SYNTHESIS AND REARRANGEMENTS OF VINYLCYCLOPROPANES IN A [2+3] CYCLOPENTENE AND OXYCYCLOPENTENE ANNULATION METHODOLOGY. APPROACH TO (-)-SPECIONIN

by

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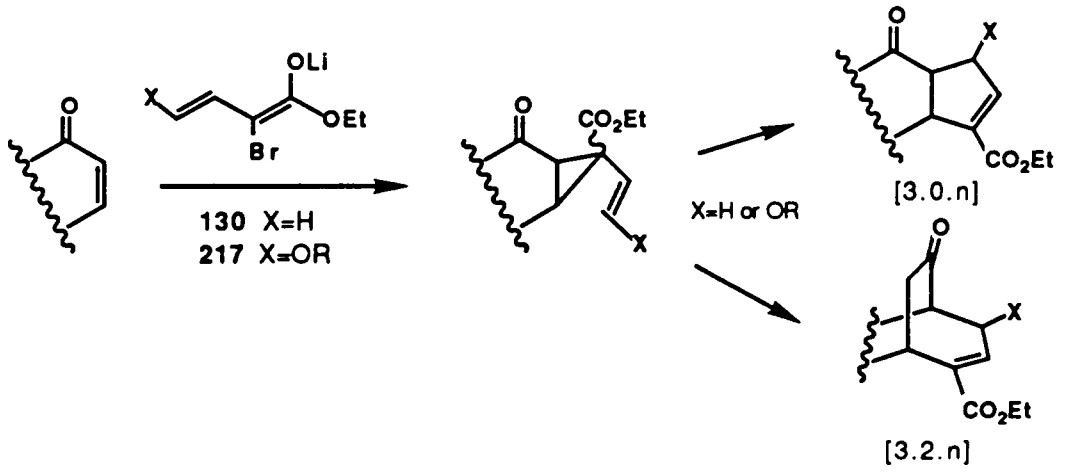
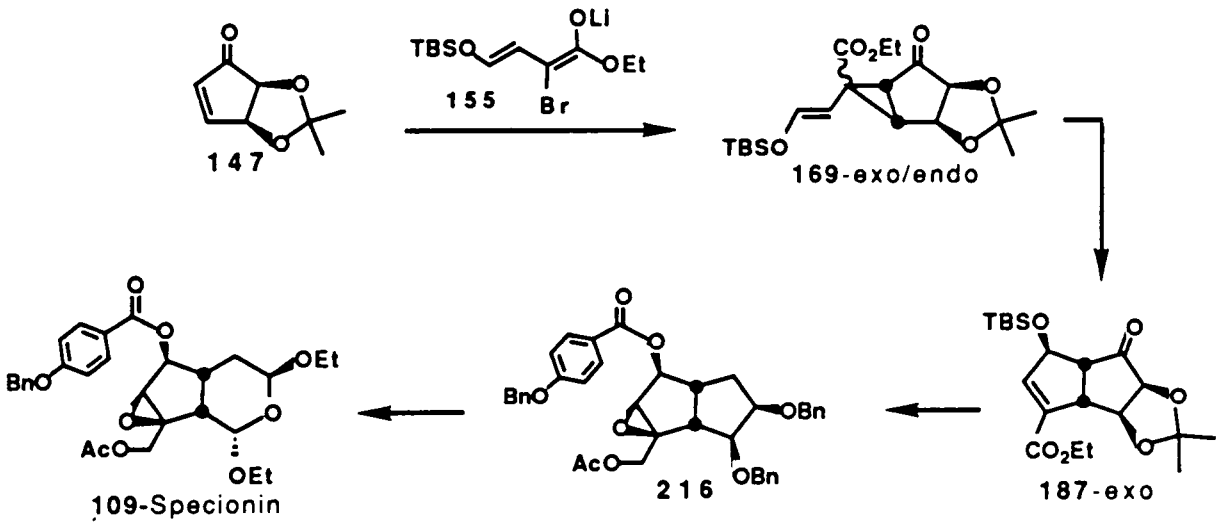
(ABSTRACT)

The addition of lithium dienolate **130**, formed from ethyl 2-bromocrotonate, to enones and aldehydes yielding vinylcyclopropanes and vinyloxiranes was optimized. Various methods, pyrolytic and nonpyrolytic, were examined for the rearrangement of the resulting vinylcyclopropanes to cyclopentenes in an overall [2+3] annulation sequence. During the course of these studies, a new rearrangement pathway of these vinylcyclopropanes to bridged [3.2.n] bicyclic systems was discovered thus establishing a new [3+4] annulation technology.

The extension of the [2+3] annulation technology to oxygenated cyclopentanoids was addressed. Several ethyl 2-bromo-4-oxycrotonates were synthesized, and the reaction of their lithium dienolates (**217**) with enones was investigated. The rearrangement of the resulting enol ether terminated vinylcyclopropanes to oxygenated cyclopentenes was also examined.



The application of this methodology was expressed in a synthetic approach to (-)-specionin (**109**). The key steps in this synthesis involved the cyclopropanation of optically pure enone **147** with lithium dienolate **155** to give vinylcyclopropanes **169**-exo/endo and the rearrangement of **169** to the oxygenated cyclopentanoid **187**-exo which possesses the correct stereochemistry for further elaboration to epoxy acetate **216**, an intermediate in a reported synthesis of specionin.



To my family

ACKNOWLEDGEMENTS

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I will always feel a very special gratitude to and . Although I left the chemistry department at Indiana University, from them I learned much about organic synthesis. My most special words of thanks are reserved for

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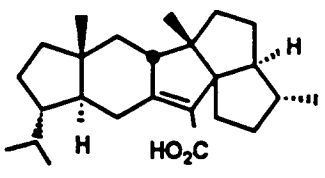
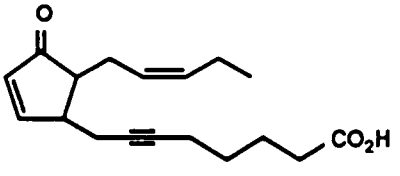
I. INTRODUCTION

During the last two decades, vinylcyclopropanes have been rising in importance as synthetic intermediates.[1a-d] The relief of the strain in the cyclopropyl ring provides a large driving force for ring cleavage making vinylcyclopropanes highly reactive molecules. Once the various modes of ring cleavage were better understood, regiocontrol was possible, and the use of vinylcyclopropanes in natural product synthesis increased. (For a comprehensive list of vinylcyclopropanes used as intermediates in natural product synthesis see Table 1, p. 24.) It is well-known that vinylcyclopropanes can be isomerized to cyclopentenes.[1d] Since many natural products contain five-membered

rings in their skeletons, this rearrangement has been widely exploited in synthesis. Compounds containing five-membered ring residues can be very diverse in their structures; they can have mono-, bi-, or tricyclic ring systems, all with a variety of substitution patterns. The importance of vinylcyclopropanes as synthetic intermediates can be seen from the fact that the same vinylcyclopropane/cyclopentene rearrangement has been applied to the synthesis of a variety of natural products ranging from the linear[2] and nonlinear[3] triquinanes to prostaglandin,[4] gibberellin,[5] and iridoid[6] terpenes. (For some recent examples see compounds **1**-**4**).



1 Retigeranic Acid



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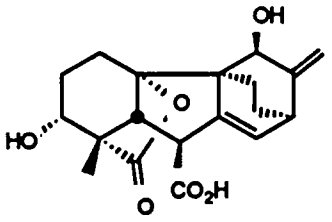
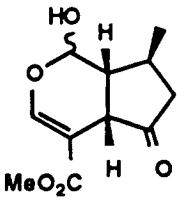
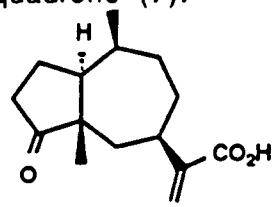


3 Antheridiogen-An

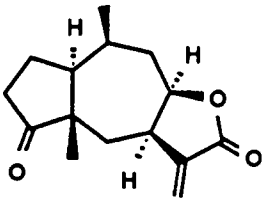


4 Verbenalol

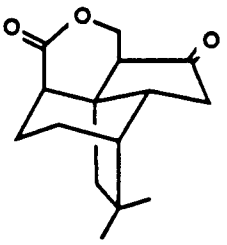
Although the vinylcyclopropane/cyclopentene isomerization may be the most commonly used vinylcyclopropane rearrangement in synthesis, it is not the only one. The [3,3] sigmatropic (or Cope) rearrangement of divinylcyclopropanes to form cycloheptadienes has also received much attention.[1a,10] Examples of this rearrangement can be seen in the syntheses of (±)-damsinic acid (**5**),[11] (±)-confertin (**6**),[11] and (±)-quadrone (**7**).[12]



5 Damsinic Acid



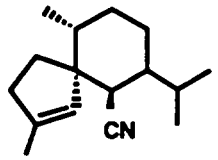
6 Confertin



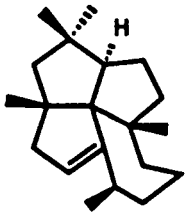
7 Quadrone

Other reactions of vinylcyclopropanes have also found application in natural product synthesis. Reductive cleavage of the cyclopropane ring in the vinylcyclopropane moiety has been used to obtain the spiro-ring system found in (-)-axisonitrile (**8**)[7] and the skeleton of (±)-laurenene (**9**),[8] while the acid-catalyzed ring opening of

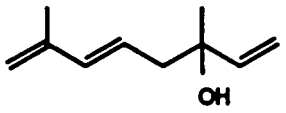
vinylcyclopropanes was used to obtain the substituted dienes found in (±)-hotrienol (**10**)[9] and (±)-santolina alcohol (**11**).[9]



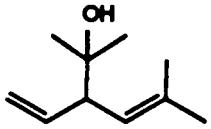
8 Axisonitrile-3



9 Laurenene

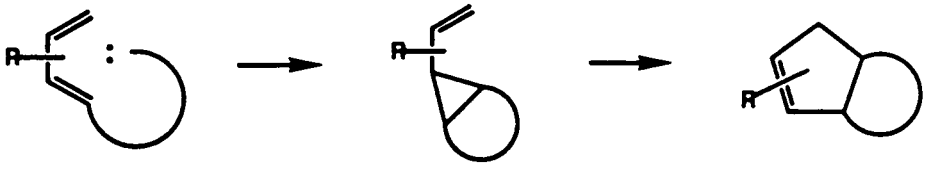


10 Hotrienol

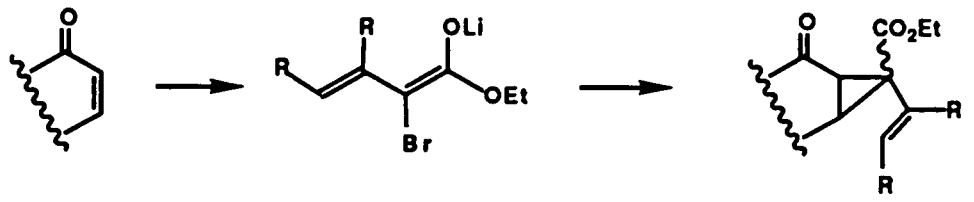


11 Santolina Alcohol

The Hudlicky group has long been interested in developing methodologies for polyquinane synthesis.[1c,d] One of their first approaches was the [4+1] annulation methodology which was successfully used for the synthesis of both linear[2] and nonlinear[3] triquinanes. This annulation is based on the carbenoid intermediate, generated upon thermolysis of a diazoketone, interacting with a dienic system. The resulting vinylcyclopropane is then rearranged to the corresponding cyclopentene.



This methodology was applied to synthesis of retigeranic acid (**1**), but was inefficient because of its linear nature.[3a] It then became apparent that a complementary, convergent methodology was needed. This led to the initial investigations of the [2+3] annulation methodology[13] where the intermediate vinylcyclopropane is formed from the reaction of α-bromodienolates with enones. This approach was amenable to the



synthesis of **1** resulting in the shortest synthesis of (-)-retigeranic acid to-date.[3a,b]

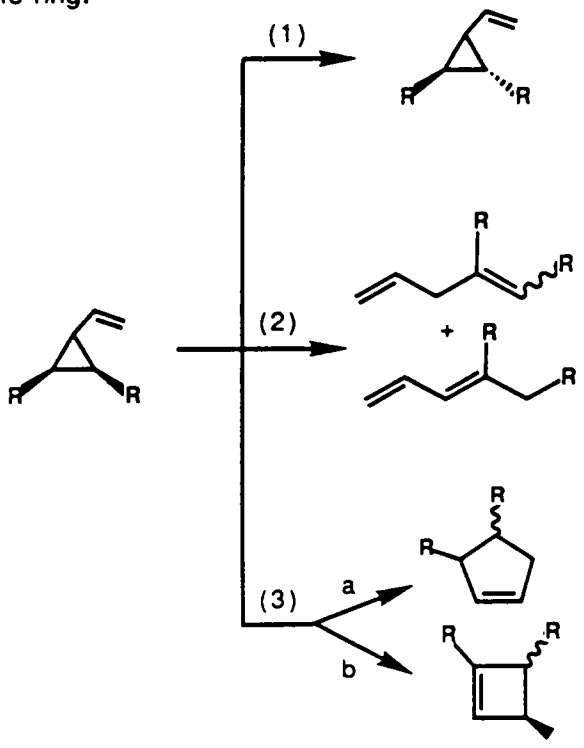
To further improve the [2+3] annulation methodology, several aspects remained to be studied: (1) improving the formation and reactions of the α-bromodienolates, (2) increasing the substitution on the dienolate and enone moieties, and (3) exploring alternative conditions and pathways for the rearrangement of the intermediate vinylcyclopropanes. The results of these studies and their application towards an approach to (-)-specionin (**109**) will be discussed. In the next section, a review of methods for both the syntheses and rearrangements of vinylcyclopropanes along with a brief history of specionin will be presented.

II. HISTORICAL

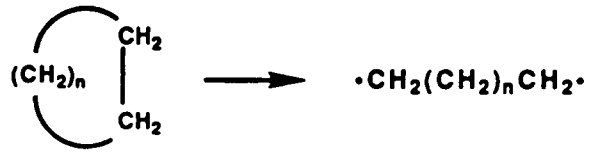
1. Rearrangements of Vinylcyclopropanes

1.1 Introduction

Because of the strain energy of the cyclopropane ring, vinylcyclopropanes have been highly useful as synthetic intermediates. They present a challenge to the synthetic chemist both in their synthesis and in controlling their rearrangement pathways. Vinylcyclopropanes undergo a great variety of ring-opening reactions depending upon the applied conditions (e.g., heat, light) or chemical reagents (e.g., electrophiles, nucleophiles, radicals).[1,10] They typically undergo three fundamental types of bond reorganizations: (1) cis-trans isomerization, (2) ring-opening to pentadienes, and (3) ring enlargement to either (a) cyclopentenes or (b) methyl cyclobutanones if an oxygen is pendant to the ring.



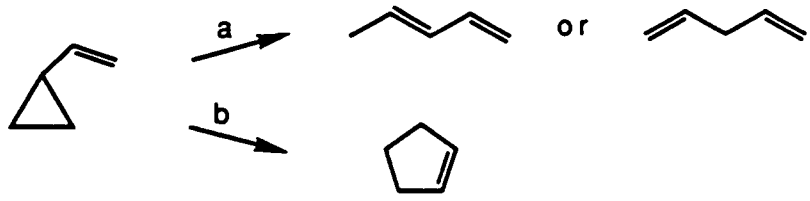
The reactivity of vinylcyclopropanes is not solely due to the angular and torsional strain of the cyclopropane ring. The strain energies of the cyclopropane and cyclobutane rings are very similar[14] (27.5 and 26.5 kcal/mol respectively) as well as the energy required for homolytic C-C cleavage of both rings (61 kcal/mol for n=1[15] and 62.5



kcal/mol for n=2[16]), yet cyclopropanes exhibit much higher reactivity. Several theories on the bonding of the cyclopropane ring have been advanced to explain the anomalous behavior of the cyclopropanes vs. cyclobutanes.[17-21] When trying to understand the reactivity of vinylcyclopropanes, it is helpful to remember that the reactivity of a cyclopropanes is similar to that of an olefin.[22] The ensuing discussion will highlight various vinylcyclopropane rearrangements classified by the conditions or reagents used to promote them.

1.2 Thermal Rearrangements of Vinylcyclopropanes

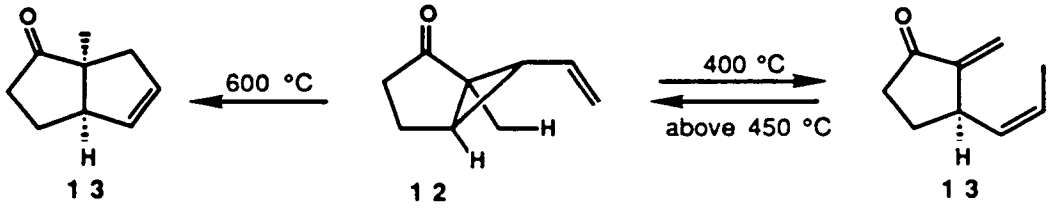
The many reviews on thermal rearrangements of vinylcyclopropanes show this mode to be the most scrutinized of all vinylcyclopropane rearrangements.[1,10b] During thermolysis two rearrangement pathways are possible (a) ring cleavage to dienes and



Scheme 1

(b) rearrangement to cyclopentenes. Some control over the thermolysis products is possible and will be discussed below.

[1,5]-Shift Pathway. When the vinylcyclopropane possesses a substituent in the 2-position with a hydrogen cis to the vinyl group, a concerted, suprafacial [1,5]-sigmatropic shift of hydrogen (or retro-ene reaction) can occur.[23,24] The concerted nature of the reaction results in the stereospecific formation of cis olefins. It is reversible[25] and has a lower Ea[23c,d,e] than radical cleavage of the cyclopropane ring (15-20 kcal/mol lower). This means that if both the [1,5]-shift of hydrogen and diradical cleavage of the cyclopropane ring (paths a and b, Scheme 1) are possible, then at lower temperature the [1,5] shift (path a, Scheme 1) will predominate.[25]

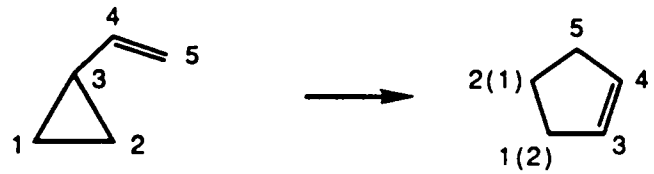


1 3 1 2 1 3

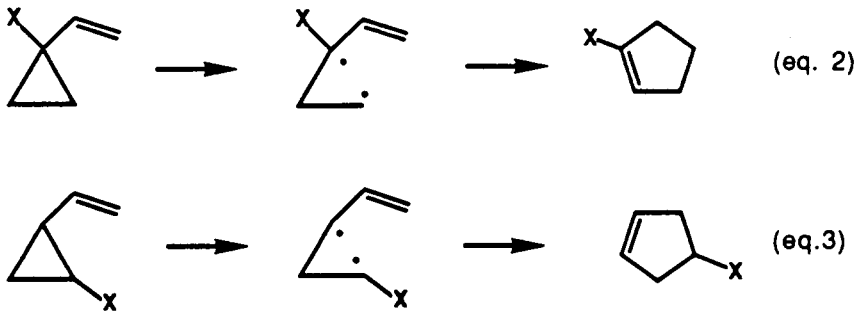
Vinylcyclopropane/Cyclopentene Rearrangement. Vinylcyclopropanes can also rearrange to cyclopentenes (path b, Scheme 1) upon thermolysis, however since radical

cleavage of the cyclopropane ring has the larger Ea (vide supra), higher reaction temperatures are needed than for the [1,5]-shift. There is still much debate over the mechanism of this reaction: it could proceed either through (1) radical cleavage of the cyclopropane ring, followed by isomerization of the allylic radical and ring closure to the cyclopentene, or (2) a concerted [1,3]-sigmatropic shift of carbon.[1,10b] Most evidence supports a biradical intermediate, but a concerted mechanism cannot be ruled out. If a biradical mechanism is correct, then cyclization of the biradical must be much faster than conformational interconversion in order to explain the formation of optically activity cyclopentenes from the pyrolysis of enantiomerically pure vinylcyclopropanes. In the most recent mechanistic study, Gajewski suggests that the mechanism may be highly dependent on the substitution of the vinylcyclopropane.[26] The substituents on the vinylcyclopropane can cause large steric interactions which make the transition state required for a concerted process too high in energy resulting in the radical mechanism being the lower energy pathway.

The substituents of the vinylcyclopropane also have a pronounced effect on the rate of formation and regiochemistry of the cyclopentene. In an unsubstituted vinylcyclopropane, the C_1-C_3 and C_2-C_3 bonds are equally activated towards cleavage.



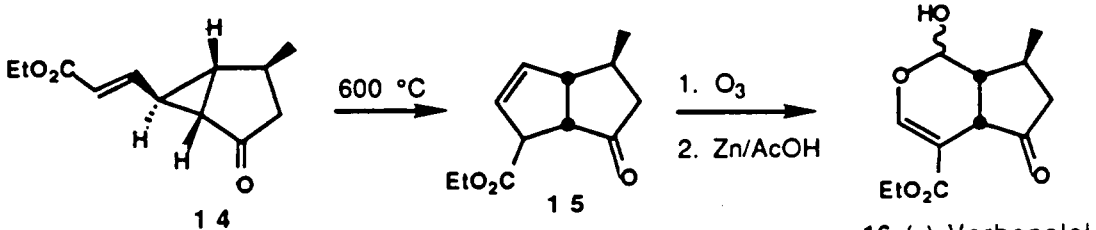
Substitution on the ring will usually render one bond more susceptible towards cleavage. Prediction of the more labile bond is based on the observation that cleavage of the cyclopropane ring always occurs regioselectively to provide the more stable diradical intermediate; one radical will always be allylic and the other would prefer be α to a hetereoatom or some other radical stabilizing group (Scheme 2). Since heteroatoms



Scheme 2

stabilize radicals, the presence of a hetereoatom (oxygen, nitrogen, sulphur, etc.) will stabilize the biradical intermediate thereby lowering the E_a of the reaction and accelerating the rearrangement to cyclopentene.[27a,c] Similarly phenyl[27a] and alkenyl[28] substituted vinylcyclopropanes rearrange to cyclopentenes much more quickly and with a lower E_a. Substitution at C_4, however, even by a radical stabilizing group, hinders cyclopentene formation by causing unfavorable steric interactions in the transition state resulting in higher E_a's for these vinylcyclopropanes.[1d]

The vinylcyclopropane/cyclopentene rearrangement has been very useful in constructing the cyclopentene rings found in many natural products. Two of the most recent applications of this rearrangement can be seen in the syntheses of (-)-verbenalol and (-)-retigeranic acid. Vinylcyclopropane **14** was thermolyzed to give diquinane **15** which was converted to verbenalol by ozonolysis of the carbon-carbon

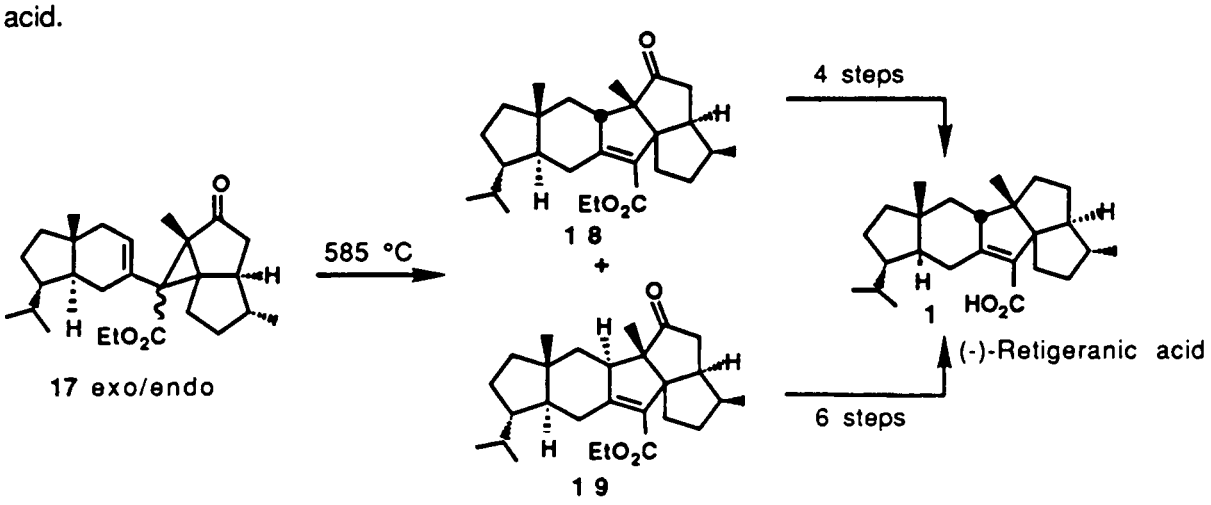


14 15 16 (-)-Verbenalol

Scheme 3

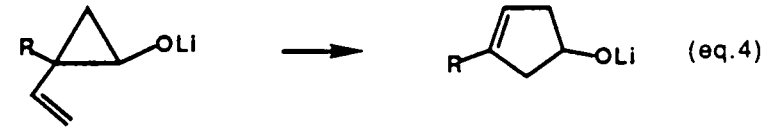
double bond.[6] Rearrangement of the highly substituted vinylcyclopropanes **17**-exo and **17**-endo was used to obtain the carbon skeleton of retigeranic acid in a very efficient

manner.[3a] Both of the pyrolysis products **18** and **19** were converted to retigeranic acid.



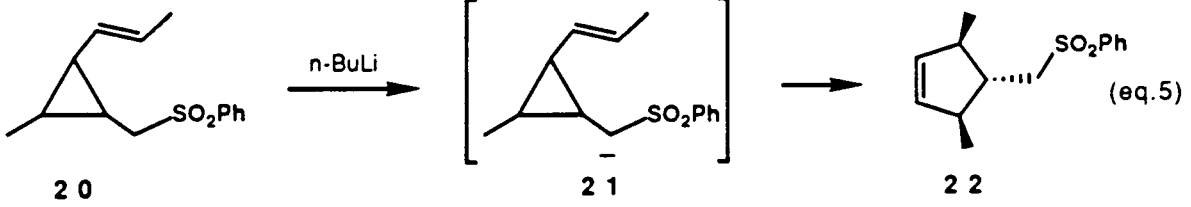
Scheme 4

Charge Accelerated Rearrangements. The vinylcyclopropane/cyclopentene rearrangement can also be accelerated by making the vinylcyclopropane a charged species. If an auxiliary group that has an acidic hydrogen at the α position is attached to the cyclopropane, then treatment with base will produce an anion which accelerates the thermal rearrangement to cyclopentene. Thus, the lithium salts of 2-vinylcyclopro-



(eq.4)

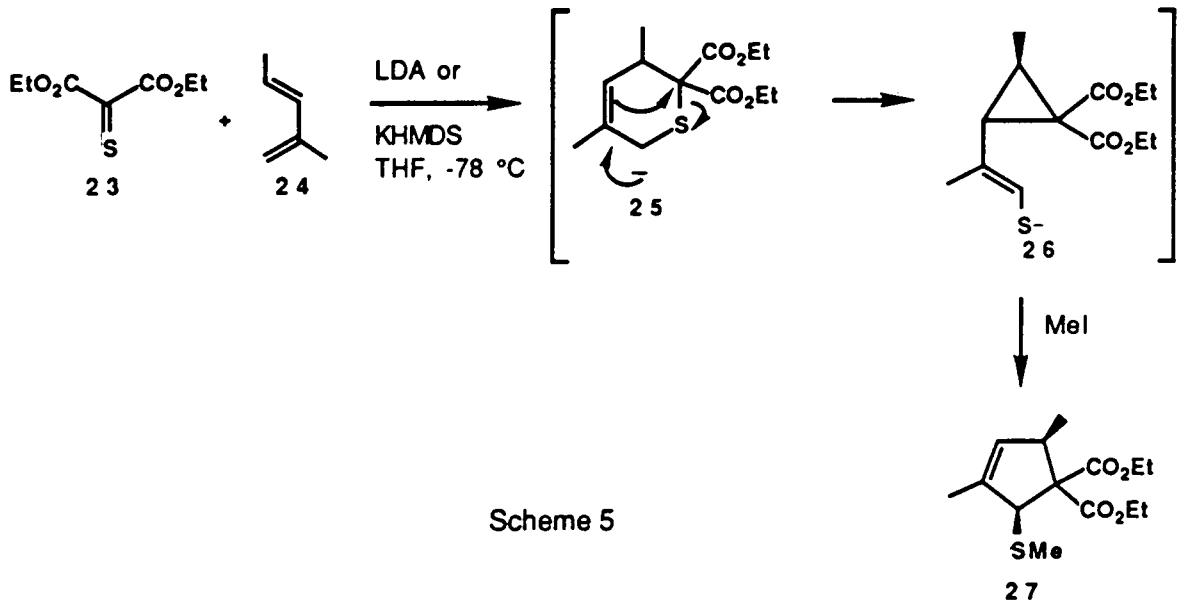
panols rearrange at 25 °C to the corresponding 3-cyclopentenols (eq. 4).[29] α-Sulphonyl carbanions also accelerate the vinylcyclopropane rearrangement with complete stereoselectivity (eq.5)[30]. Another very interesting anion accelerated



(eq.5)

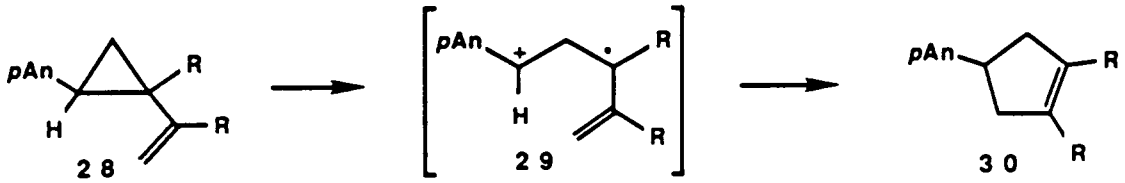
rearrangement has been used in a [4+2-1] annulation sequence (Scheme 5). The Diels-

Alder adduct **25** when treated with n-BuLi undergoes a [2,3] sigmatropic ring opening to generate a thio-enolate anion terminated vinylcyclopropane **26** which rearranges at low temperatures to the cyclopentene **27**.[31] This rearrangement is also highly stereoselective, syn substitution being favored 13:1.



Scheme 5

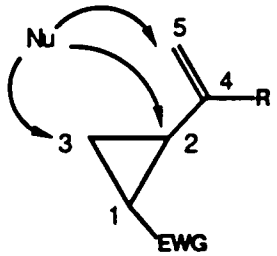
Charge acceleration of the vinylcyclopropane/cyclopentene rearrangement has also been observed by using catalytic amounts of one electron oxidants.[32] When cyclopropanes of type **28** were treated with $(p\text{-BrPh})_3N^{\bullet+}SbF_6^-$ or $O_2^{\bullet+}SbF_6^-$, they rearranged to cyclopentenes **30** in excellent yields and at least ten times faster than



under thermal conditions. It is not clear whether the mechanism is stepwise isomerization via trimethylene cation radical intermediates, such as **29**, or a concerted isomerization via odd-electron pericyclic transition states.[33]

1.3 Nucleophilic Cleavage of Vinylcyclopropanes

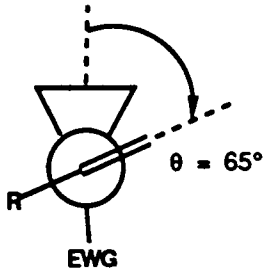
The presence of an electron withdrawing group on the cyclopropane ring of a vinylcyclopropane activates the ring towards nucleophilic attack. The vinylcyclopropane is an ambident electrophile with several possible sites for nucleophilic attack. The nucleophile can add at C_5 in a 1,5- (S_N2') fashion or at C_2 or C_3 in a 1,2-(S_N2) manner. The exact mode of opening depends on the conformation of



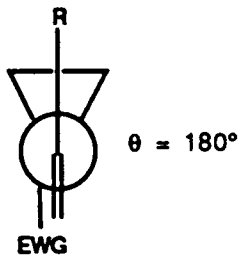
3 1

EWG = COR, CO_2R, etc.

the cyclopropane ring with the vinyl group. The vinyl group must be in a conformation that has good orbital overlap with the cyclopropane ring for it to be susceptible towards nucleophilic attack.[34] Of the two conformations, **32b** has maximum orbital overlap between the cyclopropyl ring and vinyl group, while **32a** has almost none. In rigid or

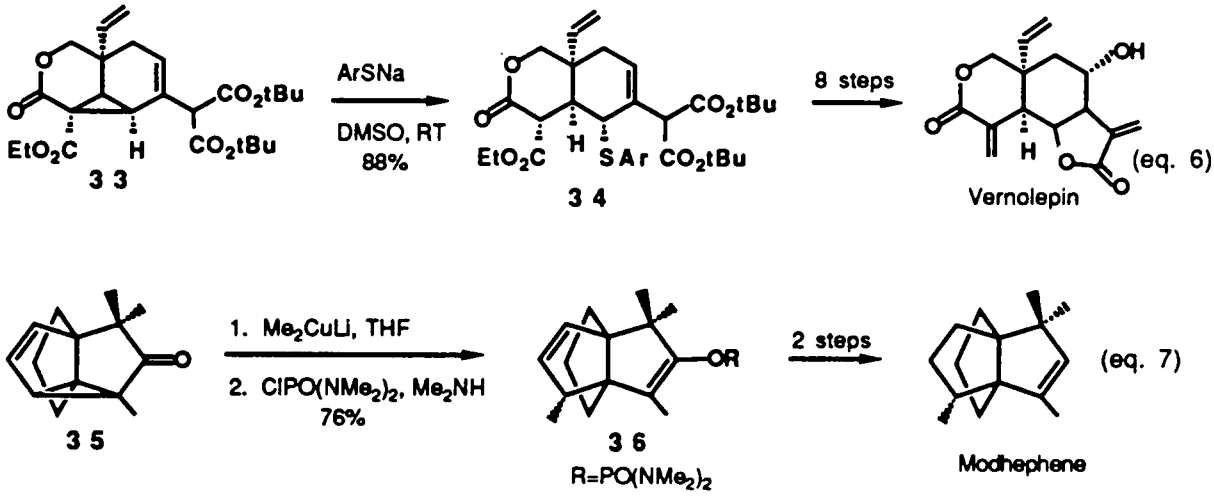


32a Synclinal (gauche)



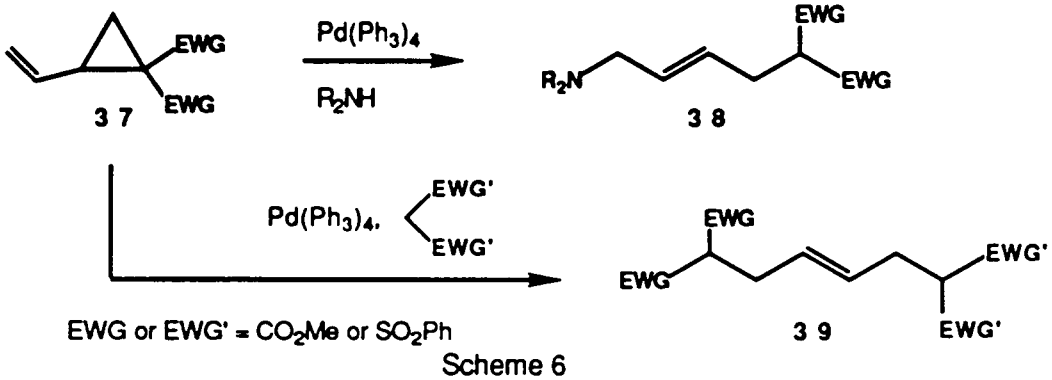
32b Antiperiplanar

cyclic structures however, this conformation can be strongly disfavored so that nucleophilic cleavage of the cyclopropane ring occurs without participation of the vinyl group as seen in eqs. 6[35] and 7[36]. Compound **34** was an intermediate in a synthesis of vernolepin, while the tricyclic compound **36** was converted to modhephene. In cases



where the double bond is in a less rigid system, the mode of nucleophilic cleavage is highly dependent on the nucleophile and reaction conditions.[37] The regioselectivity of cleavage of vinylcyclopropanes of type **31** has been studied in detail. Nucleophilic openings normally proceeded either exclusively (amines, RS^- in EtOH) or predominantly (malonate ion or RS^- in DMF) at C_2. Cuprates add in a conjugate or a 1,5-sense but these additions may involve radical intermediates which are known to add in a 1,5-manner.[38]

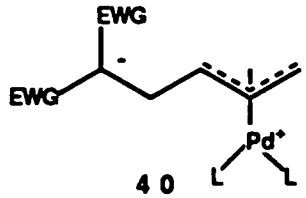
Other studies of similarly substituted vinylcyclopropanes have shown that it is possible to elicit nucleophilic attack at the vinyl group (1,5-sense) by using a palladium or nickel catalyst (Scheme 6). Secondary amines reacted with vinylcyclo-



Scheme 6

propanes of type **37** in good yields (50-98%) and with greater than 96%

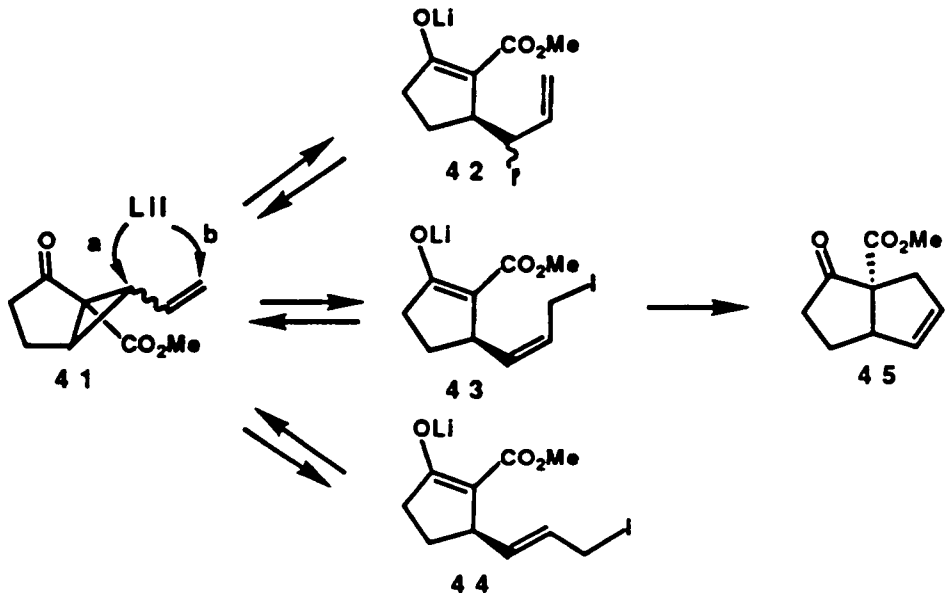
regiocontrol.[39] A latter report also used a palladium catalyst to control the mode of nucleophilic cleavage of **37**.[40] Finding that no base was necessary to generate the nucleophilic anion, led to the proposal of an intermediate such as **40** that would be



40

capable of deprotonating an active methylene compound. This reaction exhibits excellent regio- and stereoselectivity with the alkylation always occurring syn to the cyclopropane bond being cleaved in [n.1.0] bicyclic systems (n=3 or 4).

Nucleophilic opening of vinylcyclopropane **41** (also a vinylcyclopropane with two electron withdrawing groups) with LiI led to diquinane **45** directly.[41] This rearrangement was explained by the mechanism in Scheme 7. LiI can open the vinylcyclopropane by route a or b. Intermediate **42** can only revert to the starting

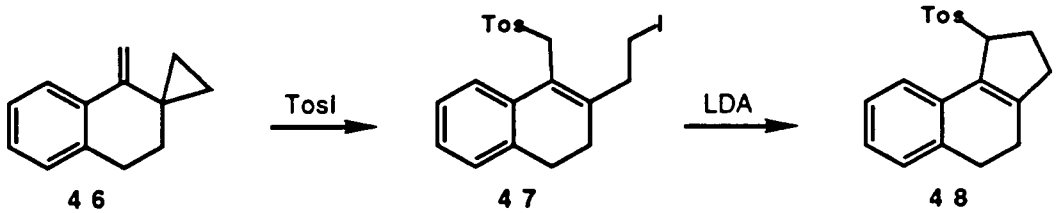


Scheme 7

vinylcyclopropane **41** because the 5-endo-trigonal process necessary for diquinane

formation is disfavored. Likewise, intermediate **44** can only recycle to vinylcyclopropane **41**, whereas only intermediate **43** can close to diquinane **45**. The only irreversible step is formation of the diquinane, so eventually all of the starting vinylcyclopropane is converted to diquinane **45**. This mild vinylcyclopropane/cyclopentene rearrangement has recently been applied to a synthesis of (±)-isocarbaryclin.[42]

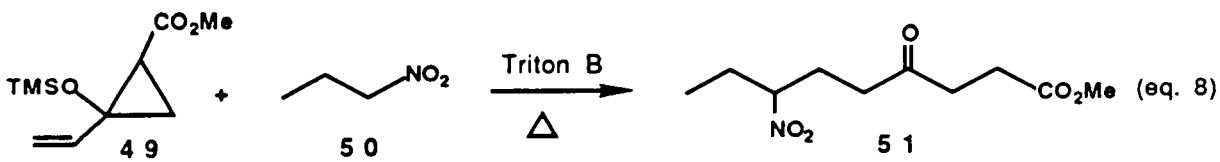
A similar opening has been observed using tosyl iodide.[43] In this case, a base, such as LDA (lithium diisopropylamide), was needed to promote closure of the intermediate iodides to cyclopentenes (Scheme 8). From mechanistic investigations, it



46 **47** **48**

Scheme 8

appears that the reaction may be proceeding through both radical and ionic intermediates. In the case of ionic intermediates, nucleophilic opening by the sulphonate anion is probably preceded by activation of the cyclopropane ring with I^+. Vinylcyclopropane **49** also underwent nucleophilic attack in a conjugate sense with α nitro carbanions. [44] The reaction of **50** with vinylcyclopropanes is a facile way to obtain highly functionalized carbon skeletons such as **51** which could be used as building

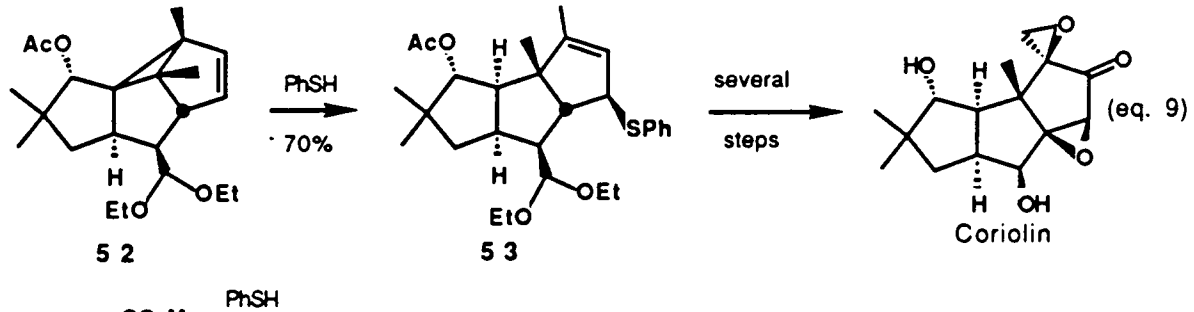


49 **50** **51** (eq. 8)

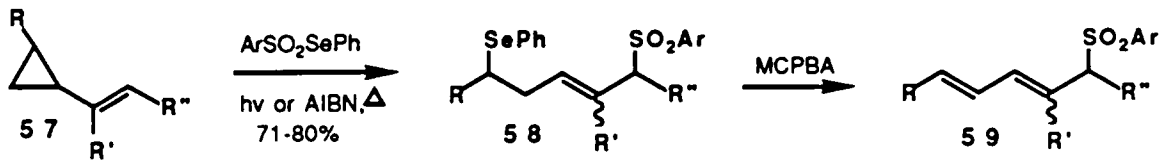
blocks for the synthesis of many different compounds. More detailed discussions of the interaction of vinylcyclopropanes with nucleophiles can be found in several recent reviews.[1a,b,10b,45]

1.4 Radical Cleavage of Vinylcyclopropanes

Radical openings of vinylcyclopropanes normally occur in a 1,5- or conjugate fashion, as was previously alluded to. Selenium, sulphur, and tin radicals have been extensively used for these types of openings, all of which proceed with attack of the radical on the terminal carbon of the vinyl group (eqs. 9[46] and 10[47]). The ring opened compound served as an intermediate in a formal synthesis of coriolin. These types of reactions have been recently reviewed.[1a,b,10b]



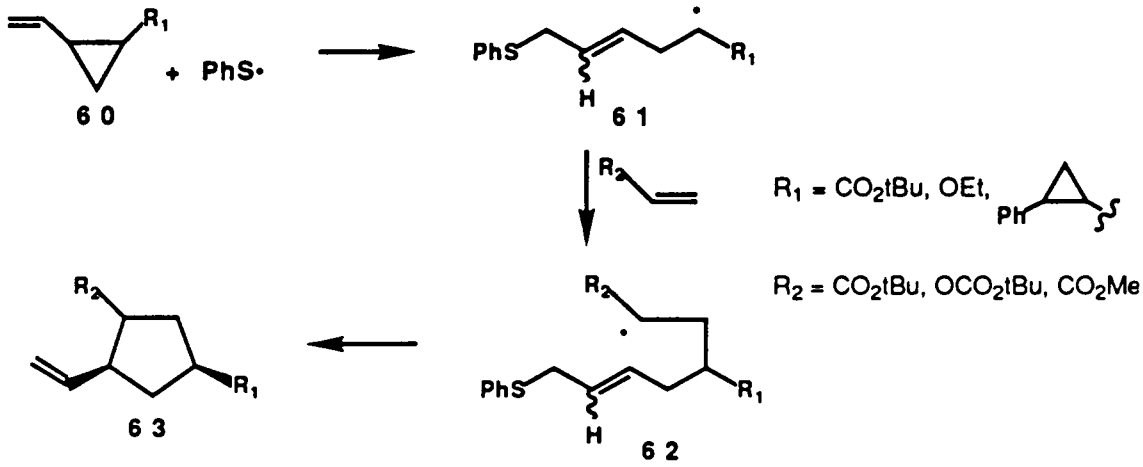
Some recent examples of radical induced cleavage of vinylcyclopropanes include the free-radical selenosulphonation of vinylcyclopropanes **57** to afford mostly 1,5-adducts.



Scheme 9

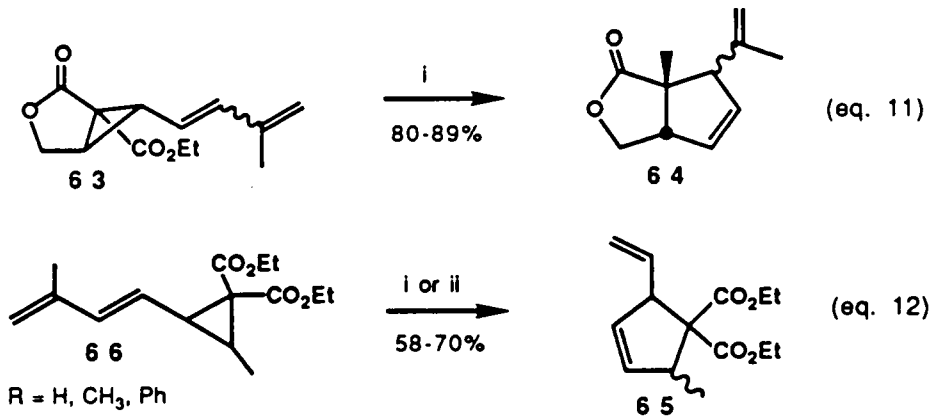
The selenoxide elimination of these products led to synthetically useful unsaturated sulphones[48] (Scheme 9). A new cyclopentene synthesis from vinylcyclopropanes uses the thiophenol radical to open a substituted vinylcyclopropane (Scheme 10). The resulting radical intermediate is then trapped with an olefin to yield cyclopentanes with

good regio- and stereoselectivity (~3:1 preference for cis substitution was observed).[49]



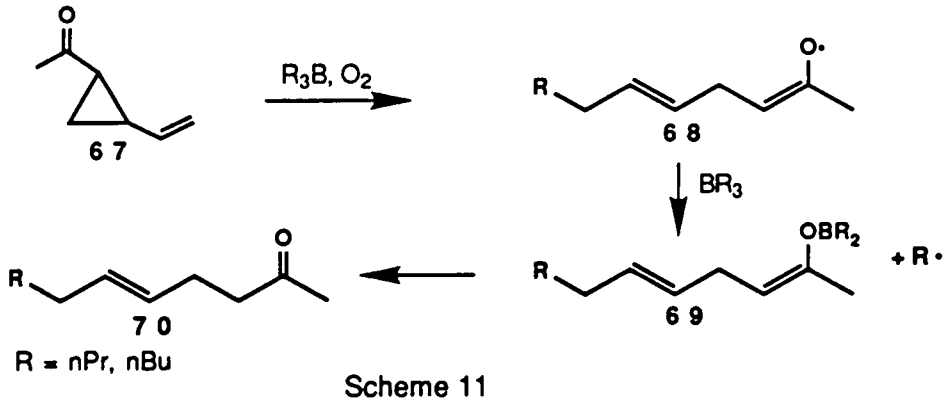
Scheme 10

Ring opening of dienylcyclopropanes with tin or sulphur radicals led directly to cyclopentenes. Unfortunately, the stereoselectivity of the ring closures was not very good (eqs. 11 & 12).[50] Finally an interesting 1,5-radical opening of vinylcyclopropyl



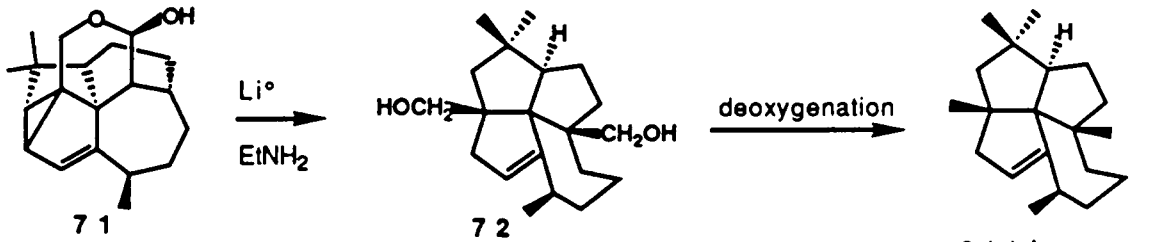
i. Ph_3SnH or PhSH, AIBN, 80 °C; ii. Ph_3GeH or nBu_3SnH, AIBN, 80 °C

ketones by alkyl boranes has been used as a route to γ–δ unsaturated ketones (Scheme 11).[51]



Scheme 11

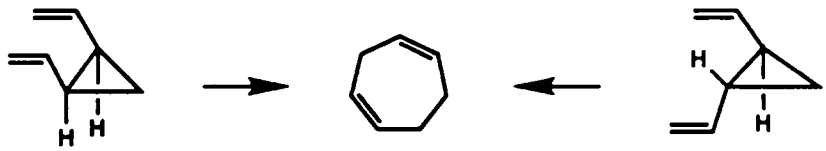
Radical cleavage of cyclopropane rings has also found use in natural product synthesis. One of the most recent applications is in a synthesis of (±)-laurenene.[52] Treatment of vinylcyclopropane **71** with Li/$EtNH_2$ gave **72** which upon deoxygenation yielded laurenene (Scheme 12).



Scheme 12

1.5 Cope Rearrangement of Divinylcyclopropanes

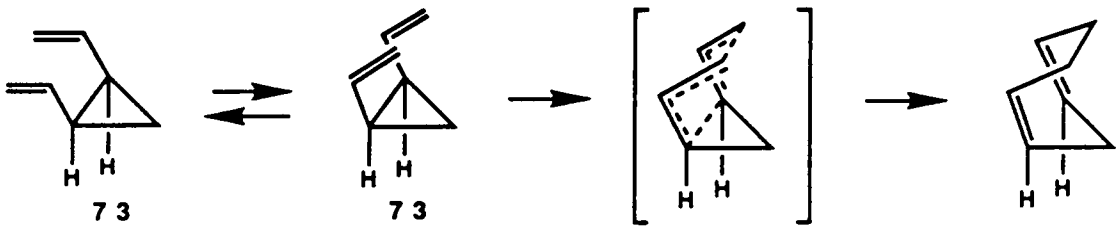
It was not until 1960 that the Cope ($\sigma^2s + \pi^2s + \pi^2s$) rearrangement of a *cis*-1,2-divinylcycloalkanes to 1,4-cycloheptadienes was investigated. Vogel examined the rearrangement of both cis- and trans-1,2-divinylcycloalkanes.[53] He found that *cis*-1,2-divinylcyclopropane (**73**) spontaneously undergoes Cope rearrangement, while the trans isomer **74** requires heating to 190 °C. In fact the Cope rearrangement of **73** is so facile that it was some time before the cis isomer could be isolated and shown to have a



73 (cis) **74** (trans)

half-life of 90 s at 35 °C and 25 min at 11 °C.[54,55] Since both isomers, cis and trans, divinylcyclopropanes will rearrange to cycloheptadienes, the divinylcyclopropanes need not be prepared stereochemically pure, which largely increases the synthetic utility of this reaction as evidenced by the large number of mono-, bi-, and tricyclic substances prepared via Cope rearrangement of a divinylcyclopropane.[10a,56]

It is widely accepted that the thermal rearrangement of a *cis*-1,2-divinylcyclopropane proceeds in a concerted manner through a boat-like transition state with the vinyl groups lying over the cyclopropane ring.[23c,57] The boat transition state leads to the

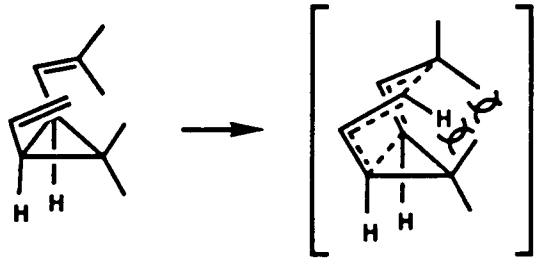


7 3 **7 3**

1,4-cycloheptadiene with both double bonds cis. A chair transition state would lead to a highly strained cycloheptadiene with both double bonds trans. In the rearrangement of trans-1,2-divinylcyclopropanes to 1,4-cycloheptadienes, thermal isomerization to the

cis-divinylcyclopropane most likely occurs first followed by Cope rearrangement of the resulting *cis*-divinylcyclopropane. The E_a for the rearrangement of **74** to 1,4-cycloheptadiene is 32.1-34.1 kcal/mol.[57,58] Comparatively, the E_a for conversion of **73** to 1,4-cycloheptadiene is only 19-20 kcal/mol.[54,59] This suggests that the rate-determining-step for the above transformation is the isomerization of **74** to **73**. Because of the facts listed above, it is generally true that for a pair of isomers, trans to cis isomerization is slower than Cope rearrangement.

