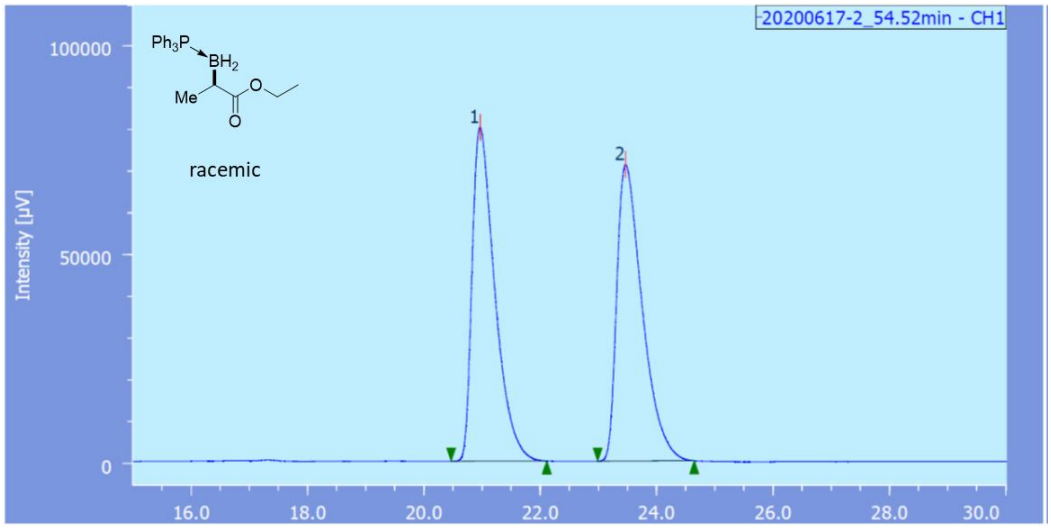
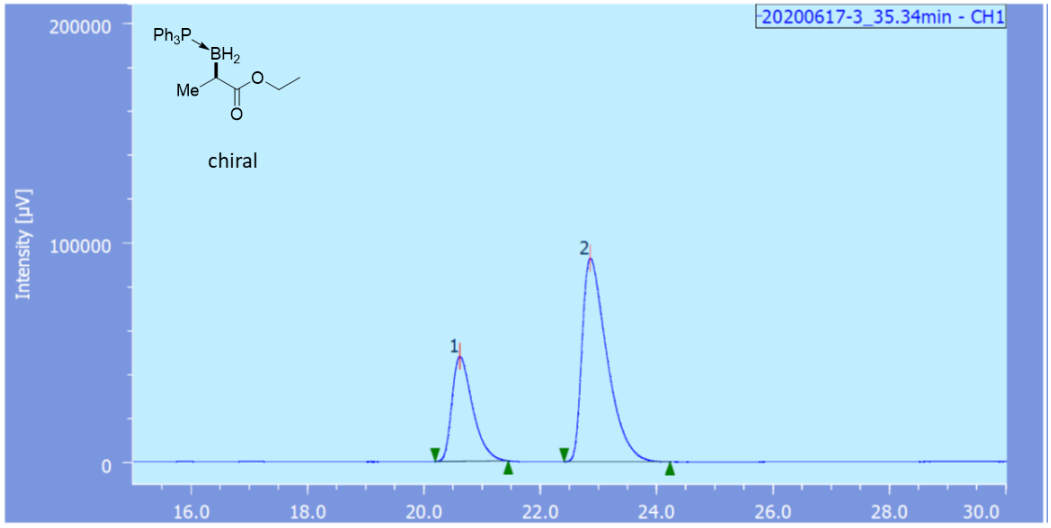
61.481
47.746
28.231
22.307
22.155


O
B
O
OMOM
4.37
1.00
2.03
1.01
2.94
1.00
12.18
abundance
X : parts per Million : Proton

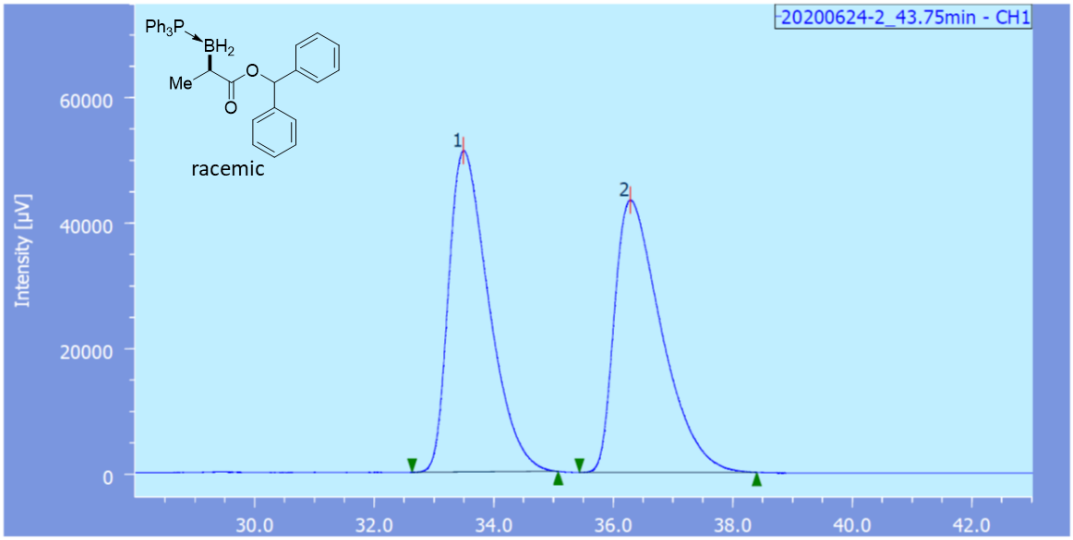
8-1-5　HPLC Spectral Data



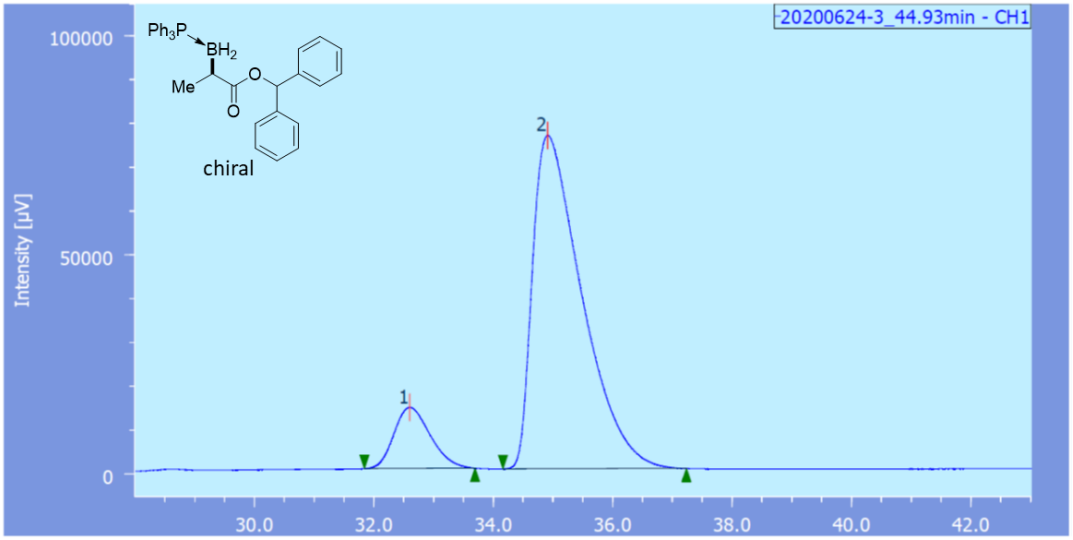
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.967	2162795	79887	50.052	52.939
2	23.467	2158345	71017	49.948	47.061



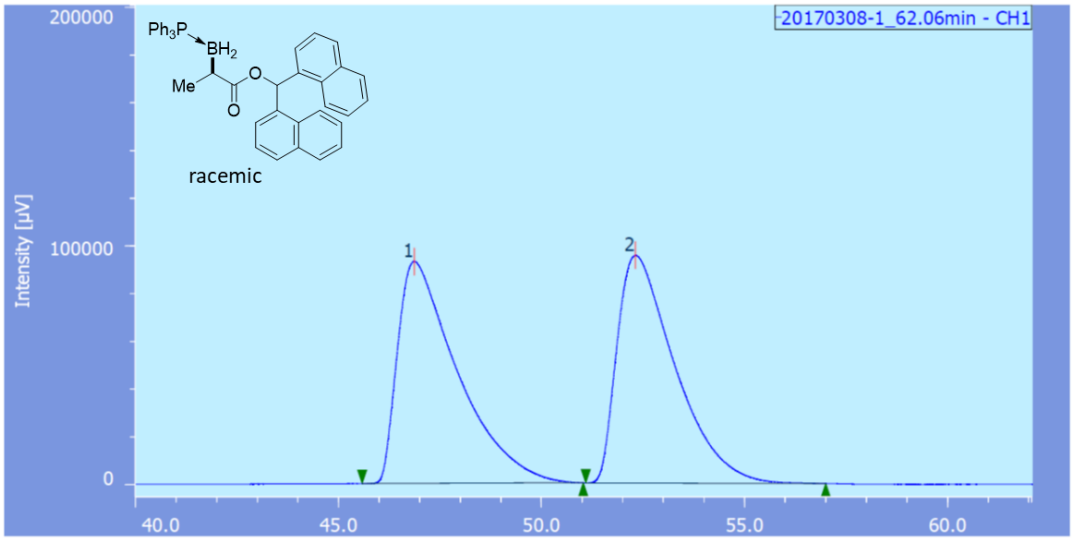
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.617	1182783	47836	29.987	34.053
2	22.858	2761503	92639	70.013	65.947



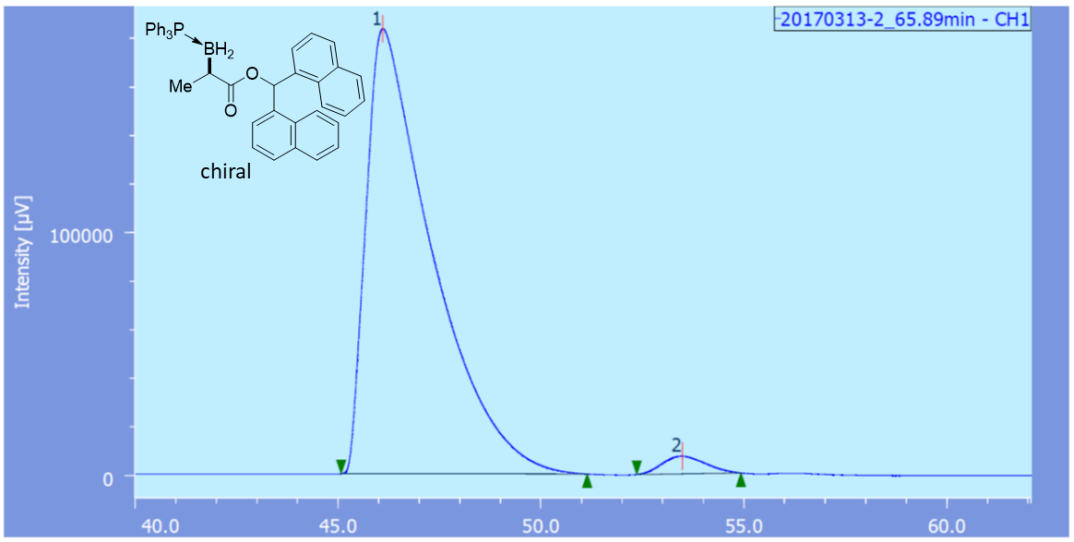
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	33.492	2388887	51151	50.221	54.117
2	36.283	2367906	43369	49.779	45.883



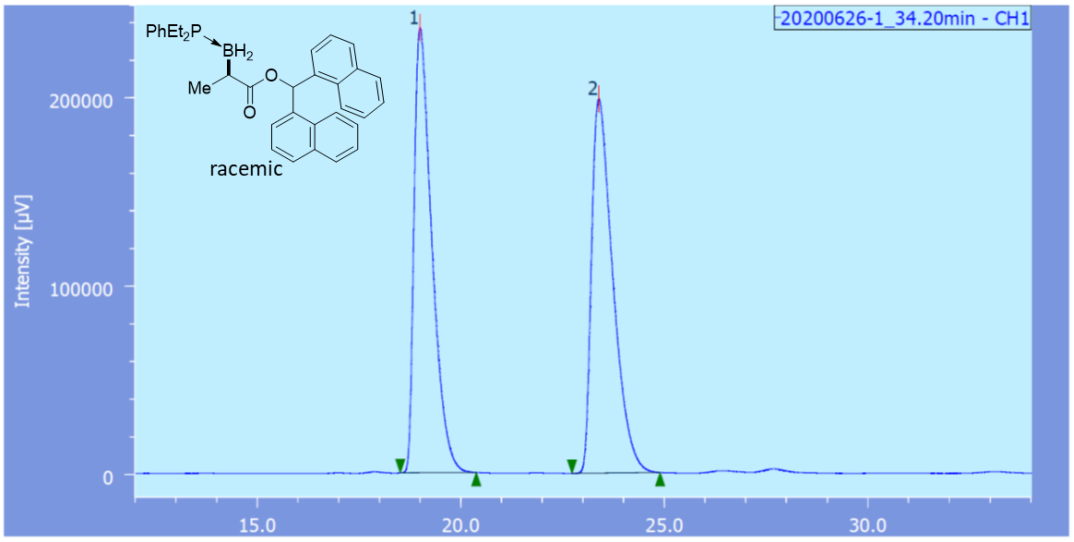
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	32.600	587467	13917	11.868	15.474
2	34.908	4362367	76020	88.132	84.526



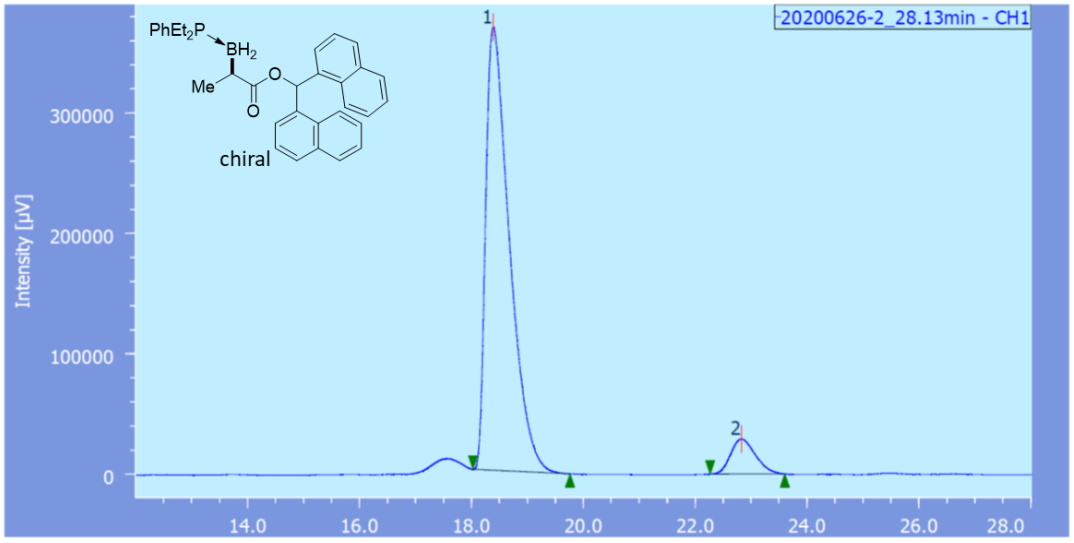
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	46.867	9546315	92955	50.219	49.352
2	52.308	9463126	95398	49.781	50.648



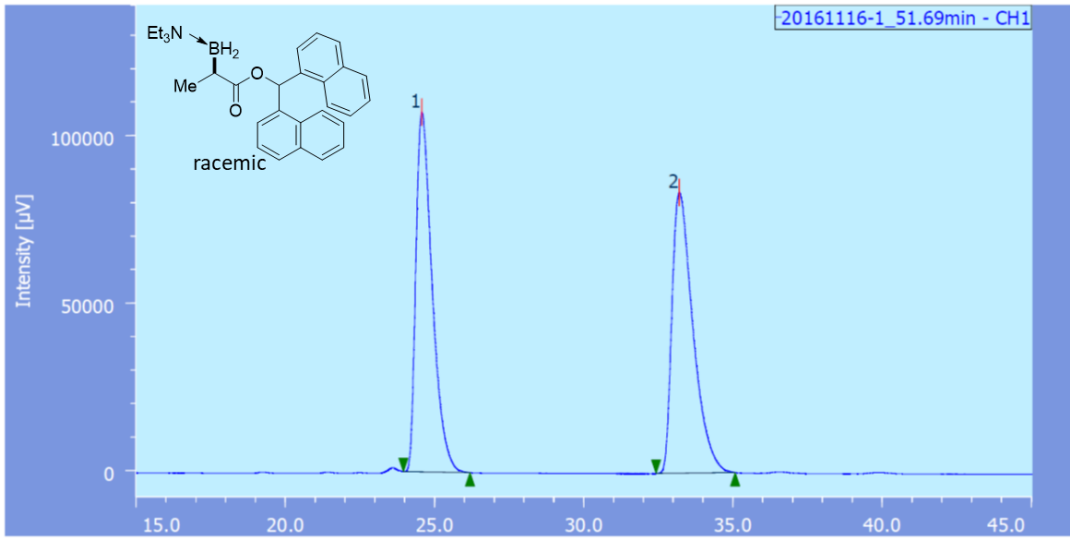
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	46.100	20718446	183187	97.462	96.185
2	53.475	539557	7267	2.538	3.815



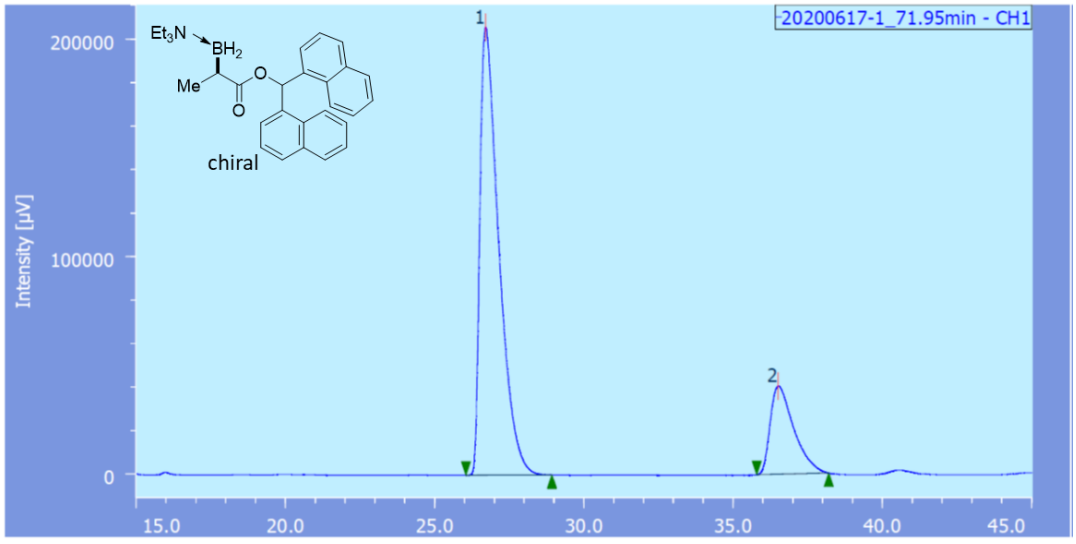
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	19.000	7154602	236225	49.700	54.332
2	23.383	7240921	198552	50.300	45.668



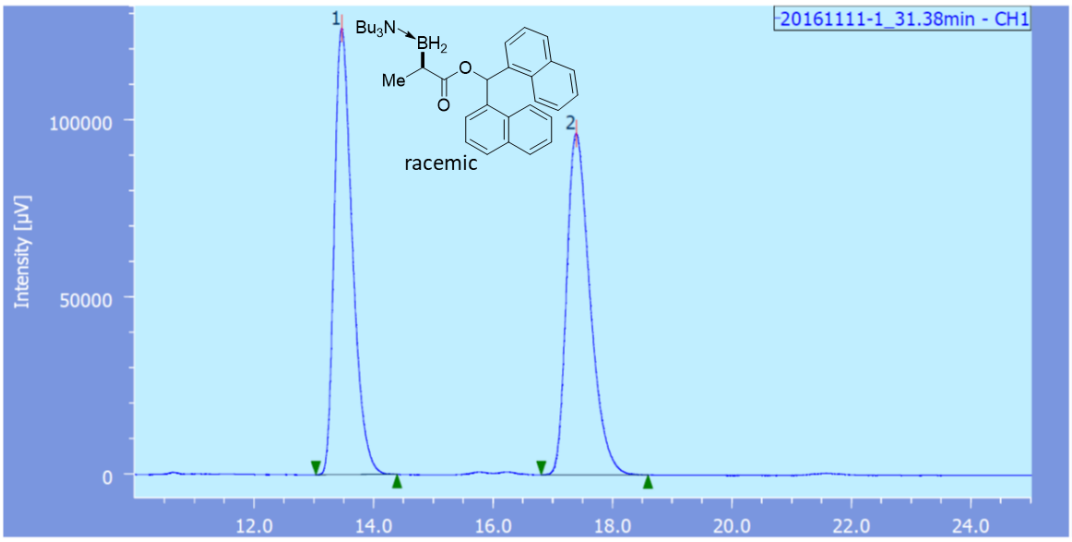
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	18.392	10804466	367920	92.284	92.693
2	22.825	903356	29003	7.716	7.307



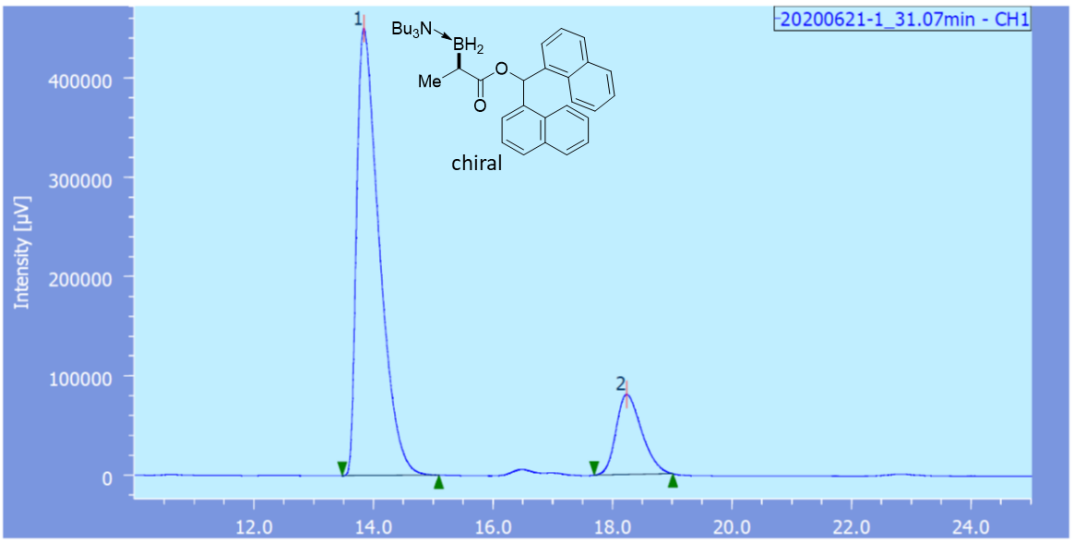
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	24.575	4071044	107339	49.869	56.156
2	33.200	4092383	83805	50.131	43.844



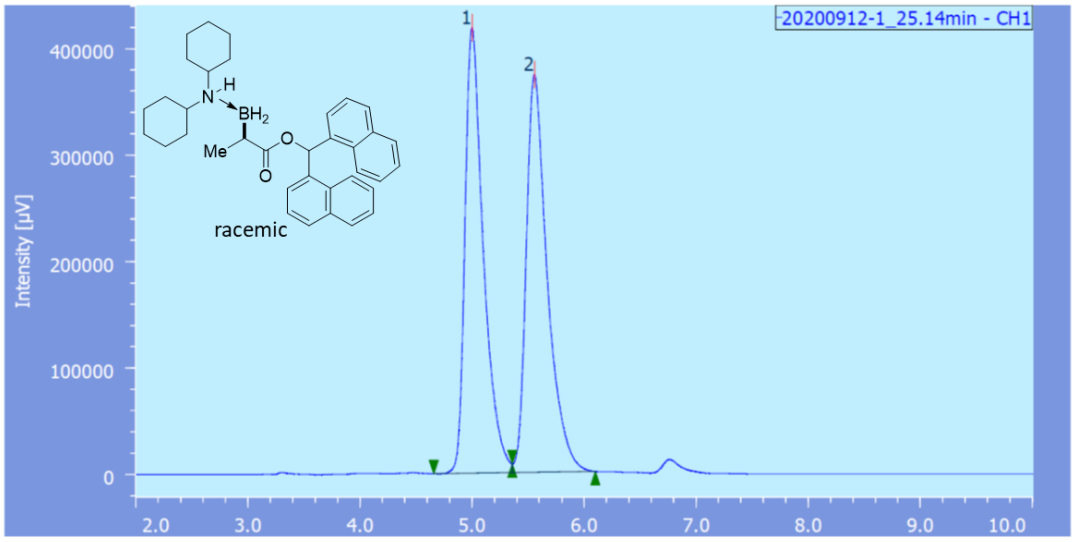
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	26.708	9050505	205964	80.216	83.566
2	36.508	2232223	40504	19.784	16.434



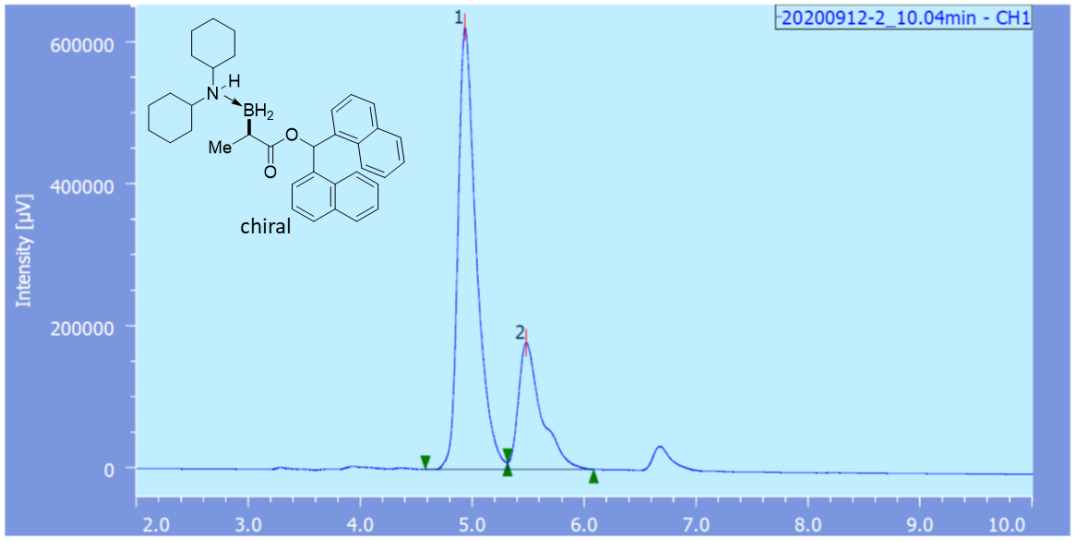
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	13.467	2635830	126007	50.141	56.668
2	17.392	2620992	96353	49.859	43.332



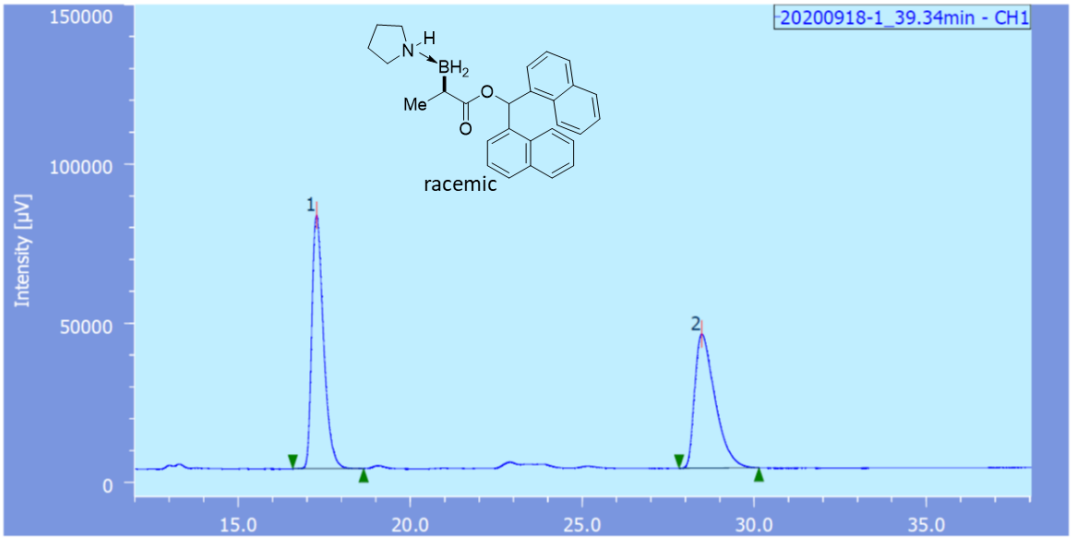
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	13.842	11810311	449919	83.037	84.804
2	18.233	2412621	80618	16.963	15.196



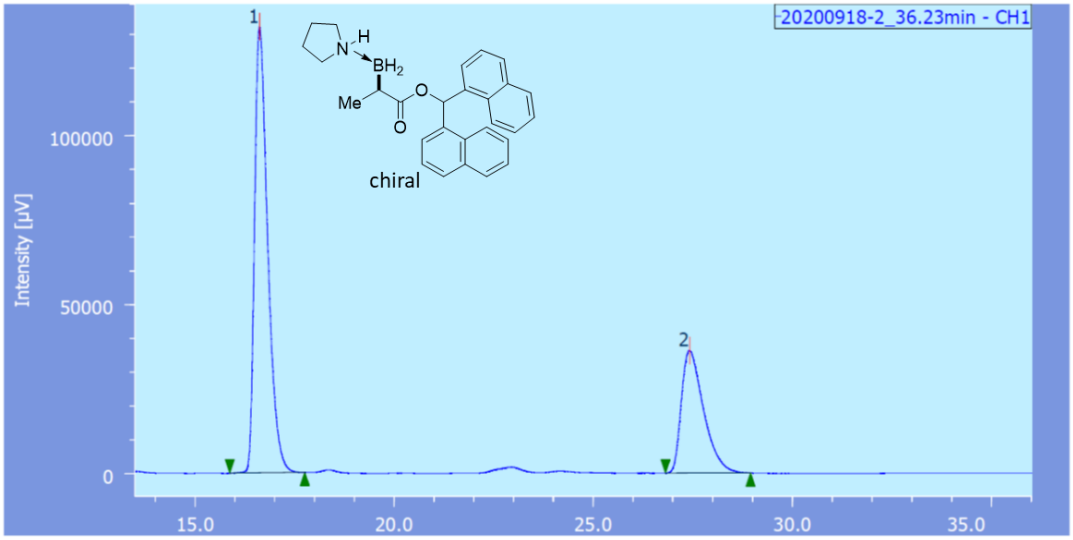
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	5.000	4779679	418239	49.471	52.839
2	5.558	4881811	373296	50.529	47.161



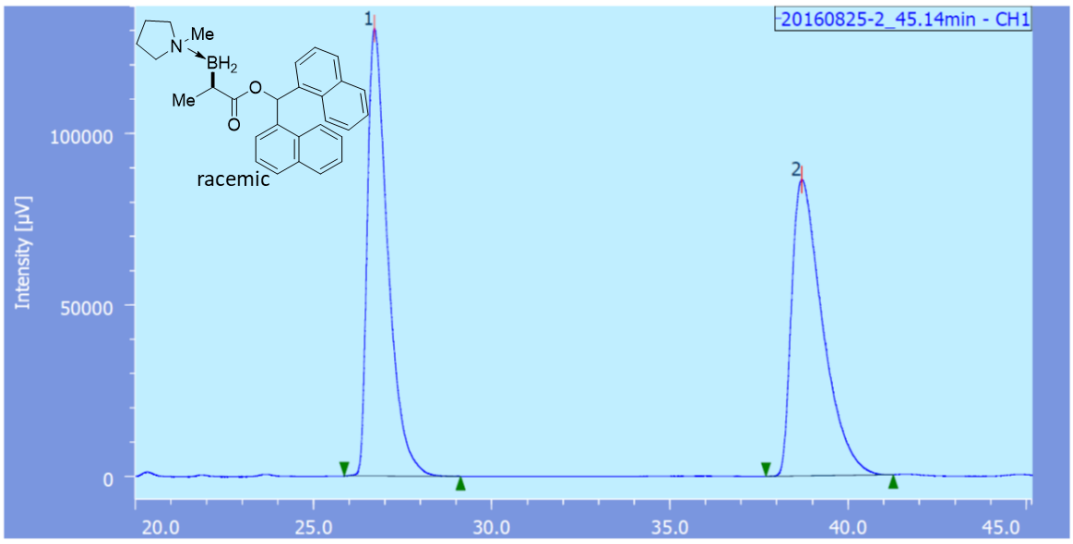
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	4.933	7155457	623163	73.727	77.719
2	5.483	2549939	178652	26.273	22.281



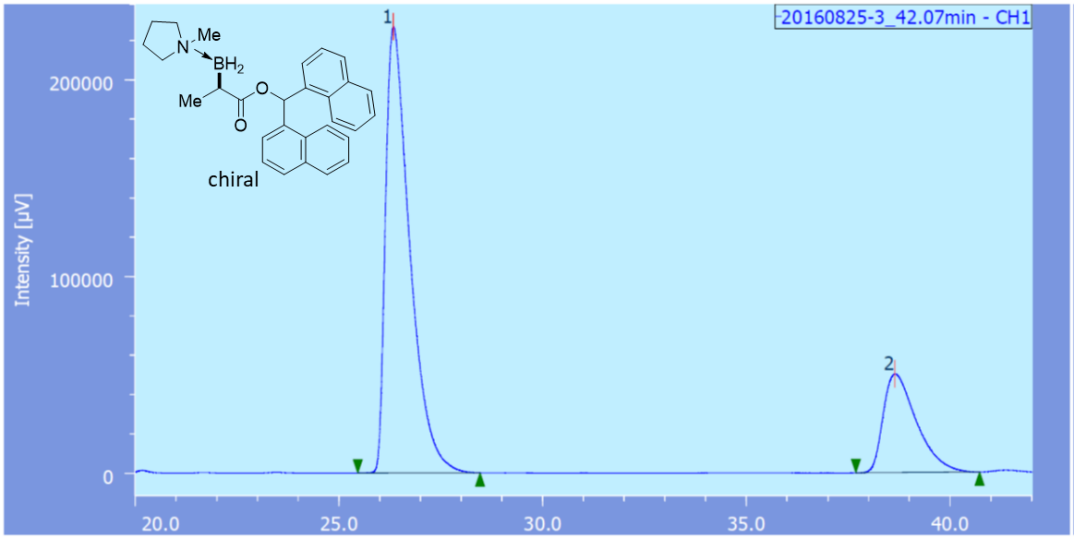
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	17.275	1869076	79570	51.989	65.400
2	28.467	1726039	42096	48.011	34.600



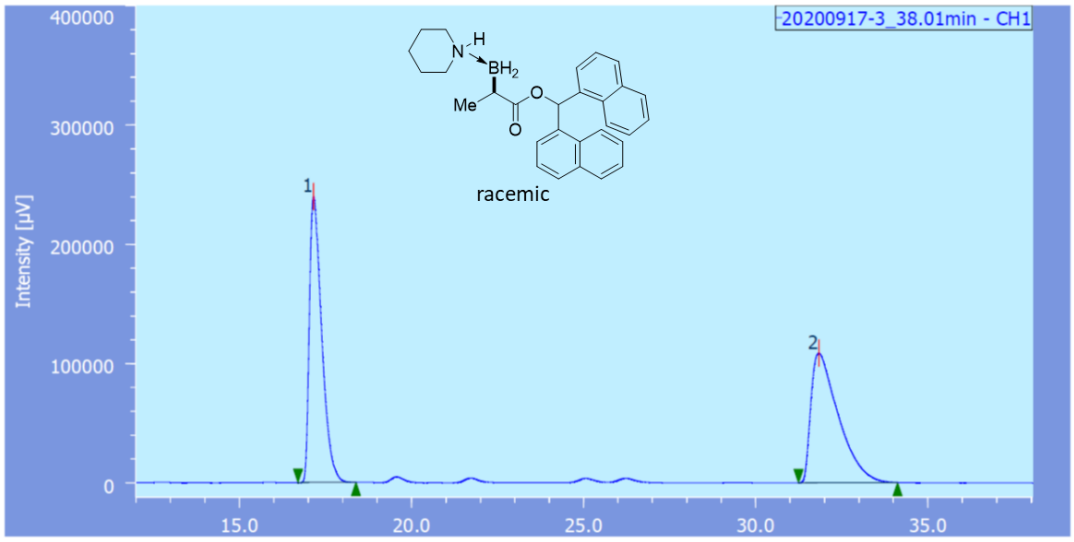
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	16.625	3026984	132001	68.364	78.456
2	27.417	1400746	36247	31.636	21.544



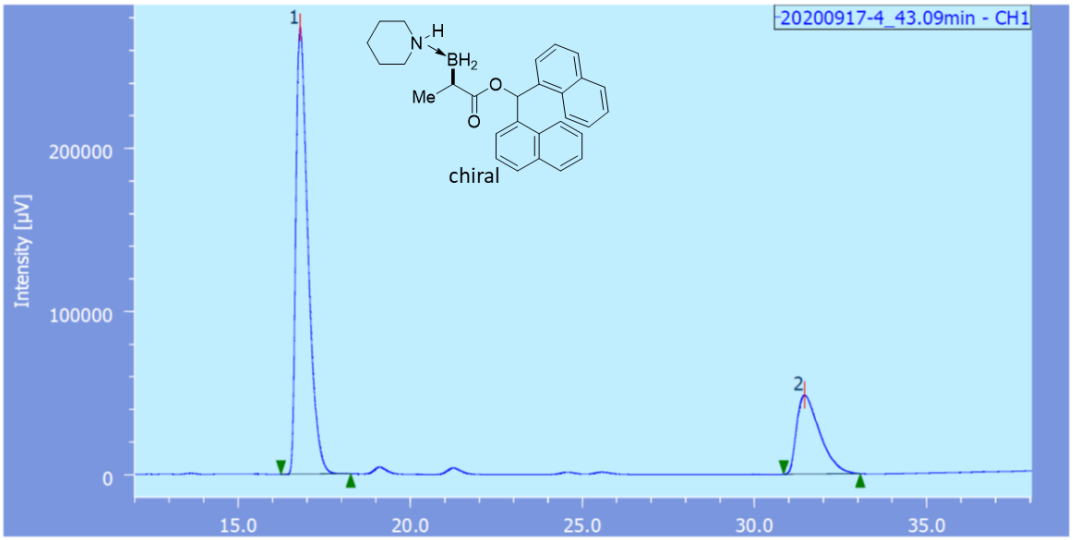
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	26.708	5183946	130383	49.964	60.169
2	38.700	5191419	86313	50.036	39.831



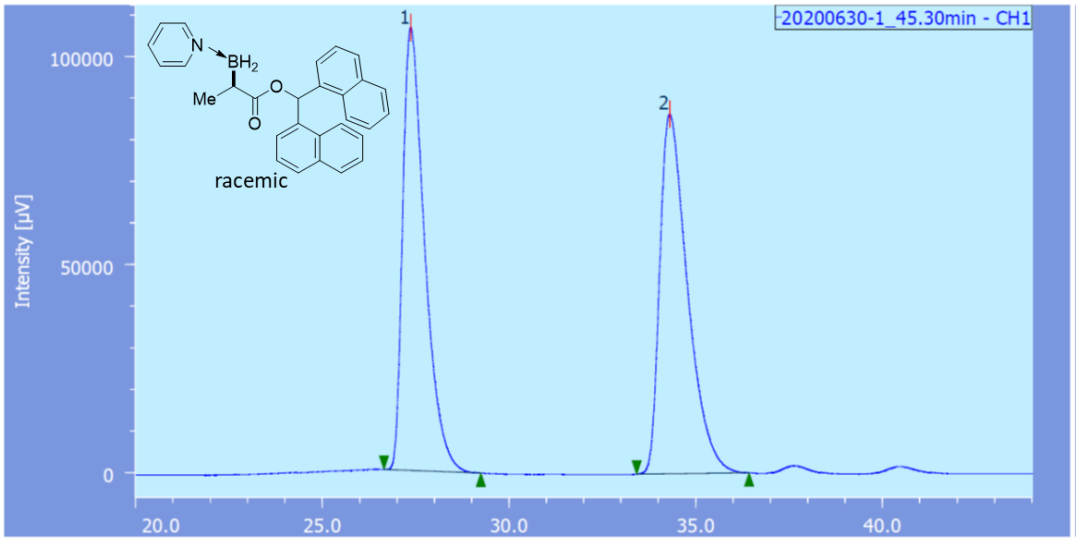
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	26.333	9374087	226791	76.632	81.869
2	38.642	2858451	50226	23.368	18.131



PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	17.158	5942859	239720	49.701	68.828
2	31.825	6014420	108566	50.299	31.172



PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	16.800	6667033	273666	74.745	84.927
2	31.442	2252622	48569	25.255	15.073



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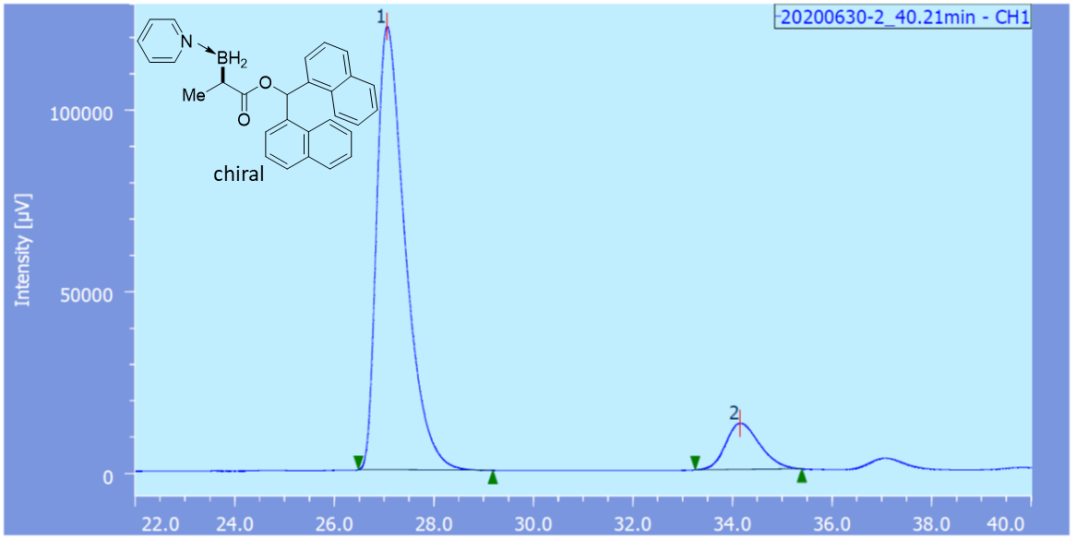
1	27.367	4335307	106381	49.305	55.181
2	34.300	4457497	86405	50.695	44.819



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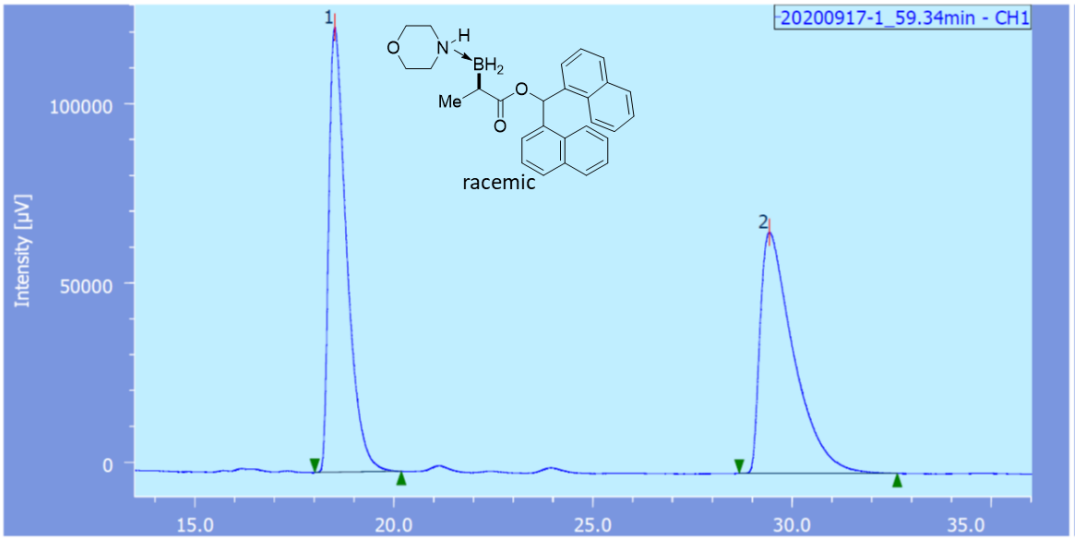
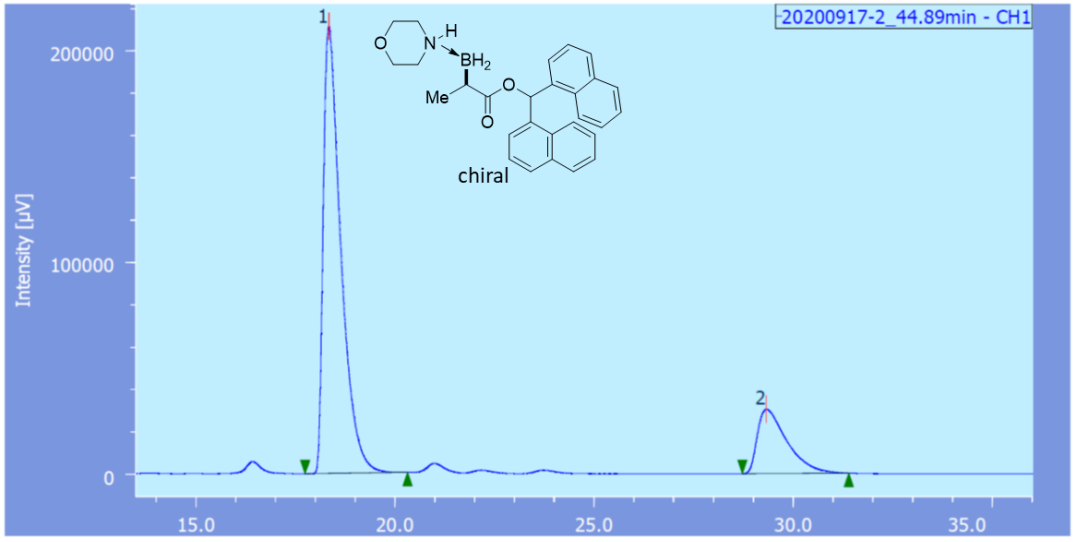
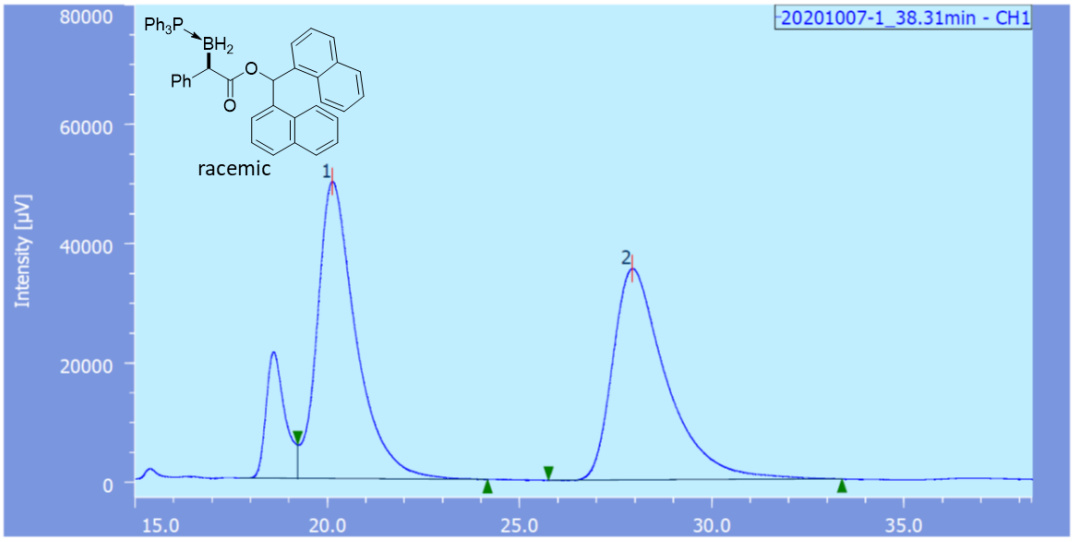
1	27.058	4852359	121997	88.862	90.567
2	34.150	608179	12707	11.138	9.433



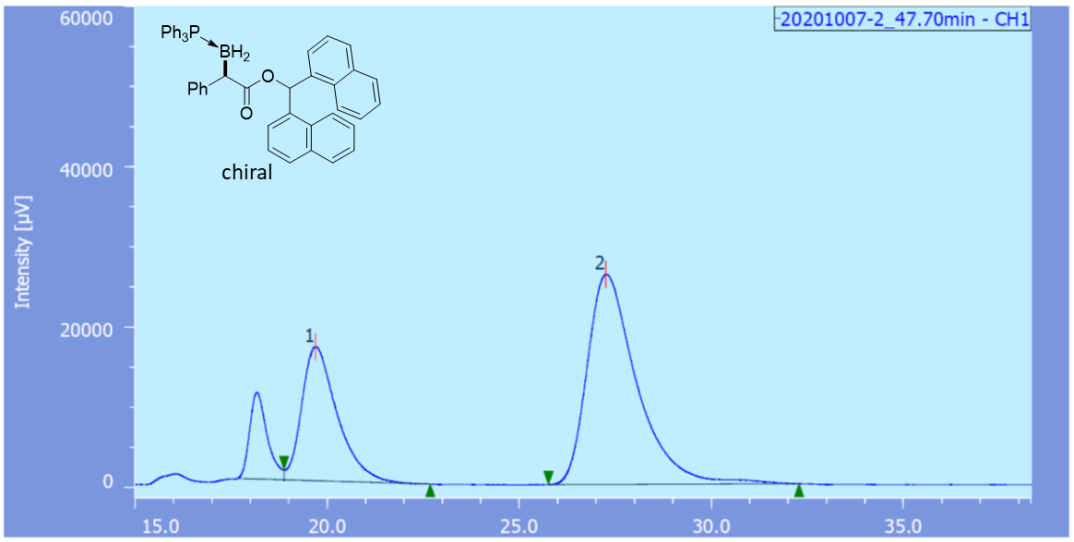
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	18.517	3867491	124105	49.714	64.864
2	29.433	3911965	67226	50.286	35.136



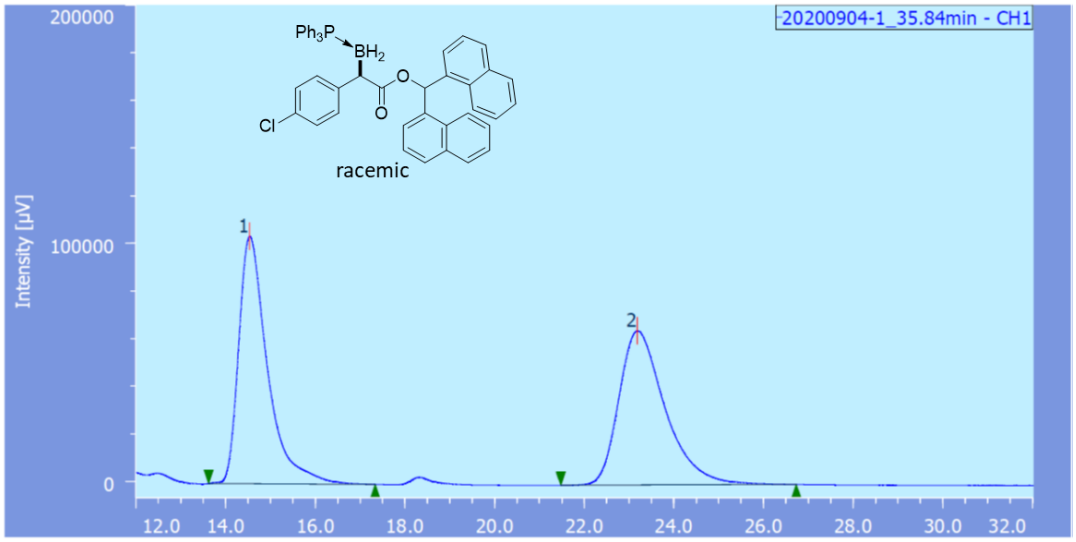
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	18.342	6494386	211151	80.511	87.387
2	29.325	1572109	30477	19.489	12.613



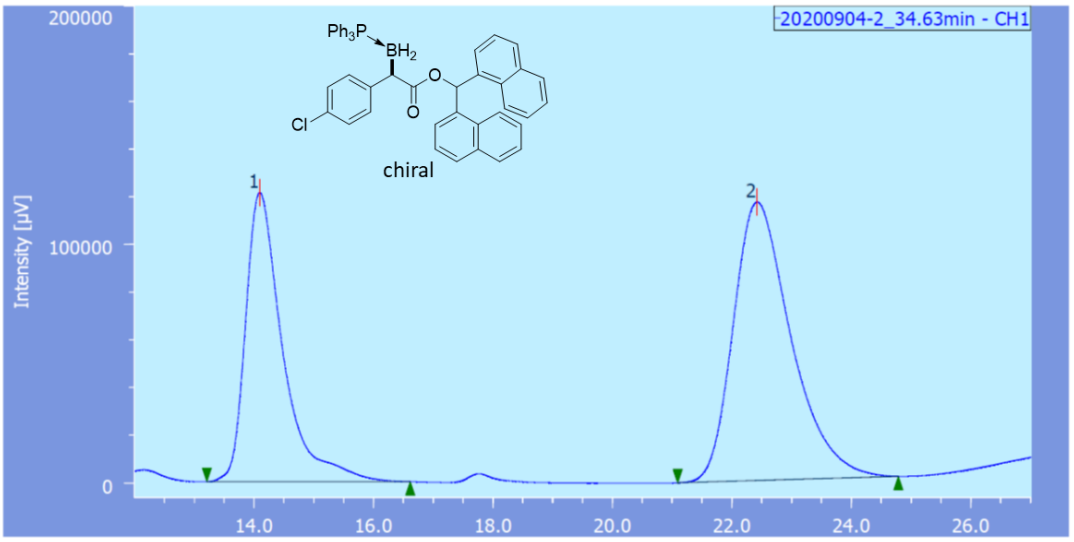
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.125	3469679	49734	50.239	58.430
2	27.925	3436689	35382	49.761	41.570



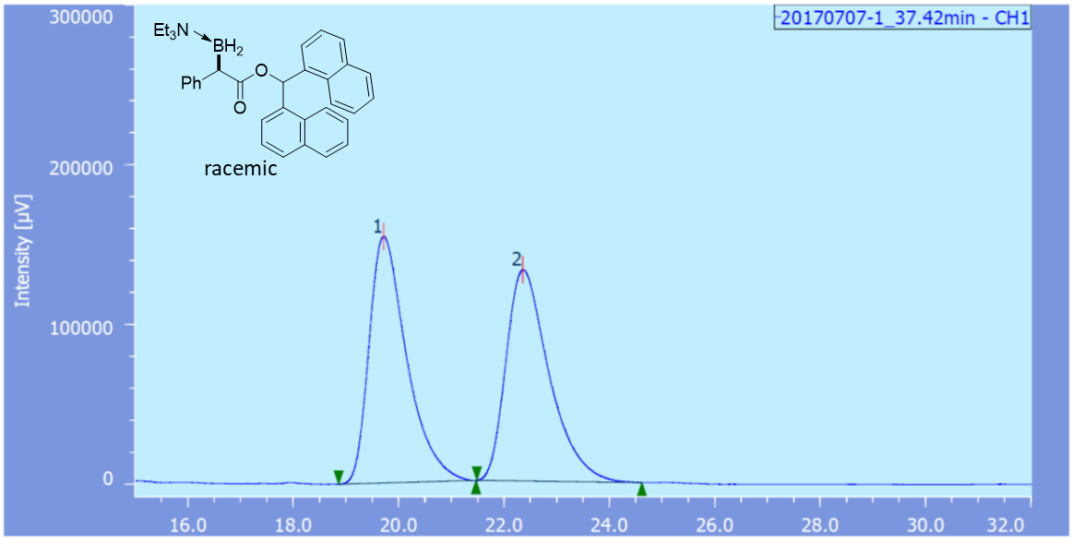
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	19.692	1077718	16738	31.335	38.983
2	27.250	2361610	26199	68.665	61.017



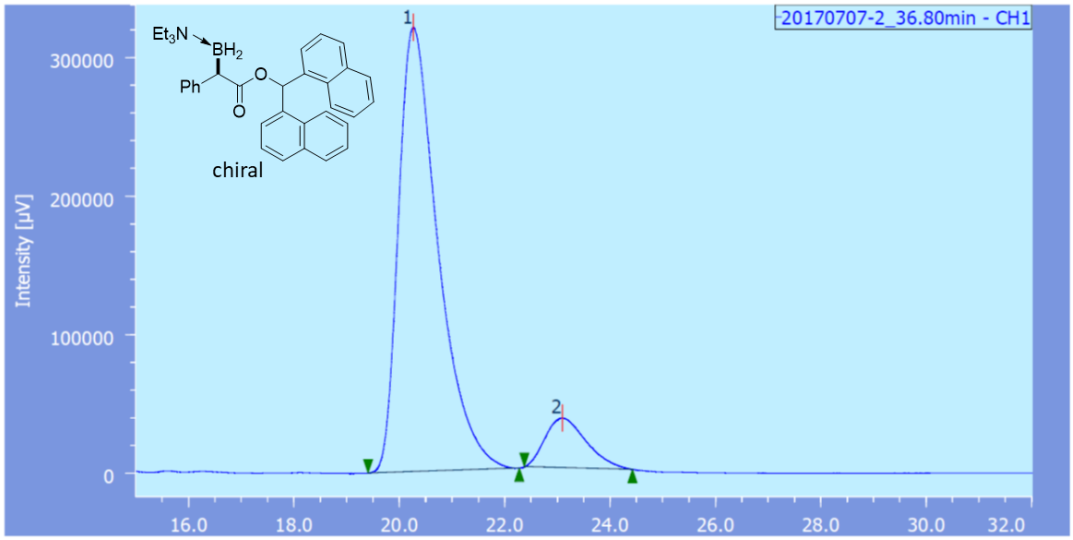
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.533	4644396	103873	49.902	61.599
2	23.183	4662644	64753	50.098	38.401



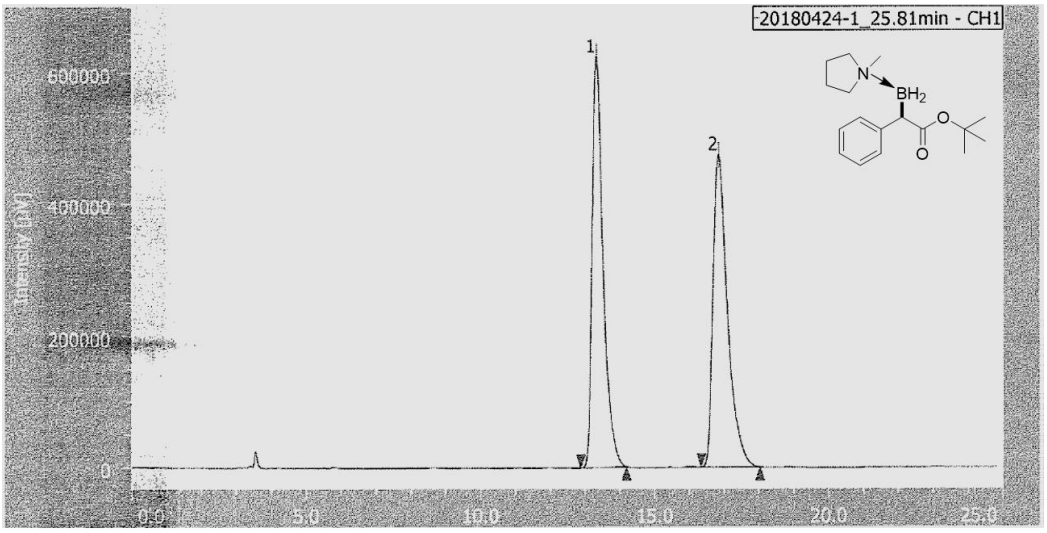
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.100	5247774	121212	40.098	50.928
2	22.417	7839575	116794	59.902	49.072



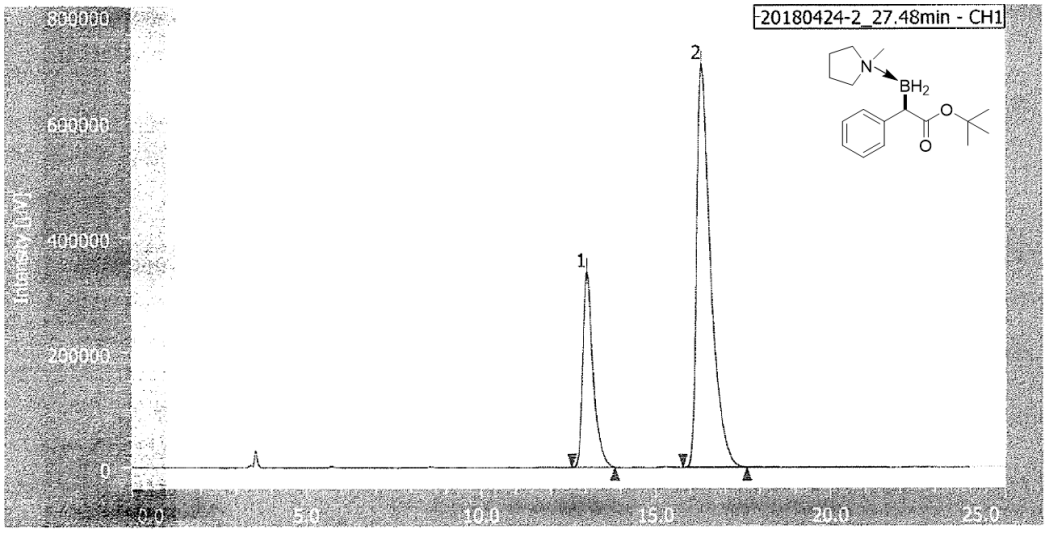
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	19.717	7664112	154269	50.474	53.850
2	22.358	7520299	132213	49.526	46.150



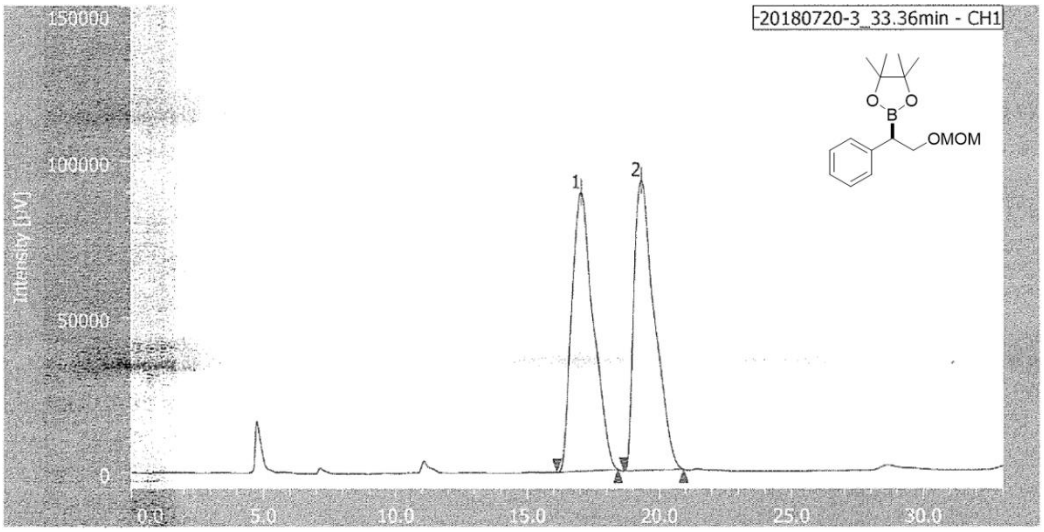
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.267	16719333	320462	89.613	89.977
2	23.092	1937890	35698	10.387	10.023



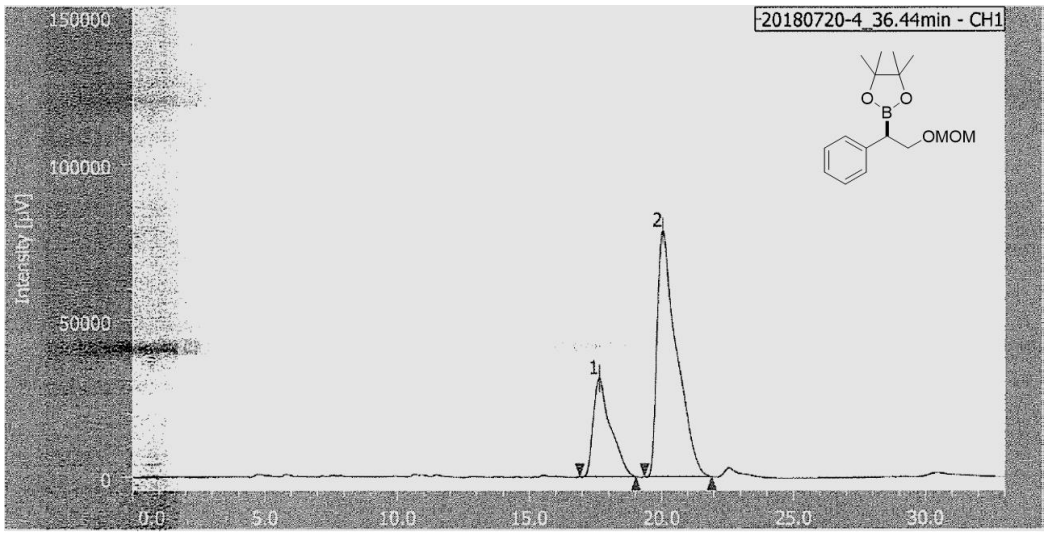
RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA %	HEIGHT %
13.325	13482276	624843	49.963	56.846
16.833	13502276	474333	50.037	43.154



RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA %	HEIGHT %
13.042	6960553	340461	26.084	32.722
16.325	19725054	700010	73.916	67.278



RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA %	HEIGHT %
17.042	5092851	89635	50.019	49.038
19.317	5089037	93152	49.981	50.962



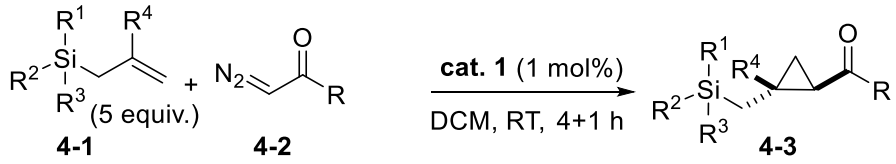
RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA %	HEIGHT %
17.642	1417767	31555	25.842	28.638
20.042	4068607	78629	74.158	71.362

8-2 Experimental Section for Chapter 4

General Information of Analysis and Reagents

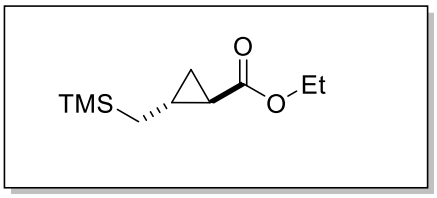
All reactions were performed under an atmosphere of argon unless otherwise noted. Acetone and Dichloromethane (DCM) were purchased from Kanto Chemical Co., Inc. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGa A 60 F_{254}, layer thickness 0.2 mm. The products were visualized by irradiation with UV light or by treatment with a solution of potassium manganate(VII) or by treatment with a solution of *p*-anisaldehyde. Column chromatography was performed using silica gel (Merck, Art. No.7734). ^{1}H NMR (500 MHz, 400 MHz) and ^{13}C NMR (125 MHz, 100 MHz) spectra were recorded on JEOL JNM-ECX500, JEOL JNM-ECS400 spectrometer. Chemical shifts are reported as δ values (ppm) relative to $CDCl_3$ (7.26 ppm), D_2O (4.79 ppm), TMS (0.00 ppm) for ^{1}H and $CDCl_3$ (77.0 ppm) for ^{13}C. Optical rotations were performed with a JASCO P-1030 polarimeter at the sodium D line (1.0 mL sample cell). Infrared (IR) spectra were recorded on an FT/IR-4600 instrument (JASCO Co., Ltd., Tokyo, Japan). Enantiomeric excesses were determined by high-performance liquid chromatography (HPLC) analyses with a JASCO GULLIVER using Daicel CHIRALPAK columns. DART mass (positive mode) analyses were performed on a LC-TOF JMS-T100LP.

8-2-1 General Procedure for the Stereoselective Cyclopropanation of Allyllsilanes



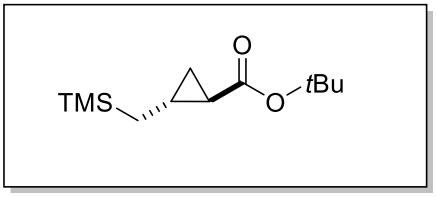
The solution of diazo compound **4-2** (0.2 mmol, 1 equiv.) in DCM (1.5 mL) was slowly added to a mixture of Ru(II)-Pheox (**cat. 1**) (1 mol%) and allylsilane **4-1** (1.0 mmol, 5 equiv.) in DCM (0.5 mL) for 4 h (using slow addition) under argon atmosphere. After the addition completed, the reaction mixture was then stirred for 1 h at room temperature. The progress of the reaction was monitored by TLC. Upon completion, solvent was removed and the residue was purified by column chromatography on silica gel eluted with Hex/EA = (20/1–4/1 v/v) to give desired product **4-3**. The d.r. ratio was determined from the crude ^{1}H NMR spectra, and the ee value was determined by chiral HPLC analysis or chiral GC analysis.

Ethyl 2-((trimethylsilyl)methyl)cyclopropanecarboxylate



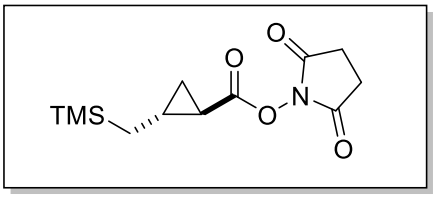
This compound was prepared according to the typical procedure for stereoselective cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and ethyl diazoacetate **4-2a** (26.8 mg, 0.20 mmol, 1 equiv.) in presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 *v*/*v*) as an eluent to give the desired product **4-3a** as a colorless liquid (72% yield, 28.9 mg, 0.144 mmol). $[\alpha]^{20}_{D} = -95.1$ (c 0.56, $CHCl_3$). d.r. = 85:15, 94% *trans* ee. The ee values were determined by GC analysis. Column (ASTEC G-TA 30 m×0.25 mm). tR = 45.18 min (major product for *trans*-isomer), tR = 47.54 min (minor product for *trans*-isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.12 (ddd, 2H, *J* = 10.7, 7.3, 2.8 Hz), 1.34–1.27 (m, 2H), 1.25 (t, 3H, *J* = 7.0 Hz), 1.22–1.18 (m, 1H), 0.78–0.73 (m, 1H), 0.63 (ddd, 1H, *J* = 10.4, 7.0, 3.7 Hz), 0.42 (dd, 1H, *J* = 14.6, 7.9 Hz), 0.03 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 60.2, 22.0, 20.9, 19.2, 17.3, 14.3, −1.6 ppm. IR (neat) ν 2955, 1725, 1150 cm^{-1}. HRMS (DART) calcd for $C_{10}H_{21}O_2Si$ $[M + H]^+$: 201.1310 found: 201.1310.

***tert*-Butyl 2-((trimethylsilyl)methyl)cyclopropanecarboxylate**



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and *tert*-butyl diazoacetate **4-2b** (28.4 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3b** as a colorless liquid (45% yield, 20.6 mg, 0.09 mmol). $[\alpha]^{20}_{D}$ = −92.4 (c 0.4, $CHCl_3$). d.r. = 84:16, 98% *trans* ee, 98% *cis* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IA), UV detector 220 nm, eluent: Hex/IPA = (400/1 v/v), flow rate = 0.25 mL/min, tR = 18.52 min (major product for *cis*-isomer), tR = 19.43 min (minor product for *cis*-isomer), tR = 23.54 min (minor product for *trans*-isomer), tR = 24.82 min (major product for *trans*-isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.30–1.18 (m, 2H), 1.14–1.10 (m, 1H), 0.66 (dd, 1H, J = 14.7, 6.1 Hz), 0.56 (ddd, 1H, J = 14.0, 11.0, 4.0 Hz), 0.45 (dd, 1H, J = 14.6, 7.3 Hz), 0.03 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 79.8, 28.2, 23.0, 20.9, 18.7, 16.9, −1.5 ppm. IR (neat) ν 2955, 1721, 1140 cm^{-1}. HRMS (DART) calcd for $C_{12}H_{25}O_2Si$ $[M+H]^+$: 229.1623 found: 229.1628.

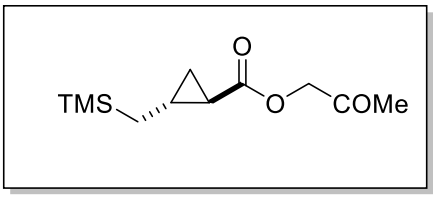
Succinimidyl 2-((trimethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and succinimidyl diazoacetate **4-2c** (36.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = (4/1 v/v) as an eluent to give the desired product **4-3c** as a white solid (45% yield, 24.2 mg, 0.09 mmol). $[\alpha]^{20}_{D}$ = −43.2 (c 0.61, $CHCl_3$). d.r. = 85:15, 91% *trans* ee, 96% *cis* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IC), UV detector 220 nm, eluent: Hex/IPA = (10/1 v/v), flow rate = 0.5 mL/min, tR = 26.17 min (major product for *cis*-isomer), tR = 28.93 min (minor product for *cis*-isomer), tR = 30.51 min (major product for *trans*-isomer), tR = 32.22 min (minor product for *trans*-

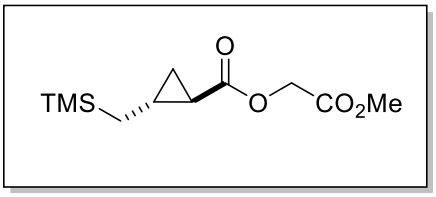
isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83 (d, 4H, *J* = 3.1 Hz), 1.60–1.50 (m, 2H), 1.44 (pent., 1H, *J* = 4.6 Hz), 0.95 (ddd, 1H, *J* = 11.3, 7.0, 4.3 Hz), 0.90 (dd, 1H, *J* = 14.6, 5.8 Hz), 0.48 (dd, 1H, *J* = 14.9, 6.4 Hz), 0.07 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 169.3, 25.5, 22.4, 21.0, 19.3, 18.8, −1.6 ppm. IR (neat) ν 2953. 1776, 1741, 1121 cm^{-1}. HRMS (DART) calcd for $C_{12}H_{23}N_2O_4Si$ $[M+NH_4]^+$: 287.1427 found: 287.1424.

Acetonyl 2-((trimethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and acetonyl diazoacetate **4-2d** (28.4 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3d** as a colorless liquid (77% yield, 35.0 mg, 0.153 mmol). $[\alpha]^{26}_D$ = −75.3 (c 1.45, $CHCl_3$). d.r. = 83:17, 98% *trans* ee, 97% *cis* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IC-3), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 1.0 mL/min, tR = 28.53 min (major product for *cis*-isomer), tR = 30.50 min (minor product for *cis*-isomer), tR = 37.66 min (major product for *trans*-isomer), tR = 41.40 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.62 (s, 2H), 2.15 (s, 3H), 1.43 (ddd, 1H, *J* = 11.8, 8.0, 3.8 Hz), 1.40–1.32 (m, 1H), 1.26 (ddd, 1H, *J* = 13.0, 8.4, 4.2 Hz), 0.78–0.70 (m, 2H), 0.47 (dd, 1H, *J* = 14.5, 8.0 Hz), 0.04 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 173.8, 68.2, 26.1, 21.5, 21.0, 20.0, 17.9, −1.6 ppm. IR (neat) ν 2956, 1727, 1156 cm^{-1}. HRMS (DART) calcd for $C_{11}H_{24}NO_3Si$ $[M+NH_4]^+$: 246.1525 found: 246.1525.

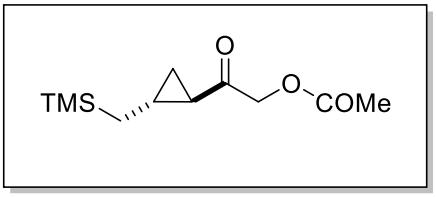
Methoxycarbonylmethyl 2-((trimethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol,

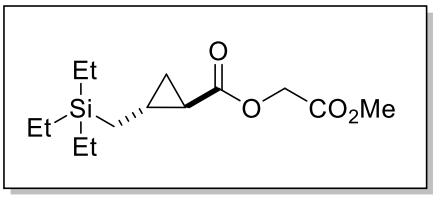
1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3e** as a colorless liquid (99% yield, 48.3 mg, 0.198 mmol). $[\alpha]^{27}_{D} = -75.54$ (c 0.84, $CHCl_3$). d.r. = 90:10, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 0.5 mL/min, tR = 25.54 min (major product for *trans*-isomer), tR = 28.48 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.60 (s, 2H), 3.74 (s, 3H), 1.43–1.34 (m, 2H), 1.27 (ddd, 1H, *J* = 13.0, 8.8, 4.4 Hz), 0.76–0.70 (m, 2H), 0.46 (dd, 1H, *J* = 14.5, 6.5 Hz), 0.03 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 168.6, 60.6, 52.3, 21.7, 21.1, 20.1, 18.0, −1.5 ppm. IR (neat) ν 3006, 2954, 2898, 1739, 1730, 1150 cm^{-1}. HRMS (DART) calcd for $C_{11}H_{21}O_4Si$ $[M+H]^+$: 245.1209 found: 245.1200.

2-Oxo-2-(2-((trimethylsilyl)methyl)cyclopropyl)ethylacetate



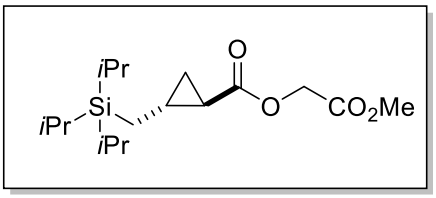
This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltrimethylsilane **4-1** (114.3 mg, 1.0 mmol, 5.0 equiv.) and diazo acetoxyacetone **4-2f** (28.4 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3f** as a colorless liquid (64% yield, 29.1 mg, 0.128 mmol). $[\alpha]^{26}_{D}$ = −89.0 (c 1.33, $CHCl_3$). d.r. = 82:18, 68% *trans* ee, 20% *cis* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IF-3), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 1.0 mL/min, tR = 15.82 min (minor product for *cis*-isomer), tR = 18.31 min (major product for *cis*-isomer), tR = 20.44 min (minor product for *trans*-isomer), tR = 22.98 min (major product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80 (d, 1H, *J* = 16.8 Hz), 4.76 (d, 1H, *J* = 16.4 Hz), 2.16 (s, 3H), 1.65 (pent., 1H, *J* = 4.2 Hz), 1.53–1.38 (m, 2H), 0.83–0.79 (m, 2H), 0.43 (dd, 1H, *J* = 14.5, 8.0 Hz), 0.03 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 170.2, 68.5, 27.2, 23.5, 21.4, 20.6, 20.5, −1.6 ppm. IR (neat) ν 2956, 1754, 1714, 1231 cm^{-1}. HRMS (DART) calcd for $C_{11}H_{21}O_3Si$ $[M+H]^+$: 229.1260 found: 229.1262.

Methoxycarbonylmethyl 2-((triethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltriethylsilane **4-1g** (156.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3g** as a colorless liquid (84% yield, 48.0 mg, 0.167 mmol). $[\alpha]^{25}_{D} = -76.2$ (c 2.04, $CHCl_3$). d.r. = 93:7, 98% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB-3), UV detector 220 nm, eluent: Hex/IPA = (500/1 v/v), flow rate = 1.0 mL/min, tR = 24.72 min (major product for *trans*-isomer), tR = 34.22 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.60 (s, 2H), 3.75 (s, 3H), 1.42 (pent., 1H, *J* = 3.4 Hz), 1.40–1.34 (m, 1H), 1.27 (pent., 1H, *J* = 4.2 Hz), 0.93 (t, 9H, *J* = 8.0 Hz), 0.81 (dd, 1H, *J* = 14.5, 5.7 Hz), 0.74 (ddt, 1H, *J* = 14.5, 10.3, 4.2 Hz), 0.56 (q, 6H, *J* = 8.0 Hz), 0.45 (dd, 1H, *J* = 14.9, 7.4 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 169.1, 61.1, 52.7, 22.6, 20.5, 18.8, 16.5, 7.9, 3.8 ppm. IR (neat) ν 3000, 2952, 1765, 1742, 1212 cm^{-1}. HRMS (DART) calcd for $C_{14}H_{30}NO_4Si$ $[M+NH_4]^+$: 304.1944 found: 304.1949.

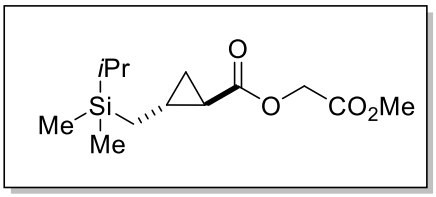
Methoxycarbonylmethyl 2-((triisopropylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltriisopropylsilane **4-1h** (198.4 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3h** as a colorless liquid (93% yield, 61.0 mg, 0.186 mmol). $[\alpha]^{25}_{D} = -61.5$ (c 0.75, $CHCl_3$). d.r. = 92:8, 98% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB-3), UV detector 220 nm, eluent: Hex/IPA = (500/1 v/v), flow rate = 1.0 mL/min, tR = 21.17 min (major product for *trans*-isomer), tR = 29.72 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.63 (d, 1H, *J* = 15.7 Hz), 4.59 (d,

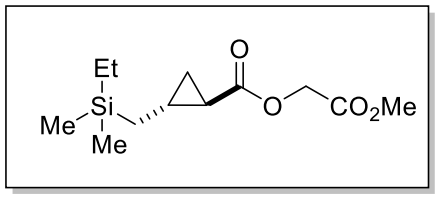
1H, *J* = 16.0 Hz), 3.76 (s, 3H), 1.48 (dt, 1H, *J* = 8.0, 4.2 Hz), 1.47–1.41 (m, 1H), 1.31 (pent., 1H, *J* = 4.2 Hz), 1.12–1.01 (m, 21H), 0.95 (dd, 1H, *J* = 14.9, 5.0 Hz), 0.81 (ddd, 1H, *J* = 9.4, 5.4, 4.2 Hz), 0.49 (dd, 1H, *J* = 15.1, 8.4 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 168.5, 60.5, 52.1, 23.0, 20.1, 19.2, 18.7, 13.8, 10.8 ppm. IR (neat) ν 2940, 2853, 1770, 1743, 1220 cm^{-1}. HRMS (DART) calcd for $C_{17}H_{33}O_4Si$ $[M+H]^+$: 329.2148 found: 329.2141.

Methoxycarbonylmethyl 2-((isopropyldimethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allylisopropyldimethylsilane **4-1i** (142.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3i** as a colorless liquid (85% yield, 46.0 mg, 0.17 mmol). $[\alpha]^{27}_D$ = −70.3 (c 1.47, $CHCl_3$). d.r. = 93:7, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (500/1 v/v), flow rate = 1.0 mL/min, tR = 24.13 min (major product for *trans*-isomer), tR = 32.03 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.60 (s, 2H), 3.75 (s, 3H), 1.42 (ddd, 1H, *J* = 11.8 Hz, 8.4, 4.2 Hz), 1.39–1.34 (m, 1H), 1.28 (pent., 1H, *J* = 4.4 Hz), 0.93 (d, 6H, *J* = 7.3 Hz), 0.81–0.72 (m, 3H), 0.46 (dd, 1H, *J* = 14.7, 8.0 Hz), 0.0 (s, 3H), −0.01 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.5, 60.4, 52.1, 21.8, 20.0, 18.1, 17.9, 17.4, 13.0, −5.4 ppm. IR (neat) ν 2953, 1768, 1737, 1156 cm^{-1}. HRMS (DART) calcd for $C_{13}H_{25}O_4Si$ $[M+H]^+$: 273.1522 found: 273.1522.

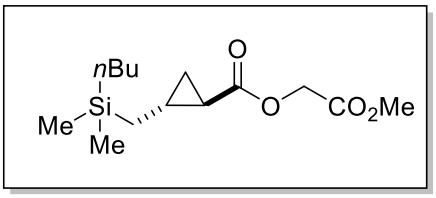
Methoxycarbonylmethyl 2-((ethyldimethylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allylethyldimethylsilane **4-1j** (128.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol,

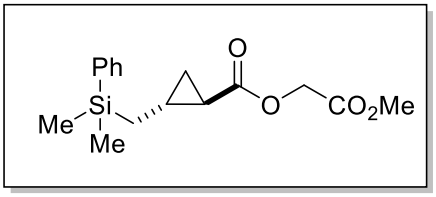
1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3j** as a colorless liquid (81% yield, 42.0 mg, 0.162 mmol). $[\alpha]^{27}_{D}$ = −81.2 (c 0.8, $CHCl_3$). d.r. = 94:6, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 1.0 mL/min, tR = 12.31 min (major product for *trans*-isomer), tR = 14.08 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61 (s, 2H), 3.76 (s, 3H), 1.42 (ddd, 1H, *J* = 11.8, 8.4, 4.2 Hz), 1.38–1.34 (m, 1H), 1.27 (pent., 1H, *J* = 4.2 Hz), 0.92 (t, 3H, *J* = 8.0 Hz), 0.79–0.71 (m, 2H), 0.53 (q, 2H, *J* = 8.0 Hz), 0.46 (dd, 1H, *J* = 14.6, 8.2 Hz), 0.02 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.5, 60.5, 52.2, 21.7, 20.0, 19.2, 18.0, 7.2, 6.8, −3.8 ppm. IR (neat) ν 2952, 1768, 1737, 1156 cm^{-1}. HRMS (DART) calcd for $C_{12}H_{23}O_4Si$ $[M+H]^+$: 259.1365 found: 259.1362.

Methoxycarbonylmethyl 2-((*n*-butyldimethylsilyl)methyl)cyclopropanecarboxylate



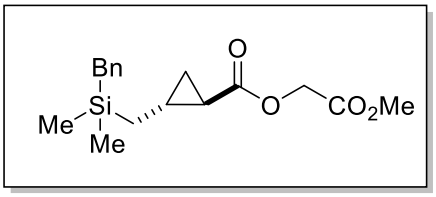
This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyl-*n*-butyldimethylsilane **4-1k** (156.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3k** as a colorless liquid (52% yield, 29.9 mg, 0.104 mmol). $[\alpha]^{27}_{D}$ = −58.1 (c 1.16, $CHCl_3$). d.r. = 92:8, 96% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (500/1 v/v), flow rate = 0.5 mL/min, tR = 45.99 min (major product for *trans*-isomer), tR = 54.57 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.61 (s, 2H), 3.76 (s, 3H), 1.44–1.35 (m, 2H), 1.34–1.22 (m, 5H), 0.87 (t, 3H, *J* = 7.3 Hz), 0.79–0.72 (m, 2H), 0.54 (dd, 2H, *J* = 8.8, 6.1 Hz), 0.45 (dd, 1H, *J* = 14.3, 8.6 Hz), 0.02 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.5, 60.5, 52.1, 26.5, 26.0, 21.7, 20.0, 19.6, 18.0, 14.8, 13.8, −3.3 ppm. IR (neat) ν 2952, 1768, 1738, 1155 cm^{-1}. HRMS (DART) calcd for $C_{14}H_{30}NO_4Si$ $[M+NH_4]^+$: 304.1944 found: 304.1942.

Methoxycarbonylmethyl 2-(dimethylphenylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyldimethylphenylsilane **4-1l** (176.3 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3l** as a colorless liquid (86% yield, 53.0 mg, 0.173 mmol). $[\alpha]^{25}_{D} = -62.9$ (c 0.67, $CHCl_3$). d.r. = 90:10, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 1.0 mL/min, tR = 13.27 min (major product for *trans*-isomer), tR = 20.16 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.50 (m, 2H), 7.36 (dd, 3H, *J* = 5.3, 2.3 Hz), 4.60 (s, 2H), 3.76 (s, 3H), 1.45–1.39 (m, 2H), 1.57 (pent., 1H, *J* = 4.2 Hz), 1.01 (dd, 1H, *J* = 14.5, 5.7 Hz), 0.74–0.69 (m, 2H), 0.35 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 168.6, 138.7, 133.7, 129.2, 127.9, 60.6, 52.3, 21.8, 20.4, 19.8, 18.1, −2.9 ppm. IR (neat) ν 3074, 3007, 2955, 2891, 1737, 1591, 1434, 1254, 1156, 1111, 995, 923, 838, 708 cm^{-1}. HRMS (DART) calcd for $C_{16}H_{23}O_4Si$ $[M+H]^+$: 307.1365 found: 307.1365.

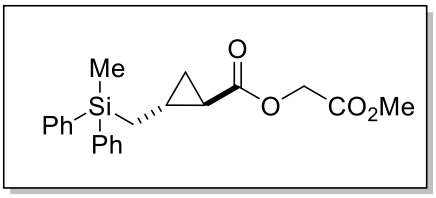
Methoxycarbonylmethyl 2-(benzyldimethylsilylmethyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allylbenzyldimethylsilane **4-1m** (190.4 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3m** as a colorless liquid (84% yield, 51.2 mg, 0.167 mmol). $[\alpha]^{17}_{D} = -68.7$ (c 0.40, $CHCl_3$). d.r. = 91:9, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IC-3), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 1.0 mL/min, tR = 28.98 min (major product for *trans*-isomer), tR = 35.55 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (t, 2H, *J* = 7.6 Hz), 7.07 (t, 1H,

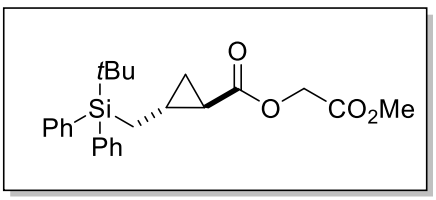
J = 7.3 Hz), 6.99 (d, 2H, *J* = 6.9 Hz), 4.63 (d, 1H, *J* = 16.0 Hz), 4.59 (d, 1H, *J* = 16.0 Hz), 3.76 (s, 3H), 2.13 (s, 2H), 1.43–1.35 (m, 2H), 1.28 (pent., 1H, *J* = 4.2 Hz), 0.77 (dd, 1H, *J* = 14.9, 6.5 Hz), 0.72 (dddd, 1H, *J* = 14.1, 10.3, 6.5, 3.8 Hz), 0.49 (dd, 1H, *J* = 14.9, 8.0 Hz), 0.05 (s, 3H), 0.04 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 168.7, 140.0, 128.4, 128.3, 124.3, 60.7, 52.4, 25.7, 21.9, 19.9, 19.3, 18.1, −3.2 ppm. IR (neat) ν 3075, 2888, 1757, 1733, 1344, 1248 cm^{-1}. HRMS (DART) calcd for $C_{17}H_{28}NO_4Si$ $[M+NH_4]^+$: 338.1787 found: 338.1787.

Methoxycarbonylmethyl 2-(methyldiphenylsilylmethyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allylmethyldiphenylsilane **4-1n** (238.4 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3n** as a colorless liquid (93% yield, 68.3 mg, 0.185 mmol). $[\alpha]^{26}_D$ = −60.6 (c 0.75, $CHCl_3$). d.r. = 92:8, 98% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), Flow Rate = 1.0 mL/min, tR = 20.30 min (major product for *trans*-isomer), tR = 60.77 min (minor product for *trans*-isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56–7.52 (m, 4H), 7.41–7.35 (m, 6H), 4.58 (d, 1H, *J* = 15.7 Hz), 4.54 (d, 1H, *J* = 16.0 Hz), 3.75 (s, 3H), 1.52–1.44 (m, 2H), 1.36 (dd, 1H, *J* = 14.5, 5.7 Hz), 1.25 (pent., 1H, *J* = 4.2 Hz), 1.35 (dd, 1H, *J* = 14.9, 8.0 Hz), 0.74 (dddd, 1H, *J* = 14.5, 10.7, 6.5, 3.2 Hz), 0.66 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 168.4, 136.5, 134.4, 129.3, 127.8, 60.5, 52.1, 21.8, 19.4, 18.8, 18.0, −4.4 ppm. IR (neat) ν 3069, 3008, 2954, 1766, 1731, 1118 cm^{-1}. HRMS (DART) calcd for $C_{21}H_{25}O_4Si$ $[M+H]^+$: 369.1522 found: 369.1521.

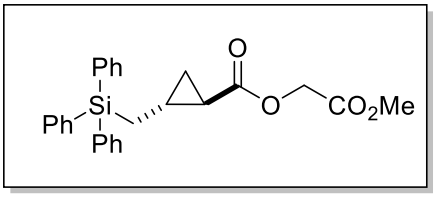
Methoxycarbonylmethyl 2-((*tert*-butyldiphenylsilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyl-*tert*-butyldiphenylsilane **4-1o** (280.5 mg, 1.0 mmol, 5.0 equiv.) and methyl

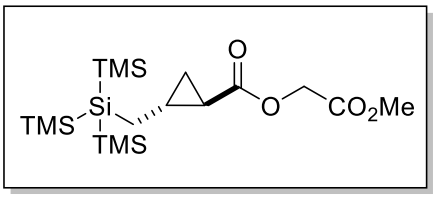
(diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3o** as a colorless liquid (86% yield, 71.0 mg, 0.173 mmol). $[\alpha]^{28}_{D} = -36.8$ (c 0.90, $CHCl_3$). d.r. = 92:8, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 1.0 mL/min, tR = 11.81 min (major product for *trans*-isomer), tR = 16.59 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (ddd, 4H, *J* = 12.6, 8.0, 4.6 Hz), 7.42–7.34 (m, 6H), 4.53 (d, 1H, *J* = 16.0 Hz), 4.43 (d, 1H, *J* = 16.0 Hz), 3.72 (s, 3H), 1.52–1.42 (m, 2H), 1.38 (pent., 1H, *J* = 4.2 Hz), 1.10–1.04 (m, 2H), 1.06 (s, 9H), 0.60 (ddd, 1H, *J* = 12.6, 8.4, 4.6 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 168.4, 136.0, 134.3, 129.1, 127.6, 60.4, 52.1, 27.8, 22.6, 19.7, 18.7, 18.0, 15.3 ppm. IR (neat) ν 3065, 2953, 2858, 1738, 1201 cm^{-1}. HRMS (DART) calcd for $C_{24}H_{34}NO_4Si$ $[M+NH_4]^+$: 428.2257 found: 428.2259.

Methoxycarbonylmethyl 2-(triphenylsilylmethyl)cyclopropanecarboxylate



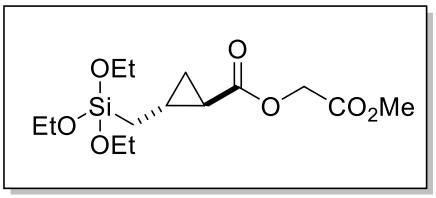
This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltriphenylsilane **4-1p** (300.5 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3p** as a colorless liquid (72% yield, 62.0 mg, 0.144 mmol). $[\alpha]^{21}_{D} = -43.0$ (c 1.34, $CHCl_3$). d.r. = 90:10, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 1.0 mL/min, tR = 19.90 min (major product for *trans*-isomer), tR = 27.98 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (dd, 6H), 7.45–7.36 (m, 9H), 4.56 (d, 1H, *J* = 16.0 Hz), 4.47 (d, 1H, *J* = 15.7 Hz), 3.71 (s, 3H), 1.70 (dd, 1H, *J* = 14.9, 5.7 Hz), 1.66–1.58 (m, 1H), 1.46 (pent., 1H, *J* = 3.4 Hz), 1.29 (dd, 1H, *J* = 14.9, 8.4 Hz), 1.18 (pent., 1H, *J* = 4.2 Hz), 0.67 (ddd, 1H, *J* = 10.9, 8.4, 4.6 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 168.6, 136.0, 134.6, 129.8, 128.2, 60.7, 52.4, 25.6, 22.6, 18.7, 18.2 ppm. IR (neat) ν 3103, 2849, 1765, 1733, 1431, 1160, 699 cm^{-1}. HRMS (DART) calcd for $C_{26}H_{30}NO_4Si$ $[M+NH_4]^+$: 448.1944 found: 448.1946.

Methoxycarbonylmethyl 2-(tri(trimethylsilyl)silylmethyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltris(trimethylsilyl)silane **4-1q** (288.7 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3q** as a colorless liquid (90% yield, 75.5 mg, 0.18 mmol). $[\alpha]^{27}_{D} = -65.7$ (c 1.05, $CHCl_3$). d.r. = 90:10, 97% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (500/1 v/v), flow rate = 0.5 mL/min, tR = 24.38 min (major product for *trans*-isomer), tR = 28.67 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.63 (d, 1H, J = 16 Hz), 4.55 (d, 1H, J = 15.7 Hz), 3.74 (s, 3H), 1.49 (td, 1H, J = 8.4, 3.8 Hz), 1.46–1.41 (m, 1H), 1.30 (pent., 1H, J = 4.2 Hz), 1.19 (dd, 1H, J = 14.5, 4.6 Hz), 0.76 (ddd, 1H, J = 10.7, 6.5, 4.2 Hz), 0.58 (dd, 1H, J = 14.5, 9.2 Hz), 0.16 (s, 27H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 168.6, 60.7, 52.3, 23.7, 23.4, 19.6, 12.5, 1.2 ppm. IR (neat) ν 2952, 1740, 1116 cm^{-1}. HRMS (DART) calcd for $C_{17}H_{42}NO_4Si_4$ $[M+NH_4]^+$: 436.2190 found: 436.2196.

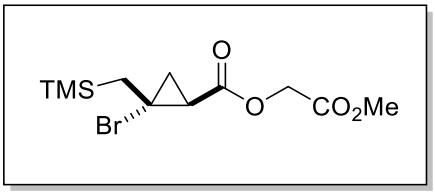
Methoxycarbonylmethyl 2-((triethoxysilyl)methyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between allyltriethoxysilane **4-1r** (408.8 mg, 2.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (63.2 mg, 0.40 mmol, 1.0 equiv.) in presence of **cat. 1** (2.5 mg, 0.004 mmol, 1 mol%) at room temperature. The resulting mixture was concentrated, washed with Et_2O, and filtered. Evaporation gave the desired product **4-3r** (92% yield by crude ^{1}H NMR). d.r. = 97:3, 92% *trans* ee. This product can not be purified by silica gel column chromatography because of reacting with silica gel. The enantioselectivity of **3r** was determined by the comparison of its synthetic transformation product **4r** of optical rotation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.58 (d, 1H, J = 15.9 Hz), 4.53 (d, 1H, J = 15.9 Hz), 3.80 (q, 6H, J = 7.0 Hz), 3.71 (s, 3H), 1.51–1.43 (m, 1H), 1.26–1.09 (m, 2H), 1.18 (t, 9H,

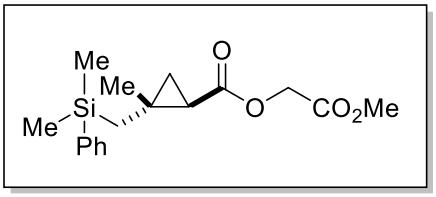
J = 7.0 Hz), 0.95–0.84 (m, 1H), 0.80 (dt, 1H, *J* = 12.5, 4.3 Hz), 0.54 (dd, 1H, *J* = 14.6, 6.7 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 168.3, 60.4, 58.4, 52.0, 21.6, 18.1, 18.0, 17.8, 14.7 ppm.

Methoxycarbonylmethyl 2-bromo-2-(trimethylsilyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between (2-bromoallyl)trimethylsilane **4-1s** (386.3 mg, 2.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (63.2 mg, 0.40 mmol, 1.0 equiv.) in presence of **cat. 1** (7.6 mg, 0.012 mmol, 3 mol%) at −50 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3s** as a colorless liquid (83% yield, 107.2 mg, 0.33 mmol). $[\alpha]^{25}_D$ = −129.8 (c 0.88, $CHCl_3$). d.r. = 95:5, 99% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (300/1 v/v), flow rate = 1.0 mL/min, tR = 7.79 min (minor product for *trans*-isomer), tR = 8.36 min (major product for *trans*-isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.69 (d, 1H, *J* = 15.9 Hz), 4.60 (d, 1H, *J* = 15.9 Hz), 3.77 (s, 3H), 2.42 (dd, 1H, *J* = 9.3, 6.7 Hz), 1.73 (dd, 1H, *J* = 9.4, 6.4 Hz), 1.52 (d, 2H, *J* = 3.7 Hz), 1.44 (t, 1H, *J* = 6.4 Hz), 0.13 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 168.1, 61.1, 52.4, 37.6, 30.2, 26.0, 24.4, −0.5 ppm. IR (neat) ν 2954, 2897, 1740, 1250, 852, 696 cm^{-1}. HRMS (DART) calcd for $C_{11}H_{23}BrNO_4Si$ $[M+NH_4]^+$: 342.0559 found: 342.0561.

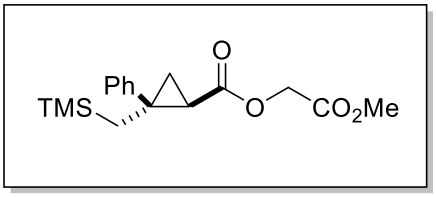
Methoxycarbonylmethyl 2-methyl -2-(dimethylphenylsilylmethyl)cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between dimethyl (2-methyl)allyl(phenyl)silane **4-1t** (190.4 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (20/1 v/v) as an eluent to give the desired product **4-3t** as a colorless liquid (96% yield, 61.5 mg, 0.192 mmol). $[\alpha]^{18}_D$ = −42.4 (c 3.0, $CHCl_3$). d.r. = 68:32, 97% *trans* ee, 98% *cis* ee. ^{1}H NMR (500

MHz, $CDCl_3$, *trans*-isomer) δ 7.54–7.51 (m, 2H), 7.35 (dd, 3H, *J* = 6.5, 3.8 Hz), 4.64 (d, 1H, *J* = 15.7 Hz), 4.57 (d, 1H, *J* = 11.9 Hz), 3.75 (s, 3H), 1.59 (td, 1H, *J* = 13.7, 5.7 Hz), 1.26 (d, 1H, *J* = 14.9 Hz), 1.14 (d, 3H, *J* = 31.0 Hz), 1.14–1.08 (m, 1H), 1.02 (dd, 1H, *J* = 35.2, 14.9 Hz), 0.91 (ddd, 1H, *J* = 23.7, 8.0, 4.6 Hz), 0.35 (s, 3H), 0.34 (s, 3H) ppm. The ee values were determined by HPLC analysis. Column (CHIRALPAK IE-3), UV detector 220 nm, eluent: Hex/IPA = (300/1 v/v), flow rate = 1.0 mL/min, tR = 24.16 min (minor product for *trans*-isomer), tR = 25.54 min (major product for *trans*-isomer), tR = 35.56 min (minor product for *cis*-isomer), tR = 39.29 min (major product for *cis*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$, *cis*-isomer) δ 7.54–7.51 (m, 2H), 7.35 (dd, 3H, *J* = 6.5, 3.8 Hz), 4.64 (d, 1H, *J* = 15.7 Hz), 4.54 (d, 1H, *J* = 12.2 Hz), 3.75 (s, 3H), 1.59 (td, 1H, *J* = 13.7, 5.7 Hz), 1.14 (d, 3H, *J* = 31.0 Hz), 1.14–1.08 (m, 1H), 1.02 (dd, 2H, *J* = 35.2, 14.9 Hz), 0.91 (ddd, 1H, *J* = 23.7, 8.0, 4.6 Hz), 0.39 (s, 3H), 0.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, mixture of *trans*, *cis*-isomers) δ 172.1, 171.9, 168.5, 139.5, 139.4, 133.5, 133.4, 128.9, 128.8, 127.8, 127.7, 60.5, 60.4, 52.1, 52.0, 29.2, 27.5, 27.2, 27.1, 26.6, 26.0, 23.7, 23.4, 19.0, 18.9, −1.78, −1.86, −1.89, −1.93 ppm. IR (neat) ν 3068, 2864, 1765, 1733, 1439, 1256 cm^{-1}. HRMS (DART) calcd for $C_{17}H_{28}NO_4Si_4$ $[M+NH_4]^+$: 338.1787 found: 338.1787.

Methoxycarbonylmethyl 2-phenyl-2-(trimethylsilyl methyl)cyclopropanecarboxylate

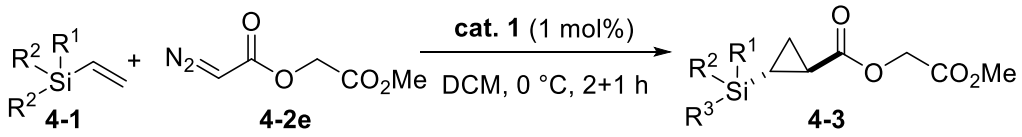


This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between dimethyl (2-phenyl)allyl trimethylsilane **1u** (190.4 mg, 1.0 mmol, 5.0 equiv.) and methyl (diazoacetoxy)acetate **2e** (31.6 mg, 0.20 mmol, 1 equiv.) in presence of **cat. 3** (1.3 mg, 0.002 mmol, 1 mol%) for 4 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (40/1 v/v) as an eluent to give the desired product **3t** as a colorless liquid (98% yield, 63.0 mg, 0.196 mmol). $[\alpha]^{26}_D$ = −109.7 (c 1.25, $CHCl_3$, major product). $[\alpha]^{27}_D$ = −104.9 (c 1.65, $CHCl_3$, minor product). d.r. = 56:44, 97% *trans* ee, 97% *cis* ee. Diastereoselectivity was separated by column chromatography. The ee values were determined by HPLC analysis. Column (CHIRALPAK IE-3), UV detector 220 nm, eluent: Hex/IPA = (300/1 v/v), flow rate = 1.0 mL/min, major product: tR = 14.84 min, tR = 16.72 min, minor product: tR = 53.42 min, tR = 77.46 min.

^{1}H NMR (500 MHz, $CDCl_3$, major product) δ 7.34 (d, 2H, *J* = 7.3 Hz), 7.28 (t, 2H, *J* = 7.6 Hz), 7.20 (t, 1H, *J* = 7.6 Hz), 4.71 (d, 1H, *J* = 15.9 Hz), 4.66 (d, 1H, *J* = 15.9 Hz), 3.78 (s, 3H), 1.92 (dd, 1H, *J* = 8.4, 6.1 Hz), 1.68 (dd, 1H, *J* = 8.2, 4.9 Hz), 1.40 (t, 1H, *J* = 5.8 Hz), 1.26 (dd, 2H, *J* = 32.6, 14.6

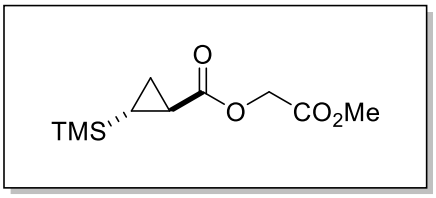
Hz), −0.24 (s, 9H) ppm. ^{1}H NMR (500 MHz, $CDCl_3$, minor product) δ 7.28 (d, 2H, *J* = 8.0 Hz), 7.24 (t, 2H, *J* = 7.6 Hz), 7.17 (t, 1H, *J* = 7.3 Hz), 4.40 (d, 1H, *J* = 15.7 Hz), 4.25 (d, 1H, *J* = 16.0 Hz), 3.67 (s, 3H), 1.99 (dd, 1H, *J* = 7.8, 5.7 Hz), 1.92 (ddd, 1H, *J* = 5.3, 5.0, 1.5 Hz), 1.71 (dd, 1H, *J* = 14.5, 1.5 Hz), 1.25 (dd, 1H, *J* = 7.7, 5.0 Hz), 0.6 (d, 1H, *J* = 14.5 Hz), −0.24 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, major product) δ 171.7, 168.5, 144.8, 128.3, 128.2, 126.8, 60.7, 52.1, 34.7, 28.0, 21.2, 20.5, −1.0 ppm. ^{13}C NMR (125 MHz, $CDCl_3$, minor product) δ 170.3, 168.4, 140.4, 129.3, 128.0, 126.8, 60.4, 52.0, 35.3, 31.4, 29.7, 20.7, −1.2 ppm. IR (neat) ν 3028, 2950, 2896, 1767, 1736, 1247, 848 cm^{-1}.

8-2-2 General Procedure for the Stereoselective Cyclopropanation of Vinylsilanes



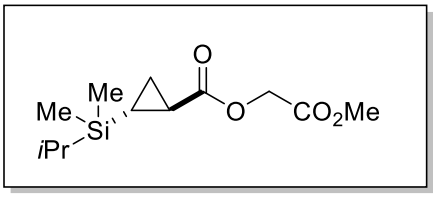
The solution of methyl (diazoacetoxy)acetate **4-2e** (0.2 mmol, 1 equiv.) in DCM (1.5 mL) was slowly added to a mixture of Ru(II)-Pheox (**cat. 1**) (3 mol%) and vinylsilane **4-1** (2.0 mmol, 10 equiv.) in DCM (0.5 mL) for 2 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The progress of the reaction was monitored by TLC. Upon completion, solvent was removed and the residue was purified by column chromatography on silica gel eluted with Hex/EA = (10/1 v/v) to give desired product **4-3**. The d.r. ratio was determined from the crude ^{1}H NMR spectra, and the ee value was determined by chiral HPLC analysis.

Methoxycarbonylmethyl 2-(trimethylsilyl)cyclopropane carboxylate



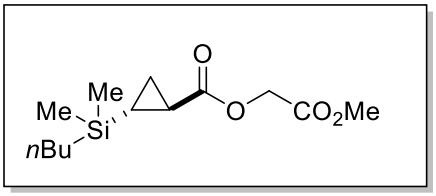
This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between vinyltrimethylsilane **4-1v** (200.4 mg, 2.0 mmol, 10.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (3.8 mg, 0.006 mmol, 3 mol%) for 2 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3v** as a colorless liquid (51% yield, 23.5 mg, 0.102 mmol). $[\alpha]^{18}_D = -30.8$ (c 0.31, $CHCl_3$). d.r. = >99:1, 98% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 0.5 mL/min, tR = 21.07 min (major product for *trans*-isomer), tR = 24.19 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.65 (d, 1H, J = 16.0 Hz), 4.59 (d, 1H, J = 16.0 Hz), 3.76 (s, 3H), 1.58 (ddd, 1H, J = 9.9, 5.7, 3.8 Hz), 1.29 (td, 1H, J = 7.3, 3.4 Hz), 0.82 (ddd, 1H, J = 10.7, 7.3, 3.4 Hz), 0.49 (ddd, 1H, J = 14.5, 8.4, 6.1 Hz), −0.01 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 168.5, 60.6, 52.2, 16.2, 12.7, 10.1, −2.7 ppm. IR (neat) ν 2955, 1739, 1159 cm^{-1}. HRMS (DART) calcd for $C_{10}H_{19}O_4Si$ $[M+H]^+$: 231.1052 found: 231.1050.

Methoxycarbonylmethyl 2-(isopropyldimethylsilyl) cyclopropanecarboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between isopropyldimethylvinylsilane **4-1w** (256.6 mg, 2.0 mmol, 10.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (3.8 mg, 0.006 mmol, 3 mol%) for 2 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3w** as a colorless liquid (46% yield, 24.0 mg, 0.092 mmol). $[\alpha]^{25}_{D} = -64.4$ (c 1.05, $CHCl_3$). d.r. = >99:1, 99% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 0.5 mL/min, tR = 14.33 min (major product for *trans*-isomer), tR = 16.45 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.64 (d, 1H, *J* = 15.7 Hz), 4.59 (d, 1H, *J* = 15.7 Hz), 3.75 (s, 3H), 1.58 (ddd, 1H, *J* = 8.6, 6.7, 4.2 Hz), 1.29 (td, 1H, *J* = 11.1, 3.8 Hz), 0.99 (d, 6H, *J* = 7.3 Hz), 0.92–0.78 (m, 2H), 0.45 (ddd, 1H, *J* = 13.4, 8.6, 6.1 Hz), −0.11 (s, 6H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 168.4, 60.6, 52.1, 17.5, 15.9, 13.6, 12.3, 7.8, −6.9 ppm. IR (neat) ν 2941, 1769, 1740, 1255, 1158, 837 cm^{-1}.

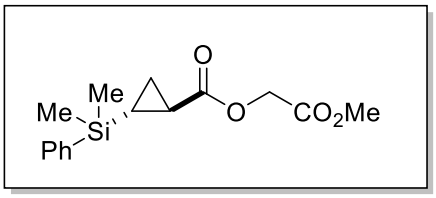
Methoxycarbonylmethyl 2-(butyldimethylsilyl) cyclopropane carboxylate



This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between butyldimethylvinylsilane **4-1x** (284.6 mg, 2.0 mmol, 10.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (3.8 mg, 0.006 mmol, 3 mol%) for 2 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3x** as a colorless liquid (61% yield, 33.2 mg, 0.122 mmol). $[\alpha]^{25}_{D} = -32.6$ (c 1.50, $CHCl_3$). d.r. = >99:1, 99% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (100/1 v/v), flow rate = 0.5 mL/min, tR = 10.71 min (minor product for *trans*-

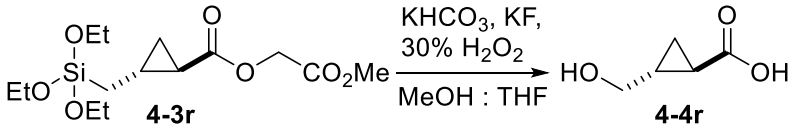
isomer), tR = 12.37 min (major product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.64 (d, 1H, *J* = 16.2 Hz), 4.58 (d, 1H, *J* = 15.9 Hz), 3.75 (s, 3H), 1.57 (ddd, 1H, *J* = 8.3, 5.9, 4.3 Hz), 1.37–1.21 (m, 5H), 0.87 (t, 3H, *J* = 7.0 Hz), 0.81 (ddd, 1H, *J* = 8.4, 7.5, 3.4 Hz), 0.53 (t, 2H, *J* = 8.1 Hz), 0.46 (ddd, 1H, *J* = 9.5, 6.1, 5.5 Hz), −0.06 (s, 3H), −0.07 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 168.4, 60.6, 52.1, 26.4, 25.9, 16.1, 14.4, 13.7, 12.5, 9.2, −4.6, −4.7 ppm. IR (neat) ν 2956, 1769, 1740, 1395, 1250, 818 cm^{-1}.

Methoxycarbonylmethyl 2-(dimethylphenylsilyl) cyclopropanecarboxylate

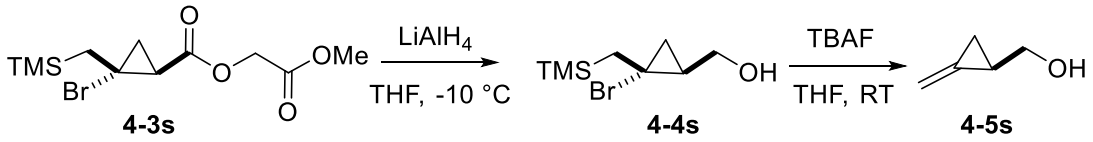


This compound was prepared according to the typical procedure for asymmetric cyclopropanation reaction between dimethylphenylvinylsilane **4-1y** (324.6 mg, 2.0 mmol, 10.0 equiv.) and methyl (diazoacetoxy)acetate **4-2e** (31.6 mg, 0.20 mmol, 1.0 equiv.) in presence of **cat. 1** (3.8 mg, 0.006 mmol, 3 mol%) for 2 h under argon atmosphere at 0 °C. After the addition completed, the reaction mixture was then stirred for 1 h at 0 °C. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (10/1 v/v) as an eluent to give the desired product **4-3y** as a colorless liquid (35% yield, 20.35 mg, 0.07 mmol). $[\alpha]^{27}_{D}$ = −18.5 (c 0.55, $CHCl_3$). d.r. = >99:1, 53% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB), UV detector 220 nm, eluent: Hex/IPA = (200/1 *v/v*), flow rate = 1.0 mL/min, tR = 14.84 min (major product for *trans*-isomer), tR = 17.28 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.52 (m, 2H), 7.40–7.33 (m, 3H), 4.65 (d, 1H, *J* = 15.7 Hz), 4.59 (d, 1H, *J* = 16.0 Hz), 3.76 (s, 3H), 1.62 (ddd, 1H, *J* = 7.5, 5.7, 4.2 Hz), 1.35 (td, 1H, *J* = 14.1, 3.4 Hz), 0.84 (ddd, 1H, *J* = 8.4, 7.6, 3.4 Hz), 0.70 (ddd, 1H, *J* = 10.7, 8.4, 6.1 Hz), 0.27 (s, 3H), 0.26 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 168.4, 137.0, 133.8, 129.3, 127.9, 60.6, 52.2, 16.4, 12.6, 9.0, −3.9, −4.2 ppm. IR (neat) ν 3067, 2954, 1737, 1157, 829 cm^{-1}.

8-2-3 応用反応



The cyclopropanation product **4-3r** (123.0 mg, 0.37 mmol, 1.0 equiv.) in MeOH/THF = (1/1 v/v) (1.0 mL) at room temperature, was successively added KF (44.2 mg, 0.76 mmol, 2.0 equiv.), $KHCO_3$ (37.0 mg, 0.37 mmol, 1.0 equiv.), and was slowly added to H_2O_2 (0.15 mL, 30% aqueous solution, 1.30 mmol, 3.5 equiv.). After the addition completed, the reaction mixture was then stirred at room temperature for 5 h. The progress of the reaction was monitored by TLC. After the reaction mixture was slowly added $Na_2S_2O_3$ (1.0 mL, 50% aqueous solution). The reaction mixture added NaOH (4.0 mL, 1.2 N), and extracted with Et_2O (3x10 mL). The water layer was added NaCl until saturation, washed with Et_2O, acidified with HCl (2M until pH=2), and extracted with Et_2O (5x10 mL). Evaporation gave the desired product **4-4r** as a colorless liquid (57% yield, 24.5 mg, 0.21 mmol). $[\alpha]^{23}_D = -74.7$ (c 0.92, MeOH). d.r. = 97:3. ^{1}H NMR (400 MHz, D_2O) δ 3.60 (s, 1H), 3.53–3.44 (m, 1H), 3.40–3.25 (m, 1H), 1.90–1.45 (m, 2H), 1.35–1.05 (m, 1H), 1.0–0.80 (m, 1H) ppm. ^{13}C NMR (100 MHz, D_2O) δ 178.7, 63.6, 24.2, 18.1, 13.1 ppm.



$LiAlH_4$ (14.1 mg, 0.37 mmol, 1.2 equiv.) was slowly added to the solution of the cyclopropanation product **4-3s** (100.0 mg, 0.31 mmol, 1.0 equiv.) in THF (1.5 mL) at −10 °C. The progress of the reaction was monitored by TLC. After quenching with H_2O, extracted three times with Et_2O, and dried over Na_2SO_4. The resulting mixture was purified by silica gel column chromatography with Hex/EA = (3/1 v/v) as an eluent to give the desired product **4-4s** as a colorless liquid (52% yield, 38.0 mg, 0.16 mmol). $[\alpha]^{20}_D = -17.6$ (c 0.98, $CHCl_3$). d.r. = 95:5, 99% *trans* ee. The ee values were determined by HPLC analysis. Column (CHIRALPAK IB-3), UV detector 220 nm, eluent: Hex/IPA = (200/1 v/v), flow rate = 0.5 mL/min, tR = 42.70 min (major product for *trans*-isomer), tR = 46.12 min (minor product for *trans*-isomer). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.62 (ddd, 2H, J = 29.8, 17.6, 11.8 Hz), 1.77 (ddt, 1H, J = 13.4, 9.9, 6.5 Hz), 1.73–1.42 (bs, 1H), 1.55 (dd, 1H, J = 14.9, 1.5 Hz), 1.36 (ddt, 1H, J = 14.5, 8.0, 6.7 Hz), 1.06 (d, 1H, J = 14.9 Hz), 0.58 (t, 1H, J = 6.7 Hz), 0.15 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 62.4, 35.5, 30.3, 25.3, 21.7, −0.3 ppm.

The solution product **4-4s** (35.7 mg, 0.15 mmol, 1.0 equiv.) in THF (1.5 mL) was slowly added to TBAF in 1M THF (0.3 mL, 0.3 mmol, 2.0 equiv.) at room temperature. After the addition completed, the reaction mixture was then stirred at −10 °C for 2 h. The progress of the reaction was monitored by TLC. After quenching with H_2O, extracted three times with Et_2O. The organic phase was washed with brine, dried over Na_2SO_4, and evaporated to give the desired product **4-5s** (91% yield by crude ^1H NMR). ^1H NMR (500 MHz, $CDCl_3$) δ 5.42 (d, 1H, *J* = 2.7 Hz), 5.4 (bs, 1H), 3.6 (dd, 1H, *J* = 11.1, 6.1 Hz), 3.40 (dd, 1H, *J* = 11.1, 7.6 Hz), 1.80–1.74 (m, 1H), 1.27 (t, 1H, *J* = 8.8 Hz), 0.87 (ddd, 1H, *J* = 19.7, 13.7, 7.6 Hz) ppm.

8-2-4 X-ray Analysis of (1*R*,2*R*)-**4-3c** (Figure 8-2)

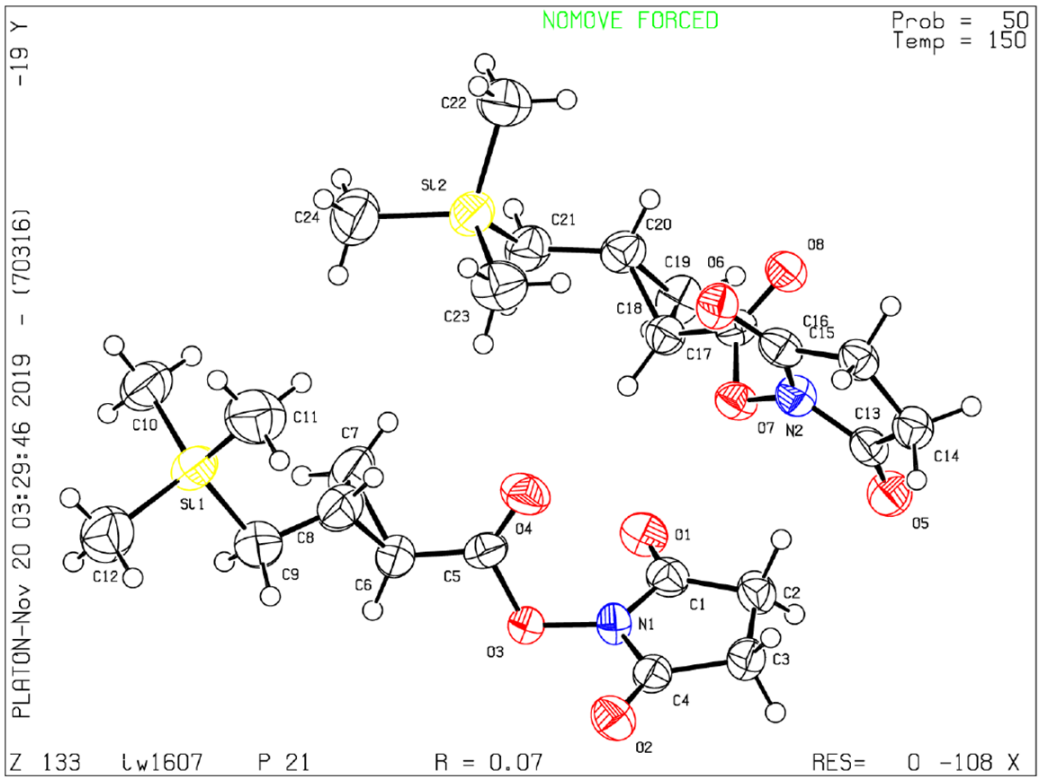
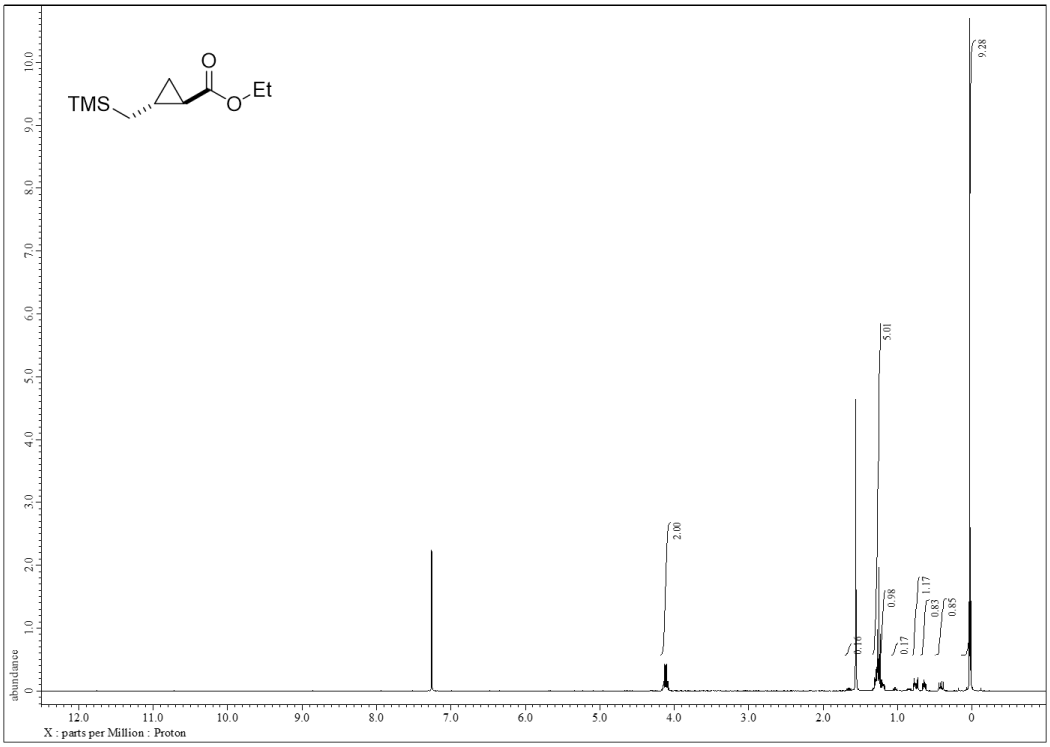


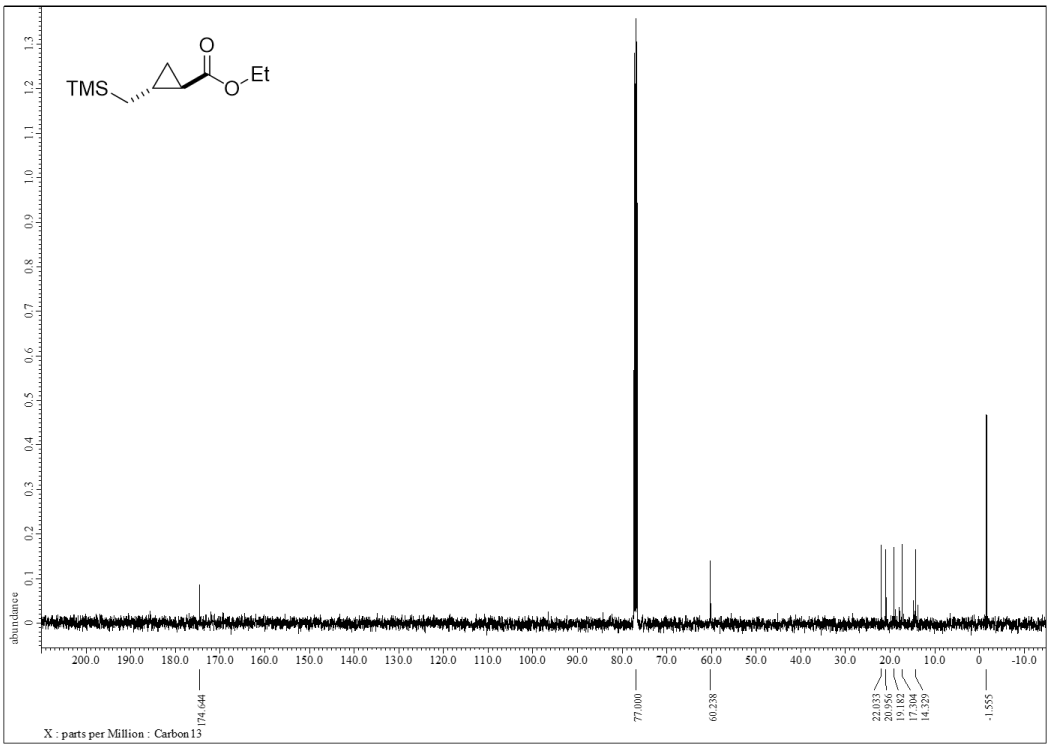
Table 8-2. Crystal data and structure refinement for **iw1607**.

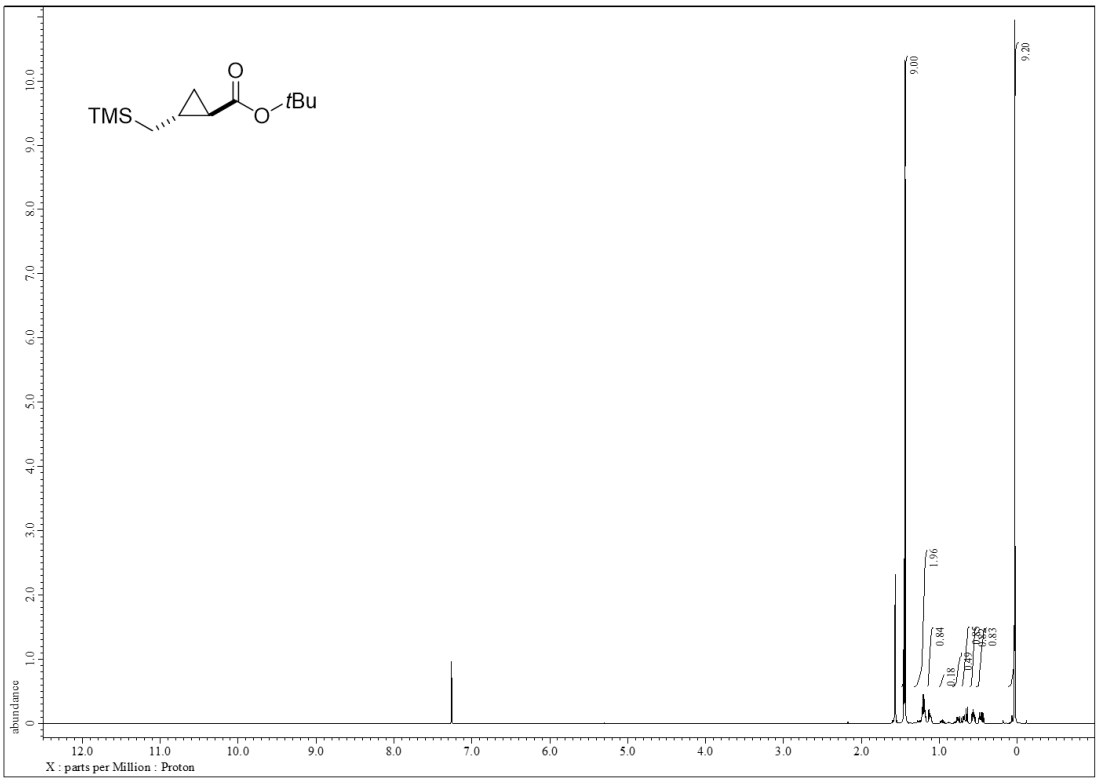
Identification code	iw1607
Empirical formula	$C_{12}H_{19}NO_4Si$
Formula weight	269.37
Temperature	150(2) K
Wavelength	0.71075 Å
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 10.315(4) Å α = 90°
	b = 8.770(3) Å β = 100.449(6)°
	c = 16.508(6) Å γ = 90°

Volume	1468.5(10) $Å^3$
Z	4
Density (calculated)	1.218 Mg/m^3
Absorption coefficient	0.166 mm^{-1}
F(000)	576
Crystal size	0.300 x 0.100 x 0.020 mm^3
Theta range for data collection	2.008 to 24.999°
Index ranges	-12<= *h* <=12, -10<= *k* <=10, -19<= *l* <=19
Reflections collected	28668
Independent reflections	5162 [*R*(int) = 0.0432]
Completeness to theta	24.999° 99.9%
Absorption correction	Numerical
Max. and min. transmission	0.988 to 0.922
Refinement method	Full-matrix least-squares on *F*2
Date / restraints / parameters	5162 / 1 / 331
Goodness of fit on *F*2	1.089
Final *R* indices [*I* > 2sigma(*I*)]	*R*1 = 0.0713, *wR*2 = 0.1879
R indices (all data)	*R*1 = 0.0767, *wR*2 = 0.1964
Absolute structure parameter	-0.01(7)
Extinction coefficient	n/a
Largest diff. peak and hole	0.411 and -0.393 e. $Å^{-3}$

8-2-5 NMR Spectral Data



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abundance
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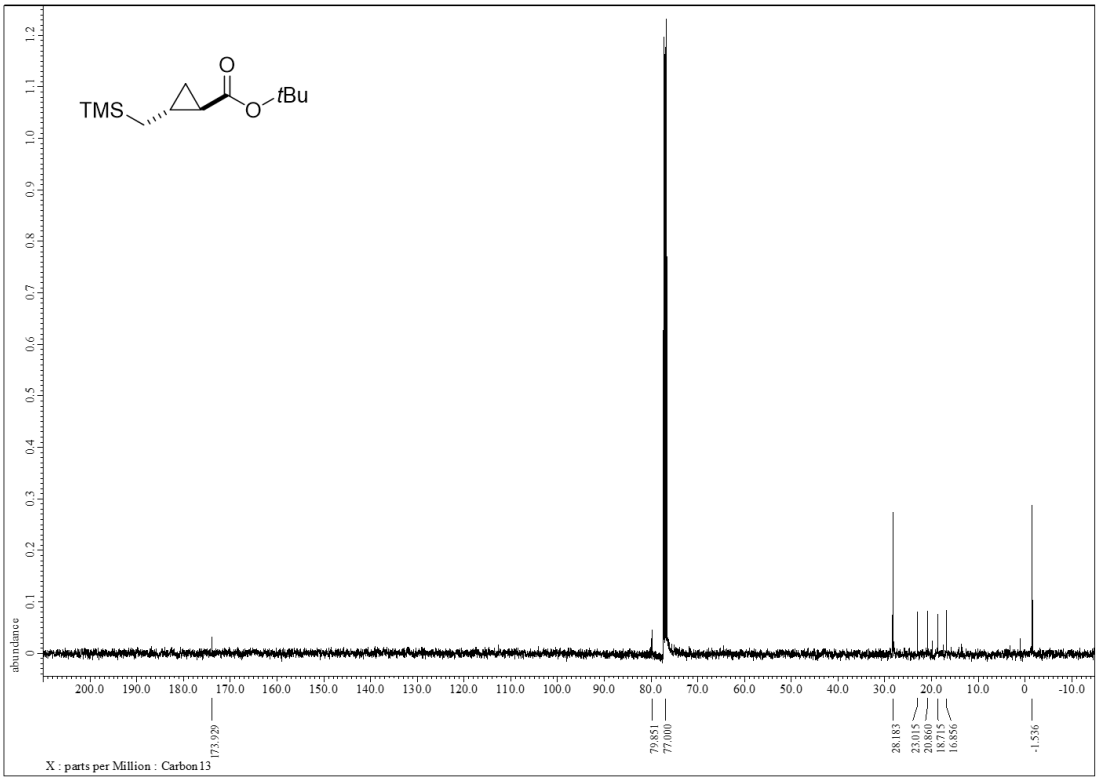
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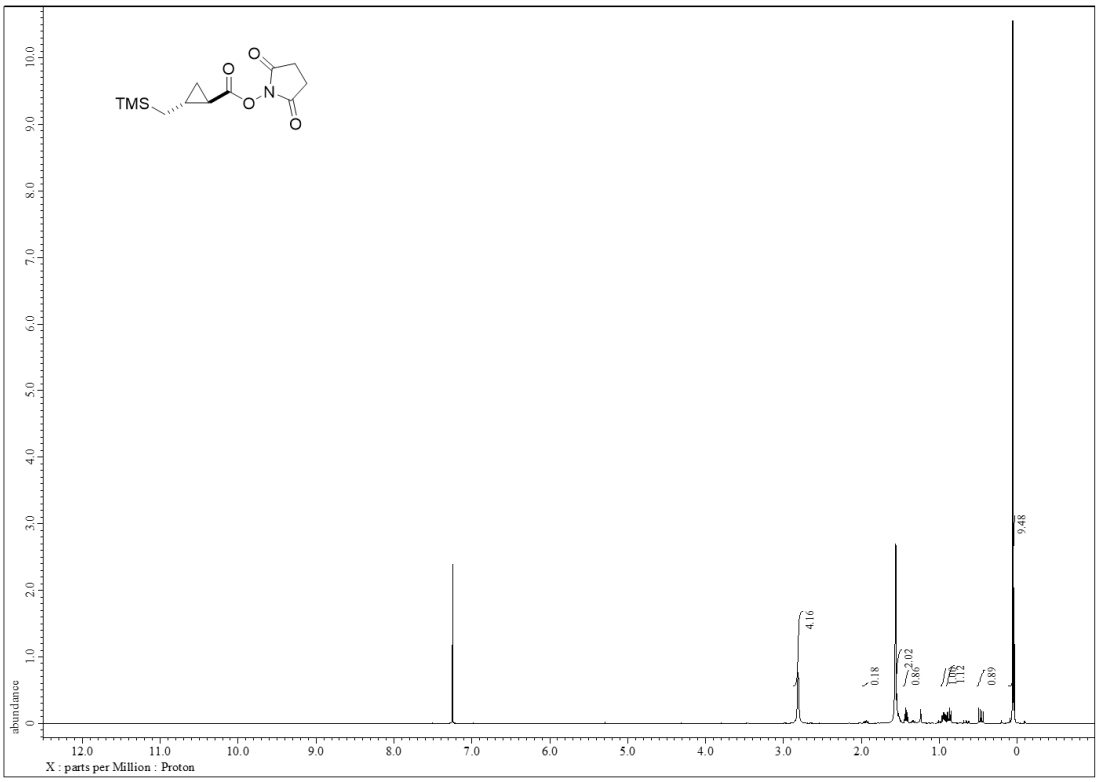
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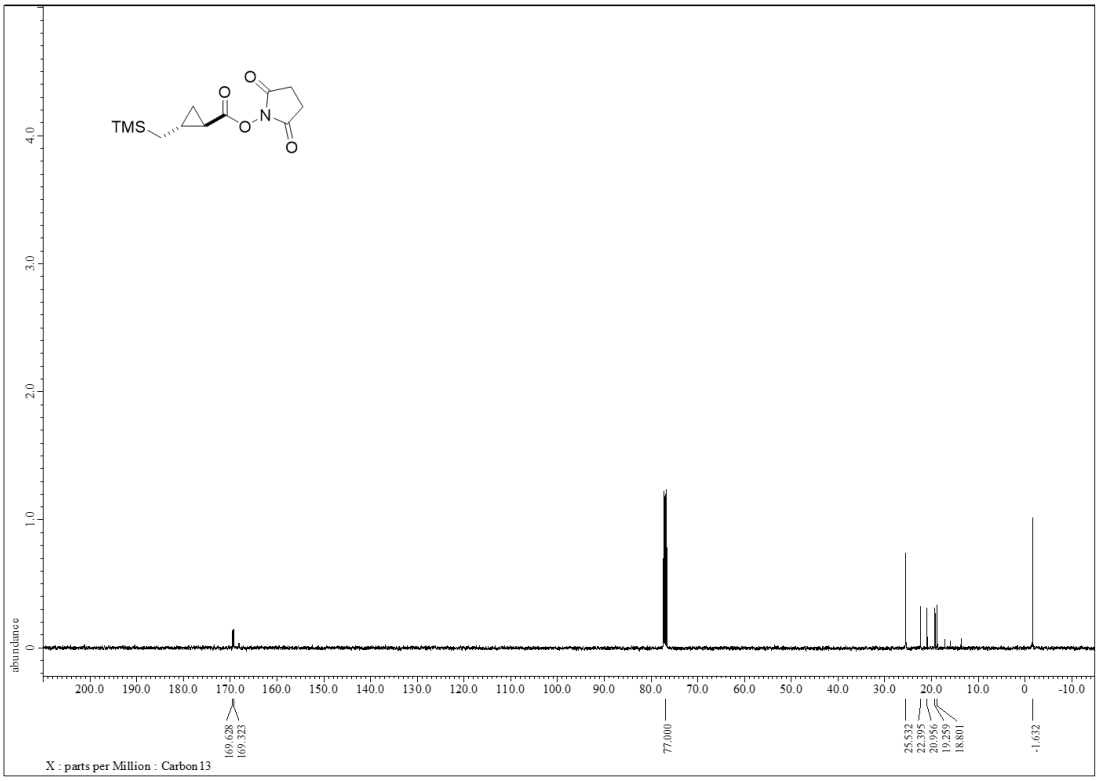
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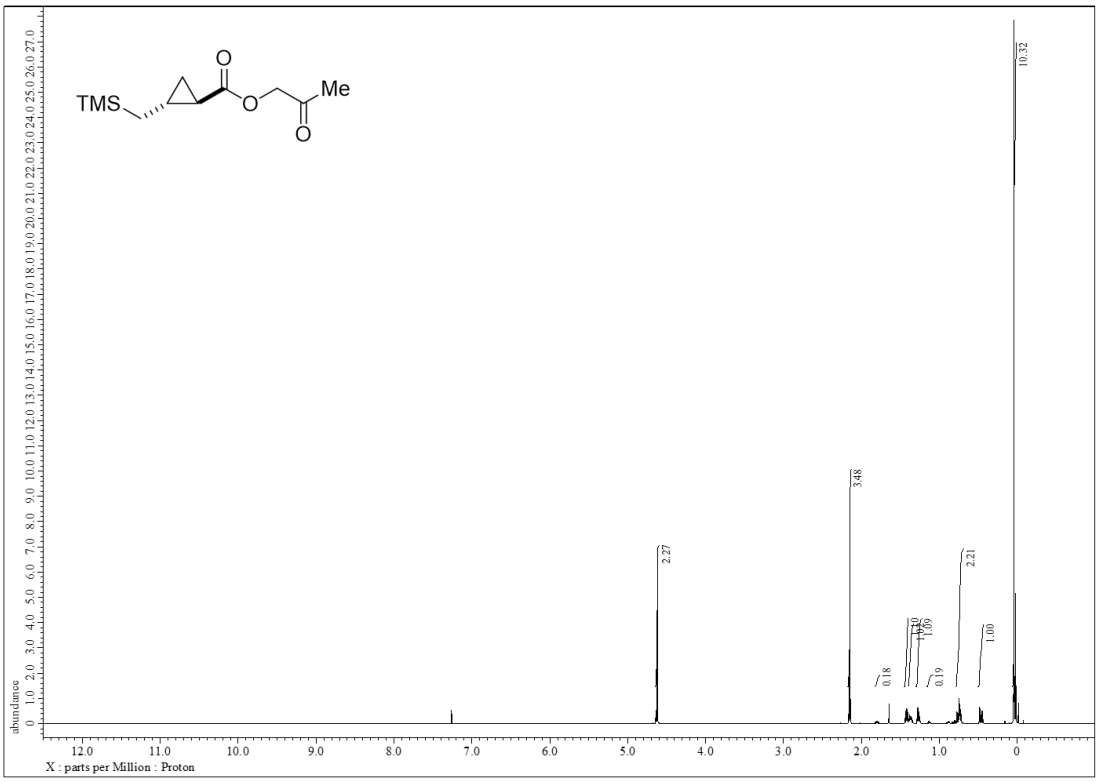
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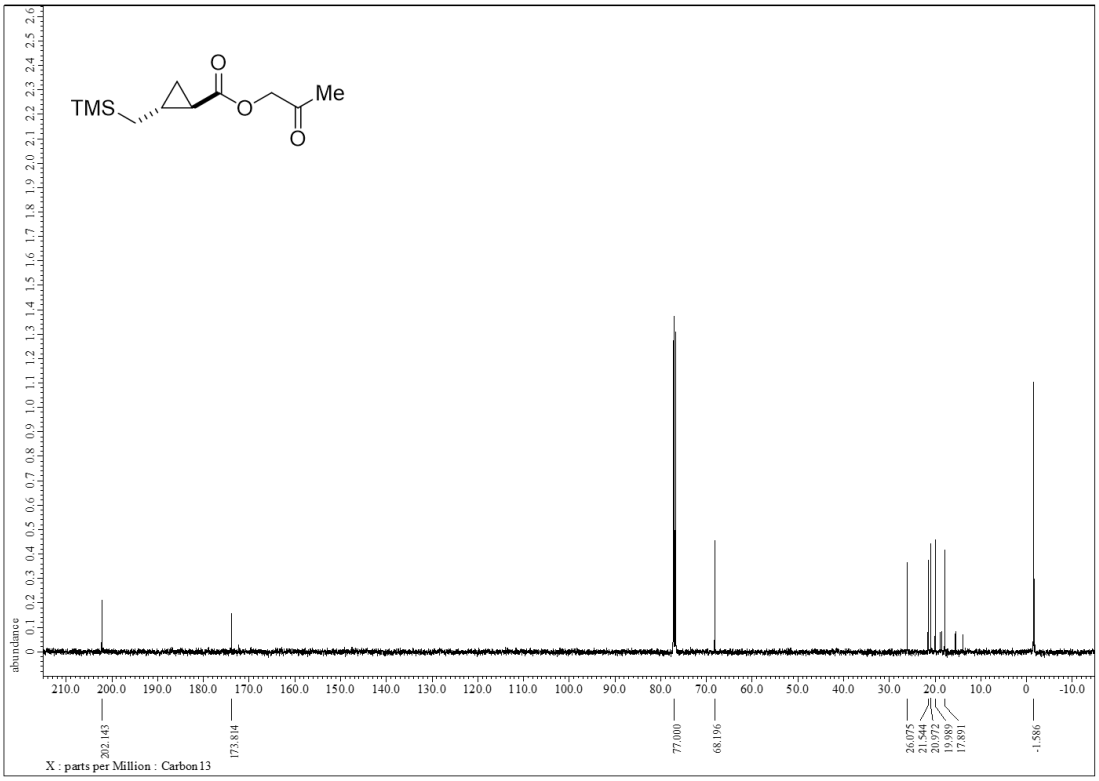
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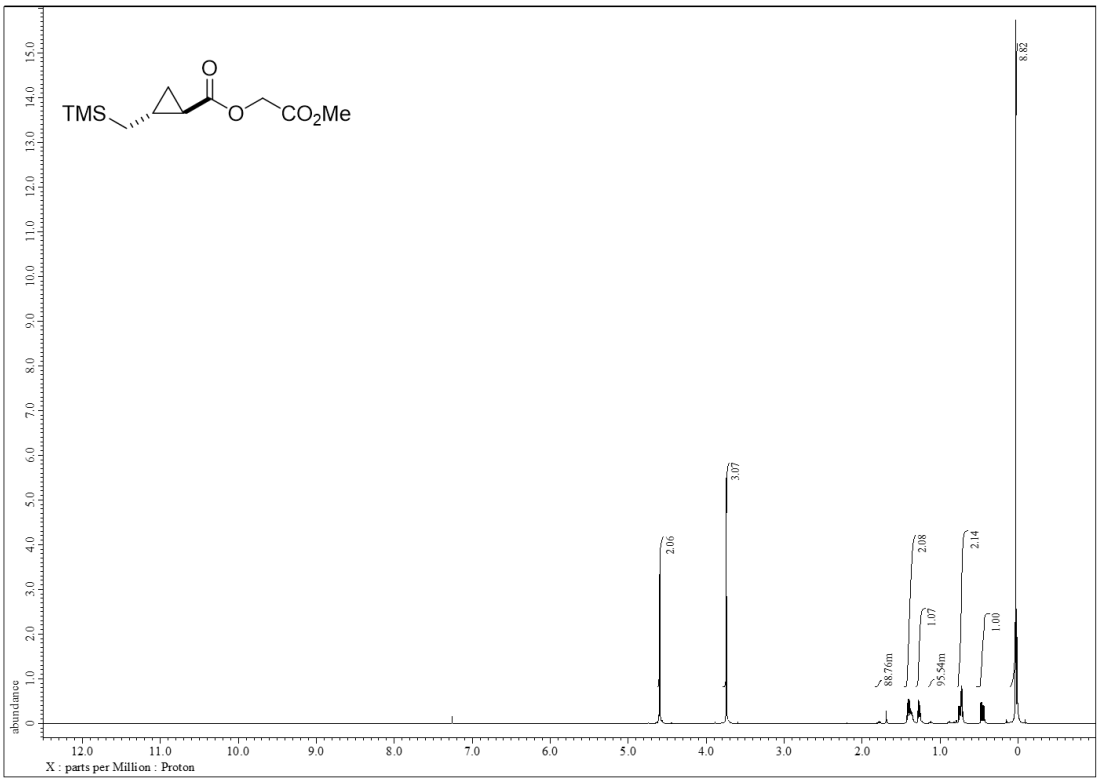
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abundance
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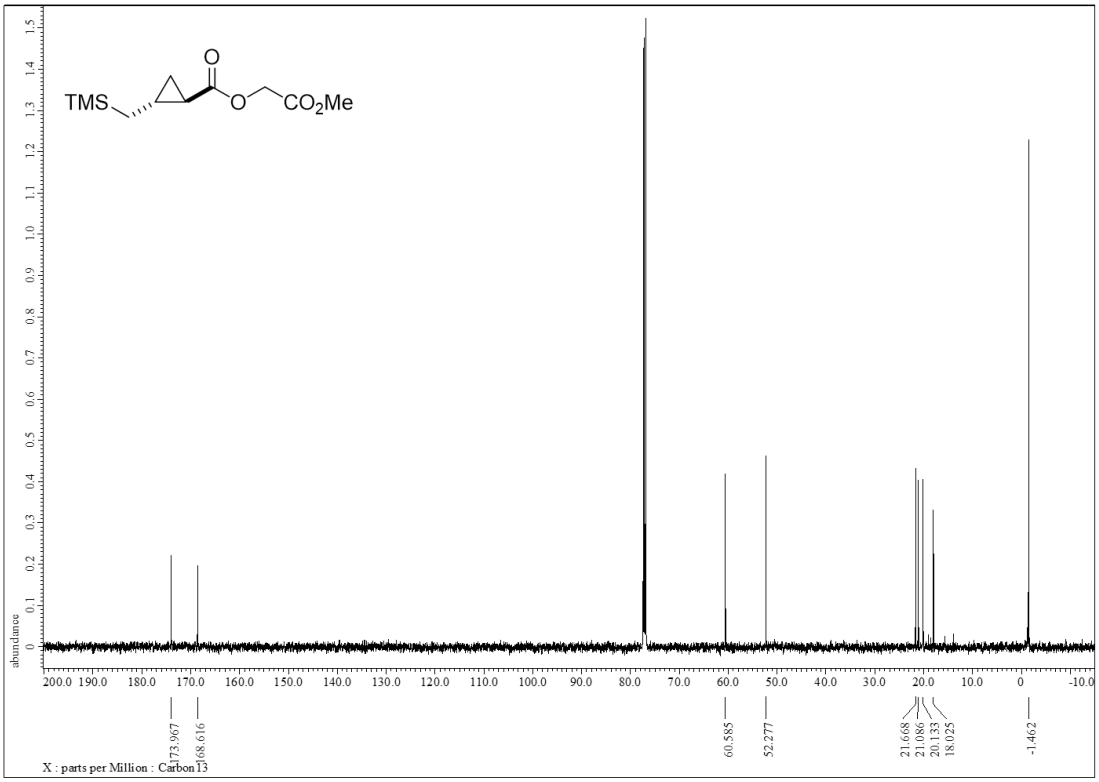
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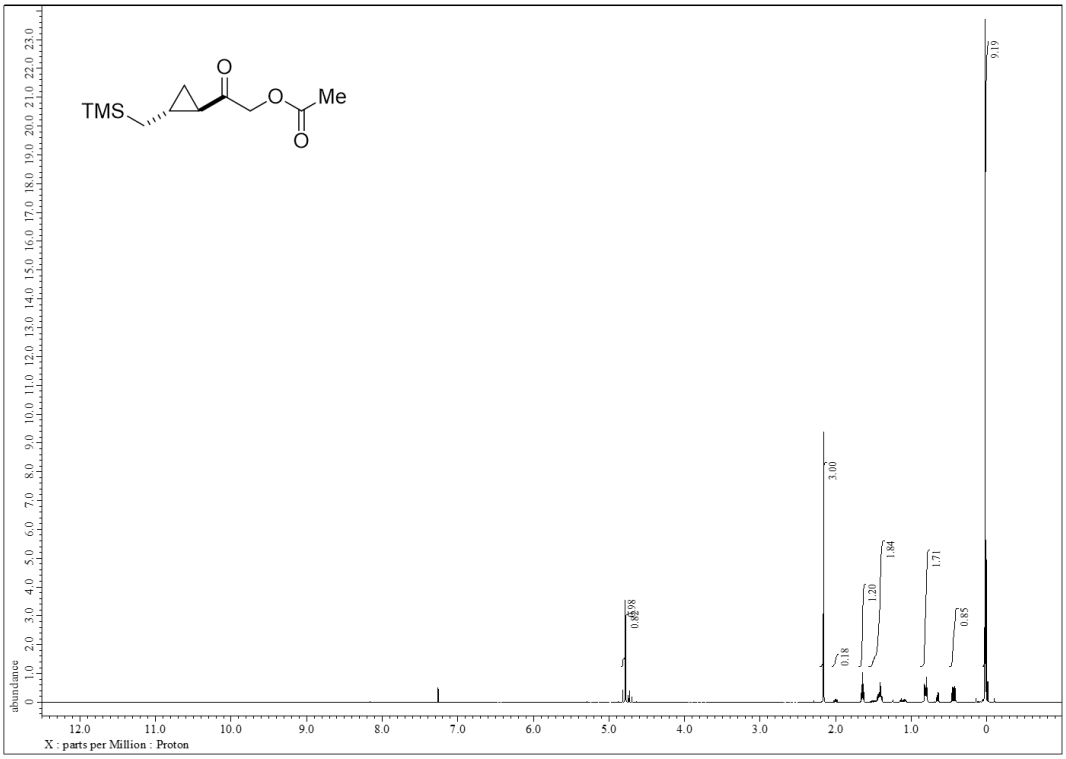
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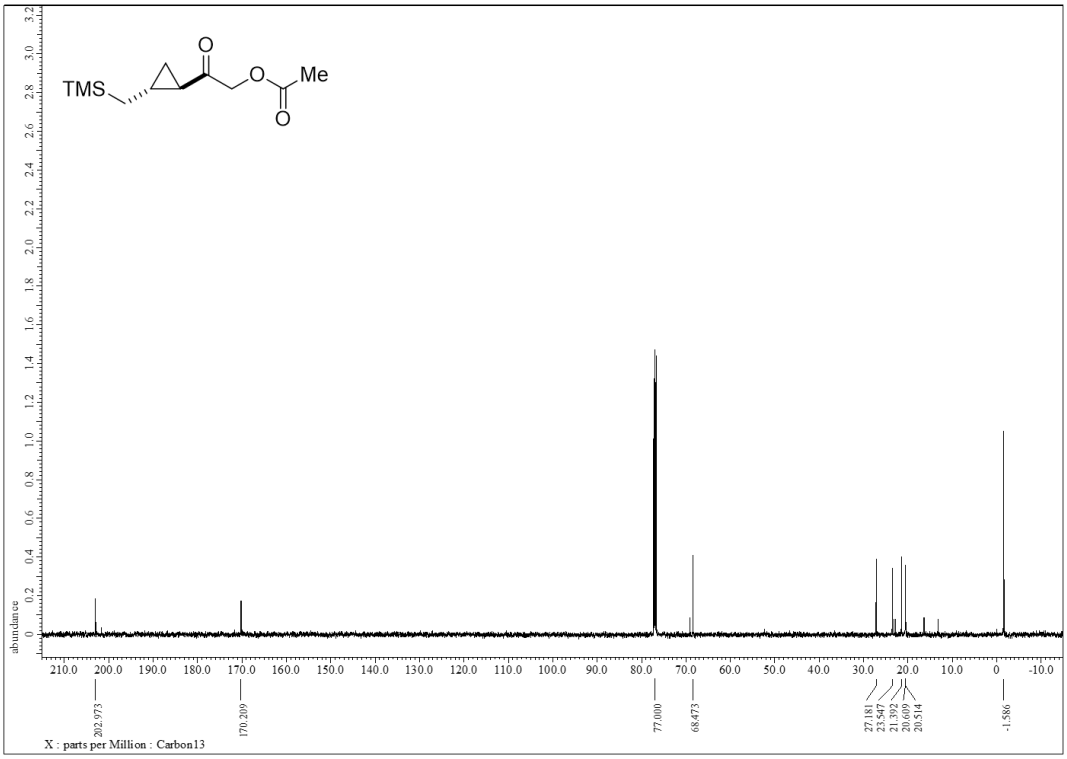
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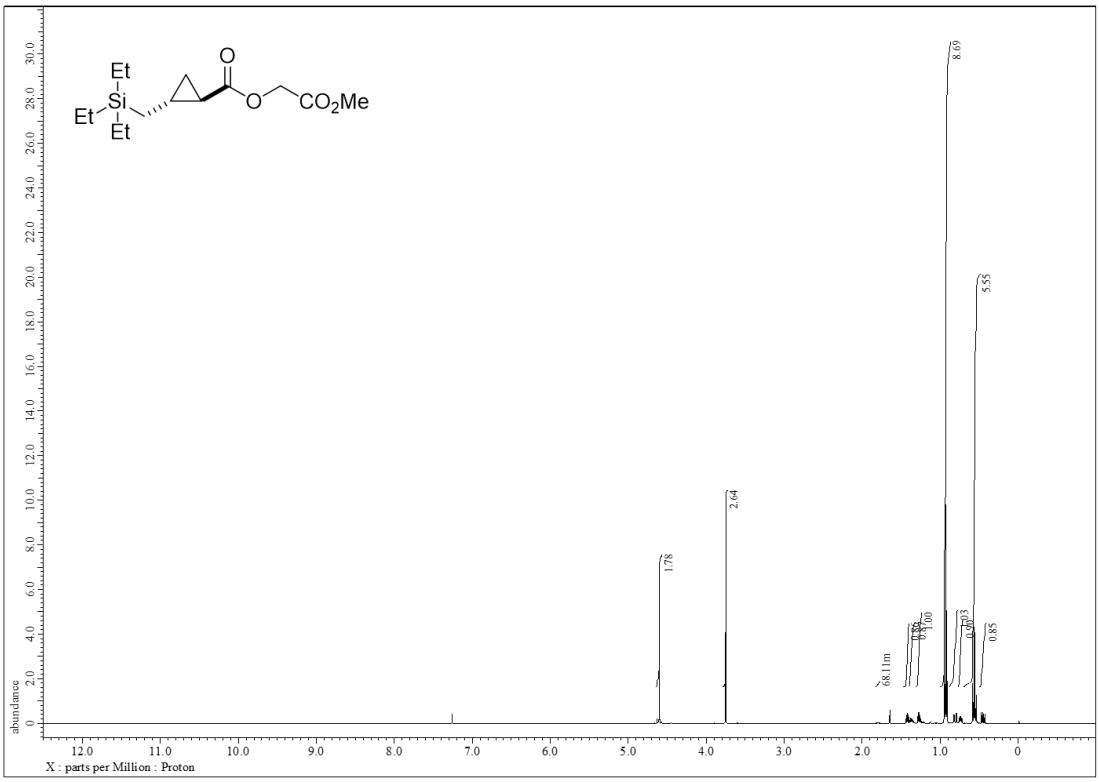
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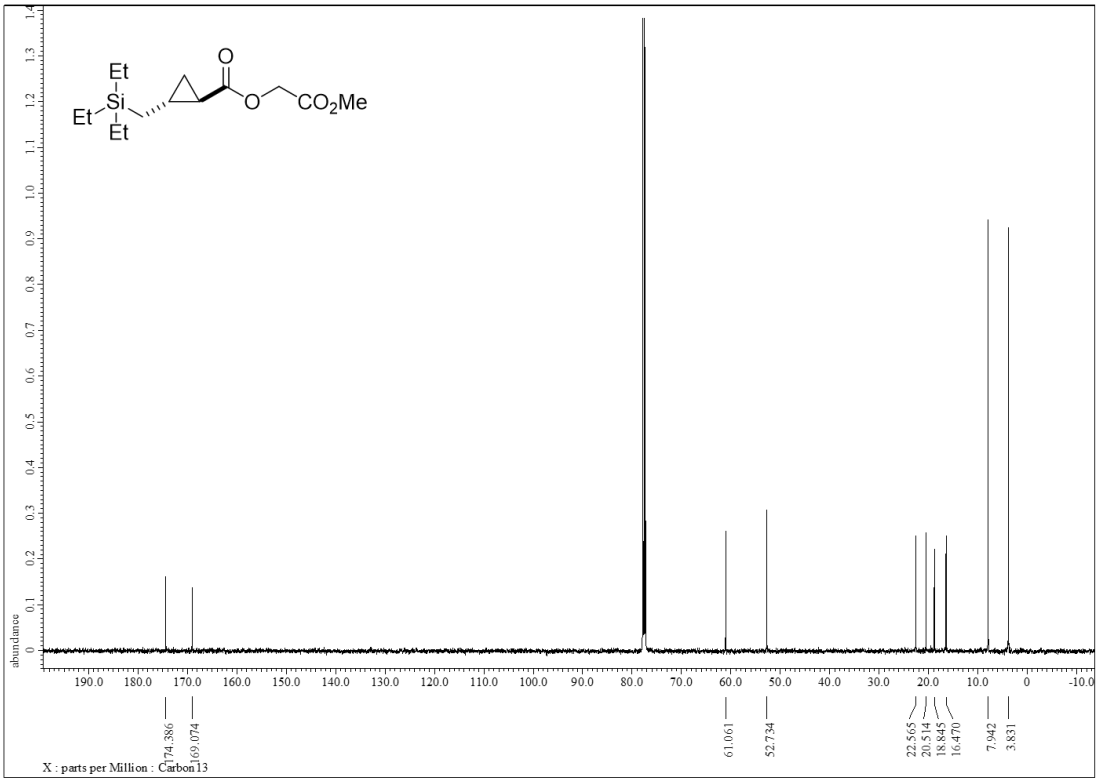
abundance
X : parts per Million : Proton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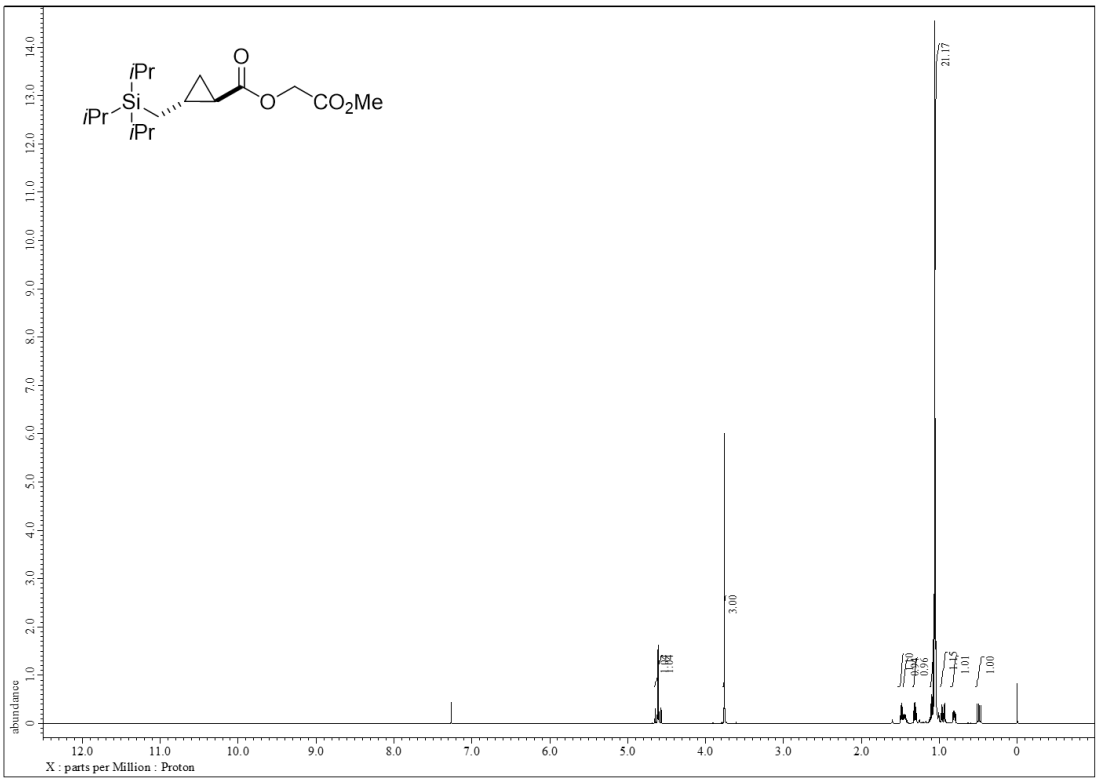
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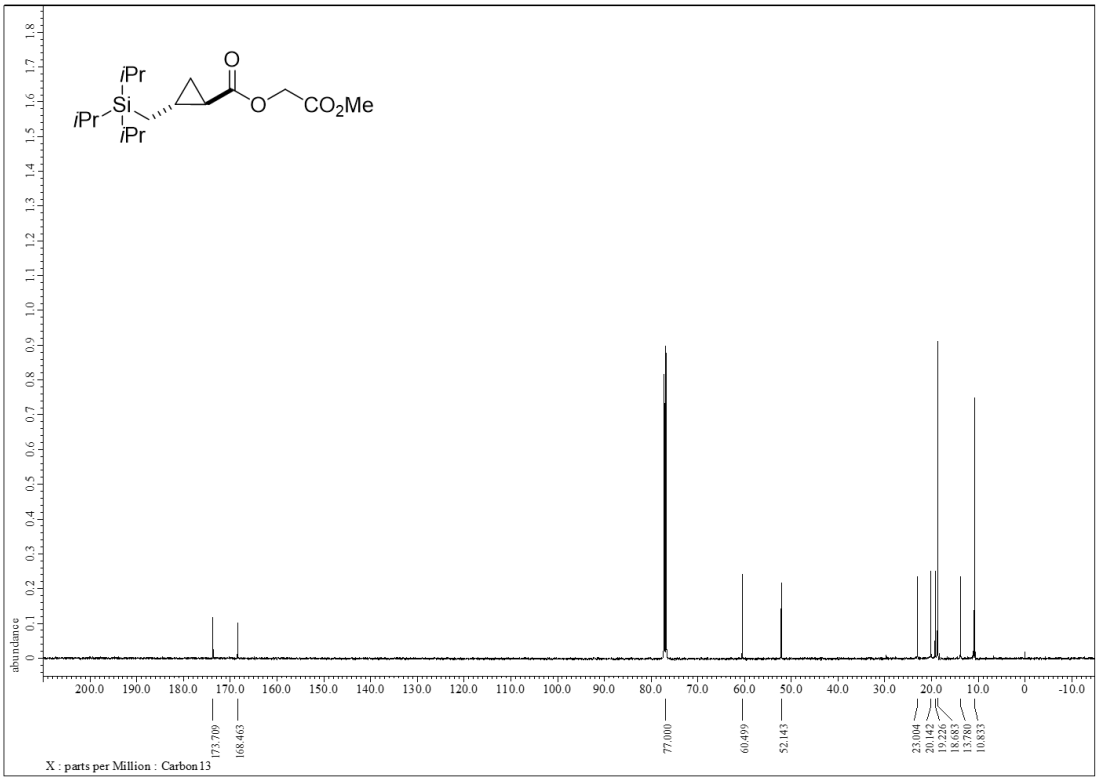
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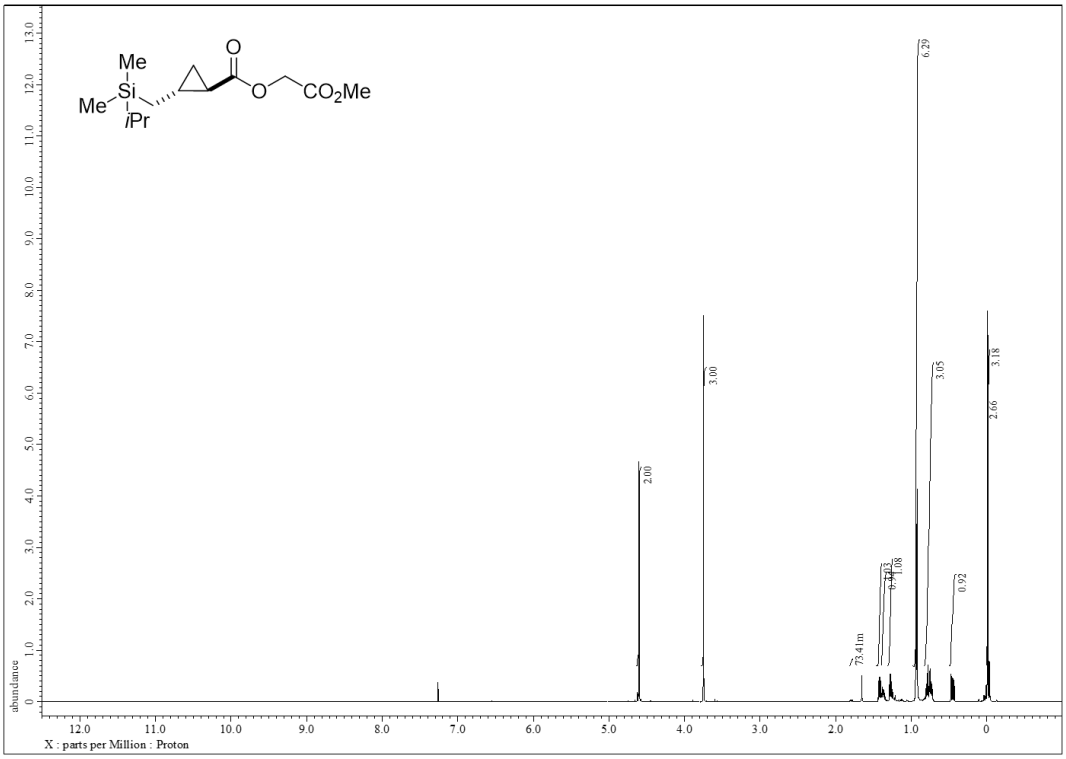
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O
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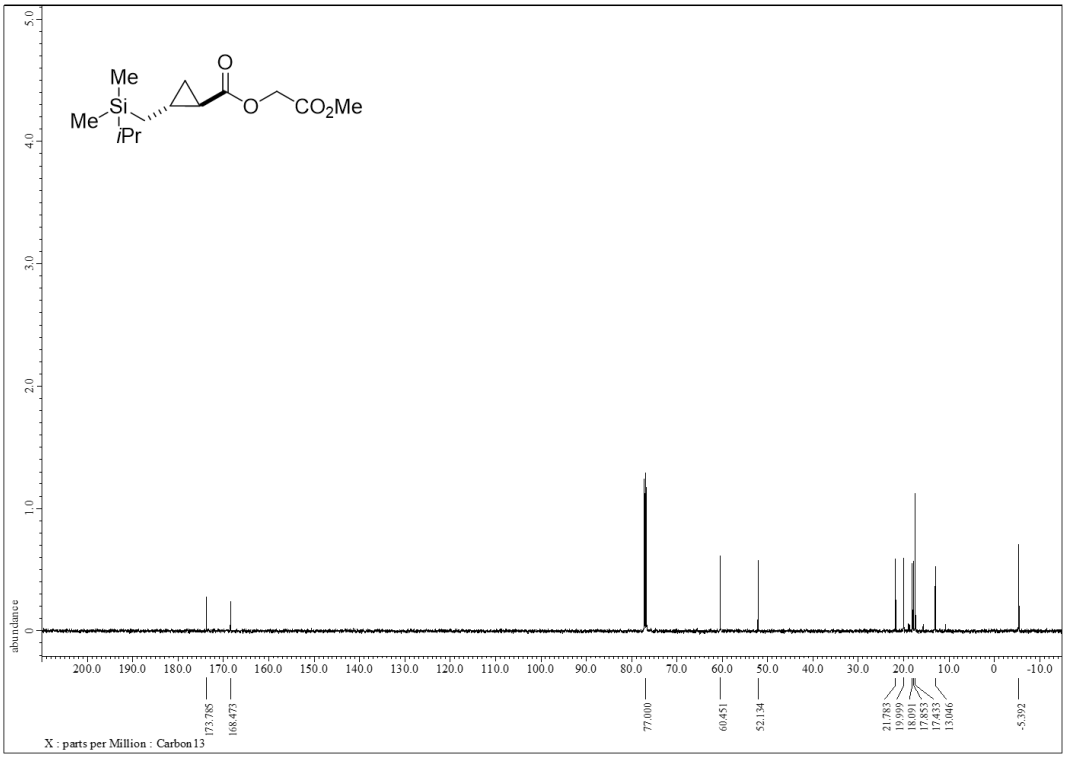
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O
CO2Me
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X : parts per Million : Carbon13
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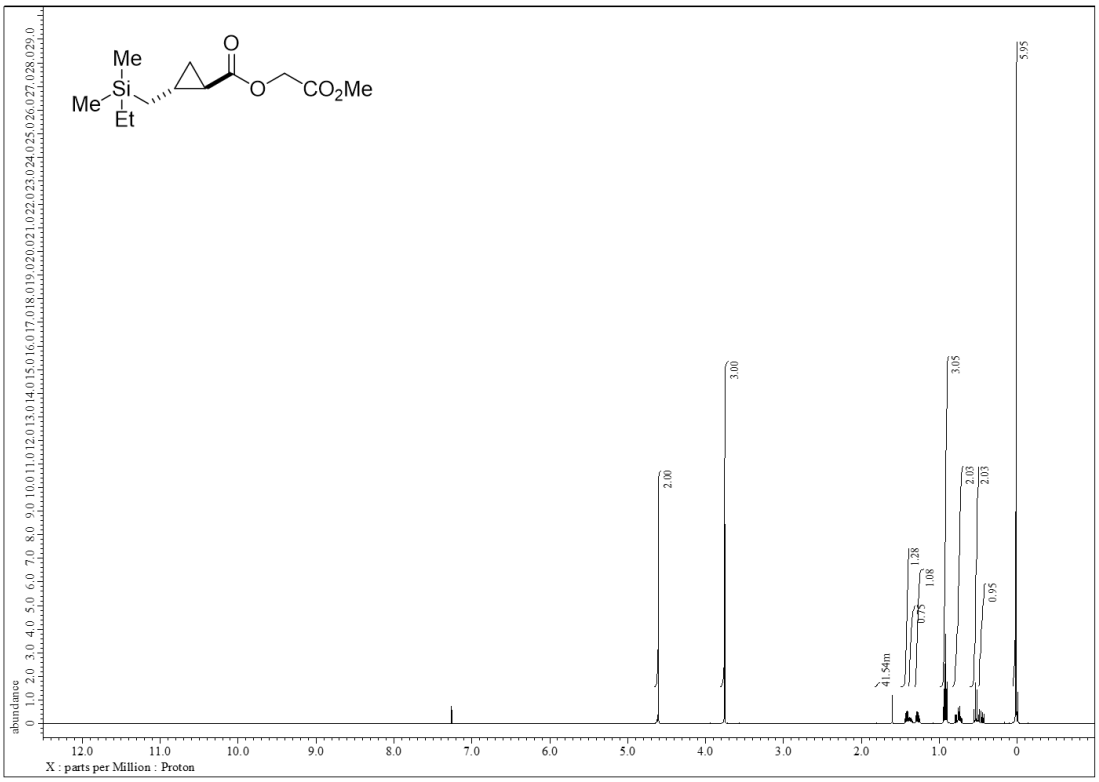
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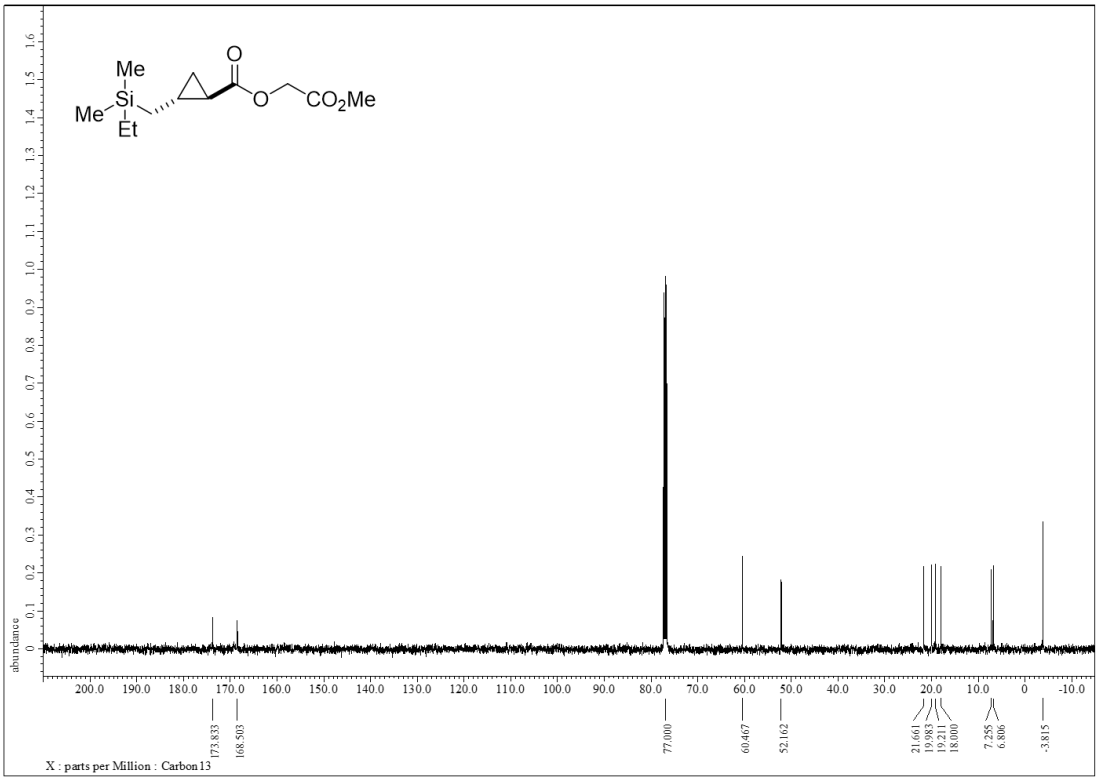
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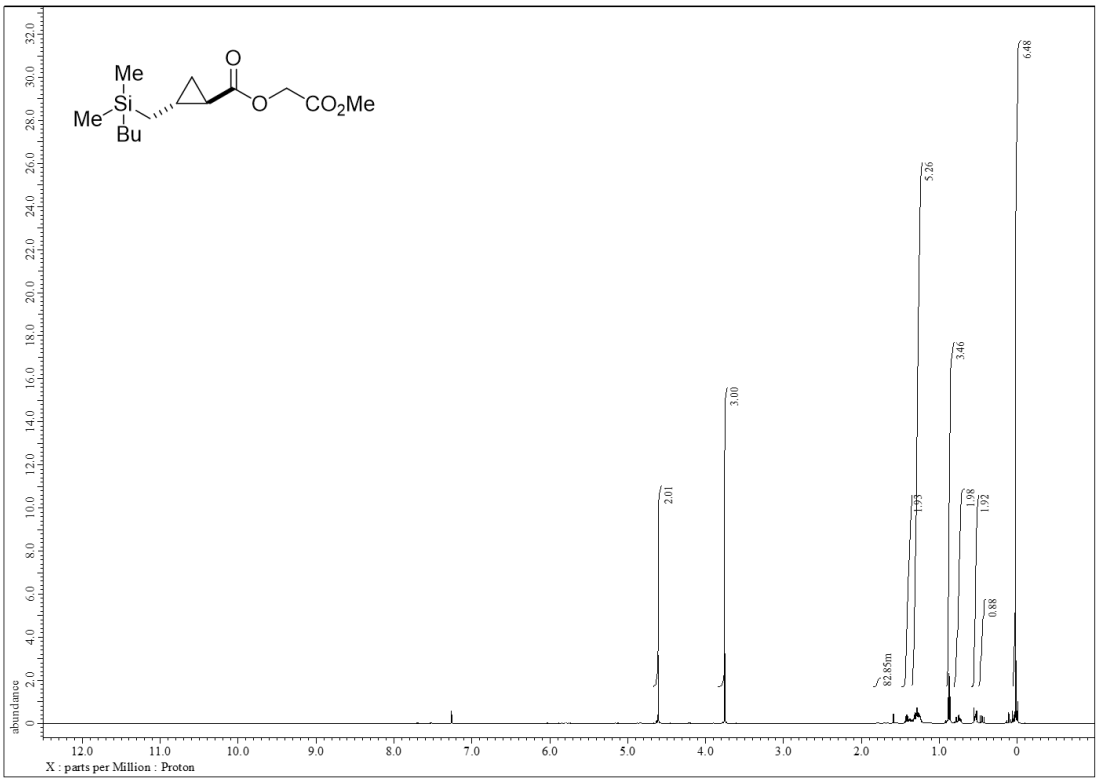
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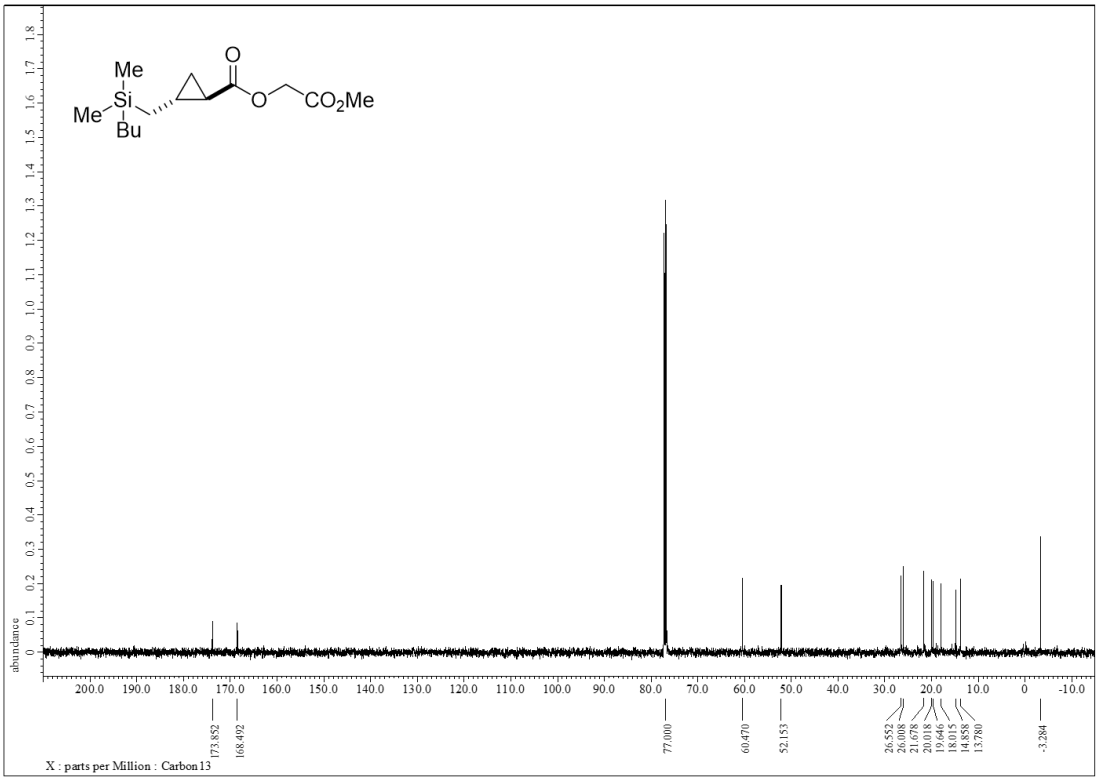
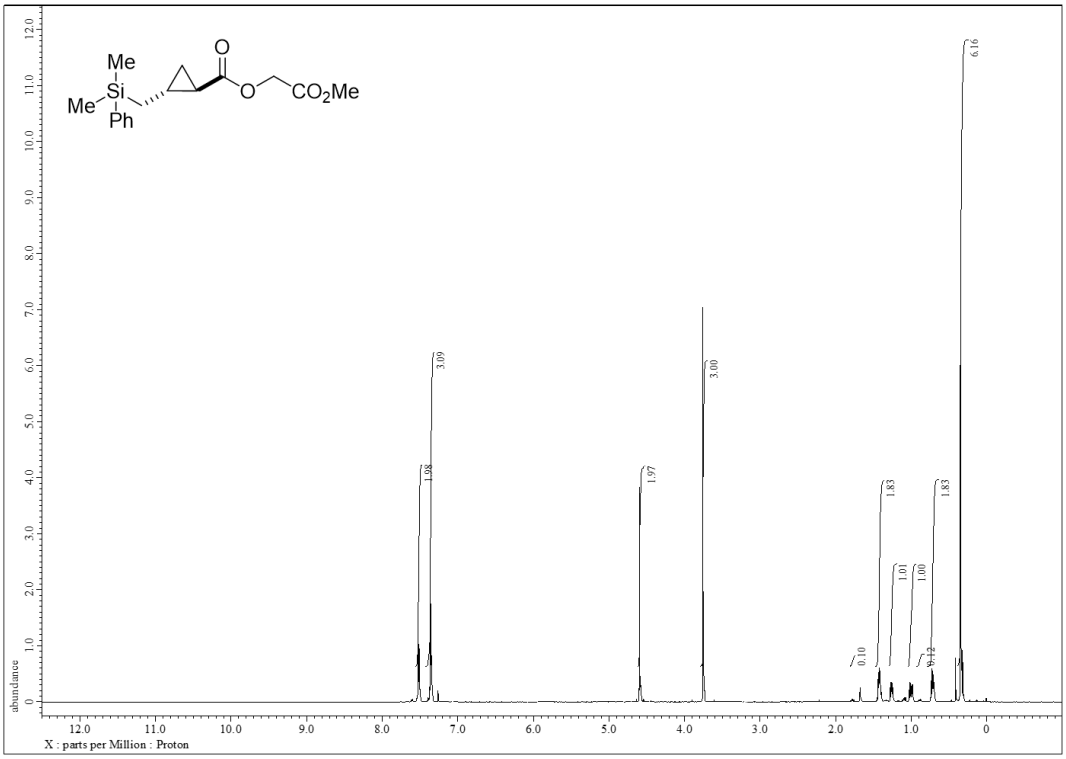
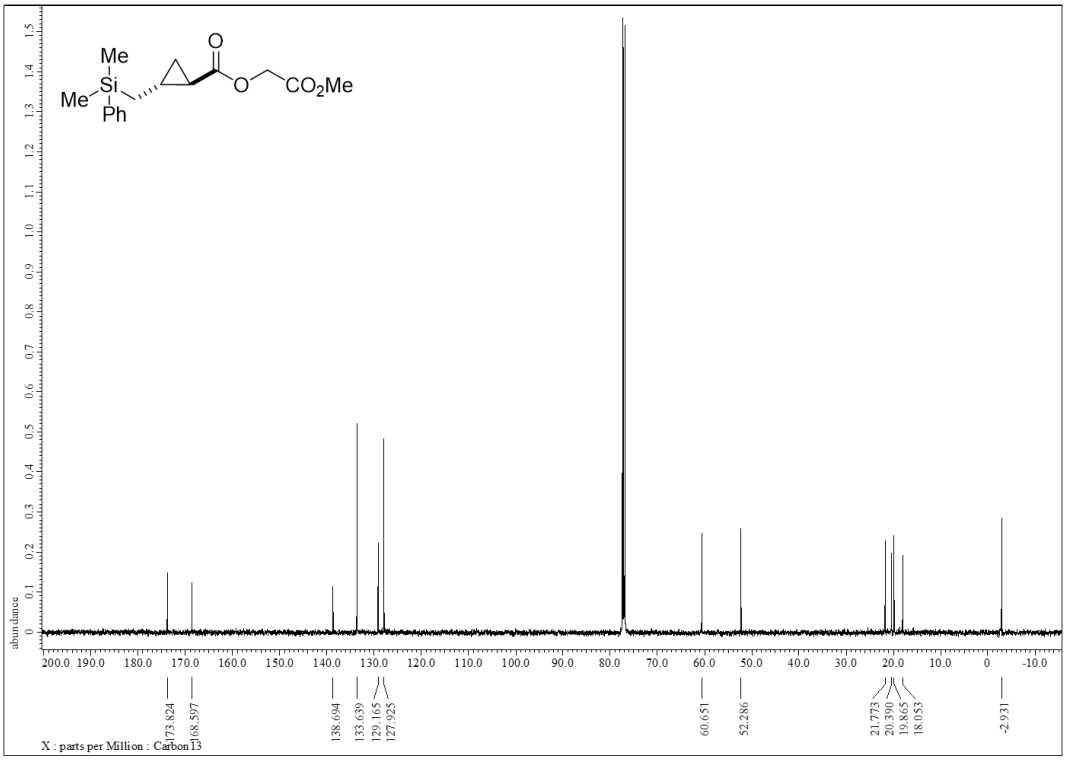
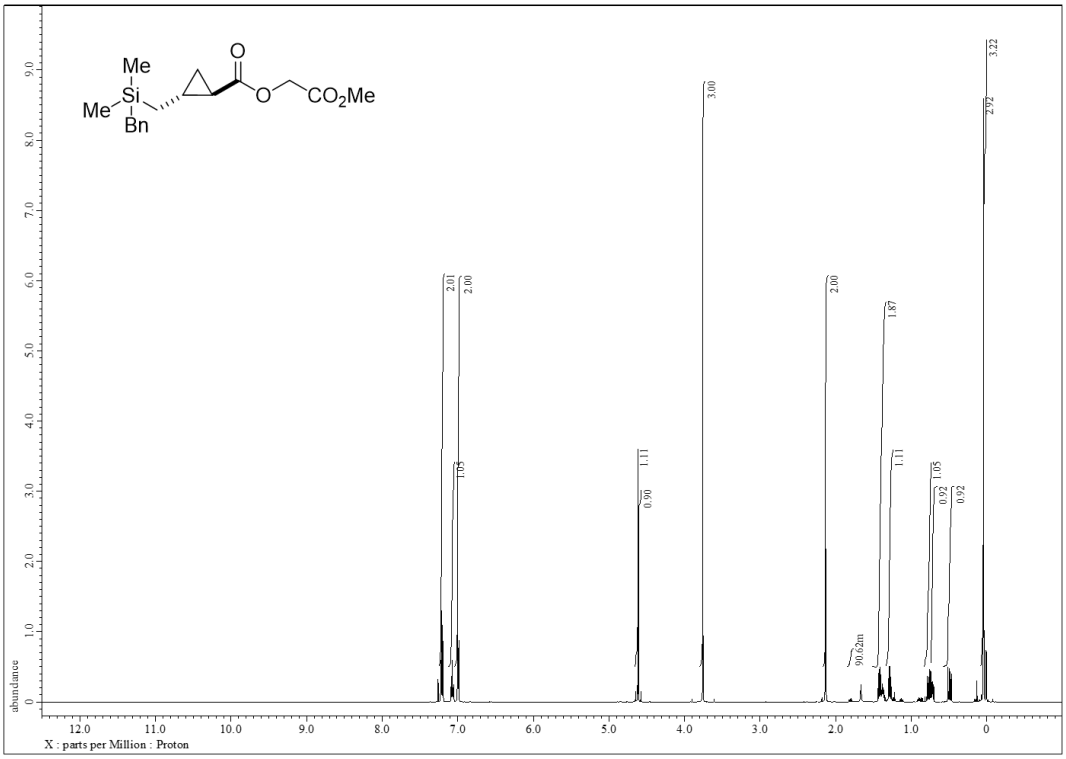
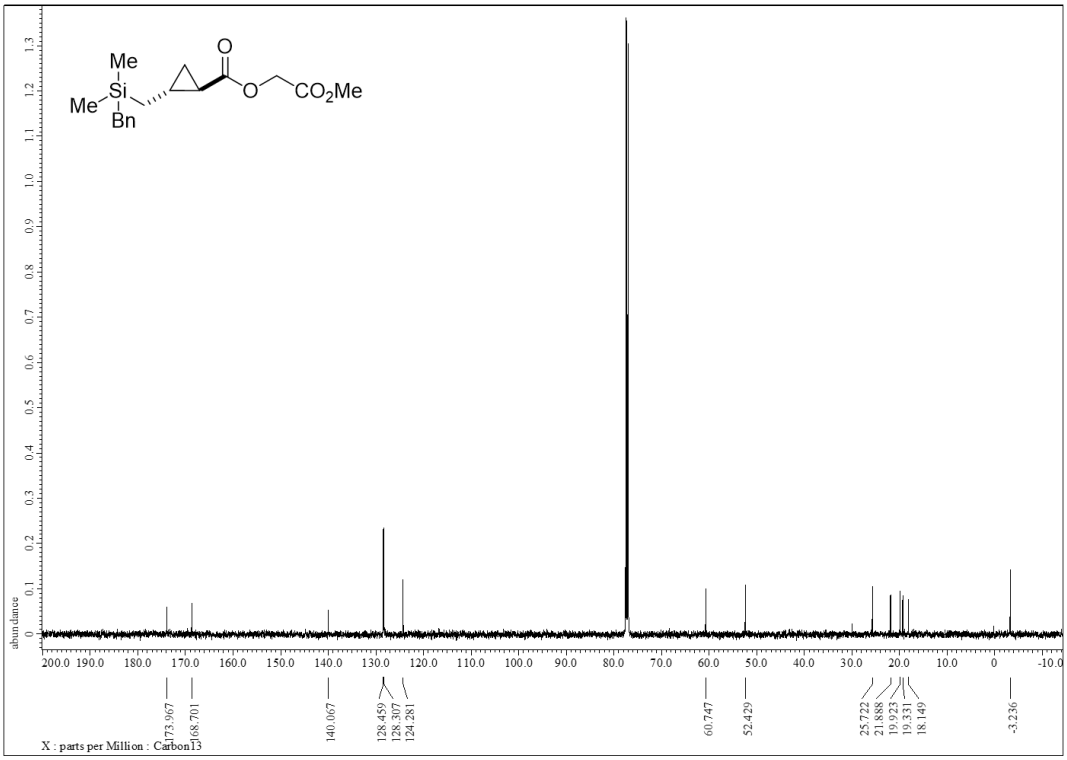
abundance
X : parts per Million : Proton

