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Part I. Fluorination of organostannanes with xenon difluoride and silver triflate. Part II. Approach to \((-\)-11-nor-\(\Delta^9\)-THC-carboxylic acid and synthesis of cannabinoid analogs

Kawakami, Joel Kenji, Ph.D.

University of Hawaii, 1994
PART I: FLUORINATION OF ORGANOSTANNANES WITH XENON DIFLUORIDE AND SILVER TRIFLATE.
PART II: APPROACH TO (-)-11-Nor-Δ9-THC-CARBOXYLIC ACID AND SYNTHESIS OF CANNABINOID ANALOGS.

A DISSERTATION SUBMITTED TO THE GRADUATE DIVISION OF THE UNIVERSITY OF HAWAII IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY DECEMBER 1994

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This dissertation is dedicated to my loving father Clyde Kenichi Kawakami who is with the Lord. From his love and encouragement, my future was changed for the better.
ACKNOWLEDGEMENTS

I would like to acknowledge Allied-Signal for their generous supply of N-fluorobenzenesulfonimide. Also, special thanks to Professor Gordon W. Gribble and his group for their gift of 2- and 3-indolyl bromides. Thank you to Professor Roger E. Cramer for suggesting the use of XeF$_2$ for the fluorination of vinyl stannanes. The most important acknowledgement goes to Professor Marcus A. Tius for his guidance and support. Thank you Marcus for coming up with the idea of using silver for the fluorination of vinyl stannanes with XeF$_2$, for without this idea, this dissertation would not exist. Special thanks to Dr. Kamali G. S. Kannangara, Jakob Busch-Petersen, and Professor Marcus A. Tius for editing this dissertation. Thank you Wesley Yoshida, Mike Burger, and Walter Niemczura for helping me obtain my NMR and MS spectra data. Also, special acknowledgement and thanks go to my wife, Nancy, for editing this dissertation, and giving me the courage and strength to complete my academic education. Finally, thank you Kira, my loving daughter, who by being herself, has comforted me through difficult periods of my graduate research.
ABSTRACT

Part I: Fluorination Of Organostannanes With Xenon Difluoride And Silver Triflate

The first successful transformation of vinyl stannanes to vinyl fluorides has been accomplished using xenon difluoride and silver(I). The reaction occurs regio- and stereospecifically. The use of silver triflate has been found to be optimal for the fluorination reaction. Although related work has appeared in the literature since our initial publication, our method still offers the fastest rate of reaction and yields for our process are competitive. The mechanism has been extensively investigated. Although our findings are not definitive, we have been able to conclusively eliminate certain mechanistic pathways. Radical mechanisms, which are common for xenon difluoride, are not occurring during our fluorination. Various functional groups in the vinyl stannane are tolerated in the fluorination. The fluorination is rapid, with typical reaction times of 5 min or less. Due to the short half-life of $^{18}$F (approx. 110 min), a short reaction time is required for in vivo metabolic studies of $^{18}$F labelled compounds using PETT. Therefore, our fluorination reaction may offer a versatile $^{18}$F labelling method.

Part II: Approach To (-)-Nor-$\Delta^9$-Tetrahydrocannabinol (THC)-9-Carboxylic Acid And Synthesis Of Cannabinoid Analogs.

The concern over marijuana abuse has led to the development of a bioassay for detecting marijuana metabolites. The major human urinary metabolite of marijuana is 11-nor-$\Delta^9$-THC-9-carboxylic acid which arises from the oxidation of $\Delta^9$-THC, a major constituent of marijuana. As a
corollary, the need for this metabolite as a standard for the bioassay has led to several synthetic studies. Notwithstanding, there is still the need for an improved synthetic route for 11-nor-Δ⁹-THC-9-carboxylic acid. This part of the dissertation will address all of the strategies for improving the previous work.

Due to Δ⁹-THC's antiemetic effect, its use for patients receiving cancer chemotherapy has been legalized in U.S.A. However, the concern over its prolonged use has led to a search for cannabinoid analogs which exhibit antiemetic and not euphoric effects. Reported in this part of the dissertation are the synthesis of cannabinoid analogs which will be bioassayed by Professor A. M. Makriyannis and coworkers at the University of Connecticut.
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LIST OF ABBREVIATIONS

[α] absolute optical rotation
Ac acetate
ACN azobis(cyclohexanecarbonitrile)
AgOTf silver triflate
Anal analytical
approx approximate(ly)
aq aqueous
β beta
bp boiling point
Bu butyl
Bz benzene
Calcd calculated
cat. catalytic
Δ heat
Δ8 delta-8-
Δ9 delta-9-
DAST diethylaminoisulfur trifluoride
DBU 1,8-diazabicyclo[5.4.0]undec-7-ene
DMF dimethylformamide
DMSO dimethyl sulfoxide
EE ethoxyethyl
eq equivalent
Et ethyl
EtOAc ethyl acetate
LIST OF ABBREVIATIONS (Continued)

GC      gas chromatography
h       hour(s)
HMBC    heteronuclear multiple bond correlation
HMQC    heteronuclear multiple quantum coherence
HOTf    triflic acid
HRMS    high resolution mass spectrum
Hz      hertz
IR      infrared (spectroscopy)
LAH     lithium aluminum hydride
lit.    literature
M       molarity
M+      molecular ion
MCPBA   meta-chloroperoybenzoic acid
Me      methyl
MeOH    methyl alcohol
MHz     megahertz
min     minute(s)
mm Hg   millimeter of mercury
µmol    micromole
mmol    millimole
mp      melting point
MS      mass spectrum
N       normal
n-BuLi  n-butylithium
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>NBS</td>
<td>N-bromosuccinimide</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance (spectroscopy)</td>
</tr>
<tr>
<td>nOe</td>
<td>nuclear Overhauser enhancement</td>
</tr>
<tr>
<td>OTf</td>
<td>trflate</td>
</tr>
<tr>
<td>π</td>
<td>pi</td>
</tr>
<tr>
<td>p-TSA</td>
<td>p-toluenesulfonic acid</td>
</tr>
<tr>
<td>PETT</td>
<td>positron emission transaxial tomography</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>PPTS</td>
<td>pyridinium p-toluenesulfonate</td>
</tr>
<tr>
<td>quant</td>
<td>quantitative</td>
</tr>
<tr>
<td>r.t.</td>
<td>room temperature (appears in figures)</td>
</tr>
<tr>
<td>Rf</td>
<td>ratio to front</td>
</tr>
<tr>
<td>s</td>
<td>second(s)</td>
</tr>
<tr>
<td>SAR</td>
<td>structure-activity relationship</td>
</tr>
<tr>
<td>t-Bu</td>
<td>t-butyl</td>
</tr>
<tr>
<td>t-BuLi</td>
<td>t-butyllithium</td>
</tr>
<tr>
<td>TBDMS</td>
<td>t-butyl-di-methylsilyl</td>
</tr>
<tr>
<td>TCA</td>
<td>trichloroacetic acid</td>
</tr>
<tr>
<td>Tf</td>
<td>trflate</td>
</tr>
<tr>
<td>Tf₂O</td>
<td>triflic anhydride</td>
</tr>
<tr>
<td>Th</td>
<td>2-thienyl</td>
</tr>
<tr>
<td>THC</td>
<td>tetrahydrocannabinol</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>tlc</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethyl silane</td>
</tr>
<tr>
<td>TMSOTf</td>
<td>trimethylsilyl trifluoromethanesulfonate</td>
</tr>
<tr>
<td>Tris</td>
<td>2,4,6-tri-isopropylbenzene</td>
</tr>
<tr>
<td>Ts</td>
<td>tosylate</td>
</tr>
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</table>
PART I

FLUORINATION OF ORGANOSTANNANES WITH XENON
DIFLUORIDE AND SILVER TRIFLATE
INTRODUCTION

In 1890, carbon tetrafluoride was thought to be synthesized by Moissan as one of the earliest known man-made organofluorine compounds.\(^1\) The first fluorination method was developed by the Belgian chemist Swarts.\(^2\) This reaction involved the conversion of methyl iodoacetate to methyl fluoroacetate using silver fluoride. Swarts went on to publish several additional fluorination methods, and can be appropriately be called the "Father of Fluorination." In fact, from 1890 though 1925, Swarts was the only researcher during this period developing fluorination methods. In the beginning of the twentieth century, chemists developed a variety of new fluorination methods which led to industrially useful organofluorine compounds. These compounds were used as refrigerants, lubricants, gaskets, and aerosol propellants to name a few applications.\(^3\) The biological activity and pharmacological potential of organofluorine compounds, on the other hand, remained largely unexplored until the 1940's. The first biologically interesting organofluorine compound was fluoroacetic acid.\(^{4a-b}\) Marais and coworkers discovered that the toxic chemical in the S. African plant \textit{Dichapetalum cymosum} (gifblaar) was fluoroacetic acid. Other plants like \textit{Oxylobium parviflorum} (box poison) and \textit{Gastrolobium bilobum} (heart lead poison) also contain the toxic fluoroacetic acid. Although the typical content of fluoroacetic acid in these plants is approximately only 1\% in the dry leaves.
or seeds, it is enough to cause the deaths of thousands of cattle in South Africa and other parts of the southern hemisphere each year. The toxicity of fluoroacetic acid stems from its ability to enter the Krebs cycle at a rate comparable to that of acetic acid. This was an interesting discovery but not unexpected when considering the physical properties of fluorine. First of all, fluorine has a van der Waals radius (ca. 1.35 angstrom) which approximates hydrogen (ca. 1.10 angstrom) more closely than any other element. Therefore, recognition by biological hosts will only be affected marginally when hydrogen is substituted by fluorine in any given molecule. However, the reactivity of the fluorinated molecule relative to the unfluorinated molecule will be dramatically altered. With fluorine having an electronegativity constant of 4.0 and hydrogen 2.1, large differences in electronic effects will be observed between the two molecules. If the reactive site of the molecule is near the fluorine substituent, a large difference in chemical reactivity between the fluorinated and the corresponding unfluorinated molecule can be anticipated. Lastly, the introduction of fluorine into a molecule usually increases its lipophilicity, thus enhancing its ability to reach biological targets situated in lipophilic environments such as the inside of the cell membrane. These basic concepts are still being applied today in medicinal chemistry. The first practical organofluorine compound synthesized on the basis of these concepts was 5-fluorouracil which is an effective cytotoxic agent used in cancer chemotherapy. The insight into the pharmacological usefulness of
organofluorine compounds has spurred the development of many different methodologies for the fluorination of organic and inorganic molecules.\textsuperscript{6a-c} It is a growing field of study with newer and better methods emerging each year. Fluorination can be carried out on an ever-increasing number of functional groups, however, prior to this study the conversion of vinyl stannanes to vinyl fluorides had not been explored as a general methodology.

In connection with a project concerning the synthesis of fluorinated cannabinoids, the need to transform a vinyl stannane into a vinyl fluoride arose. In spite of the progress made in fluorination methodologies by other research groups, as of 1990, we could not find an efficient method in the literature for the conversion of a vinyl stannane to a vinyl fluoride. This seemed odd since the halogenation of vinyl stannanes with chlorine, bromine and iodine was precedent.\textsuperscript{7} Also, few methods existed for the

\[
\begin{align*}
\text{SnMe}_3 & \quad \text{"F"}^+ \\
\begin{array}{c}
R^1 \\
R^2 \\
R^3 \\
\end{array} & \rightarrow \\
\begin{array}{c}
R^1 \\
R^2 \\
R^3 \\
\end{array}
\end{align*}
\]

synthesis of vinyl fluorides in general. These include methods using the nucleophilic fluorine reagent DAST (dialkylamino sulfor trifluoride). DAST
or sulfur tetrafluoride can be used to generate a vinyl fluoride via a two step sequence from a ketone. Another two step sequence for generating a vinyl fluoride from a ketone is the modified Horner-Wittig reaction. These two types of fluorination methods suffer from poor regio- and stereoselectivity.

The ancillary goal for this research project was to fluorinate a vinyl stannane derived from a cannabinoid regiospecifically. It would also be desirable if the fluorination method was fast enough to be suitable for $^{18}$F labeling since there is a scarcity of $^{18}$F labeling methods. As an example of this method, $^{18}$F labeled cannabinoid compounds have been studied in primate brains.
source of the label was K$^{18}$F.$^{10}$ The use of $^{18}$F labeled organic compounds
marks another advancement in fluorine chemistry.$^{3}$ $^{18}$F is a positron emitter
that can be detected in small quantities by a technique called Positron
Emission Transaxial Tomography (PETT). A $^{18}$F labeled organic compound,

SCHEME 1

\[ \text{Reagents: (a) Tf$_2$O; (b) K$^{18}$F; (c) LAH; (d) EtOAc/H}^+ \]

therefore, can be tracked by PETT in order to elucidate its metabolic pathway
within the living organism.

The short lifetime (half-life = 110 min) of the $^{18}$F isotope imposes
serious time constraints on the synthesis of the labeled compound.
Preparation and purification of the labeled organic compound must take place
immediately before injection into the biological host to be studied. Therefore
in a multistep synthesis, the $^{18}$F labeling step must be carried out in the final
reaction and preparation of both the fluorinating reagent and the labeled compound must be fast.

The project described herein concerning the transformation of vinyl stannanes to vinyl fluorides had several objectives: the method had to be high yielding, fast, show tolerance to a variety of functional groups, proceed under mild reaction conditions, and make use of easily manageable reagents. Another important goal was to be able to perform the fluorination of vinyl stannanes regio- and stereospecifically. Wulff and coworkers had shown that the regiospecific generation of vinyl stannanes from the corresponding unsymmetrical ketones could be accomplished via the enol triflates, however, the stereospecificity of Wulff's enol triflate stannylation had not been demonstrated. On the other hand, stereospecific stannylation reactions have been reported using other methods. Therefore, since

\[ \text{SCHEME 2} \]

\[ \text{Reagent: (a) kinetic base/PhNTPf2; (b) (Me}_3\text{Sn})_2, \text{Pd}^0; (c) thermodynamic base/PhNTPf2.} \]
stannylations can be accomplished regio- and stereospecifically, it would be unfortunate to lose such versatility by using a fluorination method which was not regio- and stereospecific as well.

As of 1990, the fluorination of a vinyl stannane had been reported only once, to the best of our knowledge. The fluorination had been carried out using fluorine gas, and the yield of vinyl fluoride was only $\leq 5\%$. The only other related method was the fluorination of vinyllithium which was generated by metal-halogen exchange between n-butyllithium and vinyl iodide. The fluorinating reagent was $N$-alkyl-$N$-fluoro-benzenesulfonamide. Based on this reaction, it seemed possible to generate a vinyllithium directly from a vinyl stannane via transmetallation instead of metal-halogen exchange. The vinyllithium so generated could then be fluorinated by $N$-alkyl-$N$-fluoro-benzenesulfonamide to accomplish the desired goal. However, a known example where a vinyl mercury had been subjected to this procedure had yielded little vinyl fluoride thus discouraging the investigation of this approach. Instead, it was decided to develop a method which would directly convert vinyl stannanes to vinyl fluorides. The proposed reaction between a vinyl stannane and an electrophilic fluorine
source seemed possible based on other similar known fluorinating methods. These methods involve the conversion of arylstannanes and silanes to the corresponding aryl fluorides.\textsuperscript{15a,b} The fluorinating reagents used for these reactions were either \(^{18}\text{F}_2\) or CH\(_3\)CO\(_2\)\(^{18}\text{F}\). Although both of these reagents may have accomplished the desired transformation, their high toxicity and difficult handling requirements made them unattractive.

Umemoto and coworkers have developed a new fluorinating reagent, \textit{N}-fluoropyridinium triflate, which is easily manageable and stable.\textsuperscript{16} This reagent is so stable that it has a half-life of 13 d even when stirred in water at
ambient temperature, yet the fluorination of silyl enol ethers to afford α-fluoroketones can be accomplished in good yields using N-fluoropyridinium triflate. Fluorination reactions using Umemoto’s reagent are not very fast (reaction times approx 2 h), but yields are moderate to good (50-85%). Also,

\[
\begin{align*}
\text{OM} & \quad \text{NiF} \quad \text{OTf} \\
\begin{array}{c}
R^1 \quad \text{F} \\
R^2 \\
\end{array} & \rightarrow \\
\begin{array}{c}
R^1 \quad \text{F} \\
R^2 \\
\end{array}
\end{align*}
\]

32

33

\(M = \text{SiMe}_3, \text{Li or Na.}\)

fluorination of an arylmagnesium chloride using Umemoto’s reagent yielded the corresponding aryl fluoride in moderate yield.

\[
\begin{align*}
\begin{array}{c}
\text{OMgCl} \\
\text{NiF} \quad \text{OTf} \\
\end{array} & \rightarrow \\
\begin{array}{c}
\text{F} \\
\end{array}
\end{align*}
\]

34

35

29

58%

Although other pathways of generating vinyl fluorides from ketones could have been investigated, the use of vinyl stannanes suggested itself for a practical reason: the great array of synthetic methods already developed for the generation of vinyl stannanes from various functional groups other than ketones. These include the highly versatile higher-order stannane cuprates discovered by Lipshutz and coworkers. Stannane cuprates behave just like
regular carbon cuprates, allowing trialkyl tins to be coupled regio- and stereospecifically with various organic functional groups.

Another mild method for regio- and stereospecific generation of vinyl stannanes is the palladium catalyzed hydrostannylation of alkynes. These and other known synthetic methods for the generation of vinyl stannanes make them ideal starting materials for vinyl fluorides.

Summarized here are the goals for the vinyl stannane fluorination reaction: 1) the reaction must be regio- and stereospecific; 2) the yield for the reaction must be high enough to be of practical use (approx 50% or higher); 3) the reagent or reagents must be easily manageable; 4) the fluorinating reagent can be $^{18}$F labeled; 5) the reaction should be fast enough to be used for $^{18}$F labeling; 6) the reaction conditions should be mild and tolerate other functionality present in the vinyl stannane starting material.
The method that resulted from this project met all of these goals.\textsuperscript{17a,b} Since our initial publication of a vinyl fluoride synthesis, a few other publications related to this transformation have appeared. These include a fluorination using cesium fluoroxy sulfate (CsSO\textsubscript{3}F) by Widdowson and coworkers.\textsuperscript{18} Although the yields from this fluorination were slightly inferior to ours, they successfully carried out the regiospecific fluorination of 2- and 3-trimethylstannyl indole tosylates. Our method could not accomplish this in acceptable yields. On the other hand, our reagents are milder and safer than CsSO\textsubscript{3}F. CsSO\textsubscript{3}F has been reported to be shock sensitive to detonate. However, the latest vinyl stannane fluorination paper published by McCarthy and coworkers reports a new fluorinating reagent, 1-chloromethyl-4-fluoro-1,4-diazeniabicyclo[2.2.2]octane-bis-(tetrafluoroborate), which is easily manageable and stable.\textsuperscript{19}
Finally, the investigation of the mechanism of our fluorination method has resulted in an interesting discovery. It was shown that no radical intermediates were involved in the reaction. It should be pointed out that all reactions involving XeF₂ have been shown to involve an one-electron radical process, save for one example cited by Differding and coworkers.²⁰

During the course of our work, a fluorine-containing byproduct was observed. This synthetic transformation shown below has never been reported in the literature to the best of our knowledge. Other unusual reactions were observed during the optimization experiments, but no other reaction conditions were able to surpass the efficacy of XeF₂ and AgOTf for the formation of vinyl fluorides from vinyl stanannes.
RESULTS AND DISCUSSION

The first vinyl stannane for this study was prepared using the method developed by Wulff and coworkers (Scheme 3). DAST was used in order to produce a sample of vinyl fluoride 55 for comparison. The reactions of 53 with several fluorinating reagents were examined. Nucleophilic fluorinating reagents (DAST, CsF, and LiF) could not convert 53 to a vinyl fluoride. This was not surprising, since vinyl carbons attached to tin are nucleophilic in character. Attention was turned next to electrophilic fluorinating reagents. The first electrophilic fluorinating reagent investigated was N-fluoro-N-propyl-p-toluenesulfonamide. This reagent could not convert 53 to a vinyl
fluoride. The standard reaction conditions involved adding the fluorinating reagent to a vinyl stannane dissolved in either methylene chloride or acetonitrile at room temperature. This reaction was monitored by tlc until the vinyl stannane was no longer detected. Also, the reaction was monitored

\[ \text{SCHEME 4}^a \]

\[
\begin{array}{c}
51 \quad \text{t-Bu} \quad \text{O} \\
\text{DAST} \\
\longrightarrow \\
54 \quad \text{t-Bu} \\
\text{Al}_2\text{O}_3 \quad \Delta \\
\longrightarrow \\
55 \quad \text{t-Bu} \\
\end{array}
\]

\[ a \text{Reagents: (a) DAST; (b) Al}_2\text{O}_3, 100^\circ\text{C, 1 d.}\]

using wet potassium iodide-starch paper for the detection of the fluorinating reagent. If no reaction occurred at room temperature, the reaction was heated until the solvent used for the reaction was refluxing. In the end, the crude reaction mixture was analyzed using $^1\text{H}$ and $^{19}\text{F}$-NMR. If starting material was recovered even after heating for a prolonged period (3 d), the reaction was performed in a sealed tube to achieve a reaction temperature of 100°C for 1 d. Finally, the crude mixture from the sealed tube reaction was analyzed using $^1\text{H}$ and $^{19}\text{F}$-NMR. The only observable product using $N$-fluoro-$N$-propyl-$p$-toluenesulfonamide was the corresponding alkene formed from protiodestannylation by HF. HF is formed via $\beta$-elimination of the fluorinating reagent. Another electrophilic reagent investigated was $N$-fluorobenzenesulfonimide. This reagent, unlike $N$-fluoro-$N$-propyl-$p$-toluenesulfonamide, is more strongly electrophilic and does not suffer from
\[ \text{J3-elimination. However, } N\text{-fluorobenzenesulfonimide could not convert vinyl stannanes to vinyl fluorides using our standard tests. The next electrophilic reagent that was tried was } N\text{-fluoropyridinium triflate, but again, no detectable amounts of vinyl fluoride were produced. Due to the low solubility of } N\text{-fluoropyridinium triflate in methylene chloride, the solvent most often used for fluorinating silyl enol ethers, the reactivity of this reagent must involve a heterogeneous process. Therefore, fluorination with } N\text{-fluoropyridinium triflate was attempted in a melt. This was done by mixing a vinyl stannane with } N\text{-fluoropyridinium triflate and heating the mixture (190°C) until the fluorinating reagent melted. Then, the reaction was immediately cooled to room temperature and analyzed using } ^1\text{H and } ^19\text{F-NMR. Although no vinyl stannane starting material remained, the only detectable product was the corresponding alkene arising from protiodestannylation by HF. The HF is presumed to have formed from the decomposition of } N\text{-fluoropyridinium triflate.} \]

The last electrophilic fluorinating reagent investigated was \( XeF_2 \). This was the first reagent capable of converting our vinyl stannane to the corresponding vinyl fluoride. The reaction at room temperature requires

\[
\begin{array}{c}
\text{53} \xrightarrow{XeF_2, CH_2Cl_2, r.t., 3d} \text{55, 56} \\
\leq 15\% \quad \geq 80\%
\end{array}
\]

approximately 3 d for the complete disappearance, as detected by tlc, of vinyl stannane. Unfortunately, the yield of vinyl fluoride was approximately equal
β-elimination. However, N-fluorobenzenesulfonimide could not convert vinyl stannanes to vinyl fluorides using our standard tests. The next electrophilic reagent that was tried was N-fluoropyridinium triflate, but again, no detectable amounts of vinyl fluoride were produced. Due to the low solubility of N-fluoropyridinium triflate in methylene chloride, the solvent most often used for fluorinating silyl enol ethers, the reactivity of this reagent must involve a heterogeneous process. Therefore, fluorination with N-fluoropyridinium triflate was attempted in a melt. This was done by mixing a vinyl stannane with N-fluoropyridinium triflate and heating the mixture (190°C) until the fluorinating reagent melted. Then, the reaction was immediately cooled to room temperature and analyzed using 1H and 19F-NMR. Although no vinyl stannane starting material remained, the only detectable product was the corresponding alkene arising from protiodestannylation by HF. The HF is presumed to have formed from the decomposition of N-fluoropyridinium triflate.

The last electrophilic fluorinating reagent investigated was XeF2. This was the first reagent capable of converting our vinyl stannane to the corresponding vinyl fluoride. The reaction at room temperature requires approximately 3 d for the complete disappearance, as detected by tlc, of vinyl stannane. Unfortunately, the yield of vinyl fluoride was approximately equal
to or less than 15%, and the major byproduct was the corresponding alkene. The alkene was presumed to have formed as a result of protiodestannylation by HF which was formed by hydrolysis of XeF₂. The same fluorination experiment with XeF₂ was further investigated using our standard tests. Nevertheless, the major product in all cases was the alkene, while the yield of the desired vinyl fluoride never exceeded 15%.

Attempts were made to suppress the formation of the undesired alkene by using acid scavengers. The acid scavengers were propylene oxide, 3 angstrom molecular sieves, basic alumina, potassium hydroxide, and calcium carbonate. The experiment involved adding an acid scavenger to the standard fluorination reaction of a vinyl stannane with XeF₂ at ambient temperature in methylene chloride. Analysis of the reaction using tlc, ¹H, and ¹⁹F-NMR showed that these acid scavengers had no impact on the product distribution.

Another attempt to optimize the fluorination reaction involved activation of the vinyl stannane toward electrophilic attack by the addition of fluoride. The activation of vinyl stannanes by fluoride seemed possible via an "ate" type of complex. The fluoride sources were CsF, LiF, KF, CsF-Al₂O₃, and KF-18-C-6 (CsF-Al₂O₃ is a highly reactive fluoride source, and KF-18-C-6 complex was used to increase the solubility of KF in methylene chloride). Once again, analysis showed no increase in the yield of vinyl fluoride. Further attempts to optimize the fluorination reaction involved the conversion of a vinyl stannane to a vinyl cuprate for fluorination with XeF₂ or N-fluoropyridinium triflate. The vinyl cuprate which was formed from vinyl stannane was initially reacted with cyclohexenone as an electrophile to verify that the cuprate formation was successful. The vinyl cuprate
fluorination reactions, however, afforded only alkene 56. Investigating the conversion of a vinyl stannane to a vinyl palladium complex for fluorination with XeF₂, N-fluoropyridinium triflate, or LiF also failed to produce vinyl fluoride. Pd(PPh₃)₄, Pd₂(dba)₃, and PdCl₂(PPh₃)₂ were used as the palladium catalysts for this investigation.
I. Fluorination of vinyl stannanes with XeF$_2$ and AgPF$_6$

At this point of the research, it was concluded that XeF$_2$ was the best fluorinating reagent for the conversion of vinyl stannanes to vinyl fluorides. Optimization of the fluorination reaction with XeF$_2$ by varying the reaction temperature (10°C to 100°C), changing solvent (methylene chloride, benzene, or acetonitrile), activating the vinyl stannane to a better nucleophile (ate complex, vinyl cuprate, and vinyl palladium), and attempts to suppress the alkene byproduct using acid scavengers, were all unsuccessful in optimizing the yield of vinyl fluoride beyond 15%. The only thing left to try was activation of XeF$_2$. XeF$_2$ in conjunction with boron trifluoride etherate, which is known to generate a more reactive electrophilic fluorinating reagent, was tried.$^{23}$ Unfortunately, this mixture did not fluorinate vinyl stannanes. In fact, the only observable product from this reaction was the alkene. At this point in the project, it seemed unlikely that a direct and high yielding conversion of vinyl stannanes to vinyl fluorides could be found. Although a vinyl fluoride had been formed from a vinyl stannane using XeF$_2$, a 15% yield was not a suitable result for publication as a fluorination method. A suitable method would have to generate at least a 50% yield of vinyl fluoride.

Before abandoning this fluorination project, it was decided to try one more reaction, and to activate the XeF$_2$ with silver(I).$^{26}$ Since silver(I) is known to complex or abstract halide anions, a proposal was made to activate the XeF$_2$ as shown below. If silver(I) could abstract a fluoride anion from XeF$_2$, FXe$^+$ might be formed and might be electrophilic enough to fluorinate
vinyl stannanes. In any event, the use of XeF$_2$ in conjunction with silver hexafluorophosphate (AgPF$_6$) converted a vinyl stannane, 49, to a vinyl fluoride, 50, in 51% isolated yield. Vinyl stannane 49 was formed from the

\[
\text{F-Xe-F + Ag (I)} \xrightarrow{-\text{AgF}} \text{F-Xe} \xrightarrow{-\text{Xe(g)}} \text{F}^+ 
\]

corresponding enol triflate using Wulff's procedure.$^{11}$ This vinyl stannane was used instead of vinyl stannane 53 to prevent mechanical loss of the corresponding vinyl fluoride (vinyl fluoride 55 is volatile while 50 is not). To investigate the scope and utility of this method, several vinyl stannanes were synthesized. These vinyl stannanes and fluorides are illustrated below (Figure 1).

Figure 1: Vinyl stannanes and fluorides used for fluorination investigations.
The utility of this method was demonstrated by the fluorination of several different vinyl stannane substrates (Table 1) and was the first successful vinyl stannane fluorination reported in the literature. Vinyl stannanes 59a, 60a, 61a, and 62a were synthesized from the corresponding ketones and vinyl stannane 63a from the corresponding ester using Wulff's stannylation chemistry. The formation of the Z enol triflate 65 is

Table 1: Fluorinations of vinyl stannanes with XeF₂ and AgPF₆ in CH₂Cl₂ at ambient temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinyl Stannane</th>
<th>Product</th>
<th>Reaction time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59a</td>
<td>59b</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>60a</td>
<td>60b</td>
<td>3</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>61a</td>
<td>61b</td>
<td>3</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>62a</td>
<td>62b</td>
<td>6(2)</td>
<td>35(23)</td>
</tr>
<tr>
<td>5</td>
<td>63a</td>
<td>63b</td>
<td>18(3)</td>
<td>35(43)</td>
</tr>
</tbody>
</table>

a) Reaction temperature was 35°C.

The stannylation of enol triflate 65 demonstrates the stereospecificity of Wulff's stannylation methodology for the first time. The regioisomeric vinyl stannanes 60a and 61a were both synthesized from the corresponding unsymmetrical ketone.
The examples of table 1 illustrate several important features of this method. The fluorination was regio- and stereospecific, temperature dependent, and fast, since vinyl stannanes were consumed within 3 h. The major byproduct in all cases was the corresponding alkene. Due to the increase in the rate of vinyl stannane consumption when XeF₂ was used in conjunction with AgPF₆ (3 h versus 3 d), it was concluded that AgPF₆ was activating or reacting with either the vinyl stannane or XeF₂.

II. Fluorination of vinyl stannanes with XeF₂ and AgOTf

A number of fluorinations with XeF₂/AgPF₆ unfortunately gave disappointing yields of vinyl fluoride (Table 1). As a consequence, it became clear that the methodology needed further improvement in order to become generally applicable. The most logical technique was to change the counterion of the silver(I) salt for improving the yield of vinyl fluoride. This proved to be effective. As one uses weaker bases as counterions for
silver(I), one gets a higher yield of vinyl fluoride. The best yield of vinyl fluoride with XeF₂ was accomplished using either silver tetrafluoroborate (AgBF₄) or silver triflate (AgOTf) in place of AgPF₆. In addition to the increase in yield, the rate of reaction was increased as well. Vinyl stannanes were consumed in less than 5 min when XeF₂ was used in conjunction with either AgBF₄ or AgOTf.

The fluorination reaction with XeF₂ in conjunction with either AgBF₄ or AgOTf was optimized further. The optimization experiments initially involved changing the stoichiometries of AgBF₄ and AgOTf which led to several interesting discoveries. The use of sub-stoichiometric AgOTf or AgBF₄ can effect the fluorination in moderate to good yields. The use of excess AgOTf and AgBF₄ does not improve the yield of vinyl fluoride. The use of excess AgBF₄, however, affords a different organofluorine product. The organofluorine product was shown to be the trifluorocyclohexane 66. The trifluoro compound was presumed to be formed from the corresponding vinyl fluoride. In order to substantiate this, vinyl fluoride 50 was treated with
excess XeF₂ and AgBF₄ to afford the trifluoro compound 66 in approximately 90% isolated yield. The formation of the trifluoro compound was presumed to be a HBF₄-catalyzed reaction similar to the HF-catalyzed fluorination of an electron rich alkene with XeF₂. This unusual trifluorination reaction was investigated further on a different vinyl stannane, 68. However, the optimization of this reaction could not be accomplished, and the major byproduct was determined to be the corresponding 1,1-difluoro-2-hydroxy compound, 70, which may have been formed from the solvolysis of 69. The formation of 70, therefore, may be unique for this substrate. The main difficulty in the optimization of the trifluorination of vinyl stannanes was
due to competing protiodestannylation. Therefore, converting vinyl fluoride to the corresponding trifluoro analog was a higher yielding process.

In any event, the best condition for the conversion of vinyl stannanes to vinyl fluorides required the use of XeF₂ together with AgOTf. The vinyl stannanes and fluorides used for this study are illustrated (Figure 2). All the vinyl stannanes in Table 2 were synthesized from the corresponding enol triflates,¹¹ alkynes,¹²d or trisylhydrazones.²⁹ Some of the vinyl fluorides in table 2 were volatile and actual yields may have been higher. The fluorinations were fast (< 5 min) except for the fluorination of vinyl stannane 77a which took approximately 20 min. The major product from the fluorination of vinyl stannane 77a was the corresponding dimer which was isolated in approximately 30% yield. Diluting the reaction by a factor of 2 had
Figure 2: Vinyl stannanes and fluorides.
Table 2: Fluorinations with XeF₂ and AgOTf in CH₂Cl₂ at r.t.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinyl Stannane</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>50</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>59a</td>
<td>59b</td>
<td>37</td>
</tr>
<tr>
<td>3</td>
<td>60a</td>
<td>60b</td>
<td>60</td>
</tr>
<tr>
<td>4</td>
<td>61a</td>
<td>61b</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>62a</td>
<td>62b</td>
<td>67</td>
</tr>
<tr>
<td>6</td>
<td>63a</td>
<td>63b</td>
<td>53</td>
</tr>
<tr>
<td>7</td>
<td>71a</td>
<td>71b</td>
<td>52</td>
</tr>
<tr>
<td>8</td>
<td>72a</td>
<td>72b</td>
<td>62</td>
</tr>
<tr>
<td>9</td>
<td>73a</td>
<td>73b</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>74a</td>
<td>74b</td>
<td>45</td>
</tr>
<tr>
<td>11</td>
<td>75a</td>
<td>75b</td>
<td>37</td>
</tr>
<tr>
<td>12</td>
<td>76a</td>
<td>76b</td>
<td>67</td>
</tr>
<tr>
<td>13</td>
<td>77a</td>
<td>77b</td>
<td>20</td>
</tr>
<tr>
<td>14</td>
<td>78a</td>
<td>78b</td>
<td>73</td>
</tr>
<tr>
<td>15</td>
<td>79a</td>
<td>79b</td>
<td>35</td>
</tr>
<tr>
<td>16</td>
<td>80a</td>
<td>80b</td>
<td>50</td>
</tr>
<tr>
<td>17</td>
<td>81a</td>
<td>81b</td>
<td>50</td>
</tr>
</tbody>
</table>

no noticeable effect on product distribution. Finally, the synthesis of vinyl stannane 81a is shown below (Scheme 3). Vinyl stannane 73a was synthesized from the corresponding alkyne (Scheme 4).¹²ᵈ
SCHEME 3

Reagents: (a) TMSOTf, Et3N (quant.); (b) TMSOTf (cat), HC(OMe)3 (96%); (c) TrisNHNH2, MeOH (46%); (d) n-BuLi (3 eq)/ Me3SnCl (2 eq) (30%).

