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Title(English)	
著者(和文)	土井隆行
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ネオカルチノスタチンクロモフォア，ステロイド等の  
立体選択的合成への応用

化学工学専攻

土井隆行

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## Abbreviations

Ac	acetyl-	THP	tetrahydropyranyl-
Bu	butyl-	TLC	thin layer chromatography
Bz	benzoyl-	TMS	trimethylsilyl
mCPBA	meta-chloroperbenzoic acid	Ts	para-toluenesulfonyl-
$\Delta$	heat induced reactions		
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene		
DC-18-CR-6	dicyclohexano-18-crown-6		
DHP	dihydropyran		
DMAP	4-dimethylaminopyridine		
DMSO	dimethyl sulfoxide		
EE	1-ethoxyethyl-		
Et	ethyl-		
h	hour(s)		
HMPA	hexamethylphosphoric triamide		
HPLC	high pressure liquid chromatography		
<i>i</i>	iso		
LDA	lithium diisopropylamide		
Me	methyl-		
min	minute(s)		
MOM	methoxymethyl-		
Ms	methanesulfonyl-		
<i>o</i>	ortho		
<i>p</i>	para		
PCC	pyridinium chlorochromate		
Ph	phenyl		
PPTS	pyridinium para-toluenesulfonate		
Pr	propyl-		
Py	pyridine		
r.t.	room temperature		
Rt	retention time		
<i>t</i>	tertiary		
TBDMS	<i>t</i> -butyldimethylsilyl-		
TBDPS	<i>t</i> -butyldiphenylsilyl-		
TBHP	<i>t</i> -butylhydroperoxide		
Tf	trifluoromethanesulfonyl-		
THF	tetrahydrofuran		

はじめに

現代は、コンピューター社会と言われるように、コンピューターが社会に浸透し、世の中の膨大な情報は、コンピューターで処理されている。これに対し化学の領域では、膨大な化学の情報をデータベースにした情報検索、演算能力を利用した理論計算等が行われている。データベースについては、構造、文献、各種スペクトルデータの検索であるとか、反応、合成経路検索システムに関するものが開発され、既に使われているが、コンピューターの実用化はまだまだ十分ではない。

一方、有機合成は、近年、位置及び立体選択的な合成、不斉合成が、盛んに行われ一般性のある高い選択性での合成が、可能になってきた。しかし、これまでの合成計画は、経験からくる直感と試行錯誤に頼っているため、しばしば次のような事態におちいることがある。「非常に簡略な合成計画を考え出した、がある反応の立体選択性は、どうなるかわからない。実際に合成を行ってみると、求める立体配置が得られない。」このような時は、官能基や置換基を変えて実験による条件検討を行うことになる。それでも解決できなければ、合成計画を変更しなければならない。このようになると、たとえ完成したスキームの効率が非常に良くても、実際の合成に至るまでの効率は決して良くない。

では、この立体選択性の予測が、予めできればどうであろう。これは、合成計画をたてる上で、強力な武器になるであろう。さらに、上述では、実験により行った選択性改善の条件検討を、合成計画の段階でできることになる。これが可能になれば効率のよい合成につながるであろう。

筆者は、この予想の手段にコンピューターによる理論計算を用いることにした。既に、理論計算を用いた分子の立体配座の研究は、古くから行われているが、理論計算を用いた反応の選択性の研究は、始まったばかりであり、特に理論計算を合成計画の手段、すなわち、理想の合成中間体の設計に利用する試みは、きわめて新しい分野である。そこで、筆者は、鍵反応の立体選択性を理論計算により予測し、これを新規合成中間体の設計に使うことを目的とし、本研究を行った。

# 第 一 章 序 論

## (1) 理論計算<sup>1)</sup>

理論計算は、大きく二つに分けられる。量子化学計算と分子力学計算である。量子化学計算には、ab initio法と呼ばれる非経験的計算と AM1, MNDO, MINDO/3に代表される半経験的計算とがある。これに対し分子力学計算は、経験的計算とされており MM2, AMBERと呼ばれるプログラムがよく用いられている。筆者が利用した MM2 については次に詳しく述べる。

## (2) 分子力学計算<sup>2)</sup>

分子力学とは、Born-Oppenheimer古典力学で用いられる数式を経験的に組み合わせる方法で、このポテンシャル関数の組合せは力場と呼ばれている。力場では構造、配座エネルギー、生成熱などの分子の性質に関する測定値が、最もよく再現できるようにこれらの関数に含まれるパラメーターが最適化されている。分子力場の特徴は、これらのパラメーターが、異なる分子の間で移動可能であると仮定することである。つまり簡単な化合物をいくつか集めて、標準セットを作り、これに対してパラメーターの組を決めると以後は、パラメーターの値を変えずに他の似た化合物に対してもそのまま適用する。したがって量子力学計算に比べ計算時間ははるかに短く、構造、エネルギー等を再現することができる。なかでも1977年Allingerにより報告された MM2<sup>3)</sup> は構造、エネルギーを非常によく再現することから現在最も信頼されている。

MM2は、次に示すポテンシャル関数からなっている。

結合伸縮エネルギー ( $V_c$ )

変角エネルギー ( $V_b$ )

ねじれエネルギー ( $V_t$ )

Van der Waals エネルギー ( $V_v$ )

伸縮変角エネルギー ( $V_{sb}$ )

結合能率間相互作用エネルギー ( $V_u$ ) および双極子能率 ( $V_{DPH}$ )

分子の立体エネルギーは、これらのエネルギーの和で与えられ、その和が最小

となるようにNewton-Raphson法を用いて分子構造の最適化が行われる。しかし、ここで得られる立体配座は初期入力に基づいた局所的極小点にすぎず、最安定構造を与えるわけではないことは注意する必要がある。

筆者はMM2が、大きな分子にも適用でき、実際の分子に近いレベルで計算が可能であり、さらにパソコン程度の計算機で実用できることから本研究の手段に用いることとした。

しかし、次のような問題点もある。

- 1) 炭化水素や単純な官能基を持った化合物については、実験値を再現する精度があるが、多くの複雑な官能基を持つ化合物については、パラメーター不足である。
- 2) 「真空中に浮遊する孤立単一分子」に対し適応されており、実験条件である溶液中の状態と必ずしも一致しない可能性があり、NMRなどの情報で確認することが望まれる。
- 3) 基底状態の分子構造、エネルギーを再現するように作られているため、反応の遷移状態などの計算に用いることは、標準パラメーターをそのまま用いてはできない。

(3) 合成反応への応用<sup>4)</sup>

理論計算を合成に応用するためには次の二つの場合を考慮に入れる必要がある。

1) 熱力学支配のとき

反応が主として生成物の熱力学的安定性で決定される場合には、生成物の立体配座エネルギーを計算することで容易に生成物の予測ができる。

2) 動力学支配のとき

この場合、遷移状態でのエネルギー差が生成物の分布を支配する。

例えば配座異性体 A, B 間に平衡関係があり、Aからは C, Bからは D が生成する反応の遷移状態を考察する場合、(Fig. 1-1) に示す3種の状態が可能である。

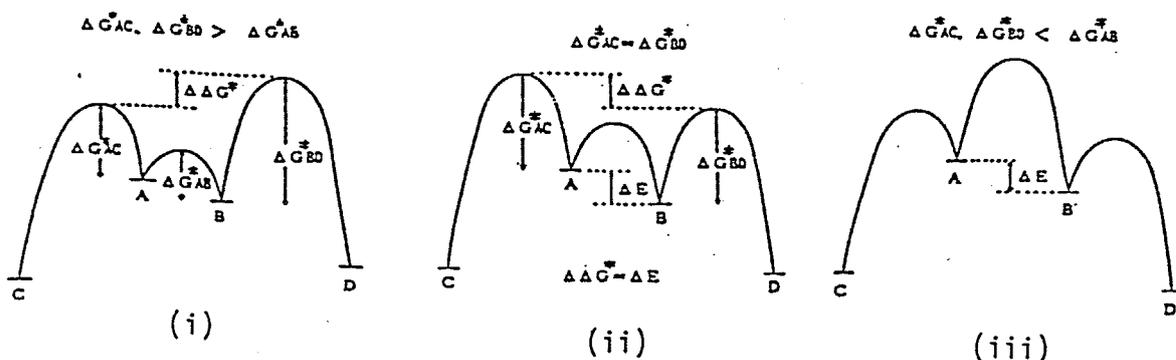
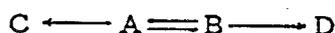
i)  $\Delta G^*_{AC}$  (AからCへの活性化エネルギー),  $\Delta G^*_{BD}$  (BからDへの活性化エネルギー) が  $\Delta G^*_{AB}$  (配座異性体 A, B間のエネルギー障壁) よりも大きい場合、Curtin-Hammettの原理<sup>5)</sup>によれば、生成物 C, Dの比は  $\Delta\Delta G^*$  によってのみ支配され、A, B間の平衡は全く関係ない。したがって A→Cの遷移状態と B→Dの遷移状態でのエネルギー差を求めなければならない。

ii)  $\Delta G^*_{AC} = \Delta G^*_{BD}$  の場合

各配座異性体から反応の活性化エネルギーがほぼ等しい場合、A, B間のエネルギー差  $\Delta E$  が生成物 C, Dの生成比に直接反映される。この場合には、分子力学計算で A, Bの基底状態のエネルギー差を計算すればよい。

iii)  $\Delta G^*_{AC}, \Delta G^*_{BD}$  が  $\Delta G^*_{AB}$  より小さい場合

A, B間の平衡よりも速く反応が進行するので、この場合も A, Bの存在比がそのまま C, Dの生成比に反映される。

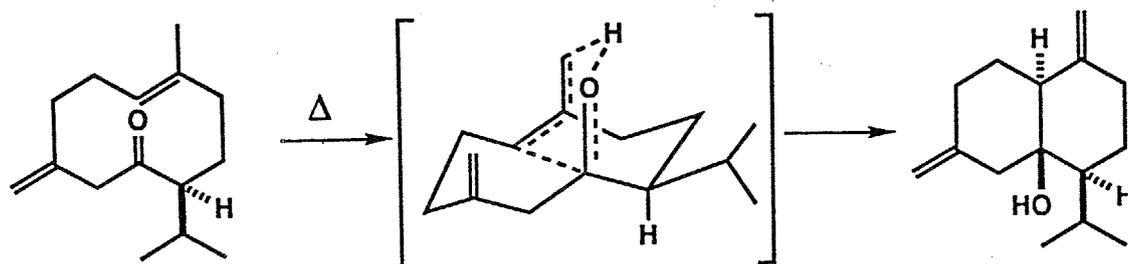


( Fig. 1-1 )

ii,iii) の場合は分子力学計算で A, B のエネルギー差を求めればよいが通常の化学反応は i の場合がほとんどであり、この場合遷移状態でのエネルギー差を求める必要がある。しかし、合成化学者の対象となる化合物では原子数が多すぎて、最も信頼性の高い *ab initio* 法で遷移状態構造を直接計算することは難しい<sup>6)</sup>。また MM2 そのままでは安定な立体配座へ最適化を行うために遷移状態構造を求めることができない。したがって、遷移状態の構造を適当に仮定するか、あるいは遷移状態に近い中間体を仮定し、その構造から立体エネルギーを見積ることによって反応性を説明する方法が用いられている。このような方法で得られたエネルギー差から  $\Delta G = \Delta H$  と仮定するとボルツマン分布の式  $\Delta G = -RT \ln K$  より、K を求めその生成比を予測することができる。実際、MM2 計算を用いて立体選択性を説明している例はこれまでにいくつか報告されている。

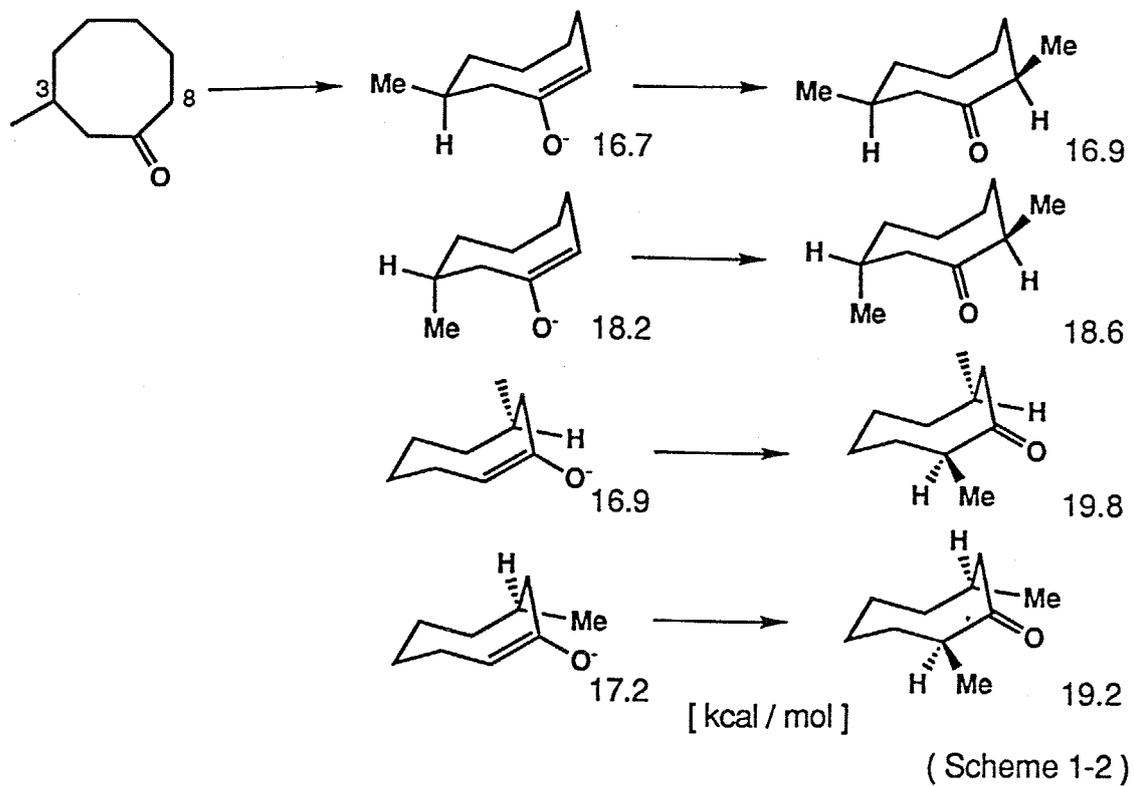
寺田、山村らは熱転位反応において、原型の立体配座の安定性では説明できなかった生成物の立体選択性を、反応点の距離が原型と生成物の中間であると仮定した遷移状態構造の MM2 計算により、説明できると報告している<sup>7)</sup>。

(Scheme 1-1)

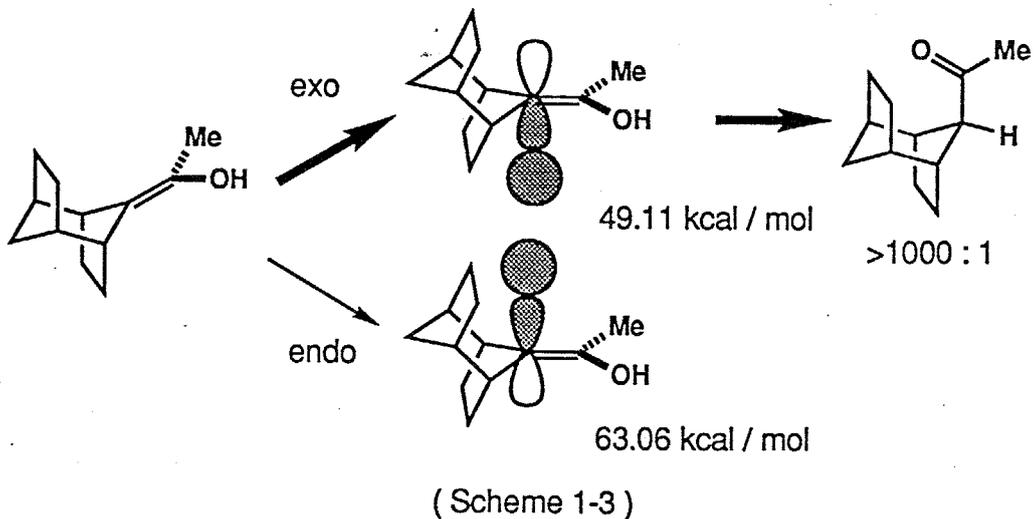


(Scheme 1-1)

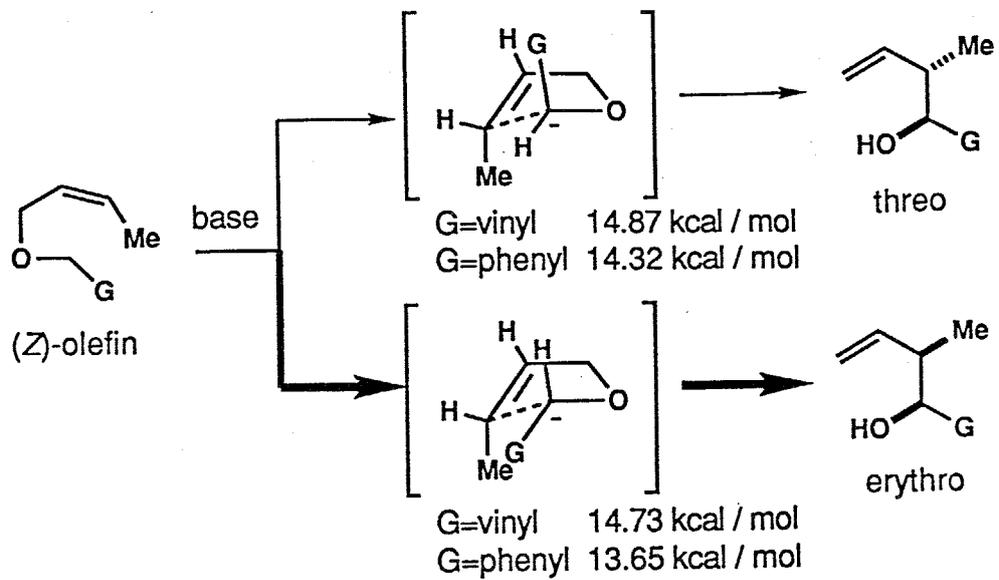
Stillらは、3-メチルシクロオクタノンの8位へのメチル化の際、エノラートの配座異性体のエネルギーと、生成する2,7-ジメチルシクロオクタノンの配座異性体とのエネルギー差から、8位のメチル化がシスの立体配置を98%という高い選択性で起こることを説明している<sup>8)</sup> (Scheme 1-2)。



また、Zimmermanらは、エノールの速度論的プロトン化において、遷移状態を鉛直方向90度からの攻撃と仮定し、エキソ方向とエンド方向からのプロトン化の立体選択性を説明している<sup>9)</sup> (Scheme 1-3)。

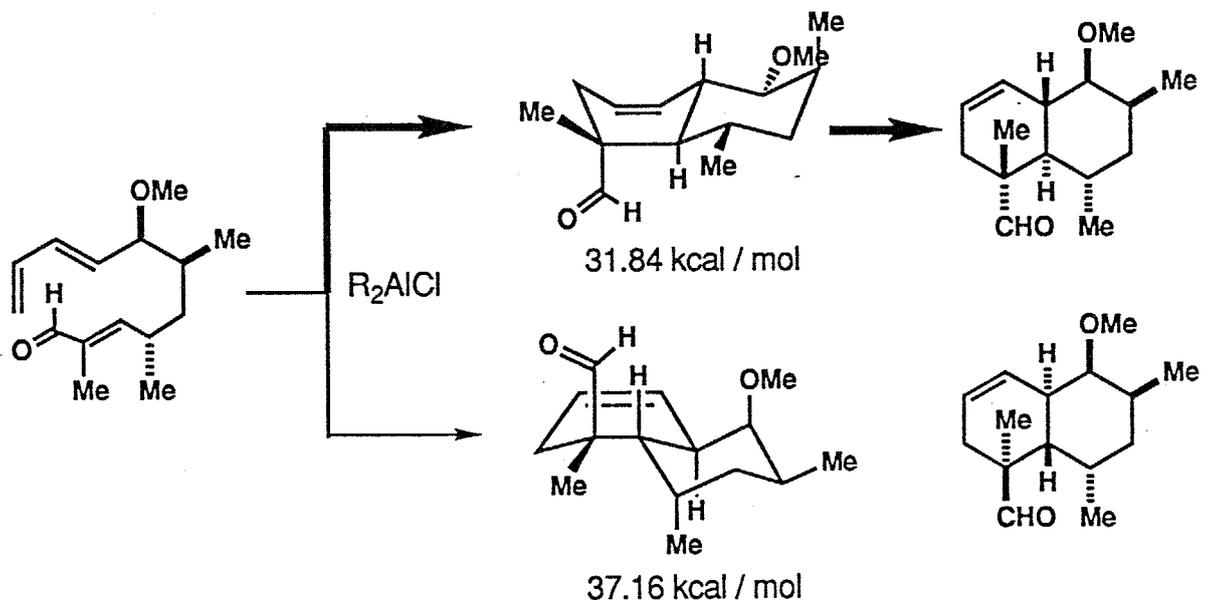


三上、中井らは[2,3]-Wittig転位反応の新しい遷移状態構造を提唱し、その遷移状態構造のMM2計算を行い、(Z)-オレフィンからの高いエリトロ立体選択性を説明している<sup>10)</sup> (Scheme 1-4)。



(Scheme 1-4)

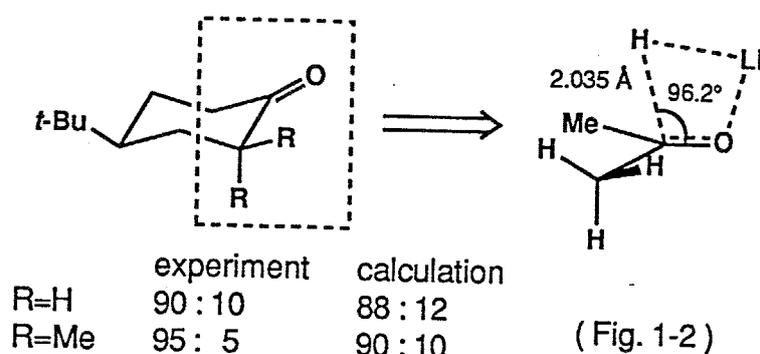
Marshallらは、Chlorotricolide, Kijanolid類の合成中間体のデカリン環の合成の際、鍵反応の分子内Diels-Alder反応における立体選択性の予測を行っている<sup>11)</sup>。彼らは、Diels-Alder反応の遷移状態が、反応が進行して直後に得られるボート型の立体配座に反映されると仮定してMM2による計算と実験結果の比較を行っている (Scheme 1-5)。



