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# ALLENE SYNTHESIS, OXIDATION AND COMPLEX MOLECULE SYNTHESIS 

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A Dissertation submitted to the<br>Graduate School-New Brunswick<br>Rutgers, The State University of New Jersey in partial fulfillment of the requirements for the degree of Doctor of Philosophy Graduate Program in Chemistry and Chemical Biology written under the direction of Professor Lawrence J. Williams, Ph.D. and approved by

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# ABSTRACT OF THE DISSERTATION Allene Synthesis, Oxidation and Complex Molecule Synthesis 

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Disclosed are studies on allene methodology, total synthesis and computational modeling. These include (1) an efficient approach to synthesize highly functionalized allenes stereospecifically; (2) the first catalytic stereoselective allene oxidation method using iminium salts to give synthetically useful furan/pyran building blocks; (3) a unified and concise route towards the total syntheses of withanolides; (4) a new mechanistic theory to understand face selectivity; and (5) a structural revision of brosimum allene.

## DEDICATION

This thesis is dedicated to my dearest cat, Chou-Chou.

He has quite a purrsonality to bring joy to me and my faraway family.

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## List of Abbreviations

| ${ }^{\circ} \mathrm{C}$ | degrees Celsius |
| :--- | :--- |
| $\AA$ | Angstroms |
| Ac | acetate |
| AD | Alzheimer's disease |
| Ar | aryl |
| Bu | butyl |
| Bn | benzyl |
| Bz | benzoyl |
| cat. | catalytic |
| calc. | calculated |
| CHCl | 3 |


| E | eletrophile |
| :---: | :---: |
| $e e$ | enantiomeric excess |
| Et | ethyl |
| $\mathrm{Et}_{2} \mathrm{O}$ | diethyl ether |
| expt. | experimental |
| FCC | flash column chromatography |
| gCosy | gradient correlation spectroscopy |
| GS | ground state |
| h | hour(s) |
| HF | Hartree-Fock |
| HMBC | heteronuclear multiple-bond correlation spectroscopy |
| HMDS | hexamethyldisilazide |
| HMPA | hexamethylphosphoramide |
| HSQC | heteronuclear single quantum coherence spectroscopy |
| Hz | hertz |
| $i$ - | iso- |
| imid. | imidazole |
| kcal | kilocalories |
| LDA | lithium diisopropylamide |
| $m$ - | meta- |
| M | molar (moles/liter) |
| $m \mathrm{CPBA}$ | $m$-chloroperbenzoic acid |
| Me | methyl |
| MeOH | methanol |
| $m / z$ | mass to charge ratio |
| mL | milliliters |
| min | minutes |


| mol | moles |
| :---: | :---: |
| MOM | methoxymethyl |
| Ms | methanesulfonyl |
| M.S. | molecular sieves |
| NBO | natural bond orbital |
| NBS | N -bromosuccinimide |
| mmol | micromole |
| NMR | nuclear magnetic resonance |
| NOESY | nuclear Overhauser effect spectroscopy |
| Nu | nucleophile |
| $o$ - | ortho- |
| [O] | oxidant |
| $p$ - | para- |
| Ph | phenyl |
| PMB | para-methoxybenzyl |
| ppm | parts per million |
| PPTS | pyridinium $p$-toluenesulfonate |
| Pr | propyl |
| R | generic alkyl group |
| $R$ | rectus (Cahn-Inglod-Prelog system) |
| Red-Al | sodium bis(2-methoxyethoxy)aluminumhydride |
| rt | room temperature |
| $S$ | sinister (Cahn-Inglod-Prelog system) |
| SAR | structure activity relationship |
| TBAF | tetrabutylammonium fluoride |
| TBDPS | tert -butyldiphenylsilyl |
| TBS | tert-butyldimethylsilyl |

$t$ -
TES
TEA
Tf

TFA
THF
TIPS
TLC
TMS

Tol.
Ts
TsDPEN
TS
tert-
triethylsilyl
triethylamine
triflate
trifluoroacetic acid
tetrahydrofuran
triisopropylsilyl
thin-layer chromatography
trimethylsilyl
toluene
p-toluenesulfonyl
TsDPEN
transition state

## Chapter I

## Stereospecific Single Flask Allene Synthesis

### 1.1. Introduction

The allenes (1.1, Figure 1.1) are useful functional groups for oxidations, additions, transition metal catalyzed cyclizations and other transformations. ${ }^{1}$ With the aid of allene chemistry, many useful intermediates can be accessed.




































Figure 1.1. Selected motifs derived from allene intermediate

Numerous methods have been reported for allene synthesis. ${ }^{1 b, 2}$ However, when it comes to chiral allenes, only a few of them are practical (Scheme 1.1). Typically, an
enantiomer-pure propargyl alcohol (1.2), obtained from Carreira's coupling method ${ }^{3}$ or Noyori reduction ${ }^{4}$, can be converted to a mesylate (1.3), followed by SN2' cuprate addition to give an enantiomer-pure tri- or tetrasubstituted allene (1.4). ${ }^{2}$ Alternatively, the propargyl alcohol (1.2) can be exposed to Myers' allene synthesis protocol to give an enantiomer-pure disubstituted allene (1.6). ${ }^{5}$ These two methods are very practical in the aspect of substrate scope. However, it takes an undesirably long sequence of reactions to make an enantiomer-pure allene. This propagates us to develop a method to simplify this process: an efficient stereospecific allene synthesis method.

## Carreira's coupling



Noyori's reduction



Scheme 1.1. Stereoselective allene synthesis methods

Additionally, our interest in highly functionalized organic moldecules, especially natural products and analogues, drew our special attention to highly functionalized allenes (Figure 1.2). Ideally, our method would be both general and efficient, and would give highly functionalized chiral allenes.





Figure 1.2. Drugs and natural products with polyols

### 1.2. Previous Allene Synthesis from Propargyl Oxirane

The first allene synthesis from propargyl oxirane was reported by Vermeer in 1974 $(\mathbf{1 . 7} \boldsymbol{\rightarrow} \mathbf{1 . 8}, \text { Scheme } 1.2)^{6}$. They demonstrated that propargyl oxirane can be attacked by Gilman cuprate to give tetrasubstituted allenic alcohol. In 1978, one of the pioneers in this field, Normant showed that when allyl magnesium bromide was used, only catalytic amount of copper (I) was required for conversion $(\mathbf{1 . 9} \rightarrow \mathbf{1 . 1 1})$, whereas for alkyl or vinyl Grignard reagents stoichometric copper (I) was required for the reaction work $(\mathbf{1 . 9} \rightarrow \mathbf{1 . 1 0})$ due to competitive metallation side reactions ${ }^{7}$



Scheme 1.2. Previous allene synthesis from propargyl oxirane

Krause recently published a lot of work on functionalizations of hydroxyl allenes ${ }^{1 b, 8}$ : gold-catalyzed isomerization reactions to give 2,5-dihydrofurans, ${ }^{2 \mathrm{~d}} 3$-pyrolines (with an additional step to convert hydroxyallene to aminoallene), ${ }^{2 \mathrm{~h}}$ and cycloisomerization of allenic hydroxyketone in basic aqueous condition to give furanones ${ }^{8 \mathrm{a}}$. In some of the reports, they used terminal alkynes containing adjacent trisubstituted epoxides as starting materials and screened the effects of copper sources, organolithium/Grignard reagents, and additives. When organolithium reagents were used, the outcome of the reactions was very highly dependent on the combinations of copper sources and additives. Either the desired SN2' product or the dimerized copper ligand (R-R) reductive elimination product was formed. The presence of certain ligands seemed to improve the selectivity. Also, ether is a better solvent than THF, presumably due to the complex formed in the latter ${ }^{8 i}$. In contrast, when Grignard reagent was used, the outcome was much less influced by these factors. And with minor modification the desired SN2' product was always obtained as the major product (Scheme 1.3) ${ }^{8 \mathrm{c}}$.


Scheme 1.3. Krause protocol for allene synthesis

### 1.3. Single Flask Allene Synthesis from Propargyl Oxirane

We wanted to take advantage of propargyl oxirane chemistry to make allenes (Scheme 1.4.). Theoretically, deprotonated propargyl oxiranes (1.14) can be attacked by different electrophiles to form the coupling products (1.15), which then can be opened by high order cuprates in situ to give highly functionalized allenes (1.16).


Scheme 1.4. Proposed single flask allene synthesis form propargyl oxirane

One of the major reasons why the method presented here is preferred is the convenience for constructing the stereochemistry of allenes. Presumably, the SN2' cuprate addition reaction is stereospecific or highly stereoselective. The stereochemistry of the allene is set up already from the stereochemistry of the oxirane, and there are already many ways to epoxidize double bonds stereoselectively. Hence, the starting material is easily accessible in only 2 steps and on large scales.

It should be noted that before the initiation of this project there were two concerns: (1) is the propargyl oxirane stable to deprotonation and/or electrophile addition? (2) will the cuprate give the desired SN2 ${ }^{\prime}$ addition or undesired SN2 addition product. ${ }^{9}$ Compared with previous examples, the substrates used here may have some disadvantages relative
to internal alkynes and more substituted epoxides (c.f. $\mathbf{1 . 1 2}$ v.s. 1.14). The epoxide here (1.14) should be more labile to direct ring opening. Also, the electronwithdrawing effect of the oxirane may deactivate the alkynylides in the event of coupling with electrophiles.

### 1.3.1 Coupling With Methyl Triflate

Propargyl oxirane (1.14) was first tested with a simple electrophile, methyl triflate (Scheme 1.5). The reaction went smoothly to give the desired coupling product $\mathbf{1 . 1 5 . 1}$ in $95 \%$ yield (shown in parenthesis). If this reaction is not stopped at the coupling stage, 1.15.1 can be subjected to direct cuprate additon to give the allene 1.16.1. This reaction sequence appears to be fairly general. Different alkyl cuprates give the corresponding allenes in moderate to excellent yields as shown in Scheme 1.5. Only a single diastereomer was observed. However, vinyl and phenyl cuprate only yielded trace amount of allene products. Instead, the SN2 product was the major side. This may be due to sterics or to the lower reactivity $\mathrm{sp}^{2}$ hybridized cuprates. ${ }^{8 \mathrm{~g}}$ Nevertheless, propargyl oxirane and methyl triflate coupling product reacted with alkyl cuprates smoothly to give allenes in a single flask stereospecifically.






Scheme 1.5. Coupling with methyl triflate

### 1.3.2. Coupling With Aldehydes and Ketones

As discussed above, we are very interested in bioactive compounds especially polyols. By coupling with aldehydes/ketones, ${ }^{10}$ it is expected to bring another functionality alpha to the allene (1.16.2) as shown in Scheme 1.6.


Scheme 1.6. Coupling with aldehydes

### 1.3.2.1. Optimization of Reaction Condition

Propargyl oxirane (1.14, Table 1) was coupled with 3-phenylpropionaldehyde followed by cuprate addition to form allene 1.16.2 ( $\mathrm{R}=\mathrm{H}$ ). Surprisingly, racemized disubstituted allene 1.16.2a was generated. For entry 1 , formation of the disubstituted allene was even the major pathway (74\% yield). Significant amounts of SN2 production accounted for the low yields of allene in entry 2-4. Excess cuprate and high temperature may facilitate the formation of the disubstituted allene (c.f. entry 3 and 4). The formation of disubstituted allene is due to reductive elimination of the high order Cu (III) intermediate, ${ }^{\text {lb }}$ whereas the racemization of allenes in cuprate addition reaction is known through a single electron transfer (SET) mechanism. ${ }^{11}$ The presence of phosphine ligand should act as a stabilizer to avoid racemization ${ }^{8,9,11 \mathrm{~b}}$ (entry 3 and 4) hence the formation of 1.16.2a was still observed and the combined yields for allene were low. One possible rationale is that the alkoxide in the intermediate (1.15.2) coordinates to the copper during the cuprate addition step which facilitates the side reaction pathways. An easy way to solve this problem is to mask the anion by protection. As shown in entry 5-8, after the
coupling step, the propargyl alkoxide (1.15.2) was exposed to TES protection followed by cuprate addition. The reaction worked very well to give the desired trisubstituted allene 1.16.2 exclusively with the help of the protection group and triethyl phosphite ligand (entry 7 and 8 ). The yield is slightly higher when diethyl ether was used instead of THF for this substrate (c.f. entry 7 and 8).

Table 1.1. Optimization of Reaction Condition


| entry | R | cuprates |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | $[\mathrm{Cu}]$ | $[\mathrm{Me}-\mathrm{M}]$ | equiv. | temp. | ligand | 2 | 2a |
| 1 | H | CuCN | MeLi | 5 | -78 to -40 | - | 4 | 73 |
| 2 | $\mathrm{H}^{\mathrm{a}}$ | CuI | MeLi | 5 | -40 | - | 5 | 14 |
| 3 | $\mathrm{H}^{\mathrm{a}}$ | CuCN | MeMgBr | 5 | -40 | $\mathrm{P}(n-\mathrm{Bu})_{3}$ | 8 | 18 |
| 4 | $\mathrm{H}^{\mathrm{a}}$ | CuCN | MeMgBr | 1.75 | -78 to -40 | $\mathrm{P}(n-\mathrm{Bu})_{3}$ | 25 | 6 |
| 5 | $\mathrm{TES}^{\mathrm{b}}$ | CuCN | MeLi | 3 | -40 | - | 4 | $<20$ |
| 6 | TES | CuCN | MeLi | 3 | -78 | - | - | $1 \%$ |
| 7 | TES | CuCN | MeMgBr | 3 | -78 | $\mathrm{P}(\mathrm{OEt})_{3}$ | 50 | - |
| $\boldsymbol{8}$ | $\boldsymbol{T E S}$ | $\boldsymbol{C u C N}$ | $\mathbf{M e M g B r}$ | $\mathbf{3}$ | $-\mathbf{7 8}$ | $\boldsymbol{P}(\boldsymbol{O E t})_{3}$ | $\mathbf{5 7}$ | - |

${ }^{\text {a. }}$ Significant amount of SN2 product was observed. ${ }^{\text {b. }}$ TESCl, rt or TESOTf, $-78{ }^{\circ} \mathrm{C}$ gave similar results. ${ }^{\mathrm{c} .} \mathrm{Et}_{2} \mathrm{O}$ was used as the solvent instead of THF.

### 1.3.2.2. Substrate Scope

With the conditions, the substrate scope was then examined (Scheme 1.7). The yields shown are for the single flask allene synthesis $(\mathbf{1 . 1 4} \rightarrow \mathbf{1 . 1 6 . 2})$. The yields in parenthesis are for the alkynylide and aldehydes/ketone coupling step for comparison $(\mathbf{1 . 1 4} \rightarrow \mathbf{1 . 1 5 . 2})$. Propargyl oxirane (1.14) reacted with different aldehydes smoothly. This method tolerates aldehydes with additional hetero-functionality (cf. $\mathbf{d}$ and $\mathbf{e}$ ), adjacent double bond (f), and tethered ring (g).



Scheme 1.7. Substrate scope for coupling with aldehydes/ketone

Poor yields wer obtained for the coupling with acetone (h, Scheme 1.7). This is mostly due to the steric hindrance during the TES protection step and cuprate additon. In this single flask allene synthesis protocol, TES protection usually takes no more than half an hour. However, TES protection of the tertiary propargyl oxide took overnight and was accomplished by many side reactions. When the protection step was omitted, the allenic diol was obtained in $60 \%$ yield $(\mathbf{1 . 1 4} \rightarrow \mathbf{1 . 1 9}$, Scheme 1.8$)$. It should be noted that the cuprate addition step is also sensitie to the steric environment of the substrate. Even though the anion of $\mathbf{1 . 1 8}$ was not masked, the allenyl diol (1.19) was obtained without racemization. Also, higher temperature seems to favor SN2' over SN2 addition. At lower temperature, SN2 addition is the major pathway. At $0{ }^{\circ} \mathrm{C}$, only $26 \%$ of SN2 product was generated and the allene was formed in $60 \%$ yield. The stability of cuprate was compromised at higher temperatures.


Scheme 1.8. Coupling with acetone

For aromatic aldehydes, the outcome becomes complicated. Propargyl oxirane (1.14) coupled with non-substituted benzaldehyde well to give the desired allene (i, Scheme 1.7). Coupling with $m$-nitrobenzaldehyde gave $\mathbf{1 . 1 5 . 2}$, however this substace was not stable upon warming up. A decent yield (70\%) was obtained when the temperature was maintained low at $-78^{\circ} \mathrm{C}$ for the coupling step, but very poor conversion was to the allene was noted, even though the sequence was conducted at $-78^{\circ} \mathrm{C}(\mathbf{l})$. Only $6 \%$ allene (j) was generated when p-methoxybenzaldehyde was employed. The side product (k) was formed in $91 \%$ yield. Probably a retro-coupling step took place featured with a para-
quinoneketene type intermediate. The para-methoxy group seemed to be the problem. To test this speculation, p-chlorobenzaldehyde was used and the desired allene product (1.16.2.12) was successfully obtained. Also, when methoxy group was at meta position instead of para to avoid quinone type intermediate, desired allene was yielded (1.21, Sheme 1.9). Interestingly, when triethyl phosphite was used as the ligand for cuprate addition, a disubstituted allene (1.20) was formed instead stereospecifically, whereas usually the formation of a disubstituted allene in such protocol is accompanied by the racemization of allene ${ }^{1 \mathrm{~b}, 9}$. Triphenyl phosphite ligand enabled the formation of the trisubstituted allene (1.21) and tri-n-butyl phosphine ligand yielded the SN2 product (1.22). It is known that manipulating ligands in the cuprate addition to propargyl oxiranes will change the anti/syn ratio of the allene generated ${ }^{8,9}$. The fact that different products are yielded with different ligands is probably because of the ligands' electronic effect rather than the steric effect. The cone angles of these three ligands are comparatively close $\left(109{ }^{\circ}, 128^{\circ}\right.$ and $132^{\circ}$ for $\mathrm{P}(\mathrm{OEt})_{3}, \mathrm{P}(\mathrm{OPh})_{3}$, and $\left.\mathrm{P}(n-\mathrm{Bu})_{3}\right)$, but the Tolman's electronic parameters $v$ are 2076.3,2085.3, and $2060.3 \mathrm{~cm}^{-1}$ correspondingly. In addition, the meta methoxy group may participate in the reaction by coordinating to the copper. All these combined contributed to stronger ligand bias for this particular substrate.


Scheme 1.9. Coupling with $p$-methoxybenzaldehyde-ligand effect

Presented here is a simple way to construct allenyl polyols in a single flask by sequential addition. Admittedly, the first coupling step was not stereoselective, therefore a mixure of two diastereomeric alcohols (1.16.2) was obtained. However, it is important that this protocol realized differential protection of the diol. At the same time, the allene can be easily converted to diverse products, for example, the diastereomerically pure keto allene (1.23, Scheme 1.10).


Scheme 1.10. Derivatization of allenol

### 1.3.3. Coupling With Iminium Salts

$\alpha$-aminoallenes are very useful building blocks in drug candidate synthesis. Limited methods are available to synthesize $\alpha$-aminoallenes stereoselectively (Scheme 1.11): cuprate addition to aziridines $(\mathbf{1 . 2 4} \rightarrow \mathbf{1 . 2 5})^{12 \mathrm{a}}$ or the use of chiral $\alpha$-aminoaldehydes are common methods for this substrate type $(\mathbf{1 . 2 6} \rightarrow \mathbf{1} \mathbf{2 9}) .{ }^{12 b}$



Scheme 1.11. Previous stereoselective $\alpha$-aminoallene synthesis

To our delight, when we coupled propargyl oxirane (1.14) with Eschenmoser's salt, the reaction gave the desired $\alpha$-aminoallene stereospecifically $(\mathbf{1 . 1 4} \rightarrow \mathbf{1 . 1 6 . 3}$, Scheme 1.12). The comparatively low yield for the coupling step may attribute to the instability of epoxide under such conditions. Change of the solvent from THF to hexane to remove lithium salts was deleterious to the yield. The polar nature of $\alpha$-aminoallene product (1.16.3) formed caused some problems in separating it from triethyl phosphite through column chromatography. However, without this ligand, the allene formed was a mixture
of diastereoisomers, which proves the importance of phosphine ligand in the cuprate addition step.


Scheme 1.12. Single flask $\alpha$-aminoallene synthesis

Propargyl oxirane (1.14) was also coupled with 1-acylpyridinium salt (generated in situ) to give the 1,2 -addition product ( $\mathbf{1} .15 .4$, not shown), followed by cuprate addition to yield pyridine-derived aminoallene (Scheme 1.13). It is known that 1-acylpyridinium salt reacts with alkynide in a 1,2 -addition fashion instead of 1,4 -addition ${ }^{13}$. Two rotamers were observed in ${ }^{1} \mathrm{H}$ NMR. Enantiomer pure propargyl oxirane (ent-1.14, prepared from Sharpless oxidation and TBDPS protection) coupled with enantiomer-pure Comins' 1acylpyridinium salt $(\mathbf{1 . 3 0})^{14}$, attacked by high order cuprate and then hydrolyzed to give the highly complex aminoallene (1.16.5) in high enantiomeric purity and excellent yield. This reaction was conducted in gram scale which demonstrates that this method is a practical means by which enantiomer-pure complex aminoallenes can be formed in a single flask. Efforts were initially made for the coupling of $\mathbf{1 . 3 0}$ and 1-acyl-4methoxypyridinium salt (not shown) with $\mathbf{1 . 1 4}$ correspondingly but were shown to be unsuccessful, in which cases, toluene were used in the pyridinium salt formation step instead of diethyl ether and no precipitate (the pyridinium salt) was observed. The solvent played an important role. The successful synthesis of $\mathbf{1 . 1 6 . 5}$ demonstrates a very promising method in complex molecule synthesis. The other three diastereomer of 1.15.5 can be easily achieved by changing the chiral ligand $\left(\mathrm{R}^{*}\right)^{14}$ and/or using the enantiomer
of the epoxide. TIPS and the chiral ligand ( $\mathrm{R}^{*}$ ) can be easily removed selectively or at the same time using basic, acidic or hydrogenation conditions. ${ }^{14} \mathrm{~A}$ lot of derivatives can be made due to the diverse functionalities in this allene.


Scheme 1.13. Single flask $\alpha$-aminoallene synthesis from 1-acylpyridinium salt

### 1.4. Conclusion

Here we presented a simple way to synthesize highly functionalized allenes stereospecifically in a single flask by sequential addition. Different electrophiles (methyl triflate, aldehydes/acetone, and iminium salts) were employed in the synthesis. Various alkyl cuprates were able to react with the coupling intermediate and gave moderate to
excellent yields. This is a practical method in the sense of generality and scalability. It is remarkable for its efficiency to provide direct entry to diverse and useful allenes in a convergent way. Nevertheless, as discussed earlier in this chapter, there are some limitations in this method. As for electrophiles, (1) the deactivating effect from the epoxide decreases it reactivity in the alkynylide coupling step: isobutyl tosylate and allyl 2,2,2-trichloroacetimidate did not participate in alkynylide coupling; (2) the epoxide may undergo side reactions, and the coupling of propargyl oxiranes with benzyl bromide, methyl iodide, ethyl iodide, triethyl orthoformate, and allyl bromide led to decomposition.

For the cuprate addition step, four possible side reaction pathways ${ }^{9,11}$ were identified: SN2 addition to the epoxide, reductive elimination of the $\mathrm{Cu}($ III ) intermediate to generate disubstituted allene, racemization of trisubstituted allene, and addition-elimination pathway to give mixed syn/anti trisubstituted allene. The hindered cuprates and unhindered epoxides facilitate SN2 addition. Catalytic cuprate condition with Grignard reagent as the alkyl source favors SN 2 addition. Electronically, non-terminal alkynes with a disubstituted epoxide inclined to give the SN2 addition product when treated with less reactive $\mathrm{sp}^{2}$ hybridized cuprates. Higher temperature favored formation of the allene (SN2') instead of the SN2 addition. The use of ligand like phosphine and phosphite and less cuprate reagent helped to avoid these side reactions.

Remarkably, even though a sterically unfavorable substrate (1.14) was used, the cuprate addition reaction worked well and gave complex allenes in a stereospecific fashion. In a few cases, very small amounts of the SN2 side products were observed. This
encouraging method the synthesis of disubstituted allenes in a single flask and with excellent selectiviy.

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## Chapter II

## First Catalytic Stereoselective Allene Epoxidation

### 2.1. Introduction

Furan/pyran containing triads can be found frequently in natural products, analogues and drugs. ${ }^{1}$ Intramolecular ring opening of spirodiepoxide (2.3) generated by allene diepoxidation enables direct excess to these motifs $(\mathbf{2 . 1} \rightarrow \mathbf{2 . 2} \rightarrow \mathbf{2 . 3} \rightarrow \mathbf{2 . 4}$, Scheme 2.1$)$. Di-, tri- and tetrasubstituted allenes can be converted to the furan/pyran cores in one step. Hence, stereoselective conversion of allenes to furanyl/pyranyl triads is important and meaningful.


Scheme 2.1. Allene diepoxidation to furan/pyran motifs

Studies of allene epoxidations can be traced back to 1960 s. ${ }^{2}$ Due to the high reactivity of allene oxide intermediate as well as spirodiepoxides, the epoxidation of allenes had been very tricky until the emergence of dioxiranes. With the help of dioxiranes, the competitive transformations $(\mathbf{2 . 1} \boldsymbol{\operatorname { 2 . 2 }} / \mathbf{2} \mathbf{5} / \mathbf{2} \mathbf{6} \text {, Scheme } 2.2)^{3}$ are usually not observed and spirodiepoxide formation is the major or exclusive pathway $\mathbf{( 2 . 1} \boldsymbol{\operatorname { 2 . 3 } / \mathbf { 2 } . 4}) .{ }^{4}$ Even with dioxiranes, usually superstoichometric amount of oxidants is necessary for complete conversion and poor stereoselectivities are observed for low biased allenic substrates. ${ }^{4 b}$


Scheme 2.2. Allene epoxidation pathways

### 2.2. Method Development

### 2.2.1. Oxidant Screen

At the outset of this study we envisioned that a catalytic, ideally stereoselective, allene oxidation method could enhance the application of spirodiepoxide chemistry in the synthesis of complex molecule synthesis. ${ }^{4 b, 4 j}$ Our research started with screening different
types of oxidants in order to effect smooth transformation of allenols to furanyl triads $(\mathbf{2 . 1} \boldsymbol{\rightarrow} \mathbf{2 . 4}$, Table 1). As expected, dimethyldioxirane (DMDO, 2.7) gave close to $1: 1$ diastereoselectivity (entries 1-2). ${ }^{5}$ Comparatively highly reactive dioxirane $\mathbf{2 . 8}$ gave slow conversion and low yield when used in a catalytic fashion (entry 3). Superstoichiometric amounts of Shi catalyst ${ }^{6,7}$ were required to drive the reaction to completion in a reasonable time (entry 4). Yet, low selectivity was observed. This was not a consequence of mismatched stereochemistry, as oxidation of the opposite enantiomer of 2.1b under these conditions gave poorer selectivity (data not shown). Davis oxaziridine $\mathbf{2 . 1 0}^{8}$ promoted smooth conversion under harsh conditions (entry 5). The highest efficiency was achieved by using oxaziridinium salt 2.11. ${ }^{9}$ Attempts to use MacMillan's iminium salt with external aldehydes (3,3-dimethylbutyraldehyde) were not successful and decomposition was always observed. ${ }^{10}$

Table 2.1. Preliminary Oxidant Screen


| entry | allene | [O] | solvent | temp. <br> $\left({ }^{\circ} \mathrm{C}\right)$ | reaction time | yield <br> (\%) | $r_{2}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | (R)-2.1a | 2.7 | $\mathrm{CHCl}_{3}$ | -40 | 10 min | 85 | 1.2:1 |
| 2 | (R)-2.1b | 2.7 | $\mathrm{CHCl}_{3}$ | -40 | 10 min | 82 | 1.5:1 |
| 3 | (R)-2.1b | $2.8{ }^{\text {a }}$ | $\mathrm{CH}_{3} \mathrm{CN} / \mathrm{H}_{2} \mathrm{O}$ | 0 | 24 h | 27 | 1.2:1 |
| 4 | (R)-2.1b | $2.9{ }^{\text {b }}$ | $\mathrm{DMM}^{\mathrm{c}} / \mathrm{CH}_{3} \mathrm{CN} /$ buffer | -10 | 2 h | 30 | 2.0:1 |
| 5 | ( $\pm$-2.1b | 2.10 | $\mathrm{CHCl}_{3}$ | 60 | 30 min | 69 | 1.4:1 |
| 6 | (土)-2.1b | 2.11 | $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ | rt | $<5 \mathrm{~min}$ | 71 | 1.3:1 |
|  |  |  |  | $-\mathrm{N}-\mathrm{SO}_{2} \mathrm{P}$ <br> 2.10 |  |  |  |

${ }^{\mathrm{a}} \mathrm{NaHCO}_{3}$, Ox one added. ${ }^{\mathrm{b}} \mathrm{K}_{2} \mathrm{CO}_{3}$, Oxone added. ${ }^{\mathrm{c}}$ dimethoxymenthane.

Shown in Scheme 2.3 are two key control experiments. In the presence of an external nucleophile, the Davis oxaziridine ( 2.2 equiv., Table 2.1) converted allene 2.1c to acetoxy ketone 2.4c. Without the addition of acetate, this reaction gave decomposition to elimination products (enone regioisomers). For the allene with an additional carbon in the tethered chain (2.1d), a pyranyl triad was obtained in moderate yield (entry 6, Table 2.1). These results led us to exam the oxaziridinium-based catalytic systems.



Scheme 2.3. Oxaziridine and oxaziridinium oxidations

### 2.2.2. Catalytic System Screen

### 2.2.2.1. Iminium Salt Screen

Given the high efficiency of the oxaziridinium salt (entry 6, Table 2.1 ), we studied the corresponding catalytic system (entry 1 , Table 2.2). We were excited to find that $20 \%$ catalyst loading and Oxone as co-oxidant gave smooth conversion of the allenol to the pyranyl triad in good yield.

Iminium-salt-based alkene epoxidation has been extensively studied. ${ }^{11}$ Encouraged by the successful catalytic allene epoxidation (entry 1, Table 2.2 ), we proceeded to study the effects of various amine substituents and carbon backbone variants of these catalysts (Table 2.2). Other isoquinoline-derived iminium salts did not improve the second oxidation selectivity (entries 2 and 3). Improvements were achieved with biphenylderived iminium salts (entries 4-7). We found that the solvent ratio is crucial. When a 97:3 ratio of $\mathrm{CH}_{3} \mathrm{CN} / \mathrm{H}_{2} \mathrm{O}$ was used instead of $1: 1$, we observed poor conversion of starting material and reduced diastereoselectivity. As an anhydrous condition alternative, tetraphenylphosphonium monoperoxybisulfate (TPPP) ${ }^{11 e, 12}$ was used instead of Oxone for entry 7. The reaction efficiency was diminished. Binaphthyl-derived iminium salts produced the highest stereoselectivity (4.2:1, entries 8 and 11) with only $10 \%$ catalyst loading. Other solvents that were screened showed a decrease in selectivity, though hydrogen bonding co-solvents did significantly increase reaction rates. ${ }^{4 \mathrm{~g}}$ Notably, certain diastereomeric catalysts gave reversed diastereoselectivity for the same enantiomer of the allene (entry 9 and 10). Similarly, the use of the same chiral catalyst $\mathbf{2 . 1 5}$ led to the same
face selectivity for the second oxidation regardless of the allene enantiomer used. Hence, the reagent controls the face selectivity of the second oxidation $\left(r_{2}\right)$ and override the intrinsic face selectivity. The difference in the degree of selectivity indicates the degree to which these are matched and mismatched cases (cf. entry 9 and 10; entry10 and 11).

Table 2.2. Iminium Salt Screen


| entry | allene | cat. | equiv. | reaction time | yield(\%) | $d r$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  |  |  | $r_{1}$ | $r_{2}$ |
| 1 | ( $\pm$ )-2.1b | 2.12a | 0.2 | 25 min | 70 | $>20: 1$ | 1:1.5 |
| 2 | (S)-2.1a | 2.12b ${ }^{\text {a }}$ | 0.2 | overnight | 59 | $>20: 1$ | 1:1 |
| 3 | (S)-2.1a | 2.12 ${ }^{\text {a }}$ | 0.2 | overnight | 81 | $>20: 1$ | 1:1 |
| 4 | (S)-2.1a | 2.13a ${ }^{\text {a }}$ | 0.2 | 3 h | 50 | $>20: 1$ | 1:2.2 |
| 5 | (S)-2.1a | 2.13 b | 0.1 | 1 h | 67 | $>20: 1$ | 1:2.5 |
| 6 | (R)-2.1a | 2.13b | 0.1 | 1 h | 72 | $>20: 1$ | 1.6:1 |
| 7 | (S)-2.1a | $2.13{ }^{\text {b }}$ | 0.1 | overnight | 47 | $>20: 1$ | 1:2.0 |
| 8 | (R)-2.1b | 2.15 | 0.1 | 1 h | 62 | $>20: 1$ | 4.2:1 |
| 9 | (S)-2.1a | 2.14 | 0.1 | 1 h | 64 | $>20: 1$ | 1:3.1 |
| 10 | (S)-2.1a | 2.15 | 0.1 | 1 h | 49 | $>20: 1$ | 2.2:1 |
| 11 | (R)-2.1a | 2.15 | 0.1 | 1 h | 65 | $>20: 1$ | 4.2:1 |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |

${ }^{\mathrm{a}}$ conditions: $\mathrm{Na}_{2} \mathrm{CO}_{3}$, rt. ${ }^{\mathrm{b}}$ conditions: TPPP, $\mathrm{CH}_{3} \mathrm{CN},-40^{\circ} \mathrm{C}$ to rt .

### 2.2.2.2. Binaphthyl-Derived Iminium Salt Catalyst Screen

Table 2.3 shows the screening of binaphthyl-derived iminium salt catalysts with diverse amino groups. Surprisingly, electron withdrawing groups did not increase the reaction rate; rather, they slowed it and an increase in catalyst loading was required (entries 6, 8, and 9). These catalysts may be unstable under the reaction conditions to facilitate allene oxidation. ${ }^{13}$ Generally, the $\alpha$-branched alkyl amino catalyst gave better dr (entry 11-19). The isopropyl amine-derived catalyst gave the highest $d r$ (5.0:1, entry 18 ). $10 \%$ catalyst loading was found to provide the best overall performance. Lower or higher catalyst loading resulted in diminished yield and/or diastereoselectivity (entry17 and 19).

Table 2.3. Binaphthyl-Derived Iminium Salt Catalyst Screen


| entry | R | reaction time | yield (\%) | $d r$ |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  |  | $r_{1}$ | $r_{2}$ |
| 1 | $\mathrm{CH}_{3}$ | 2.5 h | 63 | $>20: 1$ | 2.8:1 |
| 2 | $n-\mathrm{Pr}$ | 1 h | 70 | $>20: 1$ | 2.0:1 |
| 3 | $i-\mathrm{Bu}$ | overnight | 48 | $>20: 1$ | 1.8:1 |
| 4 | $t$-Bu | 6 h | 36 | $>20: 1$ | 1.8:1 |
| 5 | neopentyl | 40 min | 49 | $>20: 1$ | 2.6:1 |
| 6 | cyclopropyl ${ }^{\text {a }}$ | 8 h | 47 | $>20: 1$ | 2.3:1 |
| 7 | Bn | 80 min | 41 | $>20: 1$ | 3.6:1 |
| 8 | 2,4,6-trifluorobenzyl ${ }^{\text {a }}$ | overnight | 78 | $>20: 1$ | 2.7:1 |
| 9 | $p-\mathrm{CF}_{3}$-benzyl ${ }^{\text {b }}$ | overnight | 47 | $>20: 1$ | 4.2:1 |
| 10 | R ${ }^{1}$ | 5 min | 55 | $>20: 1$ | 2.7:1 |
| 11 | $\mathrm{R}^{2}$ | 30 min | 36 | $>20: 1$ | 4.5:1 |
| 12 | $\mathrm{R}^{3}$ | 1 h | 56 | $>20: 1$ | 3.4:1 |
| 13 | $\mathrm{R}^{4}$ | 1 h | 65 | $>20: 1$ | 4.2:1 |
| 14 | $\mathrm{R}^{5}$ | 2 h | 45 | $>20: 1$ | 4.0:1 |
| 15 | $\mathrm{R}^{6}$ | 50 min | 50 | $>20: 1$ | 4.6:1 |
| 16 | Cy | 1 h | 60 | $>20: 1$ | 4.8:1 |
| 17 | $i-\mathrm{Pr}^{\mathrm{c}}$ | 2.5 h | 37 | $>20: 1$ | 4.2:1 |
| 18 | $i-\mathrm{Pr}$ | 1 h | 65 | >20:1 | 5.0:1 |
| 19 | $i-\operatorname{Pr}^{\text {b }}$ | 70 min | 65 | $>20: 1$ | 3.6:1 |
|  |  |  |  | ${ }_{-0}^{-1}$ |  |
|  | $\mathrm{R}^{4}-\xi-\mathcal{L}^{t-\mathrm{Bu}}$ | $\mathrm{R}^{5}-\xi-\mathcal{K}^{\mathrm{Ph}}$ | $-\xi \nabla^{P}$ |  |  |

${ }^{a} 0.3$ equiv. cat. ${ }^{\mathrm{b}} 0.2$ equiv. cat. ${ }^{\mathrm{c}} 0.05$ equiv. cat.

### 2.2.3. Substrate Scope

The substrate scope of this transformation is summarized in Table 2.4 using catalyst
2.16 and the optimized reaction conditions. Both furans and pyrans were synthesized with moderate to outstanding diastereoselectivities as compared to DMDO oxidations. Comparatively lower dr was observed with extended carbon chain tether (cf. entry 3 and 4). Greater steric hindrance from the R group generally led to higher selectivity in the
second oxidation. When R was a cyclohexyl group (entry 7), a 14.5:1 $d r$ was achieved (vs. 2.0:1 with DMDO). The absolute configuration of the major diastereomer of these products was confirmed by X-ray crystal structure analysis of a tosylhydrazone derivative. ${ }^{14}$ Only 2.1:1 $d r$ was observed for the diphenylmethine substrate (entry 5), perhaps due to steric hindrance. For the very few disubstituted allenol substrates tested, no reaction was observed and full recovery of starting material was obtained. ${ }^{15}$

Table 2.4. Substrate Scope


| entry | R | n | reaction time | yield <br> $(\%)$ | $d r$ |  | $r_{1}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | $r_{2}$ |  |  |  |  |
| (DMDO) |  |  |  |  |  |  |

${ }^{2} 2.15$ was used as the catalyst instead.
${ }^{\mathrm{b}} 20 \%$ cat. loading with $37 \% \alpha$-ene- $\alpha^{\prime}$-hydroxyketone side product formed.

### 2.3. Stereoselective Model and Stereodivergent Behavior

### 2.3.1. Stereoselective Model

An empirical model for stereoselectivity is depicted in Scheme 2.3. The first oxidation of allene to form allene oxide $(\mathbf{2} . \mathbf{1} \boldsymbol{\rightarrow} \mathbf{2 . 2})$ always occurs exclusively on the more electron-rich double bond of the allene and from the less hindered face (syn to the hydrogen). Hence, this portion of the reaction pathway is governed by the substrate.

DMDO normally epoxidizes the allene oxide intermediate with a preference for the sterically favored diastereomer, and the relative sizes of the substituents on the nonreacting termini determine the face selectivity of the second epoxidation. In low biased linear system which is the case here, there is little to no preference at all. Our isopropylsubstituted catalyst (2.16) gives excellent selectivity. We suggest that the reaction selectivity is distinctly different for DMDO. There are two degrees of stereocontrol here: (1) the smallest group (hydrogen) fits in the space near both binaphtyl rings (interaction highlighted in red); ${ }^{16}$ and (2) the tethered amino chain (isopropyl group) gives the catalyst a higher preference to approach the allene oxide from the less hindered face, i.e. syn to the methyl. This interaction is highlighted in blue. Both affects combine to give a low-energy transition state with favorable steric complementarity between the chiral substrate and chiral catalyst.

The control from the binaphthyl ring is the major contribution here. Hydrogen preferred to stay in the nook of the binaphtyl ring junction. This is well known in alkene oxidations. ${ }^{16}$ The minor contribution is from the tethered amino side chain of the catalyst and the other terminus of the erstwhile allene. This minor contribution resulted in different stereoselctivities for enantiomers of the allenes (cf. entry 10 and 11, Table 2.2; also discussions in Section 2.3.2). Moreover, when the amino moiety is chiral, the stereoselectivities for the same substrate are different when the chirality of the amino
chain is changed (cf. entry 14 and 15, Table 2.3). Strong envidence suggests that higher stereoselectivities shall be achieved by fine tuning of the binaphthyl ring (e.g. the dihedral angle of the ring).


Scheme 2.4. Stereochemical models

### 2.3.2. Stereodivergent Behavior

Stereodivergent oxidation of racemic allene 2.1c by the enantioenriched iminium catalyst $\mathbf{2 . 1 6}$ was confirmed by chiral HPLC (Scheme 2.4). ${ }^{17}$ In the DMDO oxidation of this racemic substrate (substrate-controlled), racemic mixtures of diastereomeric products were obtained. In the chiral iminium salt-catalyzed oxidation of the same racemic substrate (reagent-controlled), enantioenriched diastereomeric mixtures were obtained. The diastereoselectivities for the first epoxidation $\left(r_{1}\right)$ of both allene enantiomers are $>20: 1$. However, the fate of these enantiomeric allene oxides is difficult and is dictated by the catalyst. For the epoxidation of allene epoxide, the $\mathrm{r}_{2}$ is excellent for the $R$ enantiomer
(14:1; (+)-I:(+)-II), consistent with our observation in entry 8, Table 2.4. For the $S$ enantiomer of the allene, a comparatively depressed $r_{2}(5: 1,(-)-\mathbf{I I}:(-)-\mathbf{I})$ was observed in favor of product $(-)-\mathbf{I I}$. Clearly, these data indicate matched and mismatched diastereoselectivities for the second epoxidation of allenes in oxaziridinium salt systems as discussed in Section 2.3.1.




Scheme 2.5. Stereodivergent allene oxidation

### 2.4. Conclusion

In summary, we have developed the first catalytic stereoselective diepoxidation of allenes. Even with these early studies, efficient oxidation and intramolecular cyclization of allenols has been achieved to afford useful triad building blocks. Chiral oxaziridinium reagents based on the binaphthyl core and the use of Oxone as the stoichiometric cooxidant afforded high stereoselectivity. The high degree of catalyst structural variation suggests that further optimization should be possible.

### 2.5. Reference

1 For example, see: (a) vitamin C, pectinotoxin, KDO, seccsyrin, citreoviral, citreoviridin, karlotoxin; (b) Topamax, Lovenox, Proscar, Taxotere, Tamiflu, Baraclude.

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13 The typical bright yellow color of the catalysts in solution fade away in reactions with insufficient catalyst loading.

14 See supporting information for more information.
15 A couple of substrates with other internal nucleophiles $\left(\mathrm{COOH}, \mathrm{CONMe}_{2}\right)$ were also studied. Formation of the desired product was often accompanied by allene oxide derived ring-closing or spirodiepoxide derived linear (ketone diol formation) pathway (stereochemistry not determined).


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## Chapter III

# Integrated Routing Strategy Towards the Total Synthesis of Withanolides 

### 3.1. Withanolide Natural Products and Bioactivities

### 3.1.1. Withanolides

Withanolides are highly oxygenated ergostane-type steroids that typically contain with a $\delta$ or $\gamma$-lactone (type A and type B, Figure 3.1). ${ }^{1}$ These $\mathrm{C}_{28}$ steroids contain functionalized carbons at $\mathrm{C}_{1}, \mathrm{C}_{22} / \mathrm{C}_{23}$ and $\mathrm{C}_{26}$ positions and more than $90 \%$ of withanolides are 1-oxosteroids. The classification of withanolides (type A or B) is based on the $\mathrm{C}_{17}$ side chain, which usually has the $\beta$ configuration. In case of the $17-\alpha$ sidechain, a hydroxyl group is present at $\mathrm{C}_{17}$ position. The number of type A withanolides is far larger than type $B$, and there is a small group of withanolides with novel skeletons that does not fall into either category. Even within the type A and B categories, some withanolides contain a modified skeleton and/or formation of additional rings.



Figure 3.1. Withaferin $A$ and withanolide categories
The first withanolide, withaferin A, was isolated in 1965 (Figure 3.1). ${ }^{1}$ So far, there are more than 560 withanolides in total. Withanolides are not widely spread in diverse plants, and they mostly originated from 19 genera, most of which are temperate and tropical. The withanolides reported within the recent 15 years are mostly isolated from Solanaceae, Myrtaceac, Taccaceae, and Labiatac families.

### 3.1.2. Structure Activity Relationship (SAR)

Studies on withanolides have been very active not only because of their complex structures but also due to their various bioactivities and great potential as drug candidates. Withanolides have shown diverse bioactivities, including neurogenic, antitumor, antifeedant, antistress, cytotoxic, immunosuppressive, antimicrobial, and antiinflammatory etc. Some of the examples are shown in Figure 3.2. The structure activity relationship is summed up in Figure 3.3. ${ }^{1}$ Generally, the $\alpha, \beta$-unsaturated ketone in the A ring (2-ene-1-one), $\Delta^{5,6}$ double bond or functionalized derivatives at C5-C6, and/or lactone side chain are considered important for the bioactivities.
Selective COX-2 Inhibitory Activity

Leishmanicidal Activity




physalin B
Immunoregulatory


Figure 3.2. Selected withanolides with known bioactivities
cytotoxicity cell differentiation induction leishmanicidal activity trypanocidal activity QR induction inhibition of NO production

inhibition of
T - and B-cell proliferation

antifeedant


Figure 3.3. Structure activity relationship of withanolides

### 3.1.3. Neurite Growth

Among all the promising bioactivities of withanolides, we are most interested in their neurogenic bioactivities, which have the potential to treat neurological disorders such as Alzheimer's disease and Parkinson's disease.

Alzheimer's disease (AD) is hard to treat and is considered a complex and multifactorial syndrome. ${ }^{2}$ Generally speaking, it is featured by (a) extracelullar deposits of amyloid beta (A $\beta$ ) protein and (b) intracellular neurofibrillary tangles (NFTs) of hyperphosphorylated tau protein, accompanied by (c) synaptic dysfunction (synaptic failure and depletion of neurotrophin and neurotransmitters) and (d) mitocondrial dysfunction (oxidative stress, insulin-signaling pathway, vascular effects, inflammation, calcium, axonal-transport deficits, aberrant cell-cycle reentry, and cholesterol metabolism). The origin of all these syndromes can be attributed to the abnormal amyloidogenic pathway (Figure 3.4). In the normal pathway (nonamyloidogenic), amyloid precursor protein (APP) is chopped by $\alpha$-secretase followed by $\gamma$-secretase to generate p3 while during the undesired competitive pathway (amyloidogenic), APP is
chopped by BACE-1 followed by $\gamma$-secretase to form $\mathrm{A} \beta$, which causes a series of dysfunctions.


Figure 3.4. Alzheimer's disease mechanism (origin) ${ }^{2}$
Due to the complexity discussed above, AD is not yet curable and is still degenerative. Currently, there are four FDA approved drugs for managing AD (Figure 3.5). ${ }^{3}$ They exhibit beneficial, however short-lived effects in alleviating the symptoms of AD. Donepezil, tacrine and rivastigmine are accompanied by various adverse side effects. Most importantly, these drugs are symptomatic, rather than disease-modifying therapeutics.


tacrine
(Brand name: Aricept)
(Brand name: Cognex)

(Brand name: Namenda)

Figure 3.5. FDA approved drugs for Alzheimer's disease
Shown below are the withanolides with pro-neurite growth bioactivities (Figure 3.6). Especially, withanolides A, IV and VI are very promising in treating AD. For example, withanolides A has been shown to significantly down-regulate BACE1 and also upregulate ADAM10 ( $\alpha$-secretase) in primary rat cortical neurons, and to significantly upregulate IDE levels, which may help in degrading excess $A \beta$ in the $A D$ brain. ${ }^{3}$ Although there is data indicating that direct binding of withanolide A to secretase is not likely, ${ }^{4}$ the detailed mechanism of action is not clear yet. The preliminary bioactivity studies of the withanolides suggest their highly promising disease modifying applications in Alzheimer's and related diseases.

Recognizing the potential of withanolides in promoting neurite growth together with their various bioactivities in other aspects, we aimed for a concise and modular route targeting aboad swath of the withanolide family.

withanolide A

withanoside IV

withanoside VI





Figure 3.6. Selected neurogenic withanolides

### 3.2. Withanolide Synthesis

Most of the reported preparations of withanolides are semi-syntheses. ${ }^{5}$ For example, the first synthesis of withanolide A involves a 13 step sequence from pregnenolone (Scheme 3.1). ${ }^{4}$ Derivatives from the semi-synthesis of withanolides A are prepared for SAR studies. Unfortunately, it was found that only A ring is practically amenable to chemical modifications using this synthetic route. Semi-synthesis is the predominant approach in steroid syntheses. Although within short sequences targets can be made successfully, synthetic flexibility is severaly limited. Ideally, similar natural products and
diverse analogues would be accessible from a limited set of intermediates derived from a single synthetic route.


Notable Features:

1) singlet-oxygen-mediated photooxygenative olefin migration
2) Warton transportation

Scheme 3.1. First withanolide A synthesis

### 3.3. Integrated Routing Synthesis to the Withanolide Core

### 3.3.1. Synthetic strategy

A short divergent route to multiple analogues of macrolides and terpenes have been successfully developed by our group. ${ }^{6}$ Similarly we aimed to realize a concise and unified route towards the synthesis of the withanolide family. We hypothesize that an advanced common intermediate with most of the functionalities in place can be rapidly assembled and that many natural products and their analogues can be synthesized efficiently (Figure 3.7).


Figure 3.7. Integrated routing synthetic strategy

We envisioned a concise synthesis of the withanolide core (3.1, Scheme 3.2) through an $\mathrm{A}+\mathrm{C}-\mathrm{D}$ ring strategy and then diverged to withanolide natural products and analogues from this common intermediate. In the field of steroid total synthesis, $\mathrm{A}+\mathrm{C}-\mathrm{D}$ ring synthetic strategy using Diels-Alder reaction has been previously employed by a Spanish group ${ }^{7}$ and recently in Corey's synthesis of nicandrenones, ${ }^{8}$ Deslongchamps' steroid total synthesis using Nazaroz reagents ${ }^{9}$ and Jung's studies towards the total synthesis of cucurbitacins B and D. ${ }^{10}$

The plan was to inverstigate the plausibility of a short route to a highly functionlized intermediate with the potential to accesess withanolide $A$ (neurogenic), physalin $B$ and withalongolide B (Scheme 3.2). Physalins and neophysalins, which display cytotoxic, leishmanicidal, and antiinflammatory activities, belong to the type A withanolide (Figure 3.1) with a modified skeleton. ${ }^{1}$ The opened C-D ring contains a 9 -membered ring that is highly oxidized. Our previous success to allenic 9-membered ring via $\mathrm{C}-\mathrm{C}$ fragmentation ${ }^{11}$ and allene oxidation/derivatization ${ }^{12}$ could provide a concise means by which to access these complex molecule types. A hydroxy group at the $\mathrm{C}_{14}$ position is necessary for the C-C fragmentation reaction. Moreover, our preliminary results proved the importance of cis-fused C-D ring $\left(\mathrm{C}_{13}-\mathrm{C}_{14}\right)$ for the fragmentation reaction to take place in the bicyclic system. C-C fragmentation reactions are highly substrate dependent and sensitive to the conformation or properties of the substrate. According for our first generation of synthesis, we elected to pursue the cis-fused C-D ring. This approach made a path to physalin steroids feasible. Withagolide $B$, isolated from the aerial parts of Physalis longifolia in 2011, has potent cytotoxicity against human head and neck squamous cell carcinoma, melanoma and normal fetal fibroblast cells. ${ }^{13}$ Unlike the
majority of withanolides, it contains a hydroxy group at $\mathrm{C}_{19}$ position. This sort of hydroxyl group is usually easier to remove than it is to install. Hence, a handle at $\mathrm{C}_{19}$ position was desired. Thus, to achieve the synthetic efficiency and diversity of the synthetic targets, the steroid core $\mathbf{3 . 1}$ was designed to contain a cis-fused C-D ring, a hydroxyl group at the $\mathrm{C}_{14}$ position and a handle for fucntionalization at the $\mathrm{C}_{19}$ position.


Scheme 3.2. Integrated routing strategy towards withanolides

### 3.3.2. Synthesis of C-D ring

The synthesis of the C-D ring started with the known one step preparation of aldehyde (3.2, Scheme 3.3). The Wittig reagent was brominated in situ and added to $\mathbf{3 . 2}$ to give vinyl bromide (3.3). Ring closure to give 3.4. This reaction is conveniently scalable. This sequence was developed and first applied in the synthesis of xenicanes by my collegues Michael A. Drahl and Huan Wang. Large quantities of $\mathbf{3 . 4}$ were prepared
( $>40 \mathrm{~g}$ in one batch). This ketone (3.4) can be reduced exclusively to give diol 3.5, which was protected to give bis-TES ester 3.6. Tuning of the $\alpha / \beta$ ratio of the reduced ketone was realized by changing the reducing reagents. However, the $\alpha$ hydroxy product (shown) always predominates. ${ }^{14}$ Large excess of $\mathrm{TMSCH}_{2} \mathrm{Li}$ (10 equiv.) was required to convert the ester to the TMS-methyl ketone, which was carefully hydrolyzed using methanol to remove the TMS group and to yield the methyl ketone 3.7 in $84 \%$ yield. This $\alpha, \beta$ unsaturated ketone was converted to the TMS-silyl enol ether in order to prepare the C-D ring (3.7 $\boldsymbol{3} \mathbf{3 . 8}$ ) for the $\mathrm{A}+\mathrm{C}-\mathrm{D}$ ring coupling step. Earlier efforts were made to convert 3.6 to methoxy diene in one step by direct methylenation using the Tebbe and Petasis reagents. Unfortunately, decomposition of the reactants was observed instead.

Alternatively, the ketone was protected first $(\mathbf{3 . 4} \rightarrow \mathbf{3 . 9}$, Scheme 3.4$)$ and then tertiary alcohol was masked by the comparatively smaller methyl group (3.9 $\boldsymbol{\rightarrow 3 . 1 0}$ ). TES-silyl enol ether diene (3.11) was then readily prepared.


Scheme 3.3. Synthesis of the bis-TES C-D ring




Scheme 3.4. Synthesis of the ketal-methoxy C-D ring
As discussed above, a cis-fused C-D ring with a hydroxy group at $\mathrm{C}_{14}$ was desired. However, since most steroids were a trans-fused C-D ring and a hydrogen at $\mathrm{C}_{14}$, we also considered the alternative routes to produce those types of products directly. This raised the question: Is the cis-fused bicycle the thermodynamic or kinetic product? Hydrindanes
3.10 and 3.13-3.15 were optimized using B3LYP/6-31G*(Figure 3.8). Not surprisingly, the $\alpha, \beta$-unsaturated ester were found to be twisted out-of-plane ( $\sim 15^{\circ}$ off), and the cishydrindanes were favored by $4.3 \mathrm{kcal} / \mathrm{mol}$. Hence, the formation of the cis-hydrindane seemed to be both thermodynamically and kinetically favored. The synthesis of transhydrindanes like 3.15 have already been extensively studied using reduction, addition, and cyclization reactions in the context of steroid synthesis. ${ }^{15}$ Yet, previous evidence suggests that Diels-Alder reactions with the $\mathbf{3 . 1 5}$ derived diene will probably yield the
undesired endo product. ${ }^{16}$ As for the synthesis of $\mathbf{3 . 1 3}$ and alike, there are a few relevant cases. For example, Rajagopalan et al. successfully made cis-hydrindane with a $\mathrm{C}_{13}-\mathrm{H}$ instead of $\mathrm{C}_{13}$ - Me through Oxy-Cope rearrangement followed by a transannular ene reaction. ${ }^{17}$ As will be shown throughout this study, the synthesis using $\mathbf{3 . 1 0}$ is the most efficient pathway to access the steroid core.



Figure 3.8. Computed energy differences in cis and trans-fused bicycles.

### 3.3.3. The A ring

As mentioned earlier, more than $90 \%$ of withanolides are 1 -oxosteroids, and SAR studies suggest that the $\alpha, \beta$-unsaturated ketone in the A ring (2-ene-1-one) is very important (Section 3.1.2). Some of the withanolides contain 1,4-dione-2-ene or 2-ene-4-ol-1-one in the A ring, for example, withalongolide B (Scheme 3.2). Hence, quinones, with functionalities at the desired positions (1,4-dioxo-2-ene) and as highly reactive dieneophiles, are good candidates of A rings.

As dienenophiles in Diels-Alder reaction, the reactivity and regioselectivity of quinones is highly dependent on the substituents. Inspired by Houk's work in the frontier molecular orbital (FMO) coefficient calculations, ${ }^{18}$ selected quinones were calculated using B3LYP/6-31G* as shown in Figure 3.9. Lowest unoccupied molecular orbital (LUMO) coefficients are labeled for each olefinic carbons in blue and red. The arrows point to the most electrophilic site as an indication of predicted regioselectivity in Diels-

Alder reactions. Additionally, the calculated relative values of frontier LUMO energy are shown in green by setting the number of $\mathbf{3 . 1 6}$ to $0 \mathrm{kcal} \mathrm{mol}^{-1}$. This demonstrates that higher frontier LUMO energy led to decreasing reactivity as dienenophiles (e.g. reactivity: 3.16 $>$ 3.17 $>$ 3.18). The model studies on $\mathbf{3 . 1 7}$ and $\mathbf{3 . 1 8}$ presented in Scheme 3.5 constitute further experimental evidence of the reliability of these predictions. The predicted regioisomers were obtained and the difference in the reaction times indicate the difference in reactivities. As discussed in Section 3.3.1, the functionality at C-19 was identified highly desirable in early-stage synthesis. With all the factors evaluated, $\mathbf{3 . 1 7}$ was considered the ideal A ring candidate.


Figure 3.9. Calculated FMO coefficients of quinones


Scheme 3.5. Diels-Alder reaction of quinones with simple silyl enol ether diene

### 3.3.4. Synthesis of the withanolides core and its reactivity

The success of this pivotal Diels-Alder reaction to construct the steroid core relies on the regioselectivity and stereoselectivity. In previous studies, unsubstituted quinone and benzoquinones were coupled with dienes dervied from Vitamin $D_{2} / D_{3}$ to make steroids by De Riccardis and Sodano. ${ }^{16}$ For all cases, the endo stereoisomer was obtained exclusively. Similar results were found in the studies on reactions of activated quinones with simple TMS-silyl ether diene. ${ }^{19}$ It should be noted that in Corey's recent nicandrenones synthesis, the exo product was obtained exclusively. ${ }^{8 a}$ However, Corey found that in model studies with monocyclic dienes, the Lewis acid was able to tune the endo/exo ratio, and the endo isomer was always formed predominantly. ${ }^{8 \mathrm{~b}}$ They reasoned that the aromaticity of the D ring (benzene) in the real system distorted the diene and increased steric repulsion in the endo approach.

In our key step to construct the steroid core, diene $\mathbf{3 . 8}$ was coupled with $\mathbf{3 . 1 7}$ to yield 3.20 as the single stereoisomer in excellent yield (Scheme3.6). The exo isomer was obtained; however, the quinone approached from the bottom face of the C-D ring (3.19)
with the formation of the undesired steroid core. The absolute structure was confirmed by extensive NMR analysis of $\mathbf{3 . 2 0}$ and X-ray diffraction analysis of its crystalline derivative $\mathbf{3 . 2 1}$ (Scheme 3.7). The formation of this stereoisomer can be ascribed to the steric hindrance from the adjacent methyl and especially OTES group, which blocks the top face of the C-D ring. Similar situations were also found by Deslongchamps. ${ }^{20} \mathbf{3 . 2 0}$ contains the desired stereochemistry in the A-B-C junction and is a suitable intermediate for the synthesis of physalins and alike (with the opening of C-D ring).


Scheme 3.6. Diels-Alder reaction of $\mathbf{3 . 1 7}$ and $\mathbf{3 . 8}$
The reactivity towards reduction, protection and acidification was then examined (Scheme 3.7). Attempts to reduce the bis-ketone and ester in one pot failed with several reagents. The double bond in the A ring is highly labile towards reduction. By careful control of the conditions, mono-reduction product $\mathbf{3 . 2 1}$ and diol derivative $\mathbf{3 . 2 2}$ were formed in moderate yields. $\mathbf{3 . 2 1}$ was then protected as the TBS ether and then subjected to acid to form the $\mathrm{C} 8-\mathrm{C} 14$ elimination product $\mathbf{3 . 2 3}$. Under milder conditions, the C-4 alcohol was protected without the effect of the joint ether bond C1-C14 (3.22 $\boldsymbol{3} \mathbf{3 . 2 5}$ ). Harsh conditions led to the opening of this ring and the production of the $\alpha, \beta$-unsaturated ketone. Sometimes thi was accompanied by the replacement of TES with TBS at C17 $(3.22 \rightarrow 3.24,3.22 \rightarrow 3.26 \rightarrow 3.24)$.


Scheme 3.7. Derivatization of the steroid core $\mathbf{3 . 2 0}$
As for the diene 3.12, stereoselectivity in the Diels-Alder reactions appears to be more complicated. More than one stereoisomers was produced in all cases (Table 3.1). The major isomer was the desired product. The ratio of the isomers is mainly dependent on the stoichiometry of quinones added and the concentration of the reaction solution. When the reaction is highly diluted, extended reaction time was required for the reaction to go to completion, and only two stereoisomers were observed by crude NMR (3.22 and 3.23). At higher concentration (entry 2-4), $\mathbf{3 . 2 1}$ was also present in the reaction solution. However, after treatment with $1 \% \mathrm{NEt}_{3}$ during purification, 3.21 was completely epimerized to $\mathbf{3 . 2 3}$, without which, $\mathbf{3 . 2 1}$ and $\mathbf{3 . 2 2}$ constitute an inseparable mixture. Due to the low solubility of quinone in diethyl ether, at higher concentration, quinone was not completely dissolved. Additionally quinone improved the stereoselectivity (entry 3).

Large excess of quinone accelerated the reaction without improving the selectivity. Even though additional quinone can be completely destroyed by $1 \% \mathrm{NEt}_{3}$ after the completion of the reaction, the quinone side product, generated during the reaction, has very similar mobility to the $\mathbf{3 . 2 3}$ and makes the separation difficult. Hence, the parameters in entry 3 were used for this reaction.

Table 3.1. Diels-Alder reaction of $\mathbf{3 . 1 7}$ and $\mathbf{3 . 1 2}$


| entry | equiv. (3.17) | conc. (in $\left.\mathrm{Et}_{2} \mathrm{O}\right)$ | temp. | $\mathbf{3 . 2 3 : 3 . 2 2}$ | total yield |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | 1.1 | 0.05 M | $0^{\circ} \mathrm{C}$ to rt | $2.5: 1$ | $83 \%$ |
| 2 | 1.1 | 0.1 M | $0^{\circ} \mathrm{C}$ to rt | $2.2: 1$ | $81 \%$ |
| $\mathbf{3}$ | $\mathbf{1 . 5}$ | $\mathbf{0 . 1 ~ M}$ | $\mathbf{0}^{\circ} \mathbf{C}$ to $\mathbf{~ r t}$ | $\mathbf{4 . 2 : 1}$ | $\mathbf{8 5 \%}$ |
| 4 | 5.0 | 0.1 M | rt | $4.0: 1$ | nd |

3.23 was subjected to elimination at C8-C14. Deprotection of the silyl enol ether and oxidative elimination to generate $\mathrm{C} 8-\mathrm{C} 9$ double bond were not successful. To our delight, treated with acid installed the C8-C14 double bond gave excellent yield (3.23 $\boldsymbol{\rightarrow} \mathbf{3 . 2 4}$ ). The C8-C14 double bond functionality is present in withanolides. ${ }^{1}$ Moreover, in principle,
3.24 can be reduced by dissolving metal (e.g. $\mathrm{Li} / \mathrm{NH}_{3}$ ) through a cis-addition ${ }^{21}$ to give trans-fused C-D ring as an important derivative.


Scheme 3.8. Transformation of the steroid core $\mathbf{3 . 2 3}$
For the Diels-Alder reaction, we also explored the possibility of making an exo adduct (e.g. 3.28 and 3.31, Scheme 3.9). One way to achieve this is having the quinone ring tethered at the C-14 tertiary alcohol to force the desired addition (3.25 $\boldsymbol{3} . \mathbf{2 6}$ ). The additional lactone formed will not be stable and shall fragment in situ to render the $\alpha, \beta$ unsaturated ketone. The ketone precursor of $\mathbf{3 . 2 9}$ was easily accessible through selective protection. It is known that the acid derivative of $\mathbf{3 . 1 7}$ is not stable and cannot be prepared for synthetic applications. For the possibility of hydrogen-bond aided DielsAlder reaction, the attempted preparation of the diene alcohol (3.29) resulted in a mixture of products.


3.17




Scheme 3.9. Attempts for the exo selectivity
The side chain seems important for bioactivity (Figure 3.3). In principle, the side chain can be installed at the C-17 ketone position within short steps directly (Scheme 3.10). ${ }^{22}$


Scheme 3.10. Proposed side chain installation

### 3.4. Conclusion

Here we report a concise route for the construction of withanolide steroid cores $\mathbf{3 . 2 0}$ and $\mathbf{3 . 2 3}$ via an $\mathrm{A}+\mathrm{C}-\mathrm{D}$ ring strategy. This synthesis was achieved in only 8 steps. Within a short sequence, a diverse range of functionalities was installed for further manipulations. Stereoselectivity of the key Diels-Alder reaction step was studied by varying reaction conditions and substrates. The reactivity of the adducts were also evaluated.

### 3.5. Reference

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## Chapter IV

# Distortional Asymmetry: A New Mechanistic Insight in Stereoinduction 

### 4.1. Introduction

For over 30 years stereoselective reactions in sterically unbiased compounds, such as in the compound types shown below (Figure 4.1), have been difficult to understand. ${ }^{1}$ We have advanced a distortional asymmetry model $^{2}$ in which we emphasize that (a) to reach the transition state the ground state becomes distorted; (b) early transition states are sensitive to the ground state energies including the substrate distortion energies; and (c) weak through-space interactions in the substrate can render the distortions asymmetric. Thus, we should expect even sterically unbiased systems to exhibit face selectivity for early transition state reactions in instances where the two faces of the reacting system participate unequally in through-space interactions.


Figure 4.1. Observed face selectivities in contrained olefins and ketones.

### 4.2. Norbornenes and Other Constrained Olefins

Norbornene contains the archetypal strained double bond that undergoes rapid and face-selective reactions (e.g. 4.1 v.s. 4.2 or 4.3, Figure 4.2). ${ }^{1,3-5}$ Huisgen claimed that an
undentified factor accounted for its exceptional reactivity and face selectivity. ${ }^{4}$ Different research groups attributed this factor to different causes. ${ }^{5}$ Here the concepts developed to understand this system are extrapolated to form foundational principles of $\pi$-bond stereoselectivity. We maintain that distortional asymmetry contributions have been overlooked in interpreting $\pi$-bond stereoselectivity and govern face selectivity in many systems especially conformationally constrained systems.


Figure 4.2. $m$ CPBA oxidation of cyclic olefins
Electronic structure calculations, using density functional theory (DFT), were carried out with the Gaussian 09 suite $^{6}$ of programs. Compounds 4.1-4.10 were all optimized using the $\mathrm{B}_{3} \mathrm{LYP}^{7} / 6-31+\mathrm{g}(\mathrm{d})^{8}$ then with single point energies for distortional potentials calculated using B3LYP/6-31g(2d,2p) (Figure 4.3-4.5). For Figure 4.6-4.8, compounds 4.1, 4.5, 4.7, 4.11 and related ground state (GS) and transition state (TS) structures were optimized using the B3LYP/6-31+g(d,p) in gas phase and/or solvents with the polarizable conductor self-consistent reaction field model (CPCM). ${ }^{9}$ Natural bond orbital (NBO) analysis was conducted using NBO $5^{10}$ incorporated in Gaussian 09 suite, and the results are shown in Figure 4.5 and 4.6.

### 4.2.1. Symmetric Constrained Olefins

The ground state distortional potentials in symmetric olefins (4.4-4.7) are shown in Figure 4.3. Symmetric out-of-plane bending in symmetric compounds gives symmetric
distortional potentials with lowest energy points (inflection points) at $0^{\circ}(\theta$, distortional angle). The distortional differentials between $\theta=0$ and $15^{\circ}$ are $3.5,3.1,2.7,2.4 \mathrm{kcal}$ $\mathrm{mol}^{-1}$ for olefins $4.4,4.5,4.6,4.7$ respectively. Interestingly, based on strain energy difference ( $\Delta$ strain, differences upon hydrogenation), ${ }^{4}$ the more strained olefin (larger $\Delta$ strain) requires less energy for distortion (c.f. 4.5: $-0.51 \mathrm{kcal} \mathrm{mol}^{-1}$ v.s 4.7: -9.96 kcal $\mathrm{mol}^{-1}$ ). Ring strain is an important factor in distortional potentials.



Figure 4.3. Ground state distortional plots of symmetric olefins. The distortional differentials at $\theta=15^{\circ}$ for 4.4 (grey), 4.5 (purple), 4.6 (green) and 4.7 (red) are highlighted.

### 4.2.2. Asymmetric Constrained Olefins

Figure 4.4 shows the ground state distortional potentials in asymmetric olefins (4.1, 4.8, 4.9, 4.10). All the olefins here are pyrimidalized to a certain degree. ${ }^{11}$ Asymmetric distortional potentials were observed in these asymmetric olefins with the lowest energy points at $0.2^{\circ},-2.3^{\circ},-5.0^{\circ}$, and $-7.0^{\circ}(\theta$, distortional angle) for olefins $4.9,4.8,4.10,4.1$ respectively. Asymmetry in the olefin requires the asymmetry in distortional potential. However, this is not the only factor. Norbornene (4.1) can be considered as a
combination of 4.8 and 4.9 , and yet it has a more asymmetric distortional potential than either 4.8 or 4.9 (the distortional differentials at $\pm 15^{\circ}$ for 4.1, 4.8 and 4.9: 5.7, 2.6, -0.5 $\mathrm{kcal} \mathrm{mol}{ }^{-1}$ ). Norbornene (4.1) is more strained than $\mathbf{4 . 8}$ or 4.9. Ring strain here amplifies the distortional asymmetry.



Figure 4.4. Ground state distortional plots of asymmetric olefins. The distortional differentials at $\theta=15^{\circ}$ for $\mathbf{4 . 1}$ (orange), 4.8 (red), 4.9 (green), and 4.10 (purple) are highlighted.