SCHEME 4

Reagents: (a) propargyl magnesium bromide (98%); (b) PdCl2(PPh3)2, Me3SnH.
XeF₂ in conjunction with AgOTf fluorinated vinyl stannanes effectively in moderate to good yields, rapidly with reaction times less than 5 min, under mild reaction conditions, regio- and stereospecifically, and with tolerance of various functionalities present in the vinyl stannane starting material. As a result of these findings, especially the rapid rate of reaction, this method appears very well suited for the use in ¹⁸F-labeling. Furthermore, ¹⁸F-labeled XeF₂ is a known reagent.³⁰

The sluggish rate of reaction between vinyl stannane ⁴⁹ and XeF₂, alone (3 d) or with AgPF₆ (3 h), is not entirely accurate. It should be mentioned that decomposition of XeF₂ at r.t. in CD₂Cl₂ is complete after approximately 3 h as judged by ¹⁹F-NMR. The decomposition product is HF. XeF₂ reacts with water to form H₂O₂ and HF.³¹ In fact, when XeF₂ is dissolved in methylene chloride at ambient temperature, bubbling occurs within 30 min followed by the flask being cleaned and etched during this period by HF. Therefore, if fluorination of a vinyl stannane is not complete within approximately 1 h, the rest of the vinyl stannane is slowly protonated by HF, a process which may take up to 3 d to proceed to completion. The long reaction time for HF protonation of the vinyl stannane is due to the low concentration of HF. During this period, the solution still contains an oxidant which was detected by potassium iodide-starch paper. This oxidant was previously thought to be leftover XeF₂ instead of the more likely H₂O₂.

\[
\text{XeF}_2 + 2\text{H}_2\text{O} \rightarrow \text{H}_2\text{O}_2 + 2\text{HF} + \text{Xe}
\]

During the further investigation of the utility of this fluorination method, several ambiguous results were obtained. First, the fluorination of
some vinyl stannanes derived from cyclic ketones (Figure 3) resulted in a poor yield of vinyl fluoride (Table 3). In particular, eight and nine membered ring vinyl stannanes were fluorinated in poor yield, whereas the fluorination of six, seven, and twelve membered ring vinyl stannanes afforded the corresponding vinyl fluorides in moderate to good yields. In addition, the fluorination of eight and nine membered ring vinyl stannanes resulted in a sluggish reaction requiring about 1 d for the complete consumption of the starting materials. This was the first indication that silver(I) might be activating the vinyl stannane substrate toward fluorination by XeF₂ and not silver(I) activating the XeF₂ in forming a more reactive fluorinating reagent. The line of reasoning for this postulate is as follows. If XeF₂ reacted with AgOTf to form a more reactive fluorinating species, one would not expect

![Diagram of vinyl stannanes derived from cyclic ketones](image)

**Figure 3: Vinyl stannanes derived from cyclic ketones.**
Table 3: Fluorination results of cyclic vinyl stannanes.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinyl Stannane</th>
<th>Product</th>
<th>Reaction time</th>
<th>Vinyl fluoride to alkene ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>50</td>
<td>5 min</td>
<td>79:21</td>
</tr>
<tr>
<td>2</td>
<td>90a</td>
<td>90b</td>
<td>5 min</td>
<td>70:30</td>
</tr>
<tr>
<td>3</td>
<td>91a</td>
<td>91b</td>
<td>1 d</td>
<td>20:80</td>
</tr>
<tr>
<td>4</td>
<td>92a</td>
<td>92b</td>
<td>1 d</td>
<td>10:90</td>
</tr>
<tr>
<td>5</td>
<td>59a</td>
<td>59b</td>
<td>12 min</td>
<td>37:63</td>
</tr>
</tbody>
</table>

To see such a difference in reactivity between substrates of varying ring size, rather it must be the strength of the Ag(I) complexation to the vinyl stannanes that varied. Such variations in complexation strengths have been reported for the interaction between Ag(I) and cycloalkenes. For example, while cis-cyclooctene does not form a π-complex with Ag(I), the more energetic trans-cyclooctene forms a complex so strong that it is water soluble. Similarly, the eight and nine membered ring vinyl stannanes may not be activated, or be activated weakly, by AgOTf for electrophilic attack by XeF₂. Therefore, XeF₂ will instead protiodestannylate the vinyl stannane to form the corresponding alkene.

An important question to ask was where did the hydrogen source come from in forming the alkene byproduct. The answer to this question might suggest a way to suppress this unwanted byproduct. The most probable answer was that the hydrogen source was coming from the solvent used in the reaction, methylene chloride. Thus, aprotic solvents were investigated in the fluorination. Reactions were carried out in hexafluorobenzene, CD₂Cl₂.
or 1,1,2-trichloro-1,2,2-trifluoroethane, but no noticeable suppression of the alkene was observed. Therefore, the solvent was then ruled out as being the hydrogen source. Since XeF₂ and AgOTf are both hygroscopic reagents, it was postulated that the hydrogen source could be a proton from H₂O. However, when the fluorination was done in the presence of excess D₂O mixed with methylene chloride, the undeuterated alkene was still formed as usual. Therefore, it seemed likely that the proton source had to be from the methyl groups of the trimethyl tin moiety. Since deleting the protons on the trimethyl tin moiety would be difficult, the efficient scavenging of HF had to be examined once again. This approach proved successful when 2,6-di-tert-butyl-4-methylpyridine²⁷ was used as an acid scavenger. The fluorination of the nine membered ring vinyl stannane, 92a, with XeF₂ in association with AgOTf and 2,6-di-tert-butyl-4-methylpyridine gave a vinyl fluoride to alkene ratio of 9 : 1 in approximately quantitative yield. This was a drastic improvement from a vinyl fluoride to alkene ratio of 1 : 9 when 2,6-di-tert-butyl-4-methylpyridine was not used. Since this pyridine base was known to be²⁷ an effective, non-nucleophilic Bronsted-Lowry acid scavenger, the hypothesis that the alkene formation was due to protiodestannylation by a Bronsted-Lowry acid, and not a hydrogen radical, was further substantiated. Experiments were carried out using 0.1, 1.0, and 2.0 eq (s) of the base and surprisingly the same high degree of alkene suppression was observed in all cases. The effective alkene suppression with 0.1 eq of 2,6-di-tert-butyl-4-methylpyridine is likely due to suppression of XeF₂ decomposition which is catalyzed by HF. The XeF₂ decomposes to generate a fluorine radical which can abstract a hydrogen radical from the methyl groups on tin. This then leads to more HF production giving rise to the alkene byproduct. This XeF₂
decomposition is initially triggered by catalytic HF. Therefore, if no HF is allowed to react with XeF₂ in the first place, no substantial amounts of HF or alkene are produced. The use of 2,6-di-tert-butyl-4-methylpyridine had no effect for fluorination reactions which proceed fast and in moderate to high yields (≥ 50%).

Another ambiguous fluorination result involved the fluorination of indolyl stannanes with XeF₂ and AgOTf (Scheme 7). The poor fluorination of indolyl stannanes can be explained by poor complexation of AgOTf to the heteroaromatic π-electrons thus providing insufficient activation for the electrophilic attack on the tin-bearing carbon by XeF₂. This hypothesis was further substantiated by the fact that 2-stannyl indole was preferentially fluorinated in the 3 position by XeF₂ and AgOTf. This was the result one would expect for an electrophilic attack on an indole system by XeF₂ alone, and it was therefore concluded that AgOTf did not partake in the reaction to any substantial degree.

An ambiguous fluorination result which has yet to be explained was the fluorination of monosubstituted E-vinyl stannane. The fluorination of this type of substrate with XeF₂ and AgOTf consistently led to poor yields of the vinyl fluoride which were always accompanied by numerous byproducts with no clear major component. Due to the complicated nature of these reactions, the fluorination of this type of vinyl stannane was not examined further.
SCHEME 7a

Reagents: (a) t-BuLi; (b) (PhSO₂)₂NF; (c) Me₃SnCl; (d) XeF₂, AgOTf, 1 min.
An interesting fluorination result involved the fluorination of 1-stannyl styrene substrates. The fluorination of these substrates predominantly gave rise to the corresponding $\alpha$-fluoro ketones. Also,

\[
\begin{align*}
\text{MeO} & \quad \text{SnMe}_3 \\
\text{MeO} & \quad \text{SnMe}_3 \\
101 & \quad \text{SnMe}_3
\end{align*}
\]

\[
\begin{align*}
\text{XeF}_2 & \quad \text{AgOTf} \\
\text{MeO} & \quad \text{MeO} \\
102 & \quad \text{MeO}
\end{align*}
\]

25%

another research group investigating the conversion of vinyl stannanes to vinyl fluorides has observed the same result when using cesium fluoroxy sulfate. In stark contrast to this, 1-stannyl-2-carboethoxy styrene, 72a, underwent smooth fluorination without ketone formation when treated with $\text{XeF}_2$ and AgOTf. It appears, however, that substrates which have the potential to form a stable carbocation on the carbon bearing the tin lead to $\alpha$-fluoro ketones upon fluorination. The fluorination of 1-stannyl-2-carboethoxy and 1-stannyl-2-phenyl styrene derivatives has not been carried out using cesium fluoroxy sulf ate.

The fluorination of 1-trimethylstannyl-1-ene-3-ol, 104, was conducted as well. The desired vinyl fluoride was formed in poor yield ($\leq 10\%$) while the major byproduct from this reaction was the corresponding enal. The byproduct is likely due to solvolysis of the corresponding vinyl fluoride 105. The formation of 1-trimethylstannyl-1-ene-3-ol, 104, is likely higher than what is reported herein. This stannylation reported herein requires further scrutiny.
All vinyl stannanes described so far were synthesized from enol triflates with either a stannyl cuprate$^{12b}$ or (Me$_3$Sn)$_2$ and Pd$^{0,11}$ or via palladium or ACN catalyzed hydrostannylations of alkynes,$^{12d}$ or

**SCHEME 8**

\[
\begin{align*}
\text{103} & \xrightarrow{a} \text{104} \\
\text{OH} & \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad \quad Pharma
isolation. Therefore, mechanical loss of vinyl fluoride due to volatility is minimized. Although trimethylstannyl hydride had been made and used in this project previously, for convenience the more stable and commercially available tributylstannyl hydride was used for the stannylation of vinyl sulfones. It should be noted, therefore, that the fluorination of a trimethylvinyl stannane afforded a slightly higher yield of a vinyl fluoride than the corresponding tributylvinyl stannane. The difference in vinyl fluoride yields between the two vinyl stannanes will be discussed later in this chapter. The various vinyl stannanes and fluorides prepared by the modified Petersen reaction are illustrated (Figure 4) along with the fluorination results (Table 4). These results demonstrate that terminal 2,2-dialkyl-1-vinyl

![Diagram of vinyl stannanes and fluorides derived via the modified Petersen reaction.](image)

Figure 4: Vinyl stannanes and fluorides derived via the modified Petersen reaction.
Table 4: Fluorinations of vinyl stannanes with XeF₂ and AgOTf in CH₂Cl₂ at ambient temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Vinyl Stannane</th>
<th>Product</th>
<th>Vinyl fluoride yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>108</td>
<td>109</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>110</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>111a</td>
<td>111b</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>112a</td>
<td>112b</td>
<td>57</td>
</tr>
<tr>
<td>5</td>
<td>113a</td>
<td>113b</td>
<td>44</td>
</tr>
<tr>
<td>6</td>
<td>114a</td>
<td>114b</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>115a</td>
<td>115b</td>
<td>40&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

a) Yield was approximated based on <sup>1</sup>H-NMR integration.

stannanes of E or Z geometry can be fluorinated efficiently by XeF₂ in conjunction with AgOTf. Only terminal 2-alkyl-1-vinyl stannanes of E geometry are not efficiently fluorinated by this reagent system, based on few examples reported herein.

The fluorination of 2,2-dialkyl-1-vinyl stannanes was recently investigated by McCarthy and coworkers. They have successfully fluorinated a series of fluoro-vinyl stannanes using 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo-[2.2.2]-octane-bis-(tetrafluoroborate) to form 1,1-difluoro olefins. The fluorination of stannane 68 by McCarthy's method proceeds in higher yield than with XeF₂ and AgOTf. Whether this is a general trend
remains to be answered. McCarthy's method uses a less expensive reagent, but reaction conditions are not as mild and the reaction is slower. For both fluorination methods, the only observable byproduct is the corresponding alkene.

The fluorination of a vinyltrimethyl stannane, vinyltributyl stannane, and vinyltrimethyl silane with XeF₂ and AgOTf was carried out for comparison. The fluorination of the vinyltrimethyl stannane afforded a
higher yield of vinyl fluoride than the fluorination of vinyltributyl stannane (79% versus 41%). The fluorination of the corresponding vinyltrimethyl silane gave a poor yield of vinyl fluoride (<10%). This is the same trend that has been reported in the literature when using electrophilic fluorine (i.e. F₂ and CsO₂SO⁻) sources for fluorination of aryl stannanes and silanes.¹⁵ᵃ,b The poor result with the vinyltrimethyl silane was disappointing. A vinyltrimethyl silane substrate would be preferable for fluorination than the corresponding stannane due to the lower toxicity associated with silanes.

The fluorination of cross- and through-conjugated divinyl stannanes was investigated. The fluorination of the through-conjugated divinyl stannane was disappointing. ¹H and ¹⁹F-NMR spectra of the crude reaction mixture showed no trace of the desired vinyl fluoride. Rather, it seemed evident from HP-tlc that a substantial amount of polymerization had occurred. Polymerized compounds typically do not move on tlc even when using highly polar solvents as the mobile phase. The fluorination of the cross conjugated divinyl stannane did not form any desired vinyl fluoride. What was observed as the major product was the corresponding aromatized compound in which the methyl group had migrated. These types of fluorinations were not investigated further.
SCHEME 9a

Reagents: (a) H+ (40%); (b) triflic anhydride, 2,5-di-tert-butyl-4-methylpyridine (66%); (c) LDA/PhNTf2 (52%); (d) (Me3Sn)2, Pd0 (15%); (e) (Me3Sn)2, Pd0 (15%); (f) XeF2, AgOTf; (g) XeF2, AgOTf (43%).
III. Mechanistic studies

A mechanistic study was undertaken in order to gain a deeper understanding of the fluorination reactions. Insight into the reaction mechanism would allow one to predict the outcome of any future fluorination reactions and lead to improved reaction conditions. With the exception of one study by Differding, all work with XeF₂ to date had implicated a radical pathway. The fluorine radical generated by XeF₂ has also been found to be electrophilic in character. Therefore, it was initially thought that a vinyl radical intermediate would be involved in the fluorination reactions, and the isolation of small amounts of dimer appeared to give support to this assumption. The dimer seemed likely to be derived from the homocoupling of the corresponding vinyl radicals. To investigate a possible vinyl radical intermediate in our fluorination reaction, several experiments were conducted. The intermolecular radical trapping experiments using acrylonitrile or vinylidene chloride, in excess or as solvents, failed in all cases. All fluorinations conducted in the presence of these radical trapping reagents gave the vinyl fluoride as the major product as if no radical trapping reagents had been present. However, these results did not rule out the possible existence of a vinyl radical by any means. If the fluorination of a vinyl radical by a fluorine radical source was very rapid, intermolecular radical trapping reagents may have been too slow to compete. Therefore, an intramolecular radical trapping experiment was carried out. A suitable substrate was synthesized and fluorinated by XeF₂ in conjunction
with AgOTf (Scheme 10). In view of the extensive literature proving that XeF₂ is an electrophilic fluorine radical source, the result of the fluorination reaction was surprising. No cyclized product was observed, and the vinyl fluoride was isolated in 84% yield, which was the highest yield obtained for any substrate under these conditions. The remainder of the material consisted of the alkene. Although one could argue that the cyclization would not be observed if the fluorination was considerably faster, a known related example suggests otherwise. Also, the cyclization of vinyl radical has been demonstrated to be even faster than the corresponding alkyl radical cyclization. The presence of AgOTf, on the other hand, could make a difference. Complexation of Ag(I) to the monosubstituted double bond might decrease its nucleophilic character, thus hampering the cyclization reaction involving a vinyl radical. Even though only one equivalent of AgOTf was used, this complexation would not
necessarily have an adverse effect on the fluorination reaction, since the
fluorination proceeded well even if a catalytic amount of AgOTf was present,

SCHEME 10

\[ \text{Reagents: (a) NaH, (MeO)\textsubscript{2}CO (97%); (b) 2 eq n-BuLi/4-bromobutene (96%); (c) LiCl, DMSO (49%); (d) LDA/PhNTf\textsubscript{2} (75%); (e) (Me\textsubscript{3}Sn)\textsubscript{2}, Pd\textsuperscript{0} (51%); (f) XeF\textsubscript{2}, AgOTf.} \]
as demonstrated earlier. Nevertheless, the failure of the vinyl stannane substrate 134 to cyclize does support a nonradical intermediate in our fluorination reaction. Furthermore, another research group has shown that

\[
\text{CCO}_2\text{H} \xrightarrow{\text{XeF}_2} \text{137} \xrightarrow{72\%} \text{138} + \text{139} \xrightarrow{25\%}
\]

in the radical pathway, XeF\textsubscript{2} generates a deep-purple colored species which is due to the formation of a cation radical of the organic substrate.\textsuperscript{34} No deep purple colored solution was observed at any point in the fluorination reactions reported herein. On the basis of these results, it was presumed that XeF\textsubscript{2} was not reacting via a radical pathway in this fluorination reaction.

The next task in this mechanistic study was to address whether the AgOTf was reacting with XeF\textsubscript{2} or the vinyl stannane. Based on several experiments, we were able to gain several lines of evidence that the silver (I) salt was reacting with the vinyl stannane rather than with XeF\textsubscript{2}. First, if XeF\textsubscript{2} reacted with AgOTf to form a more reactive fluorinating reagent, several possible species could be generated. The species shown below, or very similar species, have been reported in the literature, along with spectroscopic data.\textsuperscript{39a-c} This suggested several NMR experiments to determine if any of

\[
\text{FXe}^+ \quad \text{FXeOTf} \quad \text{FOTf}
\]

\[
\text{140} \quad \text{141} \quad \text{142}
\]
these species were being formed during the fluorination reaction. The fluorination reactions were carried out in a NMR tube and scanned at various temperatures (-80°C to r.t.). In all these NMR studies (1H-, 19F-, and 119Sn-NMR), none of the species were detected. The number of scans and scale of the reactions (0.16 mmol in 0.5 mL of CD2Cl2) in the NMR tube were performed in a manner such that a minimum of 0.5% of any steady state species should have been detected in the 19F-NMR (283 MHz). The value of 0.5% comes from the detection of 13C-satellites (-77.5 ppm, J = 320 Hz) from a saturated solution of AgOTf (0.16 mmol) in DMSO-d₆. This quantitative value could not be determined using CD2Cl₂ as the solvent due to the insoluble nature of AgOTf in this solvent. The 320 Hz coupling of 13C-F was verified by 13C-NMR of AgOTf (121 ppm, quartet, J = 322 Hz) in DMSO-d₆. Therefore, these NMR studies allowed us to conclude that AgOTf was not reacting with XeP₂ to form a more reactive, electrophilic fluorinating reagent. Nevertheless, realising that these species, if formed, could have been present in catalytic amount (< 0.5%) and/or have been short lived, other experiments were conducted to further substantiate this conclusion. These experiments, shown below, were conducted simultaneously with a control and showed that a more reactive electrophilic fluorinating reagent was not being formed. If a new electrophilic fluorinating species was being formed between XeF₂ and AgOTf, differences in organofluorine yields, amount of recovered starting material, and distribution of organofluorine products should have been observed for these reactions. However, the addition of AgOTf made no difference in the fluorination of these substrates. Therefore, AgOTf must be reacting or complexing with the vinyl stannane to create a more reactive
substrate while AgOTf does not complex any of the substrates shown below. To further substantiate this hypothesis, the fluorination of a vinyl stannane was tried using AgOTf and N-fluoropyridinium triflate in place of XeF₂. As expected, and in support of this hypothesis, the fluorination with N-fluoropyridinium triflate in conjunction with AgOTf gave some of the vinyl fluoride. Although the yield of vinyl fluoride was low, this was the first time
A vinyl stannane had been fluorinated by N-fluoropyridinium triflate, despite substantial efforts made early in this project. Therefore, the vinyl stannane becomes a better nucleophile with the aid of AgOTf. To gain further evidence for this hypothesis and to perhaps discover another synthetic method, other electrophiles were treated with vinyl stannanes mixed with AgOTf. The electrophiles were enones and ynones that readily undergo a 1,4-addition reaction when treated with nucleophiles. However, the treatment of a mixture of vinyl stannane 49, AgOTf, and several enone derivatives did not form any 1,4-adducts. Instead, the corresponding dimer was the major product, with alkene as the minor byproduct. This was the same result as when vinyl stannane 49 was treated with AgOTf alone. A few other dimers were isolated from the fluorination reactions, and it was determined that dimer formation takes place between the carbons that were directly attached to tin. All the dimers isolated and characterized are represented below.
To understand the reaction between vinyl stannanes and AgOTf in the absence of XeF₂, an intramolecular radical trapping experiment was conducted. The result of this experiment afforded no cyclized product when vinyl stannane 134 was treated with AgOTf. In fact, the only detectable product based on crude ¹H-NMR formed from this reaction was the corresponding alkene 136 which was isolated in 72% yield. The lack of dimer formation during all the other vinyl stannane fluorinations was not surprising. When vinyl stannanes which have a substituent on the carbon adjacent to the tin-bearing carbon are treated with AgOTf alone, the corresponding dimers are not formed in any detectable amount. Instead, the corresponding alkene is formed as the major product.

Due to the absence of cyclized product during the intramolecular trapping experiment of vinyl stannane 134 with AgOTf alone, a vinyl radical intermediate did not seem to be present in this reaction either. Another research group has shown that the radical cyclization should have competed well with hydrogen radical transfer.³⁸ Although the AgOTf may be complexing to the less hindered double bond thus inhibiting cyclization of a vinyl radical intermediate from vinyl stannane 134, the efficient dimer formation from vinyl stannane 49 need not be attributed to the homocoupling of two vinyl radicals. The dimer from 49 was formed in 90% isolated yield when treated with AgOTf. It is well established that radical species are short-lived and only present in low concentrations at any given time. Therefore, the probability of two vinyl radicals coupling to afford a high yield of the corresponding dimer is unlikely.

The evidences in the mechanistic studies were gained mainly from the fluorination reaction results and not from spectroscopy. After realising that
AgOTf interacted with the vinyl stannane and not XeF₂, a number of possible mechanistic pathways were mapped out. One such pathway involved Me₃SnOTf as the catalyst for the fluorination reaction (Figure 5). Although Me₃SnOTf could not be detected by ¹¹⁹Sn-NMR, both Me₃SnOTf and n-Bu₃SnOTf were synthesized and used in experiments in which a vinyl stannane was treated with the stannyl triflate and XeF₂. However, these reactions afforded vinyl fluoride in low yields (≤ 20%). Varying the stoichiometries of Me₃SnOTf or n-Bu₃SnOTf merely led to complex mixtures

![Figure 5: The postulated Me₃SnOTf catalyzed fluorination of a vinyl stannane with XeF₂ and AgOTf.](image-url)
of byproducts and no improvement of vinyl fluoride yield. From these results, the mechanism which is summarized in figure 5 seemed unlikely.

Two different mechanistic pathways could be constructed on the basis of direct interaction between Ag(I) and the vinyl stannane (Figure 6). In

PATH 1

\[
\begin{align*}
\text{Me}_3\text{Sn} & \quad \text{AgOTf} \\
& \quad \text{XeF}_2 \\
& \quad \text{SnMe}_3 \text{AgOTf} \\
& \quad \text{Me}_3\text{SnF} \\
& \quad \text{F}
\end{align*}
\]

PATH 2

\[
\begin{align*}
\text{SnMe}_3 & \quad \text{AgOTf} \\
& \quad \text{Me}_3\text{Sn} \\
& \quad \text{Ag} \\
& \quad \text{F} \quad \text{Xe}
\end{align*}
\]

Figure 6: Two postulated mechanistic pathways for the fluorination of vinyl stannanes with XeF₂ and AgOTf.

In the first pathway, silver merely complexes the vinyl stannane to facilitate fluorination, while in the second one, direct reaction takes place to form a vinyl silver, which is subsequently fluorinated by XeF₂. At first glance, Path 1 seemed to be the more likely mechanism, since E and Z vinyl stannanes are
fluorinated stereospecifically. Path 2 involves a carbocation intermediate and one would expect to see some degree of isomerization, if this was operating. Secondly, no cyclic ethers were formed in the fluorination of vinyl stannane 89 and therefore one would have to conclude, that if a carbocation is involved, it must be very short lived. One example, however, seemed to suggest that Path 2 could be in operation. Treatment of vinyl stannane 156 with XeF₂ and AgOTf afforded the first non-stereospecific fluorination and trifluorination with AgOTf. Trifluorinations had been observed only when using AgBF₄. The poor stereoselectivity and the formation of trifluoride strongly suggest a Path 2 type of mechanism when using this vinyl stannane substrate, 156, for fluorination. As can be seen (Figure 7), the first carbocation
generated is stabilized by the two metals, tin and silver. This type of stabilization by metals with d-orbital electrons is common when the carbocation is in the β position relative to the metal. The difference between this vinyl stannane relative to almost all the other E or Z vinyl stannanes is a phenyl ring which can further stabilize this proposed carbocation. Destannylation of this carbocation removes a very bulky group. As a result, the unfavorable steric interaction between the vicinal phenyl groups can now be released through rotation around the single bond created temporarily by the formation of the second carbocation. This sterically less hindered carbocation intermediate can then regenerate the double bond by losing silver(I) to form the product. Therefore, both the vinyl fluoride and the alkene (stilbene) were isolated as a 1:1 mixture of E and Z isomers. It
should be noted, however, that the isomerization of these types of vinyl fluorides to the thermodynamically favored isomer by AgOTf, or light, may be occurring. Therefore, this one example of a non-stereospecific fluorination needs further scrutiny.

Formation of the trifluoride from this substrate was suppressed by using 1.0 eq of 2,6-di-tert-butyl-4-methylpyridine instead of 0.1 eq. Although the use of 1.0 eq of 2,6-di-tert-butyl-4-methylpyridine suppressed formation of the trifluoride, the fluorination reaction was still non-stereospecific. Also, the treatment of this vinyl stannane with AgOTf in the absence of XeF2 afforded a mixture of stilbenes, but with the trans isomer predominating. Carrying out the reaction with XeF2 in the absence of AgOTf yielded another interesting result. Even though no silver was present, very little isomerization was observed and the yield of vinyl fluoride (approx 30%)

![Diagram](image)

was higher than in any previous experiment in which XeF2 had been used alone. This unusual result must also be attributed to the benzene ring $\beta$ to
the tin metal which could further stabilize a carbocation intermediate as illustrated below (Figure 8). In contrast to the silver catalyzed mechanism (Figure 7), this mechanism only involves one carbocation intermediate in which rotations are hampered, or slowed, by phenyl-stannyl steric interactions. Consequently, only relatively small amounts of the isomerized products were isolated. As far as the fluorination of all other vinyl stannanes, a carbocation intermediate is not likely due to our examples of regio- and stereospecific fluorinations. The exception belongs only to this particular vinyl stannane, 156.

Figure 8: Mechanistic explanation of the stereoselective fluorination result with XeF₂.
The more likely Path 1 mechanism in figure 6 was further investigated. The detection of Me₃SnF, a highly insoluble compound, was not attempted. The detection of Me₃SnF would not prove much, as several different mechanisms can give rise to Me₃SnF. Instead, $^{119}\text{Sn}$-, $^1\text{H}$-, and $^{13}\text{C}$-NMR were used as tools in an attempt to detect $\pi$-complexation between the vinyl stannane double bond and AgOTf. The vinyl stannane peak in the $^{119}\text{Sn}$-NMR appears at -40 ppm as expected.⁴¹ When a mixture of vinyl stannane and AgOTf in CD₂Cl₂ was examined by $^{119}\text{Sn}$-NMR, a new second peak at 0.0 ppm was detected. This peak at 0.0 ppm corresponds to a tetraalkyl stannane species where all four alkyl carbons attached to the tin are sp³ hybridized.⁴¹ Another explanation, however, for the positive shift of the vinyl stannane might be due to complexation of AgOTf with the double bond. However, the same experiment using $^1\text{H}$- and $^{13}\text{C}$-NMR did not corroborate the result from the $^{119}\text{Sn}$-NMR. Based on $^1\text{H}$- and $^{13}\text{C}$-NMR evidence, the vinyl stannane was converted to the corresponding dimer over a 50 min period with no intermediates detected. Therefore, the intermediate for the dimer, as well as the fluorination, must be short-lived and/or present in such a low concentration that detection by NMR becomes impossible.

These findings did not by any means rule out the Path 1 mechanism which is further elaborated below. The initial complexation to the double bond of the vinyl stannane would cause a weakening of the carbon-tin $\sigma$ bond. In other words, the $\pi$-Ag(I) complex (bond A) gains strength at the
expense of the carbon tin bond (bond B'). A weakening of bond B' can only result in polarization of the carbon-tin σ bond. Thereby, the vinyl carbon attached to the tin becomes more like a "naked" carbanion, due to the destabilization of the carbon-tin σ bond, for electrophilic attack by XeF₂. The electrophilic attack is more likely a cyclic decomposition of XeF₂ rather than by a highly unstable fluorine cation. Due to the high activation barrier XeF₂ has to overcome to generate a fluorine cation, a [3 + 2] cyclic intermediate (Path 1 of Figure 8) which decomposes to afford a vinyl fluoride and Me₃SnF is more probable. The [3 + 2] cyclic intermediate is mechanistically reasonable. The electrophilic fluorine of XeF₂ associates with the nucleophilic vinyl carbon due to the silver (I)-alkene π-complex and the nucleophilic fluorine of XeF₂ with the electropositive stannane. The driving force of this proposed mechanism is the formation of a noble gas, Xe (g), which boils out of the solution while Me₃SnF precipitates out as a highly insoluble compound. In fact, the fluorination reaction generated a substantial amount of gas during the first minute or two. The observed gas was most certainly Xe, since the reaction did not generate enough heat to bring the reaction mixture to boil. Furthermore, no substantial amounts of gas are generated when XeF₂ is mixed with AgOTf in the absence of vinyl stannane during the first 30 min.
after mixing. The gas is only observed when vinyl stannane is added, thus supporting the Path 1 mechanism.

To further substantiate the proposed mechanism, cuprous triflate (CuOTf) was synthesized and used in the reaction in place of AgOTf. This was done to see if another element, which is known to complex double bonds, could assume the role of silver in the fluorination. The fluorination results with CuOTf and other copper(I) salts are shown below (Table 5).

Table 5: The fluorination of vinyl stannane 49 with XeF2 and copper(I) salts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Silver (I) Salt</th>
<th>Acid Scavengers</th>
<th>Reaction Time</th>
<th>s.m. : Vinyl Fluoride : Alkene ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
<td>5 min</td>
<td>95:0:5</td>
</tr>
<tr>
<td>2</td>
<td>(CuOTf)2Bz</td>
<td>None</td>
<td>5 min</td>
<td>0:1:8</td>
</tr>
<tr>
<td>3</td>
<td>(CuOTf)2Bz</td>
<td>2,5-di-tert-butyl-4-methylpyridine</td>
<td>1d</td>
<td>1:0:1</td>
</tr>
<tr>
<td>4</td>
<td>(CuOTf)2Bz</td>
<td>N-ethyl-di-isopropylamine</td>
<td>5 min</td>
<td>0:0:1</td>
</tr>
<tr>
<td>5</td>
<td>CuCl</td>
<td>None</td>
<td>1d</td>
<td>0:1:8</td>
</tr>
<tr>
<td>6</td>
<td>CuCN</td>
<td>None</td>
<td>18 h</td>
<td>0:1:8</td>
</tr>
</tbody>
</table>

Unfortunately, the fluorination of a vinyl stannane with CuOTf and XeF2 did not afford the desired vinyl fluoride in yields (approx. 15% at best) comparable to those obtained with AgOTf. Although the rate of vinyl stannane consumption was as rapid as when using AgOTf, the fluorination with XeF2
in conjunction with CuOTf gave approximately the same yields as the fluorination of vinyl stannanes with XeF₂ alone.

CONCLUSION

In conclusion, the goals for this project were met with success. The fluorination reactions are efficient with yields typically between 50 to 87%, fast with reaction times approximately 5 min, and regio- and stereospecific. Also, the fluorination tolerates various functionalities in the vinyl stannane starting material. The functionalities include acetal, ester, carbamate, ketone, enone, and homoallylic tertiary alcohols which could readily dehydrate to form a conjugated diene. The fluorination is also a potential candidate for use as a ¹⁸F labeling method. In addition, the choice of AgOTf introduces no fluoride which might dilute the label, as is the case with AgPF₆ or AgBF₄. Finally, the first trifluorination of a vinyl stannane has been reported herein, although further optimization of this reaction is needed.