(Scheme 1-5)

以上の例では、遷移状態の構造を適当に仮定したり、近い構造に置き換えて立体選択性の説明が行われている。そのためこれらの成否は、仮定の妥当性にかかっており、定量的な予測は難しい。これに対し1986年、HoukらによりMM2遷移状態モデルが提唱された<sup>12)</sup>。MO法のなかでもab initio法は、その名のとおり非経験的な計算により最も信頼性の高い結果を与えるが、実際の複雑な分子には膨大な計算時間が必要でとても使えない。そこで直接反応に関与する部位のみab initio法でその反応の遷移状態構造を求め、この遷移状態構造を再現できるようにパラメーターをつくるか、あるいはそのまま複雑な分子でも同じと仮定し部分構造を固定する。そして、残りの反応に関与しない部分についてはMM2により構造最適化を行い、これを全体の遷移状態構造とする手法である。

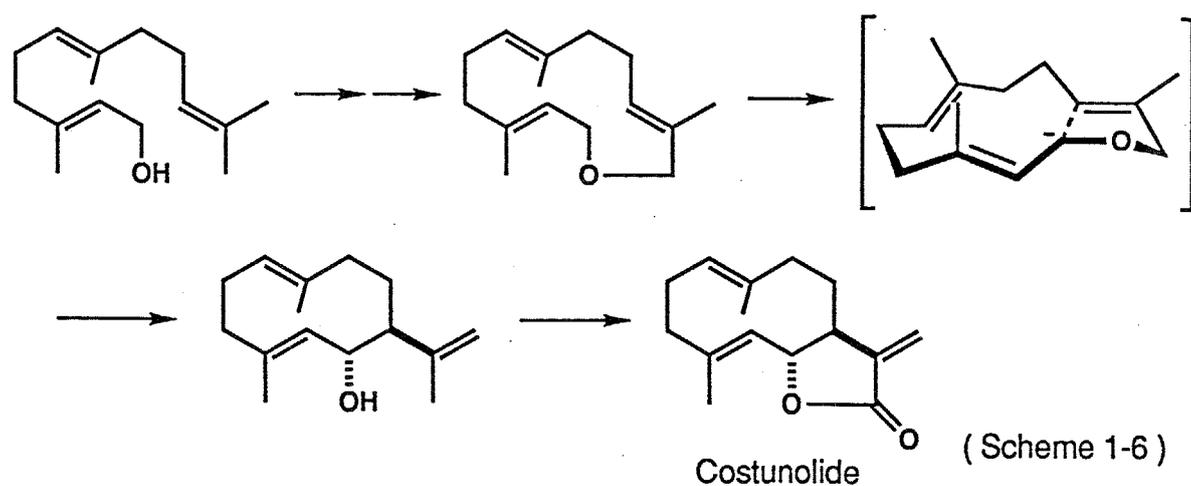
例えば、Houkらは、 $\alpha$ 位に不斉を有するカルボニル化合物のヒドリドによる還元反応の遷移状態構造をab initio法で求めFelkin-Anhモデルを支持する結果を得、この構造から非環状ケトンのLiAlH<sub>4</sub>還元のアキシャル攻撃が優先する結果を報告した<sup>13a)</sup>。さらにアセトンへのLiHの付加反応の遷移状態構造をab initio法から求め、MM2遷移状態モデルを用いて6員環ケトンへのLiAlH<sub>4</sub>のアキシャル攻撃が優先することを説明している<sup>13b)</sup> (Fig. 1-2)。



またキラルなホウ素化合物を用いるオレフィンのヒドロボレーションについても、エチレンとエチルボランの反応の遷移状態をab initio法で求め、この構造を用いて、イソピノカンフェイルボランとシス-2-ブテンとの反応が、(S)-アルコールを有利に与えるのに対し、ジイソピノカンフェイルボランからは、(R)-アルコールが優先して得られることをMM2遷移状態モデルを用いて説明している<sup>14)</sup>。さらに、Diels-Alder反応<sup>15)</sup>、ラジカル付加反応<sup>16)</sup>、エン反応<sup>17)</sup>、酸処理下でのラクトン化<sup>18)</sup>、ニトリルオキシドとキラルなアリルエーテ

ル類との付加環化反応<sup>19)</sup>、リチウム、ホウ素エノラートのアルドール反応<sup>20)</sup>、カルボニル基に対するメチルリチウムの1,2付加反応<sup>21)</sup>についても、同様にMM2遷移状態モデルを用いた例が続々と報告されている。

高橋、深沢らは、大員環内[2,3]-Wittig転位反応を行い、ゲルマクラン型セスキテルペンの一種コスタノリドを酢酸ファルネシルから6行程で全合成している<sup>22)</sup>。さらに、この際得られたトランスの環結合の高い立体選択性は *ab initio*計算で得られた遷移状態構造を基にしたMM2遷移状態モデルを用いて説明している<sup>22c)</sup> (Scheme 1-6)。

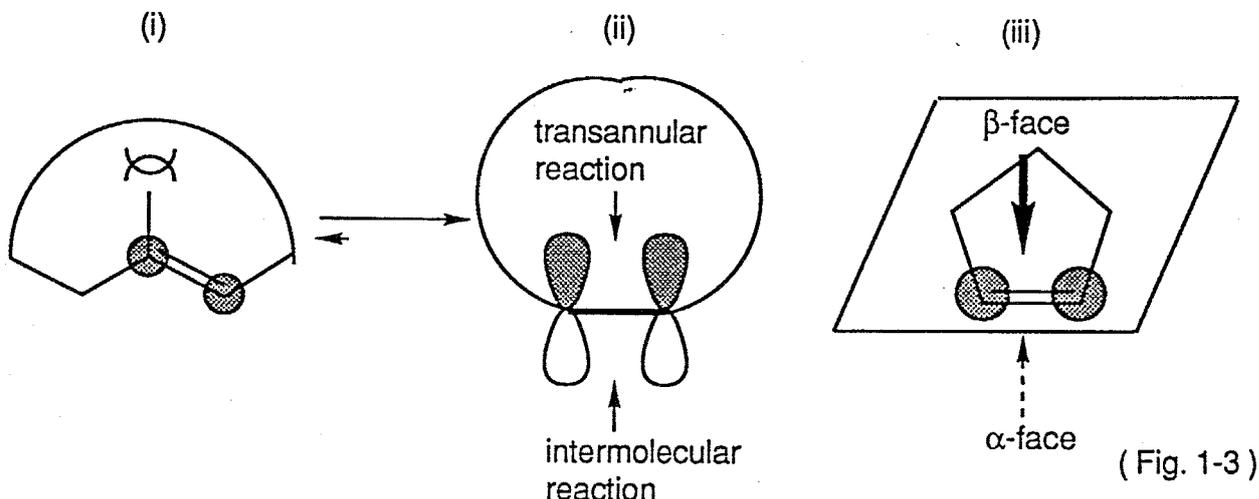


このように、現在では *ab initio* 法とMM2を組合せ、より真に近い遷移状態構造が得られることを前提として、反応の立体選択性を定量的に論議できるようになり、反応の予測に用いることのできる段階になっている。

#### (4) 中・大員環化合物の立体化学制御

鎖状、5,6員環化合物の立体化学制御は近年の有機合成化学の中心的課題の一つであり、非常に多くの研究が行われており現在では極めて高い立体制御が可能となっている。これに対し、中・大員環化合物の化学は合成研究そのものの例が少なく比較的未開発の分野といえる。

中・大員環化合物と5,6員環化合物との大きく異なる特徴は二重結合の $\pi$ 軌道を例にとるとFig. 1-3のように表せる。これらはいずれも環平面の真上から見た図である。中・大員環化合物では渡環的な接触を避けるため(i)二重結合の面は環平面に対し垂直方向に向いている(ii)。したがって、 $\pi$ 軌道は環平面に対し水平方向に向いているので、その一方は環により覆われており分子間の試薬の攻撃は必ず環の外側から起こり(peripheral attack)<sup>23)</sup>、分子内の渡環的な反応は、環の内側から起こる(ii)。すなわちオレフィンの面を制御すれば反応試薬にかかわらず、反応は一方方向から進行し高い立体化学制御が期待できる。これは、5,6員環の $\pi$ 軌道が環平面に対し垂直方向に向いているため、試薬が環平面の上下を選んで攻撃する(iii)こととは根本的に異なり、新しいタイプの立体化学制御として非常に興味もたれる。



しかし、このように特徴ある分野にも関わらず、研究があまり行われていなかったのは、次のような理由からであると考えられる<sup>24)</sup>。

- 1) 中・大員環化合物の合成自体が難しいと信じられていたこと。
- 2) 中・大員環化合物の立体配座は、鎖状化合物に比べれば自由度が制約され

ているが、5, 6員環化合物に比べるとはるかに自由であるり、その立体配座の解析が難しかった。

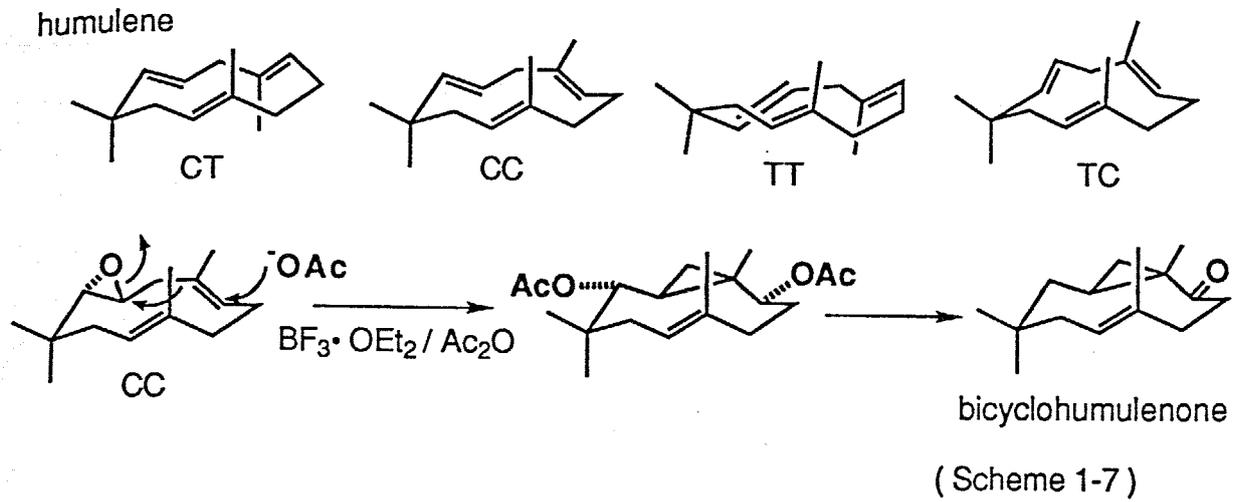
3) 同様に反応後の生成物の立体化学の証明が難しいことなどである。

1939年にRuzickaがムスコン・シベトンの合成でノーベル賞を受賞し<sup>25)</sup>, またPrelogが中・大員環化合物の研究における功績からノーベル賞を受賞した<sup>26)</sup> ことに端を発し、現在までに以下のようにいくつもの一般的な中・大員環化合物の閉環法が報告されている: 児玉ら<sup>27)</sup>はアリルフェニルスルフィドとエポキシドとのカップリングで、Frazzaら<sup>28)</sup>はトシルメチルイソニトリルとジハロゲン化合物とのアルキル化で、北原ら<sup>29)</sup>は $\alpha$ -(フェニルチオ)ニトリルとトシラートとのアルキル化で、Etournaud<sup>30)</sup>や Deslongchampsら<sup>31)</sup>はアルキルマロン酸エステルとハロゲン化アルキニルのアルキル化で、Marshallら<sup>32)</sup>はアルキルスルホンとヨウ化アリルとのアルキル化で、求める中・大員環化合物を得ている。また当研究室でも既に $\alpha$ -チオフェニルエステルとヨウ化アルキルとのアルキル化<sup>33)</sup>、さらに保護したシアノヒドリンとトシラートあるいはハロゲン化アリルとのアルキル化<sup>34)</sup>で種々の中・大員環化合物を合成することに成功している。この他にも金属を媒体としたカップリング反応もいくつか報告されている<sup>35)</sup>。またエリスロノリドの合成の際、開発された活性化エステル法は大環状ラクトンの一般合成法<sup>36)</sup>として非常に有用である。以上のことから1)の中・大員環化合物の合成自体の問題は、ほとんど解決されている。

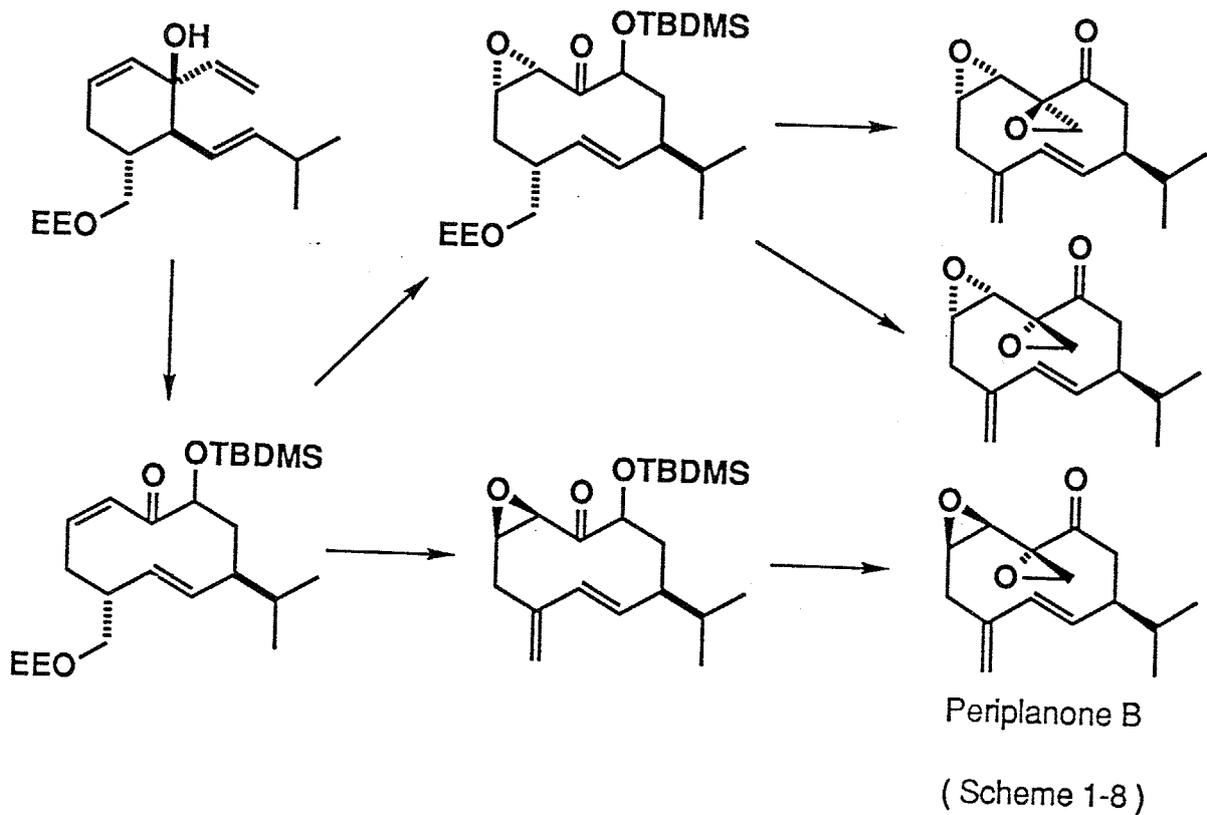
2, 3)の問題は、急激な計算機の高速化に伴い可能となった理論計算の一つであるMM2を用い、立体配座解析を行うことによって解決できると考えた。

以下に、すでに報告されている中・大員環化合物を中間体とした天然物合成と立体配座解析を利用した中・大員環化合物における立体化学制御の例を示す。

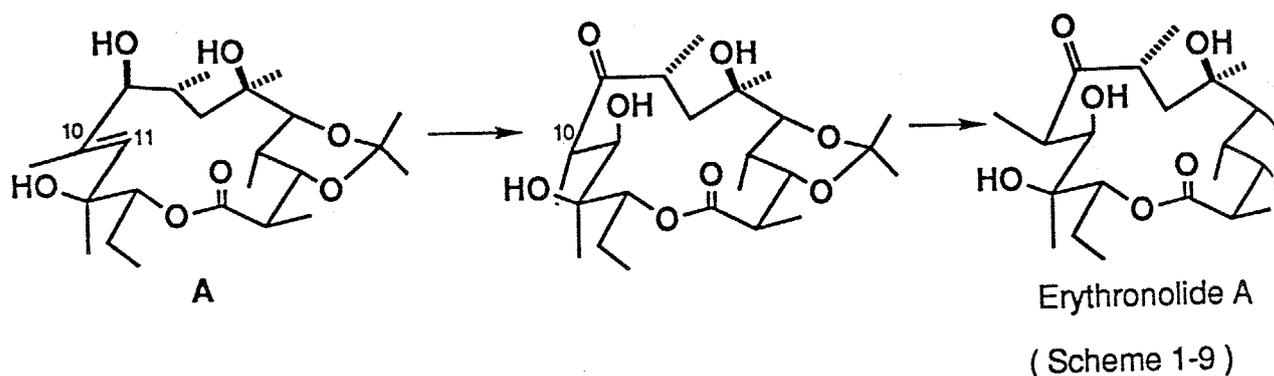
1978年、白浜、大沢らはフムレンの立体配座解析をMMIを用いて行い、4種の配座異性体を得た。特に配座C Tの他に新たに見いだした配座C Cは、ヒルスタノイド、ビシクロフムレノンの生合成前駆体であることを報告している。さらに配座C Cからの化学変換でビシクロフムレノンを合成することに成功している<sup>37)</sup> (Scheme 1-7)。この際、反応系中に求核種があるときは配座C Cから渡環反応が進行し、ないときは配座C Tから環化反応が進行することを見出し”配座選択的”反応と報告している。



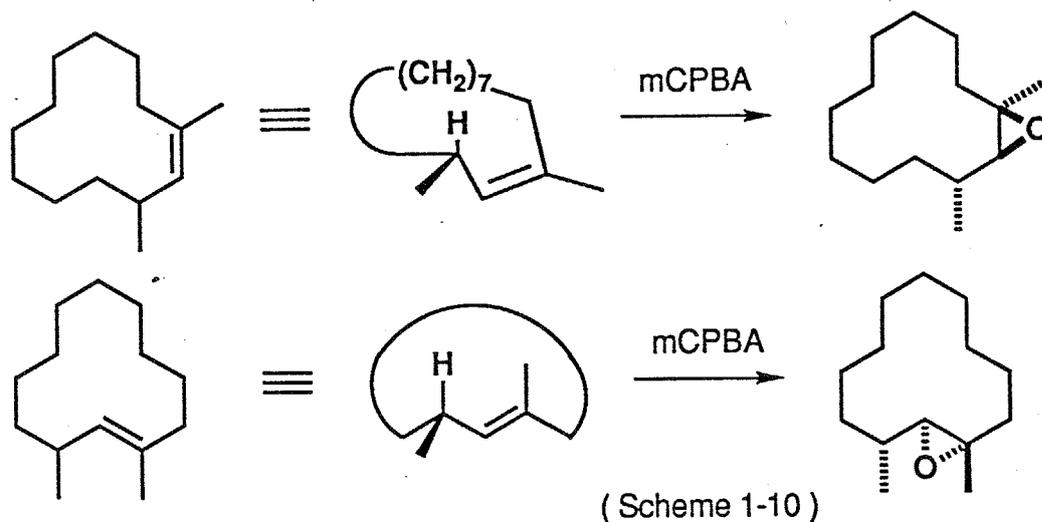
1979年、StillはOxy-Cope転位反応を用いて6員環化合物から10員環骨格を構築し、この10員環化合物へのエポキシ化反応を用いてのペリプラノンBの可能な4種のジアステレオマーのうちの3種を合成し、ペリプラノンBの立体構造を決定した<sup>23)</sup> (Scheme 1-8)。



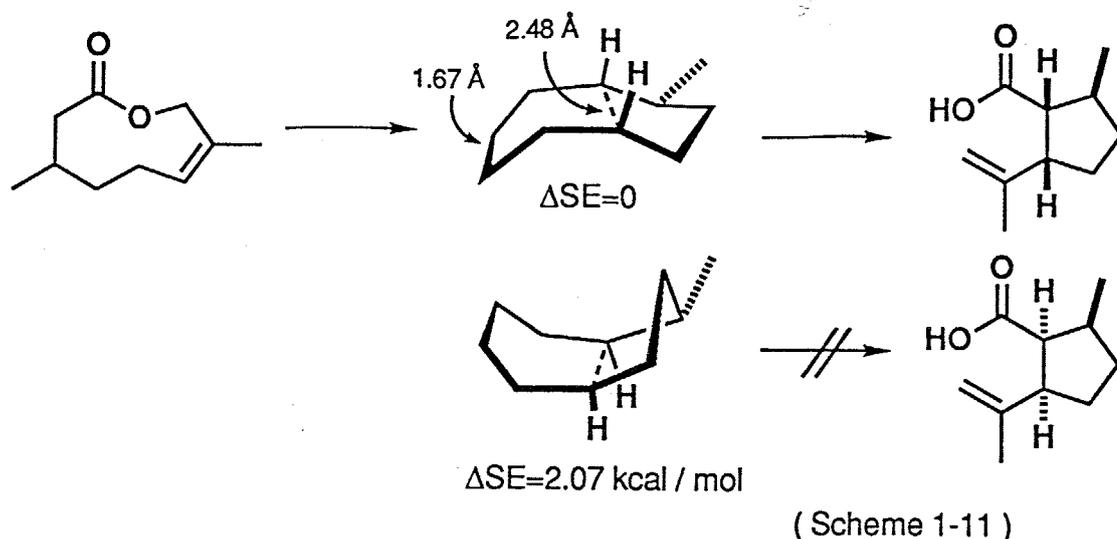
1979年、Coreyら<sup>36)</sup>は14員環ラクトンAの10,11位へβ面からの立体選択的エポキシ化、開環、ついで10位のエピ化を経てエリスノリドAの合成を行っている (Scheme 1-9)。



