INTERMOLECULAR (4+3) CYCLOADDITION REACTION OF OXIDOPYRIDINUIM IONS WITH SILYLATED DIENES, EXPLORING THE OXIDATION CHEMISTRY AND PHOTOCHEMISTRY OF CYCLOADDUCTS

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Doctor of Philosophy

by

WANNA SUNGNOI

Dr. Michael Harmata, Dissertation Supervisor

DECEMBER, 2022

The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

INTERMOLECULAR (4+3) CYCLOADDITION REACTION OF

OXIDOPYRIDINUIM IONS WITH SILYLATED DIENES, EXPLORING THE OXIDATION

CHEMISTRY AND PHOTOCHEMISTRY OF CYCLOADDUCTS

Presented by Wanna Sungnoi,

A candidate for the degree of doctor of philosophy,

and hereby certify that, in their opinion, it is worthy of acceptance.

_____

Professor Michael Harmata

_____

Professor Timothy Glass

_____

Professor Justin Walensky

_____

Professor Mark Hannink

DEDICATION

In the memory of

The one and only mom and dad, the person who let me have the freedom to live, learn, and explore of life. MaryBeth McCrumb, the beloved sister who shaped me a lot about an American's culture, life, and how to survive in the US. I wish all of you were here to celebrate with me.

And To……..

Another half of my life, Cat, who always be there when I look back. Thank you that you walk with me on the gravel road and you are still here. We will keep walking together. Sometimes the wrong train can lead us to the right destination.

A lot of love from Teresa Inkman, my sister, who is supporting me, training me very hard about critical thinking, giving me courage, and kicking my butt to continue every pathway that I chose.

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I would like to thank you, Dr. Steven Kelly, for the discussion about how to grow a better crystal throughout my Ph.D. career. Colleen Ray to help me solving the NMR's puzzle.

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LIST OF ABBREVIATIONS

CH_2Cl_2	Dichloromethane
DCM	Dichloromethane
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
Equiv	Equivalent
EtOAc	Ethyl acetate
H_2PtCl_6	Chloroplatinic acid
HFIP	Hexafluoroisopropanol
$HSiEt_3$	Triethyl silane
K_2CO_3	Potassium carbonate
KOTMS	Potassium trimethylsilanolate
LAH	Lithium aluminum hydride
Me	Methyl group
MeCN	Acetonitrile
MeOH	Methanol
n-BuLi	n-Butyllithium
NBS	N-bromosuccinimide

NIS	N-iodosuccinimide
OAc	Acetate
OMe	Methoxy group
OTf	Trifluoromethanesulfonate
$Pd(PPh_3)_4$	Palladium-tetrakis(triphenylphosphine)
Quant	Quantitative
RT	Room temperature
TBAF	Tetra-n-butylammonium fluoride
TEA	Triethylamine
TES	Triethylsilyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl
TMEDA	Tetramethylethylenediamine
TMS	Trimethylsilyl

INTERMOLECULAR (4+3) CYCLOADDITION REACTION OF OXIDOPYRIDINUIM IONS WITH SILYLATED DIENES, EXPLORING THE OXIDATION CHEMISTRY AND PHOTOCHEMISTRY OF CYCLOADDUCTS

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ABSTRACT

The development of *endo*/*exo* selectivity of intermolecular (4+3) cycloaddition reactions of an *N*-methyl oxidopyridinium ion has been studied. Dienes that contain silyl groups, R-groups, and contain both silyl group and R-groups were investigated to compare the stereoselectivity of the intermolecular (4+3) reaction. The introduction of steric hindrance in the form of 2-trialkylsilyl-4-alkylbutadienes can enhance the *endo* selectivity of the intermolecular (4+3) reaction. The *N*-methyloxidopyridinium ion reacted with 2-trialkylsilyl-4-alkylbutadienes to afford cycloadducts with high regioselectivity and *endo* selectivity.

The attempted cleavage of a trialkyl silyl of the (4+3) cycloadducts has led to a new discovery. *N*-Iodosuccinimide (NIS) was employed as the reagent and the hexafluoroisopropanol (HFIP) was employed as the solvent for the iododesilylation. However, functionalization of the cycloadducts at the bridgehead carbon was the only observed. An attempt to modify the functional group at the bridgehead carbon was unsuccessful. Based on the proposed mechanism and the product formation, HFIP acted as the nucleophile.

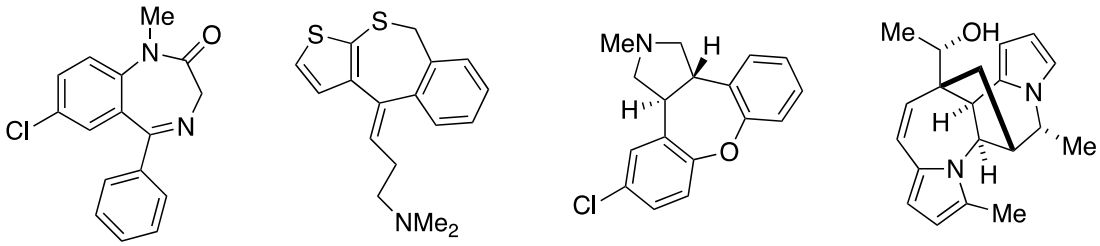
An extension of the aforementioned study investigated the efficacy of the (4+3) cycloadducts as reactants in a [2+2] photocycloaddition reaction. Irradiation by a 450-watt Hanovia medium-pressure mercury lamp of the (4+3) cycloadducts can induce a [2+2] photocycloaddition reaction. The intramolecular [2+2] photocycloaddition reaction of (4+3) cycloadducts afford polycyclic compounds possession an embedded tropane skeleton in excellent yield.

CHAPTER I

ENDO SELECTIVITY OF INTERMOLECULAR (4+3) CYCLOADDITION REACTION OF OXIDOPYRIDINIUM ION WITH TRIALKYL SILLYLATED DIENES

Introduction

Many natural and synthetic products with important biological activity contain seven-membered rings. For example, diazepam is used to treat anxiety, bisulepin is used as an antihistamine, asenapine is CNS active, carvulamine is used an anantimicrobial agent, etc. (Figure 1)[1,2]



diazepam
anti-anxiety

bisulepin
antihistamine

asenapine
CNS active

carvulamine
antimicrobial

Figure 1. Natural products contain seven-membered ring

There are several strategies for synthesizing seven-membered rings, but a key route is through cycloaddition reactions such as (4+3), (5+2), and (6+1).[3] The number in the parentheses represents the number of atoms that participate in the cycloaddition (Figure 2). The (x+y) cycloaddition is pericyclic and obeys the Woodward-Hoffmann rules.[4] Herein we will focus on the (4+3) cycloaddition reaction.

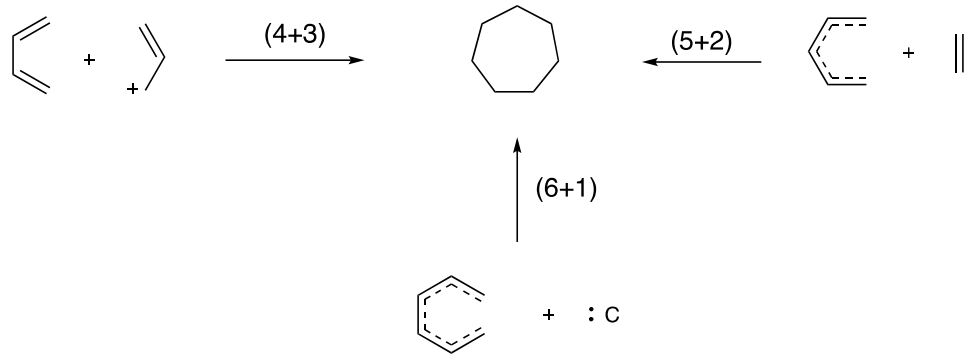


Figure 2. Method to construct the seven-membered ring

The (4+3) cycloaddition is analogous to the famous Diels-Alder reaction. The 4-carbon moiety has 4π electrons and behaves as a diene while the 3-carbon species is an allylic cation that has 2π electrons and behaves as a dienophile.[5]

To form a cycloadduct, the allylic cation has to be generated as a reactive intermediate that is stabilized by donating groups (Z) at the central carbon. Common donating groups used include O^-, OR, NR_2, CH_2SiR_3, and SR. The allylic cation intermediate can have three different forms[6]: the U form, the sickle form and the W form (Figure 3).

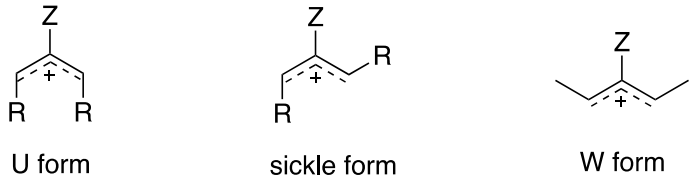


Figure 3. The allylic cation forms

If Z is nucleophilic, it will attack the electrophile (carbocation) to form species **2**, and if Z is less nucleophilic, it will generate the intermediate **1**, which reacts with the diene in a (4+3) cycloaddition (Figure 4).[7]

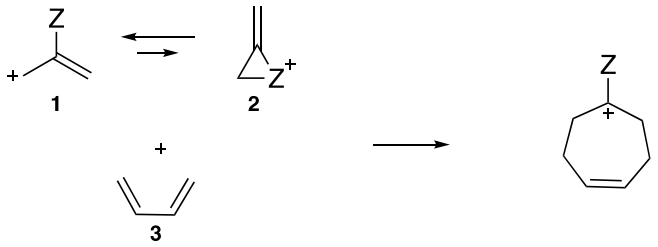


Figure 4. Diene reacts with allylic cation to form the (4+3) cycloadduct

There are two mechanisms through which an allylic cation reacts with 1,3-dienes to form the (4+3) cycloadduct,[8] a concerted and a stepwise pathway (Figure 5). The concerted pathway is favored when the dienophile is weakly electrophilic and when the diene is strongly nucleophilic.[9] In the concerted pathway, there are two transition states that can be adopted: the compact (*endo*) and extended (*exo*) configurations[7] (Figure 6). This model is similar to the Diels Alder's transition state model.

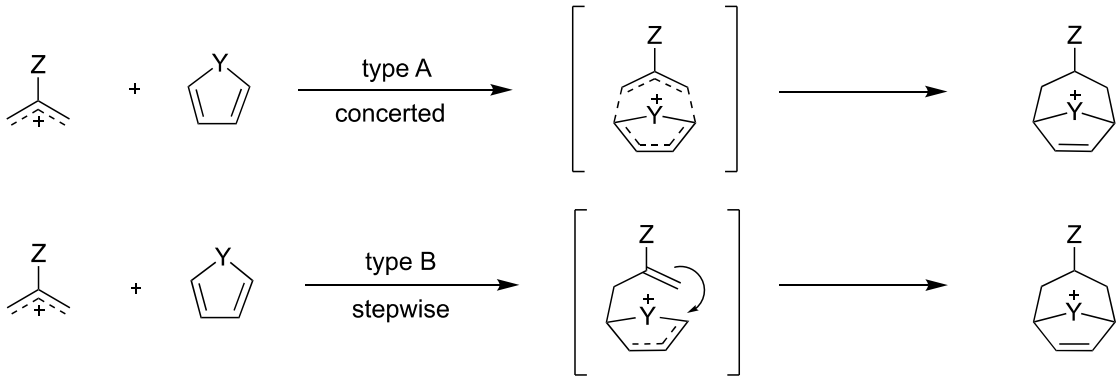
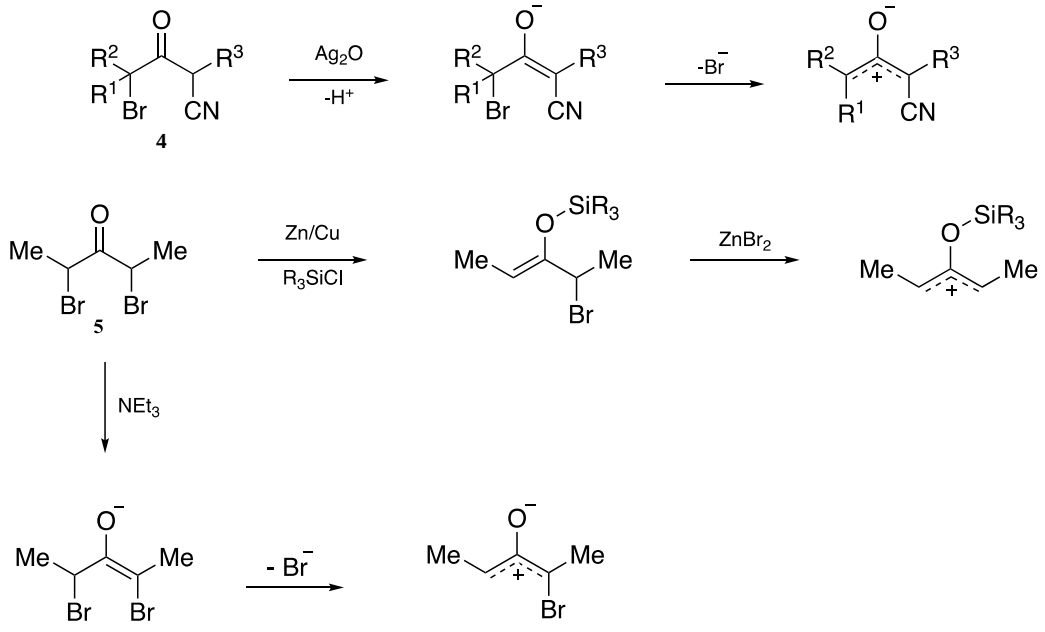


Figure 5. Mechanism of the allylic cation with 1,3-dienes

The extended (*exo*) transition state has the oxyallyl cation is pointing away from the diene (Figure 6). The stepwise pathway is reliant on the lifetime and stability of the carbocation and leads to a mixture of isomeric product.[7] Katritzky[10] stated that the steric repulsion by bulky groups should also be considered.

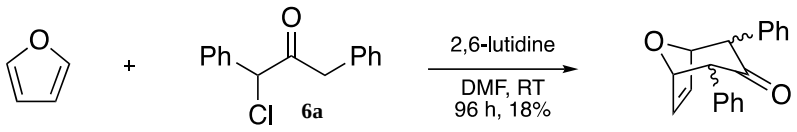
Figure 6. Transition state of the concerted pathway of allylic cation with 1,3-dienes

Hoffman and co-workers demonstrated the generation of the oxyallyl cation can be performed by Lewis acids including $SnCl_4$, AgO, Zn/Cu, and R_3SiCl, etc. (Scheme 1).[7] An enolate is formed after the deprotonation of the α-carbon of an α-halogenated propanone and then Br acts as a leaving group to give the reactive intermediate oxyallyl cation. The oxyallylic cation is stabilized by alkyl substituents **4** and **5**. Hoffman stated that highly electrophilic allyl cations tend to undergo the stepwise pathway whereas the weakly electrophilic ones tend to undergo the concerted pathway. The transition state between the oxyallyl cation and furan[9] shows the initial carbon-carbon bond formation that gives (4+3) cycloadduct in a stepwise process.[11]



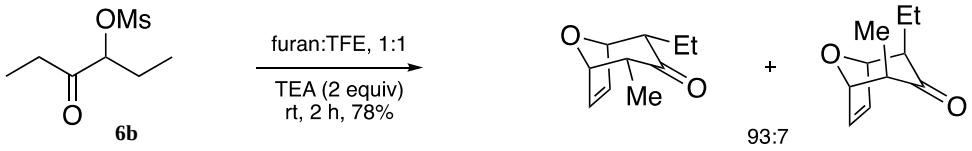
Scheme 1. Example of generating the oxyallyl cation

The first (4+3) cycloaddition reaction was reported in 1962 by Fort[12] (Scheme 2). After the deprotonation of **6a** by base and the loss of a leaving group, the chloroketone became the allylic cation then reacted with furan to form the (4+3) cycloaddition product in low yield.



Scheme 2. The first (4+3) cycloaddition reaction

Since then, additional methodologies have been developed. Föhlisch[13] used mesyloxy as a leaving group **6b** (Scheme 3) to afford the product with a good 78% yield and the stereoselectivity was excellent: *endo* 93: *exo* 7.



Scheme 3. Föhlisch (4+3) cycloaddition's method

In 1976, Katrizky reported on the 1,3-dipolar character of six-membered aromatic rings, undergoing cycloaddition reactions.[14] Katrizky demonstrated that addition at the 2- and 6-positions of 3-oxidopyridinium betaine is a (3+2) cycloaddition in the category of (4n) π-electrons while the 2- and 4-positions undergo (4+3) cycloaddition in the category (4n+2) π-electrons (Figure 7).[15]

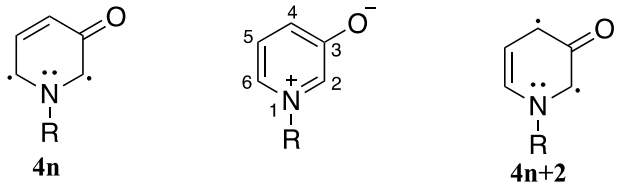
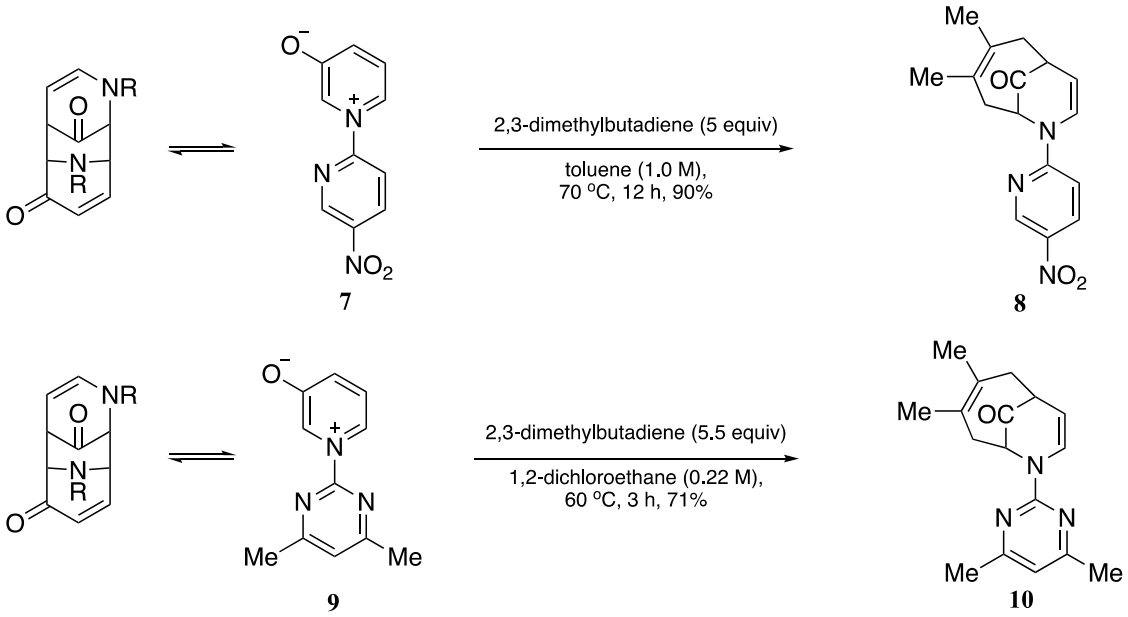


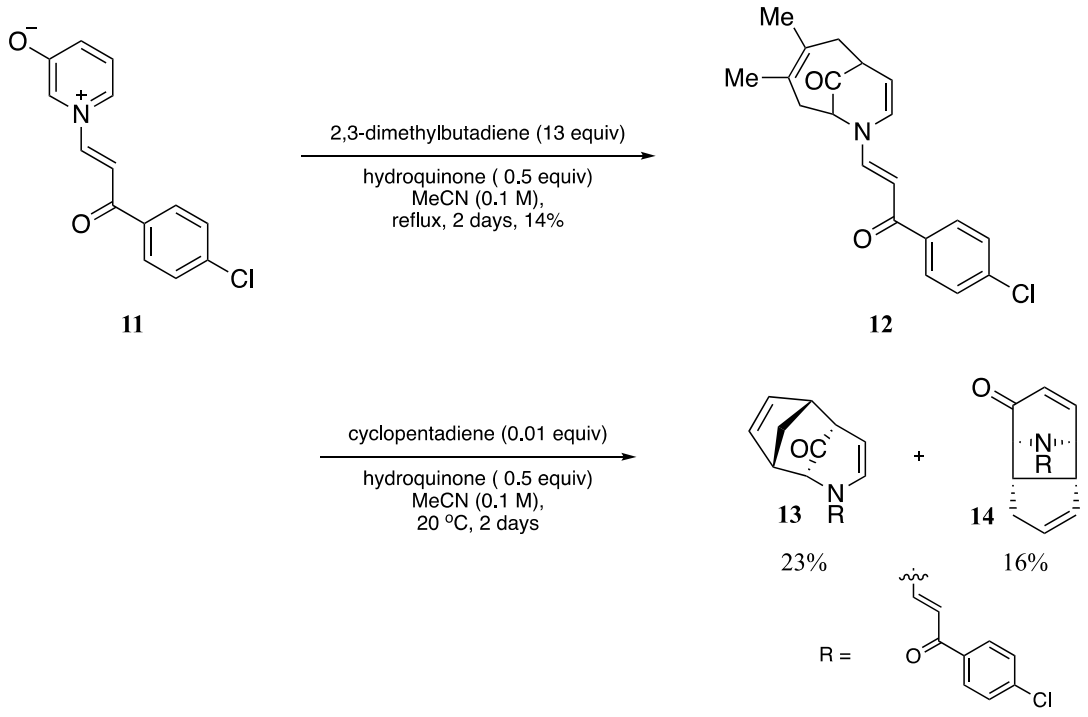
Figure 7. Oxidopyridinium betaine behaviour

Katrizky showed that nitropyridyl **7** and pyrimidinyl betaine **9** react with 2,3-dimethylbutadiene to give the (4+3) cycloaddition adducts **8** and **10** (Scheme 4).[14] Frontier Molecular Orbital (FMO) theory predicted oxidopyridinium betaine undergo thermal suprafacial cycloaddition. The addition at the 2- and 6-positions yields the thermodynamic product whereas addition at the 2- and 4-positions yields the kinetic product. The addition at the 2- and 4-positions is dependent on the LUMO of betaine, therefore the electron-withdrawing group at the nitrogen will help to lower the LUMO energy and promote a reaction with the electron-rich diene. In contrast, the addition at the 2- and 6-positions is preferred when the diene is electron-deficient.



Scheme 4. (4+3) cycloaddition reactions of oxidopyridinium ion

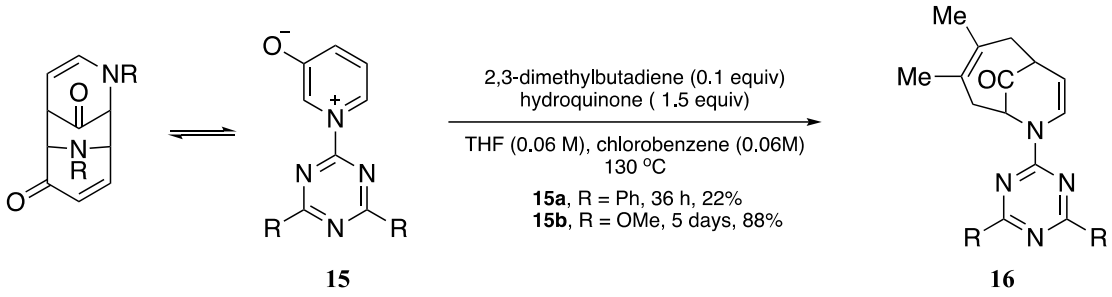
Katritzky also explored the *N*-alkenyl betaine **11** (Scheme 5).[16] The *N*-substituted betaines got activated by the substituent to lower the LUMO energy. The *N*-alkenyl betaine **11** reacted with 2,3-dimethylbutadiene to give the cycloadduct **12** in 14% yield. Conversely, when *N*-alkenyl betaine **11** reacted with cyclopentadiene, it gave two different cycloadducts. The addition at the 2- and 4-positions gave the (4+3) cycloadduct **13** as an *endo*-isomer in 23% yield while addition at the 2- and 6-positions gave the (3+2) cycloadduct **14** in 16% yield.



Scheme 5. Cycloaddition reactions of *N*-alkenyl betaine

The cycloadduct **16** can also be obtained by employing *s*-triazinylpyridinium betaine **15** in the present of 2,3-dimethylbutadiene to yield **16** (Scheme 6).[17] The *s*-triazinylpyridinium betaines were employed to increase the reactivity of the cycloaddition.

The 4,6-diphenyl-*s*-triazinyl betaines have higher electron withdrawing capacities than the 4,6-dimethoxy-*s*-triazinyl betaines. The dimer of the 4,6-diphenyl-*s*-triazinyl betaine **15a** is more stable than the dimer of the 4,6-dimethoxy-*s*-triazinyl betaine **15b**. Combined with longer reaction times (5 days) a better yield of 88% was obtained (4,6-diphenyl-*s*-triazinyl betaines gave 22%).



15 **16**

Scheme 6. The *s*-triazinylpyridinium betaines in (4+3) cycloaddition

The study of oxidopyridinium ions from Katrizky[21c,d] influenced our group to explore the reactivity of oxidopyridinium ion to construct the seven-membered ring by (4+3) cycloaddition reaction methodology in greater detail. Studies on seven-membered rings is a large field and provides an opportunity for discovery and expansion on the methodology of how we can control the regio- and stereoselectivity. Our group is especially interested in the 7-azabicyclo[4.3.1]decane ring system because we can utilize the methodology toward the formation of natural products (Figure 8).[18,19]

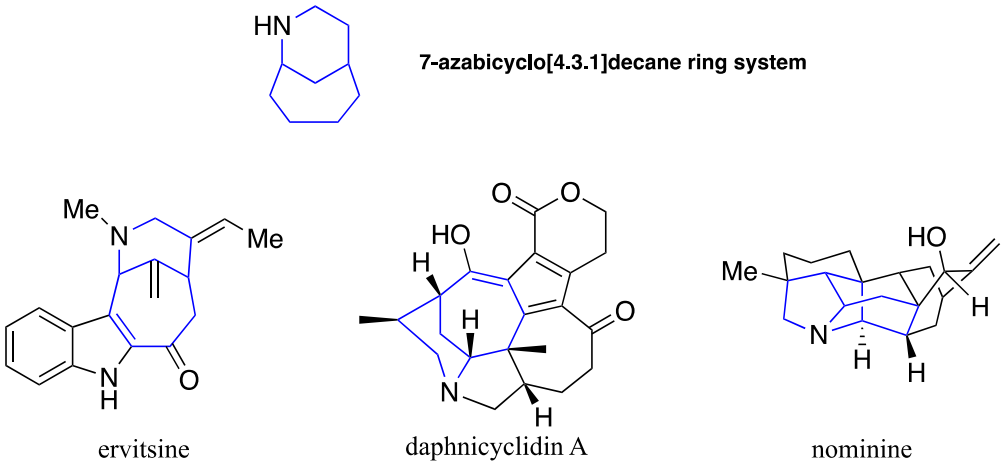
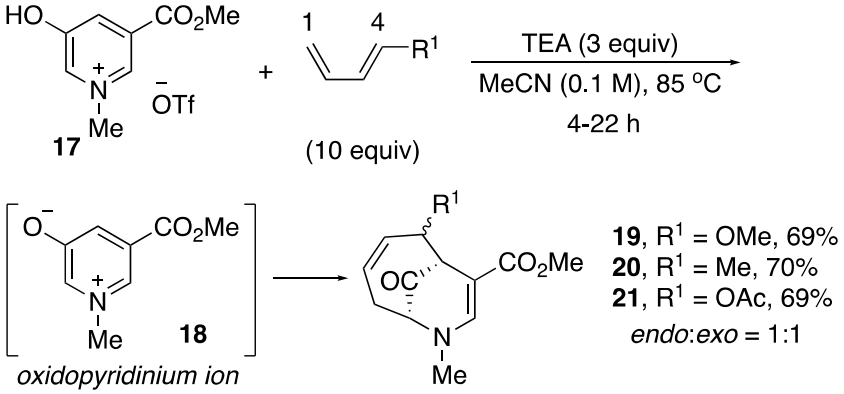


Figure 8. Natural products contain 7-azabicyclo[4.3.1]decane ring system

Previous studies from our group on the (4+3) cycloaddition reaction of oxidopyridinium ions with 4-substituted butadienes[20] showed that we could obtain cycloadducts with good yields (69-70%) and regioselectivity, but low diastereoselectivity (Scheme 7).



Scheme 7. Previous studies

Cha[22] studied its potential application in natural product synthesis. Although these studies show great promise for this type of process, the problem of poor *endo*/*exo* diastereoselectivity was not addressed. Thus, while 4- substituted 1,3-butadienes reacted

with oxidopyridinium ion **18** to afford (4 + 3) cycloadducts as single regioisomers in very good yields (Scheme 7), *endo*/*exo* selectivity was absent, with the products being formed as ca. 1:1 mixtures of diastereoisomers.

We developed a diastereoselective variant of this cycloaddition that achieves a high level of *endo* selectivity by strategically tuning the substituents on the diene.

In exploring the stereodirecting influences of the diene substituents, we were particularly interested in substituents that could be easily removed or modified, e.g., through a coupling reaction. We drew inspiration from substituent-directed stereoselectivities observed in the Diels−Alder reaction. For example, Su, Song, and co-workers recently reported high *exo* selectivity in the Diels−Alder reaction of butadienes substituted at C2 with a very bulky bis(silyl)methyl group.[23] The selectivity was rationalized on the basis of steric effects, and computational analysis showed that the *endo* transition state (TS) was destabilized by steric clashing between the $CH(SiR_3)_2$ group and the dienophile.[23] We reasoned that similar interactions might result in high *endo* selectivity in the (4 + 3) cycloaddition reaction of **18** or its congeners (Figure 9).

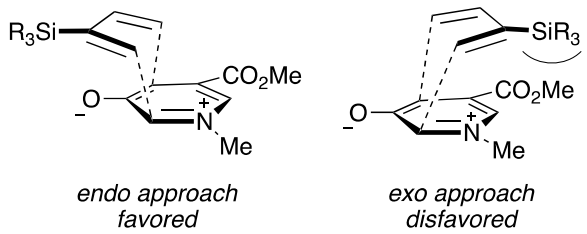
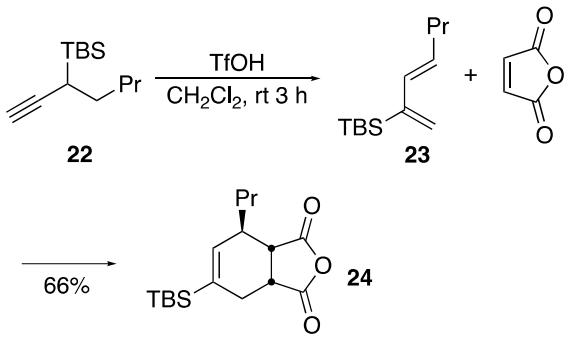


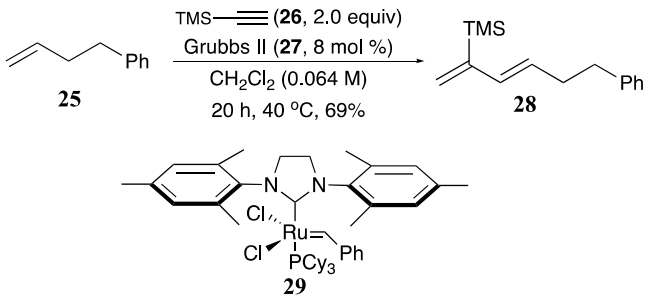
Figure 9. *Endo* and *exo* approaches of a 2-trialkylsilyl-1,3-butadiene to oxidopyridinium ion

However, we sought to further simplify the "steric steering" group and were inspired by the work of Turks, who showed that a 2-SiR_3 group was also an effective stereodirecting group for the Diels−Alder reaction to give a cycloadduct with complete *exo* selectivity (Scheme 8),[24] though *endo* selectivity has been observed more commonly observed for such dienes.[25]



Scheme 8. Highly *exo*-selective Diels-Alder reaction

Moreover, the expected (4 + 3) cycloadducts obtained from 2-silyl dienes contain a synthetically versatile vinylsilane functional group[25,26] Thus, we prepared 2-silyldienes **28** (Table 1) using the methodology introduced by Welker and others (Scheme 9).[27]

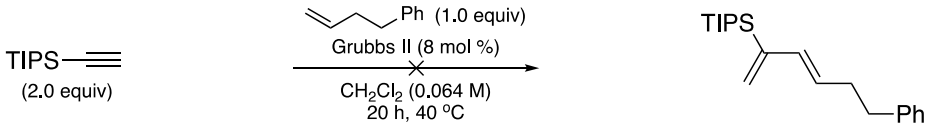


Scheme 9. Silylated diene synthesis

As a representative example, the reaction of excess trimethylsilylacetylene (**26**, 2 equiv) with 4-phenyl-1-butene **25** in the presence of 8 mol % of Grubbs II catalyst **29** at 40

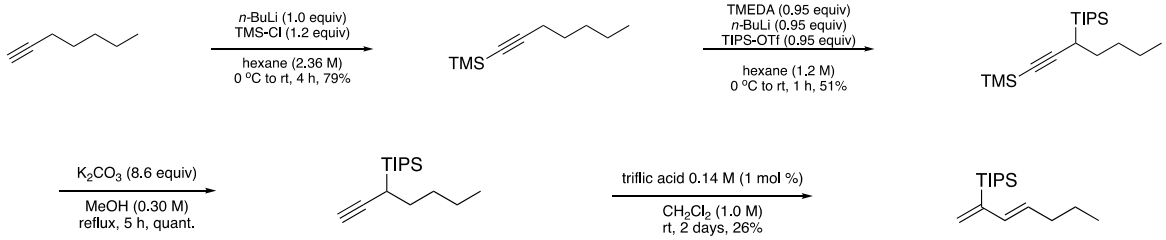
°C for 20 h afforded diene **28** in 69% yield after chromatographic purification. Other 2-silyldienes were prepared in the same general fashion, except for **30k** and **30l**, which were not accessible using the standard procedure. We solved this synthesis issue by employing ethylene gas instead of an argon atmosphere to obtain the desired dienes, as also demonstrated by Welker.[28]

The TIPS substituted diene was unable to be obtained by enyne cross metathesis. TIPS substituent was too bulky to coordinate with the Ru, no product was obtained (Scheme 10).



Scheme 10. Attempted diene synthesis

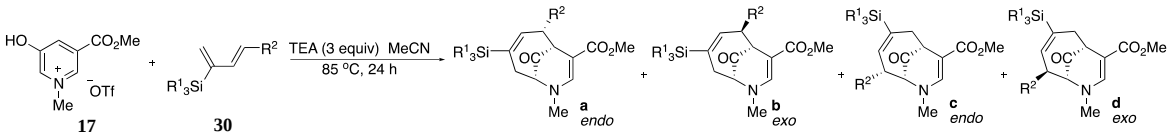
Later on, Turk's group[24] synthesized TIPS at the carbon 2 of the diene from the terminal alkyne (scheme 11). So, we employed Turk's method to synthesize the TIPS substituted diene.

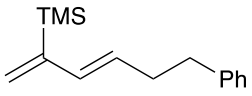
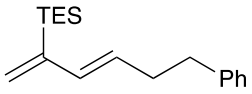
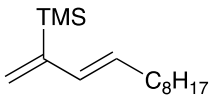
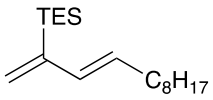
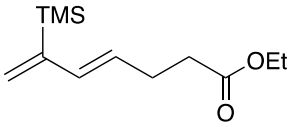
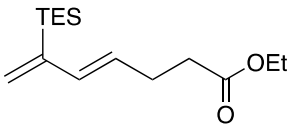


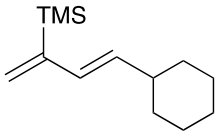
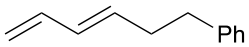
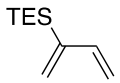
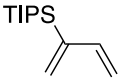
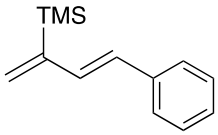
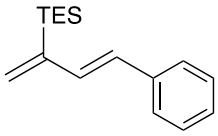
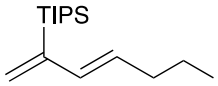
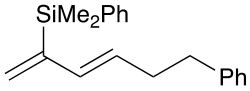
Scheme 11. Turk's method to synthesize the silyl substituted diene

The (4 + 3) cycloadditions of the silyl-substituted dienes **30** with oxidopyridinium ion **17** are summarized in Table 1.

Table 1. *Endo*-selective (4+3) cycloaddition reactions of an *N*-methyloxidopyridinium ion[49]



Entry	Diene	Product	a:b:c[a]	*endo/exo* selectivity[b]	Yield (%)[c]
1		**31**	81:13:6	87:13	93
2		**32**	81:15:4	85:15	88
3		**33**	82:14:4	86:14	71
4		**34**	89:9:2	91:9	77
5		**35**	80:16:4	84:16	87
6		**36**	83:16:1	84:16	74

Entry	Diene	Product	a:b:c[a]	*endo/exo* selectivity[b]	Yield (%)[c]
7		**37**	86:14:0	86:14	67
8		**38**	46:54:0	46:54	86
9		**39**	41:0:59	–	99
10		**40**	46:0:54	–	68
11		**41**	47:0:53	100:0	74
12		**42**	46:0:54	100:0	70
13		**43**	92:6:2	94:6	85
14		**44**	87:13:0	87:13	89

[a]Ratios were determined by integration of ^{1}H NMR spectra of crude reaction mixtures. Isomer **d** was not detected. [b]Entry = (sum of all *endo* isomers)/(sum of all *exo* isomers). [c]Yields are the average of two runs after column chromatographic purification.

Heating the oxidopyridinium precursor **17** with triethylamine (TEA, 3 equiv) and diene **30a** (3 equiv) in a sealed tube for 24 h afforded an 81:13:6 mixture of cycloadducts **31a−c**, as established by 1 H NMR analysis of the crude reaction mixture. No **31d** could be detected. This result equates to an overall endo/exo selectivity [(**31a** + **31c**)/**31b**] of 87:13. The major isomer **31a** was endo, as we had expected. Its structure was established by X-ray crystallography of its ketone reduction product (Figure 10). In this case and in

general, separation of the cycloadduct isomers proved to be very challenging when using traditional liquid chromatography approaches (normal and reversed phase). Instead, semipreparative supercritical fluid chromatography (SFC) using a chiral stationary phase column enabled separation[29,30] after which NMR analyses of the individual diastereomers (**31a−c**) could be performed.

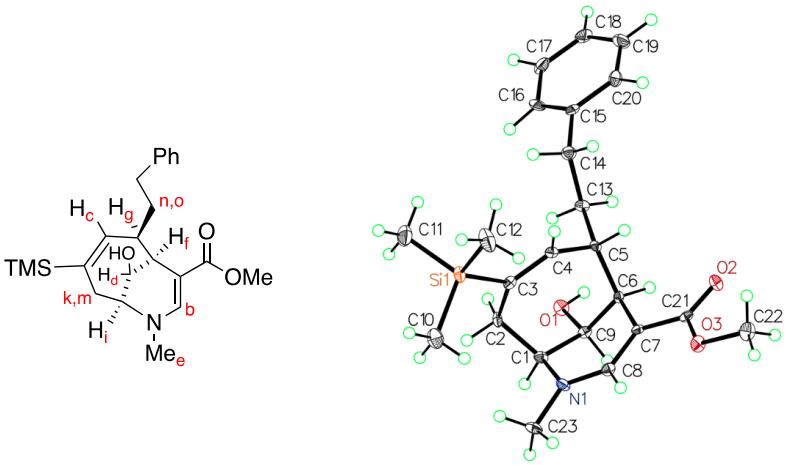


Figure 10. X-ray of the reduction of isomer **31a**

We assigned the structure of the minor isomer **31b** by NMR. Attempts to obtain crystals of the ketone reduction product of **31b** were not successful. Instead, NOESY spectra of the reduction product were used to establish the regiochemistry. In the alcohol derived from **31b**, the the triplet proton **i** on the bridgehead appeared at 3.26 ppm, a signal that correlated with the N-methyl group at 2.93 ppm and correlated (COSY and NOESY) with a 1H doublet of doublets CH_2 proton **m** at 2.45 ppm, which we assigned as one of the diastereotopic hydrogens at C-5. The latter proton was coupled to the signal of its geminal partner at 2.77 ppm and the protons of the TMS group at 0.02 ppm. This established the regiochemistry of **31b** as being the same as **31a**, confirming **31b** as the exo diastereomer of the two.

For **31c**, the stereochemistry was established in full after we fortunately grew a crystal of **31c** for X-ray analysis (Figure 11).

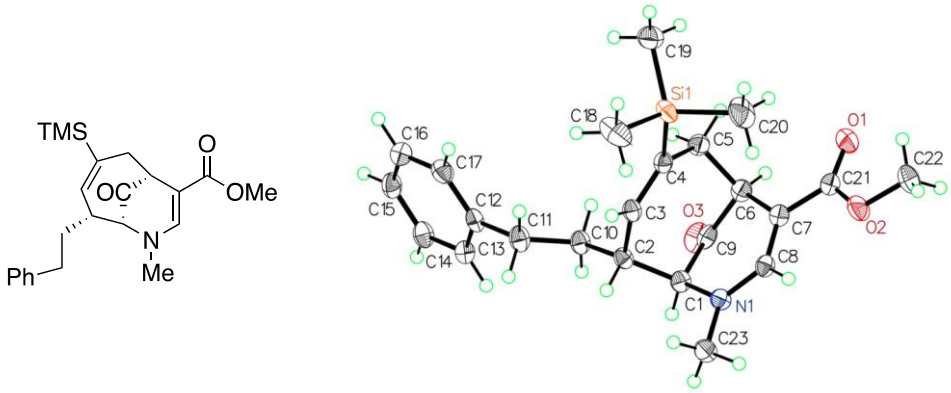


Figure 11. X-ray of the isomer **31c**

The (4 + 3) cycloadditions of a range of other silylated dienes gave results similar to **28**. The major product in each case was the expected *endo* isomer (**32a**−**37a**), and the kinetic endo/exo selectivities ranged from 84:16 to 91:9. Yields ranged from 67% to 93%. The structures of these cycloadducts were assigned by comparison to the NMR data for **31a**−**c**, and by crystallography in the cases of **33a** and **37a**.

In order to quantify the influence of the silyl group on the selectivity, we explored the reaction of diene **30h** lacking a silyl group. This diene gave two cycloadduct isomers, **38a + b**, in approximately equal amounts (46:54). As expected from our previous studies,[20] the products had identical regiochemistry. Their relative stereochemistry was assigned on the basis of their NMR spectra.[20] The lack of diastereoselectivity observed with **30h** confirms that the silyl group was indeed responsible for the highly diastereoselective cycloadditions of **30a**−**g**.

In these reactions, the silyl group leads to a slight erosion of the regioselectivity, producing small amounts (0−6%) of the minor endo regioisomers **31c**−**37c**. In our earlier

work, other 2-substituted dienes like isoprene and 2-methoxybutadiene reacted well with **17** but gave low regioselectivity.[20] Therefore, any regiochemical preference observed with 2-silyl dienes was of interest, even if it worked against the regiochemical preference of the terminal substituent on the diene. To explore this further, reactions were performed with dienes **30i** and **30j**, containing the 2-silyl group but lacking a substituent at C-4. As expected, in each case two regioisomeric cycloadducts were formed (**39a + c** or **40a + c**), in a ca. 46:54 ratio (Table 1, entries 9 and 10) in very good to near quantitative yield. This suggests that the 2-silyl group exerts a modest regiodirecting influence, favoring the "**c**" isomer. The regiodirecting influence is countered by a 4-alkyl group, to favor "**a**". Finally, entry 13 illustrates the selectivity with a TIPS group on the diene.[24] The endo/exo selectivity increases to 94:6, as might be expected from the increased size of the TIPS group.

We performed DFT computations to understand why 2-silyl-4-alkyl dienes give high levels of diastereoselectivity. The transition states calculated with M06-2X in SMD acetonitrile for the endo and exo (4 + 3) cycloadditions of **18** with two model dienes, **9o** and **9p**, in the favored regiochemistry are shown in Figure 12.

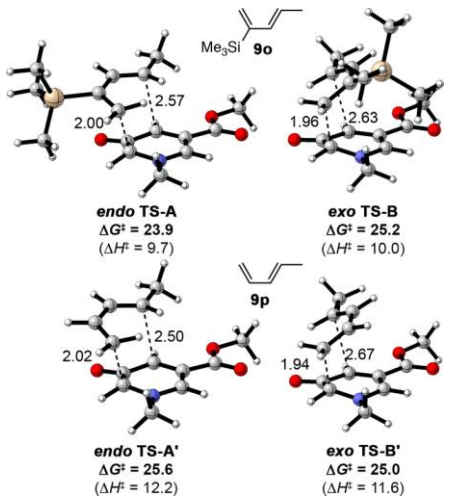


Figure 12. Transition state for (4+3) cycloadditions of dienes **9o** and **9p** with oxidopyridinium ion **18**, calculated with M06-2X/6-311+G-(d,p) in SMD acetonitrile. Distances in Å, and $\Delta G^{\ddagger}$ and $\Delta H^{\ddagger}$ in kcal/mol.[49]

The computations show that the silyl group in **9o** raises the ΔG‡ of the exo transition state (TS-B) by 1.3 kcal/mol relative to the endo transition state (TS-A). This value corresponds to a theoretical diastereomer ratio of 86:14 at 85 °C, close to that from the experiment (e.g., 81:13 for **28**). The endo selectivity originates from two effects: an enthalpic effect and an entropic effect. The enthalpic effect arises because endo TS-A can accommodate the silyl group without introducing major steric interactions, but the exo TS-B must distort to avoid the clash between the silyl group and the N-methyl group. Thus, compared to the silyl-free exo TS (TSB′), the diene and dienophile in TS-B are tilted away from each other by 0.1 Å. This distortion destabilizes TS-B. TS-B is also more compact than the endo TS-A, especially in the region of the silyl group, making TS-B entropically disfavored. Interestingly, theory predicts enhanced reactivity for silylated dienes.[31] While no quantitative experimental studies have yet been undertaken, the reaction of **28** with **17** was able to be performed at a lower temperature than is usually required for these reactions; the cycloaddition at 60 °C produced **31a−c** in an 88:10:2 ratio in 71% yield after 24 h.

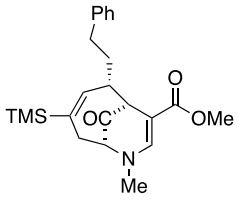
In general, a 2−3 equiv excess of diene was used in the reactions shown in Table 1. This represents a considerable decrease from the 10 equiv we used at the outset of our work on oxidopyridinium cycloadditions.[20]

Equivalents of Diene

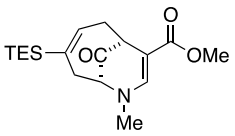
We wanted to investigate the equivalents of the diene to accommodate the formation of the (4+3) cycloaddition reaction and give a decent yield (Table 2). If we could reduce the equivalents of diene, we could reduce waste and perform the research in a more

economical way. The result of 3 different substituents was consistent with the same trend shown that the 2-3 equivalents of diene gave the best yield. Therefore, the (4+3) cycloaddition reactions performed by the 2-3 equivalents of diene in these studies.

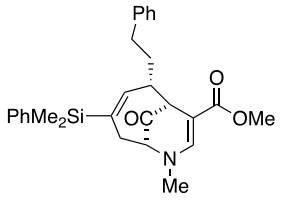
Table 2. Optimization condition of (4+3) cycloadducts



TMS Ph equiv	Yield (%)
10	87
5	88
3.0	quant.
2.0	84



TES equiv	Yield (%)
3.0	quant
2.0	quant
1.5	92
1.0	78



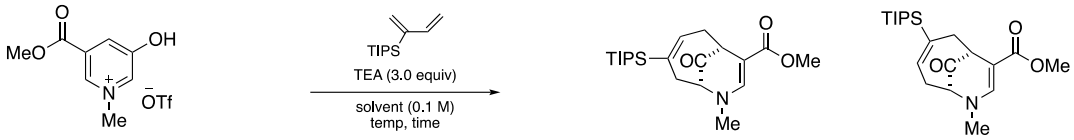
$SiMe_2Ph$ Ph equiv	Yield (%)
2.0	89
1.5	73
1.0	60

NOTE: PhCOONa 1.0 eq, diene 2.0 eq, 71% yield
2.0 eq, 84% is in the gram scale

TEMPERATURE AND SOLVENT

The diene that contains TIPS at carbon 2 has steric problem that obstructed the C-C bond formation (Table 3). When the cycloaddition was obtained under standard conditions by using CH_3CN, 85 ℃ for 24 h, a low yield of product was observed. The solvent was changed to propionitrile to obtain the cycloaddition at a higher temperature (130 ℃). Moreover, when the propionitrile was not properly dried, the cycloadduct was obtained only 43% yield. After the solvent was dried over the activated 4 Å molecular sieves for 48 h, the yield improved to 68%.

Table 3. Optimization of compound **40**



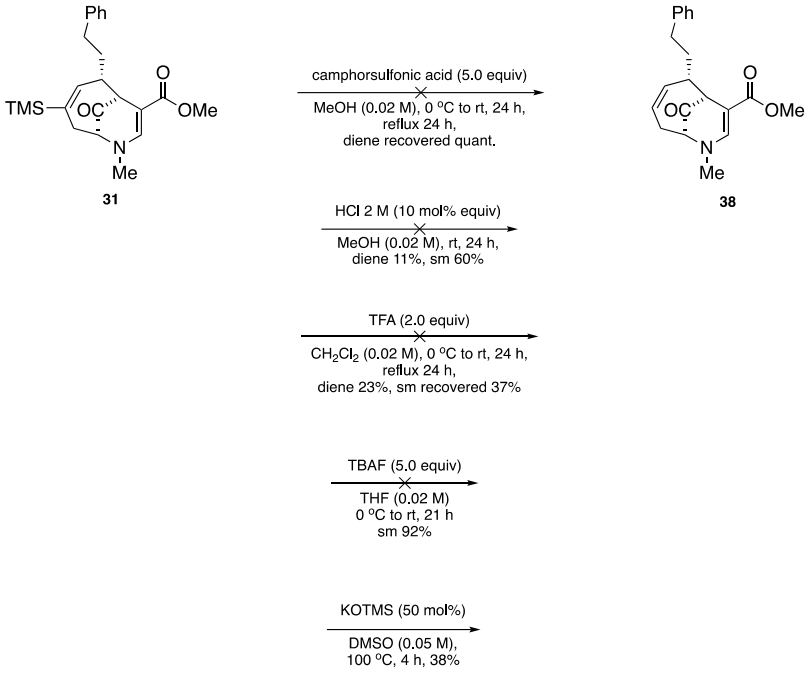
TIPS equiv	Solvent	Temp (°C)	Yield (%)
2.0	CH_3CN	85	20
2.0	Toluene	130	29
2.0	Propionitrile	130	43
2.0	Propionitrile	130	68

On a small scale, the reactions were conducted in resealable pressure tubes. However, we also performed a 1 g scale reaction in a more conventional way. On the basis of studies that had shown that the use of 2 equiv diene gave a better yield than 1 equiv, we reacted 1 g of **17** with 2 equiv of **28** in acetonitrile in the presence of TEA at reflux for 24 h. Cycloadducts **31a−c** were obtained in a respectable 84% yield in a ratio of 78:16:6. This result suggests that the process is scalable more generally than previously established without having to use pressure tubes.[32]

In our original work,[20] we established a clear example of reversibility in the cycloaddition of **2** with 1-phenyl-1,3- butadiene. The cycloadditions of the two related phenyl-substituted 2-silyl dienes, **30k** and **30l**, were performed (Table 1, entries 11 and 12) and were anticipated to afford products of thermodynamic control. Indeed, the fact that two *endo* cycloadducts were formed, as we had observed with 1-phenyl-1,3-butadiene, indicated that these two reactions likewise proceeded reversibly. Both reactions gave complete *endo* selectivity but gave low regioselectivity, affording ca. 1:1 mixture of **41a +**

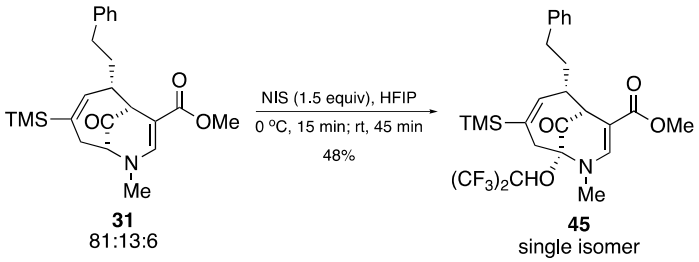
c or **42a + c**, respectively. These **a:c** ratios can be understood in terms of a situation intermediate between purely kinetic and purely thermodynamic control.[33]

To begin to establish some cycloadduct chemistry, we explored the desilylation of cycloadduct 13. Treatment of the mixture of **31a−c** with TBAF in THF at 55 °C for 22 h resulted in the recovery of the starting material.[34] With acids, retro-cycloaddition was observed: the diene could be recovered in yields ranging from 0% (excess HCl) to 99% (camphorsulfonic acid). Treatment with KOTMS in DMSO at 100 °C afforded the desilylated cycloadduct **38** in 38% yield[35] (Scheme 12).



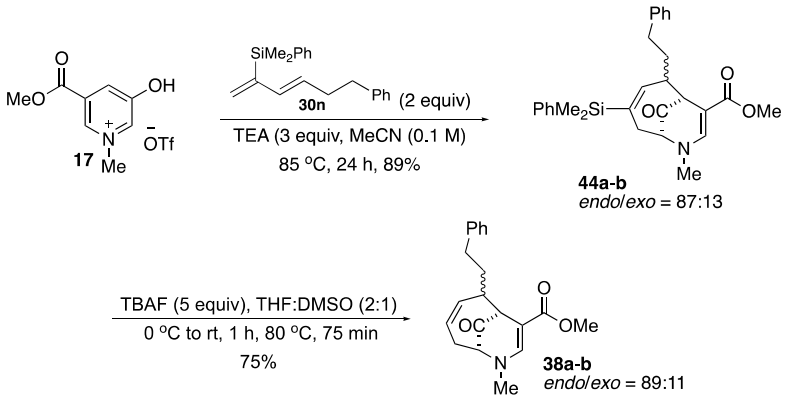
Scheme 12. Desilylation of (4+3) cycloadduct **31**

Attempts to brominate or iodinate the alkene with NBS or NIS, respectively, failed.[36,37] However, the reaction with NIS did produce a product in which functionalization had occurred at the bridgehead to afford **45** (Scheme 13). This process will be discussed in the next chapter.



Scheme 13. Reaction of **31** with NIS[49]

In contrast to the difficulty encountered in removing the TMS substituent from **31**, successful desilylation was achieved with the $SiPhMe_2$-substituted cycloadduct mixture **44**, which was obtained as an 87:13 mixture of *endo*/*exo* isomers (single regioisomer, Scheme 14 and Table 1, entry 14). The ^{13}C chemical shifts of **44a,b** for C-9 are 93.3 and 90.9 ppm, respectively. Those of **31a,b** are 93.7 and 91.4 ppm. These shifts lead to the stereochemical/regiochemical assignments shown, based on our previous work.[20] Reaction of this cycloadduct with TBAF afforded a 75% yield of the desilylated cycloadducts **38a + b** as an 89:11 mixture of isomers (Scheme 14).



Scheme 14. Synthesis and desilylation of a phenyldimethylsilyl-substituted (4+3) cycloadduct

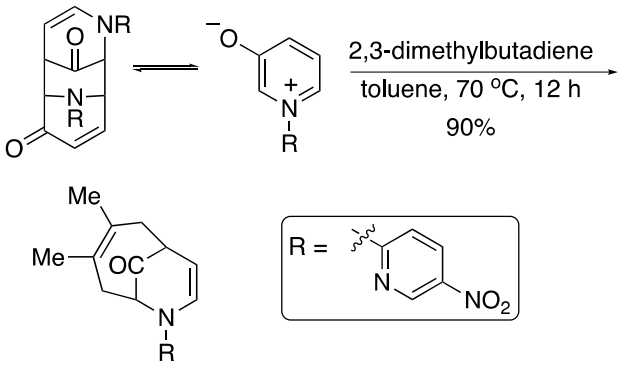
Summary

We have developed a (4 + 3) cycloaddition of an oxidopyridinium ion that is both highly diastereoselective and regioselective, by using a 2-silyl substituent on the diene as a directing group. Efforts to explore related dienes, explore the chemistry of the cycloadducts, design exo-selective processes, and broaden the scope of the dienophiles used in the cycloaddition are being undertaken.

CHAPTER II

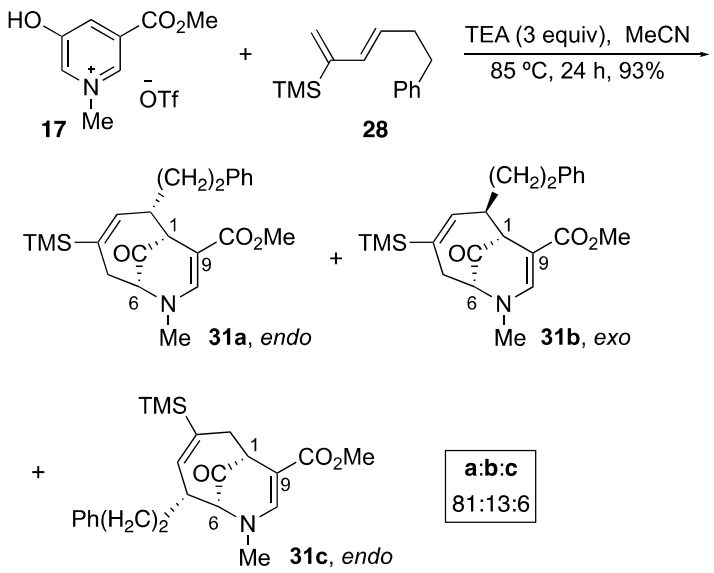
THE OXIDATION REACTION OF (4+3) CYCLOADDUCTS

Since their beginnings in the mid-1970s, the (4+3) cycloaddition reactions of *N*-substituted oxidopyridinium ions have provided an attractive and facile method for the construction of nitrogenous, heterocyclic seven-membered rings (Scheme 15)[38-47] While *N*-aryl and *N*-alkenyl substitution



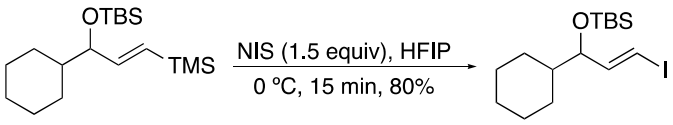
Scheme 15. Example of a (4+3) cycloaddition of an oxidopyridinium ion

of the pyridinium nitrogen have largely dominated the literature, to the best of our knowledge, there had been only one example of a (4+3) cycloaddition reaction of *N*-alkyl oxidopyridinium ions reported prior to 2017.[43] Our recent reports of the reaction of *N*-methyl oxidopyridinium ions with conjugated dienes expanded the scope of (4+3) process, due to the incorporation of an ester functional group at the 5-position of the hydroxypyridine starting material.[20,48] Cycloadducts are formed in good to excellent yields, and the reactions of select dienes proceed in high regioselectivity. Furthermore, the cycloaddition process can be steered towards a high preference for the *endo* diastereomer when the starting diene bears a bulky trialkylsilyl groups at C2, as we have recently reported (Scheme 16).[49]



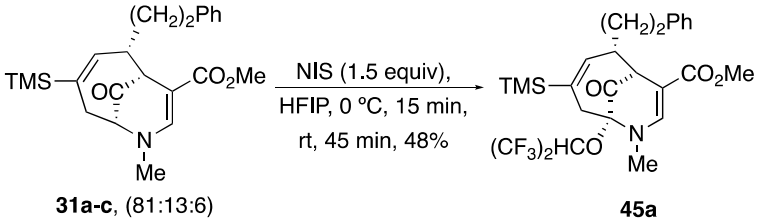
Scheme 16. *Endo* selective (4+3) cycloaddition of an oxidopyridinium ion[49]

Upon our initial exploration into the chemistry of the latter (4+3) cycloadduct products, our intentions were the replacement of the trialkylsilyl group with a halogen functional group such as iodine or bromine. We were particularly inspired by a report from the Zarkarian group, who showed that vinylsilanes react with *N*-iodosuccinimide in hexafluoroisopropanol to afford iodoalkenes stereosepecifically and in good yield (Scheme 17).[50] However, when our (4+3) cycloadducts were exposed to such reaction conditions, the replacement of the C-Si bond by a C-I bond was not observed. Thus, when a mixture of **31a-c** was treated with NIS in hexafluoroisopropanol (HFIP), a vinyl iodide was not formed.



Scheme 17. Zakarian's vinyl iodide synthesis

Instead, functionalization of the bridgehead carbon with hexafluoroisopropyl ether was observed, a formal oxidative C-H activation process, affording **45a** (Scheme 18).[49] This communication reports further examples of this process and other results that provide some insights for future studies.

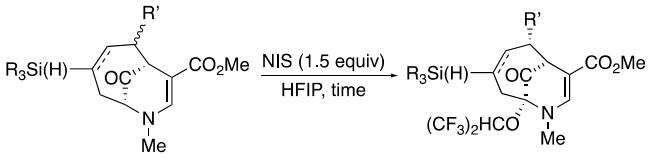


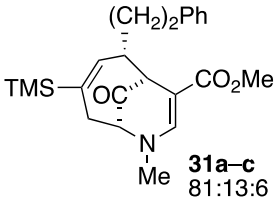
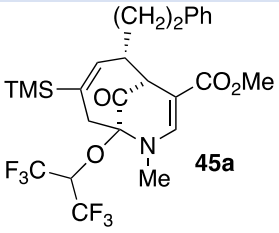
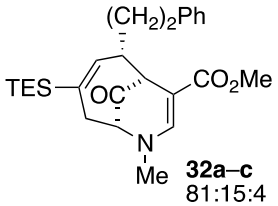
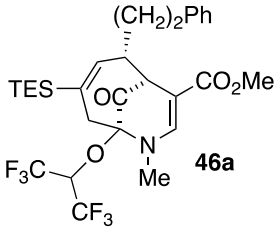
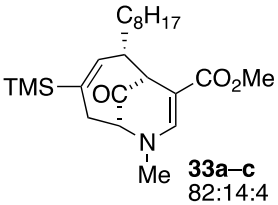
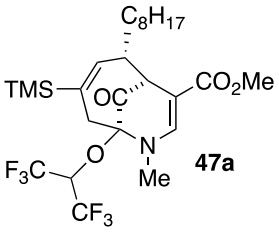
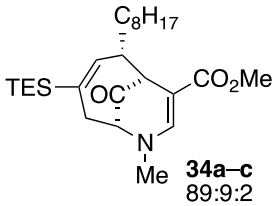
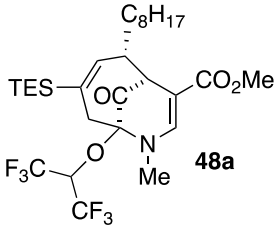
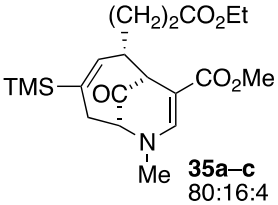
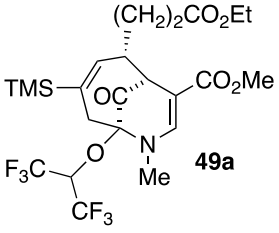
31a-c, (81:13:6) **45a**

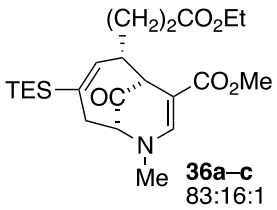
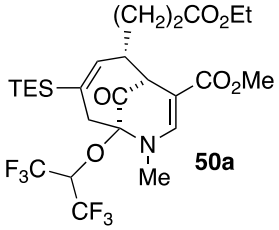
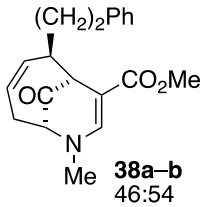
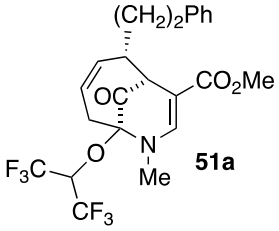
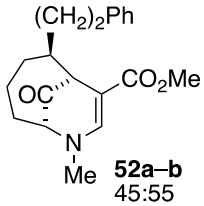
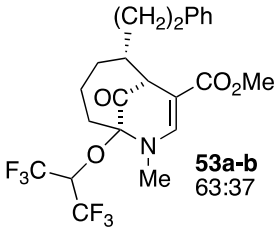
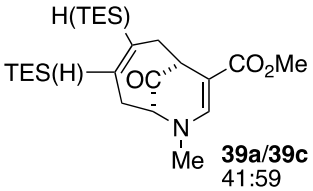
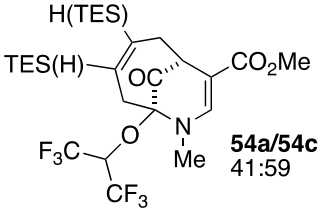
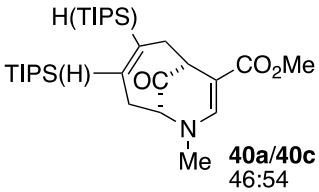
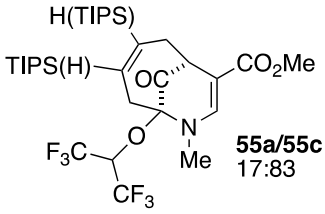
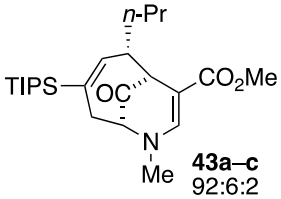
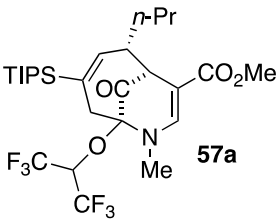
Scheme 18. First example of the bridgehead oxidation of a (4+3) cycloadduct

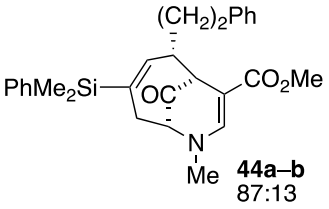
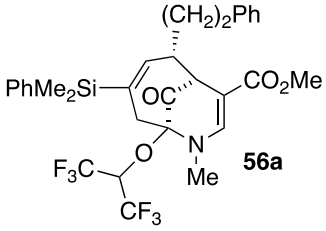
The substrates for the process are known compounds, produced in our laboratories using methodology we developed for the (4+3) cycloaddition of oxidopyridinium ions with dienes.[49] From the very first example of the process, we noted an interesting phenomenon. For example, entry 1 of Table 4 (see also Scheme 18) makes use of an inseparable mixture of diastereomers as the starting material. All three of the diastereomers are detectable by ^{1}H NMR in the mixture. Nevertheless, the product of the oxidation is a single diastereomer. The structure of **45a** was supported by ^{1}H NMR data. The fate of the minor diastereomers of the starting material is unknown at this time, as nothing else could be isolated from the reaction mixture. This is also true for similar entries in Table 4.

Table 4. Oxidation of (4+3) cycloadducts[100]



Entry	Substrate	Time (h)	Product	Yield (%)
1	 **31a–c** 81:13:6	1	 **45a**	52
2	 **32a–c** 81:15:4	23	 **46a**	54
3	 **33a–c** 82:14:4	1.5	 **47a**	52
4	 **34a–c** 89:9:2	22	 **48a**	51
5	 **35a–c** 80:16:4	21	 **49a**	44

6	 **36a–c** 83:16:1	23	 **50a**	38
7	 **38a–b** 46:54	23	 **51a**	16
8	 **52a–b** 45:55	5.5	 **53a-b** 63:37	33
9	 **39a/39c** 41:59	2	 **54a/54c** 41:59	35
10	 **40a/40c** 46:54	3	 **55a/55c** 17:83	59
11	 **43a–c** 92:6:2	23	 **57a**	64

12  4  31

[a]The major diastereomer/regioisomer of the mixture is shown. [b]Yields are based on the entire mass of the starting material, including isomers that may not have given rise to the product observed. [b]The substitution pattern of the major isomer is given in parentheses.

In general, the reactions were conducted with 0.25 mmol of substrate dissolved in 4 mL of hexafluoroisopropanol (HFIP). The stirred solution was cooled to 0 ºC in an ice bath. After addition of *N*-Iodosuccinimide (1.5 equiv), the mixture was allowed to slowly warm to the room temperature. The reaction was monitored by TLC until starting material was completely consumed.

The substrates that contained an alkyl substituent at C-2 and a trialkylsilyl group at C-4 afforded product in about 50% yield (entries 1-4, Table 4). The assignment of structure using NMR was supported by an X-ray crystal structure of **47a** (Figure 13).

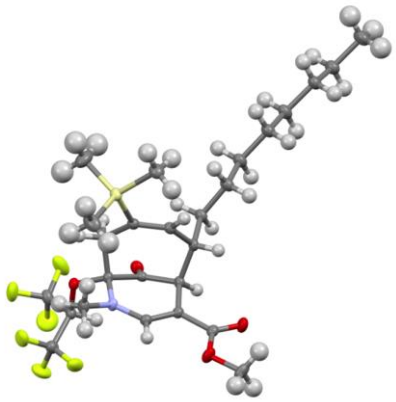


Figure 13. X-ray crystal structure of **47a**

Not all substrates bearing an alkyl substituent at C-2 and a trialkylsilyl group at C-4 afforded product in the 50% range. The lower yield of **56a** from **44a-b**, is perhaps due to the phenyl group on the silicon being sufficiently reactive to cause side product formation (entry 11, Table 4). In the case of **43a-c**, the TIPS group at C-4 may have afforded protection against side product formation, resulting in a relatively high yield for the formation of **57a** (entry 12, Table 4).

The substrate lacking a trialkylsilyl group (**38a-b**) gave a very low yield of product, indicating that the trialkylsilyl group affords some protection against degradation in the oxidation process (entry 7, Table 4). There is improvement in yield when the double bond of **38** removed, indeed the yield is doubled (entry 8, Table 4). Interestingly, this is the only case in which a substituent is located at C-2 in which both diastereomers led to product.

When no substituent appears at C-2 but a trialkylsilyl group appears at C-3 or C-4, both regioisomers appear to participate in the oxidation reaction (entries 9–10, Table 4). However, some inconsistencies are apparent. When the trialkylsilyl group is TES, the yield is low but both isomers seem to react at equal rates, as the ratio does not change in going from substrate to product (entry 9 Table 4). This is not the case for the substrate with a TIPS group, in which it is clear that one isomer behaves better than the other (entry 10 Table 4). The reasons for this are not known.

Figure 14 shows substrates that did not afford bridgehead oxidation product and led to complex reaction mixtures when treated with NIS. It does appear that the silyl group provides protection to the alkene, but the effect is clearly not universal.

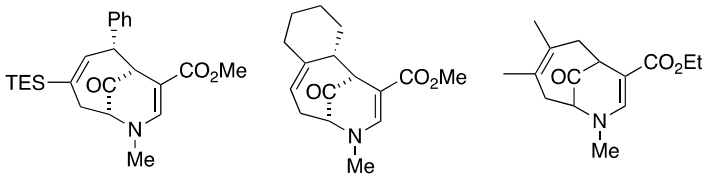


Figure 14. Substrates that did not lead to oxidation

We attempted to modify the reaction conditions in the hope of obtaining different products or limit the need for HFIP as solvent using **31a-c** as a model substrate. When LiI, NaI, or NaBr was added to the reaction mixture, oxidation products were obtained in low yield. No halogen incorporation was observed, though such products might be expected to be labile in any case, as they would likely be readily solvolyzed. Attempts to reduce the amount of HFIP used in the process (2-30 equiv in MeCN) gave bridgehead substitution products in 5-46% yield with recovered starting material ranging from 29-64%. Addition of small amounts of trifluoroacetic acid to the standard reaction mixture led to decomposition. Excess NIS (15 equiv) gave decomposition and NBS was not effective at all in producing the oxidation product under the standard reaction conditions (Table 5).

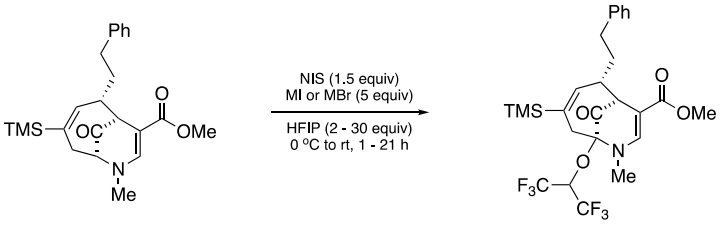
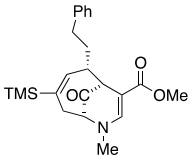
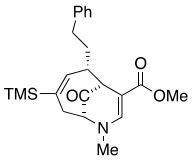
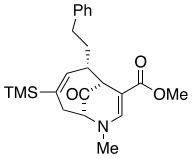
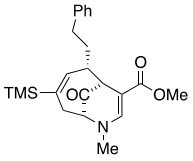
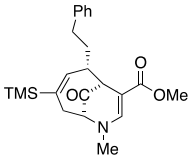
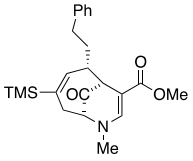
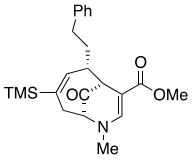
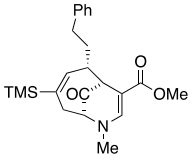


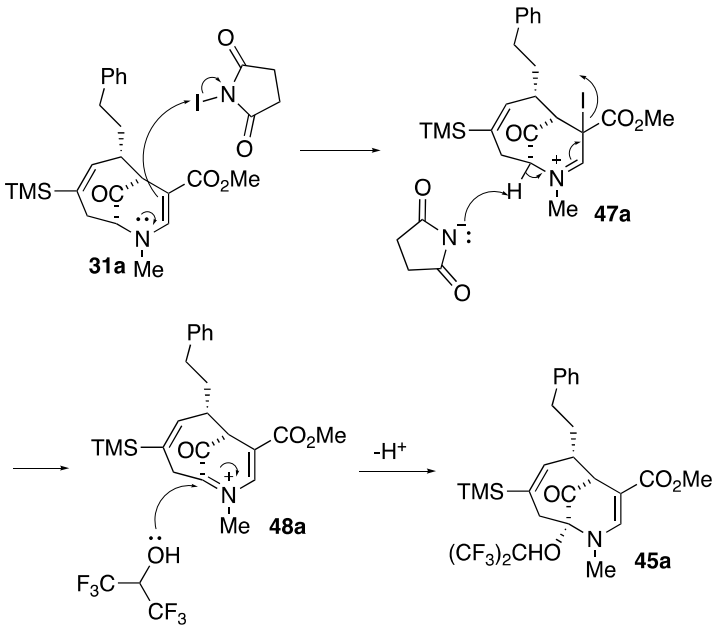
Table 5. Trapping study[100]

Substrate	NIS (eq.)	Reagents (eq.)	Solvent (M)	Time (h)	Temp. (℃)	Product

	1.5	LiI (5.0)	HFIP (0.09)	5	0 to rt	SM recovered 60% HFIP substituted (5%)
	1.5	LiI (5.0)	HFIP (400 eq.), CH_3CN (0.09)	7	0 to rt	SM recovered 60%
	1.5	NaI (5.0)	HFIP (0.09)	5	0 to rt	SM recovered 64% HFIP substituted 11%
	1.5	TFA (0.6)	TFE (0.08)	6	0 to rt	Decomposed
	-	NBS (1.5)	TFE (0.09)	8	0 to 80	Decomposed
	1.5	NaBr (5.0)	HFIP (0.09)	1	0 to rt	HFIP substituted 46%
	1.5	NaBr (5.0)	HFIP (2.0 eq.), CH_3CN (0.09)	21	0 to 85	SM recovered 29%
	1.5	NaBr (5.0)	HFIP (30.0 eq.), CH_3CN (0.09)	4	0 to rt	SM recovered 50%

Our working mechanism for this reaction is shown in Scheme 19. Reaction of **31a** with NIS produces the iminium ion **58a**.[51-53] Deprotonation of this intermediate with

succinimide anion affords the bridgehead iminium species **59a**, which is trapped with HFIP to produce the product **45a**. Inclusion of allyltrimethylsilane in the reaction in an attempt to trap **59a** led to a complex product mixture.



Scheme 19. Proposed mechanism of the oxidation

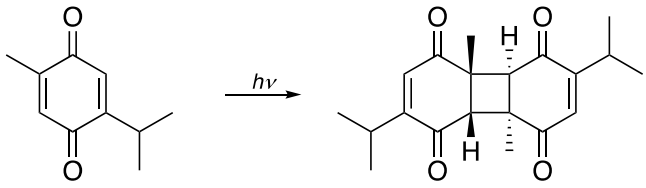
Summary

We have reported a unique bridgehead oxidation process of selected (4+3) cycloadducts derived from oxidopyridinium ions. While this process will certainly possess limitations, it raises questions about mechanism and what other reagents might be used to effect such an oxidation in a more general way and whether more general bridgehead functionalization might be possible through such a mechanism. We plan on addressing these questions.

Chapter III

EXPLORATION OF [2+2] PHOTOCHEMISTRY OF (4+3) CYCLOADDUCTS

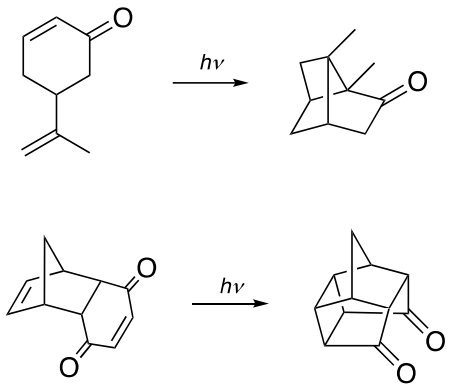
Sunlight is the most abundant, cleanest, and primary source of energy that is essential for life. Sunlight has also been used historically to propagate various physical and chemical processes. In 1599, Gesner demonstrated the distillation by sunlight in "The maner of Distilling in the Sunne"[54] Later on, Libavius reported his studies on mirrors and lens to develop many principles of optics using sunlight. In 1649, Priestley observed that liquid mercury turned into a red solid with an increase in weight when exposed to sunlight which was later revealed to be a photocatalyzed reaction between mercury and oxygen.[54] The photodimerization of anthracene was described by Fritzsche in 1867. Ten years later, Liebermann described the first photochemical [2+2] cycloaddition of thymoquinone dimerization in the solid-state using sunlight (Scheme 20).[55]



Scheme 20. Photodimerization of thymoquinone via the sunlight

In 1885, Ciamician performed photochemical experiments on alcoholic solutions of benzoquinone which were exposed to sunlight for five months to give hydroquinone and acetaldehydes. Ciamician continued to explore the reactions between organic materials and sunlight and reported the first discovery of the [2+2] photocycloaddition of an olefin and enone in 1908 by irradiation of carvone by sunlight for one year (Scheme 21).[56] Later,

Cookson performed the ultraviolet irradiation adducts of *p*-benzoquinone and cyclic dienes to obtain the cage-like structures (Scheme 21).[57]



Scheme 21. [2+2] photocycloaddition of an olefin and enone

Since then, there has been a huge expansion on intramolecular [2+2] photocycloaddition reactions containing even more complex units, such as cyclobutene. The [2+2] photocycloaddition is one of the classic methods to synthesize compounds which contain cyclobutane rings using ultraviolet or visible light. The cycloadduct can be formed by the excitation from the ground state of an olefin to first excited singlet state (S_1) which will react with another olefin to form the cycloadduct.[58]

There are 2 possible regioisomers in this reaction which are the head-to-head (HH) and head-to-tail (HT) isomers. The HH forms when the substitution is a 1,2-relationship and HT forms when it is a 1,3-relationship. The HT isomer is favored when R is an electron donating group, and the HH isomer is favored when R is an electron withdrawing group (Figure 15).[58] The relative configuration when the cyclobutene is forming a bond to another ring is differentiated via cis/trans notation and the diastereoselectivity of the intermolecular [2+2] photocycloaddition is differentiated via syn/anti notation (Figure 15).[58]

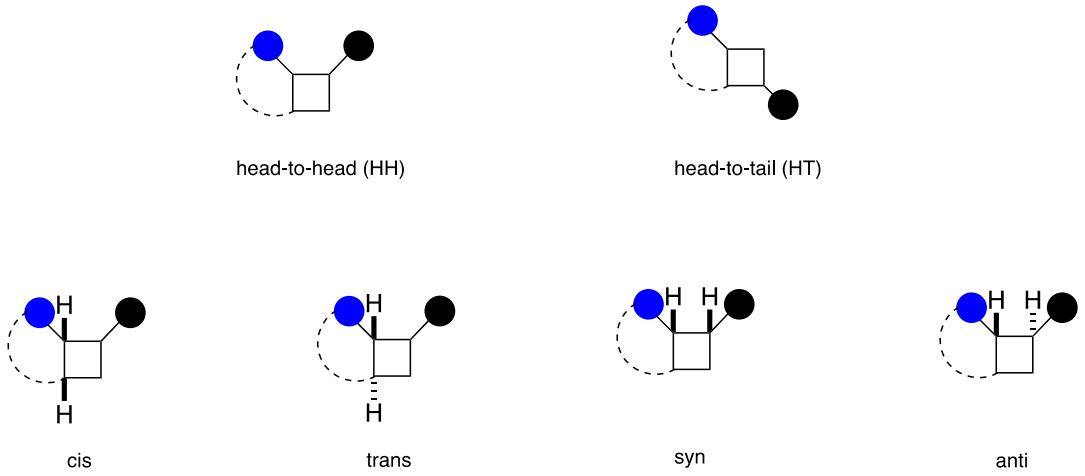


Figure 15. Regioselectivity and diastereoisomers of [2+2] photocycloaddition reaction[58]

FMO analysis of the [2+2] cycloaddition reaction indicates that thermal suprafacial [2+2] cycloaddition is symmetry forbidden but symmetry allowed under photochemical (excited state) conditions. Upon excitation, the LUMO becomes the new HOMO to react with the LUMO of another alkene (Figure 16).[59]

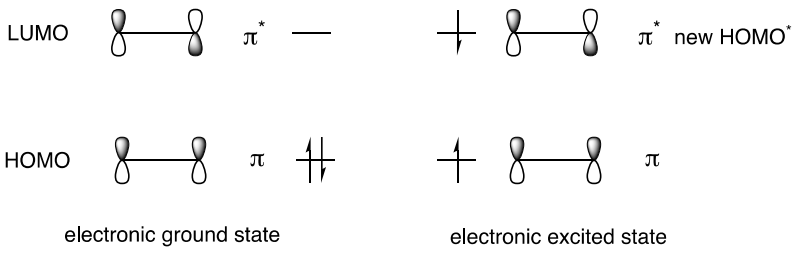
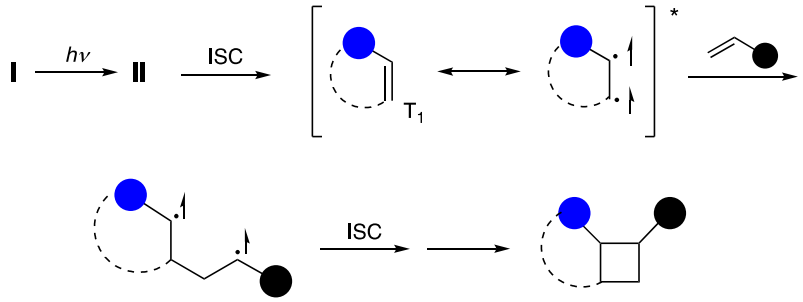


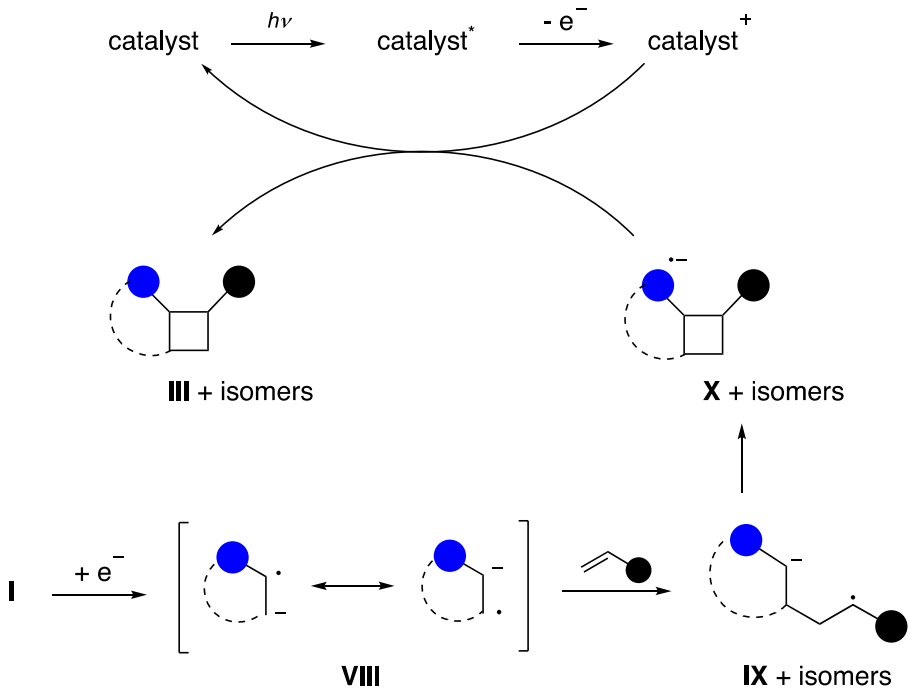
Figure 16. FMO of [2+2] photocycloaddition reaction

α,β-unsaturated ketones (I) will undergo excitation to the singlet state S_1 (II) then to the triplet state T_1 through intersystem crossing (ISC) The triplet state unsaturated ketone then reacts with an alkene to form a 1,4-diradical intermediate. After intersystem crossing (ISC) to the singlet diradical, the product is formed (Scheme 22).[60]



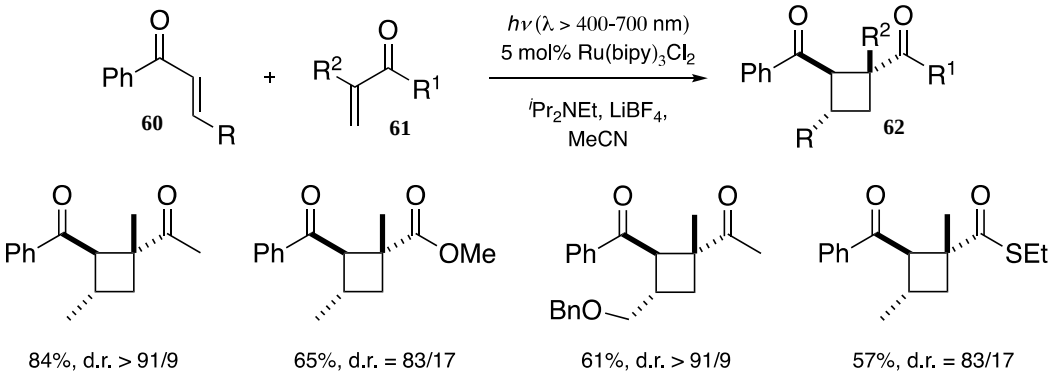
Scheme 22. [2+2] Photocycloaddition via the first excited triplet state[58]

Furthermore, [2+2] photocycloaddition can also be performed through catalytically activated single electron transfer (SET). Photoredox catalysis is photon-absorbing catalysis that is activated by visible light. After the irradiation, the olefin will be reduced or oxidized by the excited state of the photoredox catalyst via the single electron transfer.[61] The radical anion reacts with the alkene to form a 1,4-diradical intermediate and then cyclizes to form the cyclobutene (Scheme 23).[62]



Scheme 23. [2+2] Photocycloaddition by single electron transfer from a catalyst[58]

Yoon and co-worker[63] employed an aryl enone **60,** an electron acceptor which forms a radical anion intermediate reacted with the Michael acceptor, methyl vinyl ketone **61** to obtain the [2+2] photocycloadduct **62**. The role of methyl vinyl ketone **61** was helping to prevent the homocoupling of an aryl enone **60** (Scheme 24).

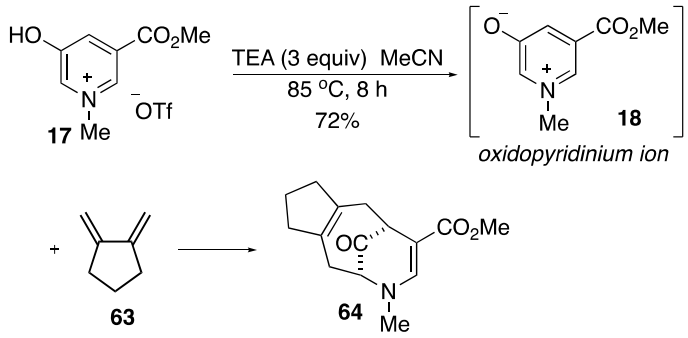


Scheme 24. Intermolecular [2+2] photocycloaddition of acyclic enones

The intramolecular reaction between enones and olefins has been well established for several decades, and we wanted to take this concept and investigate the intramolecular [2+2] photocycloaddition reaction of substituted alkenes with vinylogous carbamates obtained from the intermolecular (4+3) cycloaddition reaction of oxidopyridinium ions.