The mechanism seems to support a non-radical mechanistic pathway. There exists only one published paper which shows that XeF₂ undergoes a non-radical pathway. Although the byproducts arising from this fluorination (i.e. dimer and alkene) may have been formed from a different pathway than the one which gives rise to the vinyl fluoride, a vinyl radical intermediate is not involved. The alkene was formed via protiodestannylation which was suppressed by the addition of an acid scavenger.
Further study of this fluorination method might be pursued using other metal sources besides silver which could π-complex to double bonds. Certain metals (i.e. Co, Ir, Fe, etc.) which can complex to aromatic functionalities might prove to be useful for the fluorination of aryl stannanes in conjunction with XeF$_2$. In addition, there are other fluorinating reagents which could be investigated for the fluorination of not only vinyl stannanes but other organometallic substrates.
EXPERIMENTAL

Reagent grade dichloromethane was distilled from phosphorus pentoxide. Reagent grade ethyl ether and THF were distilled from sodium and benzophenone. Reagent grade hexane was distilled from calcium hydride. Xenon difluoride was purchased from PCR and used as received. \(^1\)H-NMR and \(^{13}\)C-NMR spectra were recorded on either General Electric QE-300 and GE-500 (Oxford magnet) NMR spectrometers. Chemical shifts were measured in ppm relative to deuterated chloroform (7.26 ppm for \(^1\)H-NMR and 77.0 for \(^{13}\)C-NMR) as an internal standard. \(^{19}\)F-NMR spectra were recorded on a Nicolet NT-300 instrument, and chemical shifts are reported upfield from either trifluoroacetic acid (-76.55 ppm) or fluorochloroform (0.00 ppm) as an external standard. \(^{119}\)Sn-NMR spectra were recorded on a Nicolet NT-300 instrument, and chemical shifts are reported relative to Me\(_4\)Sn (0.00 ppm) as an external standard. Multiplicities are designated as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). Broad signals are designated with br. High resolution mass spectra were recorded on a VG-70SE instrument. Column chromatography was performed on Brinkmann silica gel (0.040-0.063 mm) or YMC GEL ODS 120A S-50. Infrared spectra were recorded on a Perkin-Elmer 1430 double beam instrument. Solid samples were recorded on NaCl plates as thin films deposited by evaporation from dichloromethane, and oils were recorded neat. Absorptions are reported in wave numbers (cm\(^{-1}\)) and their intensities are designated as strong (s), medium (m), or weak (w). Broad signals are designated with br. Combustional analysis was done by Desert Analytics Laboratory.
I. Vinyl fluorides formed from XeF$_2$ and AgOTf

**Procedure:** In a flame dried 2-neck flask equipped with a magnetic stirrer, were added methylene chloride (4.5 mL) and silver carbonate (129 mg, 0.47 mmol) followed by triflic acid (103 mg, 0.69 mmol) under a stream of argon gas. The flask was then wrapped with aluminum foil to prevent decomposition of the AgOTf. After stirring for 30 min at ambient temperature, vinyl stannane 49 (200 mg, 0.62 mmol), dissolved in methylene chloride (4.5 mL), was transferred to the silver solution via cannula. Immediately thereafter, XeF$_2$ (116 mg, 0.69 mmol) in methylene chloride (9.0 mL) was also added to the silver solution in a similar manner. After stirring for 5 min at ambient temperature, the solution was transferred to a separatory funnel containing saturated aqueous sodium bicarbonate then extracted with methylene chloride (3 X). The organic phases were dried with anhydrous magnesium sulfate and filtered through a short pad of Celite. The solvent was evaporated under reduced pressure, and the residue chromatographed on a silica gel column eluting with pentane to afford 87 mg (79% yield) of the vinyl fluoride 50. The identical result was obtained using commercial AgOTf.
$^{1}$H-NMR (300 MHz, CDCl$_3$): 1.85-2.05 (m, 2H), 2.22-2.30 (m, 3H), 2.35-2.45 (m, 1H), 2.75-2.85 (m, 1H), 5.24-5.31 (dm, J = 16.8 Hz, 1H), 7.19-7.23 (m, 1H), 7.22-7.25 (br d, J = 7.5 Hz, 2H), 7.29-7.35 (br t, J = 7.5 Hz, 2H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -104.0 (br d, J = 11.3 Hz).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 25.7-25.9 (d, J = 24.4 Hz, 1C), 29.5-29.6 (d, J = 9.5 Hz, 1C), 30.4-30.5 (d, J = 9.5 Hz, 1C), 39.6, 101.4-101.5 (d, J = 14.9 Hz, 1C), 126.2, 126.7, 128.4, 145.6, 158.6-160.6 (d, J = 155.0 Hz, 1C).

IR (neat): 3080 (m), 3060 (m), 3020 (m), 2920 (s), 2840 (m), 1705 (s), 1600 (m), 1490 (m), 1450 (m), 1440 (m), 1370 (s), 1285 (m), 1265 (m), 1210 (m), 1150 (m), 1130 (m), 1030 (m), 980 (m), 910 (m), 880 (w), 820 (m), 800 (w).

HRMS: Calcd. for C$_{12}$H$_{13}$F (M$^+$) 176.1001, found 176.1007.

Mass spectrum m/e: 176 (M$^+$), 104.

mp: 66-68°C.

Anal Calcd for C$_{12}$H$_{13}$F: C, 81.78; H, 7.44. Found: C, 81.70; H, 7.25.

tlc: Rf = 0.5 (Hexane).

Physical characteristic: White crystalline solid.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). Vinyl fluoride 55 and alkene 56 were formed in a ratio of 6:3. Due to the extreme volatility of this organofluorine product, the isolated yield could not be determined. The scale used for this fluorination was 250 mg of vinyl stannane 53. Dimer 129 was isolated as a minor byproduct (<10%).

\[
\begin{align*}
&\text{Procedure: The procedure for vinyl fluoride 50 was used (page 62). Vinyl} \\
&\text{fluoride 55 and alkene 56 were formed in a ratio of 6:3. Due to the extreme} \\
&\text{volatility of this organofluorine product, the isolated yield could not be} \\
&\text{determined. The scale used for this fluorination was 250 mg of vinyl} \\
&\text{stannane 53. Dimer 129 was isolated as a minor byproduct (<10%).}
\end{align*}
\]

**1H-NMR** (300 MHz, CDCl3): 0.88 (s, 9H), 1.24-1.35 (m, 2H), 1.74-1.92 (m, 3H), 
2.00-2.07 (m, 1H), 2.17-2.25 (m, 1H), 5.15 (br dd, J = 16.5, 5.7 Hz, 1H).

**19F-NMR** (283 MHz, CDCl3): -104.5 (br d, J = 8.5 Hz).

**IR** (neat): 2940 (br), 1720 (br), 1600 (s), 1570 (s), 1470 (br), 1400 (s), 1360 (s), 1250 
(s), 1200 (s), 1160 (s), 1130 (s), 1030 (s), 930 (s), 900 (m), 850 (s).

**tlc:** Rf = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the vinyl hydrogens; 5.68 (s, 2H).

**tlc:** R$_f$ = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
$^1$H-NMR (300 MHz, CDCl$_3$): 0.86 (s, 18H), 1.14-1.21 (m, 2H), 1.26 (br s, 4H), 1.64 (br s, 4H), 1.70-1.80 (m, 2H), 1.91-2.00 (br s, 2H), 5.38 (br s, 2H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 23.3, 24.3, 27.2, 31.5, 32.1, 44.1, 121.3, 135.0.

IR (neat): 2950 (s), 1710 (s), 1620 (s), 1470 (s), 1250 (s).

HRMS: Calcd. for C$_{20}$H$_{34}$ (M$^+$) 274.2661, found 274.2660.

Mass spectrum m/e: 274 (M$^+$), 217, 203, 123, 95, 81.

tlc: Rf = 0.8 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 37% (32 mg) from 154 mg (0.47 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.34-1.61 (m, 16H), 1.95-2.02 (br q, $J = 6.9$ Hz, 2H), 2.23-2.35 (dt, $J = 23.4$ Hz, 6.9 Hz, 2H), 4.89-5.02 (dt, $J = 23.4$, 8.1 Hz, 1H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 21.9-22.1 (d, $J = 24.4$ Hz), 22.5-22.6 (d, $J = 10.1$ Hz), 23.5, 23.9, 24.2, 24.4, 24.4, 24.5, 24.6, 27.1, 106.6-106.8 (d, $J = 21.5$ Hz), 159.0-161.0 (d, $J = 245.6$ Hz).

$^{19}$F-NMR (283 MHz, CDCl$_3$): $^\text{-}105.1$ - $^\text{-}104.9$ (q, $J = 23.5$ Hz).

IR (neat): 2930 (s), 2860 (m), 1700 (m), 1470 (m), 1445 (br), 1370 (w), 1350 (w), 1230 (w), 1220 (w), 1180 (w), 1133 (w), 1110 (w), 1086 (w), 1070 (w), 1050 (w), 1030 (w), 927 (w), 910 (w), 860 (w), 815 (w).

HRMS: Calcd. for C$_{12}$H$_{21}$F (M$^+$) 184.1627, found 184.1627.

Mass spectrum m/e: 184 (M$^+$), 169, 131, 119, 109, 95, 81.

tlc: Rf = 0.9 (Hexane).
Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 60% (70 mg) from 205 mg (0.61 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the cis-isomer;
1.13-1.15 (d, J = 6.9 Hz, 3H), 1.56-1.68 (td, J = 12.6, 11.1 Hz, 1H), 2.04-2.12 (m, 1H), 2.19-2.35 (m, 2H), 2.60-2.70 (m, 1H), 2.79-2.90 (tm, J = 12.9 Hz, 1H), 5.20-5.27 (dm, J = 17.4 Hz, 1H), 7.19-7.23 (m, 1H), 7.21-7.24 (br d, J = 7.2 Hz, 2H), 7.29-7.34 (br t, J = 7.5 Hz, 2H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): Reported for the cis-isomer;
17.2-17.3 (d, J = 2.9 Hz), 31.4-31.5 (d, J = 8.6 Hz), 32.0-32.2 (d, J = 23.0 Hz), 39.5-39.6 (d, J = 7.2 Hz), 40.2, 101.3-101.5 (d, J = 17.2 Hz), 126.3, 126.7, 128.5, 145.7, 161.8-163.9 (d, J = 257.1 Hz).

$^{19}$F-NMR (283 MHz, CDCl$_3$): Reported for the cis-isomer;
$^{112.54}$ - $^{112.48}$ (dm, J = 17.3 Hz).

IR (neat): Reported for the cis and trans isomers;
3060 (w), 3030 (m), 2980 (s), 2920 (s), 2880 (m), 2860 (m), 2840 (m), 1697 (s), 1605 (m), 1495 (s), 1455 (s), 1435 (m), 1380 (m), 1357 (m), 1172 (m),
1160 (s), 1150 (s), 1427 (m), 1112 (s), 1097 (s), 1030 (m), 885 (m),
770 (s), 742 (m), 708 (s).

HRMS: Calcd. for C_{13}H_{15}F (M^+) 190.1158, found 190.1156.

Mass spectrum m/e: 190 (M^+), 129, 104, 91, 78.

tlc: Rf = 0.6 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 70% (106 mg) from 265 mg (0.79 mmol) of starting material.

\[ \text{Procedure:} \quad \text{The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 70\% (106 mg) from 265 mg (0.79 mmol) of starting material.} \]

\[ \text{1H-NMR (300 MHz, CDCl}_3\text{):} \quad 1.66 \text{ (br s, 3H)}, \quad 1.87-1.93 \text{ (br dd, J = 11.7, 5.7 Hz, 1H)}, \quad 1.97-2.01 \text{ (m, 1H)}, \quad 2.18-2.24 \text{ (m, 3H)}, \quad 2.32-2.39 \text{ (m, 1H)}, \quad 2.80-2.86 \text{ (m, 1H)}, \quad 7.19-7.23 \text{ (m, 1H)}, \quad 7.22-7.25 \text{ (br d, J = 7.5 Hz, 2H)}, \quad 7.30-7.35 \text{ (br t, J = 7.8 Hz, 2H).} \]

\[ \text{13C-NMR (125 MHz, CDCl}_3\text{):} \quad 14.0-14.0(2) \text{ (d, J = 5.5 Hz)}, \quad 25.8-26.0 \text{ (d, J = 24.7 Hz)}, \quad 29.1-30.1 \text{ (d, J = 9.6 Hz)} 37.1-37.2 \text{ (d, J = 5.5 Hz)}, \quad 40.0, \quad 108.6-108.7 \text{ (d, J = 12.3 Hz)}, \quad 126.2, \quad 126.8, \quad 128.4, \quad 149.3, \quad 152.4-154.4 \text{ (d, J = 249.6 Hz).} \]

\[ \text{19F-NMR (283 MHz, CDCl}_3\text{):} \quad -111.0 \text{ (br s).} \]

\[ \text{IR (neat):} \quad 3060 \text{ (m)}, \quad 3020 \text{ (m)}, \quad 2920 \text{ (s)}, \quad 2780 \text{ (s)}, \quad 1725 \text{ (m)}, \quad 1700 \text{ (w)}, \quad 1600 \text{ (w)}, \quad 1495 \text{ (m)}, \quad 1450 \text{ (m)}, \quad 1380 \text{ (w)}, \quad 1355 \text{ (m)}, \quad 1230 \text{ (w)}, \quad 1150 \text{ (s)}, \quad 1110 \text{ (s).} \]

\[ \text{HRMS:} \quad \text{Calcd. for C}_{13}\text{H}_{15}\text{F (M)}^+ 190.1158, \quad \text{found 190.1149.} \]

\[ \text{Mass spectrum m/e:} \quad 190 \text{ (M)}^+, \quad 151, \quad 133, \quad 104, \quad 91, \quad 69. \]

\[ \text{tlc:} \quad \text{Rf} = 0.9 \text{ (Hexane).} \]

\[ \text{Physical characteristic:} \quad \text{Colorless oil.} \]
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 67% (196 mg) from 560 mg (1.85 mmol) of starting material.

$^{1}$H-NMR (300 MHz, CDCl$_3$): 1.84-1.89 (br t, $J = 6.3$ Hz, 2H), 2.26-2.27 (br s, 2H), 2.37-2.39 (br s, 2H), 2.39-2.39 (br s, 2H), 3.99 (s, 4H), 5.06-5.14 (dtm, $J = 16.8$, 3.9 Hz, 1H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 24.1-24.3 (d, $J = 25.3$ Hz), 30.6-30.7 (d, $J = 9.8$ Hz), 32.8-32.9 (d, $J = 8.4$ Hz), 64.5, 64.5, 99.4-99.5 (d, $J = 19.7$ Hz), 107.2, 157.8-159.8 (d, $J = 255.4$ Hz).

$^{19}$F-NMR (283 MHz, CDCl$_3$): $^{*}$121.32 - $^{*}$121.26 (br d, $J = 15.7$ Hz).

IR (neat): 3400 (w), 2930 (s), 2880 (s), 2680 (w), 1707 (s), 1612 (w), 1511 (m), 1475 (m), 1450 (s), 1440 (s), 1380 (s), 1350 (s), 1330 (s), 1300 (m), 1260 (s), 1200 (s), 1150 (s), 1120 (s), 1060 (s), 1050 (s), 1040 (s), 1015 (s), 985 (s), 950 (s), 865 (s), 810 (s), 790 (m).

HRMS: Calcd. for C$_{8}$H$_{11}$O$_{2}$F (M$^+$) 158.0743, found 158.0745.

Mass spectrum m/e: 158 (M$^+$), 117, 99, 86, 73.

tlc: $R_f = 0.9$ (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 53% (75 mg) from 250 mg (0.76 mmol) of starting material.

\[ \text{H}_{21}\text{C}_{10}\text{SnMe}_{3} \quad \rightarrow \quad \text{H}_{21}\text{C}_{10}\text{F} \]

1\text{H-NMR} (300 MHz, CDCl\text{3}): 0.85-0.90 (br t, J = 6.9 Hz, 3H), 1.26 (br s, 16H), 2.02-2.13 (m, 2H), 4.61-4.82 (dtd, J = 43.5, 7.5, 4.5 Hz, 1H), 6.28-6.59 (ddt, J = 86.1, 4.8, 1.2 Hz, 1H).

13\text{C-NMR} (125 MHz, CDCl\text{3}): 14.1, 22.7, 29.1, 29.2, 29.3, 29.4, 29.6, 31.9, 33.8, 111.1-111.2 (d, J = 5.6 Hz), 146.5-148.5 (d, J = 255.3 Hz).

19\text{F-NMR} (283 MHz, CDCl\text{3}): *-130.2 - *-129.8 (dd, J = 86.1, 43.5 Hz).

IR (neat): 2980 (m), 2920 (s), 2850 (s), 1670 (w), 1460 (w), 1260 (w), 1100 (m), 1020 (m), 800 (w).

HRMS: Calcd. for C\text{12}H\text{23}F (M+) 186.1784, found 186.1796.

Mass spectrum m/e: 186 (M\text{+}), 140, 123, 111, 97, 83, 69.

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of 71b was 52% (60 mg) from 268 mg (0.93 mmol) of 71a. Dimer 153 was isolated as a minor byproduct (17 mg, 8%).

\begin{align*}
1^H-\text{NMR} (300 \text{ MHz, CDCl}_3): & \quad 1.09 (s, 6H), 2.21 (s, 2H), 2.39 (d, J = 3.6 \text{ Hz}, 2H), \\
& \quad 5.68 (d, J = 14.1 \text{ Hz}, 1H).
\end{align*}

\begin{align*}
1^9F-\text{NMR} (283 \text{ MHz, CDCl}_3): & \quad -74.7 (d, J = 14.0 \text{ Hz}).
\end{align*}

\begin{align*}
13C-\text{NMR} (75 \text{ MHz, CDCl}_3): & \quad 28.2, 40.3 (d, J = 17.4 \text{ Hz}), 50.6, 108.6 (d, J = 11.0 \\
& \quad \text{Hz}), 178.6 (d, J = 289.1 \text{ Hz}), 199.1 (d, J = 17.6 \text{ Hz}).
\end{align*}

\begin{align*}
\text{IR (neat):} & \quad 2960 (s), 2870 (s), 1660 (br), 1470 (s), 1450 (s), 1420 (s), 1410 (s), 1390 (s), \\
& \quad 1360 (s), 1310 (s), 1280 (s), 1250 (m), 1230 (m), 1190 (s), 1120 (s), 950 (m), 920 (m), \\
& \quad 900 (s), 890 (s), 870 (s), 840 (s), 800 (m), 730 (s).
\end{align*}

\begin{align*}
\text{HRMS:} & \quad \text{Calcd. for } C_8H_{11}FO (M^+) 142.0794, \text{ found } 142.0788.
\end{align*}

\begin{align*}
\text{Mass spectrum m/e:} & \quad 142 (M^+), 127, 114, 102.
\end{align*}

\begin{align*}
\text{tlc:} & \quad Rf = 0.2 \text{ (20% Ethyl acetate in hexane).}
\end{align*}

Physical characteristic: Colorless oil.
$^1$H-NMR (300 MHz, CDCl$_3$): 1.07 (s, 12H), 2.30 (s, 4H), 2.40 (s, 4H), 6.29 (s, 2H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 28.3, 28.3(3), 33.3, 40.1, 126.7, 126.9, 154.5, 199.8.

IR (neat): 2980 (s), 2880 (s), 1665 (s), 1580 (m), 1370 (s), 1270 (s), 1260 (s), 1140 (s), 1130 (m), 920 (m), 870 (m).

HRMS: Calcd. for C$_{16}$H$_{22}$O$_2$ (M$^+$) 246.1620, found 246.1599.

Mass spectrum m/e: 246 (M$^+$), 180, 134, 106, 84.

tlc: Rf = 0.1 (20% Ethyl acetate in hexane).

Physical characteristic: Pale-white solid.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 62% (29 mg) from 83 mg (0.2 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.33 (t, $J = 7.2$ Hz, 3H), 4.26 (q, $J = 7.2$ Hz, 2H), 5.90 (d, $J = 33.3$ Hz, 1H), 7.41-7.51 (m, 3H), 7.65 (dd, $J = 7.5$, 1.2 Hz, 2H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -96.6 (d, $J = 27.7$ Hz).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 14.3, 60.4, 97.2, 125.6 (d, $J = 6.3$ Hz), 128.8, 130.6 (d, $J = 27.0$ Hz), 131.5, 164.0, 166.2 (d, $J = 277.5$ Hz).

IR (neat): 3080 (w), 3060 (w), 2980 (s), 2930 (m), 2900 (m), 1720 (br), 1650 (br), 1600 (w), 1580 (m), 1495 (s), 1450 (s), 1390 (s), 1370 (s), 1335 (s), 1280 (br), 1160 (br), 1095 (s), 1055 (s), 1035 (s), 1020 (s), 895 (m), 830 (s), 770 (s), 690 (s), 640 (s), 620 (s).

HRMS: Calcd. for C$_{11}$H$_{11}$O$_2$F (M$^+$) 194.0743, found 194.0729.

Mass spectrum m/e: 194 (M$^+$), 166, 149, 122, 101, 75.

tlc: Rf = 0.5 (10% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was 55% (40 mg) from 51 mg (0.1 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.36 (br s, 20H), 1.45-1.70 (m, 3H), 2.32 (d, $J = 22.2$ Hz, 2H), 4.34 (dd, $J = 50.4$, 2.4 Hz, 1H), 4.69 (dd, $J = 17.7$, 2.7 Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): ~88.6 (dtd, $J = 45.0$, 25.0, 20.0 Hz).

$^{13}$C-NMR (125 MHz, CDCl$_3$): Reported for the sp$^2$ carbons; 93.8 (d, $J = 20.3$ Hz), 164.0 (d, $J = 257.7$ Hz).

IR: 3420 (br), 2920 (s), 2860 (s), 1670 (s), 1470 (s), 1440 (s), 1150 (m), 840 (m).

tlc: Rf = 0.25 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). Vinyl fluoride 74b and the corresponding alkene were isolated as an inseparable mixture (56:44, 45 mg) from 100 mg (0.30 mmol) of starting material.

\[ \text{Me}_3\text{Sn} \quad \rightarrow \quad \text{F} \]

\[ \begin{array}{c}
\text{H}_2\text{C} & \text{Me}_3\text{Sn} & \rightarrow & \text{F} \\
\text{C}_10 & & & \text{H}_2\text{C}_10
\end{array} \]

\[ 74a \quad \rightarrow \quad 74b \]

\[^{1}H\text{-NMR\ (300 MHz, CDCl}_3\text{:} \quad 0.88 \text{ (br t, J = 6.9 Hz, 3H)}, 1.26 \text{ (br s, 16H)}, 2.03 \text{ (br quintet, J = 6.6 Hz, 2H)}, 4.19 \text{ (br dd, J = 50.7, 2.7 Hz, 1H)}, 4.48 \text{ (dd, J = 17.7, 2.4 Hz, 1H)}. \]

\[^{19}F\text{-NMR\ (283 MHz, CDCl}_3\text{:} \quad -94.5 \text{ (ddt, J = 52.8, 17.1, 14.1 Hz)}. \]

\[ \text{IR\ (neat):} \quad 2920 \text{ (s)}, 2840 \text{ (s)}, 1700 \text{ (w)}, 1460 \text{ (s)}, 1380 \text{ (m)}. \]

\[ \text{tlc: \ Rf = 0.9 (Hexane).} \]

Physical characteristic: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 50 was used (page 62). The yield of 77b was approximated to be 20% (6 mg) from 63 mg (0.2 mmol) of 77a, based on $^1$H-NMR integration. Vinyl fluoride 77b is volatile. The major product from this reaction was the dimer 152 (14 mg, 25%).

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the vinyl hydrogen; 6.88 (br t, J = 8.1 Hz).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -141.9 (br t, J = 7.0 Hz).

IR (neat): 3050 (s), 2950 (br), 2850 (s), 1700 (br), 1470 (s), 1390 (s), 1370 (s), 1260 (s), 1040 (s), 900 (s), 740 (br), 700 (s).

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
$^1$H-NMR (300 MHz, CDCl$_3$): 1.05 (s, 6H), 1.51 (s, 6H), 2.60-3.00 (m, 8H), 7.86 (d, $J = 6.9$ Hz, 2H).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 22.5, 26.6, 29.7, 41.3, 43.0, 44.1, 58.8, 128.4, 155.5, 202.4.

HRMS: Calcd. for C$_{18}$H$_{22}$O$_2$ (M$^+$) 270.1620, found 270.1623.

Mass spectrum m/e: 270 (M$^+$), 255, 242, 237, 227, 214.

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was approximated to be 83% (258 mg) from 705 mg (2.72 mmol) of starting material, based on $^1$H-NMR integration.

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the vinyl proton; 5.33 (dt, $J = 21.9, 6.3$ Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): $-91.6$ (br d, $J = 20.7$ Hz).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.

Procedure: The procedure for vinyl fluoride 50 was used (page 62). The yield of product was approximated to be 22% (43 mg) from 416 mg (1.53 mmol) of starting material, based on $^1$H-NMR integration.

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the vinyl proton; 5.12 (dt).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -99.6 (dt, J = 24.9, 22.1 Hz).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 50 was used (page 62). The yield of 135 was 84% (26 mg) from 51 mg (0.1 mmol) of 134. The alkene 136 was isolated as a minor byproduct during the fluorination reaction of vinyl stannane 134. The products are isomeric mixtures (8 : 1).

This alkene was also the major product when vinyl stannane 134 was treated with AgOTf in the absence of XeF₂. The yield of 136 was 72% (23 mg) from 57 mg (0.2 mmol) of starting material.

**1H-NMR** (300 MHz, CDCl₃): 1.39-1.47 (m, 1H), 1.61 (dd, J = 23.5, 12.7 Hz, 1H), 1.85-1.92 (m, 1H), 2.04-2.15 (m, 2H), 2.15-2.21 (m, 1H), 2.21-2.26 (m, 2H), 2.62 (br s, 1H), 2.78-2.85 (m, 1H), 4.97 (dd, J = 10.1, 1.7 Hz, 1H), 5.03 (dt, J = 17.2, 1.6 Hz, 1H), 5.28 (dm, J = 17.6 Hz, 1H), 5.81 (ddt, J = 16.9, 10.1, 6.6 Hz, 1H), 7.23 (br d, J = 7.5 Hz, 3H), 7.32 (br t, J = 7.5 Hz, 2H).

**19F-NMR** (283 MHz, CDCl₃): -108.1 (br d, J = 10.9 Hz, 1F, minor isomer).

-113.4 (br d, J = 15.7 Hz, 1F, major isomer).

**13C-NMR** (125 MHz, CDCl₃): 30.4, 30.7, 31.1 (d, J = 7.4 Hz), 36.3 (d, J = 22.2 Hz), 36.7 (d, J = 7.4 Hz), 40.2, 102.2 (d, J = 16.7 Hz), 114.8, 126.4, 126.8, 128.5, 138.4, 145.7, 162.0 (d, J = 255.3 Hz).
IR: 2920 (s), 1700 (br), 1490 (m), 1450 (s), 1150 (s), 1120 (m), 920 (m), 770 (s), 700 (s).

HRMS: Calcd. for C_{16}H_{19}F (M^+) 230.1471, found 230.1487.


tlc: Rf = 0.5 (Hexane).

Physical characteristic: Colorless oil.
$^1$H-NMR (300 MHz, CDCl$_3$): 1.34-1.53 (m, 4H), 1.99-2.03 (m, 1H), 2.11-2.17 (m, 2H), 2.25-2.30 (m, 2H), 2.79-2.89 (m, 1H), 4.96 (dd, J = 10.2, 1.5 Hz, 1H), 5.02 (d, J = 16.8, 1H), 5.64 (d, J = 9.9 Hz, 1H), 5.75-5.90 (m, 2H), 7.19-7.25 (m, 3H), 7.30-7.35 (m, 2H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 30.9, 34.0, 35.6, 36.5, 36.9, 40.6, 114.4, 126.0, 126.4, 126.8, 128.4, 131.8, 138.9, 147.2.

IR: 2920 (s), 2880 (s), 1670 (s), 1490 (m), 1450 (s), 1370 (m), 920 (s), 760 (s), 700 (s).

HRMS: Calcd. for C$_{16}$H$_{20}$ (M$^+$) 212.1565, found 212.1564.

Mass spectrum m/e: 212 (M$^+$), 170, 104, 91, 79, 67.

tlc: Rf = 0.75 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 50 was used (page 62). The estimated yield of vinyl fluoride 154 was approximately 25% (18 mg) from 114 mg (0.29 mmol) of starting material, based on $^1$H-NMR integration.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.25-1.45 (br s, 21H), 1.45-1.55 (m, 2H), 1.99 (d, $J = 8.4$ Hz, 2H), 5.45 (ddt, $J = 18.9, 11.1, 8.4$ Hz, 1H), 6.52 (dd, $J = 85.5, 11.1$ Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -124.9 (dd, $J = 84.0, 22.0$ Hz).

IR: 3420 (br), 2900 (br), 1720 (br), 1580 (s), 1450 (br), 720 (s), 700 (s), 640 (s).

tlc: Rf = 0.2 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
II. Vinyl fluorides from XeF$_2$, AgOTf and 2,6-di-<i>t</i>-butyl-4-methylpyridine

![Chemical Structure](image)

**Procedure:** The procedure for vinyl fluoride 50 was used (page 62), except that 0.1 eq of 2,6-di-<i>t</i>-butyl-4-methylpyridine was added to the reaction mixture. The yield of product was 39% (39 mg) from 188 mg (0.57 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.92 (br t, $J = 7.0$ Hz, 3H), 1.37 (br s, 16H), 1.90-2.10 (m, 2H), 5.50-5.70 (m, 1H), 6.51 (dd, $J = 86.1$, 11.1 Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -130.8 (dd, $J = 84.5$, 20.7 Hz).

IR (neat): 2950 (br), 1715 (s), 1600 (s), 1570 (s), 1460 (s), 1410 (s), 1380 (s), 1350 (s), 1250 (s), 1210 (s), 1160 (s), 970 (s), 940 (s), 850 (s), 720 (s).

tlc: Rf = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
**Procedure**: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 67% (78 mg) from 200 mg (0.58 mmol) of starting material.

$^1$H-NMR (300 MHz, CDC$_3$): 0.89 (br t, J = 6.9 Hz, 3H), 1.10-1.60 (br s, 20H), 4.19 (dd, J = 50.7, 2.7 Hz, 1H), 4.48 (dd, J = 17.7, 2.7 Hz, 1H).

$^{19}$F-NMR (283 MHz, CDC$_3$): -94.5 (ddt, J = 54.3, 17.0, 12.6 Hz).

$^{13}$C-NMR (125 MHz, CDC$_3$): 14.1, 22.7, 26.0, 28.9, 29.3, 29.5, 29.6, 31.7, 31.9, 53.9 (d, J = 20.0 Hz), 89.2 (d, J = 21.6 Hz), 167.1 (d, J = 258.1 Hz).

IR (neat): 2960 (s), 2920 (br), 2850 (s), 1670 (s), 1460 (br), 1380 (s), 1350 (m), 935 (m), 910 (m), 840 (s), 720 (m).

HRMS: Calcd. for C$_{13}$H$_{25}$F (M$^+$) 200.1940, found 200.1938.

** TLC**: Rf = 0.9 (Hexane).

**Physical characteristic**: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 73% (121 mg) from 300 mg (0.93 mmol) of starting material.

\[ \text{1H-NMR (300 MHz, CDCl}_3\text{): 1.45-1.65 (m, 2H), 1.70-1.85 (m, 1H), 2.00-2.25 (m, 3H), 3.62 (br s, 1H), 5.49 (dt, J = 17.7, 3.9 Hz, 1H), 7.20-7.30 (m, 3H), 7.33 (br t, J = 7.4 Hz, 2H).} \]

\[ \text{19F-NMR (283 MHz, CDCl}_3\text{): -104.7 (br d, J = 12.9 Hz).} \]

\[ \text{13C-NMR (75 MHz, CDCl}_3\text{): 19.1, 23.0 (d, J = 7.5 Hz), 32.9 (d, J = 6.5 Hz), 42.5 (d, J = 24.4 Hz), 104.3 (d, J = 21.1 Hz), 105.5, 126.3, 127.6, 142.0, 159.5 (d, J = 255.0 Hz).} \]

\[ \text{IR (neat): 3080 (m), 3060 (m), 3020 (s), 2930 (br), 2880 (br), 1695 (s), 1600 (m), 1490 (m), 1450 (m), 1440 (m), 1370 (m), 1150 (m), 1130 (s), 885 (m), 870 (m), 750 (s), 700 (s), 630 (m), 610 (br).} \]

**HRMS:** Calcd. for C\textsubscript{12}H\textsubscript{13}F (M\textsuperscript{+}) 176.1001, found 176.0991.

**Mass spectrum m/e:** 176 (M\textsuperscript{+}), 148, 147, 133, 98, 77, 51.

**tlc:** Rf = 0.3 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was approximately 35% (65 mg) from 500 mg (1.15 mmol) of starting material, based on $^1$H-NMR integration.

$^1$H-NMR (300 MHz, CDCl$_3$): 3.80 (s, 3H), 3.81 (s, 3H), 6.08 (d, J = 15.6 Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -110.2 (d, J = 15.1 Hz).

IR (neat): 2980 (s), 2850 (s), 2880 (s), 2860 (s), 1740 (br), 1430 (s), 1240 (br), 1170 (br).

tlc: Rf = 0.1 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 50% (32 mg) from 94 mg (0.2 mmol) of starting material.

\[^1\text{H-NMR}\ (300 \text{ MHz, CDCl}_3): 0.98 \text{ (s, 3H), 1.03 \text{ (s, 3H), 1.20-1.70 \text{ (m, 9H), 1.70-2.30 \text{ (m, 7H), 2.40 \text{ (br d, J = 10.8 Hz, 1H), 3.00-3.15 \text{ (m, 1H), 3.36 \text{ (s, 3H), 4.89 \text{ (d, J = 1.2 Hz, 1H), 5.37 \text{ (d, J = 5.1 Hz, 1H).}}}}}}

\[^19\text{F-NMR}\ (283 \text{ MHz, CDCl}_3): -131.7 \text{ (br s).}}

\[^13\text{C-NMR}\ (125 \text{ MHz, CDCl}_3): 15.1, 19.2, 20.2, 26.8 \text{ (d, J = 7.7 Hz), 27.9, 29.9, 30.6, 32.8, 35.9, 37.0, 37.1, 38.7, 50.8, 54.5 \text{ (d, J = 4.6 Hz), 55.6, 80.2, 100.6 \text{ (d, J = 10.8 Hz), 121.0, 143.8, 171.8 \text{ (d, J = 289.0 Hz).}}}}

\text{IR: 2940 (br), 2840 (s), 1720 (s), 1670 (s), 1450 (m), 1380 (m), 1200 (m), 1100 (s).}

\text{tlc: Rf = 0.3 (Hexane).}

\text{Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 53% (50 mg) from 148 mg (0.38 mmol) of starting material. Vinyl fluoride 81b was isolated as a mixture (1:1) of cis and trans isomers.

$^{1}H$-NMR (300 MHz, CDCl$_3$): 1.70-2.50 (m, 2H), 2.50-3.25 (m, 3H), 3.44 (s, 6H), 4.32 (heptet, $J = 6.9$ Hz, 1H), 4.58 (d, $J = 5.4$ Hz, 1H), 5.46 (br d, $J = 17.7$ Hz, 1H), 7.23 (br t, $J = 3.3$ Hz, 2H), 7.20-7.35 (m, 3H).

$^{19}F$-NMR (283 MHz, CDCl$_3$): -107.1 (d, $J = 12.1$ Hz).

$^{13}C$-NMR (125 MHz, CDCl$_3$): Reported for the vinyl carbons; 104.7 (d, $J = 16.6$ Hz), 158.3 (d, $J = 256.2$ Hz).