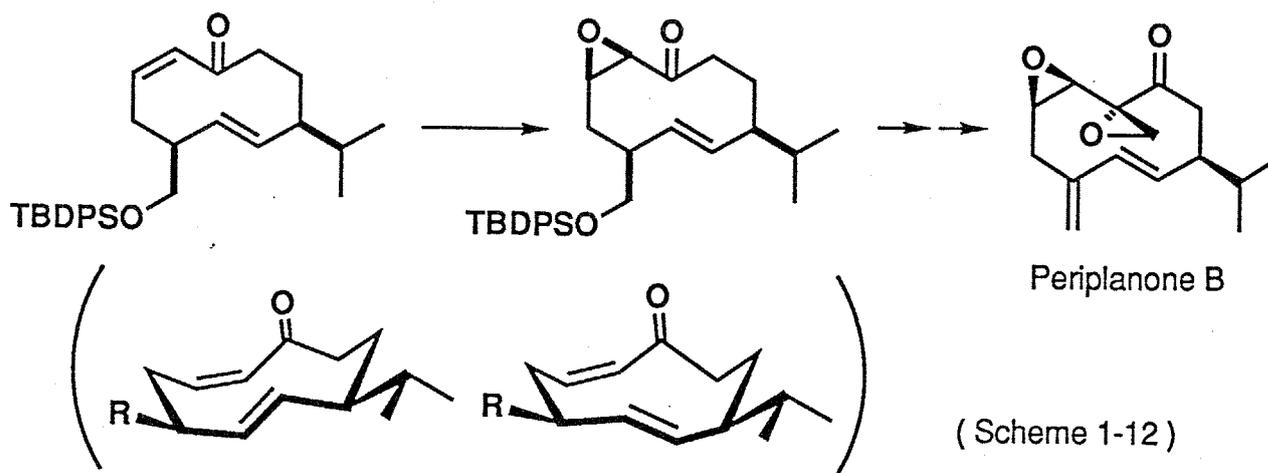
また1983年、Vedejsらは3-アルキルシクロアルケンのZ体, E体のそれぞれについて、エポキシ化あるいは、オスミウム酸化の立体選択性についての一般則を見出し報告している<sup>39)</sup> (Scheme 1-10)。



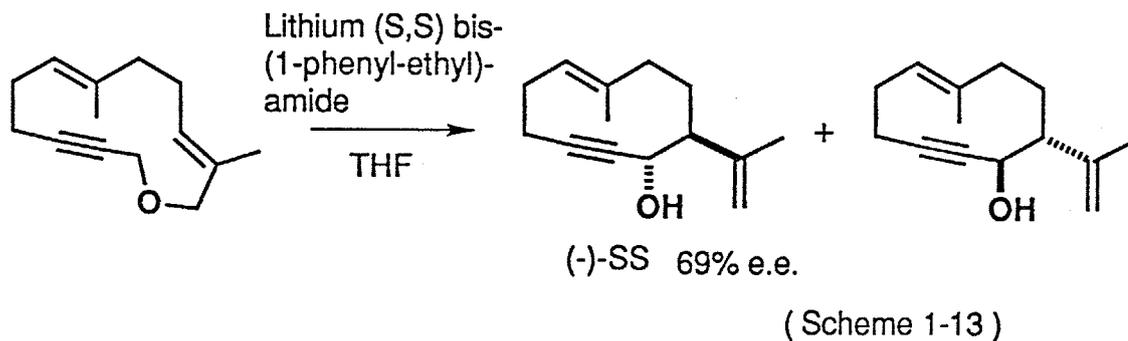
Funkらは1986年、中・大員環化合物の外側のπ軌道を用いて分子内Claisen転位反応を行い、さらにその立体選択性をCope転位アナログで近似したMM2遷移状態モデルを用いて定量的に説明している<sup>40)</sup> (Scheme 1-11)。この他Irelandらによる大員環内Ireland転位反応を用いたKijacolide合成研究<sup>41)</sup>、Paquetteらによる中員環内Oxy-Cope転位反応を用いた3環性化合物の骨格合成<sup>42)</sup>も報告されている。



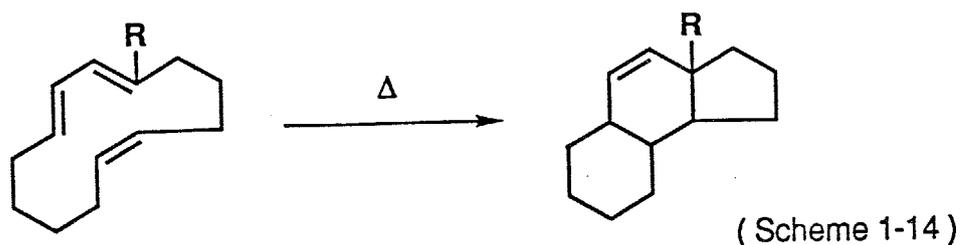
高橋らは10員環エノンに対するエポキシ化を行い、ペリプランノンBの合成を立体選択的に合成することに成功している。この際、10員環化合物の配座異性体の比がそのまま生成物の立体選択性に反映すると報告している<sup>43)</sup> (Scheme 1-12)。



Marshallらは光学活性な塩基を用いてプロキラルな大員環化合物から[2,3]-Wittig転位反応を行って光学活性体を得ている<sup>44)</sup> (Scheme 1-13)。



さらにDeslongchampsらは14員環トリエンの分子内Diels-Alder反応を各オレフィン部分のE体, Z体について反応性を比較検討している<sup>45)</sup>(Scheme 1-14)。



本研究では、従来合成の最終段階の環化反応によって作られていた中・大員環化合物をむしろ合成の鍵中間体に用い、鎖状、5,6員環とは異なる新たな第三番目の立体化学制御法を開発し、それを実際に天然物合成に応用することを目的とした。さらにこの際、分子力学計算(MM2)を用いて鍵反応の立体選択性の予測を行い、合理的な合成中間体の設計を試みた。

第二章では本研究のためのMM2の入出力の方法を詳細に述べた。

第三章ではネオカルチノスタチンクロモフォアの合成研究と、その天然物類似の渡環的ラジカル生成反応について述べた。

第四章では大員環内Diels-Alder反応の開発およびその立体選択性の予測と実証、さらに新規ステロイド骨格合成の応用とその際の立体選択性の予測について述べた。

第五章では10員環エノンへの求核的エポキシ化反応を用いたペリプラノンAの合成について述べた。

第六章では10員環エノンへのシクロプロパン環形成反応を用いたビスクロブムレノンの合成における立体選択性の予測について述べた。

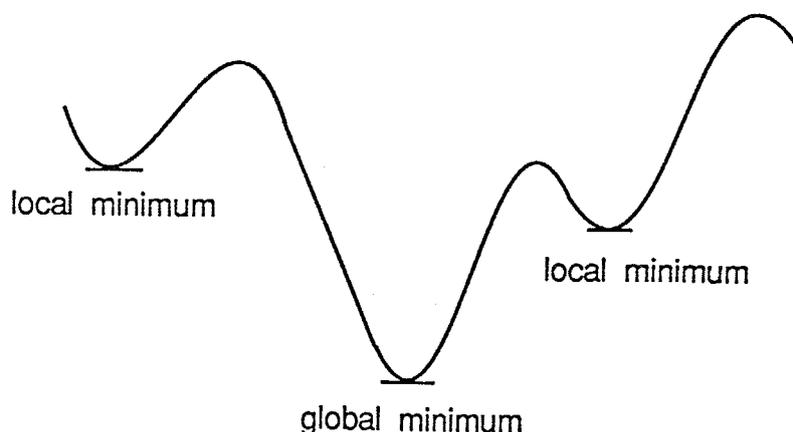
さらに第七章では、以上の結果を総括した。

## 第二章 MM2計算の方法：構造入力と出力分析

MM2計算<sup>3)</sup>は構造入力、計算、エネルギーおよび3次元構造の出力の3つの段階に分けられる。それぞれについて筆者の用いたプログラムを計算機ごとに紹介する。用いた計算機は大型計算機 (HITAC M-660H)・パソコン (PC-9801VX, 80287)・microVAXIIの3種である。

### MM2計算を行うための入力

MM2の入力文は主に分子の結合表と1つの立体配座の座標から成っており、決まった書式に基づいて作る必要がある。このときの座標はXYZ座標 (カルテジアン座標) であるので、通常の結合長・結合角・2面角を用いる内部座標 (Z-マトリックス) はXYZ座標に変換しなくてはならない。大型計算機、パソコンの入力の際は、まず分子模型から内部座標を読み取り、XYZ座標へ変換するプログラムCOORD<sup>46)</sup>を実行してXYZ座標を得る。さらにここへMM2計算に必要な結合表を書き加えMM2計算を実行する。一方microVAXIIを使った計算は、Columbia大学のStill教授らによって開発されたソフトMacroModel<sup>47\*)</sup>を用いて行っている。入力はこの中のINPUTモードで行うことができる。すなわち、マウス等を利用して画面上に分子の平面構造を描き、2面角を回転するなどして望む立体配座へ導いたり、予めテンプレートとして組み込んである3次元構造を利用して官能基を付け加えるなどして行える。しかし、これらの入力手法により得られる初期座標をMM2で構造最適化すると初期入力座標に基づく局所的極小点 (local minimum) が得られるだけである (Fig.2-1)。

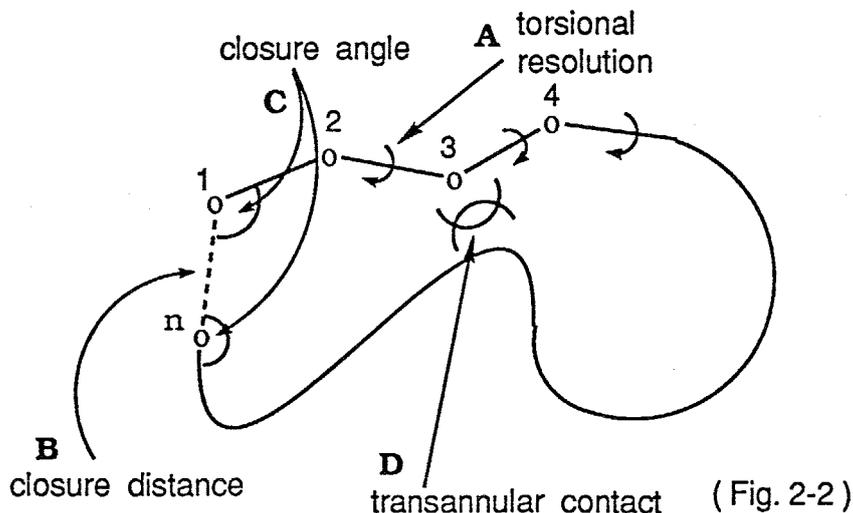


( Fig. 2-1 )

特に中・大員環化合物のように多くの配座異性体（コンホマー）が存在する場合、可能な立体配座（コンホメーション）を1つ1つ入力しなければならず、また他の重要な配座異性体を見逃す危険が多い。そこでこの問題を避けるために本研究では自動配座発生プログラムを用いて全ての可能な立体配座の初期入力座標を発生させた。

自動配座発生法には系統的な方法とランダム発生法の2種類がある<sup>4d)</sup>が、本研究ではStill教授の開発したMacroModelのMULTICモード<sup>47b)</sup>、あるいは広島大学の深沢教授の開発したMMRS<sup>48)</sup>を用い、系統的に初期入力座標を発生させた。これらのプログラムの原理は同様で、次に示す通りである<sup>4d, 8b)</sup>。

例えばn員環の初期配座を作る場合を考える。(Fig.2-2)まず1番目とn番目の原子を切断する。距離1-2, 2-3, 角度1-2-3は原子種によって定まるので、1, 2, 3の原子の位置は自動的に決まる。4の相対的な位置は距離3-4, 角度2-3-4が原子種により定まるので、2面角1-2-3-4により決まる。順に5番目からn番目の原子の位置が、それぞれの2面角によって決定される。したがって全ての2面角を独立に $\phi$ 度きざみに回転すれば(resolution:Aを例えば30や60°に設定)、全ての立体配座が得られる。ここでn員環を形成するには、1とn番目の原子が結合しなければならないので、距離1-nがある範囲にあるものだけを取り上げる(closure distance:Bを例えば1.0-3.0 Åに設定)。また角度2-1-n, 1-n-(n-1)が適当な角度にあるものだけを取り上げることできる(closure angle:Cを90-130°に設定)。さらに非結合原子間距離(transannular contact:Dを3.0 Åに設定)を定め、結合していない原子どうしがこの距離内にあるもの



すなわちぶつかり合っているものは除く。こうして得られた初期入力座標を全てMM2でエネルギー極小化することにより、全ての可能な配座異性体のエネルギーや構造を求める方法である。この方法は、環の自由度（回転可能な2面角の総数）が7個以下であれば、非常に有効である。Stillらは、シクロドデカンの立体配座解析を様々な条件設定（torsional resolution, closure distance, transannular contact等）で行い、条件次第で得られる配座異性体の数が大きく異なり、重要な配座異性体を漏らしてしまう危険性があることを報告している<sup>47b)</sup> (Table 2-1)。また分子の自由度が10以上になるとさらに多くの初期座標が存在するため、大型計算機を用いて膨大な計算を行わねばならず、それでも配座異性体が漏れてしまう危険が大きいいため、実際には自由度7~10がこの方法の限界と思われる<sup>49)</sup>。

Table 2-1 Cyclododecane

Torsional resolution	Transannular Contact	Closure		Number of conformations	
		Dist	Angle	Generated	Minimized
120°	1.5	1.0-4.0	0-180	14	8
60°	1.5	1.0-3.0	0-180	317	17
60°	1.5	1.0-3.0	65-155	153	17
60°	1.5	0.5-2.5	65-155	104	15
60°	1.5	1.0-2.0	0-180	25	15
60°	1.5	1.3-1.7	0-180	23	9
30°	1.5	1.3-1.7	90-130	240	17

## 計算

大型計算機・パソコンではMM2 (1977年)<sup>3)</sup>を用いた。

microVAXIIではMacroModel<sup>47a)</sup> (ver. 2.5) のMINIMIZEモードでMM2を用いた。

## 出力

計算の結果として得られるのは配座異性体のエネルギーとその3次元座標である。

## 配座エネルギー

おのこの初期入力座標に基づいたMM2の計算結果は、それぞれ総エネルギーと各項目 (compression, bending, stretch-bend, van der Waals, torsional

, dipole) について出力される。更に詳細な出力文では1つ1つの結合距離、結合角、2面角のデータ及びその歪エネルギーを出力することができる。

得られた配座異性体の幾つかは同じ配座異性体に収束するので、同じものは削除しエネルギーの低い順に並べる。この作業は大型計算機・パソコンでは深沢教授の作ったプログラムMDIF, ORDERを用い、microVAXIIではMacroModelのMULTICモードで行った。

ここで得られた配座異性体は、最安定配座のみを考慮するだけでなく、その近傍のエネルギー(3 Kcal/mol以内)を持つ配座異性体も含めて議論することが重要である。第一次近似としてエントロピー項を無視すれば( $\Delta G = \Delta H$ )、ボルツマン分布式( $\Delta G = -RT \ln K$ )を用いて、分子の配座異性体間のエネルギーの差 $\Delta H$ から任意の温度での平衡状態の各配座異性体の存在比 $K$ を求めることができる。

また、個々に得られる2面角に基づいてカープラスの式を用いればプロトンNMRの結合定数を計算し、それらと測定結果とを比較することで立体構造を推定することにも利用できる。

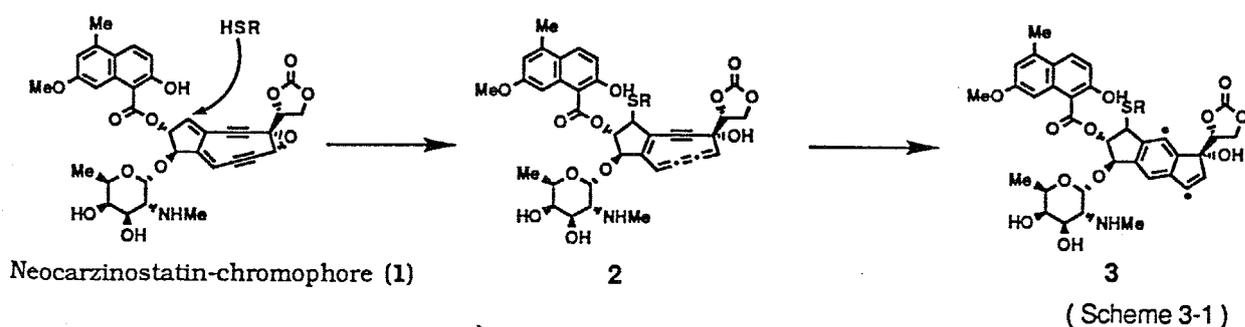
一方、得られた3次元座標からは3次元グラフィック表示を行うことで分子模型と同様に視覚で立体配座を捕えることができる。大型計算機・パソコンではORTEP<sup>2)</sup>を用いてこの3次元構造を出力している。また microVAXIIを用いたMacroModelではグラフィック画面に常に3次元構造が表示されており、入力構造から最適化の過程まで見ることができ、ANALYZEモードではグラフィック画面上の構造をマウスを使って希望の原子間距離、角度、2面角、さらにそれから算出されるプロトンNMRの結合定数を簡単に見ることができる。

以上のようにMacroModelでは入力・計算・出力は各サブモードを用いて簡単に行うことができ、数字を使うことなくグラフィック画面との対話形式で作業を進めることができる。これに対し、大型計算機・パソコンを用いた計算の場合は、数字を用いて入力し、ファイルの移動、プログラムの実行などは、すべて手作業で行なう必要がある。ただし、細かいデータの入力、特に遷移状態構造などの入力は報告されているデータをそのまま用いるため、手作業の方が通している。両方のプログラムを用いて計算を行った。

### 第三章 ネオカルチノスタチン・クロモ フォアの合成研究および合成モデルを用 いた天然物類似の渡環反応の研究<sup>51)</sup>

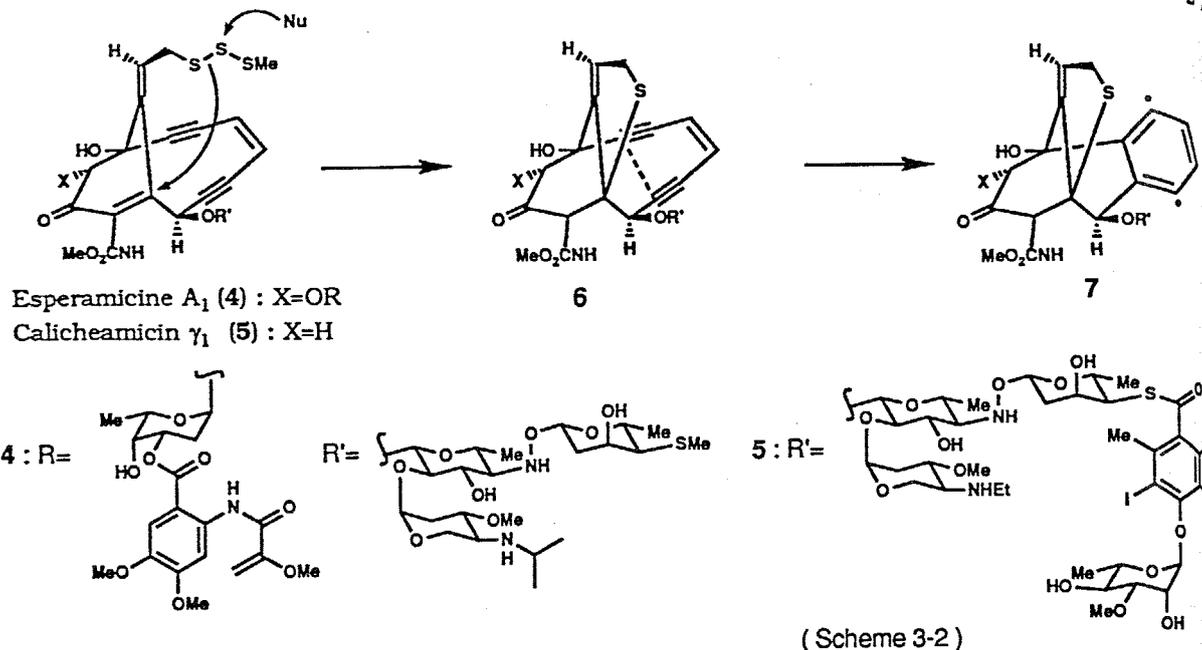
#### 3-1 背景

ネオカルチノスタチン (Neocarzinostatin, 以下NCSと略す) は1965年江戸, 石田らにより単離された抗腫瘍性抗生物質であり<sup>52)</sup>、2-メルカプトエタノールやチオグリコール酸メチルなどの付加により活性化されてDNAを切断することが知られている<sup>53)</sup>。NCSは、非蛋白クロモフォア (1) (以下NCS-chrと略す) とアポタンパク (apo-NCS) から成っているが、この活性はクロモフォア部にあり、アポタンパクは、不安定なクロモフォアを非共有結合で包み、熱や光から守りキャリアとして働くことが示唆されている<sup>54)</sup>。NCS-chrの構造は、1985年江戸, 瀬戸, 石田らにより1の平面構造が提出され<sup>52d)</sup>、さらに1988年Myersらにより渡環反応後の化合物を基に立体化学も含め1の構造が決定された<sup>52e)</sup>。この活性発現の機構は、Myersらにより次のように提唱されている<sup>55)</sup>。2-メルカプトエタノールあるいはチオグリコール酸メチルは5員環部分に付加し、エポキシドの共役的な開裂に伴って2を生じる。2において9員環のクムレンとアセチレン間で渡環反応を起こして生じるピラジカル3がDNA中のチミンのついたデオキシリボースの4'あるいは5'位の水素を引き抜きDNAを切断する (Scheme 3-1)。

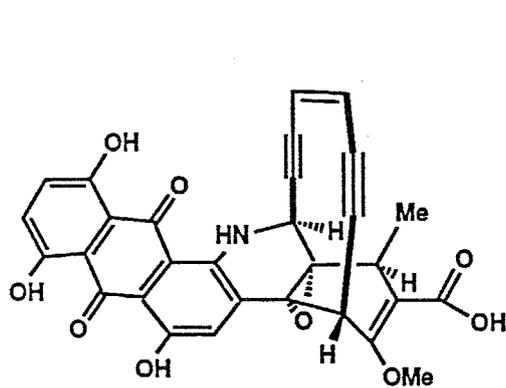


また1987年Golikらにより、構造が提出されたエスペラミシン (4)<sup>56)</sup>および、カリケミシン (5)<sup>57)</sup> (以下ESP-CALと略す) についても、その活性発現の機構が次のように報告されている。トリスルフィド部分に分子間の求核攻撃を受けて生成するチオレートが、分子内で共役付加し、6を生じる。6は5に比べ、 $sp^2$ 炭素が $sp^3$ になったため2つのアセチレンがより近づき、3-エン-1,5ジ