### 4.2.3. NBO Analysis

As summarized in Figure 4.5, NBO analysis was used to study the relationship between orbital mixing and distortional asymmetry for model compound 3,4difluorocyclobutene (4.10). Orbital interactions were turned off individually and the new resultant distortional potential, given the distortional differential in $\mathrm{kcal} \mathrm{mol}^{-1}$ at $\pm 15^{\circ}$, was compared with the parent distortional potential (black, unperturbed parent line). When $\sigma_{\mathrm{C}-\mathrm{F}}$ to $\pi{ }^{*}{ }_{\mathrm{C}=\mathrm{C}}$ orbital interaction was turned off, the distortional differential (5.3 kcal mol-1 at $\pm 15^{\circ}$, green) was slightly increased compared with the unperturbed parent distortional potential. A similar change in distortional potential ( $5.3 \mathrm{kcal} \mathrm{mol}-1$ at $\pm 15^{\circ}$,
red) was noted when $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{H}}$ orbital interaction was turned off. In contrast, turning off orbital interactions $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ led to a significant decrease in distortional potentialor, and $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}$ C-F led to an even greater change in distortional potentials (2.8 and $0.3 \mathrm{kcal} \mathrm{mol}-1$ at $\pm 15^{\circ}$ respectively, orange and purple). Therefore, $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*} \mathrm{C}=\mathrm{C}$ and $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{F}}$ are the most important contributors to the asymmetric distortional potentials. Noticeably, $\sigma_{\mathrm{C}-\mathrm{F}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}\left(\right.$ green ) and $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{H}}$ (red) interactions favor distortion towards C-F face ( $+\theta$ side), whereas $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ (orange) and $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{F}}$ (purple) interactions favor the opposite side distortion (C-H face, $-\theta$ side). The effect is pair-wise and depends on symmetry, overlap and energy. The symmetry and overlap appear subtle in this compound. However, the energies are very different for each donor and each acceptor. The lowering $\sigma^{*}{ }_{C-F}$ and the high energy $\pi_{\mathrm{C}=\mathrm{C}}$ are well matched in energy (as well as symmetry and proximity). Similarly the $\sigma_{\mathrm{C}-\mathrm{H}}$, which is significantly higher in energy than the $\sigma_{\mathrm{C}-\mathrm{F}}$, and the lowering $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ are also well matched. Not surprisingly, the $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ interatction is weaker than the $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{F}}$ interaction. These strong donor-acceptor orbital interactions dominate the distortional energetics, influence transtion-state energies for early (ground state-like) transtion structures, and thus bear on face-selective reactions in constrained systems. Distortion is favored towards the side with the strongest donor interaction.


Figure 4.5. NBO analysis of 3,4-difluorocyclobutene (4.10). The original distortional plot is in grey. In all other four plots, one of the donor-acceptor orbital interactions was turned off. The distortional differentials at $\theta=15^{\circ}$ are highlighted for $\sigma_{\mathrm{C}-\mathrm{F}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ off (green), $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{H}}$ off (red), $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ off (orange), and $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{F}}$ off (purple).

Orbital interaction theory as discussed above also applies to distortional asymmetry in norbornene (4.1) and other bicyclic olefins (4.5 and 4.7) as shown in Figure 4.6. In an unperturbed state, the $\pi$ systems in 4.5 and 4.7 were calculated to be planar of course, and vinyl C-H bonds in norbornene (4.1) were distorted to a $6.9^{\circ}$ toward the side of the cyclohexyl moiety. When the highlighted $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ and $\sigma_{\mathrm{C}-\mathrm{C}}$ orbital interactions were turned off in each molecule, only minor changes occured for $\mathbf{4 . 5} \rightarrow \mathbf{V}$ (a, Figure 4.6). However, a significant $8.9^{\circ}$ change in distortional energies occured for $\mathbf{4 . 7} \rightarrow$ VII (b). Although differencces in orbital overlap may be relevant, ring strain may account for the difference between 4.5 and 4.7. In the case of norbornene ( c and d), turning off either interaction made significant difference $\left(6.2^{\circ}\right.$ and $9.3^{\circ}$ difference for c and d). Again we see that the orbital interaction of the ethano-bridge (d) is different from the methanol-bridge, and more important. In other words, the orbital mixing identified in $d$ is more efficient, and this asymmetric orbital mixing is reflected in the ground state distortional potential
(orange, Figure 4.4). Taken together, the cyclobutene, norbornene and realted systems (Figure 4.3-4.6) show that distortion is favored towards the side of the strongest donor, and distortional differential is largely amplified by ring strain because strain increased the strength of the key interaction.
a)

b)



c)



$-13.1^{\circ}$


Figure 4.6. NBO analysis of bicyclic olefins. In each case, the $\pi^{*}{ }_{C=C}$ and $\sigma_{\mathrm{C}-\mathrm{C}}$ (red) interactions were turned off and the corresponding distortional angle ( $\mathrm{C}-\mathrm{CH}=\mathrm{C}$, red, second row) was calculated to be compared with the original one (black, first row).

### 4.2.4. Norbornenes Transition State Calculations

The distortional asymmetry properties of norbornene in transition states are similar to what has been observed in ground state as suggested in Figure 4.7. We carefully conducted transition state calculation for $m$ CPBA oxidation of norbornene. ${ }^{13}$ The transition states were early according to the small reaction barriers (12.7 and 9.4 kcal $\mathrm{mol}^{-1}$ ), the degree of bond formation (bond length of forming C-O bonds: 2.257 and $2.288 \AA$ ), and bond breaking (bond length of breaking O-O bonds: 1.781 and $1.748 \AA$ ). Reactant ground-state-based approximation $\left(2 \mathrm{kcal} \mathrm{mol}^{-1}\right.$, distortional potential at $-12.7^{\circ}$ and $+6.4^{\circ}$, orange line, Figure 4.4) suggests that distortional contributions constitute the bulk of the transition state differential ( $\sim 3 \mathrm{kcal}$ mol-1, Figure 4.7). The vinyl C-H bonds are distorted more for exo attack than for endo attack, consistant with ground state distortional potentials. The distortional angle $\left(+6.4^{\circ}\right)$ in endo attack, when compared with
the ground state distortional angle $\left(-6.9^{\circ}\right)$, is more different than in exo attack transition state $\left(-12.7^{\circ}\right)$ indicating a higher energy barrier in distorting the $\mathrm{C}-\mathrm{H}$ bonds in endo transition state. Also, the bond breaking and forming for endo attack is less starting material-like. In our previous studies on similar systems, by forcing the caculated transition strucures into a planar state $\left(\theta_{\text {syn }}=\theta_{\text {syn }}=0\right)$, the energy differences between the transition structures drop significantly. ${ }^{2}$ Thus, we see that ground state distortional contribution to these early-transition-state reactions approximates well the transition state energies.


Figure 4.7. Transition state structures of $m \mathrm{CPBA}$ oxidation of norbornene in $\mathrm{MeCN} . \mathrm{R}=$ meta-chlorophenyl. $\Delta \mathrm{H}^{\neq}{ }_{\mathrm{MeCN}(\text { endo })}=12.7 \mathrm{kcal} \mathrm{mol}^{-1} ; \Delta \mathrm{H}_{\mathrm{MeCN}(\text { exo })}^{\neq}=9.4 \mathrm{kcal} \mathrm{mol}^{-1}$. Distortional angles of $\mathrm{C}=\mathrm{C}-\mathrm{C}-\mathrm{H}$ bonds, bond lengths of forming $\mathrm{C}-\mathrm{O}$ and breaking $\mathrm{O}-\mathrm{O}$ bonds are labeled for endo (blue) and exo (red) transition states.

### 4.2.5. Distortional Asymmetry and Reaction Stages

Transition state structures of $\mathbf{4 . 1 1}$ under different reaction conditions were calculated ${ }^{13-15}$ and summed up in Figure 4.8a. By comparing the transition state energies $(\Delta \mathrm{H})$ we see that these are early transition state reactions. However, carbene addition, is earlier than $m$ CPBA oxidation, which is earlier than osmylation. The calculated transition state energy differentials $(\Delta \Delta \mathrm{H})$ correlate to the experimental data (expt. syn:anti) ${ }^{16}$ very well. Remarkably, the calculated ground state energy differentials for distortion $\left(\Delta \Delta E_{d i s}\right)$ are
almost identical to the transition state energy differentials $(\Delta \Delta \mathrm{H})$. This suggests again that ground state distortianal asymmetry contributes to transitioin state energy differences.

Distortional considerations provide altogether new insight: the degree of selctivity for one reagent to the next is readily rationalized by this theory. As illustrated in 4.8 b , for an asymmetrically distorted substrate like $4.11, \mathrm{R} \rightarrow \mathrm{P}^{\prime} / \mathrm{P}^{\prime \prime}$ corresponds to a graduated distortion reaction coordinate For a given reaction, R is the same and the anti product $\mathrm{P}^{\prime}$ and the syn product $\mathrm{P}^{\prime \prime}$ are isoenergetic. $\Delta \Delta E a$ is the activation energy difference for the anti and syn reaction pathways ( $\Delta E a-a n t i<\Delta E a-s y n$ for 4.11). A very early transition state induces a small distortion and a very small distortional differential; the reaction barrier is very low, and the face selectivity is very low. A higher distortional difference increases both the barrier height and the differential between the syn and anti attack $\left(\Delta \Delta E a_{1<} \Delta \Delta E a_{2<} \Delta \Delta E a_{3}\right)$. These predictions are reflected in experimental data (c.f. 12:88 and 44:56 for osmylation and carbene additon of 4.11). Differences in reaction stage lead to differences in reaction barriers due to ground state asymmetric distortion contributed to these starting material-like reactions.
a) Transiton State Calculations

|  |  |  |  |
| :---: | :---: | :---: | :---: |
|  | :CCl ${ }_{2}$ | $m C P B A$ | $\mathrm{OsO}_{4}$ |
| $\theta_{\text {syn }}$ | 2.4 | 3.1 | 32.1 |
| $\theta_{\text {anti }}$ | 4.6 | 7.1 | 31.4 |
| $\Delta H_{\text {syn }}$ | 1.4 | 10.6 | 13.7 |
| $\Delta H_{\text {anti }}$ | 1.0 | 9.6 | 12.4 |
| $\Delta \Delta \mathrm{H}$ | 0.4 | 1.0 | 1.3 |
| $\Delta \Delta E_{\text {dis }}$ | 0.5 | 1.1 | 1.3 |
| $\begin{aligned} & \hline \text { syn:anti } \\ & \text { (expt.) } \\ & \hline \end{aligned}$ | 44:56 | NA | 12:88 |

b) $\Delta \Delta E_{\mathrm{a} 1}<\Delta \Delta E_{\mathrm{a} 2}<\Delta \Delta E_{\mathrm{a} 3}$


Figure 4.8. a) Transition state calculations of 8-methylenetricyclo[3.2.1.0 $\left.{ }^{2,4}\right]$ octane (4.11) under different reaction conditions; b) Difference in reaction stage leads to difference in reaction barrier.

### 4.2.6. Additional Comments

Computed out-of-plane distortional potentials, transition structures, and NBO analysis provide a simple quantitative explanation for the reactivity of strained olefins. Ring strain enhances reactivity. ${ }^{4,17}$ As suggested by Huisgen, ${ }^{4}$ there is an additional X factor. For example, the reaction constants of one set of cycloaddition reactions are $5.9 \ll 1010<6340$ (units: $\mathrm{X} 10^{7}$ ) for 4.5, 4.7 and 4.1, but the ring strain energy is higher in 4.7 than in 4.1. So this factor is nothing strain. Besides, for starting material-like reactions, little ring strain is released in the transition state. This X factor can be attributed to the ground state distortional asymmetry. As discussed in 4.2.3 and 4.2.4, norbornen (4.1) is distorted $6.9^{\circ}$ in the ground state, and requires distortions to reach to the exo transition state. In comparison, 4.5 and 4.7 are symmetric, and the ring strain facilitates distortion - there is no difference in face selectivities but the ease of distortion reduces the reaction barrier. This reduction is factor X . Taken together, distortional considerations identify sizable contributions to transition barriers as well as the differentials that lead to stereoselective transformations of strained, asymmetrically substituted double bonds.

### 4.3. 5-X-2-Adamantanones and Other Constrained Ketones

For over thirty years, face selectivities in 5-X-2-adamantanones (4.12, Figure 4.9) and other sterically unbiased ketones (e.g. 4.13-15) have been perplexing. Syn attack is observed when a remote substituent, X, was an electron-withdrawing group (EWR). ${ }^{1}$ In previous work, several theories were proposed to explain the experimental results, such
as transition-state antiperiplanar hyperconjugation model, ${ }^{18}$ electrostatic effects, ${ }^{18 a}$ dipoledipole repulsion,,${ }^{19}$ and inequivalent ground state HOMO-LUMO distortions. ${ }^{20}$ However, they either overlooked the origin of remote substituents or fail to be non-paradoxical.

Di Maio et al. conducted extensive kinetic experiments of methylation and reduction reactions on conformationally rigid ketones, including 4.12. ${ }^{21}$ They concluded that only kinetic data can allow a complete understanding of the stereochemical bias, and according to their kinetic data, the two faces of the molecule behave differently.

Above, we discribed a distortional asymmetry model for sterically unbiased strained olefins in which weak through-space interactions in the substrate may render the ground state distortions asymmetric. ${ }^{2}$ This asymmetry contributes largely to transition state energy differential for early transition state reactions. Here we extend these ideas to conformationally constrained ketone systems.

For all ketones studied, the distortional potentials (Figure 4.10, 4.11 and Table 4.2), for the carbonyl group (with or without Lewis acid chelation) was manually distorted from planarity to $0^{\circ}, 5^{\circ}, 15^{\circ}$ or more and optimized using B3LYP/6-31+G* with the distortion angle $(\theta)$ fixed in order to calculate the distortional energy differential. All the potential curves were formed to be parabolic $\left(\Delta \mathrm{E}=\mathrm{a} \theta^{2}+\mathrm{b} \theta+\mathrm{c}\right)$ with an excel goodness of fit $\mathrm{R}^{2}>0.99$.


Figure 4.9. 5-X-2-Adamantanone and other strained ketones

### 4.3.1. Lewis acid effect in 5-F-2-Adamantanone

Figure 4.10. shows the effect of Lewis acid on the distortion behavior of $\mathbf{4 . 1 2}(\mathrm{X}=$ F). Distortional potentials for 4.12 without Lewis acid (LA = none, grey), with the carbonyl protonated $(\mathrm{LA}=\mathrm{H}$, red), and with hydrogen bonding to the proton of pyridinium (LA $=\mathrm{Py}-\mathrm{H}$, purple) were plotted separately. The distortion differentials at $\pm 35^{\circ}(\theta)$ were labeled. Several tends are notable, regardless of Lewis acid effects. All the plots (of $\mathbf{4 . 1 2}$ with electron-withdrawing fluorine substituent) were asymmetric and the distortioinal energy increases as the distortion angle increases. This occurs more readily away from the fluorine $(\theta<0)$. Secondly, coordination of the carbonyl group to a Lewis acid significantly lowers the distortional potentials (compare $\mathrm{LA}=$ none to H or $\mathrm{Py}-\mathrm{H}$ ). Importantly, the presence of a strong Lewis acid (protonation) increases the distortion differential more than weaker Lewis acids (cf 2.1 and $0.8 \mathrm{kcal} \mathrm{mol}^{-1}$ at $\pm 35^{\circ}$ ). In
summary, when $\mathrm{X}=\mathrm{F}$, distortions were calculated to be asymmetric and to favor the face distortions away from the fluorine group. A Lewis acid-coordinated carbonyl was found to be more easily distorted, the stronger the Lewis acid the lower the distortion energy.


Figure 4.10. Lewis acid effects on compound 4.12 distortional potential

### 4.3.2. Electronic Effect in 5-X-2-Adamantanones

As shown in Figure 4.11, ground state distortional plots of substrates with different substituents $\left(\mathrm{X}=\mathrm{NMe}_{3}, \mathrm{~F}, \mathrm{NH}_{2}\right.$ and Me$)$ were calculated for protonated 4.12. Distortional differentials for $\theta$ at $\pm 15^{\circ}$ are labeled (colors). Asymmetric distortional potential plots were observed in all the cases with strong to weak tendency in favoring distortion away from X group. A decrease in distortional differential at $\theta= \pm 15^{\circ}$ was noted when a less electron-withdrawing group was used (2.5, 1.1, 0.6 and $0.1 \mathrm{kcal} \mathrm{mol}^{-1}$ ). Therefore, the remote substituent with higher electronegativity showed a larger distortional asymmetry as illustrated in Figure 4.11.


Figure 4.11. Electronic effects on compound 4.12 distortional potential

### 4.3.3. Transition State Calculatioin of 5-X-2-Adamantanones

Transition state structures in methyl addition of $\mathbf{4 . 1 2}$ in ether (B3LYP/6-31+G**) and ground state distortional potentials with MeLi dimer as Lewis acid in ether (Figure 4.12) were calculated for several substituted ketones as summarized in Table 4.1. ${ }^{22}$ The transition state energy barrier differential of syn and anti attack ( $\left.\delta \Delta \mathrm{H}^{\ddagger}{ }_{\text {(anti-syn) }}\right)$ was compared to the experimental data (\% syn) and ground state distortional differential $\left(\delta \Delta \mathrm{E}_{\text {(anti-syn) }}^{\mathrm{GS}}\right)$ at the same syn and anti attack angles as in transition states. As suggested in experimental data, \% syn decreased as X becomes less electron-withdrawing. When X $=$ Me (entry 4), only a slight preference was shown for syn attack. A slight preference for anti attack product was observed when $\mathrm{X}=\mathrm{TMS}$ (entry 5). The calculated energy differential data for the transition states $\left(\delta \Delta \mathrm{H}^{\ddagger}{ }_{(\text {anti-syn) }}\right)$ fit the experimental data well both in terms of the overall trend and in terms of quantitative consistency. In the cases where syn attack is preferred (entry 1-4), the distortion angle in the syn transition states was larger than that in anti transition states. Additionally, a more developed C-C bond (d $\mathrm{d}_{\text {(CH3- }}$ $\mathrm{C}=0$ ) ) was observed. Remarkably, even though all the energy numbers are small because
of selectivities of reactions are moderate, the ground state distortional differentials approximate the transition state energy barriers well (compare $\delta \Delta \mathrm{E}^{\mathrm{GS}}{ }_{\text {(anti-syn) }}$ and $\delta \Delta \mathrm{H}^{\ddagger}{ }_{\text {(anti- }}$ syn).


Figure 4.12. MeLi dimer coordinated 4.12 distortional potentials in $\mathrm{Et}_{2} \mathrm{O}$

Table 4.1. Transition state calculation and ground state distortional differential data for

### 4.12



| entry | X | $\theta$ |  | $\mathrm{d}_{(\mathrm{CH} 3-\mathrm{C}=\mathrm{O})}, \AA$ |  | $\begin{gathered} \delta \Delta \mathrm{H}^{\ddagger} \\ \left(\text { (anti-syn) }{ }^{a}\right. \end{gathered}$ | $\begin{gathered} \delta \Delta \mathrm{E}^{\mathrm{GS}} \\ (\text { (anti-syn) } \end{gathered}$ | $\begin{aligned} & \% \text { syn } \\ & \text { (expt.) } \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | syn | anti | syn | anti |  |  |  |
| 1 | $\mathrm{CF}_{3}$ | 33.6 | 33.2 | 2.625 | 2.634 | +0.7 | +1.0 | 72 |
| 2 | F | 33.6 | 33.1 | 2.628 | 2.642 | +0.7 | +0.8 | 66 |
| 3 | $\mathrm{NMe}_{2}$ | 34.0 | 33.3 | 2.601 | 2.634 | +0.6 | +0.2 | 63 |
| 4 | $\mathrm{CH}_{3}$ | 34.3 | 34.3 | 2.590 | 2.597 | +0.1 | +0.05 | 54 |
| 5 | TMS | 34.6 | 35.2 | 2.576 | 2.566 | -0.05 | +0.1 | 49 |

${ }^{\mathrm{a}}$ Values given in: kcal $\mathrm{mol}^{-1}$

### 4.3.4. Other Constrained Ketones

Our distortional asymmetry model also applies to other strained ketones such as 4.13, 4.14, and 4.15 (see Figure 4.13 and Table 4.2). Differentional distortion patterns were observed in all asymmetric substrates (for $X \neq H$ ). The lowest energy structure was pyramidalized to a certain degree $(\theta \neq 0)$ in each case. The ground state distortion differentials at $\pm \theta, \delta \Delta \mathrm{E}^{\mathrm{GS}}{ }_{ \pm \theta}=2 \mathrm{~b} \theta^{2}$. Hence, when $\mathrm{b}>0, \delta \Delta \mathrm{E}^{\mathrm{GS}}{ }_{ \pm \theta}>0$, then $\operatorname{syn}$ attack is preferred. The converse where relevant is also true. The more positive b should lead to a higher \% syn with more negative b corresponds to a higher \% anti. This statement is true when compared to experimental data with some exceptions where $\mathrm{X}=$ vinyl was compared to Et and $\mathrm{X}=$ COOMe was compared to CN . This happens because from Table 4.1 we know that in the transition states $\mid \theta_{\text {antit }} /$ does not equal $/ \theta_{\text {syn }} \mid$ mostly. In the general form $\delta \Delta \mathrm{E}_{(a n t i-s y n)}^{\mathrm{GS}}=\mathrm{a}\left(\theta_{\text {anti }}{ }^{2}-\theta_{\text {syn }}{ }^{2}\right)+\mathrm{b}\left(\theta_{\text {anti }}-\theta_{\text {syn }}\right)$, the value of $\delta \Delta \mathrm{E}_{(\text {anti-syn })}$ is dependent on $\mathrm{a}, \mathrm{b}$ and $\theta$. In the cases where the differences between different groups were not big (vinyl v.s. Et, COOMe v.s. CN ), predictions simply from b may not be very accurate. Also, the occasional shoulder appeared in distortional potentials may attribute to tortional effect. This situation is especially obvious in the calculations for compound $\mathbf{4 . 1 4}$ (Figure 4.13). Nevertheless, distortional asymmetry still provided a shortcut for semi-quantitative predictions in face selectivities of sterically unbiased rigid ketones.


Figure 4.13. Ground state distortional potentials for protonated 4.13, 4.14. and 4.15.

Table 4.2. Distortional equation parameters for 4.13, 4.14 and 4.15

| Ketone | X | $\Delta \mathrm{E}=\mathbf{a} \boldsymbol{\theta}^{2}+\mathrm{b} \theta+\mathbf{c}$ |  |  | \% syn ${ }^{\text {a }}$ (expt.) |
| :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | a | b | c |  |
| 4.13- $\mathrm{H}^{+}$ | COOMe | 0.0041 | 0.0187 | 0.015 | >90 |
|  | Vinyl | 0.0041 | -0.0555 | 0.2009 | 27 |
|  | Et | 0.0041 | -0.052 | 0.1855 | 17 |
|  | $-\mathrm{CH}_{2}$ - | 0.0063 | -0.1251 | 0.6469 | 5 |
| 4.14- $\mathrm{H}^{+}$ | COOMe | 0.0059 | 0.0319 | 0.0365 | 67 |
|  | Vinyl | 0.0052 | -0.0347 | 0.0749 | 54 |
|  | Et | 0.0056 | -0.0191 | 0.0173 | 34 |
| 4.15-H ${ }^{+}$ | CN | 0.0072 | 0.0045 | -0.0077 | $75^{\text {b }}$ |
|  | COOMe | 0.0058 | 0.0098 | -0.0028 | $66^{\text {b }}$ |
|  | Et | 0.0057 | -0.0415 | 0.073 | $47^{\text {b }}$ |
|  | Vinyl | 0.0071 | -0.039 | 0.0335 | $44^{\text {b }}$ |

${ }^{\text {a }}$ All the experimental data are derived from $\mathrm{CH}_{3} \mathrm{Li}$ addition reactions.
${ }^{\text {b }}$ Limited $\mathrm{CH}_{3} \mathrm{Li}$ addition experimental data available. $\mathrm{NaBH}_{4}$ reduction experimental data is used instead here.

### 4.3.5. Additonal Comments

In summary, we described an efficient semi-quantitative model: distortional asymmetry. Ground state distortional differentials approximate face selectivities in sterically unbiased rigid ketones. In this paper, we calculated ground state distortional potentials for 4.12-4.15 with different X groups using density functional methods and compared them with transition state calculations and experimental data. It was shown that increased electronegativity of a remote functional group increased the distortional profile of carbonyl groups away from X group in the ground state. For kinetically controlled reactions, ground state distortional asymmetry becomes a significant or even major contributor to face selectivity. Nucleophiles prefer syn attack. Ground state distortion calculations approximate the transition state anti-syn barriers and account for most of the barrier difference in the two transition structures. Additionally, the effects of Lewis acid on distortional asymmetry of $\mathbf{4 . 1 2}$ was examined. In part 1 of this chapter, we discussed the origin of distortional asymmetry in olefins. In the olefin case, increased ring strain
lowers the energy of $\pi^{*}$ and enables stronger through-space interactions with bonds of proper symmetry, proximity and energy $\left(\sigma \rightarrow \pi^{*}\right)$ and hence increased asymmetry effects in distortion (Section 4.2). ${ }^{2}$ Similar factors apply to, and thereby govern, the rigid ketone systems. Moreover, Lewis acid coordinating to the carbonyl lowers $\pi^{*}$ and leads to stronger orbital interactions. This is well illustrated in Figure 4.9. Addition of a Lewis acid to the carbonyl oxygen lowers the distortional potential of the carbonyl group. The stronger the Lewis acid, the greater the distortional asymmetry. The distortion potential of 4.12 with methyl lithium dimer resembled 4.12 alone with slightly lower distortional potentials and slightly higher distortional differentials $\left(0.9 \mathrm{kcal} \mathrm{mol}^{-1}\right.$ when $\left.\theta= \pm 35^{\circ}\right) .{ }^{24}$ In reactions where strong Lewis acids are used, early transition state reactions should proceed with higher face selectivity. ${ }^{1}$ This may seem slightly counterintuitive, because faster reactions are usually accompanied by lower selectivity. Other reaction parameters, like solvents and nucleophiles, should not bias the face selectivities much unless a change of mechanism was involved. The distortional behavior did vary slightly upon solvation but not significantly. To inverstigate electronic effects of the nucleophiles, Le Nobel et al. studied $p-\mathrm{XC}_{6} \mathrm{H}_{5} \mathrm{MgBr}$ addition reactions of fluoro- $\mathbf{4} .12$ by changing the X group on the benzene ring of the Grignard reagent. ${ }^{23}$ Although it seemed electron deficient nucleophile tended to yield more syn product, again only mild change in face selectivities was observed $\left(\mathrm{X}=\mathrm{CF}_{3}\right.$ to $\mathrm{MeO}, \%$ syn from 75 to 68$)$.

### 4.4. Conclusion

For decades, stereoselective reactions in sterically unbiased olefins and ketones, such as norbornene and 5-X-2-adamantanones, had been difficult to rationalize. A semiquantitative model which values ground state asymmetric distortion as a major
contributor was discussed. Both ground state distortional potential and transition state calculations using density functional methods showed good matches to experimental data. Lewis acid, remote electronic effects and reaction stages were calculated to contribute to the reactivity, degree of distortion, and hence face selectivity. Importantly, by using distortional asymmetry, mechanistically sound qualitative predictions can also be made without computational efforts.

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(24) As the TS is approached, the changes in bonding between reagent, Lewis acid, solvent and carbonyl all change. This complicates using distortional potential of ground states to understand - quantitatively - the face selective addition. Basically the ground state is not well-defined. Accordingly, ketone additions are not as straightforward as olefin reactions. It is all the more remarkable that the distortional model and distortional data approximate the outcomes so well.

## Chapter V

## Brosimum Allene: A Structural Revision ${ }^{1}$

### 5.1. Introduction

There are over 150 allene-containing natural products ${ }^{2}$ and Brosimum allene (A, Figure 5.1.) ${ }^{3}$ was reported as one of them. It was isolated from Brosimum acutifolium Huber by Takashima, J., Asano, S., Ohsaki, A. in 2000. ${ }^{5}$ But compounds like this are generally considered not stable to isolation. Related cumulenes, e.g. quinoethylenes, are known and highly reactive as intermediates in most cases. We were interested in the structure and reactivity of Brosimum allene; however, we wondered about the structure assignment.



Figure 5.1. Structure of brosimum allene and quinoethylene

### 5.2. Computational Modeling of Brosimum Allene

The original structure assignment of the Brosimum allene was based on HRMS and ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR data, including two-dimensional NMR. The ${ }^{13} \mathrm{C}$ NMR data shows that the signal at 139 ppm was assigned to the central allenic carbon. Normally the central
allenic carbon appears near 200 ppm and often higher as shown below (Figure 5.2). ${ }^{6,7}$ There are noteworthy exceptions. Whereas this signal appears at 189 ppm for difluoroallene 5.3, ${ }^{8}$ the corresponding signal for the tetramethoxy derivative $\mathbf{5 . 4}{ }^{9}$ appears at 114 ppm and tetrafluoroallene $\mathbf{5 . 5}$. appears at 118 ppm . Interestingly, ${ }^{13} \mathrm{C}$ NMR data for the highly reactive quinoethylenes ${ }^{10}$ have not been reported.


Figure 5.2. Experimental and calculated (shown in parenthesis) allenic ${ }^{13} \mathrm{C}$ NMR sigmals

For the data mentioned above, computational modeling for the ${ }^{13} \mathrm{C}$ NMR expected for A was studied (Table 5.1). Geometry optimizations were performed with B3LYP [6$31 \mathrm{G}(2 \mathrm{~d}, 2 \mathrm{p})]$ and with HF $[6-31 \mathrm{G}(2 \mathrm{~d}, 2 \mathrm{p})] .{ }^{11}$ The spectra data were then calculated using B3LYP, mPW1PW91, and HF. ${ }^{12}$ The best-fit data was found to be the B3LYP//B3LYP one. Still, the experimental data for the central allenic carbon is 90 ppm away from the predicted data. Moreover, all calculations predict the central allenic carbon signal of $\mathbf{A}$ to be $\sim 230$ ppm. ${ }^{13}$

Table 5.1. Computed and Experimental ${ }^{13} \mathrm{C}$ NMR Signals


A


B


C

| position | A (expt) | A (calc) ${ }^{\text {a }}$ | B (calc) ${ }^{\text {a }}$ | B (expt) | C (calc) ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | 120.2 | 105.8 | 119.2 | 120.2 | 121.7 |
| 2 | 105.7 | 106.1 | 118.4 | 105.7 | 104.1 |
| 3 | 150.1 | 149.3 | 145.6 | 150.1 | 143.7 |
| 4 | 168.0 | 171.5 | 161.8 | 168.0 | 146.5 |
| 5 | 147.3 | 148.3 | 142.0 | 147.3 | 143.8 |
| 6 | 111.5 | 101.3 | 105.7 | 111.5 | 108.4 |
| 7 | 139.1 | 229.3 | 140.5 | 139.1 | 132.4 |
| 8 | 117.5 | 107.7 | 116.5 | 117.5 | 133.9 |
| 9 | 188.5 | 182.8 | 179.3 | 188.5 | 171.2 |
| 1, | 141.6 | 131.7 | 138.8 | 141.6 | 137.4 |
| $2^{\prime}$ | 110.1 | 108.5 | 113.2 | 110.1 | 116.3 |
| $3 '$ | 150.1 | 144.1 | 141.9 | 150.1 | 144.0 |
| $4{ }^{\prime}$ | 142.7 | 141.5 | 138.7 | 142.7 | 141.3 |
| 5 ' | 128.5 | 117.3 | 128.6 | 128.5 | 129.0 |
| 6 , | 114.3 | 122.4 | 114.3 | 114.3 | 111.9 |
| $7{ }^{\prime}$ | 33.6 | 36.2 | 35.9 | 33.6 | 36.1 |
| 8' | 35.9 | 39.3 | 38.9 | 35.9 | 39.0 |
| $9^{\prime}$ | 62.3 | 66.7 | 67.0 | 62.3 | 66.7 |
| $3-\mathrm{OMe}$ | 56.9 | 55.0 | 57.8 | 56.9 | 55.3 |
| 3'-OMe | 56.6 | 54.9 | 58.6 | 56.6 | 59.3 |

a. GIAO/B3LYP/6-31G (2d, 2p)//B3LYP/6-31G (2d, 2p)

Calculations were also performed on 5.1, 5.4 and $\mathbf{5 . 5}$ using the same method and
basis set (Figure 5.2). In comparison, the calculated data fits the experimental data well, which strongly suggests that the calculation in this case is reliable. Thus, it appears that there could be a problem with the brosimum allene structural assignment.

### 5.3. Model Study

The functional array of brosimum allene resembles $p$-quinonemethide, ${ }^{14}$ which is well studied in nucleophilic addition as shown in Scheme 5.1. Therefore, it is reasonable to anticipate this sort of nucleophilic addition and then aromatization for the cumulated pquinonemethides.


Scheme 5.1. Parent and Cumulated $p$-quinonemethide

The proposed key reaction to synthesis brosimum allene is to have the corresponding phenol containing a suitably positioned leaving group as starting material. By inducing the leaving group to eliminate, the phenoxide would be transformed into the desired allene, as shown in Scheme 5.2. ${ }^{15}$


Scheme 5.2. Proposed key reaction

Admitedly, this step is highly speculative. Hence, a model study was performed (Scheme 5.3). The syringealdehyde $\mathbf{5 . 1 2}$ was protected with TBS group, coupled with isopropylmagnesium chloride, and then oxidized to give the ketone 5.13. Treatment with $N$-phenyltriflimide ${ }^{16}$ yielded 5.14, which was deprotected by TBAF to give 5.15 Interestingly, the formation of vinyl sulfonamides related to $\mathbf{5 . 1 4}$ is known and thought to proceed by way of onium species. ${ }^{17}$


Scheme 5.3. Synthetic route
The reactions of $\mathbf{5 . 1 4}$ and $\mathbf{5 . 1 5}$ were further studied as shown in Table 5.2. Under neutral $\mathrm{DMF} / \mathrm{H}_{2} \mathrm{O}$ condition, $\mathbf{5 . 1 5}$ was stable at room temperature for 2 days. Similarly, 5.14 was stable under basic conditions. However, when subjected to basic conditions, 5.15 slowly formed 5.16. Mild acid hydrolysis of $\mathbf{5 . 1 6}$ gave ketone $\mathbf{5 . 1 7}$ (89\%) and $\mathbf{5 . 1 5}$ $(92 \%$, Scheme 5.4$) .{ }^{18}$ The amount of water added did not affect the yield ( $55 \sim 60 \%$ ) much, but changed the reaction rate (entries 3-6, Table 5.2). When using potassium hydroxide instead, no matter how much base added, there is no substantial influence on the yields of 5.16. Comparatively, a large excess of base and phenol was used to give $\mathbf{5 . 1 8}$ instead of
$\mathbf{5 . 1 6}$ as product. Thiophenol, on the other hand, gave $\mathbf{5 . 1 9}$ in $81 \%$ yield.
Table 5.2. Reaction of $\mathbf{5 . 1 4}$ and $\mathbf{5 . 1 5}$ in DMF

| entry | triflamide | base <br> (equiv) | Nucleophile <br> (equiv) | product <br> (yield, \%) |
| :---: | :---: | :---: | :---: | :---: |
| 1 | $\mathbf{5 . 1 5}$ | none | $\mathrm{H}_{2} \mathrm{O}(4)$ | NR |
| 2 | $\mathbf{5 . 1 4}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{H}_{2} \mathrm{O}(4)$ | NR |
| 3 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{H}_{2} \mathrm{O}(4)$ | $\mathbf{5 . 1 6}(60)$ |
| 4 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | no $\mathrm{H}_{2} \mathrm{O}$ | $\mathbf{5 . 1 6}(59)$ |
| 5 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{H}_{2} \mathrm{O}(12)$ | $\mathbf{5 . 1 6}(60)$ |
| 6 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{H}_{2} \mathrm{O}(10 \%)$ | $\mathbf{5 . 1 6}(55)$ |
| 7 | $\mathbf{5 . 1 5}$ | $\mathrm{KOH}_{(4)}$ | $\mathrm{H}_{2} \mathrm{O}(4)$ | $\mathbf{5 . 1 6}(45)$ |
| 8 | $\mathbf{5 . 1 5}$ | $\mathrm{KOH}_{(1)}$ | $\mathrm{H}_{2} \mathrm{O}(4)$ | $\mathbf{5 . 1 6}(49)$ |
| 9 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{PhOH}(1)$ | $\mathbf{5 . 1 8}$ (not formed) |
| 10 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(14)$ | $\mathrm{PhOH}(12)$ | $\mathbf{5 . 1 8}(47)$ |
| 11 | $\mathbf{5 . 1 5}$ | $\mathrm{~K}_{2} \mathrm{CO}_{3}(4)$ | $\mathrm{PhSH}(4)$ | $\mathbf{5 . 1 9}(81)$ |



Scheme 5.4. Hydrolysis of $\mathbf{5 . 1 6}$
Briefly, in this reaction water and hydroxide are not good nucleophiles and do not react. Phenoxide adds slowly and competitively in high concentration, whearas benzenethiolate gives a high yield by rapid and highly competitive addition.

Based on the analyses, a mechanistic rationale is depicted in Scheme 5.5. The phenoxide derived from deprotonation of $\mathbf{5 . 1 5}$ could promote the loss of triflate and give
rise to allenic intermediate 5.20. Addition of nucleophiles to $\mathbf{5 . 2 0}$ would lead to the observed products. A closely related pathway may also be relevant. radical anion $\mathbf{5 . 2 1}$ $(\leftrightarrow \mathbf{5 . 2 2})$ may form from rapid electron transfer from a nucleophile to $\mathbf{5 . 2 0}$ followed by selective radical coupling to give the observed products. In light of these data, as well as available data on quinoethylenes, and by analogy to p-quinonemethides, ${ }^{14}$ species like 5.20 are probably not sufficiently stable for observation and isolation under standard conditions.


Scheme 5.5. Mechanistic rationale

### 5.4. Proposed Structures and Conclusion

According to the experimental data provided in the paper, two alternative compounds $\mathbf{B}$ and $\mathbf{C}$ for brosimum allene were proposed. The calculated data for these compounds are given in Table 5.1. Compound $\mathbf{C}$ is not a known substance. Compound $\mathbf{B}$ is mururin $\mathbf{C}$, a natural product isolated by Takashima et al. in 2002 . ${ }^{4,20}$ The observed ${ }^{13} \mathrm{C}$ NMR data for $\mathbf{B}$ are also shown in Table 5.1. Importantly, the calculated data for $\mathbf{B}$ match
the experiment well and the spectral data of compound $\mathbf{A}$ and $\mathbf{B}$ are identical. ${ }^{21}$ We conclude that the structure of brosimum allene was miss-assigned and should be revised to that of mururin C. Structures like compound A are highly reactive. Although they can be employed as reactive intermediates they are not easily isolable.

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## Chapter VI

## Supporting Information

### 6.1. General

### 6.1.1. General for Experiments

Starting materials, reagents and solvents were purchased from commercial suppliers (Aldrich, Fischer, Advanced Chem Tech) and used without further purification unless otherwise stated. All reactions were conducted in oven-dried $\left(135^{\circ} \mathrm{C}\right)$ glassware under an inert atmosphere of argon. The progress of reactions was monitored by silica gel thin layer chromatography (TLC) plates (mesh size $60 \AA$ with fluorescent indicator, SigmaAldrich), visualized under UV and charred using PMA, Seebach, vanillin or anisaldehyde stain. Products were purified by flash column chromatography (FCC) on 120-400 mesh silica gel (Fisher). Infrared (FTIR) spectra were recorded on an ATI Mattson Genesis Series FT-Infrared spectrophotometer. Proton nuclear magnetic resonance spectra ( ${ }^{1} \mathrm{H}$ NMR) were recorded on either a Varian-300 instrument ( 300 MHz ), Varian-400 instrument ( 400 MHz ) or a Varian-500 instrument ( 500 MHz ) unless otherwise stated. Chemical shifts are reported in ppm relative to the residual $\mathrm{CHCl}_{3}$ signal. Data are reported as follows: chemical shift, integration, multiplicity ( $\mathrm{s}=$ singlet, $\mathrm{d}=$ doublet, $\mathrm{t}=$ triplet, $\mathrm{q}=$ quartet, $\mathrm{br}=$ broad, $\mathrm{m}=$ multiplet), and coupling constants ( Hz ). Carbon nuclear magnetic resonance spectra ( ${ }^{13} \mathrm{C}$ NMR) were recorded on either a Varian-400 instrument $(100 \mathrm{MHz})$ or a Varian-500 instrument $(125 \mathrm{MHz})$ unless otherwise stated. Mass spectra were recorded on a Finnigan LCQ-DUO mass spectrometer. HPLC analysis was conducted on an Agilent 1100 series instrument with auto sampler and multiple wavelength detectors.

### 6.1.2. General for Calculation

Electronic structure calculations, based on density functional theory (DFT), were carried out with the Gaussian 09 suite $^{1}$ of programs. We utilized the B3LYP functional ${ }^{2}$ with 6$31+\mathrm{g}(\mathrm{d}), \quad 6-31+\mathrm{g}(\mathrm{d}, \mathrm{p})$ and $6-31 \mathrm{~g}(2 \mathrm{~d}, 2 \mathrm{p})$ basis sets. ${ }^{3}$ General solvent effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM). ${ }^{4}$ All transition states were verified by observing the nature of the negative imaginary frequency. Natural bonding orbital analysis was conducted using NBO 5
incorporated in Gaussian 09 suite. ${ }^{5}$
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### 6.2. Chapter I



To a solution of trans-2-penten-4-yn-1-ol ( $5.0 \mathrm{~mL}, 53.6 \mathrm{mmol}$ ) in DCM ( $0.1 \mathrm{M}, 500 \mathrm{~mL}$ ) was added sodium phosphate dibasic $(18.0000 \mathrm{~g}, 128.7 \mathrm{mmol})$ and $m$ CPBA $(77 \%$ max, $24.0000 \mathrm{~g}, 107.2 \mathrm{mmol}$ ) at $0^{\circ} \mathrm{C}$. The reaction mixture was allowed to warm up to room temperature slowly. After overnight, the reaction mixture was quenched by 300 mL sat. $\mathrm{Na}_{2} \mathrm{CO}_{3}$ aqueous solution. After the first extraction, the aqueous layer was extracted with DCM two more times ( 2 X 300 mL ). The combined organic layers were dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo to give colorless oil as crude product. This crude product was then dissolved in $250 \mathrm{~mL}(0.2 \mathrm{M}) \mathrm{DCM}$, added imidazole ( $1.0930 \mathrm{~g}, 160.8$ $\mathrm{mmol})$ and $\operatorname{TBDPSCl}(16.7 \mathrm{~mL}, 64.3 \mathrm{mmol})$ at room temperature. After half an hour, the solution was diluted with 300 mL DCM and washed with 300 mL sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution and 300 mL brine. The organic layer was then dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo and purified by FCC ( 0.5 to $1 \%$ ethyl acetate in hexane) to give colorless oil as the product ( $16.5118 \mathrm{~g}, 49.1 \mathrm{mmol}, 92 \%$ yield). IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}: 3290$, 3071, 2958, 2931, 2893, 2858, 2128, 1472, 1428, 1390, 1362, 1112, 704; ${ }^{1} \mathrm{H}$ NMR (300 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.67-7.64(4 \mathrm{H}, \mathrm{m}), 7.44-7.36(6 \mathrm{H}, \mathrm{m}), 3.81(2 \mathrm{H}, \mathrm{ddd}, J=12,4.8,3.2 \mathrm{~Hz})$, $3.36(1 \mathrm{H}, \mathrm{t}, J=2.0 \mathrm{~Hz}), 3.31(1 \mathrm{H}, \mathrm{td}, J=3.2,2.0 \mathrm{~Hz}), 2.32(1 \mathrm{H}, \mathrm{t}, J=1.2 \mathrm{~Hz}), 1.04(9 \mathrm{H}$, $\mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 135.8,135.6,133.1,132.9,130.0,127.9,80.3,72.2,62.1$, 60.0, 42.4, 26.8, 19.3; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{21} \mathrm{H}_{24} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 359.2$, found 359.1.

General procedure for single flask allenic diol synthesis (Table 1, entry 14)


Propargyl oxirane in anh. THF or $\mathrm{Et}_{2} \mathrm{O}(0.2 \mathrm{M})$ was added $n$ - BuLi ( 1.1 equiv.) at $-78{ }^{\circ} \mathrm{C}$ slowly and the reaction mixture was stirred for 1 hr at the same temperature. 3Phenylpropinaldehyde (1 equiv.) in anh. THF/ $\mathrm{Et}_{2} \mathrm{O}$ was added at $-78^{\circ} \mathrm{C}$. After 5 min , the reaction went to completion. 10 min later, the coupling product solution was added to the methyl cuprate solution $(0.3 \mathrm{M})$ at -40 or $-78{ }^{\circ} \mathrm{C}$. The reaction was monitored by TLC. After the completion of the reaction ( 5 to 30 min ), the reaction mixture was quenched by sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution and extracted with ethyl acetate. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo and purified using FCC (10 to $30 \%$ ethyl acetate in hexane) to yield $\mathbf{A}$ and/or $\mathbf{B}$ as colorless oil.
A: IR $v_{\max }$ (neat)/cm ${ }^{-1}: 3410,3071,2930,2858,1967,1644,1428,1112,741,702 ;{ }^{1} \mathrm{H}$

NMR (500 MHz, CDCl3) 7.67 - $7.64(4 \mathrm{H}, \mathrm{m}), 7.49-7.30(6 \mathrm{H}, \mathrm{m}), 7.30-7.22(2 \mathrm{H}, \mathrm{m})$, $7.22-7.07(3 \mathrm{H}, \mathrm{m}), 5.33-5.30(1 \mathrm{H}, \mathrm{m}), 4.31-4.23(1 \mathrm{H}, \mathrm{m}), 3.70(2 \mathrm{H}, \mathrm{d}, J=5.7 \mathrm{~Hz})$, $3.66-3.54(1 \mathrm{H}, \mathrm{m}), 2.72(2 \mathrm{H}, \mathrm{t}, J=7.9 \mathrm{~Hz}), 2.08-1.81(2 \mathrm{H}, \mathrm{m}), 1.20(3 \mathrm{H}, \mathrm{d}, J=1.5$ $\mathrm{Hz}), 1.06(9 \mathrm{H}, \mathrm{d}, J=5.8 \mathrm{~Hz}, 7 \mathrm{H}) .{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 199.8,142.1,141.5$, 135.7, 133.2, 130.0, 128.6, 128.5, 128.0, 127.9, 126.0, 106.0, 104.9, 86.0, 83.8, 74.3, 65.9, 61.9, 39.7, 39.6, 31.9, 31.6, 29.8, 29.3, 27.1, 27.0, 19.4, 17.5, 13.9; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{31} \mathrm{H}_{38} \mathrm{O}_{3} \mathrm{Si}-\mathrm{H}\right]^{+}: 485.3$, found 485.2

B: IR $v_{\text {max }}$ (neat)/cm ${ }^{-1}: 3378,3070,2930,2858,1966,1428,1112,741,702 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.68(4 \mathrm{H}, \mathrm{dq}, J=6.8,3.0,2.4 \mathrm{~Hz}$ ), $7.52-7.35(6 \mathrm{H}, \mathrm{m}), 7.34-7.25$ $(2 \mathrm{H}, \mathrm{m}), 7.25-7.12(3 \mathrm{H}, \mathrm{m}), 5.51-5.23(2 \mathrm{H}, \mathrm{m}), 4.30(1 \mathrm{H}, \mathrm{dq}, J=5.2,3.3,2.7 \mathrm{~Hz})$, $4.16(1 \mathrm{H}, \mathrm{dtd}, J=12.4,7.3,6.3,3.8 \mathrm{~Hz}), 3.81-3.56(2 \mathrm{H}, \mathrm{m}), 2.92-2.60(2 \mathrm{H}, \mathrm{m}), 1.99$ $-1.76(2 \mathrm{H}, \mathrm{m}), 1.10(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 13C NMR ( $126 \mathrm{MHz}, \mathrm{CDCl} 3$ ) $\delta 202.4,202.1,202.1,201.9,141.9,135.7,135.6,133.2,133.1,130.0,128.6,128.5,127.9$, $125.9,98.8,98.3,95.0,94.9,94.6,70.3,70.2,69.9,69.7,69.2,68.7,67.9,39.1,39.0,38.9$, $32.0,31.8,29.8,29.8,29.5,27.0,22.8,19.4,14.25$; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{30} \mathrm{H}_{36} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 495.2$, found 495.3.; $\left[\mathrm{C}_{30} \mathrm{H}_{36} \mathrm{O}_{3} \mathrm{Si}-\mathrm{H}\right]^{-}: 471.2$, found 471.2.

## General procedure for single flask allene synthesis (Table 2)



Propargyl oxirane in anh. THF or $\mathrm{Et}_{2} \mathrm{O}(0.2 \mathrm{M})$ was added $n$ - BuLi (1.1 equiv.) at $-78{ }^{\circ} \mathrm{C}$ slowly and the reaction mixture was stirred for 1 hr at the same temperature. Electrophile (1.0-1.5 equiv.) in anh. THF/ $\mathrm{Et}_{2} \mathrm{O}$ was added at $-78^{\circ} \mathrm{C}$. Upon completion, the coupling product solution was added to the cuprate solution ( 3.0 equiv., 0.3 M ) at $-78{ }^{\circ} \mathrm{C}$. The reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was quenched by sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution and extracted with ethyl acetate. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo and purified by FCC. The yield of coupling product was obtained by quenching the reaction by sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution after the completion of step (ii) followed by the same work-up protocol as described above.


Entry 1-5: 95\% yield ( 142.4 mg ). IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}: 3447,2958$, 2931, 2858, 2360, 1636, 1428, 1112, 703; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.82-7.63(4 \mathrm{H}$, m), $7.58-7.36(6 \mathrm{H}, \mathrm{m}), 3.90-3.74(2 \mathrm{H}, \mathrm{ddd}, J=12.0,8.5,3.0 \mathrm{~Hz}), 3.33(1 \mathrm{H}, \mathrm{p}, J=1.9$ $\mathrm{Hz}), 3.26(1 \mathrm{H}, \mathrm{td}, J=3.5,2.1 \mathrm{~Hz}), 1.86(3 \mathrm{H}, \mathrm{d}, J=1.8 \mathrm{~Hz}), 1.07(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 135.7, 135.6, 133.2, 133.0, 129.9, 127.9, 80.6, 75.8, 62.6, 60.1, 43.3, 26.8, 19.4; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 373.2$, found 373.2.


Entry 1: $67 \%$ yield $(145.8 \mathrm{mg})$ together with disubstituted allene in $14 \%$ yield ( 29.1 mg ) as inseparable mixture ( $5: 1$ molar ratio). IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}: 3440$, 3071, 2931, 2858, 1968, 1571, 1428, 1390, 1362, 1112, 703; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.78-7.56(4 \mathrm{H}, \mathrm{m}), 7.55-7.33(6 \mathrm{H}, \mathrm{m}), 5.08(1 \mathrm{H}, \mathrm{tq}, J=6.7,3.3 \mathrm{~Hz}), 4.24(1 \mathrm{H}, \mathrm{tdd}, J$ $=10.7,8.1,4.8 \mathrm{~Hz}), 3.87-3.51(2 \mathrm{H}, \mathrm{m}), 1.70(3 \mathrm{H}, \mathrm{d}, J=3.0 \mathrm{~Hz}), 1.68(3 \mathrm{H}, \mathrm{d}, J=3.0$ $\mathrm{Hz}), 1.09(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 201.1,135.8,135.7,134.9,133.4,129.9$, 129.7, 127.9, 127.8, 98.4, 89.9, 70.6, 68.2, 27.0, 26.7, 20.7, 19.4; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{23} \mathrm{H}_{30} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 366.2$, found 389.2.


Entry 2: 77\% yield ( 82.0 mg ). IR $\nu_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3463,3071$, 2959, 2929, 2859, 1963, 1636, 1464, 1428, 1383, 1364, 1112, ; ${ }^{1}$ H NMR ( 500 MHz , $\mathrm{CDCl}_{3} 7.70(4 \mathrm{H}, \mathrm{dtd}, J=8.0,2.2,1.2 \mathrm{~Hz}), 7.42(6 \mathrm{H}, \mathrm{dtt}, J=15.8,8.3,1.4 \mathrm{~Hz}), 5.23-$ $5.12(1 \mathrm{H}, \mathrm{m}), 4.36-4.13(1 \mathrm{H}, \mathrm{m}), 3.88-3.42(2 \mathrm{H}, \mathrm{m}), 2.52(1 \mathrm{H}, \mathrm{d}, J=4.1 \mathrm{~Hz}), 1.82$ $(1 \mathrm{H}, \mathrm{d}, J=2.4 \mathrm{~Hz}), 1.71(3 \mathrm{H}, \mathrm{d}, J=2.9 \mathrm{~Hz}), 1.30(6 \mathrm{H}, \mathrm{s}), 1.09(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 199.7, 135.8, 135.7, 133.4, 133.3, 129.9, 127.9, 127.8, 108.9, 91.9, 71.0, $68.5,42.6,31.8,27.0,22.8,21.6,21.4,19.4,17.4,14.3$; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{25} \mathrm{H}_{34} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 394.2$, found 417.4.


Entry 3: $64 \%$ yield ( 134.9 mg ). IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}: 3439,2962$, 2931, 2856, 1957, 1635, 1472, 1428, 1112, 702, ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.72(4 \mathrm{H}$, dd, $J=20.7,7.0 \mathrm{~Hz}), 7.42(6 \mathrm{H}, \mathrm{dp}, J=16.2,8.3 \mathrm{~Hz}), 5.81-5.59(1 \mathrm{H}, \mathrm{m}), 5.17(1 \mathrm{H}, \mathrm{dt}, J$ $=6.4,3.2 \mathrm{~Hz}), 4.98(2 \mathrm{H}, \mathrm{dd}, J=25.4,13.5 \mathrm{~Hz}), 4.28-4.20(1 \mathrm{H}, \mathrm{m}), 3.83-3.51(2 \mathrm{H}, \mathrm{m})$, $2.72-2.62(1 \mathrm{H}, \mathrm{m}), 2.53(1 \mathrm{H}, \mathrm{s}), 1.70(3 \mathrm{H}, \mathrm{d}, J=2.9 \mathrm{~Hz}), 1.10(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 201.1, 135.8, 135.7, 135.6, 134.9, 133.4, 133.3, 129.9, 129.7, 127.9, 127.8, $116.2,101.3,91.4,70.8,68.4,38.8$, 32.1, 29.9, 27.0, 26.7, 22.9, 19.4, 18.7. 14.3; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{25} \mathrm{H}_{32} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 415.2$, found: 415.3.


Entry 3: $91 \%$ yield ( 179.4 mg ). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3443,3072$, 2957, 2931, 2858, 1956, 1641, 1471, 1428, 1112, 703; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.75 $-7.53(4 \mathrm{H}, \mathrm{m}), 7.50-7.32(6 \mathrm{H}, \mathrm{m}), 5.76(1 \mathrm{H}, \mathrm{ddt}, J=16.8,10.2,6.3 \mathrm{~Hz}), 5.16(1 \mathrm{H}, \mathrm{tt}, J$ $=6.1,3.1 \mathrm{~Hz}), 5.00-4.89(2 \mathrm{H}, \mathrm{m}), 4.21(1 \mathrm{H}, \mathrm{tt}, J=6.5,4.1 \mathrm{~Hz}), 3.75-3.56(1 \mathrm{H}, \mathrm{m})$, $2.49(1 \mathrm{H}, \mathrm{d}, J=4.1 \mathrm{~Hz}), 2.08(2 \mathrm{H}, \mathrm{ddd}, J=7.4,4.5,1.7 \mathrm{~Hz}), 2.00(2 \mathrm{H}, \mathrm{td}, J=6.6,2.5$ $\mathrm{Hz}), 1.70(3 \mathrm{H}, \mathrm{d}, J=2.9 \mathrm{~Hz}), 1.07(9 \mathrm{H}, \mathrm{d}, J=2.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 13 \mathrm{C}$ NMR ( 126 MHz , cdcl3) $\delta 200.7,138.3$, 135.7, 135.3, 134.9, 133.4, 133.3, 129.9, 129.8, $127.9,114.9,102.4,91.7,70.7,68.3,33.2,31.7,29.6,27.0,26.7,19.4,19.2$; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{26} \mathrm{H}_{34} \mathrm{O}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 429.2$, found 429.3.


Entry 7: $87 \%$ yield ( 184.0 mg ). IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}: 3406,3071$, 3050, 2958, 2931, 2859, 2241, 1471, 1428, 1113, 704; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.70$7.68(4 \mathrm{H}, \mathrm{m}), 7.47-7.40(6 \mathrm{H}, \mathrm{m}), 3.84(1 \mathrm{H}, \mathrm{qd}, J=12.0,3.0 \mathrm{~Hz}), 3.42(1 \mathrm{H}, \mathrm{d}, 2 \mathrm{~Hz}), 3.30$ $(1 \mathrm{H}, \mathrm{td}, J=2.5,0.5 \mathrm{~Hz}), 2.18(1 \mathrm{H}, \mathrm{s}, \mathrm{br}), 1.54(6 \mathrm{H}, \mathrm{s}), 1.10(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR( 125 MHz , $\mathrm{CDCl}_{3}$ ) 135.7, 135.6, 133.2, 132.9, 130.0, 127.9, 127.9, 88.7, 78.5, 65.2, 62.3, 60.2, 42.7, 31.3, 26.8, 19.4; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{24} \mathrm{H}_{30} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 417.2$, found 417.3.


Entry 7: $60 \%$ yield ( 83 mg ). IR $\nu_{\text {max }}$ (neat)/ $\mathrm{cm}^{-1}: 3422,2959$, 2930, 2858, 1967, 1636, 1462, 1428, 1365, 1112, 703; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.78$ $-7.54(4 \mathrm{H}, \mathrm{m}), 7.53-7.33(6 \mathrm{H}, \mathrm{m}), 5.29(1 \mathrm{H}, \mathrm{dq}, J=5.8,2.8 \mathrm{~Hz}), 4.28-4.19(1 \mathrm{H}, \mathrm{m})$, $3.74-3.58(2 \mathrm{H}, \mathrm{m}), 1.73(3 \mathrm{H}, \mathrm{d}, J=2.9 \mathrm{~Hz}), 1.31(3 \mathrm{H}, \mathrm{d}, J=1.7 \mathrm{~Hz}), 1.26(3 \mathrm{H}, \mathrm{s}), 1.07$ $(9 \mathrm{H}, \mathrm{d}, J=4.2 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 198.7, 135.7, 133.3, 130.0, 128.0, 127.9, 110.9, 93.9, 71.0, 70.5, 68.1, 32.1, 29.9, 29.8, 29.5, 28.9, 27.0, 22.9, 19.4, 14.8, 14.3; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{25} \mathrm{H}_{34} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 433.2$, found 433.2.


Entry 8: $55 \%$ yield ( 56.2 mg ). IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}: 3443,3071$, 2931, 2858, 2780, 2355, 1635, 1471, 1428, 1316, 1112, 703; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 7.68-7.65 ( $4 \mathrm{H}, \mathrm{m}$ ), 7.44-7.37 ( $6 \mathrm{H}, \mathrm{m}$ ), $3.80(1 \mathrm{H}, \mathrm{qd}, J=12.0,3.0 \mathrm{~Hz}$ ), 3.27-3.26 ( $3 \mathrm{H}, \mathrm{m}$ ), $2.29(6 \mathrm{H}, \mathrm{s}), 1.04(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR(125 MHz, CDCl3) 135.8, 135.6, 133.2, 130.0, 127.9, 127.8, 81.6, 79.5, 62.5, 60.3, 48.1, 44.3, 42.9, 26.9, 19.4; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{24} \mathrm{H}_{31} \mathrm{NO}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 416.2$, found 416.4.


Entry 8: 48\% yield ( 279.1 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3392,3071$, 2930, 2857, 2777, 1967, 1633, 1463, 1428, 1112, 741, 703; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.67(4 \mathrm{H}, \mathrm{d}, J=7.1 \mathrm{~Hz}), 7.41(6 \mathrm{H}, \mathrm{dq}, J=14.3,7.4 \mathrm{~Hz}), 5.29-5.08(1 \mathrm{H}, \mathrm{m}), 4.24(1 \mathrm{H}$, $\mathrm{dq}, J=10.6,5.3,4.7 \mathrm{~Hz}), 4.17-4.03(1 \mathrm{H}, \mathrm{m}), 3.87-3.50(2 \mathrm{H}, \mathrm{m}), 2.89-2.66(2 \mathrm{H}, \mathrm{m})$, $2.17(6 \mathrm{H}, \mathrm{d}, J=12.2 \mathrm{~Hz}), 1.69(3 \mathrm{H}, \mathrm{dd}, J=12.1,2.8 \mathrm{~Hz}), 1.07(9 \mathrm{H}, \mathrm{d}, J=4.5 \mathrm{~Hz}),{ }^{13} \mathrm{C}$ NMR(125 MHz, $\mathrm{CDCl}_{3}$ ) 202.2, 135.70, 135.6, 133.3, 129.9, 127.9, 100.2, 91.0, 70.6, 68.2, 63.7, 45.4, 27.0, 26.9, 19.4, 17.3, 14.34; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{25} \mathrm{H}_{35} \mathrm{NO}_{2} \mathrm{Si}+\mathrm{Na}\right]^{+}: 432.2$, found 432.3.

## Aldehydes Synthesis



To a solution of alcohol ( $5.15 \mathrm{~g}, 15.68 \mathrm{mmol}$ ) and $4 \AA \mathrm{MS}$ in $\mathrm{DCM}(80 \mathrm{~mL}, 0.19 \mathrm{M})$ at 0 ${ }^{\circ} \mathrm{C}$ was added NMO ( $2.75 \mathrm{~g}, 23.52 \mathrm{mmol}$ ) followed by TPAP ( $275.5 \mathrm{mg}, 0.784 \mathrm{mmol}$ ). The reaction mixture was allowed to slowly warm up to room temperature over 1 h . Upon
completion of reaction (1h), the reaction mixture was filtered through celite, concentrated on rotavap, and purified by FCC (ethyl actate/hexane) to give colorless oil as the product in $62 \%$ yield $(3.18 \mathrm{~g})$. IR $v_{\max }($ neat $) / \mathrm{cm}^{-1} 3071,3054,2961,2931,2889,2853,2718,1964$, 1894, 1835, 1726, 1587, 1472, 1428, 1409, 1390, 1362, 1308, 1254, 1192, 1112, 1016, $995,944,823,739 ; \delta_{\mathrm{H}}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 9.81(1 \mathrm{H}, \mathrm{s}), 7.69-7.63(4 \mathrm{H}, \mathrm{m}), 7.47-7.37$ $(6 \mathrm{H}, \mathrm{m}), 3.71(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.57(2 \mathrm{H}, \mathrm{td}, J=7.2,1.5 \mathrm{~Hz}), 1.94-1.85(2 \mathrm{H}, \mathrm{m}), 1.06$ $(9 \mathrm{H}, \mathrm{s}) ; \delta_{\mathrm{C}}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 202.75,135.77,133.83,129.91,127.92,63.15,41.00$, 27.06, 25.49, 19.42; (ESI/MS) Calcd for $m / z\left[\mathrm{C}_{20} \mathrm{H}_{27} \mathrm{O}_{2} \mathrm{Si}^{+}: 327.2[\mathrm{M}+\mathrm{H}]^{+}\right.$; found 327.2.


To a solution of alcohol ( $8.89 \mathrm{~g}, 28.27 \mathrm{mmol}$ ) and $4 \AA \mathrm{MS}$ in $\mathrm{DCM}(150 \mathrm{~mL}, 0.19 \mathrm{M})$ at $0^{\circ} \mathrm{C}$ was added NMO ( $4.97 \mathrm{~g}, 42.41 \mathrm{mmol}$ ) followed by TPAP ( $0.5 \mathrm{~g}, 1.41 \mathrm{mmol}$ ). The reaction mixture was allowed to slowly warm up to room temperature over 1 h . Upon completion of reaction (1h), the reaction mixture was filtered through celite, concentrated on rotavap, and purified by FCC (ethyl actate/hexane) to give colorless oil as the product in $68 \%$ yield $(6.0 \mathrm{~g})$. IR $v_{\max }($ neat $) / \mathrm{cm}^{-1} 3054,2931,2853,1723,1469,1388,1251,1112$, $944 ; \delta_{\mathrm{H}}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 9.83(1 \mathrm{H}, \mathrm{t}, J=2.1 \mathrm{~Hz}), 7.69-7.64(4 \mathrm{H}, \mathrm{m}), 7.48-7.36(6 \mathrm{H}$, m), $4.04(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.62(2 \mathrm{H}, \mathrm{td}, J=6.0,2.2 \mathrm{~Hz}), 1.05(9 \mathrm{H}, \mathrm{s}) ; \delta_{\mathrm{C}}(125 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ) 202.09, 135.77, 133.48, 130.04, 127.99, 58.53, 46.61, 26.98, 19.38.


To a solution of oxalyl chloride ( $1.42 \mathrm{~mL}, 16.2 \mathrm{mmol}$ ) in $\mathrm{DCM}(81 \mathrm{~mL}, 0.1 \mathrm{M})$ at $-78{ }^{\circ} \mathrm{C}$ was added DMSO ( $2.29 \mathrm{~mL}, 32.3 \mathrm{mmol}$ ). The reaction mixture was stirred at $-78^{\circ} \mathrm{C}$ for 15 min . To the reaction mixture was then added a solution of alcohol ( $2.64 \mathrm{~g}, 8.08 \mathrm{mmol}$ ) in DCM ( 5 mL ). The reaction mixture was stirred at $-78{ }^{\circ} \mathrm{C}$ for 30 min and then diisopropylethylamine ( $8.44 \mathrm{~mL}, 48.5 \mathrm{mmol}$ ) was added. The reaction mixture was stirred at $-78{ }^{\circ} \mathrm{C}$ for 45 min and was allowed to slowly warm up to room temperature over 1 h .10 mL sat. $\mathrm{NH}_{4} \mathrm{Cl}$ was added to the solution and DCM was used for extraction twice ( 15 mL X 2). The combined organic layers was dried over sodium sulfate, filtered, concentrated on rotavap, and purified by FCC (ethyl actate/hexane) to give colorless oil as the product in $84 \%$ yield $(2.2 \mathrm{~g})$. IR $v_{\max }($ neat $) / \mathrm{cm}^{-1} 3081,3052,2956,2854,1724$, $1644,1471,1389,1250,1004,918 ; \delta_{\mathrm{H}}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 9.63(1 \mathrm{H}, \mathrm{s}), 7.71-7.64(4 \mathrm{H}$, m), $7.48-7.37(6 \mathrm{H}, \mathrm{m}), 6.73(1 \mathrm{H}, \mathrm{s}), 6.17(1 \mathrm{H}, \mathrm{s}), 4.51(2 \mathrm{H}, \mathrm{s}), 1.11(9 \mathrm{H}, \mathrm{s}) ; \delta_{\mathrm{C}}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 193.67, 149.38, 135.67, 133.13, 130.11, 128.05, 60.71, 27.09, 19.56; (ESI/MS) Calcd for $m / z\left[\mathrm{C}_{20} \mathrm{H}_{25} \mathrm{O}_{2} \mathrm{Si}\right]^{+}: 325.1[\mathrm{M}+\mathrm{H}]^{+}$; found 325.1.

## General procedure for single flask allene synthesis (Table 3)



Propargyl oxirane in anh. THF or $\mathrm{Et}_{2} \mathrm{O}(0.2 \mathrm{M})$ was added $n-\mathrm{BuLi}\left(1.1\right.$ equiv.) at $-78{ }^{\circ} \mathrm{C}$ slowly and the reaction mixture was stirred for 1 hr at the same temperature. Aldehydes / ketones ( 1 equiv.) in anh. $\mathrm{THF} / \mathrm{Et}_{2} \mathrm{O}$ was added at $-78^{\circ} \mathrm{C}$ followed by addition of TESCl ( 1.5 equiv.) at room temperature or TESOTf ( 1.5 equiv.) at $-78^{\circ} \mathrm{C}$ upon completion of coupling (within 1 hr ). Cuprate solution was prepared by adding triethyl phosphite (3.0 equiv.) to copper (I) cyanide in $\mathrm{THF} / \mathrm{Et}_{2} \mathrm{O}(3.0$ equiv., 0.3 M$)$ at room temperature (the copper suspension turned clear solution), followed by addition of alkyl magnesium bromide solution ( 6.0 equiv.) at $-40^{\circ} \mathrm{C}$. After the complete disappearance of the coupling alcohol on TLC ( 30 min to 1 hr ), the reaction mixture was added to the prepared cuprate solution at $-78{ }^{\circ} \mathrm{C}$. Upon the completion of the reaction ( 30 min to 1 hr ), the reaction mixture was quenched by sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution and extracted with ethyl acetate. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo and purified by FCC. The yield of coupling product was obtained by quenching the reaction by sat. $\mathrm{NH}_{4} \mathrm{Cl}$ aqueous solution after the completion of step (ii) followed by the same work-up protocol as described above.


Table 1 \& Table 3, Entry 1: 77\% yield ( 110.3 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3411,3070,2930,2858,2349,1428,1112,702 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.71-7.68 (4H, m), 7.48-7.39 (6H, m), $7.32(2 \mathrm{H}, \mathrm{t}, J=7.5 \mathrm{~Hz}), 7.24-7.21(3 \mathrm{H}, \mathrm{m}), 4.42$ $(1 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 3.85(2 \mathrm{H}, \mathrm{qd}, J=12.0,2.5 \mathrm{~Hz}), 3.44(1 \mathrm{H}, \mathrm{d}, J=1.0 \mathrm{~Hz}), 3.31(1 \mathrm{H}, \mathrm{t}$, $J=1.5 \mathrm{~Hz}), 2.82(2 \mathrm{H}, \mathrm{t}, J=7.5 \mathrm{~Hz}), 2.06(2 \mathrm{H}$, quin, 6.5 Hz$), 1.08(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 141.2, 135.8, 135.7, 135.6, 133.1, 132.9, 130.0, 128.6, 127.9, 126.2, 84.8, 81.7, 62.3, 61.8, 60.2, 42.7, 39.0, 31.4, 26.8, 19.4; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{30} \mathrm{H}_{34} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 493.2$, found 493.1.


Table 1, Entry 5-8: 57\% yield ( 248.2 mg ). IR $v_{\max }$ (neat)/cm${ }^{1}: 3460,3070,2955,2875,1966,1459,1427,1111,742,702 ;{ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.67(4 \mathrm{H}$, dddd, $J=8.8,5.6,3.5,2.0 \mathrm{~Hz}), 7.51-7.31(6 \mathrm{H}, \mathrm{m}), 7.25(2 \mathrm{H}, \mathrm{dtd}, J=$ $8.8,7.2,2.6 \mathrm{~Hz}), 7.22-7.08(3 \mathrm{H}, \mathrm{m}), 5.17(1 \mathrm{H}, \mathrm{dt}, J=6.1,2.9 \mathrm{~Hz}), 4.25(1 \mathrm{H}, \mathrm{dtd}, J=$ $20.5,6.8,3.2 \mathrm{~Hz}), 4.19(1 \mathrm{H}, \mathrm{t}, J=6.8 \mathrm{~Hz}), 3.87-3.49(2 \mathrm{H}, \mathrm{m}), 2.72-2.51(2 \mathrm{H}, \mathrm{m})$, $1.99-1.73(2 \mathrm{H}, \mathrm{m}), 1.64(3 \mathrm{H}, \mathrm{t}, J=2.7 \mathrm{~Hz}), 1.08(9 \mathrm{H}, \mathrm{d}, J=1.5 \mathrm{~Hz}), 1.04-0.77(9 \mathrm{H}$, $\mathrm{m}), 0.58(6 \mathrm{H}, \mathrm{qqd}, J=8.9,6.2,5.3,2.6 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 200.7,200.6$, $142.3,135.7,135.6,133.3,133.2,130.0,129.9,128.5,128.4,127.9,125.9,125.8,104.6$, $104.4,91.8,91.2,74.1,73.7,73.6,70.8,70.7,68.4,68.2,38.3,38.2,32.4,32.2,32.1,29.9$,
29.8, 29.5, 27.0, 22.8, 19.4, 14.3, 13.4, 12.7, 7.0, 5.0, 4.9, 4.6; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{37} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 623.4$, found 623.3; $\left[\mathrm{C}_{37} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{TES}\right]^{+}$: 715.5, found 715.0; $\left[\mathrm{C}_{37} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}-\mathrm{H}\right]^{-}: 599.4$, found 599.4.