We have been investigating the intermolecular (4+3) cycloaddition reaction[12,39-42,64] of selected oxidopyridinium ions with dienes and have reported that the process is generally quite effective in terms of yield.[20,32] Complete control of regioselectivity and *endo*/*exo* selectivity remain to be fully optimized, though progress has been made on both fronts.[20,32,48,49] An example is shown in Scheme 25.[20] As part of that program, the chemistry of the cycloadducts has become of interest. We realized that the cycloadducts were primed for an intramolecular [2+2] photochemical cycloaddition, which would lead

to molecularly complex scaffolds in which the tropane skeleton is embedded. This letter reports our successful realization of this process.



Scheme 25. (4+3) cycloaddition of an oxidopyridinium ion[20]

Cycloadducts such as **64** possess both a simple, substituted alkene as well as a vinylogous carbamate. Some photochemistry of vinylogous carbamates and amides has been reported.[65-72] We thus expected the cycloadducts we planned to examine to be excellent candidates for intramolecular cycloaddition, with a few exceptions (vide infra).

Tropane alkaloids have a long history in drug use and abuse.[73,74] Perhaps the two most "notorious" members of this class are scopolamine **65** and cocaine **66** (Figure 17). Both are characterized by an 8-azabicyclo[3.2.1]octane ring system and have notable biological activity. Scopolamine is an anticholinergic, muscarinic receptor antagonist used medicinally as an antinauseant and antispasmodic, with potential in the treatment of depression, and as a research tool to model neural degradation associated with diseases such as dementia (e.g., Alzheimer's).[75-77] While cocaine is used medically as a local anesthetic, it has greater renown as a drug of abuse.[73,78,79] However, the synthesis of tropane alkaloids remains of interest, for the treatment of cocaine addiction and as a tool for neuroscience.[80] We were motivated by the possibility of obtaining rigid molecular scaffolds that might be useful for functionalization in the design of biologically active molecules.

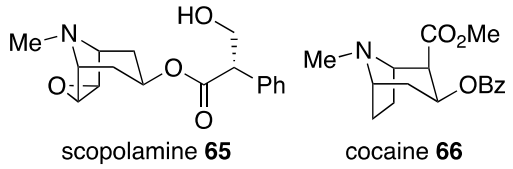
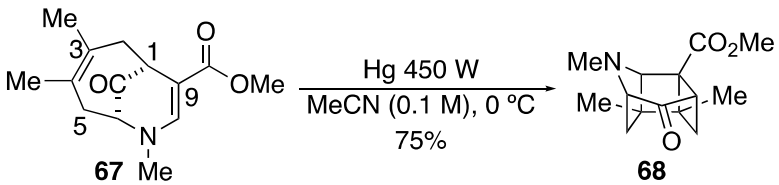


Figure 17. Examples of tropane alkaloids

The precursors used in this study are the (4+3)-cycloadducts resulting from the reaction of dienes with the oxidopyridinium ion obtained from 17 upon treatment with base. Their syntheses have been reported elsewhere.[20,32,48,49]

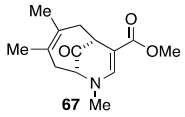
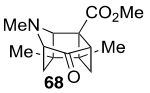
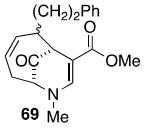
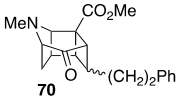
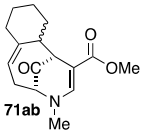
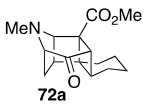
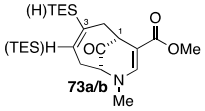
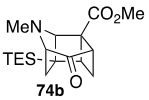
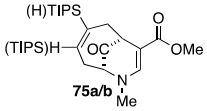
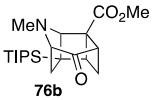
When a solution of the (4+3)-cycloadduct **67** in acetonitrile in a borosilicate test tube was irradiated at a 0 ºC (bath) using a medium pressure mercury-vapor lamp, a new product was observed.[81] The reaction mixture was purified by flash chromatography to afford the pure product as a colorless oil in 75% yield (Scheme 26).[82,83] The ^{1}H spectrum of the isolated product revealed the disappearance of the downfield vinylic proton previously assigned to the vinylogous carbamate. The two methyl singlet peaks at 1.36 ppm and 1.19 ppm showed that the two vicinal methyl groups were still connected to tertiary carbons. The methyl singlet peak at 3.76 ppm in ^{1}H NMR, along with the peak at 171.1 ppm in ^{13}C NMR indicated the retention of the methyl ester. The data collectively suggested an intramolecular [2+2] cycloaddition between the alkene of the vinylogous carbamate and the alkene on the cycloheptanone ring, as we had expected.

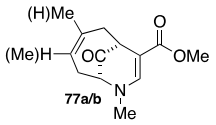
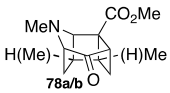
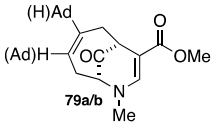
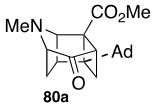
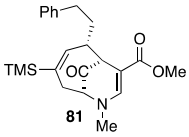
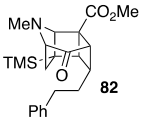
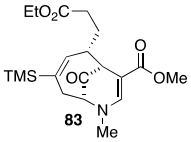
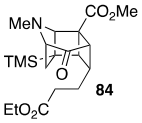
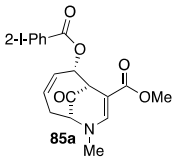
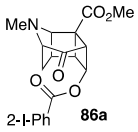


Scheme 26. First trial of intramolecular photocycloaddition[83]

Substitution at the 2 position was well tolerated regardless of stereochemistry, affording [2+2] cycloadducts in excellent yields (Table 6, entries 2). Fusing a ring between the 2 and 3 positions of the substrates led to an expected dichotomy in behavior. The photocycloaddition of **71ab** (from the mixture of **71a** and **71b**) proceeded to give **72a** in a good yield (Table 6, entry 3). Compound **71ab** and **85a** was initially performed by Dr. Fu,[83] the former lab member; however, the reproduction was required to obtain the pure product **72a** and **86a**. The compound **71a** is *exo,*[49] and produces a cycloadduct with a *cis*-fused six-membered ring. However, the *endo* isomer **71b** would be forced to produce a *trans*-fused six-membered ring on the same cyclobutane unit and consequently **72b** is not formed (Table 6, entry3). Compound **68** was initially performed by Dr. Fu,[83] it was also reproduced in the large scale 3.25 mmol.

Table 6. Intramolecular photocycloadditions producing complex Tropanoids[a,83]

entry	substrate	time (h)	product	yield (%)
1	 **67**	2.5	 **68**	96
2	 **69**	0.5 (1)	 **70**	91 (79)[b]
3	 **71ab**	2.5	 **72a**	77[c-e]
4	 **73a/b**	2.5	 **74b**	37[g]
5	 **75a/b**	1.5	 **76b**	24[h]

6		5		75[i]
7		5		32[j]
8		3		0[k]
9		2		0[l]
10		2.5		54

[a]Reactions were conducted at 0 ºC in MeCN for the time indicated. [b]The starting material was a 46:54 mixture of *endo* and *exo* isomers, respectively. The product bore the same ratio by ^{1}H NMR. Data in parentheses shows that photolysis for a longer time leads to a lower yield. [c]The starting material was a 37:63 mixture of *endo* and *exo* isomers, respectively. [d]The yield is corrected based on starting material composition; the amount of the unreactive isomer was not included in the yield calculation. [e]A 22% yield of the *endo* starting material was recovered. [g]The starting material was a 59:41 mixture of 3-TES and 4-TES isomers as determined by NMR (See ref. 3b). [h]The starting material was a 54:46 mixture of 3-TES and 4-TES isomers as determined by NMR (See ref. 3b). [i]The starting material was a 55:45 mixture of regioisomers. The regioisomeric products were partially separable and could be characterized individually. See SI. [j]The starting material was a 50:50 mixture of regioisomers. [k]The starting material was an 81:13:6 mixture of isomers (See ref. 3b); the major isomer is shown. No evidence for any [2+2] cycloadduct was found. [l]The starting material was an 80:16:4 mixture of isomers (See ref. 3b); the major isomer is shown. No evidence for any [2+2] cycloadduct was found.

Interestingly, substitution of a trialkylsilyl group on the 4 position of the substrate seems to inhibit cycloaddition. Entries 8-9 of table 6 show that when inseparable mixtures of 3 and 4 silylated substrates are photolyzed, only products derived from substrates with silyl substituents at the 4 position are isolated. The yields are low, but they represent yields calculated based on the entire mass of the starting substrate, including the isomer that does not produce a photocycloadduct. When a mixture of **77a/b** was photolyzed, both isomers

produced a photocycloadduct. When a mixture of **79a/b (**Ad = 1-adamantyl) was similarly photolyzed, only cycloadduct **80a** was obtained. Its structure was confirmed by X-ray analysis. This compound possesses a regiochemistry opposite to that of **74b** and **76b**, suggesting that while steric plays a role in the outcome of the photocycloaddition vis-à-vis the results from **77a/b**, there is likely another factor influencing and dominating the photocycloaddition of the silylated substrates. This observation warrants further investigation.

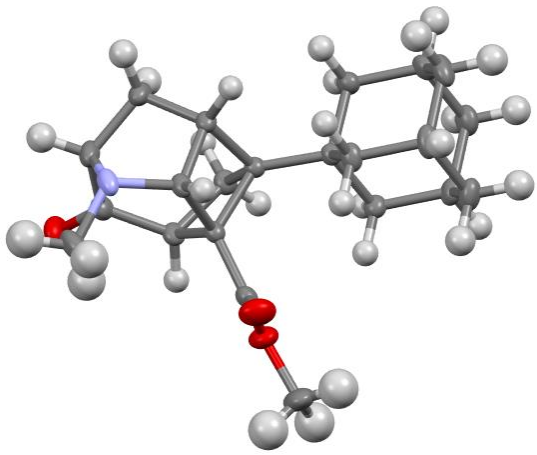
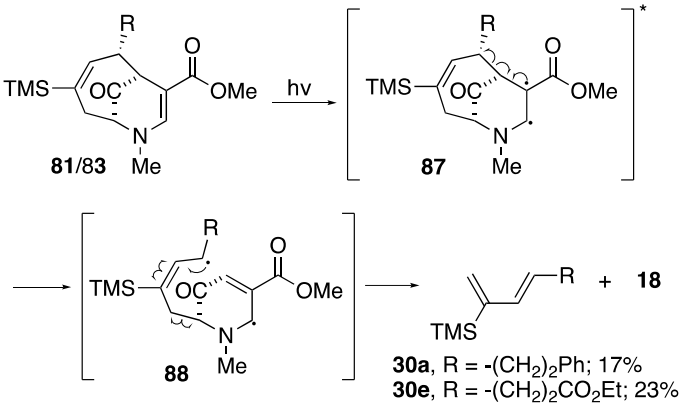


Figure 17. X-ray crystal structure of **80a**

When the *endo* substrates **81** and **83** were photolyzed, no cycloadduct was formed. This is true not only for the major diastereomers shown in Table 6, but for minor, inseparable isomers that were part of the starting material. Apparently, the combination of silyl substitution and substitution at position 4 combined to thwart the cycloaddition process. However, for both starting materials of these (4+3) cycloadducts, dienes **30a** and **30e** were produced in 17% and 23% yields, respectively. This represents a formal, photochemical retro-(4+3) cycloaddition, which we presently formulate as the result of two homolytic bond cleavages, as shown in Scheme 27.

Starting materials substituted at the 2 position with 2-iodobenzoyloxy group gave photocycloadducts in 54% yields, regardless of relative stereochemistry (Table 6, entries 10).



Scheme 27. Possible mechanism for the generation of dienes **30a** and **30e**

Summary

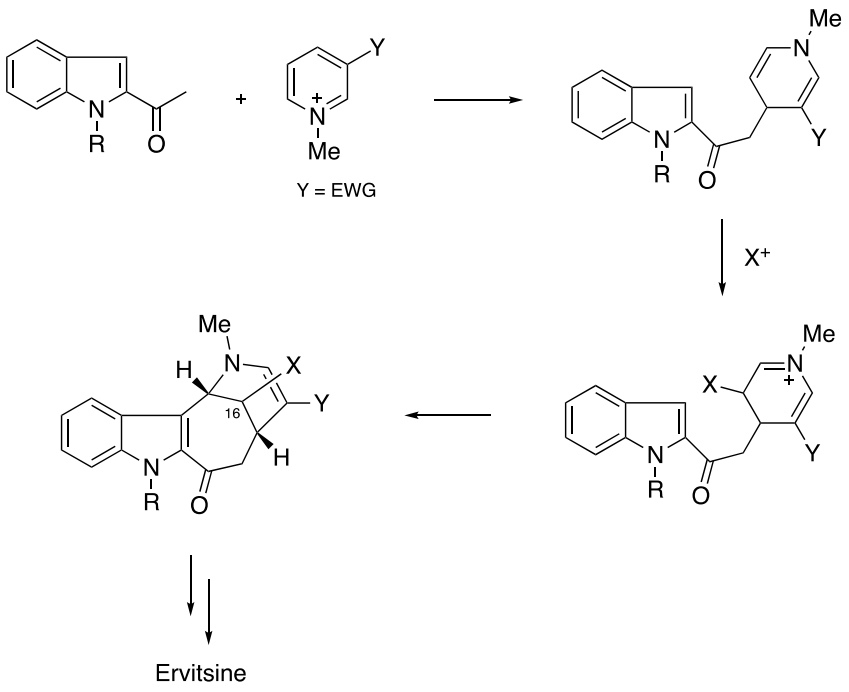
We report that the intramolecular [2+2] photocycloadditions of 7-azabicyclo[4.3.1]deca-3,8-dien-10-ones, readily available products of the (4+3) cycloaddition of oxidopyridinium ions and dienes, [20,32,48,49] afford complex polycyclic structures containing the tropane ring system. The process promises to be applicable to many, but not all, such (4+3) cycloadducts, providing rapid access to rigid molecular scaffolds that could be of use in, *inter alia*, drug development.

CHAPTER IV

INTERMOLECULAR (4+3) CYCLOADDITION REACTION OF OXIDOPYRIDINIUM AND VINYL INDOLE

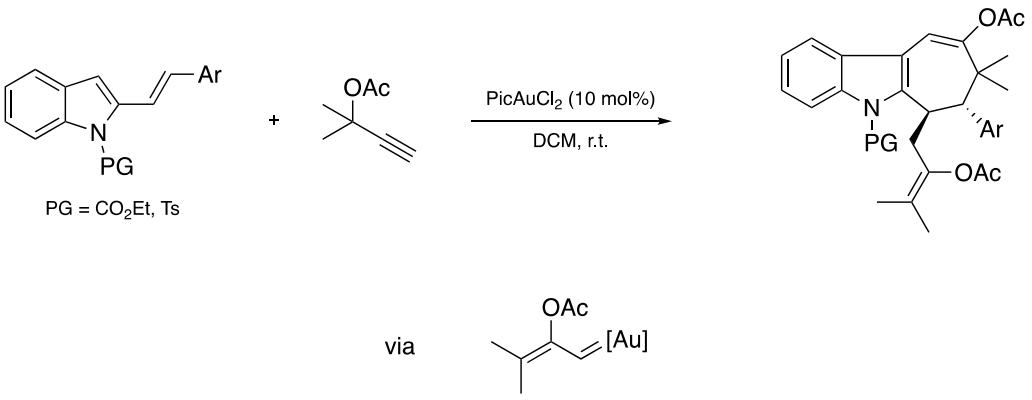
Cyclohepta[b]indoles are 6,5,7-tricyclic compounds which contain a seven-membered ring with a C2-C3 fused indole and are abundant in both natural products and pharmaceutical compounds.[84] Examples include biologically active molecules such as ambiguine, antitubercular agent, exotines and ervitsine-ervatamine alkaloids.[85]

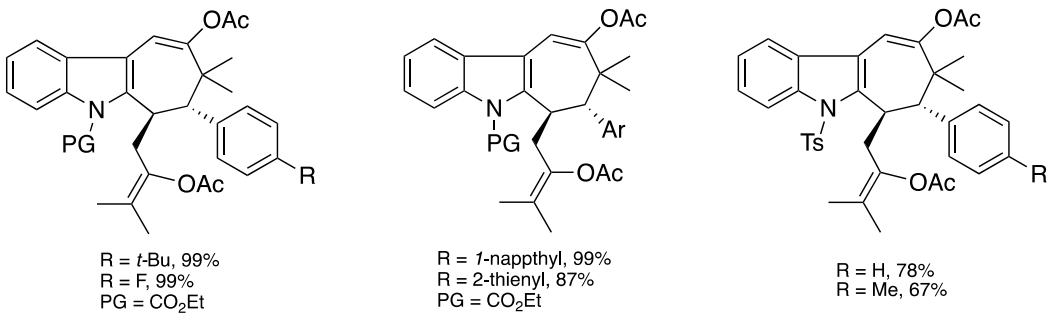
Existing methodologies to synthesize the cyclohepta[b]indoles include sigmatropic rearrangements, palladium-catalyzed cyclizations, and intermolecular (4+3) cycloadditions. Ervitsine-ervatamine alkaloids are isolated from Pandaca boiteaui.[86] Bosch and co-workers demonstrated the biomimic total synthesis of Ervitsine via 1,4-dihydropyridines.[87-89] Bosch and co-worker (scheme 28) employed the pyridinium ion which reacted with the enolate from 2-acetylindoles to give an intermediate dihydropyridine. Protection of the nitrogen of the 2-acetylindoles is needed to increase the yield from 5% to 15% yield. The functionalization with an electrophile such as BrSePh is essential at C-16 for the cyclization and then later to create the exocyclic substituent. The ervitsine was obtained in 65% yield.



Scheme 28. The synthesis of Ervitsine

In addition, there are also synthetic approaches to these tetracyclic structures through the gold-catalyzed (4+3) cycloaddition toward cyclohepta[*b*]indoles by Zhang and co-worker.[90] The gold-catalyzed intermolecular (4+3) cycloaddition of propargylic ester with 2-vinylindoles gave cyclohepta[*b*]indole derivative in a good yield (scheme 29).[91]

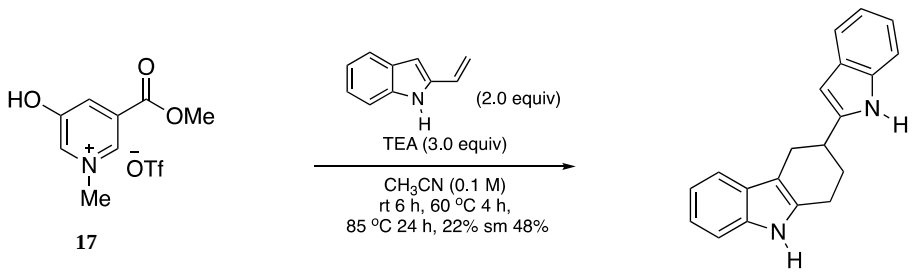




Scheme 29. The synthesis of cyclohepta[*b*]indoles

In the study of (4+3) cycloaddition of 2-vinylindoles with oxyallyl cations by Rossi and co-workers, they reported that vinylindole nitrogen is required as electron-withdrawing protecting group to facilitate the cycloaddition.[92] In contrast, the electron-donating group on the vinylindole nitrogen promotes the nucleophilic addition product.

We would like to explore the synthesis of Ervitsine; so far only a few groups have reported the synthesis of Ervitsine. We started by preparing vinylindole from the known procedure.[93-95] The first (4+3) cycloaddition reaction toward the synthesis of the ervitsine was investigated with the unprotected nitrogen of the vinylindole. No reaction occurred at ambient temperature, so the temperature was elevated, and the reaction was monitored by TLC. The result revealed that the unprotected nitrogen of the vinylindole tends to give the dimerized product with about 22% yield instead of the (4+3) cycloadduct with oxidopyridinium (Scheme 30).

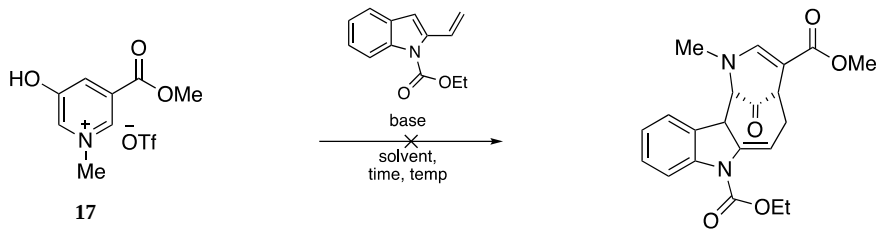


Scheme 30. The dimerization of vinyl indole

A modified procedure has been developed by protecting the amine with an electron withdrawing group.[96] The product was needed to synthesize then used it without further purification because the product was easily to decomposed. The reaction was again started at room temperature then 40 ℃ and elevated to 100 ℃ in the increment of 10 ℃. TLC showed no reaction and crude NMR showed no cycloadduct.

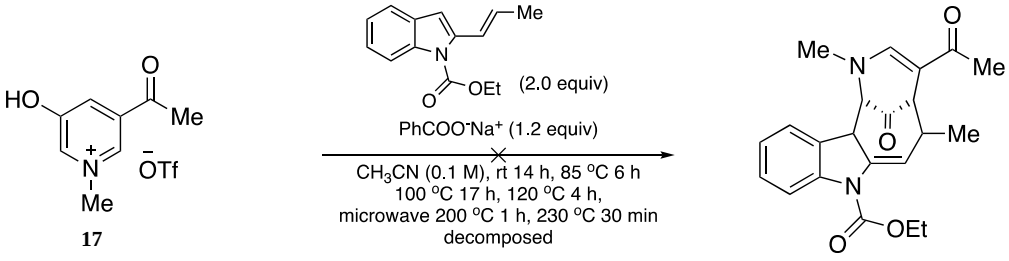
Other reactions were performed using different bases: sodium benzoate as a heterogeneous base and TEA as a homogenous base. The electron withdrawing group on oxidopyridinium ion was modified from a ketone to an ester (table 7). The reaction run using sodium benzoate for approximately 3 days, gave a complex structure by NMR after flash chromatography. Whereas the reaction with TEA showed no product even when heated to 100 ℃.

Table 7. The two bases in the (4+3) cycloaddition reaction



Diene (eq.)	Base (eq.)	Solvent (M)	Time (h)	Temp (°C)	Result
2	TEA (3.0)	CH_3CN (0.1)	14	rt	
			2	40	
			2	60	
			2	80	
			15	100	NR
2	$PhCOO^-$ Na^+ (1.2)	CH_3CN (0.1)	14	rt	
			58	85	complex structure

Another modification was done by incorporating a methyl group on the diene portion of the vinyl indole (scheme 31). The reaction was started from room temperature, then slowly heated until the temperature reached 120 °C, but no reaction progressed based on TLC. Even running the reaction at 200 °C using a microwave reactor showed no reaction. However, upon heating to 230 °C, the compound decomposed.



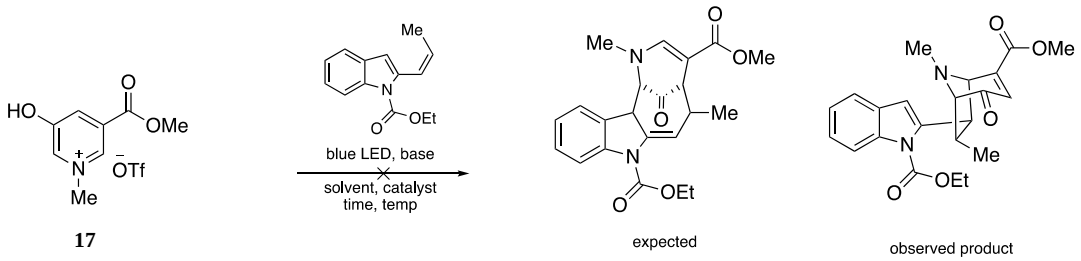
Scheme 31. (4+3) cycloaddition reaction from room temperature to 200 °C

Since thermal treatment did not yield positive results, we were motivated to pursue photochemical routes instead. The Z isomer of vinyl indole was used in the (4+3) cycloaddition reaction with the pyridinium ion under a blue LED with a wavelength of 450 nm (table 8). The reaction set with sodium benzoate for 6 days gave 7% of the observed

product 61% recovered diene. The reaction set by using triethylamine for 5 days, gave only 2% of the observed product and 88% of recovered diene. After purification by flash column chromatography, the complex structure was obtained and determined using 2D NMR spectroscopy. All attempts to grow a crystal from the yellow oil using a variation of solvent systems did not yield any crystalline material.

Based on these promising results, we started to run the reaction with the addition of photocatalyst to study if it can help to accelerate the reaction and obtained a better yield. The catalyst $Ru(bpy)_3Cl_2$ gave 43% product yield and $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$ gave a similar yield of 50% with 20% diene recovered (table 8).

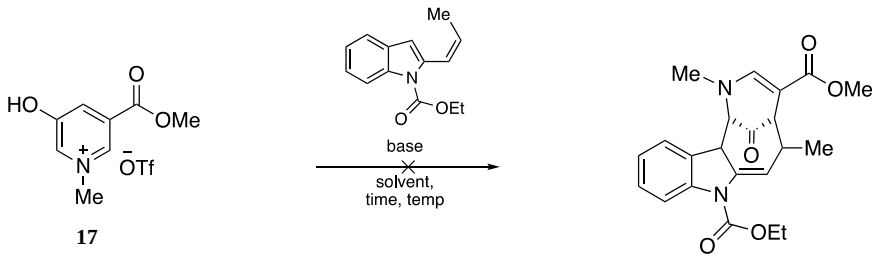
Table 8. The (4+3) cycloaddition reaction under the blue LED



Diene (eq.)	Base (eq.)	Catalyst (eq.)	Solvent (M)	Time	Temp (°C)	Result
2	TEA (3.0)	N/A	CH_3CN (0.1)	5 days	rt	2% prod., 88% diene
2	$PhCOO^-Na^+$ (1.2)	N/A	CH_3CN (0.1)	6 days	rt	7% prod., 61% diene
2	$PhCOO^-Na^+$ (1.2)	$Ru(bpy)_3Cl_2$ (2 mol%)	CH_3CN (0.1)	9 hrs	rt	43% prod.
2	$PhCOO^-Na^+$ (1.2)	$(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$ (2 mol%)	CH_3CN (0.1)	9 hrs	rt	50% prod., 20% diene

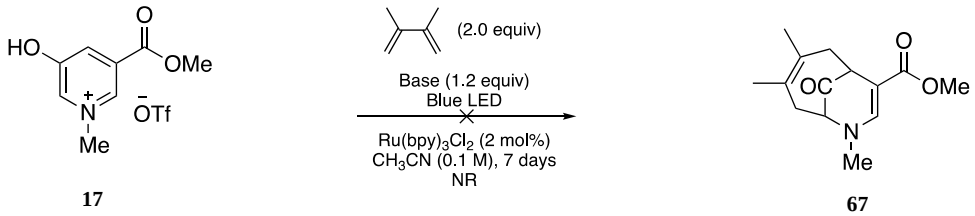
After the (4+3) cycloaddition reaction gave positive results under photochemical conditions, we chose to investigate more carefully the nature of this reaction by running the reaction of oxidopyridinium ion with 2,3-dimethylbutadiene at the room temperature for 7 days (table 9). The reaction was monitored by TLC every day, over 7 days with no sign of product formation. Similar results were obtained using triethylamine and sodium benzoate.

Table 9. The (4+3) cycloaddition reaction at room temperature



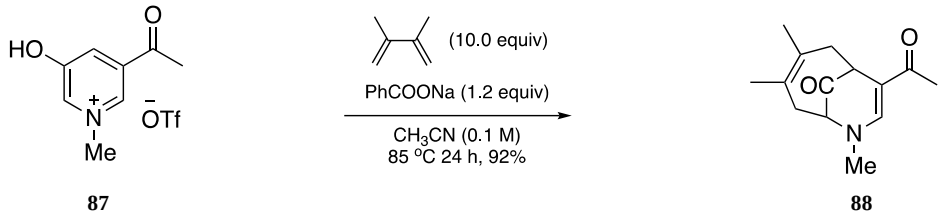
Diene (eq.)	Base (eq.)	Solvent (M)	Time (days)	Temp (°C)	Result
2	TEA (3.0)	CH_3CN (0.1)	7	rt	NR
2	$PhCOO^-Na^+$ (1.2)	CH3CN (0.1)	7	rt	NR

Investigations of this reaction using a blue LED with photocatalyst for 7 days also yielded no reaction (scheme 32).



Scheme 32. The (4+3) cycloaddition reaction under the blue LED and photocatalyst

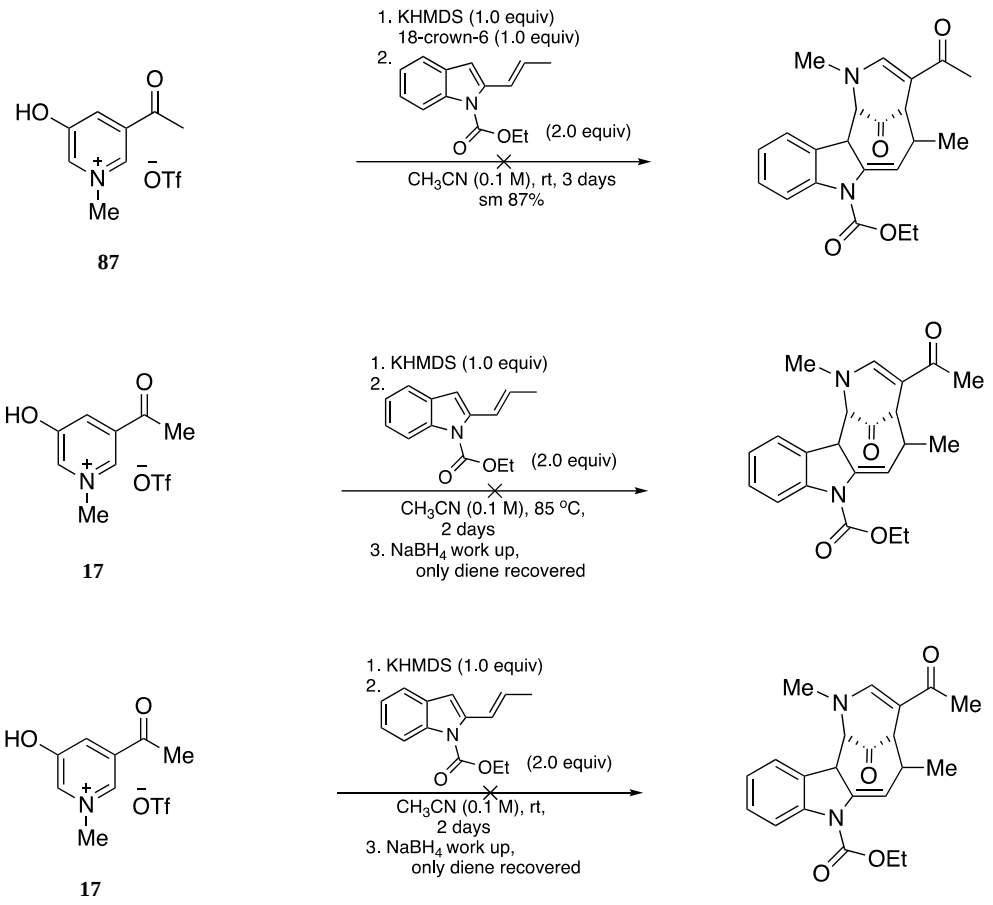
We further investigated the formation of the cycloadduct after the 2 conditions were failed. The 2,3-dimethylbutadiene did not react with the oxidopyridinium ion under the photochemical reaction. And the oxidopyridinium ion with the ketone as an electron withdrawing group[97] did not give the (4+3) cycloadduct when vinylindole was employed. Therefore, we tested the reaction of oxidopyridinium ion with 2,3-dimethylbutadiene under standard (4+3) cycloaddition conditions and obtained the cycloadduct in an excellent 92% yield (scheme 33). The result revealed that the ketone can activate the dienophile to react with the diene and yield the (4+3) cycloadduct under thermal condition and not photo condition.



87 **88**

Scheme 33. The (4+3) cycloaddition of oxidopyridinium ion with 2,3-dimethylbutadiene

With this information in mind, we went back to the vinylindole system. We began by addressing the stereochemistry issue of the substituted vinylindole. By using Suzuki coupling instead of the Wittig reaction to form the substituted vinylindole. We also postulated that the product might be forming in situ (Scheme 34), which would expose it to acidic conditions and promote decomposition so, KHMDS was employed as a base. The present or absent of 18-crown-6 did not change the outcome. Without $NaBH_4$ during the work up, 87% diene was recovered, but with $NaBH_4$ during the worked up 100% diene was recovered. Running the reaction at room temperature or 85 ℃ didn't give the product.



Scheme 34. The (4+3) cycloaddition of oxidopyridinium ion with vinyl indole under the basic condition

Summary

The results of our thermal condition studies on the reaction of oxidopyridinium ion with vinyl indole with or without the protecting group did not give the expected (4+3) cycloadduct. The unprotected vinylindole formed the dimerized product did not react with the oxidopyridinium ion. The same vinylindole did, however, react with 2-chlorocyclopentanone as the dienophile was employed in the study by Rosi[92] to give the cyclohepta[*b*]indole. The oxidopyridinium ion that was used in our study was not as reactive as the 2-chlorocyclopentanone. The photochemical reaction under the blue LED,

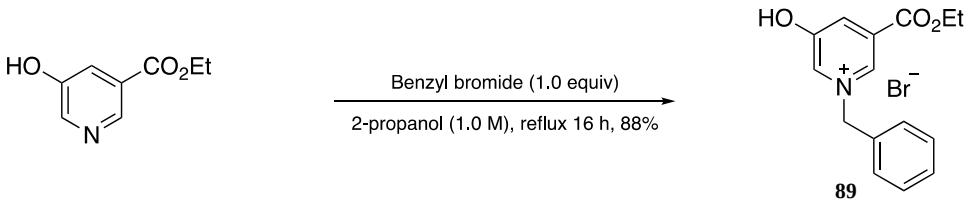
resulted only in the (3+2) cycloadduct between the oxidopyridinium ion and the vinylindole and not the (4+3) adduct.

CHAPTER V

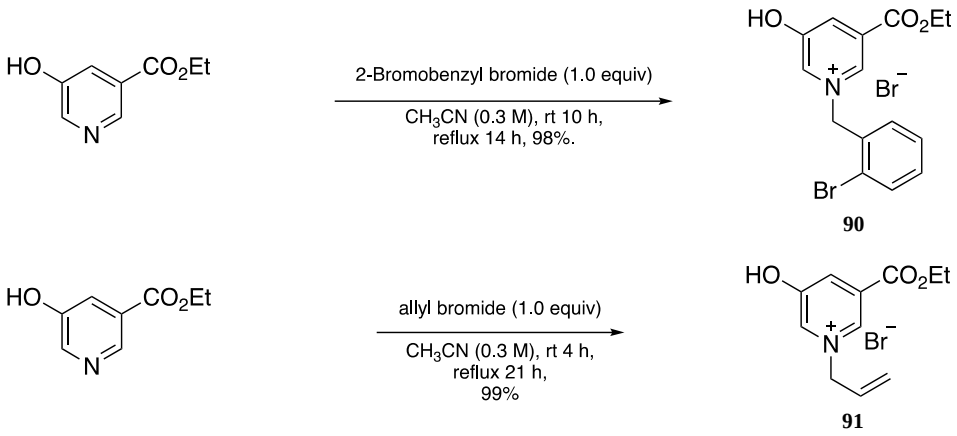
RELATED STUDIES

Since the first example of oxidopyridinium ion has been utilized in the study of intermolecular (4+3) cycloaddition reaction in our group. We have not explored the effect of the electronic effect on the nitrogen of the ethyl 5-hydroxynicotinate. Thus, we would like to create the library of the different substituent on the nitrogen of the ethyl 5-hydroxynicotinate.

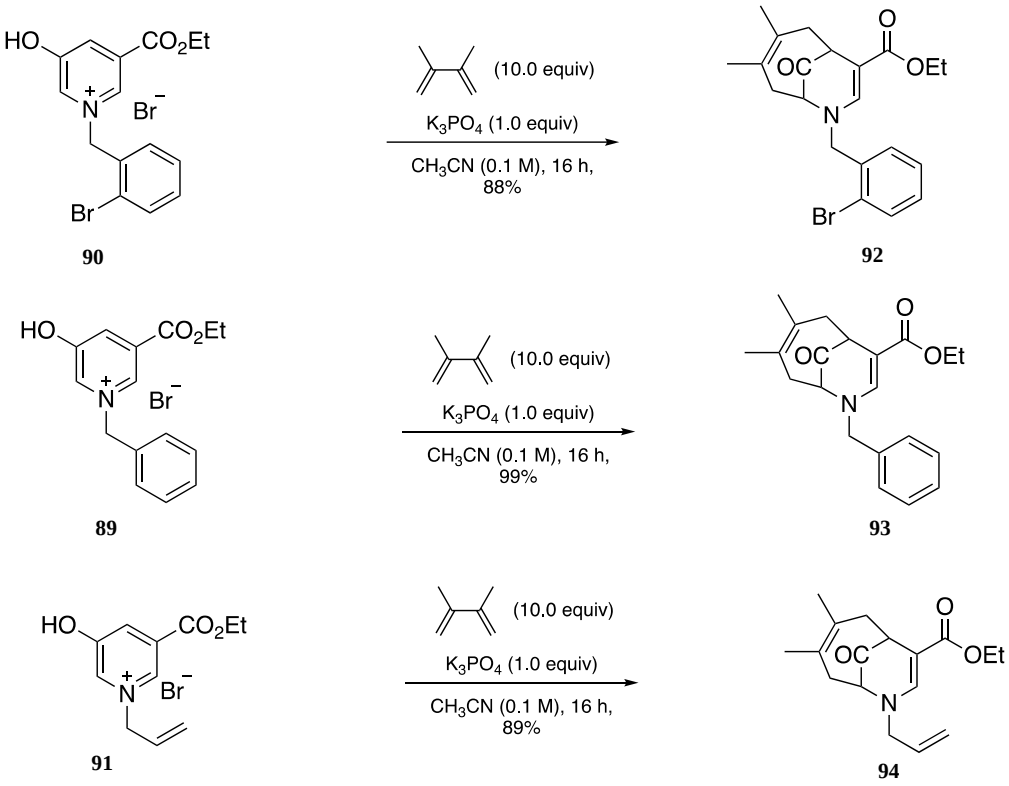
We started with benzyl bromide, 2-bromo benzyl bromide, and allyl bromide. The alkylation product on the nitrogen of ethyl 5-hydroxynicotinate was synthesized. The reactions needed to be carried out at high temperature since there were a lot of starting material left at room temperature (scheme 35). Then, we tested the reaction of oxidopyridinium with 2,3-dimethylbutadiene in the presence of K_3PO_4 under standard conditions which gave the (4+3) cycloadduct in good yield (Scheme 36). The benzyl bromide-substituted substrate gave the best result of 99% yield. The presence of the electron withdrawing group, 2-bromo on the benzyl unit gave a lower yield of 88% which was a similar to the allyl substituted substrate (89% yield). For most substrates, products were purified by flash chromatography however except for the allyl substituted substrate which was purified by silica plug to afford the product.



89



Scheme 35. The synthesis of *N*-alkylation



Scheme 36. (4+3) cycloaddition reaction of *N*-alkylation with 2,3-dimethylbutadiene

Summary

We developed the intermolecular (4+3) cycloaddition reaction of an alkylation on the nitrogen of ethyl 5-hydroxynicotinate gave an excellent yield. Further studies will be

continued using different alkyl, ester, and amide groups on the nitrogen of ethyl 5-hydroxynicotinate and will be reported in a due course.

Experimental Procedures

Endo selectivity in the (4+3) cycloaddition of oxidopyridinium ions

General Information

NMR spectra were recorded on either an AVIII-500 (500 MHz), or an AVIII-600 (600 MHz) spectrometer with chemical shifts reported in d ppm with tetramethylsilane as an internal reference (0.00 ppm). When CDCl3 does not contain tetramethylsilane, an internal reference is 7.26 ppm (s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, hept = heptet, m = multiplet, dd = doublet, ddd = doublet of doublet of doublet, dddd = doublet of doublet of doublet of doublet, td = triplet of doublet, etc). ^{13}C NMR spectra were obtained on the same instruments at 151 MHz, in $CDCl_3$ solution with $CDCl_3$ (77.16 ppm) as an internal reference. Melting points of crystalline
compound were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Thermo Nicolet Summit Pro FT-IR spectrometer and major/diagnostic peaks were picked. High-resolution mass spectra were performed by College of Science Major Instrumentation Center, Old Dominion University, on a Bruker 12 Tesla APEX-Qe FTICR-MS with an Apollo II ion source or at the Charles W. Gehrke Proteomics Center, University of Missouri, on a ThermoScientific LTQ Orbitrap XL mass spectrometer equipped with a static nanospray ECONO 12 tip (proxeon). All reactions were carried in oven-dried glassware with magnetic stir bar under an argon, ethylene atmosphere (balloon) unless otherwise noted. The reactions were heating by oil bath at the indicated temperature in the procedure. Toluene and tetrahydrofuran were order from Sigma Aldrich and distilled under a nitrogen atmosphere over sodium metal with benzophenone as an indicator. Acetonitrile and triethylamine were distilled under a nitrogen atmosphere over calcium hydride. Dichloromethane and methanol were dried over molecular sieves 4 A. Hexanes and ethyl acetate were purchased from Fisher and were used as received. Grubbs catalyst second generation were purchased from Accela ChemBio and AbaChemScene and were used as received. Upon the Grubbs catalyst second generation from different batches were given a different result. Monitoring the reaction by TLC or NMR will help to determine when the reaction will be completely done. Celite were purchased from Fisher. Analytical thin layer chromatography was performed on silica gel plates with UV indicator. The plates were strained with iodine, vanillin and KMnO4. Flash
chromatography was carried out using 40 – 63 micron silica gel purchased from ZeoChem.

Single crystal X-ray diffraction (SCXRD) data for compounds **31a** and **33** were measured on a Bruker D8 Venture diffractometer (Bruker AXS, Inc., Madison, WI, USA) equipped with a Photon 100 CMOS area detector using Mo-Kα radiation from a microfocus source. SCXRD data for compounds **31c** and **37 were** measured on a Bruker X8 Prospector diffractometer equipped with an Apex II CCD area detector using Cu-Kα radiation from a microfocus source. Crystals were cooled to their collection temperatures under streams of cold N2 gas using Oxford Cryostream 700/800 cryostats (Oxford Cryosystems, Oxford,

UK). Hemispheres of unique data were collected for each crystal using strategies of 0.5o scans about the omega and phi axes. Unit cell determination, data collection, data reduction, absorption correction, and scaling were performed using the Bruker Apex3 software suite.[1]

The crystal structures were solved by direct methods using SHELXS v.2013/1[2] and refined by full matrix least squares against F2 using SHELXL v.2017.[3] Olex2 was used for model building and as an interface for the refinement programs.[4] Non-hydrogen atoms were located from the difference map and refined anisotropically. For **31a** thermal parameters and difference map peaks for the phenyl ring indicated disorder by rotation about the C-C bond linking it to the rest of the molecule. Alternate positions could be found for three of the carbon atoms, and the other atoms are too closely overlapped to be resolved. Restraints for rigid bond behavior[5] were also applied to all nonhydrogen atoms in **31a.**

For compound **37** the crystal was weakly diffracting and required long counting times per frame; because of this the resolution of the data collection was limited to 0.90 A in order to allow the entire data collection to finish before excess ice buildup on the crystal rendered the data unusable. This results in a B-level THETM01 checkCIF alert for this model. This has no noticeable effects on the refinement as the structural features of interest are well above this resolution, and the data-to-parameters ratio for this structure is acceptable due to the large fraction of observed data in the dataset.

[1] Apex3, AXScale, and SAINT, version 2017.3-0, Bruker AXS, Inc., Madison, WI, 2017.
[2] Sheldrick, G. M. SHELXS, v.2013-1, 2013.
[3] Sheldrick, G. M. Crystal structure refinement with *SHELXL*. *Acta Cryst. Sect. C. Struct. Chem.* **2015**, *71*, 3-8.
[4] Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. *OLEX2:* A complete structure solution, refinement, and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339-341.
[5] Thorn , A.; Dittrich, B.; Sheldrick, G. M. Enhanced rigid bond restraints. *Acta Cryst. Sect. A. Found. Adv.* **2012**, *68*, 448-451.

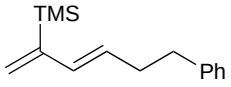
General procedure for dienes

An oven-dried 100 mL round-bottom flask equipped with a magnetic stir bar. At the room temperature and backfilled with argon three times. Then trimethylsilylacetylene (1.05 mL, 7.6 mmol, 2.0 equiv), 4-phenyl-1-butene (500 mg, 3.8 mmol, 1.0 equiv) were added in dichloromethane (63 mL, 0.064 M). The brown mixture was degassed for 5 min then Grubbs second generation (258.1 mg, 8 mol%) was added and stirred for 20 h at 40 ^{o}C by oil bath under argon atmosphere. The reaction progress was monitored by TLC using 100% hexanes. After completion of the reaction, the mixture was filtered by celite in a sintered glass funnel, rinsingwith more hexanes and the filtrate was concentrated in vacuo. The crude product was purified by flash column chromatography on silica gel (100 % hexanes, R_f = 0.63). The product was obtained
as a colorless oil (605 mg, 2.63 mmol) in 69% yield.

General procedure for (4+3) cycloadduct

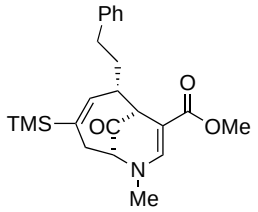
An oven-dried 15 mL seal tube equipped with a magnetic stir bar. At the room temperature, Nmethyloxidopyridinium ion (200 mg, 0.63 mmol, 1.0 equiv), (*E*)-trimethyl(6-phenylhexa-1,3-
dien-2-yl)silane (437.3 mg, 1.9 mmol, 3.0 equiv) were added in acetonitrile (6.3 mL, 0.1 M), then degassed by argon for 5 min. Triethylamine (264 μL mg, 1.9 mmol, 3.0 equiv) was added to the mixture then heating for 24 h at 85 oC by oil bath. Upon heating for 1 h, pale yellow and clear mixture turned to dark brown. After the reaction mixture was stirred for 24 h and cooled down to room temperature, 16 drops of 10% HCl was added to the mixture. Then extraction by using dichloromethane (3 x 15 mL). The combined organic layers, brown and clear solution were dried over anhydrous Na_2SO_4. The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (20% - 30% EtOAc:Hexanes)

(*E*)-trimethyl(6-phenylhexa-1,3-dien-2-yl)silane (30a)



The crude product was purified by flash column chromatography on silica gel (100 % hexanes, Rf = 0.63). The product was obtained as a colorless oil (605 mg, 2.63 mmol) in 69% yield.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 – 7.16 (m, 5H), 6.17 (d, *J* = 15.9 Hz, 1H), 5.73 (dt, *J* = 15.9, 6.9 Hz, 1H), 5.63 (d, *J* = 3.2 Hz, 1H), 5.32 (d, *J* = 3.2 Hz, 1H), 2.72 (t, *J* = 7.4 Hz, 2H), 2.43 – 2.38 (m, 2H), 0.14 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): 149.2, 142.0, 135.5, 131.8, 128.6, 128.4, 126.6, 126.0, 36.1, 35.3, -0.7; **IR** (neat) ν_{max}: 3083, 3065, 3025, 2930, 2854, 1635, 1613, 1501, 1447, 1249, 917, 840, 701 cm^{-1} ; **HRMS (m/z):** (ESI-FTICR) calcd for ($C_{15}H_{22}Si$)Na $[M+Na]^+$: 253.1383, found: 253.1384.

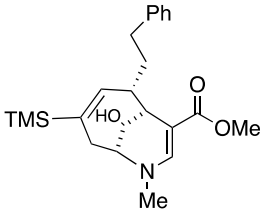
methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (31)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.42) to obtain a pale yellow oil (233 mg, 0.59 mmol) in 93% yield.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30 (s, 1H), 7.28 – 7.16 (m, 5H), 6.20 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.66 (dd, *J* = 5.4, 2.3 Hz, 1H), 3.65 (s, 3H), 3.55 (t, *J* = 3.9 Hz, 1H), 2.93 (dd, *J* = 7.7, 4.4 Hz, 1H), 2.91 (s, 3H), 2.82 (dd, *J* = 16.5, 5.9 Hz, 1H), 2.80 – 2.77 (m, 1H), 2.62 (ddd, *J* = 13.7, 10.2, 5.8 Hz, 1H), 2.12 (dt, *J* = 16.5, 2.4 Hz, 1H), 1.70 (dddd, *J* = 13.4, 10.1, 7.3, 5.9 Hz, 1H), 1.50 (dddd, *J* = 13.7, 10.1, 8.0, 5.9 Hz, 1H), 0.06 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 205.6, 167.7, 146.9, 144.1, 142.2, 137.1, 128.5, 128.4, 125.9, 93.7, 66.7, 50.8, 49.0, 40.2, 34.3, 34.2, 28.5, -1.6; **IR** (neat) ν_{max}: 3016, 2946, 2854, 1720, 1678, 1609, 1437, 1381, 1366, 1233, 1157, 1066, 833, 748, 699 cm^{-1} ; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{23}H_{31}NO_3Si)H$ $[M+H]^+$: 398.2146, found:
398.2144.

The product **31a** was confirmed the stereochemistry by the reduction of ketone then obtained the x-ray crystallography.

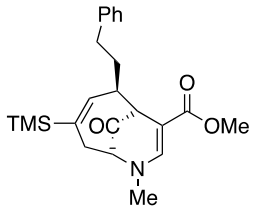
methyl(1*R*,2*R*,6*R*,10*R*)-10-hydroxy-7-methyl-2-phenethyl-4-(trimethylsilyl)-7 azabicyclo [4.3.1]deca-3,8-diene-9-carboxylate (reduction of 31a)



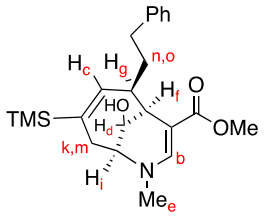
The product was obtained as a white solid (183 mg, 0.46 mmol) in 92% yield, Rf = 0.31 (30% EtOAc:Hexanes), and recrystallization by 2:8 EtOAc:Hexanes, mp = 132 - 133 ˚C.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 – 7.26 (m, 2H), 7.23 (s, 1H), 7.20 (dd, J = 8.1, 1.3 Hz, 2H), 7.16 (tt, J = 7.3, 1.2 Hz, 1H), 6.03 (dd, J = 7.6, 2.7 Hz, 1H), 4.41 (q, J = 4.9 Hz, 1H), 3.63 (s, 3H), 3.40 (dddd, J = 5.5, 3.9, 1.9 Hz, 1H), 3.14 (quin, J = 2.3 Hz, 1H), 2.95 (s, 3H), 2.86 (dddd, J = 12.3, 9.3, 7.3, 3.5 Hz, 1H), 2.82 (dt, J = 16.9, 1.9 Hz, 1H), 2.73 (ddddd, J = 23.2, 19.6, 13.6, 9.6, 6.8 Hz, 2H), 2.53 (dd, J = 16.4, 5.5 Hz, 1H), 2.11 – 2.00 (m, 2H), 1.70 (d, J = 4.3 Hz, 1H), 0.04 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): 168.3, 147.3, 144.8, 143.2, 136.5, 128.6, 128.4, 125.7, 95.9, 72.8, 59.2, 50.6, 45.6, 41.1, 37.9, 35.7, 26.3, -1.5;

IR (CH_2Cl_2) ν_{max}: 3425, 3056, 2989, 1690, 1640, 1618, 1438, 1416, 1267, 1173, 1074, 894, 840, 741, 706 cm^{-1}; **HRMS (m/z):** (ESI-FTICR)
calcd for $(C_{23}H_{33}NO_3Si)Na$ $[M+Na]^+$: 422.2122, found: 422.2120.

methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (31b)

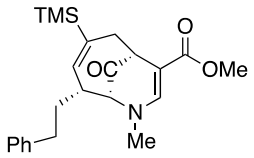


^{1}**H NMR** (600 MHz, $CDCl_3$): δ 7.33 (s, 1H), 7.28 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.21 (m, 2H), 7.19 – 7.16 (m, 1H), 5.90 (t, *J* = 3.3 Hz, 1H), 3.66 – 3.65 (m, 1H), 3.64 (s, 3H), 3.63 (ddd, *J* = 6.8, 3.1, 1.5 Hz, 1H), 2.96 (dd, *J* = 15.8, 6.6 Hz, 1H), 2.90 (s, 3H), 2.89 – 2.86 (m, 1H), 2.72 (ddd, *J* = 13.7, 9.4, 5.9 Hz, 1H), 2.14 (dddd, *J* = 13.7, 9.3, 7.9, 6.1 Hz, 1H), 2.10 – 2.04 (m, 2H), 1.89 (dddd, *J* = 13.3, 9.6, 7.1, 6.1 Hz, 1H), 0.08 (s, 9H); ^{13}**C NMR** (151 MHz, $CDCl_3$): 207.1, 168.3, 148.0, 147.7, 142.1, 139.8, 128.7, 128.5, 125.9, 91.4, 66.9, 50.8, 49.5, 43.7, 40.7, 37.0, 34.3, 30.5, -1.3; **IR** (neat) ν_{max}: 3016, 2946, 2854, 1720, 1678, 1609, 1437, 1381, 1366, 1233, 1157, 1066, 833, 748, 699 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{23}H_{31}NO_3Si)H$ $[M+H]^+$: 398.2146, found:
398.2144.



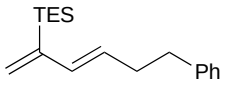
The product **31b** was assigned the stereochemistry using the NOESY spectrum of the reduction of **13b**. The NOESY spectrum indicates that the triplet proton **i** on the bridgehead at 3.26 ppm correlates with the **Mee** proton at 2.93 ppm, proton **d** on the bridge at 4.19 ppm, and CH2 proton **k** at 2.77 ppm and **m** at 2.45 ppm. The doublet proton **f** on the bridgehead at 3.06 ppm correlates with CH2 proton **n** at 2.10 ppm which indicates the exo isomer. The singlet proton **b** at 7.30 ppm correlates with the singlet **Mee** proton at 2.93 ppm. The triplet proton **c** at 5.63 ppm correlates with the proton **g** at 2.91 ppm and CH2 proton of the alkyl group **j, l, n,** and **o** at 2.83, 2.71, 2.10, and 1.85 ppm respectively. The doublet of doublet CH2 proton **m** at 2.45 ppm correlates with the proton of TMS, **Mee**, and **i** on the bridgehead at 0.02, 2.93, and 3.26 ppm respectively.

methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (31c)



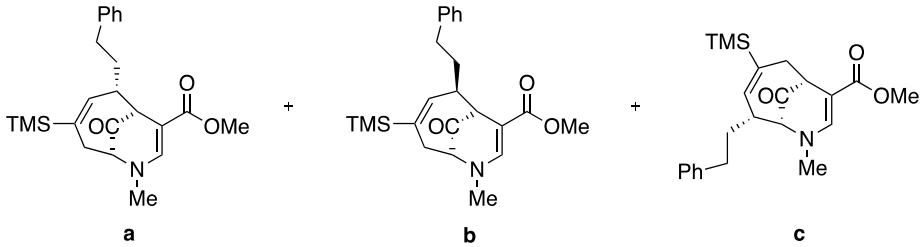
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (s, 1H), 7.27 – 7.25 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 7.0 Hz, 2H), 6.13 (dd, *J* = 7.8, 2.7 Hz, 1H), 3.64 (s, 3H), 3.62 (dd, *J* = 5.1, 3.0 Hz, 1H), 3.54 (dt, *J* = 5.5, 2.7 Hz, 1H), 2.91 – 2.89 (m, 1H), 2.88 (s, 3H), 2.85 – 2.81 (m, 1H), 2.67 (ddtt, *J* = 20.3, 13.8, 9.0, 6.6 Hz, 2H), 2.11 (dt, *J* = 15.7, 2.7 Hz, 1H), 1.66 (ddt, *J* = 13.6, 8.9, 6.6 Hz, 1H), 1.54 – 1.51 (m, 1H), 0.02 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): 205.7, 167.4, 146.5, 144.6, 141.4, 137.5, 128.6, 128.5, 126.2, 93.3, 70.2, 50.8, 45.8, 40.3, 38.4, 34.2, 32.0, 30.2, -2.4; **IR** (neat) ν_{max}: 3016, 2946, 2854, 1720, 1678, 1609, 1437, 1381, 1366, 1233, 1157, 1066, 833, 748, 699 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{23}H_{31}NO_3Si)H$ $[M+H]^+$: 398.2146, found: 398.2144.
The product **13c** was assigned stereochemistry by the x-ray crystallography.

(*E*)-triethyl(6-phenylhexa-1,3-dien-2-yl)silane (30b)



The crude product was purified by flash column chromatography on silica gel (100 % hexanes, Rf = 0.54). The product was obtained as a pale yellow oil (382 mg, 1.40 mmol) in 25% yield.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 – 7.16 (m, 5H), 6.15 (d, *J* = 15.8 Hz, 1H), 5.73 – 5.68 (m, 2H), 5.28 (d, *J* = 3.3 Hz, 1H), 2.71 (t, *J* = 7.4 Hz, 2H), 2.41 – 2.37 (m, 2H), 0.94 – 0.90 (m, 9H), 0.63 (q, *J* = 7.8 Hz, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): 146.1, 142.0, 136.0, 130.8, 128.6, 128.4, 127.7, 125.9, 36.2, 35.2, 7.5, 3.5; **IR** (neat) ν_{max}: 3033, 3026, 2952, 2879, 2874, 1462,1455, 1415, 1237, 1002, 969, 822, 700, 697 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{18}H_{28}Si)H$ $[M+H]^+$: 273.2033, found: 273.2036.

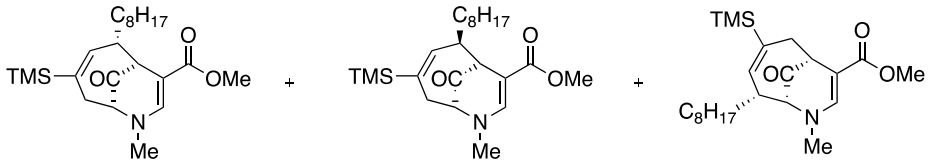
methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenethyl-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (32)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.47) to obtain a colorless oil (62 mg, 0.14 mmol) in 88% yield.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (s, 1H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.17 - 7.16 (m, 3H), 6.20 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.64 (s, 3H), 3.63 – 3.62 (m, 1H), 3.53 (t, *J* = 3.8 Hz, 1H), 2.99 - 2.93 (m, 1H), 2.92 (s, 3H), 2.80 (dd, *J* = 16.5, 5.9 Hz, 1H), 2.76 (dd, *J* = 7.9, 3.2 Hz, 1H), 2.64 (ddd, *J* = 13.5, 10.6, 5.6 Hz, 1H), 2.11 (dt, *J* = 16.4, 2.4 Hz, 1H), 1.73 (ddt, *J* = 13.1, 10.6, 6.0 Hz, 1H), 1.49 (dtt, *J* = 10.4, 8.4, 5.6 Hz, 1H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.65 - 0.52 (m, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): 207.0, 205.5, 168.0, 167.6, 148.9, 148.0, 146.8, 145.7, 142.2, 134.2, 128.6, 128.5, 128.4, 125.9, 93.9, 91.5, 66.7, 50.7, 49.1, 42.1, 40.2, 34.7, 34.5, 28.8, 7.4, 2.7; **IR** (neat) ν_{max}: 2948, 2872, 1717, 1678, 1610, 1410, 1408, 1334, 1236, 1157, 1066, 1002, 698 cm^{-1}; **HRMS (m/z):**
(ESI-FTICR) calcd for $(C_{26}H_{37}NO_3Si)H$ $[M+H]^+$: 440.2616, found: 440.2617.

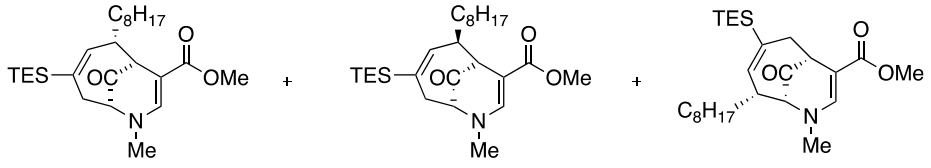
methyl (1*R*,2*R*,6*R*)-7-methyl-2-octyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (33)



a **b** **c**

The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (20% EtOAc:Hexanes, Rf = 0.58) to obtain a white solid (93 mg, 0.23 mmol) in 71% yield, and recrystallization by 20% EtOH:H2O, mp = 88 - 89˚C.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (s, 1H), 6.20 (dd, J = 7.9, 2.8 Hz, 1H), 3.67 (s, 3H), 3.65 -
3.63 (m, 1H), 3.44 (t, J = 3.7 Hz, 1H), 2.91 (s, 3H), 2.86 (td, J = 6.8, 3.1 Hz, 1H), 2.80 (dd, J =
16.5, 5.9 Hz, 1H), 2.11 (dt, J = 16.5, 2.4 Hz, 1H), 1.42 – 1.14 (m, 14H), 0.89 – 0.86 (m, 3H), 0.06 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): 205.8, 167.7, 146.8, 144.8, 136.5, 94.0, 66.8, 50.9, 49.4, 42.5, 40.2, 32.5, 32.0, 29.7, 29.6, 29.4, 28.5, 28.2, 22.8, 14.3, -1.6; **IR** (neat) ν_{max}: 2922, 2854, 1714, 1668, 1614, 1415, 1413, 1342, 1236, 1159, 1073, 833, 748 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{23}H_{39}NO_3Si)H$ $[M+H]^+$: 406.2772, found: 406.2770.

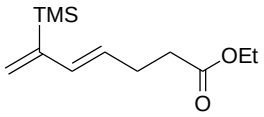
methyl (1*R*,2*R*,6*R*)-7-methyl-2-octyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (34)



a **b** **c**

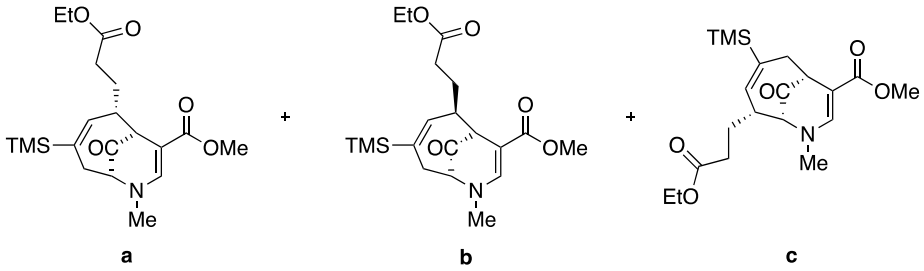
The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.44) to obtain a colorless oil (55 mg, 0.12 mmol) in 77% yield.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 (s, 1H), 6.16 (dd, *J* = 7.9, 2.9 Hz, 1H), 3.65 (s, 3H), 3.61 (dd, *J* = 6.1, 3.0 Hz, 1H), 3.42 (t, *J* = 3.8 Hz, 1H), 2.90 (s, 3H), 2.90 – 2.86 (m, 1H), 2.76 (dd, *J* = 16.5, 5.9 Hz, 1H), 2.08 (dt, *J* = 16.5, 2.4 Hz, 1H), 1.42 - 1.14 (m, 17H), 0.92 – 0.83 (m, 9H), 0.63 – 0.49 (m, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): 207.4, 205.8, 167.7, 146.7, 146.4, 133.4, 94.2, 91.7, 66.8, 50.8, 49.5, 42.6, 40.2, 32.8, 32.0, 29.7, 29.6, 29.4, 28.8, 28.2, 22.8, 14.2, 7.4, 2.8; **IR** (neat) ν_{max}: 2924, 2873, 2853, 1718, 1681, 1613, 1410, 1409, 1334, 1236, 1159, 1066, 1003, 716 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{26}H_{45}NO_3Si)H$ $[M+H]^+$: 448.3242, found: 448.3243.

ethyl (*E*)-6-(trimethylsilyl)hepta-4,6-dienoate (30e)



The crude product was purified by flash column chromatography on silica gel (3% ethyl acetate/hexanes). The product was obtained as a colorless oil (71 mg, 0.31 mmol) in 62% yield.
^{1}H NMR (600 MHz, $CDCl_3$): δ 6.18 – 6.15 (m, 1H), 5.71 – 5.66 (m, 1H), 5.62 (d, *J* = 3.2 Hz, 1H), 5.31 (d, *J* = 3.2 Hz, 1H), 4.11 (qt, *J* = 7.1, 1.5 Hz, 2H), 2.40 – 2.38 (m, 4H), 1.24 – 1.21 (m, 3H), 0.13 - 0.12 (m, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 173.1, 148.9, 136.0, 130.2, 127.0, 60.4, 34.4, 28.7, 14.4, -0.8; **IR** (neat) ν_{max}: 2954, 2899, 1732, 1373, 1247, 1162, 1026, 835, 755, 691 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{12}H_{22}O_2Si)H$ $[M+H]^+$: 227.1462, found: 227.1460.
NOTE: When the Grubbs catalyst second generation was purchased from Accela ChemBio was used, the reaction time was 19 h in contrast when the Grubbs catalyst second generation was purchased from AbaChemScene was used, the reaction time was 2 h.

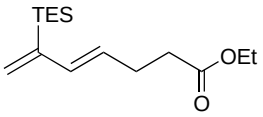
methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-7-methyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (35)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.31) to obtain a pale yellow oil (109 mg, 0.28 mmol) in 87% yield.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.32 (s, 1H), 6.19 (dd, *J* = 7.8, 2.8 Hz, 1H), 4.14 (m, 2H), 3.70 - 3.69 (m, 1H), 3.68 (s, 3H), 3.45 (t, *J* = 3.6 Hz, 1H), 2.94, (s, 3H), 2.90 (qd, *J* = 8.1,

4.5 Hz, 1H), 2.85 (dd, *J* = 16.5, 5.9 Hz, 1H), 2.48 (ddd, *J* = 15.8, 9.7, 6.2 Hz, 1H), 2.34 (ddd, *J* = 15.6, 9.6, 5.8 Hz, 1H), 2.15 (dt, *J* = 16.6, 2.4 Hz, 1H), 1.69 (dddd, *J* = 13.7, 9.6, 7.3, 6.2 Hz, 1H), 1.60 (dddd, *J* = 14.1, 9.6, 8.4, 5.8 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.09 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 206.8, 205.3, 173.3, 167.6, 146.9, 143.1, 138.2, 93.5, 91.0, 66.6, 60.5, 50.8, 49.0, 41.7, 40.2, 32.9, 28.6, 27.4, 14.3, -1.7; **IR** (neat) ν_{max}: 2949, 2910, 1722, 1677, 1610, 1438, 1409, 1335, 1243, 1153, 1067, 832, 760 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for (C20H31NO5Si)Na $[M+Na]^+$: 394.2044, found: 394.2044.

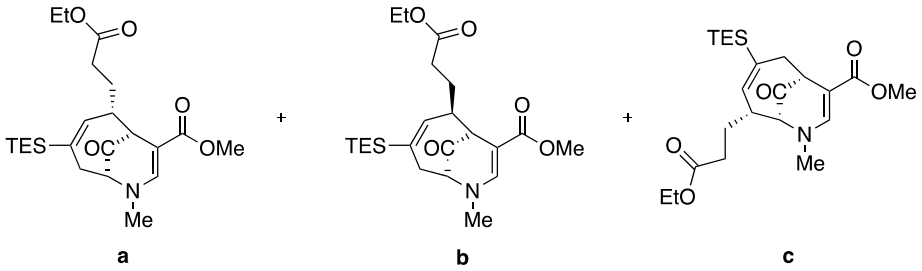
ethyl (*E*)-6-(triethylsilyl)hepta-4,6-dienoate (30f)



The crude product was purified by flash column chromatography on silica gel (5% ethyl acetate/hexanes). The product was obtained as a red oil (35 mg, 0.13 mmol) in 36% yield. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 6.18 (d, *J* = 15.8 Hz, 1H), 5.73 (d, *J* = 3.3 Hz, 1H), 5.72 – 5.67 (m, 1H), 5.30 (d, *J* = 3.3 Hz, 1H), 4.13 (qd, *J* = 7.1, 4.0 Hz, 2H), 2.40 - 2.38 (m, 4H), 1.25 (td, *J* = 7.1, 2.4 Hz, 3H), 0.92 (t, *J* = 8.1 Hz, 9H), 0.66 (q, *J* = 7.8 Hz, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): 173.0, 145.8, 136.4, 129.2, 128.0, 115.5, 60.3, 34.3, 28.6, 14.3, 7.4, 3.4; **IR** (neat) ν_{max}: 2952, 2875, 1734, 1457, 1416, 1377, 1373, 1237, 1161, 1003, 968, 719 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{15}H_{28}O_2Si)H$ $[M+H]^+$: 269.1931, found: 269.1931.

NOTE: When the Grubbs catalyst second generation was purchased from Accela ChemBio was used, the reaction time was 18 h in contrast when the Grubbs catalyst second generation was purchased from AbaChemScene was used, the reaction time was 5 h.

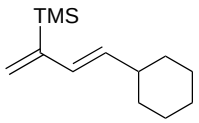
methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-7-methyl-10-oxo-4-(triethylsilyl)-7 azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (36)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.37) to obtain a pale yellow oil (104 mg, 0.24 mmol) in 74% yield.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (s, 1H), 6.12 (dd, *J* = 7.8, 2.8 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.63 (s, 3H), 3.61 (dd, *J* = 6.2, 3.6 Hz, 1H), 3.41 (t, *J* = 3.7 Hz, 1H), 2.91 (s, 3H), 2.89 (dd, *J* = 7.1, 2.6 Hz, 1H), 2.78 (dd, *J* = 16.5, 5.8 Hz, 1H), 2.44 (ddd, *J* = 15.8, 9.7, 6.3 Hz, 1H), 2.32 (ddd, *J* = 15.5, 9.7, 5.7 Hz, 1H), 2.08 (dt, *J* = 16.5, 2.4 Hz, 1H), 1.68 (ddt, *J* = 13.7, 9.7, 7.1 Hz, 1H), 1.56 (dtt, *J* = 9.6, 8.6, 5.7 Hz, 1H), 1.23 (t, *J* = 7.2 Hz, 3H),

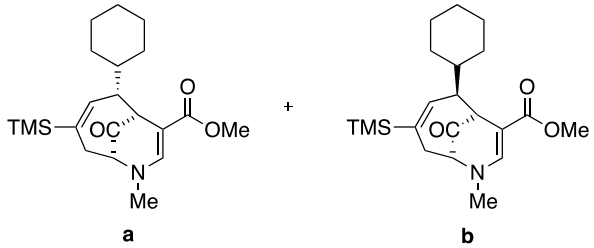
0.88 (t, *J* = 8.0 Hz, 9H), 0.56 (ddd, *J* = 22.7, 14.9, 7.5 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 205.3, 173.3, 167.5, 146.8, 144.8, 135.1, 93.7, 66.7, 60.4, 50.8, 48.9, 41.8, 40.3, 32.9, 28.9, 27.7, 14.3, 7.4, 2.7; **IR** (neat) ν_{max}: 2950, 2873, 1724, 1677, 1611, 1412, 1410, 1335, 1238, 1155, 1067, 1003, 704 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{23}H_{37}NO_5Si)H$ $[M+H]^+$: 436.2514, found: 436.2514.

(*E*)-(4-cyclohexylbuta-1,3-dien-2-yl)trimethylsilane (30g)



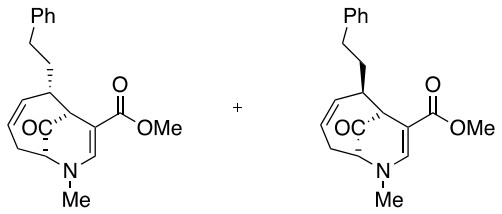
The crude product was purified by flash column chromatography on silica gel (100 % hexanes, Rf = 0.69). The product was obtained as a yellow oil (115 mg, 0.55 mmol) in 15% yield.
^{1}H NMR (600 MHz, $CDCl_3$) δ 6.12 (d, *J* = 16.0 Hz, 1H), 5.67 (dd, *J* = 16.1, 7.0 Hz, 1H), 5.64 (d, *J* = 3.3 Hz, 1H), 5.31 – 5.30 (m, 2H), 1.74 – 1.62 (m, 5H), 1.33 – 1.00 (m, 5H), 0.16 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 149.5, 139.0, 132.1, 126.1, 41.4, 34.3, 33.5, 33.4, 33.1, 26.4, 26.2, 14.2, -0.6; **IR** (neat) ν_{max}: 2922, 2850, 1448, 1247, 965, 834, 755, 689 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{13}H_{24}Si)OH$ $[M+OH]^-$: 207.1564, found: 207.1564.

methyl (1*R*,2*R*,6*R*)-2-cyclohexyl-7-methyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (37)



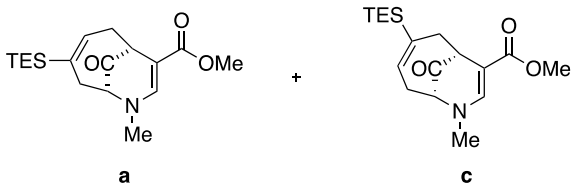
The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.42) to obtain a white solid (63 mg, 0.17 mmol) in 67% yield, and recrystallization by 10% Et2O:pentane, mp = 144-145˚C. The product **19** was confirmed the stereoisomer by the x-ray crystallography.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.29 (s, 1H), 6.19 (dd, *J* = 8.1, 2.8 Hz, 1H), 3.73 (t, *J* = 3.4 Hz, 1H), 3.66 (s, 3H), 3.62 (dt, *J* = 6.0, 2.0 Hz, 1H), 2.91 (s, 3H), 2.82 (dd, *J* = 16.3, 6.0 Hz, 1H), 2.66 (ddd, *J* = 10.1, 8.3, 4.4 Hz, 1H), 2.20 (d, *J* = 12.5 Hz, 1H), 2.10 (dt, *J* = 16.3, 2.2 Hz, 1H), 1.75 - 1.73 (m, 1H), 1.65 – 1.58 (m, 3H), 1.26 – 0.95 (m, 6H), 0.07 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 206.4, 167.7, 147.0, 145.0, 136.5, 94.1, 66.8, 50.8, 48.4, 46.3, 40.3, 39.9, 32.1, 31.5, 28,5, 26.6, 26.4, 26.0, -1.5; **IR** (neat) ν_{max}: 2926, 2849, 1709, 1661, 1615, 1415, 1411, 1338, 1236, 1160, 1064, 887, 832, 748 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{21}H_{33}NO_3Si)H$ $[M+H]^+$: 376.2303, found: 376.2298.

methyl (1*R*,2*S*,6*R*)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (38)



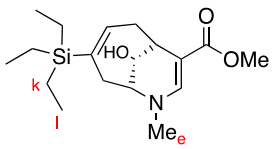
The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.26) to obtain a colorless oil (89 mg, 0.28 mmol) in 86% yield.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37 (s, 1H), 7.35 (s, 1H), 7.26 (td, *J* = 7.6, 4.2 Hz, 4H), 7.21 – 7.15 (m, 6H), 5.90 (ddd, *J* = 11.7, 8.2, 2.9 Hz, 1H), 5.78 (dddd, *J* = 11.2, 8.5, 4.0, 2.5 Hz, 1H), 5.64 (dtd, *J* = 11.9, 8.6, 2.7 Hz, 2H), 3.68 (s, 1H), 3.65 – 3.64 (m, 2H), 3.64 (s, 3H), 3.63 (s, 3H), 3.57 (t, *J* = 3.6 Hz, 1H), 2.89 (s, 3H), 2.86 (s, 3H), 2.85 – 2.62 (m, 6H), 2.14 – 2.05 (m, 5H), 1.84 (tdt, *J* = 9.0, 6.9, 5.2 Hz, 1H), 1.73 (dddd, *J* = 13.2, 10.5, 7.0, 5.8 Hz, 1H), 1.52 (dddd, *J* = 13.8, 10.4, 8.2, 5.7 Hz, 1H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 206.4, 205.4, 168.2, 167.5, 148.2, 147.1, 142.1, 141.9, 139.6, 136.7, 128.6, 128.4, 128.4, 128.3, 125.8, 124.8, 123.5, 93.7, 91.1, 66.2, 66.0, 50.7, 49.9, 49.2, 43.1, 41.1, 39.6, 39.6, 36.6, 34.5, 34.2, 34.1, 28.6, 27.0; **IR** (neat) ν_{max}: 3025, 2937, 2855, 1711, 1671, 1614, 1441, 1405, 1380, 1339, 1301, 1257, 1165, 1069, 948, 792, 749,
703, 684 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{20}H_{23}NO_3Si)H$ $[M+H]^+$: 326.1751, found: 326.1748.

methyl (1*R*,6*R*)-7-methyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (39)



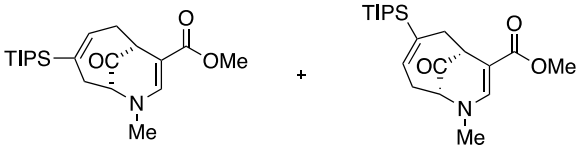
The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.33) to obtain a colorless solid (106 mg, 0.32 mmol) in 99%, and recrystallization by 20% EtOH:H2O, mp = 64 -65˚C.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26 (s, 1H), 7.23 (s, 1H), 6.10 (ddt, *J* = 11.5, 8.4, 3.0 Hz, 2H), 3.68 (dt, *J* = 5.6, 2.3 Hz, 2H), 3.66 (s, 3H), 3.65 (s, 3H), 3.60 (dt, *J* = 5.6, 2.6 Hz, 1H), 3.54 (dt, *J* = 5.6, 2.9 Hz, 1H), 3.00 (dd, *J* = 15.2, 5.8 Hz, 1H), 2.97 – 2.93 (m, 2H), 2.92 (s, 3H), 2.91 - 2.90 (m, 1H), 2.88 (s, 3H), 2.05 – 1.95 (m, 4H), 0.88 (dt, *J* = 22.9, 7.9 Hz, 18H), 0.65 – 0.45 (m, 12H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 207.3, 207.0, 167.5, 146.7, 144.6, 141.5, 137.0, 134.4, 93.3, 93.3, 67.1, 66.4, 50.8, 50.7, 46.1, 45.5, 40.4, 39.7, 32.8, 32.3, 30.5, 29.8, 7.4, 7.3, 2.8, 2.2; **IR** (neat) ν_{max}: 2950, 2873, 1715, 1661, 1616, 1412, 1409,

1345, 1273, 1164, 1066, 1002, 868, 701, 670 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{18}H_{29}NO_3Si)H$ $[M+H]^+$: 336.19895, found: 336.19859.



The NOESY spectrum of the mixtures indicates the distinct peak to assign the major and minor isomers. The peak of singlet proton **Mee** at 2.93 ppm corresponds to the major isomer and the singlet proton **Mee** at 2.90 ppm corresponds to the minor isomer. Only the minor isomer shows the correlation with the triethylsilyl group which is assigned that the minor isomer product **39** is **a** and the major isomer is **c**.

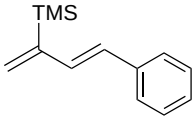
methyl (1*R*,6*R*)-7-methyl-10-oxo-4-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (40)



a **c**

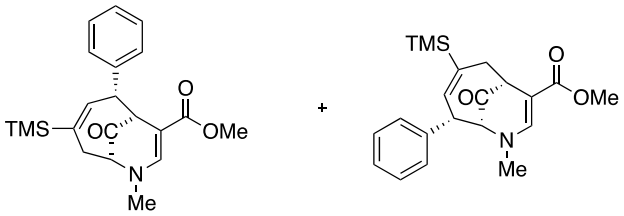
The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.32) to obtain a white solid (82 mg, 0.22 mmol) in 68% yield, and recrystallization by 30% EtOH:H2O, mp = 124 - 125˚C. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 7.27 (s, 1H), 7.26 (s, 1H), 6.10 (ddt, *J* = 15.6, 8.4, 3.1 Hz, 2H), 3.70 (dt, *J* = 6.5, 2.2 Hz, 1H), 3.65 (s, 3H), 3.64 - 3.63 (m, 1H), 3.62 (s, 3H), 3.60 (dd, *J* = 5.4, 2.8 Hz, 1H), 3.53 (dt, *J* = 5.3, 3.3 Hz, 1H), 3.02 – 2.94 (m, 3H), 2.94 (s, 3H), 2.93 - 2.91 (m, 1H), 2.89 (s, 3H), 2.11 (dq, *J* = 15.6, 3.2 Hz, 1H), 2.05 (m, 2H), 2.01 (q, *J* = 2.8 Hz, 1H), 1.13 (qd, *J* = 14.3, 7.6 Hz, 6H), 1.05 – 1.01 (m, 27H), 0.97 (d, *J* = 7.4 Hz, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.3, 207.1, 167.4, 146.6, 142.7, 142.1, 135.8, 135.5, 94.0, 93.6, 67.3, 66.4, 50.8, 50.8, 46.1, 45.4, 41.1, 39.6, 33.9, 32.5, 31.6, 30.1, 18.9, 18.8, 18.8, 18.5, 11.2, 10.9; **IR** (neat) ν_{max}: 2941, 2864, 1716, 1664, 1616, 1438, 1415, 1344, 1273, 1164, 1070, 1013, 882, 753, 646 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{21}H_{35}NO_3Si)Na$ $[M+Na]^+$: 400.2278, found: 400.2276.

(*E*)-trimethyl(4-phenylbuta-1,3-dien-2-yl)silane (30k)
The compound was prepared from the known literature.[27a]



The crude product was purified by flash column chromatography on silica gel (100 % hexanes, Rf = 0.53). The product was obtained as a colorless oil (113 mg, 0.56 mmol) in 40% yield.
^{1}H NMR (600 MHz, $CDCl_3$): δ 7.51 – 7.49 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 2H), 7.31 – 7.28 (m, 1H), 7.00 (d, *J* = 16.4 Hz, 1H), 6.70 (d, *J* = 16.4 Hz, 1H), 5.95 (d, *J* = 3.0 Hz, 1H), 5.59 (d, *J* = 3.0 Hz, 1H), 0.33 (s, 9H); **^{13}C NMR** (151 MHz, $CDCl_3$): 149.0, 137.8, 134.2, 130.7, 128.8, 128.7, 127.5, 126.4, -0.6; **IR** (neat) ν_{max}: 2935, 2922, 2851, 1448, 1247, 961, 833, 752, 692 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{13}H_{18}Si)OH$ $[M+OH]^-$: 219.1200, found: 219.1200.

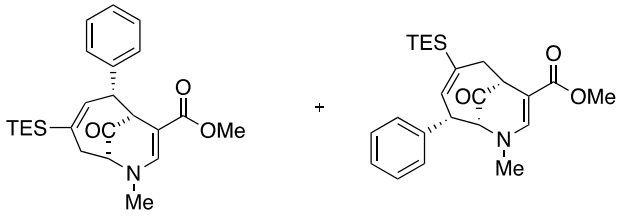
methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (41)



a **c**

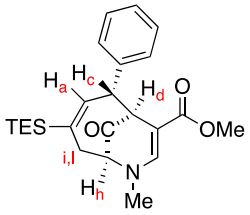
The crude product was concentrated in vacuo and purified by flash column chromatography on silica gel (20% EtOAc:Hexanes, Rf = 0.20) to obtain a white solid (30 mg, 0.08 mmol) in 74% yield, and recrystallization by 30% EtOH:H2O, mp = 154 - 155˚C.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (s, 1H), 7.34 – 7.14 (m, 11H), 6.28 (dd, *J* = 7.5, 2.7 Hz, 1H), 6.20 (dd, *J* = 7.3, 1.9 Hz, 1H), 4.28 (dd, *J* = 7.6, 3.7 Hz, 1H), 4.17 (dd, *J* = 7.3, 5.2 Hz, 1H), 3.80 (dd, *J* = 5.1, 2.8 Hz, 1H), 3.73 (s, 3H), 3.72 – 3.71 (m, 1H), 3.68 (s, 3H), 3.67 - 3.66 (m,1H), 3.49 (td, *J* = 4.7, 2.9 Hz, 1H), 3.00 (s, 3H), 2.96 (s, 3H), 2.93 (dd, *J* = 16.6, 5.5 Hz, 1H), 2.88 (dd, *J* = 15.7, 5.2 Hz, 1H), 2.41 (ddd, *J* = 15.6, 4.5, 2.2 Hz, 1H), 2.28 (dt, *J* = 16.6, 2.7 Hz, 1H), 0.14 (s, 9H), 0.06 (s, 9H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 203.8, 203.7, 167.7, 167.3, 146.7, 146.4, 145.6, 141.1, 139.5, 139.2, 137.4, 136.7, 128.9, 128.6, 128.1, 127.9, 127.4, 126.9, 94.9, 93.9, 73.6, 66.4, 53.2, 50.9, 50.9, 49.3, 46.9, 45.1, 40.8, 40.2, 32.0, 29.5, -1.7, -2.4; **IR** (neat) ν_{max}: 3001, 2946, 2895, 1711, 1684, 1598, 1439, 1329, 1240, 1153, 1074, 902, 832, 741, 696 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{21}H_{27}NO_3Si)H$ $[M+H]^+$: 370.1833, found: 370.1829.

methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-phenyl-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (42)



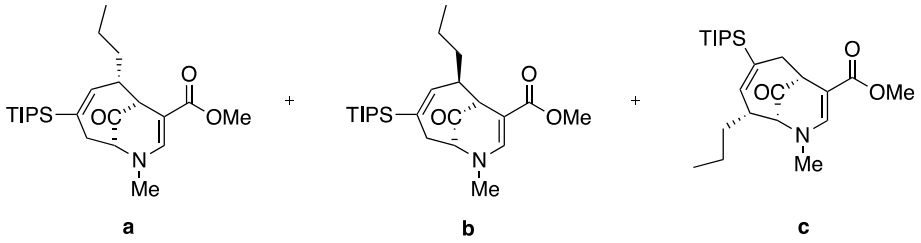
a **c**

The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (20% EtOAc:Hexanes, Rf = 0.24) to obtain a colorless oil (29 mg, 0.07 mmol) in 70% yield.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37 (s, 1H), 7.33 (s, 1H), 7.32 – 7.14 (m, 10H), 6.24 (dd, *J* = 7.5, 2.7 Hz, 1H), 6.17 (dd, *J* = 7.2, 2.0 Hz, 1H), 4.31 (dd, *J* = 7.6, 3.7 Hz, 1H), 4.19 (dd, *J* = 7.2, 5.2 Hz, 1H), 3.80 (dd, *J* = 5.1, 2.9 Hz, 1H), 3.72 (s, 3H), 3.72 – 3.70 (m, 1H), 3.68 (s, 3H), 3.65 (dt, *J* = 5.6, 2.8 Hz, 1H), 3.48 (td, *J* = 4.8, 2.9 Hz, 1H), 3.01 (s, 3H), 2.97 (s, 3H), 2.88 (td, *J* = 16.6, 5.5 Hz, 2H), 2.41 (ddd, *J* = 15.8, 4.6, 2.2 Hz, 1H), 2.26 (dt, *J* = 16.6, 2.7 Hz, 1H), 0.96 – 0.89 (m, 18H), 0.71 – 0.55 (m, 12H); **^{13}C NMR** (126 MHz, $CDCl_3$): δ 203.8, 203.8, 167.7, 167.3, 146.7, 145.6, 143.5, 142.7, 139.3, 138.4, 137.6, 136.6, 128.9, 128.6, 128.1, 128.0, 127.4, 126.9, 95.1, 94.1, 73.7, 66.5, 53.2, 50.9, 50.8, 49.6, 47.2, 45.2, 40.8, 40.3, 32.5, 29.9, 7.5, 7.4, 2.8, 2.3; **IR** (neat) ν_{max}: 2950, 2873, 1719, 1677, 1611, 1438, 1408, 1335, 1242, 1238, 1159, 1065, 1003, 916, 729, 699 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{24}H_{33}NO_3Si)H$ $[M+H]^+$: 412.2303, found: 412.2305.



The recovery of starting material from the oxidation reaction was leading to only the minor Isomer of product **42**. The minor isomer product **42** was also assigned the regiochemistry using the COSY spectrum. The COSY spectrum indicates that the triplet of doublet proton **h** on the bridgehead carbon at 3.48 ppm correlates with the proton **d** on the bridgehead carbon at 3.80 ppm, CH2 proton **I** at 2.86 ppm, and **l** at 2.42 ppm. The doublet of doublet proton **a** at 6.17 ppm correlates with the proton **c** at 4.18 ppm, proton **l** at 2.42 ppm, and proton **d** on the bridgehead carbon at 3.80 ppm.