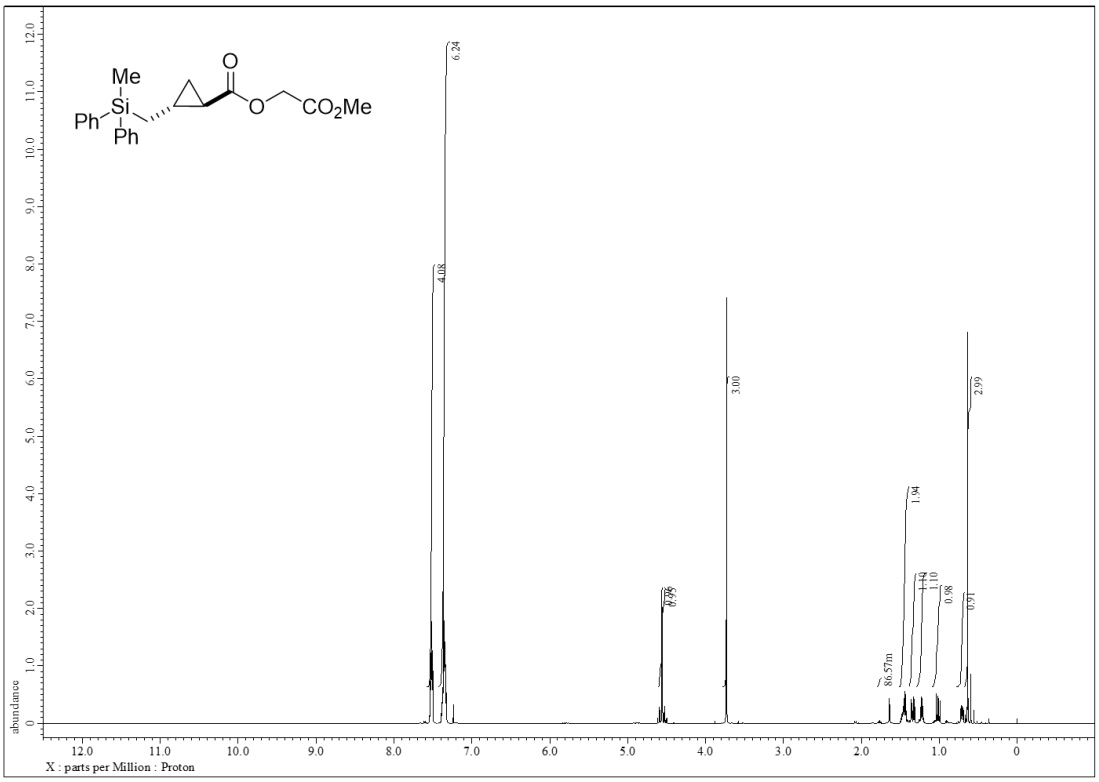

Me
Si
Me
Bu
O
O
CO2Me
abundance
173.852
168.492
77.000
60.470
52.153
26.552
26.008
21.678
20.018
19.646
18.015
14.858
13.780
-3.284
X : parts per Million : Carbon13

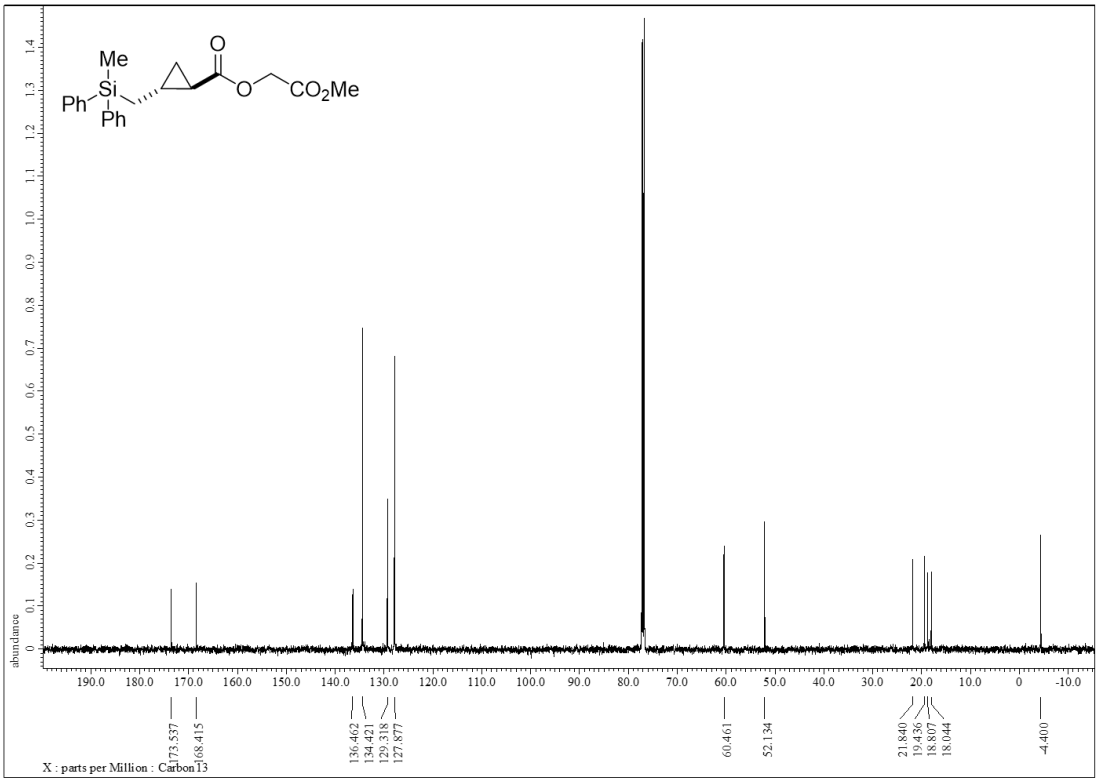

Me
Si
Me
Ph
O
O
CO2Me
6.16
3.09
3.00
1.98
1.97
1.83
1.83
1.01
1.00
0.10
0.12
abundance
X : parts per Million : Proton

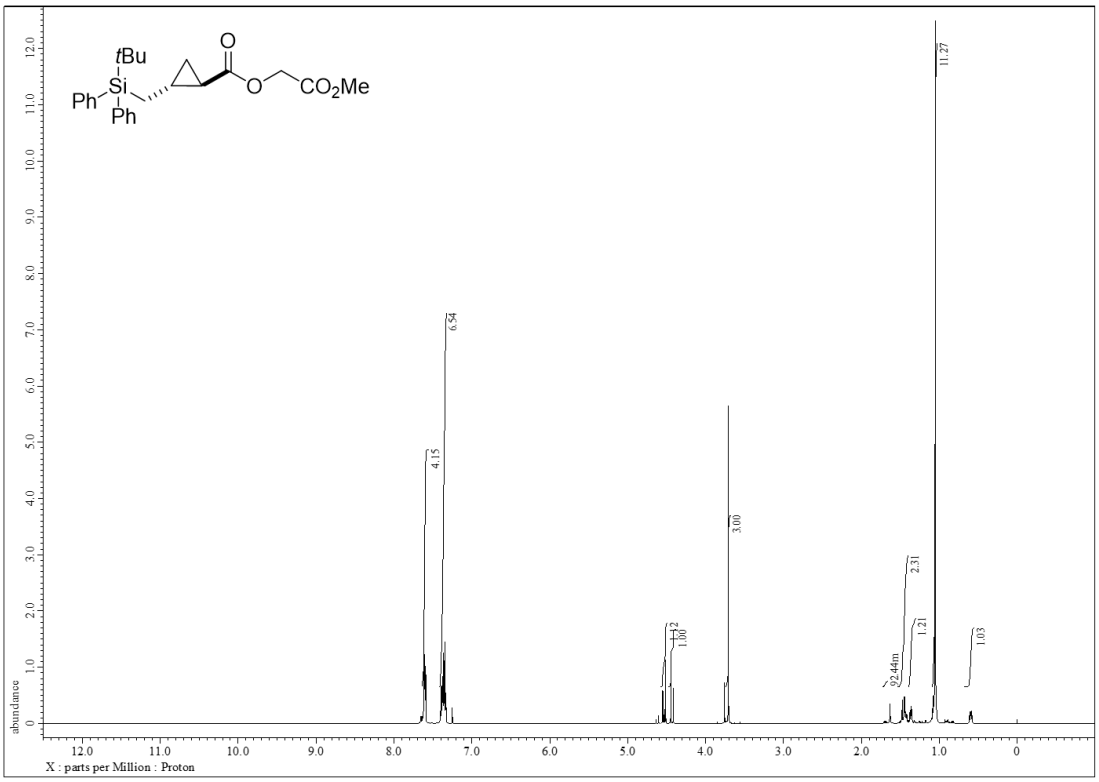

Me
Si
Me
Ph
O
O
CO2Me
abundance
173.824
168.597
138.694
133.639
129.165
127.925
60.651
52.286
21.773
20.390
19.865
18.053
-2.931
X : parts per Million : Carbon 13

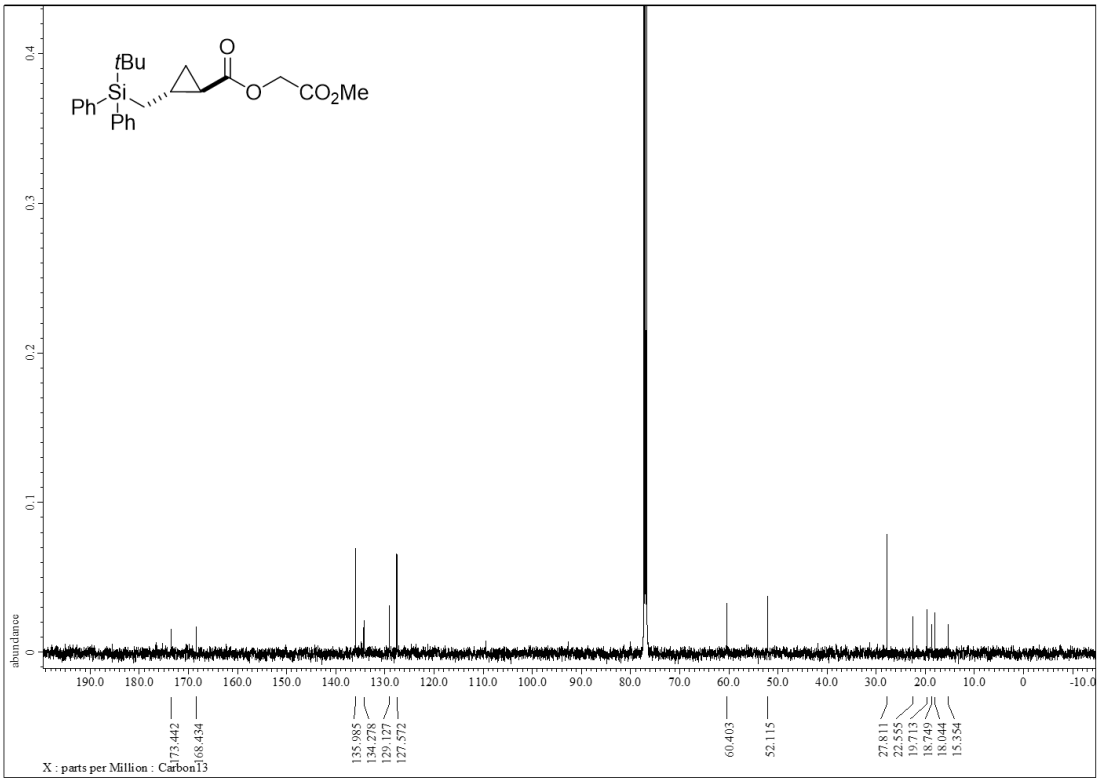

Me
Si
Me
Bn
O
O
CO2Me
abundance
X : parts per Million : Proton
2.01
2.00
1.05
1.11
0.90
3.00
2.00
90.62m
1.87
1.11
1.05
0.92
0.92
3.22
2.92

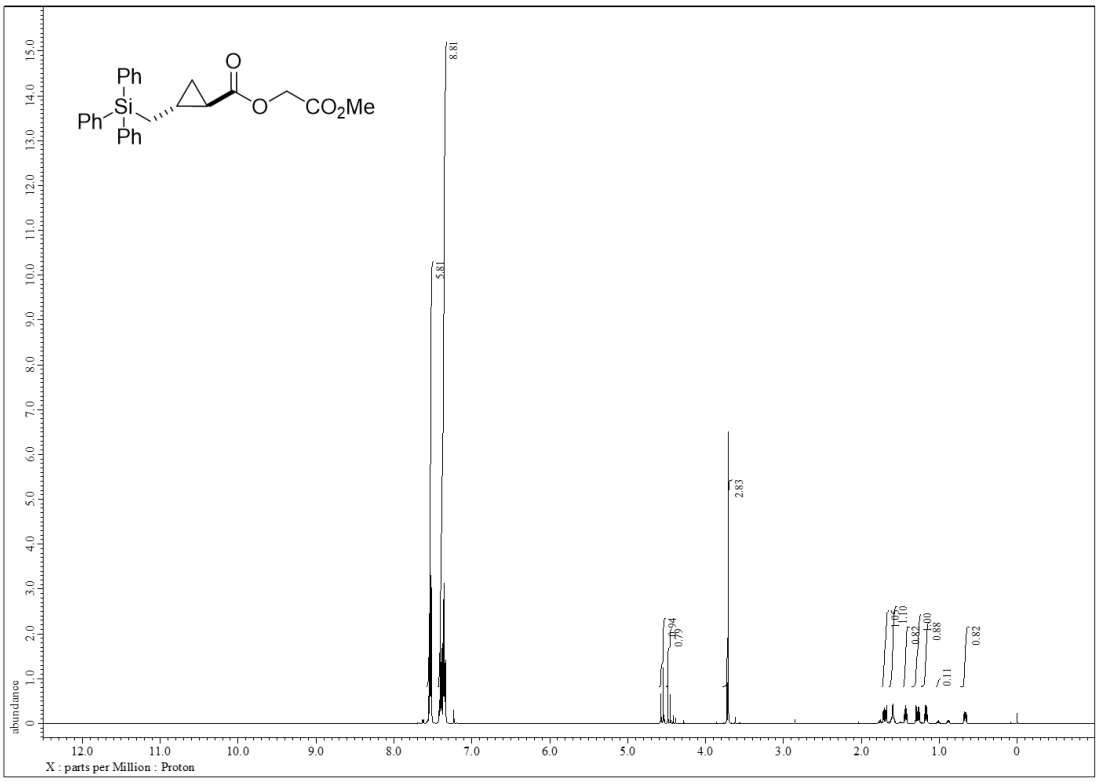

Me
Si
Me
Bn
O
O
CO2Me
abundance
X : parts per Million : Carbon13
173.967
168.701
140.067
128.459
128.307
124.281
60.747
52.429
25.722
21.888
19.923
19.331
18.149
-3.236

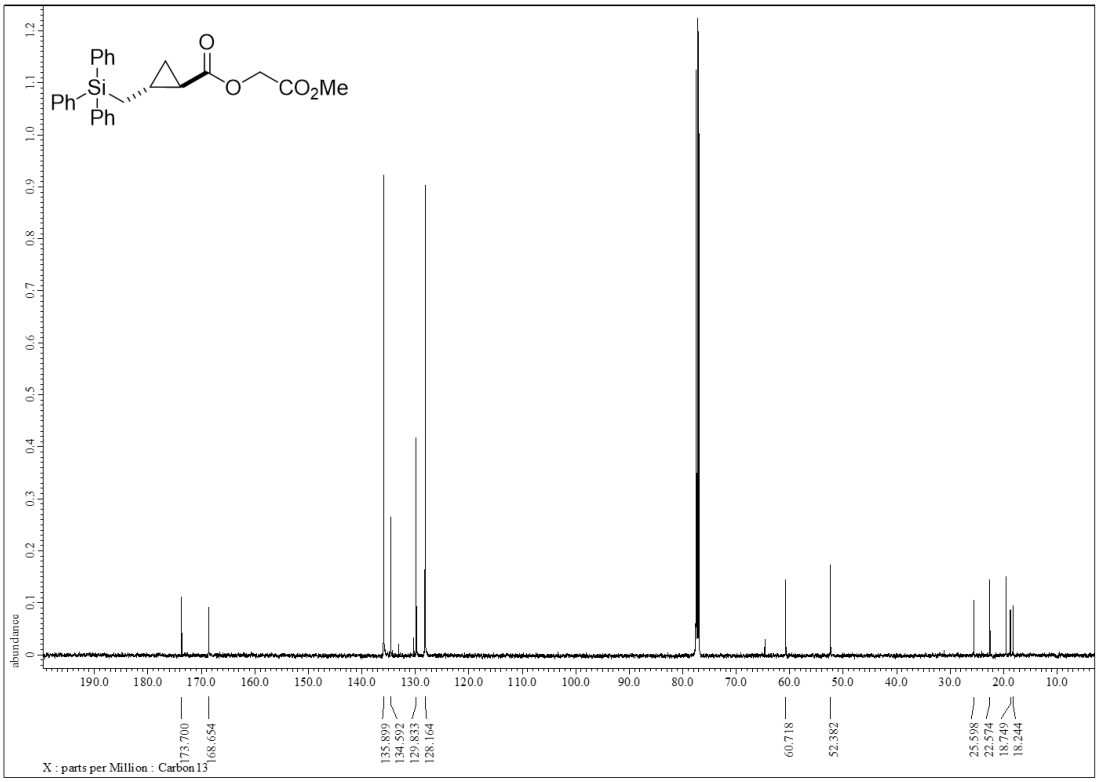

Me
Si
Ph
Ph
O
O
CO2Me
6.24
4.08
3.00
2.99
1.94
1.48
1.10
0.98
0.91
0.86
0.85
86.57m
abundance
X : parts per Million : Proton

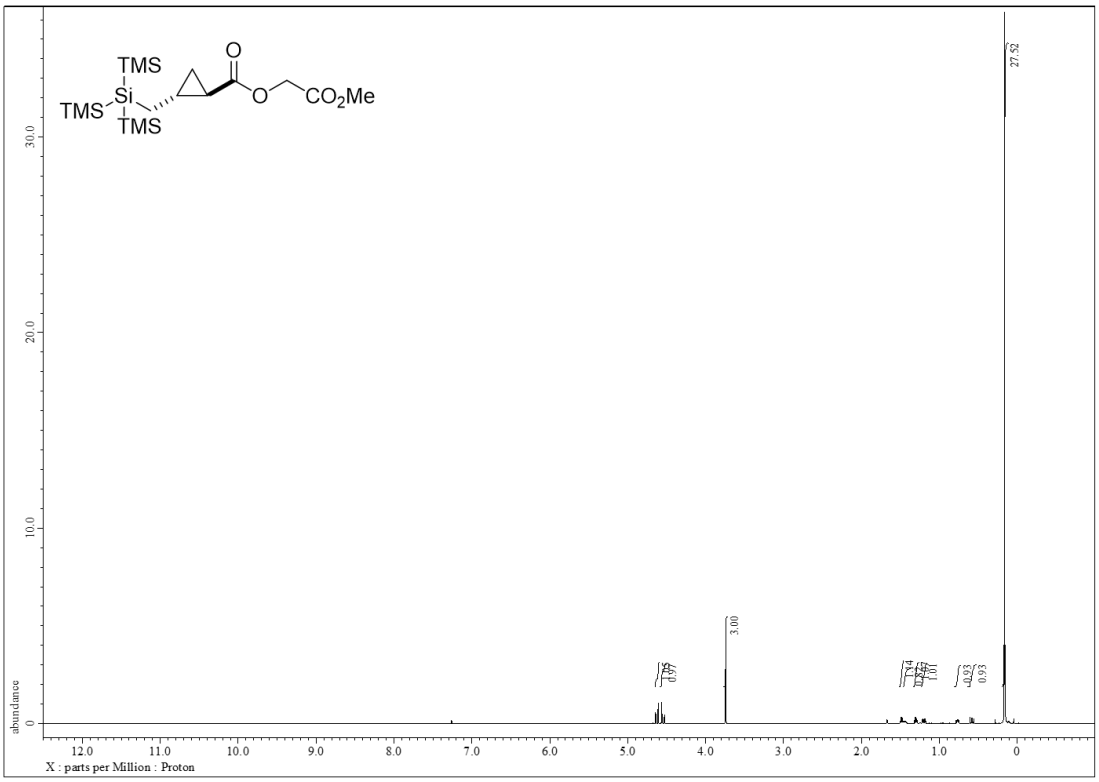

Me
Si
Ph
Ph
O
O
CO2Me
173.537
168.415
136.462
134.421
129.318
127.877
60.461
52.134
21.840
19.436
18.807
18.044
-4.400
abundance
X : parts per Million : Carbon13

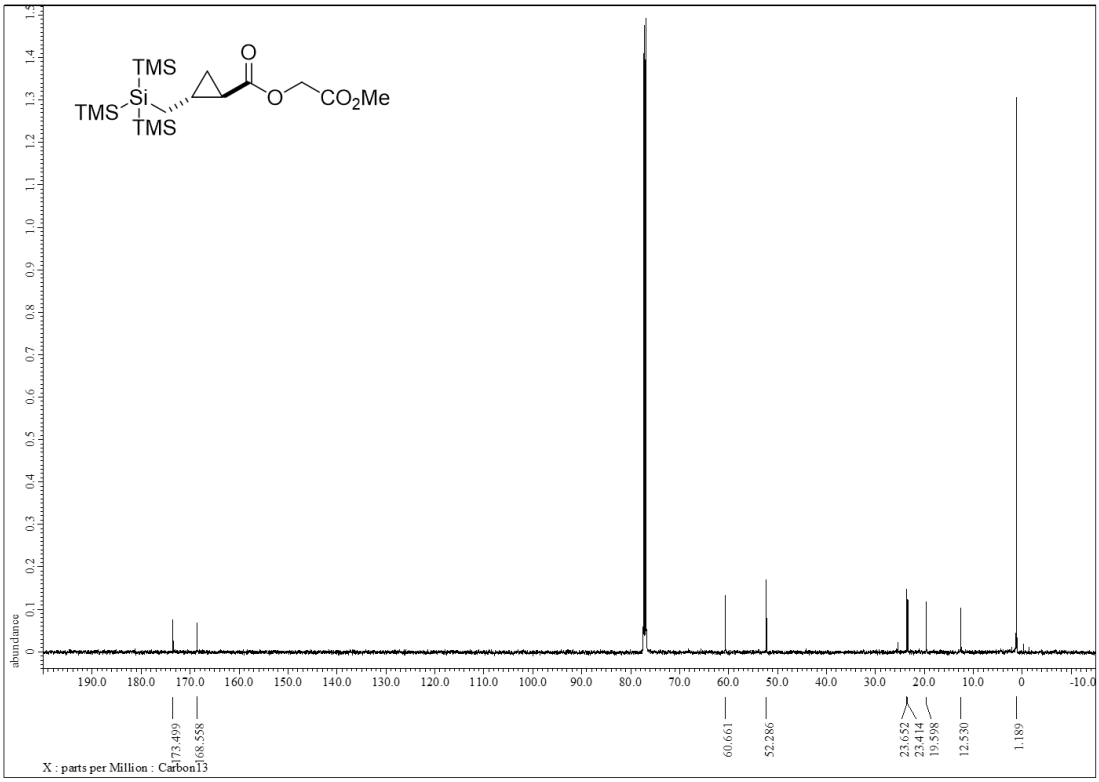

tBu
Si
Ph
Ph
O
O
CO2Me
abundance
X : parts per Million : Proton
11.27
6.54
4.15
3.00
2.31
1.21
1.03
1.02
1.00
2.44m

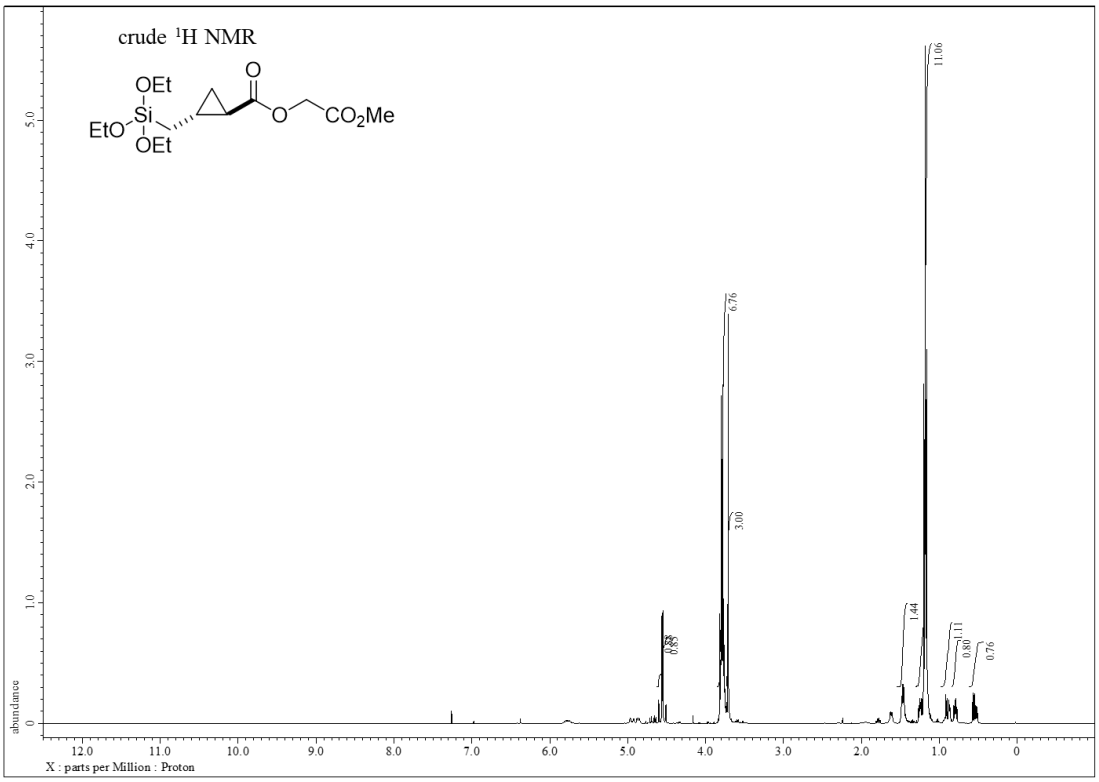

tBu
Si
Ph
Ph
O
O
CO2Me
abundance
X : parts per Million : Carbon13
173.442
168.434
135.985
134.278
129.127
127.572
60.403
52.115
27.811
22.555
19.713
18.749
18.044
15.354

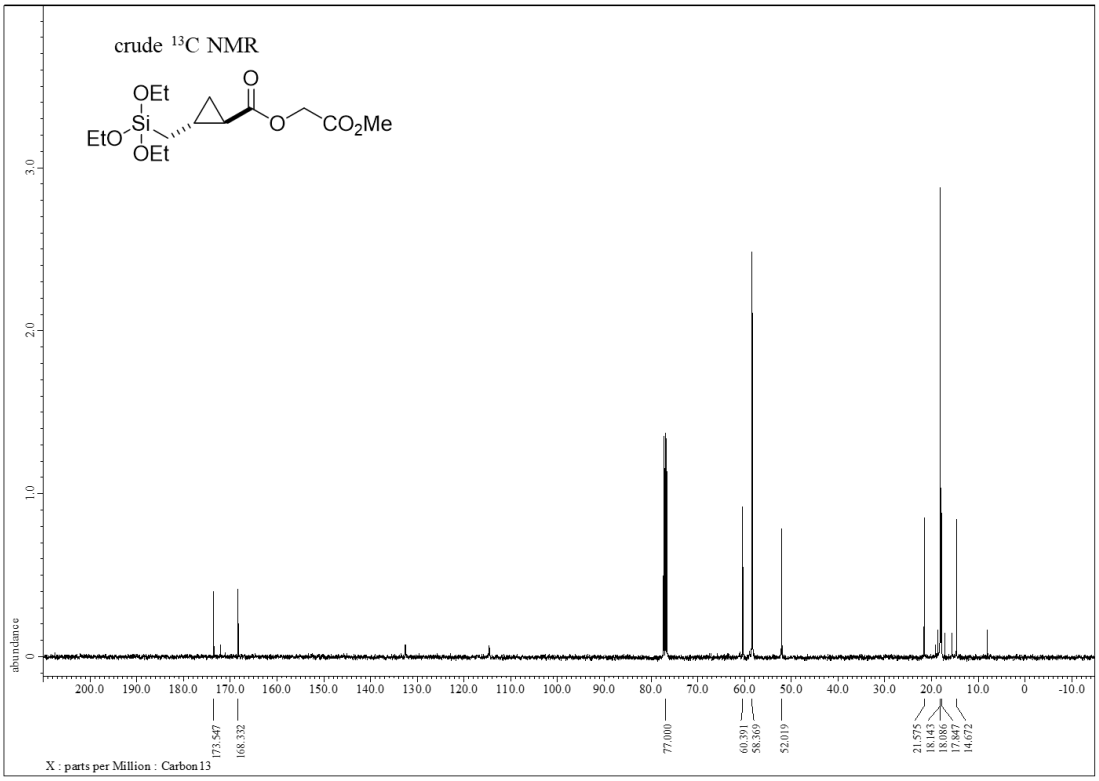

Ph
Si
Ph
Ph
O
O
CO2Me
8.81
5.81
2.83
0.82
0.88
0.11
0.82
abundance
X : parts per Million : Proton

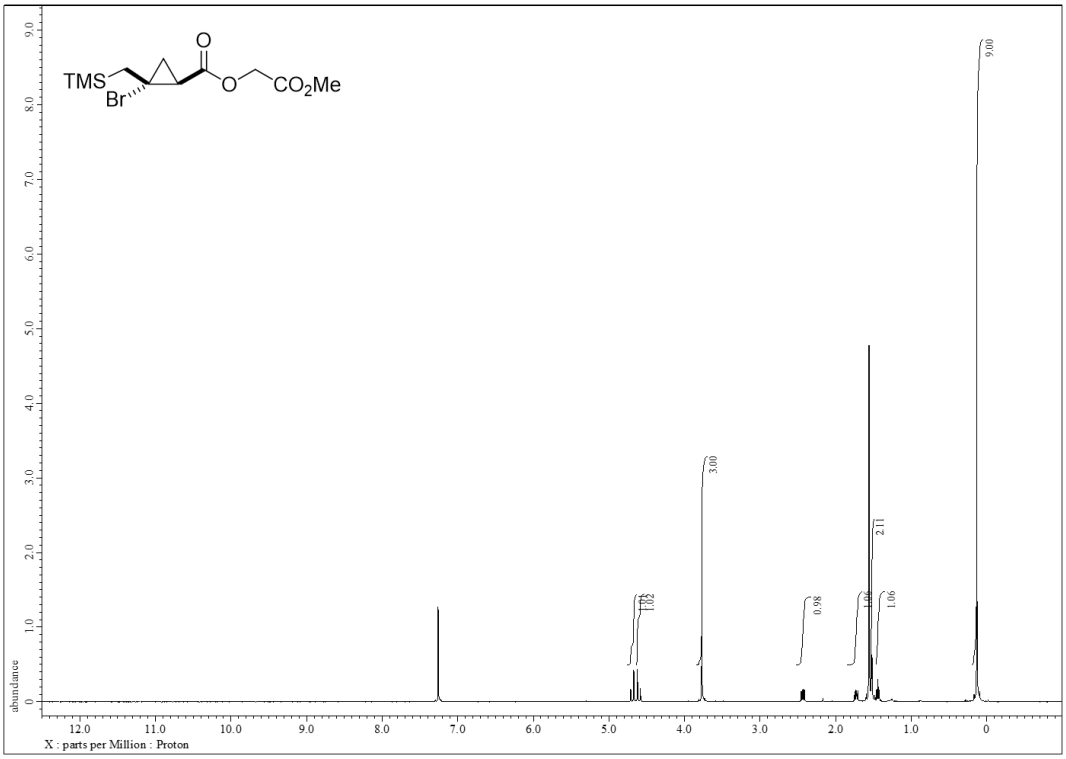

Ph
Si
Ph
Ph
O
O
CO2Me
abundance
173.700
168.654
135.899
134.592
129.833
128.164
60.718
52.382
25.598
22.574
18.749
18.244
X : parts per Million : Carbon13

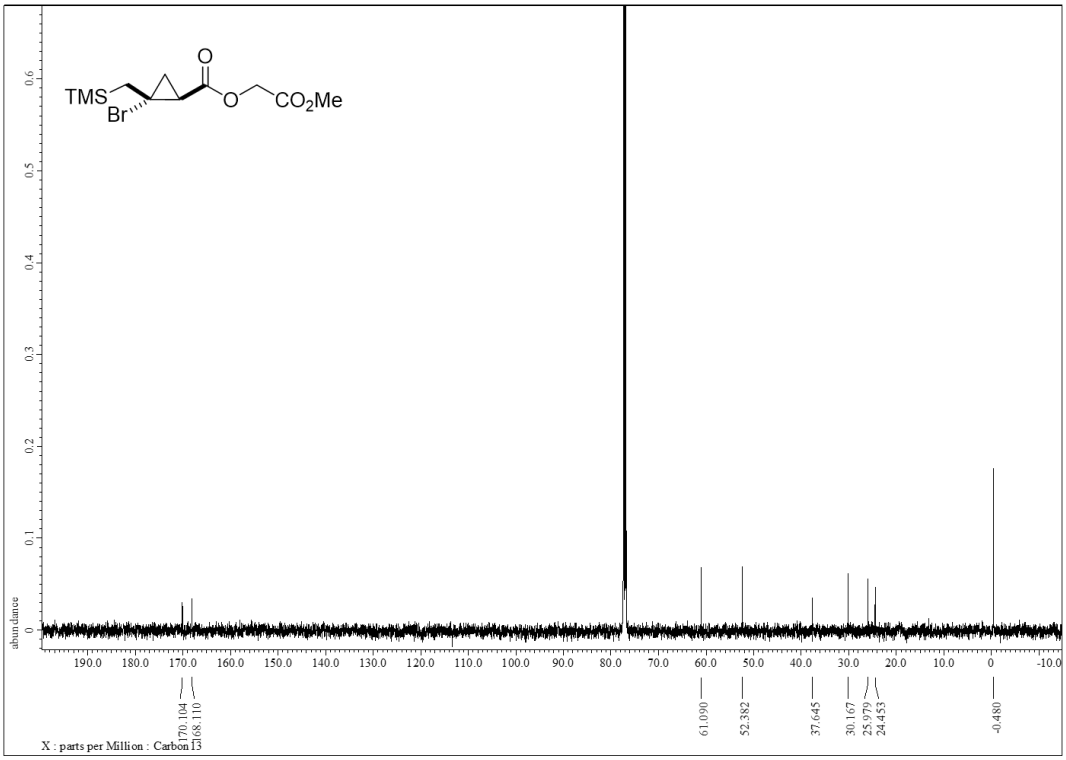

TMS
Si
TMS
TMS
O
O
CO2Me
27.52
3.00
0.97
0.93
abundance
X : parts per Million : Proton

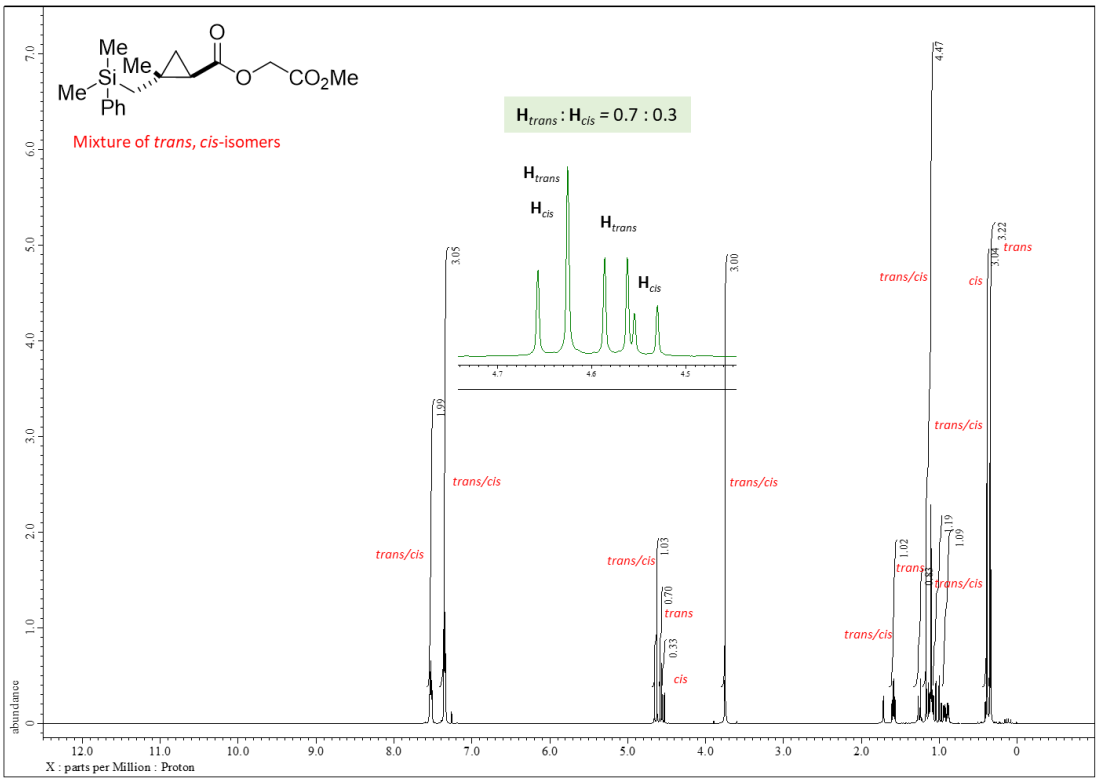

TMS
Si
TMS
TMS
O
O
CO2Me
abundance
173.499
168.558
60.661
52.286
23.652
23.414
19.598
12.530
1.189
X : parts per Million : Carbon13

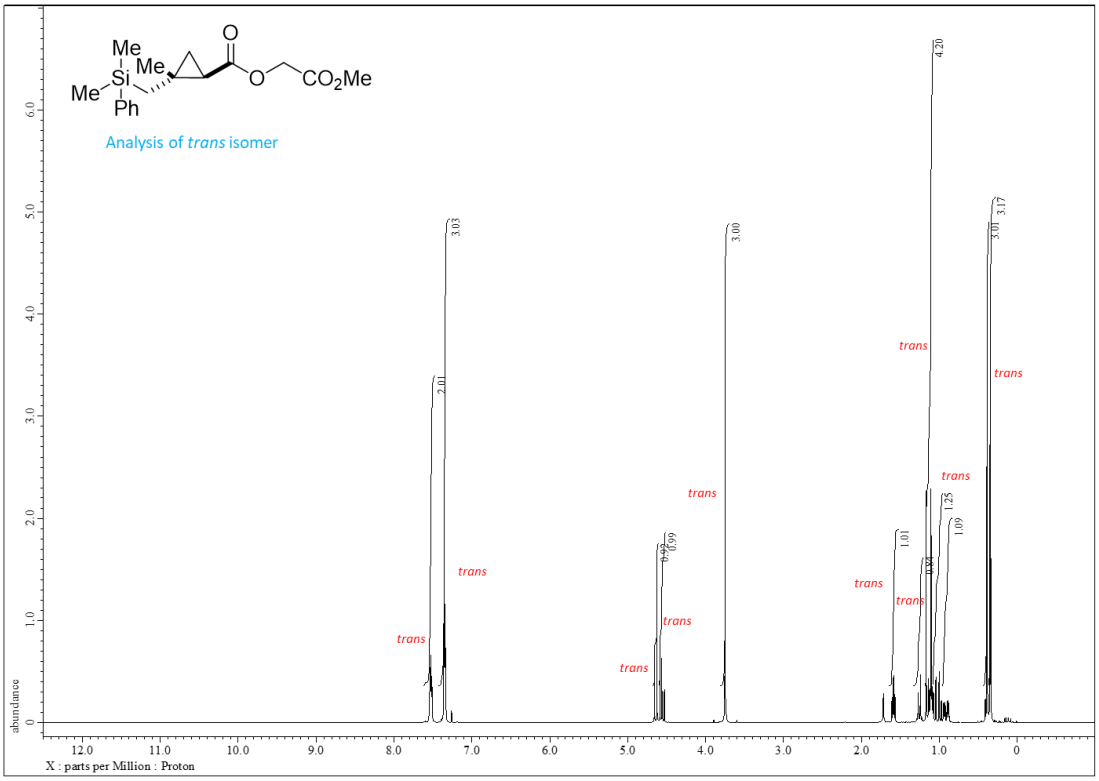

crude ^{1}H NMR
OEt
Si
EtO
OEt
O
O
CO2Me
11.06
6.76
3.00
1.44
1.11
0.80
0.76
abundance
X : parts per Million : Proton

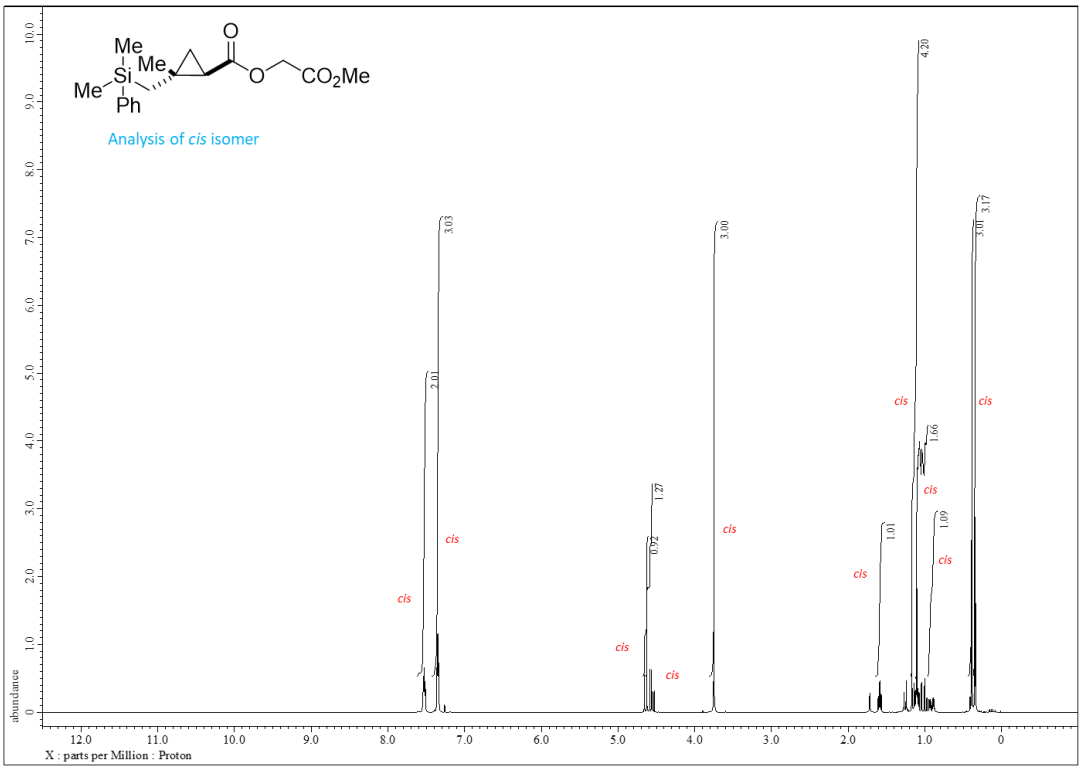

crude ^{13}C NMR
OEt
Si
EtO
OEt
O
O
CO2Me
173.547
168.332
77.000
60.391
58.369
52.019
21.575
18.143
18.086
17.847
14.672
abundance
X : parts per Million : Carbon13

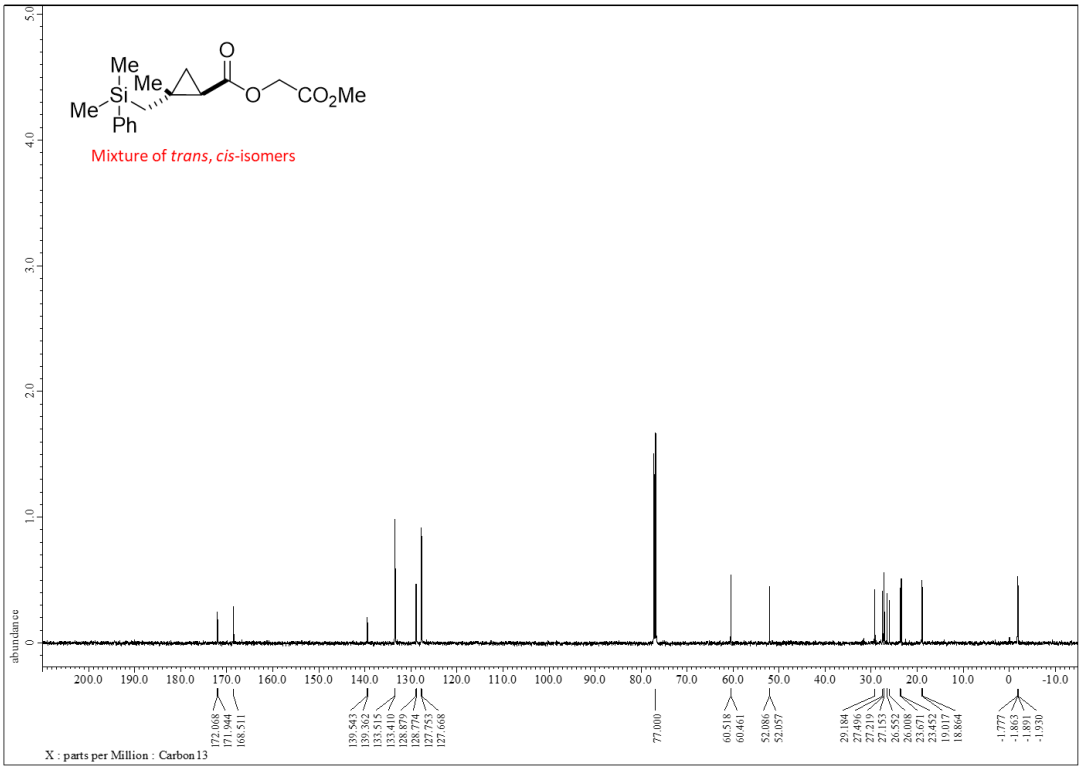

TMS
Br
O
O
CO2Me
9.00
3.00
2.11
1.06
0.98
abundance
X : parts per Million : Proton

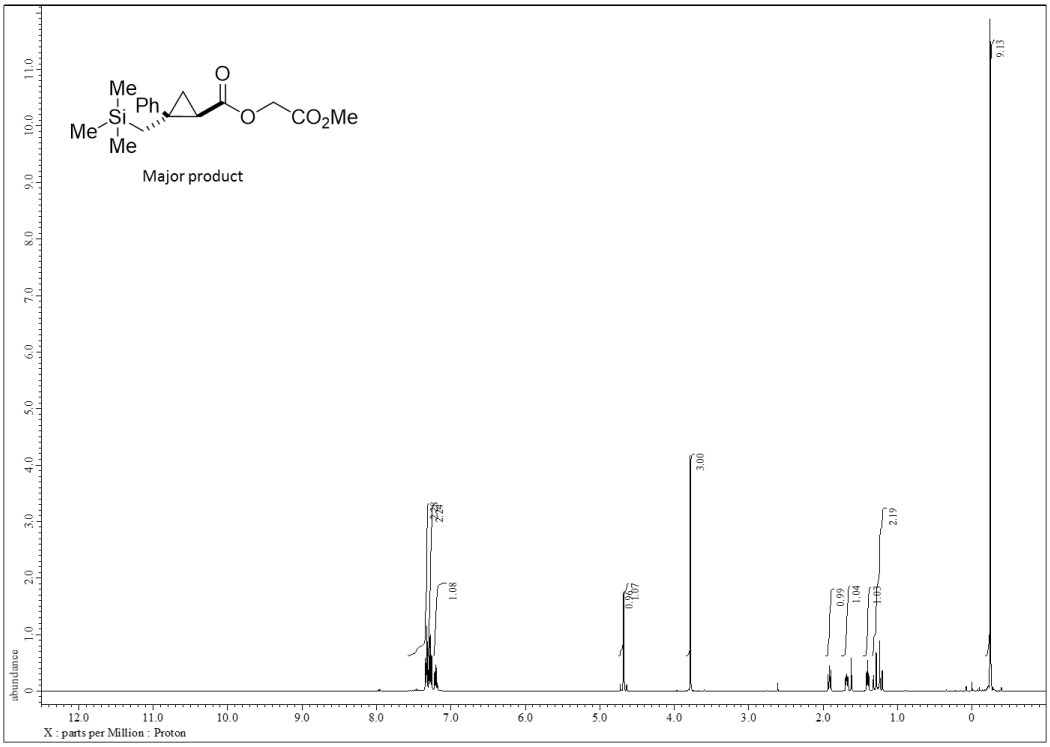

TMS
Br
O
O
CO2Me
abundance
170.104
168.110
61.090
52.382
37.645
30.167
25.979
24.453
-0.480
X : parts per Million : Carbon 13

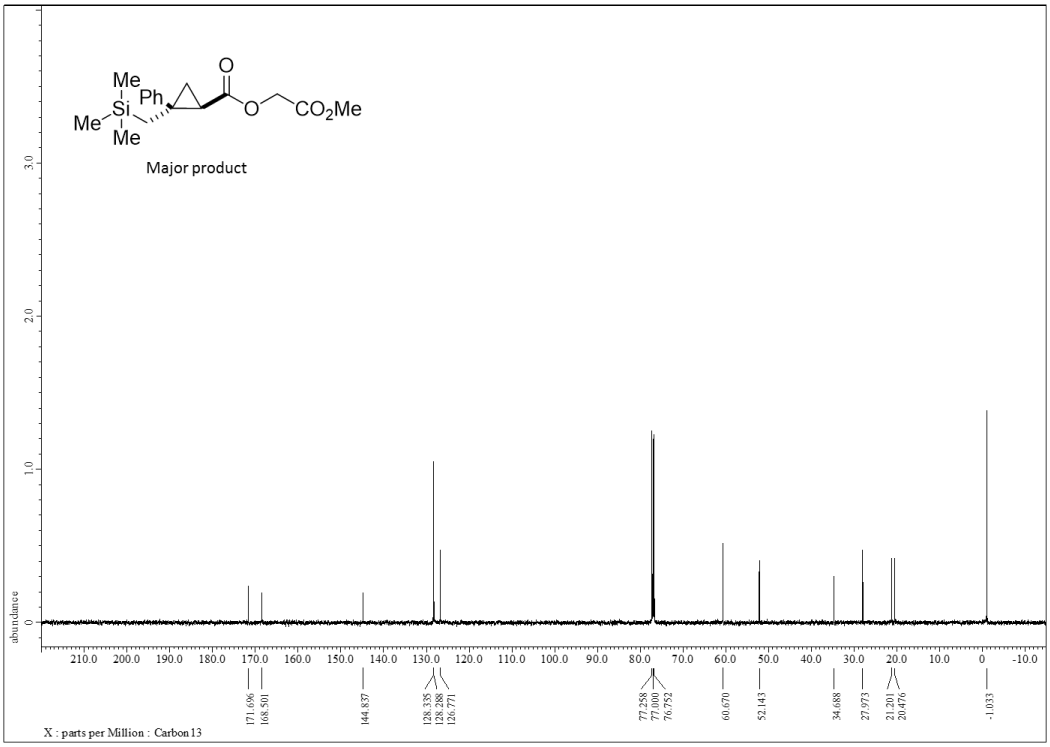

Me
Si
Me
Me
Ph
O
O
CO2Me
Mixture of trans, cis-isomers
Htrans : Hcis = 0.7 : 0.3
Htrans
Hcis
Htrans
Hcis
trans/cis
trans/cis
trans/cis
trans/cis
trans/cis
trans
cis
trans
trans/cis
trans/cis
trans
cis
abundance
X : parts per Million : Proton

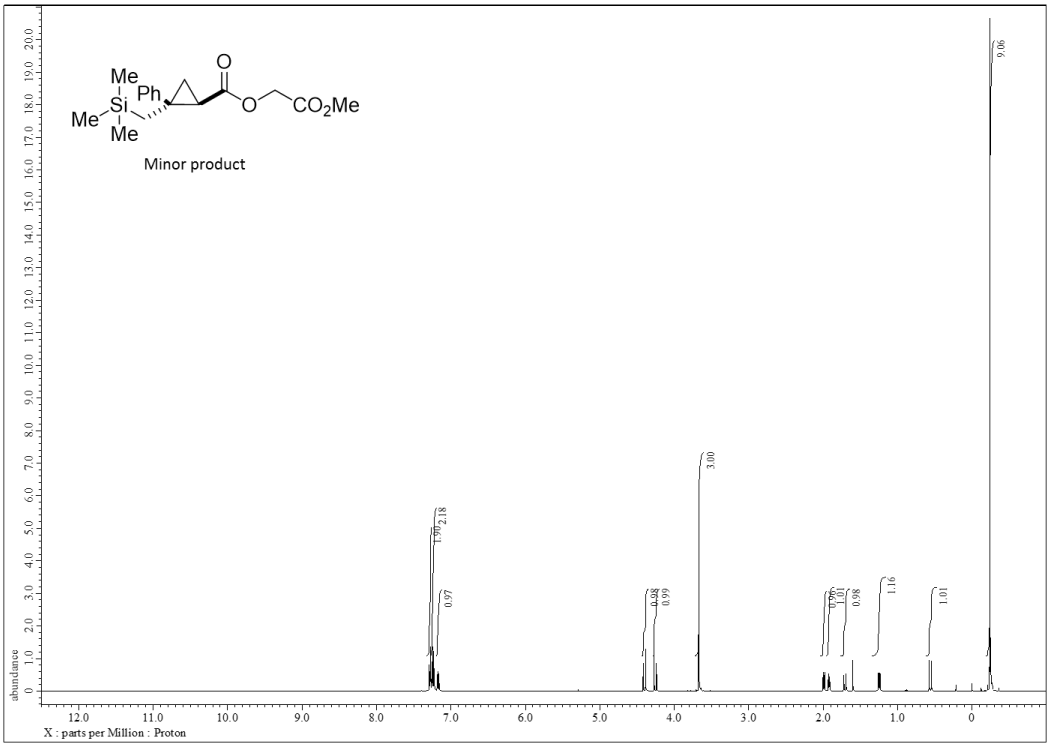

Me
Si
Me
Me
Ph
O
O
CO2Me
Analysis of trans isomer
trans
trans
trans
trans
trans
trans
trans
trans
trans
trans
trans
abundance
X : parts per Million : Proton

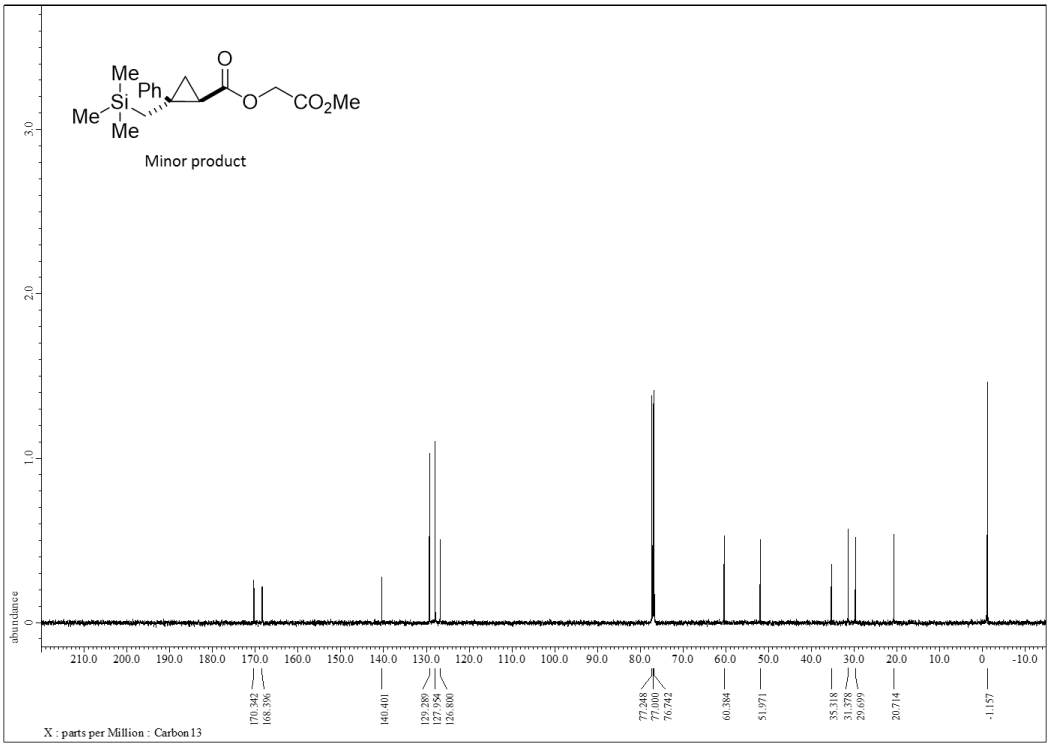

Me
Si
Me
Me
Ph
O
O
CO2Me
Analysis of cis isomer
abundance
X : parts per Million : Proton
cis
2.01
3.03
1.27
0.72
3.00
4.20
1.66
1.01
1.09
3.01
3.17

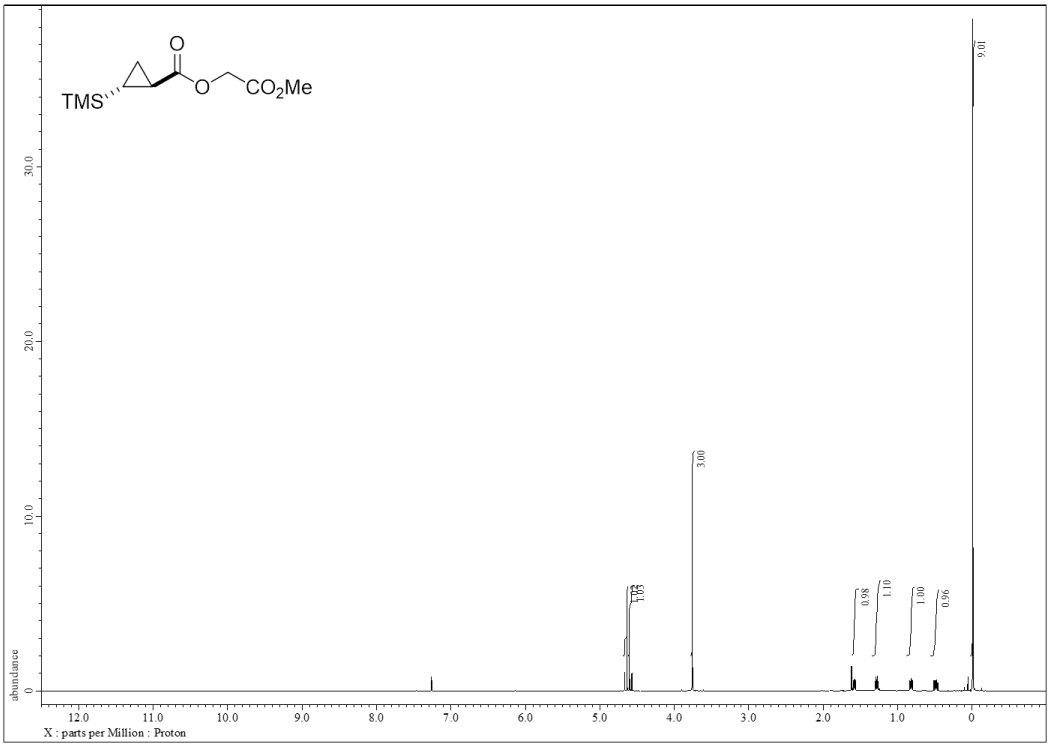

Me
Si
Me
Me
Ph
O
O
CO2Me
Mixture of trans, cis-isomers
abundance
X : parts per Million : Carbon13
172.068
171.944
168.511
139.543
139.362
133.515
133.410
128.879
128.774
127.753
127.668
77.000
60.518
60.461
52.086
52.057
29.184
27.496
27.310
27.153
26.552
26.008
23.671
23.452
19.017
18.864
-1.777
-1.863
-1.891
-1.930

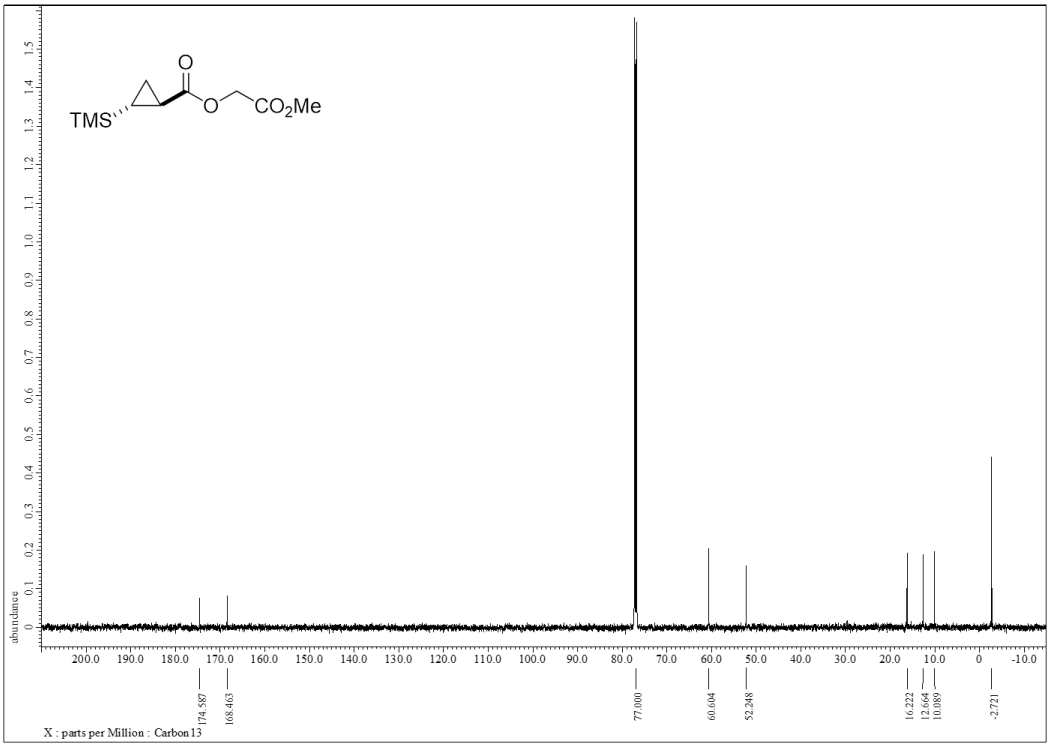

Me
Si
Ph
Me
Me
O
O
CO2Me
Major product
9.13
3.00
2.19
1.08
1.04
1.03
0.99
1.07
0.97
abundance
X : parts per Million : Proton

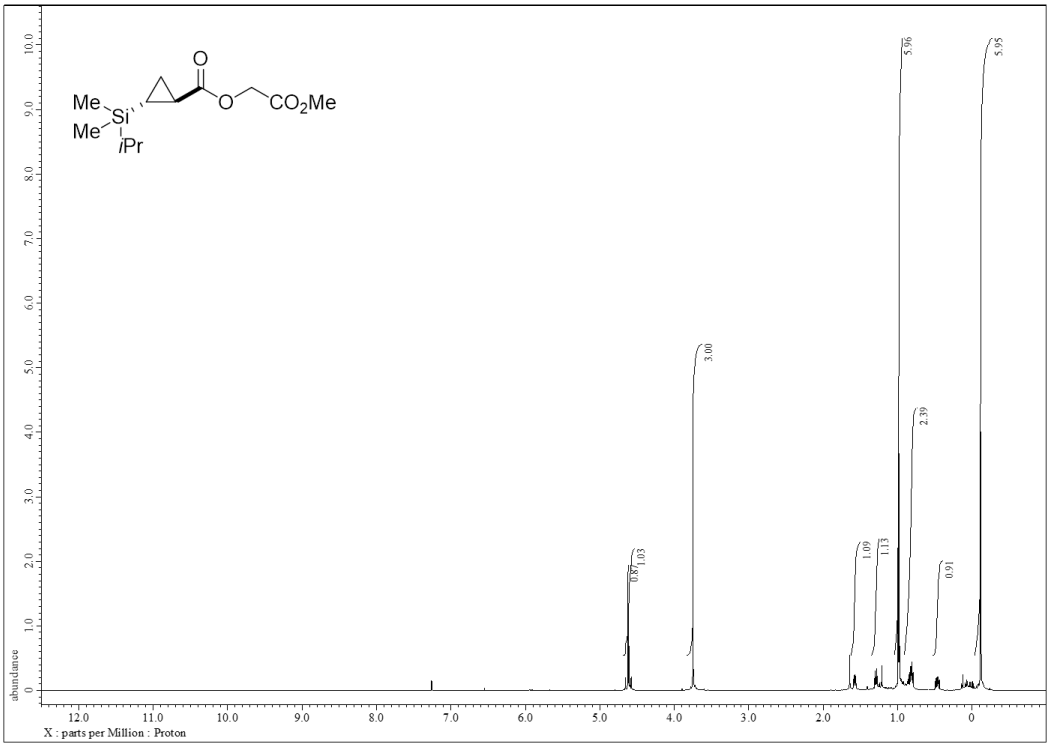

Me
Si
Ph
Me
Me
O
O
CO2Me
Major product
171.696
168.501
144.837
128.335
128.288
126.771
77.258
77.000
76.752
60.670
52.143
34.688
27.973
21.201
20.476
-1.033
abundance
X : parts per Million : Carbon13

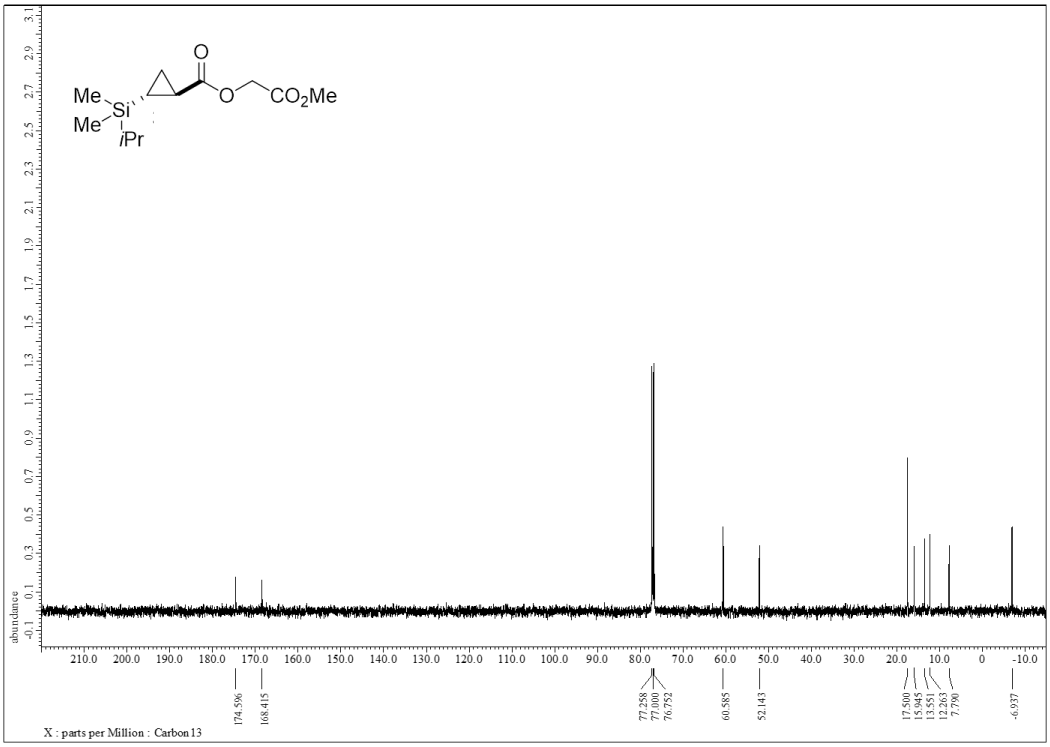

Me
Si
Ph
Me
Me
O
O
CO2Me
Minor product
abundance
X : parts per Million : Proton
9.06
3.00
2.18
1.90
0.97
0.98
0.99
0.96
1.01
0.98
1.16
1.01

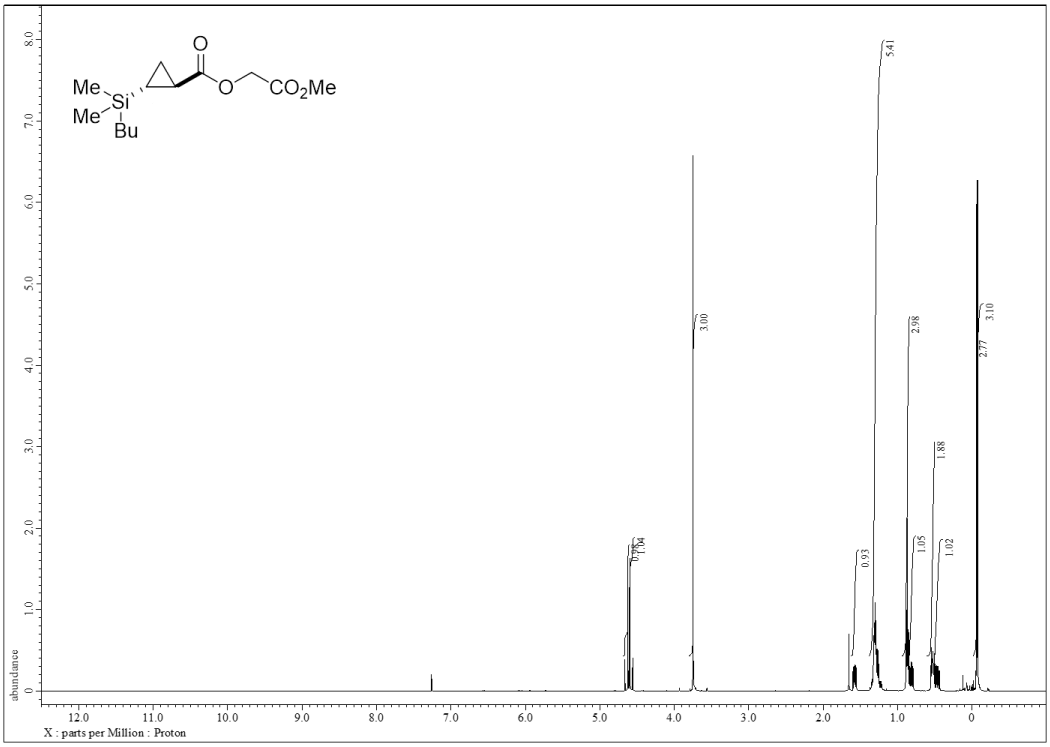

Me
Si
Ph
Me
Me
O
O
CO2Me
Minor product
abundance
X : parts per Million : Carbon13
170.342
168.396
140.401
129.289
127.954
126.800
77.248
77.000
76.742
60.384
51.971
35.318
31.378
29.699
20.714
-1.157

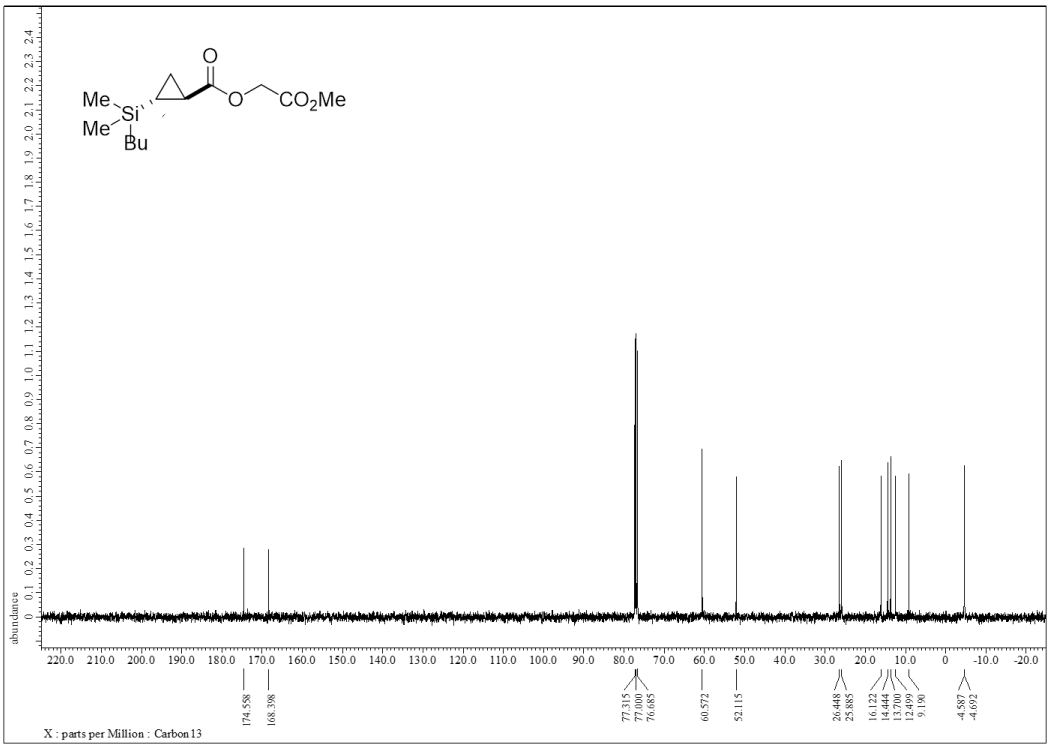

TMS
O
O
CO2Me
abundance
X : parts per Million : Proton
9.01
3.00
0.98
1.10
1.00
0.96

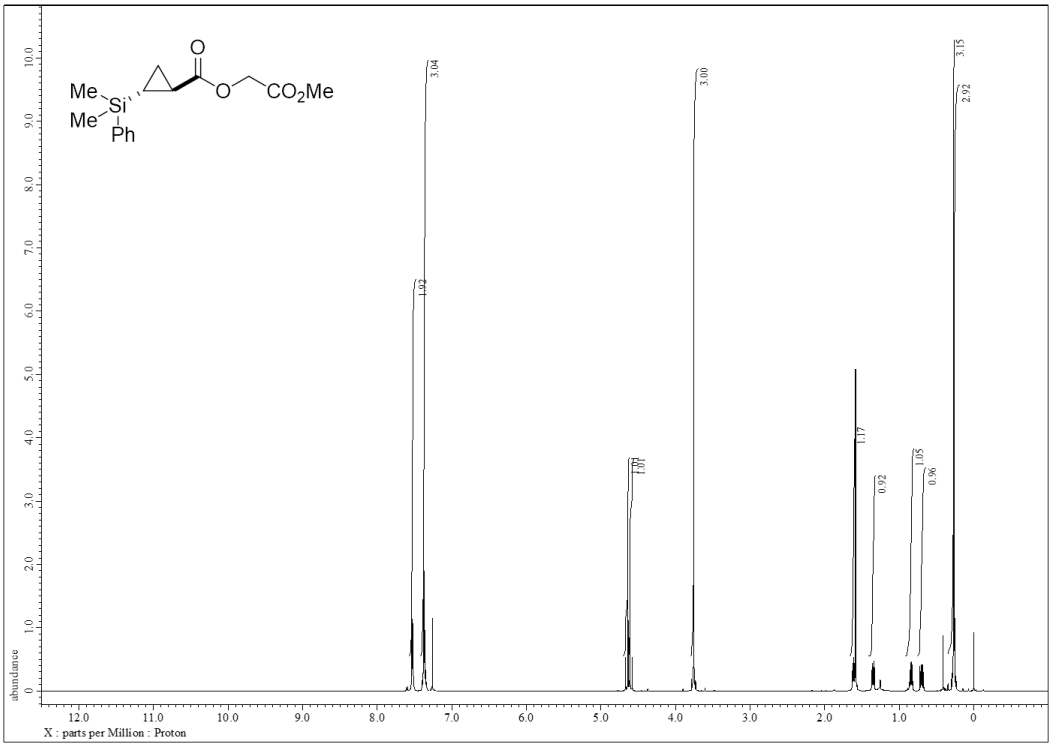

TMS
O
O
CO2Me
abundance
X : parts per Million : Carbon13
174.587
168.463
77.000
60.604
52.248
16.222
12.664
10.089
-2.721

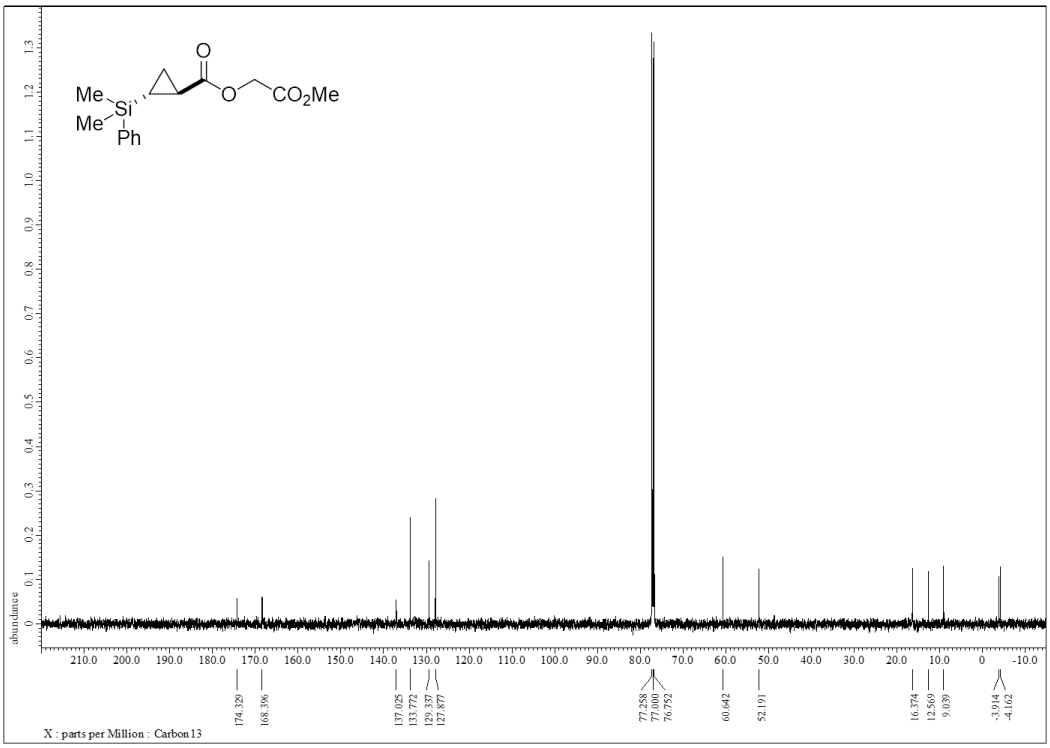

Me
Si
Me
iPr
O
O
CO2Me
5.96
5.95
3.00
2.39
1.09
1.13
1.03
0.87
0.91
abundance
X : parts per Million : Proton

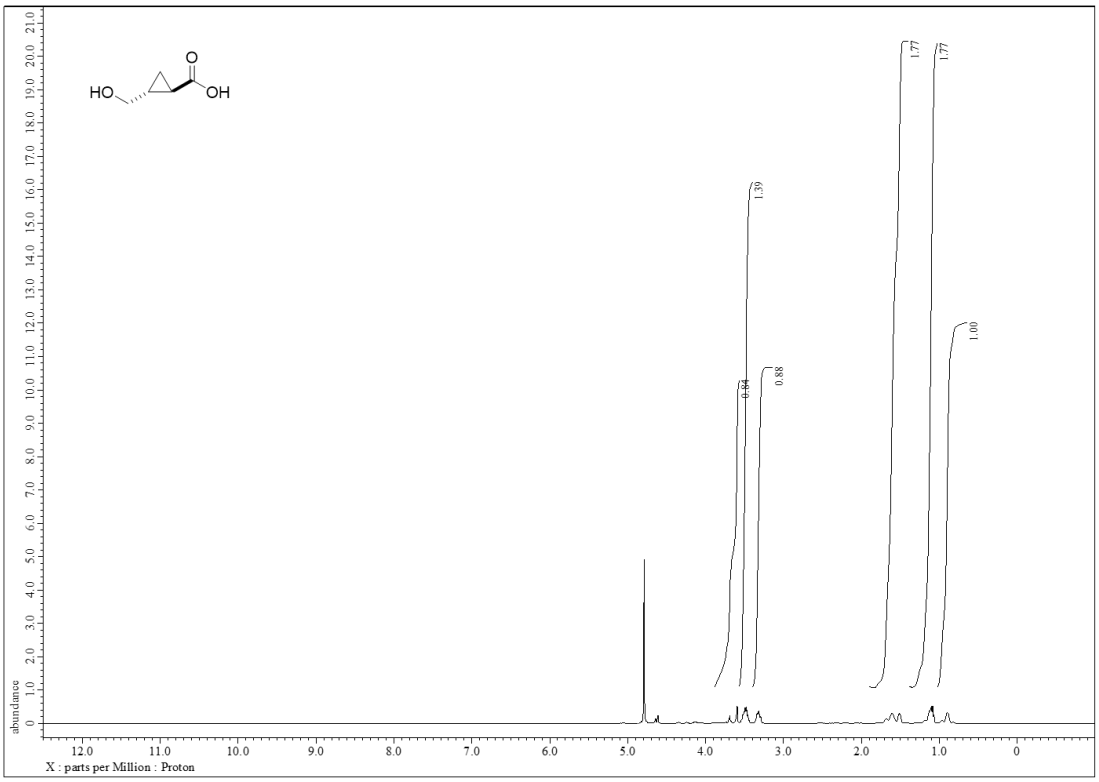

Me
Si
Me
iPr
O
O
CO2Me
174.596
168.415
77.258
77.000
76.752
60.585
52.143
17.500
15.945
13.551
12.263
7.790
-6.937
abundance
X : parts per Million : Carbon13

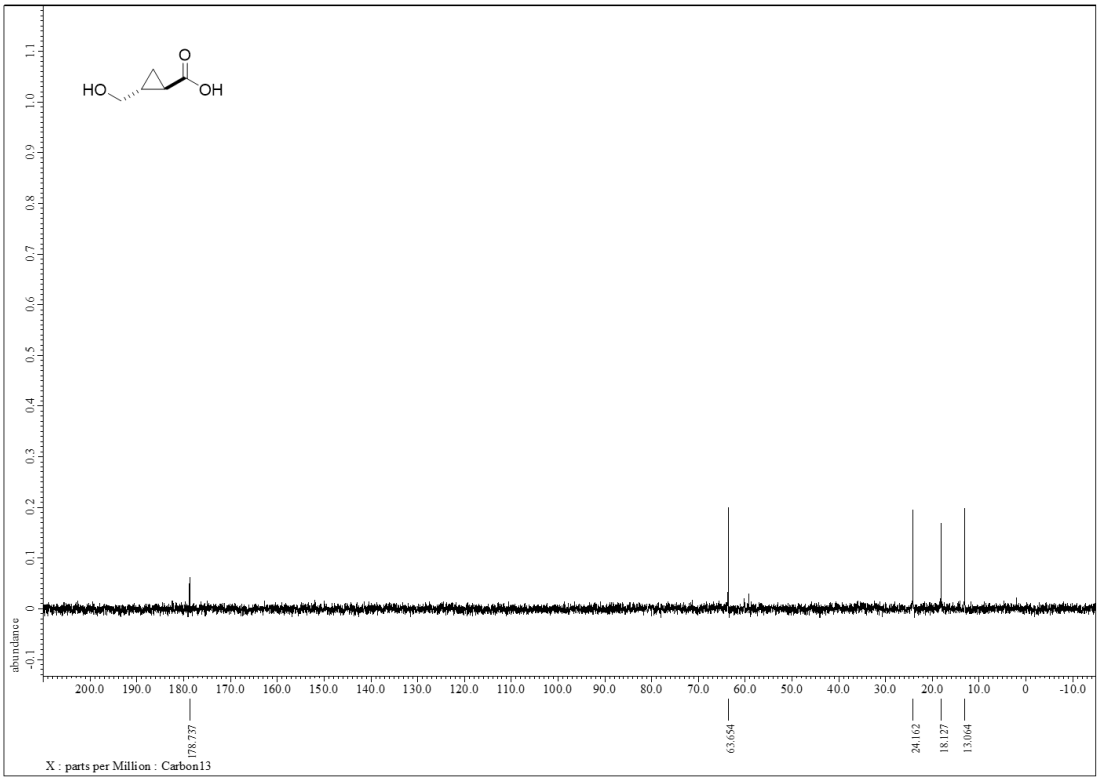

Me
Si
Me
Bu
O
O
CO2Me
5.41
3.00
2.98
3.10
2.77
1.88
1.05
1.02
0.93
1.04
1.00
abundance
X : parts per Million : Proton

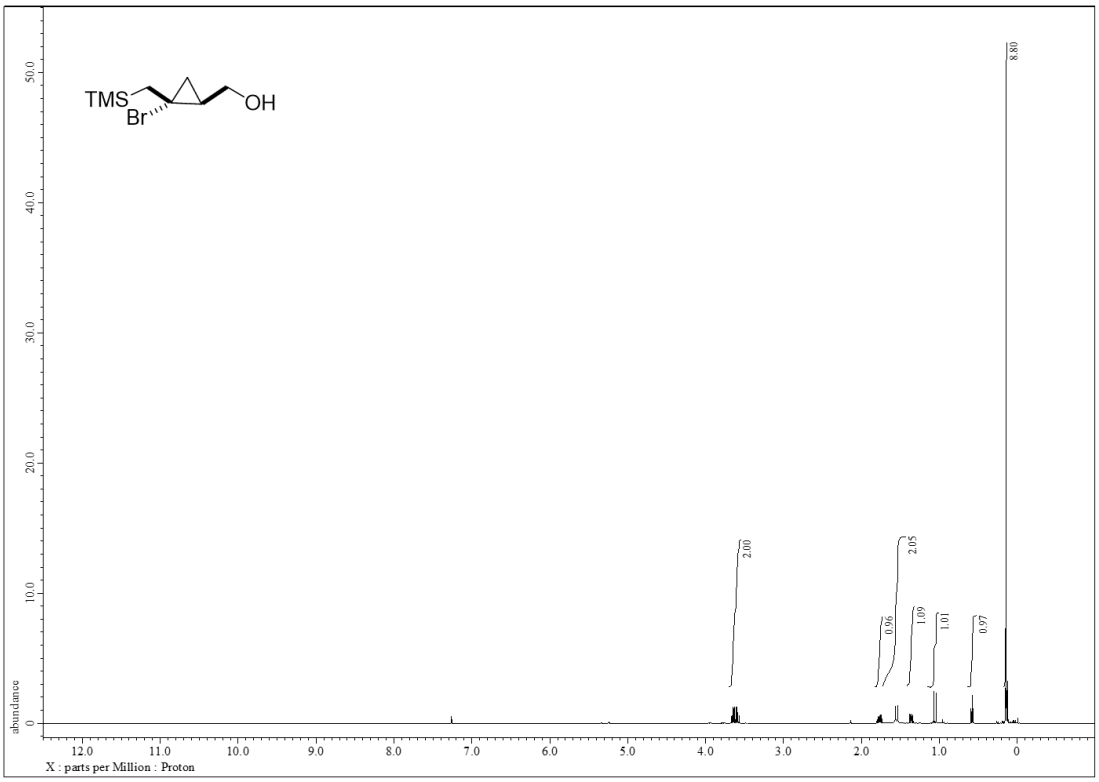

Me
Si
Me
Bu
O
O
CO2Me
174.558
168.398
77.315
77.000
76.685
60.572
52.115
26.448
25.885
16.122
14.444
13.700
13.490
9.190
-4.587
-4.692
abundance
X : parts per Million : Carbon13

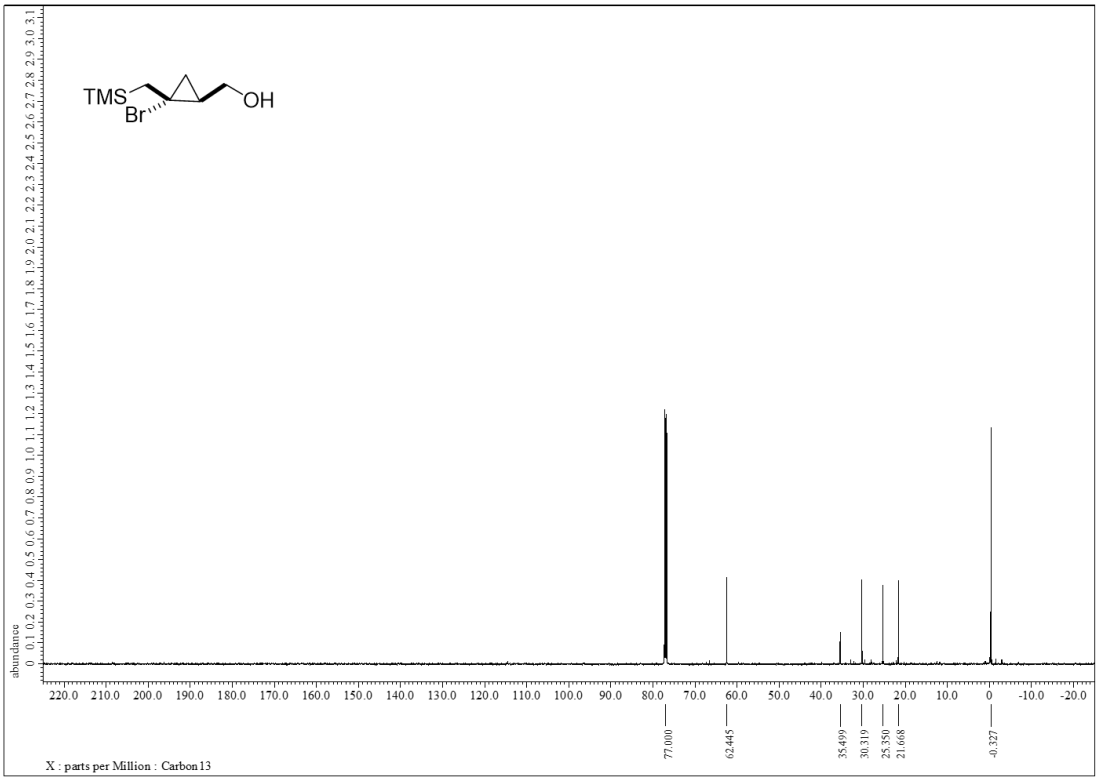

Me
Si
Me
Ph
O
O
CO2Me
3.04
3.00
3.15
2.92
1.92
1.17
1.05
0.96
0.92
abundance
X : parts per Million : Proton

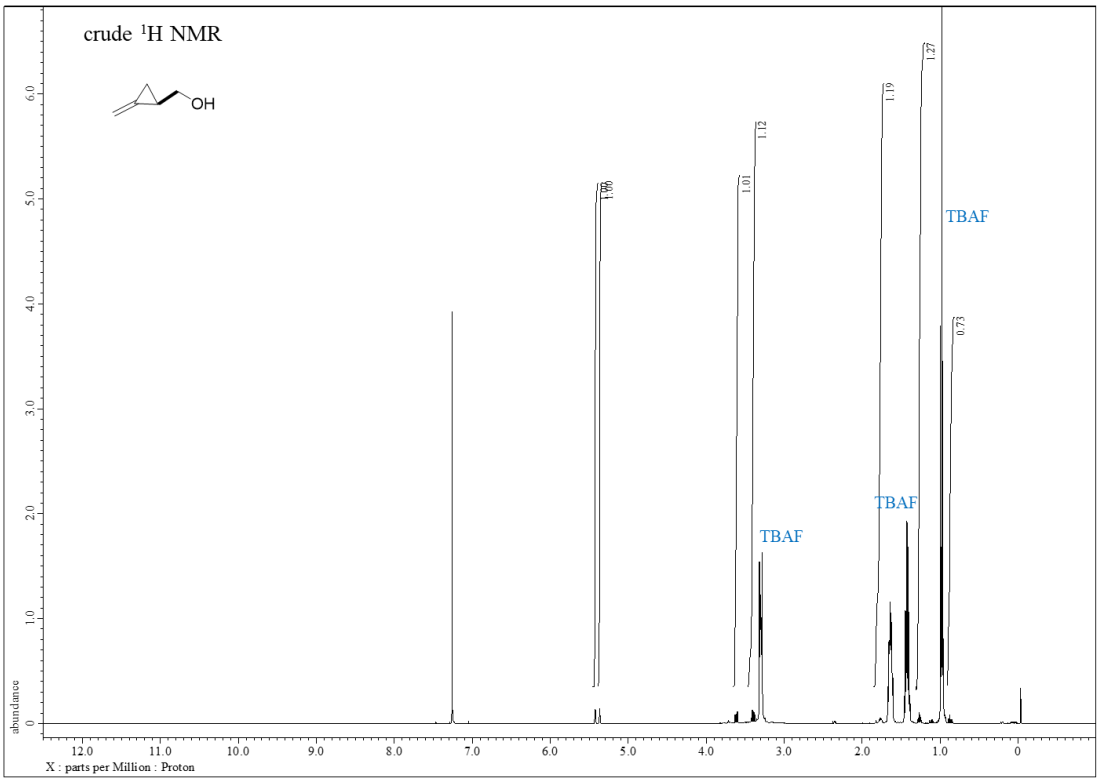

Me
Si
Me
Ph
O
O
CO2Me
abundance
174.329
168.396
137.025
133.772
129.337
127.877
77.258
77.000
76.752
60.642
52.191
16.374
12.569
9.039
-3.914
-4.162
X : parts per Million : Carbon13


HO
O
OH
1.39
0.84
0.88
1.77
1.77
1.00
abundance
X : parts per Million : Proton

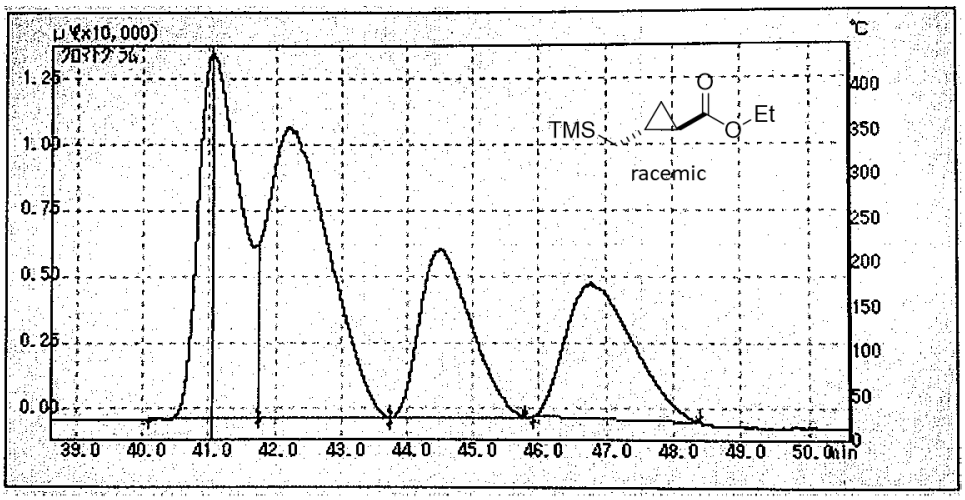

HO
O
OH
abundance
178.737
63.654
24.162
18.127
13.064
X : parts per Million : Carbon13


TMS
Br
OH
8.80
2.00
2.05
1.09
1.01
0.97
0.96
abundance
X : parts per Million : Proton

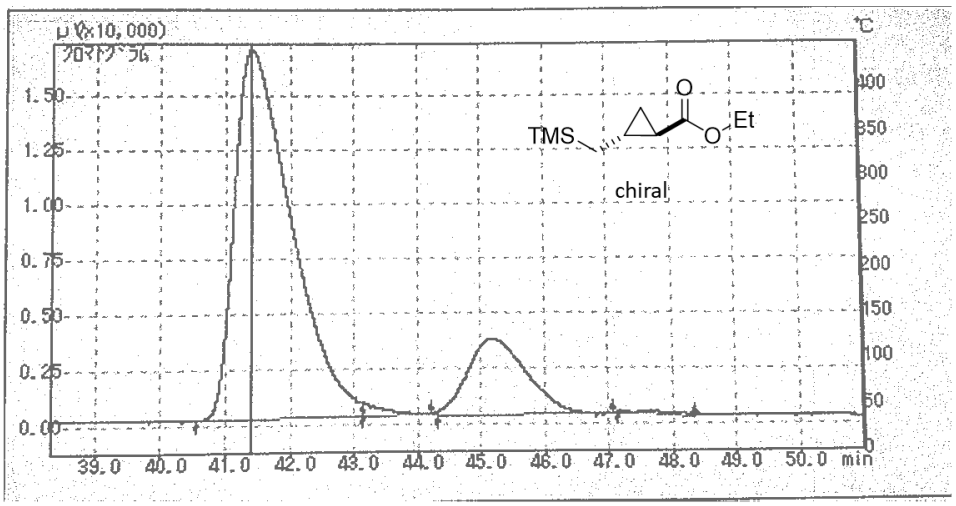

TMS
Br
OH
77.000
62.445
35.499
30.319
25.350
21.688
-0.327
abundance
X : parts per Million : Carbon13


crude ^{1}H NMR
OH
TBAF
TBAF
TBAF
1.27
1.19
1.12
1.01
0.73
abundance
X : parts per Million : Proton

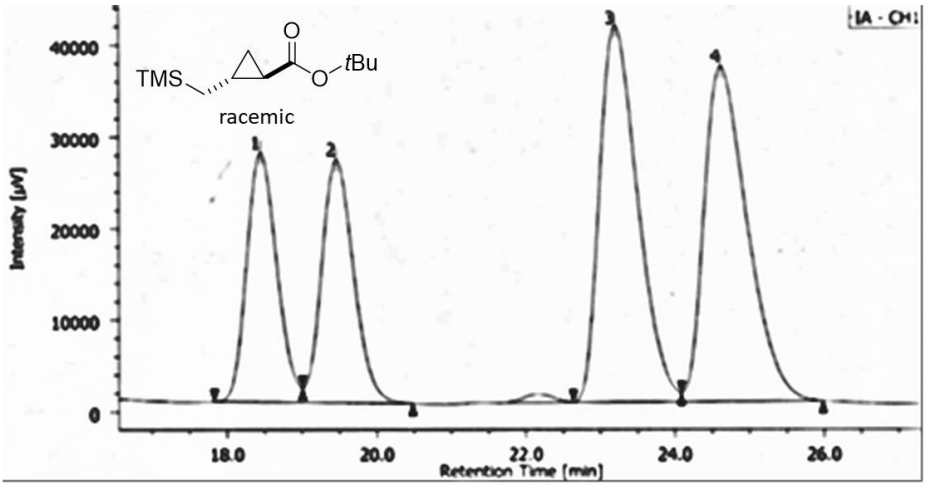
8-2-6 HPLC Spectral Data



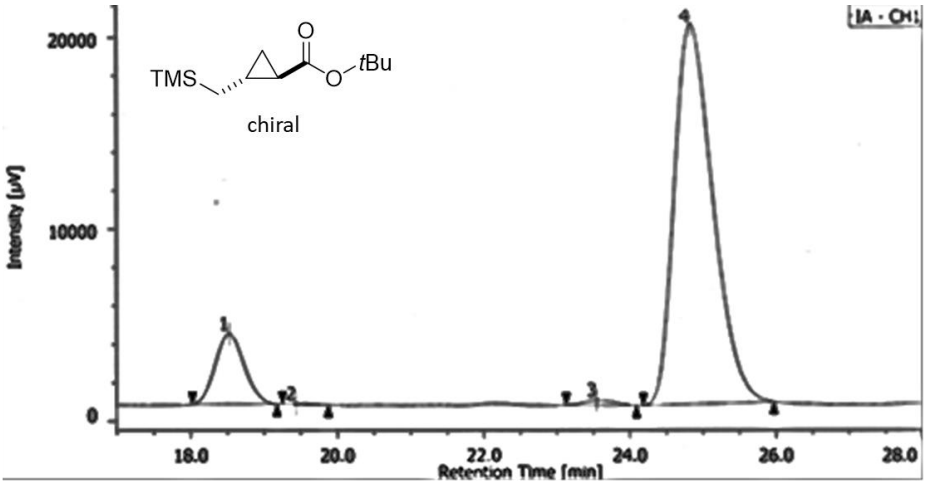
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	41.059	610572	13738	30.298	38.011
2	42.180	702573	10937	34.862	30.261
3	44.515	344622	6378	17.100	17.647
4	46.777	357476	5089	17.738	14.080



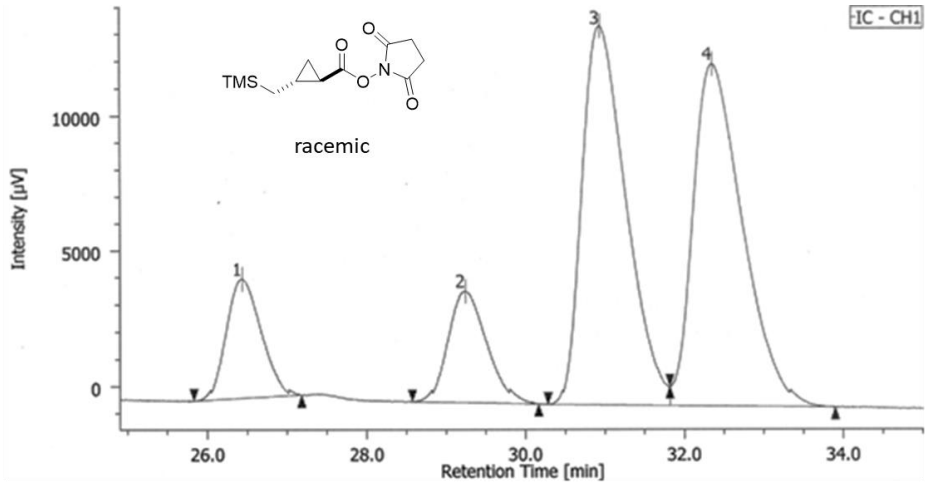
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	41.397	1033364	16885	81.556	80.538
2	43.139	11330	586	0.894	2.795
3	45.176	217175	3408	17.140	16.255
4	47.536	5184	86	0.409	0.410



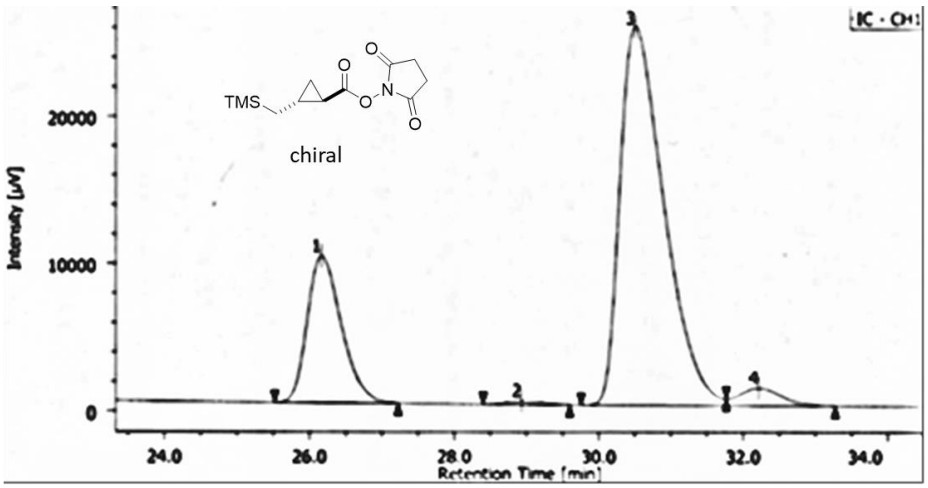
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	18.450	759974	27169	17.000	20.716
2	19.458	783279	26518	17.521	20.220
3	23.200	1462482	40976	32.714	31.244
4	24.617	1464818	36485	32.820	27.820



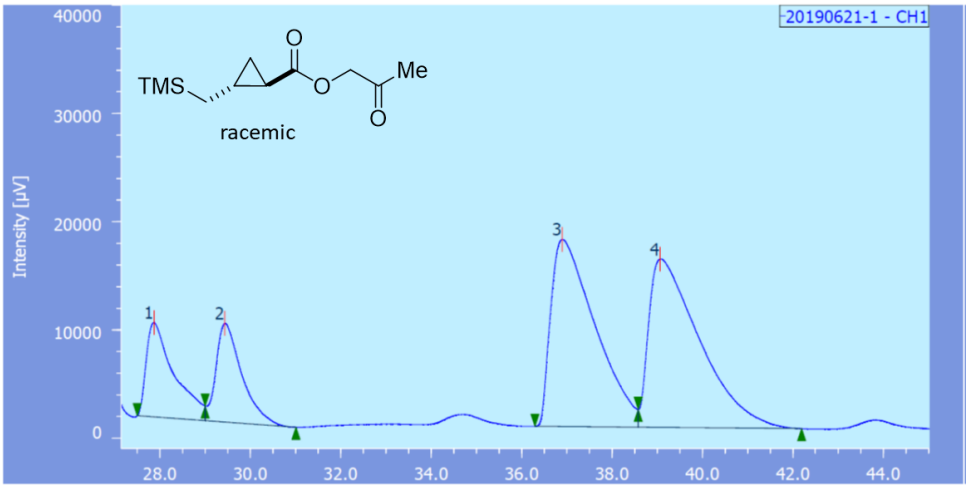
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	18.525	100622	3673	12.025	15.439
2	19.433	888	43	0.106	0.179
3	23.542	8039	280	0.961	0.961
4	24.825	727245	19795	86.909	86.207



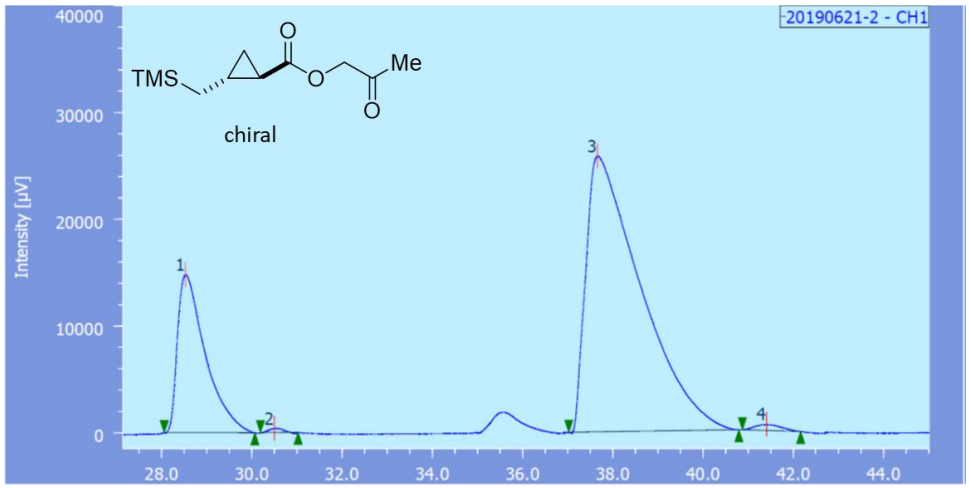
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	26.442	133452	4384	9.818	12.494
2	29.242	138942	4096	10.221	11.672
3	30.942	540145	13986	39.736	39.861
4	32.358	546793	12622	40.225	35.972



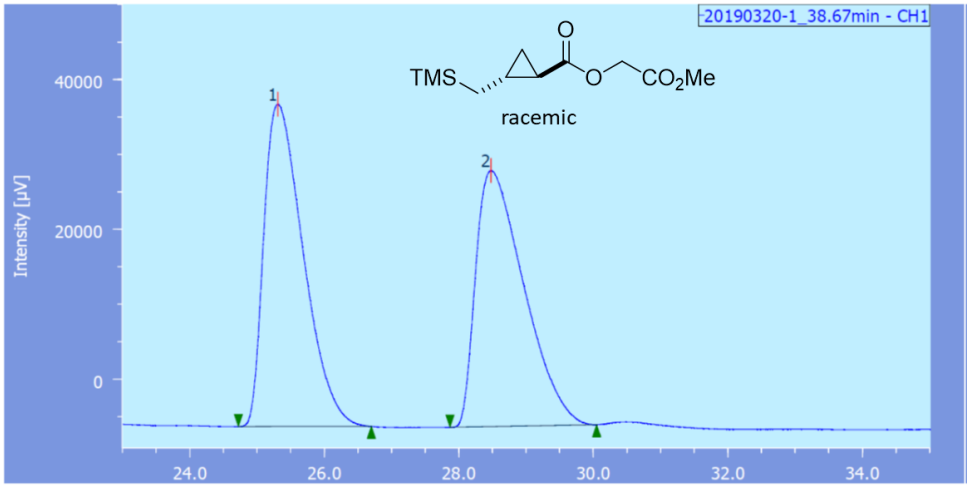
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	26.167	323848	9935	22.079	26.796
2	28.933	7338	244	0.500	0.658
3	30.508	1085778	25691	74.025	69.285
4	32.217	49817	1209	3.395	3.261



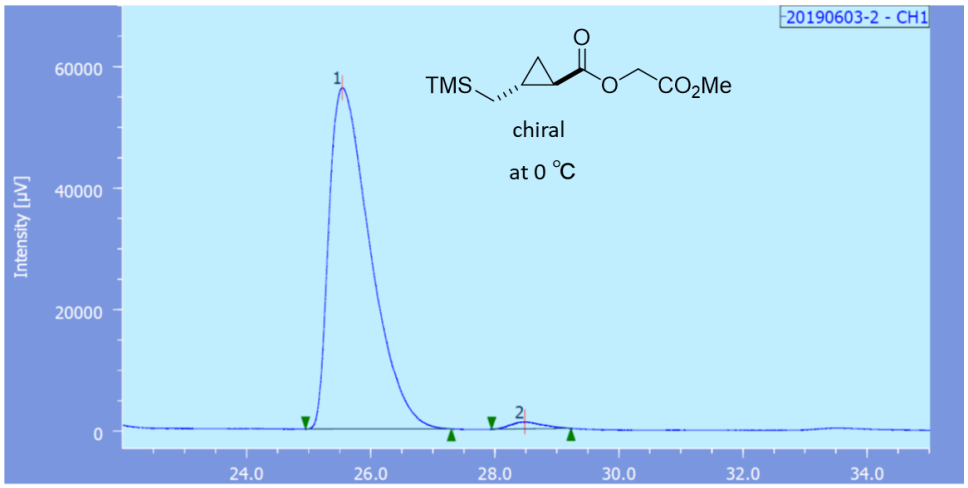
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	27.875	372576	8695	11.900	17.173
2	29.433	363496	9106	11.610	17.986
3	36.892	1176005	17281	37.561	34.133
4	39.058	1218880	15547	38.930	30.708



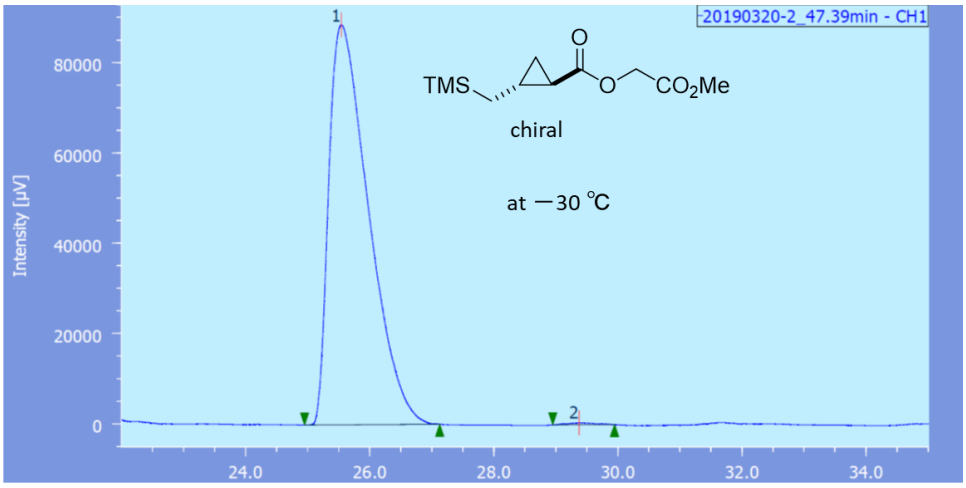
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	28.525	632405	14790	22.257	35.559
2	30.500	9142	408	0.322	0.982
3	37.658	2176559	25822	76.602	62.083
4	41.400	23288	572	0.820	1.376



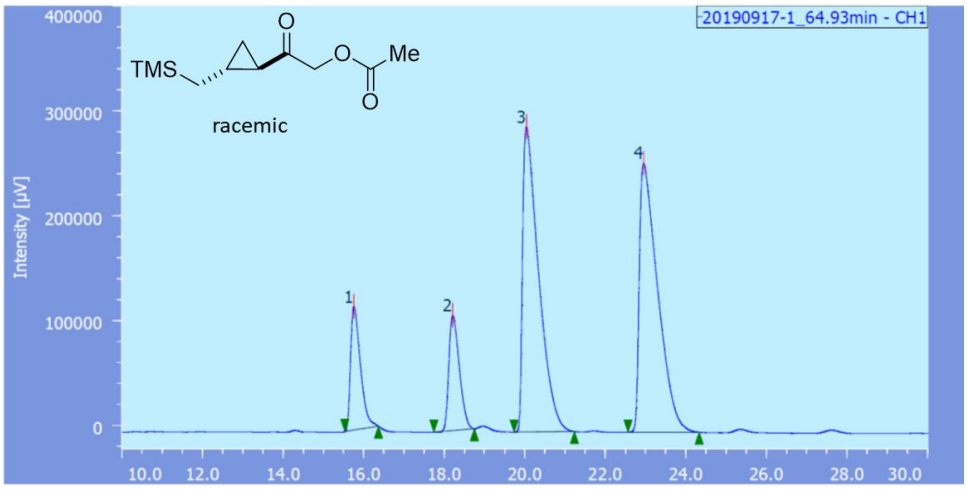
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.308	1750939	43020	50.720	55.724
2	28.475	1701245	34182	49.280	44.276



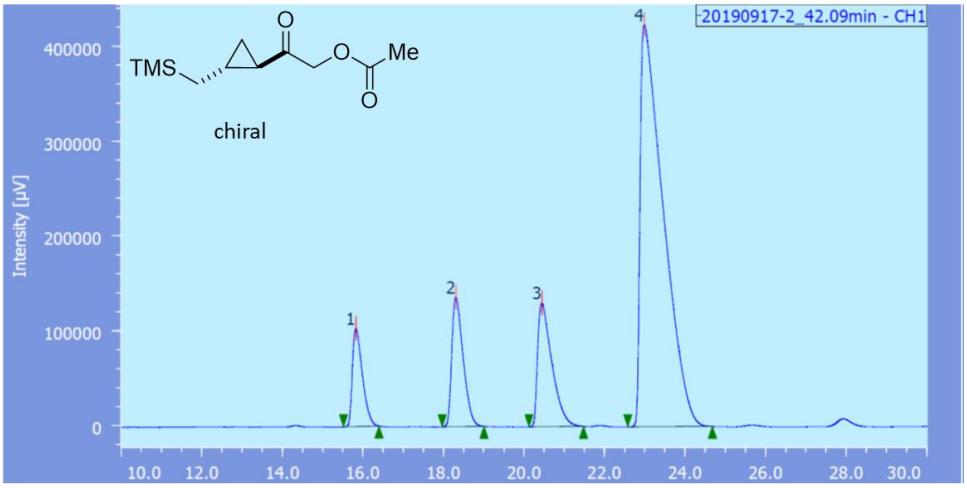
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.542	2591366	56087	98.420	97.990
2	28.483	41612	1150	1.580	2.010



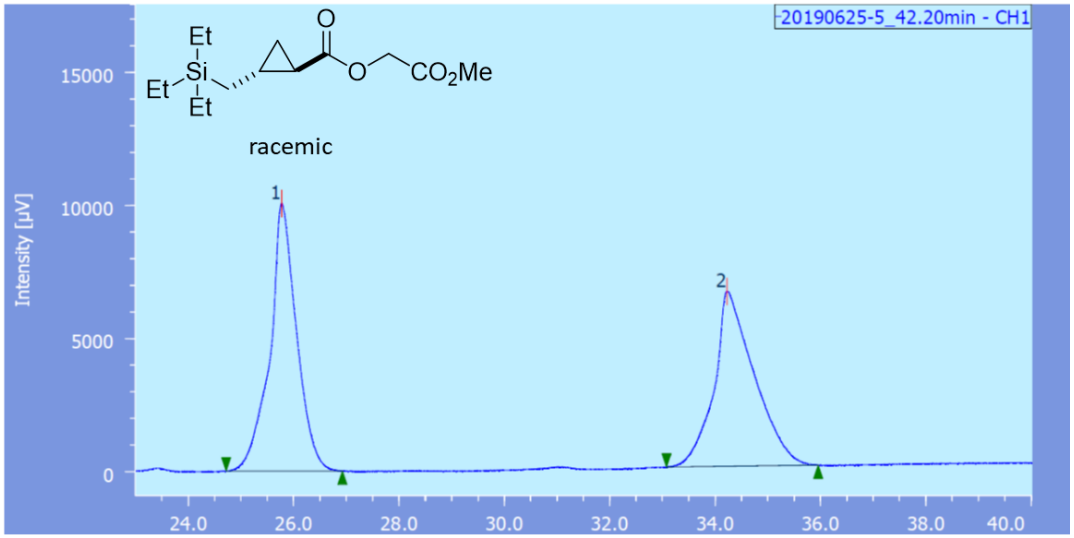
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.542	3934804	88521	99.641	99.515
2	29.375	14180	431	0.359	0.485



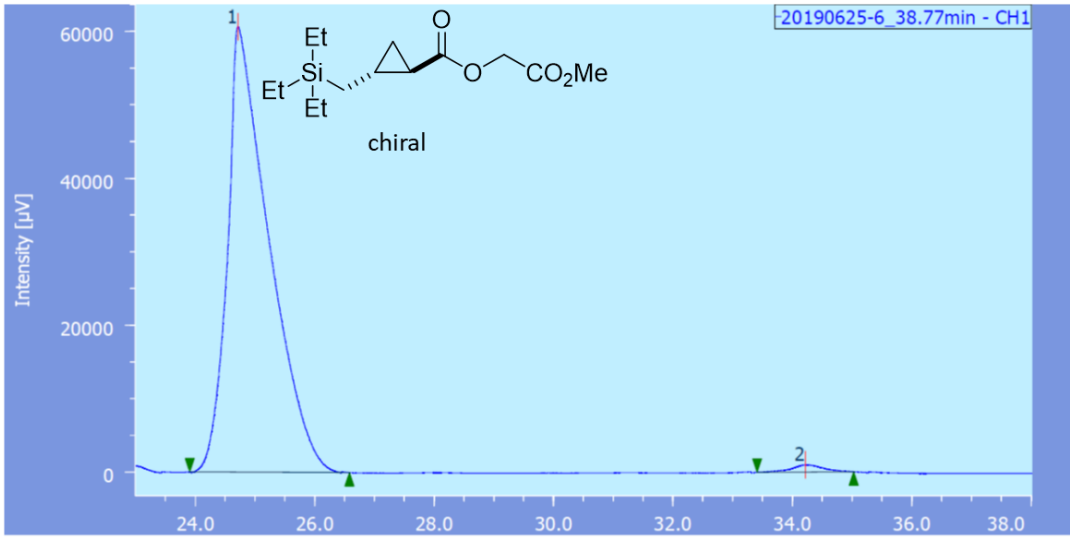
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	15.758	2007257	118103	9.961	15.229
2	18.208	1987913	109937	9.865	14.176
3	20.042	8027811	290947	39.838	37.516
4	22.950	8127950	256545	40.335	33.080



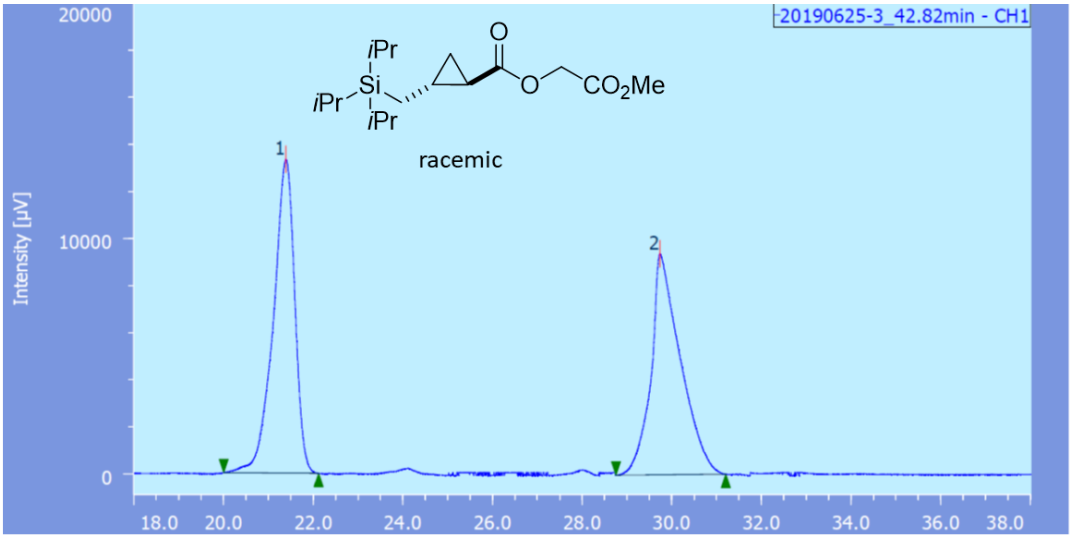
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	15.825	1793213	103603	7.309	13.044
2	18.308	2672316	136463	10.892	17.181
3	20.442	3201274	130338	13.048	16.410
4	22.983	16867481	423869	68.751	53.366



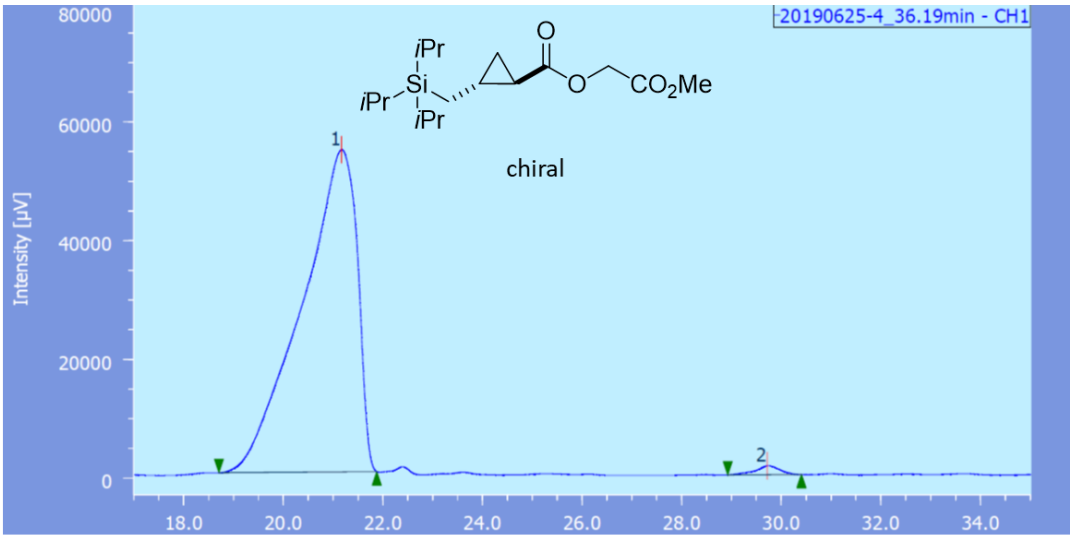
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.775	353701	10055	50.412	60.486
2	34.225	347913	6569	49.588	39.514



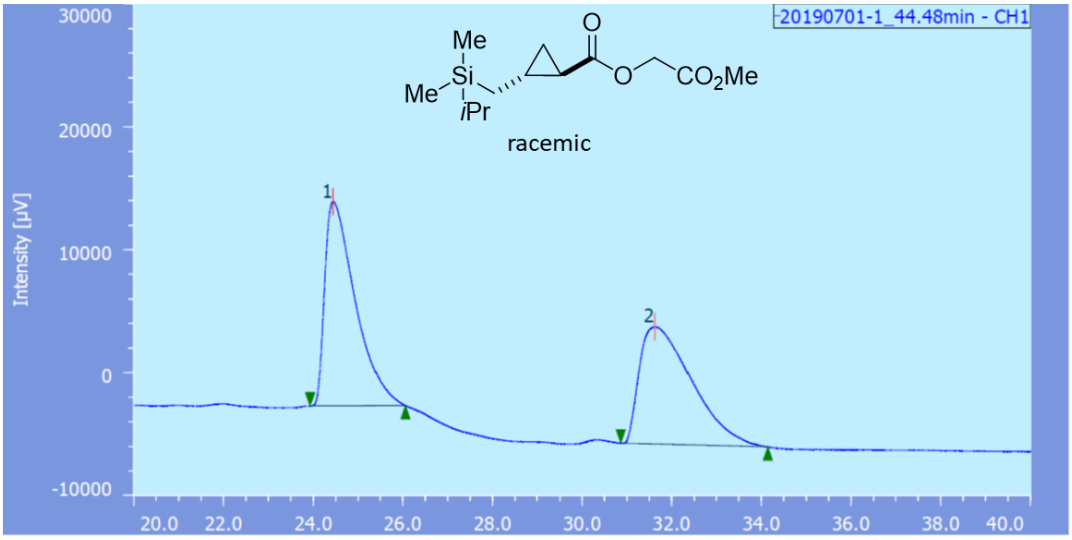
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	24.717	2930407	60573	98.763	98.417
2	34.217	36701	974	1.237	1.583



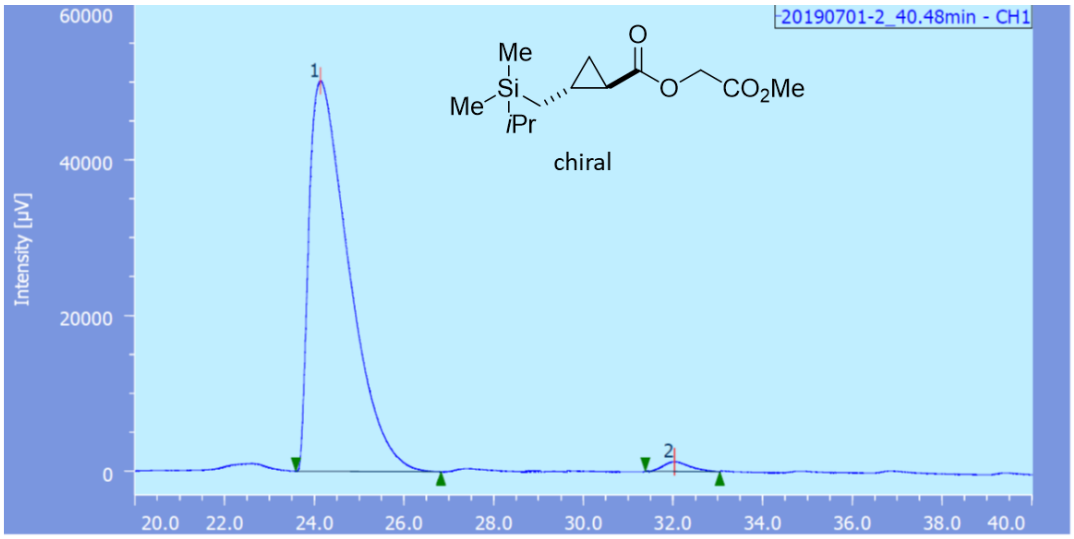
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	21.392	442549	13316	50.864	58.651
2	29.733	427516	9388	49.136	41.349



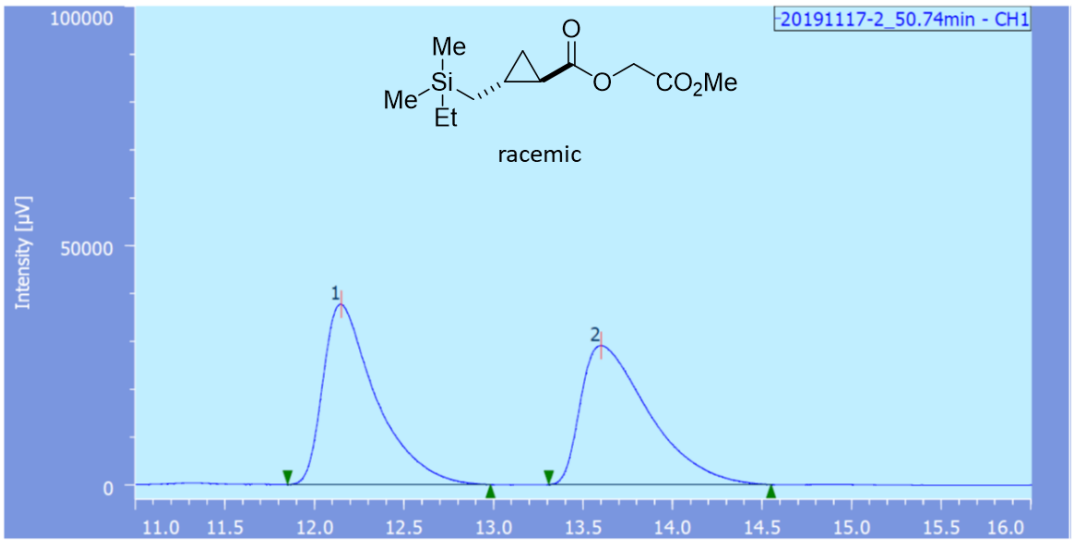
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	21.167	4181723	54243	98.758	97.270
2	29.717	52582	1523	1.242	2.730



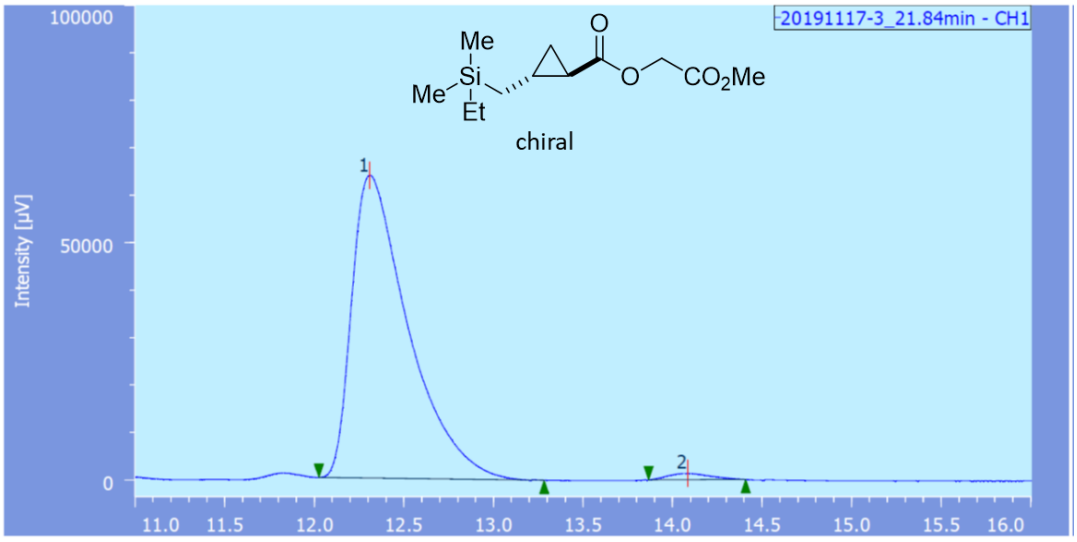
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	24.442	785230	16603	50.309	63.505
2	31.625	775593	9542	49.691	36.495



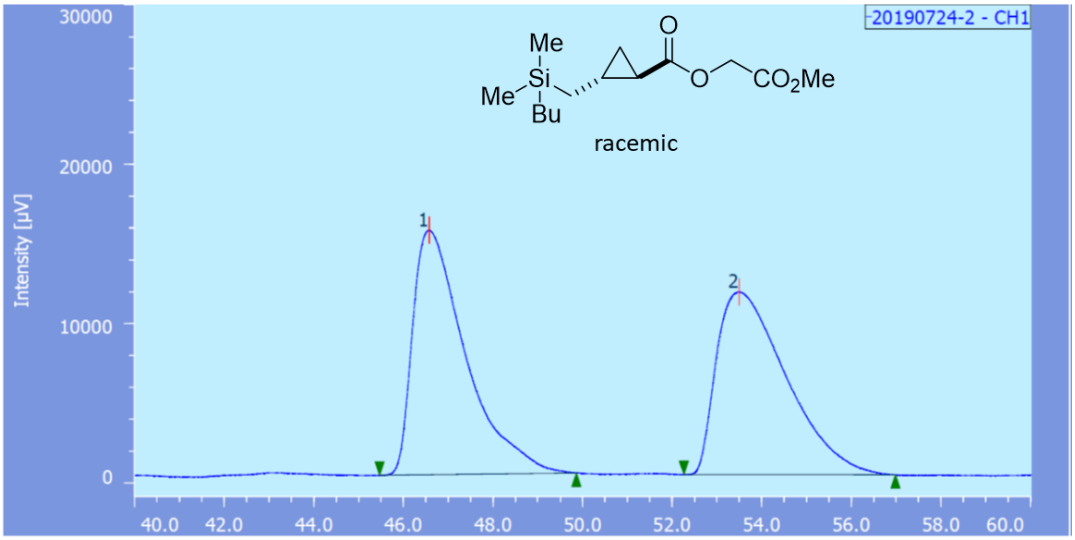
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	24.133	3092201	50122	98.317	97.534
2	32.033	52941	1267	1.683	2.466



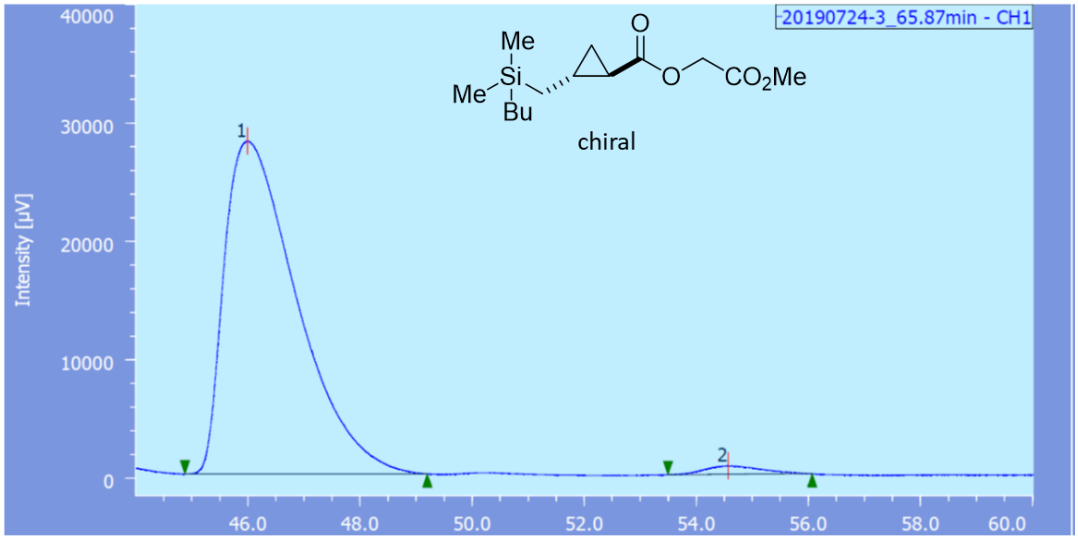
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	12.150	773253	37639	50.191	56.454
2	13.600	767380	29033	49.809	43.546



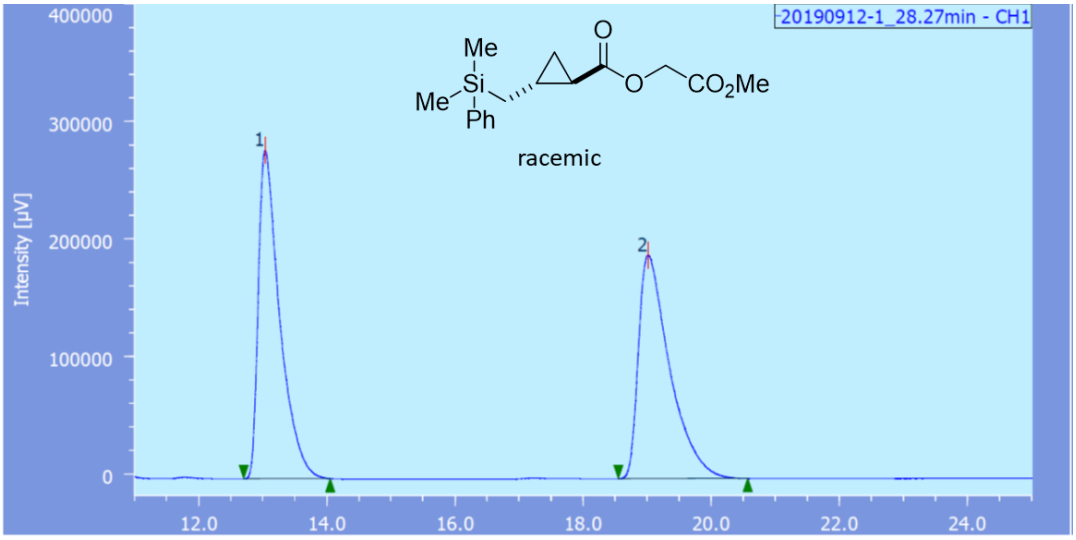
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	12.308	1402215	63823	98.415	97.923
2	14.083	22585	1354	1.585	2.077



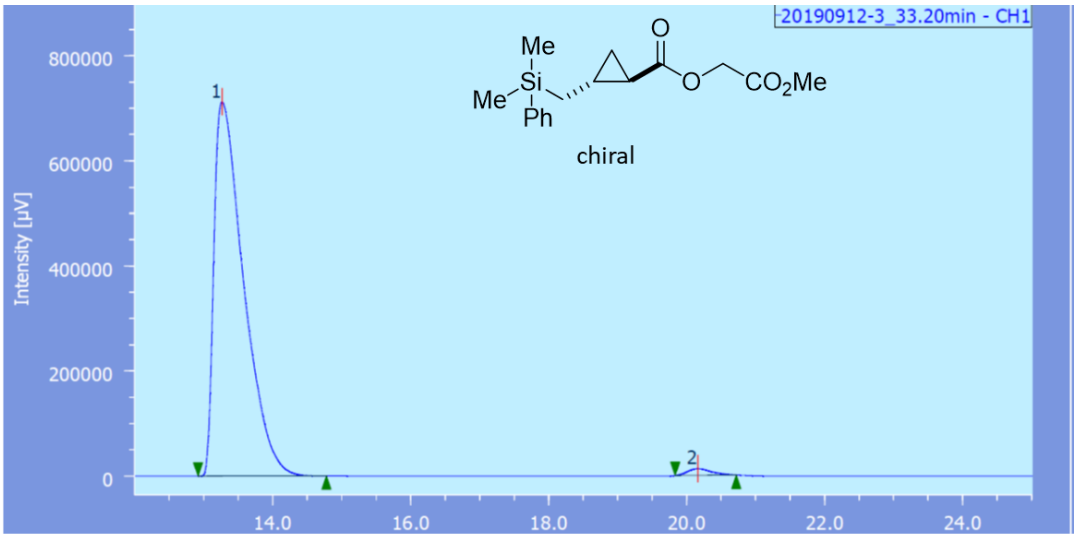
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	46.575	1258517	15336	50.379	57.246
2	53.492	1239575	11454	49.621	42.754



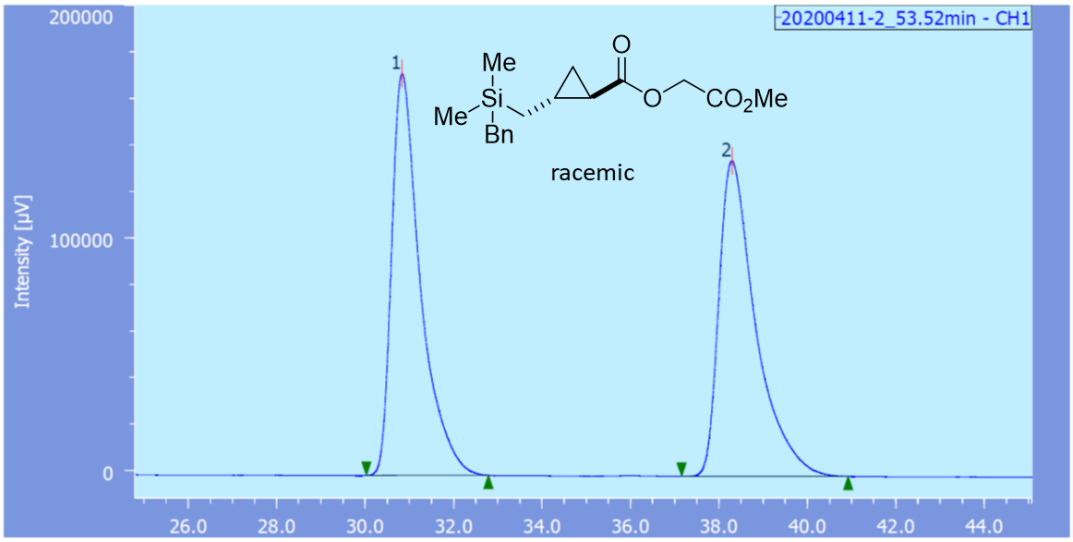
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	45.992	2533746	28090	98.035	97.521
2	54.567	50786	714	1.965	2.479



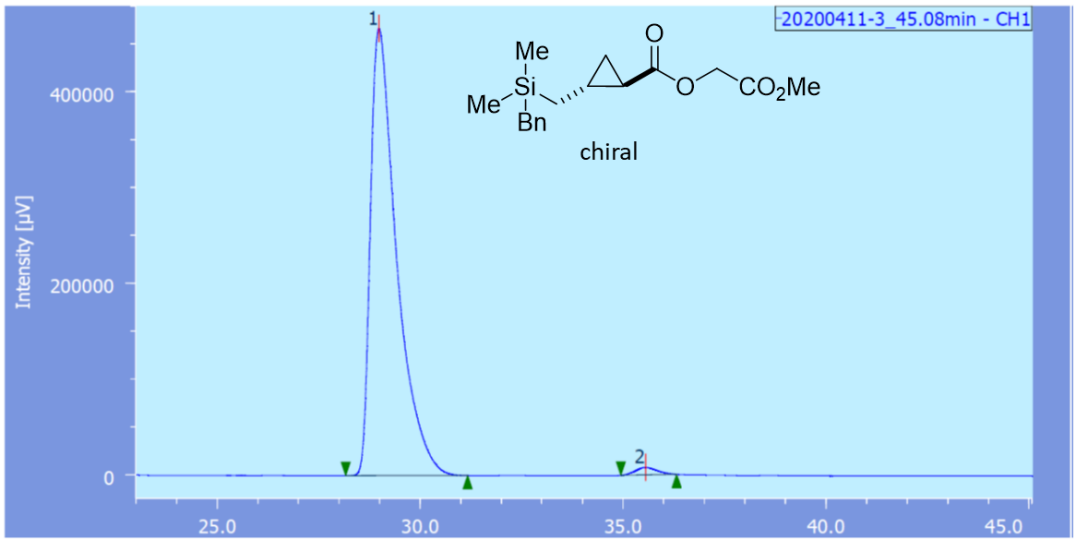
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	13.042	6449260	279306	50.133	59.515
2	19.017	6415080	189998	49.867	40.485



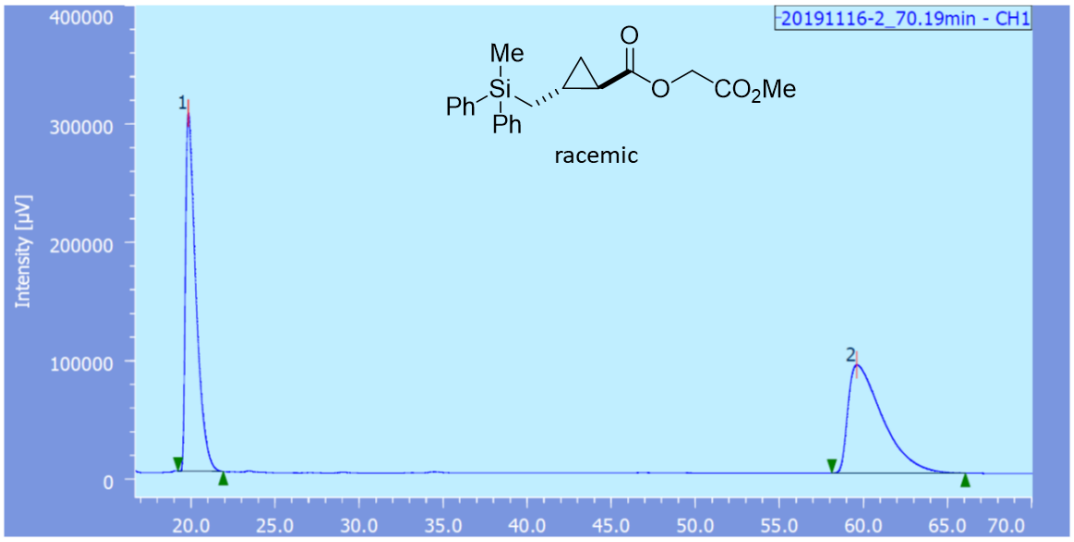
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	13.267	21217501	711911	98.575	98.265
2	20.158	306702	12573	1.425	1.735



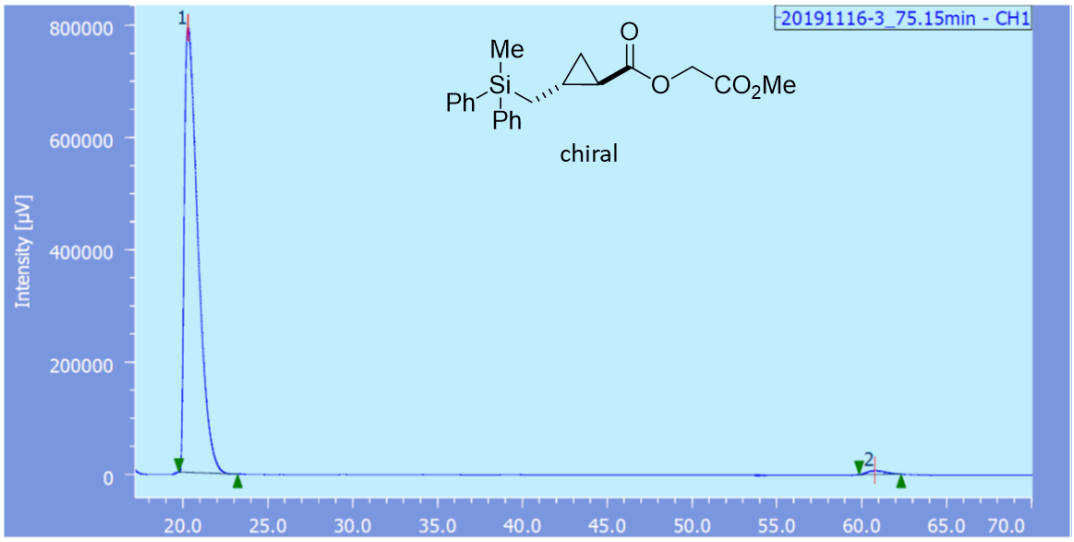
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	30.833	7811482	172741	49.935	56.024
2	38.292	7831968	135594	50.065	43.976



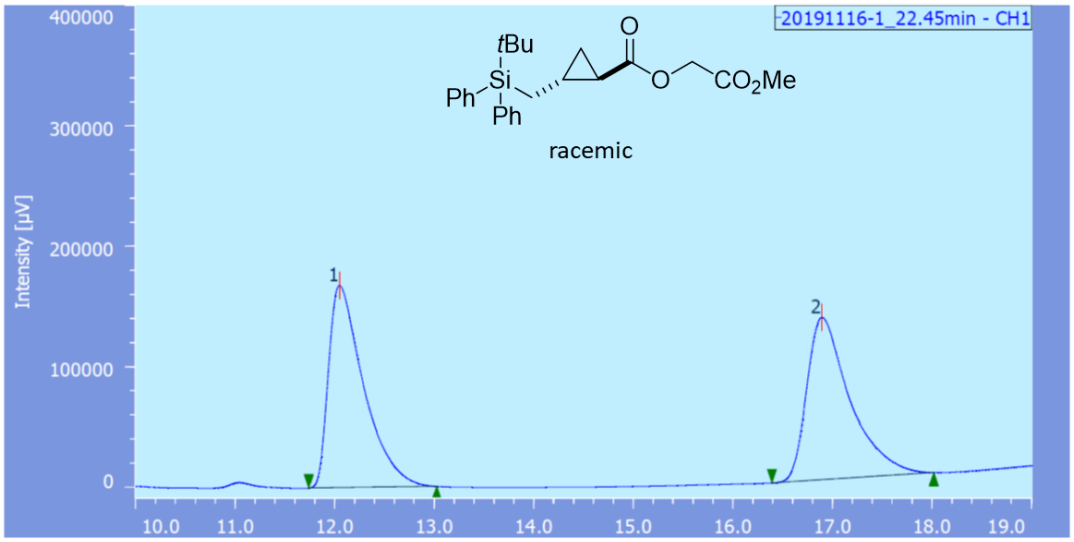
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	28.983	20963533	466595	98.600	98.356
2	35.550	297636	7799	1.400	1.644



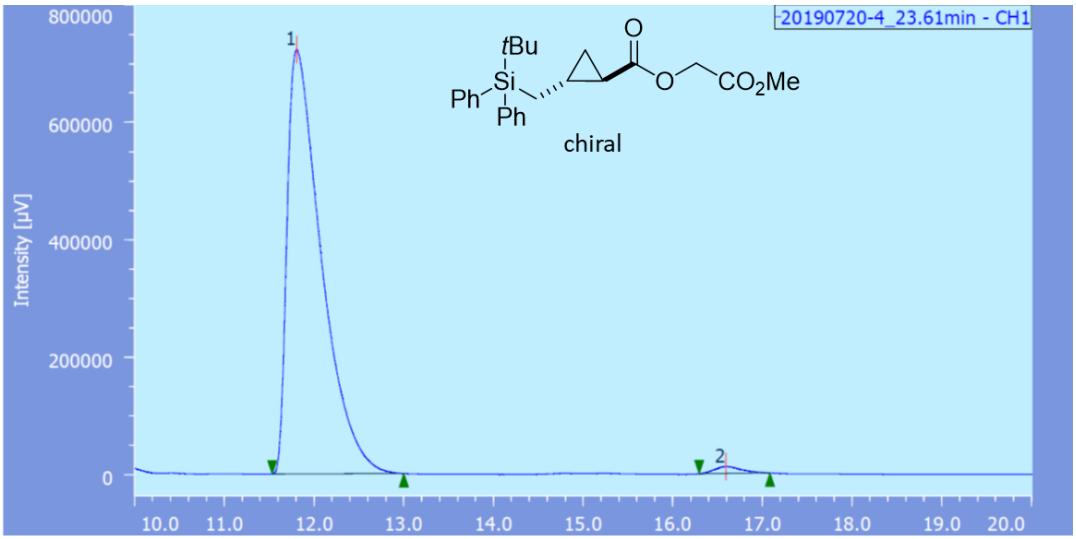
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	19.842	13019867	302275	49.916	76.777
2	59.600	13063822	91428	50.084	23.223



PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	20.300	43851764	791829	98.864	99.148
2	60.767	503834	6802	1.136	0.852



PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.050	4096094	167604	50.127	55.442
2	16.892	4075279	134702	49.873	44.558



PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
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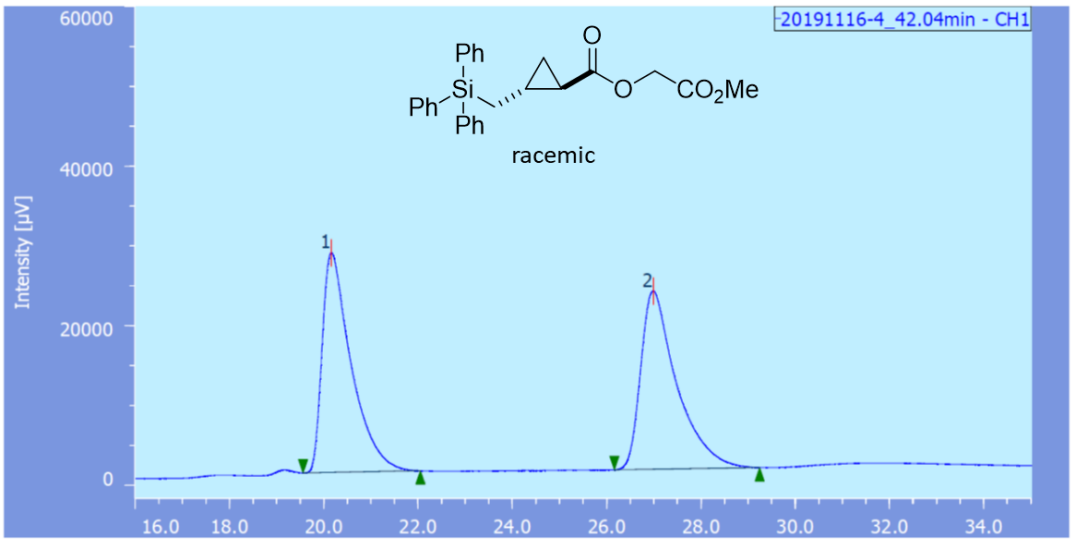
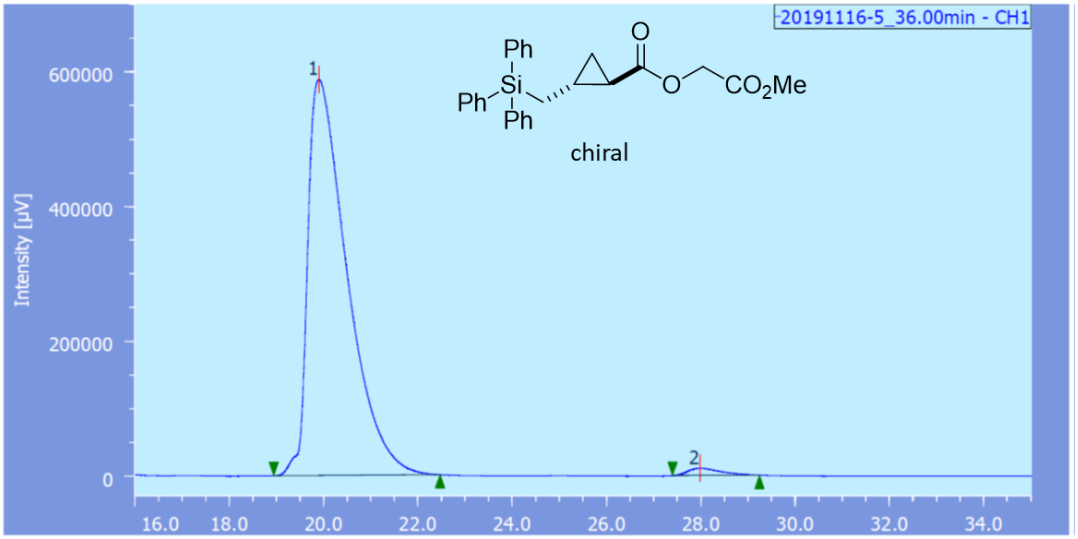
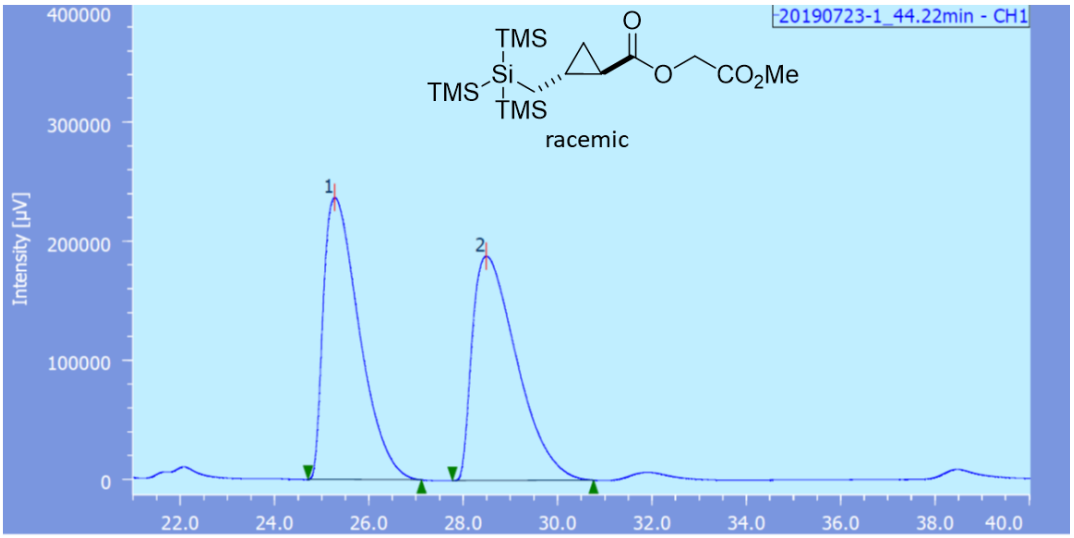
2	16.592	252912	11789	1.307	1.605



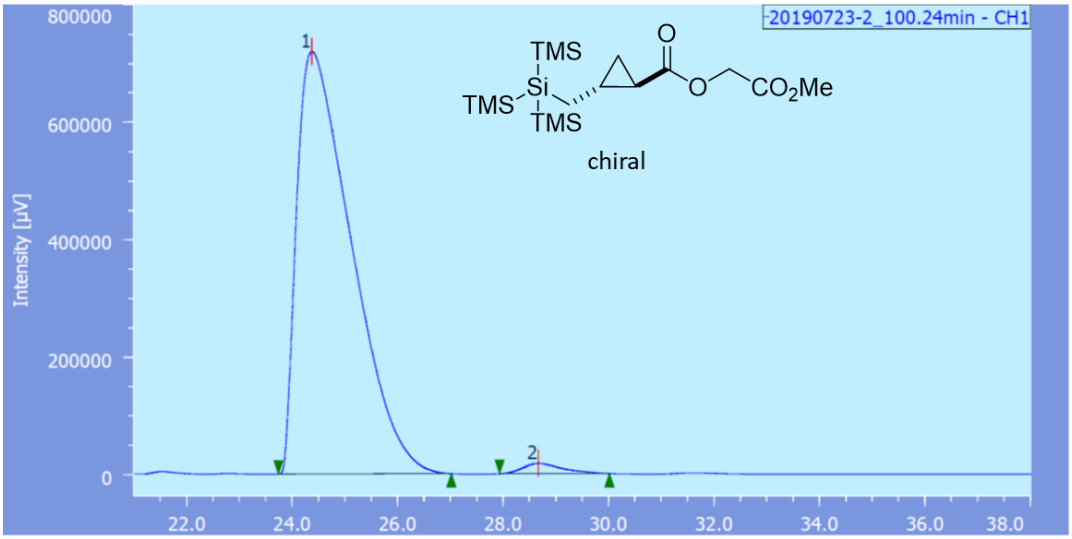
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.158	1174473	27515	49.782	55.212
2	26.992	1184744	22321	50.218	44.788