Table 3, Entry 1: $50 \%$ yield ( 242.4 mg ). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}$ : 3449, 3071, 2958, 2931, 2874, 1960, 1637, 1460, 1428, 1380, 1362, 1112, 740, 702; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.73 (4H, dddt, $J=6.3,4.6,3.1,1.6 \mathrm{~Hz}$ ), $7.57-7.34$ ( $6 \mathrm{H}, \mathrm{m}$ ), $7.31(2 \mathrm{H}, \mathrm{td}, J=7.4,6.8,2.0 \mathrm{~Hz}), 7.24-7.17(3 \mathrm{H}, \mathrm{m}), 5.42(1 \mathrm{H}, \mathrm{ddt}, J=6.2,3.2,1.4$ $\mathrm{Hz}), 4.39-4.13(2 \mathrm{H}, \mathrm{m}), 3.86-3.57(2 \mathrm{H}, \mathrm{m}), 2.73-2.50(2 \mathrm{H}, \mathrm{m}), 2.46-2.06(1 \mathrm{H}, \mathrm{m})$, $1.91(2 \mathrm{H}$, dddd, $J=19.8,17.8,8.7,4.8 \mathrm{~Hz}), 1.13(9 \mathrm{H}, \mathrm{s}), 1.07-0.88(9 \mathrm{H}+6 \mathrm{H}, \mathrm{m}), 0.64$ ( $6 \mathrm{H}, \mathrm{qd}, J=7.9,2.3 \mathrm{~Hz}$ ) ${ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 199.9,199.7,142.4,142.3,135.7$, 135.6, 133.3, 133.2, 129.9, 128.5, 128.45, 127.9, 125.8, 116.9, 116.6, 95.3, 94.7, 71.0, $68.6,39.2,38.9,32.4,32.3,32.1,29.8,29.5,27.00,26.7,26.3,23.8,23.5,23.3,23.0,22.3$, 19.4, 14.25, 7.1, 7.0, 5.0; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{39} \mathrm{H}_{56} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 651.4$, found 651.4; $\left[\mathrm{C}_{39} \mathrm{H}_{56} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{TES}\right]^{+}: 743.5$, found 743.1; $\left[\mathrm{C}_{39} \mathrm{H}_{56} \mathrm{O}_{3} \mathrm{Si}_{2}-\mathrm{H}\right]^{+}: 627.4$, found 627.3.


Table 3, Entry 2: 64\% yield ( 35.0 mg ). IR $\nu_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3418$, 3071, 2931, 2858, 1633, 1471, 1428, 1390, 1362, 1112, 703; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $7.67-7.65(4 \mathrm{H}, \mathrm{m}), 7.45-7.37(6 \mathrm{H}, \mathrm{m}), 4.29(2 \mathrm{H}, \mathrm{d}, J=4.5 \mathrm{~Hz}), 3.81(2 \mathrm{H}, \mathrm{qd}, J=12.5$, $3.0 \mathrm{~Hz}), 3.40(1 \mathrm{H}, \mathrm{d}, J=2.0 \mathrm{~Hz}), 3.28(1 \mathrm{H}, \mathrm{qd}, J=3.0,1.0 \mathrm{~Hz}), 1.04(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR(125 MHz, $\mathrm{CDCl}_{3}$ ) 135.8, 125.6, 133.1, 133.0, 130.0, 127.9, 82.3, 62.3, 60.2, 51.2, 42.7, 26.9, 19.4; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{22} \mathrm{H}_{26} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 389.2$, found 389.2.


Table 3, Entry 3: 74\% yield ( 165 mg ). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3442$, 3071, 3050, 2957, 2930, 2892, 2858, 2360, 1471, 1427, 1390, 1362, 1111, 703; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.70-7.65 (8H, m), 7.43-7.36 ( $12 \mathrm{H}, \mathrm{m}$ ), 4.74-4.68 ( $1 \mathrm{H}, \mathrm{m}$ ), 4.05-4.0 $(1 \mathrm{H}, \mathrm{m}), 3.85-3.75(3 \mathrm{H}, \mathrm{m}), 3.42-3.41(1 \mathrm{H}, \mathrm{m}), 3.32(1 \mathrm{H}, \mathrm{t}, J=7.0 \mathrm{~Hz}), 3.27-3.26(1 \mathrm{H}$, m), 2.05-1.99 ( $1 \mathrm{H}, \mathrm{m}$ ), 1.92-1.86 $(1 \mathrm{H}, \mathrm{m}), 1.04(18 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $135.8,135.7,135.6,133.2,133.0,130.0,127.9,62.3,61.9,61.7,60.2,42.7,38.6,26.9$, 19.4, 19.2; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{40} \mathrm{H}_{48} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 671.3$, found 671.4 .


Table 3, Entry 3: 56\% yield ( 166 mg ). IR $v_{\text {max }}$ (neat)/cm ${ }^{1}: 3457,3070,3050,2956,2931,2875,2858,1963,1471,1428,1111,740,702 ;{ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.83-7.54(8 \mathrm{H}, \mathrm{m}), 7.44-7.27(12 \mathrm{H}, \mathrm{m}), 5.28-5.03(1 \mathrm{H}, \mathrm{m}), 4.38$ $(1 \mathrm{H}, \mathrm{q}, J=6.2 \mathrm{~Hz}), 4.27-4.07(1 \mathrm{H}, \mathrm{m}), 3.80-3.47(4 \mathrm{H}, \mathrm{m}), 2.42(1 \mathrm{H}, \mathrm{s}), 1.85-1.62$ $(2 \mathrm{H}, \mathrm{m}), 1.58(3 \mathrm{H}, \mathrm{d}, J=2.9 \mathrm{~Hz}), 1.07(9 \mathrm{H}, \mathrm{s}), 1.04(9 \mathrm{H}, \mathrm{s}), 0.91(9 \mathrm{H}, \mathrm{td}, J=7.9,4.0$ $\mathrm{Hz}), 0.56(6 \mathrm{H}, \mathrm{p}, J=7.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 200.3,200.2,135.7,135.6$,
134.1, 133.4, 133.3, 130.0, 129.9, 129.7, 127.9, 127.8, 127.7, 104.7, 91.8, 91.7, 71.2, 70.8, 70.6, 68.4, 68.3, 61.1, 60.9, 39.5, 39.2, 27.0, 19.4, 19.3, 13.4, 12.9, 7.0, 4.9; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{47} \mathrm{H}_{66} \mathrm{O}_{4} \mathrm{Si}_{3}+\mathrm{Na}\right]^{+}: 801.4$, found 801.4.


Table 3, Entry 4: 72\% yield ( 123.7 mg ). IR $v_{\max }(\mathrm{neat}) / \mathrm{cm}^{-1}$ : $3400,3071,3050,2956,2931,2894,2858,2218,1472,1428,1111,740,703 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.73-7.68(8 \mathrm{H}, \mathrm{m}), 7.48-7.40(12 \mathrm{H}, \mathrm{m}), 4.50(1 \mathrm{H}, \mathrm{d}, J=4.0 \mathrm{~Hz}), 3.84$ $(2 \mathrm{H}, \mathrm{qdd}, J=12.5,3.0,1.5 \mathrm{~Hz}), 3.78-3.69(2 \mathrm{H}, \mathrm{m}), 3.45(1 \mathrm{H}, \mathrm{dd}, J=3.5,2.5 \mathrm{~Hz}), 3.30$ $(1 \mathrm{H}, \mathrm{qt}, J=3.0,0.5 \mathrm{~Hz}), 2.90(1 \mathrm{H}, \mathrm{dd}, J=15.5,7.5 \mathrm{~Hz}), 1.91-1.80(3 \mathrm{H}, \mathrm{m}), 1.74(1 \mathrm{H}$, quind, $J=7.5,2.0 \mathrm{~Hz}), 1.09(9 \mathrm{H}, \mathrm{d}, J=1.0 \mathrm{~Hz}), 1.08(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) 135.8,135.7,135.6,133.6,133.5,133.2,133.0,130.0,129.9,128.0,127.9,127.8$, 85.1, 81.3, 64.0, 62.3, 60.2, 42.7, 35.0, 28.3, 27.0, 26.9, 19.4, 19.3; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{41} \mathrm{H}_{50} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 685.3$, found 685.3.


Table 3, Entry 4: 57\% yield ( 117.3 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3462,3071,3050,2956,2932,2873,2859,1965,1471,1428,1111,740,702$; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.67(8 \mathrm{H}, \mathrm{ddt}, J=4.8,3.2,1.8 \mathrm{~Hz}), 7.53-7.28(16 \mathrm{H}, \mathrm{m})$, $5.22-5.06(1 \mathrm{H}, \mathrm{m}), 4.31-4.17(1 \mathrm{H}, \mathrm{m}), 4.14(2 \mathrm{H}, \mathrm{t}, J=5.8 \mathrm{~Hz}), 3.79-3.50(4 \mathrm{H}, \mathrm{m}$,$) ,$ $2.47(1 \mathrm{H}, \mathrm{d}, J=12.7 \mathrm{~Hz}), 1.76-1.41(4 \mathrm{H}, \mathrm{m}), 1.61(3 \mathrm{H}, \mathrm{s}), 1.08(9 \mathrm{H}, \mathrm{d}, J=3.8 \mathrm{~Hz})$, $1.05(9 \mathrm{H}, \mathrm{d}, J=2.3 \mathrm{~Hz}), 0.94(9 \mathrm{H}, \mathrm{dd}, J=8.6,7.2 \mathrm{~Hz}), 0.58(6 \mathrm{H}, \mathrm{qd}, J=7.9,2.9 \mathrm{~Hz})$; ${ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 200.6,200.5,135.7,134.2,133.3,130.0,129.9,129.7$, $129.6,127.9,127.8,127.7,104.7,104.5,91.6,91.1,74.4,73.9,70.9,70.8,68.4,68.2$, $63.9,63.8,32.8,32.6,29.1,28.9,27.0,19.4,13.2,12.6,7.0,5.00,4.9$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{48} \mathrm{H}_{66} \mathrm{O}_{4} \mathrm{Si}_{3}+\mathrm{Na}\right]^{+}: 815.4$, found 815.4.


Table 3, Entry 5: 73\% yield ( 269.4 mg ). IR $v \max$ (neat) $/ \mathrm{cm}^{-1}$ : 3424, 3072, 3050, 2959, 2931, 2893, 2858, 2096, 1656, 1472, 1463, 1428, 1113, 1046, 823,$740 ;{ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.88-7.59(8 \mathrm{H}, \mathrm{m}), 7.59-7.31(12 \mathrm{H}, \mathrm{m}), 5.38$ $(1 \mathrm{H}, \mathrm{s}), 5.24(1 \mathrm{H}, \mathrm{s}), 5.05(1 \mathrm{H}, \mathrm{d}, J=6.4 \mathrm{~Hz}), 4.58-4.26(2 \mathrm{H}, \mathrm{m}), 3.92-3.77(2 \mathrm{H}, \mathrm{m})$, $3.53-3.42(1 \mathrm{H}, \mathrm{m}), 3.33-3.25(1 \mathrm{H}, \mathrm{m}), 3.02(1 \mathrm{H}$, apparent $\mathrm{t}, J=6.1 \mathrm{~Hz}), 1.12(9 \mathrm{H}, \mathrm{s})$, 1.10 (9H, s); ${ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ (* indicates diastereoisomeric signal)145.3, 135.7, 135.7, 135.6*, 133.1, 132.9, 130.0, 123.0, 127.9, 113.9, 82.9, 82.6, 65.3, 65.2*, $64.6,62.2,60.1,42.6,26.9,26.8,19.4,19.3$; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{41} \mathrm{H}_{48} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}$: 683.3, found 683.3.


Table 3, Entry 5: $59 \%$ yield ( 249.0 mg ). IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}$ : $3471,3072,3050,2931,2957,2859,2859,1970,1471,1463,1428,1364,1252,1113$, $1070,884,842,825,740 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (* indicates diastereoisomeric signal) $7.71-7.55(8 \mathrm{H}, \mathrm{m}), 7.48-7.28(12 \mathrm{H}, \mathrm{m}), 5.32(1 \mathrm{H}, \mathrm{s})^{*}, 5.29(1 \mathrm{H}, \mathrm{s}), 5.21(1 \mathrm{H}$, s)*, $5.19(1 \mathrm{H}, \mathrm{s}), 5.17-5.10(1 \mathrm{H}, \mathrm{m})^{*}, 5.05-5.00(1 \mathrm{H}, \mathrm{m}), 4.63(1 \mathrm{H}, \mathrm{s}), 4.21-4.15(1 \mathrm{H}$, $\mathrm{m})^{*}, 4.13(2 \mathrm{H}, \mathrm{s}), 4.07-3.99(1 \mathrm{H}, \mathrm{m}), 3.66-3.54(2 \mathrm{H}, \mathrm{m}), 2.36(1 \mathrm{H}, \mathrm{d}, J=4.0 \mathrm{~Hz})^{*}$, $2.26(1 \mathrm{H}, \mathrm{d}, J=4.7 \mathrm{~Hz}), 1.49(3 \mathrm{H}, \mathrm{s}), 1.48(3 \mathrm{H}, \mathrm{s})^{*}, 1.06(18 \mathrm{H}, \mathrm{s}), 0.90-0.80(6 \mathrm{H}, \mathrm{m})$, $0.07-0.05(9 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \mathrm{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ (* indicates diastereoisomeric signal) 201.0, 200.9*, 148.1, 144.0*, 135.7, 133.7, 133.3, 129.9, 129.8, 127.9, 127.8, 113.9, $110.1^{*}, 103.5^{*}, 103.4,92.2^{*}, 92.0,74.1,73.4^{*}, 70.7,70.6^{*}, 68.2,68.1^{*}, 64.0^{*}, 63.9,27.0$, 26.9*, 19.4, 13.3, -0.0; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{48} \mathrm{H}_{66} \mathrm{O}_{4} \mathrm{Si}_{3}+\mathrm{Na}\right]^{+}: 813.4$, found 813.4.


Table 3, Entry 6: 77\% yield ( 101.6 mg ). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3422$, 3072, 3051, 2956, 2932, 2860, 2063, 1636, 1428, 1112, 740, 703; ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.67-7.65(4 \mathrm{H}, \mathrm{m}), 7.45-7.37(6 \mathrm{H}, \mathrm{m}), 4.25(1 \mathrm{H}, \mathrm{d}, J=6.5 \mathrm{~Hz}), 3.81(2 \mathrm{H}, \mathrm{qd}, J=$ $12,2.5 \mathrm{~Hz}), 3.39(1 \mathrm{H}, \mathrm{s}), 3.26(1 \mathrm{H}, \mathrm{m}), 2.17(1 \mathrm{H}, \operatorname{sexd}, J=8.0,0.5 \mathrm{~Hz}) ; 1.82-1.74(2 \mathrm{H}$, $\mathrm{m}), 1.68-1.53(4 \mathrm{H}, \mathrm{m}), 1.47-1.38(2 \mathrm{H}, \mathrm{m}), 1.26(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{27} \mathrm{H}_{34} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 457.2$, found 457.2.


Table 3, Entry 6: $47 \%$ yield $(89.1 \mathrm{mg})$. IR $v_{\text {max }}($ neat $) / \mathrm{cm}^{-1}$ : $3444,3072,2957,2926,2856,1957,1463,1112,704,702 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$; ${ }^{13} \mathrm{C}$ NMR( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) ; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{34} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 587.4$, found 587.4.


Table 3, Entry 7: 72\% yield ( 126.6 mg ). IR $\nu_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3070$, 2958, 2930, 2858, 2209, 1472, 1455, 1428, 1112, 740, 700; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.71-7.68(4 \mathrm{H}, \mathrm{m}), 7.55(2 \mathrm{H}, \mathrm{d}, J=7.5 \mathrm{~Hz}), 7.48-7.35(9 \mathrm{H}, \mathrm{m}), 5.51(1 \mathrm{H}, \mathrm{d}, J=3.0 \mathrm{~Hz})$, $3.85(2 \mathrm{H}$, qdd, $J=12.0,2.5,1.0 \mathrm{~Hz}), 3.49(1 \mathrm{H}, \mathrm{s}), 3.34(1 \mathrm{H}$, quin, 2.5 Hz$), 2.42(1 \mathrm{H}, \mathrm{s})$, $1.08(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $140.1,135.7,135.6,133.1,132.9,130.0,128.8$, 128.7, 127.9, 126.7, 83.7, 83.1, 64.7, 62.2, 60.2, 42.7, 26.8, 19.4; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{28} \mathrm{H}_{30} \mathrm{O}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 465.2$, found 465.1.


Table 3, Entry 7: $51 \%$ yield ( 112.3 mg ). IR $v_{\text {max }}$ (neat)/ $\mathrm{cm}^{-1}$ : 3071, 2932, 2875, 1968, 1462, 1428, 1113, 1064, 739, 700; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.68(4 \mathrm{H}, \mathrm{d}, J=7.1 \mathrm{~Hz}), 7.44-7.32(6 \mathrm{H}+2 \mathrm{H}, \mathrm{m}), 7.28-7.20(3 \mathrm{H}, \mathrm{m}), 5.29(1 \mathrm{H}, \mathrm{s}), 5.26$ $-5.22(1 \mathrm{H}, \mathrm{m}), 4.25(1 \mathrm{H}, \mathrm{p}, J=5.4 \mathrm{~Hz}), 3.90-3.45(2 \mathrm{H}, \mathrm{m}), 2.38(\mathrm{dd}, J=28.4,4.2 \mathrm{~Hz})$, $1.51(3 \mathrm{H}, \mathrm{dd}, J=12.4,2.9 \mathrm{~Hz}), 1.08(9 \mathrm{H}, \mathrm{s}), 1.03-0.77(9 \mathrm{H}, \mathrm{m}), 0.60(6 \mathrm{H}, \mathrm{qd}, J=7.5$, $4.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 201.0,143.3,135.7,133.4,133.3,130.0,129.9$, 129.4, 128.0, 127.9, 127.2, 127.0, 126.5, 126.1, 125.9, 125.8, 123.6, 106.3, 106.2, 92.3, $91.8,75.8,75.7,70.7,68.2,68.1,42.9,27.0,25.7,23.2,19.4,14.1,13.6,12.9,7.0,6.9$, 4.9; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{48} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}$: 595.3, found 595.4.


Table 3, Entry 8: 97\% yield ( 95.4 mg ). IR $v_{\text {max }}$ (neat)/ $\mathrm{cm}^{-1}: 3072$, 2958, 2931, 2858, 2207, 1637, 1487, 1253, 1113, 740, 703, 690; ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.70-7.68(4 \mathrm{H}, \mathrm{m}), 7.47-7.41(8 \mathrm{H}, \mathrm{m}), 6.93(2 \mathrm{H}, \mathrm{d}, J=8.5 \mathrm{~Hz}), 5.45(1 \mathrm{H}, \mathrm{s})$, 3.88-3.80 $(2 \mathrm{H}, \mathrm{m}), 3.49(1 \mathrm{H}, \mathrm{s}), 3.33(1 \mathrm{H}, \mathrm{s}), 2.33(1 \mathrm{H}, \mathrm{s}, \mathrm{br}), 1.07(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 159.9, 135.7, 135.6, 133.1, 132.9, 132.4, 130.0, 128.2, 127.9, 114.1, 83.9, 82.9, 64.3, 62.3, 60.2, 55.5, 42.7, 26.8, 19.4; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{32} \mathrm{O}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}$: 495.2, found .495.2.


Table 3, Entry 8: 6\% yield ( 16.2 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-}$ ${ }^{\prime}: 3073,2958,2933,2875,2859,2067,1970,1640,1510,1428,1113,1007,740,702 ;{ }^{1} \mathrm{H}$ NMR (500 MHz, CDCl 3 ) $7.73-7.59(4 \mathrm{H}, \mathrm{m}), 7.54-7.30(6 \mathrm{H}, \mathrm{m}), 7.32-7.11(2 \mathrm{H}, \mathrm{m})$, $6.87-6.72(2 \mathrm{H}, \mathrm{m}), 5.42-5.07(1 \mathrm{H}, \mathrm{m}), 5.24(1 \mathrm{H}, \mathrm{s}), 4.33-4.17(1 \mathrm{H}, \mathrm{m}), 3.80-3.58$ $(2 \mathrm{H}, \mathrm{m}), 3.76(3 \mathrm{H}, \mathrm{d}, J=6.0 \mathrm{~Hz}), 2.42(1 \mathrm{H}, \mathrm{dd}, J=24.7,4.1 \mathrm{~Hz}), 1.50(3 \mathrm{H}, \mathrm{dd}, J=11.9$, $2.9 \mathrm{~Hz}), 1.11-1.05(9 \mathrm{H}, \mathrm{m}), 1.00-0.76(9 \mathrm{H}, \mathrm{m}), 0.66-0.48(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR(125 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 200.9, 200.8, 158.9, 158.7, 135.7, 135.5, 135.1, 134.9, 133.3, 129.9, 129.8, $127.9,127.8,127.2,127.0,113.4,106.5,106.4,92.3,91.8,75.5,75.3,70.7,68.2,68.1$, $55.3,27.0,26.7,25.8,19.4,13.6,12.9,7.0,6.9,6.7,6.0,4.9$; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{36} \mathrm{H}_{48} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 611.3$, found 611.2.


Table 3, Entry 9: 75\% yield (112 mg). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 3071$, 2958, 2930, 2894, 2858, 1472, 1463, 1428, 1113, 1091, 823, 740; ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.66-7.63(4 \mathrm{H}, \mathrm{m}), 7.44-7.33(10 \mathrm{H}, \mathrm{m}), 5.44(1 \mathrm{H}, \mathrm{d}, J=4.0 \mathrm{~Hz}), 3.81(2 \mathrm{H}, \mathrm{qd}, J$ $=11,2.5 \mathrm{~Hz}), 3.44(1 \mathrm{H}, \mathrm{s}), 3.29(1 \mathrm{H}$, quin, $J=2.5 \mathrm{~Hz}), 2.35(1 \mathrm{H}, \mathrm{s}), 1.03(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$

NMR(125 MHz, CDCl3) 138.5, 135.8, 135.6, 134.5, 133.1, 132.9, 130.0, 128.9, 128.1, $127.9,83.5,83.5,83.3,83.2,64.0,62.1,60.2,42.6,26.8,19.4$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{28} \mathrm{H}_{29}{ }^{35} \mathrm{ClO}_{3} \mathrm{Si}+\mathrm{Na}\right]^{+}: 499.2$, found 499.1.


Table 3, Entry 9: $48 \%$ yield ( 99 mg ). IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}$ : 3426, 3072, 3050, 2957, 2932, 2876, 2859, 1970, 1462, 1428, 1113, 1090, 1014, 846, 824, 740,$701 ;{ }^{1} \mathrm{H}$ NMR ( $\left.500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.74-7.58(4 \mathrm{H}, \mathrm{m}), 7.50-7.32(6 \mathrm{H}, \mathrm{m}), 7.33-$ $7.12(4 \mathrm{H}, \mathrm{m}), 5.25-5.22(1 \mathrm{H}, \mathrm{m}), 5.23(1 \mathrm{H}, \mathrm{s}), 4.31-4.20(1 \mathrm{H}, \mathrm{m}), 3.77-3.52(2 \mathrm{H}, \mathrm{m})$, $2.54-2.41(1 \mathrm{H}, \mathrm{d}, J=21.0 \mathrm{~Hz}), 1.47(3 \mathrm{H}, \mathrm{dd}, J=13.5,2.7 \mathrm{~Hz}), 1.08(9 \mathrm{H}, \mathrm{d}, J=1.6$ $\mathrm{Hz}), 0.90(9 \mathrm{H}, \mathrm{tdd}, J=11.2,7.4,4.7 \mathrm{~Hz}), 0.59(6 \mathrm{H}, \mathrm{qd}, J=7.6,2.1 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}(125$ $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 201.0, 200.9, 141.8, 135.7, 133.3, 133.2, 132.7, 130.0, 128.2, 128.0, 127.9, $127.4,127.3,105.9,105.7,92.4,91.8,75.4,75.1,70.7,70.6,68.2,68.1,27.0,19.4,13.4$, 12.7, 6.9, 4.9; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{47}{ }^{35} \mathrm{ClO}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 629.3$, found 629.3.


Table 3, Entry 10: 70\% yield ( 91.6 mg ). IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}$ : $3425,3072,3050,2957,2931,2894,2858,1524,1348,1113,1043,1013,852,739,702$; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 8.23(2 \mathrm{H}, \mathrm{d}, J=3.5 \mathrm{~Hz}), 7.69(2 \mathrm{H}, J=3.5 \mathrm{~Hz}), 7.45-7.37$ $(6 \mathrm{H}, \mathrm{m}), 5.58(1 \mathrm{H}, \mathrm{s}), 3.83(2 \mathrm{H}, \mathrm{qd}, J=12.0,2.5 \mathrm{~Hz}), 3.46(1 \mathrm{H}, \mathrm{s}), 3.32-3.30(1 \mathrm{H}, \mathrm{m})$, $2.69(1 \mathrm{H}, \mathrm{s}, \mathrm{br}), 1.04(9 \mathrm{H}, \mathrm{d}, J=2.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 148.0,146.8$, 135.7, 135.6, 133.1, 132.8, 130.0, 127.9, 127.5, 124.0, 84.2, 82.5, 63.6, 63.5, 62.0, 60.3, 60.2, 42.5, 26.9, 26.8, 19.4; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{28} \mathrm{H}_{29} \mathrm{NO}_{5} \mathrm{Si}+\mathrm{Na}\right]^{+}$: 510.2, found 510.1.


Table 3, Entry 11-13: 83\% yield ( 99 mg ). IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}$ : 3416, 3071, 3050, 2958, 2931, 2894, 2858, 1601, 1488, 1471, 1428, 1262, 1113, 1042, 823, 791, $741 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.70-7.68(4 \mathrm{H}, \mathrm{m}), 7.47-7.40(6 \mathrm{H}, \mathrm{m}), 7.32$ $(1 \mathrm{H}, \mathrm{t}, J=8.0 \mathrm{~Hz}), 7.13-7.10(2 \mathrm{H}, \mathrm{m}), 6.90(1 \mathrm{H}, \mathrm{dt}, J=8.5,1.0 \mathrm{~Hz}), 5.48(1 \mathrm{H}, \mathrm{d}, J=5.0$ $\mathrm{Hz}), 3.88-3.80(2 \mathrm{H}, \mathrm{m}), 3.48(1 \mathrm{H}, \mathrm{s}), 3.35-3.32(1 \mathrm{H}, \mathrm{m}), 2.46(1 \mathrm{H}, \mathrm{t}, J=5.0 \mathrm{~Hz}), 1.07$ $(9 \mathrm{H}, \mathrm{d}, J=1.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 159.9,141.7,135.7,135.6,133.1,132.9$, $130.0,127.9,119.0,114.3,112.2,83.6,83.1,83.0,64.5,62.1,60.2,55.4,42.7,26.8$, 19.4; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{32} \mathrm{O}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}: 495.2$, found 495.3.


Table 3, Entry 11: 51\% yield ( 211.5 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3427,3071,3050,2999,2957,2875,2858,1960,1705,1600,1589,1487$, $1463,1428,1262,1113,1008,824,740 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.77-7.57(4 \mathrm{H}$, $\mathrm{m}), 7.49-7.28(6 \mathrm{H}+1 \mathrm{H}, \mathrm{m}), 7.13(1 \mathrm{H}, \mathrm{dt}, J=9.9,7.9 \mathrm{~Hz}), 6.93(1 \mathrm{H}, \mathrm{dd}, J=15.2,2.2$ $\mathrm{Hz}), 6.89-6.81(1 \mathrm{H}, \mathrm{m}), 6.73(1 \mathrm{H}, \mathrm{ddd}, J=6.5,3.0,1.6 \mathrm{~Hz}), 5.49-5.15(3 \mathrm{H}, \mathrm{m}), 4.27$ $(1 \mathrm{H}$, dddd, $J=12.8,10.8,5.2,3.2 \mathrm{~Hz}), 3.76(3 \mathrm{H}, \mathrm{d}, J=4.3 \mathrm{~Hz}), 3.75-3.52(2 \mathrm{H}, \mathrm{m})$, $1.06(9 \mathrm{H}, \mathrm{d}, J=6.2 \mathrm{~Hz}), 1.01-0.65(9 \mathrm{H}, \mathrm{m}), 0.68-0.45(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \mathrm{NMR}(125 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ) 202.6, 159.6, 145.8, 145.7, 135.7, 134.9, 130.0, 129.8, 129.2, 127.9, 127.8, 118.3, $118.2,112.9,112.8,111.3,111.2,99.5,99.4,93.8,93.4,73.4,73.0,70.4,70.2,68.0,67.9$, $55.3,55.2, ~ 27.0, ~ 26.7, ~ 19.4, ~ 14.3, ~ 6.9, ~ 5.0, ~ 4.9 ; ~(E S I / M S) ~ m / z ~ C a l c d ~ f o r ~$ $\left[\mathrm{C}_{35} \mathrm{H}_{48} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 611.3$, found 611.4.


Table 3, Entry 12: 70\% yield ( 136.2 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}-$ ${ }^{\prime}: 3388,3071,3050,2957,2932,2875,2858,1600,1588,1487,1462,1428,1260,1113$, $1007,824,740 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.80-7.52(4 \mathrm{H}, \mathrm{m}), 7.50-7.27(6 \mathrm{H}, \mathrm{m})$, $7.19(1 \mathrm{H}, \mathrm{td}, J=7.8,3.3 \mathrm{~Hz}), 7.04(1 \mathrm{H}, \mathrm{s}), 7.01(1 \mathrm{H}, \mathrm{d}, J=7.8 \mathrm{~Hz}), 6.79(1 \mathrm{H}, \mathrm{dd}, J=$ $8.4,2.4 \mathrm{~Hz}), 5.44(1 \mathrm{H}, \mathrm{d}, J=2.4 \mathrm{~Hz}), 3.77(3 \mathrm{H}, \mathrm{d}, J=2.0 \mathrm{~Hz}), 3.72-3.67(1 \mathrm{H}, \mathrm{m}), 3.60$ $(1 \mathrm{H}, \mathrm{q}, J=5.2 \mathrm{~Hz}, 1 \mathrm{H}), 2.87(1 \mathrm{H}, \mathrm{dtd}, J=8.7,6.1,5.6,2.9 \mathrm{~Hz}), 2.21(1 \mathrm{H}, \mathrm{t}, J=6.1 \mathrm{~Hz})$, $1.21(3 \mathrm{H}, \mathrm{dt}, J=7.2,2.1 \mathrm{~Hz}), 1.05(9 \mathrm{H}, \mathrm{s}), 1.00-0.89(9 \mathrm{H}, \mathrm{m}), 0.66(6 \mathrm{H}, \mathrm{qd}, J=7.8$, $3.4 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 159.7,143.8,135.7,135.6,133.4,133.3,129.9$, 129.4, 128.0, 127.9, 118.6, 113.5, 113.4, 111.6, 111.5, 86.1, 83.9, 74.4, 65.8, 64.6, 64.5, 55.3, 29.6, 29.5, 27.2, 27.0, 24.7, 19.4, 17.1, 13.9, 7.0; (ESI/MS) m/z Calcd for $\left[2 \mathrm{xC}_{36} \mathrm{H}_{50} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 1227.6$, found 1226.5.


Table 3, Entry 13: $52 \%$ yield ( 101.5 mg ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3426,3071,3049,2932,2875,2858,1969,1589,1488,1428,1194,1113$, $1070,861,824,741 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.67(4 \mathrm{H}, \mathrm{dtd}, J=6.5,2.5,1.4 \mathrm{~Hz})$, $7.40(6 \mathrm{H}$, ddtd, $J=18.6,8.8,6.8,1.8 \mathrm{~Hz}), 7.32(1 \mathrm{H}, \mathrm{dd}, J=8.7,7.2 \mathrm{~Hz}), 7.20-7.09(2 \mathrm{H}$, m), $6.95-6.88(1 \mathrm{H}, \mathrm{m}), 6.78-6.72(1 \mathrm{H}, \mathrm{m}), 5.31-5.21(1 \mathrm{H}, \mathrm{m}), 5.27(1 \mathrm{H}, \mathrm{s}), 4.26(1 \mathrm{H}$, dddd, $J=10.2,6.3,5.1,3.0 \mathrm{~Hz}), 3.78(3 \mathrm{H}, \mathrm{d}, J=1.8 \mathrm{~Hz}), 3.76-3.46(2 \mathrm{H}, \mathrm{m}), 2.41(1 \mathrm{H}$, dd, $J=28.5,4.1 \mathrm{~Hz}), 1.51(3 \mathrm{H}, \mathrm{dd}, J=13.2,2.7 \mathrm{~Hz}), 1.13-1.00(9 \mathrm{H}, \mathrm{m}), 0.93(9 \mathrm{H}, \mathrm{td}, J$ $=7.9,3.6 \mathrm{~Hz}), 0.74-0.42(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 201.1,201.0,159.5$, 145.1, 135.7, 134.9, 133.4, 133.3, 130.0, 129.9, 129.8, 129.0, 127.9, 127.8, 124.4, 120.9, $120.8,118.5,118.3,112.6,112.5,111.6,111.5,106.1,106.0,92.3,91.8,75.7,75.6,70.8$, $70.7,68.3,68.2,55.3,55.2,27.0,26.7,19.4,13.5,12.9,7.0,6.9,4.9$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{36} \mathrm{H}_{50} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 625.3$, found 625.5.


OTBDPS 1.15.4: $48 \%$ yield ( 85.0 mg ). IR $v_{\max }(\mathrm{neat}) / \mathrm{cm}^{-1}: 3470,3071$, 3050, 2956, 2931, 2894, 2858, 1726, 1588, 1442, 1428, 1378, 1338, 1316, 1283, 1258, $1113,1012,740 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.82-7.58(4 \mathrm{H}, \mathrm{m}), 7.54-7.32$ ( $6 \mathrm{H}, \mathrm{m}$ ), $6.87-6.78(1 \mathrm{H}, \mathrm{m})$ (rotamers), $6.76-6.65(1 \mathrm{H}, \mathrm{m}), 6.10-5.95(1 \mathrm{H}, \mathrm{m}), 5.73-5.27(3 \mathrm{H}$, $\mathrm{m}), 3.90-3.80(4 \mathrm{H}, \mathrm{m}), 3.80-3.72(1 \mathrm{H}, \mathrm{m}), 3.44-3.37(1 \mathrm{H}, \mathrm{m}), 3.30-3.22(1 \mathrm{H}, \mathrm{m})$, $1.04(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ (* indicates diastereoisomeric signal) 153.6, 135.7, 135.6*, 133.2, 132.9*, 129.9, 127.9, 124.7, 122.5, 118.3, 105.6, 81.3, 79.6, 62.1, 60.1, 53.7, 43.5, 42.6, 26.8, 19.3; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{28} \mathrm{H}_{31} \mathrm{NO}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}: 496.2$, found. 496.3

1.16.4: $45 \%$ yield ( 83.0 mg ). IR $\nu_{\max }$ (neat) $/ \mathrm{cm}^{-1}: 3471,3071,3050$, 2956, 2930, 2858, 1996, 1721, 1587, 1442, 1428, 1334, 1264, 1113, 1021, 824, 740; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.74-7.58(4 \mathrm{H}, \mathrm{m}), 7.48-7.30(6 \mathrm{H}, \mathrm{m}), 6.66(1 \mathrm{H}, \mathrm{d}, J=7.6$ $\mathrm{Hz}), 6.57(1 \mathrm{H}, \mathrm{d}, J=7.4 \mathrm{~Hz}$ (rotamers?), $5.95-5.82(1 \mathrm{H}, \mathrm{m}), 5.59-4.97(4 \mathrm{H}, \mathrm{m}), 4.27$ $-4.15(1 \mathrm{H}, \mathrm{m}), 3.81-3.46(5 \mathrm{H}, \mathrm{m}), 1.81-1.60(3 \mathrm{H}, \mathrm{m}), 1.12-0.96(9 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (* indicates diastereoisomeric signal) 199.5, 154.2, 135.7, 133.4, $129.9,129.8^{*}, 127.9,127.8^{*}, 126.7,125.9,125.7^{*}, 122.1,122.0^{*}, 120.3,105.5,104.5^{*}$, 94.9*, 93.9, 67.0*, 69.7, 68.4*, 67.8, 57.2, 53.5, 53.4*, 27.0, 19.4*, 14.7*, 13.3; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{35} \mathrm{NO}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}: 512.2$, found 512.2.

1.15.5: $61 \%$ yield $(257.2 \mathrm{mg})$. IR $v_{\text {max }}($ neat $) / \mathrm{cm}^{-1}: 3435$, 3072, 2960, 2727, 2252, 1728, 1713, 1667, 1574, 1455, 1428, 1113, 1020, 913, 883, 823, 741 ; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.72-7.57(5 \mathrm{H}, \mathrm{m}), 7.49-7.24(9 \mathrm{H}, \mathrm{m}), 7.21-7.07$ $(1 \mathrm{H}, \mathrm{m}), 4.97-4.81(1 \mathrm{H}, \mathrm{m}), 3.83-3.63(2 \mathrm{H}, \mathrm{m}), 3.41-2.99(3 \mathrm{H}, \mathrm{m}), 2.41(1 \mathrm{H}, \mathrm{dd}, J=$ $15.4,5.9 \mathrm{~Hz}), 2.33-1.46(7 \mathrm{H}, \mathrm{m}), 1.41-0.74(42 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $195.0,152.9,151.6,146.9,135.7,135.6,133.0,132.8,129.9,128.2,127.9,125.2,111.4$, 80.1, 78.1, 62.0, 59.9, 50.4, 43.9, 42.0, 41.8, 41.5, 39.3, 34.5, 31.5, 26.8, 26.2, 21.8, 19.3, 18.9, 11.2; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{52} \mathrm{H}_{71} \mathrm{NO}_{5} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 868.5$, found 868.4.

1.16.5: $70 \%$ yield ( 1.816 g ). IR $v_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3416$, 3071, 3052, 2957, 2929, 2864, 1970, 1721, 1661, 1574, 1462, 1428, 1301, 1246, 1113, $883,824,766,741 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.78-7.57(5 \mathrm{H}, \mathrm{m}), 7.49-7.18(9 \mathrm{H}, \mathrm{m})$, $7.14-7.01(1 \mathrm{H}, \mathrm{m}), 5.35-5.04(1 \mathrm{H}, \mathrm{m}), 5.01-4.79(1 \mathrm{H}, \mathrm{m}), 4.38-4.06(2 \mathrm{H}, \mathrm{m}), 3.78$ $-3.52(2 \mathrm{H}, \mathrm{m}), 3.28-3.10(1 \mathrm{H}, \mathrm{m}), 2.82-1.62(7 \mathrm{H}, \mathrm{m}), 1.59-0.64(46 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR(125 MHz, $\mathrm{CDCl}_{3}$ ) 200.7, 196.3, 152.8, 152.4, 147.2, 135.7, 133.2, 129.8, 128.2, $128.1,127.8,125.1,111.3,100.0,94.8,78.1,67.9,65.9,52.4,50.2,41.7,40.5,39.3,34.6$, $31.45, \quad 26.9, \quad 26.3, \quad 21.9, \quad 19.4, \quad 18.9,15.8, \quad 11.3$; (ESI/MS) $m / z$ Calcd for $\left[2 \mathrm{X}\left(\mathrm{C}_{53} \mathrm{H}_{75} \mathrm{NO}_{5} \mathrm{Si}_{2}\right)+\mathrm{Na}\right]^{+}: 1746.0$, found 1745.7.


To a solution of 1.16.2.1 ( $319.0 \mathrm{mg}, 0.532 \mathrm{mmol}$ ) in DCM ( $1.1 \mathrm{~mL}, 0.5 \mathrm{M}$ ) was added triethylamine $(111 \mu \mathrm{~L}, 0.798 \mathrm{mmol})$, acetic anhydride ( $65 \mu \mathrm{~L}, 0.692 \mathrm{mmol}$ ) and DMAP $(6.5 \mathrm{mg}, 0.0532 \mathrm{mmol})$ at $0^{\circ} \mathrm{C}$. The reaction mixture was allowed to slowly warm up to room temperature and stirred overnight. 10 mL sat. $\mathrm{NH}_{4} \mathrm{Cl}$ was added to the solution and diethyl ether was used for extraction twice ( 15 mL X 2). The combined organic layers was dried over sodium sulfate, filtered, and concentrated on rotavap to give pale yellow oil as the crude product, which was dissolved in methanol ( $13 \mathrm{~mL}, 0.04 \mathrm{M}$ ). Catalytic PPTS $(13.4 \mathrm{mg}, 0.0532 \mathrm{mmol})$ was added to the solution above at room temperature. After 30 min , the reaction mixture was quenched with saturated aq. $\mathrm{NaHCO}_{3}(10 \mathrm{~mL})$ and extracted with diethyl ether ( 20 mL X 3 ). The combined organic layers was dried over sodium sulfate, filtered, and concentrated on rotavap to give a crude product, which was purified by FCC (ethyl actate/hexane) to give colorless oil as the product in $83 \%$ yield over two steps ( 231.1 mg ).

${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) (* indicates diastereoisomeric signal) $7.77-7.66(4 \mathrm{H}, \mathrm{m}), 7.50-7.36(6 \mathrm{H}, \mathrm{m}), 7.36-7.08(5 \mathrm{H}, \mathrm{m}), 5.30-5.19(2 \mathrm{H}$, $\mathrm{m}), 4.10-3.99(1 \mathrm{H}, \mathrm{m}), 3.88-3.76(2 \mathrm{H}, \mathrm{m}), 3.68(1 \mathrm{H}, \mathrm{dt}, J=13.7,9.1 \mathrm{~Hz}), 2.88-2.62$ $(2 \mathrm{H}, \mathrm{m}), 2.05-2.01(3 \mathrm{H}, \mathrm{m}), 2.00-1.75(2 \mathrm{H}, \mathrm{m}), 1.70(3 \mathrm{H}, \mathrm{s}), 1.16-0.99(9 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR(125 MHz, $\mathrm{CDCl}_{3}$ ) (* indicates diastereoisomeric signal) 202.0, 201.7*, 171.4, 171.0*, 142.3, 142.2*, 135.7, 133.3, 129.9, 129.8*, 128.4, 127.8, 125.9, 125.8*, 106.2, 105.6*, 90. 9, 90.3*, 75.1, 74.6*, 71.6, 71.2*, 65.5, 36.9, 36.8*, 31.8, 31.7*, 26.8, 21.4, 21.3*, 19.4, 15.3, 14.5*; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{33} \mathrm{H}_{40} \mathrm{O}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}$: 551.3, found 551.3.
$174.1 \mathrm{mg}(0.330 \mathrm{mmol})$ of the alcohol obtained above was subjected to DCM ( 3.3 mL , $0.1 \mathrm{M})$ and to the resulted clear solution was added Dess-Martin reagent ( $210.0 \mathrm{mg}, 0.495$ mmol ) at room temperature. After 30 min , to the reacction mixture was added $50 \mathrm{~mL} 10 \%$ aq. $\mathrm{NaHCO}_{3}$ in sat. aq. $\mathrm{Na}_{2} \mathrm{~S}_{2} \mathrm{O}_{3}$. The suspension was filtered through Celite and the filtrate was extracted with DCM three times ( 40 mL X 3 ). The combined organic layers was dried over sodium sulfate, filtered, and concentrated on rotavap to give a crude product, which was purified by FCC (ethyl actate/hexane: $5 \%$ to $10 \%$ ) to give colorless oil 1.23 in $86 \%$ yield ( 149.6 mg ).

$1.23{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.72-7.59(\mathrm{~m}, 4 \mathrm{H}), 7.49-$ $7.33(\mathrm{~m}, 6 \mathrm{H}), 7.31-7.09(\mathrm{~m}, 5 \mathrm{H}), 5.60-5.54(\mathrm{~m}, 1 \mathrm{H}), 5.49-5.40(\mathrm{~m}, 1 \mathrm{H}), 3.88-3.73$ $(\mathrm{m}, 2 \mathrm{H}), 2.97-2.80(\mathrm{~m}, 4 \mathrm{H}), 1.97-1.90(\mathrm{~m}, 3 \mathrm{H}), 1.80-1.71(\mathrm{~m}, 3 \mathrm{H}), 1.06(\mathrm{~s}, 9 \mathrm{H}){ }^{13} \mathrm{C}$ NMR(100 MHz, $\left.\mathrm{CDCl}_{3}\right) 212.4,200.0,170.1,141.4,135.7,133.2,133.1,130.0,128.5$, 127.9, 126.1, 106.0, 92.4, 71.8, 65.4, 40.8, 30.7, 26.9, 21.0, 19.4, 13.3; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{33} \mathrm{H}_{38} \mathrm{O}_{4} \mathrm{Si}+\mathrm{Na}\right]^{+}: 549.3$, found 549.3.

### 6.3. Chapter II

## Allene Synthesis

General Procedure for Synthesis of Protected Alkynols




A
B
C

To a solution of the commercially available alkynol in dry $\mathrm{DCM}(0.4 \mathrm{M})$ at $0{ }^{\circ} \mathrm{C}$ was added imidazole ( 1.5 equiv.) and the silyl chloride ( 1.05 equiv.) dropwise. The colorless suspension was warmed to room temperature. After 20 min , the reaction was quenched with excess sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ solution. The aqueous layer was removed and extracted with DCM (x 3). The combined organic phases were dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated to crude pale yellow oil. Purification by FCC (100\% hexane to $92: 8$ hexane:ethyl acetate) afforded the silyl alkynyl ethers $\mathbf{A}(9.01 \mathrm{~g}, 91 \%), \mathbf{B}(9.42 \mathrm{~g}, 98 \%)$, and $\mathbf{C}(11.55 \mathrm{~g}$, quant.) as colorless or pale yellow oils. Their respective characterization data matched those previously reported in the literature. ${ }^{1-3}$

General Procedure for One-Pot Synthesis of Racemic Allenes


To a solution of TBDPS-protected terminal alkyne in dry THF ( 0.2 M ) was added $n$ - BuLi (1.05 equiv., 2.5 M in THF) dropwise at $-78^{\circ} \mathrm{C}$. After stirring for half an hour, a solution of aldehyde ( 1.0 equiv.) in dry THF ( 0.8 M ) was added dropwise. The cooling bath was removed, and the reaction was complete in 2-3 hours with continuous stirring (monitored by TLC). The reaction mixture was then cooled to $-40^{\circ} \mathrm{C}$, and MsCl ( 1.5 equiv.) was added dropwise, then the reaction was stirred for 1 hr . To a suspension of activated copper (I) cyanide ( 2.75 equiv.) in dry THF at $-40^{\circ} \mathrm{C}$ was added methyl lithium (2.75 equiv., 1.6 M in THF) slowly. After stirring for 10 min , a colorless homogeneous cuprate solution was formed, which was then added slowly to the mesylate solution at $-40{ }^{\circ} \mathrm{C}$. The reaction mixture was stirred for 2 hrs (monitored by TLC) and quenched with $10 \%$
$\mathrm{NH}_{3} / \mathrm{NH}_{4} \mathrm{Cl}$ sat. solution. After stirring for 30 min , the reaction mixture was diluted with ethyl acetate and the blue aqueous solution was removed. The organic phase was washed with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ and brine, dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. The residue was then dried in vacuo. The crude allene was used directly in the next step without further purification. To a solution of the allene in dry THF was added TBAF (2 equiv., 1.0 M in THF) at room temperature. After stirring for 1 hr , the reaction mixture was washed with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ and brine, dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$, and filtered. The solvent was removed by rotovap and the residue was purified by FCC (95:5 hexane:ethyl acetate) to give the pure allenol product as a colorless oil.


## 1a

Synthesized in $82 \%$ yield ( 208.4 mg ). IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3443.7,2956.4,2925.8,2855.7$, 1958.9, 1451.5, 1383.3, 1092.9; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 5.04-5.00(1 \mathrm{H}, \mathrm{m}), 3.66$ $(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 2.02-1.93(4 \mathrm{H}, \mathrm{m}), 1.76(1 \mathrm{H}, \mathrm{s}), 1.68(3 \mathrm{H}, \mathrm{s}), 1.72-1.66(2 \mathrm{H}, \mathrm{m})$, $1.40-1.30(4 \mathrm{H}, \mathrm{m}), 0.90(3 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 201.1,98.7$, $90.8,62.7,31.5,30.7,30.4,29.1,22.2,19.4,14.0 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{20} \mathrm{ONa}[\mathrm{M}+\mathrm{Na}]^{+}$191.1, found: 190.8 .


1b

Synthesized in $75 \%$ yield ( 2.5077 g ). IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3357.9$, 2954.3, 2869.3, 1964.4, $1465.4,1442.8,1382.7,1060.0,1017.9,917.9,833.7 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ $5.02-4.91(1 \mathrm{H}, \mathrm{m}), 3.65(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 2.03-1.96(2 \mathrm{H}, \mathrm{m}), 1.82(2 \mathrm{H}, \mathrm{t}, J=6.9 \mathrm{~Hz})$, $1.67(3 \mathrm{H}, \mathrm{s}), 1.73-1.56(3 \mathrm{H}, \mathrm{m}), 0.90(6 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ 201.8, 98.0, 89.7, 62.7, 39.0, 30.6, 28.7, 22.5, 22.4, 19.4; m/z (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{20} \mathrm{ONa}[\mathrm{M}+\mathrm{Na}]^{+}$191.1, found: 190.7 .


1c

Synthesized in $70 \%$ yield ( 150.2 mg ). IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3447.5,2929.1,2854.1,1961.0$, $1718.0,1448.8,1374.8,1164.5,1069.4 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 5.04-4.99(1 \mathrm{H}$, m), $3.66(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 2.02-1.87(3 \mathrm{H}, \mathrm{m}), 1.69(3 \mathrm{H}, \mathrm{s}), 1.74-1.59(6 \mathrm{H}, \mathrm{m}), 1.31-$ 0.99 ( $6 \mathrm{H}, \mathrm{m}$ ); ${ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 199.9,99.7,97.3,62.9,37.8,33.4,30.8$, 30.4, 26.2, 19.7; $m / z$ (ESIMS) calculated for $\mathrm{C}_{13} \mathrm{H}_{22} \mathrm{ONa}[\mathrm{M}+\mathrm{Na}]^{+}$217.2, found: 217.0.


1d
Synthesized in $76 \%$ yield ( 314.3 mg ). IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-1} 3444.5,2958.2,2873.1,1963.1$, $1462.9,1378.2 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 4.95(1 \mathrm{H}, \mathrm{ddt}, J=10.1,7.3,2.9 \mathrm{~Hz}$ ), 3.63 $(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 1.94(2 \mathrm{H}, \mathrm{tt}, J=6.7,2.1 \mathrm{~Hz}), 1.83(2 \mathrm{H}, \mathrm{t}, J=6.9 \mathrm{~Hz}), 1.65(3 \mathrm{H}, \mathrm{d}, J$ $=2.8 \mathrm{~Hz}), 1.64-1.54(3 \mathrm{H}, \mathrm{m}), 1.53-1.39(3 \mathrm{H}, \mathrm{m}), 0.90(6 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}),{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right.$ ) 201.9, 98.2, 89.0, 63.0, 39.1, 33.9, 32.5, 28.6, 23.8, 22.4, 19.4; m/z (ESIMS) calculated for $\mathrm{C}_{12} \mathrm{H}_{22} \mathrm{ONa}[\mathrm{M}+\mathrm{Na}]^{+}$205.2, found: 205.0.

General Procedure for Synthesis of Enantioenriched Propargyl Alcohols ${ }^{4,5}$


To a mixture of activated $\mathrm{Zn}(\mathrm{OTf})_{2}$ (1.2 equiv.) and ( + )- N -methylephedrine ( 1.3 equiv.) in dry toluene $(0.3 \mathrm{M})$ was added anhydrous $\mathrm{NEt}_{3}$ ( 1.3 equiv.) dropwise. The mixture was stirred vigorously for 2 hrs at room temperature. To the resultant white slurry was added the TBDPS-protected alkynyl ether ( 1.3 equiv.) in dry toluene ( 0.5 M ) in one portion. After stirring for 1 hr , dry aldehyde (freshly distilled if not new) was added dropwise. The reaction was stirred overnight, then diluted with ethyl acetate and washed sequentially with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ and brine. The organic phase was dried over anhydrous
$\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. The crude product was purified by FCC (95:5 hexane:ethyl acetate) to give pure propargyl alcohol as a colorless oil.


Synthesized in $30 \%$ yield ( 1.8245 g ), $90 \% e e$ as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. $[\alpha]_{\mathrm{D}}{ }^{22}+7.1200\left(c 0.0254, \mathrm{CHCl}_{3}\right.$ ); IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3416.0,3070.6$, 2955.6, 2930.6, 2858.1, 2345.0, 1471.7, 1427.7, 1387.2, 1362.2, 1110.7, 823.0, 740.1, 701.7, 613.8; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.68-7.65(4 \mathrm{H}, \mathrm{m}), 7.44-7.36(6 \mathrm{H}, \mathrm{m})$, $4.37-4.33(1 \mathrm{H}, \mathrm{m}), 3.73(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.36(2 \mathrm{H}, \mathrm{td}, J=7.2,2.0 \mathrm{~Hz}), 1.84-1.73(3 \mathrm{H}$, $\mathrm{m}), 1.60-1.44(4 \mathrm{H}, \mathrm{m}), 1.05(9 \mathrm{H}, \mathrm{s}), 0.92(3 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 0.90(3 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz})$; ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 135.7,134.0,129.7,127.8,85.0,81.9,62.5,61.4,47.4$, 31.7, 27.0, 22.7, 19.4, 15.4; m/z (ESIMS) calculated for $\mathrm{C}_{26} \mathrm{H}_{40} \mathrm{O}_{2} \mathrm{NSi}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+} 426.2$, found: 426.0.


Synthesized in $84 \%$ yield ( 2.71 g ), $94 \%$ ee as determined by HPLC of the product of benzylation and desilylation (below). $[\alpha]_{\mathrm{D}}{ }^{22}+0.027\left(c 0.027, \mathrm{CHCl}_{3}\right.$, ) ; IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-}$ ${ }^{1} 3395.8,2955.6,2919.5,2853.3,1471.1,1385.3,1255.3,1104.4,1071.0,1023.6,835.6$, $776.0 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.14(1 \mathrm{H}, \mathrm{d}, J=4.8 \mathrm{~Hz}), 3.68(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz})$, $2.29(2 \mathrm{H}, \mathrm{td}, J=6.8,1.6 \mathrm{~Hz}), 1.88-1.77(1 \mathrm{H}, \mathrm{m}), 1.77(1 \mathrm{H}, \mathrm{br} \mathrm{s}), 1.74-1.66(2 \mathrm{H}, \mathrm{m})$, $0.97(6 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz}), 0.88(9 \mathrm{H}, \mathrm{s}), 0.04(6 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $\left.100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 85.9$, 80.1, 68.3, 61.7, 34.8, 31.9, 26.1, 18.5, 18.3, 17.6, 15.2, $-5.2 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{15} \mathrm{H}_{30} \mathrm{O}_{2} \mathrm{NaSi}[\mathrm{M}+\mathrm{Na}]^{+}$293.2, found: 293.3.


HPLC conditions: Daicel Chiralpak OJ-H, $n$-hexane $/ i$-PrOH $=90 / 10$, Flow rate $=1$ $\mathrm{mL} / \mathrm{min}, \mathrm{UV}=254 \mathrm{~nm}, \mathrm{t}_{\mathrm{R}}=6.5 \mathrm{~min}$ and $\mathrm{t}_{\mathrm{R}}=7.3 \mathrm{~min}($ major, $94 \% e e)$.




Synthesized in $99 \%$ yield ( 4.01 g ), $92 \% e e$ as determined by HPLC. IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-1}$ 3396.5, 3070.7, 3049.5, 2957.3, 2931.1, 2858.7, 1471.3, 1427.8, 1111.1, 1020.7, 702.0, 505.3; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.72-7.66(4 \mathrm{H}, \mathrm{m}), 7.47-7.36(6 \mathrm{H}, \mathrm{m}), 4.18-4.13$ $(1 \mathrm{H}, \mathrm{m}), 3.69(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.24(2 \mathrm{H}, \mathrm{td}, J=7.0,2.0 \mathrm{~Hz}), 1.84(1 \mathrm{H}, \mathrm{tt}, J=12.5$, $6.5 \mathrm{~Hz}), 1.73-1.58(4 \mathrm{H}, \mathrm{m}), 1.06(9 \mathrm{H}, \mathrm{s}), 0.99(6 \mathrm{H}, \mathrm{dd}, J=7.0,2.5 \mathrm{~Hz})$, ${ }^{13} \mathrm{C}$ NMR ( 125 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 135.7,134.1,129.7,127.7,86.2,80.2,68.3,63.5,34.8,31.8,27.0,25.4$, 19.4, 18.6, 18.3, 17.6; m/z (ESIMS) calculated for $\mathrm{C}_{26} \mathrm{H}_{37} \mathrm{O}_{2} \mathrm{Si}[\mathrm{M}+\mathrm{H}]^{+} 409.3$, found: 408.9; HPLC conditions: Daicel Chiralpak AS-H, $n$-hexane $/ i-\mathrm{PrOH}=99 / 1$, Flow rate $=$ $0.5 \mathrm{~mL} / \mathrm{min}, \mathrm{UV}=210 \mathrm{~nm}, \mathrm{t}_{\mathrm{R}}=15.3 \mathrm{~min}$ (major) and $\mathrm{t}_{\mathrm{R}}=18.4 \mathrm{~min}$.




Synthesized in $96 \%$ yield ( 2.60 g ), $>95 \%$ ee as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. $[\alpha]_{\mathrm{D}}{ }^{22}-0.103\left(c 0.049, \mathrm{CHCl}_{3}\right)$; IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3419.1,3071.2,3049.8$, 2955.3, 2929.7, 2858.4, 1471.1, 1428.0, 1110.9, 701.9, 505.8; ${ }^{1} \mathrm{H}$ NMR ( 300 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 7.70-7.63(4 \mathrm{H}, \mathrm{m}), 7.46-7.34(6 \mathrm{H}, \mathrm{m}), 4.40-4.31(1 \mathrm{H}, \mathrm{m}), 3.73(2 \mathrm{H}, \mathrm{t}, J=6.0$ $\mathrm{Hz}), 2.37(2 \mathrm{H}, \mathrm{td}, J=7.2,2.1 \mathrm{~Hz}), 1.80-1.69(2 \mathrm{H}, \mathrm{m}), 1.53(1 \mathrm{H}, \mathrm{d}, J=5.7 \mathrm{~Hz}), 1.51-$ $1.38(4 \mathrm{H}, \mathrm{m}), 1.28\left(8 \mathrm{H}, \mathrm{br}\right.$ s), $1.05(9 \mathrm{H}, \mathrm{s}), 0.94-0.84(6 \mathrm{H}, \mathrm{dt}, J=5.1,1.5 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 135.7,134.0,129.7,127.8,85.8,80.5,65.5,62.6,44.5,31.8,29.9$, 29.7, 29.6, 29.5, 27.0, 23.2, 23.2, 19.4, 15.4, 14.3, 14.2; m/z (ESIMS) calculated for $\mathrm{C}_{31} \mathrm{H}_{48} \mathrm{O}_{3} \mathrm{Si}\left[\mathrm{M}+\mathrm{H}_{2} \mathrm{O}\right]^{+} 496.3$, found: 496.0.


Synthesized in quantitative yield, $92 \% e e$ as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. $[\alpha]_{\mathrm{D}}{ }^{22}+44.7400\left(c 0.0342, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3423.1,3086.3$, 3061.0, 3027.9, 2953.1, 2927.7, 2855.9, 2359.5, 2229.2, 1599.6, 1495.8, 1471.1, 1450.4, $1387.7,1360.5,1254.7,1103.4,835.5,776.1,744.9,699.4,667.7,637.6,611.9 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.57-7.28(10 \mathrm{H}, \mathrm{m}), 5.25-5.10(1 \mathrm{H}, \mathrm{m}), 4.35(1 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz})$, $3.65(2 \mathrm{H}, \mathrm{td}, J=6.1,1.5 \mathrm{~Hz}), 2.34(2 \mathrm{H}, \mathrm{td}, J=7.0,2.0 \mathrm{~Hz}), 2.03(1 \mathrm{H}, \mathrm{d}, J=6.1 \mathrm{~Hz})$, $1.77-1.65(1 \mathrm{H}, \mathrm{m}), 1.02(9 \mathrm{H}, \mathrm{s}), 0.16(6 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 141.2$, $140.5,129.0,128.6,128.4,127.0,126.9,87.6,80.1,65.5,61.6,58.2,31.6,26.1,18.4$, 15.2, $-5.2 ; m / z$ (ESIMS) calculated for $\mathrm{C}_{25} \mathrm{H}_{38} \mathrm{O}_{2} \mathrm{NSi}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}$412.2, found 412.0.


Synthesized in $89 \%$ yield ( 6.00 g ), $>95 \%$ ee as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. $[\alpha]_{\mathrm{D}}{ }^{22}-0.058\left(c 0.043, \mathrm{CHCl}_{3}\right)$; IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3382.0,3070.5,3049.0$, 2997.8, 2952.1, 1589.2, 1486.3, 1471.5, 1427.7, 1388.8, 1361.0, 1324.0, 1258.7, 1188.6, 1110.6, 1024.6, 939.3, 822.7, 791.4, 740.5, 701.0, 614.0, 505.4; ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 7.70-7.65(4 \mathrm{H}, \mathrm{m}), 7.46-7.36(6 \mathrm{H}, \mathrm{m}), 4.21-4.14(1 \mathrm{H}, \mathrm{m}), 3.75(2 \mathrm{H}, \mathrm{t}, J=6.5$ $\mathrm{Hz}), 2.37(2 \mathrm{H}, \mathrm{td}, J=7.5,2.0 \mathrm{~Hz}), 2.16-2.06(1 \mathrm{H}, \mathrm{m}), 1.81-1.67(4 \mathrm{H}, \mathrm{m}), 1.66-1.57(2 \mathrm{H}$, m), 1.56-1.47 (2H, m), 1.45-1.33 (2H, m), $1.06(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ 135.7, 134.0, 129.7, 127.8, 85.1, 81.0, 66.7, 62.5, 46.6, 31.8, 29.0, 28.5, 27.0, 25.9, 19.4, 15.4; $\mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{27} \mathrm{H}_{38} \mathrm{O}_{3} \mathrm{Si}\left[\mathrm{M}+\mathrm{H}_{2} \mathrm{O}\right]^{+} 438.3$, found: 438.0.


Synthesized in quantitative yield ( 1.385 g ), $>95 \% e e$ as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. $[\alpha]_{\mathrm{D}}{ }^{22}-1.9500\left(c 0.0235, \mathrm{CHCl}_{3}\right)$; IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-1} 3421.7$, $3070.2,3049.0,2997.8,2927.5,2854.7,2237.5,1472.7,1449.4,1427.6,1388.5,1361.3$, $1110.3,1007.3,977.0,822.7,740.4,701.5,614.0 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.69$ $(4 \mathrm{H}, \mathrm{dd}, J=7.9,1.3 \mathrm{~Hz}), 7.51-7.31(6 \mathrm{H}, \mathrm{m}), 4.10(1 \mathrm{H}, \mathrm{dd}, J=5.8,5.7 \mathrm{~Hz}), 3.75(2 \mathrm{H}, \mathrm{t}$, $J=6.0 \mathrm{~Hz}), 2.37(2 \mathrm{H}, \mathrm{td}, J=7.1,1.8 \mathrm{~Hz}), 1.85-1.37(13 \mathrm{H}, \mathrm{m}), 1.04(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 135.7,134.0,129.7,127.8,85.9,80.5,67.6,62.6,44.5,31.8,31.7$,
28.7, 28.3, 27.0, 26.6, 26.1, 26.0, 15.4; m/z (ESIMS) calculated for $\mathrm{C}_{28} \mathrm{H}_{42} \mathrm{O}_{2} \mathrm{NSi}$ $\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+} 452.2$, found: 452.3.


Synthesized in $42 \%$ yield $(1.267 \mathrm{~g}),>95 \% e e$ as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3420.4,3070.7,2957.0,2930.3,2857.2,2358.5$, 1417.9, 1427.6, 1112.7, 821.2, 700.6, 607.8; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.85-7.59$ $(4 \mathrm{H}, \mathrm{m}), 7.52-7.35(6 \mathrm{H}, \mathrm{m}), 4.40(1 \mathrm{H}, \mathrm{tt}, J=7.3,2.0 \mathrm{~Hz}), 3.70(2 \mathrm{H}, \mathrm{t}, J=5.9 \mathrm{~Hz}), 2.23$ $(2 \mathrm{H}, \mathrm{td}, J=6.9,1.9 \mathrm{~Hz}), 1.86(1 \mathrm{H}, \mathrm{dq}, J=13.5,6.8 \mathrm{~Hz}), 1.75(1 \mathrm{H}, \mathrm{s}, \mathrm{br}), 1.74-1.58(5 \mathrm{H}$, $\mathrm{m}), 1.53(1 \mathrm{H}, \mathrm{dt}, J=13.5,7.0 \mathrm{~Hz}), 1.08(9 \mathrm{H}, \mathrm{s}), 0.95(6 \mathrm{H}, \mathrm{dd}, J=9.3,6.7 \mathrm{~Hz}){ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 135.7,134.1,129.7,127.7,85.3,81.9,63.5,61.3,47.4,31.8,27.0$, 25.3, 24.9, 22.7, 19.3, 18.6; m/z (ESIMS) calculated for $\mathrm{C}_{27} \mathrm{H}_{42} \mathrm{O}_{2} \mathrm{NSi}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+} 440.3$, found: 440.3 .


Only 20-30\% yield of this propargyl alcohol was obtained using the Carreira alkynylation procedure. A Weinreb amide-Noyori sequence was used instead. To a solution of TBDPS-protected alkynyl ether ( $12.282 \mathrm{~g}, 38.4 \mathrm{mmol}$ ) in dry THF $(192 \mathrm{~mL})$ at $-78{ }^{\circ} \mathrm{C}$ was added $n$-butyllithium ( 1.6 M in THF, $25.2 \mathrm{~mL}, 40.3 \mathrm{mmol}$ ) slowly. After stirring for 5 min , the cooling bath was removed, and the reaction mixture was stirred for 40 min . A solution of the Weinreb amide ( $5.570 \mathrm{~g}, 38.4 \mathrm{mmol}$ ) in dry THF ( 30 mL ) was then added slowly at $-78^{\circ} \mathrm{C}$. The reaction mixture was stirred for an hour and left to warm to room temperature overnight. The solution was then diluted with diethyl ether ( 300 mL ) and washed with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}(400 \mathrm{~mL})$. The organic phase was dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. FCC ( $99: 1$ hexane:ethyl acetate) gave the pure ketone in $89 \%$ yield ( 13.9113 g ) for use in the next step.

Dichloro(p-cymene)ruthenium(II) dimer (63.0 mg, 0.104 mmol$),(1 R, 2 R)-\mathrm{N}-(4-$ toluenesulfonyl)-1,2-diphenylethylenediamine ( $76.0 \mathrm{mg}, 0.207 \mathrm{mmol}$ ) and $\mathrm{KOH}(87.0$ $\mathrm{mg}, 1.553 \mathrm{mmol})$ in $\mathrm{DCM}(3.5 \mathrm{~mL})$ was vigorously stirred in open air until the color
turned from orange to purple (using KOH pellets required up to 40 min for the color change; using crushed KOH pieces reduced this time to no more than 10 min ). The resultant solution was washed twice with equal amounts of distilled water. The organic layer was dried with sufficient calcium hydride, then filtered through cotton in a glass pipette into a round-bottom flask. The solvent was then removed by rotovap. The purple solid (Noyori catalyst) was then dried in vacuo, protected under argon, and dissolved in dry isopropanol ( 10 mL ) to form a light orange solution. A solution of the ketone from the previous step ( $4.2088 \mathrm{~g}, 10.35 \mathrm{mmol}$ ) in dry isopropanol ( 2 mL ) was added periodically. The color of the reaction solution changed from dark/clear orange to purple then back to orange with each addition. After complete addition of ketone, the reaction was stirred for 2 hrs . The solvent was removed by rotovap, giving crude product. FCC (92:8 hexane:ethyl acetate) gave the pure propargyl alcohol in $80 \%$ yield ( 3.384 g ), $91 \%$ $e e$ as determined by ${ }^{1} \mathrm{H}$ and ${ }^{19} \mathrm{~F}$ NMR of the MTPA esters. To remove the ruthenium catalyst during column chromatography, Florisil was placed in between the silica gel and sand. $[\alpha]_{\mathrm{D}}^{22}+7.4500\left(c 0.066, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3419.3,3070.6,2930.6$, 2858.2, 2223.8, 1472.5, 1427.8, 1388.3, 1361.5, 1110.6, 822.8, 740.0, 701.9, 613.8; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.67(4 \mathrm{H}$, dd, $J=7.7,1.4 \mathrm{~Hz}), 7.43-7.36(6 \mathrm{H}, \mathrm{m}), 4.30(1 \mathrm{H}$, dd), $3.74(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.36(2 \mathrm{H}, \mathrm{td}, J=7.1,1.8 \mathrm{~Hz}), 1.78-1.57(4 \mathrm{H}, \mathrm{m}), 1.42-1.22$ $(4 \mathrm{H}, \mathrm{m}), 1.05(9 \mathrm{H}, \mathrm{s}), 0.92(3 \mathrm{H}, \mathrm{t}, J=7.1 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ 135.7, $134.0,129.7,127.7,85.0,81.7,62.8,62.5,38.0,31.7,27.5,27.0,22.5,19.4,15.3,14.1$; $\mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{26} \mathrm{H}_{40} \mathrm{O}_{2} \mathrm{NSi}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+} 426.2$, found: 426.1.

General Procedure for Synthesis of Enantioenriched Allenols ${ }^{6}$


To a solution of propargyl alcohol in dry THF $(0.2 \mathrm{M})$ at $-40{ }^{\circ} \mathrm{C}$ was added $\mathrm{NEt}_{3}(1.5$ equiv.) slowly. MsCl ( 1.5 equiv.) was added dropwise and the reaction was stirred for 1 hr . To a solution of activated copper (I) cyanide ( 2.75 equiv.) in dry THF at $-40{ }^{\circ} \mathrm{C}$ was added methyl lithium ( 2.75 equiv., 1.6 M in THF) slowly. After stirring for 10 min , a colorless homogeneous cuprate solution was formed, which was then added to the mesylate solution slowly at $-40^{\circ} \mathrm{C}$. The reaction mixture was stirred for 2 hrs (monitored by TLC) and quenched with $10 \% \mathrm{NH}_{3} / \mathrm{NH}_{4} \mathrm{Cl}$ sat. solution. After warming to room temperature and stirring for 30 min , the reaction mixture was diluted with ethyl acetate and the blue aqueous solution was removed. The organic phase was washed with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ and brine, dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. The residue
was then dried in vacuo. The crude allene was used directly in the next step without further purification. To a solution of the allene in dry THF at room temperature was added TBAF ( 2 equiv., 1.0 M in THF). After stirring for 1 hr , the reaction mixture was washed with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$ and brine, dried over anhydrous $\mathrm{Na}_{2} \mathrm{SO}_{4}$, and filtered. The solvent was removed by rotovap and the residue was purified by FCC ( $95: 5$ hexane:ethyl acetate) to give pure allenol as a colorless oil.