Methyl (1*R*,2*R*,6*R*)-7-methyl-10-oxo-2-propyl-4-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (43)

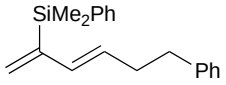


a **b** **c**

The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (20% EtOAc:Hexanes, Rf = 0.40) to obtain a white solid (224 mg, 0.53 mmol) in 85% yield, and recrystallization by 20% EtOH:H2O, mp = 89 - 90˚C.
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 (1H, s), 6.17 (1H, dd, *J* = 7.6, 2.6 Hz), 3.66 (3H, s), 3.58 (1H, dt, *J* = 5.7, 2.9 Hz), 3.43 (1H, dd, *J* = 4.2, 3.2 Hz), 2.94 (3H, s), 2.93 – 2.89 (1H, m), 2.77 (1H, dd, *J* = 16.3, 5.7 Hz), 2.18 (1H, dt, *J* = 16.3, 2.7 Hz), 1.49 – 1.40 (3H, m),

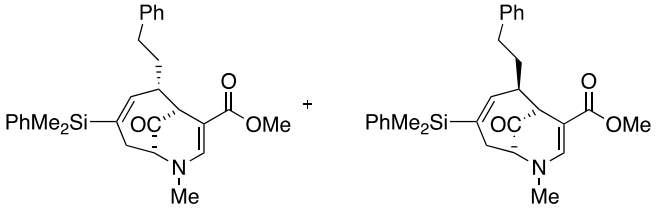
1.26 - 1.23 (1H, m), 1.20 – 1.12 (3H, m), 1.05 (18H, dd, *J* = 11.9, 7.4 Hz), 0.91 (3H, t, *J* = 7.0 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ205.7, 167.6, 147.1, 146.6, 132.8, 94.8, 67.0, 50.8, 49.2, 42.6, 41.0, 35.1, 30.1, 21.3, 18.9, 18.8, 14.1, 11.3; **IR** (neat) ν_{max}: 3011, 2943, 2864, 1717, 1680, 1610, 1443, 1438, 1408, 1334, 1239, 1160, 1065, 882, 752, 647, 645 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{24}H_{41}NO_3Si)Na$ $[M+Na]^+$: 442.2748, found: 442.2751.

(*E*)-dimethyl(phenyl)(6-phenylhexa-1,3-dien-2-yl)silane (30n)



The crude product was purified by flash column chromatography on silica gel (100 % hexanes, Rf = 0.34). The product was obtained as a red/orange oil (547 mg, 1.87 mmol) in 81% yield.
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 – 7.05 (m, 10H), 6.17 (d, *J* = 15.9 Hz, 1H), 5.76 (d, *J* = 3.1 Hz, 1H), 5.60 (dt, *J* = 15.8, 6.9 Hz, 1H), 5.39 (d, *J* = 3.2 Hz, 1H), 2.58 (t, *J* = 7.4 Hz, 2H), 2.33 – 2.29 (m, 2H), 0.39 (s, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$) δ 147.1, 141.9, 138.6, 135.1, 134.1, 132.9, 129.1, 128.6, 128.4, 127.9, 125.9, 35.9, 35.3, -2.0; **IR** (neat) ν_{max}: 3065, 3024, 2954, 2853, 1453, 1428, 1248, 1110, 967, 815, 702, 696 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{20}H_{24}Si)Na$ $[M+Na]^+$: 315.1539, found: 315.1539.

methyl (1*R*,2*R*,6*R*)-4-(dimethyl(phenyl)silyl)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (44)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.39) to obtain a pale yellow oil (131 mg, 0.29 mmol) in 89% yield.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 - 7.16 (m, 11H), 6.35 (dd, *J* = 8.0, 2.8 Hz, 1H), 3.66 (s, 3H), 3.55 (t, *J* = 3.6 Hz, 1H), 3.49 (dt, *J* = 5.4, 2.1 Hz, 1H), 2.99 (dt, *J* = 12.2, 7.7 Hz, 1H), 2.89 – 2.78 (m, 1H), 2.71 (dd, *J* = 16.5, 5.8 Hz, 1H), 2.65 (ddd, *J* = 13.8, 10.0, 5.9 Hz, 1H), 2.31 (s, 3H), 2.06 (dt, *J* = 16.5, 2.3 Hz, 1H), 1.73 (ddt, *J* = 13.4, 10.0, 7.0 Hz, 1H), 1.54 (dddd, *J* = 13.7, 9.8, 7.9, 6.0 Hz, 1H), 0.34 (d, *J* = 7.0 Hz, 6H); **^{13}C NMR** (126 MHz, $CDCl_3$): 206.9, 205.5, 168.3, 167.7, 147.0, 145.7, 142.1, 137.6, 135.8, 134.2, 129.4, 128.5, 128.4, 128.0, 125.9, 93.3, 90.8, 66.5, 50.8, 48.9, 41.9, 39.5, 34.4, 34.3, 28.6, -3.1, -3.8; **IR** (neat) ν_{max}: 3008, 2946, 2916, 1714, 1631, 1608, 1411, 1409, 1334, 1239, 1157, 1073, 1066, 809, 747, 698 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{28}H_{33}NO_3Si)Na$ $[M+Na]^+$: 482.2122, found: 482.2116.

Oxidative Functionalization of the Bridgehead Carbon of (4+3) Cycloadducts Obtained from Oxidopyridinium Ions

General Information

^{1}H and ^{13}C NMR spectra were recorded on either an AVIII-500 (^{1}H NMR: 500 MHz; ^{13}C NMR: 100 MHz) or an AVIII-600 (^{1}H NMR: 600 MHz; ^{13}C NMR: 125 MHz) spectrometer. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) as an internal standard [$CDCl_3$: ^{1}H NMR (0.00 ppm), ^{13}C NMR (77.16 ppm)]. When $CDCl_3$ does not contain tetramethylsilane, residual traces of the hydrogenated solvent were used as an internal reference (7.26 ppm). Signal splitting patterns are indicated as such: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, hept = heptet, m = multiplet, dd = doublet, ddd = doublet of doublet of doublet, dddd = doublet of doublet of doublet of doublet, td = triplet of doublet, etc. Melting points of crystalline compound were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Thermo Nicolet Summit Pro FT-IR spectrometer and characteristic peaks were highlighted. High-Resolution Mass Spectrometry (HR-MS) was recorded on a Bruker 12 Tesla APEX-Qe FTICR-MS with an Apollo II ion source (performed by College of Science Major Instrumentation Center, Old Dominion University).

All reactions were carried out in oven-dried glassware, with a magnetic stir bar, and under an atmosphere of argon (balloon) unless otherwise noted. *N*-iodosuccinimide was purchased from Ambeed and was used as received. ACS reagent grade hexanes and ethyl acetate were purchased from Fisher and were used as received. ACS reagent grade dichloromethane was purchased from Fisher and dried over 4 Å molecular sieves. ACS grade acetonitrile was purchased from Fisher and was distilled under an atmosphere of nitrogen over calcium hydride. ACS reagent grade triethylamine was purchased from Sigma Aldrich and was distilled under and atmosphere of nitrogen over calcium hydride. ACS grade hexafluoroisopropanol was purchased from Halocarbon and dried over 4 Å molecular sieves. Analytical thin layer chromatography (TLC) was performed on TLC Silica gel 60 F_{254} plates and visualized with a handheld UV lamp (254 nm). The plates were stained with iodine or vanillin for further evaluation. Flash chromatography was performed using 40 – 63 micron silica gel purchased from ZeoChem.

Single crystal X-ray diffraction data was collected on a Bruker X8 Prospector diffractometer equipped with an Apex II CCD area detector (Bruker AXS, Madison, WI, USA) using Cu-Kα radiation from a microfocus source (λ = 1.54178 Å; beam power: 45 kV, 0.65 mA). A full sphere of unique data was collected to greatest completeness possible with a 3-circle goniometer using strategies of scans about the omega and phi axes. The Bruker Apex3 software suite was used for unit cell determination, data collection, data reduction, absorption correction and scaling, and space group determination.[6]

[6] Apex3, AXScale, and SAINT, version 2017.3-0, Bruker AXS, Inc., Madison, WI, 2017.

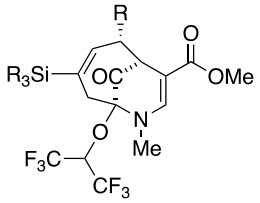
The crystal structure was solved by direct methods as implemented in SHELXS[7] and refined by full-matrix least squares refinement against $|F^2|$ using SHELXL v.2017.[8] Olex2 was used as an interface for model building and refinement programs.[9] Non-hydrogen atoms were located from the difference map and refined anisotropically. Hydrogen atoms were placed in calculated positions, and their thermal parameters and coordinates were constrained to ride on the carrier atoms. Hydrogen atoms on methyl groups were refined using a riding-rotating model.

2. Experimental Procedures

2.1 General Procedure for Preparation of Starting Materials

The starting materials were synthesized according to the known literature procedure.[10] To an oven-dried 15 mL seal tube (CG-1880-21 pressure vessel) equipped with a magnetic stir bar was added *N*-methyloxidopyridinium ion (0.63 mmol, 1.0 equiv) and diene (1.9 mmol, 3.0 equiv) in acetonitrile (6.3 mL, 0.1 M) at room temperature. The mixture was then degassed with an argon balloon for 5 min followed by addition of triethylamine (1.9 mmol, 3.0 equiv), sealed with screw cap, and heated for 24 h at 85 ^{o}C in an oil bath. Upon heating for 1 h, the reaction solution changed in color from pale-yellow to brown. After 24 h, the reaction mixture was cooled to room temperature, quenched with 16 drops of 10% HCl, and extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by flash chromatography on silica gel (20 - 30% EtOAc:Hexanes) to obtain the respective cycloadduct starting material as an isomeric mixture.

2.2 General Procedure for Synthesis of Products



To an oven-dried 10 mL RBF equipped with a magnetic stir bar was added an isomeric mixture of cycloadduct (100 mg, 0.25 mmol, 1.0 equiv) in hexafluoroisopropanol (4.0 mL,

[7] G. M. Sheldrick, SHELXS, v.2013-1, 2013.

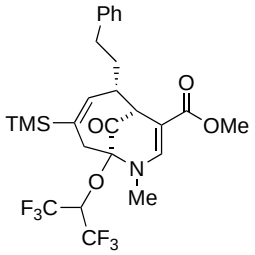
[8] G. M. Sheldrick, *Acta Cryst. Sect. C. Struct. Chem.* 2015, **71**, 3.

[9] O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard, H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339.

[10] W. Sungnoi, A. B. Keto, R. B. Roseli, J. Liu, H. Wang, C. Fu, E. L. Regalado, E. H. Krenske, M. Harmata, *Org. Lett*., 2021, **23**, 8302.

0.06 M) at room temperature. The solution was cooled to 0 °C, and upon addition of *N*-Iodosuccinimide (85.5 mg, 0.38 mmol, 1.5 equiv), the mixture changed in color from pale-yellow to orange/brown. The mixture was allowed to warm to room temperature and stir for the indicated time (1 - 23 h). Reactions were monitored by TLC (20 - 30% EtOAc:Hexanes) until all starting material was consumed. Upon completion, the reaction was quenched with water to give a dark red solution, and the resulting mixture was extracted with dichloromethane (3 x 5 mL). The combined organic layers were washed with $NaHCO_3$, dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by flash chromatography on silica gel (20 - 30% EtOAc:Hexanes) to obtain the product.

Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2 phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (45a)[5]



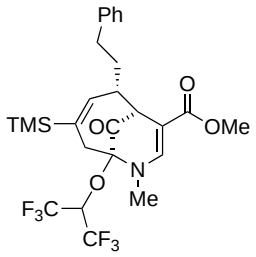
1 mmol scale

To an oven-dried 25 mL RBF equipped with a magnetic stir bar was added cycloadduct (400 mg, 1.0 mmol, 1.0 equiv, isomeric ratio of 81:13:6) in hexafluoroisopropanol (11.1 mL, 0.09 M) at room temperature. The solution was cooled to 0 °C, and upon addition of *N*-Iodosuccinimide (337.5 mg, 1.5 mmol, 1.5 equiv), the mixture changed in color from pale-yellow to orange/brown. The mixture was allowed to warm to room temperature and stirred for 21 h. The reaction was monitored by TLC (30% EtOAc:Hexanes) until all starting material was consumed. Upon completion, the reaction was quenched with water to give a dark red solution, and the resulting mixture was extracted with dichloromethane (3 x 15 mL). The combined organic layers were washed with $NaHCO_3$, dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by flash chromatography on silica gel (30% EtOAc:Hexanes, R_f = 0.72) to obtain the product as a pale-yellow solid (300 mg, 0. 53 mmol, 53%). Recrystallization (70% EtOH:H_2O) gave a white solid, mp = 150 - 151˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.27 (2H, m), 7.21 (1H, s), 7.20 – 7.17 (3H, m), 6.19 (1H, dd, *J* = 7.5, 3.0 Hz), 4.86 (1H, hept, *J* = 6.0 Hz), 3.68 (1H, s), 3.67 (3H, s), 2.90 – 2.86 (2H, m), 2.82 – 2.76 (4H, m), 2.63 (1H, ddd, *J* = 13.0, 10.5, 6.0 Hz), 2.29 (1H, dd, *J* = 17.0, 3.5 Hz), 1.70 (1H, dddd, *J* = 13.5, 10.0, 7.5, 6.0 Hz), 1.50 (1H, dddd, *J* = 13.5, 10.0, 8.0, 6.0 Hz), 0.11 (9H, s); **^{13}C NMR** (151 MHz, $CDCl_3$): 199.8, 166.8, 146.4, 143.8, 141.7, 134.0, 128.5, 128.5, 126.1, 121.5 (q, *J* = 286.9 Hz), 121.2 (q, *J* = 288.4 Hz), 97.4, 93.8, 71.5 (hept, *J* = 33.2 Hz), 51.2, 49.4, 43.3, 36.6, 34.8, 34.6, 34.1, -1.2; **IR** ($CHCl_3$) ν_{max}: 3030, 2954, 2918, 1739, 1695, 1628, 1365, 1247, 1245, 1187, 1103, 1058, 998, 837,

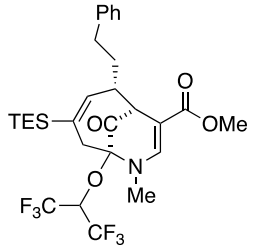
737, 691 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{26}H_{31}F_6NO_4Si)Na$ $[M+Na]^+$: 586.1819, found: 586.1813.

methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2 phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (45a)



The crude product was concentrated in vacuo, and purified by flash column chromatography on silica gel (30% EtOAc:Hexanes, Rf = 0.61) to obtain a white solid (35 mg, 0.06 mmol) in 48% yield, and recrystallization by 20% EtOH:H_2O, mp = 150 - 151˚C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.30 – 7.27 (2H, m), 7.21 (1H, s), 7.20 – 7.17 (3H, m), 6.19 (1H, dd, *J* = 7.5, 3.0 Hz), 4.86 (1H, hept, *J* = 6.0 Hz), 3.68 (1H, s), 3.67 (3H, s), 2.90 – 2.86 (2H, m), 2.82 – 2.76 (4H, m), 2.63 (1H, ddd, *J* = 13.0, 10.5, 6.0 Hz), 2.29 (1H, dd, *J* = 17.0, 3.5 Hz), 1.70 (1H, dddd, *J* = 13.5, 10.0, 7.5, 6.0 Hz), 1.50 (1H, dddd, *J* = 13.5, 10.0, 8.0, 6.0 Hz), 0.11 (9H, s); **^{13}C NMR** (151 MHz, $CDCl_3$): 199.8, 166.8, 146.4, 143.8, 141.7, 134.0, 128.5, 128.5, 126.1, 121.5 (q, *J* = 286.9 Hz), 121.2 (q, *J* = 288.4 Hz), 97.4, 93.8, 71.5 (hept, *J* = 33.2 Hz), 51.2, 49.4, 43.3, 36.6, 34.8, 34.6, 34.1, -1.2; **IR** ($CHCl_3$) ν_{max}: 3030, 2954, 2918, 1739, 1695, 1628, 1365, 1247, 1245, 1187, 1103, 1058, 998, 837, 737, 691 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{26}H_{31}F_6NO_4Si)Na$ $[M+Na]^+$: 586.1819, found: 586.1813.

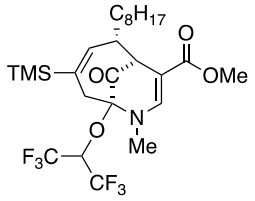
Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (46a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 81:15:4) yielded **46a** as a white solid (66 mg, 0.11 mmol, 54%) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.68). Recrystallization (20% EtOH:H_2O) gave white solid, mp = 93 - 94˚C.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30 – 7.27 (2H, m), 7.22 (1H, s), 7.20 – 7.17 (3H, m), 6.17 (1H, dd, *J* = 7.6, 3.0 Hz), 4.89 (1H, hept, *J* = 6.0 Hz), 3.68 (1H, d, *J* = 5.0 Hz), 3.67 (3H, s), 2.91 (1H, qd, *J* = 7.5, 3.9 Hz), 2.85 (1H, d, *J* = 16.5 Hz), 2.80 (3H, s), 2.77 (1H, dd, *J* = 8.0, 3.5 Hz), 2.66 (1H, ddd, *J* = 14.0, 10.5, 6.0 Hz), 2.26 (1H, dd, *J* = 16.5, 3.0 Hz), 1.72 (1H, dddd, *J* = 13.1, 10.3, 7.0, 5.9 Hz), 1.51 (1H, dddd, *J* = 13.6, 10.2, 7.8, 5.8 Hz), 0.92 (9H, t, *J* = 7.9 Hz), 0.63 (6H, tdd, *J* = 22.5, 15.1, 7.5 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.9, 166.8, 146.3, 145.0, 141.7, 131.0, 128.6, 128.6, 126.1, 121.6 (q, *J* = 288.4 Hz), 121.2 (q, *J* = 285.4 Hz), 97.3, 93.6, 71.5 (hept, *J* = 32.2 Hz), 51.3, 49.5, 43.6, 37.0, 34.9, 34.8, 34.2, 7.6, 3.2; **IR** (MeOH) ν_{max} = 3194, 2969, 2842, 1734, 1693, 1639, 1344, 1287, 1186, 1098, 938, 877, 737, 696 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{29}H_{37}F_6NO_4Si)Na$ $[M+Na]^+$: 628.2288, found 628.2280.

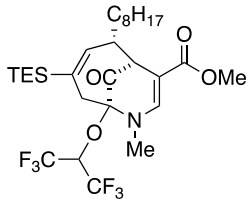
methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-2-octyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (47a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 82:14:4) yielded **47a** as a white solid (66 mg, 0.12 mmol, 46%) after purification by flash chromatography (20% EtOAc:Hexanes, R_f = 0.65). Recrystallization (80% EtOH:H_2O) gave long, white needles, mp = 78 - 79˚C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (1H, s), 6.18 (1H, dd, *J* = 7.6, 3.0 Hz), 4.84 (1H, hept, *J* = 6.0 Hz), 3.69 (3H, s), 3.58 (1H, d, *J* = 3.7 Hz), 2.85 (1H, d, *J* = 16.5 Hz), 2.81 (1H, td, *J* = 7.0, 3.5 Hz), 2.78 (3H, s), 2.27 (1H, dd, *J* = 16.5, 3.0 Hz), 1.44 - 1.16 (14H, m), 0.88 (3H, t, *J* = 6.8 Hz), 0.10 (9H, s); **^{13}C NMR** (151 MHz, $CDCl_3$): 199.9, 166.9, 146.3, 144.4, 133.3, 121.6 (q, *J* = 288.4 Hz), 121.2 (q, *J* = 280.9 Hz), 97.6, 93.9, 71.6 (hept, *J* = 34.7 Hz), 51.3, 49.6, 43.9, 36.6, 34.8, 32.8, 32.0, 29.6, 29.4, 27.8, 22.8, 14.2, -1.1; **IR** ($CHCl_3$) ν_{max}: 2931, 2922, 2853, 1734, 1676, 1641, 1361, 1279, 1234, 1188, 1102, 1070, 829, 763, 687 cm^{-1}; **HRMS (m/z):** calcd for $(C_{26}H_{39}F_6NO_4Si)H$ $[M+H]^+$: 572.2625, found: 572.2623.

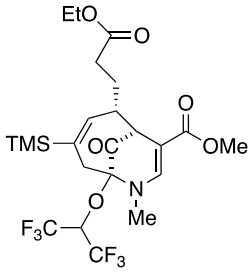
methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-2-octyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (48a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 89:9:2) yielded **48a** as a white solid (72 mg, 0.12 mmol, 52%) after purification by flash chromatography (20% EtOAc:Hexanes, R_f = 0.60). Recrystallization (70% EtOH:H_2O) gave long, white needles, mp = 66 - 67˚C.

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.21 (1H, s), 6.15 (1H, dd, *J* = 7.6, 3.0 Hz), 4.88 (1H, hept, *J* = 5.9 Hz), 3.69 (3H, s), 3.59 (1H, d, *J* = 3.8 Hz), 2.87 – 2.81 (2H, m), 2.79 (3H, s), 2.24 (1H, dd, *J* = 16.5, 3.0 Hz), 1.48 – 1.17 (14H, m), 0.91 (9H, t, *J* = 8.0 Hz), 0.88 (3H, t, *J* = 6.6 Hz), 0.68 – 0.56 (6H, m); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.9, 166.8, 146.1, 145.6, 130.2, 121.5 (q, *J* = 285.4 Hz), 121.2 (q, *J* = 285.4 Hz), 97.6, 93.7, 71.5 (hept, *J* = 33.2 Hz), 51.2, 49.6, 44.1, 36.9, 34.7, 33.1, 32.0, 29.6, 29.4, 27.9, 22.8, 14.2, 7.5; **IR (neat) ν_{max}** = 2928, 2919, 2853, 1731, 1677, 1642, 1358, 1278, 1234, 1189, 1101, 1069, 1004, 872, 688 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for (C_{29} $H_{45}F_6NO_4Si$)H $[M+H]^+$: 614.3095, found 614.3096.

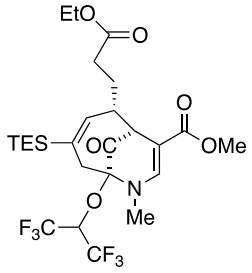
methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (49a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 80:16:4) yielded **49a** as a pale-yellow oil (56 mg, 0.10 mmol, 44%) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.63).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (1H, s), 6.16 (1H, dd, *J* = 7.6, 3.1 Hz), 4.84 (1H, hept, *J* = 6.0 Hz), 4.14 (2H, q, *J* = 7.5 Hz), 3.69 (3H, s), 3.56 (1H, d, *J* = 3.6 Hz), 2.90 – 2.83 (2H, m), 2.79 (3H, s), 2.45 (1H, ddt, *J* = 15.5, 9.0, 6.5 Hz), 2.35 (1H, dddd, *J* = 21.3, 15.4, 9.1, 6.1 Hz), 2.29 (1H, dd, *J* = 16.5, 3.0 Hz), 1.70 – 1.55 (2H, m), 1.26 (3H, t, *J* = 7.1 Hz), 0.11 (9H, s); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.7, 173.0, 166.7, 146.4, 142.8, 134.8, 121.5 (q, *J* = 286.9 Hz), 121.2 (q, *J* = 286.9 Hz), 97.2, 93.7, 71.5 (hept, *J* = 33.2 Hz), 60.6, 51.3, 49.1, 43.0, 36.7, 34.8, 32.4, 27.6, 14.3, -1.2; **IR (neat) ν_{max}** = 2951, 2865, 1731, 1646, 1637, 1196, 1188, 1067, 1059, 1010, 835, 750, 687 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for ($C_{23}H_{31}F_6NO_6Si$)H $M+H]^+$: 560.1898, found. 560.1894.

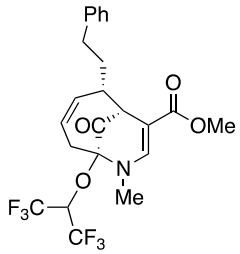
methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (50a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 83:16:1) yielded **50a** as a white solid (62 mg, 0.10 mmol, 38%) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.66). Recrystallization (70% EtOH:H_2O) gave short, white needles, mp = 87 - 88˚C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (1H, s), 6.13 (1H, dd, *J* = 7.5, 3.0 Hz), 4.87 (1H, hept, *J* = 5.9 Hz), 4.14 (2H, q, *J* = 7.2 Hz), 3.68 (3H, s), 3.57 (1H, d, *J* = 3.7 Hz), 2.89 (1H, dd, *J* = 7.8, 3.6 Hz), 2.86 (1H, d, *J* = 16.2 Hz), 2.81 (3H, s), 2.47 (1H, ddd, *J* = 16.2, 9.6, 6.6 Hz), 2.37 (1H, ddd, *J* = 15.0, 9.0, 6.0 Hz), 2.25 (1H, dd, *J* = 16.6, 3.0 Hz), 1.70 – 1.56 (2H, m), 1.26 (3H, t, *J* = 7.2 Hz), 0.92 (9H, t, *J* = 7.9 Hz), 0.69 – 0.59 (6H, m); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 199.7, 173.0, 166.7, 146.3, 144.1, 131.7, 121.5 (q, *J* = 286.9 Hz), 121.2 (q, *J* = 286.9 Hz), 97.1, 93.6, 71.5 (hept, *J* = 33.2 Hz), 60.6, 51.3, 49.1, 43.2, 37.0, 34.8, 32.4, 27.9, 14.3, 7.5, 3.1; **IR (neat) ν_{max}** = 2965, 2865, 1732, 1681, 1640, 1345, 1236, 1189, 1074, 1057, 1008, 877, 688 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $(C_{26}H_{37}F_6NO_6Si)H$ $[M+H]^+$: 602.2367, found: 602.2366.

methyl (1*R*,2*S*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (51a)

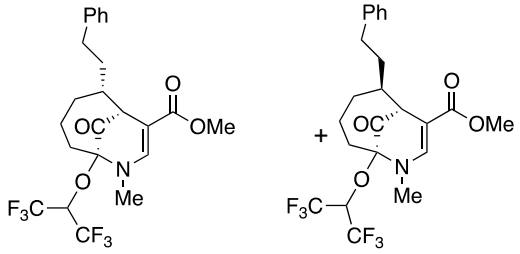


According to the general procedure, the respective cycloadduct (isomeric ratio of 46:54) yielded **51a** as a white cotton (16 mg, 0.03 mmol, 16%) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.63). Recrystallization (70 % EtOH:H_2O) gave a white cotton, mp = 129 - 130˚C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28 (2H, t, *J* = 7.5 Hz), 7.24 (1H, s), 7.21 – 7.16 (3H, m), 5.92 (1H, ddd, *J* = 11.7, 8.2, 2.9 Hz), 5.70 (1H, ddd, *J* = 12.4, 9.3, 3.4 Hz), 4.80 (1H, hept, *J* = 6.0 Hz), 3.70 (1H, d, *J* = 4.0 Hz), 3.67 (3H, s), 2.84 (1H, td, *J* = 7.7, 4.0 Hz), 2.81 (3H,

s), 2.80 – 2.75 (2H, m), 2.66 (1H, ddd, *J* = 13.8, 10.0, 5.9 Hz), 2.31 (1H, dt, *J* = 16.3, 3.2 Hz), 1.76 (1H, dddd, *J* = 13.4, 10.1, 7.0, 5.9 Hz), 1.57 (1H, dddd, *J* = 13.9, 10.1, 8.1, 5.9 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.7, 166.8, 147.0, 141.7, 136.8, 128.5, 126.1, 121.6 (q, *J* = 289.9 Hz), 121.2 (q, *J* = 285.4 Hz), 98.1, 93.5, 71.5 (hept, *J* = 34.7 Hz), 51.3, 50.2, 42.0, 34.9, 34.6, 34.3, 34.1; **IR ($CHCl_3$) ν_{max}** = 2953, 2864, 1702, 1685, 1635, 1439, 1334, 1232, 1187, 1096, 1058, 1009, 876, 753, 688 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{23}H_{23}F_6NO_4)Na$ $[M+Na]^+$: 514.1423, found: 514.1424.

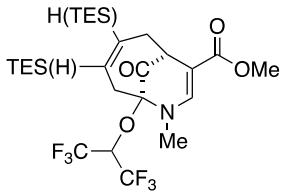
methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]dec-8-ene-9-carboxylate (53a-b)



According to the general procedure, the respective cycloadduct (isomeric ratio of 45:55) yielded **53a-b** as a white solid (10 mg, 0.02 mmol, 33%, isomeric ratio of 63:37) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.84).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (1H, s) minor isomer, 7.33 (1H, s) major isomer, 7.28 – 7.24 (4H, m), 7.20 – 7.14 (6H, m), 4.60 (1H, hept, *J* = 5.9 Hz) major isomer, 4.46 (1H, hept, *J* = 5.9 Hz) minor isomer, 3.81 (1H, s), 3.76 (1H, s), 3.70 (3H, s) major isomer, 3.69 (3H, s) minor isomer, 3.38 (1H, d, *J* = 2.5 Hz), 2.96 (3H, s) major isomer, 2.93 (3H, s) minor isomer, 2.86 – 2.59 (4H, m), 2.29 (1H, dt, *J* = 14.8, 3.8 Hz), 2.18 – 2.11 (1H, m), 2.05 – 1.91 (3H, m), 1.89 – 1.73 (4H, m), 1.68 – 1.58 (3H, m), 1.53 – 1.47 (1H, m), 1.38 (1H, dddd, *J* = 13.5, 9.8, 7.1, 6.0 Hz), 1.29 – 1.22 (2H, m), 1.05 (1H, dt, *J* = 14.3, 11.2 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.6, 200.9, 195.0, 167.5, 167.0, 164.8, 146.7, 145.4, 142.7, 142.2, 142.1, 139.9, 134.1, 130.9, 128.5, 128.5, 128.5, 128.4, 126.0, 125.9, 125.8, 121.6 (q, *J* = 284.8 Hz), 121.2 (q, *J* = 284.9 Hz), 112.6, 101.3, 96.1, 94.5, 94.4, 71.1 (hept, *J* = 32.6 Hz), 51.5, 51.3, 51.1, 50.3, 48.6, 44.6, 44.6, 42.4, 38.7, 38.3, 38.3, 36.2, 35.2, 35.0, 34.9, 34.8, 34.6, 33.9, 33.0, 31.6, 30.9, 29.6, 26.6, 21.2, 20.8, 19.4; **IR ($CHCl_3$) ν_{max}** = 3023, 2858, 1708, 1637, 1630, 1537, 1439, 1252, 1196, 1188, 1097, 871, 749, 687 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{23}H_{25}F_6NO_4Si)Na$ $[M+Na]^+$: 516.1580, found: 516.1575.

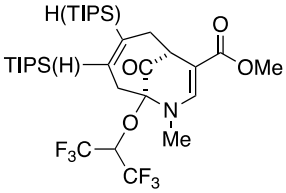
methyl (1*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-3-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (54a/54c)



According to the general procedure, the respective cycloadduct (isomeric ratio of 41:59) yielded **54a/c** as a white solid (53 mg, 0.11 mmol, 35%, isomeric ratio of 41:59) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.70). Recrystallization (70% EtOH:H_2O) gave short, white needles.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.20 (1H, s) minor isomer, 7.14 (1H, s) major isomer, 6.14 (1H, dt, *J* = 8.6, 3.4 Hz) major isomer, 6.09 (1H, dt, *J* = 8.3, 2.8 Hz) minor isomer, 4.91 (2H, hept, *J* = 6.5 Hz) major and minor isomers, 3.76 (1H, dd, *J* = 5.6, 2.7 Hz), 3.71 (1H, t, *J* = 4.2 Hz), 3.69 (3H, s) minor isomer, 3.68 (3H, s) major isomer, 3.01 – 2.88 (4H, m) major and minor isomers, 2.80 (3H, s) minor isomer, 2.79 (3H, s) major isomer, 2.26 (1H, ddd, *J* = 15.7, 3.7, 1.8 Hz), 2.23 – 2.16 (2H, m) major and minor isomers, 2.11 (1H, dq, *J* = 15.4, 2.7 Hz), 0.91 (9H, t, *J* = 7.9 Hz) minor isomer, 0.87 (9H, t, *J* = 7.9 Hz) major isomer, 0.69 – 0.46 (12H, m) major and minor isomers; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.6, 201.1, 166.8, 166.6, 146.9, 146.2, 144.9, 140.4, 133.5, 131.5, 121.6 (q, *J* = 283.9 Hz), 121.2 (q, *J* = 285.4 Hz), 97.5, 96.6, 94.7, 94.5, 71.8 (hept, *J* = 33.2 Hz), 51.3, 51.3, 47.2, 46.0, 38.4, 37.2, 35.0, 34.9, 33.4, 33.2, 7.5, 7.4, 3.2, 2.2; **IR (neat)** ν_{max} = 2966, 2875, 1733, 1674, 1642, 1364, 1247, 1242, 1187, 1102, 1062, 1016, 872, 690 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{21}H_{29}F_6NO_4Si)H$ $[M+H]^+$: 502.1843, found: 502.1847.

methyl (1*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-3-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (55a/55c)

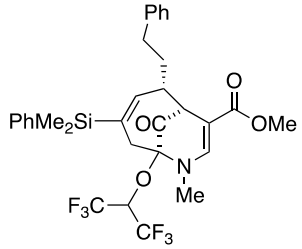


According to the general procedure, the respective cycloadduct (isomeric ratio of 46:54) yielded **55a/c** as a white solid (80 mg, 0.15 mmol, 59%, isomeric ratio of 17:83) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.55). Recrystallization (70% EtOH:H_2O) gave short, white needles.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (1H, s) major isomer, 7.18 (1H, s) minor isomer, 6.15 (1H, dt, = 8.8, 3.3 Hz) minor isomer, 6.09 (1H, dt, *J* = 8.1, 2.8 Hz) major isomer, 4.99 (1H, hept, *J* = 6.0 Hz) major isomer, 4.88 (1H, hept, = 6.1 Hz) minor isomer, 3.76 (1H, dd, = 5.2, 3.1 Hz), 3.71 (1H, t, *J* = 4.3 Hz), 3.69 (3H, s) major isomer, 3.66 (3H, s) minor isomer, 3.03 – 2.97 (3H, m) major and minor isomers, 2.92 (1H, ddd, = 16.1, 8.3, 4.6 Hz), 2.87 (3H, s) major isomer, 2.81 (3H, s) minor isomer, 2.32 – 2.28 (1H, m), 2.28 – 2.21 (2H, m),

2.16 (1H, dq, *J* = 15.5, 3.0 Hz) 1.20 – 1.11 (6H, m) major and minor isomers, 1.06 (18H, dd, *J* = 9.5, 7.2 Hz) major isomer, 1.00 (18H, dd, = 23.6, 7.4 Hz) minor isomer; **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.7, 201.1, 166.8, 166.6, 146.9, 146.1, 142.8, 140.7, 132.6, 132.5, 121.5 (q, *J* = 288.4 Hz), 121.2 (q, *J* = 283.9 Hz), 97.6, 96.5, 94.5, 94.4, 71.6 (hept, *J* = 33.2 Hz), 51.3, 46.9, 45.7, 39.4, 37.3, 35.4, 34.9, 34.3, 33.7, 19.1, 19.0, 18.8, 18.5, 11.6, 10.8; **IR (neat) ν_{max}** = 2955, 2866, 1734, 1675, 1641, 1362, 1340, 1284, 1242, 1188, 1101, 877, 659, 656 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{24}H_{35}F_6NO_4Si)Na$ $[M+Na]^+$: 566.2132, found: 566.2128.

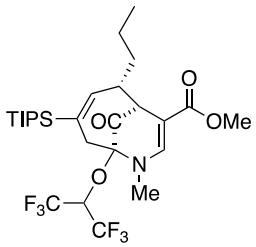
methyl (1*R*,2*R*,6*R*)-4-(dimethyl(phenyl)silyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (56a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 87:13) yielded **56a** as a pale-yellow oil (63 mg, 0.10 mmol, 31%) after purification by flash chromatography (30% EtOAc:Hexanes, R_f = 0.63).

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 – 7.48 (2H, m), 7.40 – 7.34 (3H, m), 7.28 (2H, t, *J* = 7.4 Hz), 7.21 – 7.13 (3H, m), 7.13 (1H, s), 6.29 (1H, dd, *J* = 7.6, 3.0 Hz), 4.83 (1H, hept, *J* = 5.9 Hz), 3.67 (3H, s), 3.66 (1H, d, *J* = 3.7 Hz), 2.91 (1H, qd, *J* = 7.5, 3.8 Hz), 2.84 (1H, d, *J* = 16.6 Hz), 2.78 (1H, ddd, *J* = 14.1, 10.3, 6.4 Hz), 2.63 (1H, ddd, *J* = 13.9, 10.1, 5.8 Hz), 2.36 (3H, s), 2.25 (1H, dd, *J* = 16.5, 3.0 Hz), 1.72 (1H, dddd, *J* = 13.5, 10.1, 7.0, 6.2 Hz), 1.52 (1H, dddd, *J* = 13.6, 10.0, 7.7, 5.8 Hz), 0.40 (6H, d, *J* = 9.9 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.8, 166.9, 146.5, 145.4, 141.6, 137.2, 134.2, 132.6, 129.8, 128.6, 128.6, 128.3, 126.2, 121.5 (q, *J* = 286.9 Hz), 121.2 (q, *J* = 288.4 Hz), 96.9, 93.6, 71.5 (hept, *J* = 33.2 Hz), 51.3, 49.3, 43.4, 36.7, 34.7, 34.3, 34.1, -2.8, -3.0; **IR (neat) ν_{max}** = 3023, 2951, 1704, 1643, 1631, 1428, 1296, 1241, 1199, 1188, 1098, 1061, 765, 735, 687 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{31}H_{33}F_6NO_4Si)Na$ $[M+Na]^+$: 648.1975, found: 648.1982.

methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-propyl-4-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (57a)



According to the general procedure, the respective cycloadduct (isomeric ratio of 92:6:2) yielded **57a** as a white solid (90 mg, 0.15 mmol, 64%) after purification by flash chromatography (20% EtOAc:Hexanes, R_f = 0.64). Recrystallization (70% EtOH:H_2O) gave short, white needles, mp = 126 - 127˚C.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.25 (1H, s), 6.14 (1H, dd, *J* = 7.4, 2.7 Hz), 4.94 (1H, hept, *J* = 6.0 Hz), 3.69 (3H, s), 3.39 (1H, d, *J* = 4.1 Hz), 2.90 (1H, d, *J* = 16.5 Hz), 2.87 (3H, s), 2.83 (1H, qd, *J* = 7.4, 4.1 Hz), 2.29 (1H, dd, *J* = 16.5, 2.8 Hz), 1.52 (1H, dddd, *J* = 13.0, 10.5, 7.5, 5.5 Hz), 1.47 – 1.33 (2H, m), 1.29 – 1.22 (1H, m), 1.16 (3H, hept, *J* = 7.8 Hz), 1.07 (18H, dd, *J* = 10.1, 7.3 Hz), 0.93 (3H, t, *J* = 7.2 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 199.9, 166.8, 146.0, 129.9, 121.5 (q, *J* = 285.7 Hz), 121.2 (q, *J* = 283.9 Hz), 97.5, 93.6, 71.5 (hept, *J* = 33.4 Hz), 51.2, 49.0, 44.2, 38.1, 35.2, 35.0, 20.9, 19.0, 18.9, 13.8, 11.6; **IR ($CHCl_3$) ν_{max}** = 2948, 2868, 1701, 1648, 1641, 1440, 1340, 1264, 1198, 1192, 1101, 1062, 1001, 880, 734 cm^{-1}; **HRMS (m/z)**: (ESI-FTICR) calcd for $(C_{27}H_{41}F_6NO_4Si)Na$ $[M+Na]^+$: 608.2601, found: 608.2590.

Tropane Skeleta from the Intramolecular Photocycloaddition of (4+3) Cycloadducts of Oxidopyridinium Ions and Dienes

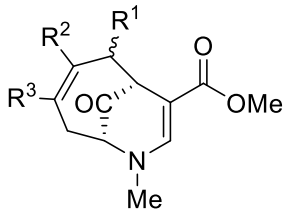
General Information

A Fisher 10 x 75 mm disposable borosilicate tube was used to carry the photocycloaddition due to its convenience and the UV cutoff at 350 nm.[11] Nuclear Magnetic Resonance (NMR) spectroscopies were measured by Bruker DRX-500 (500 MHz) and Bruker DRX-600 (600 MHz) for ^{1}H (proton) and ^{13}C (carbon). Norell® 508-up NMR tubes were used to measure NMR spectroscopy. ^{1}H NMR were reported in δ units, parts per million (ppm), relative to tetramethylsilane as an internal standard (0.00 ppm). ^{13}C NMR were reported in ppm relative to (77.16 ppm) chloroform-d. Infrared spectra were measured with a ThermoScientific Nicolet Summit PRO FTIR spectrometer with an EverestTM Diamond

[11] McMurray, T. A.; Byren, J. A.; Dunlop, P. S. M.; McAdams, E. T., Photocatalytic and Electrochemically Assisted Photocatalytic Oxidation of Formic Acid on TiO_2 Films under UVA and UVB Irradiation. *J. Appl. Electrochem.* **2005**, *35*, 723-731.

ATR Accessory spectrometer either as a neat compound or using chloroform-d as a solvent. Melting points were measured with a Fisher-Johns melting point apparatus. Samples were further characterized with high-resolution mass spectrometry with an Apollo II ion source on a Bruker 10 Tesla APEX -Qe instrument, or with an Apollo II ion source on a Bruker 12 Tesla APEX -Qe FTICR-MS, or with a Bruker's TIMS-TOF pro with an ESI positive ion source, or with FTMS positive ion on an LTQ Orbitrap XL.

General preparation procedure of (4+3) cycloadducts.



An oven-dried 15 mL seal tube equipped with a magnetic stir bar. At the room temperature, *N*-methyloxidopyridinium ion (0.32 mmol, 1.0 equiv.), diene (0.95 mmol, 3.0 equiv.) were added in acetonitrile (3.2 mL, 0.1 M), then degassed by argon for 5 min and triethylamine (132 μL mg, 0.95 mmol, 3.0 equiv) was added. The mixture was heated at 85 ^{o}C for 24 h by oil bath. After the reaction was completed, the mixture was cooled down to room temperature, and 8 drops of 10% HCl aq. was added. The mixture was extracted by dichloromethane (3 x 6 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum, and the residue was purified by flash chromatography on silica gel (EtOAc:Hexanes) to afford the resulting (4+3)-cycloadducts. All of the starting materials are known and were published by our group previously.[12]

General preparation procedure of photocycloadducts

[12] (a) Fu, C.; Lora, N.; Kirchhoefer, P. L.; Lee, D. R.; Altenhofer, E.; Barnes, C. L.; Hungerford, N. L.; Krenske, E. H.; Harmata, M., (4+3) Cycloaddition Reaction of *N*-Alkyl Oxidopyridinium Ions. *Angew. Chem. Int. Ed.* **2017**, *56*, 14682-14687; (b) Harmata, A. S.; Harmata, M., From 5-Hyrdroxynicotinic Acid to Nitrogenous (4+3) cycloadducts. *Org. Synth.* **2020**, *94*, 139-156; (c) Fu, C.; Kelley, S. P.; Tu, J.; Harmata, M., Generation of the 7-Azabicyclo[4.3.1]decane Ring System via (4+3) Cycloaddition of Oxidopyridinium Ions. *J. Org. Chem.* **2021**, *86*, 7028-7037; (d) Sungnoi, W.; Keto, A. B.; Roseli, R. B.; Liu, J.; Wang, H.; Fu, C.; Regalado, E. L.; Krenske, E. H.; Harmata, M., *Endo* Selectivity in the (4+3) Cycloaddition of Oxidopyridinium Ions. *Org. Lett.* **2021**, *23*, 8302-8306.

A solution of vinylogous amide (200 mg, 0.80 mmol) in acetonitrile (8 ml) in a borosilicate tube. The tube was capped by a rubber septum and purged with an argon balloon for 5 mins, and then the argon balloon was removed. The reaction was irradiated (450-watt Hanovia medium pressure mercury lamp) in iced water bath for 0.5-3 h. TLC analysis (50% EtOAc-hexanes) indicated the complete consumption of starting material. Evaporation of volatiles gave a brown oil. The resulting brown residue was purified by column chromatography (30-70% EtOAc-hexanes) to give cycloadduct.

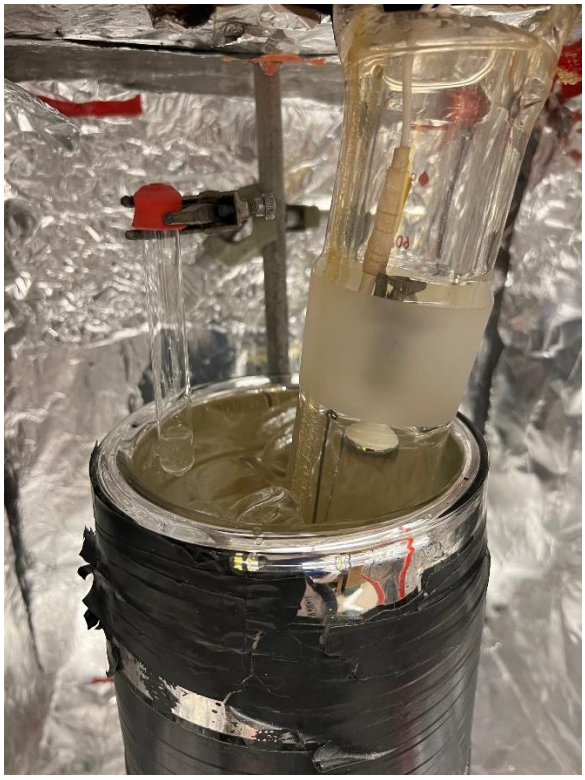


Figure 1. Starting material before starting the reaction

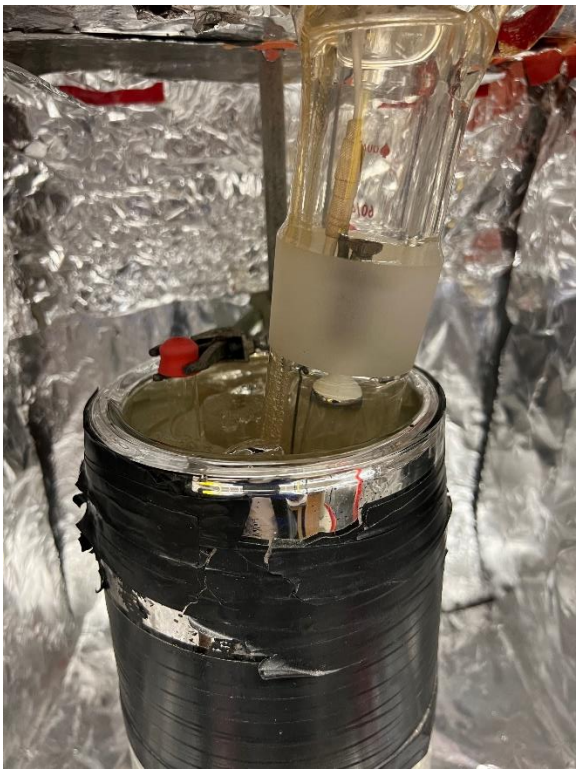


Figure 2. Submerge the starting material into the 0 ℃ bath

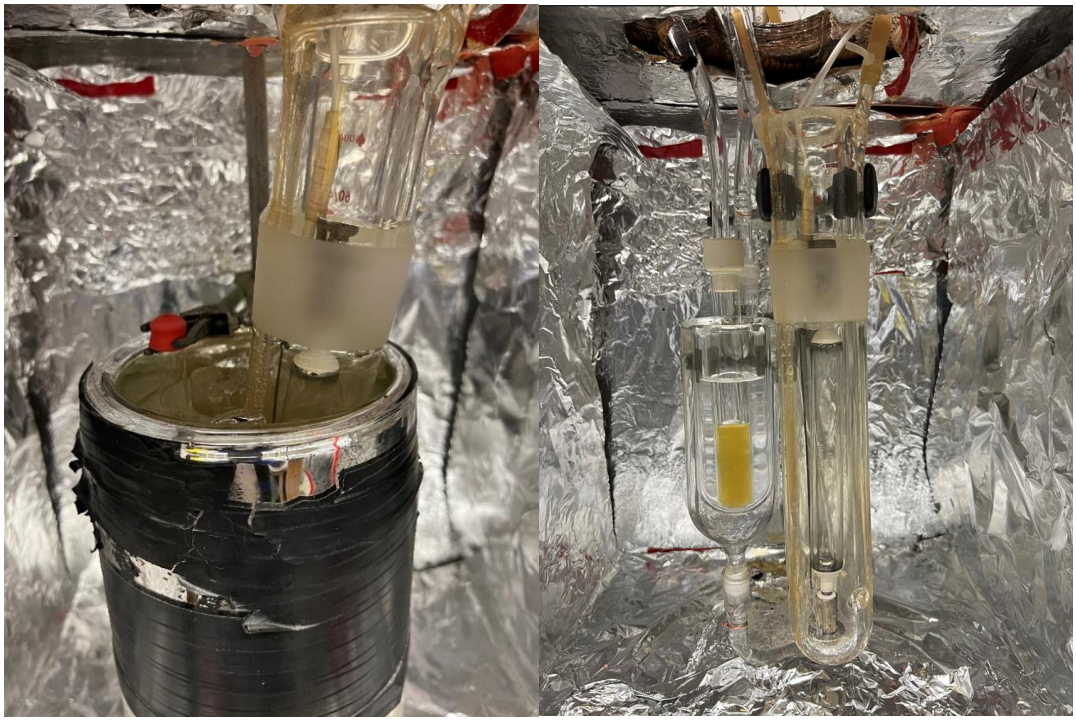


Figure 3. Starting material before closing the box and turned on the Hg lamp

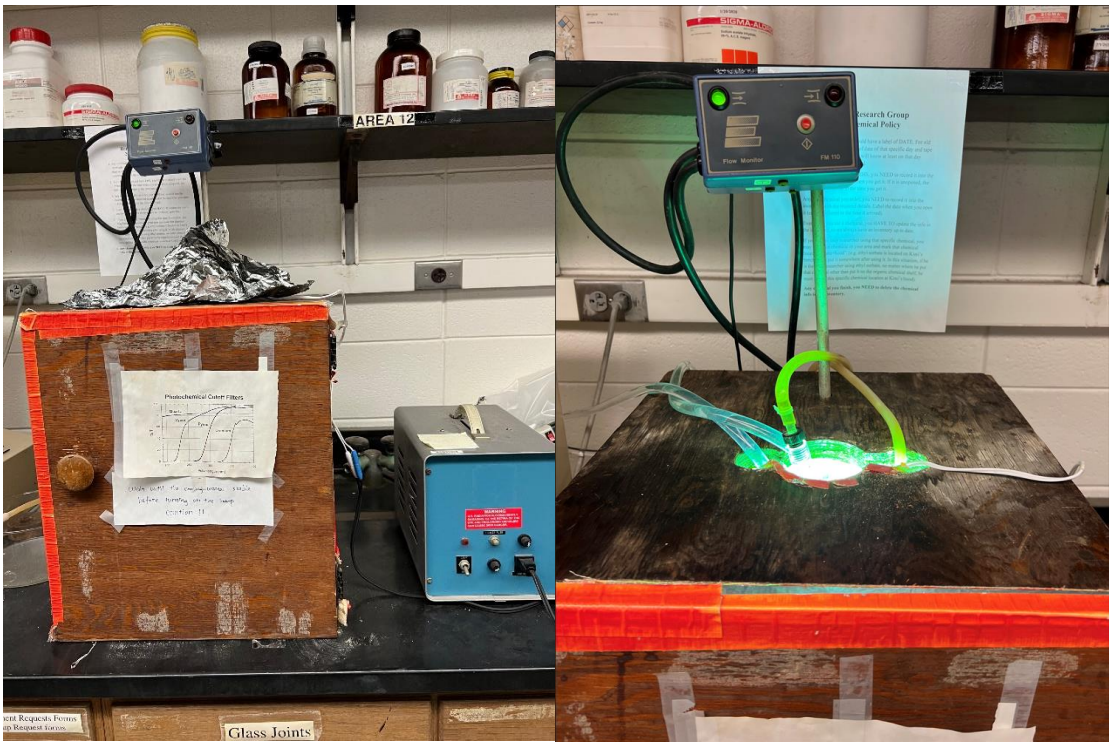
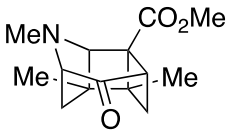
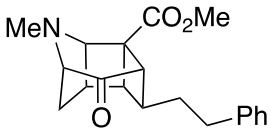


Figure 4. The box for running the [2+2] cycloaddition reaction



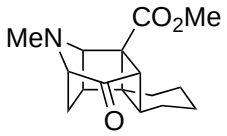
methyl 3,4,9-trimethyl-10-oxo-9-azatetracyclo[4.3.1.03,8.04,7]decane-7-carboxylate (68)

Colorless oil (2.5 h, 48 mg, 96% yield; an 1 mmol scale was also performed, affording **8** in 79% yield, 197 mg), column: Hexanes:EtOAc = 60:40; **^{1}H NMR** (800 MHz, $CDCl_3$): δ 3.80 (d, J = 0.9 Hz, 1H), 3.76 (s, 3H), 3.49 (dd, J = 6.5, 1.9 Hz, 1H), 3.23 (dtd, J = 11.5, 1.9, 1.0 Hz, 1H), 2.383 (d, J = 14.0 Hz, 1H), 2.379 (dd, J = 12.3, 11.5 Hz, 1H), 2.32 (s, 3H), 2.30 (dd, J = 12.5, 2.0 Hz, 1H), 1.96 (dd, J = 14.0, 6.5 Hz, 1H), 1.36 (s, 3H), 1.19 (s,3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 211.1, 171.1, 72.7, 67.2, 52.7, 51.9, 46.4, 45.5, 42.9, 37.6, 34.7, 34.4, 22.2, 18.7; **IR** (CH_2Cl_2): ν_{max} 3052, 2980, 2948, 1717, 1438, 1272, 1029, 890, 697 cm^{-1}; **HRMS (m/z):** (ESI) calcd. for $(C_{14}H_{19}NO_3)H^+$ $[M+H]^+$: 250.1438, found: 250.1438.



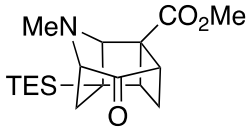
methyl 9-methyl-10-oxo-5-phenethyl-9 azatetracyclo [4.3.1.0^{3,8}.0^{4,7}] decane-7-carboxylate (70)

Colorless oil (16.8 mg, 91% yield), column: Hexanes:EtOAc = 50:50. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 (td, J = 7.5, 2.8 Hz, 2H), 7.17 (t, J = 7.4 Hz, 1H), 7.13 (d, J = 7.2 Hz, 2H), 4.15 (d, J = 7.5 Hz, 1H), 3.73 (d, J = 5.0 Hz, 3H), 3.50 (ddd, J = 22.6, 6.0, 1.5 Hz, 1H), 3.39-3.35 (m, 1H), 3.25 (q, J = 7.8 Hz, 1H), 3.10-3.06 (m, 1H), 3.00 (td, J = 7.6, 3.6 Hz, 0.5H), 2.76 (dd, J = 7.7, 3.4 Hz, 0.5H), 2.68-2.56 (m, 1H), 2.5 (ddd, J = 13.8, 9.2, 6.6 Hz, 1H), 2.39 (d, J = 7.1 Hz, 3H), 2.24-2.15 (m, 1H), 2.06 (ddd, J = 14.5, 8.7, 6.1 Hz, 1H), 1.95 (dtd, J = 14.4, 8.6, 5.9 Hz, 0.5H), 1.83 (ddt, J = 13.9, 8.8, 7.0 Hz, 0.5H), 1.74 (dtd, J = 14.1, 9.1, 5.8 Hz, 0.5H), 1.66 (ddt, J = 14.3, 9.7, 7.1 Hz, 0.5H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 210.7, 209.3, 172.7, 172.3, 141.5, 141.4, 128.6, 128.6, 128.5, 128.5, 126.1, 126.1, 71.9, 71.8, 62.9, 61.5, 52.4, 52.3, 51.4, 51.2, 50.9, 49.3, 41.5, 40.5, 39.9, 38.9, 36.9, 36.1, 35.3, 35.0, 34.8, 33.5, 32.8, 31.5, 28.7, 28.4, 0.1; **IR** ($CHCl_3$) ν_{max} = 2982, 2946, 2848, 1707, 1435, 1276, 1242, 1232, 1196, 1130, 1025, 895, 747, 699 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd. for $(C_{20}H_{23}NO_3)H^+$ $[M+H]^+$: 326.1751, found: 326.1751.



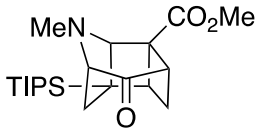
methyl (3b*S*,7a*S*)-1-methyl-3-oxodecahydro-1*H*,3a^{1}*H*-1-aza-2,8-methanocyclobuta[*de*]biphenylene-3a^{1}-carboxylate (72a)

Yellow oil (2.5 h, 32 mg, 77% yield), column: Hexanes:EtOAc = 50:50; **^{1}H NMR** (500 MHz, CDCl3): δ 4.21 (dd, J = 7.7, 0.8 Hz, 1H), 3.77 (s, 3H), 3.46 (dd, J = 6.0, 1.5 Hz, 1H), 3.02 (d, J = 1.0 Hz, 1H), 2.86 (t, J = 8.1 Hz, 1H), 2.34 (s, 3H), 2.28 (dd, J = 19.4, 9.7 Hz, 1H), 2.14- 2.10 (m, 1H), 1.66- 1.63 (m, 1H), 1.59-1.57 (m. 3H), 1.43 (dddd, J = 24.0, 16.8, 10.5, 3.2 Hz, 1H), 1.27-1.20 (m, 2H), 1.04 (qdd, J = 12.9, 4.1, 2.6 Hz, 1H), 0.90 (qd, J = 13.0, 2.6 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 209.9, 172.2, 71.4, 60.9, 52.20, 52.16, 51.49, 46.0, 44.2, 38.8, 34.7, 31.2, 31.0, 27.7, 23.5, 23.3; **IR** (CH_2Cl_2): ν_{max} 3061, 2989, 1708, 1425, 1254, 894, 773, 692 cm^{-1}.; **HRMS (m/z):** (ESI) calcd. for $(C_{16}H_{21}NO_3)H^+$ $[M+H]^+$: 276.1594, found: 276.1595.



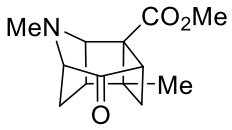
methyl 9-methyl-10-oxo-4-(triethylsilyl)-9-azatetracyclo [4.3.1.0^{3,8}.0^{4,7}] decane-7-carboxylate (74b)

Colorless oil (9 mg, 37% yield), column: Hexanes:EtOAc = 70:30. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 4.03 (d, *J* = 0.7 Hz, 1H), 3.74 (s, 3H), 3.53 (dd, *J* = 6.2, 1.8 Hz, 1H), 3.26-3.24 (m, 1H), 2.99 (dd, *J* = 6.5, 3.0 Hz, 1H), 2.80 (ddd, *J* = 12.6, 11.2, 6.7 Hz, 1H), 2.35 (s, 3H), 2.30 (d, *J* = 14.1 Hz, 1H), 2.18 (dd, *J* = 14.1, 6.3 Hz, 1H), 1.99 (dd, *J* = 12.6, 1.8 Hz, 1H), 0.98 (t, *J* = 8.0 Hz, 9H), 0.67-0.63 (m, 6H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 211.1, 172.3, 72.0, 65.3, 53.2, 52.2, 46.2, 36.8, 34.8, 33.8, 30.7, 26.3, 7.7, 2.0, 0.1; **IR** ($CHCl_3$) ν_{max} = 2951, 2876, 1712, 1457, 1434, 1268, 1219, 1177, 1068, 1011, 907, 729 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd. for $(C_{18}H_{29}NO_3Si)Na^+$ $[M+Na]^+$: 358.1809, found: 358.1809.



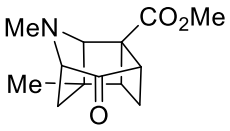
methyl 9-methyl-10-oxo-4-(triisopropylsilyl)-9-azatetracyclo [4.3.1.0^{3,8}.0^{4,7}]decane-7-carboxylate (76b)

Colorless solid (4 mg, 24% yield), Mp = 61 – 63 ºC (recrystallized in ethanol:water = 80:20), column: Hexanes:EtOAc = 80:20. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 4.26 (1H, d, *J* = 0.8 Hz), 3.73 (s, 3H), 3.50 (dt, *J* = 3.6, 1.7 Hz, 1H), 3.20-3.17 (m, 1H), 3.17 (dd, *J* = 6.8, 2.5 Hz, 1H), 2.82 (ddd, *J* = 12.6, 11.2, 6.9 Hz, 1H), 2.36 (s, 3H), 2.35 (d, *J* = 5.0 Hz, 2H), 2.04 (dd, *J* = 12.6, 1.5 Hz, 1H), 1.25 (sept, *J* = 7.8 Hz, 3H), 1.12 (dd, *J* = 12.9, 7.4 Hz, 18H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 211.9, 172.6, 71.0, 66.0, 53.5, 52.2, 46.2, 37.7, 34.7, 34.2, 32.1, 26.1, 19.4, 19.3, 11.5, 0.1 ppm; IR ($CHCl_3$) ν_{max} = 2943, 2866, 1712, 1461, 1267, 1216, 1176, 1068, 883, 749, 661 cm^{-1}. **HRMS (m/z):** (ESI-FTICR) calcd. for $(C_{21}H_{35}NO_3Si)Na+$ $[M+Na]^+$: 400.2278, found: 400.2279.



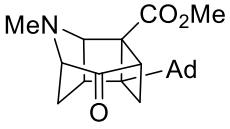
methyl 4,9-dimethyl-10-oxo-9-azatetracyclo [4.3.1.0^{3,8}.0^{4,7}]decane-7-carboxylate (78a)

Colorless oil (28 mg, 34% yield), column: Hexanes:EtOAc = 50:50. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 4.25 (dd, *J* = 7.5, 0.9 Hz, 1H), 3.75 (s, 3H), 3.49 (dd, *J* = 6.1, 1.6 Hz, 1H), 3.24 (ddd, *J* = 11.5, 2.8, 1.8 Hz, 1H), 2.94 (t, *J* = 8.0 Hz, 1H), 2.46 (t, *J* = 12.0 Hz, 1H), 2.34 (s, 3H), 2.28 (d, *J* = 14.0 Hz, 1H), 2.22 (ddd, *J* = 14.5, 8.4, 6.1 Hz, 1H), 2.16 (dd, *J* = 12.3, 1.8 Hz, 1H), 1.23 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 210.6, 171.2, 72.0, 60.5, 53.8, 52.0, 43.4, 43.1, 43.0, 35.0, 32.9, 28.9, 22.3; **IR** (CH_2Cl_2) ν_{max} = 2949, 2790, 1709, 1439, 1284, 1264, 1229, 1130, 1065, 750 cm^{-1}; **HRMS (m/z):** (ESI) calcd. for $(C_{13}H_{17}NO_3)H^+$ $[M+H]^+$: 236.1281, found: 236.1280.



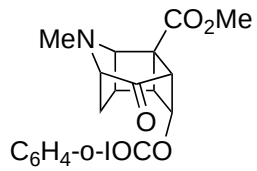
methyl 3,9-dimethyl-10-oxo-9-azatetracyclo [4.3.1.0^{3,8}.0^{4,7}]decane-7-carboxylate (78b)

Starting material contained 2 isomers, the ratio is 1.2:1 (100 mg, 0.43 mmol), the product was obtained as 2 isomers which are purified by flash chromatography to separate the 2 isomers. Colorless solid (21 mg, 21% yield), Mp = 45 – 46 ^{o}C (recrystallized in Hexanes:EtOAc = 50:50), column: Hexanes:EtOAc = 50:50. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 3.75 (s, 3H), 3.73 (s, 1H), 3.52 (dd, *J* = 6.4, 1.8 Hz, 1H), 3.30 (dddt, *J* = 11.2, 3.9, 1.9, 1.0 Hz, 1H), 2.83 (ddd, *J* = 12.5, 11.3, 6.7 Hz, 1H), 2.72 (dd, *J* = 6.7, 3.1 Hz, 1H), 2.36 (s, 3H), 2.34 – 2.32 (m, 1H), 2.05 (dd, *J* = 12.6, 1.8 Hz, 1H), 1.96 (dd, *J* = 13.8, 6.4 Hz, 1H), 1.44 (s, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 211.1, 172.3, 72.9, 68.8, 52.3, 49.5, 46.3, 44.1, 43.0, 35.7, 34.8, 27.2, 25.9; **IR** (neat) ν_{max} = 2944, 2792, 1702, 1439, 1262, 1214, 1114, 1028, 906, 751, 661 cm^{-1}; **HRMS (m/z):** (ESI) calcd. for $(C_{13}H_{17}NO_3)H^+$ $[M+H]^+$: 236.1281, Found: 236.1281.



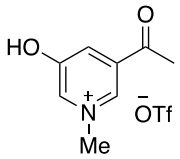
methyl 4-adamantyl-9-methyl-10-oxo-9-azatetracyclo [4.3.1.0^{3,8}.0^{4,7}]decane-7-carboxylate (80a)

Colorless solid (55 mg, 32% yield), Mp = 194 – 195 ^{o}C (recrystallized in Hexanes:EtOAc = 50:50), column: Hexanes:EtOAc = 80:20. **^{1}H NMR** (600 MHz, $CDCl_3$): δ 4.20 (dd, *J* = 8.0, 1.1 Hz, 1H), 3.74 (s, 3H), 3.45 (dd, *J* = 6.5, 1.7 Hz, 1H), 3.37 (t, *J* = 8.1 Hz, 1H), 3.26 (ddd, *J* = 12.0, 3.1, 2.0 Hz, 1H), 2.88 (t, *J* = 12.2 Hz, 1H), 2.30 (s, 3H), 2.26 – 2.18 (m, 2H), 1.98 (t, *J* = 3.2 Hz, 3H), 1.87 (dd, *J* = 12.4, 2.1 Hz, 1H), 1.70 (d, *J* = 12.3 Hz, 3H), 1.60 – 1.56 (m, 6H), 1.45 (dq, *J* = 12.1, 3.0 Hz, 3H); **^{13}C NMR** (151 MHz, $CDCl_3$): δ 210.8, 172.4, 71.9, 60.9, 54.9, 53.5, 52.0, 42.1, 37.0, 37.0, 36.0, 35.4, 34.9, 28.5, 28.1, 25.3; **IR** (neat) ν_{max} = 2900, 2849, 1699, 1697, 1435, 1433, 1261, 1222, 1121, 1065, 1021, 892, 750 cm^{-1}; **HRMS (m/z):** (ESI) calcd. for $(C_{22}H_{29}NO_3)Na^+$ $[M+Na]^+$: 378.2040, found: 378.2042.



methyl 5-((2-iodobenzoyl)oxy)-9-methyl-10-oxo-9-azatetracyclo[4.3.1.0^{3,8}.0^{4,7}]decane-7- carboxylate (86a).

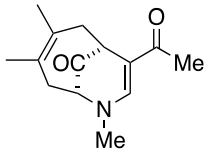
Yellow solid **(**2.5 h, 26 mg, 62% yield), mp = 120 – 122 ℃, column: Hexanes:EtOAc = 30:70. **^{1}H NMR** (500 MHz, CDCl3): δ 8.00 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.83 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.42 (td, *J* = 7.6, 1.2 Hz, 1H), 7.17 (td, *J* = 7.8, 1.7 Hz, 1H), 5.24 (s, 1H), 4.22 (d, *J* = 7.5 Hz, 1H), 3.76 (s, 3H), 3.60 (d, *J* = 4.5 Hz, 1H), 3.56-3.51 (m, 2H), 3.20 (dd, *J* = 8.1, 4.6 Hz, 1H), 2.44 (s, 3H), 2.33 (dd, *J* = 8.8, 6.1 Hz, 1H), 2.40 (d, *J* = 14.4 Hz, 1H); **^{13}C NMR** (125 MHz, CDCl3): δ 205.3, 171.1, 165.2, 141.5, 133.1, 131.3, 128.0, 94.2, 73.5, 71.5, 62.7, 53.4, 52.4, 41.0, 35.4, 34.6, 27.4; **IR** (CH_2Cl_2): ν_{max} 3065, 2998, 2997, 2948, 1726, 1267, 1236, 1142, 1101, 728, 701 cm^{-1}; **HRMS (m/z):** (ESI) calcd. for $(C_{19}H_{18}INO_5)Na^+$ $[M+Na]^+$: 468.0302, found: 468.0299.



3-acetyl-5-hydroxy-1-methylpyridin-1-ium trifluoromethanesulfonate (87)

The compound was prepared from the known literature.[32,97]

Pale orange solid (1.14 g, 91%), mp = 86 – 87 ℃. **^{1}H NMR** (600 MHz, DMSO) δ 12.24 (1H, s), 9.04 (1H, s), 8.67 (1H, s), 8.21 (1H, s), 4.35 (3H, s), 2.67 (3H, s); **^{13}C NMR** (151 MHz, DMSO) δ 194.1, 156.6, 137.0, 136.8, 135.9, 129.1, 123.9, 121.7, 119.6, 117.5, 48.3, 27.2; **IR** (neat) ν_{max} = 3091, 1702, 1631, 1291, 1216, 1169, 1022, 750 625 cm^{-1}; **HRMS** calcd for $(C_8H_9NO_2)H^+$: 303.1339, found: 303.1337.

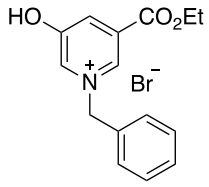


9-acetyl-3,4,7-trimethyl-7-azabicyclo[4.3.1]deca-3,8-dien-10-one (88)

Pale Orange solid (215 mg, 92%), mp = 164 – 165 ℃. **^{1}H NMR** (600 MHz, CD_3CN) δ 7.36 (1H, s), 3.64 (1H, ddd, *J* = 7.4, 2.9, 1.0 Hz), 3.43 (1H, ddd, *J* = 7.1, 2.9, 1.6 Hz), 2.99 (3H, s), 2.78 (1H, dd, *J* = 15.5, 7.4 Hz), 2.56 (1H, dd, *J* = 14.5, 7.1 Hz), 2.21 (1H, d, *J* = 15.2 Hz), 2.09 (1H, d, *J* = 14.5 Hz), 2.04 (3H, s), 1.82 (3H, s), 1.57 (3H, s); **^{13}C NMR** (151 MHz, CD_3CN) δ 207.7, 192.0, 150.4, 132.9, 126.8, 106.5, 67.0, 46.1, 40.9, 38.1, 37.2, 24.2, 23.5, 23.2; **IR** (neat) ν_{max} = 2932, 1716, 1554, 1345, 1258, 1167, 1035, 749, 633 cm^{-1}; **HRMS** calcd for $(C_{14}H_{19}NO_2)Na^+$: 256.1308, found: 256.1308.

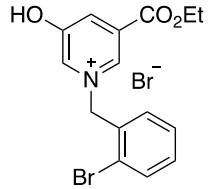
General preparation procedure of N-alkylation

To an oven-dried 50 mL RBF equipped with a magnetic stir bar was added ethyl 5-hydroxynicotinate (1.0 g, 5.98 mmol, 1.0 equiv) in CH_3CN (20 mL, 0.30 M) at room temperature. The solution was white cloudy mixture. Upon addition of 2-bromobenzyl bromide (1.50 g, 5.98 mmol, 1.0 equiv), the mixture changed in color to pale-yellow and cloudy. The mixture was stirred at room temperature for 10 h, there was still 70% of starting material and was judged by TLC (10% MeOH:CH_2Cl_2). Then the mixture was refluxed for 14 h, the mixture was pale yellow and clear. The reaction was monitored by TLC (10% MeOH:CH_2Cl_2) until all starting material was consumed. Upon completion, the reaction was cooled down to room temperature, and the resulting mixture was concentrated under reduced pressure, and purified by flash chromatography on silica gel (5 - 10% MeOH:CH_2Cl_2) to obtain the product.



1-benzyl-3-(ethoxycarbonyl)-5-hydroxypyridin-1-ium bromide (89)

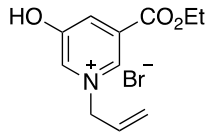
pale-yellow solid (1.81 g, 6.27 mmol, 88%). Recrystallization (10% MeOH:CH_2Cl_2) gave a pale-yellow solid, mp = 43 - 44˚C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.32 (1H, s), 8.62 (1H, s), 8.46 (1H, s), 8.05 – 7.61 (1H, broad), 7.53 (2H, dd, *J* = 7.0, 3.5 Hz), 7.44 (3H, t, *J* = 3.3 Hz), 5.93 (2H, s), 4.42 (2H, q, *J* = 7.1 Hz), 1.39 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.6, 159.7, 136.4, 133.7, 132.7, 132.1, 131.5, 130.3, 129.8, 129.5, 65.6, 63.2, 14.2; **IR** (Neat) ν_{max} = 2935, 1728, 1595, 1455, 1256, 1239, 1016, 745, 700 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{15}H_{16}NO_3$ $[M]^+$:258.1125, found: 258,1122.



1-(2-bromobenzyl)-3-(ethoxycarbonyl)-5-hydroxypyridin-1-ium bromide (90)

pale-yellow solid (2.43 g, 5.83 mmol, 98%). Recrystallization (10% MeOH:CH_2Cl_2) gave a pale-yellow solid, mp = 52 - 53˚C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.94 – 9.25 (1H, broad), 9.10 (1H, s), 8.58 (1H, s), 8.45 (1H, s), 7.92 (1H, d, *J* = 6.9 Hz), 7.66 - 7.65 (1H, m), 7.49

(1H, t, *J* = 7.0 Hz), 7.42 – 7.33 (1H, m), 6.08 (2H, s), 4.43 (2H, q, *J* = 7.1 Hz), 1.40 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.6, 159.7, 136.5, 134.0, 133.9, 133.8, 133.0, 132.5, 131.2, 131.1, 129.1, 125.4, 65.3, 63.3, 14.2; **IR** (Neat) ν_{max} = 2935, 1728, 1594, 1468, 1238, 1016, 750 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{15}H_{15}BrNO_3$ $[M]^+$:336.0230, found: 336.0231.

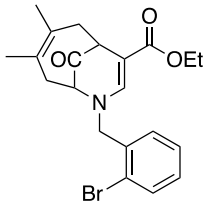


1-allyl-3-(ethoxycarbonyl)-5-hydroxypyridin-1-ium bromide (91)

pale-yellow solid (1.81 g, 6.27 mmol, 99%). Recrystallization (10% MeOH:CH_2Cl_2) gave a white solid, mp = 122 - 123˚C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.16 (1H, s), 8.90 - 8.40 (1H, broad), 8.74 (1H, s), 8.50 (1H, s), 6.17 (1H, ddt, *J* = 13.2, 10.1, 6.6 Hz), 5.68 (1H, d, *J* = 17.0 Hz), 5.61 (1H, d, *J* = 10.1 Hz), 5.43 (2H, d, *J* = 6.5 Hz), 4.46 (2H, q, *J* = 7.1 Hz), 1.43 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.5, 159.0, 136.1, 134.5, 132.7, 131.5, 129.2, 125.1, 64.5, 63.3, 14.2; **IR** (Neat) ν_{max} = 2938, 1728, 1591, 1459, 1235, 1017, 750 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{11}H_{14}NO_3$ $[M]^+$: 415.1864, found: 415.1861.

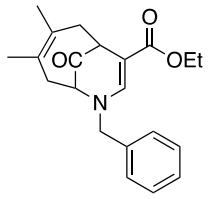
General preparation procedure of (4+3) cycloadducts

To an oven-dried 15 mL sealed tube equipped with a magnetic stir bar was added 1-(2-bromobenzyl)-3-(ethoxycarbonyl)-5-hydroxypyridin-1-ium bromide (150 mg, 0.36 mmol, 1.0 equiv) in CH_3CN (3.6 mL, 0.1 M) at room temperature. The mixture was then degassed with an argon balloon for 5 min followed by addition of 2,3-dimethyl-1,3-butadiene (410 μL, 3.6 mmol, 10.0 equiv) and potassium phosphate (76.4 mg, 0.36 mmol, 1.0 equiv) then sealed with screw cap and heated for 16 h at 85 ^{o}C in an oil bath. The reaction mixture was turned brown from pale yellow and clear upon the heating. The reaction was monitored by TLC (30% EtOAc:Hexane). The reaction was cooled down to room temperature and extracted with Satd. $NaHCO_3$ (2 x 8 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the resulting mixture was concentrated under reduced pressure, and purified by flash chromatography on silica gel (30% EtOAc:Hexane) to obtain the product.



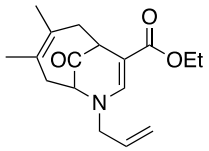
ethyl 7-(2-bromobenzyl)-3,4-dimethyl-10-oxo-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (92)

pale-yellow oil (132 g, 0.32 mmol, 88%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 (1H, dd, *J* = 7.9, 1.1 Hz), 7.48 (1H, s), 7.31 (1H, td, *J* = 7.5, 1.1 Hz), 7.18 (2H, qd, *J* = 7.7, 1.6 Hz), 4.45 (1H, d, *J* = 15.7 Hz), 4.35 (1H, d, *J* = 15.7 Hz), 4.18 (1H, dq, *J* = 10.8, 7.1 Hz), 4.13 (1H, dq, *J* = 10.8, 7.1 Hz), 3.61 (1H, dd, *J* = 6.6, 2.4 Hz), 3.53 (1H, ddd, *J* = 7.0, 2.7, 1.6 Hz), 2.69 (2H, dt, *J* = 14.3, 7.0 Hz), 2.23 (2H, t, *J* = 14.6 Hz), 1.87 (3H, s), 1.68 (3H, s), 1.26 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 206.6, 167.1, 146.7, 135.0, 133.4, 132.5, 129.9, 129.4, 128.1, 125.6, 123.8, 94.1, 63.9, 59.3, 56.4, 46.3, 38.3, 37.2, 23.6, 23.3, 14.7; **IR** (Neat) ν_{max} = 2932, 1683, 1671, 1601, 1440, 1364, 1275, 1137, 1077, 1024, 749 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{21}H_{24}BrNO_3$ $[M+Na]^+$: 440.0832, found: 440.0831.



ethyl 7-benzyl-3,4-dimethyl-10-oxo-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (93)

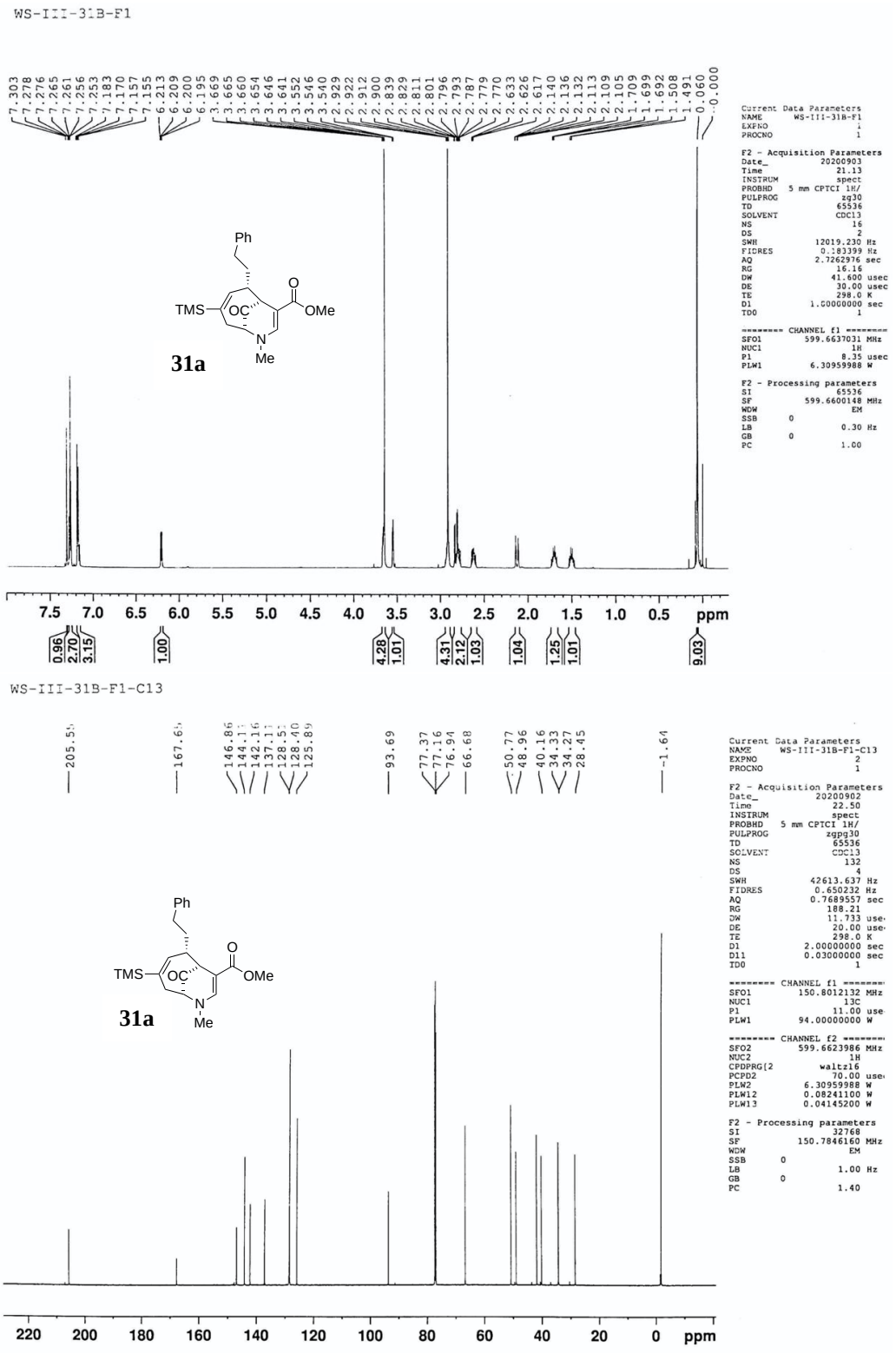
pale-yellow oil (364 mg, 1.07 mmol, 99%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (1H, s), 7.35-7.28 (3H, m), 7.19 - 7.17 (2H, m), 4.36 (1H, d, *J* = 15.2 Hz), 4.24 (1H, d, *J* = 15.2 Hz), 4.18 (1H, dq, *J* = 10.8, 7.1 Hz), 4.12 (1H, dq, *J* = 9.8, 6.1 Hz), 3.59 (1H, dd, *J* = 6.6, 2.6 Hz), 3.51 (1H, ddd, *J* = 7.1, 2.7, 1.5 Hz), 2.69 (1H, dd, *J* = 14.7, 7.1 Hz), 2.61 (1H, dd, *J* = 15.5, 7.3 Hz), 2.19 (2H, d, *J* = 15.4 Hz), 1.83 (3H, s), 1.67 (3H, s), 1.26 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 206.5, 167.1, 146.6, 135.7, 132.3, 129.0, 128.2, 127.6, 125.5, 93.4, 63.4, 59.2, 56.7, 46.2, 38.2, 36.9, 23.5, 23.2, 14.6; **IR** (Neat) ν_{max} = 2932, 1682, 1671, 1598, 1430, 1345, 1275, 1132, 1074, 750 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{21}H_{25}NO_3$ $[M+Na]^+$: 362.1727, found: 362.1730.