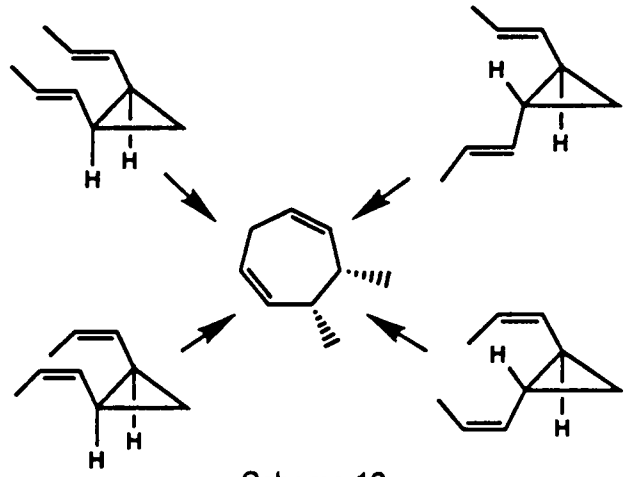
The Cope rearrangement is compatible with highly substituted compounds. Substitution only becomes a problem when large groups are placed on the terminal carbons of the vinyl groups. If substituents on the vinyl groups are placed cis to the cyclopropyl ring, then the Cope rearrangement may be precluded. The necessary conformation of the transition state can become too high in energy because of the large steric interactions between the vinyl substituents and the cyclopropane ring.[59,60] In



such an instance cis-trans isomerization will be much faster than Cope rearrangement. When the geometry of the double bonds is trans, the Cope rearrangement will proceed normally.

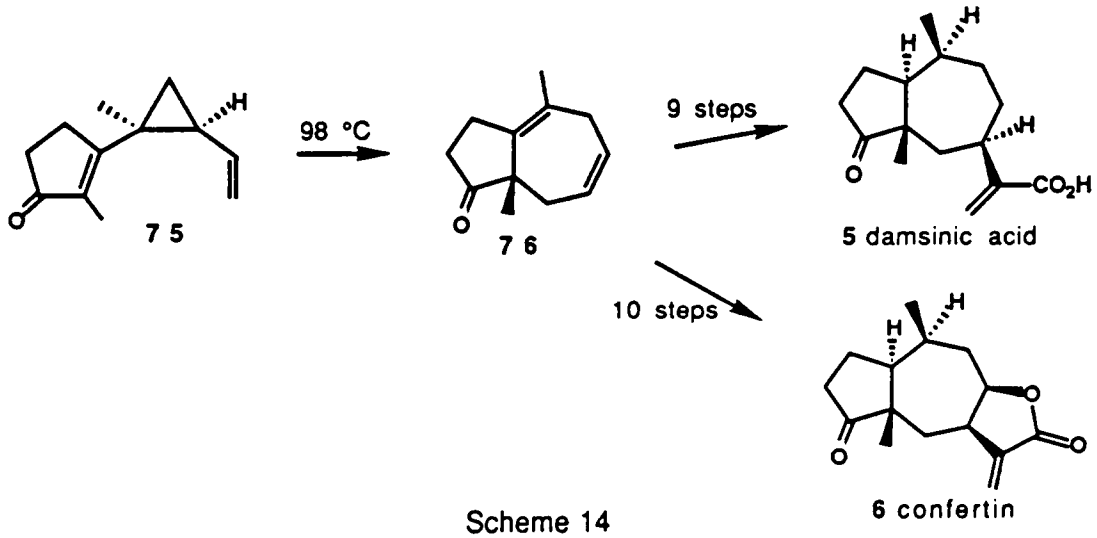
Another characteristic of this reaction is the high degree of stereospecificity observed. The stereochemistry of the rearranged cycloheptadiene depends only upon the geometry of the olefin within the vinyl substituents on the divinylcyclopropane not on their relative stereochemistry (i.e. cis or trans) on the cyclopropane ring.[10a] Divinylcyclopropanes with both double bonds of the same geometry (both either cis or

trans) give the same product, a 1,2-*cis*-disubstituted 1,4-cycloheptadienes (Scheme 13). Likewise, divinylcyclopropanes with both double bonds of different geometries (one cis and one trans) will give the same product, 1,2 trans-disubstituted 1,4-cycloheptadienes.



Scheme 13

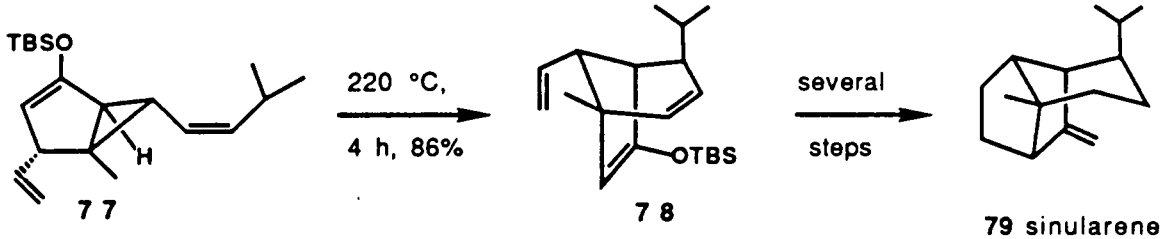
The Cope rearrangement of divinylcyclopropanes has been applied to the synthesis of pseudoguaiane sesquiterpenoids, which possess a 5-7 ring system. Wender et al. used the Cope rearrangement of divinylcyclopropane **75** to construct the skeletons of both damsinic acid (**5**) and confertin (**6**) (Scheme 14).[11]



7 5 7 6 5 damsinic acid 6 confertin

Scheme 14

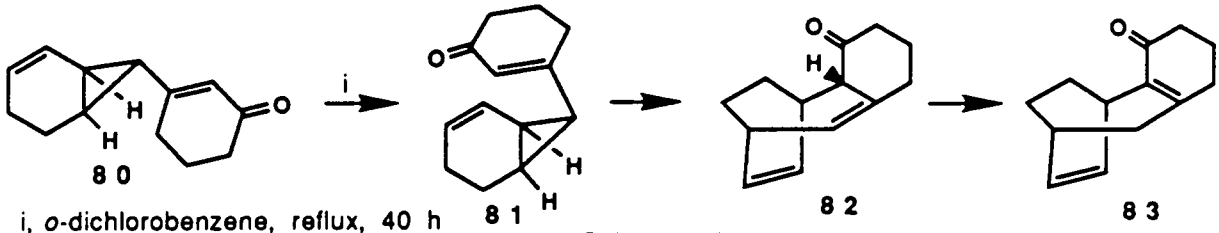
Bicyclo[3.2.1]octanes have also been constructed via the Cope rearrangement of 6-(1-alkenyl)bicyclo[3.1.0]hex-2-enes. Silyl enol ether **77** smoothly rearranges to bicyclic systems **78** stereospecifically upon heating.[61] The rearrangement is believed to have proceeded via initial isomerization of the trans to the cis divinylcyclopropane. Hydrolysis of **78** and further elaboration led to (±)-sinularene (**79**), an unusual marine natural product (Scheme 15).[62]



77 **78** **79** sinularene

Scheme 15

Bicyclo[3.2.2]nona-2,6-dienes can also be accessed via Cope rearrangement of divinylcyclopropanes.[63,64] Thermolysis of enone **80** gave tricyclic ketone **82** in



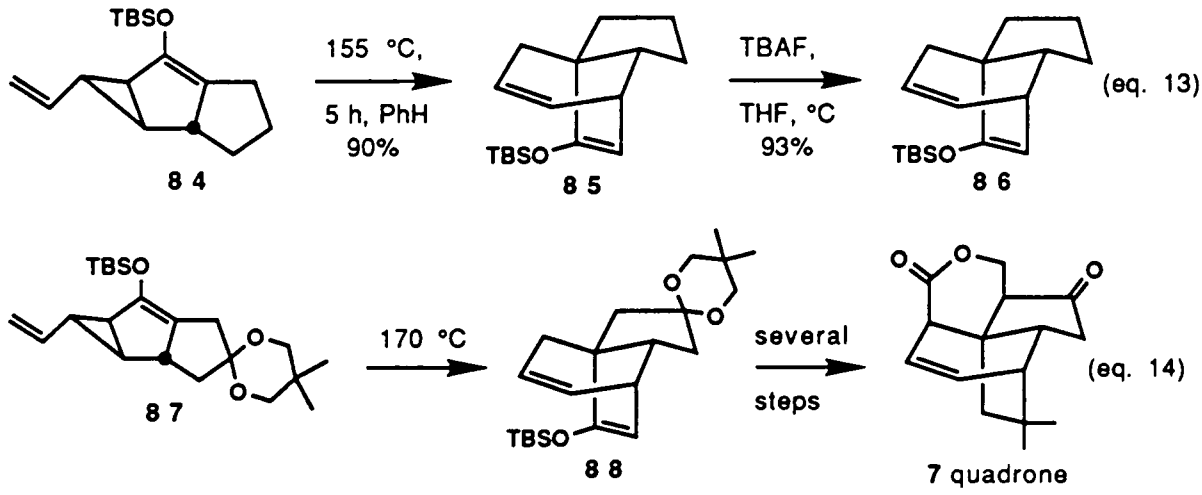
80 **81** **82** **83**

i, *o*-dichlorobenzene, reflux, 40 h

Scheme 16

excellent yield.[64] Again the Cope rearrangement is most likely proceeded by radical isomerization of **80** to its endo isomer **81**. The initially formed β,γ-unsaturated ketone isomerized under the reaction conditions to the more stable conjugated isomer, **83**.

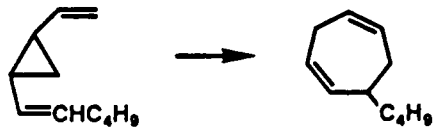
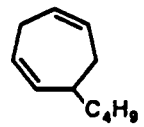
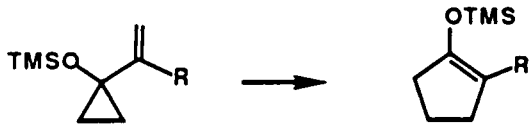
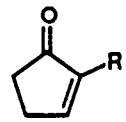
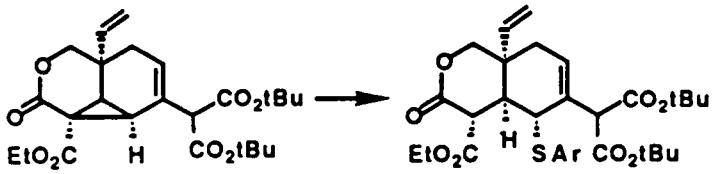
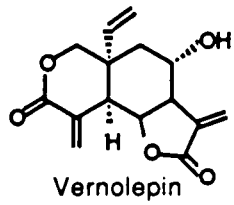
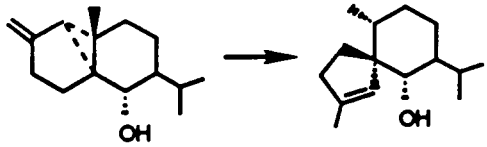
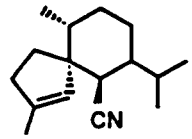
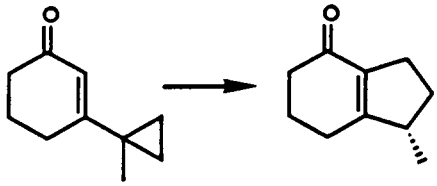
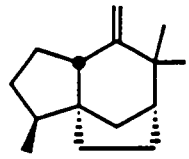
The Cope rearrangement of divinylcyclopropanes can also be used to construct tricyclic systems containing the bicyclo[3.2.1]octane carbon skeleton.[12,65] Such a rearrangement has been applied to a synthesis of quadrone[12] (Scheme 17).



Scheme 17

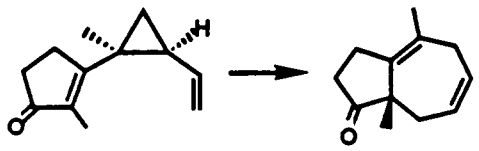
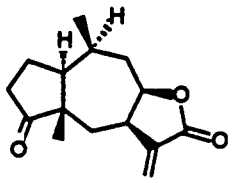
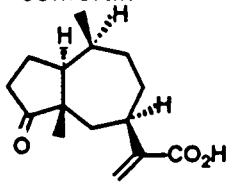
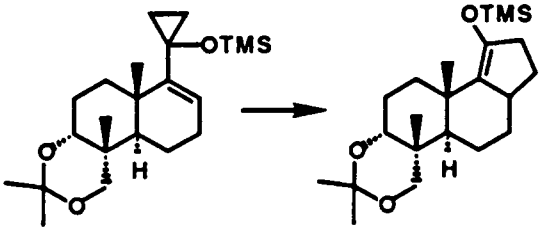
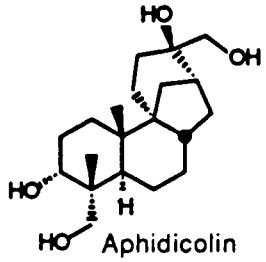
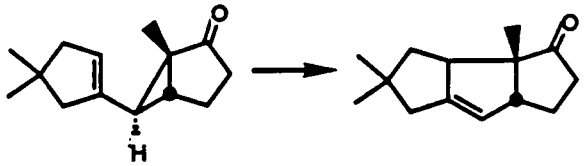
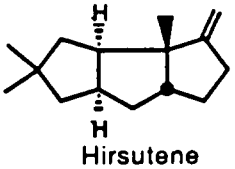
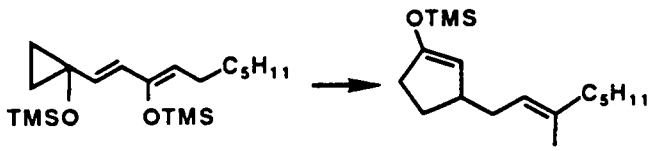
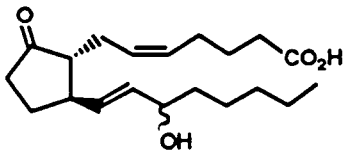
In summary, the divinylcyclopropane Cope rearrangement is a very useful reaction lending access to many structurally diverse types of compounds. Its importance can be seen in its many recent applications to natural product synthesis such as those mentioned above. The next section will summarize the different methods commonly used for the preparation of vinylcyclopropanes.

Table 1. Vinylcyclopropanes in Synthesis

Author[a](Year) Key Transformation	Target
Das[80](1969) 	 Dictyopterene A
Trost[4](1974)  R = $(CH_2)_6CO_2{}^tBu$	 Prostaglandin Intermediate
Isobe[35] (1978) 	 Vernolepin
Caine[7] (1978) 	 Axisonitrile-3
Piers[81] (1979) 	 Zizaene

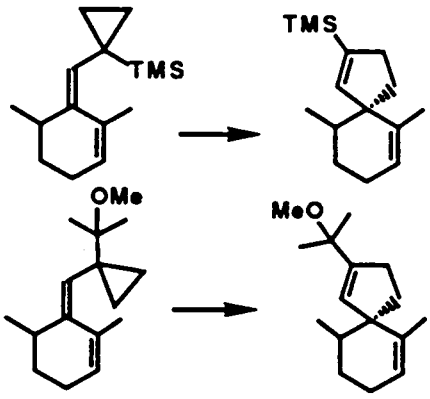
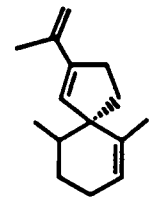
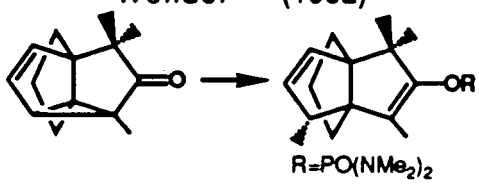
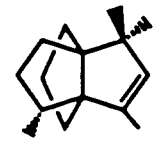
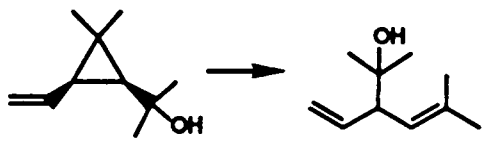
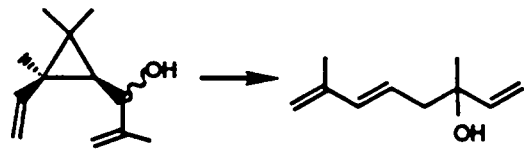
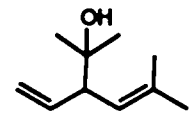
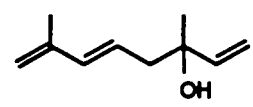
a) reference

Table 1. Vinylcyclopropanes in Syntheis, Con't.

Author[a] (Year) Key Transformation	Target
Wender[11] (1979) 	 confertin  damsinic acid
Trost[82] (1979) 	 Aphidicolin
Hudlicky[3h] (1980) 	 Hirsutene
Salaun[4b] (1981) 	 11-Deoxyprostaglandin E_2

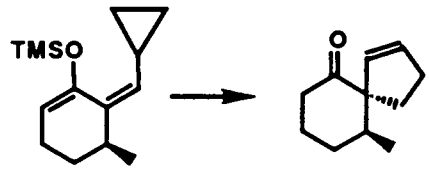
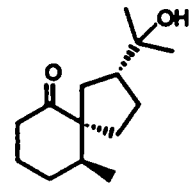
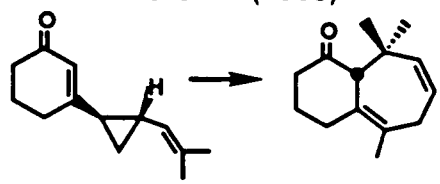
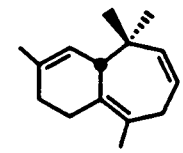
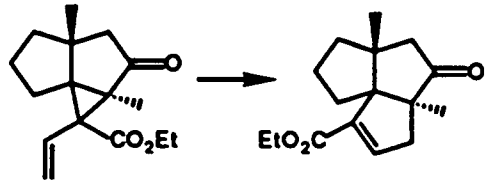
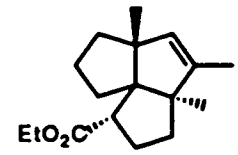
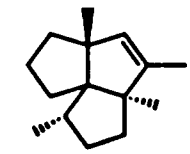
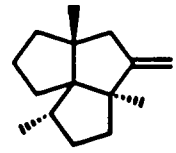
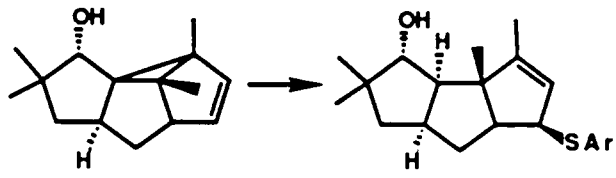
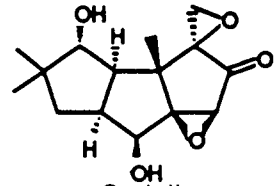
a) reference

Table 1. Vinylcyclopropanes in Synthesis, Cont'd.

Author[a] (Year) Key Transformation	Target
Paquette[83] (1982) 	 α-Vetispirene
Wender[36] (1982)  R=PO(NMe$_2$)$_2$	 Modhephene
Moiseenkov[9] (1982)  	 Santalina Alcohol  Hotrienol

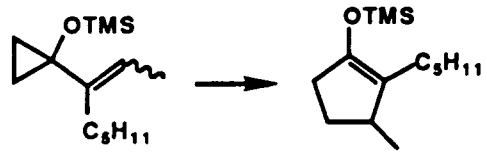
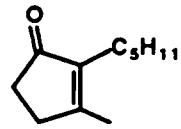
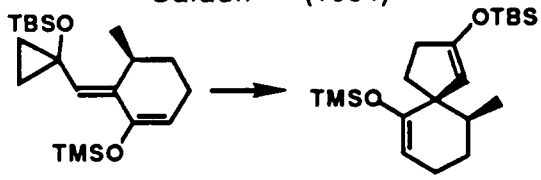
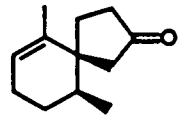
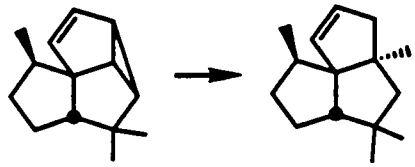
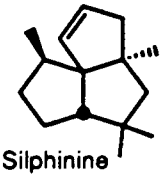
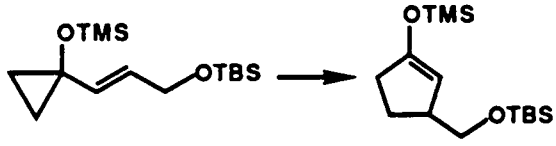
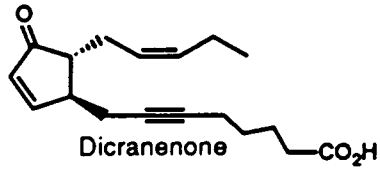
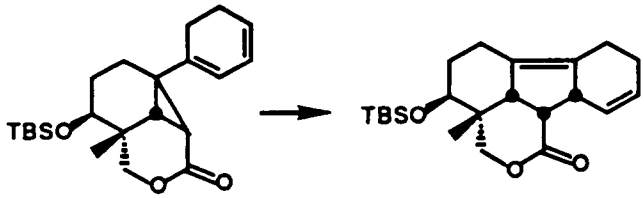
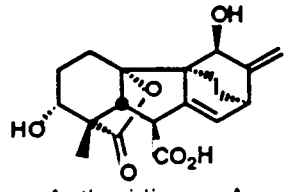
a) reference

Table 1. Vinylcyclopropanes in Synthesis, Con't.

Author[a] (Year) Key Transformation	Target
Piers[84] (1983) 	 Hinesol
Piers[85] (1983) 	 Himachalene
Hudlicky[3f] (1983) 	 Isocomenic acid  Isocomene (1984)  β-Isocomene (1984)
Wender[46] (1983) 	 Coriolin

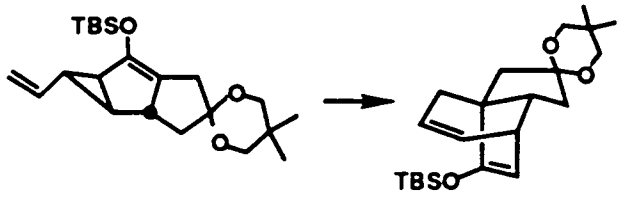
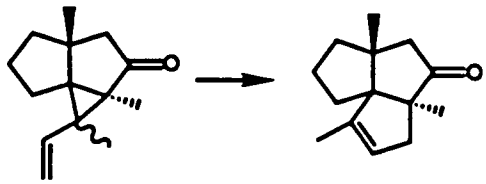
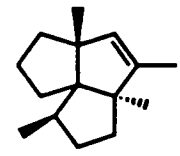
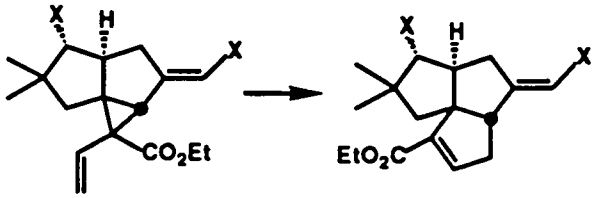
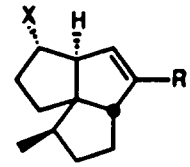
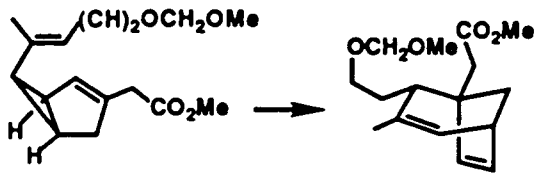
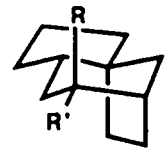
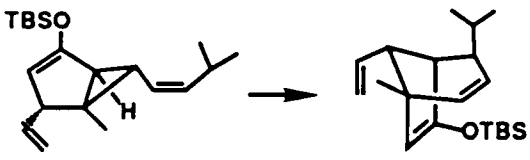
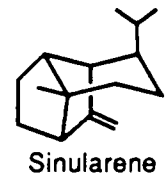
a) reference

Table 1. Vinylcyclopropanes in Synthesis, Cont'd.

Author[a] (Year) Key Transformation	Target
Salaun[86] (1983) 	 Dihydrojasmone and Jasmone
Salaun[87] (1984) 	 Spirovetivane
Wender[a] (1985) 	 Silphinine
Salaun[4a] (1985) 	 Dicranenone
Corey[5] (1985) 	 Antheridiogen-An

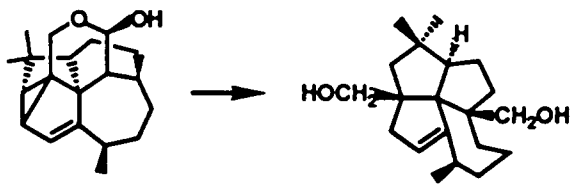
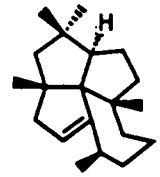
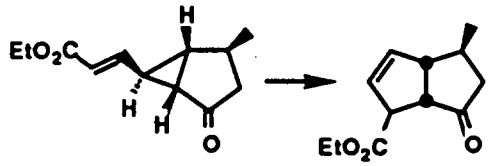
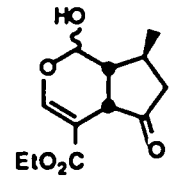
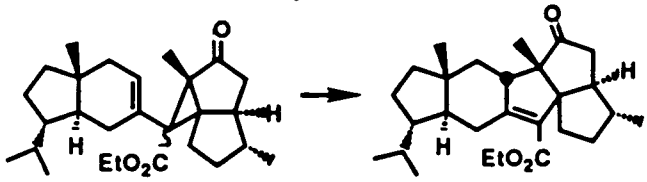
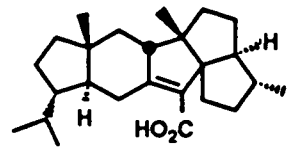
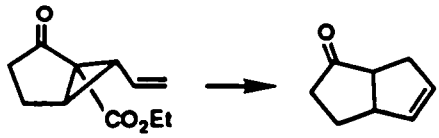
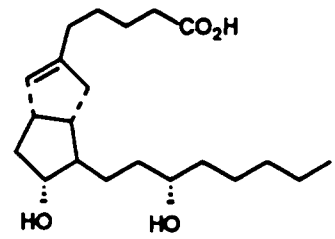
a)reference

Table 1. Vinylcyclopropanes in Synthesis, Cont'd.

Author[a] (Year) Key Transformation	Target
Piers[12] (1985) 	 Quadrone
Hudlicky[3e] (1986) 	 Epiisocomene
Hudlicky[3c] (1987) 	 Pentalenene X=H, R=CH_3 Pentalenic Acid X=OH, R=CO_2H
Piers[a] (1987) 	 R=Me, R'=H Prezizanol R,R'=CH_2 Prezizaene
Piers[62] (1987) 	 Sinularene

a) references

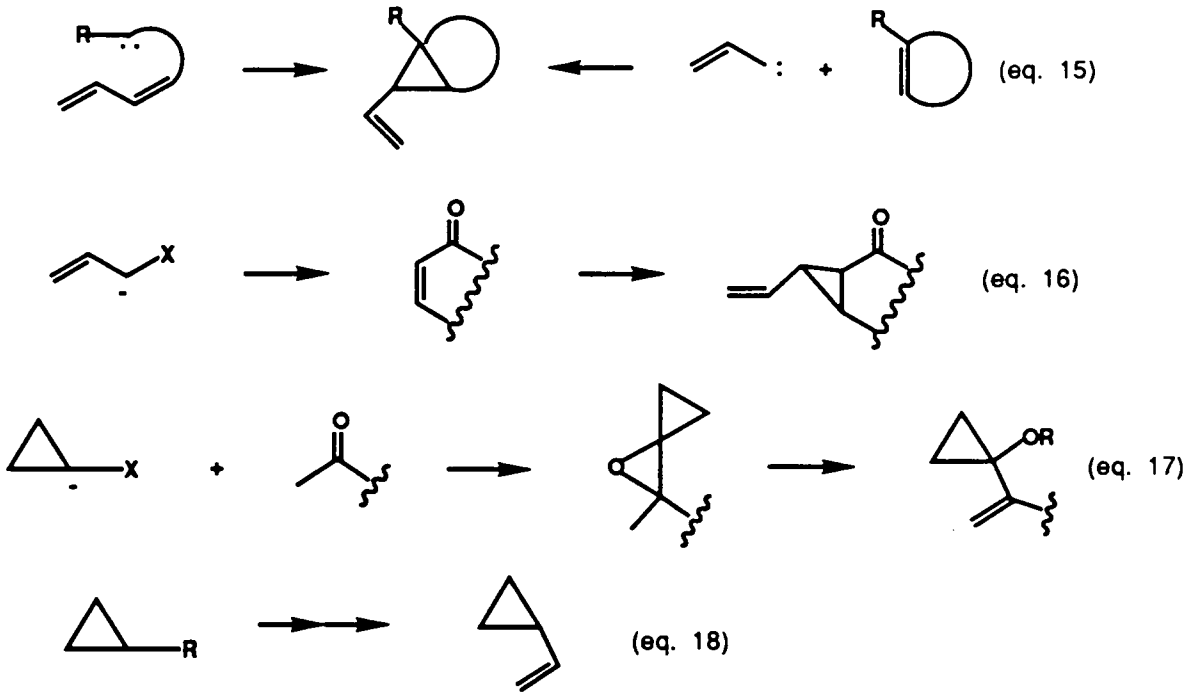
Table 1. Vinylcyclopropanes in Synthesis, Cont'd

Author[a] (Year) Key Transformation	Target
Wender[52] (1988) 	 Laurenene
Gree[6] (1988) 	 Verbenalol
Hudlicky[3a,b] (1989) 	 Retigeranic Acid
Ikegami[42] (1989) 	

a) reference

2. Synthesis of Vinylcyclopropanes

Because of the strain of cyclopropane rings, highly reactive intermediates or irreversible processes must be used for their synthesis (see Scheme 18 for examples). Two of the most common methods for the preparation of cyclopropanes involve carbene or carbenoid additions to double bonds (eq. 15) and ylides (eq. 16). These methods have also been extended to the synthesis of vinylcyclopropanes. Other methods for the

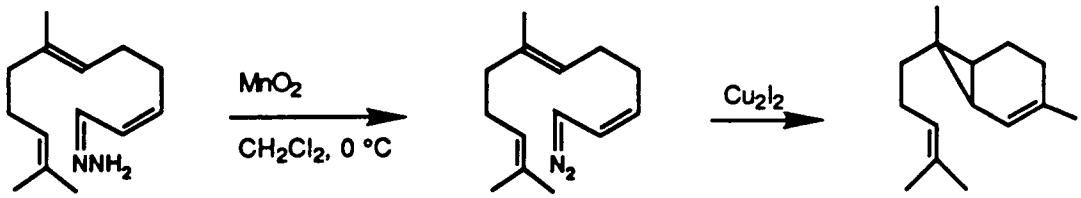


Scheme 18

synthesis of vinylcyclopropanes are ring opening of oxaspirocyclopentanes (eq. 17) and functionalization of an existing cyclopropane ring (eq. 18). These methods have been well reviewed, so only the highlights of the most common or recent methods will be discussed.[1c,66]

Carbene or carbenoid additions to carbon-carbon double bonds have long been a popular route to cyclopropanes and vinylcyclopropanes. The carbenoids obtained from decomposition of diazocompounds are more selective than "free" carbenes, so C-H

insertion reactions are suppressed, and cyclopropanes are formed in higher yields. In this manner, *cis,trans*-farnesal was converted to the hydrocarbon sesquicarene **91**.[67]

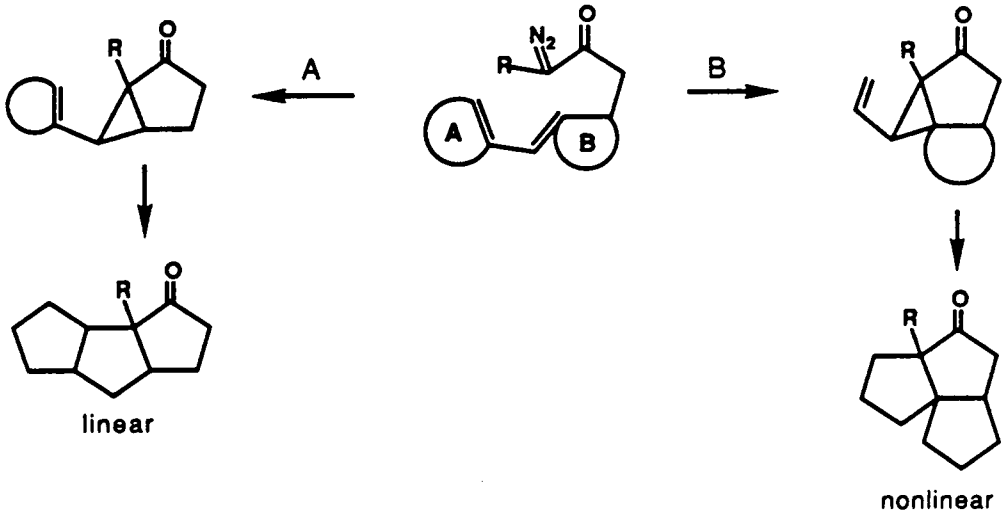


89 **90** **91**

Scheme 19

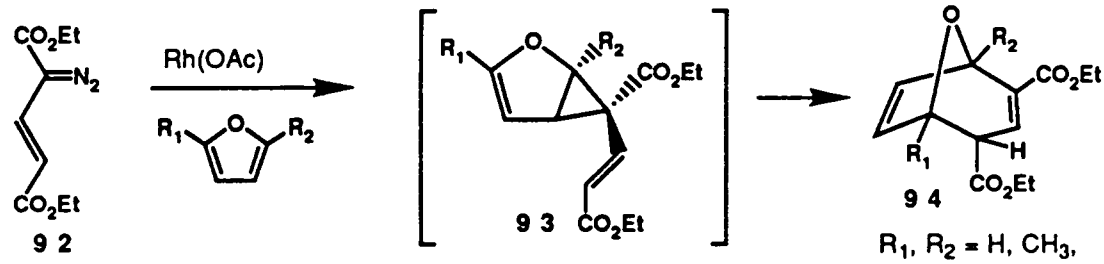
Hudlicky et al. have used diazoketones as precursors to vinylcyclopropanes which were then pyrolyzed to form annulated cyclopentenes used in the synthesis of linear and nonlinear triquinanes (Scheme 20).[1,3] Recently, the carbenoids derived from diethyl

Scheme 4



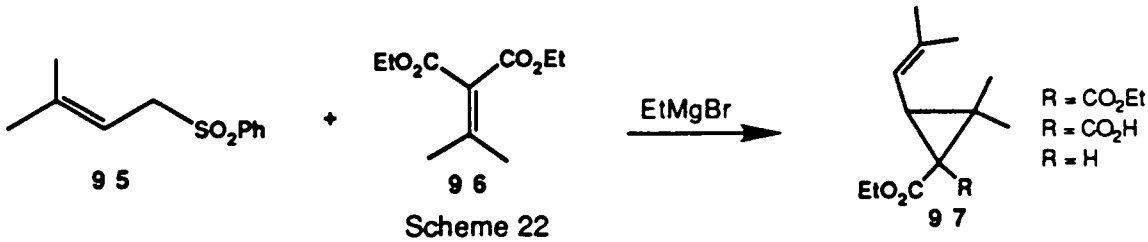
Scheme 20

4-diazo-2-pentenedioate have been added to furans yielding oxybicyclic systems. It is believed that the addition reaction produces *cis*-divinylcyclopropanes which spontaneously undergo Cope rearrangement to the bicyclic system **94** (Scheme 21).[68]



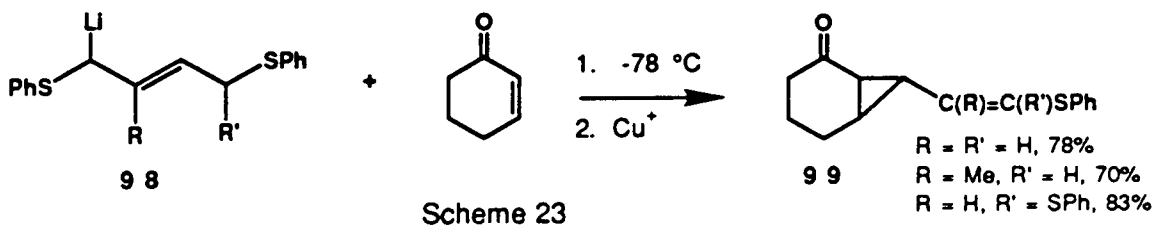
Scheme 21

Ylides have also been popular reagents for vinylcyclopropane synthesis. One of the earlier examples involved Michael addition of an sulphonyl anion to an α,β unsaturated ester to provide vinylcyclopropane **97** (R = CO_2Et) which was further elaborated to chrysanthimic acid (Scheme 22).[69] More recently, phenylthio stabilized



Scheme 22

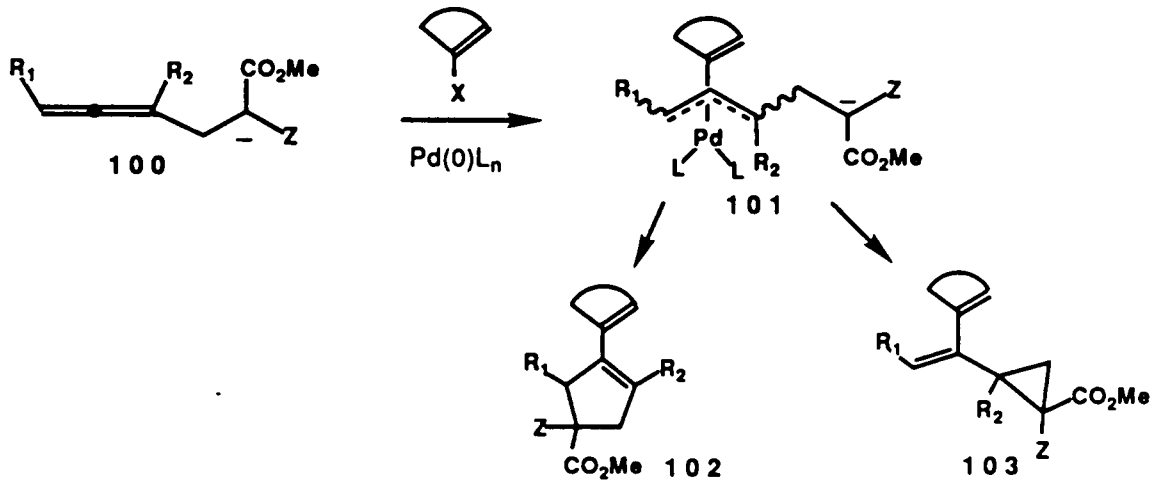
organolithium compounds have been used in a one-pot synthesis of vinylcyclopropanes (Scheme 23).[70] These anions add in a 1,4 fashion to enones. The resulting enolate anion is treated with cuprous a triflate-benzene complex to make the thiophenoxy group a good enough leaving group for displacement by the enolate anion, resulting in the formation of a mixture of exo and endo vinylcyclopropanes.



Scheme 23

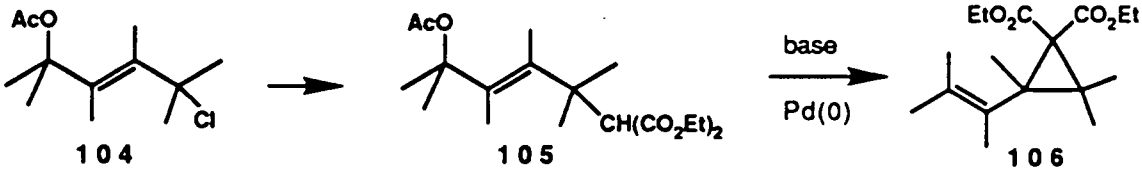
Palladium catalyzed reactions have also been used lately in two new approaches to vinylcyclopropanes. In the first, carbopalladation of the enolate of a functionalized allene such as **100** with a vinylic or aryl palladium complex leads to either

cyclopentenes **102** and/or vinylcyclopropanes **103.** These products arise from the attack of the anion at either of the terminal carbons of the intermediate π-allylic complex **101**.[71] The products are highly dependent on the vinyl or aryl halide used.



Scheme 24

Cyclopropanes are formed only when vinylbromides are used. In the second approach, the chlorine of 1-acetoxy-4-chloro-2-alkenes is stereospecifically replaced by dimethyl malonate using a palladium catalyst (Scheme 25). Subsequent palladium catalyzed cyclization affords vinylcyclopropanes in good yields.[72]



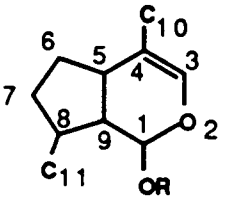
Scheme 25

Previously, most of the work on vinylcyclopropanes has been purely mechanistic. Only in the last two decades has the potential of vinylcyclopropanes as synthetic intermediates been realized. The many different types of vinylcyclopropane rearrangements, the ability to select the mode of rearrangement, the numerous methods for their preparation, and the endless number of substitution patterns possible on a

vinylcyclopropane, all illustrate the potential value vinylcyclopropanes can have in synthesis.

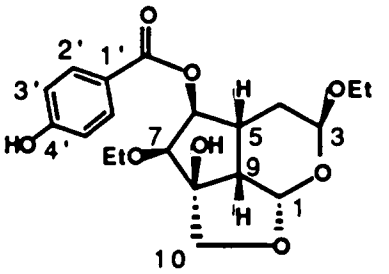
3. Isolation, Characterization, and Synthesis of Specionin

Specionin belongs to the iridoids, a large family of natural products containing a highly oxygenated, fused cyclopentapyran ring system. There are two major groups of iridoids: one has a ten carbon nucleus that contains both C-10 and C-11 and the other has a nine carbon nucleus that contains C-10 but has no C-11. While there are some



eight and fourteen carbon iridoids, most iridoids can be classified as members of one of the two groups described above.[73] Most of the naturally occurring iridoids are characterized by a link to a sugar, usually glucose. Iridoids exhibit a wide range of biological activities.[73] Some, such as luganin, have also been shown to be intermediates in the biosynthesis of many of many important families of plant-derived alkaloids.[73]

Isolation and structure elucidation. Specionin itself, has recently emerged as an important iridoid due to its strong antifeedant activity against the spruce budworm. The fir and spruce forests of North America have been infested by the Eastern spruce budworm, which in May inflicts huge damage to the lumber industry. In 1983, Nakanishi isolated specionin from the leaves of the tree *Catalpa speciosa* Warder, a tree the budworm does not attack.[74] After the initial ethanol extracts were screened and fractionated, specionin was isolated from an active fraction. Nakanishi assigned specionin the structure of **107** based on extensive NMR and mass spectroscopy. The desorption chemical ionization mass spectrum exhibited two quasi-molecular ion peaks which were interpreted as loss of ethoxy and ethanol moieties. The presence of a



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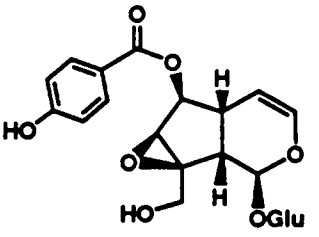
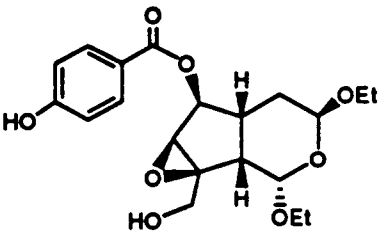
hydroxy benzoate moiety was also indicated by the mass spectra and confirmed by a λ_{max} at 254 nm in the UV spectra. The ^{13}C NMR data, especially the J-modulated spin echo spectra, showed that specionin contains two methyl groups (δ 15.6 and 15.5), one methylene (30.4, C-4), two methines (34.2 and 41.2, C-5 and C-9), three OCH_2's (61.2, 64.0, and 64.8, C-7 and CH_2O of the two ethoxy groups), two OCH's (61.4 and 80.7, C-10 and C-6), one C-O (67.3, quaternary, C-8), two hemiacetal CH's (94.8 and 97.7, C-3 and C-1), four unsubstituted aromatic carbons (116.3, 116.3, 132.8, and 132.8, C-3', C-5', C-2', and C-6'), two substituted aromatic carbons (121.5 and 164.0, C-1' and C-4'), and one carbonyl carbon (168.2). The ^1H NMR data derived from extensive decoupling experiments and two-dimensional spectroscopy showed that the two nonequivalent methylene hydrogens at δ 3.50 and 3.85 are coupled geminally and further to the methyl groups at δ 1.17 and 1.21. Nuclear Overhauser effect difference spectra were measured to determine the relative stereochemistry. Irradiation of 6-H (δ5.32) caused a 16% enhancement at 7-H, while none was observed for 5-H. Irradiation of the 5-H peak (δ 2.34) exerted NOE's of 25% on 9-H, 6% on 1-H, and 14% on 4-H_a, but no effect on 6-H. Irradiation of 9-H gave a 20 and 25% NOE for 5-H and 1-H, respectively, while irradiation of 1-H at δ 5.20 led to an 11% NOE for 9-H. The close structural relationship between specionin and the well-known iridoid glucoside catalposide **108** isolated along with specionin was noted, and thus with the



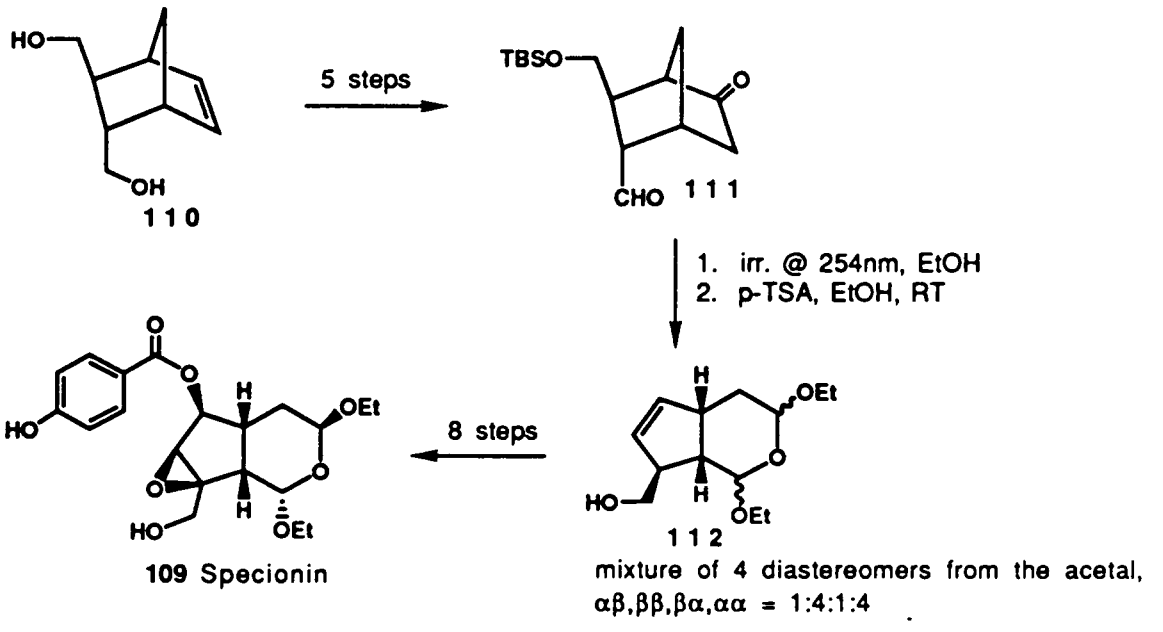
108

above spectral data, the structure of specionin was assigned as **107**. Nakanishi suggested that specionin could be an artifact derived from catalposide (**108**) during ethanol extraction, however an attempt to chemically convert catalposide to specionin by ethanolysis was not successful. Nonetheless whatever its true origin, specionin exhibits good activity (activity level = 50-100 ppm) against the spruce budworm. Also, its simple structure relative to other antifeedants make it an important compound.

In 1985, Vandewalle showed that **107** is not the correct structure of specionin by synthesis of **107** and comparison of it with natural specionin.[75] For both substances, the relative configurations of H-1, -5, -6, -7, and -9 were identical (confirmed by NOE measurements). Knowing then that the difference their structures was not a diastereotopic one, he revised the structure of specionin to **109** and confirmed the assignment by synthesis (Scheme 26).



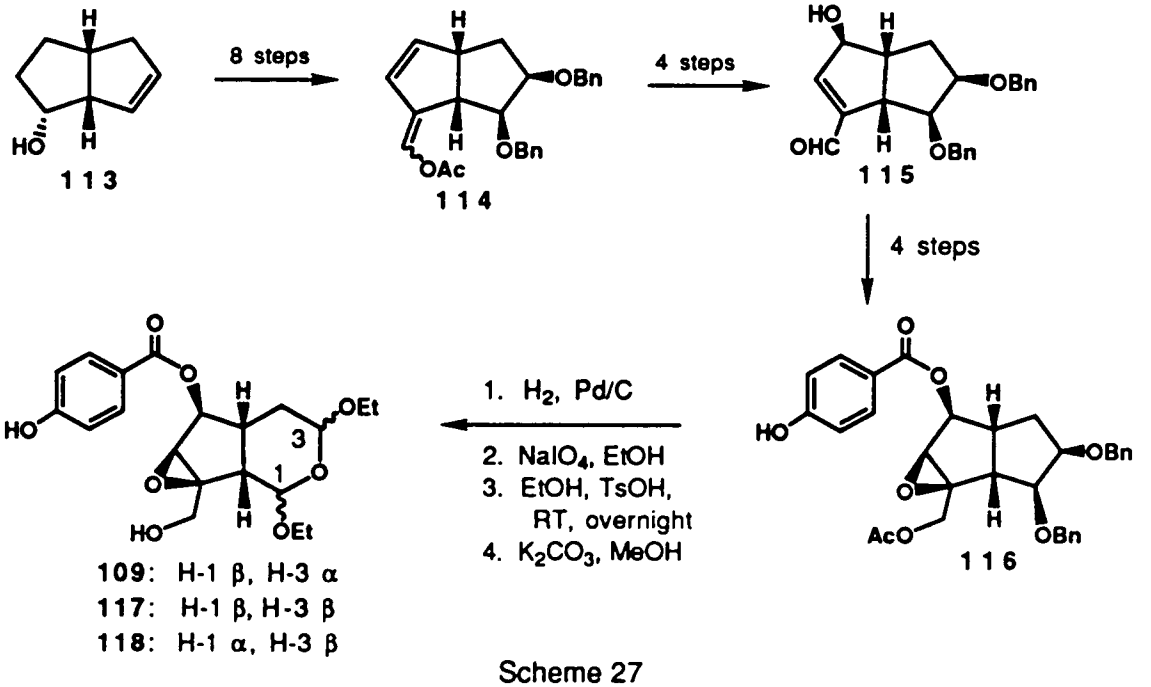
109 Specionin



Scheme 26

Syntheses of specionin. As discussed in the preceding section, Vandwalle's was the first synthesis of specionin, and this synthesis led to the correct structural elucidation of specionin. Shortly thereafter, Leonard published his approach.[76] Because of the lack of selectivity in Vandewalle's synthesis for formation of the bis acetal (obtained as a mixture of four diastereomers), Leonard decided to completely functionalize the left-hand cyclopentane ring prior to oxidative cleavage of the diol hoping that the correctly functionalized ring would elicit stereochemical control of the acetal centers during cyclization to the tetrahydropyan ring.

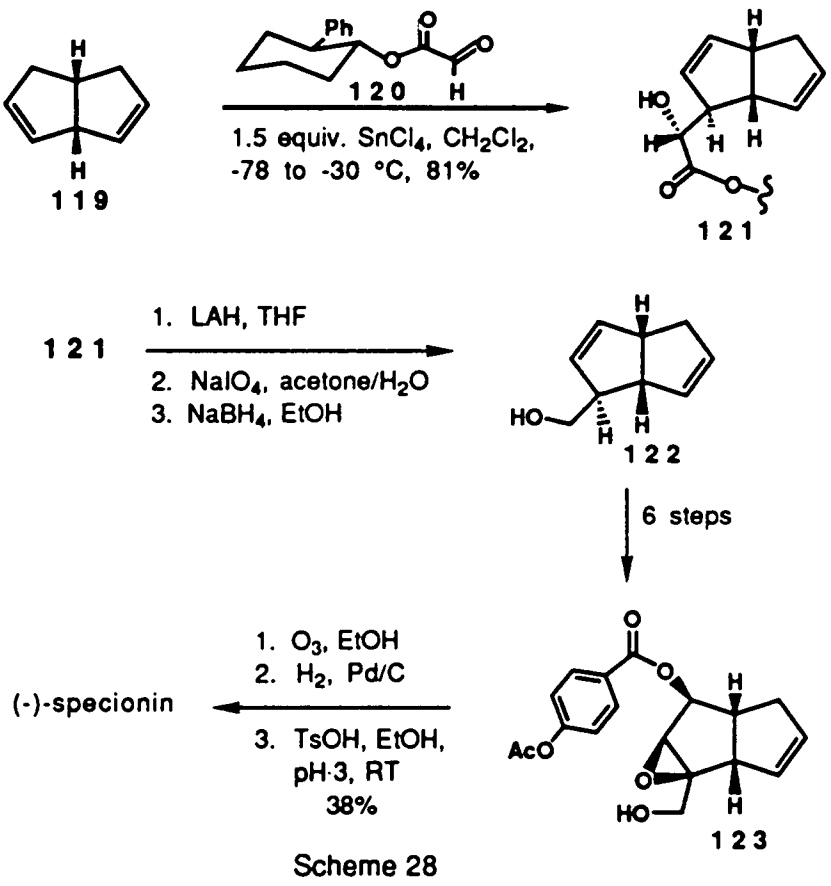
Starting with **113**, the complete carbon skeleton of the bicyclic portion was assembled in eight steps (Scheme 27). Next the left-hand ring was completely functionalized to give **116**. Oxidative cleavage of the diol did proceed with more stereochemical control. Initially a mixture of diastereomers **109**, **117**, and **118** (ca. 1:1:0.1, respectively) was obtained after 10 h. However, if this mixture was allowed to



Scheme 27

stand overnight in EtOH with a catalytic amount of p-toluenesulphonic acid, the cis isomer **117** completely equilibrated to specionin **109** and the diastereomeric trans isomer **118** in a ~4:1 ratio (Scheme 27).