Synthesized in $92 \%$ yield $(606.6 \mathrm{mg}) .[\alpha]_{\mathrm{D}}{ }^{22}+3.5900\left(c 0.0012, \mathrm{CHCl}_{3}\right)$. Characterization data matched those of the racemic substrate (above).


Synthesized in $79 \%$ yield $(159.0 \mathrm{mg}) .[\alpha]_{\mathrm{D}}{ }^{22}+4.6800\left(c 0.0267, \mathrm{CHCl}_{3}\right)$. Characterization data matched those of the racemic substrate (above).


Synthesized in quantitative yield (1.260 g). $[\alpha]_{\mathrm{D}}{ }^{22}-0.058$ (c $\left.0.004, \mathrm{CHCl}_{3}\right)$; IR $v \max$ (neat) $/ \mathrm{cm}^{-1} 3332.8,2957.9,2927.5,2868.9,1965.0,1458.1,1379.0,1363.2,1060.0$; ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 5.08-5.01(1 \mathrm{H}, \mathrm{m}), 3.67(2 \mathrm{H}, \mathrm{t}, J=8.0 \mathrm{~Hz}), 2.29-2.17$ $(1 \mathrm{H}, \mathrm{m}), 2.04-1.96(2 \mathrm{H}, \mathrm{m}), 1.69(3 \mathrm{H}, \mathrm{s}), 1.31(2 \mathrm{H}, \mathrm{s}), 0.97(6 \mathrm{H}, \mathrm{d}, J=6.8 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 199.5,100.1,98.5,62.9,30.8,30.5,28.5,22.8,22.7,19.7$; $\mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{10} \mathrm{H}_{19} \mathrm{O}[\mathrm{M}+\mathrm{H}]^{+}$155.2, found: 155.1.


Synthesized in $99 \%$ yield ( 0.770 g ). IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3344.4$, 2957.6, 2931.8, 2866.9, 1964.2, 1458.5, 1379.0, 1056.3; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 5.09-5.00(1 \mathrm{H}, \mathrm{m}), 3.65$ $(2 \mathrm{H}, \mathrm{t}, J=6.0 \mathrm{~Hz}), 2.31-2.17(1 \mathrm{H}, \mathrm{m}), 1.96(2 \mathrm{H}, \mathrm{dt}, J=7.2,3.2 \mathrm{~Hz}), 1.67(3 \mathrm{H}, \mathrm{d}, J=2.8$ $\mathrm{Hz}), 1.64-1.55(2 \mathrm{H}, \mathrm{m}), 1.54-1.44(2 \mathrm{H}, \mathrm{m}), 1.28(1 \mathrm{H}, \mathrm{br} \mathrm{s}), 0.97(6 \mathrm{H}, \mathrm{d}, J=6.8 \mathrm{~Hz}),{ }^{13} \mathrm{C}$

NMR (100 MHz, $\mathrm{CDCl}_{3}$ ) $\delta$ 199.6, 100.4, 98.2, 63.1, 34.0, 32.6, 28.5, 23.9, 22.9, 22.8, 19.6; $m / z$ (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{21} \mathrm{O}[\mathrm{M}+\mathrm{H}]^{+}$169.2, found: 169.1.


Synthesized in $99 \%$ yield $(0.252 \mathrm{~g}) .[\alpha]_{\mathrm{D}}{ }^{22}-0.0045\left(c \quad 0.0062, \mathrm{CHCl}_{3}\right)$; IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-}$ ${ }^{1} 3334.9,2955.8,2925.2,2871.5,2857.2,1964.6,1456.3,1378.4,1058.8 ;{ }^{1} \mathrm{H}$ NMR (300 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.86-4.76(1 \mathrm{H}, \mathrm{m}), 3.67(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 2.01(2 \mathrm{H}, \mathrm{dt}, J=7.8,2.4$ $\mathrm{Hz}), 1.95-1.84(1 \mathrm{H}, \mathrm{m}), 1.77-1.65(2 \mathrm{H}, \mathrm{m}), 1.69(3 \mathrm{H}, \mathrm{d}, J=2.7 \mathrm{~Hz}), 1.42-1.17(12 \mathrm{H}, \mathrm{m})$, $0.93(6 \mathrm{H}, \mathrm{brt}, J=6.5 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 200.8,98.6,95.3,62.9,40.0$, $35.5,35.3,30.8,30.5,29.8,29.6,23.0,22.9,19.6,14.3,14.3 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{16} \mathrm{H}_{31} \mathrm{O}[\mathrm{M}+\mathrm{H}]^{+}$239.2, found: 239.2.


Synthesized in $87 \%$ yield ( 1.1081 g ). $[\alpha]_{\mathrm{D}}{ }^{22}-77.7500\left(c \quad 0.0181, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3366.3,3083.4,3059.8,3025.6,2937.0,1966.0,1600.1,1492.6,1449.1$, 1058.4, 1030.8, 740.8, 698.7; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.29-7.17$ ( $10 \mathrm{H}, \mathrm{m}$ ), $5.55-$ $5.50(1 \mathrm{H}, \mathrm{m}), 4.71(1 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 3.51-3.29(2 \mathrm{H}, \mathrm{m}), 1.96-1.82(2 \mathrm{H}, \mathrm{m}), 1.62(3 \mathrm{H}$, d, $J=2.8 \mathrm{~Hz}), 1.56-1.41(2 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 202.1,144.1,143.9$, $128.6,128.5,128.3,128.3,101.1,94.7,62.4,51.8,30.3,30.1,19.1 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{20} \mathrm{H}_{22} \mathrm{ONa}[\mathrm{M}+\mathrm{Na}]^{+} 301.2$, found: 301.0.


Synthesized in quantitative yield (0.551 g). $[\alpha]_{\mathrm{D}}{ }^{22}-0.070\left(c \quad 0.018, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3333.1,2950.0,2866.9,1963.4,1449.5,1369.2,1060.3,1017.4 ;{ }^{1} \mathrm{H}$ NMR ( $\left.500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 5.05(1 \mathrm{H}, \mathrm{dt}, J=6.0,3.0 \mathrm{~Hz}), 3.65(2 \mathrm{H}, \mathrm{t}, J=6.5 \mathrm{~Hz}), 2.40$ $(1 \mathrm{H}, \mathrm{dt}, J=14.5,7.0 \mathrm{~Hz}), 2.05-1.96(2 \mathrm{H}, \mathrm{m}), 1.78-1.64(4 \mathrm{H}, \mathrm{m}), 1.67(3 \mathrm{H}, \mathrm{d}, J=2.5$ $\mathrm{Hz}), 1.63-1.57(2 \mathrm{H}, \mathrm{m}), 1.56-1.48(2 \mathrm{H}, \mathrm{m}), 1.38-1.28(2 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 199.8,99.6,95.9,62.8,39.8,33.0,32.9,30.7,30.4,25.0,25.0,19.6 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{12} \mathrm{H}_{21} \mathrm{O}[\mathrm{M}+\mathrm{H}]^{+}$181.2, found: 181.1.


Synthesized in $87 \%$ yield ( 347.1 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-44.8600$ (c $\left.0.0434, ~ \mathrm{CHCl}_{3}\right)$; Characterization data matched those of the racemic substrate (above).

## Catalyst Synthesis

General Procedure for Synthesis of Binaphthyl-Derived Iminium Salts


To a solution of $(R)-2,2$ '-bis(bromomethyl)-1,1'-binaphthyl in $\mathrm{CH}_{3} \mathrm{CN}(0.1 \mathrm{M})$ was added potassium carbonate (4 equiv.) and the primary amine ( 1.3 equiv.). The reaction mixture was refluxed for 5 hrs , at which time all dibromide was consumed (monitored by TLC). After cooling to room temperature, the mixture was filtered through Celite with DCM. The filtrate was concentrated by rotovap and dried in vacuo to give a colorless or yellow shining solid as the product. The crude tertiary amine was used directly in the next step without purification. To a solution of tertiary amine in DCM ( 0.15 M ) was added freshly recrystallized $N$-bromosuccinimide ( 1 equiv.) in small portions. The solution turned from colorless or light yellow to bright yellow. The reaction mixture was stirred for 5 min . Sodium tetraphenylborate (1 equiv.) in $\mathrm{CH}_{3} \mathrm{CN}(1.0 \mathrm{M})$ was added in one portion. The clear solution became milky. After stirring for 5 min , the mixture was diluted with DCM and washed twice with distilled water. The organic layer was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$ and filtered. Evaporation of solvent gave the very pure iminium salt as a bright yellow solid. The residue can be recrystallized from DCM/hexane. Part of the imminium catalysts are known compounds with full characterizations in literatures. ${ }^{7}$


Synthesized in $84 \%$ yield ( 502.4 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-462.1200\left(c \quad 0.0166, \mathrm{CHCl}_{3}\right)$; IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-1} 3055.1,2999.4,2984.9,2928.2,2850.0,1638.0,1613.6,1425.7,1325.1$, 1168.6, 1128.1, 1067.1, 1018.6, 818.3, 735.6, 706.9; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.97$ $(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.82(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 7.77(1 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 7.71-7.55(3 \mathrm{H}, \mathrm{m})$, $7.54-7.17(17 \mathrm{H}, \mathrm{m}), 6.96(1 \mathrm{H}, \mathrm{d}, J=8.5 \mathrm{~Hz}), 6.77(6 \mathrm{H}, \mathrm{t}, J=7.1 \mathrm{~Hz}), 6.71(2 \mathrm{H}, \mathrm{d}, J=$ $7.6 \mathrm{~Hz}), 6.54(3 \mathrm{H}, \mathrm{t}, J=6.9 \mathrm{~Hz}), 6.35(1 \mathrm{H}, \mathrm{d}, J=8.3 \mathrm{~Hz}), 4.27(1 \mathrm{H}, \mathrm{d}, J=14.2 \mathrm{~Hz})$, $4.15(1 \mathrm{H}, \mathrm{d}, J=14.2 \mathrm{~Hz}), 3.89(1 \mathrm{H}, \mathrm{d}, J=13.5 \mathrm{~Hz}), 3.59(1 \mathrm{H}, \mathrm{d}, J=13.5 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 168.8,164.6\left(\mathrm{q}, J_{\mathrm{BC}}=49.4 \mathrm{~Hz}\right), 141.9,136.1,135.4,134.9,134.2$, $133.5,131.6,131.5,131.1,130.8,130.7,129.8,129.6,129.4,128.8,128.7,127.9,127.5$, $127.3,127.2,126.9,126.3,126.1,125.9,124.5,122.2,64.6,56.2 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{30} \mathrm{H}_{21} \mathrm{~F}_{3} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 452.2$, found: 452.3.


Synthesized in $84 \%$ yield ( 476.4 mg ). $[\alpha]_{\mathrm{D}}^{22}-402.1100\left(c \quad 0.0138, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3054.7,3031.6,2978.4,2849.7,1734.1,1636.6,1558.9,1541.2,1122.5$, $732.1,705.8 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 7.99(2 \mathrm{H}, \mathrm{d}, J=4.5 \mathrm{~Hz}), 7.86(1 \mathrm{H}, \mathrm{d}, J=$ $8.0 \mathrm{~Hz}), 7.78(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.70-7.63(1 \mathrm{H}, \mathrm{m}), 7.59-7.17(14 \mathrm{H}, \mathrm{m}), 6.96(1 \mathrm{H}, \mathrm{d}, J$ $=8.6 \mathrm{~Hz}), 6.85(10 \mathrm{H}, \mathrm{t}, J=6.7 \mathrm{~Hz}), 6.66(3 \mathrm{H}, \mathrm{t}, J=6.4 \mathrm{~Hz}), 6.60(2 \mathrm{H}, \mathrm{t}, J=7.8 \mathrm{~Hz})$, $3.98(1 \mathrm{H}, \mathrm{d}, J=14.7 \mathrm{~Hz}), 3.94(1 \mathrm{H}, \mathrm{d}, J=14.7 \mathrm{~Hz}), 3.82(1 \mathrm{H}, \mathrm{d}, J=12.0 \mathrm{~Hz}), 3.79(1 \mathrm{H}$, $\mathrm{d}, J=12.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 169.1,164.2\left(\mathrm{q}, J_{\mathrm{BC}}=44.0 \mathrm{~Hz}\right), 141.9$, 136.1, 135.5, 134.3, 133.6, 131.7, 131.6, 131.1, 131.0, 130.9, 129.7, 129.6, 128.7, 128.0, 127.7, 127.4, 127.0, 126.0, 125.7, 123.8, 122.1, 101.5, 101.3, 56.1, $52.7 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{29} \mathrm{H}_{19} \mathrm{~F}_{3} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 438.2$, found: 438.4.


Synthesized in $65 \%$ yield ( 276.3 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-594.4600\left(c \quad 0.0242, \mathrm{CHCl}_{3}\right)$; IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3054.8,2961.5,2929.9,2857.1,1636.9,1427.3,1112.2,736.2,703.7$; ${ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 7.99(2 \mathrm{H}, \mathrm{dd}, J=13.8,8.4 \mathrm{~Hz}), 7.92(2 \mathrm{H}, \mathrm{dd}, J=8.3,5.4$ $\mathrm{Hz}), 7.73-7.67(1 \mathrm{H}, \mathrm{m}), 7.63-7.17(24 \mathrm{H}, \mathrm{m}), 7.02(1 \mathrm{H}, \mathrm{d}, J=8.7 \mathrm{~Hz}), 6.82(8 \mathrm{H}, \mathrm{t}, J=$ $7.3 \mathrm{~Hz}), 6.77(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.69(4 \mathrm{H}, \mathrm{t}, J=7.1 \mathrm{~Hz}), 4.27(1 \mathrm{H}, \mathrm{d}, J=12.4 \mathrm{~Hz})$,
$3.89(1 \mathrm{H}, \mathrm{d}, J=13.4 \mathrm{~Hz}), 3.54(1 \mathrm{H}, \mathrm{d}, J=13.2 \mathrm{~Hz}), 3.27(1 \mathrm{H}, \mathrm{d}, J=11.0 \mathrm{~Hz}), 3.13(1 \mathrm{H}$, d, $J=11.0 \mathrm{~Hz}), 3.02(1 \mathrm{H}, \mathrm{d}, J=13.2 \mathrm{~Hz}), 1.17(9 \mathrm{H}, \mathrm{s}), 0.74(3 \mathrm{H}, \mathrm{s}), 0.70(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 170.1,164.2\left(\mathrm{q}, J_{\mathrm{BC}}=48.9 \mathrm{~Hz}\right), 141.6,136.3,135.8,135.7$, $135.4,134.1,133.9,132.5,132.3,132.0,131.6,131.4,130.8,130.5,130.4,129.7,129.6$, $128.9,128.8,128.2,128.1,127.9,127.8,127.5,127.4,127.3,126.1,125.9,125.2,68.8$, 67.7, 58.8, 38.7, 27.3, 23.3, 22.4, 19.5; m/z (ESIMS) calculated for $\mathrm{C}_{43} \mathrm{H}_{44} \mathrm{NOSi}$ [M$\left.\mathrm{BPh}_{4}\right]^{+} 618.3$, found: 618.5.


Synthesized in $70 \%$ yiled ( 989.6 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-492.9500\left(c \quad 0.0124, \mathrm{CHCl}_{3}\right.$ ); IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3053.3,2983.2,2934.3,2876.7,1638.2,1466.3,1064.9,909.5,733.4$, $706.9 ;{ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 7.99(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.95(2 \mathrm{H}, \mathrm{dd}, J=11.7$, $8.5 \mathrm{~Hz}), 7.91(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.67(1 \mathrm{H}, \mathrm{ddd}, J=8.1,6.7,1.1 \mathrm{~Hz}), 7.51-7.15(13 \mathrm{H}$, $\mathrm{m}), 7.09(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.97(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.80(8 \mathrm{H}, \mathrm{t}, J=7.4 \mathrm{~Hz}), 6.50(4 \mathrm{H}$, $\mathrm{t}, J=7.2 \mathrm{~Hz}), 6.26(1 \mathrm{H}, \mathrm{s}), 3.58(1 \mathrm{H}, \mathrm{d}, J=13.6 \mathrm{~Hz}), 3.36(1 \mathrm{H}, \mathrm{d}, J=14.1 \mathrm{~Hz}), 2.73$ $(1 \mathrm{H}, ~ d d d, J=12.5,9.6,5.0 \mathrm{~Hz}), 2.54(1 \mathrm{H}, \mathrm{ddd}, J=13.0,10.1,6.2 \mathrm{~Hz}), 1.34-1.18(1 \mathrm{H}$, m), 1.14-0.99 ( $1 \mathrm{H}, \mathrm{m}$ ), $0.50(3 \mathrm{H}, \mathrm{t}, J=7.3 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 167.3$, $164.3\left(\mathrm{q}, J_{\mathrm{BC}}=49.1 \mathrm{~Hz}\right), 141.1,136.0,135.1,135.0,133.7,131.8,131.5,131.4,130.5$, $129.6,129.2,128.8,128.7,127.8,127.5,127.2,127.1,126.2,126.1,125.0,122.0,63.8$, 56.1, 21.6, 10.4; m/z (ESIMS) calculated for $\mathrm{C}_{25} \mathrm{H}_{22} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+}$336.2, found: 336.3.


Synthesized in $98 \%$ yield ( 397.5 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-414.5600$ (c 0.0157, $\mathrm{CHCl}_{3}$ ); IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3054.1,2962.3,2929.1,2875.9,1642.0,1594.8,1438.5,1155.5,737.3$, 701.6; ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 8.01(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.97(2 \mathrm{H}, \mathrm{dd}, J=8.5,5.3$ $\mathrm{Hz}), 7.90(1 \mathrm{H}, \mathrm{d}, J=8.3 \mathrm{~Hz}), 7.69(1 \mathrm{H}, \mathrm{ddd}, J=8.1,6.7,1.2 \mathrm{~Hz}), 7.53-7.13(14 \mathrm{H}, \mathrm{m})$, $6.98(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.89(8 \mathrm{H}, \mathrm{t}, J=7.4 \mathrm{~Hz}), 6.72(1 \mathrm{H}, \mathrm{s}), 6.68(4 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz})$, $3.80(1 \mathrm{H}, \mathrm{d}, J=13.5 \mathrm{~Hz}), 3.65(1 \mathrm{H}, \mathrm{d}, J=13.7 \mathrm{~Hz}), 2.89(1 \mathrm{H}, \mathrm{dd}, J=12.9,5.6 \mathrm{~Hz})$, $2.59(1 \mathrm{H}, \mathrm{dd}, J=12.8,10.3 \mathrm{~Hz}), 1.81-1.63(1 \mathrm{H}, \mathrm{m}), 0.76(3 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}), 0.06(3 \mathrm{H}$, $\mathrm{d}, J=6.6 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 167.5,164.4\left(\mathrm{q}, J_{\mathrm{BC}}=49.5 \mathrm{~Hz}\right), 141.5$, $136.2,135.4,134.8,133.7,131.8,131.6,131.5,131.2,131.0,130.7,129.7,129.5,128.9$,
$128.8,128.5,128.1,127.9,127.6,127.4,127.3,127.2,126.4,126.1,125.9,125.0,122.1$, $69.9,56.8,26.8,19.7,18.1 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{26} \mathrm{H}_{24} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 350.2$, found: 350.3 .


Synthesized in $72 \%$ yield ( 554.0 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}-350.4700\left(c \quad 0.0139, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3056.0,2960.4,2870.7,1638.1,1594.4,1438.6,1370.1,1101.1,819.8$, $758.6,739.9,701.3 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 8.08(1 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 8.03(1 \mathrm{H}, \mathrm{d}$, $J=8.2 \mathrm{~Hz}), 7.96(2 \mathrm{H}, \mathrm{dd}, J=8.6,2.8 \mathrm{~Hz}), 7.71(1 \mathrm{H}, \mathrm{ddd}, J=8.1,6.7,1.1 \mathrm{~Hz}), 7.52(1 \mathrm{H}$, ddd, $J=8.0,6.9,1.0 \mathrm{~Hz}), 7.47-7.21(12 \mathrm{H}, \mathrm{m}), 7.20(1 \mathrm{H}, \mathrm{s}), 7.06(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz})$, $6.85(1 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 6.83(8 \mathrm{H}, \mathrm{t}, J=7.4 \mathrm{~Hz}), 6.70(4 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz}), 4.20(1 \mathrm{H}, \mathrm{d}, J$ $=13.3 \mathrm{~Hz}), 4.08(1 \mathrm{H}, \mathrm{d}, J=14.6 \mathrm{~Hz}), 3.16(1 \mathrm{H}, \mathrm{d}, J=13.2 \mathrm{~Hz}), 2.94(1 \mathrm{H}, \mathrm{d}, J=13.3$ $\mathrm{Hz}), 0.84(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 169.9,164.2\left(\mathrm{q}, J_{\mathrm{BC}}=49.0 \mathrm{~Hz}\right), 141.6$, 136.3, 135.6, 134.9, 134.0, 132.1, 131.6, 131.2, 130.9, 129.8, 129.6, 128.9, 128.8, 128.1, 127.9, 127.6, 127.4, 127.3, 126.4, 126.3, 125.9, 125.5, 122.1, 73.2, 59.8, 33.7, 27.8; m/z (ESIMS) calculated for $\mathrm{C}_{27} \mathrm{H}_{26} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 364.2$, found: 364.3.


Synthesized in $66 \%$ yield ( 280.0 mg ). $[\alpha]_{\mathrm{D}}^{22}-822.0700\left(c 0.0101, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3054.4,2982.2,2925.0,2843.2,1640.5,1588.5,1120.2,909.3,815.7$, 734.6, 697.6; ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 7.99(1 \mathrm{H}, \mathrm{d}, J=8.2 \mathrm{~Hz}), 7.96(1 \mathrm{H}, \mathrm{d}, J=$ $8.7 \mathrm{~Hz}), 7.85(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 7.71(1 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.66(1 \mathrm{H}, \mathrm{ddd}, J=8.2,6.7$, $1.1 \mathrm{~Hz}), 7.53-7.19(15 \mathrm{H}, \mathrm{m}), 7.18(1 \mathrm{H}, \mathrm{d}, J=8.7 \mathrm{~Hz}), 6.99(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.84(8 \mathrm{H}$, $\mathrm{t}, J=7.4 \mathrm{~Hz}), 6.69(2 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}), 6.60(4 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz}), 6.56(1 \mathrm{H}, \mathrm{s}), 6.46(1 \mathrm{H}, \mathrm{d}$, $J=8.4 \mathrm{~Hz}), 3.97(1 \mathrm{H}, \mathrm{d}, J=13.2 \mathrm{~Hz}), 3.97(1 \mathrm{H}, \mathrm{d}, J=15.5 \mathrm{~Hz}), 3.88(1 \mathrm{H}, \mathrm{d}, J=14.6$ $\mathrm{Hz}), 3.63(1 \mathrm{H}, \mathrm{d}, J=14.1 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 167.9,164.3\left(\mathrm{q}, J_{\mathrm{BC}}=\right.$ $48.6 \mathrm{~Hz}), 141.7$, 136.2, 135.3, 134.8, 133.6, 131.6, 131.5, 131.3, 130.7, 130.1, 130.0, 129.7, 129.5, 129.4, 129.3, 128.9, 128.8, 128.7, 128.1, 127.9, 127.5, 127.4, 127.3, 127.2, 127.0, 126.3, 126.2, 126.1, 126.0, 124.7, 122.1, 65.6, 55.8; m/z (ESIMS) calculated for $\mathrm{C}_{29} \mathrm{H}_{22} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 384.2$, found: 384.3.


Synthesized in $67 \%$ yield ( 1.4834 g ). $[\alpha]_{\mathrm{D}}^{22}-435.1100\left(c \quad 0.0256, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3053.9,2998.2,1709.3,1427.4,1133.6,751.5,705.9 ;{ }^{1} \mathrm{H}$ NMR (400 $\mathrm{MHz}, \mathrm{CDCl} 3) \delta 8.04(1 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.98(2 \mathrm{H}, \mathrm{t}, J=9.0 \mathrm{~Hz}), 7.91(1 \mathrm{H}, \mathrm{d}, J=8.6$ $\mathrm{Hz}), 7.67(1 \mathrm{H}, \mathrm{t}, J=7.4 \mathrm{~Hz}), 7.55(1 \mathrm{H}, \mathrm{t}, J=7.5 \mathrm{~Hz}), 7.46(7 \mathrm{H}, \mathrm{s}), 7.42-7.26(4 \mathrm{H}, \mathrm{m})$, $7.05(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.85(2 \mathrm{H}, \mathrm{d}, J=13.3 \mathrm{~Hz}), 6.81(6 \mathrm{H}, \mathrm{t}, J=6.3 \mathrm{~Hz}), 6.46(4 \mathrm{H}, \mathrm{t}$, $J=6.3 \mathrm{~Hz}), 6.38(1 \mathrm{H}, \mathrm{s}), 4.19(1 \mathrm{H}, \mathrm{s}), 3.50(2 \mathrm{H}, \mathrm{s}), 3.30(2 \mathrm{H}, \mathrm{s}), 1.07(6 \mathrm{H}, \mathrm{dd}, J=19.1$, $5.1 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 166.7,164.4\left(\mathrm{q}, J_{\mathrm{BC}}=48.9 \mathrm{~Hz}\right), 141.1,136.2$, $135.6,135.2,135.0,134.0,133.8,131.9,131.7,131.6,131.5,130.5,129.6,129.2,129.0$, 128.2, 128.1, 127.8, 127.8, 127.6, 127.4, 127.2, 126.8, 126.2, 125.3, 122.1, 85.9, 65.3, 53.8, 51.0, 21.1, 20.5; m/z (ESIMS) calculated for $\mathrm{C}_{25} \mathrm{H}_{22} \mathrm{~N}\left[\mathrm{M}-\mathrm{BPh}_{4}\right]^{+} 336.2$, found: 334.3; $\mathrm{C}_{49} \mathrm{H}_{46}{ }^{11} \mathrm{BN}_{2}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+} 673.3$, found: 673.3 (100\%); $\mathrm{C}_{49} \mathrm{H}_{46}{ }^{10} \mathrm{BN}_{2}\left[\mathrm{M}+\mathrm{NH}_{4}\right]^{+}$ 672.3, found: 672.3 (23\%).


Figure 6.1. X-ray crystal structure of $i$-Pr-catalyst.
Table 6.1. Crystal data and structure refinement for of $i$-Pr-catalyst

| Empirical formula | $\mathrm{C} 50 \mathrm{H} 44 \mathrm{~B} \mathrm{Cl2} \mathrm{~N}$ |  |
| :--- | :--- | :--- |
| Formula weight | 740.57 |  |
| Temperature | $100(2) \mathrm{K}$ |  |
| Wavelength | $0.71073 \AA$ |  |
| Crystal system | Orthorhombic |  |
| Space group | $\mathrm{P} 2(1) 2(1) 2(1)$ | $=90^{\circ}$. |
| Unit cell dimensions | $\mathrm{a}=12.2648(11) \AA$ | $=90^{\circ}$. |

Volume
Z
Density (calculated)
Absorption coefficient
F(000)
Crystal size
Theta range for data collection
Index ranges
Reflections collected
Independent reflections
Completeness to theta $=25.35^{\circ}$
Absorption correction
Max. and min. transmission
Refinement method
Data / restraints / parameters
Goodness-of-fit on $\mathrm{F}^{2}$
Final R indices [ $\mathrm{I}>2 \operatorname{sigma}(\mathrm{I})$ ]
R indices (all data)
Absolute structure parameter
Largest diff. peak and hole
$\mathrm{c}=22.1690(19) \AA \quad=90^{\circ}$.
4036.7(6) $\AA^{3}$

4
$1.219 \mathrm{Mg} / \mathrm{m}^{3}$
$0.197 \mathrm{~mm}^{-1}$
1560
$0.54 \times 0.50 \times 0.05 \mathrm{~mm}^{3}$
1.84 to $25.35^{\circ}$.
$-14<=\mathrm{h}<=14,-17<=\mathrm{k}<=17,-26<=1<=26$
31148
$7394[\mathrm{R}($ int $)=0.0444]$
99.9 \%

Semi-empirical from equivalents
0.9902 and 0.9012

Full-matrix least-squares on $\mathrm{F}^{2}$
7394 / 324 / 489
1.001
$\mathrm{R} 1=0.0567, \mathrm{wR} 2=0.1393$
$\mathrm{R} 1=0.0725, \mathrm{wR} 2=0.1507$
-0.04(10)
0.579 and -0.690 e. $\AA^{-3}$

## Allene Oxidation

General Procedure for DMDO Oxidation of Allenes
To a solution of the allene in chloroform (or methanol, 0.2 M ) at $-40{ }^{\circ} \mathrm{C}$ was added freshly prepared DMDO ( 5 equiv.) in chloroform ( $\sim 0.4 \mathrm{M}$ ). After stirring for 10 to 30 $\min$ (monitored by TLC), the solvent was removed by rotovap. FCC (90:10 hexane:ethyl acetate) gave the products.

## General Procedure for Shi Oxidation of Allenes

The allene ( 0.128 mmol ) was dissolved in acetonitrile/DMM ( $1.9 \mathrm{~mL}, 1: 2 \mathrm{v} / \mathrm{v}$ ). To the solution was added buffer ( $1.4 \mathrm{~mL}, 0.05 \mathrm{M}$ solution of sodium borate in $4 \times 10^{-4} \mathrm{M}$ aq. $\mathrm{Na}_{2}$ EDTA), tetrabutylammonium hydrogen sulfate ( $5.11 \mu \mathrm{~mol}, 0.04$ equiv.), and Shi catalyst ${ }^{8}$ ( $0.192 \mathrm{mmol}, 1.5$ equiv.). The mixture was cooled in a $\mathrm{NaCl}-\mathrm{ice}$ bath. A solution of oxone ( $0.511 \mathrm{mmol}, 4$ equiv.) in aq. $\mathrm{Na}_{2}$ EDTA $\left(0.9 \mathrm{~mL}, 4 \times 10^{-4} \mathrm{M}\right)$ and a solution of $\mathrm{K}_{2} \mathrm{CO}_{3}$ ( 1.02 mmol , 8 equiv.) in water ( 0.9 mL ) were added dropwise separately over a period of 2 hrs . The reaction mixture was diluted with water ( 9 mL ) and extracted with ethyl acetate $(2 \times 12 \mathrm{~mL})$. The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered, and concentrated in vacuo. Pure products were obtained by FCC (90:10 hexane:ethyl acetate). Traces of allene oxide-derived products formed. The replacement of oxone with hydrogen peroxide as co-oxidant decreased the amount of undesired products.

## General Procedure for Davis Oxaziridine ${ }^{9}$ Oxidation of Allenes

To a solution of the allene in chloroform ( 0.2 M ) was added the Davis oxaziridine (4 equiv.). The reaction was heated to reflux and was complete in 30 min . After cooling to room temperature, the solution was diluted with DCM and quenched with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$. The organic phase was then washed with sodium sulfite, dried over sodium sulfate, filtered, and concentrated by rotovap. The crude product was purified by FCC (98:2 hexane:ethyl acetate). A major side product was formed from the allene oxide (traces to $30 \%$ yield).

## General Procedure for Oxaziridinium Salt Oxidation of Allenes

To a solution of the allene in DCM ( 0.2 M ) was added the oxaziridinium salt ${ }^{10}$ in one portion (4 equiv.). The reaction was complete in 5 min . The mixture was then diluted
with DCM, quenched with sat. aq. sodium sulfite, washed three times with water to remove the iminium salt, dried over sodium sulfate, filtered, and concentrated by rotovap. FCC (97:3 hexane:ethyl acetate) gave the pure products.

General Procedure for Iminium Salt-Catalyzed Oxidation of Allenes
To a solution of the allene in $\mathrm{CH}_{3} \mathrm{CN} / \mathrm{H}_{2} \mathrm{O}(1: 1 \mathrm{v} / \mathrm{v}$, 0.067 M$)$ was added sodium bicarbonate ( 8 equiv.) and the iminium salt catalyst ${ }^{10,11}$ ( 0.1 equiv.). The reaction mixture was stirred for 3 min , cooled to $0^{\circ} \mathrm{C}$, and stirred for another 3 min . Oxone (4 equiv.) was then added quickly in one portion with vigorous stirring. The reaction was monitored by TLC. The solution appeared bright yellow after the addition of the catalyst. Fading of the color indicated an insufficient catalyst loading. Upon completion, the reaction was quenched with sat. aq. sodium sulfite and extracted with ethyl acetate ( 1.5 v x 3 ). The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated by rotovap. FCC (95:5 hexane:ethyl acetate) gave the pure products.

## Experimental Data for Tables 1 and 2


$2 a$
IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3489.2,2957.5,2930.5,2872.3,1709.0,1640.0,1460.2,1367.9$, 1119.2, 1048.2, 718.2; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 4.49(1 \mathrm{H}, \mathrm{td}, J=7.4,3.5 \mathrm{~Hz}), 4.05-3.86(2 \mathrm{H}, \mathrm{m}), 3.27(1 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz})$, 2.28-2.12 (1H, m), 2.05-1.75 (5H, m), 1.52-1.24 (4H, m), $1.39(3 \mathrm{H}, \mathrm{s}), 0.91(3 \mathrm{H}, \mathrm{ddd}, J$ $=7.1,5.8,1.4 \mathrm{~Hz}$ ); ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 218.0,88.5,74.8,69.6,37.6,33.9$, 27.6, 25.8, 24.9, 22.5, 14.1; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR ( 500 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.58(1 \mathrm{H}, \mathrm{td}, J=7.1,3.5 \mathrm{~Hz}), 4.05-3.86(2 \mathrm{H}, \mathrm{m}), 3.34(1 \mathrm{H}, \mathrm{d}, J=6.7$ $\mathrm{Hz}), 2.28-2.12(1 \mathrm{H}, \mathrm{m}), 2.05-1.75(5 \mathrm{H}, \mathrm{m}), 1.52-1.24(4 \mathrm{H}, \mathrm{m}), 1.35(3 \mathrm{H}, \mathrm{s}), 0.91(3 \mathrm{H}$, ddd, $J=7.1,5.8,1.4 \mathrm{~Hz}$ ), ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 216.5,88.7,74.1,69.0,35.7$, $33.4,27.5,25.8,25.3,22.6,14.1 ; m / z$ (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{20} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$ 223.1, found: 223.1.


IR $v \max (\mathrm{neat}) / \mathrm{cm}^{-1} 3450.7,2959.2,2924.5,1727.4,1640.2,1462.4,1261.5,1072.9$; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.51(1 \mathrm{H}$, ddd, $J=9.7,7.3,2.1 \mathrm{~Hz}), 4.07-3.86(2 \mathrm{H}, \mathrm{m}), 3.17(1 \mathrm{H}, \mathrm{d}, J=7.5 \mathrm{~Hz}), 2.29-2.11(1 \mathrm{H}$, m), 2.04-1.74 ( $4 \mathrm{H}, \mathrm{m}$ ), $1.56-1.48(1 \mathrm{H}, \mathrm{m}), 1.40(3 \mathrm{H}, \mathrm{s}), 1.31-1.18(1 \mathrm{H}, \mathrm{m}), 0.99(3 \mathrm{H}, \mathrm{d}$, $J=6.6 \mathrm{~Hz}), 0.95(3 \mathrm{H}, \mathrm{d}, J=3.4 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 218.2,88.5,73.6$, $69.5,43.4,37.6,25.8,25.2,25.0,23.8,21.1$; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.63(1 \mathrm{H}$, ddd, $J=9.8,6.8,2.5 \mathrm{~Hz}), 4.07-3.86$ $(2 \mathrm{H}, \mathrm{m}), 3.22(1 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 2.29-2.11(1 \mathrm{H}, \mathrm{m}), 2.04-1.74(4 \mathrm{H}, \mathrm{m}), 1.56-1.48(1 \mathrm{H}$, m), $1.36(3 \mathrm{H}, \mathrm{s}), 1.31-1.18(1 \mathrm{H}, \mathrm{m}), 0.98(3 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}), 0.94(3 \mathrm{H}, \mathrm{d}, J=3.4 \mathrm{~Hz})$; ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 216.7,88.7,72.7,69.0,42.9,35.9,25.8,25.2,25.1,23.9$, 21.4; $m / z$ (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{20} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$223.1, found: 223.0.

## Experimental Data for Scheme 2



To a solution of TBS-protected allene ( $107.9 \mathrm{mg}, 0.382 \mathrm{mmol}$ ) in dry chloroform ( 2 mL ) was added the Davis oxaziridine ( $263.0 \mathrm{mg}, 0.859 \mathrm{mmol}$ ) and tetrabutylammonium acetate $(103.0 \mathrm{mg}, 0.425 \mathrm{mmol})$. The reaction mixture was stirred at reflux for 30 min . After cooling to room temperature, the solution was diluted with DCM and quenched with sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$. The organic phase was then washed with sat. aq. sodium sulfite, dried over sodium sulfate, filtered, and concentrated by rotovap. The crude product was purified by FCC ( $97: 3$ hexane:ethyl acetate) to give the ketone ( $131.0 \mathrm{mg}, 96 \%$ ) as a clear oil. Traces of enone side products were also observed. IR $v \max ($ neat $) / \mathrm{cm}^{-1} 2967.0$, 2880.7, 1738.2, 1471.3, 1253.8, 1099.9, 836.0; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 3.57(2 \mathrm{H}$, $\mathrm{dt}, J=20.1,7.8 \mathrm{~Hz}), 2.48-2.33(2 \mathrm{H}, \mathrm{m}), 2.07(3 \mathrm{H}, \mathrm{s}), 1.93-1.82(1 \mathrm{H}, \mathrm{m}), 1.79-1.61(2 \mathrm{H}$, m), 1.57-1.41 ( $4 \mathrm{H}, \mathrm{m}$ ), $1.49(3 \mathrm{H}, \mathrm{s}), 0.88(9 \mathrm{H}, \mathrm{s}), 0.87(6 \mathrm{H}, \mathrm{s}), 0.03(6 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 209.2,170.3,86.2,62.9,34.2,33.5,32.7,27.8,26.7,26.1,22.5$, 21.4, 20.6, 18.4, $-5.2 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{19} \mathrm{H}_{38} \mathrm{O}_{4} \mathrm{Si}[M]^{+} 358.3$, found: 358.2.


Following the general procedure for oxaziridinium salt oxidations, this pyran was synthesized in $53 \%$ yield ( 33.0 mg ). IR $\nu \max ($ neat $) / \mathrm{cm}^{-1} 3472.7,2955.6,2868.8,1709.3$,
1633.7, 1467.5, 1367.1, 1213.7, 1083.6, 1048.7; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.70(1 \mathrm{H}$, ddd, $J=10.1,7.6,2.5 \mathrm{~Hz}), 3.82-3.66$ $(2 \mathrm{H}, \mathrm{m}), 3.19(1 \mathrm{H}, \mathrm{d}, J=7.6 \mathrm{~Hz}), 2.01-1.87(1 \mathrm{H}, \mathrm{m}), 1.87-1.44(8 \mathrm{H}, \mathrm{m}), 1.39(3 \mathrm{H}, \mathrm{s})$, $0.99(3 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}), 0.96(3 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 217.1$, 80.7, $72.5,63.0,43.7,32.9,25.5,25.2,23.9,21.3,20.3,19.4$; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.61(1 \mathrm{H}$, ddd, $J=10.1,6.8,2.6 \mathrm{~Hz})$, $3.82-3.66(2 \mathrm{H}, \mathrm{m}), 3.40(1 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 2.01-1.87(1 \mathrm{H}, \mathrm{m}), 1.87-1.44(8 \mathrm{H}, \mathrm{m}), 1.39$ $(3 \mathrm{H}, \mathrm{s}), 0.99(3 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 0.96(3 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta 215.6,80.8,73.1,63.0,43.6,32.3,25.6,25.1,23.9,21.4,20.3,19.2 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{12} \mathrm{H}_{22} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$237.2, found: 237.2.


Following the general procedure for iminium salt-catalyzed oxidations, this pyran was synthesized in $41 \%$ yield $(15.0 \mathrm{mg})$.

## Experimental Data for Table 4



2a
Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $65 \%$ yield $(48.2 \mathrm{mg}) .[\alpha]_{\mathrm{D}}{ }^{22}+104.5100 \quad\left(c \quad 0.0193, \mathrm{CHCl}_{3}\right)$. Characterization data matched those in Table 1 and 2 (above).


Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $61 \%$ yield $(37.5 \mathrm{mg}) .[\alpha]_{\mathrm{D}}^{22}+146.0700\left(c \quad 0.0250, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3483.6,2964.7,2933.0,2874.1,1707.1,1463.3,1174.0,1115.6,1023.1$; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.42(1 \mathrm{H}$, dd, $J=7.3,1.6 \mathrm{~Hz}), 4.13-3.83(2 \mathrm{H}, \mathrm{m}), 3.16(2 \mathrm{H}, \mathrm{d}, J=7.4 \mathrm{~Hz}), 2.52-1.77(5 \mathrm{H}, \mathrm{m}), 1.38$ $(3 \mathrm{H}, \mathrm{s}), 1.11(3 \mathrm{H}, \mathrm{d}, J=4.3 \mathrm{~Hz}), 0.70(3 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 212.8,83.6,74.1,64.6,32.8,25.5,20.4,19.7,15.7,9.9$; NMR spectral data of the minor
anti product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.50(1 \mathrm{H}, \mathrm{dd}, J=6.6,2.2 \mathrm{~Hz}), 4.13-3.83$ $(2 \mathrm{H}, \mathrm{m}), 3.24(1 \mathrm{H}, \mathrm{d}, J=6.8 \mathrm{~Hz}), 2.52-1.77(5 \mathrm{H}, \mathrm{m}), 1.36(3 \mathrm{H}, \mathrm{s}), 1.09(3 \mathrm{H}, \mathrm{d}, J=7.0$ $\mathrm{Hz}), 0.73(3 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 211.1,83.8,73.3,64.0$, $30.5,25.3,20.8,20.7,15.4,10.2 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{10} \mathrm{H}_{18} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$ 209.1, found: 209.2.


Following the general procedure for iminium salt-catalyzed oxidations, this pyran was synthesized in $54 \%$ yield $(20.3 \mathrm{mg}) .[\alpha]_{\mathrm{D}}^{22}+14.9200\left(c \quad 0.0081, \mathrm{CHCl}_{3}\right)$; IR $v \max$ (neat) $/ \mathrm{cm}^{-1} 3442.8,2963.8,1810.2,1635.9,1457.0,1384.8,1364.4,1070.1,1014.2$; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.58(1 \mathrm{H}$, dd, $J=7.3,2.5 \mathrm{~Hz}), 3.81-3.70(2 \mathrm{H}, \mathrm{m}), 3.19(1 \mathrm{H}, \mathrm{d}, J=7.5 \mathrm{~Hz}), 2.38(1 \mathrm{H}$, ddtd, $J=23.2$, $13.8,6.9,2.6 \mathrm{~Hz}), 1.90-1.48(6 \mathrm{H}, \mathrm{m}), 1.37(3 \mathrm{H}, \mathrm{s}), 0.70(6 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 216.5,80.7,78.1,62.8,33.1,30.6,25.4,20.6,20.5,19.3,15.0$; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.45(1 \mathrm{H}$, dd, $J=6.5,2.7 \mathrm{~Hz}), 3.81-3.70(2 \mathrm{H}, \mathrm{m}), 3.41(1 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}), 2.38(1 \mathrm{H}, \mathrm{ddtd}, J=23.2$, $13.8,6.9,2.6 \mathrm{~Hz}), 1.90-1.48(6 \mathrm{H}, \mathrm{m}), 1.38(3 \mathrm{H}, \mathrm{s}), 0.76(6 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}$ NMR $\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 215.5,78.9,78.1,62.6,31.8,30.7,25.6,20.7,20.1,19.2,15.3 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{11} \mathrm{H}_{20} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$223.1, found: 223.0.


Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $86 \%$ yield ( 50.2 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}+178.5000\left(c \quad 0.0385, \mathrm{CHCl}_{3}\right)$; IR $\nu \max \left(\right.$ neat $/ \mathrm{cm}^{-1} 3483.7,2956.2,2931.0,2860.6,1704.5,1635.7,1457.6,1379.4,1118.4$, 1045.8; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.60$ $(1 \mathrm{H}, \mathrm{dd}, J=6.9,1.8 \mathrm{~Hz}), 4.12-3.79(2 \mathrm{H}, \mathrm{m}), 3.12(1 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 2.27-1.74(5 \mathrm{H}, \mathrm{m})$, $1.38(3 \mathrm{H}, \mathrm{s}), 1.57-1.03(12 \mathrm{H}, \mathrm{m}), 1.02-0.77(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR $\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ $218.8,88.7,76.4,69.5,40.2,38.1,30.7,29.8,25.8,23.2,23.0,14.3$; NMR spectral data of the minor anti product: 1 H NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.73(1 \mathrm{H}, \mathrm{dd}, J=6.2,1.8 \mathrm{~Hz})$, $4.12-3.79(2 \mathrm{H}, \mathrm{m}), 3.20(1 \mathrm{H}, \mathrm{d}, J=6.6 \mathrm{~Hz}), 2.27-1.74(5 \mathrm{H}, \mathrm{m}), 1.36(3 \mathrm{H}, \mathrm{s}), 1.57-1.03$ $(12 \mathrm{H}, \mathrm{m}), 1.02-0.77(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 217.1,88.8,75.8,68.9$, $40.2,35.7,30.0,29.5,25.8,23.2,22.9,14.3 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{16} \mathrm{H}_{30} \mathrm{O}_{3} \mathrm{Na}$ $[\mathrm{M}+\mathrm{Na}]^{+}$293.2, found: 293.2.


Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $84 \%$ yield ( 63.2 mg ). $[\alpha]_{\mathrm{D}}^{22}+29.6200\left(c \quad 0.0218, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3467.6,3060.6,3027.2,2977.2,2872.5,1713.1,1600.1,1495.1,1450.5$, $1368.7,1176.1,1123.0,1050.9,1032.8,1001.8,908.8,746.4,701.7$; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 7.45-7.07(10 \mathrm{H}, \mathrm{m}), 5.22(1 \mathrm{H}$, dd, $J=7.6,3.2 \mathrm{~Hz}), 4.87(1 \mathrm{H}, \mathrm{d}, J=3.0 \mathrm{~Hz}), 4.10-3.70(2 \mathrm{H}, \mathrm{m}), 3.49(1 \mathrm{H}, \mathrm{d}, J=8.6$ $\mathrm{Hz}), 2.16-2.05(1 \mathrm{H}, \mathrm{m}), 1.99-1.65(3 \mathrm{H}, \mathrm{m}), 1.29(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ $214.9,142.8,139.4,130.0,128.7,128.5,128.3,127.0,126.6,88.9,76.5,69.7,52.8,37.6$, 25.7, 24.1; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ $7.45-7.07(10 \mathrm{H}, \mathrm{m}), 5.31(1 \mathrm{H}, \mathrm{dd} J=6.5,4.5 \mathrm{~Hz}), 4.65(1 \mathrm{H}, \mathrm{d}, J=4.5 \mathrm{~Hz}), 4.10-3.70$ $(2 \mathrm{H}, \mathrm{m}), 3.40(1 \mathrm{H}, \mathrm{d}, J=6.0 \mathrm{~Hz}), 2.16-2.05(1 \mathrm{H}, \mathrm{m}), 1.99-1.65(3 \mathrm{H}, \mathrm{m}), 1.28(3 \mathrm{H}, \mathrm{s}) ;$ ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 213.2,142.2,139.8,129.8,128.8,128.5,128.4,127.0$, 126.7, 126.6, 89.1, 76.5, 69.0, 52.7, 35.0, 25.1, 24.1; m/z (ESIMS) calculated for $\mathrm{C}_{20} \mathrm{H}_{22} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+} 333.2$, found: 333.3.


Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $82 \%$ yield ( 78.5 mg ). $[\alpha]_{\mathrm{D}}{ }^{22}+137.3200\left(c 0.0523, \mathrm{CHCl}_{3}\right)$; IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3488.5,2954.2,2868.6,1705.6,1635.8,1449.6,1392.5,1387.8,1272.9$, 1163.9, 1115.3, 1055.7; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta 4.58(1 \mathrm{H}, \mathrm{dd}, J=7.3,2.9 \mathrm{~Hz}), 4.07-3.80(2 \mathrm{H}, \mathrm{m}), 3.26(1 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz})$, $2.58(1 \mathrm{H}, \mathrm{pd}, J=8.4,2.7 \mathrm{~Hz}), 2.26-2.09(1 \mathrm{H}, \mathrm{m}), 2.05-1.19(9 \mathrm{H}, \mathrm{m}), 1.38(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 217.8,88.6,76.1,69.6,41.5,37.8,29.9,26.2,25.7,24.9$; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.61(1 \mathrm{H}$, dd, $J=6.7,3.6 \mathrm{~Hz}), 4.07-3.80(2 \mathrm{H}, \mathrm{m}), 3.32(1 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 2.38(1 \mathrm{H}, \mathrm{pd}, J=8.5,3.4$ $\mathrm{Hz}), 2.26-2.09(1 \mathrm{H}, \mathrm{m}), 2.05-1.19(9 \mathrm{H}, \mathrm{m}), 1.35(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ $215.9,88.7,75.7,69.0,41.2,35.8,29.6,26.0,25.8,25.4 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{12} \mathrm{H}_{20} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$235.1, found: 235.2.


Following the general procedure for iminium salt-catalyzed oxidations, this furan was synthesized in $76 \%$ yield ( 70.0 mg ) . $[\alpha]_{\mathrm{D}}{ }^{22}+179.8000\left(c\right.$ 0.0300, $\mathrm{CHCl}_{3}$ ); IR $\nu \max$ (neat) $/ \mathrm{cm}^{-1} 3382.5,2928.8,2853.5,1706.6,1589.6,1449.4,1172.9,1118.9,1050.6$; NMR spectral data of the major syn product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.41(1 \mathrm{H}$, dd, $J=7.4,2.2 \mathrm{~Hz}), 4.10-3.79(2 \mathrm{H}, \mathrm{m}), 3.19(1 \mathrm{H}, \mathrm{d}, J=7.5 \mathrm{~Hz}), 2.34-2.13(1 \mathrm{H}, \mathrm{m}), 1.28$ $(3 \mathrm{H}, \mathrm{s}), 2.13-1.06(14 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 217.7,88.6,79.2,69.6,40.6$, $37.9,30.8,26.7,26.2,26.0,25.8,25.5,24.7$; NMR spectral data of the minor anti product: ${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 4.48(1 \mathrm{H}, \mathrm{dd}, J=6.8,2.7 \mathrm{~Hz}), 4.10-3.79(2 \mathrm{H}, \mathrm{m})$, $3.27(1 \mathrm{H}, \mathrm{d}, J=6.9 \mathrm{~Hz}), 2.34-2.13(1 \mathrm{H}, \mathrm{m}), 1.28(3 \mathrm{H}, \mathrm{s}), 2.13-1.06(14 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 216.0,88.8,78.5,69.0,40.5,35.5,30.4,26.8,26.3,26.1,25.9,25.7$, 24.7; $m / z$ (ESIMS) calculated for $\mathrm{C}_{13} \mathrm{H}_{22} \mathrm{O}_{3} \mathrm{Na}[\mathrm{M}+\mathrm{Na}]^{+}$249.2, found: 249.2.


To a solution of the ketone ( $64.3 \mathrm{mg}, 0.284 \mathrm{mmol}$ ) in DCM ( 3.6 mL ) was added acetic acid $(9.0 \mu \mathrm{~L})$ and $p$-toluenesulfonhydrazide ( $79.0 \mathrm{mg}, 0.284 \mathrm{mmol}$ ). The reaction was stirred overnight at room temperature. The mixture was then diluted with DCM ( 10 mL ) and washed with water $(2 \times 10 \mathrm{~mL})$. The organic layer was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated in vacuo. The crude product was purified by FCC (85:15 hexane:ethyl acetate), giving the tosylhydrazone ( $78.0 \mathrm{mg}, 70 \%$ ). The purified product was recrystallized from $\mathrm{CHCl}_{3} /$ hexane to give white needle-like crystals.


Figure 6.2. X-ray crystal structure of tosylhydrazone $\mathbf{X}$.


Figure 6.3. Crystal packing of tosylhydrazone $\mathbf{X}$.

Table 6.2. Crystal data and structure refinement for $\mathbf{X}$

| Empirical formula | C 20 H 30 N 2 O 4 S |  |
| :--- | :--- | :--- |
| Formula weight | 394.52 |  |
| Temperature | $100(2) \mathrm{K}$ |  |
| Wavelength | $0.71073 \AA$ |  |
| Crystal system | Orthorhombic |  |
| Space group | $\mathrm{P} 2(1) 2(1) 2(1)$ |  |
| Unit cell dimensions | $\mathrm{a}=6.1881(6) \AA$ | $=90^{\circ}$. |
|  | $\mathrm{b}=17.8049(17) \AA$ | $=90^{\circ}$. |
|  | $\mathrm{c}=18.7593(18) \AA$ | $=90^{\circ}$. |
| Volume | $2066.9(3) \AA^{3}$ |  |
| Z | 4 |  |
| Density (calculated) | $1.268 \mathrm{Mg} / \mathrm{m}^{3}$ |  |
| Absorption coefficient | $0.184 \mathrm{~mm}-1$ |  |
| $\mathrm{~F}(000)$ | 848 |  |
| Crystal size | $0.40 \times 0.09 \mathrm{x} 0.03 \mathrm{~mm}{ }^{3}$ |  |
| Theta range for data collection | $2.17 \mathrm{to} 29.57^{\circ}$. |  |
| Index ranges | $-8<=\mathrm{h}<=8,-24<=\mathrm{k}<=24,-25<=1<=26$ |  |

Reflections collected
Independent reflections
Completeness to theta $=29.57^{\circ}$
Absorption correction
Max. and min. transmission
Refinement method
Data / restraints / parameters
Goodness-of-fit on F2
Final R indices [ $\mathrm{I}>2 \operatorname{sigma}(\mathrm{I})$ ]
R indices (all data)
Absolute structure parameter
Largest diff. peak and hole

24050
$5801[\mathrm{R}(\mathrm{int})=0.0577]$
99.9 \%

Semi-empirical from equivalents
0.9945 and 0.9301

Full-matrix least-squares on $\mathrm{F}^{2}$
5801 / 0 / 252
1.004
$\mathrm{R} 1=0.0531, \mathrm{wR} 2=0.1104$
$R 1=0.0703, w R 2=0.1180$
0.11(8)
0.462 and -0.205 e. $\AA^{-3}$

## Key NMR Data for Table 4



| entry | R | key NMR spectra | entry | R | key NMR spectra |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | $n-\mathrm{Bu}$ |  | 5 | $\mathrm{Ph}_{2} \mathrm{CH}-$ |  |
| 2 | $i-\operatorname{Pr}$ |  | 6 | cyclopentyl |  |
| 3 | $i-\operatorname{Pr}(\mathrm{n}=2)$ |  | 7 | Cyc |  |
| 4 | $(\mathrm{n}-\mathrm{Bu})_{2} \mathrm{CH}-$ |  |  |  |  |

## Stereodivergent Allene Oxidation



Following the general procedure for DMDO oxidations, furans I and II were synthesized (combined mass 21.2 mg , combined yield $84 \%$ ). Use of methanol as solvent gives the sterically favored product I as the major diastereomer, whereas use of chloroform allows for hydrogen bonding with DMDO and gives the hydroxyl-directed oxidation product II as the major diastereomer. Following a reported procedure, ${ }^{7}$ the product mixture was benzoylated with 3,5-dinitrobenzoyl chloride. Both benzoylated diastereomers (III and IV, below) were racemic as determined by HPLC analysis.


HPLC conditions: Daicel Chiralcel OD-H, $n$-hexane $/ i-\mathrm{PrOH}=90 / 10$, Flow rate $=1$ $\mathrm{mL} / \mathrm{min}, \mathrm{UV}=254 \mathrm{~nm}, \mathrm{t}_{\mathrm{R}}=12.1 \mathrm{~min}[(+)-\mathbf{I I I}], \mathrm{t}_{\mathrm{R}}=13.3 \mathrm{~min}[(-)-\mathrm{III}], \mathrm{t}_{\mathrm{R}}=15.2 \mathrm{~min}[(-$ $)-\mathbf{I V}]$, and $\mathrm{t}_{\mathrm{R}}=36.6 \mathrm{~min}[(+)-\mathbf{I V}]$.


(+)-I

(+)-III
Obtained in previous synthesis (Table 4, entry 7). HPLC conditions: Daicel Chiralcel OD-H, $n$-hexane $/ i-\mathrm{PrOH}=90 / 10$, Flow rate $=1 \mathrm{~mL} / \mathrm{min}, \mathrm{UV}=254 \mathrm{~nm}, \mathrm{t}_{\mathrm{R}}=11.5 \mathrm{~min}$ $[(+)-\mathrm{III}], \mathrm{t}_{\mathrm{R}}=12.9 \mathrm{~min}[(-)-\mathrm{III}]$.



Following the general procedure for iminium salt-catalyzed oxidations (by $i$-Pr catalyst), furans I and II were synthesized (combined mass 35.7 mg , combined yield $80 \%$ ). Following a reported procedure, ${ }^{12}$ the product mixture was benzoylated with 3,5dinitrobenzoyl chloride. The benzoylated diastereomers (III and IV) were $70 \%$ ee and $86 \% e e$, respectively, as determined by HPLC analysis.

(+)-III

(-)-IV

HPLC conditions: Daicel Chiralcel OD-H, $n$-hexane $/ i$-PrOH $=90 / 10$, Flow rate $=1$ $\mathrm{mL} / \mathrm{min}, \mathrm{UV}=254 \mathrm{~nm}, \mathrm{t}_{\mathrm{R}}=11.4 \mathrm{~min}[(+)-\mathrm{III}], \mathrm{t}_{\mathrm{R}}=12.5 \mathrm{~min}[(-)-\mathrm{III}], \mathrm{t}_{\mathrm{R}}=14.1 \mathrm{~min}[(-$ $)-\mathbf{I V}]$, and $\mathrm{t}_{\mathrm{R}}=33.9 \mathrm{~min}[(+)-\mathbf{I V}]$.


## References and Notes

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5. Racemic propargyl alcohols were synthesized for the acquisition of racemic HPLC assays. General Procedure: To a solution of the protected alkynol in dry THF $(0.4 \mathrm{M})$ at $-78{ }^{\circ} \mathrm{C}$ was added $n$ - BuLi ( 1.2 equiv., 2.5 M in hexane). After stirring for 15 min , the aldehyde ( 1.2 equiv.) was added dropwise, and the reaction was slowly warmed to room temperature. After complete consumption of the starting material (as judged by TLC analysis), the reaction was quenched with
sat. aq. $\mathrm{NH}_{4} \mathrm{Cl}$. The aqueous layer was separated and extracted with diethyl ether (x3). The combined organic layers were washed with brine, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and concentrated. FCC (100\% hexane to $90: 10$ hexane/ethyl acetate) of the crude residue gave the pure racemic propargyl alcohol.
6. Running these reactions at $-40^{\circ} \mathrm{C}$ sometimes resulted in the formation of the undesired $\mathrm{S}_{\mathrm{N}} 2$ product. To prevent this side reaction, the temperature of both the mesylate and cuprate solutions was reduced to $-78^{\circ} \mathrm{C}$.
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### 6.4. Chapter III



To the mixture of the ketone $3.4(470.3 \mathrm{mg}, 2.09 \mathrm{mmol})$ in 4.2 mL THF $(0.5 \mathrm{M})$ was added ethylene glycol ( $350 \mu \mathrm{~L}, 6.16 \mathrm{mmol}$ ), $p-\mathrm{TsOH} \cdot \mathrm{H}_{2} \mathrm{O}(40.0 \mathrm{mg}, 0.209 \mathrm{mmol})$, and triethyl orthoformate ( $626 \mu \mathrm{~L}, 3.76 \mathrm{mmol}$ ) at room temperature. After 24 hrs , the reaction mixture was quenched with triethylamine ( $58 \mu \mathrm{~L}, 0.418 \mathrm{mmol}$ ) and concentrated. The residue was purified by FCC ( $15 \%$ to $20 \%$ ethyl acetate-hexanes) to give the ketal $\mathbf{3 . 9}$ in $55 \%$ yield ( $308.2 \mathrm{mg}, 1.15 \mathrm{mmol}, 76 \%$ yield brsm ) together with $28 \%$ starting material recovered ( $133.4 \mathrm{mg}, 0.595 \mathrm{mmol}$ ). IR $\nu_{\text {max }}$ (neat) $/ \mathrm{cm}^{-1}: 3501,2954,1689,1644,1436$, $1282,1250,1191,1116,1058,1006,971,951 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.00(1 \mathrm{H}, \mathrm{t}, J$ $=3.9 \mathrm{~Hz}), 4.04-3.96(2 \mathrm{H}, \mathrm{m}), 3.89(2 \mathrm{H}$, apprent $\mathrm{t}, J=6.1 \mathrm{~Hz}), 3.76(3 \mathrm{H}, \mathrm{s}), 2.35-1.97$ $(6 \mathrm{H}, \mathrm{m}), 1.75(1 \mathrm{H}, \mathrm{dd}, J=13.9,5.5 \mathrm{~Hz}), 1.61-1.51(1 \mathrm{H}, \mathrm{m}), 0.97(3 \mathrm{H}, 3 \mathrm{~s}) . ;{ }^{13} \mathrm{C}$ NMR(100 MHz, $\left.\mathrm{CDCl}_{3}\right) 167.6,138.9,134.1,119.2,79.4,65.0,64.6,51.7,49.3,38.0$, 33.5, 28.5, 23.1, 11.9; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{14} \mathrm{H}_{20} \mathrm{O}_{5}+\mathrm{Na}\right]^{+}: 291.1$, found 291.2.


Sodium hydride ( $60 \%$ dispersion in mineral oil, $169.4 \mathrm{mg}, 4.24 \mathrm{mmol}$ ) in 10.5 mL anhydrous THF was cooled to $0^{\circ} \mathrm{C}$. The alcohol 3.9 ( $947.7 \mathrm{mg}, 3.53 \mathrm{mmol}$ ) in 24.5 mL anhydrous THF was added in slowly. The reaction mixture was stirred for 10 min and warmed up to room temperature. After additional 5 min , iodomethane ( $660 \mu \mathrm{~L}, 10.6$ mmol ) was added in one portion. After overnight, the reaction was cooled to $0{ }^{\circ} \mathrm{C}$ and quenched with 35 mL sat. aqueous ammonium chloride solution. The mixture was then extracted with diethyl ether ( 40 mL X 2 ). The combined organic extractions were dried over sodium sulfate, filtered and concentrated. Further purification with FCC ( $15 \%$ ethyl acetate-hexanes) gave colorless oil 3.10 ( $722.8 \mathrm{mg}, 2.56 \mathrm{mmol}$ ) in $73 \%$ yield. IR $v_{\text {max }}$ (neat)/ $\mathrm{cm}^{-1}: 2951,2878,1721,1434,1250,1163,1065,1010,770 ;{ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.06(1 \mathrm{H}, \mathrm{t}, J=4.0 \mathrm{~Hz}), 3.98-3.90(2 \mathrm{H}, \mathrm{m}), 3.89-3.80(2 \mathrm{H}, \mathrm{m}), 3.75(3 \mathrm{H}, \mathrm{s})$, $3.25(3 \mathrm{H}, \mathrm{s}), 2.40(1 \mathrm{H}, \mathrm{ddd}, J=15.1,10.0,6.3 \mathrm{~Hz}), 2.31-2.24(2 \mathrm{H}, \mathrm{m}), 2.22-2.12(1 \mathrm{H}$, $\mathrm{m}), 1.96(1 \mathrm{H}$, ddd, $J=13.8,10.0,6.3 \mathrm{~Hz}), 1.82(1 \mathrm{H}$, ddd, $J=13.8,10.7,6.3 \mathrm{~Hz}), 1.73-$ $1.57(2 \mathrm{H}, \mathrm{m}), 1.04(3 \mathrm{H}, \mathrm{d}, J=8.3 \mathrm{~Hz}) . ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 167.4,142.1,133.9$, $119.1,83.8,64.7,64.6,53.7,51.6,50.7,34.2,33.5,29.6,23.5,16.2$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{15} \mathrm{H}_{22} \mathrm{O}_{5}+\mathrm{Na}\right]^{+}: 305.2$, found 305.2.


The ester 3.10 ( $722.8 \mathrm{mg}, 2.56 \mathrm{mmol}$ ) in 44 mL anhydrous hexane $(0.05 \mathrm{M})$ was added $\mathrm{TMSCH}_{2} \mathrm{Li}(1.0 \mathrm{M}$ in pentane, $7.7 \mathrm{~mL}, 7.68 \mathrm{mmol})$ at $0^{\circ} \mathrm{C}$. After 30 min , the reaction went to completion. To the reaction mixture was added 1 mL Methanol at $0^{\circ} \mathrm{C}$. After 10 min, the ice bath was removed and the reaction mixture continued to be stirred for another 20 min . The reaction was then quenched with 40 mL sat. aqueous ammonium chloride solution and extracted with diethyl ether ( 40 mL X 3 ). The combined organic phase was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated. The residue obtained was purified with FCC ( $15 \%$ ethyl acetate-hexanes) to give colorless oil $\mathbf{3 . 1 1}$ ( $521.2 \mathrm{mg}, 1.96$ mmol ) in $77 \%$ yield. in IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 2947,2828,1674,1374,1233,1162,1065$, 953; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $6.92(1 \mathrm{H}, \mathrm{t}, J=3.9 \mathrm{~Hz}), 4.01-3.89(2 \mathrm{H}, \mathrm{m}), 3.89-$ $3.78(2 \mathrm{H}, \mathrm{m}), 3.21(3 \mathrm{H}, \mathrm{s}), 2.46(1 \mathrm{H}$, ddd, $J=19.5,12.8,7.7 \mathrm{~Hz}), 2.37-2.24(5 \mathrm{H}, \mathrm{m})$, $2.19-2.04(1 \mathrm{H}, \mathrm{m}), 2.04-1.91(1 \mathrm{H}, \mathrm{m}), 1.84(1 \mathrm{H}, \mathrm{ddd}, J=13.7,10.9,6.0 \mathrm{~Hz}), 1.64$ ( 2 H , apparent $\mathrm{t}, J=6.1 \mathrm{~Hz}$ ), $1.05(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 199.4, 142.6, 141.4, 119.0, 84.5, 64.8, 64.6, 54.0, 50.9, 34.6, 33.5, 30.3, 29.7, 27.9, 23.6, 15.8; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{15} \mathrm{H}_{22} \mathrm{O}_{4}+\mathrm{Na}\right]^{+}: 289.2$, found 289.2.


To a solution of the ketone $\mathbf{3 . 1 1}$ ( $132.2 \mathrm{mg}, 0.500 \mathrm{mmol}$ ) in 2.5 mL DCM ( 0.2 M ) was added triethylamine ( $208 \mu \mathrm{~L}, 1.49 \mathrm{mmol}$ ) and triethylsilyl triflate ( $169 \mu \mathrm{~L}, 0.750 \mathrm{mmol}$ ) at $0{ }^{\circ} \mathrm{C}$. After 30 min , the reaction was quenched by 30 mL sat. aqueous sodium bicarbonate and extracted with diethyl ether ( 40 mL X 2 ). The combined organic phase was then dried over sodium sulfate, filtered and concentrated to give light yellow oil $\mathbf{3 . 1 2}$ and used in the next step without further purification. To a flask with diene $\mathbf{3 . 1 2} \mathrm{in} 6 \mathrm{~mL}$ diethyl ether ( 0.1 M ) was added quinone $3.17(124.5 \mathrm{mg}, 0.750 \mathrm{mmol})$ at $0{ }^{\circ} \mathrm{C}$. The reaction was allowed to warm up to room temperature and stirred for 3.5 hrs . The yellow solution was then concentrated. The silica gel was deactivated with $1 \%$ triethylaminehexanes for the later epimerization of C 5 proton in the major product $(\mathbf{3 . 2 1} \rightarrow \mathbf{3 . 2 3})$. The crude product was purified by $\operatorname{FCC}(8 \%$ to $12 \%$ ethyl acetate-hexanes) to give light yellow oils: major diastereomer $3.23(188.8 \mathrm{mg}, 0.345 \mathrm{mmol})$ in $69 \%$ yield and minor diastereomer 3.22 ( $44.9 \mathrm{mg}, 0.0822 \mathrm{mmol}$ ) in $16 \%$ yield. IR $v_{\max }$ (neat)/ $/ \mathrm{cm}^{-1}: 2955,2876$, 1723, 1688, 1659, 1651, 1455, 1315, 1227, 1206, 1077, 1060, 1006, 745; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{42} \mathrm{O}_{8} \mathrm{Si}+\mathrm{Na}\right]^{+}: 569.3$, found 569.1; 3.22: ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 6.67 $(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 6.57(1 \mathrm{H}, \mathrm{dd}, J=10.3,1.7 \mathrm{~Hz}), 3.86-3.75(4 \mathrm{H}, \mathrm{m}), 3.67(3 \mathrm{H}, \mathrm{s})$,
$3.51(1 \mathrm{H}, \mathrm{ddd}, J=12.1,7.0,1.6 \mathrm{~Hz}), 3.45-3.39(1 \mathrm{H}, \mathrm{m}), 3.20(3 \mathrm{H}, \mathrm{s}), 2.57-2.48(1 \mathrm{H}$, m), $2.33(1 \mathrm{H}, \mathrm{dd}, J=17.0,7.0 \mathrm{~Hz}$ ), $2.12(1 \mathrm{H}, \mathrm{ddd}, J=17.1,12.1,1.4 \mathrm{~Hz}), 1.94(1 \mathrm{H}$, ddd, $J=12.9,8.5,7.2 \mathrm{~Hz}), 1.83(1 \mathrm{H}, \mathrm{ddd}, J=13.1,8.5,6.6 \mathrm{~Hz}), 1.75-1.63(2 \mathrm{H}, \mathrm{m})$, $1.56-1.39(2 \mathrm{H}, \mathrm{m}), 1.38-1.30(1 \mathrm{H}, \mathrm{m}), 1.21-1.12(1 \mathrm{H}, \mathrm{m}), 1.03(3 \mathrm{H}, \mathrm{s}), 0.95-0.86$ $(9 \mathrm{H}, \mathrm{m}), 0.66-0.55(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 198.2, 192.5, 170.5, 142.7, 138.9, 138.4, 118.6, 112.2, 86.3, 64.4(2 overlapping signals), 64.4, 53.3, 52.2, 50.9, 46.0, 33.8, 32.0, 31.5, 29.4, 28.9, 25.2, 19.02, 6.8, 6.1; 3.23: ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 6.82 $(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 6.59(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 3.88-3.76(4 \mathrm{H}, \mathrm{m}), 3.62(3 \mathrm{H}, \mathrm{s}), 3.61-$ $3.54(1 \mathrm{H}, \mathrm{m}), 3.17-3.08(1 \mathrm{H}, \mathrm{m}), 3.02(3 \mathrm{H}, \mathrm{s}), 2.67(1 \mathrm{H}, \mathrm{ddd}, J=17.5,10.5,1.1 \mathrm{~Hz})$, $2.50-2.39(2 \mathrm{H}, \mathrm{m}), 2.01-1.91(1 \mathrm{H}, \mathrm{m}), 1.85-1.74(2 \mathrm{H}, \mathrm{m}), 1.74-1.65(1 \mathrm{H}, \mathrm{m}), 1.55$ $-1.45(1 \mathrm{H}, \mathrm{m}), 1.41-1.31(1 \mathrm{H}, \mathrm{m}), 1.24-1.16(1 \mathrm{H}, \mathrm{m}), 1.06(3 \mathrm{H}, \mathrm{s}), 1.01-0.92(9 \mathrm{H}$, $\mathrm{m}), 0.77-0.65(6 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR(100 MHz, $\left.\mathrm{CDCl}_{3}\right) 197.0,193.0,168.9,144.9,141.8$, 138.6, 118.7, 112.7, 86.9, 65.7, 64.4, 64.4, 53.2, 52.4, 50.5, 44.5, 34.4, 33.6, 29.7, 29.4, 28.9, 26.4, 18.8, 6.9, 6.1.