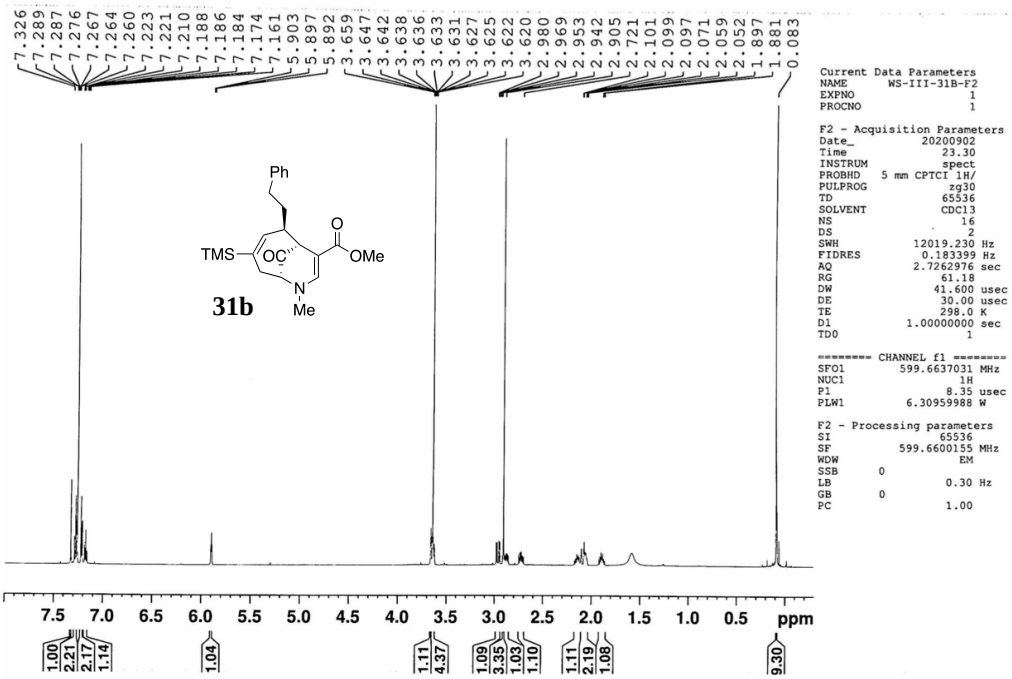
ethyl 7-allyl-3,4-dimethyl-10-oxo-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (94)

pale-yellow oil (269 mg, 0.93 mmol, 89%). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 (1H, s), 5.75 (1H, dddd, *J* = 15.4, 10.1, 6.8, 5.3 Hz), 5.26 (1H, ddd, *J* = 10.2, 2.5, 1.3 Hz), 5.23 (1H, ddd, *J* = 17.1, 2.8, 1.5 Hz), 4.17 (1H, dq, *J* = 10.8, 7.1 Hz), 4.12 (1H, dq, *J* = 10.8, 7.1 Hz), 3.76 (1H, ddt, *J* = 15.4, 5.2, 1.5 Hz), 3.71 – 3.67 (2H, m), 3.50 (1H, ddd, *J* = 7.1, 2.8, 1.6 Hz), 2.68 (1H, dd, *J* = 14.7, 7.1 Hz), 2.61 (1H, dd, *J* = 15.5, 7.3 Hz), 2.23 (2H, *J* = 22.5, 15.6 Hz), 1.81 (3H, s), 1.66 (3H, s), 1.26 (3H, t, *J* = 7.1 Hz); **^{13}C NMR** (151 MHz, $CDCl_3$) δ 207.0, 167.3, 146.2, 132.7, 132.5, 125.6, 119.5, 93.6, 64.0, 59.4, 55.7, 46.4, 38.3, 37.3, 23.6, 23.3, 14.8; **IR** (Neat) ν_{max} = 2901, 1683, 1670, 1598, 1275, 1155, 1138, 1075, 764 cm^{-1}; **HRMS (m/z):** (ESI-FTICR) calcd for $C_{17}H_{23}NO_3$ $[M+Na]^+$: 601.3248, found: 601.3241. **NOTE: Purification by silica plug instead of flash chromatography, it worked well.**

Spectral data of ^{1}H NMR and ^{13}C NMR



WS-III-31B-F2

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F2 - Processing parameters
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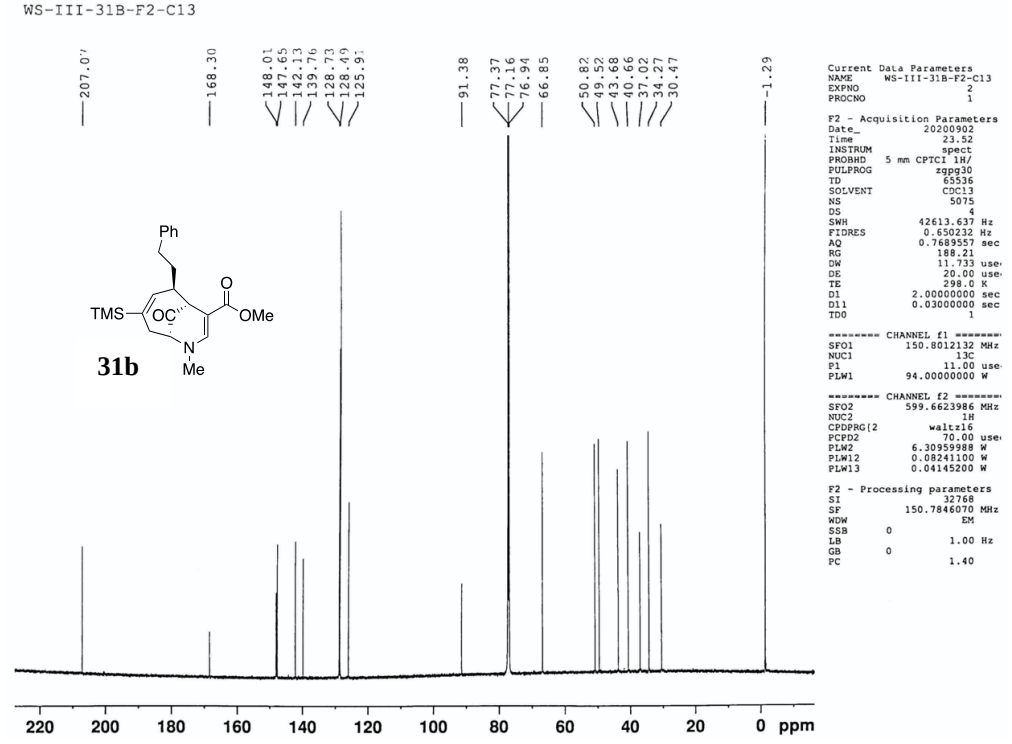
WS-III-31B-F2-C13

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NUC2                   1H
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PLW13        0.04145200 W

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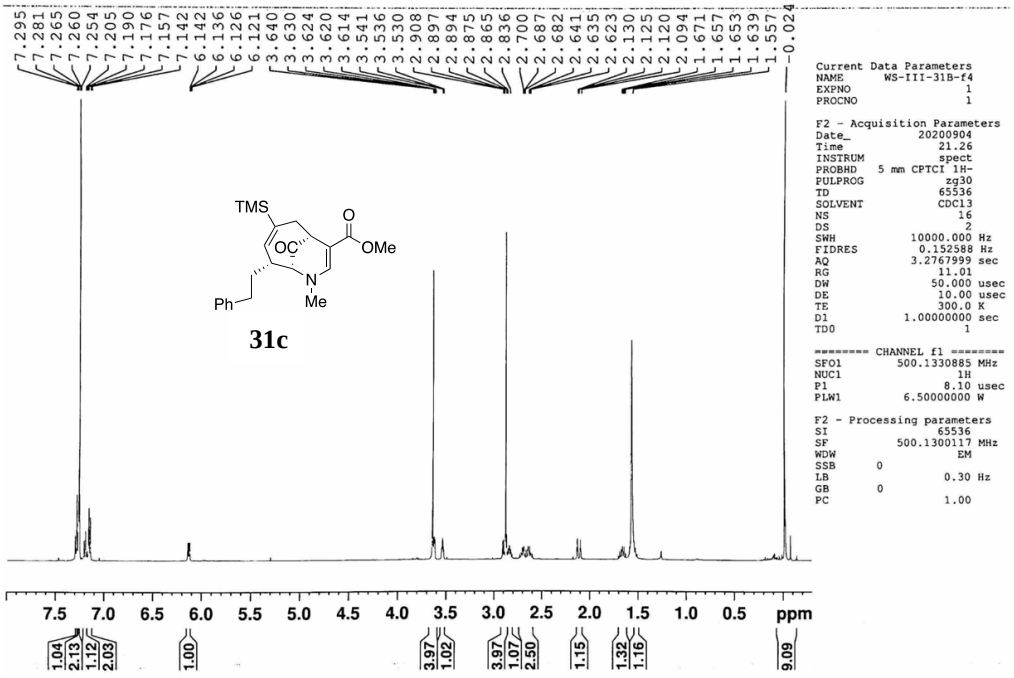
WS-III-31B-f4

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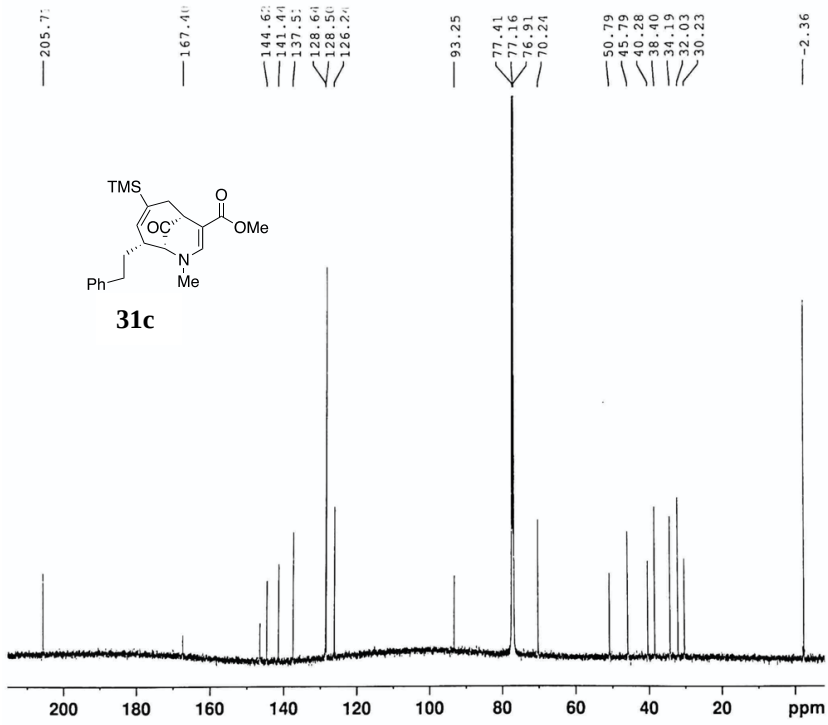
WS-III-31B-f4-C13

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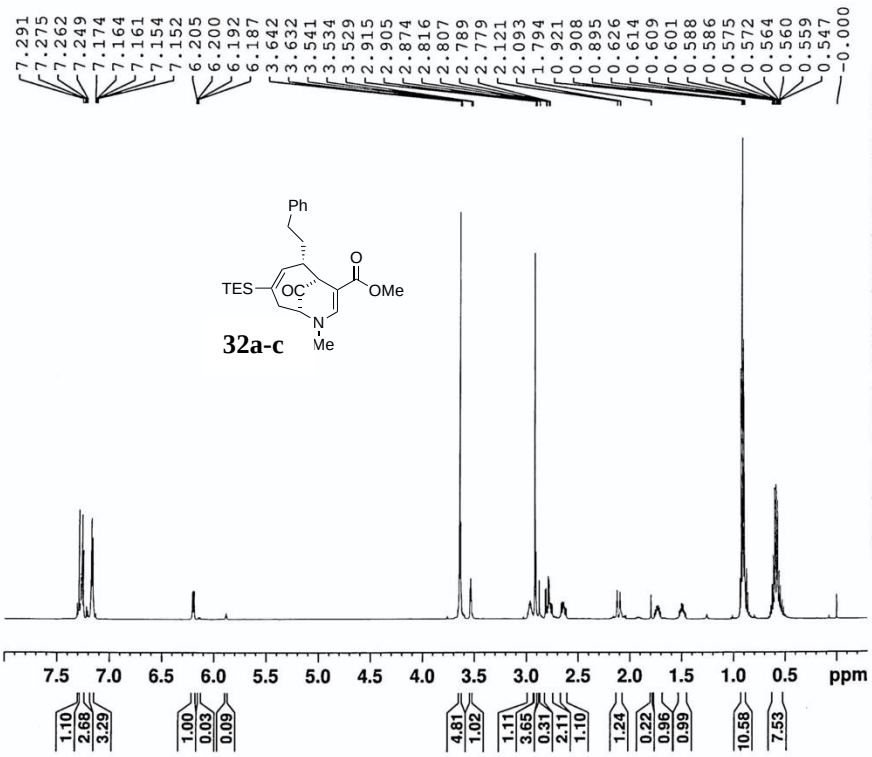
WS-III-16B

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NS                    16
DS                     2
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TE                298.0 K
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NUC1                  1H
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PLW1          6.30959988 W

F2 - Processing parameters
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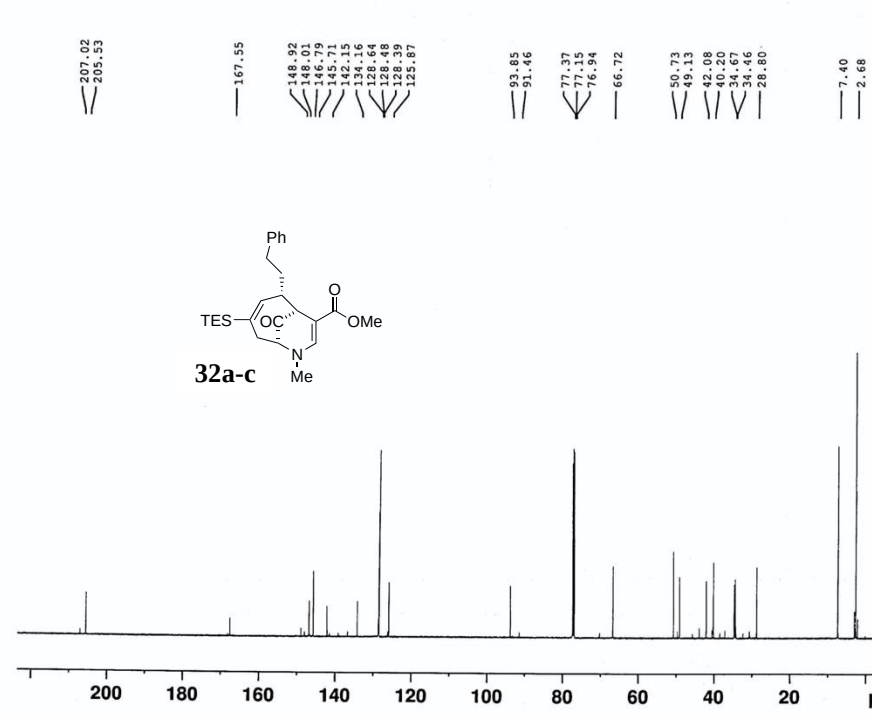
WS-III-16B-C13

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TD0                    1

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PLW1          94.00000000 W

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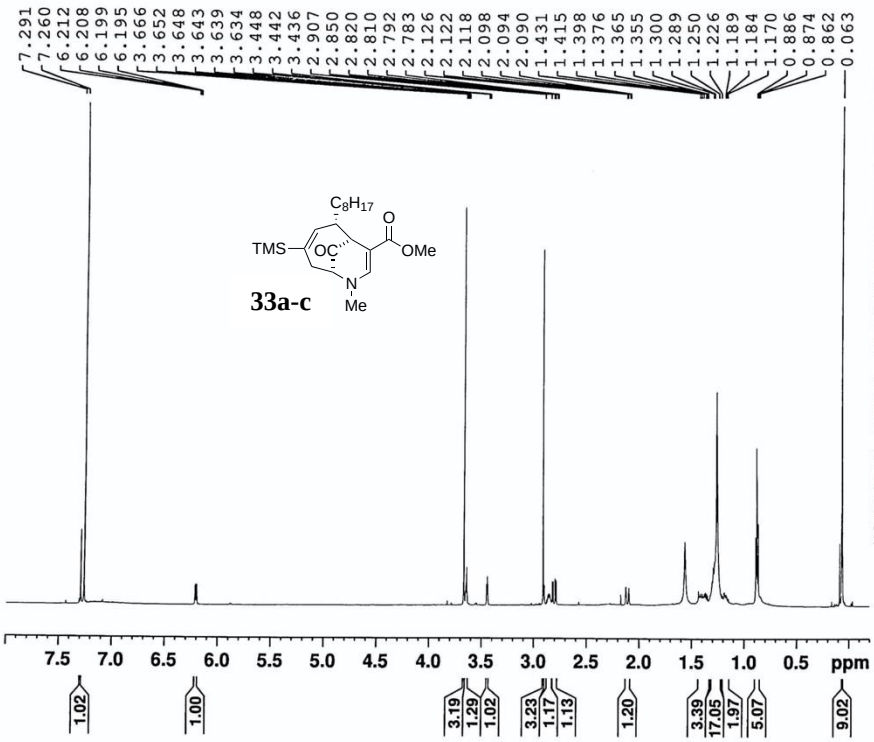
PCPD2              70.00 usec
PLW2          6.30959988 W
PLW12         0.08241100 W
PLW13         0.04145200 W

F2 - Processing parameters
SI                 32768
SF            150.7846187 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

WS-II-39B3



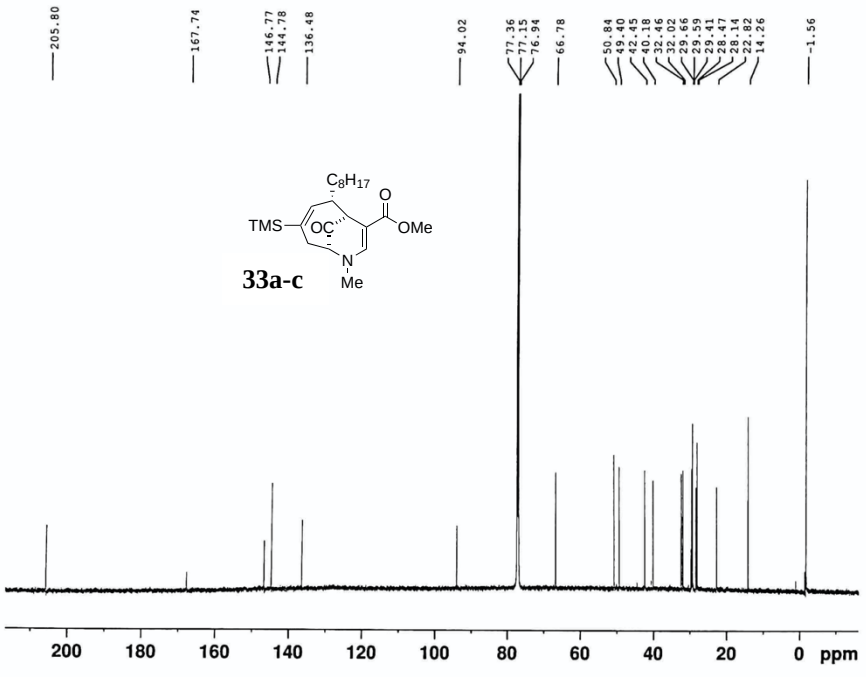

```
Current Data Parameters
NAME          WS-II-39B3
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200814
Time                1.57
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH            12019.230 Hz
FIDRES         0.183399 Hz
AQ             2.7262976 sec
RG                    56
DW                41.600 usec
DE                30.00 usec
TE                298.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          599.6637031 MHz
NUC1                  1H
P1                  8.35 usec
PLW1          6.30959988 W

F2 - Processing parameters
SI                 65536
SF            599.6600155 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

WS-II-39B3-C13




```
Current Data Parameters
NAME       WS-II-39B3-C13
EXPNO                  2
PROCNO                 1

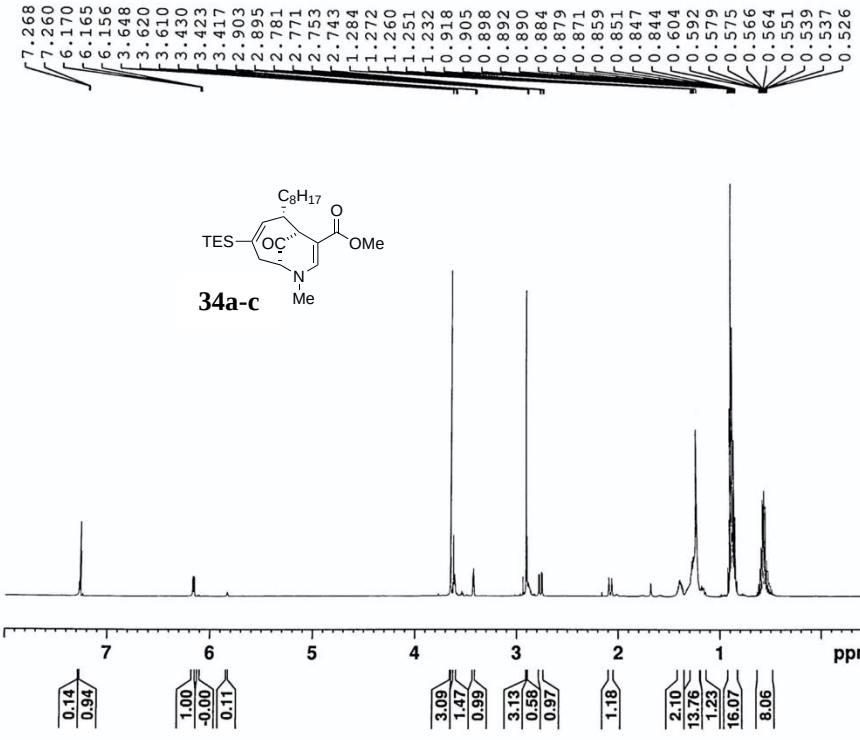
F2 - Acquisition Parameters
Date_           20200814
Time                2.30
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  2362
DS                     4
SWH            42613.637 Hz
FIDRES         0.650232 Hz
AQ             0.7689557 sec
RG                   188.21
DW                11.733 usec
DE                20.00 usec
TE                298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          150.8012132 MHz
NUC1                  13C
P1                 11.00 usec
PLW1          94.00000000 W

======== CHANNEL f2 ========
SFO2          599.6623986 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              70.00 usec
PLW2          6.30959988 W
PLW12         0.08241100 W
PLW13         0.04145200 W

F2 - Processing parameters
SI                 32768
SF            150.7846072 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

WS-III-20B2



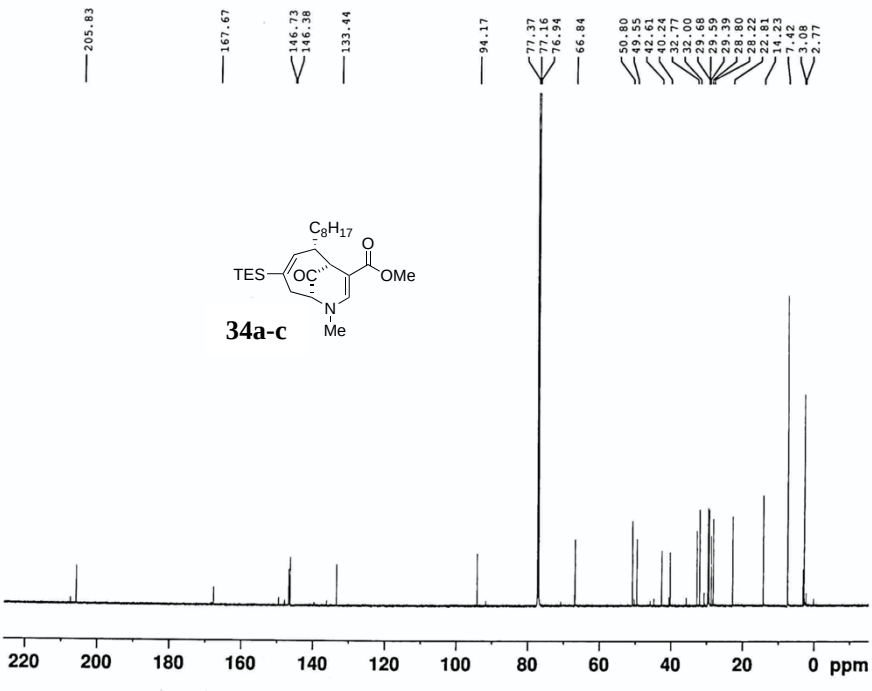

```
Current Data Parameters
NAME          WS-III-20B2
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_              20200711
Time                   1.07
INSTRUM               spect
PROBHD   5 mm CPTCI 1H/
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH              12019.230 Hz
FIDRES           0.183399 Hz
AQ               2.72629760 sec
RG                    12.91
DW                41.600 usec
DE                30.00 usec
TE                298.0 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1          599.6637031 MHz
NUC1                    1H
P1                   8.35 usec
PLW1           6.30959988 W

F2 - Processing parameters
SI                   65536
SF            599.6600141 MHz
WDW                     EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
```

WS-2-22B2-C13



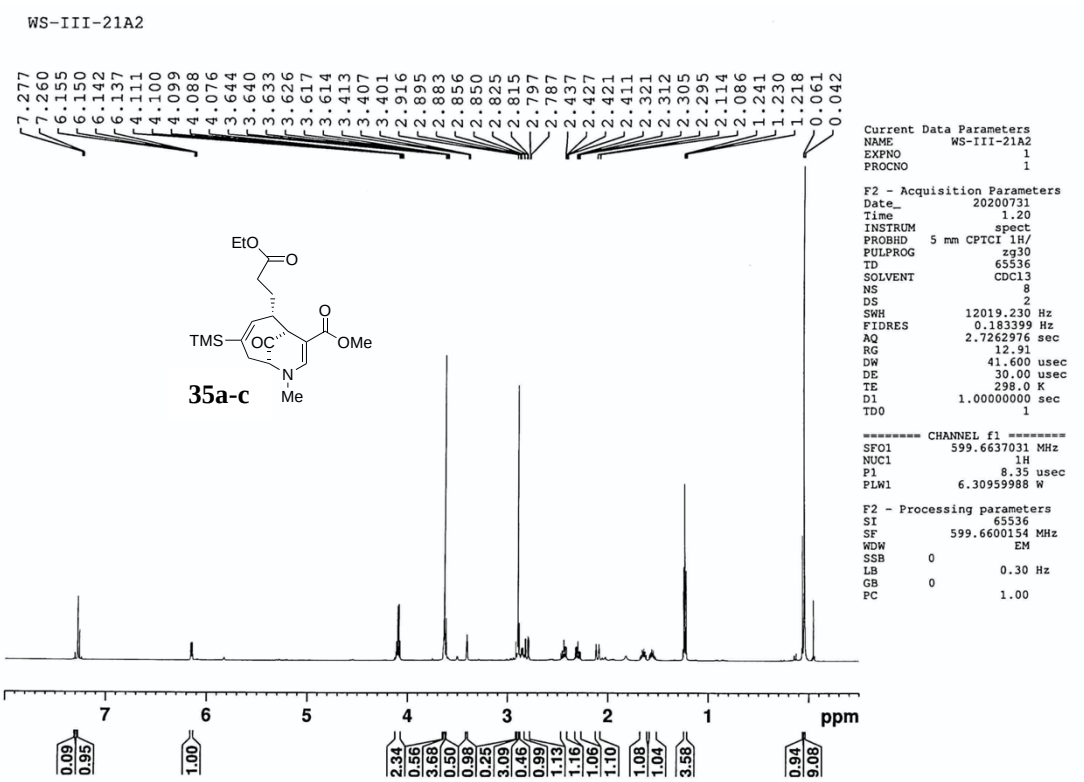

```
Current Data Parameters
NAME        WS-2-22B2-C13
EXPNO                   1
PROCNO                  1

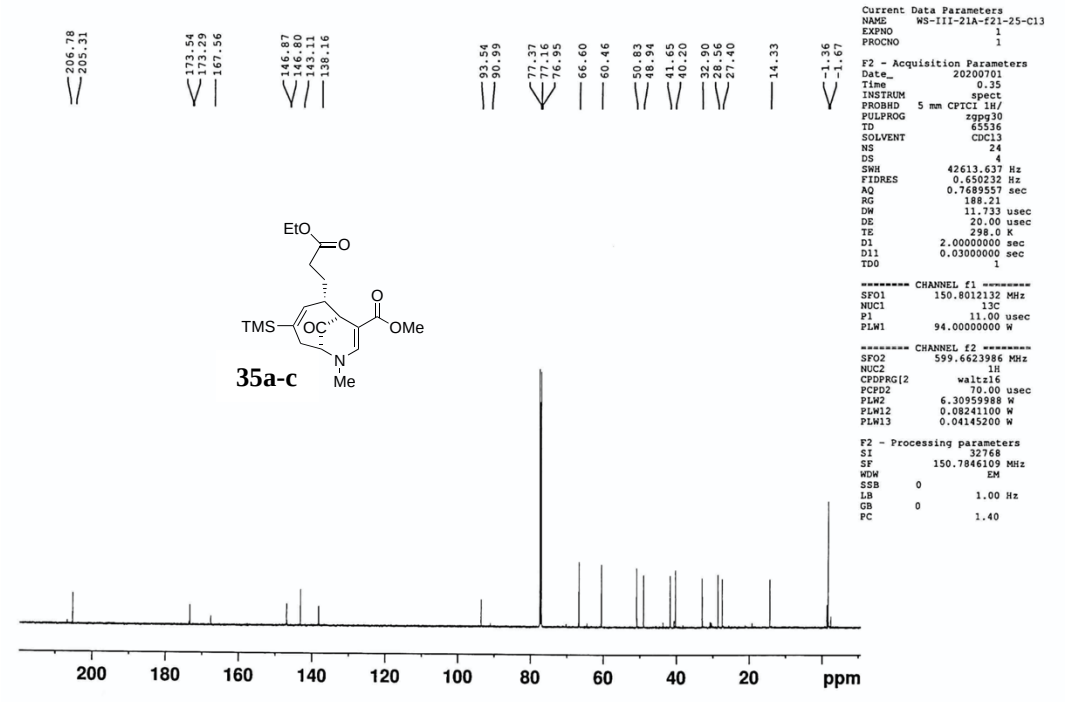
F2 - Acquisition Parameters
Date_              20191017
Time                  12.03
INSTRUM               spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     135
DS                       4
SWH              42613.637 Hz
FIDRES           0.650232 Hz
AQ               0.7689557 sec
RG                   188.21
DW                11.733 usec
DE                20.00 usec
TE                298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1          150.8012132 MHz
NUC1                    13C
P1                  11.00 usec
PLW1          94.00000000 W

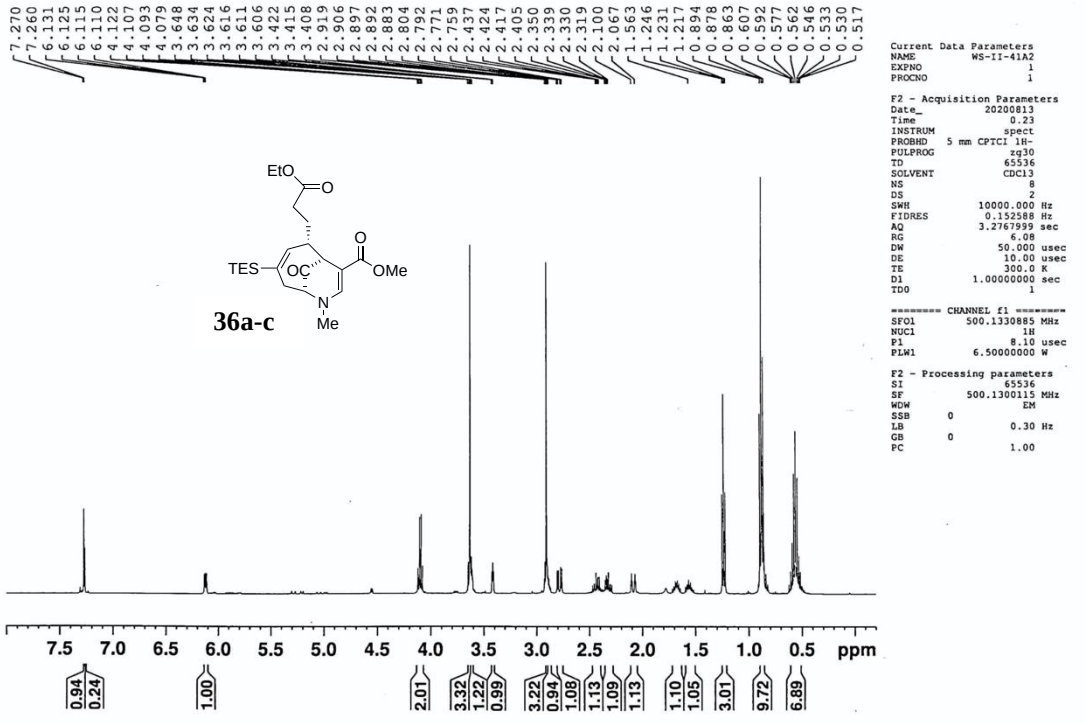
======== CHANNEL f2 ========
SFO2          599.6623986 MHz
NUC2                    1H
CPDPRG[2            waltz16
PCPD2               70.00 usec
PLW2           6.30959988 W
PLW12          0.08241100 W
PLW13          0.04145200 W

F2 - Processing parameters
SI                   32768
SF            150.7846078 MHz
WDW                     EM
SSB       0
LB                   1.00 Hz
GB        0
PC                   1.40
```


WS-III-21A2
7.277
7.260
6.155
6.150
6.142
6.137
4.111
4.100
4.099
4.088
4.076
3.644
3.640
3.633
3.626
3.617
3.614
3.413
3.407
3.401
2.916
2.895
2.883
2.856
2.850
2.825
2.815
2.797
2.787
2.437
2.427
2.421
2.411
2.321
2.312
2.305
2.295
2.114
2.086
1.241
1.230
1.218
0.061
0.042
EtO
O
O
TMS
OC
OMe
N
Me
35a-c
Current Data Parameters
NAME WS-III-21A2
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200731
Time 1.20
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 12.91
DW 41.600 usec
DE 30.00 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 599.6637031 MHz
NUC1 1H
P1 8.35 usec
PLW1 6.30959988 W
F2 - Processing parameters
SI 65536
SF 599.6600154 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7
6
5
4
3
2
1
ppm
0.09
0.95
1.00
2.34
0.56
3.66
0.50
0.98
0.25
3.09
0.46
0.99
1.13
1.16
1.06
1.10
1.08
1.04
3.58
0.94
9.08


WS-III-21A-f21-25-C13
206.78
205.31
173.54
173.29
167.56
146.87
146.80
143.11
138.16
93.54
90.99
77.37
77.16
76.95
66.60
60.46
50.83
48.94
41.65
40.20
32.90
28.56
27.40
14.33
-1.36
-1.67
EtO
O
O
TMS
OC
OMe
N
Me
35a-c
Current Data Parameters
NAME WS-III-21A-f21-25-C13
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200701
Time 0.35
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 24
DS 4
SWH 42613.637 Hz
FIDRES 0.650232 Hz
AQ 0.7689957 sec
RG 188.21
DW 11.733 usec
DE 20.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.8012132 MHz
NUC1 13C
P1 11.00 usec
PLW1 94.00000000 W
======== CHANNEL f2 ========
SFO2 599.6623986 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 6.30959988 W
PLW12 0.08241100 W
PLW13 0.04145200 W
F2 - Processing parameters
SI 32768
SF 150.7846109 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
ppm

WS-II-41A2



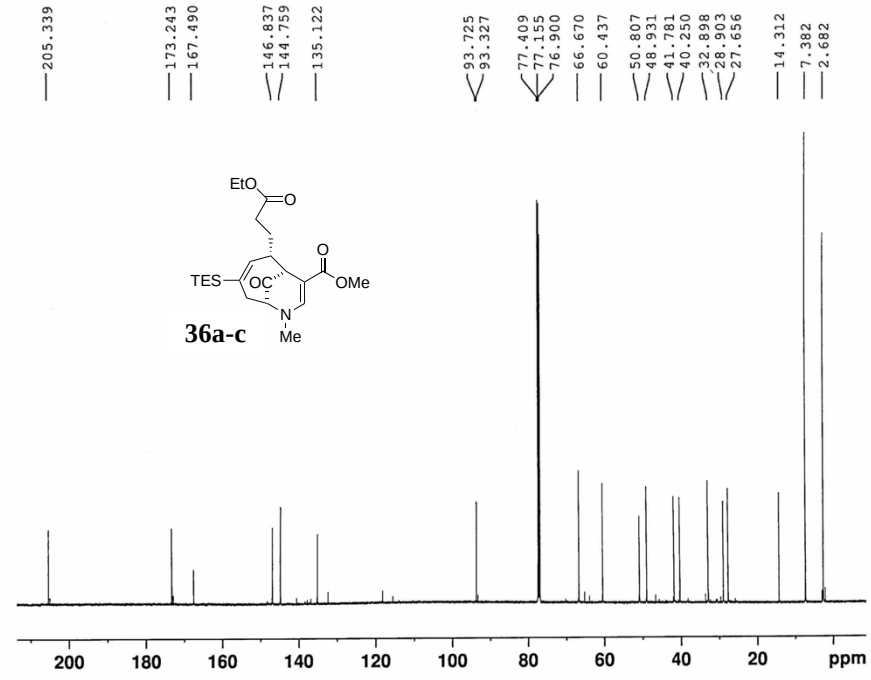

```
Current Data Parameters
NAME                  WS-II-41A2
EXPNO                          1
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20200813
Time                        0.23
INSTRUM                     spect
PROBHD    5 mm CPTCI 1H-
PULPROG                     zg30
TD                         65536
SOLVENT                    CDCl3
NS                             8
DS                             2
SWH                    10000.000 Hz
FIDRES                  0.152588 Hz
AQ                      3.2767999 sec
RG                          6.08
DW                        50.000 usec
DE                        10.00 usec
TE                        300.0 K
D1                     1.00000000 sec
TD0                            1

======== CHANNEL f1 ========
SFO1                  500.1330885 MHz
NUC1                          1H
P1                          8.10 usec
PLW1                   6.50000000 W

F2 - Processing parameters
SI                         65536
SF                    500.1300115 MHz
WDW                           EM
SSB                0
LB                          0.30 Hz
GB                 0
PC                          1.00
```

WS-II-41A2-C13




```
Current Data Parameters
NAME              WS-II-41A2-C13
EXPNO                          1
PROCNO                         1

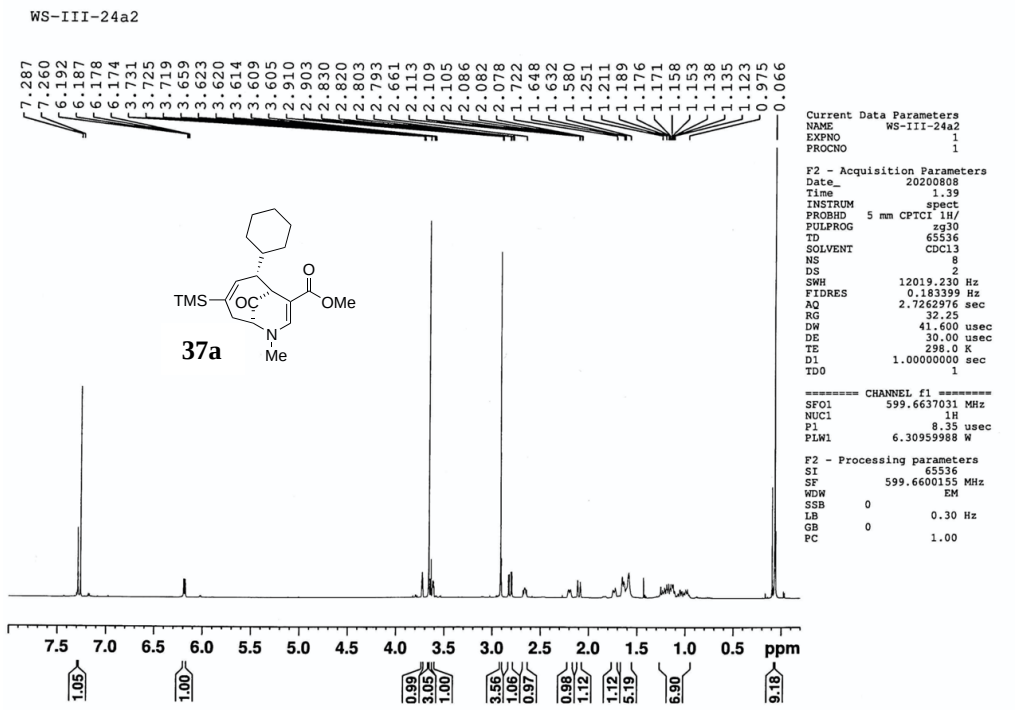
F2 - Acquisition Parameters
Date_                   20200813
Time                        0.41
INSTRUM                     spect
PROBHD    5 mm CPTCI 1H-
PULPROG                  zgpg30
TD                         65536
SOLVENT                    CDCl3
NS                           101
DS                             4
SWH                    29761.904 Hz
FIDRES                  0.454131 Hz
AQ                      1.1010048 sec
RG                        184.57
DW                        16.800 usec
DE                        35.00 usec
TE                        300.0 K
D1                     2.00000000 sec
D11                    0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
SFO1                  125.7703637 MHz
NUC1                          13C
P1                         11.29 usec
PLW1                  69.00000000 W

======== CHANNEL f2 ========
SFO2                  500.1320005 MHz
NUC2                          1H
CPDPRG[2                waltz16
PCPD2                      80.00 usec
PLW2                   6.50000000 W
PLW12                  0.06663500 W
PLW13                  0.03351700 W

F2 - Processing parameters
SI                         32768
SF                    125.7577756 MHz
WDW                           EM
SSB                0
LB                          1.00 Hz
GB                 0
PC                          1.40
```

WS-III-24a2



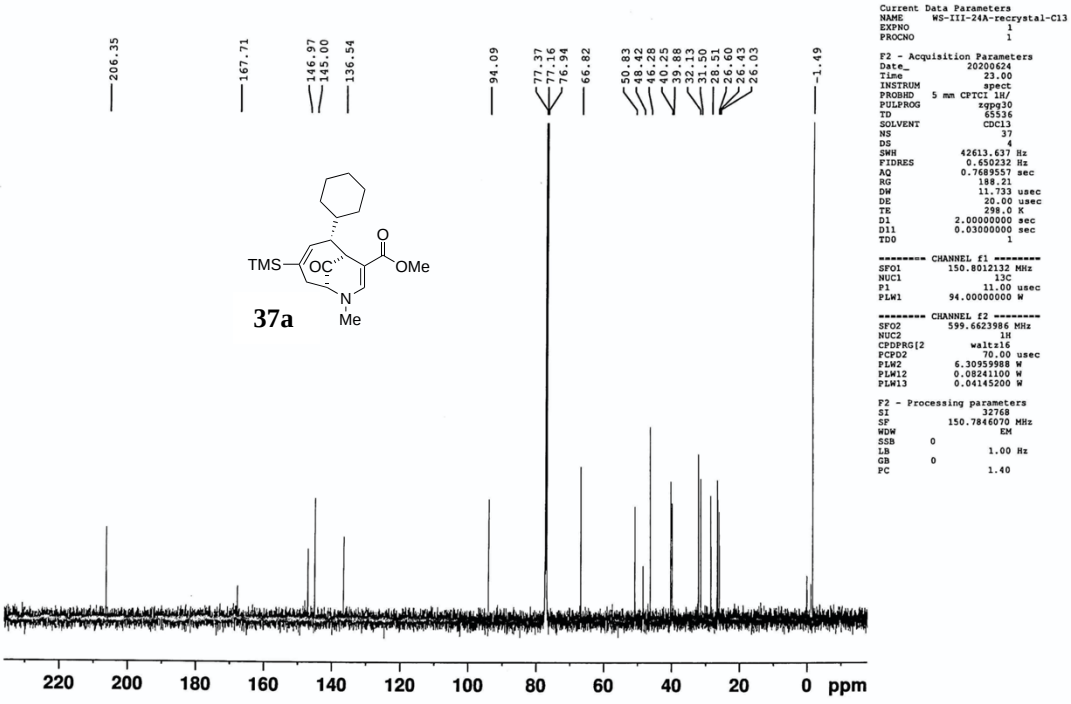

```
Current Data Parameters
NAME          WS-III-24a2
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_              20200808
Time                   1.39
INSTRUM               spect
PROBHD    5 mm CPTCI 1H/
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH              12019.230 Hz
FIDRES               0.183399 Hz
AQ                2.7262976 sec
RG                     32.25
DW                   41.600 usec
DE                   30.00 usec
TE                   298.0 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1           599.6637031 MHz
NUC1                     1H
P1                    8.35 usec
PLW1           6.30959988 W

F2 - Processing parameters
SI                   65536
SF             599.6600155 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

WS-III-24A-recrystal-C13




```
Current Data Parameters
NAME      WS-III-24A-recrystal-C13
EXPNO                   1
PROCNO                  1

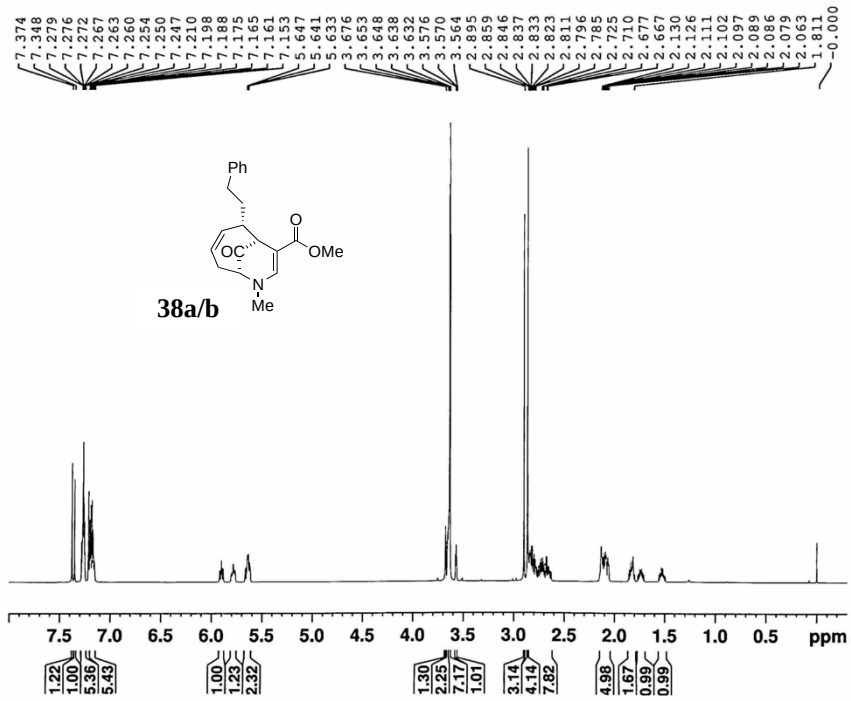
F2 - Acquisition Parameters
Date_              20200624
Time                  23.00
INSTRUM               spect
PROBHD    5 mm CPTCI 1H/
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      37
DS                       4
SWH              42613.637 Hz
FIDRES               0.650232 Hz
AQ                0.7689557 sec
RG                    188.21
DW                   11.733 usec
DE                   20.00 usec
TE                   298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
SFO1           150.8012132 MHz
NUC1                     13C
P1                   11.00 usec
PLW1          94.00000000 W

======== CHANNEL f2 ========
SFO2           599.6623986 MHz
NUC2                     1H
CPDPRG[2            waltz16
PCPD2                70.00 usec
PLW2           6.30959988 W
PLW12          0.08241100 W
PLW13          0.04145200 W

F2 - Processing parameters
SI                   32768
SF             150.7846070 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

WS-II-35B2



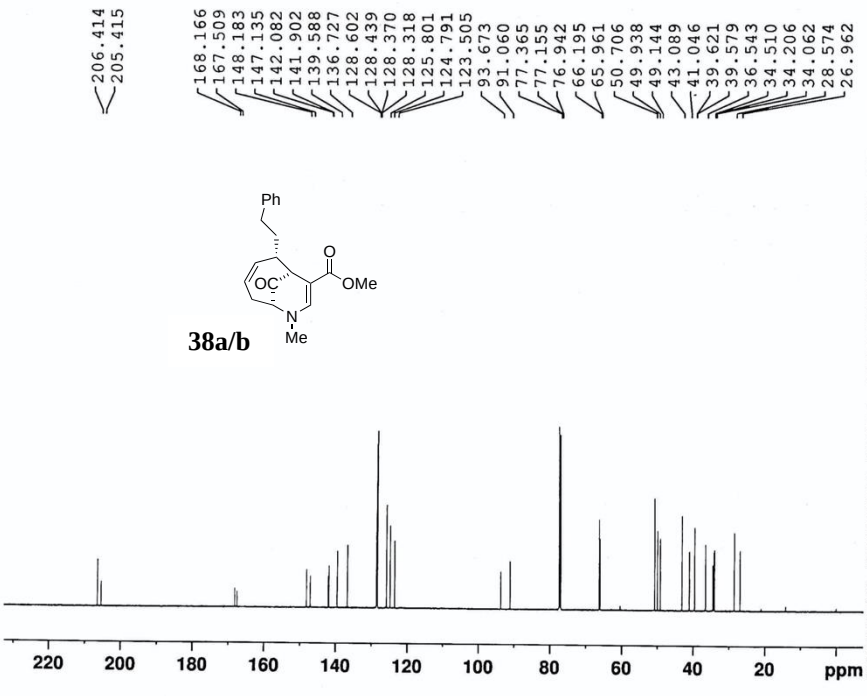

```
Current Data Parameters
NAME            WS-II-35B2
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20200625
Time                 0.08
INSTRUM             spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH            12019.230 Hz
FIDRES          0.183399 Hz
AQ              2.7262976 sec
RG                  10.15
DW                 41.600 usec
DE                 30.00 usec
TE                298.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          599.6637031 MHz
NUC1                    1H
P1                   8.35 usec
PLW1           6.30959988 W

F2 - Processing parameters
SI                     65536
SF            599.6600135 MHz
WDW                    EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

WS-II-35B-C13




```
Current Data Parameters
NAME       WS-II-35B-C13
EXPNO                  1
PROCNO                 1

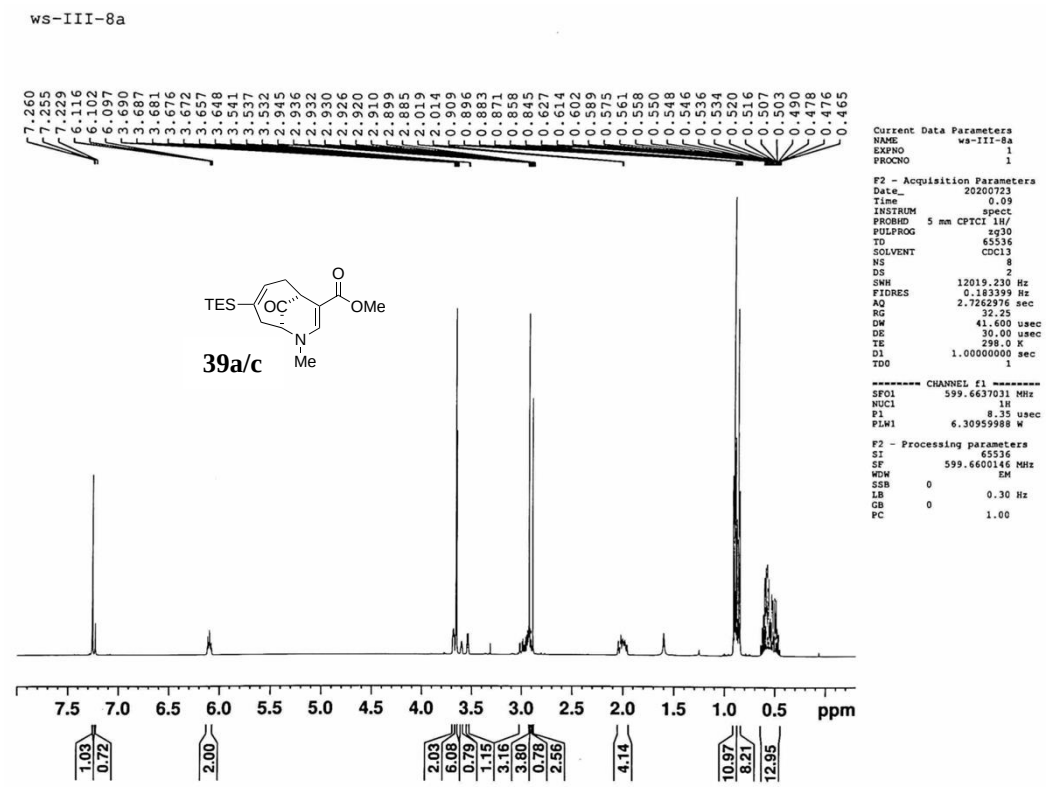
F2 - Acquisition Parameters
Date_           20191218
Time               12.26
INSTRUM           spect
PROBHD   5 mm CPTCI 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   28
DS                    4
SWH           42613.637 Hz
FIDRES         0.650232 Hz
AQ             0.7689557 sec
RG                188.21
DW                11.733 usec
DE                20.00 usec
TE                298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         150.8012132 MHz
NUC1                   13C
P1                 11.00 usec
PLW1          94.00000000 W

======== CHANNEL f2 ========
SFO2         599.6623986 MHz
NUC2                   1H
CPDPRG[2         waltz16
PCPD2              70.00 usec
PLW2           6.30959988 W
PLW12          0.08241100 W
PLW13          0.04145200 W

F2 - Processing parameters
SI                    32768
SF           150.7846251 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
```

ws-III-8a



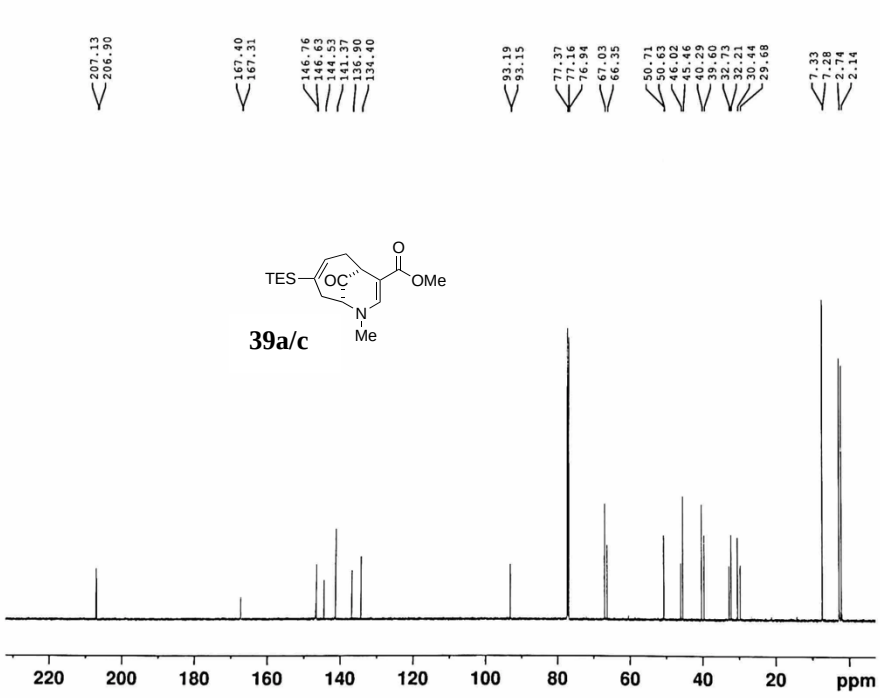
Current Data Parameters
NAME ws-III-8a
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200723
Time 0.09
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 32.25
DW 41.600 usec
DE 30.00 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 599.6637031 MHz
NUC1 1H
P1 8.35 usec
PLW1 6.30959988 W

F2 - Processing parameters
SI 65536
SF 599.6600146 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

WS-III-8B-C13



Current Data Parameters
NAME WS-III-8B-C13
EXPNO 1
PROCNO 1

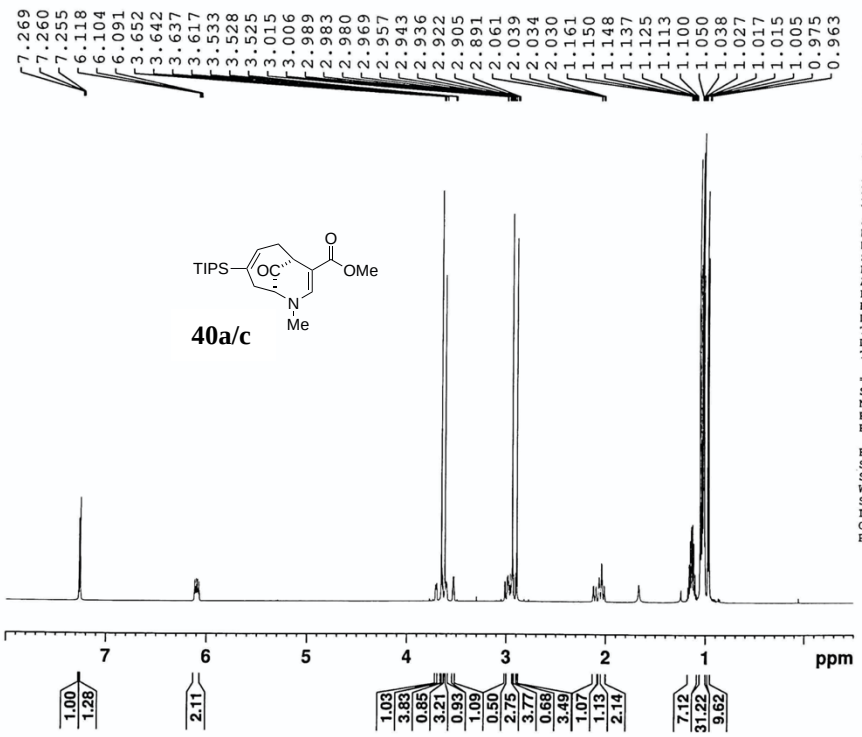
F2 - Acquisition Parameters
Date_ 20200302
Time 16.16
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 14
DS 4
SWH 42613.637 Hz
FIDRES 0.650232 Hz
AQ 0.7689557 sec
RG 188.21
DW 11.733 usec
DE 20.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 150.8012132 MHz
NUC1 13C
P1 11.00 usec
PLW1 94.00000000 W

======== CHANNEL f2 ========
SFO2 599.6623986 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 6.30959988 W
PLW12 0.08241100 W
PLW13 0.04145200 W

F2 - Processing parameters
SI 32768
SF 150.7846168 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

WS-III-28A1



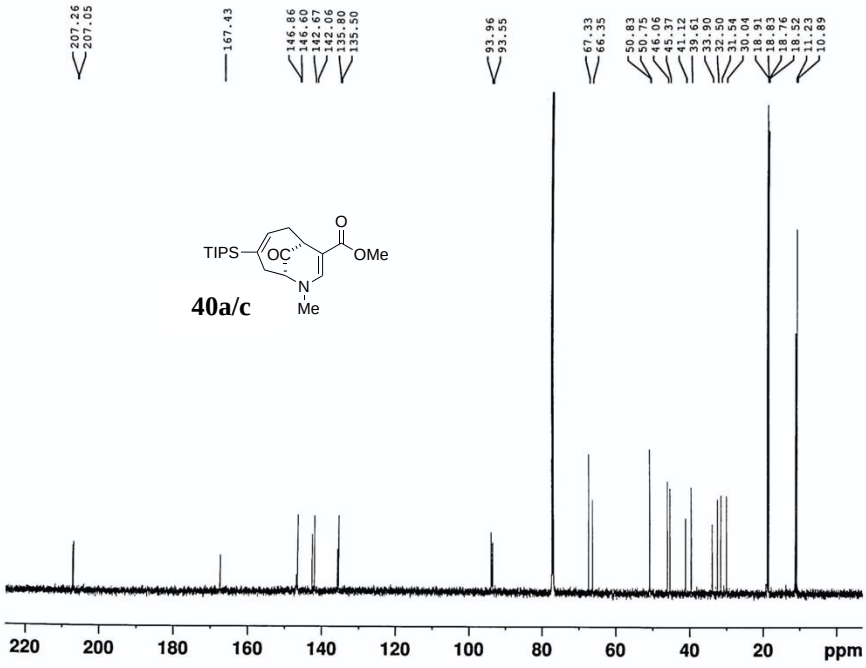

```
Current Data Parameters
NAME          WS-III-28A1
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20200711
Time                1.40
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                     8
DS                     2
SWH            12019.230 Hz
FIDRES             0.183399 Hz
AQ             2.7262976 sec
RG                 18.08
DW                 41.600 usec
DE                 30.00 usec
TE                 298.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          599.6637031 MHz
NUC1                  1H
P1                 8.35 usec
PLW1           6.30959988 W

F2 - Processing parameters
SI                 65536
SF            599.6600141 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

WS-III-28A-C13




```
Current Data Parameters
NAME       WS-III-28A-C13
EXPNO                   1
PROCNO                  1

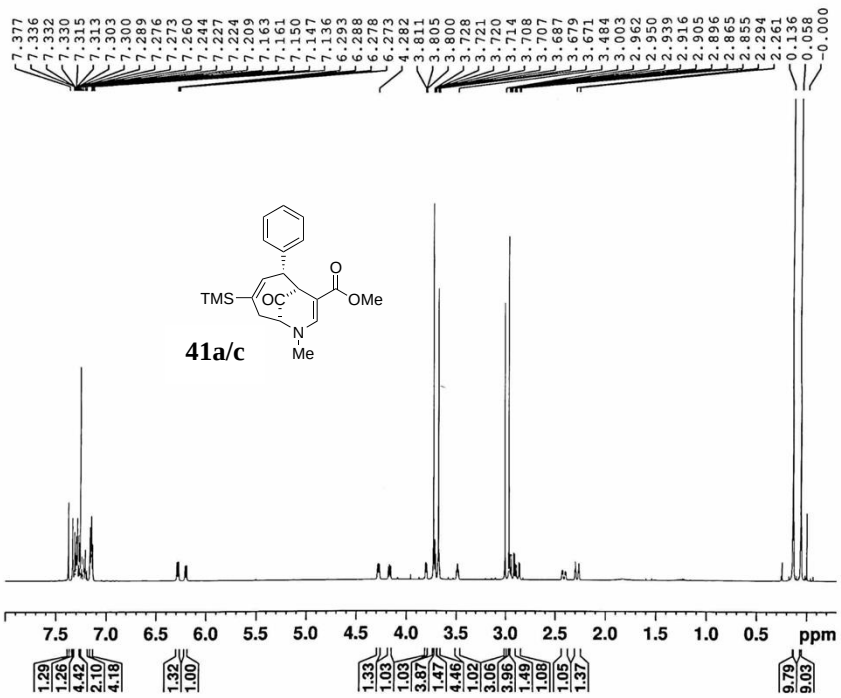
F2 - Acquisition Parameters
Date_           20200703
Time                0.46
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    72
DS                     4
SWH            42613.637 Hz
FIDRES             0.650232 Hz
AQ             0.7689557 sec
RG                 188.21
DW                 11.733 usec
DE                 20.00 usec
TE                 298.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          150.8012132 MHz
NUC1                  13C
P1                11.00 usec
PLW1          94.00000000 W

======== CHANNEL f2 ========
SFO2          599.6623986 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2             70.00 usec
PLW2           6.30959988 W
PLW12          0.08241100 W
PLW13          0.04145200 W

F2 - Processing parameters
SI                 32768
SF            150.7846082 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

WS-III-48A-f25



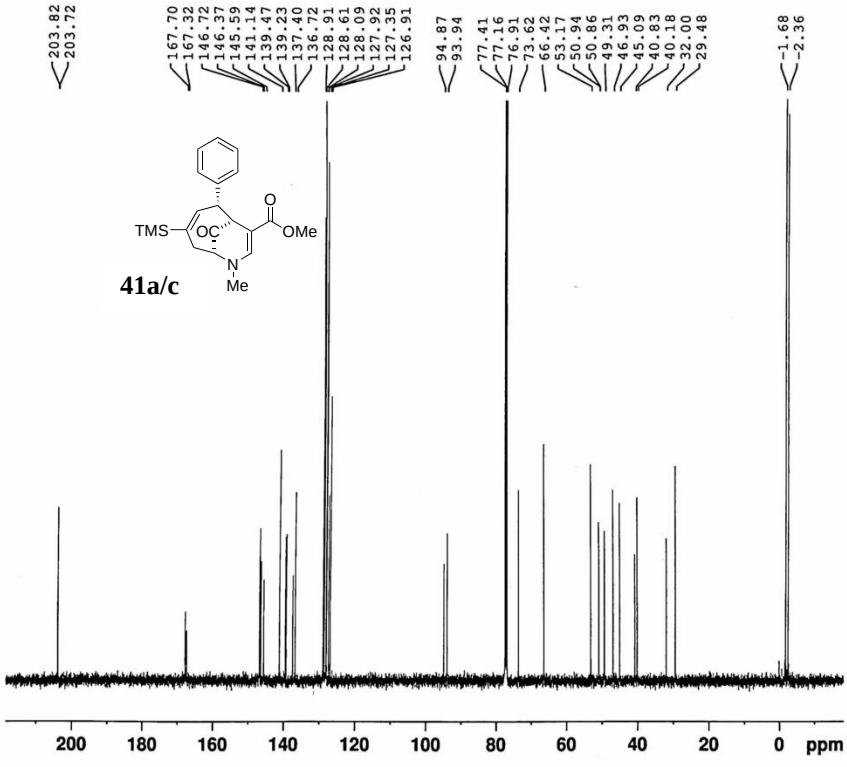

```
Current Data Parameters
NAME      WS-III-48A-f25
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20200919
Time                3.41
INSTRUM            spect
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH         10000.000 Hz
FIDRES          0.152588 Hz
AQ              3.2767999 sec
RG                  7.08
DW                 50.000 usec
DE                 10.00 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          500.1330885 MHz
NUC1                  1H
P1                  8.10 usec
PLW1          6.50000000 W

F2 - Processing parameters
SI                 65536
SF            500.1300114 MHz
WDW                   EM
SSB          0
LB                  0.30 Hz
GB           0
PC                  1.00
```

WS-III-48A-f25-C13




```
Current Data Parameters
NAME      WS-III-48A-f25-C13
EXPNO                  2
PROCNO                 1

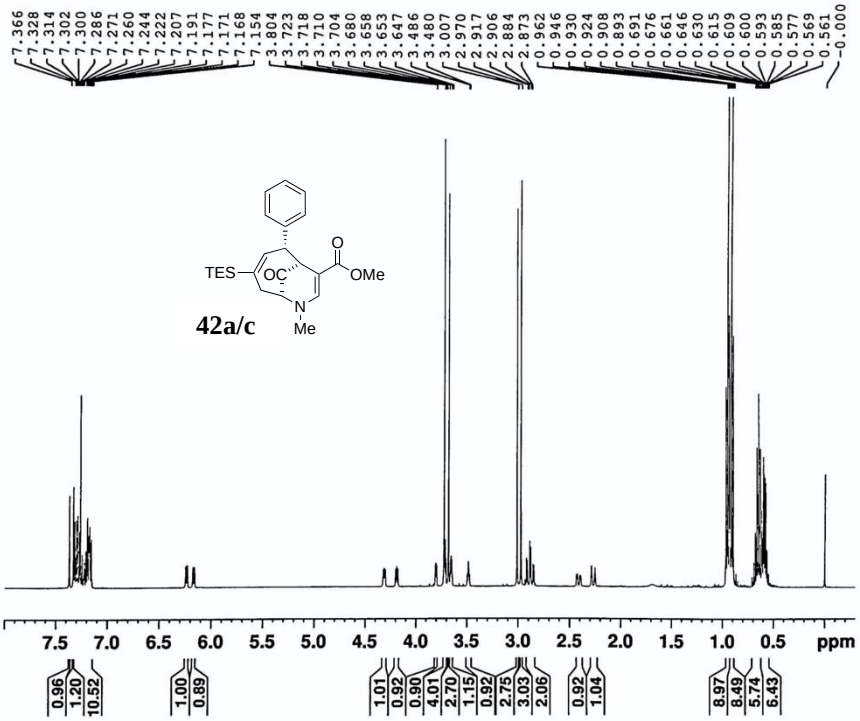
F2 - Acquisition Parameters
Date_           20200919
Time                3.50
INSTRUM            spect
PROBHD   5 mm CPTCI 1H-
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    33
DS                     4
SWH         29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                184.57
DW                16.800 use
DE                35.00 use
TE                300.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1          125.7703637 MHz
NUC1                  13C
P1                 11.29 use
PLW1          69.00000000 W

======== CHANNEL f2 ========
SFO2          500.1320005 MHz
NUC2                  1H
CPDPRG[2          waltz16
PCPD2              80.00 use
PLW2          6.50000000 W
PLW12         0.06663500 W
PLW13         0.03351700 W

F2 - Processing parameters
SI                 32768
SF            125.7577770 MHz
WDW                   EM
SSB          0
LB                  1.00 Hz
GB           0
PC                  1.40
```

WS-III-47B-f26



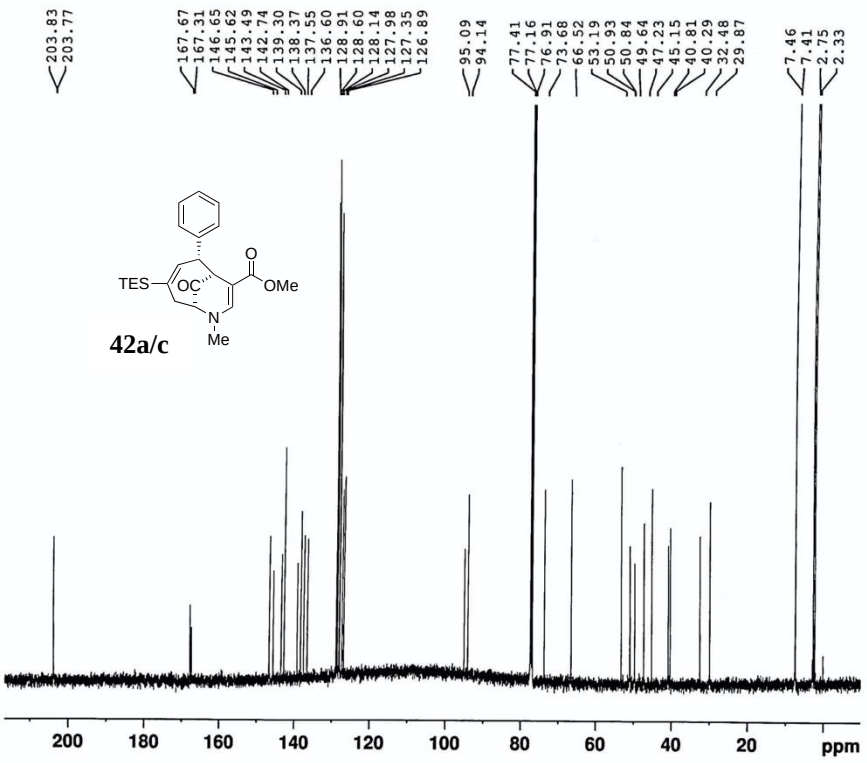

```
Current Data Parameters
NAME      WS-III-47B-f26
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20200919
Time               2.54
INSTRUM           spect
PROBHD   5 mm CPTCI 1H-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH          10000.000 Hz
FIDRES           0.152588 Hz
AQ           3.2767999 sec
RG                7.08
DW               50.000 usec
DE               10.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1       500.1330885 MHz
NUC1               1H
P1                8.10 usec
PLW1       6.50000000 W

F2 - Processing parameters
SI               65536
SF          500.1300116 MHz
WDW                EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

WS-III-47B-f26-C13




```
Current Data Parameters
NAME      WS-III-47B-f26-C13
EXPNO                 2
PROCNO                1

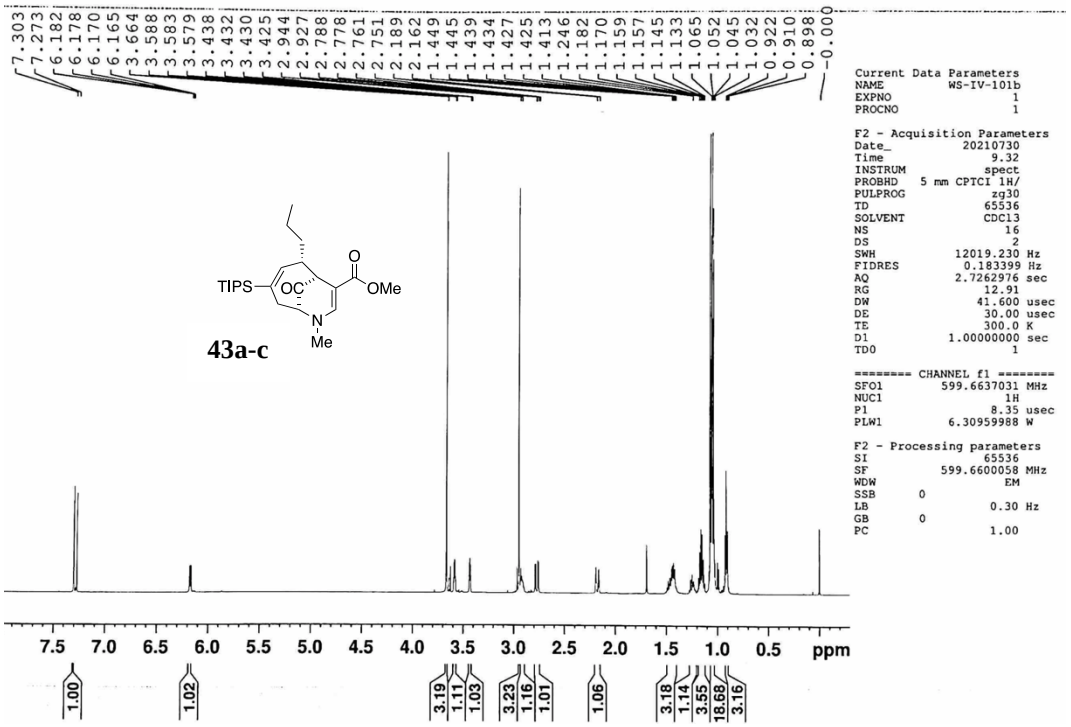
F2 - Acquisition Parameters
Date_          20200919
Time               3.07
INSTRUM           spect
PROBHD   5 mm CPTCI 1H-
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS                  45
DS                   4
SWH          29761.904 Hz
FIDRES           0.454131 Hz
AQ           1.1010048 sec
RG                184.57
DW               16.800 use
DE               35.00 use
TE                300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1       125.7703637 MHz
NUC1               13C
P1               11.29 use
PLW1       69.00000000 W

======== CHANNEL f2 ========
SFO2       500.1320005 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2             80.00 use
PLW2        6.50000000 W
PLW12       0.06663500 W
PLW13       0.03351700 W

F2 - Processing parameters
SI               32768
SF          125.7577755 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

WS-IV-101b



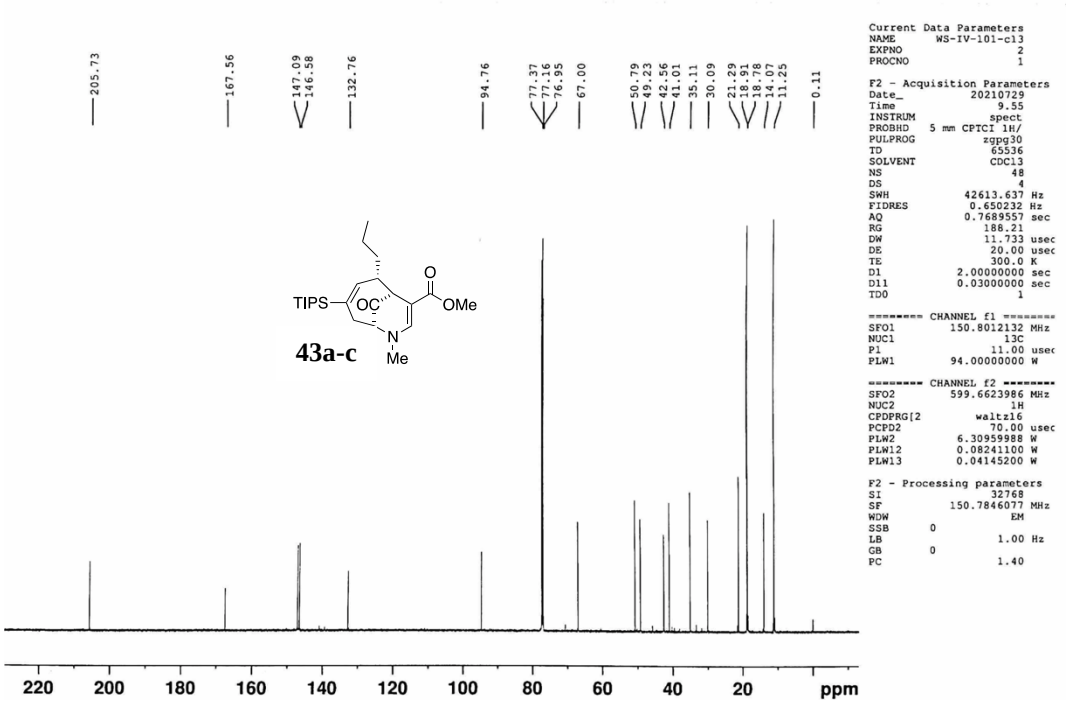

```
Current Data Parameters
NAME          WS-IV-101b
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20210730
Time                9.32
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           12019.230 Hz
FIDRES         0.183399 Hz
AQ             2.7262976 sec
RG                12.91
DW               41.600 usec
DE               30.00 usec
TE               300.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         599.6637031 MHz
NUC1                1H
P1                8.35 usec
PLW1          6.30959988 W

F2 - Processing parameters
SI                 65536
SF           599.6600058 MHz
WDW                   EM
SSB       0
LB                0.30 Hz
GB        0
PC                1.00
```

WS-IV-101-c13




```
Current Data Parameters
NAME       WS-IV-101-c13
EXPNO                  2
PROCNO                 1

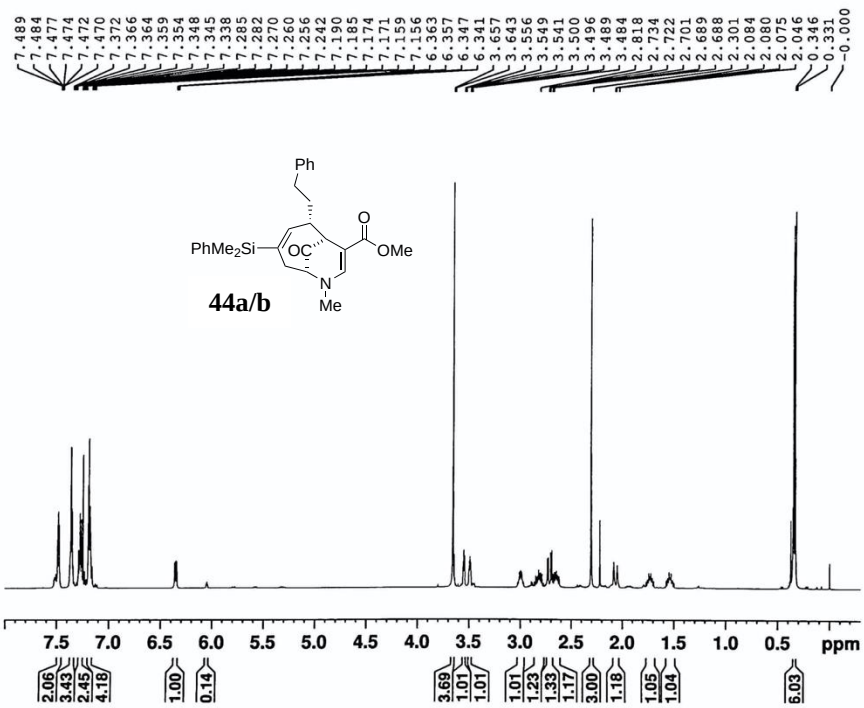
F2 - Acquisition Parameters
Date_           20210729
Time                9.55
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   48
DS                    4
SWH           42613.637 Hz
FIDRES         0.650232 Hz
AQ             0.7689557 sec
RG                188.21
DW               11.733 usec
DE               20.00 usec
TE               300.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         150.8012132 MHz
NUC1                13C
P1               11.00 usec
PLW1          94.00000000 W

======== CHANNEL f2 ========
SFO2         599.6623986 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2            70.00 usec
PLW2          6.30959988 W
PLW12         0.08241100 W
PLW13         0.04145200 W

F2 - Processing parameters
SI                 32768
SF           150.7846077 MHz
WDW                   EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

WS-IV-3



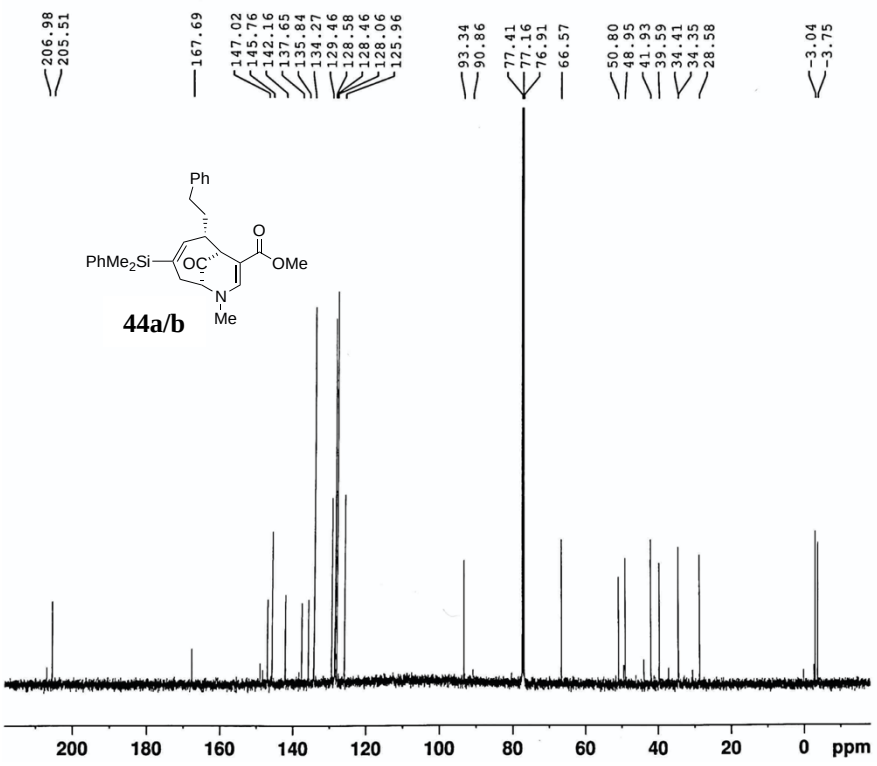

```
Current Data Parameters
NAME                  WS-IV-3
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20201016
Time                  22.50
INSTRUM               spect
PROBHD    5 mm CPTCI 1H-
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH              10000.000 Hz
FIDRES               0.152588 Hz
AQ                3.2767999 sec
RG                    4.78
DW                   50.000 usec
DE                   10.00 usec
TE                   300.1 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1            500.1330885 MHz
NUC1                      1H
P1                     8.10 usec
PLW1             6.50000000 W

F2 - Processing parameters
SI                       65536
SF              500.1300202 MHz
WDW                        EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

WS-III-49B-C13



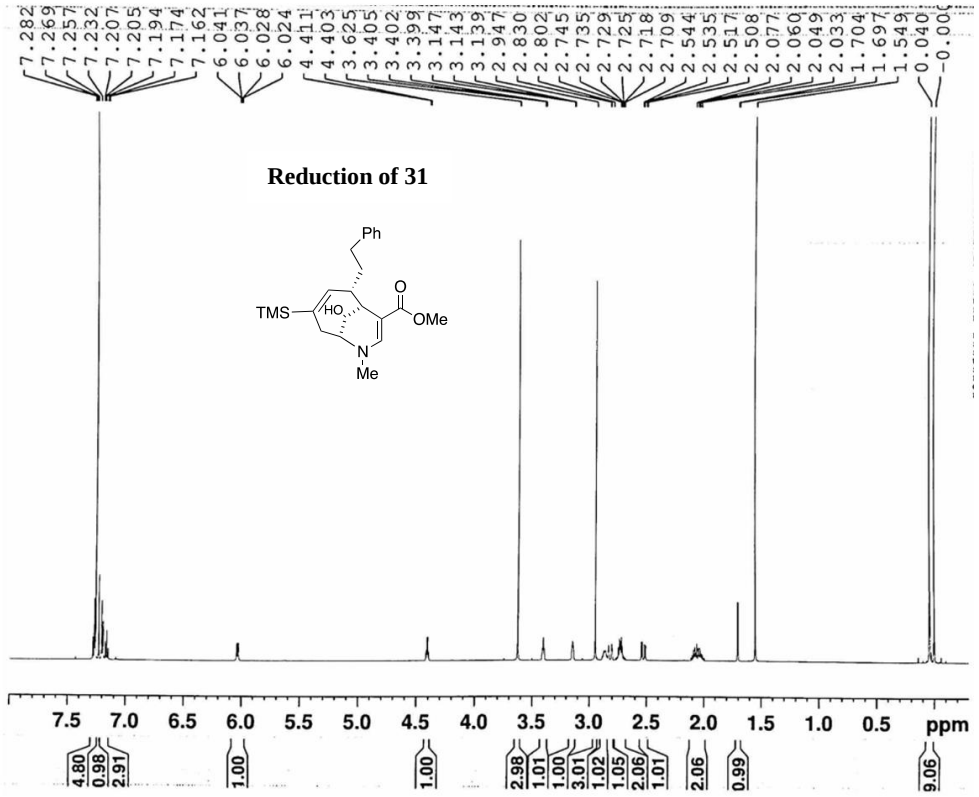

```
Current Data Parameters
NAME          WS-III-49B-C13
EXPNO                      2
PROCNO                     1

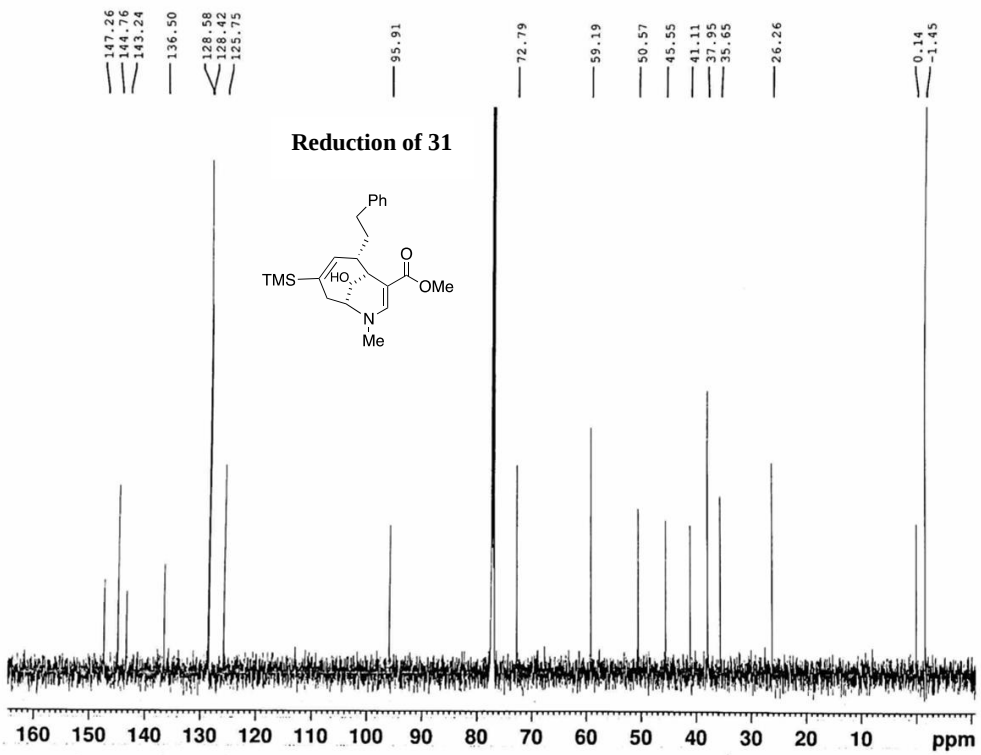
F2 - Acquisition Parameters
Date_              20201003
Time                  1.45
INSTRUM               spect
PROBHD    5 mm CPTCI 1H-
PULPROG            zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      26
DS                       4
SWH              29761.904 Hz
FIDRES               0.454131 Hz
AQ                1.1010048 sec
RG                   184.57
DW                   16.800 use
DE                   35.00 use
TE                   300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                         1

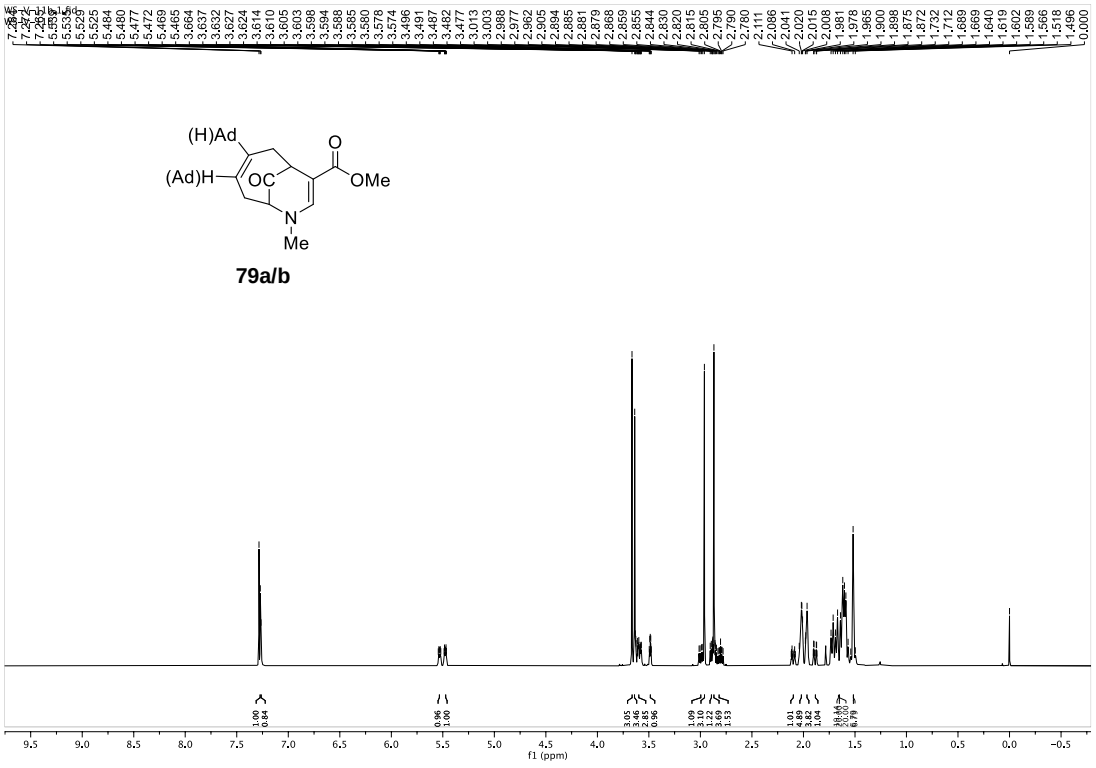
======== CHANNEL f1 ========
SFO1            125.7703637 MHz
NUC1                      13C
P1                    11.29 use
PLW1             69.00000000 W

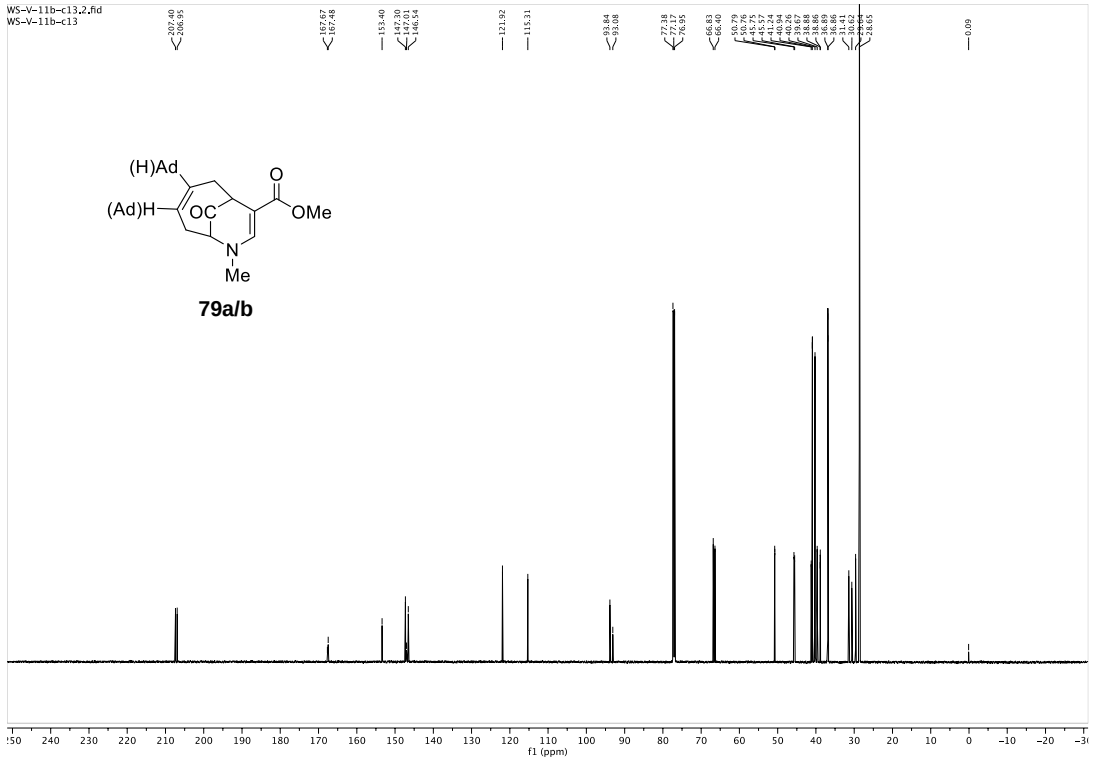
======== CHANNEL f2 ========
SFO2            500.1320005 MHz
NUC2                      1H
CPDPRG[2             waltz16
PCPD2                 80.00 use
PLW2             6.50000000 W
PLW12            0.06663500 W
PLW13            0.03351700 W