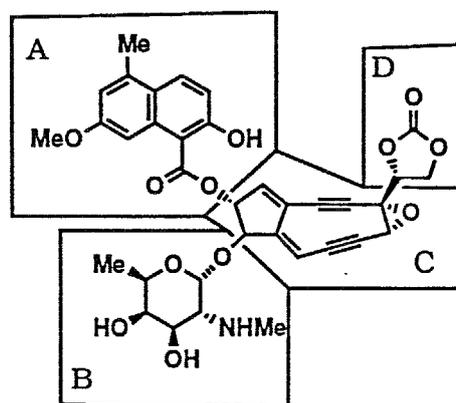
イン部分でBergman反応<sup>58)</sup>が自然に起こりベンゼン環のピラジカル7を発生する。これが直接DNAの水素を引き抜きことによりDNAが切断される (Scheme3-2)



さらに1989年小西らによって単離されたダイネミシン (8)<sup>59)</sup>についても、類似の構造が報告されている (Fig.3-1)。これらの構造は、ピシクロ[7.3.0]、[7.3.1]システムに2つのアルキンを有し極めて歪んだ特異なものである。筆者はこれらの特異な構造の骨格合成、およびそのラジカル発生、DNA切断に関する分子レベルでの機構解明に興味を持ち本研究を始めた。



(Fig. 3-1)

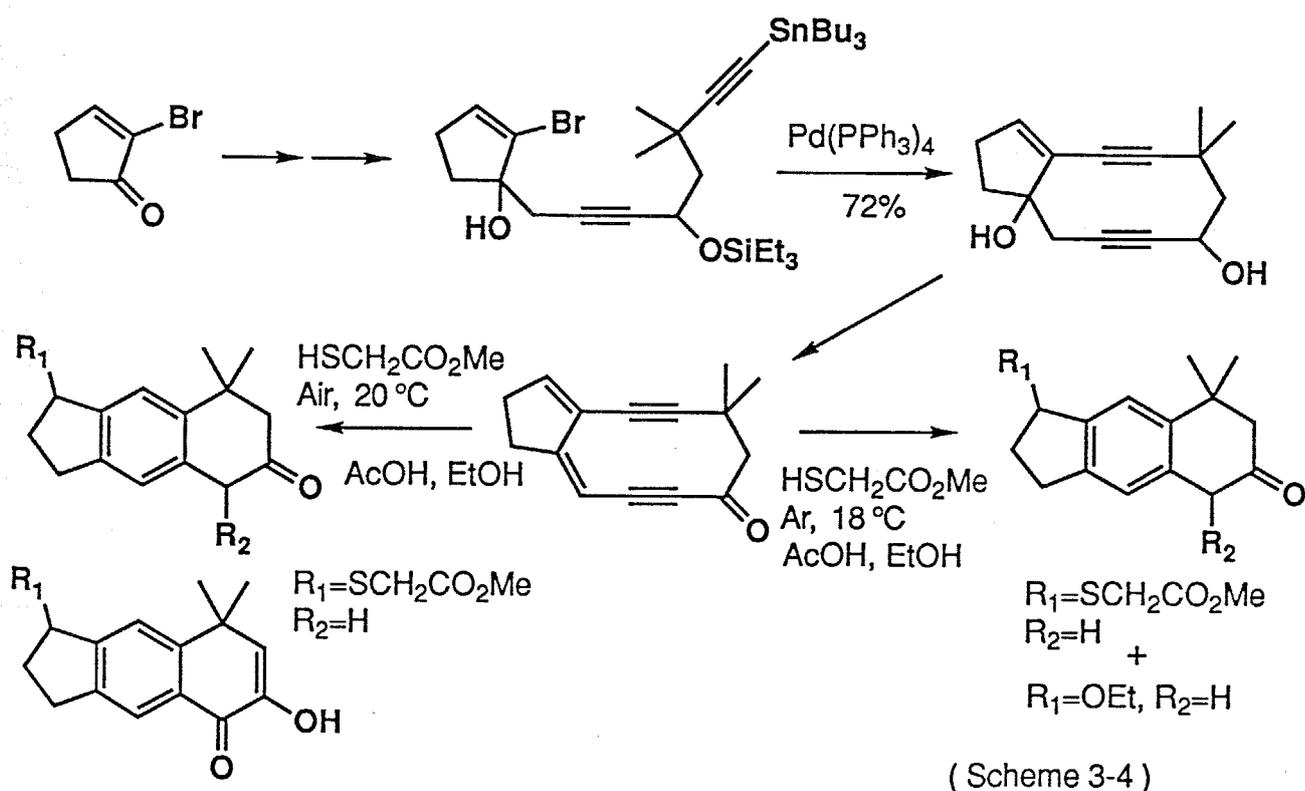
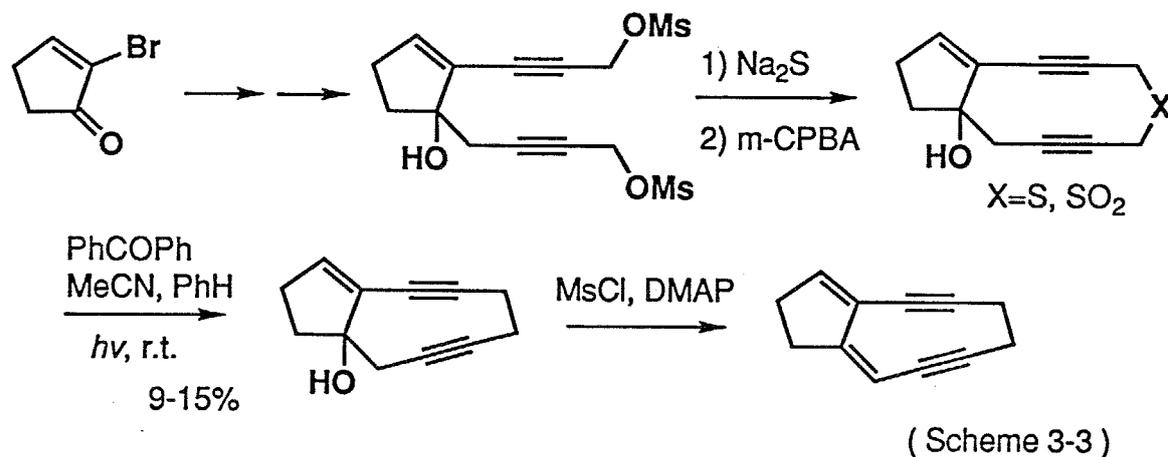


(Fig. 3-2)

NCS-chrは次のA, B, C, Dの4つの部位から成っている。A: 1-ナフトールカルボン酸, B: N-メチルフコサミン, C: ピシクロ[7.3.0]システム, D:

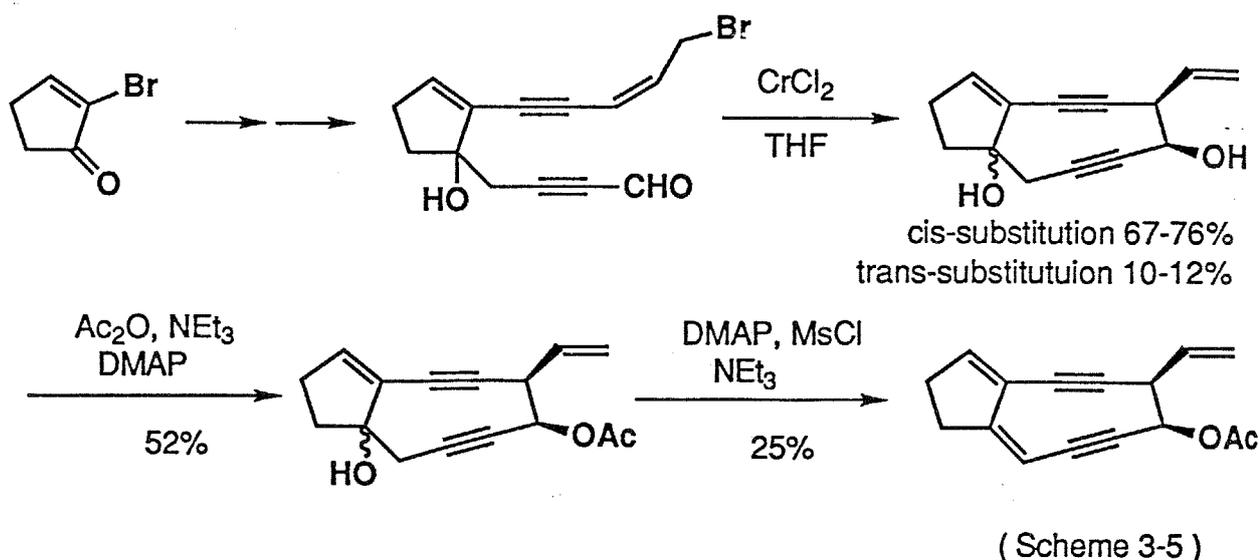
環状炭酸エステル (Fig.3-2)。これら A, B, C, D のどの部位が、アポタンバクのどの位置に接合しているか、さらに NCS-chr と apo-NCS の接合に本質的に必要なのはどれか、あるいは DNA 切断の際どのような役割をしているかを明らかにするためには、各部位を有する化合物を用いた接合試験、DNA 切断試験等を行う必要があると考えられる。しかし不安定な天然物からの誘導は困難であるため、合成により各部位を有する化合物を導く必要がある。そこでまず、ラジカル発生に重要なコア部分 C の合成研究から行うことにした。

本研究をはじめた当時、1988年 Wender らは 2つのアルキン を有するピシクロ [7.3.0] 化合物をはじめて合成し、提唱されていた天然物の NMR スペクトルによく一致することを報告している<sup>60)</sup>。ここで得られた最終化合物は非常に不安定で、室温での半減期は 48 時間と報告されている (Scheme 3-3)。



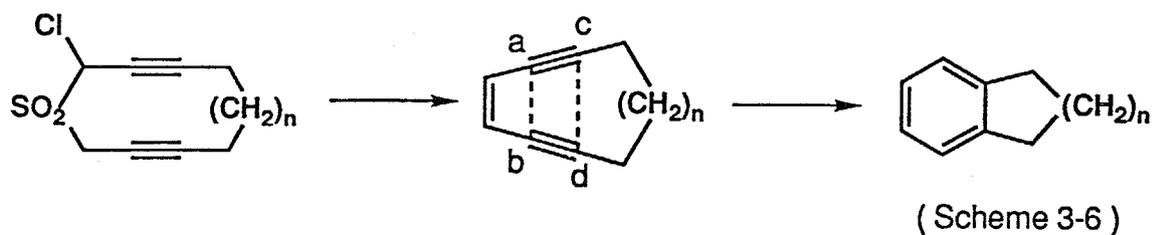
東北大学の平間らは安定なクロモフォアの合成を目的とし、アルキニルスタナンと臭化ビニルとの分子内カップリング反応で10員環を有するビシクロ[8.3.0]骨格の合成に成功し、さらにこの合成物を用いた天然物類似の渡環反応について好気・嫌気条件で比較検討している<sup>61)</sup> (Scheme 3-4)。

さらにWenderらは1990年CrCl<sub>2</sub>を用いた臭化アリルとアルデヒドとのカップリング反応で効率よく9員環骨格を合成することに成功している<sup>62)</sup>。これはクロム原子がキレートすることにより13員環の遷移状態をとって反応が進行するためと報告されている (Scheme 3-5)。



彼らは渡環的[2,3]-Wittig転位反応での構築も試みているが、低収率で単離が困難であると述べている。また、Krebsらも同様に[2,3]-Wittig転位反応による9員環構築を試みているが失敗に終わっている<sup>63)</sup>。さらに相模中央研究所の中谷、寺島らは光学活性なクロモフォアの合成研究を報告しているが、ビシクロ環の構築には至っていない<sup>64)</sup>。

これに対しESP-CALの合成研究およびそれらを用いたBergman反応によるラジカル生成、DNA切断試験等の報告が、1988年から次々と報告されている<sup>65)</sup>。特にNicolaouらは10員環以上の種々の環状化合物内のBergman反応を検討し、そのアセチレン間の距離と反応性に密接な関連があることを見出し、そのMM2計算から得られる距離がab 2.60 Å, cd 3.25 Å以下ならば室温でも反応が起こると報告している<sup>65c)</sup>。(Scheme 3-6)

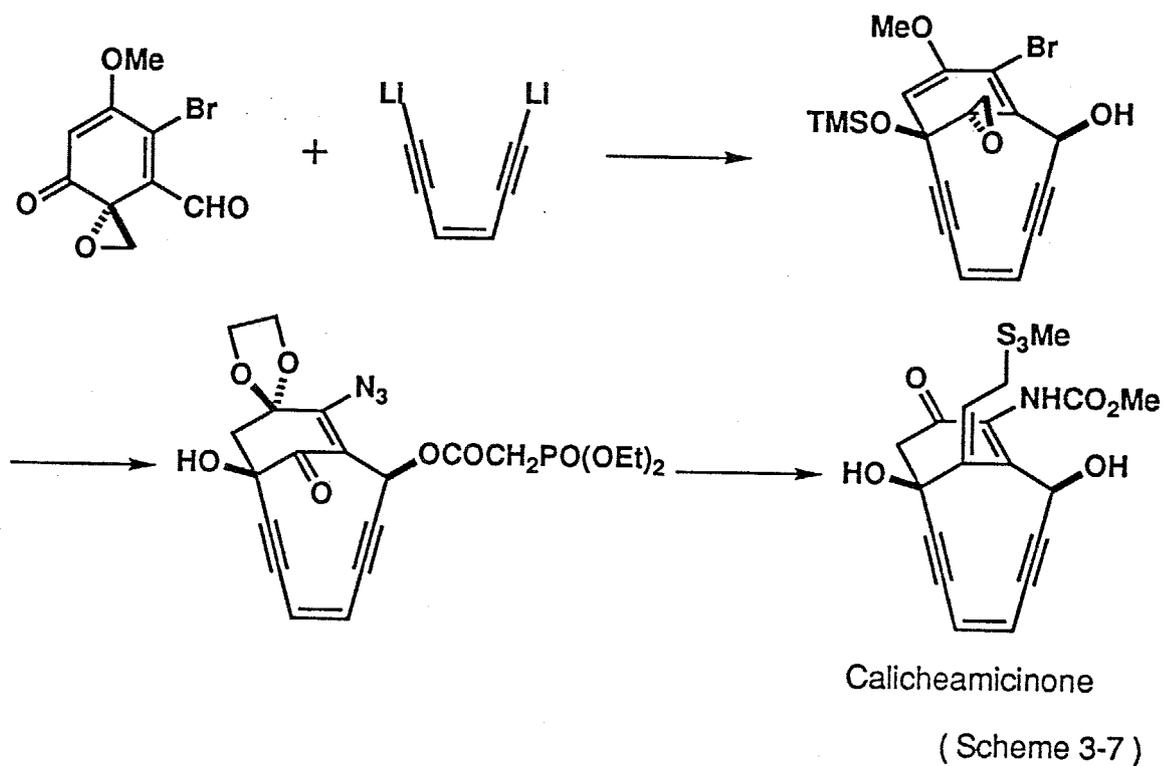


( Table 3-1 )

compound	Ring size	ab (Å)	cd (Å)	Stability
<b>6*</b>	10	2.55	3.16	spontaneous cyclization
n=2	10	2.60	3.25	cyclization at 25 °C
<b>5*</b>	10	2.65	3.35	stable at 25 °C
n=3	11	2.72	3.61	stable at 25 °C

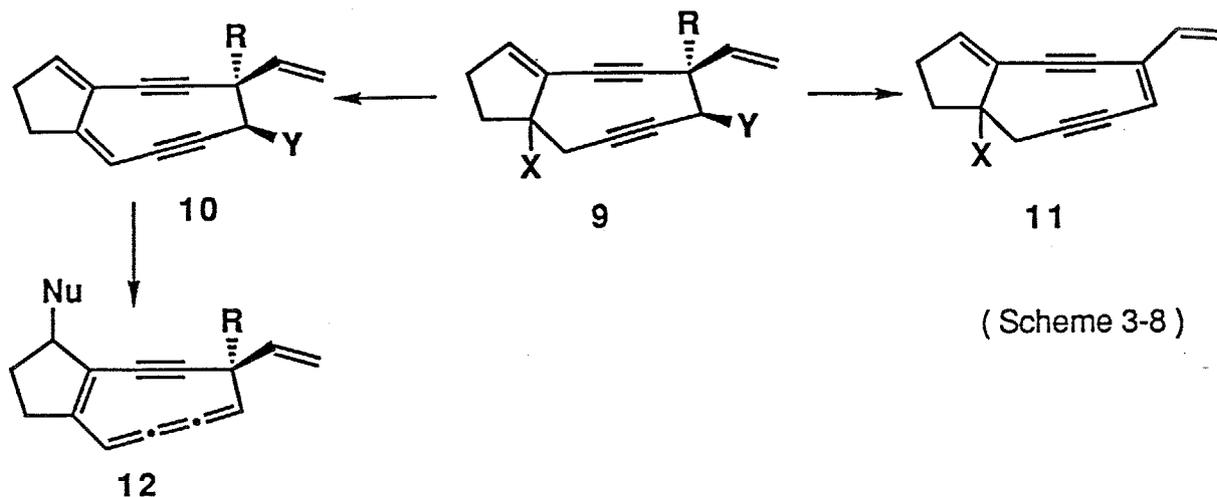
\* The compound was shown in Scheme 3-2.

またDanishefskyらは、はじめてCALのアグリコン部分である Calicheamicinone の全合成に成功している<sup>65f)</sup>。( Scheme3-7)

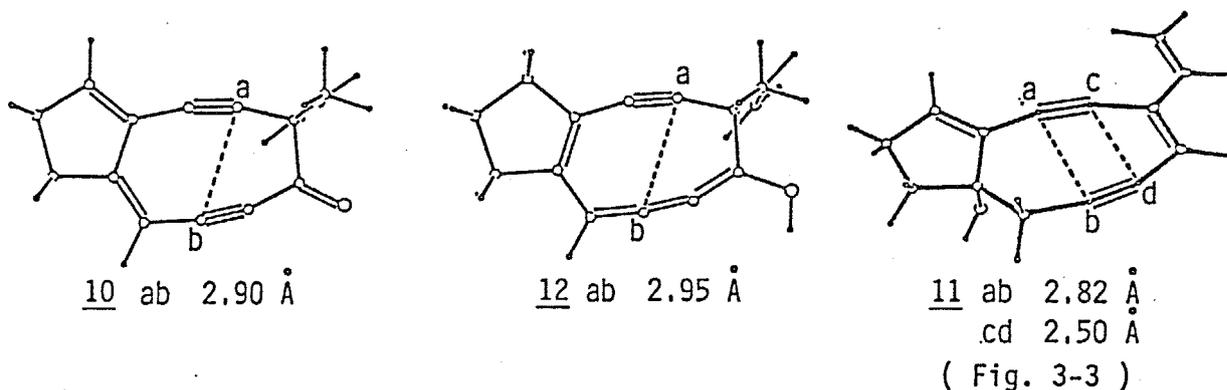


### 3-2 理論計算に基づく合成計画

NCS-chrの骨格を有し、ESP-CALタイプのBergman反応によるラジカル発生が調べられる重要中間体9の合成を計画した (Scheme 3-8)。

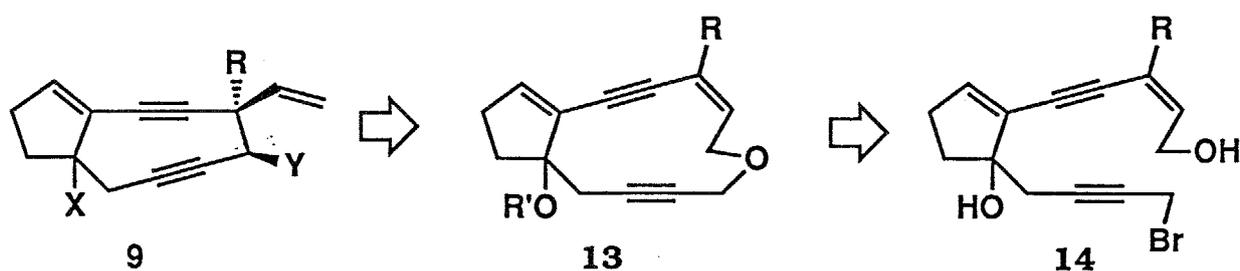


化合物9はXを脱離すればNCS-chrのモデル10が、Yを脱離すればESP-CALのモデル11へ導けると考えた。10は脱離基Yを有しており、天然型のピラジカル生成が期待できる初めてのモデルである。またBergman反応は10員環以上の報告例しかなく、11は9員環内のBergman反応が調べられる初めての例であり、その反応性が興味の対象であった。そこで各アセチレン間の反応点の距離を計算した。11 (X=OH)はMM2計算から、ab 2.82 Å, cd 2.50 Åが得られた。10 (R=Me, Y=O) および求核剤が付加してできる12 (R=Me, Nu=H)の計算は、MM2ではパラメーターがないので広島大学の深沢教授にMNDO<sup>66)</sup>で行っていただき、それぞれab 2.90, 2.95 Åを得た (Fig. 3-3)。先に述べたNicolaouらの仮定<sup>65c)</sup>から考えると、目的の渡環反応は室温で容易に起こると予想される。



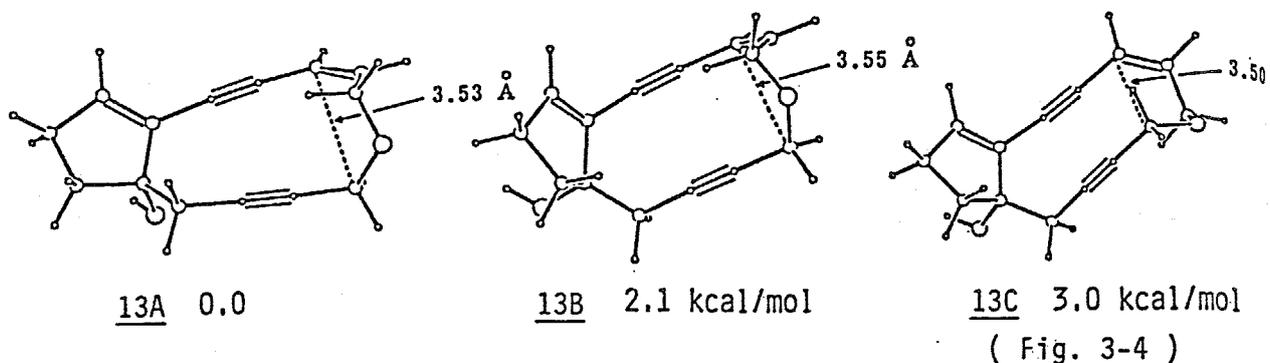
しかし、9員環内に2つのアルキンを有する9の構造は、環に大きな歪みを有するため、この骨格をいかに構築するかが第一の問題である。そこで、この9員環骨格を鎖状分子から直接つくることを避け、まずいったん歪みの小さい12員環化合物を合成し、その後エントロピー的に有利な状態で環縮小反応を行い、構築することにした。