The diol 3.5 ( $1.3543 \mathrm{~g}, 5.99 \mathrm{mmol}$ ) in 30 mL dichloromethane ( 0.2 M ) was added 2,6lutidine ( $3.5 \mathrm{~mL}, 29.9 \mathrm{mmol}$ ) and triethylsilyl triflate ( $3.4 \mathrm{~mL}, 15.0 \mathrm{mmol}$ ) at $0{ }^{\circ} \mathrm{C}$. The ice bath then removed and the mixture was stirred for 2 hrs for completion. To the mixture was added 50 mL sat. aqueous ammonium chloride solution. The mixture was extracted with 30 mL and then 60 mL diethyl ether. The combined organic layer was dried over sodium sulfate and concentrated. The residue obtained was purified by FCC ( $1 \%$ ethyl acetate-hexanes) to yield bis-TES ether $\mathbf{3 . 6}$ as colorless oil ( $2.556 \mathrm{~g}, 5.63 \mathrm{mmol}$, $94 \%$ yield). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 2954,2911,2876,1724,1461,1371,1248,1127,1090$, $1014,866,738 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $6.63-6.56(1 \mathrm{H}, \mathrm{m}), 4.18(1 \mathrm{H}, \mathrm{t}, J=8.3$ $\mathrm{Hz}), 3.71(3 \mathrm{H}, \mathrm{s}), 2.33-2.25(1 \mathrm{H}, \mathrm{m}), 2.24-2.00(4 \mathrm{H}, \mathrm{m}), 1.68-1.56(2 \mathrm{H}, \mathrm{m}), 1.45-$ $1.35(1 \mathrm{H}, \mathrm{m}), 1.01-0.87(21 \mathrm{H}, \mathrm{m}), 0.64-0.51(12 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $167.9,137.6,136.9,83.7,80.0,51.4,49.0,37.7,30.5,25.5,22.6,17.8,7.4,7.02,6.9,5.1$; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{24} \mathrm{H}_{46} \mathrm{O}_{4} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 477.3$, found 477.2.


The ester $3.6(2.2840 \mathrm{~g}, 5.03 \mathrm{mmol})$ in 100 mL anhydrous hexane $(0.05 \mathrm{M})$ was added $\mathrm{TMSCH}_{2} \mathrm{Li}(1.0 \mathrm{M}$ in pentane, $50.3 \mathrm{~mL}, 50.3 \mathrm{mmol})$ at $0^{\circ} \mathrm{C}$. After 2.5 hrs , the reaction
went to completion. To the reaction mixture was added 10 mL methanol at $0^{\circ} \mathrm{C}$. After 10 min , the ice bath was removed and the reaction mixture continued to be stirred for another 20 min . The reaction was then quenched with 60 mL sat. aqueous ammonium chloride solution and extracted with ethyl acetate ( $60 \mathrm{~mL} \mathrm{X} \mathrm{2)}$. phase was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated. The residue obtained was purified with FCC ( $0 \%$ to $0.4 \%$ ethyl acetate-hexanes) to give colorless oil 3.7 ( 1.8572 g , $4.24 \mathrm{mmol}, 84 \%$ yield) as the product. IR $v_{\max }$ (neat) $/ \mathrm{cm}^{-1}: 2955,2876,1679,1462,1415$, $1377,1240,1089,1013,912,873,739 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 6.57-6.51(1 \mathrm{H}, \mathrm{m})$, $4.18(1 \mathrm{H}, \mathrm{t}, J=8.3 \mathrm{~Hz}), 2.39-2.26(2 \mathrm{H}, \mathrm{m}), 2.25(3 \mathrm{H}, \mathrm{s}), 2.14(1 \mathrm{H}$, ddd, $J=19.4,7.3$, $3.1 \mathrm{~Hz}), 2.08-1.97(2 \mathrm{H}, \mathrm{m}), 1.68-1.52(2 \mathrm{H}, \mathrm{m}), 1.41-1.32(1 \mathrm{H}, \mathrm{m}), 1.01-0.82(21 \mathrm{H}$, $\mathrm{m}), 0.67-0.51(12 \mathrm{H}, \mathrm{m}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 199.8,146.1,137.1,83.8,79.9$, 49.1, 37.6, 30.5, 27.4, 25.3, 22.9, 17.7, 7.4, 7.0, 6.8, 5.1; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{24} \mathrm{H}_{46} \mathrm{O}_{3} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 461.3$, found 461.2.


To a solution of the ketone 3.7 ( $827.1 \mathrm{mg}, 1.89 \mathrm{mmol}$ ) in 19 mL DCM ( 0.1 M ) was added triethylamine ( $790 \mu \mathrm{~L}, 5.67 \mathrm{mmol}$ ) and trimethylsilyl triflate $(513 \mu \mathrm{~L}, 2.83 \mathrm{mmol})$ at $0{ }^{\circ} \mathrm{C}$. After 20 min , the reaction was quenched by 12 mL sat. aqueous sodium bicarbonate and extracted with 65 mL ethyl acetate. The organic phase was washed with 10 mL water, 10 mL brine and dried with sodium sulfate. The filtrate was then concentrated to give light yellow oil 3.8 and used in the next step without further purification. To a flask with quinone $3.17(161.0 \mathrm{mg}, 0.97 \mathrm{mmol})$ in 8 mL diethyl ether was added the diene $\mathbf{3 . 8}$ in 10 mL diethyl ether at $0^{\circ} \mathrm{C}$. The reaction was allowed to warm up to room temperature and stirred for 5 hrs . The yellow solution was then concentrated and purified by FCC ( $2 \%$ to $5 \%$ ethyl acetate-hexanes) to give light yellow oil 3.20 ( $556.3 \mathrm{mg}, 0.823 \mathrm{mmol}$ ) in $93 \%$ yield. IR $v_{\max }($ neat $) / \mathrm{cm}^{-1}$ : 2955, 2875, 1704, 1256, 1233, 1064, 1008, 867, 844, 740; ${ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $6.66(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 6.54(1 \mathrm{H}, \mathrm{dd}, J=10.3,1.3 \mathrm{~Hz}), 3.73$ $(1 \mathrm{H}, \mathrm{dd}, J=6.2,3.1 \mathrm{~Hz}), 3.67(3 \mathrm{H}, \mathrm{s}), 3.55(1 \mathrm{H}, \mathrm{dd}, J=10.9,6.4 \mathrm{~Hz}), 3.46-3.40(1 \mathrm{H}$, m), $2.60-2.52(1 \mathrm{H}, \mathrm{m}), 2.24(1 \mathrm{H}, \mathrm{dd}, J=16.9,6.7 \mathrm{~Hz}), 2.04(1 \mathrm{H}, \mathrm{dd}, J=16.8,12.3 \mathrm{~Hz})$, $1.98-1.89(1 \mathrm{H}, \mathrm{m}), 1.88-1.80(1 \mathrm{H}, \mathrm{m}), 1.51-1.39(3 \mathrm{H}, \mathrm{m}), 1.39-1.31(1 \mathrm{H}, \mathrm{m}), 1.24$ $-1.17(1 \mathrm{H}, \mathrm{m}), 1.01-0.89(21 \mathrm{H}, \mathrm{m}), 0.76-0.59(6 \mathrm{H}, \mathrm{m}), 0.57-0.47(6 \mathrm{H}, \mathrm{m}), 0.15(9 \mathrm{H}$, $\mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 198.4, 191.8, 170.7, 139.0, 138.2, 138.1, 117.3, 83.6, 81.1, 64.5, 53.2, 52.0, 46.2, 35.9 32.5, 32.1, 31.5, 29.4, 25.3, 23.7, 7.5, 7.1, 6.3, 5.0, 1.5; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{60} \mathrm{O}_{7} \mathrm{Si}_{3}+\mathrm{Na}\right]^{+}: 699.4$, found 699.3.


The ketone 3.20 ( $99.0 \mathrm{mg}, 0146 \mathrm{mmol}$ ) in 1.0 mL methanol $(0.15 \mathrm{M})$ was added $\mathrm{CeCl}_{3} \bullet 7 \mathrm{H}_{2} \mathrm{O}(109.1 \mathrm{MG}, 0.293 \mathrm{mmol})$ at room temperature. After the salt was completely dissolved, the solution was stirred for additional 3 min and cooled to $0^{\circ} \mathrm{C}$ and stirred for 5 min . To the mixture was added sodium borohydride ( $11.1 \mathrm{mg}, 0.293 \mathrm{mmol}$ ). Additional sodium borohydride was added three times at 15 min intervals ( $5.6 \mathrm{mg} \mathrm{X} \mathrm{3}$, $0.147 \mathrm{mmol} \mathrm{X} \mathrm{3)} \mathrm{at} 0{ }^{\circ} \mathrm{C}$. After additional 15 min stirring, the reaction mixture was quenched with 5 mL sat. aqueous ammonium chloride solution and extracted with diethyl ether ( 10 mL X 3 ). The combined organic portions was dried over sodium sulfate, filtered and concentrated. Further purification with FCC ( $5 \%$ to $8 \%$ ethyl acetate-hexanes) gave the mono-reduction product $3.21(18.2 \mathrm{mg}, 0.0268 \mathrm{mmol}, 18 \%$ yield, X-ray crystal structure availble) and di-reduction product 3.22 ( $26.4 \mathrm{mg}, 0.0482 \mathrm{mmol}, 33 \%$ yield) as colorless oils.
3.21: IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}$ : 2954, 2950, 2915, 2873, 1666, 1254, 1243, 1060, 1005, 874, 842, 739,$726 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $6.57(1 \mathrm{H}, \mathrm{dt}, J=10.4,1.8 \mathrm{~Hz}), 5.99(1 \mathrm{H}, \mathrm{dd}, J=$ $10.4,2.3 \mathrm{~Hz}), 5.26(1 \mathrm{H}, \mathrm{s}), 3.74(1 \mathrm{H}, \mathrm{dd}, J=6.1,3.5 \mathrm{~Hz}), 3.64(3 \mathrm{H}, \mathrm{s}), 3.52(1 \mathrm{H}, \mathrm{dd}, J=$ $11.3,6.4 \mathrm{~Hz}$ ), $3.10-3.00(1 \mathrm{H}, \mathrm{m}), 2.61-2.49(1 \mathrm{H}, \mathrm{m}), 2.24(1 \mathrm{H}, \mathrm{dd}, J=17.5,6.5 \mathrm{~Hz})$, $2.06-1.80(3 \mathrm{H}, \mathrm{m}), 1.56-1.31(5 \mathrm{H}, \mathrm{m}), 1.16-1.05(1 \mathrm{H}, \mathrm{m}), 1.02-0.82(21 \mathrm{H}, \mathrm{m}), 0.74$ $-0.59(6 \mathrm{H}, \mathrm{m}), 0.59-0.48(6 \mathrm{H}, \mathrm{m}), 0.17(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 191.6, $170.3,148.7,139.8,129.4,128.6,116.7,83.6,81.5,66.5,60.8,52.7,52.5,51.9,38.6$, $38.3,35.8,32.8,29.2,25.2,7.9,7.4,6.3,5.1,1.9$; (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{62} \mathrm{O}_{7} \mathrm{Si}_{3}+\mathrm{Na}\right]^{+}: 701.4$, found 700.9.
3.22: IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}$ : 2954, 2876, 1251, 1192, 1007, 878, 843, $725 ;{ }^{1} \mathrm{H}$ NMR (300 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) 6.09-5.96(1 \mathrm{H} \mathrm{m}), 5.89(\mathrm{~d}, J=1 \mathrm{H}, 9.7 \mathrm{~Hz}), 4.65(1 \mathrm{H}, \mathrm{d}, J=10.5 \mathrm{~Hz})$, $4.58-4.47(1 \mathrm{H}, \mathrm{m}), 3.79(1 \mathrm{H}, \mathrm{d}, J=10.8 \mathrm{~Hz}), 3.70(3 \mathrm{H}, \mathrm{s}), 2.78-2.52(3 \mathrm{H}, \mathrm{m}), 2.50-$ $2.32(1 \mathrm{H}, \mathrm{m}), 2.23-1.88(3 \mathrm{H}, \mathrm{m}), 1.56-1.42(1 \mathrm{H}, \mathrm{m}), 1.42-1.13(5 \mathrm{H}, \mathrm{m}), 1.05-0.78$ $(12 \mathrm{H}, \mathrm{m}), 0.66-0.46(6 \mathrm{H}, \mathrm{m}), 0.12(9 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 177.1,138.3$, $131.2,131.2,129.7,105.1,97.5,81.1,72.4,71.3,52.9,46.9,46.9,43.0,41.5,33.5,32.1$, 31.1, 27.1, $25.2,25.0,7.1,5.2,2.0$; (ESI/MS) $m / z$ Calcd for $\left[2 \mathrm{XC}_{29} \mathrm{H}_{48} \mathrm{O}_{6} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}$: 1119.6, found 1118.7.


Figure 6.4. $X$-Ray crytal structure of $\mathbf{3 . 2 1}$.
Table 6.3. Crystal data and structure refinement for $\mathbf{3 . 2 1}$

| Empirical formula | C35 H62 O7 Si3 |
| :---: | :---: |
| Formula weight | 679.12 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 £ |
| Crystal system | Monoclinic |
| Space group | P2(1)/c |
| Unit cell dimensions | $a=12.1566(13) \AA \quad=90^{\circ}$. |
|  | $\mathrm{b}=42.493(4) \AA \quad=105.781(2)^{\circ}$. |
|  | $\mathrm{c}=15.6819(16) \AA \quad=90^{\circ}$. |
| Volume | 7795.6(14) $\AA^{3}$ |
| Z | 8 |
| Density (calculated) | $1.157 \mathrm{Mg} / \mathrm{m}^{3}$ |
| Absorption coefficient | $0.164 \mathrm{~mm}^{-1}$ |
| F(000) | 2960 |
| Crystal size | $0.30 \times 0.25 \times 0.08 \mathrm{~mm}^{3}$ |
| Theta range for data collection | 1.43 to $23.03^{\circ}$. |
| Index ranges | $-13<=\mathrm{h}<=13,-46<=\mathrm{k}<=44,-17<=\mathrm{l}<=17$ |
| Reflections collected | 33842 |
| Independent reflections | 10847 [R(int) $=0.1176]$ |
| Completeness to theta $=23.03^{\circ}$ | 99.5 \% |
| Absorption correction | Semi-empirical from equivalents |

Max. and min. transmission
Refinement method
Data / restraints / parameters
Goodness-of-fit on $\mathrm{F}^{2}$
Final R indices [ $\mathrm{I}>2 \operatorname{sigma}(\mathrm{I})$ ]
R indices (all data)
Largest diff. peak and hole
0.9870 and 0.9524

Full-matrix least-squares on $\mathrm{F}^{2}$
10847 / 744 / 837
1.003
$R 1=0.0908, w R 2=0.1844$
$\mathrm{R} 1=0.1464, w R 2=0.2050$
0.474 and -0.418 e. $\AA^{-3}$




The alcohol 3.21 ( $12.9 \mathrm{mg}, 0.0190 \mathrm{mmol}$ ) in dichloromethane ( $0.2 \mathrm{~mL}, 0.1 \mathrm{M}$ ) was added imidazole ( $12.9 \mathrm{mg}, 0.190 \mathrm{mmol}$ ) and tert-butyldimethylsilyl chloride ( $\mathrm{TBSCl}, 14.3 \mathrm{mg}$, 0.0949 mmol ) at room temperature. After 30min, the reaction mixture was quenched with 2 mL sat. aqueous ammonium chloride and extracted twice with diethyl ether ( 3 mL X 2 ). The combined organic layer was dried, concentrated and used in the next step without further purifications. To the TBS-protected ether in dichloromethane:methanol solution $(1: 1,0.4 \mathrm{~mL}, 0.05 \mathrm{M})$ was added $\mathrm{TsOH} \cdot \mathrm{H}_{2} \mathrm{O}(1.6 \mathrm{mg}, 0.0085 \mathrm{mmol})$ at room temperature. After 20 min , the reaction was quenched by 2 mL sat. aqueous sodium bicarbonate and extracted three times with dichloromethane ( 5 mL X 3). The combined organic phase was dried over sodium sulfate, filtered, and concentrated to give crude product. Purification with FCC ( $15 \%$ to $50 \%$ ethyl acetate-hexanes) gave colorless oil $\mathbf{3 . 2 3}$ as the product ( 7.8 $\mathrm{mg}, 0.0165 \mathrm{mmol}, 87 \%$ yield over two steps). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 2953,2928,2857,1732$, $1674,1597,1254,1081,1060,965,868,839,805,778 ;{ }^{1} \mathrm{H} \operatorname{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 6.70$ $(1 \mathrm{H}, \mathrm{dd}, J=10.3,3.7 \mathrm{~Hz}), 6.07(1 \mathrm{H}, \mathrm{dd}, J=10.3,1.4 \mathrm{~Hz}), 4.69-4.62(1 \mathrm{H}, \mathrm{m}), 3.86(1 \mathrm{H}$, d, $J=4.1 \mathrm{~Hz}), 3.72(3 \mathrm{H}, \mathrm{s}), 3.41-3.31(1 \mathrm{H}, \mathrm{m}), 3.06(1 \mathrm{H}, \mathrm{dd}, J=11.9,6.1 \mathrm{~Hz}), 2.91$ $(2 \mathrm{H}, \mathrm{ddd}, J=12.2,7.7,3.4 \mathrm{~Hz}), 2.40(2 \mathrm{H}$, ddd, $J=25.3,18.3,6.4 \mathrm{~Hz}), 2.28-1.96(3 \mathrm{H}$, $\mathrm{m}), 1.89-1.61(3 \mathrm{H}, \mathrm{m}), 1.45-1.34(1 \mathrm{H}, \mathrm{m}), 0.95(3 \mathrm{H}, \mathrm{s}), 0.85-0.81(9 \mathrm{H}, \mathrm{m}), 0.12(6 \mathrm{H}$, d, $J=2.4 \mathrm{~Hz}$ ); ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{26} \mathrm{H}_{38} \mathrm{O}_{6} \mathrm{Si}+\mathrm{Na}\right]^{+}: 497.2$, found 497.2.


To a solution of the alcohol $3.22(40.0 \mathrm{mg}, 0.0730 \mathrm{mmol})$ in 0.8 mL dichloromethane $(0.1 \mathrm{M})$ was added triethylamine ( $100 \mu \mathrm{~L}, 0.717 \mathrm{mmol}$ ) and tert-butyldimethylsilyl triflate (TBSOTf, $134 \mu \mathrm{~L}, 0.583 \mathrm{mmol}$ ) at $0^{\circ} \mathrm{C}$. After 30 min , the reaction mixture was added 8 mL sat. aqueous ammonium chloride solution and extracted with diethyl ether $(22 \mathrm{~mL})$. The organic phase was dried and concentrated. The residue obtained was purified using FCC ( $0 \%$ to $2 \%$ ethyl acetate-hexanes) to give 3.25 in $71 \%$ yield ( 34.5 mg , 0.0521 mmol ). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}: 2955,1877,2857,1746,1728,1249,1189,1086,1056$, $1022,879,839 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $6.14(1 \mathrm{H}, \mathrm{ddd}, J=9.9,5.7,0.7 \mathrm{~Hz}$ ), 5.62 $(1 \mathrm{H}, \mathrm{ddd}, J=9.9,4.4,1.2 \mathrm{~Hz}), 4.52(1 \mathrm{H}, \mathrm{dd}, J=5.7,2.0 \mathrm{~Hz}), 3.83(1 \mathrm{H}, \mathrm{d}, J=3.9 \mathrm{~Hz})$, $3.69(1 \mathrm{H}, \mathrm{d}, J=4.3 \mathrm{~Hz}), 3.59(3 \mathrm{H}, \mathrm{s}), 2.69-2.54(2 \mathrm{H}, \mathrm{m}), 2.51-2.35(2 \mathrm{H}, \mathrm{m}), 2.11-$ $1.92(3 \mathrm{H}, \mathrm{m}), 1.58-1.37(3 \mathrm{H}, \mathrm{m}), 1.37-1.30(1 \mathrm{H}, \mathrm{m}), 1.17(1 \mathrm{H}, \mathrm{td}, J=13.3,5.1 \mathrm{~Hz})$, $0.95(9 \mathrm{H}, \mathrm{t}, J=7.9 \mathrm{~Hz}), 0.88(9 \mathrm{H}, \mathrm{s}), 0.86(3 \mathrm{H}, \mathrm{s}), 0.57(6 \mathrm{H}, \mathrm{q}, J=7.9 \mathrm{~Hz}), 0.13(9 \mathrm{H}, \mathrm{s})$, $0.07(3 \mathrm{H}, \mathrm{s}), 0.03(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 173.2,137.6,132.4,131.8,127.6$, 97.7, 81.1, 72.3, 70.7, 51.2, 46.3, 44.3, 43.3, 39.8, 34.8, 32.2, 31.3, 27.2, 26.1, 25.5, 25.3, 18.7, 7.1, 5.3, 2.1, -4.7, -4.9; (ESI/MS) $m / z$ Calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{62} \mathrm{O}_{6} \mathrm{Si}_{3}+\mathrm{H}\right]^{+}$: 663.4, found 663.1; calcd for $\left[\mathrm{C}_{35} \mathrm{H}_{62} \mathrm{O}_{6} \mathrm{Si}_{3}-\mathrm{TMS}+2 \mathrm{H}\right]^{+}$: 591.4, found 591.0.


To a solution of the alcohol $3.22(12.6 \mathrm{mg}, 0.0230 \mathrm{mmol})$ in 2.3 mL dichloromethane $(0.01 \mathrm{M})$ was added imidazole $(156.6 \mathrm{mg}, 2.30 \mathrm{mmol})$, tert-butyldimethylsilyl chloride (TBSCl, $260.0 \mathrm{mg}, 1.73 \mathrm{mmol}$ ), and DMAP ( $28.1 \mathrm{mg}, 0.230 \mathrm{mmol}$ ) at room temperature. After overnight, the reaction mixture was quenched with 8 mL sat. aqueous ammonium chloride solution and extracted with diethyl ether twice ( 15 mL X 2 ). The combined organic phase was dried and concentrated. The residue obtained was purified using FCC ( $5 \%$ ethyl acetate-hexanes) to give $3.24 \mathrm{in} 88 \%$ yield ( $12.0 \mathrm{mg}, 0.0202 \mathrm{mmol}$, dr 1:5). IR $v_{\max }$ (neat)/ $\mathrm{cm}^{-1}$ : 2956, 2858, 1658, 1462, 1259, 1079, 837, 775; ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , $\left.\mathrm{CDCl}_{3}\right) 5.83-5.77(1 \mathrm{H}, \mathrm{m}), 5.70(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 5.21(1 \mathrm{H}, \mathrm{s}), 4.12(1 \mathrm{H}, \mathrm{dd}, J=$ $8.8,2.0 \mathrm{~Hz}), 3.76(1 \mathrm{H}, \mathrm{d}, J=3.5 \mathrm{~Hz}), 3.64(3 \mathrm{H}, \mathrm{s}), 3.14-3.01(1 \mathrm{H}, \mathrm{m}), 2.99-2.85(2 \mathrm{H}$, $\mathrm{m}), 2.59(2 \mathrm{H}$, ddd, $J=23.3,18.0,4.4 \mathrm{~Hz}), 2.43(\mathrm{~d}, J=4.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.34-2.16(\mathrm{~m}, 2 \mathrm{H})$, $2.10-1.98(\mathrm{~m}, 1 \mathrm{H}), 1.95-1.84(\mathrm{~m}, 1 \mathrm{H}), 1.68(1 \mathrm{H}, \mathrm{dd}, J=13.5,9.0 \mathrm{~Hz}), 1.41-1.23$ $(2 \mathrm{H}, \mathrm{m}), 0.92(3 \mathrm{H}, \mathrm{s}), 0.87(9 \mathrm{H}, \mathrm{s}), 0.82(9 \mathrm{H}, \mathrm{s}), 0.07-0.01(12 \mathrm{H}, \mathrm{m}) . ;(\mathrm{ESI} / \mathrm{MS}) \mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{32} \mathrm{H}_{54} \mathrm{O}_{6} \mathrm{Si}_{2}+\mathrm{Na}\right]^{+}: 613.4$, found 613.4.


To a solution of the alcohol $3.22(39.3 \mathrm{mg}, 0.0718 \mathrm{mmol})$ in dichloromethane ( 1.4 mL , $0.05 \mathrm{M})$ was added imidazole ( $196.0 \mathrm{mg}, 2.87 \mathrm{mmol}$ ), tert-butyldimethylsilyl chloride (TBSCl, $216.8 \mathrm{mg}, 1.44 \mathrm{mmol}$ ), and DMAP ( $8.8 \mathrm{mg}, 0.0718 \mathrm{mmol}$ ) at room temperature. After overnight, the reaction mixture was quenched with 15 mL sat. aqueous ammonium chloride solution and extracted with diethyl ether ( 50 mL ). The combined organic phase was dried and concentrated. The residue obtained was purified using FCC ( $5 \%$ ethyl acetate-hexanes) to give $\mathbf{3 . 2 6}$ in $84 \%$ yield ( $35.6 \mathrm{mg}, 0.0603 \mathrm{mmol}, 5: 1 \mathrm{dr}$ ). ${ }^{1}$ H NMR ( 400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) 5.89-5.82(1 \mathrm{H}, \mathrm{m}), 5.74(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 5.17(1 \mathrm{H}, \mathrm{s}), 4.15(1 \mathrm{H}, \mathrm{d}, J$ $=8.6 \mathrm{~Hz}), 3.79(1 \mathrm{H}, \mathrm{d}, J=3.5 \mathrm{~Hz}), 3.63(3 \mathrm{H}, \mathrm{s}), 3.16-3.02(1 \mathrm{H}, \mathrm{m}), 3.00-2.84(2 \mathrm{H}$, $\mathrm{m}), 2.68-2.52(2 \mathrm{H}, \mathrm{m}), 2.28-2.15(2 \mathrm{H}, \mathrm{m}), 2.12-1.97(1 \mathrm{H}, \mathrm{m}), 1.91-1.79(1 \mathrm{H}, \mathrm{m})$, $1.68(1 \mathrm{H}, \mathrm{dd}, J=12.9,9.5 \mathrm{~Hz}), 1.53-1.39(1 \mathrm{H}, \mathrm{m}), 1.34-1.18(2 \mathrm{H}, \mathrm{m}), 0.91(12 \mathrm{H}, \mathrm{m})$, $0.88(9 \mathrm{H}, \mathrm{s}), 0.60-0.49(6 \mathrm{H}, \mathrm{m}), 0.08-0.02(6 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(100 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ 198.2, $174.8,167.4,132.3,130.6,128.5,80.9,71.6,70.98,55.0,51.8,49.5,43.4,39.8,34.4$, $32.3,31.0,28.7,25.9,25.5,25.0,18.1,7.0,5.1,-3.9,-4.5$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{32} \mathrm{H}_{54} \mathrm{O}_{6} \mathrm{Si}_{2}+\mathrm{NH}_{4}\right]^{+}: 608.4$, found 608.0 ; calcd for $\left[\mathrm{C}_{32} \mathrm{H}_{54} \mathrm{O}_{6} \mathrm{Si}_{2}+\mathrm{H}\right]^{+}: 591.4$, found 591.0.



72\%

To a solution of $\mathbf{3 . 2 3}(15.1 \mathrm{mg}, 0.0276 \mathrm{mmol})$ in methanol and DCM ( $1: 1,0.05 \mathrm{M}$ ) was added $\mathrm{TsOH} \cdot \mathrm{H}_{2} \mathrm{O}(2.6 \mathrm{mg}, 0.0138 \mathrm{mmol})$ at room temperature. After 20 min , the reaction mixture was quenched with sat. aqueous sodium bicarbonate solution ( 20 mL ) and extracd with DCM twice ( $30 \mathrm{~mL} \times 2$ ). The combined organic lays were dried over sodium sulfate, filtered and concentrated to give a crude product. Purification using FCC ( $18 \%$ ethyl acetate $/$ hexane) yielded 8.0 mg product 3.24 ( 0.0200 mmol ) in $72 \%$ yield. IR $\nu \max$ (neat) $/ \mathrm{cm}^{-1}: 2957,2927,1694,1241,1092,1041,735 ;{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 6.77(1 \mathrm{H}, \mathrm{d}, J=10.4 \mathrm{~Hz}), 6.71(1 \mathrm{H}, \mathrm{d}, J=10.3 \mathrm{~Hz}), 4.01-3.69(6 \mathrm{H}, \mathrm{m}), 3.84(3 \mathrm{H}, \mathrm{s})$, $3.66(1 \mathrm{H}, \mathrm{s}), 3.45(1 \mathrm{H}, \mathrm{d}, J=3.4 \mathrm{~Hz}), 2.93(1 \mathrm{H}, \mathrm{dd}, J=16.6,4.6 \mathrm{~Hz}), 2.88-2.76(1 \mathrm{H}$, $\mathrm{m}), 2.35(1 \mathrm{H}, \mathrm{dd}, J=16.8,3.7 \mathrm{~Hz}), 2.07(1 \mathrm{H}, \mathrm{ddd}, J=13.4,11.7,8.3 \mathrm{~Hz}), 1.97-1.78$ $(1 \mathrm{H}, \mathrm{m}), 1.79-1.67(1 \mathrm{H}, \mathrm{m}), 1.08(3 \mathrm{H}, \mathrm{s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR (101 MHz, $\left.\mathrm{CDCl}_{3}\right) \delta$ 198.7, $195.8,195.3,171.4,162.9,141.6,140.7,125.4,117.6,65.9,65.6,64.6,53.7,48.5,47.9$, $37.8,36.5,31.8,27.2,23.2,22.3,19.6$; (ESI/MS) m/z Calcd for $\left[\mathrm{C}_{22} \mathrm{H}_{24} \mathrm{O}_{7}+\mathrm{Na}\right]+$ : 423.2, found 423.4.


To a solution of $\mathbf{3 . 3}(9.9870 \mathrm{~g}, 32.9 \mathrm{mmol})$ in THF ( $132 \mathrm{~mL}, 0.25 \mathrm{M}$ ) was added ethylene glycol ( $5.5 \mathrm{~mL}, 98.1 \mathrm{mmol}$ ), triethyl orthoformate ( $13.1 \mathrm{~mL}, 79.0 \mathrm{mmol}$ ) and $\mathrm{TsOH} \cdot \mathrm{H}_{2} \mathrm{O}$ $(625.8 \mathrm{mg}, 3.29 \mathrm{mmol})$ at room temperature. After 6hrs, addtional ethylene glycol ( 5.5 $\mathrm{mL}, 98.1 \mathrm{mmol}$ ) and triethyl orthoformate ( $13.1 \mathrm{~mL}, 79.0 \mathrm{mmol}$ ) were added. After another 14 hrs , addtional ethylene glycol $(5.5 \mathrm{~mL}, 98.1 \mathrm{mmol})$ and triethyl orthoformate $(13.1 \mathrm{~mL}, 79.0 \mathrm{mmol})$ were added. After addtional 3 hrs , the reaction was quenched with 75 mL sat. aqueous sodium bicarbonate and extracted with diethyl ether ( 120 mL X 3 ). The combined orgnic layer was then dried over sodium sulfate, filtered, and concentrated on the rotavap. The resulted crude oil was then purified on FCC ( $10 \%$ to $20 \%$ ethyl acetate in hexanes) to give 5.4894 g yellow oil as the product ( $48 \%$ yield, $73 \% \mathrm{brsm}$ ). IR $v_{\max }$ (neat)/cm ${ }^{-1}: 1728,1658,1612,1567,1508,1261,1228,837,809,797 ;{ }^{1} \mathrm{H} \operatorname{NMR}(500$ $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.27(1 \mathrm{H}, \mathrm{t}, J=7.2 \mathrm{~Hz}), 4.06-3.97(4 \mathrm{H}, \mathrm{m}), 3.82(3 \mathrm{H}, \mathrm{s}), 2.44-2.35(4 \mathrm{H}$, $\mathrm{m}), 2.18-2.01(2 \mathrm{H}, \mathrm{m}), 1.75-1.59(2 \mathrm{H}, \mathrm{m}), 1.09(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR( $\left.125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $217.2,162.8,146.2,116.0,115.9,65.0,64.7,53.3,53.2,35.1,29.8,29.4,26.9,15.8 ;$ (ESI/MS) $\mathrm{m} / \mathrm{z}$ Calcd for $\left[\mathrm{C}_{14} \mathrm{H}_{19} \mathrm{BrO}_{5}+\mathrm{Na}\right]^{+}: 369.0$, found 369.1.

NMR Assignment of Compound 3.23


| $\mathbf{H}$ | $\delta(\mathrm{ppm})$ |
| :---: | :---: |
| $\mathbf{2}$ | 6.61 |
| $\mathbf{3}$ | 6.83 |
| $\mathbf{5}$ | 3.15 |
| $\mathbf{6} \boldsymbol{\alpha}$ | 2.46 |
| $\mathbf{6} \boldsymbol{\beta}$ | 2.68 |
| $\mathbf{7 - 1}$, | 0.73 |
| $\mathbf{7 - 2}$, | 0.98 |
| $\mathbf{9}$ | 3.60 |
| $\mathbf{1 1 \alpha}$ | 1.22 |
| $\mathbf{1 1 \beta} \boldsymbol{\beta}$ | 1.80 |
| $\mathbf{1 2 \boldsymbol { \alpha }}$ | 1.50 |
| $\mathbf{1 2 \beta}$ | 1.38 |
| $\mathbf{1 4 - 0 C H}$ | 3.03 |
| $\mathbf{1 5} \boldsymbol{\alpha}$ | 2.47 |
| $\mathbf{1 5 \beta}$ | 1.98 |
| $\mathbf{1 6 \boldsymbol { \alpha }}$ | 1.81 |
| $\mathbf{1 6 \beta}$ | 1.71 |
| $\mathbf{1 7 - O C H}$ | $3.79-3.87$ |
| $\mathbf{1 8}$ | 1.08 |
| $\mathbf{1 9 - O C H}$ | 3.64 |


| $\mathbf{C}$ | $\delta(\mathrm{ppm})$ |
| :---: | :---: |
| $\mathbf{1}$ | 192.87 |
| $\mathbf{2}$ | 138.52 |
| $\mathbf{3}$ | 141.72 |
| $\mathbf{4}$ | 196.85 |
| $\mathbf{5}$ | 44.52 |
| $\mathbf{6}$ | 29.26 |
| $\mathbf{7}$ | 144.74 |
| $\mathbf{7 - 1}$, | 5.94 |
| $\mathbf{7 - 2}$ | 6.78 |
| $\mathbf{8}$ | 112.68 |
| $\mathbf{9}$ | 34.41 |
| $\mathbf{1 0}$ | 65.59 |
| $\mathbf{1 1}$ | 26.32 |
| $\mathbf{1 2}$ | 29.54 |
| $\mathbf{1 3}$ | 52.28 |
| $\mathbf{1 4}$ | 86.75 |
| $\mathbf{1 4 - O C H}$ | 50.35 |
| $\mathbf{1 5}$ | 29.72 |
| $\mathbf{1 6}$ | 33.44 |
| $\mathbf{1 7}$ | 118.58 |
| $\mathbf{1 7 - O C H}$ | $64.24,64.27$ |
| $\mathbf{1 8}$ | 22.68 |
| $\mathbf{1 9}$ | 168.77 |
| $\mathbf{1 9 - O C H}$ | 53.12 |
|  |  |
| $\mathbf{1 9}$ |  |
| $\mathbf{1 9}$ |  |
| $\mathbf{1 9}$ |  |

## Key NOEs



### 6.5. Chapter IV

### 6.5.1. Section 4.2.

I. Ground State Cartesian Coordinates, Energies and Distortional Frequency of Compound 1-10

Compounds 1-10 were all optimized using the B3LYP/6-31+g(d). Frequency calculations were performed with the anharmonic option. The GaussView 5.0.8 package was used to display the anharmonic vibration corresponding with the olefin-bending mode at the corresponding $\mathrm{C}\left(s p^{2}\right)$-H symmetric out-of-plane vibration frequency (shown for each compound) and manual displacement of the frequency was used to isolate structures at the appropriate olefin bend. Single point energies for anharmonic distortional potentials were calculated using B3LYP/6-31g(2d,2p).


| C | -1.192248 | 0.781259 | -0.516864 |
| :--- | ---: | ---: | :---: |
| C | 0.087862 | 1.129662 | 0.323102 |
| C | -1.191924 | -0.781449 | -0.517185 |
| C | 0.088290 | -1.129789 | 0.322690 |
| C | 1.279909 | 0.672174 | -0.507261 |
| C | 1.280317 | -0.671513 | -0.507266 |
| H | -2.089124 | 1.178706 | -0.026512 |
| H | -1.147726 | 1.207742 | -1.523980 |
| H | 0.119453 | 2.159151 | 0.689734 |
| H | -1.147201 | -1.207484 | -1.524479 |
| H | -2.088682 | -1.179442 | -0.027059 |
| H | 0.120213 | -2.159390 | 0.688974 |
| H | 1.924982 | -1.328753 | -1.084157 |
| H | 1.924201 | 1.329847 | -1.084085 |
| C | 0.040175 | -0.000260 | 1.380826 |
| H | -0.881078 | -0.000596 | 1.977947 |
| H | 0.910680 | -0.000280 | 2.045356 |


| Zero-point correction= | 0.153164 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.158380 |
| Thermal correction to Enthalpy $=$ | 0.159324 |
| Thermal correction to Gibbs Free Energy= | 0.124639 |
| Sum of electronic and zero-point Energies= | -272.582875 |
| Sum of electronic and thermal Energies= | -272.577659 |
| Sum of electronic and thermal Enthalpies= | -272.576715 |
| Sum of electronic and thermal Free Energies= | -272.611400 |


|  |  |  |  |
| :---: | :---: | :---: | :---: |
|  | asses |  |  |
|  |  |  |  |
|  |  |  |  |
|  |  <br> 4 |  |  |
| C | 0.670758 | 0.664381 | 0.000001 |
| C | -0.670759 | 0.664381 | -0.000002 |
| C | 1.596153 | -0.522319 | 0.000000 |
| C | -1.596152 | -0.522320 | 0.000000 |
| H | 1.169532 | 1.634910 | 0.000001 |
| H | -1.169533 | 1.634910 | 0.000000 |
| H | 1.064519 | -1.478388 | 0.000069 |
| H | 2.252961 | -0.504483 | -0.880811 |
| H | 2.253053 | -0.504408 | 0.880739 |
| H | -1.064516 | -1.478388 | -0.000081 |
| H | -2.252952 | -0.504491 | 0.880816 |
| H | -2.253061 | -0.504403 | -0.880733 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
725.7459
1.4821
0.4599
51.1588
0.108278 (Hartree/Particle)
0.113807
0.114751
0.080383
-157.123188
-157.117659
-157.116715
-157.151083

| Frequencies | 696.3845 |
| :--- | ---: |
| Red. masses | 1.1019 |
| Frc consts | 0.3148 |
| IR Inten | 46.7325 |



| C | 0.778423 | -1.254026 | -0.674322 |
| :--- | ---: | ---: | ---: |
| C | 1.292593 | 0.000003 | 0.089940 |
| C | -0.671032 | -0.002466 | 1.468702 |
| C | 0.671037 | -0.002350 | 1.468700 |
| H | -1.170166 | 1.242007 | -1.696002 |
| H | -1.168452 | 2.161288 | -0.191365 |
| H | -2.387415 | -0.000278 | 0.130372 |
| H | 1.168131 | 2.161471 | -0.191431 |
| H | 1.169931 | 1.242140 | -1.696037 |
| H | 2.387415 | 0.000108 | 0.130365 |
| H | 1.277971 | -0.003995 | 2.371794 |
| H | -1.277962 | -0.004213 | 2.371798 |
| H | -1.168133 | -2.160821 | -0.198251 |
| H | 1.168451 | -2.160639 | -0.198191 |
| H | -1.169912 | -1.236774 | -1.699955 |
| H | 1.170137 | -1.236642 | -1.699927 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies= Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.182918 (Hartree/Particle)
0.189210
0.190154
0.152954
-311.882871
-311.876580
-311.875635
-311.912835

Frequencies
Red. masses
711.5863
1.5068

Frc consts
0.4495

IR Inten 47.5111


| C | -0.700510 | 0.786991 | 0.000235 |
| :--- | ---: | ---: | :---: |
| C | 0.815326 | -0.671678 | 0.000194 |
| C | 0.815328 | 0.671676 | -0.000369 |
| C | -0.700513 | -0.786988 | -0.000218 |
| H | -1.146676 | 1.247522 | -0.890293 |
| H | 1.603644 | -1.420931 | 0.000710 |
| H | 1.603648 | 1.420926 | -0.000252 |
| H | -1.146286 | -1.247189 | -0.891129 |
| H | -1.146259 | -1.247506 | 0.890538 |
| H | -1.145860 | 1.247181 | 0.891372 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
0.086624 (Hartree/Particle) 0.090445
0.091389

Thermal correction to Gibbs Free Energy=
0.061003

Sum of electronic and zero-point Energies= -155.893124
Sum of electronic and thermal Energies=
-155.889302
Sum of electronic and thermal Enthalpies=
-155.888358
Sum of electronic and thermal Free Energies=
-155.918745

Frequencies
650.6097

Red. masses
1.0691

Frc consts
0.2666

IR Inten 59.0479


| C | -0.279327 | 1.023732 | 0.000797 |
| :--- | ---: | :---: | :---: |
| C | -0.279315 | -1.023723 | -0.000782 |
| C | 1.216388 | 0.671393 | 0.000210 |
| C | 1.216402 | -0.671385 | -0.000264 |
| H | -0.572405 | 2.076298 | 0.001635 |
| H | -0.572370 | -2.076296 | -0.001592 |
| H | 2.046060 | -1.369290 | -0.000603 |
| H | 2.046026 | 1.369323 | 0.000472 |
| C | -0.810513 | -0.000860 | 1.065683 |
| H | -1.903301 | -0.000980 | 1.163806 |
| H | -0.329280 | -0.001624 | 2.049432 |
| C | -0.810613 | 0.000841 | -1.065651 |
| H | -1.903411 | 0.000951 | -1.163677 |
| H | -0.329448 | 0.001627 | -2.049427 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=

Frequencies
687.2225

Red. masses
1.5907

Frc consts
0.4426

IR Inten
54.4749

|  | 8 |  |  |
| :---: | :---: | :---: | :---: |
| C | 1.236658 | -0.318853 | 0.104371 |
| C | 0.000000 | -1.227451 | -0.137422 |
| C | -1.236658 | -0.318853 | 0.104371 |
| C | -0.669209 | 1.076616 | -0.047054 |
| H | 1.653994 | -0.456754 | 1.114349 |
| H | 2.053811 | -0.528164 | -0.598107 |
| H | 0.000000 | -1.567282 | -1.180120 |
| H | 0.000000 | -2.120793 | 0.496130 |
| H | -2.053811 | -0.528165 | -0.598107 |
| H | -1.653993 | -0.456753 | 1.114349 |
| C | 0.669209 | 1.076616 | -0.047054 |
| H | 1.293905 | 1.964726 | -0.105877 |
| H | -1.293904 | 1.964727 | -0.105877 |

Zero-point correction=
Thermal correction to Energy=
0.116940 (Hartree/Particle)
0.121576

Thermal correction to Enthalpy=
0.122520
0.089575

Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies= -195.217524
-195.212888
Sum of electronic and thermal Free Energies=
-195.211944
-195.244889

| Frequencies | 712.8409 |
| :--- | ---: |
| Red. masses | 1.3838 |
| Frc consts | 0.4143 |
| IR Inten | 41.1442 |



| C | 0.777254 | -1.221029 | -0.191851 |
| :--- | ---: | :---: | :---: |
| C | 1.402615 | 0.092267 | 0.344556 |
| C | -1.402519 | 0.093960 | 0.344514 |
| C | -0.778712 | -1.220137 | -0.191764 |
| H | 1.135598 | -1.371418 | -1.217243 |
| H | 1.161186 | -2.064670 | 0.395175 |
| H | -1.137336 | -1.370287 | -1.217093 |
| H | -1.163547 | -2.063241 | 0.395442 |
| C | 0.670935 | 1.303127 | -0.180701 |
| C | -0.669355 | 1.303926 | -0.180743 |


| H | 2.468270 | 0.128171 | 0.089770 |
| :--- | ---: | :--- | :---: |
| H | -2.468114 | 0.131136 | 0.089658 |
| H | -1.234890 | 2.159740 | -0.545594 |
| H | 1.237512 | 2.158264 | -0.545523 |
| H | 1.353046 | 0.088961 | 1.445691 |
| H | -1.353031 | 0.090664 | 1.445651 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.146132 (Hartree/Particle)
0.152035
0.152979
0.115620
-234.501284
-234.495381
-234.494437
-234.531797

| Frequencies | 694.4027 |
| :--- | ---: |
| Red. masses | 1.3442 |
| Frc consts | 0.3819 |
| IR Inten | 47.6743 |



| C | 0.785257 | -0.042507 | 0.478535 |
| :--- | ---: | ---: | ---: |
| F | 1.347998 | -1.055096 | -0.294090 |
| F | -1.347047 | -1.056161 | -0.294192 |
| C | -0.673079 | 1.302191 | -0.197301 |
| C | 0.671913 | 1.302776 | -0.197369 |
| C | -0.785218 | -0.043177 | 0.478608 |
| H | 1.274874 | -0.082062 | 1.457841 |
| H | -1.426120 | 2.024980 | -0.497835 |
| H | 1.424311 | 2.026130 | -0.498169 |
| H | -1.274870 | -0.083431 | 1.457862 |

Zero-point correction=
Thermal correction to Energy=
0.071671 (Hartree/Particle)
0.076861

Thermal correction to Enthalpy= 0.077805

Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies= 0.042833

$$
-354.389693
$$

Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=

$$
051201500
$$

-354.384503
-354.383559
-354.418531

| Frequencies | 777.5407 |
| :--- | ---: |
| Red. masses | 1.9567 |
| Frc consts | 0.6970 |
| IR Inten | 15.8186 |

## II. NBO Analysis of 3,4-Difluorocyclobutene

3,4-Difluorocyclobutene was optimized using the B3LYP/6-31+g(d). Frequency calculation was performed with the anharmonic ${ }^{1}$ option. The GaussView 5.0.8 package was used to display the anharmonic vibration corresponding with the olefin-bending mode at the corresponding $\mathrm{C}\left(s p^{2}\right)$-H symmetric out-of-plane vibration frequency (777.4 $\mathrm{cm}^{-1}$ ) and manual displacement of the frequency was used to isolate structures at the appropriate olefin bend. Single point energies for anharmonic distortional potentials were calculated using B3LYP/6-31g(2d,2p) for the undisturbed parent molecule (1) and the molecules with only one type of natural bond orbital interaction deletion at each time (25).

1. Undisturbed Parent Molecule


| Distortional <br> Angle $(\boldsymbol{\theta})$ | SPE <br> $(\mathbf{a . u .})$ | SPE <br> $\left.\mathbf{( k c a l ~ m o l ~}^{\mathbf{1}}\right)$ | $\boldsymbol{\Delta E}$ <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{\mathbf{1}}\right)$ |
| :---: | :---: | :---: | :---: |
| $\mathbf{+ 1 5}^{\circ}$ | -354.45050283 | -222421.0578 | 6.81 |
| $\mathbf{+ 1 0}^{\circ}$ | -354.45586716 | -222424.4240 | 3.44 |
| $\mathbf{+ 5}^{\circ}$ | -354.45904948 | -222426.4209 | 1.44 |
| $\mathbf{0}^{\circ}$ | -354.46084771 | -222427.5493 | 0.31 |
| $\mathbf{- 5}^{\circ}$ | -354.46134812 | -222427.8633 | 0.00 |
| $\mathbf{- 1 0}^{\circ}$ | -354.46053559 | -222427.3535 | 0.51 |
| $\mathbf{- 1 5}^{\circ}$ | -354.45830026 | -222425.9508 | 1.91 |

2. $\sigma_{\mathrm{C}-\mathrm{F}}$ to $\pi^{*}{ }_{\mathrm{C}=\mathrm{C}}$ Interactions Off


| Distortional <br> Angle $(\boldsymbol{\theta})$ | SPE <br> (a.u.) | SPE <br> $\left(\mathbf{k c a l ~} \mathbf{~ m o l}^{-\mathbf{1}}\right)$ | $\boldsymbol{\Delta E}$ <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{-\mathbf{1}}\right)$ |
| :---: | :---: | :---: | :---: |
| $\mathbf{+ 1 5}^{\circ}$ | -354.4473674 | -222419.0903 | 7.08 |
| $\mathbf{+ 1 0}^{\circ}$ | -354.4528503 | -222422.5309 | 3.64 |
| $\mathbf{+ 5}^{\circ}$ | -354.4561402 | -222424.5953 | 1.57 |
| $\mathbf{0}^{\circ}$ | -354.4580446 | -222425.7903 | 0.38 |
| $\mathbf{- 5}^{\circ}$ | -354.4586500 | -222426.1702 | 0.00 |
| $\mathbf{- 1 0}^{\circ}$ | -354.4579536 | -222425.7332 | 0.44 |
| $\mathbf{- 1 5}^{\circ}$ | -354.4558430 | -222424.4088 | 1.76 |

3. $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{H}}$ Interactions Off


| Distortional <br> Angle $(\boldsymbol{\theta})$ | SPE <br> $(\mathbf{a . u .})$ | SPE <br> $\mathbf{( k c a l ~ m o l ~}^{\mathbf{1}}$ ) | $\boldsymbol{\Delta E}$ <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{\mathbf{1}}\right)$ |
| :---: | :---: | :---: | :---: |
| $\mathbf{+ 1 5}^{\circ}$ | -354.4427387 | -222416.1857 | 7.05 |
| $\mathbf{+ 1 0}^{\circ}$ | -354.4481663 | -222419.5916 | 3.64 |
| $\mathbf{+ 5}^{\circ}$ | -354.4514319 | -222421.6408 | 1.59 |
| $\mathbf{0}^{\circ}$ | -354.4533382 | -222422.8370 | 0.40 |
| $\mathbf{- 5}^{\circ}$ | -354.4539717 | -222423.2346 | 0.00 |
| $\mathbf{- 1 0}^{\circ}$ | -354.4533073 | -222422.8176 | 0.42 |
| $\mathbf{- 1 5}^{\circ}$ | -354.4512395 | -222421.5201 | 1.71 |

4. $\sigma_{\mathrm{C}-\mathrm{H}}$ to $\pi^{*}{ }_{\mathrm{C}-\mathrm{F}}$ Interactions Off


| Distortional <br> Angle $(\boldsymbol{\theta})$ | SPE <br> $($ a.u. $)$ | SPE <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{\mathbf{1}}\right)$ | $\Delta \boldsymbol{E}$ <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{\mathbf{1}}\right)$ |
| :---: | :---: | :---: | :---: |
| $\mathbf{+ 1 5}^{\circ}$ | -354.4462574 | -222418.3937 | 5.46 |
| $\mathbf{+ 1 0}^{\circ}$ | -354.4510724 | -222421.4152 | 2.44 |
| $\mathbf{+ 5}^{\circ}$ | -354.4537251 | -222423.0798 | 0.78 |
| $\mathbf{0}^{\circ}$ | -354.4549612 | -222423.8554 | 0.00 |
| $\mathbf{- 5}^{\circ}$ | -354.4548733 | -222423.8003 | 0.06 |
| $\mathbf{- 1 0}^{\circ}$ | -354.4534627 | -222422.9151 | 0.94 |
| $\mathbf{- 1 5}^{\circ}$ | -354.4506145 | -222421.1279 | 2.73 |

5. $\pi_{\mathrm{C}=\mathrm{C}}$ to $\sigma^{*}{ }_{\mathrm{C}-\mathrm{F}}$ Interactions

Off


| Distortional <br> Angle $(\boldsymbol{\theta})$ | SPE <br> $(\mathbf{a} . \mathbf{.})$. | SPE <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{-\mathbf{1}}\right)$ | $\boldsymbol{\Delta} \boldsymbol{E}$ <br> $\left(\mathbf{k c a l} \mathbf{~ m o l}^{\mathbf{1}}\right)$ |
| :---: | :---: | :---: | :---: |
| $\mathbf{+ 1 5}^{\circ}$ | -354.4204233 | -222402.1826 | 4.22 |
| $\mathbf{+ 1 0}^{\circ}$ | -354.4245276 | -222404.7581 | 1.65 |
| $\mathbf{+ 5}^{\circ}$ | -354.4265412 | -222406.0216 | 0.38 |
| $\mathbf{0}^{\circ}$ | -354.4271516 | -222406.4047 | 0.00 |
| $\mathbf{- 5}^{\circ}$ | -354.4264579 | -222405.9694 | 0.44 |
| $\mathbf{- 1 0}^{\circ}$ | -354.4243993 | -222404.6776 | 1.73 |
| $\mathbf{- 1 5}^{\circ}$ | -354.4209022 | -222402.4831 | 3.92 |

## III. NBO Analysis of Bicyclic Olefins 1,5 and 7

Compounds 1, 5 and 7 were optimized with B3LYP/6-31 $+\mathrm{g}(\mathrm{d}, \mathrm{p})$ (Gaussian 03 suite) with or without the deletions of the highlighted natural bond orbital interactions ( $\sigma_{\mathrm{C}-\mathrm{c}}$ to $\pi^{*} \mathrm{C}=\mathrm{C}$ ). Coordinates of the optimized compounds ( $5, \mathrm{~V} ; 7, \mathrm{VII} ; 1, \mathrm{I}$ ) were shown below.


| H | 1.982145 | -0.895497 | 1.621316 |
| :--- | ---: | ---: | ---: |
| H | 3.034663 | 1.033107 | 0.841874 |

Energy of deletion : -312.074620455
Total SCF energy : -312.081668174
Energy change :
0.007048 a.u., $\quad 4.423 \mathrm{kcal} / \mathrm{mol}$

$$
\begin{array}{lrrr} 
& & \\
& \\
\mathrm{C} & 0.278517 & -1.023907 & 0.000671 \\
\mathrm{C} & 0.280391 & 1.023506 & -0.000535 \\
\mathrm{C} & -1.217258 & -0.670446 & -0.000085 \\
\mathrm{C} & -1.215981 & 0.671973 & -0.000667 \\
\mathrm{H} & 0.570295 & -2.075720 & 0.001051 \\
\mathrm{H} & 0.574010 & 2.074873 & -0.000797 \\
\mathrm{H} & -2.044179 & 1.369919 & -0.001149 \\
\mathrm{H} & -2.046496 & -1.367281 & 0.000065 \\
\mathrm{C} & 0.810043 & 0.000119 & 1.065774 \\
\mathrm{H} & 1.901856 & -0.000468 & 1.163752 \\
\mathrm{H} & 0.328801 & 0.001392 & 2.048370 \\
\mathrm{C} & 0.811221 & -0.001155 & -1.065288 \\
\mathrm{H} & 1.903178 & -0.002088 & -1.162174 \\
\mathrm{H} & 0.330934 & -0.001158 & -2.048341
\end{array}
$$

$$
\mathrm{HF}=-233.3853158
$$



| C | 0.000000 | 0.000000 | 0.000000 |
| :--- | ---: | :---: | :---: |
| C | 0.000000 | 0.000000 | 2.045778 |
| C | 1.512768 | 0.000000 | 0.352753 |
| C | 1.512827 | -0.000221 | 1.693376 |
| H | -0.294385 | -0.006164 | -1.051724 |
| H | -0.294605 | -0.006478 | 3.097445 |
| H | 2.336237 | -0.129877 | 2.385165 |
| H | 2.336236 | -0.129438 | -0.339039 |
| C | -0.555755 | 1.023586 | 1.022887 |
| H | -1.650410 | 1.075823 | 1.022940 |
| H | -0.122417 | 2.030035 | 1.022882 |


| C | -0.493765 | -1.102083 | 1.022843 |
| :--- | ---: | ---: | ---: |
| H | -1.580962 | -1.239032 | 1.022839 |
| H | 0.023380 | -2.065264 | 1.022846 |
|  |  |  |  |
| Energy of deletion : | -233.377291936 |  |  |
| Total SCF energy : | -233.383767207 |  |  |
| Energy change : | 0.006475 a.u., $4.063 \mathrm{kcal} / \mathrm{mol}$ |  |  |



| C | 1.192214 | -0.781135 | -0.516940 |
| :--- | ---: | ---: | ---: |
| C | -0.088260 | -1.129551 | 0.322586 |
| C | 1.192417 | 0.781330 | -0.516375 |
| C | -0.087981 | 1.129335 | 0.323391 |
| C | -1.279808 | -0.671334 | -0.508102 |
| C | -1.279531 | 0.672091 | -0.507798 |
| H | 2.088066 | -1.178477 | -0.026908 |
| H | 1.147913 | -1.206736 | -1.523436 |
| H | -0.120557 | -2.158563 | 0.687860 |
| H | 1.148260 | 1.207712 | -1.522549 |
| H | 2.088329 | 1.178087 | -0.025979 |
| H | -0.120053 | 2.158069 | 0.689472 |
| H | -1.923386 | 1.329037 | -1.083963 |
| H | -1.923911 | -1.327706 | -1.084634 |
| C | -0.041060 | -0.000648 | 1.381186 |
| H | 0.878936 | -0.001065 | 1.978327 |
| H | -0.911548 | -0.000881 | 2.044124 |

$$
\mathrm{HF}=-272.7501589
$$



| C | 0.000000 | 0.000000 | 0.000000 |
| :--- | :---: | :---: | :---: |
| C | 0.000000 | 0.000000 | 1.572461 |
| C | 1.526482 | 0.000000 | -0.344573 |
| C | 2.203089 | -0.003730 | 1.075317 |
| C | 0.557099 | 1.370377 | 1.952662 |
| C | 1.867978 | 1.368278 | 1.657091 |
| H | -0.490508 | -0.904420 | -0.375383 |
| H | -0.531181 | 0.862499 | -0.412454 |
| H | -0.949163 | -0.296592 | 2.025161 |


| H | 1.829416 | 0.863984 | -0.942916 |
| :--- | ---: | ---: | ---: |
| H | 1.807347 | -0.902942 | -0.897268 |
| H | 3.253591 | -0.304047 | 1.075461 |
| H | 2.522739 | 2.233048 | 1.613198 |
| H | -0.050452 | 2.237211 | 2.193432 |
| C | 1.219199 | -0.899672 | 1.852458 |
| H | 1.122202 | -1.906458 | 1.429650 |
| H | 1.459634 | -0.970912 | 2.918079 |

Energy of deletion : -272.746051837
Total SCF energy : -272.749317113
Energy change : $\quad 0.003265$ a.u., $2.049 \mathrm{kcal} / \mathrm{mol}$


| C | 0.000000 | 0.000000 | 0.000000 |
| :--- | ---: | ---: | ---: |
| C | 0.000000 | 0.000000 | 1.542708 |
| C | 1.534512 | 0.000000 | -0.347977 |
| C | 2.199996 | 0.008419 | 1.043707 |
| C | 0.581708 | 1.351108 | 2.056180 |
| C | 1.885972 | 1.356487 | 1.758736 |
| H | -0.497477 | -0.890350 | -0.406442 |
| H | -0.519017 | 0.877492 | -0.400713 |
| H | -0.949566 | -0.289885 | 2.004561 |
| H | 1.828428 | 0.874536 | -0.938753 |
| H | 1.809415 | -0.893417 | -0.923896 |
| H | 3.258168 | -0.273123 | 1.050964 |
| H | 2.619399 | 2.119739 | 1.997498 |
| H | 0.018418 | 2.109219 | 2.590247 |
| C | 1.227175 | -0.909178 | 1.839070 |
| H | 1.133515 | -1.913522 | 1.407448 |
| H | 1.468362 | -0.985152 | 2.902774 |

Energy of deletion : -272.732968637
Total SCF energy : -272.746862653
Energy change :
0.013894 a.u., $\quad 8.719 \mathrm{kcal} / \mathrm{mol}$
IV. $m$ CPBA Oxidation of Norbornene Calculation in MeCN .

All the compounds were optimized with B3LYP/6-31+g(d,p). General solvent effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM).

1. Ground State Calculations of Reactants and Products in MeCN

|  |  |  |  |
| :--- | ---: | ---: | ---: |
|  | -0.086998 | -1.129954 | 0.323888 |
| C | -0.037749 | 0.000015 | 1.381457 |
| C | -1.089110 | 1.129814 | 0.323832 |
| C | -1.279511 | -0.673497 | -0.506417 |
| C | -1.9272769 | 0.671279 | -0.505721 |
| C | -1.328043 | -1.085417 |  |
| H | -1.919479 | -1.331328 | -1.086591 |
| H | -0.905364 | -0.000797 | 2.048932 |
| H | 0.884367 | 0.000918 | 1.974557 |
| H | 0.189654 | 0.782185 | -0.519067 |
| C | 1.085 |  |  |
| H | 2.085256 | 1.179706 | -0.029225 |
| H | 1.142945 | 1.208958 | -1.525164 |
| C | 1.191506 | -0.780200 | -0.518412 |
| H | 2.087741 | -1.175333 | -0.027780 |
| H | 1.146250 | -1.207853 | -1.524195 |
| H | -0.120918 | 2.158796 | 0.688698 |
| H | -0.117143 | -2.158962 | 0.688823 |

```
HF=-272.751236
```



| O | -2.046608 | -1.649265 | -0.000029 |
| :--- | ---: | ---: | :---: |
| O | -2.859884 | 0.444617 | -0.000017 |
| C | -1.831683 | -0.446638 | -0.000019 |
| C | -0.506631 | 0.213733 | -0.000013 |
| C | -0.362357 | 1.609830 | -0.000007 |
| C | 0.621204 | -0.621192 | 0.000004 |
| C | 0.916219 | 2.166134 | 0.000006 |
| H | -1.234709 | 2.252267 | -0.000015 |
| C | 1.884499 | -0.039827 | 0.000002 |
| H | 0.499194 | -1.697657 | -0.000009 |
| C | 2.048803 | 1.347238 | 0.000001 |
| H | 1.037178 | 3.244151 | -0.000005 |
| H | 3.043371 | 1.779188 | 0.000003 |
| Cl | 3.305901 | -1.077085 | 0.000008 |
| O | -4.133335 | -0.228746 | 0.000037 |
| H | -3.847055 | -1.176024 | 0.000117 |

```
HF =-955.5814662
```

|  |  |  |  |
| :--- | ---: | ---: | ---: |
| endo |  |  |  |
| C | -0.317979 | 0.520890 | -1.091021 |
| C | -0.800770 | 1.358074 | 0.127001 |
| C | -0.317216 | 0.309713 | 1.168571 |
| C | 1.168204 | 0.343029 | -0.707112 |
| H | 1.168357 | 0.205843 | 0.758146 |
| H | 1.964989 | 0.549127 | 1.413180 |
| O | 1.964334 | 0.802549 | -1.287418 |
| H | -0.283290 | -0.922512 | -0.086441 |
| H | -1.883185 | 1.319791 | 0.216555 |
| C | -1.080456 | -0.954520 | 0.143482 |
| H | -2.097783 | -0.940345 | 1.101668 |
| H | -0.597422 | -1.877524 | 1.027372 |
| C | -1.080735 | -0.808922 | -0.861446 |
| H | -2.098281 | -0.720843 | -1.256149 |
| H | -0.597211 | -1.654420 | -1.357121 |
| H | -0.461386 | 0.562107 | 2.221650 |
| H | -0.462693 | 0.963792 | -2.079069 |

$\mathrm{HF}=-347.9556741$


| C | 0.211193 | 1.139059 | 0.344543 |
| :--- | ---: | ---: | ---: |
| C | 0.208809 | 0.000185 | 1.387730 |
| C | 0.211130 | -1.138936 | 0.344639 |
| C | -0.947689 | 0.734638 | -0.570488 |
| C | -0.947582 | -0.734538 | -0.570488 |
| H | -1.231281 | -1.337750 | -1.429050 |
| H | -1.231351 | 1.337884 | -1.429053 |
| O | -2.031566 | -0.000173 | 0.057282 |
| H | 0.181946 | -2.161196 | 0.728851 |
| H | 0.182092 | 2.161456 | 0.728367 |
| H | 1.114288 | 0.000069 | 2.002071 |
| H | -0.668422 | 0.000236 | 2.036239 |
| C | 1.485631 | -0.785151 | -0.479119 |
| C | 1.485669 | 0.784948 | -0.479269 |
| H | 2.379257 | 1.184301 | 0.010439 |
| H | 1.451872 | 1.202606 | -1.491246 |
| H | 2.379098 | -1.184451 | 0.010858 |

$\begin{array}{llll}\mathrm{H} & 1.452063 & -1.203008 & -1.491027\end{array}$
$\mathrm{HF}=-347.9641624$
2. Transition State Cartesian Coordinates, Energies and Low Frequencies in MeCN.

| C | 4.706743 | -0.230502 | -1.132805 |
| :--- | ---: | ---: | :---: |
| C | 5.739536 | -0.491473 | 0.000434 |
| C | 4.706187 | -0.230125 | 1.133084 |
| C | 3.613202 | -1.184797 | -0.686296 |
| C | 3.612868 | -1.184600 | 0.686361 |
| O | 0.178435 | 0.727077 | 0.000349 |
| O | -0.510237 | -1.407968 | -0.000699 |
| H | 3.031401 | -1.818993 | 1.344461 |
| H | 3.031871 | -1.819234 | -1.344480 |
| H | 1.257479 | -0.976173 | -0.000344 |
| C | -0.753737 | -0.190451 | -0.000194 |
| O | 1.748113 | -0.114530 | 0.000161 |
| H | 6.134469 | -1.511791 | 0.000697 |
| H | 6.569705 | 0.223515 | 0.000535 |
| C | 4.275373 | 1.234016 | 0.779805 |
| H | 5.017095 | 1.931656 | 1.180804 |
| H | 3.302097 | 1.487155 | 1.202164 |
| C | 4.275716 | 1.233754 | -0.780249 |
| H | 5.017562 | 1.931301 | -1.181182 |
| H | 3.302600 | 1.486652 | -1.203123 |
| H | 5.039191 | -0.364868 | 2.163280 |
| H | 5.040230 | -0.365592 | -2.162801 |
| C | -2.158748 | 0.340593 | -0.000125 |
| C | -3.211001 | -0.586129 | -0.000028 |
| C | -2.429707 | 1.716163 | -0.000167 |
| C | -4.521126 | -0.117581 | 0.000046 |
| H | -2.994012 | -1.647363 | -0.000005 |
| C | -3.752254 | 2.161630 | -0.000123 |
| H | -1.611972 | 2.427307 | -0.000255 |
| C | -4.810264 | 1.248316 | -0.000009 |
| H | -5.839074 | 1.590891 | 0.000037 |
| Cl | -5.848183 | -1.279378 | 0.000206 |
| H | -3.966750 | 3.225448 | -0.000179 |


| Zero-point correction $=$ | 0.260640 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.276775 |
| Thermal correction to Enthalpy= | 0.277720 |
| Thermal correction to Gibbs Free Energy= | 0.212949 |
| Sum of electronic and zero-point Energies= | -1228.051763 |
| Sum of electronic and thermal Energies= | -1228.035628 |
| Sum of electronic and thermal Enthalpies $=$ | -1228.034684 |
| Sum of electronic and thermal Free Energies= | -1228.099454 |


| C | 4.516180 | 0.196926 | -1.133744 |
| :--- | ---: | ---: | ---: |
| C | 4.368828 | 1.241251 | -0.001207 |
| C | 4.515881 | 0.198977 | 1.133240 |
| C | 3.534155 | -0.863100 | -0.684252 |
| C | 3.533955 | -0.861854 | 0.685406 |
| O | 0.007740 | 0.874322 | -0.000402 |
| O | -0.578598 | -1.291415 | 0.000114 |
| H | 3.096713 | -1.615460 | 1.331003 |
| H | 3.096986 | -1.617818 | -1.328610 |
| H | 1.174862 | -0.761959 | 0.000114 |
| C | -0.882020 | -0.089350 | -0.000122 |
| O | 1.592830 | 0.136642 | -0.000089 |
| H | 4.414938 | 0.546511 | 2.162120 |
| H | 4.415508 | 0.542603 | -2.163275 |
| C | -2.307330 | 0.379738 | -0.000098 |
| C | -3.317871 | -0.592377 | -0.000020 |
| C | -2.637717 | 1.742382 | -0.000117 |
| C | -4.647234 | -0.181599 | 0.000037 |
| H | -3.054680 | -1.643115 | 0.000001 |
| C | -3.978421 | 2.129334 | -0.000050 |
| H | -1.852259 | 2.488980 | -0.000170 |
| C | -4.995359 | 1.170507 | 0.000027 |
| H | -6.038038 | 1.468104 | 0.000081 |
| C | -5.922346 | -1.399745 | 0.000130 |
| H | -4.239244 | 3.182737 | -0.000052 |
| H | 5.174291 | 1.982343 | -0.001771 |
| H | 3.400216 | 1.743212 | -0.001770 |
| C | 5.927447 | -0.400063 | 0.781528 |
| C | 5.927656 | -0.401472 | -0.780570 |
| H | 6.710417 | 0.249773 | -1.181852 |
| H | 6.072859 | -1.398256 | -1.206383 |
| H | 6.710109 | 0.251897 | 1.181840 |
| H | 6.072529 | -1.396081 | 1.209173 |
|  |  |  |  |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies= Sum of electronic and thermal Energies= Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=

0.260522 (Hartree/Particle)
0.276772
0.277716
0.212871
-1228.057202
-1228.040952
-1228.040008
-1228.104852

Low frequencies $-413.9572,17.0641,21.3574,33.4844,42.9184$
V. Transition State Calculations of $\mathbf{1 1}$ in Gas Phase and Solvent.

1. Compound 11 was optimized using the B3LYP/6-31+g(d,p). Frequency calculations were performed. The GaussView 5.0.8 package was used to display the vibration corresponding with the olefin-bending mode at the corresponding $\mathrm{C}\left(s p^{2}\right)$ - H symmetric
out-of-plane vibration frequency and manual displacement of the frequency was used to isolate structures at the appropriate olefin bend. Single point energies for distortional potentials were calculated using B3LYP/6-31 $+\mathrm{g}(\mathrm{d}, \mathrm{p})$.


| C | -0.087778 | 1.501555 | -0.785203 |
| :--- | ---: | ---: | ---: |
| C | 0.256851 | 0.028605 | -1.137544 |
| C | -0.087372 | 1.501346 | 0.785663 |
| C | 0.256501 | 0.028190 | 1.137425 |
| C | -0.902725 | -0.931512 | -0.764894 |
| C | -0.903189 | -0.932140 | 0.764824 |
| H | 0.688377 | 2.166726 | -1.176113 |
| H | -1.041865 | 1.821433 | -1.215423 |
| H | 0.632811 | -0.114339 | -2.152742 |
| H | -1.040800 | 1.822172 | 1.216542 |
| H | 0.689843 | 2.165493 | 1.176226 |
| H | 0.632304 | -0.115236 | 2.152627 |
| C | 1.220649 | -0.296555 | -0.000060 |
| H | -0.978624 | -1.860191 | 1.324573 |
| H | -0.979075 | -1.859253 | -1.325131 |
| C | 2.477770 | -0.737011 | -0.000080 |
| H | 3.012903 | -0.927945 | -0.926759 |
| H | 3.012797 | -0.928158 | 0.926621 |
| C | -2.110297 | -0.441943 | -0.000267 |
| H | -2.377444 | 0.609392 | 0.001112 |
| H | -2.973677 | -1.103303 | -0.000721 |


| Zero-point correction $=$ | 0.186422 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.193337 |
| Thermal correction to Enthalpy= | 0.194281 |
| Thermal correction to Gibbs Free Energy= | 0.155662 |
| Sum of electronic and zero-point Energies= | -349.946309 |
| Sum of electronic and thermal Energies= | -349.946309 |
| Sum of electronic and thermal Enthalpies= | -349.938450 |
| Sum of electronic and thermal Free Energies= | -349.977069 |


| Frequencies | 707.6798 |
| :--- | ---: |
| Red. masses | 5.0210 |
| Frc consts | 1.4815 |
| IR Inten | 10.8587 |

## 2. Dichlorocarbene Addition to $\mathbf{1 1}$ Calculations.

All the compounds were optimized with B3LYP/6-31+g(d,p). General solvent effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM) for calculation in chloroform.
a. Ground State Calculations of Reactants and Products in Gas Phase and Chloroform.