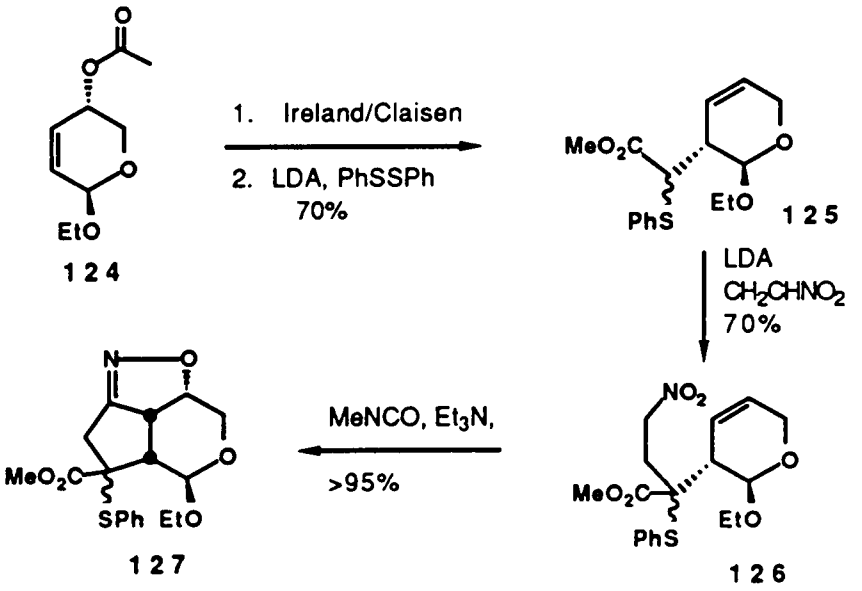
In 1988 several enantioselective syntheses of specionin were completed. Whitesell's approach used a modification of the asymmetric ene reaction he had developed earlier using Corey's chiral auxiliary 8-phenylmenthol.[77] He had found that changing the chiral auxiliary to *trans*-2-phenylcyclophexanol was necessary to obtain the natural enantiomer of specionin. In this reaction a discrimination between the π systems of a diene with internal mirror symmetry is possible, consequently the ene reaction of **119** with **120** gave optically pure **121**. Removal of the chiral auxiliary with LAH and oxidative cleavage of the resulting 1,2 diol gave after reduction with $NaBH_4$ primary alcohol **122** (Scheme 28). As in Leonard's previous synthesis, the



Scheme 28

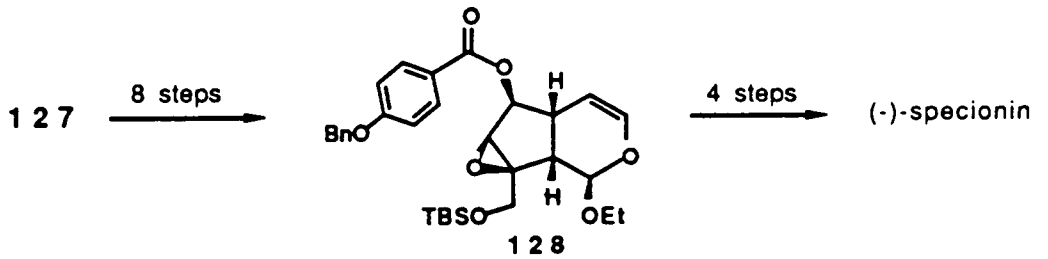
left-hand cyclopentene ring was completely functionalized in six steps prior to formation of the bis-acetal unit. Under Whitesell's conditions (TsOH, EtOH, pH=3, RT) no diastereomers were formed in the cyclization reaction. It is possible that under these conditions kinetic rather than thermodynamic control predominates.

Curran also published an enantioselective synthesis of (-)-specionin.[78] Unlike the previous synthesis, his started with a cyclic acetal moiety and then functionalized the left-hand ring (Scheme 29). Enantiocontrol was incorporated by using the chiral



Scheme 29

glycal **124** derived from D-xylal using a procedure developed by Fraser-Reid.[79] A combination of an Ireland-Claisen rearrangement followed by a nitrile oxide cycloaddition yielded chiral **127**. Functional group manipulation gave **128** in eight steps. Introduction of the remaining acetal group via ethoxymercuration followed by desilylation and debenzylation produced (-)-specionin (Scheme 30).



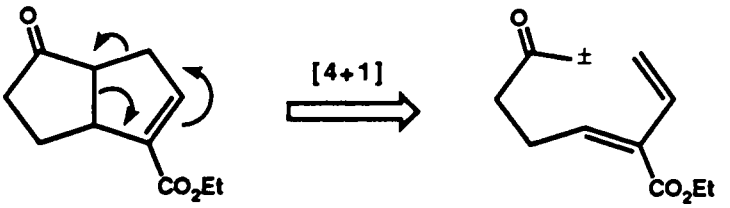
Scheme 30

III. DISCUSSION

1. Introduction

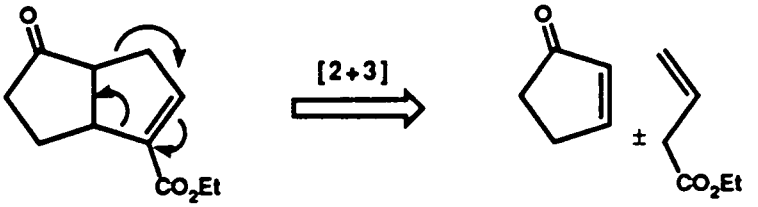
In the early seventies, the triquinanes, a new class of natural products containing one or more fused five-membered rings, were discovered.[1, 73-75] This spurred much activity in developing new methodologies for the construction of such ring systems. Many problems are encountered in the formation of five-membered rings. Hudlicky[1c] attributes these to the following factors: (1) charge disonance resulting from an odd number of carbons, (2) difficulty in predicting the stereoelectronic behavior of cyclopentanes as a result of the strain imparted by the distorted tetrahedral angles, and (3) the lack of methods for constructing cyclopentanes independently of their substitution patterns. Various cyclopentannulation methodologies have been developed, but to date no very general or versatile method has been discovered.[1,90-96]

The challenge of finding new approaches for the synthesis of five-membered rings has been accepted by many chemists, including the Hudlicky group. One of the first approaches developed in the Hudlicky group for the synthesis of both linear and nonlinear triquinanes was the intramolecular [4+1] cyclopentene annulation.[1-3] This method involved formation of dienic diazoketones which when decomposed formed vinylcyclopropanes through carbenoid intermediates. The vinylcyclopropanes were then thermolytically rearranged to their corresponding cyclopentenes. The rationale behind this methodology can be easily seen by viewing the intermediate carbene as a resonance structure of the cyclopentene. This procedure served quite well for the synthesis of

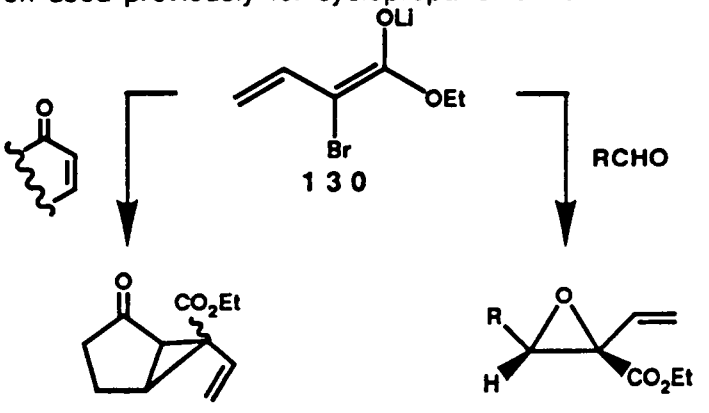


several triquinanes; however, some shortcomings were apparent, namely the consistently low yields of the decomposition reaction and the difficultly in constructing more substituted dienic diazoketones for more functionalized systems. These problems clearly pointed out the need for a complementary methodology.

Invoking the same type of reasoning using resonance structures led to the idea of an intermolecular reaction to form the same vinylcyclopropanes. The carbenoid intermediate would be replaced by its isoelectronic equivalent: an anion equipped with a



good leaving group. The carbenoid equivalent became the dienolate formed from the reaction of ethyl 2-bromocrotonate with LDA (lithium diisopropyl amide). This dienolate was found to react with aldehydes in a vinylogous Darzen reaction to give vinyloxiranes and with enones to give vinylcyclopropanes (Scheme 31).[3a,13] Similar reactions have been used previously for cyclopropane formation.[69,98,99]



Scheme 31

The mechanism and topological implications of the vinylcyclopropanation reaction are depicted in Figure 1. Following Michael addition of the dienolate to enone **129**, the resulting enolate anion will, in the case of proper orbital alignment (**131a**), immediately displace bromine leading to *endo*- and *exo*-vinylcyclopropanes (**132**-exo/endo) or if improperly aligned, there may be sufficient time for its equilibration to **131b** prior to displacement of the bromine in an S_N2 or vinylogous manner producing bridged bicyclic systems such as **136** or **137**. It should also be possible to obtain the bridged bicyclic system **136** by another pathway: Cope rearrangement of the enol ether of the *endo*-vinylcyclopropane **132**. Rearrangement of the vinylcyclopropanes could in principle lead to two regioisomeric diquinanes, **134** or **135**. Pyrolysis would be expected to give diquinane **135** resulting from cleavage of bond a (Figure 1), which is activated by the ketone group. Bond b of the cyclopropane is not activated towards cleavage unless an electron donating group (X) is present. Under such circumstances, nucleophilic opening/reclosure would lead to **135**, whereas thermolysis would lead to **134**.

It was felt that the vinylcyclopropanation reaction could offer a shorter alternate route to bicyclic systems, only it was plagued with consistently low isolated yields (20-35%). If this problem could be overcome, then this reaction could lead to a new methodology for cyclopentene annulation. Several details of this reaction required investigation, among them the optimization of the dienolate formation and improvement in its reaction with aldehydes, ketones, and enones; a study of the possible substitution patterns of both the dienolate and the enone; and finally a synthetic application to underscore its utility. In the following discussion, the above points are addressed and a new method of cyclopentanoid synthesis is described.

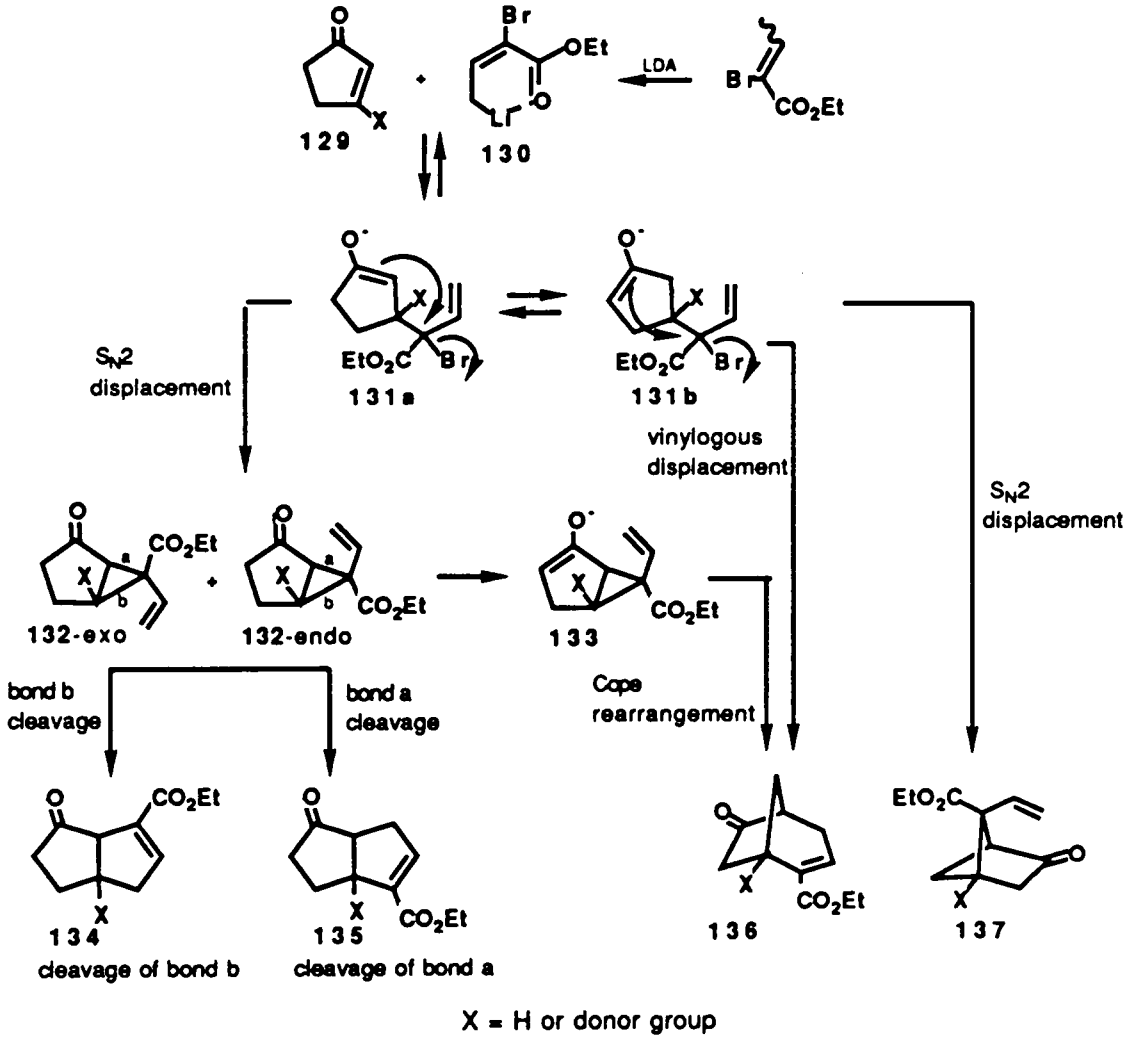
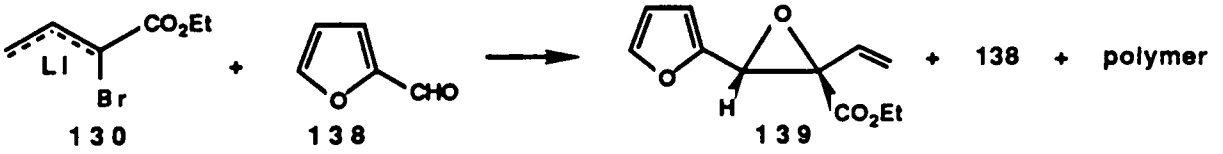


Figure 1. Mechanistic pathways for the addition of the dienolate of ethyl 2-bromocrotonate to enones and the rearrangements of the resulting vinylcyclopropanes.

2. Optimization of the Reaction of the Lithium Dienolate of Ethyl 2-Bromocrotonate with Electrophiles.

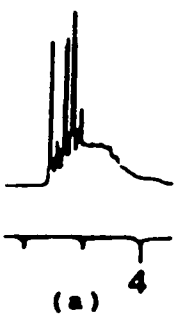
The vinylcyclopropanation and vinyloxiranation reactions were originally performed at -78 °C, at a 1 M concentration, and with THF/HMPA as the solvent. The ethyl 2-bromocrotonate and the enone or aldehyde, neat and at room temperature, were introduced into the reaction via syringe.[13] Rathke mentions that more dilute solutions were necessary to successfully form the dienolate of ethyl crotonate.[100] He also observed that the dienolate of ethyl crotonate while stable at -78 °C, undergoes complete decomposition at higher temperatures. With these facts in mind, a detailed investigation of the effects of temperature and concentration on the formation of the dienolate of ethyl 2-bromocrotonate and its reaction with electrophiles was initiated (see Table 2). For these studies, 2-furaldehyde was chosen as the electrophile. It was observed that the in the ^1H NMR, the signals from the decomposition product of the dienolate, a polymer, appeared underneath the signals for the ethyl ester pattern of the vinyloxiranes and vinylcyclopropanes (see footnote a, Table 2). (This is what led to the initial reporting of incorrect yields for this reaction.[13]) The relative amounts of decomposition product, or polymer, could therefore be calculated by the percent of excess integration found for the methylene pattern for the ethyl ester at δ 4.1 ppm. In this way the relative effects of changing any parameter of the reaction could be measured by comparing the integrations of the methylene patterns in the proton spectra of the crude reaction mixtures. The closer this integration was to two protons, the better the reaction conditions, because less polymer was present. An improvement in the yield was first observed by simply adding the crotonate as a precooled solution in THF and lowering the temperature of the reaction to -90 °C (entry 3, Table 2). This decreased the amount of

Table 2. Optimization of the Vinyloxiranation of 2-Furaldehyde.[101]

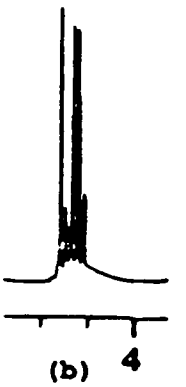


Entry	Mode of Addition of crotonate	Mode of Addition of 138	Conc. of 130	Time (h)	Temp (°C)	Composition 139(%)	138(%)	polymer[a]
1	neat, RT	neat, RT	1.0 M	0.66	-78	48	52	73
2	3 M, -78 °C	neat, RT	1.0 M	1.0	-78 to -45	62	38	56
3	3 M -90 °C	neat, RT	1.0 M	1.5	-90 to -40	61	39	36
4	0.3 M, -78 °C	neat, RT	0.2 M	1.0	-78 to -40	67	33	43
5	0.3 M, -90 °C	neat, RT	0.2 M	1.5	-90 to -50	87	13	43
6	0.3 M, -90 °C	1 M, -90 °C	0.2 M	1.5	-90 to -50	85	15	21
7	0.3M, -95 °C	1 M, -110 °C	0.2 M	2.5	-105 to -60	89	11	18

a) The relative amount of polymer is estimated in percent of excess integration of the quartet at δ=4.1 ppm, corresponding to the methylene of the ethyl ester in both the polymer and the pure oxirane.



(a)
Unoptimized, entry 1

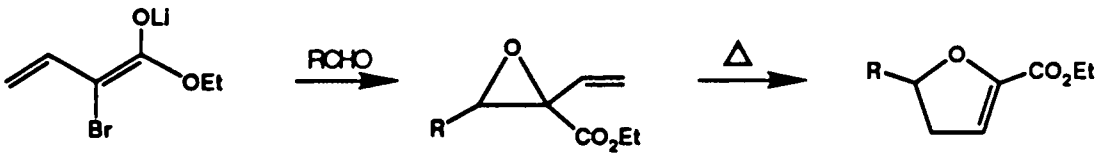


(b)
Optimized, entry 9

b) The singlet at δ=4.17 ppm corresponds to the oxirane H.

polymer by 50%. The next major increase in yield was obtained by adding the enone, also as a precooled solution in THF, and further lowering the temperature of the reaction to -110 °C (entry 7, Table 2). Under these conditions, the reaction was no longer a dark-brown color, but a clear bright yellow which lightened to a very pale yellow after the addition of the aldehyde.

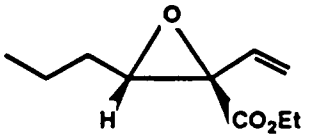
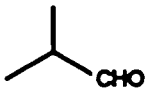
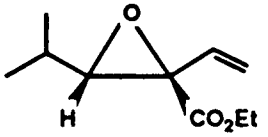
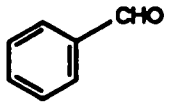
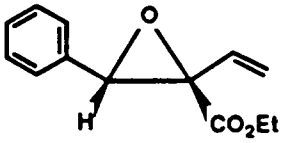
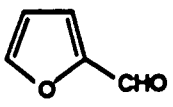
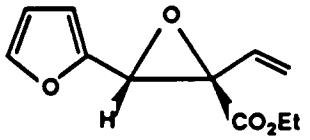
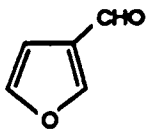
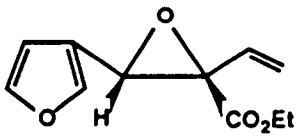
The yields of oxiranes obtained from both aldehydes and ketones were now substantially improved (see Table 3). For aromatic aldehydes, the vinyloxiranes were formed in yields of 85% or greater. The lower than expected isolated yields are due to the instability of the oxiranes on silica gel, the adsorbent used in the column/filtration of the crude reaction mixtures. It has since been observed that the oxiranes are much more stable on florisil. However, since the oxiranes are only intermediates to be converted into the desired dihydrofurans via pyrolysis,[101] an overall higher yield of



dihydrofurans can be obtained by pyrolyzing the crude products directly. The aliphatic aldehydes gave vinyloxiranes in only low yields. This is probably from competing enolization of the aldehyde by the dienolate occurring in preference to nucleophilic addition. (The α-protons of an aldehyde are at least 4-5 units of pKa more acidic than those of an ester.)

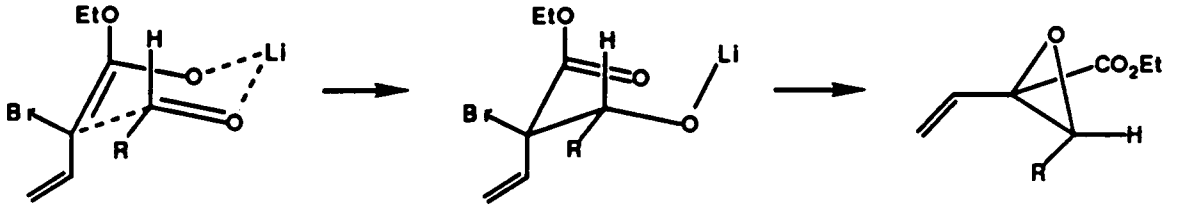
To our surprise the vinyloxiranation reaction was completely stereoselective: only one isomer of each vinyloxirane was detected (stereochemistry determined by NOE studies). In all cases, the isomer with the carbethoxy group and the oxirane hydrogen cis to each other was isolated. Although the exact nature of the reacting dienolate and the mechanism of the reaction are still under investigation, one possible explanation of this

Table 3. Vinyloxiranation of Carbonyl Compounds with 2-Bromocrotonate.[101]

Aldehyde	Oxirane[a]
	 **140** (47)[a](56)[b]
	 **141** (49)[a](78)[b]
	 **142** (68)[a](95)[b]
	 **139** (51)[a](86)[b]
	 **143** (70)[a](86)[b]

a) isolated yield, b) GC or ^{1}H NMR yield

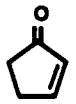
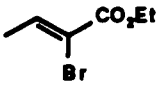
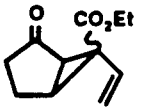
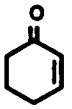
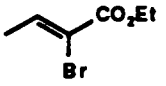
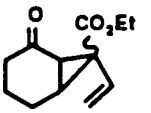
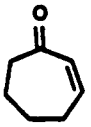
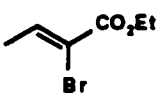
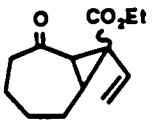
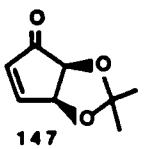
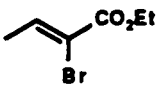
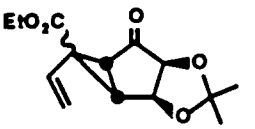
phenomenon could be that only one isomer of the dienolate is reacting and that the reaction is proceeding through a chair transition state similar to the one proposed for the Aldol reaction where lithium coordinates to the carbonyl oxygens of both the enolate anion and the electrophile.[101] The electrophile, the aldehyde, reacts with the enolate



anion in the least sterically demanding manner forming the chair conformation with the hydrogen and the ethoxy group diaxial, rather than the alkyl portion of the aldehyde in the axial position. Immediately after addition of the dienolate to the aldehyde, the bromine is suitably situated in an antiperiplanar arrangement for immediate displacement by the oxygen anion. No bond rotation is necessary prior to the displacement, thus the syn disposition of the hydrogen and the ethoxy group in the transition state is preserved in the product.

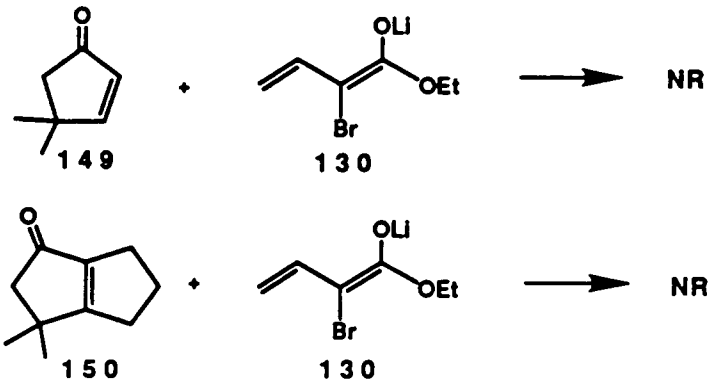
The enones were also found to react in much higher yields under the optimized conditions (see Table 4). (With the unoptimized conditions, the vinylcyclopropanes were isolated in yields of 20-35%.) For the reactions with cyclopentenone and cyclohexenone, pure *endo*- and *exo*-vinylcyclopropanes were isolated. Purification was only necessary to separate the exo and endo isomers for complete characterization. Since both the *endo*- and *exo*-vinylcyclopropanes converge to the same cyclopentene upon pyrolysis, the crude product can be pyrolyzed directly. This is especially desirable for the cyclopropanes formed from cyclopentenone, since these cyclopropanes are not very stable to silica gel, resulting in lower isolated yields after chromatographic separation. Surprisingly, while γ-disubstituted enones **149** and **150** had reacted to give

Table 4. Vinylcyclopropanation of Enones with 2-Bromocrotonate.[3a]

Enone	Crotonate	Vinylcyclopropane
		 **144-exo/144-endo** (57/43) (67)[a] (98)[b]
		 **145-exo/145-endo** (68/32) (90)[a] (93)[b]
		 **146-exo/146-endo** (63/37) (83)[a] (84)[b]
 **147**		 **148-exo/148-endo** (66/34) (72)[a] (97)[b]

a) isolated yield, b) GC yield, c) exo/endo refers to the orientation of the vinyl group

vinylcyclopropanes under the unoptimized conditions,[13] these same enones would not react under the optimized conditions even with $BF_3 \cdot Et_2O$ activation.

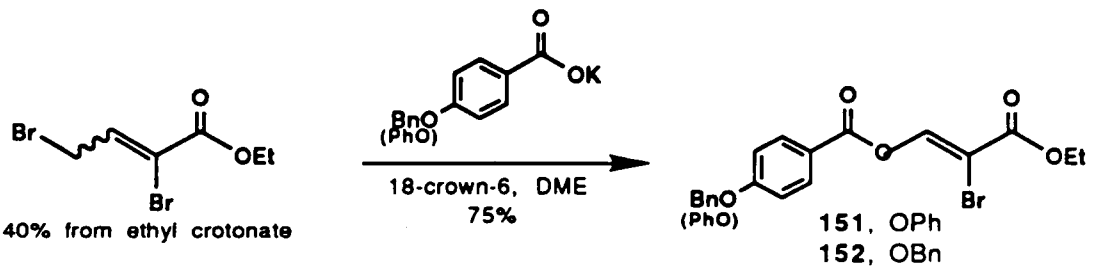


Finally, in order to make this reaction even more applicable to natural product synthesis, it was necessary to see if enantiocontrol could be introduced into the vinylcyclopropanation. The results of an investigation of asymmetric induction using chiral auxiliaries as the ester alkoxide were misinterpreted[102] and later found to be incorrect, and the use of 4-alkoxy groups was also unsuccessful.[102b] It therefore appeared that using a chiral enone might be the only way to introduce chirality into the vinylcyclopropanation reaction. The optically active enone must be such as to clearly render one face more sterically hindered than the other. The Hudlicky group had already developed a synthesis of such an enone from the microbial oxidation of toluene for use as a prostaglandin precursor.[103,104] Enone **147** (see Table 4) with an acetonide group in the 4,5 position should be bulky enough to completely block the α-face of the enone from nucleophilic attack by the dienolate, which did indeed prove to be the case. Cyclopropanation of enone **147** gave the expected optically active vinylcyclopropanes **148**-exo/endo. No diastereomers were detected from GC or ^1H NMR analysis of the crude reaction mixture, and it was clear from analysis of the coupling constants that the dienolate had added to **147** from the face opposite the acetonide. The results of these studies have been published.[3a]

3. Vinylcyclopropanation of Enones with Ethyl 2-Bromo-4-oxycrotonates

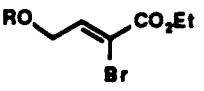
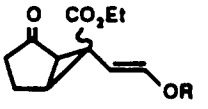
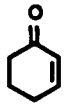
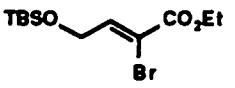
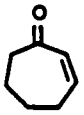
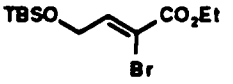
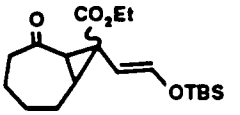
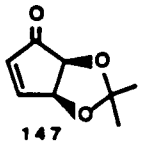
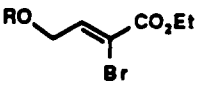
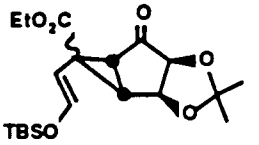
This vinylcyclopropanation methodology would become more general and applicable to natural product synthesis if it could be extended to more functionalized crotonates. A highly substituted crotonate had been used successfully in a recent synthesis of retigeranic acid.[3a,b] We were particularly interested in obtaining more highly oxygenated systems, which would allow entry into the iridoid or prostaglandin domains and therefore decided to investigate the stereoelectronic effects of oxygen substitution at the 4-position of the crotonate.

Synthesis of the Crotonates. Various oxygenated crotonates (see Table 5) were prepared for this study. The 4-benzoyloxy crotonates were prepared from ethyl 2,4-dibromocrotonate, previously prepared in our laboratory, as shown below. Displacement of the allylic bromide with the potassium salt of the appropriate carboxylic acid in the presence of 18-crown-6 with DME as the solvent gave crotonates **151** and **152** as E and Z mixtures in good yields. The other oxygenated crotonates were prepared starting from the readily available ethyl 4-hydroxycrotonate.[105] The



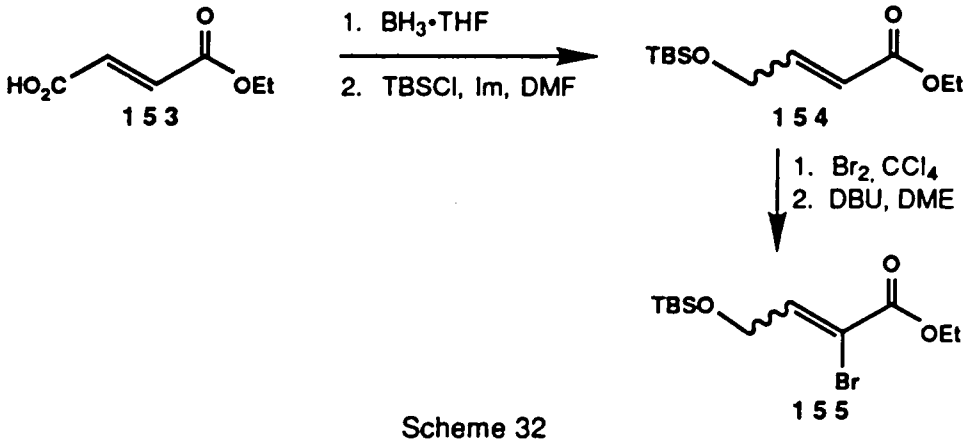
stability of the 4-hydroxyl protecting group towards bromine dictated the exact order of the steps. Most of the protecting groups, t-butyldimethylsilyl (TBS), t-

Table 5. Vinylcyclopropanation of Enones with the 4-Oxycrotonates.[3a]

Enone	Crotonate	Vinylcyclopropane
		
	155, R=TBS	**163**- exo/**163**-endo (44/56) (50)[a] (65)[b]
	151, R=CO(C$_6$H$_4$)OPh-*p*	**164**- exo/**164**-endo (70/30) (40)[a] (78)[b]
	157, R=MEM	**165**-exo/**165**-endo (87:13) (26)[a]
	158, R=SEM	**166**-exo/**166**-endo (66:33) (64)[a]
		
		167-exo/**167**-endo (45:55) (40)[a]
		
		168-exo/**168**-endo (45/55) (4.5)[a]
		
	155, R=TBS	**169**-exo/**169**-endo (66/34) (47)[a]
	158 R=SEM	**170**-exo/**170**-endo (85/15) (53-64)[a]

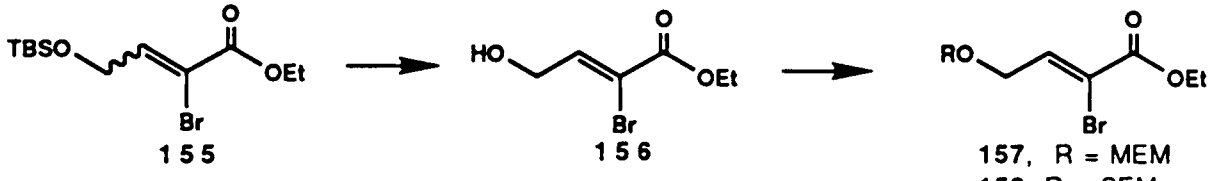
a) isolated yield, b) GC yield, c) exo/endo refers to the orientation of the vinyl group

butyldiphenylsilyl (TBDPS), and triisopropyl (TIPS), were stable under the bromination conditions, so those crotonates could be prepared as shown in Scheme 32.



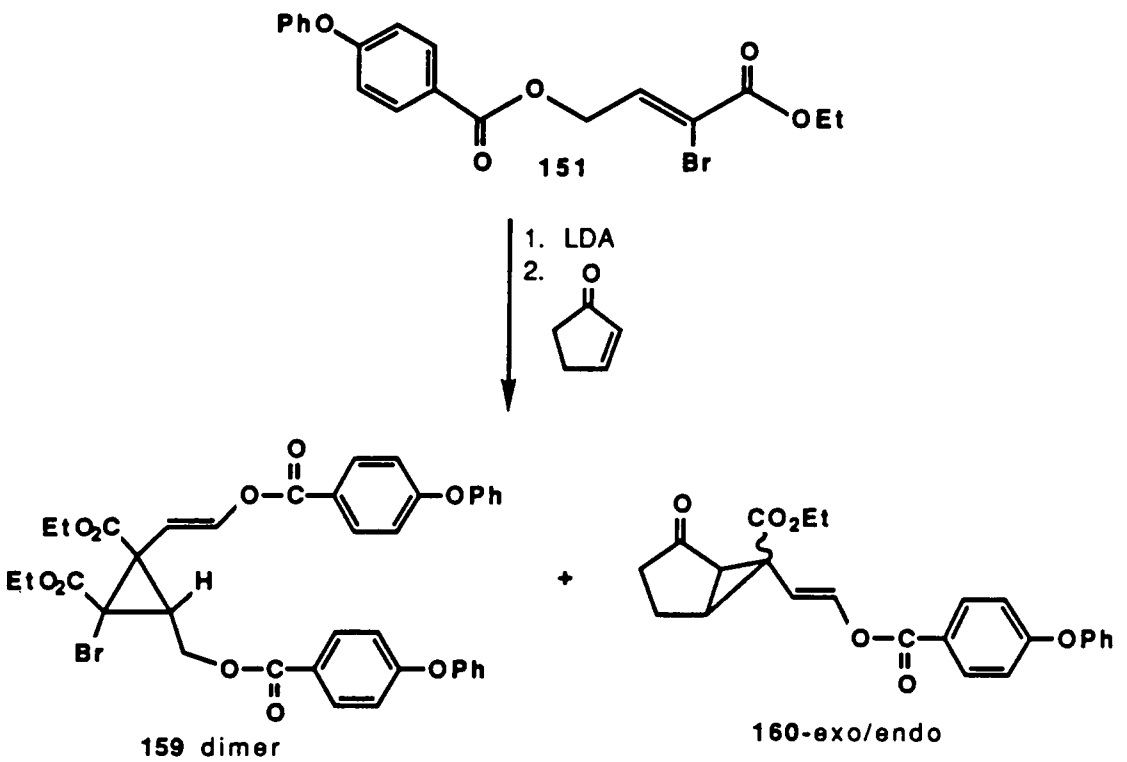
Scheme 32

The SEM [2-(trimethylsilyl)ethoxymethyl] and MEM (methoxyethoxymethyl) groups, however, were cleaved during bromination, so it was necessary to use another protecting group during the bromination/debromination sequence, remove it, and then introduce the desired protecting group as shown in Scheme 33.



Scheme 33

Vinylcyclopropanation. Next the vinylcyclopropanation reactions of the above crotonates were studied. One of the expected hazards of placing an oxygen in the 4-position of the crotonate is lowering the acidity of the γ-protons thereby hampering enolization of the crotonate. This was definitely the case with ethyl [4-(4'-phenoxy)benzoyl]-2-bromo-2-crotonate (**151**) (see Figure 2). At -110 °C, self-condensation was the major reaction yielding the undesired cyclopropane **159**. By raising the temperature of the reaction to -78 °C to facilitate enolization, the desired vinylcyclopropane became the major product (40% isolated yield), but self-



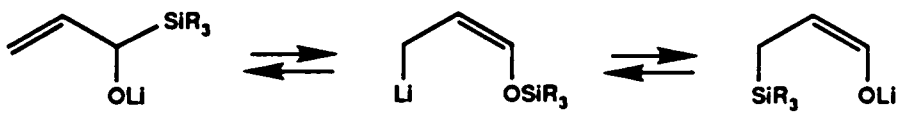
Reaction Temp	Dimer:Endo:Exo
-100 °C	1:1.5:2
-78 °C	0.5:1:2
-40 °C	polymer

Figure 2. Vinyclopropanation of 2-cyclopentanone with ethyl 2-bromo-4-[(4'-phenoxybenzoyl)oxy]-2-butenoate.

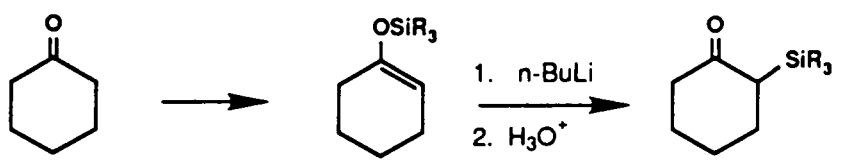
condensation of the dienolate still interfered. Increasing the temperature further to -40 °C only led to complete decomposition of the dienolate.. With [4-(4'-benzoxy)benzoyl]-2-bromocrotonate (**152**) the problem was exacerbated. At -78 °C, the dimer (**161**) was the major product, so an even lower yield of vinylcyclopropanes was obtained (see Figure 3).

Changing the oxygen functionality from an ester to a *tert*-butyldimethylsilyl (TBS) protected alcohol improved the yield of the vinylcyclopropanation reaction (see Table 5). The enol ether terminated vinylcyclopropanes were isolated as their endo- and exo-isomers. Surprisingly in all of the vinylcyclopropanes only the E-isomer of the enol ether double bond was formed. The dienolate of this crotonate appeared to be even more unstable than the one formed from ethyl 2-bromocrotonate. Polymerization was extremely facile. Increasing the dilution of the reaction did not lessen the amount of decomposition of the dienolate, so the isolated yields of vinylcyclopropanes were only 40-50% from cyclopentenone and cyclohexenone and 4.5% from cycloheptenone. Lowering the reaction temperature was not possible because the solvent began to freeze.

This increased tendency towards decomposition could be from interfering silicon migrations. Migrations of silicon from oxygen to carbon in anions of this type has been



well documented.[106] Recently Corey has utilized such a migration as the basis for preparing α-silyl ketones.[107] Evans had similar problems which he overcame by



increasing the bulk of the alkyl groups on the silicon thus impeding its migration.[108] In

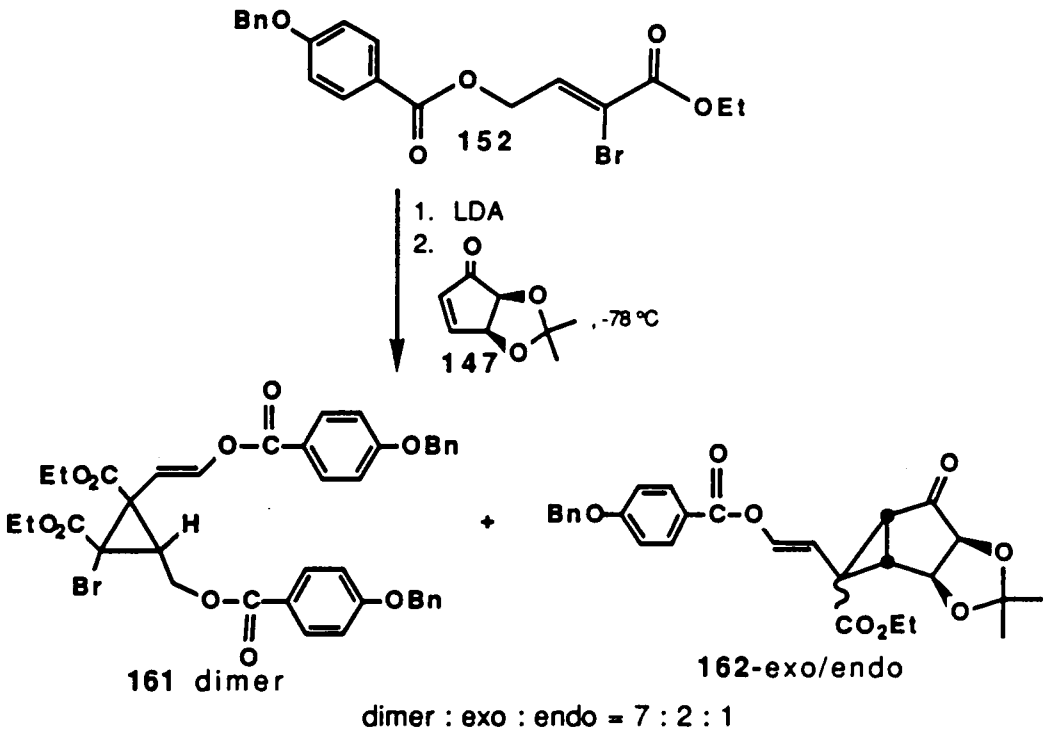
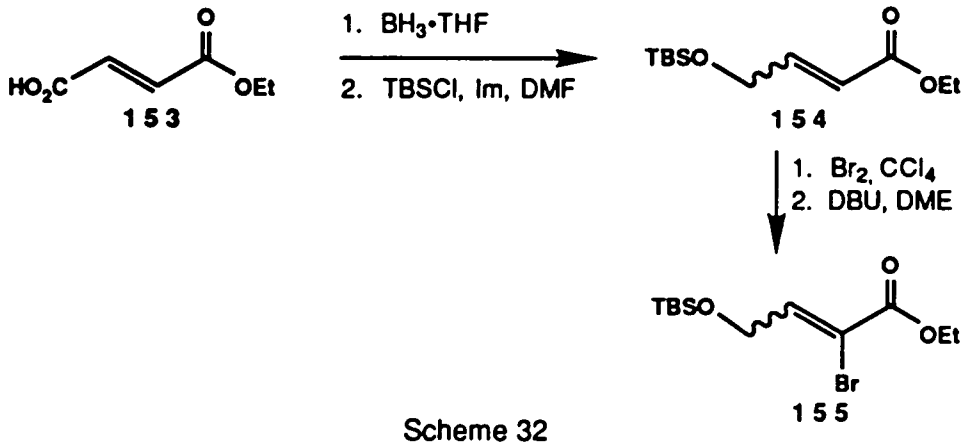


Figure 3. Vinylcyclopropantion of 2-cyclopentanone with ethyl 2-bromo-4-[(4'-benzyloxybenzoyl)oxy]-2-butenoate.

this vein, various silyl protecting groups with bulkier alkyl groups were tried. This only led to a decrease in the yields of vinylcyclopropanes. It was immediately apparent



Scheme 32

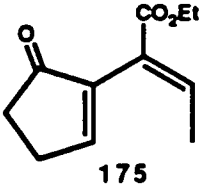
that the bulkier groups were only hindering enolization. At -110 °C, the starting crotonate was recovered. At higher temperatures (-78 °C), in analogy with the ethyl 4-benzoate-2-bromocrotonates, the vinylcyclopropanes were formed but in very low yields due to the instability of the dienolate at this temperature. For the bulkier alkyl groups, the higher temperatures required for enolization resulted in substantial decomposition of the dienolate, so the vinylcyclopropanes were formed in only very low quantities.

Moving the silicon further from the oxygen of crotonate by using a SEM protecting group, as in crotonate **158**, gave the best yields in the vinylcyclopropanation reactions (64%, see Table 5). Surprisingly, the MEM group did not follow suit. Only a 26% yield of vinylcyclopropanes was isolated using crotonate **157**. Clearly the full implications of placing an oxygen-containing substituent in the 4-position of the crotonate are not totally understood. Perhaps when this reaction is better understood, it will be possible of control the deleterious side-reactions and improve the yield of vinylcyclopropanes. For the purpose of present applications, however, the unoptimized yields sufficed for continuing the study of this reaction by its application to synthesis.

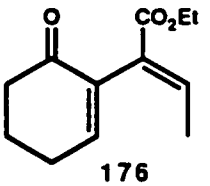
4. Rearrangements of Vinylcyclopropanes

The last part of the [2+3] annulation methodology requires the conversion of the vinylcyclopropanes to their corresponding diquinanes. Ultimately it is desired that the overall transformation from enone to diquinane be a mild, one-pot procedure. For such a procedure, mild alternatives to pyrolysis would have to be found. In the following sections, the results of the pyrolytic and nonpyrolytic conditions for vinylcyclopropane rearrangements will be presented.

Pyrolytic Rearrangements. When the vinylcyclopropanes in Tables 4 and 5 were subjected to flash vacuum pyrolysis (10^{-4} to 10^{-6} mmHg) and the corresponding cyclopentenes were isolated. Apparently two competing processes were possible during pyrolysis as evidenced by isolation of enones **175** and **176** in addition to diquinanes

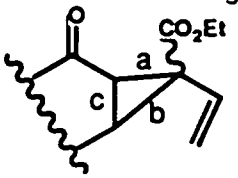


175



176

178 and **179**. Enones of this type have been observed when cleavage of bond b of the cyclopropane is possible.[1,10b] Such diradical cleavage followed by hydrogen abstraction



could in principle lead to **175** and **176**. However the steric integrity of these enones (only the E isomer was formed) makes a concerted [1,5]-sigmatropic hydrogen shift (or a retro-ene reaction) followed by conjugation of the double bond the more likely pathway. In accordance with the known dominance of retro-ene processes at lower temperatures[1d], enones **175** and **176** were not formed at higher temperatures

(see Table 6). Thus at lower temperatures (500 °C) enone **175** and diquinanes **178** were formed in a ~1:1 ratio from **144**-endo, while at higher temperatures (550 °C) the diquinane was the exclusive product. With the endo-vinylcyclopropanes an additional side product **177** was formed at low temperatures (see Table 6). This is the bicyclic product that would be expected from a Cope rearrangement of the enol form of vinylcyclopropane **144**-endo. As with the other side products, its formation was completely suppressed at higher temperatures.

Another attempt at minimizing enone formation was made by subjecting the silyl enol ethers of the vinylcyclopropanes to pyrolysis. By placing a double bond in the starting material, it was thought that formation of a product which would introduce one more double bond into the ring (enones **175** or **176**) would be unfavored. When the silyl enol ether of **144**-exo was pyrolyzed, none of the enone was detected, but another unexpected bicyclic product, resulting from a Cope rearrangement, was isolated in addition to the silyl enol ether of diquinane **178**. This was the same product formed in trace quantities form pyrolysis of **144**-endo at lower temperatures. The reaction cannot obviously proceed directly via the Cope rearrangement, since in the exo isomer the vinyl group and the carbon-carbon double bond of the enol ether are on opposite faces of the cyclopropane ring. This reaction must involve prior cleavage of the cyclopropane ring followed by bond rotation and ring closure yielding the isomeric endo vinylcyclopropane which can undergo Cope rearrangement. The endo isomer exhibited completely different behavior leading to the discovery of yet another rearrangement pathway, which will be discussed in the section on nonpyrolytic rearrangements.

Even with the temperatures of pyrolysis optimized, only the vinylcyclopropanes derived from cyclopentenones furnished cyclopentenes in synthetically useful yields (see Table 7). Pyrolysis of vinylcyclopropanes **146**-exo/endo furnished the

Table 6. Pyrolysis Temperature Profile for the Vinylcylopropanes.[3a]

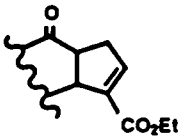
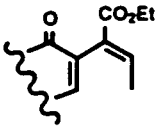
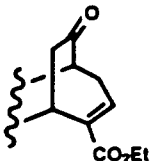
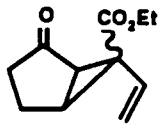
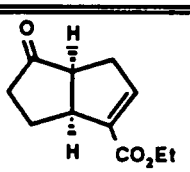
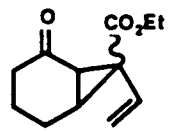
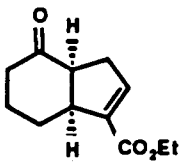
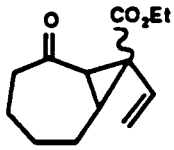
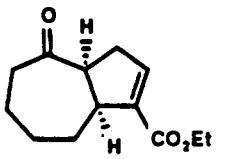
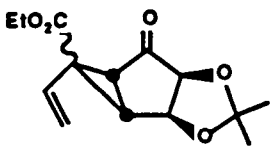
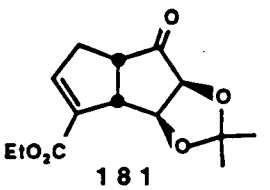
Vinylcyclopropane	temperature	 178 and 179	 175 and 176	 177
8-endo	500 °C	47	42	11
8-endo	550 °C	98	2	0
silylenolether of 8-exo	550 °C	48	0	52
25-exo	575 °C	69	31	0
25-exo	600 °C	100	0	0

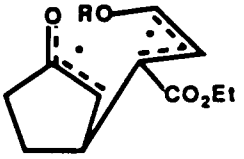
Table 7. Pyrolysis of the Unsubstituted Vinylcyclopropanes.[3a]

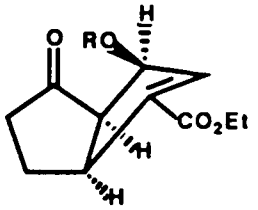
Vinylcyclopropane	Cyclopentene
 144-exo/144-endo	 178 (43)[a] (550°)[b]
 145-exo/145-endo	 179 (19)[a] (600°)[b]
 146-exo/146-endo	 180 (21)[a] (600°)[b]
 148-exo/148-endo	 181 (51)[a] (550°)[d]

a) isolated yield, b) temperature of pyrolysis

corresponding cis-fused cyclopentene **180** in low yield. In spite of the low yield, formation of perhydroazulene skeleton **180** is a particularly useful result, since it has been shown that intramolecular cyclopropanation of dienes by keto carbenoids does not reproducibly lead to seven-membered rings.[109]

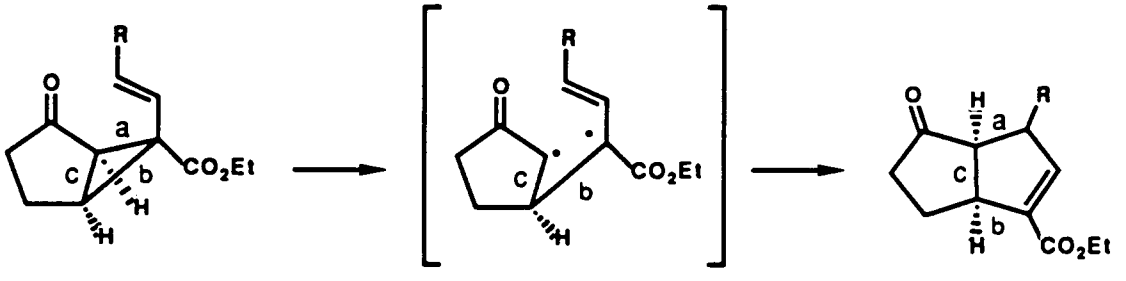
The enol ether terminated, or oxygenated vinylcyclopropanes, were also pyrolyzed to give two isomeric cyclopentenes, the one with the 4-oxy substituent endo predominating (see Table 8). These results parallel the observation that radical closures of five-membered rings usually produce the less stable, endo isomer as the





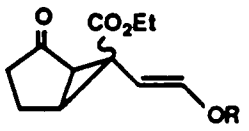
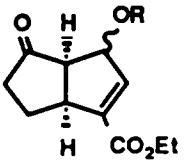
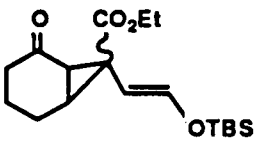
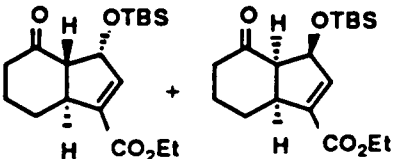
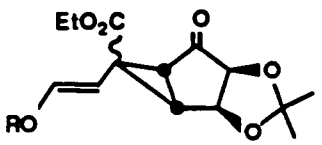
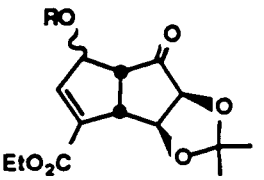
major product.[110] Pyrolysis of vinylcyclopropane **164** gave diquinanes **183**-exo/endo in low yield. The poor yield can most likely be attributed to the difficulty in evaporating such a high molecular weight compound, since the more volatile derivatives **163**, **165**, **166** gave diquinanes **182**, **184**, and **185** respectively in yields greater than 50%.

The chirality of the optically active vinylcyclopropanes derived from chiral enone **147** was preserved after pyrolysis in diquinanes **187**-exo/endo and **188**-exo/endo. Although bond a is cleaved during pyrolysis, since bonds b and c are left undisturbed and reclosure must lead to the *cis*-fused ring system, the stereochemistry,



and therefore the chirality, of the vinylcyclopropane is transmitted to the diquinane.

Table 8. Pyrolysis of the Oxygenated Vinylcyclopropanes.[3a]

Vinylcyclopropane	Cyclopentene
	
163, R=TBS	**182** endo/exo (72/28) (52)[a] (525°)[b]
164, R=CO(C_6H_4)OPh-*p*	**183** endo/exo (99/1) (28)[a] (525°)[b]
165, R=MEM	**184** endo/exo (73/27) (51)[a] (550°)[b]
166, R=SEM	**185** endo/exo (75/25) (57)[a] (550°)[b]
 **167**	 **186**, trans : **186**, cis 4 : 1 (57)[a] (550°)[b]
 **169**, R=OTBS	 **187** endo/exo (99/1) (75)[a] (525°)[b]
170, R=SEM	**188** endo/exo (76/24) (61)[a] (535°)[b]

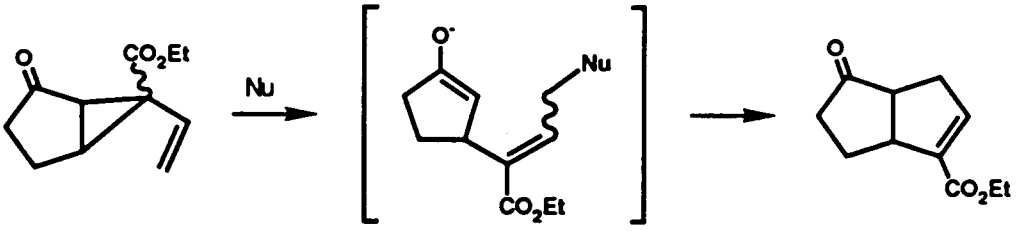
a) isolated yield, b) temperature of pyrolysis

This is the best method found so far for introducing chirality into this methodology, since the use of chiral auxiliaries on the crotonate have resulted in only poor optical induction.[102]

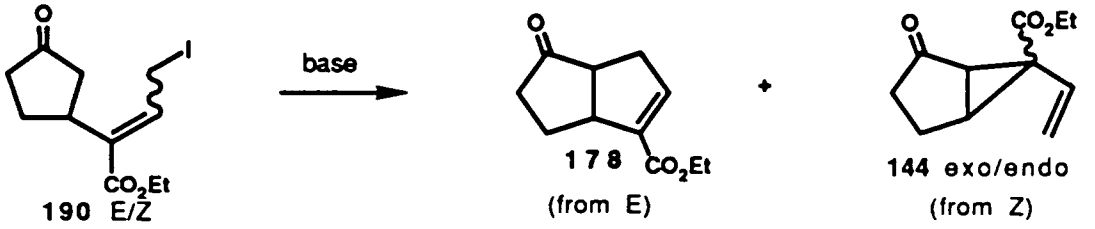
In view of the problems encountered with using flash vacuum pyrolysis on high molecular weight compounds, as seen in the pyrolysis of **164**, and the incompatibility of thermolysis with sensitive functionalities, it is apparent that there is a great need for nonpyrolytic conditions suitable for the vinylcyclopropane/cyclopentene rearrangement. Finding nonpyrolytic alternatives would therefore greatly extend the scope of this methodology.