IR (neat): 2960 (s), 2940 (s), 2900 (s), 1720 (br), 1600 (s), 1500 (s), 1450 (s), 1240 (br), 1150 (br), 1080 (s), 1020 (s), 760 (s), 700 (s), 680 (s).

tlc: $R_f = 0.2$ (Hexane).

Physical characteristic: Colorless oil.

**Procedure:** The procedure for vinyl fluoride 75b was used (page 86). The yield of product was approximated to be 80% (20 mg) from 50 mg (0.2 mmol) of starting material, based on \(^1\)H-NMR integration.

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): Reported for the vinyl proton; 5.09 (dt, J = 21.6, 9.0 Hz, 1H).

tlc: Rf = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 60% (124 mg) from 500 mg (1.08 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.49 (tt, $J = 12.6$, 4.8 Hz, 1H), 1.50-1.58 (m, 1H), 1.84 (br t, $J = 13.8$ Hz, 1H), 1.90-2.10 (m, 3H), 2.22 (br d, $J = 13.2$ Hz, 1H), 2.67 (tt, $J = 12.3$, 3.3 Hz, 1H), 2.97 (br d, $J = 13.5$ Hz, 1H), 6.46 (d, $J = 87.0$ Hz, 1H), 7.21 (br d, $J = 6.6$ Hz, 3H), 7.31 (br t, $J = 7.2$ Hz, 2H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -140.3 (d, $J = 85.7$ Hz).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 24.4 (d, $J = 6.3$ Hz), 27.9 (d, $J = 7.8$ Hz), 33.8, 34.9, 44.3, 120.5 (d, $J = 6.3$ Hz), 126.1, 126.8, 128.4, 140.8 (d, $J = 250.4$ Hz), 146.6.

IR (neat): 3080 (w), 3060 (w), 3030 (m), 2930 (s), 2860 (s), 1690 (s), 1600 (w), 1495 (m), 1450 (s), 1100 (s), 1075 (m), 1060 (s), 810 (w), 755 (m), 700 (s).

HRMS: Calcd. for C$_{13}$H$_{15}$F (M$^+$) 190.1112, found 190.1135.


tlc: Rf = 0.5 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 48% (103 mg) from 509 mg (1.08 mmol) of starting material.

\[ \text{SnBu}_3 \text{SnBu}_3 \rightarrow \text{F} \]

68 \rightarrow 110

**1H-NMR** (300 MHz, CDCl\(_3\)): 6.97 (d, J = 8.31 Hz, 1H), 7.20-7.27 (m, 2H), 7.30-7.37 (m, 4H), 7.36 (br s, 4H).

**19F-NMR** (283 MHz, CDCl\(_3\)): -128.0 (d, J = 79.2 Hz).

**13C-NMR** (125 MHz, CDCl\(_3\)): 127.8 (d, J = 4.9 Hz), 128.2, 128.5, 128.7, 129.7 (d, J = 3.2 Hz), 145.8 (d, J = 268.6 Hz).

**IR** (neat): 3120 (s), 3100 (s), 3060 (s), 1650 (m), 1640 (w), 1500 (s), 1455 (s), 1175 (s), 1090 (s), 1070 (s), 1030 (w), 945 (w), 920 (w), 825 (w), 760 (s), 730 (m), 700 (s), 635 (s).

**HRMS**: Calcd. for C\(_{14}\)H\(_{11}\)F (M\(^+\)) 198.0829, found 198.0837.

**Mass spectrum m/e**: 198 (M\(^+\)), 183, 178, 165, 98, 89, 76, 63, 51.

**tlc**: Rf = 0.45 (Hexane).

**Physical characteristic**: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 70% (49 mg) from 165 mg (0.35 mmol) of starting material.

**\(^1\)H-NMR** (300 MHz, CDCl\textsubscript{3}): 0.62 (br s, 10H), 0.98-1.14 (m, 4H), 1.27-1.35 (m, 2H), 1.40-1.49 (m, 1H), 1.63 (br t, \(J = 13.0\) Hz, 1H), 1.87 (br d, \(J = 9.9\) Hz, 2H), 2.12 (br dd, \(J = 15.6, 2.1\) Hz, 1H), 2.87 (br d, \(J = 13.5\) Hz, 1H), 6.38 (br d, \(J = 87.6\) Hz, 1H).

**\(^19\)F-NMR** (283 MHz, CDCl\textsubscript{3}): -141.7 (d, \(J = 87.6\) Hz).

**\(^{13}\)C-NMR** (125 MHz, CDCl\textsubscript{3}): 24.5 (d, \(J = 5.6\) Hz), 27.3, 27.6, 28.1 (d, \(J = 7.4\) Hz), 28.3, 29.3, 30.1, 121.6 (d, \(J = 5.6\) Hz), 140.1 (d, \(J = 249.7\) Hz).

**IR** (neat): 2960 (s), 2920 (s), 2860 (s), 2850 (s), 1460 (s), 1440 (s), 1380 (s), 1370 (s), 700 (m).

**tlc:** \(R_f = 0.7\) (Hexane).

**Physical characteristic:** Colorless oil.
**Procedure:** The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 57% (53 mg) from 228 mg (0.50 mmol) of starting material.

\[
\begin{array}{c}
\text{EtO}_2\text{C} - \text{SnBu}_3
\end{array}
\rightarrow
\begin{array}{c}
\text{EtO}_2\text{C} - \text{F}
\end{array}
\]

1H-NMR (300 MHz, CDCl₃): 1.26 (t, J = 7.2 Hz, 3H), 2.02 (br s, 2H), 2.30 (br s, 2H), 3.46 (br t, J = 5.4 Hz, 4H), 4.14 (q, J = 7.2 Hz, 2H), 6.34 (d, J = 85.5 Hz, 1H).

19F-NMR (283 MHz, CDCl₃): -138.4 (d, J = 85.8 Hz).

13C-NMR (125 MHz, CDCl₃): 14.6, 44.0, 45.1, 61.4, 117.6 (d, J = 6.9 Hz), 142.0 (d, J = 252.4 Hz), 155.4.

IR (neat): 2950 (br), 2880 (m), 1710 (br), 1475 (m), 1430 (s), 1280 (m), 1250 (m), 1230 (s), 1210 (m), 1120 (m), 1090 (s), 990 (m).

HRMS: Calcd. for C₉H₁₄FNO₂ (M⁺) 187.1009, found 187.1000.

Mass spectrum m/e: 187 (M⁺), 158, 114, 94, 67.

**tlc:** Rf = 0.5 (20% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 44% (80 mg) from 446 mg (0.97 mmol) of starting material.

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): Reported for the E and Z isomers;
2.05 (dd, J = 4.8, 1.5 Hz, 3H), 2.21 (dd, J = 3.9, 1.5 Hz, 3H), 6.79 (dd, J = 84.3, 1.2 Hz, 1H), 7.11 (dd, J = 84.9, 1.5 Hz, 1H), 7.46-7.54 (m, 4H), 7.78 (br t, J = 12.3 Hz, 4H), 7.82-7.91 (m, 4H), 7.93 (br d, J = 11.7 Hz, 2H).

\(^1^9\)F-NMR (283 MHz, CDCl\(_3\)): Reported for the E and Z isomers;
-130.0 (d, J = 84.9 Hz), -128.0 (d, J = 84.3 Hz).

\(^{13}\)C-NMR (125 MHz, CDCl\(_3\)): Reported for the E and Z isomers;
12.1 (d, J = 5.9 Hz), 16.1 (d, J = 7.4 Hz), 108.4 (d, J = 28.0 Hz), 113.0, 116.9, 120.0 (d, J = 10.3 Hz), 123.9, 124.5, 125.8, 126.0, 126.5, 127.5, 127.6, 127.7, 127.9, 128.1, 128.2, 131.0, 132.6, 132.7, 133.2, 133.4, 134.8, (d, J = 8.8 Hz), 144.5 (d, J = 263.3 Hz), 146.4 (d, J = 257.4 Hz).

IR (neat): 3060 (s), 2980 (br), 2920 (m), 1660 (s), 1600 (m), 1510 (m), 1140 (m), 1110 (br), 890 (m), 860 (s), 810 (s), 750 (s).

tlc: Rf = 0.8 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 50% (56 mg) from 255 mg (0.52 mmol) of starting material.

**$^1$H-NMR (300 MHz, CDCl$_3$):** Reported for the E and Z isomers; 0.89 (br t, $J = 6.6$ Hz, 6H), 1.10-1.50 (br s, 36H), 1.63 (br s, 3H), 1.72 (br s, 3H), 2.01 (br t, $J = 6.9$ Hz, 2H), 2.10 (br t, $J = 6.6$ Hz, 2H), 6.37 (br d, $J = 86.7$ Hz, 1H), 6.39 (br d, $J = 86.7$ Hz, 1H).

**$^{19}$F-NMR (283 MHz, CDCl$_3$):** Reported for the E and Z isomers; -137.5 (d, $J = 88.6$ Hz), -136.4 (d, $J = 87.5$ Hz).

**$^{13}$C-NMR (125 MHz, CDCl$_3$):** Reported for the E and Z isomers; 8.7, 11.8 (d, $J = 9.3$ Hz), 13.7, 14.8 (d, 9.3 Hz), 22.4, 27.0, 27.3, 27.4, 27.7, 27.8, 27.82, 29.1, 29.3, 29.4, 29.45, 29.5, 29.7, 31.4 (d, $J = 7.8$ Hz), 118.2 (d, $J = 4.6$ Hz), 118.3 (d, $J = 6.2$ Hz), 142.9 (d, $J = 250.3$ Hz), 143.3 (d, $J = 250.3$ Hz).

**IR (neat):** 2960 (s), 2920 (s), 2860 (s), 1690 (m), 1465 (m), 1455 (m), 1380 (w), 1250 (w), 1130 (m), 1095 (br), 890 (w), 840 (w), 805 (w), 720 (w).

**Anal Calcd for C$_{14}$H$_{27}$F:** C, 78.44; H, 12.70. Found C, 74.24; H, 12.12.

**tlc:** Rf = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 32% (20 mg) from 147 mg (0.31 mmol) of starting material.

\[ \text{Ph} \text{SnBu}_3 \xrightarrow{\text{Ph}} \text{PhF} \]

156 \hspace{1cm} 157

\[ \text{IH-NMR (300 MHz, CDCl}_3\text{)}: \ 6.49 \ (d, \ J = 21.6 \text{ Hz, 1H}), \ 7.23 \ (\text{br t, } J = 7.5 \text{ Hz, 4H}), \]
\[7.35 \ (\text{br t, } J = 7.8 \text{ Hz, 3H}), \ 7.46 \ (\text{br d, } J = 7.8 \text{ Hz, 2H}), \ 7.50-7.58 \ (\text{m, 1H}).\]

\[ \text{19F-NMR (283 MHz, CDCl}_3\text{): } -95.9 \ (d, \ J = 21.0 \text{ Hz}).\]

\[ \text{13C-NMR (125 MHz, CDCl}_3\text{): 109.3} \ (d, \ J = 31.0 \text{ Hz}), \ 127.0, \ 128.3, \ 128.4, \ 128.8,
\[129.5, \ 131.6, \ 131.9 \ (d, \ J = 29.2 \text{ Hz}), \ 133.8 \ (d, \ J = 12.4 \text{ Hz}), \ 136.3 \ (d, \ J = 226.0 \text{ Hz}).\]

\[ \text{IR (neat): 3080} \ (s), \ 3060 \ (s), \ 3020 \ (s), \ 1660 \ (\text{br}), \ 1600 \ (s), \ 1580 \ (m), \ 1500 \ (s), \ 1440 \ (s), \ 1360 \ (\text{br}), \ 1220 \ (s), \ 1180 \ (s), \ 1080 \ (m), \ 1050 \ (s), \ 1025 \ (s), \ 920 \ (m), \ 870 \ (m), \ 850 \ (\text{br}), \ 775 \ (s), \ 760 \ (s), \ 730 \ (s), \ 690 \ (s), \ 640 \ (s), \ 620 \ (s).\]

\[ \text{HRMS: Calcd. for C}_{14}\text{H}_{11}\text{F (M+)} 198.0845, \text{ found } 198.0852.\]

\[ \text{Mass spectrum m/e: } 198 (M^+), 178, 165, 152, 98, 89, 76, 63.\]

\[ \text{tlc: } \text{Rf} = 0.8 \ (\text{Hexane}).\]

\[ \text{Physical characteristic: Colorless oil.}\]
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 32% (20 mg) from 147 mg (0.31 mmol) of starting material.

\[ \text{Ph} \begin{array}{c} \rightarrow \text{SnBu}_3 \\ \text{Ph} \end{array}, \quad \begin{array}{c} \rightarrow \text{F} \\ \text{Ph} \end{array} \]

\[ \text{156} \quad \text{158} \]

\(^1\text{H}-\text{NMR}\ (300\ \text{MHz, CDCl}_3):\ 6.35\ (d, J = 39.6\ \text{Hz, 1H}),\ 7.20-7.50\ (m, 6\text{H}),\ 7.50-7.60\ (m, 2\text{H}),\ 7.68\ (\text{br} d, J = 7.8\ \text{Hz, 2H}).\]

\(^{19}\text{F}-\text{NMR}\ (283\ \text{MHz, CDCl}_3):\ -114.0\ (d, J = 38.3\ \text{Hz}).\]

\(^{13}\text{C}-\text{NMR}\ (125\ \text{MHz, CDCl}_3):\ 105.8\ (d, J = 9.8\ \text{Hz}),\ 124.3\ (d, J = 7.7\ \text{Hz}),\ 126.5\ (d, J = 6.6\ \text{Hz}),\ 127.3,\ 128.2,\ 128.3,\ 128.6,\ 129.0,\ 131.6,\ 132.5\ (d, J = 284.8\ \text{Hz}).\]

\text{IR}\ (\text{neat}):\ 3050\ (s),\ 3020\ (s),\ 2960\ (s),\ 2950\ (w),\ 1880\ (w),\ 1765\ (w),\ 1650\ (br),\ 1600\ (s),\ 1570\ (w),\ 1495\ (s),\ 1450\ (s),\ 1440\ (s),\ 1330\ (s),\ 1280\ (s),\ 1270\ (br),\ 1200\ (m),\ 1170\ (m),\ 1100\ (br),\ 1070\ (br),\ 1050\ (br),\ 1035\ (s),\ 1010\ (br),\ 910\ (s),\ 800\ (br),\ 765\ (s),\ 690\ (s).\]

\text{HRMS: Calcd. for C}_{14}\text{H}_{11}\text{F (M+)}\ 198.0845,\ \text{found}\ 198.0848.\]

\text{Mass spectrum m/e: 198 (M+), 178, 165, 152, 98, 89, 76, 63.}\]

\text{tlc: Rf = 0.7 (Hexane).}\]

\text{Physical characteristic: Colorless oil.}
III. Byproducts arising from fluorination reactions


Procedure: The procedure for vinyl fluoride 50 was used (page 62). α-Fluoroketone 102 was formed as the major product during the fluorination of vinyl stannane 101. The yield of 102 was 25% (43 mg) from 284 mg (0.88 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl₃): Reported for the methine at C-F;
5.09 (ddd, $J = 47.7$, 12.3, 5.1 Hz).

$^{19}$F-NMR (283 MHz, CDCl₃): -190.2 (br d, $J = 54.3$ Hz).

tlc: Rf = 0.1 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** The procedure for vinyl fluoride 50 was used (page 62). This compound was formed as the major product during the fluorination of vinyl stannane 126. The yield of 127 was 43% (51 mg) from 255 mg (0.82 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.75-1.90 (m, 4H), 2.25 (s, 3H), 2.66 (t, $J = 6.0$ Hz, 2H), 2.82 (t, $J = 6.0$ Hz, 2H), 6.97 (br d, $J = 7.5$ Hz, 1H), 7.03 (br d, $J = 4.2$ Hz, 1H), 7.05 (br t, $J = 9.9$ Hz, 1H).

**IR:** 2930 (s), 1670 (s), 1590 (s), 1470 (s), 1180 (s).

**tLC:** Rf = 0.6 (Hexane).

**Physical characteristic:** Viscous oil.
IV. Trifluoride formations

![Diagram of molecules 50 and 66]

**Procedure:** In a dry 25 mL 2-neck flask containing a stirred solution of vinyl fluoride 50 (88 mg, 0.5 mmol) in 7.1 mL of dichloromethane, was added silver tetrafluoroborate (292 mg, 1.50 mmol) under a stream of nitrogen. XeF₂ (101 mg, 0.60 mmol) dissolved in 3.8 mL of dichloromethane was then added rapidly via cannula using positive nitrogen pressure. The flask was covered with aluminum foil and stirred for 1 d. The reaction mixture was then partitioned between saturated aqueous sodium bicarbonate and dichloromethane, and the organic phase was dried with anhydrous magnesium sulfate and filtered through a short pad of silica eluting with dichloromethane. After solvent evaporation, the products were isolated and purified by silica gel column chromatography eluting with hexane to afford 96 mg (90% yield) of 66 as a mixture (1 : 2) of cis and trans isomers.

**¹H-NMR (300 MHz, CDCl₃):** Reported for the cis and trans isomers;
1.70-1.95 (m, 2H), 2.00-2.08 (m, 1H), 2.08-2.40 (m, 3H), 2.65-2.80 (m, 1H), 4.65-4.83 (dm, J = 42.6 Hz, 1H), 7.14-7.19 (m, 1H), 7.21-7.24 (br d, J = 8.1 Hz, 2H), 7.28-7.36 (m, 2H).

**¹⁹F-NMR (283 MHz, CDCl₃):** Reported for the cis isomer;
-186.7 - -186.5 (dt, J = 46.0, 11.0 Hz, 1F), -98.4 - -97.4 (dd, J = 235.4, 13.6 Hz, 1F), -
97.0 - -96.1 (dd, J = 235.4, 6.8 Hz, 1F).

Reported for the trans isomer;
-183.5 - -183.0 (dddd, J = 47.0, 45.0, 14.0, 12.0 Hz, 1F), -98.4 - -97.4 (dd, J = 258.4,
48.1 Hz, 1F), -94.2 - -93.3 (dd, J = 258.1, 12.7 Hz, 1F).

HRMS: Calcd. for C_{12}H_{13}F_{3} (M+) 214.0969, found 214.0970.

Mass spectrum m/e: 214 (M+), 153, 119, 103, 91, 78, 65, 51.

tlc: Rf = 0.20 (Hexane).

Physical characteristic: Yellowish oil.
Procedure: In a dry 25 mL 2-neck flask containing a solution of AgOTf (226 mg, 0.85 mmol) in 6.1 mL of methylene chloride, vinyl stannane 68 (400 mg, 0.85 mmol) and XeF2 (144 mg, 0.85 mmol), dissolved in 6.1 mL and 5.5 mL of methylene chloride, respectively, were transferred by cannula into this solution. After stirring the solution for 20 min, more XeF2 (188 mg, 1.11 mmol) dissolved in 7.1 mL of methylene chloride was transferred by cannula into this solution followed by the addition of powdered AgBF4 (498 mg, 2.56 mmol) under a stream of argon. The solution was stirred overnight and worked-up with methylene chloride and saturated aqueous sodium bicarbonate. Column chromatography, eluting with hexane, afforded 65 mg (32% yield) of trifluoro compound 69. The difluorohydroxy 70 was formed as a byproduct (yield approx. 30%; 60 mg).

$^1$H-NMR (300 MHz, CDCl$_3$): 6.21 (td, $J = 54.3, 5.4$ Hz, 1H), 7.00-7.70 (m, 10H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): Reported for the geminal difluoride; -127.8 (dd, $J = 54.1, 10.2$ Hz).

IR (neat): 3000 (s), 1490 (s), 1440 (s), 650 (s), 600 (s).

Anal Calcd for C$_{14}$H$_{11}$F$_3$: C, 71.18; 4.69. Found: C, 70.93; H, 4.59.

tlc: Rf = 0.4 (Hexane).

Physical characteristic: Colorless oil.
$^{1}$H-NMR (300 MHz, CDCl$_3$): 2.84 (s, exchangeable with D$_2$O, 1H), 6.23 (t, $J = 55.2$ Hz, 1H), 7.32-7.40 (m, 4H), 7.36 (d, $J = 7.5$ Hz, 2H), 7.40-7.48 (m, 2H), 7.47 (d, $J = 6.9$ Hz, 2H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -127.4 (d, $J = 55.4$ Hz).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 78.0 (t, $J = 21.7$ Hz), 116.8 (t, $J = 250.9$ Hz), 127.0, 128.2, 128.3, 140.5.

IR: 3470 (br), 3070 (s), 1665 (s), 1600 (s), 1585 (s), 1500 (s), 1450 (s), 1380 (s), 1375 (s), 1350 (s), 1330 (s), 1295 (s), 1265 (s), 1240 (s), 1180 (s), 1140 (s), 1075 (s), 1050 (s), 1000 (s), 975 (s), 930 (s), 900 (s), 850 (m), 810 (s), 760 (s), 725 (s), 700 (s), 760 (s), 640 (s), 615 (s).

tlc: Rf = 0.3 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for trifluoride 69 was used (page 105). The yield of product was 60% (63 mg) from 158 mg (0.49 mmol) of starting material. Purification of this trifluoride could not be achieved beyond 70%. The estimated yield, based on weight and \(^1\)H-NMR integration, was approximately 60%. The trifluoride is a mixture (1 : 1) of cis and trans isomers.

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): 1.50-2.50 (m, 6H), 2.50-3.25 (m, 1H), 4.74 (br d, \(J = 47.7\) Hz, 1H), 7.00-7.50 (m, 5H).

\(^19\)F-NMR (283 MHz, CDCl\(_3\)): Reported for the cis and trans isomers; 
-200.1 (d, \(J = 45.8\) Hz), -188.7 (d, \(J = 40.0\) Hz), -131.6 (br d, \(J = 236.0\) Hz), -119.7 (dd, \(J = 264.6, 30.3\) Hz), -111.8 (dd, \(J = 238.1, 12.5\) Hz), -107.8 (br d, \(J = 275.9\) Hz).

\(^13\)C-NMR (125 MHz, CDCl\(_3\)): The carbons attached to the fluorine(s) could not be detected after 4000 scans. Reported for the methylene carbons adjacent to the carbons attached to the fluorine(s); 
21.8 (d, \(J = 11.4\) Hz), 26.6 (t, \(J = 18.8\) Hz).

IR (neat): 2960 (s), 2860 (s), 1730 (s), 1510 (s), 1490 (s), 1450 (s), 1120 (s), 1090 (s), 760 (s), 700 (s).

\textit{tlc}: \(R_f = 0.4\) (Hexane).
\textbf{Physical characteristic}: Colorless oil.
Procedure: The procedure for trifluoride 69 was used (page 105). The yield of product was 20% (28 mg) from 200 mg (0.58 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.89 (br t, J = 6.9 Hz, 3H), 1.20-1.40 (br s, 16H), 1.40-1.65 (m, 2H), 1.65-2.05 (m, 2H), 4.42 (dt, J = 46.2, 11.7 Hz, 1H).

$^{19}$F-NMR (283 MHz, CDCl$_3$): -234.4 (br dt, J = 47.6, 13.3 Hz, 1F), -108.8 (m, 2F).

$^{13}$C-NMR (125 MHz, CDCl$_3$): 14.1, 22.7, 29.2, 29.3, 29.31, 29.4, 29.5, 29.51, 29.6, 31.9, 33.0 (t, J = 22.6 Hz), 81.5 (dt, J = 178.0, 37.3 Hz), 121.1 (td, J = 242.1, 22.0 Hz).

IR (neat): 2920 (s), 2840 (s), 1470 (s), 1380 (m).

HRMS: Calcd. for C$_{13}$H$_{25}$F$_3$ (M$^+$) 238.1908, found 238.1913.


tlc: Rf = 0.6 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl fluoride 75b was used (page 86). The yield of product was 27% (20 mg) from 147 mg (0.31 mmol) of starting material.

\[ \text{Ph-SnBu}_3 \xrightarrow{\text{156}} \text{Ph-}\begin{array}{c} F \\ F \end{array} \xrightarrow{\text{159}} \]

**1H-NMR (300 MHz, CDCl}_3):** 5.67 (dt, \( J = 44.7, 9.0 \) Hz, 1H), 7.18 (br d, \( J = 7.2 \) Hz, 2H), 7.29 (br d, \( J = 7.8 \) Hz, 2H), 7.36 (br t, \( J = 6.9 \) Hz, 4H), 7.44 (br t, \( J = 6.9 \) Hz, 2H).

**19F-NMR (283 MHz, CDCl}_3):** -191.6 (dt, \( J = 45.8, 14.0 \) Hz, 1F), -109.3 (br d, \( J = 249.0 \) Hz, 1F), -105.5 (br d, \( J = 253.8 \) Hz, 1F).

**13C-NMR (125 MHz, CDCl}_3):** 93.0 (dt, \( J = 185.1, 35.2 \) Hz), 126.3 (t, \( J = 5.8 \) Hz), 127.3 (d, \( J = 6.8 \) Hz), 128.0, 129.4, 130.3. The quaternary benzylic carbon bearing the geminal difluoride could not be detected after 4000 scans.

**IR (neat):** 3060 (m), 3040 (m), 2930 (m), 1495 (m), 1450 (s), 1330 (m), 1260 (s), 1240 (s), 1205 (s), 1175 (s), 1155 (m), 1110 (m), 1095 (m), 1080 (m), 1060 (s), 1040 (s), 1030 (s), 1005 (s), 1000 (s), 920 (m), 840 (s), 820 (s), 760 (s), 745 (s), 700 (s), 680 (m).

**HRMS:** Calcd. for C\(_{14}\)H\(_{11}\)F\(_3\) (M\(^+\)) 236.0813, found 236.0816.

**Mass spectrum m/e:** 236 (M\(^+\)), 127, 109, 58.

**Anal Calcd for C\(_{14}\)H\(_{11}\)F\(_3\):** C, 71.18; H, 4.69. Found C, 70.19; H, 4.53.

**tlc:** Rf = 0.5 (Hexane).

**Physical characteristic:** Colorless oil.
V. Vinyl stannane syntheses


**Procedure:** In a dry 100 mL 2-neck flask under a static nitrogen atmosphere and equipped with a magnetic stirrer, were added LiCl (683 mg, 16.1 mmol), Pd(PPh₃)₄ (53 mg, 0.046 mmol), and 14 mL of THF. The reaction mixture was heated to 60°C. At this time, enol triflate (777 mg, 2.54 mmol) in 7 mL of THF was added to the reaction mixture via cannula. Likewise, (Me₃Sn)₂ (789 mg, 2.41 mmol) in 7 mL of THF was added to the reaction mixture. After stirring at 60°C for 9 h, the reaction was worked up in the usual manner with saturated aqueous sodium bicarbonate and ether/hexane (1:1). The organic phase was dried (MgSO₄), evaporated and purified by flash column chromatography (2% Et₃N in hexane) to afford 694 mg (90% yield) of 49.

**¹H-NMR (300 MHz, CDCl₃):** 0.12 (s, 9H), 1.70-1.84 (m, 1H), 1.92-1.96 (m, 1H), 2.20-2.28 (m, 1H), 2.30-2.36 (br s, 3H), 2.76-2.85 (m, 1H), 5.93-5.95 (br s, 1H), 7.19-7.22 (m, 1H), 7.24 (br s, 2H), 7.28-7.34 (br t, J = 7.2 Hz, 2H).

**¹³C-NMR (75 MHz, CDCl₃):** -10.4, 30.6, 31.7, 35.7, 40.1, 125.9, 126.8, 128.3, 136.3, 140.4, 147.4.
**IR (neat):** 3080 (w), 3060 (m), 3020 (s), 9080 (s), 2910 (s), 2840 (s), 2820 (s), 1620 (s), 1600 (s), 1490 (s), 1450 (s), 1430 (s), 1185 (m), 1140 (m), 1050 (w), 1030 (w), 920 (s), 760 (s), 690 (s), 610 (s).

**tlf:** Rf = 0.6 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 90% (694 mg) from 777 mg (2.54 mmol) of starting material.

\(^1\)H-NMR (300 MHz, C\(_6\)D\(_6\)): 0.16 (s, 9H), 0.83 (s, 9H), 1.13-1.33 (m, 3H), 1.68-1.74 (m, 1H), 1.80-1.86 (m, 1H), 1.97-2.05 (m, 1H), 2.20-2.28 (m, 1H), 5.90 (m, 1H).

\(^13\)C-NMR (75 MHz, C\(_6\)D\(_6\)): 10.4, 25.3, 27.3, 29.5, 32.3, 32.9, 44.3, 137.5, 139.7.

IR (neat): 2950 (br), 1615 (s), 1460 (s), 1480 (s), 1430 (s), 1390 (s), 1365 (s), 1295 (w), 1255 (s), 1230 (m), 1190 (s), 1170 (w), 1155 (m), 1070 (w), 1050 (w), 920 (s), 765 (br), 710 (br).

tlc: Rf = 0.85 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 28% (315 mg) from 1.08 g (3.45 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.10 (s, 9H), 1.20-1.50 (br t, J = 27.0 Hz, 16H), 2.15-2.21 (br q, J = 6.6 Hz, 2H), 2.34-2.39 (br t, J = 6.6 Hz, 2H), 5.48-5.53 (br t, J = 7.2 Hz, 1H).

nOe (500 MHz, CDCl$_3$): Positive nOe between 2.15-2.21 and 2.34-2.39.

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.

**Procedure:** The procedure for vinyl stannane 49 was used (page 110). The yield of product was 42% (604 mg) from 1.44 g (4.49 mmol) of starting material. Purification via normal phase flash column chromatography, eluting with 2% triethylamine in hexane, afforded vinyl stannane 60a as a mixture (8 : 1) of cis and trans isomers.

**1H-NMR** (300 MHz, CDCl₃): Reported for the cis isomer;
0.15 (s, 9H), 1.07-1.10 (d, J = 7.2 Hz, 3H), 1.40-1.52 (td, J = 12.6, 10.8 Hz, 1H), 1.96-2.03 (m, 1H), 2.11-2.22 (m, 1H), 2.28-2.35 (m, 1H), 2.50-2.55 (br s, 1H), 2.78-2.88 (m, J = 11.6 Hz, 1H), 5.90-5.93 (td, J = 2.4, 2.1 Hz, 1H), 7.20 (br s, 1H), 7.23 (br s, 2H), 7.29-7.33 (br t, J = 7.2 Hz, 2H).

**13C-NMR** (125 MHz, C₆D₆): Reported for the cis and trans isomers;
-9.5, -8.8, 22.0, 23.7, 35.0, 35.5, 36.1, 36.3, 37.5, 37.9, 40.6, 41.1, 126.3, 127.1, 127.3, 128.3, 128.7, 128.7, 133.4, 136.2, 136.6, 146.4, 147.5, 147.5.

**IR** (neat): Reported for the cis and trans isomers;
3060 (w), 3020 (m), 2950 (s), 2910 (s), 2880 (m), 2840 (m), 1600 (m), 1490 (m), 1450 (s), 1370 (w), 1210 (w), 930 (w), 760 (s), 700 (s), 680 (w).

**tlc:** Rf = 0.6 (Hexane).
**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 54% (570 mg) from 1.06 g (3.68 mmol) of starting material.

^1H-NMR (300 MHz, C₆D₆): 0.09 (s, 9H), 1.76-1.80 (t, J = 6.0 Hz, 2H), 2.37-2.47 (m, 4H), 3.55 (br s, 4H), 5.72 (br s, 1H).

tlc: Rf = 0.44 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 75% (959 mg) from 1.280 g (4.05 mmol) of starting material.

$^{1}$H-NMR (300 MHz, C$_6$D$_6$): 0.20 (s, 9H), 0.89-0.93 (br t, J = 6.6 Hz, 3H), 1.27 (br s, 16H), 2.08-2.14 (br q, J = 6.9 Hz, 2H), 5.94-5.98 (d, J = 12.3 Hz, 1H), 6.52-6.61 (dt, J = 12.3, 6.9 Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): -8.6, 14.4, 23.1, 29.76, 29.8, 30.1, 32.4, 36.9, 128.8, 149.0.

IR (neat): 2980 (s), 2920 (s), 2850 (s), 1595 (s), 1465 (br), 1380 (m), 1190 (m), 985 (m), 910 (m), 770 (s), 720 (s).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 29% (268 mg) from 938 mg (3.45 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.00 (s, 9H), 0.75 (s, 6H), 2.00 (d, J = 2.1 Hz, 2H), 2.11 (s, 2H), 6.41 (t, J = 1.8 Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): -10.6, 28.2, 34.4, 46.0, 51.7, 138.0, 168.4, 195.0.

IR (neat): 2950 (s), 2880 (s), 2810 (m), 1680 (s), 1660 (s), 1580 (m), 1460 (m), 1410 (m), 1380 (m), 1360 (m), 1340 (m), 1290 (m), 1270 (s), 1250 (s), 1190 (m), 1140 (m), 990 (m), 910 (m), 860 (m), 770 (br).

tlc: Rf = 0.6 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 16% (83 mg) from 5.23 mg (1.61 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.37 (s, 9H), 0.93 (t, $J = 7.2$ Hz, 3H), 3.95 (q, $J = 7.2$ Hz, 2H), 6.61 (s, 1H), 7.00-7.04 (m, 2H), 7.07-7.13 (m, 3H).

nOe (500 MHz, CDCl$_3$): Positive nOe between the ortho phenyl protons and vinyl proton.

$^{13}$C-NMR (125 MHz, C$_6$D$_6$): -6.1, 14.1, 60.6, 126.8, 127.3, 128.4, 130.5, 145.2, 168.1, 173.6.

IR (neat): 2980 (s), 2900 (s), 1700 (s), 1585 (s), 1485 (s), 1440 (m), 1390 (m), 1365 (s), 1310 (s), 1270 (m), 1220 (s), 1180 (br), 1120 (m), 1095 (m), 1030 (s), 880 (s), 770 (br), 695 (s).

tlc: Rf = 0.3 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 46% (63 mg) from 136 mg (0.48 mmol) of starting material.

$^1$H-NMR (300 MHz, C₆D₆): 0.29 (s, 9H), 0.84 (s, 3H), 1.10 (s, 3H), 1.76 (d, J = 9.0 Hz, 1H), 2.07 (br q, J = 6.0 Hz, 1H), 2.34 (dt, J = 9.0, 5.7 Hz, 1H), 2.70 (t, J = 6.0 Hz, 1H), 7.26 (d, J = 6.3 Hz, 1H).

$^{13}$C-NMR (125 MHz, C₆D₆): -9.7, 22.8, 26.2, 41.4, 46.4, 53.5, 59.0, 140.4, 164.9, 205.2.