## Gas Phase

| C | 0.000000 | 0.000000 | 0.855194 |
| :--- | ---: | ---: | ---: | ---: |
| Cl | 0.000000 | 1.426844 | -0.150917 |
| Cl | 0.000000 | -1.426844 | -0.150917 |

$\mathrm{HF}=-958.3889178$

## In Chloroform

| C | 0.000000 | 0.000000 | 0.847756 |
| :--- | ---: | ---: | ---: | ---: |
| Cl | 0.000000 | 1.425110 | -0.149604 |
| Cl | 0.000000 | -1.425110 | -0.149604 |

$H F=-958.3907557$


Gas Phase

|  | C | 2.269544 | 0.762776 |
| :--- | ---: | ---: | :---: |
|  | -0.773042 |  |  |
| C | 1.001463 | 1.137270 | 0.032748 |
| C | 2.269421 | -0.762870 | -0.772883 |
| C | 1.001493 | -1.137254 | 0.033040 |
| C | 1.144155 | 0.784398 | 1.534755 |
| C | 1.144311 | -0.783980 | 1.534955 |
| H | 2.474754 | 1.327155 | -1.678523 |
| H | 0.649575 | 2.153034 | -0.155229 |
| H | 2.474725 | -1.327511 | -1.678182 |
| H | 0.649611 | -2.153069 | -0.154701 |
| C | 0.066232 | -0.000074 | -0.425382 |
| H | 0.286727 | -1.176355 | 2.089386 |
| H | 0.286481 | 1.176782 | 2.089038 |
| C | -0.758150 | -0.000154 | -1.696782 |
| H | -0.82885 | 0.916566 | -2.277334 |
| H | -0.822875 | -0.916964 | -2.277189 |
| C | -1.427065 | -0.000033 | -0.348425 |
| Cl | -2.288874 | -1.478449 | 0.171945 |
| Cl | -2.288857 | 1.478449 | 0.171786 |
| C | 3.402107 | -0.000073 | -0.125679 |
| H | 3.526809 | -0.000090 | 0.951452 |
| H | 4.345048 | -0.000284 | -0.666579 |
| H | 2.046028 | 1.217272 | 1.977190 |
| H | 2.046312 | -1.216567 | 1.977415 |

$H F=-1308.6215536$

## In Chloroform

| C | 2.268801 | 0.762834 | -0.774318 |
| :--- | ---: | ---: | ---: |
| C | 1.003430 | 1.137774 | 0.035494 |
| C | 2.268718 | -0.762884 | -0.774193 |
| C | 1.003445 | -1.137795 | 0.035661 |
| C | 1.150379 | 0.784205 | 1.536931 |
| C | 1.150394 | -0.784008 | 1.537056 |
| H | 2.469312 | 1.325477 | -1.681737 |
| H | 0.652144 | 2.153474 | -0.153481 |


| H | 2.469369 | -1.325718 | -1.681466 |
| :--- | ---: | ---: | :---: |
| H | 0.652158 | -2.153518 | -0.153215 |
| C | 0.068433 | -0.000063 | -0.422873 |
| H | 0.295055 | -1.176053 | 2.095534 |
| H | 0.295053 | 1.176340 | 2.095362 |
| C | -0.753474 | -0.000091 | -1.696274 |
| H | -0.814696 | 0.916720 | -2.276949 |
| H | -0.814751 | -0.916952 | -2.276864 |
| C | -1.424416 | -0.000013 | -0.350227 |
| Cl | -2.294877 | -1.477778 | 0.171364 |
| Cl | -2.294832 | 1.477809 | 0.171295 |
| C | 3.403910 | -0.000024 | -0.130128 |
| H | 3.531683 | -0.000037 | 0.946746 |
| H | 4.344078 | -0.000162 | -0.675832 |
| H | 2.053949 | 1.215747 | 1.976866 |
| H | 2.053985 | -1.215455 | 1.977041 |

$H F=-1308.6243146$


## Gas Phase

| C | -2.186025 | 0.783855 | 1.206480 |
| :--- | ---: | ---: | ---: |
| C | -1.033156 | 1.136701 | 0.232536 |
| C | -2.185959 | -0.784344 | 1.206259 |
| C | -1.033137 | -1.136804 | 0.232121 |
| C | -1.373699 | 0.762912 | -1.229976 |
| C | -1.373727 | -0.762478 | -1.230253 |
| H | -1.964262 | 1.174928 | 2.204719 |
| H | -3.139498 | 1.218395 | 0.893165 |
| H | -0.650198 | 2.152661 | 0.341894 |
| H | -3.139411 | -1.218873 | 0.892874 |
| H | -1.964107 | -1.175689 | 2.204372 |
| H | -0.650152 | -2.152795 | 0.341093 |
| C | -0.048644 | -0.000108 | 0.572343 |
| H | -0.876760 | -1.323990 | -2.015818 |
| H | -0.876702 | 1.324698 | -2.015326 |
| C | 0.955186 | -0.000297 | 1.712395 |
| H | 1.105782 | 0.916567 | 2.276757 |
| H | 1.105806 | -0.917354 | 2.276436 |
| C | -2.633921 | 0.000308 | -1.566259 |
| H | -3.481593 | 0.000213 | -0.889946 |
| H | -2.923907 | 0.000514 | -2.613989 |
| C | 1.413397 | -0.000041 | 0.278552 |
| Cl | 2.189812 | -1.477549 | -0.364408 |
| Cl | 2.189783 | 1.477696 | -0.363910 |

```
HF =-1308.6216391
```


## In Chloroform

| C | 2.184977 | -0.784341 | 1.207848 |
| :--- | ---: | ---: | ---: |
| C | 1.035115 | -1.137271 | 0.230082 |
| C | 2.185080 | 0.783738 | 1.208095 |
| C | 1.035145 | 1.137150 | 0.230585 |
| C | 1.378610 | -0.762514 | -1.231778 |
| C | 1.378575 | 0.763043 | -1.231439 |
| H | 1.958260 | -1.175604 | 2.204594 |
| H | 3.139454 | -1.218323 | 0.897197 |
| H | 0.652679 | -2.153262 | 0.340190 |
| H | 3.139588 | 1.217699 | 0.897497 |
| H | 1.958505 | 1.174701 | 2.204991 |
| H | 0.652754 | 2.153106 | 0.341162 |
| C | 0.050966 | -0.000124 | 0.570834 |
| H | 0.885525 | 1.324614 | -2.019720 |
| H | 0.885592 | -1.323751 | -2.020316 |
| C | -0.949923 | -0.000359 | 1.713378 |
| H | -1.096495 | -0.917270 | 2.278574 |
| H | -1.096498 | 0.916314 | 2.278963 |
| C | 2.640222 | 0.000375 | -1.564905 |
| H | 3.485477 | 0.000257 | -0.885674 |
| H | 2.930964 | 0.000632 | -2.612477 |
| C | -1.411421 | -0.000054 | 0.281919 |
| Cl | -2.195864 | 1.477017 | -0.364183 |
| Cl | -2.195893 | -1.476839 | -0.364799 |
| HF $=-1308.6245231$ |  |  |  |
|  |  |  |  |

## b. Transition State Calculations in Gas Phase and Chloroform.

## Endo: Gas Phase

| C | 0.409797 | -0.000131 | 1.800923 |
| :--- | ---: | :---: | :---: |
| C | -0.518286 | -0.000094 | 0.809962 |
| C | 2.397955 | 0.000012 | 0.777859 |
| Cl | 2.515978 | -1.455009 | -0.271350 |
| Cl | 2.515793 | 1.455102 | -0.271276 |
| H | 0.677325 | -0.922466 | 2.305265 |
| H | 0.677299 | 0.922174 | 2.305333 |
| C | -1.245210 | -1.141469 | 0.115077 |
| C | -1.245141 | 1.141387 | 0.115180 |
| C | -2.682184 | 0.769422 | 0.566942 |
| C | -2.682231 | -0.769451 | 0.566876 |
| C | -1.002996 | -0.784261 | -1.376454 |
| C | -1.002941 | 0.784297 | -1.376384 |
| C | -3.608486 | 0.000054 | -0.341580 |
| H | -0.034170 | 1.173417 | -1.700225 |
| H | -1.765682 | 1.218568 | -2.029353 |
| H | -0.034254 | -1.173417 | -1.700343 |


| H | -1.765776 | -1.218420 | -2.029454 |
| :--- | ---: | ---: | ---: |
| H | -0.946922 | 2.152706 | 0.395556 |
| H | -3.101873 | 1.327178 | 1.398871 |
| H | -3.101955 | -1.327254 | 1.398754 |
| H | -3.462800 | 0.000097 | -1.416045 |
| H | -4.655897 | 0.000073 | -0.049462 |
| H | -0.947059 | -2.152835 | 0.395359 |


| Zero-point correction= | 0.192057 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.203064 |
| Thermal correction to Enthalpy= | 0.204008 |
| Thermal correction to Gibbs Free Energy= | 0.153805 |
| Sum of electronic and zero-point Energies= | -1308.328402 |
| Sum of electronic and thermal Energies= | -1308.317394 |
| Sum of electronic and thermal Enthalpies $=$ | -1308.316450 |
| Sum of electronic and thermal Free Energies= | -1308.366654 |

Low frequencies
$-118.5231 \quad 29.447270 .3246$

## Endo: In Chloroform

| C | 0.345553 | 0.000000 | 1.823529 |
| :--- | ---: | ---: | :---: |
| C | -0.564775 | 0.000000 | 0.822868 |
| C | 2.475199 | 0.000000 | 0.774893 |
| Cl | 2.575930 | -1.448590 | -0.270487 |
| Cl | 2.575930 | 1.448590 | -0.270487 |
| H | 0.634850 | -0.924638 | 2.311729 |
| H | 0.634850 | 0.924637 | 2.311729 |
| C | -1.285318 | -1.141759 | 0.120548 |
| C | -1.285318 | 1.141759 | 0.120549 |
| C | -2.728204 | 0.769328 | 0.551471 |
| C | -2.728204 | -0.769329 | 0.551471 |
| C | -1.021043 | -0.784500 | -1.367225 |
| C | -1.021043 | 0.784501 | -1.367225 |
| C | -3.641820 | 0.000000 | -0.370809 |
| H | -0.047964 | 1.174617 | -1.677985 |
| H | -1.774295 | 1.217018 | -2.031978 |
| H | -0.047964 | -1.174616 | -1.677986 |
| H | -1.774295 | -1.217017 | -2.031978 |
| H | -0.992301 | 2.153101 | 0.406136 |
| H | -3.159752 | 1.326189 | 1.377835 |
| H | -3.159752 | -1.326189 | 1.377834 |
| H | -3.479998 | 0.000000 | -1.443151 |
| H | -4.692862 | 0.000000 | -0.092191 |
| H | -0.992301 | -2.153102 | 0.406135 |


| Zero-point correction $=$ | 0.191505 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy= | 0.202647 |
| Thermal correction to Enthalpy= | 0.203591 |
| Thermal correction to Gibbs Free Energy= | 0.152881 |
| Sum of electronic and zero-point Energies= | -1308.332064 |
| Sum of electronic and thermal Energies= | -1308.320922 |
| Sum of electronic and thermal Enthalpies= | -1308.319978 |

Low frequencies

## Exo: Gas Phase

| C | -0.465037 | -0.019741 | -1.885387 |
| :--- | ---: | ---: | :---: |
| C | 0.541645 | -0.010167 | -0.971674 |
| C | -2.316051 | -0.007522 | -0.736127 |
| Cl | -2.360603 | -1.453883 | 0.331876 |
| Cl | -2.360729 | 1.460336 | 0.301968 |
| H | -0.759620 | -0.947093 | -2.365137 |
| H | -0.758798 | 0.897148 | -2.385357 |
| C | 1.298186 | -1.143301 | -0.296919 |
| C | 1.300139 | 1.136711 | -0.322778 |
| C | 2.733625 | 0.776177 | -0.809936 |
| C | 2.732397 | -0.796336 | -0.791906 |
| C | 1.098538 | -0.752045 | 1.190281 |
| C | 1.099900 | 0.779709 | 1.172913 |
| H | 0.358900 | 1.346070 | 1.725945 |
| H | 0.356437 | -1.304347 | 1.755904 |
| H | 0.975947 | 2.145914 | -0.581618 |
| H | 2.889022 | 1.155472 | -1.824526 |
| H | 2.887769 | -1.199158 | -1.797387 |
| H | 0.972323 | -2.157565 | -0.532838 |
| C | 2.157653 | 0.021466 | 1.938038 |
| H | 2.054662 | 0.033819 | 3.020339 |
| H | 3.190186 | 0.016819 | 1.607232 |
| H | 3.503824 | -1.222814 | -0.144254 |
| H | 3.506039 | 1.216321 | -0.172688 |

$-85.2707 \quad 29.0176 \quad 62.1004$


Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy= Sum of electronic and zero-point Energies= Sum of electronic and thermal Energies= Sum of electronic and thermal Enthalpies= Sum of electronic and thermal Free Energies=

Low frequencies
$-152.7280 \quad 28.602972 .4178$

## Exo: In Chloroform

```
0.400316 -0.003681 -1.908604
-0.586725 -0.001892-0.980263
2.378932 -0.001236 -0.743263
2.409535 1.452369 0.306716
2.409950 -1.451088 0.311885
0.711248
```

| 0.711220 | -0.929188 | -2.381590 |  |
| :---: | :---: | :---: | :---: |
| -1.336068 | 1.140165 | -0.311500 |  |
| -1.336158 | -1.141394 | -0.307255 |  |
| -2.777534 | -0.787515 | -0.773999 |  |
| -2.777483 | 0.784664 | -0.776906 |  |
| -1.107949 | 0.768740 | 1.176689 |  |
| -1.107997 | -0.764495 | 1.179532 |  |
| -0.357617 | -1.323727 | 1.727795 |  |
| -0.357542 | 1.329939 | 1.722898 |  |
| -1.016120 | -2.153418 | -0.559812 |  |
| -2.949156 | -1.180471 | -1.780552 |  |
| -2.949183 | 1.173933 | -1.784874 |  |
| -1.015961 | 2.151228 | -0.567788 |  |
| -2.151767 | 0.003594 | 1.954756 |  |
| -2.026179 | 0.005613 | 3.034757 |  |
| -3.190113 | 0.003026 | 1.642774 |  |
| -3.538550 | 1.218423 | -0.122117 |  |
| -3.538689 | -1.218828 | -0.117699 |  |
| Zero-point | correction= |  | 0.191544 (Hartree/Particle) |
| Thermal cor | rrection to | Energy= | 0.202701 |
| Thermal cor | rrection to | Enthalpy= | 0.203645 |
| Thermal cor | rrection to | Gibbs Free Energy= | 0.152858 |
| Sum of ele | ctronic and | zero-point Energies= | -1308.331325 |
| Sum of ele | ctronic and | hermal Energies= | -1308.320168 |
| Sum of ele | ctronic and | hermal Enthalpies= | -1308.319224 |
| Sum of ele | ctronic and | hermal Free Energies= | -1308.370010 |

Low frequencies

## 3. $m$ CPBA Oxidation of $\mathbf{1 1}$ Calculations.

All the compounds were optimized with B3LYP/6-31+g(d,p). General solvent effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM) for calculation in chloroform.
a. Ground State Calculations of Reactants and Products in Gas Phase and Chloroform.


## Gas Phase

| O | 2.041508 | -1.649474 | -0.000219 |
| :--- | ---: | ---: | ---: |
| O | 2.859179 | 0.444010 | -0.000159 |
| C | 1.834438 | -0.447040 | -0.000375 |
| C | 0.506979 | 0.214945 | -0.000182 |
| C | 0.362672 | 1.610390 | -0.000097 |
| C | -0.619917 | -0.619633 | -0.000085 |
| C | -0.916453 | 2.165236 | 0.000068 |


| H | 1.238122 | 2.249057 | -0.000169 |
| :--- | ---: | ---: | :---: |
| C | -1.885858 | -0.041911 | 0.000080 |
| H | -0.492619 | -1.695807 | -0.000148 |
| C | -2.048023 | 1.345666 | 0.000157 |
| H | -1.038212 | 3.243740 | 0.000128 |
| H | -3.044346 | 1.774216 | 0.000287 |
| Cl | -3.303664 | -1.075870 | 0.000191 |
| O | 4.131517 | -0.228749 | 0.000190 |
| H | 3.838684 | -1.173642 | 0.000755 |

$H F=-955.57458$

## In Chloroform

| O | 2.045667 | -1.649361 | -0.000057 |
| :--- | ---: | ---: | :---: |
| O | 2.859666 | 0.444440 | -0.000038 |
| C | 1.832353 | -0.446896 | -0.000121 |
| C | 0.506643 | 0.213844 | -0.000060 |
| C | 0.362449 | 1.609817 | -0.000033 |
| C | -0.620986 | -0.620942 | -0.000029 |
| C | -0.916215 | 2.165892 | 0.000018 |
| H | 1.235541 | 2.251351 | -0.000055 |
| C | -1.884867 | -0.040319 | 0.000024 |
| H | -0.497901 | -1.697357 | -0.000049 |
| C | -2.048620 | 1.346878 | 0.000048 |
| H | -1.037261 | 3.244033 | 0.000037 |
| H | -3.043577 | 1.778074 | 0.000089 |
| Cl | -3.305521 | -1.076677 | 0.000060 |
| O | 4.133015 | -0.228444 | 0.000063 |
| H | 3.845737 | -1.175323 | 0.000143 |

$H F=-955.5800433$


## Gas Phase

| C | 0.981237 | -0.192983 | -0.000008 |
| :--- | ---: | ---: | ---: |
| C | -0.012794 | 0.072348 | 1.142109 |
| C | -0.012897 | 0.072165 | -1.142084 |
| C | -0.437070 | 1.519817 | -0.785643 |
| C | -0.436730 | 1.520031 | 0.785512 |
| C | -1.097605 | -0.960478 | -0.767762 |
| C | -1.097694 | -0.960243 | 0.768050 |
| H | 0.380047 | -0.045745 | 2.154183 |
| H | 0.379847 | -0.046047 | -2.154184 |
| H | -1.121003 | -1.891009 | -1.328183 |
| H | -1.121199 | -1.890615 | 1.328733 |
| H | 0.303862 | 2.225317 | -1.173045 |
| H | 0.304508 | 2.225468 | 1.172445 |
| C | -2.331805 | -0.551826 | -0.000018 |


| H | -1.405297 | 1.787832 | 1.217431 |
| :--- | ---: | ---: | ---: |
| H | -3.146752 | -1.271124 | -0.000027 |
| H | -2.670554 | 0.478542 | -0.000246 |
| H | -1.405884 | 1.787316 | -1.217215 |
| C | 2.152669 | -1.066224 | 0.000015 |
| O | 2.289481 | 0.378968 | -0.000126 |
| H | 2.471391 | -1.553585 | 0.921124 |
| H | 2.471314 | -1.553734 | -0.921040 |

```
HF = -425.339741
```


## In Chloroform

| C | 0.980187 | -0.189166 | -0.000009 |
| :--- | ---: | ---: | :---: |
| C | -0.011868 | 0.076738 | 1.142649 |
| C | -0.011976 | 0.076537 | -1.142625 |
| C | -0.445024 | 1.521487 | -0.785533 |
| C | -0.444658 | 1.521720 | 0.785392 |
| C | -1.090613 | -0.962843 | -0.767970 |
| C | -1.090721 | -0.962580 | 0.768288 |
| H | 0.381558 | -0.041392 | 2.154357 |
| H | 0.381346 | -0.041716 | -2.154361 |
| H | -1.106074 | -1.894501 | -1.326428 |
| H | -1.106314 | -1.894059 | 1.327043 |
| H | 0.288790 | 2.234058 | -1.174457 |
| H | 0.289496 | 2.234218 | 1.173810 |
| C | -2.327613 | -0.561563 | -0.000025 |
| H | -1.415464 | 1.783011 | 1.215838 |
| H | -3.136480 | -1.287666 | -0.000041 |
| H | -2.672870 | 0.466758 | -0.000276 |
| H | -1.416096 | 1.782441 | -1.215603 |
| C | 2.145744 | -1.068346 | 0.000021 |
| O | 2.296033 | 0.382186 | -0.000139 |
| H | 2.461590 | -1.555189 | 0.921513 |
| H | 2.461509 | -1.555358 | -0.921410 |

$$
\mathrm{HF}=-425.343755
$$



## Gas Phase

| C | -1.005073 | -0.086454 | -0.000016 |
| :--- | ---: | ---: | ---: |
| C | 0.003624 | 0.122187 | -1.140845 |
| C | 0.003531 | 0.122374 | 1.140865 |
| C | 0.499227 | 1.546376 | 0.786476 |
| C | 0.499587 | 1.546142 | -0.786610 |
| C | 1.041422 | -0.961330 | 0.764720 |
| C | 1.041355 | -0.961531 | -0.764462 |
| H | -0.392121 | 0.017001 | -2.153233 |
| H | -0.392304 | 0.017298 | 2.153228 |
| H | 1.013819 | -1.893109 | 1.321639 |


| H | 1.013682 | -1.893444 | -1.321153 |
| :--- | ---: | ---: | ---: |
| H | -0.198215 | 2.294926 | 1.176607 |
| H | -0.197509 | 2.294749 | -1.177247 |
| C | 2.296344 | -0.609401 | 0.000004 |
| H | 1.482252 | 1.762888 | -1.214878 |
| H | 3.079868 | -1.363082 | 0.000008 |
| H | 2.681590 | 0.404688 | -0.000193 |
| H | 1.481641 | 1.763478 | 1.215120 |
| O | -1.904737 | -1.190101 | 0.000045 |
| C | -2.449836 | 0.154255 | -0.000117 |
| H | -2.957900 | 0.439768 | -0.921096 |
| H | -2.958001 | 0.439939 | 0.920752 |

```
HF}=-425.337913
```


## In Chloroform

| C | -1.003773 | -0.087601 | -0.000007 |
| :--- | ---: | ---: | ---: |
| C | 0.003281 | 0.120136 | -1.141284 |
| C | 0.003230 | 0.120251 | 1.141300 |
| C | 0.493131 | 1.546585 | 0.786451 |
| C | 0.493345 | 1.546444 | -0.786534 |
| C | 1.045251 | -0.960046 | 0.765053 |
| C | 1.045210 | -0.960167 | -0.764899 |
| H | -0.392945 | 0.015300 | -2.153441 |
| H | -0.393046 | 0.015480 | 2.153443 |
| H | 1.025686 | -1.891616 | 1.323253 |
| H | 1.025605 | -1.891819 | -1.322961 |
| H | -0.208498 | 2.290836 | 1.176421 |
| H | -0.208073 | 2.290731 | -1.176809 |
| C | 2.298955 | -0.602479 | 0.000001 |
| H | 1.475125 | 1.767043 | -1.214522 |
| H | 3.084584 | -1.353976 | 0.000001 |
| H | 2.678234 | 0.413799 | -0.000115 |
| H | 1.474758 | 1.767404 | 1.214662 |
| O | -1.906434 | -1.197718 | 0.000028 |
| C | -2.446241 | 0.156248 | -0.000071 |
| H | -2.952109 | 0.441115 | -0.921469 |
| H | -2.952176 | 0.441215 | 0.921259 |

$$
\mathrm{HF}=-425.3422409
$$

## b. Transition State Calculations in Gas Phase and Chloroform.

## Endo: Gas Phase

| C | -3.345901 | -0.314638 | 0.770249 |
| :--- | ---: | :---: | :---: |
| C | -2.919325 | -0.918928 | 1.916524 |
| O | 0.446657 | -1.565053 | 0.206304 |
| O | 0.682519 | 0.533531 | 0.959739 |
| H | -2.560625 | -0.333816 | 2.757960 |
| H | -0.836941 | -0.293104 | 1.058198 |
| C | 1.152471 | -0.496034 | 0.442849 |
| O | -1.215062 | -1.177979 | 0.791862 |
| C | 2.598523 | -0.585495 | 0.043665 |
| C | 3.411706 | 0.536148 | 0.253569 |
| C | 3.132913 | -1.751050 | -0.521085 |



|  |  |  |  |
| :--- | ---: | ---: | :---: |
| C | 4.754249 | 0.473896 | -0.108259 |
| H | 2.985147 | 1.429896 | 0.693143 |
| C | 4.481731 | -1.791199 | -0.875619 |
| H | 2.491167 | -2.610938 | -0.675099 |
| C | 5.303344 | -0.679241 | -0.672655 |
| H | 6.352610 | -0.703803 | -0.946231 |
| H | -3.083436 | -1.976430 | 2.086919 |
| C | -4.063534 | -0.881870 | -0.441673 |
| C | -3.425195 | 1.154128 | 0.382652 |
| C | -4.973084 | 1.244858 | 0.321700 |
| C | -5.403154 | -0.127917 | -0.235816 |
| C | -2.792317 | 1.126809 | -1.032975 |
| C | -3.224534 | -0.273452 | -1.595893 |
| Cl | 5.783329 | 1.878598 | 0.150837 |
| H | 4.901752 | -2.691884 | -1.313078 |
| H | -4.170102 | -1.966802 | -0.477814 |
| H | -2.972341 | 1.867651 | 1.073082 |
| H | -3.135745 | 1.965077 | -1.645771 |
| H | -1.704828 | 1.197960 | -0.954637 |
| H | -3.797980 | -0.206999 | -2.525067 |
| H | -2.349896 | -0.900958 | -1.779552 |
| C | -5.704604 | 1.140382 | -0.992414 |
| H | -5.202303 | 1.362705 | -1.927188 |
| H | -6.743808 | 1.459615 | -0.973965 |
| H | -5.480329 | 1.683007 | 1.175917 |
| H | -6.221587 | -0.679709 | 0.216796 |


| Zero-point correction $=$ | 0.294983 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy= | 0.312715 |
| Thermal correction to Enthalpy= | 0.313659 |
| Thermal correction to Gibbs Free Energy= | 0.245872 |
| Sum of electronic and zero-point Energies= | -1305.393639 |
| Sum of electronic and thermal Energies= | -1305.375907 |
| Sum of electronic and thermal Enthalpies= | -1305.374962 |
| Sum of electronic and thermal Free Energies= | -1305.442750 |

## Endo: In Chloroform

| C | 3.408790 | 0.204465 | 0.798095 |
| :--- | ---: | ---: | ---: |
| C | 2.922276 | 0.640752 | 1.992648 |
| O | -0.485352 | 1.427872 | 0.332116 |
| O | -0.798312 | -0.709395 | 0.937820 |
| H | 2.562279 | -0.060941 | 2.739192 |
| H | 0.817203 | 0.095505 | 1.085615 |
| C | -1.230543 | 0.363486 | 0.488171 |
| O | 1.141673 | 1.010355 | 0.881087 |
| C | -2.664990 | 0.537417 | 0.079200 |
| C | -3.526887 | -0.559236 | 0.220674 |
| C | -3.145338 | 1.752431 | -0.428856 |
| C | -4.860793 | -0.419695 | -0.150346 |
| H | -3.147264 | -1.494378 | 0.614395 |
| C | -4.486908 | 1.867759 | -0.795026 |
| H | -2.472435 | 2.595389 | -0.534045 |


| C | -5.356761 | 0.782329 | -0.658908 |
| :--- | ---: | ---: | ---: |
| H | -6.400105 | 0.867568 | -0.941984 |
| H | 3.039238 | 1.673951 | 2.298830 |
| C | 4.140733 | 0.949316 | -0.304733 |
| C | 3.557419 | -1.198192 | 0.230448 |
| C | 5.108384 | -1.225138 | 0.217020 |
| C | 5.501492 | 0.223483 | -0.144579 |
| C | 2.971040 | -1.009845 | -1.193715 |
| C | 3.367087 | 0.464265 | -1.558048 |
| Cl | -5.950460 | -1.794315 | 0.026588 |
| H | -4.863271 | 2.806386 | -1.189144 |
| H | 4.207005 | 2.032576 | -0.197048 |
| H | 3.112108 | -2.009368 | 0.808182 |
| H | 3.365571 | -1.749296 | -1.896047 |
| H | 1.884442 | -1.127566 | -1.167901 |
| H | 3.973433 | 0.536041 | -2.465274 |
| H | 2.476678 | 1.081158 | -1.700440 |
| C | 5.879360 | -0.926190 | -1.043795 |
| H | 5.419974 | -1.044256 | -2.018817 |
| H | 6.929559 | -1.206738 | -1.022216 |
| H | 5.603339 | -1.748521 | 1.029157 |
| H | 6.279824 | 0.740738 | 0.407870 |

## Zero-point correction=

Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.294288 (Hartree/Particle)
0.312209
0.313153
0.244911
-1305.403158
-1305.385238
-1305.384293
-1305.452535

Low frequencies
$-433.7206 \quad 15.7550 \quad 22.3558$

## Exo: Gas Phase

| C | 3.454011 | -0.549153 | -0.684819 |
| :--- | ---: | ---: | ---: |
| C | 3.021673 | -1.525614 | -1.536731 |
| O | -0.397849 | -1.750852 | 0.063002 |
| O | -0.501888 | 0.267678 | -0.908923 |
| H | 2.672802 | -1.280085 | -2.534836 |
| H | 0.976666 | -0.624857 | -0.862425 |
| C | -1.038855 | -0.682742 | -0.309032 |
| O | 1.315307 | -1.495042 | -0.508588 |
| C | -2.502458 | -0.661869 | 0.036093 |
| C | -3.250215 | 0.466690 | -0.325131 |
| C | -3.115383 | -1.734112 | 0.697400 |
| C | -4.606889 | 0.505148 | -0.016592 |
| H | -2.763249 | 1.287241 | -0.838334 |
| C | -4.477053 | -1.674448 | 0.995930 |
| H | -2.523254 | -2.600499 | 0.968944 |
| C | -5.234018 | -0.554379 | 0.641968 |
| H | -6.292814 | -0.501628 | 0.871167 |
| H | 3.221977 | -2.570798 | -1.331810 |
| C | 4.135208 | -0.634671 | 0.669138 |



|  |  |  |  |
| :--- | ---: | ---: | :---: |
| C | 3.475644 | 0.965905 | -0.819753 |
| C | 5.012714 | 1.187222 | -0.717048 |
| C | 5.466910 | 0.085093 | 0.308263 |
| C | 2.752745 | 1.355183 | 0.494792 |
| C | 3.193346 | 0.280984 | 1.491557 |
| Cl | -5.553495 | 1.920098 | -0.466063 |
| H | -4.957748 | -2.502881 | 1.507484 |
| H | 4.257590 | -1.633781 | 1.089277 |
| H | 3.017804 | 1.386089 | -1.716805 |
| H | 1.710029 | 1.645238 | 0.412735 |
| H | 2.467975 | -0.210331 | 2.131428 |
| H | 5.481685 | 1.032910 | -1.693577 |
| H | 6.161133 | -0.621158 | -0.157325 |
| C | 3.533278 | 1.731868 | 1.730719 |
| H | 5.960673 | 0.495237 | 1.193568 |
| H | 2.961208 | 2.225296 | 2.512393 |
| H | 4.555649 | 2.087401 | 1.660807 |
| H | 5.252796 | 2.204051 | -0.394073 |


| Zero-point correction= | 0.294940 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.312685 |
| Thermal correction to Enthalpy= | 0.313630 |
| Thermal correction to Gibbs Free Energy= | 0.245690 |
| Sum of electronic and zero-point Energies= | -1305.391833 |
| Sum of electronic and thermal Energies= | -1305.374088 |
| Sum of electronic and thermal Enthalpies= | -1305.373144 |
| Sum of electronic and thermal Free Energies= | -1305.441083 |

Low frequencies $\quad-425.4642 \quad 10.8555 \quad 22.0806$

## Exo: In Chloroform

| C | 3.514888 | -0.527502 | -0.705737 |
| :--- | ---: | ---: | ---: |
| C | 3.037158 | -1.452306 | -1.585613 |
| O | -0.437856 | -1.661257 | 0.007888 |
| O | -0.606041 | 0.355734 | -0.960185 |
| H | 2.690593 | -1.155854 | -2.570634 |
| H | 0.963324 | -0.539831 | -0.911799 |
| C | -1.112342 | -0.601765 | -0.352615 |
| O | 1.238851 | -1.425386 | -0.559195 |
| C | -2.566574 | -0.623412 | 0.025202 |
| C | -3.356030 | 0.478561 | -0.332286 |
| C | -3.134028 | -1.705090 | 0.712824 |
| C | -4.705873 | 0.478336 | 0.005889 |
| H | -2.909365 | 1.309831 | -0.864243 |
| C | -4.490057 | -1.682230 | 1.041557 |
| H | -2.516439 | -2.553032 | 0.984935 |
| C | -5.288259 | -0.589810 | 0.690868 |
| H | -6.342471 | -0.567979 | 0.944141 |
| H | 3.186776 | -2.511736 | -1.411909 |
| C | 4.200658 | -0.691735 | 0.638790 |
| C | 3.606068 | 0.987767 | -0.791163 |
| C | 5.152465 | 1.134350 | -0.692471 |
| C | 5.561485 | -0.022181 | 0.290730 |
| C | 2.909351 | 1.364147 | 0.541582 |


| C | 3.307693 | 0.237696 | 1.499647 |
| :--- | ---: | ---: | :---: |
| Cl | -5.704064 | 1.861052 | -0.441794 |
| H | -4.933782 | -2.517430 | 1.574060 |
| H | 4.280803 | -1.709281 | 1.022970 |
| H | 3.164282 | 1.457419 | -1.671210 |
| H | 1.881921 | 1.709905 | 0.481956 |
| H | 2.569189 | -0.237986 | 2.136909 |
| H | 5.605163 | 0.990740 | -1.677828 |
| H | 6.216792 | -0.744345 | -0.205007 |
| C | 3.714834 | 1.663473 | 1.783099 |
| H | 6.080149 | 0.333733 | 1.184997 |
| H | 3.170090 | 2.154522 | 2.585607 |
| H | 4.751764 | 1.973854 | 1.714744 |
| H | 5.442055 | 2.127045 | -0.337081 |


| Zero-point correction $=$ | 0.294357 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.312286 |
| Thermal correction to Enthalpy= | 0.313230 |
| Thermal correction to Gibbs Free Energy= | 0.244411 |
| Sum of electronic and zero-point Energies= | -1305.401568 |
| Sum of electronic and thermal Energies= | -1305.383640 |
| Sum of electronic and thermal Enthalpies $=$ | -1305.382696 |
| Sum of electronic and thermal Free Energies= | -1305.451514 |

Low frequencies $\quad \begin{array}{lllll}-449.8550 & 6.3917 & 10.7821 & 21.8740\end{array}$

## 4. Compound 11 Osmylation Calculations.

All the compounds were optimized with B3LYP/6-31+g(d,p), SDD. General solvent effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM) for calculation in pyridine.
a. Ground State Calculations of Reactants and Products in Gas Phase and Pyridine.


| Os | -0.000091 | 0.000045 | 0.000009 |
| :--- | ---: | ---: | ---: |
| O | 0.853645 | -0.393823 | 1.439739 |
| O | 0.562560 | -0.990535 | -1.288109 |
| O | -1.681590 | -0.269500 | 0.238208 |
| O | 0.266253 | 1.653431 | -0.389927 |

$\mathrm{HF}=-391.5944162$


## Gas Phase

| C | -1.214311 | 0.282129 | 0.225497 |
| :---: | :---: | :---: | :---: |
| C | -0.638653 | 1.672066 | 0.030450 |
| Os | 1.638594 | -0.051225 | -0.024058 |
| O | -0.089805 | -0.536083 | 0.642958 |
| O | 0.692101 | 1.535391 | -0.523539 |
| O | 2.762512 | 0.299394 | 1.219815 |
| O | 2.053253 | -1.037202 | -1.362080 |
| H | -0.555754 | 2.200890 | 0.989262 |
| H | -1.202029 | 2.290115 | -0.670958 |
| C | -2.407945 | 0.119929 | 1.209593 |
| H | -2.224007 | 0.485039 | 2.223278 |
| C | -1.995118 | -0.346408 | -0.978396 |
| H | -1.443406 | -0.395671 | -1.920724 |
| C | -3.484162 | 0.926025 | 0.447489 |
| C | -3.209272 | 0.605132 | -1.027033 |
| C | -2.371117 | -1.727178 | -0.388938 |
| C | -2.657666 | -1.405806 | 1.119257 |
| H | -3.216438 | 1.382669 | -1.786154 |
| H | -3.688987 | 1.940449 | 0.779965 |
| H | -1.531611 | -2.419936 | -0.485724 |
| H | -1.959593 | -1.938129 | 1.769658 |
| H | -3.671100 | -1.669390 | 1.434085 |
| H | -3.225956 | -2.169695 | -0.907790 |
| C | -4.522884 | 0.221802 | -0.391240 |
| H | -4.773769 | -0.817399 | -0.211337 |
| H | -5.378233 | 0.825975 | -0.682424 |

$H F=-741.7783003$

## In Pyridine

| C | 1.211042 | -0.274327 | 0.199138 |
| :--- | :---: | :---: | :---: |
| C | 0.632204 | -1.660896 | -0.013960 |
| Os | -1.644807 | 0.052496 | -0.022125 |
| O | 0.084922 | 0.551722 | 0.612191 |
| O | -0.703939 | -1.518820 | -0.568368 |
| O | -2.696639 | -0.354671 | 1.278211 |
| O | -2.057195 | 1.064222 | -1.352208 |
| H | 0.544195 | -2.200749 | 0.936879 |
| H | 1.195704 | -2.269329 | -0.722562 |
| C | 2.387276 | -0.125582 | 1.206169 |
| H | 2.181322 | -0.495266 | 2.213621 |
| C | 2.015848 | 0.356117 | -0.986972 |
| H | 1.480379 | 0.412807 | -1.937887 |
| C | 3.468486 | -0.937876 | 0.459151 |


| C | 3.222214 | -0.607140 | -1.018266 |
| :--- | ---: | ---: | :---: |
| C | 2.395009 | 1.730037 | -0.384559 |
| C | 2.653208 | 1.398396 | 1.126501 |
| H | 3.232694 | -1.384925 | -1.776615 |
| H | 3.652495 | -1.957460 | 0.786634 |
| H | 1.565028 | 2.432956 | -0.493830 |
| H | 1.952673 | 1.936956 | 1.769658 |
| H | 3.664314 | 1.650688 | 1.457212 |
| H | 3.264018 | 2.166082 | -0.884921 |
| C | 4.529064 | -0.239477 | -0.357399 |
| H | 4.787383 | 0.796359 | -0.167575 |
| H | 5.381824 | -0.852921 | -0.636554 |

$H F=-741.7921889$


## Gas Phase

| C | 1.210150 | 0.468331 | -0.170782 |
| :--- | ---: | ---: | ---: |
| C | 0.504996 | 1.803222 | -0.007371 |
| Os | -1.608502 | -0.114532 | 0.006583 |
| O | 0.172813 | -0.450374 | -0.604515 |
| O | -0.823790 | 1.557110 | 0.509743 |
| O | -2.719989 | 0.118636 | -1.275845 |
| O | -1.974088 | -1.120862 | 1.343775 |
| H | 0.407105 | 2.314252 | -0.974605 |
| H | 0.984998 | 2.478913 | 0.703909 |
| C | 2.431716 | 0.390487 | -1.131041 |
| H | 2.231459 | 0.704337 | -2.158607 |
| C | 2.015729 | -0.092725 | 1.049602 |
| H | 1.446054 | -0.210850 | 1.975106 |
| C | 3.435218 | 1.293970 | -0.371685 |
| C | 3.157863 | 0.948448 | 1.135370 |
| C | 2.517421 | -1.430069 | 0.459131 |
| C | 2.797760 | -1.105945 | -1.003653 |
| C | 3.917737 | -1.558019 | -0.095671 |
| H | 4.706899 | -0.877385 | 0.204645 |
| H | 4.270657 | -2.573953 | -0.253685 |
| H | 4.033678 | 0.547259 | 1.651210 |
| H | 2.841760 | 1.833020 | 1.697166 |
| H | 4.467453 | 1.099338 | -0.674330 |
| H | 3.236137 | 2.350796 | -0.581010 |
| H | 1.983132 | -2.333275 | 0.736201 |
| H | 2.465706 | -1.770270 | -1.794976 |

$H F=-741.7752684$

## In Pyridine

| C | 1.206077 | 0.460922 | -0.159953 |
| :--- | ---: | :---: | :---: |
| C | 0.499797 | 1.794820 | 0.005679 |
| Os | -1.612353 | -0.119002 | 0.005582 |
| O | 0.168364 | -0.467283 | -0.590423 |
| O | -0.836484 | 1.550788 | 0.516429 |
| O | -2.687080 | 0.145888 | -1.312497 |
| O | -1.961093 | -1.111809 | 1.367484 |
| H | 0.403520 | 2.307875 | -0.959211 |
| H | 0.976823 | 2.466200 | 0.721755 |
| C | 2.420997 | 0.395488 | -1.129624 |
| H | 2.210812 | 0.713044 | -2.153786 |
| C | 2.022838 | -0.098579 | 1.052992 |
| H | 1.458865 | -0.224570 | 1.980604 |
| C | 3.420167 | 1.306498 | -0.372842 |
| C | 3.155170 | 0.953948 | 1.134727 |
| C | 2.534912 | -1.429225 | 0.454888 |
| C | 2.803190 | -1.097569 | -1.009119 |
| C | 3.933890 | -1.540601 | -0.108958 |
| H | 4.716245 | -0.851002 | 0.188458 |
| H | 4.294936 | -2.552851 | -0.272948 |
| H | 4.038207 | 0.559852 | 1.643563 |
| H | 2.832665 | 1.833447 | 1.699962 |
| H | 4.452378 | 1.122032 | -0.681614 |
| H | 3.208210 | 2.361043 | -0.577827 |
| H | 2.015579 | -2.340963 | 0.733815 |
| H | 2.478725 | -1.764815 | -1.801682 |
| HF $=-741.7895732$ |  |  |  |
| H |  |  |  |

b. Transition State Calculations in Gas Phase and Pyridine.

## Endo: Gas Phase

| C | -1.638188 | 0.585476 | 0.000041 |
| :--- | ---: | ---: | :---: |
| C | -0.968428 | 1.797151 | -0.000036 |
| Os | 1.747309 | -0.039153 | -0.000007 |
| O | 0.135276 | -0.757805 | 0.000431 |
| O | 1.144162 | 1.618557 | -0.000382 |
| O | 2.587023 | -0.402178 | 1.461261 |
| O | 2.586559 | -0.403050 | -1.461324 |
| H | -0.850377 | 2.354954 | 0.922045 |
| H | -0.850516 | 2.354920 | -0.922156 |
| C | -2.455757 | -0.024430 | 1.142849 |
| H | -2.118396 | 0.201681 | 2.155981 |
| C | -2.455608 | -0.024596 | -1.142772 |
| H | -2.118120 | 0.201361 | -2.155896 |
| C | -3.798299 | 0.662922 | 0.770953 |
| C | -3.798197 | 0.662808 | -0.771152 |
| C | -2.483576 | -1.529929 | -0.783626 |
| C | -2.483683 | -1.529835 | 0.783939 |
| H | -4.068945 | 1.557760 | -1.324136 |
| H | -4.069118 | 1.557958 | 1.323765 |
| H | -1.592235 | -2.026692 | -1.171238 |
| H | -1.592405 | -2.026553 | 1.171748 |
| H | -3.356771 | -2.028033 | 1.215096 |
| H | -3.356600 | -2.028206 | -1.214823 |



| C | -4.866347 | -0.071589 | -0.000113 |
| :--- | ---: | ---: | ---: |
| H | -4.911008 | -1.154884 | -0.000036 |
| H | -5.846688 | 0.399325 | -0.000214 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.200414 (Hartree/Particle)
0.212827
0.213772
0.160268
-741.506983
-741.494570
-741.493626
-741.547129

Low frequencies
$\begin{array}{llll}-230.7147 & 8.5174 & 37.2765 & 63.8825\end{array}$

## Endo: In Pyridine

| C | -1.657162 | 0.591935 | -0.033459 |
| :--- | ---: | ---: | :---: |
| C | -0.978453 | 1.798120 | -0.055650 |
| Os | 1.756359 | -0.038711 | 0.004524 |
| O | 0.146841 | -0.751811 | 0.004982 |
| O | 1.164554 | 1.617675 | -0.112844 |
| O | 2.523157 | -0.314553 | 1.532666 |
| O | 2.610264 | -0.502083 | -1.430340 |
| H | -0.824405 | 2.351443 | 0.863708 |
| H | -0.885569 | 2.351200 | -0.983232 |
| C | -2.435418 | -0.026890 | 1.130605 |
| H | -2.068799 | 0.197469 | 2.133449 |
| C | -2.497108 | -0.018981 | -1.156830 |
| H | -2.188639 | 0.216112 | -2.176696 |
| C | -3.788457 | 0.657896 | 0.799485 |
| C | -3.830830 | 0.663251 | -0.744427 |
| C | -2.506766 | -1.524985 | -0.802467 |
| C | -2.469793 | -1.531321 | 0.764699 |
| H | -4.116731 | 1.561723 | -1.283174 |
| H | -4.044524 | 1.551634 | 1.360739 |
| H | -1.621229 | -2.013552 | -1.214940 |
| H | -1.570877 | -2.030786 | 1.130942 |
| H | -3.332860 | -2.032388 | 1.211889 |
| H | -3.385911 | -2.029254 | -1.213674 |
| C | -4.874585 | -0.077071 | 0.054208 |
| H | -4.916251 | -1.160660 | 0.051181 |
| H | -5.854597 | 0.393549 | 0.083308 |


| Zero-point correction $=$ | 0.200106 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.212396 |
| Thermal correction to Enthalpy= | 0.213340 |
| Thermal correction to Gibbs Free Energy= | 0.160964 |
| Sum of electronic and zero-point Energies= | -741.521090 |
| Sum of electronic and thermal Energies= | -741.508800 |
| Sum of electronic and thermal Enthalpies $=$ | -741.507856 |
| Sum of electronic and thermal Free Energies= | -741.560232 |

## Exo: Gas Phase

| C | 1.612449 | 0.766632 | 0.000059 |
| :--- | :---: | :---: | :---: |
| C | 0.884224 | 1.941688 | -0.000158 |
| Os | -1.692774 | -0.076921 | -0.000003 |
| O | -0.033578 | -0.673781 | 0.001396 |
| O | -1.220848 | 1.621780 | -0.001414 |
| O | -2.502012 | -0.504994 | -1.460731 |
| O | -2.503521 | -0.502063 | 1.460744 |
| H | 0.727874 | 2.489759 | -0.922731 |
| H | 0.727363 | 2.489808 | 0.922302 |
| C | 2.470165 | 0.203754 | -1.139713 |
| H | 2.110440 | 0.382848 | -2.154775 |
| C | 2.470488 | 0.204131 | 1.139791 |
| H | 2.111021 | 0.383539 | 2.154887 |
| C | 3.785789 | 0.961779 | -0.787865 |
| C | 3.786015 | 0.962034 | 0.787338 |
| C | 2.580451 | -1.291306 | 0.761198 |
| C | 2.580222 | -1.291547 | -0.760673 |
| C | 3.776255 | -1.818314 | 0.000173 |
| H | 4.722906 | -1.289104 | -0.000070 |
| H | 3.893570 | -2.899120 | 0.000343 |
| H | 4.665015 | 0.473464 | 1.217238 |
| H | 3.750626 | 1.982672 | 1.180082 |
| H | 4.664670 | 0.473079 | -1.217863 |
| H | 3.750282 | 1.982287 | -1.180936 |
| H | 1.965368 | -1.991754 | 1.316329 |
| H | 1.964963 | -1.992158 | -1.315412 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=

0.200376 (Hartree/Particle)
0.212777
0.213721
0.160219
-741.504948
-741.492547
-741.491603
$-741.545105$

Low frequencies
$-249.6160 \quad 18.0028 \quad 37.9058 \quad 67.4426$

## Exo: In Pyridine

| C | 1.635928 | 0.766237 | -0.022999 |
| :--- | ---: | ---: | ---: |
| C | 0.897486 | 1.932925 | -0.042910 |
| Os | -1.706865 | -0.076968 | 0.002022 |
| O | -0.058829 | -0.692680 | 0.024215 |
| O | -1.223073 | 1.611258 | -0.113535 |
| O | -2.518348 | -0.593184 | -1.439179 |
| O | -2.483758 | -0.387841 | 1.518874 |
| H | 0.768276 | 2.480142 | -0.969964 |
| H | 0.706106 | 2.473238 | 0.877567 |
| C | 2.515654 | 0.209190 | -1.145316 |
| H | 2.180444 | 0.396191 | -2.166951 |
| C | 2.462844 | 0.199041 | 1.135442 |
| H | 2.076695 | 0.373367 | 2.141175 |


| C | 3.820919 | 0.970491 | -0.756201 |
| :--- | ---: | ---: | ---: |
| C | 3.784213 | 0.962149 | 0.818710 |
| C | 2.585334 | -1.294655 | 0.750751 |
| C | 2.618669 | -1.287476 | -0.771027 |
| C | 3.799962 | -1.814932 | 0.013411 |
| H | 4.743324 | -1.280320 | 0.035353 |
| H | 3.919732 | -2.895608 | 0.011554 |
| H | 4.654354 | 0.473189 | 1.265865 |
| H | 3.734506 | 1.979946 | 1.216381 |
| H | 4.712143 | 0.488423 | -1.167677 |
| H | 3.787859 | 1.992831 | -1.143778 |
| H | 1.963901 | -2.002252 | 1.289752 |
| H | 2.020368 | -1.987865 | -1.345143 |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy= Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.199881 (Hartree/Particle)
0.212295
0.213240
0.160325
-741.519138
-741.506723
-741.505779
-741.558693

### 6.5.2. Section 4.3.

I. Ground State Cartesian Coordinates, and Energies of Compound $\mathbf{1}$ with different Lewis acids in diethyl ether (Figure 2).

Compound 1 with or without Lewis acid coordination were all optimized using the B3LYP/6-31+G*. The carbonyl group in the ketone was distorted away from planarity both ways to $0^{\circ}, 5^{\circ}, 15^{\circ}, 20^{\circ}, 25^{\circ}, 30^{\circ}, 35^{\circ}$ and optimized using B3LYP/6-31+G* with the distortion angle $(\theta)$ frozen to get the distortional energies at these distortional angles. General solvent (diethyl ether) effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM).


|  |  |  |  |
| :--- | ---: | ---: | ---: |
| C | 0.704004 | 1.301056 | -1.257741 |
| C | 0.830852 | -0.246624 | -1.269310 |
| C | -0.586375 | -0.879134 | -1.257092 |
| C | -1.319755 | -0.405802 | 0.000008 |
| C | 1.556080 | -0.664800 | 0.000046 |
| C | -0.066617 | 1.750632 | -0.000069 |
| C | -0.586402 | -0.879029 | 1.257161 |
| C | 0.830825 | -0.246521 | 1.269353 |
| C | 0.703984 | 1.301158 | 1.257651 |
| C | -1.476686 | 1.114214 | -0.000056 |
| O | 2.628991 | -1.260149 | 0.000082 |
| F | -2.628536 | -0.996934 | 0.000018 |
| H | 0.180264 | 1.620153 | -2.168201 |
| H | 1.700643 | 1.759873 | -1.276139 |
| H | 1.398133 | -0.589897 | -2.139532 |
| H | -0.522999 | -1.973692 | -1.262839 |
| H | -1.134458 | -0.566412 | -2.153906 |
| H | -0.163339 | 2.843108 | -0.000114 |
| H | -0.523027 | -1.973587 | 1.263002 |
| H | -1.134502 | -0.566232 | 2.153938 |
| H | 1.398089 | -0.589722 | 2.139616 |
| H | 0.180233 | 1.6203336 | 2.168077 |
| H | 1.700625 | 1.759970 | 1.276023 |
| H | -2.040960 | 1.426746 | -0.887416 |
| H | -2.040978 | 1.426820 | 0.887267 |
| HF=-564.015523 |  |  |  |
|  |  |  |  |



| C | 0.584753 | 0.081931 | 0.660260 |
| :--- | ---: | ---: | :---: |
| O | -0.569318 | -0.031134 | 1.081810 |
| C | 0.921279 | 0.494331 | -0.757803 |
| H | -0.001704 | 0.656879 | -1.322853 |
| C | 1.800684 | -0.181896 | 1.523343 |
| H | 1.477777 | -0.484893 | 2.523437 |
| C | 1.769343 | 1.794775 | -0.685175 |
| H | 2.025763 | 2.102093 | -1.706592 |
| H | 1.179976 | 2.604629 | -0.237069 |
| C | 2.642968 | 1.123065 | 1.574631 |
| H | 2.068001 | 1.922726 | 2.057996 |
| H | 3.531641 | 0.940405 | 2.191265 |
| C | 2.636719 | -1.306422 | 0.853351 |
| H | 3.537228 | -1.490633 | 1.450182 |
| H | 2.065840 | -2.241078 | 0.805044 |
| C | 1.766305 | -0.635421 | -1.406556 |
| H | 2.045330 | -0.338437 | -2.423968 |
| H | 1.189871 | -1.565762 | -1.471783 |
| C | 3.020673 | -0.854457 | -0.557346 |
| C | 3.874057 | 0.412047 | -0.512809 |
| C | 3.043039 | 1.539163 | 0.145138 |
| H | 4.788672 | 0.221244 | 0.061451 |
| H | 4.167035 | 0.694875 | -1.531109 |
| H | -2.200716 | 0.095073 | 0.367309 |
| C | -3.831582 | 1.051046 | -0.470036 |
| C | -3.864955 | -1.090101 | 0.539475 |
| C | -5.190042 | 0.974585 | -0.737624 |
| H | -3.214209 | 1.900630 | -0.732513 |
| C | -5.223921 | -1.214888 | 0.294576 |
| H | -3.268929 | -1.846324 | 1.034600 |
| H | -5.683090 | 1.799186 | -1.238917 |
| H | -5.743602 | -2.113574 | 0.604944 |
| N | -3.215014 | 0.027403 | 0.154537 |
| C | -5.893937 | -0.170071 | -0.349651 |
| H | -6.957938 | -0.247188 | -0.548704 |
| F | 3.786376 | -1.901609 | -1.165211 |
| H | 3.643007 | 2.455761 | 0.185294 |
|  |  |  |  |

$\mathrm{HF}=-812.7670795$


|  |  |  |  |
| :--- | ---: | ---: | ---: |
| C | 0.658828 | 1.301451 | -1.270644 |
| C | 0.817272 | -0.261234 | -1.250040 |
| C | -0.595813 | -0.917017 | -1.238448 |
| C | -1.353668 | -0.4253228 | -0.000008 |
| C | 1.486883 | -0.585625 | 0.030571 |
| C | -0.134954 | 1.752592 | -0.032832 |
| C | -0.621063 | -0.864797 | 1.271367 |
| C | 0.792682 | -0.212153 | 1.281554 |
| C | 0.639083 | 1.350257 | 1.233913 |
| C | -1.533369 | 1.092326 | -0.032928 |
| O | 2.652781 | -1.111700 | 0.116227 |
| F | -2.636198 | -1.042090 | -0.002240 |
| H | 0.138715 | 1.555734 | -2.200611 |
| H | 1.643901 | 1.779992 | -1.299778 |
| H | 1.405017 | -0.604354 | -2.106395 |
| H | -0.516044 | -2.0090558 | -1.226095 |
| H | -1.117476 | -0.621653 | -2.154216 |
| H | -0.244523 | 2.842624 | -0.056007 |
| H | -0.543325 | -1.956340 | 1.307852 |
| H | -1.158936 | -0.530296 | 2.164030 |
| H | 1.371927 | -0.525884 | 2.152338 |
| H | 0.107052 | 1.646221 | 2.144519 |
| H | 1.625821 | 1.825877 | 1.256707 |
| H | -2.092866 | 1.377421 | -0.931153 |
| H | -2.110214 | 1.413575 | 0.841735 |
| H | 3.059190 | -1.304287 | -0.757601 |

$H F=-564.4096818$
II. Ground State Cartesian Coordinates, and Energies of Compound 1 with different 5-X subsituents (Figure 3).

Compound 1 with different $5-\mathrm{X}$ substituents were all optimized using the B3LYP/6$31+\mathrm{G}^{*}$ in gas phase. The carbonyl group in the ketone was distorted away from planarity both ways to $0^{\circ}, 5^{\circ}, 15^{\circ}$ and optimized using B3LYP/6-31+G* with the distortion angle $(\theta)$ frozen to get the distortional energies at these distortional angles.


|  |  |  |  |  |
| :--- | ---: | ---: | ---: | :---: |
| C | 0.661591 | 1.301634 | -1.270372 |  |
| C | 0.814196 | -0.268561 | -1.250944 |  |
| C | -0.605288 | -0.916534 | -1.240041 |  |
| C | -1.366953 | -0.426490 | 0.001331 |  |
| C | 1.482749 | -0.586576 | 0.028784 |  |
| C | -0.132954 | 1.751156 | -0.031453 |  |
| C | -0.625325 | -0.867270 | 1.271116 |  |
| C | 0.794857 | -0.2221284 | 1.281138 |  |
| C | 0.643518 | 1.348100 | 1.234040 |  |
| C | -1.532735 | 1.095406 | -0.030659 |  |
| O | 2.659430 | -1.104069 | 0.114007 |  |
| F | -2.626618 | -1.033328 | -0.000928 |  |
| H | 0.146638 | 1.556804 | -2.203174 |  |
| H | 1.647968 | 1.799697 | -1.302576 |  |
| H | 1.403048 | -0.612756 | -2.110067 |  |
| H | -0.540500 | -2.010504 | -1.237457 |  |
| H | -1.126485 | -0.618813 | -2.155679 |  |
| H | -0.234789 | 2.842473 | -0.054520 |  |
| H | -0.560613 | -1.960316 | 1.314530 |  |
| H | -1.160838 | -0.533739 | 2.165863 |  |
| H | 1.381707 | -0.535957 | 2.148094 |  |
| H | 0.115727 | 1.641142 | 2.148322 |  |
| H | 1.630860 | 1.823792 | 1.263491 |  |
| H | -2.099241 | 1.384135 | -0.923400 |  |
| H | -2.112752 | 1.415560 | 0.841186 |  |
| H | 3.071464 | -1.299495 | -0.755959 |  |
|  |  |  |  |  |
| HF $=-564.3264324$ |  |  |  |  |



| C | 0.715005 | 1.277970 | -1.287302 |
| :--- | ---: | ---: | ---: |
| C | 0.831775 | -0.292160 | -1.240321 |
| C | -0.605212 | -0.904483 | -1.225113 |
| C | -1.397444 | -0.402805 | 0.003554 |
| C | 1.487349 | -0.614588 | 0.041195 |
| C | -0.071694 | 1.761643 | -0.057674 |
| C | -0.619683 | -0.818830 | 1.281026 |


| C | 0.819083 | -0.201874 | 1.285033 |
| :--- | ---: | ---: | :---: |
| C | 0.695726 | 1.366066 | 1.214417 |
| C | -1.481731 | 1.138669 | -0.052293 |
| O | 2.632771 | -1.201854 | 0.132695 |
| N | -2.744290 | -0.953258 | -0.078740 |
| H | 0.204871 | 1.529718 | -2.223635 |
| H | 1.711908 | 1.733434 | -1.326407 |
| H | 1.412755 | -0.664995 | -2.093366 |
| H | -0.548965 | -2.000866 | -1.226570 |
| H | -1.112333 | -0.605628 | -2.147919 |
| H | -0.150609 | 2.854748 | -0.099194 |
| H | -0.560822 | -1.912181 | 1.356014 |
| H | -1.132582 | -0.461351 | 2.181422 |
| H | 1.400423 | -0.516355 | 2.156262 |
| H | 0.171154 | 1.684147 | 2.122341 |
| H | 1.691638 | 1.824158 | 1.238751 |
| H | -2.039814 | 1.432641 | -0.948576 |
| H | -2.049401 | 1.507268 | 0.812502 |
| H | 3.025234 | -1.434513 | -0.736747 |
| H | -2.757672 | -1.968523 | 0.009671 |
| H | -3.356964 | -0.571723 | 0.639946 |
| $\mathrm{HF}=-520.4372078$ |  |  |  |



| C | 0.745432 | 1.302997 | -1.268708 |
| :--- | ---: | ---: | ---: |
| C | 0.846009 | -0.265968 | -1.246033 |
| C | -0.602657 | -0.867952 | -1.235085 |
| C | -1.389679 | -0.376132 | 0.000230 |
| C | 1.486688 | -0.632867 | 0.028967 |
| C | -0.032560 | 1.777230 | -0.030012 |
| C | -0.620033 | -0.821474 | 1.263003 |
| C | 0.828675 | -0.220709 | 1.276577 |
| C | 0.727704 | 1.347899 | 1.235149 |
| C | -1.450304 | 1.170994 | -0.030119 |
| O | 2.599406 | -1.282902 | 0.112971 |
| C | -2.802430 | -0.980520 | -0.000661 |
| H | 0.236039 | 1.578065 | -2.199132 |
| H | 1.747831 | 1.746534 | -1.303822 |
| H | 1.420395 | -0.635494 | -2.105189 |
| H | -0.552743 | -1.963991 | -1.253667 |
| H | -1.088419 | -0.552937 | -2.165967 |
| H | -0.096753 | 2.871986 | -0.052161 |
| H | -0.569694 | -1.915779 | 1.324556 |
| H | -1.120452 | -0.472863 | 2.173853 |
| H | 1.400426 | -0.563015 | 2.143529 |
| H | 0.205449 | 1.658749 | 2.146932 |


| H | 1.730310 | 1.790560 | 1.269639 |
| :--- | ---: | ---: | ---: |
| H | -2.000333 | 1.501967 | -0.920514 |
| H | -2.012742 | 1.534536 | 0.839328 |
| H | 2.981939 | -1.518498 | -0.759929 |
| H | -3.370568 | -0.644566 | 0.874004 |
| H | -3.357804 | -0.676684 | -0.895175 |
| H | -2.769190 | -2.076346 | 0.020108 |
|  |  |  |  |
| HF=-504.405382 |  |  |  |

III. MeLi Addition Reaction to Compound $\mathbf{1}$ in diethyl ether

1. Gound State Distortional Potentials of Compound $\mathbf{1}$ with MeLi Coordinated in diethyl ether.

Compound $\mathbf{1}$ with MeLi dimmer coordination were all optimized using the B3LYP/6$31+\mathrm{G}^{*}$. The carbonyl group in the ketone was distorted away from planarity both ways to $0^{\circ}, 5^{\circ}, 15^{\circ}$ and optimized using B3LYP/6-31+G* with the distortion angle $(\theta)$ frozen to get the distortional energies at these distortional angles. General solvent (diethyl ether) effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM). Distortional Potential v.s. Distortional Angle ( $\theta$ ) graphs were ploted. Parabola's equations were obtained from the s. $\delta \Delta \mathrm{E}^{\mathrm{GS}}{ }_{\text {(anti-syn) }}$ were calculated with $\theta_{\text {syn/anti }}$ (from the transition state calculation) incorporated to these ground state parabola's equations: $\delta \Delta \mathrm{E}^{\mathrm{GS}}{ }_{(\text {anti-syn })}=\mathrm{a}\left(\theta_{\text {anti }}{ }^{2}-\theta_{\text {syn }}{ }^{2}\right)+\mathrm{b}\left(\theta_{\text {anti }}-\theta_{\text {syn }}\right)$.


| C | 1.165458 | -0.323767 | -0.595169 |
| :--- | ---: | ---: | ---: |
| O | 2.281710 | -0.042318 | -1.036321 |
| C | 0.740719 | -0.062539 | 0.831967 |
| H | 1.543546 | 0.457845 | 1.363168 |
| C | 0.105314 | -1.009575 | -1.426304 |
| H | 0.473796 | -1.140048 | -2.448086 |
| C | -0.543369 | 0.806172 | 0.822384 |
| H | -0.853270 | 0.980592 | 1.858676 |
| H | -0.330948 | 1.782203 | 0.371978 |
| C | -1.179387 | -0.143484 | -1.425741 |
| H | -0.983177 | 0.817814 | -1.913770 |
| H | -1.947485 | -0.660059 | -2.011722 |
| C | -0.192031 | -2.381606 | -0.759384 |
| H | -0.962827 | -2.896429 | -1.346921 |
| H | 0.706612 | -3.010668 | -0.774565 |
| C | 0.439525 | -1.439491 | 1.486066 |
| H | 0.126704 | -1.273360 | 2.524725 |
| H | 1.350344 | -2.049946 | 1.511346 |
| C | -0.667403 | -2.154041 | 0.688214 |
| C | -1.949759 | -1.297555 | 0.692351 |
| C | -1.662355 | 0.078132 | 0.032136 |
| H | -0.887176 | -3.121536 | 1.156003 |
| H | -2.746418 | -1.815398 | 0.145773 |
| H | -2.296310 | -1.153586 | 1.722445 |
| Li | 3.940952 | 0.598666 | -0.289564 |


| Li | 5.967305 | 1.249002 | 0.531540 |
| :--- | ---: | ---: | ---: |
| C | 4.457477 | 2.704487 | 0.049150 |
| H | 4.190332 | 2.997879 | -0.985386 |
| H | 3.567049 | 2.947149 | 0.661847 |
| H | 5.216862 | 3.450680 | 0.359962 |
| C | 5.523536 | -0.835867 | 0.232666 |
| H | 5.514676 | -1.328239 | -0.759789 |
| H | 6.542520 | -1.025935 | 0.627004 |
| H | 4.861523 | -1.452592 | 0.872210 |
| C | -2.929795 | 0.930899 | 0.027718 |
| F | -2.741285 | 2.153373 | -0.544190 |
| F | -3.952063 | 0.347958 | -0.659506 |
| F | -3.408027 | 1.171844 | 1.280741 |

$H F=-896.7467504$


|  |  |  |  |
| :--- | ---: | ---: | ---: |
| C | -0.418541 | -0.068494 | 0.486592 |
| O | -1.593083 | 0.023752 | 0.845223 |
| C | 0.030928 | 0.080652 | -0.952669 |
| H | -0.828415 | 0.333235 | -1.580496 |
| C | 0.706618 | -0.390474 | 1.447728 |
| H | 0.306994 | -0.461521 | 2.463227 |
| C | 1.107754 | 1.196862 | -1.020889 |
| H | 1.466353 | 1.290458 | -2.052422 |
| H | 0.687051 | 2.163215 | -0.719604 |
| C | 1.777638 | 0.728411 | 1.354647 |
| H | 1.362208 | 1.692486 | 1.671159 |
| H | 2.614181 | 0.485245 | 2.019986 |
| C | 1.331293 | -1.740568 | 0.994620 |
| H | 2.152087 | -1.992078 | 1.677884 |
| H | 0.586193 | -2.542477 | 1.067443 |
| C | 0.664389 | -1.272762 | -1.385174 |
| H | 1.001477 | -1.183649 | -2.425508 |
| H | -0.090375 | -2.068095 | -1.352593 |
| C | 1.844132 | -1.614654 | -0.453940 |
| C | 2.909679 | -0.495222 | -0.532815 |
| C | 2.263706 | 0.817821 | -0.093221 |
| H | 2.293053 | -2.564798 | -0.767018 |
| H | 3.759448 | -0.724895 | 0.121493 |
| H | 3.288207 | -0.395447 | -1.557489 |
| Li | -3.383233 | 0.195334 | 0.174860 |
| Li | -5.611908 | 0.269406 | -0.316435 |
| F | 3.249646 | 1.857337 | -0.167029 |
|  |  |  |  |


| C | -4.479960 | 2.082131 | -0.048038 |
| :--- | ---: | ---: | ---: |
| H | -4.271333 | 2.520842 | 0.947255 |
| H | -3.681695 | 2.469388 | -0.712641 |
| H | -5.397288 | 2.600300 | -0.394770 |
| C | -4.577765 | -1.613539 | -0.213797 |
| H | -4.277983 | -2.121770 | 0.723746 |
| H | -5.558571 | -2.063369 | -0.470872 |
| H | -3.887529 | -1.998330 | -0.990843 |
|  |  |  |  |
| $\mathrm{HF}=-658.93342$ |  |  |  |



| C | 1.026624 | -0.536873 | -0.524989 |
| :--- | ---: | ---: | :---: |
| O | 2.168193 | -0.391115 | -0.971862 |
| C | 0.609554 | -0.112871 | 0.860928 |
| H | 1.461846 | 0.339684 | 1.378301 |
| C | -0.093296 | -1.157406 | -1.319797 |
| H | 0.273106 | -1.425460 | -2.315809 |
| C | -0.546632 | 0.911819 | 0.727646 |
| H | -0.827290 | 1.214134 | 1.741522 |
| H | -0.203893 | 1.810926 | 0.200782 |
| C | -1.248841 | -0.128849 | -1.430682 |
| H | -0.922573 | 0.754926 | -1.993697 |
| H | -2.046973 | -0.609496 | -2.005598 |
| C | -0.596655 | -2.410075 | -0.553330 |
| H | -1.413960 | -2.865579 | -1.127375 |
| H | 0.205462 | -3.155340 | -0.478648 |
| C | 0.100699 | -1.369623 | 1.618293 |
| H | -0.209786 | -1.066813 | 2.626757 |
| H | 0.913973 | -2.098022 | 1.731610 |
| C | -1.078125 | -1.992272 | 0.847604 |
| C | -2.227706 | -0.966363 | 0.729973 |
| C | -1.755928 | 0.303653 | -0.030855 |
| H | -1.436147 | -2.878433 | 1.387820 |
| H | -3.078031 | -1.422974 | 0.206963 |
| H | -2.571496 | -0.693685 | 1.735362 |
| Li | 3.769189 | 0.479240 | -0.341318 |
| Li | 5.626200 | 1.514423 | 0.482376 |
| C | 3.929545 | 2.674170 | -0.139245 |
| H | 3.452454 | 2.712594 | -1.139168 |
| H | 3.135478 | 2.966443 | 0.574651 |
| H | 4.632598 | 3.532461 | -0.143360 |
| C | 5.596804 | -0.614335 | 0.202970 |
|  |  |  |  |


| H | 5.522792 | -1.151687 | -0.763486 |
| :--- | ---: | ---: | ---: |
| H | 6.686362 | -0.564126 | 0.404454 |
| H | 5.203647 | -1.318699 | 0.961685 |
| N | -2.805835 | 1.355597 | -0.182121 |
| C | -3.407136 | 1.811561 | 1.077054 |
| H | -4.011183 | 2.701959 | 0.871994 |
| H | -4.068334 | 1.059789 | 1.544322 |
| H | -2.642455 | 2.093150 | 1.803197 |
| C | -3.879257 | 1.047315 | -1.133722 |
| H | -4.564980 | 1.900385 | -1.162820 |
| H | -3.488486 | 0.909248 | -2.143717 |
| H | -4.470879 | 0.154263 | -0.860248 |