Nonpyrolytic rearrangements. We were interested in examining other conditions using nucleophiles, radicals, or Lewis acids for promoting vinylcyclopropane rearrangement. Electrophiles such as Lewis or Bronsted acids have been used in conjunction with nucleophilic reagents for cleaving cyclopropanes. However, the conditions required for these reactions were often too vigorous and led to poor regioselectivity. Recently, the use of reagents that consist of a soft nucleophile and a hard acid or oxygenophile has led to mild procedures which cleave cyclopropanes conjugated to carbonyls with good regioselectivity. Acetyl methanesulphonate[111] and trimethylsilyl halides have been employed for such reactions.[112,113] The coordination of an oxygenophile such as silicon to the carbonyl oxygen of the carbonyl group conjugated with the cyclopropane ring both assists and directs nucleophilic cleavage of the ring. In analogy to nucleophilic additions to enones, the softer the nucleophile the more likely the nucleophilic attack will occur at the conjugated carbon, rather than directly at the carbonyl carbon.[114] Halides are usually classified as soft nucleophiles,[115] so they should open a vinylcyclopropane in an S_N2' fashion. They can

then function as good leaving groups which could be displaced by the resulting enolate anion.

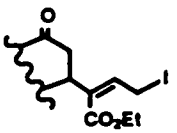
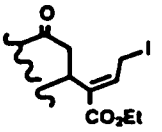
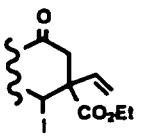
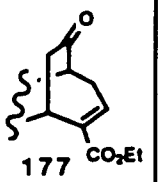
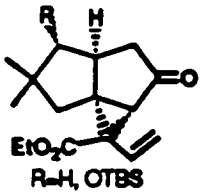


The opening of cyclopropyl ketones by TMSI (trimethylsilyl iodide) to yield iodo ketones has been reported by Miller[112] and Dieter.[113] Since iodide is soft and can act both as a nucleophile or a good leaving group, we adopted Miller's TMSI procedure. These reaction conditions were applied to vinylcyclopropanes **144**-exo/endo and **145**-exo/endo. When vinylcyclopropane **144**-exo was treated with TMSI, a mixture of isomer allylic iodides (E:Z=65:35) was formed quantitatively (see Table 9). The intermediate is most likely not an enolate anion, but the silyl enol ether of the ketone, which apparently is not nucleophilic enough to displace the iodide in situ, so the allylic iodides had to be treated with a base (either NaH or Et_4NOH) to promote cyclization. From the E allylic iodide, the diquinane was formed, while a mixture of the starting *endo*- and *exo*-vinylcyclopropanes was obtained from the Z allylic iodide. In the heterocyclic series, treatment of vinylaziridine **192** with TMSI yielded the correspond-

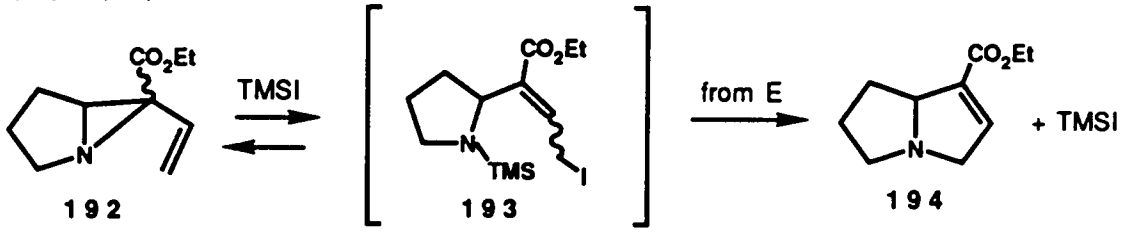


ing pyrolizidine quantitatively.[116] In contrast to the carbocyclic case, the intermediate **193** is a silylamine not a silyl enol ether. The nucleophilicity of the silylamine is responsible for the immediate displacement of the iodide in the E isomer and S_N2'

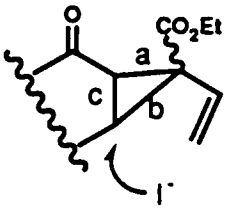
Table 9. Nucleophilic Cleavage of Vinylcyclopropanes.[3a,97]

vinylcyclopropane	nucleophile	 190-Z	 190-E	 191	 177
144-endo	TMSI	19	21	42	18
144-exo	TMSI	40	60	0	0
145-endo	TMSI	46	32	22	0
145-exo	TMSI	55	27	18	0
144-exo	TMSI/$TiCl_4$	20	80	0	0
145-exo	TMSI/$TiCl_4$	25	75	0	0
 189	TMSI	100	0	0	0
	TMSI/$TiCl_4$	100	0	0	0

displacement in the Z so that an in situ recycling of the iodides occurs leading to eventual quantitative formation of the pyrolizidine skeleton. This is similar to the openings of vinylcyclopropanes with LiI discussed in Section 1.3 of the historical.



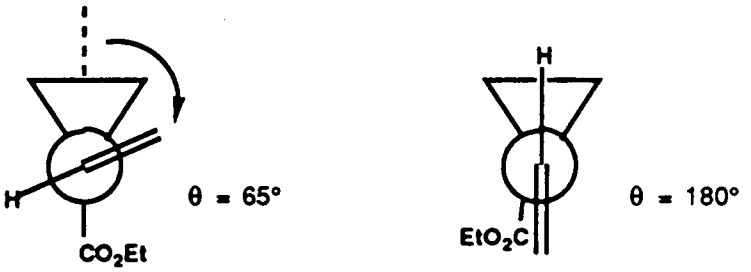
The endo isomer of **144** exhibited slightly different reactivity; a ring expanded product **191** was formed in equal amounts as the allylic iodides, and the same bicyclic compound **177** from the Cope rearrangement was formed in trace amounts. The ring expanded product results from cleavage of bond c in the cyclopropane ring. Such cleavage will occur when the π-orbitals of vinyl group are not properly aligned with those of the carbonyl (see discussion in Section 1.3).



Other vinylcyclopropanes followed suit (see Table 9) giving random mixtures of allylic iodides and sometimes a ring expanded product. One exception was vinylcyclopropanes **189**-exo and **189**-endo, the tricyclic precursors to pentalenene terpenes (see Table 9). When subjected to TMSI, these tricyclic vinylcyclopropanes gave exclusively the Z allylic iodides, which unfortunately could not be converted to cyclopentenes upon base treatment.

Although constant recycling of the recovered vinylcyclopropanes would in theory eventually lead to complete conversion of the vinylcyclopropanes to cyclopentenes, such an approach would not be very practical. Conditions needed to be found either for

controlling the stereochemistry of the allylic iodides or for in situ recycling of the Z iodides via the starting vinylcyclopropane. Changes in the reaction temperature had no substantial effect on the E:Z ratio. This was rather unexpected since this ratio (E:Z iodides) should be dependent on the conformer populations which are usually influenced by temperature. Nucleophilic attack of conformer **32a** would lead to the desired, E allylic iodide, while attack of conformer **32b** would lead to the wrong, Z allylic iodide.



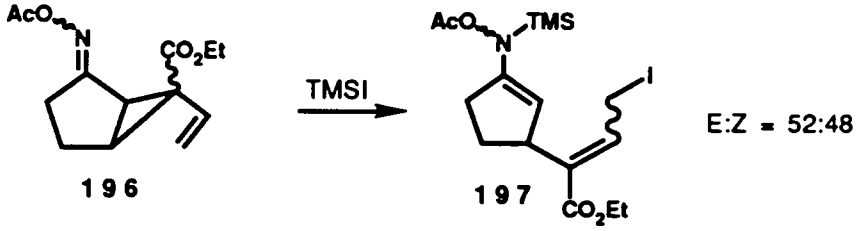
32a Synclinal (gauche)

32b Antiperiplanar

From examination of molecular models it was apparent that a Lewis acid complexing with both the ester and ketone carbonyls of the vinylcyclopropane should provide enough steric bulk to force conformer **32a** to predominate, making the desired E allylic iodide the major isomer. This prediction was borne out: $TiCl_4$ used in conjunction with TMSI lead to an improved ratio of allylic iodides (E:Z=80:20, see Table 9). This was successful, however, only for the simple vinylcyclopropanes **145**-exo/endo and **146**-exo/endo. For the tricyclic pentalenene terpene precursors **189**-exo/endo, $TiCl_4$ did not affect the reaction, and the Z-allylic iodide was still the exclusive product.[3c,97]

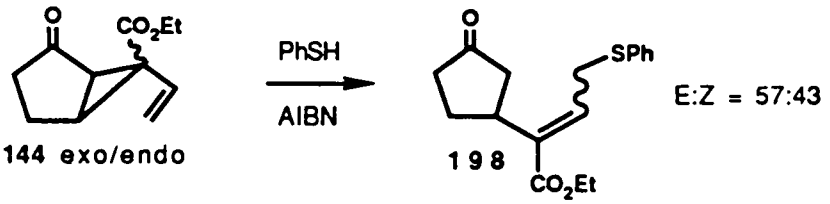
Some other attempts at improving the nonpyrolytic ring opening of the vinylcyclopropanes were briefly examined. The first involved treating the acylated oxime derivative of the vinylcyclopropyl ketone (**196**) with TMSI. It was hoped that the nitrogen of the oxime would be nucleophilic enough to displace the iodide thereby

recycling the iodides in situ as in the case of the vinylaziridine. The nitrogen of the oxime was not nucleophilic, and only the isomeric allylic iodides were isolated in a ~1:1



196 197

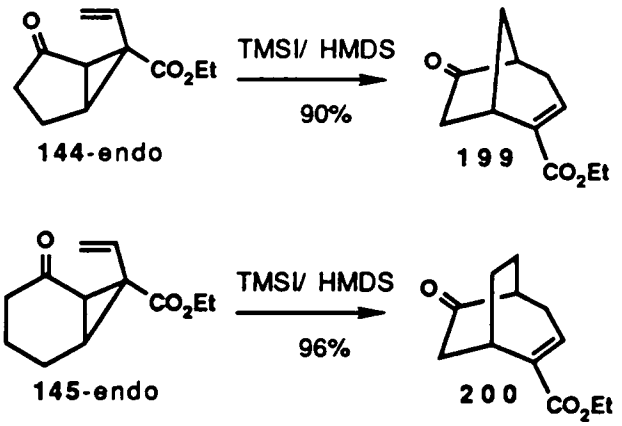
ratio. The last attempt was to open the vinylcyclopropane ring using the radical generated from thiophenol and AIBN in refluxing benzene.[47,49] The sulfur of the resulting thio ether group in **198** E and Z could then be oxidized to a sulphone to convert it to a good leaving group. Unfortunately the E:Z ratio was still poor-only ~1:1.



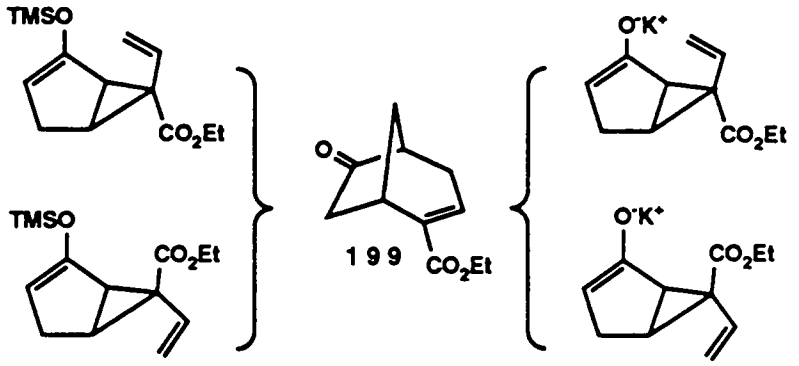
144 exo/endo 198

Similar conditions, TMSI/HMDS, TBAF (tetrabutylammonium fluoride), and $FeCl_3$, have been applied to the silyl enol ether terminated vinylcyclopropanes.[117] These conditions offer a mild alternative to pyrolysis. They also complement the pyrolytic rearrangement since the substituted diquinanes normally obtained from these conditions are those with the 4-oxy substituent exo, while the major isomer from pyrolyses is the endo (see Table 8).

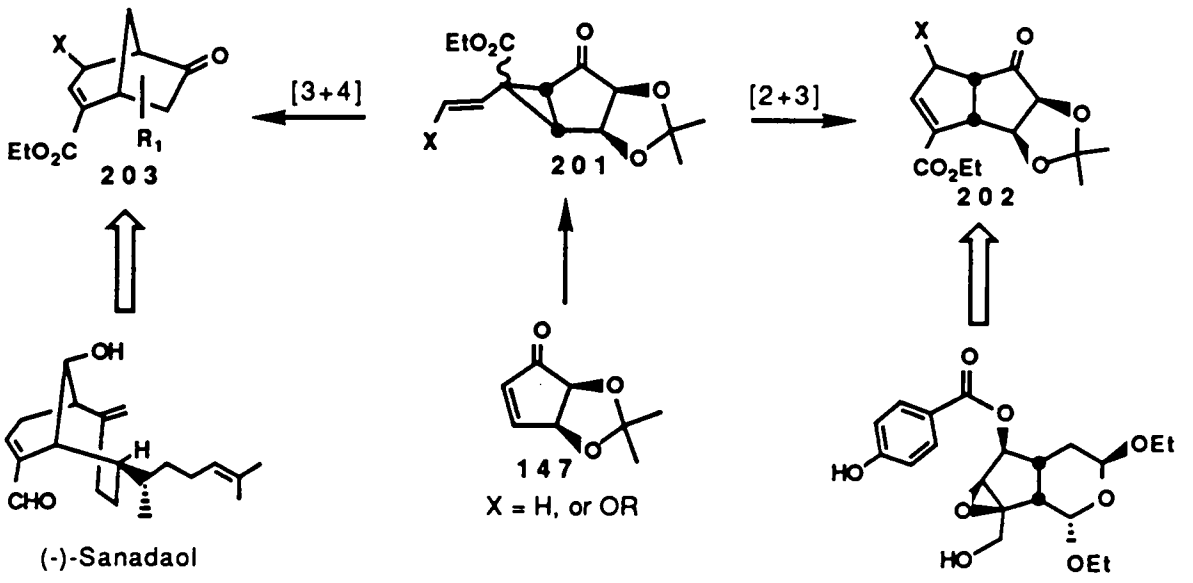
[3+4] annulations. As previously mentioned, an unexpected rearrangement occurred when the *endo*-vinylcyclopropanes were transformed into their silyl enol ethers. Treatment of vinylcyclopropanes **144**-endo and **145**-endo with TMSI/HMDS[118] (hexamethyldisilazane) at -20 °C yielded the bicyclic systems **199** and



200, in excellent yields, through a divinylcyclopropane Cope rearrangement. The same bicyclic product **199** was isolated from the pyrolysis of the silyl enol ether of **144**-exo. Later it was found that the potassium enolate anion of **144**-endo, formed from KHMDS (potassium hexamethyldisilazane) in THF, also undergoes Cope rearrangement at room temperature.



These types of bridged bicyclic skeletons are found in many natural products, therefore this mild and high-yielding rearrangement serves to make the vinylcyclopropanes more valuable synthetic intermediates. For example, from the same vinylcyclopropane, two different carbocyclic skeletons can be obtained (Scheme 34). The substituted vinylcyclopropane **201** could be converted to either a [3.3.0] or a [3.2.1] bicyclic system, **202** or **203** respectively, depending upon the conditions employed for the rearrangement. The [3.3.0] bicyclic system (**202**) is suitably

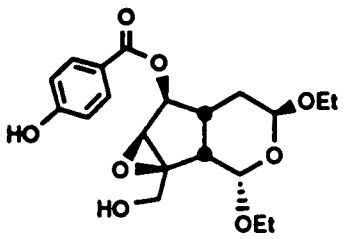


Scheme 34

functionalized for conversion into (-)-specionin,[74] while the [3.2.1] bicyclic system (**203**) could be transformed to (-)-sanadaol[119] (its unnatural enantiomer). The following section contains a discussion of the progress made in the elaboration of a vinylcyclopropane such as **201** to (-)-specionin.

5. Synthesis of (-)-Specionin.

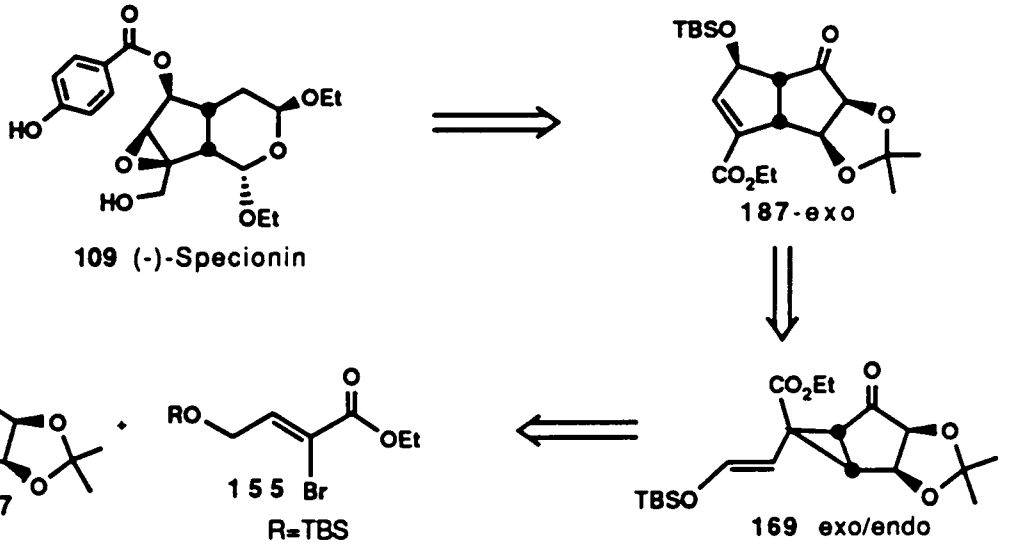
The iridoids, a highly oxygenated class of terpenes, appeared ideal for application of the new [2+3] annulation methodology. An attractive target emerged as (-)-specionin. This molecule would test the applicability of this new technology to



109 (-)-Specionin

more functionalized compounds. Having already determined that chirality of enone **147** introduces complete enantiocontrol into the vinylcyclopropanation reaction and that this chirality is preserved in the diquinane after pyrolysis (see Sections 3 and 4 of the discussion), the stage was set for application of this methodology to a synthesis of (-)-specionin.

The retrosynthetic analysis for specionin began with the realization that the skeleton of specionin could be obtained from diquinane **187**-exo by oxidative cleavage of

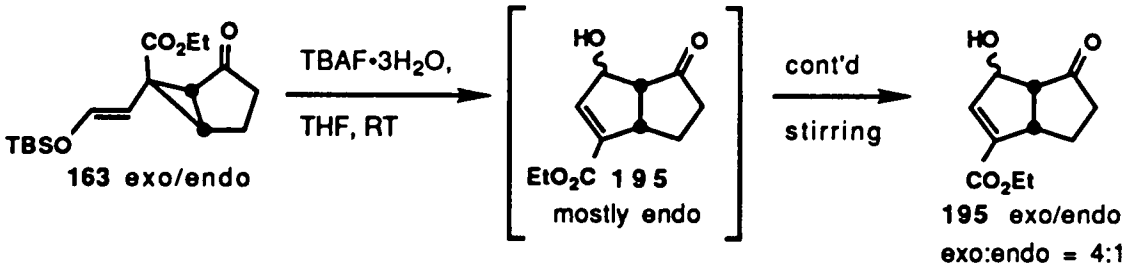


the protected diol followed by cyclization to the bis hemiacetal. The key intermediate, diquinane **187**, had been obtained by pyrolysis of vinylcyclopropanes **169**-exo/endo, which were derived from chiral enone **147** and crotonate **155**.

The initial synthetic sequence involved introduction of the benzoate ester directly into the vinylcyclopropane via the appropriately substituted 4-oxy-2-bromocrotonate **152**. This approach unfortunately had to be abandoned for it not only led to serious problems with the cyclopropanation but also with the pyrolysis (see Sections 3 and 4). This meant that a protected alcohol, not an ester, must be used in the 4-position of the crotonate. After studying various protecting groups, the SEM (trimethylsilylethoxymethyl) group was chosen because it interfered the least with the cyclopropanation reaction (see Section 3).

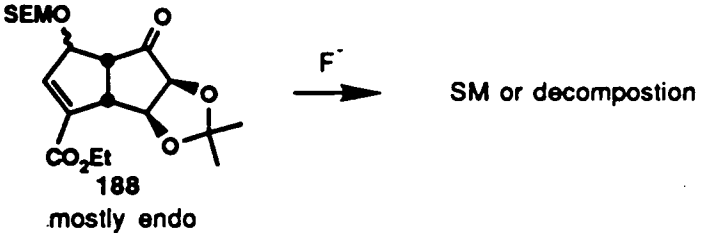
Now that the conditions for the cyclopropanation and pyrolysis reactions had been determined, the next critical step toward specionin was obtaining the correct stereochemistry (exo) for the protected alcohol of diquinane **187**. At that time pyrolysis was the only known method for promoting the vinylcyclopropane/cyclopentene rearrangement, but it gave the endo not the exo isomer as the major product. However, treatment of the endo diquinane with a base under protic conditions should lead to the more thermodynamically stable exo isomer. Equilibration studies were performed on diquinane **187**-endo. These experiments were totally unsuccessful; NaOEt/EtOH, t-BuOK/t-BuOH, and Et_4NOH/aq. DMF at room temperature all led to complete decomposition.

Concurrently in the Hudlicky group, fluoride ion had been found to catalyze both the rearrangement of vinylcyclopropanes **163**-exo/endo to diquinane **195** and the epimerization of the resulting endo alcohol to the exo alcohol.[117] Since the SEM group



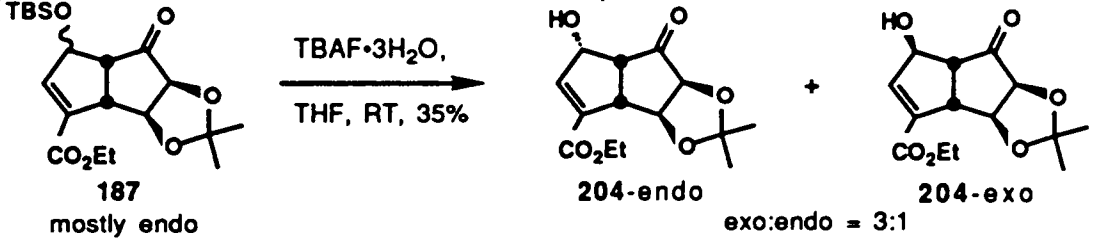
Scheme 35

is normally cleaved under similar conditions, treatment of diquinane **188**-endo with TBAF in THF should lead to exo alcohol **204**. Unfortunately, all attempts at removing the SEM group with fluoride ion were unsuccessful. Various reaction conditions, using different sources of fluoride ion, were explored to no avail; only starting material or complete decomposition were observed. Such phenomena are not unknown with

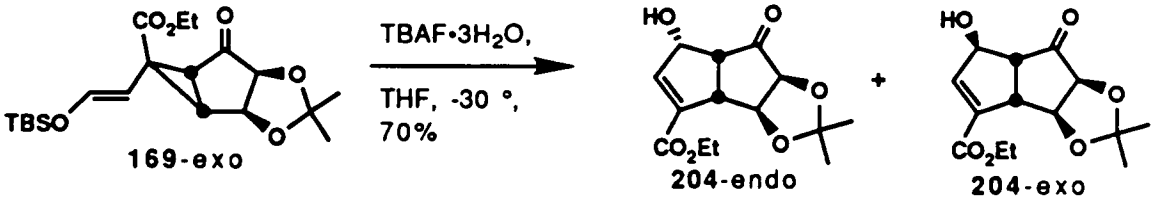


protecting groups like the SEM group.[120] This protecting group appears to be rather capricious with respect to its removal.

This left us with little choice but to use the more readily cleaved TBS (*tert*-butyldimethylsilyl) group to protect the alcohol. It was also believed that the fluoride ion used for cleavage of the TBS group could also epimerize the resulting alcohols as observed with alcohols **195**-exo/endo. Exposure of diquinane **187**, obtained from pyrolysis, to TBAF in THF at room temperature for 1 h gave a 3:1 exo:endo mixture of diquinane alcohols **204**-exo/endo. The next question to be answered was whether it



would be more efficient to use pyrolytic conditions for the rearrangement and then epimerize with fluoride, or to promote the rearrangement and epimerization directly with fluoride. Pyrolysis of the vinylcyclopropanes **169**-exo and **169**-endo gave predominantly **187**-endo (75%, endo:exo=75:25; see Table 8, Section 4). The fluoride catalyzed rearrangements usually proceeded in lower yields but with predominate formation of the desired exo isomer. The low yields of the fluoride reactions were most likely from the prolonged exposure and higher temperatures needed for epimerization; the rearrangement itself occurs instantaneously according to TLC. To test this hypothesis, a small quantity of vinylcyclopropane **169**-exo was treated with TBAF in THF at -40 °C, and the diquinane alcohols were isolated in a 70% yield (exo:endo = 1:1).

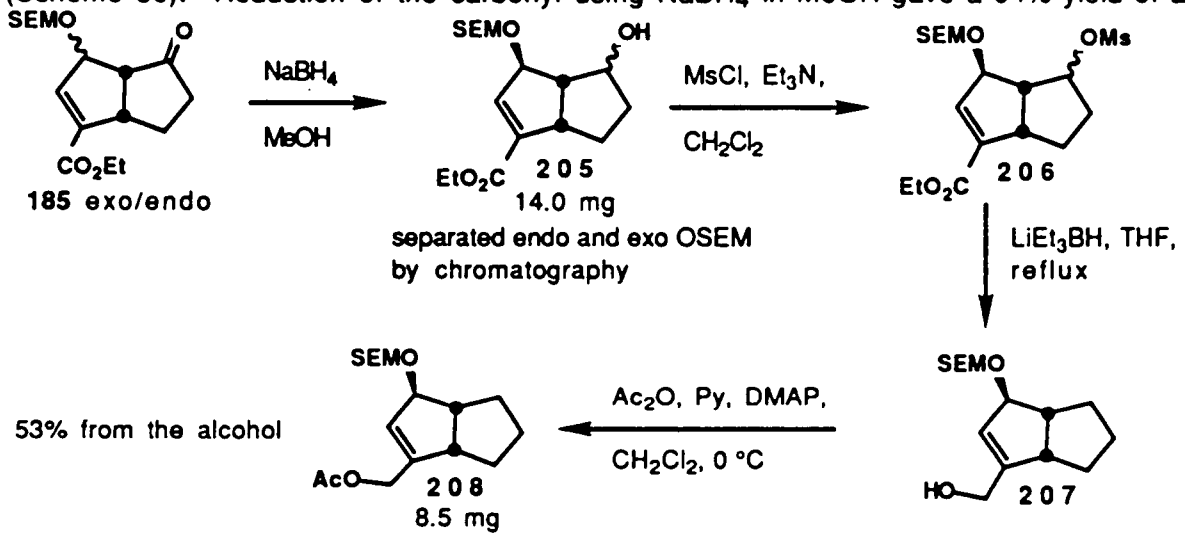


This yield was comparable to that of the pyrolysis and the exo:endo ratio was better, so it appeared that the best method for the rearrangement and epimerization was immediate termination of the fluoride rearrangement reaction, separation of the isomeric alcohols, and then treatment of the endo isomer with fluoride for an extended period to promote epimerization to the exo alcohol. In this manner, the initially formed exo alcohol **204**-exo would not be decomposed by the basic fluoride ion. When this sequence was carried out on a larger scale the initial rearrangement proceeded in 86% yield (exo:endo =1:2). Retreating the endo isomer gave an overall 46% yield of the exo isomer and 16% yield of the endo.

The next major hurdle was conversion of the ketone to a methylene. Not only is this carbonyl very hindered, but the neighboring acetonide may preclude using many

well-known methods for converting hindered carbonyls to methylenes.[121] Most of the methods for such hindered ketones either proceed through radical anion intermediates, which could result in elimination of the acetonide through cleavage of the C-O bond α to the ketone,[122] or use acidic conditions which may also cleave the acetonide. In view of this possibility, it appeared that the best route would be conversion of the ketone to a sulphonate and displacement of this sulphonate with super hydride.[123] Another advantage to this sequence was that the super hydride should also simultaneously reduce the ester carbonyl to the required allylic alcohol.

Because of the difficulties in obtaining large quantities of enone **147**,[124] a model study was performed. At the time the model study was run, it was still thought that the SEM group would be used in the synthesis, so diquinanes **185**-exo/endo were chosen for the study. Although the ketone group in **185** is not hindered, this would test the hypothesis that concomitant reduction of the ester would not interfere with the reaction and that the reduction would occur exclusively 1,2. This sequence proved to be quite effective (Scheme 36). Reduction of the carbonyl using $NaBH_4$ in MeOH gave a 94% yield of a

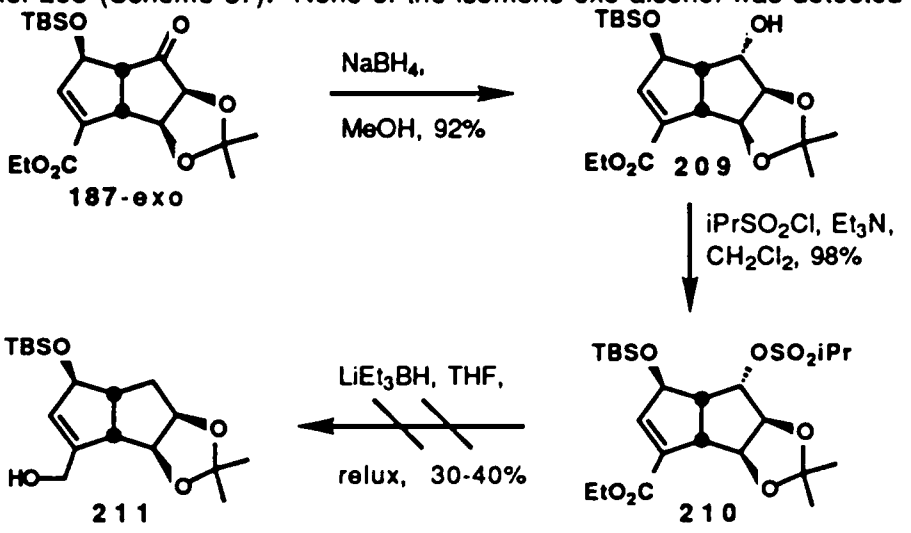


Scheme 36

mixture of α and β alcohols (**205**). At this point the diquinanes with the endo and exo

OSEM groups were easily separable by flash chromatography,[125] so only the diquinane with the correct stereochemistry of the OSEM group (exo) was carried on. Treatment of the alcohols with methane sulphonyl chloride and triethylamine in CH_2Cl_2 gave crude mesylates **206**, which were subjected to super hydride ($LiEt_3BH$) without purification. At room temperature in THF, super hydride only reduced the ester to the allylic alcohol; no displacement of the sulphonate was observed. Higher temperatures were necessary to induce displacement of the sulphonate. Acetylation of the allylic alcohol gave acetate **208** in 53% overall yield from the epimeric alcohols.

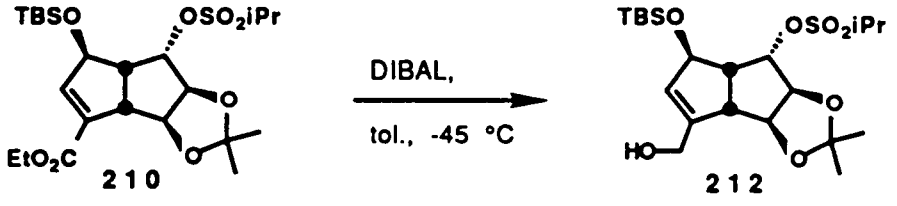
For diquinane **187**-exo, it seemed prudent to make one more slight modification. Besides using the TBS protecting group rather than the SEM, the isopropyl sulphonate not the methyl sulphonate would be used. Hua had found during his hirsutene synthesis that with hindered ketones, a side reaction, attack of the hydride at sulphur, can occur resulting in recovery of the of the starting alcohol.[126] By using the more bulky isopropyl sulphonate, this side reaction could be avoided. Following suit, the ketone of diquinane **187**-exo was reduced to the alcohol with $NaBH_4$ to give a 92% yield of the endo alcohol **209** (Scheme 37). None of the isomeric exo alcohol was detected by TLC or



Scheme 37

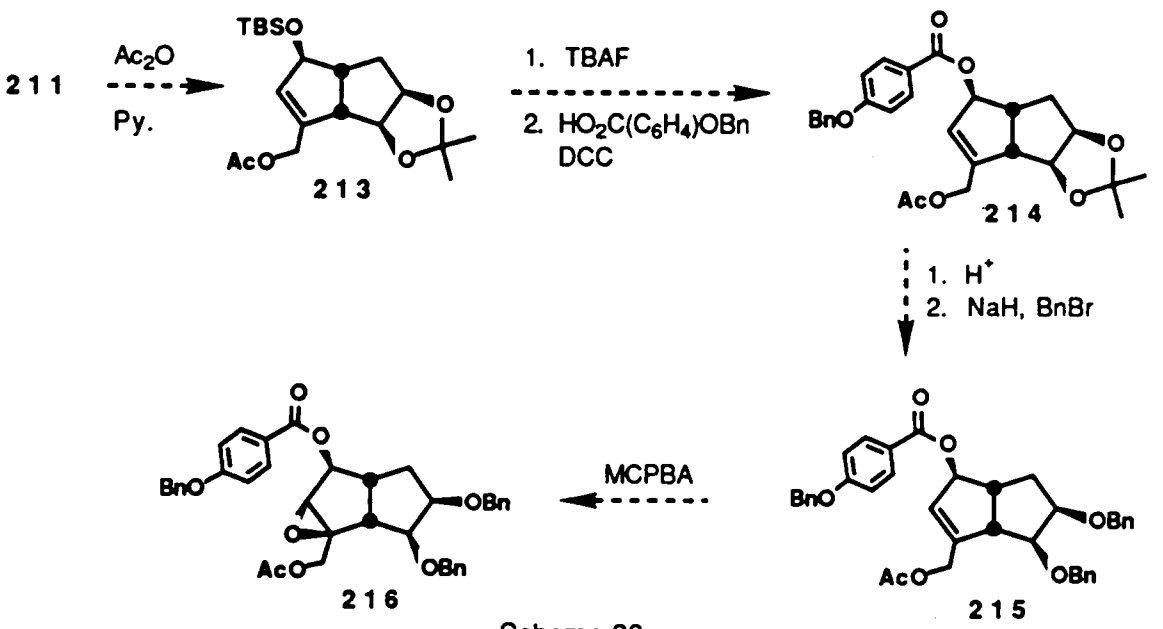
proton NMR. Sulphonation of the alcohol was straightforward (98% isolated yield).

Treatment of sulphonate **210** with superhydride in refluxing THF for 1 h yielded a mixture of products, one of which being so nonpolar was easily isolated (30%). From the ^{1}H NMR, MS, and HRMS spectra, the nonpolar compound was tentatively identified as desired alcohol **211**. The more polar products were not readily separated, but the sulphonate group was easily visible in the ^{1}H NMR spectrum, so alcohol **212** (p. 72), from 1,2 reduction of the ester, was assumed to be present in the mixture. Thus it was thought that prolonged reaction time should allow for complete conversion of **210** to the reduced diquinane **211**. This initial study was carried out on a small amount of material, precluding complete spectral analysis of the compound. When more material was obtained, the IR, ^{13}C NMR, and two-dimensional proton/carbon correlation NMR spectra revealed that this compound was <u>not</u> allylic alcohol **211**. The compound must be a structural isomer of **211** because of the mass spectra data. The ^{13}C NMR spectrum shows no vinylic carbons, and instead of a quaternary carbon, it has an additional CH resonance, while the IR spectrum clearly shows that there is no OH group. This suggests the presence of additional ring rather than a carbon-carbon double bond, so the compound is most likely a cyclic ether. The low yield of the displacement reaction may then be attributed to side reactions from concomitant reduction of the ester. It has already been shown that the ester in sulphonate **210** may be reduced quantitatively by DIBAL (diisobutylaluminum hydride) to a allylic alcohol **212**. Protection of the allylic



alcohol prior to treatment with super hydride may eliminate the side reactions. The deoxygenated product **211** may then be obtained as a protected alcohol.

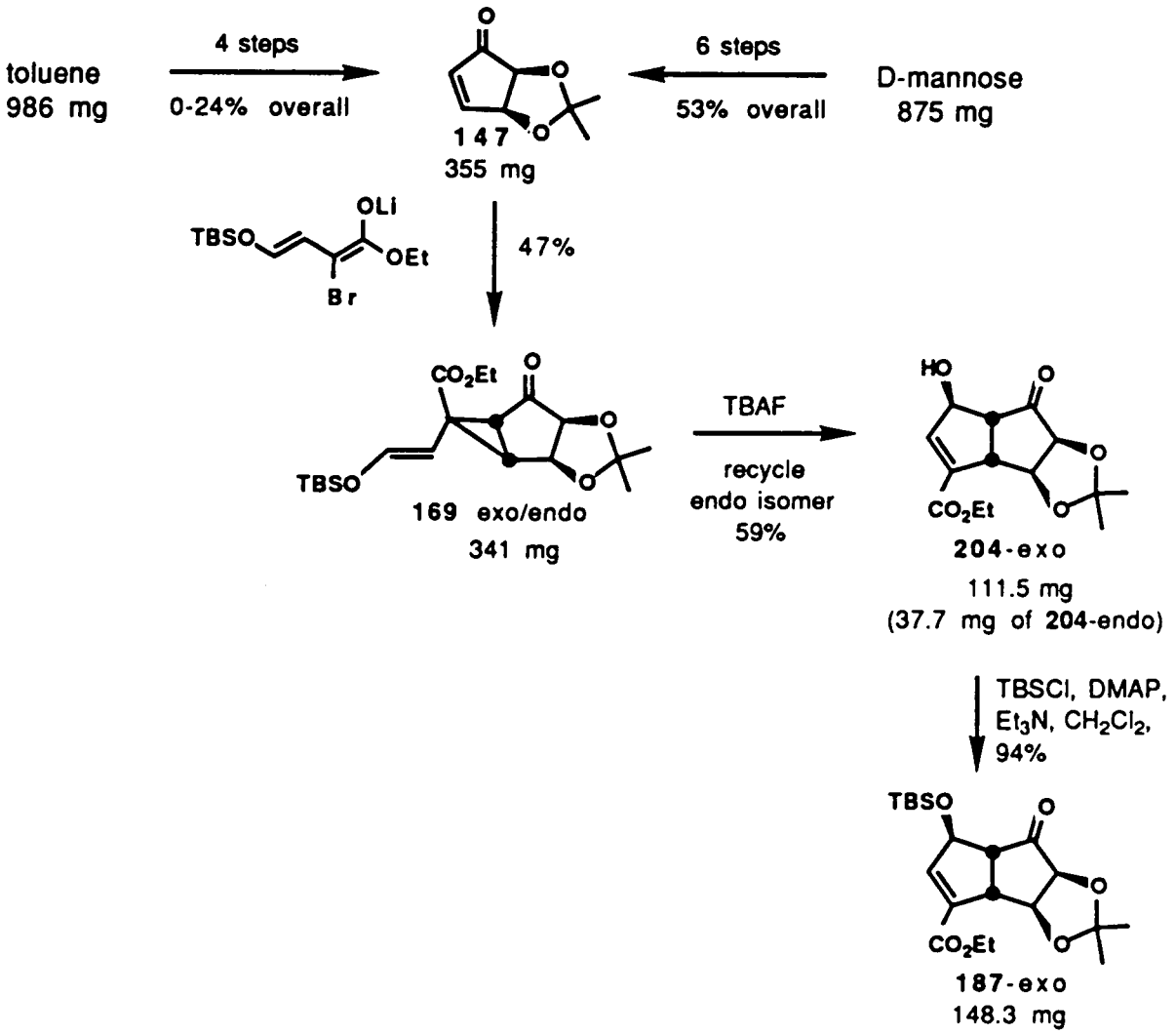
Diquinane **187**-exo has the carbocyclic skeleton with the correct stereochemistry and functionality for conversion to specionin. The remaining steps of the synthesis involve functional group manipulation only. If the route described above does give **211**, then the synthesis could be completed as shown in Scheme 38. The primary alcohol in diquinane **211** would be acetylated using standard conditions. Next the benzoate ester moiety could be introduced via DCC (dicyclohexylcarbodiimide) coupling of the alcohol obtained from exposure of the acetylated diquinane **213** to TBAF. The final step would involve changing the diol protecting group of **214** from an acetonide to a dibenzyl ether. Epoxidation of compound **215** would conclude a formal synthesis of specionin, since epoxide **216** has already been converted to specionin by Leonard.[76]



Scheme 38

The overall approach to (-)-specionin can be summarized as shown in Scheme 39. Enone **147** is available in optically pure form from either toluene via a microbial oxidation[103] or from D-mannose.[104b] Vinylcyclopropanation of enone **147** with the lithium dienolate of crotonate **155** gives vinylcyclopropanes **169**-exo/endo. After a

fluoride catalyzed rearrangement and epimerization, reprotection of the alcohol **204**-exo as a TBS ether yields diquinane **187**-exo which possesses the correct stereochemistry for further elaboration to (-)-specionin.



6. Conclusions

The [2+3] annulation methodology was studied in more detail, and the vinylcyclopropanation and pyrolysis reactions for this sequence were optimized. Various conditions for nonpyrolytic conversion of the vinylcyclopropanes to the corresponding cyclopentenes were examined. A new rearrangement pathway, resulting in the formation of [3.2.n] bicyclic systems was discovered.

The [2+3] annulation sequence was then extended by using 4-oxycrotonates in the vinylcyclopropanation reactions. These enol ether terminated vinylcyclopropanes were pyrolyzed to give the substituted diquinanes.

The versatility of the vinylcyclopropanation reaction can be seen in the incorporation of enantiocontrol by using chiral enone **147**, its extension to more oxygenated systems, and the potential of the resulting vinylcyclopropanes to rearrange to two totally different bicyclic systems. Future work in this area would include optimization of the vinylcyclopropanation reaction using the dienolates of 4-oxy crotonates and its application to the synthesis of vinyloxiranations by using aldehydes and ketones as the electrophiles.

An approach to the formal synthesis of the iridoid specionin using the [2+3] annulation technology was examined. Diquinanes **187**-exo and **204**-exo have the carbon skeleton with the correct stereochemistry for elaboration to (-)-specionin. Future work would involve improving the yield of the vinylcyclopropanation and finding an alternative method for the vinylcyclopropane/cyclopentene rearrangement that would give both better stereocontrol and an improved yield of diquinane **187**-exo. It is also necessary to find a method for deoxygenation of diquinane **187**-exo in order to access **211**, which would allow for completion of the synthesis by the path illustrated in Scheme 38.

IV. EXPERIMENTAL

All nonhydrolytic reactions were carried out in an argon atmosphere with standard techniques for the exclusion of air and moisture. Glassware used for moisture-sensitive reactions was flame-dried under vacuum. THF, ether, DME, and benzene were distilled from benzophenone ketyl. Dichloromethane, diisopropylamine, diisopropylethylamine, triethylamine, and toluene were distilled from calcium hydride. Thin layer chromatography was performed on Kieselgel 60F-254 plates (analytical 0.25mm thickness, preparative, 0.5mm; EM Reagents). Flash chromatography[103] was performed on Kieselgel 60 (EM Reagents, 230-400 mesh). Mass spectra were recorded on a Varian MAT-112 instrument (low resolution) or on a double focusing VG 7070 E-HF instrument (exact mass). Infrared spectra were recorded on a Perkin-Elmer 283B or 710B instruments. Proton NMR spectra were obtained on a Bruker WP-270 instrument. Proton chemical shifts are reported in parts per million (ppm) relative to $CHCl_3$ as an internal reference (7.24 ppm). Carbon NMR spectra were recorded on Bruker WP-270 or NR-80 instruments. Carbon chemical shifts are reported in ppm relative to the center line of the $CHCl_3$ triplet (77.0 ppm) and the multiplicity is indicated by CH_3, CH_2 CH, C (INEPT experiments). Rotations were recorded on a Perkin Elmer 241 digital polarimeter.

Z Ethyl 2-bromo-4-[(4-phenoxybenzoyl)oxy]-2-butenoate (151). To a solution of 18-crown-6 (80 mg, 0.3 mmol) in DME (30 mL) at room temperature was added potassium 4-phenoxybenzoate (3.0 g, 11.9 mmol). Stirring was continued for 40 min, after which neat ethyl 2,4-dibromo-2-butenoate (1.63 g, 0.6 mmol) was added. The whitish suspension slowly turned dark-brown upon continued stirring at room temperature. After 6 h, the reaction mixture was filtered through celite. Evaporation of the solvent gave 2.66 g of a green viscous oil.

Purification by flash chromatography (silica gel, 10% deactivated with H_20; 6:1 hexane/ethyl acetate) gave 1.83 g of a cream-colored solid (75%). **151: mp** 49.5-51.5 °C; R_f=0.26 (15:1 hexane/ethyl acetate); **IR** (neat) 3050, 2980, 1735, 1725, 1610, 1585, 1508, 1490, 1240, 1160, 1100 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.32 (t, 3H, J=7.2 Hz), 4.28 (q, 2H, J=7.2 Hz), 5.02 (d, 2H, J=5.3 Hz), 6.98 (d, 2H, J=8.8 Hz), 7.05 (d, 2H, J=7.6 Hz), 7.18 (t, 1H, J=7.6 Hz), 7.38 (t, 2H, J=7.6 Hz), 7.46 (t, 1H, 5.3 Hz), 8.01 (d, 2H, J=8.8 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 62.5 (CH_2), 63.8 (CH_2), 117.1 (CH, double intensity), 119.9 (CH, double intensity), 123.5 (C), 124.4 (CH), 129.8 (CH, double intensity), 131.7 (CH, double intensity), 139.8 (CH), 143.6 (C), 155.3 (C), 161.2 (C), 162.0 (C), 165.2 (C); **MS** (70 eV, *m/e* (rel. int.)) 406 (4.4) M^++2, 404 (4.6) M^+, 197 (100), 162 (10), 141 (12), 115 (11), 113 (10), 86 (32), 84 (51); **HRMS**, calcd for $C_{19}H_{17}BrO_5$: 404.0259. Found: 404.0248. **Anal Calcd for** $C_{19}H_{17}BrO_5$: C, 56.43; H, 4.20. Found: C, 56.23; H, 4.13.

E and Z Ethyl 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]-2-butenoate (155). To a solution of ethyl 4-hydroxy-2-butenoate (32.43 g, 0.25 mol) in DMF (150 mL) was added *tert*-butyldimethylsilyl chloride (45.2 g, 0.30 mol) and imidazole (25.5 g, 0.37 mol). Stirring was continued at room temperature for 4.5 h, whereupon TLC indicated that none of the alcohol remained. The reaction was quenched slowly with saturated aqueous $NaHCO_3$ and extracted with ether (3x100 mL). The combined ether extracts were washed with saturated aqueous $NaHCO_3$, water, and brine, and then dried ($MgSO_4$). Evaporation of the solvent gave 50.5 g (83%) of a very pale yellow liquid. R_f=0.62 (3:1 hexane/ethyl acetate); **^{1}H NMR** ($CDCl_3$) δ 1.04 (s, 3H), 1.06 (s, 3H), 1.90 (s, 9H), 1.27 (t, 3H, J=7.1 Hz), 4.17 (q, 2H, J=7.1 Hz), 4.31

(dd, 2H, J_1=3.4, J_2=2.4 Hz), 6.07 (dt, 1H, J_1=15.5, J_2=2.4 Hz), 6.97 (dt, 1H, J_1=15.5, J_2=3.4 Hz).

The crude ethyl 4-[(*tert*-butyldimethylsily)oxy]-2-butenoate was dissolved in CCl_4 (150 mL), cooled to 0 °C, and a solution of bromine (44.4 mL, 0.75 mol) in CCl_4 (100 mL) was added over 1 h. Stirring was continued at 0 °C for 1 h then at room temperature for 1.0 h. The reaction mixture was quenched with saturated aqueous Na_2SO_3 and the aqueous layer extracted with CH_2Cl_2. The organic extracts were combined, washed with brine and dried ($MgSO_4$). Removal of the solvent gave 66.72 g (79%) of a yellow oil pure enough to be used without distillation. **^{1}H NMR** ($CDCl_3$) δ 0.09 (s, 6H), 0.91 (s, 9H), 1.31 (t, 3H, J=7.1 Hz), 4.00 (dd, 1H, J_1=11.8, J_2=1.9 Hz), 4.20-4.30 (m, 3H), 4.40 (ddd, 1H, J_1=10.9, J_2=2.9, J_3=2.0 Hz), 4.58 (d, 1H, J=10.9 Hz).

The crude dibromides (66.72 g, 0.17 mol) in DME (250 mL) were cooled to 0 °C, and a solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (27.4 mL, 0.18 mol) in DME (100 mL) was added over 45 min. Stirring was continued at 0 °C for 1 h. The resulting black solution was then filtered through a plug of silica gel with ether as the eluant. The ether solution was washed twice with 3N HCl. The aqueous layer was extracted twice with ether, and the combined ether extracts were washed with brine and dried ($MgSO_4$). Evaporation of the solvent gave 40.5 g of a brown-orange liquid. The crude material was distilled in three portions to give 21.72 g (38%) of a 1:1 mixture of E and Z ethyl 2-bromocrotonates (**155**) as a pale yellow liquid. There is significant loss of material due to decomposition of the dibromides in the distillation pot. **bp**=90-105 °C (0.2 mmHg); **IR** (neat) 2915, 2815, 1717, 1615, 1250, 1225, 730 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.05 (s, 6H), 0.07 (s, 6H), 0.88 (s, 9H), 0.89 (s, 9H), 1.31 (t, 6H, J=7.1 Hz), 4.19-4.30 (m, 4H), 4.38 (d, 2H, J=4.9 Hz) 4.56 (d, 2H, J=4.9 Hz), 6.81 (t, 1H,

J=4.9 Hz), 7.36 (t, 1H, J=4.9 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.4 (CH_3, quadruple intensity), 14.0 (CH_3, double intensity), 18.2 (C, double intensity), 25.8 (CH_3, sextuplet intensity), 62.2 (CH_2), 62.5 (CH_2), 62.6 (CH_2), 63.7 (CH_2), 109.5 (C), 113.7 (C), 146.1 (CH), 150.9 (CH), 161.8 (C), 162.5 (C); **MS** (70 eV, *m/e* (rel. int.)) 323 (16) M^+, 321 (16), 281 (23), 279 (22), 237, (30, 235 (30), 163 (31), 75 (100), 73 (61); **HRMS,** calcd for $C_{12}H_{24}BrO_3Si$: 323.0678. Found: 323.0708. **Anal. calcd** for $C_{12}H_{24}Br0_3Si$: C, 44.58; H, 7.17. Found: C, 44.73; H, 7.25.

Ethyl 2-bromo-4-[(triisopropylsilyl)oxy]-2-butenoate (173). Prepared in 71% yield in an analogous fashion as ethyl 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]-2-butenoate. **173-E and Z isomers**: R_f=0.31 (15:1 hexane/ethyl acetate); **IR** (neat) 2939, 1730, 1710, 1610, 1461, 1367, 1224, 875 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.05 (s, 18H), 1.06 (s, 18H), 1.09-1.20 (m, 6H), 1.32 (t, 6H, J=7.1 Hz), 4.18-4.32 (m, 4H), 4.46 (d, 1H, J=4.9 Hz), 4.64 (d, 2H, J=4.9 Hz), 4.79 (d, 1H, J=4.9 Hz), 6.87 (t, 1H, J=4.9 Hz), 7.40 (t, 1H, J=4.9 Hz); **^{13}C NMR** ($CDCl_3$) δ 11.9 (CH, sextuple intensity), 12.8 (CH_3), 14.0 (CH_3), 17.9 (CH_3, 18 of them), 62.2 (CH_2), 62.5 (CH_2), 63.1 (CH_2), 64.1 (CH_2), 109.3 (C), 113.4 (C), 146.5 (CH), 151.5 (CH), 161.8 (C), 162.5 (C); **MS** (70 eV, *m/e* (rel. int.)) 323 (70), 321 (71), 159 (49), 131 (98), 103 (100), 75 (98), 61 (59); **HRMS**, calcd for $C_{15}H_{30}BrO_3Si$: 365.1148. Found: 365.1149.

Ethyl 2-bromo-4-[(*tert*-butyldiphenylsilyl)oxy]-2-butenoate (174). Prepared in 44% yield in an analogous fashion as ethyl 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]2-butenoate. **174-E and Z isomers**: R_f=0.35 (15:1 hexane/ethyl acetate); **IR** (neat) 2927, 1727, 1585, 1421, 1262, 1105, 818, 733, 699 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.047 (s, 9H), 1.05 (s, 1H), 1.17 (t, 3H, J=7.1 Hz),

1.32 (t, 3H, J=7.1 Hz), 4.12 (q, 2H, J=7.1 Hz), 4.27 (q, 2H, J=7.1 Hz), 4.43 (d, 2H, J=4.9 Hz), 4.60 (d, 2H, J=4.9 Hz), 6.93 (t, 1H, J=4.9 Hz) 7.32-7.72 (m, 20H); **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 14.0 (CH_3), 19.1 (C, double intensity), 26.8 (CH_3, sextuple intensity), 62.1 (CH_2), 62.4 (CH_2), 63.4 (CH_2), 64.4 (CH_2), 110.0 (C), 113.9 (C), 127.8 (CH, octuple intensity), 129.8 (CH, quadruple intensity), 132.9 (C), 133.1 (C), 135.4 (octuple intensity), 145.5 (CH), 150.0 (CH), 161.6 (C), 162.2 (C); **MS** (CI, *m/e* (rel. int.)) 271 (20), 257 (40), 239 (41), 199 (100), 179 (37).

Ethyl 2-bromo-4-[(methoxyethoxymethyl)oxy]-2-butenoate (157). To a solution of ethyl 2,3-dibromo-4-hydroxybutanoate (44.3 mmol) in CH_2Cl_2 at 0 °C was added diisopropylethylamine (10 equiv.) and methoxyethyoxymethylchloride (2 equiv.). The reaction mixture was allowed to slowly warm to room temperature overnight. The CH_2Cl_2 was removed *in vacuo*, and the black residue filtered through silica gel (3:1 hexane/ethyl acetate). After removal of the hexane, more ethyl acetate was added, and the organic layer was washed with H_2O, 3N HCl, and brine. It was dried (MgSO4), and the solvent removed to give 5.05 g of an orange-brown oil which was chromatographed (silica gel, 4:1 hexane ethyl acetate) to give 2.65 g of a bright yellow liquid. This liquid was kugelrohred (108 °C, 10^{-4} mmHg) yielding 2.31 g (20%) of an almost colorless liquid. **157-E isomer**: **R_f**=0.22 (4:1 hexane/ethyl acetate); **IR** (neat) 2937, 1724, 1618, 1370, 1312, 1230, 1035 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.32 (t, 3H, J=7.1 Hz), 3.40 (s, 3H), 3.55 (m, 2H), 3.70 (m, 2H), 4.24 (q, 2H, J=7.1 Hz), 4.50 (d, 2H, J=5.0 Hz), 4.72 (s, 2H), 6.84 (t, 1H, J=5.0 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 59.0 (CH_3), 62.4 (CH_2), 66.8 (CH_2), 67.2 (CH_2), 71.8 (CH_2), 95.4 (CH_2), 111.3 (C), 146.7 (CH),

162.4 (C); **MS** (CI, *m/e* (rel. int.)) 223 (52), 221 (50), 193 (41), 191 (38), 163 (35), 161 (38), 89 (100).