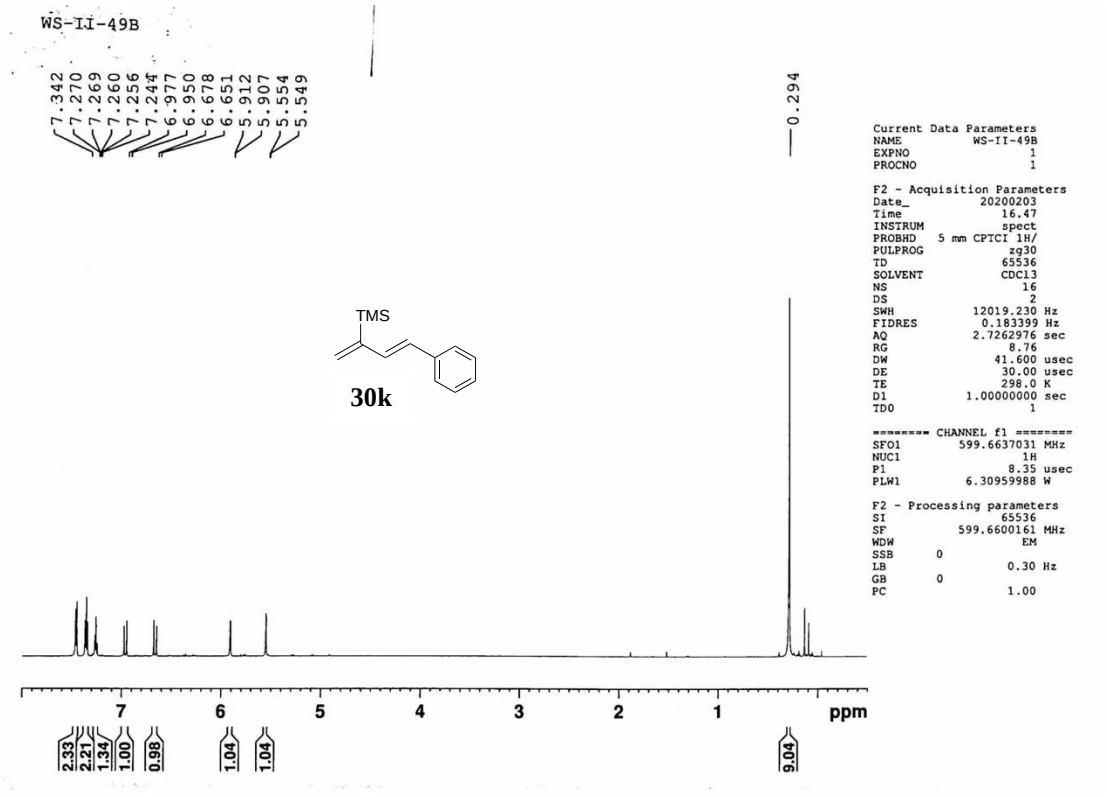
F2 - Processing parameters
SI                       32768
SF              125.7577751 MHz
WDW                        EM
SSB          0
LB                     1.00 Hz
GB           0
PC                     1.40
```

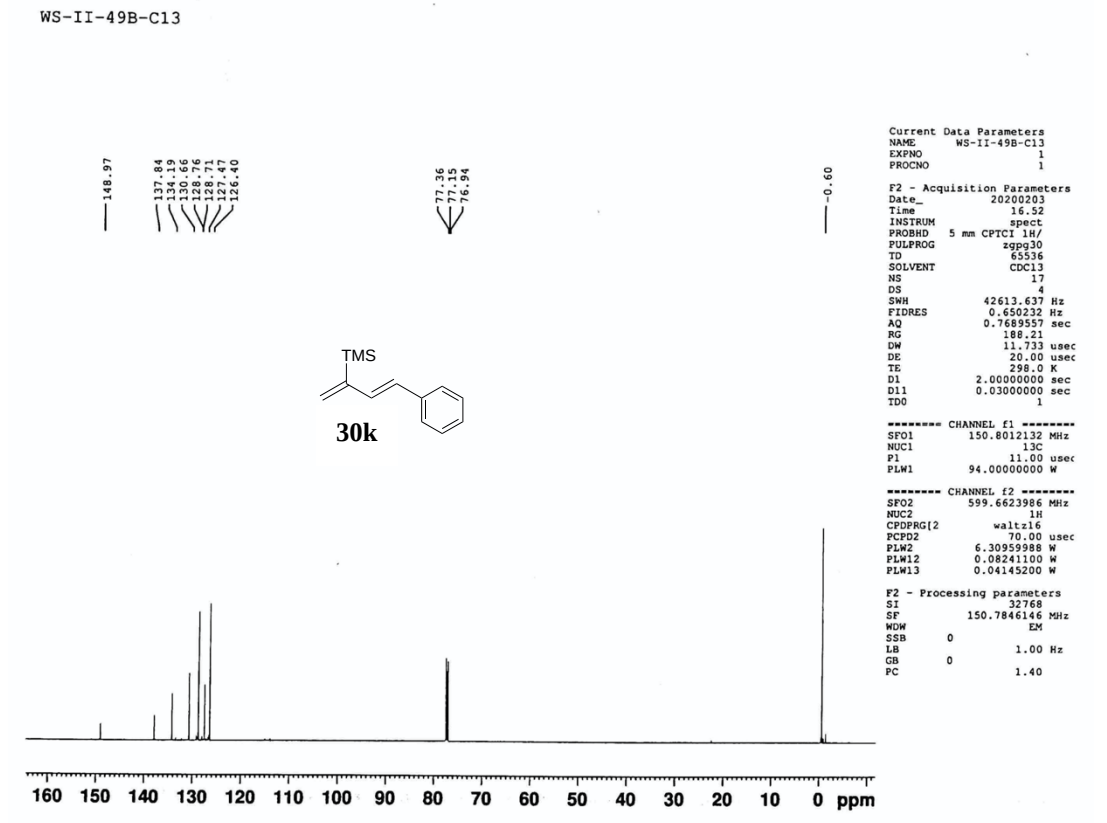

Reduction of 31
Ph
TMS
HO
O
OMe
N
Me
ppm


Reduction of 31
Ph
TMS
HO
O
OMe
N
Me
ppm

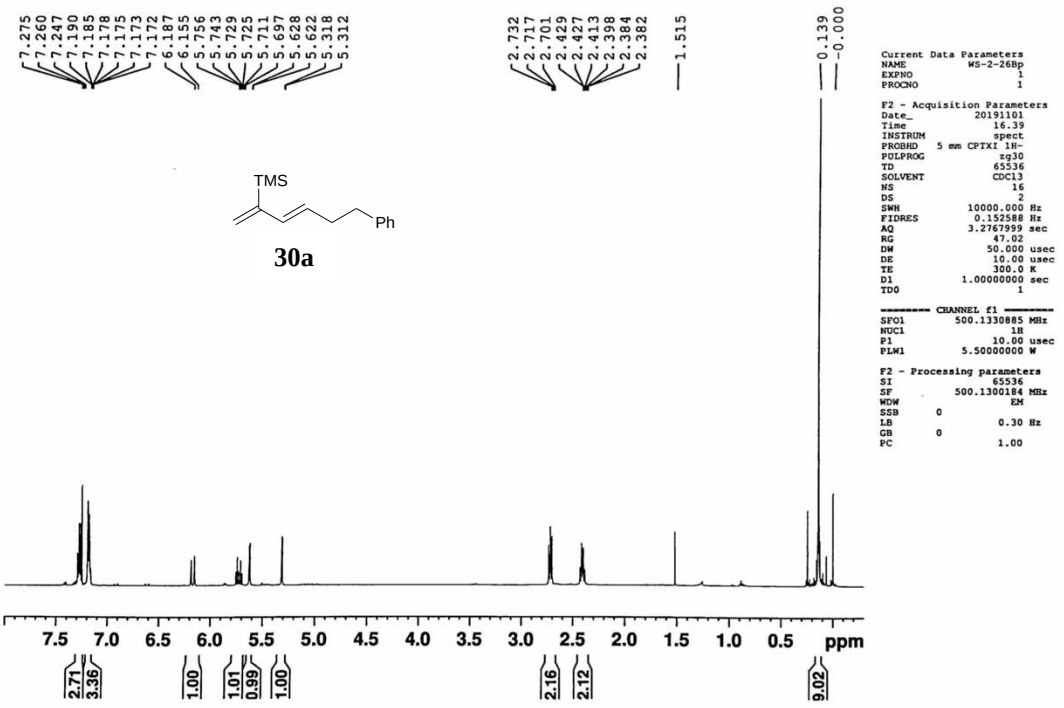

(H)Ad
(Ad)H
OC
O
OMe
N
Me
79a/b
f1 (ppm)


WS-V-11b-c13.2.fid
WS-V-11b-c13
(H)Ad
(Ad)H
OC
O
OMe
N
Me
79a/b
f1 (ppm)


WS-II-49B
7.342
7.270
7.269
7.260
7.256
7.244
6.977
6.950
6.678
6.651
5.912
5.907
5.554
5.549
0.294
TMS
30k
Current Data Parameters
NAME WS-II-49B
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200203
Time 16.47
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 8.76
DW 41.600 usec
DE 30.00 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 599.6637031 MHz
NUC1 1H
P1 8.35 usec
PLW1 6.30959988 W
F2 - Processing parameters
SI 65536
SF 599.6600161 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7
6
5
4
3
2
1
ppm
2.33
2.21
1.34
1.00
0.98
1.04
1.04
9.04


WS-II-49B-C13
148.97
137.84
134.19
130.66
128.76
128.71
127.47
126.40
77.36
77.15
76.94
-0.60
TMS
30k
Current Data Parameters
NAME WS-II-49B-C13
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20200203
Time 16.52
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 17
DS 4
SWH 42613.637 Hz
FIDRES 0.650232 Hz
AQ 0.7689557 sec
RG 188.21
DW 11.733 usec
DE 20.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.8012132 MHz
NUC1 13C
P1 11.00 usec
PLW1 94.00000000 W
======== CHANNEL f2 ========
SFO2 599.6623986 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 6.30959988 W
PLW12 0.08241100 W
PLW13 0.04145200 W
F2 - Processing parameters
SI 32768
SF 150.7846146 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

WS-2-26Bp



30a

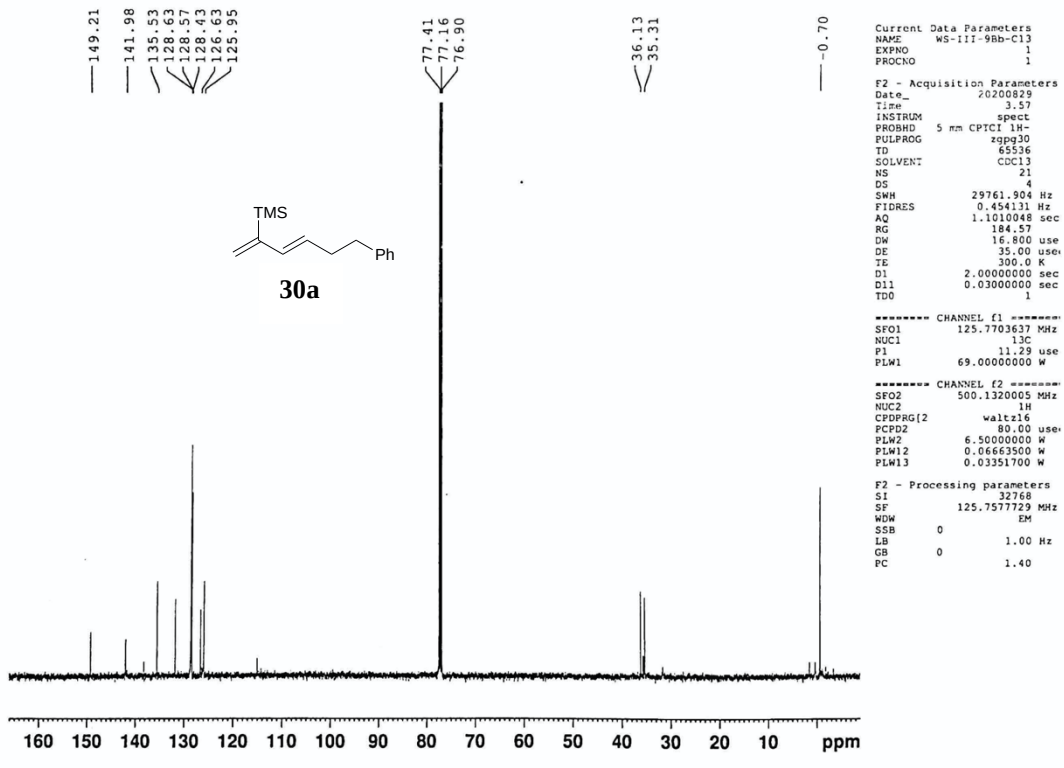
```
Current Data Parameters
NAME            WS-2-26Bp
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_          20191101
Time              16.39
INSTRUM           spect
PROBHD   5 mm CPTXI 1H-
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH          10000.000 Hz
FIDRES           0.152588 Hz
AQ            3.2767999 sec
RG                47.02
DW              50.000 usec
DE              10.00 usec
TE                300.0 K
D1           1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1         500.1330885 MHz
NUC1               1H
P1              10.00 usec
PLW1         5.50000000 W

F2 - Processing parameters
SI                65536
SF           500.1300184 MHz
WDW                EM
SSB       0
LB              0.30 Hz
GB        0
PC              1.00
```

WS-III-9Bb-C13



30a

```
Current Data Parameters
NAME        WS-III-9Bb-C13
EXPNO                   1
PROCNO                  1

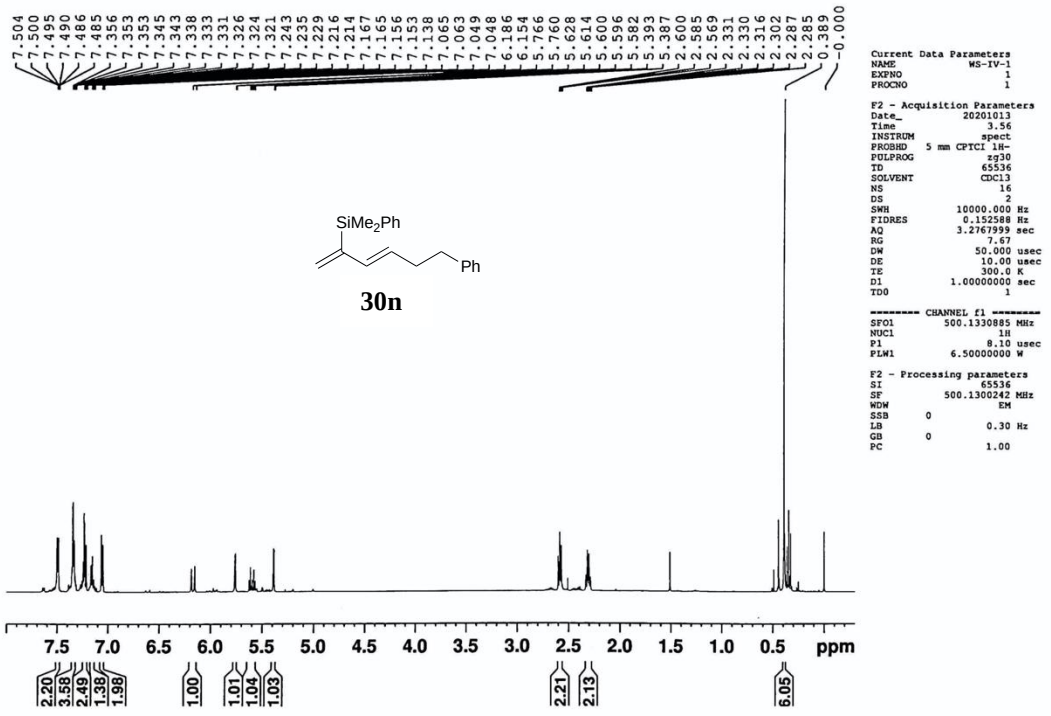
F2 - Acquisition Parameters
Date_          20200829
Time              3.57
INSTRUM           spect
PROBHD   5 mm CPTCI 1H-
PULPROG          zgpg30
TD               65536
SOLVENT          CDCl3
NS                  21
DS                   4
SWH          29761.904 Hz
FIDRES           0.454131 Hz
AQ            1.1010048 sec
RG                184.57
DW              16.800 use
DE              35.00 use
TE                300.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1         125.7703637 MHz
NUC1               13C
P1              11.29 use
PLW1        69.00000000 W

======== CHANNEL f2 ========
SFO2         500.1320005 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2           80.00 use
PLW2         6.50000000 W
PLW12        0.06663500 W
PLW13        0.03351700 W

F2 - Processing parameters
SI                32768
SF           125.7577729 MHz
WDW                EM
SSB       0
LB              1.00 Hz
GB        0
PC              1.40
```

WS-IV-1



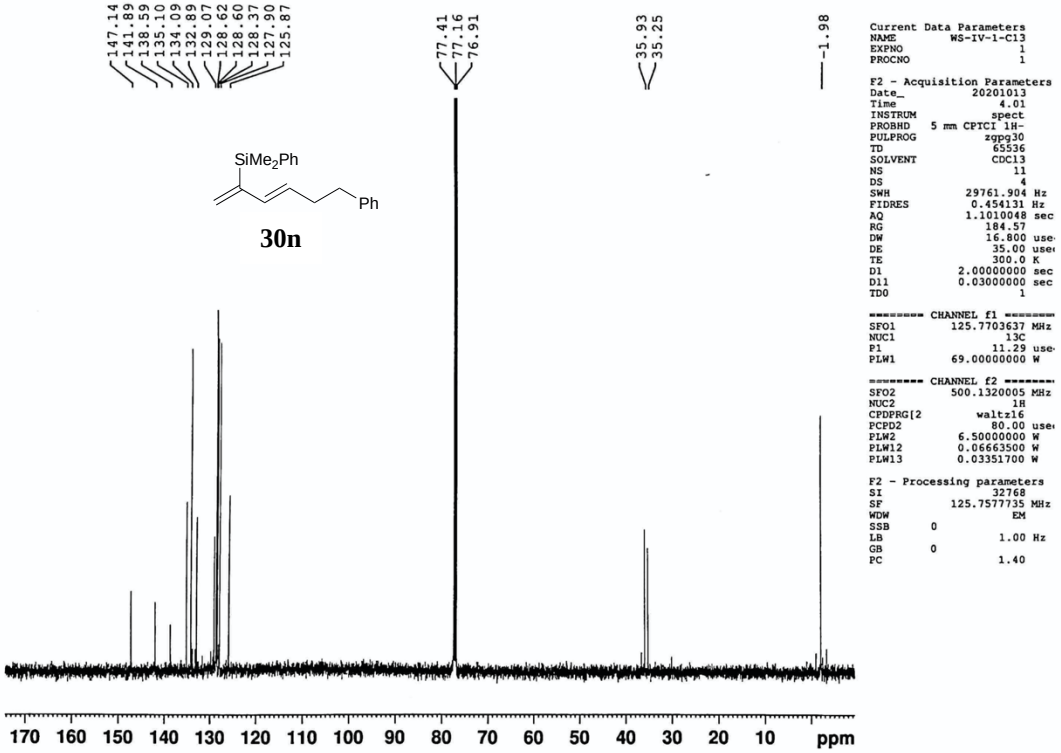

```
Current Data Parameters
NAME                  WS-IV-1
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20201013
Time                   3.56
INSTRUM               spect
PROBHD    5 mm CPTCI 1H-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH             10000.000 Hz
FIDRES              0.152588 Hz
AQ                3.2767999 sec
RG                     7.67
DW                   50.000 usec
DE                   10.00 usec
TE                   300.0 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1            500.1330885 MHz
NUC1                      1H
P1                     8.10 usec
PLW1             6.50000000 W

F2 - Processing parameters
SI                    65536
SF              500.1300242 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

WS-IV-1-C13




```
Current Data Parameters
NAME              WS-IV-1-C13
EXPNO                       1
PROCNO                      1

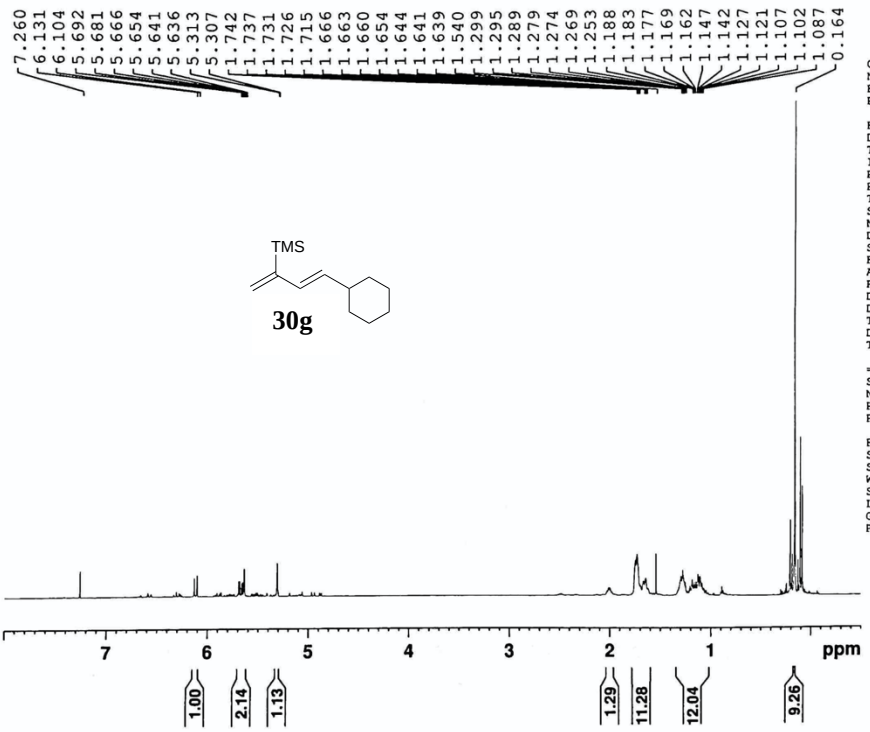
F2 - Acquisition Parameters
Date_              20201013
Time                   4.01
INSTRUM               spect
PROBHD    5 mm CPTCI 1H-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                       11
DS                        4
SWH             29761.904 Hz
FIDRES              0.454131 Hz
AQ                1.1010048 sec
RG                   184.57
DW                   16.800 use
DE                   35.00 use
TE                   300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
SFO1            125.7703637 MHz
NUC1                      13C
P1                    11.29 use
PLW1             69.00000000 W

======== CHANNEL f2 ========
SFO2            500.1320005 MHz
NUC2                      1H
CPDPRG[2             waltz16
PCPD2                 80.00 use
PLW2              6.50000000 W
PLW12             0.06663500 W
PLW13             0.03351700 W

F2 - Processing parameters
SI                    32768
SF              125.7577735 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

WS-III-17B1



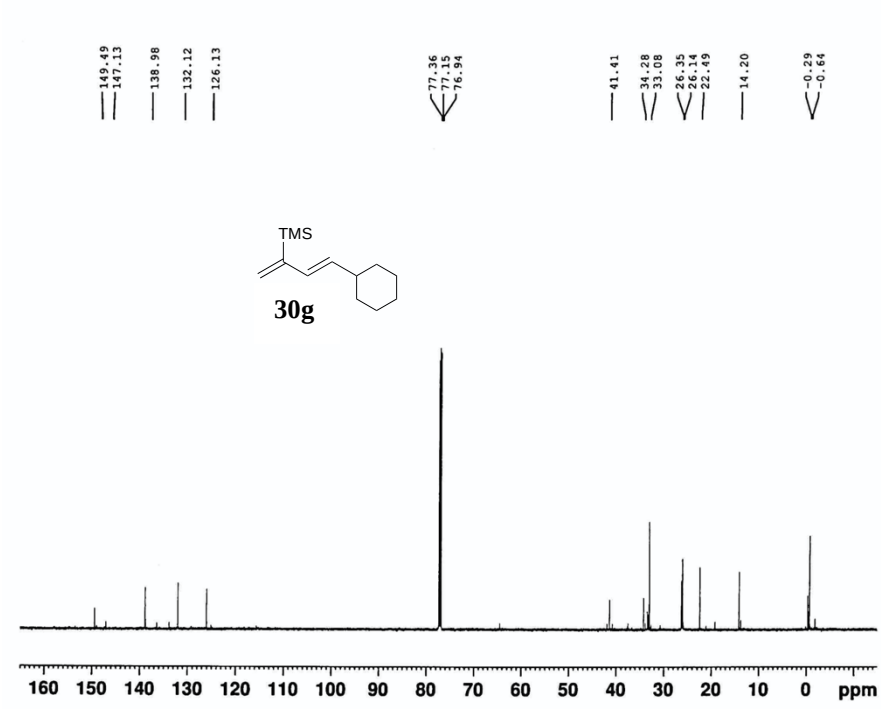

```
Current Data Parameters
NAME          WS-III-17B1
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20200529
Time                0.17
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           12019.230 Hz
FIDRES         0.183399 Hz
AQ            2.7262976 sec
RG                 12.91
DW                41.600 usec
DE                30.00 usec
TE                298.0 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        599.6637031 MHz
NUC1                   1H
P1                 8.35 usec
PLW1          6.30959988 W

F2 - Processing parameters
SI                 65536
SF          599.6600155 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

WS-III-22B-C13




```
Current Data Parameters
NAME      WS-III-22B-C13
EXPNO                   1
PROCNO                  1

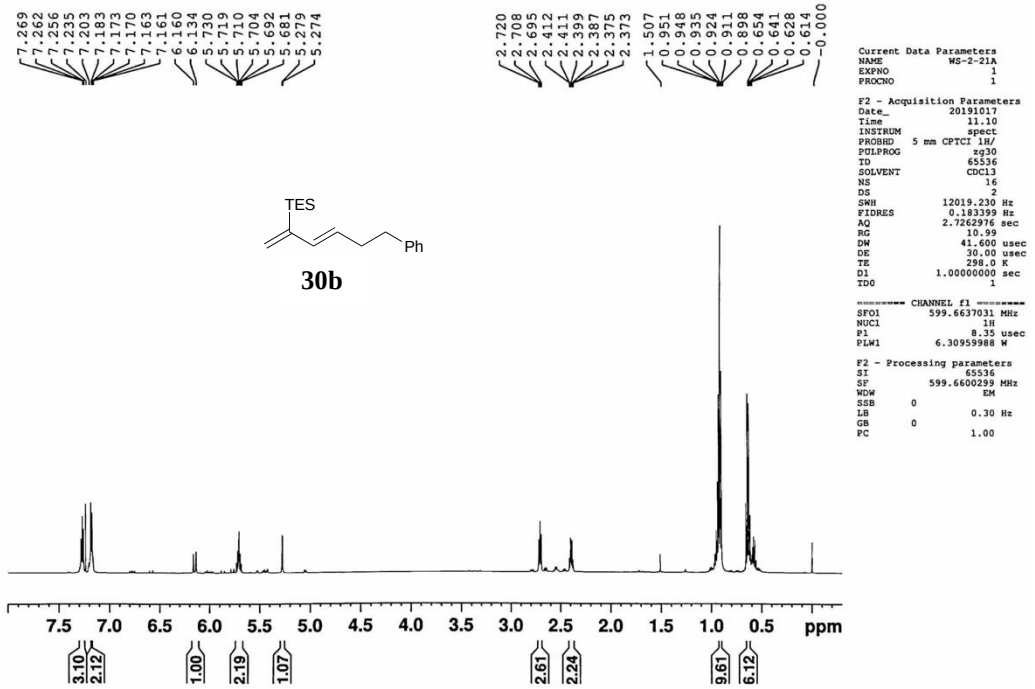
F2 - Acquisition Parameters
Date_           20200612
Time               22.57
INSTRUM            spect
PROBHD   5 mm CPTCI 1H/
PULPROG          zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    13
DS                     4
SWH           42613.637 Hz
FIDRES         0.650232 Hz
AQ            0.7689557 sec
RG                188.21
DW                11.733 usec
DE                20.00 usec
TE                298.0 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1        150.8012132 MHz
NUC1                   13C
P1                11.00 usec
PLW1         94.00000000 W

======== CHANNEL f2 ========
SFO2        599.6623986 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2             70.00 usec
PLW2          6.30959988 W
PLW12         0.08241100 W
PLW13         0.04145200 W

F2 - Processing parameters
SI                 32768
SF          150.7846057 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

WS-2-21A



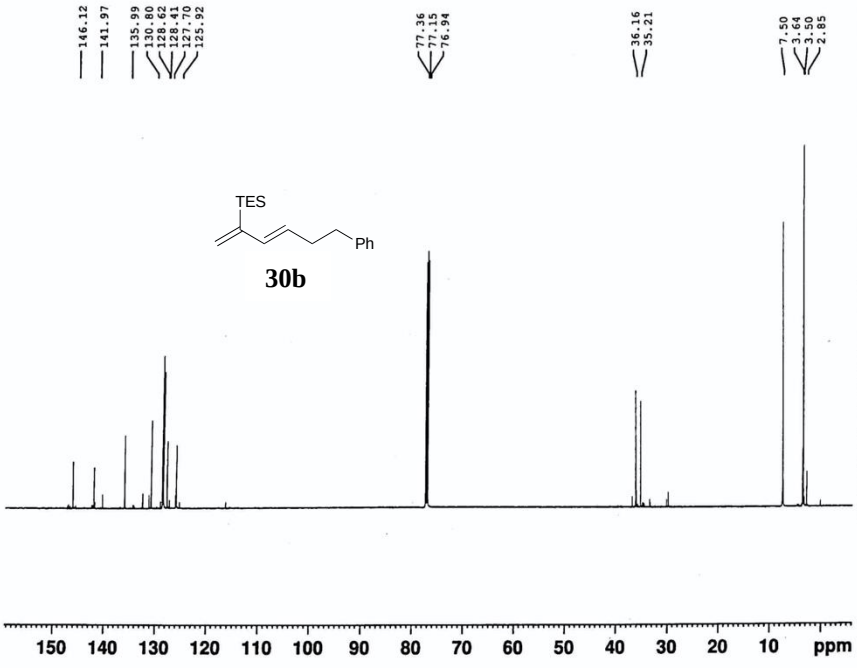

```
Current Data Parameters
NAME                  WS-2-21A
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20191017
Time                     11.10
INSTRUM                  spect
PROBHD    5 mm CPTCI 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                  12019.230 Hz
FIDRES                0.183399 Hz
AQ                    2.7262976 sec
RG                       10.99
DW                      41.600 usec
DE                      30.00 usec
TE                      298.0 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1                599.6637031 MHz
NUC1                        1H
P1                        8.35 usec
PLW1                6.30959988 W

F2 - Processing parameters
SI                      65536
SF                  599.6600299 MHz
WDW                         EM
SSB                  0
LB                        0.30 Hz
GB                   0
PC                        1.00
```

WS-2-21A-C13




```
Current Data Parameters
NAME                WS-2-21A-C13
EXPNO                        1
PROCNO                       1

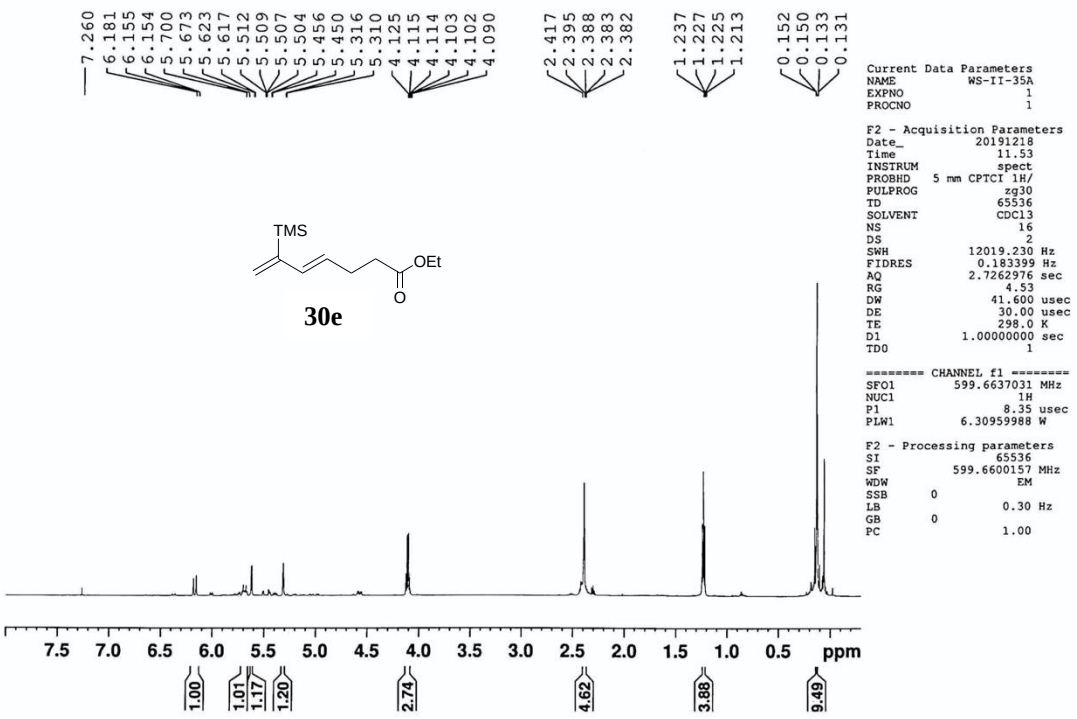
F2 - Acquisition Parameters
Date_                 20191017
Time                     11.18
INSTRUM                  spect
PROBHD    5 mm CPTCI 1H/
PULPROG                zgpg30
TD                      65536
SOLVENT                  CDCl3
NS                         103
DS                           4
SWH                  42613.637 Hz
FIDRES                0.650232 Hz
AQ                    0.7689557 sec
RG                       188.21
DW                      11.733 usec
DE                      20.00 usec
TE                      298.0 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1                150.8012132 MHz
NUC1                        13C
P1                      11.00 usec
PLW1                94.00000000 W

======== CHANNEL f2 ========
SFO2                599.6623986 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                    70.00 usec
PLW2                6.30959988 W
PLW12               0.08241100 W
PLW13               0.04145200 W

F2 - Processing parameters
SI                      32768
SF                  150.7846096 MHz
WDW                         EM
SSB                  0
LB                        1.00 Hz
GB                   0
PC                        1.40
```

WS-II-35A



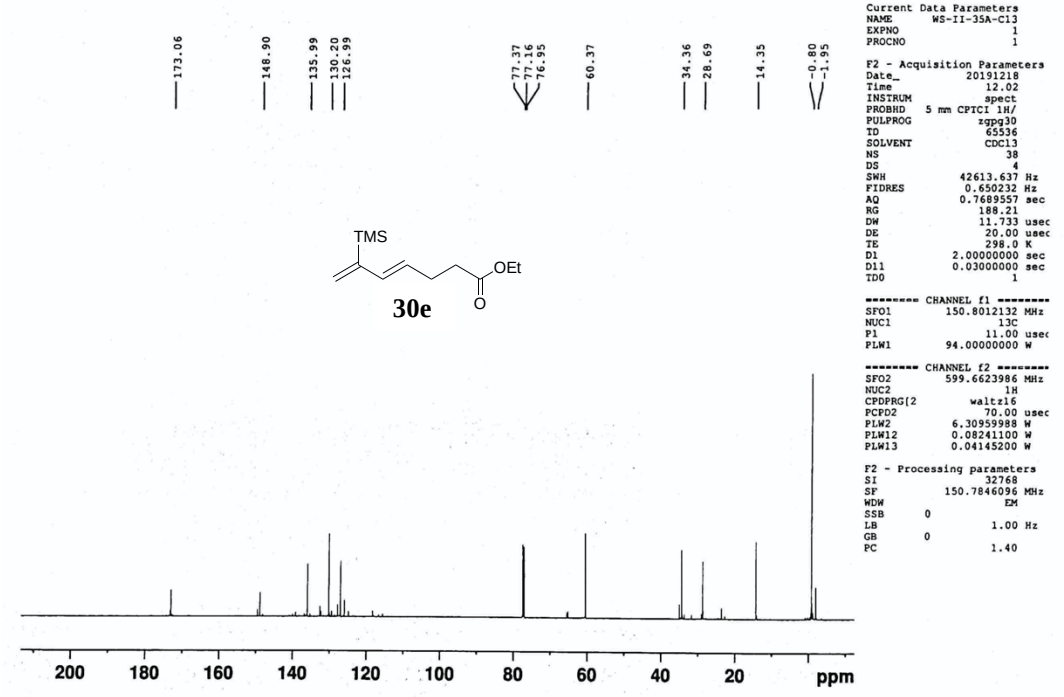

```
Current Data Parameters
NAME                  WS-II-35A
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20191218
Time                      11.53
INSTRUM                   spect
PROBHD    5 mm CPTCI 1H/
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                  12019.230 Hz
FIDRES                0.183399 Hz
AQ                   2.7262976 sec
RG                         4.53
DW                       41.600 usec
DE                       30.00 usec
TE                       298.0 K
D1                   1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
SFO1                599.6637031 MHz
NUC1                        1H
P1                        8.35 usec
PLW1                6.30959988 W

F2 - Processing parameters
SI                           65536
SF                  599.6600157 MHz
WDW                             EM
SSB                  0
LB                            0.30 Hz
GB                   0
PC                            1.00
```

WS-II-35A-C13



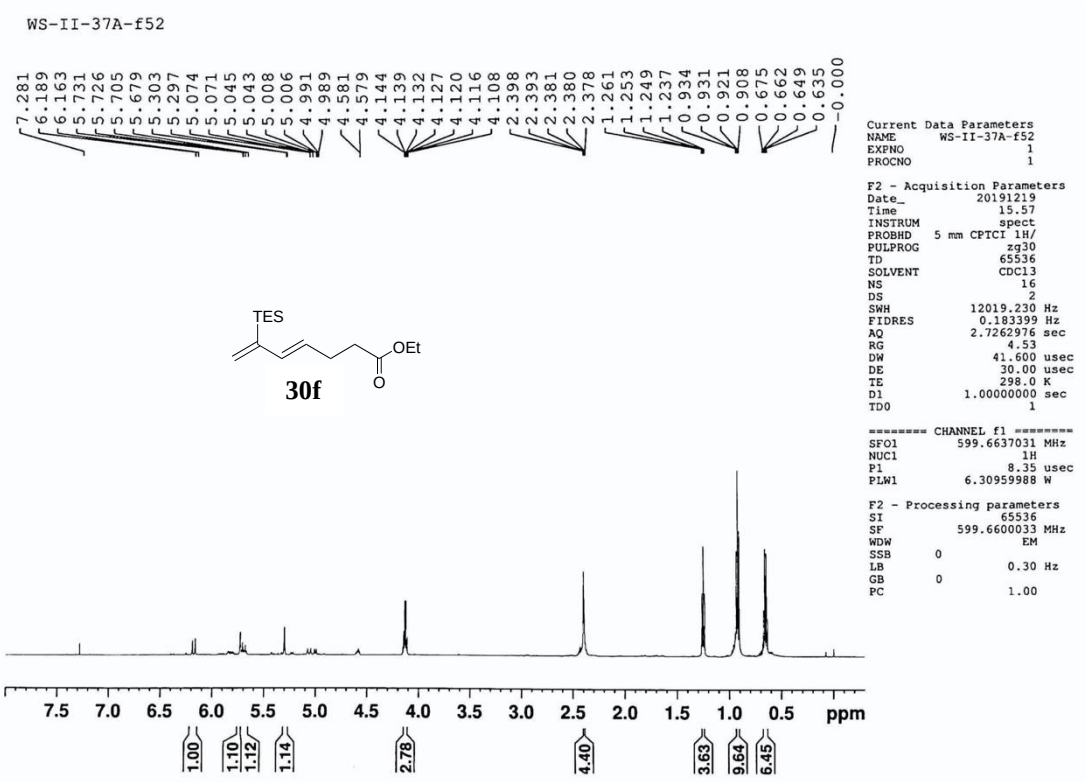

```
Current Data Parameters
NAME               WS-II-35A-C13
EXPNO                         1
PROCNO                        1

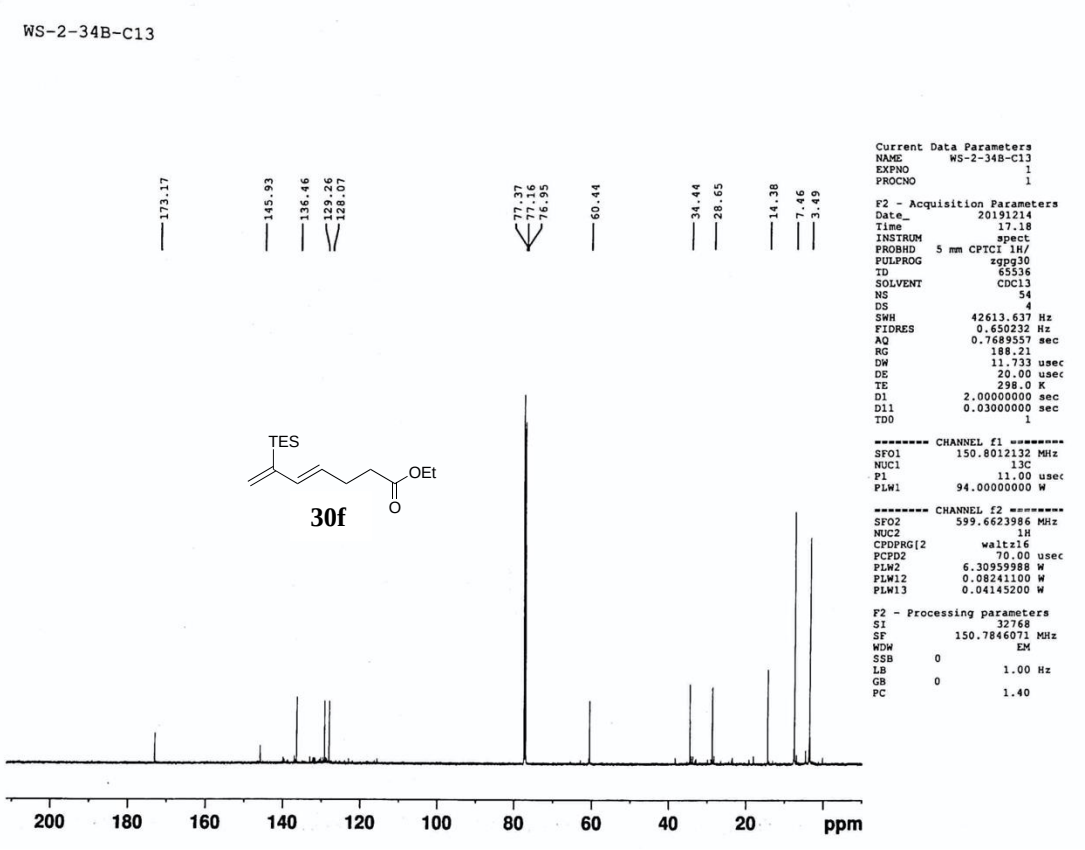
F2 - Acquisition Parameters
Date_                  20191218
Time                      12.02
INSTRUM                   spect
PROBHD    5 mm CPTCI 1H/
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          38
DS                           4
SWH                  42613.637 Hz
FIDRES                0.650232 Hz
AQ                   0.7689557 sec
RG                       188.21
DW                       11.733 usec
DE                       20.00 usec
TE                       298.0 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                           1

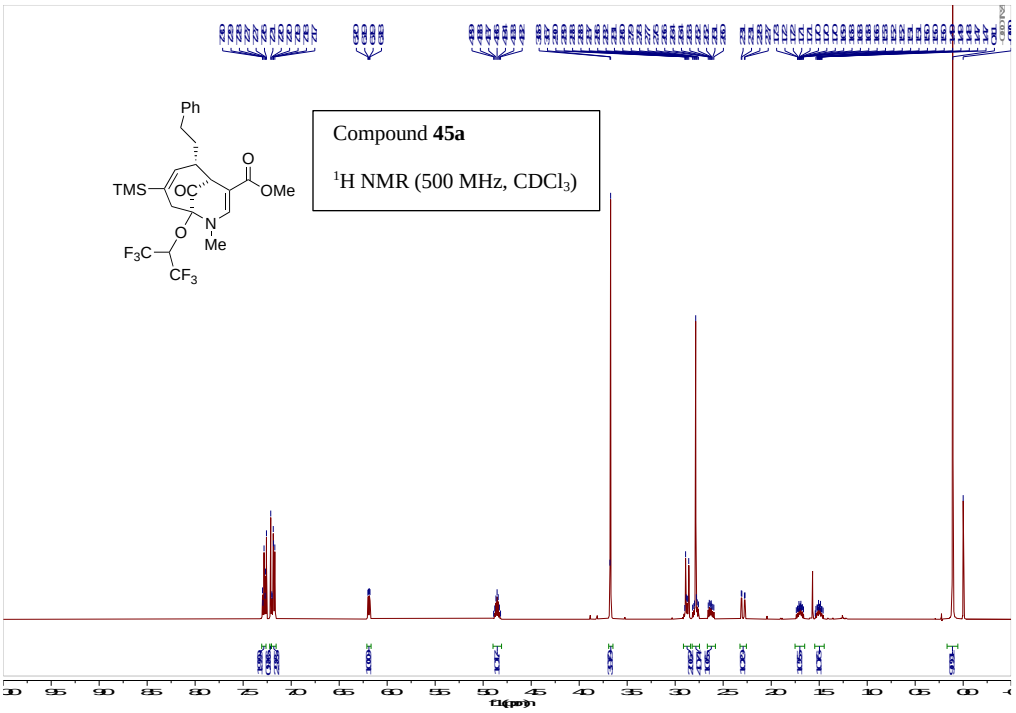
======== CHANNEL f1 ========
SFO1                150.8012132 MHz
NUC1                        13C
P1                       11.00 usec
PLW1                94.00000000 W

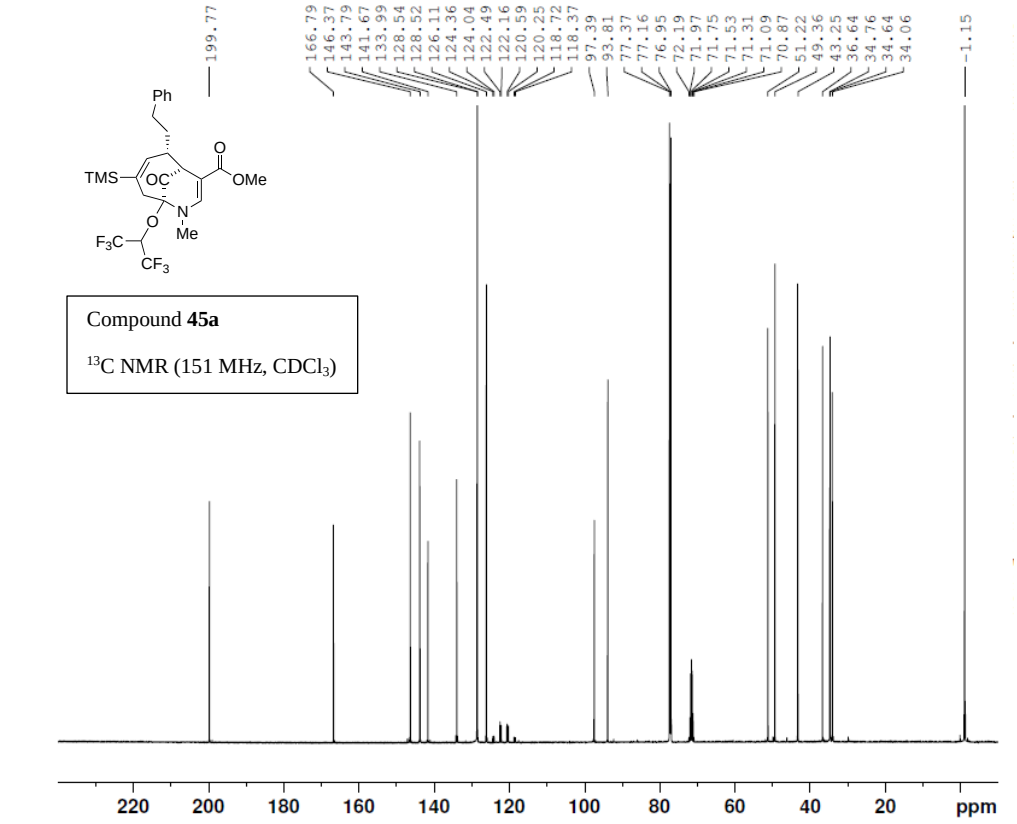
======== CHANNEL f2 ========
SFO2                599.6623986 MHz
NUC2                        1H
CPDPRG[2                waltz16
PCPD2                    70.00 usec
PLW2                6.30959988 W
PLW12               0.08241100 W
PLW13               0.04145200 W