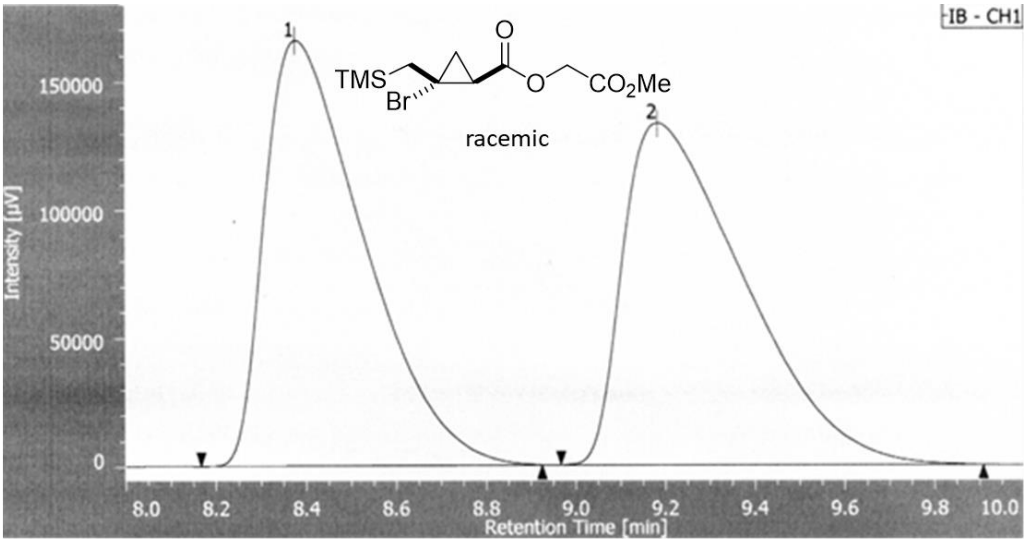
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	19.900	33912305	587800	98.483	98.199
2	27.983	522376	10781	1.517	1.801



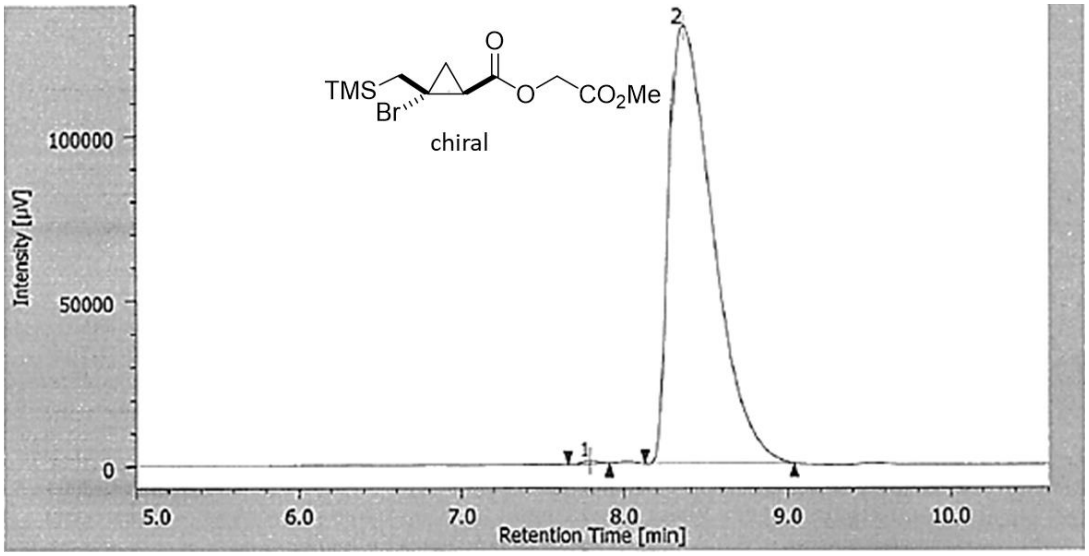
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	25.275	12490831	236737	50.256	55.673
2	28.483	12363629	188492	49.744	44.327



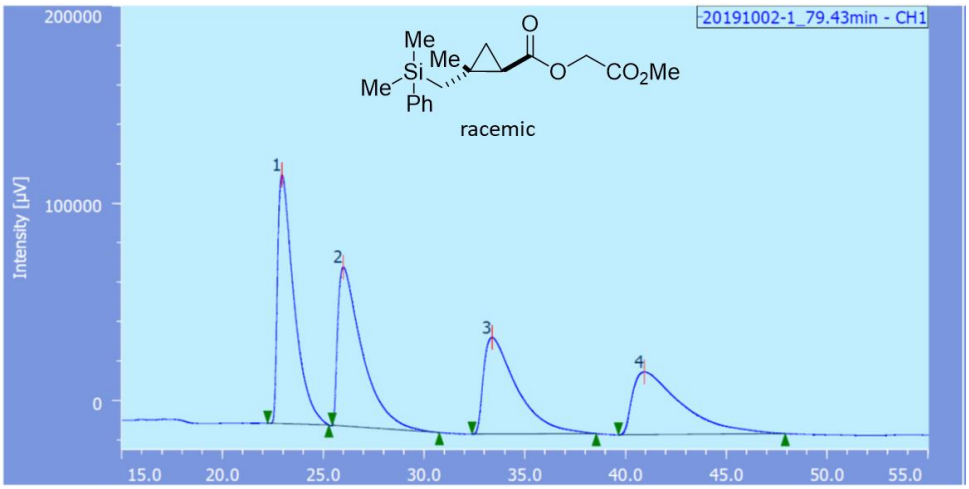
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	24.375	51895300	719286	98.257	97.617
2	28.667	920561	17559	1.743	2.383



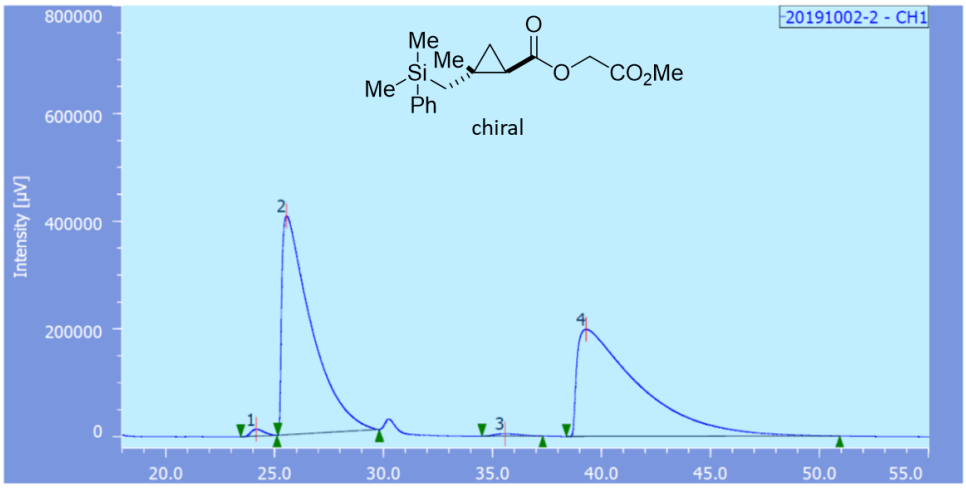
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	8.375	2528307	165397	50.352	55.405
2	9.183	2492997	133129	49.648	44.595



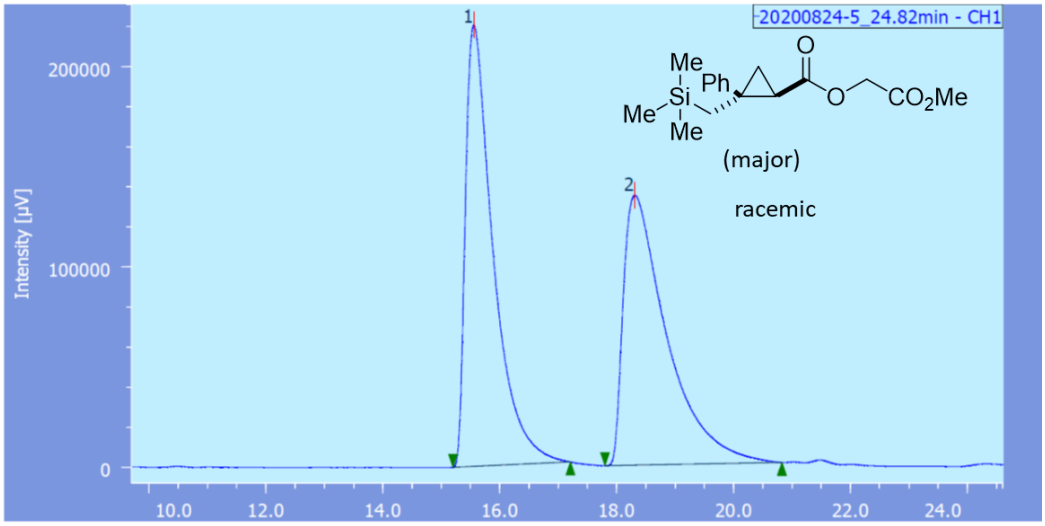
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	7.792	6713	976	0.275	0.735
2	8.360	2437716	131687	99.265	99.265



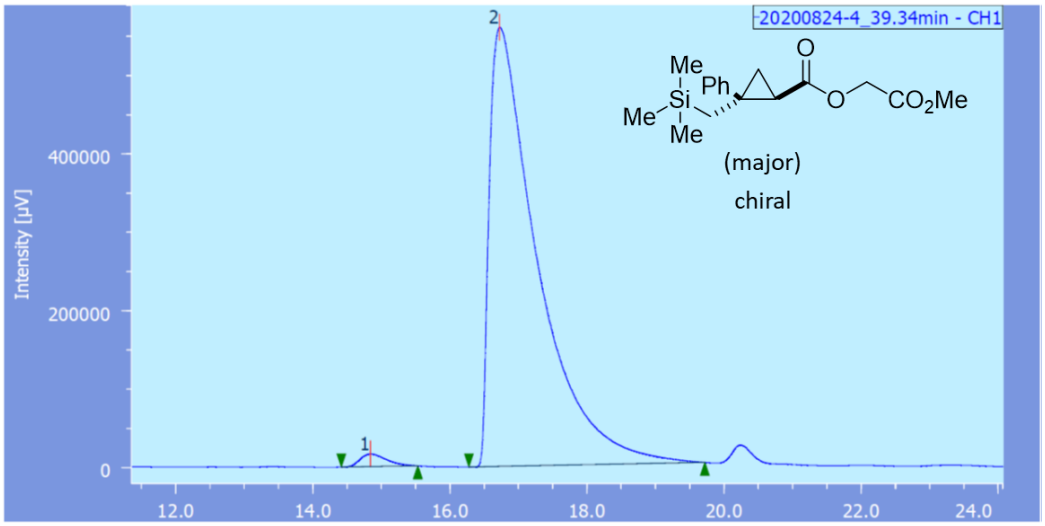
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	22.950	7155138	126137	28.706	43.878
2	25.992	6803285	80565	27.295	28.025
3	33.375	5585243	48981	22.408	17.038
4	40.933	5381674	31791	21.591	11.059



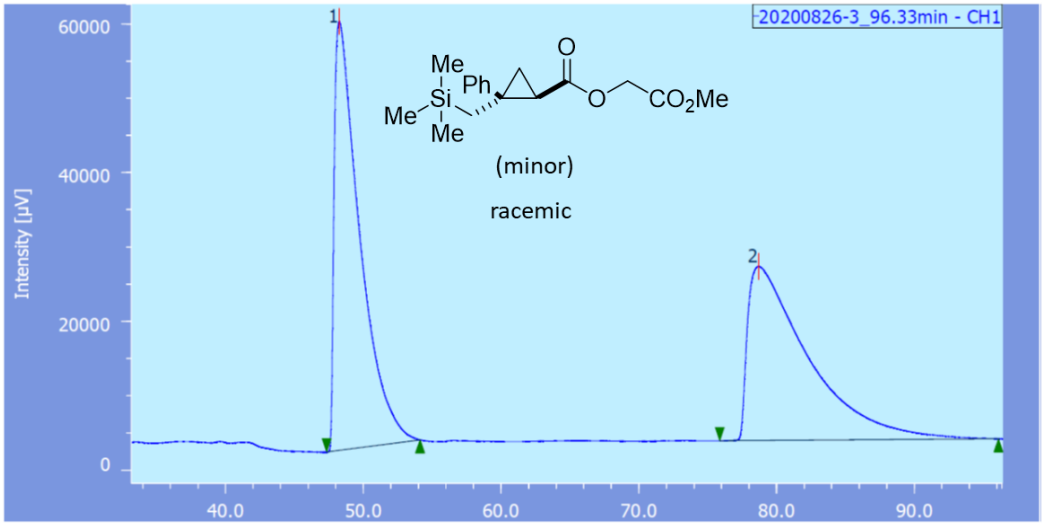
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	24.158	567539	13154	0.726	2.112
2	25.542	38053150	406227	48.654	65.223
3	35.558	388760	4678	0.497	0.751
4	39.292	39202813	198771	50.124	31.914



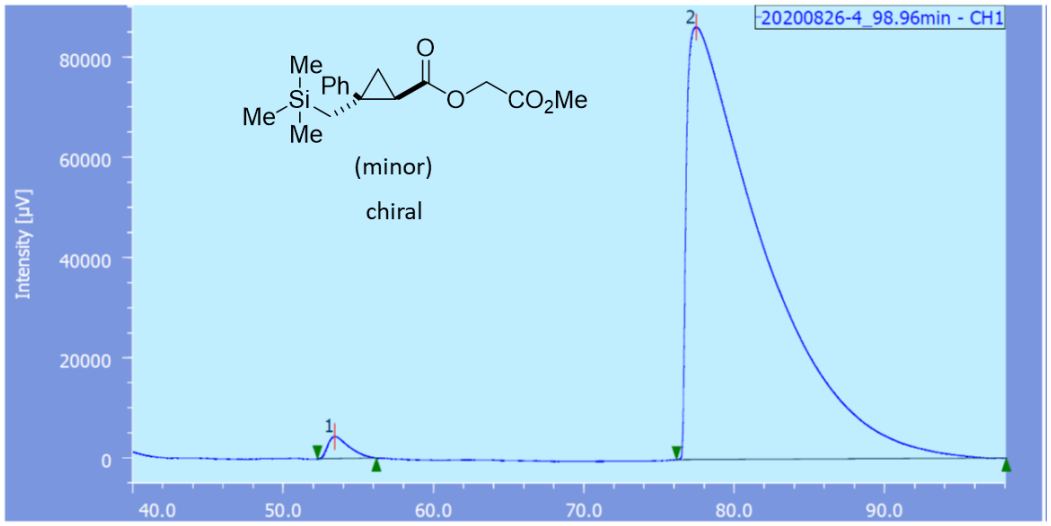
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	15.558	7261876	220166	51.018	62.043
2	18.308	6971989	134696	48.982	37.957



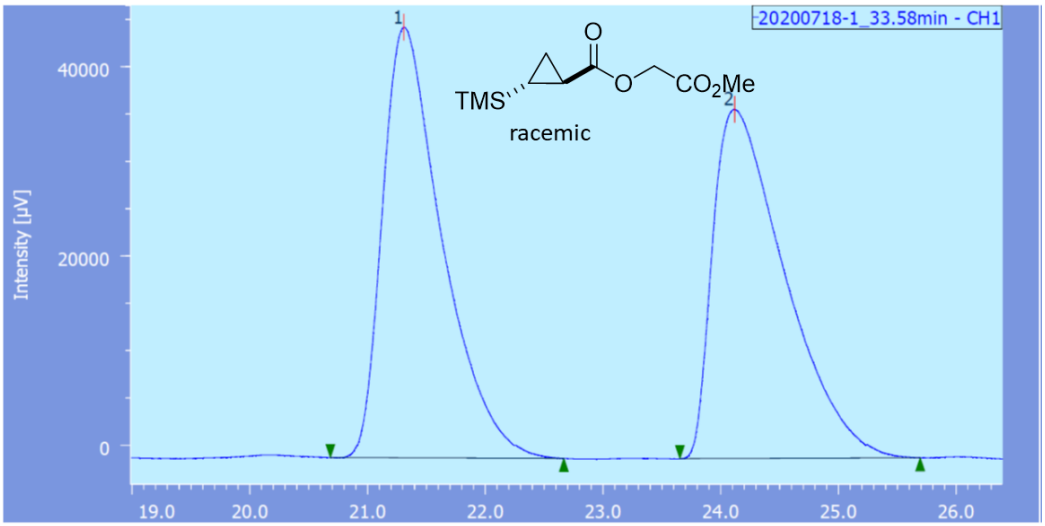
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	14.842	440017	16189	1.586	2.812
2	16.725	27310150	559581	98.414	97.188



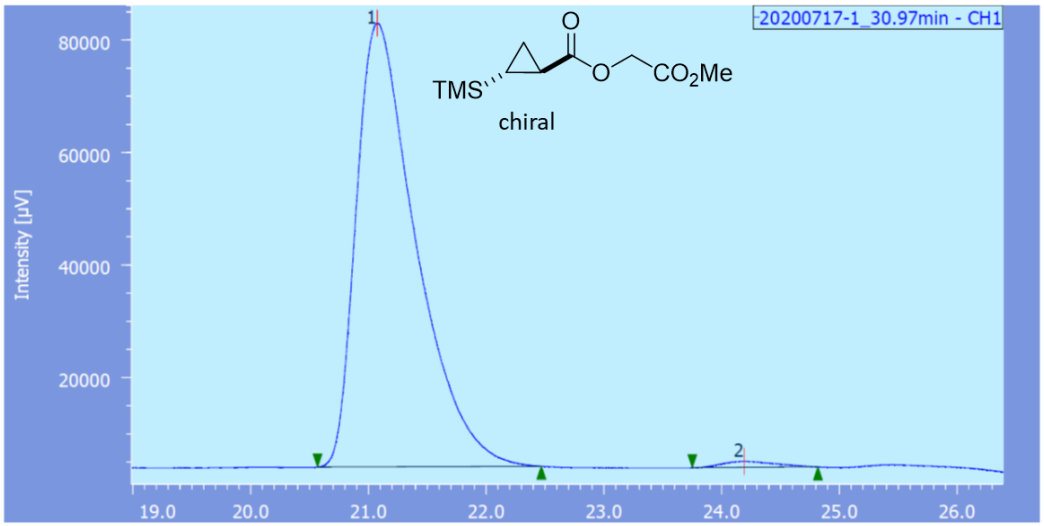
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	48.250	7400964	57627	50.851	71.141
2	78.683	7153277	23377	49.149	28.859



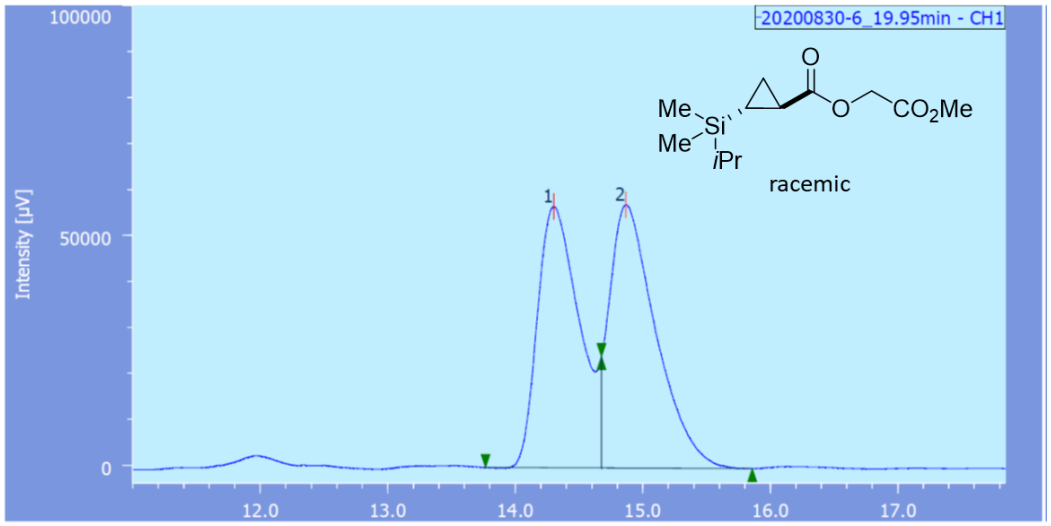
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	53.425	440499	4413	1.415	4.868
2	77.458	30699955	86238	98.585	95.132



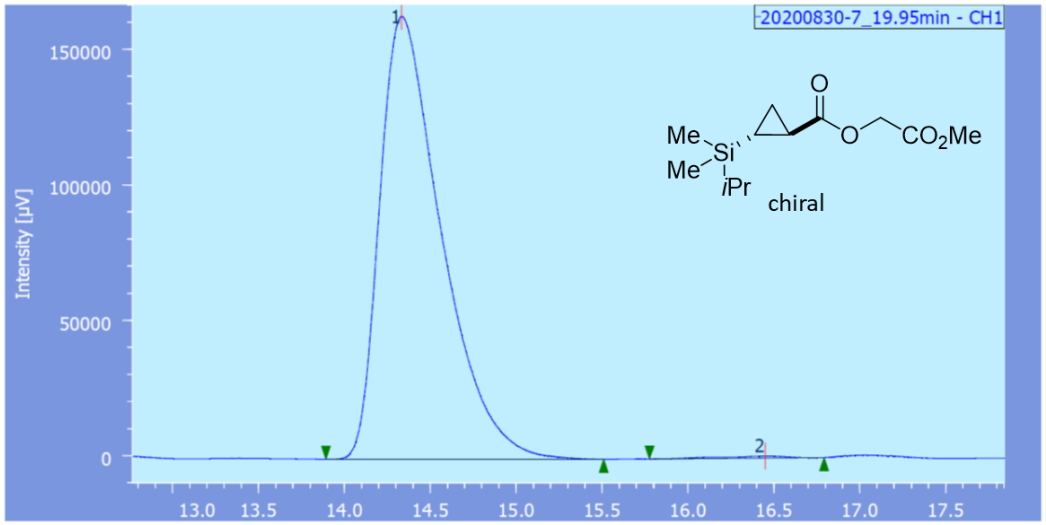
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	21.308	1603068	45475	50.501	55.229
2	24.117	1571240	36863	49.499	44.771



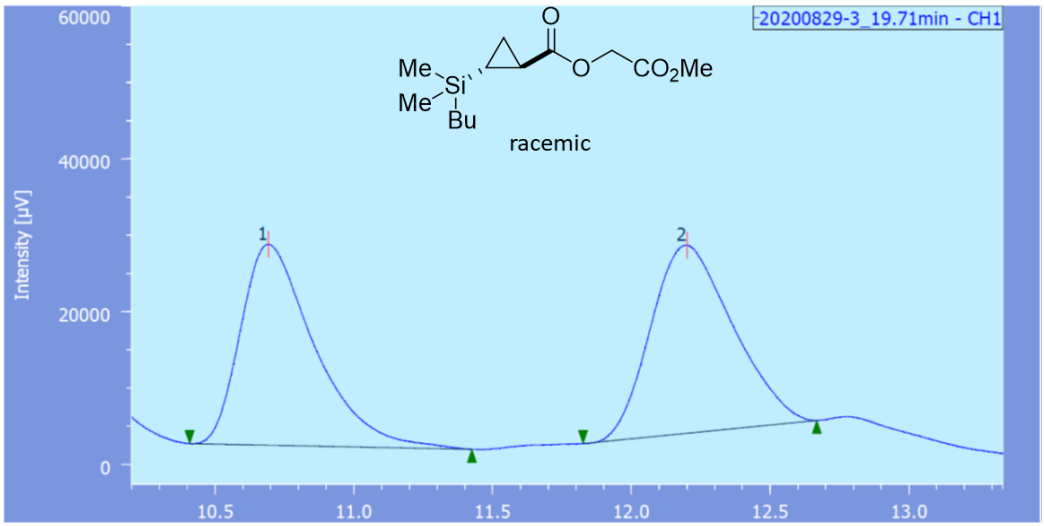
PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	21.075	2777278	78834	98.777	98.646
2	24.192	34394	1082	1.223	1.354



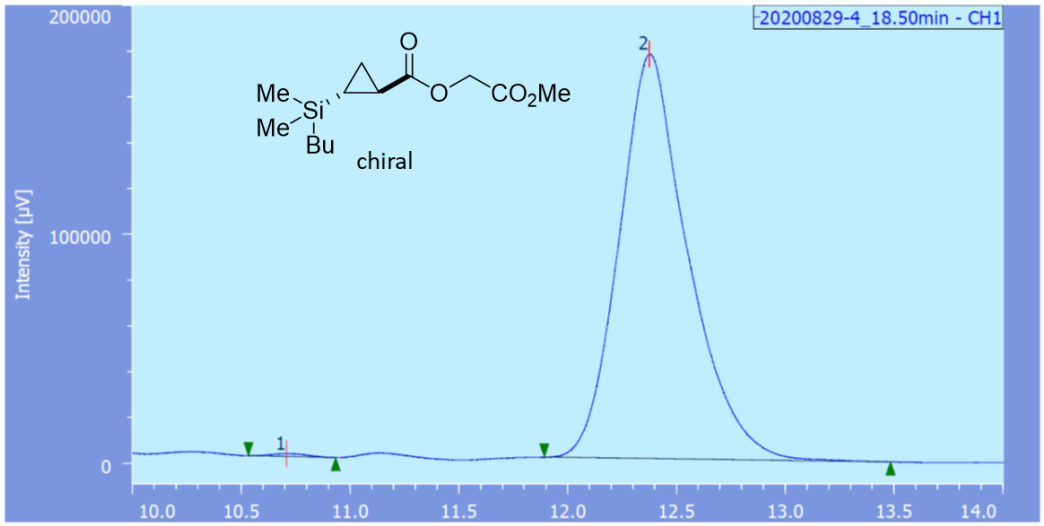
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.00	1308769	56808	47.564	49.824
2	14.867	1442813	57209	52.436	50.176



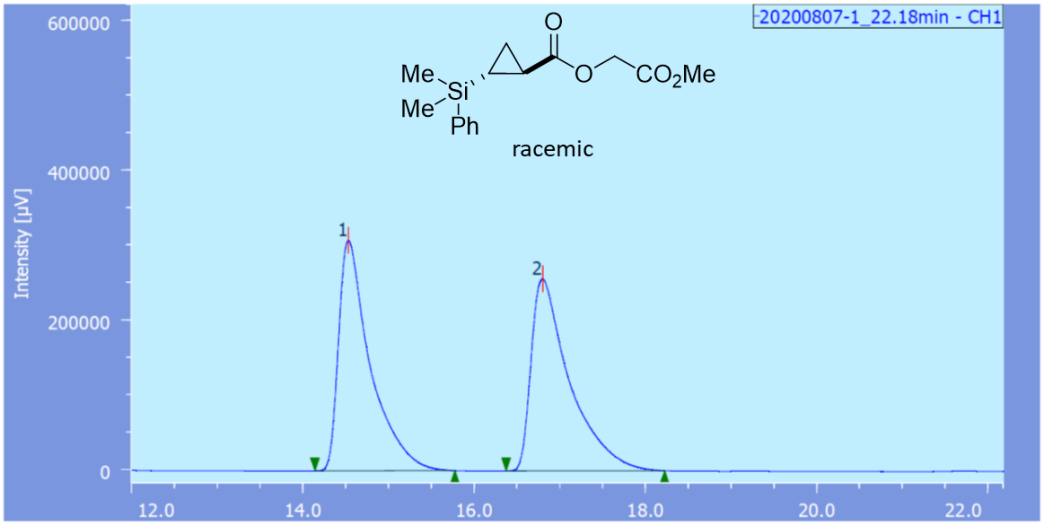
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.333	4077390	163355	99.511	99.548
2	16.450	20017	741	0.489	0.452



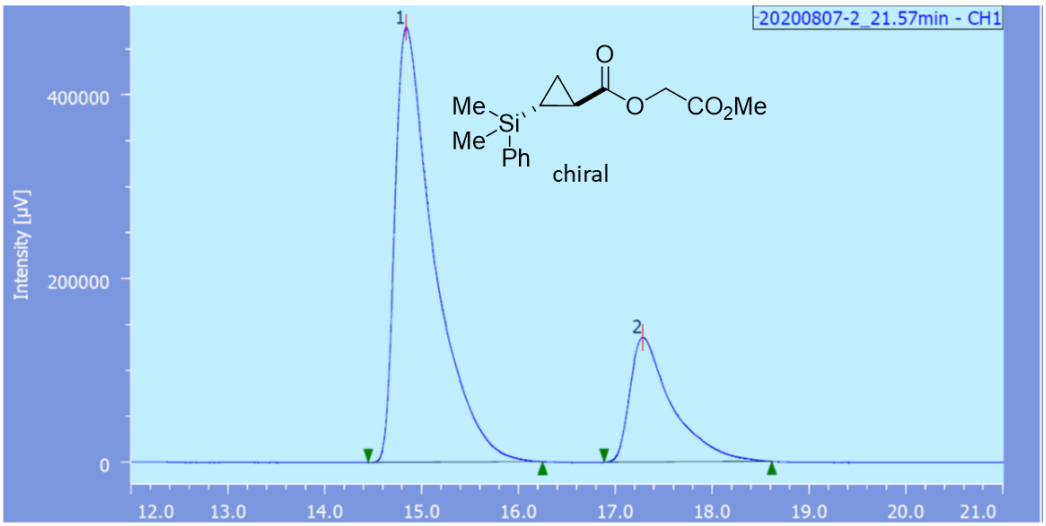
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	10.692	487250	26298	49.238	51.744
2	12.200	502322	24525	50.762	48.256



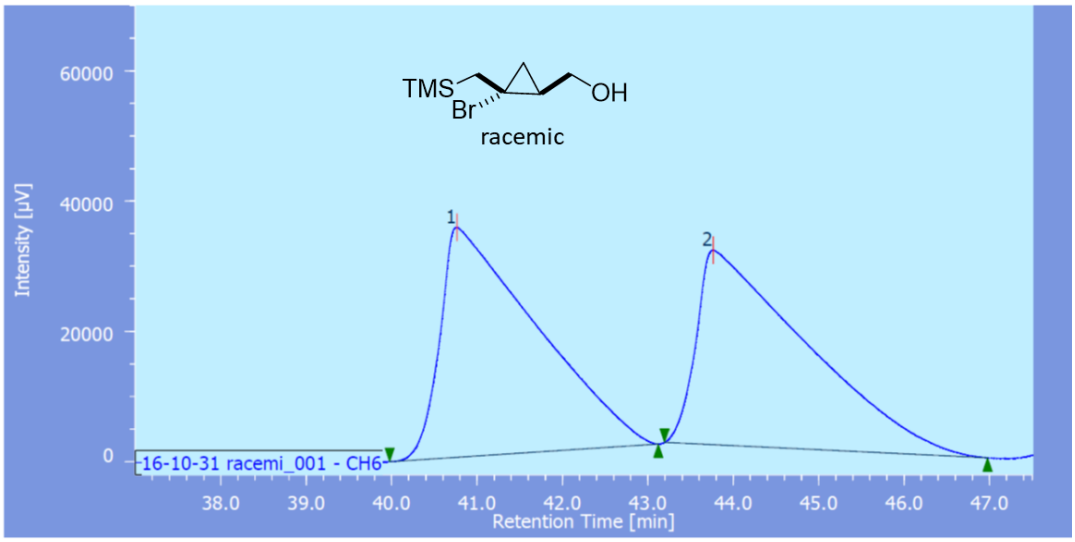
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	10.708	15252	1284	0.390	0.722
2	12.375	3896025	176586	99.610	99.278



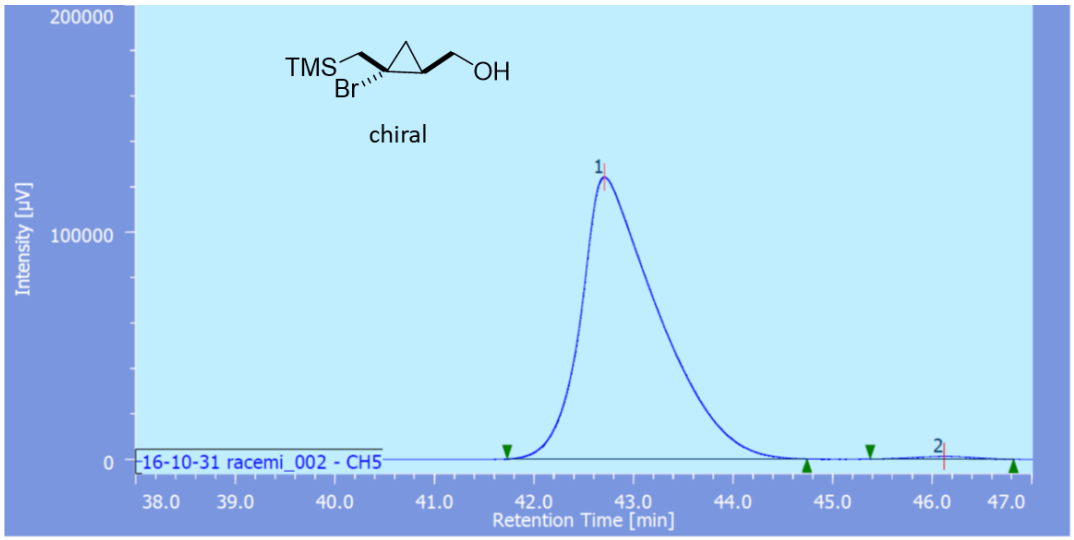
PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.533	7876379	307624	49.607	54.527
2	16.800	8001074	256541	50.393	45.473



PEAK	RT [min]	AREA [μV·sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	14.842	13336373	473290	76.518	77.736
2	17.283	4092648	135554	23.482	22.264



PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	40.763	2754595	35272	50.636	54.147
2	43.763	2685401	29869	49.364	45.853



PEAK	RT [min]	AREA [µV·sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	42.705	6721402	123927	99.281	99.059
2	46.118	48648	1178	0.719	0.941

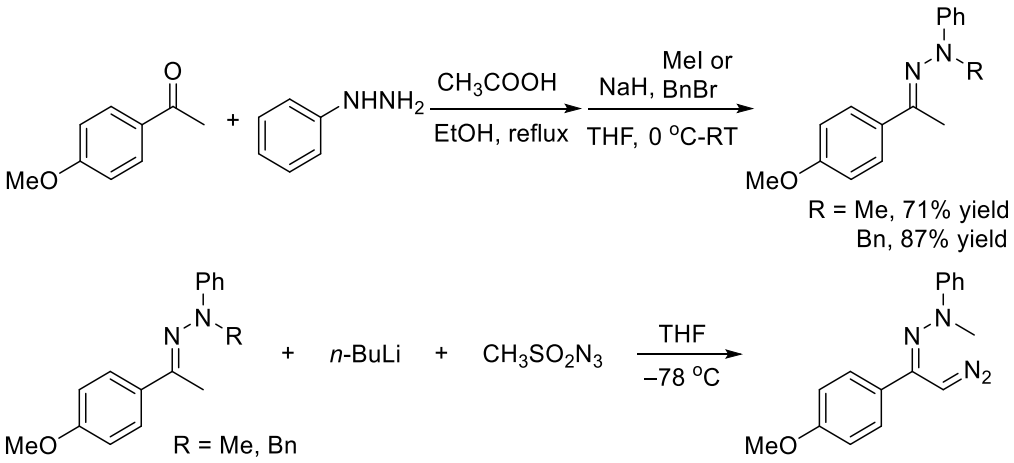
8-3 Experimental Section for Chapter 5

General Experimental Information

All reactions were carried out under an atmosphere of argon unless otherwise noted.
Dichloromethane (CH_2Cl_2) was purchased from Kanto Chemical Co., Inc.. All the staring materials are commercially available and were used without further purification unless otherwise stated. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGaA 60 F254, layer thickness 0.2 mm. The products were visualized by irradiation with UV light or by treatment with a solution of phosphomolybdic acid or by treatment with a solution of p-anisaldehyde. Flash column chromatography was performed using silica gel (Merck, Art. No. 7734). ^{1}H NMR (500 MHz, 400 MHz) and ^{13}C NMR (125 MHz, 100 MHz) spectra were collected on JEOL JNM-ECX500, JEOL JNM-ECS400 spectrometer. Chemical shifts are reported as δ values (ppm) relative to internal tetramethylsilane (0.00 ppm) in $CDCl_3$, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (Hz), and integration. DART mass (positive mode) analyses were performed on a LC-TOF JMS-T100LP. Optical rotations were performed with a JASCO P-1030 polarimeter at the sodium D line (1.0 mL sample cell). Enantiomeric excesses were determined by high-performance liquid chromatography (HPLC) analyses with a JASCO GULLIVER using Daicel CHIRALPAK or CHIRALCEL columns.

8-3-1 General Procedures for the Synthesis of Diazo Compounds

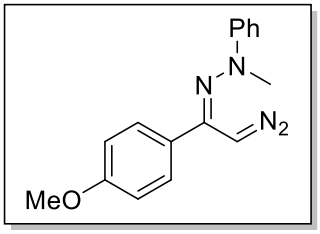
a) Synthesis of α-Diazo Hydrazones



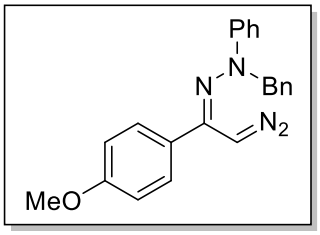
A three-necked flask was charged with 2.5 mL anhydrous ethanol, ketone (1 mmol, 1 equiv.) and hydrazine (1.25 mmol, 1.25 equiv.) and acetic acid (0.1 mmol, 10 mol%). The reaction mixture was then refluxed for 3 h. After removal of ethanol, the residue was dissolved in EA (5 mL), washed with a mixture of acetic acid (5 mL) and water (5 mL), and the organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give desired hydrazone, which was used for next step without further purification.

To a solution of hydrazone in dry THF (4 mL) was added NaH (9.5 mmol, 9.5 equiv.) at 0 ℃. The mixture was stirred for 15 min, and then MeI or BnBr (1.5 mmol, 1.5 equiv.) was added by dropwise. After stirring at RT for 3 h. The reaction mixture was cooled to the RT, and then the solvent was removed under reduced pressure. The residue was diluted with water (5 mL), extracted with ether (5mLx3) and dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash chromatography column on silica gel (Hex/EA = 20/1) to give the desired hydrazone.

The reaction condition was applied for Shatzmiller's procedure. To a solution of hydrazone (1 mmol) in dry THF (3 mL) was added a solution of BuLi (1.6 M in *n*-hexane, 1 mL, 1.6 mmol, 1.6 equiv.) during 20 min at −78 °C and the reaction mixture was stirred for another 1 hour. Then, a solution of methanesulfonyl azide (1.3 mmol, 1.3 equiv.) in THF (1 mL) was added slowly over 20 min and the mixture was allowed to stirr for another 1 hour. Water (3 mL) was then added to the cold reaction mixture. The organic material was extracted with ether (2x3 mL) and CH_2C1_2 (2x3 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvents removed in vacuo. The residue was purified by flash chromatography on silica gel using Hex/EA (20/1 ($^v/_v$)) to afford coressponding α-diazo hydrazones.

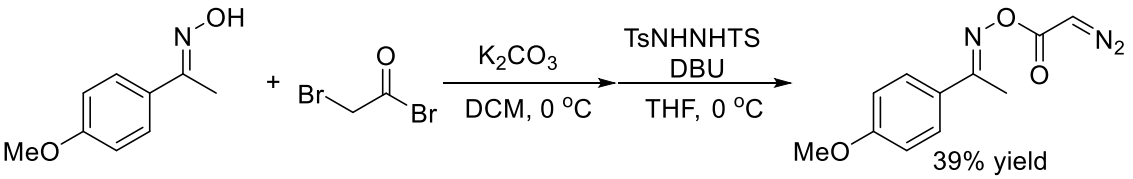


α-Diazo hydrazone **1a** was obtained according to the typical procedure in 10% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 1.91 Hz, 1H), 7.61 (d, *J* = 2.29 Hz, 1H), 7.25 (dd, *J* = 6.50, 2.68 Hz, 2H), 6.96 (dd, *J* = 6.69, 2.29 Hz, 2H), 6.93–6.80 (m, 3H), 5.54 (s, 1H), 3.84 (s, 3H), 3.10 (s, 3H) ppm.



α-Diazo hydrazone **1b** was obtained according to the typical procedure in 20% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 6.69, 1.91 Hz, 2H), 7.40 (d, *J* = 7.64 Hz, 2H), 7.32 (t, *J* = 7.64 Hz, 3H), 7.28–7.20 (m, 3H), 6.69 (d, *J* = 7.64 Hz, 2H), 6.94–6.85 (m, 3H), 5.43 (s, 1H), 4.71 (s, 2H), 3.83 (s, 3H) ppm.

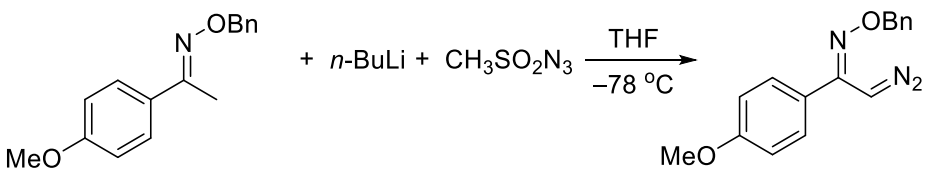
b) Synthesis of α-Diazo Oxime Ethers



To a solution of oxime (143.3 mg, 0.87 mmol, 1 equiv), K_2CO_3 (240.5 mg, 1.74 mmol, 2 equiv.) in DCM (2 mL) was added dropwise bromoacetyl bromide (1.04 mmol, 1.2 equiv.) at 0 °C. The reaction mixture was stirred for 30 min at RT. The organic product was then extracted with DCM, dried Na_2SO_4. After evaporation of the solvent, the residue was used for next step without purification.

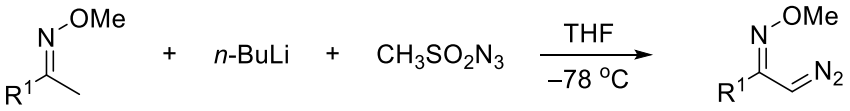
The resulting product (226 mg, 0.79 mmol) and TsNHNHTs (403.3 mg, 1.18 mmol, 1.5 equiv.) were dissolved in THF (2 mL) and cooled down to 0 °C, then DBU (0.23 mL, 1.58 mmol, 2 equiv.) was added dropwise and stirred at 0 °C for 1 h. After quenched with water and extracted with ether, the combined organic phase dried over Na_2SO_4 and evaporated to give the crude product. Purification was performed with column chromatography on silica gel eluted with Hex/EA=10/1 to give diazo compound **1c** as a yellow oil (67.0 mg. 39% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.79 Hz, 2H), 5.70–5.20 (bs, 1H), 3.83 (s, 3H), 2.34 (s, 3H) ppm.

c) Synthesis of α-Diazo Oxime Ethers



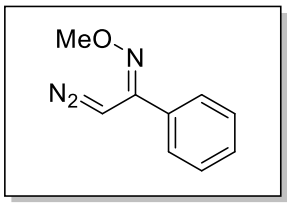
The reaction condition was applied for Shatzmiller's procedure. To a solution of oxime ether (490.0 mg, 1.92 mmol) in dry THF (6 mL) was added a solution of BuLi (1.6 M in *n*-hexane, 1.4 mL, 2.3 mmol) during 20 min at −78 °C and the reaction mixture was stirred for another 1 hour. Then, a solution of methanesulfonyl azide (302.8 mg, 2.5 mmol) in THF (1 mL) was added slowly over 20 min and the mixture was allowed to stirr for another 1 hour. Water (6 mL) was then added to the cold reaction mixture. The organic material was extracted with ether (2 x 6 mL) and CH_2C1_2 (2 x 6 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvents removed in vacuo. The residue was purified by flash chromatography on silica gel using EtOAc/*n*-Hexane (1/10 ($^v/_v$)) to afford coressponding α-diazo oxime ether **1e** in 32% yield as a yellow oil (172.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 6.69, 1.91 Hz, 2H), 7.40 (d, *J* = 7.64 Hz, 2H), 7.32 (t, *J* = 7.64 Hz, 3H), 7.28–7.20 (m, 3H), 6.69 (d, *J* = 7.64 Hz, 2H), 6.94–6.85 (m, 3H), 5.43 (s, 1H), 4.71 (s, 2H), 3.83 (s, 3H) ppm.

d) Synthesis of α-Diazo Oxime Ethers



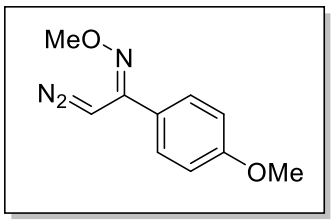
The reaction condition was applied for Shatzmiller's procedure. To a solution of oxime ether (5 mmol) in dry THF (15 mL) was added a solution of BuLi (1.6 M in *n*-hexane, 5 mL, 8 mmol) during 20 min at −78 °C and the reaction mixture was stirred for another 1 hour. Then, a solution of methanesulfonyl azide (787.4 mg, 6.5 mmol) in THF (5 mL) was added slowly over 20 min and the mixture was allowed to stirr for another 1 hour. Water (15 mL) was then added to the cold reaction mixture. The organic material was extracted with ether (2 x 15 mL) and CH_2C1_2 (2 x 15 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvents removed in vacuo. The residue was purified by flash chromatography on silica gel using EtOAc/*n*-Hexane (1/50 ($^v/_v$)) to afford coressponding α-diazo oxime ethers.

(*Z*)-2-Diazo-1-phenylethanone *O*-methyl oxime



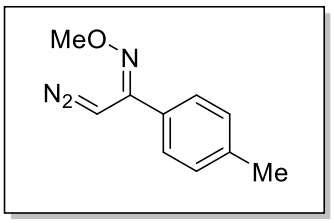
α-Diazo oxime ether **5-2a** was obtained according to the typical procedure in 65% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.46 (m, 2H), 7.40–7.38 (m, 3H), 5.37 (s, 1H), 3.97 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 132.7, 129.7, 128.7, 127.6, 62.0, 43.5 ppm. HRMS (DART) calcd for $[C_9H_9N_3O+H]^+$: 176.0824, found: 176.0823. The configuration of (*Z*)-Diazo *O*-methyl oxime **5-2a** was confirmed by ROSEY spectra.

(*Z*)-2-Diazo-1-(4-methoxyphenyl)ethanone *O*-methyl oxime



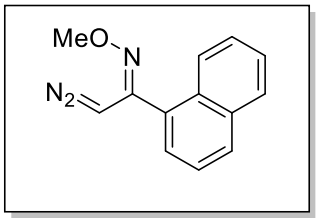
α-Diazo oxime ether **5-2m** was obtained according to the typical procedure in 45% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.79 Hz, 2H), 6.92 (d, *J* = 8.79 Hz, 2H), 5.38 (s, 1H), 3.96 (s, 3H), 3.82 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 147.7, 128.9, 124.9, 113.9, 61.9, 55.4, 43.5 ppm. HRMS (DART) calcd for $[C_{10}H_{11}N_3O_2+H]^+$: 206.0930, found: 206.0930.

(*Z*)-2-Diazo-1-(*p*-tolyl)ethanone *O*-methyl oxime



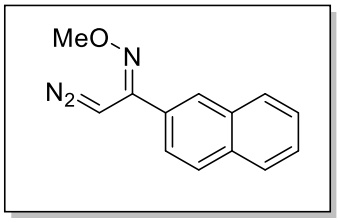
α-Diazo oxime ether **5-2n** was obtained according to the typical procedure in 50% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) 7.37 (d, *J* = 8.03 Hz, 2H), 7.20 (d, *J* = 8.03 Hz, 2H), 5.38 (s, 1H), 3.96 (s, 3H), 2.34 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 139.7, 129.7, 129.4, 127.5, 61.9, 43.5, 21.3 ppm. HRMS (DART) calcd for $[C_{10}H_{11}N_3O+H]^+$: 190.0980, found: 190.0980.

(*Z*)-2-Diazo-1-(naphthalen-1-yl)ethanone *O*-methyl oxime



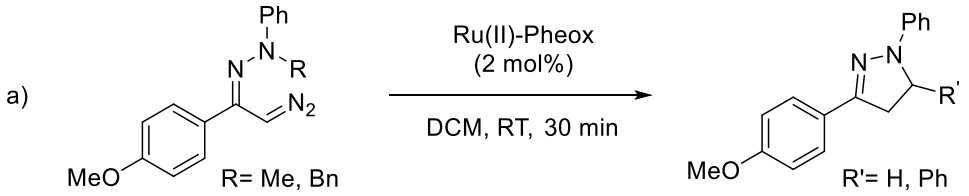
α-Diazo oxime ether **5-2o** was obtained according to the typical procedure in 72% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13–8.11 (m, 1H), 7.89–7.84 (m, 2H), 7.56-7.46 (m, 4H), 5.67 (s, 1H), 4.02 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 133.6, 131.4, 130.0, 129.5, 128.4, 127.4, 127.0, 126.2, 125.1, 124.6, 62.0, 45.8 ppm. HRMS (DART) calcd for $[C_{13}H_{11}N_3O+H]^+$: 226.0980, found: 226.0981.

(*Z*)-2-Diazo-1-(naphthalen-2-yl)ethanone *O*-methyl oxime

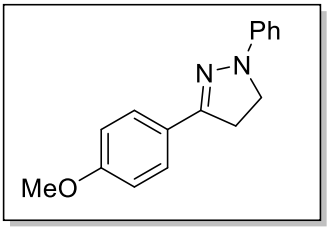


α-Diazo oxime ether **5-2p** was obtained according to the typical procedure in 43% yield as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.87–7.82 (m, 3H), 7.62–7.60 (m, 1H), 7.52-7.48 (m, 2H), 5.46 (s, 1H), 4.02 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.0, 133.7, 133.0, 130.1, 128.5, 128.4, 127.7, 127.2, 126.8, 126.5, 124.7, 62.1, 43.7 ppm. HRMS (DART) calcd for $[C_{13}H_{11}N_3O+H]^+$: 226.0980, found: 226.0980.

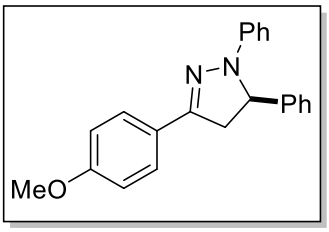
8-3-2 General Procedure for Catalytic Asymmetric C−H Insertion Reaction of α-Diazo Hydrazone and α-Diazo Oxime Ethers



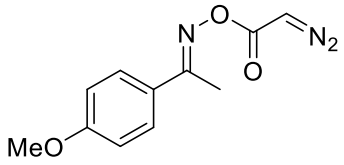
To a solution of Ru(II)-Pheox catalyst (2 mol%) in CH_2Cl_2 (1 mL) was slowly added a solution of *α*-diazo hydrazone **1** (0.1 mmol) in CH_2Cl_2 (2 mL) under an argon atmosphere at room temperature. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel (eluted with EtOAc/*n*-Hexane) to give the desired product **2**.



2a was prepared according to the typical procedure for asymmetric C−H insertion reaction of *α*-diazo hydrazone **1a** (22.0 mg, 0.078 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/10 ($^{v}/_{v}$)) as an eluent to give the desired product in 80% yield (15.8 mg) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 9.16 Hz, 2H), 7.28 (dd, *J* = 15.41, 6.41 Hz, 2H), 712 (d, *J* = 7.63 Hz, 2H), 6.91 (d, *J* = 6.71 Hz, 2H), 6.83 (t, *J* = 7.2 Hz, 1H), 3.85 (dd, *J* = 10.38, 3.66 Hz, 2H), 3.84 (s, 3H), 3.23 (t, *J* = 10.07 Hz, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 149.0, 146.1, 129.0, 127.1, 125.7, 118.8, 113.9, 112.8, 55.3, 48.2, 32.1 ppm.



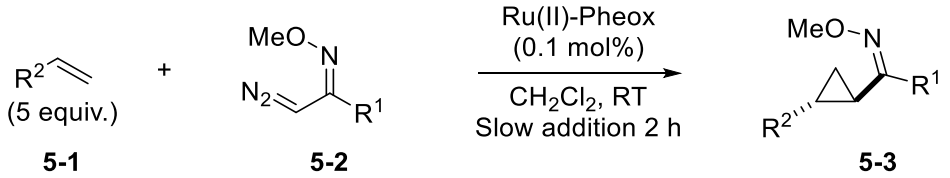
2b was prepared according to the typical procedure for asymmetric C−H insertion reaction of *α*-diazo hydrazone **1b** (21.4 mg, 0.06 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/10 ($^{v}/_{v}$)) as an eluent to give the desired product in 72% yield (14.1 mg) as a white solid. 2% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IC-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 15/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 5.78, tR (minor) = 6.88. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.79 Hz, 2H), 7.33 (d, *J* = 4.20 Hz, 4H), 725 (d, *J* = 7.63 Hz, 2H), 7.16 (t, *J* = 7.69 Hz, 2H), 7.05 (d, *J* = 8.79 Hz, 2H), 6.91 (d, *J* = 8.79 Hz, 2H), 5.22 (dd, *J* = 12.23, 7.260 Hz, 1H), 3.83 (s, 3H), 3.90-3.70 (m, 1H), 3.11 (dd, *J* = 17.01, 7.64 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.0, 146.7, 145.1, 142.7, 129.0, 128.8, 127.4, 127.1, 125.8, 125.4, 118.7, 113.9, 113.2, 64.4, 55.3, 43.7 ppm.

b) 

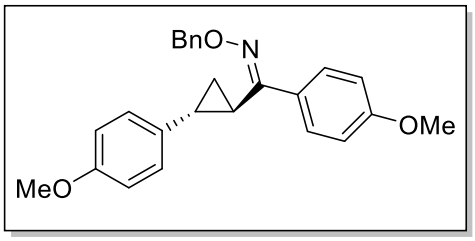
Ru(II)-Pheox (2 mol%)
DCM, RT, 30 min
Dimerization

To a solution of Ru(II)-Pheox catalyst (1.3 mg, 0.002 mmol, 2 mol%) in CH_2Cl_2 (1 mL) was slowly added a solution of *α*-diazo oxime ether **1c** (21.9 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) under an argon atmosphere at room temperature. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel (eluted with EtOAc/*n*-Hexane) to give the dimer product **2c** as a white solid (17.6 mg, 86% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.43 (dd, J = 6.88, 2.29 Hz, 2H), 6.89 (dd, J = 6.88, 1.92 Hz, 2H), 3.81 (s, 3H), 1.89 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 159.9, 151.1, 130.5, 130.3, 126.6, 113.9, 113.6, 109.5, 55.3, 28.3 ppm.

8-3-3 General Procedure for Catalytic Asymmetric Cyclopropanation of α-Diazo Oxime Ethers with Olefins



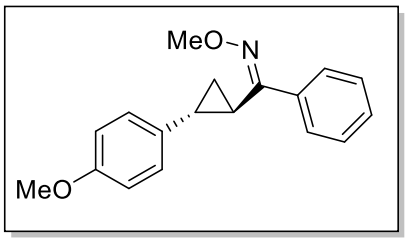
To a solution of Ru(II)-Pheox catalyst (0.0002 mmol) and olefin **5-1** (1.0 mmol) in CH_2Cl_2 (2 mL) was slowly added a solution of *α*-diazo oxime ether **5-2** (0.2 mmol) in CH_2Cl_2 (2 mL) over 2 hours under an argon atmosphere at room temperature. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel (eluted with EtOAc/*n*-Hexane) to give the desired product **5-3**. The *trans/cis* ratio was determined from the crude ^{1}H NMR spectra and the enantiomeric excess of the product was determined by chiral HPLC analysis.



Cyclopropyl oxime ether **2f** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **1e** (28.1 mg, 0.1 mmol) and 4-methoxystyrene (67.1 mg, 0.5 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/20 ($^v/_v$)) as an eluent to give the desired product in 69% yield (26.6 mg) as a white solid. The *trans/cis* ratio = 85:15. *trans*: 51% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-H), UV detector 254 nm, eluent: *n*-Hexane/IPA = 150/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 55.32 min (*trans*), tR (minor) = 85.03 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 6.7, 2.1 Hz, 2H), 7.38 (d, *J* = 6.5 Hz, 2H), 7.36-7.28 (3H), 7.07 (d, *J* = 8.8 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 5.22 (s, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 2.36 (dt, *J* = 8.79, 5.35 Hz, 1H), 2.14 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.35 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 1.27 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 159.1, 157.9, 138.1, 133.4, 129.4, 129.2, 129.0, 128.2, 128.1, 128.0, 127.5, 127.5, 127.0, 113.7, 113.5, 113.2, 113.0, 76.0, 55.2, 23.0, 20.8, 15.0 ppm.

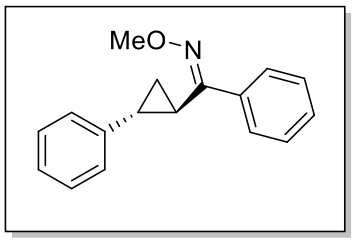
]

(*E*)-(2-(4-Methoxyphenyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



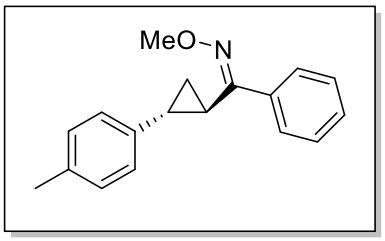
Cyclopropyl oxime ether **5-3a** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 4-methoxystyrene **5-1a** (134.2 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 91% yield (99% yield of product was observed when 3 mol% catalyst was used) as a colorless oil. The *trans/cis* ratio = 80:20. $[\alpha]_D^{23.1}$ = –98.2 (c 1.10, $CHCl_3$), *trans*: 93% ee, *cis*: 86% ee. The ee was determined by chiral HPLC analysis. Column (Chiral OD-H), UV detector 254 nm, eluent: *n*-Hexane/IPA = 800/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 20.8 and 24.8 min (*trans*), tR (minor) = 29.2 and 36.4 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.43 (m, 2H), 7.38–7.35 (m, 3H), 7.10 (d, *J* = 8.41 Hz, 2H), 6.84 (d, *J* = 8.79 Hz, 2H), 3.98 (s, 3H), 3.79 (s, 3H), 2.38 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H), 2.09 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.31 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 1.22 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 158.0, 134.4, 133.2, 129.2, 128.7, 128.2 127.4, 113.8, 62.0, 55.3, 22.8, 20.6 15.0 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO_2+H]^+$: 282.1494, found: 282.1495.

(*E*)-(2-Phenylcyclopropyl)(phenyl)methanone *O*-methyl oxime



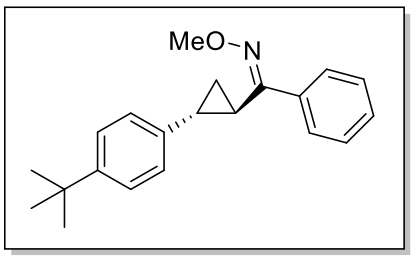
Cyclopropyloxime ether **5-3b** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and styrene **5-1b** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 84% yield as a colorless oil. The *trans/cis* ratio = 81:19. $[\alpha]_D^{22.5}$ = –106.3 (c 1.10, $CHCl_3$), *trans*: 92% ee, *cis*: 78% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-H), UV detector 254 nm, eluent: *n*-Hexane/IPA = 100/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 5.4 and 7.1 (*trans*), tR (minor) = 5.9 and 6.5 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.45 (m, 2H), 7.38–7.36 (m, 3H), 7.31–7.28 (m, 2H), 7.18–7.14 (m, 3H), 3.98 (s, 3H), 2.46 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H), 2.13 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.48 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H), 1.27 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 141.3, 134.3, 128.8, 128.2, 128.0, 127.9, 127.6, 126.2, 62.0, 23.6, 21.0, 15.4 ppm. HRMS (DART) calcd for $[C_{17}H_{17}NO+H]^+$: 252.1388, found: 252.1389.

(*E*)-(2-(*p*-Tolyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime (3c)



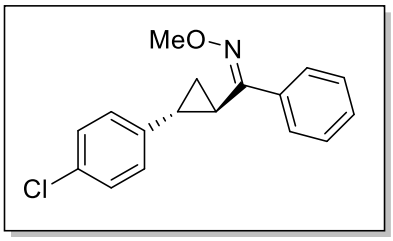
Cyclopropyloxime ether **5-3c** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 4-methylstyrene **5-1c** (118.2 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 82% yield as a colorless oil. The *trans/cis* ratio = 79:21. $[\alpha]_D^{25.5}$ = –119.8 (c 1.20, $CHCl_3$), *trans*: 94% ee, *cis*: 76% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-H), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 8.2 and 12.2 (*trans*), tR (minor) = 6.0 and 6.4 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.37–7.35 (m, 3H), 7.10 (d, *J* = 8.41 Hz, 2H), 7.05 (d, *J* = 8.03 Hz, 2H), 3.97 (s, 3H), 2.42 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H), 2.32 (s, 3H), 2.10 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.34 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 1.24 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 138.2, 135.6, 134.4, 129.1, 128.7, 128.3, 128.2, 126.1, 62.0, 23.2, 21.0, 20.9 15.2 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO+H]^+$: 266.1545, found: 266.1544.

(*E*)-(2-(4-(*tert*-Butyl)phenyl)cyclopropyl)(phenyl)methanone O-methyl oxime



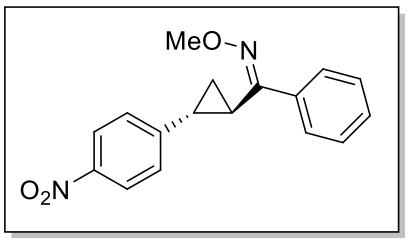
Cyclopropyloxime ether **5-3d** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 4-*tert*-butylstyrene **5-1d** (160.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 88% yield as a colorless oil. The *trans/cis* ratio = 85:15. $[\alpha]_D^{25.6}$ = –134.382 (c 1.00, $CHCl_3$), *trans*: 92% ee, *cis*: 84% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 150/1 ($^{v}/_{v}$), Flow late = 0.7 mL/min, tR (major) = 8.7 and 12.4 min (*trans*), tR (minor) = 9.3 and 9.9 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.38–7.36 (m, 3H), 7.32 (d, *J* = 8.60 Hz, 2H), 7.10 (d, *J* = 8.03 Hz, 2H), 3.97 (s, 3H), 2.46 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H), 2.11 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.35 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 1.28 (s, 9H), 1.24 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 149.0, 138.2, 134.4, 128.7, 128.3, 128.2, 125.9, 125.3, 62.0, 31.4, 23.1, 20.8, 15.3 ppm. HRMS (DART) calcd for $[C_{21}H_{25}NO+H]^+$: 308.2014, found: 308.2013.

(*E*)-(2-(4-Chlorophenyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



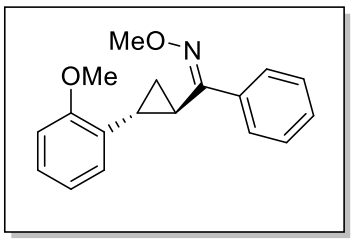
Cyclopropyloxime ether **5-3e** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 4-chlorostyrene **5-1e** (138.0 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 77% yield as a colorless oil. The *trans/cis* ratio = 80:20. $[\alpha]_D^{23.2}$ = –112.9 (c 1.10, $CHCl_3$), *trans*: 96% ee, *cis*: 99% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-H), UV detector 254 nm, eluent: *n*-Hexane/IPA = 300/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 9.4 and 20.9 min (*trans*), tR (minor) = 7.3 and 7.8 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.37–7.36 (m, 3H), 7.25 (d, *J* = 8.54 Hz, 2H), 7.09 (d, *J* = 8.54 Hz, 2H), 3.98 (s, 3H), 2.38 (ddd, *J* = 8.85, 6.10, 5.04 Hz, 1H), 2.09 (dt, *J* = 8.85, 5.49 Hz, 1H), 1.34 (dt, *J* = 8.85, 5.49 Hz, 1H), 1.28 (ddd, *J* = 8.85, 6.10, 5.04 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 139.8, 134.2, 131.7, 128.8, 128.5, 128.2, 128.1, 127.6, 62.0, 23.0, 21.1, 15.3 ppm. HRMS (DART) calcd for $[C_{17}H_{16}ClNO+H]^+$: 286.0999, found: 286.0998.

(*E*)-(2-(4-Nitrophenyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



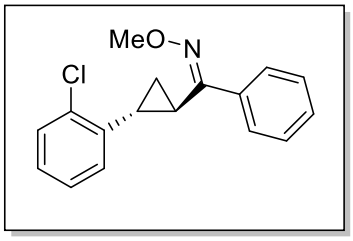
Cyclopropyloxime ether **5-3f** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 4-nitrostyrene **5-1f** (149.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 70% yield as a pale yellow solid. The *trans/cis* ratio = 75:25. $[\alpha]_D^{25}$ = –144.6 (c 1.05, $CHCl_3$), *trans*: 95% ee, *cis*: 70% ee. *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.79 Hz, 2H), 7.48–7.44 (m, 2H), 7.40–7.38 (m, 3H), 7.28 (d, *J* = 8.41 Hz, 2H), 3.98 (s, 3H), 2.47 (ddd, *J* = 8.98, 6.50, 4.97 Hz, 1H), 2.21 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.48 (dt, *J* = 8.98, 5.35 Hz, 1H), 1.42 (ddd, *J* = 8.98, 6.50, 4.97 Hz, 1H) ppm. ^{13}C NMR (10 The ee was determined by chiral HPLC analysis. Column (Chiral ID-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 22.3 and 39.2 min (*trans*), tR (minor) = 13.9 and 16.5 min (*cis*).0 MHz, $CDCl_3$) δ 157.6, 149.7, 146.3, 134.0, 129.0, 128.4, 128.0, 126.7, 123.7, 62.2, 23.7, 22.4, 16.3 ppm. HRMS (DART) calcd for $[C_{17}H_{16}N_2O_3+H]^+$: 297.1239, found: 297.1239.

(*E*)-(2-(2-Methoxyphenyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



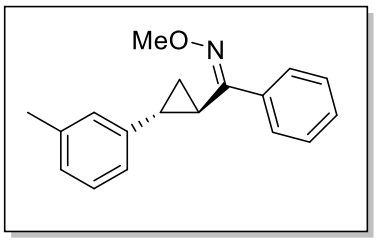
Cyclopropyloxime ether **5-3g** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 2-methoxystyrene **5-1g** (134.2 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 85% yield as a white solid. The *trans/cis* ratio = 68:32. $[\alpha]_D^{23.6}$ = –99.1 (c 1.00, CHCl3), *trans*: 90% ee, *cis*: 66% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IF-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 0.7 mL/min, tR (major) = 17,2 and 18.6 min (*trans*), tR (minor) = 20.9 and 24.6 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.47 (m, 2H), 7.01 (dd, *J* = 7.64, 1.53 Hz, 1H), 6.91 (td, *J* = 7.64, 1.15 Hz, 1H), 6.85 (dd, *J* = 8.13, 1.15 Hz, 1H), 3.96 (s, 3H), 3.84 (s, 3H), 2.51 (dt, *J* = 9.17, 6.12 Hz, 1H), 2.42 (dt, *J* = 9.17, 6.12 Hz, 1H), 1.34 (ddd, *J* = 9.17, 6.31, 4.97 Hz, 1H), 1.18 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 158.3, 134.2, 128.7, 128.6, 128.1, 127.7, 127.1, 125.8, 120.5, 110.1, 61.9, 55.4, 19.6, 18.1, 13.9 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO_2+H]^+$: 282.1494, found: 282.1494.

(*E*)-(2-(2-Chlorophenyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



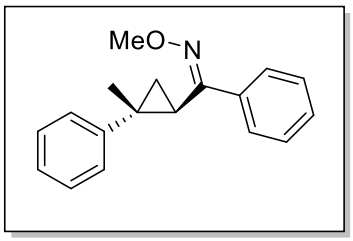
Cyclopropyloxime ether **5-3h** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 2-chlorostyrene **5-1h** (138.0 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 82% yield as a colorless oil. The *trans/cis* ratio = 65:35. $[\alpha]_D^{24.3}$ = –72.6 (c 1.10, $CHCl_3$), *trans*: 93% ee, *cis*: 73% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 6.5 and 10.2 min (*trans*), tR (minor) = 7.3 and 8.3 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47–7.45 (m, 2H), 7.39–7.37 (m, 3H), 7.21–7.20 (m, 3H), 7.15 (td, *J* = 7.64, 1.91 Hz, 1H), 6.85 (dd, *J* = 7.64, 1.53 Hz, 1H), 3.98 (s, 3H), 2.55 (ddd, *J* = 8.79, 6.12, 5.35 Hz, 1H), 2.43 (dt, *J* = 8.79, 6.12 Hz, 1H),1.34 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H), 1.29 (ddd, *J* = 8.79, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 138.5, 135.3, 133.8, 129.2, 128.5, 128.2, 127.9, 127.6, 127.3, 126.8, 62.0, 21.2, 20.0, 14.2 ppm. HRMS (DART) calcd for $[C_{17}H_{16}ClNO+H]^+$: 286.0999, found: 286.0999.

(*E*)-(2-(*m*-Tolyl)cyclopropyl)(phenyl)methanone *O*-methyl oxime



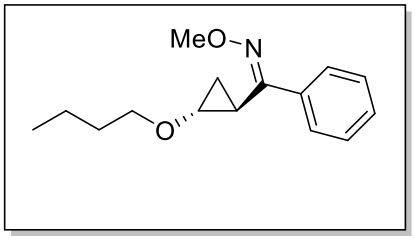
Cyclopropyloxime ether **5-3i** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and 3-methylstyrene **5-1i** (118.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 81% yield as a colorless oil. The *trans/cis* ratio = 79:21. $[\alpha]_D^{26.5}$ = –104.1 (c 1.05, $CHCl_3$), *trans*: 90% ee, *cis*: 71% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 100/0.6 ($^{v}/_{v}$), Flow late = 0.5 mL/min, tR (major) = 13.0 and 15.0 min (*trans*), tR (minor) = 14.5 and 15.8 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.38–7.36 (m, 3H), 7.18 (t, *J* = 7.26 Hz, 1H), 7.01 (d, *J* = 7.26 Hz, 1H), 6.96 (s, 1H), 6.95 (d, *J* = 7.64, 1.53 Hz, 1H), 3.98 (s, 3H), 2.45 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 2.33 (s, 3H), 2.10 (dt, *J* = 9.17, 5.35 Hz, 1H), 1.36 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 1.25 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 141.2, 138.0, 134.3, 128.7, 128.3, 128.2, 128.1, 126.9, 126.8, 123.2, 62.0, 23.4, 21.4, 21.0, 15.4 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO+H]^+$: 266.1545, found: 266.1545.

(*E*)-(2-Methyl-2-phenylcyclopropyl)(phenyl)methanone *O*-methyl oxime



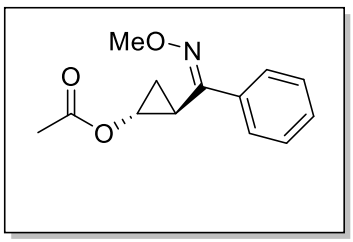
Cyclopropyloxime ether **5-3j** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and *α*-methylstyrene **5-1j** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 92% yield as a colorless oil. The *trans/cis* ratio = 75:25. $[\alpha]_D^{24.6}$ = +17.3 (c 1.11, $CHCl_3$), *trans*: 92% ee, *cis*: 93% ee. The ee was determined by chiral HPLC analysis. Column (Chiral OJ-H), UV detector 280 nm, eluent: *n*-Hexane/IPA = 50/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 8.7 and 24.7 min (*trans*), tR (minor) = 5.1 and 5.9 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 6.5, 1.91 Hz, 2H), 7.47 (dd, *J* = 8.41, 1.15 Hz, 2H), 7.36 (d, *J* = 7.26 Hz, 2H), 7.32 (t, *J* = 7.26 Hz, 2H), 7.22 (tt, *J* = 7.26, 1.15 Hz, 1H), 7.15 (tt, *J* = 6.50, 1.15 Hz, 1H), 4.07 (s, 3H), 2.26 (dd, *J* = 8.79, 6.88 Hz, 1H), 1.55 (s, 1H), 1.51 (dd, *J* = 8.41, 4.97 Hz, 1H), 1.19 (s, 3H), 0.89 (d, *J* = 6.88, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 147.0, 136.2, 128.7, 128.2, 128.1, 127.9, 127.5, 126.1, 62.1 27.7, 24.6, 22.5, 20.7 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO+H]^+$: 266.1545, found: 266.1545.

(*E*)-(2-Butoxycyclopropyl)(phenyl)methanone *O*-methyl oxime



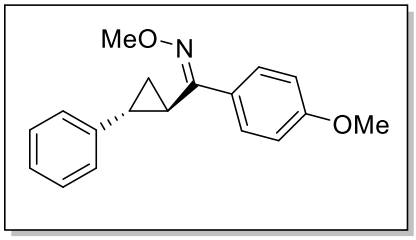
Cyclopropyloxime ether **5-3k** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and *n*-butyl vinyl ether **5-1k** (100.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 83% yield as a colorless oil. The *trans/cis* ratio = 84:16. $[\alpha]_D^{23.3}$ = +19.1 (c 0.725, $CHCl_3$), *trans*: 74% ee, *cis*: 57% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IC-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 800/1 ($^{v}/_{v}$), Flow late = 0.8 mL/min, tR (major) = 16.6 and 24.4 min (*trans*), tR (minor) = 13.0 and 15.1 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42–7.40 (m, 2H), 7.34–7.33 (m, 3H), 4.07 (s, 3H), 3.63 (dt, *J* = 9.74, 6.87 Hz, 1H), 3.55 (dt, *J* = 9.74, 6.87 Hz, 1H), 3.43 (dt, *J* = 6.30, 2.86 Hz, 1H), 2.25 (ddd, *J* = 10.03, 6.87, 2.86 Hz, 1H), 1.59–1.53 (m, 2H), 1.41–1.33 (m, 2H), 1.27–1.23 (m, 2H), 0.93 (t, *J* = 7.16 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 134.7, 128.7, 128.2, 127.9, 70.5, 61.9, 58.9, 31.6, 19.3, 18.4, 14.3, 13.8 ppm. HRMS (DART) calcd for $[C_{15}H_{21}NO_2+H]^+$: 248.1651, found: 248.1650.

(*E*)-(2-Acetylcyclopropyl)(phenyl)methanone *O*-methyl oxime



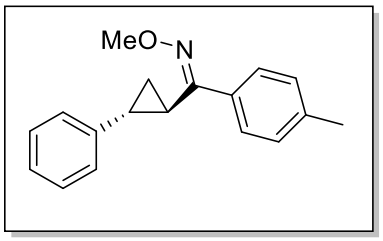
Cyclopropyloxime ether **5-3l** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2a** (35.0 mg, 0.2 mmol) and vinyl acetate **5-1l** (100.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 35% yield (64% yield of product was observed when 3 mol% catalyst was used) as a colorless oil. The *trans/cis* ratio = 58:42. $[\alpha]_D^{22.1}$ = +27.1 (c 1.35, $CHCl_3$, *trans* product), $[\alpha]_D^{22.3}$ = –37.1 (c 1.00, $CHCl_3$, *cis* product), *trans*: 77% ee, *cis*: 60% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 8.7 and 11.3 min (*trans*); Column (Chiral AD-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 17.5 and 19.9 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.49 (m, 2H), 7.38–7.34 (m, 3H), 4.59 (ddd, *J* = 6.88, 3.82, 6.88 Hz, 1H), 4.00 (s, 3H), 2.27 (ddd, *J* = 9.56, 7.64, 6.88 Hz, 1H), 1.82 (s, 3H), 1.36 (dt, *J* = 9.56, 6.88 Hz, 1H), 1.01 (ddd, *J* = 8.03, 3.82, 6.88 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 154.8, 135.6, 128.7, 128.2, 127.7, 61.2, 51.9, 20.6, 15.6, 11.9 ppm. HRMS (DART) calcd for $[C_{13}H_{15}NO_3+H]^+$: 234.1130, found: 234.1131.

(*E*)-(2-Phenylcyclopropyl)(4-methoxyphenyl)methanone *O*-methyl oxime



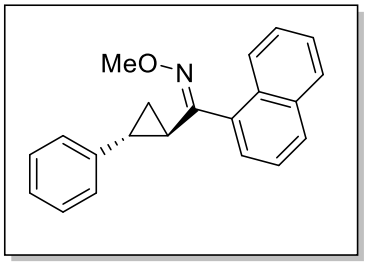
Cyclopropyloxime ether **5-3m** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2m** (41.0 mg, 0.2 mmol) and styrene **5-1b** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 85% yield as a colorless oil. The *trans/cis* ratio = 81:19. $[\alpha]_D^{27.2}$ = –111.6 (c 1.01, $CHCl_3$), *trans*: 93% ee, *cis*: –79% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 150/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 8.1 and 10.2 min (*trans*), tR (minor) = 11.4 and 12.6 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 9.56 Hz, 2H), 7.30–7.27 (m, 2H), 7.20 (t, *J* = 7.26 Hz, 1H), 7.16 (dd, *J* = 7.26, 1.15 Hz, 2H), 6.89 (d, *J* = 9.56 Hz, 2H), 3.96 (s, 3H), 3.81 (s, 3H), 2.12 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.37 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H), 1.27 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.6, 141.4, 129.5, 128.4 127.5, 126.2, 126.0, 113.6, 61.9, 55.3, 23.5, 18.4 15.4 ppm. HRMS (DART) calcd for $[C_{13}H_{15}NO_3+H]^+$: 234.1130, found: 234.1131.

(*E*)-(2-Phenylcyclopropyl)(p-tolyl)methanone *O*-methyl oxime



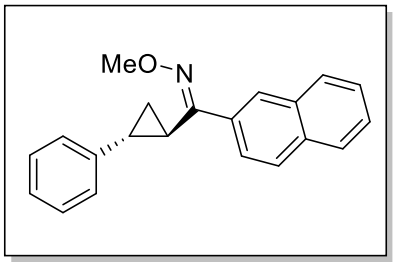
Cyclopropyloxime ether **5-3n** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2n** (37.8 mg, 0.2 mmol) and styrene **5-1b** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 86% yield as a colorless oil. The *trans/cis* ratio = 81:19. $[\alpha]_D^{23}$ = –109.3 (c 0.93, $CHCl_3$), *trans*: 92% ee, *cis*: –78% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 1.0 mL/min, tR (major) = 14.8 and 23.2 min (*trans*), tR (minor) = 16.0 and 21.4 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.03 Hz, 2H), 7.29 (t, *J* = 7.26 Hz, 2H), 7.21–7.14 (m, 5H), 3.96 (s, 3H), 2.44 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H), 2.36 (s, 3H), 2.12 (dt, *J* = 9.17, 5.35 Hz, 1H), 1.37 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H), 1.27 (ddd, *J* = 9.17, 6.12, 4.97 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 141.4, 138.7, 131.4, 128.9, 128.4, 128.1, 126.2, 126.0, 61.9, 23.5, 21.3, 21.1, 15.4 ppm. HRMS (DART) calcd for $[C_{18}H_{19}NO+H]^+$: 266.1545, found: 266.1545.

(*E*)-(2-Phenylcyclopropyl)(naphthalen-1-yl)methanone *O*-methyl oxime



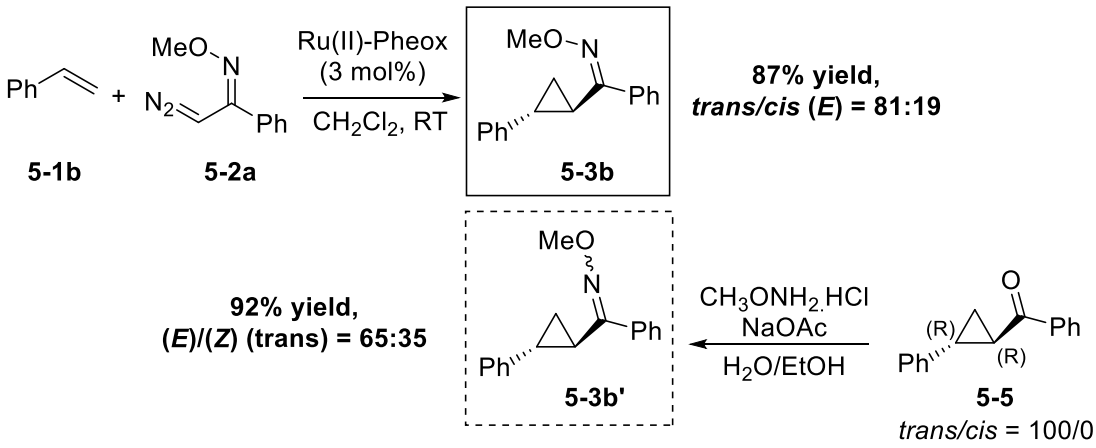
Cyclopropyloxime ether **5-3o** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2o** (45.0 mg, 0.2 mmol) and styrene **5-1b** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 84% yield as a colorless oil. The *trans/cis* ratio = 95:5. $[\alpha]_D^{22.6}$ = –162.1 (c 1.00, $CHCl_3$), *trans*: 93% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 0.8 mL/min, tR (major) = 8.6 and 9.2 min (*trans*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.03 Hz, 1H), 7.87 (t, *J* = 8.41 Hz, 2H), 7.55–7.46 (m, 3H), 7.35 (dd, *J* = 6.88, 1.20 Hz, 1H), 7.26 (t, *J* = 7.45 Hz, 2H), 7.18 (t, *J* = 7.45 Hz, 1H), 7.05 (d, *J* = 7.26 Hz, 2H), 4.00 (s, 3H), 2.98 (ddd, *J* = 8.79, 5.73, 4.97 Hz, 1H), 1.87 (dt, *J* = 8.79, 5.73 Hz, 1H), 1.34 (ddd, *J* = 8.79, 5.73, 4.97 Hz, 1H), 0.99 (dt, *J* = 8.79, 5.73 Hz, 1H), ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 140.9, 133.5, 132.4, 130.3, 129.3, 128.4, 128.2, 127.5, 126.6, 126.2, 126.1, 125.5, 124.9, 61.9, 24.1, 22.3, 15.4 ppm. HRMS (DART) calcd for $[C_{21}H_{19}NO+H]^+$: 302.1545, found: 302.1545.

(*E*)-(2-Phenylcyclopropyl)(naphthalen-2-yl)methanone *O*-methyl oxime



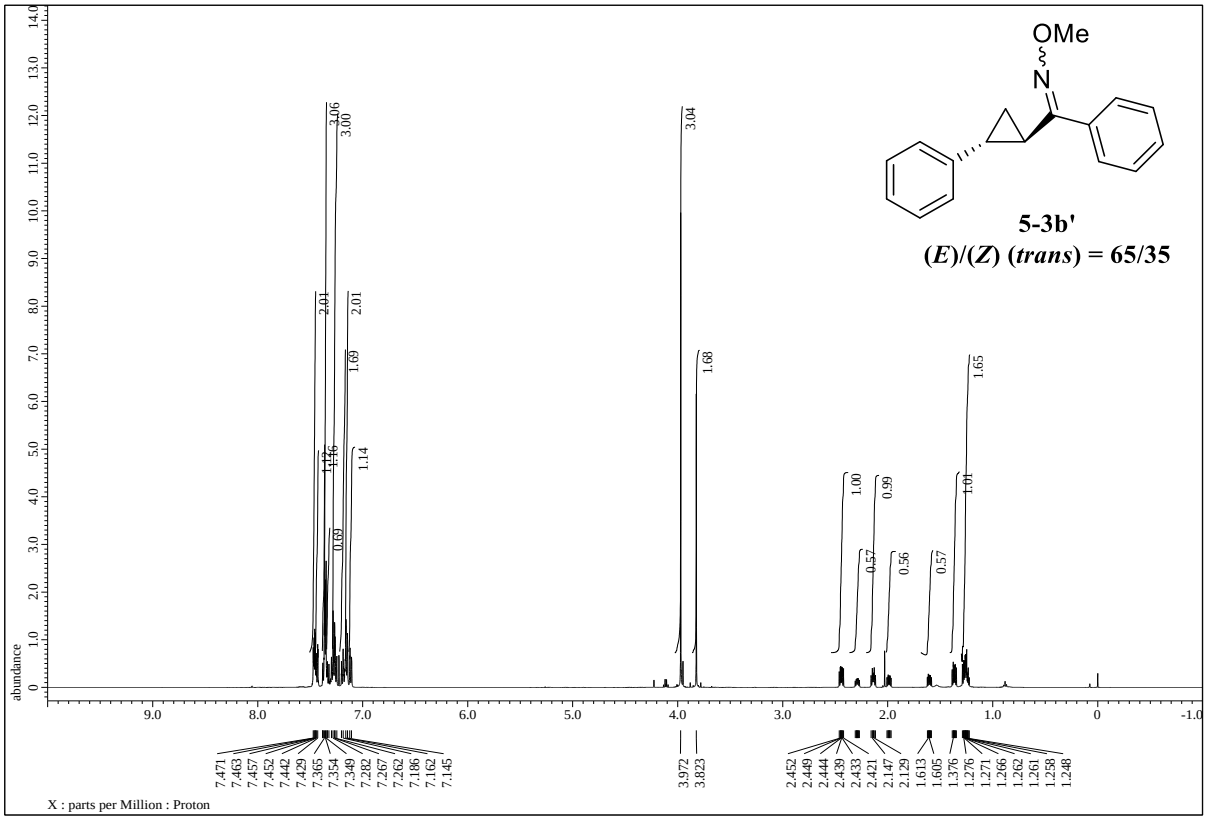
Cyclopropyloxime ether **5-3p** was prepared according to the typical procedure for asymmetric cyclopropanation reaction of *α*-diazo oxime ether **5-2p** (45.0 mg, 0.2 mmol) and styrene **5-1b** (104.1 mg, 1.0 mmol). The crude mixture was purified by silica gel column chromatography with EtOAc/*n*-Hexane (1/50 ($^{v}/_{v}$)) as an eluent to give the desired product in 92% yield as a colorless oil. The *trans/cis* ratio = 85:15. $[\alpha]_D^{25.4}$ = –127.0 (c 1.04, $CHCl_3$), *trans*: 98% ee, *cis*: –71% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^{v}/_{v}$), Flow late = 0.8 mL/min, tR (major) = 14.5 and 19.6 min (*trans*), tR (minor) = 12.4 and 13.2 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.85–7.82 (m, 3H), 7.64 (dd, *J* = 8.41, 1.91 Hz, 1H), 7.50–7.48 (m, 2H), 7.31 (t, *J* = 7.64 Hz, 2H), 7.22 (t, *J* = 7.84 Hz, 1H), 7.18 (dd, *J* = 8.41, 1.53 Hz, 2H), 4.02 (s, 3H), 2.47 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H), 2.17 (dt, *J* = 9.17, 5.73 Hz, 1H), 1.45 (ddd, *J* = 9.17, 6.12, 5.35 Hz, 1H), 1.33 (ddd, *J* = 8.79, 6.12, 5.35 Hz, 1H), ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 141.5, 133.4, 133.1, 132.0, 128.6, 128.5, 128.0, 127.9, 127.8, 126.7, 126.5, 126.3, 126.2, 125.6, 62.3, 23.9, 21.4, 15.7 ppm. HRMS (DART) calcd for $[C_{21}H_{19}NO+H]^+$: 302.1545, found: 302.1546.

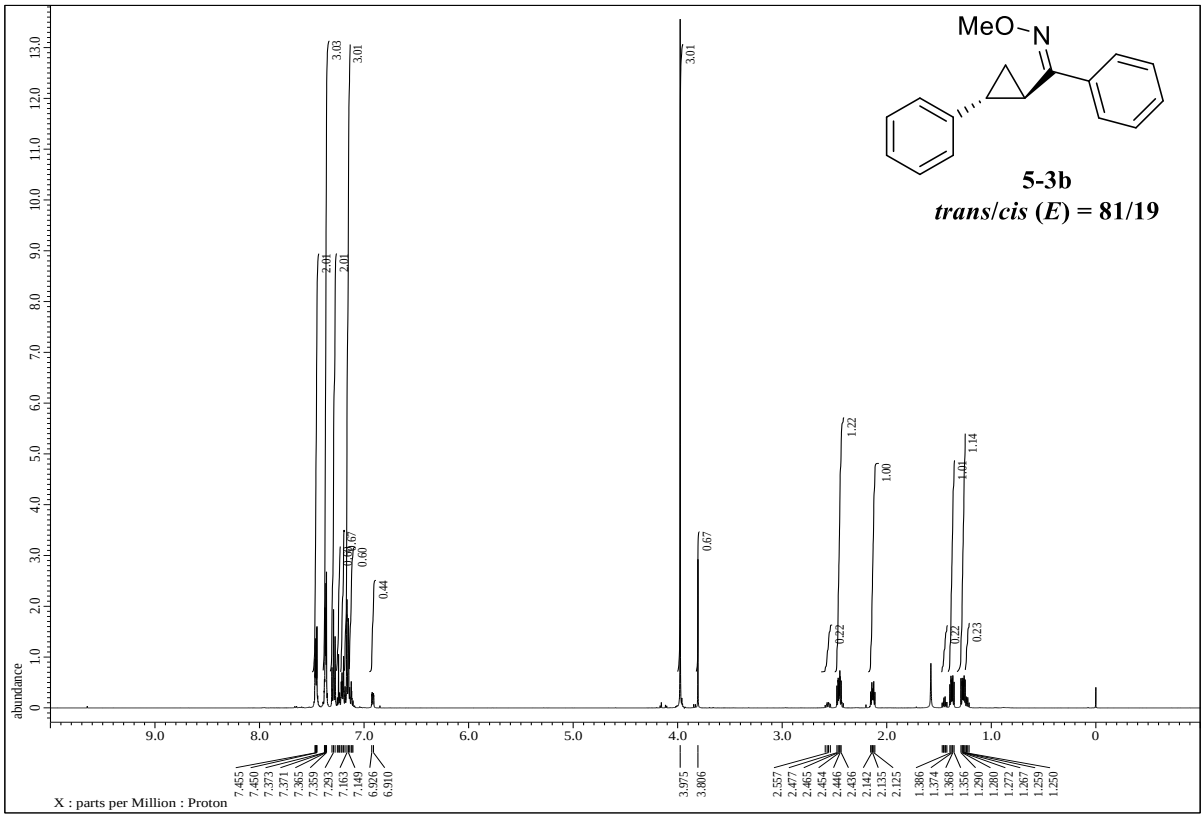
8-3-4 Determination of Diastereomers of Cyclopropyl Oxime Product by Synthetic Transformation



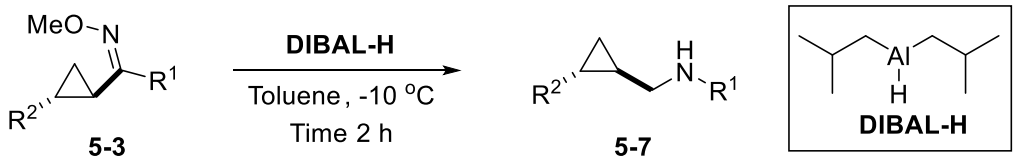
The mixture **5-3b** incuding *trans* and *cis* isomers was prepared as the general procedure in section 8-3-2. Besides, the product mixrure **5-3b'** was achieved from the transformation reaction of corresponding cyclopropyl ketone (**5-5**, *trans* isomer only). The reaction conditions are described below in detail. To a 20 mL round bottom flask equipped with a stir bar was combined *trans* isomer of cyclopropyl ketone **5-5** (1 mmol, 1 equiv.), $MeONH_2 \cdot HCl$ (0.250 g, 3 mmol, 3 equiv.), NaOAc (0.369 g, 4.5 mmol, 4.5 equiv.), H_2O (4.5 mL), and EtOH (1.5 mL). The flask was equipped with a reflux condenser and heated at 70 °C for 2 hours. After cooling to room temperature, the mixture was extracted with EtOAc (3 x 25 mL). The organic layers were combined, dried with Na_2SO_4, and concentrated to yield the crude product. The crude product was purified by column chromatography on silica gel using EtOAc/*n*-Hexane (1/10 ($^{v}/_{v}$)) to give product mixrure **5-3b'** in 92% yield as a colorless oil. The (***E***)/(***Z***) ratio = 65:35**.**

By comparing ^{1}H NMR of product **5-3b** and **5-3b'**, we could determine identified structures of *trans* and *cis* isomers in product **5-3b** and diasteroselectivity as well.

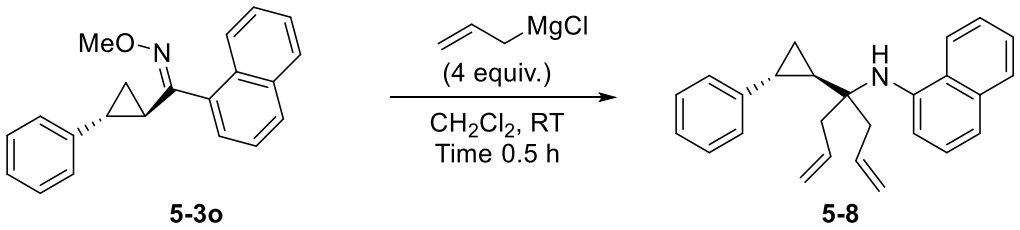

OMe
N
5-3b'
(E)/(Z) (trans) = 65/35
abundance
X : parts per Million : Proton


MeO
N
5-3b
trans/cis (E) = 81/19
abundance
X : parts per Million : Proton

8-3-5 DIBALH Mediated and Grignard Mediated Reductive Beckmann Rearrangement of Cyclopropyl Oxime Ethers

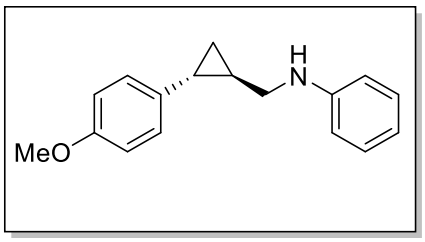


To a solution of cyclopropyl oxime ether **5-3** (0.15 mmol) in dry toluene (4 mL) was added dropwise a solution of DIBALH (1.0 M in toluene, 0.6 mL, 0.6 mmol) at −10 °C and the reaction mixture was stirred for 2 hours. After that, 10% aq. HCl was added slowly until a precipitate was formed, followed by 10% aq. NaOH until the solution was alkaline. The mixture was extracted with ether (2 x 5 mL) and CH_2C1_2 (2 x 5 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvents removed in vacuo. The residue was purified by flash chromatography on silica gel using EtOAc/*n*-Hexane (1/5 ($^v/_v$)) to afford coressponding secondary amine **5-7**.



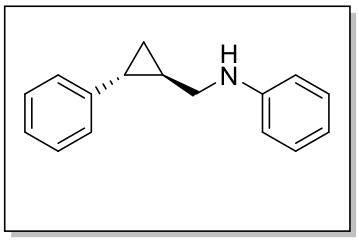
To a solution of cyclopropyl oxime ether **5-3o** (0.15 mmol) in dry CH_2CL_2 (4 mL) was added dropwise a solution of Allylmagnesium chloride (2.0 M in THF, 0.3 mL, 0.6 mmol) at room temperature and the reaction mixture was stirred for 30 minutes. After that, 10% aq. HCl was added slowly until a precipitate was formed, followed by 10% aq. NaOH until the solution was alkaline. The mixture was extracted with ether (2 x 5 mL) and CH_2C1_2 (2 x 5 mL). The combined organic layers were dried with Na_2SO_4, filtered and the solvents removed in vacuo. The residue was purified by chromatography on silica gel using EtOAc/*n*-Hexane (1/20 ($^v/_v$)) to afford **5-8**.

***N*-((2-(4-Methoxyphenyl)cyclopropyl)methyl)aniline**



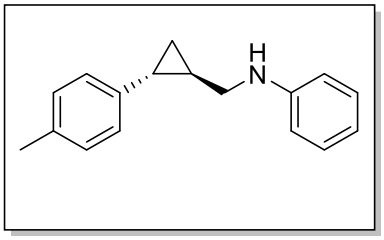
Cyclopropyl methyl amine **5-7a** was prepared according to the typical procedure in 87% yield as a yellow oil. The *trans/cis* ratio = 80:20. $[\alpha]_D^{25.9}$ = –67.7 (c 1.10, $CHCl_3$), *trans*: 93% ee, *cis*: 78% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-3), UV detector 280 nm, eluent: *n*-Hexane/IPA = 200/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 37.5 and 39.3 min (*trans*), tR (minor) = 23.5 and 26.0 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19–7.16 (m, 2H), 7.00 (d, *J* = 8.39 Hz, 2H), 6.83–6.80 (m, 2H), 6.71 (t, *J* = 7.26 Hz, 1H), 6.62 (d, *J* = 8.79 Hz, 2H), 3.77 (s, 3H), 3.14 (dd, *J* = 12.61, 6.88 Hz, 1H), 3.11 (dd, *J* = 12.61, 6.88 Hz, 1H), 1.80 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.41–1.34 (m, 1H), 0.90 (dddd, *J* = 13.38, 8.41, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.7, 148.3, 134.5, 129.2, 126.8, 117.4, 113.8, 112.7, 55.3, 48.4, 22.3, 21.4, 14.1 ppm. HRMS (DART) calcd for $[C_{17}H_{19}NO+H]^+$: 254.1545, found: 254.1548.

***N*-((2-Phenylcyclopropyl)methyl)aniline**



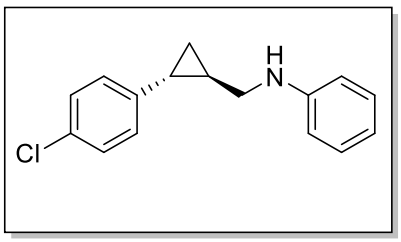
Cyclopropyl methyl amine **5-7b** was prepared according to the typical procedure in 86% yield as a yellow oil. The *trans/cis* ratio = 85:15. $[\alpha]_D^{27.8}$ = –108.4 (c 1.2, $CHCl_3$), *trans*: 93% ee, *cis*: 79% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IE-3), UV detector 280 nm, eluent: *n*-Hexane/IPA = 160/1 ($^v/_v$), Flow late = 0.7 mL/min, tR (major) = 12.8 and 13.3 min (*trans*), tR (minor) = 10.7 and 11.6 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.23 (m, 2H), 7.19–7.16 (m, 3H), 7.01 (d, *J* = 7.26 Hz, 2H), 6.71 (t, *J* = 7.26 Hz, 1H), 6.63 (d, *J* = 7.64 Hz, 2H), 3.14 (d, 6.88 Hz, 2H), 1.84 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.48–1.42 (m, 1H), 0.97 (dddd, *J* = 16.05, 8.79, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 142.6, 129.1, 128.3, 125.7, 125.6, 117.5, 112.8, 48.4, 22.8, 22.1, 14.7 ppm. HRMS (DART) calcd for $[C_{16}H_{17}N+H]^+$: 224.1439, found: 224.1439.

***N*-((2-(*p*-Tolyl)cyclopropyl)methyl)aniline**



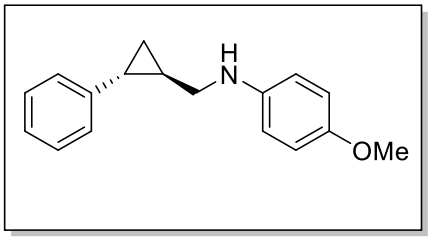
Cyclopropyl methyl amine **5-7c** was prepared according to the typical procedure in 82% yield as a yellow oil. The *trans/cis* ratio = 80:20. $[\alpha]_D^{27.5}$ = –82.2 (c 1.25, $CHCl_3$), *trans*: 94% ee, *cis*: 77% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-3), UV detector 280 nm, eluent: *n*-Hexane/IPA = 200/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 12.4 and 15.2 min (*trans*), tR (minor) = 8.0 and 9.2 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19–7.15 (m, 2H), 7.08 (d, *J* = 7.64 Hz, 2H), 6.96 (d, *J* = 8.03 Hz, 2H), 6.70 (t, *J* = 7.26 Hz, 1H), 6.61 (d, *J* = 7.26 Hz, 2H), 3.75 (br, 1H), 3.13 (dd, *J* = 12.61, 6.88 Hz, 1H), 3.12 (dd, *J* = 12.61, 6.88 Hz, 1H), 2.31 (s, 3H), 1.80 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.44–1.38 (m, 1H), 0.94 (dddd, *J* = 15.29, 8.79, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 139.5, 135.1, 129.2, 129.0, 125.6, 117.3, 112.7, 48.3, 22.6, 21.7, 21.0, 14.5 ppm. HRMS (DART) calcd for $[C_{17}H_{19}N+H]^+$: 238.1596, found: 238.1592.

***N*-((2-(4-Chlorophenyl)cyclopropyl)methyl)aniline**



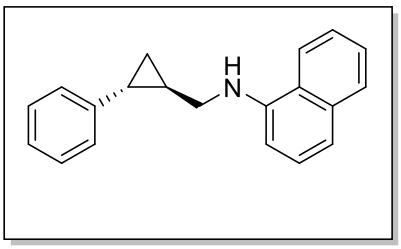
Cyclopropyl methyl amine **5-7e** was prepared according to the typical procedure in 84% yield as a yellow oil. The *trans/cis* ratio = 80:20. $[\alpha]_D^{25.7}$ = –77.2 (c 1.05, $CHCl_3$), *trans*: 94% ee, *cis*: 98% ee. The ee was determined by chiral HPLC analysis. Column (Chiral AD-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 100/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 21.3 and 24.4 min (*trans*), tR (minor) = 13.4 and 15 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.41 Hz, 2H), 7.19–7.16 (m, 2H), 6.97 (d, *J* = 8.41 Hz, 2H), 6.72 (t, *J* = 7.26 Hz, 1H), 6.62 (d, *J* = 7.64 Hz, 2H), 3.76 (br, 1H), 3.16 (dd, *J* = 12.23, 6.88 Hz, 1H), 3.12 (dd, *J* = 12.23, 6.88 Hz, 1H), 1.81 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.44–1.37 (m, 1H), 0.96 (dddd, *J* = 13.38, 9.17, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 141.1, 131.2, 129.3, 128.4, 127.1, 117.5, 112.8, 48.1, 23.0, 21.5, 14.7 ppm. HRMS (DART) calcd for $[C17H16ClN+H]^+$: 258.1049, found: 258.1049.

***N*-((2-Phenylcyclopropyl)methyl)-4-methoxyaniline**



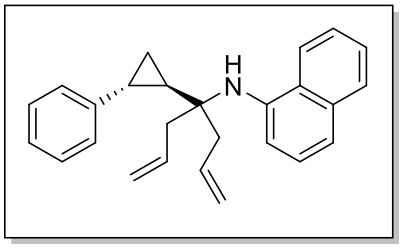
Cyclopropyl methyl amine **5-7m** was prepared according to the typical procedure in 95% yield as a yellow oil. The *trans/cis* ratio = 81:19. $[\alpha]_D^{27.8}$ = –99.7 (c 1.25, $CHCl_3$), *trans*: 92% ee, *cis*: 79% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 28.6 and 30.3 min (*trans*), tR (minor) = 20.5 and 23.5 min (*cis*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27–7.22 (m, 2H), 7.16 (t, *J* = 7.26 Hz, 1H), 7.06 (d, *J* = 6.88 Hz, 2H), 6.78 (d, *J* = 8. 89 Hz, 2H), 6.59 (d, *J* = 8.79 Hz, 2H), 3.74 (s, 3H), 3.11 (dd, *J* = 12.23, 6.88 Hz, 1H), 3.08 (dd, *J* = 12.23, 6.88 Hz, 1H), 1.82 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.47–1.41 (m, 1H), 0.96 (dddd, *J* = 15.67, 8.79, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 142.7, 142.5, 128.3, 125.7, 125.6, 114.8, 114.4, 55.7, 49.4, 22.9, 22.1, 14.7 ppm. HRMS (DART) calcd for $[C_{17}H_{19}NO+H]^+$: 254.1545, found: 254.1545.

***N*-((2-Phenylcyclopropyl)methyl)naphthalen-1-amine**



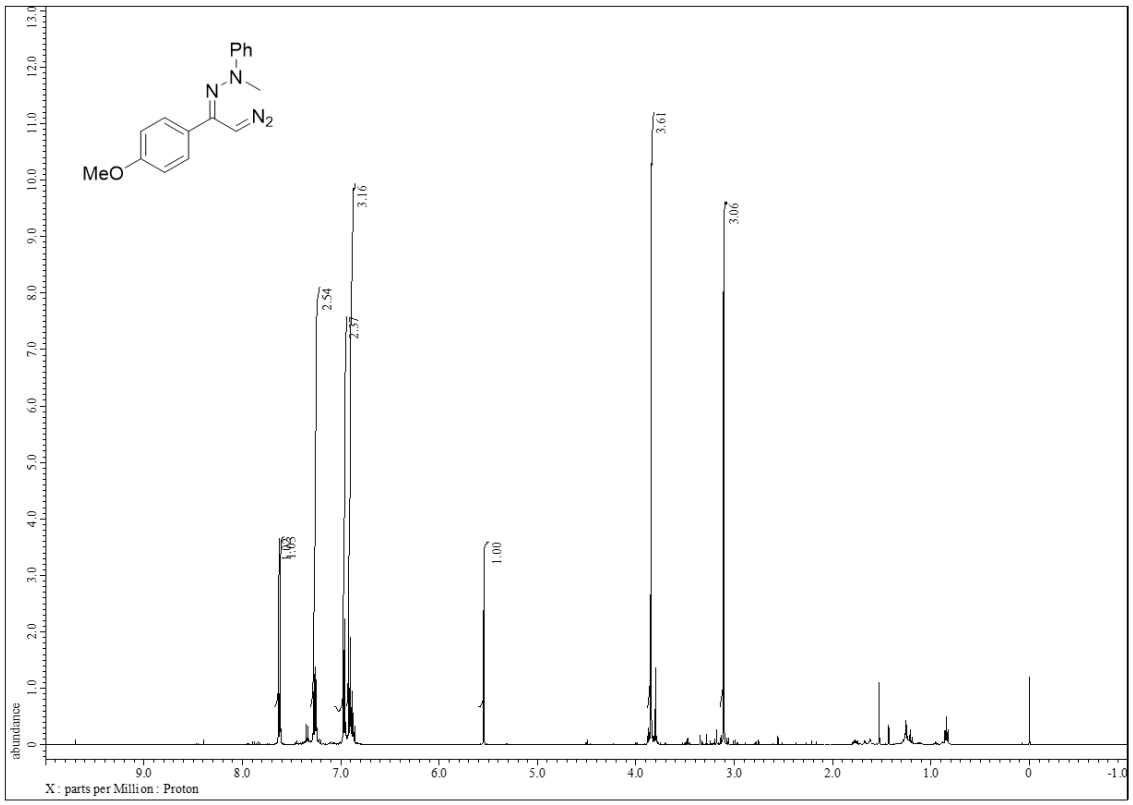
Cyclopropyl methyl amine **5-7o** was prepared according to the typical procedure in 85% yield as a yellow oil. $[\alpha]_D^{27.6}$ = –60.3 (c 1.21, $CHCl_3$), *trans*: 92% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IC-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 16.2 and 19.8 min (*trans*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84–7.78 (m, 2H), 7.46–7.41 (m, 2H), 7.35 (t, *J* = 7.46 Hz, 1H), 7.29 (t, *J* = 7.45 Hz, 2H), 7.24 (d, *J* = 8.41, 1H), 7.19 (t, *J* = 7.45 Hz, 1H), 7.11 (dd, *J* = 8.41, 1.53 Hz, 2H), 6.61 (d, *J* = 7.26 Hz, 1H), 4.50 (br, 1H), 3.32 (dd, *J* = 12.23, 6.88 Hz, 1H), 3.29 (dd, *J* = 12.23, 6.88 Hz, 1H), 1.93 (ddd, *J* = 9.17, 4.97, 4.97 Hz, 1H), 1.65–1.58 (m, 1H), 1.06 (dddd, *J* = 16.05, 8.79, 4.97, 4.97 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.4, 142.6, 134.2, 128.6, 128.4, 126.6, 125.8, 125.7, 125.6, 124.7, 123.3, 119.9, 117.4, 104.3, 48.7, 22.7, 22.3, 14.8 ppm. HRMS (DART) calcd for $[C_{20}H_{19}N+H]^+$: 274.1596, found: 274.1596.

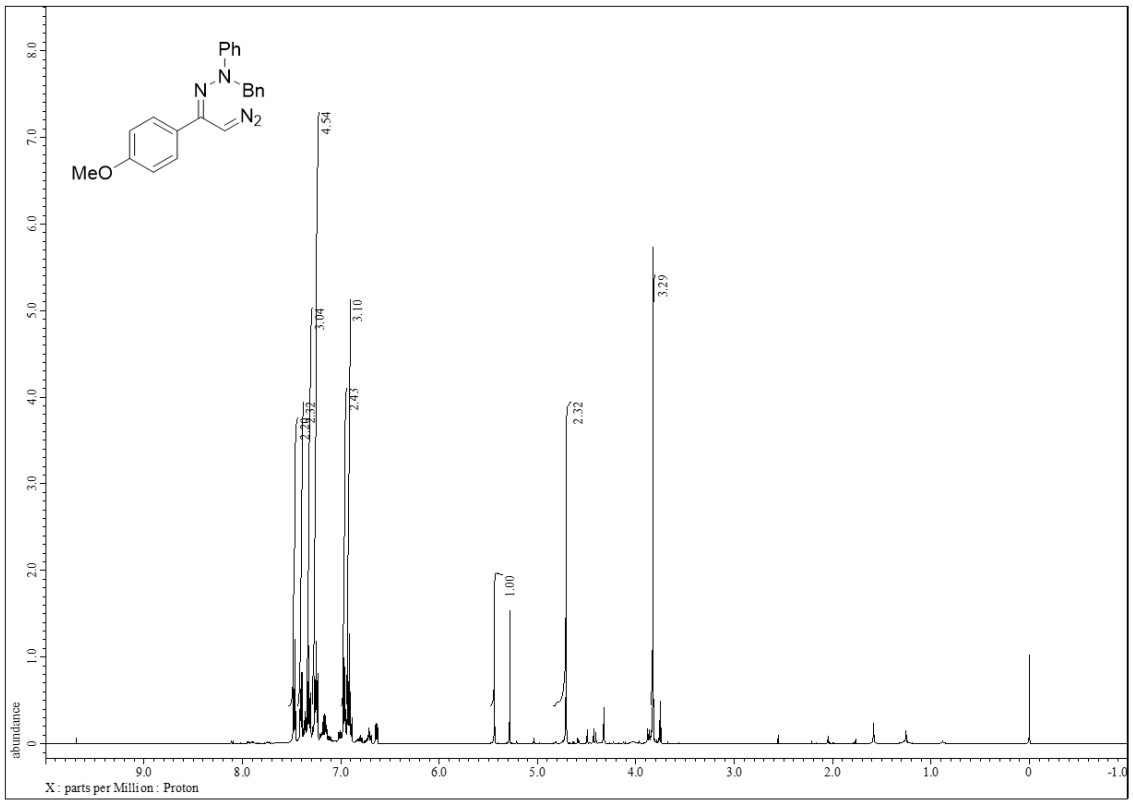
***N*-(4-(-2-Phenylcyclopropyl)hepta-1,6-dien-4-yl)naphthalen-1-amine**

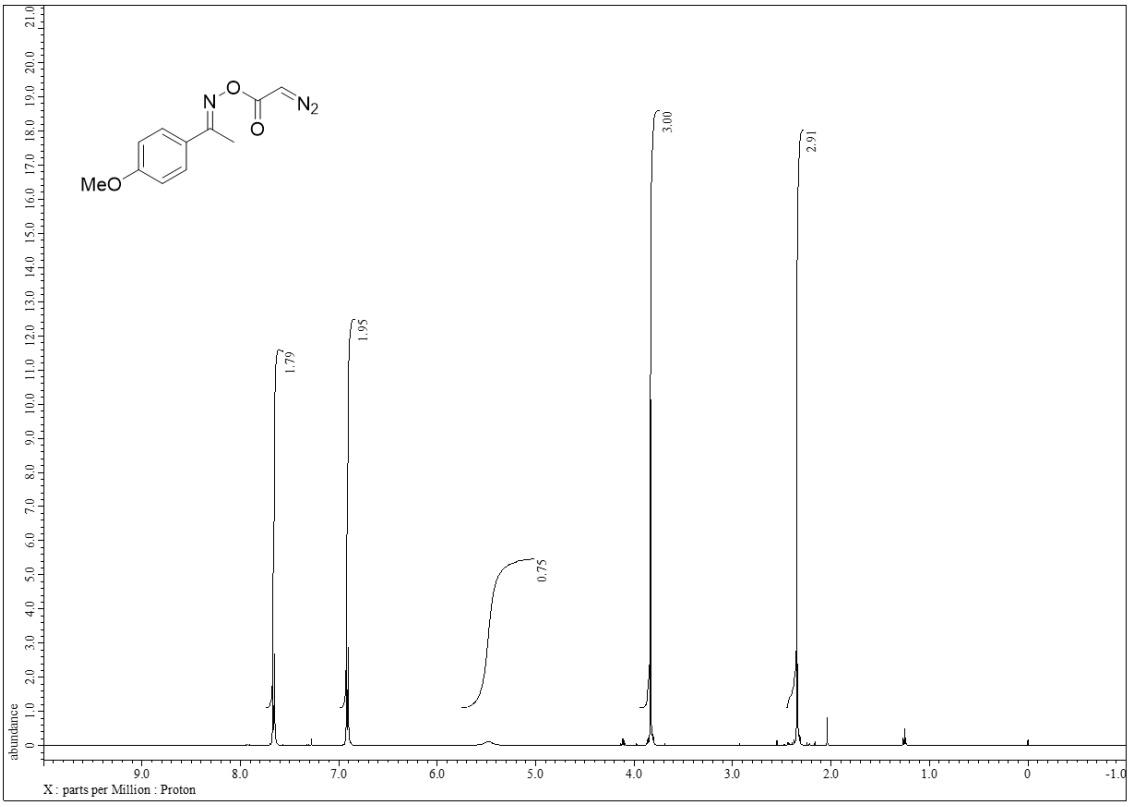


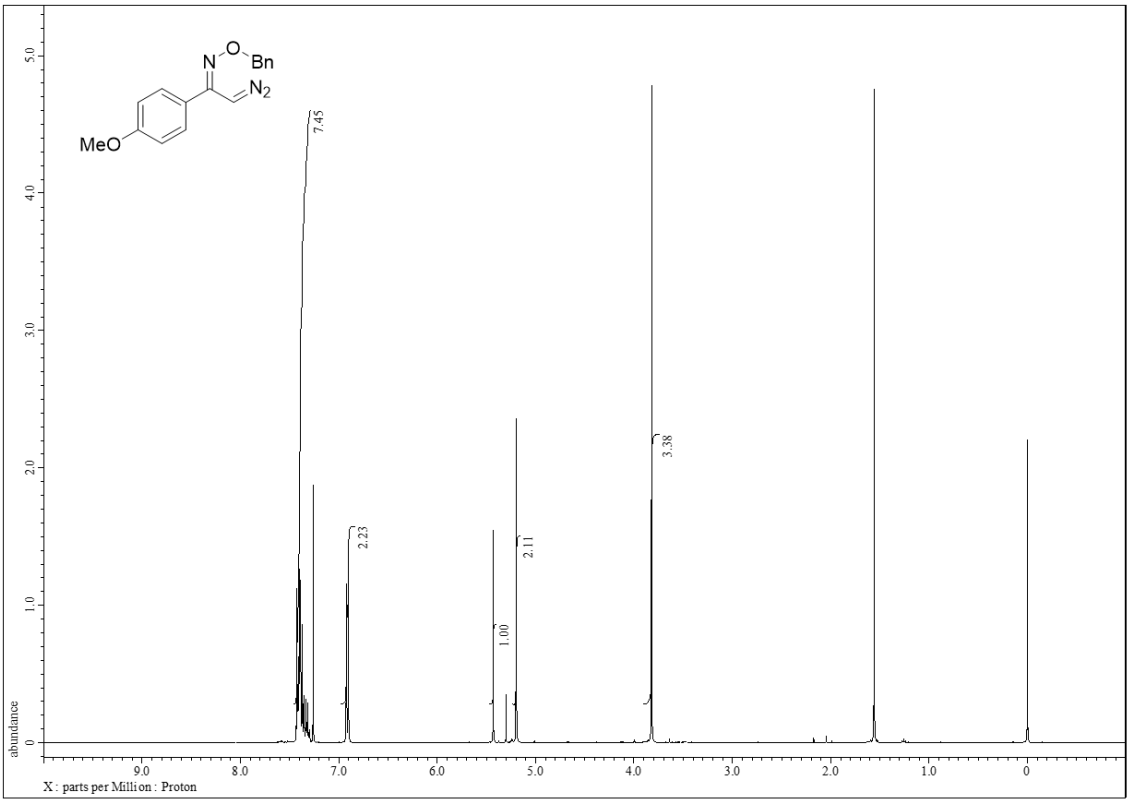
Compound **5-8** was obtained in 60% yield as a yellow oil. $[\alpha]_D^{27.3}$ = –39.0 (c 1.10, $CHCl_3$), *trans*: 93% ee. The ee was determined by chiral HPLC analysis. Column (Chiral IA-3), UV detector 254 nm, eluent: *n*-Hexane/IPA = 200/1 ($^v/_v$), Flow late = 1.0 mL/min, tR (major) = 5.6 and 6.0 min (*trans*). *trans*: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.43–7.38 (m, 2H), 7.26–7.20 (m, 4H), 7.14 (t, *J* = 7.26 Hz, 1H), 7.09–7.05 (m, 3H), 5.49–5.84 (m, 2H), 5.18–5.11 (m, 4H), 4.51 (br, 1H), 2.67–2.73 (m, 2H), 2.48–2.39 (m, 2H), 2.12 (dt, *J* = 8.79, 5.35 Hz, 1H), 1.46 (ddd, *J* = 8.79, 6.50, 5.35 Hz, 1H), 1.29 (ddd, *J* = 9.17, 6.50, 5.35 Hz, 1H), 1.10 (dt, *J* = 9.17, 5.35 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7141.0, 134.6, 134.1, 134.0, 128.8, 128.3, 126.1, 125.7, 125.5, 125.4, 124.7, 120.0, 118.9, 118.8, 117.5, 109.3, 57.0, 42.3, 41.2, 32.7, 21.3, 14.1 ppm. HRMS (DART) calcd for $[C_{26}H_{27}N+H]^+$: 354.2222, found: 354.2223.

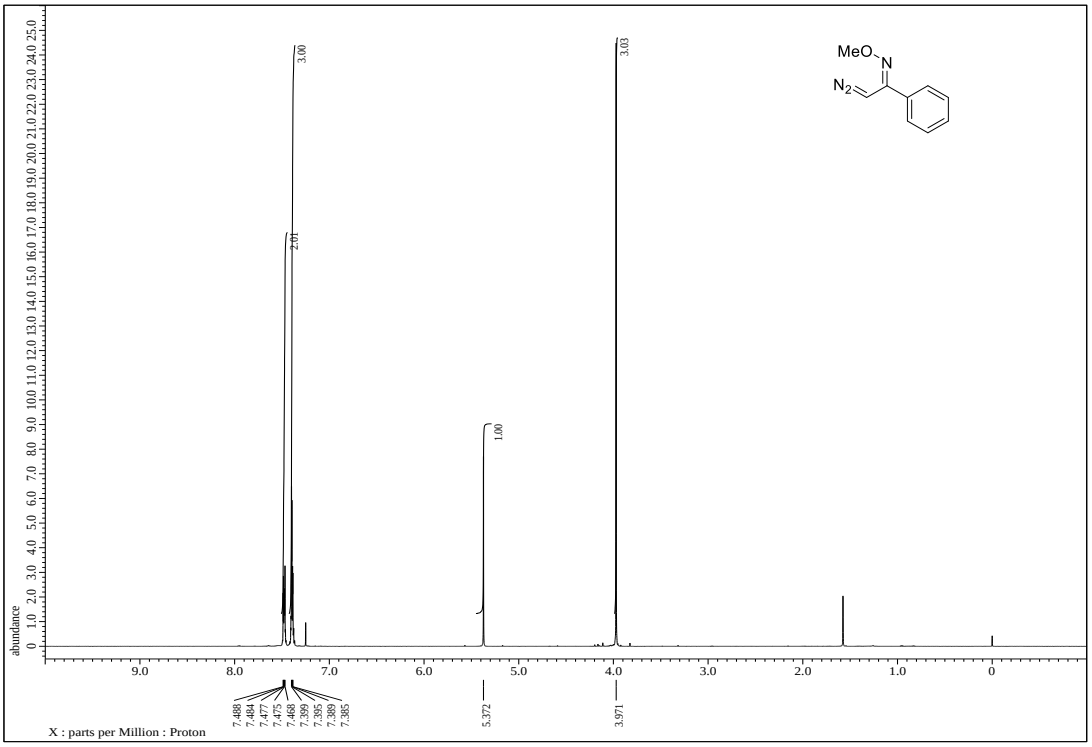
8-3-6 NMR Spectral Data

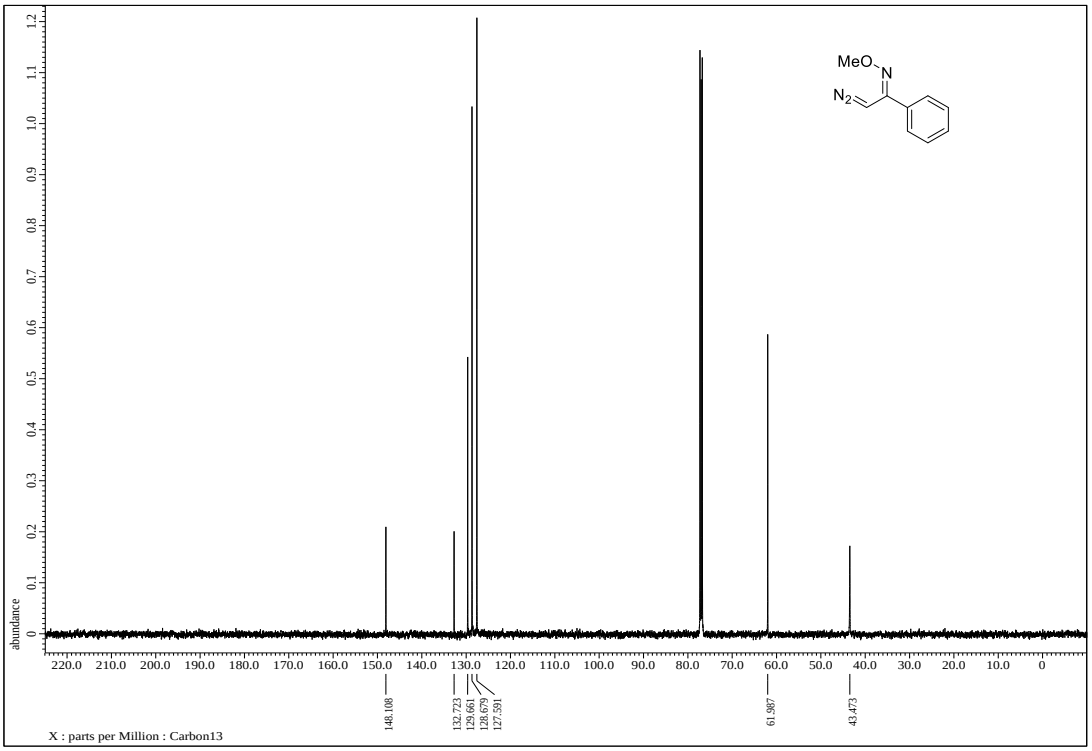


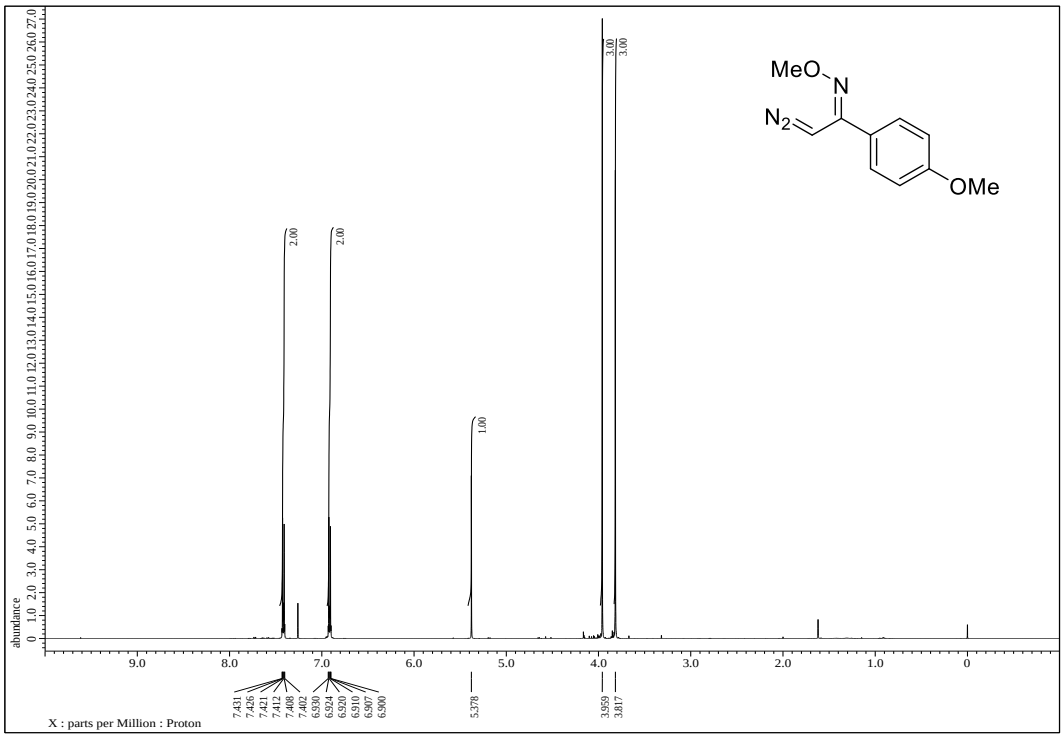


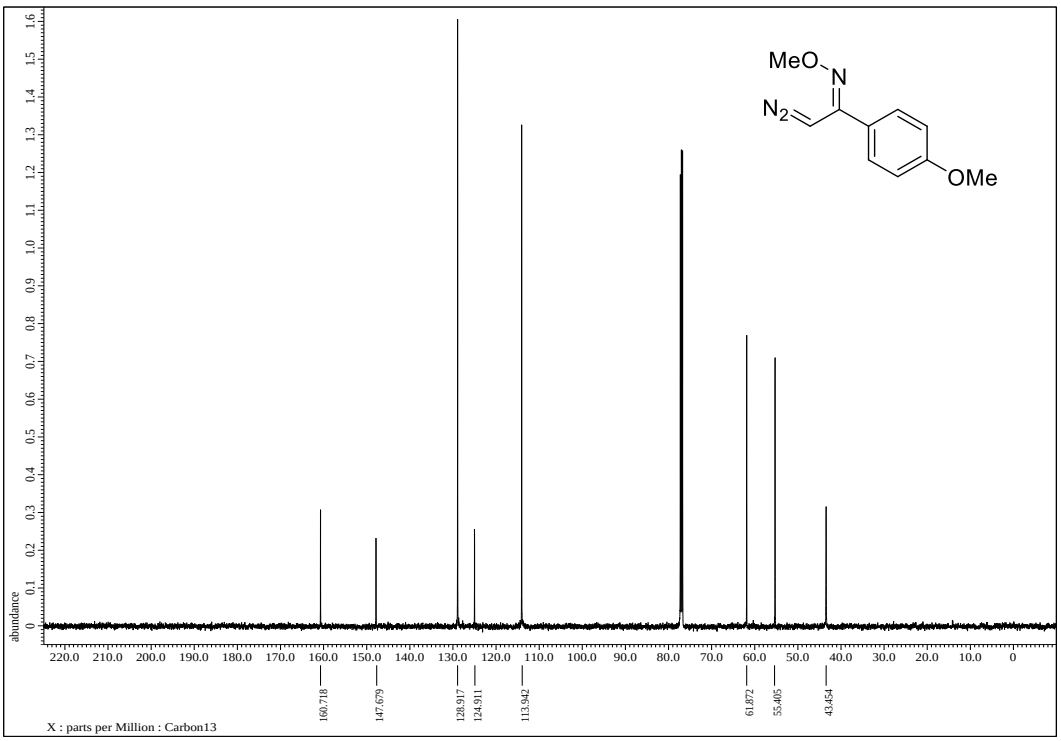

MeO
N
O
O
N2
1.79
1.95
0.75
3.00
2.91
abundance
X : parts per Million : Proton

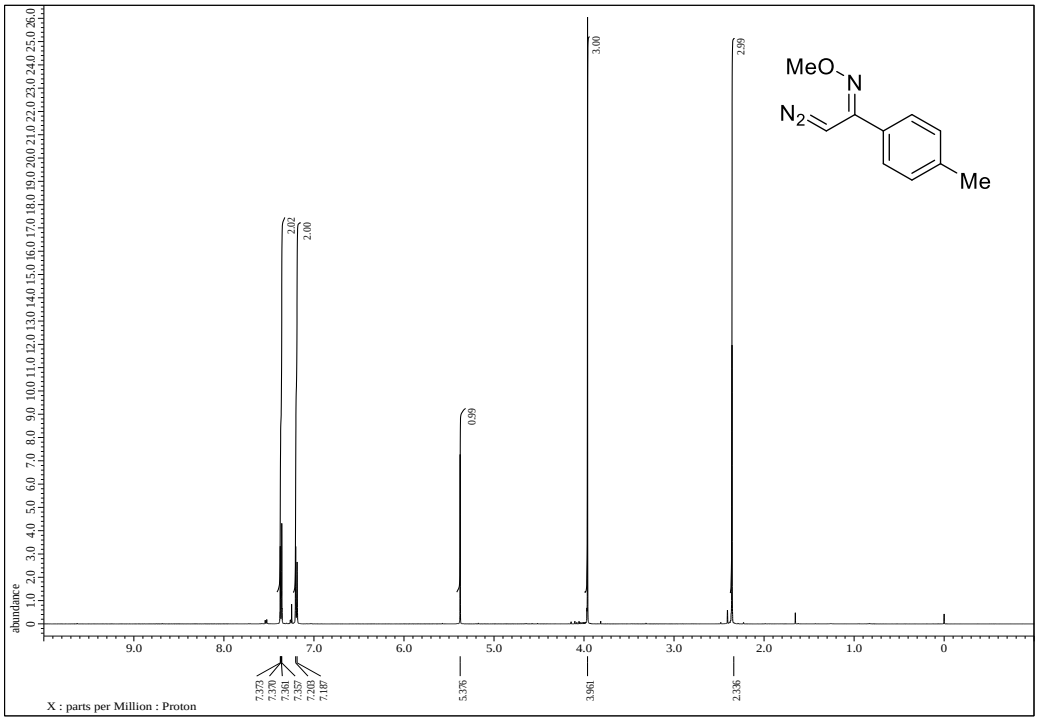

MeO
N
O
Bn
N2
7.45
2.23
1.00
2.11
3.38
abundance
X : parts per Million : Proton

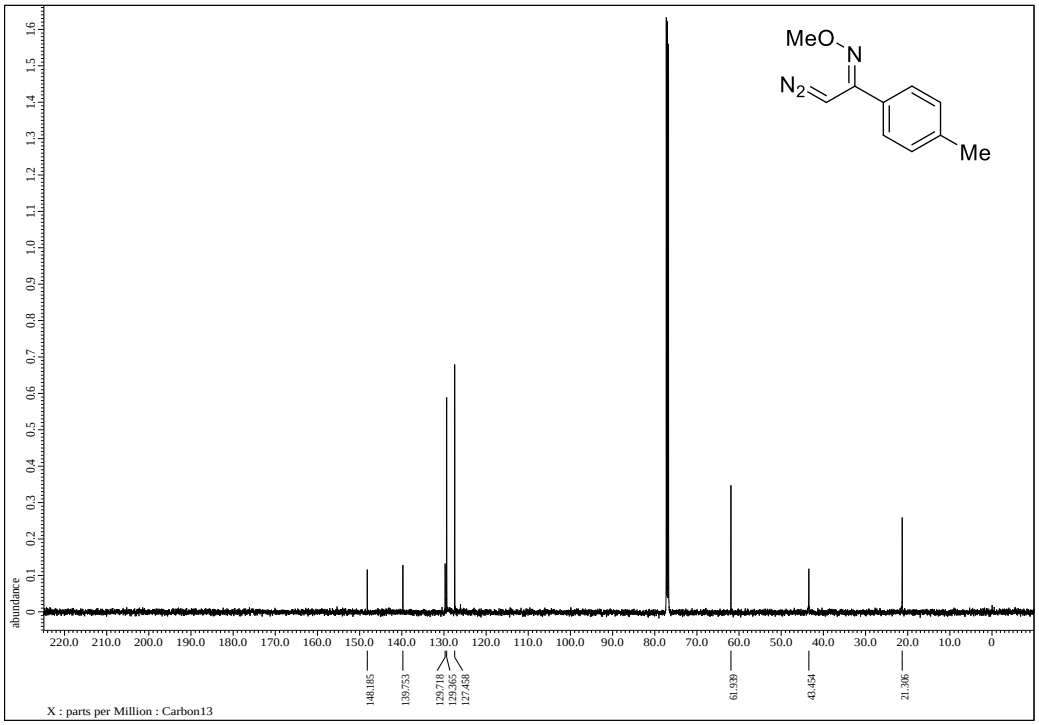

MeO
N
N2
3.00
3.03
2.01
1.00
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.488
7.484
7.477
7.475
7.468
7.399
7.395
7.389
7.385
5.372
3.971
X : parts per Million : Proton

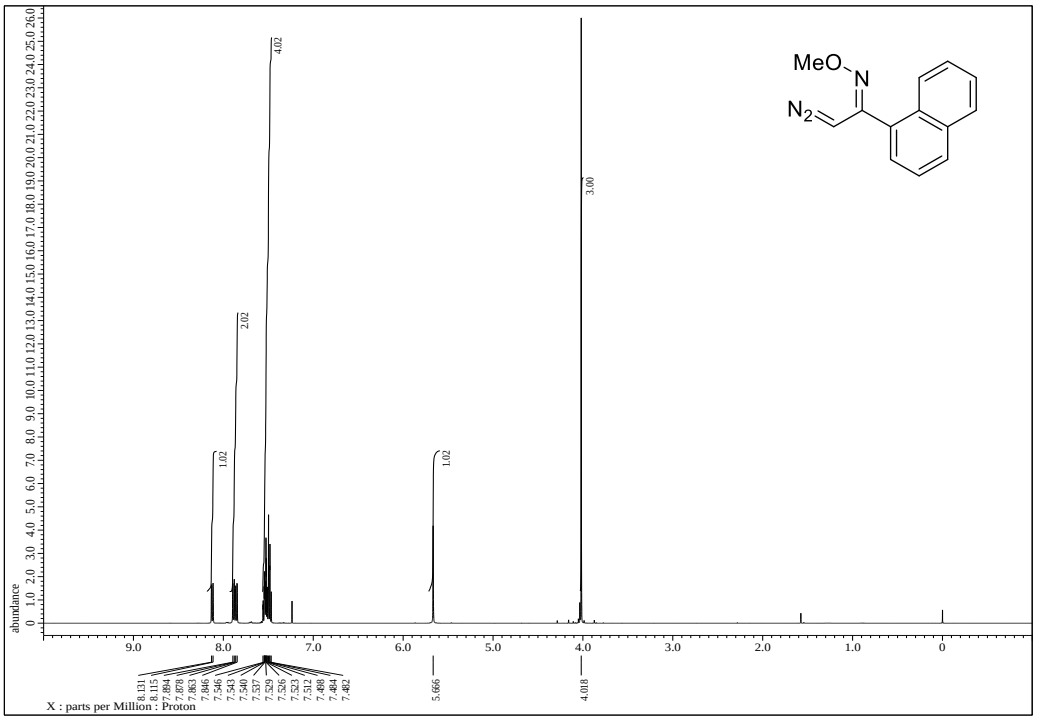

MeO
N
N2
abundance
220.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
148.108
132.723
129.661
128.979
127.591
61.987
43.473
X : parts per Million : Carbon13

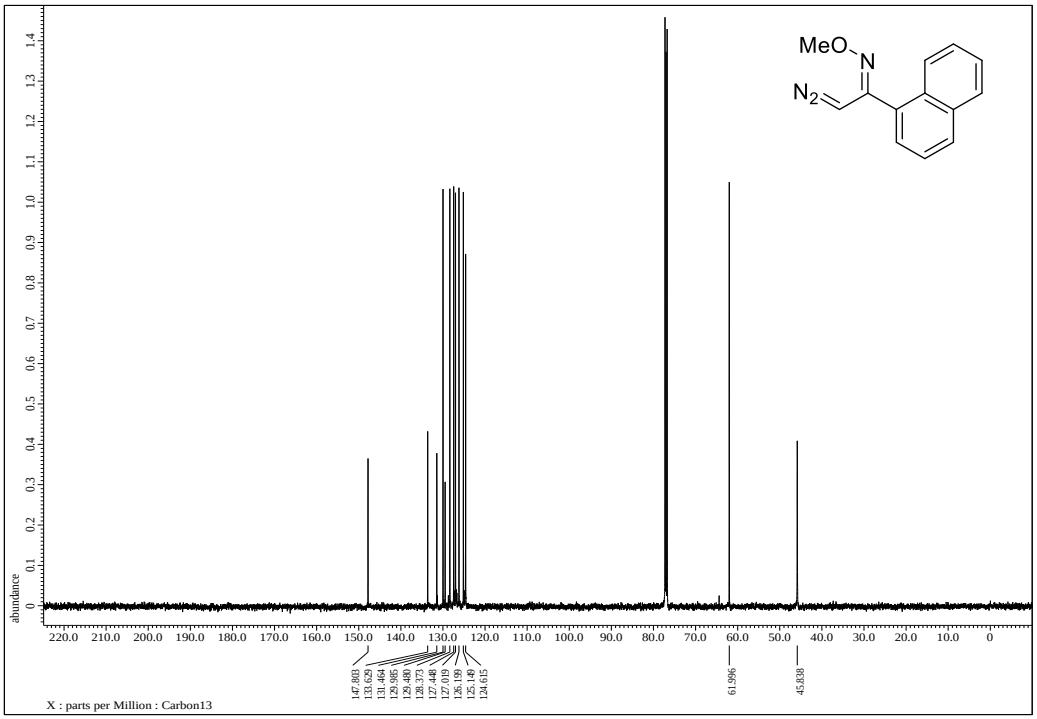

MeO
N
N2
OMe
abundance
X : parts per Million : Proton
7.431
7.426
7.421
7.412
7.408
7.402
6.930
6.924
6.920
6.910
6.907
6.900
5.378
3.959
3.817

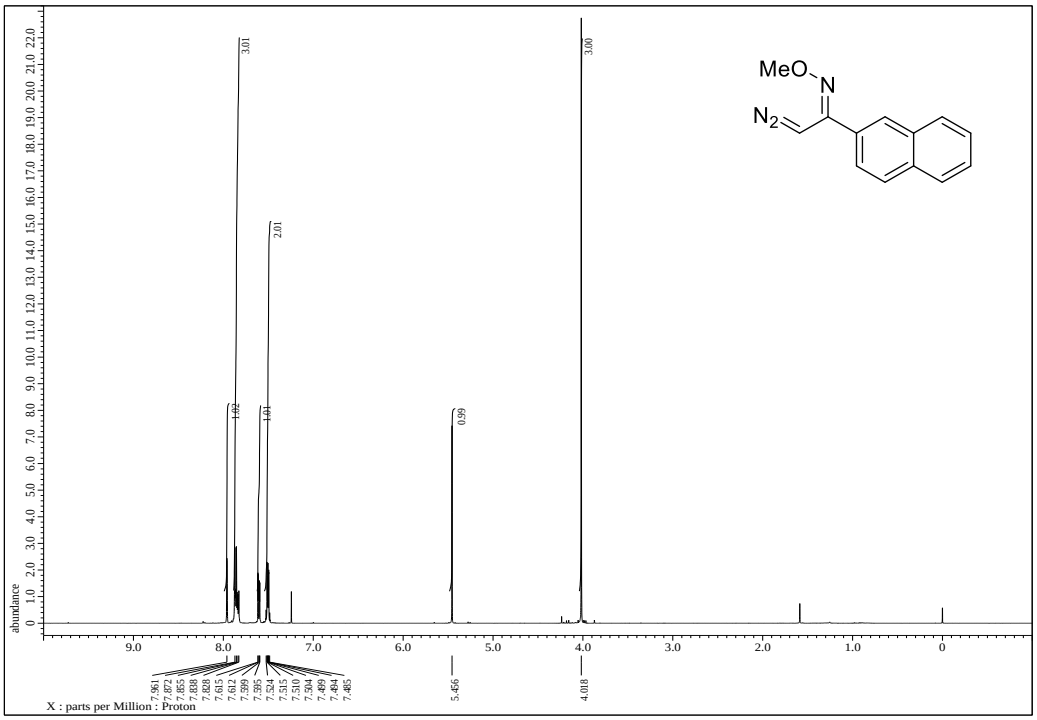

MeO
N
N2
OMe
abundance
X : parts per Million : Carbon13
160.718
147.679
128.917
124.911
113.942
61.872
55.405
43.454

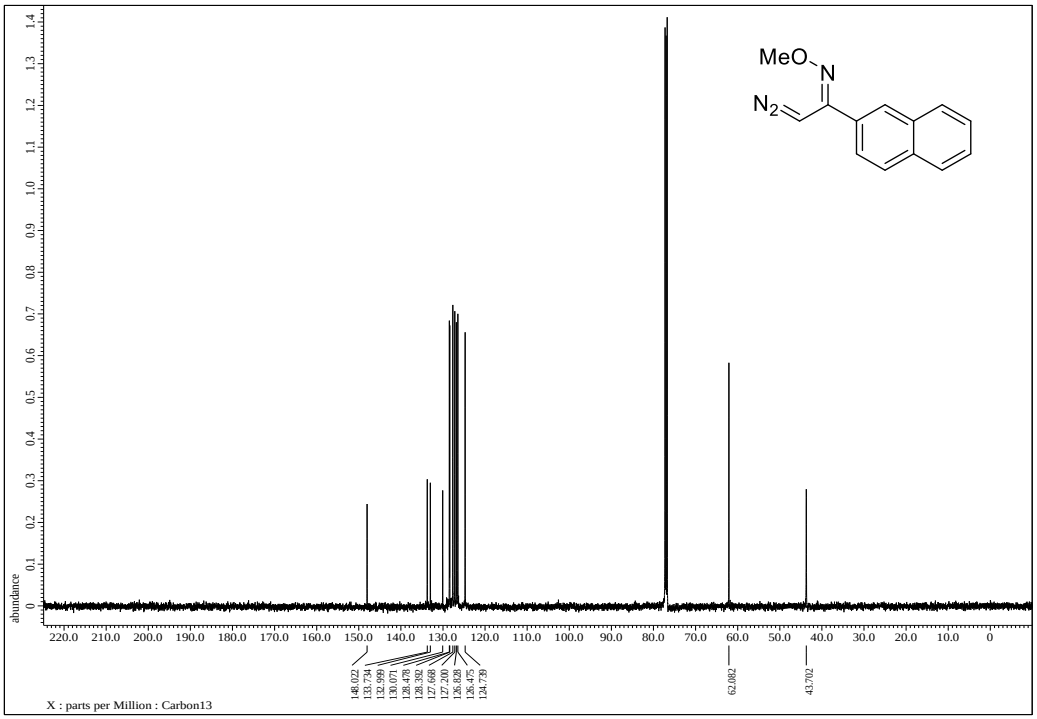

MeO
N
N2
Me
abundance
3.00
2.99
2.02
2.00
0.99
7.373
7.370
7.361
7.357
7.209
7.187
5.376
3.961
2.336
X : parts per Million : Proton

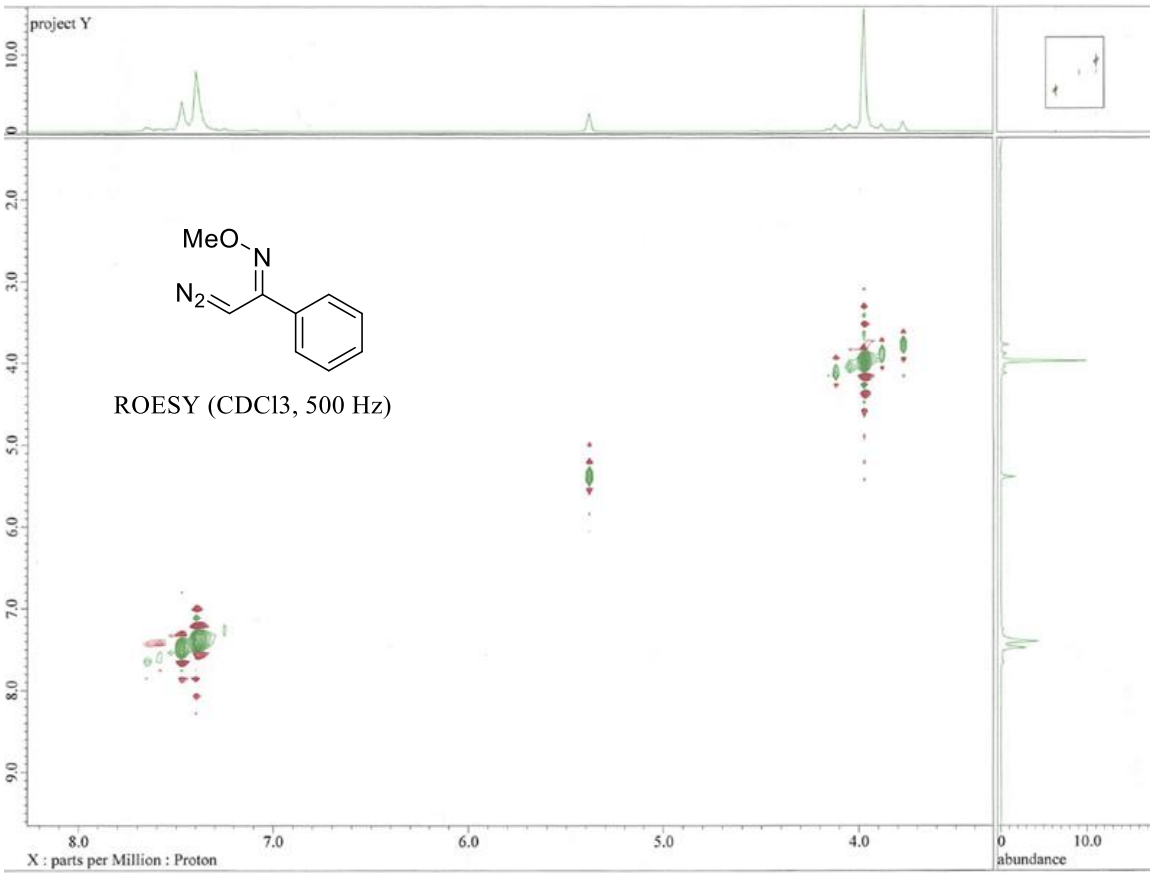

MeO
N
N2
Me
abundance
148.185
139.753
129.718
129.365
127.458
61.939
43.454
21.306
X : parts per Million : Carbon13

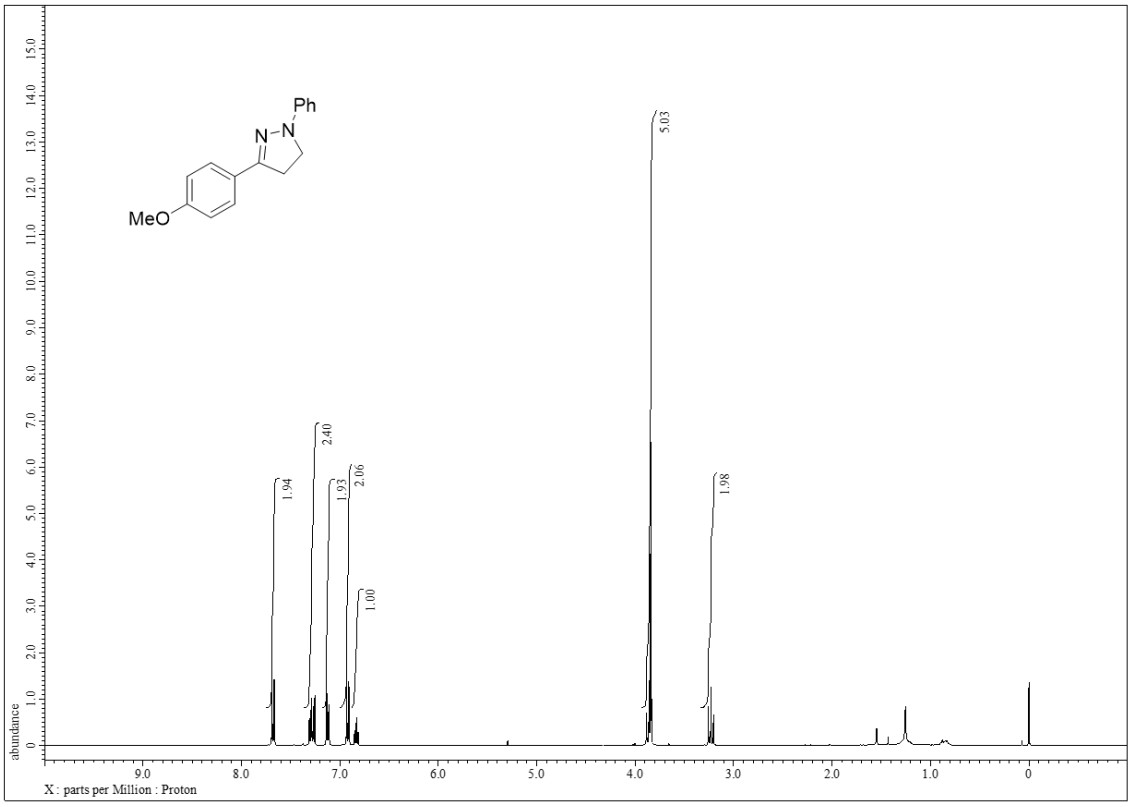

MeO
N
N2
abundance
4.02
3.00
2.02
1.02
1.02
8.131
8.115
7.894
7.878
7.863
7.846
7.545
7.543
7.540
7.537
7.529
7.526
7.523
7.512
7.498
7.494
7.482
5.666
4.018
X : parts per Million : Proton

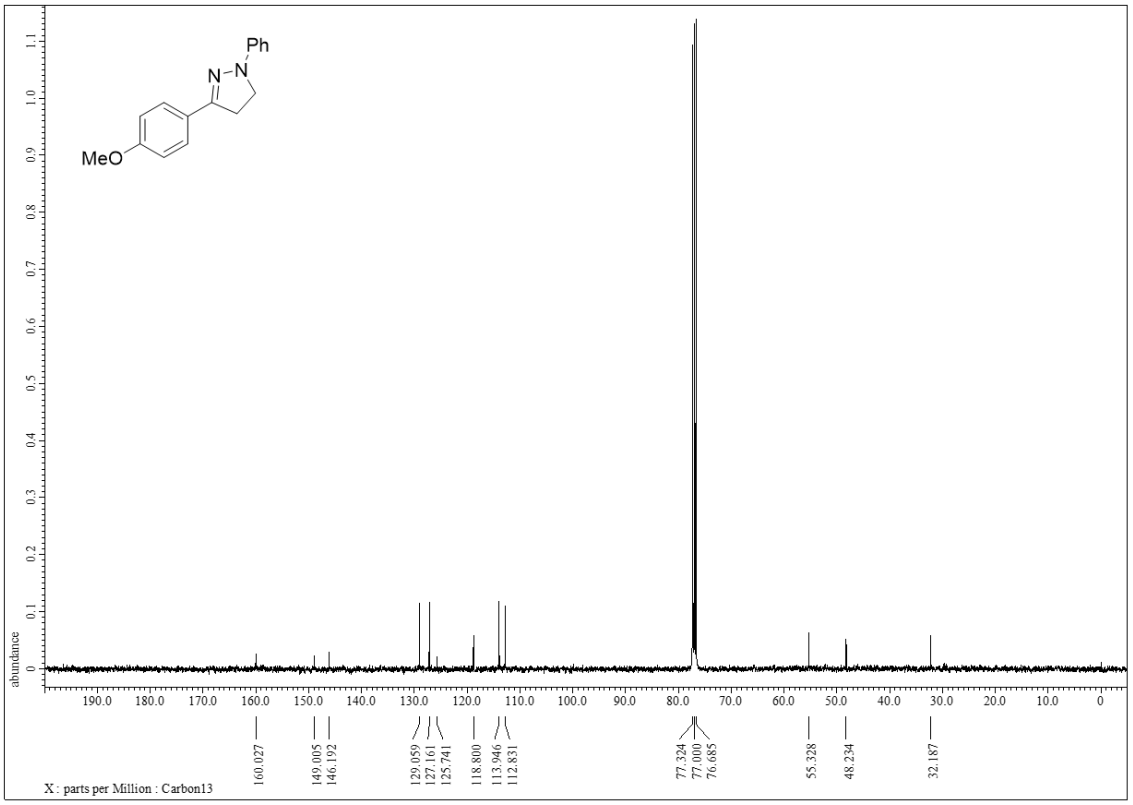

MeO
N
N2
abundance
147.803
133.629
131.464
129.985
129.489
128.373
127.448
127.019
126.199
125.149
124.615
61.996
45.838
X : parts per Million : Carbon13

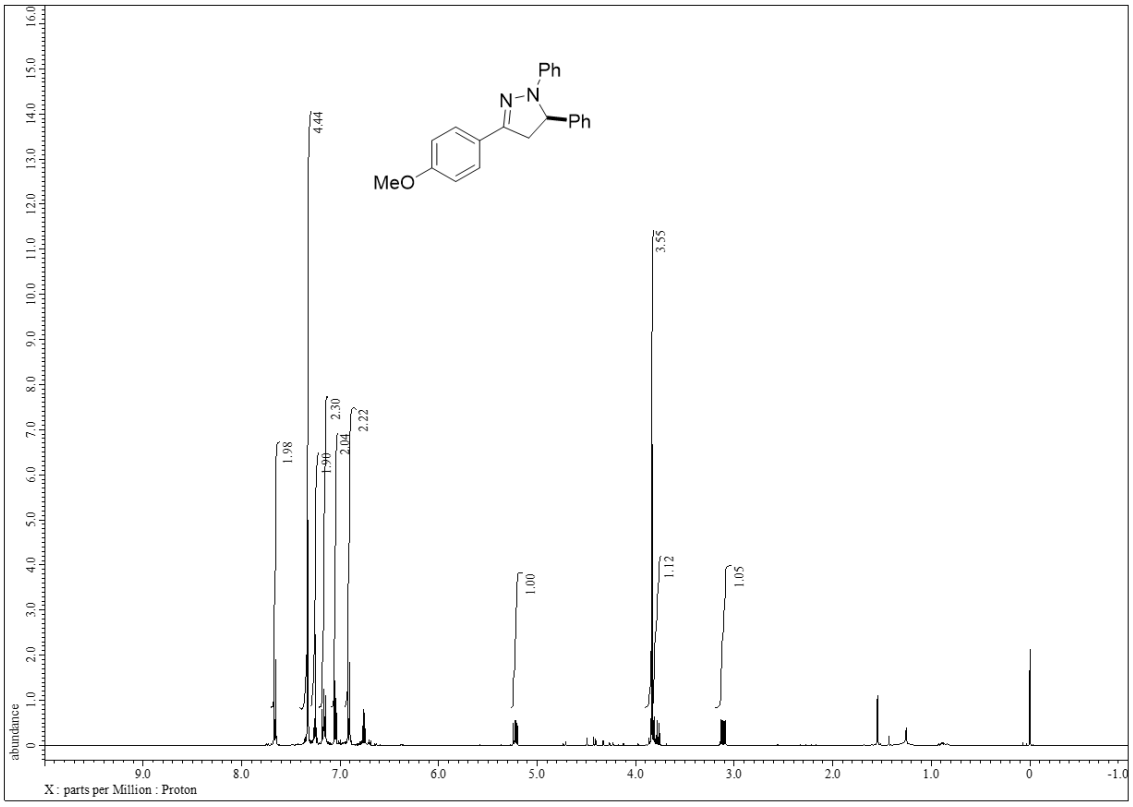

MeO
N
N2
abundance
3.01
2.01
1.02
1.01
0.99
3.00
7.961
7.872
7.855
7.838
7.828
7.615
7.613
7.596
7.595
7.524
7.515
7.510
7.504
7.499
7.494
7.485
5.456
4.018
X : parts per Million : Proton

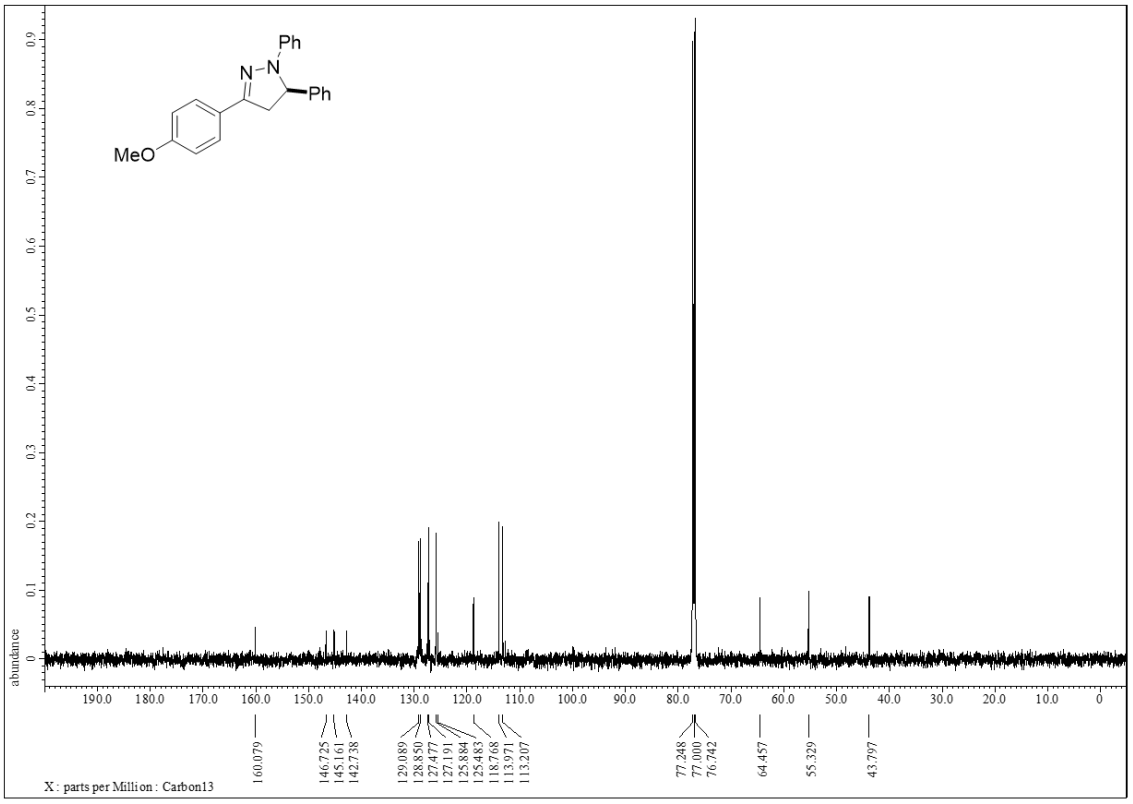

MeO
N
N2
abundance
148.022
133.734
132.999
130.071
128.478
128.392
127.698
127.200
126.928
126.475
124.739
62.082
43.702
X : parts per Million : Carbon13

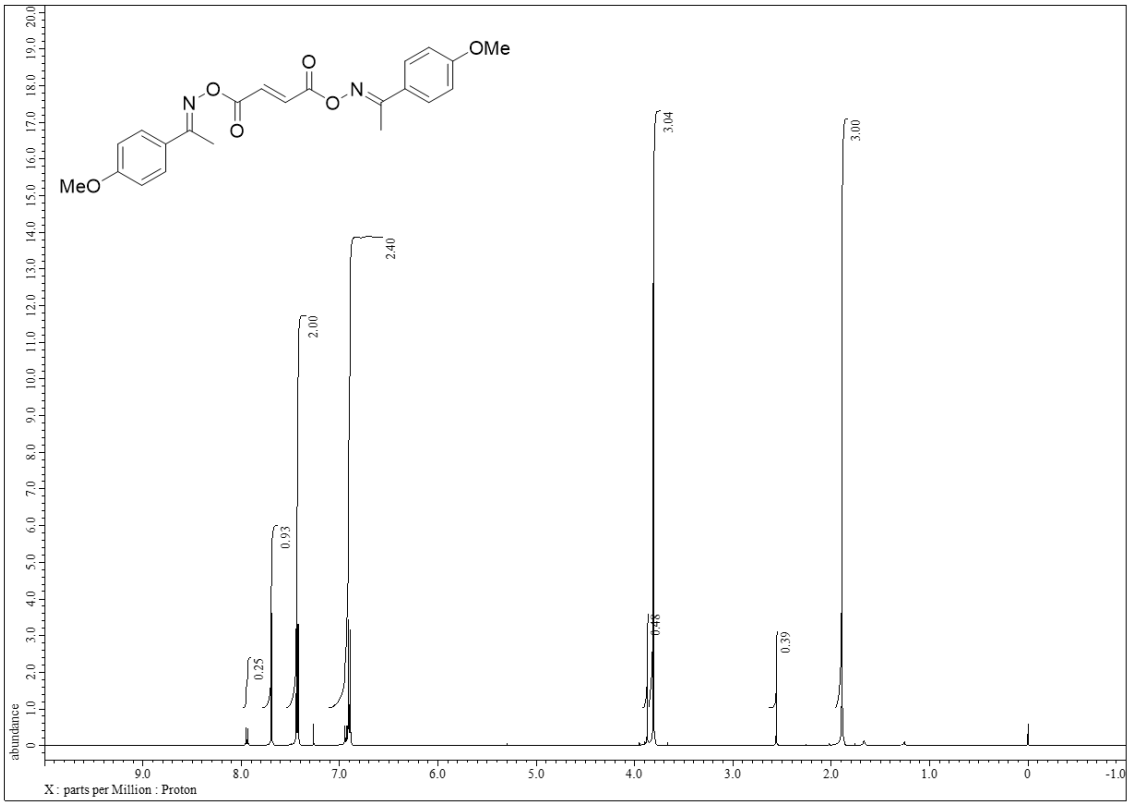

project Y
MeO
N
N2
ROESY (CDCl3, 500 Hz)
X : parts per Million : Proton
abundance

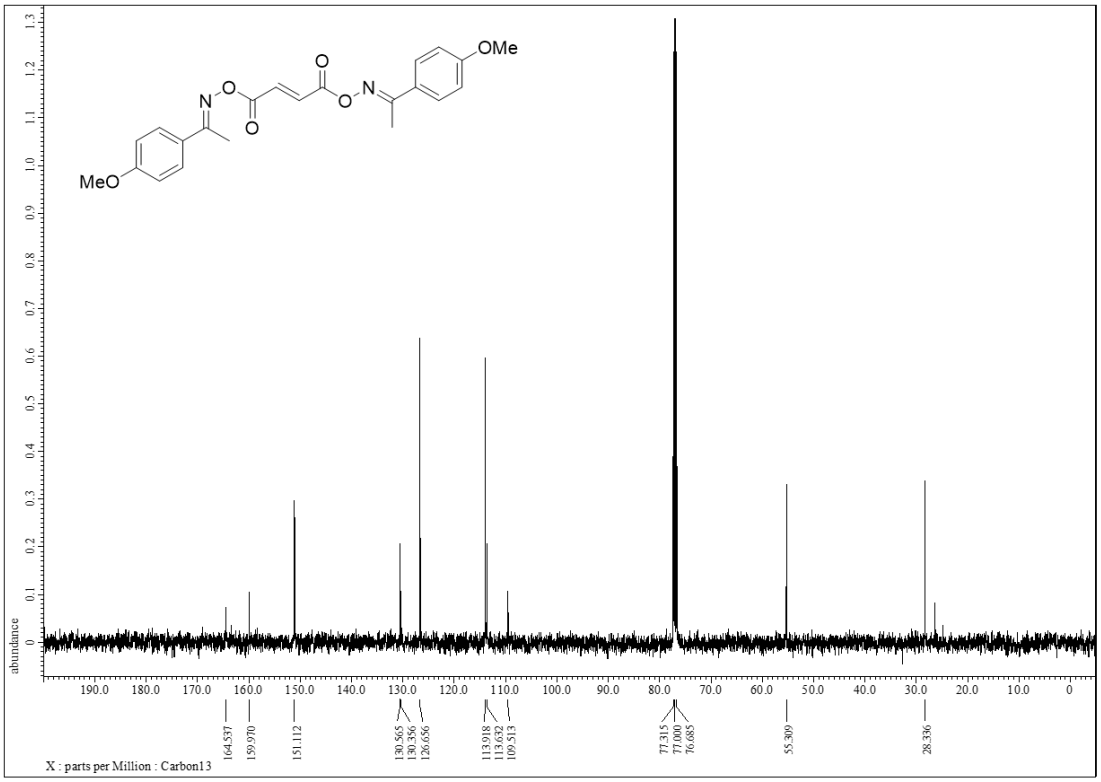

Ph
N
N
MeO
5.03
2.40
1.94
1.93
2.06
1.98
1.00
abundance
X : parts per Million : Proton

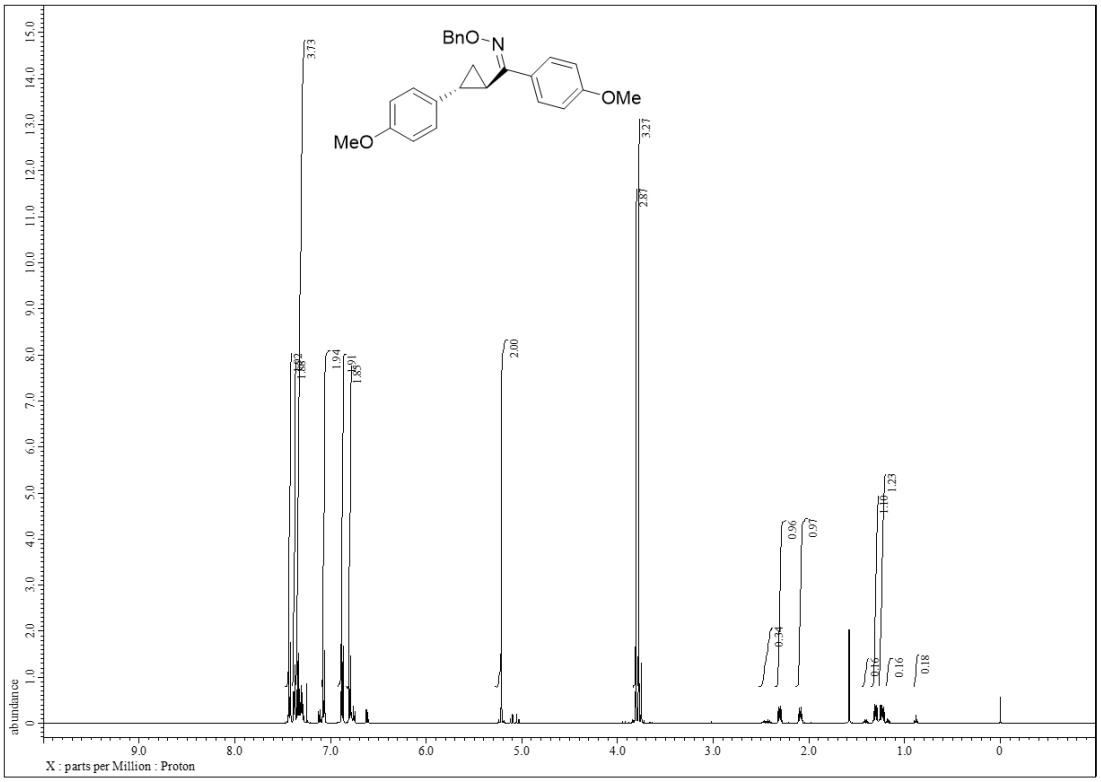

Ph
N
N
MeO
abundance
160.027
149.005
146.192
129.059
127.161
125.741
118.800
113.946
112.831
77.324
77.000
76.685
55.328
48.234
32.187
X : parts per Million : Carbon13

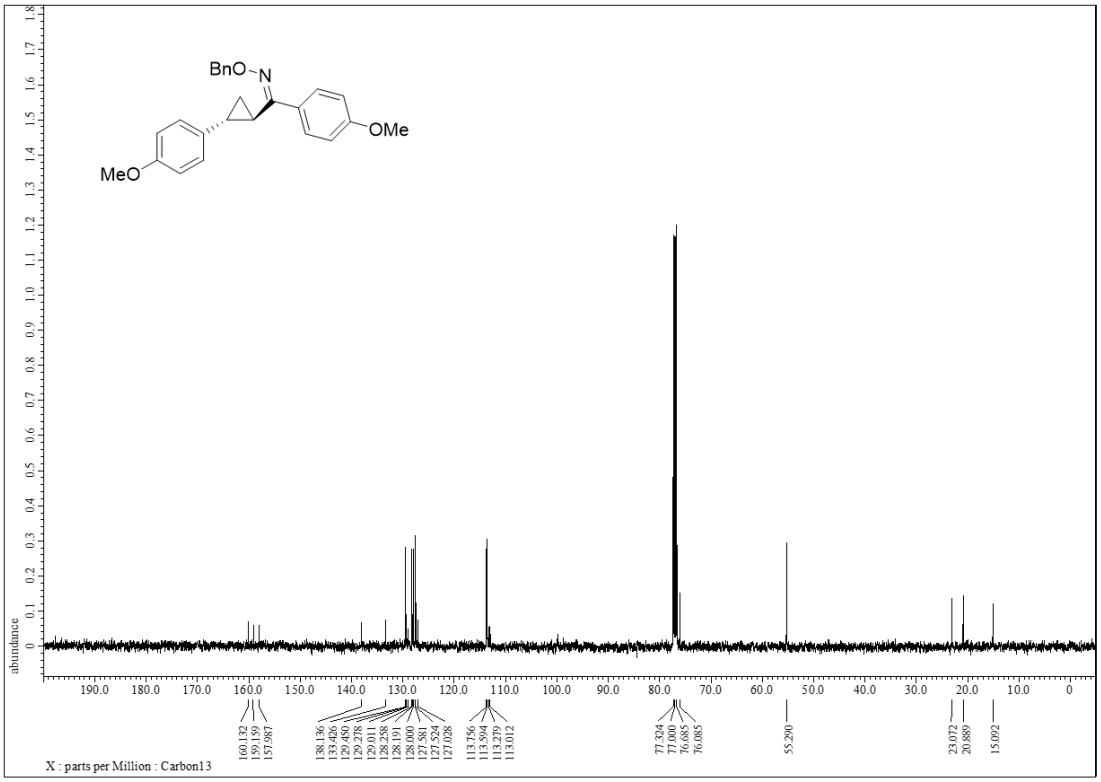

Ph
N
N
Ph
MeO
4.44
3.55
2.30
2.22
2.04
1.98
1.90
1.00
1.12
1.05
abundance
X : parts per Million : Proton

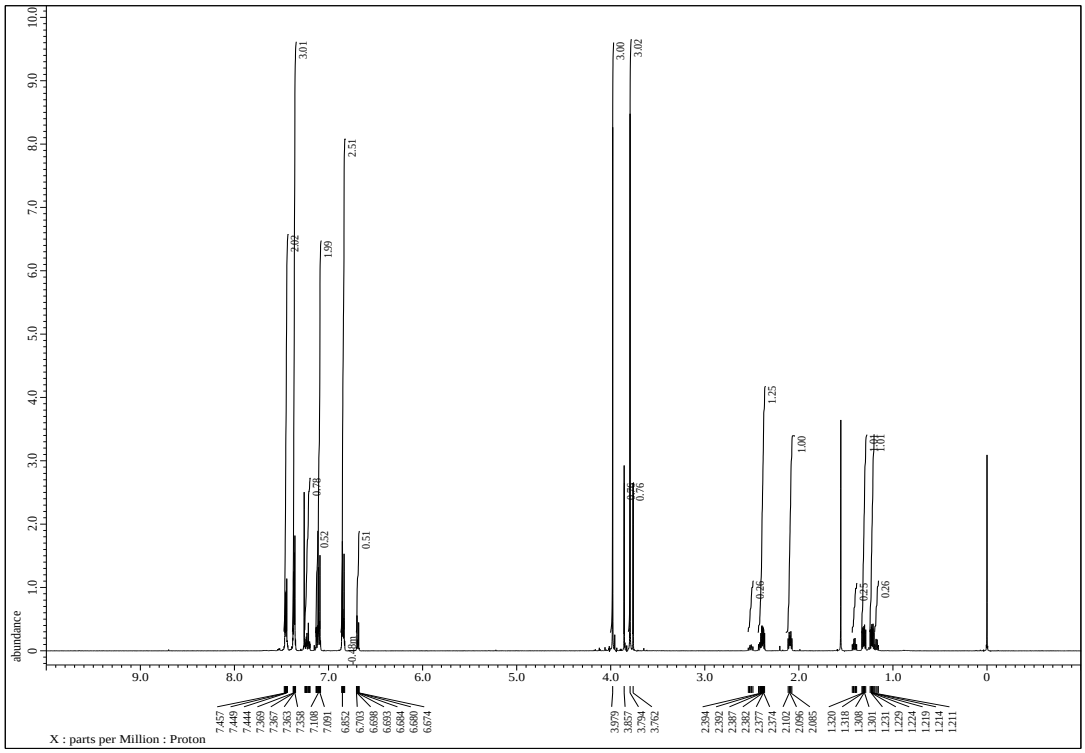

Ph
N
N
Ph
MeO
160.079
146.725
145.161
142.738
129.089
128.850
127.477
127.191
125.884
125.483
118.768
113.971
113.207
77.248
77.000
76.742
64.457
55.329
43.797
abundance
X : parts per Million : Carbon13

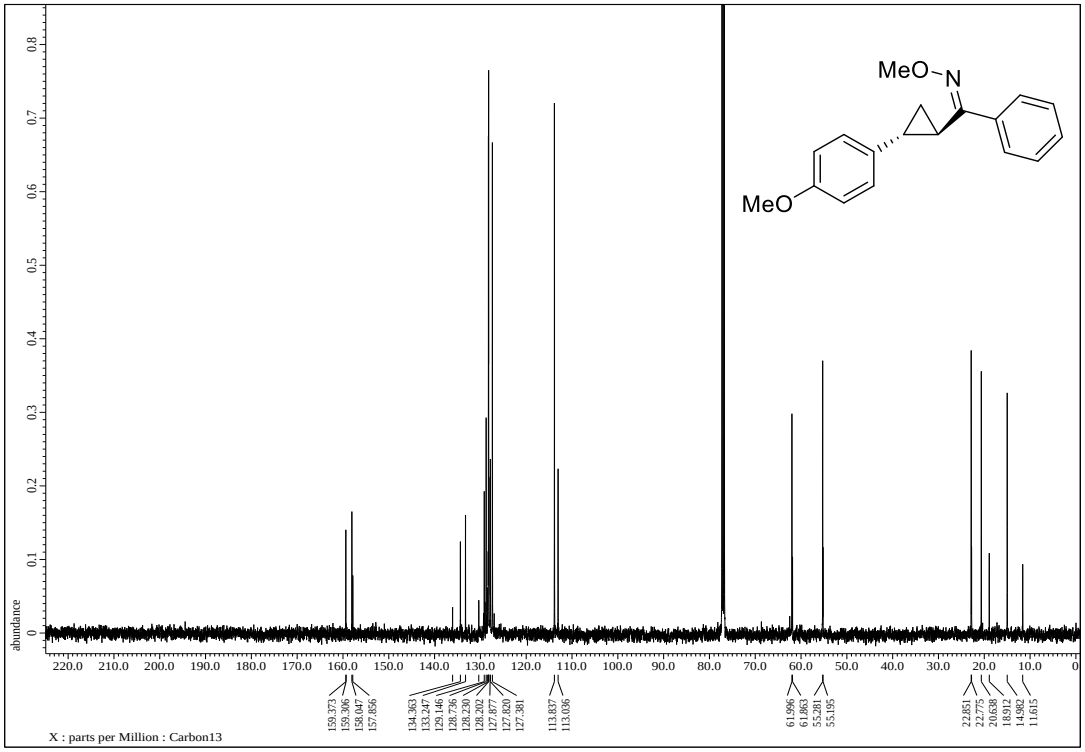

OMe
MeO
0.25
0.93
2.00
2.40
3.04
0.48
0.39
3.00
abundance
X : parts per Million : Proton