Ethyl 2-bromo-4-[((trimethylsilyl)ethoxymethyl)oxy]-2-butenoate (158). A solution of ethyl 2-bromo-4-hydroxycrotonate (5.17 g) in AcOH/THF/H_2O (3:1:1) was stirred at room temperature for 0.5 h. Enough NaOH was added to neutralize 85% of the AcOH. Then the pH was adjusted to eight using $NaHCO_3$. The aqueous layer was extracted with ethyl acetate. The combined organic extracts were washed with sat'd aq. $NaHCO_3$ and brine and then dried ($MgSO_4$). Evaporation of the solvent gave 3.51 g of an orange oil which was chromatographed (silica gel, 4:1 hexane/ethyl acetate) to give 1.54 g (46%) of the alcohol To a solution of the alcohol in CH_2Cl_2 at 0 °C was added diisopropylethylamine (12 equiv.) and then after ten minutes trimethylsilylethoxymethylchloride (3 equiv) . Stirrring was continued at 0 °C for 10 h then at room temperature for 11 h, whereupon the reaction mixture was quenched with sat'd. aq. NH_4Cl solution. The black organic layer was filtered through silica gel and dried ($MgSO_4$). Removal of the solvent gave 2.27 g of a dark-brown liquid. Flash chromatography (silica gel, 15:1 hexane/ethyl acetate) yielded 1.89 g of a colorless liquid. **158-E isomer:** R_f=0.48 (5:1 hexane/ethyl acetate); **IR** (neat) 2950, 1726, 1628, 1255, 1029 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.002 (s, 9H), 0.93 (dd, 1H, J_1=9.0, J_2=7.7 Hz), 1.30 (t, 3H, J=7.1 Hz), 3.61 (dd, 1H, J_1=9.0, J_2=7.7 Hz), 4.25 (q, 2H, J=7.1 Hz), 4.30 (d, 1H, J=5.1 Hz), 4.69 (s, 2H), 7.41 (t, 1H, J=5.1 Hz); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.1 (CH_3), 18.1 (CH_2), 62.6 (CH_2), 65.5 (CH_2), 67.4 (CH_2), 94.9 (CH_2), 115.6 (C), 142.9 (CH), 161.6 (C); **MS** (CI, *m/e* (rel. int.)) 313 (100), 31 (99), 283 (42), 281 (41), 267 (21) 265 (20), 201 (30), 165 (28) 163 (30), 101 (96), 103 (91).

General Procedure for Cyclopropanation/Vinyloxirination:

To a stirred solution of lithium diisopropylamide (1.04 equiv., 5.2 mmol), prepared from diisopropylamine and n-butyllithium, in 8 mL of THF and HMPA (1.14 equiv., 5.7 mmol) at -110 °C was added a solution of the 2-bromo-2-butenoate (1.0 equiv., 5.0 mmol) in 17 mL of THF, cooled to -110 °C, over a period of 25 min while maintaining the temperature of the reaction at or below -95 °C. After the addition was complete, the reaction mixture was stirred for 5 min and then treated with a solution of the electrophile (1.0 equiv., 5.0 mmol; either the aldehyde or the enone) in 7 mL of THF cooled to -105 °C. This addition took 5 min and was also done at a rate which kept the temperature of the reaction at or below -95 °C Stirring was continued between -100 and -110 °C for 0.5 h and at -78 °C for 1 h. The reaction mixture was then warmed to -50 °C over 0.5 h, quenched with saturated NH_4Cl solution, and diluted with ether. The layers were separated, and the aqueous layer extracted twice more with ether. The combined ether extracts were washed with water then brine and dried (Na_2SO_4). The solvent was removed *in vacuo* to give a mixture of the crude *endo*- and *exo*-vinylcyclopropanes or vinyloxiranes.

r-3-Propyl-2-*trans*-carbethoxy-2-ethenyloxirane (140). Butyraldhyde (0.44 mL) gave 940 mg of a clear yellow liquid which by GC contained 56% of the desired oxirane. The crude material was filtered through 20 g of silica gel (10% deactivated with H_2O) with 95:5 hexane/ether as eluant to give **140** (523 mg, 83% pure by GC). An analytical sample was obtained by flash chromatography (silica gel, 10% deativated with H_2O; 95:5 hexane/ether). **140:** R_f = 0.47 (9:1 hexane/ethyl acetate); **IR** (neat) 2930, 1750, 1732, 1300, 1250, 1075 cm^{-1}; ^1H **NMR** ($CDCl_3$) δ 0.89 (t, 3H, J=7.1 Hz),1.25 (t, 3H, J=7.0 Hz), 1.37-1.49 (m, 4H), 3.22 (t, 1H, J=5.8 Hz), 4.20 (q, 2H, J=7.0 Hz), 5.30 (dd, 1H, J_1=17.1, J_2=1.8 Hz),

5.35 (dd, 1H, J_1=10.8, J_2=1.8 Hz), 6.26 (dd, 2H, J_1=17.1, J_2=10.8 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.1 (CH_3), 13.5 (CH_3), 18.6 (CH_2, double intensity), 27.9 (CH_2), 60.2 (C), 60.9 (CH_2), 63.9 (CH), 118.3 (CH_2), 128.2 (CH), 169.1 (C); **MS** (CI, *m/e* (rel. int.)) 185 (80) M^++1, 167 (22), 157 (15), 139 (100), 115 (41), 111 (86), 101 (47), 83 (30). **HRMS**, calcd for $C_{10}H_{17}O_3$: 185.1177. Found: 185.1177.

r-3-Isopropyl-2-*trans*-carbethoxy-2-ethenyloxirane (141). Isobutyraldeyde (o.46 mL) gave 710 mg of a clear yellow liquid which by GC contained 78% of the desired oxirane. The residue was filtered through 20 g of silica gel (10% deactivated with H_2O) with 95:5 hexane ether as eluant to give **141** (540 mg, 83% pure by GC). An analytical sample of **141** was obtained by flash chromatography (silica gel, 10% deactivated with H_2O; 95:5 hexane/ether). R_f = 0.50 (4:1 hexane/ethyl acetate); **IR** (neat) 2960, 1750, 1730, 1244, 1033 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.87 (d, 3H, J=8.1 Hz), 1.03 (d, 3H, J=7.1 Hz), 1.24 (t, 3H, J=7.1 Hz), 1.41-1.57 (m,1H), 2.89 (d, 1H, J=9.2 Hz), 4.17 (q, 2H, J=7.0 Hz), 5.27-5.33 (m, 2H), 6.25-6.39 (m, 1H); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 17.9 (CH_3), 19.4 (CH_3), 25.9 (CH), 61.1 (C), 61.5 (CH_2), 70.1 (C), 118.8 (CH_2), 128.3 (CH), 169.6 (C); **MS** (CI, *m/e* (rel. int.)) 185 (83) M^++1, 169 (63), 157 (14), 139 (98), 129 (25) 123 (19), 111 (55). **HRMS**, calcd for $C_{10}H_{16}O_3$: 184.1019. Found 184.1103.

r-3-Phenyl-2-*trans*-carbethoxy-2-ethenyloxirane (142). Benzaldehyde (0.51 mL) afforded 1.03 g of a clear yellow liquid which was 95% pure by GC. The residue was filtered through 20 g of silica gel (10% deactivated with H_2O) with 9:1 hexane/ether as eluant to give pure **142** (736 mg 68%). R_f = 0.57 (4:1 hexane/ethyl acetate); **IR** (neat) 1745, 1730, 1258, 1140, 1040 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.32 (t, 3H, J=7.1 Hz), 4.29 (qd, 2H, J_1=7.1, J_2=0.7 Hz), 4.43 (s, 1H,

5.20), (dd, 1H, J_1=10.4 , J_2=1.5 Hz), 5.41 (dd, 1H, J_1=17.3, J_2=1.5 Hz), 5.91 (dd, 1H, J_1=17.3, J_2=10.4 Hz), 7.24 (m, 5H); **^{13}C NMR** ($CDCl_3$) δ 13.6 (CH_3), 61.3 (CH_2), 62.5 (C), 63.8 (CH), 119.9 (CH_2), 126.6 (CH, double intensity), 126.9 (CH), 127.4 (CH, double intensity), 127.7 (CH), 132.4 (C), 168.4 (C); **MS** (70 eV, *m/e* (rel. int.)) 162 (12), 145 (19), 135 (100), 117 (29), 107 (65), 79 (25), 55 (78). **Anal. Calcd** for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.36; H, 6.26.

3-(2'-Furyl)-2-carbethoxy-2-ethenyloxirane (139). 2-Furaldehyde (0.41 mL) gave 1.04 g of a 9:1 mixture of oxirane **139** and 2-furaldehyde. The residue was filtered through silical gel (10% deactivated with H_2O) with 95:5 hexane ether as eluant to give pure **139** (527 mg, 51%). R_f=0.34 (9:1 hexane/ethyl acetate); **IR** (neat) 3010, 1735, 1255 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.31 (t, 3H, J=7.1 Hz), 4.26 (qd, 2H, J_1=7.1, J_2=1.2 Hz), 4.33 (s, 1H), 5.37 (dd, 1H, J_1=10.9, J_2=1.5 Hz), 5.50 (dd, 1H, J_1=17.4, J_2=1.5 Hz), 6.13 (dd, 1H, J_1=17.4, J_2=10.9 Hz), 6.26 (d, 1H, J=3.1 Hz), 6.32 (dd, 1H, J_1=3.1, J_2=1.9 Hz), 7.37 (dd, 1H, J_1=1.9, J_2=0.8 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.1 (CH_3), 58.8 (CH), 62.1 (CH_2), 62.9 (C), 110.1 (CH), 110.4 (CH), 120l4 (CH_2), 127.3 (CH), 143.3 (CH), 147.3 (C), 168.4 (C); **MS** (70 eV, *m/e* (rel. int.)) 208 (30) M^+, 162 (15), 134 (65), 107 (100), 79 (50). **HRMS**, calcd for $C_{11}H_{12}O_4$: 208.0736. Found: 208.0737.

3-(3'-Furyl)-2-carbethoxy-2-ethenyloxirane (143). 3-Furaldehyde (0.43 mL) gave 1.04 g of a 6:1 mixture of oxirane **143** and 3-furaldehyde. The residue was filtered through silica gel (10% deactivated with H_2O) with 95:5 hexane/ether as eluant to give pure **143** (730 mg, 68%). R_f = 0.44 (4:1 hexane/ethyl acetate); **IR** (neat) 3145, 3080, 1775, 1640, 1595, 1045, 1025 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.31 (t, 3H, J=7.2 Hz), 4.22 (s, 1H), 4.26 (qd, 2H, J_1=7.2, J_2=1.5 Hz), 5.37 (dd, J_1=10.8, J_2=1.5 Hz), 5.45 (dd, 1H, J_1=17.2, J_2=1.5 Hz),

6.09 (dd, 1H, J_1=17.2, J_2=10.8 Hz), 6.32 (m, 1H), 7.32 (m, 1H), 7.37 (m, 1H); **^{13}C NMR** ($CDCl_3$) δ 13.7 (CH_3), 58.4 (CH), 61.5 (CH_2), 62.4 (C), 109.4 (CH), 118.3 (C), 119.8 (CH_2), 127.5 (CH), 141.6 (CH), 142.6 (CH), 168.6 (C); **MS** (70 eV, *m/e* (rel. intl.)) 208 (3) M^+, 125 (100), 107 (28), 97 (55), 55 (59). **HRMS**, calcd for $C_{11}H_{12}O_4$: 208.0736. Found: 208.0744.

6-Carbethoxy-6-vinylbicyclo[3.1.0]hexan-2-one (144-exo and 144-exo isomers). The general procedure for cyclopropantion was followed using ethyl 2-bromo-2-butenoate (5.0 mmol) and 2-cyclcopentenone (5.0 mmol). Flash chromatography (silica gel, 15:1, 9:1, 3:1, 2:1 pentane/ether) gave 260 mg of *endo*- and 390 mg of *exo*-vinylcyclopropanes (67%). **144-exo:** R_f = 0.23 (3:1 hexane/ethyl acetate); **IR** (neat) 2980, 1720, 1630, 1190 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.23 (t, 3H, J=7.0 Hz), 1.99-2.33 (m, 6H), 4.10-4.22 (m, 2H), 4.98 (d, 1H, J=17.3 Hz), 5.05 (d, 1H, J=10.7 Hz), 5.85 (dd, 1H, J_1=17.3, J_2=10.7 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 20.8 (CH_2), 36.3 (CH_2), 36.7 (CH), 41.0 (CH, C), 61.6 (CH_2), 114.6 (CH_2), 135.3 (CH), 168.8 (C), 211.1 (C); **MS** (70 eV, *m/e* (rel. int.)) 194 (6) M^+, 138 (90), 110 (86), 91 (89), 77 (100), 65 (57), 53 (52). **HRMS**, calcd for $C_{11}H_{14}O_3$: 194.0943. Found: 194.0943. **144-endo:** R_f = 0.29 (3:1 hexane/ethyl acetate); **IR** (neat) 2990, 1770, 1740, 1227 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.20 (t, 3H, J=7.0 Hz), 1.86-2.34 (m, 4H), 2.56 (m, 2H), 4.09 (q, 2H, J=7.0 Hz), 5.31 (d, 1H, J=17.3 Hz), 5.40 (d, 1H, J=10.6 Hz), 5.95 (dd, 1H, J_1=17.3, J_2=10.6 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.7 (CH_3), 19.4 (CH_2), 35.4 (CH), 35.8 (C, CH_2), 40.8 (CH), 61.3 (CH_2), 122.6 (CH_2), 128.7 (CH), 170.4 (C), 212.3 (C); **MS** (CI, *m/e* (rel. int.)) 195 (100) M+1, 167 (8), 149 (12), 123 (11), 109 (15), 95 (29), 91 (20), 81 (62). **HRMS**, calcd for $C_{11}H_{15}O_3$: 195.1021. Found: 195.1105.

6-Carbethoxy-6-[2-vinyl(4-phenoxybenzoate)]bicyclo[3.1.0]-hexan-2-one (164-exo and 164-endo Isomers). Following the general procedure using ethyl 2-bromo-4-(4-phenoxybenzoyloxy)-2-butenoate (**151**) (0.91 mmol) and 2-cyclopentanone (0.91 mmol) and keeping the temperaute at -78 °C not -100 °C gave after preparative TLC (4:1 hexane/ethyl acetate, two elutions) 99 mg of the exo isomer, 50 mg of the endo, and 34 mg of the dimer 1-bromo-1,2-dicarbethoxy-3-(4-phenoxybenzoyloxy)-2-[2-(4-phenoxybenzoyl)oxyvinyl]cyclo-propane (40% yield of vinylcyclopropanes). **164-exo:** R_f=0.30 (2:1 hexane/ethyl acetate); **IR** (neat) 3045, 2970, 1720, 1682, 1482, 1260, 1235, 1156, 730 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.28 (t, 3H, J=7.0 Hz), 2.06-2.39 (m, 5H), 2.45 (t, 1H, J=5.9 Hz), 4.12-4.25 (m, 2H), 5.77 (d, 1H, J=12.6 Hz), 6.97 (d, 2H, J=9.0 Hz), 7.04 (d, 2H, J=8.5 Hz), 7.19 (t, 1H, J=7.5 Hz), 7.38 (t, 2H, J=7.5 Hz), 7.45 (d, 1H, J=12.6 Hz), 8.0 (d, 2H, J=9.0 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 20.7 (CH_2), 36.4 (CH), 36.9 (CH_2), 37.3 (C), 41.0 (CH), 61.9 (CH_2), 112.9 (CH), 117.3 (CH, double intensity), 120.2 (CH, double intensity), 122.7 (C), 124.7 (CH), 130.1 (CH, double intensity), 131.8 (C), 132.2 (CH, double intensity), 138.5 (C), 155.4 (C), 162.7 (C), 168.2 (C), 211.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 406 (6) M^+, 214 (9), 197 (100), 141 (26), 115 (18), 77 (20); **HRMS**, calcd for $C_{24}H_{22}O_6$: 406.1416. Found: 406.1359. **164-endo:** R_f=0.35 (2:1 hexane/ethyl acetate); **IR** (neat) 3050, 2960, 1720, 1582 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.24 (t, 3H, J=7.2 Hz), 1.90-2.45 (m, 4H), 2.60 (d, 1H, J=5.9 Hz), 2.70 (t, 1H, J=5.9 Hz), 4.13 (q, 2H, J=7.2 Hz), 5.63 (d, 1H, J=12.2 Hz), 6.98 (d, 2H, J=9.4 Hz), 7.05 (d, 2H, J=7.5 Hz), 7.19 (t, 1H, J=7.5 Hz), 7.39 (t, 2H, J=7.5 Hz), 7.51 (d, 1H, J=12.2 Hz), 8.03 (d, 2H, J=9.4 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 20.2 (CH_2), 31.5 (CH), 35.3 (CH), 35.7 (CH_2), 41.5 (CH), 61.8 (CH_2), 105.7 (CH), 117.3 (CH,

double intensity), 120.1 (CH, double intensity), 122.6 (C), 124.7 (CH), 130.0 (CH, double intensity), 131.9 (C), 132.2 (CH, double intensity), 142.2 (CH), 155.3 (C), 162.6 (C), 170.6 (C), 211.9 (C); **MS** (70 eV, *m/e* (rel. int.)) 406 (4) M^+, 214 (11), 197 (100), 168 (7), 141 (33), 115 (20), 77 (28); **HRMS**, calcd for $C_{24}H_{22}O_6$: 406.1416. Found: 406.1395.

1-Bromo-1,2-dicarbethoxy-3-[(4-phenoxybenzoyl)oxy]-2-[((4-phenoxybenzoyl)oxy)vinyl]cyclopropane (159). Isolated along with 164-endo/exo. R_f=0.55 (2:1 hexane/ethyl acetate); **IR** (neat) 3060, 2975, 1730, 1610, 1585 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.25 (t, 3H, J=7.1 Hz), 1.29 (t, 3H, J=7.2 Hz), 2.95 (t, 1H, J=7.2 Hz), 4.18 (m, 4H), 4.40 (dd, 1H, J_1=11.9, J_2=7.4 Hz), 4.56 (dd, 1H, J_1=11.9, J_2=7.1 Hz), 5.67 (d, 1H, J=13.0 Hz), 6.98 (d, 4H, J=7.4 Hz), 6.98-7.12 (m, 4H), 7.13-7.26 (m, 2H), 7.33-7.43 (m, 4H), 7.70 (d, 1H, J=13.0 Hz), 8.02 (d, 4H, J=7.4 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.6 (CH_3), 13.7 (CH_3), 31.1 (CH), 37.5 (C), 42.5 (C), 62.0 (CH_2), 62.1 (CH_2), 62.7 (CH_2), 106.2 (CH), 117.0 (CH, quadruple intensity) 119.8 (CH, double intensity), 119.9 (CH, double intensity), 122.1 (C), 123.6 (C), 124.2 (CH), 124.5 (CH), 129.7 (CH, double intensity), 129.8 (CH, double intensity), 131.6 (CH, double intensity), 132.0 (CH, double intensity), 142.2 (CH), 154.9 (C), 155.3 (C), 161.7 (C), 162.1 (C), 162.3 (C), 165.3 (C), 166.1 (C), 167.8 (C); **MS** (70 eV, *m/e* (rel. int.)) 730 (<1) M^+, 379 (21), 238 (95), 225 (50), 214 (91), 199 (92), 198 (100), 164 (51), 141 (100), 115 (99) 77 (99).

6-Carbethoxy-6-[(2-(*tert*-butyldimethylsily)oxy)vinyl]-bicyclo[3.1.0]hexan-2-one (163-exo and 163-endo isomers). Following the general procedure for cyclopropanation, using ethyl 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]-2-butenoate (**155**) (3.4 mmol) and 2-cyclopentanone (3.4

mmol) gave after flash chromatography (silica gel, 10% deactivated with H_20; 9:1 hexane/ethyl acetate) 225 mg of the exo isomer and 159 mg of the endo (38%). **163-exo:** R_f=0.39 (3:1 hexane/ethyl acetate); **IR** (neat) 2925, 1722, 1650, 1178, 830 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.09 (s, 6H), 0.86 (s, 9H), 1.22 (t, 3H, J=7.1 Hz), 2.01-2.28 (m, 6H), 4.05-4.19 (m, 2H), 5.10 (d, 1H, J-11.9 Hz), 6.40 (d, 1H, J=11.9 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.3 (CH_3, double intensity), 14.0 (CH_3), 18.2 (C), 20.7 (CH_2), 25.5 (CH_3, triple intensity), 35.7 (CH), 36.3 (CH_2), 37.7 (C), 40.7 (CH),61.5 (CH_2), 108.9 (CH), 144.8 (CH), 169.5 (C), 212.0 (C); **MS** (CI, *m/e* (rel. int.)) 325 (32) M^++1, 305 (19), 267 (19), 193 (100), 133 (57), 85 (16); **HRMS**, calcd for $C_{20}H_{32}O_6Si$: 324.1757. Found: 324.1788. **163-endo:** R_f=0.49 (3:1 hexane/ethyl acetate); **IR** (neat) 2912, 1720, 1650, 1252, 1218, 1162, 839 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.106 (s, 3H), 0.11 (s, 3H), 0.88 (s, 9H), 1.20 (t, 3H, J=7.2 Hz), 1.90-2.29 (m, 4H), 2.48-2.56 (m, 2H), 4.07 (q, 2H, J=7.2 Hz), 5.03 (d, 1H, J=12.3 Hz), 6.38 (d, 1H, J=12.3 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.3 (CH_3), -5.2 (CH_3), 14.2 (CH_3), 18.2 (C), 19.9 (CH_2), 25.6 (CH_3, triple intensity), 31.8 (CH_2), 35.1 (CH), 36.2 (C), 41.4 (CH), 61.6 (CH_2), 101.1 (CH), 148.0 (CH), 171.9 (C), 213.4 (C); **MS** (70 eV *m/e* (rel. int.)) 324 (21) M^+, 267 (20), 223 (38), 193 (11), 105 (12), 103 (11), 75 (71), 73 (71), 59 (18).; **HRMS**, calcd for $C_{20}H_{32}O_6Si$: 324.1757. Found: 324.1797.

6-Carbethoxy-6-[(2-methoxyethoxymethyl)oxy)vinyl]bicyclo-[3.1.0]hexan-2-one (165-exo and 165-endo Isomers). Following the general procedure for cyclopropanation, using 2-bromo-4-[(methoxyethoxymethyl)-oxy]-2-butenoate (2.0 mmol) and 2-cyclopentenone (2.0 mmol) gave after flash chromatography (silica gel, 1:1 hexane/ethyl acetate) 20 mg of endo and 136 mg of the exo isomer (26%). **165-exo:** R_f=0.23 (1:1 hexane/ethyl acetate); **IR** (neat)

2930, 1735, 1728, 1668, 1185 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.25 (t, 3H, J=7.1 Hz), 1.98-2.37 (m, 6H), 3.36 (s, 3H), 3.53 (m, 2H), 3.69 (m, 2H), 4.17 (m, 2H), 4.87 (s, 2H), 5.20 (d, 1H, J=12.5 Hz), 6.40 (d, 1H, J=12.5 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 20.7 (CH_2), 35.7 (CH), 36.3 (CH_2), 37.6 (C), 40.8 (CH), 58.9 (CH_3), 61.5 (CH_2), 67.6 (CH_2), 71.5 (CH_2), 95.0 (CH_2), 106.1 (CH), 147.2 (CH), 169.3(C), 211.4 (C); **MS** (70 eV, *m/e* (rel int.)) 298 (2) M^+, 280 (15), 89 (100), 79 (22), 77 (21), 59 (100); **HRMS**, calcd for $C_{15}H_{22}O_6$: 298.1416. Found: 298.1438. **165-endo:** R_f=0.25 (1:1 hexane/ethyl acetate); **IR** (neat) 2939, 1725, 1670, 1220, 1186 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.18 (td, 3H, J_1=7.1 Hz, J_2=1.0 Hz). 1.78-2.36 (m, 5H), 2.48-2.52 (m, 1H), 3.32 (d, 3H, J=0.9 Hz), 3.48 (m, 2H), 3.68 (m, 2H), 4.06 (qd, 2H, J_1=7.1, J_2=0.9 Hz), 4.85 (d, 1H, J=7.0 Hz), 4.90 (d, 1H, J=7.0 Hz), 5.11 (dd, 1H, J_1=12.7, J_2=0.9 Hz), 6.38 (dd, 1H, J_1=12.7, J_2=1.0 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.0 (CH_3), 19.7 (CH_2), 31.8 (C), 35.0 (CH), 36.0 (CH_2), 41.3 (CH), 58.9 (CH_3), 61.5 (CH_2), 67.6 (CH_2), 71.5 (CH_2), 94.8 (CH_2), 98.6 (CH), 150.5 (CH), 171.4 (C), 212.7 (C); **MS** (70 eV, *m/e* (rel. int.)) 298 (1.6) M^+, 280 (6), 209, (3), 89 (100), 77 (9), 59 (73); **HRMS**, calcd for $C_{15}H_{22}O_6$: 298.1416. Found: 298.1392.

6-Carbethoxy-6-[(2-trimethylsilylethoxymethyl)oxy)vinyl]-bicyclo[3.1.0]hexan-2-one (166-exo and 166-endo Isomers). Following the general procedure for cyclopropanation, using 2-bromo-4-[(methoxyethoxymethyl)oxy]-2-butenoate (**158**) (0.97 mmol) and 2-cyclopentanone (0.97 mmol) gave after flash chromatography (silica gel, 8:1, 6:1 hexane/ethyl acetate) 72 mg of endo and 140 mg of the exo isomer (64%). **166-exo:** R_f= 0.13 (5:1 hexane/ethyl acetate); **IR** (neat) 2950, 1735, 1722, 1665, 1172, 1055, 830 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.02 (s, 9H), 0.89 (dd, 2H, J=8.3 Hz), 1.24 (t, 3H,

J=7.1 Hz), 1.96-2.35 (m, 6H), 3.60 (dd, 2H, J=8.3 Hz), 4.14 (m, 2H), 4.80 (s, 2H), 5.16 (d, 1H, J=12.5 Hz), 6.39 (d, 1H, J=12.5 Hz); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.0 (CH_3), 17.9 (CH_2), 20.7 (CH_2), 35.7 (CH), 36.2 (CH_2), 37.6 (C), 40.8 (CH), 61.5 (CH_2), 66.1 (CH_2), 94.4 (CH_2), 105.7 (CH), 147.5 (CH), 169.3 (C), 211.3 (C); **MS** (CI, *m/e* (rel. int.)) 283 (27), 211 (30), 193 (100), 101 (32), 91 (58), 85 (48); **Anal. Calcd for** $C_{17}H_{28}O_5Si$: C, 59.95; H, 8.30. Found: C, 59.93; H, 8.31. **166-endo:** R_f=0.21 (5:1 hexane/ethyl acetate); **IR** (neat) 2950, 1723, 1665, 1227, 830 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.01 (s, 9H), 0.90 (dd, 2H, J=8.3 Hz), 1.21 (t, 2H, J= 7.1 Hz), 1.87-2.36 (m, 4H), 2.50-2.60 (m, 2H), 3.60 (td, 2H, J_1=8.4, J_2=1.2 Hz), 4.08 (q, 2H, J=7.1Hz), 4.83 (d, 1H, J=6.5 Hz), 4.86 (d, 1H, J=6.5 Hz), 5.10 (d, 1H, J=12.7 Hz), 6.40 (d, 1H, J=12.7 Hz); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.1 (CH_3), 18.1 (CH_2), 20.0 (CH_2), 32.0(C), 35.1 (CH), 36.1 (CH_2), 41.3 (CH), 61.6 (CH_2), 66.1(CH_2), 94.4 (CH_2), 98.2 (CH), 150.8 (CH), 171.6 (C), 212.7 (C); **MS** (CI, *m/e* (rel. int.)) 283 (50), 237 (27), 193 (100, 165 (19).

7-Carbethoxy-7-vinylbicyclo[4.1.0]heptan-2-one (145-exo and 145-endo Isomers). Following the general procedure for vinylcyclopropanation, using ethyl 2-bromo-2-butenoate (5.0 mmol) and 2-cyclohexenone (5.0 mmol) gave after flash chromatography (silica gel 19:1, 9:1, 3:1 hexane/ether) 270 mg of the endo isomer and 480 mg of the exo (90%). **145-exo:** R_f = 0.25 (3:1 hexane/ethyl acetate); **IR** (neat) 2950, 1725, 1700, 1638 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.20 (t, 3H, J=7.2 Hz), 1.55-2.30 (m, 8H), 4.12 (qd, 2H, J_1=7.2, J_2=1.5 Hz), 5.00 (d, 1H, J=10.6 Hz), 5.00 (d, 1H, J=17.2 Hz), 5.88 (dd, 1H, J_1=17.2, J_2=10.6 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 18.9 (CH_2), 21.8 (CH_2), 30.8 (CH), 33.6 (CH), 38.0 (CH_2),40.8 (C), 61.5 (CH_2), 114.0 (CH_2), 136.9 (CH), 169.1 (C), 205.1 (C); **MS**

(70 eV, *m/e* (rel. int.)) 208 (30) M^+, 180 (31), 162 (100,) 134 (72), 79 (78). **HRMS**, calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1111. **Anal. Calcd** for C12H16O3: C, 69.23; H, 7.69. Found: C, 68.54; H, 7.83. **145-endo:** R_f = 0.35 (3:1 hexane/ethyl acetate); **IR** (neat) 2950, 1720, 1705, 1240 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.19 (t, 3H, J=7.0 Hz), 1.60-1.87 (m, 3H), 1.97-2.24 (m, 4H), 2.45 (d, 1H, J=7.0 Hz), 4.07 (q, 2H, J=7.0 Hz), 5.21 (dd, 1H, J_1=17.5, J_2=0.8 Hz), 5.42 (d, 1H, J=10.5 Hz), 5.94 (dd, 1H, J_1=17.5, J_2=10.5 Hz), **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 18.2 (CH_2), 22.9 (CH_2), 34.1 (CH), 36.6 (C), 39.2 (CH_2), 61.5 (CH_2), 123.7 (CH_2), 130.1 (CH), 171.9 (C), 206.7 (C); **MS** (70 eV, *m/e* (rel. int.)) 208 (13) M^+, 180 (31), 162 (100), 134 (62), 79 (73). **HRMS**, calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1101.

7-Carbethoxy-7-[(2-(*tert*-butyldimethylsilyl)oxy)vinyl]-bicyclo[4.1.0]heptan-2-one (167-exo and 167-endo Isomers). Following the general procedure for cyclopropanation, using 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]-2-butenoate (3.4 mmol) and 2-cyclohexanone (3.4 mmol) gave after flash chromatography (silica gel, 10:1 hexane/ethyl acetate) 230 mg of endo and 190 mg of the exo isomer (40%). **167-exo:** R_f=0.23 (5:1 hexane/ethyl acetate); **IR** (neat) 2945, 2930, 1725, 1697, 1655, 1180, 830 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.10 (s, 3H), 0.11 (s, 3H), 0.87 (s, 9H), 1.23 (t, 3H, J=7.2 Hz), 1.60-2.35 (m, 8H), 4.12 (q, 2H, J=7.2 Hz), 5.22 (d, 1H, J=12.0 Hz), 6.44 (d, 1H, J=12.0 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.3 (CH_3), 14.0 (CH_3), 18.2 (C), 19.1 (CH_2), 22.1 (CH_2), 25.6 (CH_3, triple intensity), 30.0 (CH), 33.6 (CH), 37.3 (C), 38.2 (CH_2), 61.4, (CH_2), 111.1 (CH), 144.5 (CH), 169.9 (C), 205.9 (C); **MS** (70 eV, *m/e* (rel. int.)) 338 (5) M^+, 281 (31), 235 (37), 75 (100); **HRMS**, calcd for $C_{18}H_{31}O_4Si$: 339.1992. Found: 339.1997. **167-endo:** R_f=0.36 (5:1 hexane/ethyl

acetate); **IR** (neat) 2903, 1710, 1695, 1650, 1225, 1163, 822 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.09 (s, 3H), 0.10 (s, 3H), 0.87 (s, 9H), 1.19 (t, 2H, J=7.1 Hz), 1.51-1.80 (m, 3H), 1.87-2.16 (m, 4H), 2.41 (d, 1H, J=8.1 Hz), 4.06 (qd, 2H, J_1=7.1, J_2=1.8 Hz), 5.00 (d, 1H, J=12.2 Hz), 6.25 (d, 1H, J=12.2 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.2 (CH_3, double intensity), 14.1 (CH_3), 18.2 (C), 18.4 (CH_2), 23.1, (CH_2), 25.6 (CH_3, triple intensity), 28.8 (CH), 32.6 (C), 34.7 (CH), 39.4 (CH_2), 61.5 (CH_2), 102.6 (CH), 148.5 (CH), 173.0 (C), 207.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 338 (2.5) M^+, 281 (28), 235 (33), 75 (89), 73 (100), 57 (44); **HRMS**, calcd for $C_{18}H_{31}O_4Si$: 339.1992. Found: 339.2051. **Anal. Calcd for** $C_{18}H_{31}O_4Si$: C, 63.92; H, 8.96: Found C, 62.74; H, 8.90.

8-Carbethoxy-8-vinylbicyclo[5.1.0]octan-2-one (146-exo and 146-endo isomers). Following the general procedure for vinylcyclopropanation using ethyl 2-bromo-2-butenoate (5.0 mmol) and 2-cycloheptanone (5.0 mmol) gave after flash chromatography (silica gel, 19:1, 9:1, 3:1 hexane/ether) 980 mg of a 1.4:1 mixture of exo- and endovinylcylopropanes, respectively (83%). For analytical puropses the isomers were separated by preparative TLC (95:5 hexane/ethyl acetate). **146-exo:** R_f=0.45 (7:3 hexane/ethyl acetate); **IR** (neat) 3050, 2965, 1730, 1710, 1650, 1300 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.25 (t, 3H, J=7.2 Hz), 1.55-1.73 (m, 3H), 1.73-1.90 (m, 3H), 2.02-2.12 (m, 1H), 2.18 (d, 1H, J=8.5 Hz), 2.45-2.55 (m, 2H), 4.15 (qd, 2H, J_1=7.2, J_2=1.3 Hz), 4.98 (d, 1H, J=17.2 Hz), 5.00 (d, 1H, J=10.2 Hz), 6.34 (dd, 1H, J_1=17.2, J_2=10.2 Hz); **^{13}C NMR** ($CDCl_3$) δ 13.8 (CH_3), 21.6 (CH_2, double intensity), 25.4 (CH_2), 30.1 (CH), 36.6 (C), 38.8 (CH), 42.7 (CH_2), 60.9 (CH_2), 112.8 (CH_2), 136.8 (CH), 169.5 (C), 206.3 (C); **MS** (70 eV, *m/e* (rel. int.)) 222 (15) M^+, 194 (50), 177 (90), 148 (90), 120 (60), 105 (50), 91 (95), 79 (100); **HRMS**, calcd for $C_{13}H_{18}O_3$: 222.1256. Found:

222.0899. **146-endo:** R_f=0.58 (7:3 hexane/ethyl acetate); **IR** (neat) 2960, 1735, 1710, 1235 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.23 (t, 3H, J=7.1 Hz), 1.35-1.65 (m, 3H), 1.78-2.00 (m, 3H), 2.09-2.21 (m, 1H), 2.29-2.40 (m, 1H), 2.48-2.61 (m, 2H), 4.11 (q, 2H, J=7.1 Hz), 5.26 (dd, 1H, J_1=17.7, J_2=1.6 Hz), 5.38 (dd, 1H, J_1=10.9, J_2=1.6 Hz), 6.01 (dd, 1H, J_1=17.7, J_2=10.9 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.1 (CH_3), 22.9 (CH_2), 23.8 (CH_2, double intensity), 25.7 (CH), 32.0 (C), 39.1 (CH), 43.8 (CH_2), 61.4 (CH_2), 121.9 (CH_2), 129.6 (CH), 172.5 (C), 205.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 222 (5) M^+, 176 (100), 148 (50), 120 (20), 105 (30) 91 (53)79 (90); **HRMS**, calcd for $C_{13}H_{18}O_3$. 222.1256. Found: 222.1254.

8-Carbethoxy-8-[(2-(*tert*-butyldimethylsilyl)oxy)vinyl]-bicyclo[5.1.0]octan-2-one (168-exo and 168-endo Isomers). Following the general procedure for cyclopropanation, using 2-bromo-4-[(*tert*-butyldimethylsilyl)oxy]-2-butenoate (**155**) (3.4 mmol) and 2-cycloheptanone (3.4 mmol) gave after flash chromatography (silica gel, 15:1 hexane/ethyl acetate) 54 mg of endo (4.5%) and only impure exo isomer contaminated with 2-cycloheptanone. A sample of the pure exo isomer was obtained by preparative TLC. **168-exo:** R_f=0.15 (10:1 hexane /ethyl acetate); **IR** (neat) 2930, 1770, 1720, 1658, 1180, 840 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.12 (s, 6H), 0.88 (s, 9H), 1.23 (t, 3H, J=7.1 Hz), 1.47-1.92 (m, 6H), 2.06 (d, 2H, J=9.4 Hz), 2.35-2.58 (m, 2H), 4.11 (qd, 2H, J_1=7.1, J_2=2.1 Hz), 5.39 (d, 1H, J=12.0 Hz), 6.37 (d, 1H, J=12.0 Hz); **MS** (70 eV, *m/e* (rel. int.)) 352 (2) M^+, 295 (37), 249 (41), 221 (20), 75 (72), 73 (100); **HRMS**, calcd for $C_{19}H_{33}O_4Si$: 353.2148 Found: 353.2152. **168-endo:** R_f= 0.23 (10:1 hexane/ethyl acertate); **IR** (neat) 2920, 1708, 1655, 1250, 1165, 830 cm^{-1}: **^{1}H NMR** ($CDCl_3$) δ 0.135 (s, 3H), 0.139 (s, 3H), 0.90 (s, 9H), 1.00-1.19 (m, 1H), 1.22 (t, 3H, J=7.1 Hz), 1.37-2.58 (m, 9H), 4.08 (q, 2H, J=7.1 Hz), 5.08 (d, 1H,

J=12.3 Hz), 6.42 (d, 1H, J=12.3 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.3 (CH_3), 14.0 (CH_3), 18.0 (C), 23.0 (CH_2), 25.1 (CH_2, double intensity), 25.5 (CH_3, triple intensity), 27.3 (CH), 31.5 (C), 38.6 (CH), 43.4 (CH_2), 61.1 (CH_2), 102.3 (CH), 148.0 (CH), 173.3 (C), 206.4 (C); **MS** (70 eV, *m/e* (rel. int.)) 352 (2.5) M^+, 295 (43), 249 (53), 221 (25), 75 (85), 73 (100); **HRMS**, calcd for $C_{19}H_{33}O_4Si$: 353.2148. Found: 353.2160.

(3S,4R)-6-Carbethoxy-3,4-(isopropylidenedioxy)-6-vinyl-bicyclo[3.1.0]hexan-2-one (148-exo and 148-endo Isomers). Following the general procedure for vinylcyclopropanation using ethyl 2-bromo-2-butenoate (0.64 mmol) and (2S,3R)-2,3-isopropylidenedioxycyclopent-4-enone (**147**) (0.64 mmol) gave after flash chromatography (silica gel, 10% deactivated with H_20; 6:1 hexane/ethyl acetate) 111 mg of a mixture of endo- and exo vinylcyclopropanes (72%). For analytical purposes the isomers were separated by proparative TLC (6:1 hexane/ethyl acetate, two elutions). **148-exo:** $[\alpha]_D$ +14.2° (c 0.38, MeOH); R_f=0.48 (2:1 hexane/ethyl acetate); **IR** (neat) 2970, 1737, 1722, 1630 cm-^{1}; **^{1}H NMR** ($CDCl_3$) δ 1.23 (t, 3H, J=7.0 Hz), 1.29 (s, 3H), 1.42 (s, 3H), 2.40 (d, 1H, J=5.5 Hz), 2.54 (d, 1H, J=5.5 Hz), 4.13 (q, 2H, J=7.0 Hz), 4.40 (d, 1H, J=5.0 Hz), 4.65 (d, 1H, J=5.0 Hz), 4.96 (d, 1H, J=17.2 Hz), 5.06 (d, 1H, J=10.7 Hz), 6.15 (dd, 1H, J_1=17.2, J_2=10.7 Hz; **^{13}C NMR** ($CDCl_3$) δ 13.9 (CH_3), 24.7 (CH_3), 26.8 (CH_3), 39.7 (CH), 41.0 (C), 41.2 (CH), 62.3 (CH_2), 76.6 (CH), 81.8 (CH) 112.5 (C), 115.2 (CH_2), 133.9 (CH), 169.4 (C), 204,5 (C); **MS** (70 eV*m/e* (rel. int.)) 266 (11) M^+, 162 (46), 138, (85), 123 (79), 107 (100), 79 (95), 77 (92); **HRMS**, calcd for $C_{14}H_{14}O_5$: 266.1154. Found: 266.1146.

(3S,4R)-6-[((2-*tert*-Butyldimethylsilyl)oxy)vinyl]-6-carbethoxy-3,4-(isopropylidenedioxy)bicyclo[3.1.0]hexan-2-one (169-exo and 169-endo Isomers). Following the general procedure for vinylcyclopropanation, using ethyl 2-bromo-4-[(*tert*-butyldimethylsily)oxy]-2-butenoate (3.38 mmol) and (2S,3R)-2,3-isopropylidenedioxy-cyclopent-4-enone (**147**) (2.6 mmol) gave after flash chromatography (silica gel; 8:1 hexane/ethyl acetate) 73.6 mg of the endo- and 408.0 mg of the exovinylcyclopropanes (47%). **169-exo:** $[\alpha]_D$ = +9.51 (MeOH; c, 0.93); R_f=0.21 (8:1 hexane/ethyl acetate); **IR** (neat) 2933, 1748, 1720, 1659, 1375, 1200, 828 cm^{-1}; ^{1}**H NMR** ($CDCl_3$) δ 0.12 (s, 6H), 0.88 (s, 9H), 1.24 (t, 3H, J=7.1 Hz), 1.32 (s, 3H), 1.45 (s, 3H), 2.34 (d, 1H, J=5.5 Hz), 2.50 (d, 1H, J=5.5 Hz), 4.13 (q, 2H, J=7.1 Hz), 4.42 (d, 1H, J=5.0 Hz) 4.68 (d, 1H, J=5.0 Hz), 5.22 (d, 1H, J=12.0 Hz), 6.38 (d, 1H, J=12.0 Hz); ^{13}**C NMR** ($CDCl_3$) δ -5.3 (CH_3, double intensity), 14.0 (CH_3),.18.2 (C), 24.7 (CH_3), 25.5 (CH_3, triple intensity), 26.9 (CH_3), 38.4 (C), 39.6 (CH), 40.6 (CH), 62.2 (CH_2), 76.5 (CH), 82.1 (CH), 108.1 (CH), 12.4 (C), 145.0 (CH), 170.3 (C), 205.1 (C); **MS** (70 eV*m/e* (rel. int.)) 396 (12) M^+, 281 (40), 237 (31), 75 (45), 73 (100); **HRMS**, calcd for $C_{20}H_{32}O_6Si$: 396.1968 Found: 396.1978. **Anal. Calcd** for: $C_{20}H_{32}Si$: C, 60.63; H, 8.14. Found: C, 60.46; H, 8.19. **169-endo:** $[\alpha]_D$ = +23.54 (MeOH c, 0.48); R_f=0.25 (8:1 hexane/ethyl acetate); **IR** (neat) 2930, 1742, 1725, 1653, 1255, 1222, 1175, 840 cm^{-1}; ^{1}**H NMR** ($CDCl_3$) δ 0.10 (s, 6H), 0.86 (s, 9H), 1.20 (t, 3H, J=7.1 Hz), 1.30 (s, 3H), 1.40 (s, 3H), 2.65 (d, 1H, J=5.6 Hz), 2.82 (d, 1H, J=5.6 Hz) 4.05-4.13 (m, 3H), 4.64 (d, 1H, J=5.2 Hz), 5.02 (d, 1H, J=12.2 Hz), 6.33 (d, 1H, J=12.2 Hz); ^{13}**C NMR** ($CDCl_3$) δ -5.3 (CH_3, double intensity), 14.0 (CH_3), 18.1 (C), 25.0 (CH_3), 25.5 (CH_3, triple intensity), 27.0 (CH_3), 32.3 (C), 37.6 (CH), 38.7 (CH), 62.0 (CH_2), 76.2 (CH), 80.1 (CH),

101.3 (CH), 112.5 (C), 149.6 (CH), 170.6 (C), 207.1 (C); **MS** (70 eV, *m/e* (rel. int.)) 396 (7), 281 (19), 237 (24), 75 (40), 73 (100); **HRMS**, calcd for $C_{20}H_{32}O_6Si$: 396.1968. Found: 396.1956.

(3S,4R)-6-[2-(Trimethylsilyl)ethoxymethyl)oxy)vinyl]-6-carbethoxy-3,4-(isopropylidenedioxy)bicyclo[3.1.0]hexan-2-one (170-exo and 170-endo isomers). Following the general procedure for vinylcyclopropanation using ethyl 2-bromo-4-[(trimethylsilylethoxymethyl)oxy]-2-butenoate (**158**) (468.6 mg ,1.38 mmol) and enone **147** (170 mg, 1.1 mmol) gave after flash chromatography (silica gel, 5:1 hexane.ethyl acetate) 86.7 mg of a 2:3 mixture of endo to exo vinylcyclopropanes and 152.7 mg of the exo isomer. **170-exo**: R_f = 0.26 (4:1 hexane/ethyl acetate); **IR** (neat) 2955, 2247, 1742, 1721, 1670, 1374, 1250, 170, 1060, 853, 826 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.01 (s, 9H), 0.90 (dd, 2H, J_1=8.3, J_2=8.2 Hz), 1.25 (t, 3H, J=7.1 Hz), 1.32 (s, 3H), 1.45 (s, 3H), 2.37 (d, 1H, J=5.5 Hz), 2.54 (d, 1H, J=5.5 Hz), 3.61 (dd, 2H, J_1=8.3, J_2=8.2 Hz), 4.13 (q, 2H, J=7.1Hz), 4.43 (d, 1H, J=5.0 Hz), 4.68 (d, 1H, J=5.0 Hz), 4.82 (s, 2H), 5.30 (d, 1H, J=12.5 Hz), 6.36 (d, 1H, J=12.5 Hz); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.1 (CH_3), 18.0 (C), 24.8 (CH_3), 27.0 (CH_3), 38.4 (C), 39.8 (CH), 40.7 (CH), 62.3 (CH_2), 76.5 (CH), 82.2 (CH), 94.6 (CH_2), 104.9 (CH), 12.5 (C), 147.7 (CH), 170.1 (C), 207.7 (C); **MS** (CI, *m/e* (rel. int.)) 413 (<1) M^++1, 355 (48), 297 (85), 237 (47), 207 (100), 179 (71), 131 (41), 103 (55), 91 (84); **HRMS**, calcd for $C_{20}H_{33}O_7Si$: 413.1997. Found: 413.1973. **Anal. Calcd** for $C_{20}H_{32}O_7Si$: C, 58.25; H, 7.77. Found: C, 58.09; H, 7.86.

General Procedure for Pyrolysis:

A sample of the vinylcyclopropane was evaporated (10^{-4} mmHg) through a horizontally situated Vycor tube (41 cm, 5 mm i.d.) which was heated to the specified temperature after being thoroughly cleaned (nitric acid; 50% aq. KOH) and preheated with a slurry of $PbCO_3$. The pryrolysate was condensed in a trap cooled with liquid nitrogen. The apparatus was rinsed with ether, the solution was filtered to remove inorganic impurities, and the solvent was evaporated to give the crude pyrolysate.

2-Carbethoxybicyclo[3.3.0]oct-2-en-6-one (178). The vinylcyclopropane **144-endo** (79 mg, 0.41 mmol) was pyrolyzed (550 °C) according to the general procedure to give after preparative TLC (9:1 hexane/ethyl acetate, three elutions) 23 mg of diquinane **178** (43%). R_f=0.35 (3:1 hexane/ethyl acetate); **IR** (neat) 2950, 1732, 1709, 1620, 1260 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.27 (t, 3H, J=7.0 Hz), 2.00-2.35 (m, 4H), 2.65-2.72 (m, 2H), 2.76-2.84 (m, 1H) 3.69-3.78 (m, 1H), 4.12-4.25 (m, 2H), 6.78 (dd, 1H, J_1=4.5, J_2=2.3 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 25.0 (CH_2), 36.3 (CH_2), 36.6 (CH_2), 46.8 (CH), 49.4 (CH), 60.3 (CH_2), 138.0 (C), 143.2 (CH), 164.4 (C), 222.1 (C); **MS** (70 eV, *m/e* (rel. int.))194 (100) M^+, 166 (20), 149 (45), 138 (22), 121 (30), 105 (33), 93 (35), 79 (56), 65(60); **HRMS**, calcd for $C_{11}H_{14}O_3$: 194.0943. Found: 194.0932.

2-Carbethoxy-4-endo[(4-phenoxybenzoyl)oxy]bicyclo[3.3.0]oct-2-en-6-one (183). Vinylcyclopropane **164-exo** (145 mg, 0.36 mmol) was pyrolyzed (525 °C) according to the general procedure to give after flash chromatography (silica gel, 10% deactivated with H_2O; 4:1 hexane/ethyl acetate) 39 mg of diquinane **183** (28%). R_f=0.31 (4:1 hexane/ethyl acetate); **IR** (neat) 2980, 2250, 1740, 1728, 1715, 1610, 1600, 1490, 1250, 1080, 910, 730 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.32 (t, 3H, J=7.1 Hz), 2.01-2.50 (m, 4H), 3.24 (dd, 1H, J_1=9.1,

J_2=8.1 Hz), 3.78 (t, 1H, J=7.5 Hz), 4.16-4.31 (m, 2H), 6.13 (m, 1H), 6.75 (t, 1H, J=1.9 Hz), 6.94 (d, 2H, J=8.8 Hz), 7.03 (d, 2H, J=7.4 Hz), 7.17 (t, 1H, J=7.4 Hz), 7.37 (t, 2H, J=7.4 Hz), 7.90 (d, 2H, J=8.8 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 24.8 (CH_2), 38.3 (CH_2) 46.2 (CH), 50.7 (CH), 60.9 (CH_2), 77.5 (CH), 117.4 (CH, double intensity), 120.1 (CH, double intensity), 124.4 (CH), 130.0 (CH, double intensity), 131.8 (CH, double intensity), 133.1 (C), 139.1 (CH), 141.4 (C), 155.7 (C), 162.1 (C), 163.8 (C), 165.1 (C), 213.7 (C); **MS** (70 eV, *m/e* (rel. int.)) 406 (19) M^+, 214 (26), 198 (65), 197 (100) 141 (29), 105 (22), 77 (30); **HRMS**, calcd for $C_{24}H_{22}O_6$: 406.1416. Found: 406.1383.

4-[(*tert*-Butyldimethylsilyl)oxy]-2-carbethoxybicyclo[3.3.0]oct-2-en-6-one (182-endo and 182-exo Isomers). A mixture of the vinylcyclopropanes **163-exo** and **163-endo** (53.5 mg, 0.17 mmol) was pyrolyzed (550 °C) according to the general procedure to give after preparative TLC (8:1 hexane/ethyl acetate, two elutions) 8.0 mg of the exo isomer and 20 mg of the endo (52%). **182-endo:** R_f=0.18 (9:1 hexane/ethyl acetate); **IR** (neat) 2930, 1740, 1710, 1632, 1260 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.84 (s, 9H), 1.30 (t, 3H, J=7.1 Hz), 1.94-2.37 (m, 4H), 2.91 (t, 1H, J=8.8 Hz), 3.50-3.61 (m, 1H), 4.13-4.33 (m, 2H), 5.03 (dd, 1H, J_1=8.8, J_2=2.0 Hz), 6.53 (t, 1H, J=2.0 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.1 (CH_3, double intensity), 14.1 (CH_3), 18.1 (C), 25.4 (CH_2), 25.7 (CH_3, triple intensity) 38.6 (CH_2), 45.7 (CH), 53.6 (CH), 60.5 (CH_2), 77.0 (CH), 139.8 (C), 141.8 (CH), 164.4 (C), 214.3 (C); **MS** (CI,*m/e* (rel. int.)) 325 (42) M^++1, 267 (30), 193 (100), 133 (21); **HRMS**, calcd for $C_{17}H_{29}O_4Si$. 325.1835. Found: 325.1866; **Anal Calcd** for $C_{17}H_{29}O_4Si$: C, 62.79; H, 8.70. Found: C, 62.63; H, 8.67. **182-exo:** R_f=0.22 (9:1 hexane/ethyl acetate); **IR** (neat) 2950, 1735, 1720, 1629,

1250 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.11 (s, 3H), 0.12 (s, 3H), 0.87 (s, 9H), 1.30 (t, 3H, J=7.1 Hz), 2.03-2.30 (m, 4H), 2.74 (d, 1H, J=7.4 Hz), 3.89 (m, 1H), 4.15-4.28 (m, 2H), 4.83 (bs, 1H), 6.55 (t, 1H, J=2.1 Hz); **^{13}C NMR** ($CDCl_3$) δ -4.7 (CH_3, double intensity), 14.2 (CH_3), 18.1 (C), 24.2 (CH_2), 25.8 (CH_3, triple intensity), 36.6 (CH_2), 45.6 (CH), 60.6 (CH,CH_2), 79.4 (CH), 140.8 (C), 142.6 (CH), 164.4(C), 218.3 (C); **MS** (CI, *m/e* (rel. int.)) 325 (20) M^++1, 267 (21), 193 (100), 133 (42); **HRMS**, calcd for $C_{17}H_{29}O_4Si$: 325.1835. Found: 325.1872.