$H F=-693.6407812$


| C | -0.431978 | -0.415600 | 0.584425 |
| :--- | ---: | ---: | ---: |
| O | -1.581601 | -0.439622 | 1.035972 |
| C | -0.113348 | -0.124356 | -0.863009 |
| H | -1.044492 | 0.040351 | -1.415258 |
| C | 0.788285 | -0.660586 | 1.439409 |
| H | 0.473698 | -0.864030 | 2.468157 |
| C | 0.784037 | 1.141337 | -0.907790 |
| H | 1.030440 | 1.357095 | -1.956087 |
| H | 0.230661 | 2.006770 | -0.519838 |
| C | 1.676584 | 0.611318 | 1.372866 |
| H | 1.142256 | 1.465845 | 1.809406 |
| H | 2.572809 | 0.441556 | 1.985015 |
| C | 1.569498 | -1.863814 | 0.844651 |
| H | 2.465642 | -2.034510 | 1.455619 |
| H | 0.959027 | -2.774520 | 0.899195 |
| C | 0.671081 | -1.334746 | -1.438988 |
| H | 0.914205 | -1.124863 | -2.488879 |
| H | 0.042042 | -2.234176 | -1.423155 |
| C | 1.954224 | -1.558148 | -0.615520 |
| C | 2.833418 | -0.292221 | -0.667756 |
| C | 2.078433 | 0.928626 | -0.087224 |
| H | 2.508437 | -2.409626 | -1.031404 |
| H | 3.759650 | -0.456356 | -0.098683 |
| H | 3.126432 | -0.082173 | -1.706396 |
| Li | -3.290598 | 0.082272 | 0.309291 |
| Li | -5.287118 | 0.807756 | -0.532686 |
| C | -3.782865 | 2.220185 | 0.067816 |
|  |  |  |  |


|  |  | -3.515653 | 2.445933 |
| :--- | ---: | ---: | :---: |
| H | 1.119132 |  |  |
| H | -2.885372 | 2.482593 | -0.526268 |
| H | -4.528061 | 2.996565 | -0.200792 |
| C | -4.882156 | -1.295386 | -0.331988 |
| H | -4.698217 | -1.886823 | 0.586662 |
| H | -5.961571 | -1.443943 | -0.539357 |
| H | -4.363271 | -1.844869 | -1.141842 |
| C | 2.956492 | 2.184640 | -0.137291 |
| H | 3.876727 | 2.042523 | 0.443955 |
| H | 3.243419 | 2.422805 | -1.169561 |
| H | 2.426929 | 3.053263 | 0.275180 |

$H F=-598.997744$


| C | 1.517073 | -0.447532 | -0.676662 |
| :--- | ---: | ---: | ---: |
| O | 2.583672 | -0.037189 | -1.150567 |
| C | 1.122939 | -0.262402 | 0.767043 |
| H | 1.920776 | 0.268356 | 1.298182 |
| C | 0.483431 | -1.169459 | -1.502000 |
| H | 0.842690 | -1.261420 | -2.532775 |
| C | -0.205163 | 0.556442 | 0.801052 |
| H | -0.487563 | 0.690957 | 1.853736 |
| H | -0.023348 | 1.557252 | 0.387273 |
| C | -0.838565 | -0.343677 | -1.443633 |
| H | -0.677489 | 0.632829 | -1.920679 |
| H | -1.589222 | -0.873384 | -2.045570 |
| C | 0.239671 | -2.566195 | -0.867323 |
| H | -0.525732 | -3.088824 | -1.456754 |
| H | 1.156190 | -3.168972 | -0.917436 |
| C | 0.878029 | -1.664939 | 1.388058 |
| H | 0.575989 | -1.534511 | 2.435953 |
| H | 1.809618 | -2.245650 | 1.387790 |
| C | -0.219565 | -2.396648 | 0.593031 |
| C | -1.526660 | -1.574361 | 0.636693 |
| C | -1.321122 | -0.168541 | 0.015263 |
| H | -0.391030 | -3.386780 | 1.037022 |
| H | -2.315393 | -2.116918 | 0.096265 |
| H | -1.861001 | -1.482397 | 1.679539 |
| Li | 4.139389 | 0.805224 | -0.393340 |
| Li | 5.794803 | 1.754872 | 0.856461 |
| C | 4.413301 | 2.987784 | -0.232958 |
| H | 4.099978 | 2.968974 | -1.296373 |


|  | 3.548027 | 3.407410 | 0.315949 |
| :--- | ---: | ---: | :---: |
| H | 5.186206 | 3.782781 | -0.196445 |
| C | 5.685416 | -0.379637 | 0.650488 |
| H | 5.804340 | -0.967700 | -0.281469 |
| H | 6.695898 | -0.387402 | 1.108311 |
| H | 5.069749 | -1.011328 | 1.319573 |
| Si | -3.004242 | 0.853380 | 0.073812 |
| C | -2.820258 | 2.680679 | -0.556115 |
| H | -3.790881 | 3.188937 | -0.478738 |
| H | -2.098621 | 3.245398 | 0.048822 |
| H | -2.496579 | 2.736955 | -1.604058 |
| C | -3.610989 | 0.979794 | 1.911087 |
| H | -4.525833 | 1.585889 | 1.962247 |
| H | -3.839595 | -0.003634 | 2.343011 |
| H | -2.859492 | 1.459564 | 2.552547 |
| C | -4.394275 | -0.022156 | -0.955616 |
| H | -5.338641 | 0.527110 | -0.841701 |
| H | -4.156674 | -0.056448 | -2.027158 |
| H | -4.564501 | -1.052056 | -0.615713 |

$H F=-968.3791429$

## 2. Ground State Calculations of Reactants and Products

All the ground state structures were all optimized using the B3LYP/6-31+G**. General solvent (diethyl ether) effects were incorporated with the polarizable conductor selfconsistent reaction field model (CPCM).

| H | 1.360927 | 2.854387 | -0.000102 |
| :--- | ---: | ---: | :---: |
| H | -0.259512 | -1.691013 | 1.281451 |
| H | -0.471563 | -0.177654 | 2.169749 |
| H | 1.940512 | -0.869043 | 2.134614 |
| H | 1.363834 | 1.587166 | 2.166752 |
| H | 2.865081 | 1.311213 | 1.276256 |
| H | -0.811526 | 2.022476 | -0.883690 |
| H | -0.811513 | 2.022535 | 0.883570 |
| C | -2.180149 | -0.191532 | 0.000015 |
| F | -2.792400 | 0.355132 | 1.088584 |
| F | -2.521105 | -1.510749 | -0.000042 |
| F | -2.792427 | 0.355232 | -1.088488 |

$H F=-801.8459449$


| C | -0.707618 | 1.298722 | 1.258524 |
| :--- | ---: | ---: | :---: |
| C | -0.830623 | -0.249101 | 1.270180 |
| C | 0.588467 | -0.877105 | 1.257025 |
| C | 1.323339 | -0.404467 | -0.000005 |
| C | -1.558668 | -0.670039 | -0.000042 |
| C | 0.061646 | 1.750156 | 0.000073 |
| C | 0.588490 | -0.877002 | -1.257087 |
| C | -0.830600 | -0.248996 | -1.270216 |
| C | -0.707594 | 1.298826 | -1.258429 |
| C | 1.473103 | 1.116819 | 0.000060 |
| O | -2.627799 | -1.264649 | -0.000077 |
| F | 2.625806 | -0.989584 | -0.000018 |
| H | -0.186323 | 1.621556 | 2.167918 |
| H | -1.704375 | 1.755129 | 1.278125 |
| H | -1.398925 | -0.594533 | 2.138123 |
| H | 0.531404 | -1.971426 | 1.265218 |
| H | 1.138122 | -0.564074 | 2.151854 |
| H | 0.154889 | 2.842005 | 0.000120 |
| H | 0.531426 | -1.971322 | -1.265371 |
| H | 1.138161 | -0.563897 | -2.151880 |
| H | -1.398887 | -0.594355 | -2.138198 |
| H | -0.186282 | 1.621736 | -2.167786 |
| H | -1.704351 | 1.755235 | -1.278010 |
| H | 2.037807 | 1.430220 | 0.885816 |
| H | 2.037823 | 1.430294 | -0.885659 |

$H F=-564.0254838$


|  |  |  |  |
| :--- | ---: | ---: | ---: |
| C | -1.503526 | -0.804639 | 1.537445 |
| C | -1.361004 | -1.305733 | 0.075568 |
| C | 0.142564 | -1.411117 | -0.282211 |
| C | 0.855064 | -0.040717 | -0.138261 |
| C | -2.011747 | -0.287701 | -0.836397 |
| C | -0.825359 | 0.571201 | 1.677237 |
| C | 0.132841 | 0.950450 | -1.088890 |
| C | -1.369688 | 1.079246 | -0.734661 |
| C | -1.511480 | 1.573157 | 0.729468 |
| C | 0.674206 | 0.456451 | 1.322855 |
| O | -2.962703 | -0.541103 | -1.572193 |
| H | -1.035449 | -1.536186 | 2.207997 |
| H | -2.562996 | -0.739392 | 1.813738 |
| H | -1.852965 | -2.273904 | -0.057911 |
| H | 0.269629 | -1.779270 | -1.307485 |
| H | 0.582109 | -2.153370 | 0.390394 |
| H | -0.926952 | 0.922028 | 2.711832 |
| H | 0.256070 | 0.611152 | -2.124375 |
| H | 0.569792 | 1.950841 | -1.018032 |
| H | -1.867605 | 1.762243 | -1.429593 |
| H | -1.049330 | 2.564654 | 0.813495 |
| H | -2.571036 | 1.684458 | 0.990250 |
| H | 1.162261 | -0.237399 | 2.017821 |
| H | 1.153041 | 1.434697 | 1.449533 |
| N | 2.279177 | -0.180583 | -0.570947 |
| C | 3.046501 | -1.223249 | 0.121537 |
| H | 2.579477 | -2.202228 | 0.009885 |
| H | 4.038964 | -1.281119 | -0.335606 |
| H | 3.189355 | -1.025497 | 1.198688 |
| C | 3.058813 | 1.063420 | -0.558661 |
| H | 4.034877 | 0.864476 | -1.011699 |
| H | 2.576225 | 1.841558 | -1.150917 |
| H | 3.238818 | 1.460562 | 0.455987 |
|  |  |  |  |

$\mathrm{HF}=-598.7468949$


| C | -0.808188 | 1.274096 | 1.256391 |
| :--- | ---: | ---: | ---: |
| C | -0.849078 | -0.277150 | 1.266934 |
| C | 0.600483 | -0.829437 | 1.253473 |
| C | 1.367157 | -0.342469 | 0.000049 |
| C | -1.546860 | -0.740018 | 0.000063 |
| C | -0.061556 | 1.764230 | -0.000129 |
| C | 0.600445 | -0.829646 | -1.253227 |
| C | -0.849030 | -0.277324 | -1.266809 |
| C | -0.808289 | 1.273917 | -1.256531 |
| C | 1.376421 | 1.205676 | -0.000093 |
| O | -2.571164 | -1.416267 | -0.000013 |
| C | 2.799020 | -0.892575 | -0.000067 |
| H | -0.301669 | 1.620579 | 2.166830 |
| H | -1.828161 | 1.679364 | 1.278787 |
| H | -1.402424 | -0.651769 | 2.136199 |
| H | 0.585283 | -1.927551 | 1.279581 |
| H | 1.115009 | -0.493516 | 2.164056 |
| H | -0.030632 | 2.862338 | -0.000196 |
| H | 0.585079 | -1.927764 | -1.279031 |
| H | 1.114996 | -0.493976 | -2.163872 |
| H | -1.402384 | -0.652110 | -2.135998 |
| H | -0.301950 | 1.620307 | -2.167121 |
| H | -1.828321 | 1.679041 | -1.278822 |
| H | 1.920224 | 1.569043 | 0.883108 |
| H | 1.920262 | 1.568797 | -0.883389 |
| H | 3.349643 | -0.554365 | -0.886168 |
| H | 3.349748 | -0.554660 | 0.886082 |
| H | 2.801456 | -1.989411 | -0.000259 |
| HF | -504.0976098 |  |  |
| H |  |  |  |



| C | -2.147406 | -1.113564 | -1.256302 |
| :--- | ---: | ---: | ---: |
| C | -1.808464 | 0.399507 | -1.264543 |
| C | -0.263110 | 0.583411 | -1.254175 |
| C | 0.368867 | -0.078081 | -0.000007 |
| C | -2.367303 | 1.024593 | -0.000040 |
| C | -1.544630 | -1.770600 | 0.000038 |
| C | -0.263112 | 0.583450 | 1.254139 |
| C | -1.808467 | 0.399577 | 1.264499 |
| C | -2.147410 | -1.113495 | 1.256339 |
| C | -0.011297 | -1.585074 | 0.000018 |
| O | -3.178989 | 1.944349 | -0.000067 |
| H | -1.741720 | -1.574686 | -2.165982 |
| H | -3.235009 | -1.257252 | -1.280507 |
| H | -2.250941 | 0.898490 | -2.132859 |
| H | -0.025223 | 1.654155 | -1.287351 |


|  |  |  |  |
| :--- | ---: | ---: | :---: |
| H | 0.138916 | 0.139496 | -2.173717 |
| H | -1.782097 | -2.842002 | 0.000067 |
| H | -0.025190 | 1.654188 | 1.287308 |
| H | 0.138890 | 0.139529 | 2.173685 |
| H | -2.250946 | 0.898606 | 2.132788 |
| H | -1.741727 | -1.574565 | 2.166047 |
| H | -3.235013 | -1.257183 | 1.280548 |
| H | 0.413655 | -2.082728 | -0.881456 |
| H | 0.413689 | -2.082712 | 0.881488 |
| Si | 2.286554 | 0.139494 | 0.000024 |
| C | 2.741296 | 1.980421 | -0.001194 |
| H | 2.354443 | 2.498004 | 0.883868 |
| H | 3.831891 | 2.095243 | -0.000439 |
| H | 2.355848 | 2.496369 | -0.887822 |
| C | 3.032010 | -0.676891 | -1.541709 |
| H | 4.122494 | -0.561726 | -1.534937 |
| H | 2.812936 | -1.749945 | -1.581896 |
| H | 2.657357 | -0.222330 | -2.465898 |
| C | 3.031718 | -0.674898 | 1.542952 |
| H | 4.122288 | -0.560576 | 1.535744 |
| H | 2.657618 | -0.218506 | 2.466459 |
| H | 2.811834 | -1.747718 | 1.584976 |
| $\mathrm{HF}=-873.4595634$ |  |  |  |



| C | 1.155643 | 0.305678 | 0.695045 |
| :--- | ---: | ---: | ---: |
| O | 2.286049 | -0.025975 | 1.059937 |
| C | 0.744710 | 0.416828 | -0.755441 |
| H | 1.584055 | 0.129335 | -1.393916 |
| C | 0.054470 | 0.664679 | 1.666112 |
| H | 0.421503 | 0.543469 | 2.688834 |
| C | -0.463927 | -0.521786 | -1.000847 |
| H | -0.770481 | -0.427834 | -2.047509 |
| H | -0.171000 | -1.563076 | -0.833782 |
| C | -1.154695 | -0.272832 | 1.414815 |
| H | -0.874837 | -1.309376 | 1.628269 |
| H | -1.958224 | 0.002739 | 2.105180 |
| C | -0.359415 | 2.136097 | 1.388452 |
| H | -1.160671 | 2.411999 | 2.084272 |
| H | 0.486750 | 2.806065 | 1.579022 |
| C | 0.324295 | 1.889062 | -1.016838 |
| H | 0.018194 | 1.983125 | -2.065397 |


| H | 1.180041 | 2.556433 | -0.864308 |
| :--- | ---: | ---: | ---: |
| C | -0.830783 | 2.268637 | -0.071731 |
| C | -2.038170 | 1.342141 | -0.321694 |
| C | -1.629404 | -0.131179 | -0.054844 |
| H | -1.133578 | 3.304189 | -0.264516 |
| H | -2.867413 | 1.622624 | 0.336636 |
| H | -2.383720 | 1.451275 | -1.355357 |
| Li | 3.925105 | -0.483458 | 0.130049 |
| Li | 5.843502 | -1.107850 | -0.947451 |
| C | 5.177906 | -2.153310 | 0.804985 |
| H | 5.179639 | -1.742414 | 1.832453 |
| H | 4.407279 | -2.946730 | 0.805986 |
| H | 6.139704 | -2.696522 | 0.724136 |
| C | 4.743750 | 0.610640 | -1.614076 |
| H | 4.460278 | 1.529711 | -1.065885 |
| H | 5.691979 | 0.882745 | -2.119525 |
| H | 4.007388 | 0.520164 | -2.434036 |
| C | -2.821103 | -1.055132 | -0.299719 |
| F | -2.521420 | -2.369372 | -0.098151 |
| F | -3.299555 | -0.969702 | -1.572678 |
| F | -3.875778 | -0.780184 | 0.518256 |
|  |  |  |  |
| $\mathrm{HF}=-896.7741765$ |  |  |  |



|  |  |  |  |
| :--- | ---: | ---: | ---: |
| C | -0.426354 | 0.000036 | 0.162711 |
| O | -1.639482 | 0.137833 | 0.285737 |
| C | 0.279167 | -0.027365 | -1.179865 |
| H | -0.450562 | 0.148302 | -1.974598 |
| C | 0.502362 | -0.204691 | 1.343663 |
| H | -0.076170 | -0.150277 | 2.269435 |
| C | 1.378182 | 1.069157 | -1.184963 |
| H | 1.918288 | 1.039009 | -2.137444 |
| H | 0.936156 | 2.066410 | -1.082549 |
| C | 1.598419 | 0.893679 | 1.310716 |
| H | 1.156746 | 1.889631 | 1.426300 |
| H | 2.295865 | 0.738512 | 2.140973 |
| C | 1.164965 | -1.601471 | 1.174961 |
| H | 1.842462 | -1.772965 | 2.019671 |
| H | 0.400357 | -2.386135 | 1.208077 |
| C | 0.945168 | -1.425311 | -1.325498 |
| H | 1.463510 | -1.468166 | -2.290592 |
| H | 0.178110 | -2.208144 | -1.334768 |


| C | 1.930968 | -1.654147 | -0.162237 |
| :--- | ---: | ---: | ---: |
| C | 3.020113 | -0.555271 | -0.179997 |
| C | 2.342123 | 0.806066 | -0.024733 |
| H | 2.404295 | -2.635943 | -0.273148 |
| H | 3.733606 | -0.705329 | 0.638326 |
| H | 3.580196 | -0.581439 | -1.121710 |
| Li | -3.535892 | 0.203073 | -0.014048 |
| Li | -5.818713 | 0.193538 | -0.065188 |
| F | 3.344465 | 1.819750 | -0.042149 |
| C | -4.711090 | 2.049998 | -0.029022 |
| H | -4.225204 | 2.490805 | 0.862038 |
| H | -4.201266 | 2.504668 | -0.899790 |
| H | -5.723320 | 2.501199 | -0.039332 |
| C | -4.699310 | -1.655414 | -0.056453 |
| H | -4.218607 | -2.101569 | 0.834791 |
| H | -5.707098 | -2.115880 | -0.082959 |
| H | -4.176136 | -2.094528 | -0.927259 |
|  |  |  |  |
| $\mathrm{HF}=-658.9572647$ |  |  |  |



| C | -1.022019 | -0.557680 | -0.559455 |
| :--- | ---: | ---: | ---: |
| O | -2.157860 | -0.425666 | -1.024919 |
| C | 0.107963 | -1.200042 | -1.321129 |
| H | -0.246726 | -1.496500 | -2.312499 |
| C | -0.623556 | -0.093769 | 0.819238 |
| H | -1.482618 | 0.374326 | 1.309133 |
| C | 1.257608 | -0.166658 | -1.443441 |
| H | 2.062531 | -0.646839 | -2.007146 |
| H | 0.928996 | 0.706358 | -2.019130 |
| C | 0.538581 | 0.924087 | 0.684283 |
| H | 0.206102 | 1.817922 | 0.143353 |
| H | 0.808732 | 1.233437 | 1.697874 |
| C | -0.129002 | -1.330017 | 1.619307 |
| H | 0.164966 | -0.998938 | 2.622688 |
| H | -0.943609 | -2.054312 | 1.739244 |
| C | 0.602869 | -2.429362 | -0.512115 |
| H | 1.429813 | -2.897652 | -1.059584 |
| H | -0.197900 | -3.173727 | -0.429082 |
| C | 1.061447 | -1.972071 | 0.884811 |
| C | 2.214620 | -0.951975 | 0.752202 |
| C | 1.752786 | 0.297745 | -0.048025 |
| H | 1.410847 | -2.842271 | 1.454033 |


| H | 2.556258 | -0.652221 | 1.750207 |
| :--- | ---: | ---: | ---: |
| H | 3.062310 | -1.428528 | 0.246391 |
| Li | -3.764407 | 0.455305 | -0.427660 |
| Li | -5.537936 | 1.521628 | 0.546634 |
| C | -3.924985 | 2.657393 | -0.296496 |
| H | -3.121918 | 3.010206 | 0.376788 |
| H | -3.470460 | 2.632683 | -1.305573 |
| H | -4.643687 | 3.498888 | -0.345602 |
| C | -5.532693 | -0.614139 | 0.344912 |
| H | -5.226487 | -1.209693 | 1.225163 |
| H | -6.636283 | -0.547937 | 0.416142 |
| H | -5.360231 | -1.274306 | -0.526658 |
| N | 2.809367 | 1.337322 | -0.231604 |
| C | 3.206411 | 2.053558 | 0.986816 |
| H | 3.949545 | 2.808328 | 0.713133 |
| H | 2.360793 | 2.577036 | 1.434441 |
| H | 3.662298 | 1.403444 | 1.754715 |
| C | 4.020007 | 0.875836 | -0.922969 |
| H | 4.646311 | 1.745874 | -1.142407 |
| H | 4.626292 | 0.172032 | -0.326355 |
| H | 3.778255 | 0.398224 | -1.873253 |
|  |  |  |  |
| $\mathrm{HF}=-693.6758366$ |  |  |  |



| C | -0.443027 | -0.009854 | 0.161816 |
| :--- | ---: | ---: | :---: |
| O | -1.653281 | 0.170215 | 0.285953 |
| C | 0.260070 | -0.048831 | -1.176943 |
| H | -0.469510 | 0.136995 | -1.970826 |
| C | 0.478015 | -0.236029 | 1.339490 |
| H | -0.103743 | -0.178606 | 2.264178 |
| C | 1.373683 | 1.032554 | -1.177578 |
| H | 1.894246 | 0.998273 | -2.143073 |
| H | 0.928374 | 2.031852 | -1.089143 |
| C | 1.588712 | 0.846906 | 1.310550 |
| H | 1.147658 | 1.842602 | 1.447651 |
| H | 2.265876 | 0.677141 | 2.157321 |
| C | 1.121717 | -1.640461 | 1.169247 |
| H | 1.797779 | -1.820520 | 2.014061 |
| H | 0.347876 | -2.416922 | 1.202762 |
| C | 0.906299 | -1.454422 | -1.327946 |
| H | 1.426253 | -1.498995 | -2.292719 |
| H | 0.129087 | -2.228018 | -1.343271 |


| C | 1.888705 | -1.697914 | -0.166051 |
| :--- | ---: | ---: | :---: |
| C | 2.988232 | -0.616473 | -0.179868 |
| C | 2.374839 | 0.796456 | -0.021426 |
| H | 2.345285 | -2.688648 | -0.279338 |
| H | 3.703596 | -0.798797 | 0.633295 |
| H | 3.552941 | -0.667957 | -1.120424 |
| Li | -3.541425 | 0.243892 | -0.016099 |
| Li | -5.826341 | 0.237753 | -0.049327 |
| C | -4.719571 | 2.093307 | -0.033403 |
| H | -4.234476 | 2.536213 | 0.857073 |
| H | -4.203385 | 2.539409 | -0.904872 |
| H | -5.729250 | 2.549984 | -0.050915 |
| C | -4.717106 | -1.613046 | -0.053651 |
| H | -4.390575 | -2.077966 | 0.895716 |
| H | -5.705931 | -2.068573 | -0.261841 |
| H | -4.056815 | -2.037929 | -0.833760 |
| C | 3.470666 | 1.869653 | -0.036315 |
| H | 4.182081 | 1.715410 | 0.783418 |
| H | 4.032147 | 1.844128 | -0.977588 |
| H | 3.042629 | 2.873197 | 0.073414 |
| $\mathrm{HF}=-599.0279045$ |  |  |  |



| C | 1.477210 | -0.348545 | -0.109899 |
| :--- | ---: | ---: | ---: |
| O | 2.604923 | 0.132479 | -0.217349 |
| C | 0.775603 | -0.525279 | 1.215243 |
| H | 1.432407 | -0.177783 | 2.018833 |
| C | 0.657931 | -0.798914 | -1.295044 |
| H | 1.234818 | -0.638385 | -2.211025 |
| C | -0.537204 | 0.312143 | 1.174652 |
| H | -1.044034 | 0.186640 | 2.139376 |
| H | -0.284819 | 1.375466 | 1.083074 |
| C | -0.655026 | 0.039294 | -1.315908 |
| H | -0.407790 | 1.095025 | -1.482538 |
| H | -1.248398 | -0.288380 | -2.178433 |
| C | 0.307057 | -2.299697 | -1.106576 |
| H | -0.299201 | -2.627986 | -1.959877 |
| H | 1.221905 | -2.905017 | -1.109028 |
| C | 0.423210 | -2.027370 | 1.386836 |
| H | -0.098410 | -2.158018 | 2.343010 |
| H | 1.339907 | -2.628261 | 1.435011 |
| C | -0.463409 | -2.486086 | 0.214113 |


| C | -1.762888 | -1.651429 | 0.184256 |
| :--- | ---: | ---: | ---: |
| C | -1.450631 | -0.139232 | 0.004582 |
| H | -0.713663 | -3.546564 | 0.341628 |
| H | -2.403302 | -2.005998 | -0.633869 |
| H | -2.318813 | -1.813224 | 1.116411 |
| Li | 4.403072 | 0.752502 | -0.059583 |
| Li | 6.556812 | 1.518989 | 0.046595 |
| C | 4.882274 | 2.881707 | 0.112161 |
| H | 4.250433 | 3.190120 | -0.742742 |
| H | 4.267191 | 3.061328 | 1.015041 |
| H | 5.672811 | 3.656345 | 0.161590 |
| C | 6.158899 | -0.590372 | -0.094289 |
| H | 6.789032 | -0.797057 | -0.981449 |
| H | 6.762674 | -0.910552 | 0.777174 |
| H | 5.346783 | -1.339639 | -0.154771 |
| Si | -3.076656 | 0.902997 | -0.028306 |
| C | -2.667129 | 2.750334 | -0.145433 |
| H | -3.594844 | 3.333850 | -0.184121 |
| H | -2.095494 | 3.097201 | 0.722935 |
| H | -2.089955 | 2.988619 | -1.045669 |
| C | -4.135022 | 0.408785 | -1.521587 |
| H | -4.384058 | -0.658269 | -1.510715 |
| H | -5.078121 | 0.968386 | -1.510182 |
| H | -3.632525 | 0.628270 | -2.470238 |
| C | -4.075815 | 0.601126 | 1.554910 |
| H | -4.985468 | 1.213421 | 1.540034 |
| H | -4.384233 | -0.445862 | 1.652022 |
| H | -3.511057 | 0.871269 | 2.454466 |

$\mathrm{HF}=-968.3922257$


| C | 1.407428 | 0.708557 | 0.019255 |
| :--- | ---: | ---: | ---: |
| O | 2.763667 | 0.341256 | 0.021428 |
| C | 0.669522 | 0.105824 | 1.261271 |
| H | 1.137828 | 0.513343 | 2.167740 |
| C | 0.681961 | 0.128065 | -1.240575 |
| H | 1.159565 | 0.551300 | -2.134968 |
| C | -0.832429 | 0.471155 | 1.271517 |
| H | -1.303480 | 0.041162 | 2.163444 |
| H | -0.971855 | 1.554379 | 1.326959 |
| C | -0.819827 | 0.493108 | -1.260277 |
| H | -0.959115 | 1.577067 | -1.298550 |


| H | -1.281383 | 0.078471 | -2.164402 |
| :--- | ---: | ---: | ---: |
| C | 0.807705 | -1.410191 | -1.262392 |
| H | 0.332323 | -1.806813 | -2.169640 |
| H | 1.861415 | -1.707816 | -1.298595 |
| C | 0.793053 | -1.432808 | 1.258526 |
| H | 0.305115 | -1.843399 | 2.152811 |
| H | 1.845138 | -1.734604 | 1.304297 |
| C | 0.128515 | -2.002431 | -0.010981 |
| C | -1.368785 | -1.636189 | -0.015739 |
| C | -1.517140 | -0.091893 | -0.002820 |
| H | 0.221423 | -3.095990 | -0.020311 |
| H | -1.855080 | -2.051306 | -0.906074 |
| H | -1.864458 | -2.066934 | 0.861924 |
| Li | 4.286067 | 1.333474 | -0.097255 |
| C | 1.355148 | 2.252458 | 0.032660 |
| H | 1.872785 | 2.621286 | 0.927079 |
| H | 1.881676 | 2.636810 | -0.850311 |
| H | 0.349609 | 2.679811 | 0.030428 |
| Li | 4.026585 | -0.939870 | 0.057049 |
| C | 5.977332 | -0.020388 | -0.023585 |
| H | 6.354584 | -0.629620 | 0.819859 |
| H | 6.404060 | -0.486698 | -0.930963 |
| H | 6.526318 | 0.936556 | 0.075778 |
| C | -2.994389 | 0.284378 | -0.006921 |
| F | -3.201755 | 1.633902 | 0.003703 |
| F | -3.659925 | -0.183935 | -1.102797 |
| F | -3.670799 | -0.202827 | 1.073878 |
|  |  |  |  |
| $\mathrm{HF}=-896.8325251$ |  |  |  |
|  |  |  |  |



| C | -1.618353 | -0.826158 | -0.000091 |
| :--- | ---: | ---: | ---: |
| O | -2.284618 | 0.410908 | -0.000279 |
| C | -0.687181 | -0.948405 | 1.251296 |
| H | -1.314319 | -0.879154 | 2.150634 |
| C | -0.687009 | -0.948625 | -1.251328 |
| H | -1.314042 | -0.879524 | -2.150752 |
| C | 0.099856 | -2.277827 | 1.259644 |
| H | 0.727443 | -2.325006 | 2.160072 |
| H | -0.577729 | -3.137290 | 1.303727 |
| C | 0.100015 | -2.278054 | -1.259357 |
| H | -0.577580 | -3.137512 | -1.303354 |
| H | 0.727700 | -2.325405 | -2.159707 |


|  |  |  |  |
| :--- | ---: | ---: | :---: |
| C | 0.327219 | 0.215002 | -1.267057 |
| H | 0.952774 | 0.145297 | -2.164401 |
| H | -0.197002 | 1.173596 | -1.311051 |
| C | 0.327076 | 0.215199 | 1.266969 |
| H | 0.952538 | 0.145579 | 2.164384 |
| H | -0.197100 | 1.173825 | 1.310805 |
| C | 1.220434 | 0.148235 | 0.000010 |
| C | 1.994629 | -1.195689 | 0.000160 |
| C | 0.984806 | -2.362277 | 0.000205 |
| H | 2.639322 | -1.257591 | -0.884307 |
| H | 2.639225 | -1.257441 | 0.884706 |
| Li | -4.042632 | 0.883967 | -0.000421 |
| C | -2.699606 | -1.929115 | -0.000082 |
| H | -3.332597 | -1.811964 | 0.888512 |
| H | -3.332524 | -1.812074 | -0.888745 |
| H | -2.313159 | -2.951388 | -0.000005 |
| Li | -2.164113 | 2.210137 | 0.000123 |
| C | -4.148866 | 3.046484 | 0.000154 |
| H | -4.008587 | 3.702531 | 0.879542 |
| H | -4.009106 | 3.702945 | -0.879002 |
| H | -5.234047 | 2.824499 | 0.000430 |
| H | 1.541561 | -3.307769 | 0.000330 |
| C | 2.201186 | 1.315679 | -0.000040 |
| F | 3.024563 | 1.322712 | 1.087831 |
| F | 3.024617 | 1.322568 | -1.087868 |
| F | 1.577396 | 2.532228 | -0.000140 |

$H F=-896.8334034$


| C | 0.721203 | 0.729887 | 0.027569 |
| :--- | ---: | ---: | ---: |
| O | 2.029949 | 0.240262 | 0.051006 |
| C | -0.089368 | 0.215416 | 1.268683 |
| H | 0.406901 | 0.584314 | 2.176052 |
| C | -0.044290 | 0.209298 | -1.239550 |
| H | 0.484479 | 0.573606 | -2.130303 |
| C | -1.554875 | 0.720521 | 1.245242 |
| H | -2.096545 | 0.345896 | 2.122987 |
| H | -1.609392 | 1.813148 | 1.273686 |
| C | -1.509414 | 0.714556 | -1.271301 |
| H | -1.562298 | 1.807059 | -1.306722 |
| H | -2.019193 | 0.335889 | -2.166248 |
| C | -0.072254 | -1.334100 | -1.243567 |


| H | -0.573525 | -1.693288 | -2.152670 |
| :--- | ---: | ---: | ---: |
| H | 0.947697 | -1.730529 | -1.264298 |
| C | -0.118010 | -1.327998 | 1.279513 |
| H | -0.652454 | -1.682416 | 2.171471 |
| H | 0.899939 | -1.725603 | 1.340460 |
| C | -0.819777 | -1.846679 | 0.006088 |
| C | -2.275655 | -1.323226 | -0.021429 |
| C | -2.230645 | 0.202947 | -0.024392 |
| H | -0.834056 | -2.943892 | 0.008477 |
| H | -2.799889 | -1.679456 | -0.916821 |
| H | -2.832401 | -1.675173 | 0.855830 |
| Li | 3.644661 | 1.108873 | -0.038914 |
| C | 0.804644 | 2.274484 | 0.025110 |
| H | 1.347090 | 2.604536 | 0.919915 |
| H | 1.369235 | 2.601292 | -0.857424 |
| H | -0.156649 | 2.795339 | 0.011012 |
| F | -3.581527 | 0.693960 | -0.050149 |
| Li | 3.187129 | -1.140495 | 0.094789 |
| C | 5.220775 | -0.393253 | -0.045148 |
| H | 5.762767 | -0.339089 | 0.917278 |
| H | 5.450886 | -1.401016 | -0.442903 |
| H | 5.772193 | 0.285395 | -0.725013 |
|  |  |  |  |
| $\mathrm{HF}=-659.0226525$ |  |  |  |



| C | -0.672756 | -0.930148 | -0.000066 |
| :--- | ---: | :---: | :---: |
| O | -1.886868 | -0.236795 | -0.000552 |
| C | 0.185603 | -0.543690 | 1.254152 |
| H | -0.384218 | -0.814597 | 2.152910 |
| C | 0.186229 | -0.544348 | -1.254097 |
| H | -0.383158 | -0.815713 | -2.152991 |
| C | 1.558423 | -1.257578 | 1.260912 |
| H | 2.117966 | -0.969082 | 2.161271 |
| H | 1.436676 | -2.345243 | 1.305829 |
| C | 1.559093 | -1.258146 | -1.259884 |
| H | 1.437450 | -2.345833 | -1.304433 |
| H | 2.119081 | -0.969974 | -2.160073 |
| C | 0.439705 | 0.981818 | -1.259241 |
| H | 1.016990 | 1.270639 | -2.146424 |
| H | -0.505599 | 1.531186 | -1.285747 |
| C | 0.439171 | 0.982461 | 1.258680 |
| H | 1.016107 | 1.271648 | 2.145972 |


| H | -0.506058 | 1.531979 | 1.284573 |
| :--- | :---: | :---: | :---: |
| C | 1.222210 | 1.351620 | -0.000203 |
| C | 2.587488 | 0.666375 | 0.000303 |
| C | 2.357059 | -0.863809 | 0.000629 |
| H | 3.156568 | 0.972426 | -0.886186 |
| H | 3.156150 | 0.972871 | 0.886907 |
| Li | -3.627347 | -0.805144 | -0.000769 |
| C | -0.996806 | -2.441655 | 0.000329 |
| H | -1.595679 | -2.679337 | 0.888400 |
| H | -1.594627 | -2.679982 | -0.888274 |
| H | -0.126765 | -3.103030 | 0.001081 |
| Li | -2.777461 | 1.335348 | 0.000340 |
| C | -4.909556 | 0.948588 | -0.000291 |
| H | -5.152718 | 1.574359 | 0.879471 |
| H | -5.152573 | 1.574765 | -0.879799 |
| H | -5.698733 | 0.170579 | -0.000515 |
| F | 1.432065 | 2.775573 | -0.000511 |
| H | 3.328744 | -1.373006 | 0.000994 |
|  |  |  |  |
| $\mathrm{HF}=-659.0234566$ |  |  |  |



| C | -1.246741 | 0.843959 | -0.000986 |
| :--- | ---: | ---: | :---: |
| O | -2.594649 | 0.460178 | -0.000190 |
| C | -0.510941 | 0.255234 | -1.245583 |
| H | -0.982037 | 0.668976 | -2.147583 |
| C | -0.510696 | 0.259228 | 1.245327 |
| H | -0.981679 | 0.675774 | 2.146100 |
| C | 0.993546 | 0.606616 | -1.250406 |
| H | 1.430303 | 0.185176 | -2.162653 |
| H | 1.157084 | 1.688631 | -1.294505 |
| C | 0.993719 | 0.610726 | 1.248772 |
| H | 1.157296 | 1.692880 | 1.289184 |
| H | 1.430632 | 0.192378 | 2.162360 |
| C | -0.638285 | -1.278620 | 1.261770 |
| H | -0.160322 | -1.682385 | 2.164473 |
| H | -1.694071 | -1.575871 | 1.319303 |
| C | -0.638016 | -1.282726 | -1.257300 |
| H | -0.159789 | -1.689053 | -2.158707 |
| H | -1.693575 | -1.581323 | -1.314547 |
| C | 0.028980 | -1.868967 | 0.003246 |
| C | 1.530578 | -1.505851 | 0.002561 |
| C | 1.713975 | 0.038366 | 0.000070 |


| H | -0.075933 | -2.962604 | 0.004986 |
| :--- | ---: | ---: | ---: |
| H | 2.015401 | -1.941436 | 0.885648 |
| H | 2.015390 | -1.944310 | -0.879133 |
| Li | -4.228819 | 1.131104 | 0.011145 |
| C | -1.208088 | 2.386254 | -0.003454 |
| H | -1.733070 | 2.755784 | -0.893216 |
| H | -1.732133 | 2.758576 | 0.885754 |
| H | -0.205926 | 2.821468 | -0.004497 |
| Li | -3.620231 | -0.982836 | -0.012663 |
| C | -5.655399 | -0.430254 | -0.000525 |
| H | -5.983839 | -1.005238 | -0.885074 |
| H | -5.975642 | -1.029513 | 0.870878 |
| H | -6.366182 | 0.420704 | 0.014857 |
| N | 3.136393 | 0.488320 | -0.000726 |
| C | 3.912232 | 0.148191 | 1.190858 |
| H | 4.886030 | 0.644372 | 1.124279 |
| H | 3.427261 | 0.510834 | 2.097926 |
| H | 4.102693 | -0.935592 | 1.308600 |
| C | 3.911523 | 0.146721 | -1.192342 |
| H | 3.426489 | 0.509061 | -2.099498 |
| H | 4.885689 | 0.642270 | -1.126476 |
| H | 4.101200 | -0.937285 | -1.309346 |
|  |  |  |  |
| $\mathrm{HF}=-693.7041798$ |  |  |  |



| C | -1.482782 | -0.840562 | 0.000114 |
| :--- | ---: | ---: | ---: |
| O | -2.261581 | 0.331217 | -0.001272 |
| C | -0.540821 | -0.871511 | 1.244907 |
| H | -1.167973 | -0.852508 | 2.147683 |
| C | -0.540490 | -0.874425 | -1.244374 |
| H | -1.167398 | -0.857643 | -2.147364 |
| C | 0.358293 | -2.128748 | 1.258962 |
| H | 0.984928 | -2.118719 | 2.161516 |
| H | -0.242305 | -3.044146 | 1.304008 |
| C | 0.358694 | -2.131661 | -1.255107 |
| H | -0.241873 | -3.047174 | -1.298261 |
| H | 0.985652 | -2.123714 | -2.157459 |
| C | 0.378237 | 0.365498 | -1.254439 |
| H | 0.986339 | 0.324796 | -2.164181 |
| H | -0.207089 | 1.290576 | -1.307683 |
| C | 0.378177 | 0.368240 | 1.252553 |
| H | 0.986381 | 0.328856 | 2.162277 |


|  |  |  |  |
| :--- | :---: | ---: | ---: |
| H | -0.206916 | 1.293604 | 1.304291 |
| C | 1.290861 | 0.404730 | -0.000912 |
| C | 2.156416 | -0.884594 | 0.000624 |
| C | 1.250947 | -2.136985 | 0.002099 |
| H | 2.807034 | -0.902952 | -0.882833 |
| H | 2.807526 | -0.900686 | 0.883811 |
| Li | -4.023833 | 0.762874 | -0.002245 |
| C | -2.457322 | -2.038541 | 0.001344 |
| H | -3.099233 | -1.980269 | 0.889482 |
| H | -3.099403 | -1.981868 | -0.886778 |
| H | -1.975121 | -3.019450 | 0.002173 |
| Li | -2.182937 | 2.134255 | -0.002449 |
| C | -4.183689 | 2.927648 | -0.002577 |
| H | -4.050690 | 3.585748 | 0.876620 |
| H | -4.052749 | 3.586072 | -0.881809 |
| H | -5.265632 | 2.691266 | -0.001325 |
| H | 1.882122 | -3.035758 | 0.003226 |
| N | 2.080609 | 1.679162 | -0.002680 |
| C | 2.901302 | 1.907623 | 1.192596 |
| H | 3.728222 | 1.183761 | 1.305838 |
| H | 3.346539 | 2.905124 | 1.122148 |
| H | 2.297225 | 1.882048 | 2.100130 |
| C | 2.914240 | 1.895481 | -1.191229 |
| H | 2.321436 | 1.851949 | -2.105469 |
| H | 3.351999 | 2.896961 | -1.130654 |
| H | 3.747297 | 1.175717 | -1.283732 |



| C | 0.735752 | 0.729299 | 0.031603 |
| :--- | ---: | ---: | ---: |
| O | 2.053913 | 0.257688 | 0.056124 |
| C | -0.070721 | 0.205830 | 1.268597 |
| H | 0.425313 | 0.577519 | 2.176701 |
| C | -0.022479 | 0.202578 | -1.234458 |
| H | 0.508548 | 0.571644 | -2.123717 |
| C | -1.538483 | 0.692818 | 1.244264 |
| H | -2.062872 | 0.315443 | 2.134440 |
| H | -1.593233 | 1.786982 | 1.295515 |
| C | -1.489610 | 0.689782 | -1.268333 |
| H | -1.541602 | 1.783834 | -1.324079 |
| H | -1.978948 | 0.310548 | -2.177498 |
| C | -0.031135 | -1.340530 | -1.240730 |
| H | -0.528297 | -1.703028 | -2.151608 |
| H | 0.993211 | -1.727799 | -1.262367 |


| C | -0.079994 | -1.337280 | 1.278788 |
| :--- | ---: | ---: | ---: |
| H | -0.612692 | -1.697108 | 2.170477 |
| H | 0.942334 | -1.725615 | 1.342582 |
| C | -0.776684 | -1.861490 | 0.005710 |
| C | -2.233119 | -1.354997 | -0.023142 |
| C | -2.268721 | 0.191576 | -0.026094 |
| H | -2.748614 | -1.736865 | -0.916256 |
| H | -2.783139 | -1.734374 | 0.850216 |
| Li | 3.654260 | 1.139225 | -0.047035 |
| C | 0.803704 | 2.274745 | 0.030305 |
| H | 1.342111 | 2.610198 | 0.926426 |
| H | 1.365749 | 2.609084 | -0.850988 |
| H | -0.163713 | 2.784091 | 0.016356 |
| Li | 3.217211 | -1.112180 | 0.098531 |
| C | 5.248563 | -0.349780 | -0.052904 |
| H | 5.795071 | -0.283851 | 0.906283 |
| H | 5.483406 | -1.359387 | -0.443384 |
| H | 5.791602 | 0.327058 | -0.741337 |
| C | -3.716644 | 0.696159 | -0.055515 |
| H | -4.239696 | 0.341750 | -0.952672 |
| H | -4.276356 | 0.342408 | 0.819489 |
| H | -3.753884 | 1.792759 | -0.056801 |
| H | -0.772584 | -2.960184 | 0.007205 |
|  |  |  |  |
| $\mathrm{HF}=-599.0883281$ |  |  |  |



| C | -0.694305 | -0.942679 | -0.000818 |
| :--- | ---: | ---: | ---: |
| O | -1.902539 | -0.234590 | -0.002815 |
| C | 0.168009 | -0.566534 | 1.251897 |
| H | -0.408996 | -0.830802 | 2.149816 |
| C | 0.170594 | -0.568635 | -1.252369 |
| H | -0.404534 | -0.834394 | -2.151046 |
| C | 1.524206 | -1.310568 | 1.261442 |
| H | 2.089306 | -1.030094 | 2.161744 |
| H | 1.380857 | -2.396108 | 1.311250 |
| C | 1.526797 | -1.312669 | -1.257832 |
| H | 1.383339 | -2.398290 | -1.306137 |
| H | 2.093748 | -1.033696 | -2.157439 |
| C | 0.455972 | 0.947648 | -1.257920 |
| H | 1.027287 | 1.213946 | -2.159135 |
| H | -0.483939 | 1.510107 | -1.304080 |
| C | 0.453768 | 0.949680 | 1.255770 |


| H | 1.023629 | 1.217092 | 2.157581 |
| :--- | ---: | ---: | ---: |
| H | -0.485908 | 1.512676 | 1.299690 |
| C | 1.257367 | 1.366143 | -0.000690 |
| C | 2.594277 | 0.584927 | 0.001213 |
| C | 2.331763 | -0.934223 | 0.002302 |
| H | 3.186835 | 0.864386 | -0.882000 |
| H | 3.185282 | 0.865949 | 0.884971 |
| Li | -3.648396 | -0.755555 | -0.001341 |
| C | -1.042663 | -2.449464 | 0.000039 |
| H | -1.645488 | -2.677871 | 0.888283 |
| H | -1.644532 | -2.679036 | -0.888549 |
| H | -0.183114 | -3.124535 | 0.000970 |
| Li | -2.745268 | 1.357908 | -0.000106 |
| C | -4.897001 | 1.023787 | 0.001237 |
| H | -5.123350 | 1.656059 | 0.880917 |
| H | -5.128538 | 1.653912 | -0.878571 |
| H | -5.703307 | 0.263239 | 0.004696 |
| H | 3.290094 | -1.470932 | 0.003716 |
| C | 1.517716 | 2.877166 | -0.001636 |
| H | 2.088144 | 3.180940 | 0.885136 |
| H | 2.089678 | 3.179584 | -0.887879 |
| H | 0.575604 | 3.440052 | -0.002877 |
|  |  |  |  |
| $\mathrm{HF}=-599.0884537$ |  |  |  |



| C | 1.704385 | 0.703228 | 0.043178 |
| :--- | ---: | ---: | :---: |
| O | 3.067530 | 0.380612 | 0.050973 |
| C | 0.974530 | 0.075025 | 1.277302 |
| H | 1.430910 | 0.491023 | 2.187562 |
| C | 1.000409 | 0.110854 | -1.223499 |
| H | 1.475664 | 0.552508 | -2.111843 |
| C | -0.542434 | 0.386875 | 1.274773 |
| H | -0.995247 | -0.059957 | 2.171116 |
| H | -0.709960 | 1.467325 | 1.354484 |
| C | -0.515364 | 0.424254 | -1.243381 |
| H | -0.679844 | 1.506843 | -1.292727 |
| H | -0.949320 | 0.006485 | -2.162910 |
| C | 1.174788 | -1.421756 | -1.252661 |
| H | 0.716970 | -1.829959 | -2.164996 |
| H | 2.238206 | -1.682867 | -1.286381 |
| C | 1.149648 | -1.457815 | 1.265861 |
| H | 0.674361 | -1.892172 | 2.156929 |


| H | 2.212695 | -1.719522 | 1.313103 |
| :--- | ---: | ---: | ---: |
| C | 0.508418 | -2.043235 | -0.008582 |
| C | -1.000596 | -1.718259 | -0.019866 |
| C | -1.229589 | -0.179768 | -0.000376 |
| H | -1.461944 | -2.160856 | -0.913734 |
| H | -1.481143 | -2.186131 | 0.850870 |
| Li | 4.560850 | 1.413855 | -0.107810 |
| C | 1.595970 | 2.245863 | 0.063662 |
| H | 2.103893 | 2.629757 | 0.957441 |
| H | 2.103937 | 2.654412 | -0.819594 |
| H | 0.575578 | 2.637164 | 0.067399 |
| Li | 4.365295 | -0.871461 | 0.073753 |
| C | 6.302078 | 0.107709 | -0.077371 |
| H | 6.740229 | -0.430617 | 0.784674 |
| H | 6.699409 | -0.403376 | -0.974470 |
| H | 6.822185 | 1.086154 | -0.070347 |
| H | 0.642442 | -3.134128 | -0.022848 |
| Si | -3.104517 | 0.244817 | -0.017659 |
| C | -3.361973 | 2.126432 | -0.036137 |
| H | -4.434233 | 2.356960 | -0.027977 |
| H | -2.912995 | 2.608997 | 0.839360 |
| H | -2.931263 | 2.587896 | -0.931902 |
| C | -3.942330 | -0.483054 | -1.558528 |
| H | -3.891884 | -1.577615 | -1.570759 |
| H | -5.001827 | -0.200290 | -1.579605 |
| H | -3.482928 | -0.115587 | -2.483331 |
| C | -3.966887 | -0.457845 | 1.521114 |
| H | -5.031578 | -0.194829 | 1.508616 |
| H | -3.896758 | -1.550608 | 1.563950 |
| H | -3.537307 | -0.057582 | 2.446608 |
| HF | --968.4522633 |  |  |
|  |  |  |  |



| C | 2.033981 | -0.515012 | -0.000708 |
| :--- | ---: | ---: | ---: |
| O | 2.373152 | 0.844157 | -0.001862 |
| C | 1.161210 | -0.869622 | -1.251115 |
| H | 1.754668 | -0.647426 | -2.150290 |
| C | 1.161958 | -0.867698 | 1.250733 |
| H | 1.755948 | -0.644084 | 2.149210 |
| C | 0.736708 | -2.355935 | -1.257985 |
| H | 0.139561 | -2.560993 | -2.158149 |
| H | 1.609043 | -3.018457 | -1.306758 |


|  | 0.737438 | -2.353997 | 1.2 |
| :---: | :---: | :---: | :---: |
| H | 1.609800 | -3.016449 | 1.3 |
| H | 0.140826 | -2.557664 |  |
| C | -0.116654 | -0.002042 | 1.2 |
| H | -0.692928 | -0.225192 | 2.169501 |
| H | 0.160358 | 1.056 |  |
| C | -0. | -0.0039 |  |
| H | -0.6942 | -0.22 |  |
| H | 1595 | 1.05403 |  |
| C | -0.98790 | -0.273 |  |
| C | -1.367615 | -1.781866 | 0.00125 |
| C | -0.098902 | -2.6615 | 0.00155 |
| H | -1.976770 | -2.020803 | 0.88409 |
| H | -1.977319 | -2.022186 | -0.8 |
| Li | 3.975676 | 1.714400 | -0.003 |
| C | 3.353585 | -1.319997 | -0.000 |
| H | 3.939049 | -1.051740 | -0.8 |
| H | 96 | -1.050575 | 0.8877 |
| H | 3.232169 | -2.4064 |  |
| Li | 1.835709 | . 56 | 0.001 |
| C | 5648 | 3.856443 | 0.000993 |
| H | 268279 | 4.459852 | -0.878 |
|  | 3.266511 | 45774 |  |
| H | 4.671272 | 3.912642 | . 002 |
| H | -0.392350 | -3.720501 | 0.02 |
| Si | -2.556883 | 0.834780 | -0.00025 |
| C | -3.617727 | 0.502806 | 1.53956 |
| H | -4.513055 | 1.136019 | 1.52 |
|  | -3.951177 | -0.540119 |  |
| H | -3.073821 | 0.723306 | 2.4 |
| C | -2.074373 | 2.672558 | -0.002 |
| H | -1.488111 | 2.94071 |  |
|  | -1.489194 | . 939312 |  |
| H | -2.975141 | 3.298138 | -0. |
| C | -3.619373 | 0.499898 | -1.5382 |
| H | -3.953269 | -0.543003 | -1.58 |
| H | -4.514439 | 1.133494 | -1.52145 |
| H | -3.076261 | 0.718119 | -2.46 |

3. Transition State Cartesian Coordinates, Energies and Low Frequencies

All the transition state structures were all optimized using the B3LYP/6-31+G**. General solvent (diethyl ether) effects were incorporated with the polarizable conductor self-consistent reaction field model (CPCM).

## $\mathrm{CF}_{3}$-synTS



| Thermal correction to Energy $=$ | 0.317383 |
| :--- | ---: |
| Thermal correction to Enthalpy= | 0.318327 |
| Thermal correction to Gibbs Free Energy= | 0.250525 |
| Sum of electronic and zero-point Energies= | -896.449381 |
| Sum of electronic and thermal Energies= | -896.429615 |
| Sum of electronic and thermal Enthalpies $=$ | -896.428670 |
| Sum of electronic and thermal Free Energies= | -896.496472 |

Low frequencies $\quad-249.0921 \quad 19.4878 \quad 26.7411 \quad 56.1262$

## $\mathrm{CF}_{3}$-antiTS



| C | 1.288973 | -0.282786 | -0.140426 |
| :--- | ---: | ---: | ---: |
| O | 1.781822 | -1.444267 | -0.253387 |
| C | 0.681574 | 0.150114 | 1.191677 |
| H | 1.288039 | -0.240012 | 2.014470 |
| C | 0.562388 | 0.341901 | -1.329176 |
| H | 1.085233 | 0.083124 | -2.254635 |
| C | 0.470763 | 1.670811 | 1.310676 |
| H | -0.046631 | 1.883474 | 2.254955 |
| H | 1.432196 | 2.188363 | 1.345094 |
| C | 0.345003 | 1.861026 | -1.201903 |
| H | 1.297979 | 2.391730 | -1.258607 |
| H | -0.265535 | 2.201951 | -2.047836 |
| C | -0.831782 | -0.361934 | -1.318989 |
| H | -1.415907 | 0.004948 | -2.169505 |
| H | -0.703991 | -1.441329 | -1.438406 |
| C | -0.711198 | -0.554131 | 1.209733 |
| H | -1.210206 | -0.324014 | 2.156724 |
| H | -0.580760 | -1.638703 | 1.152813 |
| C | -1.563823 | -0.045263 | 0.014724 |
| C | -1.753038 | 1.489089 | 0.142003 |
| C | -0.373072 | 2.176886 | 0.124375 |
| H | -2.367791 | 1.859212 | -0.685930 |
| H | -2.276450 | 1.724778 | 1.075436 |
| Li | 3.562778 | -0.993950 | -0.158052 |
| C | 3.496303 | 1.152242 | -0.065612 |
| H | 4.001549 | 1.151979 | 0.919684 |
| H | 4.232798 | 1.124584 | -0.893383 |


| H | 3.003505 | 2.122166 | -0.146539 |
| :--- | ---: | ---: | ---: |
| C | 5.548513 | -1.802871 | 0.105702 |
| Li | 5.725352 | 0.287417 | 0.238874 |
| H | 6.655046 | -1.797786 | 0.118223 |
| H | 5.294981 | -2.423976 | -0.773494 |
| H | 5.264702 | -2.410866 | 0.984184 |
| H | -0.518474 | 3.260054 | 0.213615 |
| C | -2.924473 | -0.738501 | 0.026114 |
| F | -3.739288 | -0.318197 | -0.983948 |
| F | -2.832298 | -2.091547 | -0.107093 |
| F | -3.617973 | -0.521972 | 1.180416 |

Zero-point correction=
0.297487 (Hartree/Particle)

Thermal correction to Energy= 0.317298

Thermal correction to Enthalpy= 0.318242

Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies= 0.250471
-896.448386
-896.428575
Sum of electronic and thermal Free Energies=
-896.427631
-896.495402

Low frequencies
$-255.5967 \quad 16.7334 \quad 31.9920 \quad 52.3960$

## F-synTS



| C | -0.687619 | -0.577657 | -0.032305 |
| :--- | ---: | ---: | ---: |
| O | -1.608891 | -1.447326 | -0.033548 |
| C | 0.174049 | -0.401725 | -1.282424 |
| H | -0.451149 | -0.479899 | -2.176169 |
| C | 0.102045 | -0.324818 | 1.251566 |
| H | -0.573028 | -0.348027 | 2.111510 |
| C | 0.994046 | 0.905123 | -1.291518 |
| H | 1.662997 | 0.907753 | -2.159876 |
| H | 0.343811 | 1.778870 | -1.365820 |
| C | 0.921617 | 0.982746 | 1.225041 |


| H | 0.269270 | 1.857717 | 1.206660 |
| :--- | ---: | ---: | ---: |
| H | 1.540510 | 1.041620 | 2.127856 |
| C | 1.095592 | -1.530055 | 1.314771 |
| H | 1.690319 | -1.451027 | 2.232871 |
| H | 0.536525 | -2.470485 | 1.361108 |
| C | 1.167301 | -1.607330 | -1.212981 |
| H | 1.813610 | -1.584849 | -2.098759 |
| H | 0.609718 | -2.549576 | -1.232288 |
| C | 2.014541 | -1.506129 | 0.074133 |
| C | 2.817228 | -0.183508 | 0.056328 |
| C | 1.823504 | 0.973831 | -0.009332 |
| H | 2.712085 | -2.350496 | 0.119636 |
| H | 3.431276 | -0.092275 | 0.959903 |
| H | 3.483838 | -0.148701 | -0.813193 |
| Li | -3.050599 | -0.313519 | -0.140966 |
| C | -2.117564 | 1.627395 | -0.071209 |
| H | -2.804419 | 1.901971 | -0.896477 |
| H | -2.569914 | 1.845258 | 0.916027 |
| H | -1.269371 | 2.307046 | -0.163604 |
| C | -5.204037 | -0.224688 | 0.001888 |
| Li | -4.489543 | 1.742109 | 0.249940 |
| H | -6.204868 | 0.239955 | 0.084111 |
| H | -5.202400 | -1.009790 | 0.780057 |
| H | -5.237892 | -0.765869 | -0.962324 |
| F | 2.567379 | 2.207170 | -0.025948 |


| Zero-point correction= | 0.285242 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy= | 0.302095 |
| Thermal correction to Enthalpy= | 0.303039 |
| Thermal correction to Gibbs Free Energy= | 0.242709 |
| Sum of electronic and zero-point Energies= | -658.648570 |
| Sum of electronic and thermal Energies= | -658.631717 |
| Sum of electronic and thermal Enthalpies= | -658.630773 |
| Sum of electronic and thermal Free Energies= | -658.691103 |

Low frequencies -265.8464 $18.9718 \quad 42.9410 \quad 76.2453$

## F-antiTS



| C | 0.639773 | -0.388633 | -0.028484 |
| :--- | ---: | ---: | ---: |
| O | 1.350963 | -1.434651 | -0.055860 |
| C | -0.101629 | -0.018042 | 1.257328 |
| H | 0.530408 | -0.241515 | 2.121512 |
| C | -0.134630 | 0.026184 | -1.280813 |
| H | 0.474329 | -0.166649 | -2.168593 |
| C | -0.613199 | 1.435783 | 1.281730 |
| H | -1.208128 | 1.584771 | 2.191676 |
| H | 0.224620 | 2.135415 | 1.325929 |
| C | -0.647575 | 1.479347 | -1.241862 |
| H | 0.187604 | 2.181943 | -1.286091 |
| H | -1.267695 | 1.657654 | -2.129449 |
| C | -1.370765 | -0.932518 | -1.276773 |
| H | -1.994026 | -0.728667 | -2.154333 |
| H | -1.049582 | -1.977751 | -1.318724 |
| C | -1.337871 | -0.976234 | 1.252848 |
| H | -1.938058 | -0.802749 | 2.152730 |
| H | -1.016042 | -2.022167 | 1.250895 |
| C | -2.174200 | -0.678300 | 0.003454 |
| C | -2.697719 | 0.755541 | 0.035106 |
| C | -1.480908 | 1.711345 | 0.035822 |
| H | -3.331471 | 0.936040 | -0.841099 |
| H | -3.308779 | 0.905245 | 0.933030 |
| Li | 3.008975 | -0.642066 | -0.018495 |
| C | 2.530779 | 1.455998 | -0.017927 |
| H | 3.145835 | 1.579318 | 0.895022 |
| H | 3.145950 | 1.575498 | -0.931593 |
| H | 1.838911 | 2.299062 | -0.019980 |
| C | 5.127994 | -1.041796 | 0.031435 |
| Li | 4.890624 | 1.046738 | -0.018260 |
| H | 6.213424 | -0.828895 | 0.011480 |
| H | 4.973408 | -1.739806 | -0.811923 |
| H | 4.985233 | -1.648983 | 0.944452 |
| F | -3.301637 | -1.572670 | 0.002489 |
| H | -1.838011 | 2.747402 | 0.058620 |
|  |  |  |  |

Zero-point correction=
Thermal correction to Energy=
0.285241 (Hartree/Particle)
0.302128

| Thermal correction to Enthalpy= | 0.303073 |
| :--- | ---: |
| Thermal correction to Gibbs Free Energy= | 0.241352 |
| Sum of electronic and zero-point Energies= | -658.647419 |
| Sum of electronic and thermal Energies $=$ | -658.630532 |
| Sum of electronic and thermal Enthalpies $=$ | -658.629588 |
| Sum of electronic and thermal Free Energies= | -658.691309 |

Low frequencies $-232.5914 \quad 11.0159 \quad 23.4535 \quad 34.1746$

## $\mathrm{NMe}_{2}$-synTS

llan

| C | -2.157712 | -1.865732 | -0.143191 |
| :--- | ---: | ---: | ---: |
| H | -2.535257 | -2.225246 | 0.834074 |
| H | -2.764438 | -2.267008 | -0.979979 |
| H | -1.170166 | -2.313035 | -0.261622 |
| C | -5.609109 | -0.836427 | 0.064641 |
| Li | -4.423272 | -2.575982 | 0.149907 |
| H | -6.466451 | -1.534021 | 0.112982 |
| H | -5.818124 | -0.214622 | -0.825851 |
| H | -5.749557 | -0.164564 | 0.931081 |
| N | 2.576385 | -1.411315 | -0.012507 |
| C | 3.398947 | -1.519105 | 1.197755 |
| H | 2.780525 | -1.622154 | 2.090136 |
| H | 4.014513 | -2.420730 | 1.119231 |
| H | 4.082068 | -0.663825 | 1.346026 |
| C | 3.456973 | -1.434090 | -1.186027 |
| H | 4.088920 | -2.325670 | -1.126367 |
| H | 2.883860 | -1.501515 | -2.111380 |
| H | 4.126586 | -0.558163 | -1.254307 |


| Zero-point correction $=$ | 0.366153 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy= | 0.386297 |
| Thermal correction to Enthalpy= | 0.387242 |
| Thermal correction to Gibbs Free Energy $=$ | 0.318892 |
| Sum of electronic and zero-point Energies= | -693.280865 |
| Sum of electronic and thermal Energies= | -693.260720 |
| Sum of electronic and thermal Enthalpies $=$ | -693.259776 |
| Sum of electronic and thermal Free Energies $=$ | -693.328126 |

## NMe $_{2}$-antiTS



| C | 1.152310 | -0.333183 | 0.074619 |
| :--- | ---: | ---: | :---: |
| O | 1.707668 | -1.467129 | 0.119705 |
| C | 0.415669 | 0.190934 | 1.301500 |
| H | 0.968013 | -0.087987 | 2.204474 |


| C | 0.491178 | 0.134363 | -1.215944 |
| :--- | ---: | ---: | :--- |
| H | 1.097314 | -0.181781 | -2.070812 |
| C | 0.118899 | 1.701090 | 1.261039 |
| H | -0.488425 | 1.966308 | 2.136750 |
| H | 1.045470 | 2.276044 | 1.325557 |
| C | 0.200173 | 1.646064 | -1.254758 |
| H | 1.133476 | 2.213694 | -1.279561 |
| H | -0.345652 | 1.878816 | -2.178905 |
| C | -0.866916 | -0.632096 | -1.237339 |
| H | -1.371340 | -0.375465 | -2.173952 |
| H | -0.695861 | -1.713953 | -1.236644 |
| C | -0.943419 | -0.575697 | 1.273422 |
| H | -1.503109 | -0.275473 | 2.164474 |
| H | -0.773680 | -1.656264 | 1.333957 |
| C | -1.747557 | -0.248168 | -0.015345 |
| C | -1.991749 | 1.285846 | -0.057281 |
| C | -0.646749 | 2.047013 | -0.030662 |
| H | -2.546765 | 1.552553 | -0.965309 |
| H | -2.606083 | 1.592031 | 0.798816 |
| Li | 3.464234 | -0.914060 | 0.121341 |
| C | 3.280632 | 1.217736 | 0.042462 |
| H | 4.025199 | 1.209019 | 0.863496 |
| H | 3.787031 | 1.287374 | -0.940324 |
| H | 2.732328 | 2.153955 | 0.158307 |
| C | 5.500486 | -1.654996 | -0.043371 |
| Li | 5.613964 | 0.443422 | -0.307174 |
| H | 6.605260 | -1.595854 | -0.075390 |
| H | 5.240567 | -2.355585 | -0.857884 |
| H | 5.292395 | -2.203331 | 0.894626 |
| H | -0.843234 | 3.126424 | -0.060818 |
| N | -2.993482 | -1.071667 | -0.036748 |
| C | -3.846221 | -0.959500 | 1.150246 |
| H | -4.278772 | 0.047311 | 1.296503 |
| H | -4.680059 | -1.659948 | 1.042232 |
| H | -3.306753 | -1.236477 | 2.056783 |
| C | -3.825026 | -0.920990 | -1.234524 |
| H | -3.250858 | -1.104261 | -2.143397 |
| H | -4.624041 | -1.668158 | -1.197949 |
| H | -4.304257 | 0.071136 | -1.322317 |
|  |  |  |  |

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
0.365923 (Hartree/Particle)

Low frequencies
$-220.2495 \quad 17.8037 \quad 32.2648 \quad 37.2028$

## Me-synTS



| C | -0.717978 | -0.566946 | -0.033679 |
| :--- | ---: | ---: | ---: |
| O | -1.656759 | -1.424274 | -0.035907 |
| C | 0.149405 | -0.413811 | -1.280177 |
| H | -0.479991 | -0.477161 | -2.173761 |
| C | 0.077687 | -0.337131 | 1.248274 |
| H | -0.601394 | -0.346020 | 2.107010 |
| C | 1.010111 | 0.862959 | -1.287670 |
| H | 1.666988 | 0.839129 | -2.168047 |
| H | 0.379706 | 1.751659 | -1.384989 |
| C | 0.937769 | 0.940610 | 1.224598 |
| H | 0.303982 | 1.831994 | 1.229117 |
| H | 1.543266 | 0.973723 | 2.140800 |
| C | 1.031550 | -1.573126 | 1.312361 |
| H | 1.628146 | -1.512102 | 2.231485 |
| H | 0.443866 | -2.496627 | 1.359901 |
| C | 1.102708 | -1.650717 | -1.212387 |
| H | 1.750379 | -1.646554 | -2.098310 |
| H | 0.516126 | -2.575854 | -1.234906 |
| C | 1.952620 | -1.575493 | 0.073831 |
| C | 2.792735 | -0.282723 | 0.057678 |
| C | 1.875199 | 0.962042 | -0.007565 |
| H | 2.618895 | -2.446539 | 0.119305 |
| H | 3.419772 | -0.230814 | 0.958693 |
| H | 3.470292 | -0.285986 | -0.807493 |
| Li | -3.073877 | -0.274304 | -0.143547 |
| C | -2.080141 | 1.635881 | -0.071915 |
| H | -2.760439 | 1.910711 | -0.902377 |
| H | -2.536285 | 1.852650 | 0.913663 |
| H | -1.224179 | 2.305760 | -0.159810 |
| C | -5.226708 | -0.121906 | 0.002541 |
| Li | -4.464708 | 1.825526 | 0.248149 |
| H | -6.217687 | 0.363047 | 0.087183 |
| H | -5.237662 | -0.903678 | 0.784044 |
| H | -5.275363 | -0.666274 | -0.959152 |
| C | 2.709732 | 2.248009 | -0.023529 |
| H | 3.328188 | 2.326736 | 0.879039 |
| H | 3.378681 | 2.271539 | -0.892574 |
|  |  | 0 |  |

$\begin{array}{llll}\mathrm{H} & 2.066402 & 3.135295 & -0.069541\end{array}$

Zero-point correction=
Thermal correction to Energy=
Thermal correction to Enthalpy=
Thermal correction to Gibbs Free Energy=
Sum of electronic and zero-point Energies=
Sum of electronic and thermal Energies=
Sum of electronic and thermal Enthalpies=
Sum of electronic and thermal Free Energies=
0.320824 (Hartree/Particle)
0.338211
0.339156
0.278090
-598.678675
-598.661287
-598.660343
-598.721409

Low frequencies
$-259.5154 \quad 12.1295 \quad 38.2424 \quad 81.4316$

## Me-antiTS



| C | 0.658527 | -0.362660 | -0.017479 |
| :--- | ---: | ---: | ---: |
| O | 1.342675 | -1.433294 | -0.035805 |
| C | -0.084878 | 0.020503 | 1.258483 |
| H | 0.543858 | -0.199182 | 2.127516 |
| C | -0.104322 | 0.051857 | -1.271975 |
| H | 0.510696 | -0.145905 | -2.155918 |
| C | -0.588051 | 1.476590 | 1.274898 |
| H | -1.188059 | 1.630318 | 2.181679 |
| H | 0.251603 | 2.175206 | 1.323796 |
| C | -0.608394 | 1.507503 | -1.244772 |
| H | 0.229539 | 2.208255 | -1.290981 |
| H | -1.223510 | 1.682292 | -2.137518 |
| C | -1.343509 | -0.898609 | -1.270737 |
| H | -1.944597 | -0.696187 | -2.166946 |
| H | -1.012629 | -1.942420 | -1.325774 |
| C | -1.324087 | -0.929793 | 1.253117 |
| H | -1.91178 | -0.749691 | 2.163263 |
| H | -0.992521 | -1.974611 | 1.277306 |
| C | -2.204617 | -0.677743 | 0.000810 |
| C | -2.665611 | 0.799878 | 0.022871 |
| C | -1.450295 | 1.747796 | 0.025073 |


| H | -3.297501 | 1.000350 | -0.853620 |
| :--- | ---: | ---: | ---: |
| H | -3.283616 | 0.978022 | 0.913990 |
| Li | 3.014351 | -0.695700 | -0.010230 |
| C | 2.553660 | 1.413191 | -0.011535 |
| H | 3.177120 | 1.508970 | 0.898917 |
| H | 3.165230 | 1.509600 | -0.930124 |
| H | 1.890622 | 2.278928 | -0.006781 |
| C | 5.134535 | -1.103867 | 0.021911 |
| Li | 4.909470 | 0.986914 | -0.025321 |
| H | 6.222014 | -0.902226 | -0.001145 |
| H | 4.969216 | -1.796778 | -0.823687 |
| H | 4.988855 | -1.713572 | 0.932857 |
| C | -3.413152 | -1.621557 | -0.001808 |
| H | -4.031057 | -1.468508 | 0.891269 |
| H | -4.043967 | -1.446885 | -0.881815 |
| H | -3.094580 | -2.670765 | -0.016983 |
| H | -1.797239 | 2.788957 | 0.040642 |


| Zero-point correction= | 0.320769 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.338255 |
| Thermal correction to Enthalpy= | 0.339199 |
| Thermal correction to Gibbs Free Energy= | 0.276417 |
| Sum of electronic and zero-point Energies= | -598.678622 |
| Sum of electronic and thermal Energies= | -598.661136 |
| Sum of electronic and thermal Enthalpies= | -598.660192 |
| Sum of electronic and thermal Free Energies= | -598.722974 |