すなわち9は、12員環アリルエーテル13の分子内[2,3]-Wittig転位反応により構築することにした。[2,3]-Wittig転位反応は低温下で行え、不可逆であることが知られている<sup>67)</sup>。また大員環内での渡環反応は、すでに反応点が接近し、 $\pi$ 軌道も環の内側を向いていることからエントロピー的に有利である。したがって、高歪みで不安定と予想される9員環化合物9も構築できると考えた。また転位と同時に脱離基として必要な水酸基Yと、環状炭酸エステル(D) (Fig.3-2)に変換可能なビニル基を一挙に導入することができ、不安定と考えられる9員環化合物での骨格変換を最小限にすることができる点でも非常に有効であると考えた。12員環アリルエーテル13は14の分子内エーテル化により得られると考えた (Scheme 3-9)。



(Scheme 3-9)

まず[2,3]-Wittig転位反応が進行しやすいかどうかを予想するために13 ( $R=R'=H$ )の立体配座解析をMM2計算を用いて行った。MacroModelのMULTICを用いてtorsional angleを15度刻み、closure distanceを1.0-3.0 Åの条件で初期入力座標を発生させMM2で構造最適化を行って、次に示す3つの配座異性体13A, 13B, 13Cを得た。(Fig. 3-4)



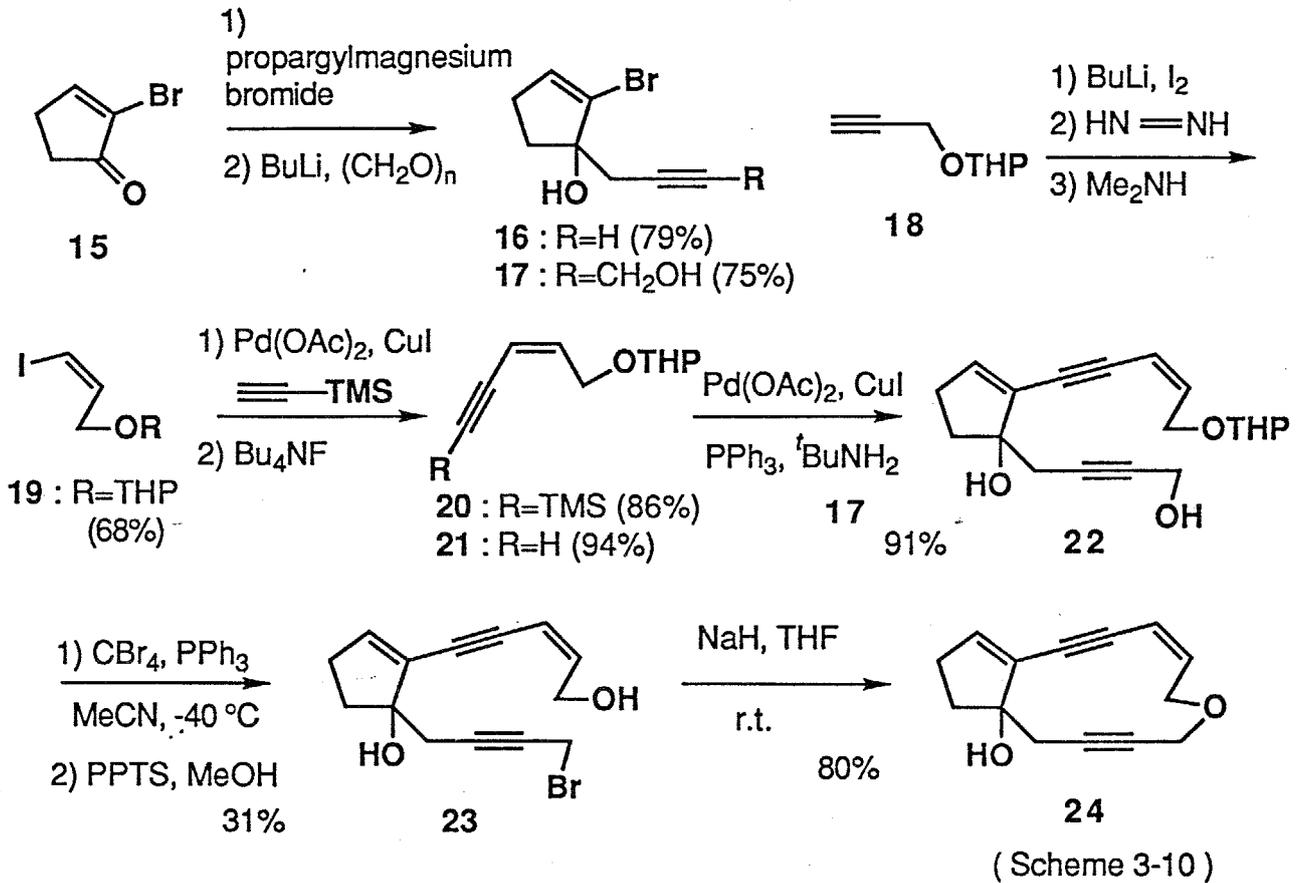
いずれの配座異性体も基底状態で反応点は約3.5 Åと非常に接近しており、軌道の重なりもよく13の[2,3]-Wittig転位反応が進行しやすいことが予想された<sup>22a)</sup>。さらに生成物のビニル基と水酸基の立体化学は、いずれの配座異性体からもシス配置だけが得られると予測された。9から11に導くためには9の水酸基Yを脱離する必要がある。この際、ビニル基と水酸基がシス従って脱離する水酸基とβ位の水素がトランスの立体化学であることが重要である。逆にNCS-chr型の10に導く際、Yのβ-脱離反応が副反応として考えられ、β-脱離を抑える必要性が示唆された。

### 3-3 NCS-chrモデルおよびESP-CALモデル化合物の合成と 合成モデルを用いた天然物類似の渡環反応

#### 3-3-1 大員環内[2,3]-Wittig転位反応を用いたビスクロ[7.3.0]骨格の構築

2-プロモ-2-シクロペンテノン (15)<sup>68)</sup>に臭化プロパルギルマグネシウム<sup>69)</sup>を1,2-付加し、生成したアルキン16を1.9当量のBuLiで処理した後、パラホルムアルデヒドを付加しジオール17を収率75%で得た。同時に原料16を23%回収した。一方、プロパルギルアルコールをDHPで保護して得られる18を既知法で(Z)-臭化ビニル19へ導いた<sup>70)</sup>。19とトリメチルシリルアセチレンとをPd,Cu触媒<sup>71)</sup>を用いてカップリングし(86%)、生成する20のTMS基をBu<sub>4</sub>NFを用いて除去してエンイン21を得た(94%)。続いて臭化ビニル17とエンイン21をPd,Cu触媒を用いてカップリングし、エンジン22とした(91%)。22の1級の水酸基だけをMeCN溶媒中、CBr<sub>4</sub>, PPh<sub>3</sub>, Py条件下-40~

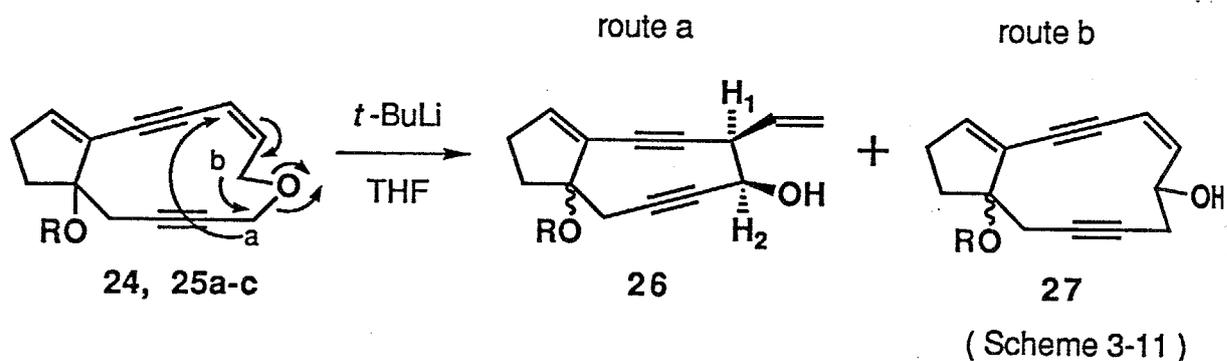
10 °Cでブロム化し、PPTS, MeOHでTHPを除去してプロモヒドリン 23 を収率31%で得た。このブロム化は、0 °Cで行うとTHPが脱保護されるためか低収率に終わった。23の分子内エーテル化は、次のように行った。23 (57 mg, 0.19 mmol)のdry THF(20 mL)溶液を、NaH(90 mg, 3.7 mmol), EtOH(0.02 mL), THF(20 mL)中へ20 °Cで5時間かけて滴下し、収率80%で12員環エーテル 24 を得た (Scheme 3-10)。



24を直接塩基で処理したが、TLC上で棒状になってしまった。TLC上で化合物が壊れることも考えられたので、そのままMeI, AcCl等での捕捉も試みたが、望む[2,3]-Wittig転位生成物は得られなかった。そこで、3級水酸基を保護して検討することにした。イソプロペニルメチルエーテル, 塩化テトラブチルジメチルシリル (TBDMS-Cl)での保護は立体障害のためか進行しなかったが、塩化メトキシメチル (MOM-Cl), TBDMS(OTf), TMS(OTf)を用いたところ保護体 25 を得ることができた。

25の[2,3]-Wittig転位反応を塩基としてt-BuLiを1.1~1.5当量使い、THF

溶媒中-100または-78 °Cで行ったところ、2.5は10分内に消失し、望むaの位置にカルボアニオンが発生して[2,3]転位が進行したと考えられる2.6を主生成物として得た。この際、bにカルボアニオンが発生し、[1,2]転位反応が進行して得られたと考えられる化合物2.7も確認した。これらの生成比はHPLCにより決定した (Scheme 3-11, Table 3-2)。-78 °Cより-100 °Cの方が選択性がよいことから速度論的なa,bのプロトン引き抜きが、生成物の比を支配していると考えられる。そこで、よりaを選択的に引き抜ける塩基を求め、LiN(TMS)<sub>2</sub>等の塩基を用いて検討したが現在までのところ成功していない。前述したように反応点の距離が接近していることやπ軌道の重なりが良いことが、この反応に有利に作用し、歪の大きい9員環骨格を構築できたと考えられる。



( Table 3-2 )

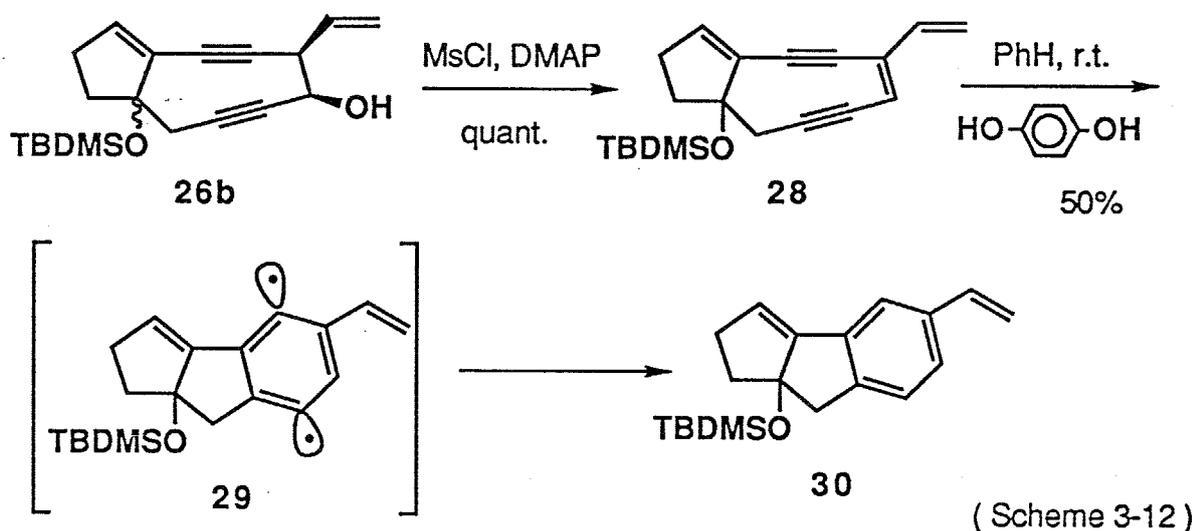
compound	temp	yield	[2,3]-rearrangement	:	[1,2]-
<b>24</b> : R=H	-78 °C	—			
<b>25a</b> : R=MOM	-78 °C	84%	( 26a : 26a' = 4:1 )	1.7	1 27a
	-100 °C	93%	( 26a : 26a' = 4:1 )	2.3	1 27a
<b>25b</b> : R=TBDMS	-100 °C	80%	26b (>10 : 1)	4.7	1 27b
<b>25c</b> : R=TMS	-100 °C	80%	26c (>10 : 1)	3.0	<1 27c

生成物 2.6 a はHPLC分析から2種のジアステレオマーが得られたが、いずれのジアステレオマーも H<sub>1</sub>, H<sub>2</sub> において6%のNOEが観測されたのはじめの予測通り、ビニル基と水酸基はシス配置であることを確認した。したがって、これらのジアステレオマーは3級水酸基とのものであることがわかったが、その相対配置は

未決定である。先の立体配座解析で得られた (Fig. 3-4) 13 A, 13 Bからは2級と3級の水酸基はシス、13 Cからはトランスがそれぞれ異なる5員環遷移状態構造を通して得られると考えられる。生成物がジアステレオマー混合物になるという実験結果は[2,3]-Wittig転位反応が、少なくとも2つの遷移状態構造を通して進行したことを示している。この立体選択性を予測するためには異なるそれぞれの5員環遷移状態を求めなければならないので、分子軌道計算を行なってゆく必要がある。

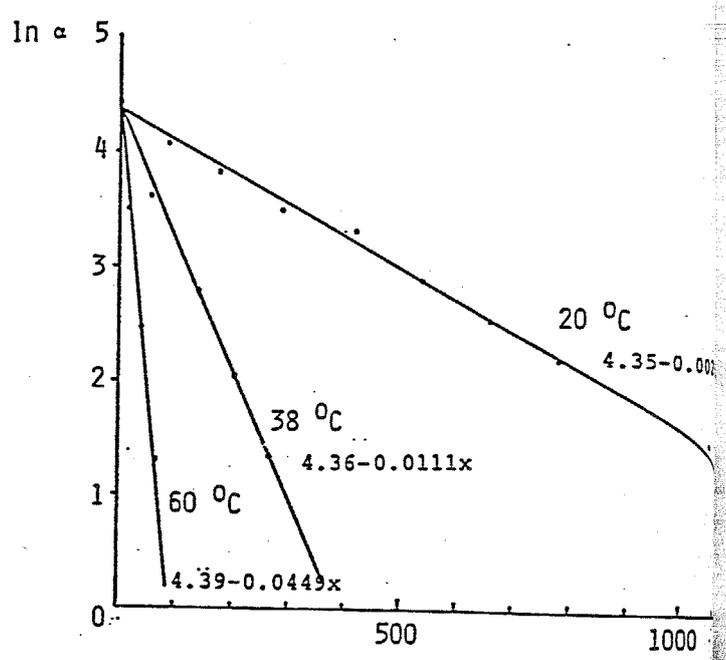
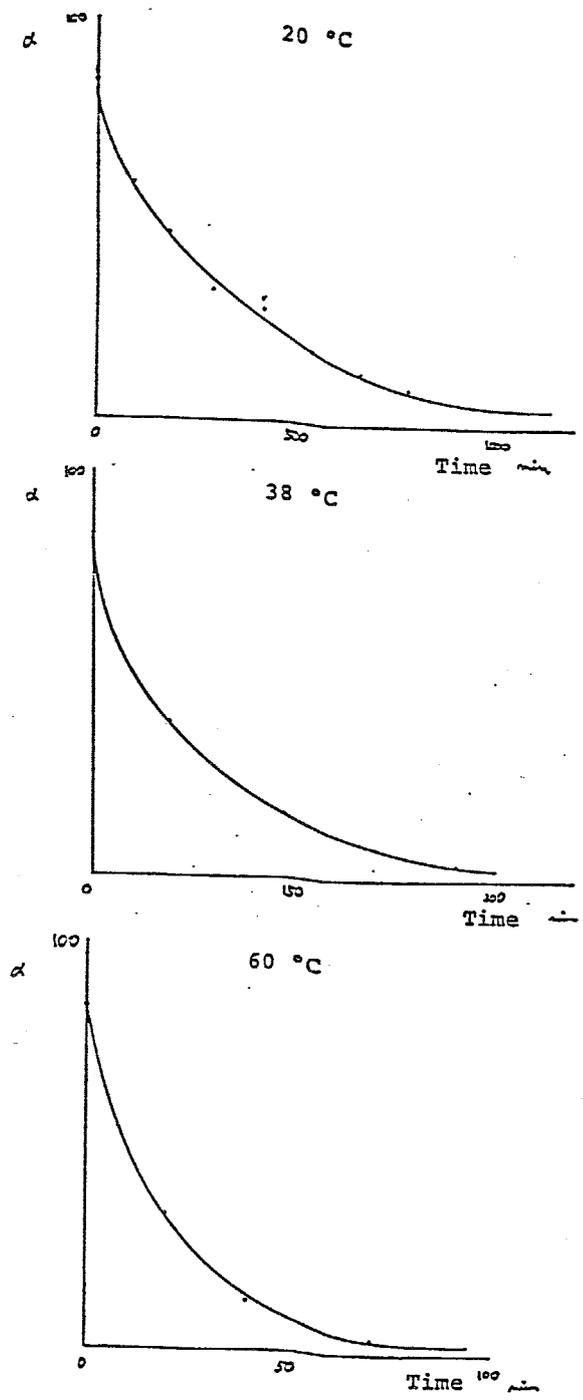
### 3-3-2 9員環内Bergman反応

まず、最も選択性の良かった 26 b を用いて2級水酸基の脱水を試みた。すなわちWenderらの報告<sup>60)</sup>と同様に水酸基のメシル化、同時にβ脱離が起こり 28 を得ることができた。28 は濃縮すると黒い粉になって壊れてしまったが、ベンゼン溶液中ヒドロキノン存在下室温でBergman反応が進行し、収率50%で 30 を与えることが確認できた (Scheme 3-12)。すなわち9員環の合成モデルから天然のESP-CAL型と同様に渡環反応が室温で進行し、ピラジカル 29 を生成していると推測できる。

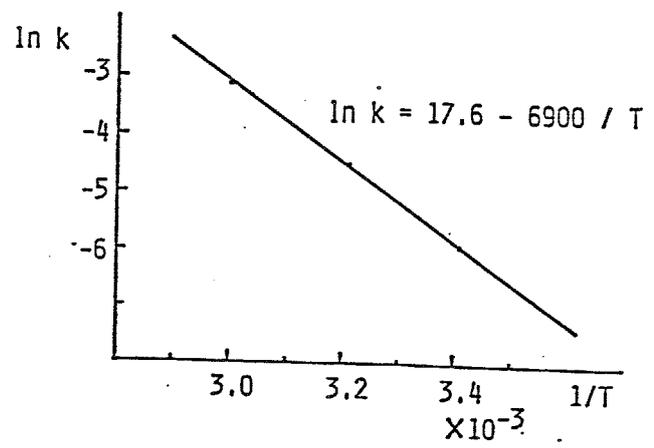


さらに天然の10員環と9員環でのBergman反応の反応性を比較する目的で反応速度を測定した。20, 38, 60 °Cでピフェニルに対する 28 の減少をHPLCで分析し、この反応が 28 の濃度に対して一次反応であることがわかった。各温度での反応速度定数  $k$  ( $\text{min}^{-1}$ ) と温度  $T$  (K) の関係を Arrheniusプロットし、そ

の傾きから 14 kcal/molの活性化エネルギーを算出した (Fig. 3-5)。  
 Nicolaouら<sup>65c)</sup>の報告している3-シクロデセン-1, 5-ジイン (Scheme 3-6, n=2) のBergman反応の活性化エネルギーが23.8 kcal/molであることと比較すると約10kcal/mol小さく、反応点の距離の減少が大きく反応性を増していることがわかった。



T (K)	k (min <sup>-1</sup> )
293	0.00266
311	0.0111
333	0.0449



Kinetic Data for 28 to 29  
 hexane solution (0.001 M) of enediynes 28  
 $\alpha = [28] / [\text{biphenyl}]$

Arrhenius :  $k = A \exp(-E_a/RT)$   
 $E_a = 14 \text{ kcal/mol}$

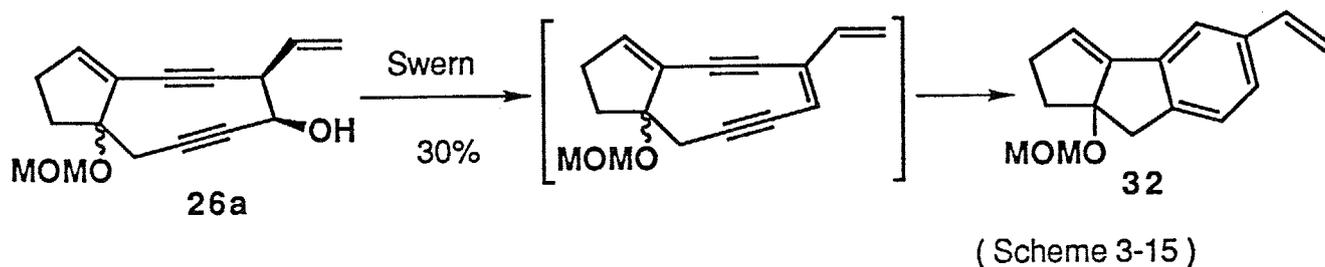
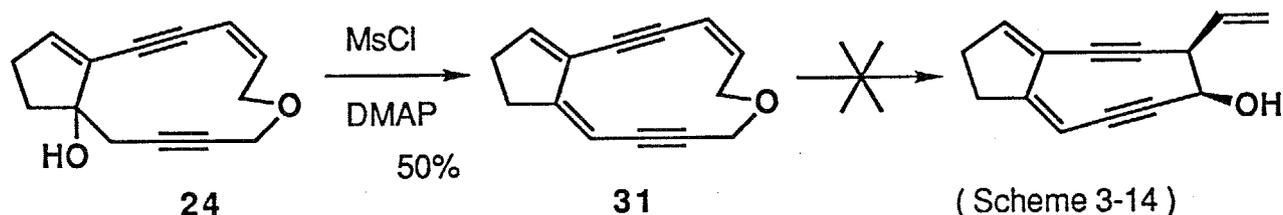
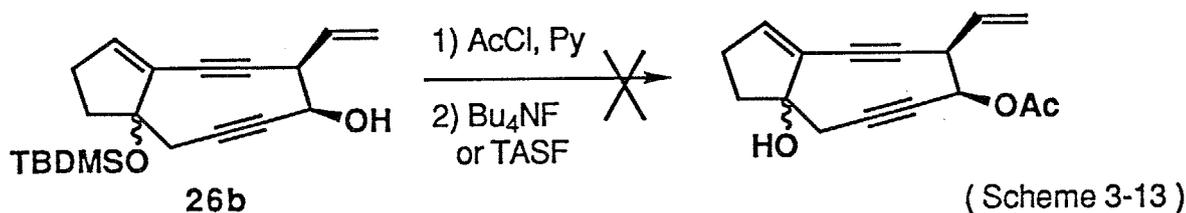
(Fig. 3-5)