2-Carbethoxy-4-[(methoxyethoxymethyl)oxy]bicyclo[3.3.0]oct-2-en-6-one (184-endo and 182-exo Isomers). Vinylcyclopropane **165-exo** (82.1 mg) was pyrolyzed (550 °C) according to the general procedure to give after flash chromatography (silica gel, 2:1 hexane/ethyl acetate) 11.3 mg of the endo isomer and 30.6 mg of the exo (51%). **184-endo:** R_f=0.32 (1:1 hexane/ethyl acetate); **IR** (neat) 2970, 1740, 1720, 1634, 1260, 1025 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.28 (td, 3H, J_1=7.1, J_2=0.7 Hz), 2.00-2.40 (m, 4H), 3.04 (t, 1H, J=8.7 Hz), 3.36 (d, 3H, 0.96 Hz), 3.50-3.81 (m, 5H), 4.22 (m. 2H), 4.67 (d, 1H, J=6.8 Hz), 4.80 (d, 1H, J=6.8 Hz), 5.01 (dd, 1H, J_1=9.2, J_2=2.0 Hz), 6.66 (bs, 1H); **^{13}C NMR** ($CDCl_3$) δ.14.1 (CH_3), 25.3 (CH_2), 38.6 (CH_2), 45.8 (CH), 52.1 (CH), 58.9 (CH_3), 60.6 (CH_2), 67.1 (CH_2), 71.7 (CH_2), 80.8 (CH), 95.3 (CH2), 140.2 (C), 140.8 (CH), 164.2 (C), 215.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 298 (<1) M^++1, 209 (30), 195 (40), 193 (79), 165 (30), 105 (50), 89 (100), 59 (100); **HRMS**, calcd for $C_{15}H_{23}O_6$: 299.1495. Found: 299.1541. **Anal Calcd** for $C_{15}H_{23}O_6$: C, 60.43; H, 7.44. Found: C, 60.45; H, 7.44. **184-exo:** R_f=0.34 (1:1 hexane/ethyl acetate); **IR** (neat) 2935, 1728, 1712, 1628, 1259, 1030 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.29 (td, 3H, J_1=7.2, J_2=1.2Hz), 2.08-2.39 (m, 4H), 2.89 (d, 1H, J=7.5 Hz), 3.37 (d, 3H, J=1.3 Hz), 3.51-3.79 (m, 4H), 3.89 (bs, 1H), 4.24 (m,

2H), 4.73 (m, 1H), 4.75 (dd, 1H, J_1=6.9, J_2=1.1 Hz), 4.83 (dd, 1H, J_1=6.9, J_2=1.1 Hz), 6.71 (m, 1H); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 24.4 (CH_2), 36.7 (CH_2), 45.7 (CH), 58.2 (CH_3), 59.0 (CH), 60.7 (CH_2), 67.2 (CH_2), 71.8 (CH_2), 83.8 (CH), 94.9 (CH_2), 140.8 (CH), 142.3 (C) 164.2 (C), 217.9 (C); **MS** (70 eV, *m/e* (rel. int.)) 298 (<1) M^+, 193 (45), 165 (25), 105 (40), 89 (100), 59 (100), 55 (39); **HRMS**, calcd for $C_{15}H_{23}O_6$: 229.1495. Found: 299.1486.

2-Carbethoxy-4-[(trimethylsilyl)ethoxymethyl)oxy]bicyclo-[3.3.0]oct-2-en-6-one (185-endo and 185-exo Isomers). Vinylcyclopropane **166-exo** (77.6 mg) was pyrolyzed (550 °C) according to the general procedure to give after flash chromatography (silica gel, 15:1, 12:1, 9:1 hexane/ethyl acetate) 29.7 mg of the endo isomer and 14.2 mg of a mixture of both isomers (57%). **185-endo:** R_f=0.22 (5:1 hexane/ethyl acetate); **IR** (neat) 2950, 1742, 1720, 1632, 1260, 1023 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.01 (s, 9H), 0.80-1.0 (m, 2H), 1.28 (t, 2H, J=7.1 Hz), 1.97-2.37 (m, 4H), 3.04 (t, 1H, J=8.7 Hz), 3.42-3.72 (m, 3H), 4.21 (q, 2H, J=7.1 Hz), 4.63 (d, 1H J=7.1 Hz, 4.74 (d, 1H, J=7.1 Hz), 4.98 (dd, 1H, J_1=9.1, J_2=2.1 Hz), 6.63 (bs, 1H); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.2 (CH_3), 18.1 (CH_2), 25.4 (CH_2), 38.6 (CH_2), 45.8 (CH), 52.2 (CH), 60.6 (CH_2), 65.4 (CH_2), 80.7 (CH), 94.7 (CH_2), 140.2 (C), 140.9 (CH), 164.3 (C), 215.0 (C); **MS** (CI, *m/e* (rel int.)) 341 (6) M^++1, 283 (81), 267 (28), 265 (28), 237 (32), 223 (33), 193 (100), 101 (32), 91 (49). **Anal. Calcd for** $C_{17}H_{28}O_5Si$: C, 59.95; H, 8.30: Found: C, 59.77; H, 8.29. **185-exo:** R_f=0.25 (5:1 hexane/ethyl acetate); **IR** (neat) 2945, 1738, 1722, 1255, 1023, 831 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.01 (s, 9H), 0.81-1.00 (m, 2H), 1.29 (t, 3H, J=7.2 Hz), 2.05-2.35 (m, 4H), 2.88 (d, 1H, J=7.3 Hz), 3.48-3.70 (m, 2H), 3.87 (m, 1H), 4.14-4.29 (m, 2H), 4.707 (s, 1H), 4.711 (d, 1H, J=6.9 Hz), 4.78

(d, 1H, J=6.9 Hz) 6.69 (t, 1H, J=2.1 Hz); **^{13}C NMR** ($CDCl_3$) δ -1.4 (CH_3, triple intensity), 14.2 (CH_3), 18.1 (CH_2), 24.4 (CH_2), 36.6 (CH_2), 45.7 (CH), 58.2 (CH), 60.7 (CH_2), 65.5 (CH_2), 83.7 (CH), 94.3 (CH_2), 141.0 (CH), 142.2 (C), 164.2 (C), 217.8 (C); **MS** (CI, *m/e* (rel int.)) 341 (6) M^++1, 339 (8), 283 (60), 211 (51), 193 (100), 91 (70), 85 (26).

7-Carbethoxybicyclo[4.3.0]non-7-en-2-one (179). Vinylcyclopropane **145-exo** (770 mg, 3.7 mmol) was pyrolyzed (600 °C) according to the general procedure to give after preparative TLC (9:1 hexane/ethyl acetate, three elutions) 146 mg of hydrindane **179** (19%). R_f=0.19 (3:1 hexane/ethyl acetate); **IR** (neat) 2950, 1720, 1710, 1260, 1110 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.25 (t, 3H, J=7.2 Hz), 1.32-1.50 (m, 1H), 1.70-1.90 (m, 2H) 2.10-2.20 (m, 1H), 2.30-2.40 (m, 2H), 2.55-2.83 (m, 2H), 2.98 (dd, 1H, J_1=17.0, J_2=8.8 Hz), 3.27-3.40 (m, 1H), 4.18 (m, 2H), 6.73 (dd, 1H, J_1=4.5, J_2=2.3 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 22.1 (CH_2), 27.3 (CH_2), 34.4 (CH_2), 39.1 (CH_2), 46.1 (CH), 50.4 (CH), 60.2 (CH_2), 139.6 (C), 141.9 (CH), 164.4 (C), 213.2 (C); **MS** (70 eV, *m/e* (rel. int.)) 208 (65) M^+, 179 (20), 162 (40), 135 (100), 117 (50), 91 (45), 79 (60), 65 (40); **HRMS**, calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1105.

9-[(tert-Butyldimethylsilyl)oxy]-7-carbethoxybicyclo[4.3.0]-non-7-en-2-one (186-trans and 186-cis isomers). Vinylcyclopropane **167-endo** (115.5 mg) was pyrolyzed (575 °C) according to the general procedure to give after flash chromatography (silica gel, 5% deactivated with H_2O; 19:1, 15:1 hexane/ethyl acetate) 40 mg of the trans isomer and 10.4 mg of the cis (44%). **186-trans isomer:** R_f=0.30 (6:1 hexane/ethyl acetate); **IR** (neat) 2945, 2920, 1715, 1624, 1255, 1208, 1040, 825 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.03, (s, 3H), 0.01 (s, 3H), 0.79 (s, 9H), 1.27 (t, 3H, J=7.1Hz), 1.33-2.47 (m, 6H), 2.84 (t, 1H, J=7.3

Hz), 3.0 (m, 1H), 4.19 (m, 2H), 4.90 (dd, 1H, J_1=7.0, J_2=2.4 Hz), 6.60 (d, 1H, J=2.3 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.1 (CH_3), -4.7 (CH_3), 14.2 (CH_3), 17.9 (C), 23.4 (CH_2) 25.7 (CH_3, triple intensity), 30.0 (CH_2), 42.6 (CH_2), 45.0 (CH), 55.0 (CH), 60.5 (CH_2), 77.5 (CH), 139.9 (CH), 143.7 (C), 164.6 (C), 211.2 (C); **MS** (70 eV, *m/e* (rel int.)) 338 (3) M^+, 281 (100), 207 (40), 105 (20), 75 (79), 73 (32), 57 (18); **HRMS**, calcd for $C_{18}H_{31}O_4Si$: 339.1992: Found: 339.2000. **Anal Calcd for** $C_{18}H_{31}O_4Si$: C, 63.92; H, 8.96: Found: C, 63.69; H, 8.91. **186-cis isomer:** R_f=0.32 (6:1 hexane/ethyl acetate); **IR** (neat) 2930, 2907, 1717, 1613, 1243, 835 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.06 (s, 6H), 0.86 (s, 9H), 1.28 (t, 3H, J=7.1 Hz), 1.67-1.95 (m, 2H), 2.10-2.50 (m, 4H), 2.84 (dd, 1H, J_1=8.4, J_2=6.0 Hz), 3.44 (m, 1H), 4.20 (qd, 2H, J_1=7.1, J_2=1.7 Hz), 5.15 (dt, 1H, J_1=6.0, J_2=2.0 Hz), 6.55 (t, 1H, J=1.4 Hz); **^{13}C NMR** ($CDCl_3$) δ -4.8 (CH_3), 14.2 (CH_3), 18.1 (C), 22.1 (CH_2), 25.7 (CH_3, triple intensity), 28.2 (CH_2), 39.3 (CH_2), 45.3 (CH), 60.5 (CH_2), 60.9 (CH), 78.3 (CH), 140.0 (C), 143.0 (CH), 164.4 (C), 210.7 (C); **MS** (70 eV, *m/e* (rel. int.)) 338 (1) M^+, 281 (100), 207 (59), 105 (21), 75 (90), 73 (40), 57 (20); **HRMS**, calcd for $C_{18}H_{31}O_4Si$: 339.1992. Found: 339.1994.

8-Carbethoxybicyclo[5.3.0]dec-8-en-2-one (180). A mixture of *endo*- and *exo*-vinylcyclopropanes **146-exo** and **146-endo** (237 mg, 1.07 mmol) was pyrolyzed (600 °C) according to the general procedure to give after flash chromatography (silica gel, 98:2, 95:5, 9:1 hexane/ether) then preparative TLC 50 mg of hydroazulene **180** (21%). R_f=0.28 (7:3 hexane/ethyl acetate); **IR** (neat) 2920, 2240, 1700, 1628, 1255, 728 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.03 (m, 1H), 1.26 (t, 3H, J=7.2 Hz), 1.42-1.67 (m, 2H), 1.80-2.02 (m, 3H), 2.35-2.48 (m, 2H), 2.55-2.66 (m, 1H), 2.98 (m, 1H), 3.26 (bt, 1H, J=8.9 Hz), 3.48 (q, J=8.9 Hz), 4.16 (q, 2H, J=7.2 Hz), 6.68 (m, 1H); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 26.1 (CH_2), 29.0

(CH_2), 30.1 (CH_2), 31.7 (CH_2), 43.1 (CH_2), 45.5 (CH), 55.7 (CH), 60.1 (CH_2), 137.5 (C), 141.6 (CH), 164.3 (C), 211.8 (C); **MS** (70 eV, *m/e* (rel. int.)) 222 (43) M^+, 176 (76) 149 (60) 91 (90), 79 (90) 65 (77), 55 (100); **HRMS**, calcd for $C_{13}H_{18}O_3$: 222.1256. Found: 222.1275.

(7S,8R)-2-Carbethoxy-7,8-(isopropylidenedioxy)bicyclo-[3.3.0]oct-2-en-6-one (181). Vinylcyclopropane **148-exo** (41 mg, 0.15 mmol) was pyrolyzed (550 °C) according to the general procedure to give after preparative TLC (9:1 hexane/ethyl acetate, two elutions then 6:1, one elution) 21 mg of diquinane **181** (51%). $[\alpha]_D$ +64.4 ° (c 0.25, MeOH); R_f=0.35 (3:1 hexane/ethyl acetate); **IR** (neat) 2980, 2930, 1755, 1712, 1621, 1370, 1260 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.27 (t, 3H, J=7.1 Hz), 1.30 (s, 3H), 1.38 (s, 3H), 2.67-2.75 (m, 2H), 3.18 (m, 1H), 3.79 (m, 1H), 4.12 (d, 1H, J=5.1 Hz), 4.19 (qd, 2H, J_1=7.1, J_2=1.8 Hz), 4.99 (d, 1H, J=5.1 Hz), 6.74 (dd, 1H, J_1 4.8, J_2=2.4 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 25.0 (CH_3), 27.0 (CH_3), 36.1 (CH_2), 46.7 (CH), 50.3 (CH), 60.6 (CH_2), 78.9 (CH, double intensity), 112.2 (C), 135.1 (C), 145.4 (CH), 163.7 (C), 217.3 (C); **MS** (70 eV, *m/e* (rel. int.)) 266 (8) M^+, 251 (29), 208 (46), 134 (48), 100 (100), 85 (87) 79 (75); **HRMS**, calcd for $C_{14}H_{18}O_5$: 266.1154. Found: 266.1171.

2-Carbethoxy-4-endo[((4'-benzyloxy)benzoyl)oxo]bicyclo-[3.3.0]-oct-2-en-6-one (183a). A mixture of vinylcyclopropanes **164a-exo/endo** (35.2 mg, 0.07mmol) was pyrolyzed (480 °C) according to the general procedure to give after preparative TLC (3:1 hexane/ethyl acetate, three elutions; then 6:1 hexane/ethyl acetate, one elution) 11.9 mg of diquinane **183a** (34%). R_f=0.12 (3:1 hexane/ethyl acetate); **IR** (neat) 2980, 2925, 1746, 1712, 1599, 1145, 630 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.36 (t, 3H, J=7.2 Hz), 3.57 (t, 1H, J=9.0 Hz), 3.85 (d,

1H, J=9.0 Hz), 4.29 (qd, 2H, J_1=7.2, J_2=2.0 Hz), 4.45 (d, 1H, J=4.9 Hz), 4.80 (d, 1H, J=4.9 Hz), 5.09 (s, 2H), 6.12 (bd, 1H, J=9.0 Hz), 6.85 (t, 1H, J=2.0 Hz), 6.93 (d, 2H, J=8.5 Hz), 7.28-7.47 (m, 5H), 7.84 (d, 2H, J=8.5 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.2 (CH_3), 25.6 (CH_3), 27.1 (CH_3), 48.4 (CH), 49.3 (CH), 61.3 (CH_2), 70.3 (CH_2), 77.2 (CH), 77.8 (CH), 80.6 (CH), 112.7 (C), 114.8 (CH), 121.3 (C), 127.4 (CH), 128.2 (CH), 128.7 (CH), 131.8 (CH), 136.3 (C), 138.8 (C), 141.0 (CH), 163.0 (C), 163.3 (C), 165.1 (C), 211.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 492 (1.5) M^+, 211 (56), 91 (100).

(7S,8R)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-carbethoxy-7,8-(isopropylidenedioxy)bicyclo[3.3.0]oct-2-en-6-one (187-endo and 187-exo Isomers). Vinylcyclopropane **169-exo** (158 mg, 0.40 mmol) was pyrolyzed (525 °C) according to the general procedure to give after flash chromatography (silica gel, 10% deactivated with H_2O; 19:1, 15:1, 12:1 hexane/ethyl acetate) 118 mg of the endo isomer and traces of the endo isomer. **187-endo:** (75%) $[\alpha]_D$ = +84.30 (MeOH c, 0.395); R_f=0.35 (8:1 hexane ethyl acetate); **IR** (neat) 2910, 2240, 1755, 1716, 1636, 1247 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.79 (s, 9H), 1.30 (t, 3H, J=7.1 Hz), 3.25 (t, 1H, J=9.0 Hz), 3.58 (bd, 1H, J=9.0 Hz), 4.18-4.32 (m, 2H), 4.35 (d, 1H, J=5.1 Hz), 4.58 (d, 1H, J=5.1 Hz), 5.02 (dd, 1H, J_1=9.0 , J_2=2.2 Hz), 6.56 (t, 1H, J=2.0 Hz); **^{13}C NMR** ($CDCl_3$) δ -5.8 (CH_3), -5.7 (CH_3), 13.6 (CH_3), 17.5 (C), 25.1 (CH_3, triple intensity), 26.4 (CH_3), 26.5 (CH_3), 47.6 (CH), 51.9 (CH), 60.3 (CH_2), 76.2 (CH), 77.5 (CH), 80.6 (CH), 117.7 (C), 136.4 (C), 142.9 (CH), 163.2 (C), 210.7 (C); **MS** (70 eV,*m/e* (rel. int.)) 396 (1.5) M^+, 339 (26), 281 (100), 179 (13), 165 (19), 85 (13), 75 (55), 73 (59), 57 (18); **HRMS**, calcd for $C_{20}H_{32}O_6Si$: 396.1968. Found: 396.1934. **187-exo:** **mp** 73.5-75.5 °C; $[\alpha]_D$ = +29.22 (MeOH c, 0.575); R_f =

0.26 (6:1 hexane/ethyl acetate); **IR** (neat) 2922, 1752, 1720, 1627, 1253, 1074, 841 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 0.11 (s, 3H), 0.13 (s, 3H), 0.37 (s, 9H), 1.29-1.34 (m, 6H), 1.42 (s, 3H), 3.07 (d, 1H, J=7.3 Hz), 3.98 (m, 1H), 4.13 (d, 1H, J=5.1 Hz), 4.26 (q, 2H, J=7.1 Hz), 4.83 (bs, 1H), 4.93 (bs, 1H), 4.93 (d, 1H, J=5.1 Hz), 6.61 (t, 1H, J=2.4 Hz); **^{13}C NMR** ($CDCl_3$) δ -4.7 (CH_3, double intensity), 14.3 (CH_3), 18.2 (C), 25.0 (CH_3), 25.8 (CH_3, triple intensity), 27.1 (CH_3), 49.1 (CH), 57.9 (CH), 61.1 (CH_2), 78.0 (CH), 79.0 (CH, double intensity), 112.3 (C), 137.8 (C), 144.6 (CH), 164.9 (C), 214.0 (C); **MS** (70 eV, *m/e* (rel. int.)) 396 (<1) M^+, 339 (30), 281 (100), 75 (77), 73 (60); **HRMS** calcd for $C_{20}H_{32}O_6Si$: 396.1968. Found: 396.1945.

(7S,8R)-4-[(trimethylsilylethoxymethyl)oxy]-2-carbethoxy-7,8-(isopropylidenedioxy)bicyclo[3.3.0]oct-2-en-6-one (188-endo and 188-exo isomers). Following the general procedure for flash vacuum pyrolysis, vinylcyclopropane **170** (179.6 mg) was pyrolyzed (535 °C) to give after flash chromatography (silica gel, 12:1, 9:1, 6:1 hexane/ethyl acetate) 15.6 mg of the endo diquinane and 109.8 mg of the exo isomer as a cream-colored solid (61%). Traces of the vinylcyclopropane were recovered during chromatography suggesting that a higher pyrolysis temperature is needed on this scale. **188-endo: mp** 74-82 °C; **R_f** = 0.24 (4:1 hexane/ethyl acetate); IR (neat) 2959. 1762, 1720, 1640, 1372, 1250, 1015, 832cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ -0.03 (s, 9H), 1.29 (t, 3H, J=7.1 Hz), 1.30 (s, 3H), 1.36 (s, 3H), 3.39 (t, 1H, J=9.1 Hz), 3.45-3.69 (m, 3H), 4.25 (q, 2H, J=7.1 Hz), 4.37 (d, 1H, J=5.2 Hz), 4.58 (d, 1H, J=7.2 Hz), 4.63 (d, 1H, J=5.2 Hz), 4.68 (d, 1H, J=7.2 Hz), 4.98 (dd, 1H, J_1=9.1, J_2=2.4 Hz), 6.69 (m, 1H); **^{13}C NMR** ($CDCl_3$) δ -1.5 (CH_3, triple intensity), 14.2 (CH_3), 18.0 (C), 25.5 (CH_3), 27.1 (CH_3), 48.3 (CH), 51.2 (CH), 61.0 (CH_2), 65.6 (CH_2), 78.1 (CH), 80.2 (CH),

80.9 (CH), 94.6 (CH_2), 112.4 (C), 137.7 (C), 142.5 (CH), 163.6 (C), 21.6 (C); **MS** (CI, *m/e* (rel. int.)) 413 (<1) M^++1, 237 (30), 209 (32), 207 (28), 179 (77), 101 (45), 91 (100); **HRMS**, calcd for $C_{20}H_{33}O_7Si$: 413.1996. Found: 413.1980. **Anal. Calcd** for C_{20} $H_{32}O_7Si$: C, 58.25; H, 7.77. Found: C, 57.74; H, 7.87.

2-Carbethoxybicyclo[3.2.1]hept-2-en-6-one. (199). To a solution of vinylcylopropane **144-endo** (145 mg, 0.75 mmol) in 3:1 pentane/CH_2Cl_2 (4mL) cooled to -20 °C was added hexamethyldisilazane (190 μL, 0.90 mmol) then trimethylsilyl iodide (129 μL, 0.90 mmol). Stirring was continued at -20 °C for 1 h then at room temperature for 3 h. The reaction mixture was quenched with 3N HCl and diluted with ether. The ether layer was washed with water and the aqueous layers combined and extracted with ether. The combined ether extracts were washed with brine and dried (Na_2SO_4). Purification by flash chromatography (silica gel, 10% deactivated with H_2O; 5:1 hexane/ethyl acetate) gave 130 mg of a pale yellow oil (90%). Note: If there are two spots by TLC, the less polar spot is the silylenol ether which can be hydrolyzed to the ketone with cat. $HClO_4$ in THF/H_2O at room temperature prior to chromatography. **199**: R_f=0.23 (5:1 hexane/ethyl acetate); **IR** (neat) 2970, 1746, 1708, 1635, 1250, 1070 cm^{-1}; ^{1}**H NMR** ($CDCl_3$) δ 1.21 (t, 3H, J=7.0 Hz), 1.85 (m, 1H), 2.05-2.60 (m, 4H), 3.31 (bs, 1H), 4.11 (q, 2H, J=7.0 Hz), 6.63 (m, 1H); ^{13}**C NMR** ($CDCl_3$) δ 14.1 (CH_3), 31.8 (CH_2), 31.9 (CH), 33.2 (CH_2), 44.3 (CH), 48.9 (CH_2), 60.5 (CH_2), 128.7 (C), 135.7 (CH), 165.7 (C), 219.4 (C); **MS** (70 eV, *m/e* (rel. int.)) 194 (45) M^+, 155 (57), 123 (49), 107 (32), 88 (49), 79 (100); **HRMS**, calcd for $C_{11}H_{14}O_3$: 194.0943. Found: 194.0980.

2-Carbethoxybicyclo[3.2.2]hept-2-en-6-one (200). Following the same procedure used for the preparation of **199**, vinylcycloprpane **145-endo** (113

mg, 0.55 mmol) gave after flash chromatography (silica gel, 10% deactivatedwith H_2O; 8:1 hexane ethyl/acetate) 109 mg of a cream-colored solid (96%). **200: mp** 29.5-31.5 °C; R_f=0.14 (8:1 hexane/ethyl acetate); **IR** (neat) 2930, 1720, 1712, 1640, 1250, 1040 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.24 (t, 3H, J=7.1 Hz), 1.86-2.15 (m, 3H), 2.49-2.71 (m, 4H), 3.36 (bs, 1H), 4.14 (q, 2H, J=7.1 Hz), 6.81 (t, 1H, J=4.0 Hz); **^{13}C NMR** ($CDCl_3$) δ 14.1 (CH_3), 24.4 (CH_2), 27.5 (CH_2), 28.3 (CH), 35.5 (CH_2), 45.8 (CH), 46.1 (CH_2), 60.7 (CH_2) 137.9 (C), 138.7 (CH), 166.7 (C), 213.7 (C); **MS** (70 eV, *m/e* (rel. int.)) 208 (49) M^+, 166 (89), 137 (31), 107 (32), 93 (100), 91 (62), 79 (43), 77 (41).; **HRMS**, calcd for $C_{12}H_{16}O_3$: 208.1099. Found: 208.1089.

(7S,8R)-2-Carbethoxy-4-hydroxy-7,8-isopropylidenedioxy-bicyclo[3.3.0]oct-2-en-6-one (204-endo and 204-exo Isomers). To a solution of the vinylcyclopropane **169** (341.8 mg, 0.86 mmol) in 15 mL of THF at -40 °C was added the TBAF•$3H_2O$ (0.543 g 1.73 mmol). The cooling bath was removed, stirring was continued for 10 min, and the reaction was quenched with sat'd aqueous NH_4Cl sol'n. The aqueous layer was extracted three times with ethyl acetate. The organic extracts were combined, washed with brine, and dried ($MgSO_4$). Flash chromatography (silica gel, 3:1, 2:1, 1:1 hexane/ethyl acetate) gave 73.6 mg of the exo alcohol and 134.7 mg of the endo alcohol (86 %).

The endo isomer was retreated with TBAF•$3H_2O$ (0.5 equiv., 75 mg) at room temperature for 6 h. Following the same procedure for workup and chromatography gave 37.9 mg of the exo alcohol and 37.7 mg of the endo. The overall yield was 111.5 mg (44%) of the exo alcohol and 37.7 mg (15%) of the endo. **204-exo:** R_f = 0.34 (1:1 hexane/ethyl acetate); **IR** (neat) 3465 (broad) 2980, 2935, 1755, 1720, 1628, 1375, 1260 cm^{-1}; **^{1}H NMR** ($CDCl_3$) δ 1.28-1.34 (m, 6H), 1.4 (s, 3H), 2.38 (bd,

1H, J=6.2 Hz), 3.19 (d, 1H, J=7.2 Hz), 4.00 (bd, 1H, J=7.3 Hz), 4.15 (d, 1H, J=4.8 Hz), 4.26 (m, 2H), 4.89 (bs, 1H), 4.95 (d, 1H, J=4.8 Hz), 6.73 (t, 1H, J=2.4 Hz). **204-endo:** R_f = 0.29 (1:1 hexane/ethyl acetate); **IR** (neat) 3460, 2990, 1755, 1720, 1635, 1383, 1250 cm^{-1}; ^1H **NMR** ($CDCl_3$) δ 1.32 (m, 6H), 1.41 (s, 3H), 2.88 (m, 1H), 3.34 (dd, 1H, J=8.6 Hz), 3.74 (d, 1H, J=8.0 Hz), 4.23-4.31 (m, 3H), 4.83 (d, 1H, J=5.1 Hz), 5.16 (m, 1H), 6.73 (dd, 1H J=2.0 Hz).

(7S,8R)-4-*exo*-[(*tert*-Butyldimethylsilyl)oxy]-2-carbethoxy-7,8-(isopropylidenedioxy)bicyclo[3.3.0]oct-2-en-6-ol (6-*endo* Isomer, 209). A solution of ketone **187** (148.3 mg, 0.37 mmol) in MeOH was cooled to -20 °C , and $NaBH_4$ (14.0 mg, 0.37 mmol) was added. After 30 min, TLC indicated that all of the ketone had been consumed, so the reaction was slowly quenched with sat'd aq. NH_4Cl sol'n and warmed to room temperature. The aqueous layer was extracted three times with ethyl acetate; the extracts were combined, washed with brine, and dried (MgSO4). Flash chromatography (silica gel, 4:1, 3:1 hexane/ethyl acetate) gave 126.9 mg of the ethyl ester-alcohol (86%) and 8.86 mg of the methyl ester alcohol (6.2%) as white waxy solids. **209:** **mp** 87.5-89.5 °C; R_f = 0.25 (3:1 hexane/ethyl acetate); **IR** (neat) 3500, 2940, 1715, 1617, 1260, 1055, 840 cm^{-1}; ^1H **NMR** ($CDCl_3$) d 0.09 (s, 3H), 0.10 (s, 3H), 0.87 (s, 9H), 1.29 (m, 6H), 1.51 (s, 3H), 2.30 (d, 1H, J=10 Hz), 2.57 (dd, 1H, J=7.6 Hz), 3.52 (bd, 11H, J=8.1 Hz), 4.23 (a, 2H, J=7.1 Hz), 4.44 (dd, 1H, J=5.0 Hz) 4.67 (d, 1H, J=5.3 Hz), 4.75(bs, 1H), 6.54 (bs, 1H).

(7S,8R)-4-*exo*-[(*tert*-Butyldimethylsilyl)oxy]-2-carbethoxy-7,8-isopropylidenedioxy-6-*endo*-[(isopropylsulfonyl)oxy]bicyclo-[3.3.0]oct-2-ene (210). Et_3N (0.42 mL, 3.0 mmol) and isopropylsulfonyl chloride (0.17 mL, 1.52 mmol) were added to a solution of alcohol **209** in 10 mL of

CH_2Cl_2 at 0 °C. The ice-bath was removed, and stirring was continued at room temperature for 50 min. The reaction was quenched with sat'd aqueous NH_4Cl sol'n, and the aqueous layer extracted three times with ethyl acetate. The organic extracts were combined, washed with brine, and dried ($MgSO_4$). Purification by flash chromatography (silica gel, 5:1 hexane/ethyl acetate) yielded the pure sulfonate (149.2 mg, 98%). **210:** R_f = 0.31 (3:1 hexane ethyl/acetate); **IR** (neat) 2930, 1715, 622, 1340, 1263, 1158, 1065, 839 cm^{-1}: **^{1}H NMR** ($CDCl_3$) δ 0.06 (S, 3H), 0.07 (s, 3H), 0.84 (s, 9H), 1.27 (m, 6H), 1.43 (d, 6H, J=6.8 Hz), 1.49, (s, 3H), 2.91 (dd, 1H, J=8.4 Hz), 3.31 (h, 1H, J=7.0 Hz), 3.51 (bd, 1H, J=7.7 Hz), 4.20 (q, 2H, J=7.2 Hz), 4.38 (dd, 1H, J_1=9.4, J_2 = 4.1 Hz), 4.56 (dd, 1H, J_1=4.5, J_2=4.1 Hz), 4.62 (d, 1H, J=4.9 Hz), 4.78 (bs, 1H), 6.52 (bs, 1H).

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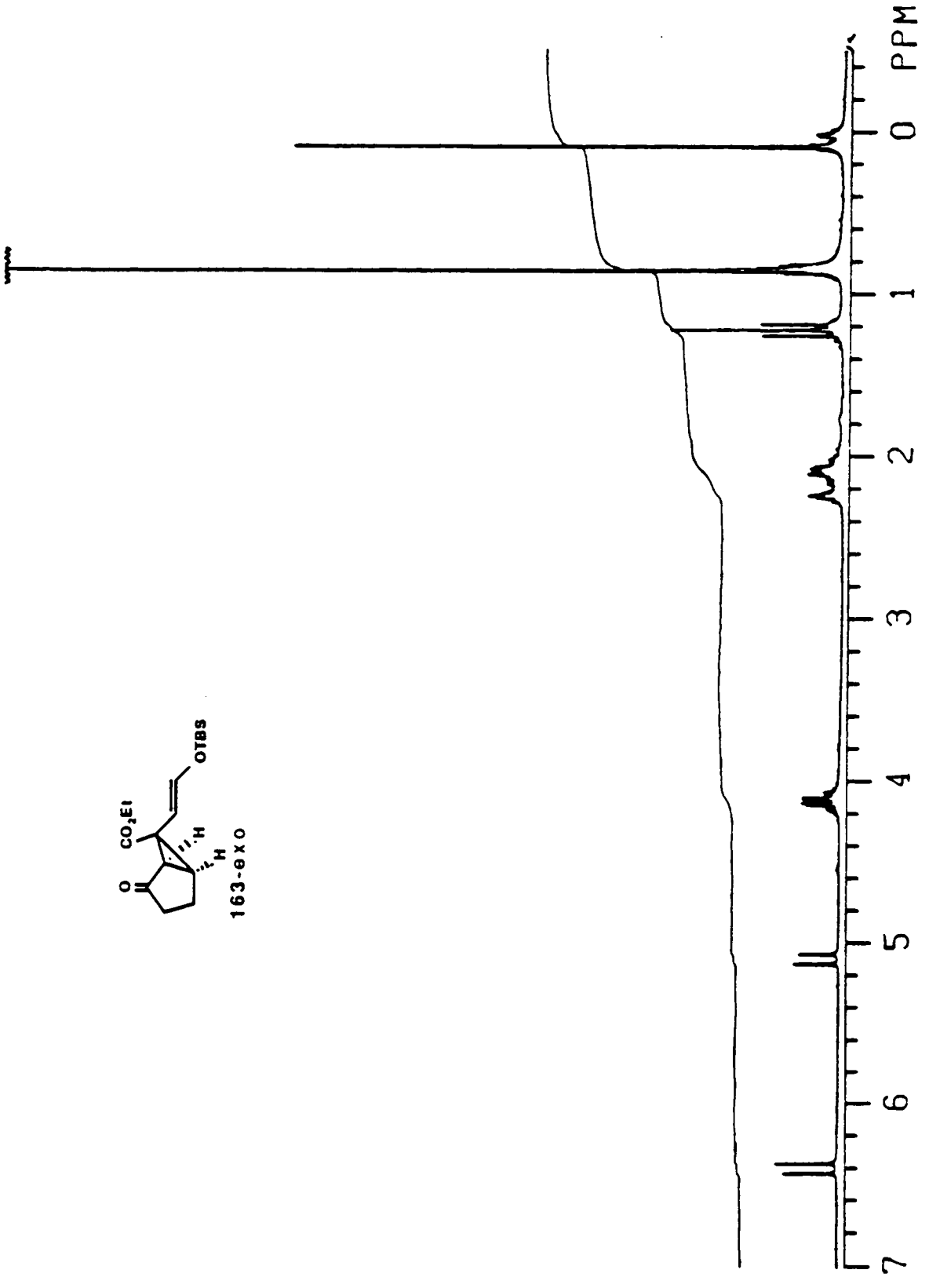
VI. APPENDIX

SELECTED SPECTRA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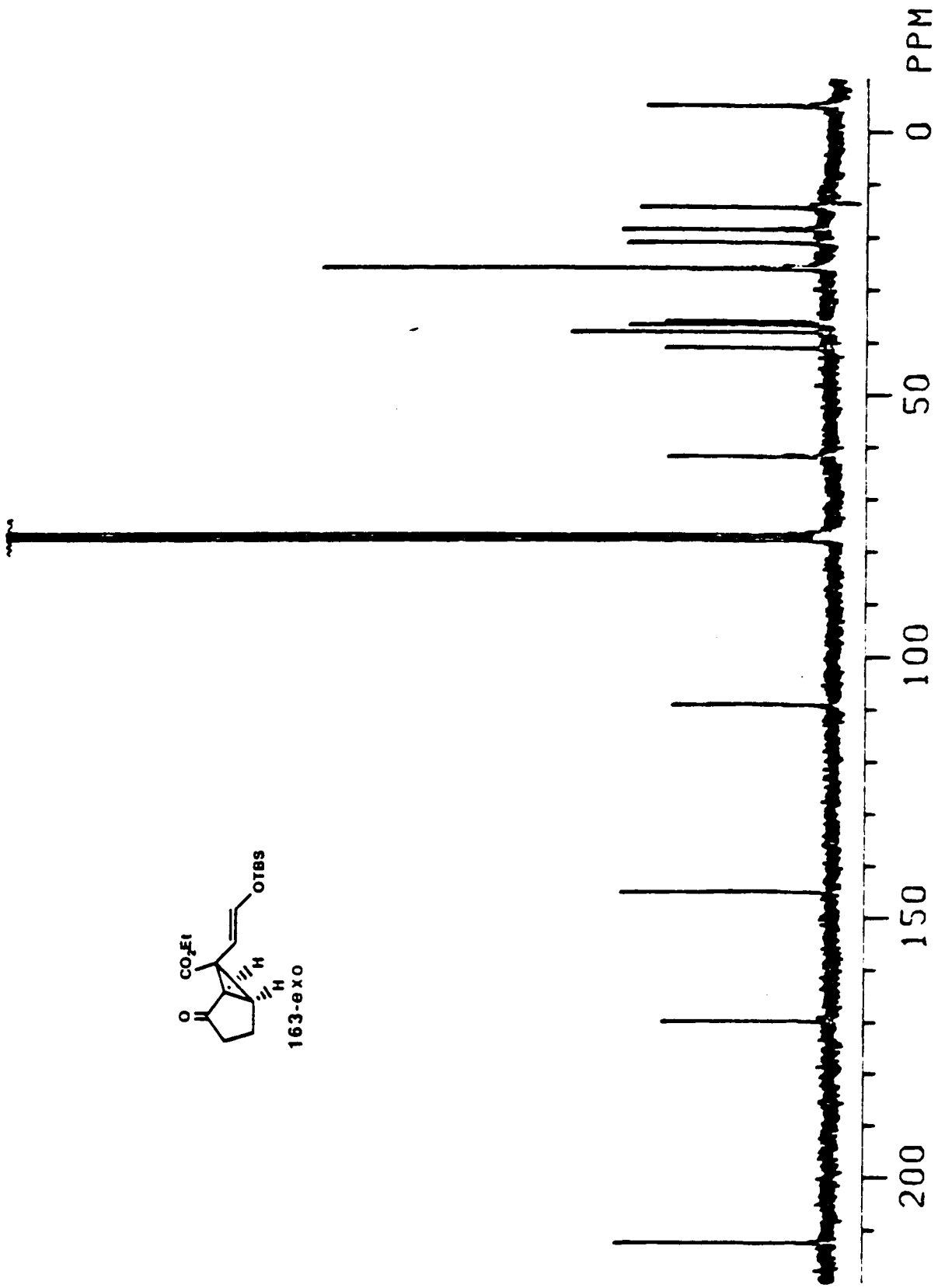
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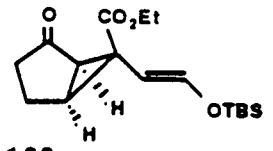
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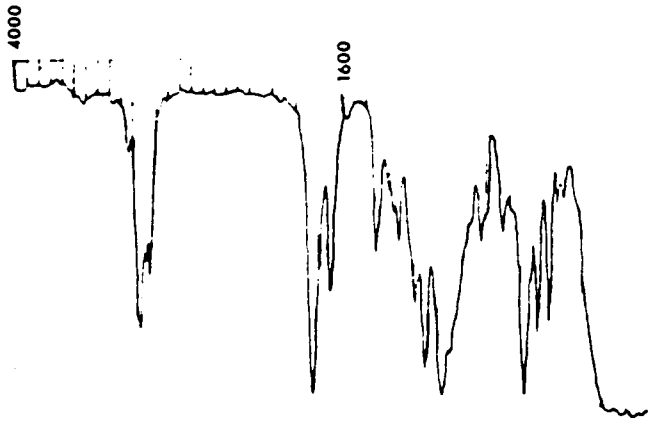
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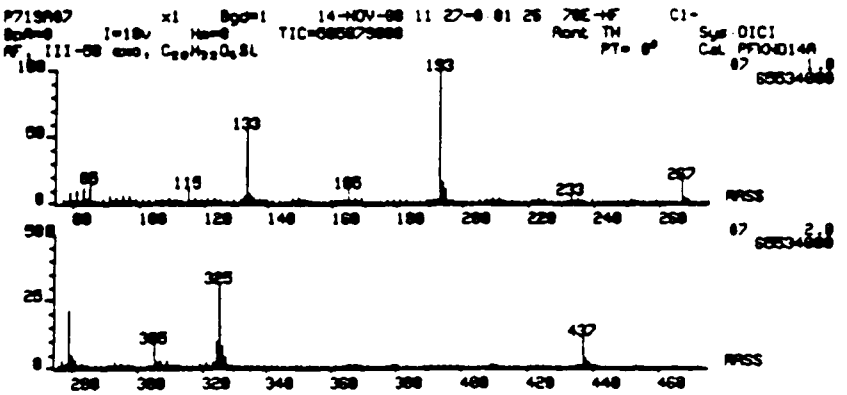
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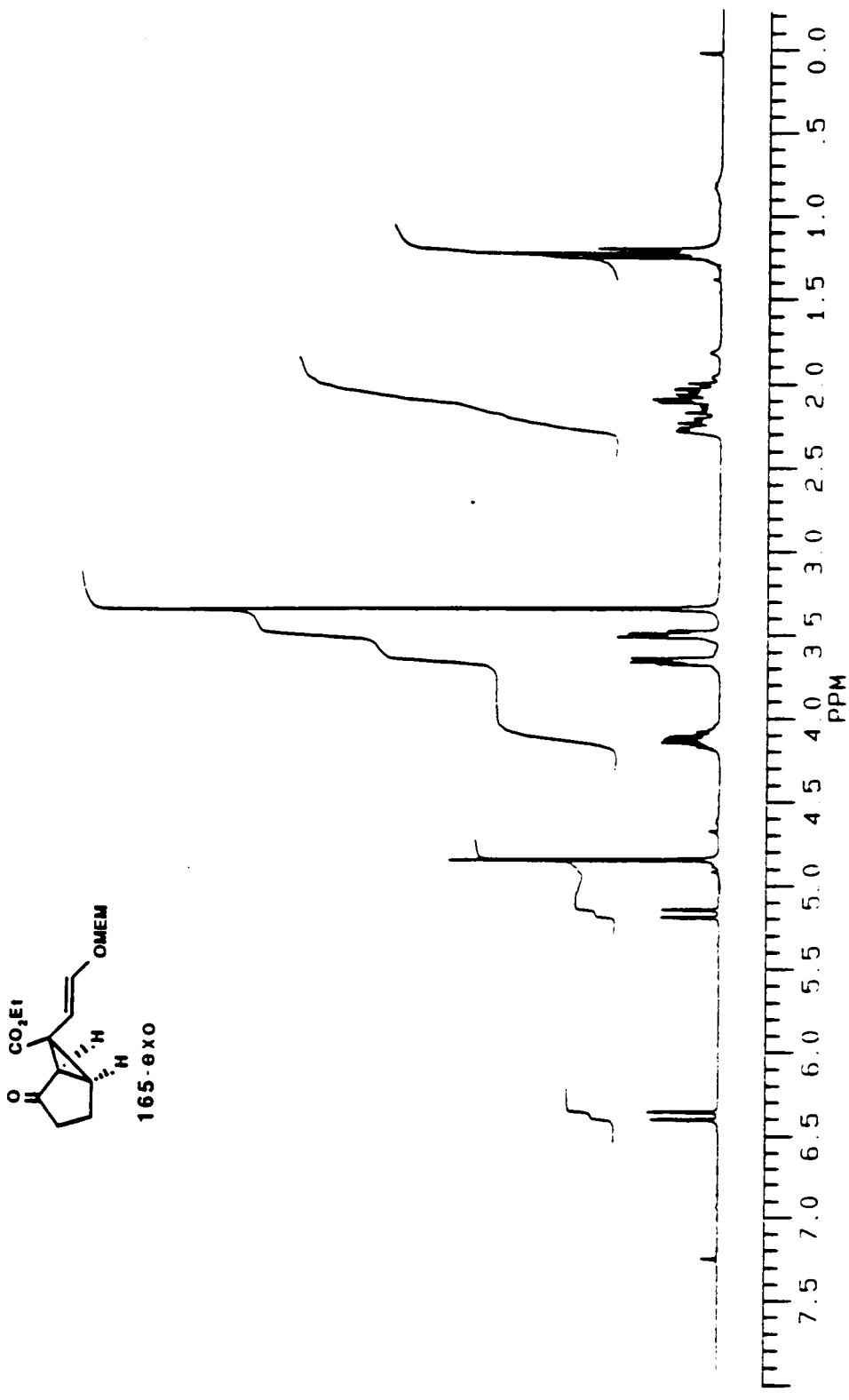
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OMEM
H
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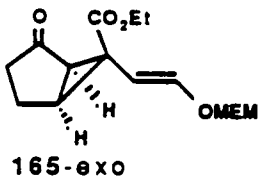
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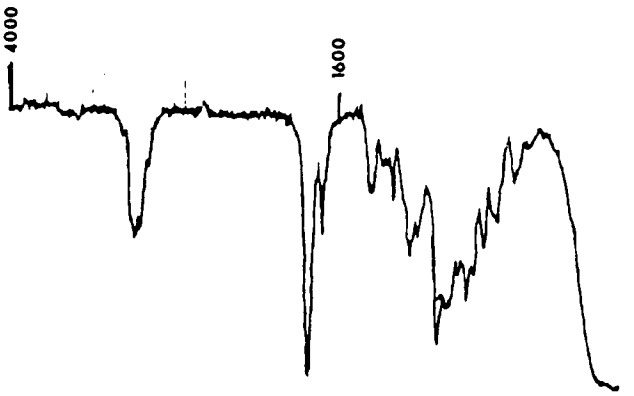
165-exo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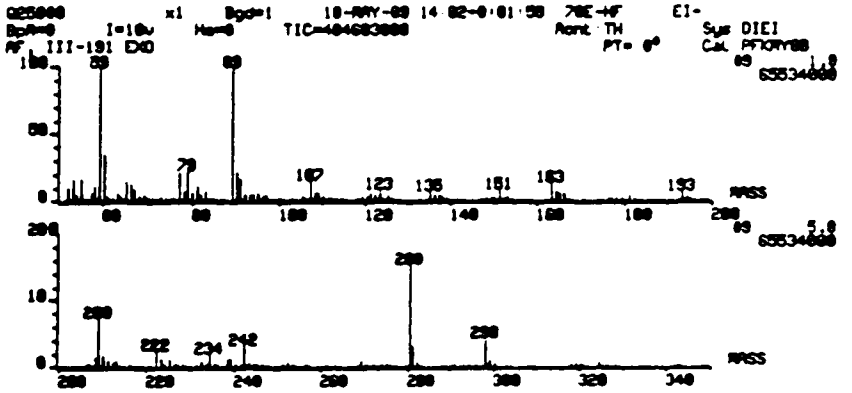