$\begin{array}{llllll}\text { Low frequencies } & -246.0523 & 8.0646 & 20.5293 & 37.1008\end{array}$

## SiMe $_{3}$-synTS



| C | -1.831377 | -0.608005 | -0.043350 |
| :--- | :--- | :--- | :--- |
| O | -3.030806 | -1.034841 | -0.047694 |
| C | -0.972337 | -0.800830 | -1.289233 |
| H | -1.577630 | -0.609622 | -2.182280 |


| C | -1.011077 | -0.715427 | 1.237800 |
| :--- | ---: | :---: | :---: |
| H | -1.642544 | -0.463912 | 2.097222 |
| C | 0.324676 | 0.037402 | -1.294127 |
| H | 0.908893 | -0.246292 | -2.180884 |
| H | 0.083489 | 1.098087 | -1.405243 |
| C | 0.281016 | 0.128291 | 1.220551 |
| H | 0.028539 | 1.192247 | 1.238807 |
| H | 0.835988 | -0.080885 | 2.145239 |
| C | -0.616025 | -2.225943 | 1.295642 |
| H | -0.043199 | -2.406247 | 2.214731 |
| H | -1.518040 | -2.846837 | 1.341703 |
| C | -0.579238 | -2.312654 | -1.228575 |
| H | 0.019890 | -2.557184 | -2.115413 |
| H | -1.480382 | -2.935894 | -1.257509 |
| C | 0.231550 | -2.582177 | 0.056662 |
| C | 1.512595 | -1.719626 | 0.047234 |
| C | 1.159687 | -0.210035 | -0.011506 |
| H | 0.502853 | -3.645810 | 0.096710 |
| H | 2.103906 | -1.937313 | 0.947782 |
| H | 2.132777 | -1.998652 | -0.816184 |
| Li | -3.890604 | 0.573901 | 0.040933 |
| C | -2.226172 | 1.936155 | -0.139764 |
| H | -2.699908 | 2.298093 | -1.073312 |
| H | -2.629080 | 2.458819 | 0.749755 |
| H | -1.177121 | 2.225565 | -0.204377 |
| C | -5.799705 | 1.579205 | 0.113625 |
| Li | -4.344077 | 3.069857 | -0.162820 |
| H | -6.515530 | 2.422567 | 0.147907 |
| H | -5.983699 | 1.032429 | 1.057505 |
| H | -6.190281 | 0.922379 | -0.685044 |
| Si | 2.786968 | 0.879368 | -0.007463 |
| C | 2.298302 | 2.758862 | -0.050767 |
| H | 1.692135 | 3.028861 | 0.822066 |
| H | 3.201585 | 3.381952 | -0.034222 |
| H | 1.728680 | 3.022777 | -0.950098 |
| C | 3.982177 | 0.502394 | -1.472308 |
| H | 4.847570 | 1.174308 | -1.417148 |
| H | 4.355181 | -0.528364 | -1.433729 |
| H | 3.503878 | 0.650444 | -2.448262 |
| C | 3.807540 | 0.653873 | 1.617475 |
| H | 4.157484 | -0.377232 | 1.752156 |
| H | 4.691543 | 1.303168 | 1.582140 |
| H | 3.226305 | 0.929931 | 2.505513 |
|  |  |  |  |

Zero-point correction=
0.392099 (Hartree/Particle)

Thermal correction to Energy=
0.416166

Thermal correction to Enthalpy=
0.417110

Thermal correction to Gibbs Free Energy=
0.341587

Sum of electronic and zero-point Energies= -967.997420
Sum of electronic and thermal Energies= -967.973354
Sum of electronic and thermal Enthalpies $=\quad-967.972409$
Sum of electronic and thermal Free Energies= -968.047932

## SiMe $_{3}$-antiTS

|  |  |  |  |
| :---: | :---: | :---: | :---: |
| C | 1.584365 | 0.238325 | 0.067232 |
| O | 1.962572 | 1.454141 | 0.119850 |
| C | 0.981639 | -0.290595 | -1.228320 |
| H | 1.548776 | 0.097436 | -2.081510 |
| C | 0.930172 | -0.380842 | 1.296316 |
| H | 1.460488 | -0.054308 | 2.197582 |
| C | 0.859212 | -1.825277 | -1.279040 |
| H | 0.334014 | -2.106017 | -2.202162 |
| H | 1.847971 | -2.291327 | -1.319069 |
| C | 0.801920 | -1.914644 | 1.236937 |
| H | 1.785379 | -2.389751 | 1.293493 |
| H | 0.232333 | -2.253399 | 2.113044 |
| C | -0.513497 | 0.231944 | 1.283167 |
| H | -1.043626 | -0.134467 | 2.171845 |
| H | -0.440009 | 1.321562 | 1.373931 |
| C | -0.461898 | 0.321065 | -1.233641 |
| H | -0.954547 | 0.019578 | -2.167459 |
| H | -0.385801 | 1.414057 | -1.243925 |
| C | -1.275558 | -0.166757 | -0.007256 |
| C | -1.347928 | -1.715030 | -0.064297 |
| C | 0.069502 | -2.330116 | -0.054511 |
| H | -1.918649 | -2.100216 | 0.792374 |
| H | -1.878541 | -2.036510 | -0.971379 |
| Li | 3.764911 | 1.183716 | 0.107316 |
| C | 3.844596 | -0.976855 | 0.031155 |
| H | 4.379360 | -0.936444 | -0.938061 |
| H | 4.544535 | -0.885799 | 0.885631 |
| H | 3.428298 | -1.982383 | 0.098438 |
| C | 5.711045 | 2.112285 | -0.041456 |
| Li | 5.998828 | 0.034573 | -0.198063 |
| H | 6.816554 | 2.163625 | -0.041430 |
| H | 5.416682 | 2.687993 | 0.855878 |
| H | 5.406112 | 2.735462 | -0.902010 |
| H | -0.004670 | -3.425182 | -0.095209 |
| Si | -3.051335 | 0.640007 | -0.012350 |
| C | -4.042657 | 0.138809 | 1.573937 |


| H | -5.045049 | 0.584219 | 1.547204 |
| :--- | ---: | ---: | ---: |
| H | -4.162152 | -0.947921 | 1.662548 |
| H | -3.540746 | 0.497999 | 2.480278 |
| C | -2.895680 | 2.551036 | -0.012761 |
| H | -2.381735 | 2.917973 | -0.909329 |
| H | -3.892440 | 3.010131 | 0.009387 |
| H | -2.343263 | 2.915798 | 0.861638 |
| C | -4.037520 | 0.139003 | -1.602097 |
| H | -4.194777 | -0.944401 | -1.668839 |
| H | -5.023437 | 0.620457 | -1.599949 |
| H | -3.510430 | 0.459627 | -2.508798 |


| Zero-point correction= | 0.392073 (Hartree/Particle) |
| :--- | ---: |
| Thermal correction to Energy $=$ | 0.416160 |
| Thermal correction to Enthalpy= | 0.417104 |
| Thermal correction to Gibbs Free Energy= | 0.341374 |
| Sum of electronic and zero-point Energies= | -967.997530 |
| Sum of electronic and thermal Energies= | -967.973444 |
| Sum of electronic and thermal Enthalpies= | -967.972500 |
| Sum of electronic and thermal Free Energies= | -968.048230 |

Low frequencies $\begin{array}{llllll}-278.4739 & 25.8962 & 33.4456 & 56.7907\end{array}$
IV. Ground State Cartesian Coordinates, and Energies of Compound 2-4 in Table 2

Protonated compound 2-4 were all optimized using the B3LYP/6-31+G*. The carbonyl group in the ketone was distorted away from planarity both ways to $0^{\circ}, 5^{\circ}, 15^{\circ}$ and optimized using B3LYP/6-31+G* with the distortion angle $(\theta)$ frozen to get the distortional energies at these distortional angles.


| C | -1.695726 | -0.563415 | 1.542962 |
| :--- | ---: | ---: | ---: |
| C | -1.775487 | -1.100935 | 0.070388 |
| C | -1.693719 | 0.999607 | 1.379755 |
| C | -1.608250 | 1.210397 | -0.171176 |
| C | -0.417540 | -0.899986 | -0.673667 |
| C | -0.238044 | 0.673937 | -0.747749 |
| H | -2.562105 | -0.907604 | 2.113148 |
| H | -0.795185 | -0.941405 | 2.024687 |
| H | -2.232363 | -2.080749 | -0.058250 |


| H | -0.851483 | 1.476210 | 1.882912 |
| ---: | ---: | ---: | ---: |
| H | -2.615079 | 1.449647 | 1.763281 |
| H | -1.899617 | 2.198386 | -0.533269 |
| C | -2.473584 | 0.055055 | -0.534070 |
| 0 | -3.582711 | 0.006737 | -1.163855 |
| H | -0.143991 | 0.992131 | -1.788322 |
| H | -0.526703 | -1.257856 | -1.705540 |
| H | -3.900785 | 0.878705 | -1.488073 |
| C | 0.720625 | -1.742228 | -0.087693 |
| 0 | 0.574051 | -2.553487 | 0.797657 |
| O | 1.847323 | -1.512730 | -0.765001 |
| C | 0.949087 | 1.244508 | 0.026804 |
| O | 1.346587 | 0.794340 | 1.081323 |
| 0 | 1.441643 | 2.317495 | -0.592679 |
| C | 3.020216 | -2.257552 | -0.335127 |
| H | 2.825509 | -3.328870 | -0.412347 |
| H | 3.812911 | -1.953355 | -1.016710 |
| H | 3.262174 | -1.992457 | 0.695929 |
| C | 2.566120 | 2.982363 | 0.047044 |
| H | 2.813991 | 3.812200 | -0.612442 |
| H | 2.272839 | 3.339240 | 1.036384 |
| H | 3.402558 | 2.286432 | 0.134225 |

$H F=-804.0626781$

| $\theta\left({ }^{\circ}\right)$ | HF (a.u.) | HF $\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -804.0607277 | -504555.7 | 1.2 |
| 10 | -804.0617191 | -504556.4 | 0.6 |
| 5 | -804.0623391 | -504556.8 | 0.2 |
| 0 | -804.0626411 | -504556.9 | 0.0 |
| -2.3 | -804.0626781 | -504557.0 | 0.0 |
| -5 | -804.0626378 | -504556.9 | 0.0 |
| -10 | -804.0623112 | -504556.7 | 0.2 |
| -15 | -804.0616227 | -504556.3 | 0.7 |



| C | -1.117601 | -0.838651 | 1.543714 |
| :--- | ---: | ---: | :---: |
| C | -1.004874 | -1.171721 | 0.028352 |
| C | -1.114660 | 0.731999 | 1.587667 |
| C | -1.018268 | 1.147473 | 0.090748 |
| C | 0.446776 | -0.789143 | -0.522396 |


| C | 0.433025 | 0.813485 | -0.493136 |  |
| :--- | ---: | ---: | ---: | ---: |
| H | -2.049417 | -1.242947 | 1.949288 |  |
| H | -0.298718 | -1.289939 | 2.105990 |  |
| H | -1.350142 | -2.157431 | -0.281878 |  |
| H | -0.285748 | 1.149215 | 2.161365 |  |
| H | -2.038184 | 1.117996 | 2.028639 |  |
| H | -1.370191 | 2.151242 | -0.155505 |  |
| C | -1.705387 | -0.003691 | -0.535766 |  |
| O | -2.594205 | -0.052292 | -1.457942 |  |
| H | 0.454990 | 1.163561 | -1.531594 |  |
| H | 0.485801 | -1.101679 | -1.571529 |  |
| H | -2.914775 | 0.830073 | -1.746586 |  |
| C | 1.544803 | 1.509772 | 0.236402 |  |
| H | 1.739425 | 1.221249 | 1.266764 |  |
| C | 1.562981 | -1.486678 | 0.198981 |  |
| H | 1.750166 | -1.215163 | 1.235466 |  |
| C | 2.307287 | 2.453117 | -0.327308 |  |
| H | 2.165931 | 2.772640 | -1.358089 |  |
| H | 3.113063 | 2.930683 | 0.222798 |  |
| C | 2.334652 | -2.415095 | -0.376912 |  |
| H | 3.140446 | -2.897145 | 0.169284 |  |
| H | 2.198593 | -2.719220 | -1.412964 |  |
|  |  |  |  |  |
| HF=-503.09727 |  |  |  |  |



| C | 1.507493 | 1.036674 | 1.314712 |
| :---: | ---: | ---: | :---: |
| C | 1.253905 | 1.121213 | -0.219006 |
| C | 1.321586 | -0.487003 | 1.642184 |
| C | 1.103491 | -1.144777 | 0.247561 |
| C | -0.263004 | 0.787710 | -0.551516 |
| C | -0.344411 | -0.800533 | -0.304528 |
| H | 2.523962 | 1.369425 | 1.546300 |


| H | 0.821476 | 1.683261 | 1.863258 |
| :--- | ---: | ---: | ---: |
| H | 1.645542 | 2.002847 | -0.726564 |
| H | 0.467720 | -0.681531 | 2.293809 |
| H | 2.207278 | -0.902068 | 2.131089 |
| H | 1.371171 | -2.200383 | 0.161881 |
| C | 1.814624 | -0.181918 | -0.620594 |
| O | 2.624440 | -0.367519 | -1.594694 |
| H | -0.426161 | -1.274677 | -1.291010 |
| H | -0.397728 | 0.962511 | -1.625239 |
| C | -1.467421 | -1.397711 | 0.577349 |
| H | -1.047670 | -2.197859 | 1.200257 |
| H | -1.847862 | -0.644639 | 1.275102 |
| C | -1.232686 | 1.729937 | 0.185353 |
| H | -0.793469 | 2.736489 | 0.168297 |
| H | -1.321360 | 1.456279 | 1.242748 |
| C | -2.620560 | -1.989627 | -0.246923 |
| H | -2.276429 | -2.837165 | -0.851568 |
| H | -3.413286 | -2.354749 | 0.414322 |
| H | -3.065632 | -1.255061 | -0.926064 |
| C | -2.628715 | 1.805430 | -0.449744 |
| H | -2.569714 | 2.106518 | -1.502348 |
| H | -3.163978 | 0.853275 | -0.399384 |
| H | -3.235806 | 2.551100 | 0.074157 |
| H | 2.860611 | -1.309790 | -1.740580 |
|  |  |  |  |
| $\mathrm{HF}=-505.5625587$ |  |  |  |


| $\theta\left({ }^{\circ}\right)$ | HF (a.u.) | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -505.56200 | -317245.0 | 0.4 |
| 10 | -505.56247 | -317245.3 | 0.1 |
| 6.6 | -505.56256 | -317245.3 | 0.0 |
| 5 | -505.56254 | -317245.3 | 0.0 |
| 0 | -505.56226 | -317245.1 | 0.2 |
| -5 | -505.56161 | -317244.7 | 0.6 |
| -10 | -505.56078 | -317244.2 | 1.1 |
| -15 | -505.55958 | -317243.4 | 1.9 |


$\begin{array}{llll}\text { C } & -0.754157 & 1.453611 & -0.773373\end{array}$
C $\quad 0.168457 \quad 0.284443-1.184829$
$\begin{array}{llll}\text { C } & -0.735075 & 1.450343 & 0.797700\end{array}$
C $\quad 0.195890 \quad 0.276945 \quad 1.180077$

| C | -0.376781 | -1.111376 | -0.828864 |
| :--- | ---: | ---: | ---: |
| C | -0.358621 | -1.116118 | 0.827515 |
| H | -0.349502 | 2.391001 | -1.165324 |
| H | -1.756602 | 1.334823 | -1.192050 |
| H | 0.637289 | 0.336776 | -2.166076 |
| H | -1.725788 | 1.326991 | 1.242371 |
| H | -0.320824 | 2.385420 | 1.185408 |
| H | 0.673329 | 0.326528 | 2.159272 |
| C | 1.081331 | 0.136846 | -0.017316 |
| O | 2.322841 | -0.222679 | -0.113712 |
| H | 0.072005 | -1.976043 | 1.329655 |
| H | 0.054783 | -1.965029 | -1.340118 |
| H | 2.764912 | -0.352324 | 0.749795 |
| C | -1.599391 | -1.256255 | 0.010834 |
| H | -2.350647 | -0.474021 | 0.021523 |
| H | -2.011617 | -2.263321 | 0.014773 |
|  |  |  |  |
| HF $=-386.3789543$ |  |  |  |


| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -386.3785861 | -242456.2 | 0.2 |
| 10 | -386.3789528 | -242456.5 | 0.0 |
| 9.3 | -386.3789543 | -242456.5 | 0.0 |
| 5 | -386.3787093 | -242456.3 | 0.2 |
| 0 | -386.3779127 | -242455.8 | 0.7 |
| -5 | -386.3766172 | -242455.0 | 1.5 |
| -10 | -386.3748815 | -242453.9 | 2.6 |
| -15 | -386.3727258 | -242452.6 | 3.9 |



| C | 1.335308 | -0.985047 | 1.641078 |
| :--- | :---: | :---: | :---: |
| C | 1.303884 | -1.586446 | 0.218518 |
| C | 0.128045 | -1.003811 | -0.599978 |
| C | 1.641114 | 0.532165 | 1.556972 |
| C | 0.199872 | 0.562280 | -0.606327 |
| C | 1.563331 | 1.021022 | 0.053385 |
| C | 2.602348 | -1.193355 | -0.511367 |
| C | 2.655663 | 0.284312 | -0.589987 |
| H | 0.371363 | -1.155906 | 2.123637 |
| H | 2.095210 | -1.494122 | 2.243037 |
| H | 1.215979 | -2.673563 | 0.264300 |
| H | 2.627716 | 0.781676 | 1.962940 |


| H | 0.909476 | 1.124524 | 2.111607 |  |
| :--- | ---: | ---: | ---: | ---: |
| H | 1.686536 | 2.107001 | -0.025800 |  |
| H | 0.247921 | -1.323068 | -1.644588 |  |
| H | 0.177898 | 0.937107 | -1.632266 |  |
| O | 3.677781 | 0.829454 | -1.155243 |  |
| H | 3.647707 | 1.810549 | -1.164771 |  |
| C | -0.926461 | 1.276872 | 0.153371 |  |
| O | -1.387187 | 0.892798 | 1.206996 |  |
| O | -1.276025 | 2.399678 | -0.479705 |  |
| C | -1.218324 | -1.604683 | -0.181939 |  |
| O | -1.342647 | -2.492675 | 0.630432 |  |
| O | -2.213234 | -1.075623 | -0.908135 |  |
| C | -2.325516 | 3.193932 | 0.138109 |  |
| H | -2.462174 | 4.045692 | -0.526028 |  |
| H | -3.239686 | 2.601676 | 0.209383 |  |
| H | -2.012383 | 3.516050 | 1.133418 |  |
| C | -3.546815 | -1.578856 | -0.631552 |  |
| H | -4.198497 | -1.054952 | -1.329390 |  |
| H | -3.579273 | -2.656915 | -0.800873 |  |
| H | -3.816224 | -1.356034 | 0.403021 |  |
| H | 2.673820 | -1.605979 | -1.530003 |  |
| H | 3.510422 | -1.543093 | 0.005907 |  |
|  |  |  |  |  |
| HF=-843.4038365 |  |  |  |  |



| C | 0.555244 | -1.523187 | 1.375484 |
| :--- | ---: | ---: | :---: |
| C | 0.322630 | -1.600573 | -0.147957 |
| C | -0.811987 | -0.628983 | -0.594521 |
| C | 0.889752 | -0.060613 | 1.776085 |
| C | -0.351578 | 0.859171 | -0.314868 |
| C | 1.040634 | 0.837898 | 0.507289 |


| C | 1.632686 | -1.182824 | -0.845891 |
| :--- | ---: | ---: | ---: |
| C | 1.956040 | 0.201724 | -0.430781 |
| H | -0.326144 | -1.879860 | 1.913683 |
| H | 1.376093 | -2.193663 | 1.654031 |
| H | 0.065740 | -2.621003 | -0.444930 |
| H | 1.807442 | -0.002292 | 2.369356 |
| H | 0.099894 | 0.386386 | 2.385655 |
| H | 1.334354 | 1.861723 | 0.762110 |
| H | -0.915068 | -0.726331 | -1.682215 |
| H | -0.145338 | 1.340966 | -1.277906 |
| O | 2.972222 | 0.779187 | -0.982293 |
| H | 3.125983 | 1.691383 | -0.655520 |
| C | -1.324505 | 1.750890 | 0.410093 |
| C | -2.149493 | -1.000868 | 0.000955 |
| C | -3.189842 | -1.421635 | -0.723238 |
| C | -1.758072 | 2.914211 | -0.086798 |
| H | -2.256391 | -0.939023 | 1.083143 |
| H | -1.690081 | 1.418796 | 1.379113 |
| H | -1.435632 | 3.287096 | -1.057438 |
| H | -3.144178 | -1.499086 | -1.808173 |
| H | -4.129781 | -1.701738 | -0.256191 |
| H | -2.473397 | 3.526583 | 0.454819 |
| H | 1.580774 | -1.221403 | -1.944796 |
| H | 2.478902 | -1.833294 | -0.571515 |
|  |  |  |  |
| HF=-542.4358509 |  |  |  |


| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -542.4346239 | -340382.9 | 0.8 |
| 10 | -542.435514 | -340383.4 | 0.2 |
| 5 | -542.4358445 | -340383.6 | 0.0 |
| 4.4 | -542.4358509 | -340383.6 | 0.0 |
| 0 | -542.4356868 | -340383.5 | 0.1 |
| -5 | -542.4350728 | -340383.2 | 0.5 |
| -10 | -542.4343926 | -340382.7 | 0.9 |
| -15 | -542.4330366 | -340381.9 | 1.8 |



| C | 0.597383 | -0.874171 | 1.843092 |
| :--- | ---: | :---: | :---: |
| C | 0.380986 | -1.600750 | 0.498682 |
| C | -0.733943 | -0.912251 | -0.339714 |
| C | 1.183727 | 0.538215 | 1.574654 |


| C | -0.394012 | 0.625228 | -0.474836 |
| :--- | ---: | ---: | :---: |
| C | 1.105097 | 0.872618 | 0.049461 |
| C | 1.687368 | -1.530156 | -0.320928 |
| C | 1.922781 | -0.109265 | -0.654333 |
| H | -0.353491 | -0.805607 | 2.379435 |
| H | 1.274142 | -1.450347 | 2.482836 |
| H | 0.127914 | -2.651414 | 0.666927 |
| H | 2.224516 | 0.613529 | 1.907598 |
| H | 0.635777 | 1.318182 | 2.108377 |
| H | 1.417474 | 1.899420 | -0.165948 |
| H | -0.659643 | -1.340106 | -1.350819 |
| H | -0.398878 | 0.894897 | -1.538402 |
| O | 2.791170 | 0.168145 | -1.569116 |
| H | 2.899758 | 1.131011 | -1.724053 |
| C | -2.155266 | -1.259972 | 0.157389 |
| C | -3.241168 | -1.128185 | -0.921108 |
| H | -2.424039 | -0.664048 | 1.036782 |
| H | -2.141685 | -2.303473 | 0.498125 |
| H | -4.222118 | -1.392813 | -0.512836 |
| H | -3.318170 | -0.111949 | -1.324303 |
| H | -3.040760 | -1.802487 | -1.762610 |
| C | -1.345001 | 1.618889 | 0.229781 |
| C | -1.010552 | 3.098602 | 0.002201 |
| H | -1.408068 | 1.410827 | 1.303526 |
| H | -2.345571 | 1.425231 | -0.169887 |
| H | -1.817863 | 3.728621 | 0.388988 |
| H | -0.092867 | 3.412875 | 0.513843 |
| H | -0.901682 | 3.326447 | -1.065820 |
| H | 1.672770 | -2.130414 | -1.240505 |
| H | 2.558721 | -1.886354 | 0.255628 |

$\mathrm{HF}=-544.903301$

| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -544.90167 | -341931.0 | 1.0 |
| 10 | -544.90274 | -341931.6 | 0.4 |
| 5 | -544.90324 | -341932.0 | 0.0 |
| 2.4 | -544.90330 | -341932.0 | 0.0 |
| 0 | -544.90325 | -341932.0 | 0.0 |
| -5 | -544.90285 | -341931.7 | 0.3 |
| -10 | -544.90207 | -341931.2 | 0.8 |
| -15 | -544.90083 | -341930.4 | 1.6 |



| C | -0.192619 | -0.726715 | 0.511549 |
| :--- | ---: | ---: | ---: |
| C | 0.176475 | 1.246747 | -0.113285 |
| C | -1.472744 | -0.314589 | -0.058678 |
| C | -1.302177 | 1.087888 | -0.549430 |
| H | -0.061224 | -1.728197 | 0.921396 |
| H | 0.665252 | 2.196178 | -0.324727 |
| H | -1.490067 | 1.160114 | -1.629633 |
| C | 0.142926 | 0.622999 | 1.305611 |
| H | 1.121519 | 0.527452 | 1.780717 |
| H | -0.598854 | 0.984182 | 2.022896 |
| C | 0.773811 | -0.107163 | -0.624789 |
| H | 0.554231 | -0.396299 | -1.658175 |
| O | -2.575206 | -0.955464 | -0.155817 |
| H | -1.995575 | 1.774437 | -0.045271 |
| C | 2.179994 | -0.347150 | -0.338130 |
| N | 3.303336 | -0.539368 | -0.117008 |
| H | -2.550974 | -1.870685 | 0.201297 |
|  |  |  |  |
| HF=-401.1911754 |  |  |  |


| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -401.1887203 | -251749.7 | 1.5 |
| 10 | -401.1901347 | -251750.6 | 0.7 |
| 5 | -401.1909396 | -251751.1 | 0.1 |
| 0 | -401.1911743 | -251751.3 | 0.0 |
| -5 | -401.1908663 | -251751.1 | 0.2 |
| -10 | -401.1899759 | -251750.5 | 0.8 |
| -15 | -401.1885141 | -251749.6 | 1.7 |


$\begin{array}{lrrr}\text { C } & -1.035591 & -0.867735 & 0.112910 \\ \text { C } & -0.588709 & 1.122702 & 0.614937\end{array}$

| C | -2.221127 | -0.142650 -0.322 |  |  |
| :---: | :---: | :---: | :---: | :---: |
| C | -1.991177 | $1.306154-0.02$ |  |  |
| H | -0.956658 | -1.947579 -0.007 |  |  |
| H | -0.079351 | 2.0184570 .96 |  |  |
| H | -2.014795 | $1.911340-0.93$ |  |  |
| C | -0.837146 | -0.112104 1.5183 |  |  |
| H | 0.048536 | -0.517356 2.007 |  |  |
| H | -1.685404 | -0.095661 2.208 |  |  |
| C | 0.069985 | $0.151567-0.41$ |  |  |
| H | 0.007409 | $0.447425-1.46$ |  |  |
| O | -3.303928 | -0.576191 -0.853 |  |  |
| H | -2.757349 | 1.7001130 .658 |  |  |
| H | -3.320123 | -1.547630-0.99 |  |  |
| C | 1.488212 | -0.333082-0.12 |  |  |
| O | 1.755412 | -1.405735 0.37 |  |  |
| O | 2.361744 | $0.594854-0.50$ |  |  |
| C | 3.772651 | $0.284396-0.31$ |  |  |
| H | 4.027650 | -0.616292-0.87 |  |  |
| H | 4.303702 | $1.152681-0.70$ |  |  |
| H | 3.977978 | 0.1355910 .74 |  |  |
| $\mathrm{HF}=-536.8472777$ |  |  |  |  |
| $\theta\left({ }^{\circ}\right)$ |  | HF (a.u.) | HF (kcal mol ${ }^{-1}$ ) | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}{ }^{-1}\right)$ |
|  | 15 | -536.8449664 | -336875.3 | 1.4 |
|  | 10 | -536.8461918 | -336876.1 | 0.7 |
|  | 5 | -536.8469562 | -336876.6 | 0.2 |
|  | 0 | -536.8472695 | -336876.8 | 0.0 |
|  | -5 | -536.8471279 | -336876.7 | 0.1 |
|  | -10 | -536.8465193 | -336876.3 | 0.5 |
|  | -15 | -536.8454199 | -336875.6 | 1.2 |



| C | -0.593555 | -0.546781 | 0.828028 |
| :--- | ---: | :---: | ---: |
| C | 0.116297 | 1.158723 | -0.172222 |
| C | -1.645846 | -0.267291 | -0.129353 |
| C | -1.260941 | 0.978911 | -0.863562 |
| H | -0.662873 | -1.412929 | 1.487407 |
| H | 0.718925 | 2.008903 | -0.490000 |
| H | -1.227012 | 0.810733 | -1.947706 |
| C | -0.265463 | 0.927983 | 1.309746 |


| H | 0.577588 | 0.923139 | 1.999234 |
| :--- | ---: | ---: | ---: |
| H | -1.090574 | 1.507144 | 1.735182 |
| C | 0.651202 | -0.307122 | -0.217303 |
| H | 0.525095 | -0.812379 | -1.183451 |
| O | -2.706692 | -0.935059 | -0.412951 |
| H | -1.977550 | 1.789567 | -0.670928 |
| H | -2.838249 | -1.731048 | 0.145364 |
| C | 2.028172 | -0.657644 | 0.342921 |
| C | 3.144688 | -0.188129 | -0.605391 |
| H | 2.082817 | -1.747411 | 0.459425 |
| H | 2.184900 | -0.228115 | 1.337847 |
| H | 4.119367 | -0.489271 | -0.208776 |
| H | 3.039941 | -0.631754 | -1.602182 |
| H | 3.153840 | 0.901994 | -0.714998 |
|  |  |  |  |
| HF=-387.6024267 |  |  |  |


| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -387.6007021 | -243223.1 | 1.1 |
| 10 | -387.6018504 | -243223.8 | 0.3 |
| 5 | -387.6023923 | -243224.2 | 0.0 |
| 0 | -387.6023016 | -243224.1 | 0.1 |
| -5 | -387.6017338 | -243223.8 | 0.4 |
| -10 | -387.6006038 | -243223.1 | 1.1 |
| -15 | -387.5988549 | -243222.0 | 2.2 |



| C | -0.398502 | -0.678139 | 0.666595 |
| :--- | ---: | ---: | ---: |
| C | 0.235830 | 1.118677 | -0.228686 |
| C | -1.593164 | -0.206795 | 0.001418 |
| C | -1.261866 | 1.108133 | -0.631342 |
| H | -0.395068 | -1.628443 | 1.200939 |
| H | 0.820984 | 1.980297 | -0.548590 |
| H | -1.462607 | 1.094703 | -1.710620 |
| C | 0.150204 | 0.682325 | 1.255355 |
| H | 1.120163 | 0.511475 | 1.722978 |
| H | -0.511175 | 1.234593 | 1.929526 |
| C | 0.647310 | -0.337391 | -0.589359 |
| H | 0.288808 | -0.711440 | -1.556303 |
| O | -2.741816 | -0.768548 | -0.140454 |
| H | -1.851687 | 1.923185 | -0.189887 |
| H | -2.825298 | -1.629070 | 0.322978 |


| C | 2.035589 | -0.831297 | -0.345872 |
| :--- | :--- | ---: | ---: |
| H | 2.170660 | -1.904394 | -0.476877 |
| C | 3.095336 | -0.062653 | -0.068304 |
| H | 4.086124 | -0.496765 | 0.029631 |
| H | 3.029207 | 1.017077 | 0.041031 |

$H F=-386.3661578$

| $\theta\left({ }^{\circ}\right)$ | $\mathrm{HF}($ a.u. $)$ | $\mathrm{HF}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ | $\Delta \mathrm{E}\left(\mathrm{kcal} \mathrm{mol}^{-1}\right)$ |
| :---: | :---: | :---: | :---: |
| 15 | -386.3649575 | -242447.7 | 0.7 |
| 10 | -386.3658066 | -242448.2 | 0.2 |
| 5 | -386.3661483 | -242448.4 | 0.0 |
| 0 | -386.3660172 | -242448.3 | 0.1 |
| -5 | -386.3654587 | -242448.0 | 0.4 |
| -10 | -386.3644636 | -242447.4 | 1.1 |
| -15 | -386.3629932 | -242446.4 | 2.0 |

### 6.6. Chapter V

### 6.6.1. Computational Section

General Information: All of the compounds were optimized at B3LYP/6-31G(2d,2p).



```
H
```

$H F=-574.7280571$

|  |  |  |  |
| :--- | :--- | :--- | :--- |
| C | 0.000171 | 1.296857 | 0.000000 |
| C | 0.000411 | -0.000004 | 0.000000 |
| F | 0.000034 | -1.296865 | 0.000000 |
| F | 0.000034 | 2.059683 | 1.074822 |
| F | -1.075069 | -2.059349 | 0.000000 |
| F | 1.074589 | -2.060009 | 0.000000 |

$H F=-513.5930027$


A


A
$\begin{array}{llll}\text { C } & 3.556853 & -1.450374 & 0.290482\end{array}$
$\begin{array}{llll}\text { C } & 3.855890 & -0.137611 & -0.041629\end{array}$
$\begin{array}{llll}\text { C } & 2.882426 & 0.681720 & -0.637555\end{array}$

| C | 1.627745 | 0.144739 | -0.896325 |
| :---: | :---: | :---: | :---: |
| C | 1.306505 | -1.184523 | -0.575007 |
| C | 2.278527 | -1.978853 | 0.032978 |
| O | 4.407605 | -2.349184 | 0.878217 |
| H | 4.842569 | 0.263427 | 0.154552 |
| C | 3.200576 | 2.124127 | -0.964312 |
| H | 0.867577 | 0.755660 | -1.370406 |
| C | -0.042023 | -1.747106 | -0.864967 |
| O | 1.990269 | -3.259027 | 0.395964 |
| C | 3.144178 | 3.043547 | 0.267671 |
| C | 3.466303 | 4.493197 | -0.065262 |
| O | 3.418645 | 5.238007 | 1.143833 |
| C | -0.139696 | -3.114982 | $-1.500348$ |
| O | -1.160565 | -3.742727 | -1.620084 |
| C | 5.720856 | -1.919161 | 1.195952 |
| H | 4.198153 | 2.187476 | -1.415754 |
| H | 2.496201 | 2.485283 | -1.721080 |
| H | 2.798201 | -3.636547 | 0.769869 |
| H | 2.149425 | 2.996132 | 0.722215 |
| H | 3.850556 | 2.694161 | 1.028403 |
| H | 4.462210 | 4.556315 | -0.532056 |
| H | 2.740394 | 4.877248 | -0.798503 |
| H | 3.580596 | 6.162648 | 0.933201 |
| H | 0.827530 | -3.492605 | -1.882216 |
| H | 6.218069 | -2.773242 | 1.653697 |
| H | 6.268856 | -1.619240 | 0.296335 |
| H | 5.704510 | -1.084619 | 1.904992 |
| C | -1.147786 | -1.075080 | -0.645073 |
| C | -2.290554 | -0.424597 | -0.455772 |
| C | -2.828168 | 0.453610 | -1.482904 |


| C | -3.984633 | 1.112138 | -1.253429 |
| :--- | :--- | :--- | :--- |
| C | -4.732431 | 0.970677 | 0.013205 |
| C | -4.170810 | 0.069625 | 1.035687 |
| C | -3.007801 | -0.588799 | 0.804360 |
| O | -5.777148 | 1.602876 | 0.149999 |
| O | -4.562921 | 1.944729 | -2.133669 |
| O | -4.928611 | 0.002061 | 2.147602 |
| C | -4.481484 | -0.846052 | 3.192747 |
| H | -2.298236 | 0.564735 | -2.419794 |
| H | -5.371090 | 2.248877 | -1.673767 |
| H | -5.223743 | -0.764309 | 3.985018 |
| H | -4.415179 | -1.887636 | 2.858694 |
| H | -3.504098 | -0.527331 | 3.572720 |
| H | -2.577538 | -1.257738 | 1.536005 |

$\mathrm{HF}=-1300.7017823$


B
$\begin{array}{llll}\text { C } & 2.161238 & 1.826585 & -0.640559\end{array}$
$\begin{array}{llll}\text { C } & 3.448784 & 1.300455 & -0.769465\end{array}$
$\begin{array}{lllll}\text { C } & 3.729311 & -0.071299 & -0.666309\end{array}$

| C | 2.696267 | -0.978492 | -0.434234 |
| :---: | :---: | :---: | :---: |
| C | 1.147515 | 0.895475 | -0.398093 |
| C | 1.398562 | -0.480103 | -0.303700 |
| O | -0.201176 | 1.141976 | -0.227423 |
| C | -0.813774 | -0.062965 | -0.029226 |
| C | 0.107605 | -1.090584 | -0.049064 |
| C | -0.127934 | -2.495798 | 0.254475 |
| H | -1.152315 | -2.747524 | 0.589789 |
| O | 0.730222 | -3.356239 | 0.184851 |
| C | -2.257300 | -0.009378 | 0.159384 |
| C | -3.088902 | $-1.044505$ | -0.285119 |
| C | -4.467899 | -0.997857 | -0.089237 |
| C | $-5.038661$ | 0.104953 | 0.559404 |
| C | -4.207110 | 1.158646 | 0.969943 |
| C | -2.837478 | 1.112388 | 0.776975 |
| O | -5.213773 | -2.068742 | -0.490932 |
| O | -6.375003 | 0.153384 | 0.793801 |
| O | -4.869074 | 2.194672 | 1.580479 |
| O | 2.042865 | 3.176101 | -0.756317 |
| C | 5.159941 | -0.551647 | -0.783193 |
| C | 5.925544 | -0.472450 | 0.548786 |
| C | 7.359801 | -0.966301 | 0.429218 |
| O | 7.975906 | -0.833755 | 1.703603 |
| H | 4.247929 | 2.007275 | -0.964105 |
| H | 2.875270 | -2.042203 | $-0.358302$ |
| H | -2.211452 | 1.928850 | 1.117731 |
| H | -6.556823 | 0.985168 | 1.251753 |
| H | 5.163096 | -1.586213 | -1.142606 |
| H | 5.685979 | 0.043182 | -1.538836 |
| H | 5.937741 | 0.560422 | 0.912469 |


| H | 5.408574 | -1.065548 | 1.310036 |
| :--- | :--- | :--- | :--- |
| H | 7.365632 | -2.014500 | 0.092227 |
| H | 7.894791 | -0.377890 | -0.333001 |
| H | 8.875913 | -1.166861 | 1.636486 |
| C | 0.750538 | 3.763031 | -0.834781 |
| H | 0.920653 | 4.821228 | -1.032681 |
| H | 0.159710 | 3.330578 | -1.647025 |
| H | 0.200448 | 3.653778 | 0.103877 |
| C | -6.234588 | -1.811265 | -1.459136 |
| H | -4.234429 | 2.837112 | 1.912333 |
| H | -2.689218 | -1.893720 | -0.821534 |
| H | -6.673476 | -2.780777 | -1.693683 |
| H | -7.003994 | -1.144211 | -1.066451 |
| H | -5.802519 | -1.380663 | -2.369382 |

```
HF=-1300.7590791
```



$\begin{array}{llll}\mathrm{C} & 2.865473 & 1.906661 & -0.241680\end{array}$
$\begin{array}{llll}\text { C } & 3.533617 & 0.695057 & -0.412831\end{array}$
C $\quad 2.872298 \quad-0.542294 \quad-0.532812$
C $\quad 1.483961 \quad-0.589806 \quad-0.498582$
$\begin{array}{llll}\text { C } & 1.465793 & 1.830999 & -0.202870\end{array}$

| C | 0.778519 | 0.611585 | -0.340162 |
| :---: | :---: | :---: | :---: |
| O | 0.590463 | 2.860482 | -0.022587 |
| C | -0.667351 | 2.311857 | -0.049800 |
| C | -0.623630 | 0.946021 | -0.232728 |
| O | 3.631592 | 3.017245 | -0.117115 |
| C | 3.687612 | -1.810841 | -0.664376 |
| C | 4.186590 | -2.341357 | 0.690569 |
| C | 5.010131 | -3.613670 | 0.554164 |
| O | 5.416386 | -4.012474 | 1.856456 |
| H | 4.616756 | 0.735911 | -0.450567 |
| H | 0.957269 | -1.532145 | -0.584434 |
| H | 3.082052 | -2.580089 | -1.155453 |
| H | 4.547039 | -1.626722 | -1.319418 |
| H | 4.794578 | -1.579868 | 1.189982 |
| H | 3.334094 | -2.539993 | 1.348278 |
| H | 4.407909 | -4.397498 | 0.068483 |
| H | 5.880789 | -3.426248 | -0.093828 |
| H | 5.938078 | -4.816548 | 1.774002 |
| C | 3.020559 | 4.306980 | -0.161932 |
| H | 3.845801 | 5.017720 | -0.135126 |
| H | 2.448361 | 4.444728 | -1.082955 |
| H | 2.363109 | 4.472696 | 0.693543 |
| C | -1.755958 | 0.009866 | -0.288646 |
| C | -1.797434 | -0.974561 | -1.282778 |
| C | -2.866493 | -1.864708 | $-1.346136$ |
| C | -3.897830 | -1.778446 | -0.411701 |
| C | -3.858497 | -0.803453 | 0.589675 |
| C | -2.792988 | 0.088942 | 0.659050 |
| O | -2.904289 | -2.809552 | -2.322261 |
| O | -4.924777 | -2.674233 | -0.509887 |

```
O 
    H
    H
H
C
H
H
H
H
C 
O 
H
```

Table 6.4. Calculated NMR data for brosimum allene $\mathbf{A}$


A

| Position | Expt | B3LYP* |  |  |  | HF |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | B3LYP | mPW1PW91** | mPW1PW91 | HF | B3LYP | mPW1PW91 | HF |
| $\mathbf{1}$ | 120.2 | 105.8 | 100.4 | 100.4 | 94.9 | 104.8 | 104.3 | 93.0 |
| $\mathbf{2}$ | 105.7 | 106.1 | 100.6 | 101.7 | 106.2 | 106.7 | 107.1 | 104.9 |
| $\mathbf{3}$ | 150.1 | 149.3 | 143.1 | 144.3 | 143.8 | 153.8 | 153.3 | 146.0 |
| $\mathbf{4}$ | 168.0 | 171.5 | 166.5 | 167.5 | 176.2 | 170.8 | 171.5 | 171.8 |
| $\mathbf{5}$ | 147.3 | 148.3 | 141.5 | 143.2 | 142.9 | 151.4 | 151.2 | 145.1 |
| $\mathbf{6}$ | 111.5 | 101.3 | 95.3 | 96.7 | 100.9 | 109.8 | 110.4 | 109.5 |
| $\mathbf{7}$ | 139.1 | 229.3 | 223.5 | 224.1 | 229.2 | 226.8 | 226.5 | 225.5 |
| $\mathbf{8}$ | 117.5 | 107.7 | 102.5 | 102.5 | 97.8 | 108.1 | 108.0 | 97.3 |
| $\mathbf{9}$ | 188.5 | 182.8 | 177.4 | 179.1 | 180.4 | 184.7 | 186.1 | 181.9 |
| $\mathbf{1}$ | 141.6 | 131.7 | 126.0 | 126.7 | 129.9 | 132.6 | 132.5 | 129.3 |
| $\mathbf{2}$ | 110.1 | 108.5 | 102.9 | 104.4 | 108.0 | 123.1 | 123.9 | 121.1 |
| $\mathbf{3}$ | 150.1 | 144.1 | 137.0 | 138.6 | 139.3 | 147.9 | 147.2 | 140.4 |
| $\mathbf{4}$ | 142.7 | 141.5 | 134.1 | 136.0 | 137.2 | 145.8 | 145.4 | 140.0 |
| $\mathbf{5}$, | 128.5 | 117.3 | 111.4 | 112.1 | 114.9 | 121.3 | 121.1 | 117.5 |
| $\mathbf{6}$ | 114.3 | 122.4 | 116.9 | 118.3 | 121.1 | 128.3 | 129.0 | 126.3 |
| $\mathbf{7}$ | 33.6 | 36.2 | 29.8 | 30.2 | 26.4 | 36.5 | 35.5 | 25.7 |
| $\mathbf{8}$ | 35.9 | 39.3 | 32.4 | 32.9 | 31.1 | 39.2 | 37.7 | 29.7 |
| $\mathbf{9}$, | 62.3 | 66.7 | 59.1 | 60.1 | 54.5 | 68.9 | 67.2 | 55.6 |
| $\mathbf{3 - O M e}$ | 56.9 | 55.0 | 49.0 | 49.8 | 46.6 | 55.7 | 55.2 | 46.0 |
| $\mathbf{3} \mathbf{\prime} \mathbf{- O M e}$ | 56.6 | 54.9 | 48.9 | 49.6 | 46.2 | 62.5 | 62.0 | 52.6 |

*This 1st row shows the methods used to optimize the structure, while the 2nd row shows the methods exployed to calculate the NMR values.
**All of the calcalations in this table were done by using $6-31 \mathrm{G}(2 \mathrm{~d}, 2 \mathrm{p})$ basis set except this one $6-31 \mathrm{G}(\mathrm{d}, \mathrm{p})$.
6.6.2. Experimental Section


To solution of syringaldehyde $12(3.287 \mathrm{~g}, 18.04 \mathrm{mmol})$ in DMF $(120 \mathrm{~mL})$ was added imidazole ( $2.457 \mathrm{~g}, 36.10 \mathrm{mmol}$ ) and $\mathrm{TBSCl}(4.580 \mathrm{~g}, 30.40 \mathrm{mmol})$, sequentially. The reaction mixture was stirred at room temperature for 30 min . The mixture was diluted with $\mathrm{H}_{2} \mathrm{O}(125 \mathrm{~mL})$, and extracted with ethyl acetate ( $3 \times 125 \mathrm{~mL}$ ). The organic extracts were combined, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and the residue was then purified by FCC using hexane:ethyl acetate (4:1) to provide TBS-protected syringaldehyde $13 \mathrm{a}(5.240 \mathrm{~g}, 98 \%)$. $\mathrm{R}_{\mathrm{F}} 0.5$ (2:1-hexane:ethyl acetate); IR vmax (neat) $/ \mathrm{cm}^{-1}$ 2931, 2887, 2857, 2738, 1692, 1584, 1505, 1463, 1423, 1389, 1334, 1129, 904, 840; ${ }^{1} \mathrm{H}$ NMR (500 MHz, CDCl3) $9.82(1 \mathrm{H}, \mathrm{s}) 7.09(2 \mathrm{H}, \mathrm{s}) 3.86(6 \mathrm{H}, \mathrm{s}) 1.01(9 \mathrm{H}, \mathrm{s}) 0.16(6 \mathrm{H}, \mathrm{s})$; ${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 191.3, 152.3, 140.9, 129.6, 106.9, 56.1, 25.9, 19.1, -4.7; $m / z$ (ESIMS) calculated for $\mathrm{C}_{15} \mathrm{H}_{25} \mathrm{O}_{4} \mathrm{Si}[\mathrm{MH}]^{+}$297.3, found: 297.2.


The TBS-protected syringaldehyde 13a ( $560 \mathrm{mg}, 1.89 \mathrm{mmol}$ ) was dissolved in dry THF $(10 \mathrm{~mL})$, cooled to $0{ }^{\circ} \mathrm{C}$, and then isopropyl magnesium chloride ( $1.89 \mathrm{~mL}, 3.78 \mathrm{mmol}$ ) was added drop-wise. The reaction was stirred at $0{ }^{\circ} \mathrm{C}$ for 30 min , quenched with saturated $\mathrm{NH}_{4} \mathrm{Cl}$ (aq.) $(50 \mathrm{~mL})$, and extracted with ethyl acetate $(2 \times 50 \mathrm{~mL})$. The organic extracts were combined, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and then the residue was purified by FCC using hexane:ethyl acetate (20:1) to give the alcohol 13b ( $450 \mathrm{mg}, 70 \%$ ). $\mathrm{R}_{\mathrm{F}} 0.4$ (10:1-hexane:ethyl acetate); IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3483,2956,2933$, $2895,2858,1588,1510,1463,1420,1331,1249,1130,919,901,839$; 1H NMR (500 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) 6.49(2 \mathrm{H}, \mathrm{s}) 4.23(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=7.06 \mathrm{~Hz}) 3.78(6 \mathrm{H}, \mathrm{s}) 1.90(1 \mathrm{H}, \mathrm{m}) 1.87(1 \mathrm{H}$, bs) $1.01(12 \mathrm{H}, \mathrm{bs}) 0.77(3 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.82 \mathrm{~Hz}) 0.12(5 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 151.8, 136.7, 133.8, 103.9, 80.8, 56.1, 35.8, 26.2, 19.4, 18.9, 18.7, -4.3; m/z (ESIMS) calculated for $\mathrm{C}_{18} \mathrm{H}_{32} \mathrm{O}_{4} \mathrm{SiNa}[\mathrm{MNa}]^{+} 363.2$, found: 363.2.


To a solution of the alcohol $\mathbf{1 3 b}(402 \mathrm{mg}, 1.18 \mathrm{mmol})$ in hexane $(11.9 \mathrm{~mL})$ was added activated $\mathrm{MnO}_{2}(2.330 \mathrm{~g}, 23.62 \mathrm{mmol})$ at room temperature, stirred for 6 h , and then filtered through a plug of silica gel to remove excess manganese oxides with ethyl acetate $(200 \mathrm{~mL})$. The filtrate was concentrated in vacuo and the residue was purified by FCC using hexane:ethyl acetate (10:1) to give $\mathbf{1 3}$ ( $352 \mathrm{mg}, 88 \%$ ). $\mathrm{R}_{\mathrm{F}} 0.6$ (5:1-hexane:ethyl acetate); IR $v \max ($ neat $) / \mathrm{cm}^{-1} 2963,2932,2857,2709,1677,1580,1510,1464,1416$, $1352,1322,1145,915,863 ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 7.21(2 \mathrm{H}, \mathrm{s}) 3.84(6 \mathrm{H}, 2) 3.52$ $(1 \mathrm{H}, \mathrm{m}) 1.20(6 \mathrm{H}, \mathrm{d}, \mathrm{J}=6.79 \mathrm{~Hz}) 1.00(9 \mathrm{H}, \mathrm{s}) 0.14(6 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 203.4, 151.6, 139.6, 129.0, 106.1, 56.2, 35.1, 25.9, 19.8, 19.0, -4.3; m/z (ESIMS) calculated for $\mathrm{C}_{18} \mathrm{H}_{30} \mathrm{O}_{4} \mathrm{SiNa}[\mathrm{MNa}]^{+} 361.2$, found: 361.2.


A solution of $\mathbf{1 3}(1.234 \mathrm{~g}, 3.650 \mathrm{mmol})$ in dry THF $(36.5 \mathrm{~mL})$ was cooled to $-78{ }^{\circ} \mathrm{C}$, to which was added NaHMDS ( $7.29 \mathrm{~mL}, 7.29 \mathrm{mmol}$ ) drop-wise. The reaction mixture was stirred for 40 min and $N$-phenyl bis-trifluoromethane sulfonimide ( $2.60 \mathrm{~g}, 7.29 \mathrm{mmol}$ ) was added in one portion. The resultant reaction mixture was stirred for 4 h , and allowed to warm (final temperature $\sim 0{ }^{\circ} \mathrm{C}$ ). The mixture was quenched with saturated $\mathrm{NH}_{4} \mathrm{Cl}$ (aq.) $(100 \mathrm{~mL})$, extracted with ethyl acetate $(2 \times 100 \mathrm{~mL})$. The organic extracts were combined, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and then the residue was purified by FCC using the gradient: $1 \%(\sim 200 \mathrm{~mL}), 3 \%(\sim 500 \mathrm{~mL}), 5 \%(\sim 300 \mathrm{~mL})$ ethyl ether in hexane to afford 14 ( $651 \mathrm{mg}, 32 \%$ ). $\mathrm{R}_{\mathrm{F}} 0.6$ (7:1-hexane:ethyl ether), IR $v \max ($ neat $) / \mathrm{cm}^{-1}$ 2997, 2934, 2857, 1580, 1511, 1453, 1391, 1219, 1130, 940; ${ }^{1} \mathrm{H}$ NMR ( 500 MHz , $\left.\mathrm{CDCl}_{3}\right) 7.31(3 \mathrm{H}, \mathrm{m}) 7.18(2 \mathrm{H}, \mathrm{m}) 6.27(2 \mathrm{H}, \mathrm{s}) 3.66(6 \mathrm{H}, \mathrm{s}) 2.16(3 \mathrm{H}, \mathrm{s}) 1.70(3 \mathrm{H}, \mathrm{s}) 1.01$ $(9 \mathrm{H}, \mathrm{s}) 0.13(6 \mathrm{H}, \mathrm{s}){ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 151.4, 139.4, 138.7, 134.5, 132.4, 129.7, 129.3, 128.7, 128.4, 107.5, 55.9, 26.0, 22.3, 21.7, 19.0, -4.5; m/z (ESIMS) calculated for $\mathrm{C}_{25} \mathrm{H}_{34} \mathrm{~F}_{3} \mathrm{NO}_{5} \mathrm{SSiNa}[\mathrm{MNa}]^{+}$568.7, found: 568.7.


Compound I was observed as the major by-product for the formation of $\mathbf{1 4}$ (see above). For example, when the above procedure was followed using 13 ( $103 \mathrm{mg}, 0.304 \mathrm{mmol}$ ), THF ( 3 mL ), NaHMDS ( $609 \mu \mathrm{~L}, 0.609 \mathrm{mmol}$ ), and $N$-phenyl bis-trifluoromethane sulfonimide ( $163 \mathrm{mg}, 0.456 \mathrm{mmol}$ ). The desired product was obtained [ $\mathbf{1 4}(51 \mathrm{mg}, 31 \%$ yield)] as was I ( $93 \mathrm{mg}, 50 \%$ yield). RF 0.4 (7:1-hexane:ethyl ether); IR $v \max ($ neat $) / \mathrm{cm}-1$ $3068,2933,2857,2252,2161,1954,1726,1672,1581,1510,1464,1394,1343,1229$, $1194,1129,1067,1028,909 ; 1 \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.41(3 \mathrm{H}, \mathrm{m}) 7.31(2 \mathrm{H}, \mathrm{m})$ $6.45(2 \mathrm{H}, \mathrm{s}) 3.80(2 \mathrm{H}, \mathrm{bs}) 3.75(6 \mathrm{H}, \mathrm{s}) 3.37(2 \mathrm{H}, \mathrm{t}) 1.74(3 \mathrm{H}, \mathrm{s}) 1.65(3 \mathrm{H}, \mathrm{s}) 1.59(4 \mathrm{H}, \mathrm{m})$ $1.03(9 \mathrm{H}, \mathrm{s}) 0.15(6 \mathrm{H}, \mathrm{s})$; 13 C NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 151.3, 148.1, 136.9, 134.0, 129.8, 129.4, 129.2, 128.3, 114.9, 106.9, 68.3, 56.0, 53.4, 26.8, 26.0, 25.4, 20.1, 19.0, 17.8, -4.4; $\mathrm{m} / \mathrm{z}$ (ESIMS) calculated for [MNa]+ 640.8, found: 640.7.


To a solution of $\mathbf{1 4}(651.3 \mathrm{mg}, 1.195 \mathrm{mmol})$ in THF $(9.2 \mathrm{~mL})$ was added TBAF $(2.80 \mathrm{~mL}$, 2.80 mmol ) at $0{ }^{\circ} \mathrm{C}$. The reaction mixture was stirred for 10 min , quenched with saturated $\mathrm{NH}_{4} \mathrm{Cl}$ (aq.) $(50 \mathrm{~mL})$, extracted with ethyl acetate ( 2 x 50 mL ). The organic extracts were combined, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, and then concentrated in vacuo. The residue was purified by FCC using hexane:ethyl acetate (5:1) to give 15 (468 mg, 93\%). $\mathrm{R}_{\mathrm{F}} 0.32$ (2:1 hexane:ethyl ether); IR $v \max$ (neat) $/ \mathrm{cm}^{-1} 3515,2998,2939,2841,1608,1513,1389,1334$, $1216,1196,1112 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $7.33(3 \mathrm{H}, \mathrm{m}) 7.24(2 \mathrm{H}, \mathrm{m}) 6.31(2 \mathrm{H}, \mathrm{s})$ $3.76(6 \mathrm{H}, \mathrm{s}) 2.17(3 \mathrm{H}, \mathrm{s}) 1.69(3 \mathrm{H}, \mathrm{s}){ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 146.9, 139.8, 138.6, 134.9, 132.2, 129.4, 128.8, 128.5, 128.4, 107.2, 56.5, 22.2, 21.7; m/z (ESIMS) calculated for $\mathrm{C}_{19} \mathrm{H}_{20} \mathrm{~F}_{3} \mathrm{NO}_{5} \mathrm{SNa}[\mathrm{MNa}]^{+} 454.1$, found: 454.1.



15
16
To a solution of $\mathbf{1 5}(79 \mathrm{mg}, 0.19 \mathrm{mmol})$ in DMF $(10 \mathrm{~mL})$ was added $\mathrm{K}_{2} \mathrm{CO}_{3}(92 \mathrm{mg}, 0.66$ $\mathrm{mmol})$ and water ( $12 \mathrm{~L}, 0.66 \mathrm{mmol}$ ) at room temperature. The reaction mixture was stirred for 24 h , diluted with ethyl acetate ( 25 mL ), washed distilled water ( $2 \times 25 \mathrm{~mL}$ ), and then with saturated $\mathrm{NH}_{4} \mathrm{Cl}\left(\mathrm{aq}\right.$.) $(25 \mathrm{~mL})$. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and then the residue was purified by FCC using toluene:ethyl acetate (7:1) to give $\mathbf{1 6}(36 \mathrm{mg}, 60 \%) . \mathrm{R}_{\mathrm{F}} 0.6$ (1:1 hexane:ethyl acetate); IR $v \max ($ neat $) / \mathrm{cm}^{-1} 3504,2937,2856,1701,1586,1502,1452,1413,1389,1337,1195$, $1110,1030,979,942 ;{ }^{1} \mathrm{H}$ NMR ( $500 \mathrm{MHz}, \mathrm{CD}_{3} \mathrm{COCD}_{3}$ ) $6.53(2 \mathrm{H}, \mathrm{s}) 6.13(2 \mathrm{H}, \mathrm{s}) 3.73$ $(6 \mathrm{H}, \mathrm{s}) 3.66(6 \mathrm{H}, \mathrm{s}) 2.13(3 \mathrm{H}, \mathrm{s}) 1.91(3 \mathrm{H}, \mathrm{s}) 1.68(3 \mathrm{H}, \mathrm{s}) 1.62(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR (125 $\mathrm{MHz}, \mathrm{CDCl} 3) 152.6,148.8,146.9,139.1,138.2,135.9,134.8,132.2,129.5,129.1,128.8$, $128.4,125.2,109.2,107.6,106.9,55.8,55.5,21.3,20.9,19.5,17.1 ; \mathrm{m} / \mathrm{z}$ (ESIMS) calculated for $\mathrm{C}_{18} \mathrm{H}_{20} \mathrm{O}_{4} \mathrm{Na}[\mathrm{MNa}]^{+} 660.2$, found: 660.2.


To a solution of HCl in $\mathrm{MeOH}(0.1 \mathrm{M}, 5 \mathrm{~mL})$ was added compound $16(32 \mathrm{mg}, 0.050$ mmol ) and the reaction mixture was allowed to stand at room temperature for 15 min . The reaction was then diluted with ethyl acetate $(25 \mathrm{~mL})$, washed with saturated $\mathrm{Na}_{2} \mathrm{CO}_{3}$ (aq.) $(25 \mathrm{~mL})$ and then distilled water $(25 \mathrm{~mL})$. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and then purified by FCC using hexane:ethyl acetate (5:1) to give $\mathbf{1 5}(20 \mathrm{mg}, 0.046 \mathrm{mmol}, 92 \%)$ and $\mathbf{1 7}(10 \mathrm{mg}, 0.045$ $\mathrm{mmol}, 89 \%$ ). Experimental data for 17: $\mathrm{R}_{\mathrm{F}} 0.4$ ( $1: 1$ hexane:ethyl acetate); IR $v \max ($ neat $) / \mathrm{cm}^{-1}$ 3407, 2970, 2936, 2873, 2841, 1667, 1605, 1515, 1463, 1421, 1382,

1352, 1316, 1197, 1114, 1050, 900; ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CD}_{3} \mathrm{COCD}_{3}$ ) $5.91(2 \mathrm{H}, \mathrm{s}) 3.96$ $(6 \mathrm{H}, \mathrm{s}) 3.52(1 \mathrm{H}, \mathrm{m}) 1.22(6 \mathrm{H}, \mathrm{d}) ;{ }^{13} \mathrm{C}$ NMR ( $100 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 203.2, 147.0, 139.7, 127.9, 105.9, 56.7, 35.0, 19.7; m/z (ESIMS) calculated for $\mathrm{C}_{12} \mathrm{H}_{16} \mathrm{O}_{4} \mathrm{Na}[\mathrm{MNa}]^{+} 247.2$, found: 247.2.


15
18
To a solution of $\mathbf{1 5}(62.3 \mathrm{mg}, 0.148 \mathrm{mmol})$ in $\mathrm{DMF}(8 \mathrm{~mL})$ was added $\mathrm{K}_{2} \mathrm{CO}_{3}(314 \mathrm{mg}$, $2.27 \mathrm{mmol})$ and phenol ( $165 \mathrm{mg}, 1.75 \mathrm{mmol}$ ) at room temperature. The reaction mixture was stirred for 16 h , diluted with ethyl acetate ( 25 mL ), washed with distilled water ( 25 $\mathrm{mL})$ and then saturated $\mathrm{NH}_{4} \mathrm{Cl}($ aq. $)(25 \mathrm{~mL})$. The organic extract was dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered, concentrated in vacuo, and then the residue was purified by FCC using hexane:ethyl acetate ( $7: 1$ ) to give $\mathbf{1 8}(21 \mathrm{mg}, 47 \%)$. $\mathrm{R}_{\mathrm{F}} 0.4$ (2:1 hexane:ethyl acetate); ${ }^{1} \mathrm{H}$ NMR ( $\left.500 \mathrm{MHz}, \mathrm{CD}_{3} \mathrm{COCD}_{3}\right) 7.18(2 \mathrm{H}, \mathrm{m}) 6.94(2 \mathrm{H}, \mathrm{m}) 6.85(1 \mathrm{H}, \mathrm{m}) 6.73(2 \mathrm{H}, \mathrm{s}) 3.78$ $(6 \mathrm{H}, \mathrm{s}) 1.95(3 \mathrm{H}, \mathrm{s}) 1.80(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CD}_{3} \mathrm{COCD}_{3}$ ) 157.8, 144.5, 129.4, 126.2, 121.3, 119.6, 116.4, 107.5, 55.9, 19.6, 18.0; m/z (ESIMS) calculated for $\mathrm{C}_{18} \mathrm{H}_{20} \mathrm{O}_{4} \mathrm{Na}[\mathrm{MNa}]^{+}$323.1, found: 323.1.


To a solution of $\mathbf{1 5}(74.1 \mathrm{mg}, 0.172 \mathrm{mmol})$ in DMF ( 8.5 mL ) was added $\mathrm{K}_{2} \mathrm{CO}_{3}(95 \mathrm{mg}$, $0.69 \mathrm{mmol})$, and benzenethiol ( $70 \mu \mathrm{~L}, 0.67 \mathrm{mmol}$ ). The reaction mixture was allowed to stir overnight at room temperature. The mixture was then diluted with distilled water ( 25 mL ), extracted with ethyl acetate ( $1 \times 20 \mathrm{~mL}, 1 \times 5 \mathrm{~mL}$ ). The organic extracts were combined, washed with water ( $2 \times 25 \mathrm{~mL}$ ), dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, concentrated in vacuo, and then the residue was purified by FCC using hexane:ethyl acetate (3:1) to afford 19 (44 $\mathrm{mg}, 81 \%$ ). $\mathrm{R}_{\mathrm{F}} 0.36$ (2:1-hexane:ethyl ether); ${ }^{1} \mathrm{H}$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) 7.03-7.39(5H,
m) $6.42(2 \mathrm{H}, \mathrm{s}) 5.39(1 \mathrm{H}, \mathrm{s}) 3.77(6 \mathrm{H}, \mathrm{s}) 2.17(3 \mathrm{H}, \mathrm{s}) 1.85(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}$ NMR ( 125 MHz , $\mathrm{CDCl}_{3}$ ) 146.5, 140.4, 136.4, 133.7, 132.3, 129.9, 128.7, 128.1, 126.0, 107.1, 56.5, 23.6, 23.4; $m / z$ (ESIMS) calculated for $\mathrm{C}_{18} \mathrm{H}_{20} \mathrm{O}_{3} \mathrm{SK}[\mathrm{MK}]^{+} 355.2$, found: 355.2.

1.14


1.16.2














|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| 9.0 | 8.5 | 8.0 | 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 | 0.0 |







1.16.1


1.16.1


1.16.1


1.16.1








### 1.15.3



1.15.3



1.16.3


${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$
TBDPSO~~~~~~


|  | T | 1 | 1 | 1 | 1 | 1 | T | 1 | 1 | 1 | 1 | 1 | T | 1 | 1 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 4 | 13 | 12 | 11 | 10 | 9 | 8 | 7 | $\stackrel{6}{\mathrm{f} 1}(\mathrm{ppm})$ | 5 | 4 | 3 | 2 | 1 | 0 | -1 |

${ }^{13} \mathrm{C} \operatorname{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$
$\underbrace{\sim}_{\text {TBDPSO }}$


${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$
$\overbrace{\text { TBDPSO }}^{\sim} \sim_{\mathrm{H}}$

${ }^{13} \mathrm{C}$ NMR ( $125 \mathrm{MHz}, \mathrm{CDCl}_{3}$ )

${ }^{1} \mathrm{H}$ NMR $\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$

${ }^{13} \mathrm{C}$ NMR $\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$


| T | T | T | 1 | 1 | 1 | 1 | T | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | - |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 220 | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | $\underset{f 1}{110}$ | $\begin{aligned} & 100 \\ & \mathrm{ppm}) \end{aligned}$ | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 | -10 |


1.15.2 (a-m)


|  |  | T | T |  | T |  |  |  | T |  | 1 | 1 |  | T |  | T |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 8.0 | 7.5 | 7.0 | 6.5 | 6.0 | 5.5 | 5.0 | 4.5 | $\begin{gathered} 4.0 \\ \mathrm{f} 1(\mathrm{ppm}) \end{gathered}$ | 3.5 | 3.0 | 2.5 | 2.0 | 1.5 | 1.0 | 0.5 | 0.0 |



1.16.2 (a-m)






|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |
| 8.5 | 8.0 | 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 | 0.0 |


1.16.2 (a-m)


|  |  |  |  | 1 | , |  |  |  | , |  |  |  |  |  | , |  |  |  | 1 | 1 | 1 |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 220 | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 |  |  | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 |



### 1.15.2 (a-m)



1.15.2 (a-m)



### 1.15 .2 (a-m)


$\xlongequal{ }$ $\qquad$ M M A $\qquad$ $\sim$


|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 8.5 | 8.0 | 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 | 0.0 |



### 1.16.2 (a-m)












1.16.2 (a-m)



### 1.15.2 (a-m)



### 1.15.2 (a-m)



### 1.16.2 (a-m)



### 1.16 .2 (a-m)




1.15.2 (a-m)




### 1.16.2 (a-m)




1.15.2 (a-m)





### 1.16.2 (a-m)



1.15.2 (a-m)

1.15.2 (a-m)





1.16.2 (a-m)


[^0]
1.15.2 (a-m)





1.16.2 (a-m)


### 1.15.2 (a-m)





### 1.16.2 (a-m)



1.16.2 (a-m)





1.16.4









| T | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 220 | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 140 | 130 | 120 | 110 | 100 | 90 | 80 | 70 | 60 | 50 | 40 | 30 | 20 | 10 | 0 |
|  |  |  |  |  |  |  |  |  |  |  | f 1 (ppm) |  |  |  |  |  |  |  |  |  |  |  |









2.1 precursor







Table 2.4 2.1 precursor




Table 2.4 2.1 precursor




Table 2.4
2.1 precursor







Table 2.4
2.1 precursor





Table 2.4
2.1 precursor





2.1




2.1


















Table 2.3





Table 2.3






Table 2.3




Table 2.3







Table 2.3









2.2b







2.2

Table 2.4






2.2

Table 2.4







2.2

Table 2.4




2.2

Table 2.4












Chapter III
3.6-3.11



| 220 | 210 | 200 | 190 | 180 | 170 | 160 | 150 | 0 | 130 |  | 110 |  |  | 80 | 70 | 60 | 50 |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | 190 |  | 170 | 160 | 150 | - | , | 120 | f1 pp |  | 90 | 80 | 70 | 60 | 0 | 40 | 30 | 0 | 10 | 0 |





Chapter III
3.6-3.11





Chapter III
3.6-3.11




Chapter III
3.29 precursor




Chapter III
3.29 precursor







Chapter III
3.20-3.26





Chapter III
3.20-3.26





## 1D TOCSY spectrum

Chapter III
3.20-3.26


1D TOCSY spectrum
Chapter III
3.20-3.26
$\mathrm{H} 1 \quad \mathrm{H} 10^{\mathrm{b}}$


${ }_{21}$




## DPFGSENOE

spectrum


22-OCH3

















## Expreimental (a) and calcualted (b) ${ }^{1} \mathrm{H}$ NMR specrtra




Protons of the methylene $11-\mathrm{CH}_{2}$ and $12-\mathrm{CH}_{2}$ groups
complex non - first order splitting patterns + ovelapping of H11b and H12 b with H15b cannot be detremined precisely






## Expanded portion of the NOESY spectrum



## Expanded portion of the NOESY spectrum






${ }^{13} \mathrm{C}$ NMR spectrum in $\mathrm{CDCl}_{3}$



## Chapter III

3.20-3.26


[^1]


[^2]

## Chapter III

3.20-3.26





## Chapter III

3.20-3.26





Chapter III
3.20-3.26




Chapter III
3.20-3.26

































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## Publications

Hu, G,; Liu, K.; Williams, L. J. Org. Lett. 2008, 10, 5493. "The Brosimum Allene: A Structural Revision."

Hu, G.; Wang, H.; Liu, L.; Pu, M.; He, J.; Evans, D. G. J. Phys. Chem. Solids 2010, 71, 1290. "Supramolecular structural control and characteristics of p-hydroxybenzoate intercalated hydrotalcite."


[^0]:    

[^1]:    | 7.5 | 7.0 | 6.5 | 6.0 | 5.5 | 5.0 | 4.5 | 4.0 | $\begin{array}{r}3.5 \\ \mathrm{f1}(\mathrm{ppm})\end{array}$ | 3.0 | 2.5 | 2.0 | 1.5 | 1.0 | 0.5 |
    | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- | :--- |

[^2]:    $\begin{array}{llllllllllllllllllllllllllllll}220 & 210 & 200 & 190 & 180 & 170 & 160 & 150 & 140 & 130 & 120 & 110 & 100 & 90 & 80 & 70 & 60 & 50 & 40 & 30 & 20 & 10 & 0 & -10\end{array}$