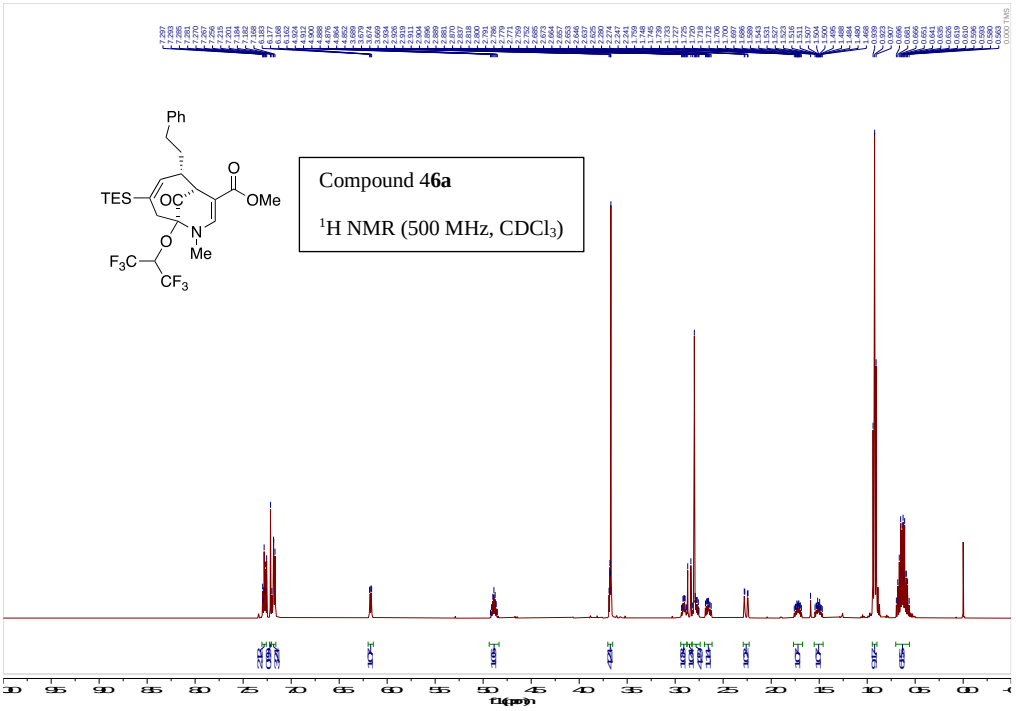
F2 - Processing parameters
SI                           32768
SF                  150.7846096 MHz
WDW                             EM
SSB                  0
LB                            1.00 Hz
GB                   0
PC                            1.40
```

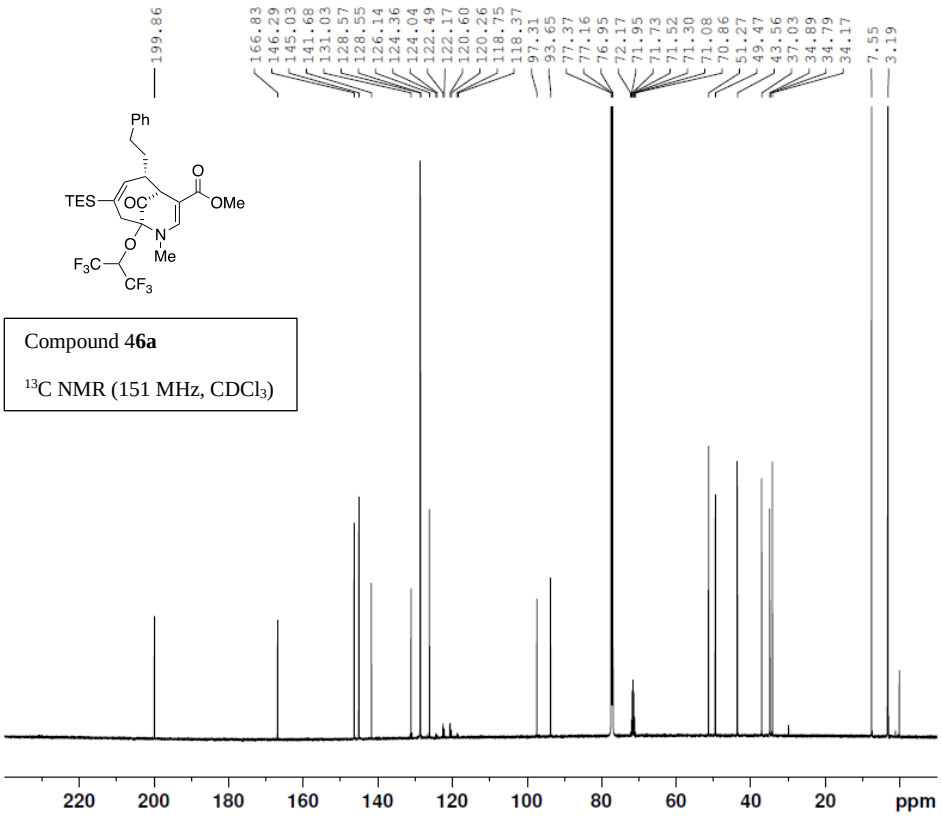

WS-II-37A-f52
7.281
6.189
6.163
5.731
5.726
5.705
5.679
5.303
5.297
5.074
5.071
5.045
5.043
5.008
5.006
4.991
4.989
4.581
4.579
4.144
4.139
4.132
4.127
4.120
4.116
4.108
2.398
2.393
2.381
2.380
2.378
1.261
1.253
1.249
1.237
0.934
0.931
0.921
0.908
0.675
0.662
0.649
0.635
-0.000
TES
OEt
O
30f
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.10
1.12
1.14
2.78
4.40
3.63
9.64
6.45
Current Data Parameters
NAME WS-II-37A-f52
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191219
Time 15.57
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7262976 sec
RG 4.53
DW 41.600 usec
DE 30.00 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 599.6637031 MHz
NUC1 1H
P1 8.35 usec
PLW1 6.30959988 W
F2 - Processing parameters
SI 65536
SF 599.6600033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

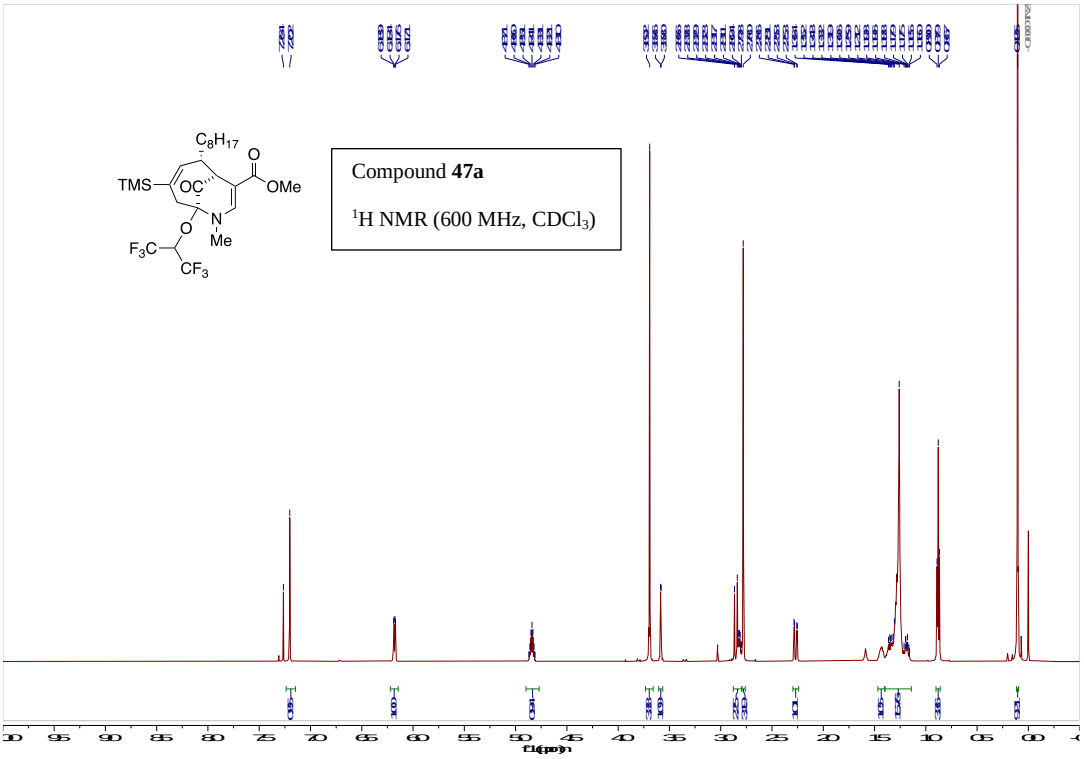

WS-2-34B-C13
173.17
145.93
136.46
129.26
128.07
77.37
77.16
76.95
60.44
34.44
28.65
14.38
7.46
3.49
TES
OEt
O
30f
200 180 160 140 120 100 80 60 40 20 ppm
Current Data Parameters
NAME WS-2-34B-C13
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20191214
Time 17.18
INSTRUM spect
PROBHD 5 mm CPTCI 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 54
DS 4
SWH 42613.637 Hz
FIDRES 0.650232 Hz
AQ 0.7689557 sec
RG 188.21
DW 11.733 usec
DE 20.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 150.8012132 MHz
NUC1 13C
P1 11.00 usec
PLW1 94.00000000 W
======== CHANNEL f2 ========
SFO2 599.6623986 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 70.00 usec
PLW2 6.30959988 W
PLW12 0.08241100 W
PLW13 0.04145200 W
F2 - Processing parameters
SI 32768
SF 150.7846071 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

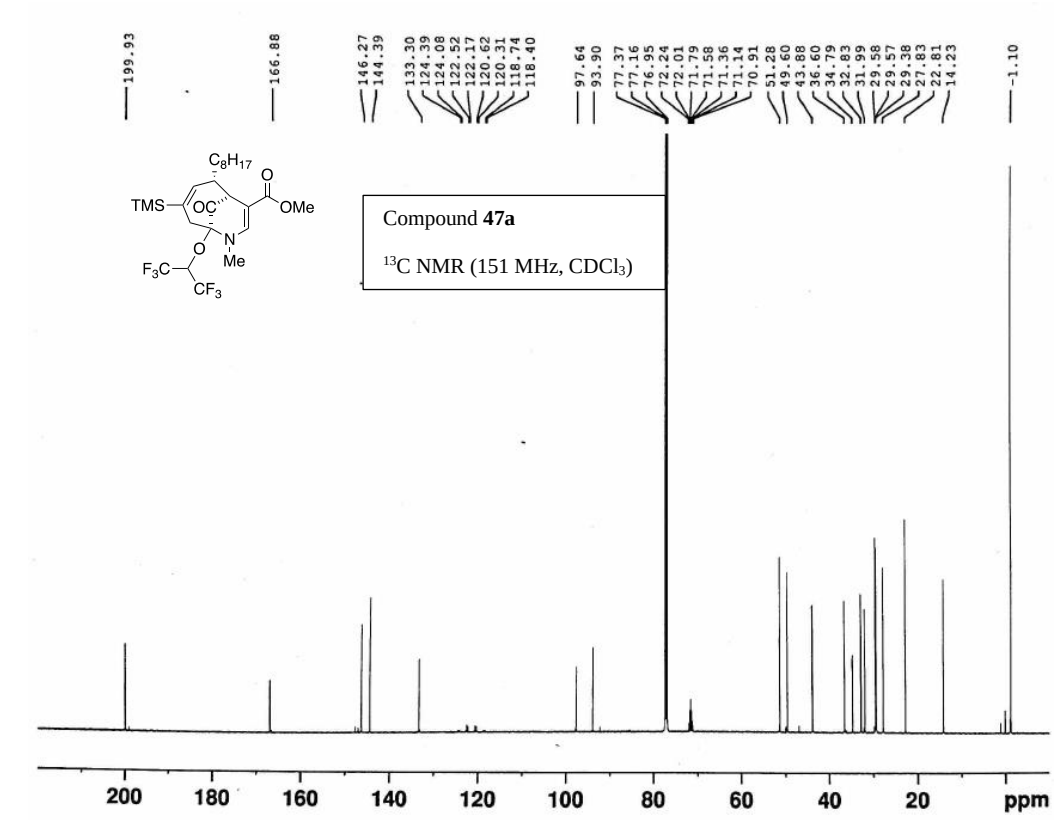

Ph
TMS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 45a
1H NMR (500 MHz, CDCl3)

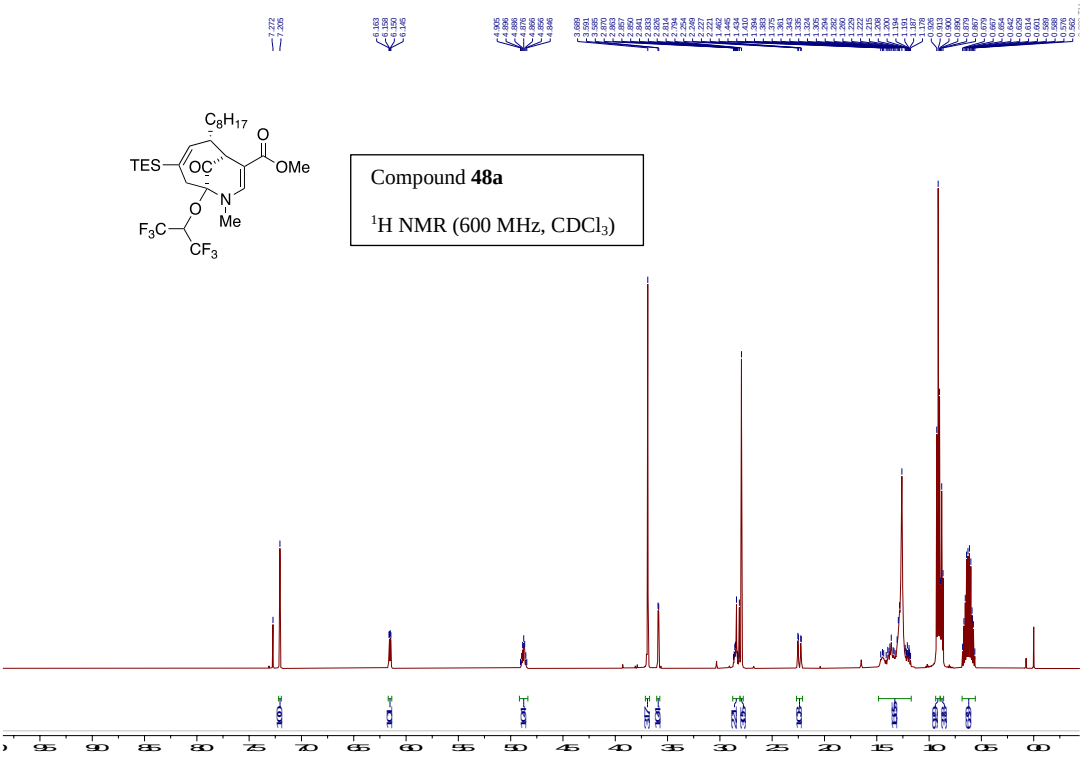

199.77
166.79
146.37
143.79
141.67
133.99
128.54
128.52
126.11
124.36
124.04
122.49
122.16
120.59
120.25
118.72
118.37
97.39
93.81
77.37
77.16
76.95
72.19
71.97
71.75
71.53
71.31
71.09
70.87
51.22
49.36
43.25
36.64
34.76
34.64
34.06
-1.15
Ph
TMS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 45a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

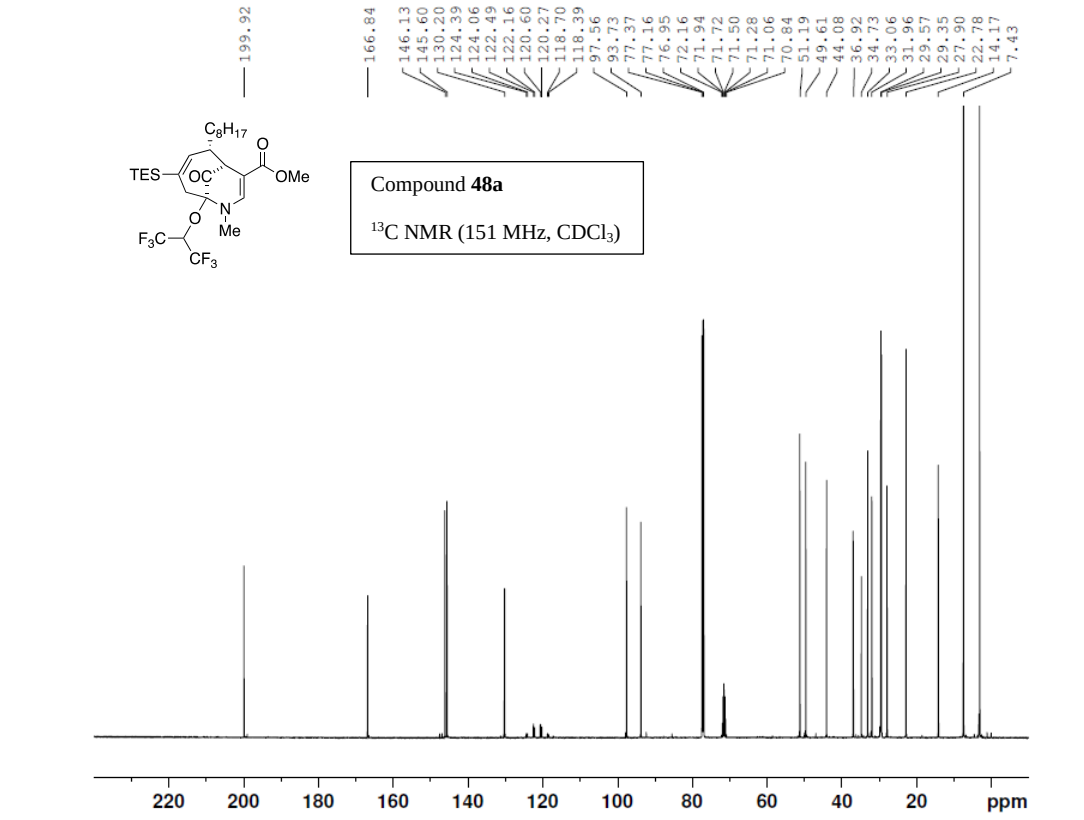

Ph
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 46a
1H NMR (500 MHz, CDCl3)

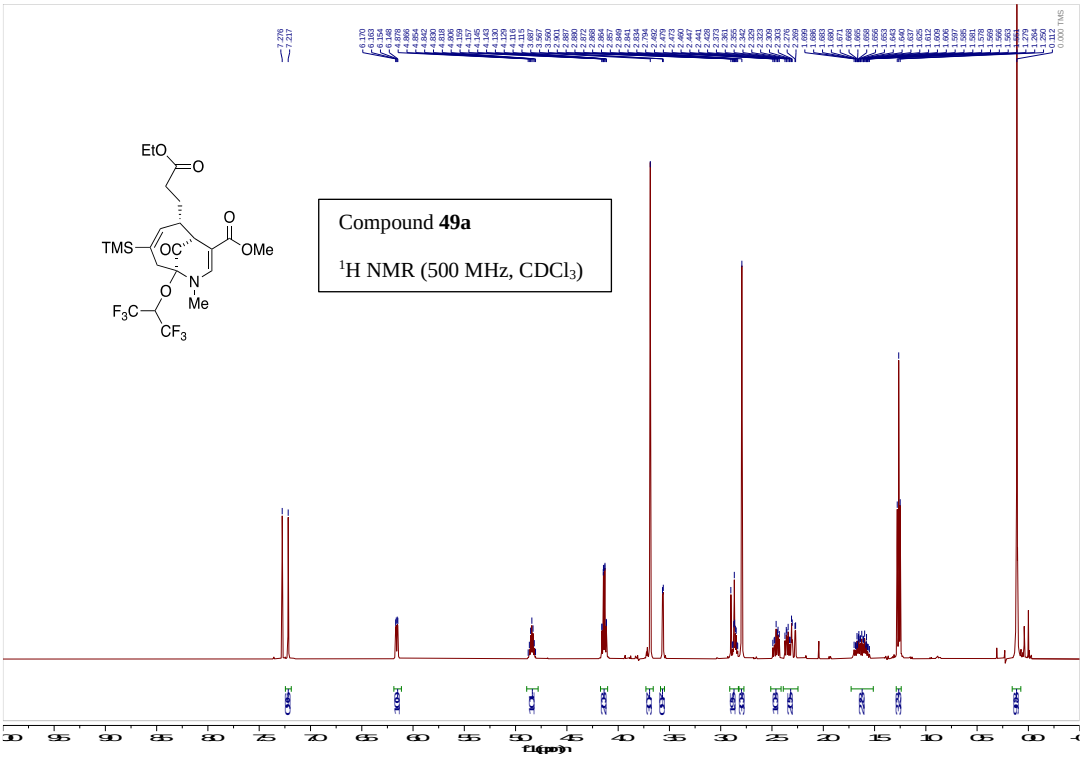

199.86
166.83
146.29
145.03
141.68
131.03
128.57
128.55
126.14
124.36
124.04
122.49
122.17
120.60
120.26
118.75
118.37
97.31
93.65
77.37
77.16
76.95
72.17
71.95
71.73
71.52
71.30
71.08
70.86
51.27
49.47
43.56
37.03
34.89
34.79
34.17
7.55
3.19
Ph
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 46a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

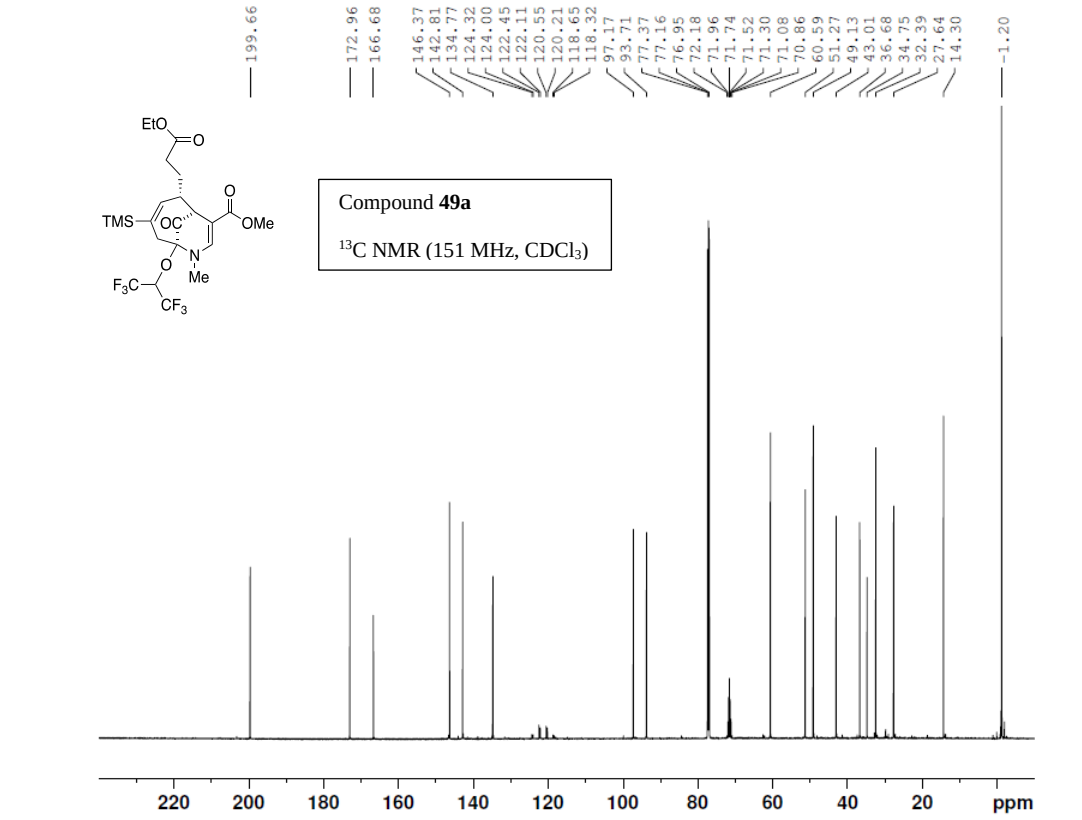

Compound **47a**
^{1}H NMR (600 MHz, $CDCl_3$)

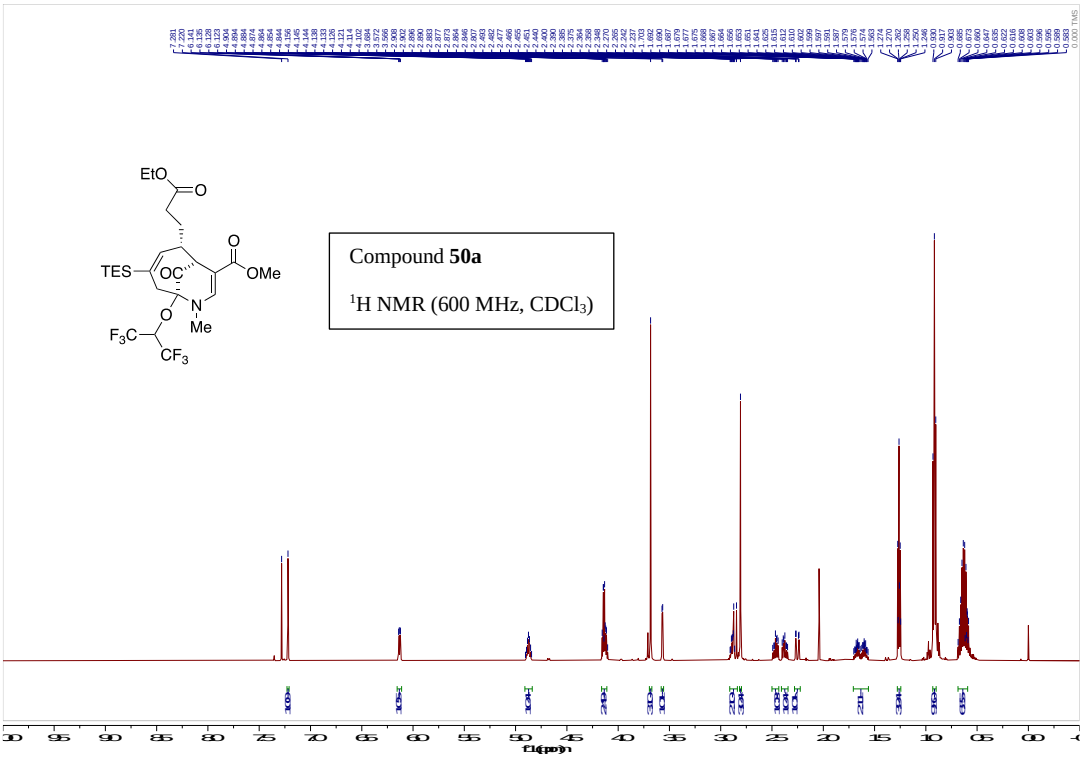

Compound **47a**
^{13}C NMR (151 MHz, $CDCl_3$)
ppm

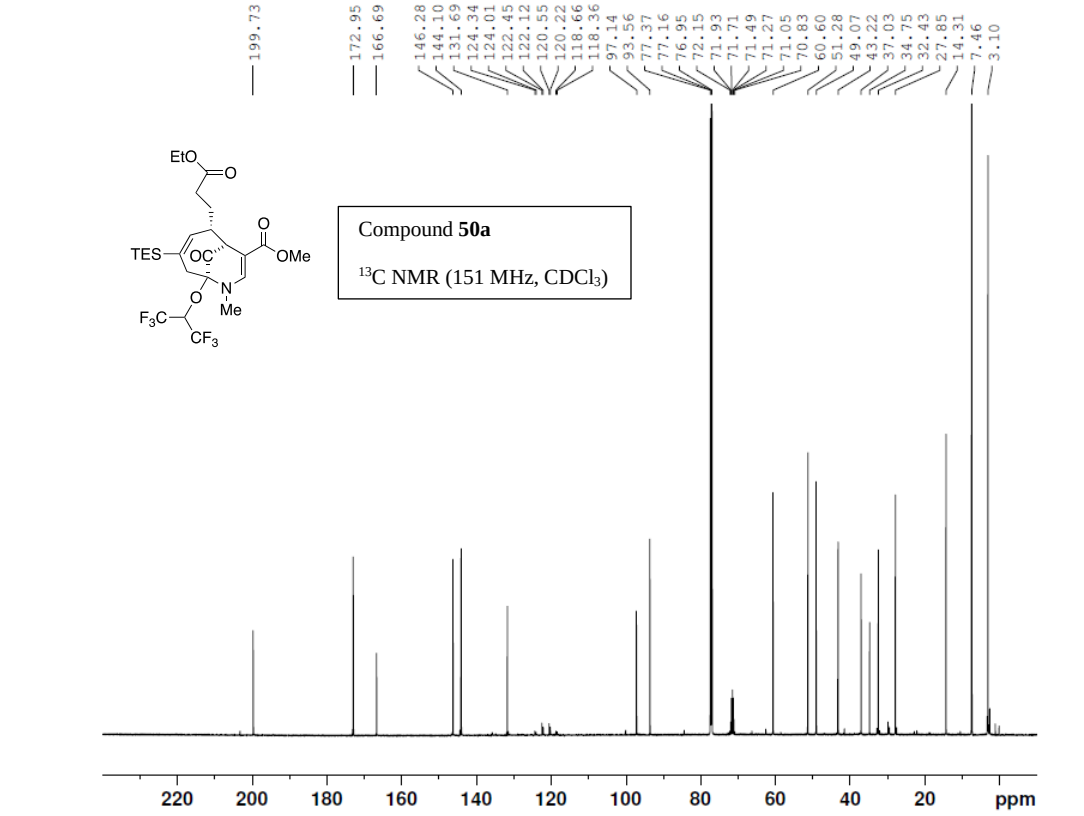

C8H17
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 48a
1H NMR (600 MHz, CDCl3)

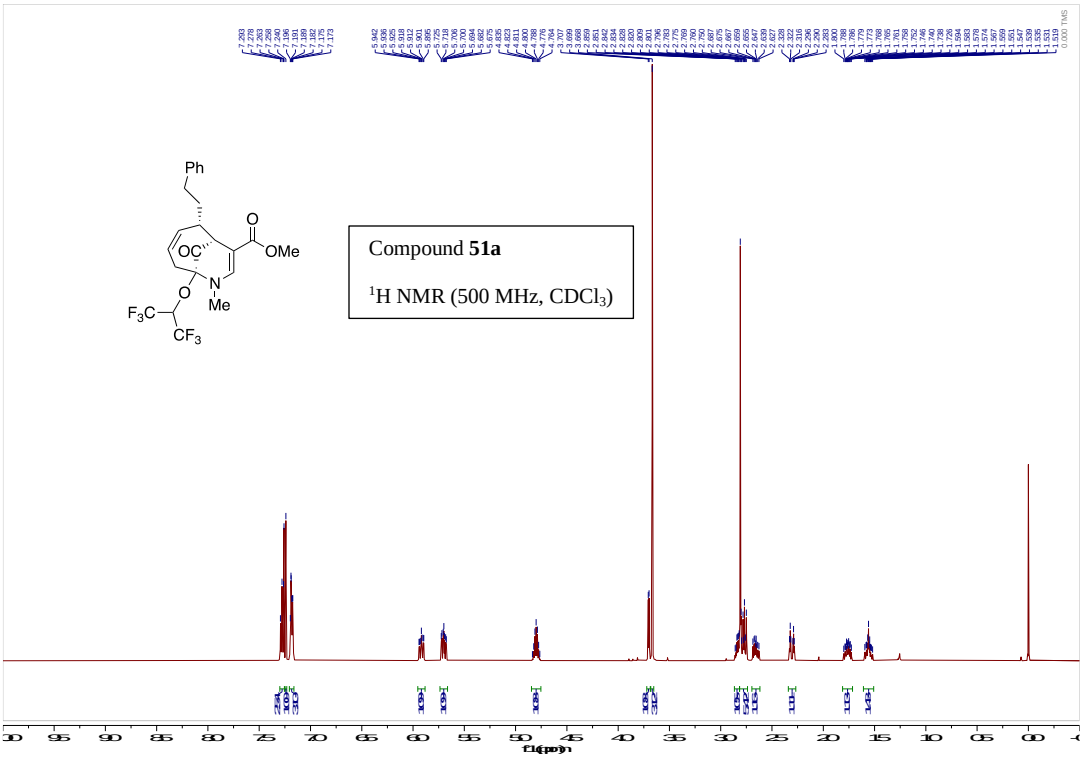

C8H17
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 48a
13C NMR (151 MHz, CDCl3)
ppm

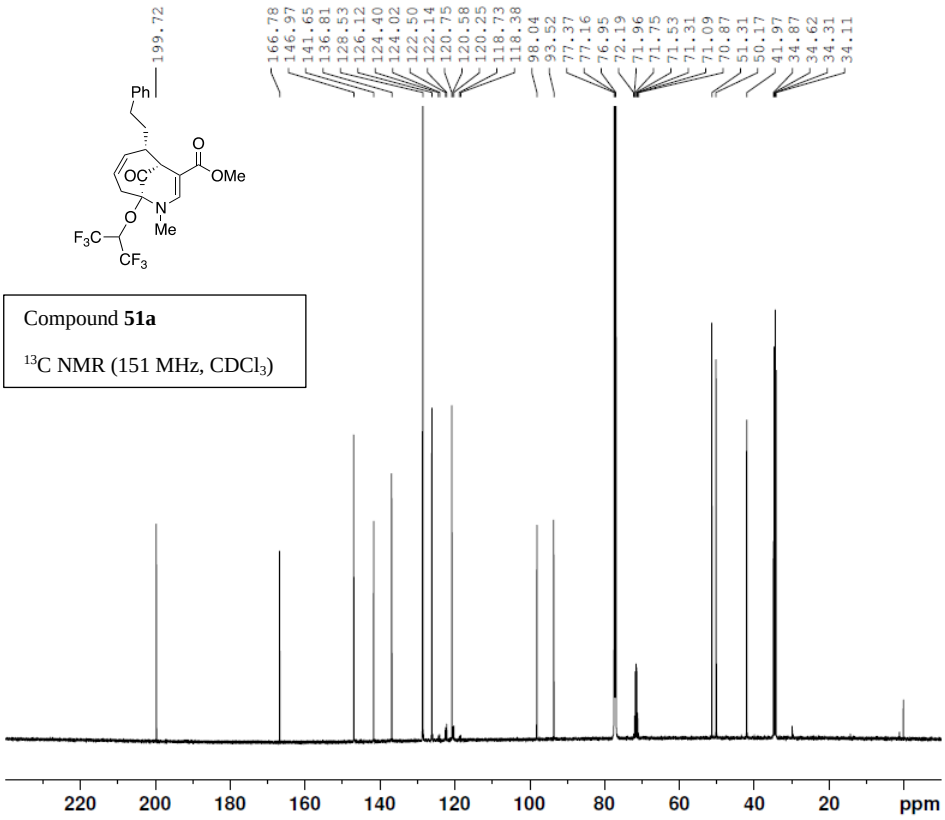

EtO
O
TMS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 49a
1H NMR (500 MHz, CDCl3)

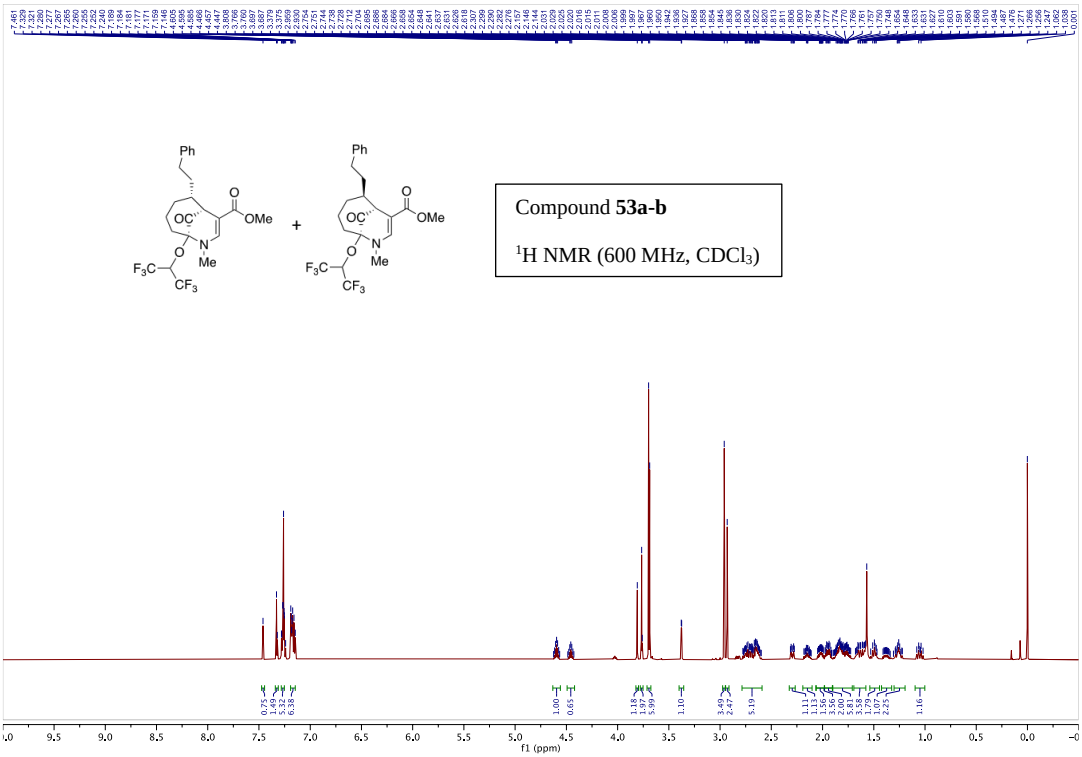

199.66
172.96
166.68
146.37
142.81
134.77
124.32
124.00
122.45
122.11
120.55
120.21
118.65
118.32
97.17
93.71
77.37
77.16
76.95
72.18
71.96
71.74
71.52
71.30
71.08
70.86
60.59
51.27
49.13
43.01
36.68
34.75
32.39
27.64
14.30
-1.20
EtO
O
TMS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 49a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

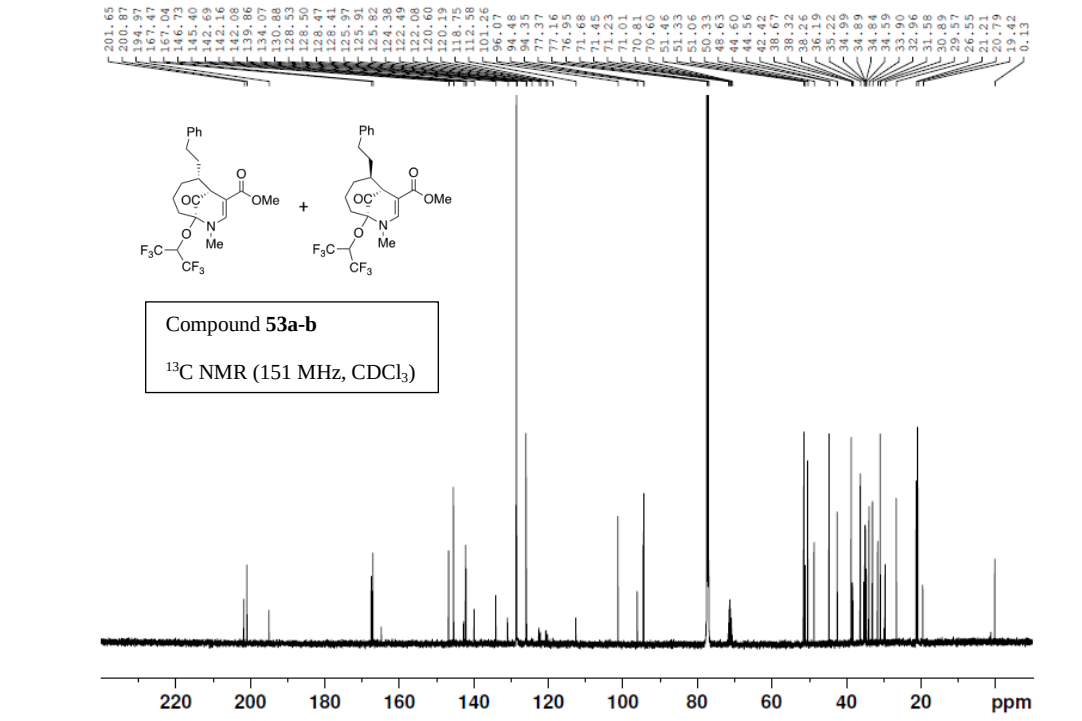

EtO
O
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 50a
1H NMR (600 MHz, CDCl3)

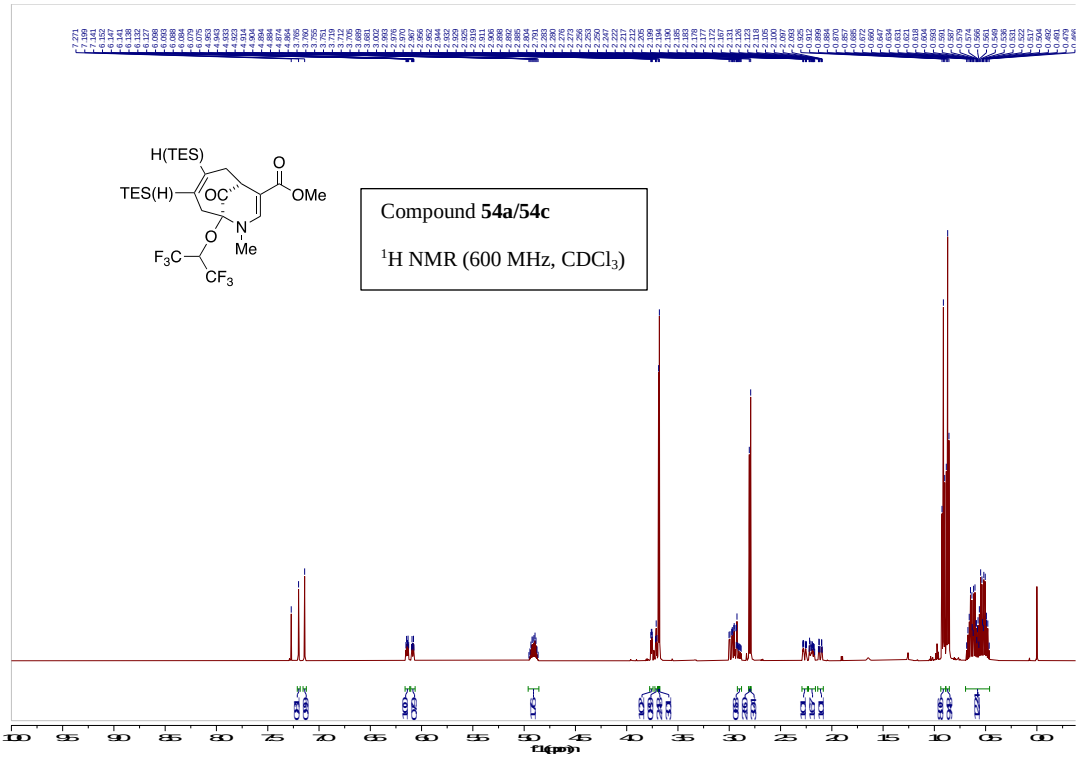

199.73
172.95
166.69
146.28
144.10
131.69
124.34
124.01
122.45
122.12
120.55
120.22
118.66
118.36
97.14
93.56
77.37
77.16
76.95
72.15
71.93
71.71
71.49
71.27
71.05
70.83
60.60
51.28
49.07
43.22
37.03
34.75
32.43
27.85
14.31
7.46
3.10
EtO
O
TES
OC
O
OMe
N
Me
O
F3C
CF3
Compound 50a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

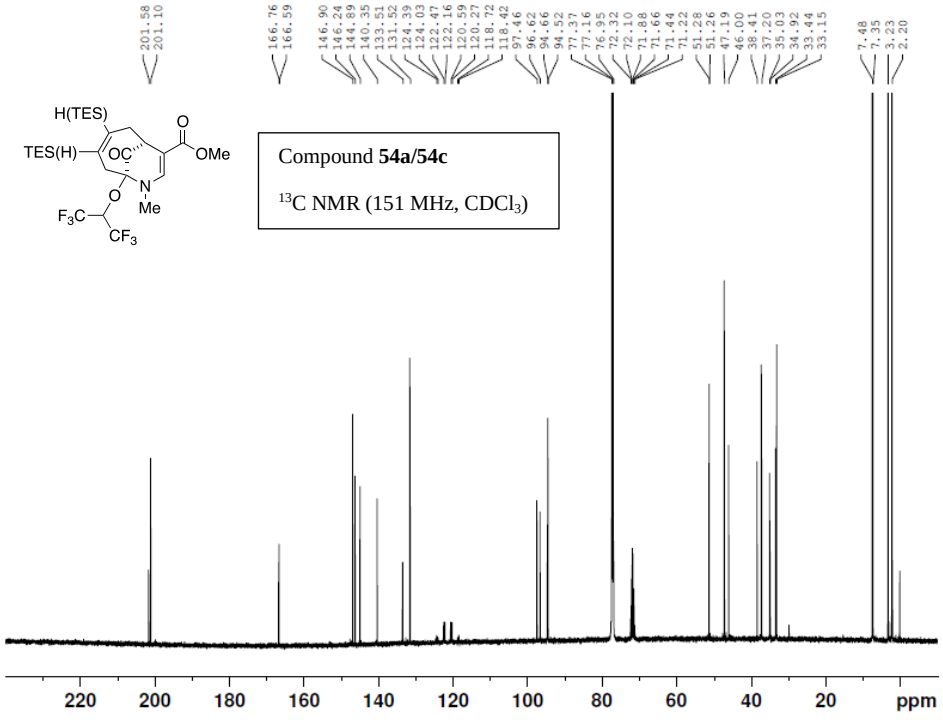

Ph
O
OMe
OC
N
Me
O
F3C
CF3
Compound 51a
1H NMR (500 MHz, CDCl3)

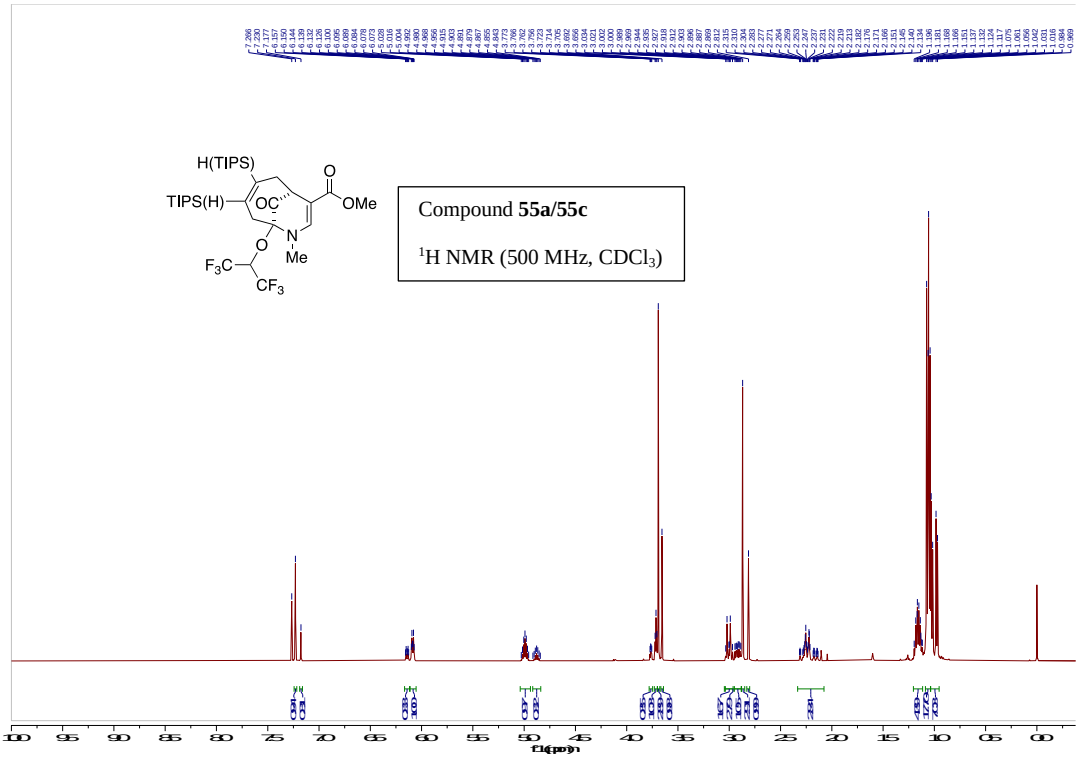

199.72
166.78
146.97
141.65
136.81
128.53
126.12
124.40
124.02
122.50
122.14
120.75
120.58
120.25
118.73
118.38
98.04
93.52
77.37
77.16
76.95
72.19
71.96
71.75
71.53
71.31
71.09
70.87
51.31
50.17
41.97
34.87
34.62
34.31
34.11
Ph
O
OMe
OC
N
Me
O
F3C
CF3
Compound 51a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

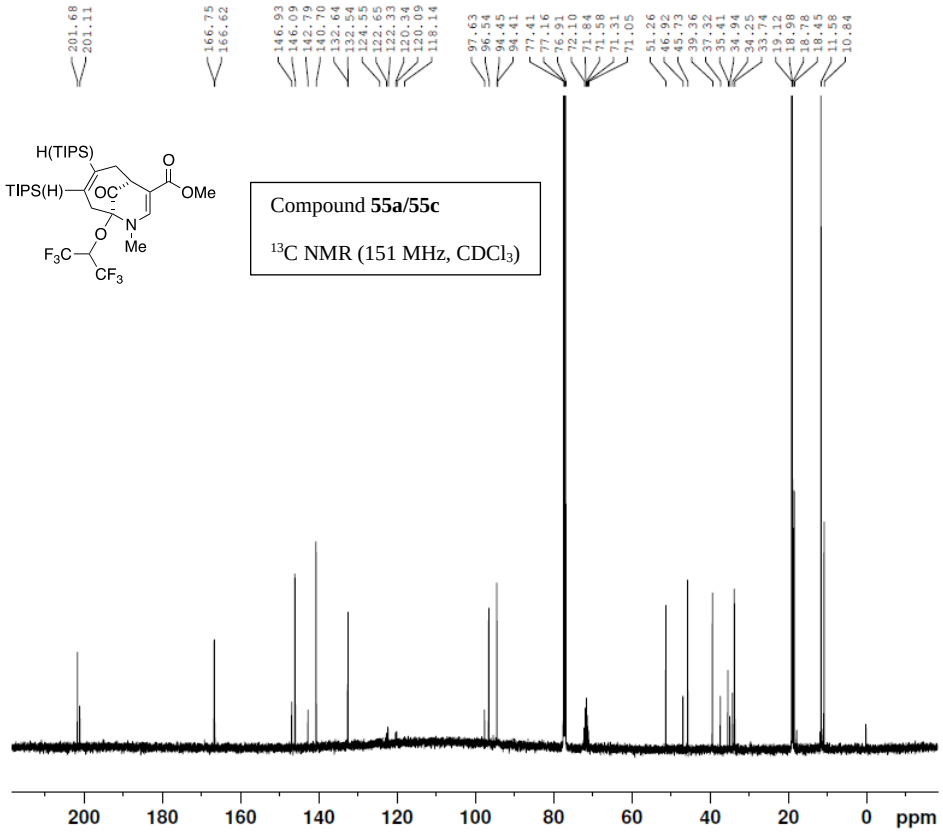

Ph
OMe
Me
F3C
CF3
Compound 53a-b
1H NMR (600 MHz, CDCl3)
f1 (ppm)

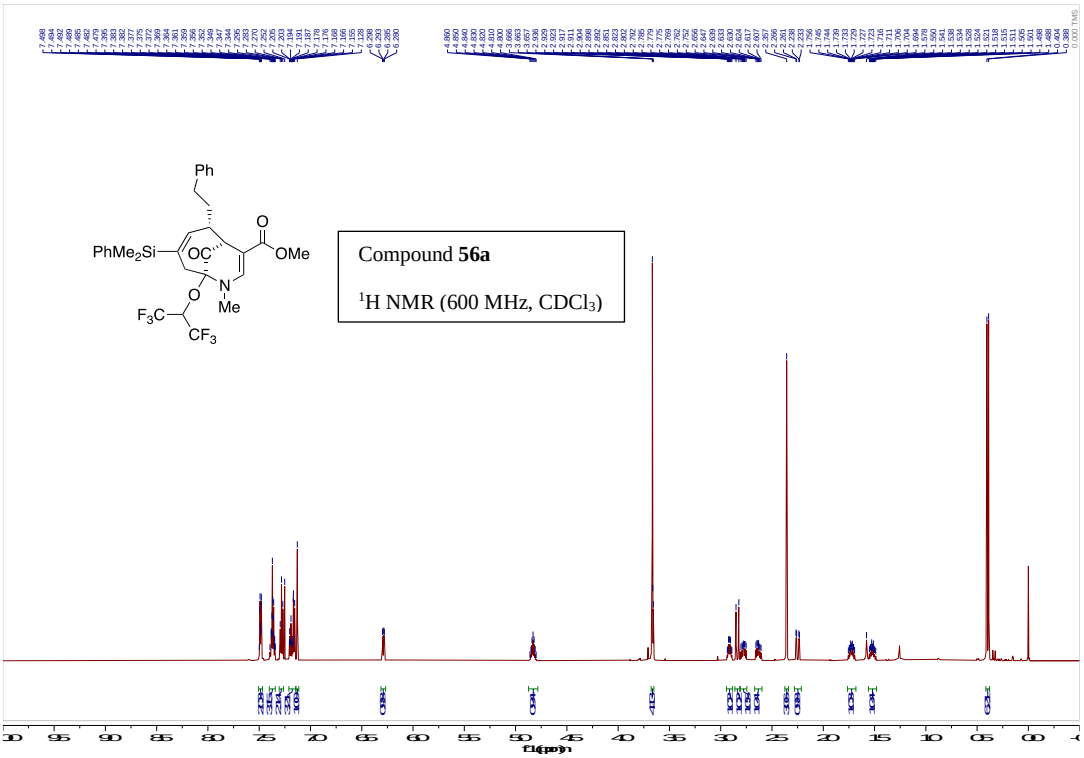

Ph
OMe
Me
F3C
CF3
Compound 53a-b
13C NMR (151 MHz, CDCl3)
ppm

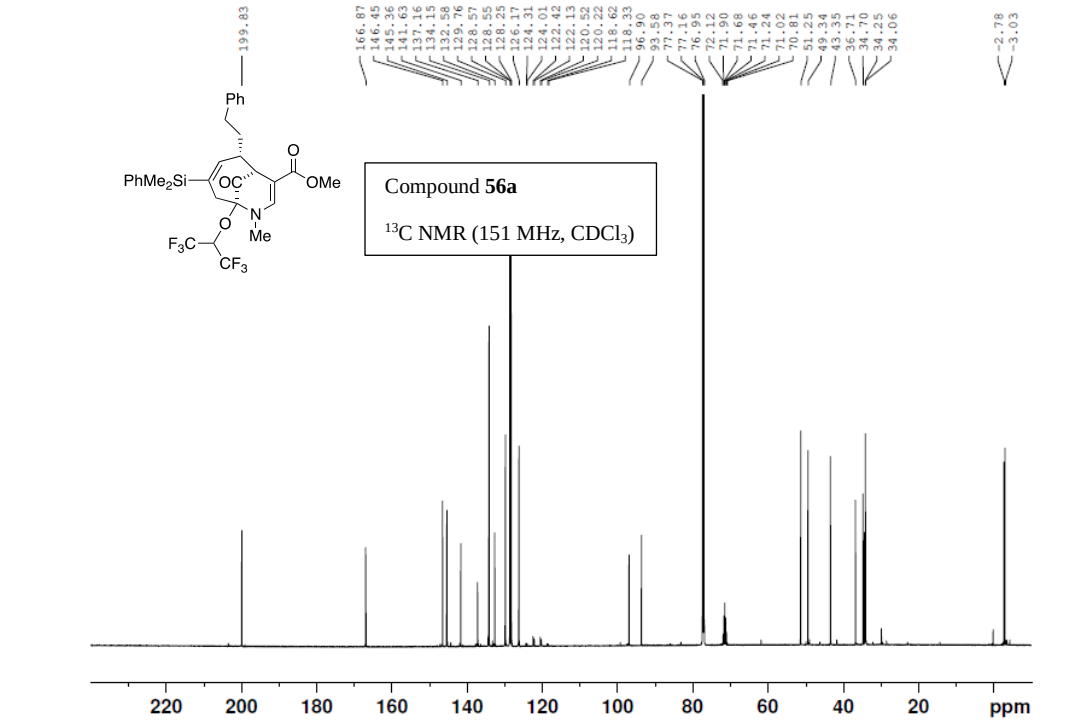

H(TES)
TES(H)
OC
O
OMe
N
Me
O
F3C
CF3
Compound 54a/54c
1H NMR (600 MHz, CDCl3)

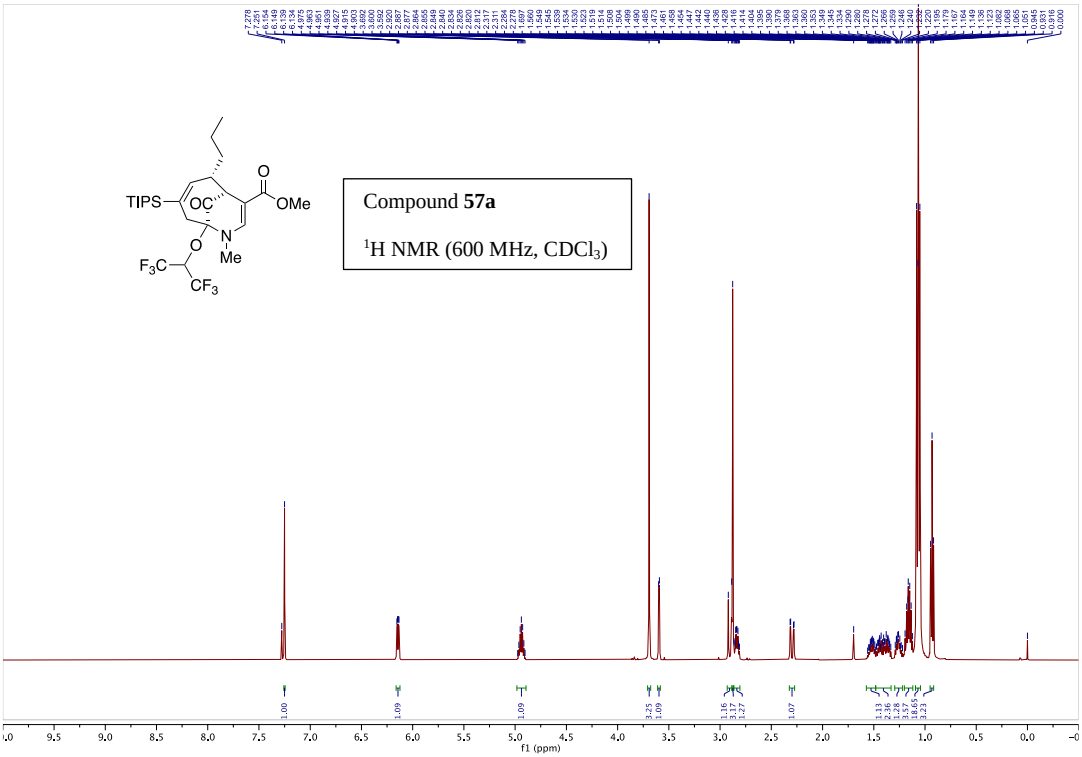

H(TES)
TES(H)
OC
O
OMe
N
Me
O
F3C
CF3
Compound 54a/54c
13C NMR (151 MHz, CDCl3)
ppm

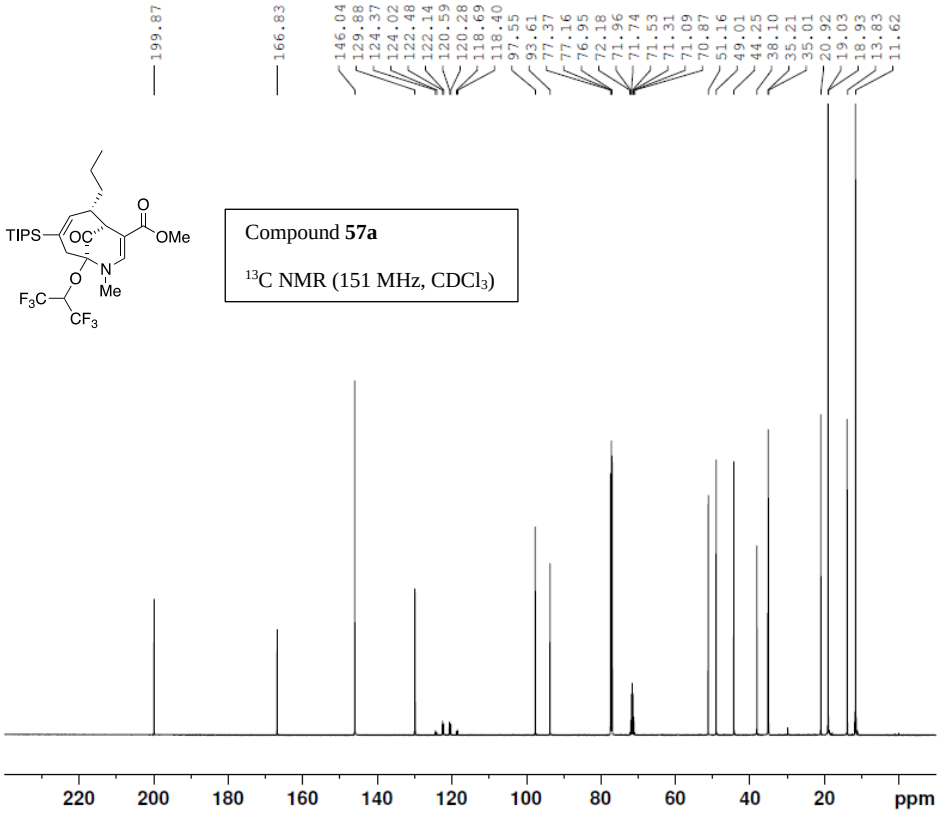

H(TIPS)
TIPS(H)
OC
O
OMe
N
Me
O
F3C
CF3
Compound 55a/55c
1H NMR (500 MHz, CDCl3)

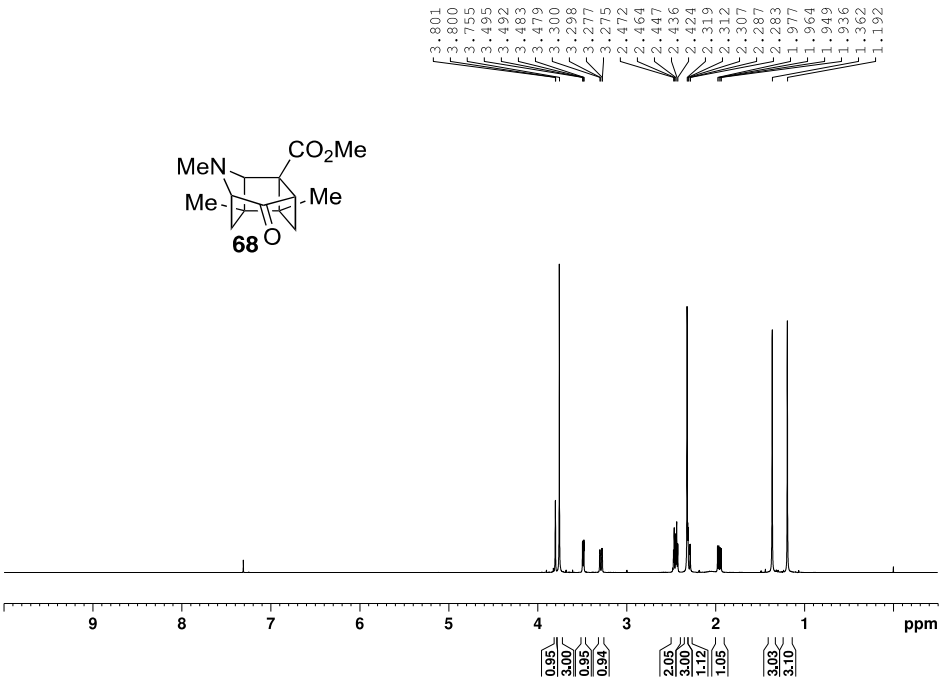

H(TIPS)
TIPS(H)
OC
O
OMe
N
Me
O
F3C
CF3
Compound 55a/55c
13C NMR (151 MHz, CDCl3)
ppm

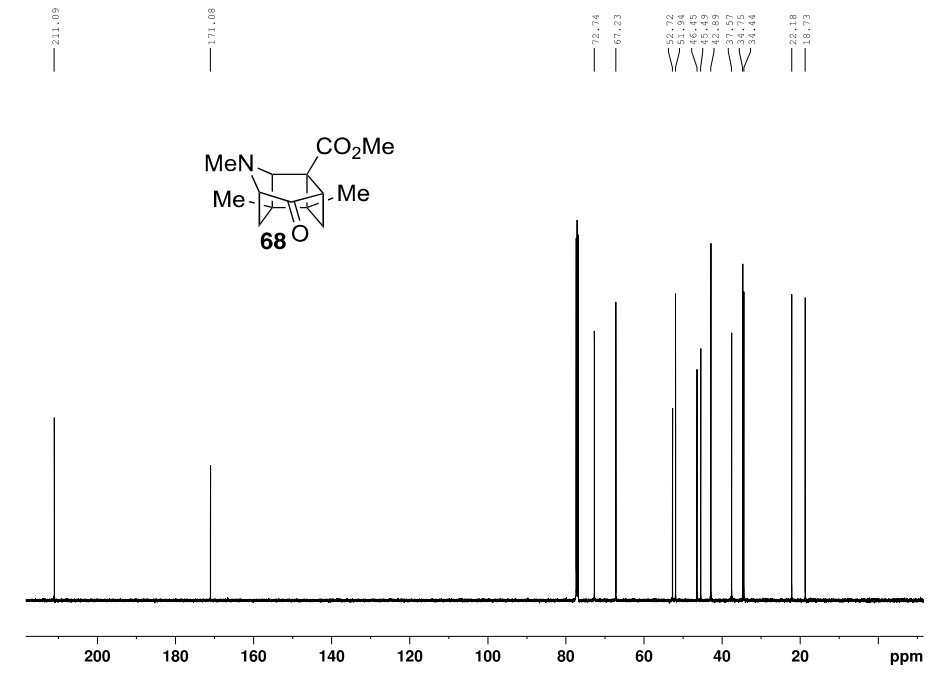

Ph
PhMe2Si
OC
O
OMe
N
Me
O
F3C
CF3
Compound 56a
1H NMR (600 MHz, CDCl3)

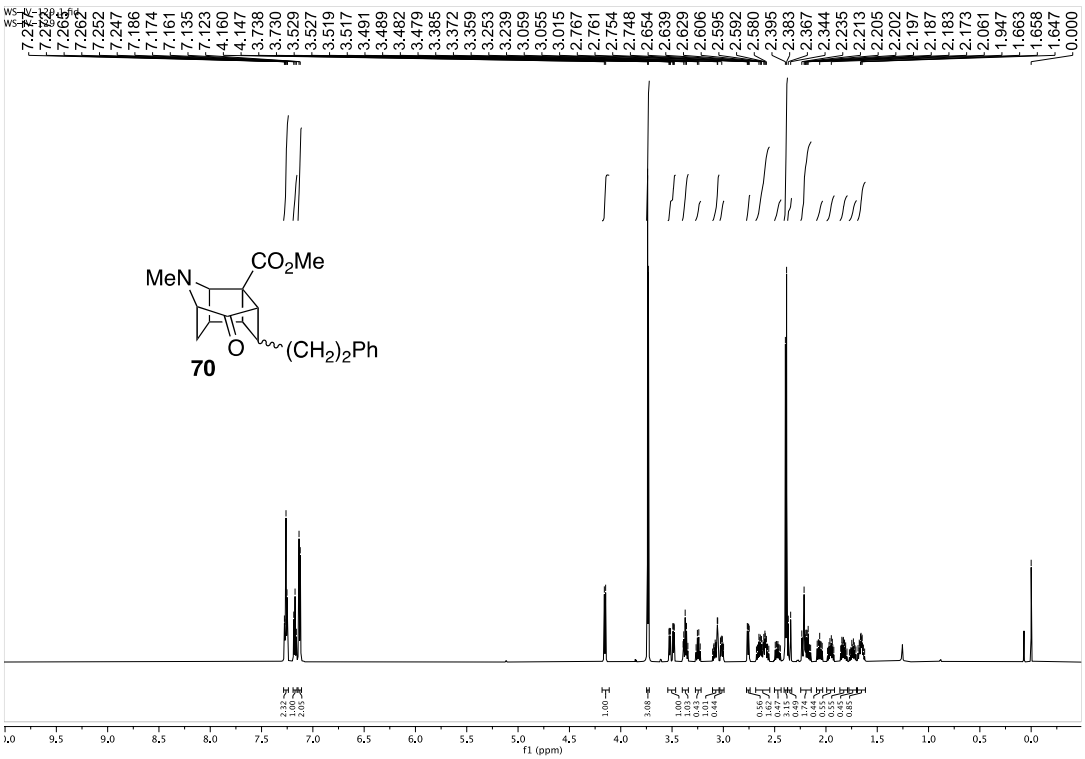

199.83
166.87
146.45
145.36
141.63
137.16
134.15
132.58
129.76
128.57
128.55
128.25
126.17
124.31
124.01
122.42
122.13
120.52
120.22
118.62
118.33
96.90
93.58
77.37
77.16
76.95
72.12
71.90
71.68
71.46
71.24
71.02
70.81
51.25
49.34
43.35
36.71
34.70
34.25
34.06
-2.78
-3.03
Ph
PhMe2Si
OC
O
OMe
N
Me
O
F3C
CF3
Compound 56a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

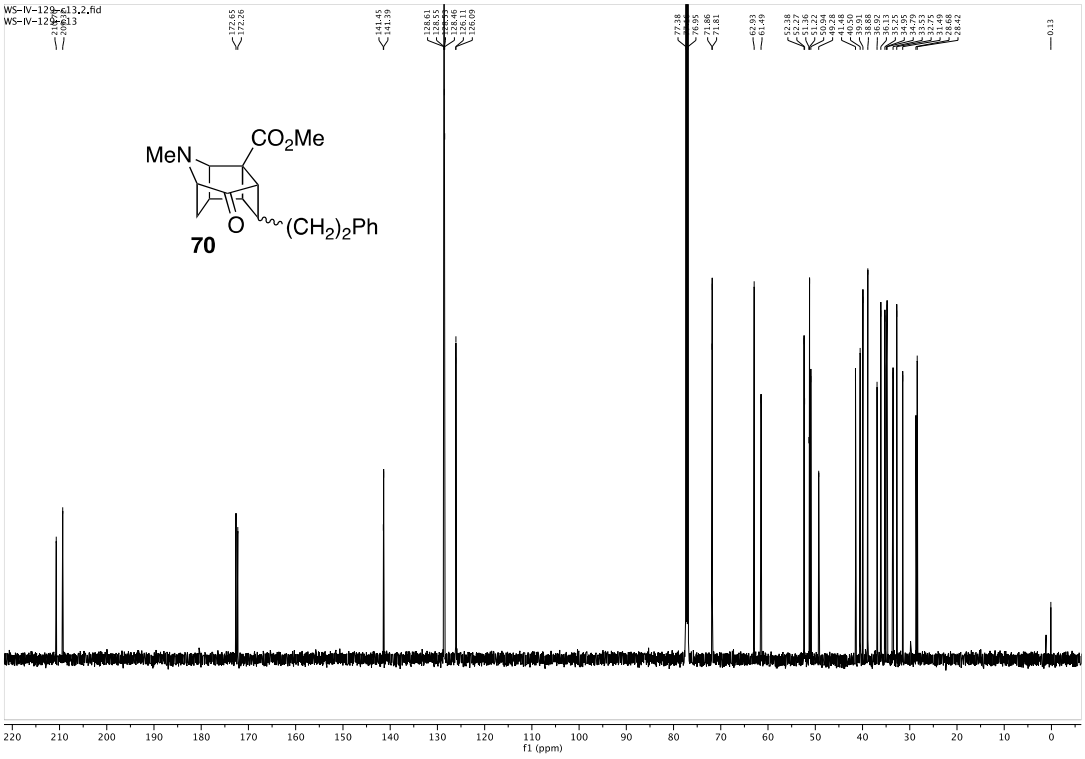

TIPS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 57a
1H NMR (600 MHz, CDCl3)
f1 (ppm)

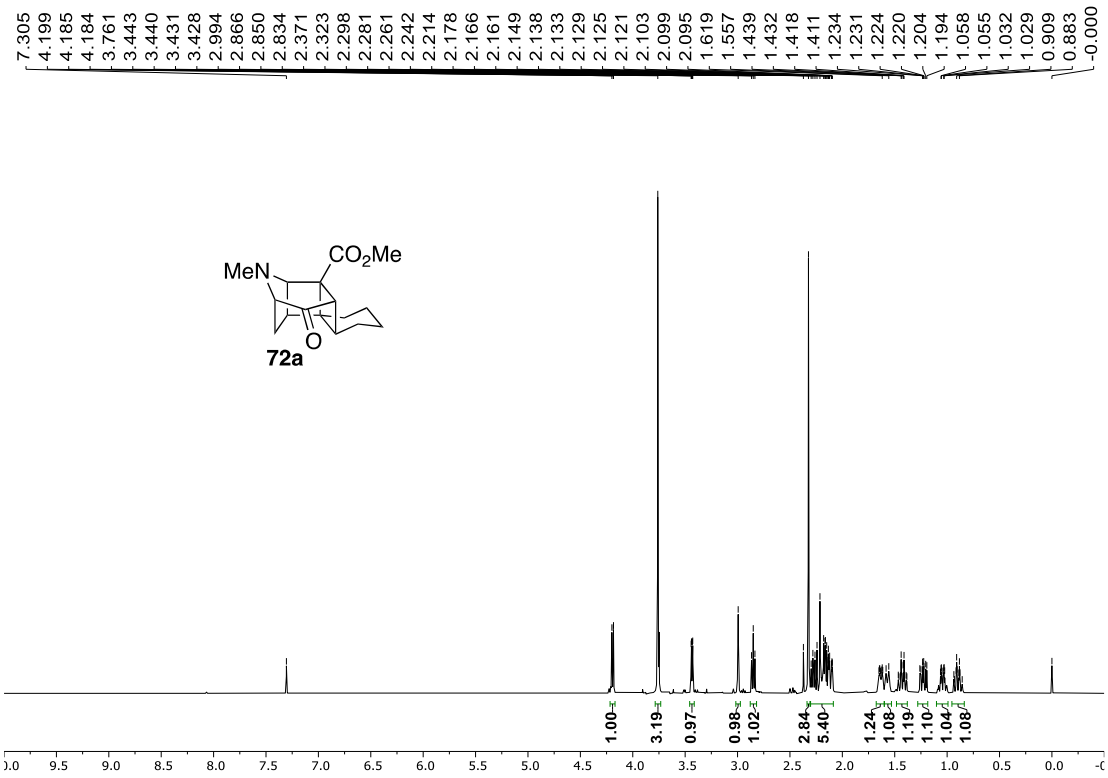

199.87
166.83
146.04
129.88
124.37
124.02
122.48
122.14
120.59
120.28
118.69
118.40
97.55
93.61
77.37
77.16
76.95
72.18
71.96
71.74
71.53
71.31
71.09
70.87
51.16
49.01
44.25
38.10
35.21
35.01
20.92
19.03
18.93
13.83
11.62
TIPS
OC
O
OMe
N
Me
O
F3C
CF3
Compound 57a
13C NMR (151 MHz, CDCl3)
220
200
180
160
140
120
100
80
60
40
20
ppm

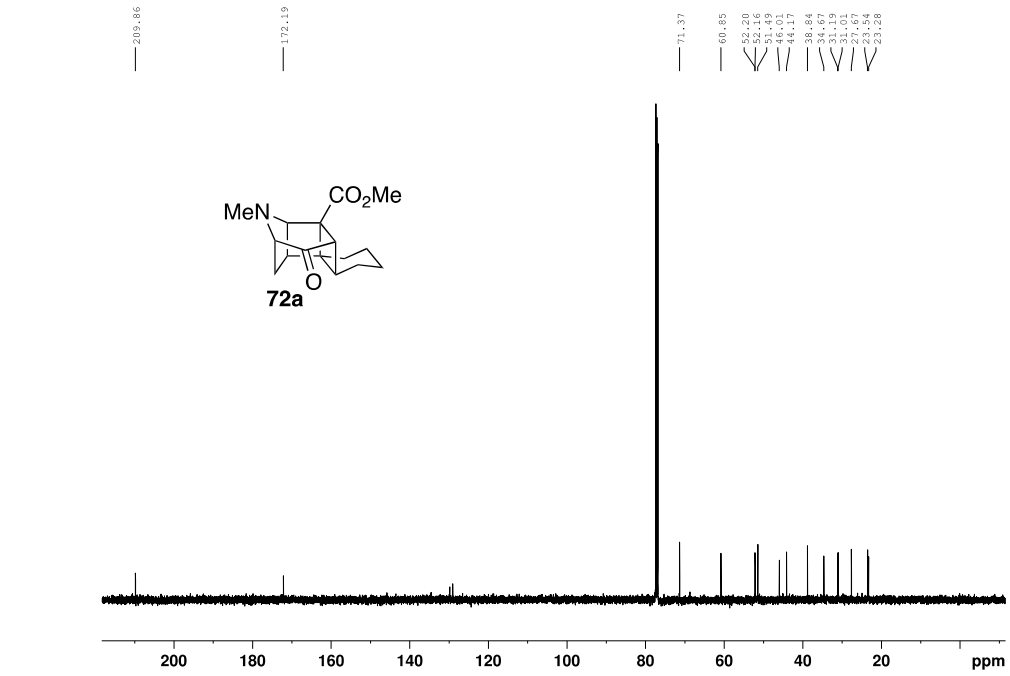

3.801
3.800
3.755
3.495
3.492
3.483
3.479
3.300
3.298
3.277
3.275
2.472
2.464
2.447
2.436
2.424
2.319
2.312
2.307
2.287
2.283
1.977
1.964
1.949
1.936
1.362
1.192
MeN
CO2Me
Me
Me
68
O
9
8
7
6
5
4
3
2
1
ppm
0.95
3.00
0.95
0.94
2.05
3.00
1.12
1.05
3.03
3.10

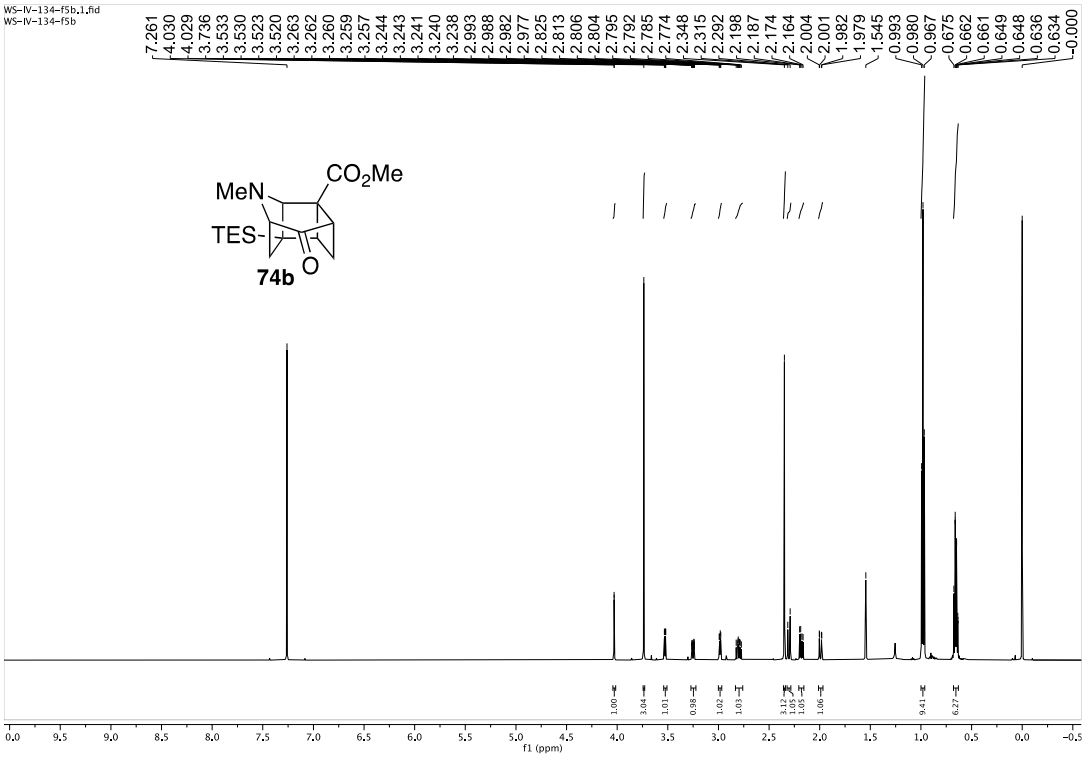

211.09
171.08
72.74
67.23
52.72
51.94
46.45
45.49
42.89
37.57
34.75
34.44
22.18
18.73
MeN
CO2Me
Me
Me
68
O
200
180
160
140
120
100
80
60
40
20
ppm

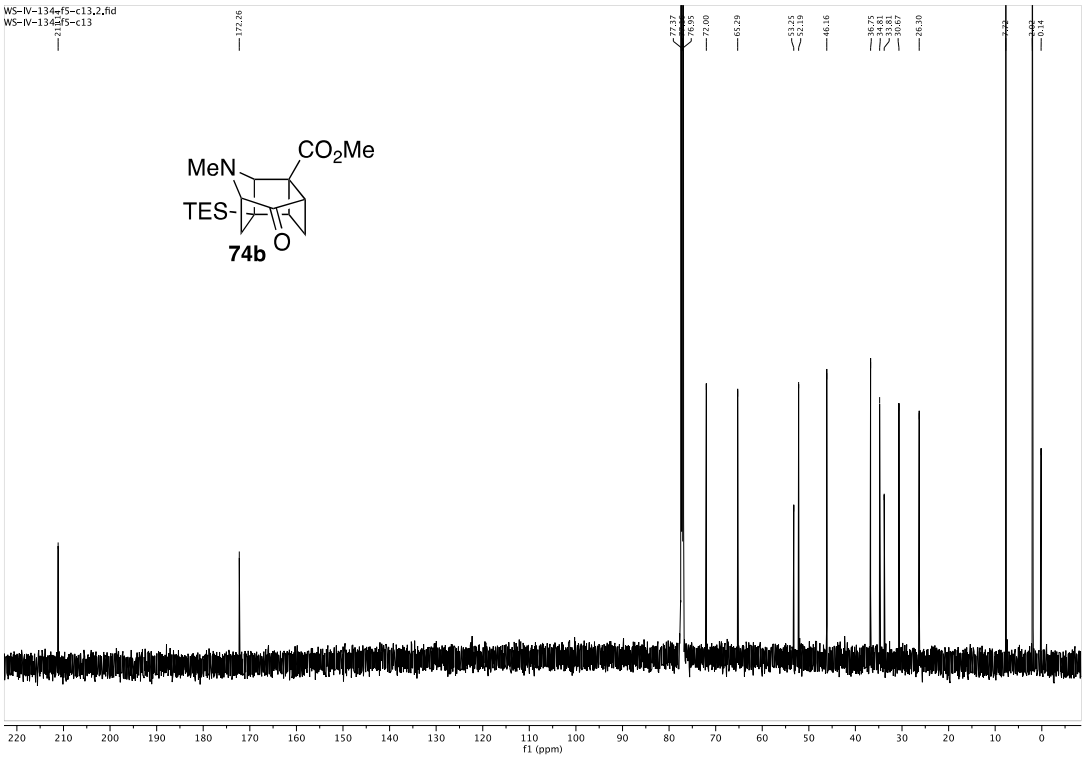

MeN
CO2Me
O
(CH2)2Ph
70
f1 (ppm)

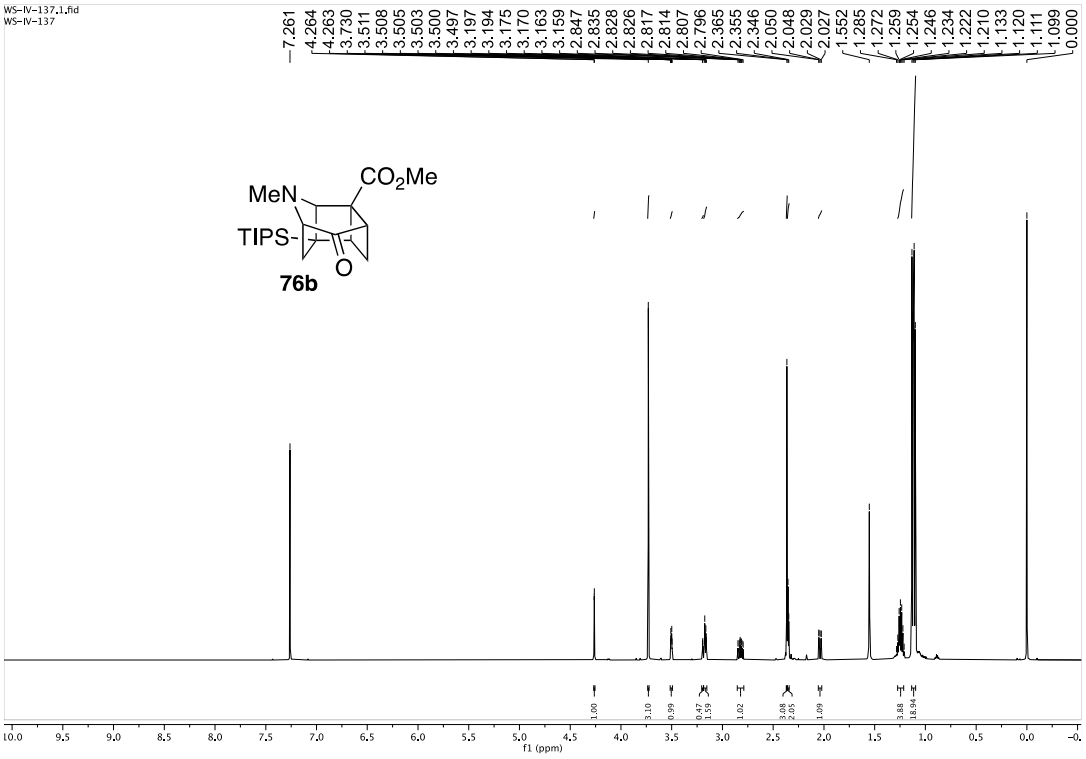

MeN
CO2Me
O
(CH2)2Ph
70
f1 (ppm)

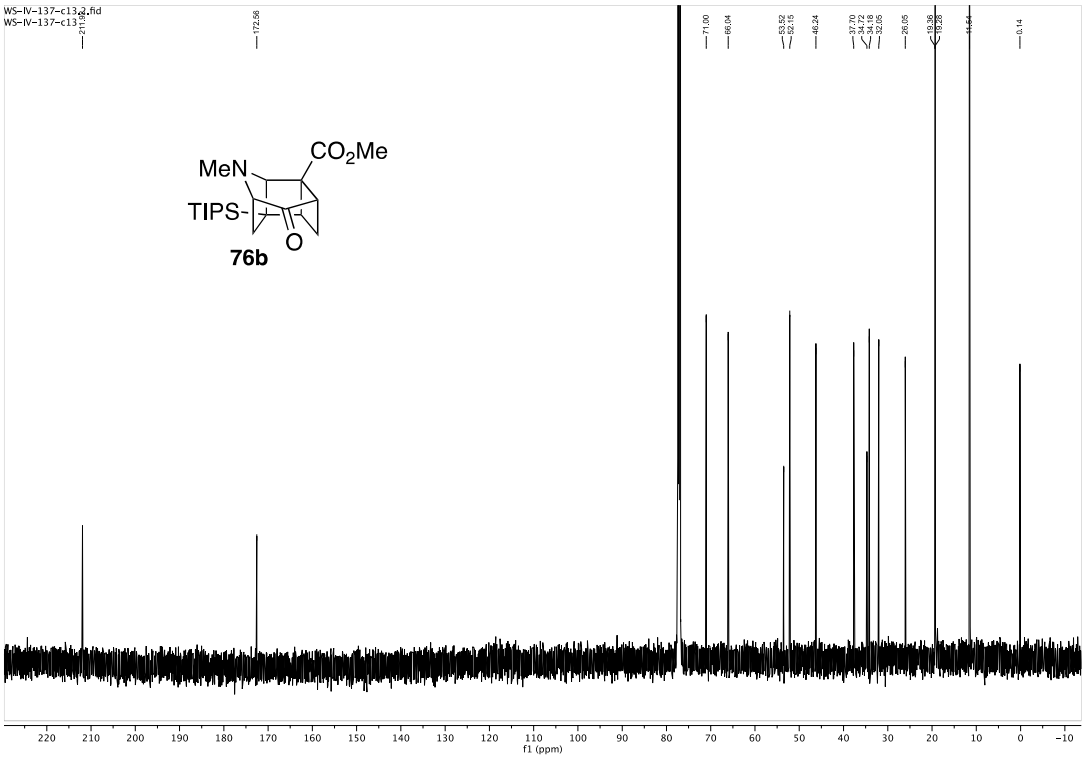

7.305
4.199
4.185
4.184
3.761
3.443
3.440
3.431
3.428
2.994
2.866
2.850
2.834
2.371
2.323
2.298
2.281
2.261
2.242
2.214
2.178
2.166
2.161
2.149
2.138
2.133
2.129
2.125
2.121
2.103
2.099
2.095
1.619
1.557
1.439
1.432
1.418
1.411
1.234
1.231
1.224
1.220
1.204
1.194
1.058
1.055
1.032
1.029
0.909
0.883
-0.000
MeN
CO2Me
O
72a
1.00
3.19
0.97
0.98
1.02
2.84
5.40
1.24
1.08
1.19
1.10
1.04
1.08

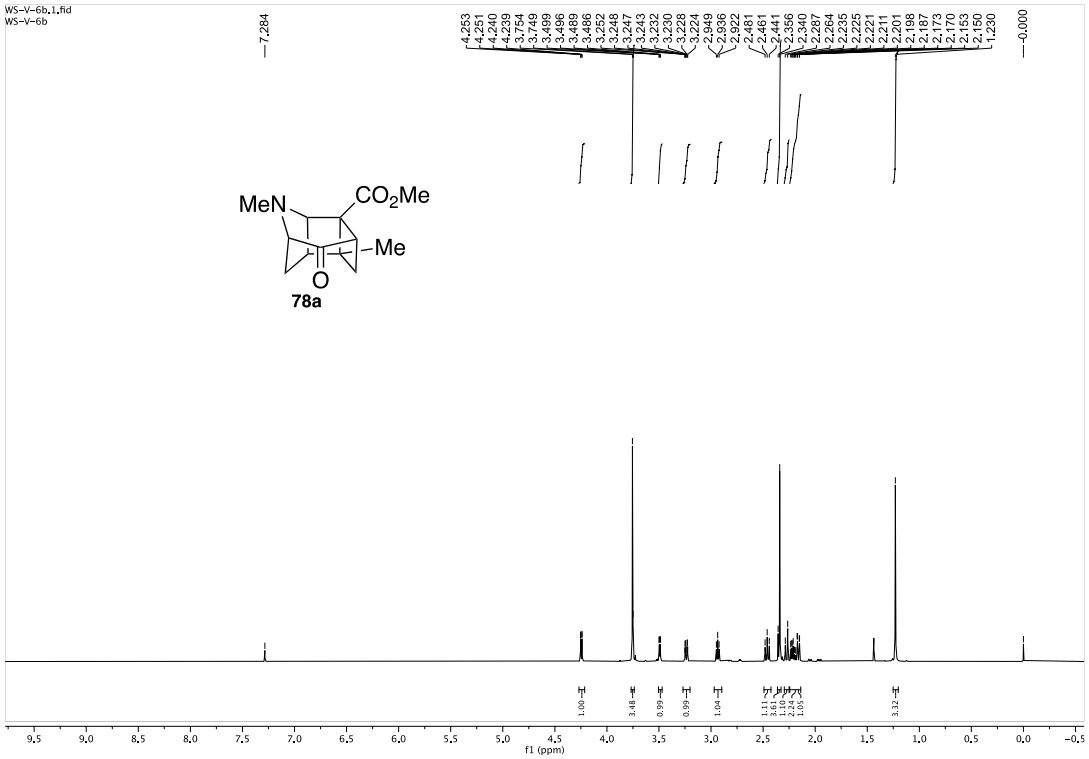

209.86
172.19
71.37
60.85
52.20
52.16
51.89
46.01
44.17
38.84
34.67
31.19
31.01
27.67
25.54
23.28
MeN
CO2Me
O
72a
200
180
160
140
120
100
80
60
40
20
ppm

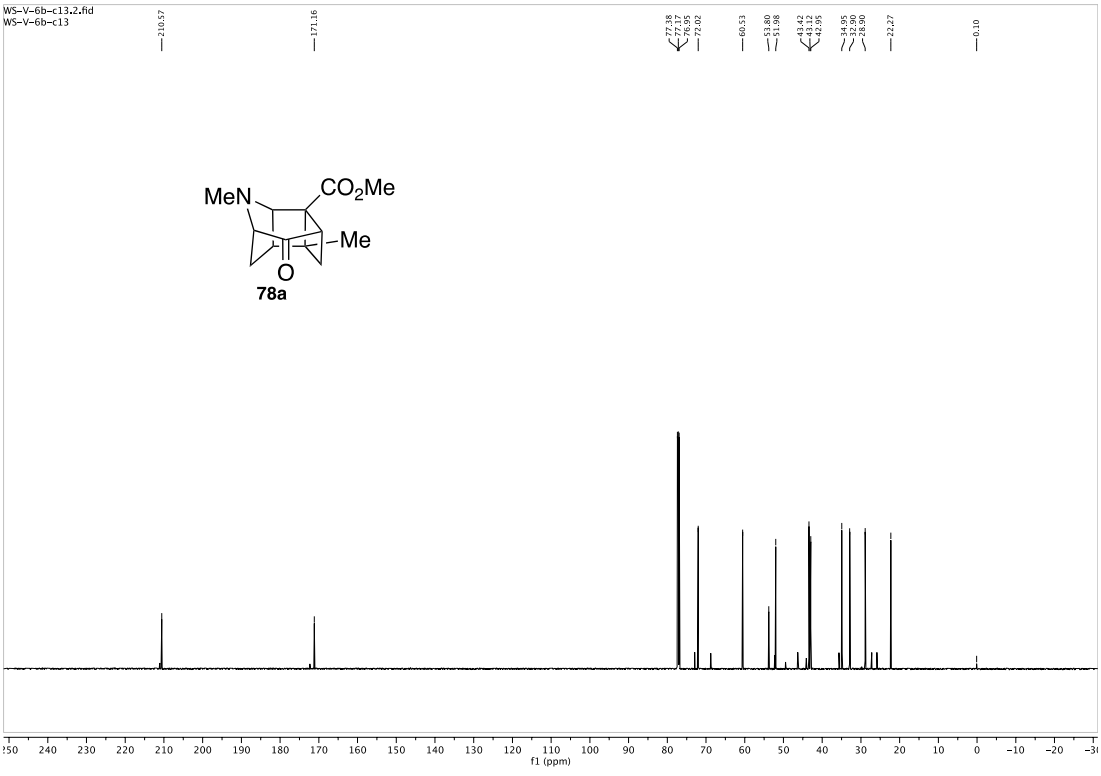

WS-IV-134-f5b.1.fid
WS-IV-134-f5b
MeN
CO2Me
TES-
O
74b
f1 (ppm)

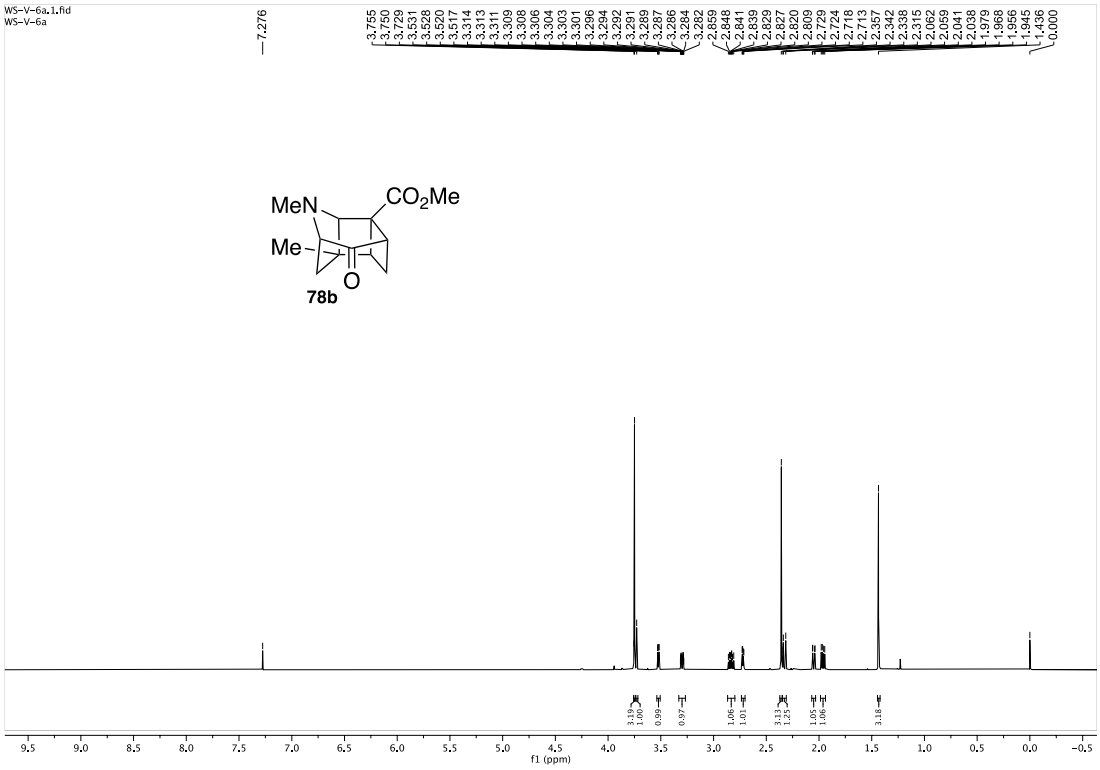

WS-IV-134-f5-c13.2.fid
WS-IV-134-f5-c13
MeN
CO2Me
TES-
O
74b
f1 (ppm)

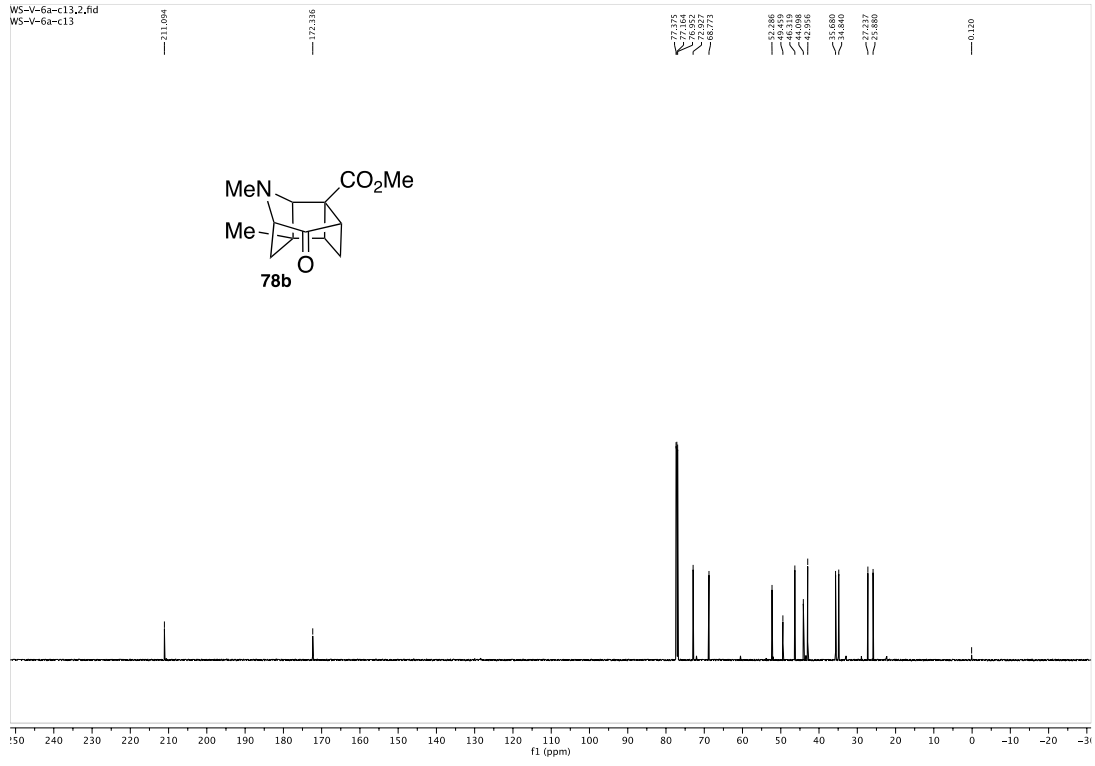

WS-IV-137.1.fid
WS-IV-137
MeN
CO2Me
TIPS-
O
76b
f1 (ppm)

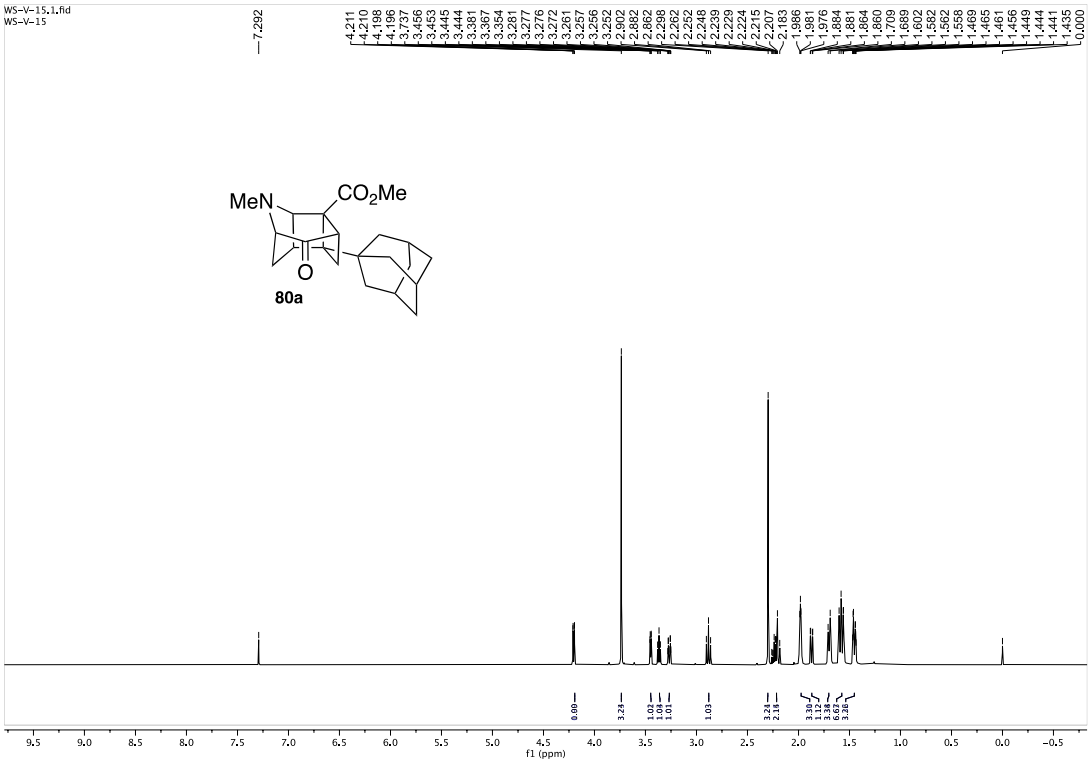

WS-IV-137-c13.1.fid
WS-IV-137-c13
MeN
CO2Me
TIPS-
O
76b
f1 (ppm)

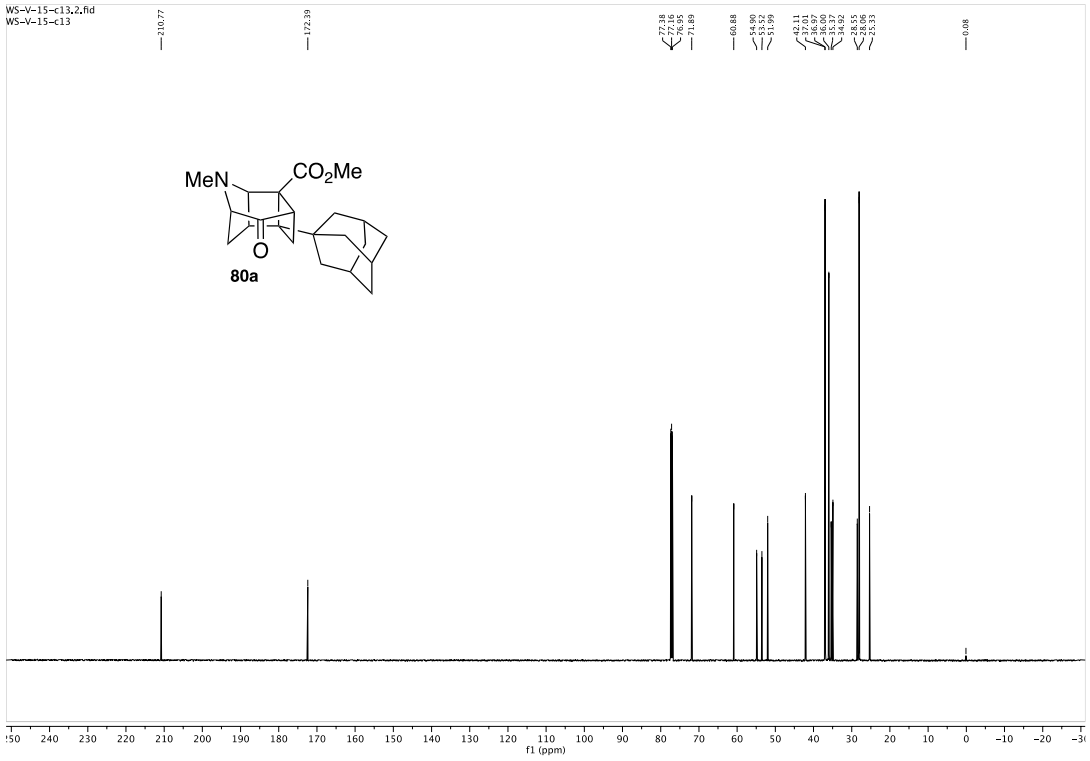

WS-V-6b.1.fid
WS-V-6b
MeN
CO2Me
Me
O
78a
f1 (ppm)


WS-V-6b-c13.2.fid
WS-V-6b-c13
MeN
CO2Me
Me
O
78a
f1 (ppm)


WS-V-6a.1.fid
WS-V-6a
MeN
CO2Me
Me
O
78b
f1 (ppm)

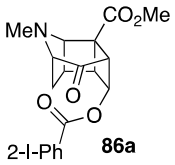

WS-V-6a-c13.2.fid
WS-V-6a-c13
MeN
CO2Me
Me
O
78b
f1 (ppm)


WS-V-15.1.fid
WS-V-15
MeN
CO2Me
O
80a
f1 (ppm)

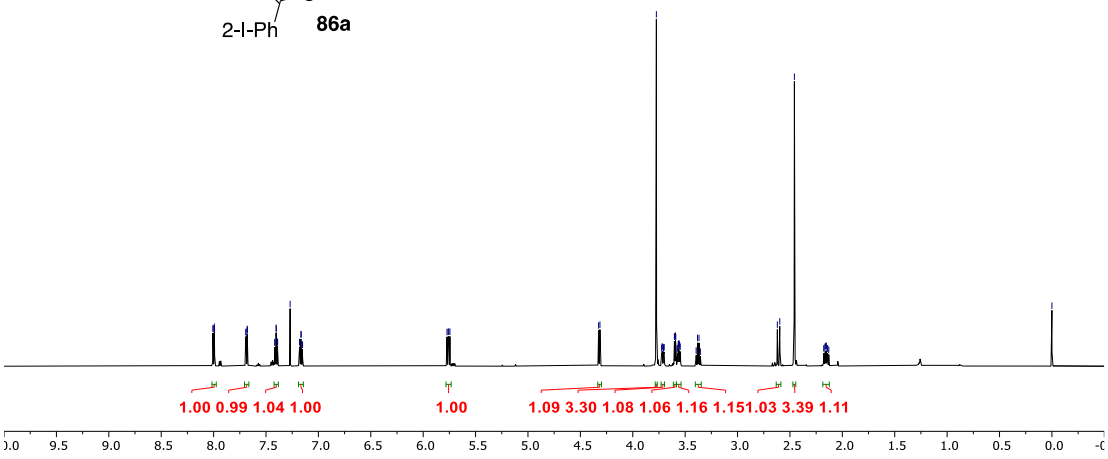

WS-V-15-c13.2.fid
WS-V-15-c13
MeN
CO2Me
O
80a
f1 (ppm)

WS-V-23.1.fid — WS-V-23

8.006 8.004 7.993 7.991 7.693 7.690 7.680 7.677 7.416 7.414 7.404 7.402 7.391 7.389 7.270 7.179 7.177 7.167 7.164 7.154 7.151 5.773 5.762 5.756 5.745 4.326 4.313 3.775 3.721 3.718 3.704 3.701 3.603 3.600 3.592 3.590 3.565 3.564 3.560 3.558 3.553 3.547 3.382 3.368 2.620 2.597 2.458 2.163 2.155 2.152 0.000

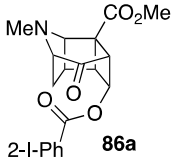


86a

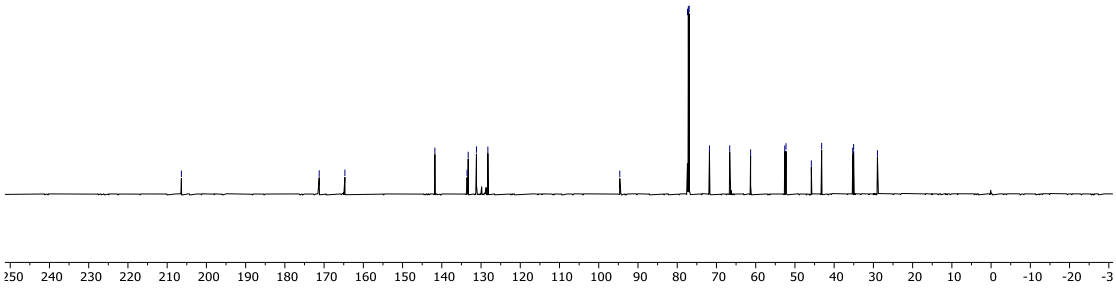


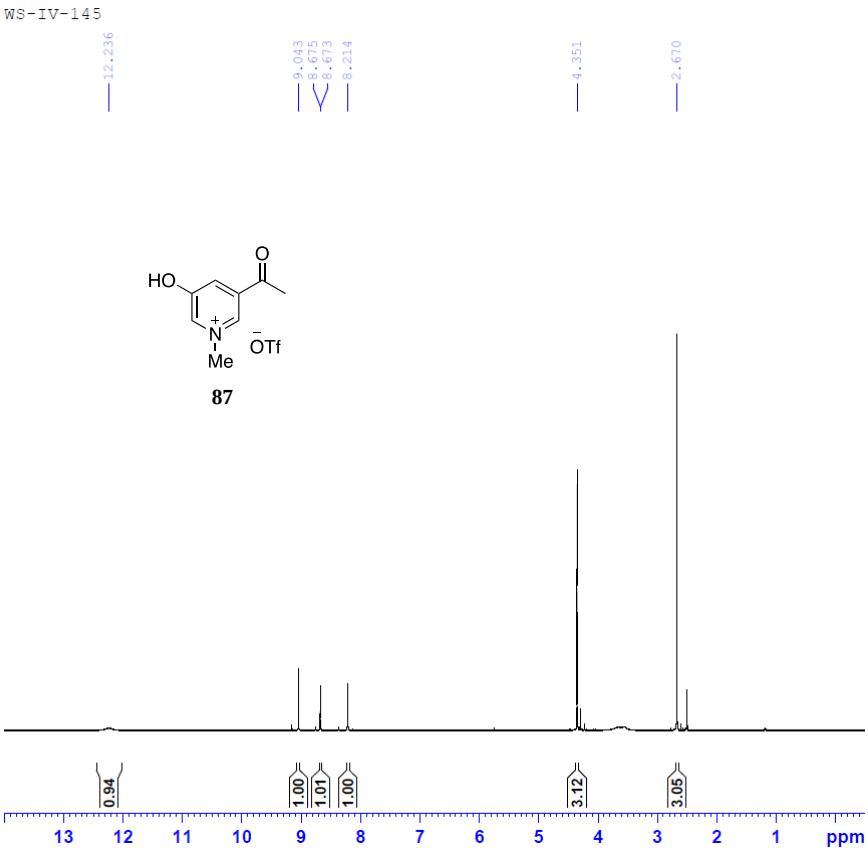
WS-V-23-c13.2.fid — WS-V-23-c13

206.38 171.25 164.70 141.77 133.56 133.27 131.17 128.26 94.64 77.38 77.16 76.95 71.79 66.62 61.30 52.60 52.28 45.82 43.19 35.28 35.04 28.97

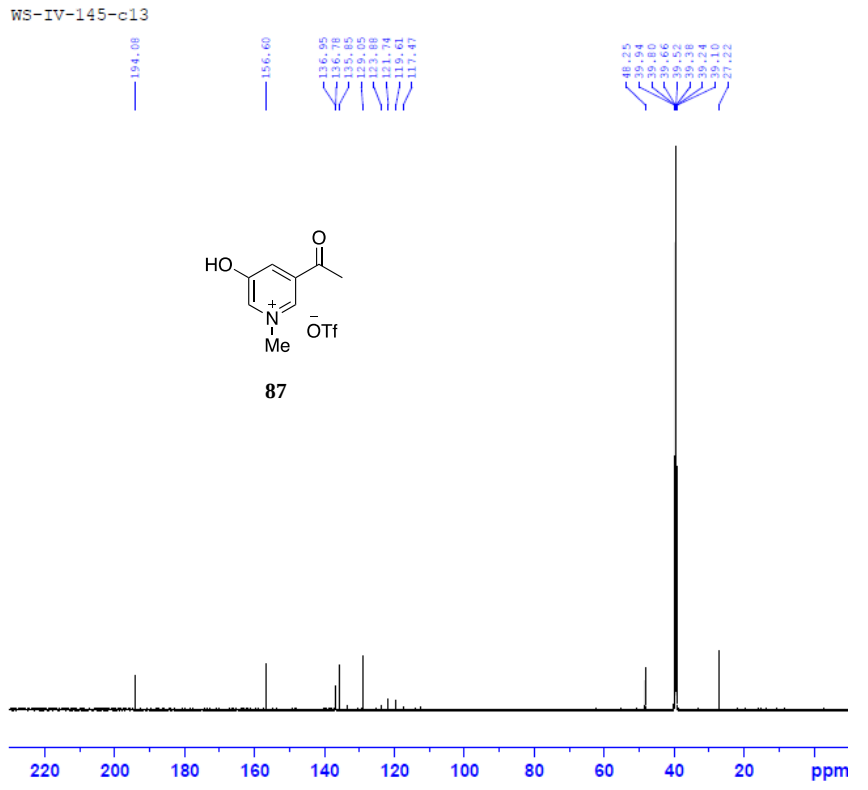


86a



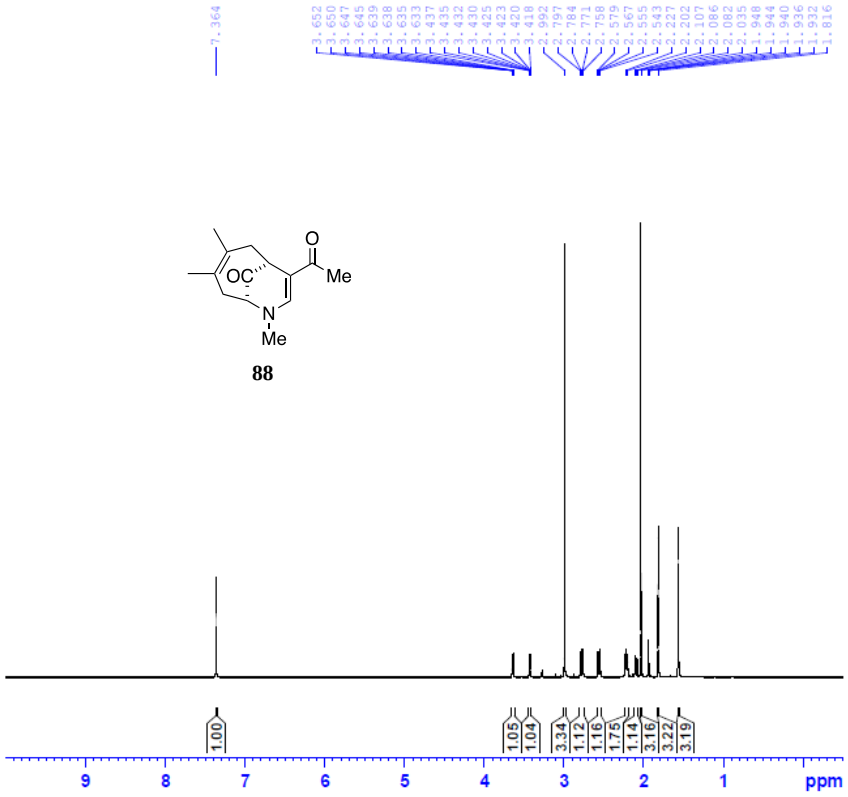

WS-IV-145
12.236
9.043
8.675
8.673
8.214
4.351
2.670
HO
O
N
Me
OTf
0.94
1.00
1.01
1.00
3.12
3.05
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

87


WS-IV-145-c13
194.08
156.60
136.95
136.78
135.85
129.65
123.88
121.74
119.61
117.47
48.25
39.94
39.80
39.66
39.52
39.38
39.24
39.10
27.22
HO
O
N
Me
OTf
220
200
180
160
140
120
100
80
60
40
20
ppm

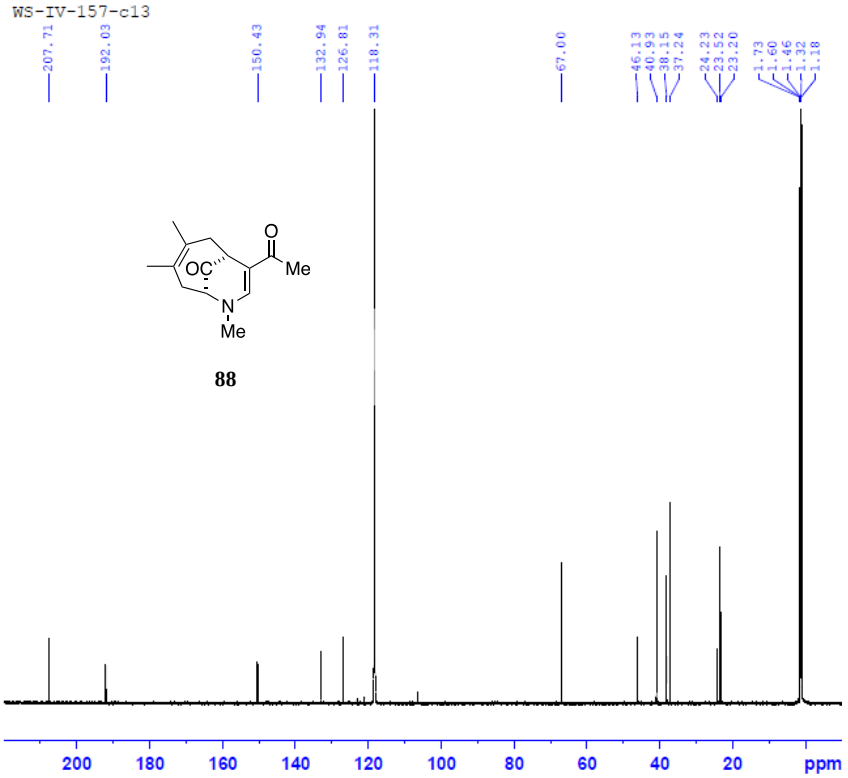
87

WS-IV-157



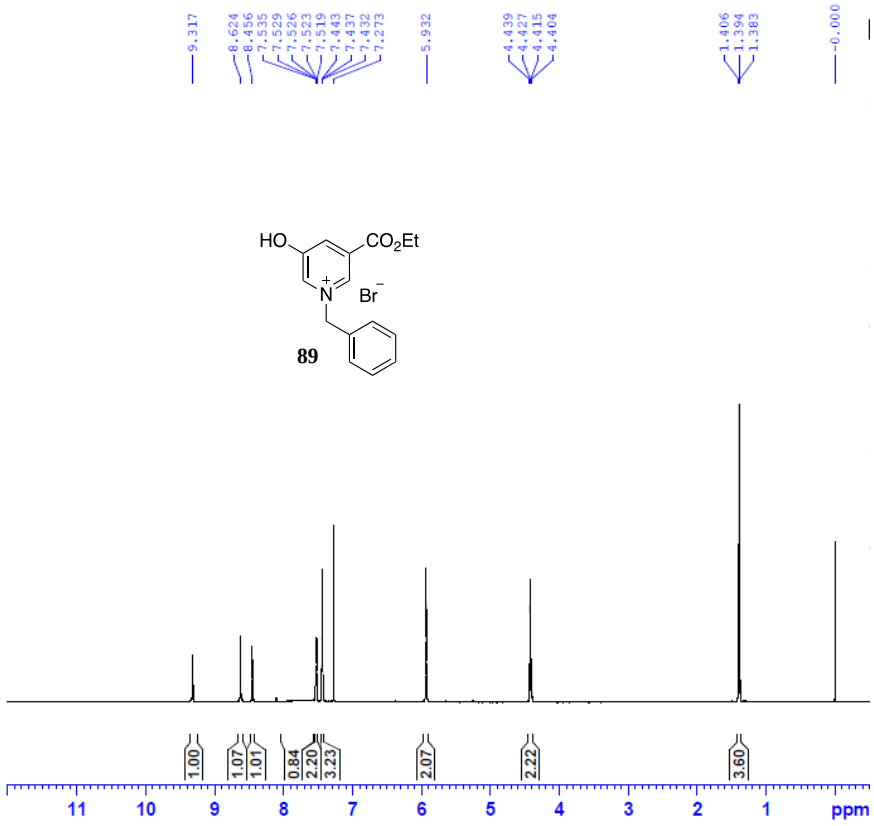
88

WS-IV-157-c13

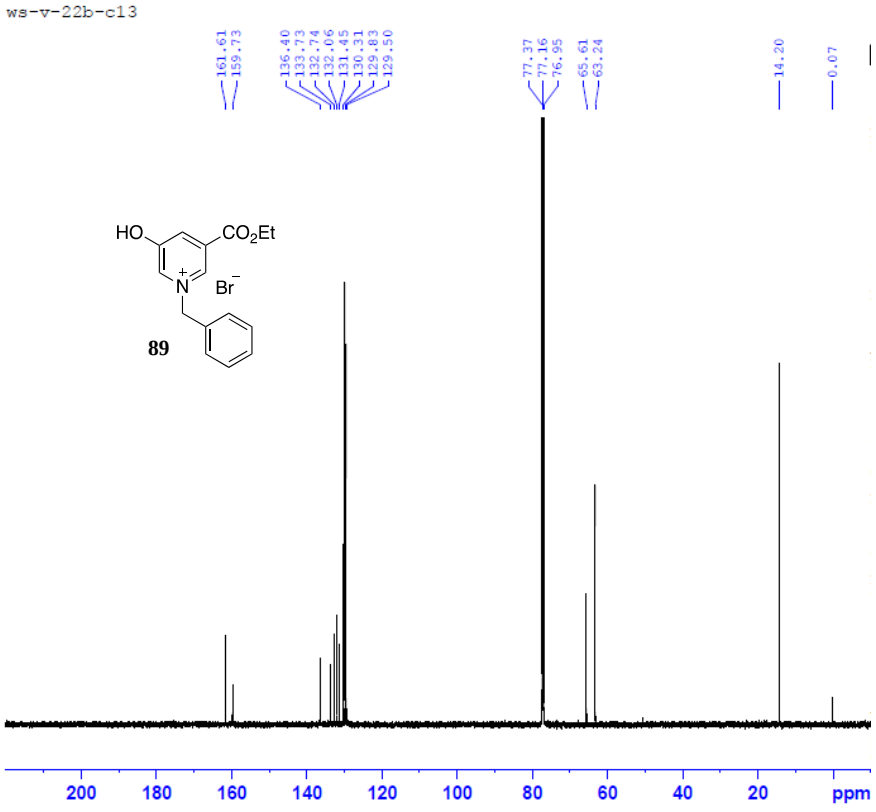


88

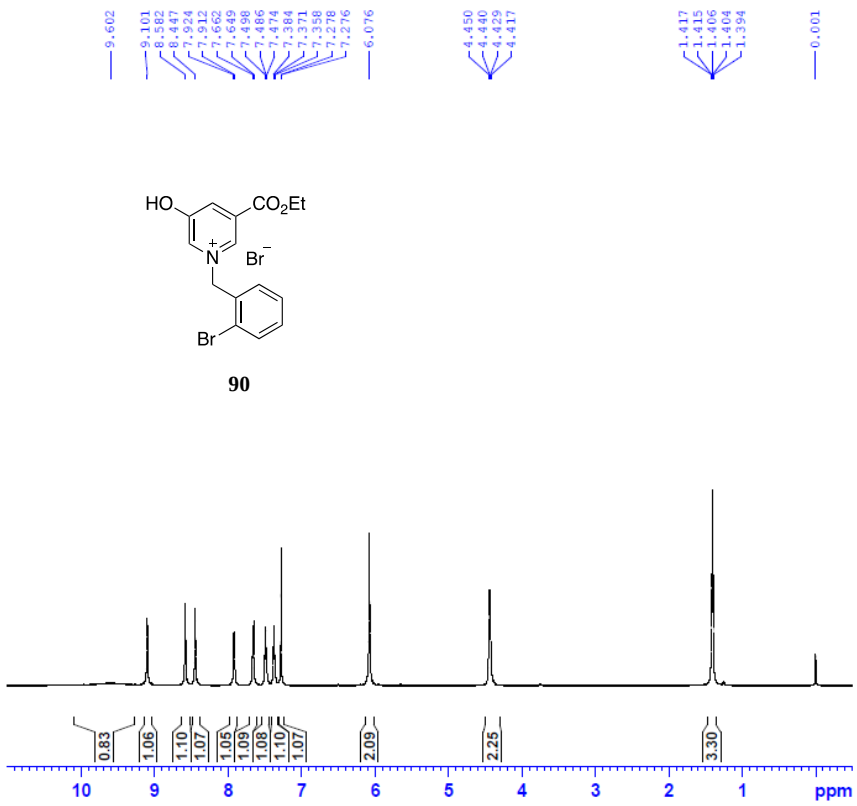
ws-v-22a



ws-v-22b-c13

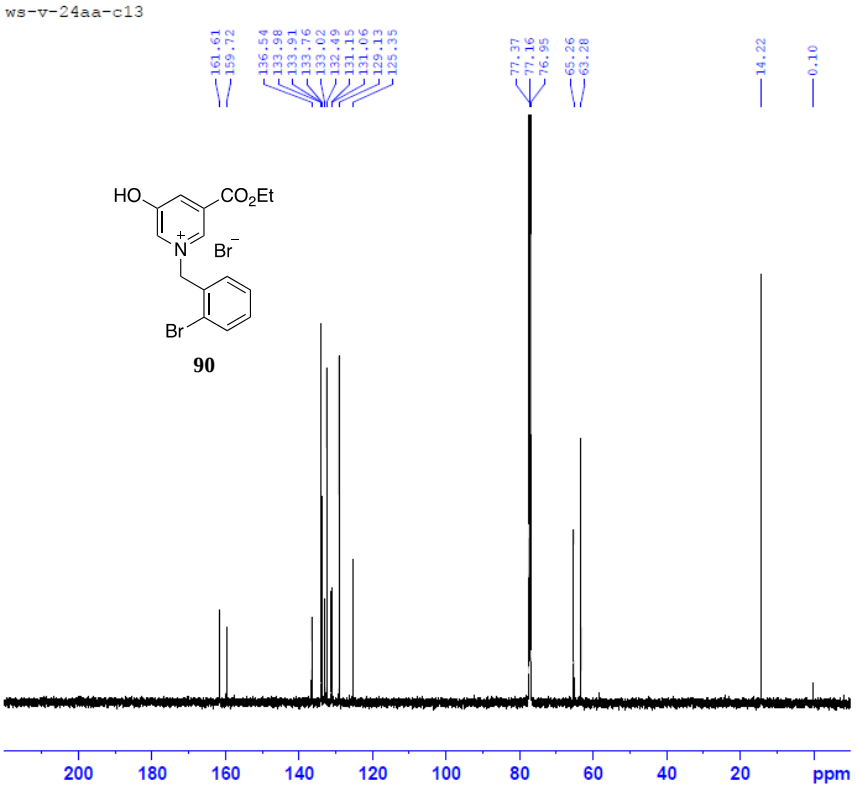


WS-V-24a



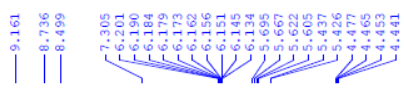
90

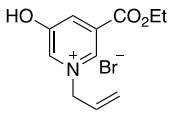
ws-v-24aa-c13



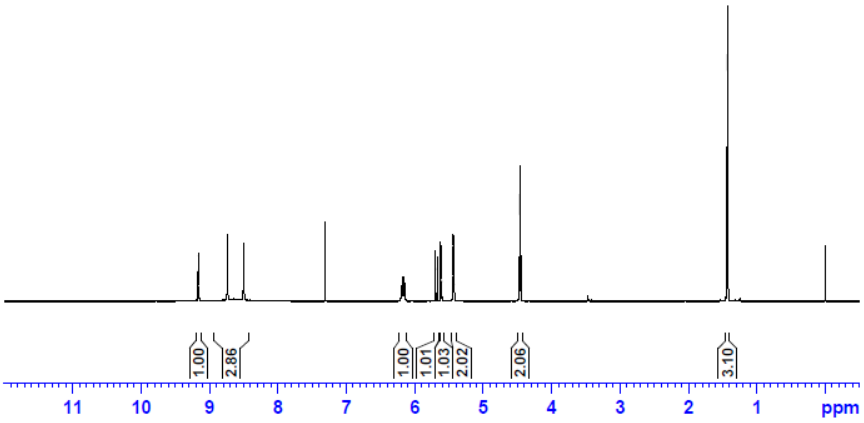
90

ws-v-33b

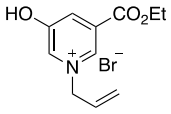




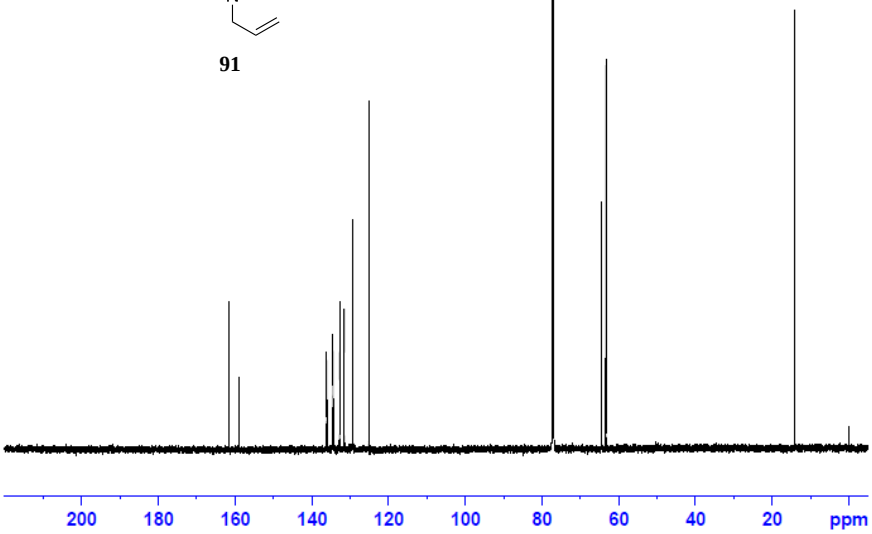
91

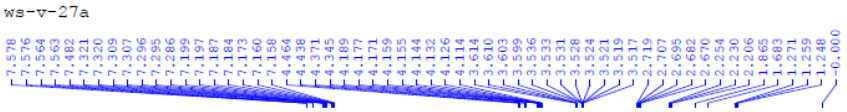


ws-v-33b-c13



91




ws-v-27a
7.578
7.576
7.564
7.563
7.482
7.321
7.320
7.309
7.307
7.296
7.295
7.286
7.199
7.197
7.187
7.184
7.173
7.160
7.158
4.464
4.438
4.371
4.345
4.189
4.177
4.171
4.159
4.155
4.144
4.132
4.126
4.114
3.614
3.610
3.603
3.599
3.536
3.533
3.531
3.528
3.524
3.521
3.519
3.517
2.719
2.707
2.695
2.682
2.670
2.254
2.230
2.206
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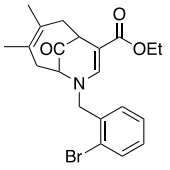
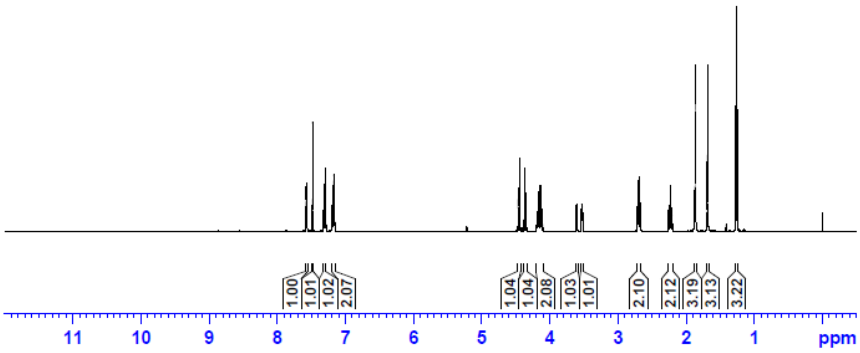
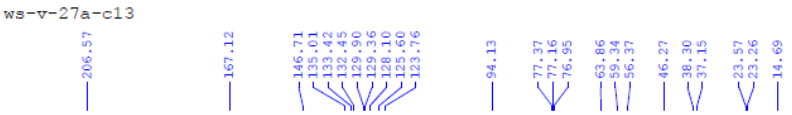
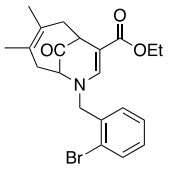
1.683
1.271
1.259
1.248
0.000


O
OC
OEt
N
Br

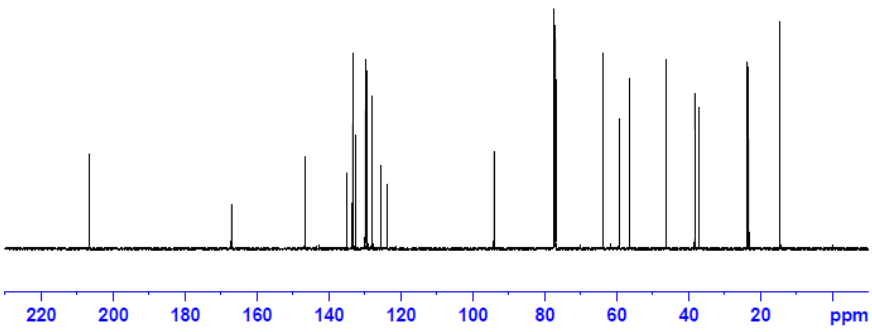
92

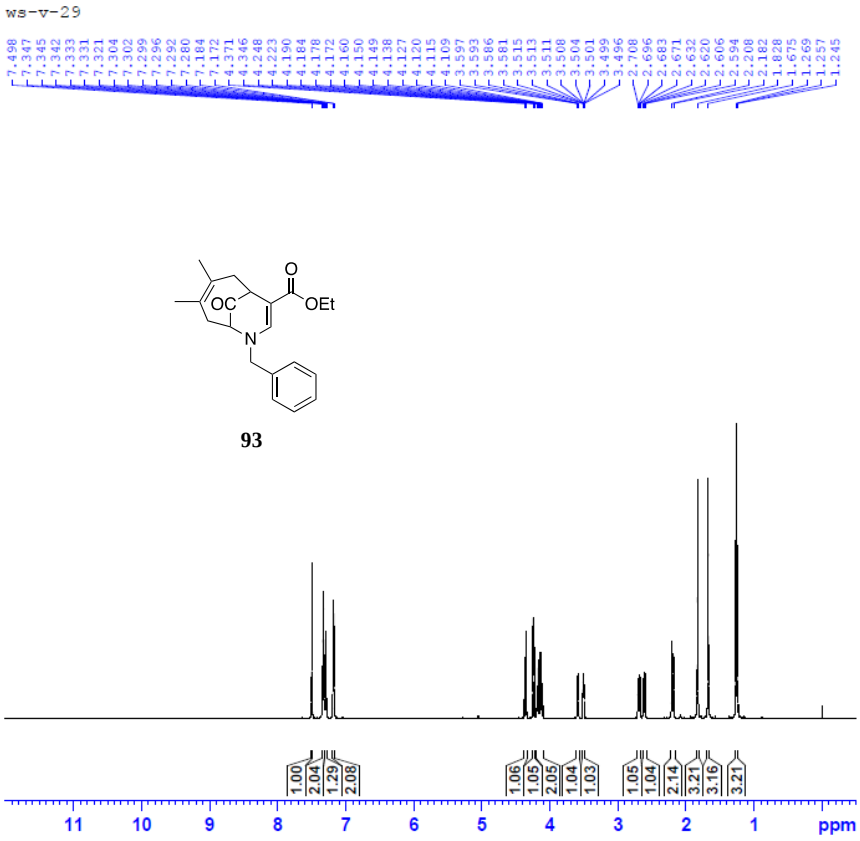

1.00
1.01
1.02
2.07
1.04
1.04
2.08
1.03
1.01
2.10
2.12
3.19
3.13
3.22
11
10
9
8
7
6
5
4
3
2
1
ppm


ws-v-27a-c13
206.57
167.12
146.71
135.01
133.42
132.45
129.90
129.36
128.10
125.60
123.76
94.13
77.37
77.16
76.95
63.86
59.34
56.37
46.27
38.30
37.15
23.57
23.26
14.69

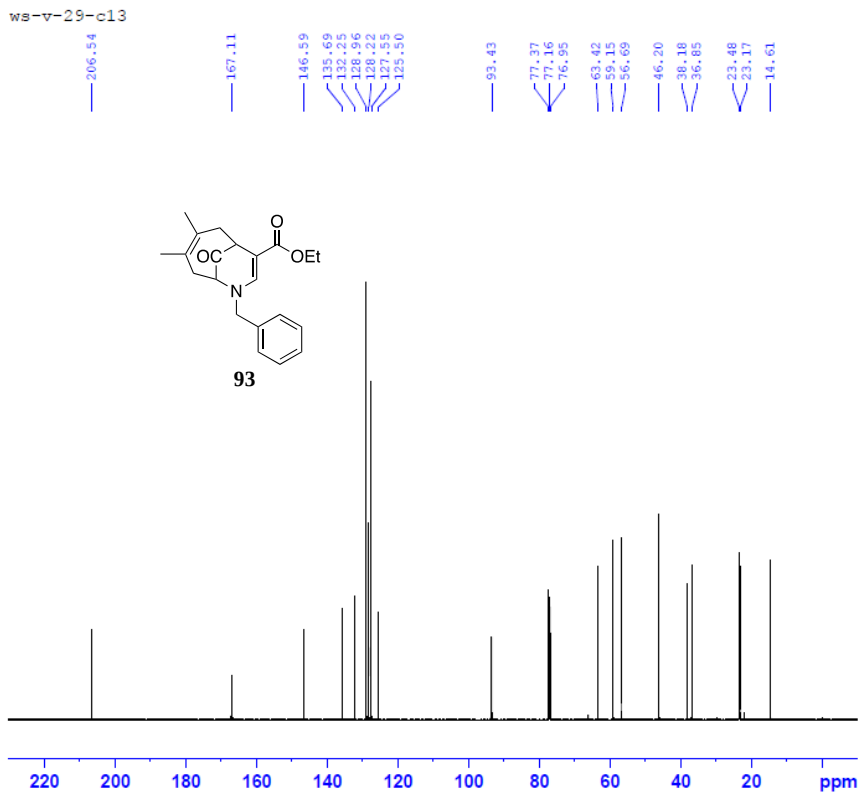

O
OC
OEt
N
Br

92

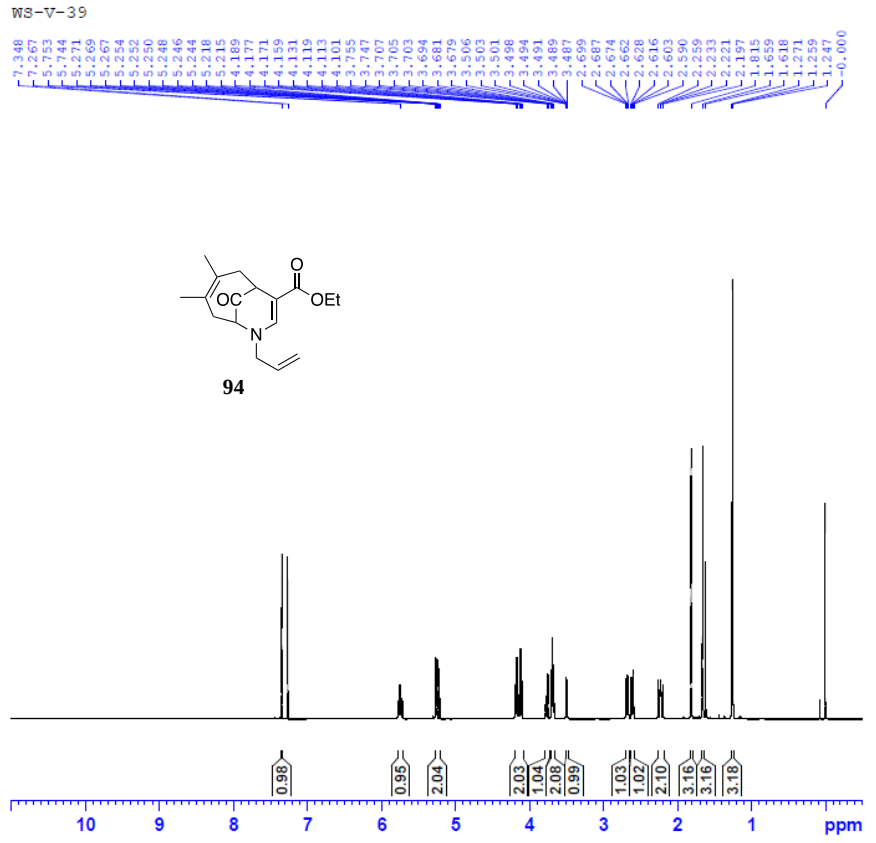

220
200
180
160
140
120
100
80
60
40
20
ppm

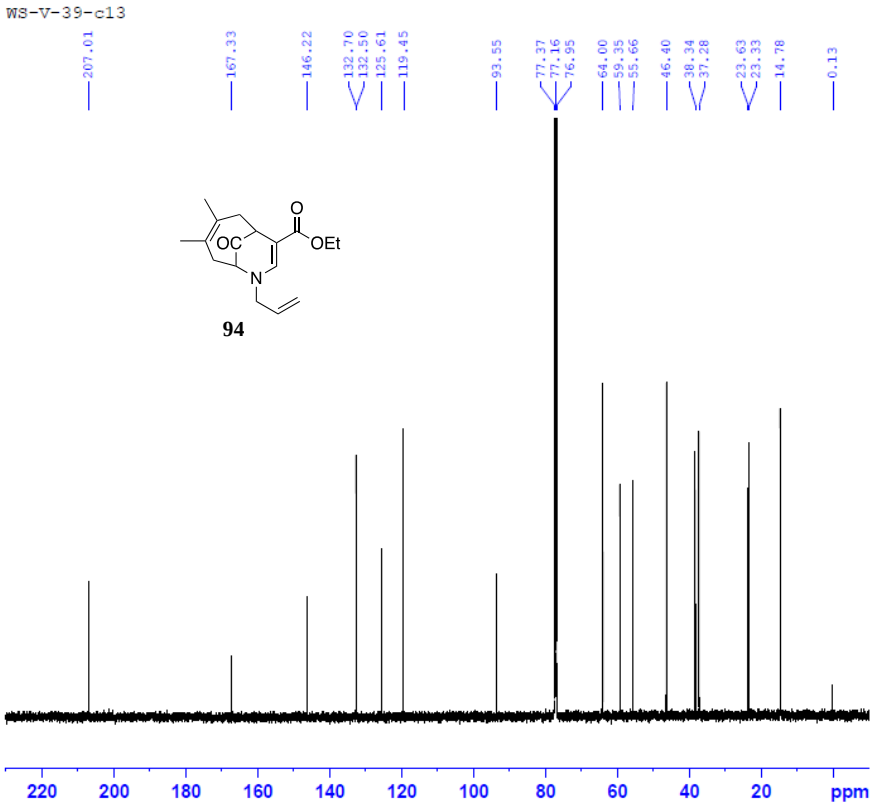

ws-v-29
7.498
7.347
7.345
7.342
7.333
7.331
7.321
7.304
7.302
7.299
7.296
7.292
7.280
7.184
7.172
4.371
4.346
4.248
4.223
4.190
4.184
4.178
4.172
4.160
4.150
4.149
4.138
4.127
4.120
4.115
4.109
3.597
3.593
3.586
3.581
3.515
3.513
3.511
3.508
3.504
3.501
3.499
3.496
2.708
2.696
2.683
2.671
2.632
2.620
2.606
2.594
2.208
2.182
1.828
1.675
1.269
1.257
1.245
O
OEt
OC
N
1.00
2.04
1.29
2.08
1.06
1.05
2.05
1.04
1.03
1.05
1.04
2.14
3.21
3.16
3.21
11
10
9
8
7
6
5
4
3
2
1
ppm

93

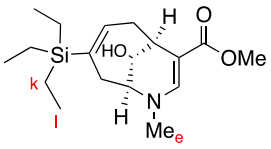

ws-v-29-c13
206.54
167.11
146.59
135.69
132.25
128.96
128.22
127.55
125.50
93.43
77.37
77.16
76.95
63.42
59.15
56.69
46.20
38.18
36.85
23.48
23.17
14.61
O
OEt
OC
N
220
200
180
160
140
120
100
80
60
40
20
ppm

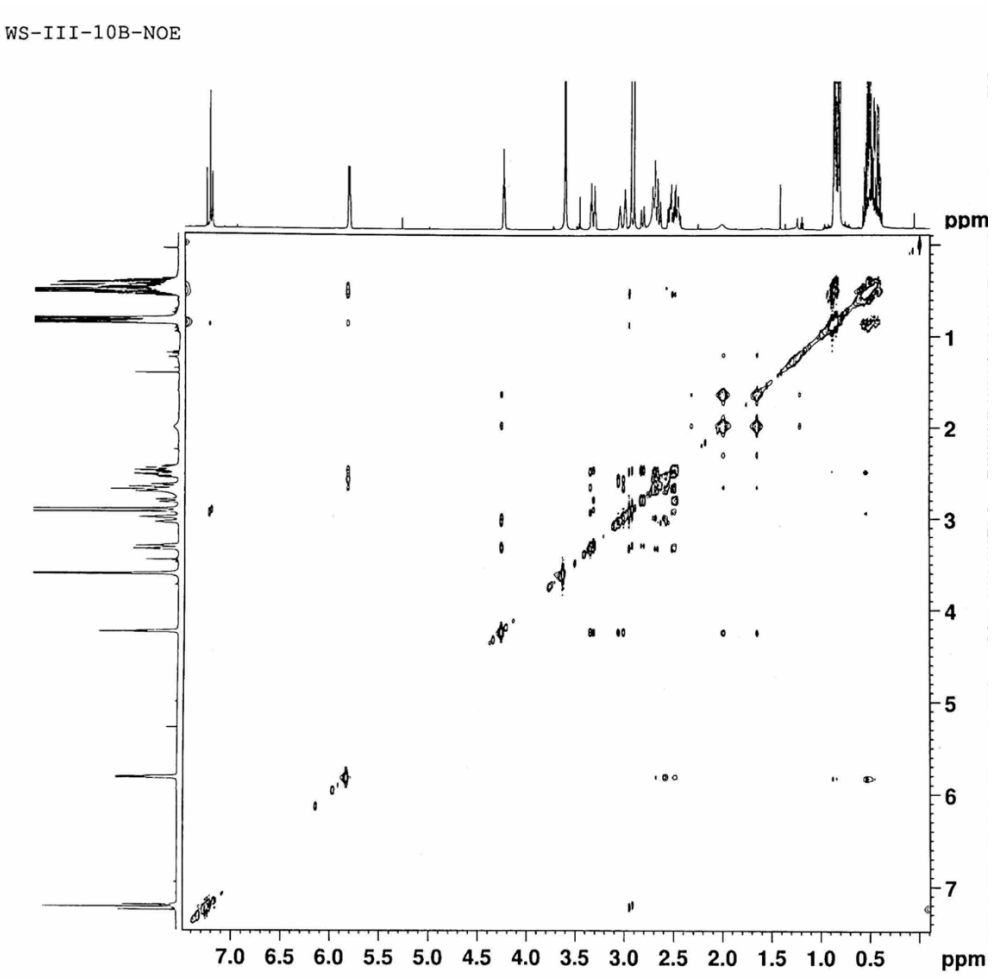
93


WS-V-39
OC
OEt
O
N
94
0.98
0.95
2.04
2.03
1.04
2.08
0.99
1.03
1.02
2.10
3.16
3.16
3.18
10
9
8
7
6
5
4
3
2
1
ppm

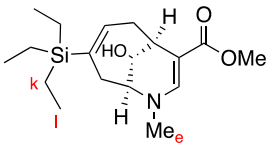

WS-V-39-c13
207.01
167.33
146.22
132.70
132.50
125.61
119.45
93.55
77.37
77.16
76.95
64.00
59.35
55.66
46.40
38.34
37.28
23.63
23.33
14.78
0.13
OC
OEt
O
N
94
220
200
180
160
140
120
100
80
60
40
20
ppm

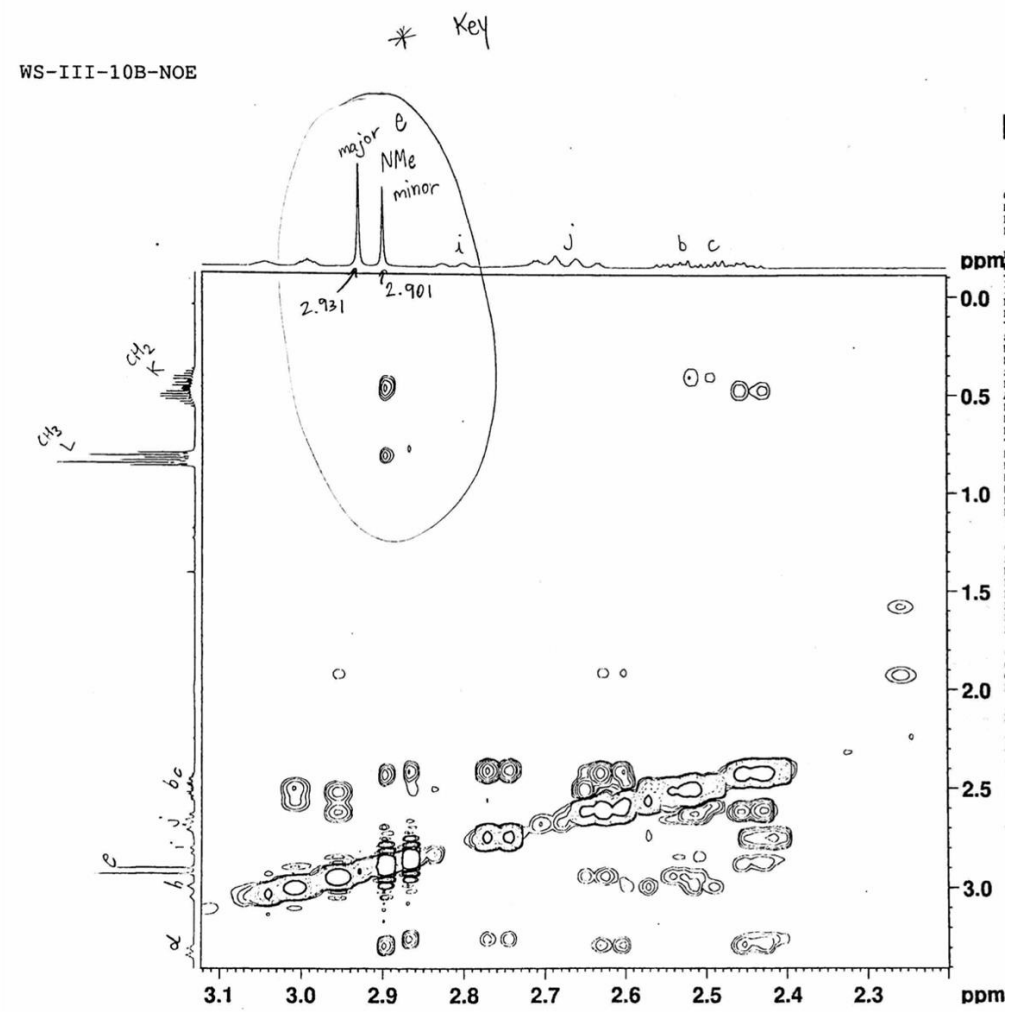
NOESY of the Reduction of Compound **39**



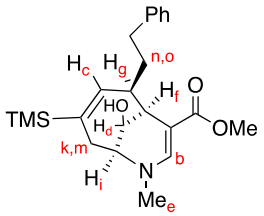


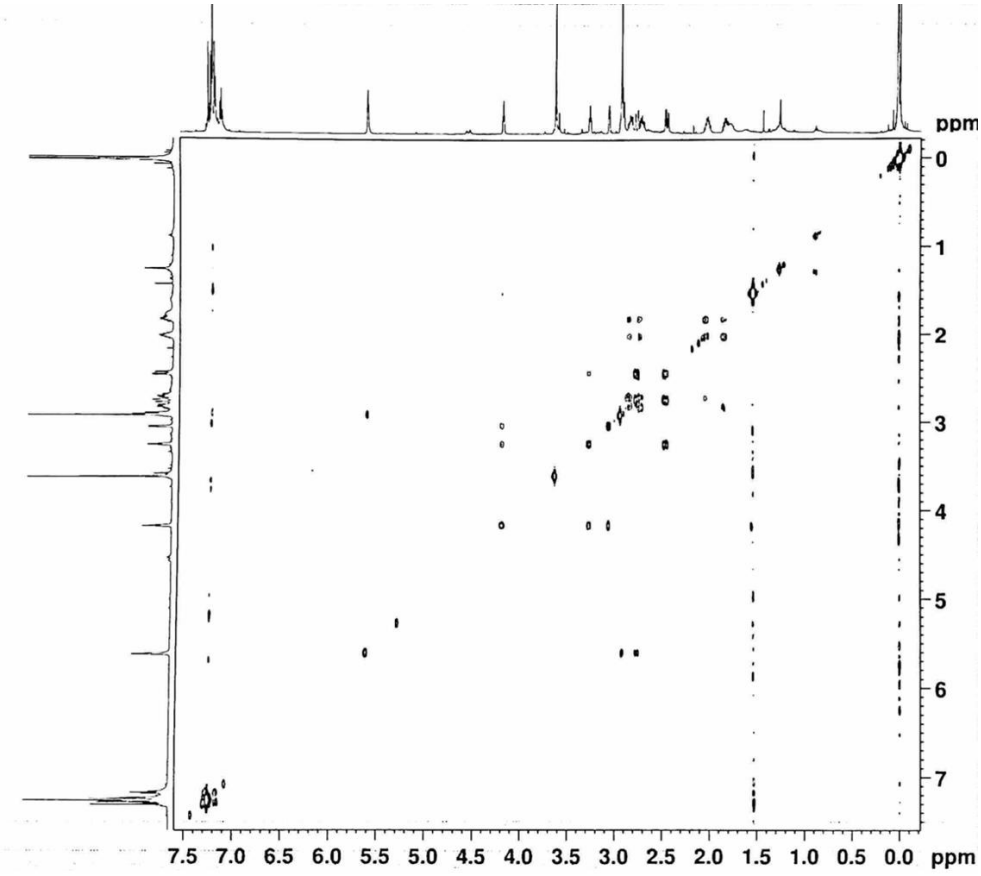
Zoom in NOESY of the Reduction of Compound **39**



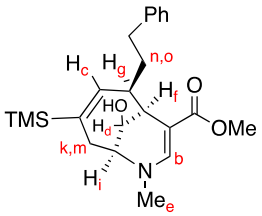


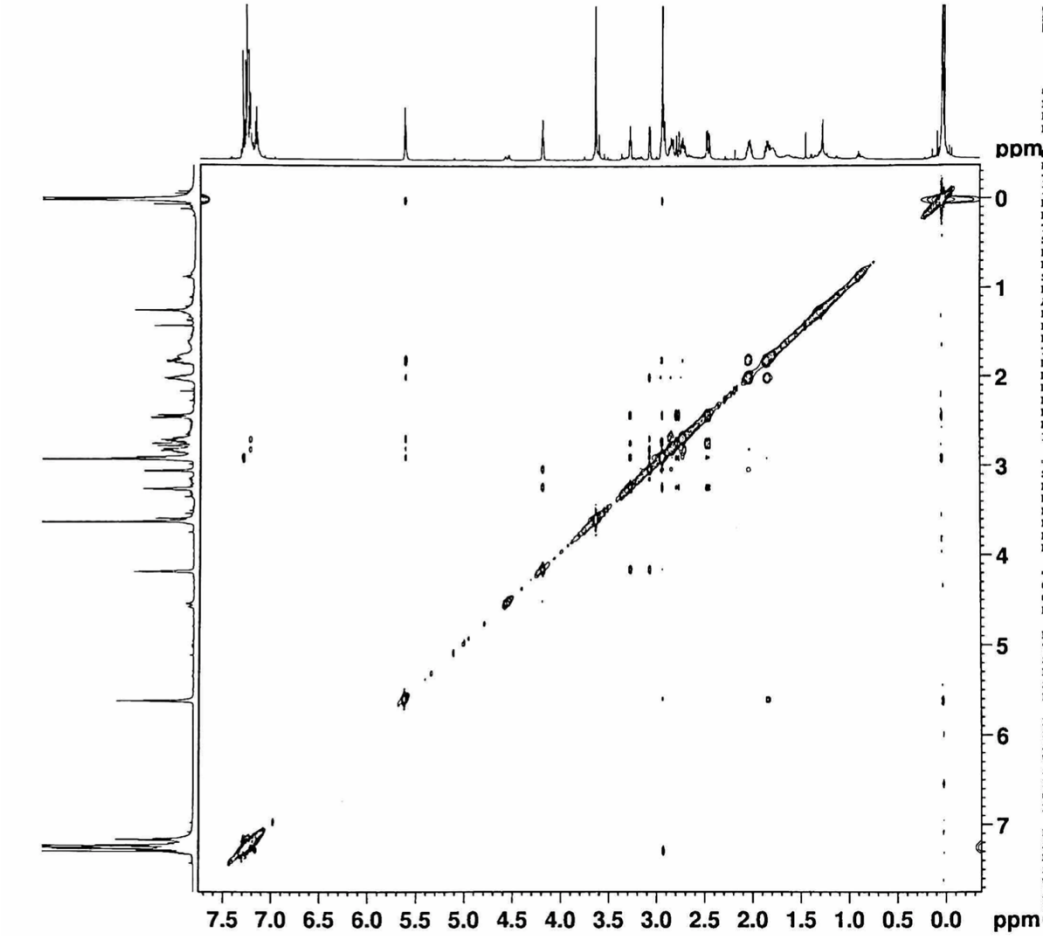
COSY of the Reduction of Compound **31b**



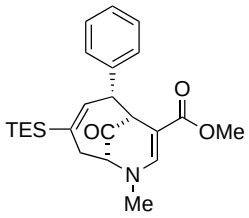


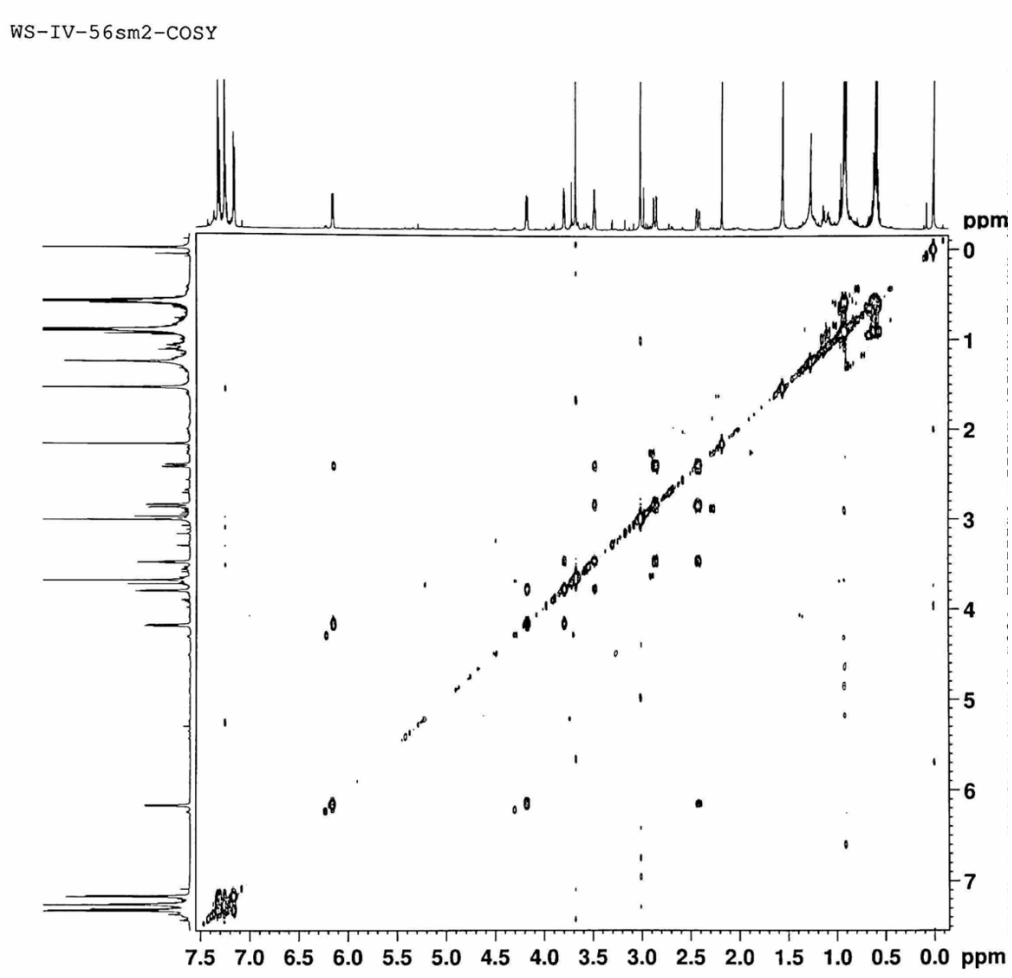
NOESY of the Reduction of Compound **31b**



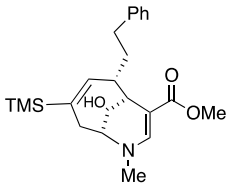


COSY of the Minor Isomer of Compound **42**





X-Ray Crystallographic of Compound **31a**



Bond precision: C-C = 0.0039 A Wavelength=0.71073

Cell: a=15.8194(10) b=6.6586(5) c=21.5171(15) alpha=90 beta=92.423(3) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2264.5(3)	2264.5(3)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C23 H33 N O3 Si	C23 H33 N O3 Si
Sum formula	C23 H33 N O3 Si	C23 H33 N O3 Si
Mr	399.59	399.59
Dx,g cm-3	1.172	1.172
Z	4	4
Mu (mm-1)	0.126	0.126
F000	864.0	864.0
F000’	864.66	
h,k,lmax	19,8,26	19,8,26
Nref	4645	4643
Tmin,Tmax	0.998,0.999	0.671,0.745
Tmin’	0.959	

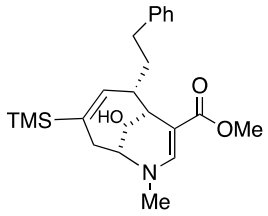
Correction method= # Reported T Limits: Tmin=0.671 Tmax=0.745

AbsCorr = MULTI-SCAN

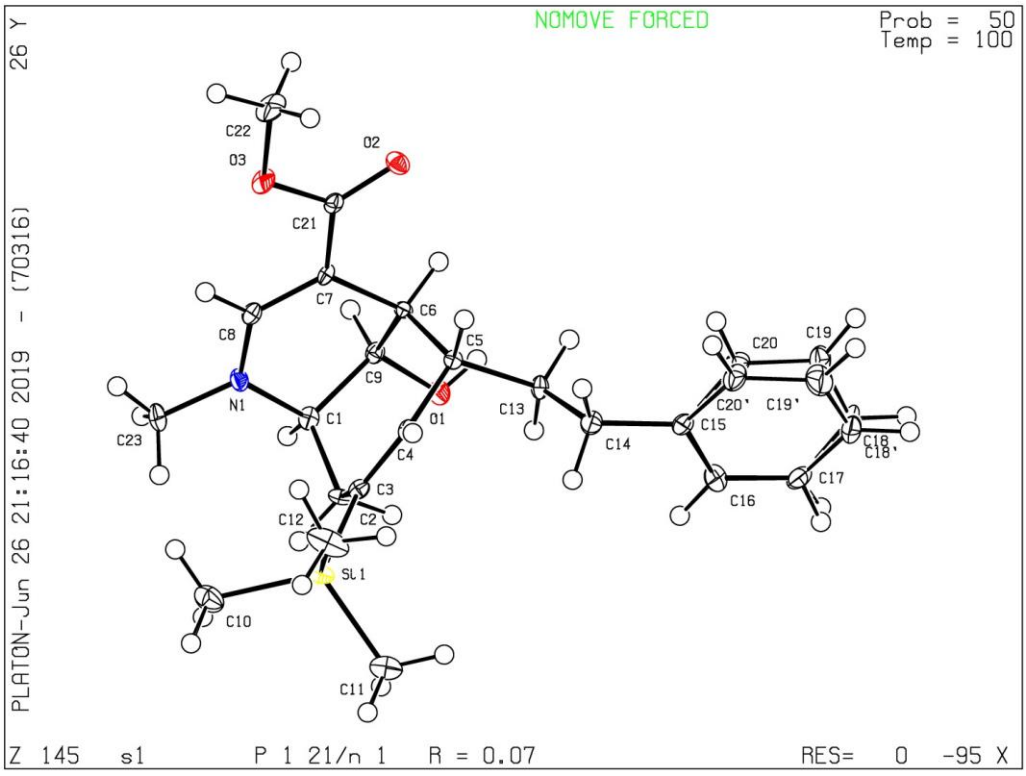
Data completeness= 1.000 Theta(max)= 26.375

R(reflections)= 0.0687(3090) wR2(reflections)= 0.1236(4643)

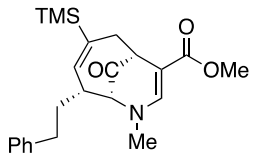
S = 1.086 Npar= 288



Thermal ellipsoids are set at the 50% probability level



Compound **31c**



Bond precision: C-C = 0.0018 A Wavelength=1.54178

Cell: a=7.0770(3) b=10.0844(4) c=17.0797(6)
alpha=103.8327(15) beta=92.2183(16) gamma=108.9342(15)

Temperature: 150 K

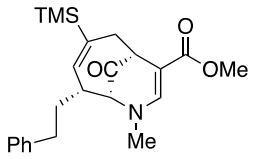
	Calculated	Reported
Volume	1110.53(8)	1110.53(8)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C23 H31 N O3 Si	C23 H31 N O3 Si
Sum formula	C23 H31 N O3 Si	C23 H31 N O3 Si
Mr	397.58	397.58
Dx,g cm-3	1.189	1.189
Z	2	2
Mu (mm-1)	1.106	1.106
F000	428.0	428.0
F000’	429.64	
h,k,lmax	8,12,21	8,12,21
Nref	4508	4365
Tmin,Tmax	0.798,0.967	0.652,0.754
Tmin’	0.615	

Correction method= # Reported T Limits: Tmin=0.652 Tmax=0.754. AbsCorr = MULTI-SCAN

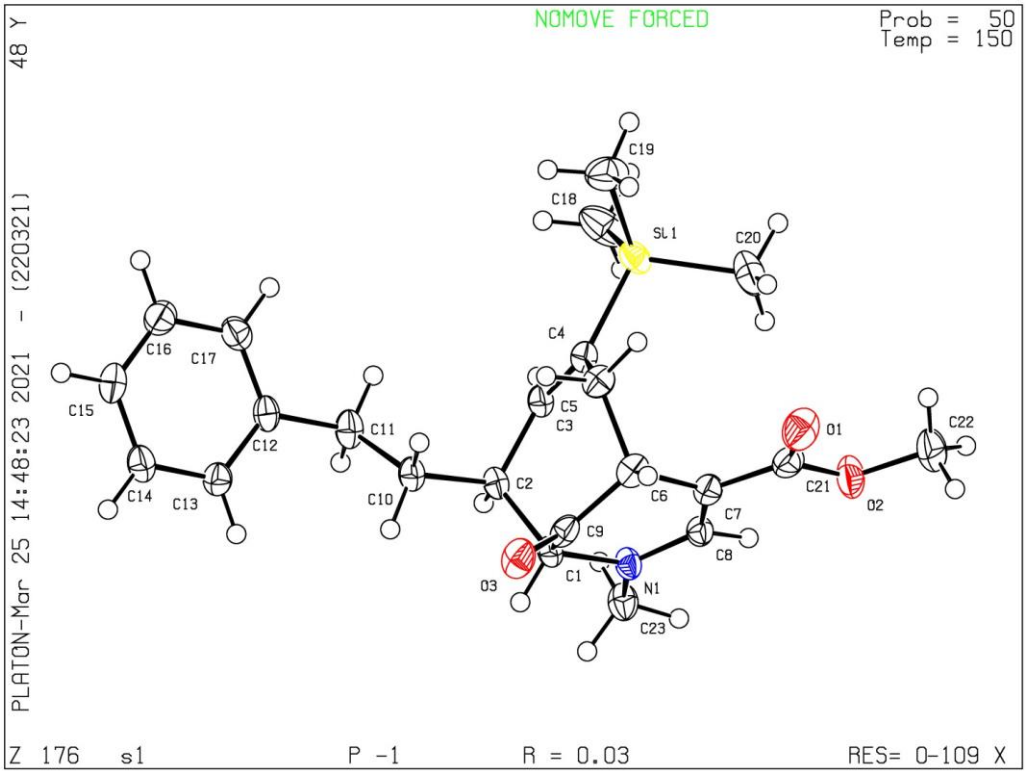
Data completeness= 0.968 Theta(max)= 73.950

R(reflections)= 0.0333(4092) wR2(reflections)= 0.0900(4365)

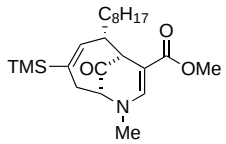
S = 1.038 Npar= 276



Thermal ellipsoids are set at the 50% probability level



Compound **33**



Bond precision: C-C = 0.0052 A Wavelength=0.71073

Cell: a=7.0328(11) b=39.280(6) c=9.0010(14)

alpha=90 beta=98.548(6) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2458.9(7)	2458.9(6)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C23 H39 N O3 Si	C23 H39 N O3 Si
Sum formula	C23 H39 N O3 Si	C23 H39 N O3 Si
Mr	405.64	405.64
Dx,g cm-3	1.096	1.096
Z	4	4
Mu (mm-1)	0.116	0.116
F000	888.0	888.0
F000’	888.66	
h,k,lmax	8,49,11	8,49,11
Nref	5074	5059
Tmin,Tmax	0.990,0.999	0.629,0.745
Tmin’	0.986	

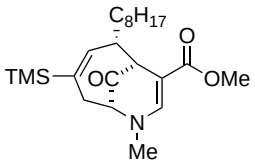
Correction method= # Reported T Limits: Tmin=0.629 Tmax=0.745

AbsCorr = MULTI-SCAN

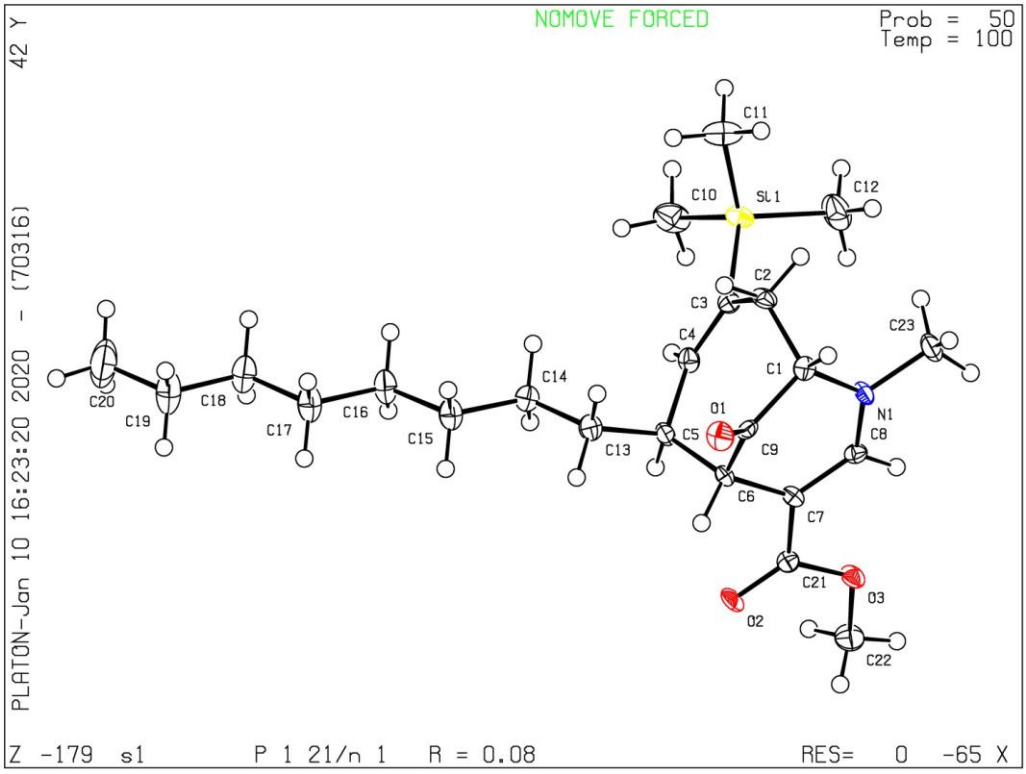
Data completeness= 0.997 Theta(max)= 26.444

R(reflections)= 0.0814(3292) wR2(reflections)= 0.1557(5059)

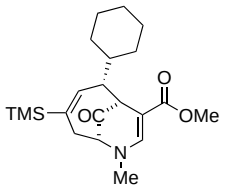
S = 1.154 Npar= 259



Thermal ellipsoids are set at the 50% probability level



Compound **37**



Bond precision: C-C = 0.0049 A Wavelength=1.54178

Cell: a=16.5870(19) b=7.2183(9) c=17.885(2) alpha=90 beta=105.909(10) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	2059.4(4)	2059.4(4)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C21 H33 N O3 Si	C21 H33 N O3 Si
Sum formula	C21 H33 N O3 Si	C21 H33 N O3 Si
Mr	375.57	375.57
Dx,g cm-3	1.211	1.211
Z	4	4
Mu (mm-1)	1.158	1.158
F000	816.0	816.0
F000’	819.14	
h,k,lmax	18,8,19	18,8,19
Nref	2962	2950
Tmin,Tmax	0.933,0.977	0.547,0.752
Tmin’	0.601	

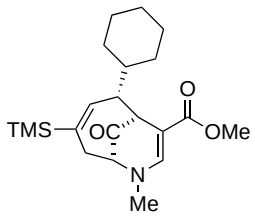
Correction method= # Reported T Limits: Tmin=0.547 Tmax=0.752

AbsCorr = NONE

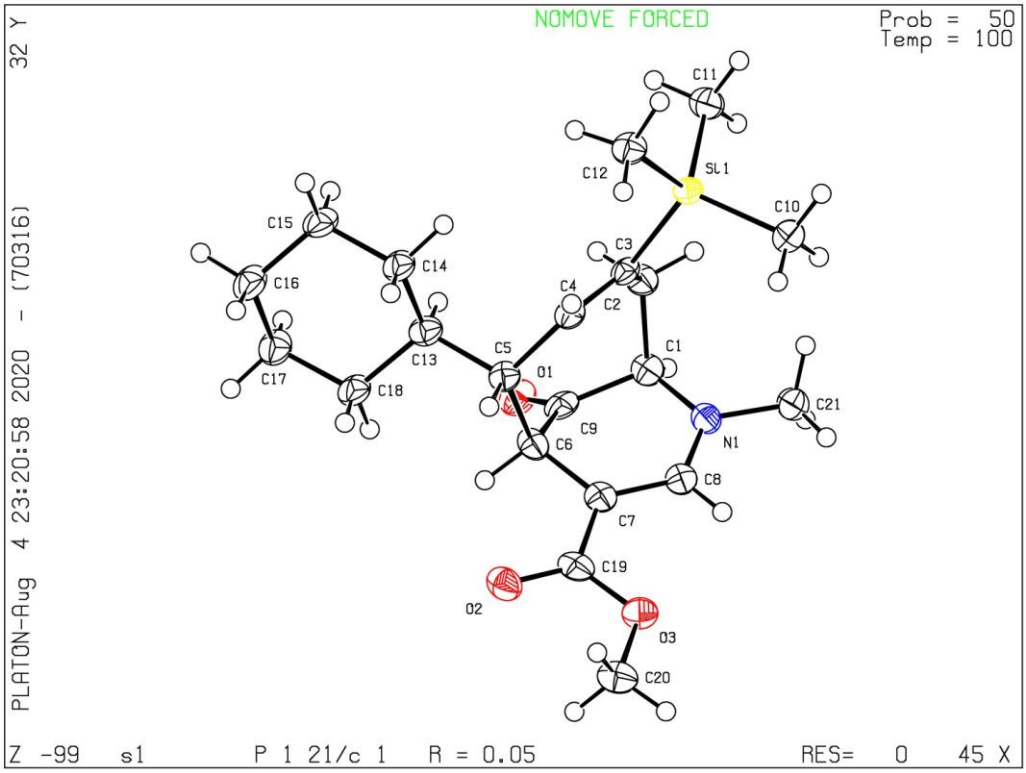
Data completeness= 0.996 Theta(max)= 59.049

R(reflections)= 0.0545(2284) wR2(reflections)= 0.1396(2950)

S = 1.046 Npar= 240



Thermal ellipsoids are set at the 50% probability level



Crystal data and structure refinement for **80a**.

Bond precision: C-C = 0.0017 A Wavelength=1.54178

Cell: a=6.4954(1) b=11.6955(2) c=12.1509(2)
alpha=85.8963(11) beta=78.5840(9) gamma=82.2282(9)
Temperature: 173 K

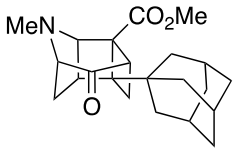
	Calculated	Reported
Volume	895.54(3)	895.54(3)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C22 H29 N O3	C22 H29 N O3
Sum formula	C22 H29 N O3	C22 H29 N O3
Mr	355.46	355.46
Dx,g cm-3	1.318	1.318
Z	2	2
Mu (mm-1)	0.688	0.688
F000	384.0	384.0
F000'	385.10	
h,k,lmax	8,14,15	8,14,15
Nref	3650	3514
Tmin,Tmax	0.855,0.921	0.694,0.754
Tmin'	0.797	

Correction method= # Reported T Limits: Tmin=0.694 Tmax=0.754
AbsCorr = MULTI-SCAN

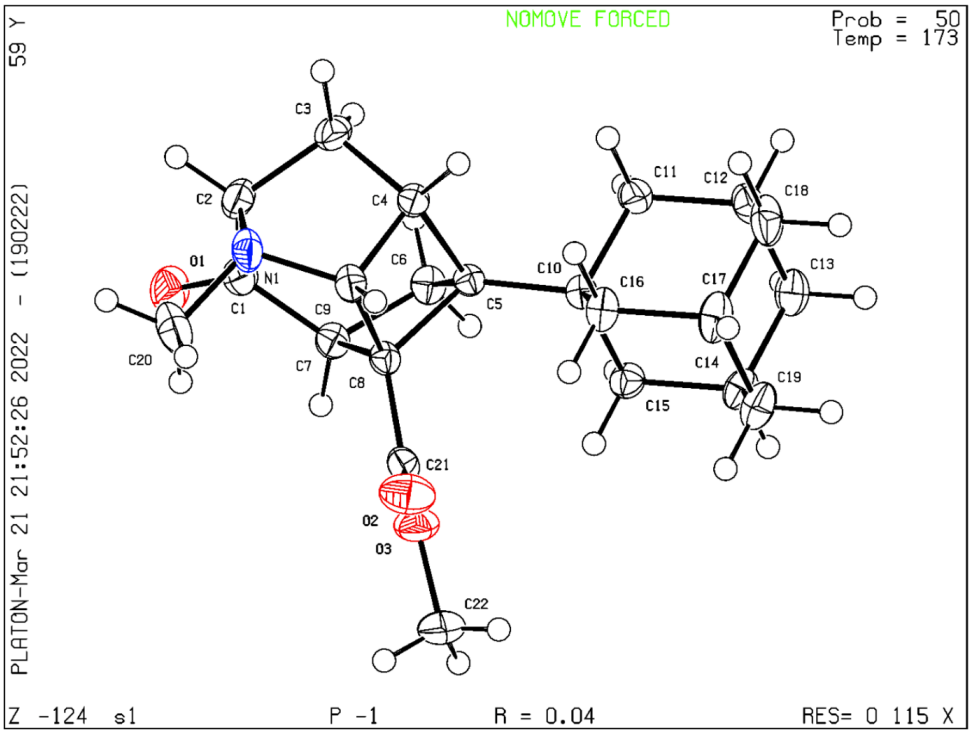
Data completeness= 0.963 Theta(max)= 74.217

R(reflections)= 0.0395(3347) wR2(reflections)= 0.1056(3514)

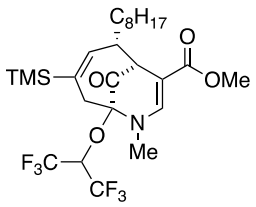
S = 1.037 Npar= 238



Thermal ellipsoids are set at the 50% probability level



X-Ray Crystallographic Data of Compound **47a**



Bond precision: C-C = 0.0019 A Wavelength=1.54178

Cell:	a=7.2552(2)	b-13.8552(4)	c=15.7314(5)
	alpha=105.3326(16)	beta=99.3403(19)	gamma=101.6075(17)

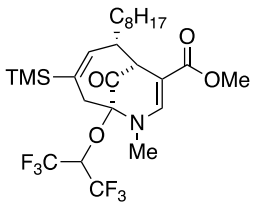
Temperature: 150 K

	Calculated	Reported
Volume	1454.49 (8)	1454.49(8)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C26 H39 F6 N O4 Si	C26 H39 F6 N O4 Si
Sum formula	C26 H39 F6 N O4 Si	C26 H39 F6 N O4 Si
Mr	571.67	571.67
Dx, g cm-3	1.305	1.305
Z	2	2
Mu (mm-1)	1.335	1.335
F000	604.0	604.0
F000’	606.71	
h, k, lmax	9, 17, 19	9, 17, 19
Nref	5928	5717
Tmin, Tmax	0.880, 0.961	0.661, 0.754
Tmin’	0.563	

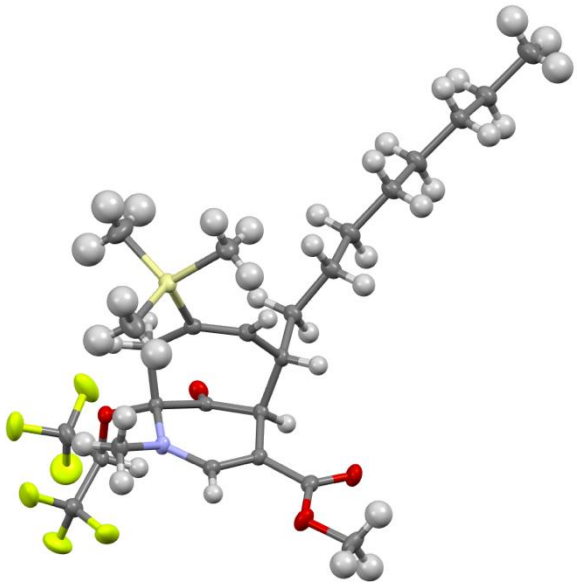
Correction method= # Reported T Limits: Tmin=0.661 Tmax=0.754

AbsCorr = NONE

Data completeness= 0.964	Theta(max)= 74.291
R(reflections)= 0.0340 (5225)	wR2(reflections)= 0.0899 (5717)
S = 1.020	Npar= 349

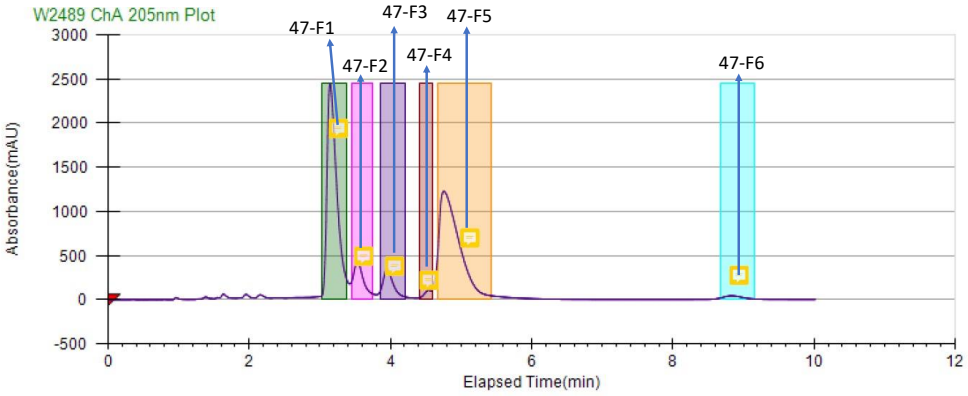


Thermal ellipsoids are set at the 50% probability level



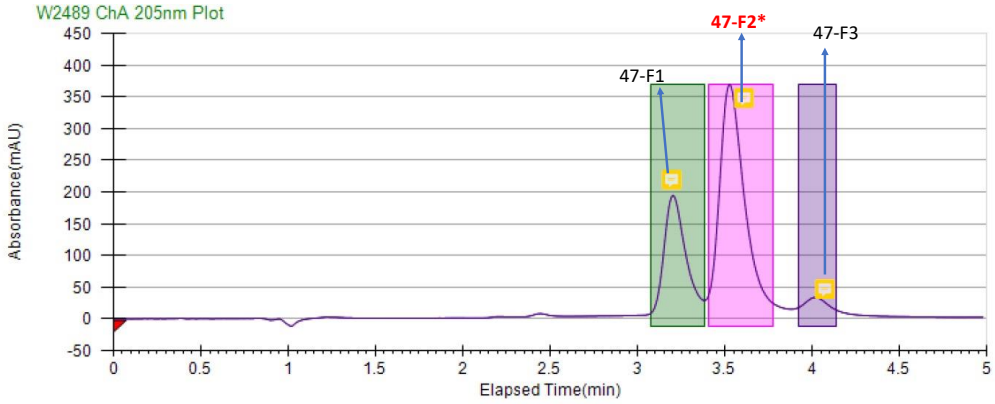
HPLC of Compound **31a, 31b, and 31c**

Preparative sub-critical fluid chromatography (SFC-UV) – **Rxn Mixture**



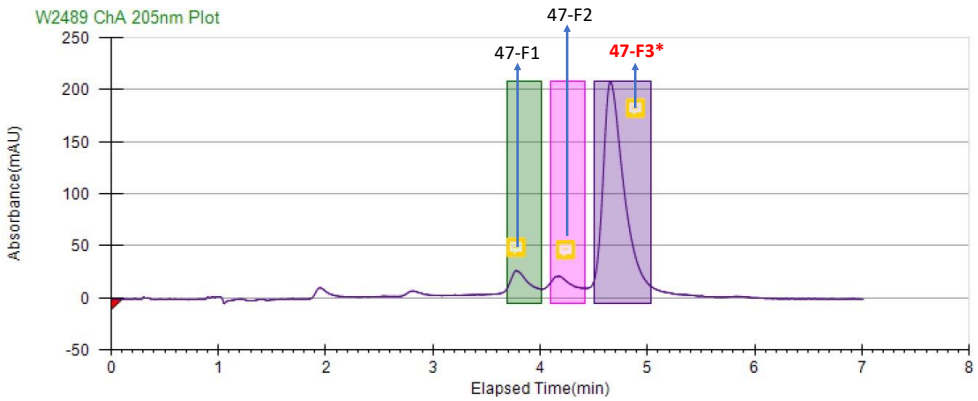
Column: Chiralpak IC (21 x 250 mm, 5um), Mobile phase: 15% MeOH/85% CO_2 at 80 mL/min, UV: 205 nm, BPR: 100 bar
Sample in 10 ml of MeOH, 0.35 mL injection **ELN 5025104-0047, tab: "Sep on Ic"**

Preparative SFC-UV – **2nd pass purification of 47-F2**



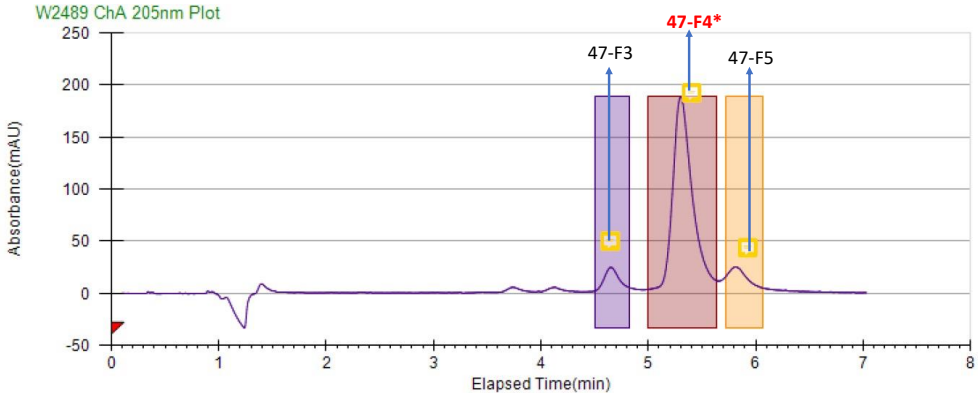
Column: Chiralpak IC (21 x 250 mm, 5um), Mobile phase: 15% MeOH/85% CO_2 at 80 mL/min, UV: 205 nm, BPR: 100 bar
Sample in MeOH, 0.6 mL injection **ELN 5025104-0047, tab: "Sep 47-F2"**

Preparative SFC-UV – 2nd pass purification of 47-F3

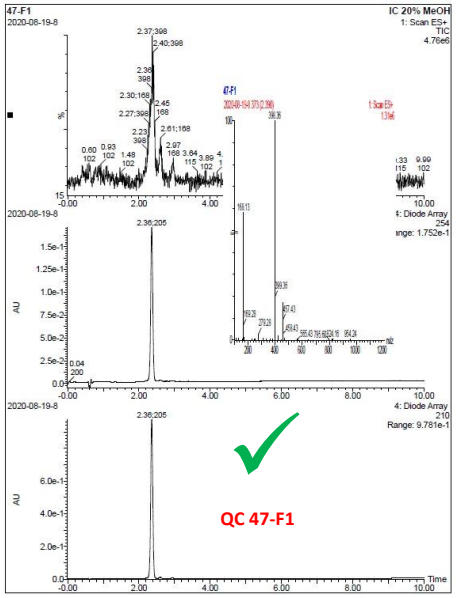


Column: Chiralpak IC (21 x 250 mm, 5um), Mobile phase: 15% MeOH/85% CO_2 at 70 mL/min, UV: 205 nm, BPR: 100 bar
Sample in MeOH, 1.7 mL injection **ELN 5025104-0047, tab: "Sep 47-F3"**

Preparative SFC-UV – 2nd pass purification of 47-F4



Column: Chiralpak IC (21 x 250 mm, 5um), Mobile phase: 15% MeOH/85% CO_2 at 70 mL/min, UV: 205 nm, BPR: 100 bar
Sample in MeOH, 1.5 mL injection **ELN 5025104-0047, tab: "Sep 47-F3"**

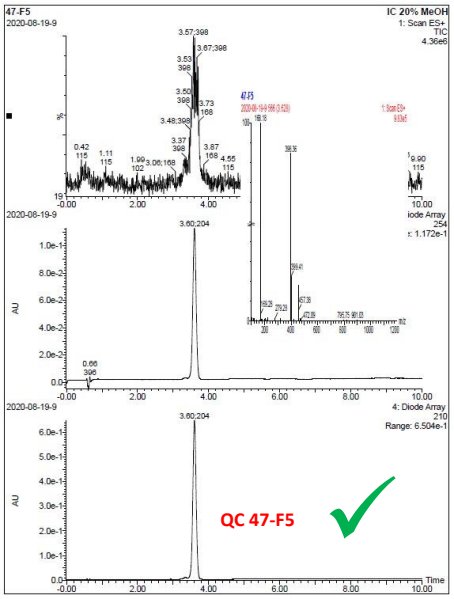


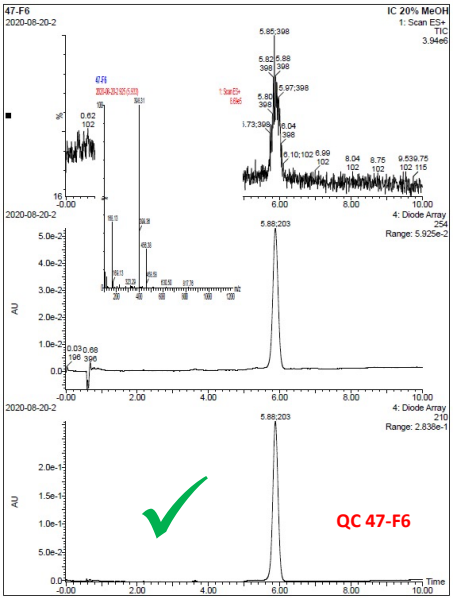
Analytical SFC-UV – **Fractions**

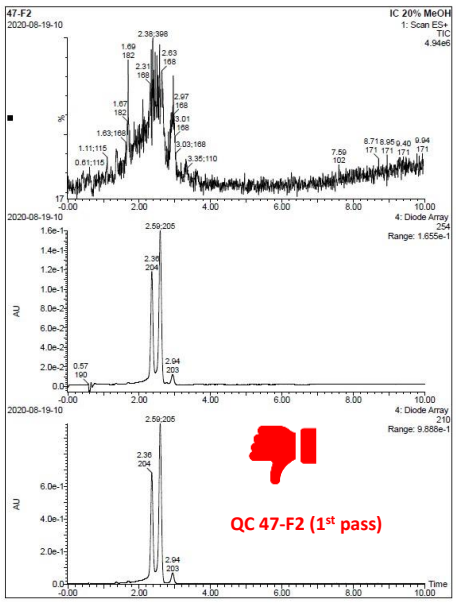
- ✓ **Slide 7 → QC 47-F1**
- ✓ **Slide 8 → QC 47-F5 and 47-F5**
- ✓ **Slide 9 → QC 47-F2 (1st and 2nd passes)**
- ✓ **Slide 10 → QC 47-F3 (1st and 2nd passes)**
- ✓ **Slide 11 → QC 47-F4 (1st and 2nd passes)**

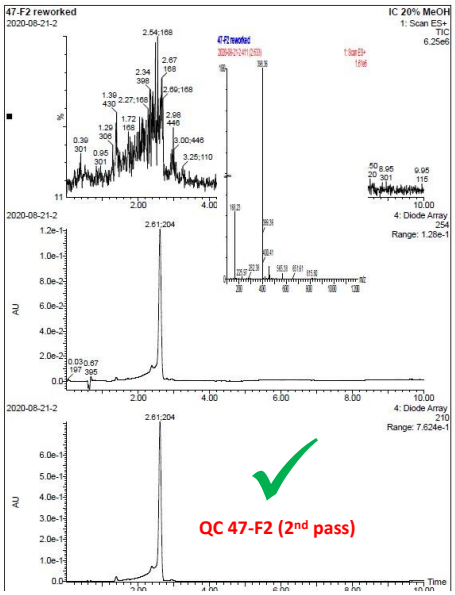
Fractions 47-F2, F3 and F4 required the application of offline 2D-SFC to upgrade purity

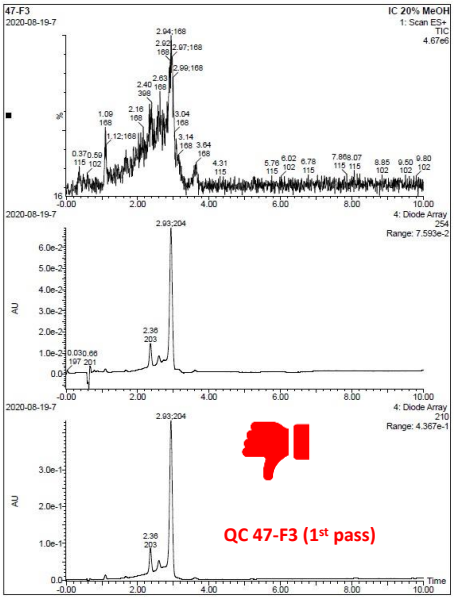
sent 82 mg 47-F1, 3 mg 47-F2, 6 mg 47-F3, 2 mg 47-F4, 84 mg 47-F5, and 3 mg 47-F6 to Harmata***

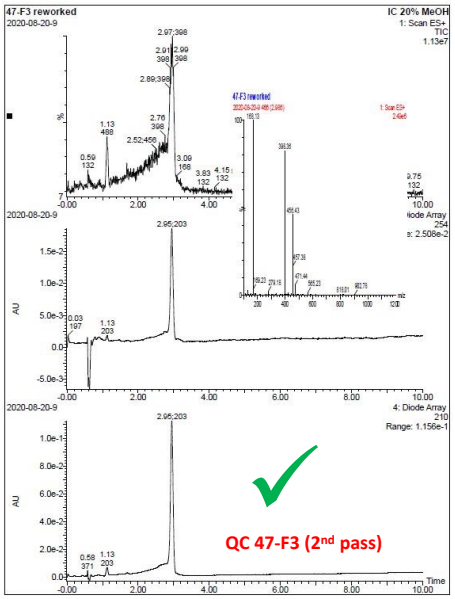


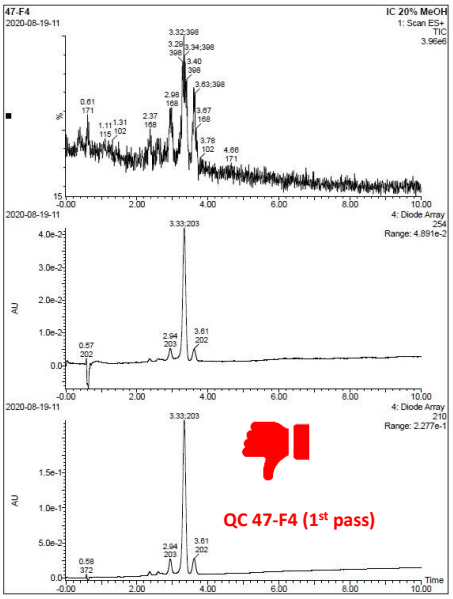


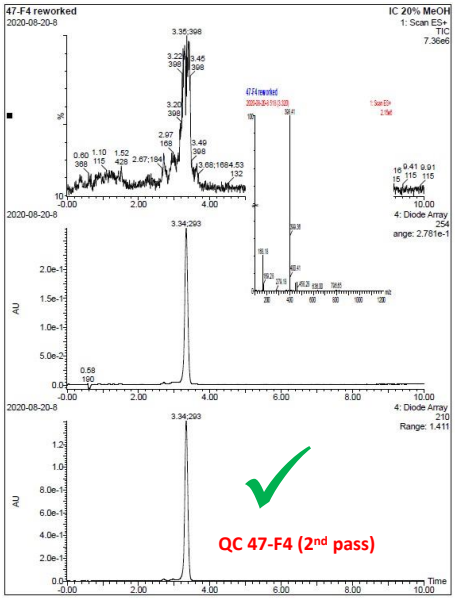

47-F2
IC 20% MeOH
1: Scan ES+
TIC
4.94e6
4: Diode Array
254
Range: 1.655e-1
4: Diode Array
210
Range: 9.886e-1
AU
Time
QC 47-F2 (1st pass)


47-F2 reworked
IC 20% MeOH
1: Scan ES+
TIC
6.25e6
4: Diode Array
254
Range: 1.28e-1
4: Diode Array
210
Range: 7.624e-1
AU
Time
QC 47-F2 (2nd pass)


47-F3
IC 20% MeOH
1: Scan ES+
TIC
4.67e6
4: Diode Array
254
Range: 7.593e-2
4: Diode Array
210
Range: 4.367e-1
AU
Time
QC 47-F3 (1st pass)


47-F3 reworked
IC 20% MeOH
1: Scan ES+
TIC
1.13e7
4: Diode Array
254
Range: 2.508e-2
4: Diode Array
210
Range: 1.156e-1
AU
Time
QC 47-F3 (2nd pass)


47-F4
2020-08-19-11
IC 20% MeOH
1: Scan ES+
TIC
3.96e6
4: Diode Array
254
Range: 4.891e-2
4: Diode Array
210
Range: 2.277e-1
AU
Time
QC 47-F4 (1st pass)


47-F4 reworked
2020-08-20-8
IC 20% MeOH
1: Scan ES+
TIC
7.36e6
4: Diode Array
254
4: Diode Array
210
Range: 1.411
AU
Time
QC 47-F4 (2nd pass)

Computational Methods

Density functional theory calculations were performed in Gaussian 16.[13] The calculations were performed with M06-2X/6-311+G(d,p),[14] using the SMD model[15] of acetonitrile solvent. We previously used a similar method to explore the kinetics and thermodynamics of the (4+3) cycloadditions of the oxidopyridinium ion **2** with other dienes [in that case we performed M06-2X/6-311+G(d,p) single point energies in solution on geometries optimized with M06-2X/6-31G(d)].[16] The computations employed the ultrafine integration grid of Gaussian 16. Vibrational frequency calculations were performed to characterize each species as a minimum or transition state, and to determine thermochemical quantities. In order to reduce errors in entropy associated with the harmonic treatment of low-frequency vibrational modes, a quasi-harmonic correction[17] was applied, in which all vibrational frequencies less than 100 cm^{-1} were raised to exactly 100 cm^{-1} before evaluation of the vibrational component of the thermal contribution to entropy. Gibbs free energies are reported at a standard state of 298.15 K and 1 mol/L.

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13. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16, Revision C.01, Gaussian, Inc., Wallingford CT, 2016.
14. Zhao, Y.; Truhlar, D. G. The M06 suite of density functionals for main group thermochemistry, thermochemical kinetics, noncovalent interactions, excited states, and transition elements: two new functionals and systematic testing of four M06-class functionals and 12 other functionals. *Theor. Chem. Account.* **2008**, *120*, 215–241.
15. Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.
16. Fu, C.; Lora, N.; Kirchhoefer, P. L.; Lee, D. R.; Altenhofer, E.; Barnes, C. L.; Hungerford, N. L.; Krenske, E. H.; Harmata, M. (4+3) Cycloaddition reactions of *N*-Alkyl Oxidopyridinium Ions. *Angew. Chem. Int. Ed.* **2017**, *56*, 14682–14687.
17. Zhao, Y.; Truhlar, D. G. Computational characterization and modeling of buckyball tweezers: density functional study of concave–convex p···p interactions. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2813–2818.

Computed Activation Energies and Reaction Energies of (4+3) Cycloadditions

The computed values of D*G* and D$G^{‡}$ for the (4+3) cycloadditions of oxidopyridinium ion **2** with dienes **9o**, **9p**, and **9k** are listed in Tables S1–S3. The theoretical isomer ratios predicted under kinetic control (based on the activation free energies and the Eyring equation) and under thermodynamic control (based on the products' relative free energies) are listed. These data indicate that for both of the 2-silyl dienes (**9o** and **9k**), the *endo* cycloadduct "**a**" is predicted to be the major cycloadduct (at least 78% of the total products formed) under conditions of kinetic control. The "**a**" product is not the most stable product for either of these two dienes, however. Instead, "**c**" is most stable and is therefore the expected major product under conditions of thermodynamic control. These results agree with the experiments, in which the cycloaddition of **9a** (a diene similar to **9o**) gave primarily product "**a**" with little evidence of reversibility, while the cycloaddition of **9k** gave a 47:53 ratio of "**a**" and "**c**" and showed evidence of reversibility.

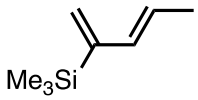
The barrier heights for the reverse reactions (retro-cycloadditions) are overall smaller for diene **9k** (D$G^{‡}$ = 30–34 kcal/mol) than for **9o** (D$G^{‡}$ = 35–38 kcal/mol), consistent with the experimental observation that the cycloaddition with **9k** showed a greater degree of reversibility than that of **9a** (which is modeled by **9o**).

Moreover, the barrier for the cycloaddition in the kinetically favored mode "**a**" is lower for diene **9k** (D$G^{‡}$ = 22 kcal/mol) than for **9o** (D$G^{‡}$ = 24 kcal/mol). This is consistent with the greater nucleophilicity of **9k** compared to **9o**. The HOMO of **9k** is 0.4 eV higher in energy than that of **9o**. The transition state is polarized, with charge transfer of 0.11–0.20 *e* from the diene to the oxidopyridinium ion. The preferred transition state for each diene is the one in which the more nucleophilic carbon of the diene is forming a bond to the more electrophilic carbon of the oxidopyridinium ion (the carbon adjacent to the NMe group).[18]

[18]. This was also observed in previous computations on related oxidopyridinium ion (4+3) cycloadditions (see ref. 16 for details).

Tables S1–S3. Computed $\Delta G^{\ddagger}$ and ΔG values for the (4+3) cycloadditions of oxidopyridinium ion **2** with dienes **9o**, **9p**, and **9k**, and the theoretically predicted isomer ratios at 85 °C under conditions of kinetic and thermodynamic control.

Table S1.

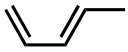


9o

(HOMO = –7.56 eV)

Isomer	$\Delta G^{\ddagger}$ (kcal/mol)	Isomer % if kinetically controlled	ΔG (kcal/mol)	Isomer % if thermodynamically controlled
a	23.9	78	–11.2	12
b	25.2	13	–10.4	4
c	25.6	7	–12.3	55
d	26.3	3	–11.8	29

Table S2.

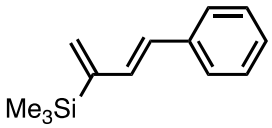


9p

(HOMO = –7.58 eV)

Isomer	$\Delta G^{\ddagger}$ (kcal/mol)	Isomer % if kinetically controlled	ΔG (kcal/mol)	Isomer % if thermodynamically controlled
a	25.6	29	–10.6	42
b	25.0	65	–10.2	25
c	26.9	5	–10.2	25
d	28.0	1	–9.3	7

Table S3.



9k

(HOMO = –7.16 eV)

Isomer	$\Delta G^{\ddagger}$ (kcal/mol)	Isomer % if kinetically controlled	ΔG (kcal/mol)	Isomer % if thermodynamically controlled
a	21.5	80	–8.1	18
b	22.5	18	–8.1	18
c	24.3	2	–8.7	41
D	25.6	0	–8.2	22

Distortion/Interaction Analysis of (4+3) Cycloaddition Transition States

In order to gain further insights into the factors that influence the (4+3) cycloaddition transition state energies, we analysed the transition states **TS-A**/**B** and **TS-A'**/**B'** using the distortion/interaction model of reactivity.[19] The results are shown in Figure S1.

[19]. Bickelhaupt, F. M.; Houk, K. N. Analyzing Reaction Rates with the Distortion/Interaction-Activation Strain Model. *Angew. Chem. Int. Ed.* **2017**, *56*, 10070–10086.

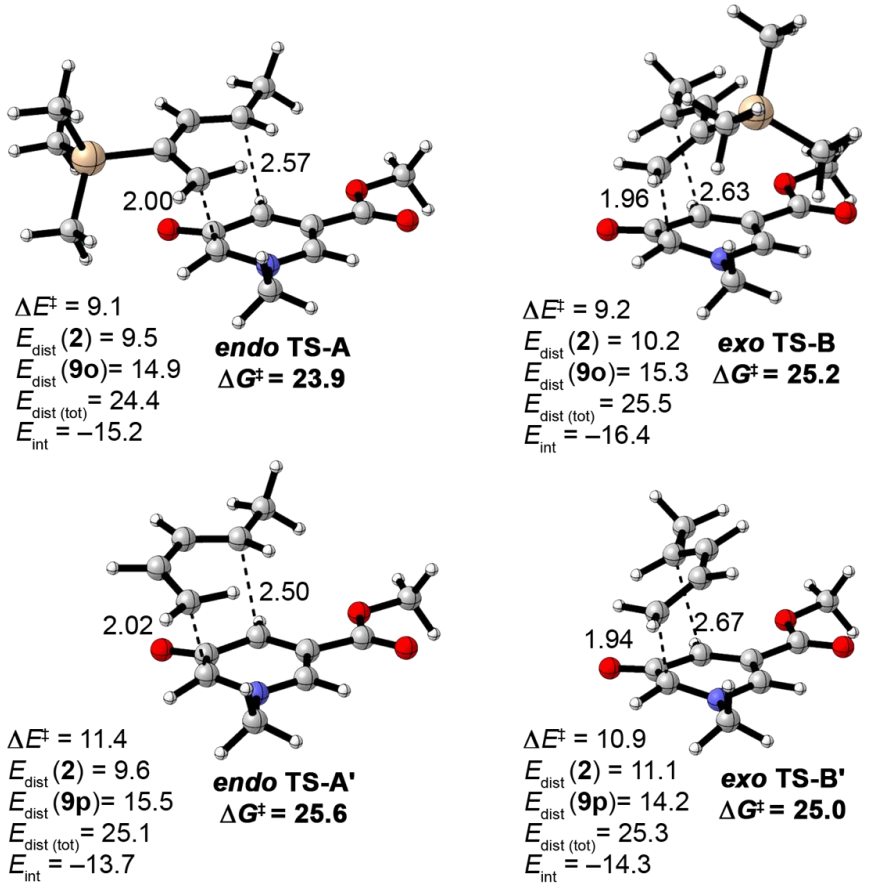


Figure S1. Distortion/interaction analyses for (4+3) cycloaddition transition states. Energies in kcal/mol.

For the 2-silyl diene, both the diene and the oxidopyridinium ion are less distorted in the favored (*endo*) transition state **TS-A** than in the disfavored (*exo*) transition state **TS-B**; the total distortion energy is 1.1 kcal/mol smaller in **TS-A** than in **TS-B**. This feature is countered by a stronger interaction between the more distorted diene and oxidopyridinium ion in **TS-B**. Overall, these two influences almost cancel each other out, such that the activation energies D$E^{‡}$ for the two reactions differ by only 0.1 kcal/mol, favoring the *endo* TS. In contrast, for the non-silylated diene, the total distortion energies are similar in both *endo* and *exo* TSs, while the interaction energy is 0.6 kcal/mol larger in the favored (*exo*) **TS-B'**. Overall, the activation energies (D$E^{‡}$) for this diene favor **TS-B'** by 0.5 kcal/mol.

Computed Coordinates and Energies

The Cartesian coordinates of optimized structures are shown below. Underneath each set of coordinates are listed the following energies, all calculated with M06-2X/6-311+G(d,p) in SMD acetonitrile:

E: electronic potential energy

H: enthalpy at 298.15 K

G: Gibbs free energy at 298.15 K and 1 mol/L including quasi-harmonic energy correction

Oxidopyridinium ion 2

C	-0.308829	-0.101096	-0.006464
C	0.135468	1.205830	-0.002976
C	1.537601	1.517924	-0.004281
C	2.383221	0.362734	-0.009604
N	1.902400	-0.888966	-0.011818
C	0.590757	-1.163576	-0.011103
O	1.999880	2.683546	-0.002037
C	2.866710	-2.005900	0.030700
C	-1.761642	-0.458541	-0.008468
O	-2.168626	-1.594265	-0.031153
O	-2.549873	0.609622	0.018144
C	-3.962167	0.349775	0.019213
H	3.461384	0.463110	-0.011084
H	-0.572819	2.026175	-0.000856
H	0.292356	-2.200451	-0.013275
H	3.676983	-1.793741	-0.662940
H	2.354733	-2.920237	-0.255872
H	3.253129	-2.092043	1.045429
H	-4.244810	-0.193083	-0.882796
H	-4.438591	1.326197	0.040128

H -4.236933 -0.227288 0.902252

0 imaginary frequencies

E = -590.626673

H = -590.449113

G = -590.495280

Diene 9o

C -3.689967 -0.482833 0.000001

C -2.203937 -0.304231 0.000009

H -4.205783 0.479414 -0.000024

H -4.012178 -1.051108 0.878038

H -4.012164 -1.051145 -0.878018

C -1.587225 0.883142 0.000003

C -0.131006 1.108983 0.000015

C 0.315541 2.376380 0.000017

H -2.205001 1.783371 -0.000006

H -1.614712 -1.218720 0.000022

H -0.375273 3.218854 0.000012

H 1.372658 2.622609 0.000024

Si 1.124314 -0.315962 0.000001

C 2.854236 0.411243 0.000031

H 3.038990 1.024699 0.886434

H 3.585759 -0.403223 0.000053

H 3.039025 1.024682 -0.886377

C 0.915830 -1.368972 -1.542913

H -0.039072 -1.899809 -1.564538

H 0.980331 -0.751187 -2.443794

H 1.715033 -2.115760 -1.591583

C 0.915816 -1.369065 1.542846

H 1.714902 -2.115988 1.591367

H 0.980534 -0.751358 2.443767

H -0.039172 -1.899738 1.564553

0 imaginary frequencies

E = -603.898566

H = -603.668660

G = -603.718510

Transition state "a" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o (TS-A)

N 0.786225 2.355323 -0.009636

C -0.242983 1.585268 0.498905

C 2.008291 1.837256 -0.216835

C 0.440554 3.667575 -0.555731

C 2.326533 0.574451 0.243407

C 1.360792 -0.211629 0.908249

C 3.702357 0.096456 -0.015903

C 0.085191 0.349768 1.212846

O -0.797501 -0.207534 1.888460

O 3.915643 -1.128679 0.475187

O 4.553806 0.725498 -0.603826

C 5.216657 -1.682427 0.245845

C -1.797420 -0.364062 -0.708147

C -1.002276 -1.546081 -0.658758

H 5.196689 -2.673787 0.691937

H 5.980881 -1.068339 0.723005

H 5.415670 -1.752391 -0.823961

H 1.352915 4.233667 -0.729542

H -0.190417 4.195178 0.158837

H -0.100219 3.543023 -1.497243

C -1.227378 0.857402 -1.088437

C	0.326992	-1.618998	-0.977131
C	1.117508	-2.890175	-0.894797
H	2.134041	-2.703124	-0.540343
H	0.639869	-3.612366	-0.228932
H	1.203981	-3.348634	-1.886882
H	-0.347295	0.860920	-1.730950
H	-1.885356	1.707492	-1.253387
H	0.796027	-0.801887	-1.513653
H	-1.456165	-2.439522	-0.232173
H	2.729511	2.465930	-0.721059
H	1.640287	-1.142349	1.385720
H	-1.072910	2.162476	0.889469
Si	-3.553083	-0.374494	-0.020525
C	-3.859667	1.218351	0.926103
H	-4.896158	1.254451	1.277047
H	-3.199214	1.276390	1.794930
H	-3.691326	2.101460	0.301970
C	-3.801807	-1.854881	1.104403
H	-4.796015	-1.818159	1.561132
H	-3.722990	-2.799863	0.559045
H	-3.054460	-1.851799	1.902449
C	-4.774421	-0.467032	-1.451512
H	-5.806006	-0.459310	-1.084660
H	-4.650647	0.385850	-2.126379
H	-4.630235	-1.381381	-2.035177

1 imaginary frequency

E = -1194.510733

H = -1194.102282

G = -1194.175676

Product “a” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N	-0.033140	1.410688	1.512682
C	-1.053217	0.547369	1.613452
C	-1.859498	0.168741	0.579302
C	-1.631002	0.709141	-0.813429
C	-0.890347	2.015127	-0.720293
C	0.282280	2.058095	0.241101
C	-2.905381	-0.798353	0.859210
O	-3.150134	-1.311359	1.937462
O	-3.628037	-1.094873	-0.244119
C	-4.683917	-2.040388	-0.065118