IR (neat): 2950 (br), 1665 (s), 1570 (m), 1470 (br), 1390 (m), 1370 (m), 1315 (m), 1225 (m), 1190 (br), 775 (br).

tlc: Rf = 0.80 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 15% (139 mg) from 907 mg (3.06 mmol) of starting material.

\[^{1}H-NMR\ (300\ MHz,\ CDCl_3):\ 0.11\ (s,\ 9H),\ 0.91\ (s,\ 3H),\ 1.22-1.32\ (m,\ 2H),\ 1.41-1.57\ (m,\ 1H),\ 1.60-1.66\ (m,\ 2H),\ 1.75-1.79\ (m,\ 1H),\ 1.96-2.04\ (dd,\ J = 16.8,\ 6.0\ Hz,\ 1H),\ 2.08-2.25\ (m,\ 3H),\ 5.62\ (s,\ 1H),\ 5.78-5.84\ (m,\ 1H).\]

tlc: \(R_f = 0.60\) (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 49 was used (page 110). The yield of product was 15% (176 mg) from 1.180 g (3.98 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl₃): 0.11 (s, 9 H), 1.01 (s, 3 H), 1.26-1.40 (m, 2 H), 1.42-1.48 (m, 2 H), 1.60-1.73 (m, 1 H), 1.70-1.84 (m, 1 H), 2.15-2.17 (br s, 2 H), 2.22-2.36 (td, J = 18.0, 5.1 Hz, 1 H), 2.35-2.50 (m, 1 H), 5.39 (br s, 1 H), 6.10 (s, 1 H).

tlc: Rf = 0.60 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** In a dry 50 mL round bottom flask, PdCl₂ (500 mg, 2.82 mmol) was added followed by PPh₃ (1.84 g, 7.05 mmol) and 17 mL of dry DMF. The reaction mixture was then heated to 140°C - 150°C. When the solution became homogeneous, the reaction was cooled to ambient temperature, filtered and washed with ethyl ether to afford 1.98 g (100% yield) of Pd(PPh₃)₂Cl₂ as a bright yellow crystalline solid.

In a dry 25 mL 2-neck flask under a static nitrogen atmosphere and equipped with a magnetic stirrer, Pd(PPh₃)₂Cl₂ (136 mg, 0.19 mmol) was added under a stream of nitrogen. Then 4.8 mL of THF was added to this flask followed by 1.16 mL of a 1.0 M THF solution (1.16 mmol) of diisobutylaluminum hydride. The reaction mixture was then stirred at room temperature for 30 min. A 3.0 mL aliquot of this solution was transferred via syringe to another dry 50 mL 2-neck flask containing LiCl (521 mg, 12.3 mmol) and Li₂CO₃ (143 mg, 1.93 mmol). This reaction mixture was heated to 60°C. At this time, enol triflate (620 mg, 1.93 mmol) in 10 mL of THF was added to the reaction mixture via cannula. Likewise, (Me₃Sn)₂ (602 mg, 1.84 mmol) in 11.5 mL of THF was added to the reaction mixture via cannula. After stirring at 60°C for 1 d, the reaction was worked up in the usual manner with saturated aqueous sodium bicarbonate and ether/hexane (1:1). Column chromatography, eluting with 2% triethylamine in hexane, and distillation afforded 106 mg (17% yield) of vinyl stannanes 61a and 60a in a ratio of 2:1.
$^1$H-NMR (300 MHz, C$_6$D$_6$): Reported for 61a;

0.23 (s, 9H), 0.92-1.02 (dd, $J = 24.3, 7.5$ Hz, 1H), 1.57-1.59 (m, 1H), 1.68 (s, 3H),
1.79-1.84 (m, 1H), 1.99-2.04 (br t, $J = 7.5$ Hz, 1H), 2.10-2.12 (br d, $J = 7.8$ Hz, 1H),
2.22 (br s, 1H), 2.60-2.72 (m, 1H), 7.10-7.15 (m, 3H), 7.19-7.24 (br t, $J = 7.2$ Hz, 2H).

tlc: Rf = 0.65 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 61a was used (page 122). The yield of product was 27% (284 mg) from 1.06 mg (3.45 mmol) of starting material.

**$^{1}$H-NMR** (300 MHz, C$_6$D$_6$): 0.28 (s, 9H), 2.09 (td, $J$ = 8.1, 4.5 Hz, 2H), 2.57 (t, $J$ = 8.1 Hz, 2H), 3.35 (s, 3H), 6.11 (t, $J$ = 4.5 Hz, 1H), 6.64 (dd, $J$ = 8.4, 2.7 Hz, 1H), 6.73 (d, $J$ = 2.7 Hz, 1H), 7.08 (d, $J$ = 8.4 Hz, 1H).

**$^{13}$C-NMR** (125 MHz, C$_6$D$_6$): -8.9, 24.9, 28.9, 54.8, 111.3, 114.8, 128.8, 131.7, 136.9, 137.9, 140.1, 158.9.

**IR** (neat): 2940 (br), 1600 (s), 1580 (m), 1560 (s), 1500 (s), 1470 (m), 1430 (s), 1320 (m), 1300 (s), 1280 (s), 1250 (s), 1190 (m), 1165 (m), 1150 (m), 1130 (s), 1115 (m), 1045 (s), 840 (s), 810 (m), 770 (s), 670 (m).

**tlc**: Rf = 0.5 (Hexane).

**Physical characteristic**: Colorless oil.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, was added powdered CuCN (163 mg, 1.82 mmol). The flask was again flame dried until the CuCN could be stirred freely with the magnetic stirrer. After the flask had cooled to ambient temperature, THF (15 mL) was added followed by cooling of this solution to -78°C with a dry ice-acetone bath. Then, 1.6 mL of a 2.34 M solution of n-BuLi (3.60 mmol) in hexane was added dropwise. After stirring this solution for 30 min at -78°C, trimethyltin hydride (601 mg, 3.65 mmol) in THF (2.0 mL) was added rapidly via cannula. After stirring this solution for an additional 30 min at -78°C, enol triflate 133 (348 mg, 1.09 mmol) in THF (2.0 mL) was added rapidly via cannula. The reaction was stirred at -78°C for 30 min and quenched with aqueous NH₄OH/NH₄Cl (1 : 9, 15 mL). The dry ice-acetone bath was removed, and the reaction was allowed to warm to ambient temperature. The aqueous phase was extracted with ethyl ether (3 X). The combined organic extracts were washed with brine (3 X), dried with anhydrous sodium sulphate, filtered, and the solvent was evaporated under reduced pressure. Column chromatography eluting with 2% triethylamine in hexane, afforded 207 mg (51% yield) of 134.

$^1$H-NMR (300 MHz, C₆D₆): 0.21 (s, 9H), 0.87-0.96 (m, 2H), 1.25-1.46 (m, 3H), 1.66-1.75 (m, 1H), 1.92-2.01 (m, 1H), 2.14-2.24 (m, 1H), 2.38-2.43 (m, 1H), 2.63-2.74 (m, 1H), 4.98 (dd, J = 10.5, 1.8 Hz, 1H), 5.03 (dd, J = 17.1, 1.8 Hz, 1H), 5.78
(ddt, J = 16.5, 10.2, 6.9 Hz, 1H), 5.94 (m, 1H), 7.12 (br d, J = 7.2 Hz, 3H), 7.22 (br t, J = 7.4 Hz, 2H).

$^{13}$C-NMR (125 MHz, C$_6$D$_6$): -8.7, 30.8, 36.5, 37.2, 37.4, 40.9, 41.6, 114.8, 126.4, 127.2, 128.7, 137.4, 138.8, 146.4, 147.5.

IR (neat): 3070 (m), 3050 (m), 3020 (m), 2960 (s), 2900 (s), 2840 (s), 1635 (m), 1600 (m), 1490 (m), 1450 (m), 910 (s), 750 (s), 695 (s).

tlc: Rf = 0.85 (Hexane).

Physical characteristic: Colorless oil.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer and a reflux condenser, were added the corresponding vinyl sulphone (859 mg, 2.68 mmol) and toluene (29 mL) followed by ACN (13 mg, 0.1 mmol). Tri-n-butyl tin hydride was then added, and the solution was heated to 105°C overnight. After cooling the solution to ambient temperature, water was added followed by extractive work-up with ethyl ether (3 X). The combined organic extracts were then filtered through a short pad of basic alumina and further eluted with hexane. After solvent evaporation under reduced pressure, the residue was heated to 80°C at approx. 1.5 mm Hg for 2 h. The residue contained 509 mg (40% yield) of 68.

\[
\begin{align*}
1^H\text{-NMR (300 MHz, C}_6\text{D}_6):} & \quad 0.81 (\text{br t, J} = 8.1 \text{ Hz, 6H}), 0.91 (\text{t, J} = 7.2 \text{ Hz, 9H}), 1.33 \quad (
\text{sixtet, J} = 7.5 \text{ Hz, 6H}), 1.50 \quad (\text{sextet, J} = 7.8 \text{ Hz, 6H}), 6.83 \quad \text{(s, 1H)}, 7.08-7.15 \quad \text{(m, 10H)}. \\
1^{13}\text{C-NMR (75 MHz, C}_6\text{D}_6):} & \quad 10.6, 13.5, 27.3, 29.2, 127.3, 127.5, 127.9, 129.3, 144.8, 159.2. \\
\text{IR (neat):} & \quad 2960 \quad \text{(s), 2920 \quad (s), 2880 \quad (s), 2860 \quad (s), 1600 \quad (w), 1490 \quad (m), 1460 \quad (m), 1440} \\
& \quad \text{(m), 1380 \quad (m), 1075 \quad (m), 775 \quad (m), 760 \quad (m), 700 \quad (s).} \\
\text{tlc:} & \quad R_f = 0.9 \quad \text{(Hexane).} \\
\text{Physical characteristic:} & \quad \text{Colorless oil.}
\end{align*}
\]
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 37% (165 mg) from 306 mg (0.95 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.82 (br s, 8H), 0.94 (t, $J = 7.2$ Hz, 9H), 1.00-1.20 (m, 12H), 1.08 (br t, $J = 9.9$ Hz, 4H), 1.39 (sextet, $J = 7.5$ Hz, 6H), 1.61 (octet, $J = 7.5$ Hz, 6H), 2.13 (br quintet, $J = 11.4$ Hz, 2H), 2.31 (br dd, $J = 12.9, 2.4$ Hz, 1H), 2.45 (br d, $J = 2.1$ Hz, 1H), 5.55 (s, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): 10.6, 14.0, 27.5, 27.8, 28.6, 29.7, 29.8, 32.4, 38.1, 40.4, 48.2, 118.5, 159.4.

IR (neat): 2980 (br), 2960 (br), 2875 (s), 2865 (s), 1610 (s), 1625 (s), 1565 (s), 1555 (s), 14.80 (s), 1465 (s), 1070 (s), 1000 (m), 960 (m), 930 (w), 875 (m), 865 (m), 820 (w), 810 (s), 765 (w), 755 (w), 730 (w), 690 (s), 665 (br), 590 (s).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 77% (228 mg) from 200 mg (0.65 mmol) of starting material.

\(^1\)H-NMR (300 MHz, C\(_6\)D\(_6\)): 0.86-0.98 (m, 3H), 0.96 (t, J = 7.2 Hz, 9H), 1.08 (br t, J = 8.4 Hz, 6H), 1.30-1.50 (m, 6H), 1.56 (quintet, J = 8.1 Hz, 4H), 1.70 (quintet, J = 7.8 Hz, 6H), 2.11 (br t, J = 5.4 Hz, 4H), 4.12 (q, J = 7.2 Hz, 2H), 5.53 (br s, 1H).

\(^13\)C-NMR (75 MHz, C\(_6\)D\(_6\)): 10.5, 14.0, 27.6, 28.6, 29.6, 46.0, 46.2, 61.2, 121.9, 155.1.

IR (neat): 2980 (s), 2920 (s), 2880 (s), 2860 (s), 1710 (br), 1540 (br), 1460 (br), 1440 (br), 1370 (br), 1235 (s), 1220 (m), 675 (br).

tlc: Rf = 0.5 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 37% (446 mg) from 823 mg (2.67 mmol) of starting material.

\[ \text{1H-NMR (300 MHz, C}_6\text{D}_6): \text{ Reported for the E and Z isomers;} \]
\[ 0.75 \text{ (br t, } J = 9.9 \text{ Hz, 6H)}, 0.83 \text{ (t, } J = 7.2 \text{ Hz, 9H)}, 0.96 \text{ (t, } J = 7.2 \text{ Hz, 9H)}, 1.11 \text{ (br t, } J = 7.2 \text{ Hz, 6H)}, 1.23 \text{ (sextet, } J = 7.5 \text{ Hz, 6H)}, 1.42 \text{ (sextet, } J = 7.5 \text{ Hz, 12H)}, 1.68 \text{ (heptet, } J = 7.8 \text{ Hz, 6H)}, 2.31 \text{ (br s, 6H)}, 6.14 \text{ (br d, } J = 1.2 \text{ Hz, 1H)}, 6.66 \text{ (br s, 1H)}, 7.20-7.30 \text{ (m, 4H)}, 7.37 \text{ (dd, } J = 8.4, 1.8 \text{ Hz, 2H)}, 7.50-7.65 \text{ (m, 2H)}, 7.62 \text{ (d, } J = 8.7 \text{ Hz, 2H)}, 7.69 \text{ (td, } J = 8.4, 1.8 \text{ Hz, 2H)}, 7.77 \text{ (br s, 1H)}, 7.87 \text{ (br s, 1H)}. \]

\[ \text{13C-NMR (75 MHz, C}_6\text{D}_6): \text{ 10.2, 13.5, 27.3, 29.1, 29.3, 112.6, 123.7, 124.0, 124.3, 125.4, 125.8, 126.0, 127.2, 127.4, 127.5, 127.6, 127.8, 128.0, 128.2, 128.4, 132.8, 133.5, 140.7, 143.6, 151.8, 155.6.} \]

\[ \text{IR (neat): 3060 (m), 2960 (s), 2920 (s), 2870 (s), 2850 (s), 1600 (w), 1585 (w), 1510 (w), 1465 (m), 1455 (m), 1450 (w), 1380 (m), 890 (m), 855 (m), 810 (s), 755 (s), 690 (m), 670 (s), 620 (s).} \]

\[ \text{tlc: Rf = 0.9 (Hexane).} \]

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 29% (255 mg) from 600 mg (1.78 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): Reported for the E and Z isomers;
0.89 (t, J = 7.2 Hz, 6H), 0.95 (t, J = 7.2 Hz, 9H), 0.96 (t, J = 7.2 Hz, 9H), 1.04 (t, J = 7.8 Hz, 6H), 1.05 (t, J = 8.4 Hz, 6H), 1.32 (br s, 36H), 1.30-1.60 (m, 12H), 1.64 (heptet, J = 4.5 Hz, 12H), 1.83 (s, 3H), 1.92 (s, 3H), 2.19 (br q, J = 5.7 Hz, 4H), 5.69 (d, J = 0.9 Hz, 1H), 5.74 (br s, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): Reported for the E and Z isomers;
10.0, 10.2, 13.6, 14.0, 23.2, 27.8, 27.9, 28.6, 29.8, 30.2, 32.4, 121.7, 123.1.

IR (neat): 2960 (s), 2920 (s), 2850 (s), 1605 (m), 1465 (m), 1455 (m), 1375 (m), 1070 (w), 860 (br), 840 (w), 690 (m), 665 (m).

tlc: $R_f$ = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 28% (300 mg) from 721 mg (2.66 mmol) of starting material.

\(^1\)H-NMR (300 MHz, C\(_6\)D\(_6\)): Reported for the E and Z isomers;
0.95 (br t, J = 7.2 Hz, 18H), 1.13 (br t, J = 8.4 Hz, 12H), 1.45 (sixtet, J = 7.5 Hz, 12H), 1.70 (sixtet, J = 7.5 Hz, 12H), 2.14 (d, J = 1.2, Hz, 6H), 6.55 (d, J = 0.9 Hz, 2H), 6.59 (br t, J = 7.5 Hz, 2H), 6.94 (d, J = 8.1 Hz, 2H), 7.02 (td, J = 8.1, 1.2 Hz, 2H), 8.25 (br d, J = 4.8 Hz, 2H).

\(^1\)C-NMR (75 MHz, C\(_6\)D\(_6\)): Reported for the E and Z isomers;
13.4, 14.0, 14.1, 24.0, 27.8, 28.0, 29.7, 30.0, 119.6, 121.8, 136.8, 138.1, 146.6, 147.3, 156.8.

IR (neat): 2960 (s), 2920 (s), 2880 (s), 2850 (s), 1590 (s), 1560 (m), 1475 (s), 1465 (s), 1455 (s), 1430 (s), 1375 (s), 1070 (m), 830 (s), 770 (m), 740 (s), 675 (br), 630 (m).

tlc: Rf = 0.8 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 68 was used (page 127). The yield of product was 100% (2.00 g) from 1.36 g (4.35 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.96 (t, J = 7.2 Hz, 9H), 1.02-1.07 (m, 6H), 1.41 (sixtet, J = 7.2 Hz, 6H), 1.65 (octet, J = 7.5 Hz, 6H), 1.87-2.00 (m, 3H), 2.25 (dt, J = 12.9, 4.5 Hz, 2H), 2.36 (br s, 1H), 2.43 (br s, 1H), 2.48 (br s, 1H), 2.53 (tt, J = 12.0, 3.3 Hz, 1H), 5.65 (s, 1H), 7.10 (br t, J = 6.9 Hz, 2H), 7.15 (br s, 2H), 7.18 (br t, J = 6.9 Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): 10.6, 14.1, 27.8, 29.8, 36.6, 38.0, 40.4, 119.9, 126.3, 127.0, 128.6, 146.8, 157.9.

IR (neat): 3060 (w), 3030 (w), 2960 (s), 2930 (s), 2880 (s), 2860 (s), 1810 (w), 1615 (m), 1495 (m), 1460 (m), 1450 (m), 1440 (m), 1380 (w), 1070 (w), 810 (w), 750 (w), 700 (w).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** In a dry 2-neck flask under argon was added \( \text{PdCl}_2(\text{PPh}_3)_2 \) (32 mg, 0.05 mmol). The flask was purged with argon. The homopropargyl alcohol \( 87 \) (504 mg, 2.27 mmol) dissolved in THF (11 mL) was transferred to the flask containing the catalyst via cannula using positive nitrogen pressure. Immediately thereafter, trimethyltin hydride (374 mg, 2.27 mmol) in THF (1.0 mL) was transferred in the same manner. After a few minutes, the reaction was worked up in the usual manner with saturated aqueous sodium bicarbonate and ethyl ether. Drying of the organic phase with anhydrous sodium sulfate and evaporation of the solvent afforded the crude reaction mixture. The mixture was then separated using silica gel column chromatography eluting with 2% triethylamine in 20% ethyl acetate in hexane to afford the vinyl stannane \( 73a \) as a minor product (\( \leq 30\% \) yield). Additional vinyl stannanes, \( 88 \) (50% yield) and \( 89 \) (\( \leq 10\% \) yield), were also isolated from this reaction. The yield of \( 88 \) was determined to be 50% (1.30 g) when using 1.49 g (6.71 mmol) of \( 87 \).

The minor byproduct \( 89 \) is presumed to have been formed from hexamethyl ditin, present in the reagent, trimethyl tin hydride, in small quantities.
\( ^1H\text{-NMR} \) (300 MHz, C\(_6\)D\(_6\)): 0.31 (s, 9H), 1.20 (br s, 22H), 2.32 (s, 2H), 5.47 (d, \( J = 3.3 \) Hz, 1H), 5.81 (dt, \( J = 3.3, 1.2 \) Hz, 1H).

\( ^{13}C\text{-NMR} \) (125 MHz, CDCl\(_3\)): -7.9, 19.2, 22.1, 22.6, 26.0, 26.4, 34.5, 51.5, 75.5, 127.9, 152.5.

IR: 3400 (br), 2950 (br), 1600 (m), 1475 (m), 1450 (m), 1070 (br), 770 (br), 640 (m).

mp: Near room temperature.

tlc: \( R_f = 0.8 \) (20% Ethyl acetate in hexane).

Physical characteristic: Transparent crystalline solid.
$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.13 (s, 9H), 1.27 (br s, 20H), 1.42-1.53 (m, 2H), 2.26 (d, $J = 6.6$ Hz, 2H), 6.14 (d, $J = 18.9$ Hz, 1H), 6.37 (dt, $J = 19.2$, 6.6 Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): ~9.3, 19.8, 22.5, 22.9, 26.4, 26.9, 34.9, 49.8, 74.3, 132.8, 145.4.

IR: 2400 (br), 2940 (s), 2850 (s), 1600 (s), 1485 (s), 1450 (s), 1070 (s), 1000 (s), 900 (s), 770 (br), 640 (s).

mp: 76 - 78$^\circ$C.

tlc: Rf = 0.7 (20% Ethyl acetate in hexane).

Physical characteristic: Off-white crystalline solid.
**1H-NMR** (300 MHz, CDCl₃): 0.14 (s, 9H), 0.17 (s, 9H), 1.21 (s, 1H), 1.27-1.48 (m, 23H), 6.68 (s, 1H).

**13C-NMR** (125 MHz, C₆D₆): -7.5, -5.3, 19.5, 22.5, 22.9, 26.4, 26.7, 34.9, 57.8, 75.8, 146.9, 166.5.

**nOe** (500 MHz, C₆D₆): Positive nOe between the allyl methylene hydrogens (2.44 ppm) and vinyl hydrogen (6.68 ppm). Positive nOe between the two trimethyl tin hydrogens (0.14 and 0.17 ppm).

**IR**: 3610 (m), 2940 (s), 2860 (s), 1470 (s), 1445 (s), 1380 (m), 1350 (m), 1250 (m), 1190 (m), 1070 (m), 1010 (m), 900 (m), 770 (s), 725 (m), 715 (m), 620 (m).

**tlc**: Rf = 0.8 (20% Ethyl acetate in hexane).

**Physical characteristic**: White-crystalline solid.
Procedure: The procedure for vinyl stannane 73a was used (page 134). The yield of product was 4% (100 mg) from 1.17 g (7.04 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl₃): 0.13 (s, 9H), 0.88 (br t, J = 6.3 Hz, 3H), 1.20-1.40 (br s, 16H), 2.26 (t, J = 6.9 Hz, 2H), 5.12 (d, J = 2.7 Hz, 1H), 5.64 (br s, 1H).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 73a was used (page 134). The yield of product was 43% (1.00 g) from 1.170 g (7.04 mmol) of starting material.

$^{1}$H-NMR (300 MHz, CDCl$_3$): 0.10 (s, 9H), 0.88 (br t, $J = 6.9$ Hz, 3H), 1.26 (br s, 16H), 2.00-2.20 (m, 2H), 5.91 (d, $J = 18.6$ Hz, 1H), 6.00 (dt, $J = 18.9$, 5.1 Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): -9.8, 14.4, 23.2, 29.7, 29.9, 30.1, 32.4, 38.1, 128.0, 149.5.

IR (neat): 2960 (s), 2920 (s), 2860 (s), 1600 (m), 1470 (br), 1380 (w), 1190 (w), 990 (br), 770 (br), 720 (br), 630 (br).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.

**Procedure:** The procedure for vinyl stannane 73a was used (page 134). The yield of product was 100% (1.520 g) from 500 mg (3.52 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): Reported for the vinyl hydrogen; 6.19 (s).

tlc: Rf = 0.2 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl stannane 73a was used (page 134). The yield of product was 52% (1.02 g) from 750 mg (4.21 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.90 (t, $J = 7.2$ Hz, 9H), 1.04 (br t, $J = 8.1$ Hz, 6H), 1.35 (sixtet, $J = 7.2$ Hz, 6H), 1.58 (heptet, $J = 7.5$ Hz, 6H), 6.89 (br d, $J = 6.6$ Hz, 1H), 6.96 (br t, $J = 7.5$ Hz, 2H), 6.96-7.02 (m, 1H), 7.10-7.20 (br s, 7H).

nOe: A positive nOe between the vinyl hydrogen and methylene hydrogens attached to the tin.

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): 10.4, 13.9, 27.7, 29.4, 125.5, 126.7, 127.1, 128.3, 129.1, 129.7, 137.9, 139.2, 146.2, 149.9.

IR (neat): 3080 (m), 3060 (m), 3020 (m), 2960 (s), 2880 (s), 2860 (s), 1600 (m), 1495 (m), 1490 (m), 1475 (m), 1470 (m), 1460 (m), 1380 (m), 1070 (m), 790 (m), 765 (m), 695 (s), 665 (br).

tlc: Rf = 0.3 (Hexane).

Physical characteristic: Colorless oil.

**Procedure:** The isolated yield of product was 45% (438 mg) from 1.350 g (2.81 mmol) of starting material using the referenced procedure cited above.

$^1$H-NMR (300 MHz, CDCl₃): 0.13 (s, 9H), 0.89 (br t, J = 7.2 Hz, 3H), 1.26 (br s, 18H), 2.26 (br t, J = 7.2 Hz, 2H), 5.12 (d, J = 2.7 Hz, 1H), 5.64 (br s, 1H).

$^{13}$C-NMR (75 MHz, C₆D₆): −9.4, 14.5, 23.2, 29.7, 29.9, 30.1, 30.2, 32.5, 41.4, 125.0, 155.5.

IR (neat): 2950 (s), 2910 (s), 2840 (s), 1460 (br), 1375 (w), 1185 (w), 910 (m), 765 (br), 715 (br).

*tlc:* Rf = 0.9 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 72% (680 mg) from 1.330 g (2.93 mmol) of starting material.

\(^1\)H-NMR (300 MHz, C\(_6\)D\(_6\)): 0.04 (s, 9H), 0.85-1.05 (m, 1H), 1.25-1.75 (m, 3H), 1.85-2.05 (m, 1H), 2.07 (br s, 1H), 3.49 (br s, 1H), 6.10 (dd, J = 5.7, 3.6 Hz, 1H), 7.02-7.14 (m, 2H), 7.14-7.22 (m, 3H).

\(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): -9.6, 20.5, 27.3, 33.5, 47.3, 125.8, 127.9, 128.4, 137.6, 144.2, 146.6.

IR (neat): 3080 (m), 3040 (m), 3020 (s), 2980 (s), 2920 (s), 2840 (s), 2820 (s), 1600 (m), 1490 (s), 1450 (s), 1440 (s), 1185 (m), 890 (m), 760 (br), 700 (s).

tlc: Rf = 0.6 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 24% (94 mg) from 500 mg (0.86 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.22 (s, 9H), 0.77 (s, 3H), 0.80-1.00 (m, 5H), 0.98 (s, 3H), 1.30 (br heptet, $J$ = 7.2 Hz, 3H), 1.40-1.60 (m, 3H), 1.60-2.00 (m, 3H), 2.05-2.15 (m, 1H), 2.38 (br t, $J$ = 7.2 Hz, 1H), 2.45-2.60 (m, 1H), 3.00-3.10 (m, 1H), 3.22 (s, 3H), 5.37 (br d, $J$ = 5.1 Hz, 1H), 5.91 (br t, $J$ = 1.2 Hz, 1H).

$^{13}$C-NMR (125 MHz, C$_6$D$_6$): 9.2, 13.9, 19.5, 21.4, 28.6, 31.2, 32.5, 34.2, 35.9, 37.5, 37.7, 39.4, 46.8, 51.3, 55.4, 57.1, 80.5, 121.6, 140.1, 141.4, 158.0.

IR (neat): 2930 (s), 2900 (s), 2850 (br), 1450 (br), 1370 (s), 1250 (s), 1190 (s), 1100 (s).

tlc: Rf = 0.5 (10% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
**Procedure:** The procedure for vinyl stannane 76a was used (page 142). The yield of product was 30% (148 mg) from 656 mg (1.24 mmol) of starting material. Vinyl stannane 81a is a mixture (1:1) of cis and trans isomers.

**$^1$H-NMR (300 MHz, C$_6$D$_6$):** Reported for the cis and trans isomers;
0.27 (s, 9H), 2.97 (s, 3H), 3.08 (s, 3H), 4.24 (d, J = 8.1 Hz, 1H), 6.11 (br s, 1H), 7.00-7.20 (m, 5H).

**$^{13}$C-NMR (75 MHz, C$_6$D$_6$):** Reported for the cis and trans isomers;
-8.0, -6.1, 24.7, 30.0, 31.9, 34.4, 36.0, 36.3, 41.7, 41.8, 50.2, 55.2, 107.0, 124.2, 127.2, 128.7, 139.3, 141.8, 146.3, 147.3, 152.8.

**IR (neat):** 2960 (br), 2920 (br), 1600 (s), 1465 (s), 1455 (s), 1370 (s), 1340 (s), 1170 (br), 1120 (br), 1055 (br), 770 (br), 760 (s), 700 (s), 670 (s), 660 (s).

**tlc:** Rf = 0.5 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 64% (2.10 g) from 5.00 g (12.7 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.16 (s, 9H), 1.40-1.50 (m, 4H), 1.69 (dd, $J = 11.4$, 5.7 Hz, 2H), 2.16 (dd, $J = 11.4$, 6.0 Hz, 2H), 2.34-2.37 (m, 2H), 6.13 (t, $J = 6.2$ Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): -10.0, 27.5, 27.6, 31.1, 33.2, 34.8, 143.0, 147.3.

IR (neat): 2960 (s), 2920 (s), 2850 (s), 2840 (s), 1610 (m), 1445 (s), 1355 (m), 1190 (m), 850 (m), 770 (s), 710 (s).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 65% (2.18 g) from 5.00 g (12.3 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.15 (s, 9H), 1.44 (br s, 8H), 2.16 (br dd, J = 7.8, 3.6 Hz, 2H), 2.40 (br s, 2H), 5.90 (t, J = 7.8 Hz, 1H).

$^{13}$C-NMR (125 MHz, C$_6$D$_6$): 9.9, 26.2, 26.8, 27.4, 29.5, 29.6, 30.7, 140.8, 144.4.

IR (neat): 2980 (m), 2920 (s), 2840 (s), 1610 (m), 1470 (m), 1450 (m), 1190 (m), 900 (m), 830 (m), 760 (m), 710 (m).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 50% (733 mg) from 2.15 g (5.10 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.16 (s, 9H), 1.41-1.49 (br s, 10H), 2.16 (dd, $J = 11.4, 8.1$ Hz, 2H), 2.42 (br s, 2H), 5.82 (t, $J = 8.1$ Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): -9.6, 24.8, 26.3, 26.4, 26.5, 26.7, 28.0, 31.4, 140.9, 144.4.

IR (neat): 2920 (s), 2860 (s), 1608 (m), 1475 (s), 1450 (s), 1190 (m), 765 (s), 715 (s).

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for vinyl stannane 76a was used (page 142). The yield of product was 80% (2.40 g) from 3.05 g (6.71 mmol) of starting material.

$^1$H-NMR (300 MHz, C$_6$D$_6$): 0.89-1.03 (m, 2H), 0.96 (t, $J = 7.2$ Hz, 9H), 1.30-1.36 (m, 1H), 1.41 (sextet, $J = 7.2$ Hz, 6H), 1.50-1.58 (m, 1H), 1.62 (sextet, $J = 7.8$ Hz, 6H), 1.70-1.80 (m, 1H), 1.80-1.95 (m, 1H), 2.20-2.40 (m, 6H), 2.77 (br t, $J = 11.1$ Hz, 1H), 6.01 (br s, 1H), 7.11 (br t, $J = 7.5$ Hz, 2H), 7.13-7.17 (overlapping with C$_6$D$_6$, m, 2H), 7.20 (br t, $J = 7.5$ Hz, 1H).

$^{13}$C-NMR (75 MHz, C$_6$D$_6$): 9.2, 14.0, 27.0, 29.8, 31.2, 33.0, 36.2, 40.6, 126.2, 127.2, 128.6, 137.2, 140.2, 147.6.

tlc: Rf = 0.9 (Hexane):

Physical characteristic: Colorless oil.
VI. Vinyl triflate syntheses

![Chemical Structure](image)


Procedure: In a dry 50 mL two-neck flask under a static nitrogen atmosphere and equipped with a magnetic stirrer, diisopropyl amine (0.80 mL, 5.7 mmol) was added followed by 20 mL of THF. After cooling this solution to 0°C, 3.59 mL of a 1.60 M hexane solution (5.7 mmol) of n-BuLi was added dropwise. The solution was allowed to stir for 20 min and transferred via cannula using positive nitrogen pressure to another 250 mL two-neck flask containing the ketone 82 (1.00 g, 5.70 mmol) in 40 mL of THF, previously cooled to -78°C. The solution was warmed to 0°C after 1 h. At this temperature, N-phenyltrifluoromethanesulfonimide (2.19 g, 6.10 mmol) in 40 mL of THF was transferred to the flask via cannula, and the reaction mixture was warmed to ambient temperature. After stirring for 6 h, the reaction was worked up in the usual manner with saturated aqueous sodium bicarbonate and ethyl ether. Anhydrous magnesium sulphate was used to dry the organic phase. Purification via flash column chromatography, eluting with hexane, afforded 1.52 g (87% yield) of the corresponding enol triflate.
$^{1}$H-NMR (300 MHz, CDCl$_3$): 1.92-2.02 (m, 1H), 2.03-2.12 (m, 1H), 2.34-2.56 (m, 4H), 2.81-2.91 (m, J = 10.8 Hz, 1H), 5.83-5.87 (br t, J = 2.7 Hz, 1H), 7.21 (br s, 1H), 7.24 (br s, 2H), 7.31-7.36 (br t, J = 7.2 Hz, 2H).

IR (neat): 3080 (w), 3020 (w), 2920 (m), 1690 (m), 1600 (m), 1490 (m), 1440 (s), 1412 (s), 1360 (m), 1250 (s), 1210 (s), 1140 (s), 1070 (m), 1050 (s), 1025 (s), 950 (m), 930 (m), 920 (m), 890 (s), 860 (s), 830 (m), 760 (s), 700 (s).

tlc: Rf = 0.4 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 84% (2.34 g) from 1.50 g (9.72 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.89 (s, 9H), 1.25-1.43 (m, 2H), 1.90-2.01 (m, 2H), 2.15-2.30 (m, 1H), 2.34 (br s, 1H), 2.30-2.45 (m, 1H), 5.74 (br s, 1H).

IR (neat): 2990(br), 1415 (br), 1250 (s), 1210 (br), 1140 (s), 1060 (m), 1040 (m), 875 (br), 610 (s).

tlc: Rf = 0.6 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 63% (1.08 g) from 1.00 g (5.49 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.33 (br s, 7H), 1.37 (br s, 5H), 1.47-1.55 (m, 2H), 1.61-1.70 (m, 2H), 2.11-2.18 (dt, $J = 8.1$, 6.1 Hz, 2H), 2.43-2.47 (t, $J = 6.6$ Hz, 2H), 5.45-5.51 (t, $J = 8.1$ Hz, 1H).

tlc: Rf = 0.7 (Hexane).

Physical characteristic: Colorless oil.
**Procedure:** The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 6% (1.45 g) from 1.30 g (6.91 mmol) of starting material.