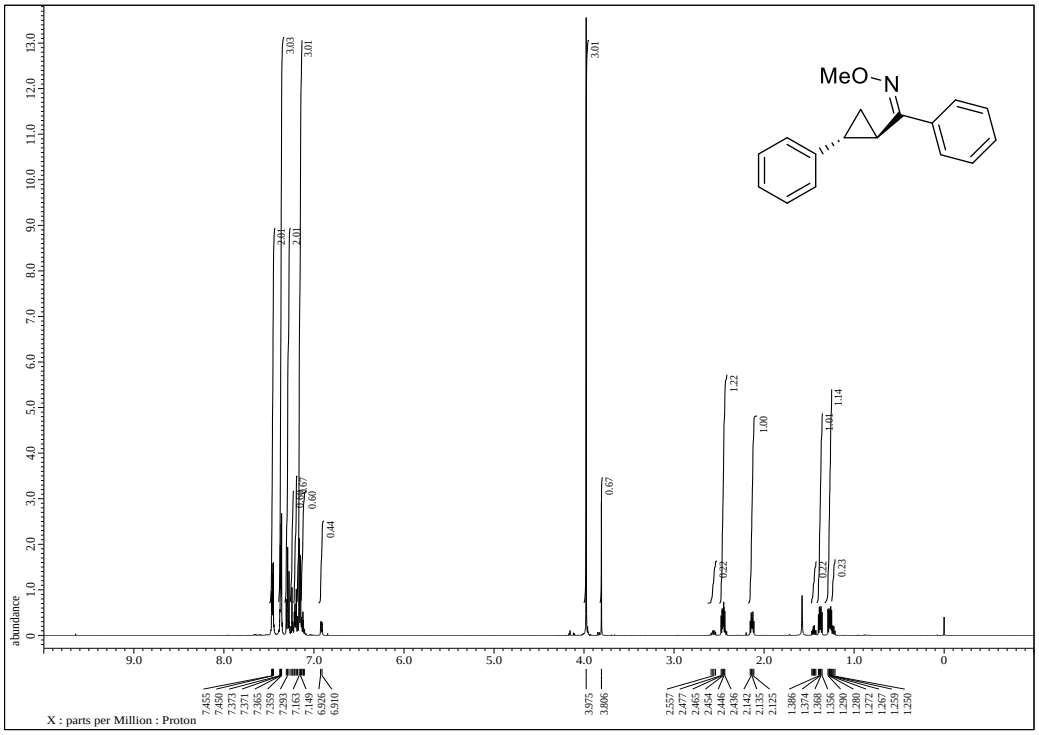

OMe
MeO
abundance
164.537
159.970
151.112
130.565
130.356
126.656
113.918
113.632
109.513
77.315
77.000
76.685
55.309
28.336
X : parts per Million : Carbon13

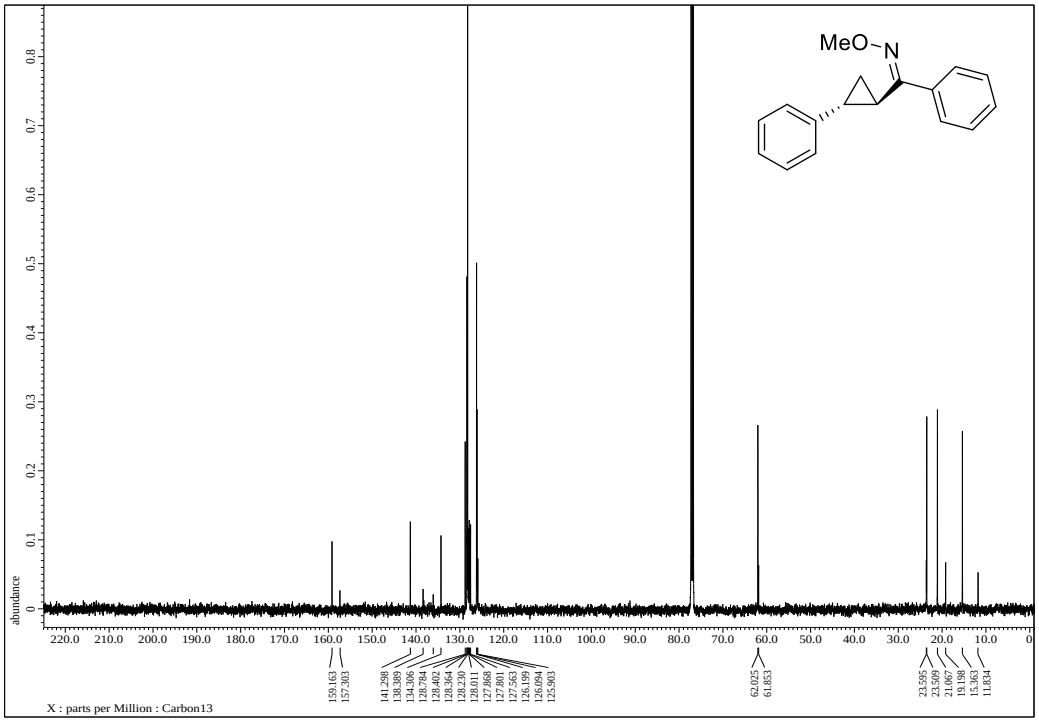

BnO
N
OMe
MeO
3.73
3.27
2.87
2.00
1.94
1.91
1.92
1.89
0.96
0.97
1.23
1.16
0.34
0.16
0.16
0.18
abundance
X : parts per Million : Proton

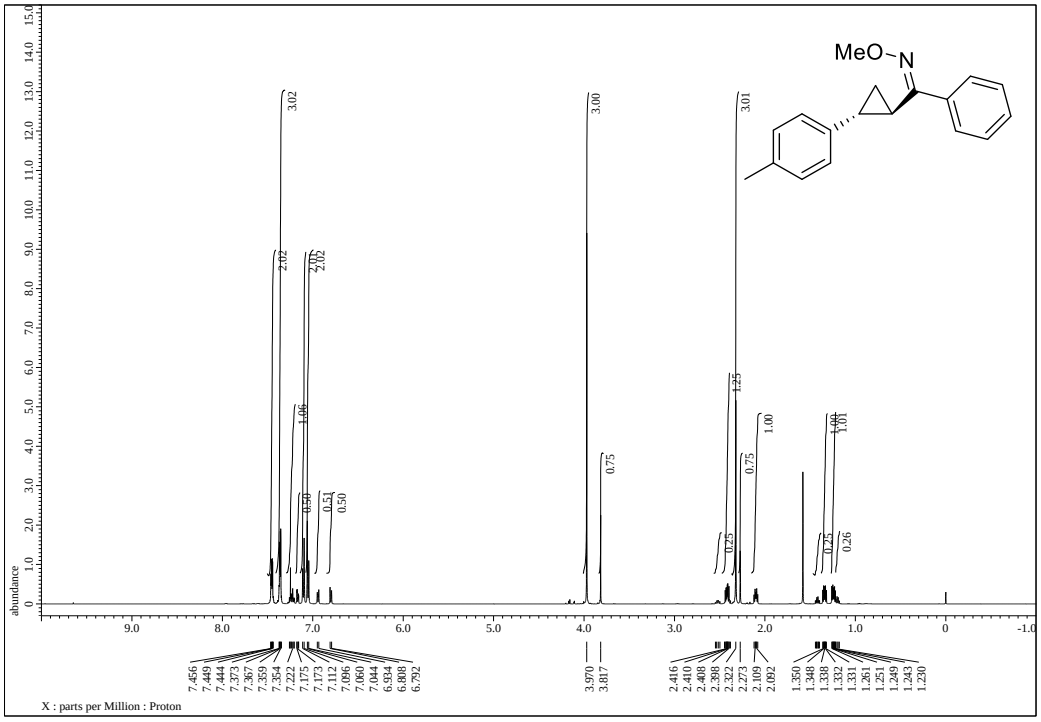

BnO
N
OMe
MeO
abundance
160.132
159.159
157.987
138.136
137.450
129.460
129.278
129.011
128.258
128.191
128.000
127.581
127.524
127.028
113.756
113.594
113.279
113.012
77.324
77.000
76.685
76.085
55.290
23.072
20.889
15.092
X : parts per Million : Carbon13

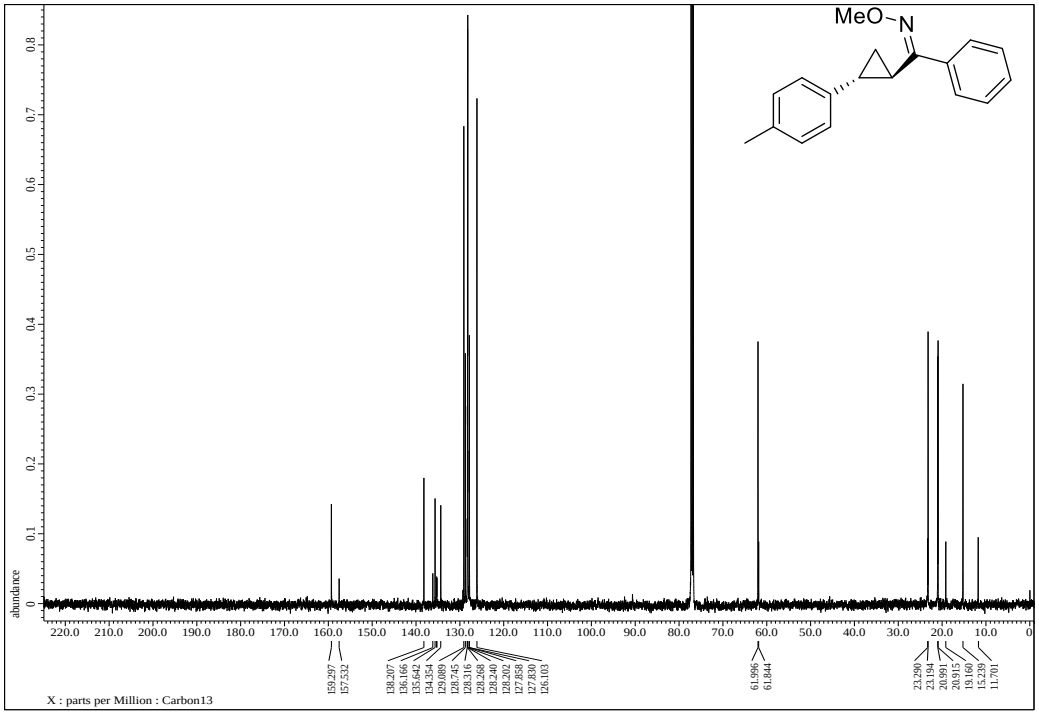

abundance
X : parts per Million : Proton

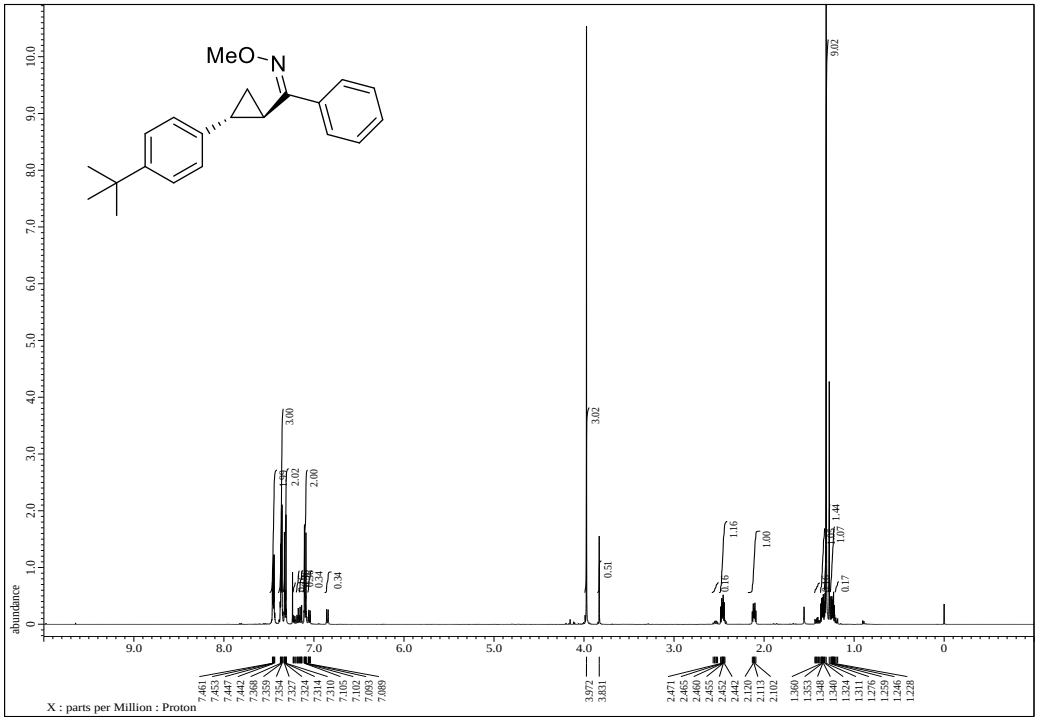

MeO
N
MeO
abundance
X : parts per Million : Carbon13


MeO
N
abundance
X : parts per Million : Proton


MeO
N
abundance
X : parts per Million : Carbon13


MeO
N
abundance
X : parts per Million : Proton


MeO
N
abundance
X : parts per Million : Carbon13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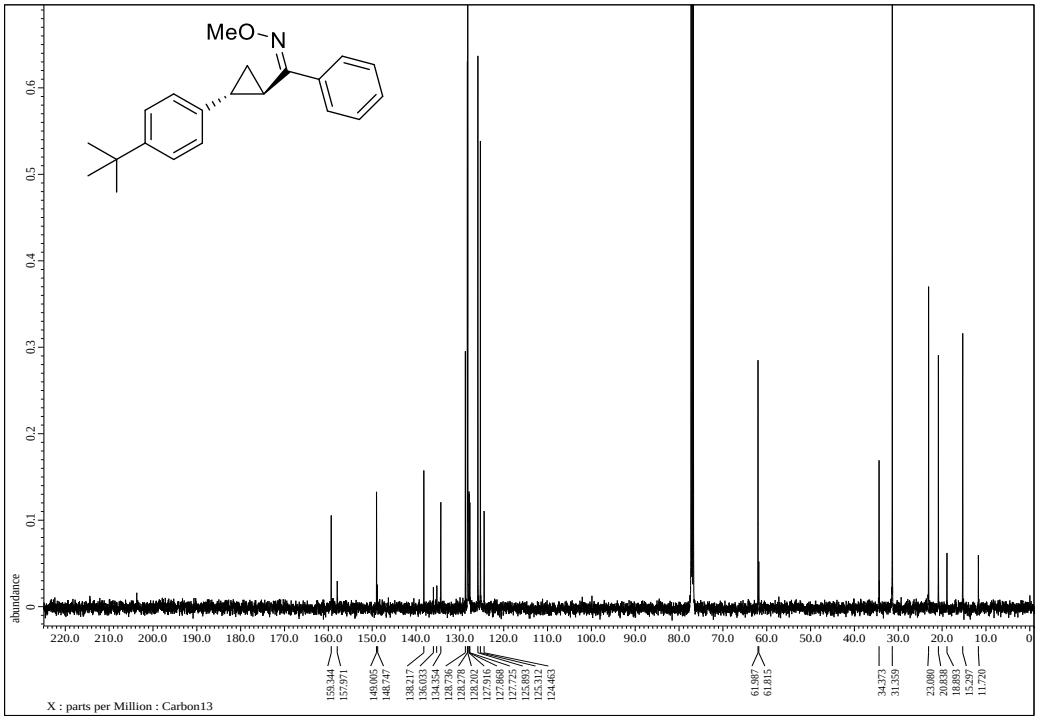
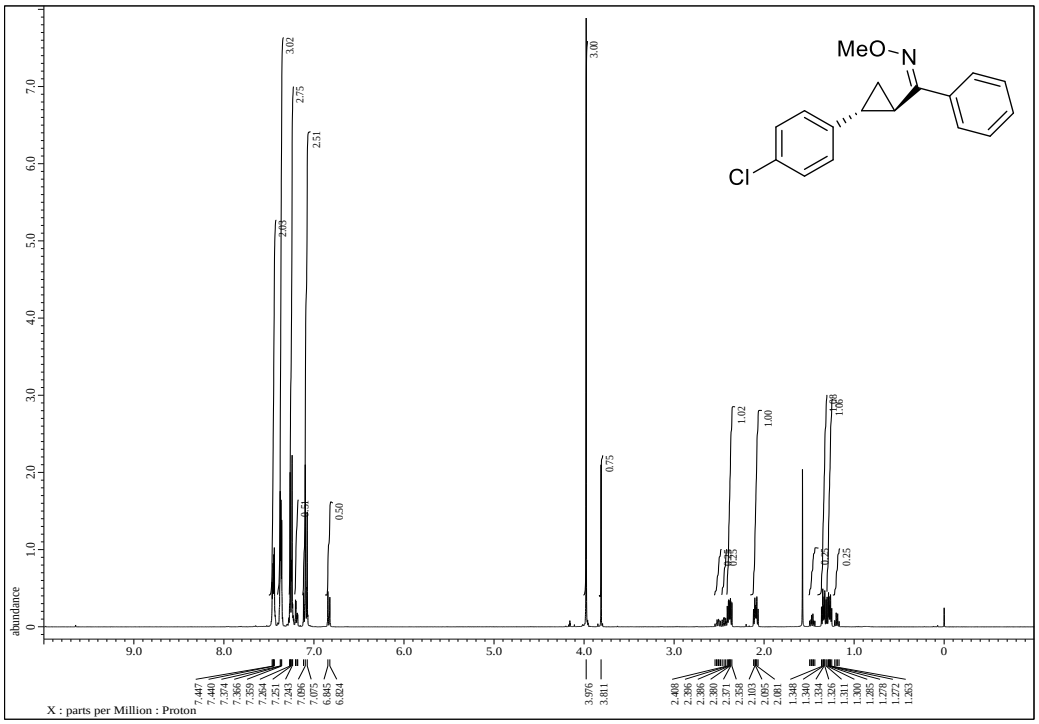
N
abundance
X : parts per Million : Proton


MeO
N
abundance
X : parts per Million : Carbon13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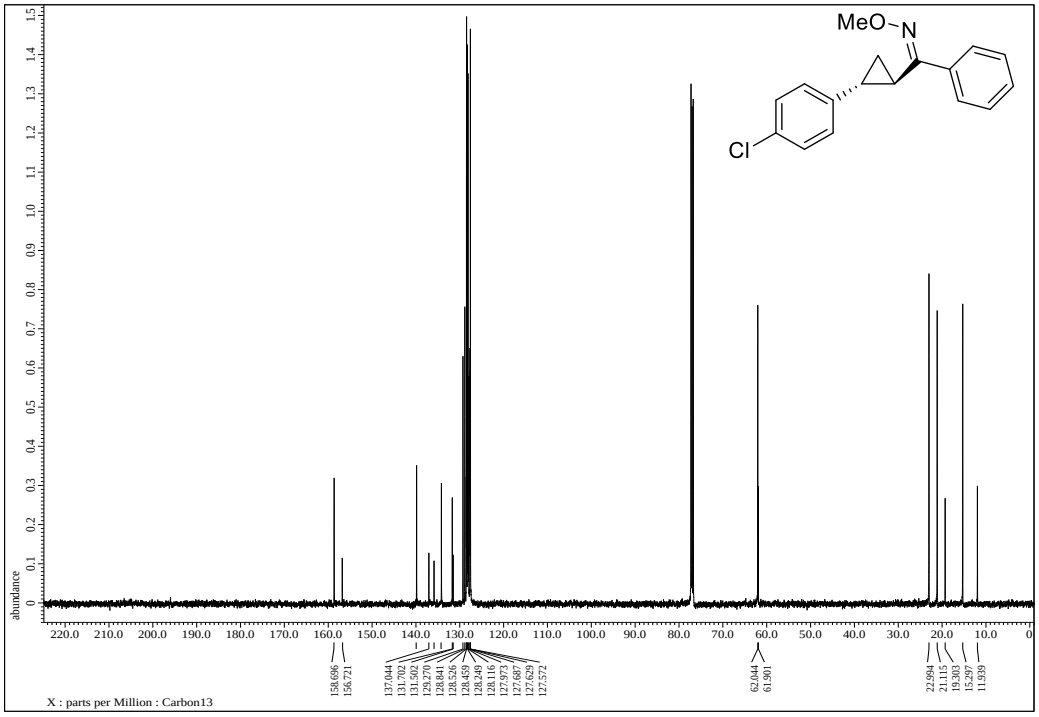
N
Cl
abundance
X : parts per Million : Proton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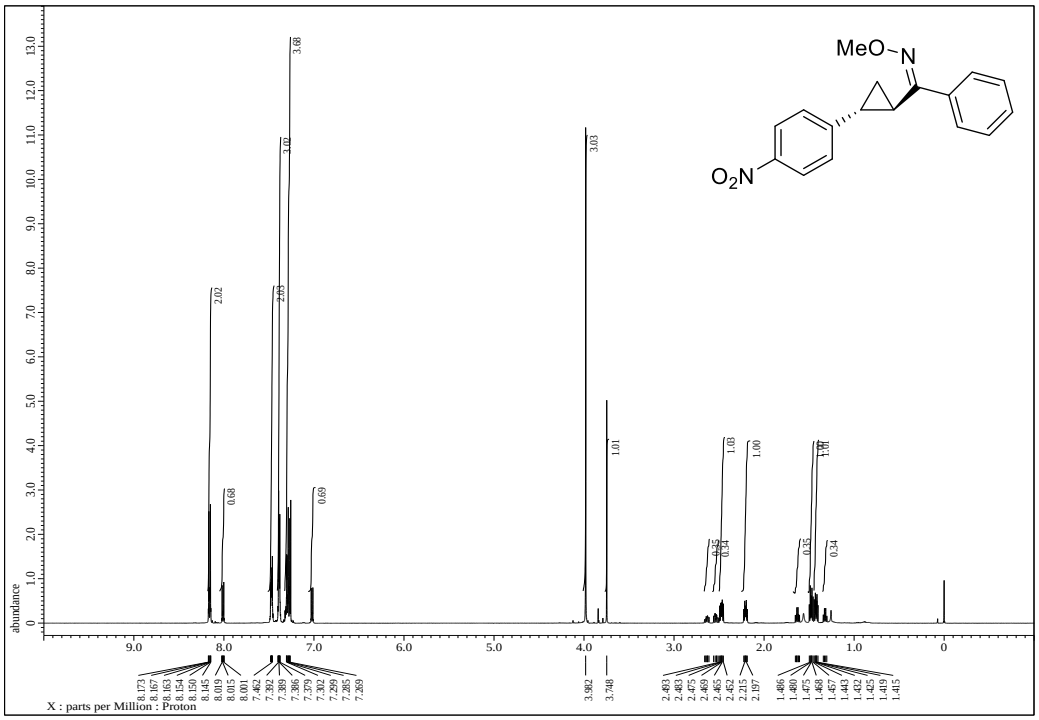
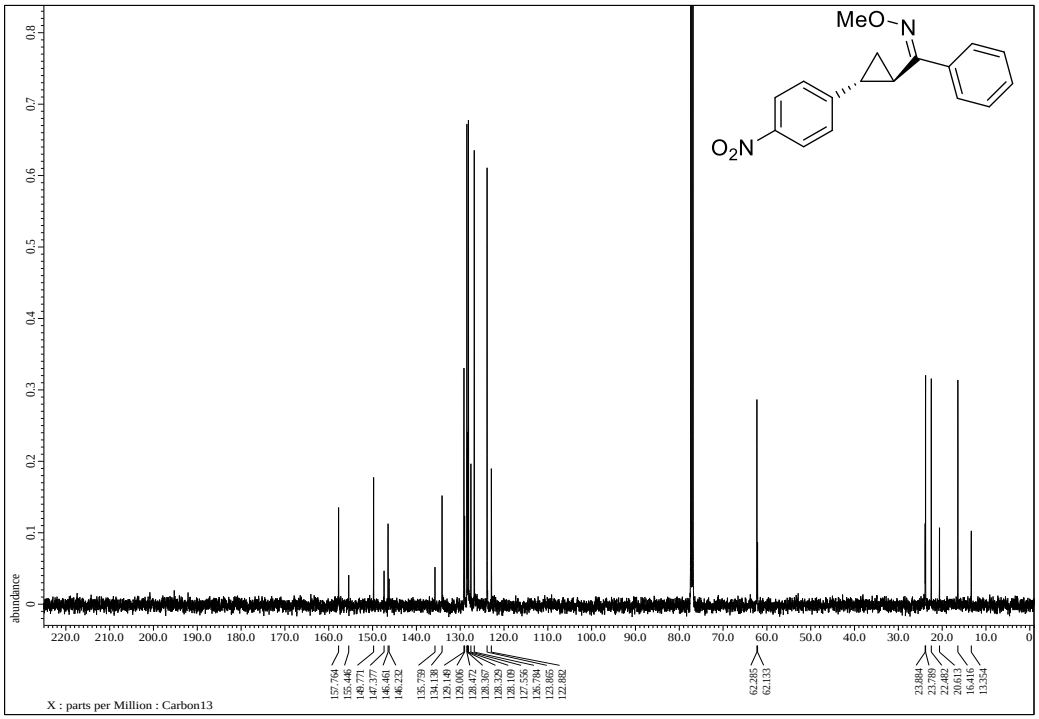
abundance
X : parts per Million : Carbon13


MeO
N
O2N
abundance
X : parts per Million : Proton


MeO
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O2N
abundance
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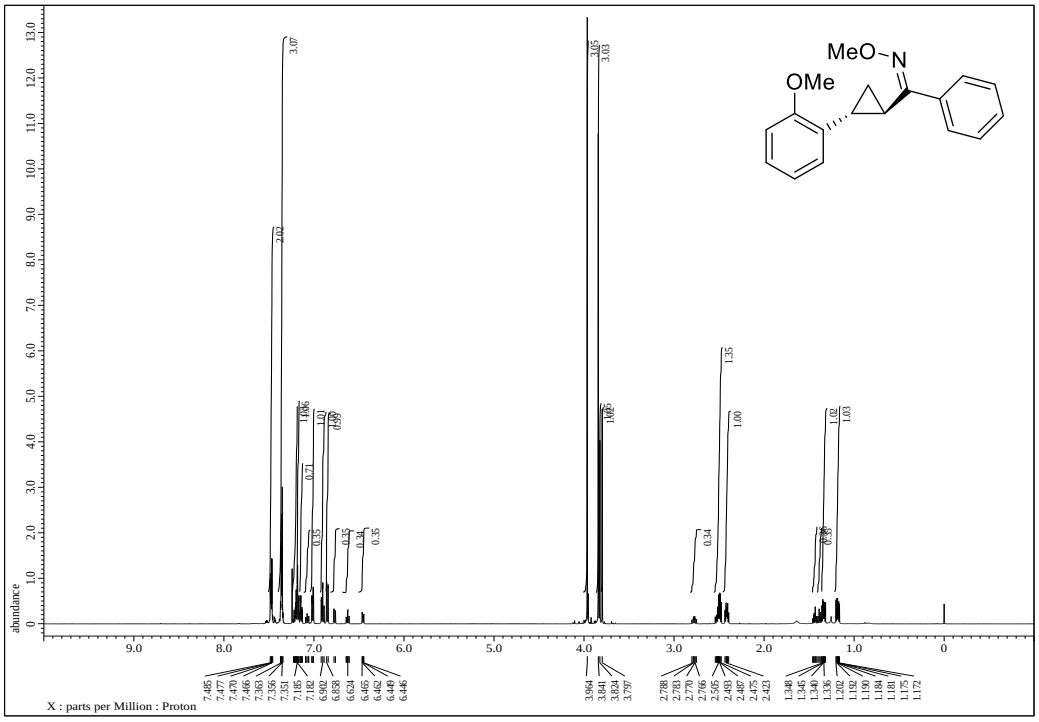
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OMe
abundance
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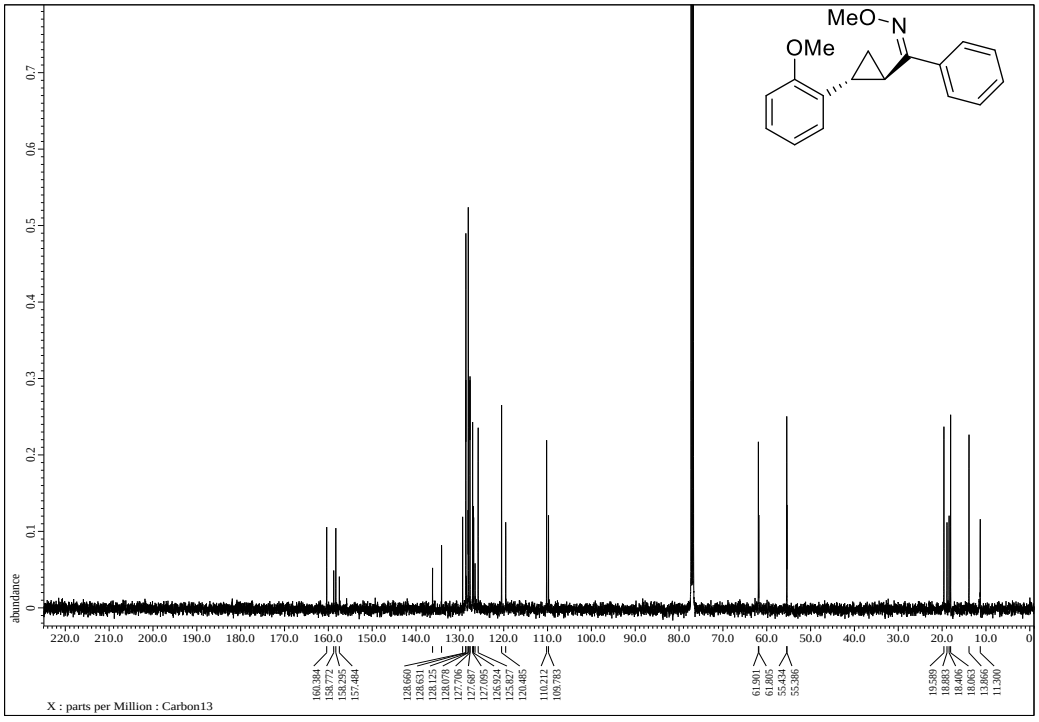
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abundance
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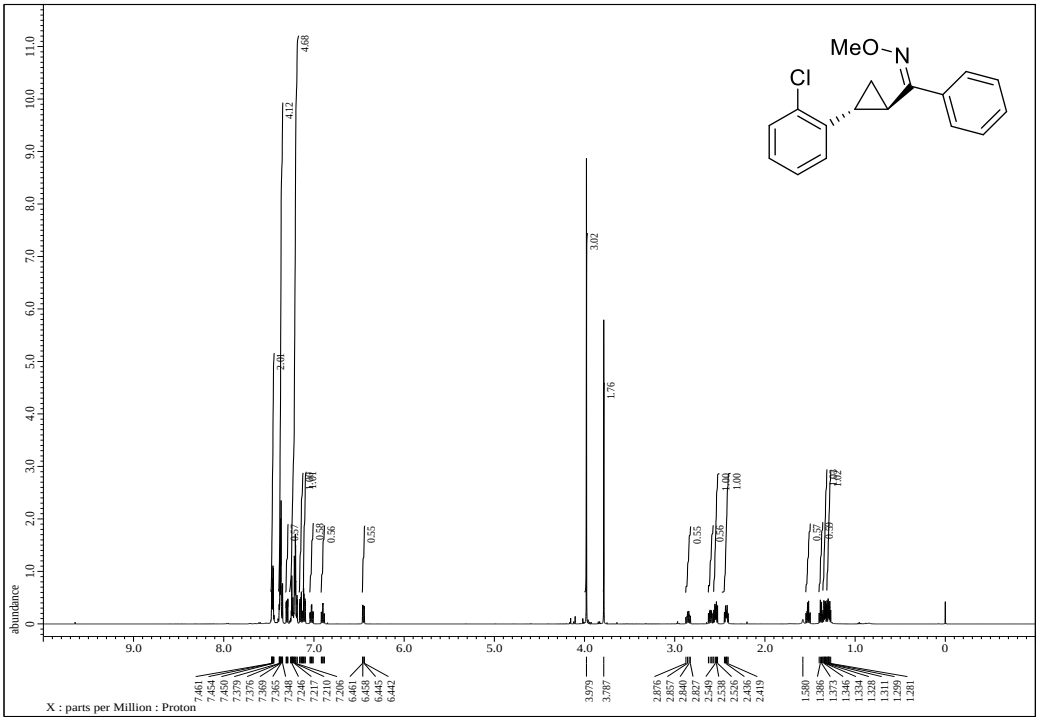
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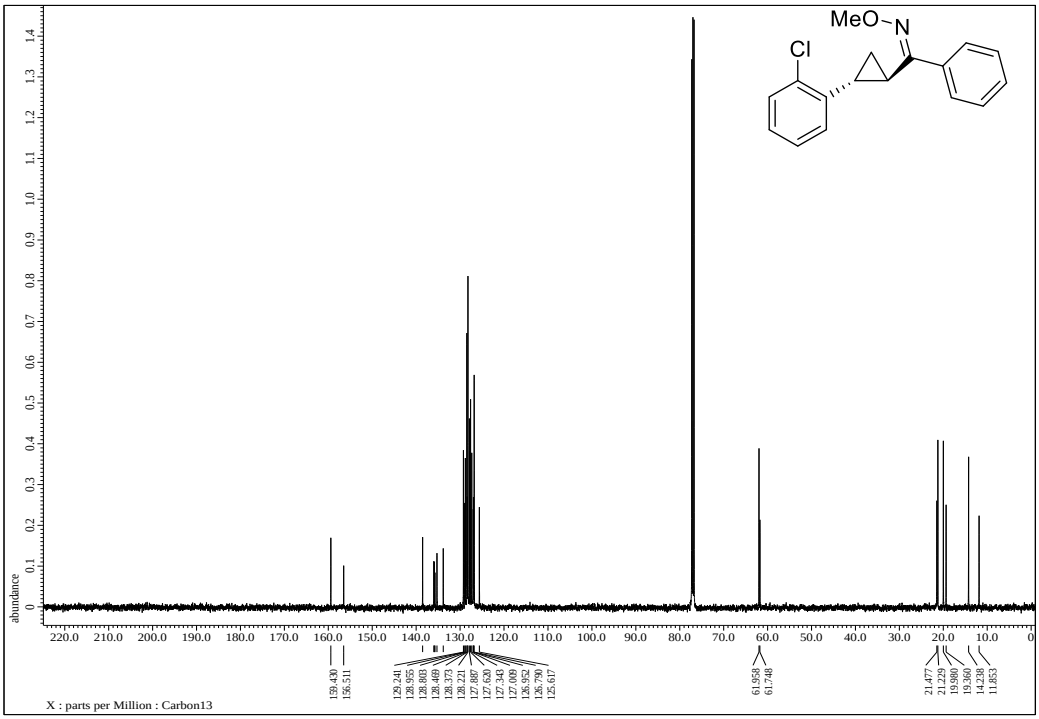
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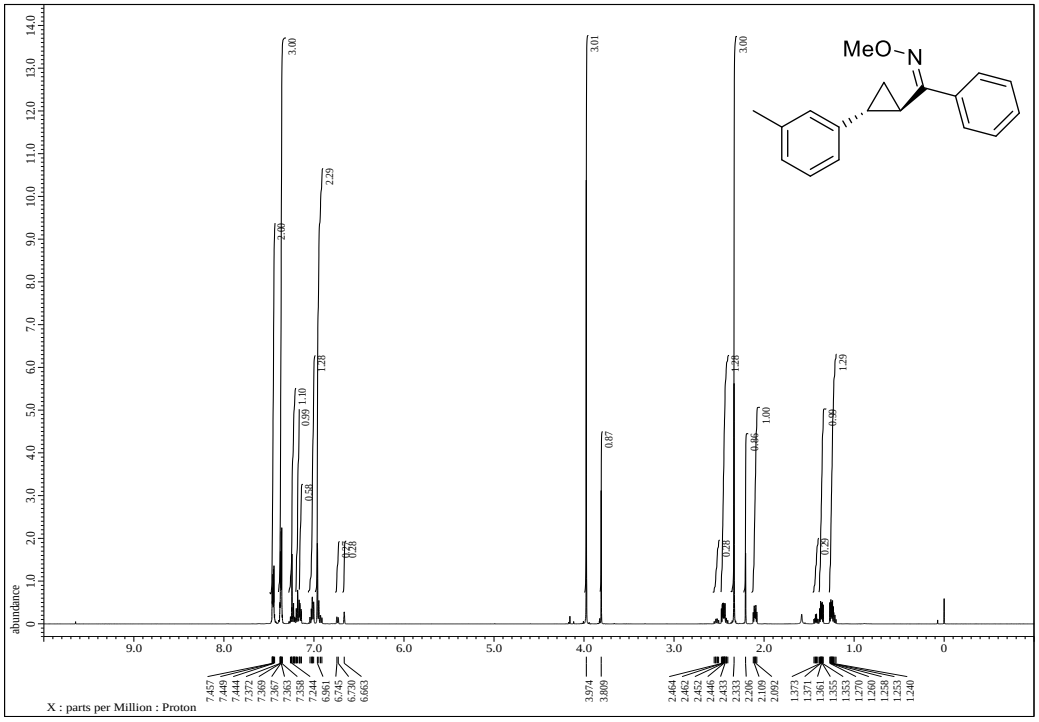
Cl
abundance
X : parts per Million : Carbon13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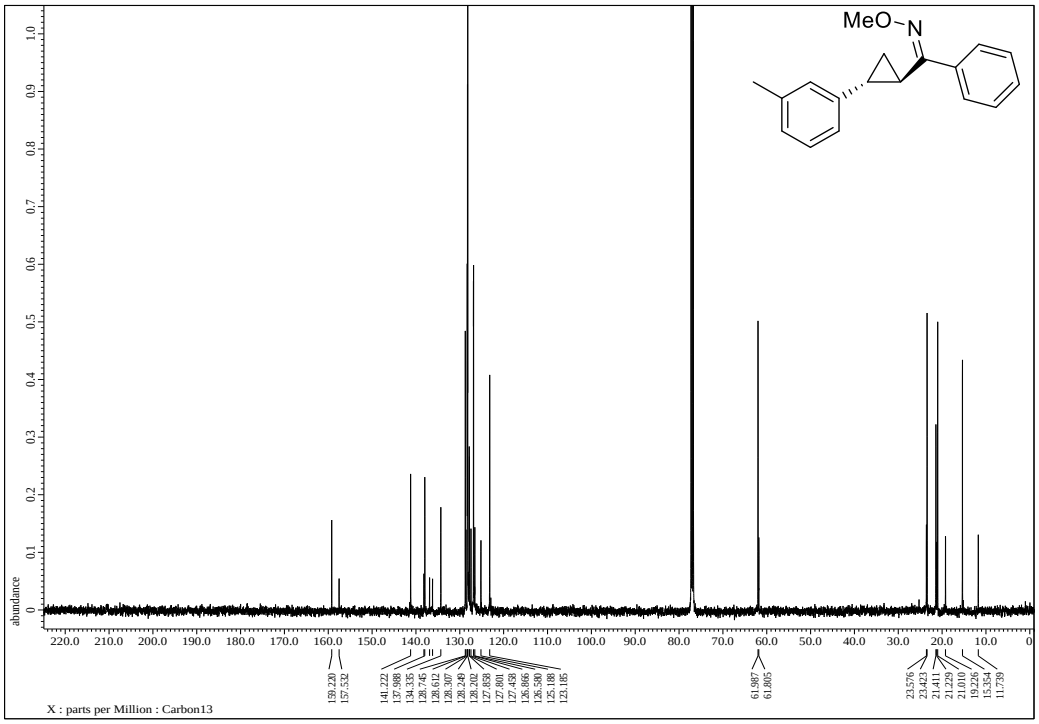
abundance
X : parts per Million : Proton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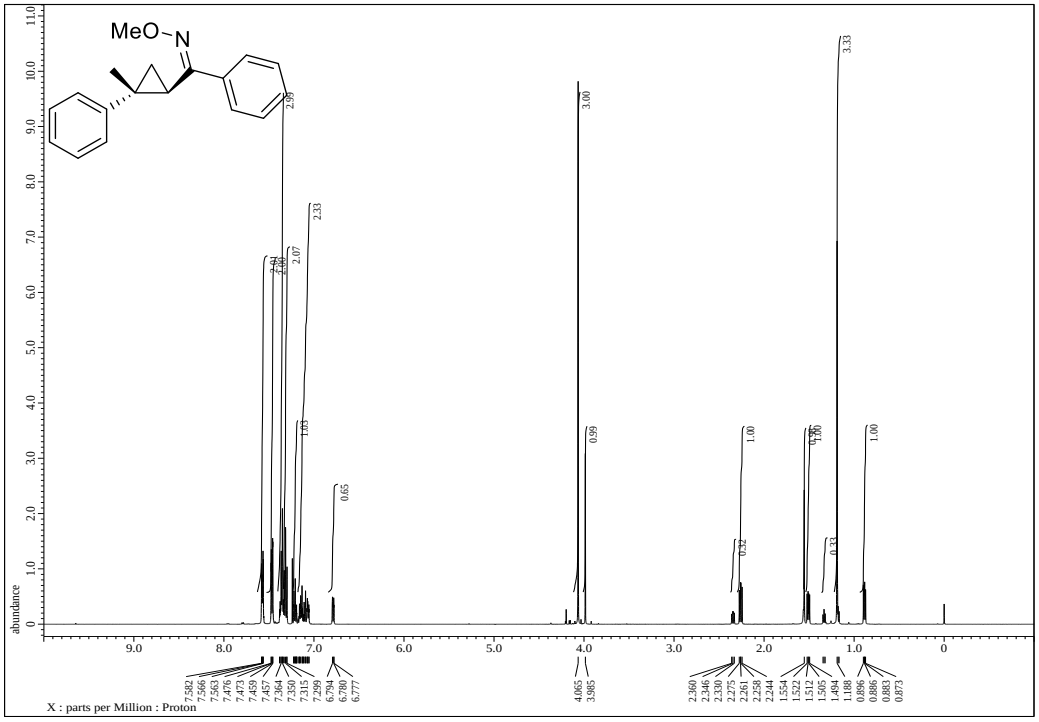
abundance
X : parts per Million : Carbon13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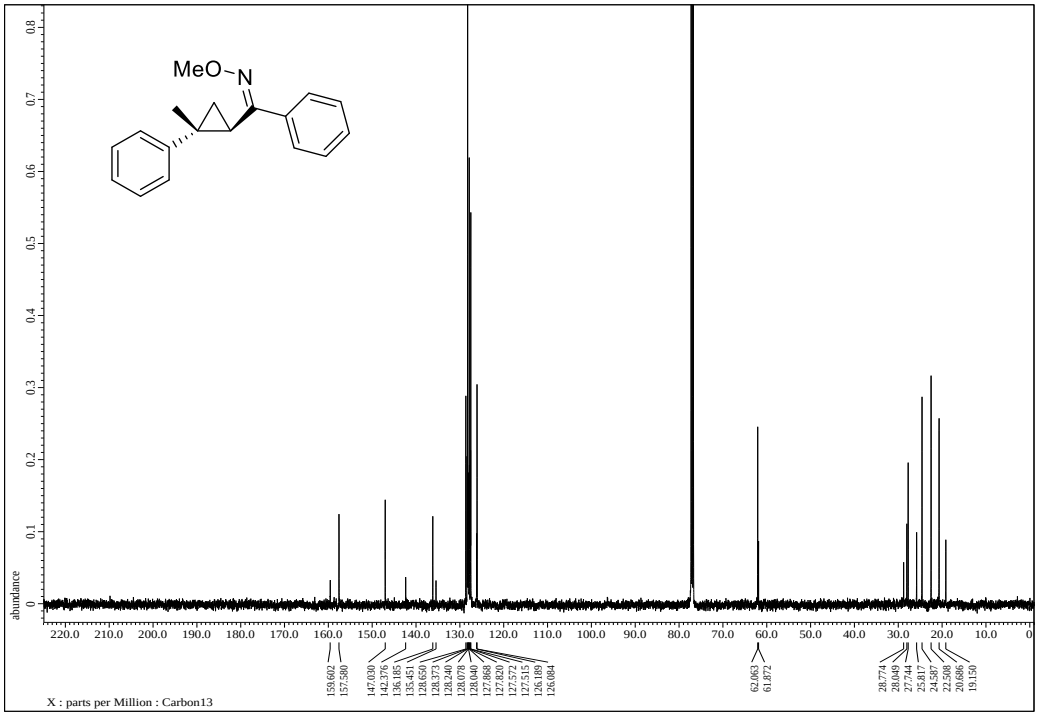
abundance
X : parts per Million : Proton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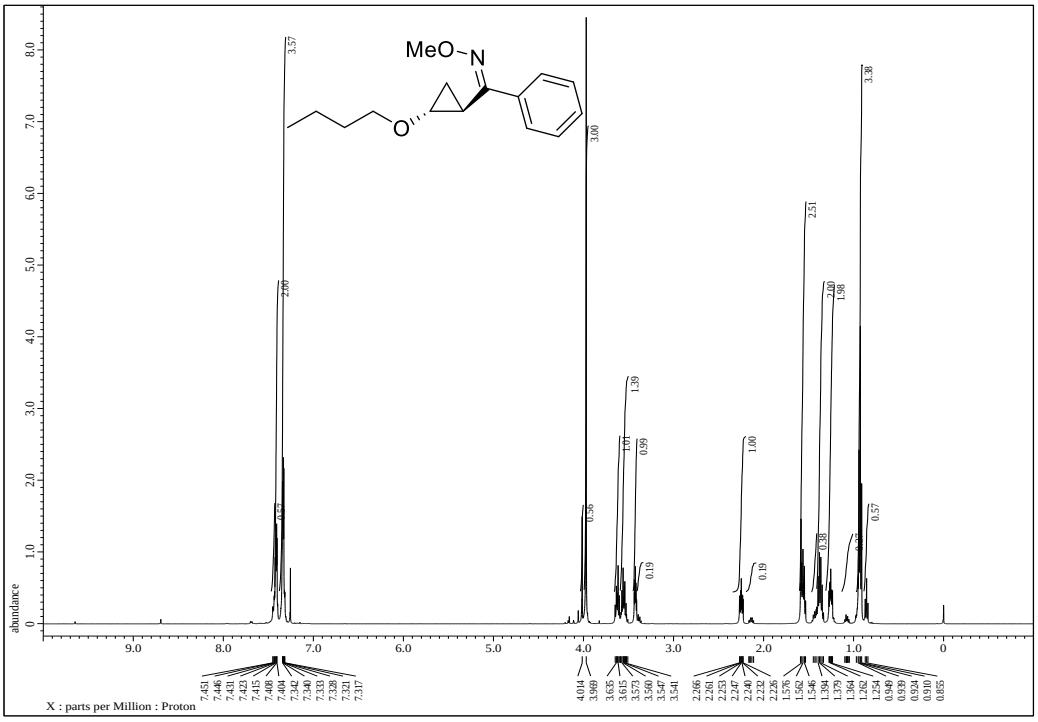
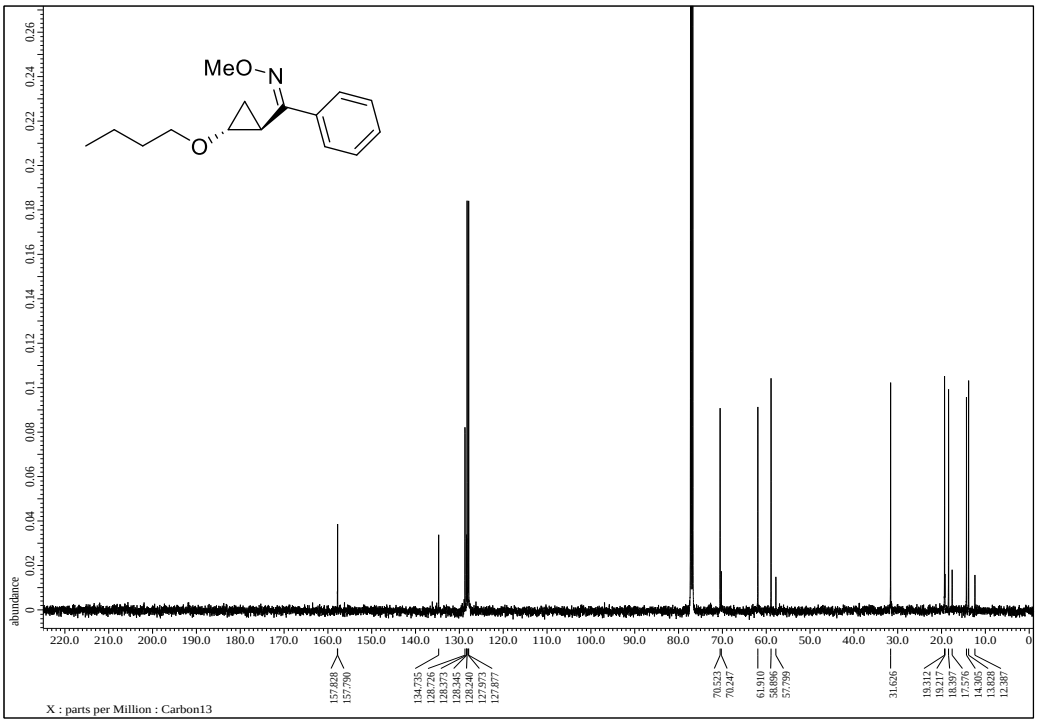
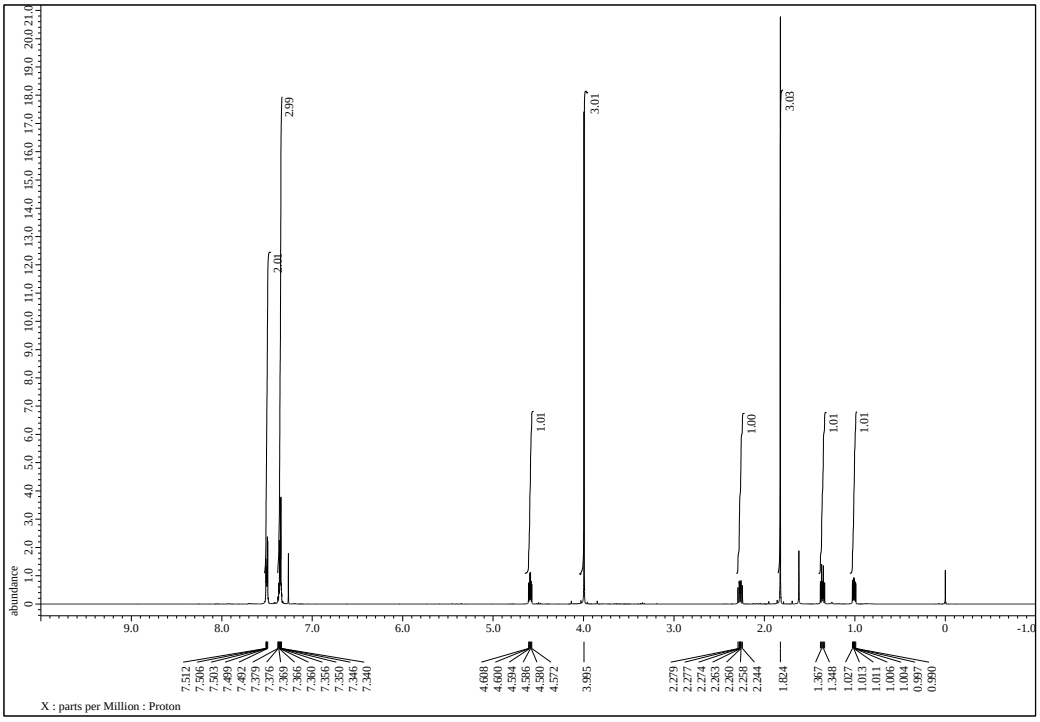
N
abundance
X : parts per Million : Carbon13


MeO
N
O
abundance
X : parts per Million : Proton


MeO
N
O
abundance
X : parts per Million : Carbon13


abundance
2.99
2.01
3.01
3.03
1.01
1.00
1.01
1.01
7.512
7.506
7.503
7.499
7.492
7.379
7.376
7.369
7.366
7.360
7.356
7.350
7.346
7.340
4.608
4.600
4.594
4.586
4.580
4.572
3.995
2.279
2.277
2.274
2.263
2.260
2.258
2.244
1.824
1.367
1.348
1.027
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1.011
1.006
1.004
0.997
0.990
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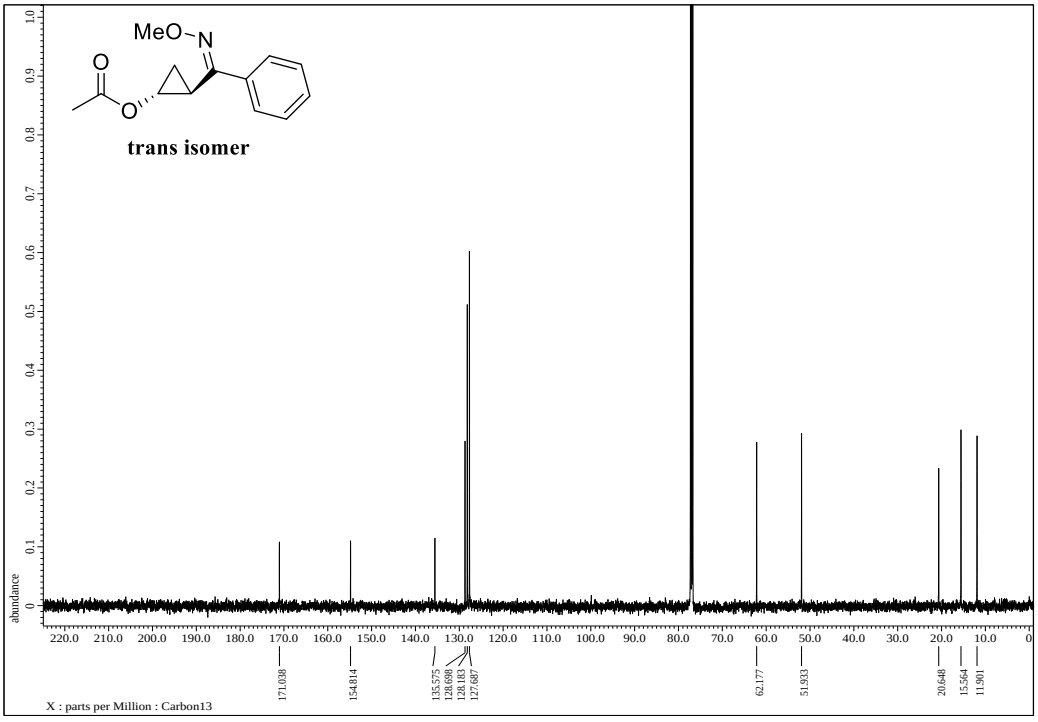
MeO
N
O
O
trans isomer
abundance
171.038
154.814
135.575
128.698
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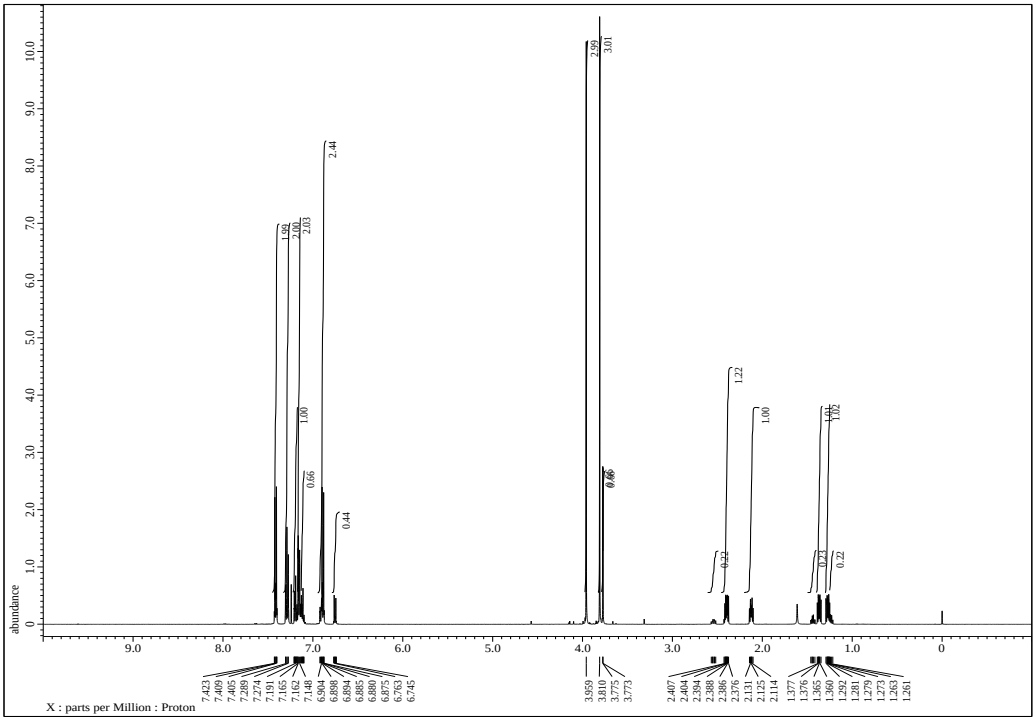
127.687
62.177
51.933
20.648
15.564
11.901
X : parts per Million : Carbon13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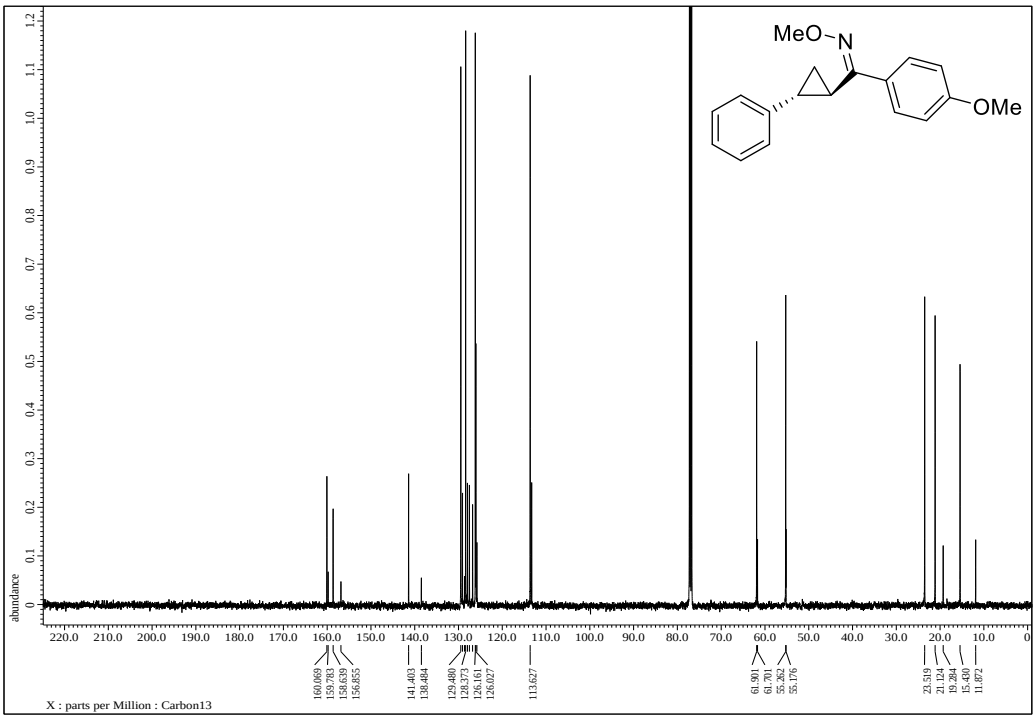
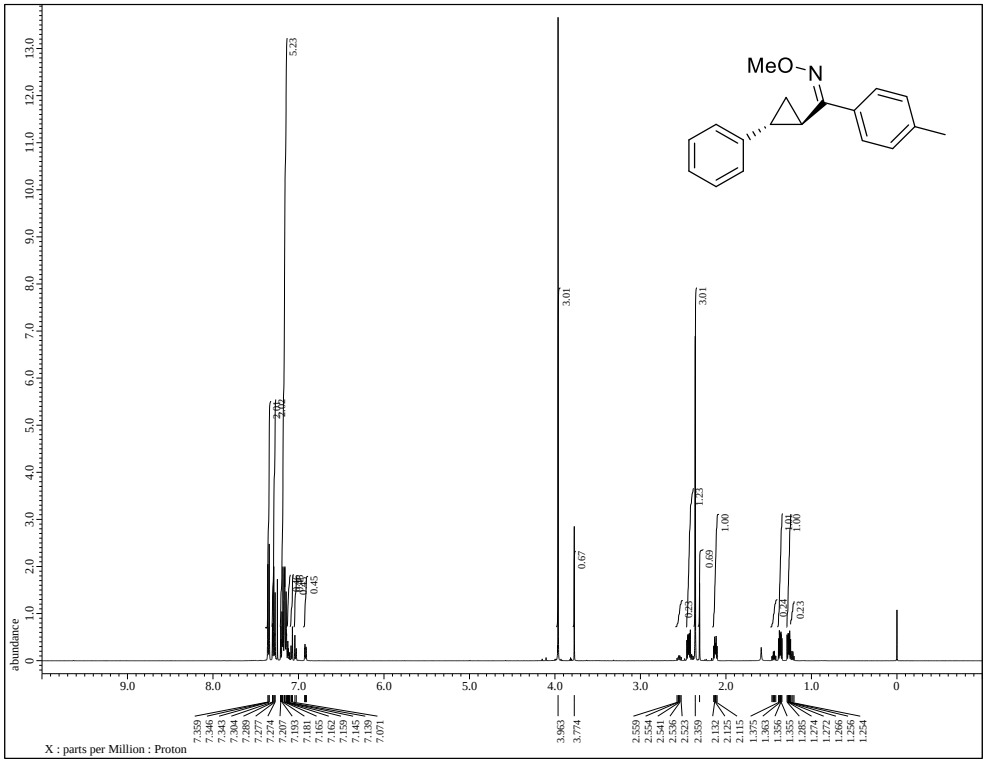

MeO
N
OMe
abundance
X : parts per Million : Carbon13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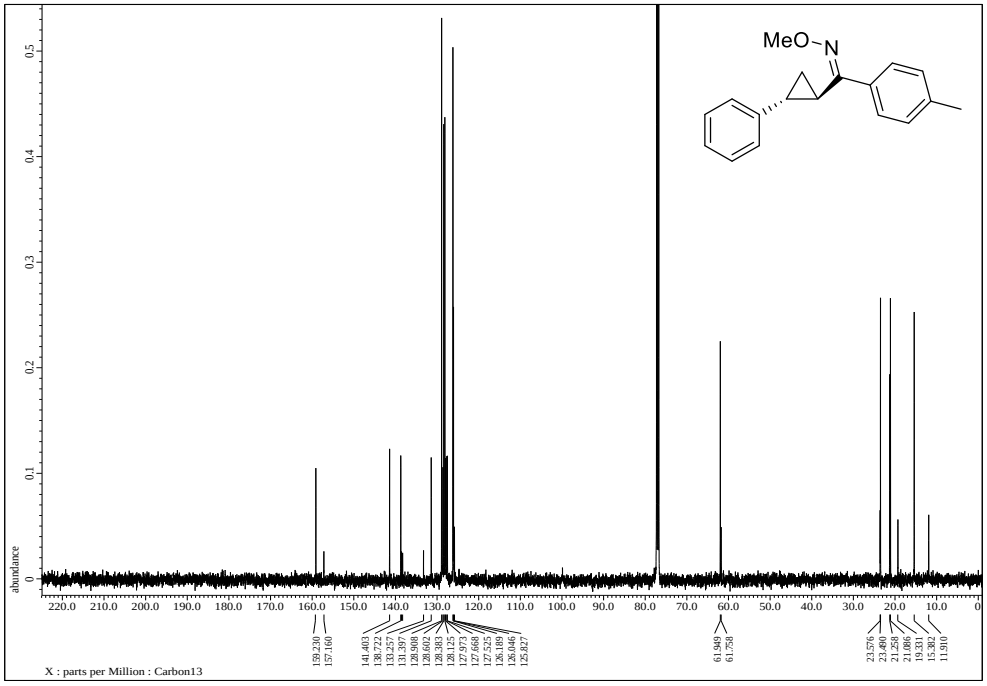
X : parts per Million : Proton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abundance
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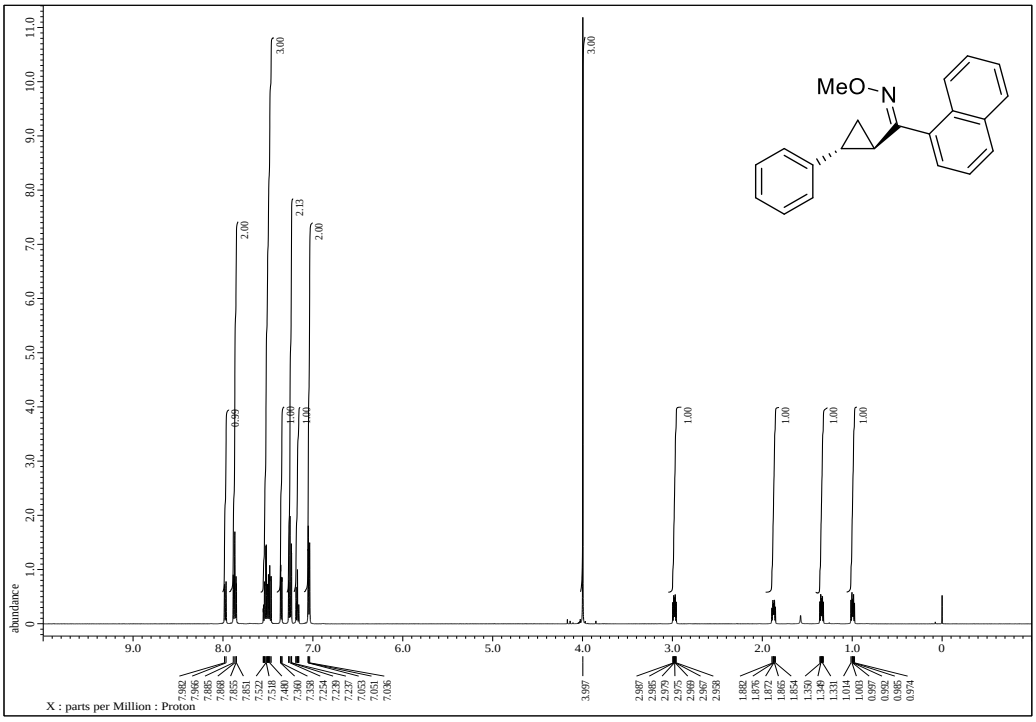
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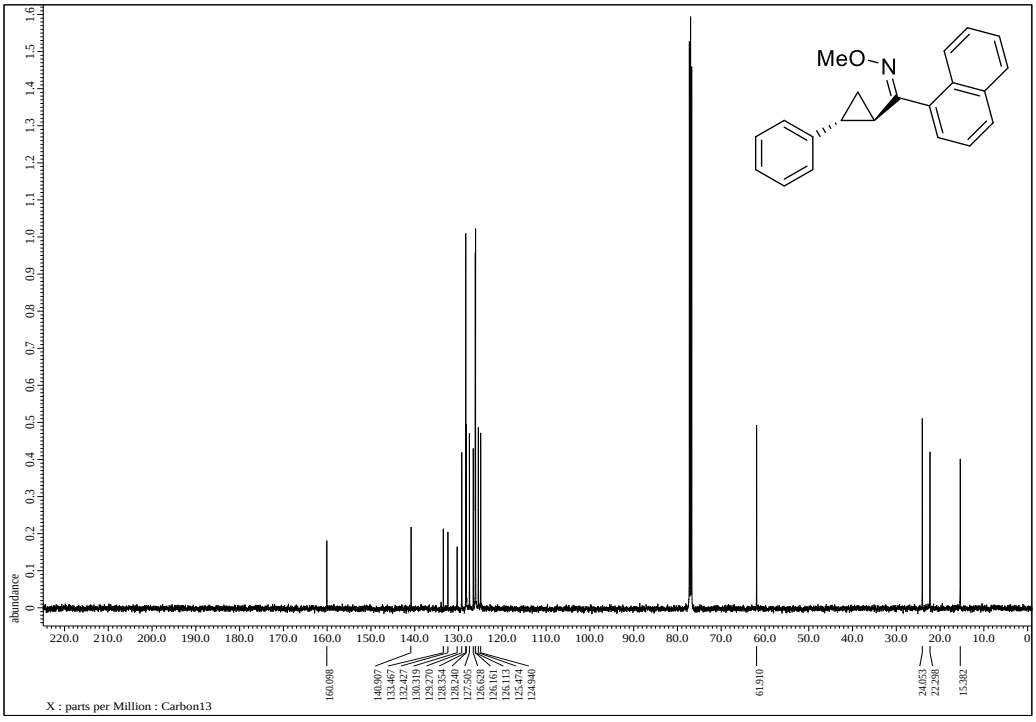
N
abundance
X : parts per Million : Proton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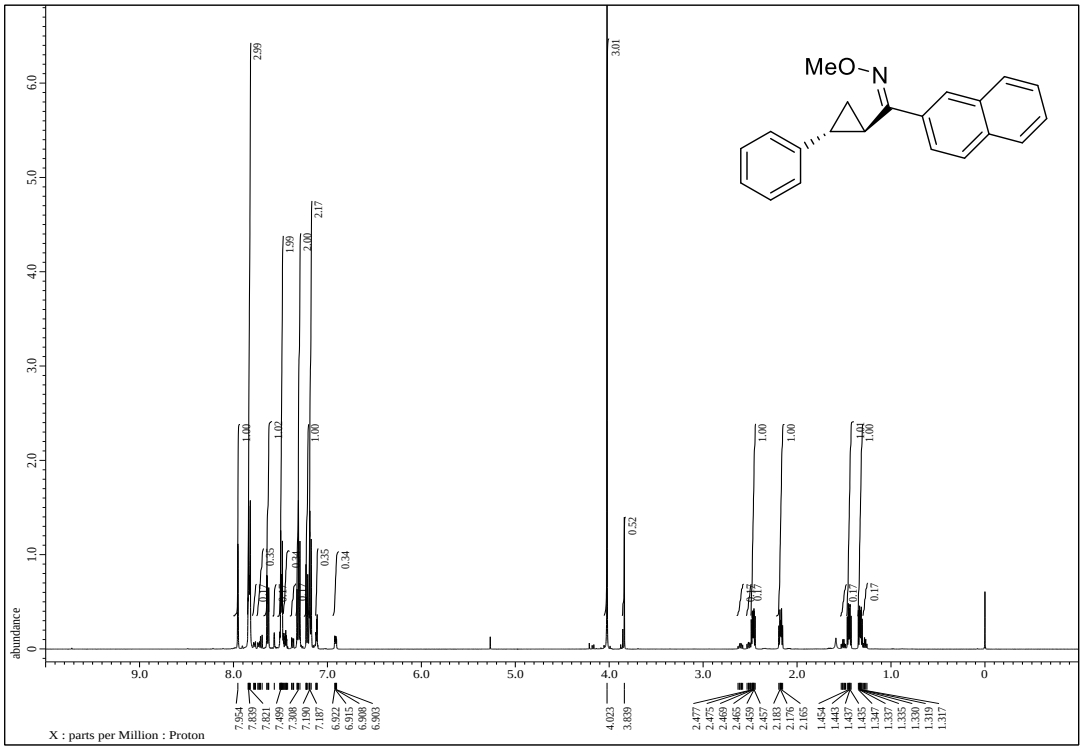
abundance
X : parts per Million : Carbon13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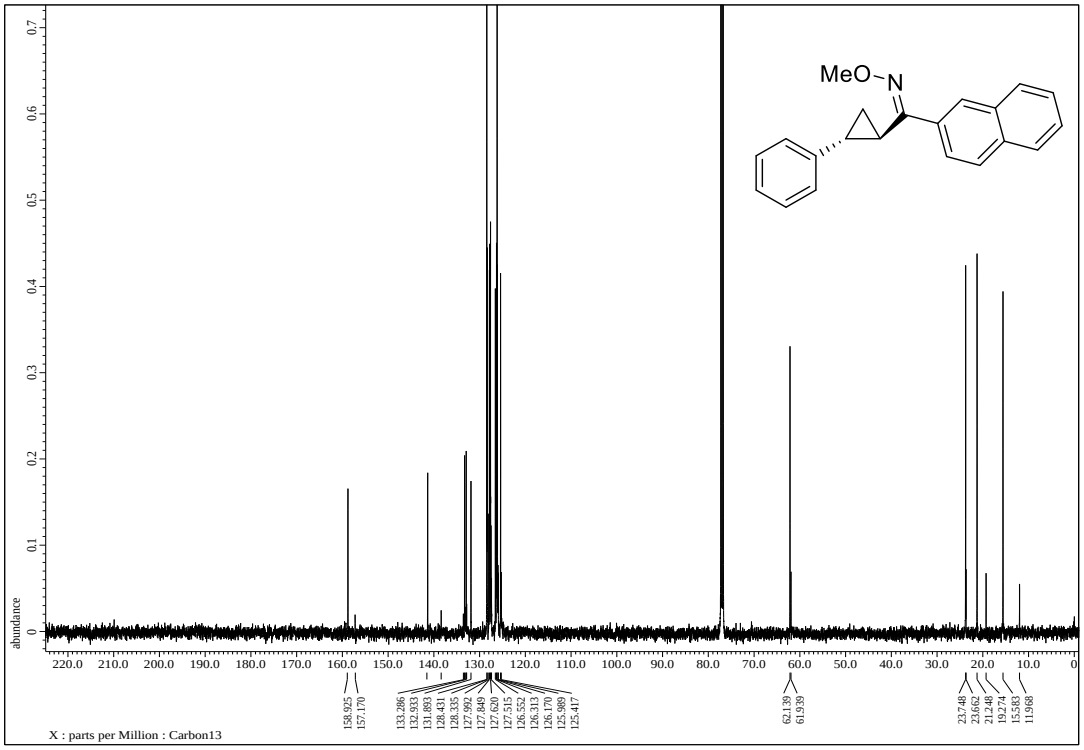
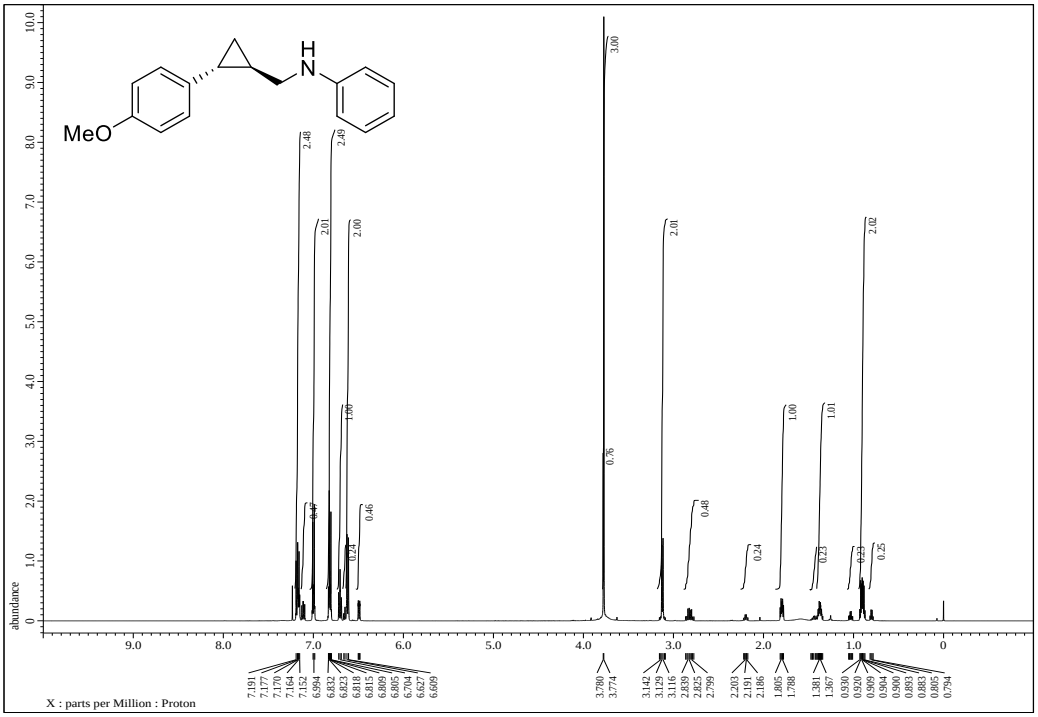
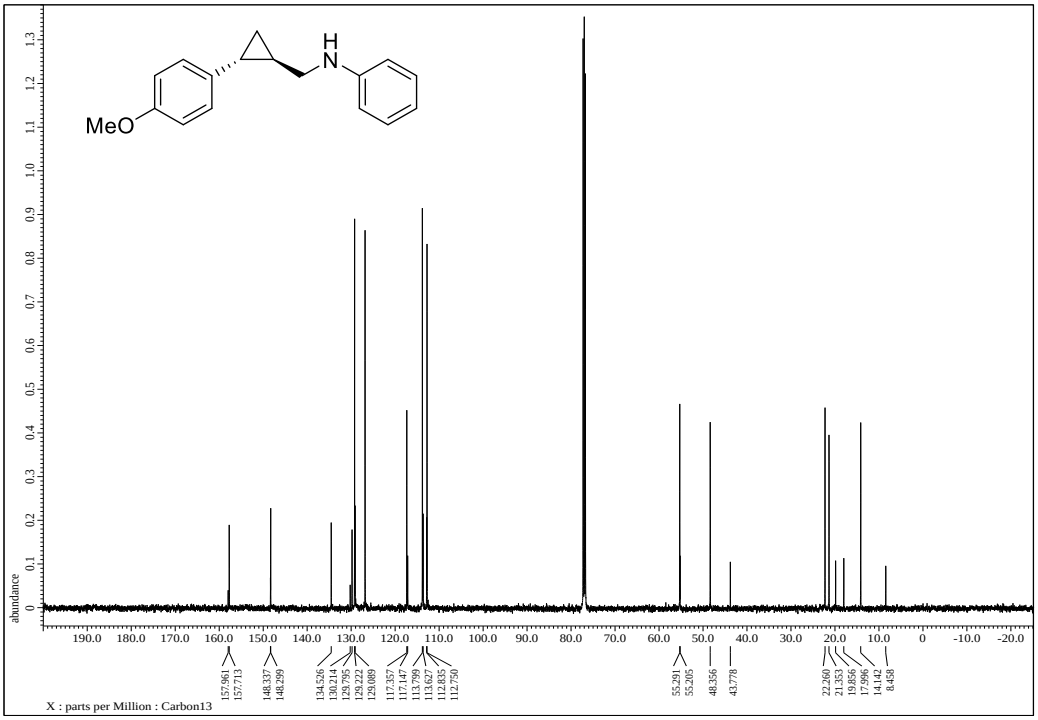
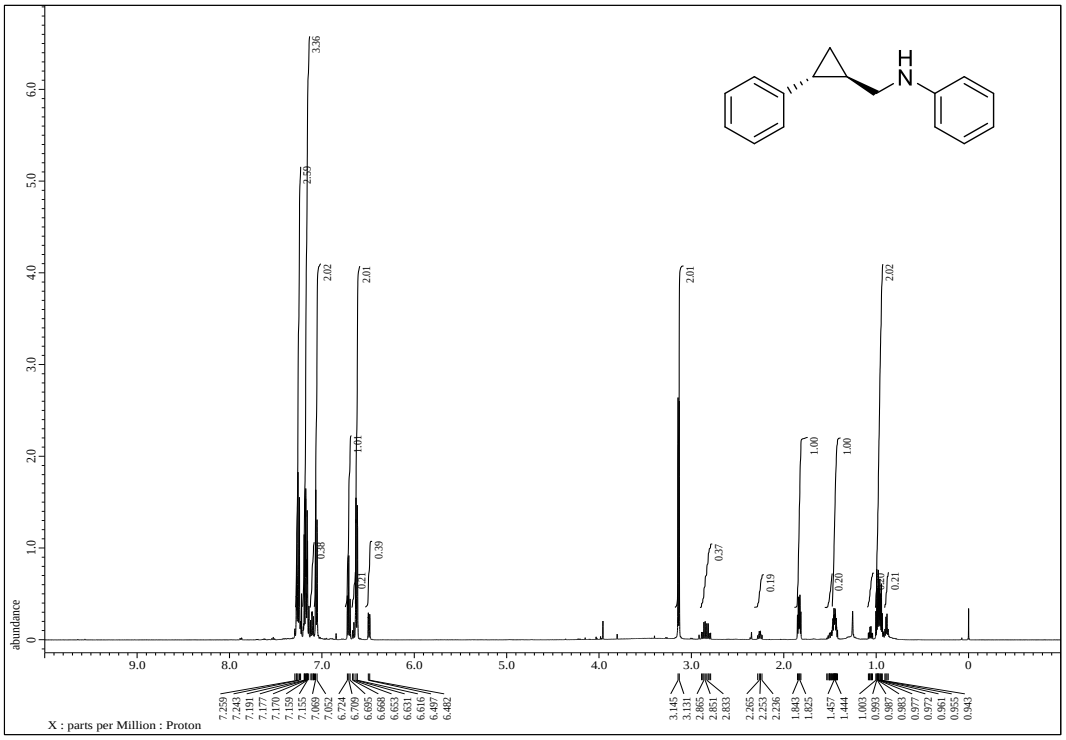
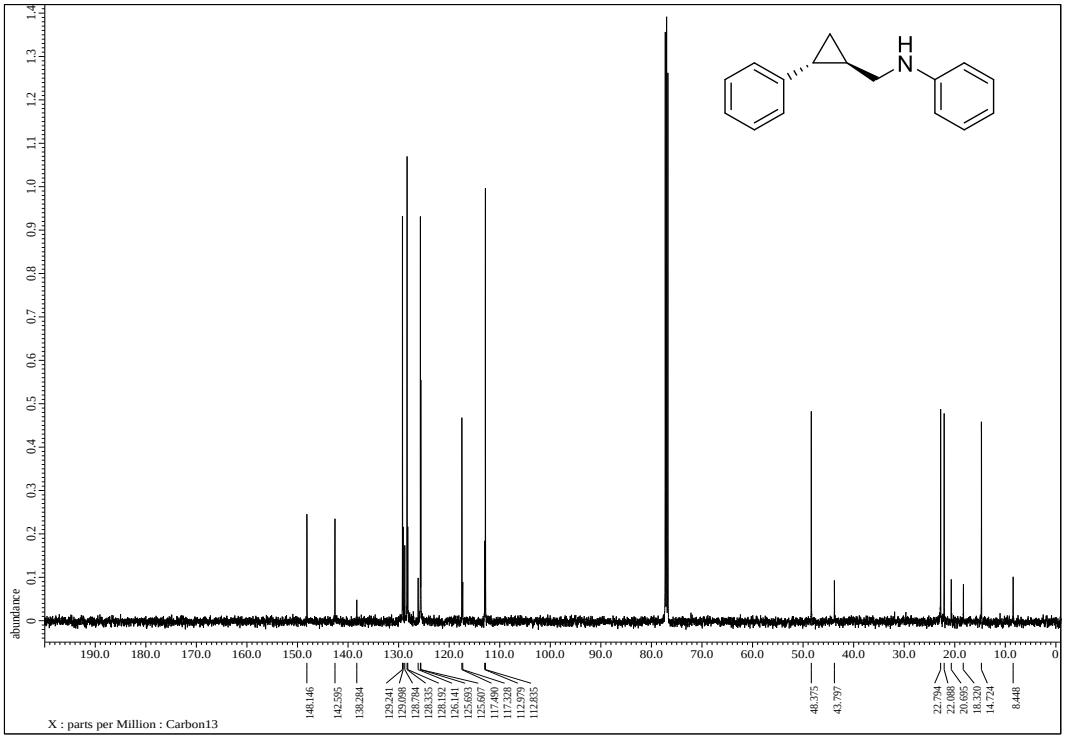
abundance
X : parts per Million : Proton


MeO
N
abundance
X : parts per Million : Carbon13


MeO
H
N
abundance
X : parts per Million : Proton


MeO
H
N
abundance
X : parts per Million : Carbon13


abundance
X : parts per Million : Proton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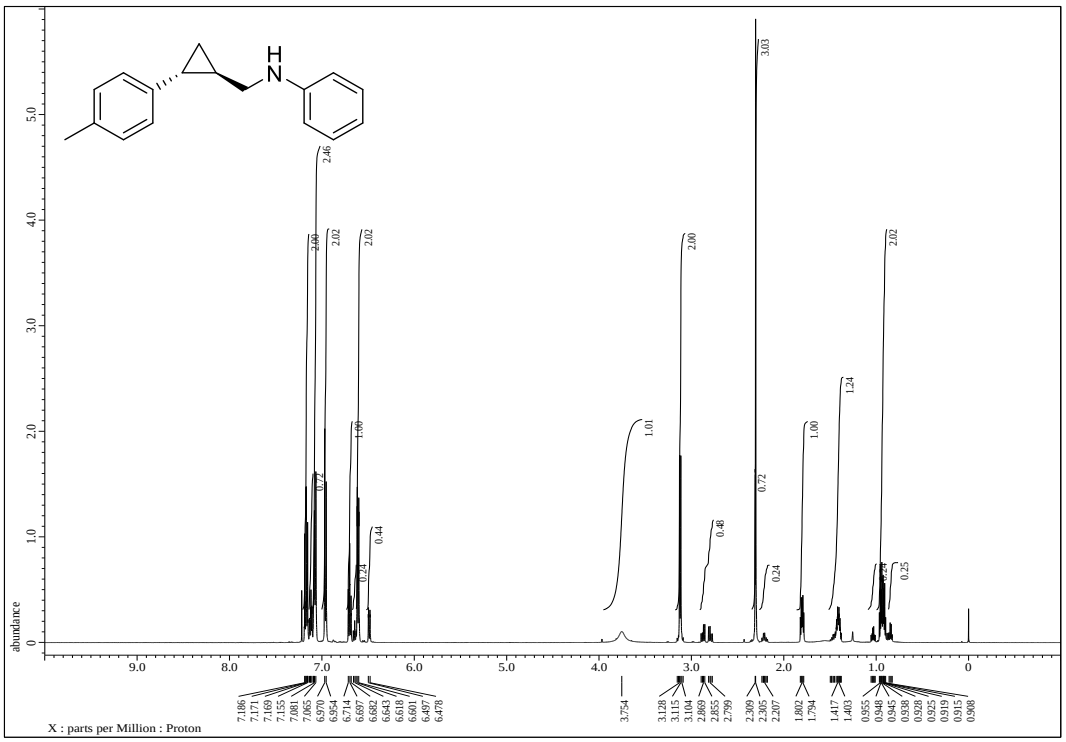
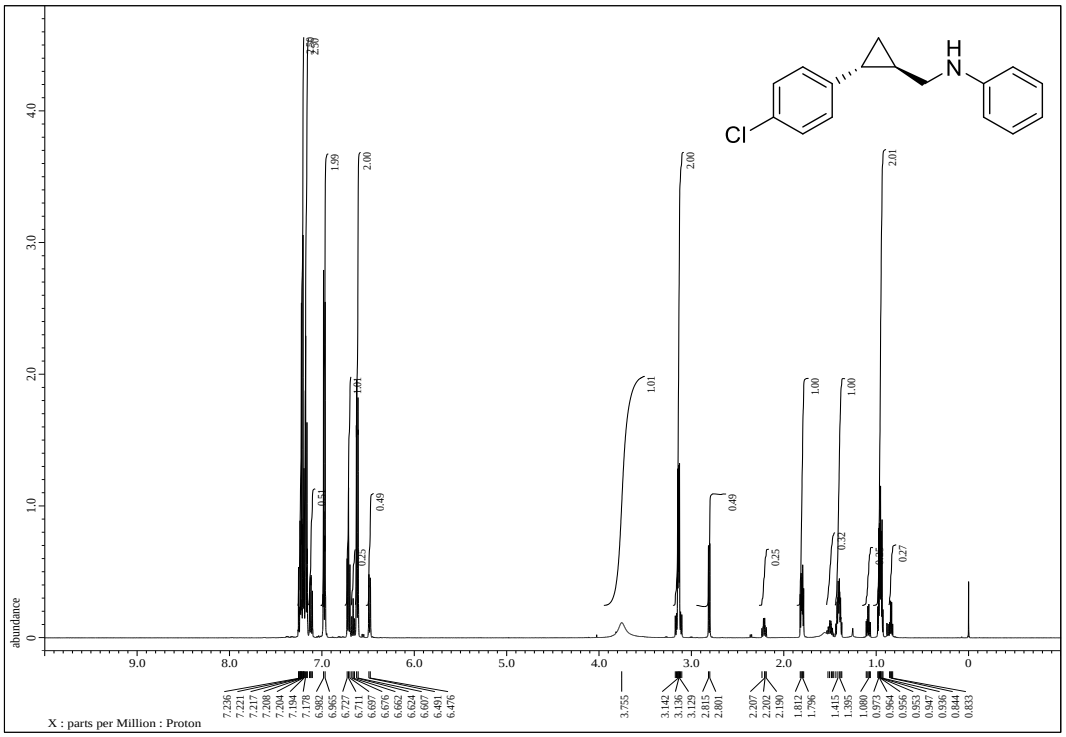
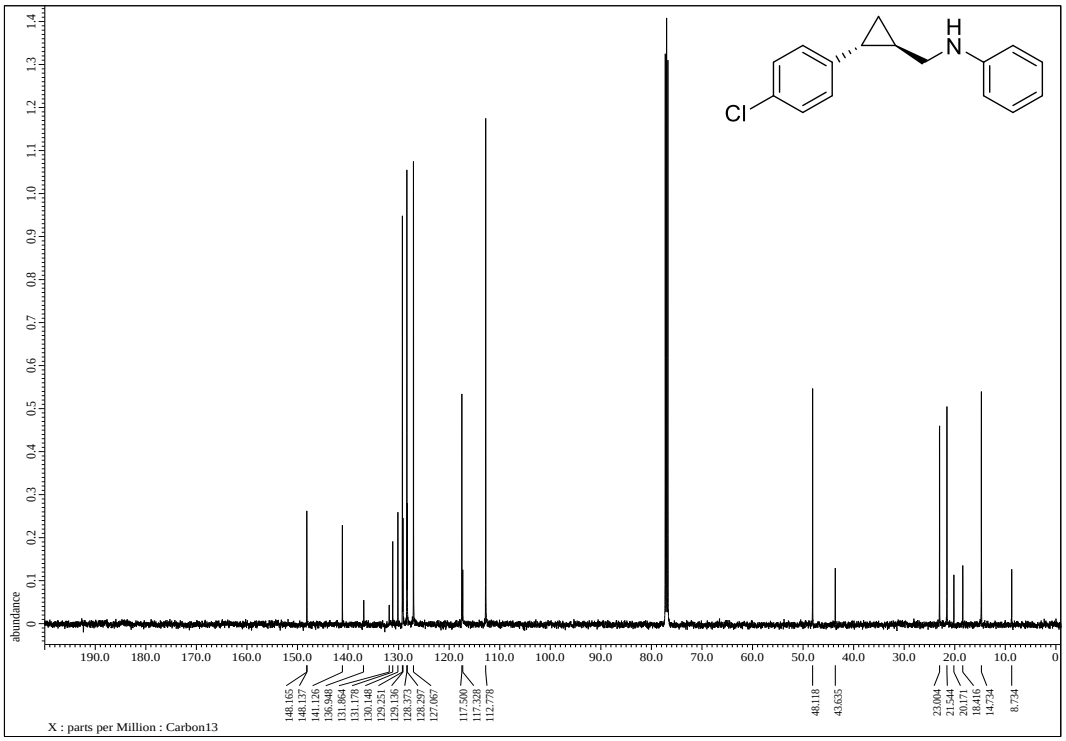
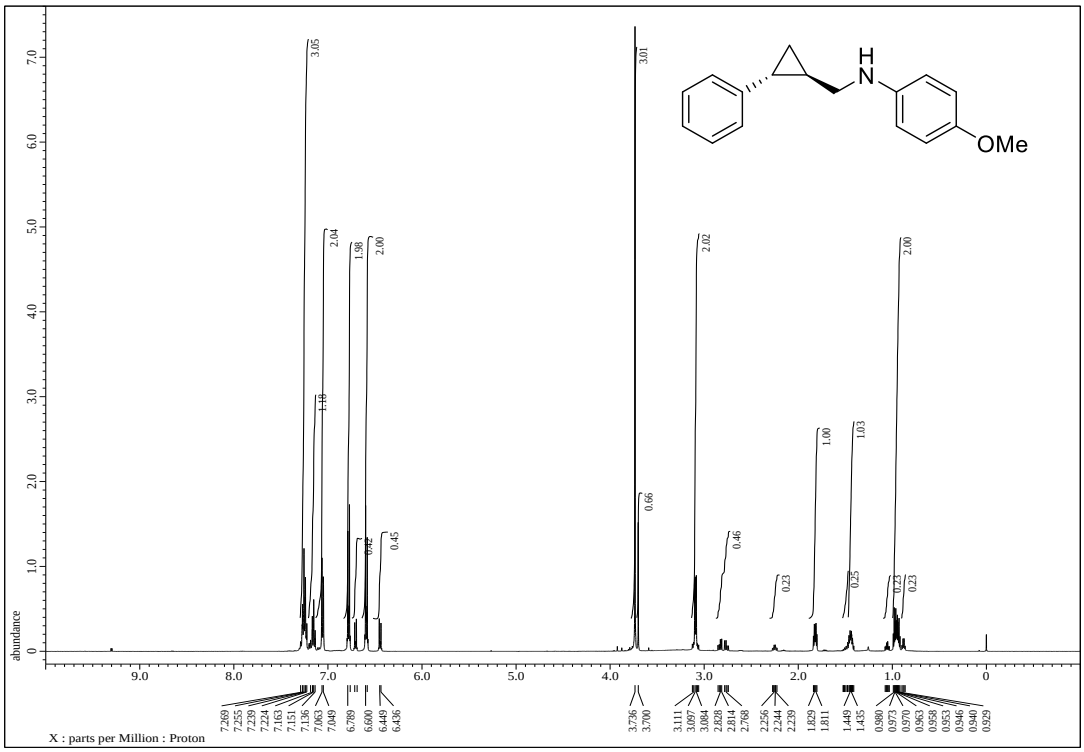
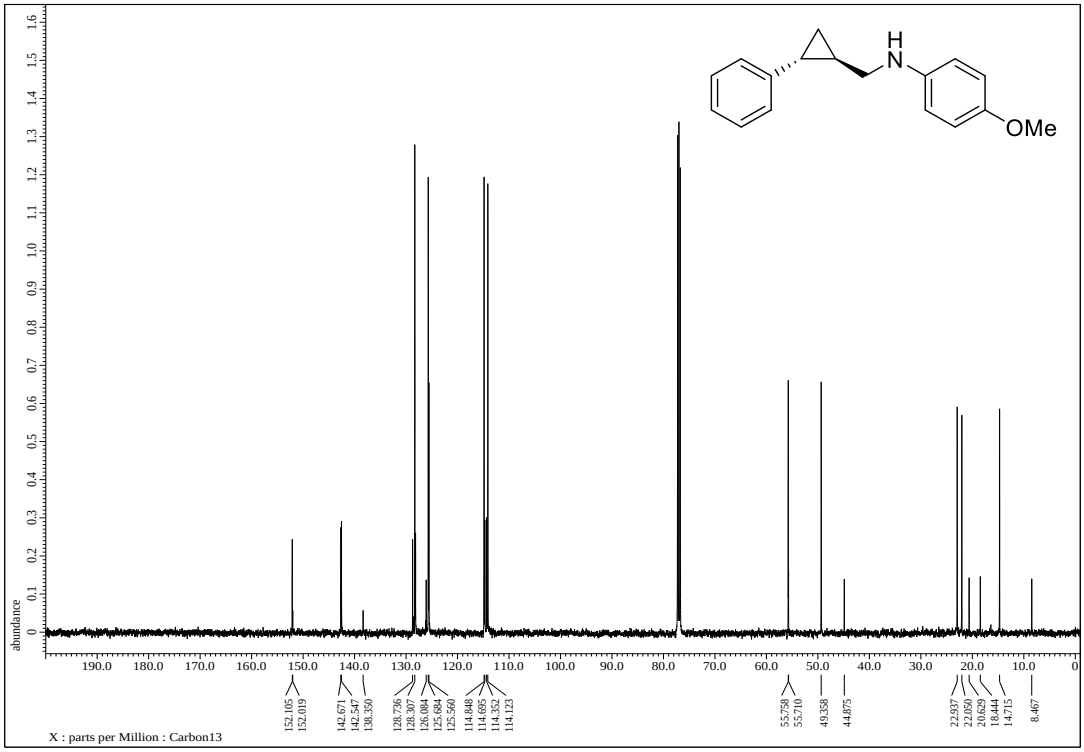

abundance
X : parts per Million : Proton


abundance
X : parts per Million : Carbon13


Cl
H
N
abundance
X : parts per Million : Proton


Cl
H
N
abundance
X : parts per Million : Carbon13


abundance
X : parts per Million : Proton
OMe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X : parts per Million : Carbon13
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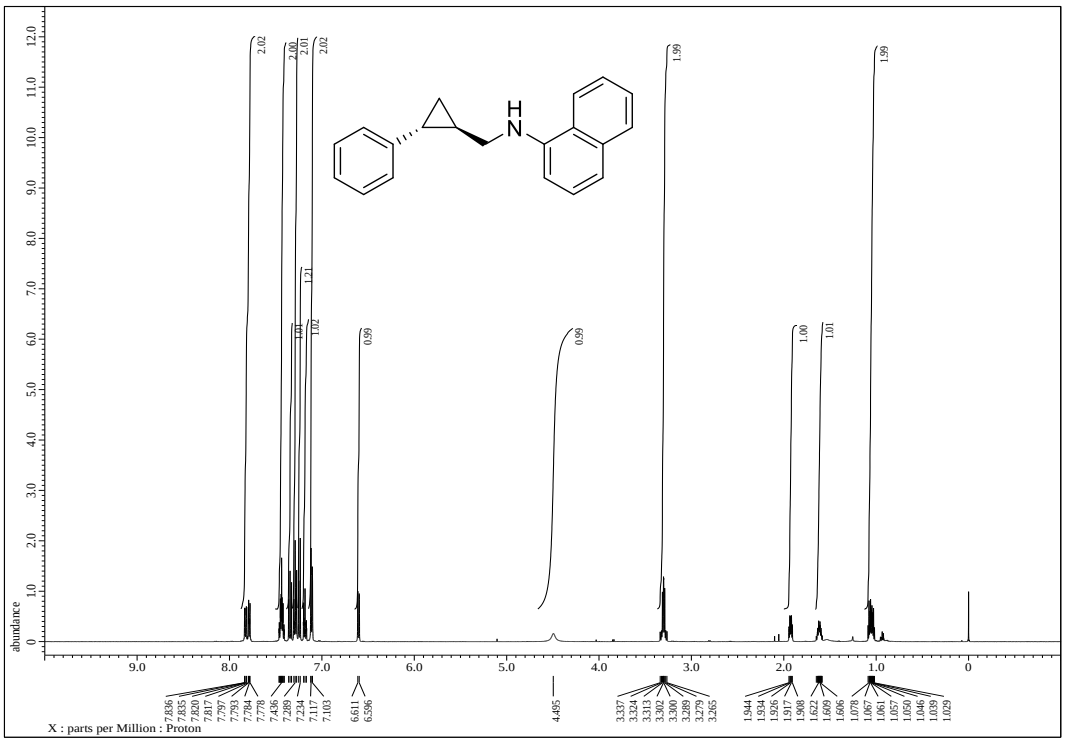
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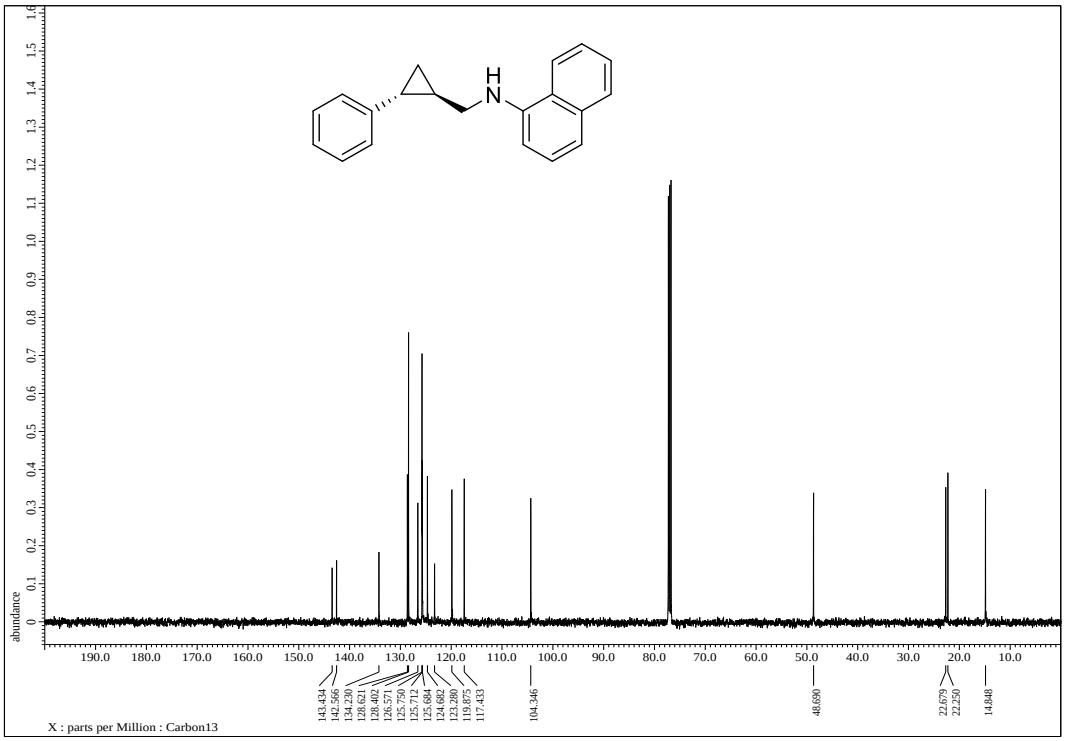
X : parts per Million : Proton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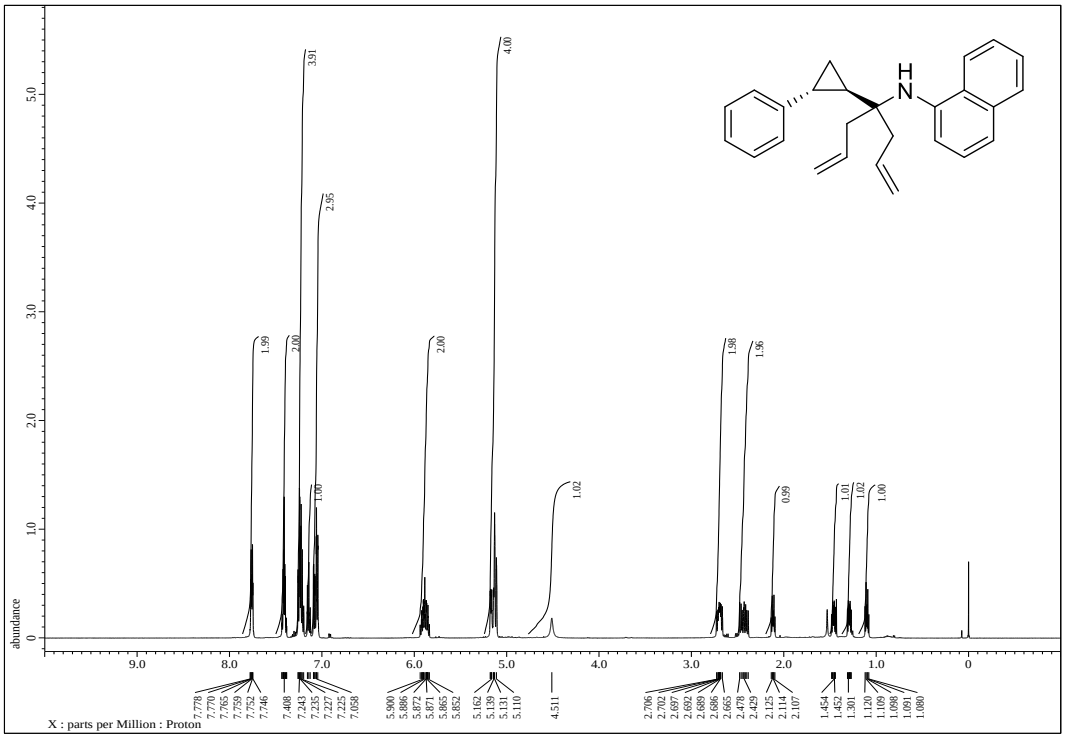
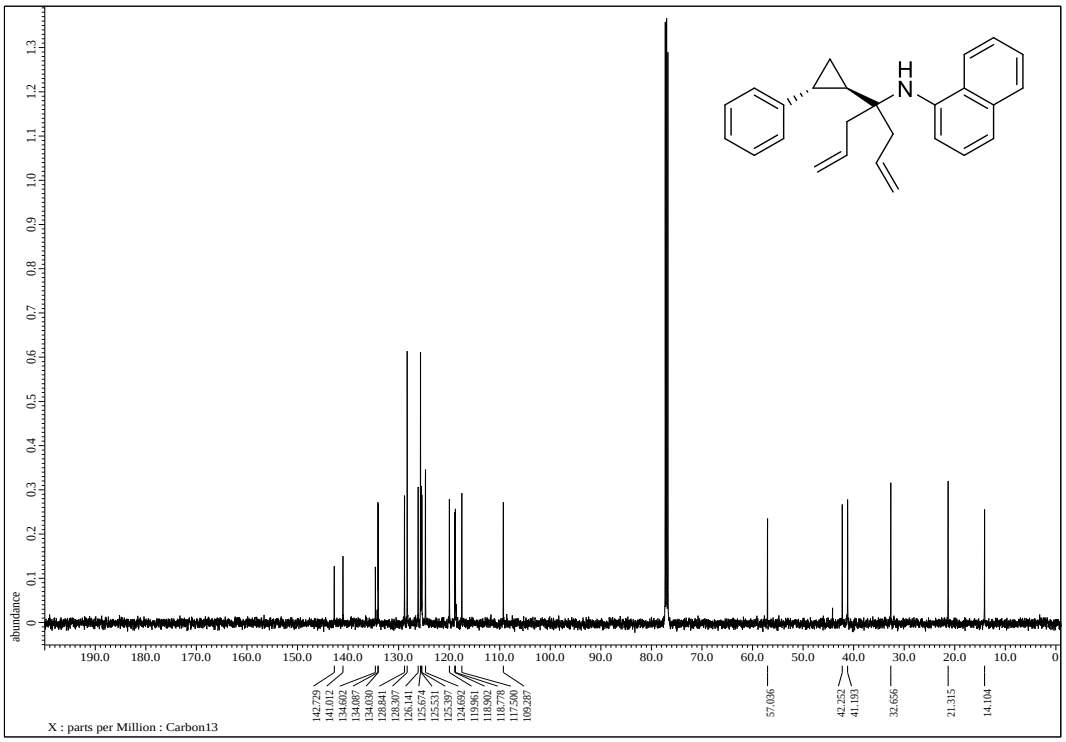
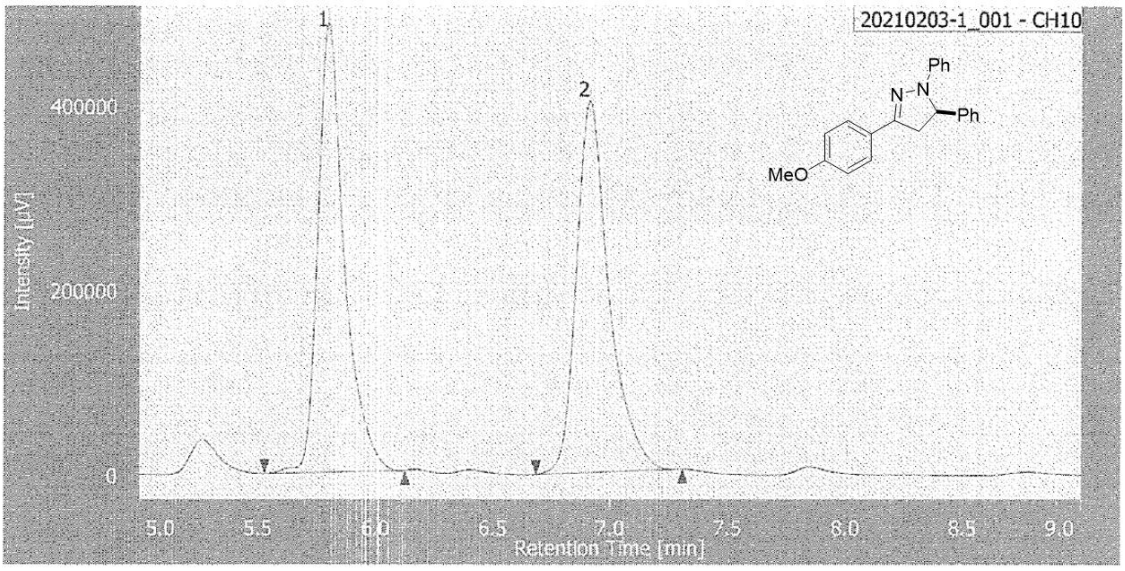
X : parts per Million : Carbon13

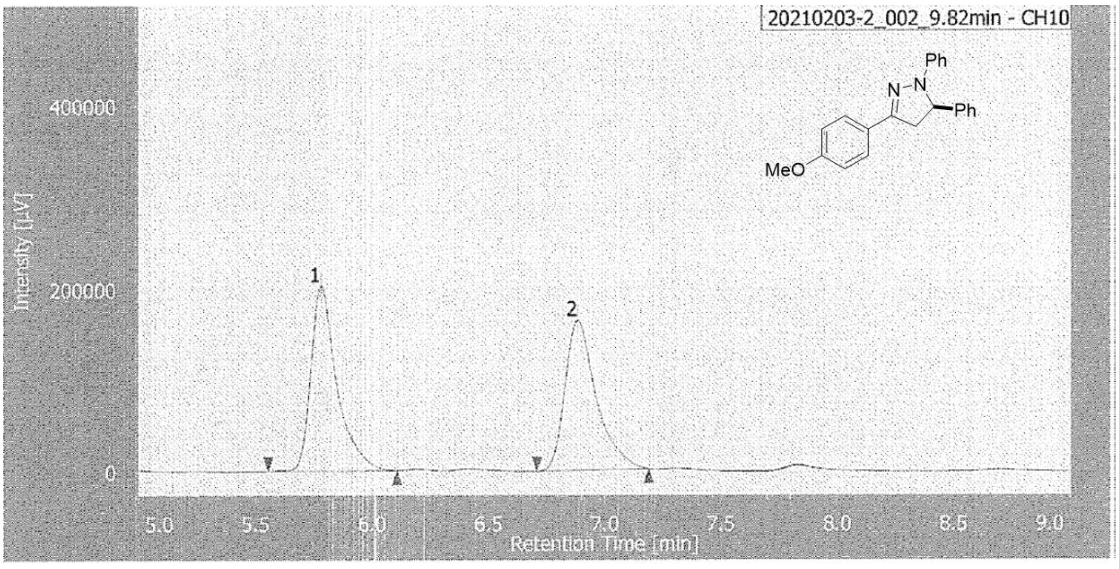

abundance
X : parts per Million : Proton
H
N


abundance
X : parts per Million : Carbon13
H
N

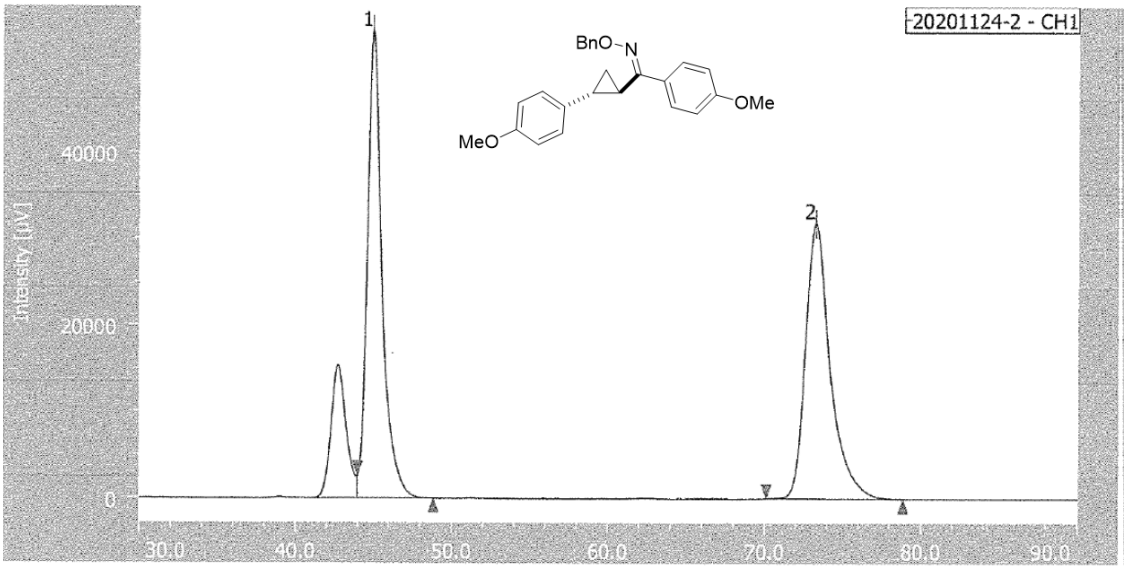
8-3-7 HPLC Spectral Data



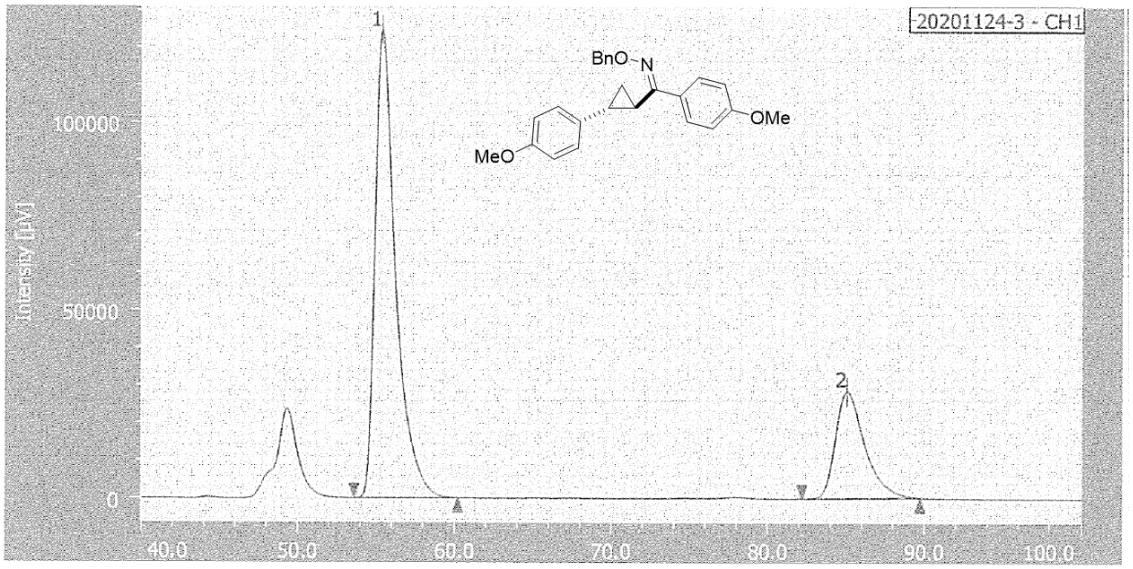
PEAK	RT [min]	AREA [μV･sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.798	3817204	487296	49.722	54.756
2	6.913	3859944	402637	50.278	45.244



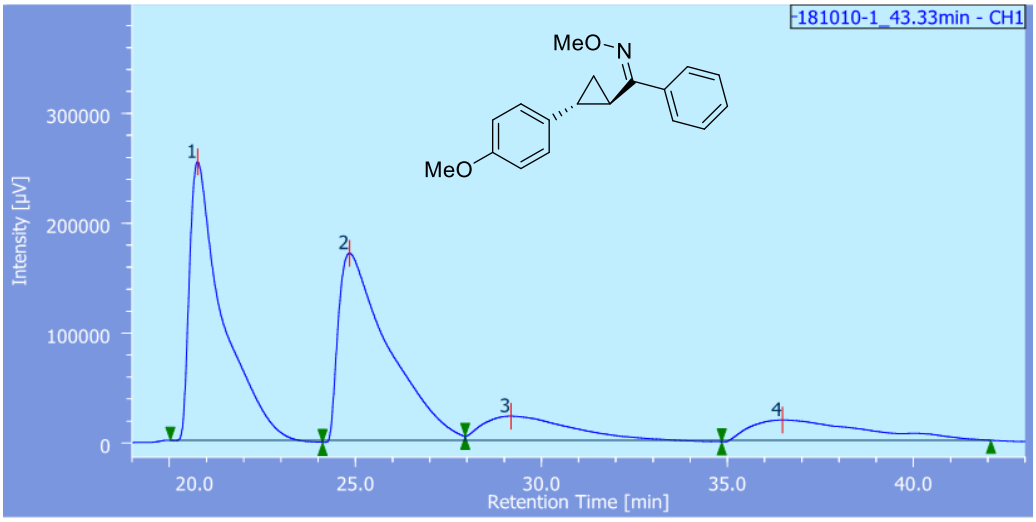
PEAK	RT [min]	AREA [μV･sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.782	1579586	203060	50.898	55.263
2	6.885	1523849	164380	49.102	44.737



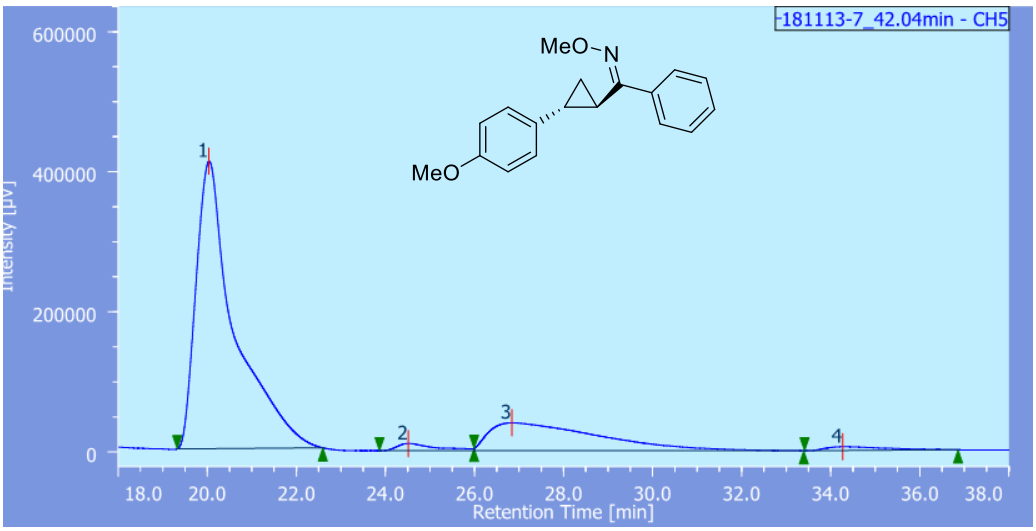
PEAK	RT [min]	AREA [μV･sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	44.967	3572484	54209	50.340	62.986
2	73.283	3524180	31856	49.660	37.014



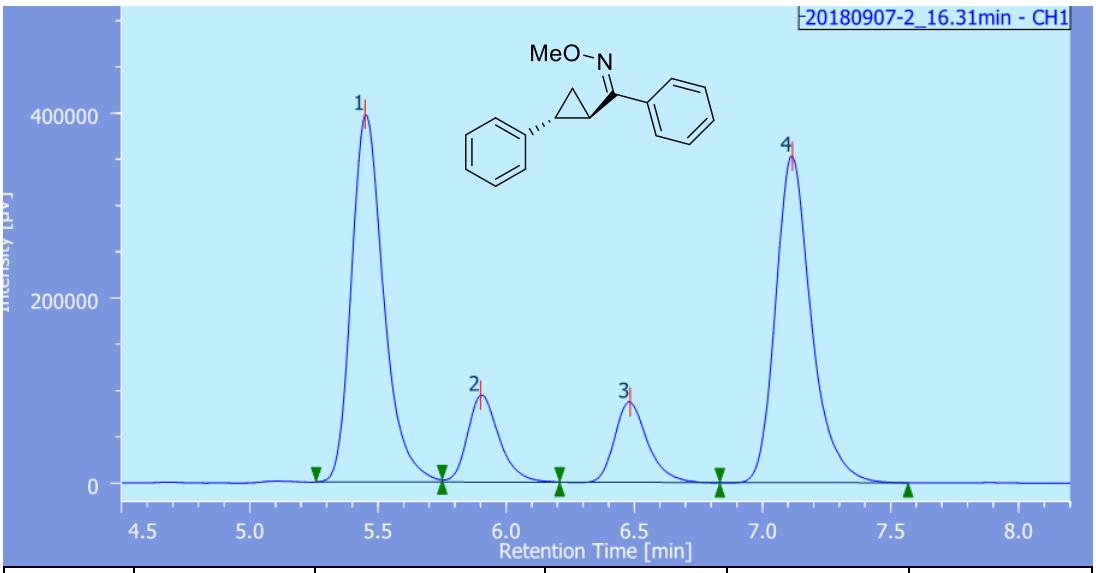
PEAK	RT [min]	AREA [μV･sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	55.325	11354780	124601	75.439	81.359
2	85.033	3696900	28548	24.561	18.641



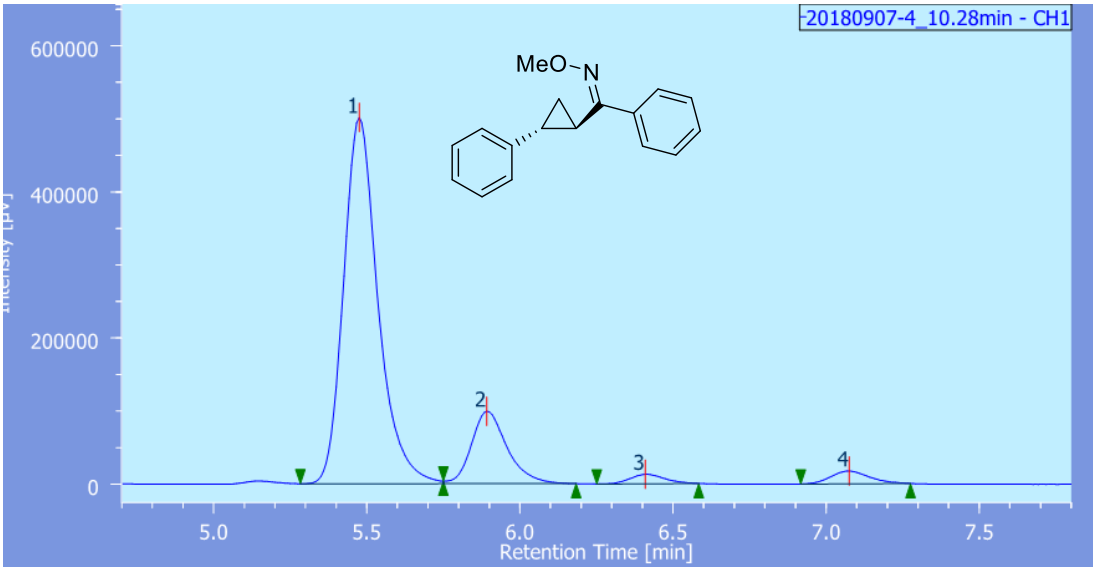
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.758	15660602	253428	40.093	54.630
2	24.842	15877012	170197	40.647	36.688
3	29.183	3576568	21839	9.156	4.708
4	36.475	3946691	18437	10.104	3.974



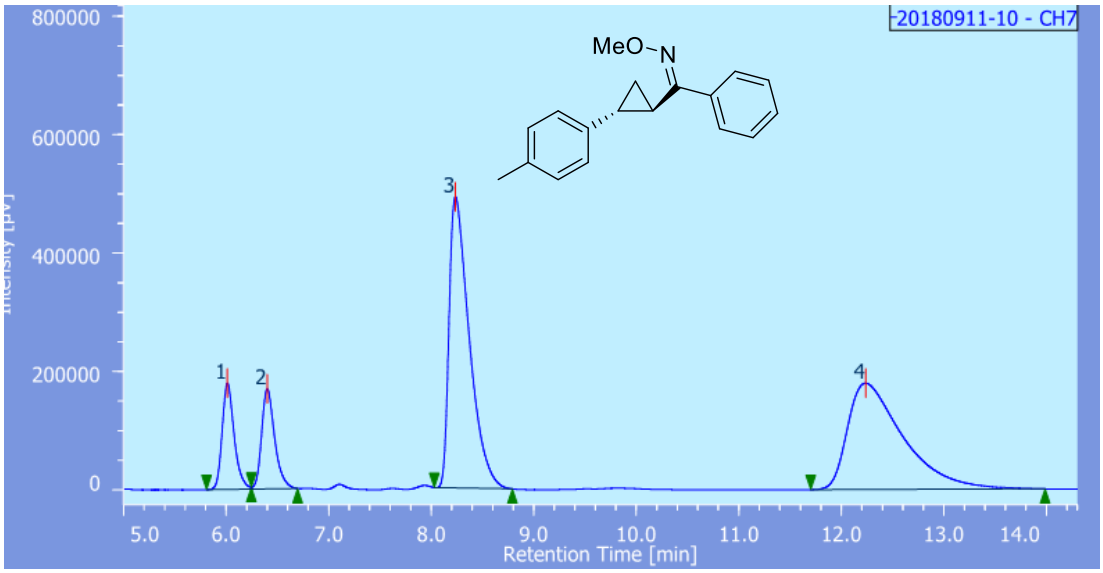
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.035	24667009	410216	75.810	88.118
2	24.513	609843	10209	1.874	2.193
3	26.835	6761280	39761	20.780	8.541



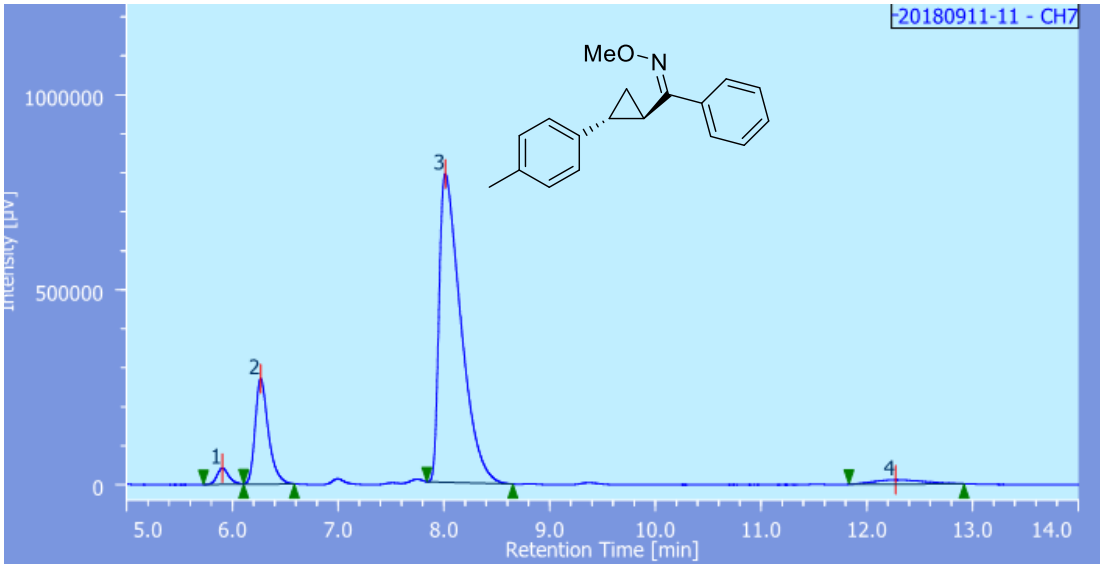
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.450	3468303	397300	40.883	42.670
2	5.900	810435	94160	9.553	10.113
3	6.483	774893	86868	9.134	9.330
4	7.117	3429753	352770	40.429	37.887



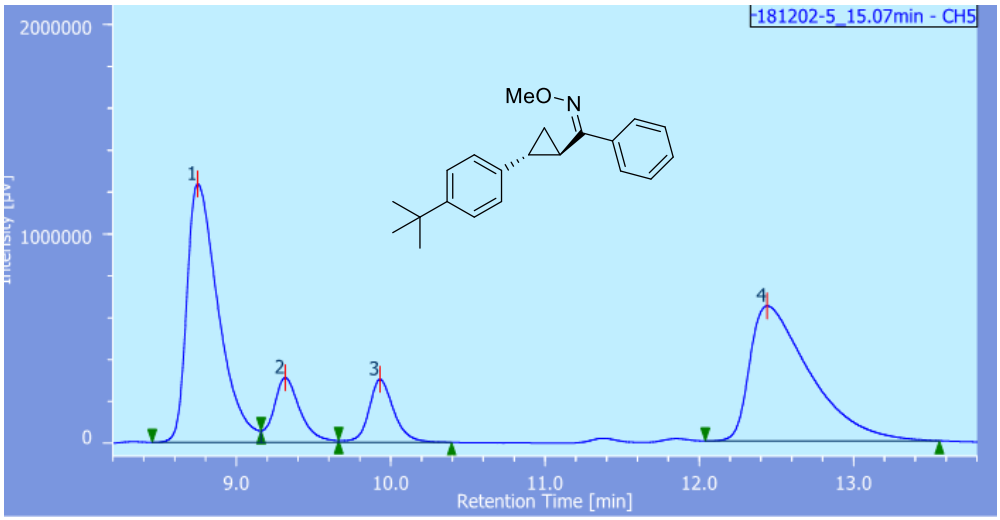
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.475	3911598	501024	78.799	79.497
2	5.892	801354	99128	16.143	15.728



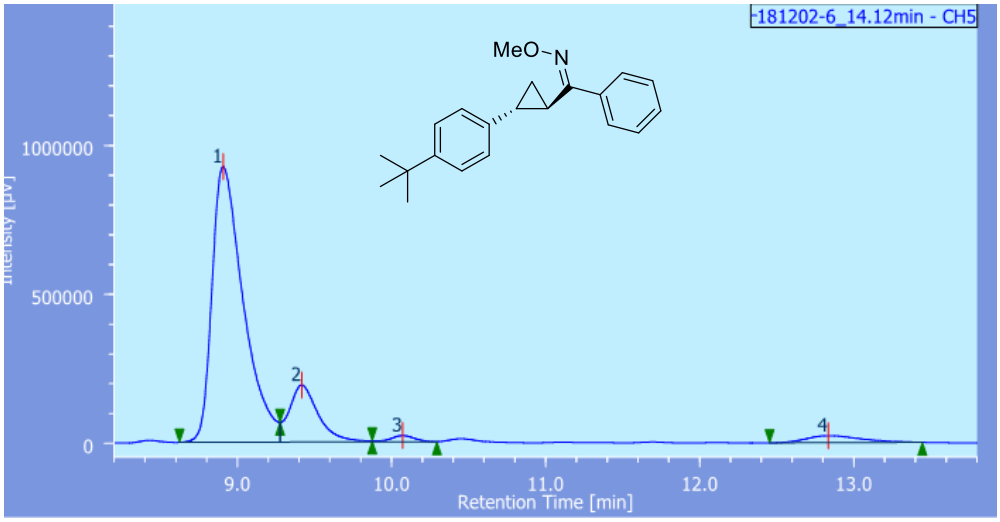
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	6.012	1463367	179193	8.905	17.579
2	6.400	1498626	169117	9.120	16.591
3	8.235	6724137	491681	40.920	48.235
4	12.235	6746236	179364	41.055	17.596



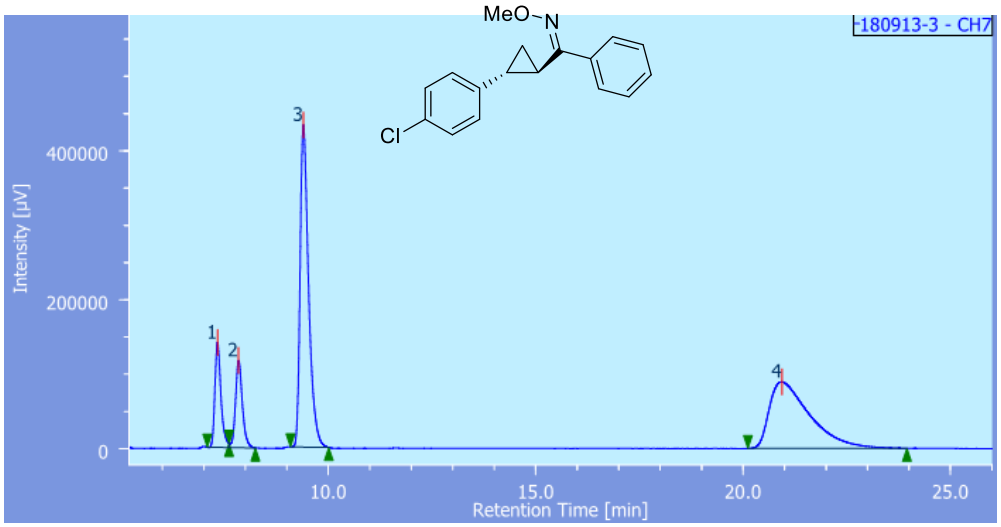
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.905	322929	41591	2.249	3.734
2	6.267	2350125	270429	16.370	24.276



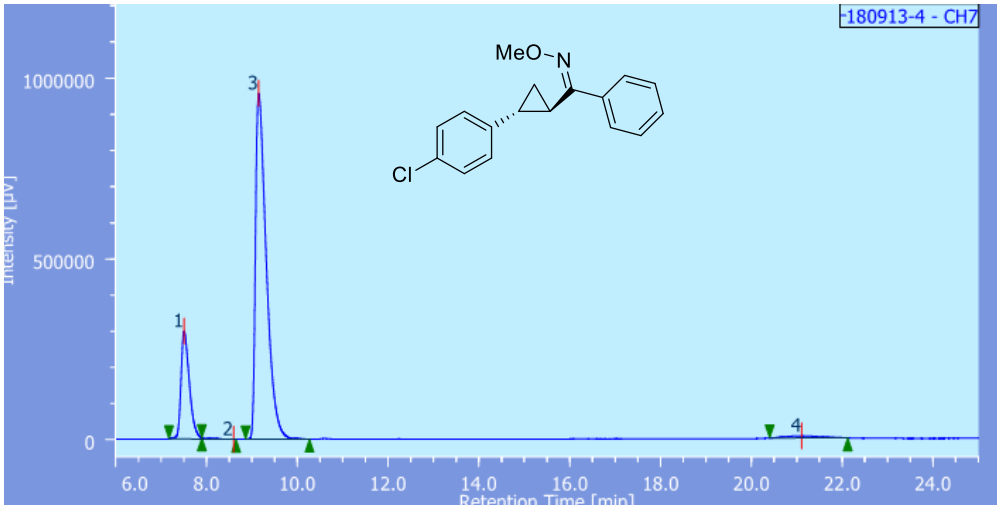
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	8.748	17560104	1234868	41.685	49.560
2	9.317	3686333	309553	8.751	12.424
3	9.930	3390727	301353	8.049	12.095
4	12.438	17488112	645869	41.515	25.921



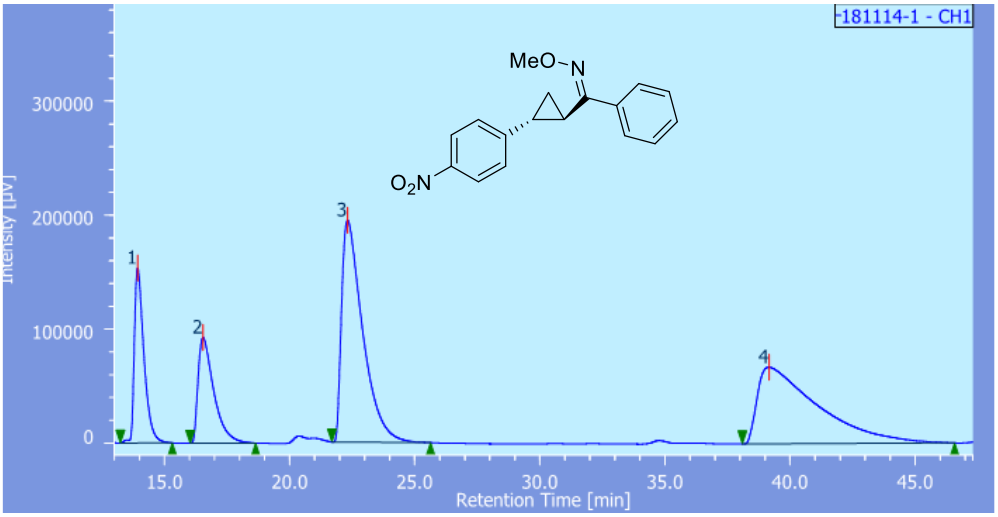
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	8.907	13095000	924368	79.857	79.686
2	9.417	2505491	191530	15.279	16.511
3	10.072	223006	20818	1.360	1.795
4	12.833	574562	23291	3.504	2.008



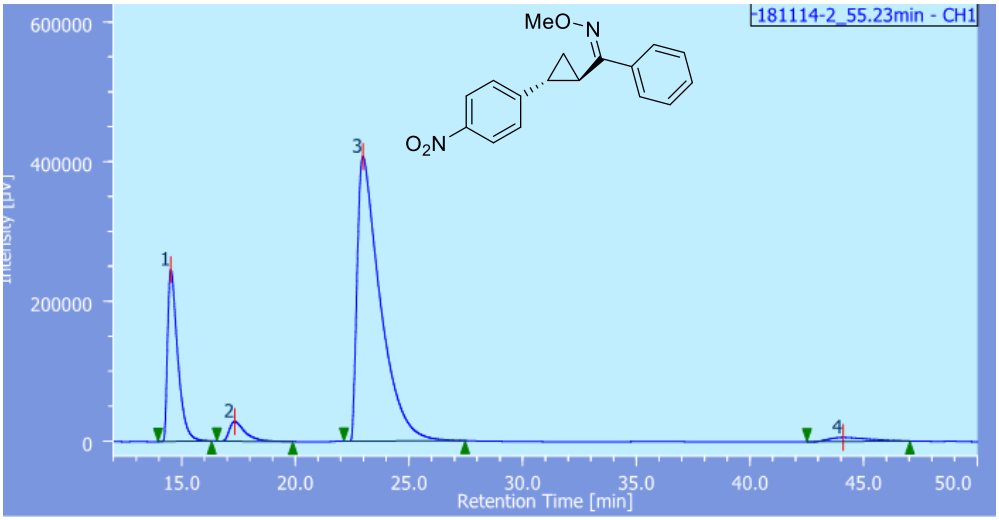
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	7.327	1431594	140701	9.552	18.056
2	7.837	1352278	116869	9.023	15.005
3	9.397	6121450	431890	40.845	55.451
4	20.938	6081837	89402	40580	11.479



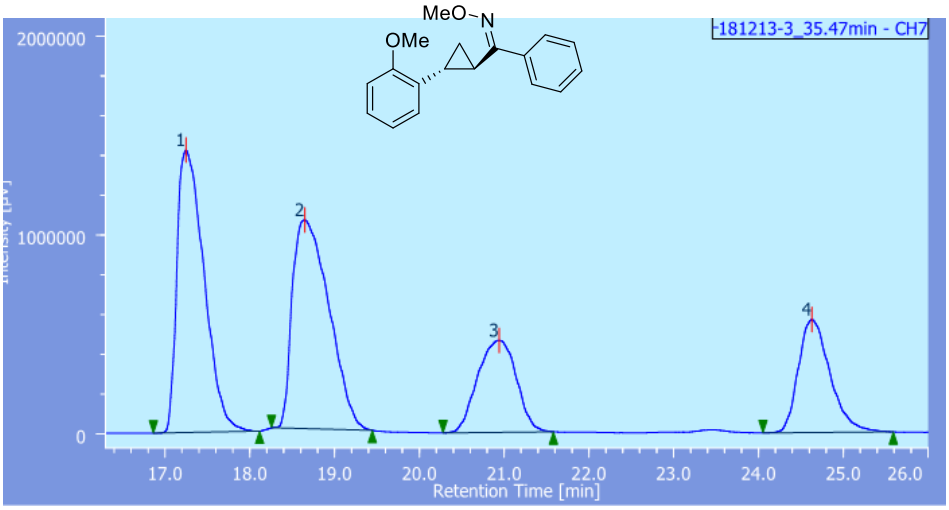
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	7.508	3798719	297755	19.047	23.639
2	8.598	1191	177	0.006	0.014
3	9.150	15819950	956029	79.324	75.899
4	21.105	323628	5644	1.623	0.448



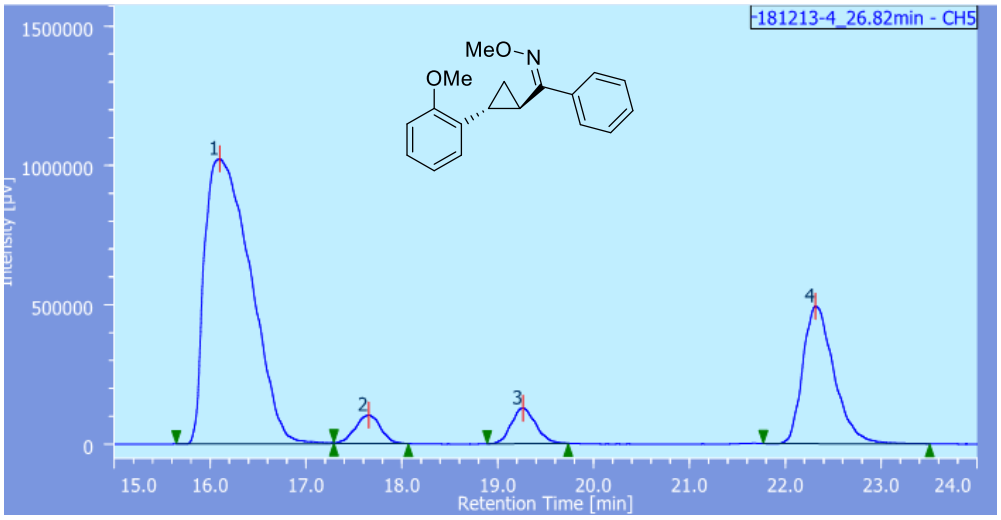
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	13.925	4134348	153552	13.372	30.219
2	16.542	4067360	92753	13.156	18.254
3	22.317	11432294	194589	36.977	38.295
4	39.150	1128335	67241	36.495	13.233



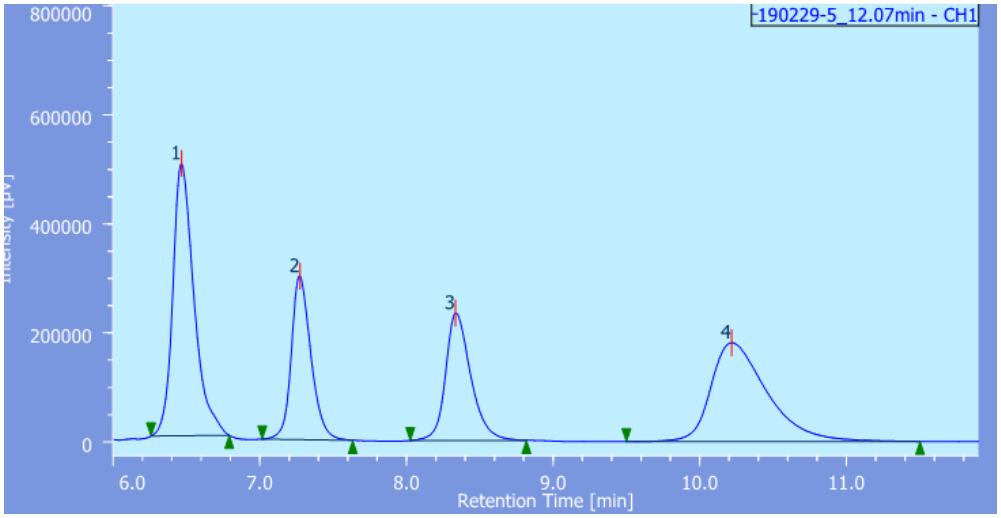
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	14.525	7642223	245778	19.895	35.792
2	17.333	1353344	28172	3.523	4.103
3	22.975	28698155	406954	74.708	59.263
4	44.092	719985	5785	1.874	0.842



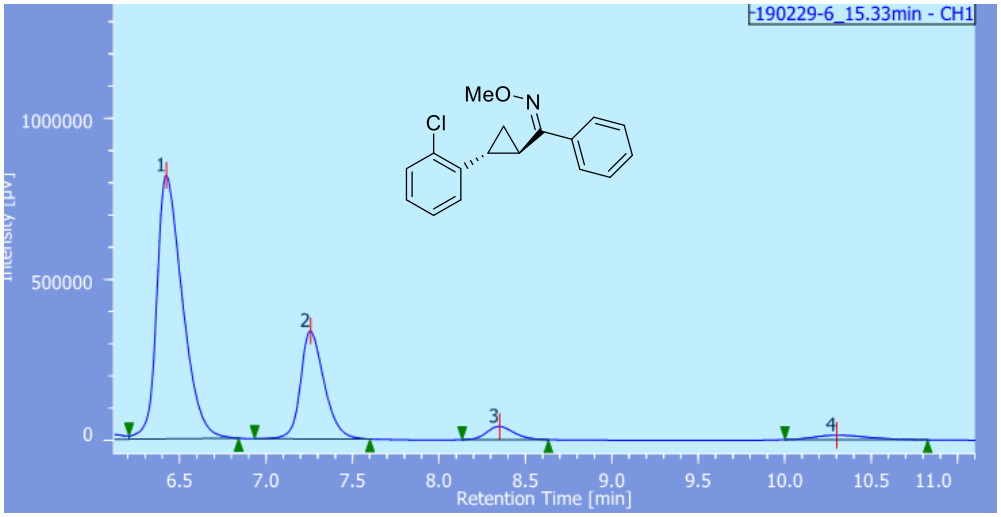
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	17.247	31463751	1418552	34.090	40.599
2	18.648	31468209	1046946	34.095	29.964
3	20.940	14627963	461271	15.849	13.202
4	24.628	14735786	567290	15.849	16..236



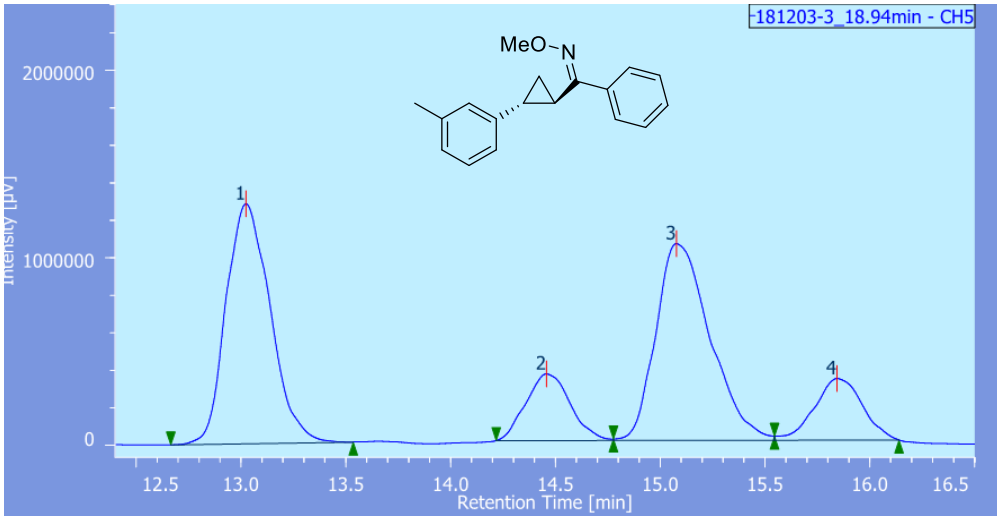
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	16.100	34148841	1022447	69.050	58.611
2	17.653	1887151	102328	3.826	5.866
3	19.263	2254854	127070	4.559	7.284
4	22.313	11164178	492612	22.574	28.239



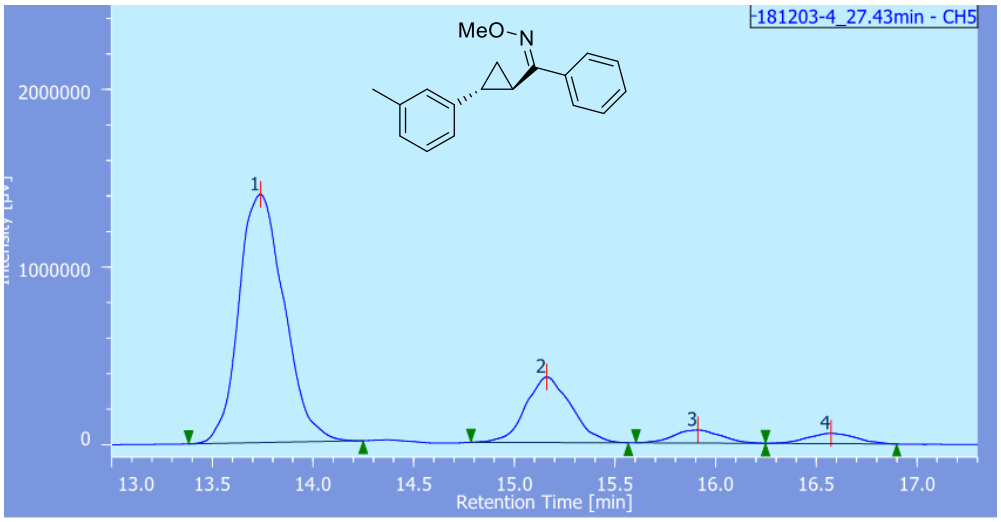
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	6.467	5035563	499484	32.606	41.138
2	7.275	2791822	299563	18.077	24.672
3	8.333	2792781	233668	18.083	19.245
4	10.217	4823660	181447	31.234	14.944



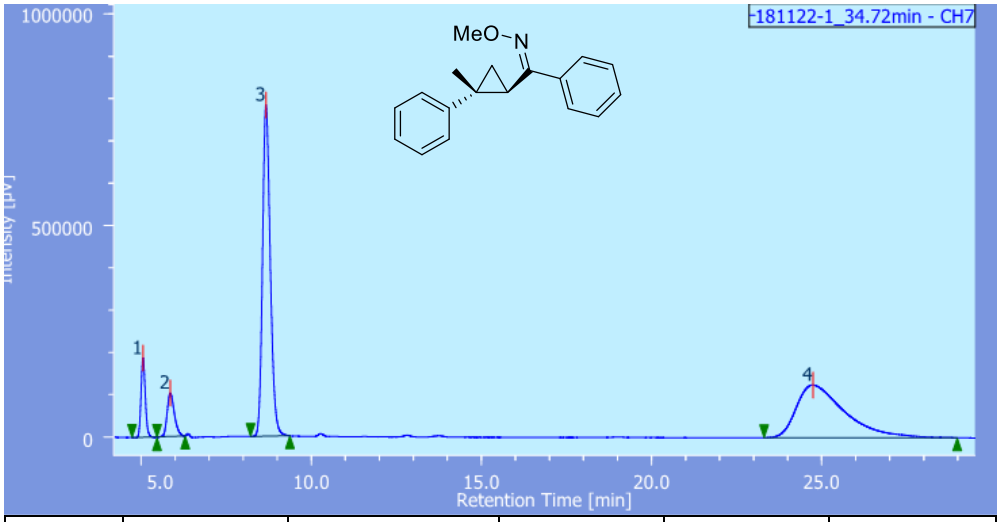
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	6.425	8454552	817882	68.042	67.664
2	7.258	3191509	335192	25.685	27.731
3	8.350	459358	41208	3.697	3.409
4	10.300	320078	14456	2.576	1.196



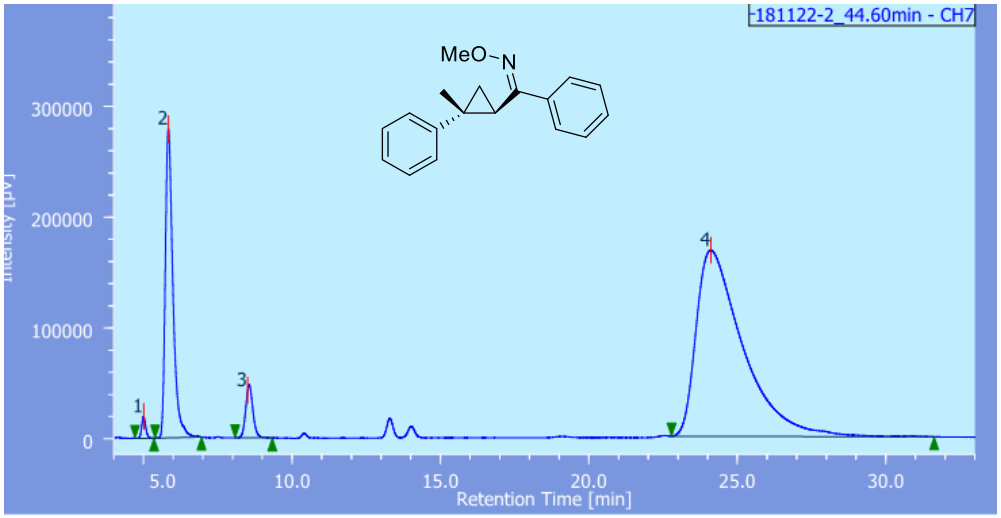
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	13.023	18787951	1279358	39.082	42.488
2	14.457	5218874	354776	10.856	11.782
3	15.077	18847032	1048658	39.205	34.827
4	15.843	5219608	328284	10.858	10.903



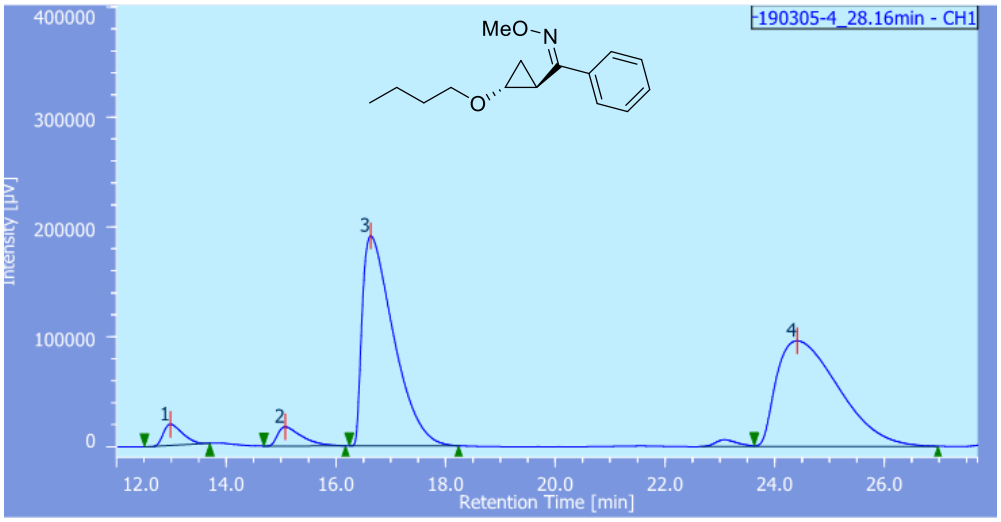
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	13.740	21815032	1396905	73.290	73.575
2	15.160	5761230	368666	19.356	19.418
3	15.910	1207728	74298	4.058	3.913
4	16.572	981201	58734	3.296	3.094



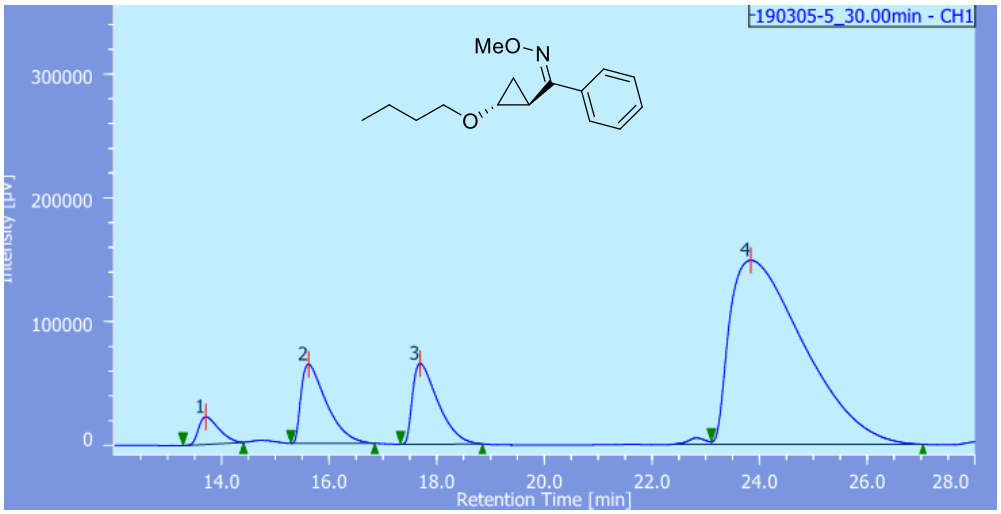
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	5.057	1632098	187227	5.847	15.643
2	5.858	1511429	102504	5.415	8.565
3	8.668	12413468	782488	44.474	65.380
4	24.745	12354945	124621	44.264	10.412



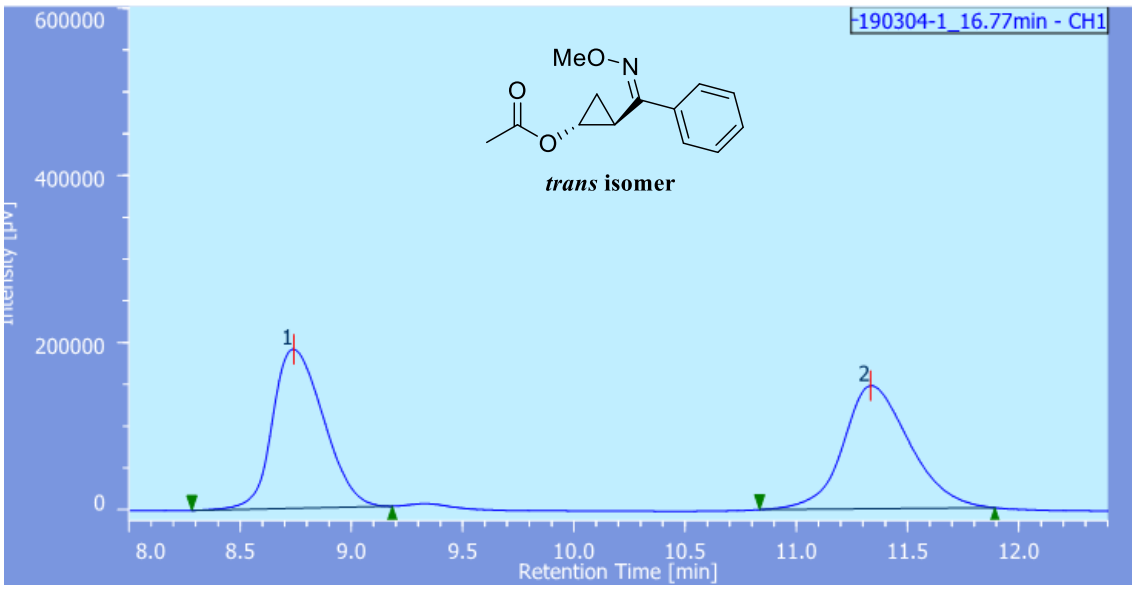
PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	5.002	183416	19551	0.752	3.838
2	5.837	4966906	278888	20.353	54.752
3	8.507	806869	43006	3.306	8.443
4	24.102	18446174	167923	75.589	32.967



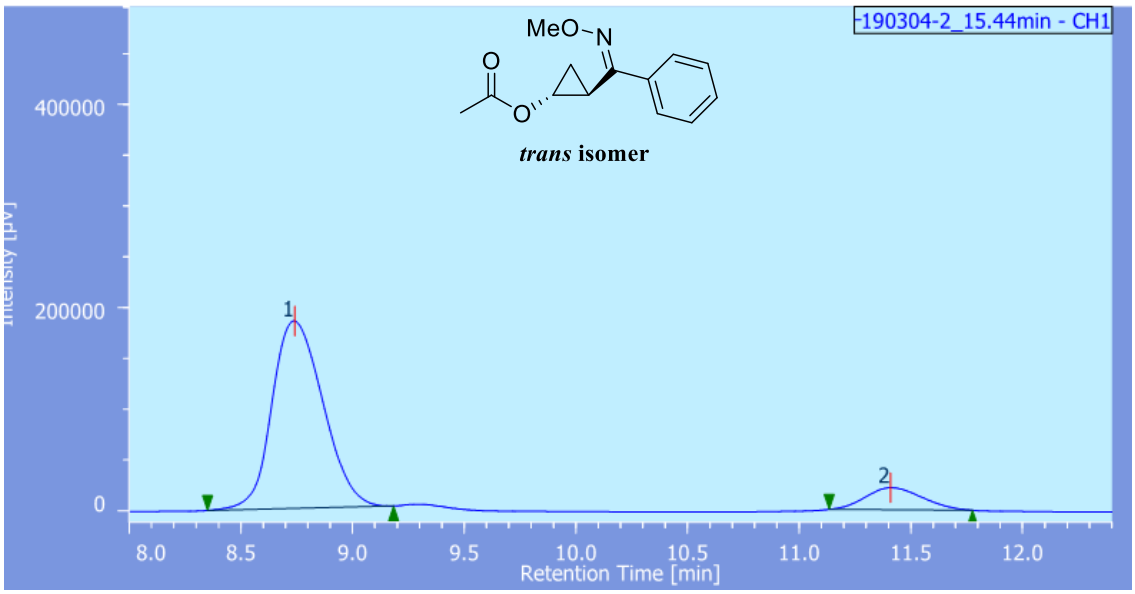
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.983	461480	19169	2.857	5.923
2	15.075	538946	17491	3.337	5.404
3	16.633	7582808	190944	46.951	58.996
4	24.408	7567113	96050	46.854	29.677



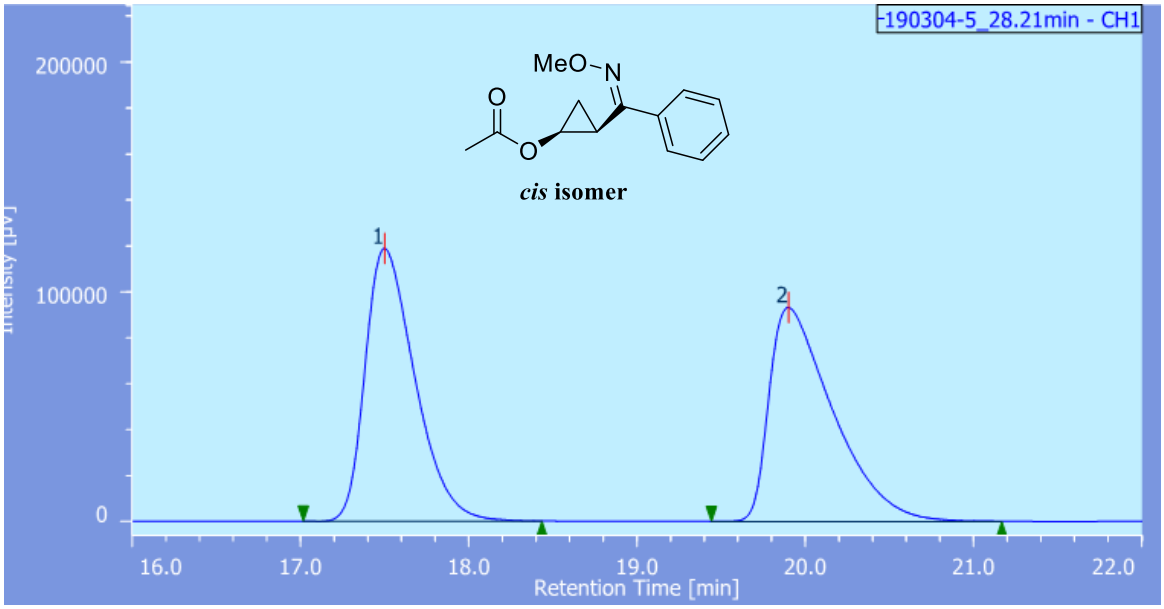
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	13.708	577192	22113	3.034	7.378
2	15.617	2111637	63966	11.101	21.341
3	17.692	2141655	65170	11.258	21.743
4	23.833	14192102	148479	74.607	49.538



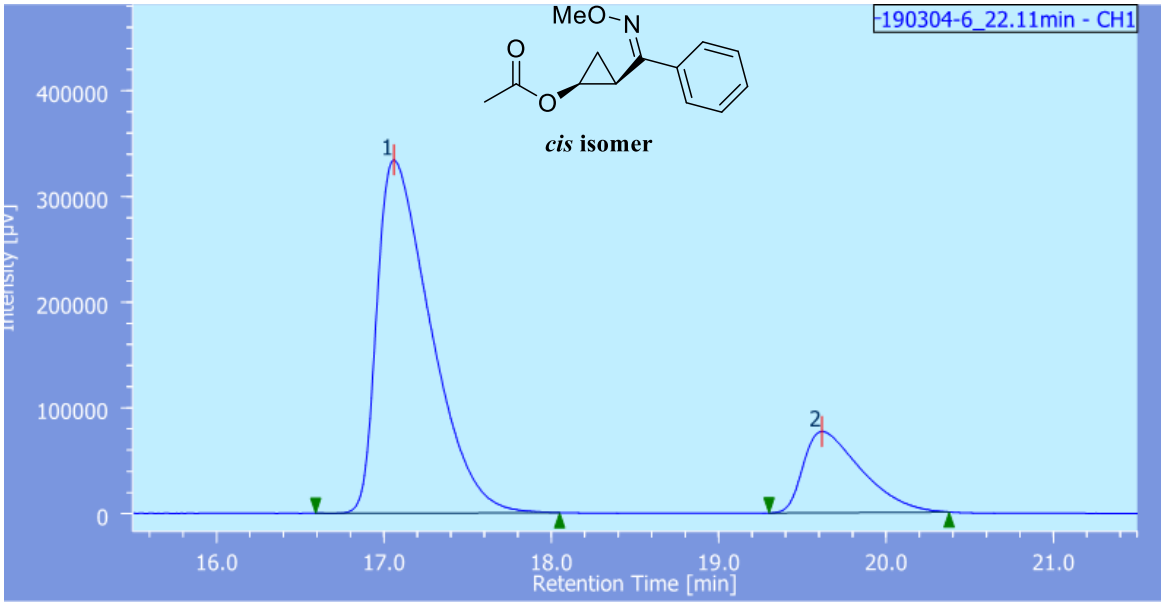
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.742	3165403	192776	49.747	56.395
2	11.333	3197544	149054	50.253	43.605



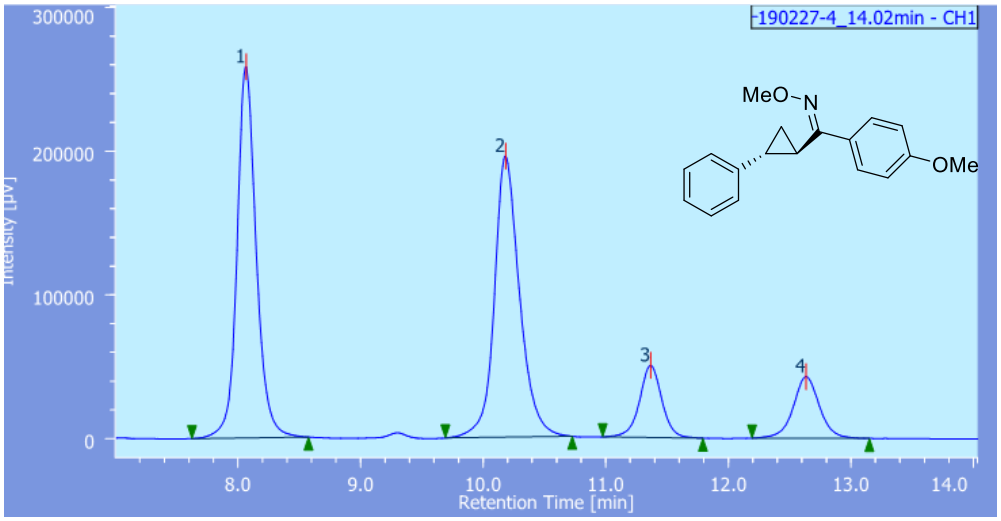
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.742	2930556	184335	88.419	89.455
2	11.408	383839	21730	11.581	10.545



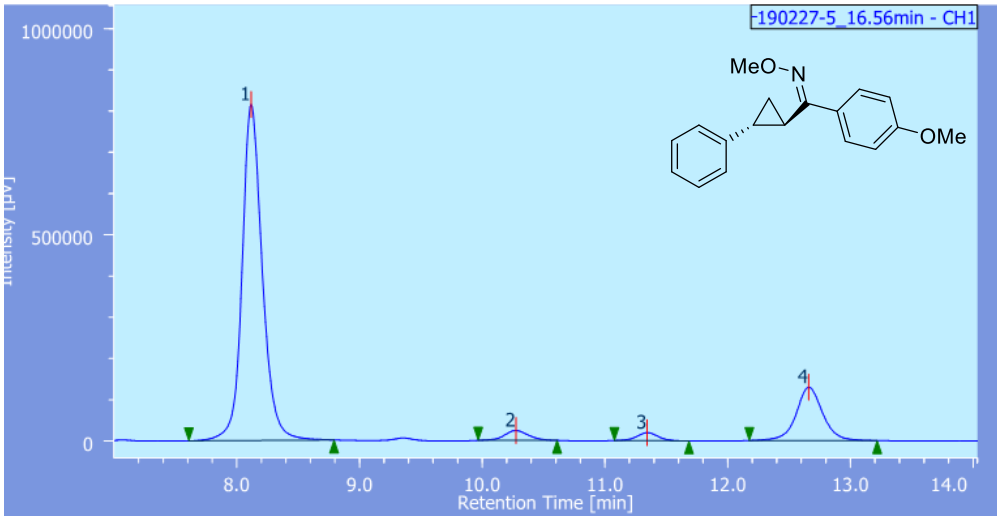
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	17.500	2441617	118736	49.866	56.044
2	19.900	2454696	93127	50.134	43.956



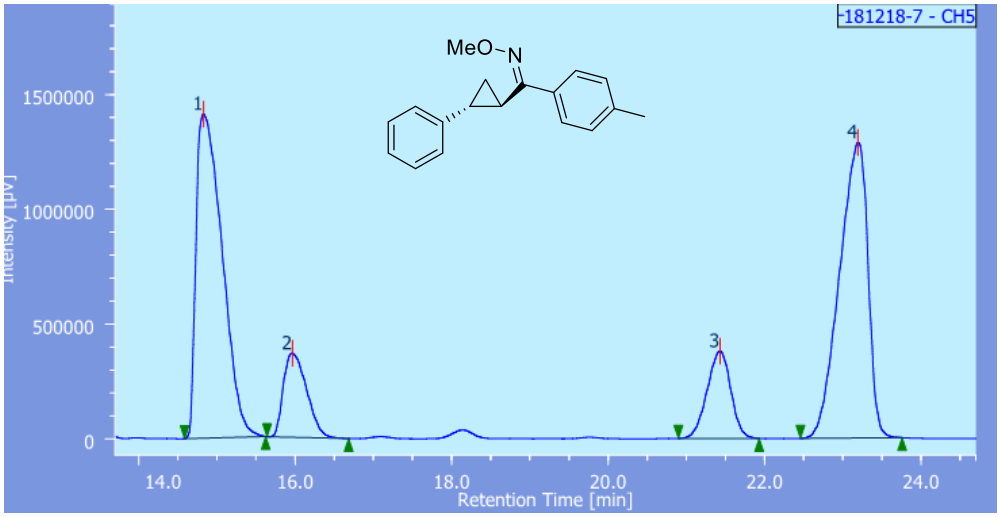
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	17.058	7446953	334108	80.104	81.297
2	19.617	1849682	76862	19.896	18.703



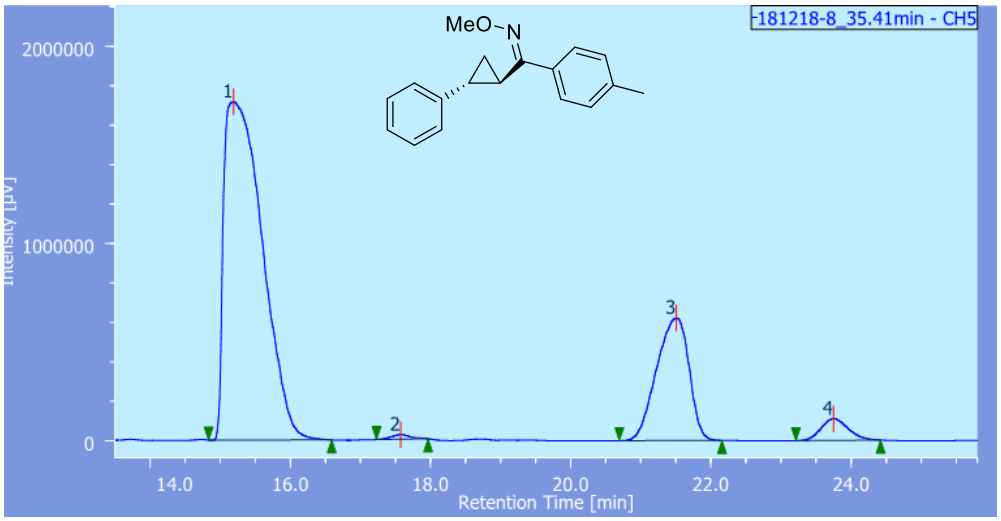
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.067	2811425	258048	40.879	47.228
2	10.183	2796471	195426	40.662	35.767
3	11.367	632693	50104	9.200	9.170
4	12.633	636762	42813	9.259	7.836



PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.117	9336199	814277	78.853	82.549
2	10.275	318892	23601	2.697	2.393
3	11.342	230755	19291	1.951	1.956
4	12.658	1939180	129242	16.399	13.102



PEAK	RT [min]	AREA [µV-sec]	HEIGHT [µV]	AREA%	HEIGHT%
1	14.828	32946184	1413787	40.585	40.953
2	15.965	7755631	370900	9.554	10.744
3	21.430	7999830	380245	9.855	11.014
4	23.190	32477376	1287309	40.007	37.289