### 3-3-3 NCS-chrモデルの合成とNCS類似の渡環反応

26bの2級水酸基を保護したのち、 $\text{Bu}_4\text{NF}$ あるいはTASFを用いてTBDMS基の除去を試みたが、濃縮に極めて不安定なアセチル基のない化合物だけが得られ、望むシリル基の脱保護はできなかった (Scheme 3-13)。

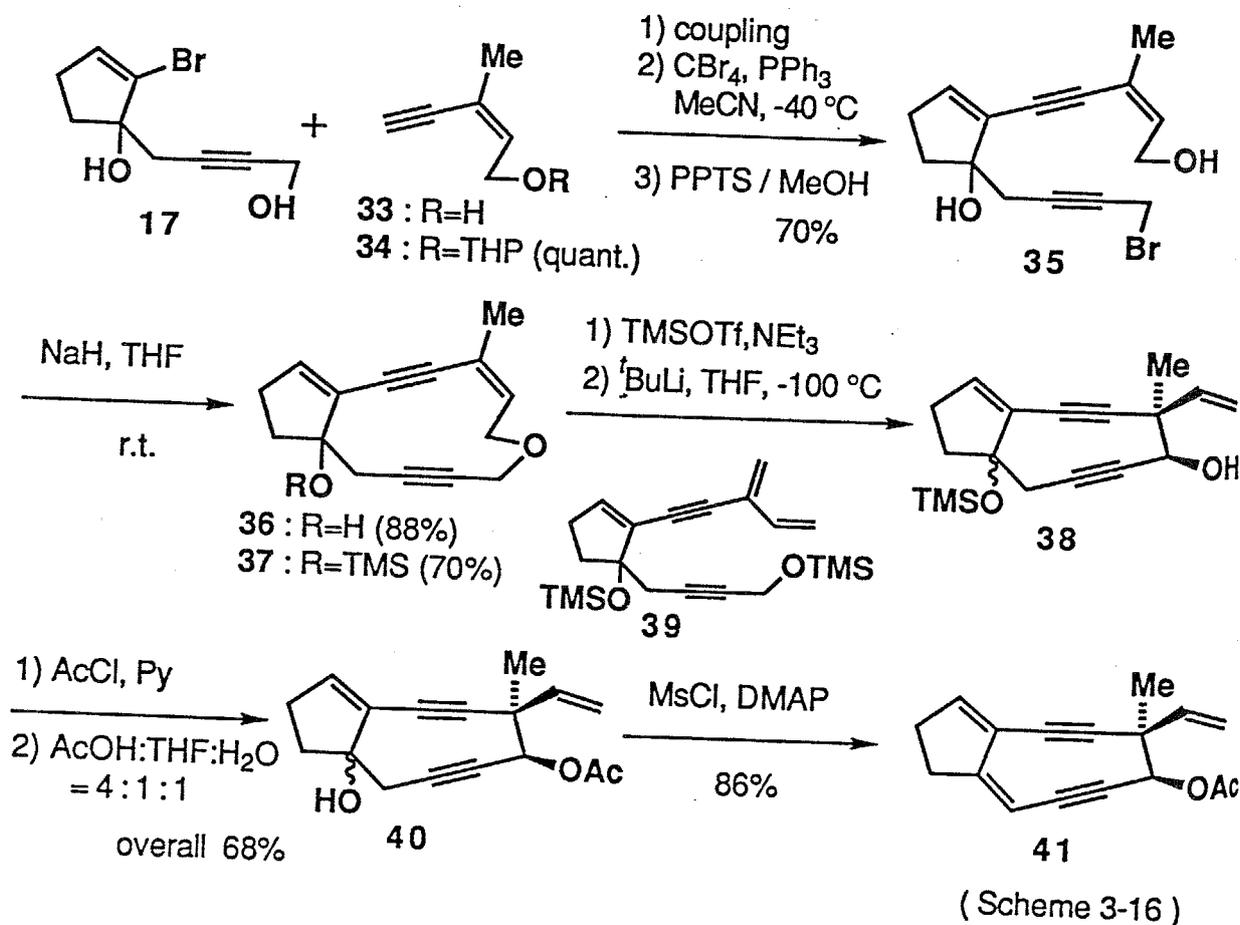
また12員環エーテル24の3級水酸基をあらかじめ脱離した31で塩基として $t\text{-BuLi}$ ,  $\text{LiN}(\text{TMS})_2$ を用いて[2,3]-Wittig転位反応を検討したが、求める転位生成物を得ることはできなかった (Scheme 3-14)。

次に26aの2級水酸基の酸化、続くMOM基の脱離を検討した。2級水酸基のSwern酸化を試みたところ、 $\beta$ 脱離反応が進行し、さらにBergman反応を経て得られたと考えられる化合物32を得た (Scheme 3-15)。

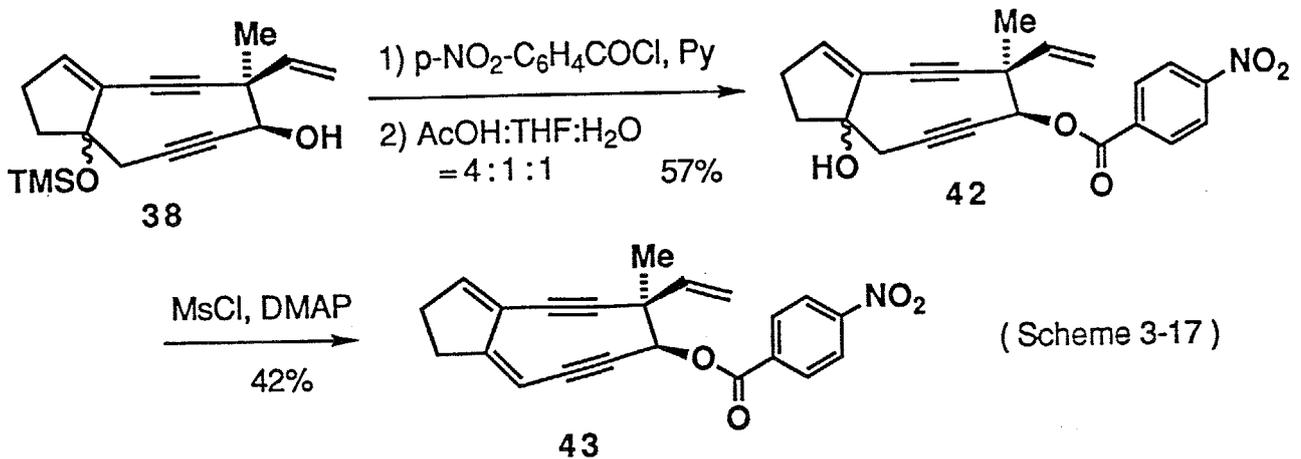


このことは、たとえば10 (Scheme 3-8,  $\text{R}=\text{H}$ ) が合成できても、そのラジカル発生を調べる際、 $\beta$ 脱離反応が問題になることを示している。この問題を避けるため、 $\beta$ -水素をメチル基に変えてNCS-chrモデル化合物として合成することにした (Scheme 3-8, 9  $\text{R}=\text{Me}$ )。また3級水酸基の保護基は、弱い酸で脱保護できるTMS基を用いることとした。

すなわち市販の3-メチル-2-ペンチン-4-イン-1-オール (33) をDHPで保護して得られる34を用いて、同様に12員環エーテル36を得、TMS(OTf)を用い3級水酸基を保護した後、同じく37をt-BuLiで処理したところ、先と同様の収率(83%)、選択性(>80%)で求める38を得た。ただし、30 °CでTMS基による保護を行うと、エーテル環が開いて生成したジエン39が副生した。続いて38の2級水酸基をアセチル基で保護した後、酢酸: THF: 水=4: 1: 1で室温下処理しTMS基を除去した(68%)。さらに得られた40の3級水酸基をメシル化を経て脱離し、NCS-chrモデル化合物41を収率86%で得ることに成功した(Scheme 3-16)。41は非常に不安定で重クロロホルム中では分解したが、-30 °Cで濃縮し、重ベンゼン溶液で<sup>1</sup>Hおよび<sup>13</sup>C-NMRを測定することによってその構造を確認することができた。

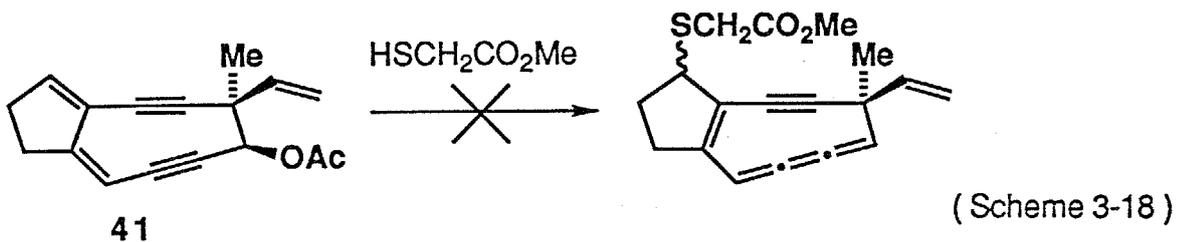


NCS-chrはX線により分解するため、その3次元構造は明らかではない。そこで、合成化合物のX線構造解析を行ってその3次元構造を明らかにしようと考え、合成化合物の結晶化を試みた。38の2級水酸基を塩化パラニトロベンゾイルで保護した後、希酸でTMS基を除去し42へ導いた(57%)。さらに3級水酸基を脱離させ43へ導くことに成功した(42%)。しかし、現在までのところX線結晶解析を行える単結晶を得るには至っていない(Scheme 3-17)。

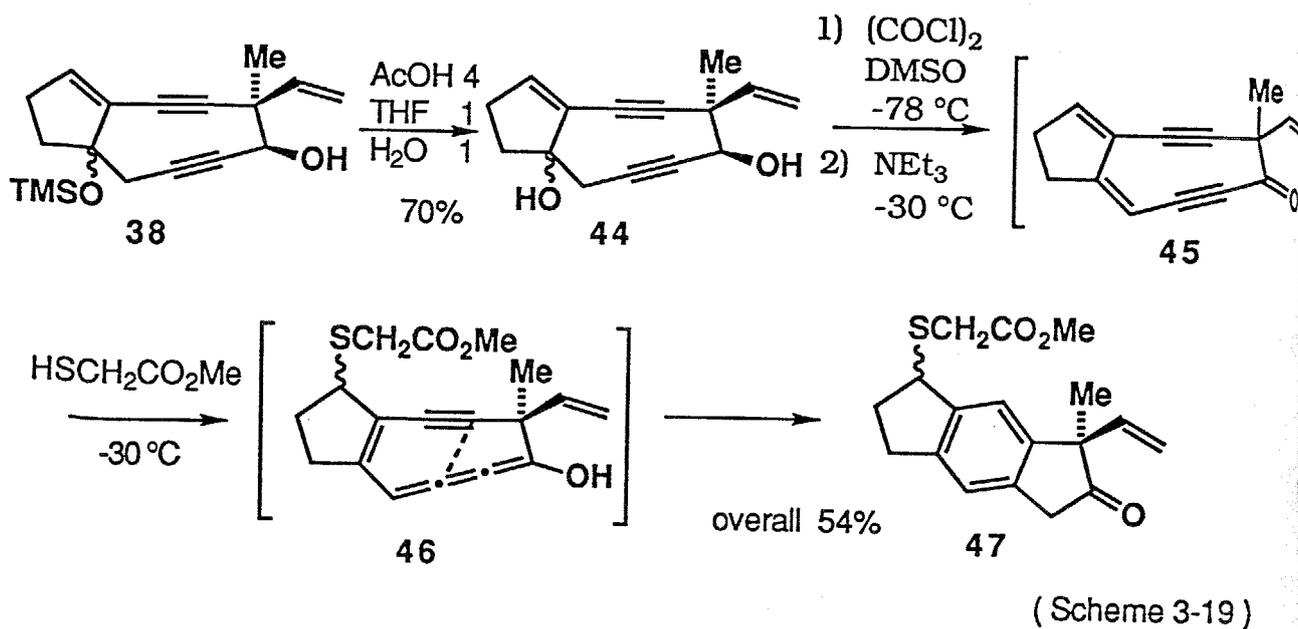


次に天然物と類似の渡環反応が起こるかどうかを検討した。

41をチオグリコール酸メチルで処理したが、望む付加・渡環反応は進行せず41が分解した(Scheme 3-18)。



そこで 41 の求核付加を受けやすくするために共役ケトンへ導いた<sup>61)</sup>。すなわち [2,3]-Wittig転位生成物 38 を酢酸: THF: 水 = 4: 1: 1 で室温下処理し TMS 基を除去した (70%)。さらに得られたジオール 44 を -78 °C で Swern 酸化を行い同条件下で 3 級水酸基が脱離して得られると考えられる共役ケトン 45 に、-30 °C で *in situ* にチオグリコール酸メチルを加えたところ化合物 47 を 1: 1 のジアステレオマー混合物で得た (54%) (Scheme 3-19)。これは天然物と同様に 45 の 5 員環部分にチオグリコール酸メチルが付加し、9 員環にクムレンが生成し、46 の渡環反応を経て 47 が得られたと推測される。

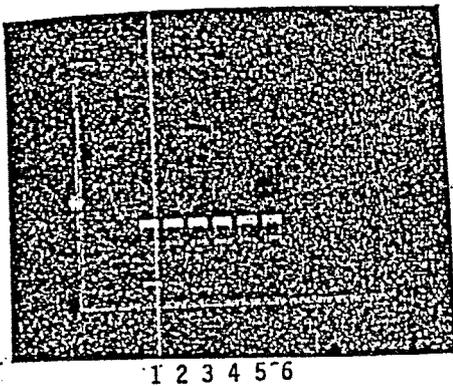


### 3-4 合成モデルを用いた活性試験

#### 3-4-1 DNA切断活性試験<sup>65k, 1)</sup>

φX174 Form I DNA (5 nM) と 28 (2.6, 0.26, 0.026 mM) を pH 8.05 のトリス (ヒドロキシ) アミノメタン-酢酸の緩衝溶液中, 37 °C で 18 時間培養し、アガロースゲルを用いて電気泳動を行った (Fig. 3-6)。また φX174 Form I DNA (6 nM) と 41 (0.4, 0.04 mM) を 2-メルカプトエタノール (10 mM) 存在下、pH 7.5 のトリス (ヒドロキシ) アミノメタン-塩酸の緩衝溶液中, 37 °C で 1 または 20 時間培養し、アガロースゲルを用いて電気泳動を行った (Fig. 3-7)。Fig. 3-7 の lane 12 に見られるように、NCS と 2-メルカプトエタノールを加えた系では Form III への DNA の切断を確認できるが、合成物 28 と 41 ではいずれの場合も DNA の切断活性は、まったく見られない。これは、28 と 41 の水溶性に難があることが最も大きな原因ではないかと考えている。

agarose gel electrophoresis

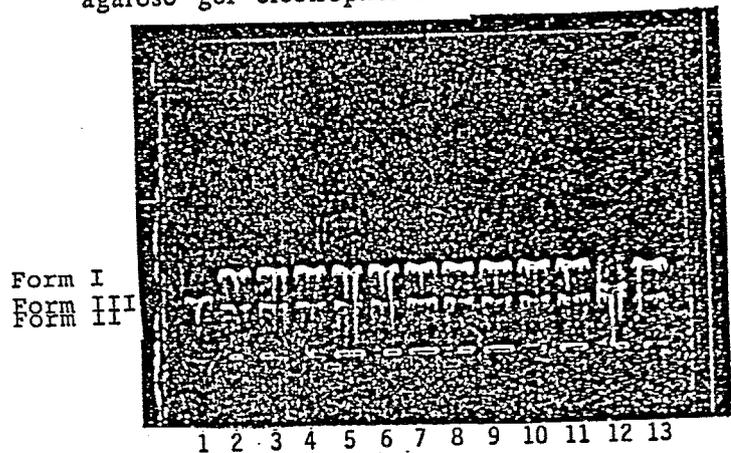


φX174 Form I DNA (5 nM) was incubated with compound 28 in Tris-acetate buffer at 37 °C for 18 h.

- lane 1: DNA + (2.6 mM)
- lane 2: DNA + (0.26 mM)
- lane 3: DNA + (0.26 mM)
- lane 4: DNA + (0.026 mM)
- lane 5: DNA + (0.026 mM)
- lane 6: DNA alone

(Fig. 3-6)

agarose gel electrophoresis



φX174 Form I DNA (6 nM) was incubated with compound 41 in Tris-HCl buffer (pH. 7.5) at 37 °C for 1 or 20 h.

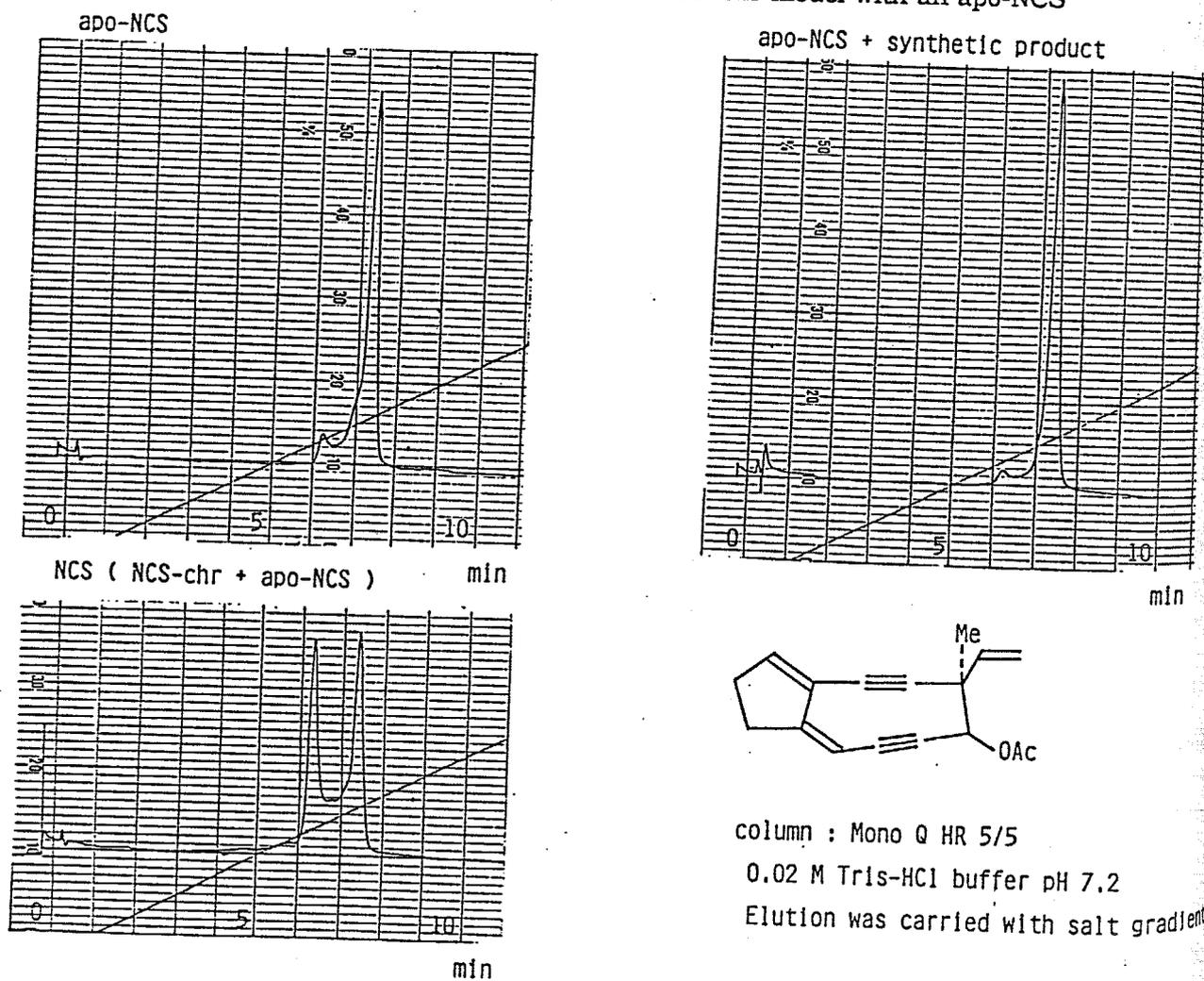
- lane 1: Form III DNA
- lane 2: DNA alone, 20 h
- lane 3: DNA + (0.04 mM), 20 h
- lane 4: DNA + (0.04 mM) + 2-mercaptoethanol, 20 h
- lane 5: DNA + (0.04 mM), 1 h
- lane 6: DNA + (0.04 mM) + 2-mercaptoethanol, 1 h
- lane 7: DNA + (0.4 mM), 20 h
- lane 8: DNA + (0.4 mM) + 2-mercaptoethanol, 20 h
- lane 9: DNA + (0.4 mM), 1 h
- lane 10: DNA + (0.4 mM) + 2-mercaptoethanol, 1 h
- lane 11: DNA + NCS (1 μM), 1 h
- lane 12: DNA + NCS (1 μM) + 2-mercaptoethanol, 1 h
- lane 13: DNA alone, 1 h

(Fig. 3-7)