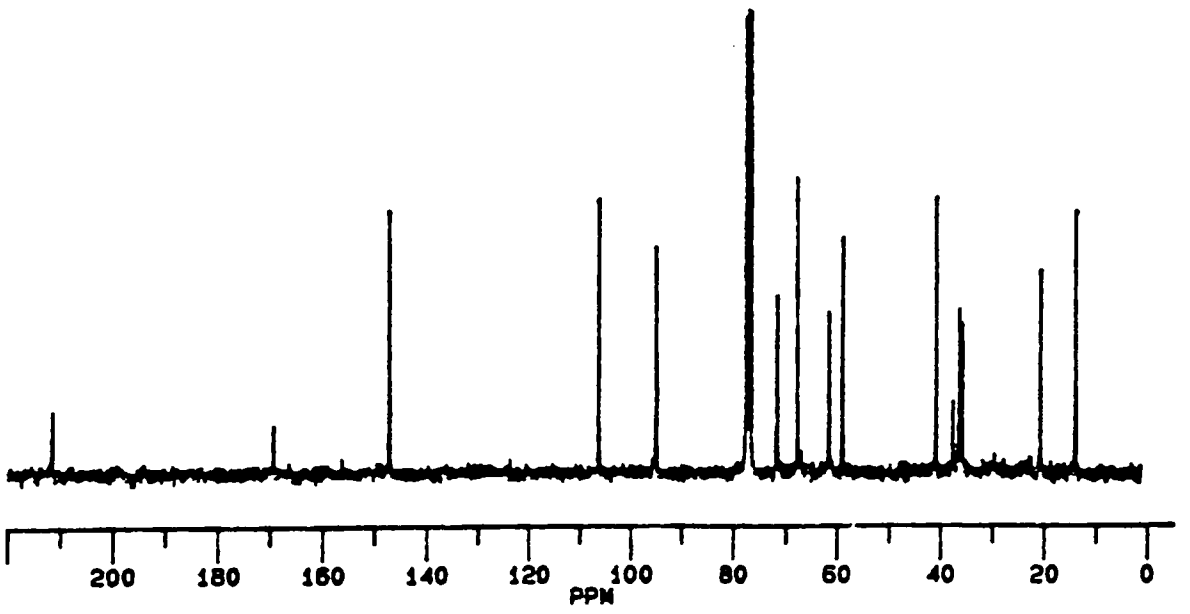
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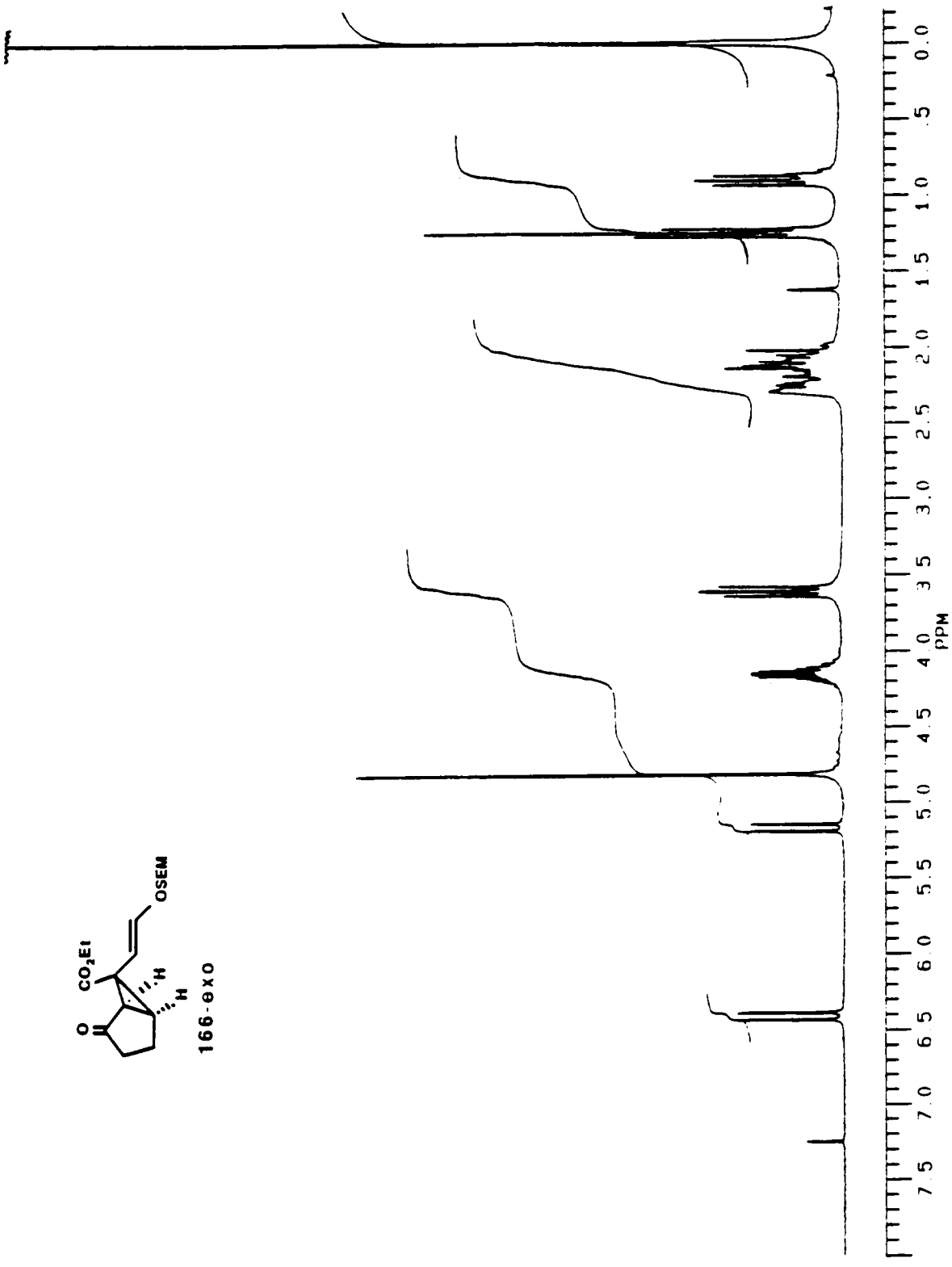
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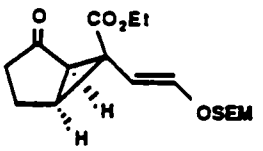
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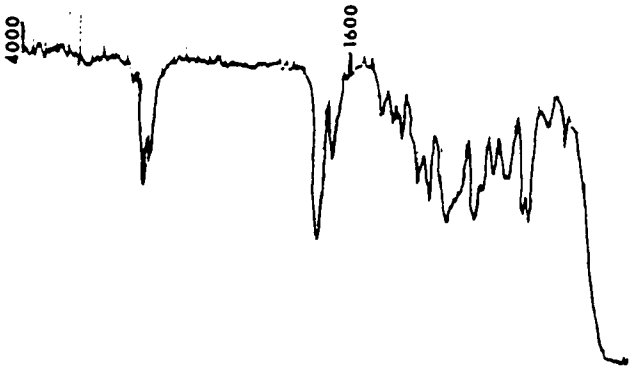
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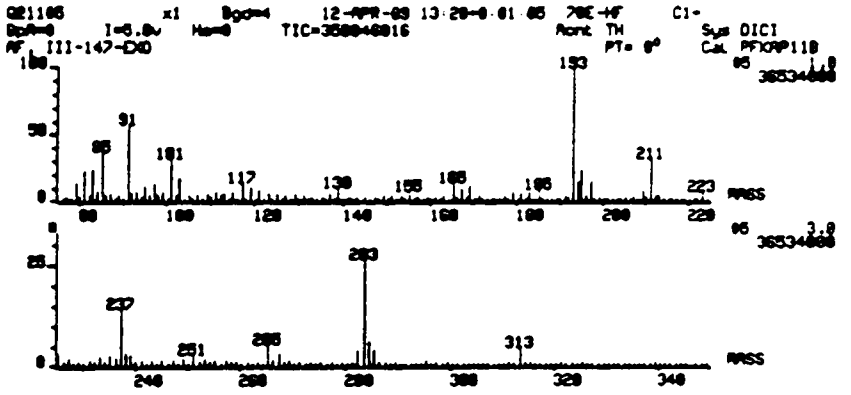
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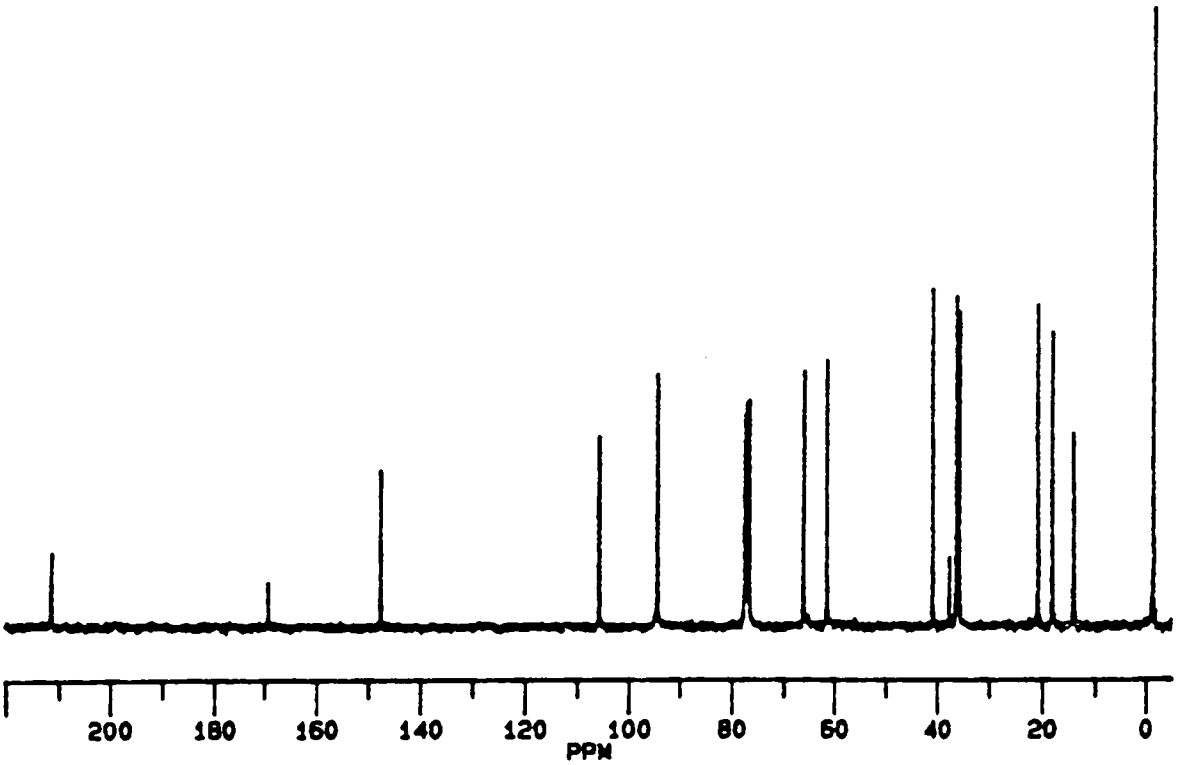
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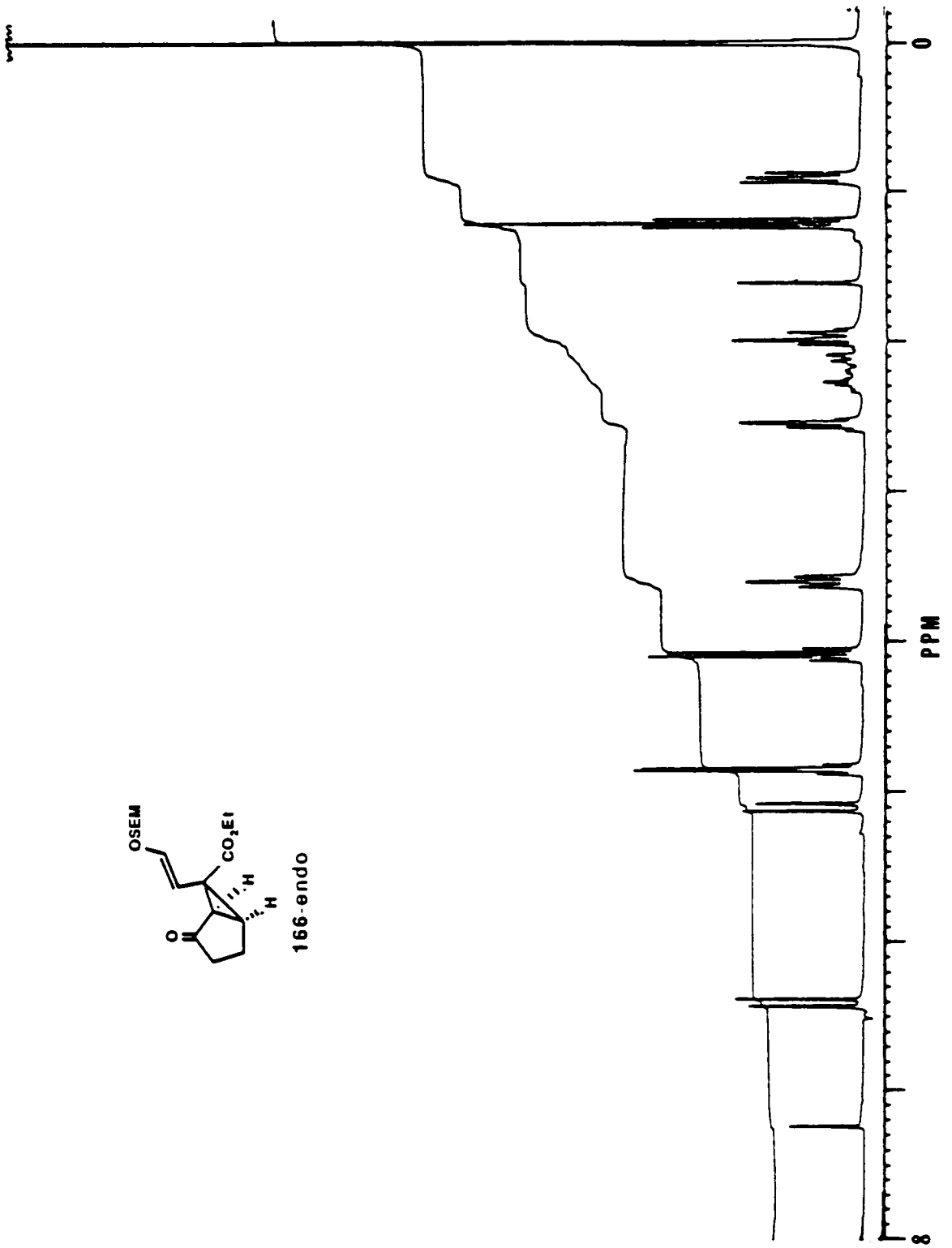
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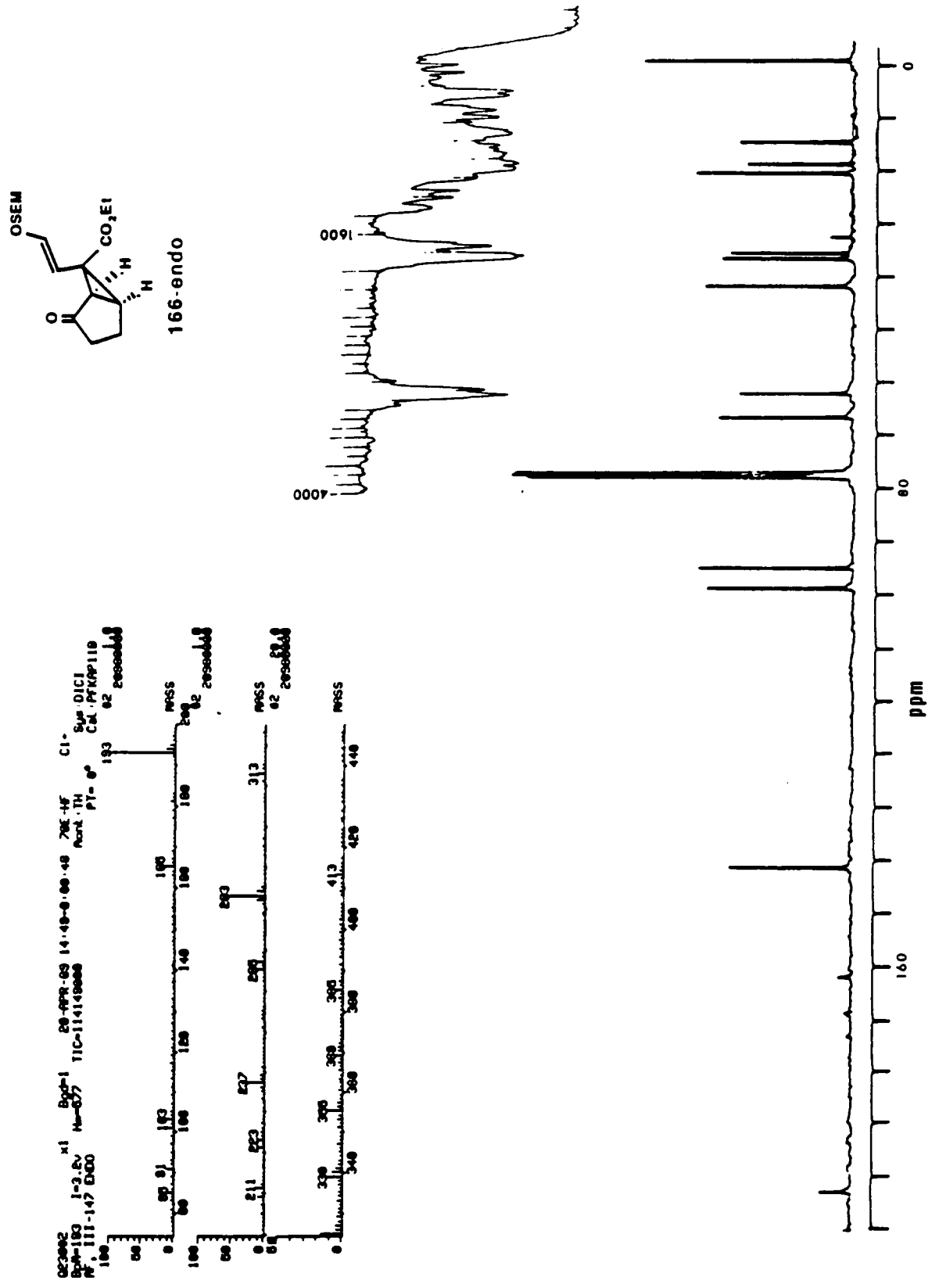
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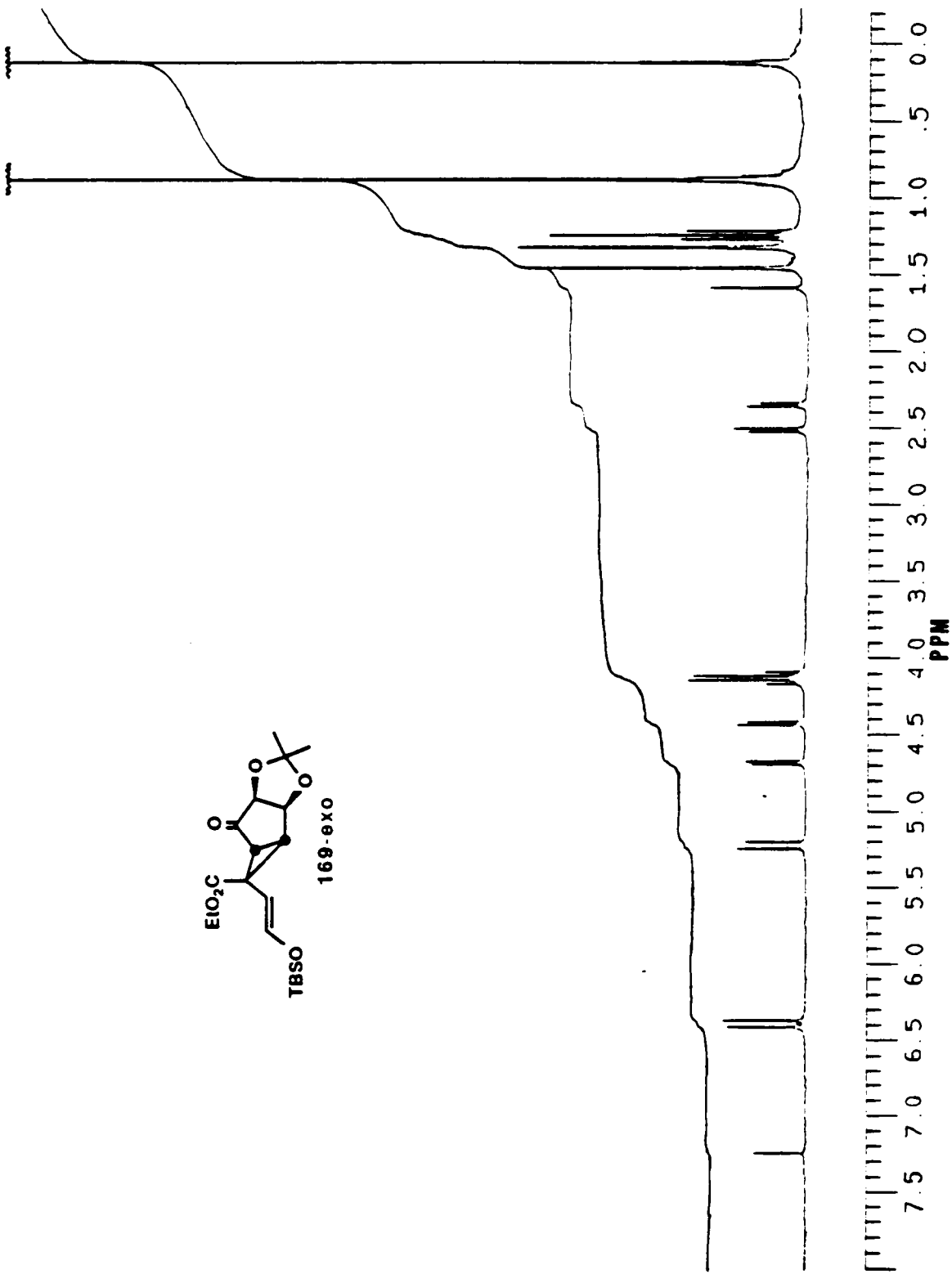
MASS


EtO2C
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TBSO
169-exo
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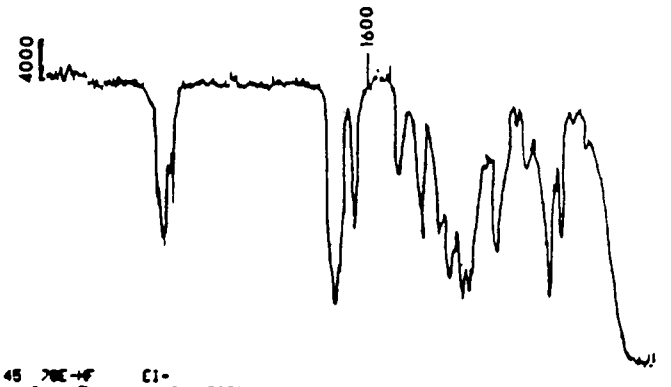
PPM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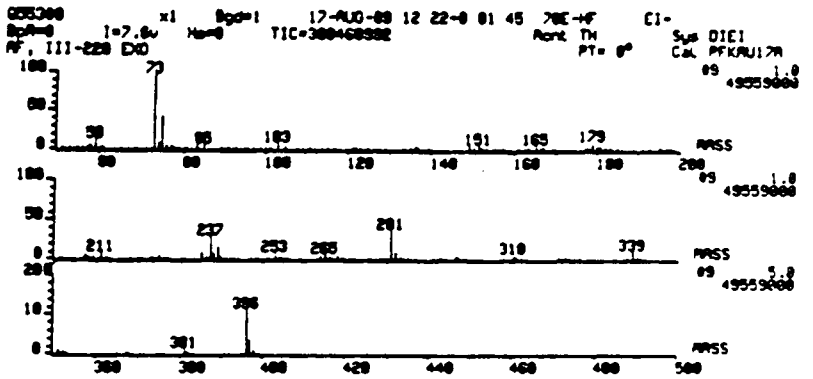
AF, III-228 EXO
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MASS
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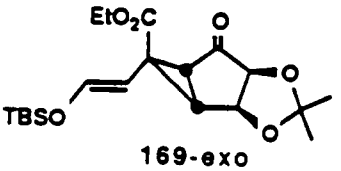
301
MASS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169-exo

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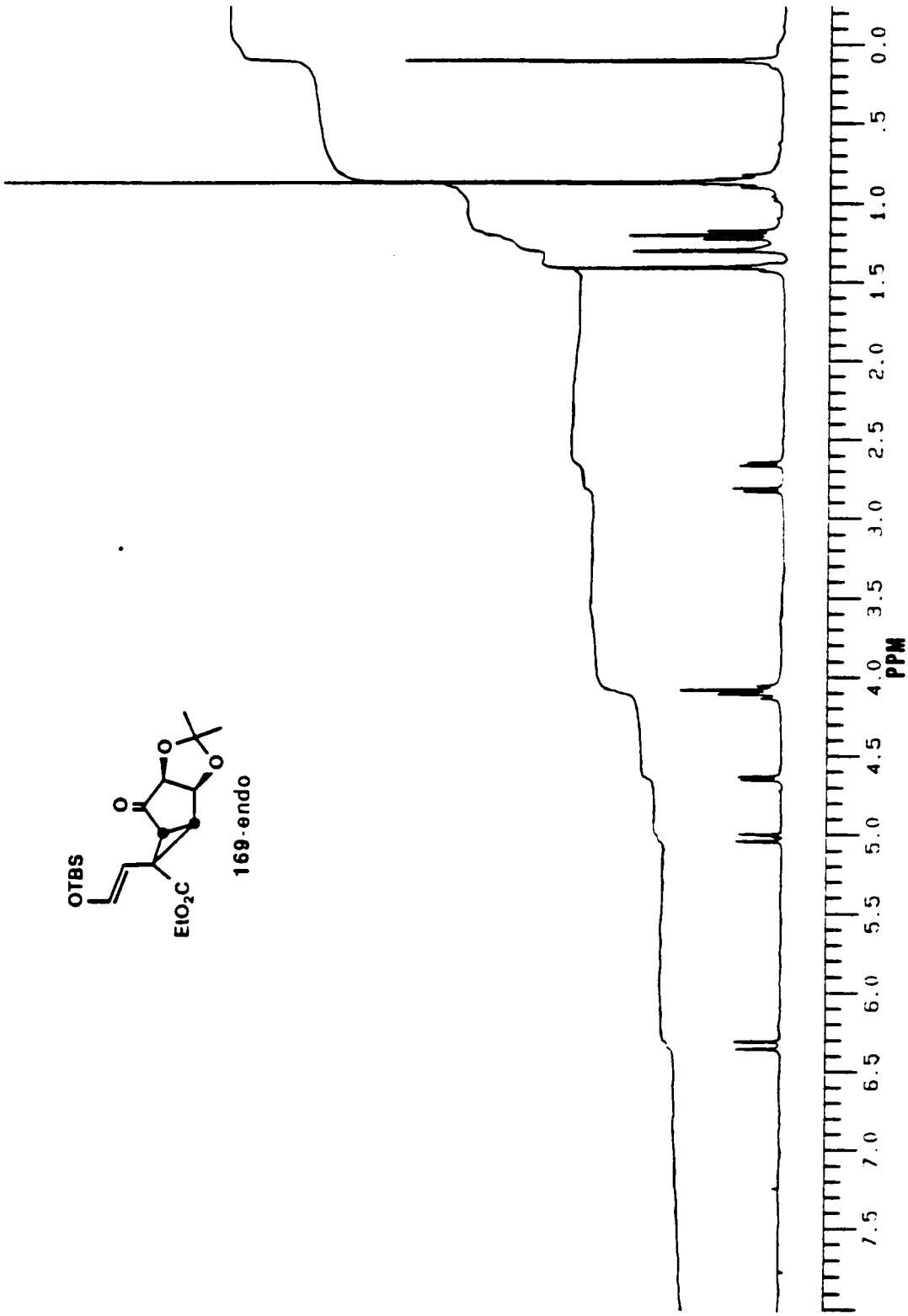
OTBS
EtO2C
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169-endo
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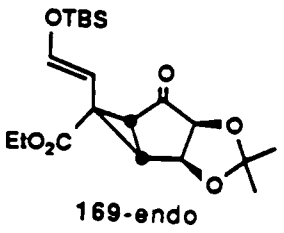
PPM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EtO2C
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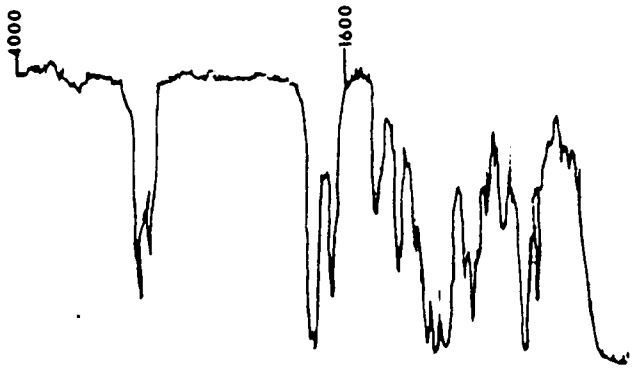
169-endo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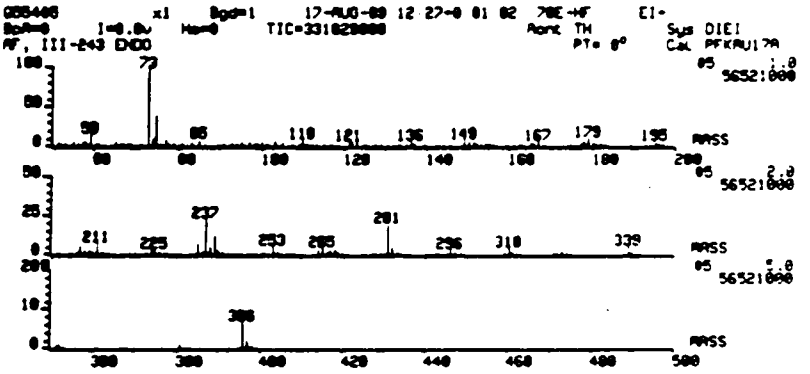
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RRSS
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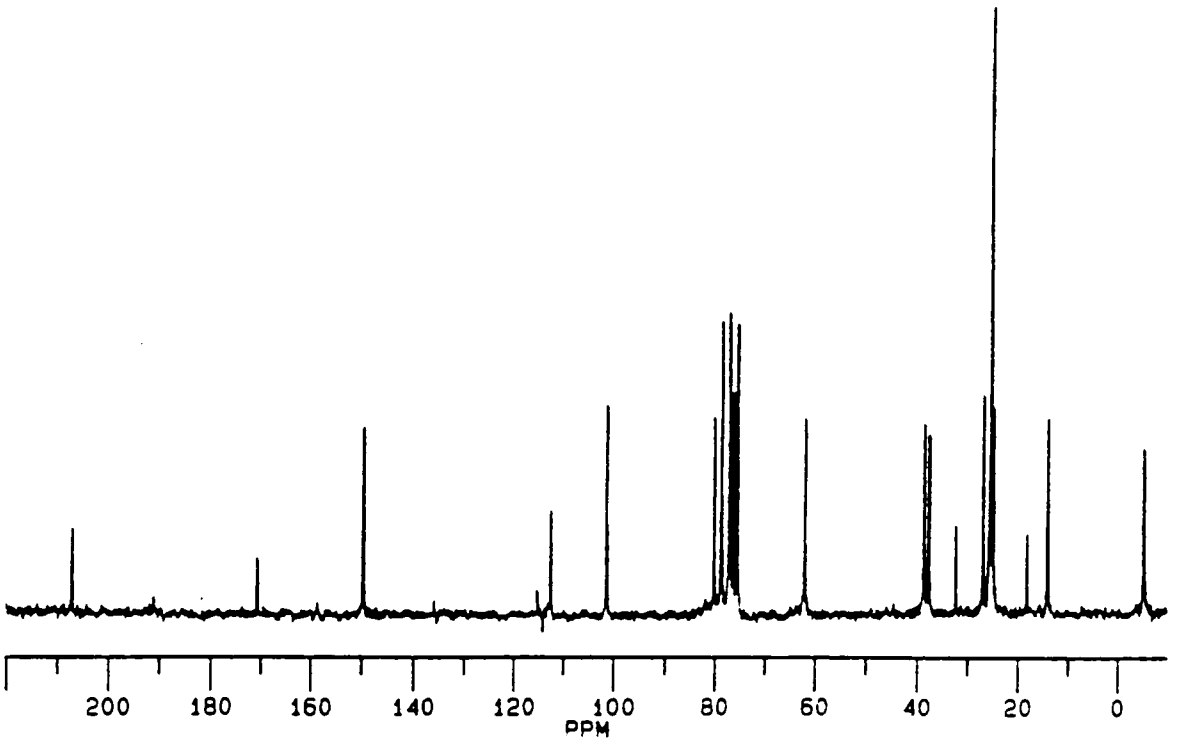
RRSS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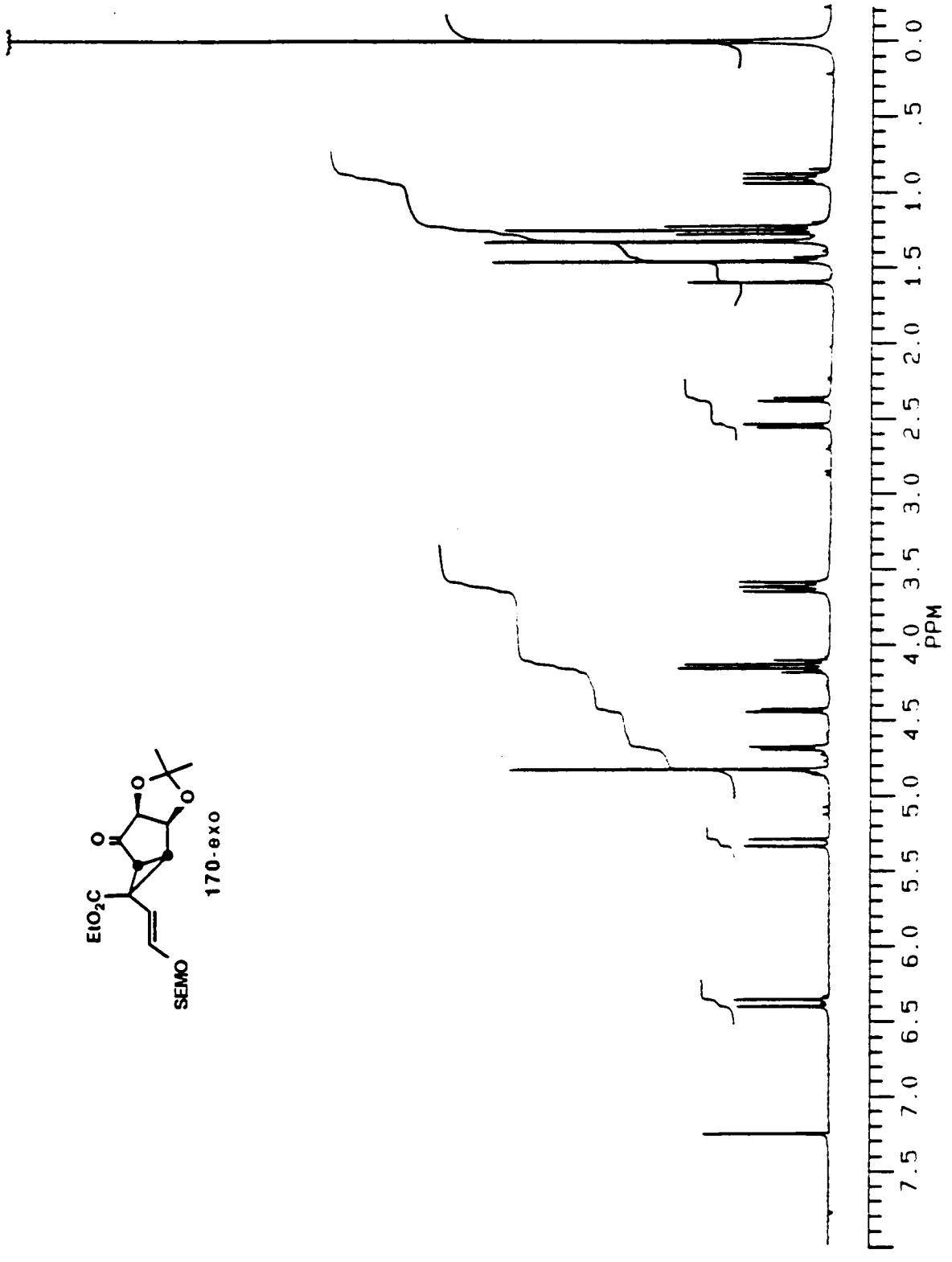
PPM


EtO2C
SEMO
170-exo
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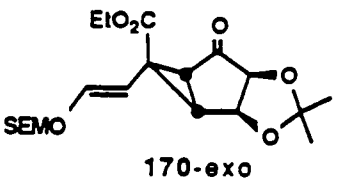
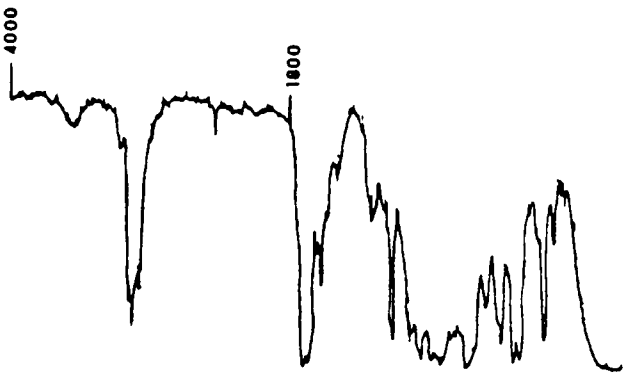
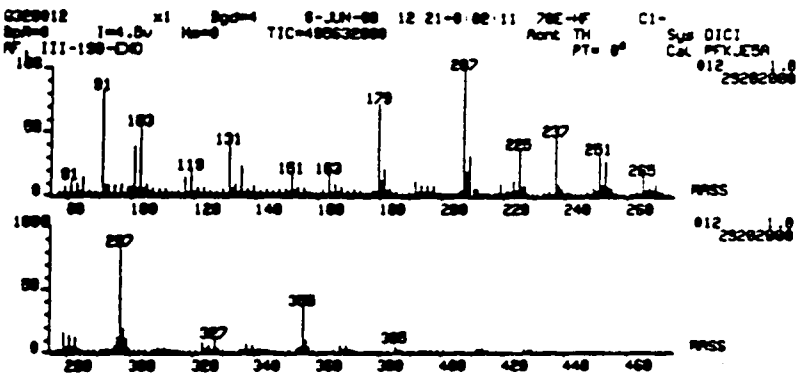
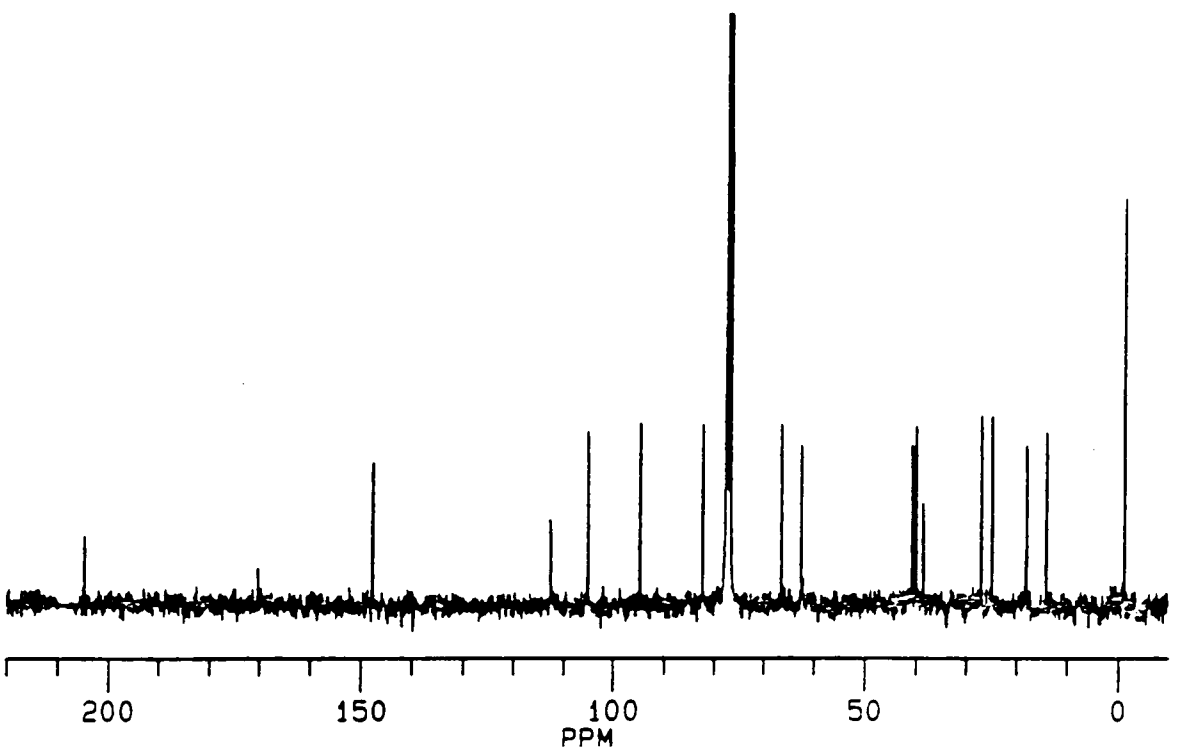
PPM

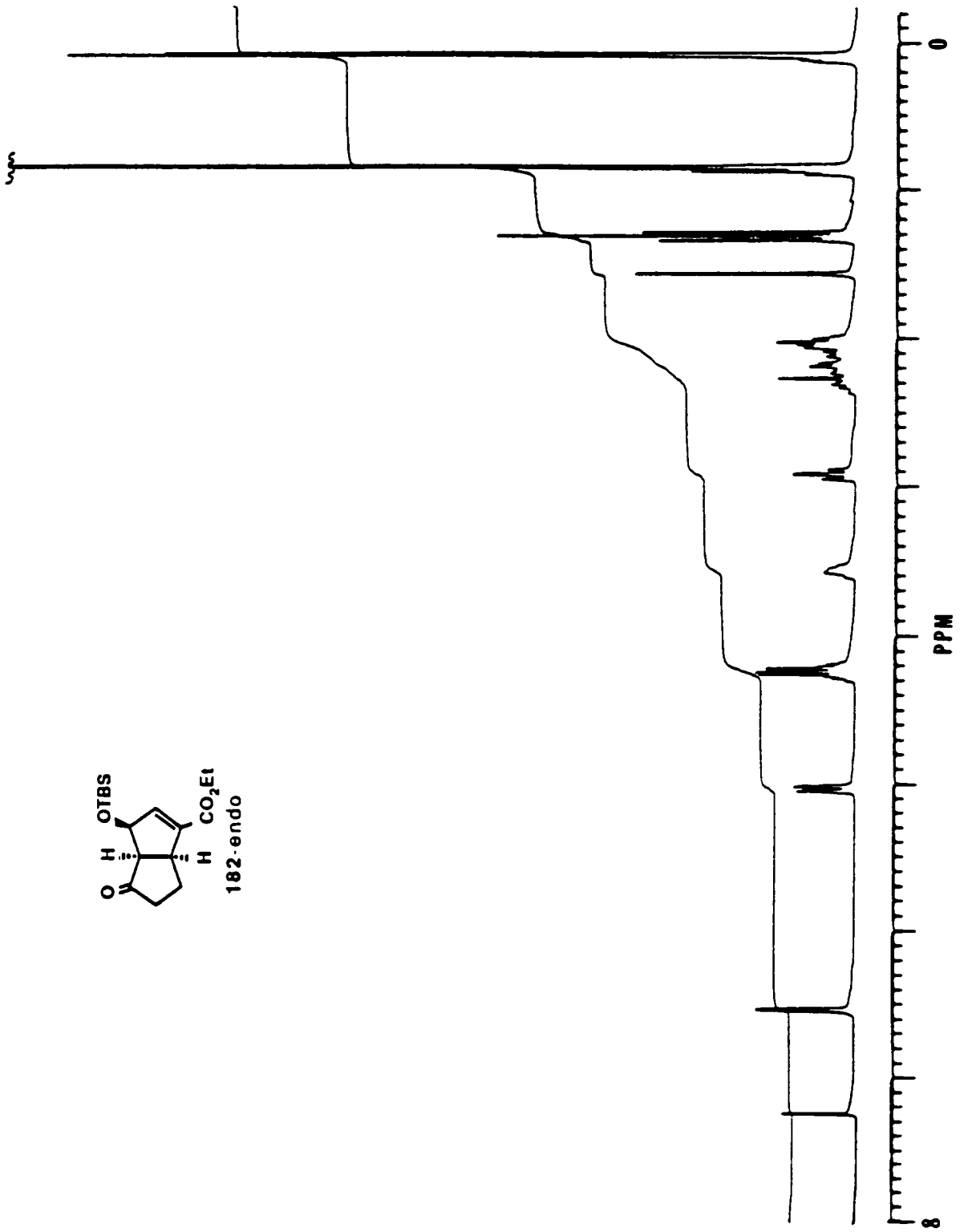


170-exo





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182-endo
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PPM
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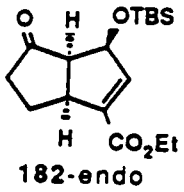
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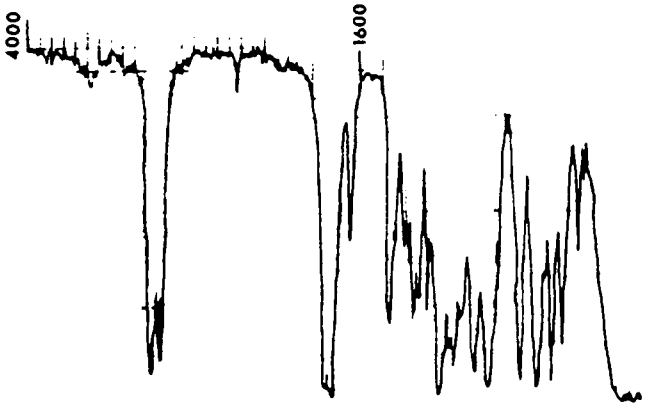
OTBS
H
CO2Et

182-endo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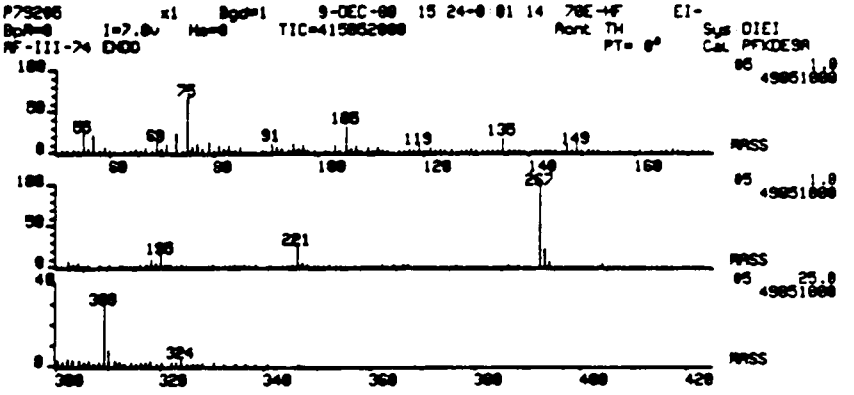
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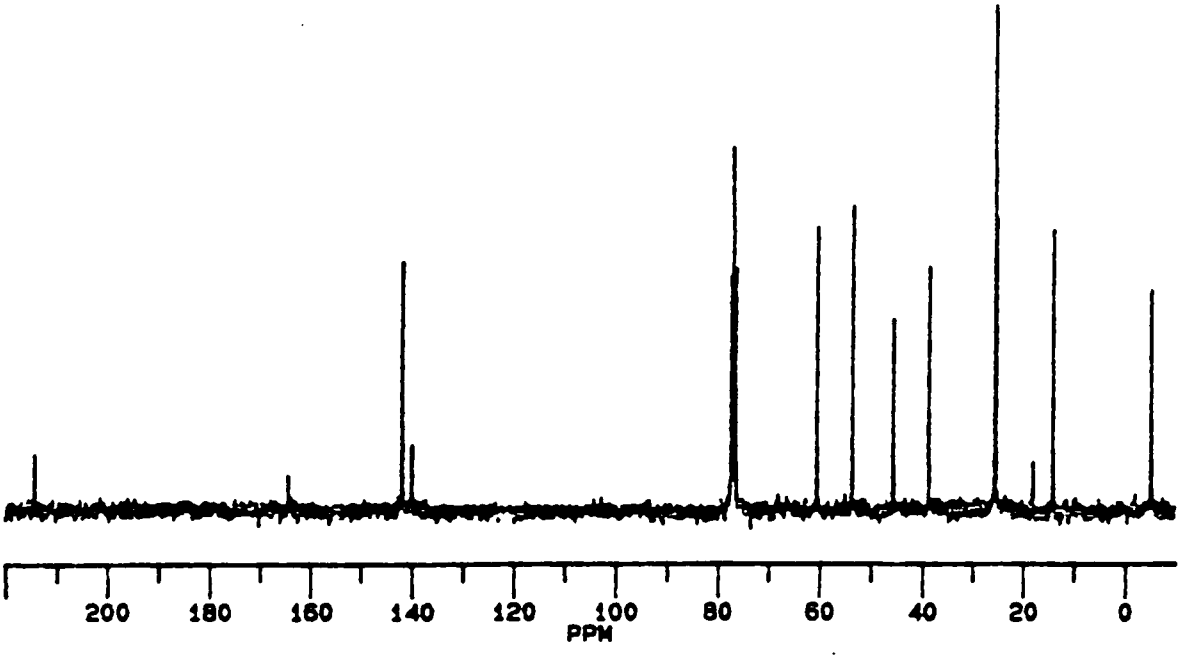
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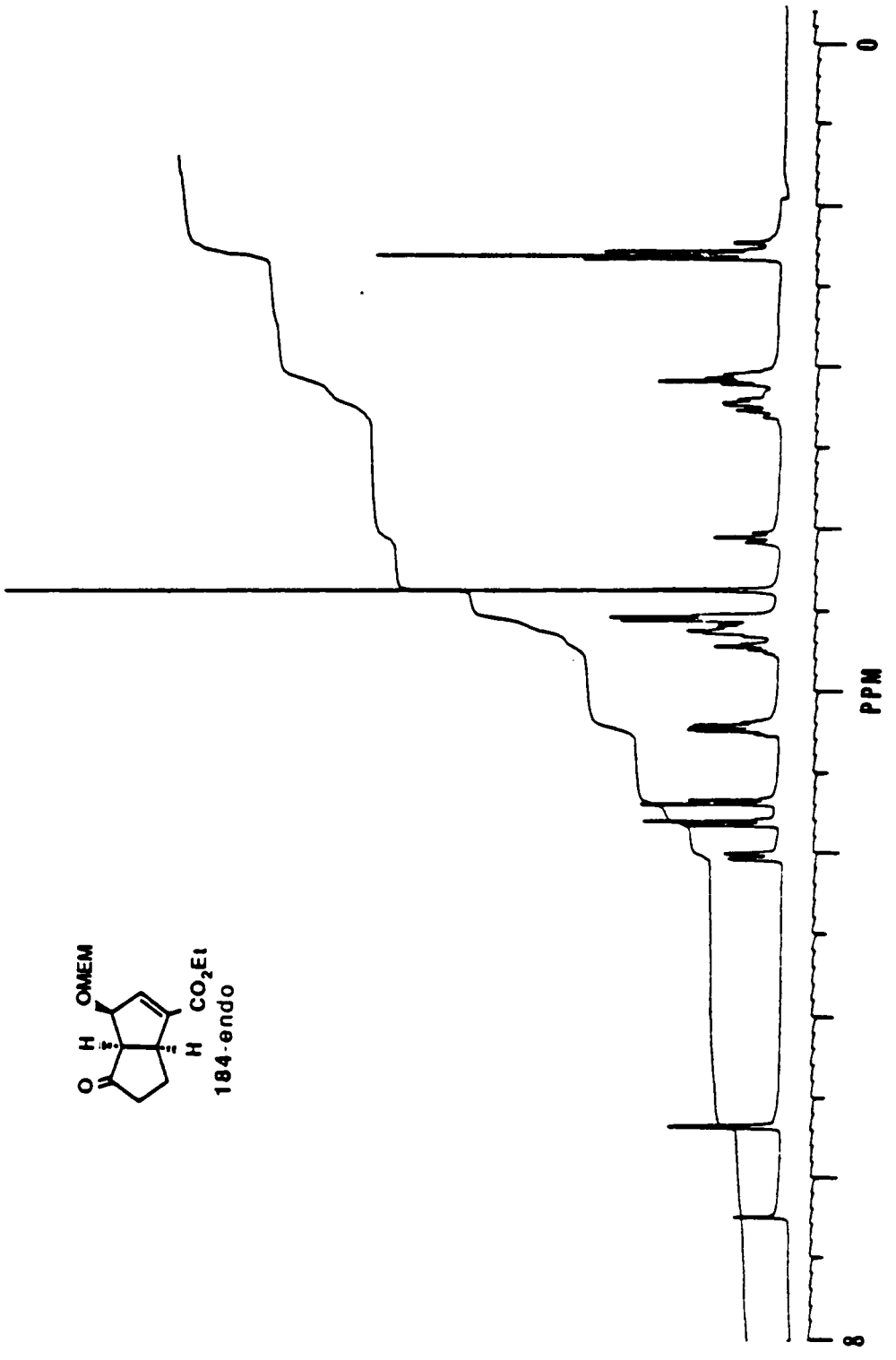
PPM


O H OMEM
H CO2Et
184-endo
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PPM
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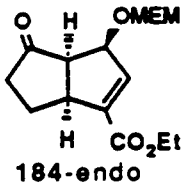
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OMEM
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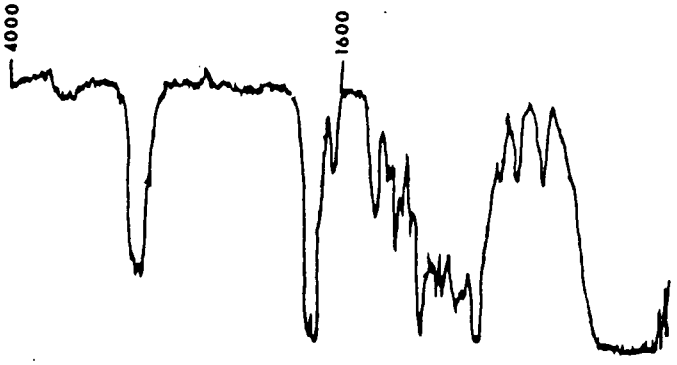
CO_2Et

184-endo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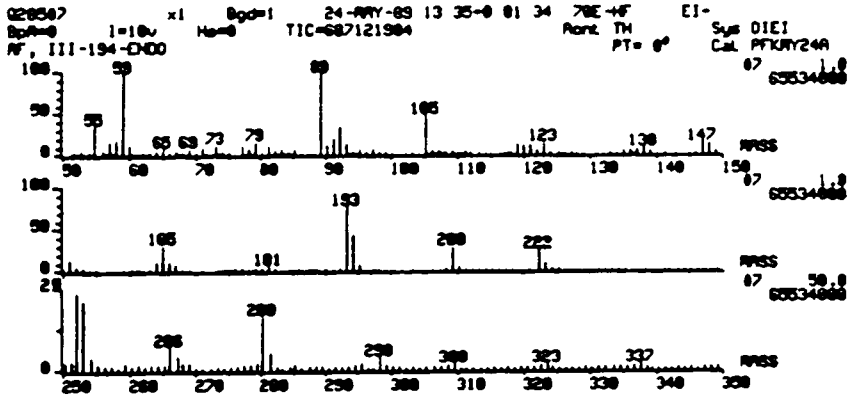

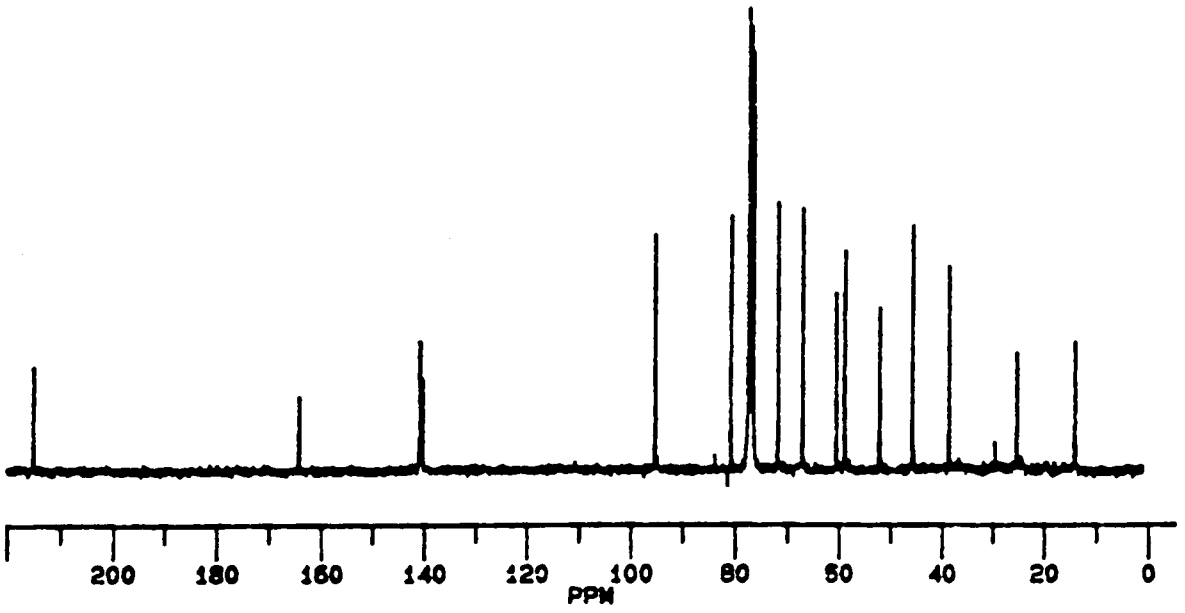
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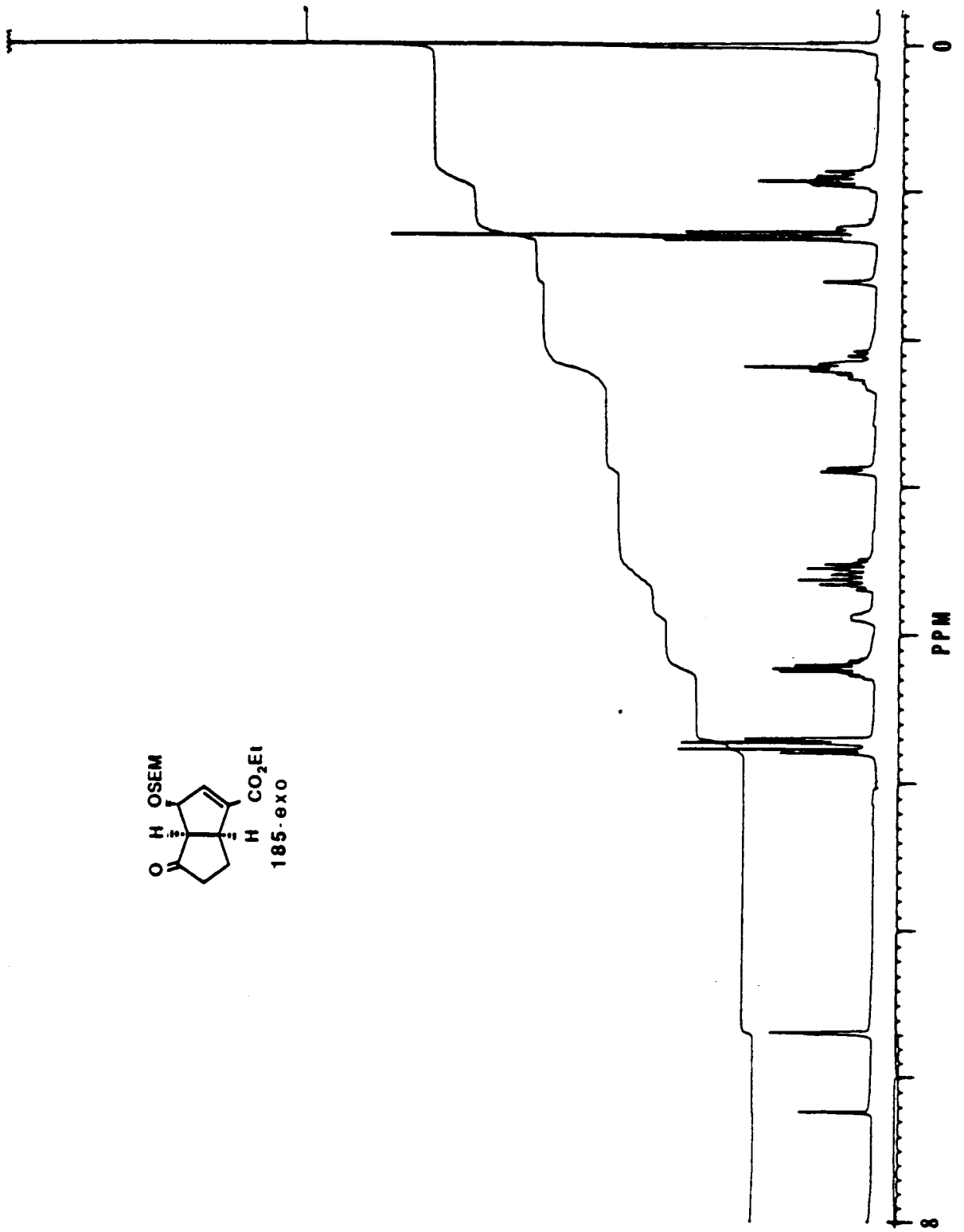
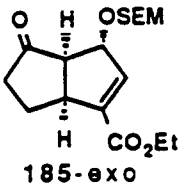

O H OSEM
H CO2Et
185-exo
0
PPM
8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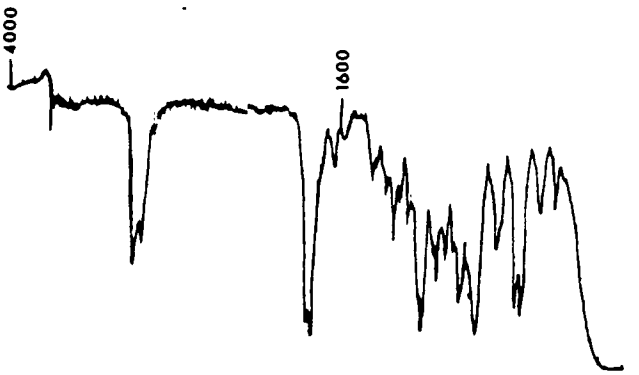
OSEM
H
CO2Et