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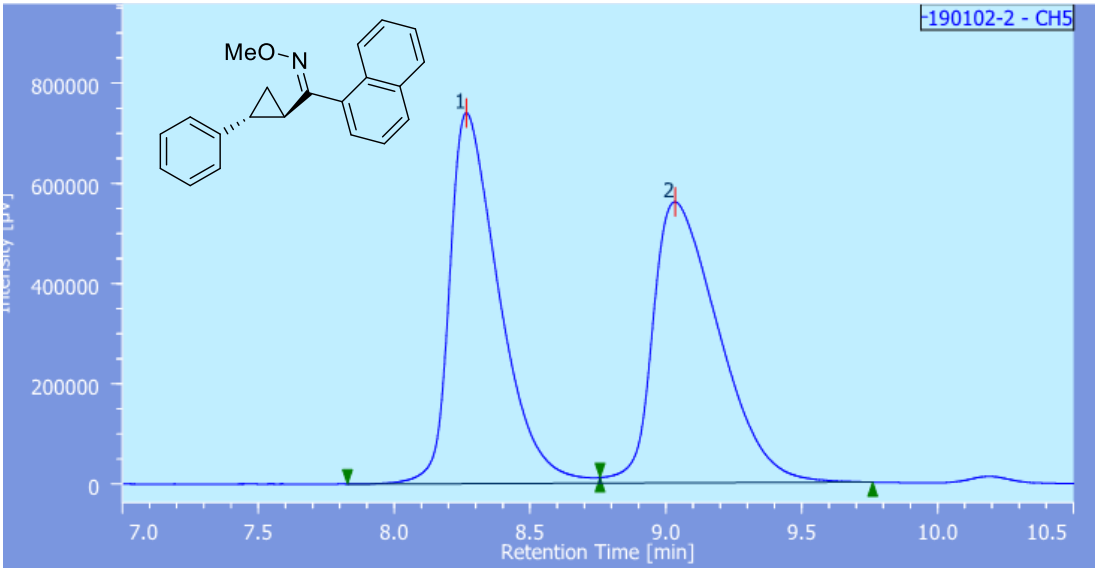
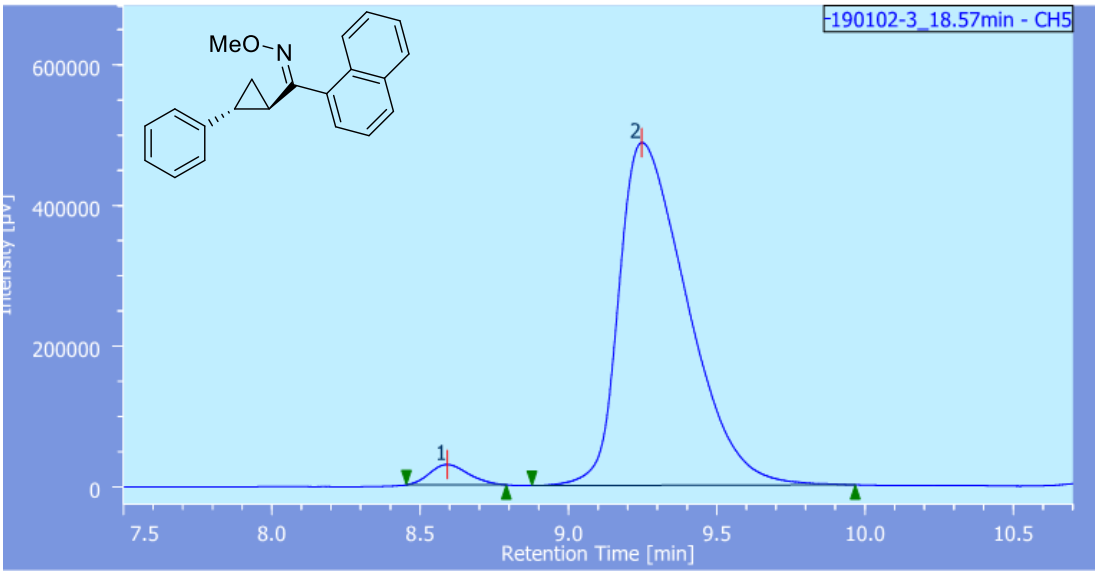
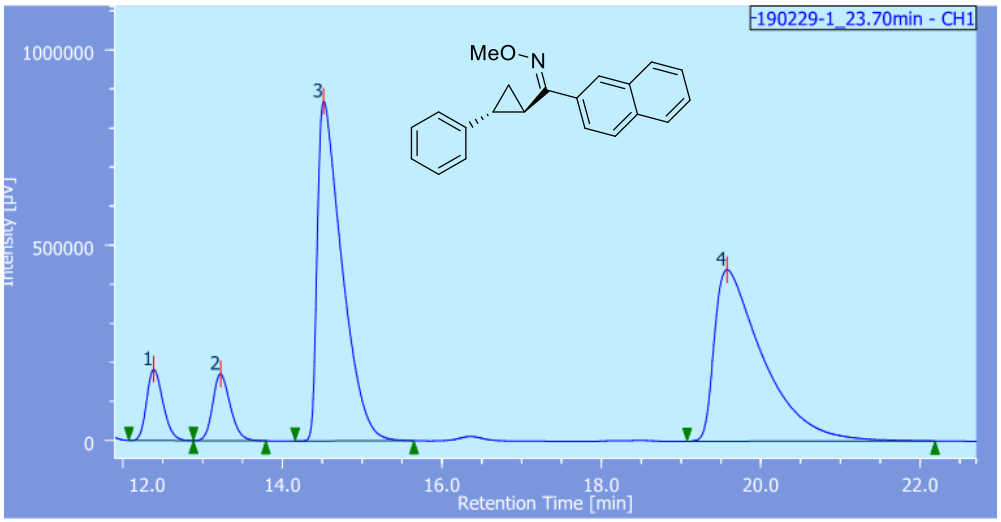
1	15.190	65575299	1714532	73.751	69.480
2	17.573	449330	23020	0.505	0.933
3	21.505	19954211	620514	22.442	25.146
4	23.748	2935705	109612	3.302	4.442



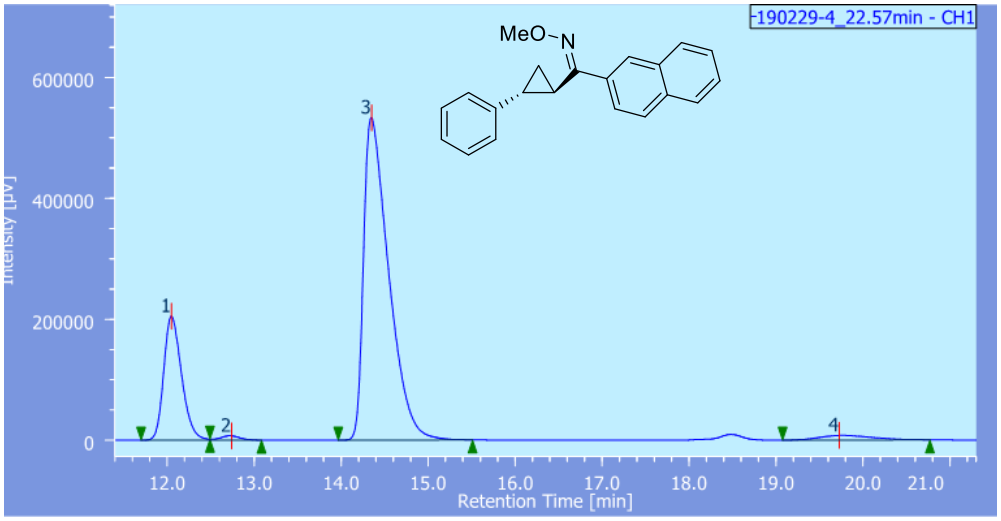
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.265	9344545	739230	49.725	56.904
2	9.033	9447897	559846	50.275	43.096



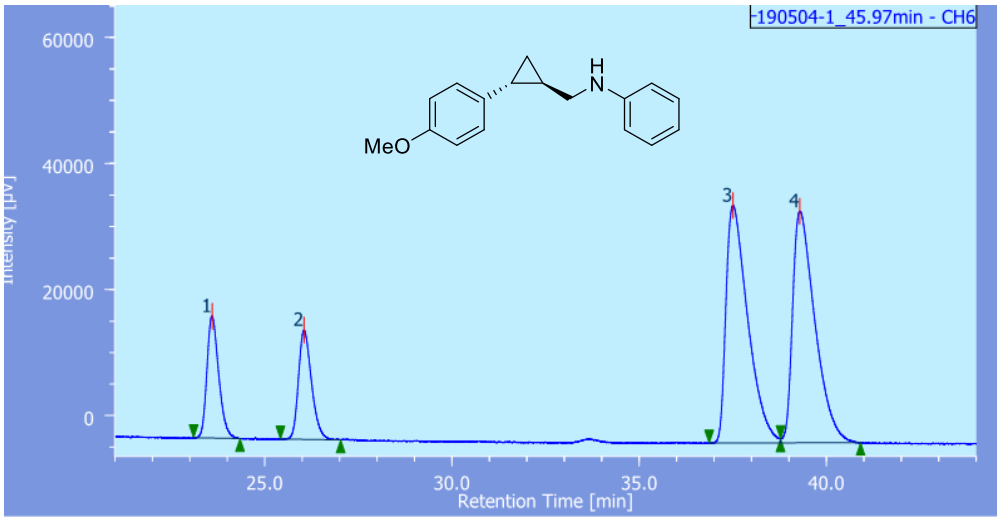
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.592	259809	28741	3.219	5.571
2	9.247	7811773	487141	96.781	94.429



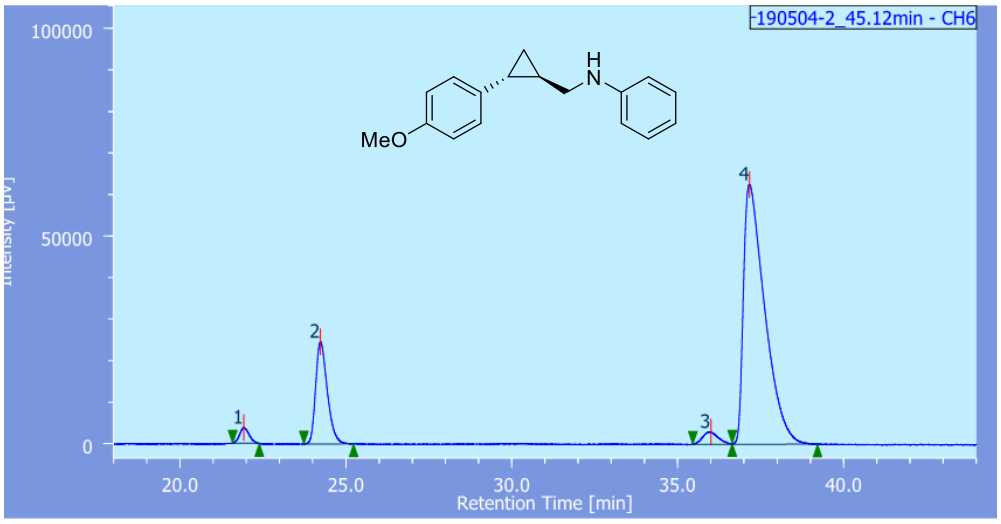
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.383	2608996	183055	6.126	11.008
2	13.225	2622756	171105	6.159	10.289
3	14.517	18717178	869700	43.951	52.298
4	19.575	18637416	439125	43.764	26.406



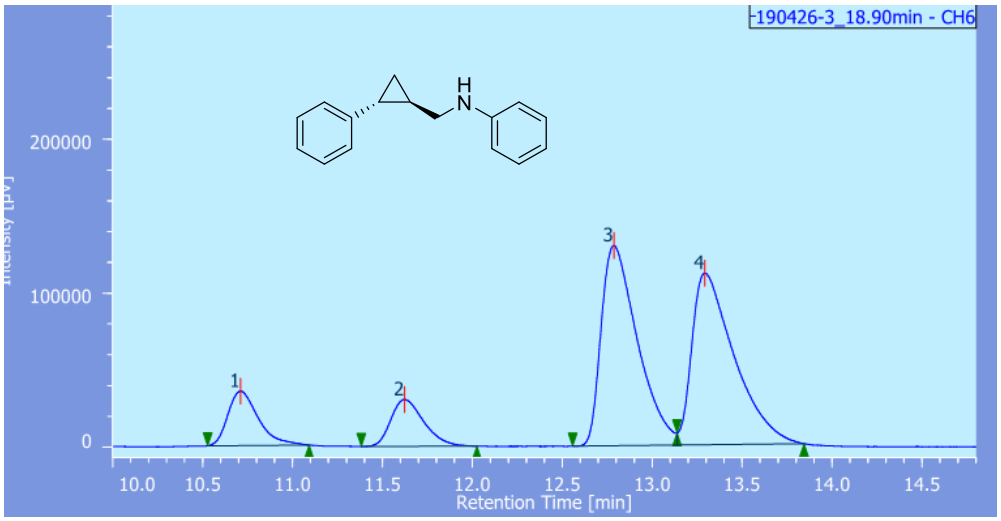
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.050	2920821	205182	20.771	27.251
2	12.742	113779	7212	0.811	0.958
3	14.350	10700201	532898	76.092	70.778
4	19.725	327231	7628	2.327	1.013



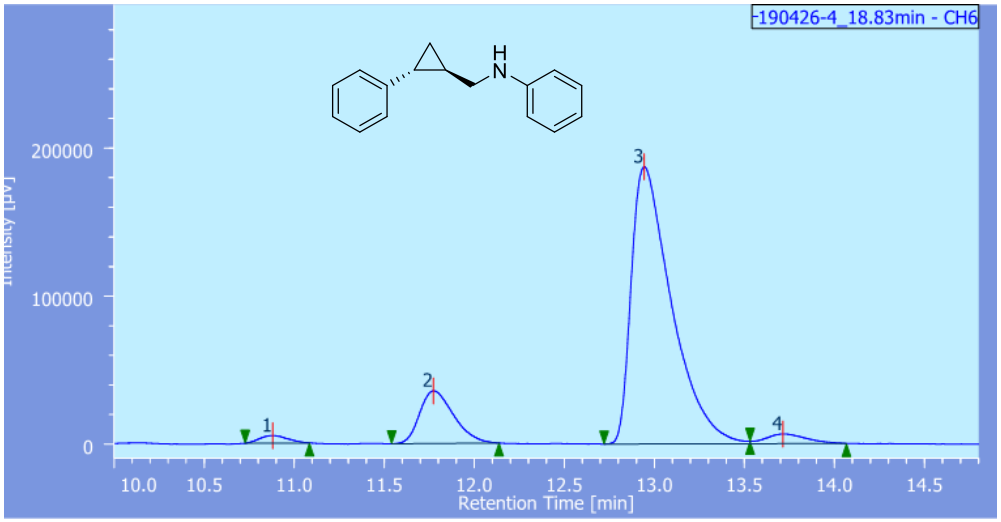
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	23.598	422528	19308	10.860	17.390
2	26.052	418575	17338	10.758	15.617
3	37.505	1525464	37668	39.208	33.927
4	39.287	1524171	36712	39.174	33.066



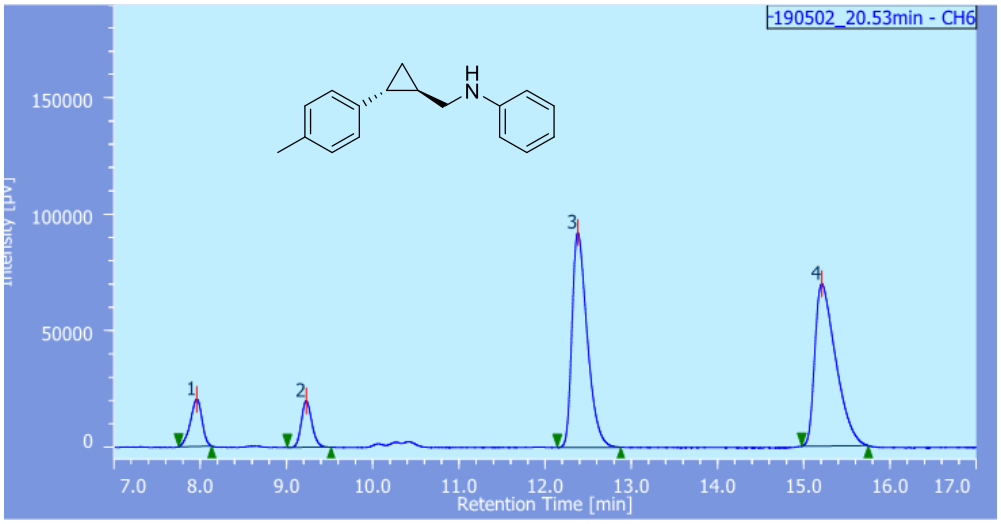
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	21.922	75840	3810	2.129	4.055
2	24.230	599080	24633	16.819	26.214
3	36.000	97883	2971	2.748	3.161
4	37.158	2789074	62553	78.304	66.569



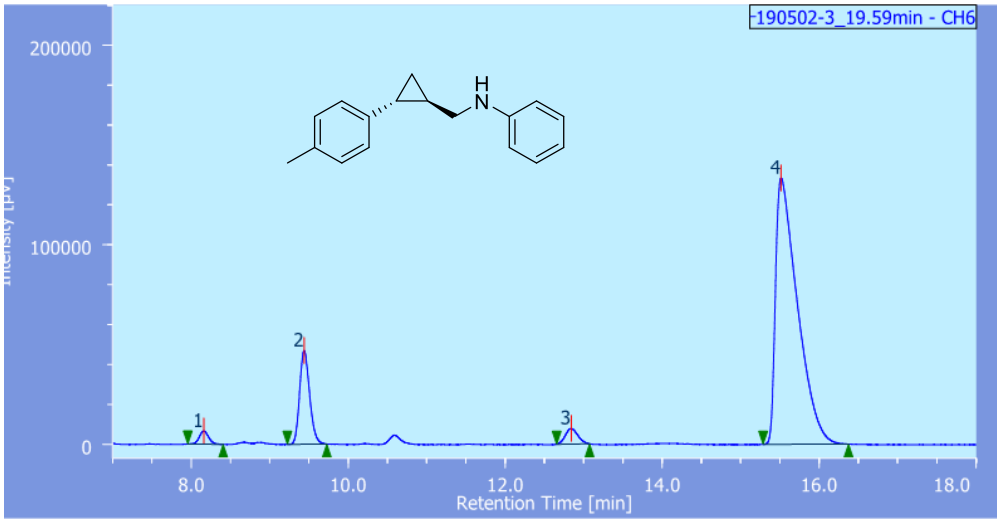
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	10.710	415522	35330	9.366	11.507
2	11.622	387127	30451	8.698	9.918
3	12.787	1820540	129896	40.905	42.307
4	13.292	1827504	111352	41.061	36.268



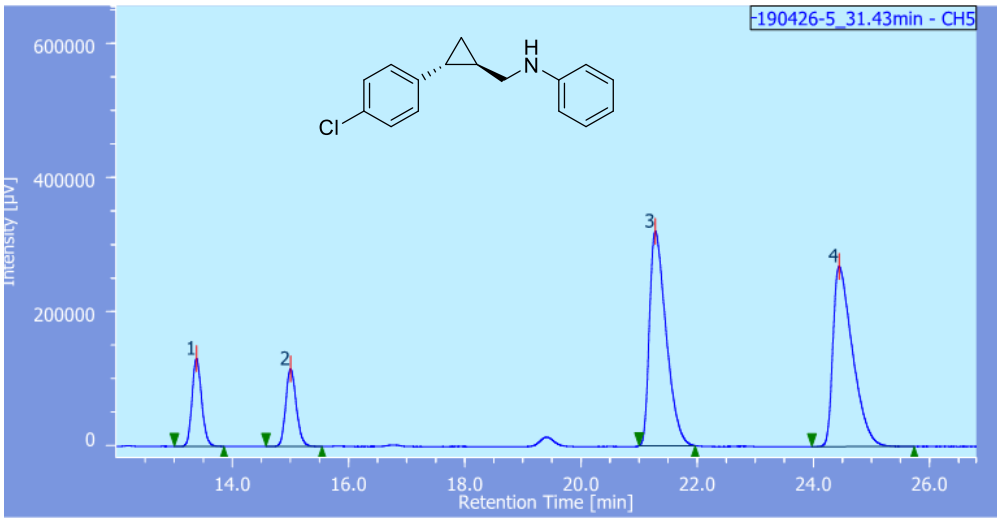
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	10.880	55.217	5107	1.565	2.180
2	11.772	465461	35561	13.191	15.182
3	12.942	2907548	187063	82.399	79.862
4	13.713	100409	6501	2.846	2.775



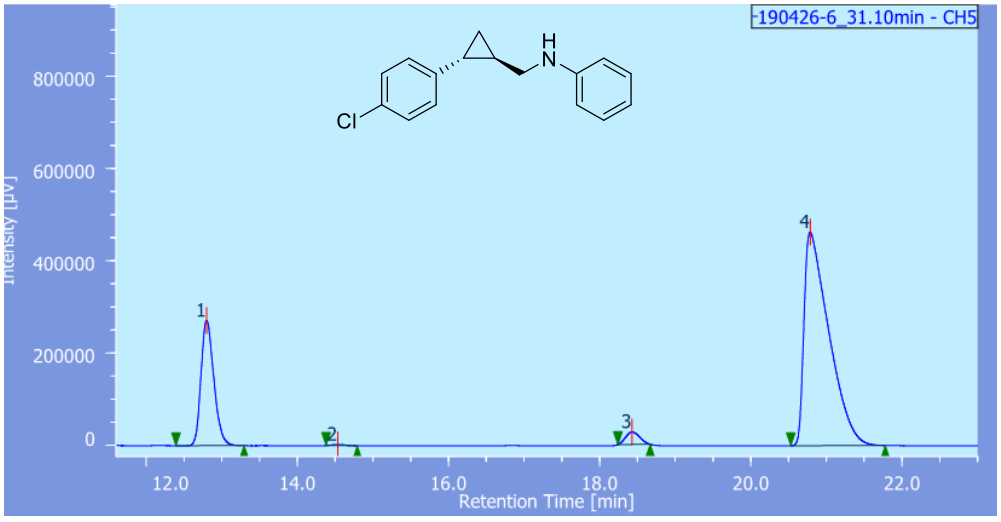
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	7.96	189753	20250	7.120	10.028
2	9.230	169679	19921	6.367	9.865
3	12.378	1128081	92170	42.327	45.643
4	15.208	1177586	69596	44.187	34.464



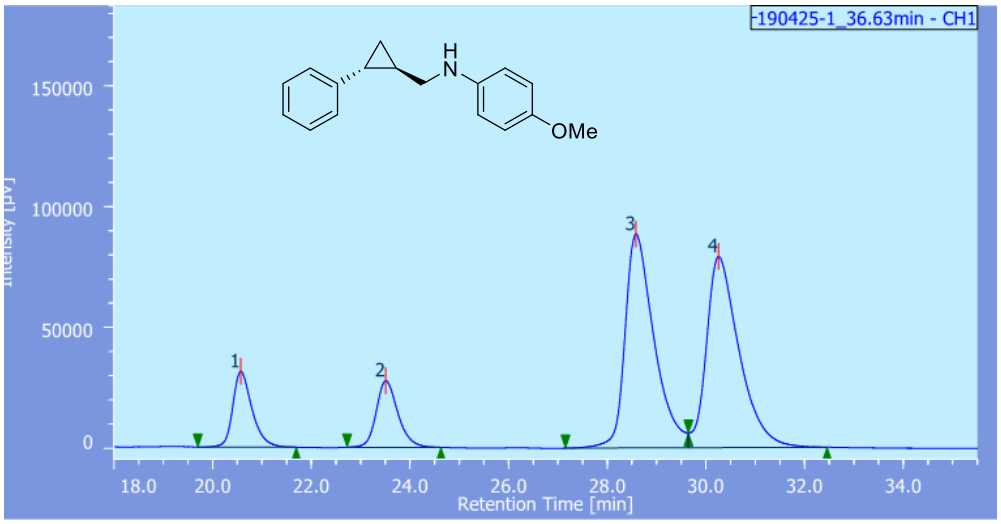
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	8.160	54113	6576	1.722	3.379
2	9.438	415588	46887	13.224	24.090
3	12.840	85824	7802	2.731	4.008
4	15.513	2587064	133365	82.323	68.522



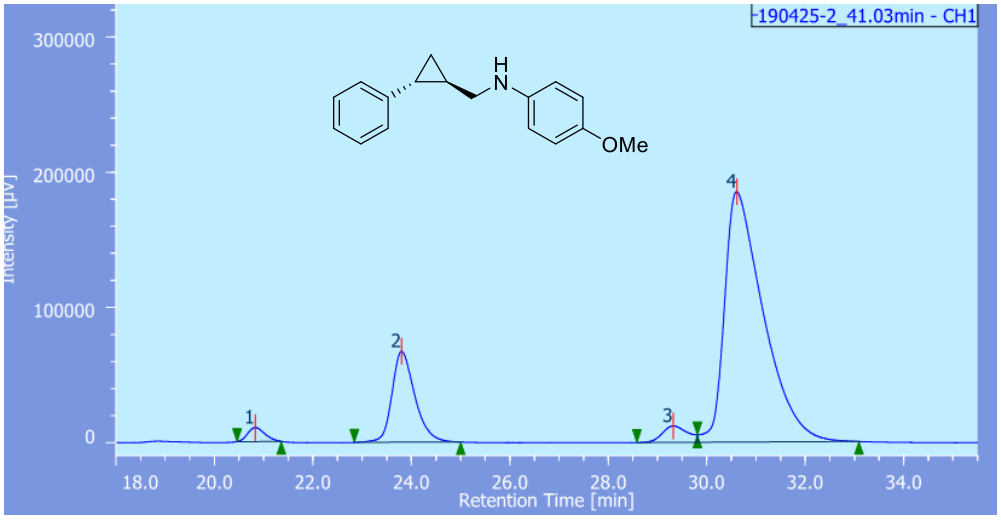
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	13.283	1504466	130814	9.625	15.669
2	14.978	1462561	115711	9.357	13.860
3	21.151	6363369	319663	40.712	38.289
4	24.193	6299849	268688	40.306	32.183



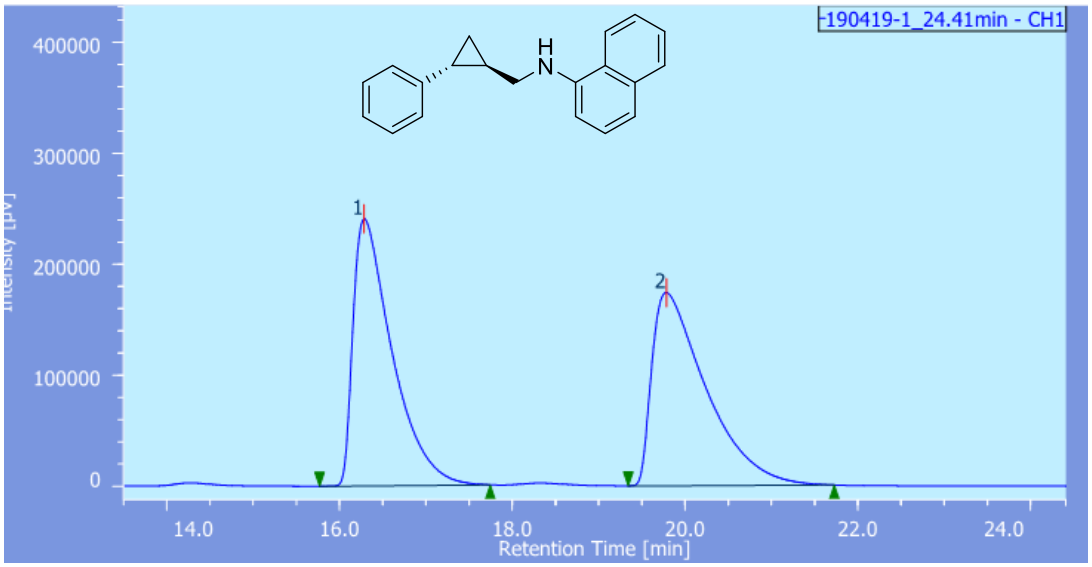
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.812	3205539	271125	22.704	35.538
2	14.573	27051	2282	0.192	0.299
3	18.495	347351	26950	2.460	3.533
4	20.825	10538908	462560	74.644	60.630



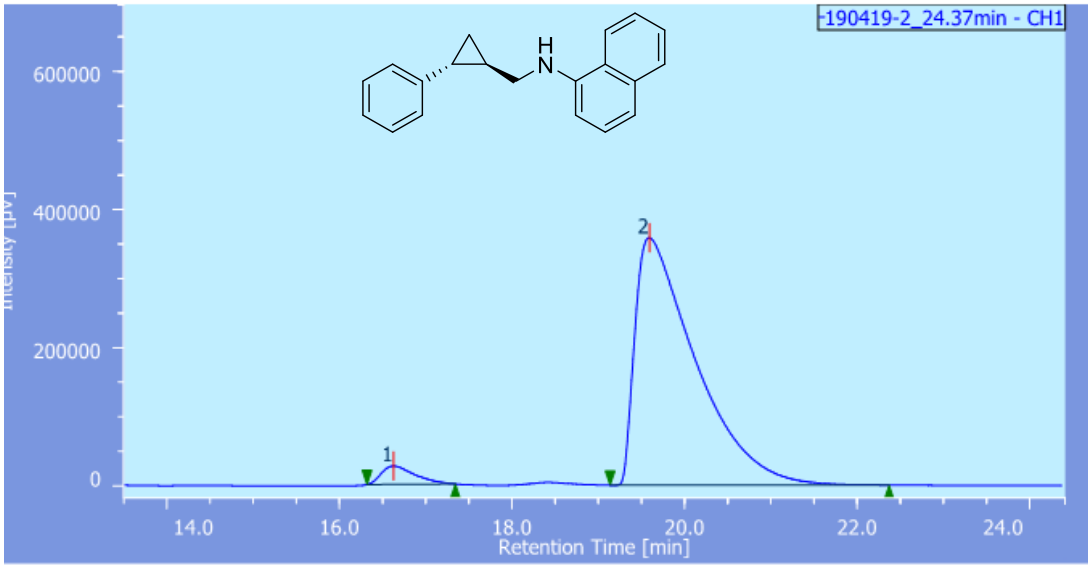
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.567	856546	31436	9.541	13.877
2	23.508	842578	27547	9.386	12.161
3	28.575	3632763	88502	40.467	39.069
4	30.250	3645229	79042	40.606	34.893



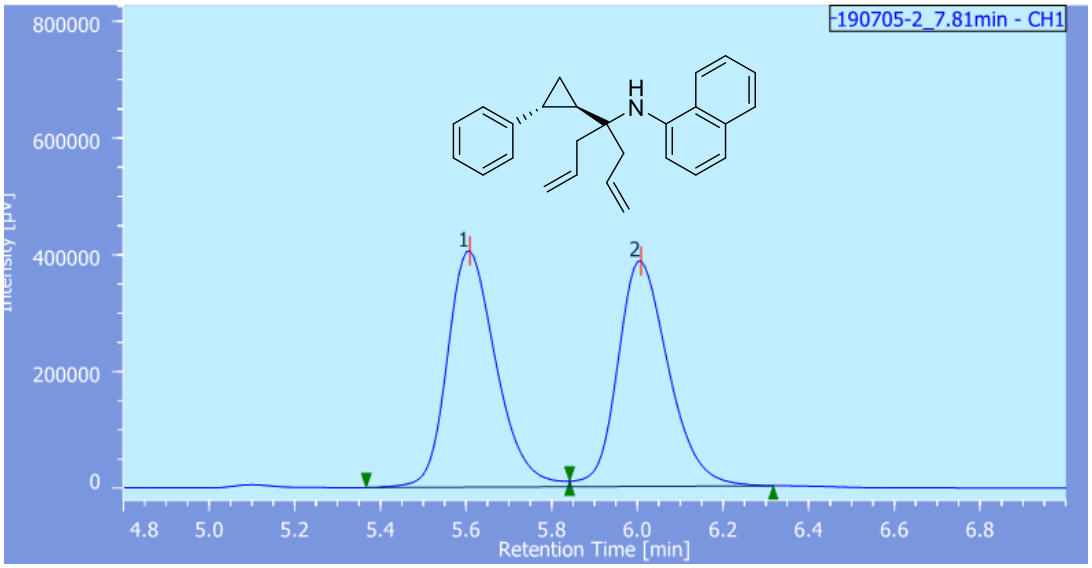
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.825	250902	10323	1.926	3.760
2	23.800	2165116	67133	16.621	24.453
3	29.317	436771	12136	3.353	4.421
4	30.608	10137880	184948	78.100	67.366



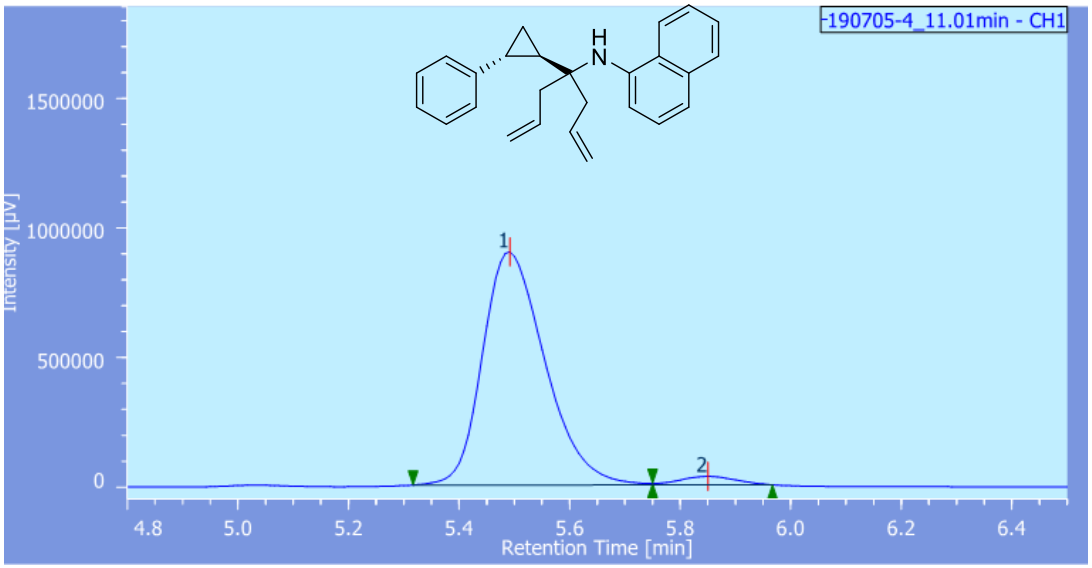
PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	16.283	7552262	240497	49.860	58.024
2	19.783	7594603	173982	50.140	41.976



PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	16.625	722092	26679	3.960	6.932
2	19.592	17504133	358209	96.040	93.068



PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.608	3195156	404591	50.081	51.197
2	6.,008	3184813	385665	49.919	48.803



PEAK	RT [min]	AREA [μV-sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	5.492	7069247	899066	96.860	96.490
2	5.850	229168	32703	3.140	3.510

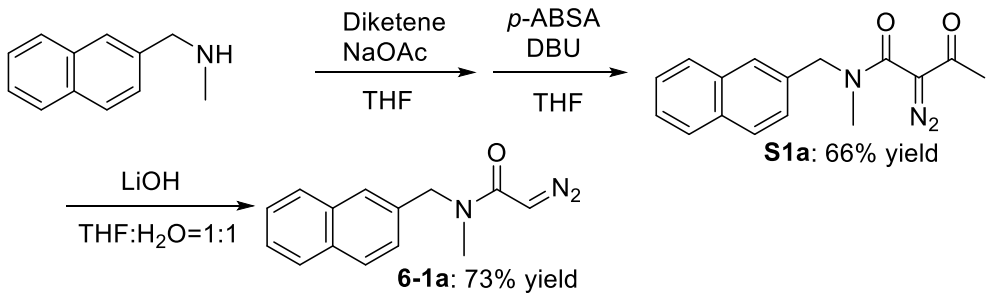
8-4 Experimental Section for Chapter 6

General Information

All reactions were performed under an atmosphere of argon unless otherwise noted. Dichloromethane (CH_2Cl_2) was purchased from Kanto Chemical Co., Inc. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGa A 60 F_{254}, layer thickness 0.2 mm. The products were visualized by irradiation with UV light or by treatment with a solution of *p*-anisaldehyde or by treatment with a solution of phosphomolybdic acid. Column chromatography was performed using silica gel (Merck, Art. No.7734). ^{1}H NMR (500 MHz, 400 MHz) and ^{13}C NMR (125 MHz, 100 MHz) spectra were recorded on JEOL JNM-ECX500, JEOL JNM-ECS400 spectrometer. Chemical shifts are reported as δ values (ppm) relative to $CDCl_3$ (7.26 ppm), TMS (0.00 ppm), $(CD_3)_2CO$ (2.05 ppm) for ^{1}H and $CDCl_3$ (77.0 ppm), $(CD_3)_2CO$ (29.85 ppm) for ^{13}C. Optical rotations were performed with a JASCO P-1030 polarimeter at the sodium D line (1.0 mL sample cell). Infrared (IR) spectra were recorded on an FT/IR-4600 instrument (JASCO Co., Ltd., Tokyo, Japan). Enantiomeric excesses were determined by high-performance liquid chromatography (HPLC) analyses with a JASCO GULLIVER using Daicel CHIRALPAK columns. HRMS (ESI) was recorded on a Bruker micrOTOF II.

8-4-1 Preparing Diazoacetamides

***N*-(Methyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide (6-1a)**



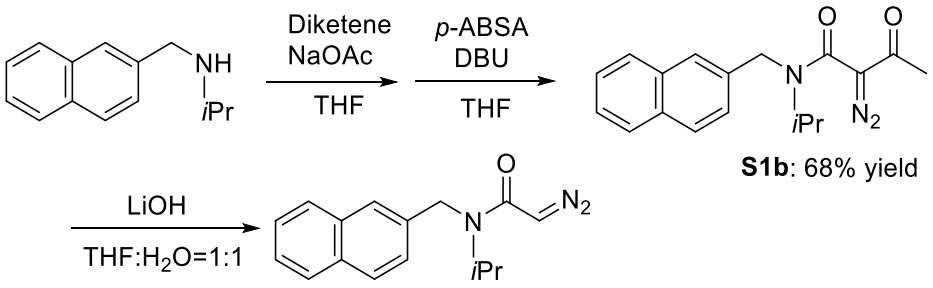
To a solution of secondary amine (847.6 mg, 4.95 mmol, 1 equiv.) in THF (10 mL) was slowly added diketene (1.9 mL, 24.75 mmol, 5 equiv.) and NaOAc (81.2 mg, 0.99 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (2 mL) and the combined mixture was extracted with EA (3x10 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (4.95 mmol, 1 equiv.) and *p*-ABSA (1783.8 mg, 7.42 mmol, 1.5 equiv.) in THF (20 mL) was slowly added DBU (1.11 mL, 7.42 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (20 mL) and the combined mixture was extracted with EA (3x20 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1a** as a yellow liquid (66% yield, 926.0 mg, 3.29 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (t, *J* = 7.83 Hz, 3H), 7.70 (s, 1H), 7.60-7.44 (m, 2H), 7.38 (dd, *J* = 8.6, 1.3 Hz, 1H), 4.75 (s, 2H), 2.95 (s, 3H), 2.40 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 133.4, 133.2, 132.8, 128.7, 127.7, 126.6, 126.4, 126.1, 125.4, 52.9, 35.7, 27.3 ppm. IR (neat) ν 3055, 2962, 2919, 2107, 1633, 1397, 1290, 1269, 821, 740 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1a** (926.0 mg, 3.29 mmol, 1 equiv.) in THF (10 mL) was slowly added LiOH (158.1 mg, 6.6 mmol, 2 equiv.) in H_2O (10 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x10 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1a** as a yellow solid (73% yield, 574.1 mg, 2.4 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.41, 6.88 Hz, 3H),

7.63 (s, 1H), 7.51-7.34 (m, 2H), 7.34 (s, 1H), 5.01 (s, 1H), 5.0-4.20 (bs, 2H), 3.50-2.40 (bs, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 133.2, 132.7, 128.5, 127.6, 126.2, 125.9, 46.5, 34.2 ppm. IR (neat) ν 3055, 2923, 2104, 1612, 1406, 1107, 813, 756 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{14}H_{13}N_3NaO$: 262.0951, found: 262.0950.

***N*-(Isopropyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide (6-1b)**



S1b: 68% yield

6-1b: 94% yield

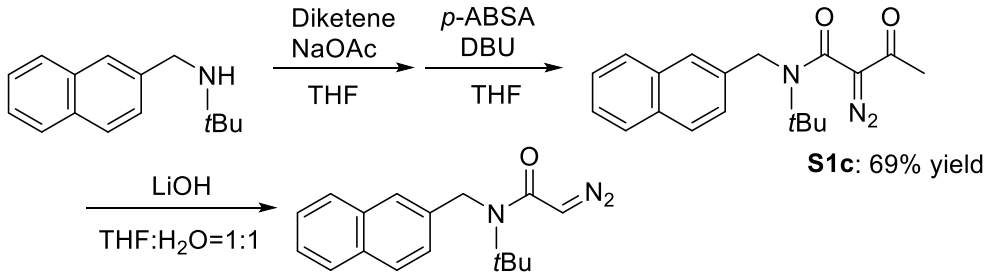
To a solution of secondary amine (398.0 mg, 2.0 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.77 mL, 10.0 mmol, 5 equiv.) and NaOAc (32.8 mg, 0.4 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x4 mL) The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (2.0 mmol, 1 equiv.) and *p*-ABSA (720.6 mg, 3.0 mmol, 1.5 equiv.) in THF (6 mL) was slowly added DBU (0.45 mL, 3.0 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (6 mL) and the combined mixture was extracted with EA (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(isopropyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1b** as a yellow liquid (68% yield, 418.0 mg, 1.35 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.03 Hz, 3H), 7.66 (s, 1H), 7.41 (td, *J* = 14.14, 6.88 Hz, 2H), 7.33 (d, *J* = 8.41 Hz, 1H), 4.62 (s, 2H), 4.24 (bs, 1H), 2.25 (s, 3H), 1.23 (s, 3H), 1.22 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 161.1, 135.2, 133.0, 132.3, 128.1, 127.4, 127.3, 125.9, 125.5, 125.0, 124.4, 73.5, 50.2, 46.2, 26.8, 20.6 ppm. IR (neat) ν 3051, 2973, 2931, 2103, 1651, 1410, 1271, 817, 752 cm^{-1}.

To a solution of *N*-(isopropyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1b** (187.0 mg, 0.60 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (71.85 mg, 3.0 mmol, 5 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature.

The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(isopropyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1b** as a yellow liquid (94% yield, 150.0 mg, 0.56 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 6.31, 4.59 Hz, 3H), 7.64 (s, 1H), 7.44 (td, *J* = 16.05, 7.26 Hz, 2H), 7.33 (d, *J* = 8.03 Hz, 1H), 5.70-4.0 (bs, 4H), 1.13 (s, 3H), 1.25 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 133.1, 132.3, 128.2, 127.5, 127.4, 126.1, 125.6, 124.5, 47.3, 45.2, 20.4 ppm. IR (neat) ν 3057, 2976, 2873, 2108, 1595, 1430, 1200, 1072, 818, 733 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{16}H_{17}N_3NaO$: 290.1264, found: 290.1269.

***N*-(*tert*-Butyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide (6-1c)**

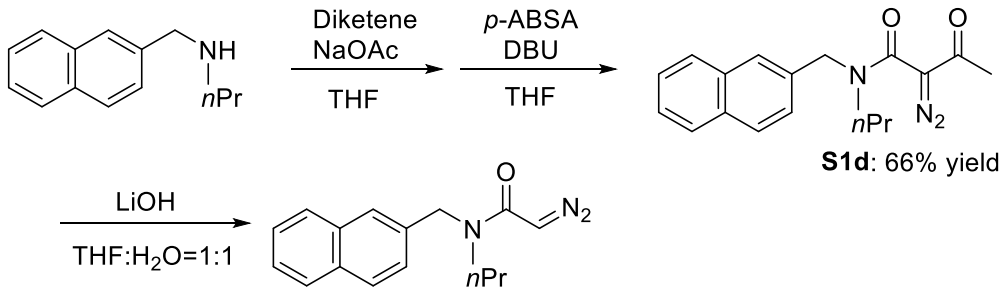


To a solution of secondary amine (418.0 mg, 1.96 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.76 mL, 9.8 mmol, 5 equiv.) and NaOAc (32.2 mg, 0.39 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.96 mmol, 1 equiv.) and *p*-ABSA (706.3 mg, 2.94 mmol, 1.5 equiv.) in THF (6 mL) was slowly added DBU (0.44 mL, 2.94 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (6 mL)and the combined mixture was extracted with EA (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(*tert*-butyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1c** as a yellow liquid (69% yield, 448.6 mg, 1.38 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 10.51, 8.41 Hz, 3H), 7.62 (s, 1H), 7.45 (td, *J* = 14.14, 6.88 Hz, 2H), 7.27 (d, *J* = 8.03 Hz, 1H), 4.73 (s, 2H), 2.22 (s, 3H), 1.44 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.1, 162.9, 136.1, 132.9, 132.3, 128.4, 127.4, 127.3, 126.3, 125.8, 124.7, 123.9, 75.5, 58.7, 51.0, 28.3, 26.8 ppm. IR (neat) ν 3059, 2973, 2927, 2102, 1361, 1258, 1195, 960, 748 cm^{-1}.

To a solution of *N*-(*tert*-butyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1c** (166.0 mg, 0.51 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (61.0 mg, 2.55 mmol, 5 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(*tert*-butyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1c** as a yellow liquid (91% yield, 131.1 mg, 0.46 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 13.0, 6.88 Hz, 3H), 7.65 (s, 1H), 7.45 (td, *J* = 17.97, 8.79 Hz, 2H), 7.29 (dd, *J* = 8.41, 1.53 Hz, 1H), 4.75 (s, 1H), 4.54 (s, 2H), 1.50 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 136.2, 133.2, 132.4, 128.5, 127.5, 126.3, 125.7, 124.1, 123.6, 58.1, 48.8, 48.6, 28.7 ppm. IR (neat) ν 3059, 2969, 2927, 2104, 1620, 1403, 1193, 813, 731 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}N_3NaO$: 304.1420, found: 304.1489.

_N_-(Propyl)-2-diazo-_N_-((naphthalen-2-yl)methyl)acetamide (6-1d)



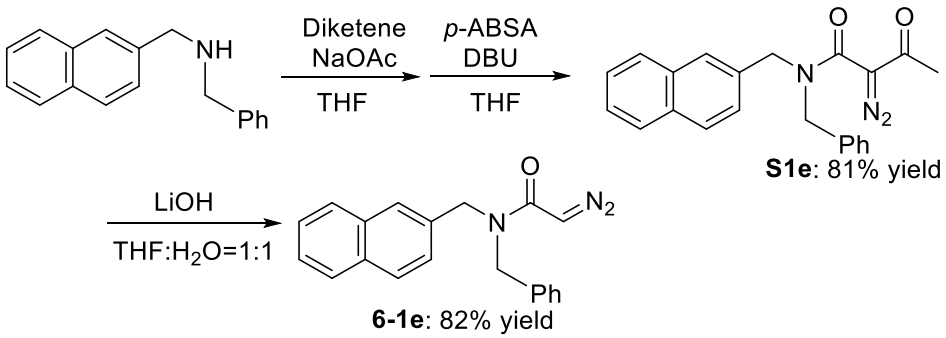
To a solution of secondary amine (589.5 mg, 2.95 mmol, 1 equiv.) in THF (6 mL) was slowly added diketene (1.1 mL, 14.75 mmol, 5 equiv.) and NaOAc (48.4 mg, 0.59 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1.5 mL) and the combined mixture was extracted with EA (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (2.95 mmol, 1 equiv.) and *p*-ABSA (1063.1 mg, 4.42 mmol, 1.5 equiv.) in THF (10 mL) was slowly added DBU (0.66 mL, 4.42 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (10 mL) and the combined mixture was extracted with EA (3x10 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(propyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1d** as a yellow liquid (66% yield, 605.2 mg, 1.96 mmol). ^{1}H NMR (500

MHz, $CDCl_3$) δ 7.81 (s, 3H), 7.66 (s, 1H), 7.47 (s, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 4.73 (s, 2H), 3.27 (t, *J* = 7.3 Hz, 2H), 2.35 (s, 3H), 1.78-1.46 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 161.3, 133.5, 133.0, 132.6, 128.5, 127.5, 126.2, 125.9, 125.8, 124.9, 72.9, 50.4, 48.9, 27.0, 20.6, 10.9 ppm. IR (neat) ν 3047, 2962, 2837, 2103, 1652, 1417, 1270, 1247, 813, 752 cm^{-1}.

To a solution of *N*-(propyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1d** (139.0 mg, 0.45 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (21.5 mg, 0.9 mmol, 2 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 5 h at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(propyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1d** as a yellow liquid (85% yield, 102.7 mg, 0.38 mmol). ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.54 Hz, 3H), 7.61 (s, 1H), 7.50-7.40 (m, 2H), 7.33 (s, 1H), 4.95 (s, 1H), 4.80-4.30 (bs, 2H), 3.80-2.70 (bs, 2H), 1.70-1.40 (bs, 2H), 0.85 (t, *J* = 7.32 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 133.2, 132.6, 128.5, 127.6, 126.2, 125.8, 48.6, 46.7, 21.4, 11.2 ppm. IR (neat) ν 3055, 2966, 2935, 2877, 2106, 1614, 1434, 1224, 817, 752 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{16}H_{17}N_3NaO$: 290.1264, found: 290.1269.

_N_-(Benzyl)-2-diazo-_N_-((naphthalen-2-yl)methyl)acetamide (6-1e)



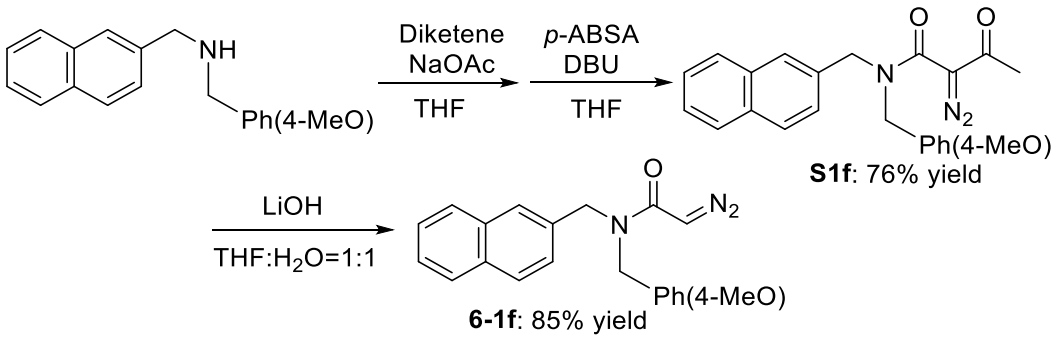
To a solution of secondary amine (296.8 mg, 1.2 mmol, 1 equiv.) in THF (4.8 mL) was slowly added diketene (0.46 mL, 6.0 mmol, 5 equiv.) and NaOAc (19.8 mg, 0.24 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.6 mL) and the combined mixture was extracted with EA (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.2 mmol, 1 equiv.) and *p*-ABSA (432.4 mg, 1.8 mmol, 1.5 equiv.) in THF (3.6 mL) was slowly added DBU (0.27 mL, 1.8 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with

H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(benzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1e** as a yellow liquid (81% yield, 347.8 mg, 0.97 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.8 Hz, 2H), 7.79 (t, *J* = 4.6 Hz, 1H), 7.59 (s, 1H), 7.49 (t, *J* = 4.2 Hz, 2H), 7.43-7.27 (m, 4H), 7.18 (d, *J* = 6.9 Hz, 2H), 4.67 (s, 2H), 4.55 (s, 2H), 2.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 162.0, 135.8, 133.2, 133.1, 132.8, 128.8, 128.7, 127.8, 127.7, 127.6, 127.5, 126.5, 126.4, 126.1, 125.2, 75.0, 50.4, 50.3, 27.3 ppm. IR (neat) ν 3059, 2923, 2105, 1633, 1416, 1274, 1245, 731 cm^{-1}.

To a solution of *N*-(benzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1e** (323.1 mg, 0.90 mmol, 1 equiv.) in THF (3 mL) was slowly added LiOH (107.8 mg, 4.5 mmol, 5 equiv.) in H_2O (3 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x3 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(benzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1e** as a yellow liquid (82% yield, 232.2 mg, 0.74 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 11.85, 8.41 Hz, 3H), 7.58 (s, 1H), 7.53-7.40 (m, 2H), 7.40-6.93 (m, 6H), 4.96 (s, 1H), 4.89-3.78 (bs, 4H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 133.1, 132.6, 128.6, 128.5, 127.5, 127.4, 126.2, 125.9, 49.2, 46.9 ppm. IR (neat) ν 3059, 2923, 2105, 1608, 1426, 1212, 813, 728 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{20}H_{17}N_3NaO$: 338.1264, found: 338.1261.

***N*-(4-methoxyBenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide (6-1f)**



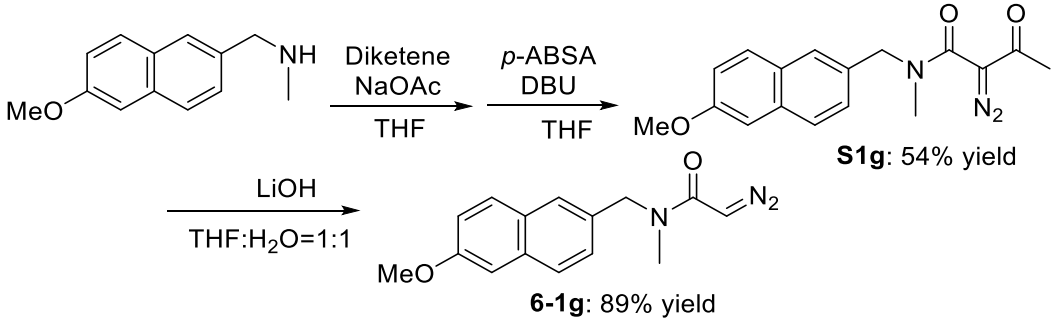
To a solution of secondary amine (332.8 mg, 1.2 mmol, 1 equiv.) in THF (4.8 mL) was slowly added diketene (0.46 mL, 6.0 mmol, 5 equiv.) and NaOAc (19.8 mg, 0.24 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.6 mL) and the combined mixture was extracted with EA (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure

to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.2 mmol, 1 equiv.) and *p*-ABSA (432.4 mg, 1.8 mmol, 1.5 equiv.) in THF (3.6 mL) was slowly added DBU (0.27 mL, 1.8 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(4-methoxybenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1f** as a yellow liquid (76% yield, 346.7 mg, 0.894 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.78-7.80 (m, 1H), 7.58 (s, 1H), 7.49 (t, *J* = 3.8 Hz, 2H), 7.30 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.10 (d, *J* = 9.0 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 4.64 (s, 2H), 4.48 (s, 2H), 3.81 (s, 3H), 2.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 159.2, 133.2, 132.8, 129.0, 128.7, 127.6, 126.4, 126.3, 126.1, 125.2, 114.1, 55.2, 50.2, 49.7, 27.2 ppm. IR (neat) ν 3051, 3000, 2931, 2834, 2104, 1638, 1412, 1246, 1177, 817 cm^{-1}.

To a solution of *N*-(4-methoxybenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)-3-oxobutanamide **S1f** (323.2 mg, 0.83 mmol, 1 equiv.) in THF (2.5 mL) was slowly added LiOH (99.4 mg, 4.15 mmol, 5 equiv.) in H_2O (2.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x3 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(4-methoxybenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1f** as a yellow liquid (85% yield, 244.5 mg, 0.71 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (t, *J* = 8.6 Hz, 3H), 7.56 (s, 1H), 7.43 (bs, 2H), 7.29 (bs, 1H), 7.11 (bs, 2H), 6.83 (d, *J* = 8.4 Hz, 2H), 4.97 (s, 1H), 4.89-3.92 (bs, 4H), 3.73 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 158.8, 133.0, 132.5, 128.4, 127.4, 126.1, 125.7, 113.9, 54.9, 48.5, 46.7 ppm. IR (neat) ν 3059, 2954, 2927, 2106, 1609, 1511, 1247, 821 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{21}H_{19}N_3NaO_2$: 368.1369, found: 368.1380.

_N_-(Methyl)-2-diazo-_N_-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1g)

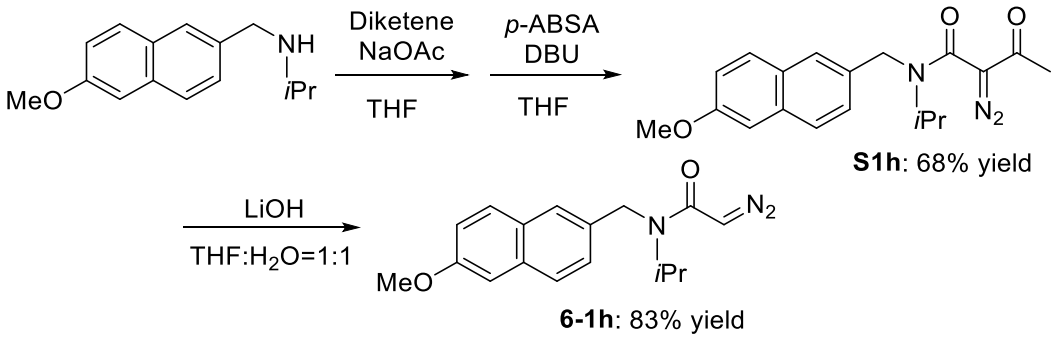


To a solution of secondary amine (201.3 mg, 1.0 mmol, 1 equiv.) in THF (2 mL) was slowly added diketene (0.38 mL, 5.0 mmol, 5 equiv.) and NaOAc (16.4 mg, 0.2 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x2 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.0 mmol, 1 equiv.) and *p*-ABSA (360.4 mg, 1.5 mmol, 1.5 equiv.) in THF (3 mL) was slowly added DBU (0.22 mL, 1.5 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (3 mL) and the combined mixture was extracted with EA (3x3 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 2/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1g** as a yellow liquid (54% yield, 166.6 mg, 0.54 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 12.4, 8.6 Hz, 2H), 7.60 (s, 1H), 7.33 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.15 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.11 (d, *J* = 2.3 Hz, 1H), 4.68 (s, 2H), 3.88 (s, 3H), 2.91 (s, 3H), 2.37 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 161.4, 157.6, 133.8, 130.9, 128.9, 128.4, 127.3, 126.4, 125.9, 118.9, 105.4, 73.3, 55.0, 52.5, 35.4, 27.1 ppm. IR (neat) ν 3004, 2954, 2935, 2842, 2107, 1636, 1392, 1266, 1030, 856 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1g** (166.0 mg, 0.53 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (25.4 mg, 1.06 mmol, 2 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 2 h at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/2 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1g** as a yellow solid (89% yield, 127.1 mg, 0.47 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (t, *J* = 8.4 Hz, 2H), 7.53 (s, 1H), 7.29 (s, 1H), 7.13 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.10 (d, *J* = 2.3 Hz, 1H), 4.99 (s, 1H), 4.60 (s, 2H), 3.86 (s, 3H), 2.78 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 157.5, 133.7, 128.9, 128.5, 127.2, 118.8, 105.4, 55.0, 46.3, 33.9 ppm. IR (neat) ν 3055, 2962, 2935, 2104, 1608, 1408, 1266, 1171, 1027, 856 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{15}H_{15}N_3NaO_2$: 292.1056, found: 292.1057.

***N*-(Isopropyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1h)**



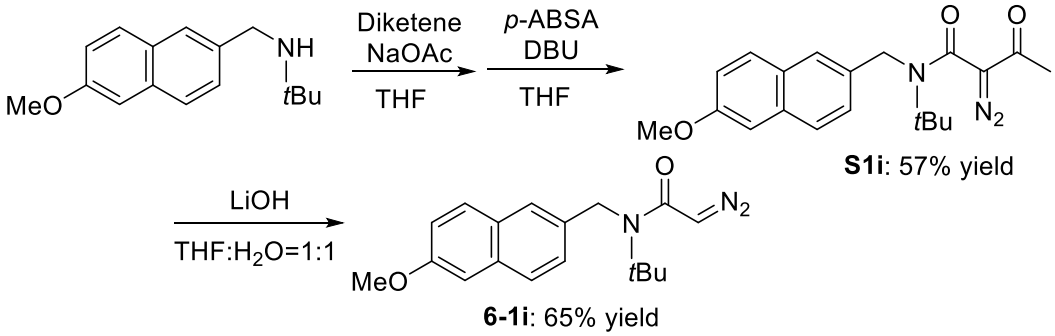
To a solution of secondary amine (436.0 mg, 1.9 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.73 mL, 9.5 mmol, 5 equiv.) and NaOAc (31.1 mg, 0.38 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.9 mmol, 1 equiv.) and *p*-ABSA (684.7 mg, 2.85 mmol, 1.5 equiv.) in THF (9 mL) was slowly added DBU (0.42 mL, 2.85 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (9 mL) and the combined mixture was extracted with EA (3x9 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(isopropyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide as a yellow liquid **S1h** (68% yield, 437.4 mg, 1.29 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (t, *J* = 8.60 Hz, 2H), 7.59 (s, 1H), 7.31 (dd, *J* = 8.41, 1.53 Hz, 1H), 7.13 (dd, *J* = 8.79, 2.68 Hz, 1H), 7.10 (d, *J* = 2.29 Hz, 1H), 4.62 (s, 2H), 4.27 (bs, 1H), 3.88 (s, 3H), 2.27 (s, 3H), 1.27 (s, 3H), 1.25 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 161.3, 157.5, 133.6, 132.9, 129.0, 128.6, 127.1, 125.2, 125.1, 119.0, 105.5, 73.8, 55.1, 50.3, 46.4, 27.0, 20.8 ppm. IR (neat) ν 2966, 2931, 2838, 2102, 1632, 1265, 1030, 848 cm^{-1}.

To a solution of *N*-(isopropyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1h** (263.8 mg, 0.78 mmol, 1 equiv.) in THF (2 mL) was slowly added LiOH (93.4 mg, 3.9 mmol, 5 equiv.) in H_2O (2.0 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(isopropyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1h** as a yellow liquid (83% yield, 193.3 mg, 0.65 mmol). ^{1}H NMR (500 MHz,

$CDCl_3$) δ 7.68 (dd, *J* = 11.28, 8.79 Hz, 2H), 7.56 (s, 1H), 7.29 (d, *J* = 8.03, 1H), 7.13 (dd, *J* = 8.98, 2.68 Hz, 1H), 7.10 (d, *J* = 2.29 Hz, 1H), 4.83 (bs, 1H), 4.44 (bs, 2H), 3.86 (s, 3H), 1.13 (bs, 3H), 1.12 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 157.4, 133.5, 128.9, 128.6, 127.0, 124.4, 118.8, 105.4, 55.0, 47.2, 45.1, 20.4 ppm. IR (neat) ν 3059, 2973, 2939, 2838, 2104, 1606, 1428, 1267, 1026, 852, 724 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}N_3NaO_2$: 320.1369, found: 320.1359.

***N*-(tert-Butyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1i)**

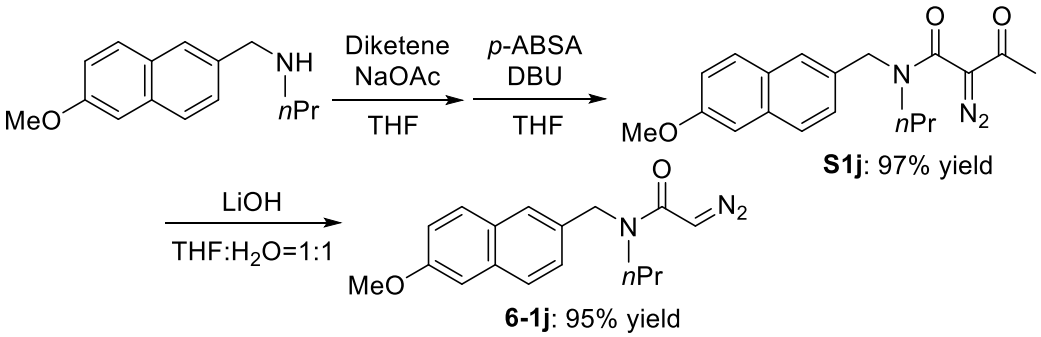


To a solution of secondary amine (730.0 mg, 3.0 mmol, 1 equiv.) in THF (6 mL) was slowly added diketene (1.15 mL, 15.0 mmol, 5 equiv.) and NaOAc (49.2 mg, 0.6 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1.5 mL) and the combined mixture was extracted with EA (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (3.0 mmol, 1 equiv.) and *p*-ABSA (1081.0 mg, 4.5 mmol, 1.5 equiv.) in THF (9 mL) was slowly added DBU (0.67 mL, 4.5 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (9 mL) and the combined mixture was extracted with EA (3x9 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(tert-butyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1i** as a yellow solid (57% yield, 605.8 mg, 1.71 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.8 Hz, 1H), 7.69 (d, *J* = 9.2 Hz, 1H), 7.56 (s, 1H), 7.25 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.16 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.12 (d, *J* = 2.3 Hz, 1H), 4.72 (s, 2H), 3.91 (s, 3H), 2.25 (s, 3H), 1.45 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.1, 157.7, 133.9, 133.7, 129.0, 128.6, 127.4, 124.8, 124.6, 119.3, 105.6, 58.9, 55.2, 51.2, 28.5, 27.0 ppm. IR (neat) ν 3055, 2973, 2931, 2842, 2102, 1644, 1266, 1030, 852, 744 cm^{-1}.

To a solution of *N*-(tert-butyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1i** (162.0 mg, 0.46 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (55.1 mg, 2.3 mmol, 5 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(tert-butyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1i** as a yellow liquid (65% yield, 93.2 mg, 0.30 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 16.63, 8.79 Hz, 2H), 7.57 (s, 1H), 7.26 (dd, *J* = 8.60, 1.53 Hz, 1H), 7.15 (dd, *J* = 8.98, 2.68 Hz, 2H), 4.79 (s, 1H), 4.53 (s, 2H), 3.90 (s, 3H), 1.50 (s, 9H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 157.6, 133.9, 133.6, 129.0, 128.8, 127.4, 124.2, 124.0, 119.1, 105.6, 58.2, 55.2, 48.8, 48.7, 28.8 ppm. IR (neat) ν 3055, 2966, 2838, 2103, 1608, 1402, 1194, 1030, 848, 731 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{18}H_{21}N_3NaO_2$: 334.1526, found: 334.1535.

_N_-(Propyl)-2-diazo-_N_-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1j)



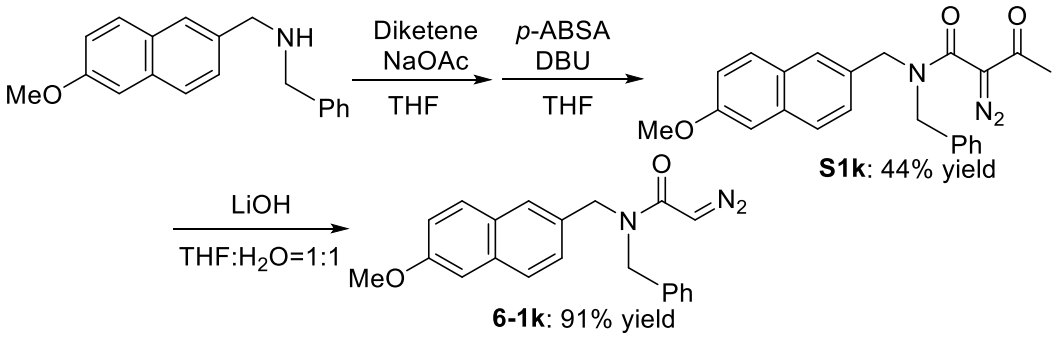
To a solution of secondary amine (654.0 mg, 2.85 mmol, 1 equiv.) in THF (6 mL) was slowly added diketene (1.1 mL, 14.25 mmol, 5 equiv.) and NaOAc (47.0 mg, 0.57 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1.5 mL) and the combined mixture was extracted with EA (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (2.85 mmol, 1 equiv.) and *p*-ABSA (1027.0 mg, 4.27 mmol, 1.5 equiv.) in THF (12 mL) was slowly added DBU (0.64 mL, 4.27 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (12 mL) and the combined mixture was extracted with EA (3x12 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 5/1 ($^v/_v$)) to give *N*-(propyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1j** as a yellow liquid (97% yield, 937.6 mg, 2.76 mmol). ^{1}H NMR

(500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 12.61, 8.79 Hz, 2H), 7.58 (s, 1H), 7.29 (dd, *J* = 8.41, 1.53 Hz, 1H), 7.15 (dd, *J* = 8.98, 2.29 Hz, 1H), 7.11 (d, *J* = 2.29 Hz, 1H), 4.68 (s, 2H), 3.88 (s, 3H), 3.26 (t, *J* = 7.64 Hz, 2H), 2.34 (s, 3H), 1.61 (sixt., *J* = 7.26 Hz, 2H), 0.86 (t, *J* = 7.26 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 161.2, 157.6, 133.8, 131.1, 128.9, 128.4, 127.3, 125.9, 125.5, 119.0, 105.4, 72.9, 55.0, 50.3, 48.7, 27.0, 20.5, 10.9 ppm. IR (neat) ν 2958, 2935, 2877, 2103, 1634, 1266, 1026, 852 cm^{-1}.

To a solution of *N*-(propyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1j** (200.0 mg, 0.60 mmol, 1 equiv.) in THF (1.8 mL) was slowly added LiOH (71.8 mg, 3.0 mmol, 5 equiv.) in H_2O (1.8 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(propyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide as a yellow liquid **6-1j** (95% yield, 169.3 mg, 0.57 mmol). ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 8.03, 6.12 Hz, 2H), 7.55 (s, 1H), 7.30 (bs, 1H), 7.14 (dd, *J* = 9.17, 2.29 Hz, 1H), 7.10 (d, *J* = 2.29 Hz, 1H), 4.96 (bs, 1H), 4.90-4.30 (bs, 2H), 3.88 (s, 3H), 3.60-2.80 (bs, 2H), (bs, 2H), 0.86 (t, *J* = 7.26 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 157.5, 133.7, 129.0, 128.6, 127.2, 118.9, 105.5, 55.1, 48.5, 46.6, 21.3, 11.1 ppm. IR (neat) ν 3059, 2963, 2935, 2875, 2097, 1636, 1165, 1123, 1032, 729 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}N_3NaO_2$: 320.1369, found: 320.1360.

_N_-(Benzyl)-2-diazo-_N_-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1k)

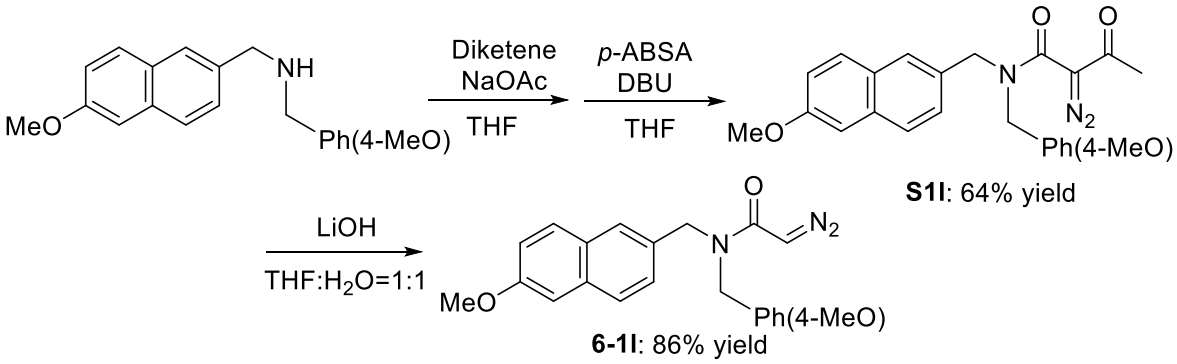


To a solution of secondary amine (554.0 mg, 2.0 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.77 mL, 10.0 mmol, 5 equiv.) and NaOAc (32.8 mg, 0.4 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (2.0 mmol, 1 equiv.) and *p*-ABSA (720.7 mg, 3.0 mmol, 1.5 equiv.) in THF (4 mL) was slowly added DBU (0.45 mL, 3.0 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 5/1 ($^v/_v$)) to give *N*-(benzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1k** as a yellow solid (44% yield, 341.0 mg, 0.88 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.46 (s, 1H), 7.29 (t, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 5.2 Hz, 2H), 7.14 (d, *J* = 7.3 Hz, 2H), 7.11 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.08 (d, *J* = 1.9 Hz, 1H), 4.58 (s, 2H), 4.49 (s, 2H), 3.81 (s, 3H), 2.30 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 161.5, 157.4, 135.5, 133.6, 130.5, 128.8, 128.4, 128.3, 127.3, 127.2, 127.1, 126.0, 125.5, 118.8, 105.3, 73.0, 54.8, 50.0, 49.8, 26.8 ppm. IR (neat) ν 3055, 2935, 2842, 2105, 1634, 1411, 1266, 1026, 860, 735 cm^{-1}.

To a solution of *N*-(benzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1k** (246.5 mg, 0.63 mmol, 1 equiv.) in THF (1 mL) was slowly added LiOH (75.44 mg, 3.15 mmol, 5 equiv.) in H_2O (1.0 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x1 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(benzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1k** as a yellow liquid (91% yield, 197.5 mg, 0.57 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 21.98, 8.79 Hz, 2H), 7.48 (s, 1H), 7.35-7.0 (m, 8H), 4.95 (s, 1H), 4.90-4.05 (m, 4H), 3.84 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 157.5, 133.7, 128.9, 128.6, 128.5, 127.3, 118.9, 105.5, 55.0, 49.1, 46.8 ppm. IR (neat) ν 3063, 2958, 2931, 2110, 1613, 1416, 1266, 1030, 853, 732 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{21}H_{20}N_3O_2$: 346.1550, found: 346.1565.

***N*-(4-methoxyBenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1l)**

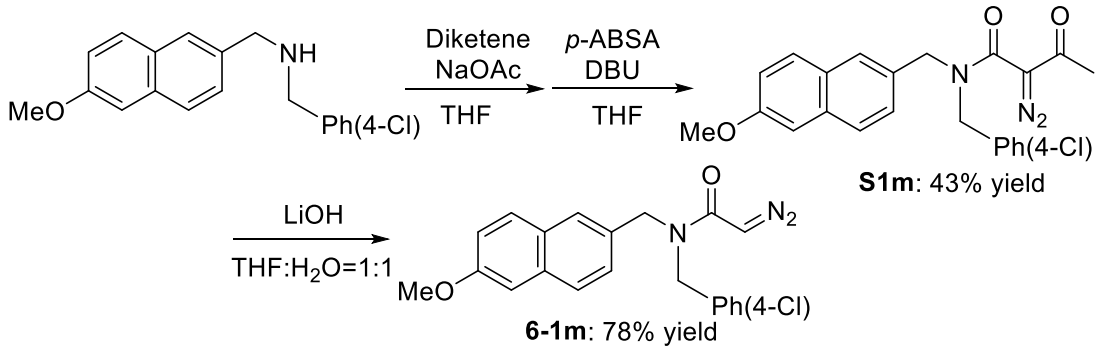


To a solution of secondary amine (614.78 mg, 2.0 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.77 mL, 10.0 mmol, 5 equiv.) and NaOAc (32.8 mg, 0.4 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (2.0 mmol, 1 equiv.) and *p*-ABSA (720.7 mg, 3.0 mmol, 1.5 equiv.) in THF (4 mL) was slowly added DBU (0.45 mL, 3.0 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 5/1 ($^v/_v$)) to give *N*-(4-methoxybenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide as a yellow liquid **S1l** (64% yield, 534.0 mg, 1.28 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H), 7.47 (s, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.12 (dd, *J* = 8.8, 2.7 Hz, 1H), 7.06-7.09 (m, 3H), 6.83 (d, *J* = 8.4 Hz, 2H), 4.57 (s, 2H), 4.43 (s, 2H), 3.82 (s, 3H), 3.71 (d, *J* = 1.9 Hz, 4H), 2.32 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 161.3, 158.7, 157.4, 133.6, 130.5, 128.7, 128.5, 128.2, 127.3, 127.1, 125.9, 125.4, 118.7, 113.7, 105.2, 72.9, 54.7, 54.7, 49.7, 49.2, 26.7 ppm. IR (neat) ν 3000, 2954, 2935, 2834, 2105, 1632, 1610, 1266, 1026, 848, 813 cm^{-1}.

To a solution of *N*-(4-methoxybenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1l** (236.0 mg, 0.71 mmol, 1 equiv.) in THF (2 mL) was slowly added LiOH (85.0 mg, 3.55 mmol, 5 equiv.) in H_2O (2.0 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(4-methoxybenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1l** as a yellow liquid (86% yield, 228.0 mg, 0.61 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 15.86, 8.79 Hz, 2H), 7.51 (s, 1H), 7.27 (s, 1H), 7.13 (td, *J* = 8.98, 2.29 Hz, 4H), 6.85 (d, *J* = 11.47 Hz, 2H), 4.99 (s, 1H), 4.80-4.0 (bs, 4H), 3.88 (s, 3H), 3.77 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4, 158.9, 157.6, 133.8, 129.0, 128.6, 127.4, 119.0, 114.0, 105.6, 55.1, 49.3, 48.6, 46.9 ppm. IR (neat) ν 3059, 2954, 2935, 2106, 1608, 1266, 1174, 1031, 852, 810 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{22}H_{21}N_3NaO_3$: 398.1475, found: 398.1475.

***N*-(4-chloroBenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide (6-1m)**



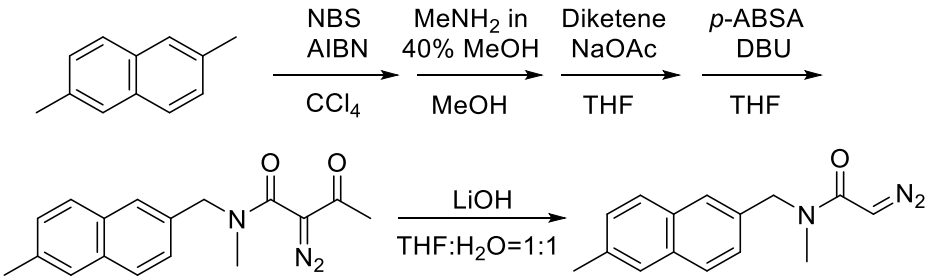
To a solution of secondary amine (597.0 mg, 1.91 mmol, 1 equiv.) in THF (4 mL) was slowly added diketene (0.74 mL, 9.55 mmol, 5 equiv.) and NaOAc (31.3 mg, 0.38 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA(3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1.91 mmol, 1 equiv.) and *p*-ABSA (688.3 mg, 2.86 mmol, 1.5 equiv.) in THF (4 mL) was slowly added DBU (0.43 mL, 2.86 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 4/1 ($^v/_v$)) to give *N*-(4-chlorobenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1m** as a yellow liquid (43% yield, 342.6 mg, 0.81 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.4 Hz, 1H), 7.64 (d, *J* = 9.2 Hz, 1H), 7.45 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.23 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.13 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.11-7.02 (m, 3H), 4.57 (s, 2H), 4.46 (s, 2H), 3.85 (s, 3H), 2.33 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 161.7, 157.6, 134.3, 133.8, 133.1, 130.3, 128.9, 128.8, 128.6, 128.3, 127.3, 126.1, 125.5, 119.0, 105.4, 73.6, 54.9, 50.5, 49.0, 26.9 ppm. IR (neat) ν 3051, 2996, 2931, 2106, 1633, 1266, 1169, 848 cm^{-1}.

To a solution of *N*-(4-chlorobenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)-3-oxobutanamide **S1m** (338.0 mg, 0.8 mmol, 1 equiv.) in THF (2 mL) was slowly added LiOH (96.0 mg, 4.0 mmol, 5 equiv.) in H_2O (2.0 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(4-chlorobenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1m** as a yellow liquid (78% yield, 238.2 mg, 0.63

mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 23.70, 9.17 Hz, 2H), 7.46 (s, 1H), 7.24 (d, *J* = 8.03 Hz, 3H), 7.18-7.0 (m, 4H), 4.99 (s, 1H), 4.90-4.0 (bs, 4H), 3.84 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.5, 133.7, 133.0, 128.9, 128.6, 128.4, 127.3, 119.0, 105.4, 55.0, 48.4, 46.8 ppm. IR (neat) ν 3059, 2935, 2834, 2107, 1608, 1212, 1031, 852, 731 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{21}H_{18}ClN_3NaO_2$: 402.0980, found: 402.0988.

***N*-(Methyl)-2-diazo-*N*-((6-methylnaphthalen-2-yl)methyl)acetamide (6-1n)**



S1n: 8% yield **6-1n**: 85% yield

A mixture of *N*-bromosuccinimide (228.0 mg, 1.28 mmol, 2 equiv.) and 2,6-dimethylnaphthalene (100.0 mg, 0.64 mmol, 1 equiv) were dissolved in 3 mL of CCl_4 under argon atmosphere. Then a catalytic quantity of AIBN (3.2 mg, 0.019 mmol, 3 mol%) was added which was then heated 80 ℃ for 4 h. After the reaction was completed, concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 50/1 ($^{v}/_{v}$)) to give mixture of 2,6-bis(bromomethyl)naphthalene and 2-(bromomethyl)-6-methylnaphthalene (134.0 mg).

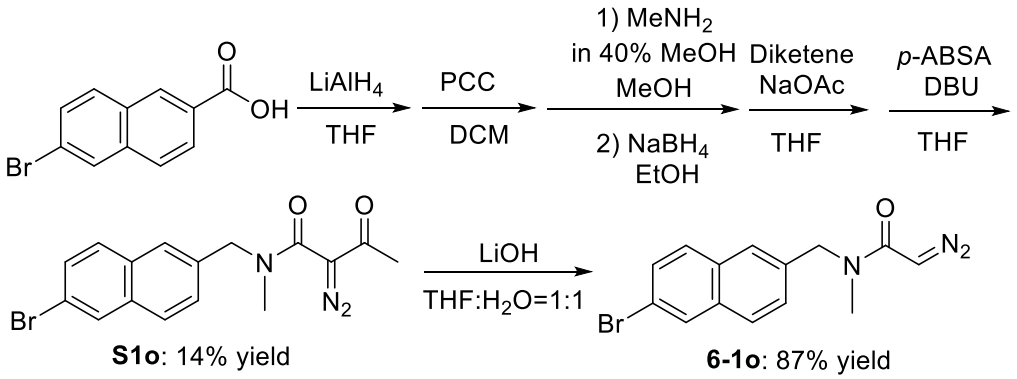
To a stirred suspension of 2,6-bis(bromomethyl)naphthalene and 2-(bromomethyl)-6-methylnaphthalene (134.0 mg) in MeOH (1 mL) was added a 40% solution of methylamine in MeOH (1.3 mL) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. The residue was dissolved in CH_2Cl_2 (1 mL) and washed with a 20% NaOH (1 mL) solution and water. The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give mixture of secondary amines, which was used for next step without further purification.

To a solution of the mixture of secondary amines in THF (1.2 mL) was slowly added diketene (0.33 mL) and NaOAc (14.1 mg) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA(3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired mixture of β-ketoamides, which was used for next step without further purification.

To a solution of the mixture of β-ketoamides and *p*-ABSA (309.9 mg) in THF (2 mL) was slowly added DBU (0.19 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (2 mL) and the combined mixture was extracted with EA (3x2 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-methylnaphthalen-2-yl)methyl)-3-oxobutanamide **S1n** as a yellow liquid (8% yield, 29.8 mg, 0.10 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.64 (s, 1H), 7.60 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 4.72 (s, 2H), 2.94 (s, 3H), 2.51 (s, 3H), 2.39 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 135.8, 133.0, 132.4, 131.4, 128.6, 128.1, 127.4, 126.6, 126.4, 125.5, 52.9, 35.6, 27.3, 21.6 ppm. IR (neat) ν 2923, 2858, 2105, 1633, 1289, 1046, 821 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((6-methylnaphthalen-2-yl)methyl)-3-oxobutanamide **S1n** (29.0 mg, 0.098 mmol, 1 equiv.) in THF (0.3 mL) was slowly added LiOH (11.7 mg, 0.49 mmol, 5 equiv.) in H_2O (0.3 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x1 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-methylnaphthalen-2-yl)methyl)acetamide **6-1n** as a yellow solid (85% yield, 21.0 mg, 0.083 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.59 (s, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 5.00 (s, 1H), 4.64 (bs, 2H), 2.87 (bs, 3H), 2.50 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 135.6, 132.9, 131.5, 128.6, 127.9, 127.4, 126.6, 46.6, 34.2, 21.6 ppm. IR (neat) ν 3051, 2919, 2858, 2104, 1608, 1267, 813, 728 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{15}H_{15}N_3NaO$: 276.1107, found: 276.1103.

***N*-(Methyl)-2-diazo-*N*-((6-bromonaphthalen-2-yl)methyl)acetamide (6-1o)**



To a solution of 6-bromo-2-naphthoic acid (690.0 mg, 2.75 mmol, 1 equiv.) in THF (30 mL) was added by slowly $LiAlH_4$ (208.7 mg, 5.5 mmol, 2 equiv.) at 0 ℃ in an ice bath. The reaction mixture was allowed to warm to room temperature for 1 h. It was quenched by addition H_2O (3 mL) and extracted with Et_2O (3x10 mL) and dried over Na_2SO_4, and concentrated under reduced pressure to give mixture of (6-bromonaphthalen-2-yl)methanol and 2-naphthalenmethanol, which were used for next step without further purification.

To a solution of the mixture of (6-bromonaphthalen-2-yl)methanol and 2-naphthalenmethanol in CH_2Cl_2 (15 mL) was added pyridium chlorochromate (592.8 mg, 2.75 mmol, 1 equiv.) and the reaction mixture was heated to reflux for 5 h. After the reaction was completed, concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 10/1 ($^{v}/_{v}$)) to give mixture of 6-bromo-2-naphthaldehyde and naphthaldehyde (376.8 mg).

To a stirred suspension of 6-bromo-2-naphthaldehyde and 2-naphthaldehyde (376.8 mg) in MeOH (3.2 mL) and CH_2Cl_2 (1.6 mL) was added a 40% solution of methylamine in MeOH (1.6 mL) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (4.8 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (60.5 mg) was added, and stirring was continued for 1 h at room temperature. The reaction was quenched with the addition of H_2O (5 mL) and Na_2CO_3 (125.0 mg), and extracted with CH_2Cl_2 (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give mixture of secondary amines, which was used for next step without further purification.

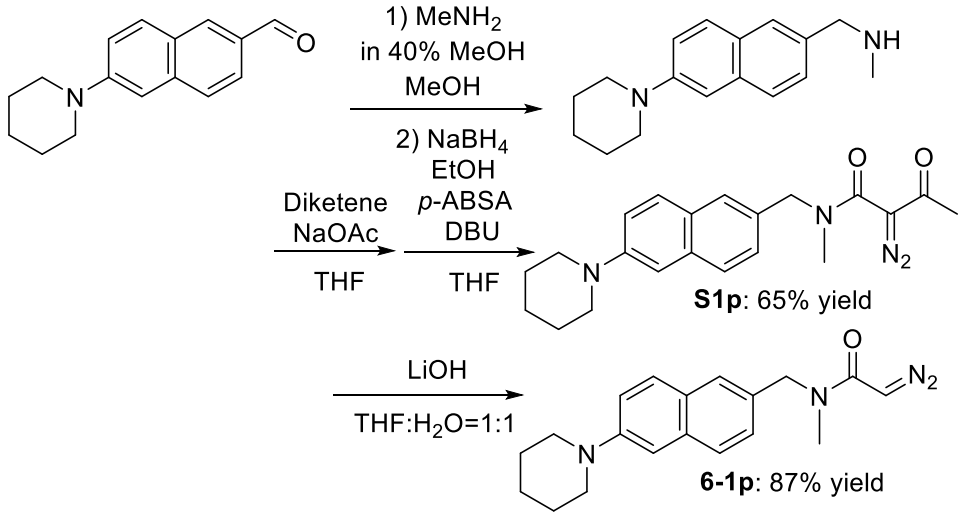
To a solution of the mixture of secondary amines in THF (3.2 mL) was slowly added diketene (0.62 mL) and NaOAc (26.2 mg) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x3 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired mixture of β-ketoamides, which was used for next step without further purification.

To a solution of the mixture of β-ketoamides and *p*-ABSA (576.6 mg) in THF (3.2 mL) was slowly added DBU (0.36 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (3 mL) and the combined mixture was extracted with EA (3x3 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 5/1 ($^{v}/_{v}$)) to give *N*-(methyl)-2-diazo-*N*-((6-bromonaphthalen-2-yl)methyl)-3-oxobutanamide **S1o** as a yellow

liquid (14% yield, 143.0 mg, 0.397 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 2H), 7.55 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.41 (dd, *J* = 8.4, 1.1 Hz, 1H), 4.72 (s, 2H), 2.95 (s, 3H), 2.39 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 161.7, 134.0, 133.8, 131.6, 129.6, 129.3, 127.7, 126.5, 119.9, 73.7, 52.6, 35.8, 27.2 ppm. IR (neat) ν 3051, 2962, 2925, 2106, 1621, 1268, 1050, 813, 736 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((6-bromonaphthalen-2-yl)methyl)-3-oxobutanamide **S1o** (143.0 mg, 0.40 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (47.5 mg, 2.0 mmol, 5 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 5/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-bromonaphthalen-2-yl)methyl)acetamide **6-1o** as a yellow solid (87% yield, 109.8 mg, 0.35 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.72 (d, *J* = 8.41 Hz, 1H), 7.67 (d, *J* = 8.79 Hz, 1H), 7.61 (s, 1H), 7.55 (d, *J* = 8.79 Hz, 1H), 7.37 (s, 1H), 5.01 (s, 1H), 4.90-4.0 (bs, 2H), 3.70-2.60 (bs, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 133.8, 131.7, 129.7, 129.3, 127.7, 119.8, 49.5, 34.3 ppm. IR (neat) ν 3063, 2919, 2104, 1607, 1111, 879, 806 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{14}H_{12}BrN_3NaO$: 340.0056, found: 340.0073.

***N*-(Methyl)-2-diazo-*N*-((6-piperidinenaphthalen-2-yl)methyl)acetamide (6-1p)**



To a stirred suspension of 6-piperidine-2-naphthaldehyde (66.0 mg, 0.28 mmol, 1 equiv.) in MeOH (0.5 mL) was added a 40% solution of methylamine in MeOH (0.28 mL, 2.8 mmol, 10 equiv.) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (1.5 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (10.6 mg, 0.28 mmol. 1 equiv.) was added, and stirring was continued for 1 h

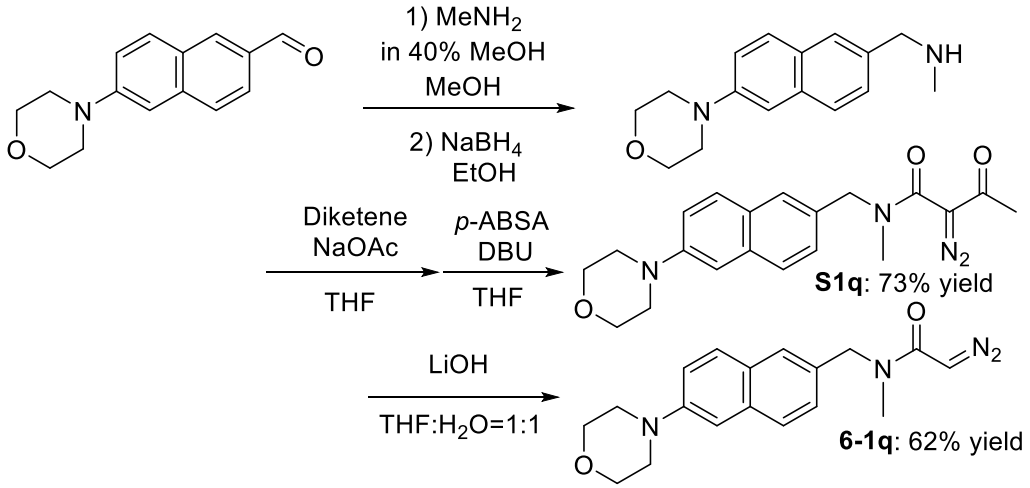
at room temperature. The reaction was quenched with the addition of H_2O (1 mL) and Na_2CO_3 (21.6 mg), and extracted with CH_2Cl_2 (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give secondary amine (94% yield, 66.0 mg, 0.26 mmol).

To a solution of the secondary amine (66.0 mg, 0.26 mmol, 1 equiv.) in THF (0.6 mL) was slowly added diketene (0.1 mL, 1.3 mmol, 5 equiv.) and NaOAc (4.3 mg, 0.052 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a solution of β-ketoamide (0.26 mmol, 1 equiv.) and *p*-ABSA (93.7 mg, 0.39 mmol, 1.5 equiv.) in THF (1 mL) was slowly added DBU (58 μL, 0.39 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (1 mL) and the combined mixture was extracted with EA (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-piperidinenaphthalen-2-yl)methyl)-3-oxobutanamide **S1p** as a yellow liquid (65% yield, 62.0 mg, 0.17 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 4.2 Hz, 1H), 7.65 (d, *J* = 3.4 Hz, 1H), 7.54 (s, 1H), 7.28-7.30 (m, 1H), 7.26-7.28 (m, 1H), 7.10 (d, *J* = 2.3 Hz, 1H), 4.67 (s, 2H), 3.25 (t, *J* = 5.5 Hz, 4H), 2.91 (s, 3H), 2.38 (s, 3H), 1.81-1.68 (m, 4H), 1.68-1.52 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 161.5, 150.2, 134.1, 130.3, 128.2, 127.8, 127.4, 126.4, 125.7, 120.4, 109.9, 73.4, 50.9, 50.7, 35.4, 27.3, 25.7, 24.2 ppm. IR (neat) ν 2939, 2106, 1653, 1507, 1270, 748 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((6-piperidinenaphthalen-2-yl)methyl)-3-oxobutanamide **S1p** (62.0 mg, 0.17 mmol, 1 equiv.) in THF (0.5 mL) was slowly added LiOH (20.4 mg, 0.85 mmol, 5 equiv.) in H_2O (0.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x1 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-piperidinenaphthalen-2-yl)methyl)acetamide **6-1p** as a yellow solid (87% yield, 47.9 mg, 0.15 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 8.22, 7.64 Hz, 2H), 7.49 (s, 1H), 7.27 (dd, *J* = 9.36, 7.17 Hz, 2H), 7.09 (s, 1H), 4.98 (s, 1H), 4.90-4.10 (bs, 2H), 3.24 (t, *J* = 5.35 Hz, 4H), 3.10 (bs, 3H), 1.80-1.70 (m, 4H), 1.70-1.5 (m, 2H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 150.1, 134.0, 128.2, 127.9, 127.3, 120.4, 110.0, 51.0, 50.8, 46.5, 34.1, 25.7, 24.2 ppm. IR (neat) ν 3055, 2933, 2850, 2103, 1605, 1214, 852, 724 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{19}H_{23}N_4O$: 323.1866, found: 323.1860.

***N*-(Methyl)-2-diazo-*N*-((6-morpholinenaphthalen-2-yl)methyl)acetamide (6-1q)**



To a stirred suspension of 6-morpholine-2-naphthaldehyde (190.6 mg, 0.79 mmol, 1 equiv.) in MeOH (2 mL) was added a 40% solution of methylamine in MeOH (0.80 mL, 7.9 mmol, 10 equiv.) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (3 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (29.9 mg, 0.79 mmol, 1 equiv.) was added, and stirring was continued for 1 h at room temperature. The reaction was quenched with the addition of H_2O (3 mL) and Na_2CO_3 (70.0 mg), and extracted with CH_2Cl_2 (3x3 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give secondary amine (94% yield, 190.7 mg, 0.74 mmol).

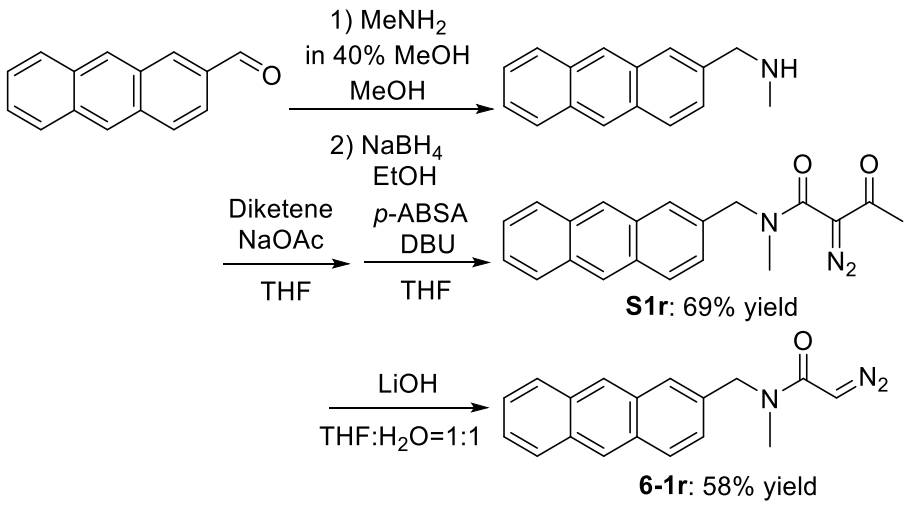
To a solution of the secondary amine (190.7 mg, 0.74 mmol, 1 equiv.) in THF (2 mL) was slowly added diketene (0.29 mL, 3.7 mmol, 5 equiv.) and NaOAc (12.1 mg, 0.15 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x2 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a solution of β-ketoamide (0.74 mmol, 1 equiv.) and *p*-ABSA (266.6 mg, 1.11 mmol, 1.5 equiv.) in THF (2 mL) was slowly added DBU (0.17 mL, 1.11 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (2 mL) and the combined mixture was extracted with EA (3x2 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 1/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-morpholinenaphthalen-2-yl)methyl)-3-oxobutanamide **S1q** as a yellow liquid (73% yield, 197.0 mg, 0.54 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 12.2, 8.8 Hz, 2H), 7.58 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.26 (dd, *J* =

9.0, 2.1 Hz, 1H), 7.10 (d, *J* = 1.9 Hz, 1H), 4.68 (s, 2H), 3.89 (t, *J* = 4.8 Hz, 4H), 3.24 (t, *J* = 4.8 Hz, 4H), 2.92 (s, 3H), 2.38 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.1, 161.4, 149.2, 133.9, 130.8, 128.5, 128.1, 127.5, 126.3, 125.9, 119.1, 109.6, 73.4, 66.7, 52.7, 49.4, 35.5, 27.2 ppm. IR (neat) ν 3055, 2962, 2915, 2850, 2107, 1633, 1606, 1266, 964, 731 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((6-morpholinenaphthalen-2-yl)methyl)-3-oxobutanamide **S1q** (120.4 mg, 0.33 mmol, 1 equiv.) in THF (1 mL) was slowly added LiOH (39.5 mg, 1.65 mmol, 5 equiv.) in H_2O (1 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x1 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 1/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((6-morpholinenaphthalen-2-yl)methyl)acetamide **6-1q** as a yellow solid (62% yield, 66.2 mg, 0.20 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 9.17 Hz, 1H), 7.67 (d, *J* = 8.41 Hz, 1H), 7.52 (s, 1H), 7.25 (d, *J* = 8.41 Hz, 2H), 7.08 (s, 1H), 5.0 (s, 1H), 4.90-4.20 (bs, 2H), 3.89 (t, *J* = 4.59 Hz, 4H), 3.23 (t, *J* = 4.20 Hz, 4H), 3.20-2.60 (bs, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 149.1, 133.8, 128.5, 128.2, 127.4, 119.1, 109.7, 66.7, 49.5, 46.4, 34.0 ppm. IR (neat) ν 3059, 2962, 2854, 2106, 1607, 1219, 1111, 852, 728 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{18}H_{20}N_4NaO_2$: 347.1478, found: 347.1478.

***N*-(Methyl)-2-diazo-*N*-((anthracen-2-yl)methyl)acetamide (6-1r)**



To a stirred suspension of anthracene-2-carbaldehyde (18.0 mg, 0.087 mmol, 1 equiv.) in MeOH (0.5 mL) was added a 40% solution of methylamine in MeOH (90 μL, 0.87 mmol, 10 equiv.) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (1 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (3.3 mg, 0.087 mmol. 1 equiv.) was added, and stirring was continued for 1 h at room temperature. The reaction was quenched with the addition of H_2O (0.5 mL) and Na_2CO_3 (7 mg), and

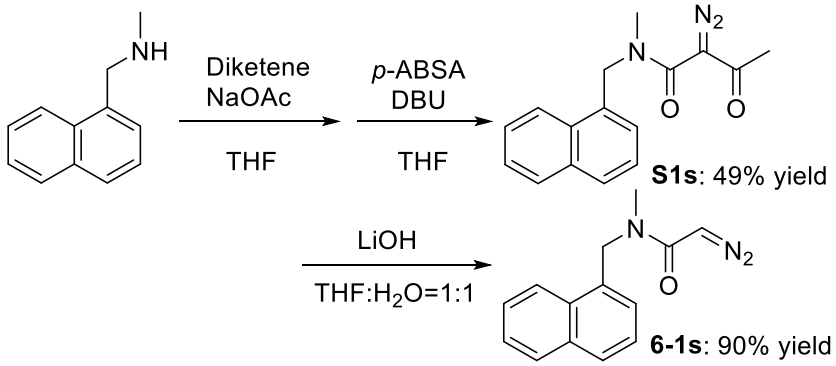
extracted with CH_2Cl_2 (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give secondary amine.

To a solution of the secondary amine (0.087 mmol, 1 equiv.) in THF (0.5 mL) was slowly added diketene (33.5 μL, 0.43 mmol, 5 equiv.) and NaOAc (1.4 mg, 0.017 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a solution of β-ketoamide (0.087 mmol, 1 equiv.) and *p*-ABSA (31.3 mg, 0.13 mmol, 1.5 equiv.) in THF (1 mL) was slowly added DBU (19 μL, 0.13 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 2 h at room temperature. The reaction mixture was diluted with H_2O (1 mL) and the combined mixture was extracted with EA (3x1 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((anthracen-2-yl)methyl)-3-oxobutanamide **S1r** as a yellow solid (69% yield, 19.8 mg, 0.06 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 9.9 Hz, 2H), 8.01 (d, *J* = 8.8 Hz, 3H), 7.84 (s, 1H), 7.48 (dd, *J* = 6.12, 3.03 Hz, 2H), 7.36 (dd, *J* = 8.6, 1.3 Hz, 1H), 4.78 (s, 2H), 2.99 (s, 3H), 2.41 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 132.9, 132.0, 131.8, 131.2, 131.0, 129.2, 128.1, 128.1, 126.6, 126.2, 126.1, 125.6, 125.5, 125.0, 35.8, 29.6, 27.3 ppm. IR (neat) ν 3055, 2927, 2854, 2129, 1590, 1164, 756 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((anthracen-2-yl)methyl)-3-oxobutanamide **S1r** (19.8 mg, 0.06 mmol, 1 equiv.) in THF (1 mL) was slowly added LiOH (7.2 mg, 0.3 mmol, 5 equiv.) in H_2O (1 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x1 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 10/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((anthracen-2-yl)methyl)acetamide **6-1r** as a yellow solid (58% yield, 10.0 mg, 0.035 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 10.3 Hz, 2H), 7.99 (dd, *J* = 8.41, 6.31 Hz, 3H), 7.77 (s, 1H), 7.47 (s, 2H), 7.41-7.28 (s, 1H), 5.0 (s, 1H), 4.90-4.40 (bs, 2H), 3.40-2.60 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 131.9, 131.7, 131.3, 130.9, 129.0, 128.1, 128.0, 126.1, 126.0, 125.5, 125.4, 46.6, 34.5 ppm. IR (neat) ν 3051, 2919, 2112, 1607, 1409, 887, 740 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{18}H_{15}N_3NaO$: 312.1107, found: 312.1097.

***N*-(Methyl)-2-diazo-*N*-((naphthalen-1-yl)methyl)acetamide (6-1s)**



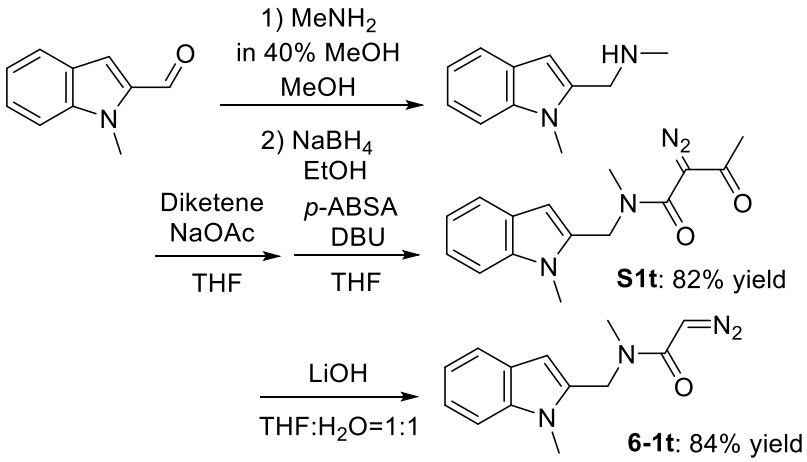
To a solution of secondary amine (171.2 mg, 1.0 mmol, 1 equiv.) in THF (2 mL) was slowly added diketene (0.40 mL, 5.0 mmol, 5 equiv.) and NaOAc (16.4 mg, 0.2 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (0.5 mL) and the combined mixture was extracted with EA (3x2 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a mixture of β-ketoamide (1 mmol, 1 equiv.) and *p*-ABSA (360.4 mg, 1.5 mmol, 1.5 equiv.) in THF (4 mL) was slowly added DBU (0.22 mL, 1.5 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for 1 h at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 5/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((naphthalen-1-yl)methyl)-3-oxobutanamide **S1s** as a yellow liquid (49% yield, 136.6 mg, 0.49 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.45-7.51 (m, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 6.9 Hz, 1H), 5.03 (s, 2H), 2.83 (s, 3H), 2.34 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 161.1, 133.4, 130.9, 130.8, 128.5, 128.3, 126.2, 125.7, 124.9, 122.5, 72.9, 50.0, 35.5, 27.0 ppm. IR (neat) ν 3051, 2962, 2923, 2106, 1636, 1284, 794, 779 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((naphthalen-1-yl)methyl)-3-oxobutanamide **S1s** (136.6 mg, 0.49 mmol, 1 equiv.) in THF (2 mL) was slowly added LiOH (23.5 mg, 0.98 mmol, 2 equiv.) in H_2O (2 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 2/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((naphthalen-1-

yl)methyl)acetamide **6-1s** as a yellow liquid (90% yield, 105.0 mg, 0.44 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.20-7.90 (s, 1H), 7.85 (d, *J* = 7.64 Hz, 1H), 7.78 (d, *J* = 8.41 Hz, 1H), 7.56-7.46 (m, 2H), 7.42 (t, *J* = 7.26 Hz, 1H), 7.28 (d, *J* = 7.26 Hz, 1H), 5.0-4.40 (bs, 3H), 3.30-2.40 (bs, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 133.6, 128.6, 128.2, 126.4, 125.9, 125.2, 46.5, 29.5 ppm. IR (neat) ν 3063, 2923, 2104, 1606, 1407, 1169, 793, 779 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{14}H_{13}N_3NaO$: 262.0951, found: 262.0950.

***N*-(Methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-2-yl)methyl)acetamide (6-1t)**



To a stirred suspension of 1-methylindole-2-carbaldehyde (286.6 mg, 1.8 mmol, 1 equiv.) in MeOH (4 mL) was added a 40% solution of methylamine in MeOH (1.8 mL, 18 mmol, 10 equiv.) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (6 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (68.1 mg, 1.8 mmol, 1 equiv.) was added, and stirring was continued for 1 h at room temperature. The reaction was quenched with the addition of H_2O (5 mL) and Na_2CO_3 (150.0 mg), and extracted with CH_2Cl_2 (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give secondary amine (100% yield, 314.0 mg).

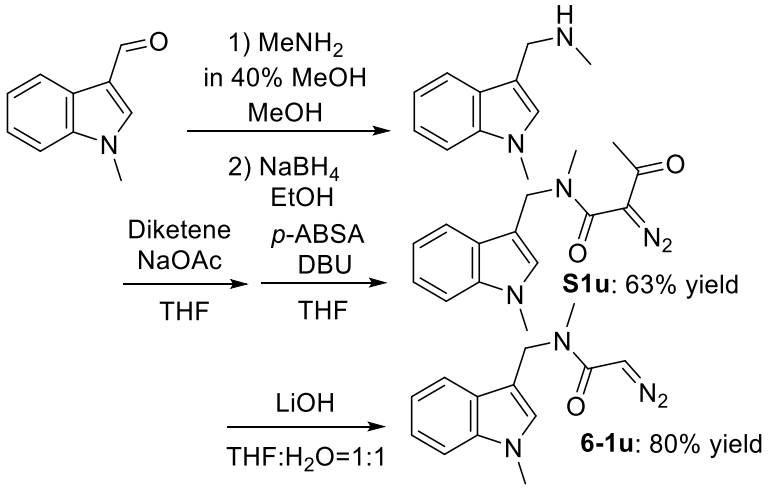
To a solution of the secondary amine (1.8 mmol, 1 equiv.) in THF (5.4 mL) was slowly added diketene (0.7 mL, 9.0 mmol, 5 equiv.) and NaOAc (29.5 mg, 0.36 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

To a solution of β-ketoamide (1.8 mmol, 1 equiv.) and *p*-ABSA (648.6 mg, 2.7 mmol, 1.5 equiv.) in THF (3.6 mL) was slowly added DBU (0.4 mL, 2.7 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the

reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-2-yl)methyl)-3-oxobutanamide **S1t** as a yellow liquid (82% yield, 417.6 mg, 1.47 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.23 (dd, *J* = 9.6, 8.4 Hz, 1H), 7.11 (t, *J* = 7.1 Hz, 1H), 6.47 (s, 1H), 4.80 (s, 2H), 3.68 (s, 3H), 2.89 (s, 3H), 2.36 (3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.6, 161.0, 137.7, 133.5, 126.8, 121.5, 120.1, 119.3, 108.9, 102.7, 73.4, 44.0, 35.2, 29.4, 26.9 ppm. IR (neat) ν 3059, 2923, 2106, 1652, 1634, 1470, 1286, 1261, 740 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-2-yl)-3-oxobutanamide **S1t** (400.0 mg, 1.4 mmol, 1 equiv.) in THF (3 mL) was slowly added LiOH (167.6 mg, 7.0 mmol, 5 equiv.) in H_2O (3 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x3 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 1/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-2-yl)methyl)acetamide **6-1t** as a yellow solid (84% yield, 284.4 mg, 1.17 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.35 (s, 1H), 4.87 (s, 1H), 4.65 (s, 2H), 3.58 (s, 3H), 2.61 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 137.6, 134.6, 126.9, 121.3, 119.9, 119.2, 108.9, 102.4, 46.1, 42.5, 32.6, 29.4 ppm. IR (neat) ν 3109, 3047, 2931, 2105, 1607, 1406, 1172, 737 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{13}H_{14}N_4NaO$: 265.1060, found: 265.1082.

_N_-(Methyl)-2-diazo-_N_-((1-methyl-1_H_-indol-3-yl)methyl)acetamide (6-1u)



To a stirred suspension of 1-methylindole-3-carbaldehyde (318.4 mg, 2.0 mmol, 1 equiv.) in MeOH (4 mL) was added a 40% solution of methylamine in MeOH (2.0 mL, 20 mmol, 10 equiv.) and stirred for overnight at room temperature. The mixture was concentrated under reduced pressure to remove solvent. EtOH (6 mL) was added to the residue. The resulting solution was cooled to 0 ℃ in an ice bath, $NaBH_4$ (75.7 mg, 2.0 mmol, 1 equiv.) was added, and stirring was continued for 1 h at room temperature. The reaction was quenched with the addition of H_2O (6 mL) and Na_2CO_3 (150.0 mg), and extracted with DCM (3x6 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give secondary amine (100% yield, 347.6 mg).

To a solution of the secondary amine (1.98 mmol, 1 equiv.) in THF (5 mL) was slowly added diketene (0.76 mL, 9.9 mmol, 5 equiv.) and NaOAc (32.5 mg, 0.40 mmol, 0.2 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was heated to reflux at 70 ℃ for 1 h. The reaction mixture was quenched with the addition of 1 M aqueous K_2CO_3 (1 mL) and the combined mixture was extracted with EA (3x5 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to give desired β-ketoamide, which was used for next step without further purification.

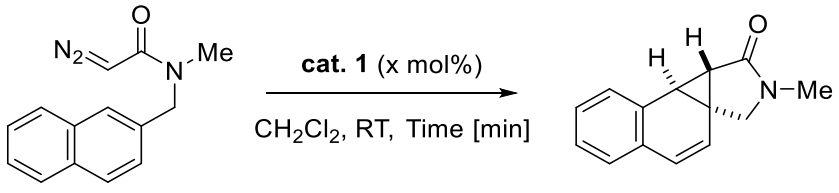
To a solution of β-ketoamide (1.98 mmol, 1 equiv.) and *p*-ABSA (713.5 mg, 2.97 mmol, 1.5 equiv.) in THF (4 mL) was slowly added DBU (0.44 mL, 2.97 mmol, 1.5 equiv.) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The reaction mixture was diluted with H_2O (4 mL) and the combined mixture was extracted with EA (3x4 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (Hex/EA = 1/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-3-yl)methyl)-3-oxobutanamide **S1u** as a yellow liquid (63% yield, 354.1 mg, 1.24 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.23-7.26 (m, 1H), 7.13 (t, *J* = 6.9 Hz, 1H), 7.07 (s, 1H), 4.73 (s, 2H), 3.76 (s, 3H), 2.91 (s, 3H), 2.37 (s, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.9, 136.9, 128.5, 127.1, 121.9, 119.5, 118.8, 109.3, 109.1, 43.8, 35.2, 32.6, 27.2 ppm. IR (neat) ν 3055, 2923, 2104, 1632, 1288, 1042, 743 cm^{-1}.

To a solution of *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-3yl)-3-oxobutanamide **S1u** (117.3 mg, 0.41 mmol, 1 equiv.) in THF (1.5 mL) was slowly added LiOH (49.3 mg, 2.1 mmol, 5 equiv.) in H_2O (1.5 mL) at 0 ℃ in an ice bath, and the reaction mixture was stirred for overnight at room temperature. The combined mixture was extracted with Et_2O (3x2 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 1/1 ($^v/_v$)) to give *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-3-yl)methyl)acetamide **6-1u** as a yellow solid (80% yield, 79.8 mg, 0.33 mmol). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 4.93 (bs, 1H), 4.67 (bs,

2H), 3.72 (s, 3H), 2.74 (bs, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.4, 136.9, 128.1, 126.8, 121.76 119.2, 110.0, 109.1, 46.2, 41.9, 33.5, 32.5 ppm. IR (neat) ν 3101, 3055, 2931, 2102, 1603, 1407, 1107, 744 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{13}H_{14}N_4NaO$: 265.1060, found: 265.1043.

8-4-2 General Procedure for Asymmetric Intramolecular Arene Cyclopropanation Reaction of Diazoacetamides

Table S1. Efficiency of Ru(II)-Pheox Catalyst

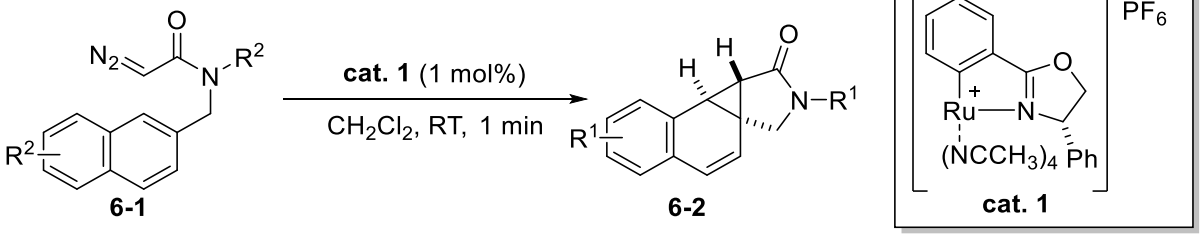


6-1a **6-2a**

entry	x [mol%]	time [min]	yield [%][a]	ee [%][b]	TON[c]	TOF [min^{-1}][d]
1	1	1	93	98	93	93
2	0.5	1	95	97	189	189
3	0.2	30	80	96	402	13.4
4[e]	0.1	1440	11	91	111	0.08

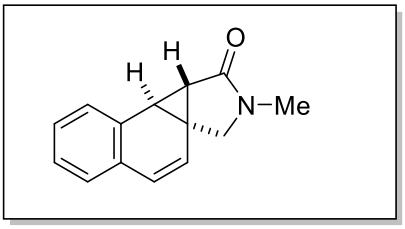
[a]Isolated yield. [b]Determined by chiral HPLC. [c]TON (turnover number) = Product [mol]/cat. [mol]. [d]TOF (turnover frequency) = TON/Time [min]. [e]Reaction did not proceed to completion even after 24 h of stirring.

Catalytic Asymmetric Carbene Transfer Reaction of Naphthyl Diazoacetamides

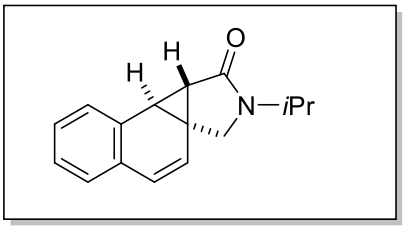


6-1 **6-2** **cat. 1**

To a solution of Ru(II)-Pheox (**cat. 1**) (1 mol%) in CH_2Cl_2 (2 mL) was slowly added a solution of diazoacetamide **6-1** (0.2 mmol, 1 equiv.) in CH_2Cl_2 (2 mL) under argon atmosphere at room temperature. The reaction mixture was stirred at room temperature for 1 min. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel to give the desired product **6-2**.

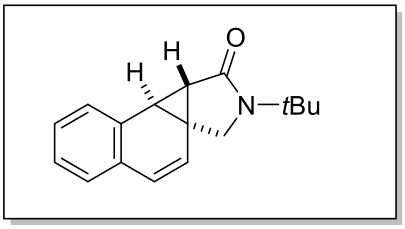


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1a** (47.9 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2a** as a white solid (93% yield, 39.5 mg, 0.187 mmol), 98% ee. $[\alpha]^{9}_{D}$ = +332.7 (c 1.50 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 19.60 min (minor product), tR = 25.40 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 6.88 Hz, 1H), 7.28-7.20 (m, 2H), 7.17 (d, *J* = 6.88 Hz, 1H), 6.41 (d, *J* = 9.56 Hz, 1H), 6.13 (d, *J* = 9.56 Hz, 1H), 3.73 (d, *J* = 10.32 Hz, 1H), 3.46 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.84 (s, 3H), 2.71 (d, *J* = 2.87 Hz, 1H), 0.87 (bs, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 131.7, 130.9, 128.5, 128.1, 127.8, 126.8, 125.4, 125.0, 55.4, 34.2, 29.2, 28.8, 23.9 ppm. IR (neat) ν 3055, 3000, 2915, 2869, 1681, 1492, 1253, 784, 752 cm^{-1}. HRMS(ESI) $[M+Na]^{+}$ calcd for $C_{14}H_{13}NNaO$: 234.0889, found: 234.0884.

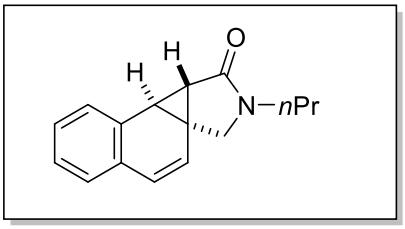


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(isopropyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1b** (53.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 3/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2b** as a white solid (93% yield, 44.3 mg, 0.185 mmol), 98% ee. $[\alpha]^{16}_{D}$ = +216.7 (c 2.2 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 15.30 min (minor product), tR = 15.90 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 6.88 Hz, 1H), 7.23 (ddd, 2H), 7.17 (d, *J* = 7.26 Hz, 1H), 6.42 (d, *J* = 9.56 Hz, 1H), 6.14 (d, *J* = 9.56 Hz, 1H), 4.33 (sept., *J* = 6.88 Hz, 1H), 3.67 (d, *J* = 10.32 Hz, 1H), 3.44 (dd, *J* = 10.51, 1.53 Hz, 1H), 2.59 (d, *J* = 2.68 Hz, 1H), 1.20 (d, *J* = 6.50 Hz, 3H), 1.09 (d, *J* = 6.88 Hz, 3H), 0.87 (dd, *J* = 2.68, 1.15 Hz, 1H) ppm. ^{13}C NMR

(125 MHz, $CDCl_3$) δ 173.6, 131.7, 130.9, 128.6, 128.1, 127.8, 126.8, 125.4, 125.2, 48.1, 42.1, 33.9, 28.4, 24.2, 20.4, 19.4 ppm. IR (neat) ν 3032, 2971, 2931, 2873, 1681, 1426, 1239, 784, 751 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{16}H_{18}NO$: 240.1383, found: 240.1381.

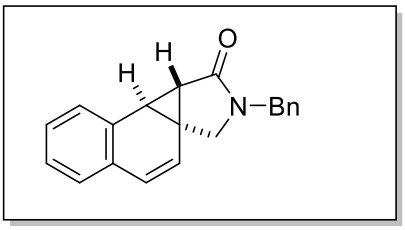


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(tert-butyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1c** (52.0 mg, 0.185 mmol, 1 equiv.) in the presence of **cat. 1** (1.2 mg, 0.0018 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-2c** as a white solid (94% yield, 44.0 mg, 0.174 mmol), 99% ee. $[\alpha]^{16}_D$ = +219.4 (c 2.2 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 17.29 min (minor product), tR = 17.93 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 6.88 Hz, 1H), 7.22 (td, *J* = 16.08, 7.26 Hz, 2H), 7.16 (d, *J* = 7.26 Hz, 1H), 6.40 (d, *J* = 11.08 Hz, 1H), 6.11 (d, *J* = 9.56 Hz, 1H), 3.76 (dd, *J* = 10.51, 2.29 Hz, 1H), 3.58 (d, *J* = 10.32 Hz, 1H), 2.63 (s, 1H), 1.41 (s, 9H), 0.8 (d, *J* = 1.91 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 131.9, 131.0, 128.6, 128.0, 127.7, 126.7, 125.3, 125.2, 53.6, 51.7, 33.6, 28.0, 27.6, 25.3 ppm. IR (neat) ν 3059, 2969, 2923, 2869, 1679, 1405, 1231, 783, 752 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{17}H_{20}NO$: 254.1539, found: 254.1563.

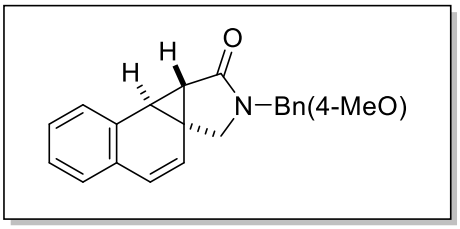


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(propyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1d** (53.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 4/1 ($^v/_v$) as an eluent to give desired product **6-2d** as a white solid (64% yield, 30.8 mg, 0.129 mmol), 96% ee. $[\alpha]^{10}_D$ = +250.5 (c 1.50 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 26.80 min (major product), tR = 29.66 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 6.56, 1.83 Hz, 1H), 7.23

(ddd, *J* = 6.87, 4.12, 1.83 Hz, 2H), 7.17 (dd, *J* = 6.56, 2.75 Hz, 1H), 6.42 (d, *J* = 9.77 Hz, 1H), 6.13 (d, *J* = 9.46 Hz, 1H), 3.72 (d, *J* = 10.38 Hz, 1H), 3.48 (dd, *J* = 10.53, 1.53 Hz, 1H), 3.27 (ddd, *J* = 13.73, 7.02, 6.71 Hz, 1H), 3.19 (ddd, *J* = 13.89, 7.02, 6.29 Hz, 1H), 2.67 (d, *J* = 2.75 Hz, 1H), 1.60-1.50 (m, 2H), 0.97 (t, *J* = 7.63 Hz, 3H), 0.88 (dd, *J* = 2.75, 1.53 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 131.7, 130.9, 128.6, 128.1, 127.8, 126.8, 125.4, 125.1, 53.2, 43.7, 34.2, 28.7, 24.1, 20.7, 11.1 ppm. IR (neat) ν 3032, 2963, 2923, 2873, 1682, 1429, 1252, 784, 748 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{16}H_{18}NO$: 240.1383, found: 240.1381.

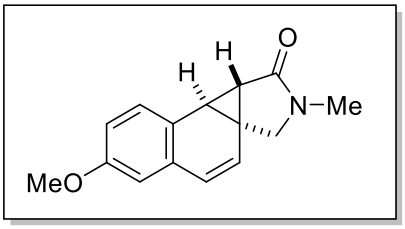


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(benzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1e** (63.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-2e** as a white solid (83% yield, 47.5 mg, 0.165 mmol), 99% ee. $[\alpha]^{18}_D$ = +112.6 (c 0.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 41.84 min (major product), tR = 44.62 min (minor product). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.10 (m, 9H), 6.39 (bs, 1H), 6.07 (bs, 1H), 4.46 (bs, 2H), 3.61 (bs, 1H), 3.36 (bs, 1H), 2.69 (bs, 1H), 0.93 (bs, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 136.5, 131.6, 130.9, 128.7, 128.6, 128.2, 128.1, 127.9, 127.6, 126.9, 125.5, 125.0, 52.7, 46.3, 34.1, 28.8, 23.8 ppm. IR (neat) ν 3024, 2915, 2861, 1686, 1427, 1251, 783, 750 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{20}H_{18}NO$: 288.1383, found: 288.1384.

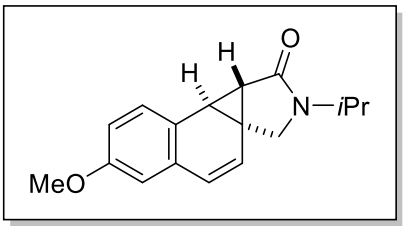


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-methoxybenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1f** (69.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-2f** as a white solid (46% yield, 29.0 mg, 0.091 mmol), 98% ee. $[\alpha]^{17}_D$ = +79.5 (c 1.0 in

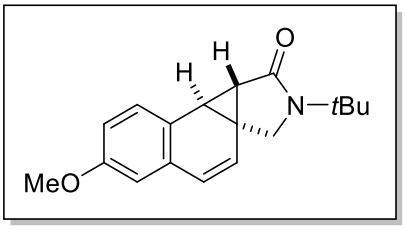
$CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 35.16 min (major product), tR = 42.07 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.26 Hz, 1H), 7.26-7.15 (m, 5H), 6.88 (d, *J* = 8.41 Hz, 2H), 6.38 (d, *J* = 9.56 Hz, 1H), 6.06 (d, *J* = 9.56 Hz, 1H), 4.41 (d, *J* = 14.52 Hz, 1H), 4.34 (d, *J* = 14.52 Hz, 1H), 3.80 (s, 3H), 3.58 (d, *J* = 10.13 Hz, 1H), 3.33 (dd, *J* = 10.51, 1.53 Hz, 1H), 2.66 (d, *J* = 2.68 Hz, 1H), 0.90 (bs, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 159.1, 131.6, 130.9, 129.5, 128.6, 128.5, 128.1, 127.8, 126.9, 125.4, 125.0, 114.0, 55.2, 52.6, 45.6, 34.1, 28.7, 23.9 ppm. IR (neat) ν 3000, 2915, 2838, 1680, 1511, 1247, 783, 752 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{21}H_{19}NNaO_2$: 340.1308, found: 340.1336.



This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1g** (53.9 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^v/_v$) as an eluent to give desired product **6-2g** as a white solid (98% yield, 47.5 mg, 0.196 mmol), 99% ee. $[\alpha]^{21}_D$ = +207.8 (c 2.2 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 32.92 min (minor product), tR = 48.61 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.54 Hz, 1H), 6.81 (dd, *J* = 8.24, 2.75 Hz, 1H), 6.70 (d, *J* = 2.75 Hz, 1H), 6.36 (d, *J* = 9.77 Hz, 1H), 6.14 (d, *J* = 9.77 Hz, 1H), 3.79 (s, 3H), 3.71 (d, *J* = 10.68 Hz, 1H), 3.45 (dd, *J* = 10.38, 1.53 Hz, 1H), 2.83 (s, 3H), 2.66 (d, *J* = 2.75 Hz, 1H), 0.85 (dd, *J* = 2.75, 1.83 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 158.4, 131.9, 129.4, 125.8, 125.4, 124.1, 113.9, 112.6, 55.3, 55.2, 33.7, 29.2, 28.5, 24.3 ppm. IR (neat) ν 2993, 2935, 2834, 1684, 1495, 1263, 1037, 871, 752 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{15}H_{16}NO_2$: 242.1176, found: 242.1169.

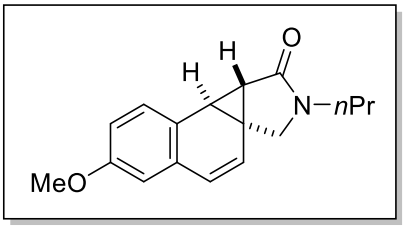


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(isopropyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1h** (59.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 3/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2h** as a white solid (95% yield, 51.0 mg, 0.189 mmol), 99% ee. $[\alpha]^{12}_{D}$ = +189.8 (c 2.5 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 44.75 min (minor product), tR = 53.57 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.41 Hz, 1H), 6.81 (d, *J* = 8.41 Hz, 1H), 6.69 (s, 1H), 6.36 (d, *J* = 9.56 Hz, 1H), 6.14 (d, *J* = 9.56 Hz, 1H), 4.32 (sept., *J* = 6.88 Hz, 1H), 3.79 (s, 3H), 3.65 (dd, *J* = 10.32, 1.53 Hz, 1H), 3.42 (d, *J* = 10.32 Hz, 1H), 2.54 (s, 1H), 1.19 (d, *J* = 8.41 Hz, 3H), 1.08 (d, *J* = 6.88 Hz, 3H), 0.84 (d, *J* = 1.53 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 158.3, 132.0, 129.5, 126.0, 125.4, 124.1, 113.9, 112.6, 55.1, 48.0, 42.1, 33.3, 28.1, 24.6, 20.4, 19.3 ppm. IR (neat) ν 2937, 2931, 2873, 1679, 1430, 1264, 1240, 1038, 748 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}NNaO_2$: 292.1308, found: 292.1343.

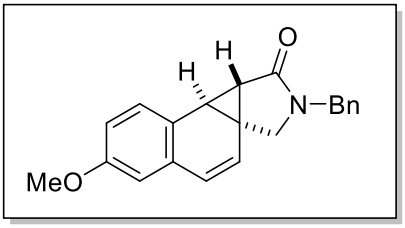


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(*tert*-butyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1i** (44.0 mg, 0.14 mmol, 1 equiv.) in the presence of **cat. 1** (0.9 mg, 0.0014 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2i** as a white solid (98% yield, 38.7 mg, 0.137 mmol), 99% ee. $[\alpha]^{13}_{D}$ = +185.7 (c 1.9 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 28.84 min (minor product), tR = 30.14 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.41 Hz, 1H), 6.81 (dd, *J* = 8.31, 2.48 Hz, 1H), 6.69 (d, *J* = 2.68 Hz, 1H), 6.34 (d, *J* = 9.56 Hz, 1H), 6.12 (d, *J* = 9.56 Hz, 1H), 3.78 (s, 3H), 3.75 (d, *J* = 10.70 Hz, 1H), 3.57 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.58 (d, *J* = 2.29 Hz, 1H), 1.40 (s, 9H), 0.78 (bs, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.9, 158.3, 132.1, 129.5,

126.1, 125.3, 124.3, 113.9, 112.6, 55.2, 53.5, 51.7, 33.1, 27.8, 27.5, 25.7 ppm. IR (neat) ν 2966, 2838, 1675, 1407, 1262, 1034, 867, 752 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{18}H_{22}NO_2$: 284.1645, found: 284.1649.

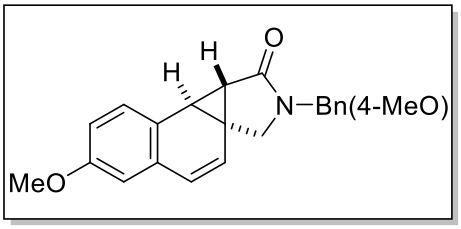


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(propyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1j** (59.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 4/1 ($^v/_v$) as an eluent to give desired product **6-2j** as a white solid (66% yield, 35.4 mg, 0.131 mmol), 98% ee. $[\alpha]^{21}_D$ = +158.1 (c 1.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 52.25 min (minor product), tR = 56.07 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.41 Hz, 1H), 6.81 (dd, *J* = 8.22, 2.29 Hz, 1H), 6.70 (d, *J* = 2.68 Hz, 1H), 6.37 (d, *J* = 9.56 Hz, 1H), 6.15 (d, *J* = 9.94 Hz, 1H), 3.79 (s, 3H), 3.70 (d, *J* = 10.32 Hz, 1H), 3.47 (dd, *J* = 10.32, 1.53 Hz, 1H), 3.27 (ddd, *J* = 10.51, 7.26, 6.88 Hz, 1H), 3.17 (ddd, *J* = 12.23, 7.26, 6.88 Hz, 1H), 2.62 (d, *J* = 2.68 Hz, 1H), 1.61-1.49 (m, 2H), 0.92 (t, *J* = 7.26 Hz, 3H), 0.86 (dd, *J* = 2.68, 1.34 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 158.4, 132.0 129.5, 125.9, 125.4, 124.2, 113.9, 112.7, 55.2, 53.2, 43.7, 33.6, 28.5, 24.6, 20.7, 11.1 ppm. IR (neat) ν 2958, 2927, 2873, 1681, 1432, 1262, 1038, 871 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{17}H_{20}NO_2$: 270.1489, found: 270.1497.

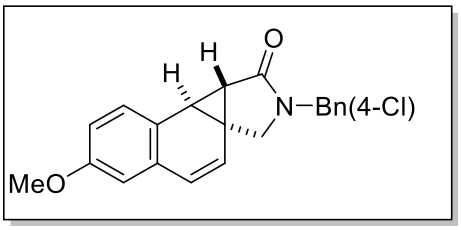


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(benzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1k** (69.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-2k** as a white solid (71% yield, 45.0 mg, 0.141 mmol), 99% ee. $[\alpha]^{20}_D$ = +87.2 (c 1.9 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV

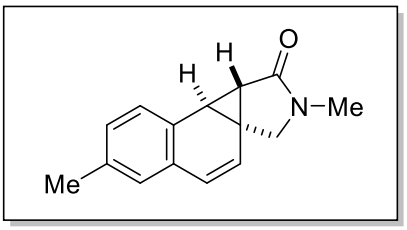
detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 54.89 min (minor product), tR = 56.50 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.22, 3.06 Hz, 3H), 7.29 (d, *J* = 7.26 Hz, 1H), 7.25 (d, *J* = 6.88 Hz, 2H), 6.81 (dd, *J* = 8.41, 2.68 Hz, 1H), 6.68 (d, *J* = 2.29 Hz, 1H), 6.24 (d, *J* = 9.56 Hz, 1H), 6.07 (d, *J* = 9.56 Hz, 1H), 4.43 (s, 2H), 3.78 (s, 3H), 3.58 (d, *J* = 10.70 Hz, 1H), 3.34 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.65 (d, *J* = 2.68 Hz, 1H), 0.91 (dd, *J* = 2.68, 1.34 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.2, 158.4, 136.5, 132.0, 129.6, 128.7, 128.1, 127.6, 125.8, 125.5, 124.0, 113.9, 112.7, 55.2, 52.6, 46.2, 33.5, 28.5, 24.3 ppm. IR (neat) ν 3024, 2915, 2834, 1682, 1436, 1261, 756, 704 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{21}H_{20}NO_2$: 318.1489, found: 318.1485.



This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-methoxybenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1l** (75.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2l** as a white solid (46% yield, 32.0 mg, 0.092 mmol), 99% ee. $[\alpha]^{20}_{D}$ = +55.4 (c 1.6 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 57.38 min (major product), tR = 70.50 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.41 Hz, 1H), 7.18 (d, *J* = 8.41 Hz, 2H), 6.87 (d, *J* = 8.41 Hz, 2H), 6.81 (dd, *J* = 8.41, 2.68 Hz, 1H), 6.68 (d, *J* = 2.29 Hz, 1H), 6.33 (d, *J* = 9.56 Hz, 1H), 6.07 (d, *J* = 9.56 Hz, 1H), 4.36 (d, *J* = 6.12 Hz, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.57 (d, *J* = 10.70 Hz, 1H), 3.32 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.62 (d, *J* = 2.68 Hz, 1H), 0.90 (dd, *J* = 2.68, 1.34 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 159.0, 158.4, 132.0, 129.6, 129.5, 128.5, 125.8, 125.5, 124.1, 114.0, 113.9, 112.7, 55.3, 55.2, 52.5, 45.6, 33.5, 28.5, 24.4 ppm. IR (neat) ν 3000, 2954, 2912, 2831, 1681, 1512, 1261, 1246, 1035, 756 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{22}H_{22}NO_3$: 348.1594, found: 348.1592.

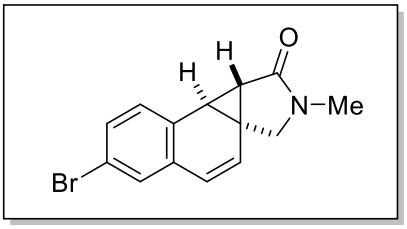


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-chlorobenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1m** (76.0 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA=5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2m** as a white solid (81% yield, 57.0 mg, 0.161 mmol), 99% ee. $[\alpha]^{22}_{D}$ = +76.9 (c 2.8 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 34.60 min (major product), tR = 40.36 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.79, 6.69 Hz, 3H), 7.20 (d, *J* = 8.41 Hz, 2H), 6.83 (dd, *J* = 8.50, 2.68 Hz, 1H), 6.69 (d, *J* = 2.68 Hz, 1H), 6.35 (d, *J* = 9.56 Hz, 1H), 6.08 (d, *J* = 9.56 Hz, 1H), 4.40 (d, *J* = 6.12 Hz, 2H), 3.80 (s, 3H), 3.58 (d, *J* = 10.70 Hz, 1H), 3.34 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.64 (d, *J* = 2.68 Hz, 1H), 0.92 (dd, *J* = 2.68, 1.34 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 158.4, 135.0, 133.4, 132.0, 129.6, 129.5, 128.8, 125.6, 123.9, 114.0, 112.7, 55.2, 52.6, 45.5, 33.5, 28.5, 24.2 ppm. IR (neat) ν 2993, 2912, 2838, 1684, 1491, 1262, 1034, 756 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{21}H_{19}ClNO_2$: 352.1099, found: 352.1106.

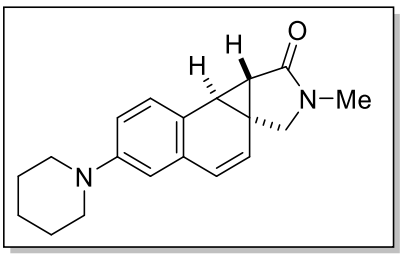


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((6-methylnaphthalen-2-yl)methyl)acetamide **6-1n** (17.7 mg, 0.07 mmol, 1 equiv.) in the presence of **cat. 1** (0.4 mg, 0.0007 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2n** as a white solid (91% yield, 14.3 mg, 0.063 mmol), 94% ee. $[\alpha]^{22}_{D}$ = +164.2 (c = 0.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 24.71 min (minor product), tR = 46.50 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.64 Hz, 1H), 7.06 (d, *J* = 7.64 Hz, 1H), 6.99 (s, 1H), 6.37 (d, *J* = 9.56 Hz, 1H), 6.11 (d, *J* = 9.56 Hz, 1H), 3.72 (d, *J* = 10.32 Hz, 1H), 3.46 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.84 (s, 3H), 2.68 (d, *J* = 2.68 Hz, 1H), 2.32 (s,

3H), 0.86 (dd, *J* = 2.68, 1.91 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 136.5, 130.8, 128.9, 128.8, 128.7, 128.4, 125.5, 125.1, 55.5, 34.0, 29.3, 28.7, 24.2, 21.0 ppm. IR (neat) ν 2919, 2861, 1686, 1494, 1251, 810 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{15}H_{16}NO$: 226.1226, found: 226.1234.

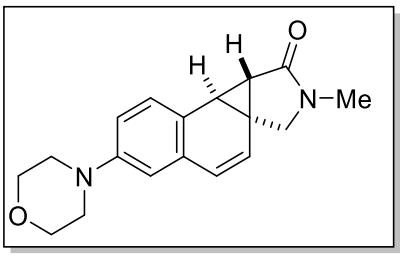


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((6-bromonaphthalen-2-yl)methyl)acetamide **6-1o** (63.6 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^v/_v$) as an eluent to give desired product **6-2o** as a white solid (90% yield, 52.0 mg, 0.18 mmol), 97% ee. $[\alpha]^{28}_D$ = +185.8 (c 2.0 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 25.15 min (minor product), tR = 32.28 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (td, *J* = 11.47, 1.91 Hz, 2H), 7.27 (d, *J* = 8.03 Hz, 1H), 6.33 (d, *J* = 9.56 Hz, 1H), 6.19 (d, *J* = 9.56 Hz, 1H), 3.74 (d, *J* = 10.70 Hz, 1H), 3.47 (dd, *J* = 10.51, 1.53 Hz, 1H), 2.84 (s, 3H), 2.66 (d, *J* = 2.68 Hz, 1H), 0.86 (dd, *J* = 2.68, 1.91 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 132.8, 130.6, 130.5, 130.1, 126.6, 124.2, 120.4, 55.2, 33.7, 29.3, 28.9, 23.9 ppm. IR (neat) ν 3040, 2915, 2877, 1676, 1432, 1247, 844 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{14}H_{12}BrNNaO$: 311.9994, found: 312.0005.

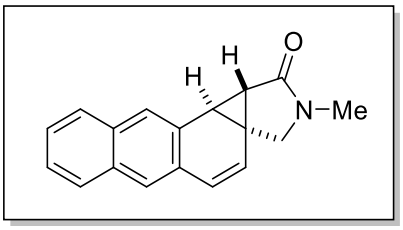


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((6-piperidinenaphthalen-2-yl)methyl)acetamide **6-1p** (18.0 mg, 0.056 mmol, 1 equiv.) in the presence of **cat. 1** (0.4 mg, 0.00056 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 3/2 with 1% of Et_3N ($^v/_v$) as an eluent to give desired product **6-2p** as a yellow oil (83% yield, 13.6 mg, 0.046 mmol), 96% ee. $[\alpha]^{23}_D$ = +323.9 (c 0.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min,

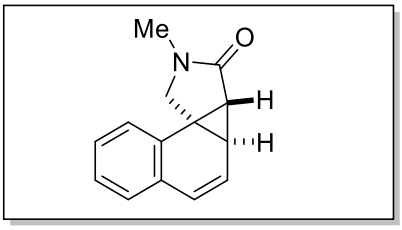
tR = 50.78 min (major product), tR = 72.59 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.41 Hz, 1H), 6.86 (dd, *J* = 8.60, 2.68 Hz, 1H), 6.72 (d, *J* = 2.68 Hz, 1H), 6.35 (d, *J* = 9.56 Hz, 1H), 6.10 (d, *J* = 9.56 Hz, 1H), 3.70 (d, *J* = 10.70 Hz, 1H), 3.45 (dd, *J* = 10.32, 1.53 Hz, 1H), 3.14 (t, *J* = 5.35 Hz, 4H), 2.83 (s, 3H), 2.64 (d, *J* = 2.87 Hz, 1H), 1.78-1.66 (m, 4H), 1.60-1.50 (m, 2H), 0.88 (dd, *J* = 2.68, 1.91 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6, 151.2, 131.5, 129.1, 126.1, 125.2, 122.7, 116.7, 115.7, 55.5, 50.6, 33.8, 29.3, 28.5, 25.7, 24.7, 24.2 ppm. IR (neat) ν 2932, 2858, 2804, 1682, 1497, 1245, 952, 748 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{19}H_{22}NaN_2O$: 317.1624, found: 317.1628.



This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((6-mopholinenaphthalen-2-yl)methyl)acetamide **6-1q** (32.4 mg, 0.1 mmol, 1 equiv.) in the presence of **cat. 1** (0.6 mg, 0.001 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 with 1% of Et_3N ($^{v}/_{v}$) as an eluent to give desired product **6-2q** as a yellow solid (94% yield, 28.0 mg, 0.094 mmol), 98% ee. $[\alpha]^{23}_{D}$ = +133.6 (c 1.4 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IB), UV detector 254 nm, eluent: Hex/IPA = 4/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 32.54 min (minor product), tR = 107.77 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.41 Hz, 1H), 6.84 (dd, *J* = 8.22, 2.68 Hz, 1H), 6.70 (d, *J* = 2.29 Hz, 1H), 6.36 (d, *J* = 9.56 Hz, 1H), 6.13 (d, *J* = 9.56 Hz, 1H), 3.85 (t, *J* = 4.97 Hz, 4H), 3.72 (d, *J* = 10.32, 1H), 3.46 (dd, *J* = 10.70, 1.53 Hz, 1H), 3.14 (dd, *J* = 5.73, 4.01 Hz, 4H), 2.84 (s, 3H), 2.66 (d, *J* = 2.68 Hz, 1H), 0.87 (dd, *J* = 2.68, 1.72 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 150.2, 131.7, 129.2, 125.8, 125.6, 123.6, 115.8, 114.8, 66.8, 55.4, 49.3, 33.7, 29.3, 28.5, 24.6 ppm. IR (neat) ν 2954, 2850, 2823, 1681, 1494, 1244, 1120, 906, 752 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{18}H_{21}N_2O_2$: 297.1598, found: 297.1607.

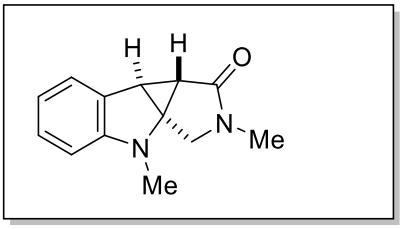


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((anthracen-2-yl)methyl)acetamide **6-1r** (5.8 mg, 0.02 mmol, 1 equiv.) in the presence of **cat. 1** (0.1 mg, 0.0002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2r** as a yellow solid (96% yield, 5.0 mg, 0.019 mmol), 98% ee. $[\alpha]^{15}_{D}$ = +229.9 (c 0.3 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 38.08 min (minor product), tR = 66.17 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.78 (t, *J* = 4.59 Hz, 2H), 7.62 (s, 1H), 7.44 (ddd, *J* = 11.37, 6.88, 4.97 Hz, 2H), 6.58 (d, *J* = 9.56 Hz, 1H), 6.20 (d, *J* = 9.56 Hz, 1H), 3.76 (d, *J* = 10.70 Hz, 1H), 3.55 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.88 (s, 3H), 2.86 (d, *J* = 2.68 Hz, 1H), 1.14 (dd, *J* = 2.68, 1.15 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 133.1, 132.5, 129.6, 129.4, 127.7, 127.5, 127.2, 126.9, 126.2, 126.0, 125.9, 125.8, 55.5, 33.5, 29.4, 28.0, 27.5 ppm. IR (neat) ν 3051, 2996, 2919, 1670, 11436, 1251, 892, 752 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{18}H_{16}NO$: 262.1226, found: 262.1259.

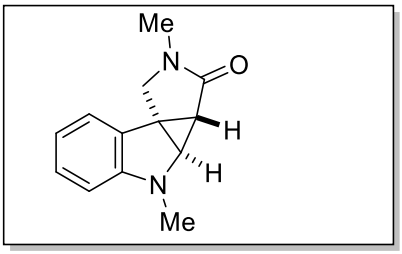


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((naphthalen-1-yl)methyl)acetamide **6-1s** (53.0 mg, 0.22 mmol, 1 equiv.) in the presence of **cat. 1** (1.4 mg, 0.0022 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2s** as a white solid (95% yield, 44.0 mg, 0.208 mmol), 25% ee. $[\alpha]^{17}_{D}$ = −68.1 (c 2.2 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 20.43 min (major product), tR = 24.83 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.63 Hz, 1H), 7.31 (dt, *J* = 7.63 1.22 Hz, 1H), 7.25 (t, *J* = 7.32 Hz, 1H), 7.19 (d, *J* = 6.41 Hz, 1H), 6.44 (d, *J* = 9.77 Hz, 1H), 6.30 (dd, *J* = 9.61, 4.88 Hz, 1H), 4.31(d, *J* = 10.99 Hz, 1H), 3.40 (dd, *J* = 10.68, 1.53 Hz, 1H), 2.89 (s, 3H), 2.19 (dd, *J* = 4.88, 2.75 Hz, 1H), 0.94 (s, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.4, 130.8,

130.5, 128.4, 127.7, 126.6, 126.2, 125.3, 124.9, 52.3, 31.9, 29.3, 29.2, 24.1 ppm. IR (neat) ν 3028, 2915, 2877, 1686, 1491, 1289, 785, 771 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{14}H_{14}NO$: 212.1070, found: 212.1090.



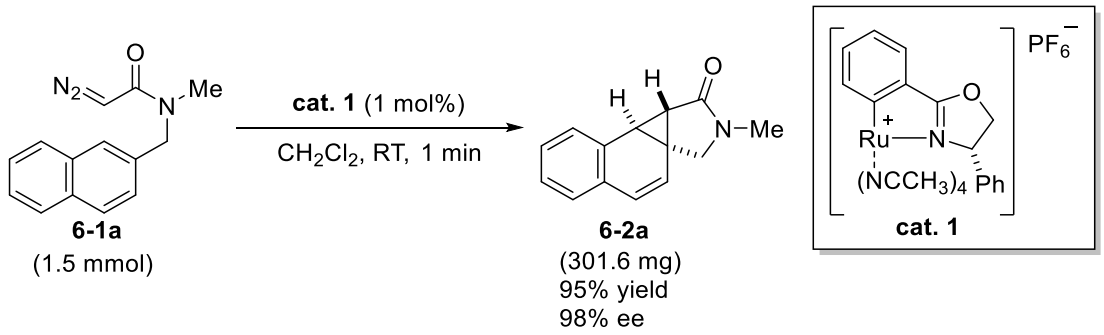
This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-2-yl)methyl)acetamide **6-1t** (48.5 mg, 0.20 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 2/3 with 2% of Et_3N ($^v/_v$) as an eluent to give desired product **6-2t** as a yellow liquid (89% yield, 38.0 mg, 0.177 mmol), 21% ee. $[\alpha]^{15}_D$ = +230.8 (c 1.7 in MeOH). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 32.96 min (major product), tR = 38.54 min (minor product). ^{1}H NMR (500 MHz, $(CD_3)_2CO$)) δ7.28 (dd, *J* = 7.07, 1.15 Hz, 1H), 7.11 (td, *J* = 7.84, 1.15 Hz, 1H), 6.76 (dd, *J* = 15.48, 7.26 Hz, 2H), 3.97 (d, *J* = 10.32 Hz, 1H), 3.58 (dd, *J* = 10.32, 1.91 Hz, 1H), 2.93 (s, 3H), 2.78 (d, *J* = 1.10 Hz, 1H), 2.78 (s, 3H), 0.89 (t, *J* = 1.53 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $(CD_3)_2CO$)) δ 172.5, 152.7, 130.4, 128.2, 125.5, 120.1, 111.1, 52.4, 49.5, 33.4, 32.8, 29.2, 19.9 ppm. IR (neat) ν 3044, 2923, 2881, 1635, 1473, 1235, 743 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{13}H_{15}N_2O$: 215.1179, found: 215.1174.



This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(methyl)-2-diazo-*N*-((1-methyl-1*H*-indol-3-yl)methyl)acetamide **6-1u** (48.5 mg, 0.20 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 1/1 with 1% of Et_3N ($^v/_v$) as an eluent to give desired product **6-2u** as a brown liquid (82% yield, 35.2 mg, 0.164 mmol), 71% ee. $[\alpha]^{18}_D$ = −25.7 (c 1.7 in MeOH). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IB), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR =

27.65 min (major product), tR = 31.57 min (minor product). ^{1}H NMR (500 MHz, $(CD_3)_2CO$)) δ 7.27 (d, *J* = 7.64 Hz, 1H), 7.09 (td, *J* = 7.64, 1.15 Hz, 1H), 6.70 (td, *J* = 7.26, 1.15 Hz, 1H), 6.58 (d, *J* = 7.64 Hz, 1H), 4.16 (d, *J* = 10.32 Hz, 1H), 3.61 (s, 1H), 3.59 (dd, *J* = 10.32, 1.53 Hz, 1H), 2.99 (s, 3H), 2.78 (s, 3H), 0.79 (d, *J* = 1.53 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $(CD_3)_2CO$)) δ 172.1, 150.6, 128.2, 127.9, 123.0, 118.1, 108.3, 52.0, 49.3, 33.7, 33.2, 29.3, 23.3 ppm. IR (neat) ν 3045, 2923, 2877, 1682, 1488, 1247, 1011, 743 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{13}H_{15}N_2O$: 215.1179, found: 215.1176.

3.3 Large Scale Synthesis of 6-2a

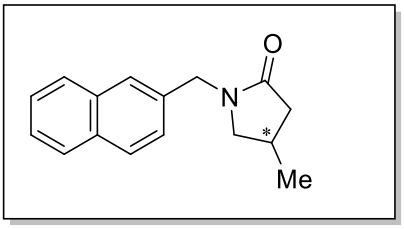


6-1a
(1.5 mmol)

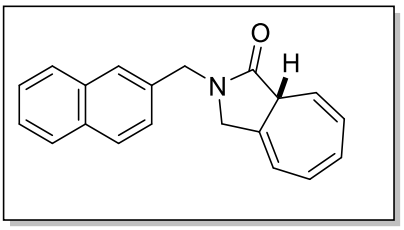
6-2a
(301.6 mg)
95% yield
98% ee

To a solution of Ru(II)-Pheox (**cat. 1**) (9.5 mg, 0.015 mmol, 1 mol%) in CH_2Cl_2 (15 mL) was slowly added a solution of naphthyl 2-diazoacetamide **6-1a** (358.9 mg, 1.5 mmol, 1 equiv.) in CH_2Cl_2 (15 mL) under argon atmosphere at room temperature. The reaction mixture was stirred at room temperature for 1 min. The completion of the reaction was confirmed by TLC. After the reaction was complete, solvent was removed under reduced pressure and the residue was purified using column chromatography on silica gel with Hex/EA = 1/1 ($^{v}/_{v}$) as an eluent to give desired product **6-2a** as a white solid (95% yield, 301.6 mg, 1.43 mmol), 98% ee.

8-4-3 Analytical Data for Products **6-3d**, **6-3e**, **6-3f**, **6-3j**, **6-3k**, **6-3l**, **6-3m**

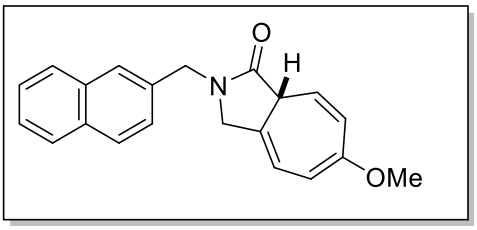


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(propyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1d** (53.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 4/1 ($^{v}/_{v}$) as an eluent to give desired product **6-3d** as a white solid (30% yield, 14.3 mg, 0.06 mmol), 33% ee. $[\alpha]^{21}_{D}$ = +3.7 (c 0.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK AD-3), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 12.39 min (major product), tR = 13.02 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.84 (m, 3H), 7.68 (s, 1H), 7.47-7.49 (m, 2H), 7.36 (dd, *J* = 8.5, 1.8 Hz, 1H), 4.60 (s, 2H), 3.38 (dd, *J* = 9.6, 7.8 Hz, 1H), 2.83 (dd, *J* = 9.8, 6.1 Hz, 1H), 2.64 (q, *J* = 8.3 Hz, 1H), 2.41 (sept., 1H), 2.11 (dd, *J* = 16.6, 6.9 Hz, 1H), 1.06 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 134.0, 133.2, 132.7, 128.5, 127.6, 126.9, 126.2, 126.0, 125.9, 53.8, 46.6, 39.4, 26.3, 19.7 ppm. IR (neat) ν 3047, 2959, 2925, 1686, 1267, 753 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{16}H_{17}NNaO$: 262.1202, found: 262.1211.

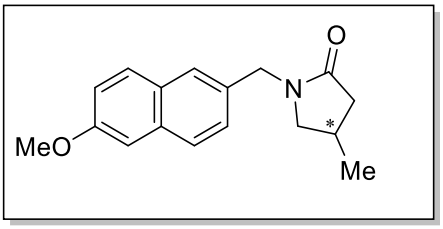


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(benzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1e** (63.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-3e** as a white solid (16% yield, 9.1 mg, 0.031 mmol), 42% ee. The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 57.72 min (minor product), tR = 62.21 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (t, *J* = 8.03 Hz, 2H), 7.71 (s, 1H), 7.48 (t, *J* = 3.82 Hz, 1H), 7.39 (d, *J* = 8.41 Hz, 1H), 7.33 (dd, *J* = 16.44, 6.88 Hz, 2H), 6.48 (bs, 2H), 6.20 (bs, 1H), 6.07 (bs, 1H), 5.35 (ddd, *J* = 14.24, 9.75, 3.82 Hz, 1H), 4.74 (dd, *J* = 48.54, 14.52 Hz, 1H), 4.58 (dd, *J* = 30.20, 14.52 Hz,

1H), 4.08 (d, J = 9.94 Hz, 2H), 3.17 (d, J = 15.79 Hz, 1H) ppm. IR (neat) ν 3020, 2959, 2950, 1688, 1266, 753 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{20}H_{18}NO$: 288.1383, found: 288.1382.

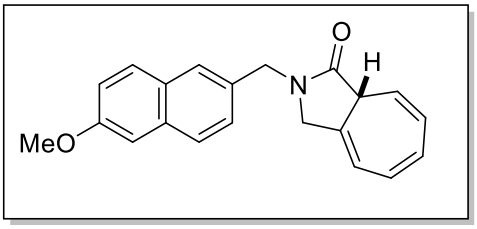


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-methoxybenzyl)-2-diazo-*N*-((naphthalen-2-yl)methyl)acetamide **6-1f** (69.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-3f** as a green solid (45% yield, 28.7 mg, 0.09 mmol), 99% ee. $[\alpha]^{20}_D$ = −5.2 (c 1.0 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 27.18 min (major product), tR = 31.40 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (t, J = 8.03 Hz, 3H), 7.70 (s, 1H), 7.48 (t, J = 3.82 Hz, 2H), 7.38 (dd, J = 8.41, 1.53 Hz, 1H), 6.07 (dt, J = 11.28, 1.91 Hz, 1H), 5.95 (dd, J = 6.69, 2.29 Hz, 1H), 5.66 (d, J = 6.88 Hz, 1H), 5.55 (dd, J = 10.32, 4.20 Hz, 1H), 4.77 (d, J = 14.52 Hz, 1H), 4.67 (d, J = 14.52 Hz, 1H), 4.03 (d, J = 11.85 Hz, 2H), 3.62 (s, 3H), 3.25 (s, 1H)ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 159.2, 133.4, 133.2, 132.8, 128.7, 127.6, 127.0, 126.3, 126.0, 125.9, 125.1, 123.1, 123.0, 117.6, 102.6, 54.6, 50.3, 46.7, 45.8 ppm. IR (neat) ν 3000, 2927, 2831, 1690, 1436, 1214, 753 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{21}H_{20}NO_2$: 318.1489, found: 318.1497.

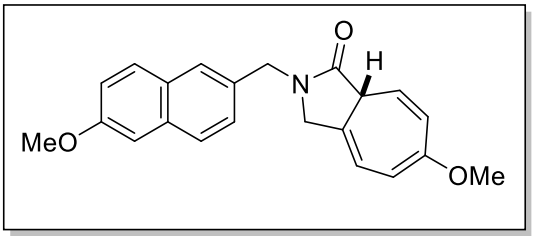


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(propyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1j** (59.5 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 4/1 ($^v/_v$) as an eluent to give desired product **6-3j** as a white solid (28% yield, 15.1 mg, 0.056 mmol), 31% ee. $[\alpha]^{21}_D$ = −1.4 (c 0.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 49.28 min (minor product), tR = 52.75 min (major product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, J = 8.60, 3.82 Hz, 2H), 7.60 (s, 1H),

7.32 (dd, *J* = 8.41, 1.53 Hz, 1H), 7.15 (dd, *J* = 8.79, 2.68 Hz, 1H), 7.12 (d, *J* = 2.29 Hz, 1H), 4.55 (s, 2H), 3.91 (s, 3H), 3.37 (dd, *J* = 9.56, 7.64 Hz, 1H), 2.82 (dd, *J* = 9.52, 5.73 Hz, 1H), 2.62 (dd, *J* = 16.82, 8.41 Hz, 1H), 2.39 (nonet, *J* = 6.88 Hz, 1H), 2.09 (dd, *J* = 16.82, 6.88 Hz, 1H), 1.05 (d, *J* = 6.88 Hz, 3H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.5, 157.7, 133.9, 131.7, 129.1, 128.7, 127.3, 126.8, 126.6, 119.0, 105.6, 55.2, 53.8, 46.5, 39.4, 26.3, 19.7 ppm. IR (neat) ν 3050, 2954, 2919, 1682, 1266, 1030, 852 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{17}H_{19}NNaO_2$: 292.1308, found: 292.1315.

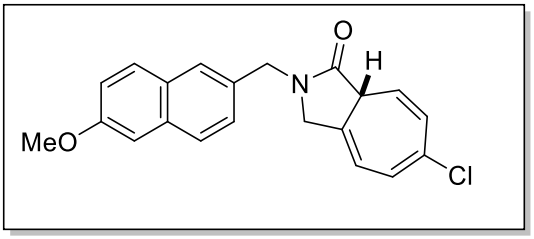


This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(benzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1k** (69.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^v/_v$) as an eluent to give desired product **6-3k** as a white solid (11% yield, 7.3 mg, 0.023 mmol), 79% ee. The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 10/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 61.31 min (major product), tR = 68.83 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4, 6.1 Hz, 2H), 7.63 (s, 1H), 7.35 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.16 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.12 (d, *J* = 2.7 Hz, 1H), 6.47 (t, *J* = 3.1 Hz, 2H), 6.26-6.15 (m, 1H), 6.10-5.98 (m, 1H), 5.36 (dd, *J* = 9.6, 3.4 Hz, 1H), 4.75 (d, *J* = 14.5 Hz, 1H), 4.65 (d, *J* = 14.5 Hz, 1H), 4.08 (s, 2H), 3.92 (s, 3H), 3.18 (s, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.0, 158.1, 134.0, 130.3, 129.8, 129.1, 128.7, 127.5, 127.0, 126.5, 120.6, 119.5, 119.2, 105.6, 55.3, 50.5, 46.6, 46.4 ppm. IR (neat) ν 3024, 2954, 2919, 1688, 1266, 708 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{21}H_{19}NaNO_2$: 340.1309, found: 340.1308.



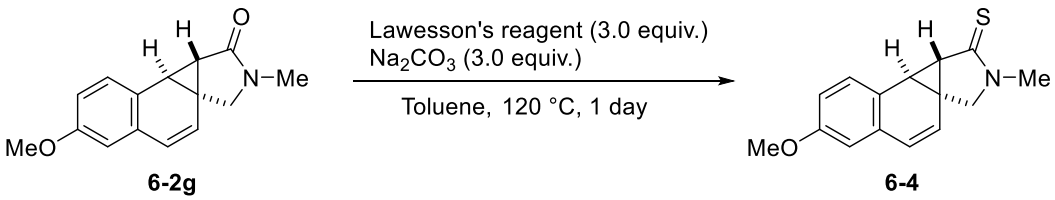
This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-methoxybenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1l** (75.1 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The

resulting mixture was purified by silica gel column chromatography with Hex/EA = 5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-3l** as a white solid (50% yield, 35.0 mg, 0.10 mmol), 97% ee. $[\alpha]^{21}_{D}$ = −8.9 (c 1.7 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK ID), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 51.30 min (major product), tR = 59.36 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 8.60, 5.73 Hz, 2H), 7.62 (s, 1H), 7.34 (dd, *J* = 8.41, 1.53 Hz, 1H), 7.15 (dd, *J* = 8.98, 2.68 Hz, 1H), 7.12 (d, *J* = 2.68 Hz, 1H), 6.07 (dt, *J* = 10.32, 2.29 Hz, 1H), 5.97 (dd, *J* = 6.69, 2.29 Hz, 1H), 5.66 (d, *J* = 6.50 Hz, 1H), 5.54 (dd, *J* = 10.32, 4.20 Hz, 1H), 4.73 (d, *J* = 14.52 Hz, 1H), 4.63 (d, *J* = 14.52 Hz, 1H), 4.05 (d, *J* = 15.10 Hz, 1H), 4.0 d, *J* = 14.91 Hz, 1H), 3.91 (s, 3H), 3.62 (s, 3H), 3.24 (s, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 159.2, 157.7, 134.0, 131.0, 129.1, 128.6, 127.5, 126.9, 126.5, 125.0, 123.1, 119.1, 117.6, 105.6, 102.7, 55.2, 54.6, 50.3, 46.6, 45.8 ppm. IR (neat) ν 3008, 2935, 2842, 1634, 1608, 1437, 1266, 1026, 753 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{22}H_{22}NO_3$: 348.1594, found: 348.1591.



This compound was prepared according to the typical procedure for catalytic asymmetric carbene transfer reaction of *N*-(4-chlorobenzyl)-2-diazo-*N*-((6-methoxynaphthalen-2-yl)methyl)acetamide **6-1m** (76.0 mg, 0.2 mmol, 1 equiv.) in the presence of **cat. 1** (1.3 mg, 0.002 mmol, 1 mol%). The resulting mixture was purified by silica gel column chromatography with Hex/EA=5/1 ($^{v}/_{v}$) as an eluent to give desired product **6-3m** as a white solid (18% yield, 12.7 mg, 0.036 mmol), 97% ee. The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^{v}/_{v}$), Flow rate = 1.0 ml/min, tR = 54.91 min (major product), tR = 60.48 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (t, *J* = 8.03 Hz, 2H), 7.62 (s, 1H), 7.33 (dd, *J* = 8.41, 1.53 Hz, 1H), 7.16 (dd, *J* = 8.98, 2.68 Hz, 1H), 7.12 (d, *J* = 2.68 Hz, 1H), 6.66 (d, *J* = 6.50 Hz, 1H), 6.19 (d, *J* = 9.94 Hz, 1H), 5.98 (dd, *J* = 6.50, 2.29 Hz, 1H), 5.41 (dd, *J* = 9.94, 4.20 Hz, 1H), 4.73 (d, *J* = 14.52 Hz, 1H), 4.63 (d, *J* = 14.52 Hz, 1H), 4.07 (d, *J* = 16.05 Hz, 1H), 4.02 (d, *J* = 16.05 Hz, 1H), 3.91 (s, 3H), 3.28 (s, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 157.8, 134.9, 134.0, 130.7, 129.4, 129.1, 128.8, 128.6, 128.5, 127.6, 127.1, 126.5, 122.3, 119.2, 118.1, 105.6, 55.3, 50.3, 46.6, 46.0 ppm. IR (neat) ν 3004, 2935, 2842, 1699, 1267, 1230, 755 cm^{-1}. HRMS(ESI) $[M+H]^+$ calcd for $C_{21}H_{19}ClNO_2$: 352.1099, found: 352.1093.

8-4-4 Synthetic Transformation of Product



6-2g **6-4**

To a solution of product **6-2g** (36.0 mg, 0.149 mmol, 1 equiv.) in toluene (3 mL) was added Lawesson's reagent (181.0 mg, 0.448 mmol, 3 equiv.) and Na_2CO_3 (47.5 mg, 0.448 mmol, 3 equiv.) under an argon atmosphere. The reaction mixture was heated to reflux at 120 ℃ for 1 day. The combined mixture was extracted with EA (3x3 mL) and dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (Hex/EA = 3/1 ($^v/_v$)) to give desired product **6-4** as a white solid (99% yield, 38.0 mg, 0.148 mmol), 99% ee. $[\alpha]^{31}_D$ = +349.1 (c 1.25 in $CHCl_3$). The *ee* value was determined by chiral HPLC analysis. Column (CHIRALPAK IE-3), UV detector 254 nm, eluent: Hex/IPA = 5/1 ($^v/_v$), Flow rate = 1.0 ml/min, tR = 54.47 min (major product), tR = 72.11 min (minor product). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.41 Hz, 1H), 6.82 (dd, *J* = 8.41, 2.68 Hz, 1H), 6.70 (d, *J* = 2.68 Hz, 1H), 6.37 (d, *J* = 9.56 Hz, 1H), 6.10 (d, *J* = 9.56 Hz, 1H), 4.09 (d, *J* = 12.23 Hz, 1H), 3.82 (d, *J* = 1.91 Hz, 1H), 3.80 (s, 3H), 3.23 (s, 3H), 2.67 (d, *J* = 2.68 Hz, 1H), 1.55 (t, *J* = 2.29 Hz, 1H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.7, 158.6, 131.9, 129.8, 125.9, 124.7, 123.9, 114.1, 112.8, 62.9, 55.2, 37.7, 36.9, 34.8, 31.5 ppm. IR (neat) ν 3028, 2931, 2834, 1603, 1499, 1322, 1262, 1122, 934, 813 cm^{-1}. HRMS(ESI) $[M+Na]^+$ calcd for $C_{15}H_{15}NNaOS$: 280.0767, found: 280.0769.

8-4-5 X-ray Crystallographic Data

Product **6-4**:

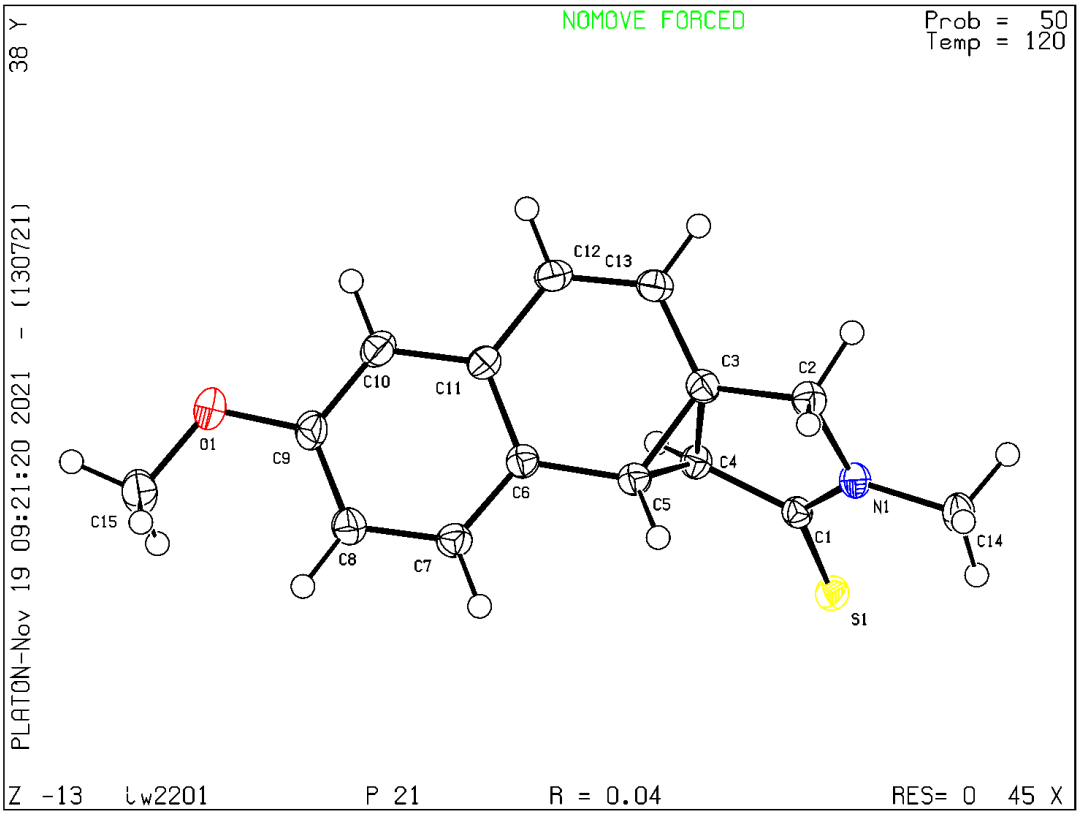
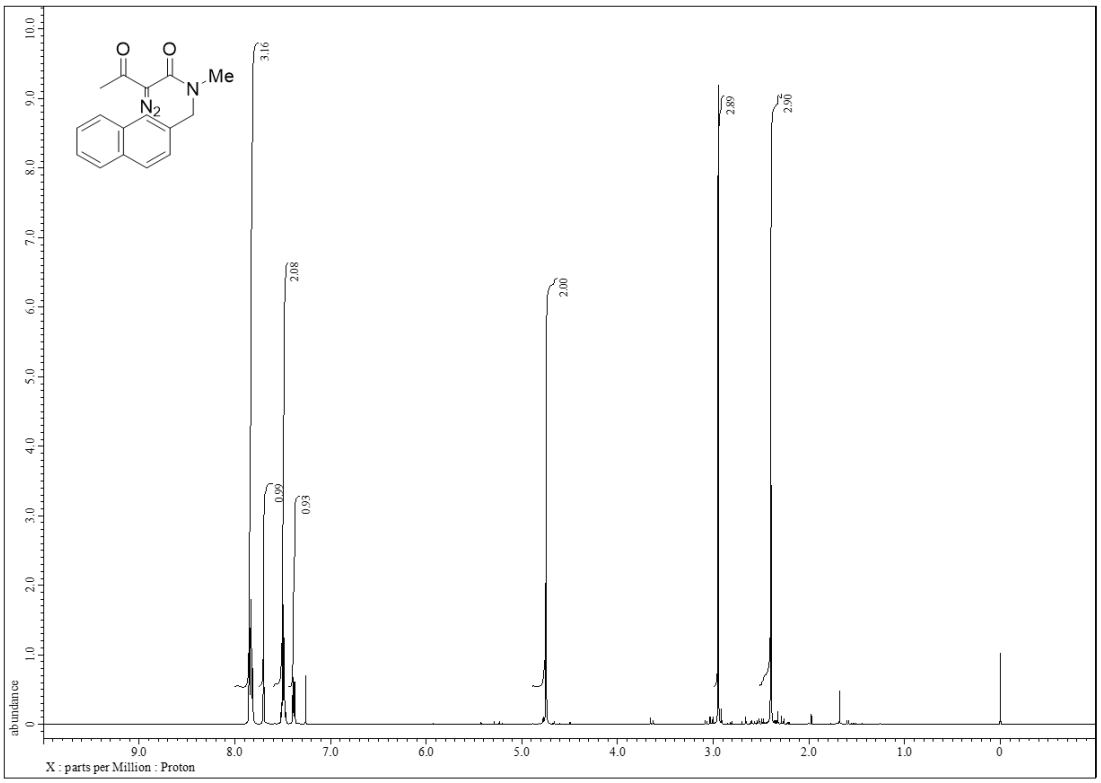


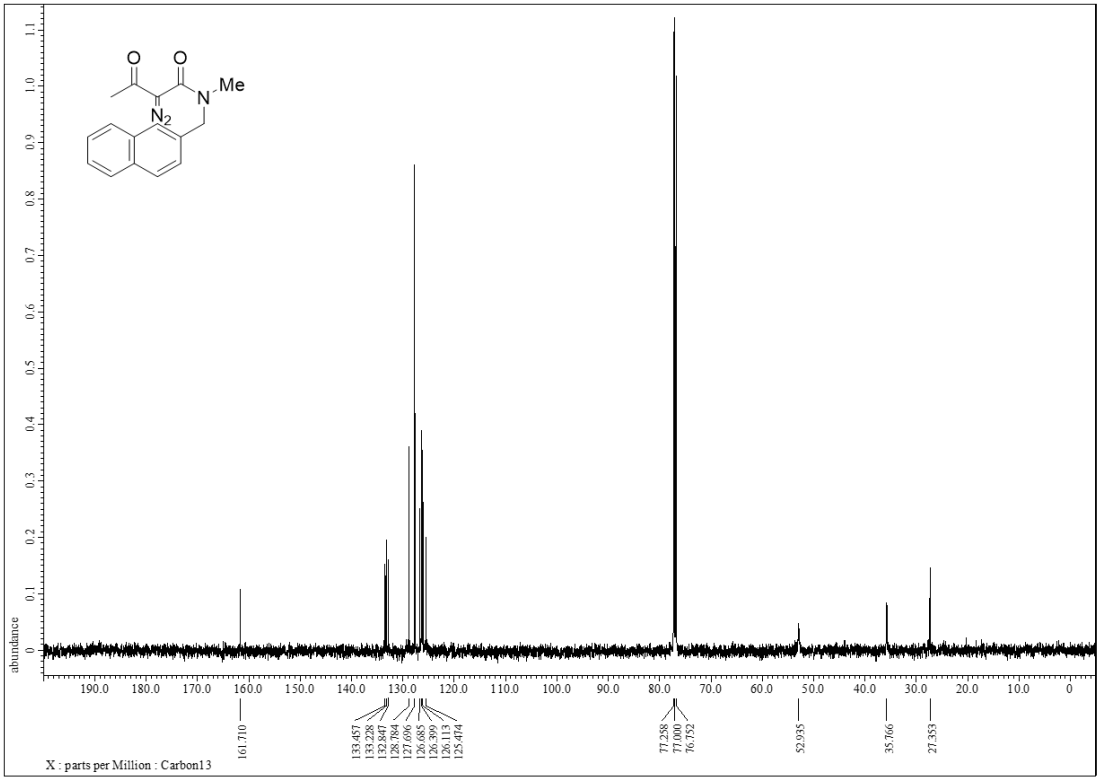
Table S2. Crystal data and structure refinement for **iw2201**.