**$^1$H-NMR (300 MHz, CDCl$_3$):** Reported for the cis isomer;

1.19-1.21 (d, $J = 6.6$ Hz, 3H), 1.60-1.72 (td, $J = 12.9, 10.5$ Hz, 1H), 2.12-2.18 (m, 1H), 2.30-2.44 (m, 2H), 2.75-2.80 (m, 1H), 2.85-2.95 (tm, $J = 10.5$ Hz, 1H), 5.80-5.83 (m, 1H), 7.21 (br s, 1H), 7.23 (br s, 2H), 7.31-7.35 (br t, $J = 7.2$ Hz, 2H).

**IR (neat):** Reported for the cis and trans isomers;

2970(s), 2930(s), 2880(s), 1490(s), 1450(s), 1415(s), 1300(s), 1250(s), 1210(s), 1140(s), 1090(m), 1065(m), 1030(s), 980(s) 900(s), 860(s), 840(s), 820(s), 760(s).

**tlc:** $R_f = 0.3$ (Hexane)

**Physical characteristic:** Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 98% (361 mg) from 200 mg (1.28 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.88-1.93 (t, $J = 6.6$ Hz, 2H), 2.40-2.44 (br s, 2H), 2.50-2.57 (tm, $J = 6.6$ Hz, 2H), 3.99 (s, 4H), 5.64-5.68 (br t, $J = 3.9$ Hz, 1H).

tlc: Rf = 0.21 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The isolated yield of the corresponding enol triflate was 53% (1.44 g) from dimedone (1.40 g, 9.99 mmol) using Tf₂O instead of PhNTf₂.

\[^{1}H\text{-NMR}\, (300\, \text{MHz, CDCl}_3)\,:\, 1.14\, (s, \, 6\, \text{H}),\, 2.31\, (s, \, 2\, \text{H}),\, 2.55\, (d, \, J = 1.2\, \text{Hz}, \, 2\, \text{H}),\, 6.07\, (s, \, 1\, \text{H}).\]

\[^{13}C\text{-NMR}\, (75\, \text{MHz, CDCl}_3)\,:\, 27.6,\, 33.1,\, 42.0,\, 50.3,\, 118.0,\, 118.2\, (q, \, J = 318.3\, \text{Hz}),\, 165.9,\, 197.1.\]

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The isolated yield of the corresponding enol triflate was 21% (523 mg) from the corresponding ketoester (1.50 g, 7.80 mmol) using Tf₂O instead of PhNTf₂.

**¹H-NMR (300 MHz, CDCl₃):** 1.31 (t, J = 6.9 Hz, 3H), 4.30 (q, J = 6.9 Hz, 2H), 7.30-7.47 (m, 4H), 7.51-7.60 (m, 2H).

**tlc:** Rf = 0.2 (10% Ethyl acetate in hexane; the same Rf as the starting material).

**Physical characteristic:** Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 97% (1.06 g) from 1.00 g (3.54 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 2.48 (td, $J = 8.4$, 4.8 Hz, 2H), 2.84 (t, $J = 8.1$ Hz, 2H), 3.82 (s, 3H), 5.86 (t, $J = 4.8$ Hz, 1H), 6.74 (br s, 1H), 6.77 (dd, $J = 8.4$, 2.4 Hz, 1H), 7.27 (d, $J = 8.4$ Hz, 1H).

tlc: $R_f = 0.5$ (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 52% (187 mg) from 200 mg (1.22 mmol) of starting material.

\[
\begin{array}{c}
\text{1H-NMR (300 MHz, CDCl3):} \\
1.02 (s, 3H), 1.25-1.36 (br td, J = 13.2, 3.6 Hz, 2H), \\
1.46-1.55 (tt, J = 13.2, 3.3 Hz, 1H), 1.62-1.73 (ttm, J = 13.2, 3.3 Hz, 2H), 1.75-1.83 (br d, J = 13.2 Hz, 1H), 2.08-2.16 (dd, J = 17.1, 6.9 Hz, 1H), 2.23-2.26 (br d, J = 6.9 Hz, 2H), 2.31-2.36 (br d, J = 15.9 Hz, 1H), 5.47 (br s, 1H), 5.50-5.55 (br td, J = 6.9, 2.7 Hz, 1H).
\end{array}
\]

tlc: Rf = 0.42 (Hexane).

Physical characteristic: Colorless oil.
Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 75% (1.20 g) from 1.01 g (4.44 mmol) of starting material.

\[ \text{Procedure: The same procedure for the enol triflate derived from 4-phenylcyclohexanone was used (page 150). The yield of product was 75\% (1.20 g) from 1.01 g (4.44 mmol) of starting material.} \]

\[ \text{\textsuperscript{1}H-NMR (300 MHz, CDCl}_3): \ 1.48 \ (qt, \ J = 9.0, 4.8 \text{ Hz, } 1\text{H}), \ 1.65 \ (br \ q, \ J = 12.6 \text{ Hz, } 1\text{H}), \ 1.93 \ (qt, \ J = 9.9, 3.3 \text{ Hz, } 1\text{H}), \ 2.07 \ (br \ quintet, \ J = 6.9 \text{ Hz, } 1\text{H}), \ 2.14-2.33 \ (m, 2\text{H}), \ 2.23-2.50 \ (m, 2\text{H}), \ 2.76 \ (br \ s, 1\text{H}), \ 2.85-2.95 \ (m, 1\text{H}), \ 5.01 \ (br \ dd, \ J = 10.2, 1.2 \text{ Hz, } 1\text{H}), 5.05 \ (br \ dd, \ J = 17.4, 1.5 \text{ Hz, } 1\text{H}), 5.80 \ (ddt, \ J = 16.8, 10.2, 6.3 \text{ Hz, } 1\text{H}), \ 5.88 \ (br \ dt, \ J = 6.0, 2.1 \text{ Hz, } 1\text{H}), 7.25 \ (br \ td, \ J = 6.9, 1.5 \text{ Hz, } 3\text{H}), 7.35 \ (br \ t, \ J = 6.9 \text{ Hz, } 2\text{H}). \]

\[ \text{\textsuperscript{19}F-NMR (283 MHz, CDCl}_3): \ -77.6 \ (s). \]

\[ \text{\textsuperscript{13}C-NMR (75 MHz, CDCl}_3): \ 29.8, 30.6, 32.2, 36.6, 37.9, 39.3, 115.2, 116.6 \ (q, \ J = 192.8 \text{ Hz, } 1\text{H}), 118.9, 126.6, 128.6, 129.9, 137.4, 144.6, 151.9. \]

\[ \text{IR (neat): } 3060 \ (s), 3020 \ (s), 2920 \ (br), 2860 \ (s), 1680 \ (s), 1640 \ (s), 1600 \ (s), 1490 \ (s), 1430 \ (br), 1340 \ (s), 1220 \ (br), 1140 \ (br), 1020 \ (br), 940 \ (s), 900 \ (br), 860 \ (br), 840 \ (s). \]

\[ \text{HRMS: Calcd. for C}_{17}\text{H}_{19}\text{F}_{3}\text{O}_3\text{S (M\textsuperscript{+}) 360.0998, found 360.0993.} \]

\[ \text{Mass spectrum m/e: } 360 \ (M\textsuperscript{+}), 318, 303, 281, 256, 227, 210, 185, 104, 91, 77. \]

\[ \text{tlc: Rf = 0.5 (Hexane).} \]

\[ \text{Physical characteristic: Colorless oil.} \]

Procedure: Into a dry 100 mL 2-neck flask, equipped with a reflux condenser and a magnetic stirrer, were added 35 mL of dichloromethane, the methyl ketone (995 mg, 5.28 mmol), triflic anhydride (1.11 mL, 6.60 mmol), and 2,6-di-t-butyl-4-methylpyridine (1.63 g, 7.92 mmol). The solution was then refluxed for 1.5 d. The solvent was evaporated and 50 mL of pentane was added to the residue. The solid pyridinium triflate salt was filtered off and washed further with 10 mL of pentane. The combined organic phases were washed with ice-cold 1 N HCl (aq) and then with brine. The organic phase was dried with anhydrous magnesium sulfate, and the solvent was evaporated. Purification via normal phase flash column chromatography eluting with hexane afforded 620 mg (37% yield) of the desired tetrasubstituted enol triflate and the trisubstituted enol triflate in an approximate ratio of 2 : 1, which were not separated.

\[ \begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O} \quad \text{Tf}
\end{align*} \]

\(^{1}\text{H-NMR} (300 \text{ MHz, CDCl}_3): 1.81 (s, 3H), 1.91-2.00 (td, J = 11.4, 5.7 Hz, 1H), 2.01-2.08 (m, 1H), 2.35-2.37 (br d, J = 6.9 Hz, 2H), 2.41 (br s, 1H), 2.50-2.60 (m, 1H), 2.85-2.95 (m, 1H), 7.20 (br s, 1H), 7.23 (br s, 2H), 7.31-7.35 (br t, J = 7.2 Hz, 2H).

IR (neat): 2920 (w), 1410 (s), 1250 (m), 1210 (s), 1140 (s), 1030 (m), 1005 (w).

tlc: Rf = 0.3 (Hexane).

Physical characteristic: Colorless oil.

Procedure: Into a 100 mL 2-neck flask, equipped with a reflux condenser and a magnetic stirrer, were added 43 mL of dichloromethane, dodecanal (1.19 g, 6.46 mmol), triflic anhydride (1.36 mL, 8.07 mmol), and 2,6-di-tert-butyl-4-methylpyridine (1.99 g, 9.69 mmol). The solution was refluxed for 2 d. The solvent was then evaporated and 50 mL of pentane added to the residue. The solid pyridinium triflate salt was filtered off and washed further with 10 mL of pentane. The combined organic phases were washed with ice-cold 1 N HCl (aq) and then with brine. The organic phase was dried with anhydrous magnesium sulfate, and the solvent was evaporated. Purification via normal phase flash column chromatography eluting with hexane afforded 801 mg (39% yield) of enol triflate 65 as a mixture (6.6 : 1) of Z and E stereoisomers.

\[ H_{23}C_{11}O \rightarrow H_{21}C_{10}OTf \]

65

\( ^1H\text{-NMR} \) (300 MHz, CDCl\(_3\)): 0.86-0.90 (br t, J = 6.6 Hz, 3H), 1.26 (br s, 16H), 2.15-2.22 (dt, J = 7.5, 6.6 Hz, 2H), 5.21-5.28 (td, J = 7.5, 5.7 Hz, 1H), 6.51-6.53 (d, J = 5.4 Hz, 1H).

\( ^{13}C\text{-NMR} \) (75 MHz, CDCl\(_3\)): 112.3-125.0 (q, J = 318.6 Hz), 120.2, 134.8-134.9 (br d, J = 7.3 Hz).

\( ^{19}F\text{-NMR} \) (283 MHz, CDCl\(_3\)): -72.62 (s).
**IR** (neat): 3110 (w), 2920(s), 2850(s), 1665(s), 1465(s), 1420(s), 1380(m), 1250(s), 1210(s), 1140(s), 1010(s), 970(s), 850(s), 740(s), 640(s), 600(s).

**tlc:** Rf = 0.40 (Hexane).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for the enol triflate 65 was used (page 162). The yield of product was 66% (1.19 g) from 1.00 g (6.09 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.02 (s, 3H), 1.26-1.36 (td, $J = 13.2, 4.2$ Hz, 1H), 1.44-1.54 (td, $J = 12.6, 5.7$ Hz, 1H), 1.52-1.64 (m, 2H), 1.70-1.85 (m, 2H), 2.01-2.23 (m, 2H), 2.31-2.39 (dd, $J = 19.0, 5.4$ Hz, 1H), 2.57-2.69 (m, 1H), 5.59 (t, $J = 3.6$ Hz, 1H), 6.01 (s, 1H).

tlc: $R_f = 0.40$ (Hexane).

Physical characteristic: Colorless oil.
VII. Hydrazine syntheses


Procedure: To a stirred suspension of finely ground TrisNHNH2 (1.20 g, 4.02 mmol) in 4 mL of methanol was added the ketone 82 (1.01 g, 5.78 mmol) after which a granular product crystallized. The reaction mixture was chilled overnight in the freezer and filtered. The product was triturated with cold methanol and dried at ambient temperature at 2.5 mm Hg over P2O5 for 1 d to afford 1.37 g (75% yield) of corresponding trisyl hydrazine.

$^1$H-NMR (300 MHz, CDCl3): 1.26-1.28 (d, J = 6.9 Hz, 12H), 1.27-1.29 (d, J = 6.9 Hz, 6H), 1.56-1.80 (m, 2H), 1.92-2.03 (td, J = 14.1, 5.1 Hz, 1H), 1.99-2.10 (m, 2H), 2.02 (br s, 1H), 2.04-2.06 (br s, 1H), 2.23-2.33 (td, J = 13.5, 4.8 Hz, 1H), 2.49-2.56 (br d, J = 15.3 Hz, 1H), 2.73-2.82 (br d, J = 15.3 Hz, 1H), 2.85-3.00 (heptet, J = 6.9 Hz, 1H), 4.18-4.32 (heptet, J = 6.9 Hz, 2H), 7.15-7.17 (m, 1H), 7.17-7.23 (m, 2H), 7.18 (s, 2H), 7.27-7.32 (br t, J = 7.2 Hz, 2H).
**Physical characteristic:** White crystalline solid.
Procedure: The procedure for the trisyl hydrazone derived from 4-phenylcyclohexanone was used (page 165). The yield of product was 63% (2.51 g) from 1.40 g (9.08 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.84 (s, 9H), 1.25 (d, J = 6.9 Hz, 12H), 1.27 (d, J = 6.6 Hz, 6H), 1.76 (td, J = 13.5, 5.4 Hz, 2H), 1.93 (br d, J = 12.9 Hz, 2H), 2.09 (br t, J = 12.6 Hz, 1H), 2.42 (d, J = 13.8 Hz, 2H), 2.68 (br d, J = 13.5 Hz, 2H), 2.90 (heptet, J = 6.9 Hz, 1H), 4.22 (heptet, J = 6.9 Hz, 2H), 7.16 (s, 2H).

Physical characteristic: White crystalline solid.
**Procedure:** The procedure for the trisyl hydrazone derived from 4-phenylcyclohexanone was used (page 165). The yield of product was 46% (656 mg) from 670 mg (2.70 mmol) of starting material. Trisyl hydrazone 85 was used in the stannylation reaction without any further purification.
VIII. Vinyl sulfone syntheses

![Chemical Structure]

**Procedure:** In a dry 100 mL 2-neck flask containing a solution of phenyl trimethylsilylmethyl sulfone (1.10 g, 4.79 mmol) in 24 mL of DME cooled to -78°C, 2.1 mL of a 2.5 M hexane solution of n-BuLi (5.27 mmol) was added dropwise. After stirring this solution for 15 min at this temperature, benzophenone (961 mg, 5.27 mmol) dissolved in 3.1 mL of DME was transferred by cannula into this solution. The -78°C dry-ice bath was removed and replaced with an ice bath. After stirring this solution for 1 h at 0°C, 24 mL of saturated NH₄Cl (aq) was added, followed by removal of the ice bath and extractive work-up with ethyl ether. Column chromatography, eluting with 10% ethyl acetate in hexane, afforded 1.54 g (100% yield) of the corresponding sulphonyl derivative.

**¹H-NMR (300 MHz, CDCl₃):** 7.02 (s, 1H), 7.08 (d, J = 6.9 Hz, 2H), 7.21 (d, J = 7.8 Hz, 2H), 7.29 (d, J = 6.6 Hz, 2H), 7.28-7.37 (m, 2H), 7.35 (d, J = 7.8 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.58 (d, J = 7.8 Hz, 2H), 7.81 (d, J = 7.2 Hz, 1H).

**tlc:** Rf = 0.3 (20% Ethyl acetate in hexane).

**Physical characteristic:** White crystalline solid.
Procedure: The procedure for the vinyl sulfone derived from benzophenone was used (page 169). The yield of product was 86% (838 mg) from 712 mg (3.12 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.47-1.70 (m, 2H), 2.00-2.10 (m, 3H), 2.34-2.37 (m, 2H), 2.75 (tt, J = 12.1, 3.6 Hz, 1H), 3.80 (dt, J = 15.3, 5.5 Hz, 1H), 6.24 (s, 1H), 7.15, (d, J = 7.2 Hz, 2H), 7.20 (t, J = 6.9 Hz, 1H), 7.29 (t, J = 6.9 Hz, 2H), 7.55 (t, J = 7.5 Hz, 2H), 7.62 (t, J = 7.2 Hz, 1H), 7.94 (d, J = 6.9 Hz, 2H).

IR: 3060 (w), 3020 (w), 2930 (m), 2860 (w), 1620 (s), 1490 (m), 1450 (s), 1350 (w), 1305 (s), 1250 (w), 1220 (w), 1150 (s), 1085 (s), 1070 (m), 1020 (w), 1000 (w), 980 (w), 930 (w), 905 (w), 885 (w), 840 (s), 810 (m), 765 (s), 720 (m), 700 (s), 690 (s), 610 (s), 785 (s), 560 (s).

tlc: Rf = 0.15 (20% Ethyl acetate in hexane).

Physical characteristic: White crystalline solid.
Procedure: The procedure for the vinyl sulfone derived from benzophenone was used (page 169). The yield of product was 34% (306 mg) from 641 mg (2.81 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.83 (br s, 8H), 0.98-1.14 (m, 3H), 1.16-1.27 (m, 3H), 1.82 (td, J = 13.8, 4.2 Hz, 2H), 1.94 (br d, J = 11.7 Hz, 2H), 2.14 (td, J = 11.7, 2.7 Hz, 2H), 2.29 (dd, J = 13.5, 2.1 Hz, 1H), 3.69 (br dd, J = 13.5, 2.4 Hz, 1H), 6.15 (br s, 1H), 7.53 (t, J = 6.9 Hz, 2H), 7.60 (t, J = 6.9 Hz, 1H), 7.91 (dd, J = 8.4, 1.5 Hz, 2H).

tlc: Rf = 0.25 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
**Procedure:** The procedure for the vinyl sulfone derived from benzophenone was used (page 169). The yield of product was 33% (525 mg) from 1.18 g (5.15 mmol) of starting material.

\[ \text{EtO}_2\text{C} \begin{array}{c} \text{N} \\ \text{O} \end{array} \rightarrow \text{EtO}_2\text{C} \begin{array}{c} \text{N} \\ \text{SO}_2\text{Ph} \end{array} \]

$^1$H-NMR (300 MHz, CDCl$_3$): 1.25 (t, $J = 7.2$ Hz, 3H), 2.25 (br t, $J = 5.7$ Hz, 4H), 2.89 (br t, $J = 6.0$ Hz, 4H), 4.14 (q, $J = 7.2$ Hz, 2H), 6.25 (s, 1H), 7.54 (br t, $J = 6.9$ Hz, 2H), 7.61 (d, $J = 6.9$ Hz, 1H), 7.90 (d, $J = 7.2$ Hz, 2H).

**tlc:** Rf = 0.6 (Ethyl ether).

**Physical characteristic:** Colorless oil.
Procedure: The procedure for the vinyl sulfone derived from benzophenone was used (page 169). The yield of product was 68% (823 mg) from 900 mg (3.94 mmol) of starting material.

$^{1}$H-NMR (300 MHz, CDCl$_3$): Reported for the E and Z isomers;
2.24 (br s, 6H), 5.33 (s, 1H), 5.74 (s, 1H), 7.14 (dd, J = 8.4, 1.5 Hz, 2H), 7.21 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 7.5 Hz, 2H), 7.35-7.45 (m, 2H), 7.47 (dd, J = 8.1, 1.8 Hz, 4H), 7.52 (t, J = 10.8 Hz, 2H), 7.60-7.70 (m, 2H), 7.72 (d, J = 8.7 Hz, 2H), 7.76 (br d, J = 5.1 Hz, 2H), 7.78-7.87 (m, 4H).

tlc: Rf = 0.2 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: The procedure for the vinyl sulfone derived from benzophenone was used (page 169). The yield of product was 50% (1.01 g) from 1.19 g (6.02 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for the vinyl hydrogens of the E and Z isomers;
4.75 (s), 5.02 (s).

tlc: Rf = 0.2 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
IX. Difluoride, vinyl silane and dimer syntheses

\[
\begin{align*}
\text{51} & \quad \text{54}
\end{align*}
\]


**Procedure:** In a flame dried 2-neck flask equipped with a magnetic stirrer, were added ketone 51 (100 mg, 0.69 mmol) and methylene chloride (1.0 mL). The flask was cooled to 0°C followed by the dropwise addition of Me-DAST (0.253 mL, 2.60 mmol). The syringe used to transfer the Me-DAST was cautiously thrown into a bucket full of water. The reaction was stirred at ambient temperature for 18 h. At the end of this period, the reaction was cooled to -78°C with a dry ice-acetone bath and water (2.0 mL) was added to the reaction dropwise. The reaction was immediately warmed to r.t. followed by extractive work-up with methylene chloride. The combined organic phases were back washed with water and dried with anhydrous magnesium sulphate. After solvent evaporation under reduced pressure, column chromatography eluting with hexane afforded 111 mg (97% yield) of the geminal difluoride 54.

\[ ^1\text{H-NMR} \ (300 \text{ MHz, CDCl}_3): \ 0.88 \ (s, 9H), \ 1.25-1.37 \ (m, 2H), \ 1.59 \ (br \ t, J = 13.8 \ Hz, 1H), \ 1.64-1.82 \ (m, 2H), \ 2.00-2.20 \ (m, 4H) \]
\textbf{19F-NMR} (283 MHz, CDC\textsubscript{3}): 51.2 (dtt, J = 246.9, 35.1, 9.9 Hz, 1F), 62.8 (d, J = 246.9 Hz, 1F).

tlc: Rf = 0.9 (20\% Ethyl acetate in hexane). Using this solvent system, the starting material has a Rf = 0.5.

Physical characteristic: Colorless oil.

Procedure: The procedure for vinyl stannane 76a was used (page 142) except that Me₃SiCl was used in place of Me₃SnCl. The yield of product was 40% (404 mg) from 2.00 g (4.39 mmol) of starting material.

$^1$H-NMR (300 MHz, C₆D₆): 0.06 (s, 9H), 1.50-1.64 (m, 1H), 1.80 (br d, J = 9.9 Hz, 1H), 2.06 (br s, 2H), 2.17 (br t, J = 16.5 Hz, 2H), 2.59 (br s, 1H), 6.00 (br s, 1H), 7.05 (br s, 2H), 7.00-7.12 (m, 2H), 7.15 (br t, J = 7.2 Hz, 1H).

$^{13}$C-NMR (75 MHz, C₆D₆): -2.0, 27.8, 30.4, 35.5, 40.4, 126.3, 127.2, 128.7, 135.7, 138.2, 147.7.

tlc: Rf = 0.9 (Hexane).

Physical characteristic: Colorless oil.
Procedure: In a dry 5 mL 2-neck flask under a static nitrogen atmosphere and equipped with a magnetic stirrer, silver carbonate (97 mg, 0.4 mmol) was added under a stream of nitrogen followed by 1.2 mL of dichloromethane. Triflic acid was then added to the solution under a stream of nitrogen. The flask was covered with aluminum foil and stirred at ambient temperature for 30 min. Vinyl stannane 49 (56 mg, 0.18 mmol) in 1.3 mL of dichloromethane was transferred to the reaction mixture via cannula using positive nitrogen pressure. After stirring for 1 d, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate and dichloromethane, and the organic phase was separated, dried with anhydrous magnesium sulfate and filtered through a short pad of Celite eluting with dichloromethane. After solvent evaporation, silica gel column chromatography eluting with pentane afforded 49 mg (88% yield) of dimer 129 as a diastereomeric mixture (1:1).

\[\text{1}^H\text{-NMR (300 MHz, CDCl}_3\text{)}: 1.79-1.92 \text{ (qd, J = 12.0, 5.7 Hz, 2H), 2.08-2.15 \text{ (dm, J = 12.0 Hz, 2H), 2.29-2.55 \text{ (m, 4H), 2.47-2.48 \text{ (br d, J = 2.7 Hz, 4H), 2.80-2.90 \text{ (m, 2H), 5.96 \text{ (br s, 2H), 7.23-7.28 \text{ (br t, J = 6.9 Hz, 2H), 7.29-7.31 \text{ (br d, J = 6.6 Hz, 4H), 7.34-7.39 \text{ (br t, J = 7.2 Hz, 4H).}}}\]}

\[\text{13}C\text{-NMR (125 MHz, CDCl}_3\text{)}: 26.1, 26.4, 29.9, 30.2, 30.4, 34.1, 34.2, 40.0, 40.1, 40.2, 121.2, 121.4, 121.6, 125.9, 126.1, 126.7, 127.0, 128.2, 128.5, 136.3, 136.3, 147.0, 147.1.]}\]
IR: 3050 (m), 3040 (m), 3020 (m), 2930 (s), 2920 (s), 2880 (s), 2850 (m), 1490 (m), 1450 (s), 1430 (m), 920 (m), 910 (w), 785 (s), 760 (s), 710 (s).


Mass spectrum m/e: 314 (M+), 210, 195, 156, 130, 117, 104, 91, 980.

tlc: Rf = 0.15 (Hexane).

Physical characteristic: White crystalline solid.
X. Vinyl stannane precursors and a model reaction

**Procedure**: In a flame dried 2-neck flask equipped with a magnetic stirrer, was added CuCN (130 mg, 1.46 mmol). The flask was flame dried again until all the CuCN freely stirred in the flask. After the CuCN was allowed to cool to ambient temperature, THF (2.0 mL) was added followed by cooling this solution to 0°C with an ice-water bath. At this temperature, 2.24 mL of a solution containing 1.30 M MeLi (2.91 mmol) in ethyl ether was added dropwise. After stirring this solution at 0°C for an additional 30 min, vinyl stannane 53 in THF (1.0 mL) was added via cannula using positive argon pressure. The solution was stirred at that temperature for an additional 30 min followed by the addition of 2-cyclohexenone in THF (1.0 mL). The solution was allowed to warm to r.t. (ca. 2 h) followed by extractive work-up with brine and ethyl ether. Purification by column chromatography eluting with 10% ethyl acetate in hexane afforded 51 mg (68% yield) of 58.

**1H-NMR** (300 MHz, CDCl3): 0.86 (s, 9H), 1.05-1.25 (m, 3H), 1.50-1.70 (m, 2H), 1.70-1.90 (m, 4H), 2.00 (br s, 2H), 2.06 (br s, 1H), 2.20-2.40 (m, 4H), 5.43 (br s, 1H).

**IR** (neat): 2040 (br), 2880 (s), 1720 (s), 1470 (m), 1450 (m), 1440 (m), 1390 (m).

**Tlc**: Rf = 0.5 (20% Ethyl acetate in hexane).

**Physical characteristic**: Colorless oil.
**Procedure:** In a dry 250 mL 2-neck flask under static a nitrogen atmosphere and equipped with a magnetic stirrer, diisopropyl amine (4.42 mL, 31.6 mmol) was added followed by 30 mL of THF, and the mixture was cooled to 0°C. Then, 11.5 mL of 2.50 M hexane solution of n-BuLi (28.7 mmol) was added dropwise. After stirring for 20 min at 0°C, ketone 82 (5.00 g, 28.7 mmol) in 60 mL of THF, was added to the solution via cannula and stirred for 30 min at 0°C. Neat MeI (2.0 mL, 32 mmol) was added dropwise, and the solution allowed to warm to ambient temperature (ca. 3 h). The reaction mixture was partitioned between saturated aqueous sodium bicarbonate and ethyl ether, and the organic phase was dried with anhydrous magnesium sulfate. After solvent evaporation, purification by silica gel column chromatography, eluting with 10% ethyl acetate in hexane, afforded 3.05 g (56% yield) of the methyl ketone as a mixture (8:1) of cis and trans isomers.

**1H-NMR (300 MHz, CDCl3):** Reported for the cis isomer;

1.06-1.08 (d, J = 6.6 Hz, 3H), 1.61-1.73 (q, J = 12.9 Hz, 1H), 1.85-2.00 (m, 1H), 2.21-2.28 (m, 2H), 2.50-2.66 (m, 3H), 3.09-3.21 (ttm, J = 12.3, 3.3Hz, 1H), 7.23 (br s, 1H), 7.25 (br s, 2H), 7.30-7.35 (m, 2H).

**IR (neat):** Reported for the cis and trans isomers;

2960 (s), 2920 (s), 2860 (s), 1710 (s), 1600 (m), 1495 (s), 1450 (s), 1430 (m), 1380 (m).

**tlc:** Rf = 0.2 (20% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
**Procedure:** In a dry 250 mL 2-neck flask under a static nitrogen atmosphere and equipped with a magnetic stirrer, was added ethyl laurate, 64, under a stream of nitrogen followed by 50 mL of THF. After cooling this solution to ~78°C, 18.0 mL of a 1.0 M THF solution (18.0 mmol) of lithium aluminum hydride was added dropwise. The reaction was then allowed to warm to ambient temperature (approx. 5 h). Solid NaF (3.00 g, 52.6 mmol) was added to this solution under a stream of nitrogen followed by 1.0 mL of water very slowly. After stirring for 2 h, the solution was filtered through Celite and the solvent evaporated to afford 2.49 g (100% yield) of the corresponding alcohol.

**\(^1\)H-NMR** (300 MHz, CDCl3): 0.85-0.90 (br t, J = 6.9 Hz, 3H), 1.24-1.30 (br s, 18H), 1.51-1.60 (br quintet, J = 6.9 Hz, 2H), 3.61-3.65 (t, J = 6.6 Hz, 2H), 3.72-3.76 (br t, J = 6.6 Hz, 1H).

**IR** (neat): 3340 (br), 2920 (s), 2850 (s), 1465 (s), 1380 (m), 1120 (w), 1055 (s), 900 (w), 720 (m).

**tlc:** Rf = 0.20 (20% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
Procedure: Chromium trioxide (7.88 g, 79 mmol) was added, under a stream of nitrogen, to a mechanically stirred solution of pyridine (12.8 mL, 158 mmol) in 197 mL of dichloromethane. The solution was then stirred at room temperature for 15 min. At the end of this period, a solution of the alcohol in 10 mL of dichloromethane was added to the solution and stirred for an additional 15 min. The solution was decanted from the residue, and the residue was washed with 600 mL of ethyl ether. The combined organic phases were washed with three 100-mL portions of 1 N NaOH (aq), 1 N HCl (aq), water, saturated aqueous sodium bicarbonate, brine, and were dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded 2.42 g (100% yield) of the corresponding aldehyde.

\[ H_{21}C_{10}OH \rightarrow H_{23}C_{11}O \]

\[ ^1H-NMR \text{(300 MHz, CDCl}_3\text{): 0.85-0.90 (br t, } J = 6.9 \text{ Hz, 3H), 1.25 (br s, 16H), 1.60-1.65 (m, 2H), 2.39-2.44 (td, } J = 7.2, 1.5 \text{ Hz, 2H), 9.75-9.76 (t, } J = 1.5 \text{ Hz, 1H).} \]

\[ \text{IR (neat): 2960 (s), 2920 (s), 2860 (s), 2715 (m), 1760 (m), 1740 (s), 1710 (m), 1470 (m), 1415 (w), 1380 (w).} \]

\[ \text{tlc: Rf = 0.60 (20\% Ethyl acetate in hexane).} \]

\[ \text{Physical characteristic: Colorless viscous oil.} \]
**Procedure:** In a dry 2-neck flask under argon were added magnesium turnings (2.67 g, 110 mmol). The flask was then flame dried while stirring. Upon cooling to ambient temperature, 6.11 mL of propargyl bromide (80% in toluene, 54.9 mmol) was added followed by anhydrous ethyl ether (250 mL). A catalytic amount of iodine (ca. 5 mg) was added to the solution, which was heated briefly (5 min) to vigorous reflux. The solution became slightly grey at this time. The solution was allowed to stir at a mild reflux for an additional 5 h. The solution was then cooled to 20°C, and cyclododecanone 86 (5.00 g, 27.4 mmol) in ethyl ether (20 mL) was transferred to the solution via cannula using positive nitrogen pressure. The solution was stirred overnight at ambient temperature. Brine (ca. 250 mL) was added followed by acidification of the aqueous phase with 1N HCl (aq) to pH 4. Extractive work up with ethyl ether was followed by drying of the organic phase with anhydrous magnesium sulfate and solvent evaporation. Filtration through a short pad of silica gel eluting with 10% ethyl acetate in hexane afforded 6.00 g (98% yield) of the corresponding homopropargyl alcohol, 87.

**1H-NMR** (300 MHz, CDCl₃): 1.31 (br s, 16H), 1.35-1.49 (m, 3H), 1.57-1.65 (m, 3H), 1.89 (br s, exchangeable with D₂O, 1H), 2.04 (t, J = 2.7 Hz, 1H), 2.28 (d, J = 2.7 Hz, 2H).
$^{13}$C-NMR (75 MHz, CDCl$_3$): 19.5, 21.9, 22.4, 25.9, 26.2, 31.6, 33.6, 71.2, 73.9, 80.6.

IR: 3440 (br), 3300 (s), 2920 (s), 2850 (s), 2110 (m), 1470 (s), 1450 (s), 1420 (m), 1350 (m), 1280 (m), 1250 (m), 1160 (m), 1070 (m), 1020 (m), 1010 (m), 895 (m), 725 (m), 630 (br).

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

Physical characteristic: White solid.
Procedure: In a flame dried 2-neck flask equipped with magnetic stirrer, were added 4-phenylcyclohexanone (2.20 g, 12.6 mmol), methylene chloride (51 mL), and triethylamine (2.64 mL, 18.9 mmol). To this flask was then added TMSOTf (3.05 mL, 15.8 mmol) dropwise. After stirring this solution for 5 min, the solvent was removed under reduced pressure. The residue was diluted with ethyl ether (31 mL) and filtered through a short pad of Celite. Evaporation of the organic solvent afforded 3.11 g (100% yield) of pure silyl enol ether 83.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.21 (s, 9H), 1.70-2.10 (m, 3H), 2.10-2.30 (m, 3H), 2.75 (br s, 1H), 4.95 (br s, 1H), 7.20-7.35 (m, 5H).

tlc: Rf = 0.8 (Hexane).

Physical characteristic: Colorless oil.
Reference: See *J. Am. Chem. Soc.* 1980, 102, 3248 for the procedure. The yield of product was 96% (3.03 g) from 3.13 g (12.7 mmol) of starting material.