185-exo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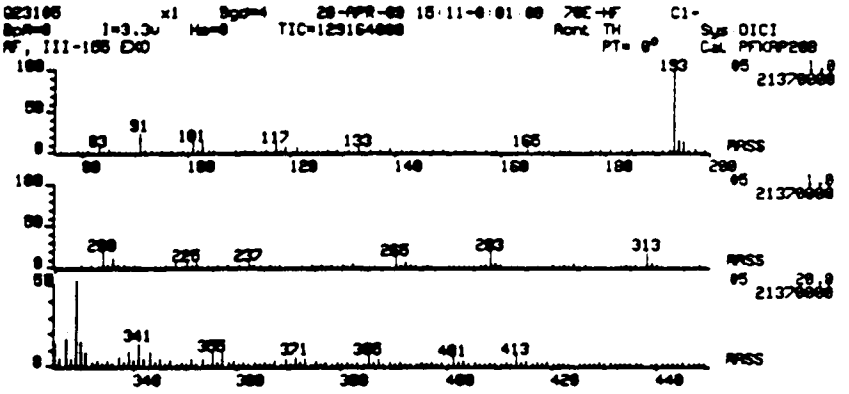
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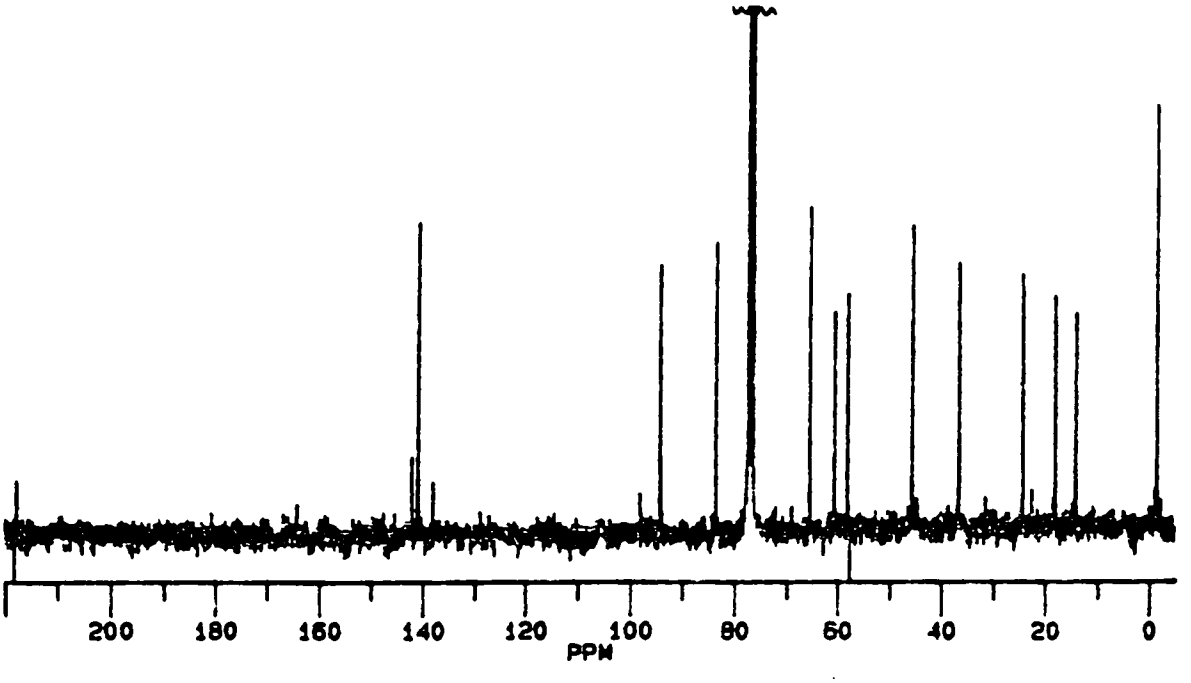
RRSS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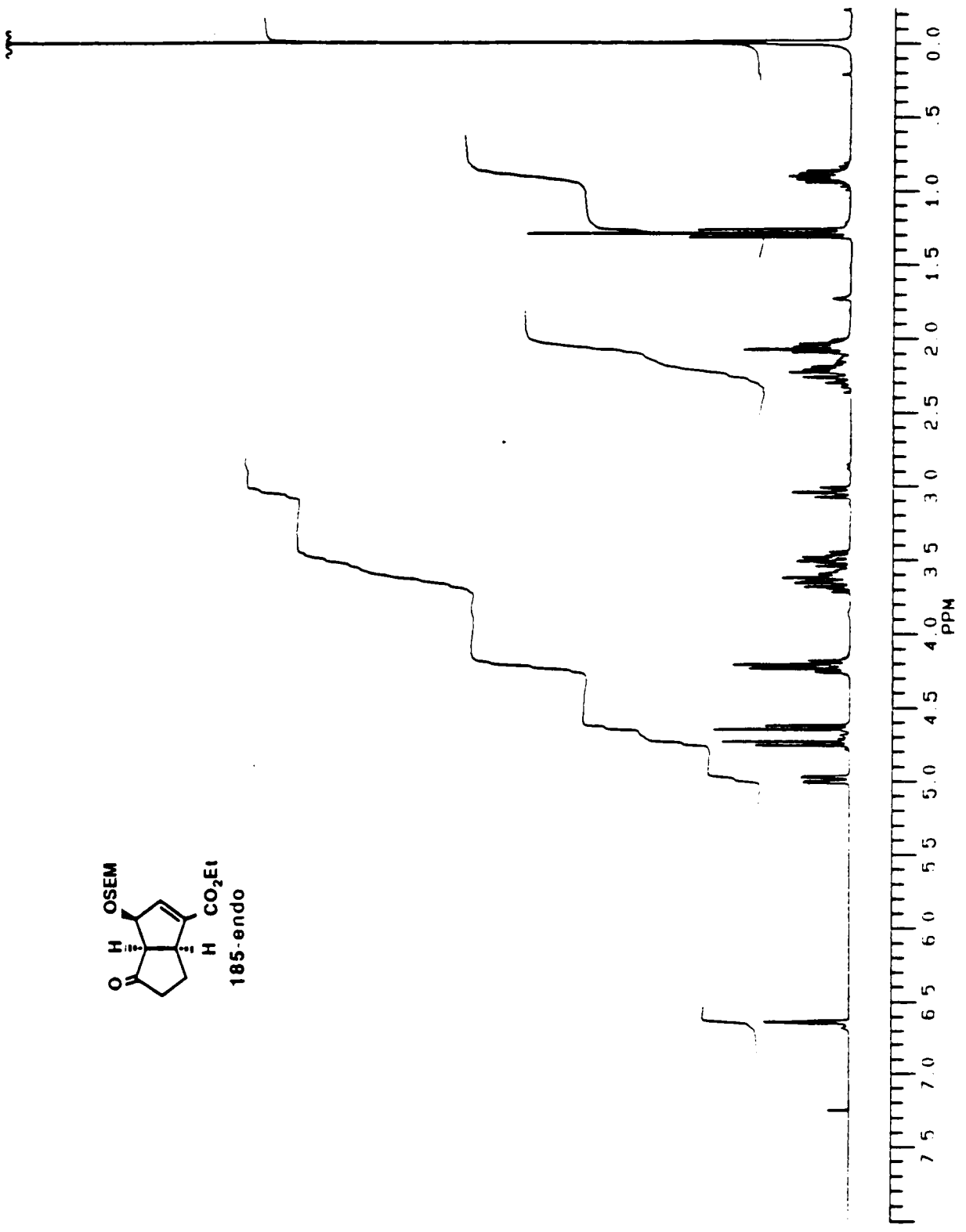
PPM


OSEM
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CO2Et
185-endo
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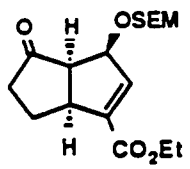
PPM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OSEM
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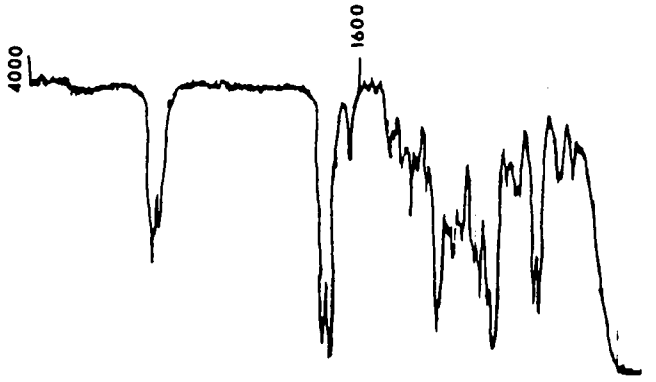
CO2Et

185-endo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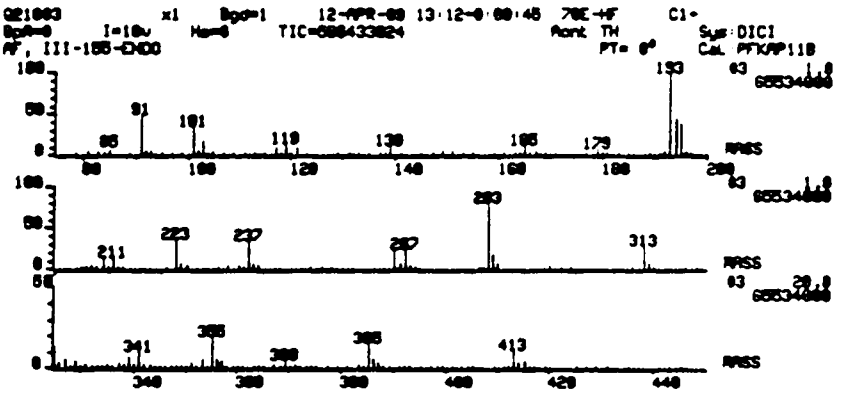
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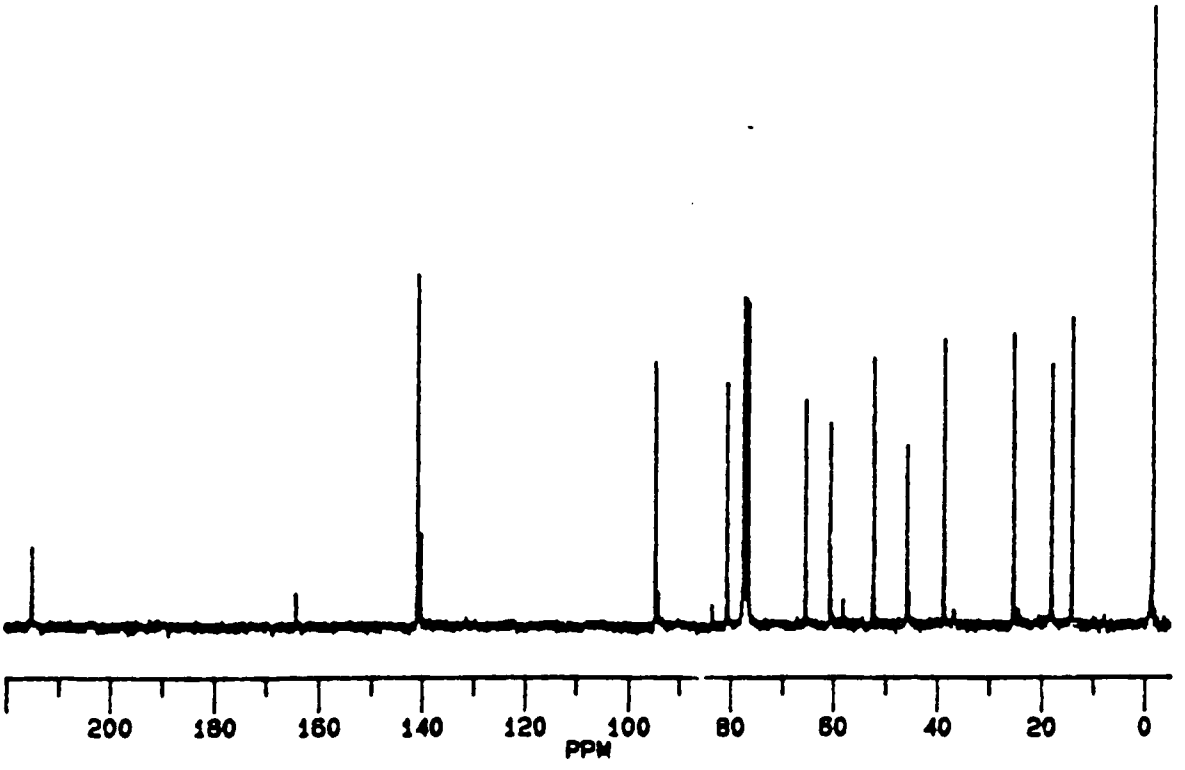
RRSS
RRSS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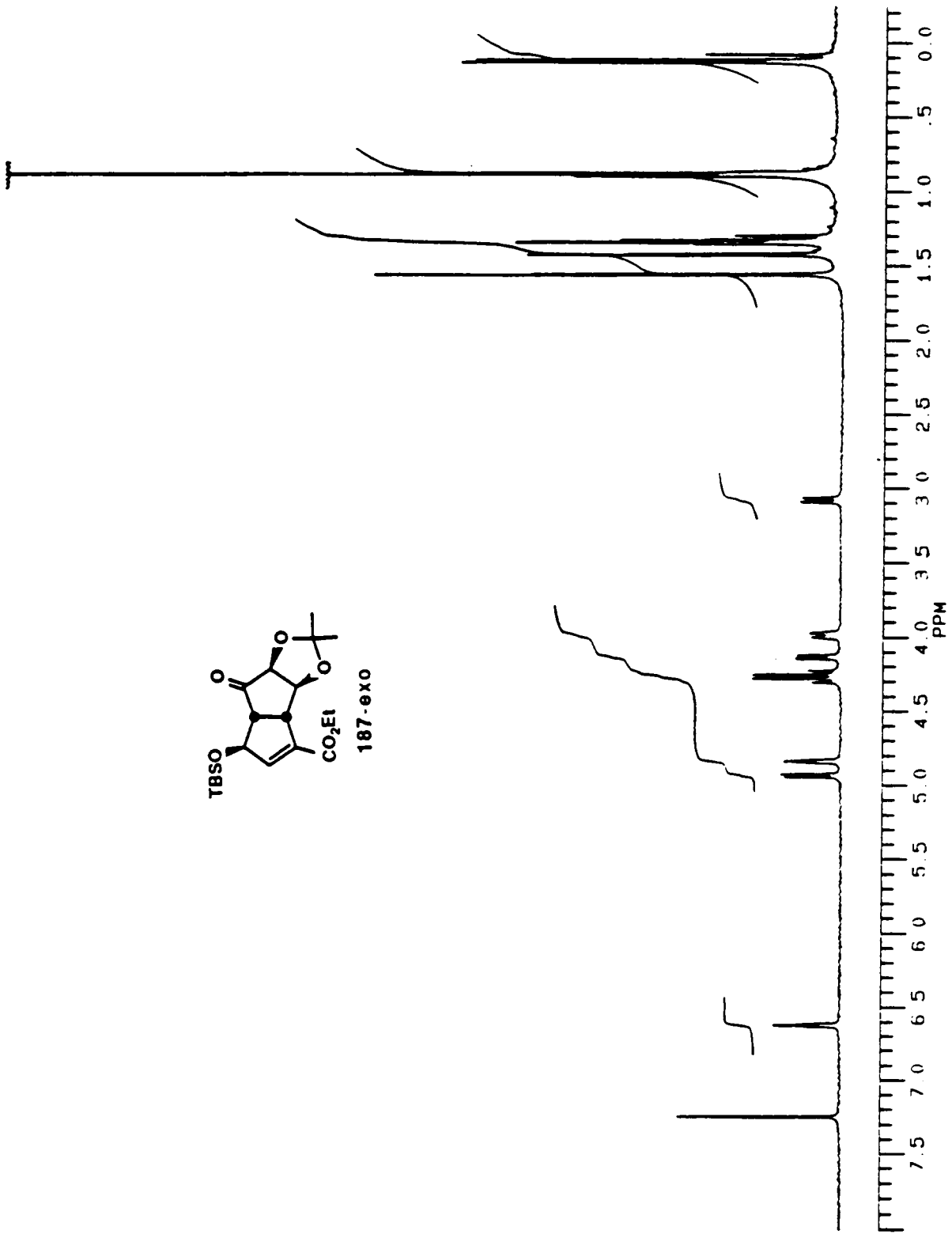
PPM


TBSO
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CO2Et
187-exo
7.5
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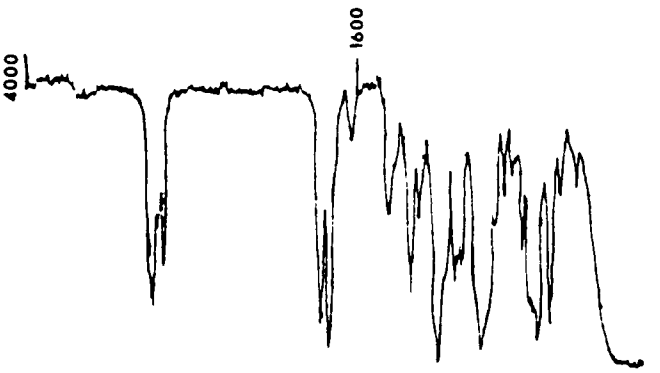
PPM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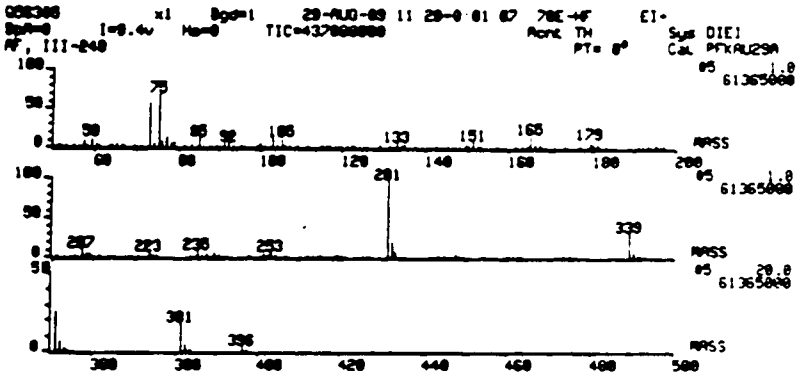
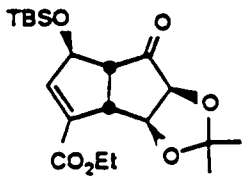

RRSS
RRSS
RRSS


TBSO
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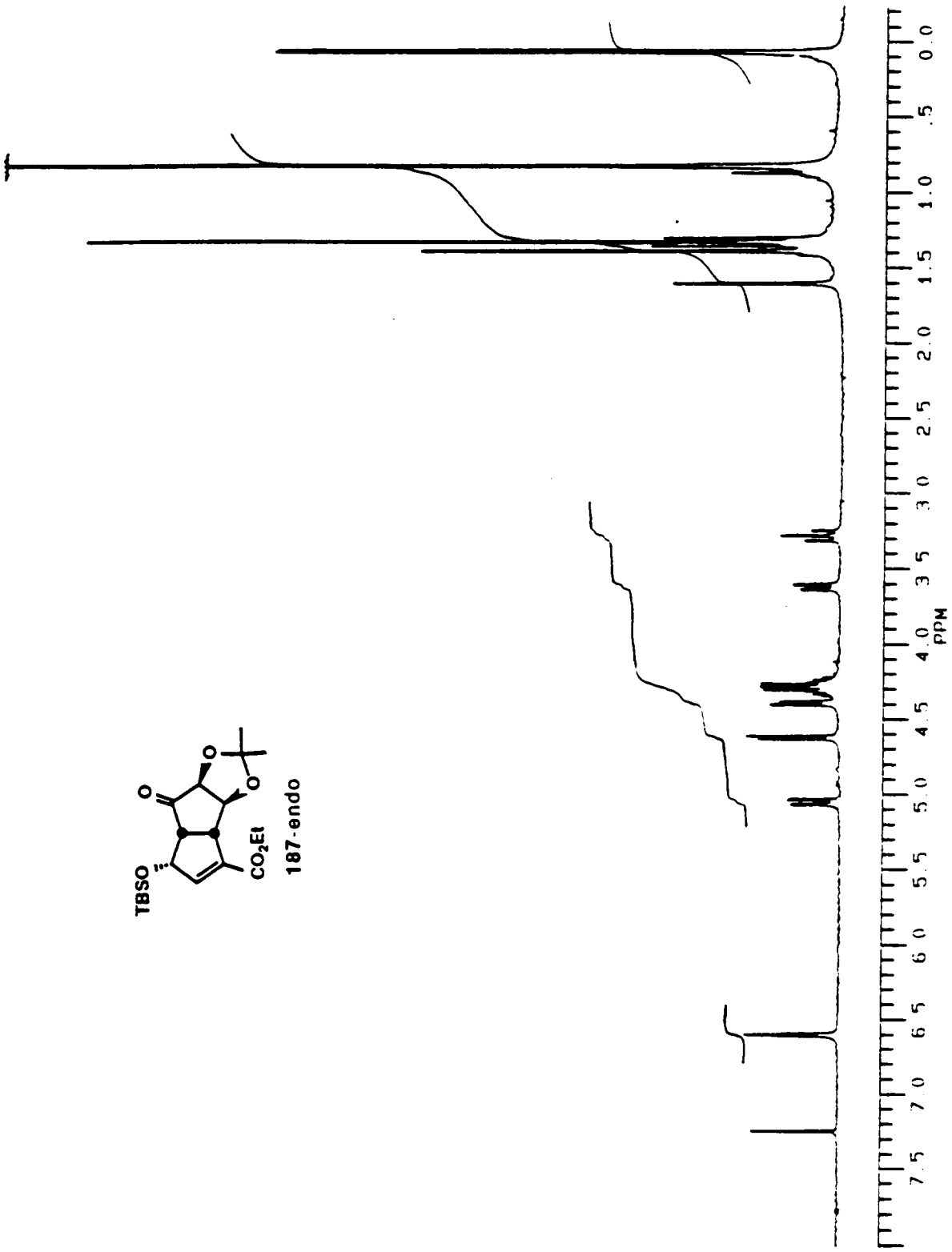
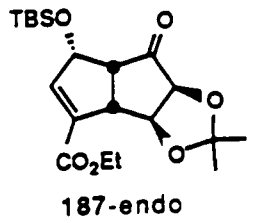
O
O
CO2Et

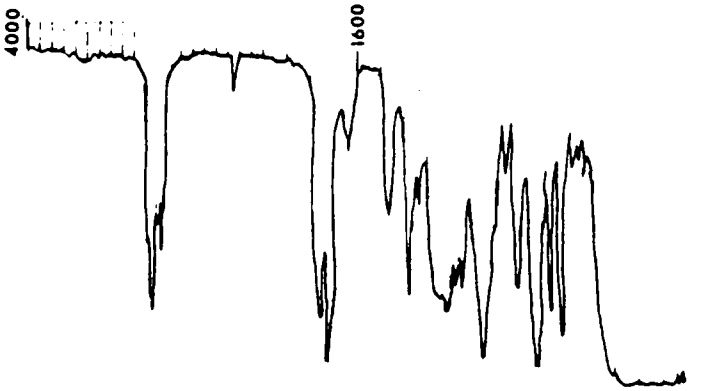
187-exo

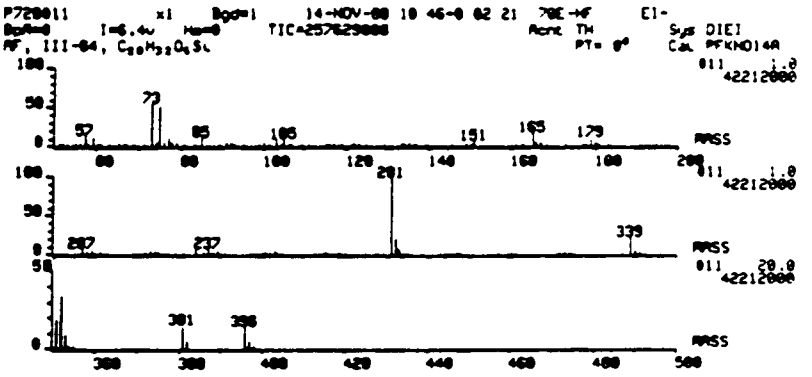
200
180
160
140
120
100
80
60
40
20
0
PPM

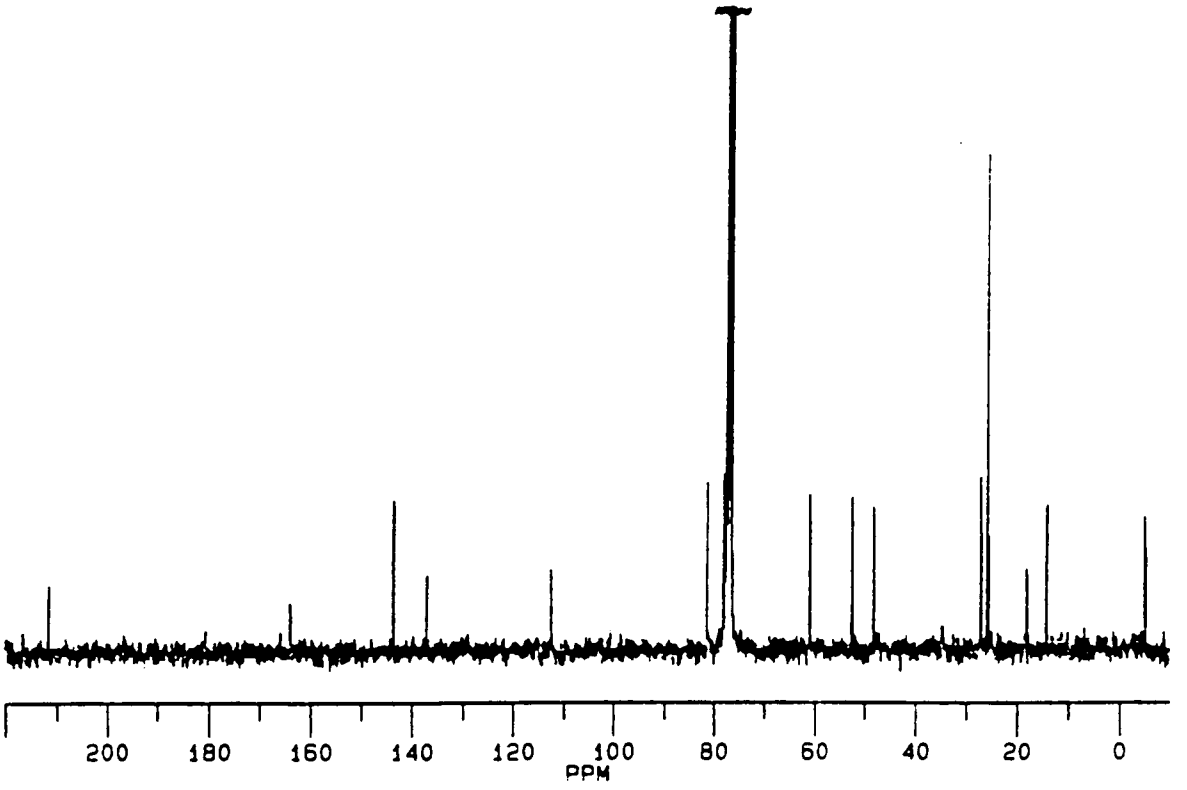

TBSO
CO2Et
O
O
O
O
187-endo
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0.0
PPM


TBSO
O
O
O
CO_2Et

187-endo


4000
1600


RRSS
RRSS
RRSS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120
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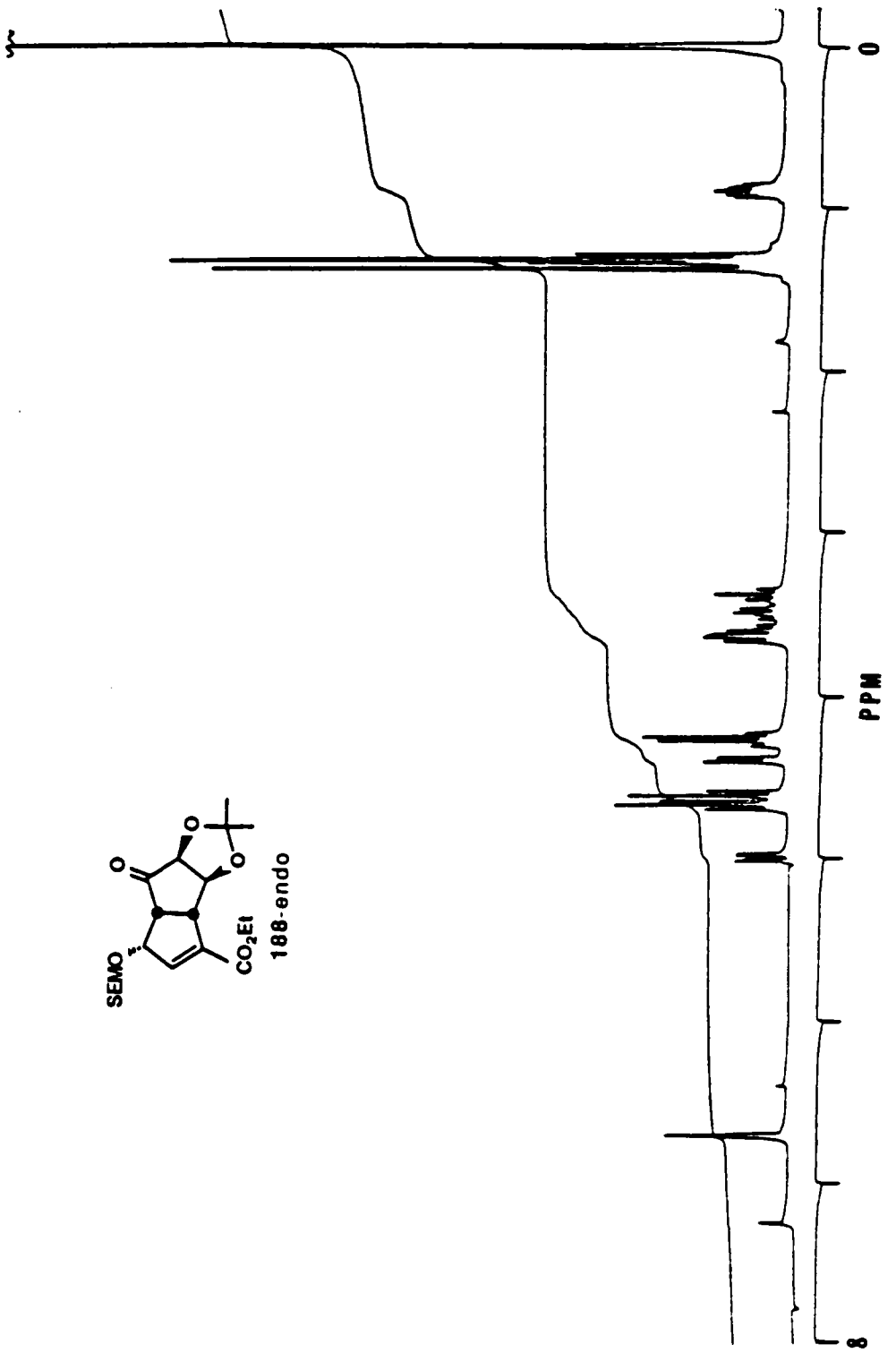
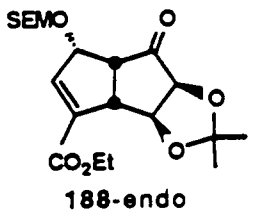
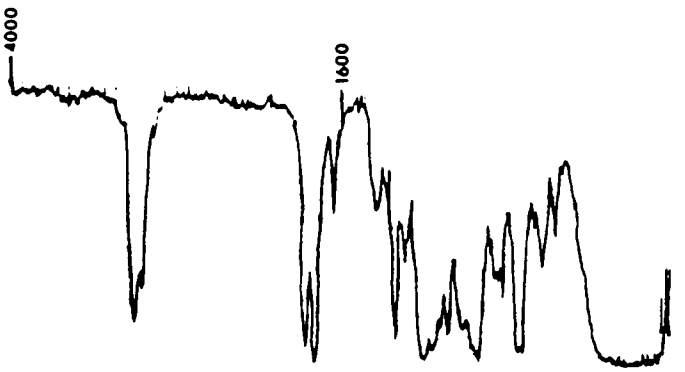
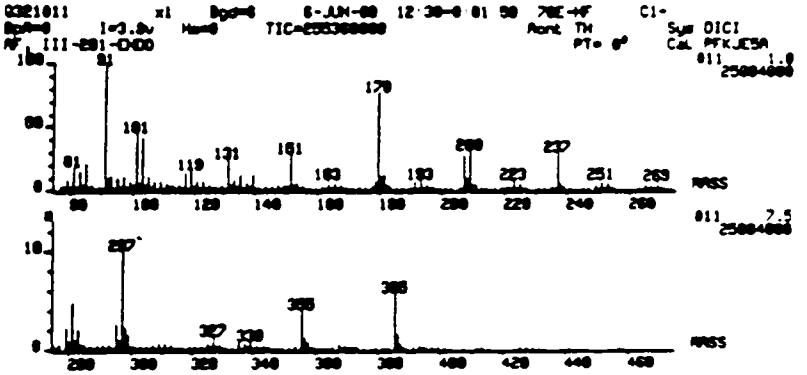
0
PPM

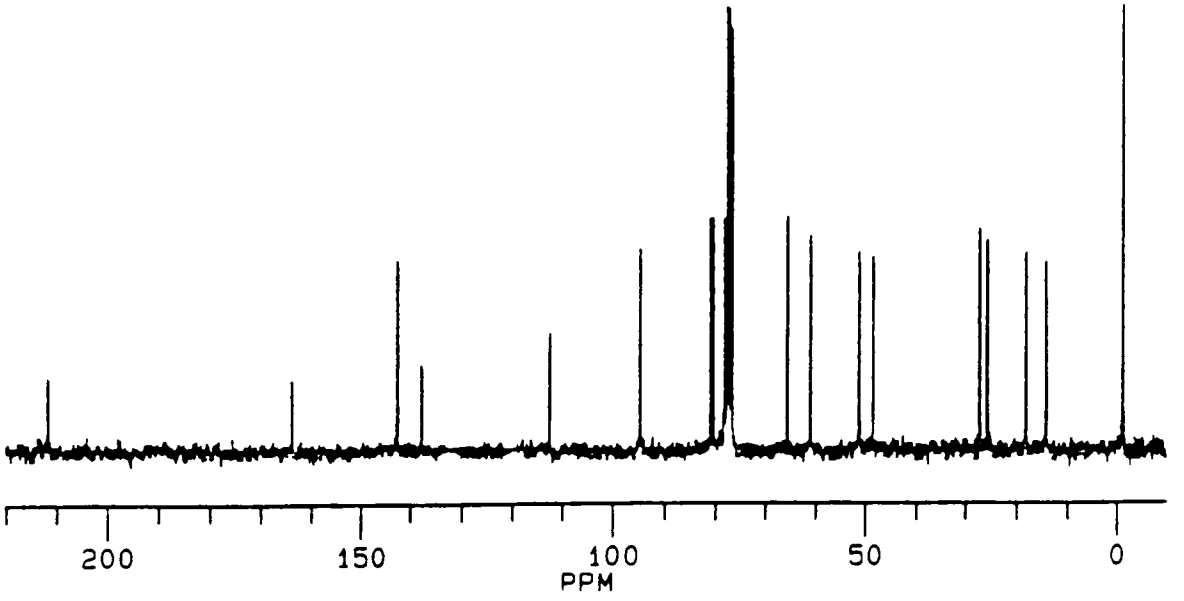

O
O
O
SEMO
CO2Et
188-endo
0
PPM
8

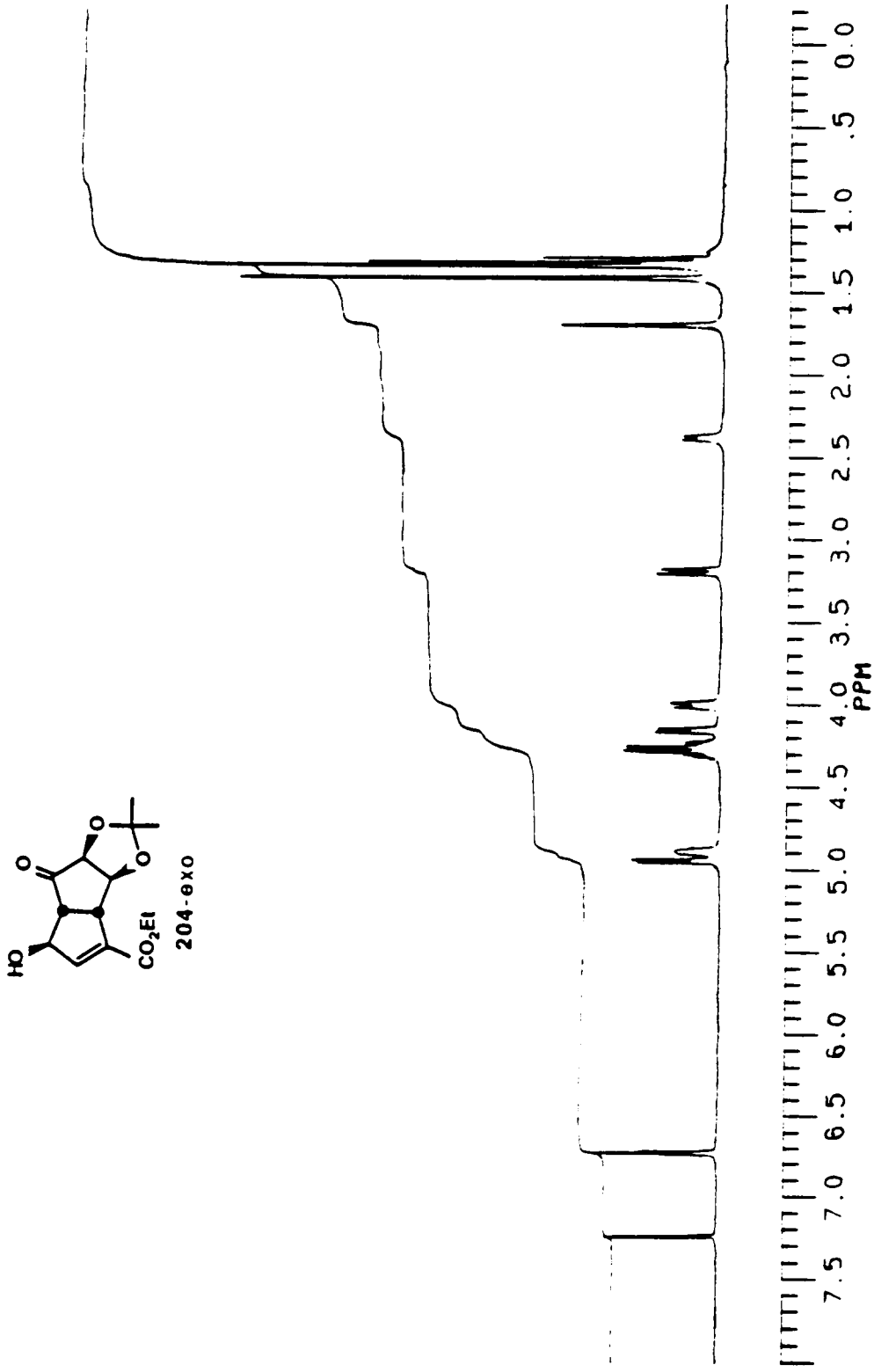


188-endo








HO
O
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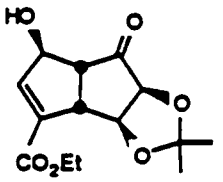
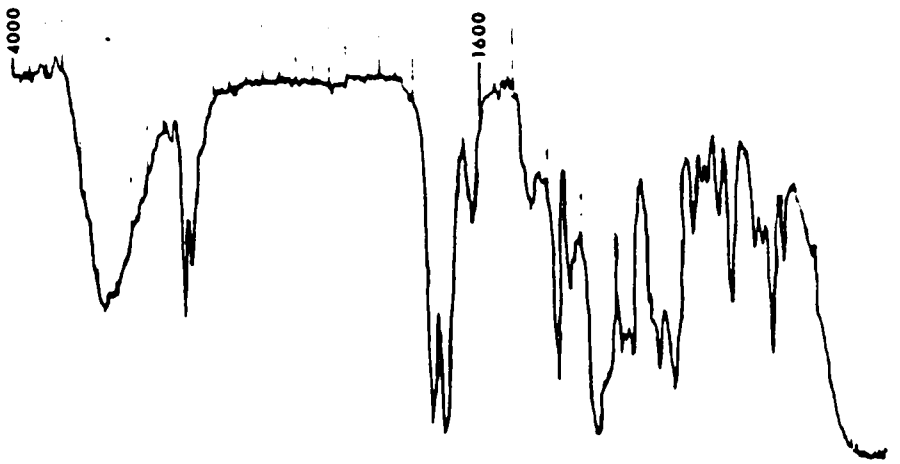
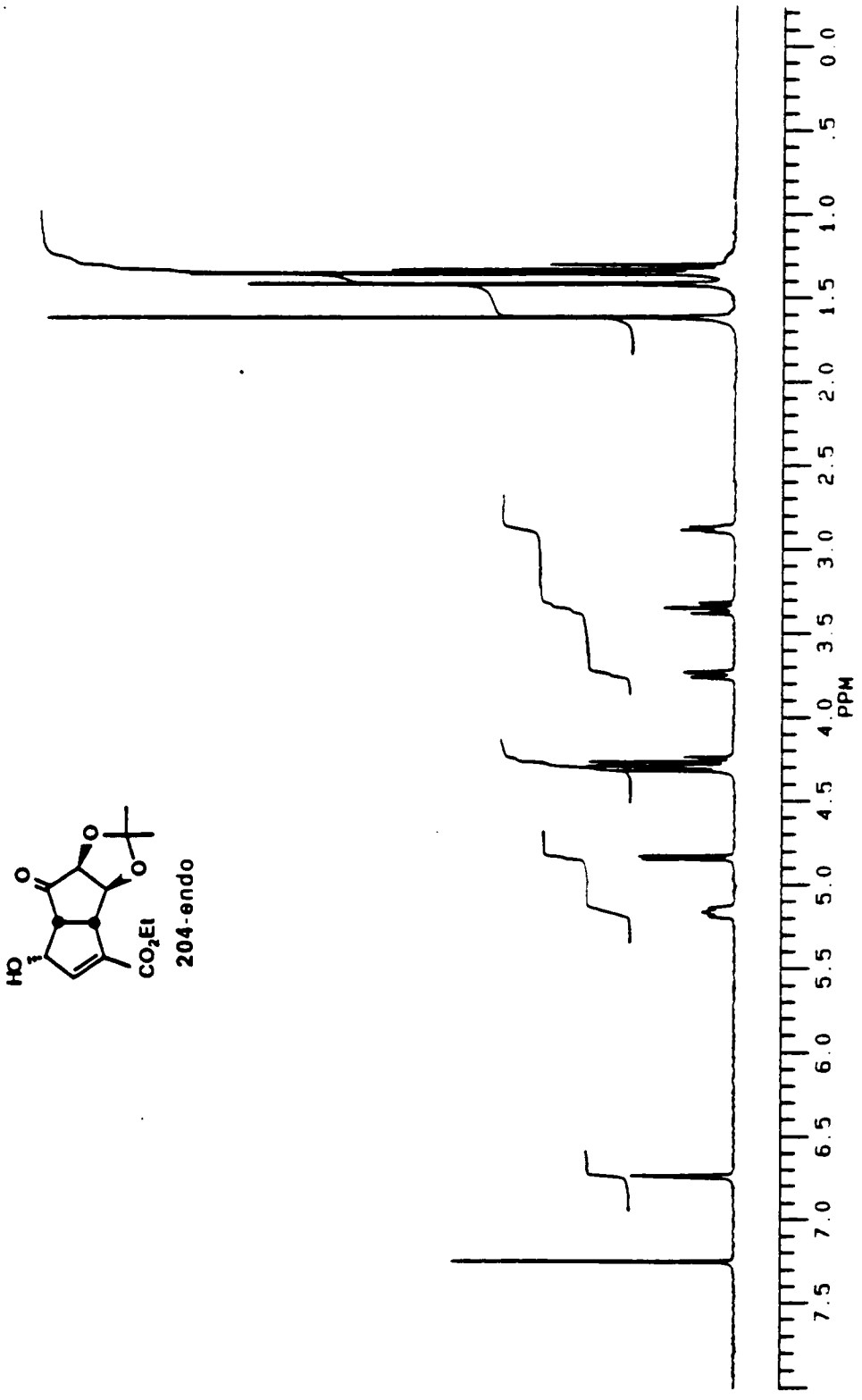
CO2Et
204-exo
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0.0
PPM



204-exo




HO
CO2Et
204-endo
7.5
7.0
6.5
6.0
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1.5
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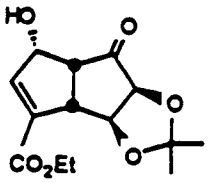
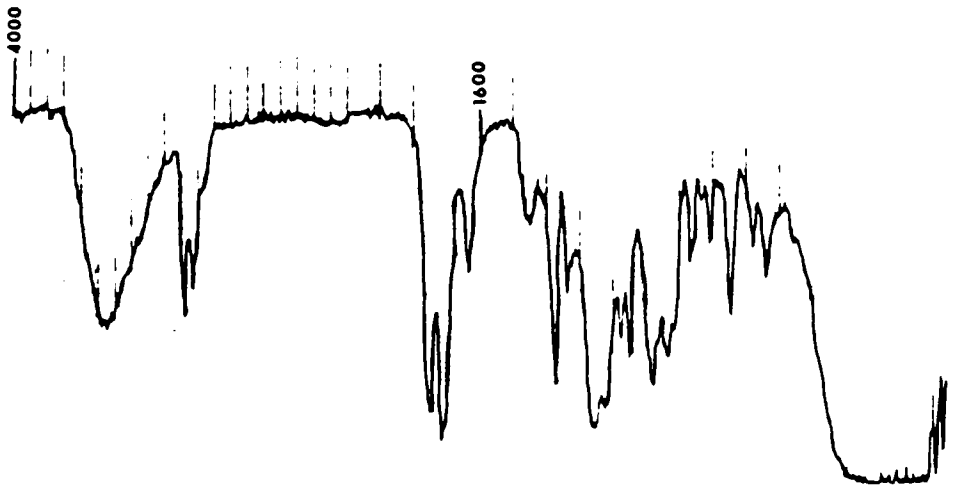
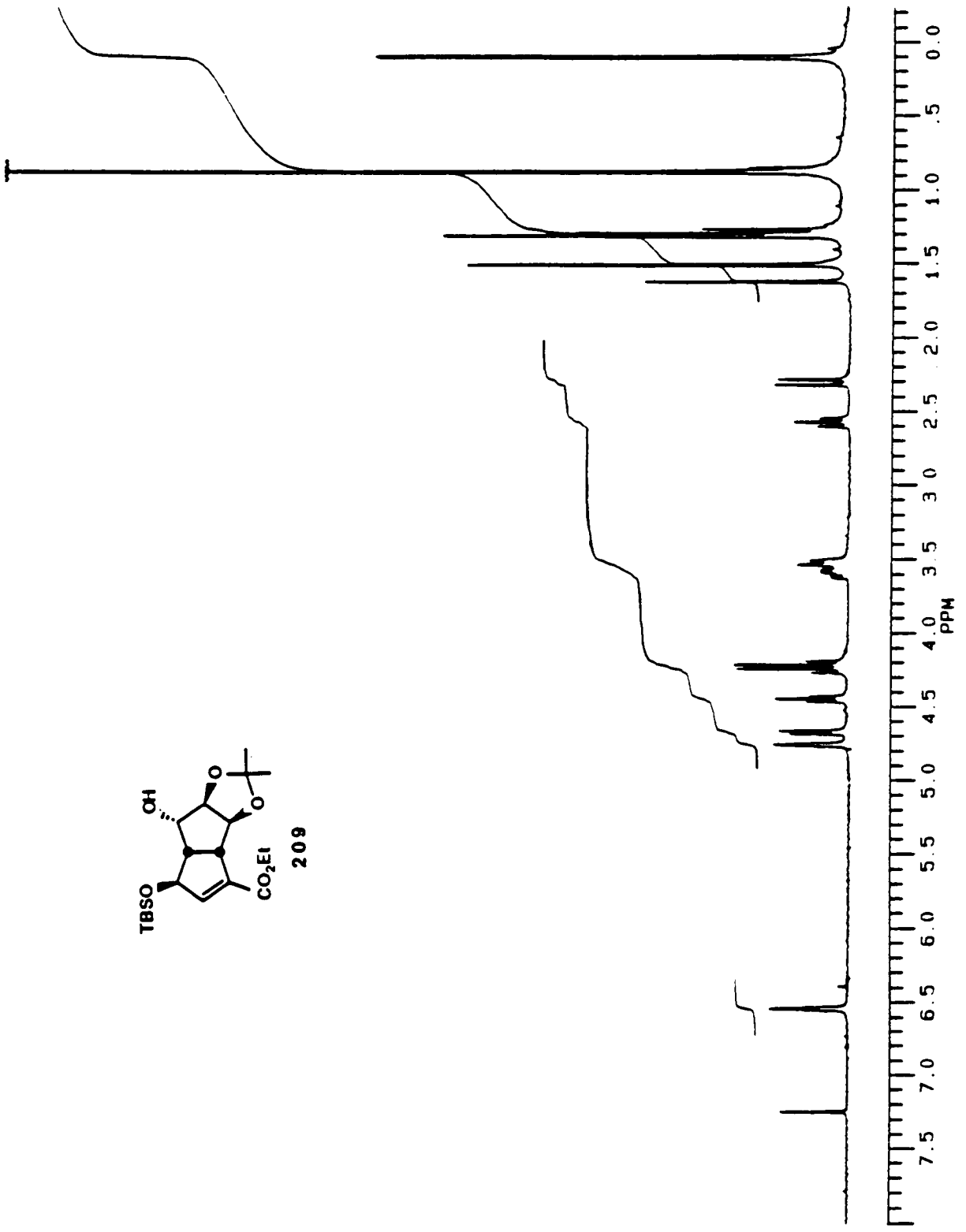
PPM



204-endo




OH
TBSO
CO2Et
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O
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209
7.5
7.0
6.5
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1.5
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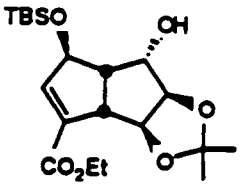
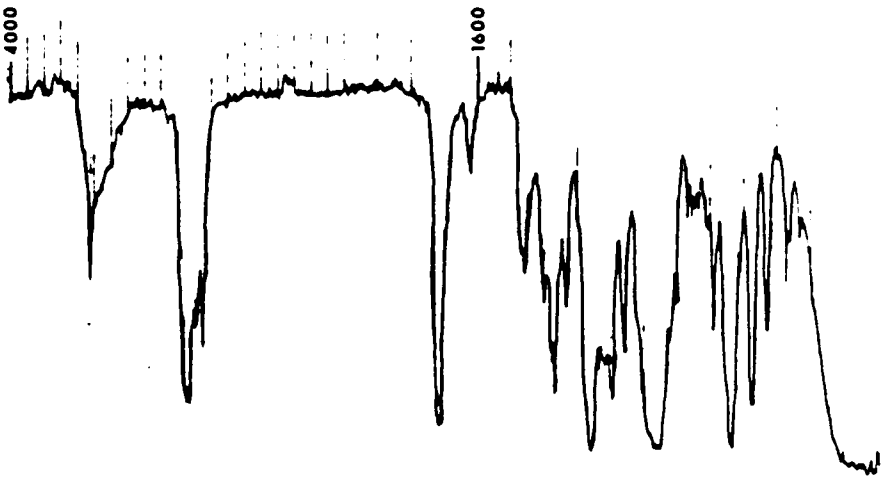
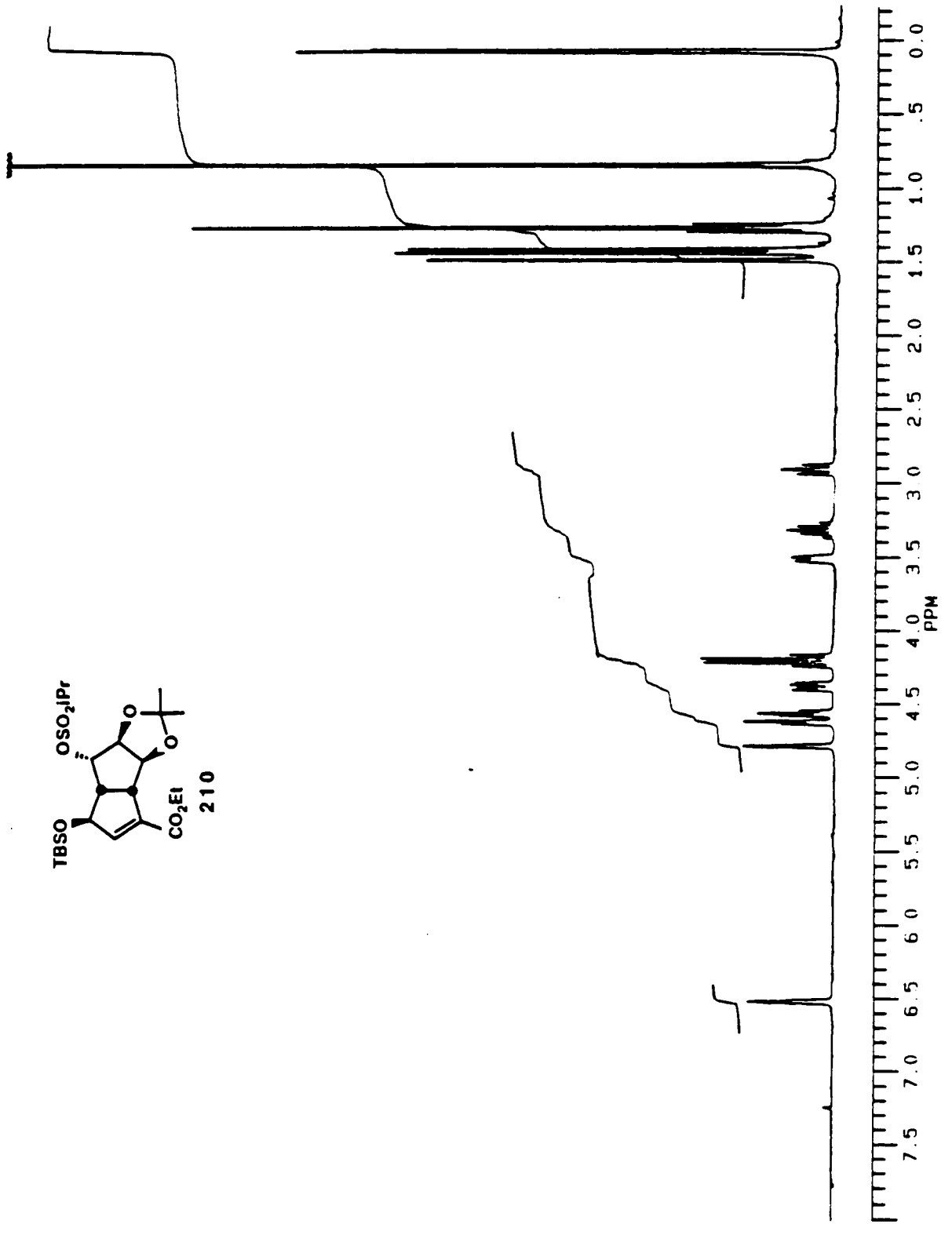
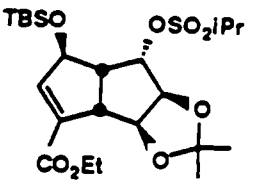
PPM



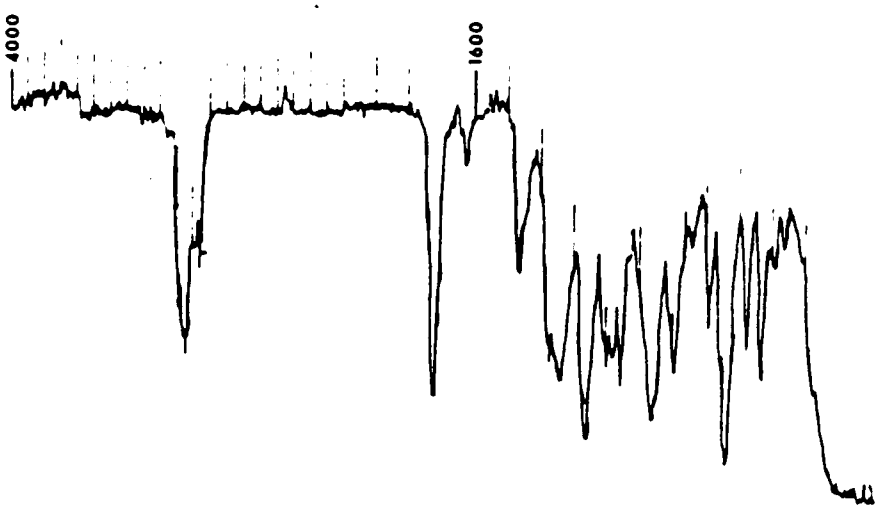
209




OSO2iPr
TBSO
CO2Et
210
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 .5 0.0
PPM



210



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