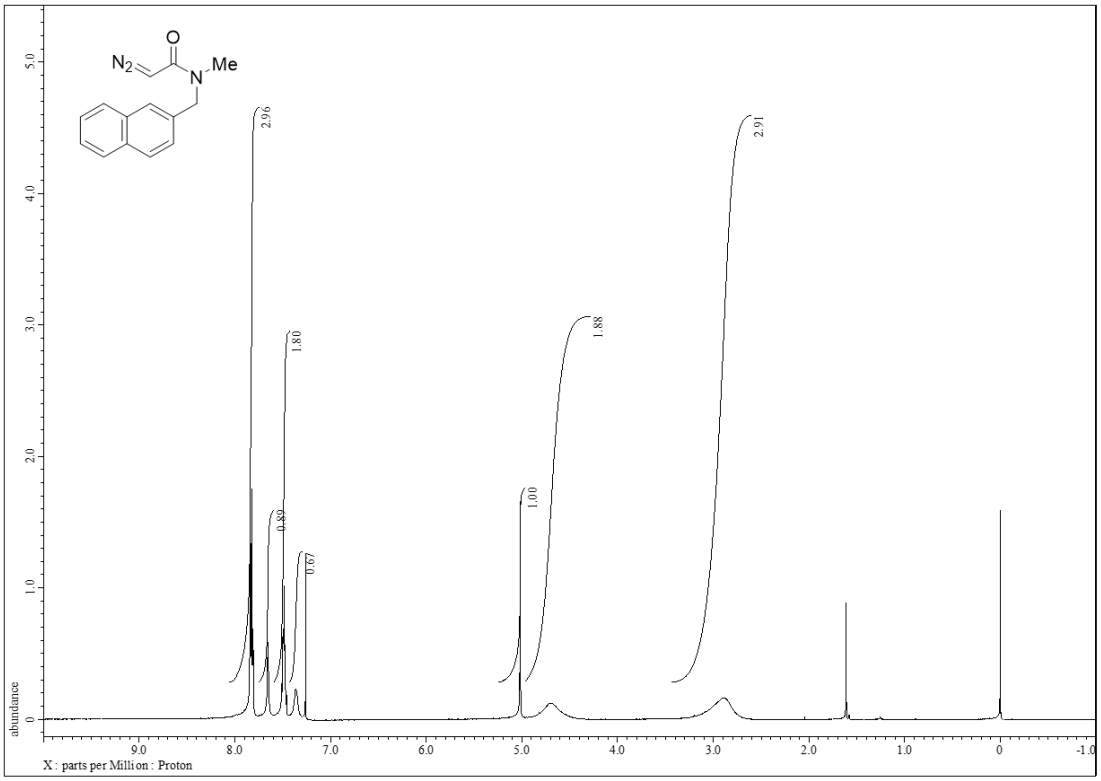
Identification code	iw2201	
CCDC number	2143554	
Empirical formula	C15 H15 N O S	
Formula weight	257.34	
Temperature	120 K	
Wavelength	0.71075 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.4659(14) Å	α = 90°.
	b = 7.0218(15) Å	β = 94.163(4)°.
	c = 14.113(3) Å	γ = 90°.
Volume	639.1(2) Å^3	
Z	2	
Density (calculated)	1.337 Mg/m^3	
Absorption coefficient	0.240 mm^{-1}	
F(000)	272	
Crystal size	0.35 x 0.30 x 0.03 mm^3	
Theta range for data collection	2.894 to 32.033°.	
Index ranges	-9<= h <=9, -10<= k <=10, -18<= l <=21	
Reflections collected	12012	
Independent reflections	4426 [R(int) = 0.0329]	
Completeness to theta = 25.242°	99.4 %	
Absorption correction	Numerical	
Max. and min. transmission	0.972 and 0.876	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4426 / 1 / 223	
Goodness-of-fit on F^2	1.081	
Final R indices [I >2sigma(I)]	R1 = 0.0399, wR2 = 0.0943	
R indices (all data)	R1 = 0.0430, wR2 = 0.0977	
Absolute structure parameter	-0.04(2)	

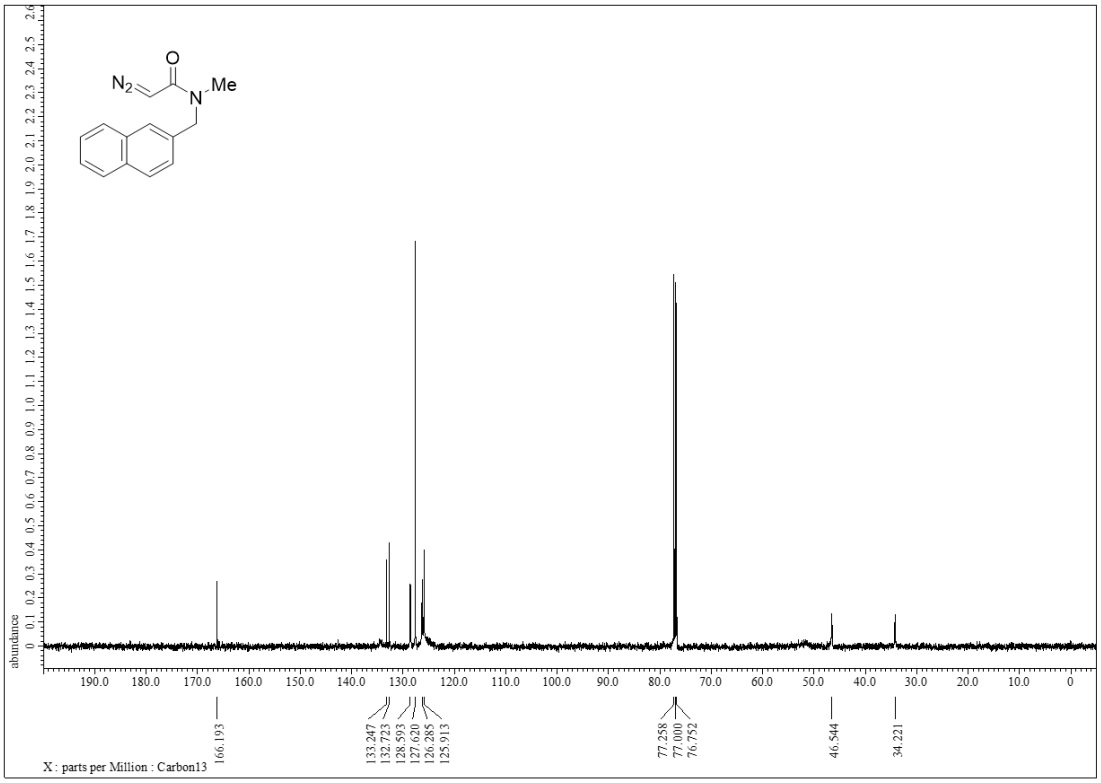
Extinction coefficient	n/a
Largest diff. peak and hole	0.289 and -0.535 e.Å^{-3}

8-4-6 NMR Spectral Data






N2
O
N
Me
2.96
1.80
0.89
0.67
1.00
1.88
2.91
abundance
X : parts per Million : Proton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O
N
Me
abundance
166.193
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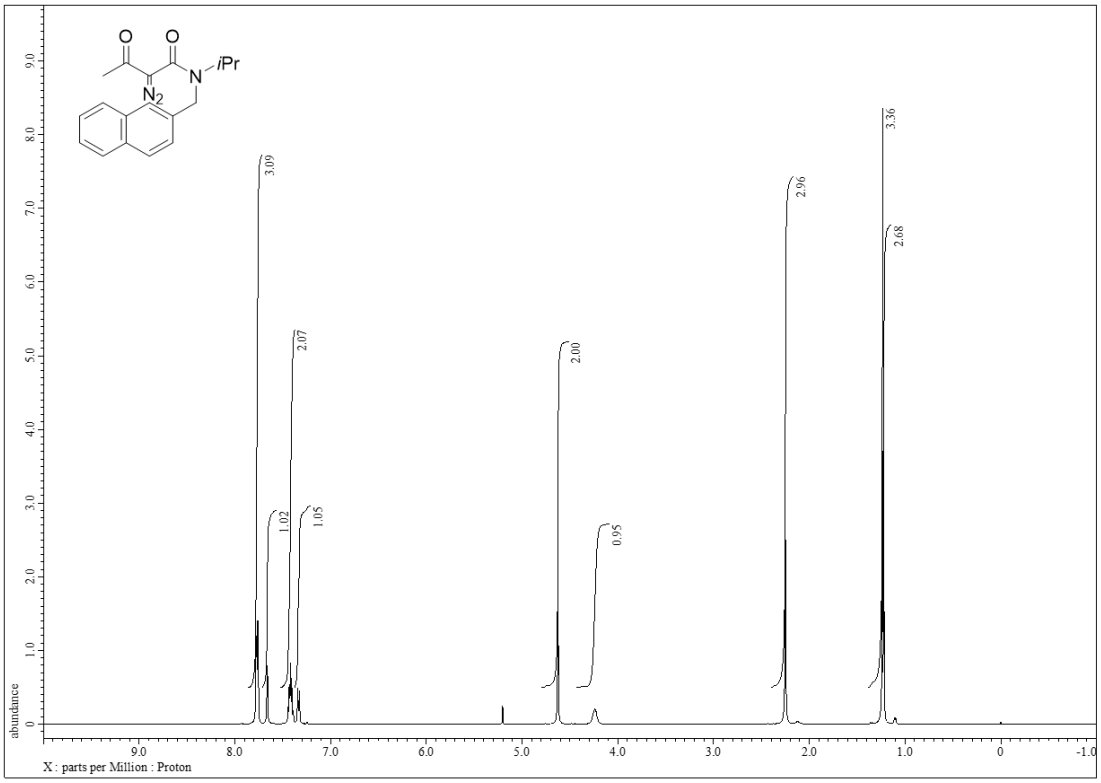
132.723
128.593
127.620
126.285
125.913
77.258
77.000
76.752
46.544
34.221
X : parts per Million : Carbon13


O
O
N
iPr
N2
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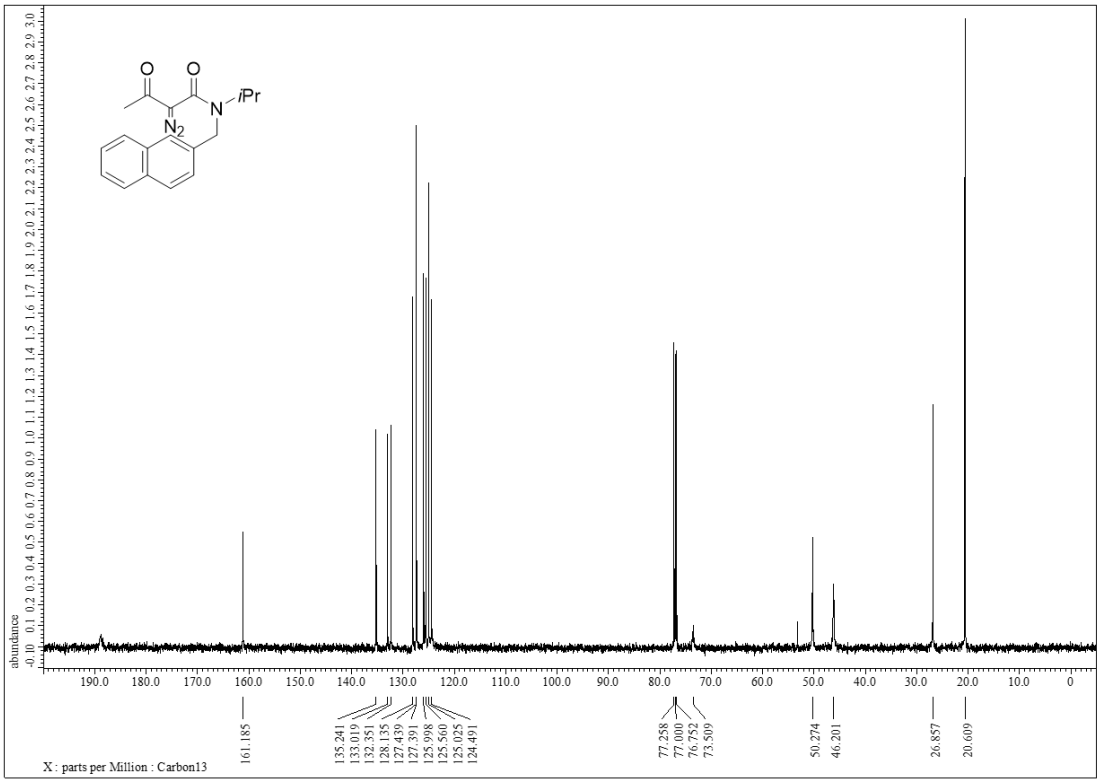
1.02
2.07
1.05
2.00
0.95
2.96
3.36
2.68
abundance
X : parts per Million : Proton


O
O
N
iPr
N2
abundance
161.185
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133.019
132.351
128.135
127.439
127.391
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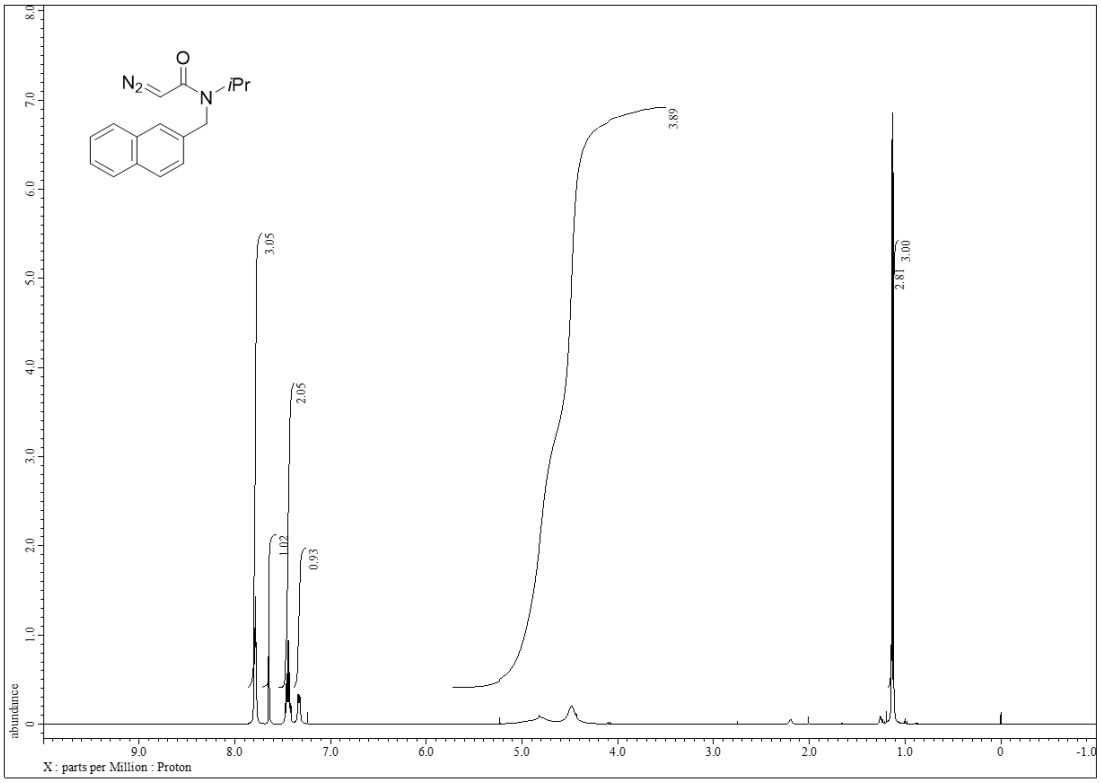
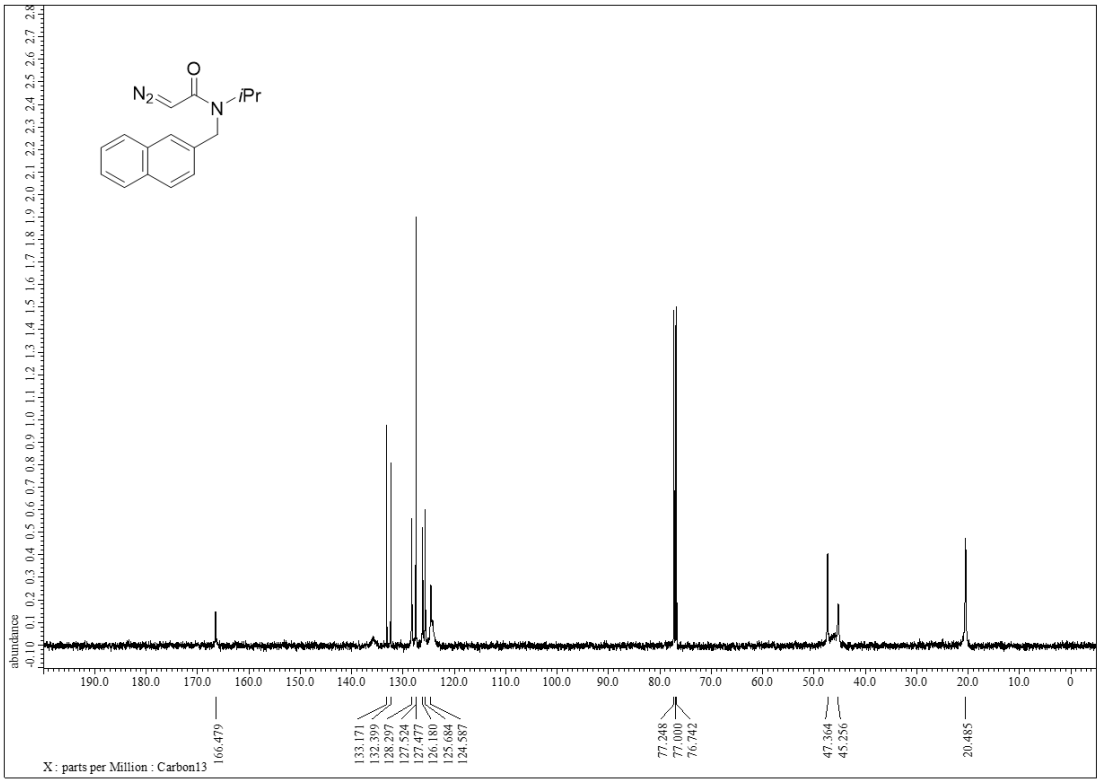
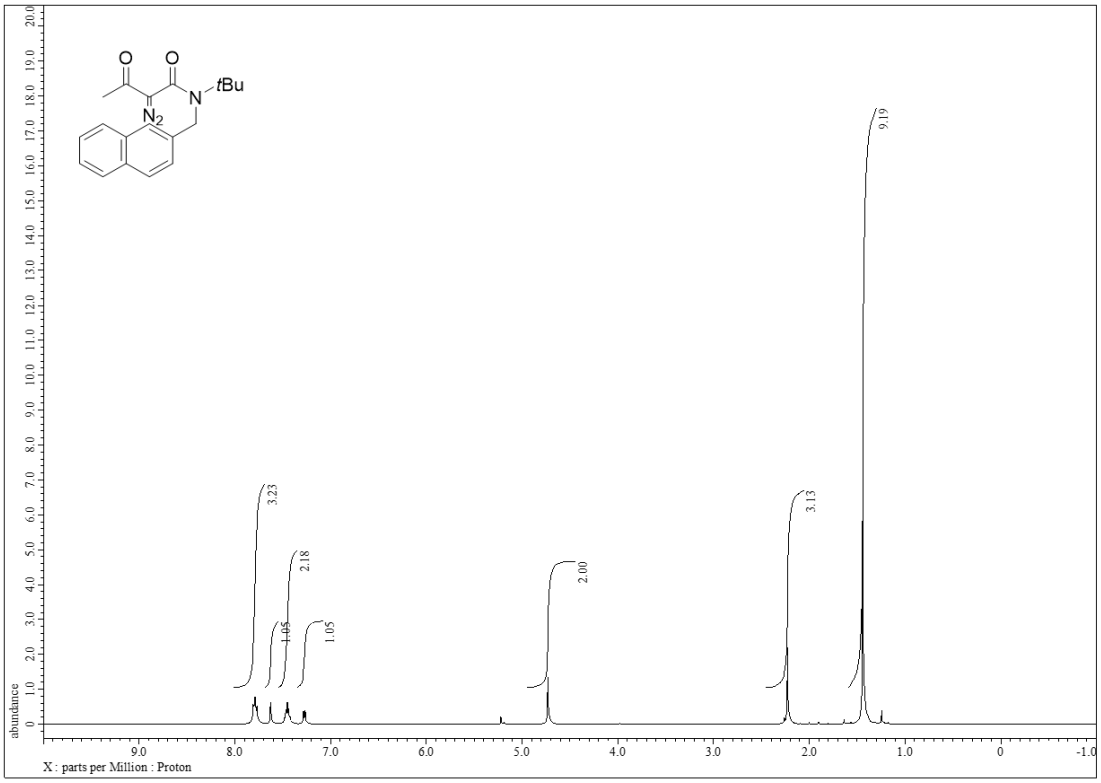
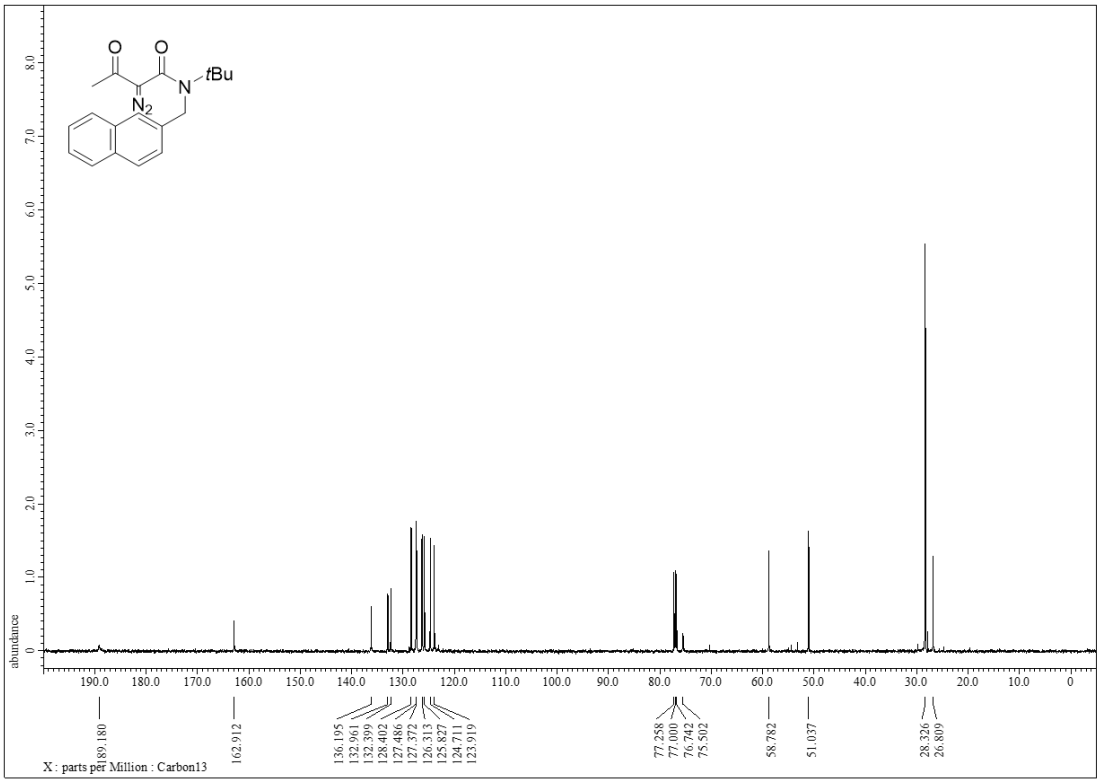
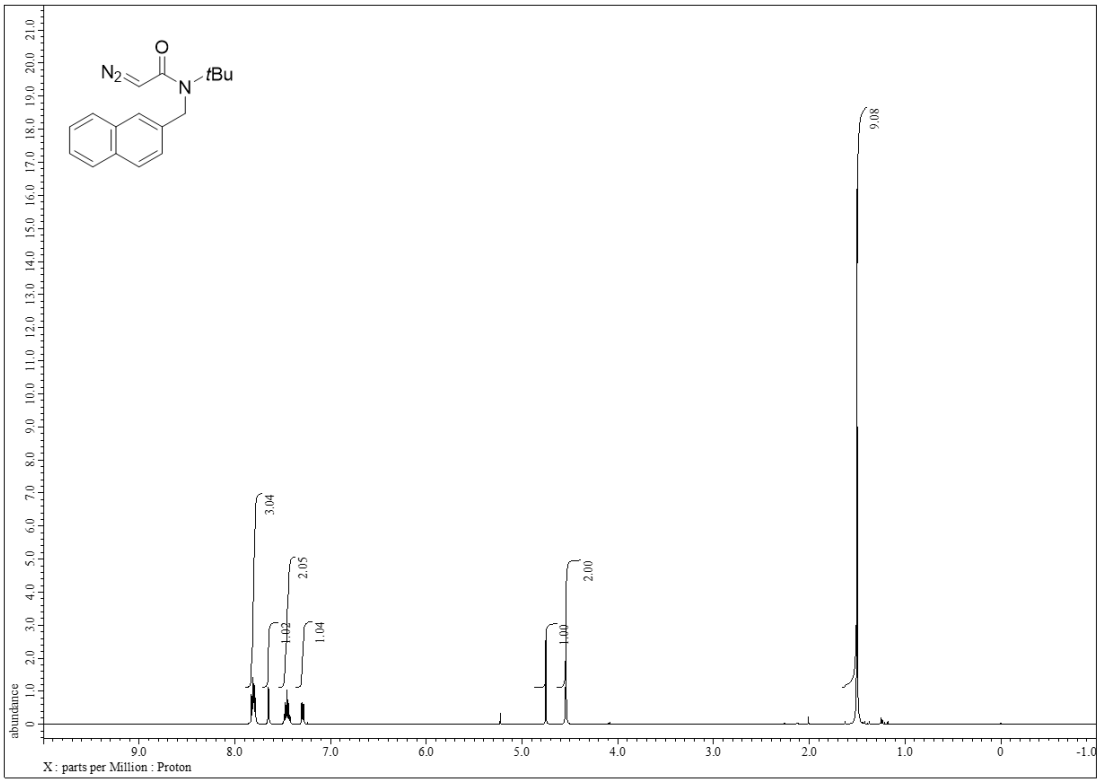
125.025
124.491
77.258
77.000
76.752
73.509
50.274
46.201
26.857
20.609
X : parts per Million : Carbon13

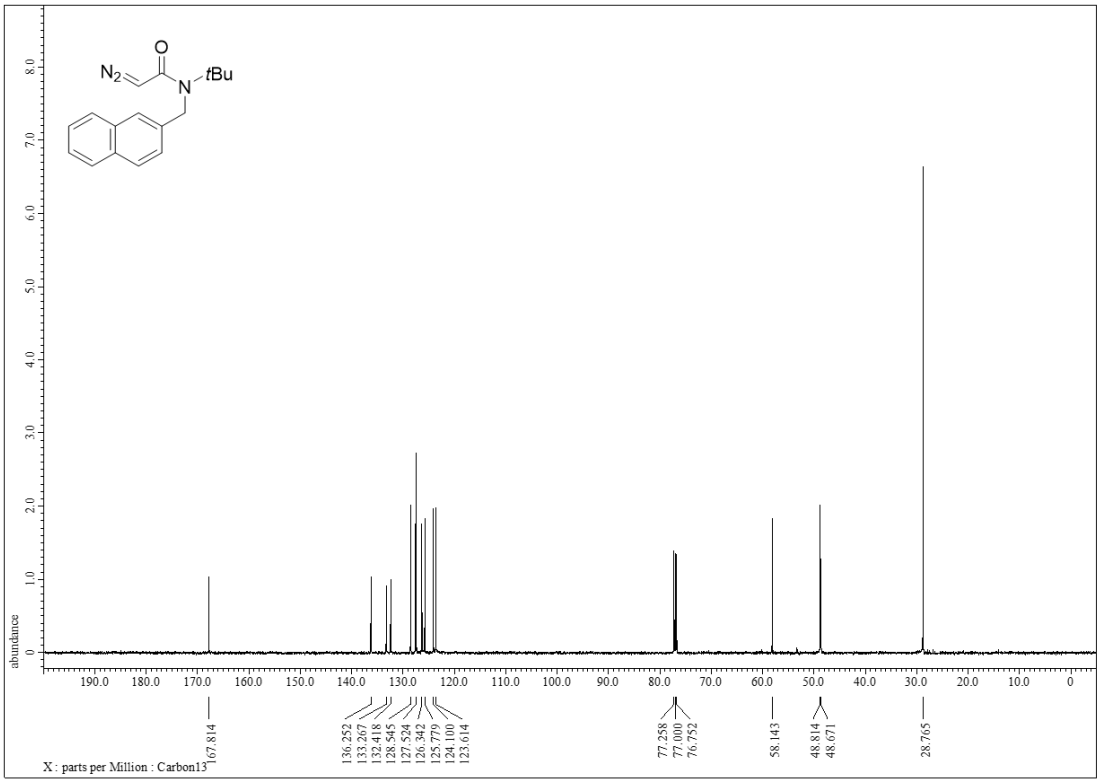

N2
O
N
iPr
3.05
1.02
2.05
0.93
3.89
2.81
3.00
abundance
X : parts per Million : Proton

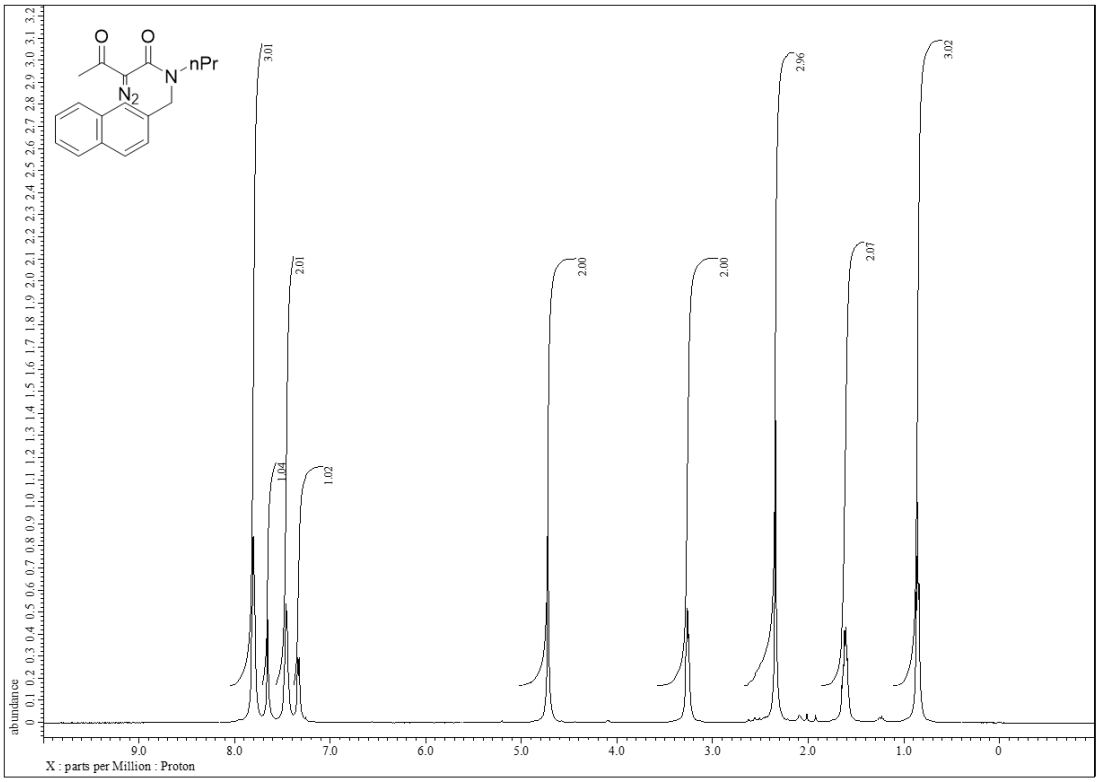

N2
O
N
iPr
abundance
166.479
133.171
132.399
128.297
127.524
127.477
126.180
125.684
124.587
77.248
77.000
76.742
47.364
45.256
20.485
X : parts per Million : Carbon13

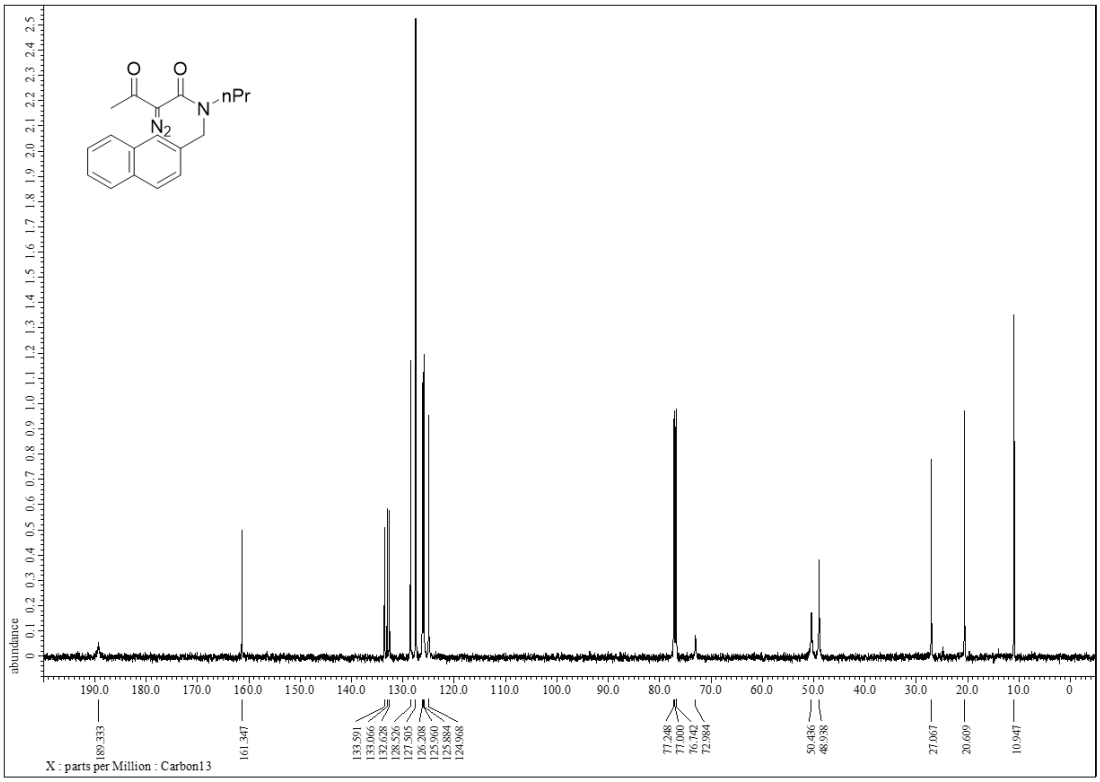

O
O
N
tBu
N2
abundance
3.23
2.18
1.05
1.05
2.00
3.13
9.19
X : parts per Million : Proton

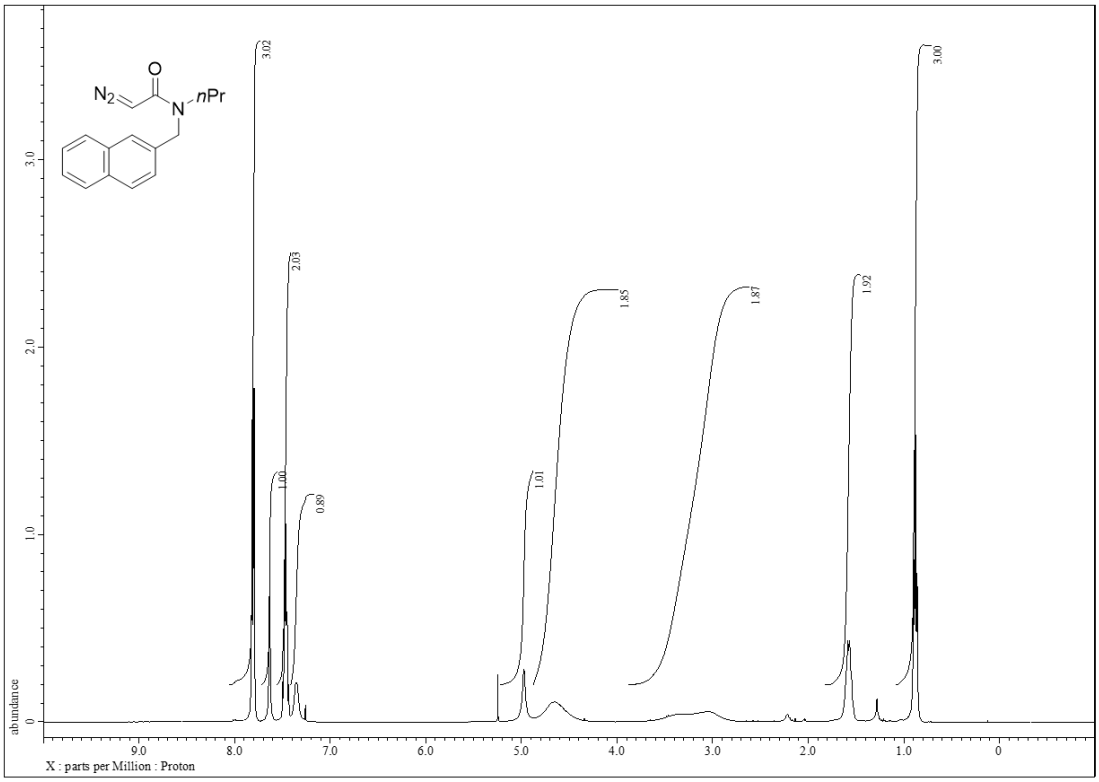

O
O
N
tBu
N2
abundance
189.180
162.912
136.195
132.961
132.399
128.402
127.486
127.372
126.313
125.827
124.711
123.919
77.258
77.000
76.742
75.502
58.782
51.037
28.326
26.809
X : parts per Million : Carbon13

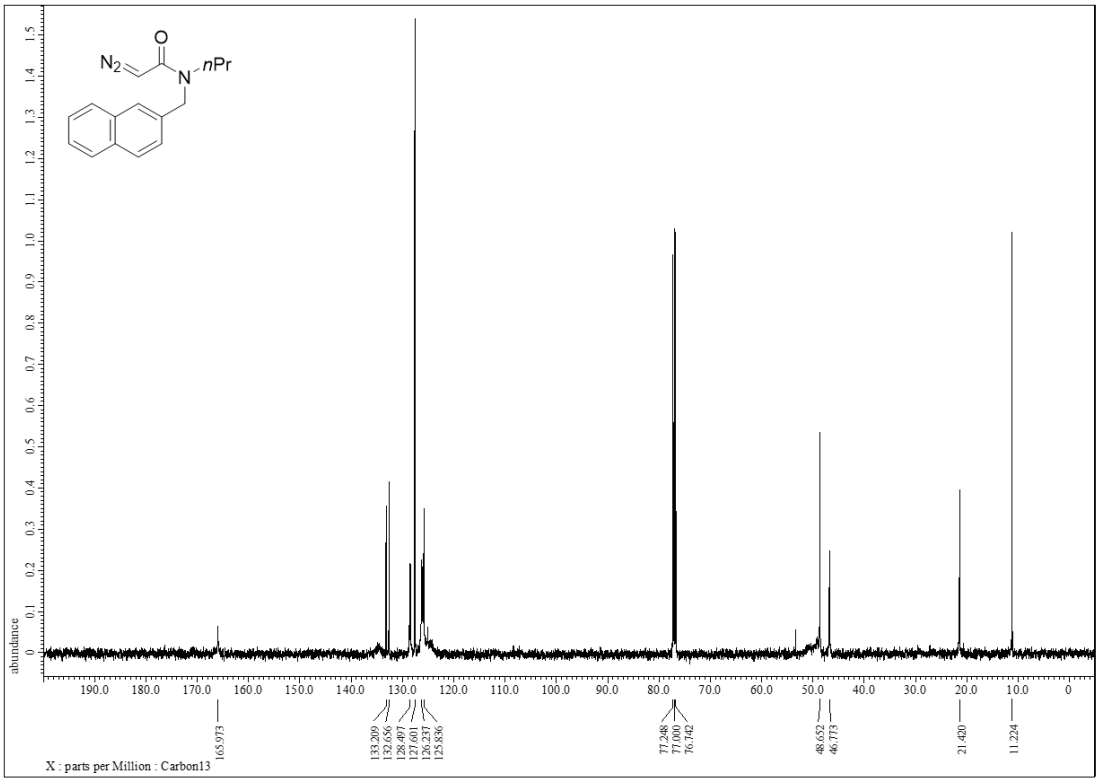

O
N2
N
tBu
3.04
2.05
1.02
1.04
1.00
2.00
9.08
abundance
X : parts per Million : Proton

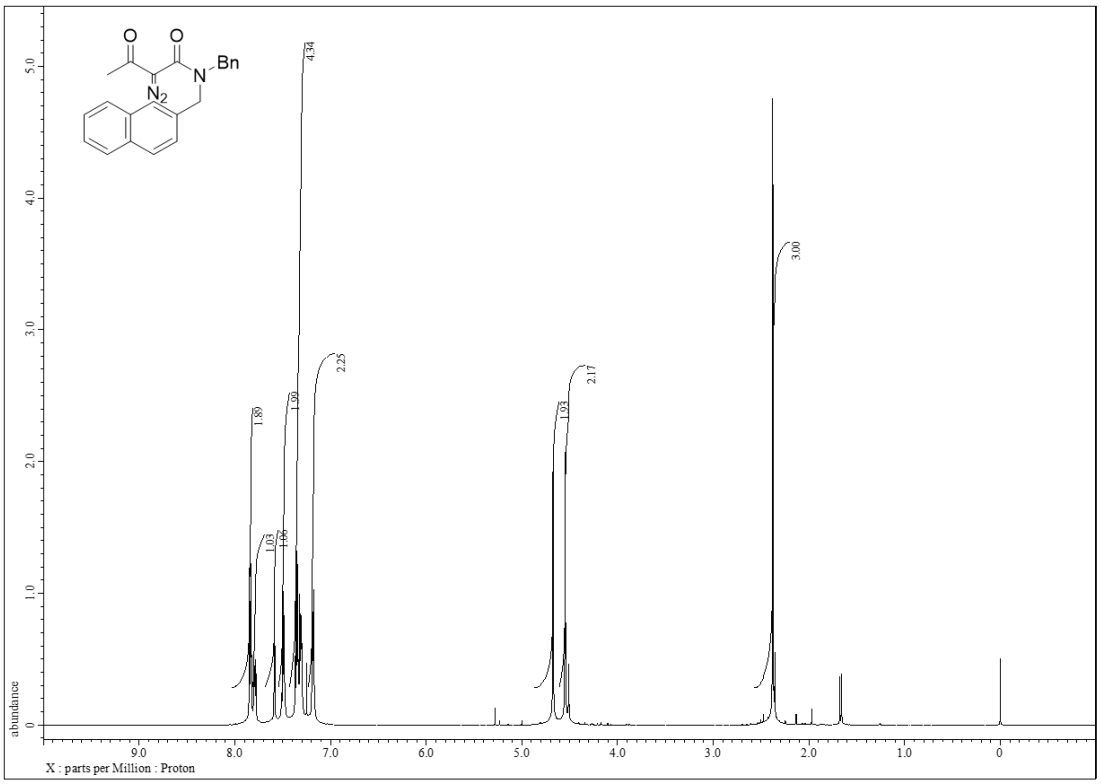

O
N2
N
tBu
abundance
167.814
136.252
133.267
132.418
128.545
127.524
126.342
125.779
124.100
123.614
77.258
77.000
76.752
58.143
48.814
48.671
28.765
X : parts per Million : Carbon13

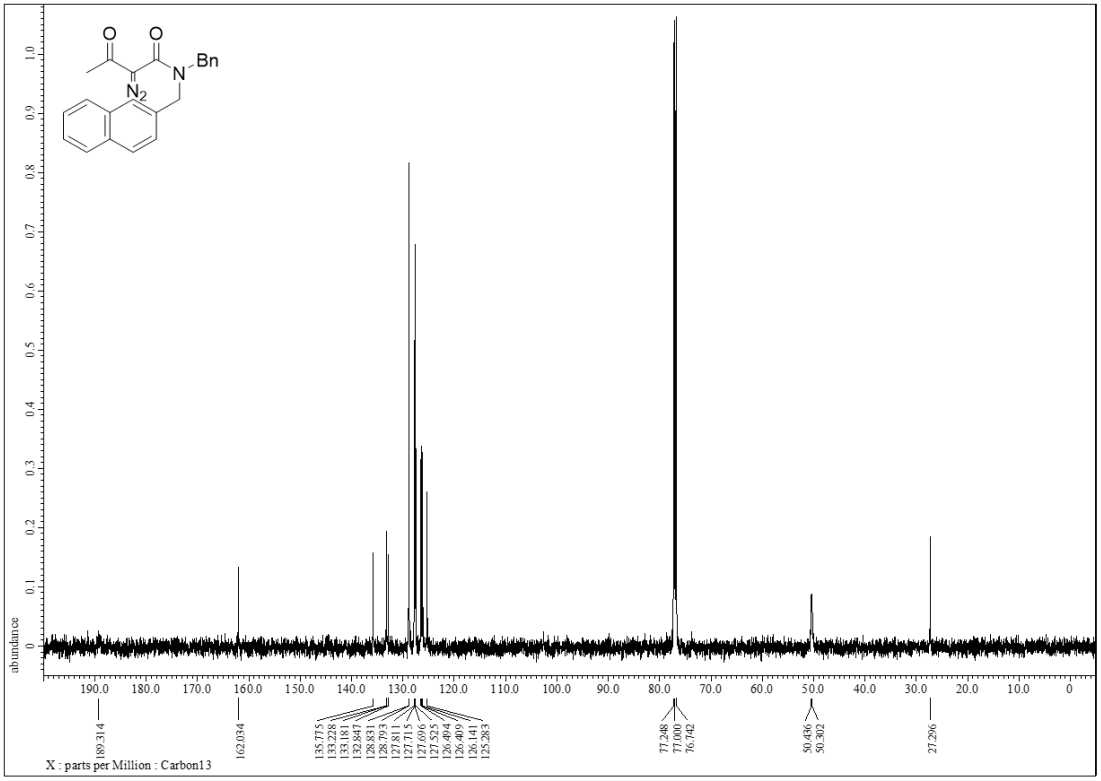

O
O
N
nPr
N2
3.01
1.04
2.01
1.02
2.00
2.00
2.96
2.07
3.02
abundance
X : parts per Million : Proton

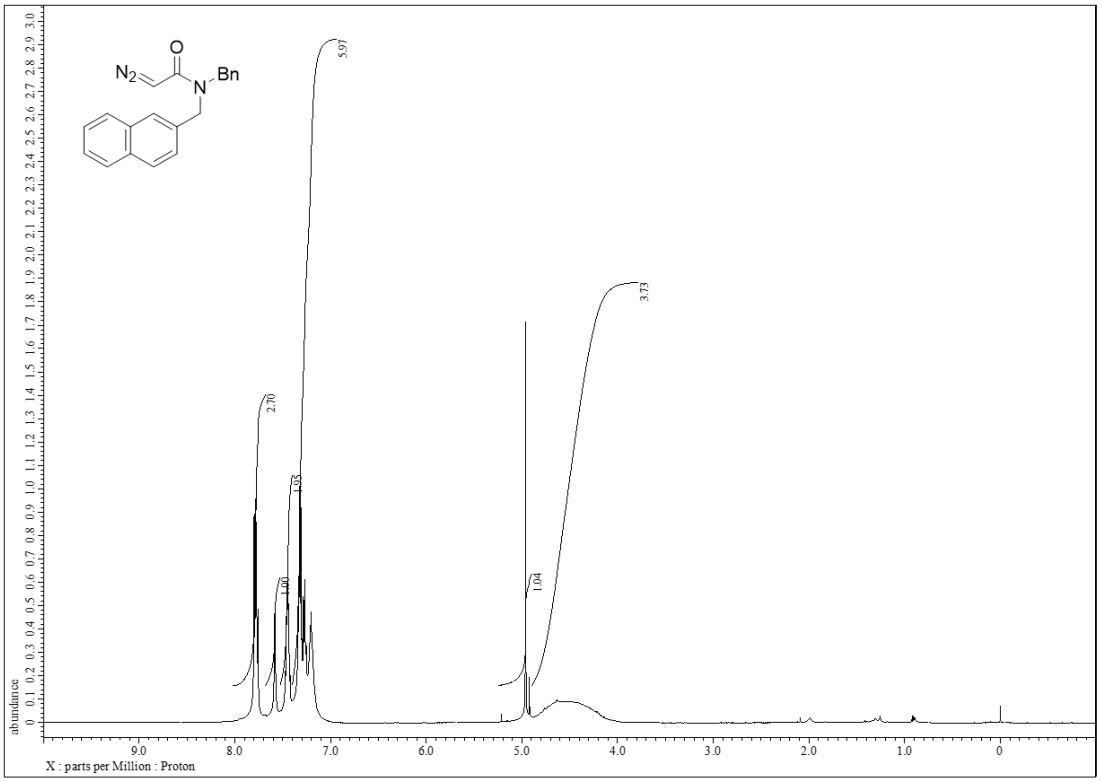

O
O
N
nPr
N2
abundance
189.333
161.347
133.591
133.066
132.628
128.526
127.505
126.208
125.960
125.884
124.968
77.248
77.000
76.742
72.984
50.436
48.938
27.067
20.609
10.947
X : parts per Million : Carbon13

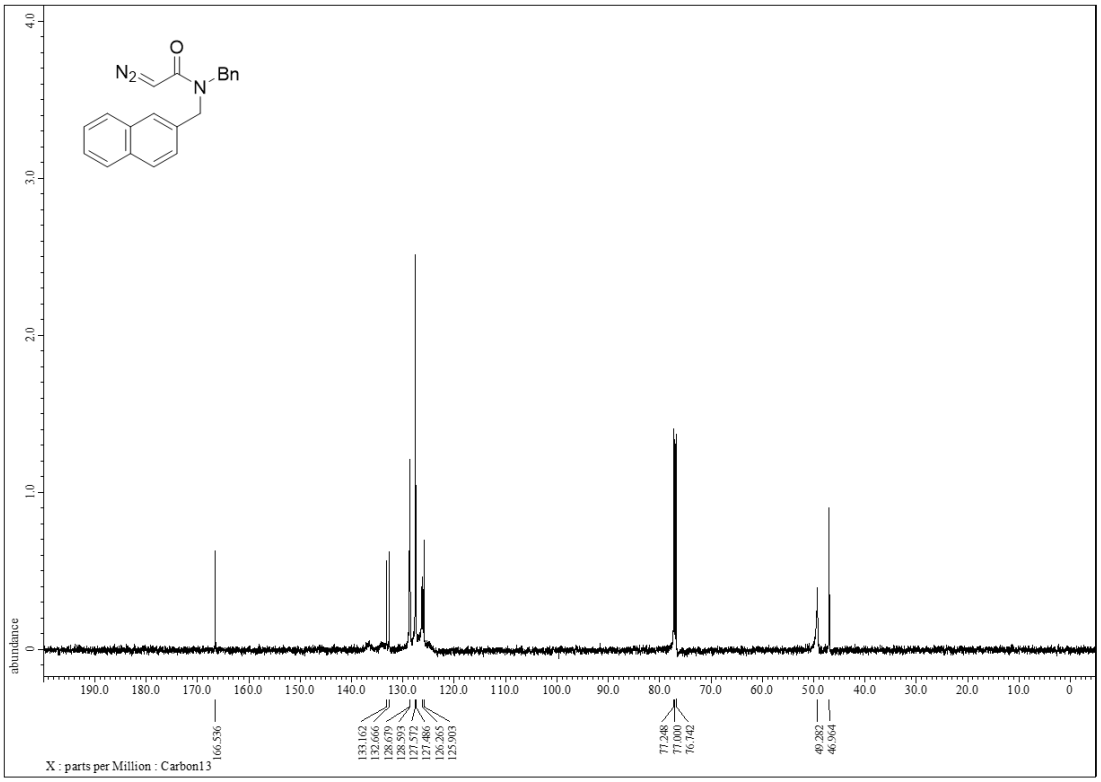

O
N2
N
nPr
3.02
2.03
1.00
0.89
1.01
1.85
1.87
1.92
3.00
abundance
X : parts per Million : Proton

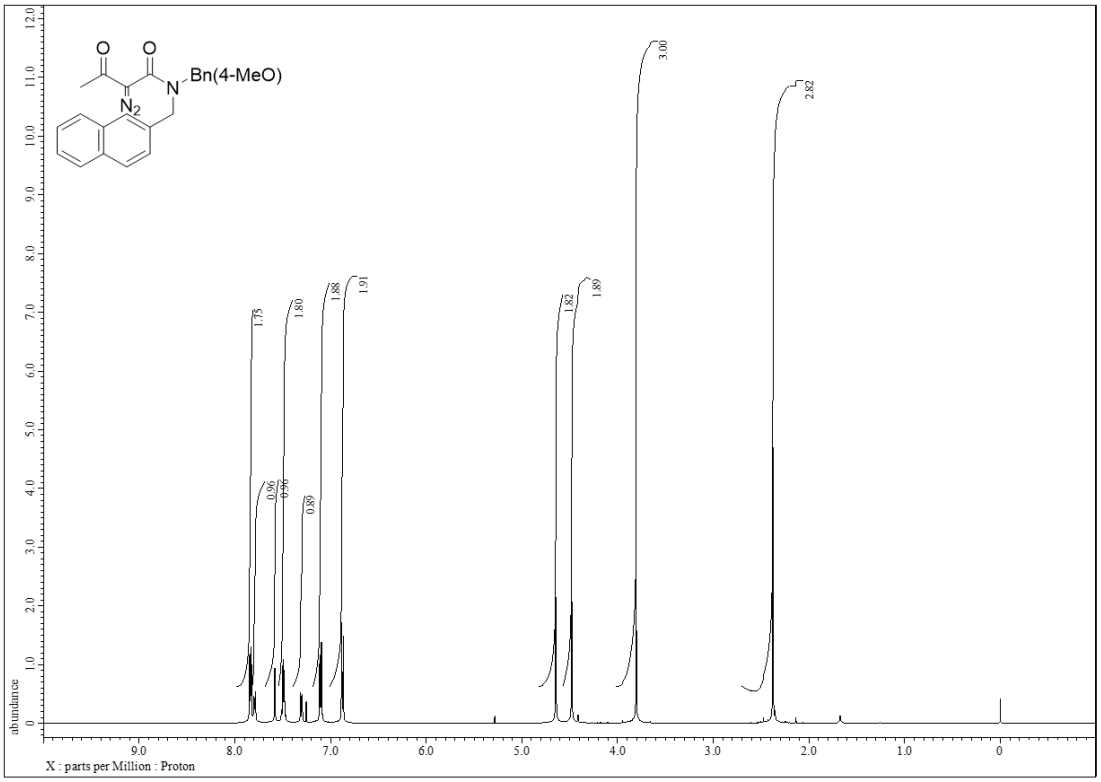

O
N2
N
nPr
abundance
165.973
133.209
132.656
128.497
127.601
126.237
125.836
77.248
77.000
76.742
48.652
46.773
21.420
11.224
X : parts per Million : Carbon13

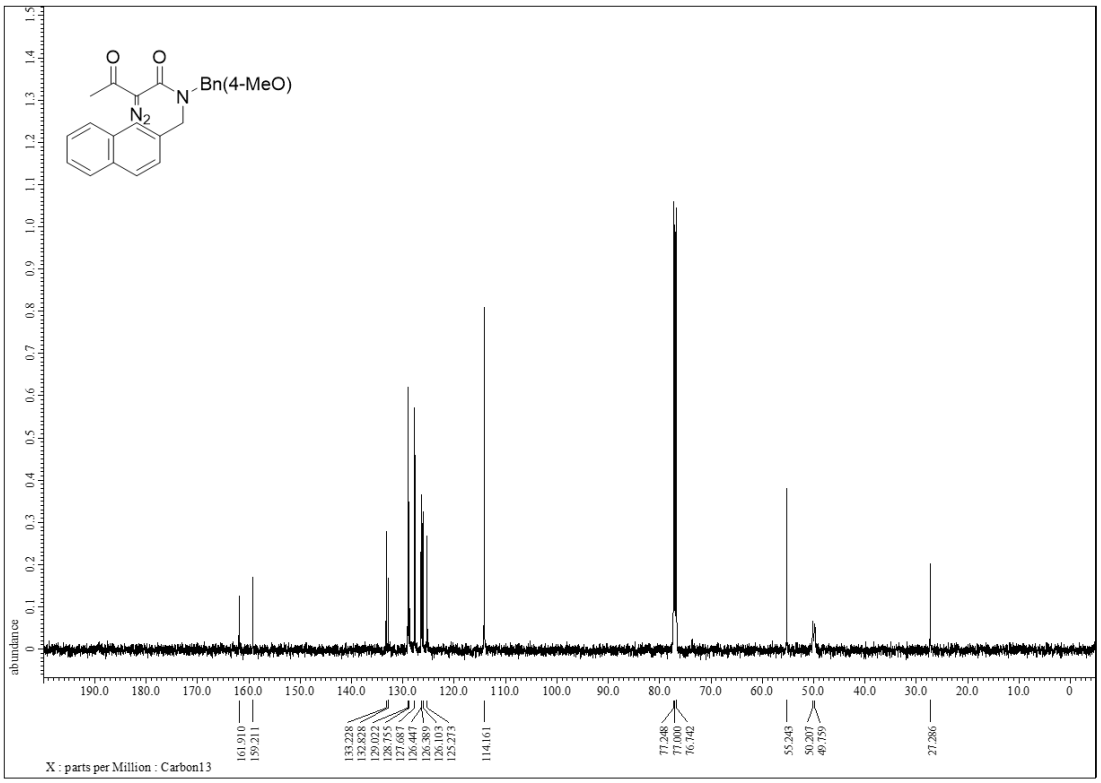

O
O
N
Bn
N2
4.34
2.25
1.89
1.99
1.03
1.06
2.17
1.93
3.00
abundance
X : parts per Million : Proton

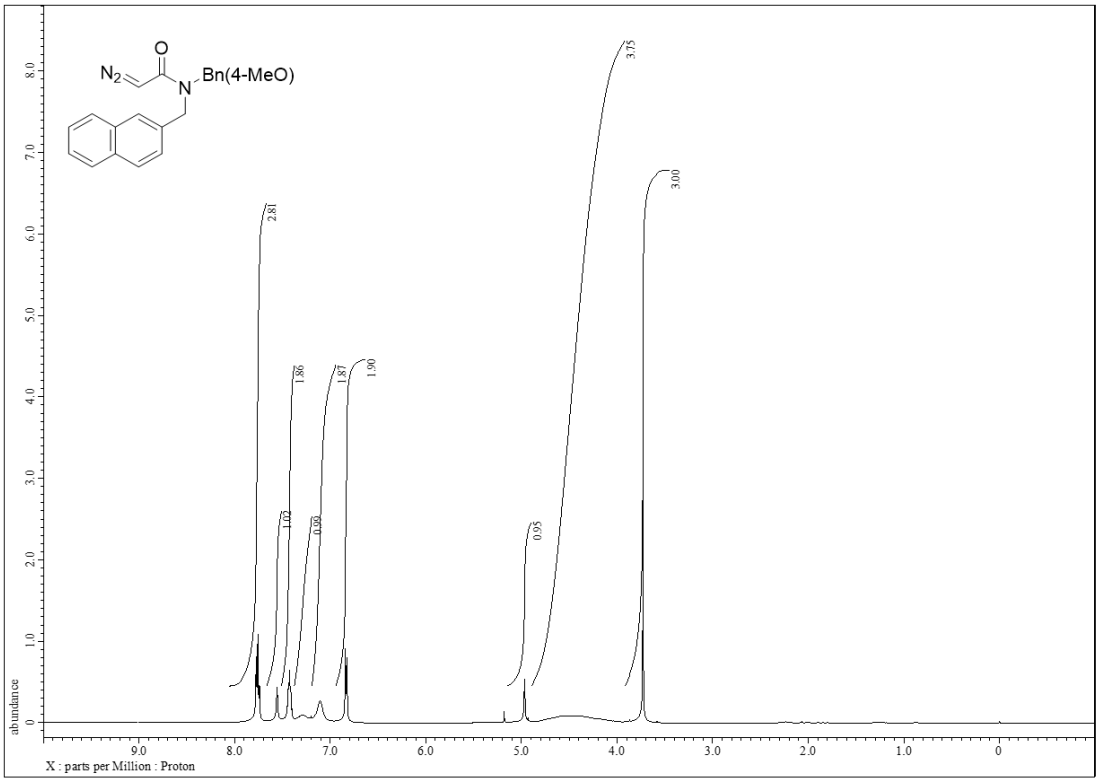

O
O
N
Bn
N2
abundance
189.314
162.034
135.775
133.228
133.181
132.847
128.831
128.793
127.811
127.715
127.696
127.525
126.494
126.409
126.141
125.285
77.248
77.000
76.742
50.436
50.302
27.296
X : parts per Million : Carbon13

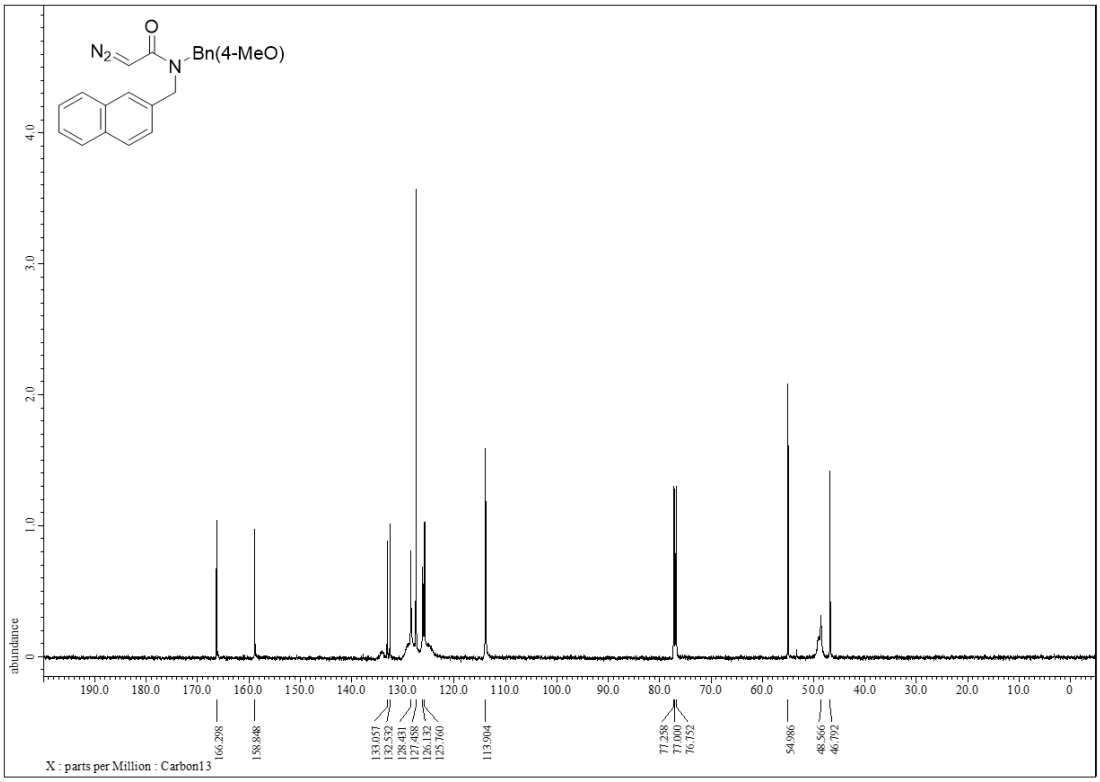

O
N2
N
Bn
5.97
3.73
2.70
1.03
1.00
1.04
abundance
X : parts per Million : Proton

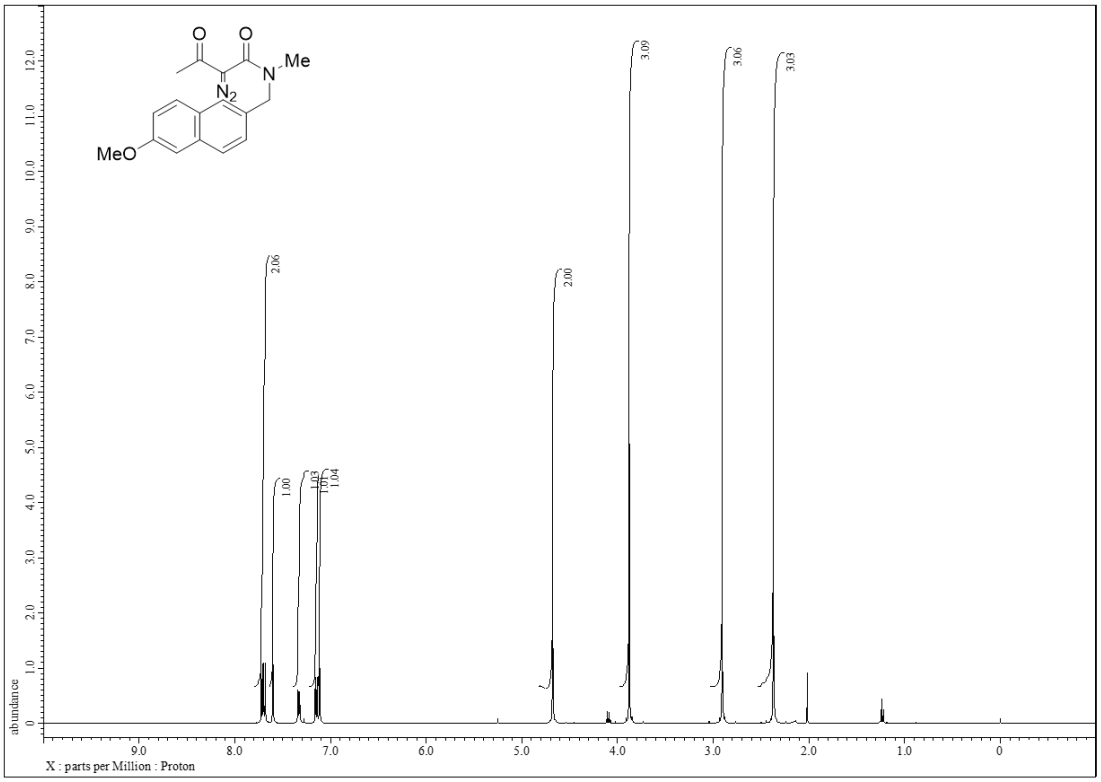

O
N2
N
Bn
abundance
166.536
133.162
132.666
128.670
128.593
127.572
127.486
126.265
125.903
77.248
77.000
76.742
49.282
46.964
X : parts per Million : Carbon13

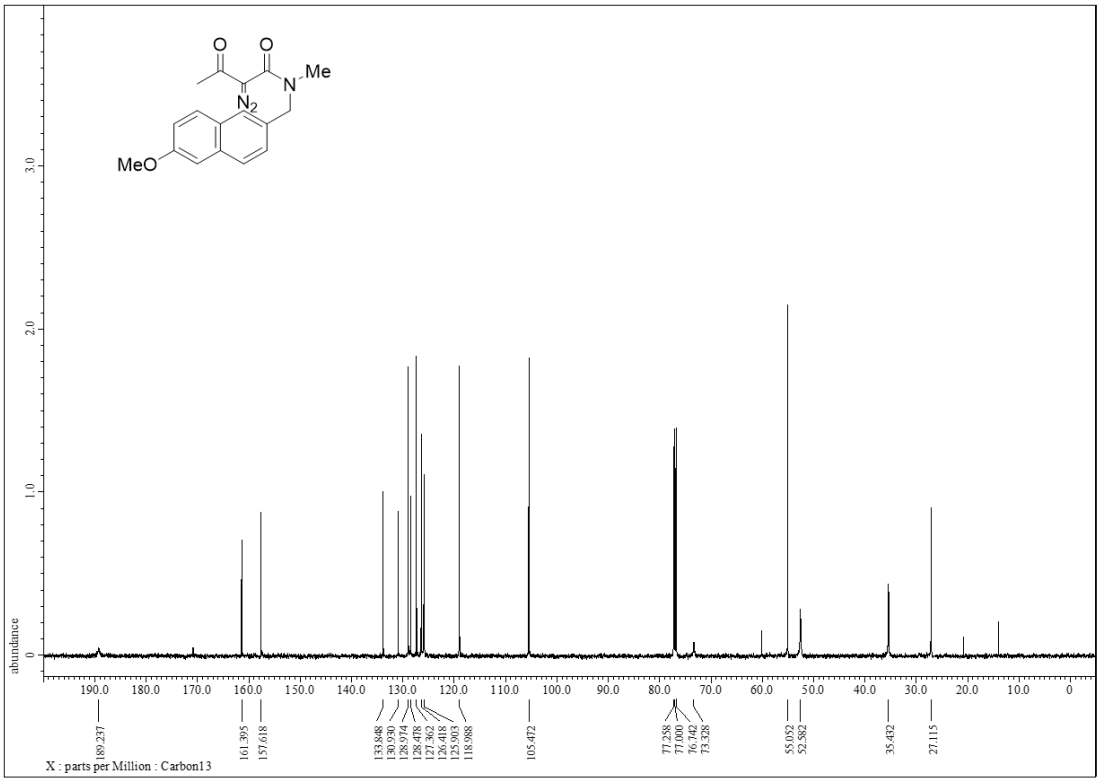

Bn(4-MeO)
N2
abundance
X : parts per Million : Proton
1.75
1.80
1.88
1.91
0.96
0.96
0.89
1.82
1.89
3.00
2.82

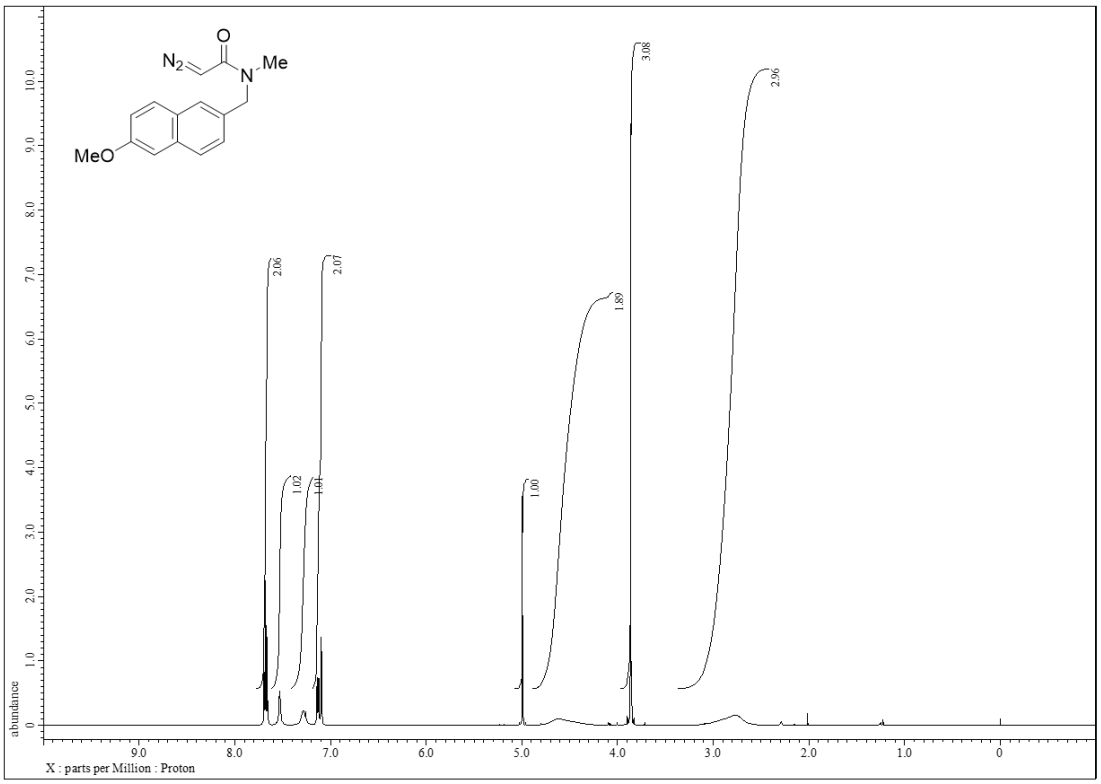

Bn(4-MeO)
N2
abundance
X : parts per Million : Carbon13
161.910
159.211
133.228
132.828
129.213
128.755
127.687
126.447
126.389
126.103
125.273
114.161
77.248
77.000
76.742
55.243
50.207
40.759
27.286

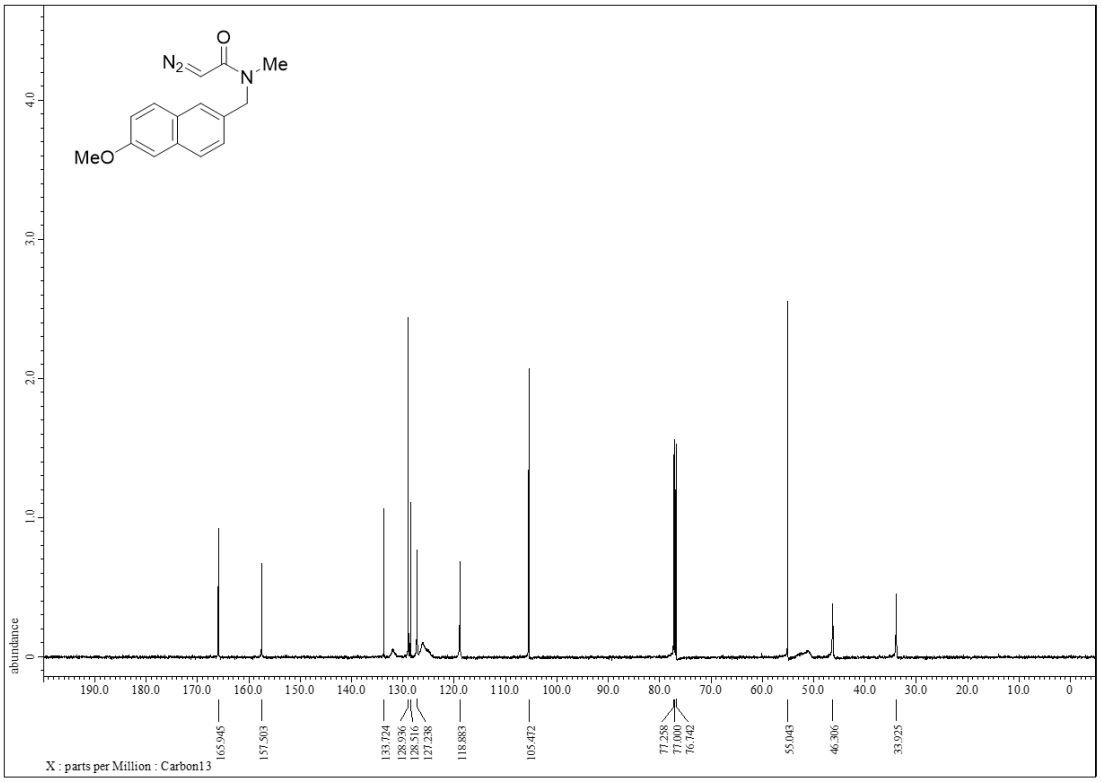

O
N2
N
Bn(4-MeO)
2.81
1.02
1.86
0.98
1.87
1.90
0.95
3.75
3.00
abundance
X : parts per Million : Proton

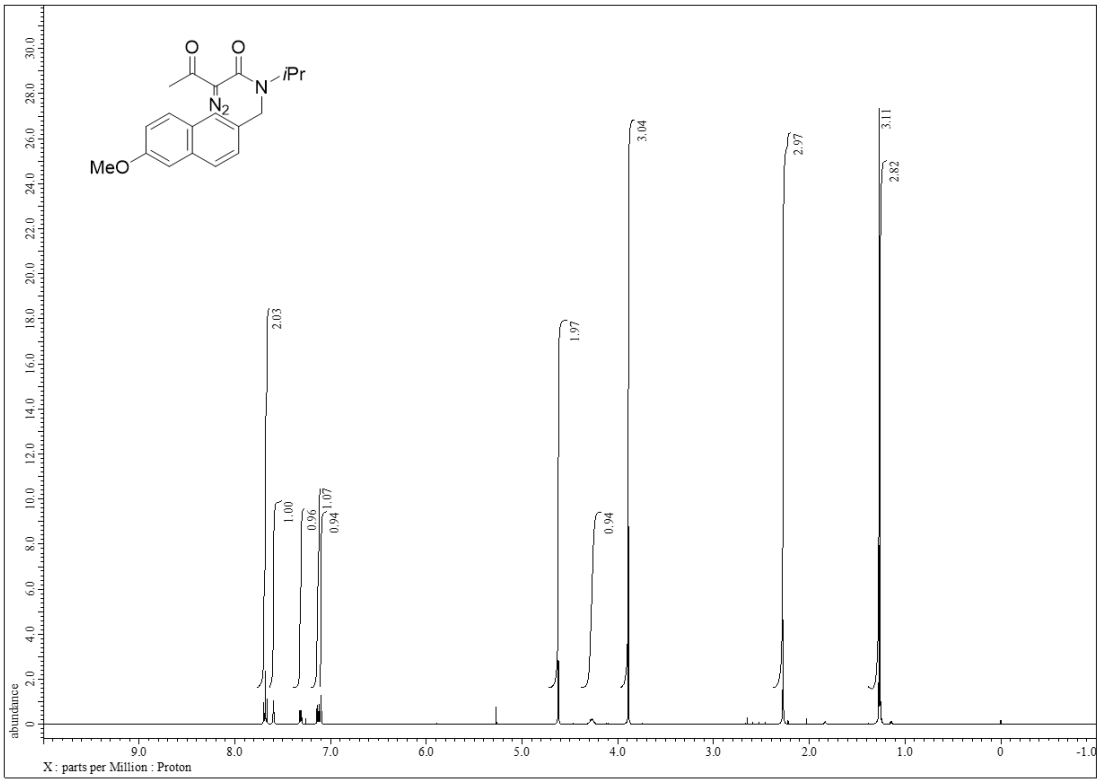

O
N2
N
Bn(4-MeO)
abundance
166.298
158.848
133.057
132.553
128.481
127.458
126.132
125.760
113.904
77.258
77.000
76.752
54.986
48.566
46.792
X : parts per Million : Carbon13

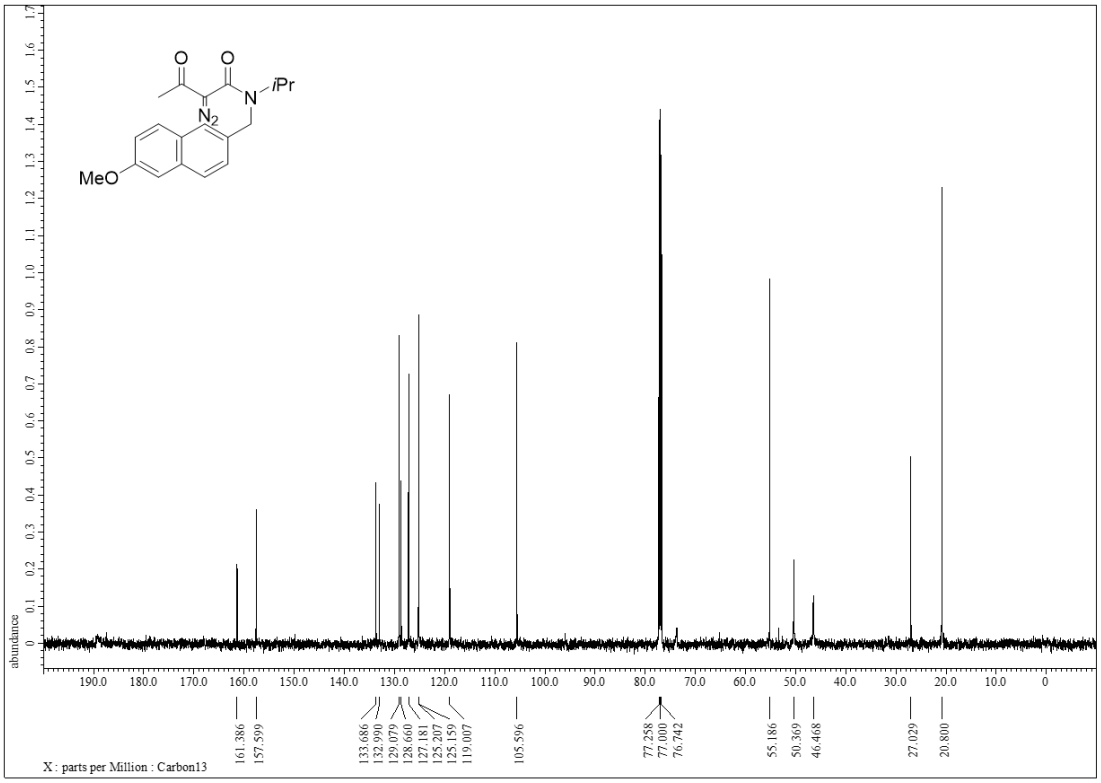

O
O
N
Me
N2
MeO
2.06
1.00
1.03
1.01
1.04
2.00
3.09
3.06
3.03
abundance
X : parts per Million : Proton

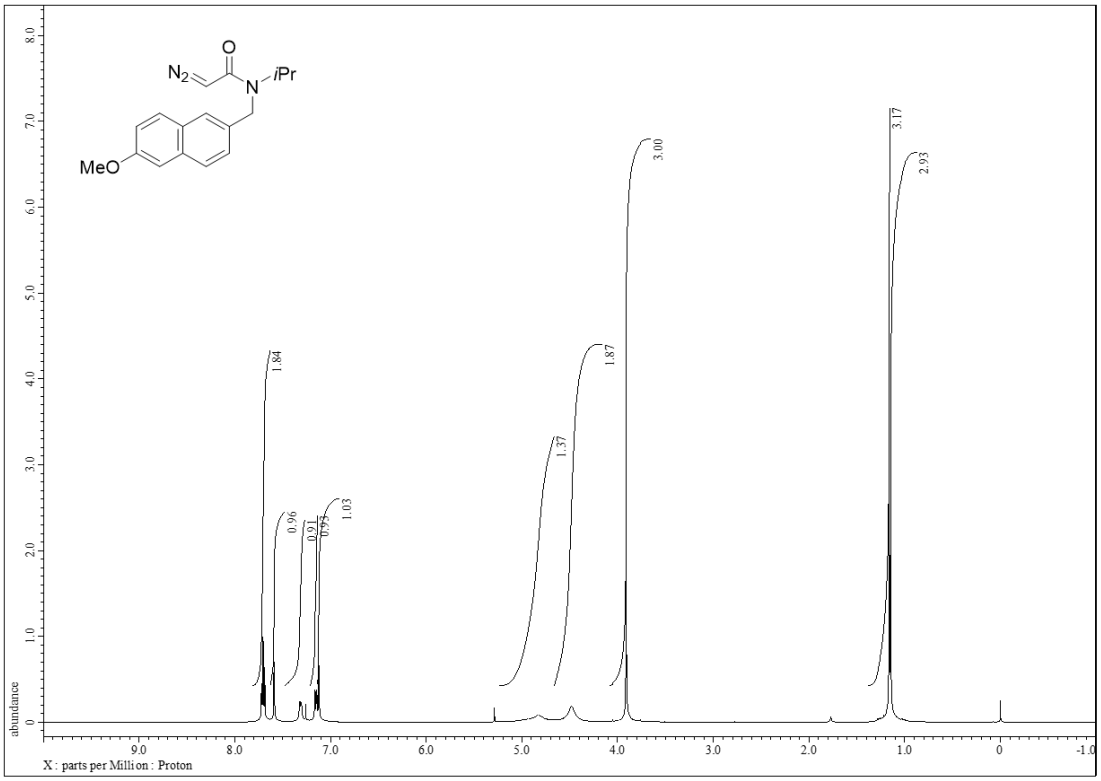

O
O
N
Me
N2
MeO
abundance
189.237
161.395
157.618
133.848
130.930
128.974
128.478
127.365
126.418
125.903
118.988
105.472
77.258
77.000
76.742
73.328
55.052
52.582
35.432
27.115
X : parts per Million : Carbon13

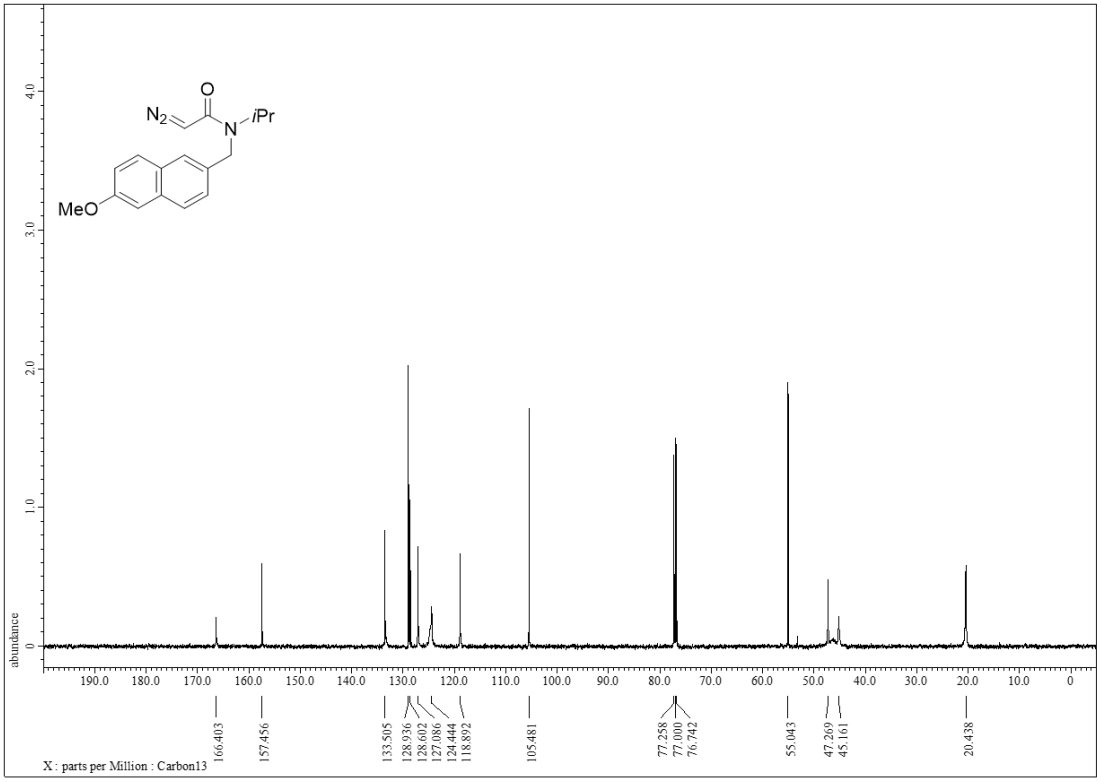

O
N2
N
Me
MeO
2.06
1.02
1.01
2.07
1.00
1.89
3.08
2.96
abundance
X : parts per Million : Proton

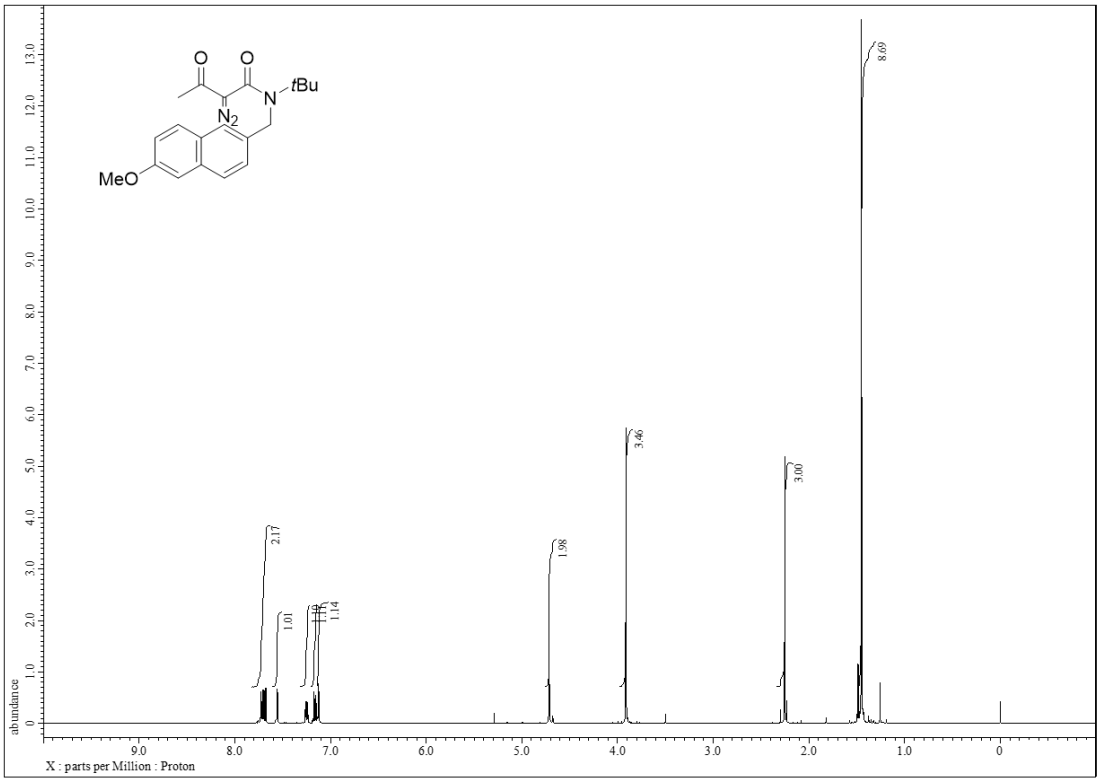

O
N2
N
Me
MeO
abundance
165.945
157.503
133.724
128.936
128.516
127.238
118.883
105.472
77.258
77.000
76.742
55.043
46.306
33.925
X : parts per Million : Carbon13

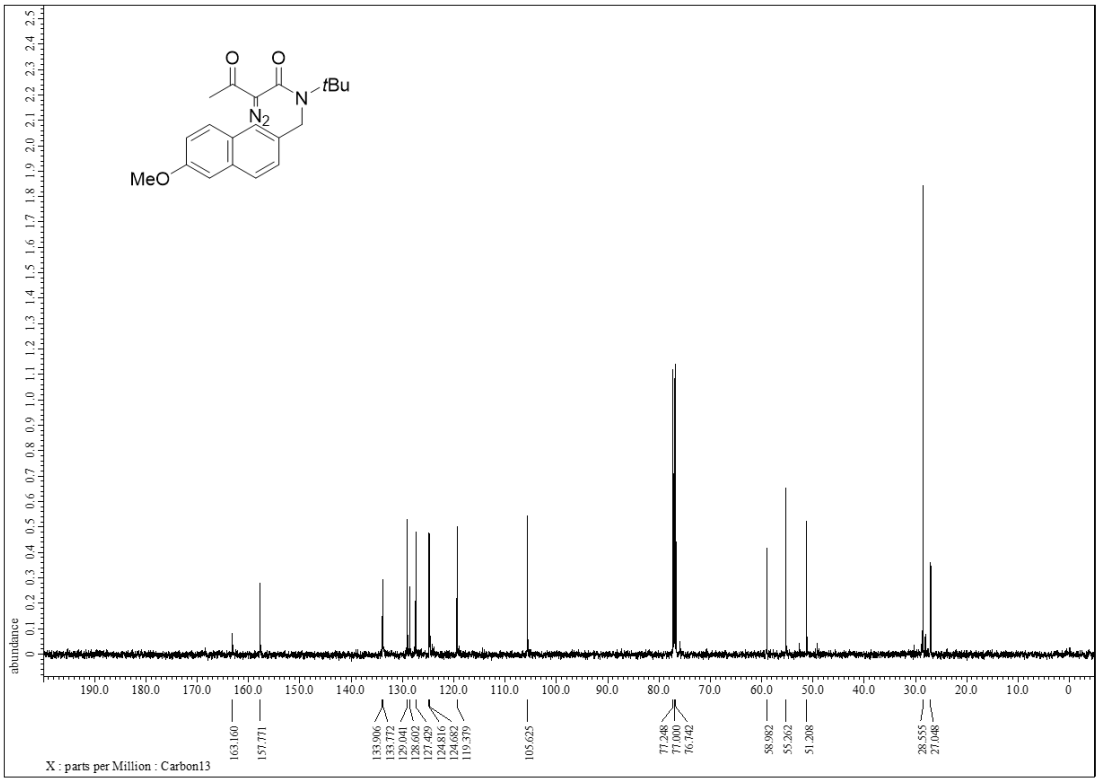

O
O
N
iPr
N2
MeO
2.03
1.00
0.96
1.07
0.94
1.97
0.94
3.04
2.97
3.11
2.82
abundance
X : parts per Million : Proton

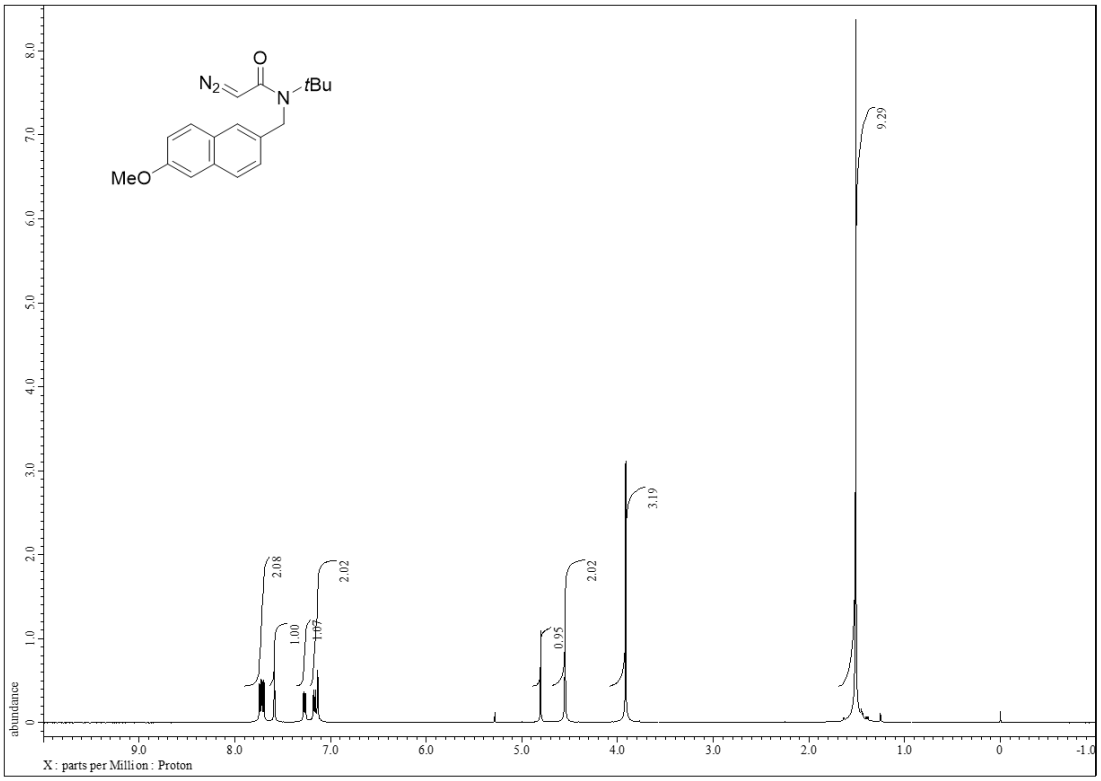

O
O
N
iPr
N2
MeO
abundance
161.386
157.599
133.686
132.990
129.079
128.660
127.181
125.207
125.159
119.007
105.596
77.258
77.000
76.742
55.186
50.369
46.468
27.029
20.800
X : parts per Million : Carbon13

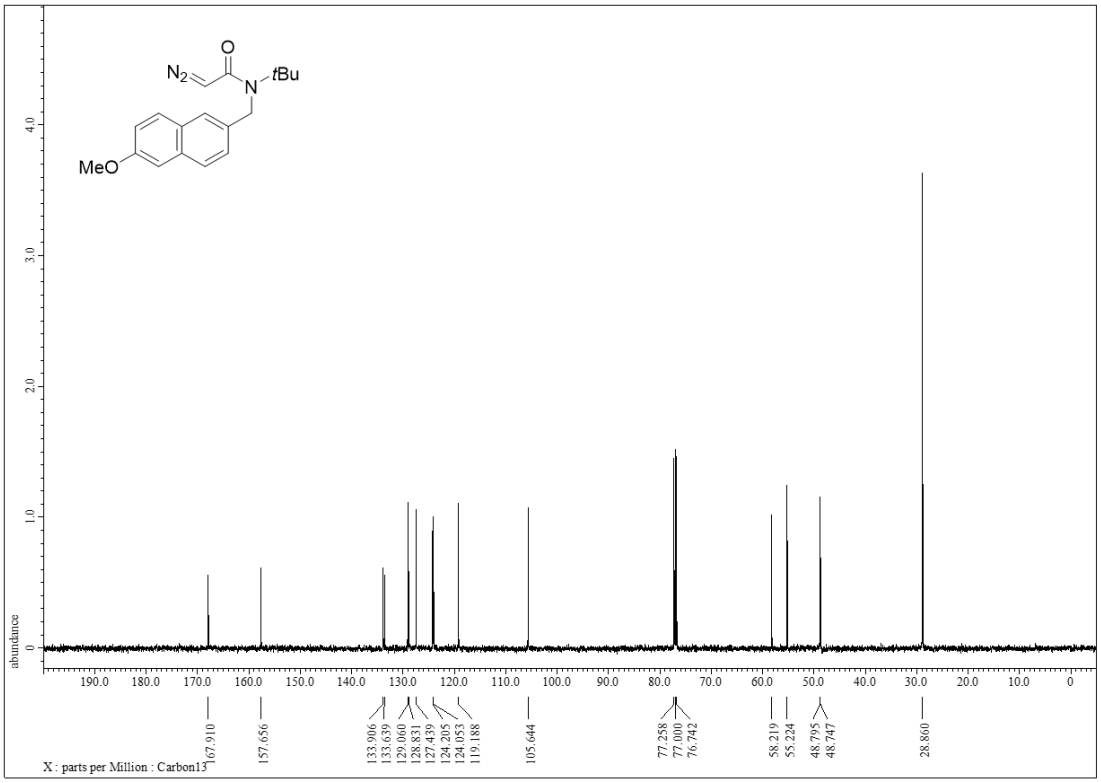

N2
O
N
iPr
MeO
abundance
X : parts per Million : Proton
1.84
0.96
0.91
0.93
1.03
1.37
1.87
3.00
3.17
2.93

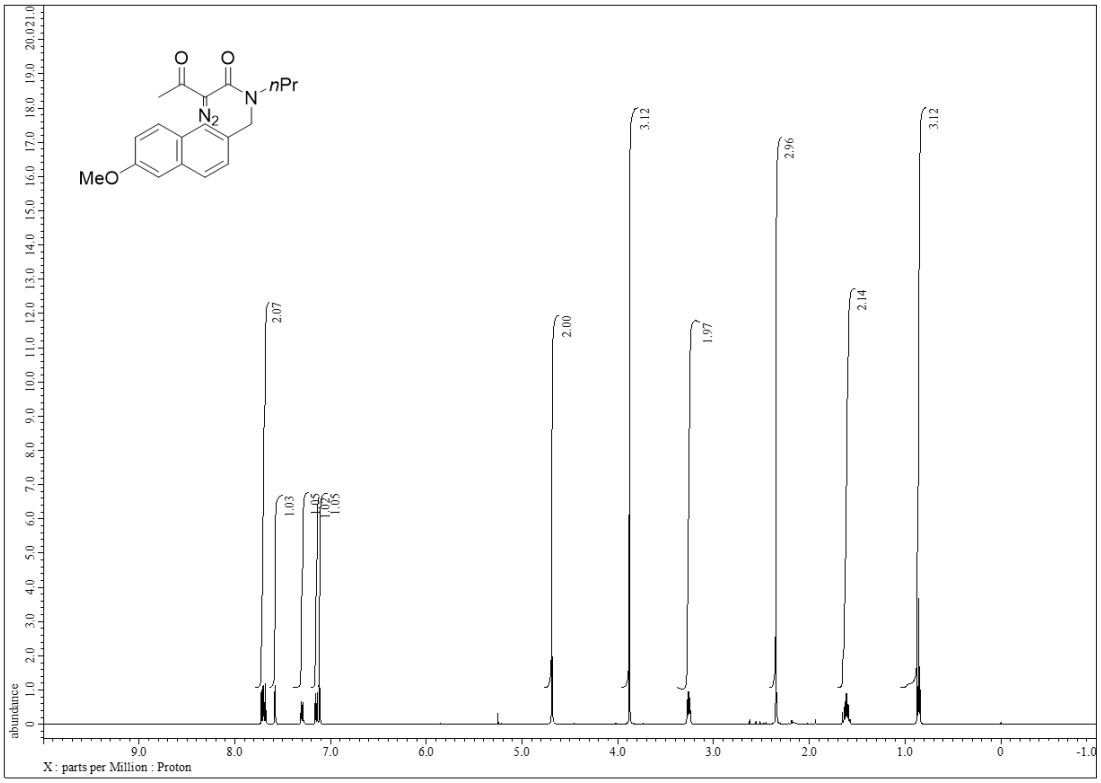

N2
O
N
iPr
MeO
abundance
X : parts per Million : Carbon13
166.403
157.456
133.505
128.936
128.602
127.086
124.444
118.892
105.481
77.258
77.000
76.742
55.043
47.269
45.161
20.438

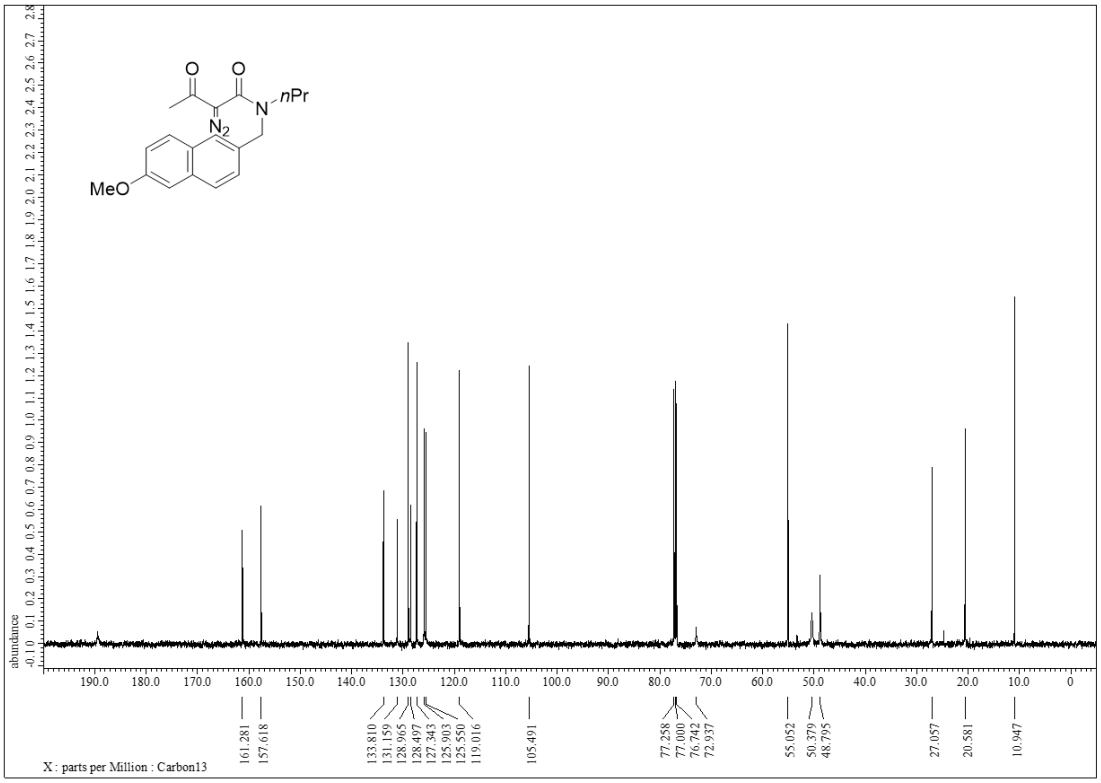

O
O
N
tBu
N2
MeO
abundance
2.17
1.01
1.18
1.14
1.98
3.46
3.00
8.69
X : parts per Million : Proton

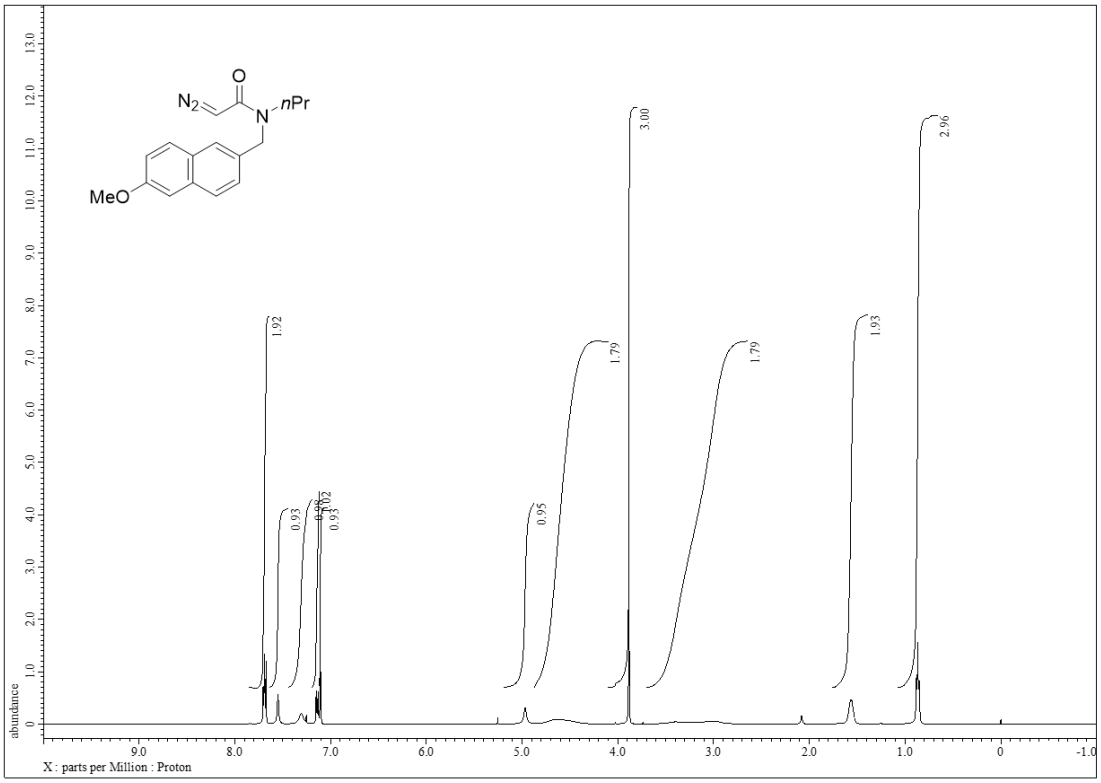

O
O
N
tBu
N2
MeO
abundance
163.160
157.771
133.906
133.772
129.041
128.602
127.429
124.816
124.682
119.379
105.625
77.248
77.000
76.742
58.982
55.262
51.208
28.555
27.048
X : parts per Million : Carbon13

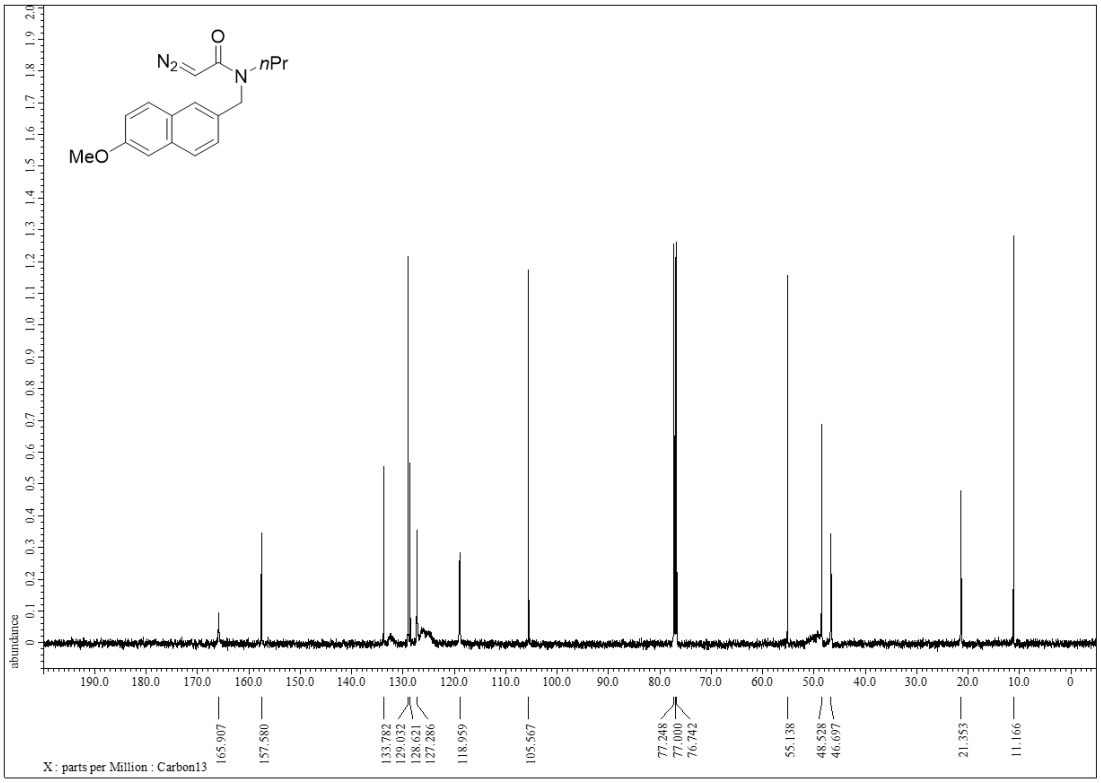

N2
O
N
tBu
MeO
2.08
1.00
1.07
2.02
0.95
2.02
3.19
9.29
abundance
X : parts per Million : Proton

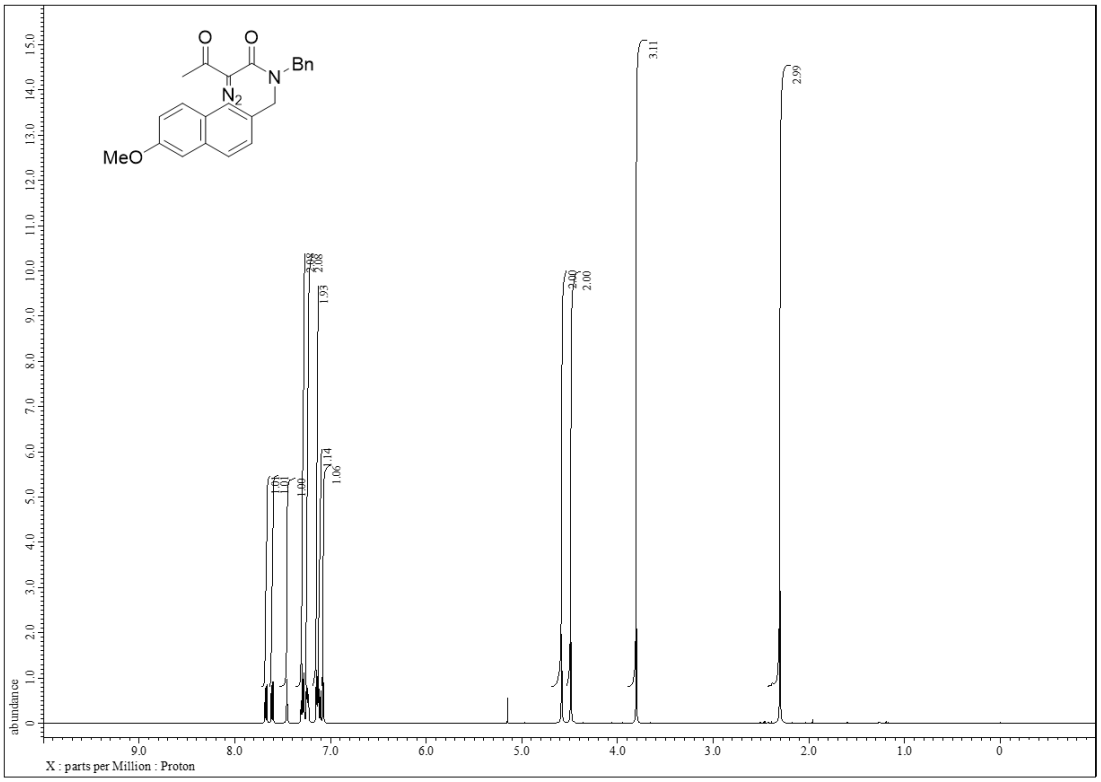

N2
O
N
tBu
MeO
abundance
167.910
157.656
133.906
133.639
129.060
128.831
127.439
124.205
124.053
119.188
105.644
77.258
77.000
76.742
58.219
55.224
48.795
48.747
28.860
X : parts per Million : Carbon13

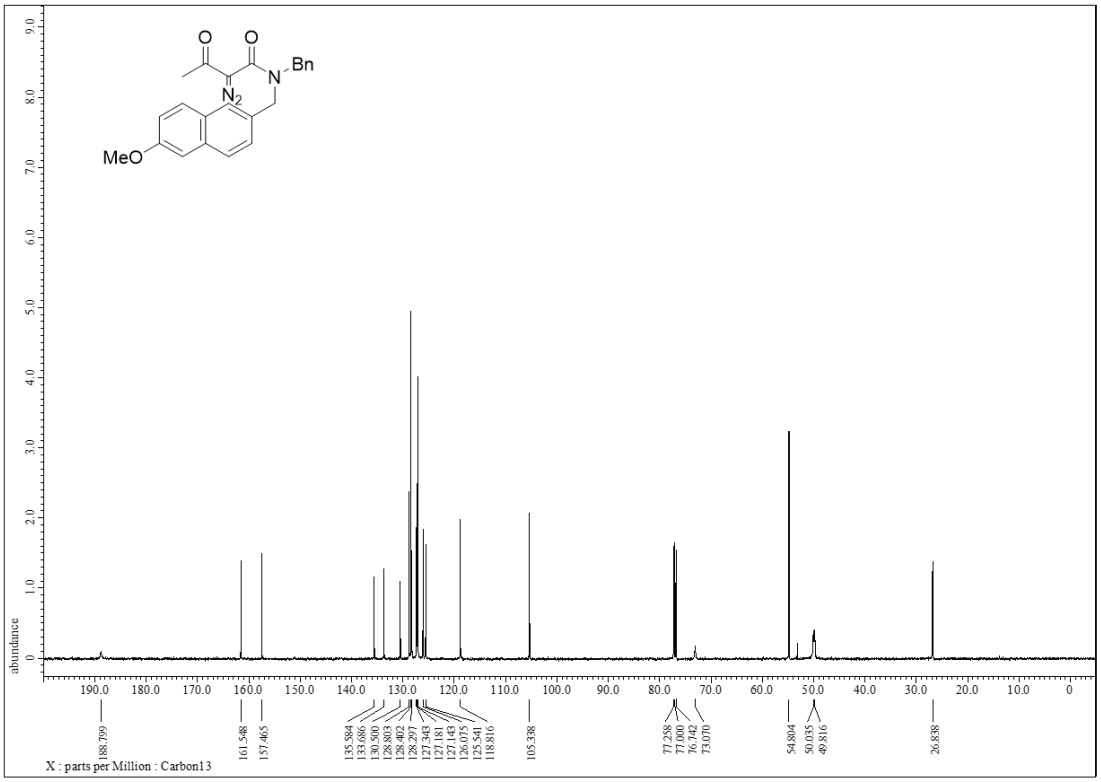

O
O
N
nPr
N2
MeO
2.07
1.03
1.05
1.02
1.05
2.00
3.12
1.97
2.96
2.14
3.12
abundance
X : parts per Million : Proton

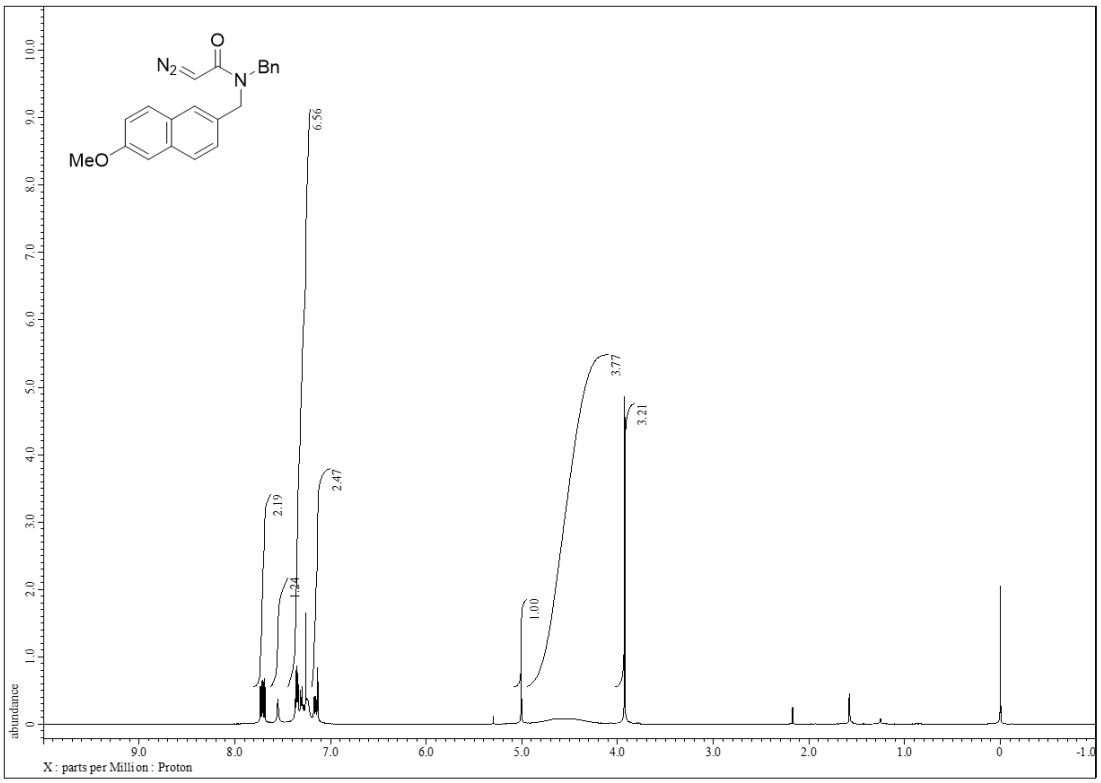

O
O
N
nPr
N2
MeO
abundance
161.281
157.618
133.810
131.159
128.965
128.497
127.343
125.903
125.550
119.016
105.491
77.258
77.000
76.742
72.937
55.052
50.379
48.795
27.057
20.581
10.947
X : parts per Million : Carbon13

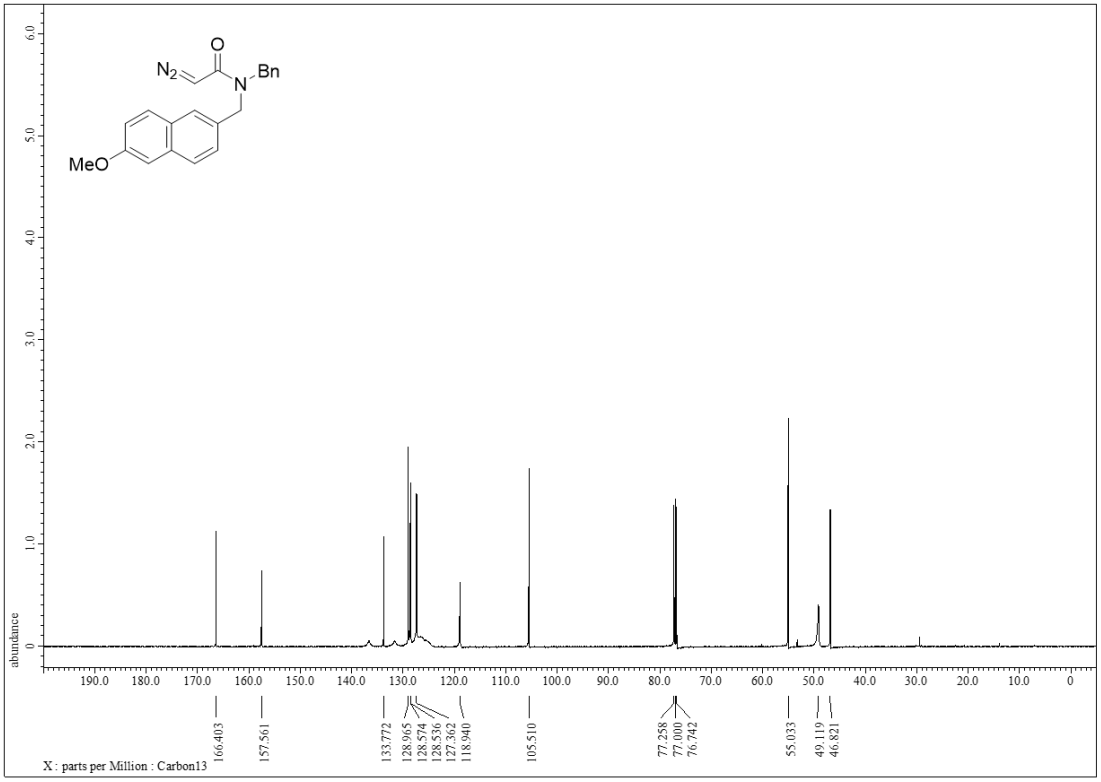

O
N2
N
nPr
MeO
1.92
0.93
0.96
1.02
0.95
0.95
1.79
3.00
1.79
1.93
2.96
abundance
X : parts per Million : Proton

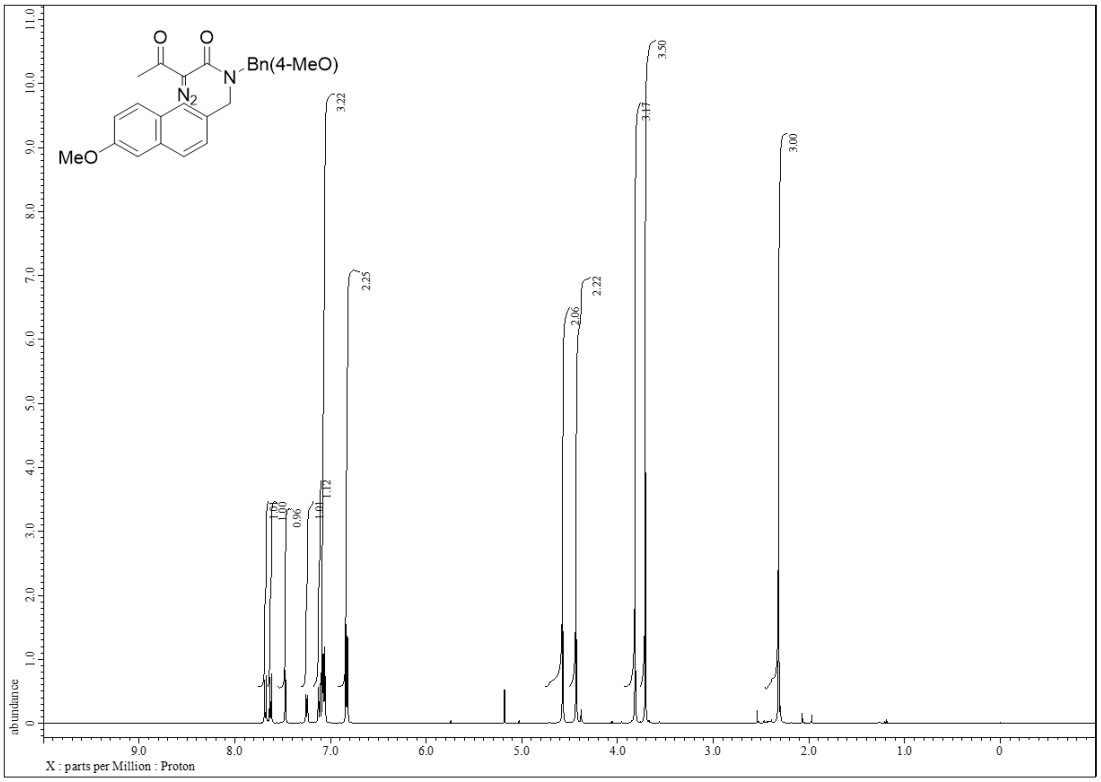

O
N2
N
nPr
MeO
abundance
165.907
157.580
133.782
129.032
128.621
127.286
118.959
105.567
77.248
77.000
76.742
55.138
48.528
46.697
21.353
11.166
X : parts per Million : Carbon13

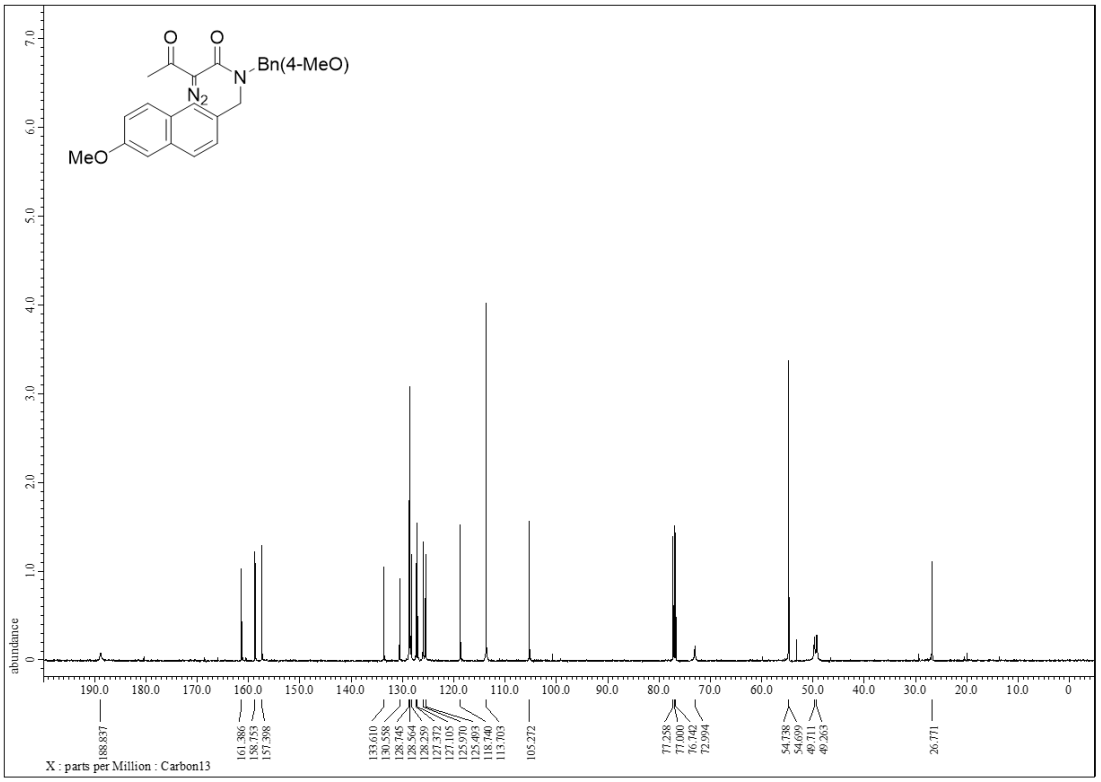

O
O
N
Bn
N2
MeO
3.11
2.99
2.40
2.00
1.93
2.08
1.06
1.00
abundance
X : parts per Million : Proton

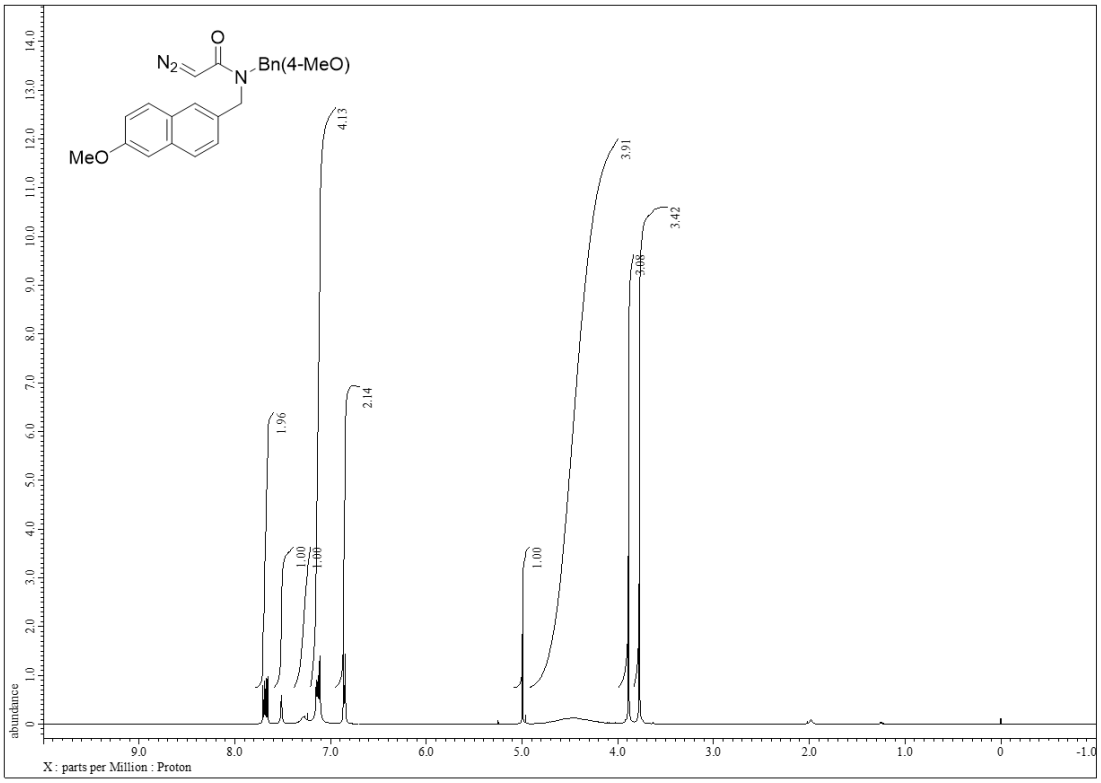

O
O
N
Bn
N2
MeO
abundance
188.799
161.548
157.465
135.584
133.686
130.503
128.803
128.402
128.297
127.345
127.181
127.143
126.075
125.541
118.816
105.338
77.258
77.000
76.742
73.070
54.804
50.035
49.816
26.838
X : parts per Million : Carbon13

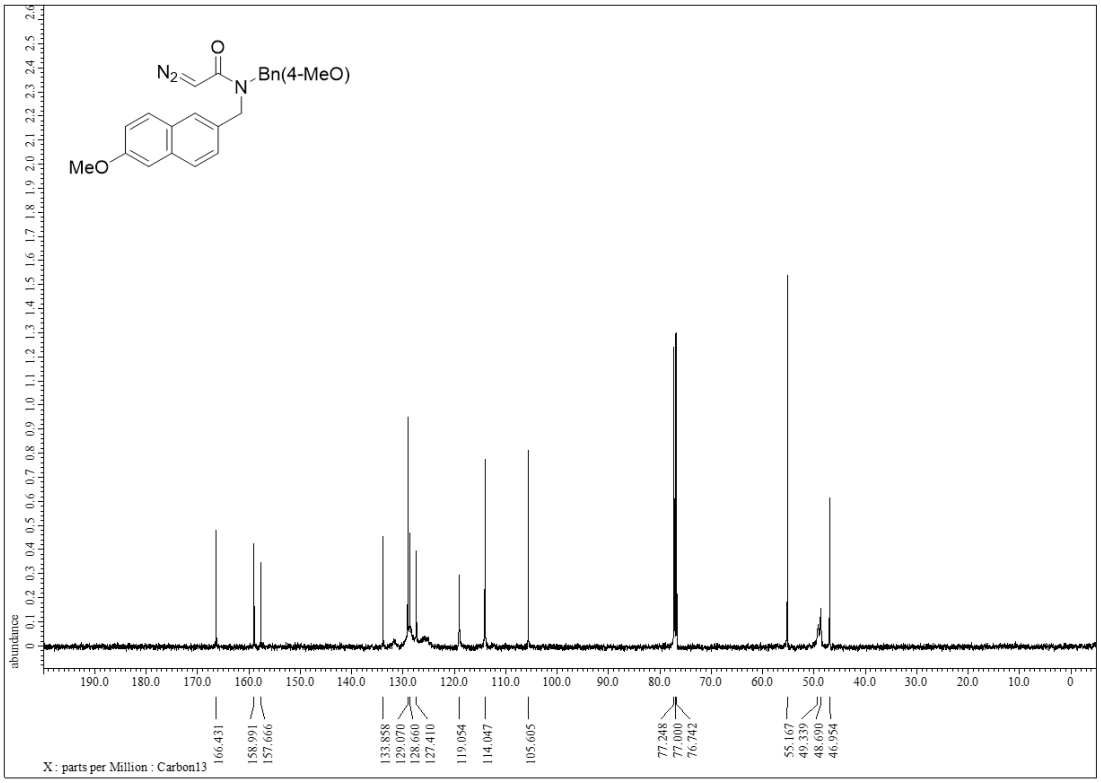

N2
O
N
Bn
MeO
6.56
3.77
3.21
2.47
2.19
1.34
1.00
abundance
X : parts per Million : Proton

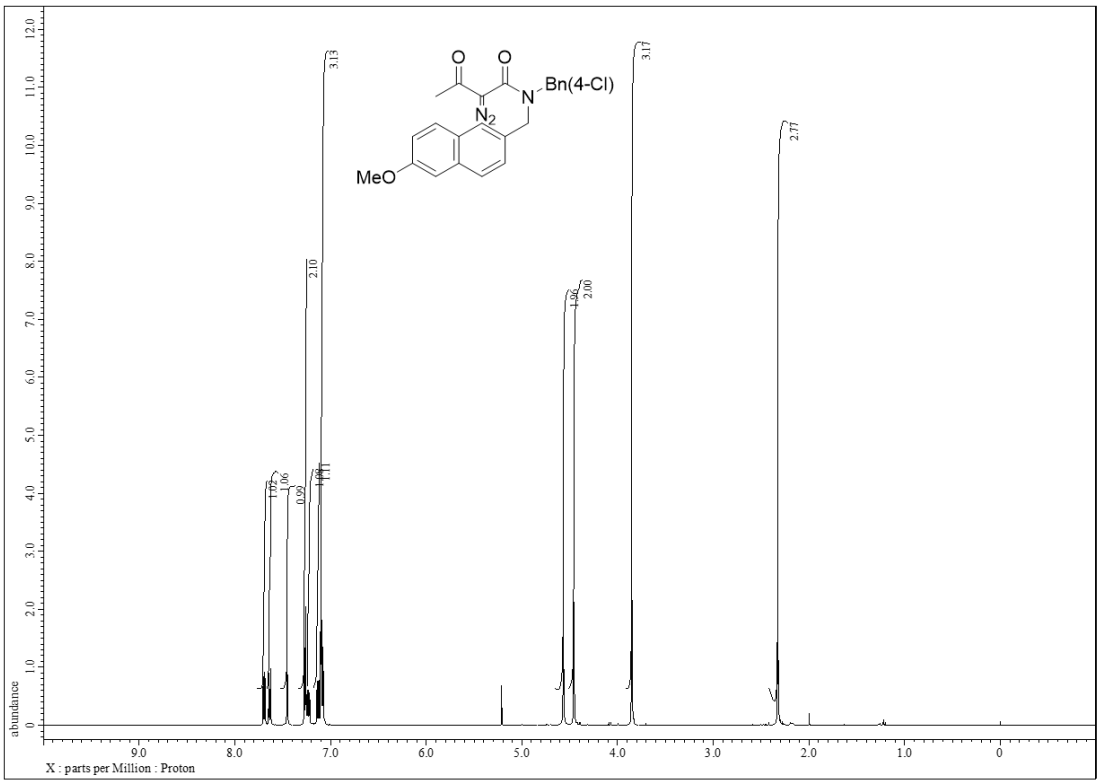

N2
O
N
Bn
MeO
abundance
166.403
157.561
133.772
128.965
128.574
128.536
127.362
118.940
105.510
77.258
77.000
76.742
55.033
49.119
46.821
X : parts per Million : Carbon13

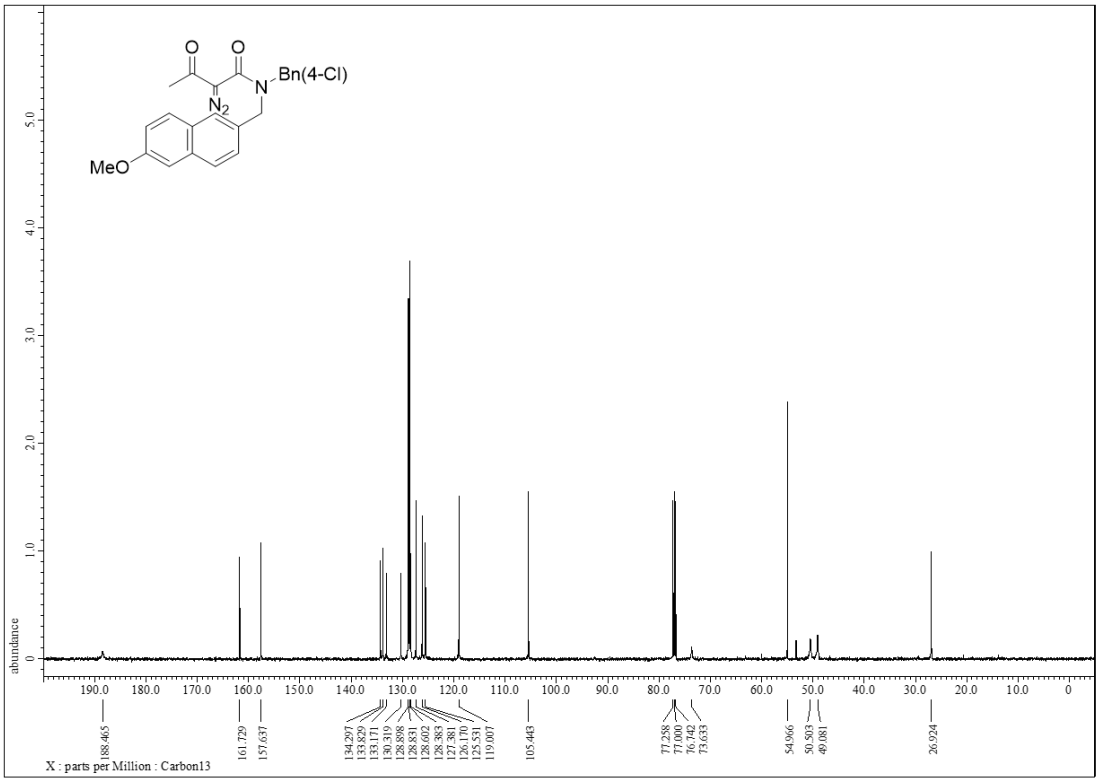

Bn(4-MeO)
MeO
N2
3.22
2.25
2.22
2.06
3.50
3.17
3.00
1.72
1.07
0.96
1.00
1.09
abundance
X : parts per Million : Proton

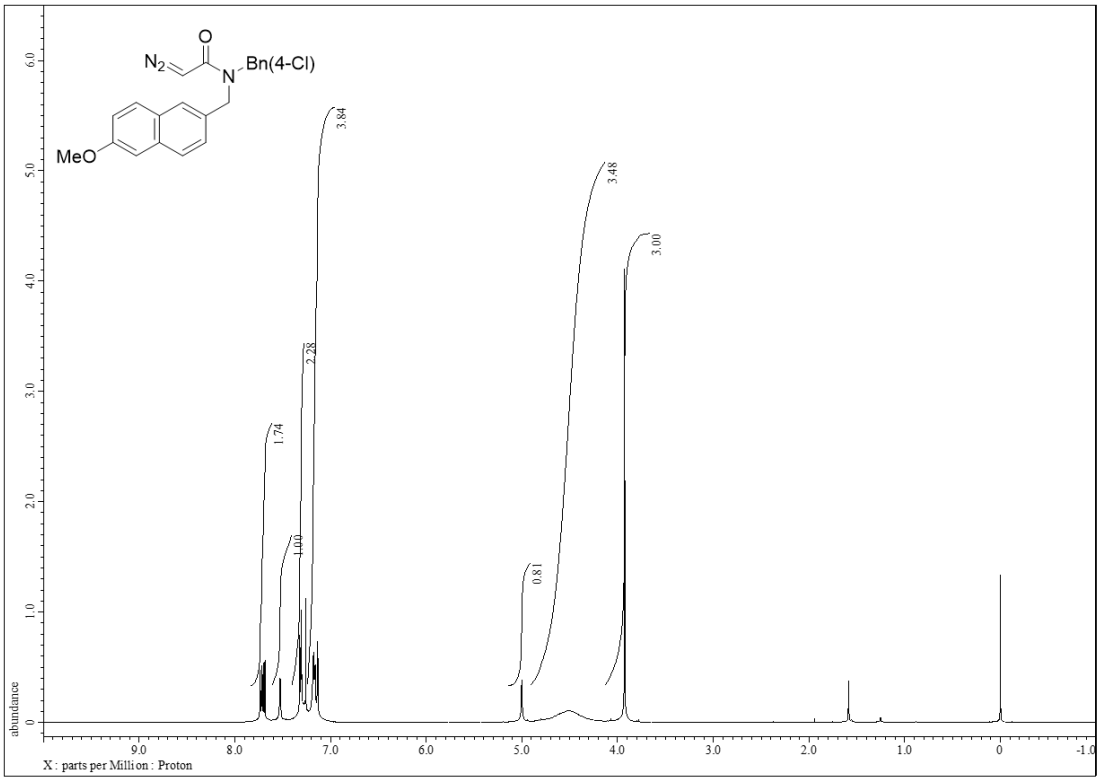

Bn(4-MeO)
MeO
N2
abundance
188.837
161.386
158.753
157.398
133.610
130.558
128.745
128.564
128.259
127.372
127.105
125.970
125.493
118.746
113.703
105.272
77.258
77.000
76.742
72.994
54.738
54.699
49.711
49.263
26.771
X : parts per Million : Carbon13

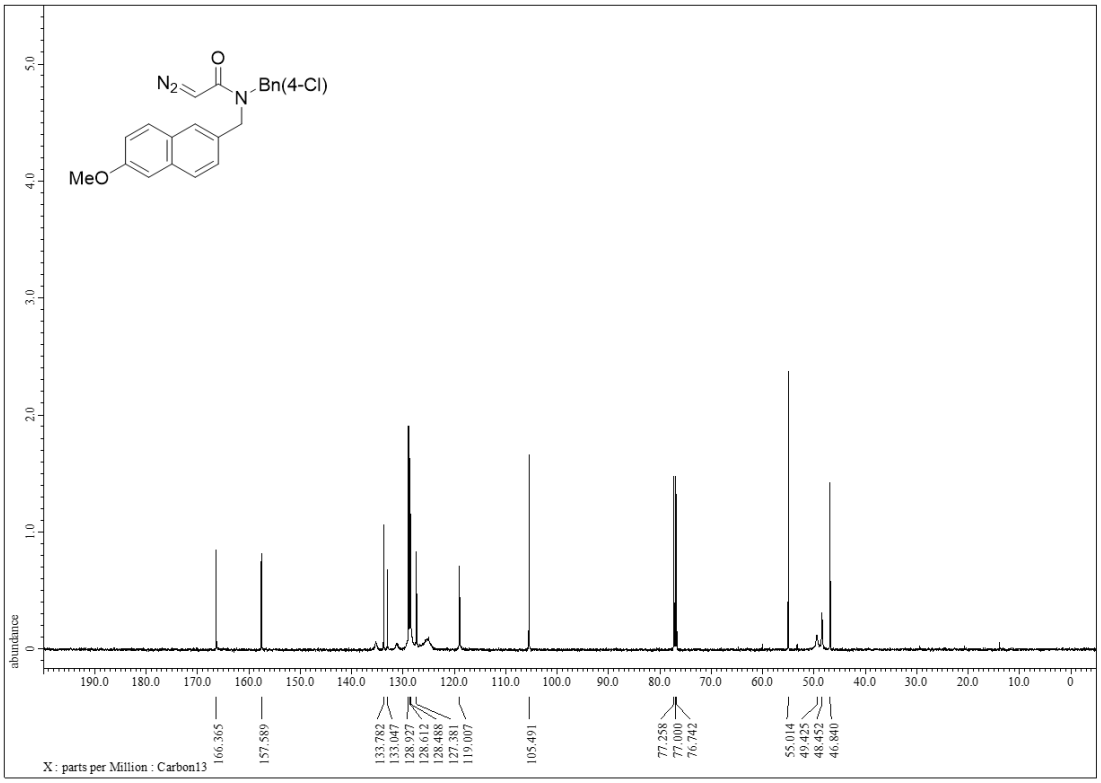

O
N2
N
Bn(4-MeO)
MeO
4.13
3.91
3.42
3.08
2.14
1.96
1.00
1.00
1.00
abundance
X : parts per Million : Proton

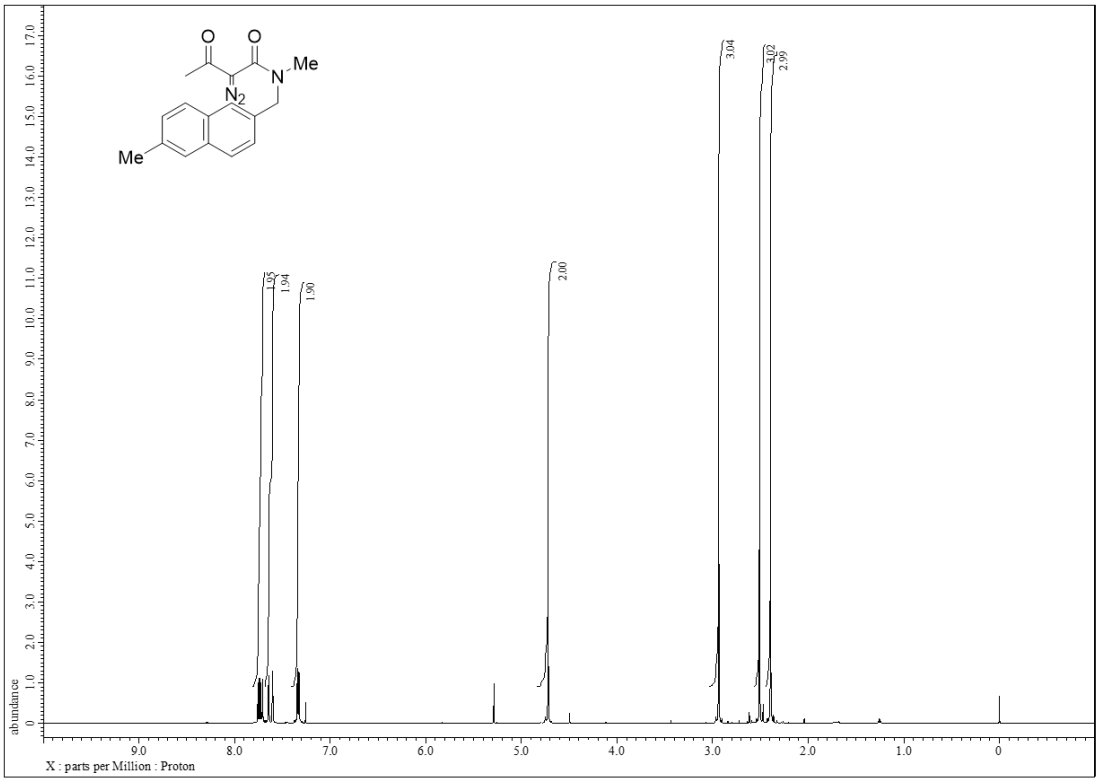

O
N2
N
Bn(4-MeO)
MeO
abundance
166.431
158.991
157.666
133.858
129.070
128.660
127.410
119.054
114.047
105.605
77.248
77.000
76.742
55.167
49.339
48.690
46.954
X : parts per Million : Carbon13

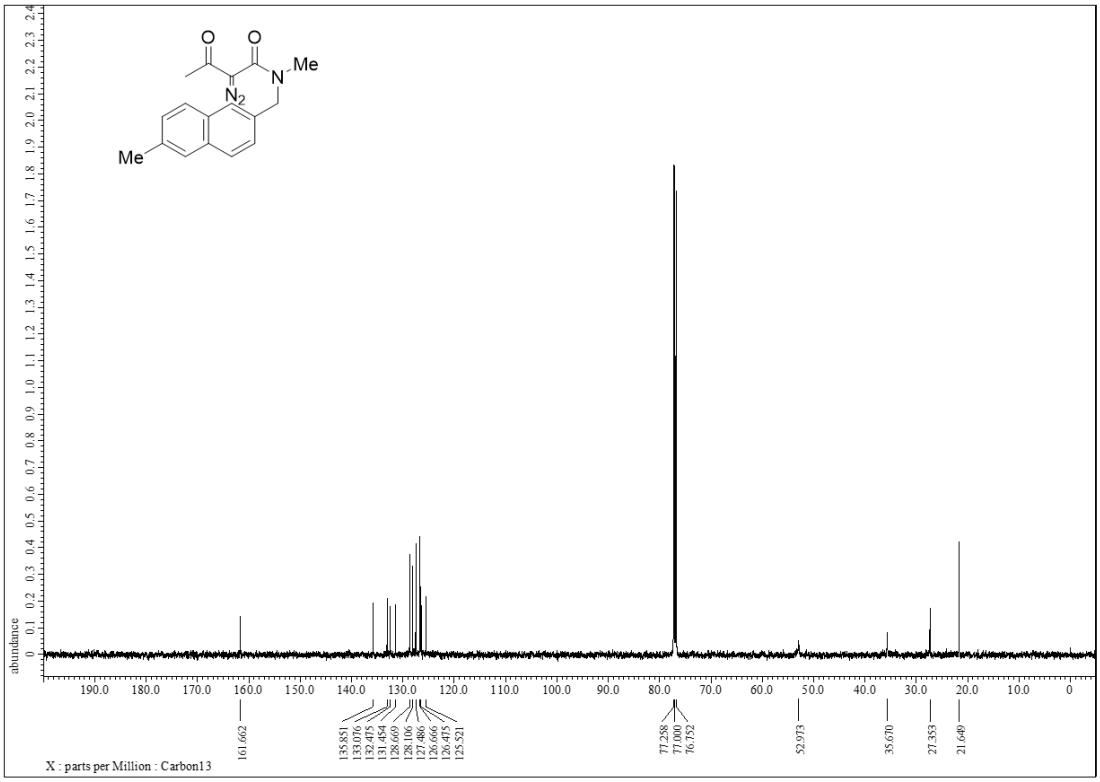

O
O
N
Bn(4-Cl)
N2
MeO
3.13
3.17
2.77
2.10
2.00
1.06
0.92
abundance
X : parts per Million : Proton

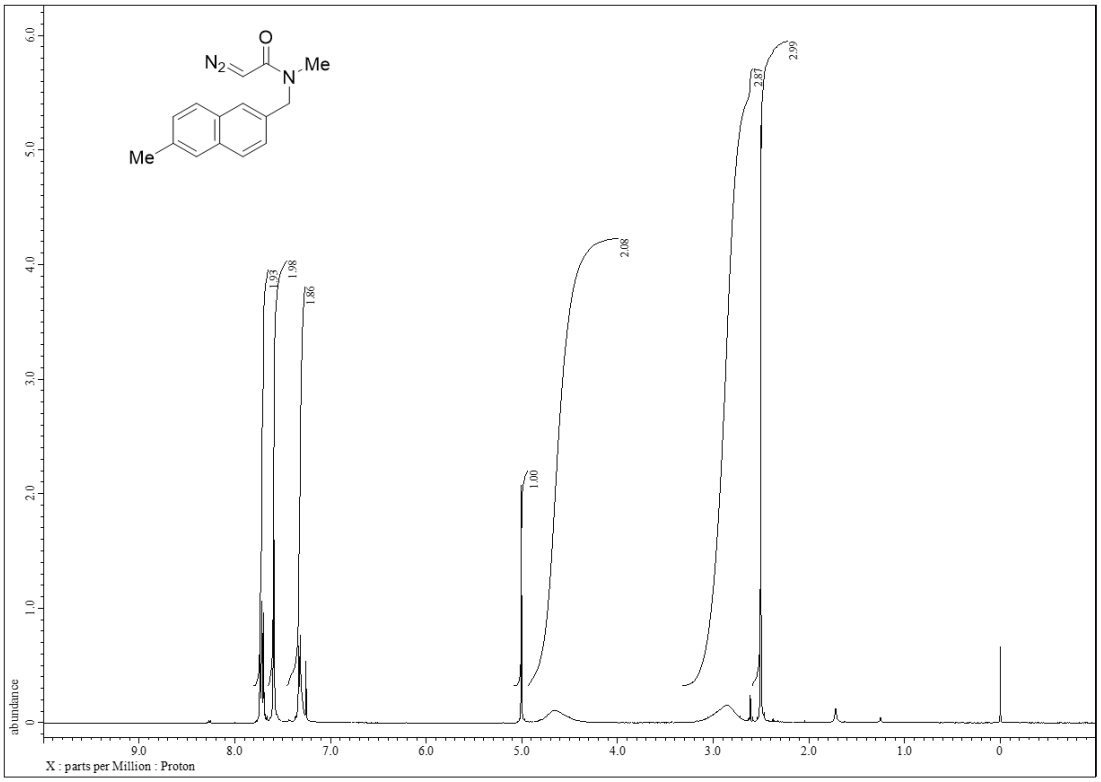

O
O
N
Bn(4-Cl)
N2
MeO
abundance
188.465
161.729
157.637
134.297
133.929
133.171
130.310
128.898
128.831
128.602
128.383
127.381
126.170
125.531
119.007
105.443
77.258
77.000
76.742
73.633
54.966
50.503
49.081
26.924
X : parts per Million : Carbon13

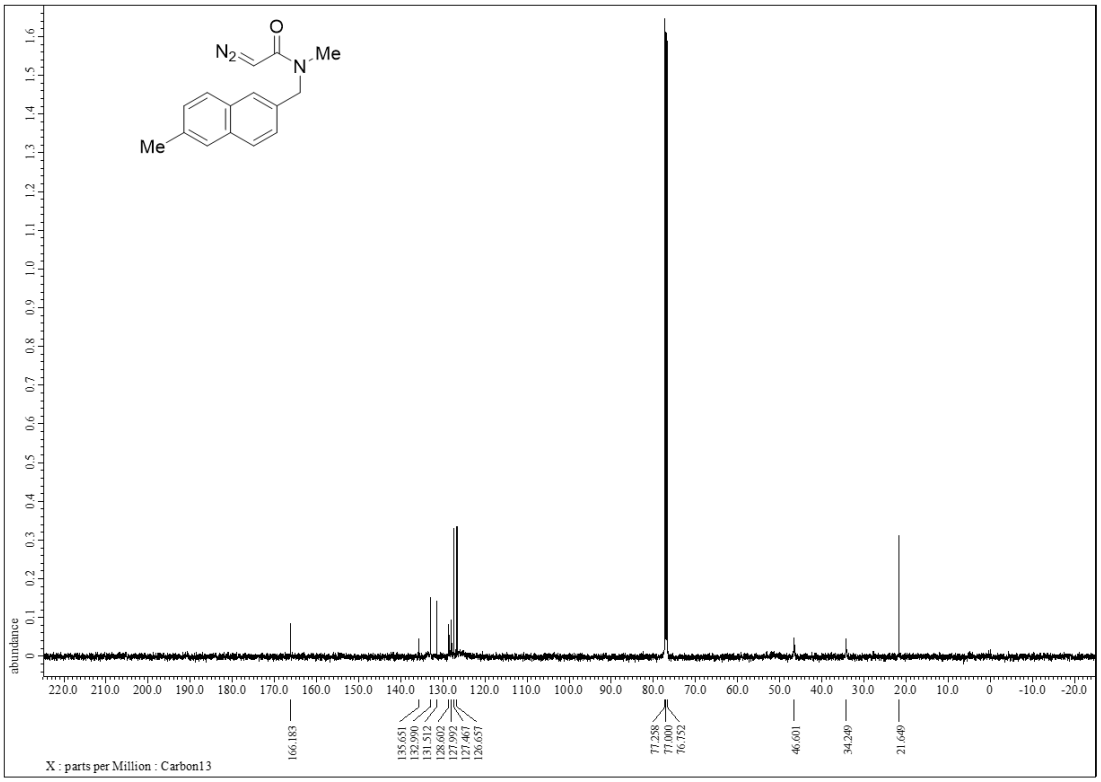

N2
O
N
Bn(4-Cl)
MeO
3.84
3.48
3.00
2.28
1.74
1.00
0.81
abundance
X : parts per Million : Proton

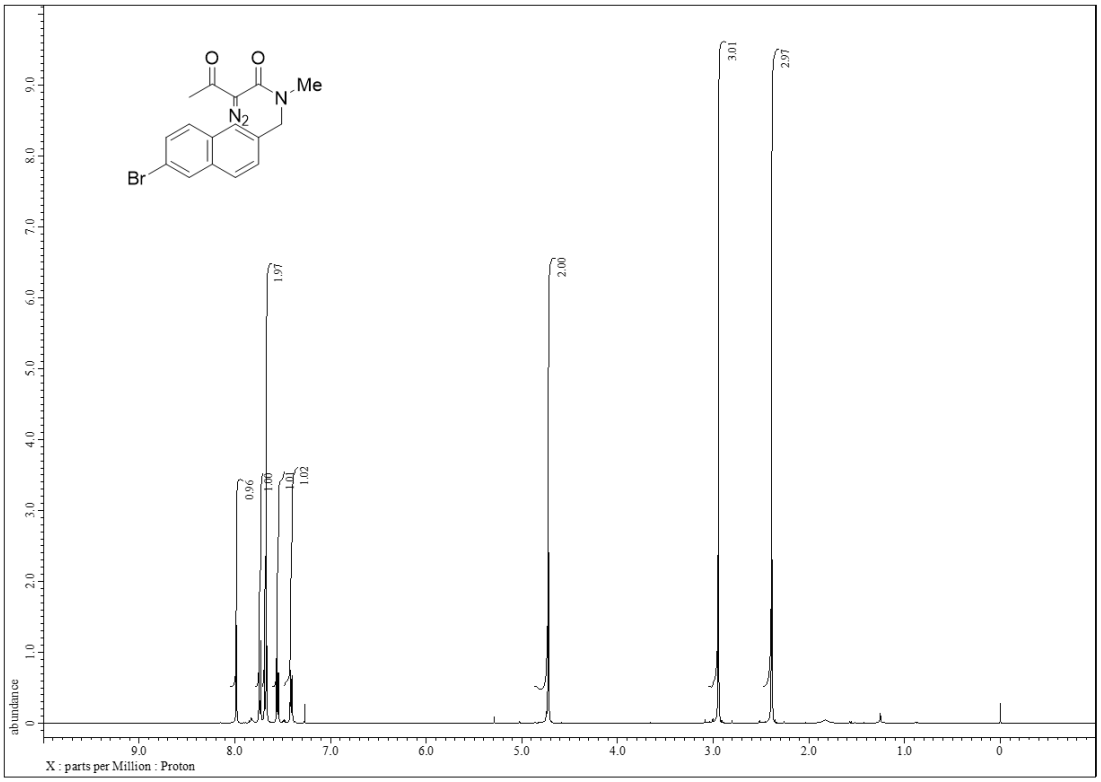

N2
O
N
Bn(4-Cl)
MeO
abundance
166.365
157.589
133.782
133.047
128.927
128.612
128.488
127.381
119.007
105.491
77.258
77.000
76.742
55.014
49.425
48.452
46.840
X : parts per Million : Carbon13

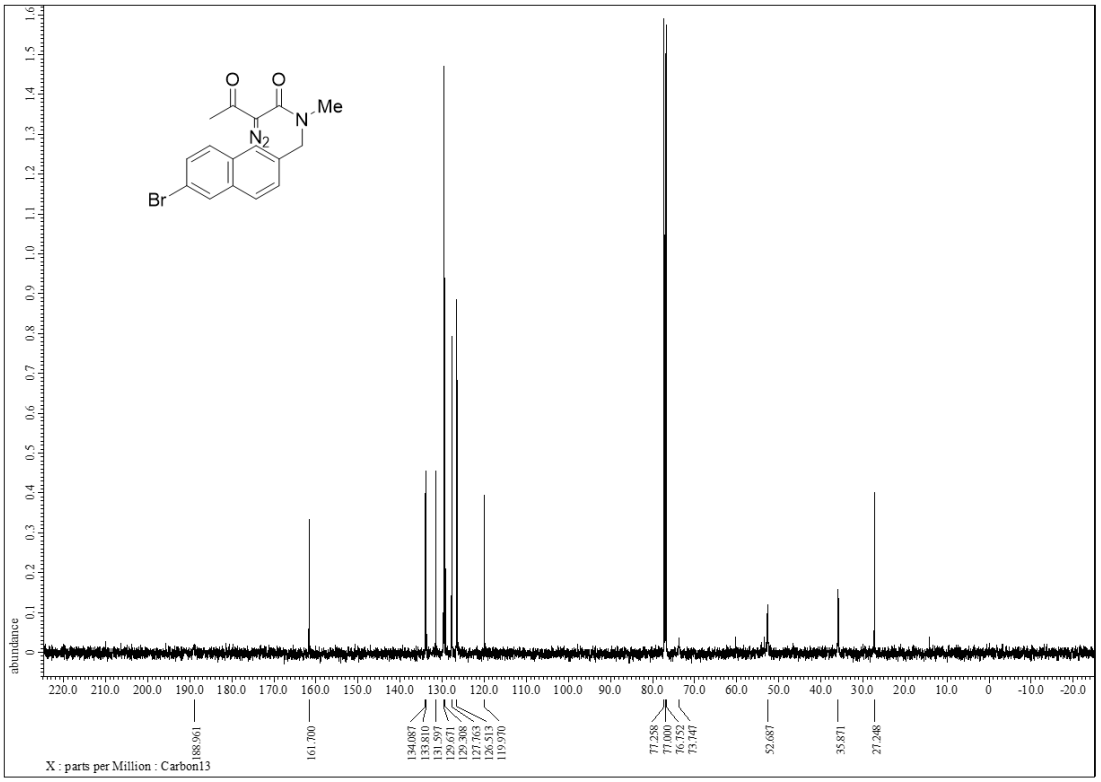

O
O
N
Me
N2
Me
3.04
3.02
2.99
2.00
1.95
1.94
1.90
abundance
X : parts per Million : Proton

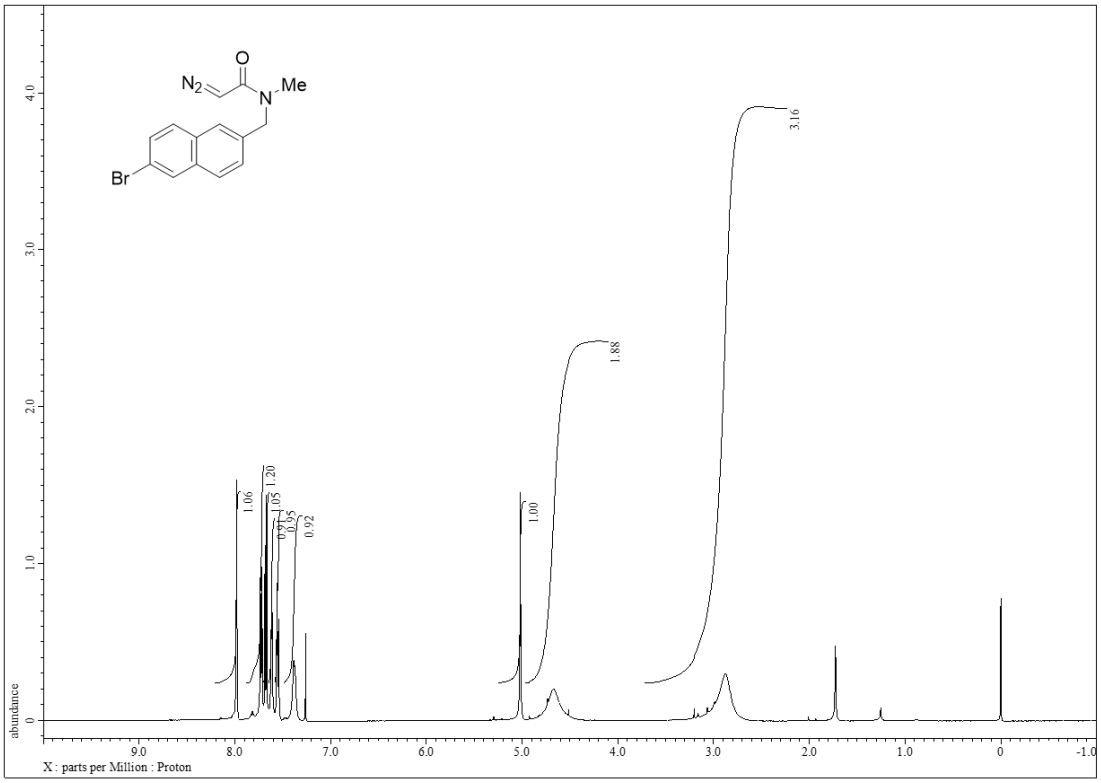

O
O
N
Me
N2
Me
abundance
161.662
135.851
133.076
132.475
131.454
128.669
128.106
127.486
126.666
126.475
125.521
77.258
77.000
76.752
52.973
35.670
27.353
21.649
X : parts per Million : Carbon13

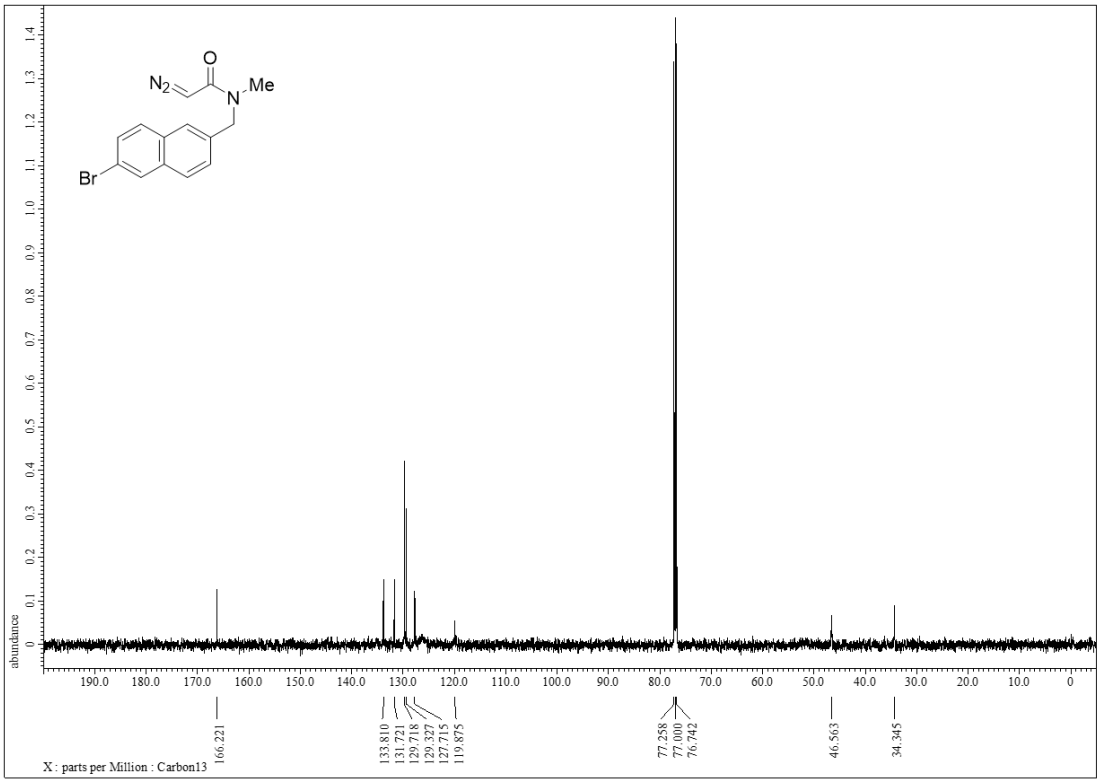

O
N2
N
Me
Me
1.93
1.98
1.86
2.08
1.00
2.87
2.99
abundance
X : parts per Million : Proton

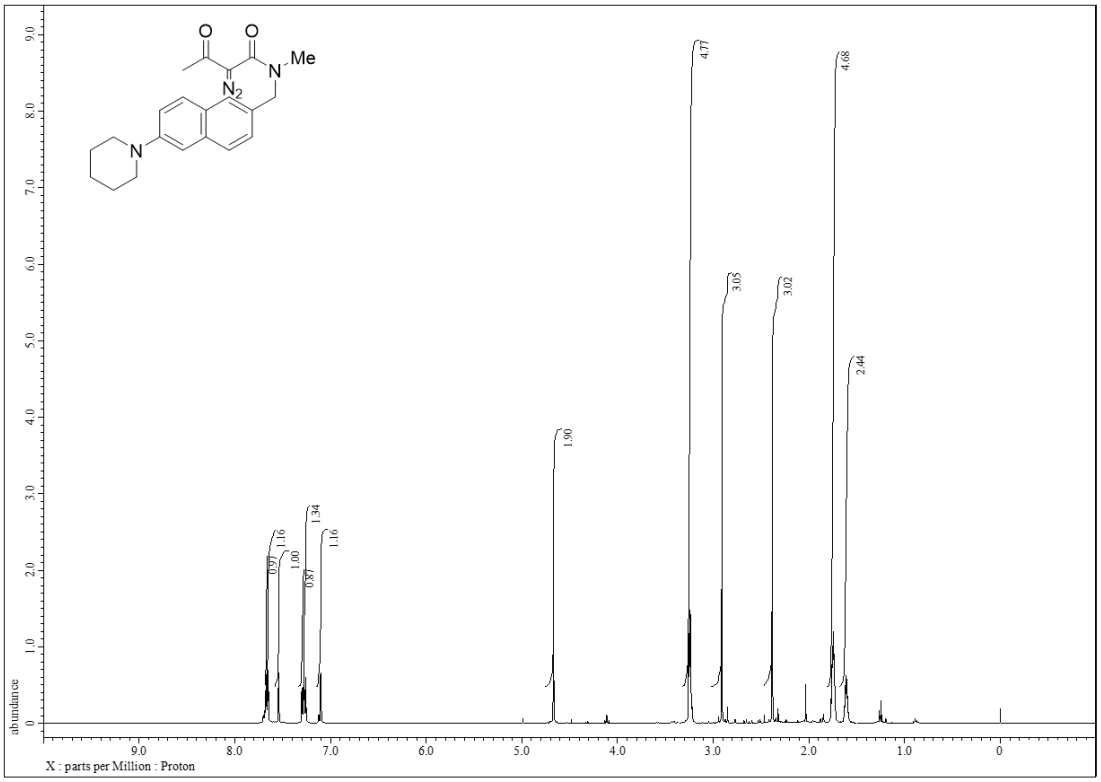

O
N2
N
Me
Me
abundance
166.183
135.651
132.990
131.512
128.602
127.992
127.467
126.657
77.258
77.000
76.752
46.601
34.249
21.649
X : parts per Million : Carbon13

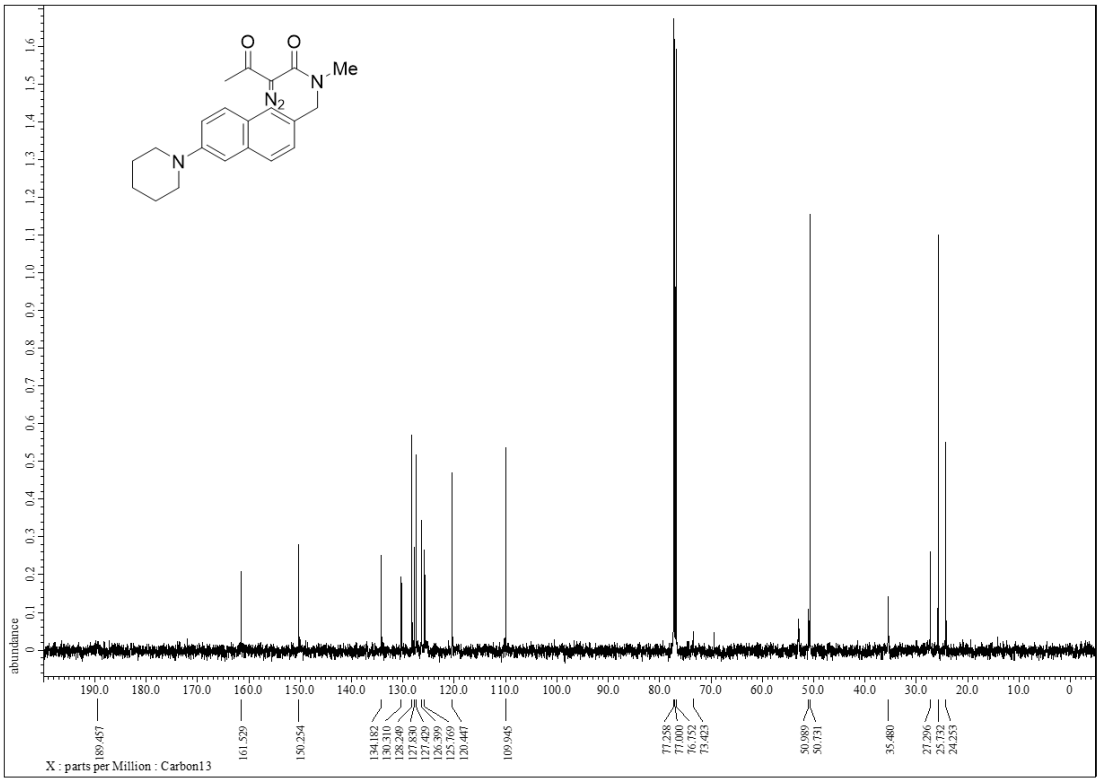

O
O
N
Me
N2
Br
3.01
2.97
2.00
1.97
0.96
1.00
1.01
1.02
abundance
X : parts per Million : Proton

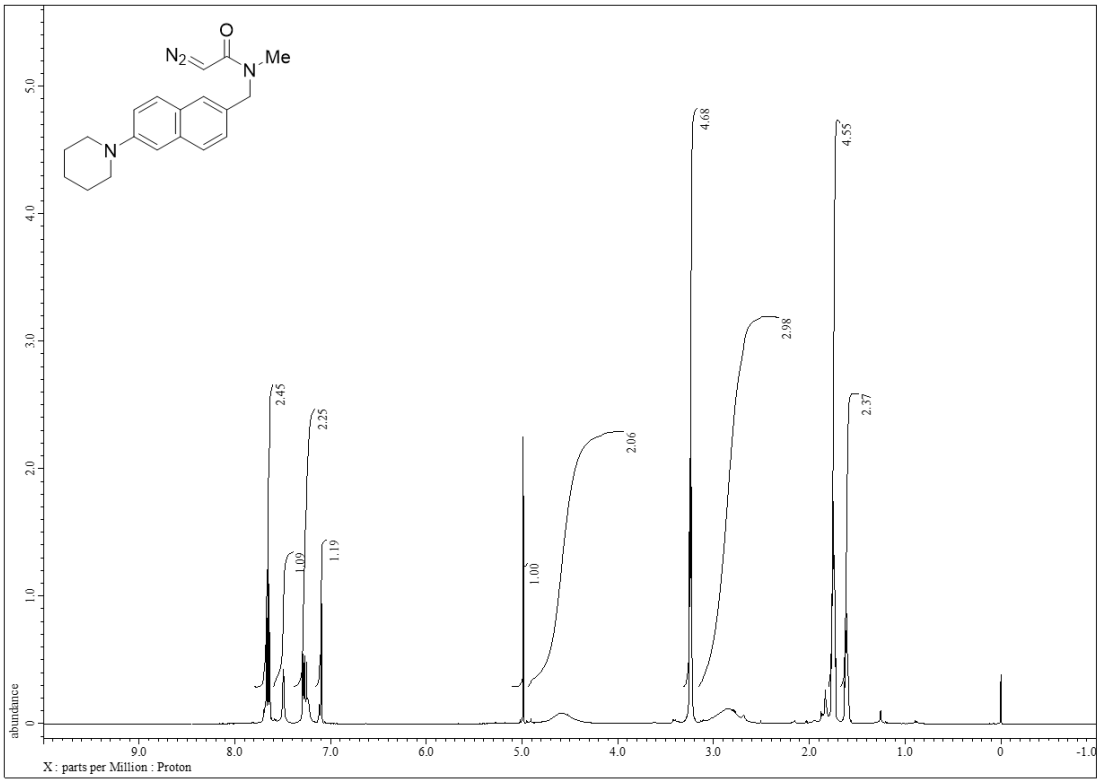

O
O
N
Me
N2
Br
abundance
188.961
161.700
134.087
133.810
131.597
129.671
129.308
127.763
126.513
119.970
77.258
77.000
76.732
73.747
52.687
35.871
27.248
X : parts per Million : Carbon13