C	0.705977	1.872460	2.676978
O	-1.140759	2.969487	-1.421870
C	-0.842391	-0.283954	-1.723177
C	1.515622	1.418622	-0.441252
C	1.476351	-0.094340	-0.596126
C	0.459094	-0.786912	-1.132569
C	-0.616286	0.286398	-3.129160
H	-1.224190	0.139149	2.604539
H	0.502224	3.109750	0.438763
H	-5.143533	-2.160180	-1.043822
H	-4.290092	-2.995948	0.283595
H	-5.418136	-1.667525	0.650212
H	0.528603	1.194168	3.510584
H	1.774777	1.888042	2.457330
H	0.389621	2.882191	2.957229
H	-1.507038	-1.146858	-1.814162
H	2.386026	1.708001	0.155627
H	1.644922	1.901901	-1.416795
H	0.571505	-1.868414	-1.196052

H -0.199538 -0.482750 -3.783359

H -1.558541 0.632809 -3.562474

H 0.082534 1.126916 -3.111410

H -2.579132 0.912413 -1.314881

Si 2.999114 -1.017650 0.027007

C 4.510837 -0.381747 -0.892390

H 5.420062 -0.860498 -0.515065

H 4.437760 -0.592152 -1.963537

H 4.627147 0.699148 -0.767144

C 2.818710 -2.864662 -0.243847

H 3.719277 -3.373036 0.115319

H 1.964660 -3.273676 0.303596

H 2.697299 -3.111045 -1.302518

C 3.210480 -0.661705 1.861426

H 3.459486 0.388114 2.040480

H 2.300419 -0.899594 2.421039

H 4.025828 -1.268032 2.269606

0 imaginary frequencies

E = -1194.573584

H = -1194.160329

G = -1194.231677

Transition state "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o (TS-B)

N -0.416341 1.710787 -1.473753

C -0.355356 2.354447 -0.251696

C 0.388668 0.669620 -1.717219

C -1.596114 1.943721 -2.301858

C 1.488269 0.425330 -0.906571

C 1.775051 1.245220 0.189520

C	2.308913	-0.762352	-1.240657
C	0.912861	2.349792	0.489909
O	1.114658	3.190837	1.385206
O	3.276523	-0.974493	-0.346265
O	2.128616	-1.476866	-2.201206
C	4.113864	-2.112933	-0.582807
C	-1.509435	1.382957	1.006348
C	-1.288342	-0.006887	0.993307
C	-0.171028	-0.586461	1.671063
C	0.806977	0.086409	2.342758
C	1.972375	-0.597707	2.988716
H	0.685320	1.140018	2.575815
H	-1.140071	1.971588	1.847051
H	-2.465642	1.736173	0.626589
H	-0.033628	-1.663750	1.568456
H	1.863149	-0.588867	4.079366
H	2.059144	-1.635570	2.660652
H	2.909670	-0.080922	2.764124
H	4.826670	-2.128344	0.237951
H	4.634440	-2.009907	-1.535374
H	3.518793	-3.026547	-0.584873
H	2.712324	1.154062	0.722818
H	0.192171	0.084896	-2.605501
H	-0.914154	3.283581	-0.221491
H	-1.447497	1.479757	-3.274424
H	-1.741366	3.016678	-2.423513
H	-2.476584	1.511632	-1.817260
Si	-2.513267	-1.177962	0.150210
C	-2.675260	-2.709677	1.230573
H	-1.748006	-3.289194	1.255298

H -2.938006 -2.446101 2.259364

H -3.462190 -3.360882 0.836629

C -4.194376 -0.347317 0.025399

H -4.558796 -0.050270 1.013503

H -4.183953 0.540911 -0.612041

H -4.917522 -1.050082 -0.401144

C -1.958136 -1.735396 -1.558268

H -2.621570 -2.529077 -1.919362

H -1.985369 -0.918488 -2.284229

H -0.939175 -2.133767 -1.528061

1 imaginary frequency

E = -1194.510639

H = -1194.101824

G = -1194.173586

Product "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N 0.243556 1.589985 1.196573

C -0.750092 0.726683 1.450772

C -1.670817 0.299176 0.535459

C -1.570897 0.741190 -0.907092

C -0.839502 2.054595 -0.963418

C 0.428368 2.152406 -0.137436

C -2.746744 -0.547005 1.022501

O -3.701253 -0.747493 0.088664

O -2.835601 -1.032497 2.137427

C 1.216116 1.982142 2.202085

O -1.163245 2.961035 -1.698197

C -0.803289 -0.259748 -1.848271

C 1.578484 1.446215 -0.912064

C 1.534505 -0.065988 -0.809300

C	0.479132	-0.776525	-1.233447
C	-1.703579	-1.430256	-2.240706
H	-0.817968	0.383637	2.478288
H	-2.559003	0.899534	-1.341442
H	0.673941	3.211520	-0.032775
H	0.969529	1.505016	3.149513
H	2.225234	1.679093	1.905616
H	1.202562	3.067927	2.330832
H	-0.558040	0.308031	-2.755714
H	0.503682	-1.860578	-1.107493
H	-1.187208	-2.071792	-2.959621
H	-1.954191	-2.034503	-1.364939
H	-2.634066	-1.080243	-2.691701
C	-4.780067	-1.602504	0.467211
H	-5.432550	-1.657877	-0.401653
H	-5.323124	-1.187267	1.317249
H	-4.411454	-2.597155	0.722746
H	1.519316	1.769737	-1.957842
H	2.521935	1.831999	-0.521024
Si	2.923595	-1.014648	0.059852
C	3.345776	-2.555112	-0.928185
H	4.149532	-3.111286	-0.435277
H	2.485124	-3.224074	-1.018189
H	3.681563	-2.296670	-1.936714
C	4.449505	0.068915	0.215008
H	4.784698	0.429500	-0.762381
H	4.272458	0.938151	0.855296
H	5.268414	-0.507125	0.657604
C	2.328538	-1.536472	1.766079
H	2.091793	-0.675370	2.397208

H 1.426620 -2.151366 1.681520

H 3.094138 -2.128291 2.278627

0 imaginary frequencies

E = -1194.572233

H = -1194.159344

G = -1194.230374

Transition state "c" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N 2.096987 2.023758 0.390024

C 0.811090 2.003742 0.854454

C 2.743916 0.883685 0.066628

C 2.729560 3.311478 0.086361

C 2.157211 -0.342447 0.259394

C 0.807563 -0.436596 0.722766

C 2.937997 -1.534689 -0.122981

C 0.202206 0.764541 1.266378

O -0.872646 0.747557 1.886963

O 2.215839 -2.658143 -0.033376

O 4.094193 -1.524596 -0.485070

C 2.895097 -3.870514 -0.381207

C -1.612533 1.444986 -0.793860

C -1.583658 0.029053 -0.730511

H 2.165382 -4.665264 -0.247119

H 3.751262 -4.028128 0.275392

H 3.229056 -3.834522 -1.418517

H 2.527706 3.590476 -0.949448

H 3.803608 3.221666 0.238458

H 2.326857 4.069865 0.755640

C -0.523523 2.256390 -1.045063

C -0.396431 -0.658680 -0.991839

H	3.746569	0.989471	-0.325547
H	0.464531	-1.372670	1.144680
H	0.437814	2.937192	1.255575
C	-0.676136	3.750907	-1.132186
H	0.350778	1.834564	-1.535223
H	-2.530632	1.945803	-0.489738
H	-0.398047	-1.745244	-1.004022
H	0.357462	-0.213157	-1.633360
H	-1.520437	4.091389	-0.528171
H	-0.860186	4.052156	-2.169638
H	0.218728	4.279721	-0.799639
Si	-3.049766	-0.922630	-0.023557
C	-2.421394	-2.274029	1.119358
H	-1.903191	-1.833685	1.974857
H	-3.258040	-2.874490	1.491341
H	-1.730994	-2.950821	0.606325
C	-4.001238	-1.726459	-1.437009
H	-4.852396	-2.301813	-1.058556
H	-4.385319	-0.973532	-2.132218
H	-3.358603	-2.408813	-2.002377
C	-4.195960	0.234838	0.907656
H	-5.011123	-0.332877	1.367759
H	-3.649001	0.755625	1.698114
H	-4.645657	0.981829	0.246897

1 imaginary frequency

E = -1194.508770

H = -1194.100132

G = -1194.172990

Product “c” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N	-2.052702	-0.963360	1.272236
C	-0.829712	-1.519727	1.262746
C	-0.040953	-1.656033	0.159683
C	-0.479379	-1.084236	-1.166883
C	-1.980040	-0.958977	-1.181790
C	-2.620195	-0.372686	0.062000
C	1.254370	-2.290746	0.328086
O	1.967178	-2.291727	-0.820409
O	1.697130	-2.776557	1.353887
C	-2.732148	-0.675216	2.525969
O	-2.651773	-1.227058	-2.152294
C	0.134511	0.316384	-1.464294
C	-2.493089	1.178454	0.057447
C	-1.081940	1.673730	0.301168
C	0.049108	1.331219	-0.335535
H	-0.480761	-1.891436	2.221084
H	-0.203581	-1.744632	-1.990210
H	-3.684929	-0.618000	0.029618
H	-2.395205	-1.380668	3.284856
H	-2.525668	0.343119	2.870521
H	-3.808947	-0.790367	2.387241
H	-0.337237	0.715582	-2.369916
H	-3.102996	1.510390	0.901969
C	-3.103638	1.787824	-1.210733
H	-1.011357	2.417403	1.093905
H	1.182014	0.134384	-1.720152
H	-3.148410	2.874101	-1.110262
H	-2.509882	1.556193	-2.097791
H	-4.119153	1.415468	-1.370129
C	3.275025	-2.860883	-0.741054

H 3.712556 -2.738034 -1.729506

H 3.219358 -3.919962 -0.485121

H 3.877047 -2.338873 0.004515

Si 1.692975 2.089523 0.195402

C 2.457035 2.974726 -1.276668

H 3.440651 3.377491 -1.014903

H 2.590055 2.294279 -2.123302

H 1.827881 3.806688 -1.606672

C 1.451588 3.294409 1.612278

H 1.031113 2.803067 2.494451

H 2.418555 3.720896 1.897587

H 0.792512 4.121770 1.333704

C 2.834851 0.690396 0.721056

H 2.409568 0.118628 1.551599

H 3.020292 0.002550 -0.109304

H 3.801141 1.091073 1.044613

0 imaginary frequencies

E = -1194.575802

H = -1194.162547

G = -1194.233400

Transition state “d” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N -1.649176 -1.277458 1.272823

C -2.265530 -1.352189 0.054066

C -0.306409 -1.329117 1.391286

C -2.454348 -0.846837 2.413165

C 0.493893 -1.572717 0.300752

C -0.074411 -1.608961 -1.002067

C 1.946594 -1.646329 0.529196

C -1.512251 -1.747642 -1.123240

O	-2.088291	-2.049972	-2.182390
O	2.634741	-1.773292	-0.613156
O	2.484551	-1.596082	1.614930
C	4.059228	-1.849284	-0.481753
C	-2.753571	0.684955	-0.666040
C	-1.639617	1.419126	-0.283371
C	-0.338773	1.294690	-0.824756
C	-0.062167	0.402816	-1.856828
C	-4.108659	0.984655	-0.080528
H	4.445404	-1.908560	-1.496414
H	4.340526	-2.739144	0.082532
H	4.444847	-0.960639	0.019309
H	0.517405	-1.985335	-1.827471
H	0.094577	-1.216989	2.390076
H	-3.326152	-1.568156	0.083438
H	-2.544828	0.243573	2.394304
H	-1.970319	-1.161044	3.335762
H	-3.444816	-1.294712	2.341953
H	-4.025452	1.408706	0.922255
H	-4.742575	0.096337	-0.032922
H	-4.628179	1.712196	-0.713675
H	-2.768700	0.236741	-1.657485
H	-0.837470	0.081148	-2.548804
H	0.946177	0.353739	-2.257670
H	-1.767717	2.070952	0.582925
Si	1.059835	2.250546	0.015888
C	0.688459	4.086999	-0.136936
H	-0.255743	4.339894	0.355205
H	1.479647	4.680967	0.331378
H	0.613195	4.387352	-1.186132

C 2.690073 1.852090 -0.823334

H 3.508491 2.364277 -0.307546

H 2.902070 0.778929 -0.804112

H 2.695590 2.178401 -1.867649

C 1.169087 1.811397 1.841477

H 1.563351 0.802502 1.990068

H 1.839526 2.512796 2.349780

H 0.190079 1.873495 2.327106

1 imaginary frequency

E = -1194.508844

H = -1194.100112

G = -1194.171884

Product "d" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9o

N -1.908886 -1.089696 1.113881

C -0.620235 -1.446537 1.250291

C 0.266013 -1.596783 0.225635

C -0.148595 -1.258915 -1.185764

C -1.639001 -1.442867 -1.298645

C -2.475295 -0.808912 -0.201929

C 1.620851 -2.002579 0.553088

O 2.418064 -2.018650 -0.538149

O 2.043237 -2.298808 1.656798

C -2.714477 -0.789078 2.288661

O -2.169145 -1.971982 -2.249517

C 0.215884 0.202474 -1.606396

C -2.591876 0.715518 -0.555526

C -1.358417 1.479570 -0.133702

C -0.110493 1.271406 -0.578128

H -0.297598 -1.635226 2.269726

H	0.314668	-1.934143	-1.905909
H	-3.475380	-1.247003	-0.245099
H	-2.391007	-1.421835	3.115442
H	-2.617487	0.259627	2.585230
H	-3.762181	-1.000864	2.069223
H	-0.291855	0.420603	-2.554351
C	-3.868106	1.343648	0.005291
H	-1.532336	2.252769	0.614794
H	1.288218	0.198612	-1.819429
H	-2.665216	0.747167	-1.650583
H	-3.977225	2.360223	-0.380799
H	-4.748283	0.769814	-0.292891
H	-3.845936	1.402846	1.094907
C	3.784676	-2.363384	-0.306126
H	4.278294	-2.286607	-1.272587
H	3.865806	-3.381953	0.076081
H	4.240236	-1.672049	0.404811
Si	1.325228	2.307947	0.068220
C	0.734989	3.494255	1.395814
H	0.306945	2.962169	2.250482
H	1.579849	4.086942	1.760894
H	-0.017740	4.189431	1.013066
C	2.060741	3.267949	-1.371342
H	2.387277	2.595260	-2.170442
H	1.331169	3.965334	-1.793542
H	2.931574	3.845158	-1.044802
C	2.643389	1.161711	0.761894
H	2.263852	0.570436	1.600408
H	3.008104	0.473874	-0.006914
H	3.497730	1.746694	1.118276

0 imaginary frequencies

E = -1194.574730

H = -1194.161810

G = -1194.232662

Diene 9p

C	2.462252	-0.215452	0.000021
C	1.107992	0.418364	-0.000010
H	2.392002	-1.304826	-0.000341
H	3.035800	0.096969	0.878125
H	3.036141	0.097558	-0.877645
C	-0.049373	-0.252277	-0.000051
C	-1.356873	0.399209	-0.000023
C	-2.518706	-0.260135	0.000035
H	-0.041875	-1.341795	-0.000100
H	1.076505	1.507400	0.000049
H	-2.548570	-1.346166	0.000049
H	-1.354494	1.487823	-0.000034
H	-3.467257	0.264782	0.000068

0 imaginary frequencies

E = -195.265811

H = -195.145221

G = -195.178030

Transition state “a” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p (TS-A')

N	-1.239577	1.943737	0.036868
C	-1.923376	0.871074	0.572915
C	0.079916	1.869409	-0.212125
C	-2.030505	3.050787	-0.500964

C	0.824391	0.796770	0.234268
C	0.208521	-0.270466	0.929381
C	2.272627	0.821915	-0.065658
C	-1.172264	-0.164580	1.284597
O	-1.783488	-0.970151	2.004483
O	2.912431	-0.242516	0.429879
O	2.836217	1.696308	-0.685548
C	4.318830	-0.312226	0.166795
C	-2.679788	-1.526419	-0.647196
C	-1.551441	-2.367276	-0.527892
H	4.659138	-1.234209	0.631864
H	4.830628	0.544376	0.606222
H	4.502512	-0.339760	-0.907655
H	-1.375390	3.897570	-0.693901
H	-2.790059	3.331498	0.227689
H	-2.514402	2.740685	-1.430568
C	-2.597614	-0.185316	-1.014296
C	-0.266300	-1.983139	-0.821714
C	0.902330	-2.913333	-0.685134
H	1.809890	-2.374726	-0.405010
H	0.707190	-3.686867	0.060998
H	1.103765	-3.409830	-1.641634
H	-1.764622	0.135422	-1.636576
H	-3.523413	0.352775	-1.189931
H	-0.103430	-1.095709	-1.422771
H	-3.634767	-1.915082	-0.308177
H	-1.702243	-3.345322	-0.077045
H	0.529388	2.701252	-0.736966
H	0.808260	-1.023247	1.425082
H	-2.898650	1.122688	0.971914

1 imaginary frequency

E = -785.874325

H = -785.574814

G = -785.632585

Product “a” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N	-1.309295	-1.681353	-0.249885
C	0.016439	-1.674695	-0.037217
C	0.832684	-0.600267	-0.230966
C	0.252518	0.744008	-0.599943
C	-1.057406	0.532076	-1.311911
C	-2.007628	-0.481870	-0.700659
C	2.255274	-0.781439	0.000936
O	2.810268	-1.817239	0.322937
O	2.947040	0.364988	-0.180076
C	4.358748	0.283198	0.024869
C	-2.141207	-2.785892	0.200373
O	-1.398986	1.182079	-2.274025
C	0.050345	1.673687	0.638975
C	-2.787572	0.206820	0.445714
C	-1.972382	0.488858	1.682999
C	-0.777839	1.081567	1.758288
C	-0.505527	3.042941	0.226749
H	0.438975	-2.617016	0.297398
H	-2.722093	-0.772285	-1.474469
H	4.743556	1.283248	-0.162693
H	4.582193	-0.018361	1.049010
H	4.808331	-0.427540	-0.669815
H	-1.536209	-3.689842	0.261472
H	-2.576224	-2.581274	1.184164

H -2.949028 -2.946391 -0.516477

H 1.060403 1.823069 1.029037

H -3.627862 -0.437822 0.708860

H -3.218963 1.129178 0.041170

H -2.423209 0.165871 2.617681

H -0.353427 1.199656 2.752548

H -0.503582 3.722790 1.081696

H 0.102798 3.485283 -0.566734

H -1.534405 2.960148 -0.134048

H 0.908550 1.278185 -1.289539

0 imaginary frequencies

E = -785.938327

H = -785.634178

G = -785.690152

Transition state "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p (TS-B')

N 1.859894 -1.430191 0.192737

C 2.197271 -0.167463 0.642966

C 0.576657 -1.703658 -0.086065

C 2.916804 -2.244353 -0.401206

C -0.437019 -0.897694 0.410730

C -0.153926 0.239914 1.172789

C -1.824878 -1.274338 0.046818

C 1.209062 0.602007 1.418345

O 1.580473 1.561090 2.119446

O -2.720671 -0.393519 0.495442

O -2.126053 -2.254872 -0.595596

C -4.089209 -0.666230 0.170043

C 2.382966 0.961323 -0.930460

C 1.281434 0.842710 -1.786541

C 0.040999 1.505947 -1.600701

C -0.276474 2.288555 -0.530851

C -1.623858 2.912068 -0.343013

H 0.498663 2.603707 0.162247

H 2.492627 1.873408 -0.346190

H 3.322120 0.554182 -1.293795

H 1.359258 0.162505 -2.629892

H -0.748599 1.279362 -2.315004

H -1.568889 3.996080 -0.495532

H -2.354702 2.501929 -1.042858

H -1.991137 2.757382 0.675489

H -4.662653 0.147478 0.607067

H -4.398330 -1.620418 0.597614

H -4.223656 -0.686309 -0.911822

H -0.939862 0.781841 1.682323

H 0.368767 -2.614773 -0.631439

H 3.223934 -0.084909 0.983310

H 2.573423 -3.273981 -0.477923

H 3.800784 -2.198764 0.233099

H 3.160013 -1.861712 -1.397308

1 imaginary frequency

E = -785.875068

H = -785.575784

G = -785.633496

Product "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N -1.571570 1.480255 0.080773

C -0.255614 1.562425 -0.174198

C 0.665549 0.607560 0.144068

C	0.214241	-0.718854	0.707279
C	-1.086082	-0.520623	1.439730
C	-2.143443	0.310376	0.737231
C	2.067513	0.935959	-0.062084
O	2.891922	0.000396	0.453438
O	2.500412	1.931125	-0.616531
C	-2.513514	2.423049	-0.499941
O	-1.340870	-1.067444	2.489282
C	-0.001261	-1.842057	-0.369208
C	-2.898583	-0.610149	-0.260800
C	-2.104498	-0.924947	-1.500156
C	-0.869049	-1.428077	-1.537974
C	1.344550	-2.353870	-0.882875
H	0.068190	2.488397	-0.639209
H	0.934170	-1.106997	1.429073
H	-2.853148	0.652628	1.493889
H	-1.995622	3.354623	-0.725652
H	-2.953489	2.028071	-1.421812
H	-3.313479	2.623466	0.215686
H	-0.501417	-2.663956	0.160206
H	-2.584800	-0.694269	-2.447133
H	-0.423402	-1.576200	-2.519714
H	1.187135	-3.199811	-1.556835
H	1.868975	-1.571639	-1.438697
H	1.985221	-2.676273	-0.060304
C	4.289141	0.215831	0.252746
H	4.788955	-0.631016	0.718235
H	4.609099	1.145609	0.724767
H	4.523410	0.250042	-0.812416
H	-3.174165	-1.522998	0.278987

H -3.830056 -0.113807 -0.536894

0 imaginary frequencies

E = -785.937657

H = -785.633760

G = -785.689564

Transition state "c" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N -0.830603 1.741981 0.323006

C -1.508461 0.670447 0.848872

C 0.474394 1.656611 -0.004214

C -1.581028 2.944814 -0.048731

C 1.199564 0.518531 0.255037

C 0.559361 -0.636029 0.795505

C 2.622480 0.520005 -0.133908

C -0.774198 -0.476864 1.336842

O -1.330210 -1.344795 2.024760

O 3.193181 -0.678143 0.038596

O 3.225509 1.478362 -0.565449

C 4.581376 -0.767896 -0.303370

C -2.406100 -1.704830 -0.620696

C -1.204737 -2.435684 -0.620051

H 4.870025 -1.795093 -0.094313

H 5.167778 -0.078878 0.305197

H 4.727863 -0.541448 -1.359823

H -1.962202 2.846552 -1.067114

H -0.919066 3.806616 0.011709

H -2.412269 3.071701 0.642795

C -2.497438 -0.347837 -0.890974

C 0.027030 -1.864682 -0.903627

H 0.920651 2.533871 -0.453216

H 1.165162 -1.419316 1.232272

H -2.470177 0.899694 1.290614

C -3.845830 0.321875 -0.945658

H -1.707544 0.118104 -1.476320

H -3.301507 -2.209531 -0.266150

H 0.912355 -2.490665 -0.914964

H 0.075061 -0.986425 -1.535701

H -1.235647 -3.452401 -0.240911

H -4.540483 -0.151035 -0.247422

H -4.268477 0.234844 -1.952634

H -3.793605 1.385396 -0.708467

1 imaginary frequency

E = -785.872598

H = -785.572966

G = -785.630500

Product "c" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N 1.000942 1.647943 -0.300168

C -0.323167 1.550993 -0.097228

C -1.057048 0.413121 -0.251742

C -0.379073 -0.893402 -0.586222

C 0.927976 -0.606943 -1.279901

C 1.796212 0.480034 -0.672068

C -2.488216 0.492296 -0.016317

O -3.085922 -0.712715 -0.141937

O -3.122485 1.493348 0.266441

C 1.731800 2.843360 0.091949

O 1.321345 -1.248555 -2.227529

C -0.105407 -1.777071 0.663549

C 2.601320 -0.082422 0.534512

C 1.752390 -0.388176 1.747082

C 0.628828 -1.108438 1.800186

H -0.817527 2.471927 0.195710

H -0.984064 -1.483410 -1.275770

H 2.517151 0.787454 -1.434367

H 1.059081 3.699710 0.059757

H 2.140059 2.750703 1.103346

H 2.553236 3.009970 -0.607551

H 0.439650 -2.670840 0.337058

H 3.290443 0.719753 0.810680

C 3.447452 -1.293721 0.123398

H 2.134070 0.003380 2.686968

H 0.181709 -1.243389 2.781690

H -1.077536 -2.116333 1.024884

H 4.118824 -1.566857 0.939937

H 2.821037 -2.160055 -0.102433

H 4.052128 -1.065587 -0.758323

C -4.498079 -0.737614 0.074217

H -4.801287 -1.772442 -0.069503

H -5.009027 -0.094150 -0.643153

H -4.737988 -0.414173 1.087948

0 imaginary frequencies

E = -785.937857

H = -785.633614

G = -785.689490

Transition state “d” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N -1.009880 1.513426 0.468097

C -1.583171 0.388301 0.998925

C 0.285434 1.534288 0.096080

C	-1.898666	2.587320	0.030621
C	1.120761	0.475071	0.363915
C	0.594994	-0.727642	0.902845
C	2.528614	0.602984	-0.053483
C	-0.745198	-0.711355	1.452738
O	-1.213757	-1.624127	2.153883
O	3.212533	-0.534616	0.117114
O	3.030568	1.608677	-0.506868
C	4.596607	-0.496090	-0.249951
C	-2.623474	-0.725369	-0.562369
C	-1.763005	-0.640104	-1.650844
C	-0.516811	-1.283134	-1.738819
C	0.023925	-2.089010	-0.753558
C	-3.997302	-0.109556	-0.625275
H	4.983662	-1.490730	-0.042817
H	5.126966	0.247639	0.345602
H	4.702704	-0.262292	-1.309582
H	1.271271	-1.478877	1.291989
H	0.639727	2.442947	-0.372396
H	-2.529453	0.546891	1.501344
H	-2.294277	2.344952	-0.960014
H	-1.341490	3.521145	-0.014112
H	-2.721337	2.680992	0.738227
H	-4.017055	0.758443	-1.287207
H	-4.358687	0.193363	0.359901
H	-4.708906	-0.846303	-1.013427
H	-2.537721	-1.587312	0.096820
H	-0.609358	-2.611279	-0.043034
H	1.001770	-2.528156	-0.919272
H	0.116300	-1.012813	-2.579619

H -2.025957 0.053708 -2.447065

1 imaginary frequency

E = -785.871260

H = -785.571692

G = -785.628706

Product "d" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9p

N -1.138343 1.378810 0.392972

C 0.182552 1.445743 0.156563

C 1.054152 0.402880 0.261760

C 0.545992 -0.979204 0.590565

C -0.748610 -0.849067 1.349836

C -1.770342 0.122136 0.783903

C 2.455267 0.654736 -0.024595

O 3.192692 -0.475148 0.045427

O 2.957505 1.729029 -0.303809

C -1.991131 2.528846 0.124415

O -1.024631 -1.542228 2.302792

C 0.302212 -1.863578 -0.673235

C -2.516481 -0.626328 -0.373518

C -1.700405 -0.659947 -1.643130

C -0.485216 -1.195742 -1.771440

H 0.553133 2.426788 -0.124359

H 1.244363 -1.514365 1.234728

H -2.496493 0.334869 1.571947

H -1.434173 3.443920 0.327227

H -2.332252 2.544443 -0.914455

H -2.860663 2.492439 0.782602

H -0.198682 -2.784017 -0.349325

C -3.915129 -0.059347 -0.621072

H -2.153976 -0.191597 -2.514234

H -0.005546 -1.138562 -2.744574

H 1.283788 -2.148689 -1.053757

H -2.640910 -1.653977 -0.007863

H -4.453646 -0.705829 -1.318457

H -4.486249 -0.009922 0.308570

H -3.875446 0.939712 -1.058490

C 4.588407 -0.329629 -0.223638

H 5.015117 -1.324892 -0.120630

H 5.049784 0.351705 0.492386

H 4.748111 0.044076 -1.235886

0 imaginary frequencies

E = -785.935984

H = -785.632186

G = -785.688152

Diene 9k

C 0.611324 0.049495 -0.003739

C -0.152121 1.153373 0.024625

C -1.622053 1.176664 0.024035

C -2.229825 2.376174 0.045857

H 0.326394 2.132031 0.052437

H 0.137115 -0.928451 -0.024537

H -1.653974 3.300662 0.063858

H -3.309902 2.482540 0.046471

C 4.887029 -0.207547 0.002932

C 4.274099 1.045420 -0.029563

C 2.889537 1.152957 -0.034363

C 2.082467 0.005025 -0.004453

C 2.712106 -1.246650 0.024623

C 4.099413 -1.354378 0.029172

H 5.968130 -0.285897 0.005918

H 4.880587 1.943897 -0.053074

H 2.437383 2.137630 -0.064971

H 2.100439 -2.143139 0.044863

H 4.563322 -2.333993 0.052812

Si -2.680888 -0.401454 -0.007449

C -2.330355 -1.447147 1.513911

H -3.017026 -2.299444 1.542534

H -1.310603 -1.839254 1.533262

H -2.485031 -0.862630 2.425961

C -4.489502 0.095962 0.008605

H -4.754760 0.697984 -0.865094

H -5.109559 -0.806103 -0.007732

H -4.749042 0.661994 0.907708

C -2.339597 -1.379658 -1.575227

H -2.504914 -0.756880 -2.459678

H -1.318325 -1.765673 -1.620223

H -3.022928 -2.233066 -1.634725

0 imaginary frequencies

E = -795.617450

H = -795.330491

G = -795.386910

Transition state “a” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N -0.555302 2.969521 -0.186140

C -1.335265 1.975503 0.378726

C 0.776357 2.848738 -0.287527

C -1.253002 4.052558 -0.880794

C 1.441320 1.810139 0.342252

C	0.722137	0.840072	1.058052
C	2.913672	1.753835	0.189910
C	-0.688759	0.972737	1.226770
O	-1.393512	0.212317	1.912835
O	3.469839	0.823218	0.968255
O	3.554868	2.468238	-0.548516
C	4.884349	0.651990	0.829534
C	-2.161829	-0.456213	-0.671485
C	-1.029615	-1.306921	-0.522873
H	5.141907	-0.195679	1.460170
H	5.408928	1.547404	1.166023
H	5.141855	0.444120	-0.209232
H	-1.673804	3.675434	-1.815991
H	-0.549869	4.854882	-1.091143
H	-2.055911	4.422305	-0.243842
C	-2.007120	0.855191	-1.143027
C	0.257721	-0.927882	-0.806159
H	-1.167591	1.096753	-1.793266
H	-2.902476	1.429496	-1.369023
H	0.426781	-0.019959	-1.373973
H	-1.192082	-2.281853	-0.069228
H	1.299387	3.616911	-0.840989
H	1.237988	0.080527	1.631981
H	-2.317089	2.312017	0.690496
C	3.836974	-3.206380	-0.265902
C	3.809291	-2.109702	-1.123684
C	2.634642	-1.383541	-1.289330
C	1.459576	-1.744222	-0.612442
C	1.504079	-2.846385	0.256447
C	2.679314	-3.567651	0.424735

H	4.751580	-3.772357	-0.130710
H	4.704173	-1.817912	-1.662251
H	2.617695	-0.523139	-1.952661
H	0.621266	-3.128343	0.819850
H	2.696277	-4.413183	1.103567
Si	-3.843937	-0.987904	-0.005480
C	-4.924265	-1.555305	-1.439891
H	-4.474677	-2.406827	-1.959793
H	-5.914465	-1.860012	-1.085696
H	-5.060554	-0.749977	-2.168552
C	-4.668370	0.480829	0.824712
H	-5.667707	0.203922	1.176087
H	-4.077666	0.809224	1.683526
H	-4.782474	1.324842	0.137389
C	-3.641310	-2.398896	1.213534
H	-2.964091	-2.108593	2.021286
H	-4.610123	-2.658928	1.651901
H	-3.243957	-3.298213	0.733833

1 imaginary frequency

E = -1386.234342

H = -1385.769030

G = -1385.847982

Product “a” for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N	-1.209527	1.699500	1.661892
C	-0.467964	2.454973	0.842502
C	0.728050	2.078152	0.303760
C	1.310787	0.716330	0.593234
C	0.729697	0.178778	1.872806
C	-0.761596	0.372102	2.076042

C	1.395810	3.016271	-0.580427
O	0.998987	4.124493	-0.895357
O	2.565026	2.524185	-1.048050
C	3.295881	3.378492	-1.929977
C	-2.426924	2.198097	2.282629
O	1.378009	-0.450999	2.677231
C	1.057928	-0.297767	-0.577203
C	-1.513908	-0.745478	1.320333
C	-1.487171	-0.663612	-0.197778
C	-0.396225	-0.484575	-0.958923
H	-0.874695	3.434719	0.612838
H	2.391497	0.776885	0.729235
H	-0.961686	0.262856	3.144501
H	4.188022	2.822217	-2.209443
H	2.705602	3.611262	-2.817184
H	3.574604	4.304454	-1.425279
H	-2.740123	3.110356	1.776786
H	-3.223960	1.457317	2.196189
H	-2.256472	2.410463	3.342517
H	-2.548997	-0.719995	1.674258
H	-1.107806	-1.706523	1.657090
H	-0.541990	-0.483904	-2.037900
H	1.543797	0.179362	-1.432705
C	3.296652	-3.932562	0.163578
C	3.942723	-2.746363	-0.182980
C	3.201712	-1.596657	-0.429088
C	1.805030	-1.603865	-0.332860
C	1.168422	-2.798345	0.004039
C	1.909286	-3.953856	0.253194
H	3.871269	-4.831533	0.355626

H 5.023571 -2.719374 -0.265869

H 3.710160 -0.676336 -0.702429

H 0.086660 -2.836920 0.064650

H 1.395714 -4.872649 0.514081

Si -3.165154 -0.883700 -1.037211

C -2.997902 -0.807121 -2.902997

H -2.338716 -1.591628 -3.285424

H -3.982586 -0.947580 -3.360233

H -2.610878 0.159779 -3.237196

C -4.314222 0.480059 -0.441330

H -5.259091 0.442807 -0.993379

H -4.549413 0.372078 0.621272

H -3.872061 1.469204 -0.596653

C -3.865716 -2.550045 -0.521848

H -4.861336 -2.700588 -0.951022

H -3.223326 -3.367350 -0.863572

H -3.957193 -2.623563 0.566119

0 imaginary frequencies

E = -1386.287278

H = -1385.817530

G = -1385.895117

Transition state "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N -2.087136 -1.985127 -0.539622

C -1.643897 -1.501642 -1.755431

C -1.274214 -1.982890 0.521654

C -3.525961 -2.176870 -0.374251

C 0.097035 -1.818147 0.356038

C 0.647036 -1.613385 -0.907107

C 0.930456 -1.817351 1.583701

C	-0.207765	-1.550027	-2.058437
O	0.190824	-1.427389	-3.229450
O	2.234103	-1.783197	1.309227
O	0.488225	-1.833741	2.710025
C	3.114604	-1.687451	2.434425
C	-1.938163	0.452967	-1.787676
C	-1.531618	1.080976	-0.595984
C	-0.157450	1.342792	-0.322729
C	0.902455	1.013969	-1.124155
H	0.733378	0.720877	-2.156090
H	-1.325018	0.554339	-2.683945
H	-3.004685	0.436821	-1.999587
H	0.069851	1.777136	0.649601
H	4.118119	-1.634032	2.019328
H	3.013918	-2.567676	3.070521
H	2.893985	-0.789250	3.012451
H	1.719093	-1.617790	-1.056528
H	-1.711405	-2.203654	1.485866
H	-2.310169	-1.721866	-2.582290
H	-3.715453	-2.655866	0.583962
H	-3.895867	-2.807434	-1.182065
H	-4.031468	-1.207967	-0.411336
C	5.041539	1.452067	-0.125079
C	4.078669	1.494160	0.883765
C	2.730813	1.357190	0.577713
C	2.309982	1.187467	-0.751930
C	3.291006	1.134151	-1.754105
C	4.640669	1.267430	-1.446222
H	6.092836	1.553879	0.118715
H	4.382966	1.621067	1.917104

H 2.003302 1.358698 1.382315

H 2.982257 0.986924 -2.784562

H 5.380073 1.225254 -2.238294

Si -2.803518 1.669493 0.676980

C -2.938588 0.519007 2.158814

H -3.564300 0.983312 2.929027

H -3.389669 -0.440954 1.894158

H -1.953472 0.326752 2.595110

C -2.247859 3.354618 1.300304

H -2.100786 4.055283 0.473096

H -3.007402 3.773678 1.968146

H -1.311473 3.291516 1.861981

C -4.484296 1.850707 -0.142273

H -5.200674 2.250095 0.583001

H -4.436714 2.548012 -0.984164

H -4.883962 0.902000 -0.510495

1 imaginary frequency

E = -1386.233446

H = -1385.768132

G = -1385.846302

Product "b" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N 1.592344 -2.131168 -0.262633

C 0.460983 -1.949611 -0.959931

C -0.721056 -1.514459 -0.431743

C -0.790459 -1.082733 1.011941

C 0.268023 -1.810168 1.795339

C 1.646189 -1.873135 1.171245

C -1.890290 -1.523989 -1.298102

O -3.037021 -1.358452 -0.608513

O	-1.888046	-1.682527	-2.506645
C	2.840142	-2.527992	-0.892288
O	0.080052	-2.242002	2.910452
C	-0.581902	0.470743	1.232937
C	2.373533	-0.538607	1.496888
C	1.924792	0.629725	0.644498
C	0.649328	1.036067	0.554392
C	-1.849107	1.184783	0.804235
C	-2.063662	1.569364	-0.522295
C	-3.270398	2.147084	-0.907836
C	-4.282076	2.350121	0.027385
C	-4.076747	1.972874	1.352363
C	-2.868786	1.395594	1.734303
H	0.514889	-2.212933	-2.011496
H	-1.752665	-1.335159	1.457674
H	2.190788	-2.691186	1.648242
H	2.657757	-2.756865	-1.941393
H	3.584229	-1.727469	-0.829746
H	3.240732	-3.414885	-0.394020
H	-0.478220	0.598808	2.318007
H	3.444461	-0.712036	1.375802
H	2.213160	-0.327977	2.560640
H	0.445643	1.896317	-0.081405
H	-1.293282	1.403612	-1.269129
H	-3.421350	2.434500	-1.942684
H	-5.221281	2.800806	-0.273034
H	-4.855724	2.130529	2.090145
H	-2.714686	1.098301	2.767427
C	-4.229148	-1.262598	-1.386689
H	-5.029482	-1.054541	-0.679231

H -4.425818 -2.200281 -1.909350

H -4.150167 -0.452194 -2.112879

Si 3.169743 1.535435 -0.462642

C 4.924453 1.071087 0.016443

H 5.635039 1.644140 -0.587659

H 5.124438 1.294755 1.068816

H 5.128881 0.009446 -0.150470

C 2.834650 1.045502 -2.247119

H 1.813656 1.322157 -2.529974

H 3.524139 1.554203 -2.928796

H 2.944686 -0.032345 -2.398299

C 2.939396 3.390575 -0.285556

H 3.106933 3.711367 0.746785

H 3.651092 3.922159 -0.925248

H 1.932310 3.701340 -0.578117

0 imaginary frequencies

E = -1386.286982

H = -1385.817701

G = -1385.895144

Transition state "c" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N -0.853795 -2.235639 -0.924768

C -0.863169 -0.946704 -1.345742

C 0.266365 -2.787149 -0.401437

C -2.065704 -3.059212 -1.045108

C 1.438699 -2.079188 -0.338525

C 1.499314 -0.704188 -0.746147

C 2.608652 -2.766180 0.248436

C 0.348867 -0.185823 -1.470304

O 0.358298 0.927623 -2.021371

O 3.660173 -1.948576 0.368079

O	2.634196	-3.926909	0.592508
C	4.846495	-2.527897	0.925385
C	-0.734396	1.472656	0.582664
C	0.677743	1.577740	0.647376
H	5.582772	-1.728220	0.945387
H	5.196875	-3.349963	0.300669
H	4.653010	-2.889718	1.935509
H	-2.241302	-3.584280	-0.107462
H	-1.932326	-3.780174	-1.852878
H	-2.911935	-2.412148	-1.264157
C	-1.423594	0.285576	0.711007
C	1.451636	0.444993	0.942393
H	-0.920306	-0.571805	1.150094
H	1.030606	-0.341268	1.560989
H	-1.297199	2.360820	0.304255
H	0.191192	-3.813461	-0.067818
H	2.459499	-0.300766	-1.043125
H	-1.759257	-0.607859	-1.849080
C	-5.670758	-0.201649	0.485471
C	-4.886476	-1.102609	1.201249
C	-3.508190	-0.926303	1.270476
C	-2.885493	0.155042	0.631672
C	-3.686347	1.050874	-0.093535
C	-5.062893	0.874813	-0.161392
H	-6.744502	-0.337832	0.426565
H	-5.347920	-1.944552	1.705309
H	-2.898347	-1.631675	1.827047
H	-3.225913	1.877696	-0.623830
H	-5.665276	1.574720	-0.729888
Si	1.542915	3.157634	0.091876

H 2.524290 0.562477 1.068583

C 2.091659 4.123170 1.613732

H 2.772187 3.526963 2.229932

H 2.614447 5.041498 1.326965

H 1.234507 4.402443 2.234201

C 3.065196 2.710480 -0.912210

H 3.610761 3.616704 -1.195003

H 3.752217 2.075223 -0.344495

H 2.774304 2.180880 -1.822593

C 0.373881 4.220140 -0.919913

H -0.006899 3.656153 -1.775519

H -0.477104 4.566123 -0.325653

H 0.897109 5.106026 -1.293914

1 imaginary frequency

E = -1386.229809

H = -1385.764573

G = -1385.843515

Product "c" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N -0.110543 -2.086225 1.475152

C 1.171820 -1.999112 1.080025

C 1.583378 -1.582344 -0.148931

C 0.580249 -1.089875 -1.162873

C -0.778843 -1.659949 -0.852786

C -1.199940 -1.656252 0.605119

C 3.012799 -1.548847 -0.408333

O 3.895610 -1.911514 0.348354

O 3.289922 -1.048135 -1.632280

C 4.675816 -0.936201 -1.961112

C -0.447026 -2.367282 2.862969

O	-1.544471	-2.033887	-1.711555
C	0.457813	0.460127	-1.189604
C	-1.738949	-0.245963	1.019951
C	-0.668138	0.825263	1.063545
C	0.273424	1.135308	0.158873
C	-2.982457	0.113301	0.214741
C	-3.010238	1.141877	-0.726155
C	-4.173647	1.415642	-1.445515
C	-5.325551	0.667367	-1.230960
C	-5.311593	-0.355670	-0.283713
C	-4.151492	-0.625485	0.432265
H	1.906987	-2.306681	1.816984
H	-2.020416	-2.369250	0.712251
H	4.710346	-0.485346	-2.950631
H	5.191820	-0.300699	-1.239558
H	5.147674	-1.919553	-1.980912
H	0.345861	-2.966755	3.309147
H	-0.565981	-1.446609	3.443121
H	-1.380595	-2.931942	2.899075
H	-0.364782	0.729898	-1.862455
H	1.372734	0.825527	-1.663967
H	-2.081844	-0.386685	2.049216
H	-0.693818	1.408462	1.982631
H	-2.126085	1.745710	-0.894310
H	-4.176064	2.221009	-2.171638
H	-6.229434	0.882303	-1.789513
H	-6.206905	-0.938578	-0.098372
H	-4.150175	-1.417509	1.175654
H	0.844112	-1.416355	-2.169821
Si	1.516149	2.505732	0.538666

C 1.355554 3.836713 -0.778553

H 2.095045 4.627992 -0.619738

H 1.516742 3.425655 -1.779789

H 0.361521 4.293455 -0.756181

C 3.239675 1.758750 0.450919

H 3.446599 1.363722 -0.548224

H 3.994382 2.520943 0.670743

H 3.359142 0.945383 1.173233

C 1.211826 3.239841 2.236766

H 1.944335 4.030294 2.429088

H 0.215307 3.684083 2.314354

H 1.315850 2.489900 3.026235

0 imaginary frequencies

E = -1386.288557

H = -1385.818789

G = -1385.896043

Transition state "d" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N -0.423232 -1.324198 1.422757

C -1.011002 -1.747662 0.276654

C 0.918578 -1.166794 1.529810

C -1.285004 -0.839470 2.501637

C 1.744453 -1.443052 0.473432

C 1.176970 -1.710578 -0.811273

C 3.192176 -1.270327 0.678740

C -0.212735 -2.145581 -0.861506

O -0.718473 -2.697949 -1.852716

O 3.889253 -1.446307 -0.451162

O 3.715936 -0.994951 1.736996

C 5.309465 -1.290626 -0.342517

C	-1.878794	0.157287	-0.881913
C	-0.918722	1.095829	-0.546928
C	0.430287	1.062173	-0.966388
C	0.912051	0.061189	-1.822575