\(^1\text{H-NMR}\) (300 MHz, CDCl\(_3\)): Reported for the cis and trans isomers;
1.88 (t, J = 12.9 Hz, 1H), 1.90-2.10 (m, 3H), 2.15-2.28 (m, 3H), 2.29-2.40 (m, 1H),
2.40-2.65 (m, 4H), 2.80-2.87 (br s, 2H), 3.07 (tt, J = 12.3, 3.3 Hz, 1H), 3.23 (tt, J =
11.4, 3.6 Hz, 1H), 3.36 (s, 3H), 3.37 (s, 3H), 3.44 (s, 3H), 3.46 (s, 3H), 4.72 (d, J = 5.1
Hz, 1H), 4.86 (d, J = 7.2 Hz, 1H), 7.23 (br t, J = 7.5 Hz, 6H), 7.33 (br t, J = 7.2 Hz,
4H).

tlc: Rf = 0.2 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Reference: See *Tetrahedron Lett.*, 1971, 52, 4995 for procedure. The yield of enone 122 was 17.6 g (50%) from 24.0 g (0.21 mol) of 2-methylcyclohexanone, 121.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.22 (s, 3H), 1.28-1.45 (m, 2H), 1.63-1.67 (m, 2H), 1.75-1.79 (m, 1H), 1.82-1.92 (m, 3H), 2.21-2.55 (m, 4H), 5.70 (br s, 1H).

bp: 97°C-103.0°C at 2.5 mm Hg.

tlc: Rf = 0.15 (20% Ethyl acetate in hexane).

Physical characteristic: Yellowish oil.
Procedure: In a dry 25 mL 2-neck flask containing a suspension of NaH (372 mg, 11.5 mmol: 74% dispersion in mineral oil) and dimethyl carbonate (2.37 mL, 28.1 mmol) in 4.6 mL of DME, ketone 82 (1.00 g, 5.74 mmol) in 2.3 mL of DME was transferred dropwise to the reaction mixture via cannula using positive nitrogen pressure (CAUTION: substantial amounts of H2 gas are generated). The solution was allowed to reflux. After refluxing for 2 h, the solution was neutralized to pH 7 with sat. AcOH (aq). The organic solvent was evaporated, and the residue was diluted with water, extracted with ethyl ether, and dried with anhydrous magnesium sulphate. Evaporation of the solvent and purification by filtration through a short pad of silica gel afforded 1.30 g (97% yield) of the β-ketoester 130.

**1H-NMR** (300 MHz, CDCl3): 1.80-1.95 (m, 1H), 1.99-2.03 (m, 1H), 2.44 (br s, 3H), 2.60-2.67 (dd, J = 15.6, 4.8 Hz, 1H), 2.73-2.85 (tm, J = 11.1 Hz, 1H), 3.75 (s, 3H), 7.19-7.22 (m, 1H), 7.23-7.25 (br d, J = 7.2 Hz, 2H), 7.30-7.35 (tm, J = 7.2 Hz, 2H), 12.20 (s, 1H).

**IR** (neat): 2940 (s), 2930 (s), 2890 (s), 2850 (s), 1747 (s), 1717 (s), 1660 (s), 1650 (s), 1615 (s), 1490 (s), 1440 (s), 1420 (s), 1380 (s), 1360 (s), 1330 (s), 1310 (s), 1280 (s), 1260 (s), 1225 (s), 1200 (s), 820 (s), 760 (s), 700 (s), 540 (s).

**tlc**: Rf = 0.65 (20% Ethyl acetate in hexane).

**Physical characteristic**: Colorless oil.
Procedure: To a suspension of sodium hydride (300 mg, 9.26 mmol; 74% dispersion in mineral oil) in 10.5 mL of THF cooled to 0°C, was added β-keto ester 130 (1.08 g, 4.63 mmol). Stirring was continued for 10 min at 0°C. Then, 1.85 mL of a 2.50 M solution of n-BuLi (4.63 mmol) in hexane was added dropwise to the suspension. After stirring 10 min at 0°C, 4-bromo-1-butene (0.43 mL, 4.21 mmol) in 0.84 mL of THF was added via cannula. Stirring was continued for 10 min at 0°C and for an additional hour at ambient temperature. The mixture was cooled to 0°C and neutralized by addition of 1 N HCl (aq). After extraction with ethyl ether, the organic phases were dried with anhydrous magnesium sulfate, filtered, and the solvent was evaporated to afford 1.16 g (96% yield) of 131 as a mixture of isomers (8 : 1).

**1H-NMR** (300 MHz, CDCl3): 0.84-0.93 (q, J = 7.5 Hz, 2H), 1.25-1.34 (m, 1H), 1.51-1.72 (m, 1H), 1.83-2.14 (m, 2H), 2.22-2.45 (m, 3H), 2.51-2.65 (m, 1H), 3.74 (s, 3H), 4.96-5.08 (m, 2H), 5.72-5.90 (m, 1H), 7.20-7.23 (m, 1H), 7.23-7.28 (m, 2H), 7.30-7.35 (m, 2H), 12.2 (s, 1H).

**IR** (neat): 3020 (s), 2930 (s), 2850 (s), 1740 (s), 1715 (s), 1650 (s), 1610 (s), 1492 (s), 1437 (s), 1357 (s), 1310 (s), 1260 (s), 1220 (s), 1200 (s), 1170 (s), 910 (s), 820 (s), 760 (s), 735 (s), 700 (s).

**tlc: Rf = 0.65 (10% Ethyl acetate in hexane).**

**Physical characteristic:** Light yellowish oil.
Procedure: A solution of 131 (5.40 g, 18.6 mmol) and LiCl (4.68 g, 111 mmol) in a mixture of DMSO (91 mL) and water (2.6 mL) was heated to 145°C for 4 h then allowed to cool to ambient temperature. The solution was diluted with brine and extracted with 1 : 1 ethyl ether/hexane (6 x 25 mL). The combined organic extracts were washed with brine (2 x 10 mL) and dried over anhydrous magnesium sulphate. Concentration and purification by flash column chromatography afforded 2.10 g (49% yield) of 132 as a mixture of isomers (8 : 1).

${^1}$H-NMR (300 MHz, CDCl3): 0.86-0.93 (td, J = 6.9, 6.0 Hz, 1H), 1.22-1.33 (td, J = 6.9, 6.3 Hz, 2H), 1.56-1.69 (q, J = 12.6 Hz, 2H), 1.85-2.00 (m, 1H), 2.03-2.11 (q, J = 7.2 Hz, 2H), 2.20-2.33 (m, 1H), 2.46-2.56 (m, 2H), 3.06-3.17 (tt, J = 12.3, 3.6 Hz, 1H), 4.94-4.98 (br d, J = 10.8 Hz, 1H), 4.98-5.04 (br d, J = 16.8 Hz, 1H), 5.72-5.86 (ddt, J = 16.8, 10.8, 6.6 Hz, 1H), 7.21-7.24 (m, 1H), 7.22-7.25 (br d, J = 6.3 Hz, 2H), 7.29-7.35 (m, 2H).

${^{13}}$C-NMR (75 MHz, CDCl3): 27.7, 30.6, 34.4, 40.7, 41.3, 42.8, 48.4, 114.3, 126.0, 126.2, 128.0, 137.9, 144.3, 210.8.

IR (neat): 3060 (s), 3020 (s), 3000 (m), 2920 (s), 2860 (s), 1700 (s), 1640 (s), 1600 (s), 1490 (s), 1450 (s), 1430 (s), 1210 (s), 1155 (s), 995 (s), 910 (s), 760 (s), 700 (s).

tlc: Rf = 0.50 (10% Ethyl acetate in hexane).
Physical characteristic: Light yellowish oil.
PART II

APPROACH TO (-)-11-NOR-Δ⁹-THC-CARBOXYLIC ACID AND SYNTHESIS OF CANNABINOID ANALOGS
INTRODUCTION

One of the oldest and best documented plants is *Cannabis sativa* L. This plant has been mentioned in the Bible (King James Version) as well as in other older historical documents. *Cannabis sativa* has been used by man as a source of fiber, food, medicine and for social and religious rituals. Today, most people know this plant as "marijuana." Marijuana has been specifically used as an anesthetic, antiinflammatory, antidepressant, hypnotic and antivomiting agent by many different cultures. In spite of the great array of positive uses of this plant, marijuana can only be used legally for a few purposes in the U.S.A. The two legal uses of marijuana in the United States are for the treatment of glaucoma and nausea caused by cancer chemotherapy. Although there is no evidence supporting the physical addiction of marijuana, it is believed that psychological addiction does occur from prolonged use. In addition, marijuana has been labeled as a mind altering drug when used for a prolonged period of time. Also, due to the strong euphoric effect of marijuana, it is undesirable for workers to be under the influence of marijuana. This concern has led to the development of a cannabinoid assay which detects marijuana metabolites in urine. The major marijuana metabolite present in human urine is (-)-nor-Δ⁹-trans-6a,10a-THC-9-carboxylic acid. This metabolite originates from the major active compound, (-)-Δ⁹-THC, in marijuana. (-)-Δ⁹-THC is oxidized to the carboxylic acid within the human body at C11. The assay for detecting the marijuana metabolite in urine involves the use of GC/MS. This
analytical assay requires a quantitative standard for the calibration of the instrumental method. As a consequence, there is a need for synthetic (-)-nor-Δ⁹-THC-9-carboxylic acid as an analytical standard.

![Chemical Structures](image)

The strategies for the total synthesis of (-)-nor-Δ⁹-THC-9-carboxylic acid are discussed herein. At the beginning of this project, the challenge was overwhelming because several good synthetic routes to (-)-nor-Δ⁹-THC-9-carboxylic acid existed. This project was investigated in order to address important problems that faced all of the other synthetic routes which are discussed below. Three of the most important works will be discussed regarding the total synthesis of (-)-nor-Δ⁹-THC-9-carboxylic acid. A convenient synthesis of racemic (±)-nor-Δ⁹-cis-6a,10a-THC-9-carboxylic acid was accomplished in 1989 in our group.⁵⁰ All the reactions proceeded in good
yields, and the C11 carbon was carried through the synthesis in oxidized form. One of the shortcomings in this total synthesis is the undesired cis ring junction. The required trans ring junction and enantiospecificity were addressed in a different work by the same group (Scheme 11). This total synthesis work is efficient and short. The only reaction which suffers a low yield is the acid catalyzed coupling of olivetol with the tertiary alcohol (ca. 30%). In any event, this paper set the standard for future work in the total enantiospecific synthesis of (-)-11-nor-Δ⁹-THC-9-carboxylic acid with regard to the total number of steps involved.

SCHEME 11
SCHEME 11 (Continued)a

(-)-11-nor-Δ⁹-THC-9-methanol

aReagents: (a) TBDMSOTf, Et₃N; (b) MCPBA (excess); (c) LAH (66% over 2 steps); (d) MeOCCI, pyridine; (e) boron trifluoride etherate (30%); (f) LAH (94%).

A common regioselectivity problem encountered during the coupling of a terpenoid unit with an aromatic unit for cannabinoid synthesis is illustrated below using olivetol, 169, as an example. Huffman and coworkers, another prominent research group in this area, used a lithiated
resorcinol derivative which does not suffer from this problem.\textsuperscript{53} They have also described an efficient synthesis of nabilone using the lithiated resorcinol.\textsuperscript{54} Nabilone is used as an antiemetic for patients receiving cancer chemotherapy.\textsuperscript{55a,b}

Another prominent researcher in the area is Razdan. Razdan and coworkers have developed a synthetic strategy for the synthesis of 11-nor-\textDelta^9-THC-9-carboxylic acid.\textsuperscript{56} A major problem in this synthetic strategy is the low yielding, acid catalyzed coupling step between olivetol and the monoterpene unit. The low yield is due to the regioselectivity problem. A remedy for this regioselectivity problem was published by Chan and coworkers in which they used a carboxyl group \textit{ortho} to the n-pentyl side chain on olivetol.\textsuperscript{57} This olivetol analog does not suffer from the regioselectivity problem when coupled to the monoterpene unit. However, the additional steps involved in the formation and subsequent removal of the carboxyl group on olivetol resulted in an inefficient solution to the regioselectivity problem. Another solution for the regioselectivity problem was published by our group. This solution involves the use of a higher-order cuprate which undergoes 1,4-addition to apoverbenone.\textsuperscript{58} The utility of this method for the total synthesis
of (-)-11-nor-Δ⁸-THC-9-carboxylic acid methyl ester is illustrated below (Scheme 12). This cannabinoid with the double bond in the C-8 position is another major metabolite of marijuana.⁵⁹ This synthetic strategy involving the higher-order cuprate was subsequently applied to the enantiospecific total synthesis of (-)-11-nor-Δ⁹-tetrahydrocannabinol acid methyl ester methyl ether (Scheme 13).⁶⁰ The use of an α-bromo ketone was necessary for the
SCHEME 13

Reagents: (a) NBS (60%); (b) Li₂CO₃, LiBr (76%); (c) boron trifluoride etherate (83%); (d) (Me₃SiO)₂, TMSOTf (65%); (e) HClO₄ (aq) (66-71%); (f) LiCuMe₂; (g) PhNTf₂ (75-81% over 2 steps); (h) TMSI (47%); (i) Pd (II), CO (g) (82%).
formation of the Δ⁹ double bond. Formation of the Δ⁹ double bond from a nabilone analog lacking a bromine in the α-position was unsuccessful due to the kinetically and thermodynamically favored formation of the Δ⁸ enolate.⁶⁰

Lastly, the cyclobutane ring cleavage required the use of TMSI and therefore a robust phenolic protecting group was required to survive these conditions. Therefore, the methyl ether was used instead of the EE as a phenolic protecting group. Unfortunately, the cleavage of the methyl ether was difficult. Although the methyl ether was not deprotected in the final product, Δ⁹-THC-carboxylic acid derivative 191 has been used as an analytical standard for GC/MS.⁴⁶d

The synthesis which is summarized in scheme 13 is very efficient. This synthesis might be streamlined, however, by generating the Δ⁹ double bond directly from a non-halogenated ketone, rather than from 188. It would also be desirable to use an EE phenolic protecting group instead of the more robust methyl ether which is difficult to remove.

Reported herein are the results of these proposals for the total synthesis of (-)-Δ⁹-THC-9-carboxylic acid. The synthesis of several cannabinoid analogs, required for biological study, is also included.
RESULTS AND DISCUSSION

I. Approaches to (-)-11-nor-Δ⁹-THC-carboxylic acid

The total synthesis of (-)-11-nor-Δ⁹-THC-9-carboxylic acid involved much the same convergent strategy that had been used for the synthesis of Δ⁸-methyl ester 181 (Scheme 12). Ketone 178 was chosen as starting material for the synthesis. It was prepared by the previously described cuprate addition of bis-EE-olivetol to apoeverbenone, 176. The EE-protecting groups were removed by exposure to PPTS. Treatment with either stannic chloride or boron trifluoride etherate completed the cannabinoid skeleton to afford the corresponding ketone 194. Although stannic chloride gave a slightly higher yield, the cyclization with boron trifluoride etherate afforded a cleaner reaction making purification simpler. An unprecedented problem occurred when the cyclization with boron trifluoride etherate was performed on a large scale (> 1 g). Large scale cyclizations required long reaction times relative to small scale reactions. Four days were required for a 2 g scale cyclization while several hours were sufficient for a 100 mg scale cyclization. The reason for this ambiguous result is not known and bears further scrutiny. Benzylation of the phenolic function with iodobenzyl chloride yielded 195, which was the starting material for the key step in the proposed total synthesis of (-)-11-nor-
\( \Delta^9 \)-THC-9-carboxylic acid. The key step was to form the \( \Delta^9 \) double bond directly from the corresponding ketone 195 via metal-iodide exchange with an alkyl lithium. The aryllithium, so generated, might deprotonate C10 carbon intramolecularly to afford the \( \Delta^9 \) double bond. In order to thoroughly investigate this reaction, a sufficient amount of precursor 195 had to be prepared. This research project was conducted as a team effort, and my task was to synthesize sufficient amounts of 195.

Although the preparation of 195 in sufficient quantity was accomplished, direct formation of the \( \Delta^9 \) double bond was unsuccessful. This reaction was thoroughly investigated using several different conditions and alkylolithiums for the attempted synthesis of vinyl triflate 196. The corresponding vinyl triflate, with the unprotected phenol, is a known compound which has been converted to the corresponding \( \Delta^9 \)-THC-carboxylic acid.\(^{54} \)
Other methods for the direct generation of the $\Delta^9$ double bond from cannabinoid ketone 194 were investigated instead. The proposed method for $\Delta^9$ double bond formation involved a geminal ditriflate as a key intermediate. The formation of a geminal ditriflate from a ketone was investigated using 4-phenylcyclohexanone, 82, as a model. The geminal ditriflate 197 was formed as the major product along with the corresponding vinyl triflate 198, as the minor product. Other geminal ditriflates have also been prepared, as reported in the literature, using the same condition as above. Also, it is well precededent that geminal ditriflates which have $\alpha$-hydrogens readily form the corresponding vinyl triflates when treated with base.

Based on these facts, a synthesis of the $\Delta^9$-vinyl triflate via intramolecular phenoxide assisted elimination of geminal ditriflate was investigated. However, the proposed reaction did not work as anticipated.
Instead, the \( \Delta^8 \)-vinyl triflate \( \text{199} \) was formed exclusively. Also, formation of the aryl triflate was not desired. It was hoped that a phenoxide-pyridinium ion pair would be too bulky for aryl triflate formation to occur, and that rapid geminal ditriflate formation would be followed by phenoxide induced elimination of triflate to form the desired vinyl triflate. Since the aryl triflate had been formed, it was assumed that the geminal ditriflate and phenoxide anion might not have been present simultaneously in the reaction mixture.

In order to address this problem of generating a phenoxide anion in the presence of a geminal ditriflate, another reaction was investigated. In this approach to the \( \Delta^9 \)-vinyl triflate, the geminal ditriflate is formed from the phenolic silyl ether \( \text{200} \) prior to the generation of the phenoxide anion which is subsequently generated via desilylation by fluoride. This reaction, however, also led to \( \text{199} \). The formation of the aryl triflate might be suppressed by using less triflic anhydride. However, due to the formation of the undesired \( \Delta^8 \) double bond, the investigation of geminal ditriflates as the
means for introducing the $\Delta^9$ double bond was not pursued any further. Also, other means of introducing the $\Delta^9$ double bond directly from ketone 194 was not pursued.
II. Synthesis of triol cannabinoid analog

In another project involving cannabinoids, the total synthesis of a series of cannabinoid analogs required for SAR studies was investigated. All of these analogs could be synthesized from a common intermediate. This project was performed as a team effort, and my responsibility was the synthesis of this intermediate. The synthesis involved a convergent strategy between a suitable terpenoid and aromatic unit. The synthesis of the terpenoid unit was accomplished following a known literature procedure, but with a slight variation (Scheme 14). The difference lay in the lead tetraacetate reaction. The reported yield for diacetates and never exceeded 40%. The diacetates, however, were found to be thermally labile, undergoing

SCHEME 14a

\[ \text{201} \xrightarrow{a} \text{182} \xrightarrow{b} \text{202} \xrightarrow{c} \]

\[ \begin{align*}
\text{201} & \quad \text{AcO} \quad \text{OAc} \\
\text{203} & + \quad \text{204} \quad \text{OAc} \\
\text{176} & \quad (65 : 30 : 5)
\end{align*} \]

aReagents: (a) O₃/thiourea (75%); (b) p-TSA/isopropenyl acetate (quant); (c) Pb(OAc)₄, Δ, 2 h (quant).
decomposition to give apovernone when heated. In the published procedures, distillation\textsuperscript{63} and GC/MS\textsuperscript{54} have been used for purification and analysis, but these techniques may have had an adverse effect on the yields. Indeed, when the workup was conducted without exposing the material to heat, the \textsuperscript{1}H-NMR of the crude product showed a 95\% yield of diacetates, based on integration and weight of the mixture.

The aromatic portion of the cannabinoid analogs was prepared using known literature procedures (Scheme 15).\textsuperscript{64} All the results of these reactions

\textbf{SCHEME 15\textsuperscript{a}}

\begin{align*}
\text{205} & \xrightarrow{a} \text{206} + \text{207} \\
\text{208} & \xrightarrow{c} \text{209} \xrightarrow{d,e} \text{210}
\end{align*}

\textsuperscript{a}Reagents: (a) MeMgBr (quant); (b) p-TSA (98\%); (c) HPO(OEt)\textsubscript{2}, Et\textsubscript{3}N (80\%); (d) Li/NH\textsubscript{3} (95\%); (e) BBr\textsubscript{3} (75\%).
correlate closely with those reported in the literature.\textsuperscript{64} In the beginning of any total synthesis, large scale reactions which do not require column chromatography are desirable. The large scale preparation of the aromatic unit, as well as the terpenoid unit, contain only a few chromatographic purifications, and yields are typically good to excellent.

The coupling of the terpenoid and aromatic unit was accomplished using a known procedure.\textsuperscript{63} This procedure is very easy compared to the previously described cuprate reaction which was used for coupling reactions with olivetol.\textsuperscript{58} This acid catalyzed condensation, however, is limited to Cl\textsuperscript{1} substituted resorcinols in which the substituent is very sterically demanding.

\[
\begin{align*}
\ce{AcO} \ce{OAc} + \ce{OAc} \ce{OAc} + \ce{OAc} \ce{OAc} + \ce{HO,\text{OH}} &\xrightarrow{\text{p-TSA}} \ce{C_6H_{13}} \\
203 &+ 204 &+ 176 &+ 210 \\
(65:30:5)
\end{align*}
\]

Otherwise, the reaction will suffer from poor regioselectivity (see 173 and 174). Another advantage of this procedure involved the purification method.
The coupled product 211 could be recrystallized efficiently to high optical purity, \([\alpha]^{21}_D = 53.0^\circ\) (c = 1, CHCl3) [lit.\(^{63}\) \([\alpha]^{20}_D = 55.8^\circ\) (c = 1, CHCl3)].

This coupled product was transformed into the desired intermediate (Scheme 16). Attention must be paid to several important factors for successful, high yielding reactions. First, the ring opening reaction, 211 to 212, had to be slowly warmed to approximately 50°C from 0°C before complete disappearance of starting material was observed. Second, the elimination of the tertiary iodide from 212 had to be accomplished by adding DBU very slowly (approx 1 drop per 2 s), and the reaction time should not exceed 4 h. Care had to be taken during the Wittig reaction of 213 since the solvent had a tendency to boil violently during the first hour. The hydrolysis of 214 was accomplished with wet TCA (aq), taken from the liquid phase of a sample which had deliquesced. Lastly, the epimerization of aldehyde 216 takes

\[ \text{SCHEME 16} \]
Reagents: (a) TBDMSCl, imidazole, DMF (quant); (b) I₂, allyltrimethylsilane; (c) DBU (66% over 2 steps); (d) [Ph₃P⁺(CH₂)OCH₃]Cl⁻, sodium t-amylate; (e) TCA (aq); (f) K₂CO₃, EtOH; (g) NaBH₄, EtOH (66% over 4 steps); (h) TBDMSCl, imidazole, DMF (quant).

approx 1 d as monitored by ¹H-NMR of a concentrated aliquot (approx 100 mg per 0.5 mL of CDCl₃) of the crude reaction mixture. The advanced intermediate 218 was prepared on a large scale (approx 3 g). It should be noted
that the two TBDMS ethers of 213 - 219 are unequivalent, as seen in the $^1$H-
NMR spectrum, due to hindered rotation.

The intermediate was later used to produce 100 mg of the desired
cannabinoid analog 221 (Scheme 17). Triol 221 was one of the final target
molecules required for biological study. The SAR study required a
hydroxyalkyl group attached to the B ring of the cannabinoid. Triol 221 was
obtained as a 4 : 1 isomeric mixture.

SCHEME 17a

\[
\begin{align*}
\text{218} & \quad \text{R} = \text{TBDMS} \\
\text{219} & \\
\text{220} & \\
\text{221} & \\
\end{align*}
\]

\( a \text{Reagent: (a) AlMe}_3, \text{ trioxane, 2,6,-di-phenylphenol; (b) TBAF; (c)} \text{Hg(OAc)}_2/\text{NaBH}_4. \)
III. Synthesis of fluorocannabinoid analogs

Finally, an efficient synthesis of 2-fluoronabilone, 222, was also desired for biological study. The initial strategy was to form the 2-fluoronabilone directly from nabilone, 175. Some questions were how stable nabilone would be towards mildly oxidizing fluorinating reagents and the regiospecificity of the fluorination, whether the C2 or C4 position would be fluorinated. To answer the former question, olivetol was subjected to 1 eq of XeF$_2$. Based on crude $^1$H- and $^{19}$F-NMR, approximately 40% of olivetol was fluorinated to give 2 regioisomeric aryl fluorides. The rest of the material was unreacted olivetol. From this result, it seemed likely that oxidation of nabilone with XeF$_2$ would not be a problem since olivetol was not oxidized to any detectable degree.

The synthesis of nabilone involved the use of substrate 211. Diol 211 was cyclized by a method previously developed in this group using TMSOTf in MeNO$_2$ at ambient temperature for 5 h. The isolated yield of nabilone was 99% on a 100 mg scale. The cyclization reaction might actually be faster than
5 h. It is very difficult to tell by tlc when the reaction is over since both starting material and product have roughly the same Rf values. This method of cyclization is superior to the method previously reported in the literature for the synthesis of nabilone (the reported yield is approx 73%\textsuperscript{22}).

The fluorination of nabilone with XeF\textsubscript{2} was disappointing. The use of 2 eq of the fluorinating reagent gave unreacted nabilone and a complex reaction mixture containing several fluorinated cannabinoids. \textit{N}-Fluoropyridinium triflate,\textsuperscript{16} an alternative source of fluorine, known as Umemoto's reagent after its discoverer, was very reactive and nabilone was completely consumed using the standard fluorination conditions for this reagent. Based on crude \textsuperscript{19}F-NMR, two different organofluorine cannabinoids were formed. The two organofluorine cannabinoids were inseparable using flash column chromatography. IR, MS, \textsuperscript{1}H- and \textsuperscript{19}F-NMR of the mixture revealed the
structures represented above. This reaction was performed in a sealed tube at 90°C using excess Umemoto's reagent. The di- and trifluorocannabinoids were isolated in approx 80% yield in a ratio of 3:1. The rest of the material was 2-fluoronabilone, 222. To see whether 223 was a precursor of 224, the mixture (3:1) of 223 and 224 was treated under the conditions set forth above. This led to no change in product distribution. Therefore, these two products must be coming from two different reaction pathways. Lower reaction temperatures did not change the ratio of di- and trifluorocannabinoids formed from nabilone.

It seemed possible that a stoichiometric amount of Umemoto's reagent could be used effectively to monofluorinate nabilone at C2. In fact, 2-fluoronabilone was synthesized when nabilone was treated to 1 eq of Umemoto's reagent at ambient temperature. The reaction was very efficient, giving 2-fluoronabilone as the only detectable organofluorine cannabinoid by 19F-NMR in the crude reaction mixture. That the fluorine was at the C2 position, and not the C4 position, was verified from a series of NMR experiments. There were no nOe correlations between the phenolic and aryl hydrogens. This suggested that the two hydrogens were not close to each
other, since an aryl hydrogen ortho to a phenolic moiety usually shows a NOE correlation in cannabinoid substrates. Furthermore, it was shown that the hydrogen which appears at 5.49 ppm as a doublet with a coupling constant of $J = 8.4$ Hz in the $^1$H-NMR exchanges with D$_2$O, proof that this hydrogen corresponded to the phenolic hydrogen. This coupling constant could only arise if the fluorine was in the C2 position and not C4. With the fluorine in the C2 position, the phenolic hydrogen can couple to the fluorine via an intramolecular hydrogen bond. Finally, the aryl hydrogen showed a HMBC correlation to the C4a carbon. This correlation could arise only if the aryl hydrogen was in the C4 position and not C2.
CONCLUSION

In conclusion, efficient synthetic routes have been demonstrated for the intermediates 194 and 218. The synthesis of 218 of high optical purity was accomplished. The synthetic routes are both high yielding as well as regio- and stereospecific. Also, since both R and S terpenoid starting materials are commercially available, both enantiomeric series can be synthesized if desired.

Finally, an efficient cyclization method, previously developed by this group, has been applied to the synthesis of nabilone, 175. A high yielding and regiospecific fluorination of nabilone has been developed for the synthesis of 2-fluoronabilone. Also, a moderately regiospecific difluorination of nabilone has been developed. These fluorination methods, by mildly oxidizing reagents, are advantageous since the free phenol of nabilone can be used directly without detectable amounts of oxidized byproducts being formed.
**EXPERIMENTAL**

**Procedure:** (+)-β-Pinene (25.0 g, 184 mmol) in MeOH (164 mL) was ozonized at -78°C for 2.5 h. Thiourea (6.98 g, 91.8 mmol) was added to the solution at -78°C and allowed to warm to ambient temperature overnight. The reaction was partitioned between ethyl ether and brine. After evaporation of the solvent, but before distillation, wet starch-KI paper was used to determine that no ozonide was present. Distillation of the crude reaction mixture under reduced pressure (0.5 mm Hg) led to 22.1 g (87% yield) of nopinone, 182.

**1H-NMR** (300 MHz, CDCl₃): 0.84 (s, 3H), 1.32 (s, 3H), 1.57 (d, J = 10.2 Hz, 1H), 1.91-2.08 (m, 2H), 2.20-2.37 (m, 2H), 2.47-2.61 (m, 3H).

**13C-NMR** (75 MHz, CDCl₃): 21.3, 22.3, 25.2, 25.8, 32.7, 40.3, 41.1, 57.9, 215.0.

**IR** (neat): 2920 (s), 1710 (s), 1460 (s), 1200 (s).

**bp:** 51-53°C (0.5 mm Hg).

**tlc:** Rf = 0.4 (15% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
Procedure: To nopinone, 182 (22.0 g, 0.16 mmol), was added isopropenyl acetate (439 mL, 0.36 mmol) and a catalytic amount of p-TSA monohydrate (2.42 g, 12.7 mmol). The solution was refluxed for 12 h. The solvent was then evaporated under reduced pressure. The crude reaction mixture was distilled to afford 26.2 g of pure enol acetate 202 (91% yield).

\[ ^{1}H\text{-NMR} \text{ (300 MHz, CDCl} _3\text{):} \] 0.95 (s, 3H), 1.44 (d, J = 8.7 Hz, 1H), 2.10 (s, 3H), 2.10-2.13 (m, 1H), 2.25 (dt, J = 12.9, 2.7 Hz, 2H), 2.48 (dt, J = 9.0, 5.4 Hz, 2H), 5.17 (br s, 1H).

bp: 42-44°C (1.5 mm Hg).

tlc: Rf = 0.5 (15% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.

Procedure: The isolated yield of product was 80% (3.60 g) from 4.77 g (26.5 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 1.02 (s, 3H), 1.49 (s, 3H), 2.12 (d, J = 9.0 Hz, 1H), 2.55-2.61 (m, 1H), 2.69 (t, J = 6.6 Hz, 1H), 2.79-2.86 (m, 1H), 5.93 (d, J = 9.0 Hz, 1H), 7.51 (dd, J = 9.0, 6.9 Hz, 1H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 22.3, 26.6, 42.0, 43.9, 55.0, 58.7, 125.7, 157.0, 204.1.

IR (neat): 2960 (s), 2860 (s), 1685 (s).

tlc: Rf = 0.3 (15% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: In a flame dried 2-neck flask, olivetol (5.58 g, 31.0 mmol) was added, followed by ethyl ether (111 mL), ethyl vinyl ether (7.4 mL, 77.0 mmol), and p-TSA monohydrate (59 mg, 0.3 mmol) at 0°C. The solution was maintained at this temperature and stirred for 12 h. The solution was diluted with ethyl ether and washed with saturated aqueous sodium bicarbonate, brine, then dried with anhydrous magnesium sulfate. The organic solvent was evaporated under reduced pressure, and the residue chromatographed on silica gel with 5% ethyl acetate in hexane to afford the desired product (8.04 g, 80% yield).

$^1$H-NMR (300 MHz, CDCl$_3$): 0.89 (t, $J = 6.3$ Hz, 3H), 1.21 (t, $J = 6.9$ Hz, 6H), 1.49 (d, $J = 5.4$ Hz, 6H), 2.52 (t, $J = 7.5$ Hz, 2H), 3.49-3.59 (m, 2H), 3.73-3.81 (m, 2H), 5.35 (q, $J = 5.1$ Hz, 2H), 6.50 (br s, 1H), 6.62 (s, 1H), 6.62 (s, 1H).

IR (neat): 2985 (s), 2920 (s), 2850 (s), 1590 (s), 1450 (s), 1380 (s), 1340 (s), 1290 (s).


tlc: Rf = 0.4 (10% Ethyl acetate in hexane).

Physical characteristic: Yellowish oil.

Procedure: See reference for procedure. The crude reaction mixture was used for the next reaction without purification.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.89 (t, $J = 6.7$ Hz, 3H), 0.98 (s, 3H), 1.16-1.22 (m, 6H), 1.35 (s, 3H), 1.48 (d, $J = 5.1$ Hz, 6H), 2.22 (br s, 1H), 2.45-2.56 (m, 5H), 3.29-3.38 (m, 1H), 3.46-3.57 (m, 2H), 3.64-3.74 (m, 2H), 4.09-4.16 (m, 1H), 5.39-5.46 (m, 2H), 6.55 (s, 1H), 6.59 (s, 1H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 13.9, 15.2, 20.1, 22.0, 22.4, 24.7, 26.3, 29.1, 30.9, 31.4, 36.0, 38.3, 42.3, 46.9, 57.7, 60.6, 60.9, 61.0, 98.8, 99.0, 108.4, 108.6, 108.61, 108.7, 118.7, 142.4, 156.0, 156.1, 215.7.

IR (neat): 2975 (s), 2925 (s), 2860 (s), 1710 (s), 1605 (s), 1570 (s), 1430 (s), 1380 (s), 1071 (s), 1050 (s).

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

Physical characteristic: Thick colorless oil.
Procedure: Removal of the EE protecting groups was accomplished using PPTS (1 mole%) and MeOH (0.123 M) as the solvent. Yields are typically quantitative from 178 and 63% overall (100 mg to 5 g scale) from apoverbenone, 176.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.89 (t, $J = 6.9$ Hz, 3H), 0.99 (s, 3H), 1.26-1.31 (m, 4H), 1.36 (s, 3H), 2.30 (t, $J = 5.4$ Hz, 1H), 2.39-2.68 (m, 5H), 3.47 (dd, $J = 18.9$, 7.8 Hz, 1H), 3.95 (t, $J = 8.1$ Hz, 1H), 5.13 (s, exchanges with D$_2$O, 2H), 6.17 (s, 2H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 14.0, 22.1, 22.5, 24.4, 26.2, 29.5, 30.6, 31.5, 35.2, 37.9, 42.3, 46.8, 58.0, 108.6, 113.7, 142.6, 155.3, 171.7.

IR: 3350 (s), 2950 (s), 2920 (s), 2850 (s), 1680 (s), 1620 (s), 1590 (s), 1430 (s), 1265 (s), 1020 (s).

Mass spectrum m/e: 316 (M$^+$), 301, 273, 247, 233, 219, 206, 193, 150, 83, 69, 57.

tlc: Rf = 0.45 (40% Ethyl acetate in hexane).

Procedure: Isolated yield of product was 80% (170 mg) from 310 mg (0.67 mmol) of starting material.