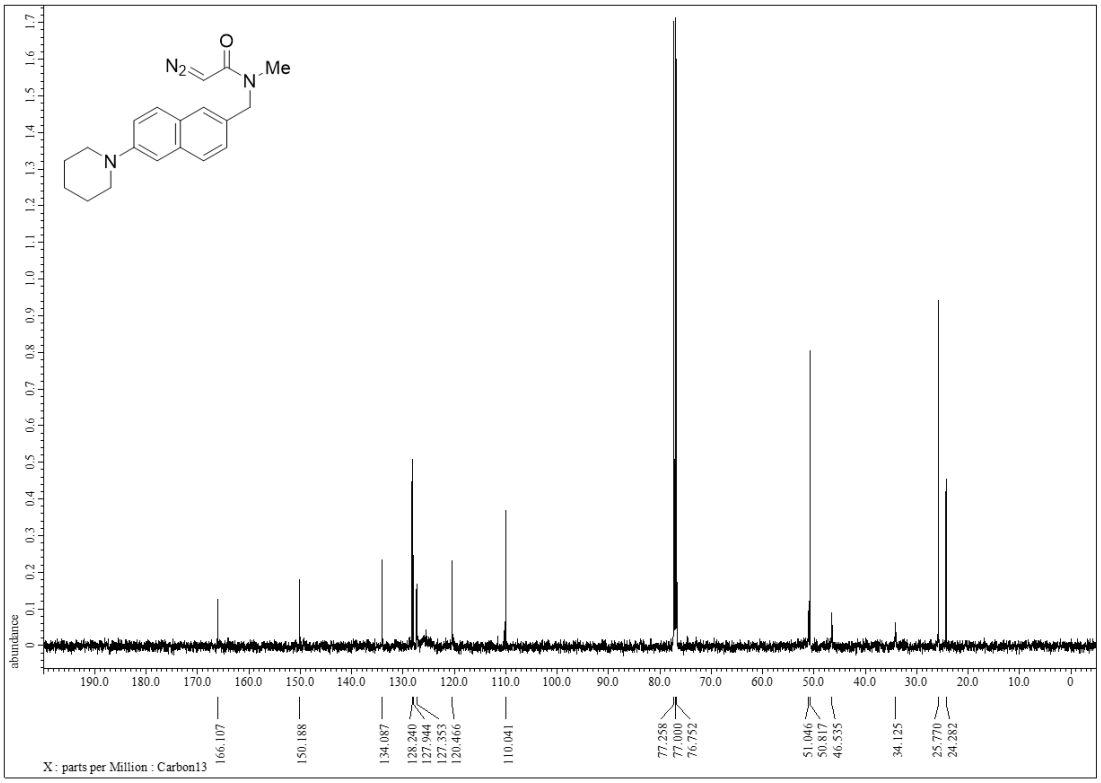

O
N2
N
Me
Br
1.06
1.20
1.05
0.95
0.92
1.00
1.88
3.16
abundance
X : parts per Million : Proton

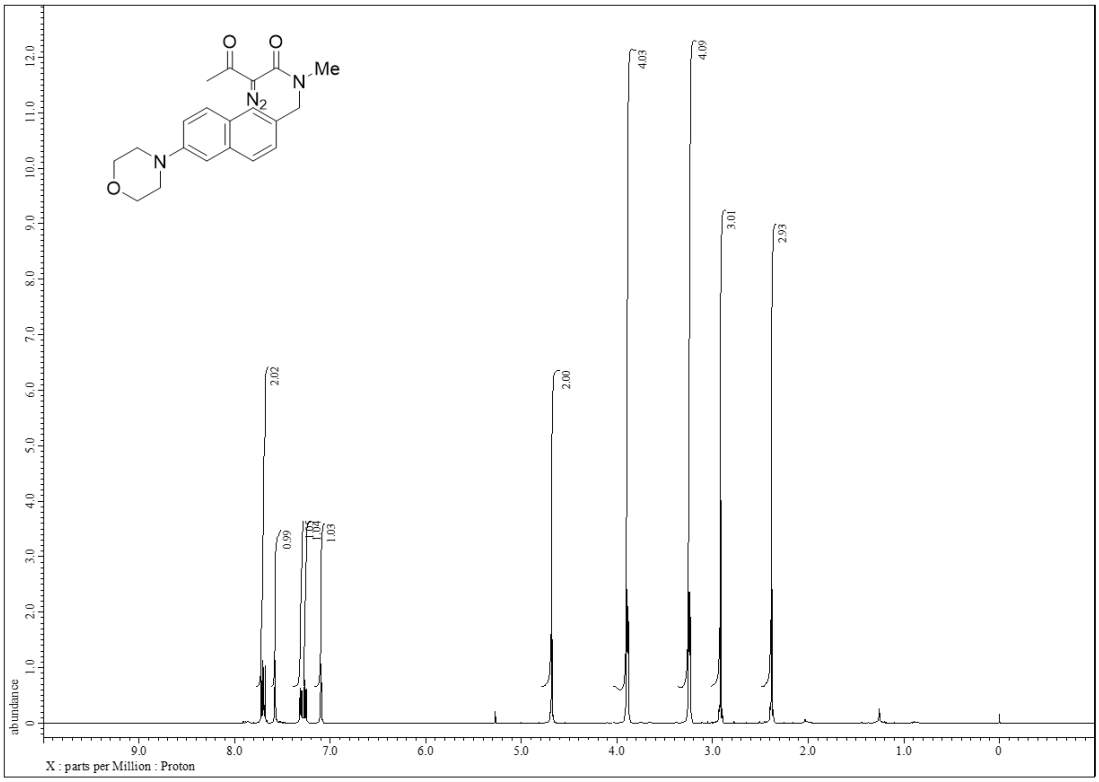

O
N2
N
Me
Br
abundance
166.221
133.810
131.721
129.718
129.327
127.715
119.875
77.258
77.000
76.742
46.563
34.345
X : parts per Million : Carbon13

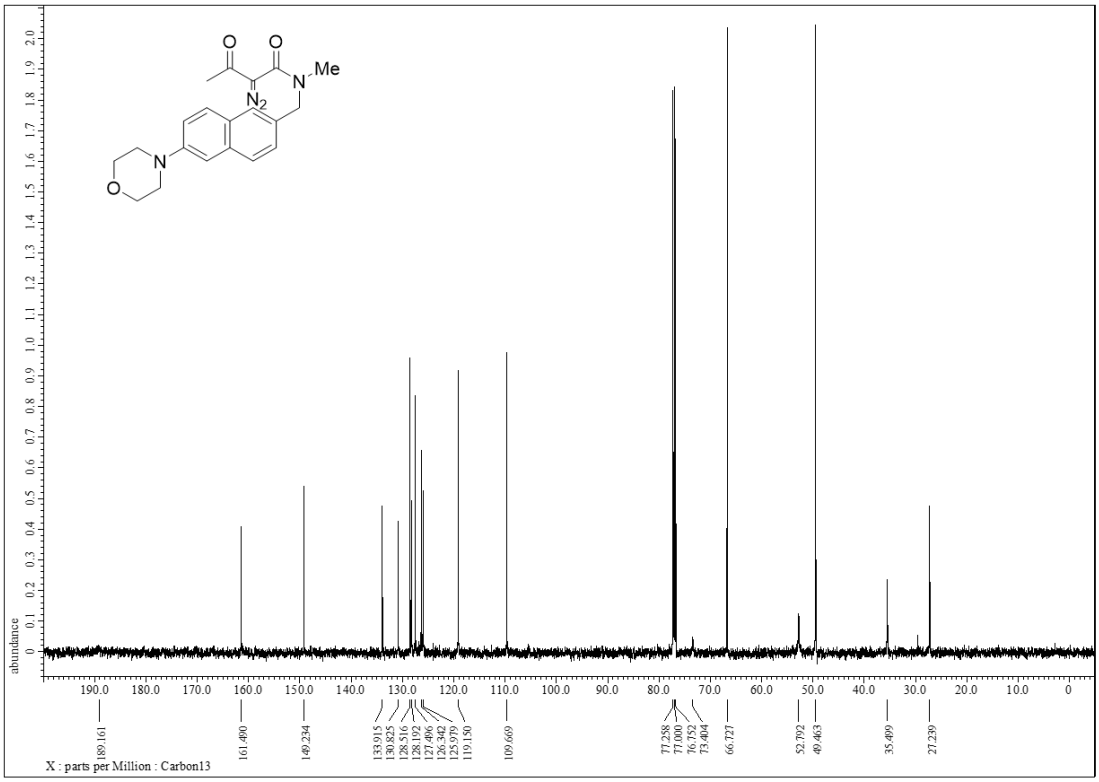

O
O
N
Me
N2
N
4.77
4.68
3.05
3.02
2.44
1.90
1.34
1.16
1.16
1.00
0.97
0.87
abundance
X : parts per Million : Proton

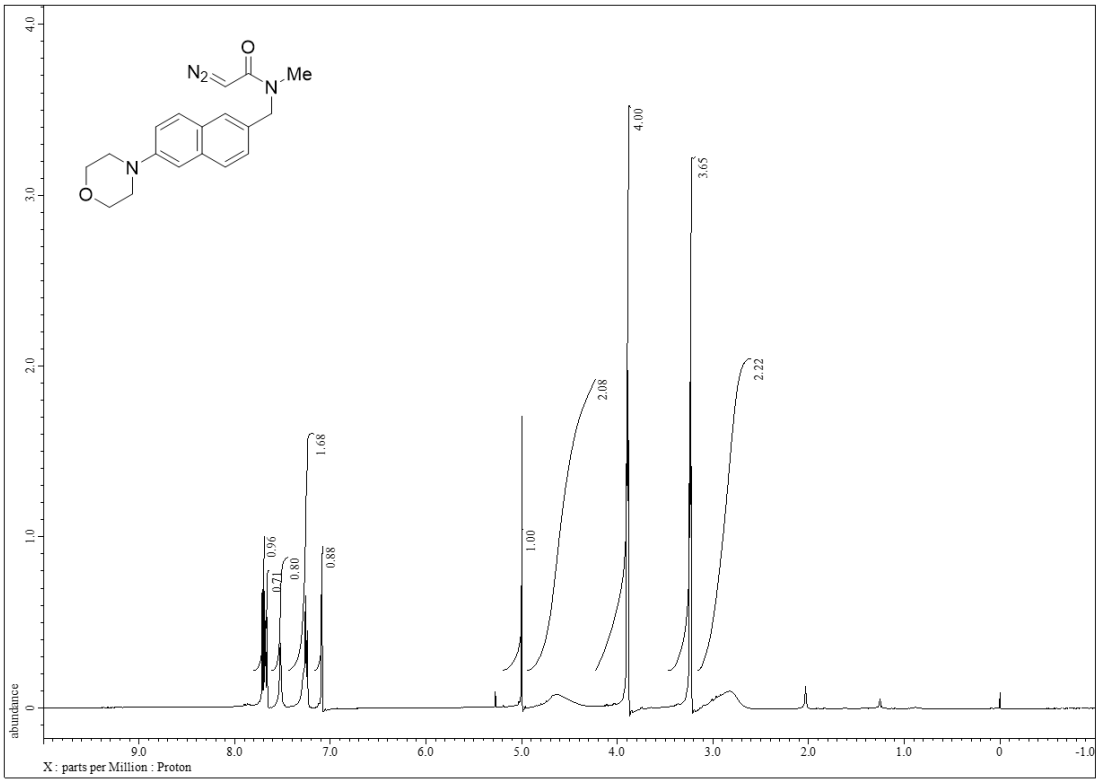

O
O
N
Me
N2
N
abundance
189.457
161.529
150.254
134.182
130.310
128.296
127.830
127.429
126.399
125.760
120.447
109.945
77.258
77.000
76.752
73.423
50.989
50.731
35.480
27.296
25.732
24.253
X : parts per Million : Carbon13

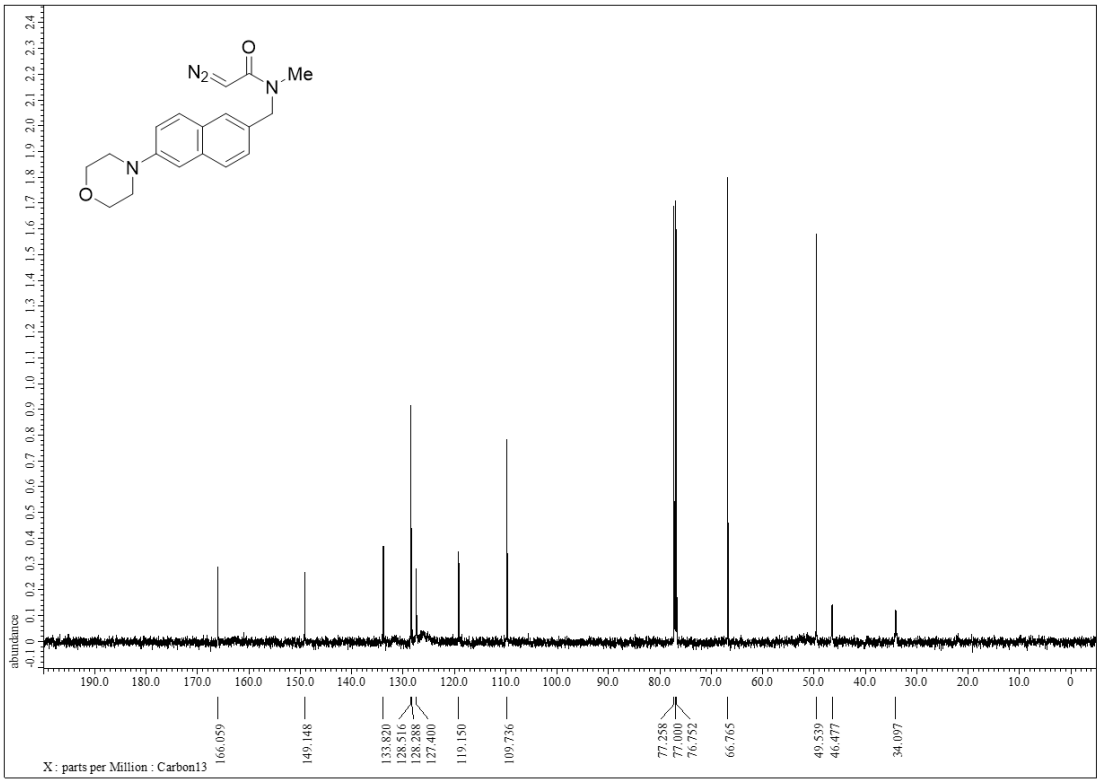

N2
O
N
Me
N
2.45
1.09
2.25
1.19
1.00
2.06
4.68
2.98
4.55
2.37
abundance
X : parts per Million : Proton

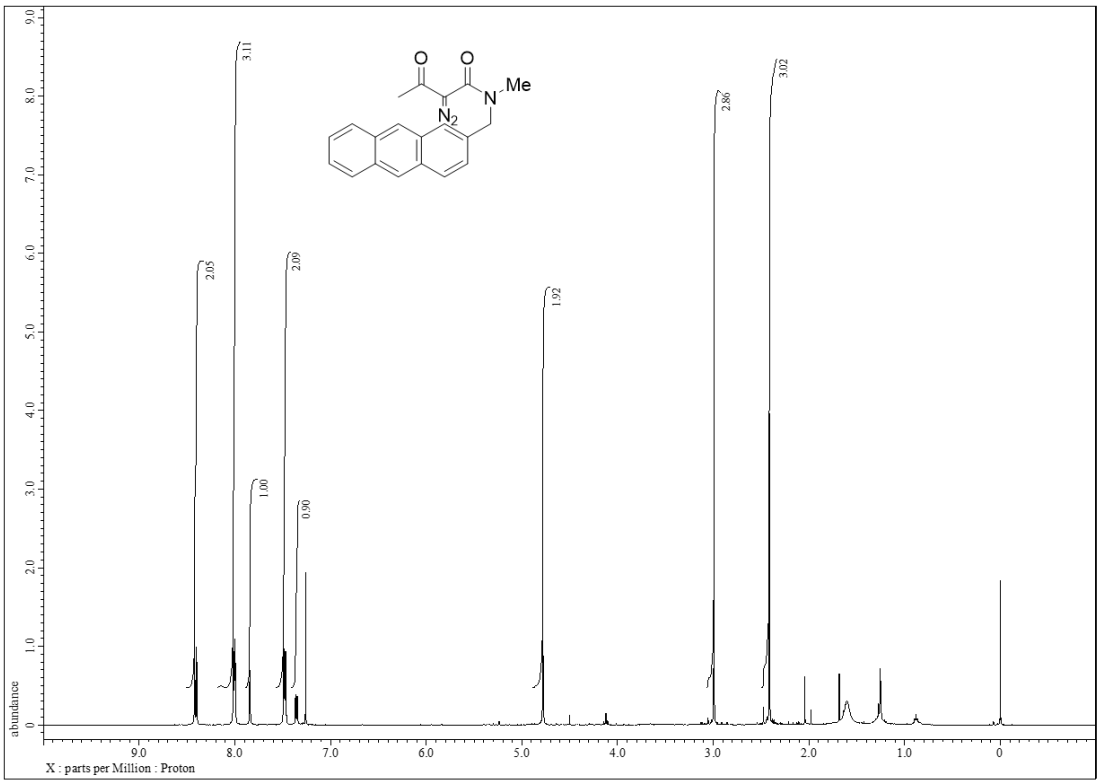

N2
O
N
Me
N
abundance
X : parts per Million : Carbon13
166.107
150.188
134.087
128.240
127.944
127.353
120.466
110.041
77.258
77.000
76.752
51.046
50.817
46.535
34.125
25.770
24.282

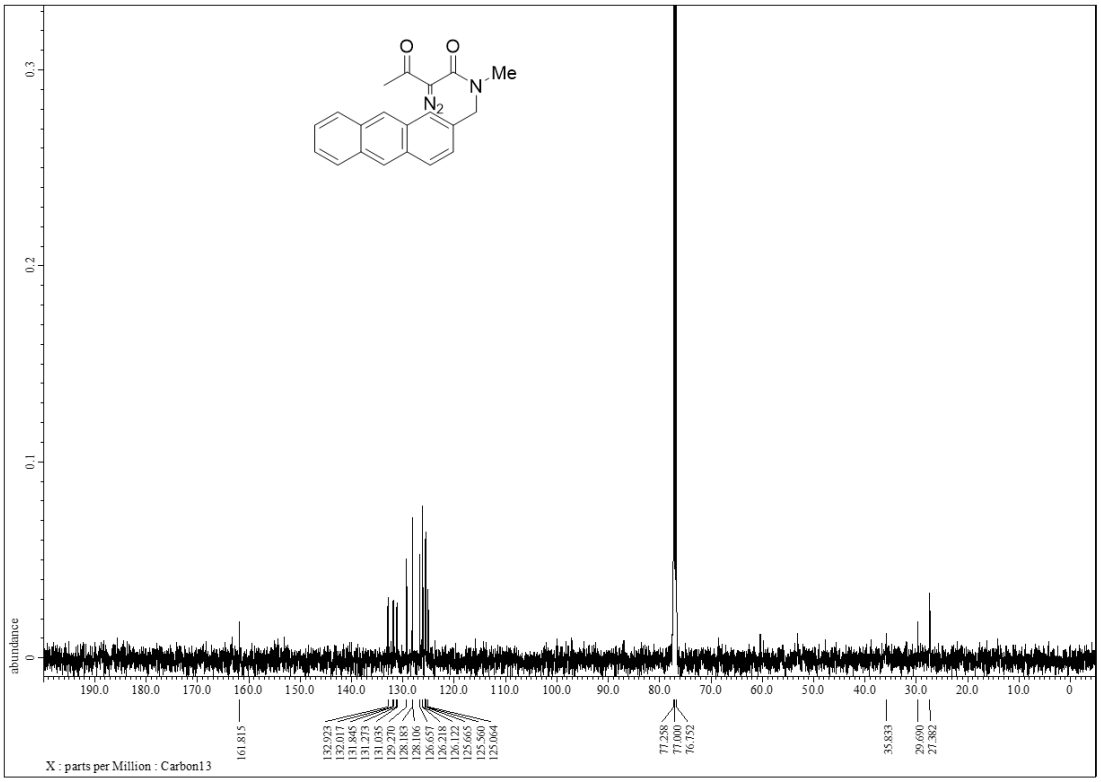

O
O
N
Me
N2
N
O
2.02
0.99
1.04
1.04
1.03
2.00
4.03
4.09
3.01
2.93
abundance
X : parts per Million : Proton

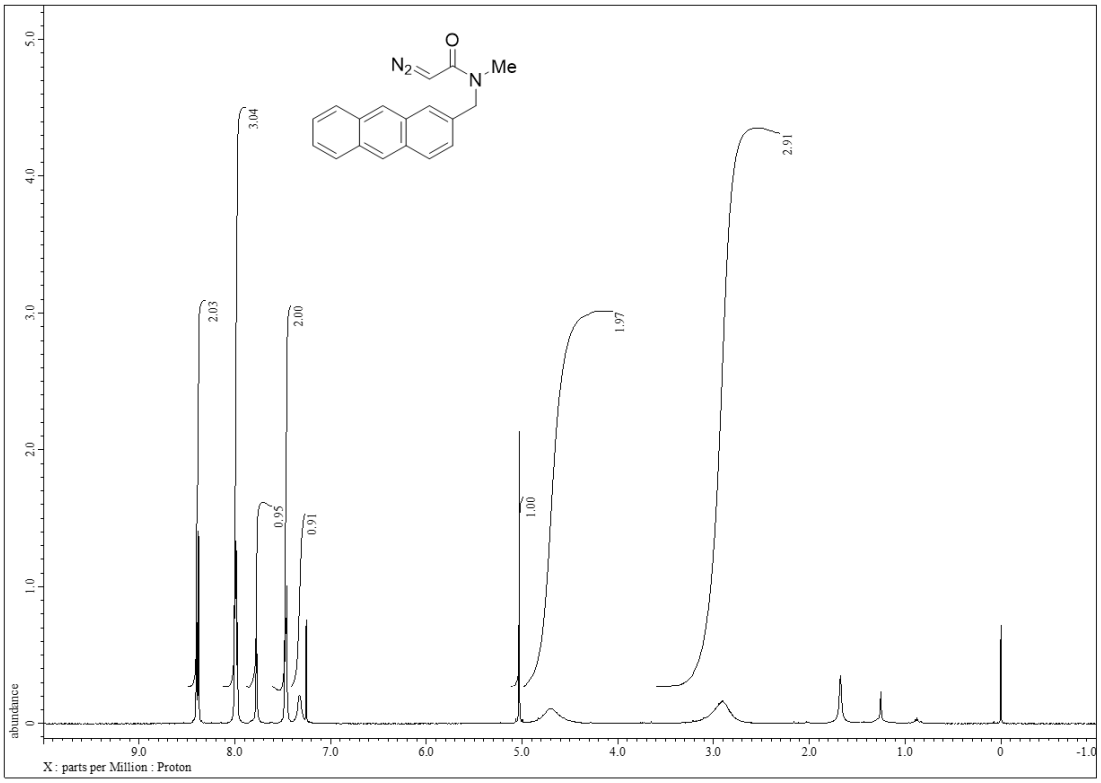

O
O
N
Me
N2
N
O
abundance
189.161
161.490
149.234
133.915
130.825
128.516
128.102
127.496
126.342
125.979
119.150
109.669
77.258
77.000
76.752
73.404
66.727
52.792
49.463
35.409
27.239
X : parts per Million : Carbon13

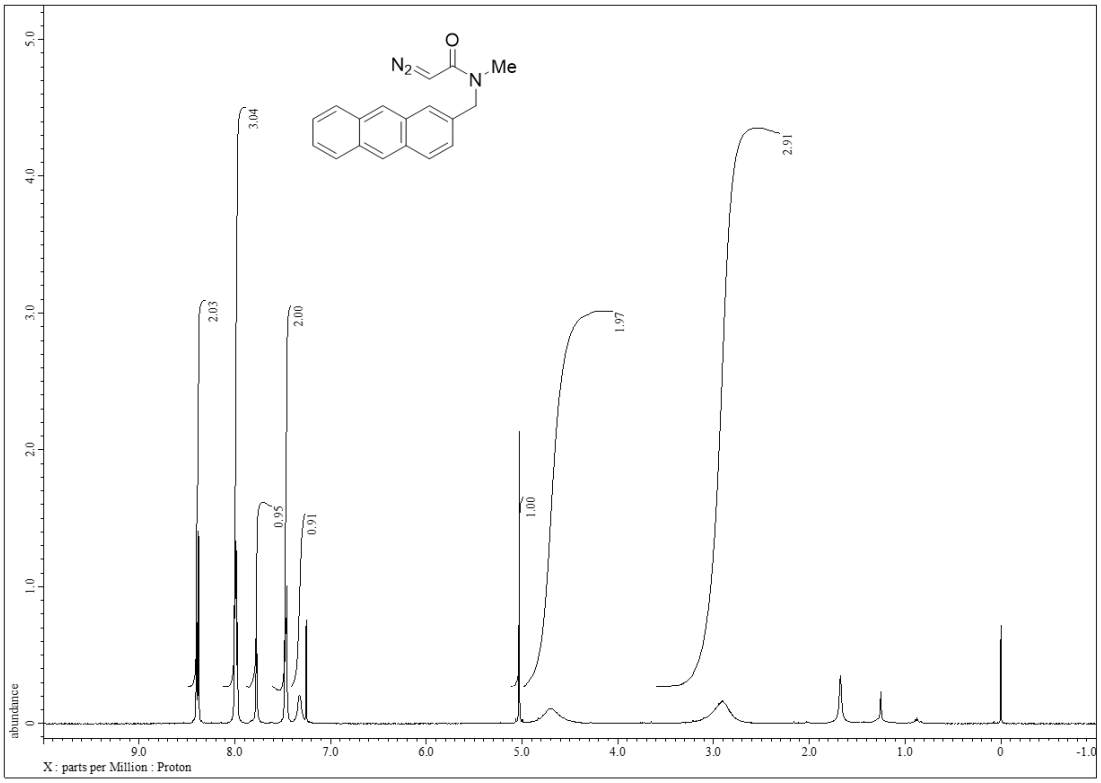

N2
O
N
Me
O
N
abundance
X : parts per Million : Proton
0.96
0.71
0.80
1.68
0.88
1.00
2.08
4.00
3.65
2.22

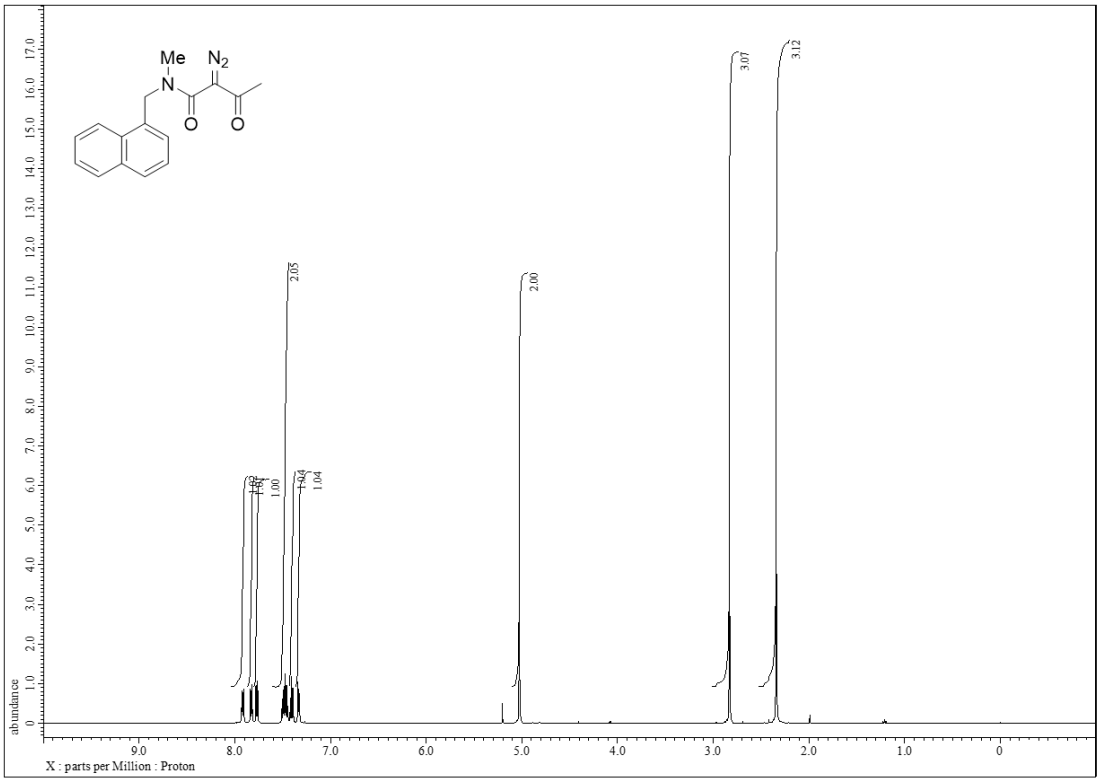

N2
O
N
Me
O
N
abundance
X : parts per Million : Carbon13
166.059
149.148
133.820
128.516
128.288
127.400
119.150
109.736
77.258
77.000
76.752
66.765
49.539
46.477
34.097

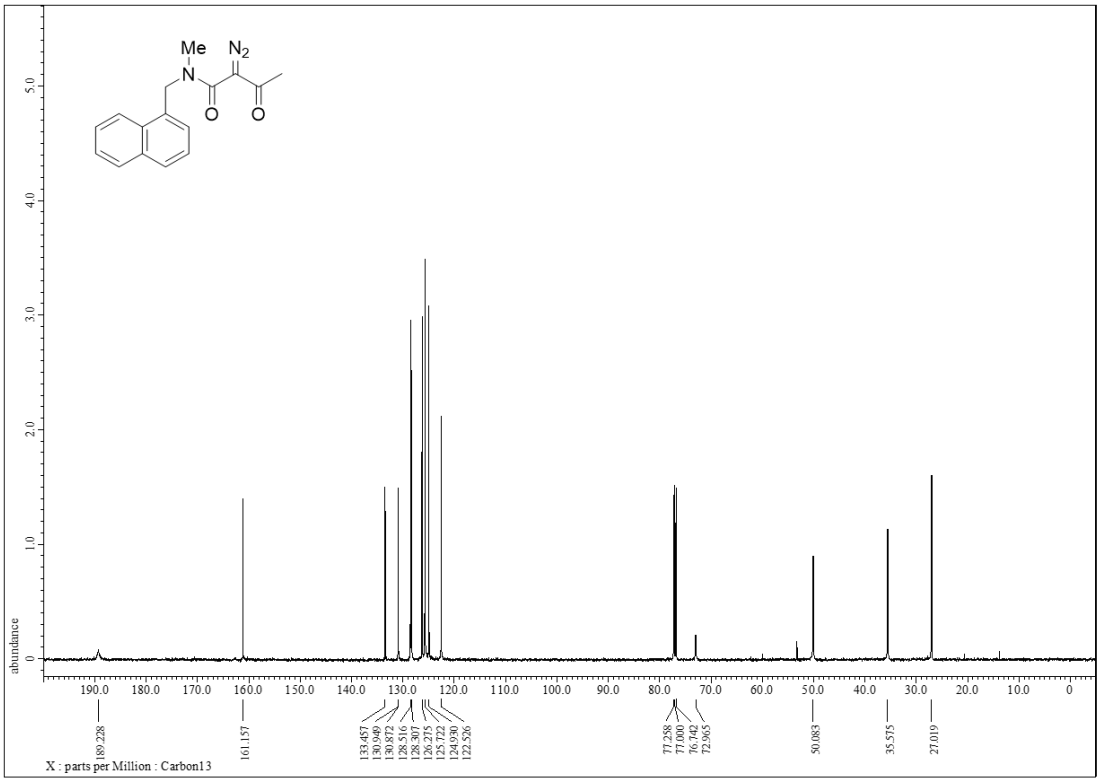

O
O
N
Me
N2
2.05
3.11
1.00
2.09
0.90
1.92
2.86
3.02
abundance
X : parts per Million : Proton

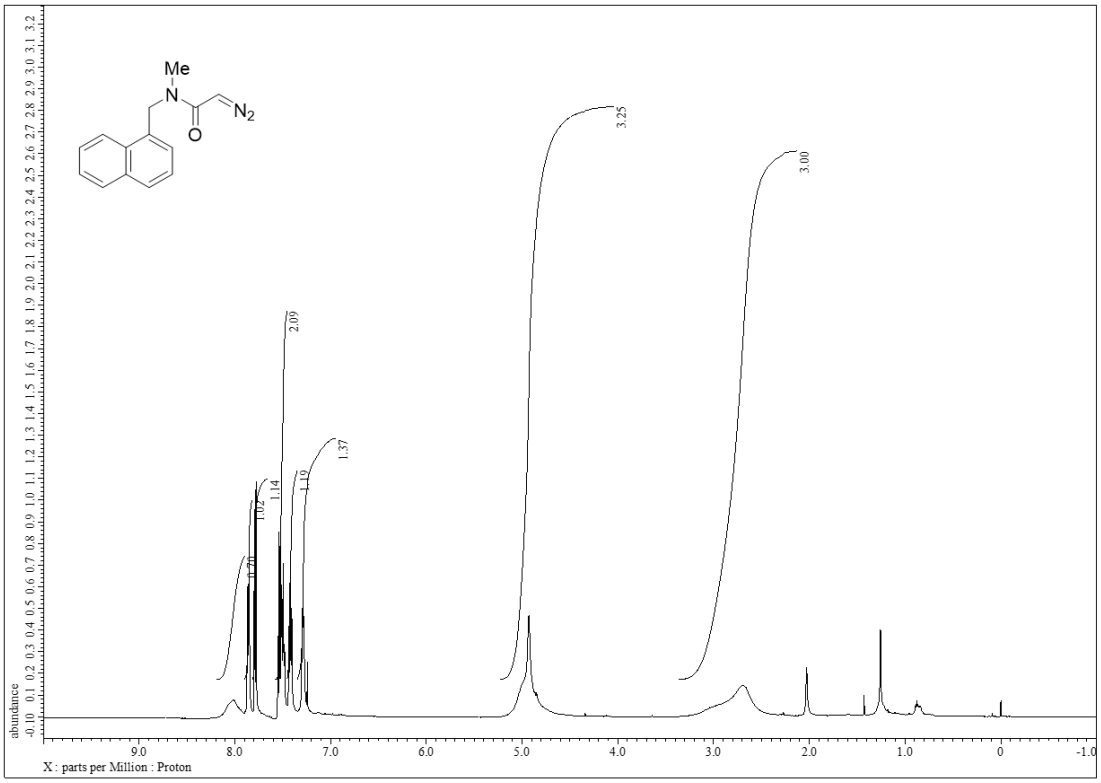

O
O
N
Me
N2
abundance
161.815
132.923
132.017
131.845
131.273
131.035
129.270
128.183
128.100
126.657
126.218
126.122
125.665
125.560
125.064
77.258
77.000
76.752
35.833
29.690
27.382
X : parts per Million : Carbon13

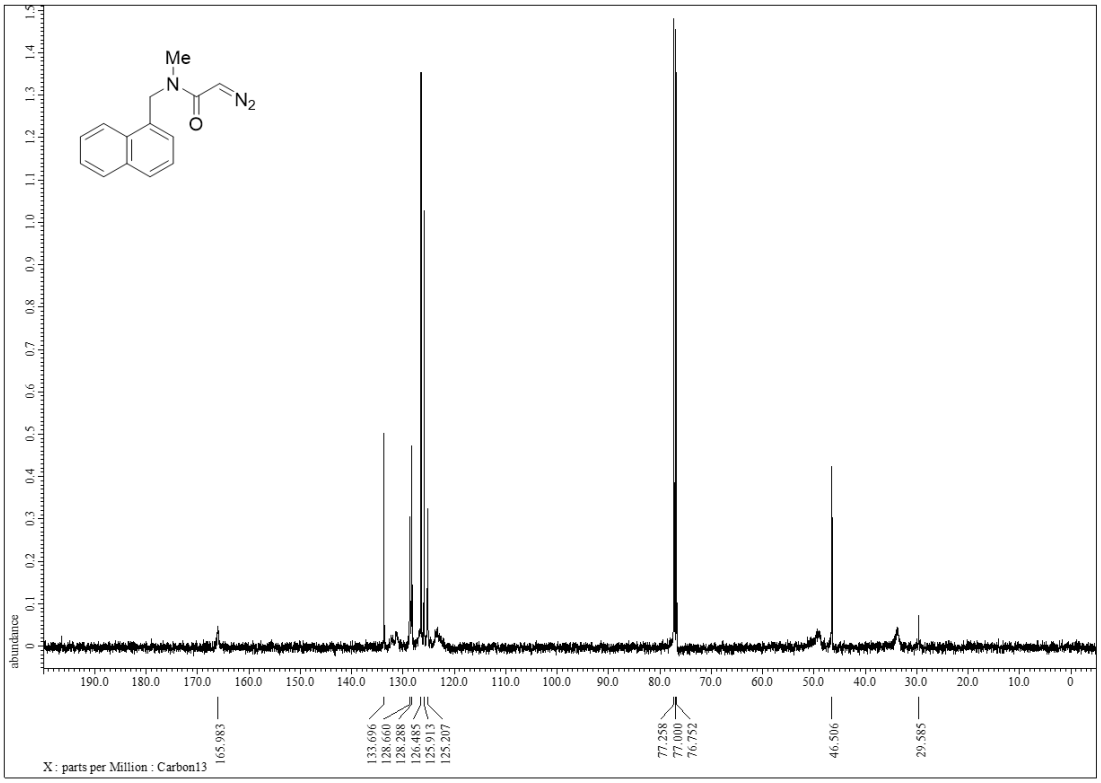

O
N2
N
Me
3.04
2.91
2.03
2.00
1.97
1.00
0.95
0.91
abundance
X : parts per Million : Proton

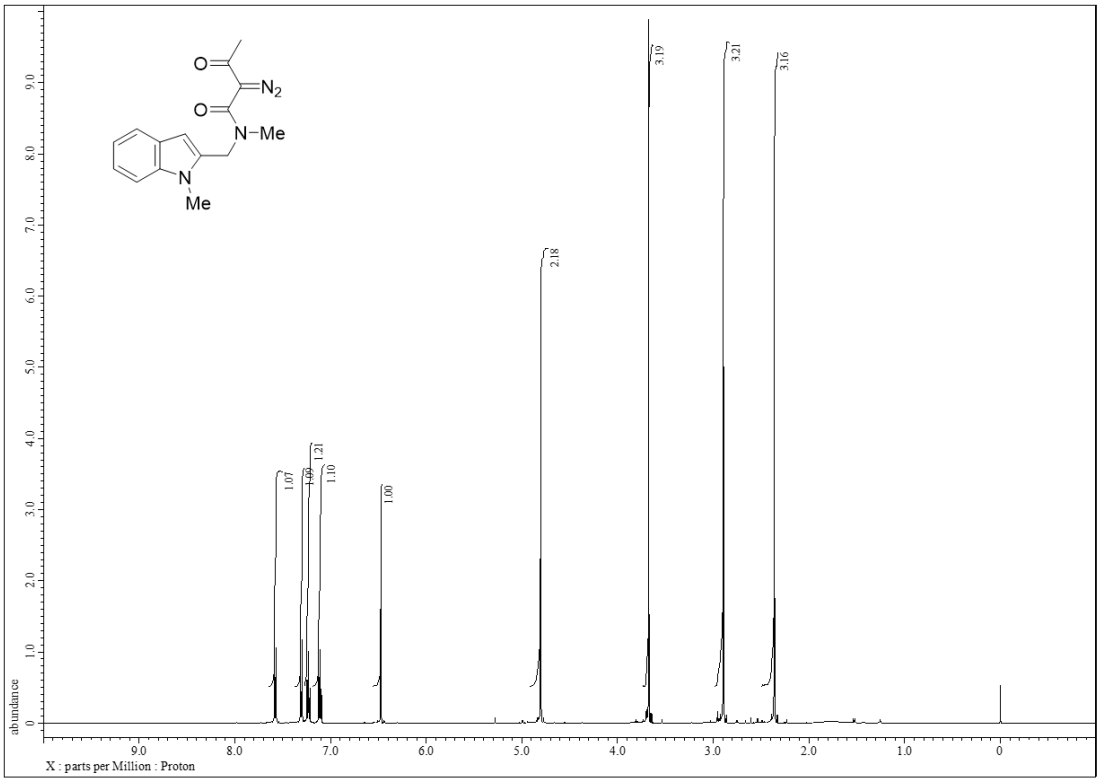

O
N2
N
Me
3.04
2.91
2.03
2.00
1.97
1.00
0.95
0.91
abundance
X : parts per Million : Proton

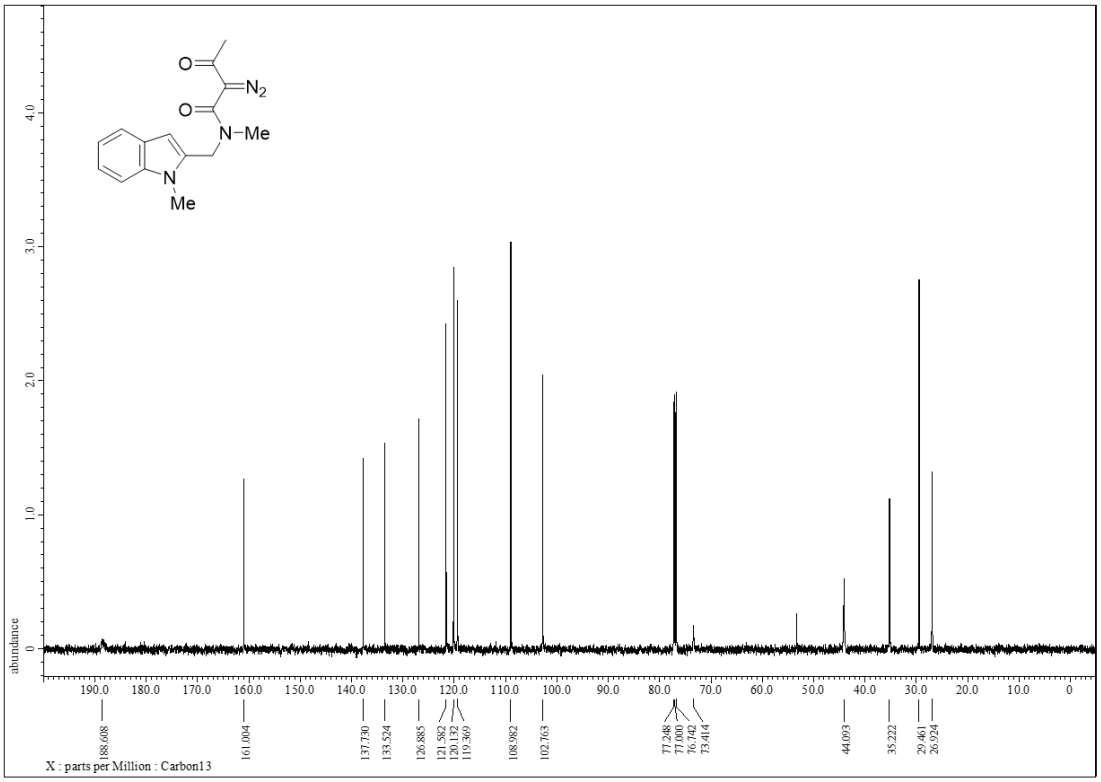

Me
N2
N
O
O
3.07
3.12
2.05
2.00
1.00
1.04
abundance
X : parts per Million : Proton

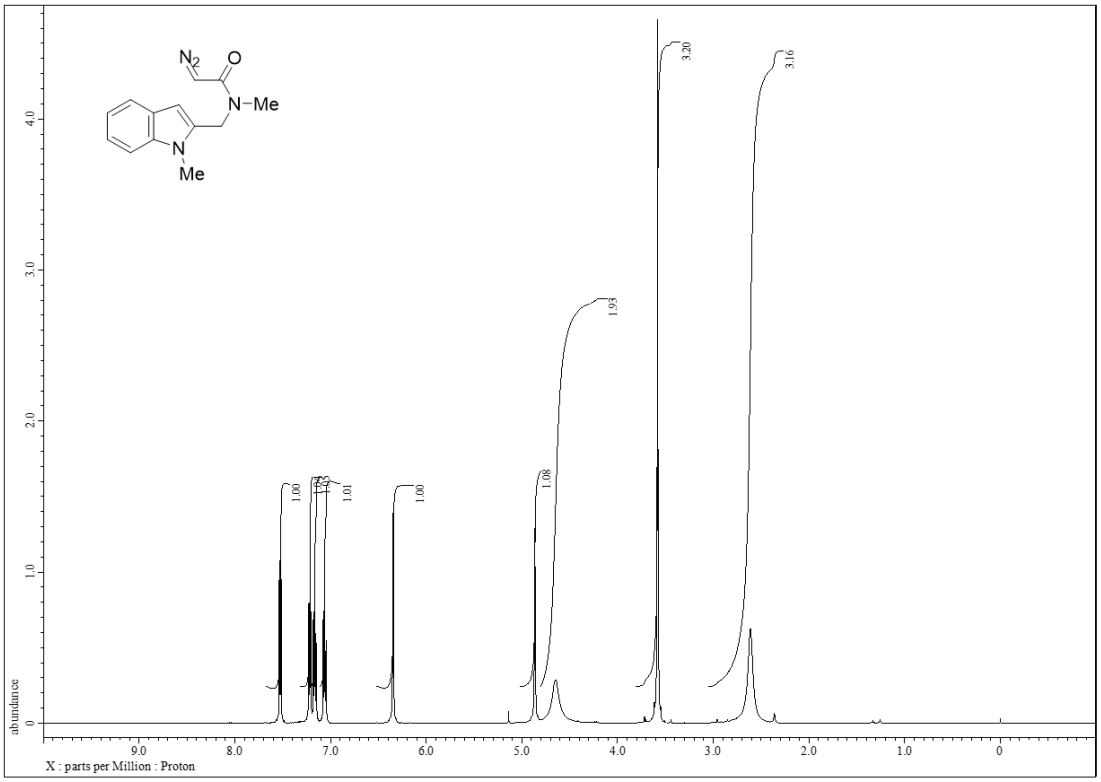

Me
N2
N
O
O
abundance
189.228
161.157
133.457
130.949
130.872
129.515
128.301
126.275
125.722
124.930
122.526
77.258
77.000
76.742
72.965
50.083
35.575
27.019
X : parts per Million : Carbon13

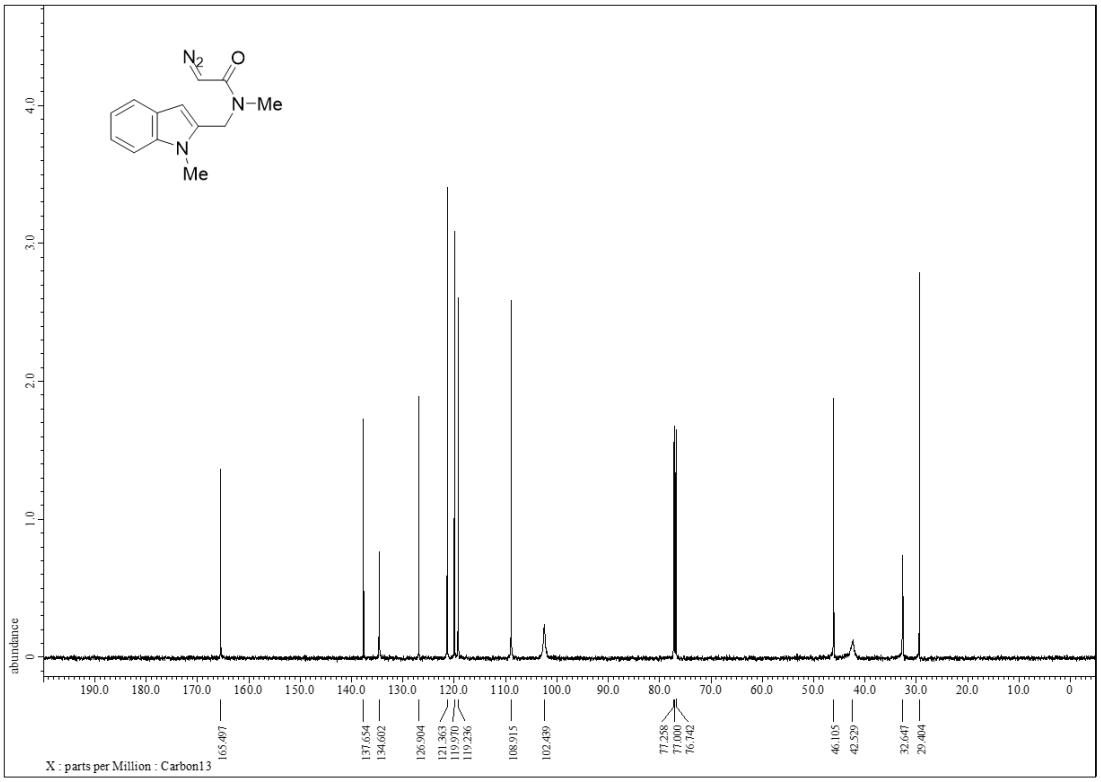

Me
N
O
N2
3.25
3.00
2.09
1.37
1.19
1.14
1.02
1.00
abundance
X : parts per Million : Proton

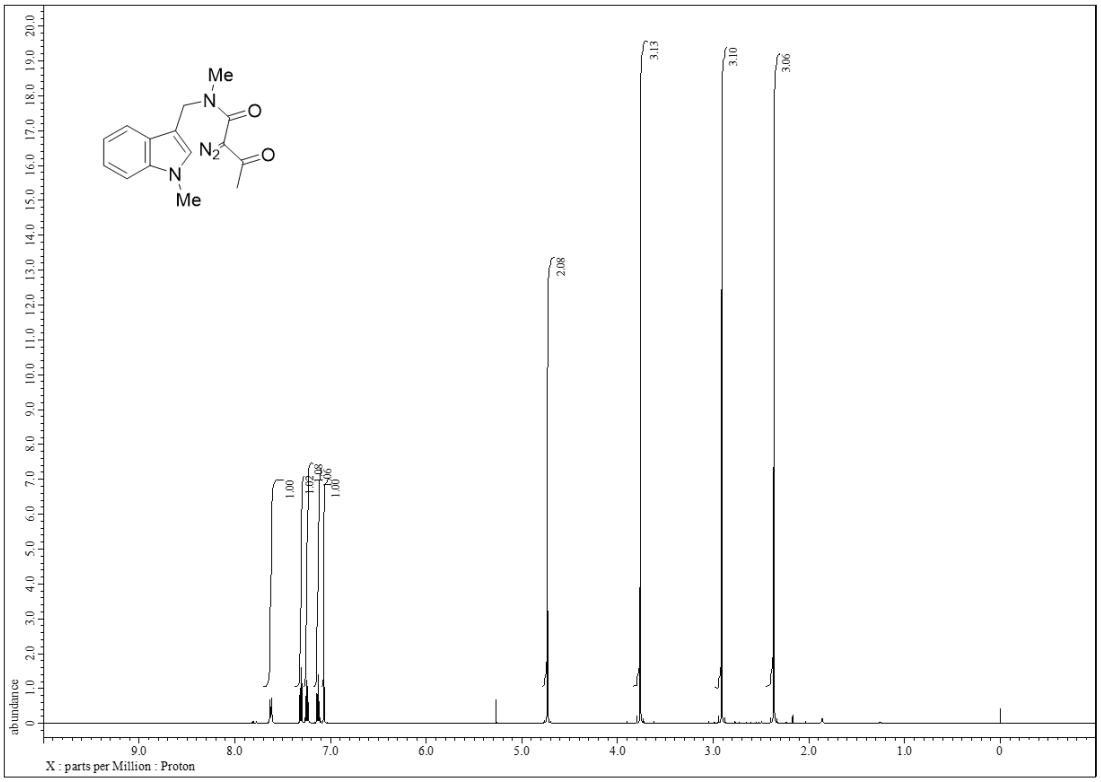

Me
N
O
N2
abundance
165.983
133.696
128.660
128.288
126.485
125.913
125.207
77.258
77.000
76.752
46.506
29.585
X : parts per Million : Carbon13

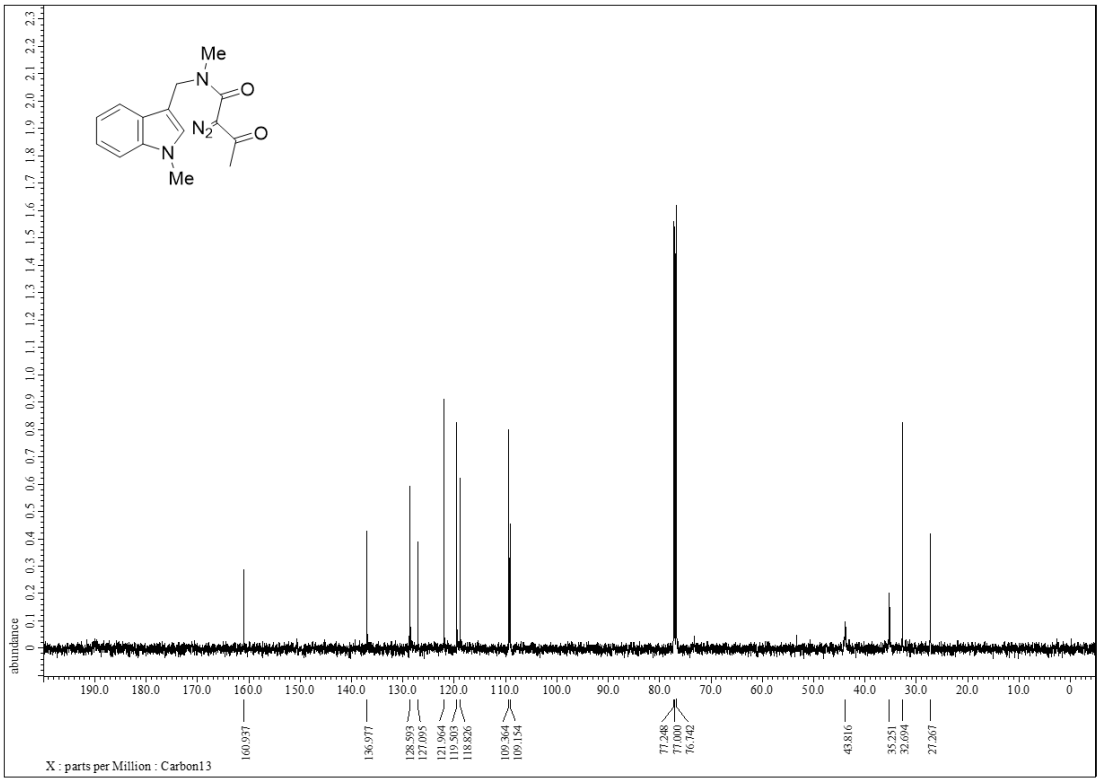

O
O
N2
N–Me
N
Me
3.19
3.21
3.16
2.18
1.07
1.09
1.21
1.10
1.00
abundance
X : parts per Million : Proton

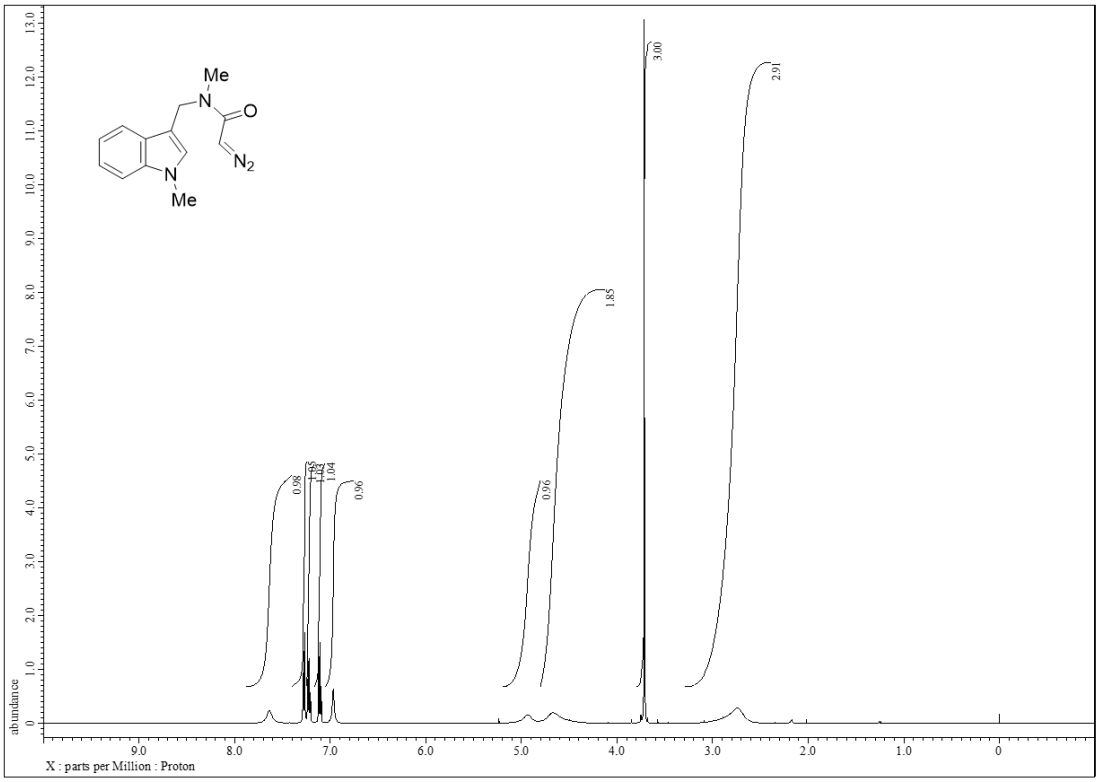

O
O
N2
N–Me
N
Me
abundance
188.608
161.004
137.730
133.524
126.885
121.582
120.132
119.369
108.982
102.763
77.248
77.000
76.742
73.414
44.093
35.222
29.461
26.924
X : parts per Million : Carbon13

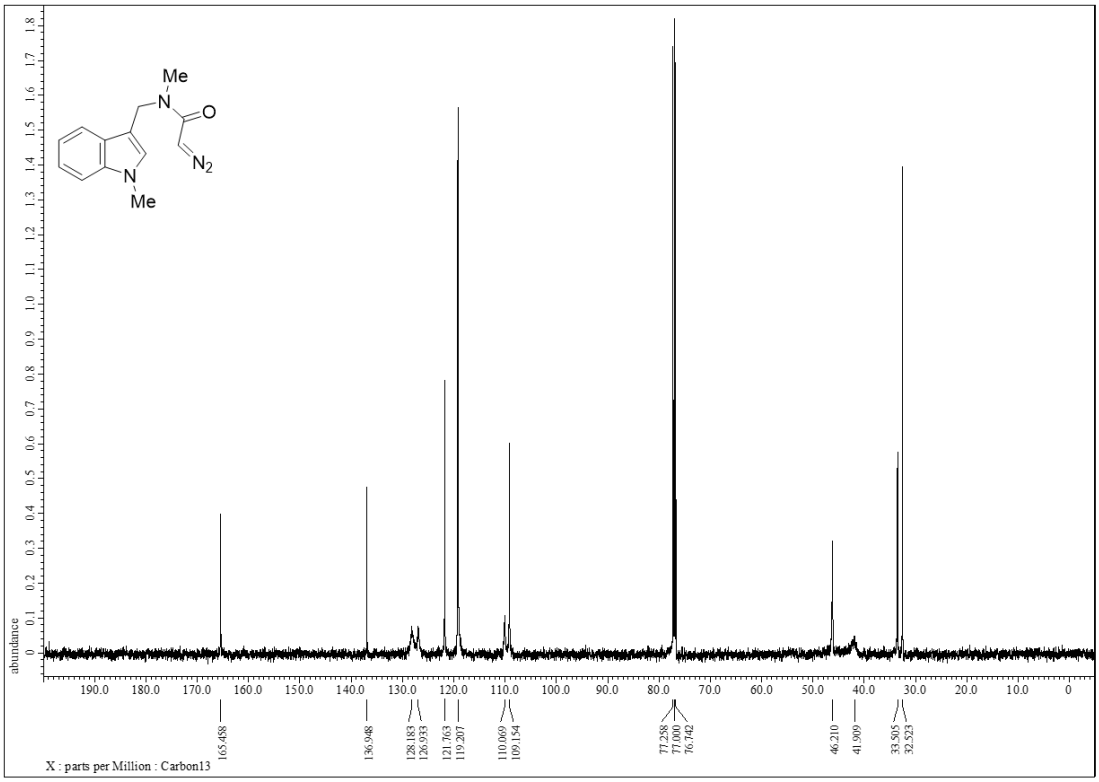

N2
O
N–Me
N
Me
3.20
3.16
1.93
1.08
1.00
1.01
1.00
abundance
X : parts per Million : Proton

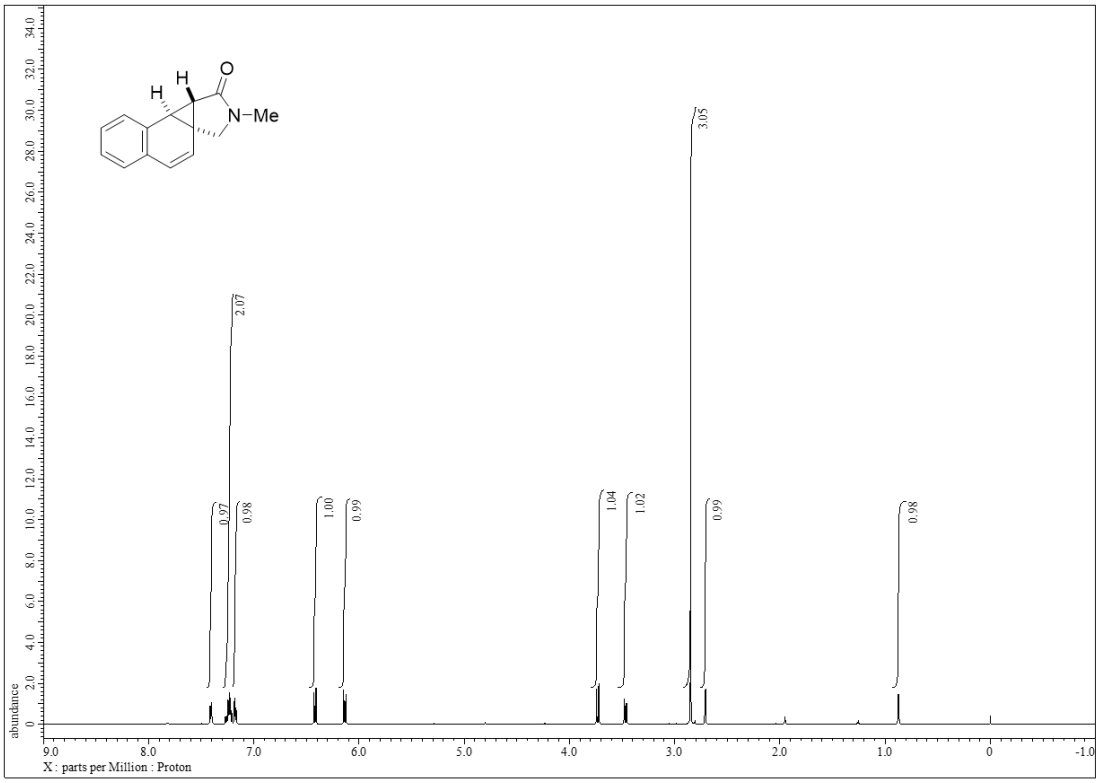

N2
O
N–Me
N
Me
abundance
165.497
137.654
134.602
126.904
121.363
119.970
119.236
108.915
102.439
77.258
77.000
76.742
46.105
42.529
32.647
29.404
X : parts per Million : Carbon13

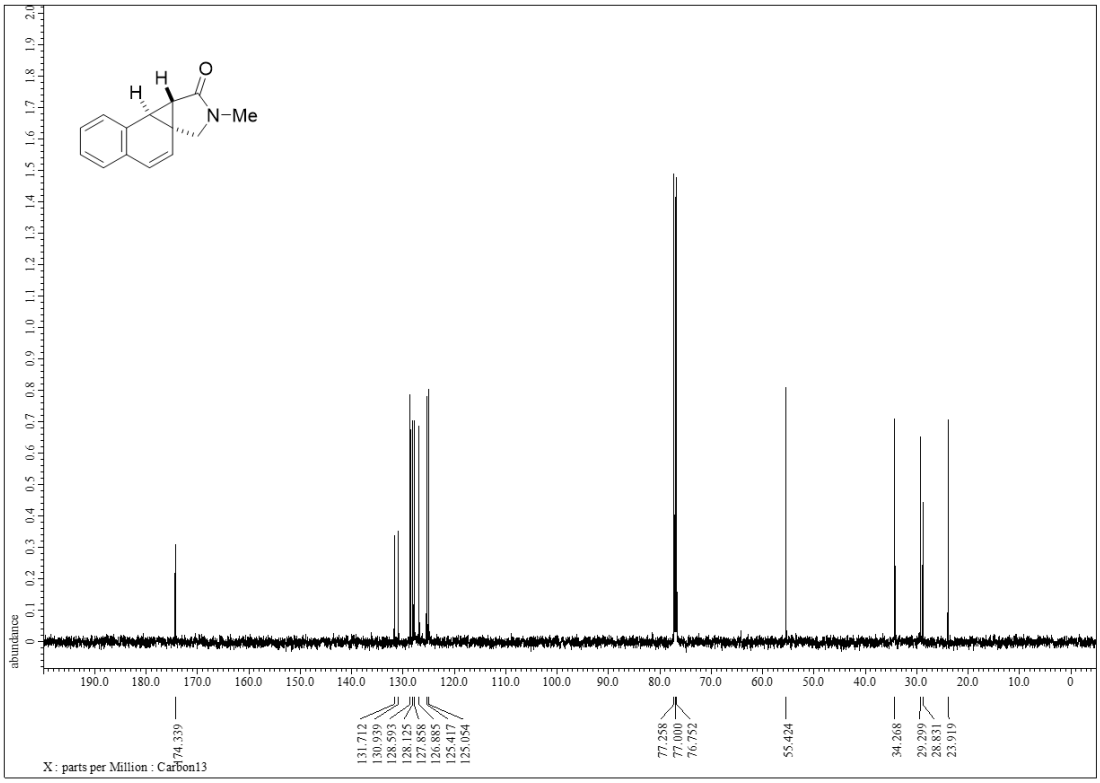

Me
N
O
N2
O
N
Me
abundance
X : parts per Million : Proton
1.00
1.02
1.08
2.08
3.13
3.10
3.06
1.00

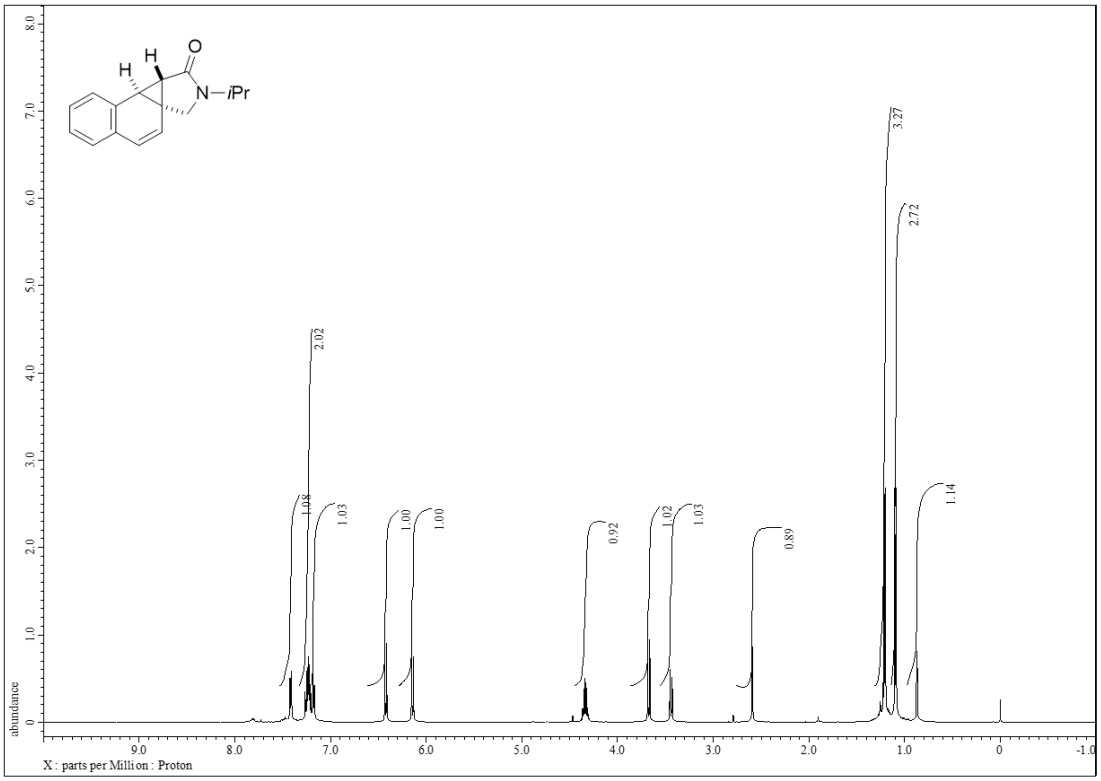

Me
N
O
N2
O
N
Me
abundance
X : parts per Million : Carbon13
160.937
136.977
128.593
127.095
121.964
119.503
118.826
109.364
109.154
77.248
77.000
76.742
43.816
35.251
32.694
27.267

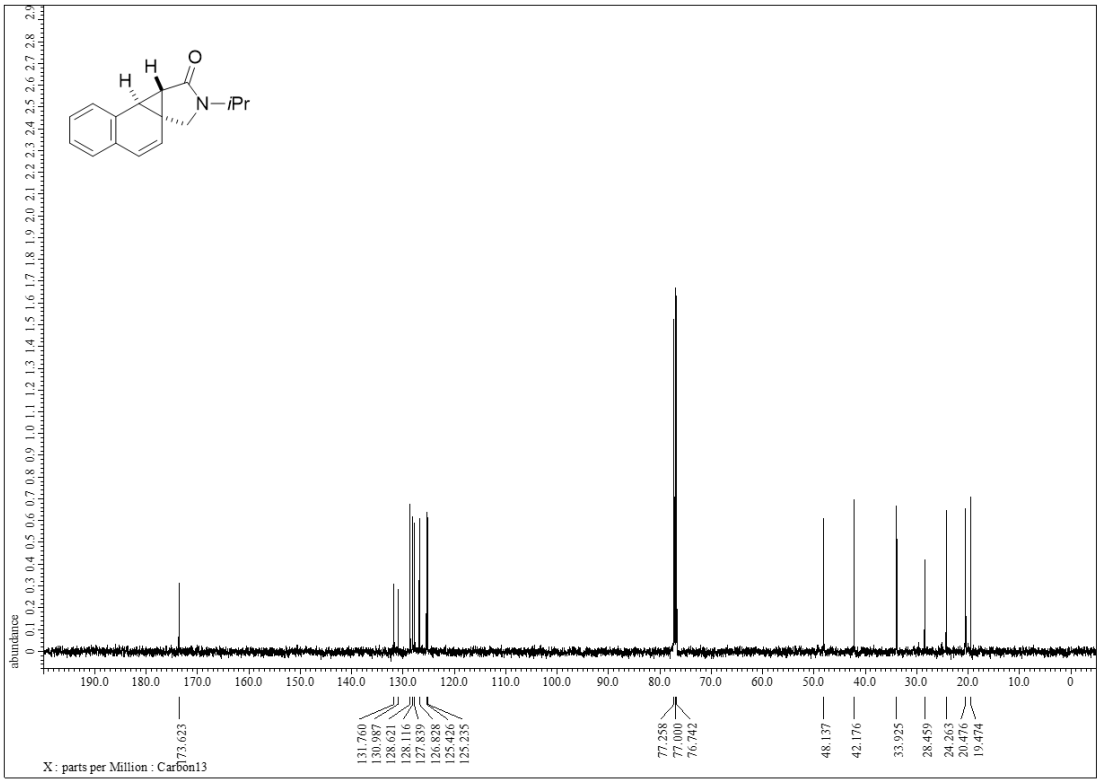

Me
N
O
N2
N
Me
abundance
X : parts per Million : Proton
0.98
1.85
0.96
3.00
2.91
0.96

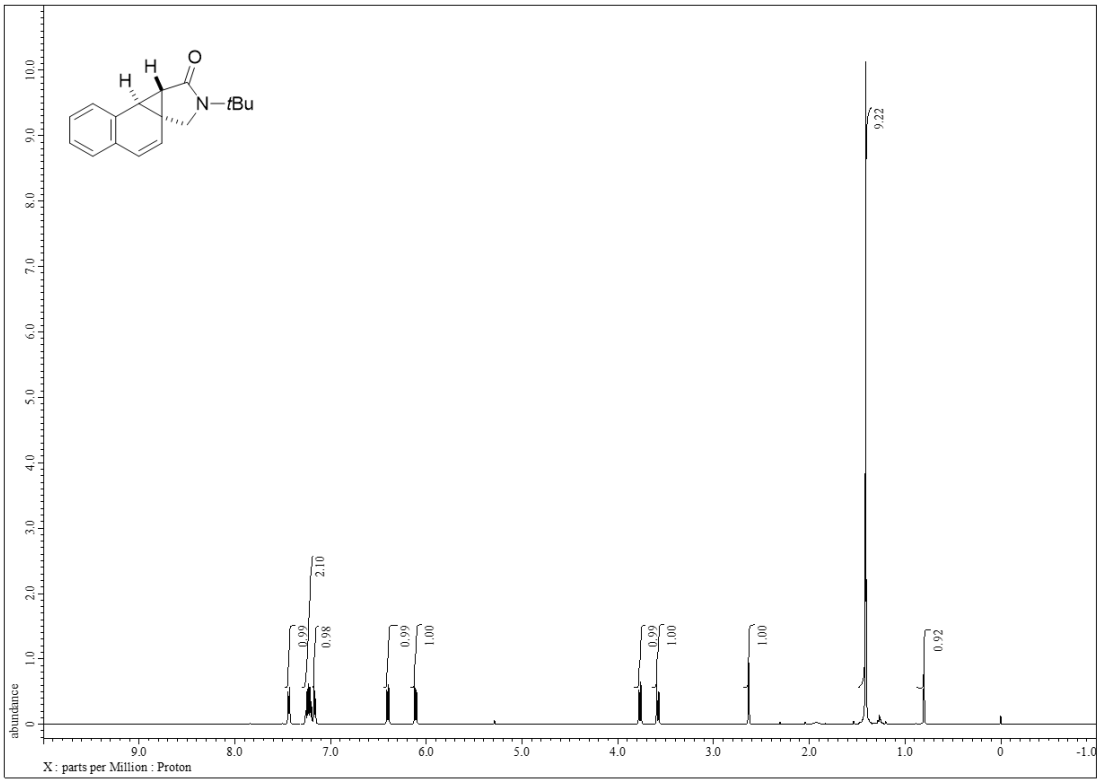

Me
N
O
N2
N
Me
abundance
X : parts per Million : Carbon13
165.458
136.948
128.183
126.933
121.763
119.207
110.069
109.154
77.258
77.000
76.742
46.210
41.909
33.505
32.523

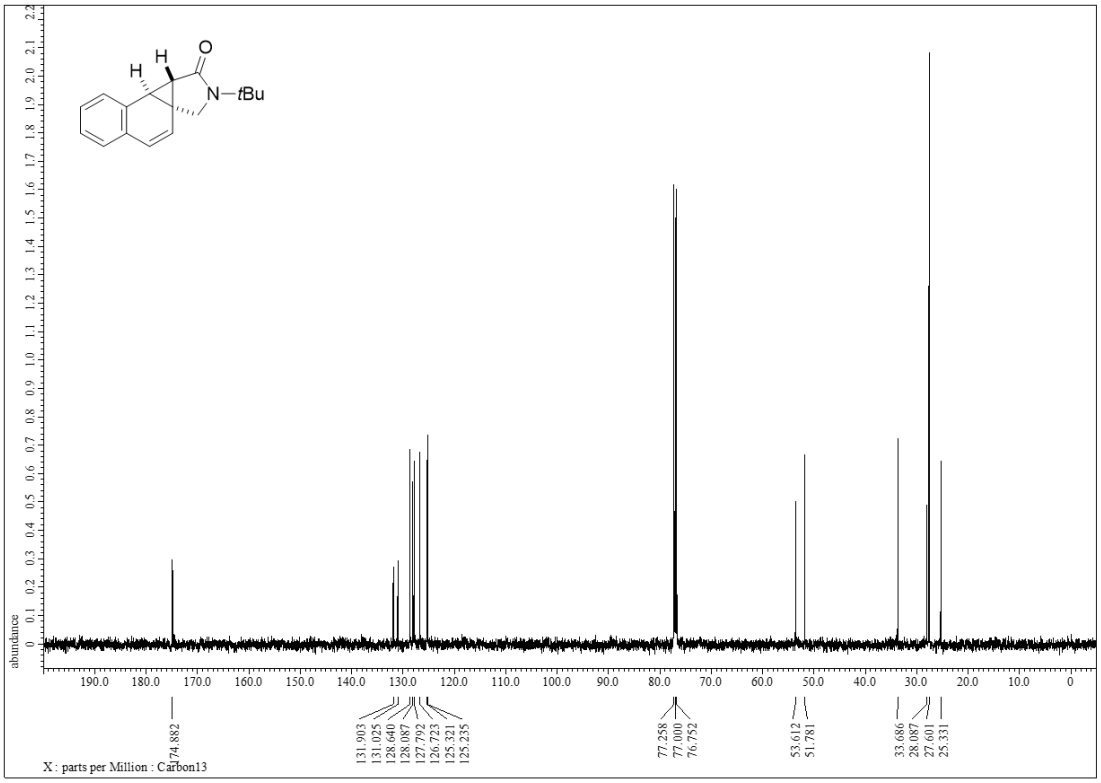

H
H
O
N−Me
3.05
2.07
0.97
0.98
1.00
0.99
1.04
1.02
0.99
0.98
abundance
X : parts per Million : Proton

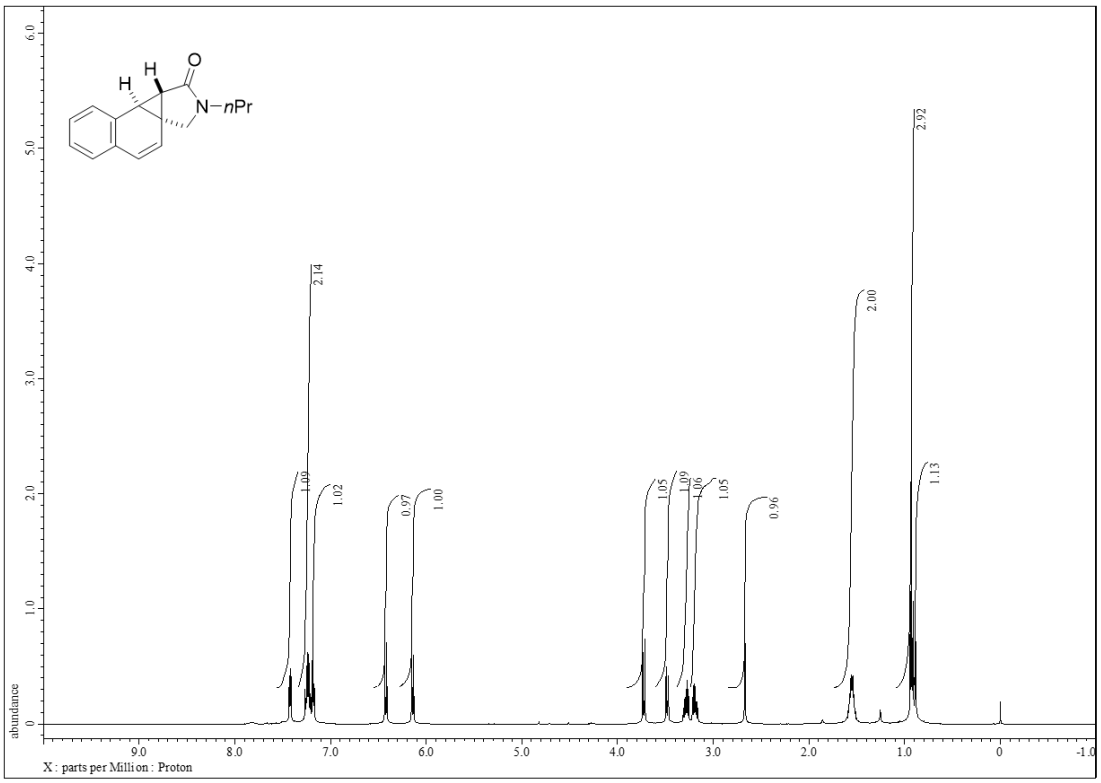

H
H
O
N−Me
abundance
174.339
131.712
130.939
128.593
128.125
127.858
126.885
125.417
125.054
77.258
77.000
76.752
55.424
34.268
29.299
28.831
23.919
X : parts per Million : Carbon13

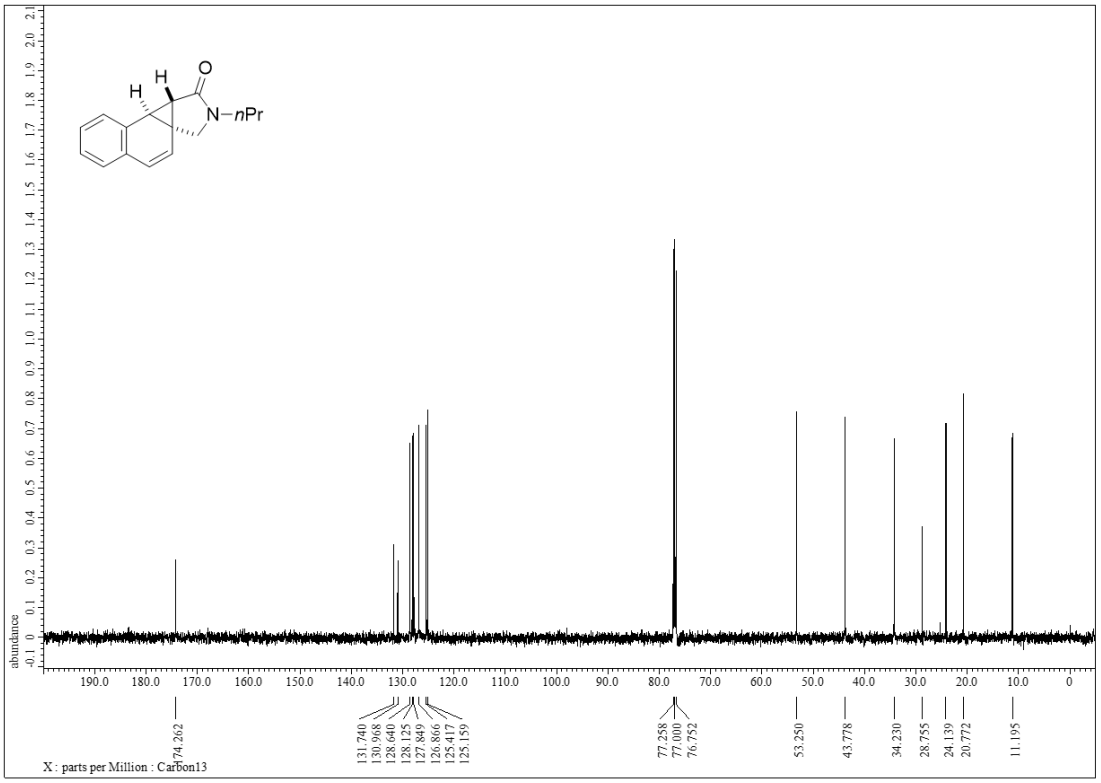

H
H
O
N—iPr
abundance
X : parts per Million : Proton
2.02
1.08
1.03
1.00
1.00
0.92
1.02
1.03
0.89
3.27
2.72
1.14

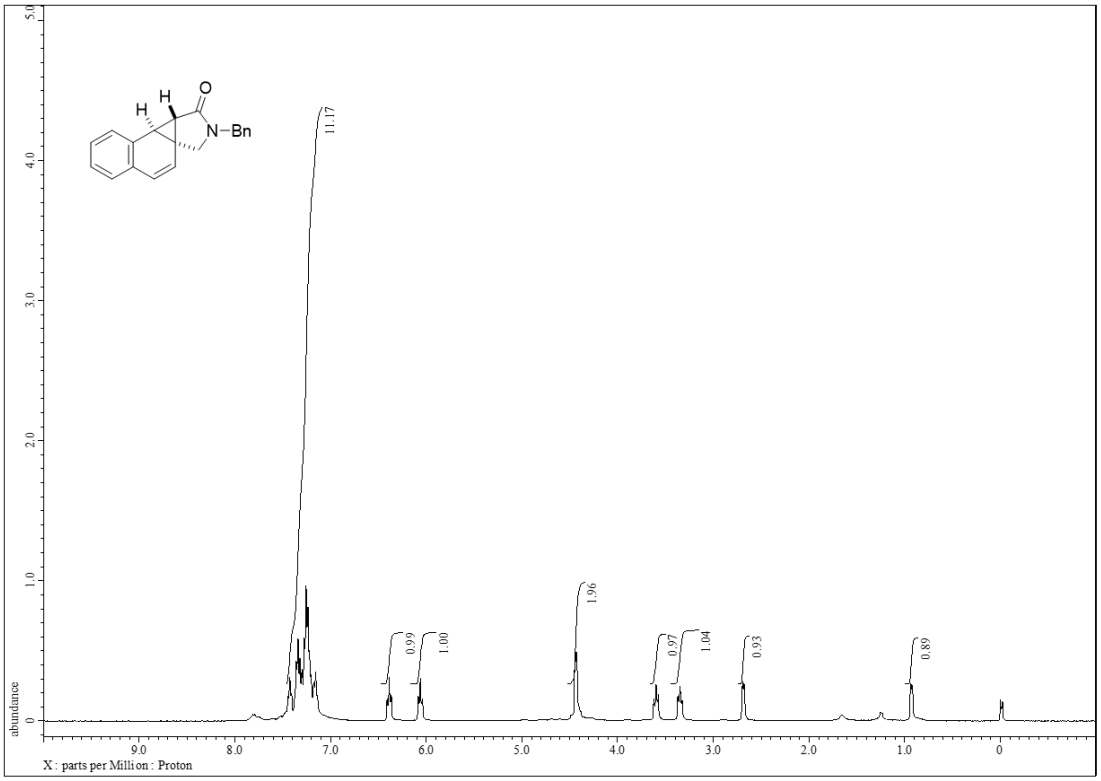

H
H
O
N—iPr
abundance
X : parts per Million : Carbon13
173.623
131.760
130.987
128.621
128.116
127.839
126.828
125.426
125.235
77.258
77.000
76.742
48.137
42.176
33.925
28.459
24.263
20.476
19.474

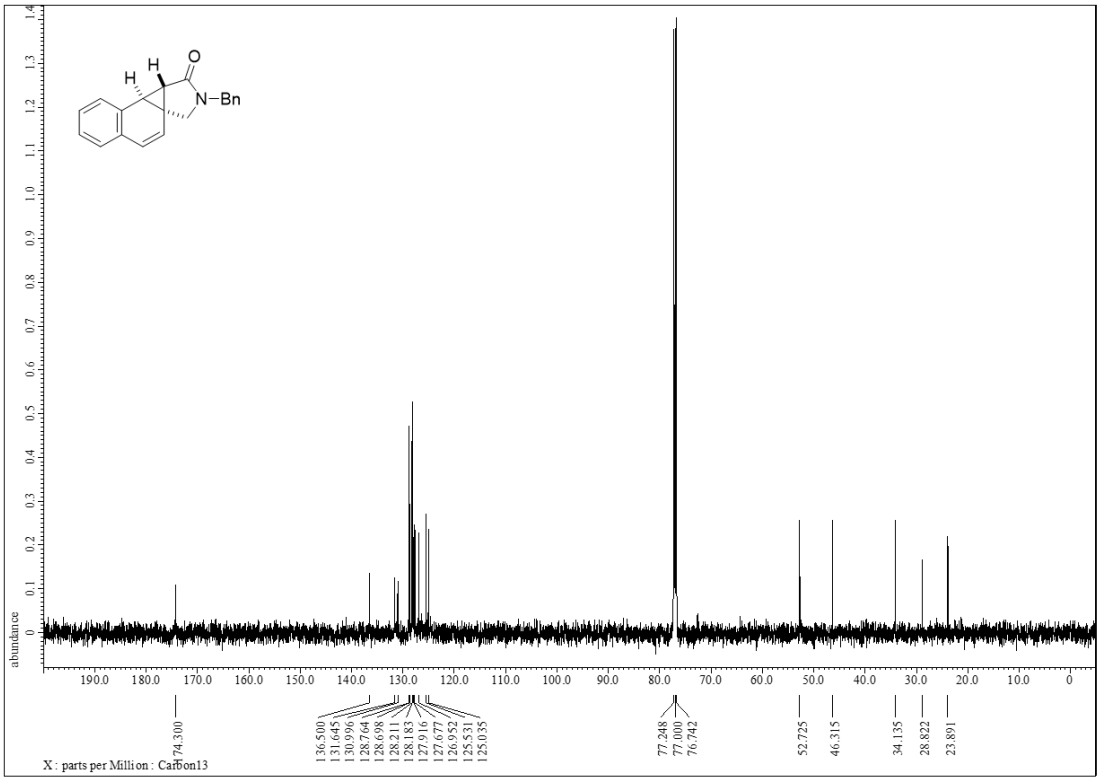

H
H
O
N—tBu
9.22
2.10
0.99
0.98
0.99
1.00
0.99
1.00
1.00
0.92
abundance
X : parts per Million : Proton

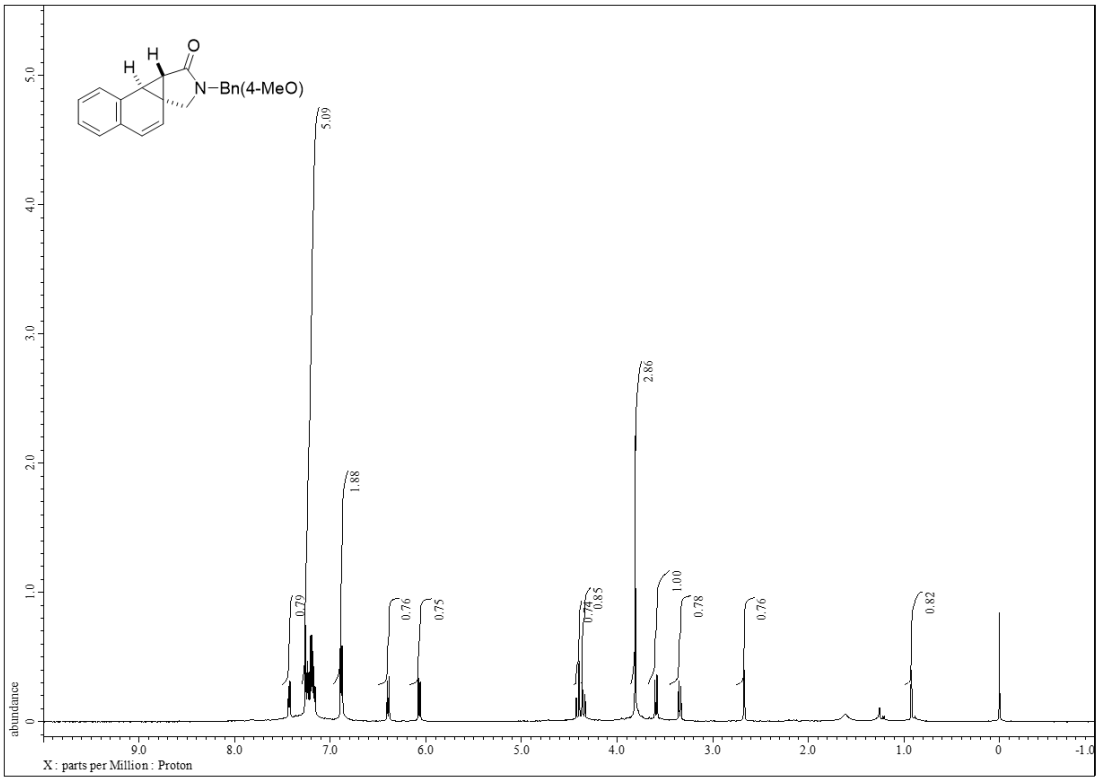

H
H
O
N—tBu
abundance
174.882
131.903
131.025
128.640
128.087
127.792
126.723
125.321
125.235
77.258
77.000
76.752
53.612
51.781
33.686
28.087
27.601
25.331
X : parts per Million : Carbon13

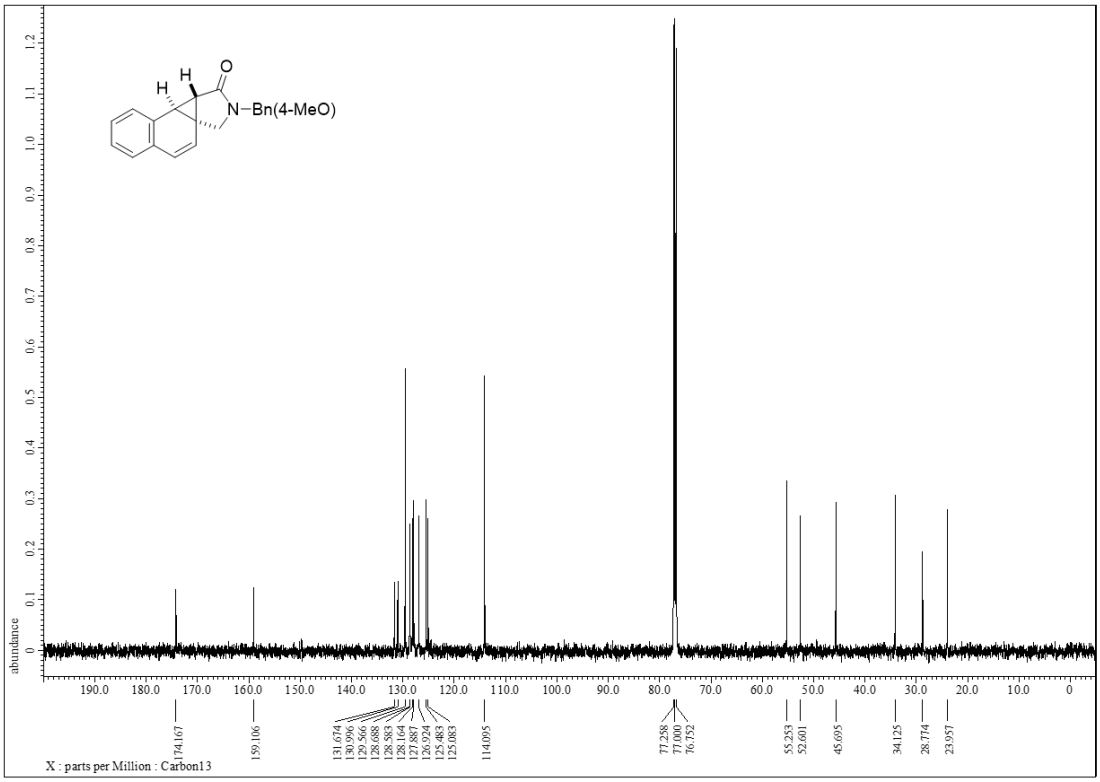

H
H
O
N–nPr
2.14
2.00
2.92
1.09
1.02
0.97
1.00
1.05
1.09
1.06
1.05
0.96
1.13
abundance
X : parts per Million : Proton

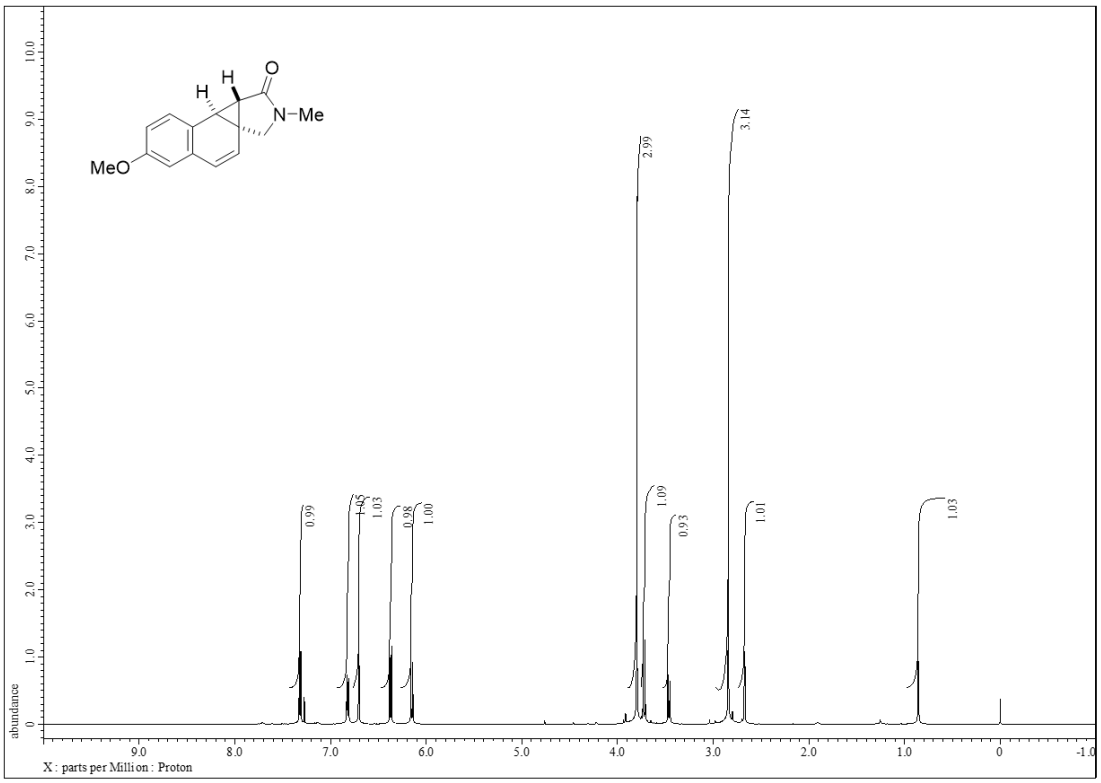

H
H
O
N–nPr
abundance
X : parts per Million : Carbon13
174.262
131.740
130.968
128.640
128.125
127.849
126.866
125.417
125.159
77.258
77.000
76.752
53.250
43.778
34.230
28.755
24.139
20.772
11.195

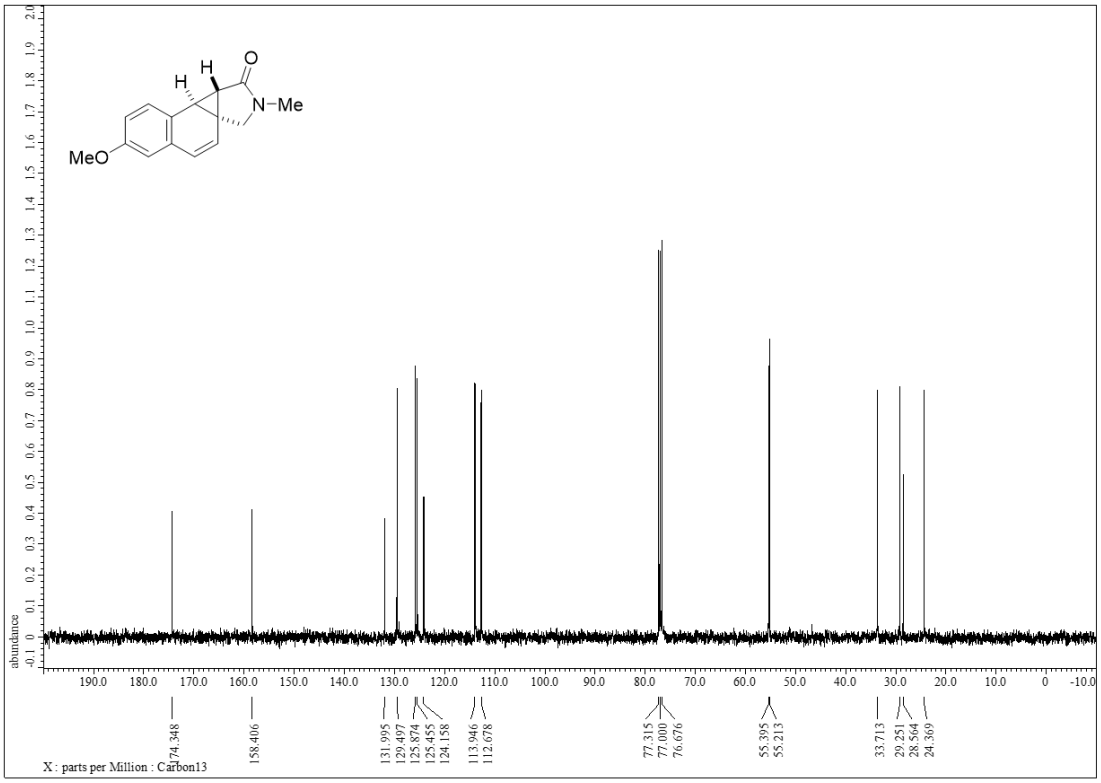

H
H
O
N–Bn
11.17
0.99
1.00
1.96
0.97
1.04
0.93
0.89
abundance
X : parts per Million : Proton

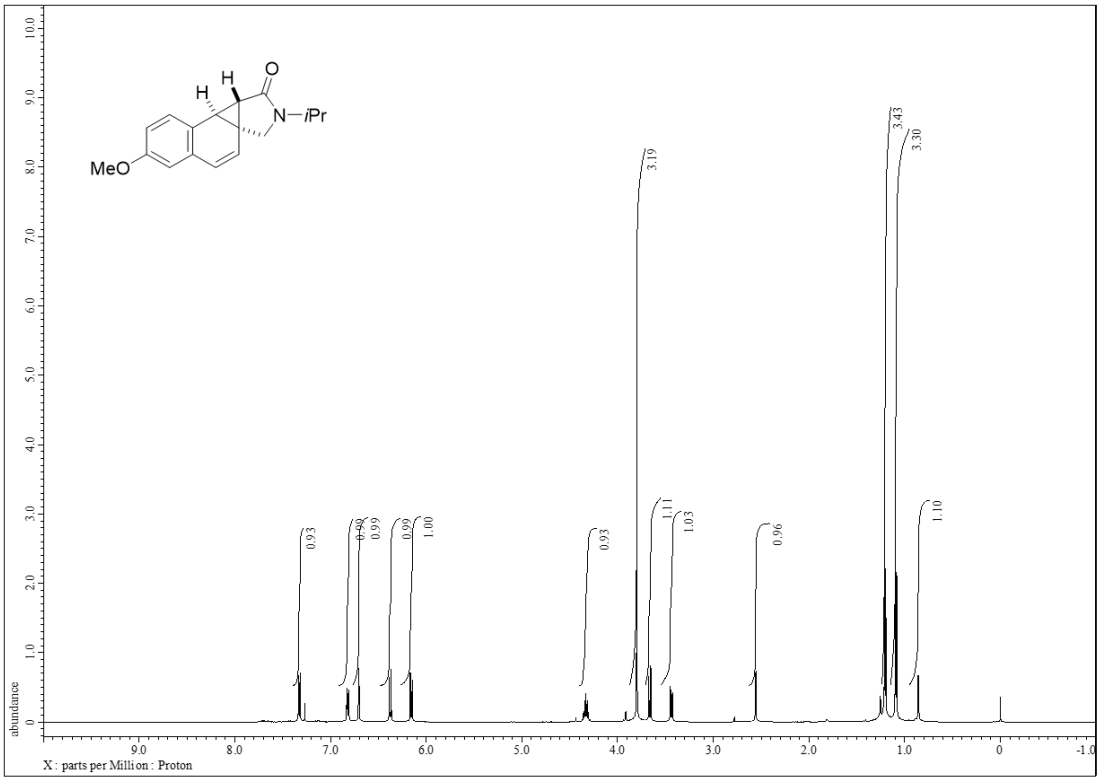

H
H
O
N–Bn
abundance
74.300
136.500
131.645
130.996
128.764
128.698
128.211
128.183
127.916
127.677
126.952
125.531
125.035
77.248
77.000
76.742
52.725
46.315
34.135
28.822
23.891
X : parts per Million : Carbon13

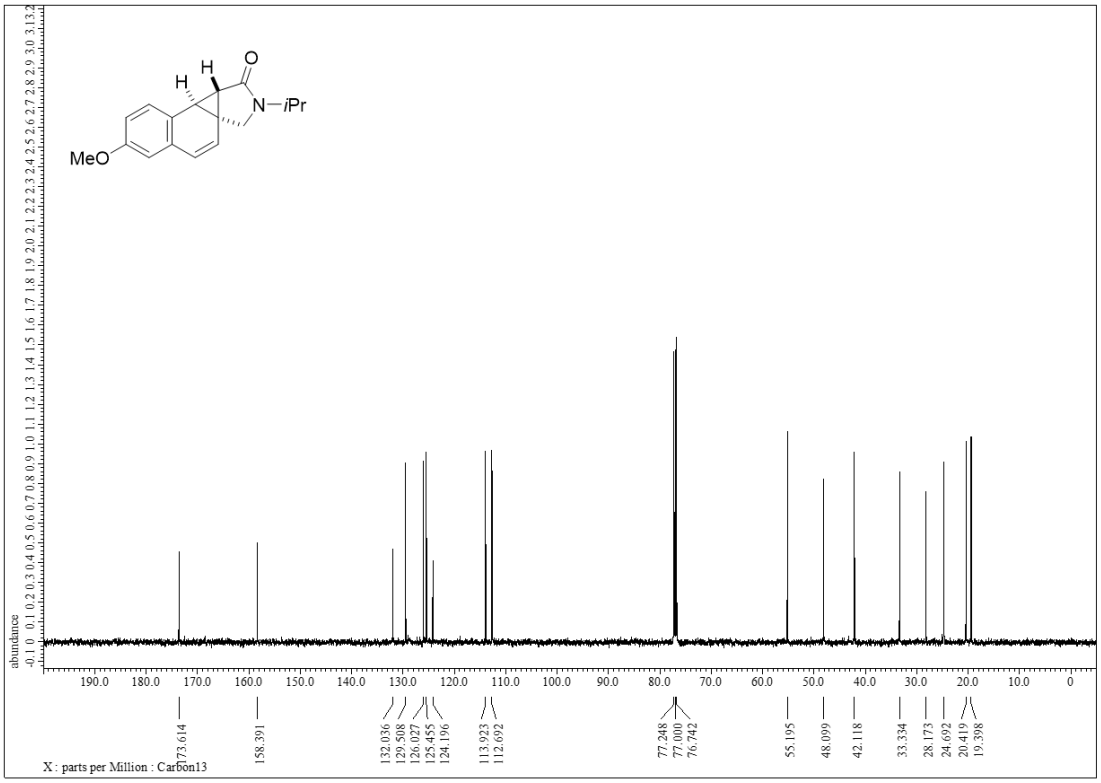

N–Bn(4-MeO)
5.09
1.88
2.86
0.79
0.76
0.75
0.74
0.85
1.00
0.78
0.76
0.82
abundance
X : parts per Million : Proton

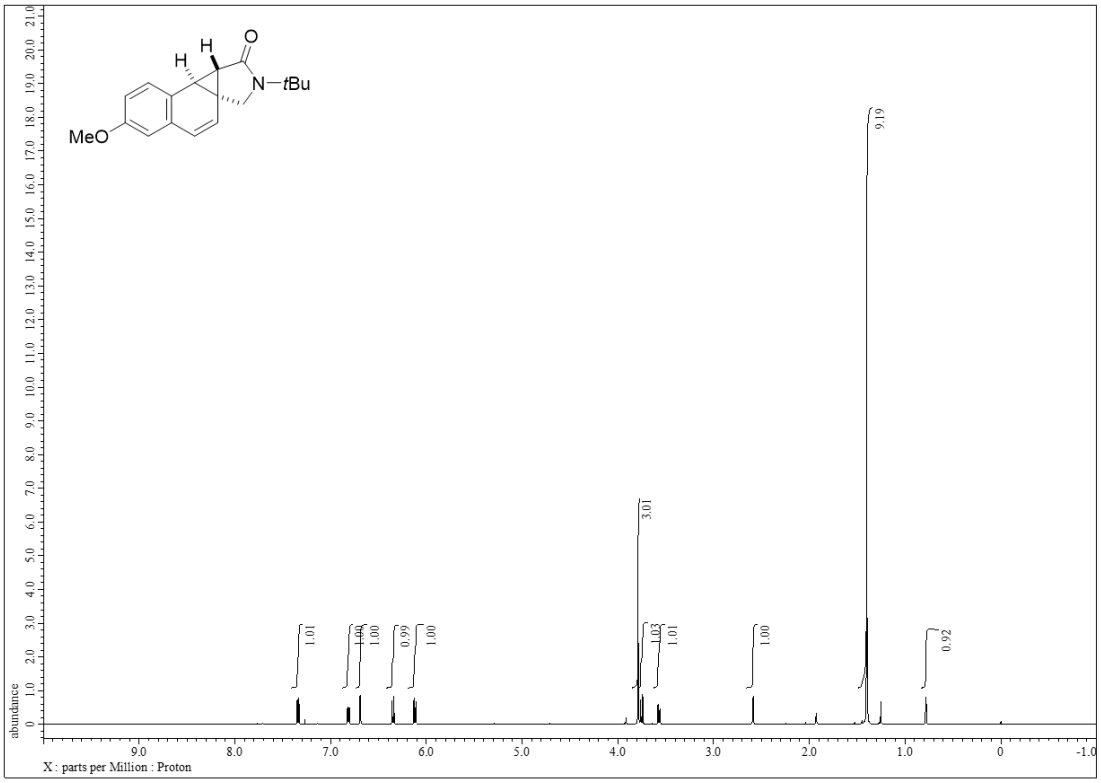

N–Bn(4-MeO)
abundance
174.167
159.106
131.674
130.996
129.566
128.688
128.164
127.887
126.924
125.483
125.083
114.095
77.258
77.000
76.752
55.253
52.601
45.695
34.125
28.774
23.957
X : parts per Million : Carbon13

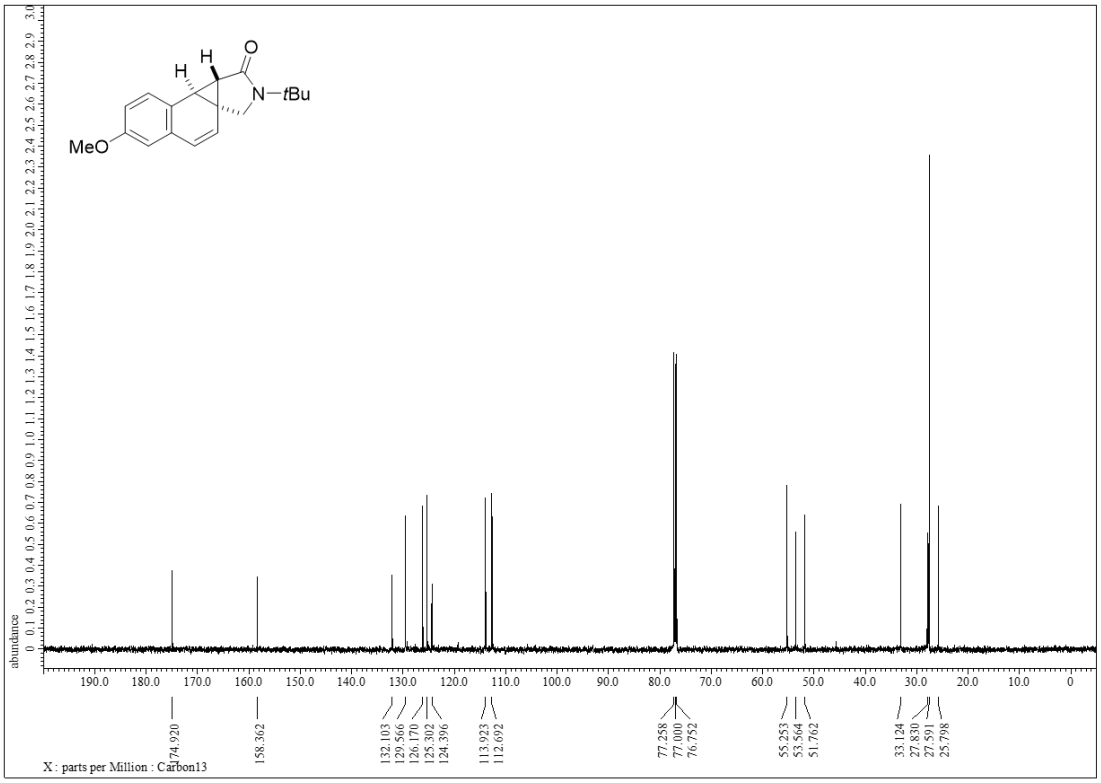

H
H
O
N–Me
MeO
0.99
1.05
1.03
0.98
1.00
2.99
1.09
0.93
3.14
1.01
1.03
abundance
X : parts per Million : Proton

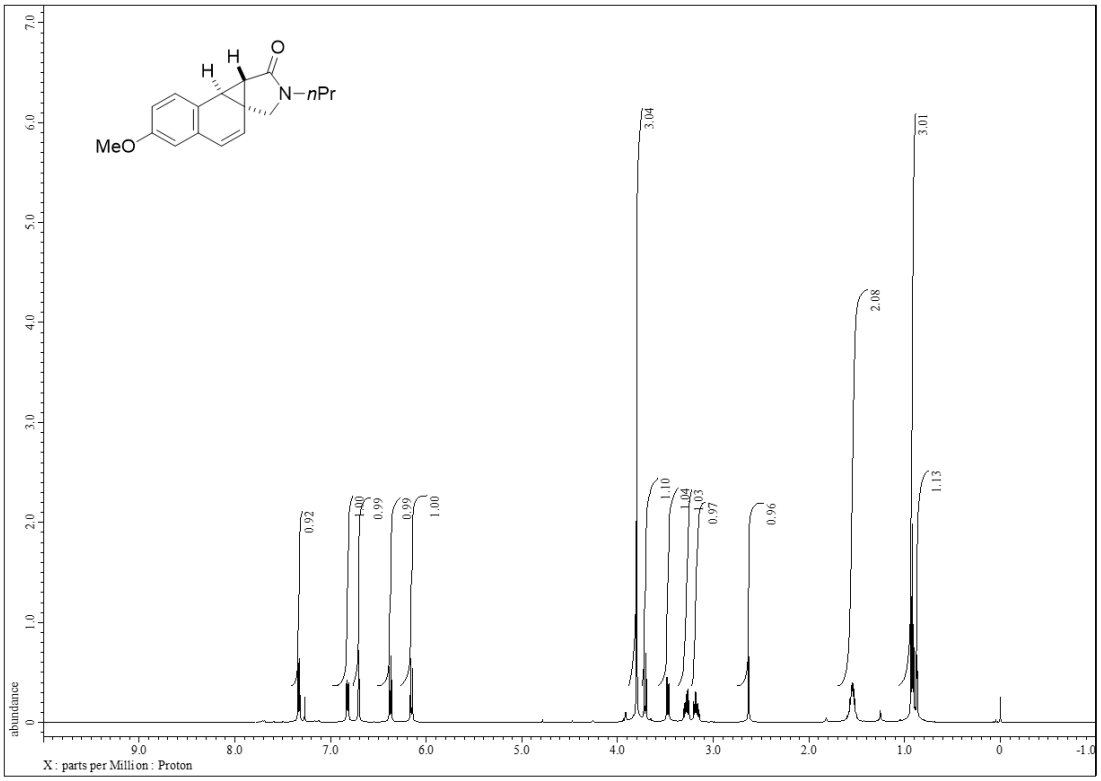

H
H
O
N–Me
MeO
abundance
174.348
158.406
131.995
129.497
125.874
125.455
124.158
113.946
112.678
77.315
77.000
76.676
55.395
55.213
33.713
29.251
28.564
24.369
X : parts per Million : Carbon13

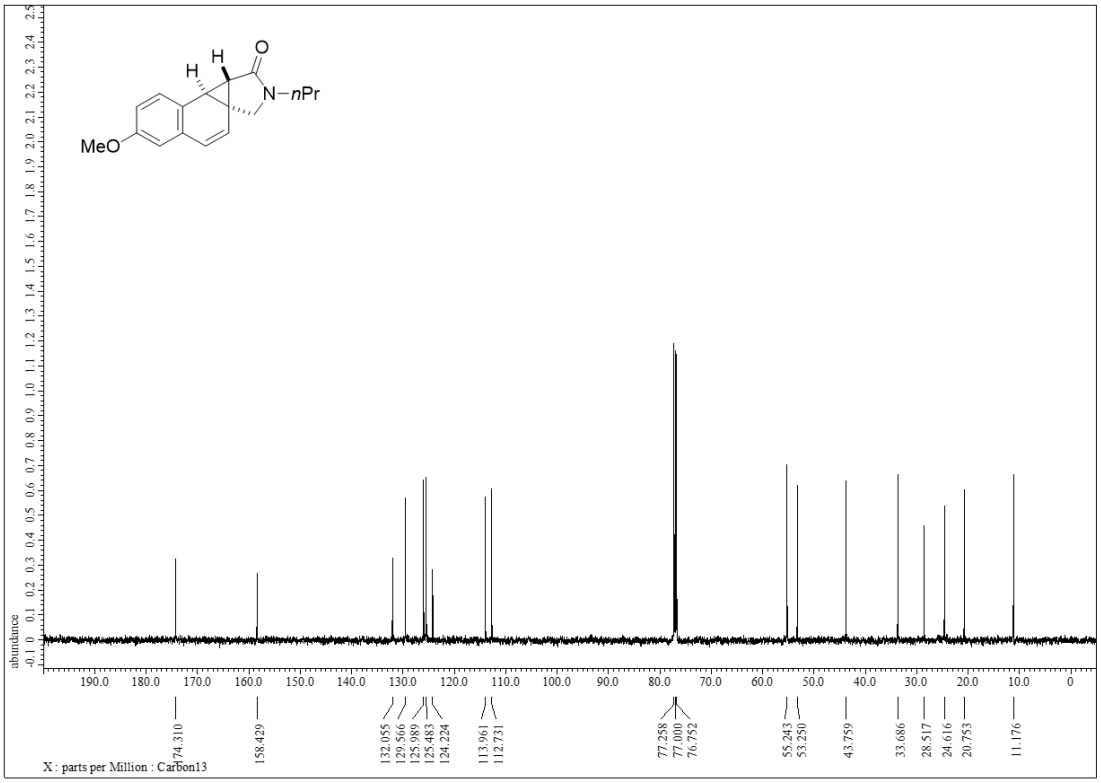

MeO
N—iPr
0.93
0.98
0.99
0.99
1.00
0.93
3.19
1.11
1.03
0.96
3.43
3.30
1.10
abundance
X : parts per Million : Proton

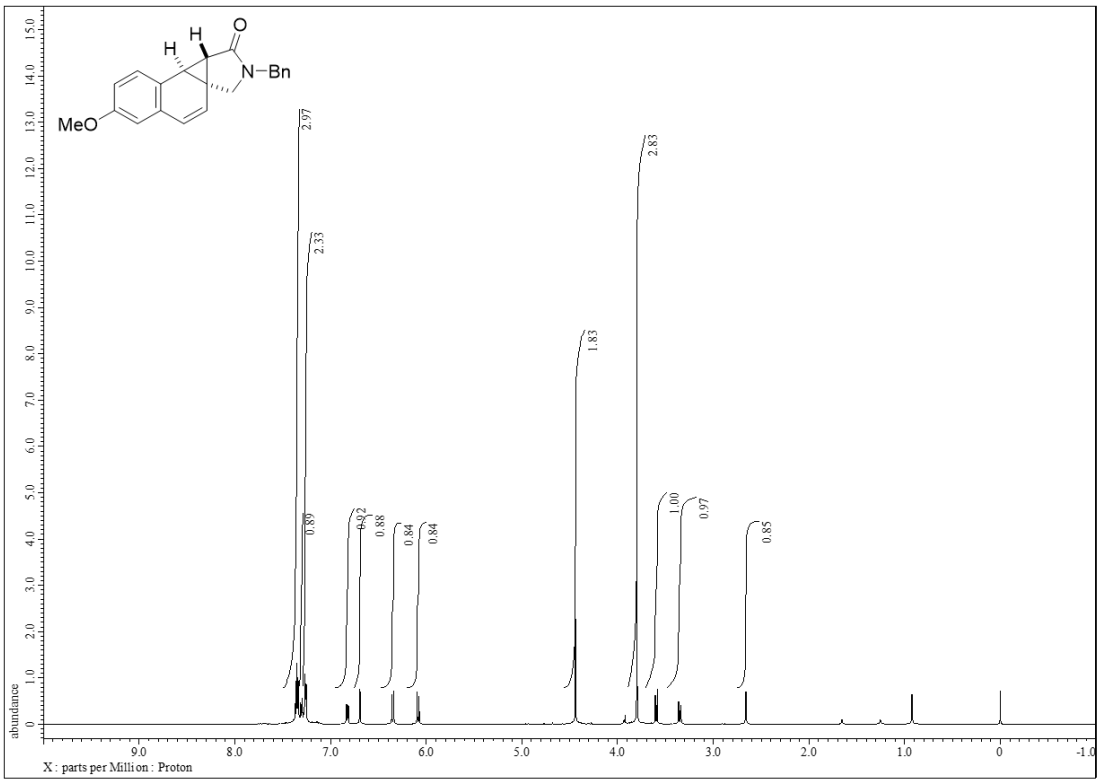

MeO
N—iPr
abundance
173.614
158.391
132.036
129.508
126.027
125.455
124.196
113.923
112.692
77.248
77.000
76.742
55.195
48.099
42.118
33.334
28.173
24.692
20.419
19.398
X : parts per Million : Carbon13

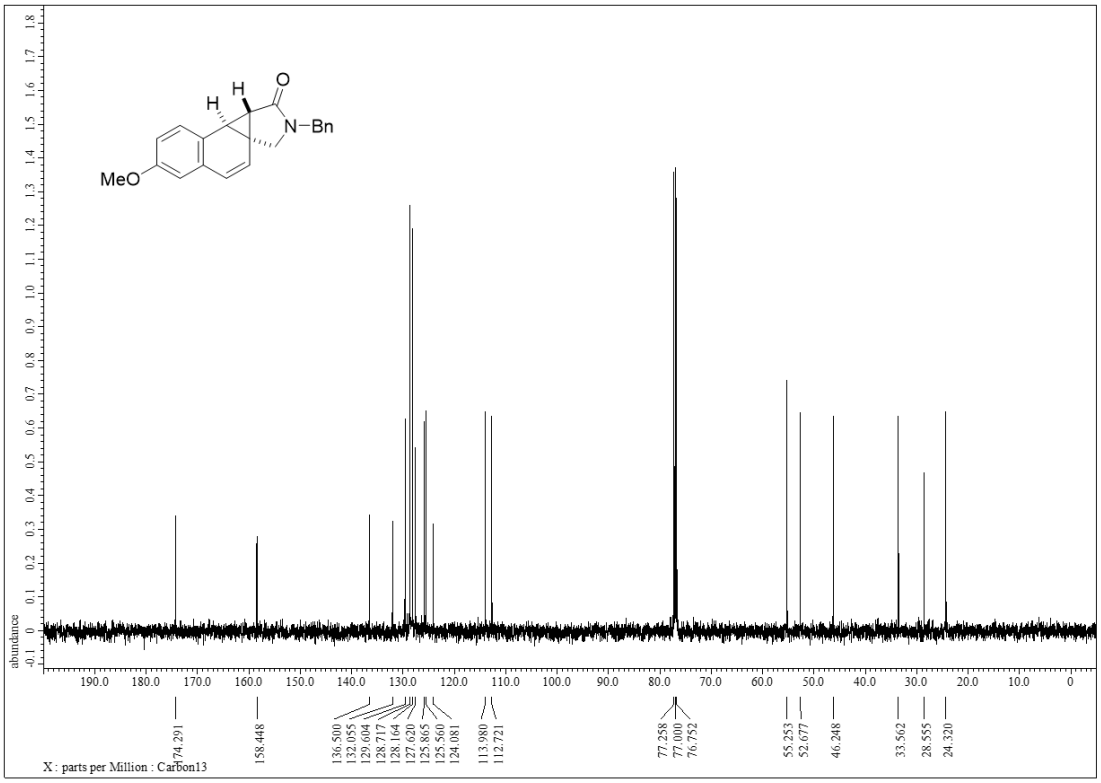

MeO
N—tBu
1.01
1.00
1.00
0.99
1.00
3.01
1.03
1.01
1.00
9.19
0.92
abundance
X : parts per Million : Proton

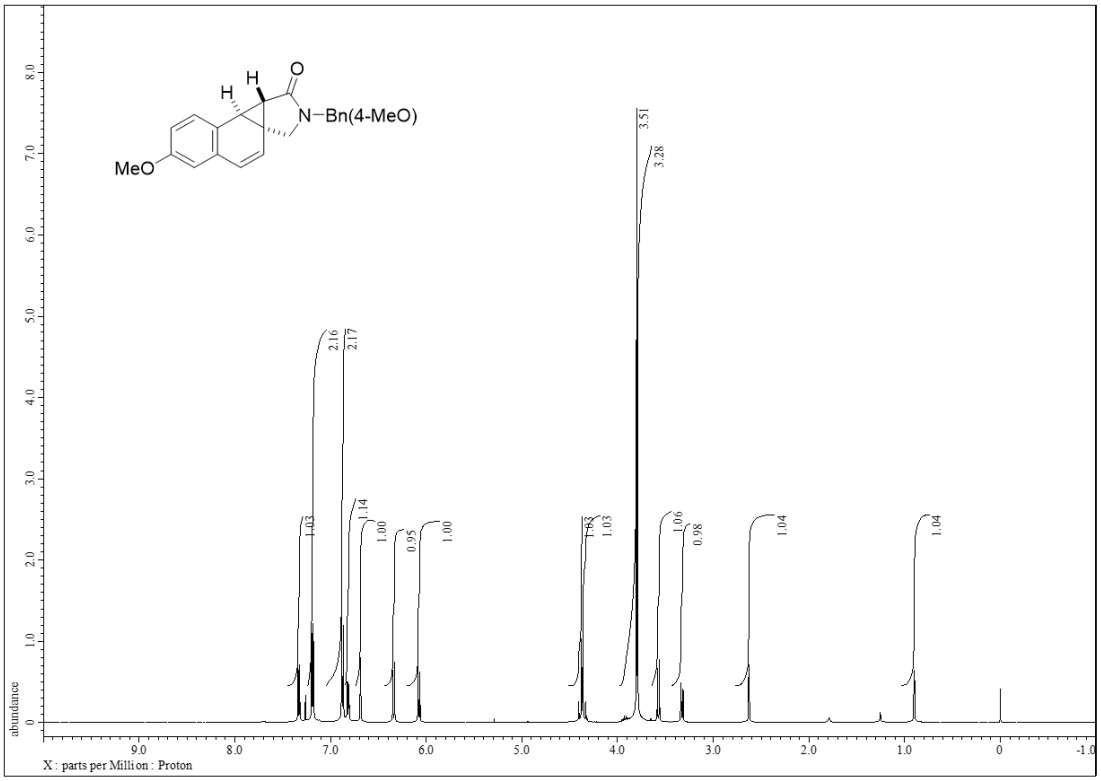

MeO
N—tBu
abundance
174.920
158.362
132.103
129.566
126.170
125.302
124.396
113.923
112.692
77.258
77.000
76.752
55.253
53.564
51.762
33.124
27.830
27.591
25.798
X : parts per Million : Carbon13

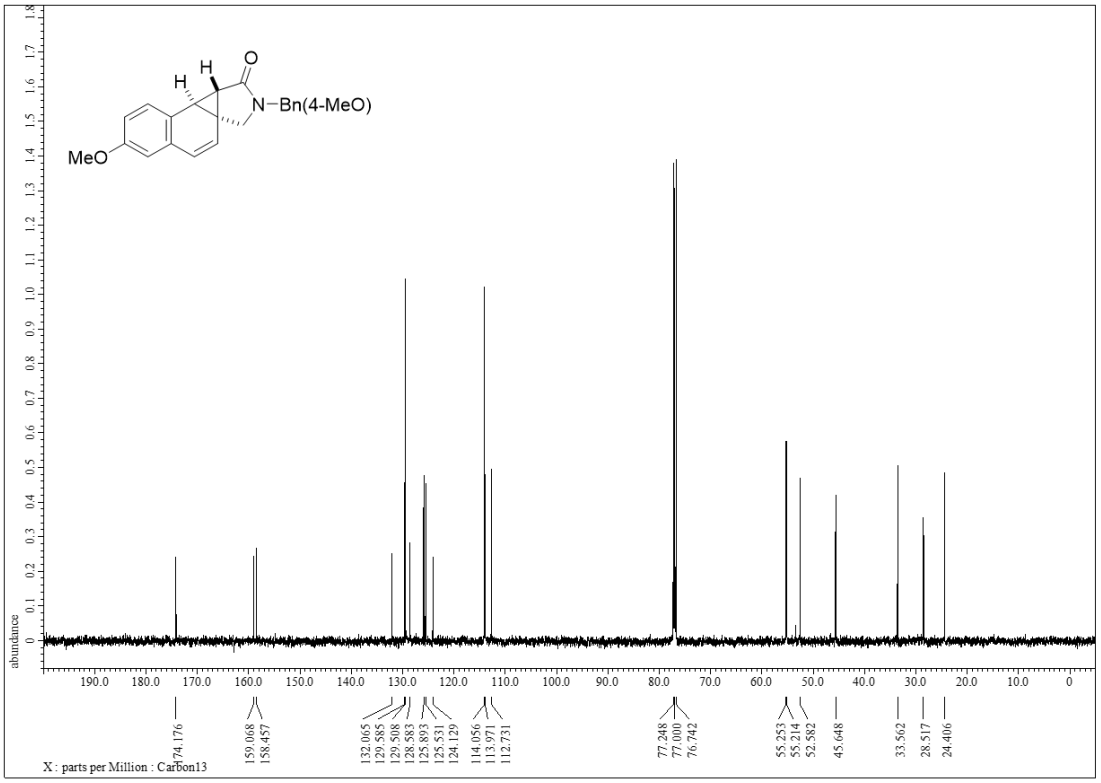

H
H
O
N–nPr
MeO
3.04
3.01
2.08
1.13
1.10
1.04
1.03
1.00
0.99
0.99
0.97
0.96
0.92
abundance
X : parts per Million : Proton

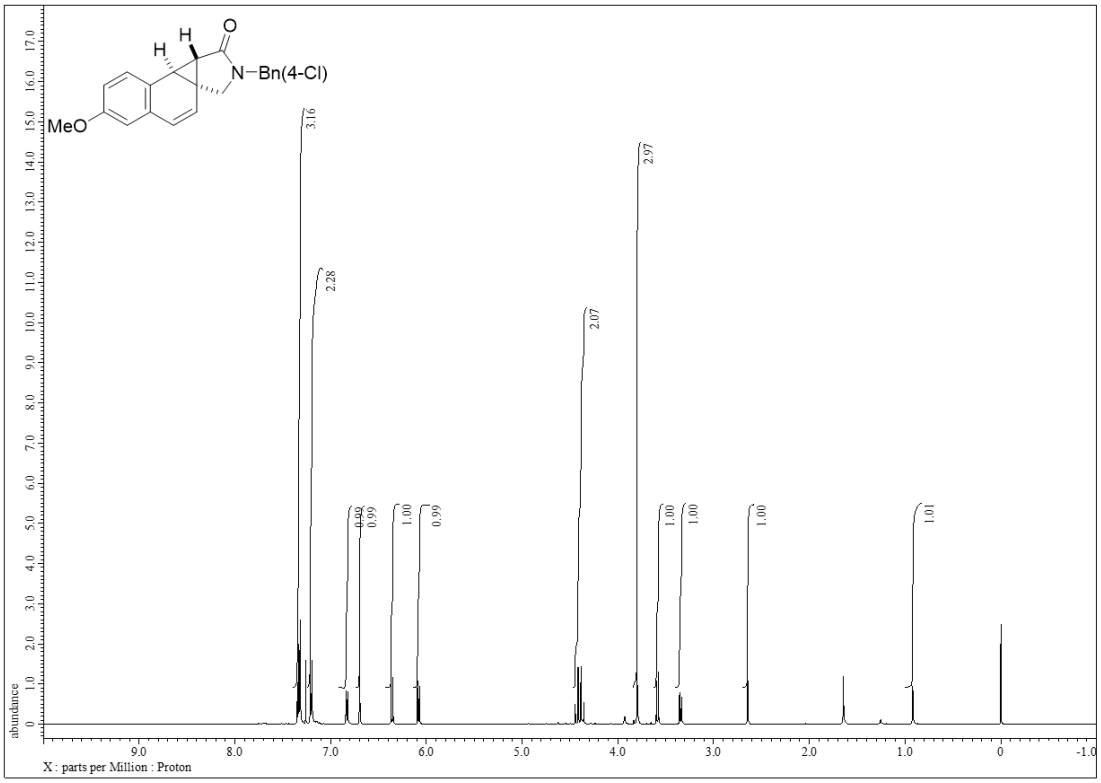

H
H
O
N–nPr
MeO
abundance
X : parts per Million : Carbon13
174.310
158.429
132.055
129.566
125.989
125.483
124.224
113.961
112.731
77.258
77.000
76.752
55.243
53.250
43.759
33.686
28.517
24.616
20.753
11.176

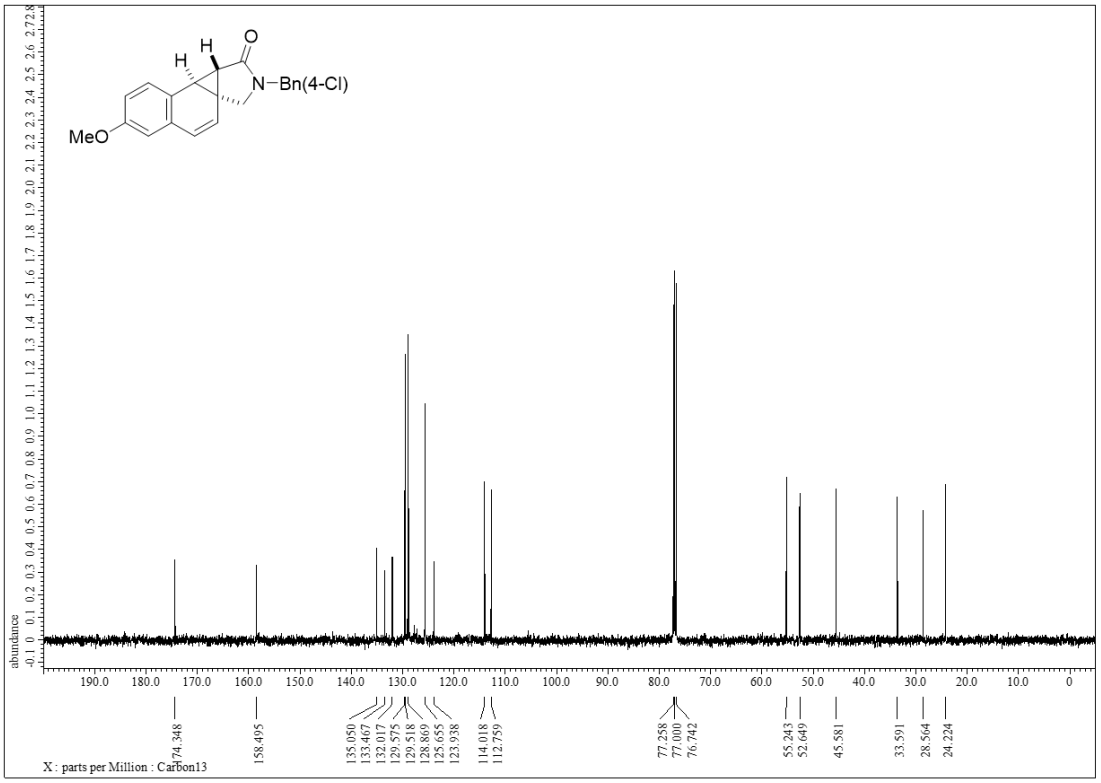

MeO
N–Bn
O
H
H
2.97
2.33
0.89
4.12
0.88
0.84
0.84
1.83
2.83
1.00
0.97
0.85
abundance
X : parts per Million : Proton

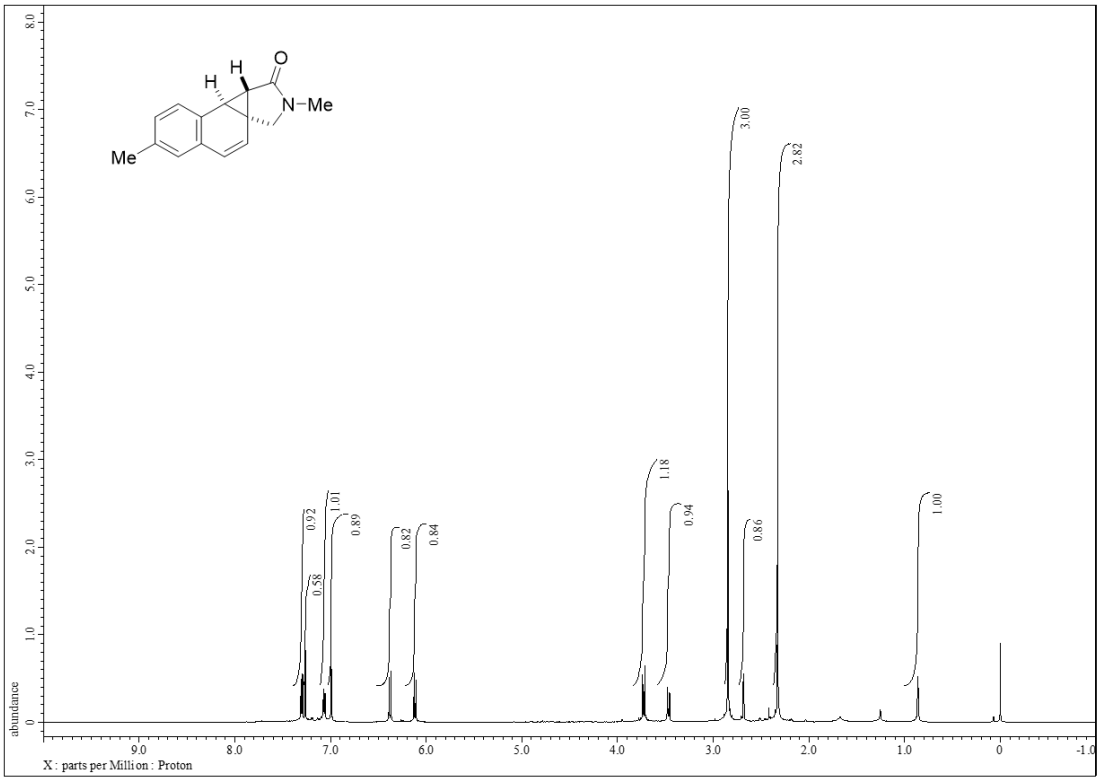

MeO
N–Bn
O
H
H
abundance
X : parts per Million : Carbon13
174.291
158.448
136.500
132.055
129.604
128.717
128.164
127.620
125.865
125.560
124.081
113.980
112.721
77.258
77.000
76.752
55.253
52.677
46.248
33.562
28.555
24.320

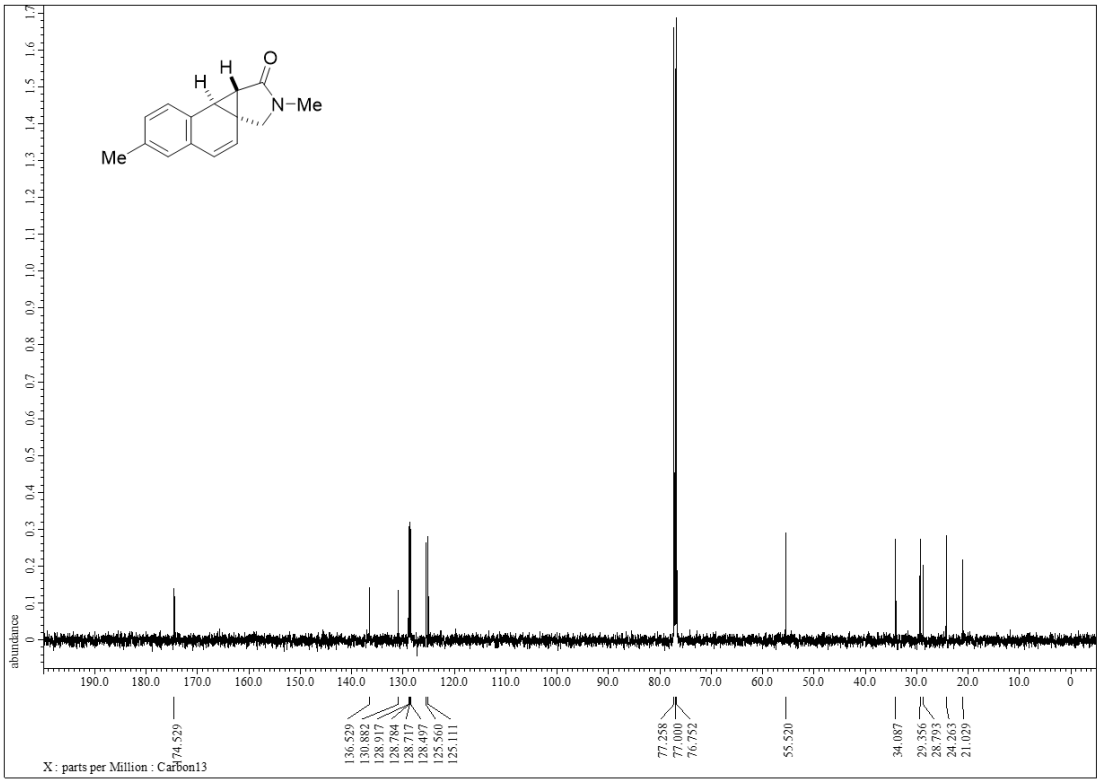

H
H
O
N–Bn(4-MeO)
MeO
3.51
3.28
2.16
2.17
1.14
1.03
1.00
0.95
1.00
1.83
1.03
1.06
0.98
1.04
1.04
abundance
X : parts per Million : Proton

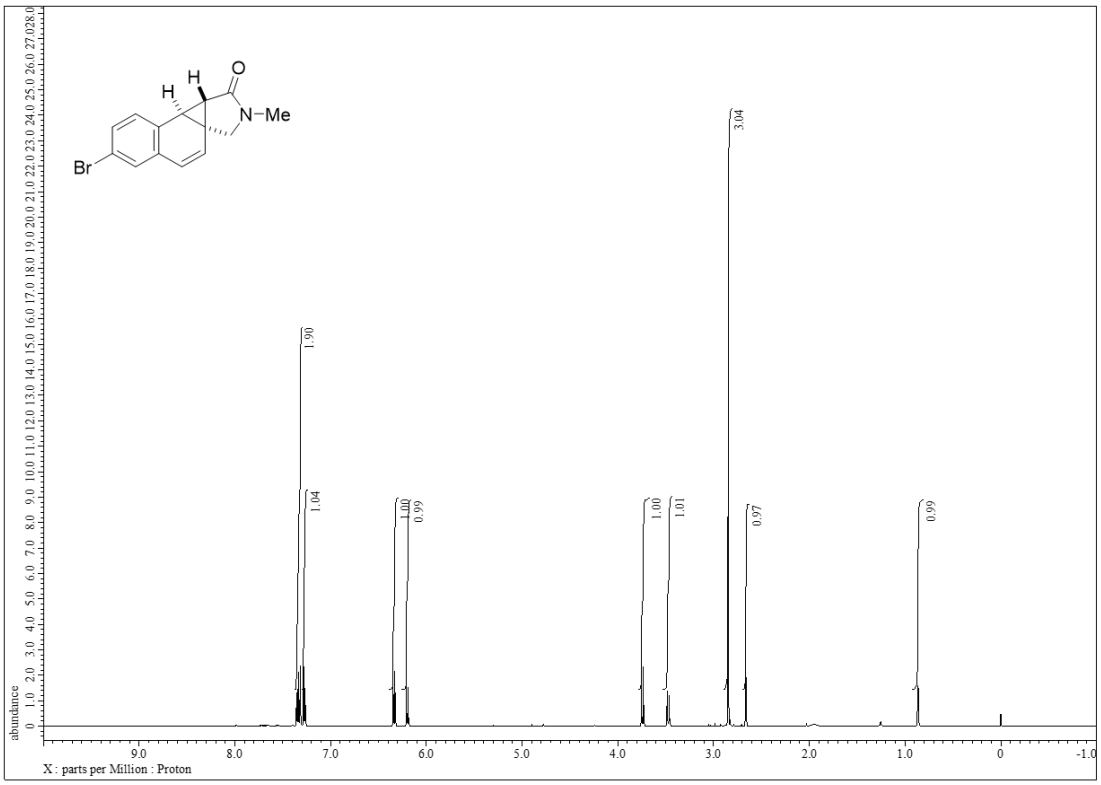

H
H
O
N–Bn(4-MeO)
MeO
abundance
174.176
159.068
158.457
132.065
129.585
129.508
128.583
125.893
125.531
124.129
114.056
113.971
112.731
77.248
77.000
76.742
55.253
55.214
52.582
45.648
33.562
28.517
24.406
X : parts per Million : Carbon13

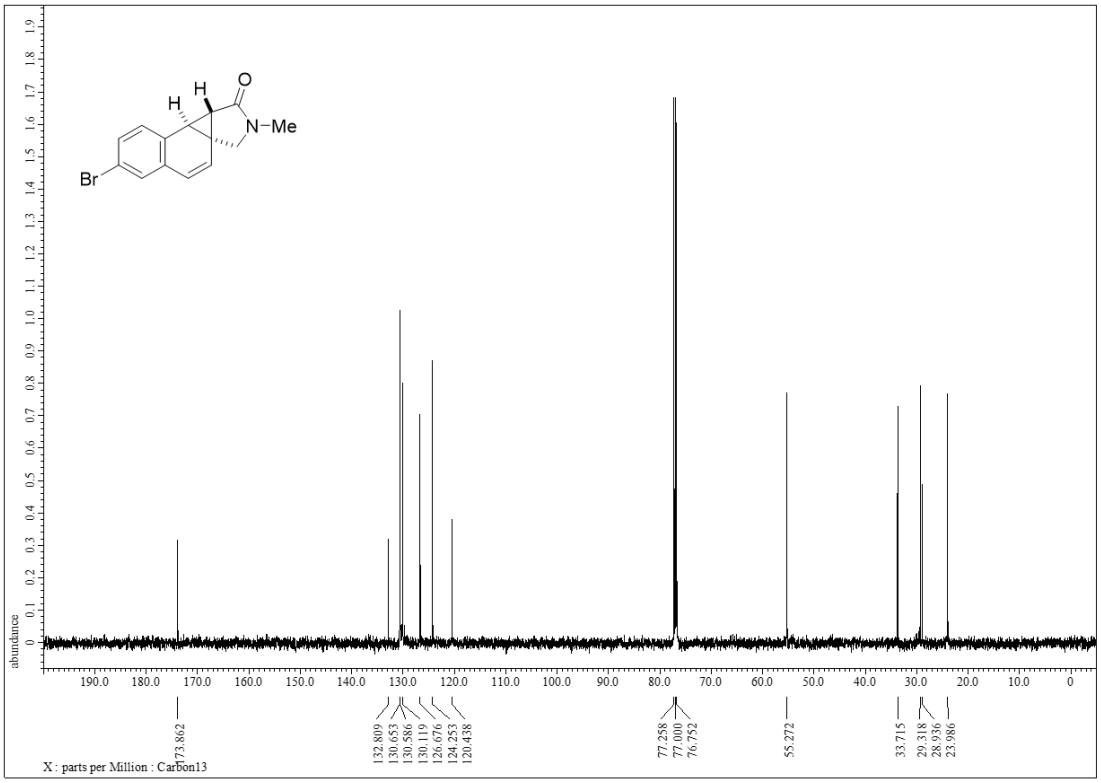

MeO
N–Bn(4-Cl)
3.16
2.28
0.99
0.99
1.00
0.99
2.07
2.97
1.00
1.00
1.00
1.01
abundance
X : parts per Million : Proton

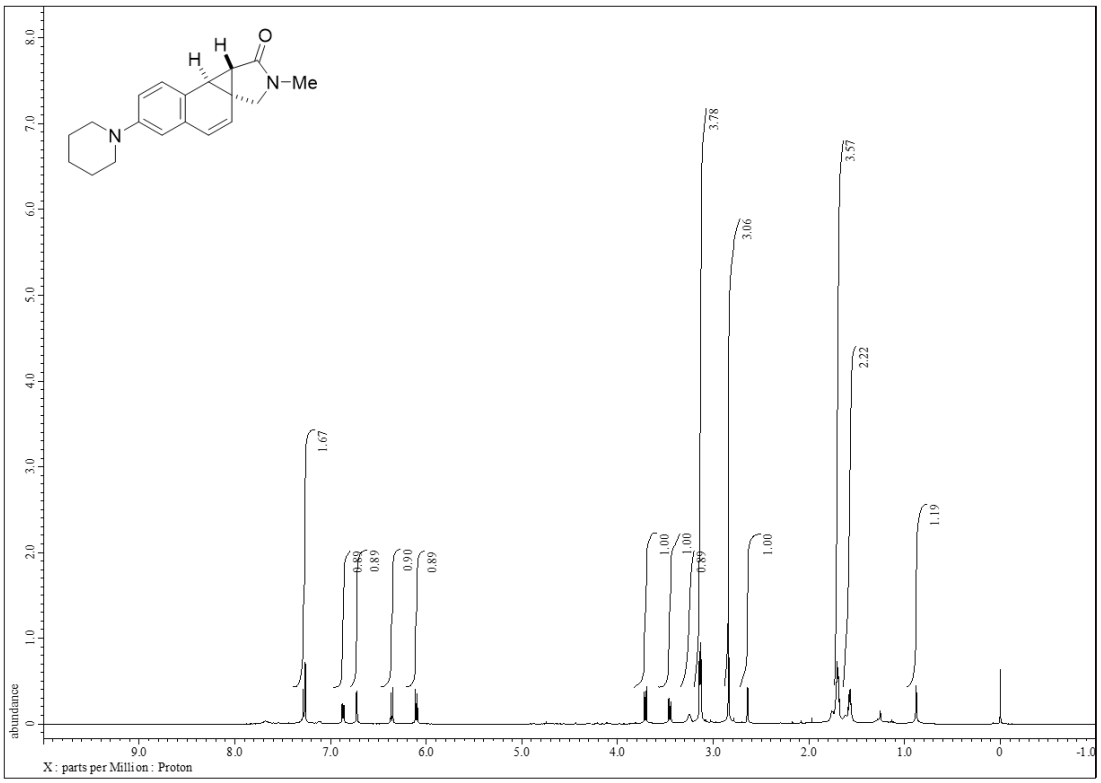

MeO
N–Bn(4-Cl)
abundance
X : parts per Million : Carbon13
174.348
158.495
135.050
133.467
132.017
129.575
129.518
128.869
125.655
123.938
114.018
112.759
77.258
77.000
76.742
55.243
52.649
45.581
33.591
28.564
24.224

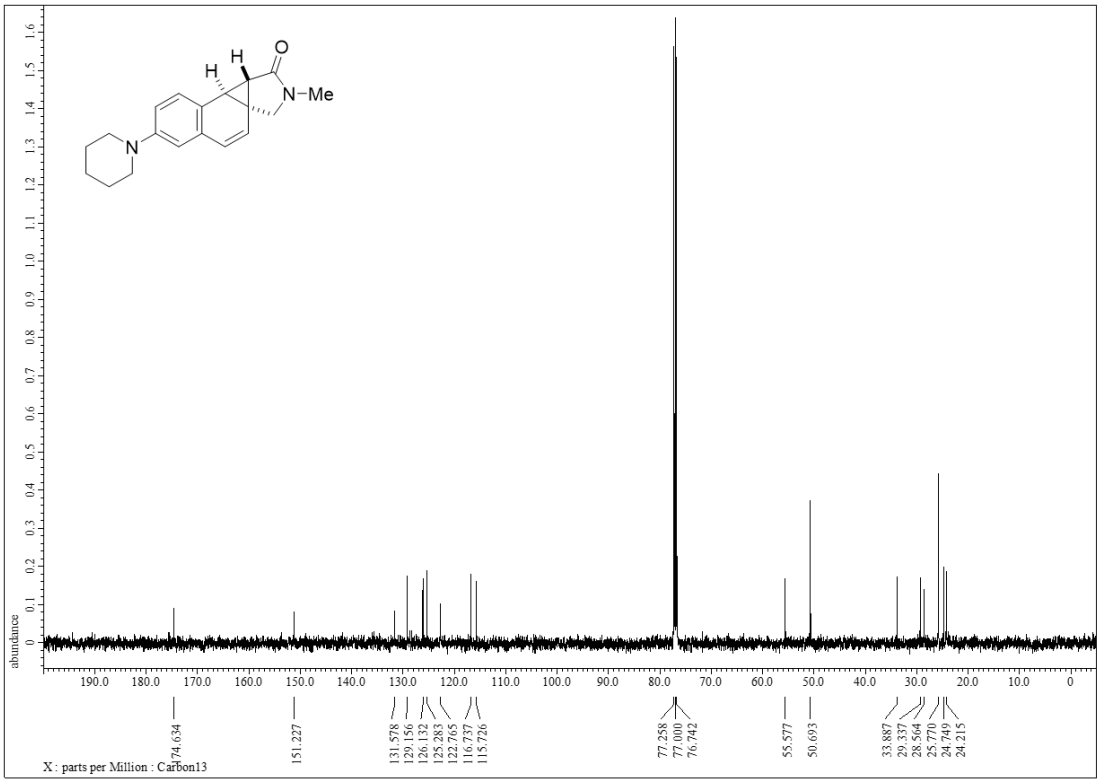

H
H
O
N–Me
Me
0.92
0.58
1.01
0.89
0.82
0.84
1.18
0.94
3.00
2.82
0.86
1.00
abundance
X : parts per Million : Proton

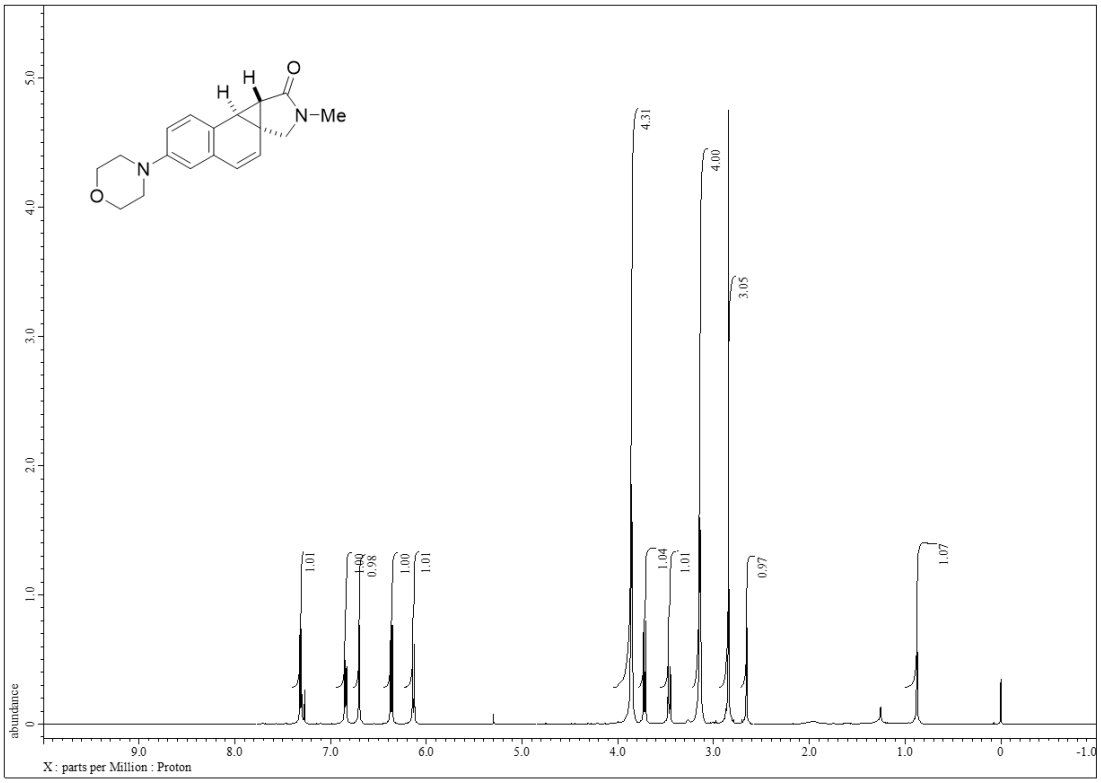

H
H
O
N–Me
Me
abundance
74.529
136.529
130.882
128.917
128.784
128.717
128.497
125.560
125.111
77.258
77.000
76.752
55.520
34.087
29.356
28.793
24.263
21.029
X : parts per Million : Carbon13

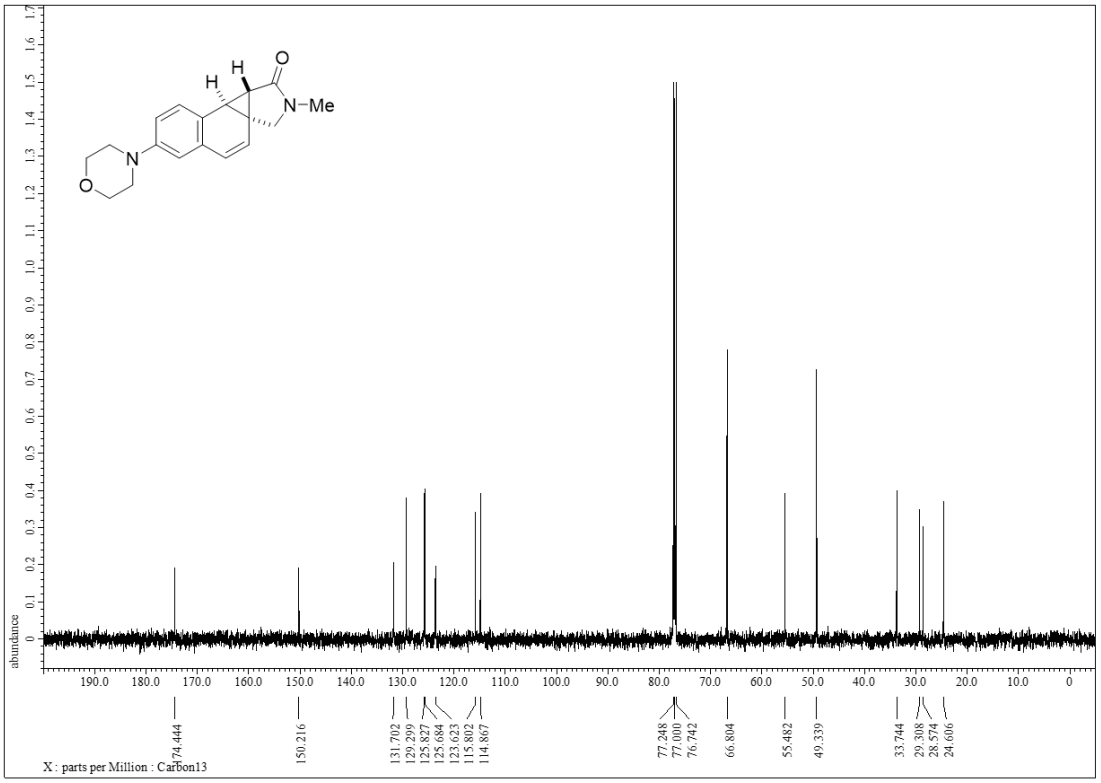

H
H
O
N–Me
Br
1.90
1.04
1.00
0.99
1.00
1.01
3.04
0.97
0.99
abundance
X : parts per Million : Proton

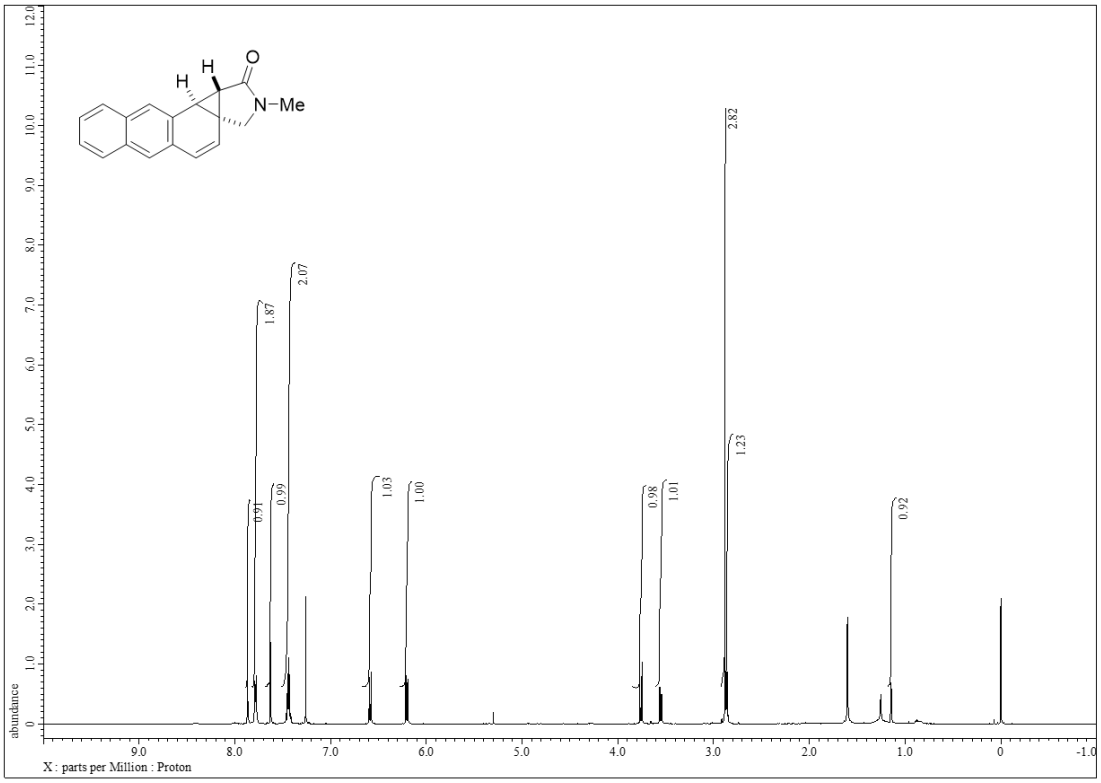

H
H
O
N–Me
Br
abundance
X : parts per Million : Carbon13
173.862
132.809
130.653
130.586
130.119
126.676
124.253
120.438
77.258
77.000
76.752
55.272
33.715
29.318
28.936
23.986

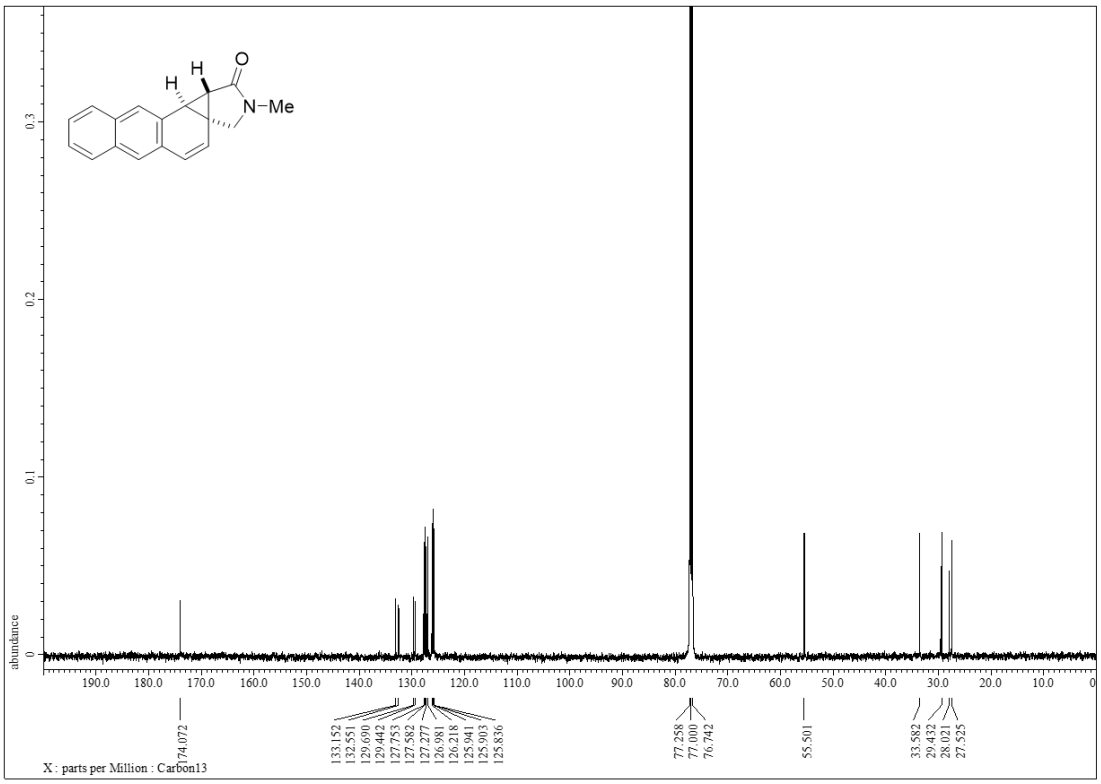

H
H
O
N–Me
N
1.67
0.89
0.89
0.90
0.89
1.00
1.00
0.89
3.78
3.06
1.00
3.57
2.22
1.19
abundance
X : parts per Million : Proton

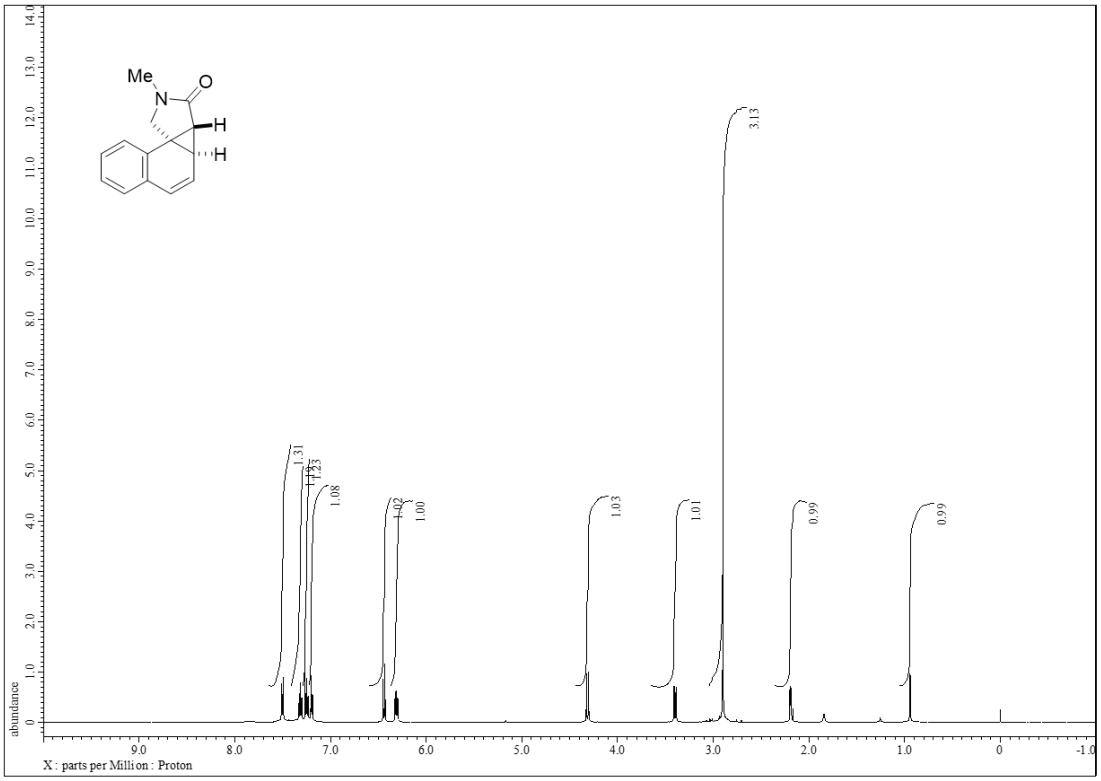

H
H
O
N–Me
N
abundance
174.634
151.227
131.578
129.156
126.132
125.283
122.765
116.737
115.726
77.258
77.000
76.742
55.577
50.693
33.887
29.337
28.564
25.770
24.749
24.215
X : parts per Million : Carbon13

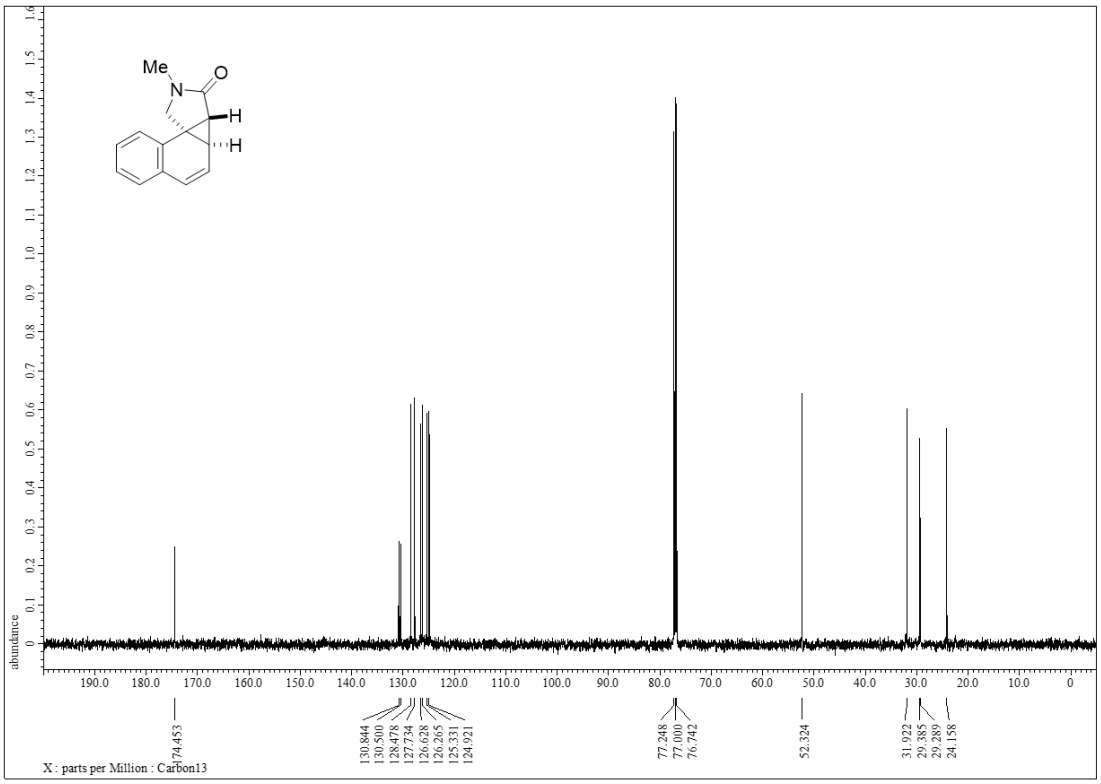

H
H
O
N–Me
N
O
4.31
4.00
3.05
1.01
1.00
0.98
1.00
1.01
1.04
1.01
0.97
1.07
abundance
X : parts per Million : Proton

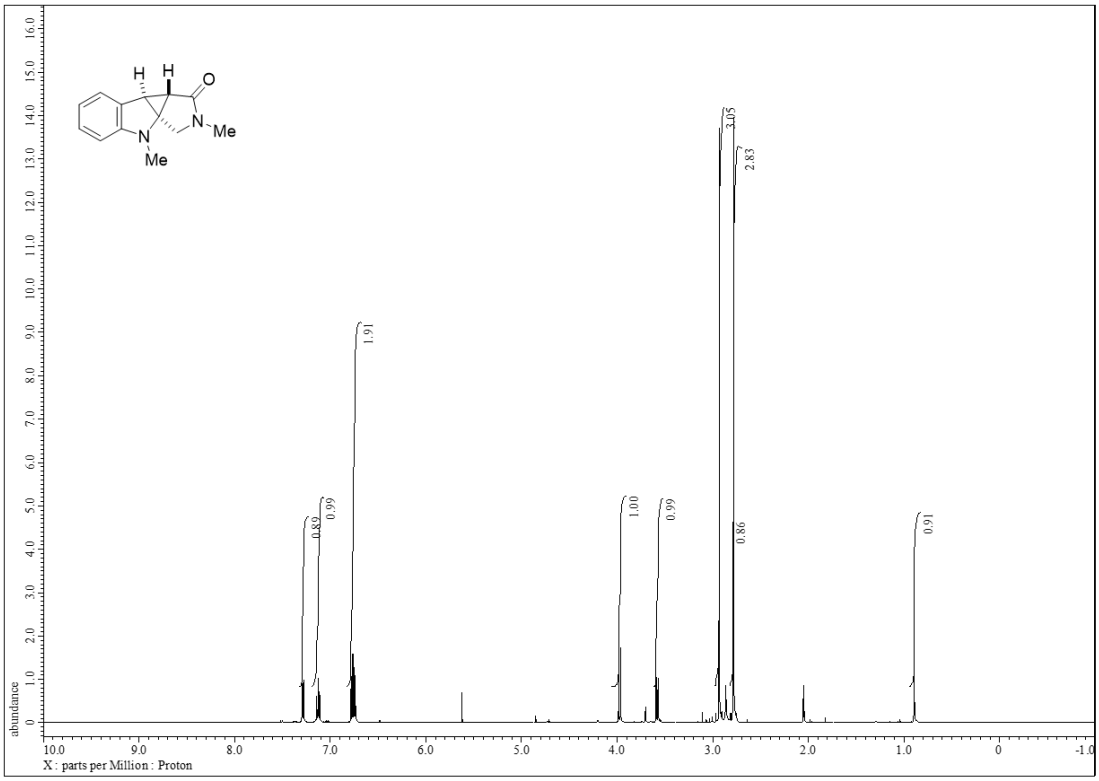

H
H
O
N–Me
N
O
abundance
X : parts per Million : Carbon13
174.444
150.216
131.702
129.299
125.827
125.684
123.623
115.802
114.867
77.248
77.000
76.742
66.804
55.482
49.339
33.744
29.308
28.574
24.606

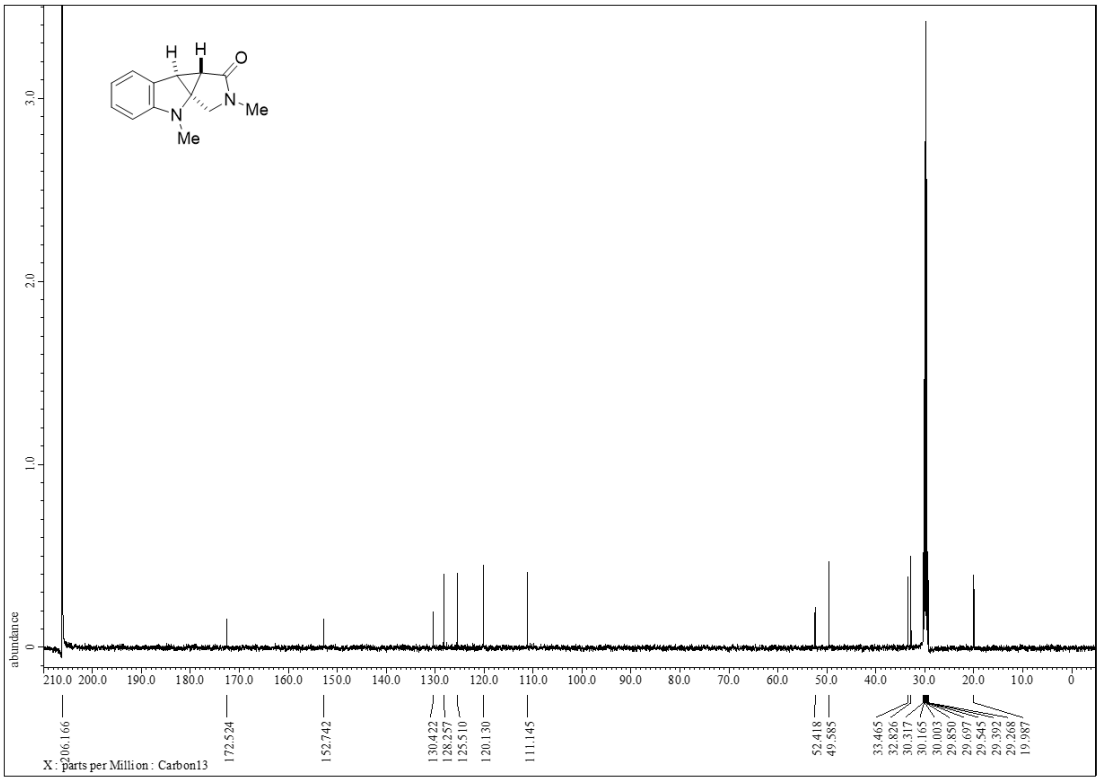

H
H
O
N–Me
2.82
2.07
1.87
1.23
1.03
1.00
0.99
0.98
1.01
0.92
0.91
abundance
X : parts per Million : Proton