### 3-4-2 NCSアポタンパクとの構成試験

NCS-chrがアポタンパクと再構成すると、アポタンパクのHPLCの保持時間が変化することが知られているので<sup>72)</sup>、合成品がアポタンパクと構成できればこの変化が期待できると考えた。41 (0.1  $\mu\text{mol}$ , 0.03 mL, EtOH) をアポタンパク (0.01  $\mu\text{mol}$ ) とpH 7.2のトリス(ヒドロキシ)アミノメタン-塩酸の緩衝溶液中、37  $^{\circ}\text{C}$ で1.5時間培養し、Mono Q カラムを用いてHPLCで分析したが、期待したアポタンパクの保持時間の変化は見られず、合成モデル41とアポタンパクは構成しないことがわかった (Fig. 3-8)。

The binding-test of the synthetic NCS-chr model with an apo-NCS



(Fig. 3-8)

### 3-5 まとめ

本研究ではNCS-chrのコア部位Cの骨格合成を確立すると共に、合成モデルを用いて天然物と類似のラジカル発生と考えられる渡環反応を確認することができた。しかし、Cの部位だけではアボタンパクとの構成、DNAの切断が行われなことがわかった。次の段階としてA, B, D (Fig. 3-2)を導入した化合物を合成することにより、それぞれの部位の働きを明らかにしていくことができると考えられる。

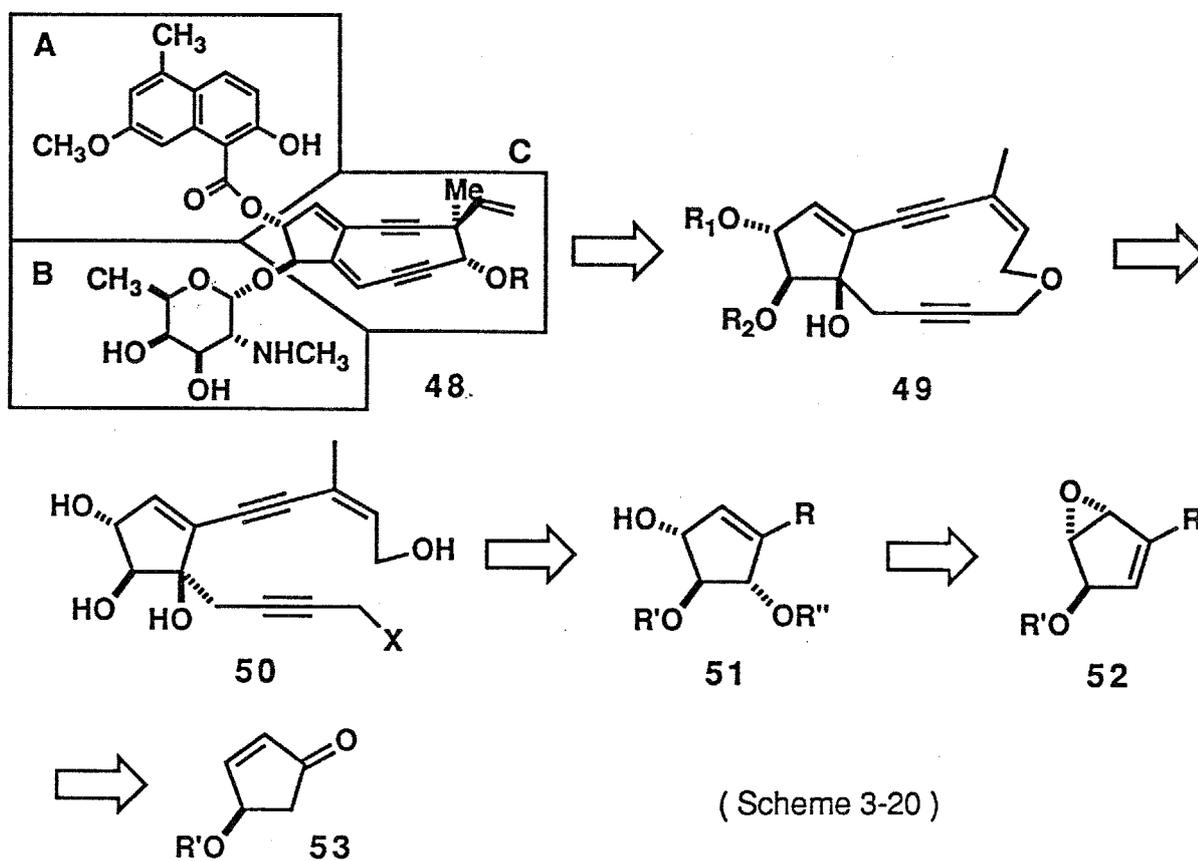
### 3-6 官能基化されたモデル化合物の合成研究

#### 3-6-1 背景

ネオカルチノスタチンに $\beta$ ナフトールやD-ガラクトサミンを作用させると、クロモフォア1がアポタンパクから遊離することが報告されており<sup>72b)</sup>、A、B (Fig. 3-2)の部位が、接合に重要な働きをしていることが示唆される。そこで次にCに対しA、Bの導入を計画した。

#### 3-6-2 合成計画

A、Bの導入には、5員環部位に2つの水酸基が不可欠である。その合成計画をscheme 3-20に示した。

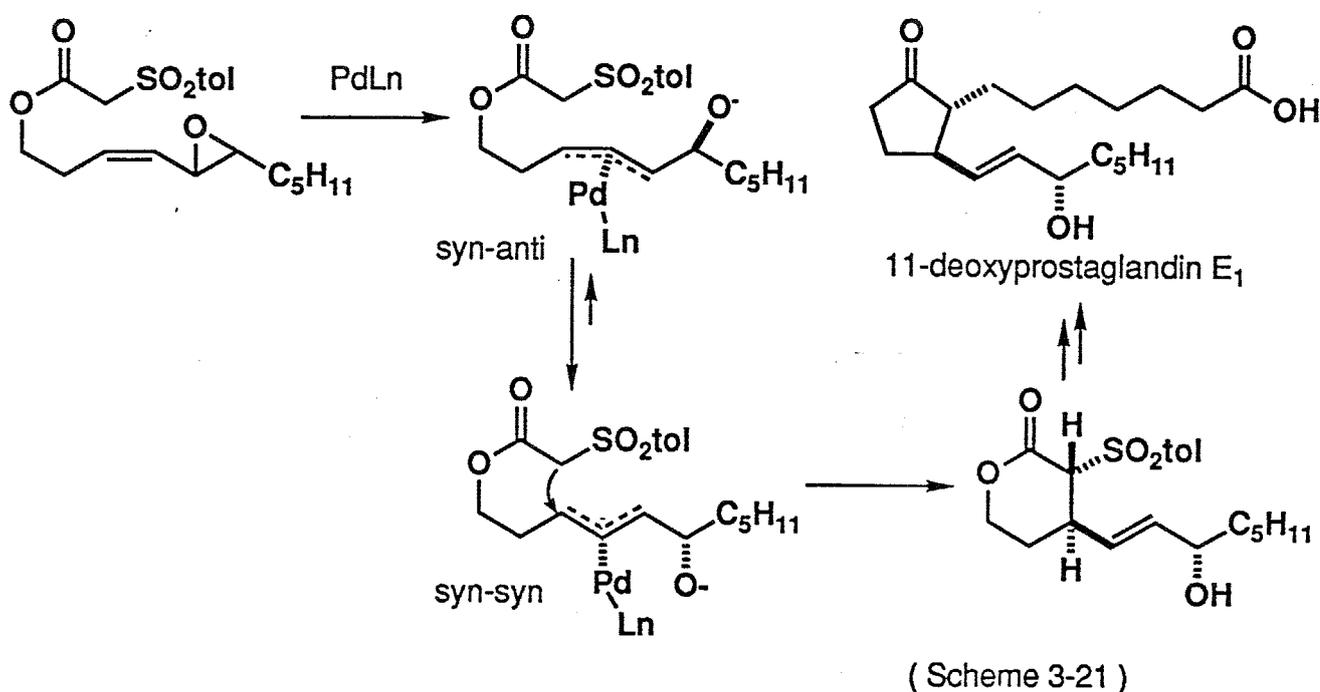


化合物49を合成できれば、水酸基のエステル化および、グルコシル化を経て既に述べた[2,3]-Wittig転位反応を用いて48へ導けると考えられる。49は50の分子内エーテル化により構築し、50の下の側鎖は51のアルコキシ基

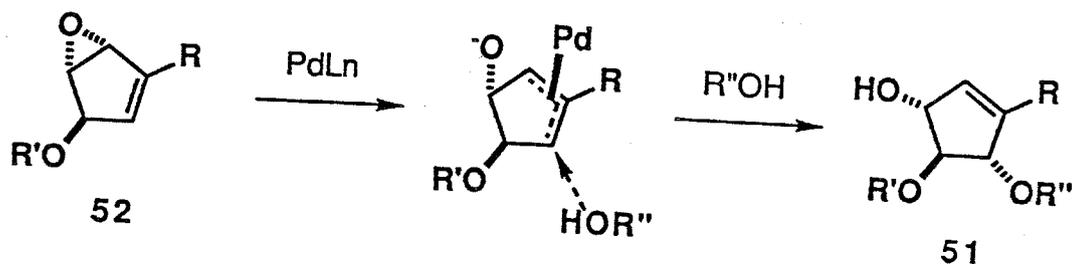
(OR<sup>n</sup>) からケトンへ導き、1,2-付加反応で得る。5.1の2-エン-1,4-ジオール部は、ジエンモノエポキシド 5.2のPd触媒を用いた開環、カルボキシラートの付加反応により構築する。この反応の反応機構については3-6-3で詳しく述べる。エポキシド 5.2はエノン 5.3へアルコキシ基と反対側から立体選択的にエポキシ基を導入後、ケトン部分へ上の側鎖Rを1,2付加し、生成する3級水酸基をβ-脱離して得ることにした。5.3はプロスタグランジン合成の際の重要中間体であり、光学活性体としての導入も可能であるが、今回はdl-体で検討した。

### 3-6-3 Pd触媒を用いる1,3-ジエンモノエポキシドの反応

当研究室では1,3-ジエンモノエポキシドに対しPd触媒存在下、求核試薬が1,4付加することを見出し、この反応を分子内で行って位置及び立体選択的に6員環ラクトンを構築し、11-デオキシプロスタグランジンE<sub>1</sub>を合成することに成功している。この際1,3-ジエンモノエポキシドのPd<sup>0</sup>錯体への酸化的付加反応はエポキシドに対し立体反転で起こり、π-アリルパラジウム錯体を形成した後、シン-アンチ錯体は不安定なのでπ-σ-πの異性化で安定なシン-シン錯体となり、続くアルキル化も立体反転で進行することを報告している (Scheme-3-21)<sup>73)</sup>。



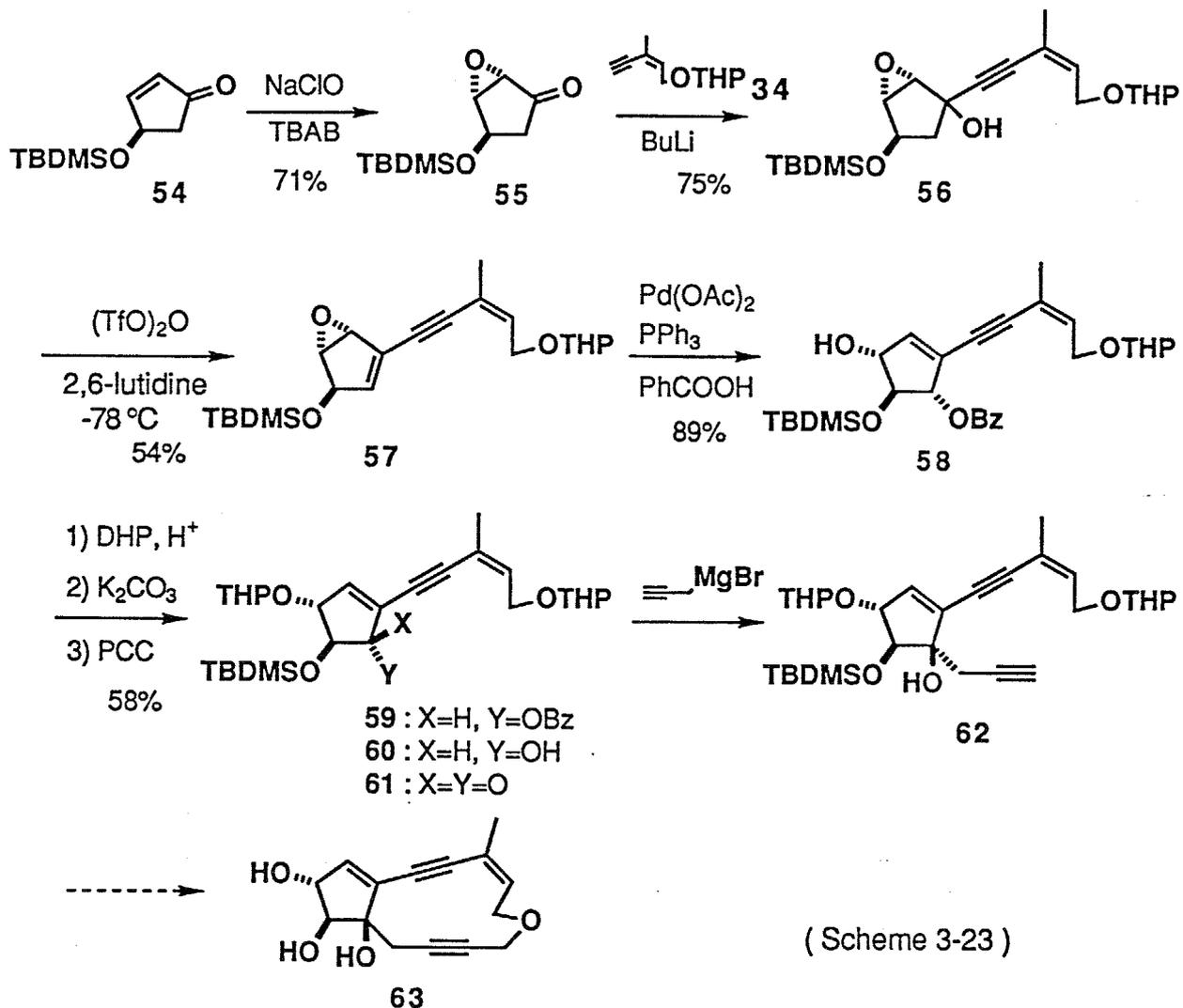
したがって同様にして5員環のジエンモノエポキシド 52 を用いてPd触媒存在下、求核試薬（カルボキシラート）を作用させれば、求める立体化学を有する 51 が得られると考えた（Scheme 3-22）<sup>74)</sup>。



(Scheme 3-22)

### 3-6-4 合成

3-*t*-ブチルジメチルシロキシ-2-シクロペンテノン (54)<sup>75)</sup> に次亜塩素酸ナトリウムと硫酸水素テトラブチルアンモニウムを作用させエポキシド 55 を収率71%で得た。この際、カリウム-*t*-ブチルペルオキシドを用いても検討したが、アルコキシ基のβ-脱離反応が進行するためか、求める 55 は得られなかった。続いて 34 をBuLiでアセチリドに導き、55 へ1,2-付加反応を行ったところ収率75%で 56 を得た。56 の3級水酸基を2,6-ルチジン存在下、無水トリフルオロメタンスルホン酸で脱離させ、ジエンモノエポキシド 57 へ導いた。57 はこの反応の条件下で分解するので、-78 °Cで希釈した無水トリフルオロメタンスルホン酸を-78 °Cで滴下したところ収率54%まで向上した。57 から 58 への変換は次のように行った。Pd(OAc)<sub>2</sub>を20 mol%触媒としPPh<sub>3</sub>を80 mol%存在下、安息香酸を3当量用いたところ、反応は室温で進行し、求める 58 を収率89%で得た。すなわち、この反応によりNCS-chrモデルに必要な5員環部位のトランスの2つの水酸基とオレフィンを構築することができた。さらに生成した水酸基をDHPで保護した後、59 のベンゾイル基をK<sub>2</sub>CO<sub>3</sub>, MeOHで除去し、生成した 60 の水酸基をPCCで酸化しエノン 61 へ 58 から収率58%で導いた。続いて 61 に臭化プロパルギルマグネシウムを1,2-付加し 62 を得た。62 から12員環エーテル 63 への変換は現在検討中である (Scheme 3-23)。



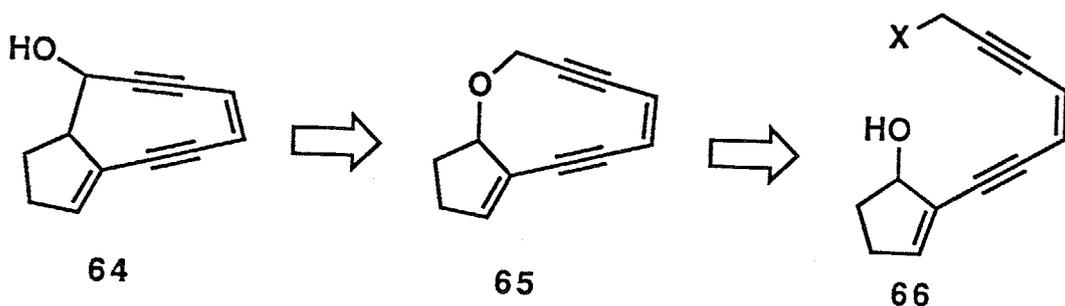
### 3-6-5 結論

Pd触媒を用いたジエンモノエポキシドの開環、安息香酸の付加反応により、NCS-chrモデルとして A, B の導入に不可欠な2つのトランス水酸基を有する5員環部位の合成に成功することができた。今後12員環エーテルを構築した後、5員環部位の2つの2級水酸基を利用して A, B の誘導を行い、アポタンパクとの構成、あるいは[2,3]-Wittig転位反応により9員環部分の構築を検討することが可能であると考えられる。

### 3-7 10員環エーテルから9員環骨格の合成研究

#### 3-7-1 合成計画

先の研究と同時にScheme 3-24に示す9員環骨格の構築法の検討も行った。高歪みの9員環化合物64を10員環化合物65の分子内[1,2]-あるいは[2,3]-Wittig転位反応から得られると考えた。65は[1,2]-転位が進行しても[2,3]-転位反応が進行しても64を与えるため都合が良く、64からは9員環のBergman反応が調べられると考えた。65は66の分子内エーテル化反応により得られると考えた。

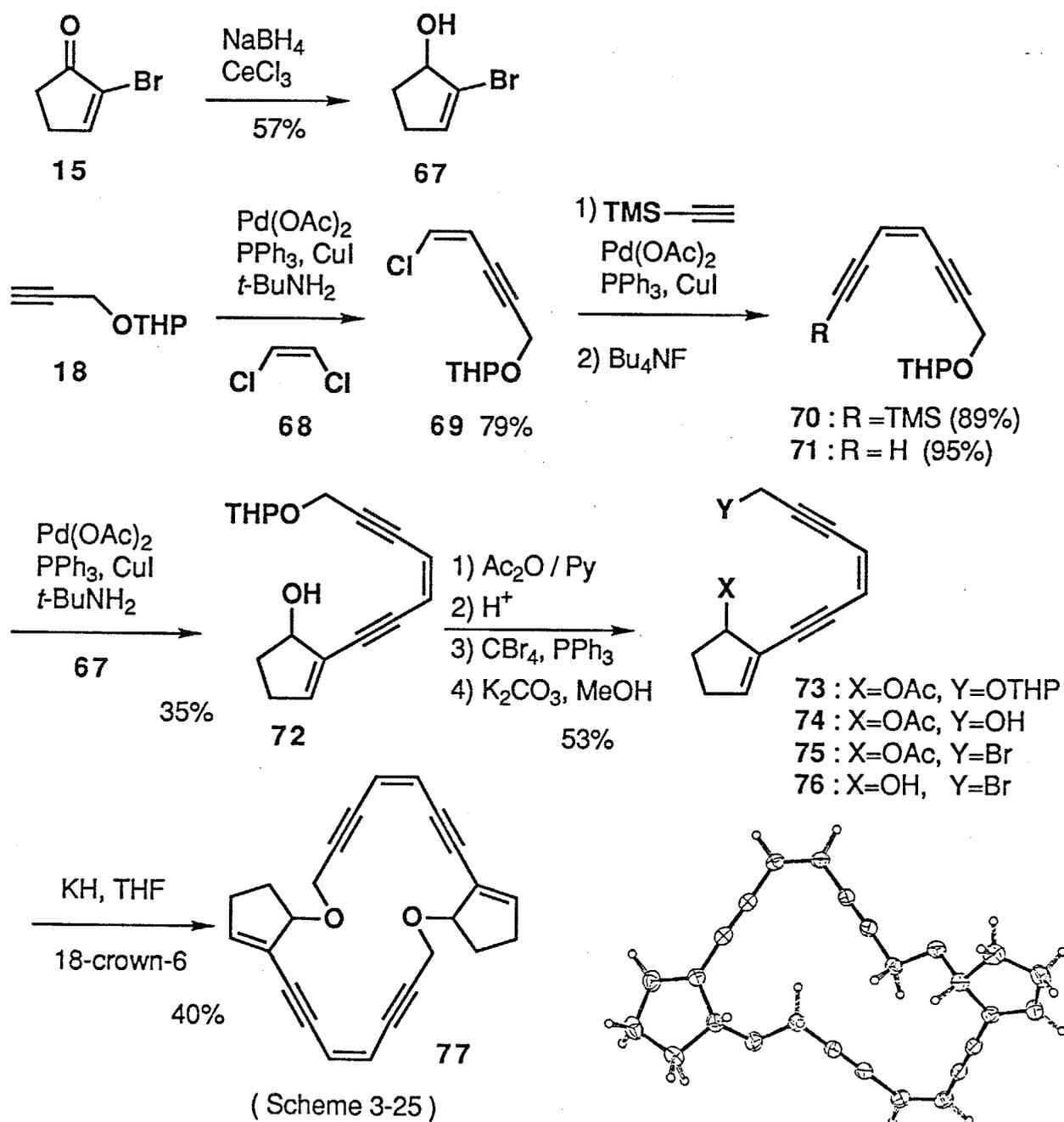


(Scheme 3-24)

#### 3-7-2 合成

2-ブromo-2-シクロペンテノン (15)<sup>68)</sup>を塩化セリウム存在下NaBH<sub>4</sub>でケトンだけを還元し、2-ブromo-2-シクロペンタノール (67)を収率57%で得た。一方、パラジウムと銅触媒存在下、プロパルギルエーテル18とシス-1,2-ジクロロエチレン (68)とをカップリングし、エンイン69を収率79%で得た<sup>71)</sup>。この際68を5当量用いることにより、一方のみカップリングした化合物を得ることができた。続いて同様にパラジウム、銅触媒を用いてトリメチルシリルアセチレンとカップリングした後(89%)、70のトリメチルシリル基をフッ化テトラブチルアンモニウムを用いて除去した(95%)。得られたエンジン71と67をパラジウム、銅触媒下カップリング反応を行って、ジエンジン化合物72へ導いた(35%)。さらに72の水酸基をアセチル化した後、73のTHP基を希酸により除去した。得られたアルコール74は四臭化炭素とPPh<sub>3</sub>を用いてブrom化し、塩基により75のアセチル基を除去してブromoアルコール76を73から収率53%で得た。得られた76を高希釈条件で、NaH,

THF中へ滴下したが、求める分子内エーテル化は進行しなかった。そこで塩基にKHを用いて高希釈条件で検討したところ、分子間反応が進行した後、分子内反応が進行したと考えられる2量体77だけが得られた(40%)。77の構造はX線結晶構造解析から明らかにすることができた。このことは76が分子内でエーテル化するためには歪みが大きすぎるため、高希釈条件にもかかわらず分子間反応が起こり、次の分子内エーテル化は歪が小さいために、高希釈条件で容易に進行したものと考えられる。すなわち10員環エーテル65でさえ環を構築することは歪が大きくて困難であることがわかった。10員環エーテル化合物から9員環骨格を構築することは断念せざるを得なかった(Scheme 3-25)。



## EXPERIMENTAL SECTION

### Methods and Instrumentation

Proton magnetic resonance ( $^1\text{H}$  NMR) spectra were recorded on Jeol Model FX-90Q, GSX-500, or Varian Gemini-200 (90, 500, or 200 MHz, respectively), and are recorded in parts per million using tetramethylsilane as a standard on the  $\delta$  scale. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, and coupling constants (Hz).  $^{13}\text{C}$  NMR spectra were recorded on Jeol Model FX-90Q, GSX-500, or Varian Gemini-200 (22.5, 50, or 125 MHz, respectively), and are recorded in parts per million using  $\text{CDCl}_3$  (77.1 $\delta$ ) as a standard on the  $\delta$  scale. Infrared spectra were recorded on a Jasco Model IRA-2 or IR-700 spectrometer ( $\nu_{\text{max}}$  in  $\text{cm}^{-1}$ ). HPLC was performed on a Nihon Seimitsu Kagaku apparatus. Optical rotations were measured on a Yanako OR-50 polarimeter.