H	0.242091	-0.423711	-2.531371
H	-1.710809	-0.484597	-1.742224
H	-1.199445	1.873083	0.163147
H	5.699088	-1.437643	-1.346832
H	5.721428	-2.037940	0.336513
H	5.557219	-0.291470	0.017724
H	1.819455	-2.119622	-1.582187
H	1.288989	-0.850086	2.495404
H	-2.042082	-2.068101	0.352381
H	-2.204676	-1.422661	2.514691
H	-1.521330	0.211812	2.317647
H	-0.764324	-0.941469	3.451739
H	1.935986	0.143377	-2.176352
C	-5.986332	0.164955	0.344286
C	-5.545251	-0.659408	-0.687227
C	-4.207989	-0.643106	-1.069622
C	-3.280978	0.196585	-0.434059
C	-3.739020	1.015594	0.609759
C	-5.075469	1.001761	0.989107
H	-7.027303	0.155367	0.646110
H	-6.242406	-1.315771	-1.195946
H	-3.868433	-1.286064	-1.875945
H	-3.049449	1.665019	1.136832
H	-5.408799	1.644520	1.796322
Si	1.615519	2.334127	-0.222123
C	3.317393	2.125740	-0.984452

H 4.018765 2.830095 -0.526073

H 3.709982 1.116225 -0.829033

H 3.302856 2.318932 -2.061335

C 0.942561 4.048305 -0.598210

H 0.844801 4.205804 -1.676214

H -0.042265 4.195468 -0.144331

H 1.612041 4.817722 -0.200785

C 1.741358 2.135979 1.644703

H 2.341886 1.263061 1.914401

H 2.220673 3.020721 2.077522

H 0.753730 2.030427 2.104919

1 imaginary frequency

E = -1386.228640

H = -1385.763253

G = -1385.841387

Product "d" for (4+3) cycloaddition of oxidopyridinium ion 2 with 9k

N 0.934581 -1.727332 -0.697331

C -0.360554 -1.787071 -1.074311

C -1.426925 -1.580263 -0.255930

C -1.236927 -1.328155 1.219749

C 0.139062 -1.762557 1.641701

C 1.273971 -1.426435 0.692242

C -2.753981 -1.606396 -0.855938

O -3.724041 -1.421629 0.063710

O -3.011454 -1.778941 -2.032923

C 1.943646 -2.415380 -1.499262

O 0.369197 -2.261592 2.720140

C -1.394655 0.170208 1.622677

C 1.674748 0.074211 0.913125

C	0.642775	1.079453	0.434339
C	-0.662825	1.152405	0.731146
C	3.036078	0.311117	0.285226
C	4.190863	0.095264	1.040858
C	5.453197	0.241353	0.472719
C	5.577880	0.604390	-0.866197
C	4.433037	0.820618	-1.628729
C	3.171416	0.675879	-1.056947
H	-0.526111	-2.025293	-2.120640
H	-1.953624	-1.902217	1.808963
H	2.127445	-2.041819	0.981904
H	1.690533	-2.313976	-2.554967
H	2.921048	-1.968019	-1.326736
H	1.988278	-3.478509	-1.239743
H	-1.064051	0.283700	2.662333
H	-2.467393	0.379898	1.612940
H	1.789335	0.175970	1.999876
H	1.053355	1.855941	-0.206125
H	4.097040	-0.190329	2.084383
H	6.338348	0.074434	1.076276
H	6.559660	0.720398	-1.310994
H	4.520284	1.100001	-2.672796
H	2.288562	0.832130	-1.668538
C	-5.062987	-1.408332	-0.435748
H	-5.696732	-1.189190	0.420921
H	-5.324886	-2.379998	-0.857029
H	-5.180666	-0.637877	-1.199246
Si	-1.708195	2.540451	-0.007155
C	-2.410395	3.573725	1.397116
H	-3.070399	4.355515	1.008078

H -2.994316 2.957743 2.087934

H -1.612004 4.057856 1.967232

C -3.131340 1.764338 -0.958893

H -3.772547 1.177997 -0.294579

H -3.748801 2.545354 -1.414637

H -2.771292 1.108739 -1.757769

C -0.675581 3.615425 -1.144955

H -1.303369 4.404514 -1.570969

H 0.148371 4.097940 -0.611427

H -0.256052 3.038618 -1.974508

0 imaginary frequencies

E = -1386.287200

H = -1385.817814

G = -1385.895316

Computational NMR Analysis of Structures **13**, **20**, and **23**

I. Summary

A computational analysis of structures 13, 20, and 23 was undertaken to verify their experimental NMR spectra and identify diagnostic peaks as well as conclude their mixture compositions in the case of the latter two structures. Computational spectra supported the experimental assignments in structure 13 and determined the structure 20 reaction mixture was of isomers A and B while the structure 23 reaction mixture was isomers A and C.

The DP4-AI workflow developed by the Goodman group[98] was used in combination with diagnostic peaks to assign the spectra. Computational methods were chosen in accordance to best practice for DP4-AI[99]. Geometry optimizations used B3LYP/6-31G(d), energy calculations used M06-2X/def2tzvp, and NMR shift calculations used mPW19PW91/6-311G(d).

II. Structure 13

Experimental assignment of major isomer A and minor isomers B and C was supported by computational NMR and certain bridgehead atoms were located as diagnostic peaks for further experimental work. A theoretical exo regioisomer, D, was created but did not match experimental spectra. Discriminating between minor isomers B and C was also supported by DP4-AI analysis.

The newly formed bridgehead carbons of 13B exhibit different shifts at 70 ppm and 50 ppm for C-xx and C-yy respectively. The proton attached to C-xx resonates at 3.63 ppm and couples to proton H_1-zz and geminal H_2-zz attached to C-zz. The former exhibits a doublet of doublets at 2.97 ppm and the latter is contained in the multiplet between 2.10-2.04 ppm. These carbons are identified in Figure 1 below.

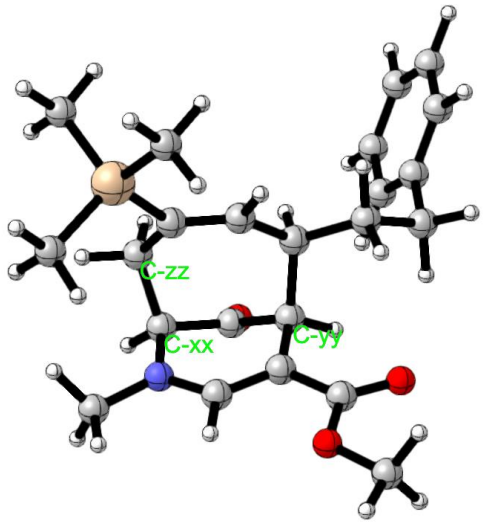


Figure 1. Minor isomer 13B shown with labelled carbon atoms.

Corresponding couplings and shifts were observed for 13C but centered around C-yy rather than C-xx. The proton attached to C-yy resonated at 3.62 ppm and coupled with two geminal partners on C-aa with proton shifts of 2.99-2.97 ppm and 2.19 ppm. Figure 2 below shows 13C with carbon labels.

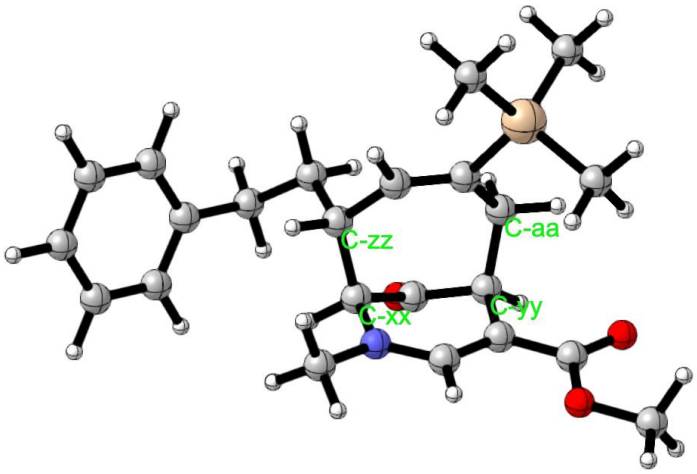


Figure 2. Minor isomer 13C shown with labelled carbon atoms.

Although other protons such as those alpha to the phenyl ring exhibited different computational shifts, the aforementioned protons are easily detectable and suited for experiments.

III. Structure 20

Computational analysis determined that the structure 20 product mixture was of isomers A and B. As before, the exo regiosomer D was created for further validation.

The first diagnostic region was the alkyl chain protons closest to the stereocentre which correlated to three experimental peaks for three protons below 2 ppm at 1.52, 1.73, and 1.84 ppm. Computationally (mPW19PW91/6-311G(d)), isomers A, B, C, and D had 2, 1, 2, and 0 peaks respectively in this region. The lowest shift for 13D was 2.06 ppm. To achieve the three peaks seen experimentally, this meant a combination of B (1) and either A (2) or C (2). The next diagnostic region involved the bridgehead protons shown in Figure 3. Experimentally, there is a peak at 3.57 ppm which corresponds well with computational shifts (mPW19PW91/6-311G(d)) for isomer A (3.53 ppm) but not as well with isomer C (3.39 ppm). In addition, amine methyl peaks supported the presence of both A and B. Peak height analysis guided by computational shifts for the amine and ester groups suggested that isomer B was the major product.

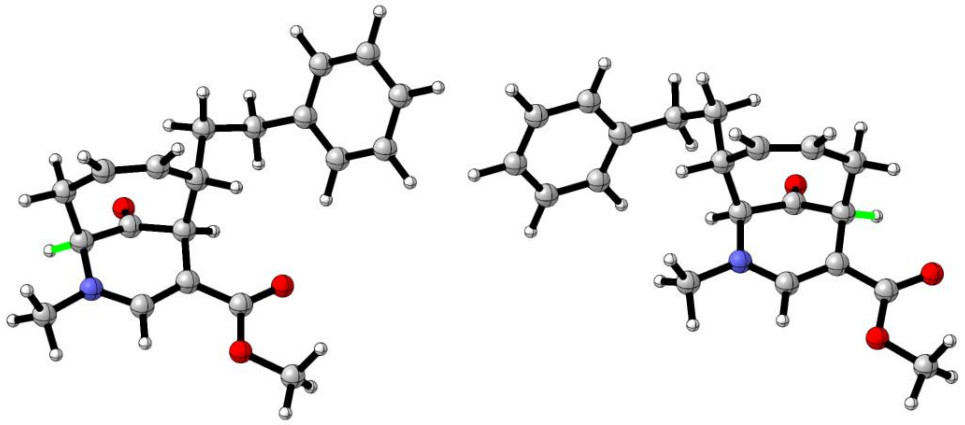


Figure 3. Structures 20A (right) and 20C (left) with diagnostic bridgehead protons shown by green bond.

IV. Structure 23

Identification of the structure 23 mixture followed the same general procedure as for structure 20 and determined that the experimental spectra of structure 23 was an approximately 50:50 mixture of isomers A and C. As before, the exo regiosomer D was created for further validation.

The proton peaks corresponding to the amine and ester functionalities were used as diagnostic peaks because the phenyl ring exerts an observable influence on the shifts of these two functionalities. The amine methyl group saw average computational shifts of 3.00, 2.97, 3.12, and 2.51 ppm (mPW19PW91/6-311G(d)) for isomers A, B, C, and D. Isomers A, B, and C corroborated well with experimental singlets at 2.96 ppm and 3.00 ppm. Experimental ester shifts of 3.68 ppm and 3.73 ppm were then used to eliminate isomer B since computational shifts of 3.69, 2.95, and 3.64 ppm (mPW19PW91/6-311G(d)) were observed for isomers A, B, and C respectively. The positioning of the phenyl ring on B as shown in Figure 4 likely leads to anisotropic interactions with the ester methyl in a similar manner to isomer D and the amine methyl. Peak height analysis guided by computational shifts for the OTMS, amine, and ester functionalities suggested that isomer A was the major product.

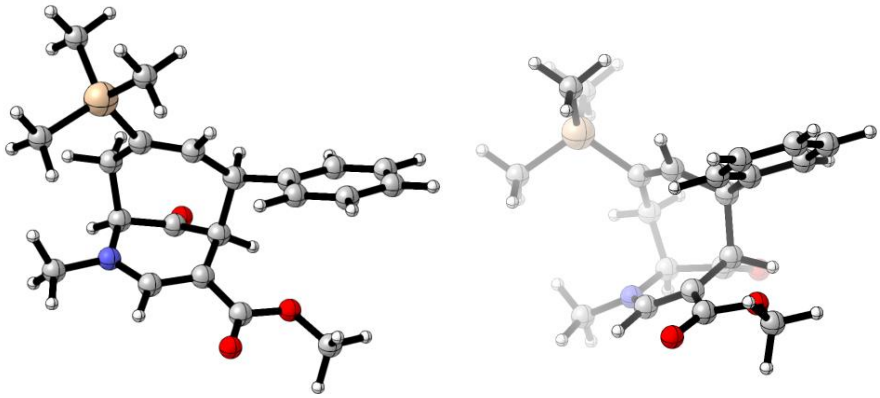


Figure 4. Top conformer of structure 23B shown from two different perspectives with phenyl ring pointed towards ester methyl group.

V. Computational Data

V.I. Proton Computational NMR Data

Calculated Proton Shift (6-311G(d)) /ppm			
13A	**13B**	**13C**	**13D**
-0.02	-0.01	-0.25	-0.3
0	0.01	-0.08	-0.17
0	0.06	-0.06	-0.16
0.03	0.07	-0.03	-0.04
0.04	0.07	0	0.05
0.04	0.08	0	0.11
0.08	0.09	0.01	0.14
0.1	0.1	0.04	0.19
0.12	0.11	0.13	0.19
1.59	1.89	1.67	2.1
1.71	2.07	1.71	2.26
2.08	2.08	2.1	2.27
2.79	2.22	2.8	2.39
2.9	2.84	2.84	2.74

2.91	3.1	2.85	3.03
3.04	2.93	2.83	2.92
2.86	2.98	2.61	2
2.92	2.84	2.71	2.6
2.91	3.05	2.97	3.33
3.45	3.54	3.44	3.33
3.46	3.67	3.5	3.41
3.48	3.69	3.67	3.63
3.56	3.51	3.63	3.65
3.6	3.62	3.61	3.35
6.46	6.18	6.42	6.25
7.44	7.42	7.44	7.5
7.45	7.5	7.48	7.58
7.53	7.53	7.5	7.62
7.55	7.55	7.55	7.64
7.56	7.55	7.6	7.69
7.26	7.31	7.19	7.04

Calculated Proton Shift (6-311G(d)) /ppm			
20A	**20B**	**20C**	**20D**
1.63	1.81	1.63	2.06
1.68	2.05	1.79	2.1
2.1	2.14	2.18	2.11
2.79	2.14	2.62	2.18
2.81	2.85	2.72	2.79
2.81	2.93	2.88	2.86
2.92	3.12	2.91	2.94
2.8	2.68	2.79	2.9
2.94	3.03	2.81	3.09

3.04	2.95	2.39	2.83
3.53	3.7	3.39	3.35
3.44	3.71	3.58	3.51
3.53	3.66	3.6	3.65
3.56	3.55	3.62	3.64
3.6	3.58	3.73	3.53
5.96	5.93	6.04	6.01
6.2	6.11	6.12	6.18
7.32	7.37	7.25	7.27
7.45	7.42	7.49	7.41
7.48	7.51	7.49	7.47
7.53	7.52	7.51	7.48
7.53	7.53	7.57	7.54
7.57	7.6	7.6	7.55

Calculated Proton Shift (6-311G(d)) /ppm			
23A	**23B**	**23C**	**23D**
0.06	-0.06	-0.2	-0.08
0.08	0.04	-0.07	-0.06
0.11	0.06	0	-0.04
0.12	0.09	0.04	-0.01
0.12	0.13	0.05	-0.01
0.16	0.19	0.09	0.01
0.2	0.19	0.13	0.15
0.23	0.21	0.27	0.18
0.24	0.25	0.34	0.19
2.28	2.27	2.28	2.23
3.05	3.22	3.17	3.27

2.84	3.02	2.92	2.29
2.92	3.03	3.02	2.6
3.25	2.85	3.43	2.63
3.51	3.46	3.41	3.42
3.58	2.93	3.51	3.61
3.73	2.66	3.7	3.62
3.77	3.27	3.72	3.74
3.64	3.63	3.68	3.51
4.44	3.73	4.46	3.58
6.58	6.65	6.56	6.69
7.26	7.43	7.23	7.62
7.46	7.5	7.29	7.67
7.46	7.52	7.5	7.67
7.49	7.59	7.52	7.67
7.54	7.6	7.55	7.71
7.34	7.36	7.31	7.33

V.I.I. Carbon Computational NMR Data

Calculated Carbon Shift (6-311G(d)) /ppm			
13A	**13B**	**13C**	**13D**
-1.71	-1.51	-2.15	-2.4
-1.18	-0.91	-1.96	-2.11
-0.87	-0.7	-1.46	-0.97
32.1	34.17	34.66	36.71
37.9	37.69	36.32	39.1
38.87	41.98	37.27	40.34
42.25	42.46	41.37	43.59
46.73	48.63	41.83	50.95

52.58	52.76	50.85	52.32
53.21	53.35	52.78	52.71
70.76	70.78	74.16	72.04
97.79	95.6	97.55	97.41
131	130.74	131.39	131.59
133.33	133.05	133.49	133.98
133.52	133.47	133.83	134.13
134.06	134.14	133.84	134.17
134.51	134.92	134.58	136.53
146.26	148.63	148.05	149.65
149.47	149.54	148.53	150.77
153.36	154.5	152.8	152.97
155.17	158.06	154.72	156.08
173.65	174.7	174.09	173.98
215.71	216.64	215.54	216.81

Calculated Carbon Shift (6-311G(d)) /ppm			
20A	**20B**	**20C**	**20D**
30.87	33.04	34.17	35.72
37.47	37.36	36.3	38.23
39.04	41.26	36.36	43.3
41.28	41.34	40	44.5
46.12	48.14	41.28	47.07
52.62	52.84	50.02	50.67
52.64	53.18	52.75	52.77
70.6	70.92	73.15	76.92
98.16	95.65	97.62	97.38
130.9	130.71	131.4	131.39
131.59	132.48	133.62	133.58

133.23	133.18	133.72	133.61
133.46	133.25	133.73	134.15
133.61	134.31	134.53	134.71
134.84	134.71	138.76	140.6
146.06	148.75	139.07	141.12
149.42	149.53	148.12	148.04
153.36	154.39	152.85	153.57
173.81	174.97	173.65	173.52
215.82	216.02	216.13	215.99

Calculated Carbon Shift (6-311G(d)) /ppm			
23A	**23B**	**23C**	**23D**
-1.6	-2.08	-2.34	-2.2
-1.27	-0.47	-1.85	-1.61
-0.76	-0.38	-0.99	-1.34
33.1	36.27	35.73	38.18
42.33	42.36	42	45.15
52.91	52.19	50.22	51.21
55.27	56.42	51.01	52.97
58.71	57.95	52.85	55.09
70.58	71.45	78.39	78.4
97.99	94.49	98.23	100.33
131.81	131.7	132.35	132.73
133.19	133.35	133.64	134.18
133.24	133.4	133.72	134.24
133.55	133.77	133.87	134.26
134.19	134.49	134.06	134.37
146.22	149.88	143.49	149.66

149.25	152.15	145.69	151.35
151.36	154.38	152.58	154.35
153.21	155.61	156.5	156.75
173.96	174.6	174.14	173.95
212.69	215.44	212.6	216.42

Bibliography

1. Joule, J. A. Chapter four-natural products containing nitrogen heterocycles-some highlights 1990-2015. *Adv. Heterocycl. Chem*. **2016**, *119*, 81 – 106.

2. Reekie, T. A., Kavanagh, M. E.; Longworth, M.; Kassiou, M. Synthesis of biologically active seven-membered-ring heterocycles. *Synthesis*, **2013**, *45*, 3211 – 3227.

3. Oliveira, K. T. D.; Servilha, B. M.; Alves, L. D. C.; Desiderá, A. L.; Brocksom, T. J. The synthesis of seven-menbered rings in natural products. *Stud. Nat. Prod. Chem*. **2014**, *42*, 421 – 463.

4. Woodward, R. B.; Hoffmann, R. The conservation of orbital symmetry. *Angew. Chem. Internat. Edit*. **1969**, *8*, 781 – 932.

5. Rigby, J. H.; Pigge, F. C. [4+3] Cycloaddition Reactions. *Org. React*. **1997**, *51*, 351 – 478.

6. Rigby, J. H.; Pigge, C. F. Organic Reactions, Vol. 51 (Eds.: L. A. Paquette), *Wiley*, Hoboken, **1997**, 351 - 478.

7. Hoffmann, H. M. R. The cycloaddition of allyl cations to 1,3-dienes: general method for the synthesis of seven-membered carbocycles. *Angew. Chem. Int. Ed. Engl*. **1984**, *23*, 1 – 19.

8. Harmata, M. Intramolecular Cycloaddition Reactions of Allylic Cations. *Tetrahedron*. **1997**, *53*, 6235 – 6280.

9. Cramer, C. J.; Barrows, S. E. Quantum chemical characterization of cycloaddition reactions between the hydroxyallyl cation and dienes of verifying nucleophilicity. *J. Org. Chem*., **1998**, *63*, 5523 – 5532.

10. Dennis, N.; Ibrahim, B.; Katritzky, A. R. 1,3-Dipolar character of six-membered aromatic rings. Part xxi. Thermal cycloadditions of 1-(5-nitro-2-pyridyl)-and 1-(4,6-dimethyl-pyrimidin—2-yl)-3-oxidopyridinium with 2, 4, and 6 π-electron components. *J. Chem. Soc. Perkin Trans*. **1976**, *1*, 2307 – 2328.

11. Cramer, C. J.; Barrows, S. E. Quantum chemical characterization of cycloaddition reactions between 1,3-butadiene and oxyallyl cations of varying electrophilicity. *J. Phys. Org. Chem.* **2000**, *13*, 176 – 186.

12. Harmata, M. The (4+3)-cycloaddition reaction: simple allylic cations as dienophiles. *Chem. Commun*. **2010**, *46*, 8886 – 8903.

13. Föhlisch, B.; Herter, R.; Wolf, E.; Stezowski.; Eckle, E. *Chem. Ber*., **1982**, *115*, 335 – 380.

14. Dennis, N.; Ibrahim, B.; Katritzky, A. R. 1,3-Dipolar character of six-membered aromatic rings. Part XXI. Thermal cycloadditions of 1-(5-nitro-2-pyridyl)-and 1-(4,6-dimethyl-pyrimidin—2-yl)-3-oxidopyridinium with 2, 4, and 6 π-electron components. *J. Chem. Soc. Perkin Trans*. **1976**, *1*, 2307 – 2328.

15. Dennis, N.; Ibrahim, B.; Katritzky, A. R. 1,3-Dipolar character of six-membered aromatic rings. Part XX. Preparation and dimerization of 1-(5-nitro-2-pyridyl)- and 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium. *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2296 – 2307.

16. Katrizky, A. R.; Rahimi-Rastgoo, S.; Sabongi, G. J. 1,3-Dipolar character of six-membered aromatic rings. Part 51. Cycloaddition of 1-(β-benzoylvinyl)-3-oxidopyridiniums and subsequent transformations. J. Chem. Soc., Perkin Trans.1, **1980**, 362 – 371.

17. Dennis, N.; Katrizky, A. R.; Sabounji, G. J.; Turker, L. 1,3-Dipolar character of six-membered aromatic rings. Part 33. Transformations of cycloadducts derived from 3-oxido-1-triazinylpyridiniums. *J. Chem. Soc. Perkin Trans*. *1*, **1977**, 1930 – 1940.

18. Shoemarker, A. H.; Griffith, D. R. Synthetic approaches to non-tropane, bridged, azapolycyclic ring systems containing seven-membered carbocycles. *Synthesis*, **2021**, *53*, 65 – 78.

19. Peese, K. M.; Gin, D. Y. Asymmetric synthesis access to the hetisine alkaloids: total synthesis of (+)-Nominine. *Chem. Eur. J*. **2008**, *14*, 1654 – 1665.

20. Fu, C.; Lora, N.; Kirchhoefer, P. L.; Lee, D. R.; Altenhofer, E.; Barnes, C. L.; Hungerford, N. L.; Krenske, E. H.; Harmata, M. (4+3) Cycloaddition Reactions of *N*-Alkyl Oxidopyridinium Ions. *Angew. Chem. Int. Ed.* **2017,** *56*, 14682–14687.

21. (a) Dennis, N.; Ibrahim, B.; Katritzky, A. R. The dimer of 1-(5- nitro-2-pyridyl)-3-oxidopyridinium and its reactions. *J. Chem. Soc., Chem. Commun*. **1974**, 500−501. (b) Dennis, N.; Ibrahim, B.; Katritzky, A. R. Rationalization of the variation or reactivity towards cycloaddition with structure in 3-oxidopyridinium and -azinium betaines and a study of 1-(4,6-dimethyl-2-pyrimidyl)-3-oxidopyridi- nium. J. *Chem. Soc., Chem. Commun*. **1975**, 425−427. (c) Dennis, N.; Ibrahim, B.; Katritzky, A. R. 1,3-Dipolar character of six-membered aromatic rings. Part XXI. Thermal cycloadditions of 1-(5-nitro-2- pyridyl)- and 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium with 2, 4, and 6- π-electron components. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2307−2328. (d) Dennis, N.; Katritzky, A. R.; Rittner, R. 1,3- Dipolar character of six-membered aromatic rings. Part XXV. 5-Aryl- 1-methyl-3-oxidopyridiniums. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2329−2334. (e) Dennis, N.; Katritzky, A. R.; Sabounji, G. J.; Turker, L. 1,3-Dipolar

character of six-membered aromatic rings. Part 33. Transformations of cycloadducts derived from 3-oxido-1-triazinylpyr- idiniums. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1930−1940. (f) Katritzky, A. R.; Banerji, J.; Boonyarakvanich, A.; Cutler, A. T.; Dennis, N.; Rizvi, S. Q. A.; Sabongi, G. J.; Wilde, H. 1,3-Dipolar character of six-membered aromatic rings. Part 34. The search for superior 1-substituents to facilitate cycloadditions of 3-oxidopyridi- nium. J. *Chem. Soc., Perkin Trans. 1* **1979**, 399−407. (g) Katritzky, A. R.; Dennis, N.; Chaillet, M.; Larrieu, C.; El Mouhtadi, M. 1,3-Dipolar character of six-membered aromatic rings. Part 38. FMO treatment of peri-, site, regio, and stereo-selectivity, and relative reaction rates of cycloaddition reactions. *J. Chem. Soc., Perkin Trans. 1* **1979**, 408−417. (h) Katritzky, A. R.; Dennis, N.; Sabongi, G. J.; Turker, L. 1,3-Dipolar character of six-membered aromatic rings. Part 43. Cycloadditions leading to tricyclic adducts. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1525− 1535. (i) Katritzky, A. R.; Rahimi-Rastgoo, S.; Sabongi, G. J.; Fischer, G. W. 1,3-Dipolar character of six-membered aromatic rings. Part 51. Cycloadditions of 1-(β-benzoylvinyl)-3-oxidopyridiniums and sub- sequent transformations. *J. Chem. Soc., Perkin Trans. 1* **1980**, 362− 371. (j) Katritzky, A. R.; Dennis, N. Cycloaddition reactions of heteroaromatic six-membered rings. *Chem. Rev*. **1989**, *89*, 827−861.

22. (a) Kun Cha, J.; Ik Lee, H.; Je Sung, M.; Bong Lee, H. Synthetic studies toward sarain A: An improved synthesis of the tricyclic core of sarains by a 3-oxidopyridinium betaine cycloaddition. *Heterocycles* **2004**, *62*, 407−422. (b) Sung, M. J.; Lee, H. I.; Chong, Y.; Cha, J. K. Facile Synthesis of the Tricyclic Core of Sarain A. 3-Oxidopyridinium Betaine Cycloaddition Approach. *Org. Lett*. **1999**, 1, 2017−2019.

23. (a) Liu, Z.; Lin, X.; Yang, N.; Su, Z.; Hu, C.; Xiao, P.; He, Y.; Song, Z. Unique steric effect of geminal bis(silane) to control the high exo-selectivity in intermolecular Diels−Alder reaction. *J. Am. Chem. Soc*. **2016**, *138*, 1877−1883. (b) Wang, J.; Liu, Z.; Li, J.; Song, Z.; Hu, C.; Su, Z. exo/endo selectivity control in Diels-Alder reactions of geminal bis(silyl) dienes: Theoretical and experimental studies. *J. Org. Chem*. **2019**, *84*, 3940−3952.

24. Puriņs, M.; Mishnev, A.; Turks, M. Brønsted Acid Catalyzed 1,2- silyl shift in propargyl silanes: synthesis of silyl dienes and silyl indenes. *J. Org. Chem*. **2019**, *84*, 3595−3611.

25. (a) Pidaparthi, R. R.; Junker, C. S.; Welker, M. E.; Day, C. S.; Wright, M. W. Preparation of 2-silicon-substituted 1,3-dienes and their Diels-Alder/cross-coupling reactions. *J. Org. Chem*. **2009**, *74*, 8290−8297. (b) Junker, C. S.; Welker, M. E.; Day, C. S. Synthesis of 4-aryl- and 4-alkyl-2-silyl-1,3-butadienes and their Diels-Alder/cross-coupling reactions. *J. Org. Chem*. **2010**, *75*, 8155−8165. (c) Kaminsky, L.; Clark, D. A. Ruthenium catalyzed cycloisomerization of silicon- tethered 1,7-enynes to give exocyclic 1,3-dienes. *Org. Lett*. **2014**, *16*, 5450−5453.

26. Fleming, I.; Dunogues, J.; Smithers, R. The electrophilic substitution of allylsilanes and vinylsilanes. *Org. React*. **1989**, *37*, 57−575.

27. (a) Choudhury, P. P.; Junker, C. S.; Pidaparthi, R. R.; Welker, M. E. Syntheses of 2-silicon-substituted 1,3-dienes. *J. Organomet. Chem*. **2014**, *754*, 88−93. (b) Ostrowska, S.; Powała, B.; Jankowska-Wajda, M.; Ż ak, P.; Rogalski, S.; Wyrzykiewicz, B.; Pietraszuk, C. Regio- and steroselective cross-metathesis of silylacetylenes with terminal olefins and α,ω-dienes. *J. Organomet. Chem*. **2015**, *783*, 135−140.

28. Choudhury, P. P.; Welker, M. E. Preparation and reaction chemistry of novel silicon-substituted 1,3-dienes. *Molecules* **2015**, *20*, 16892−16907.

29. Conditions as follows: injection volume, 1.7 mL sample in CH_3OH; column, Chiralpak IC (21 mm × 250 mm, 5 μm); mobile phase, isocratic 15% MeOH/85% CO_2; flow rate, 70 mL/min; detection, UV at 205 nm; backpressure regulator (BPR), 100 bar.

30. In this process, we also separated the enantiomers of each individual diastereomer, but this is not relevant to the present study.

31. See Supporting Information for a discussion of this point.

32. Harmata, A. S.; Harmata, M. From 5-hydroxynicotinic acid to nitrogenous (4 + 3)-cycloadducts. *Org. Synth*. **2020**, *97*, 139−156.

33. Consistent with this idea, the isomeric TS energies for the (4 + 3) cycloaddition of 2 with 9k follow a similar order to those with 9a (i.e., 23a is kinetically favored), but the product energies predict that 23c is the most stable product. Details are provided in the Supporting Information.

34. Oda, H.; Sato, M.; Morizawa, Y.; Oshima, K.; Nozaki, H. Cleavage of vinyl carbon-silicon bond with tetrabutylammonium fluoride. *Tetrahedron*, **1985**, *41*, 3257−3268.

35. Yao, W.; Li, R.; Jiang, H.; Han, D. An additive-free, base- catalyzed protodesilylation of organosilanes. *J. Org. Chem*., **2018**, *83*, 2250−2255.

36. Szudkowska-Fratczak, J.; Marciniec, B.; Hreczycho, G.; Kubicki, M.; Pawluc, P. Ruthenium-catalyzed silylation of 1,3-butadienes with vinylsilanes. Org. Lett., 2015, 17, 2366−2369.

37. Ilardi, E. A.; Stivala, C. E.; Zakarian, A. Hexafluoroisopropanol as a unique solvent for stereoselective iododesilylation of vinylsilanes. *Org. Lett*., **2008**, *10*, 1727−1730.

38. Harmata, M. The (4 + 3)-cycloaddition reaction: simple allylic cations as dienophiles. *Chem. Commun.* **2010**, *46*, 8886-8903.

39. Harmata, M. The (4+3)-cycloaddition reaction: heteroatom-substituted allylic cations as dienophiles. *Chem. Commun.* **2010**, *46*, 8904-8922.

40. Mascareñas, J. L.; Gulias, M.; Lopez, F. (4+3) cycloadditions. In *Cycloaddition Reactions in Organic Syntheses*, Nishiwaki, N., Ed.; John Wiley & Sons: Hoboken, 2014, pp 595-655.

41. Lam, S. Y. Y.; Chiu, P. [4+3] Cycloadditions of enol silane derivatives. In *Methods and Applications of Cycloaddition Reactions in Organic Syntheses,* Nishiwaki, N., Ed.; Wiley: New York, 2014; Chapter 18.

42. Jones, D. E.; Harmata, M. Application of the [4+3]-Cycloaddition Reaction to the Synthesis of Natural Products. In *Methods and Applications of Cycloaddition Reactions in Organic Synthesis*; Nishiwaki, N., Ed.; Wiley: New York, 2014; Chapter 19.

43. Dennis, N.; Katritzky, A. R.; Rittner, R. 1,3-Dipolar Character of Six-Membered Aromatic Rings. Part XXV. 5-Aryl-1-methyl-3-oxidopyridiniums. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2329-2334.

44. Katritzky, A. R.; Rahimi-Rastgoo, S.; Sabongi, G. J.; Fischer, G. W. 1,3-Dipolar Character of Six-Membered Aromatic Rings. Part 51. Cycloadditions of 1-(β-Benzoylvinyl)-3-oxidopyridiniums and Subsequent Transformations. *J. Chem. Soc., Perkin Trans. 1* **1980**, 362-371.

45. Katritzky, A. R.; Dennis, N. Cycloaddition Reactions of Heteroaromatic Six-Membered Rings. *Chem. Rev.* **1989**, *89*, 827-861.

46. Sung, M. J.; Lee, H. I.; Chong, Y.; Cha, J. K. Facile Synthesis of the Tricyclic Core of Sarain A. 3-Oxidopyridinium Betaine Cycloaddition Approach. *Org. Lett.* **1999**, *1*, 2017-2019.

47. Lee, H. I.; Sung, M. J.; Lee, H. B.; Cha, J. K. Synthetic studies toward sarain A: An improved synthesis of the tricyclic core of sarains by a 3-oxidopyridinium betaine cycloaddition. *Heterocycles* **2004**, *62*, 407-422.

48. Fu, C.; Kelley, S. P.; Tu, J.; Harmata, M., Generation of the 7-azabicyclo[4.3.1]decane ring system via (4 + 3) cycloaddition of oxidopyridinium ions. *J. Org. Chem.* **2021**, *86*, 7028-7037.

49. Sungnoi, W.; Keto, A. B.; Roseli, R. B.; Liu, J.; Wang, H.; Fu, C.; Regalado, E. L.; Krenske, E. H.; Harmata, M., *Endo* selectivity in the (4+3) cycloaddition of oxidopyridinium ions. *Org. Lett.* **2021,** *23*, 8302-8306.

50. Iiardi, E. A.; Stivala, C. E.; Zakarian, A. Hexafluoroisopropanol as a unique solvent for stereoselective iododesilylation of vinylsilanes. *Org. Lett*. **2008**, *10*, 1727-1730.

51. Brummond, K. M.; Hong, S.-p. A Formal total synthesis of (-)-FR901483, Using a tandem cationic aza-Cope rearrangement/Mannich cyclization approach. *J. Org. Chem.* **2005**, *70*, 907-916.

52. Franz, M. H.; Roeper, S.; Wartchow, R.; Hoffmann, H. M. R. The first and second Cinchona rearrangement. Two fundamental transformations of alkaloid chemistry. *J. Org. Chem.* **2004**, *69*, 2983-2991.

53. Maryanoff, B. E.; Zhang, H.-C.; Cohen, J. H.; Turchi, I. J.; Maryanoff, C. A. Cyclizations of *N*-acyliminium ions. *Chem. Rev.* **2004**, *104*, 1431-1628.

54. Roth, H. D. The beginnings of organic photochemistry. *Angew. Chem. Int. Ed. Engl*., **1989**, *28*, 1193 – 1207.

55. Liebermann, C. *Ann. Chem. Pharm*., **1871**, *158*, 300.

56. Crimmins, M. T. Synthetic applications of intramolecular enone-olefin photocycloadditions. *Chem. Rev*., **1988**, *88*, 1453 – 1473.

57. Cookson, R. C.; Crundwell, E.; Hill, R. R.; Hudec, J. Photochemical cyclisation of Diels-alder adducts. *Chem. Ind*., **1958**, 1003.

58. Poplata, S.; Tröster, A.; Zou, Y-Q.; Bach, T. Recent advances in the synthesis of cyclobutanes by olefin [2+2] photocycloaddition reactions. *Chem. Rev*., **2016**, *116*, 9748 – 9815.

59. Woodward, R. B.; Hoffmann, R. The conservation of orbital symmetry. *Angew. Chem. Internat. Edit*., **1969**, *8*, 781 – 932.

60. Schuster, D. I.; Lem, G.; Kaprinidis, N. A. New insights into an old mechanism: [2+2] photocycloaddition of enones to alkenes. *Chem. Rev*., **1993**, *93*, 3 – 22.

61. Shaw, M. H.; Twilton, J.; MacMillan, D. W. C. Photoredox catalysis in organic chemistry. *J. Org. Chem.* **2016**, *81*, 6898 – 6926.

62. Xi, Y.; Yi, H.; Lei, A. Synthetic applications of photoredox catalysis with visible light. *Org. Biomol. Chem*., **2013**, *11*, 2387 – 2403.

63. Yoon, T. P. and Du, J. Crossed intermolecular [2+2] cycloadditions of acyclic enones via visible light photocatalysis. *J. Am. Chem. Soc*., **2009**, *131*, 14604 – 14605.

64. Harmata, M. Fun with (4 + 3) cycloadditions. Synlett 2019, 30, 532−541.

65. Winkler, J. D.; Hershberger, P. M.; Springer, J. P., A stereoselective synthesis of the azaspiroundecane ring system of (-)-histrionicotoxin from (+)-glutamic acid. *Tetrahedron Lett.* **1986**, *27*, 5177-5180.

66. Winkler, J. D.; Hershberger, P. M., A stereoselective synthesis of (-) perhydrohistrionicotoxin. *J. Am. Chem. Soc.* **1989**, *111*, 4852-4856.

67. Winkler, J. D.; Scott, R. D.; Williard, P. G., Asymmetric induction in the vinylogous amide photocycloaddition reaction. A formal synthesis of vindorosine. *J. Am. Chem. Soc.* **1990**, *112*, 8971-8975.

68. Comins, D. L.; Zheng, X., A novel approach to the perhydrohistrionicotoxin ring system. *J. Chem. Soc., Chem. Commun.* **1994**, 2681-2682.

69. Kwak, Y.-S.; Winkler, J. D., Synthesis of 6-aza-bicyclo[3,2,1]octan-3-ones via vinylogous imide photochemistry: An approach to the synthesis of the hetisine alkaloids. *J. Am. Chem. Soc.* **2001**, *123*, 7429-7430.

70. Ragains, J. R.; Winkler, J. D., Pseudosymmetry in azabicyclo[2.1.1]hexanes. A stereoselective construction of the bicyclic core of peduncularine. *Org. Lett.* **2006**, *8*, 4437-4440.

71. White, J. D.; Ihle, D. C., Tandem photocycloaddition-retro-Mannich fragmentation of enaminones. A route to spiropyrrolines and the tetracyclic Core of koumine. *Org. Lett.* **2006**, *8*, 1081-1084.

72. Sahn, J. J.; Comins, D. L., [2 + 2] Photochemical cycloaddition/ring opening of 6-alkenyl-2,3-dihydro-4-pyridones. *J. Org. Chem.* **2010**, *75*, 6728-6731.

73. Drake, L. R.; Scott, P. J. H., DARK classics in chemical neuroscience: Cocaine. *ACS Chem. Neurosci.* **2018**, *9*, 2358-2372.

74. Afewerki, S.; Wang, J. X.; Liao, W. W.; Córdova, A. In The Alkaloids: Chemistry and Biology; Knölker, H. J., Ed.; Elsevier:Cambridge, MA, 2019; Vol. 81, Chapter 3, pp 151−233.

75. Ullrich, S. F.; Hagels, H.; Kayser, O., Scopolamine: a journey from the field to clinics. *Phytochem. Rev.* **2017**, *16*, 333-353.

76. Drevets, W. C.; Bhattacharya, A.; Furey, M. L., The antidepressant efficacy of the muscarinic antagonist scopolamine: past findings and future directions. *Adv. Pharmacol.* **2020**, *89*, 357-386.

77. Tang, K. S., The cellular and molecular processes associated with scopolamine-induced memory deficit: A model of Alzheimer's biomarkers. *Life Sci.* **2019,** *233*, 116695.

78. Bezerra, M. M.; Leao, R. A. C.; Miranda, L. S. M.; de Souza, R. O. M. A., A brief history behind the most used local anesthetics. *Tetrahedron* **2020**, *76*, 131628.

79. Brain, P. F.; Coward, G. A., A review of the history, actions, and legitimate uses of cocaine. *J. Subst. Abuse* **1989**, *1*, 431-451.

80. Kohnen-Johannsen, K. L.; Kayser, O., Tropane alkaloids: chemistry, pharmacology, biosynthesis and production. *Molecules* **2019**, *24*, 796/1.

81. We conducted the photolysis at 0 ºC to mitigate against any untoward effects of the heat generated by the lamp.

82. Repeated sampling for TLC analysis may have lowered the yield.

83. Fu, C.; Sungnoi, W.; Tu, J.; Kelley, S. P.; Harmata, M. Tropane skeletal from the intramolecular photocycloaddition of (4+3) cycloadducts of oxidopyridinium ions and dienes. *Org. Lett*. **2022**, *24*, 3521 – 3525.

84. Stempel, E.; Gaich, T. Cyclohepta[b]indoles: a privileged structure motif in natural products and drug design. *ACC. Chem. Res*. **2016**, *49*, 2390 – 2402.

85. Li, Y.; Zhu, C. Z.; Zhang, J. Gold-catalyzed [4+3]cycloaddition/C-H functionalization cascade: regio- and diastereoselective route to cyclohepta[b]indoles. *Eur. J. Org. Chem*. **2017**, 6609 – 6613.

86. Andraintsiferana, M.; Besselievre, R.; Riche, C.; Husson, H. –P. *Tetrahedron Lett*. **1977**, 2587.

87. Bennasar, M. –L.; Vidal, B.; Bosch, J. Biomimic total synthesis of Ervitsine and indole alkaloids of the ervatamine group via 1,4-dihydropyridines. *J. Org. Chem*., **1997**, *62*, 3597 – 3609.
88. Husson, H. –P.; Bannai, K.; Freire, R.; Mompon, B.; Reis, F. A. M. *Tetrahedron*. **1978**, *34*, 1363.

89. Bennasar, M. –L.; Vidal, B.; Bosch, J. *Chem. Commun*. **1996**, 2755.

90. Bosch, J.; Rubiralta, M.; Bolos, J. *Tetrahedron.* **1987**, *43*, 391.

91. Li, Y.; Zhu, C.-Z.; Zhang, J. Gold-catalyzed (4+3) cycloaddition/c-h functionalization cascade: regio- and diastereoselective route to cyclohepta[*b*]indoles. *Eur. J. Org. Chem*., **2017**, 6609 – 6613.

92. Pirovano, V.; Brambilla, E.; Moretti, A.; Rizzato, S.; Abbiati, G.; Nava, D.; Rossi, E. Synthesis of cyclohepta[b]indoles by (4+3) cycloaddition of 2-vinylindoles or 4*H*-furo[3,2-*b*]indoles with oxyallyl cations. *J. Org. Chem*. **2022**, *85*, 3265 – 3276.

93. Pirovano, V.; Decataldo, L.; Rossi, E.; Vicente, R. Gold-catalyzed synthesis of tetrahydrocarbazole derivatives through an intermolecular cycloaddition. *Chem. Commun*., **2013**, *49*, 3594 – 2596.

94. Qin, W. B.; Li, W. W.; Zhu, P. F.; Mo, X. G.; Zhang, H. J.; Wen, T. B. Rh(III)-catalyzed regio- and stereoselective bisindolylation of vinyl acetate: an efficient approach toward (*E*)-1,2-bis(2-indolyl)ethenes. *Org. Chem. Front*., **2018**, *5*, 1096 - 1100.

95. Porcs-Makkay, M.; Argay, G.; Kalman, A.; Simig, G. Synthesis of 1,3-di[alkoxy(aryloxy)]carbonyl]-2-oxo-2,3-dihydroindoles. *Tetrahedron*, **2000**, *56*, 5893 – 5903.

96. Rossi, E.; Abbiati, G.; Canevari, V.; Celentano, G.; Magri, E. 2-Trifluoromethanesulfonyloxyindole-1-carboxylic acid ethyl ester: a practical intermediate for the synthesis of 2-carbosubstitute indoles. *Synthesis*, **2006**, *2*, 299 – 304.

97. The compound was prepared from the known procedure WO2006100413 A2 2006-09-28.

98. Howarth, A.; Ermanis, K.; Goodman, J. M., DP4-AI automated NMR data analysis: straight from spectrometer to structure. *Chemical Science* **2020,** *11* (17), 4351-4359.

99. Ermanis, K.; Parkes, K. E. B.; Agback, T.; Goodman, J. M., The optimal DFT approach in DP4 NMR structure analysis - pushing the limits of relative configuration elucidation. *Org Biomol Chem* **2019,** *17* (24), 5886-5890.

100. Sungnoi, W.; Harmata, M. Oxidative bridgehead functionalization of (4+3) cycloadducts obtained from oxidopyridinium ions. *RSC Adv*., **2022**, *12*, 28572 – 28575.

VITA

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