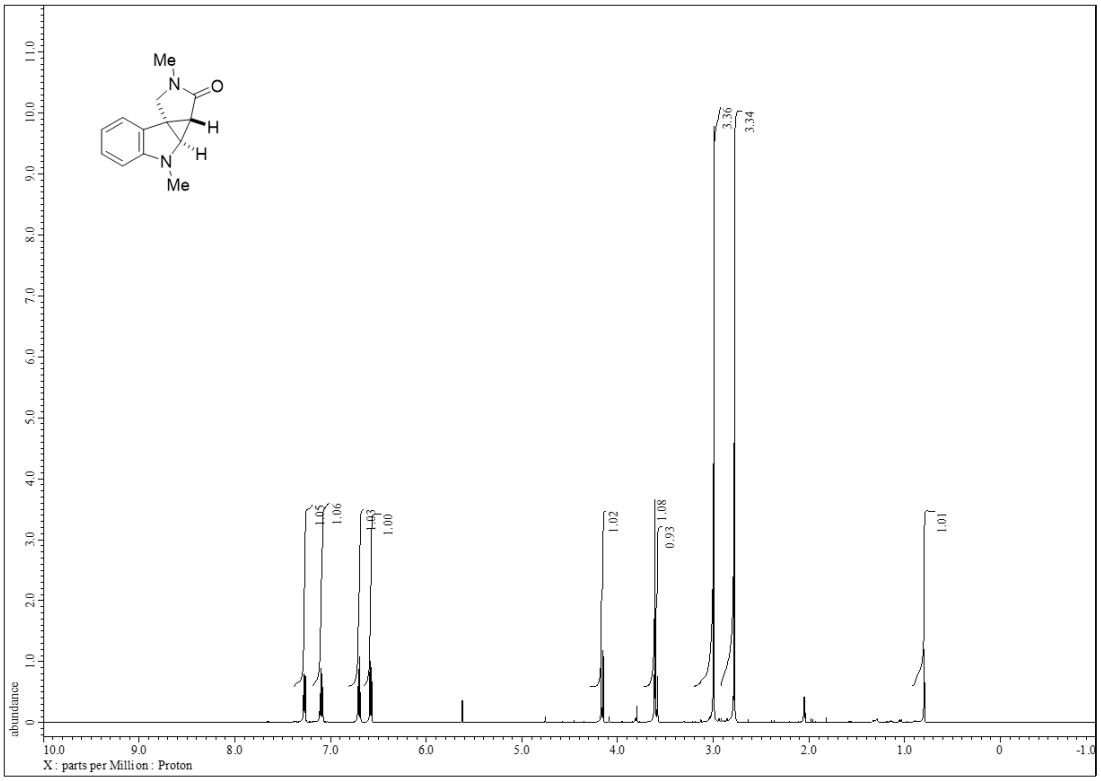

H
H
O
N–Me
abundance
174.072
133.152
132.551
129.690
129.442
127.753
127.582
127.277
126.981
126.218
125.941
125.903
125.836
77.258
77.000
76.742
55.501
33.582
29.432
28.021
27.525
X : parts per Million : Carbon13

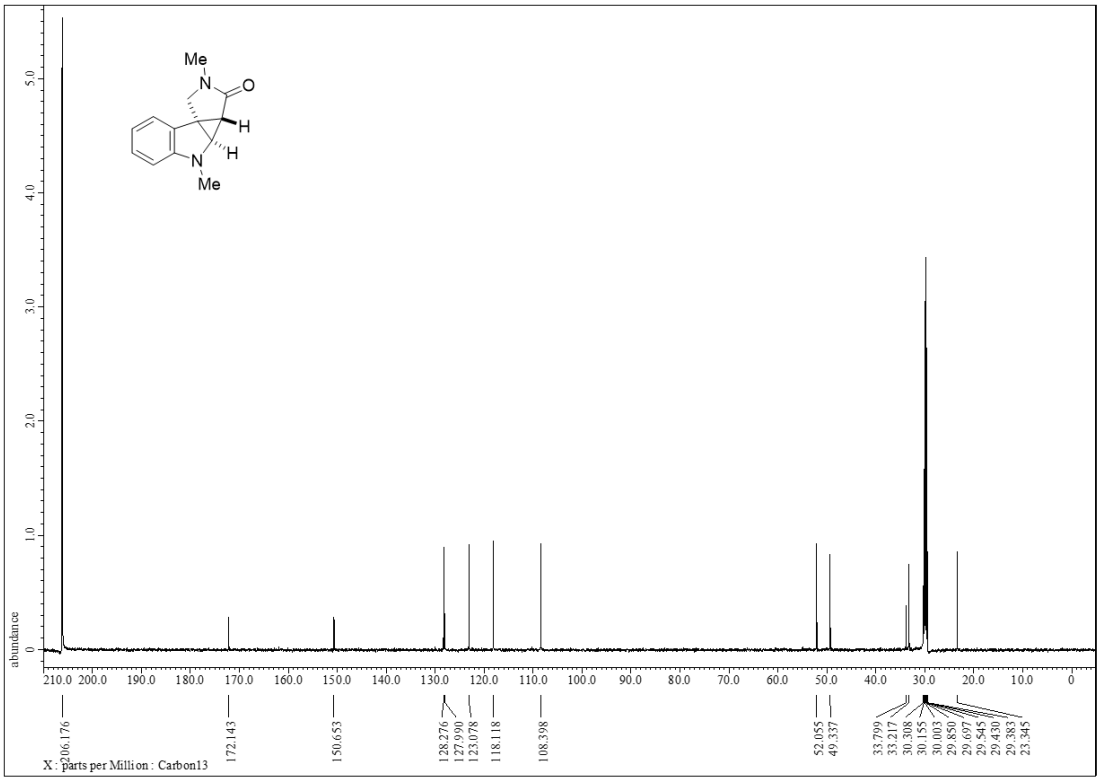

Me
N
O
H
H
abundance
X : parts per Million : Proton
1.31
1.12
1.25
1.08
1.02
1.00
1.03
1.01
3.13
0.99
0.99

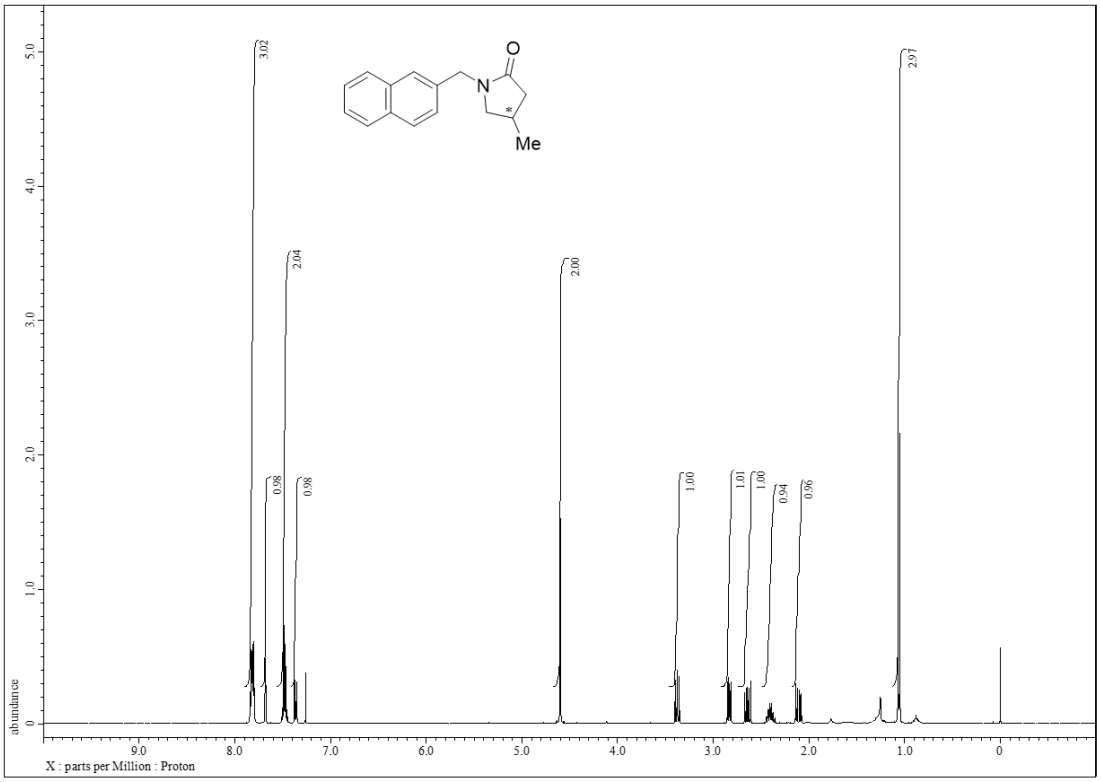

Me
N
O
H
H
abundance
X : parts per Million : Carbon13
174.453
130.844
130.500
128.478
127.734
126.628
126.265
125.331
124.921
77.248
77.000
76.742
52.324
31.922
29.385
29.289
24.158

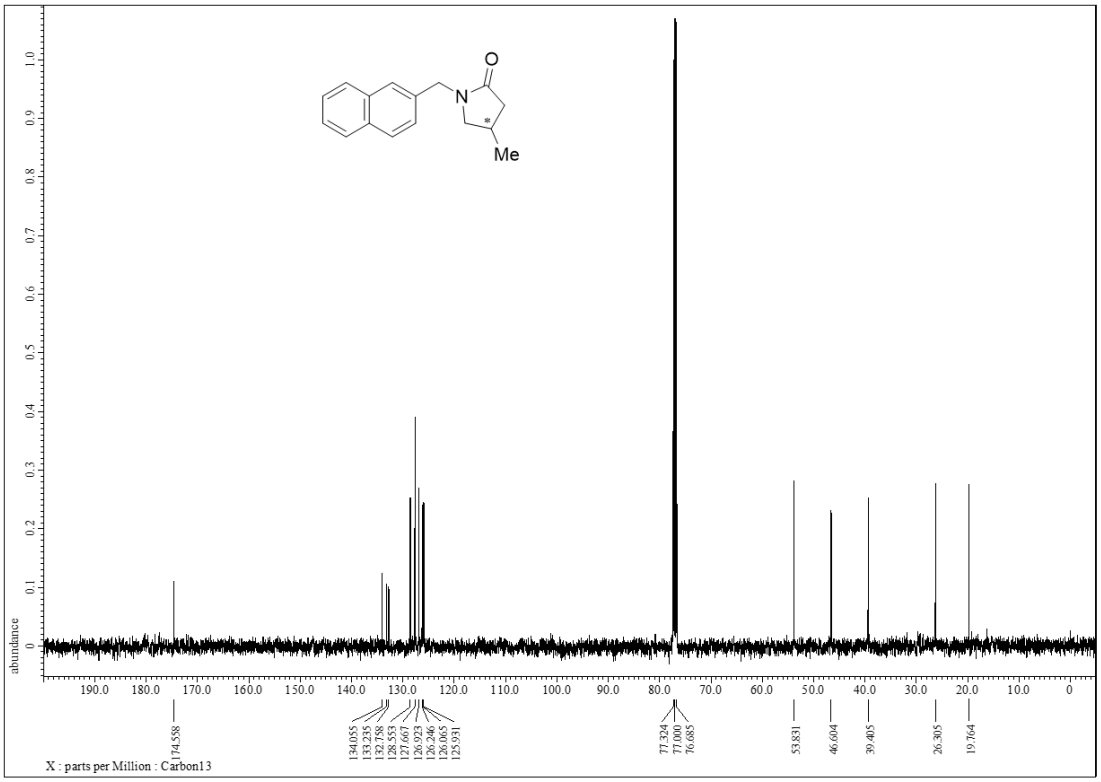

H
H
O
N
Me
N
Me
0.89
0.99
1.91
1.00
0.99
3.05
2.83
0.86
0.91
abundance
X : parts per Million : Proton

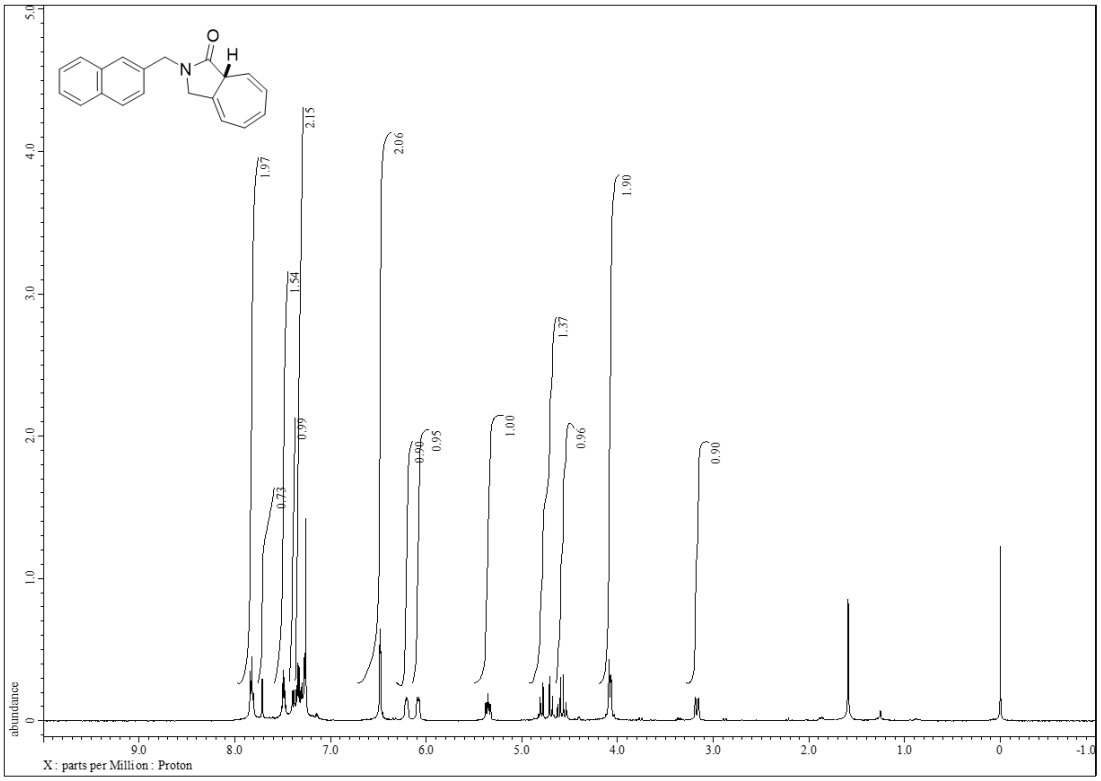

H
H
O
N
Me
N
Me
abundance
X : parts per Million : Carbon13
206.166
172.524
152.742
130.422
128.257
125.510
120.130
111.145
52.418
49.585
33.465
32.826
30.317
30.165
30.003
29.850
29.697
29.545
29.392
29.268
19.987

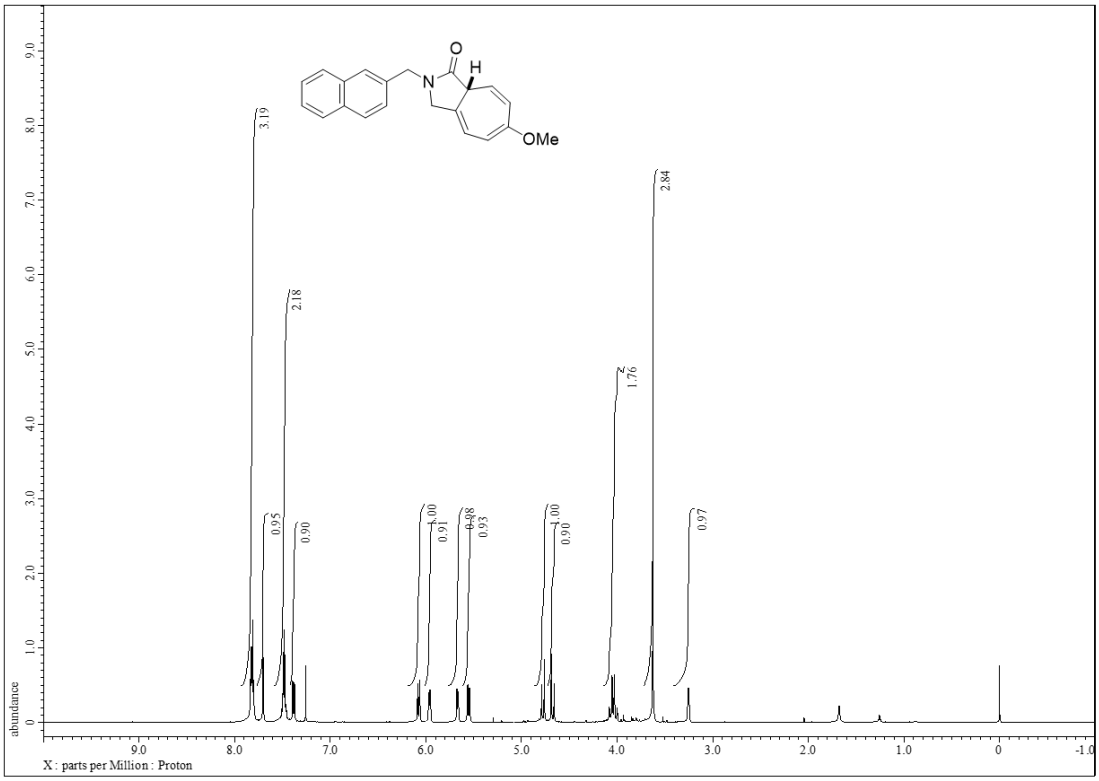

Me
N
O
H
H
N
Me
abundance
X : parts per Million : Proton
1.05
1.06
1.03
1.00
1.02
1.08
0.93
3.36
3.34
1.01

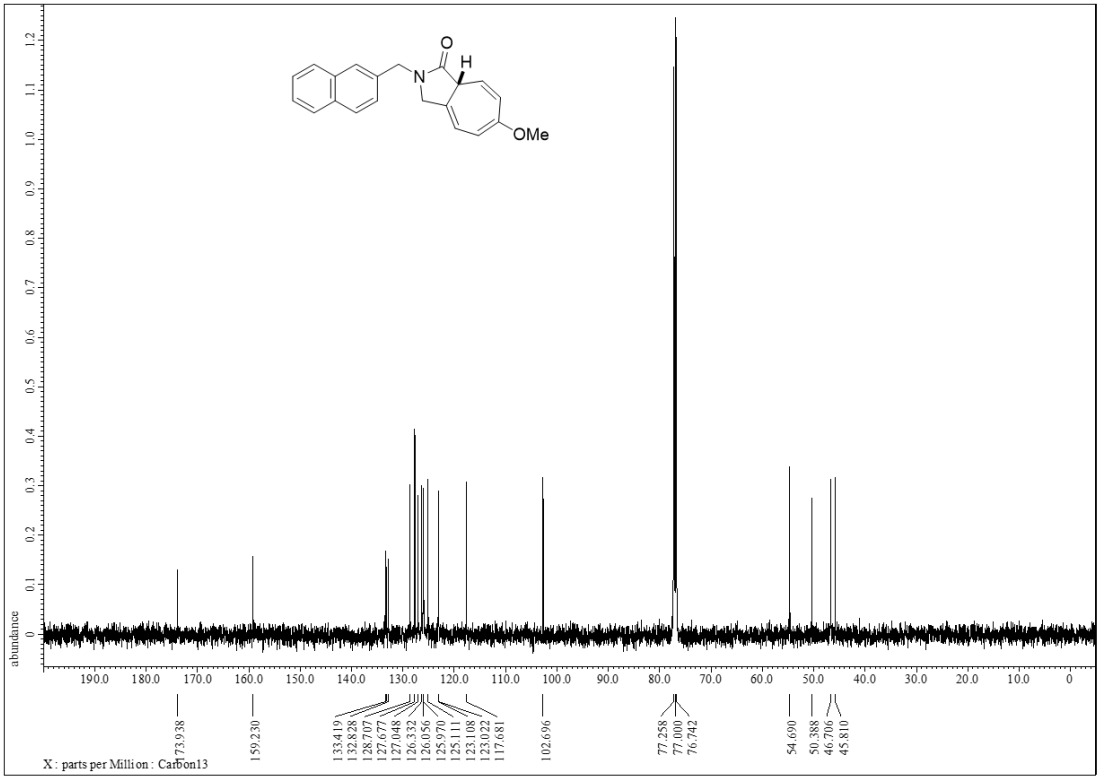

Me
N
O
H
H
N
Me
abundance
X : parts per Million : Carbon13
106.176
172.143
150.653
128.276
127.990
123.078
118.118
108.398
52.055
49.337
33.799
33.217
30.308
30.155
30.003
29.850
29.697
29.545
29.430
29.383
23.345

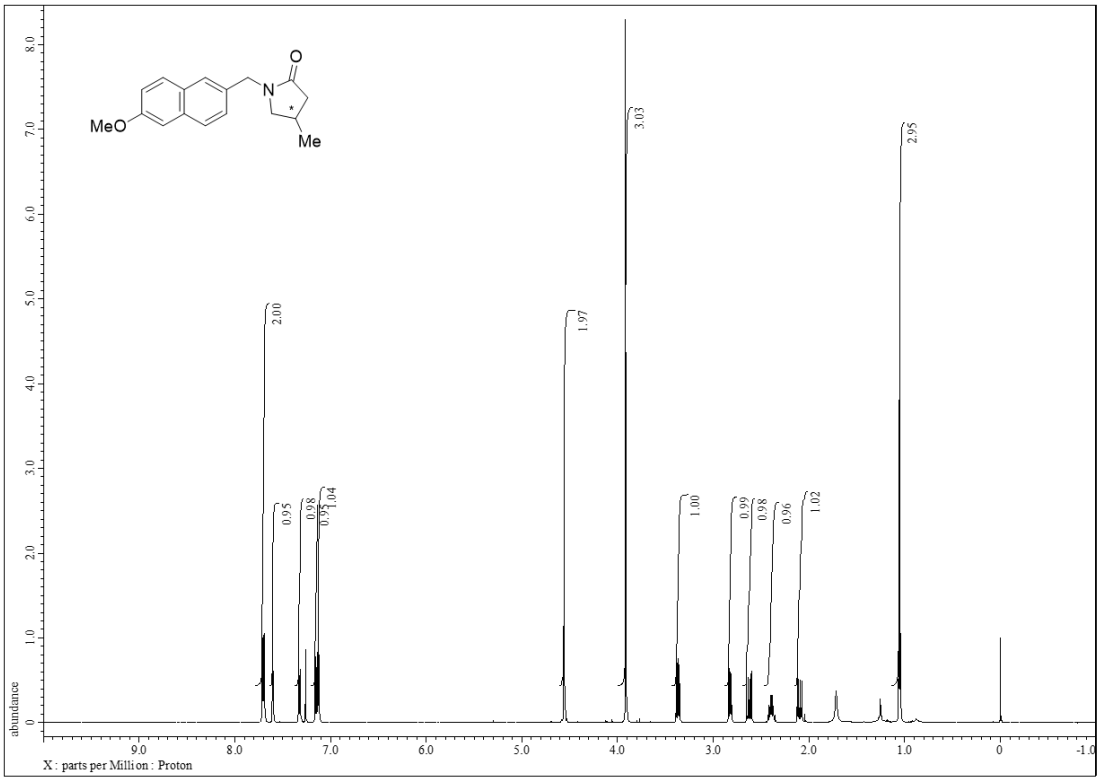

O
N
*
Me
3.02
2.04
2.00
2.97
0.98
0.98
1.00
1.01
1.00
0.94
0.96
abundance
X : parts per Million : Proton

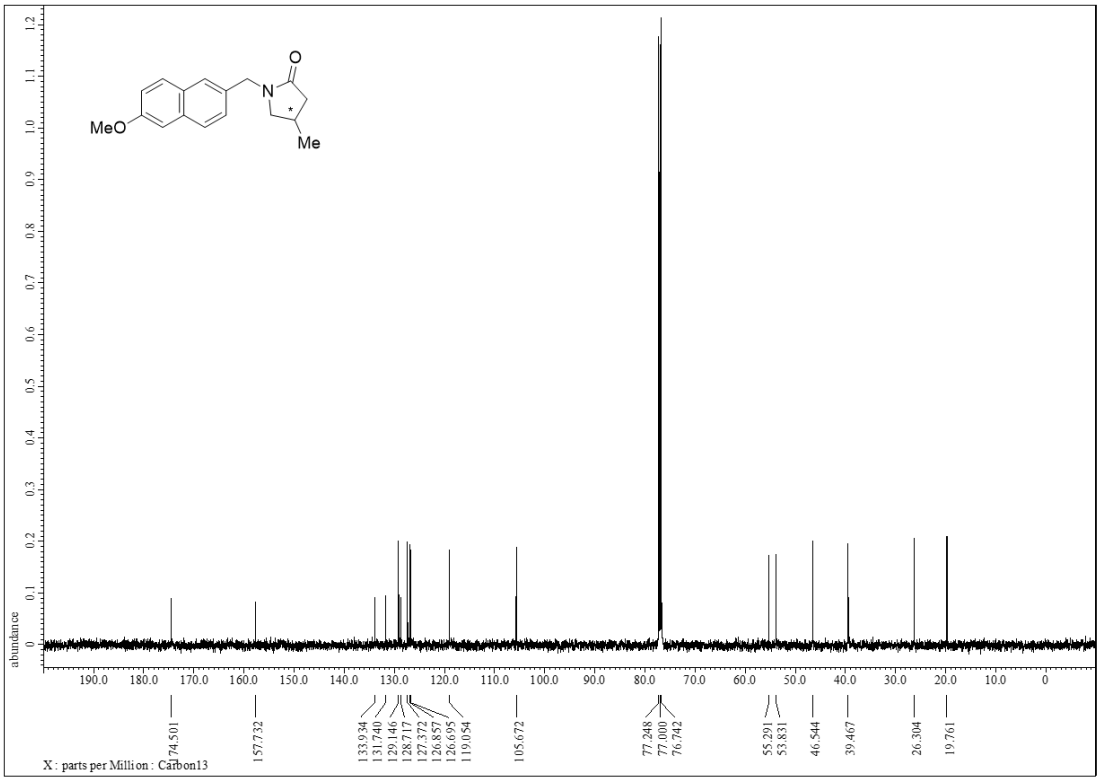

O
N
*
Me
abundance
174.558
134.055
133.235
132.758
128.553
127.667
126.923
126.268
126.065
125.931
77.324
77.000
76.685
53.831
46.604
39.405
26.305
19.764
X : parts per Million : Carbon13

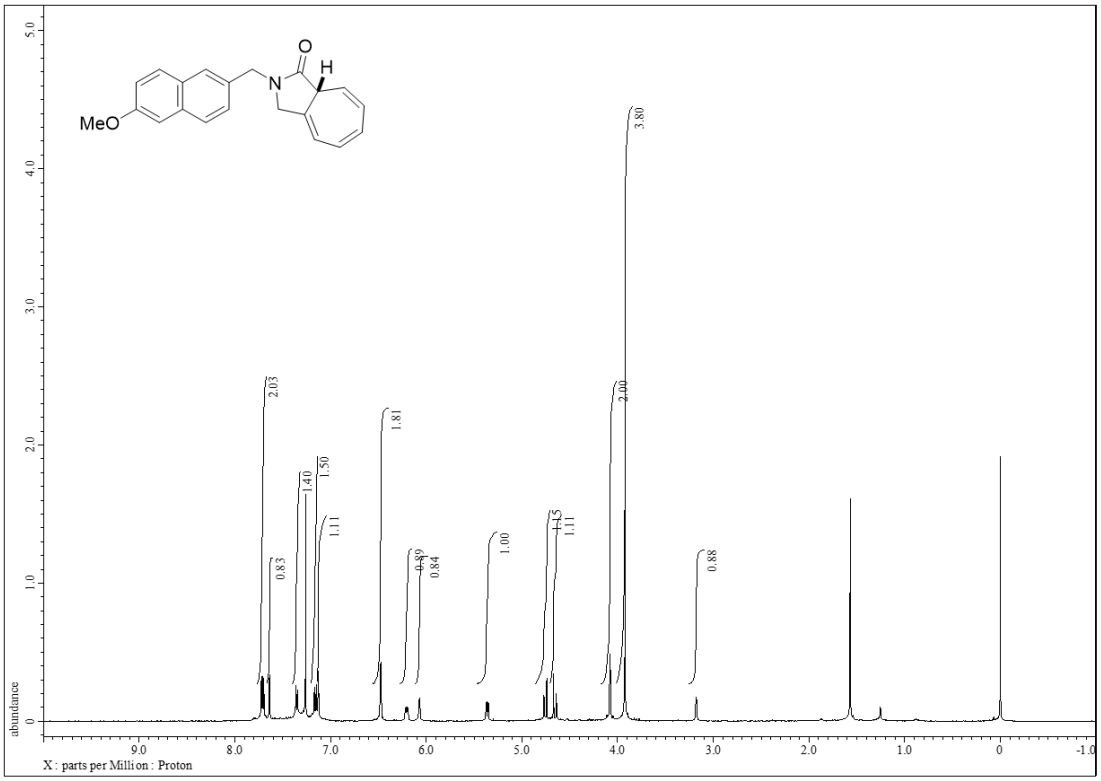

O
H
N
1.97
0.73
1.54
2.15
0.99
2.06
0.99
0.95
1.00
1.37
0.96
1.90
0.90
abundance
X : parts per Million : Proton

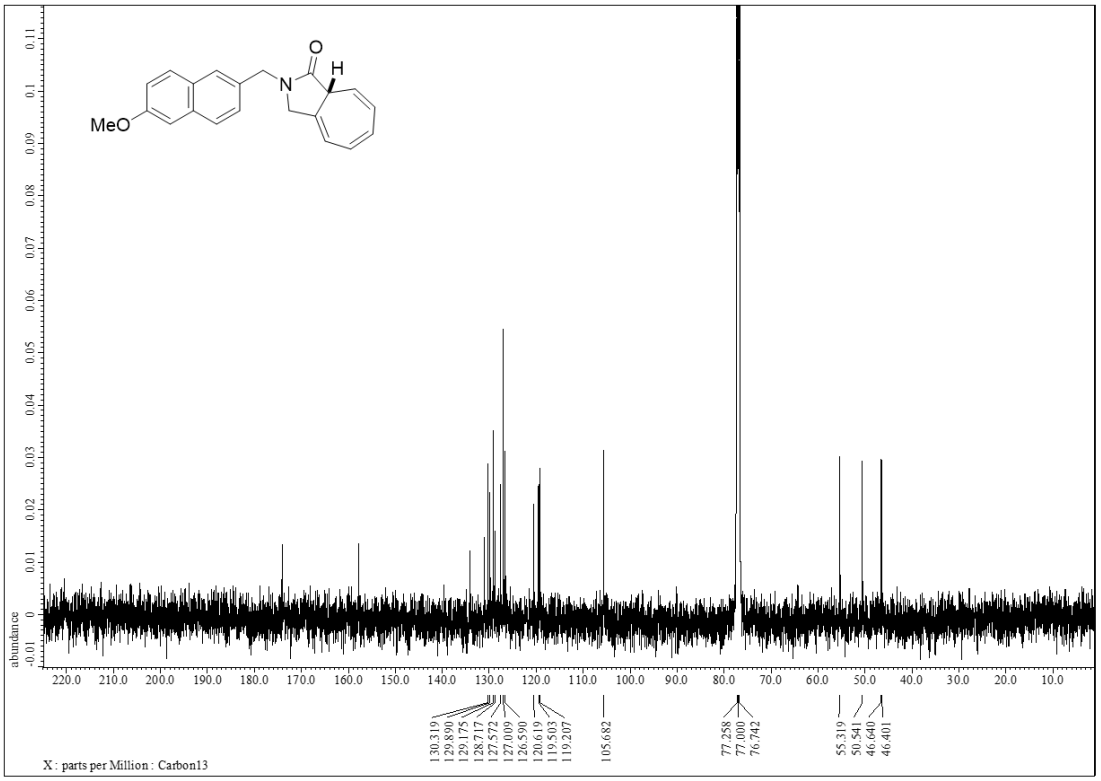

O
H
N
OMe
3.19
0.95
2.18
0.90
1.00
0.91
0.98
0.93
1.00
0.90
2
1.76
2.84
0.97
abundance
X : parts per Million : Proton

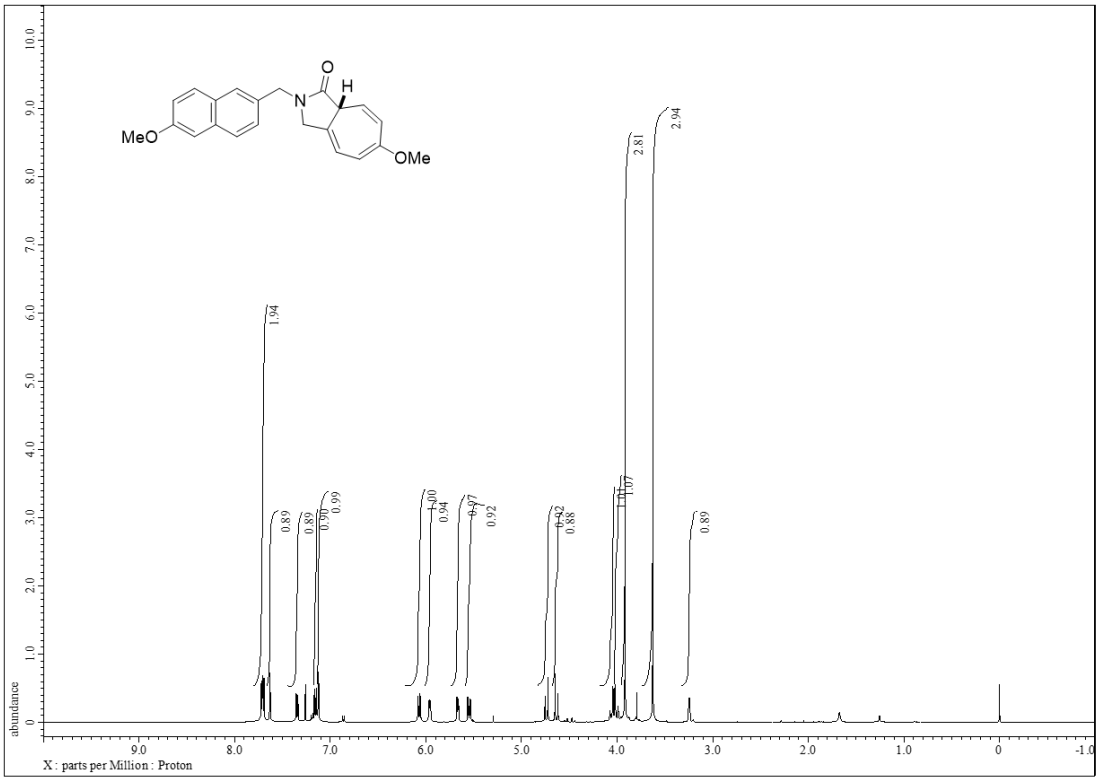

O
H
N
OMe
abundance
X : parts per Million : Carbon13
173.938
159.230
133.419
132.828
128.707
127.677
127.048
126.332
126.056
125.970
125.111
123.108
123.022
117.681
102.696
77.258
77.000
76.742
54.690
50.388
46.706
45.810

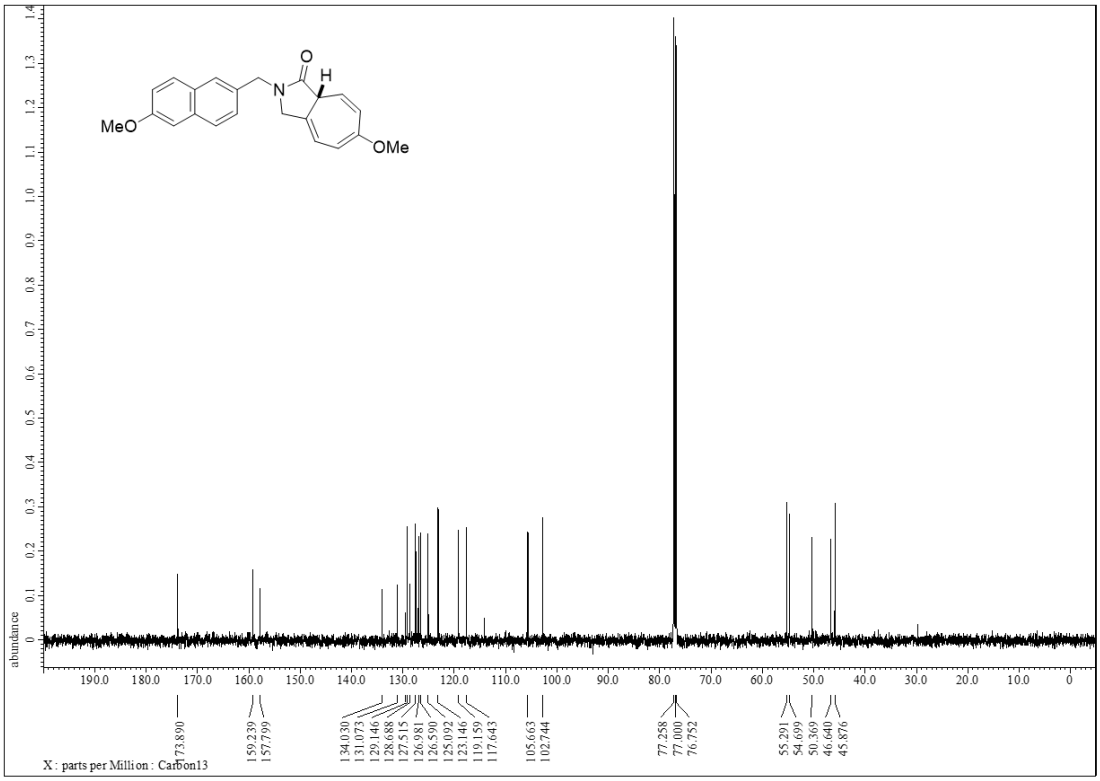

MeO
Me
O
N
*
2.00
0.95
0.98
0.95
1.04
1.97
3.03
1.00
0.99
0.98
0.96
1.02
2.95
abundance
X : parts per Million : Proton

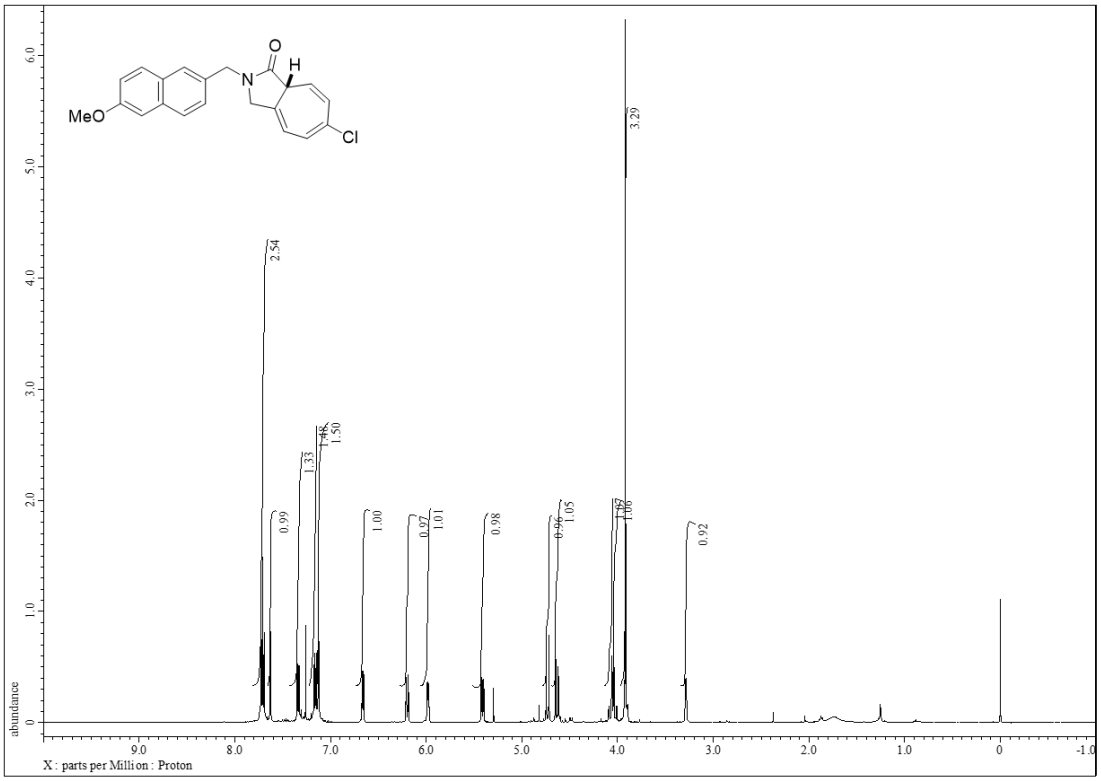

MeO
Me
O
N
*
abundance
X : parts per Million : Carbon13
174.501
157.732
133.934
131.740
129.146
128.717
127.372
126.857
126.695
119.054
105.672
77.248
77.000
76.742
55.291
53.831
46.544
39.467
26.304
19.761

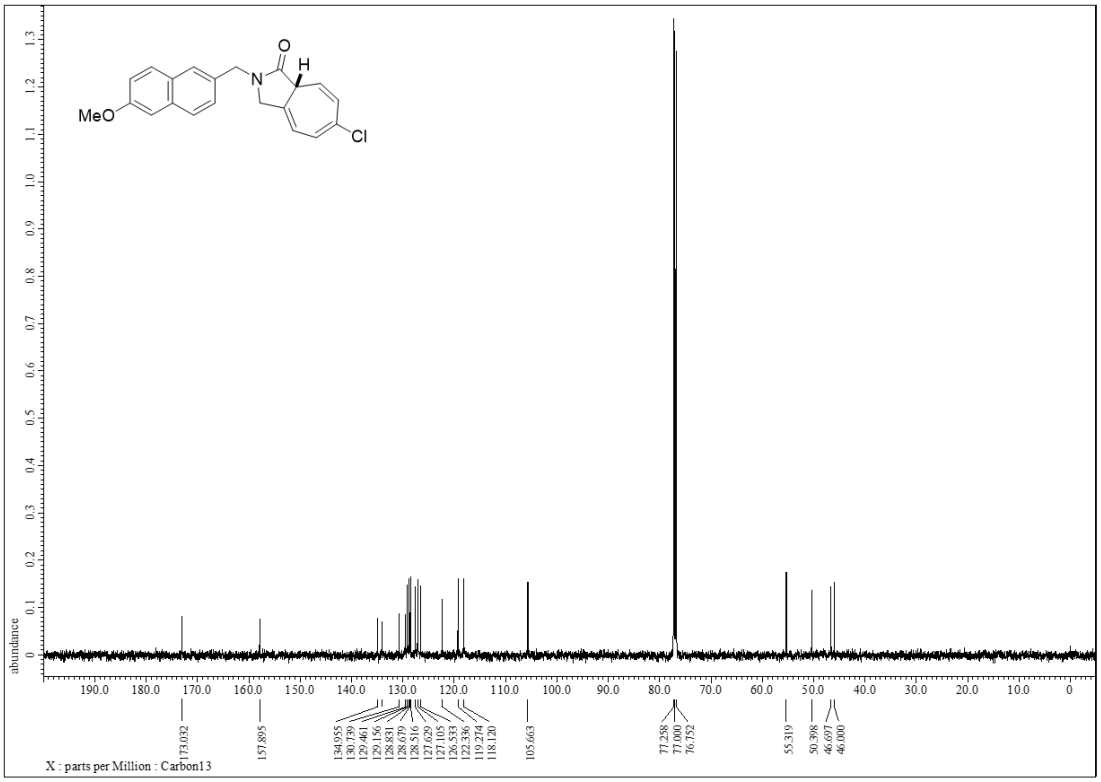

MeO
O
H
N
2.03
0.83
1.40
1.50
1.11
1.81
0.89
0.84
1.00
1.15
1.11
2.00
3.80
0.88
abundance
X : parts per Million : Proton

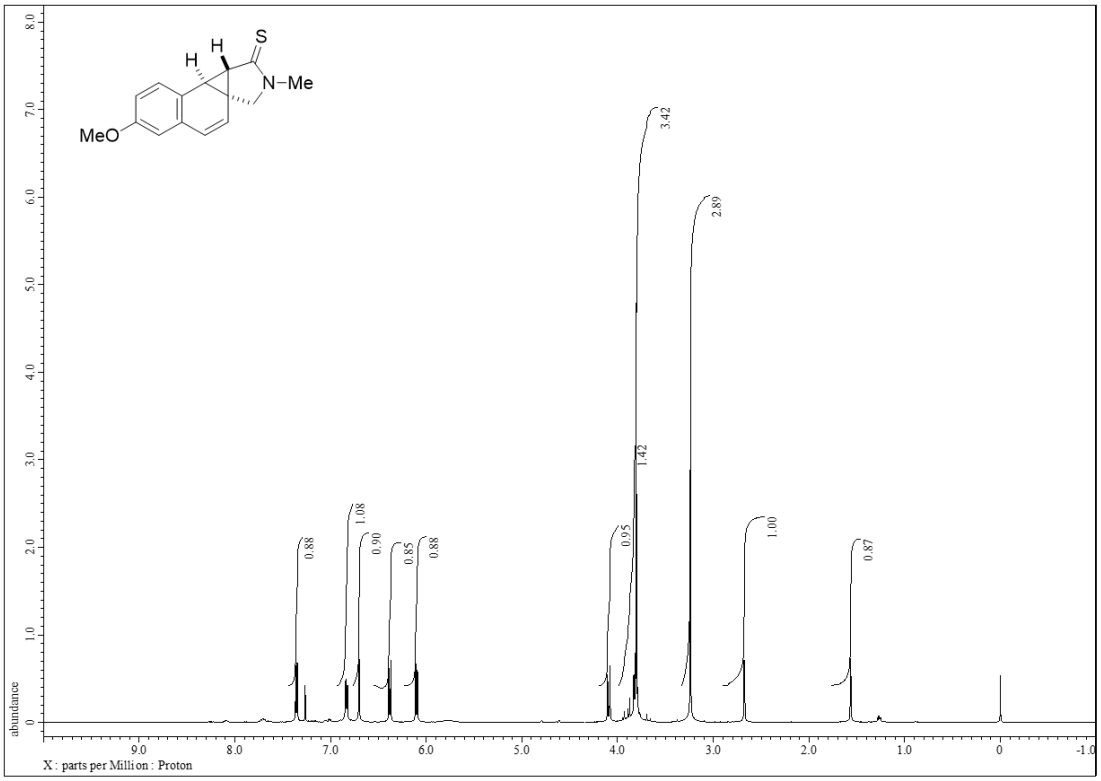

MeO
O
H
N
abundance
X : parts per Million : Carbon13
130.319
129.890
129.175
128.717
127.572
127.009
126.590
120.619
119.503
119.207
105.682
77.258
77.000
76.742
55.319
50.541
46.640
46.401

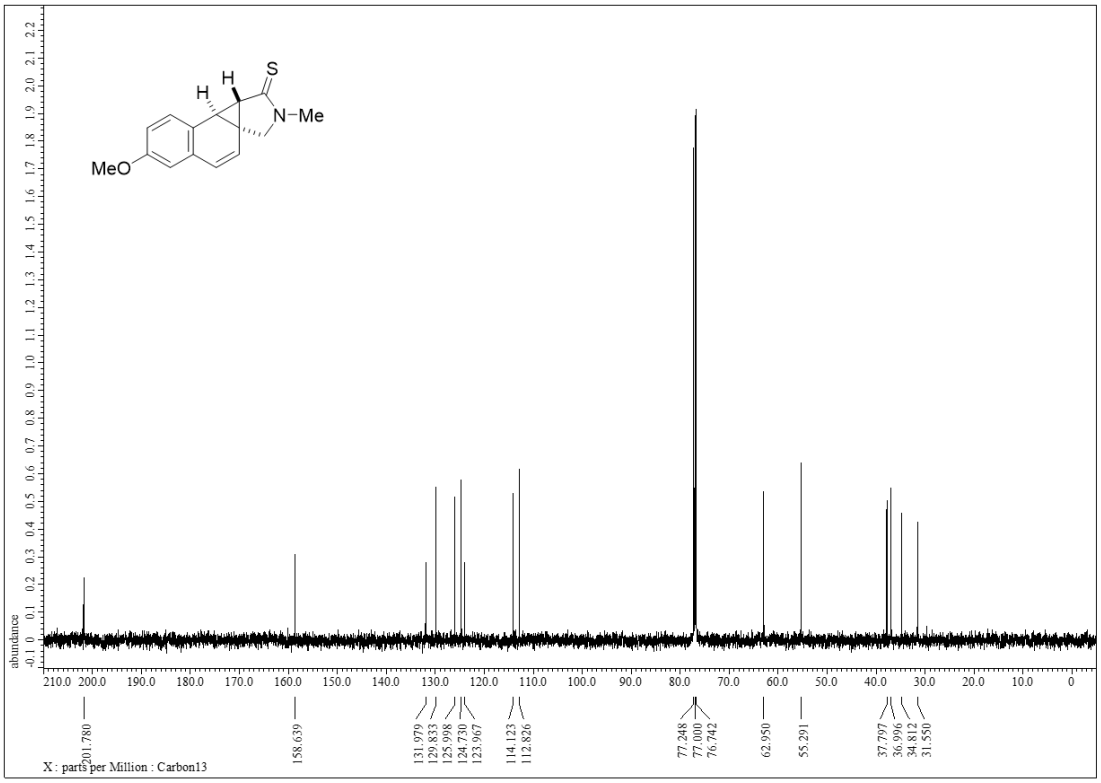

MeO
OMe
O
H
N
1.94
0.89
0.89
0.90
0.99
1.00
0.94
0.97
0.92
0.82
0.88
1.07
1.07
2.81
2.94
0.89
abundance
X : parts per Million : Proton


MeO
OMe
O
H
N
abundance
X : parts per Million : Carbon13
173.890
159.239
157.799
134.030
131.073
129.146
128.688
127.515
126.981
126.590
125.092
123.146
119.159
117.643
105.663
102.744
77.258
77.000
76.752
55.291
54.699
50.369
46.640
45.876

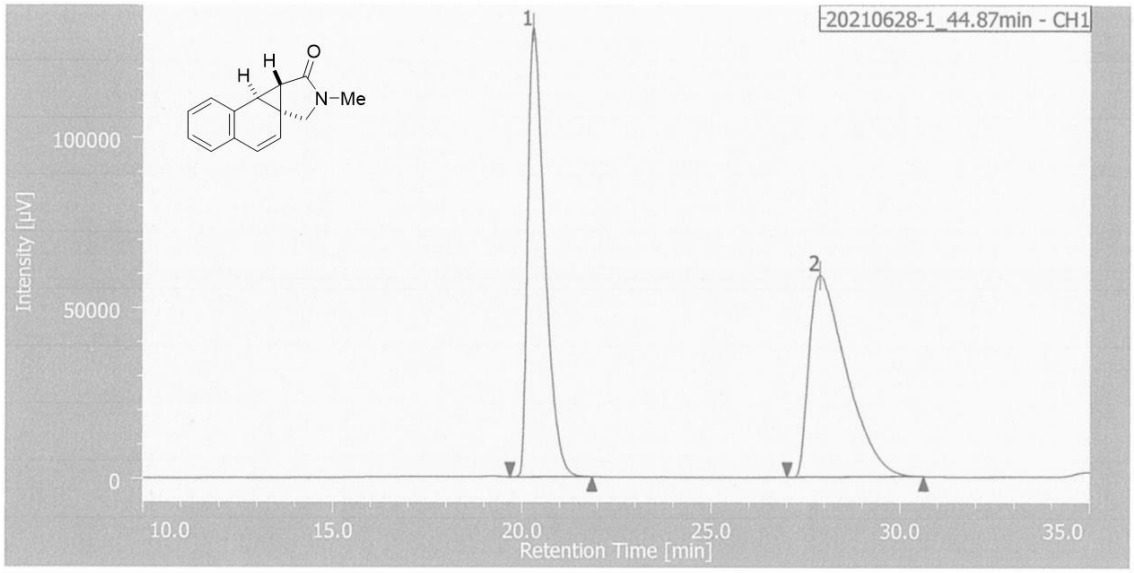

MeO
Cl
O
H
N
abundance
X : parts per Million : Proton
2.54
0.99
1.33
1.48
1.50
1.00
0.97
1.01
0.98
0.96
1.05
1.07
1.06
3.29
0.92


MeO
Cl
O
H
N
abundance
X : parts per Million : Carbon13
173.032
157.895
134.955
130.739
129.460
129.156
128.851
128.670
128.516
127.629
127.105
126.533
122.336
119.274
118.120
105.663
77.258
77.000
76.752
55.319
50.398
46.697
46.000

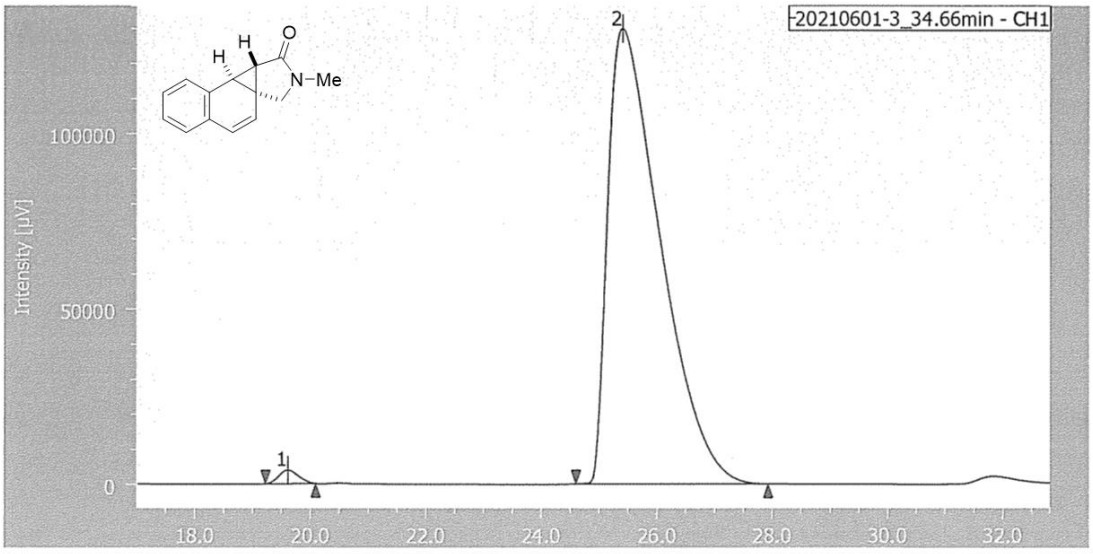

H
H
S
N–Me
MeO
3.42
2.89
1.42
1.08
0.90
0.88
0.85
0.88
0.95
1.00
0.87
abundance
X : parts per Million : Proton


H
H
S
N–Me
MeO
abundance
201.780
158.639
131.979
129.833
125.998
124.730
123.967
114.123
112.826
77.248
77.000
76.742
62.950
55.291
37.797
36.996
34.812
31.550
X : parts per Million : Carbon13

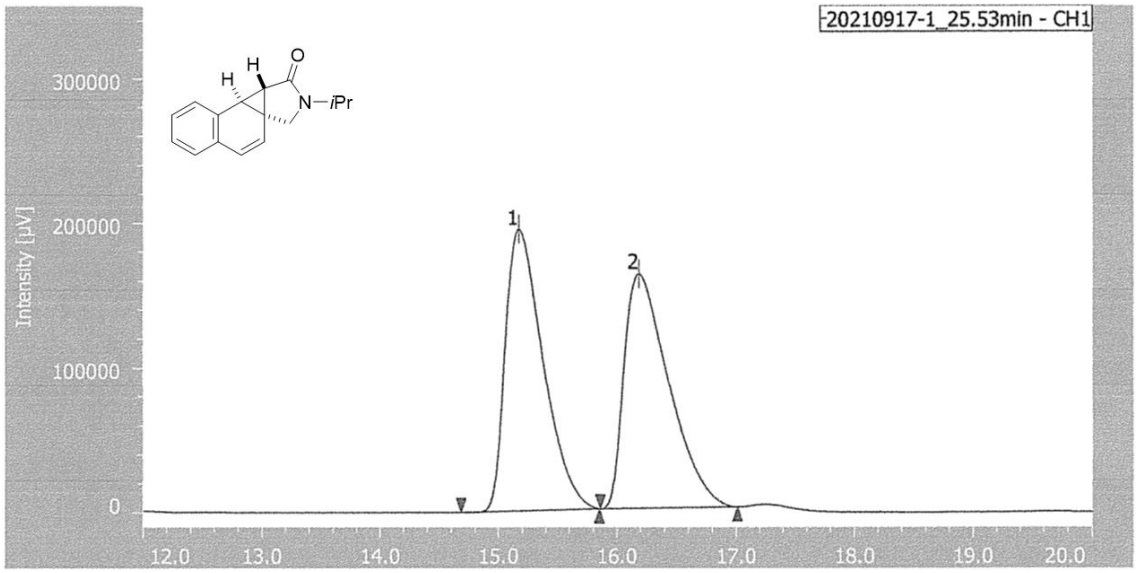
8-4-7 HPLC Spectral Data



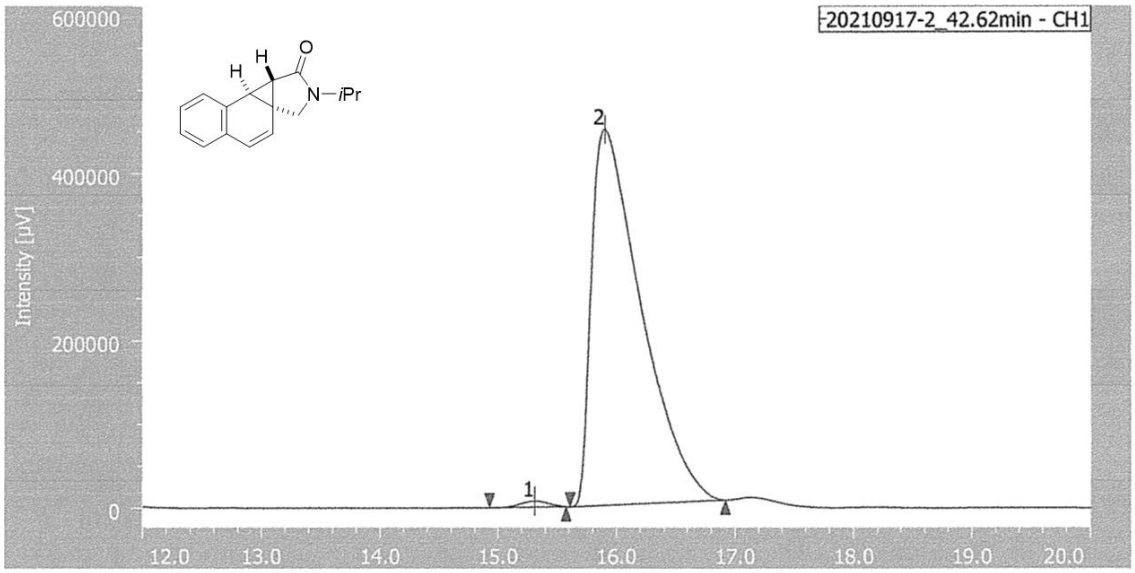
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.283	4091564	131722	49.834	68.991
2	27.875	4118833	59206	50.166	31.009



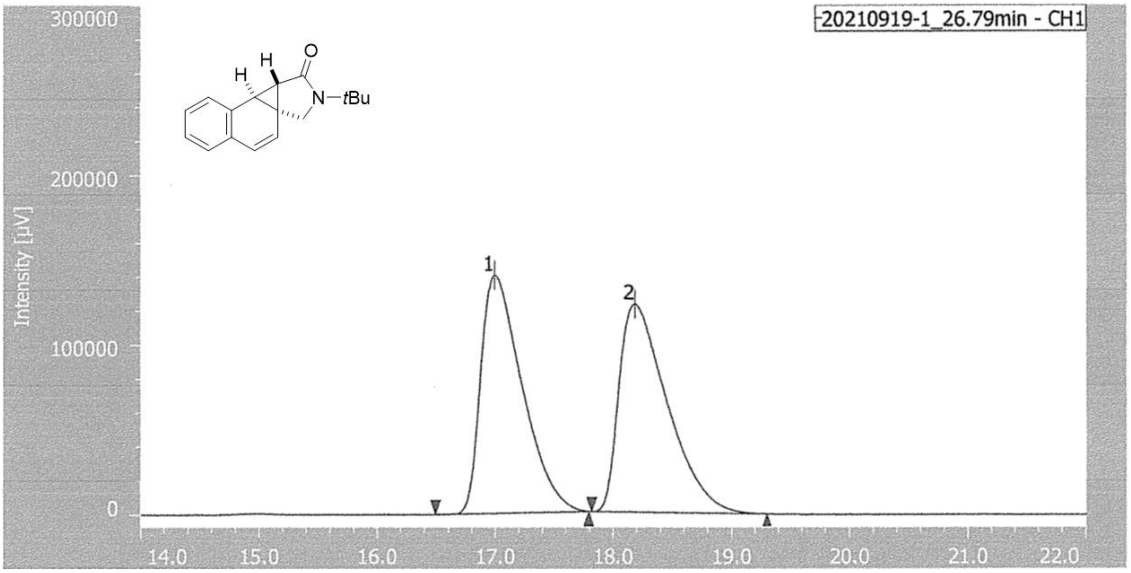
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	19.608	90564	3843	1.094	2.878
2	25.400	8189568	129655	98.906	97.122



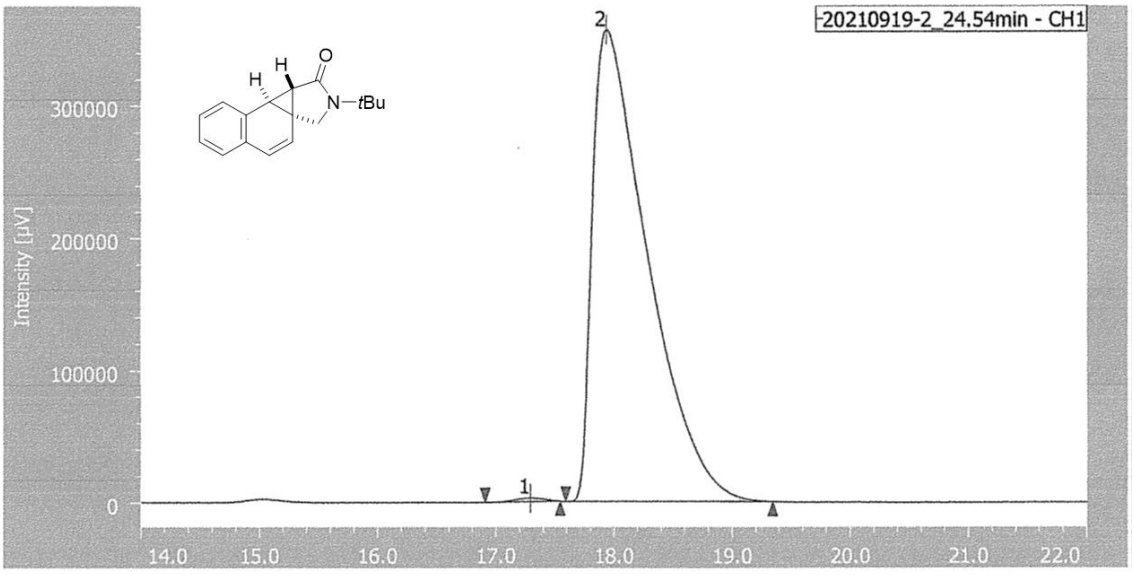
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	15.167	4299562	194569	50.456	54.557
2	16.183	4221779	162064	49.544	45.443



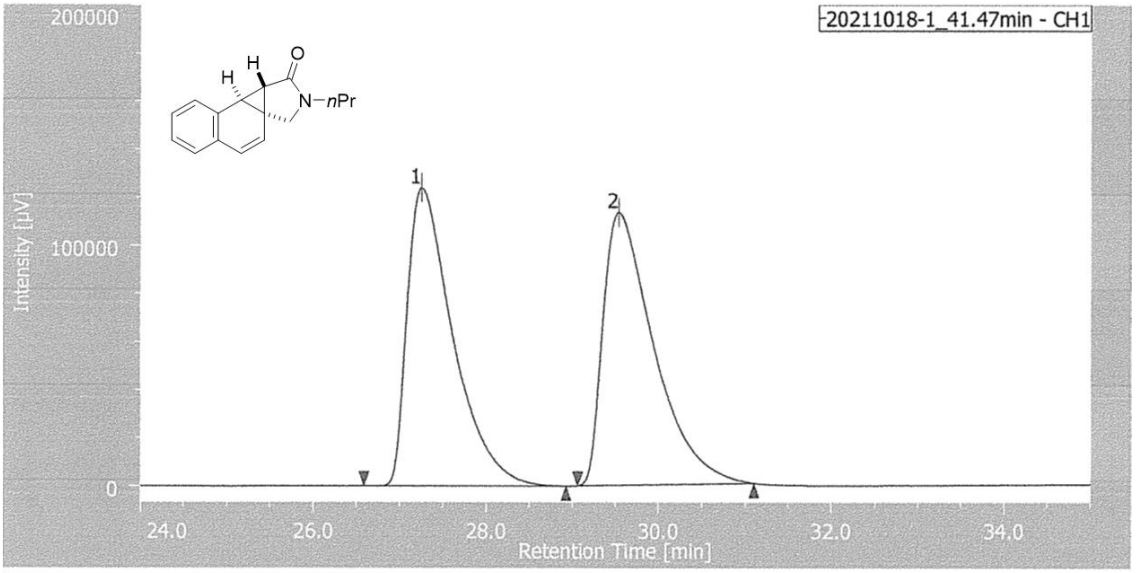
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	15.308	121958	7265	0.924	1.591
2	15.900	13079080	449515	99.076	98.409



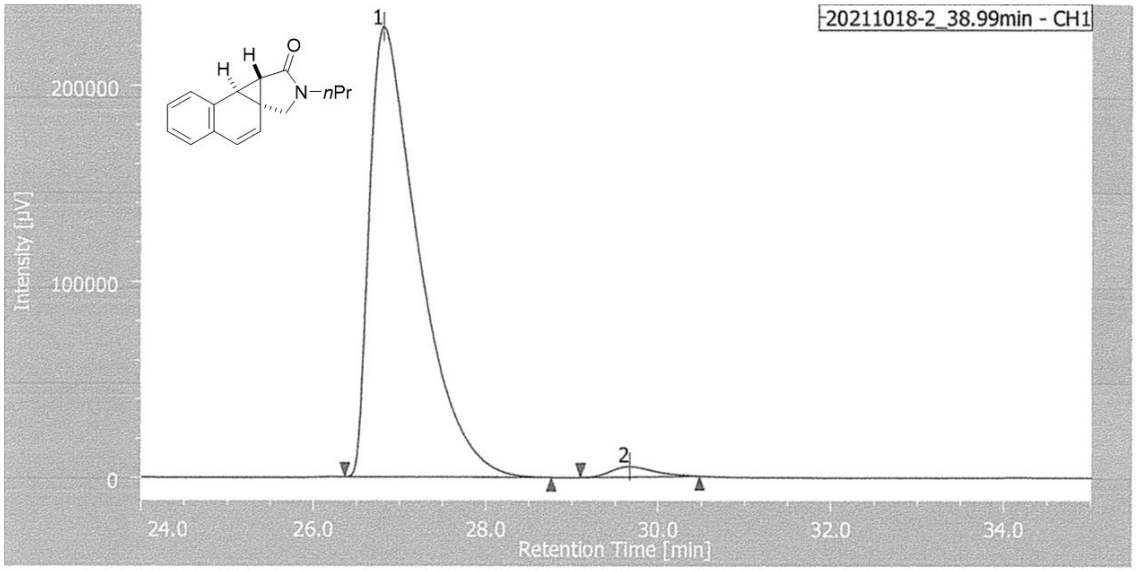
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	16.992	3429223	140352	49.746	53.391
2	18.183	3464260	122522	50.254	46.609



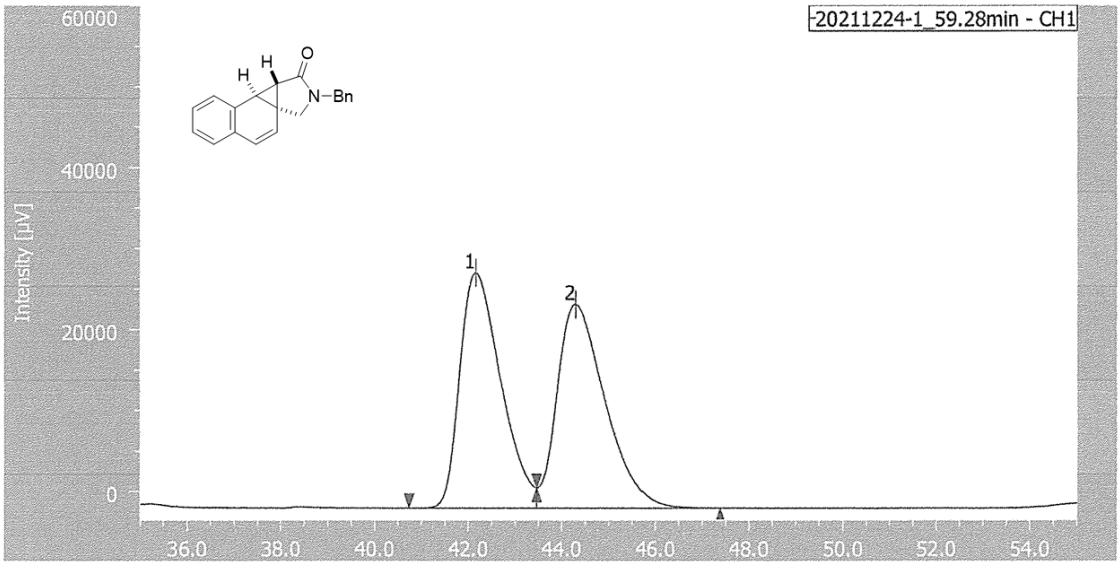
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	17.292	48173	2722	0.413	0.757
2	17.933	11612040	356628	99.587	99.243



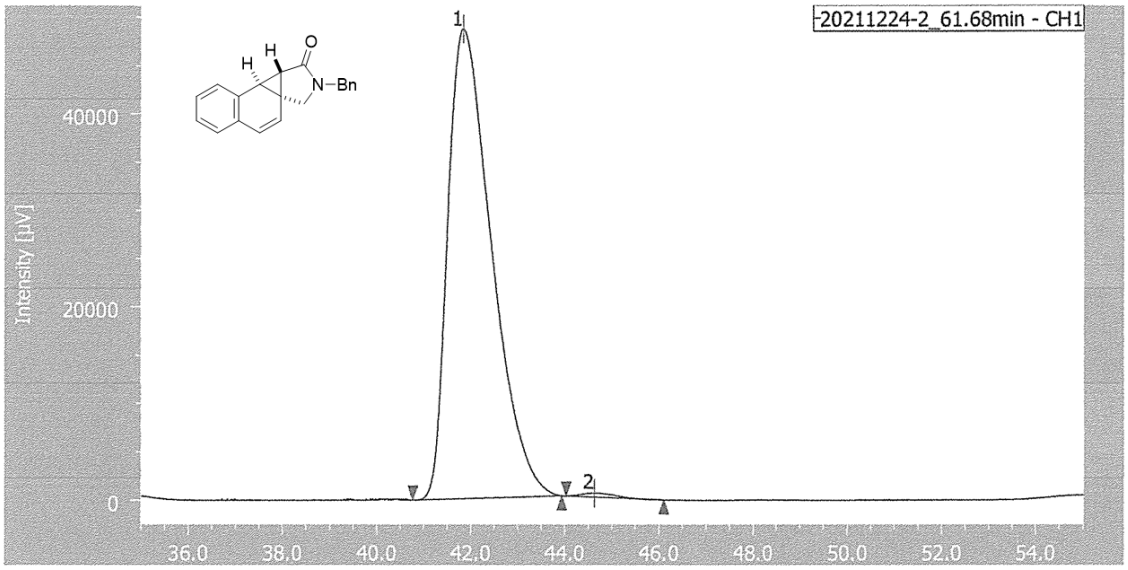
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	27.250	4537126	123959	49.369	52.231
2	29.533	4653086	113369	50.631	47.769



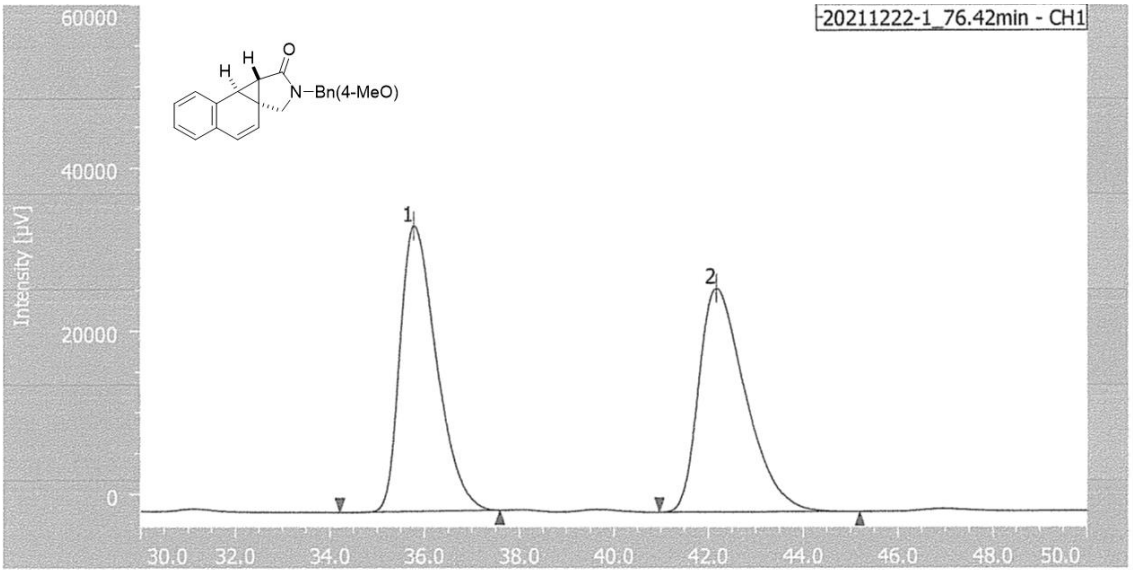
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	26.808	9064886	229495	97.998	97.744
2	29.667	185231	5298	2.002	2.256



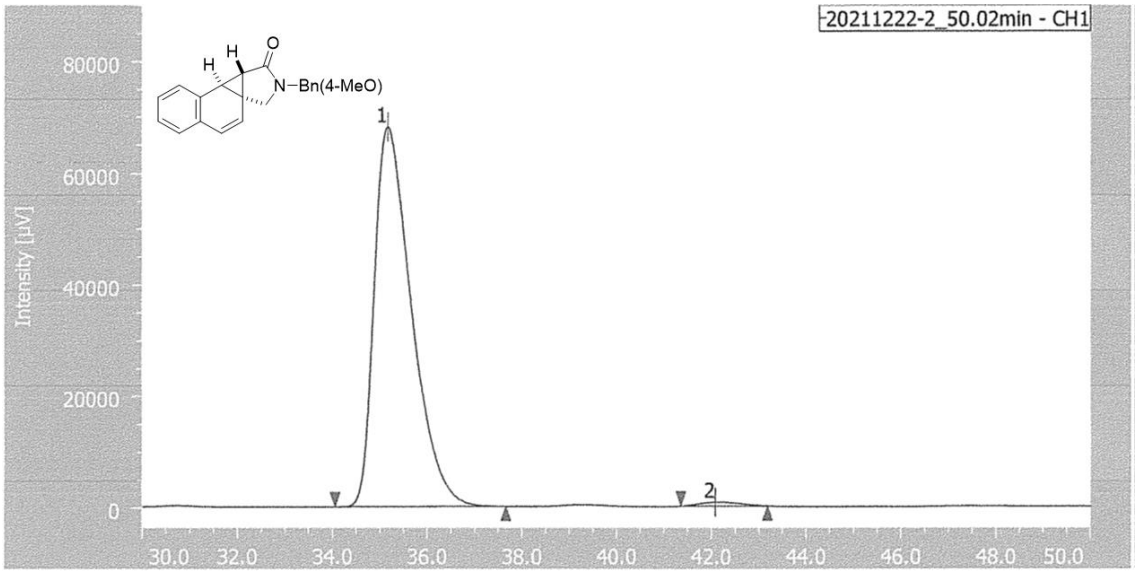
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	42.158	1765194	29033	49.690	53.596
2	44.292	1787185	25136	50.310	46.404



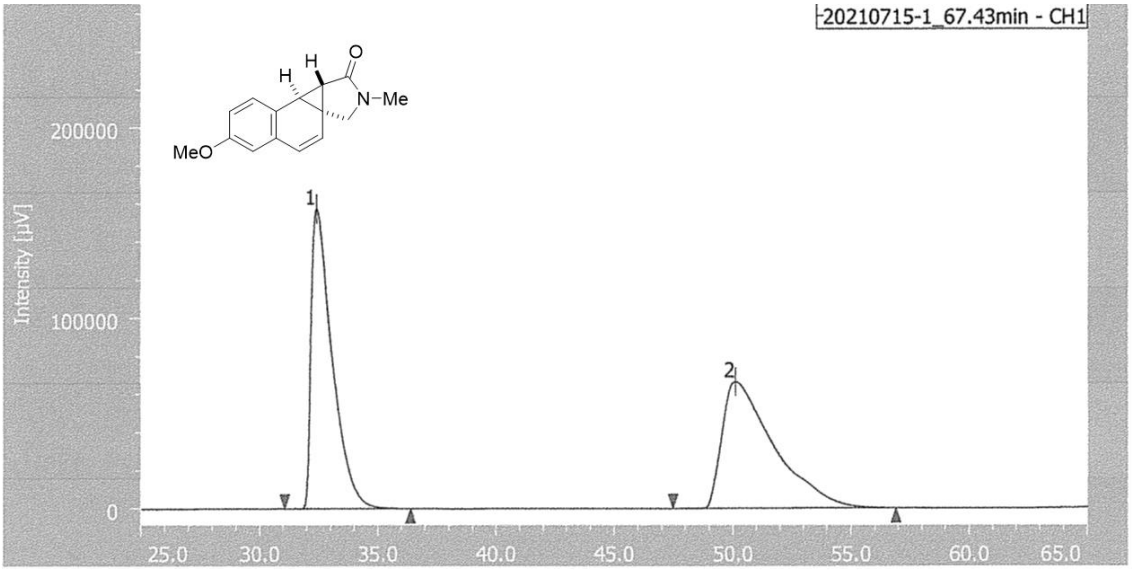
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	41.842	3133368	48627	99.335	99.134
2	44.625	20976	425	0.665	0.866



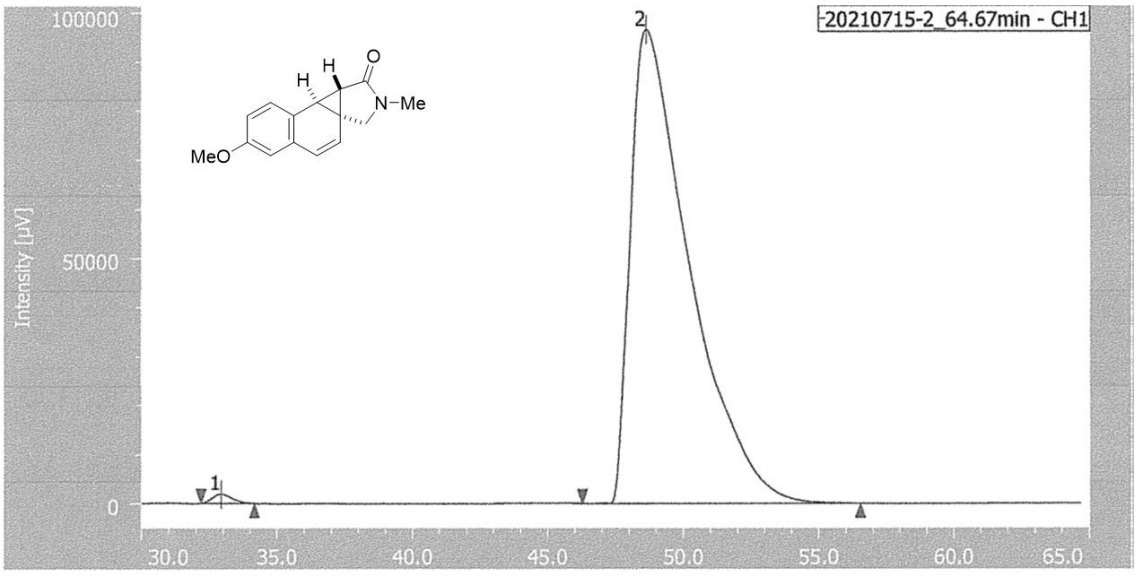
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	35.775	1865856	34961	49.804	56.061
2	42.167	1880554	27402	50.196	43.939



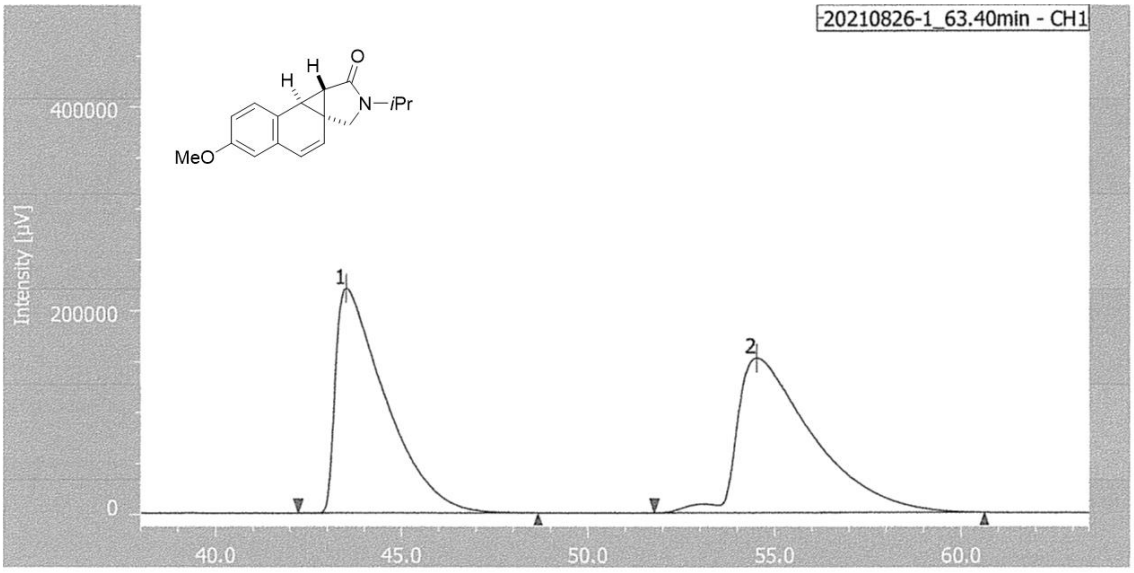
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	35.167	3721249	67927	98.907	98.960
2	42.075	41129	714	1.093	1.040



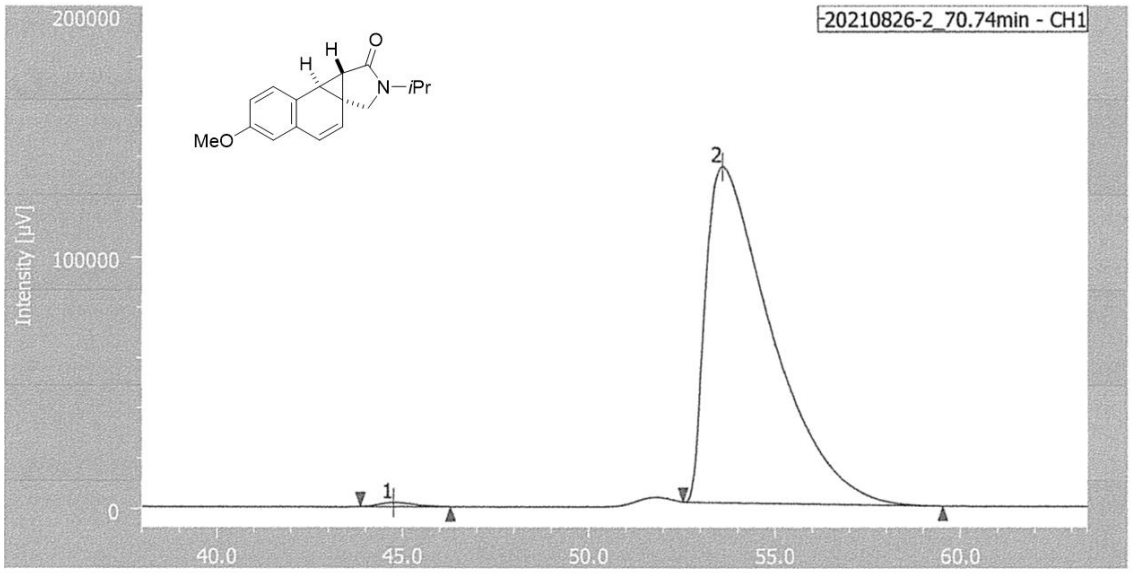
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	32.400	9682949	157401	48.891	70.311
2	50.092	10122117	66463	51.109	29.689



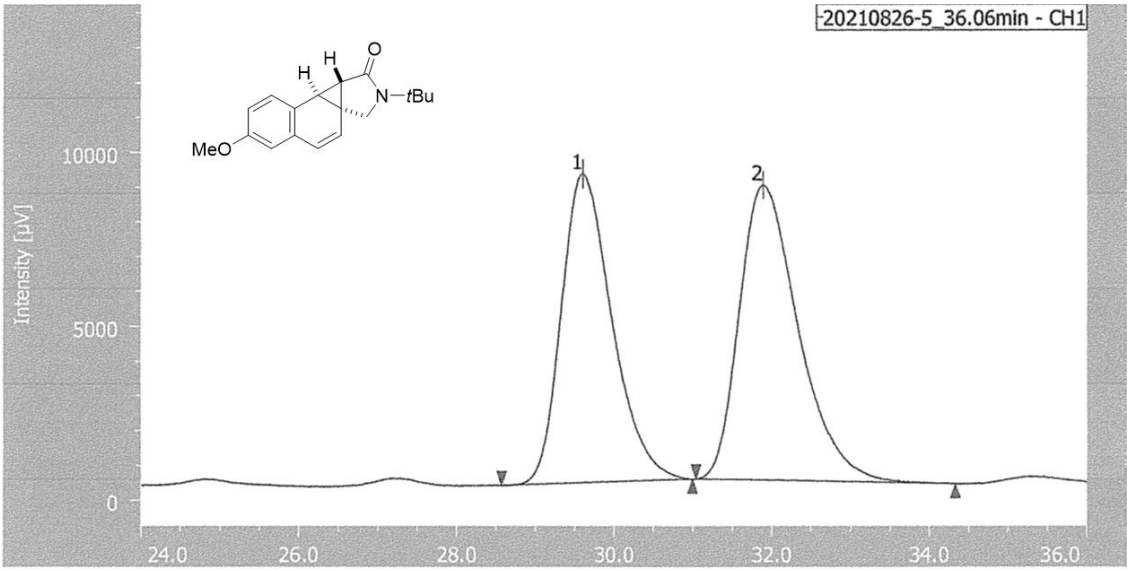
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	32.925	95311	1878	0.647	1.908
2	48.617	14630328	96575	99.353	98.092



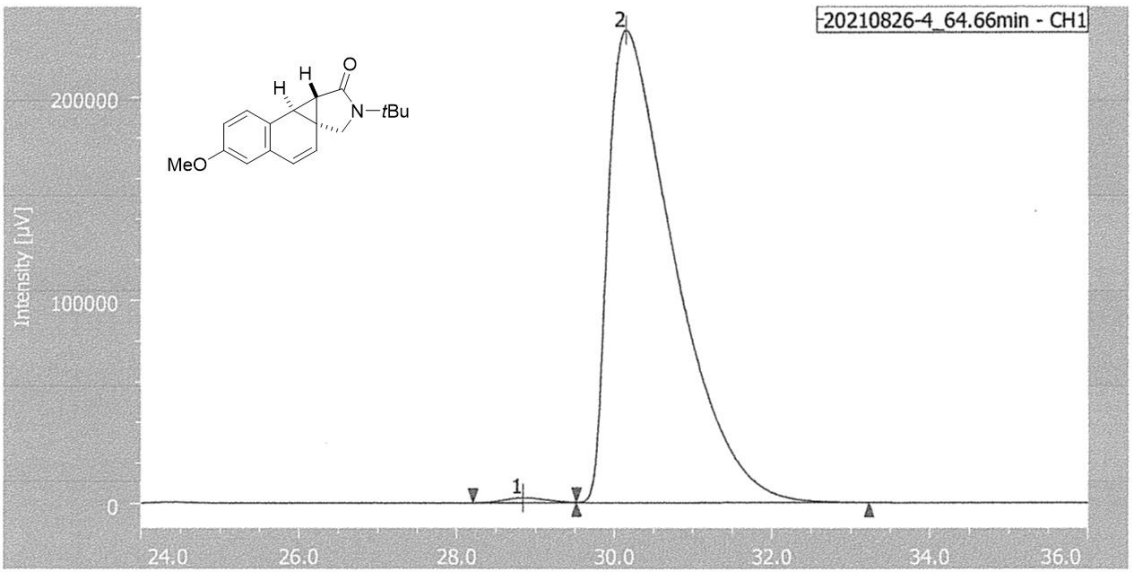
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	43.500	20599136	220436	48.815	59.204
2	54.508	21599060	151896	51.185	40.796



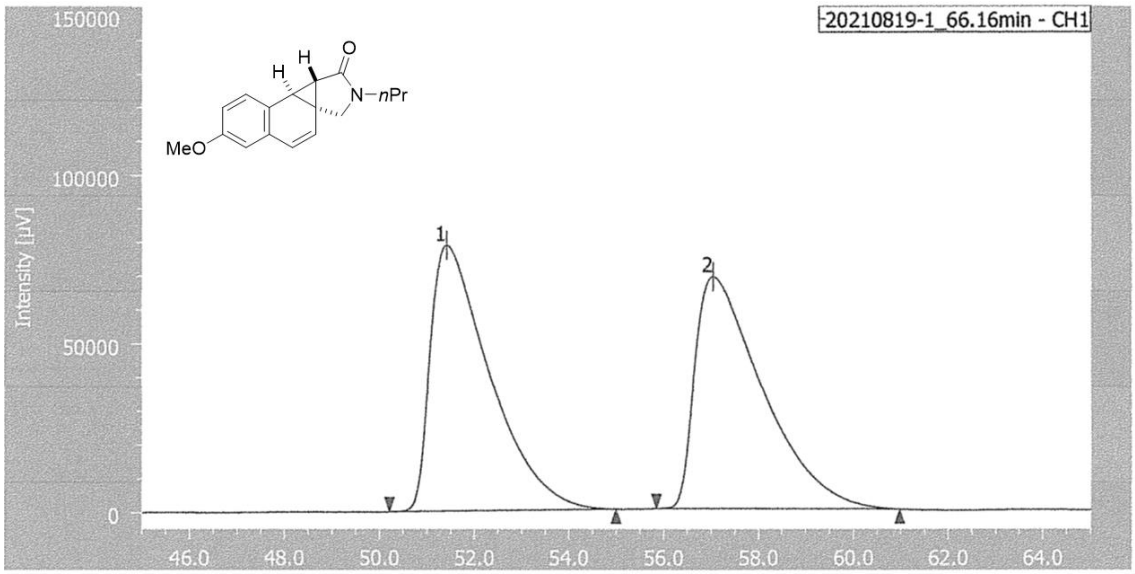
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	44.750	104754	1647	0.628	1.217
2	53.575	16562664	133671	99.372	98.783



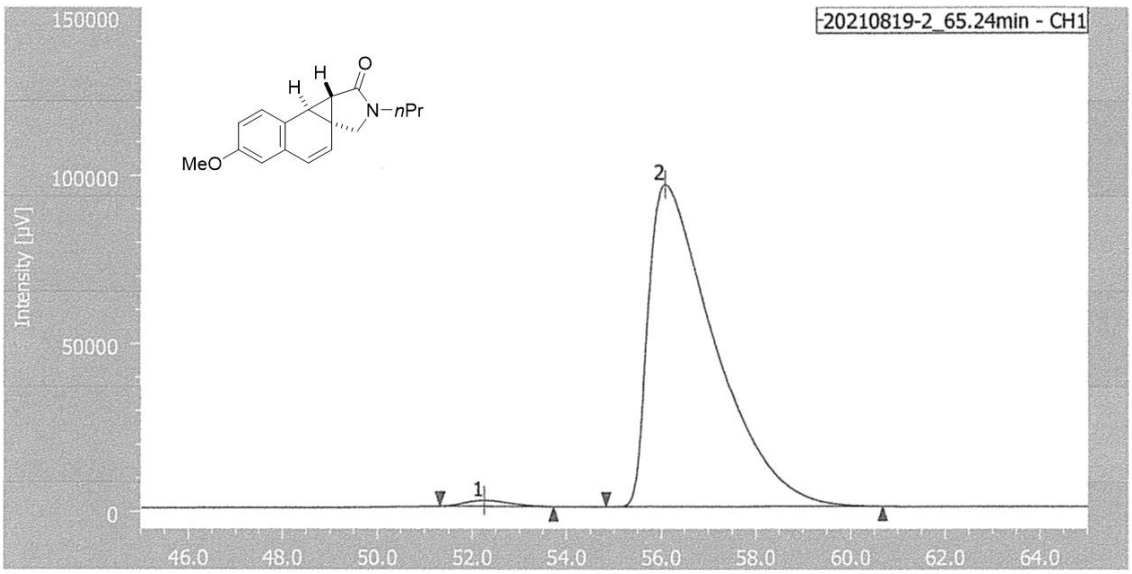
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	29.600	398447	8877	47.363	51.162
2	31.883	442818	8473	52.637	48.838



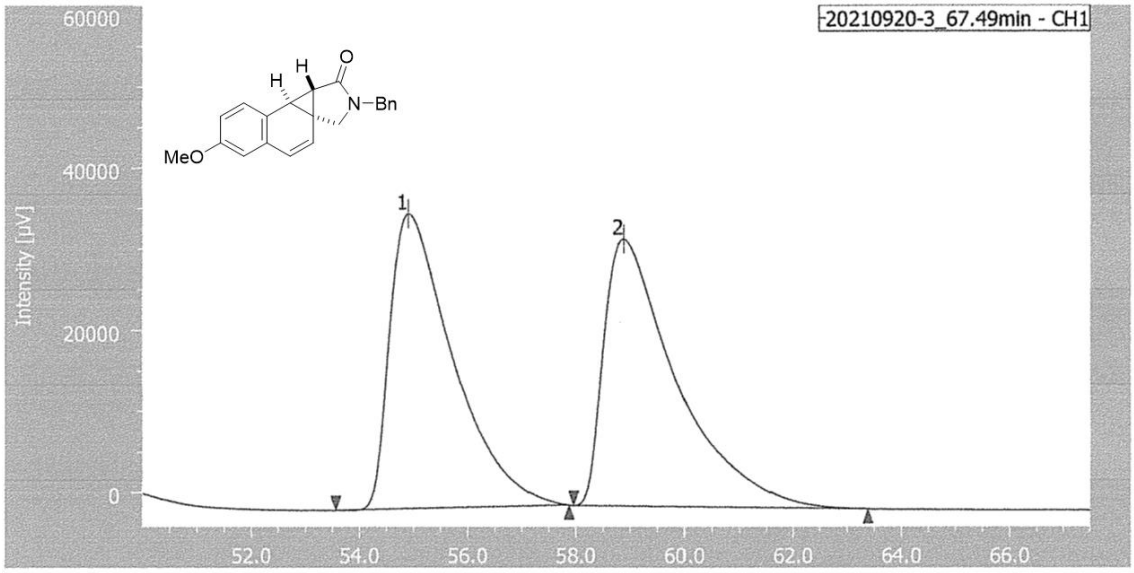
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	28.842	95748	2468	0.697	1.051
2	30.142	13637236	232374	99.303	98.949



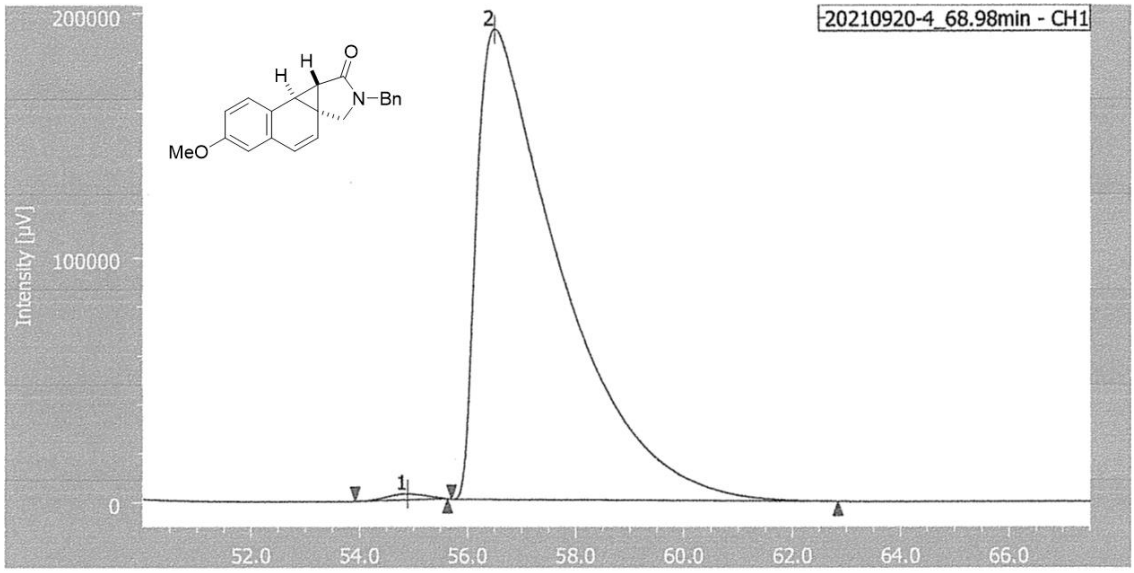
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	51.408	6873180	78753	50.125	53.379
2	57.033	6838901	68783	49.875	46.621



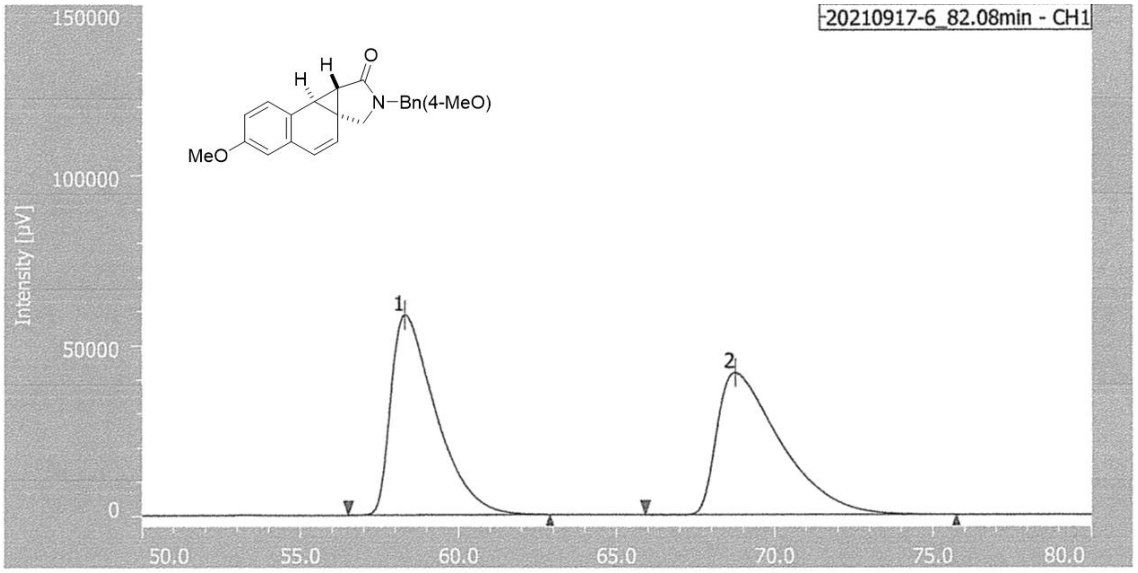
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	52.250	117851	1777	1.242	1.819
2	56.075	9371925	95918	98.758	98.181



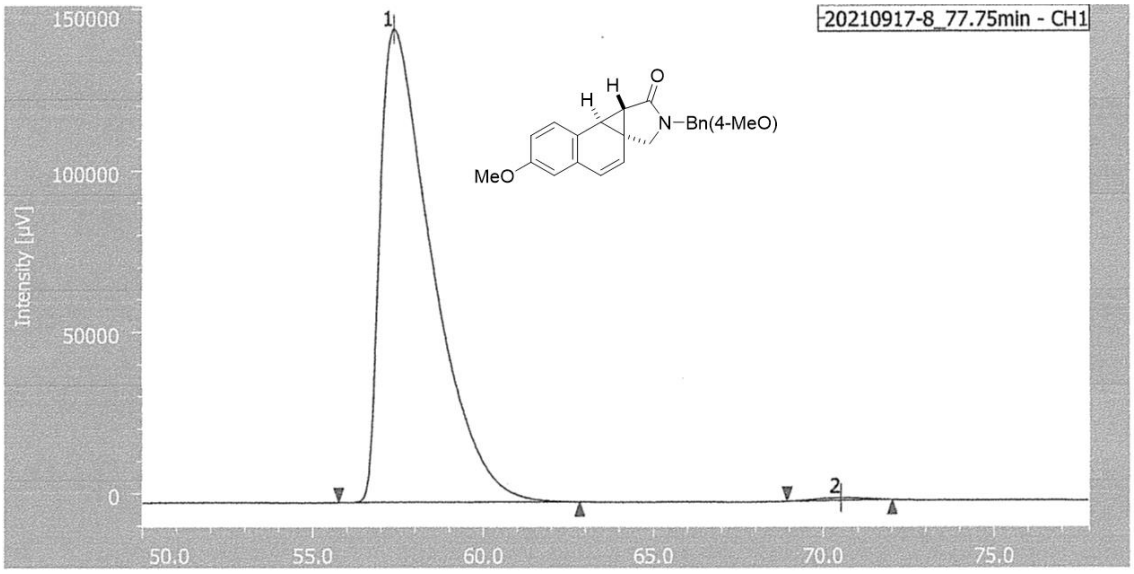
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	54.900	2948038	36310	49.277	52.486
2	58.875	3034522	32870	50.723	47.514



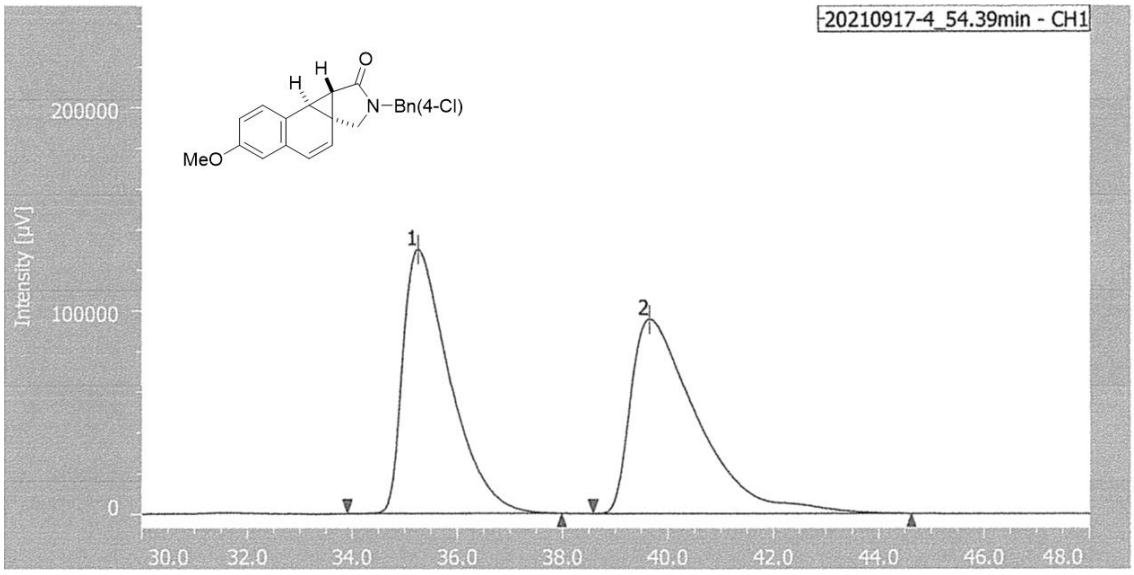
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	54.892	126515	2451	0.603	1.259
2	56.500	20857113	192316	99.397	98.741



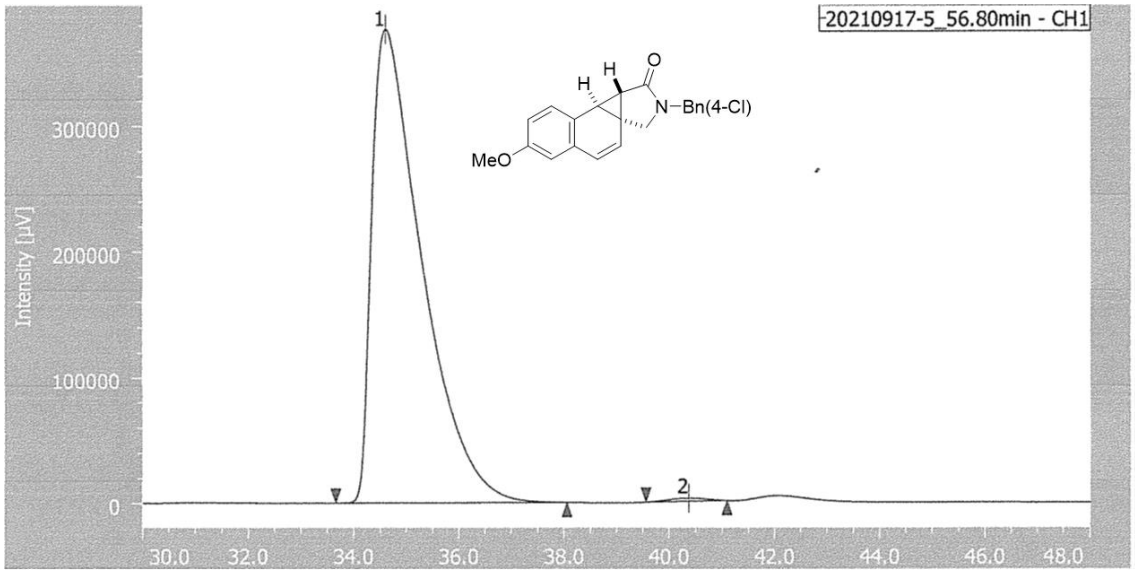
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	58.300	58.16887	58609	49.949	58.447
2	68.750	58.28785	41668	50.051	41.553



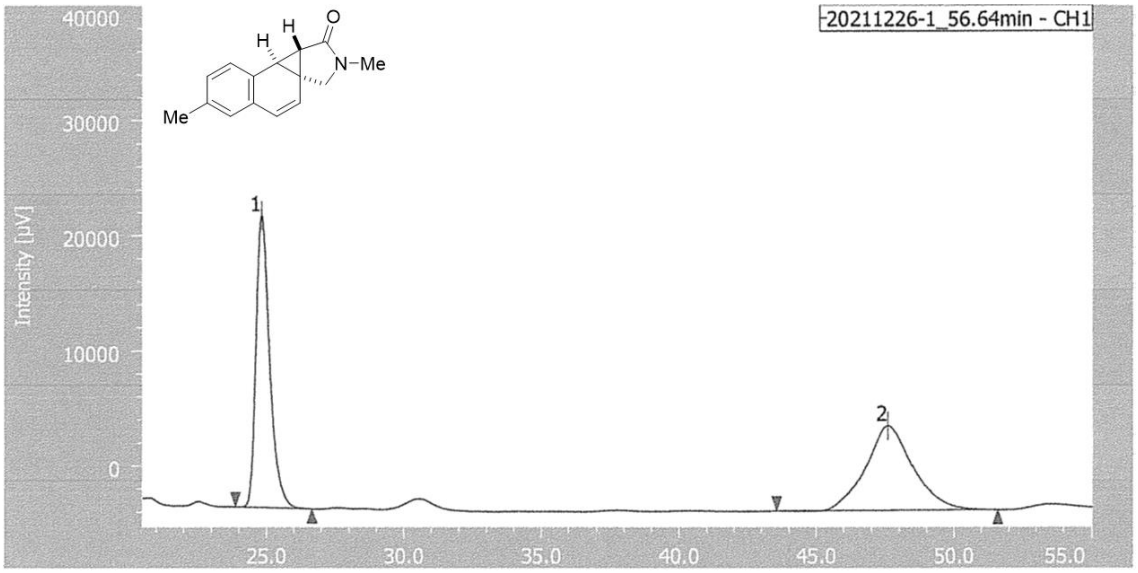
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	57.383	15600330	146455	99.487	99.442
2	70.508	80413	822	0.513	0.558



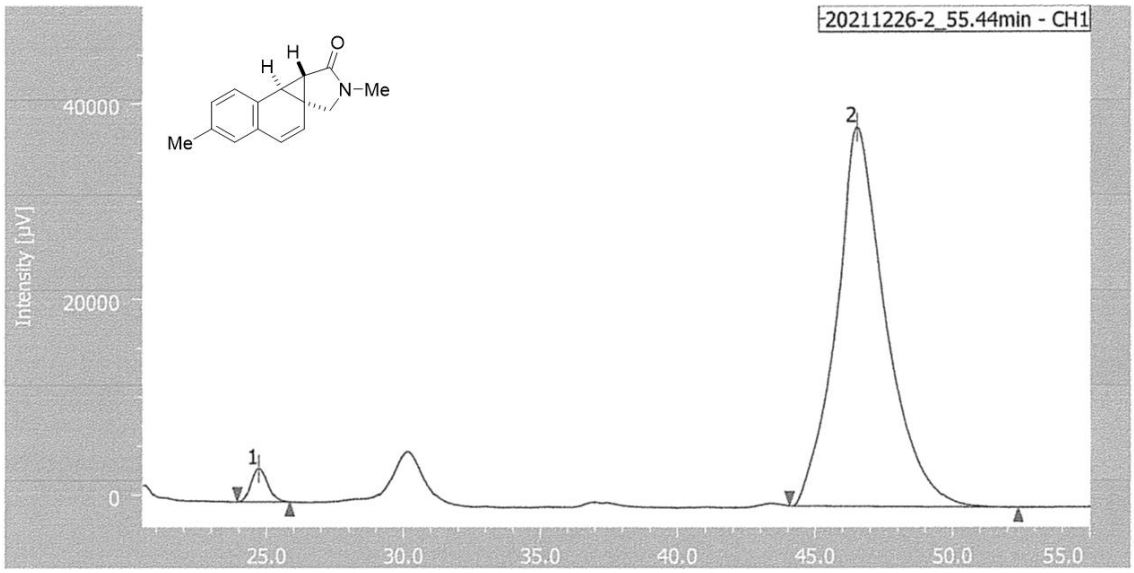
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	35.250	8032823	129839	48.941	57.627
2	39.650	8380303	95469	51.059	42.373



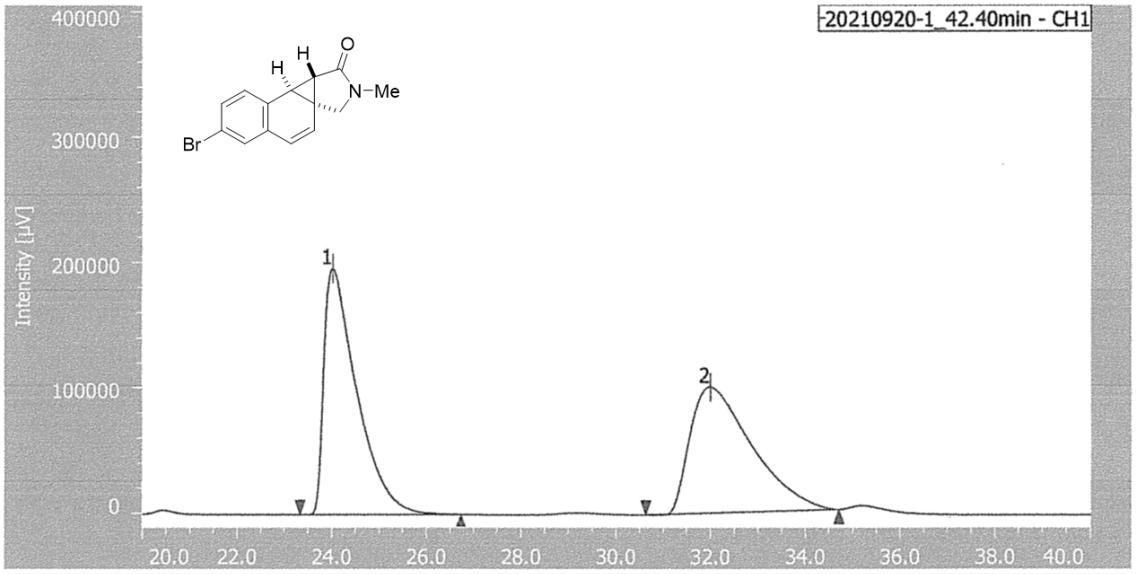
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	34.600	24967597	376623	99.485	99.337
2	40.367	129330	2515	0.515	0.663



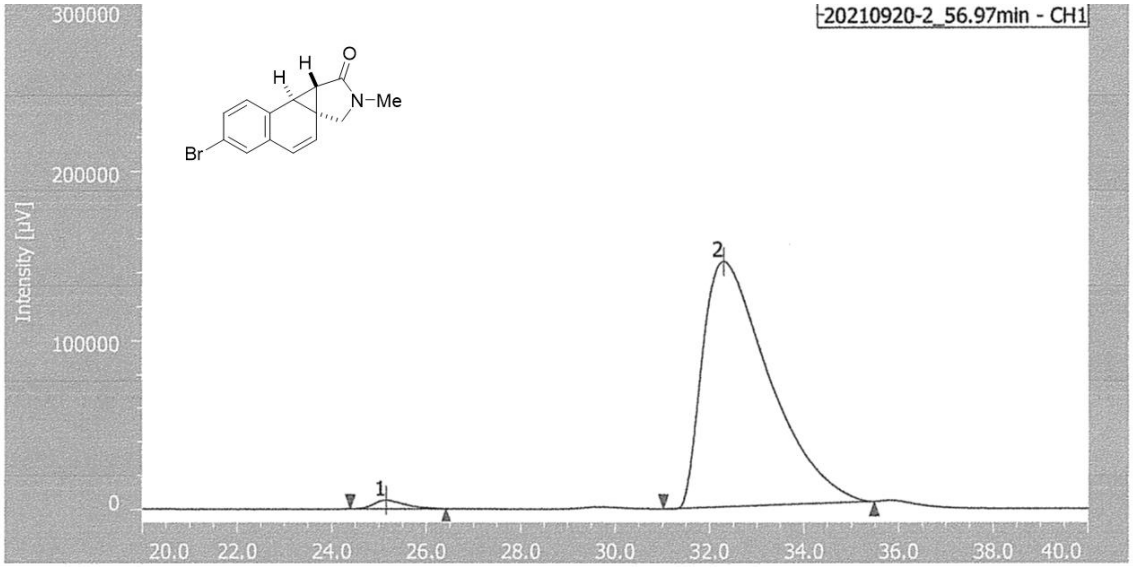
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	24.825	877694	25320	50.141	77.580
2	47.583	872772	7317	49.859	22.420



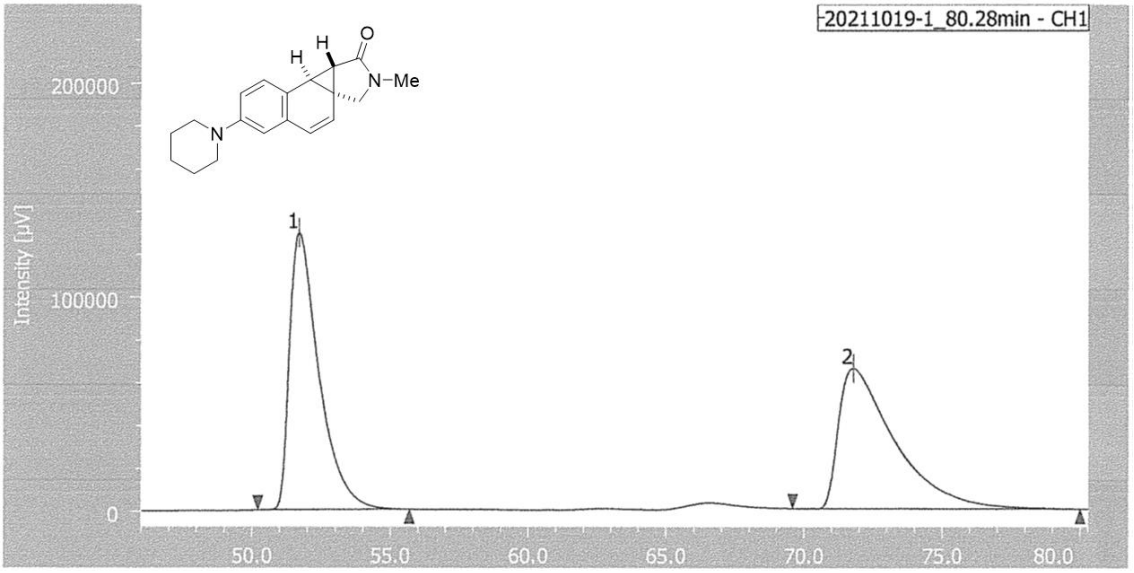
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	24.717	143494	3400	2.882	8.063
2	46.508	4834896	38773	97.118	91.937



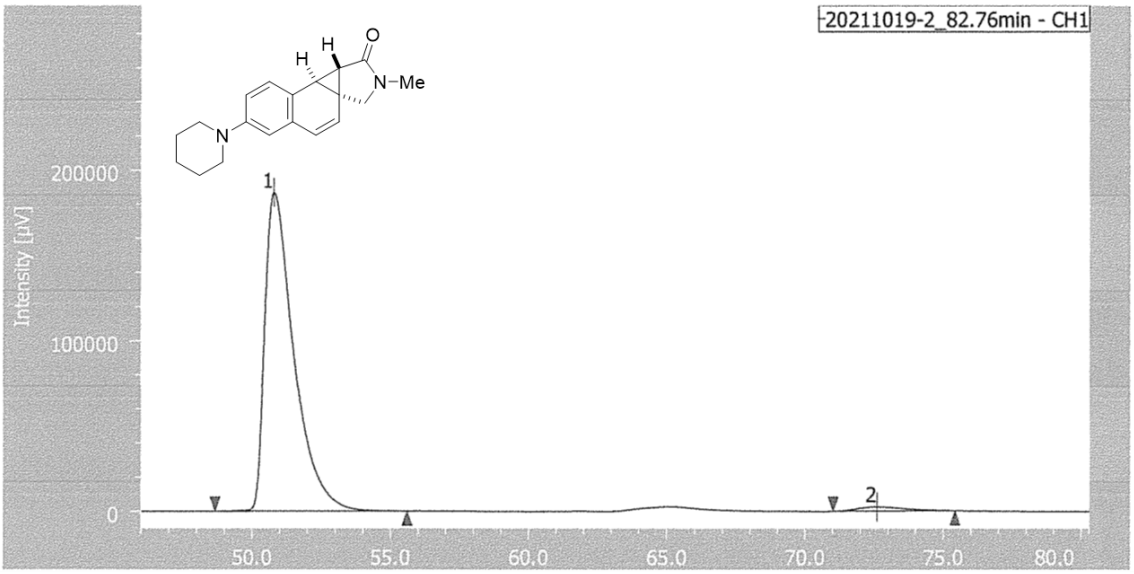
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	24.017	9417073	196175	50.809	66.169
2	31.992	9117104	100301	49.191	33.831



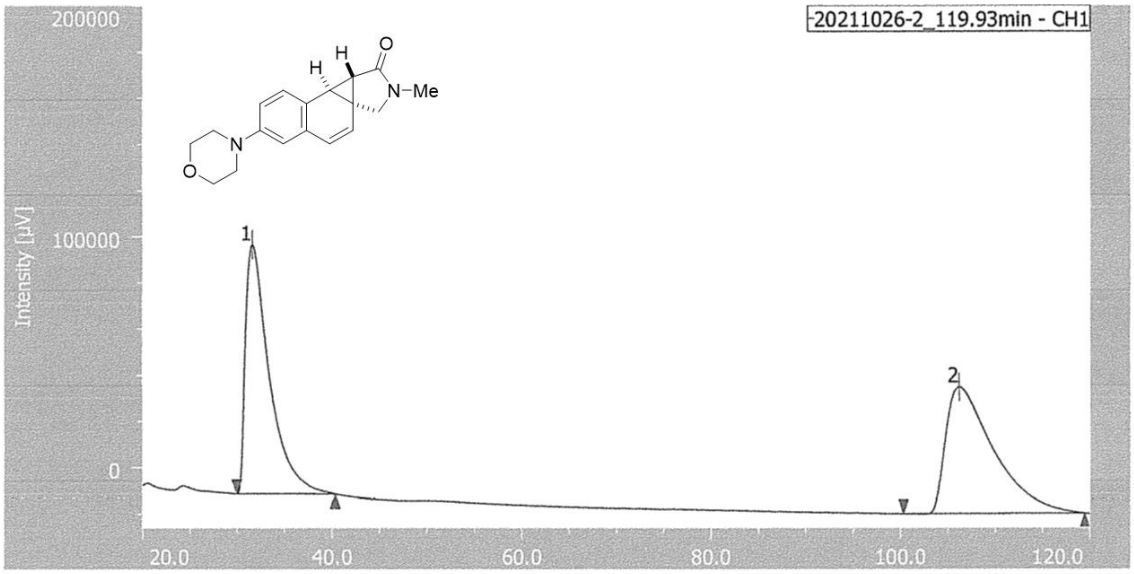
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.150	229554	5020	1.578	3.342
2	32.283	14317977	14159	98.422	96.658



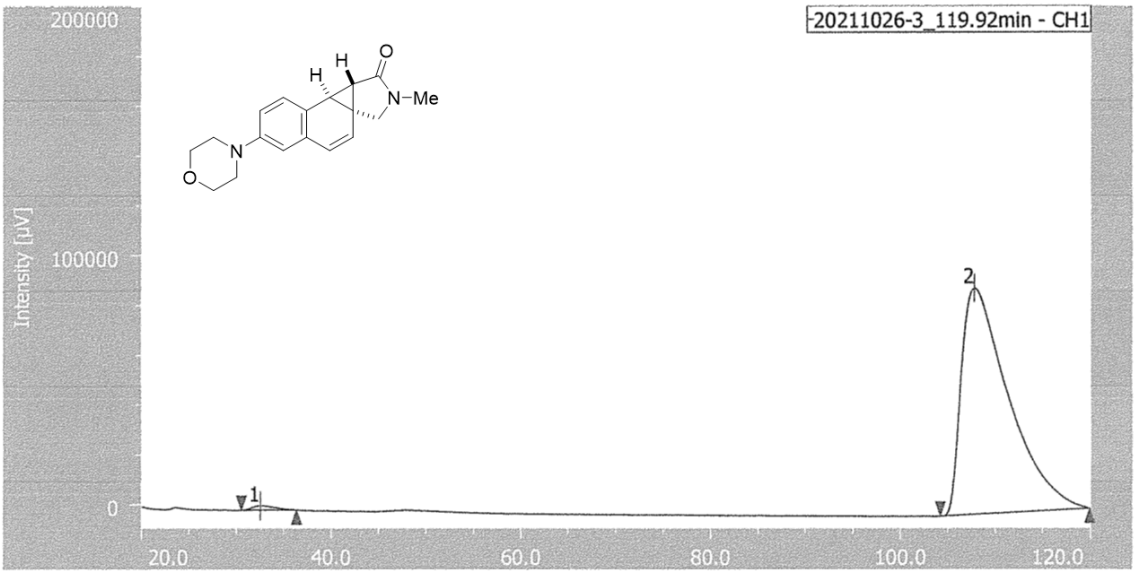
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	51.692	9522639	129254	50.686	66.313
2	71.775	9265008	65661	49.314	33.687



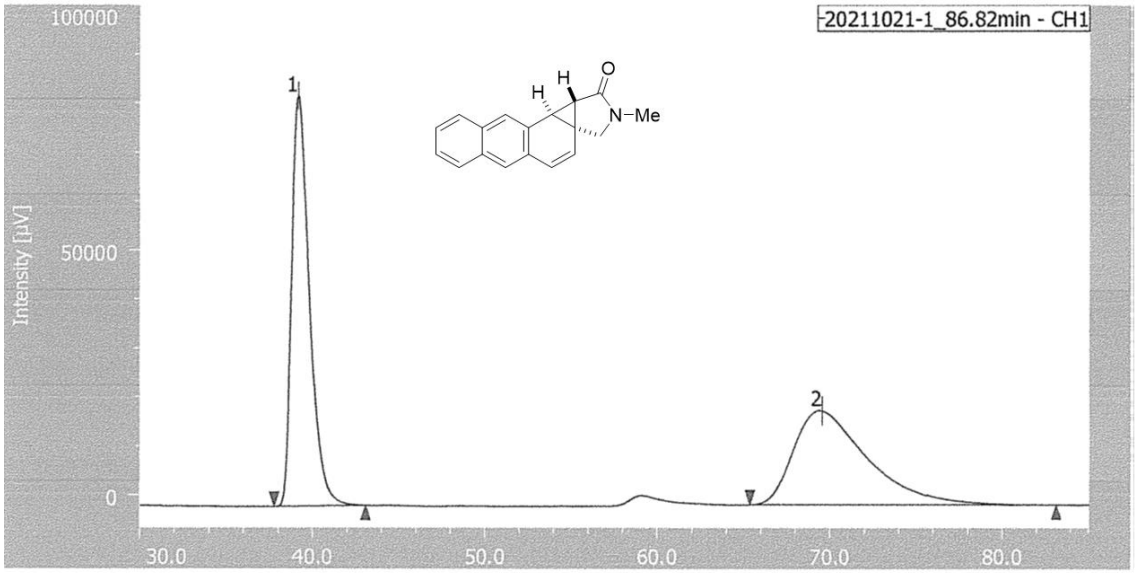
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	50.783	13628840	186828	97.885	98.701
2	72.592	294484	2458	2.115	1.299



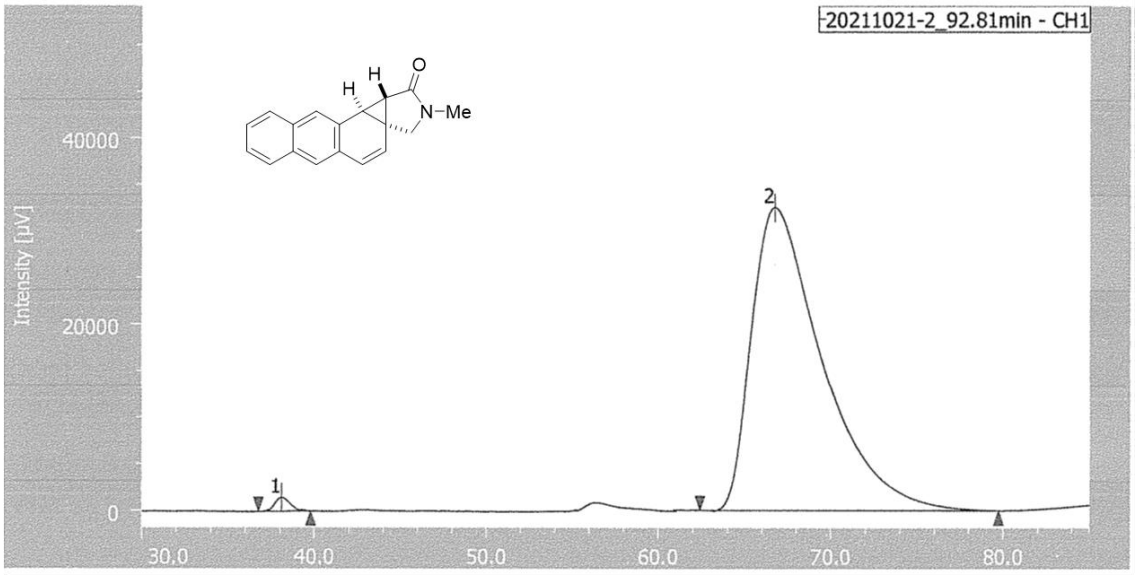
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	31.558	18935328	107962	49.855	66.421
2	106.175	19045611	54581	50.145	33.579



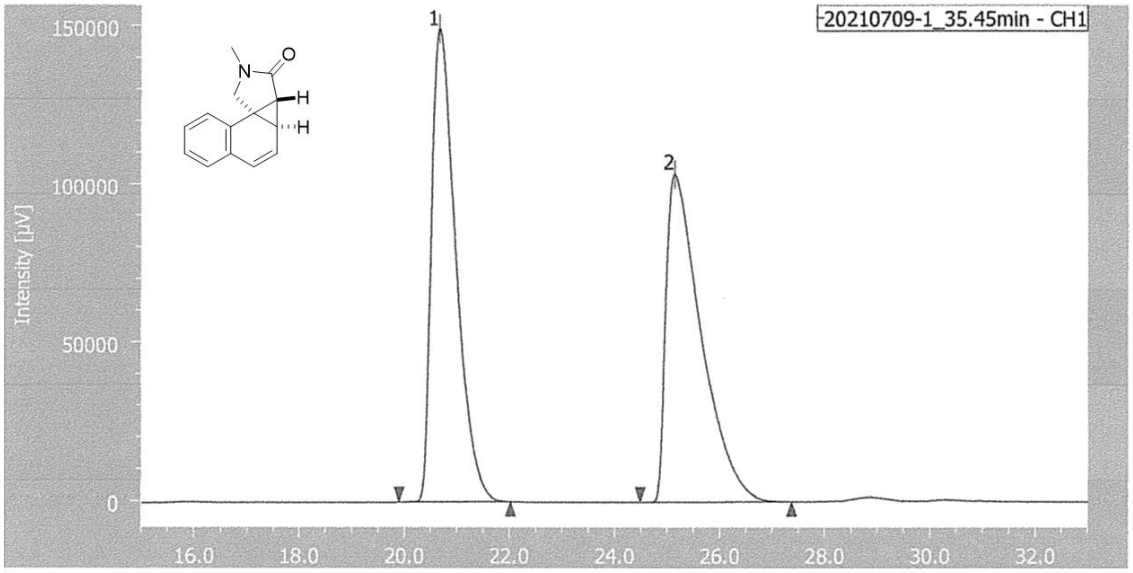
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	32.542	295148	1783	0.928	1.925
2	107.775	31513860	90848	99.072	98.075



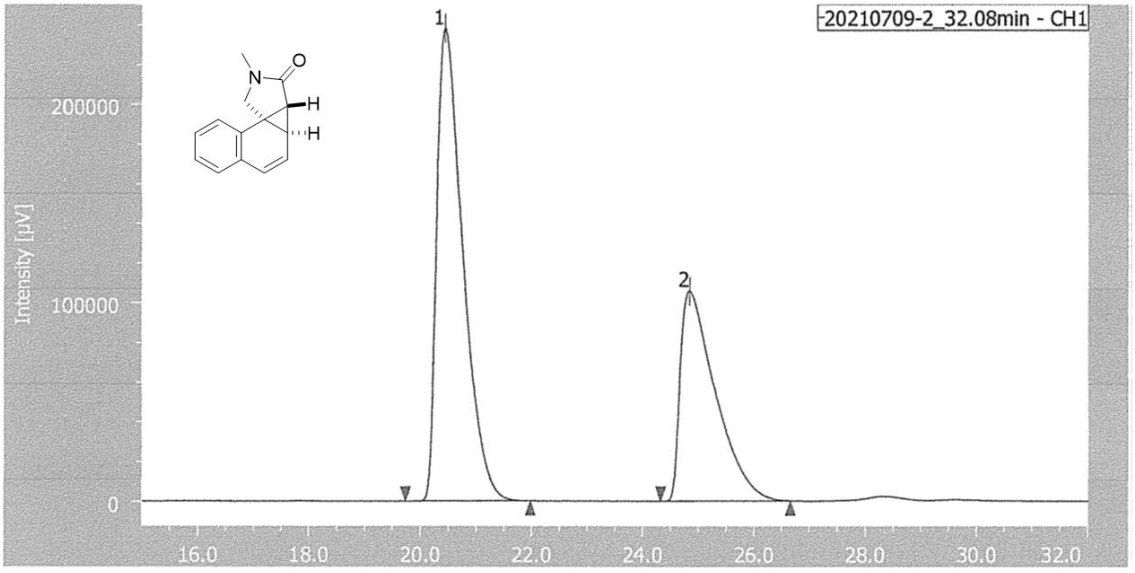
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	39.142	6006781	83677	51.199	81.312
2	69.525	5725480	19232	48.801	18.688



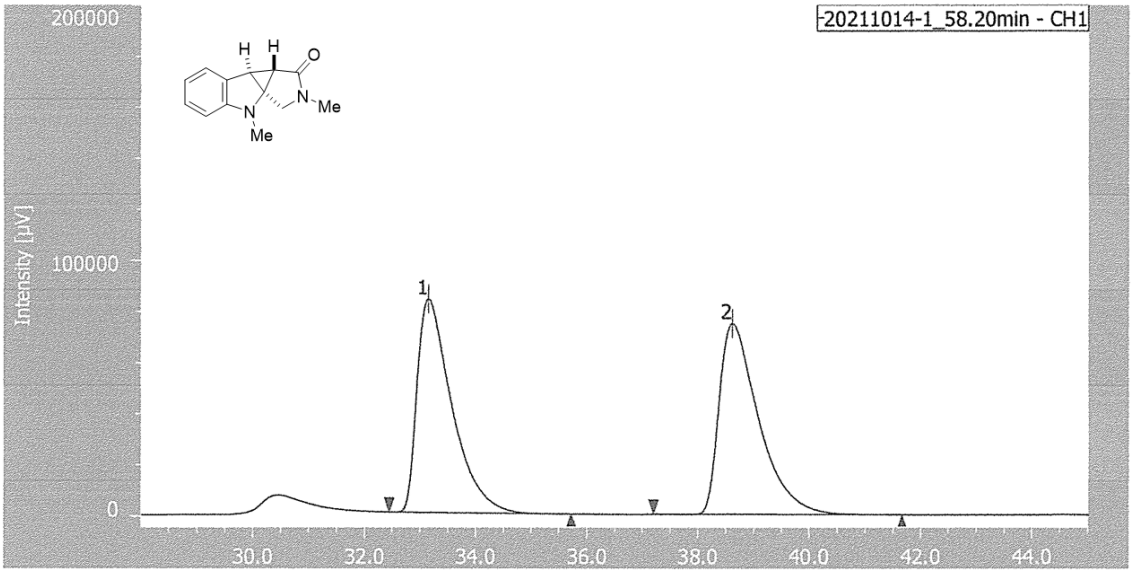
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	38.083	90584	1468	0.967	4.318
2	66.717	9277632	32521	99.033	95.682



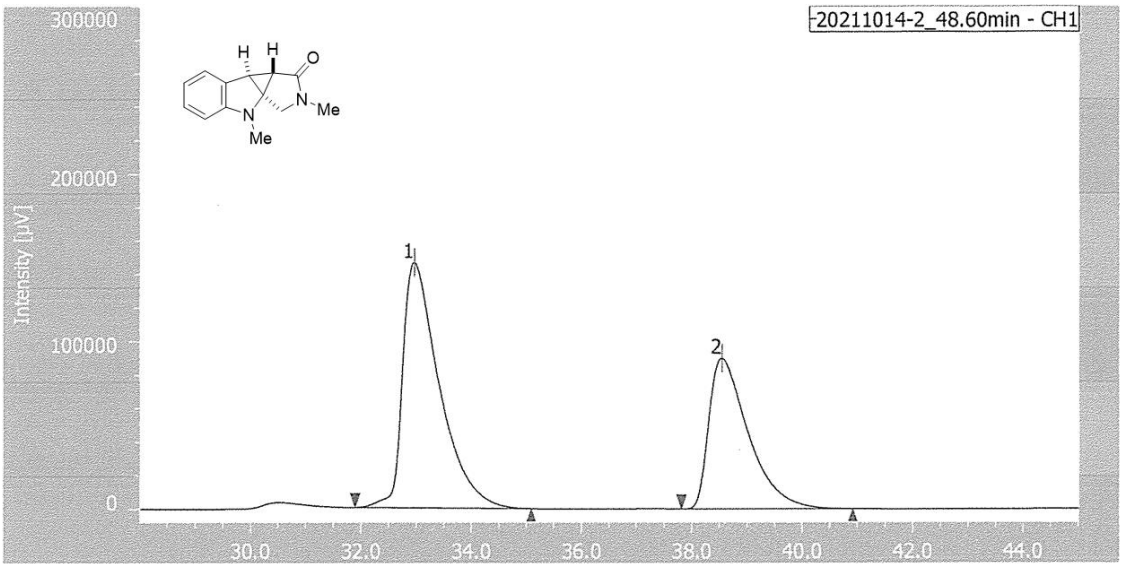
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.667	4786915	149310	49.923	59.067
2	25.142	4801717	103471	50.077	40.933



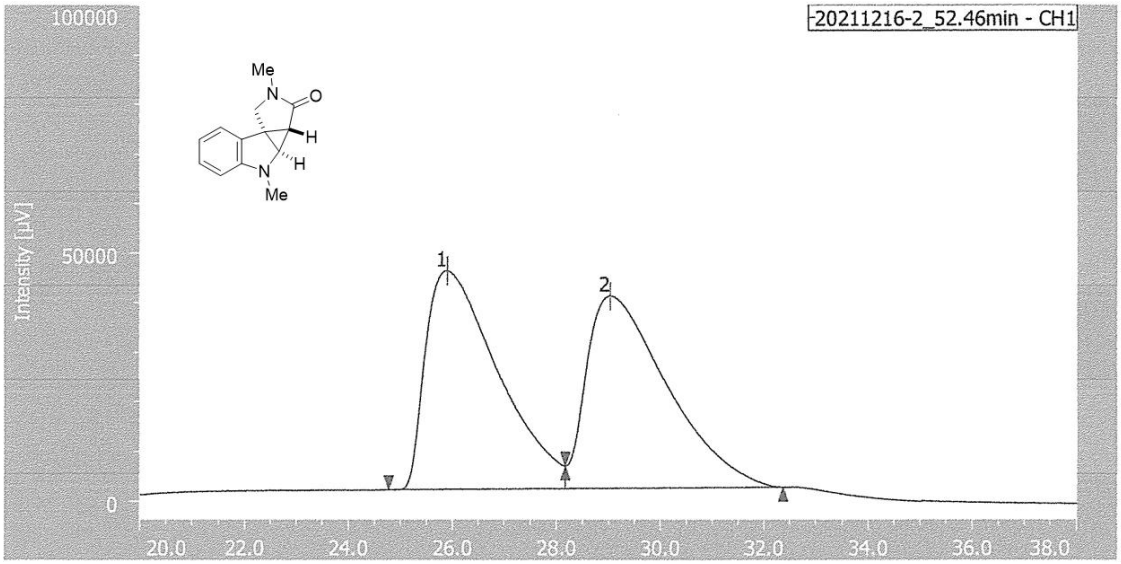
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	20.433	7730078	238136	62.414	69.252
2	24.833	4655005	105735	37.586	30.748



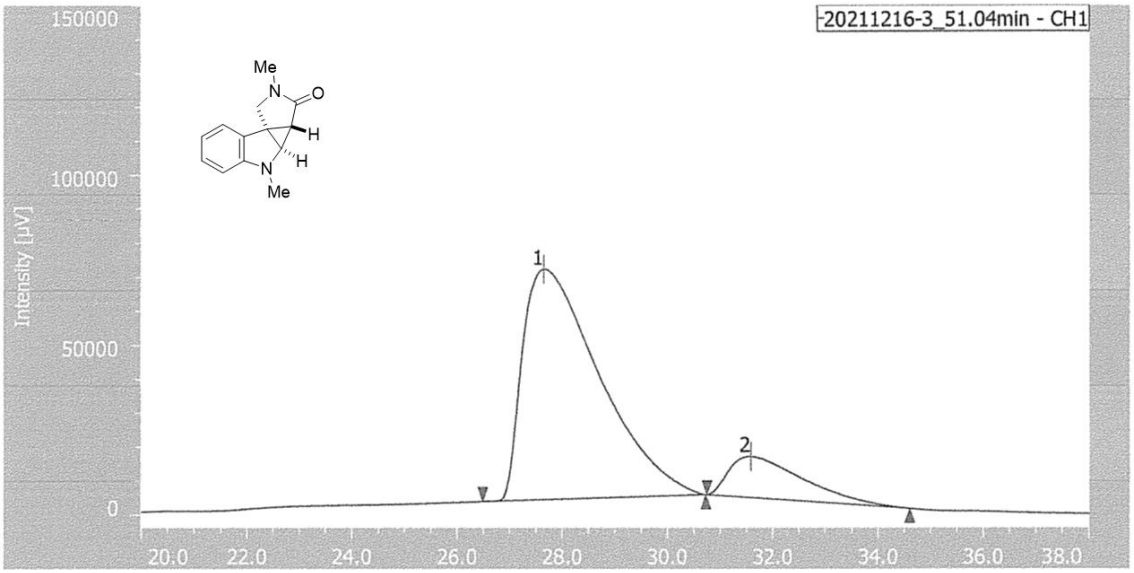
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	33.150	3629641	83533	49.757	52.813
2	38.608	3665126	74633	50.243	47.187



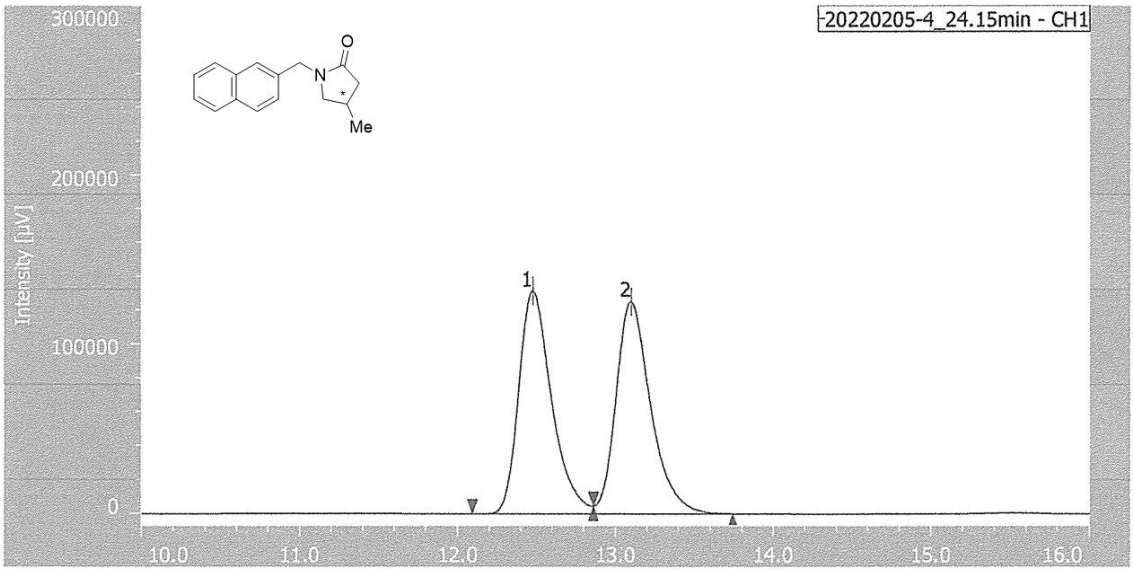
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	32.967	6771558	146531	60.404	61.957
2	38.542	4438828	89973	39.596	38.043



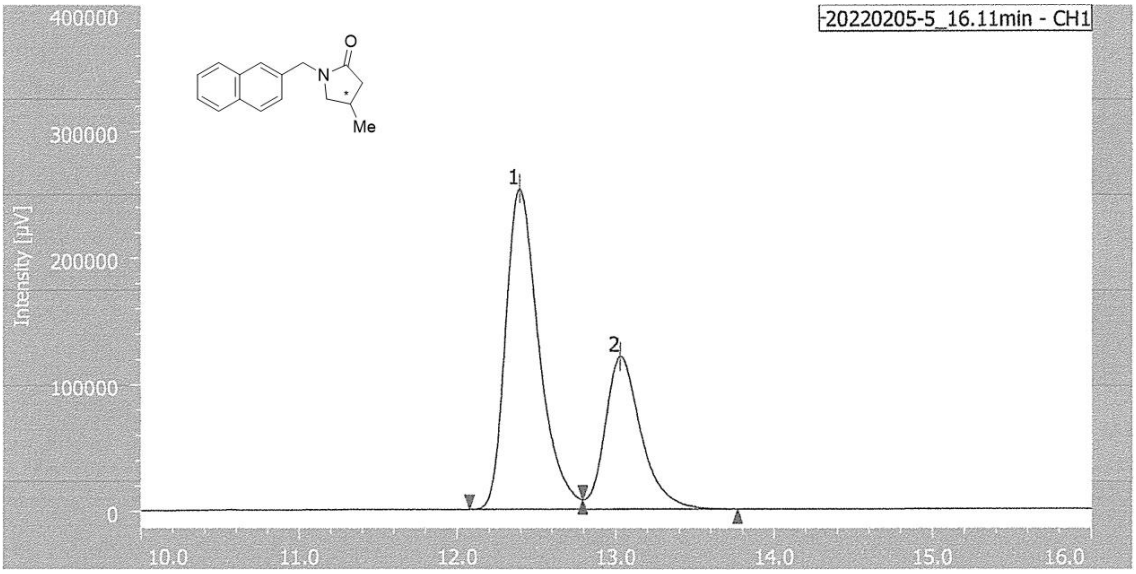
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	25.900	4269477	44060	50.482	53.241
2	29.033	4187926	38696	49.518	46.759



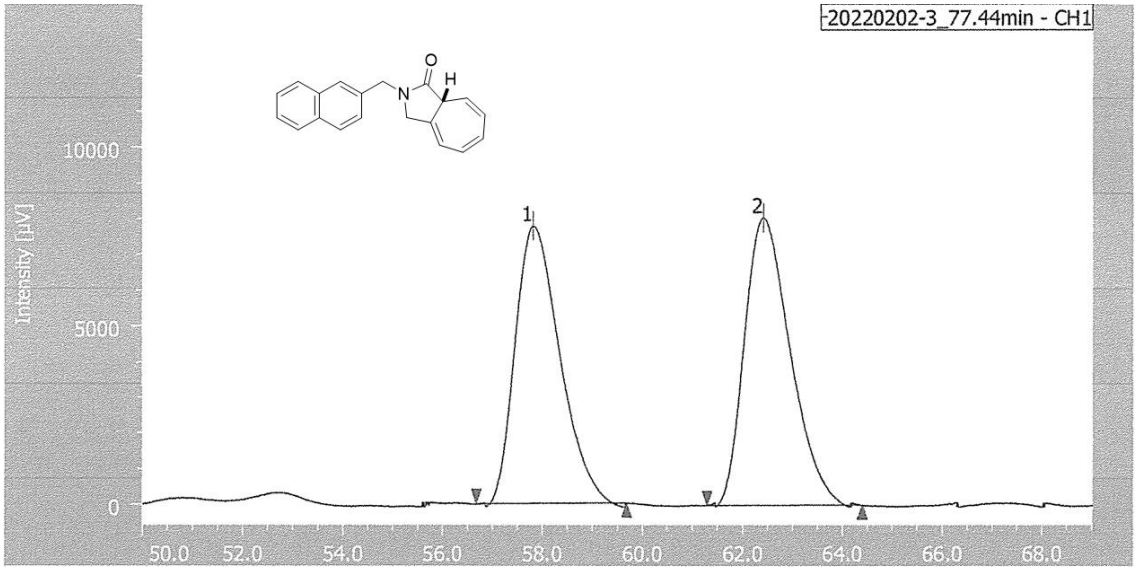
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	27.650	6910919	68000	85.270	84.858
2	31.575	1193830	12134	14.730	15.142



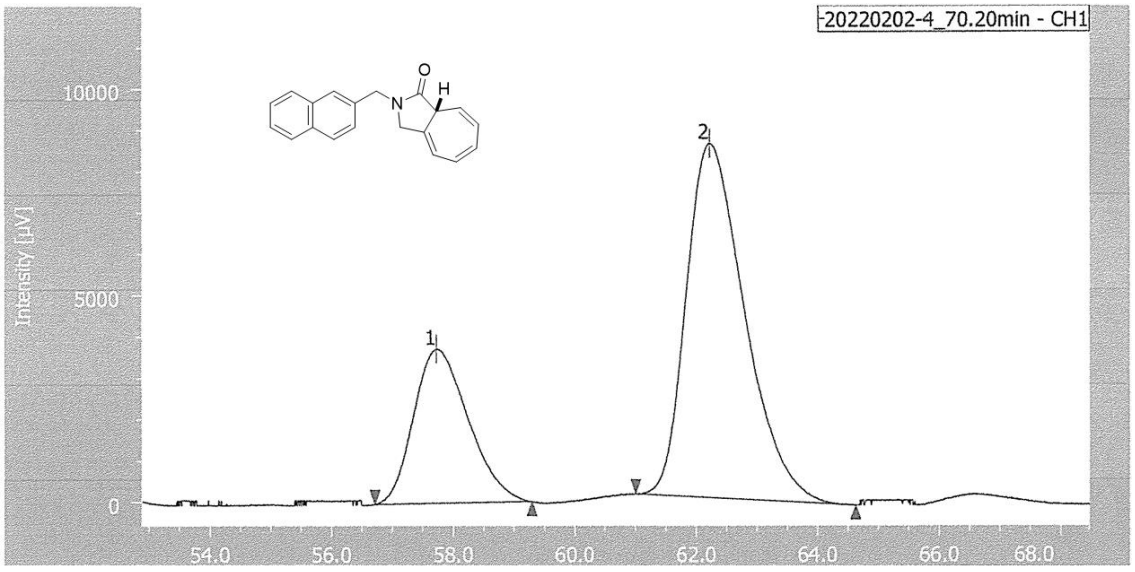
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.475	1900142	131747	49.786	51.236
2	13.100	1916465	125393	50.214	48.764



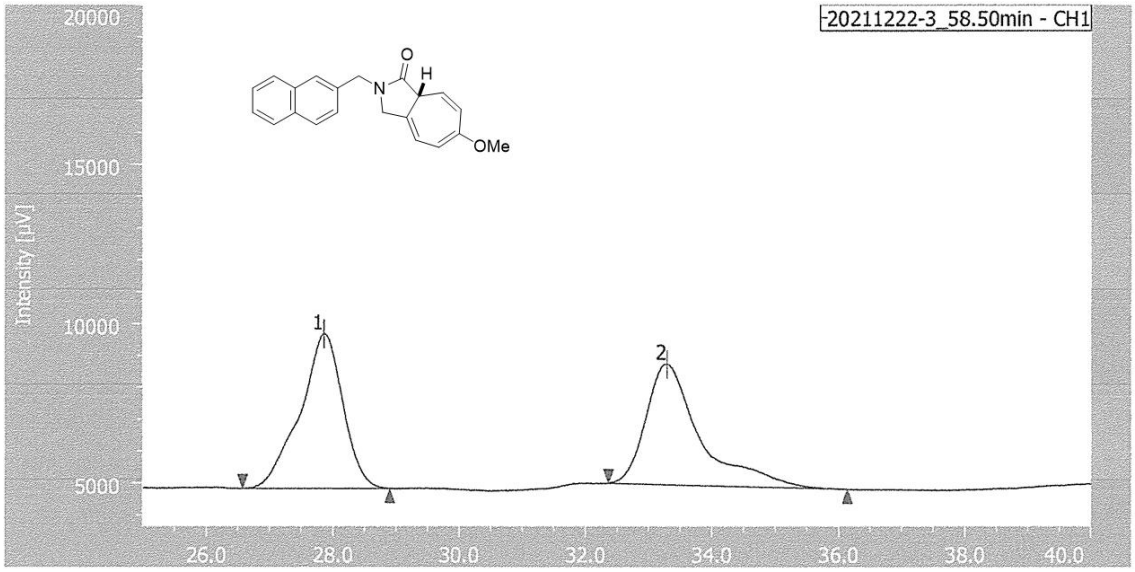
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	12.392	3732528	253321	66.313	67.726
2	13.025	1896128	120719	33.687	32.274



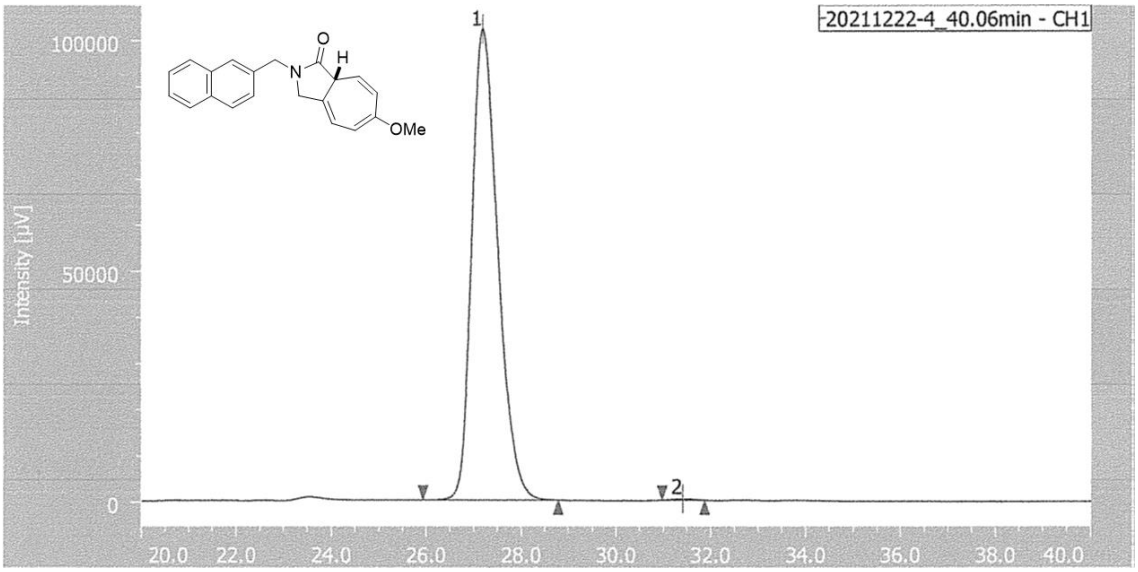
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	57.808	480576	7767	48.361	49.118
2	62.408	513154	8046	51.639	50.882



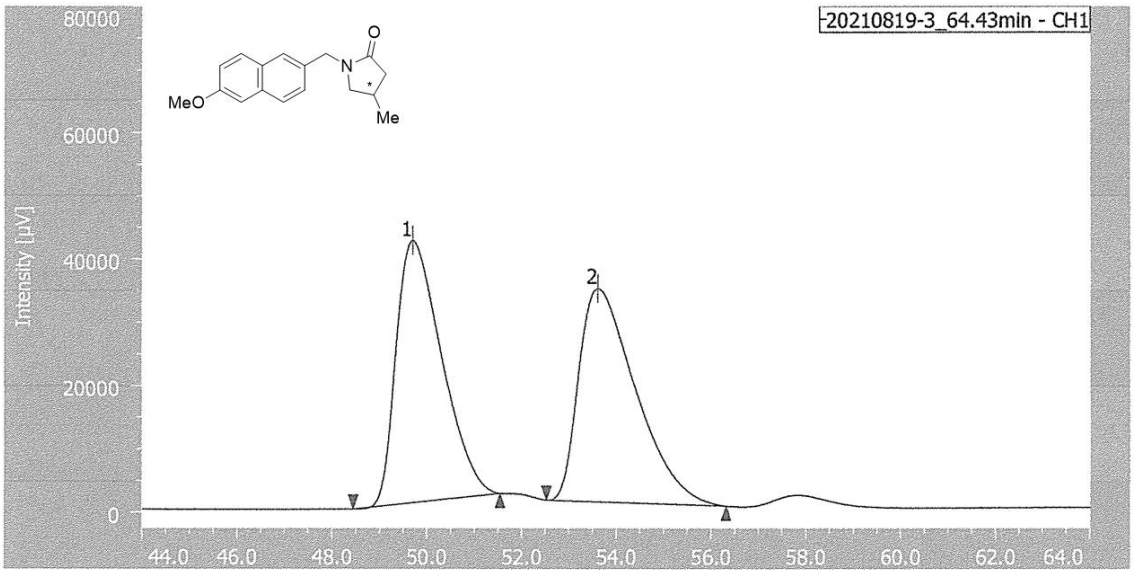
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	57.725	232333	3737	28.866	30.357
2	62.217	572541	8573	71.134	71.134



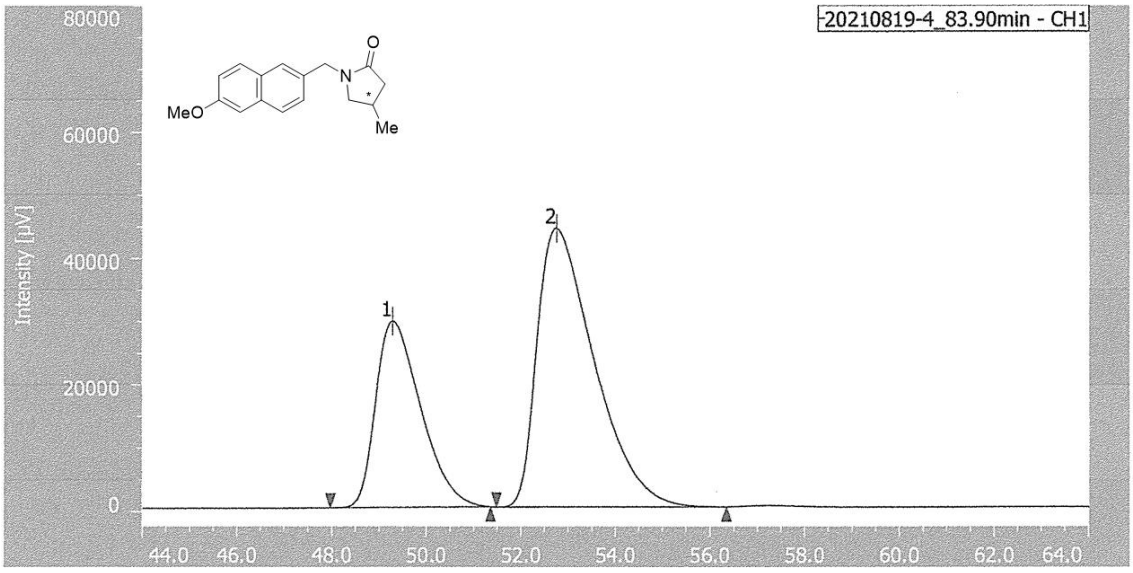
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	27.858	227862	4851	50.193	56.156
2	33.292	226114	3787	49.807	43.844



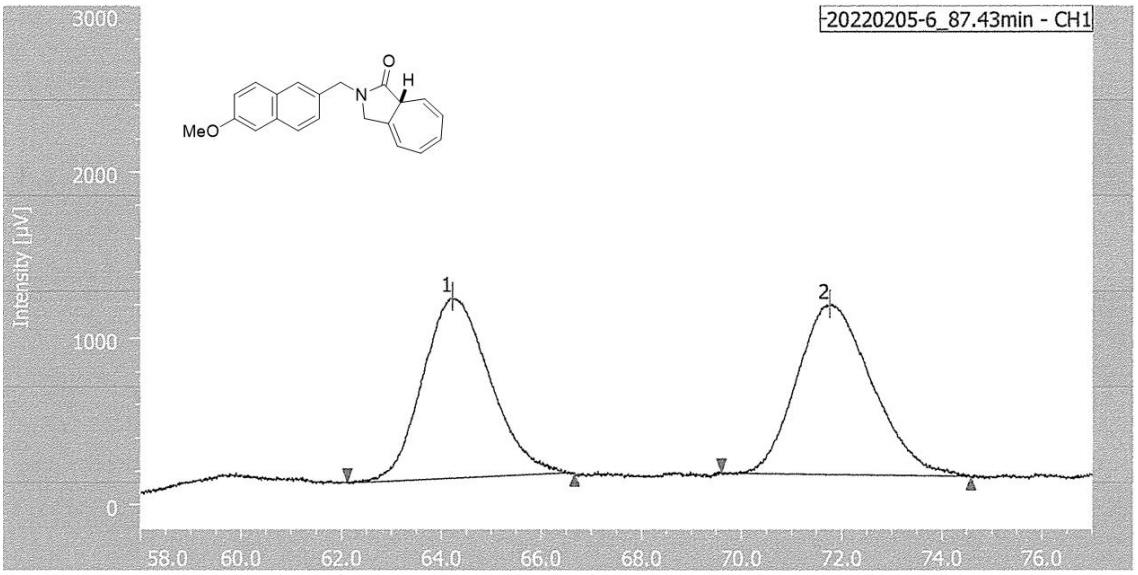
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	27.183	3883341	102047	99.768	99.709
2	31.408	9018	298	0.232	0.291



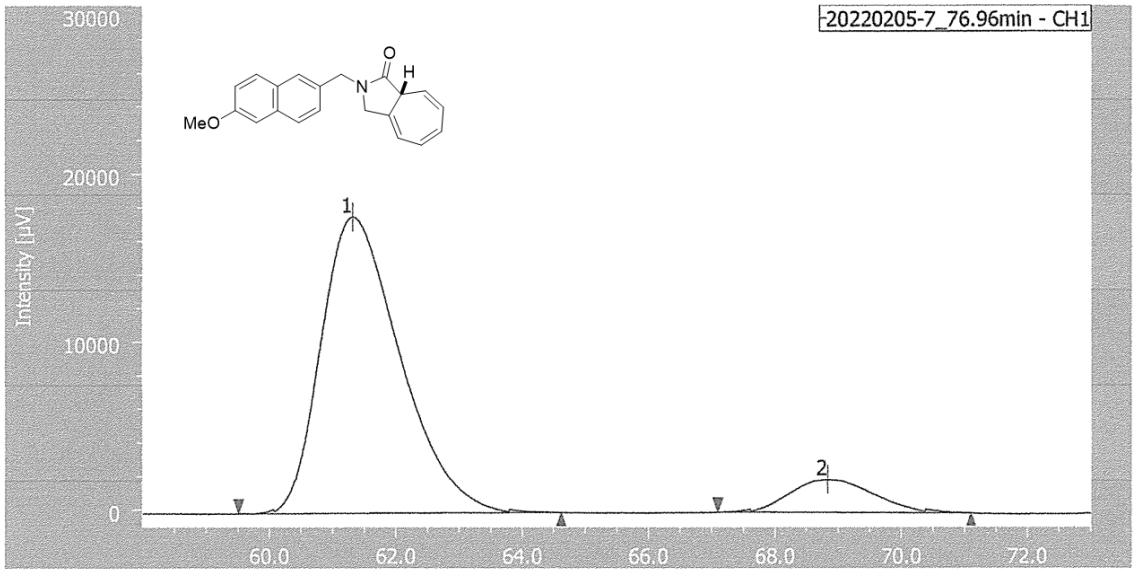
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	49.692	2772457	41481	49.544	55.138
2	53.600	2823458	33750	50.456	44.862



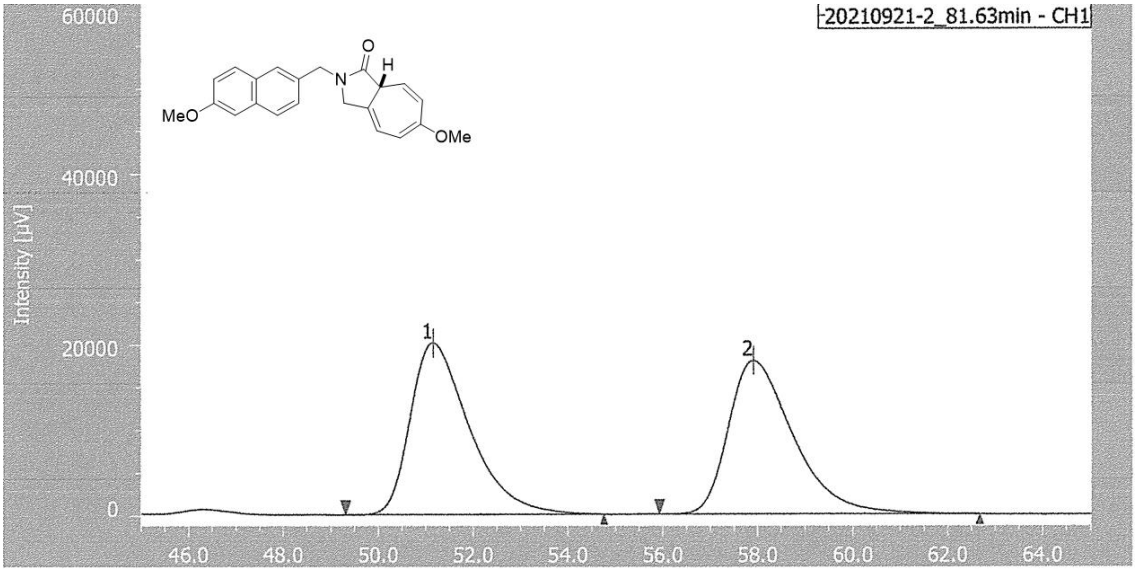
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	49.283	1951126	29451	34.481	40.066
2	52.750	3707470	44057	65.519	59.934



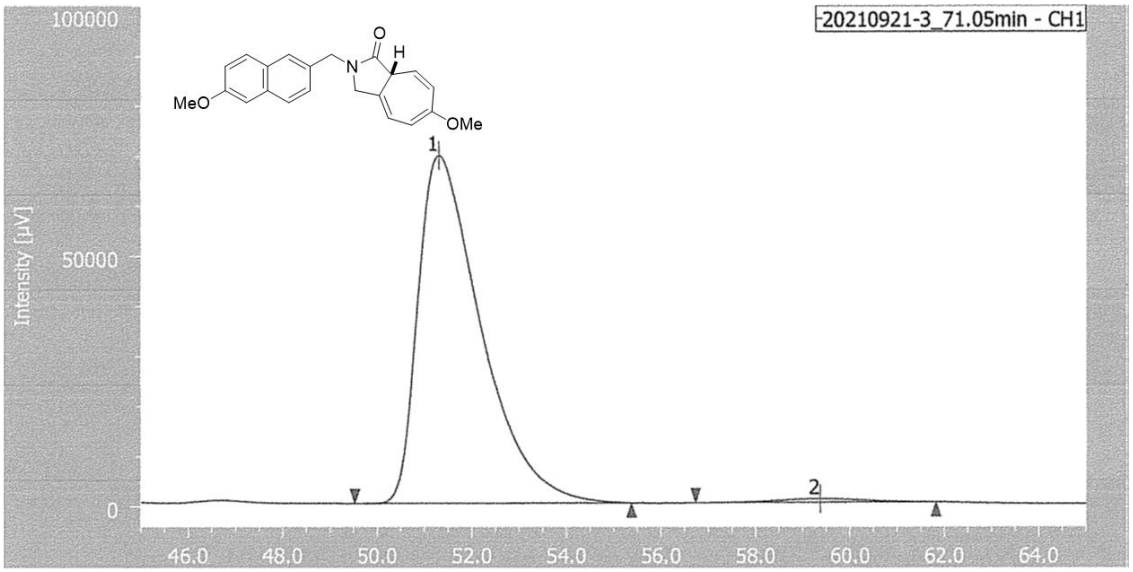
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	64.217	101521	1092	48.806	51.537
2	71.758	106490	1027	51.194	48.463



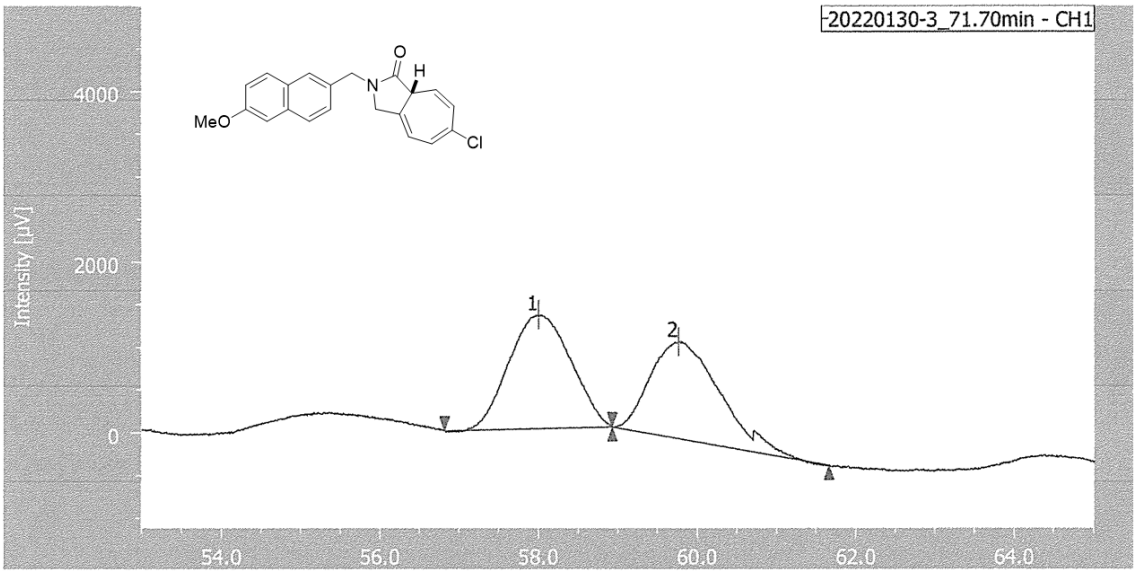
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	61.317	1536622	17606	89.524	89.889
2	68.833	179822	1980	10.476	10.111



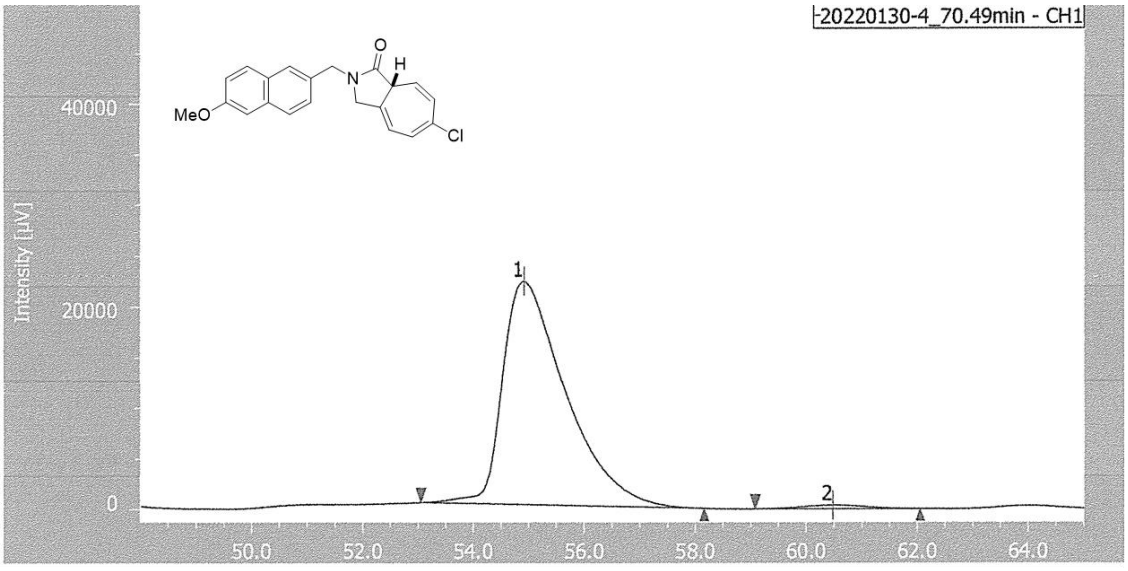
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	51.158	1742989	20105	50.444	52.780
2	57.908	1712303	17987	49.556	47.220



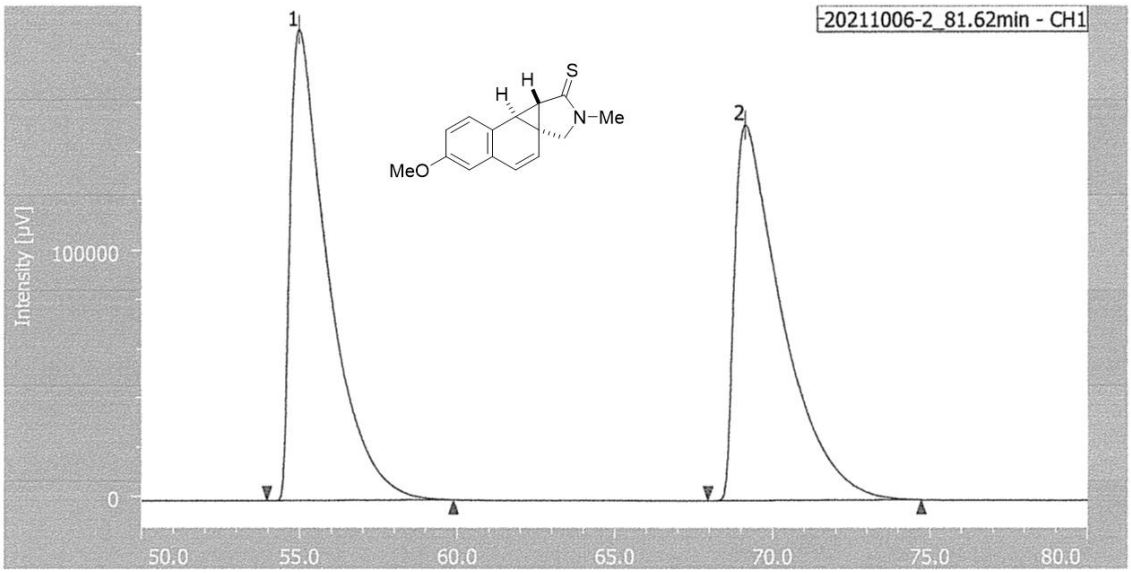
PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	51.308	6410426	69489	98.591	98.972
2	59.367	91586	722	1.409	1.028



PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	58.000	72288	1331	51.068	53.932
2	59.767	69264	1137	48.932	46.068



PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	54.917	1745053	22063	98.337	98.270
2	60.483	29514	388	1.663	1.730



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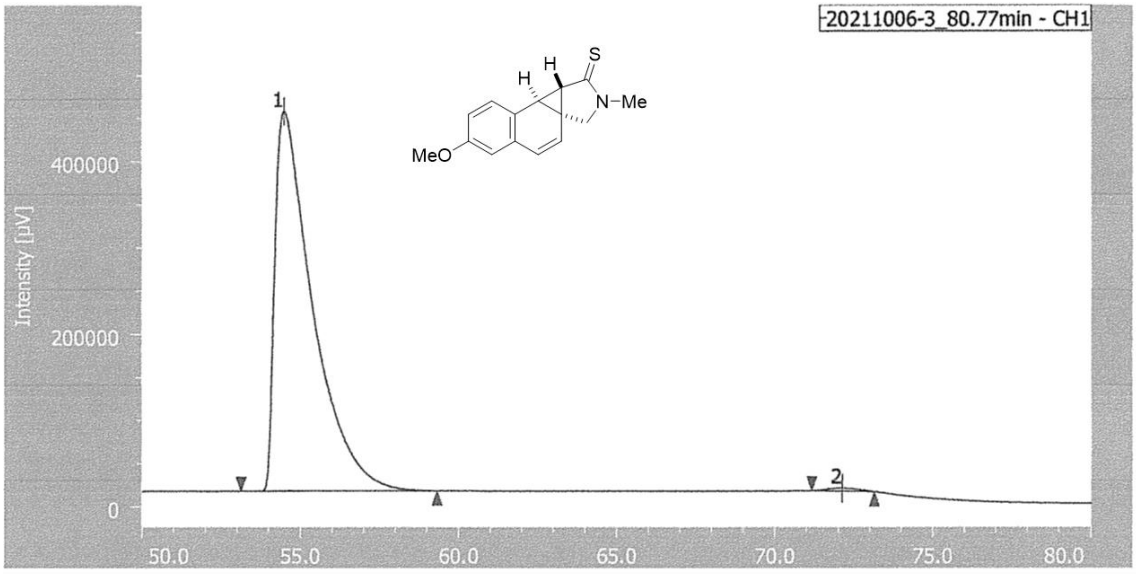
1	54.975	16042999	191444	50.028	55.644
2	69.125	16025200	152607	49.972	44.356



PEAK	RT [min]	AREA [μV・sec]	HEIGHT [μV]	AREA%	HEIGHT%
1	54.475	36475216	440072	99.375	99.224
2	72.117	229354	3441	0.625	0.776

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第 2 章

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