$^1$H-NMR (300 MHz, CDCl$_3$): 0.88 (t, $J = 6.7$ Hz, 3H), 1.12 (s, 3H), 1.47 (s, 3H), 1.96 (t, $J = 12.0$ Hz, 1H), 2.14-2.19 (m, 2H), 2.44 (t, $J = 7.2$ Hz, 1H), 2.58-2.67 (m, 1H), 2.89 (t, $J = 12.0$ Hz, 1H), 4.03 (d, $J = 14.7$ Hz, 1H), 6.18 (s, 1H), 6.22 (s, exchanges with D$_2$O, 1H), 6.27 (s, 1H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 14.0, 18.9, 22.5, 26.9, 27.8, 30.7, 31.6, 34.8, 35.5, 40.8, 45.0, 47.4, 76.4, 107.8, 108.0, 109.1, 143.6, 154.5, 155.3, 214.7.

IR: 3260 (s), 2940 (s), 2920 (s), 2840 (s), 1685 (s), 1615 (s), 1570 (s), 1420 (s), 1350 (s), 1250 (s), 1175 (s), 1090 (s), 1030 (s).

Mass spectrum m/e: 316 (M$^+$), 301, 273, 260, 233, 150, 95, 83, 69, 57.

tlc: Rf = 0.25 (20% Ethyl acetate in hexane).
Procedure: Ketophenol 194 (18 mg, 56 µmol) was added to a oven dried, sealed tube. Potassium carbonate (156 mg, 1.13 mmol), NaI (8 mg, 60 µmol), 2-iodobenzyl chloride (19 mg, 73 µmol), and acetone (2.0 mL) were added to the tube under an argon atmosphere. The reaction mixture was heated to 80°C and stirred at that temperature overnight. After cooling the reaction mixture to ambient temperature, the crude reaction mixture was purified by column chromatography on silica gel, eluting with 10% ethyl acetate in hexane, to afford pure ketone 195 (26 mg, 82% yield).

$^1$H-NMR (300 MHz, CDCl$_3$): 0.88 (br t, J = 6.6 Hz, 3H), 1.12 (s, 3H), 1.20-1.32 (m, 4H), 1.47 (s, 3H), 1.49-1.61 (m, 3H), 1.97 (td, J = 12.0, 2.4 Hz, 1H), 2.15 (dd, J = 15.0, 13.2 Hz, 2H), 2.37-2.62 (m, 2H), 2.49 (t, J = 8.4 Hz, 2H), 2.91 (td, J = 12.6, 2.1 Hz, 1H), 3.80 (br d, J = 13.7 Hz, 1H), 5.04 (d, J = 3.0 Hz, 2H), 6.25 (s, 1H), 6.36 (s, 1H), 7.03 (br t, J = 8.4 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H).

tlc: Rf = 0.6 (10% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, 4-phenylcyclohexanone (500 mg, 2.87 mmol), sodium carbonate (574 mg, 5.42 mmol), and methylene chloride (12 mL) were added. Triflic anhydride in methylene chloride (6 mL) was then transferred to the solution using a syringe. After stirring this solution for 30 h at ambient temperature, the reaction mixture was poured into a beaker containing ice and saturated aqueous sodium bicarbonate. The mixture, once allowed to warm to ambient temperature, was extracted with ethyl ether, and the organic phase dried with anhydrous sodium sulphate and filtered. After evaporation of the solvent under reduced pressure, the crude products 197 and 198 (approx 1.3 g, 99% yield) were analyzed using $^1$H-NMR, which showed the purity of 197 to be approx 80%. The balance of the material was the corresponding vinyl triflate 198.

$^1$H-NMR (300 MHz, C$_6$D$_6$): Reported for the mixture 197 and 198; 1.20-1.60 (m), 1.60-1.90 (m), 1.86 (br d, $J = 17.4$ Hz, 2H), 2.00-2.40 (m), 2.46 (br s, 1H), 2.72 (br s, 1H), 5.31 (br t, $J = 2.7$ Hz, 1H), 6.83 (br d, $J = 6.9$ Hz, 2H), 6.95 (br d, $J = 7.8$ Hz, 1H), 7.12-7.21 (m).

IR (neat): Reported for the mixture 197 and 198; 3010 (s), 2920 (br), 1690 (m), 1605 (m), 1495 (s), 1455 (s), 1425 (s), 1255 (s), 1210 (br), 1140 (s), 1050 (w), 1025 (s), 890 (s), 860 (s), 760 (s), 700 (s), 600 (br).

tlc (neat): Rf = 0.75 (20% Ethyl acetate in hexane).
Physical characteristic: Colorless oil.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, ketophenol 194 (50 mg, 0.2 mmol), 2,6-di-t-butyl-4-methylpyridine (49 mg, 0.24 mmol), and methylene chloride (0.42 mL) were added. Triflic anhydride (0.03 mL, 0.2 mmol) in methylene chloride (0.53 mL) was transferred to the reaction mixture via syringe. After stirring this solution for 1 d, the reaction mixture was poured into a beaker containing ice and saturated aqueous sodium bicarbonate. The mixture was allowed to warm to ambient temperature and extracted with ethyl ether, and the organic phase dried with anhydrous sodium sulphate and filtered. After evaporation of the solvent under reduced pressure, the crude products were analyzed using ¹H-NMR. The analysis of the ¹H-NMR showed 199 as the major component of the crude reaction mixture (approx 60 mg, 80-90% yield).

¹H-NMR (300 MHz, CDCl₃): 0.89 (br t, J = 6.9 Hz, 3H), 1.14 (s, 3H), 1.20-1.35 (m, 4H), 1.44 (s, 3H), 1.48 (br d, J = 7.8 Hz, 1H), 1.58 (br quintet, J = 6.9 Hz, 2H), 1.86 (td, J = 11.1, 3.9 Hz, 1H), 2.02 (br tt, J = 14.1, 2.1 Hz, 1H), 2.20-2.45 (m, 2H), 2.54 (t, J = 7.8 Hz, 2H), 3.00 (td, J = 11.1, 4.8 Hz, 1H), 3.29 (br d, J = 17.1 Hz, 1H), 5.87 (br t, J = 3.0 Hz, 1H), 6.64 (s, 1H), 6.70 (s, 1H).
IR (neat): 2960 (s), 2930 (s), 2860 (s), 1740 (w), 1690 (w), 1630 (s), 1560 (s), 1420 (s), 1390 (s), 1375 (s), 1365 (s), 1350 (m), 1330 (s), 1245 (s), 1210 (br), 1180 (s), 1140 (s), 1080 (m), 1050 (s), 1040 (m), 1010 (m), 975 (s), 910 (s), 880 (br), 855 (br), 820 (s), 775 (m), 665 (m), 610 (br).

tlc: Rf = 0.5 (20% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.

Procedure: The identical procedure was followed as reported in the reference cited above. The exception is the method of work-up. The crude reaction mixture was not warmed above ambient temperature. The mixture was then analyzed by $^1$H-NMR to show the corresponding ratio of 65 : 30 : 5 of 203, 204, and 176, respectively, based on integration. The yield of the products was approx quant (scale 1.00 g to 20 g) based on weight of the crude material.

Procedure: Isolated yield of product was 76% (9.6 g) from 8.0 g (34 mmol) of starting material. The purification of this product was accomplished via recrystallization from methylene chloride, ethyl acetate, and hexane (1 : 1 : 20).

$^1$H-NMR (300 MHz, CDCl$_3$): 0.84 (dd, J = 6.9, 6.6 Hz, 3H), 0.99 (s, 2H), 1.05-1.25 (m, 6H), 1.19 (s, 6H), 1.35 (s, 3H), 1.46-1.51 (m, 2H), 1.68 (s, 2H), 2.31 (t, J = 5.4 Hz, 1H), 2.45-2.67 (m, 5H), 3.52 (dd, J = 18.6, 7.5 Hz, 1H), 3.94 (t, J = 8.1 Hz, 1H), 5.25 (s, 2H), 6.28 (s, 2H).

$^{13}$C-NMR (75 MHz, CDCl$_3$): 14.1, 22.2, 22.7, 24.4, 24.6, 26.2, 28.7, 29.5, 30.0, 31.8, 37.2, 37.9, 42.2, 44.4, 46.8, 57.9, 106.6, 113.5, 150.0, 154.7, 216.9.
IR: 3300 (s), 2920 (s), 1680 (s), 1580 (s), 1420 (s), 1370 (s), 1330 (s), 1265 (s).

HRMS: Calcd. for C_{24}H_{36}O_{3} (M^+) 372.2647, found 372.2652.

Mass spectrum m/e: 372 (M^+), 355, 329, 289, 269, 249, 217, 178, 149, 109, 83.

mp = 171-174°C.

Optical rotation: [\alpha]^{21}_{D} = +53.0 (c = 1, CHCl_3).

tlc: Rf = 0.4 (40% Ethyl acetate in hexane).

Physical characteristic: White crystalline solid.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, imidazole (6.03 g, 88.5 mmol) was added followed by DMF (10 mL). TBDMSCl (10.6 g, 70.3 mmol) in DMF (31.7 mL) was transferred to the imidazole solution via cannula followed by ketodiol 211 (8.50 g, 22.8 mmol) in DMF (20 mL). After stirring the solution overnight, ethyl ether (200 mL) was added, and the reaction mixture was washed with water, saturated aqueous sodium bicarbonate, then brine. The organic phase was dried with anhydrous magnesium sulphate and evaporated under reduced pressure. Purification by silica gel column chromatography, eluting with hexane, afforded the product (13.7 g, 100% yield).

\[ \text{Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, imidazole (6.03 g, 88.5 mmol) was added followed by DMF (10 mL). TBDMSCl (10.6 g, 70.3 mmol) in DMF (31.7 mL) was transferred to the imidazole solution via cannula followed by ketodiol 211 (8.50 g, 22.8 mmol) in DMF (20 mL). After stirring the solution overnight, ethyl ether (200 mL) was added, and the reaction mixture was washed with water, saturated aqueous sodium bicarbonate, then brine. The organic phase was dried with anhydrous magnesium sulphate and evaporated under reduced pressure. Purification by silica gel column chromatography, eluting with hexane, afforded the product (13.7 g, 100% yield).} \]

\[ \text{\textsuperscript{1}H-NMR (300 MHz, CDCl\textsubscript{3}): 0.27 (s, 12H), 0.85 (t, J = 7.8 Hz, 3H), 0.98 (s, 16H), 1.20 (s, 6H), 1.11-1.26 (m, 6H), 1.32 (s, 3H), 1.46-1.52 (m, 2H), 1.58 (s, 6H), 2.23 (t, J = 5.4 Hz, 1H), 2.39-2.55 (m, 5H), 3.68 (dd, J = 18.6, 7.5 Hz, 1H), 3.98 (br t, J = 8.0 Hz, 1H), 6.40 (s, 2H).} \]

\[ \text{\textsuperscript{13}C-NMR (75 MHz, CDCl\textsubscript{3}): 14.1, 18.8, 22.2, 22.7, 24.2, 24.7, 25.7, 26.0, 26.3, 28.9, 30.0, 30.2, 31.8, 37.3, 41.9, 44.6, 47.4, 57.9, 110.0, 119.6, 148.2, 154.7, 215.4.} \]

\[ \text{IR (neat): 2950 (s), 2860 (s), 1620 (s), 1605 (s), 1565 (s), 1470 (s), 1420 (s), 1260 (s).} \]
HRMS: Calcd. for C$_{36}$H$_{64}$O$_3$Si$_2$ (M$^+$) 600.4400, found 600.4375.

Mass spectrum m/e: 543 (M$^+$), 503, 435, 119, 73.

Optical rotation: $[\alpha]^D_{21} = +48.5$ (c = 1, CHCl$_3$).

tlc: Rf = 0.65 (5% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, iodine (570 mg, 2.25 mmol) was added followed by carbon tetrachloride (22.5 mL). This flask was cooled to 0°C and protected from light with aluminum foil. To this solution was added allyltrimethylsilane (0.357 mL, 2.25 mmol) very slowly (approx 1 drop per 2 s). After stirring the solution at this temperature for 2 h, the ketone (1.00 g, 1.66 mmol) in carbon tetrachloride (5.7 mL) was transferred to the reaction mixture via cannula. The solution was allowed to warm to 5°C within a 4 h period. The reaction mixture was then diluted with ethyl ether and quenched with saturated Na₂S₂O₃ (aq). After stirring this solution at ambient temperature for 1 h, the organic phase was separated, and the aqueous phase further extracted with ethyl ether. The combined organic phases were dried with anhydrous magnesium sulphate, filtered, and the solvent was evaporated under reduced pressure at ambient temperature in the dark. Note: This reaction may be HI catalyzed, since generating the trimethylsilyl iodide from absolutely dry allyltrimethylsilane prevents the reaction from occurring, or this reaction may be trimethylsilyl triiodide catalyzed. Finally, the work up should also include a cold saturated aqueous sodium bicarbonate wash since concentration of the crude reaction mixture may result in some deprotection to afford the diol 211 as a byproduct.
The crude reaction mixture, continuously protected from light, was dissolved in benzene (27.7 mL) under argon. To this solution was added DBU (0.995 mL) very slowly (approx 1 drop per 5 s) using a pressure equalizing dropping funnel. After stirring this solution for 4 h, the reaction mixture was diluted with ethyl ether and washed with water. The organic phase was dried with anhydrous magnesium sulphate, and the solvent was evaporated under reduced pressure. Column chromatography on silica gel, eluting with 2.5% ethyl acetate in hexane, afforded 213 (2.00 g, 66% yield over two steps).

\(^1\)H-NMR (300 MHz, CDCl\(_3\)): 0.14 (s, 3H), 0.22 (s, 3H), 0.32 (br s, 6H), 0.83 (t, J = 6.6 Hz, 3H), 0.99 (s, 9H), 1.05 (s, 9H), 1.17 (m, 4H), 1.19 (s, 6H), 1.43-1.48 (m, 3H), 1.55 (s, 3H), 1.58 (s, 3H), 1.71-1.79 (m, 1H), 1.97-2.04 (m, 1H), 2.31 (dd, J = 14.4, 3.9 Hz, 1H), 2.46 (m, 2H), 3.19 (t, J = 14.1 Hz, 1H), 3.39 (td, J = 8.6, 3.3 Hz, 1H), 3.63 (m, 1H), 4.49 (s, 1H), 4.63 (s, 1H), 6.33 (br s, 2H).

\(^{13}\)C-NMR (75 MHz, CDCl\(_3\)): 14.1, 19.3, 22.5, 24.6, 25.9, 26.4, 28.6, 28.9, 29.9, 31.8, 32.0, 37.3, 38.8, 41.6, 44.8, 45.1, 45.9, 109.6, 109.8, 110.7, 119.2, 147.4, 148.4, 211.6.

IR (neat): 3065 (s), 2900 (s), 1720 (s), 1650 (s), 1610 (s), 1570 (s), 1420 (s).

HRMS: Calcd. for C\(_{36}\)H\(_{64}\)O\(_3\)Si\(_2\) (M\(^+\)) 600.4389, found 600.4374.

tlc: Rf = 0.2 (10% Ethyl acetate in hexane).

Physical characteristic: Colorless oil.
**Procedure:** In a flame dried 2-neck flask equipped with a magnetic stirrer, was added NaH (670 mg, 74% dispersion in mineral oil, 20.7 mmol) followed by hexane (10 mL). After stirring this solution for 1 min, the hexane was carefully syringed out leaving behind a powder of NaH. Benzene (4 mL) was then added to this flask to make a stock suspension of NaH in benzene. t-Amylalcohol (2.26 mL, 20.7 mmol) was then added to the NaH benzene suspension, dropwise, then heated to 70°C for 3 h. In a separate flask, methoxymethyltriphenyl phosphonium chloride (3.47 g, 10.1 mmol) was dissolved in benzene (63 mL). To this solution was added the warm solution of sodium t-amylate (2 mL). The mixture was stirred for 10 min at ambient temperature. To this solution was added the ketone 213 (2.00 g, 3.33 mmol) in benzene (12.3 mL), via cannula. The combined solution was heated to 70°C and stirred at this temperature for 3 h [Caution: exothermic during the first 30 min]. After cooling to ambient temperature, saturated aqueous ammonium chloride was added. The aqueous phase was extracted with ethyl ether (3 X). The combined organic phases were washed with brine, dried with anhydrous magnesium sulphate, filtered, and the solvent was evaporated under reduced pressure. This crude reaction mixture was used in the next reaction without purification.
Procedure: The crude mixture from the previous reaction was dissolved in methylene chloride (197 mL), and wet trichloroacetic acid (aq) (1.87 g, 11.4 mmol) was added. This solution was stirred at ambient temperature for 15 min then diluted with methylene chloride. The organic layers were washed with water, saturated aqueous sodium bicarbonate, brine, dried with anhydrous magnesium sulphate, filtered, and the solvent was evaporated under reduced pressure. The crude product was used in the next reaction without purification.

Procedure: The crude mixture from the previous reaction was dissolved in absolute ethyl alcohol (119 mL), and powdered potassium carbonate (909 mg, 6.58 mmol) was added. This solution was stirred for 1 d at ambient
temperature before being diluted with ethyl ether (318 mL). The organic phase was washed with 1 N HCl (aq), water, saturated aqueous sodium bicarbonate, brine, dried with anhydrous magnesium sulphate, and filtered. The solvent was then evaporated under reduced pressure. The crude reaction mixture was used for the next reaction without purification.

Procedure: The crude mixture from the previous reaction was dissolved in ethyl alcohol (318 mL), and sodium borohydride (433 mg, 11.5 mmol) was added at 0°C. This solution was warmed to ambient temperature and stirred for 5 h. The solution was diluted with water and extracted with ethyl ether (3 X). The organic phases were dried with anhydrous magnesium sulphate, filtered, and the solvent was evaporated. The crude reaction mixture was chromatographed on silica gel to afford pure 217 (0.09 g, 62% overall yield over 4 steps).

**1H-NMR (500 MHz, CDCl3):** 0.16 (s, 3H), 0.24 (s, 3H), 0.31 (s, 6H), 0.84 (br t, J = 6.9 Hz, 3H), 1.03 (s, 9H), 1.06 (s, 9H), 1.00-1.25 (m, 12H), 1.19 (br s, 6H), 1.38-1.44 (m, 1H), 1.42-1.55 (m, 3H), 1.58-1.68 (m, 1H), 1.76-1.84 (m, 1H), 1.86-1.92 (m,
1H), 3.01 (td, J = 11.7, 2.9 Hz, 1H), 3.26 (td, J = 11.9, 3.1 Hz, 1H), 3.47 (br heptet, J = 5.9 Hz, 2H), 4.41 (d, J = 1.0 Hz, 1H), 4.57 (d, J = 1.9 Hz, 1H), 6.30 (d, J = 1.7 Hz, 1H), 6.31 (d, J = 1.7 Hz, 1H).

nOe: Positive nOe from C1 hydrogen (1.60 ppm) to benzylic hydrogen, C3, (3.25 ppm). The assignments of C1 and benzylic hydrogens were based on HMQC AND HMBC NMR experiments.

Table 6: HMQC correlations of cannabinoid 217

<table>
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<th>Hydrogen(s) δ (ppm)</th>
<th>Carbon</th>
<th>Carbon δ (ppm)</th>
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<td>1.6</td>
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Table 7: HMBC correlations of cannabinoid 217

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<th>Hydrogen(s) δ (ppm)</th>
<th>Carbon(s)</th>
<th>Carbon(s) δ (ppm), respectively</th>
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<td>41 &amp; 33</td>
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<td>1.6</td>
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<td>69 &amp; 38</td>
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<tr>
<td>3.3</td>
<td>C1</td>
<td>41</td>
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</table>
$^{13}$C-NMR (125 MHz, CDCl$_3$): -4.4, -3.8, -3.7, -3.5, 14.0, 18.3, 18.8, 19.4, 22.6, 24.6, 25.9, 26.4, 28.6, 28.9, 29.3, 29.9, 31.8, 32.4, 33.0, 37.2, 37.8, 41.1, 44.8, 46.7, 68.8, 109.2, 109.3, 109.9, 121.8, 147.3, 149.7, 153.4, 154.9.

tlc: Rf = 0.1 (5% Ethyl acetate in hexane).
Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, imidazole (233 mg, 3.43 mmol) was added followed by DMF (1 mL). TBDMSCI (410 mg, 2.72 mmol) in DMF (2.23 mL) was transferred to the imidazole solution via cannula followed by alcohol 217 (1.09 g, 1.77 mmol) in DMF (2.0 mL). After stirring the solution overnight, ethyl ether was added, and the organic phase was washed with water, saturated aqueous sodium bicarbonate, then brine. The organic phase was dried with anhydrous magnesium sulphate, and the solvent was evaporated under reduced pressure. Purification of the crude reaction material by silica gel column chromatography, eluting with hexane, afforded 218 (1.29 g, 100% yield).

$^{1}$H-NMR (300 MHz, CDCl$_3$): 0.01 (s, 3H), 0.02 (s, 3H), 0.13 (s, 3H), 0.22 (s, 3H), 0.29 (s, 6H), 0.80-1.00 (m, 11H), 0.87 (s, 9H), 1.01 (s, 9H), 1.05 (s, 9H), 1.18 (br s, 6H), 1.18-1.26 (m, 3H), 1.40-1.45 (m, 1H), 1.45-1.60 (m, 3H), 1.53 (s, 3H), 1.60-1.80 (m, 1H), 1.80-1.95 (m, 1H), 2.99 (td, J = 11.4, 2.7 Hz, 1H), 3.12 (td, J = 11.4, 3.9 Hz, 1H), 3.40 (br dd, J = 6.3, 1.5 Hz, 2H), 4.39 (d, J = 0.9 Hz, 1H), 4.55 (d, J = 1.5 Hz, 1H), 6.29 (s, 1H), 6.294 (s, 1H).

Optical rotation: $[\alpha]_{D}^{27} = -80.9$ (c = 1, CHCl$_3$).

Tlc: Rf = 0.8 (Hexane).

Physical characteristic: Colorless oil.

Procedure: In a flame dried 2-neck flask equipped with a magnetic stirrer, was added diol 211 followed by nitromethane (26.4 mL) and methylene chloride (18.0 mL). This solution was slightly warmed using a hot water bath to dissolve 211. The solution was cooled to 0°C with an ice-water bath followed by the dropwise addition of a 0.50 M solution of TMSOTf in nitromethane (1.00 mL, 0.45 mmol). The ice-water bath was then removed, and the reaction stirred at ambient temperature for 5 h. The reaction mixture was poured into a mixture of ice and saturated aqueous sodium bicarbonate and was diluted with brine. The aqueous phase was extracted with a mixture of ethyl acetate and hexane (4:1, 3 X). The combined organic phases were dried with anhydrous magnesium sulfate, filtered though a short pad containing silica gel on the top layer and Celite on the bottom, and the solvent was evaporated under reduced pressure. The product so obtained was pure with respect to tlc and NMR. The isolated yield of nabilone, 175, was 99% (255 mg).

$^1$H-NMR (300 MHz, CDCl$_3$): 0.84 (br t, J = 6.3 Hz, 3H), 1.35-1.85 (m, 11H), 1.12 (s, 3H), 1.20 (s, 6H), 1.48 (s, 3H), 1.96 (td, J = 12.0, 2.7 Hz, 1H), 2.16 (br t, J = 13.8 Hz, 2H), 2.44 (br td, J = 12.6, 7.2 Hz, 1H), 2.60 (dm, J = 15.3 Hz, 1H), 2.87 (td, J =
12.6, 3.6 Hz, 1H), 3.93 (br d, J = 14.7 Hz, 1H), 5.60 (br s, exchangeable with D₂O, 1H), 6.25 (d, J = 1.2 Hz, 1H), 6.38 (d, J = 1.5 Hz, 1H).

**13C-NMR (75 MHz, CDCl₃):** 14.1, 18.9, 22.6, 24.6, 26.9, 27.8, 28.7, 30.0, 31.7, 34.7, 37.3, 40.8, 44.4, 45.0, 47.4, 105.5, 107.0, 107.7, 150.8, 154.1, 155.0, 214.4.

**IR:** 3300 (br), 2960 (s), 2940 (s), 2880 (m), 2860 (m), 1700 (s), 1625 (m), 1580 (m), 1420 (s), 1390 (w), 1365 (w), 1340 (m), 1275 (m), 1190 (m), 1095 (m), 1045 (m), 970 (m).

**tlc:** Rf = 0.2 (20% Ethyl acetate in hexane).

**Physical characteristic:** Colorless oil.
**Procedure:** In a flame dried 2-neck flask equipped with a magnetic stirrer, were added nabilone (100 mg, 0.27 mmol), N-fluoropyridinium triflate (66 mg, 0.27 mmol), and methylene chloride (3.8 mL). This solution was stirred at ambient temperature for 1 d under an argon atmosphere. The solution was diluted with methylene chloride and washed with saturated aqueous sodium bicarbonate. The aqueous phase was back extracted with methylene chloride (2 X). The combined organic extracts were dried with anhydrous magnesium sulfate, filtered, and solvent was evaporated under reduced pressure. Column chromatography on silica gel, eluting with 15% ethyl acetate in hexane, afforded 91 mg of 2-fluoronabilone, **222**, in 88% isolated yield.

**¹H-NMR** (300 MHz, CDCl₃): 0.84 (t, J = 6.9 Hz, 3H), 1.00-1.30 (m, 8H), 1.11 (s, 3H), 1.28 (s, 6H), 1.46 (s, 3H), 1.40-1.75 (m, 3H), 1.93 (td, J = 12.0, 2.7 Hz, 1H), 2.10-2.20 (m, 1H), 2.17 (t, J = 14.1 Hz, 1H), 2.43 (td, J = 12.6, 6.9 Hz, 1H), 2.60 (dm, J = 15.3 Hz, 1H), 2.90 (td, J = 12.3, 3.6 Hz, 1H), 3.86 (dq, J = 15.3, 2.1 Hz, 1H), 5.49 (d, J = 8.4 Hz, exchangeable with D₂O, 1H), 6.23 (d, J = 7.2 Hz, 1H).

**¹⁹F-NMR** (283 MHz, CDCl₃): -149.6 (br s).
nOe: Neither phenolic (5.49 ppm) nor aryl (6.23 ppm) hydrogens show any nOe correlations, which is consistent with the structure shown for 222.

$^{13}$C-NMR (125 MHz, CDCl$_3$): 14.1, 18.8, 22.6, 24.9, 26.6, 27.8, 28.0, 29.9, 31.7, 34.8, 37.6 (d, $J = 3.4$ Hz), 40.8, 41.9 (d, $J = 5.2$ Hz), 45.0, 47.0, 76.5, 107.1 (d, $J = 5.2$ Hz), 109.7, 135.4 (d, $J = 12.0$ Hz), 142.6, 144.8 (d, $J = 228.7$ Hz), 148.9, 210.8.

Table 8: HMQC correlations of cannabinoid 222

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Table 8: (Continued) HMQC correlations of cannabinoid 222

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<tr>
<td>C1'''</td>
<td>28.0</td>
<td>1.28</td>
</tr>
</tbody>
</table>
### Table 9: HMBC correlations of cannabinoid 222

<table>
<thead>
<tr>
<th>Position of Hydrogen</th>
<th>$^1$H-NMR (δ)</th>
<th>Correlation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C4</td>
<td>6.24</td>
<td>C2, C4a, C10b, C1'</td>
</tr>
<tr>
<td>C11</td>
<td>1.11</td>
<td>C6, C6a, C12</td>
</tr>
<tr>
<td>C12</td>
<td>1.46</td>
<td>C6, C6a, C11</td>
</tr>
<tr>
<td>C6a</td>
<td>1.93</td>
<td>C6</td>
</tr>
<tr>
<td>C7</td>
<td>1.50</td>
<td>C6a, C8, C10a</td>
</tr>
<tr>
<td>C7</td>
<td>2.17</td>
<td>C6a, C8, C10a</td>
</tr>
<tr>
<td>C8</td>
<td>2.43</td>
<td>C6a, C7, C9</td>
</tr>
<tr>
<td>C8</td>
<td>2.60</td>
<td>C6a, C7, C9</td>
</tr>
<tr>
<td>C10</td>
<td>2.20</td>
<td>C6a, C9, C10a, C10b</td>
</tr>
<tr>
<td>C10a</td>
<td>3.86</td>
<td>C6a, C9, C10a</td>
</tr>
<tr>
<td>C10a</td>
<td>2.90</td>
<td>C4a, C6a, C9, C10a, C10b</td>
</tr>
<tr>
<td>C1'' &amp; C1'''</td>
<td>1.20 &amp; 1.28</td>
<td>C1, C1', C2'</td>
</tr>
<tr>
<td>C2'</td>
<td>1.60</td>
<td>C1', C1'', C1'''</td>
</tr>
</tbody>
</table>

**IR:** 3300 (br), 2960 (s), 2930 (s), 2860 (s), 1710 (s), 1630 (s), 1580 (s), 1495 (s), 1440 (s), 1390 (s), 1380 (s), 1360 (s), 1340 (s), 1260 (s), 1245 (s), 1205 (s), 1190 (s), 1150 (s), 1120 (s), 1100 (s), 1070 (s), 1020 (s), 1005 (s), 970 (s), 940 (s), 880 (m), 850 (m), 810 (m), 770 (m).

**HRMS:** Calcd. for C$_2$H$_{35}$O$_3$F (M$^+$) 390.2570, found 390.2574.

Optical rotation: \([\alpha]^{21}_D = -53.3 \) (c = 1, CHCl₃).

tlc: Rf = 0.2 (20% Ethyl acetate in hexane).

Physical characteristic: Light, yellowish oil.
Procedure: In a dry sealed tube, were added nabilone, 175, (26 mg, 70 µmol), N-fluoropyridinium triflate (70 mg, 0.28 mmol), and methylene chloride (3.0 mL). The tube was then filled with argon, sealed, and heated using a sand bath (90°C). After stirring at this temperature for 1 d, the reaction was partitioned between saturated aqueous sodium bicarbonate and methylene chloride. Column chromatography on silica gel, eluting with 15% ethyl acetate in hexane, afforded an inseparable 3:1 mixture of 223 and 224 (23.0 mg, 79% yield).

$^1$H-NMR (300 MHz, CDCl$_3$): Reported for 223;

0.86 (br t, $J = 6.6$ Hz, 3H), 1.15-1.65 (m, 9H), 1.19 (s, 3H), 1.23 (s, 6H), 1.53 (s, 3H), 1.83 (br td, $J = 11.4$, 2.7 Hz, 1H), 1.93-2.13 (m, 4H), 2.33-2.45 (m, 1H), 2.53-2.65 (m, 2H), 3.64 (dm, $J = 15.0$ Hz, 1H), 5.98 (s, not exchangeable with D$_2$O, 1H). The
IH-NMR spectra of 223 and 224 are identical except for the aryl hydrogen peak which belongs to 223.

IH-NMR (300 MHz, CDCl₃): Reported for 224;
0.86 (br t, J = 6.6 Hz, 3H), 1.15-1.65 (m, 9H), 1.19 (s, 3H), 1.23 (s, 6H), 1.53 (s, 3H),
1.83 (br td, J = 11.4, 2.7 Hz, 1H), 1.93-2.13 (m, 4H), 2.33-2.45 (m, 1H), 2.53-2.65 (m, 2H), 3.64 (dm, J = 15.0 Hz, 1H). The IH-NMR spectrum of 223 and 224 are identical except for the aryl hydrogen peak which belongs to 223.

19F-NMR (283 MHz, CDCl₃): Reported for 223;
-108.3 (d, J = 335.7 Hz, 1F), -100.8 (d, J = 335.7 Hz, 1F).

19F-NMR (283 MHz, CDCl₃): Reported for 224;
-118.2 (t, J = 16.2 Hz, 1F), -102.7 (dd, J = 336.4, 13.0 Hz, 1H), -97.4 (dd, J = 336.3, 12.3 Hz, 1F).

13C-NMR (125 MHz, CDCl₃): Reported for the mixture 223 and 224;
14.0, 19.8, 19.9, 22.6, 24.6, 25.0, 26.1, 26.2, 27.1, 27.2, 27.6, 27.7, 27.72, 27.8, 29.7,
29.8, 31.7, 32.2, 39.4, 40.4, 40.5, 42.1, 42.6, 43.7, 43.9, 45.6, 45.8, 82.2, 82.3, 106.5 (t, J = 245.8 Hz), 106.9, 108.0, 124.8 (t, J = 8.3 Hz), 185.4 (t, J = 24.8 Hz), 208.1, 208.7.

IR: Reported for the mixture 223 and 224;
2980 (s), 2940 (s), 2870 (s), 1740 (s), 1680 (s), 1600 (s), 1465 (m), 1395 (s), 1320 (m),
1280 (m), 1250 (w), 1210 (m), 1185 (s), 1130 (s), 1105 (m), 1045 (s), 965 (m), 930 (s),
865 (w), 780 (w).
**HRMS:** Reported for 223;
Calcd. for C_{24}H_{34}O_{3}F_{2} (M^+) 408.2476, found 408.2472.

**HRMS:** Reported for 224;
Calcd. for C_{24}H_{33}O_{3}F_{3} (M^+) 426.2382, found 426.2398.

**Mass spectrum m/e:** Reported for the mixture 223 and 224;
426 (M^+, for 224), 408 (M^+, for 223), 390, 375, 341, 323, 305, 237, 195, 167, 137, 111, 83, 69.

tlc: Rf = 0.15 (20% Ethyl acetate in hexane).

**Physical characteristic:** Yellowish oil.
NOTES


35, 2231. (b) Lipshutz, B. H.; Reuter, D. C. Tetrahedron Lett. 1989, 30,
Commun. 1989, 19, 285. (d) Zhang, H. X.; Gube, F.; Balavoine, G.
Chem. 1986, 51, 3561.
1973, 596.
15. (a) Adam, M. J.; Ruth, T. J.; Jivan, S.; Pate, B. D. J. Fluorine Chem.
1984, 25, 329. (b) Adam, M. J.; Berry, J. M.; Hall, L. D.; Pate, B. D.; Ruth,
17. (a) Tius, M. A.; Kawakami, J. K. SYNLETT 1993, 207. (b) Tius, M. A.;


(b) Gillespie, R. J.; Schrobilgen, G. J. *Inorg. Chem. 1974*, 13, 765. (c)


66. Jakob Busch-Petersen, research assistant of Professor M. A. Tius.
REFERENCES


Clark, J. H.; Cork, D. G.; Robertson, M. S. Chemistry Lett. 1983, 1145.


Hodson, H. F.; Madge, D. J.; Widdowson, D. A. *SYNLETT* 1992, 831.


Lothian, A. P.; Ramsden, C. A. *SYNLETT*, 1993, 753.


Matthews, D. P.; Miller, S. C.; Jarvi, E. T.; Sabol, J. S.; McCarthy, J. R.


Moissan, H. *Compt. Rend.* 1890, 110, 276.


1980, 63, 1.
Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K.-S.; Faron, K. L.;