Solvents were distilled under argon as follows: Benzene, dioxane, ether, hexane, THF, toluene, and xylene were distilled over sodium. Dichloromethane was distilled over  $\text{P}_2\text{O}_5$ . Triethylamine, pyridine, hexamethylphosphoric triamide (HMPA), dimethyl sulfoxide (DMSO), and acetonitrile were distilled over  $\text{CaH}_2$ . Reactions were monitored by analytical thin-layer chromatography (TLC) using Merck silica gel 60 F254. Column chromatography separations were performed under pressure by using silica gel (Fuji Davison BW820 MH or Daiso IR-60) or activated alumina (Wako 200 mesh).

Calculations were performed using Allinger's MM2 program. Specific parameters were input to calculate structures with enone system, diene moiety, and epoxide. Input data containing listings of added parameters for each calculated structure, and final energies and all coordinates for optimized geometries were described in this section. All atom types utilized were shown below.

#### Atom types utilized

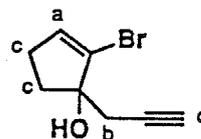
1	C $\text{sp}^3$ carbon	7	O (carbonyl)
2	C (olefin)	21	H (alcohol)
3	C (carbonyl)	22	C (3-membered ring)
5	H (C-H bond)	29	C (inside atom of diene)
6	O (alcohol)	30	O (epoxide)

### 1-(2-propynyl)-2-bromo-2-cyclopenten-1-ol (16)

In a flask were placed 9.6 g of magnesium turnings and 40 mL of dry ether and 600 mg of mercury(II) chloride were added successively. After stirring for 30 min at room temperature an additional 100 mL of ether were added and the mixture was cooled in a bath of ice and ice-water. After the temperature has reached 0 °C, 2.0 mL of propargyl bromide were added. As soon as the temperature began to rise (5 °C), the bath was removed and replaced with dry-ice and acetone. The temperature was lowered to 0 °C, the remainder of the bromide (18.0 mL) was added dropwise in 45 min at -10 °C. After the addition, the temperature was allowed to rise to 5 °C in 30 min. The grey solution obtained was then decanted from the excess of magnesium and transferred into another reaction flask.

To the solution of propargylmagnesium bromide<sup>69</sup> was added a solution of 2-bromo-2-cyclopentenone (15)<sup>68</sup> (21.3 g, 132 mmol) in dry ether(80 mL) dropwise over 1 h at 0 °C. After addition was complete, the reaction mixture was poured into ice-cooled saturated ammonium chloride with vigorous stirring. The aqueous layer was extracted with ether. Then the combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 10 : 1) to give the alcohol 16 (21.0 g, 104 mmol, 79%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.09 (t, 1H, a, J = 2.64 Hz), 2.61 (dd, 1H, b, J = 16.2, 2.64 Hz), 2.55 (dd, 1H, b, J = 16.2, 2.64 Hz), 2.16-2.5 (m, 4H, c), 2.02 (t, 1H, d, J = 2.64 Hz)  
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 134.5, 126.9, 84.3, 79.6, 70.5, 35.5, 30.0, 29.9  
IR (neat) 3300, 2925, 2850, 1720, 1620, 1265, 1060, 940, 740



16

### 1-(2-bromo-2-cyclopentenylidene)-3-pentyne-1,5-diol (17)

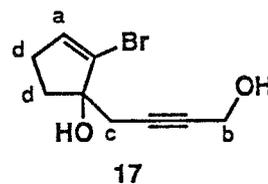
To a solution of the alkyne 16 (12.8 g, 63.7 mmol) in dry ether(25 mL) was added dropwise a solution of butyllithium (1.69 N, 71.6 mL, 1.9 eq.) at -78 °C. After 10 min paraformaldehyde (1.1 eq. 2.10 g) was added in one portion at the same temperature. After being stirred for 1 h at -40 °C, the reaction mixture was stirred for 12 h at room temperature. The reaction mixture was washed with ice-cooled water and the aqueous solution was extracted with dichloromethane. The combined

organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with ethyl acetate : hexane = 1 : 1) to give the diol **17** (11.0 g, 47.6 mmol, 75%), and the recovered alkyne **16** ( 3.0 g, 14.9 mmol, 23%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.05 (t, 1H, a, J = 2 Hz), 4.23 (brs, 2H, b), 2.64 (dd, 1H, c, J = 16.6, 2.0 Hz), 2.50 (dd, 1H, c, J = 16.6, 2.1 Hz), 2.2 -2.42 (m, 4H, d)

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 134.2, 127.2, 84.3, 81.3, 80.7, 50.9, 35.6, 30.0, 29.8

IR (neat) 3300, 2920, 2850, 2220, 1620, 1480, 1380, 1250, 1170, 1140, 1060, 1010, 970, 940, 900, 840



#### tetrahydro-2-[(Z)-3-iodo-2-propenyloxy]-2H-pyran (**19**)

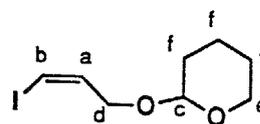
To a solution of tetrahydro-2-(2-propynyloxy)-2H-pyran (**18**) (9.5 g, 67.9 mmol) in dry ether (100 mL) was added dropwise a solution of butyllithium (1.73N, 1.05 eq., 41.2 mL) at -78 °C. After 30 min a solution of iodine (21 g, 82.7 mmol) in dry THF (40 mL) was added dropwise to the white solution at the same temperature. The temperature gradually rose up to -20 °C. The reaction mixture was poured into an aqueous solution of sodium bicarbonate and sodium thiosulfate, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was used for the next reaction without further purification.

To a solution of the crude alkyne iodide and potassium azodicarboxylate (28 g, 144 mmol) in methanol (250 mL) was added dropwise acetic acid (16 mL) at room temperature. After 3 h the reaction mixture was poured into water with stirring. The aqueous solution was extracted with ether and the combined organic layer was washed with ice-cooled saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, 50% aqueous dimethylamine (150 mL) was added to the residue at 0 °C. After being stirred for 10 h, the reaction solution was extracted with ether. The combined organic layer was washed with saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 50 : 1) to give the alkenyl iodide **19** (12.9 g, 48 mmol, 68%).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.484 (ddd, 1H, a,  $J = 7.69, 5.99, 5.13$  Hz), 6.381 (ddd, 1H, b,  $J = 7.69, 1.71, 1.71$  Hz), 4.654 (t, 1H, c,  $J = 3.63$  Hz), 4.291 (ddd, 1H, d,  $J = 13.7, 5.13, 1.71$  Hz), 4.103 (ddd, 1H, d,  $J = 13.7, 5.99, 1.71$  Hz), 3.88 (m, 1H, e), 3.53 (m, 1H, e), 1.5 -1.9 (m, 6H, f)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  138.4, 98.4, 82.5, 70.0, 62.2, 30.6, 25.4, 19.4

IR (neat) 3066, 2940, 2868, 1612, 1453, 1439, 1385, 1345, 1280, 1200, 1120, 1066, 1027, 903, 869, 814



19

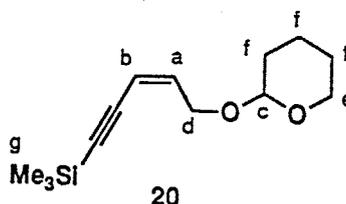
#### tetrahydro-2-[(*Z*)-(5-trimethylsilyl-2-penten-4-ynoxy)]-2*H*-pyran (20)

To a mixture of palladium acetate (3 mol%, 280 mg), triphenylphosphine (12 mol%, 1.5 g), CuI (6 mol%, 550 mg) and *t*-butylamine (10 mL, 97 mmol) in benzene (90 mL) was added a solution of alkenyl iodide **19** (13 g, 48.5 mmol) in benzene (20 mL) and a solution of trimethylsilyl acetylene (10 mL, 73 mmol) in benzene (10 mL) at 5 °C. After being stirred for 4 h at room temperature, the reaction mixture was diluted with hexane and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution, 1N HCl, saturated sodium bicarbonate, brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 50 : 1) to give the enyne **20** (9.9 g, 41.8 mmol, 86%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.04 (ddd, 1H, a,  $J = 10.0, 6.59, 5.93$  Hz), 5.59 (ddd, 1H, b,  $J = 10.0, 1.54, 1.54$  Hz), 4.63 (br, 1H, c), 4.46 (ddd, 1H, d,  $J = 13.2, 5.93, 1.54$  Hz), 4.32 (ddd, 1H, d,  $J = 13.2, 6.59, 1.54$  Hz), 3.3 -4.1 (m, 2H, e), 1.4 -2.0 (m, 6H, f), 0.18 (s, 9H, g)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  140.7, 111.1, 98.6, 65.2, 62.2, 30.7, 25.5, 22.7, 19.5, 14.1, -0.1

IR (neat) 2930, 2140, 1250, 1200, 1120, 1030, 840, 760



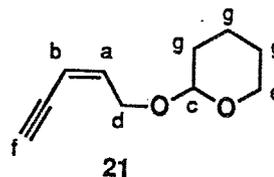
20

**tetrahydro-2-[(Z)-(2-penten-4-ynyloxy)]-2H-pyran (21)**

To a solution of the protected enyne **20** (11.6 g, 48.9 mmol) in THF (120 mL) was added tetrabutylammonium fluoride (4.6 g) in several portions at 0 °C. After being stirred for 10 min, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ether = 50 : 1) to give the deprotected enyne **21** (7.59 g, 45.7 mmol, 94%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.13 (dddd, 1H, a, J = 11.0, 7.3, 6.4, 0.94 Hz), 5.60 (dddd, 1H, b, J = 11.0, 1.7, 1.7, 2.6 Hz), 4.65 (brs, 1H, c), 4.42 (ddd, 1H, d, J = 13, 6.4, 1.7 Hz), 4.30 (ddd, 1H, d, J = 13, 7.3, 1.7 Hz), 3.46-4.04 (m, 2H, e), 3.16 (brd, 1H, f, J = 2.6 Hz), 1.4 -2.0 (m, 6H, g)

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 141.7, 109.9, 98.6, 83.1, 79.4, 65.2, 62.2, 30.6, 25.5, 19.5  
IR (neat) 3250, 2920, 2850, 1200, 1120, 1020, 900, 865, 810

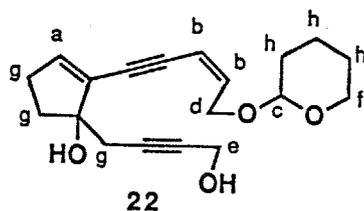


**2-[(Z)-5-(tetrahydro-2H-pyran-2-yloxy)-3-penten-1-ynyl]-2-cyclopentenylidene-3-pentyne-1,5-diol (22)**

To a mixture of palladium acetate (3 mol%, 222 mg), triphenylphosphine (12 mol%, 1.2 g), CuI (6 mol%, 435 mg) and *t*-butylamine (8.0 mL, 76 mmol) in benzene (80 mL) was added a solution of alkenyl bromide **17** (8.80 g, 38.1 mmol) in benzene (40 mL) and a solution of the enyne **21** (7.59 g, 45.7 mmol) in benzene (40 mL) at room temperature. After being stirred for 10 h at the same temperature, the reaction mixture was diluted with ethyl acetate and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution, 1N HCl, saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ethyl acetate = 1 : 1) to give the dienediyne **22** (11.0 g, 34.8 mmol, 91%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.17 (brs, 1H, a), 5.68-6.24 (m, 2H, b), 4.6-4.8 (br, 1H, c), 4.1-4.6 (m, 2H, d), 4.2 (brt, 2H, e), 3.4-4.0 (m, 2H, f), 1.9-2.9 (m, 6H, g), 1.3-1.8 (m, 6H, h)

IR (neat) 3370, 2925, 2850, 2170, 1440, 1380, 1320, 1260, 1200, 1140, 1120, 1060, 1020, 960, 900, 860, 780, 760



**1-(4-bromo-2-butynyl)-2-[(Z)-5-hydroxy-3-penten-1-ynyl]-2-cyclopenten-1-ol (23)**

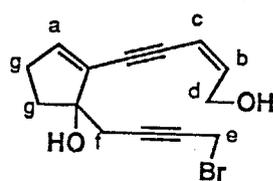
To a mixture of the diol **22** (4.66 g, 14.7 mmol) and pyridine (1.19 mL, 14.7 mmol) in dry acetonitrile (90 mL) was added tetrabromomethane (1.01 eq, 4.91 g) and triphenylphosphine (1.01 eq, 3.89 g) in three portions at  $-40\text{ }^\circ\text{C}$ . After being stirred for 1 h at the  $-20\text{ }^\circ\text{C}$ , the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with ethyl acetate and the combined organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was stirred with pentane (40 mL), ether (40 mL), ethyl acetate (4 mL), and water (4 mL) for 1 h. After decantation, the solution was washed with saturated sodium bicarbonate, brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was diluted with methanol (50 mL). A catalytic amount of pyridinium *p*-toluenesulfonate was added to the solution at room temperature. After being stirred for 12 h, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After the removal of the solvent, the residue was purified by the column chromatography on silica gel (elution with hexane : ethyl acetate = 1: 1) to give the bromo alcohol **23** (1.36 g, 4.6 mmol, 31%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.23 (t, 1H, a,  $J = 1.8$  Hz), 6.19 (dt, 1H, b,  $J = 11.0, 6.2$  Hz), 6.07 (brd, 1H, c,  $J = 11.0$  Hz), 4.43 (brd, 2H, d,  $J = 6.2$  Hz), 3.92 (t, 2H, e,  $J = 2.4$  Hz), 2.72 (dt, 1H, f,  $J = 16, 2.4$  Hz), 2.68 (dt, 1H, f,  $J = 16, 2.4$  Hz), 1.8-2.6 (m, 4H, g)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  141.7, 140.0, 129.6, 110.4, 89.1, 88.7, 85.1, 83.9, 77.1,

60.5, 36.9, 30.6, 30.4, 15.3

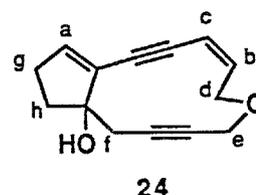
IR (neat) 3300, 2900, 2850, 2230, 2180, 1210, 1160, 1060, 1010, 960, 920, 840, 780, 760, 600



### 6-oxabicyclo[10.3.0]pentadec-8,12-diene-3,10-diyne-1-ol (24)

To a suspension of NaH (60%, 150 mg) which was already washed with dry hexane (3 mL X 3) in dry THF (20 mL) and ethanol (0.02 mL) was slowly added a solution of the bromo alcohol **23** (57 mg, 0.19 mmol) in dry THF (20 mL) dropwise over 5 h at 20 °C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into saturated ammonium chloride and the aqueous solution was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ethyl acetate = 5 : 1) to give the cyclic ether **24** (33 mg, 0.15 mmol, 80%).

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 6.185 (t, 1H, a, J = 2.79 Hz), 6.087 (ddd, 1H, b, J = 10.5, 7.76, 7.22 Hz), 5.988 (d, 1H, c, J = 10.5 Hz), 4.431 (dd, 1H, d, J = 10.7, 7.76 Hz), 4.383 (dd, 1H, d, J = 10.7, 7.22 Hz), 4.19 (dt, 1H, e, J = 16.1, 2.2 Hz), 4.18 (dt, 1H, e, J = 16.1, 2.0 Hz), 2.744 (dt, 1H, f, J = 16.8, 2.2 Hz), 2.619 (dt, 1H, f, J = 16.8, 2.0 Hz), 2.553 (dddd, 1H, g, J = 18.2, 8.7, 3.8, 2.8 Hz), 2.374 (dddd, 1H, g, J = 18.2, 7.8, 6.4, 2.8 Hz), 2.149 (ddd, 1H, h, J = 13.5, 8.7, 6.4 Hz), 1.948 (ddd, 1H, h, J = 13.5, 7.8, 3.8 Hz)  
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 139.1, 136.5, 130.4, 117.1, 90.6, 89.5, 83.7, 82.9, 80.0, 63.9, 56.3, 38.4, 31.9, 29.8.  
IR (neat) 3430, 3030, 2940, 2850, 2280, 2200, 1450, 1360, 1320, 1140, 1060, 1020, 960, 920, 900, 880, 840, 790, 760



### methoxymethyl ether 25a

To a mixture of the alcohol **24** (121 mg, 0.56 mmol), dry dichloromethane (1 mL) and diisopropylethylamine (2 mL) was added chloromethyl methyl ether (6 eq, 0.26 mL) dropwise at 0 °C. After being stirred for 18 h at room temperature, the reaction mixture was diluted with ether. The solution was washed with saturated copper sulfate, saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was passed through a short pad of silica gel (elution with hexane : ether = 2 : 1) to give the ether **25a** (126 mg, 0.485 mmol, 87%), which was used for the next reaction.

### ***t*-butyldimethylsilyl ether 25b**

To a mixture of the alcohol **24** (117 mg, 0.55 mmol), dry triethylamine (0.37 mL, 2.75 mmol) and dry dichloromethane (5 mL) was added *t*-butyldimethylsilyl triflate (0.25 mL, 1.1 mmol) dropwise at 0 °C. After being stirred for 10 h at room temperature, the reaction mixture was diluted with ether. The solution was washed with saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was passed through a short pad of silica gel (elution with hexane : ether = 3 : 1) to give the ether **25b** (160 mg, 0.49 mmol, 90%), which was used for the next reaction

### **trimethylsilyl ether 25c**

To a mixture of the alcohol **24** (31 mg, 0.145 mmol), dry triethylamine (0.24 mL, 1.45 mmol), and dry dichloromethane (2 mL) was added trimethylsilyl trifluoromethanesulfonate (0.1 mL, 0.435 mmol) dropwise at 0 °C. After being stirred for 6 h at room temperature, the reaction mixture was diluted with ether. The solution was washed with saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was passed through a short pad of silica gel (elution with hexane : ether = 1 : 1) to give the ether **25c** (29 mg, 0.10 mmol, 70%), which was used for the next reaction.

### **A general procedure of [2,3]-Wittig reactions**

To a solution of the protected cyclic ether **25** (0.33 mmol) in dry THF (20 mL) was added *t*-butyllithium (1.93 N, 1.2 eq, 0.21 mL) dropwise at -100 °C. After 30 min, 3 mL of saturated ammonium chloride was added to the reaction mixture in one portion at the same temperature. After being stirred for 10 min at room temperature, the mixture was diluted with ether. The organic layer was washed with saturated ammonium chloride, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel to give the mixture of rearrangement products (80-92%).

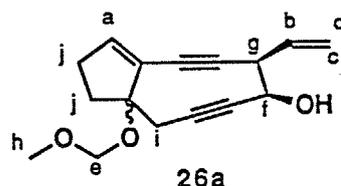
the [2,3]-rearrangement product 26a (major isomer)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 3% *i*-PrOH in hexane, 3.4 mL/min);

Rt=8.5-9 min

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.199 br s (1H, a), 5.851 (ddd, 1H, b,  $J = 16.95, 10.08, 6.42$  Hz), 5.429 (dd, 1H, c,  $J = 16.95, 1.37$  Hz), 5.286 (dd, 1H, d,  $J = 10.08, 1.37$  Hz), 4.786 (d, 1H, e,  $J = 7.34$  Hz), 4.742 (d, 1H, e,  $J = 7.34$  Hz), 4.447 (br, 1H, f), 3.753 (br dd, 1H, g,  $J = 6.42, 3.9$  Hz), 3.414 (s, 3H, h), 2.843 (d, 1H, i,  $J = 17.2$  Hz), 2.565 (m, 1H, j), 2.558 (d, 1H, i,  $J = 17.2$  Hz), 2.382 (m, 1H, j), 2.279 (m, 1H, j), 1.846 (m, 1H, j)

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  138.4, 132.6, 126.8, 118.9, 97.8, 95.5, 93.9, 92.3, 87.1, 86.7, 67.9, 55.7, 48.9, 36.7, 31.8, 30.4

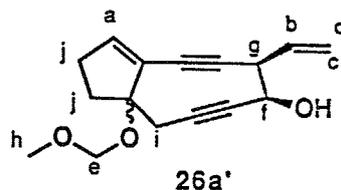


the [2,3]-rearrangement product 26a' (minor isomer)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 3% *i*-PrOH in hexane, 3.4 mL/min);

Rt=13-14 min

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.190 (t, 1H, a,  $J = 2.75$  Hz), 5.828 (ddd, 1H, b,  $J = 16.95, 10.08, 6.87$  Hz), 5.436 (dd, 1H, c,  $J = 16.95, 1.38$  Hz), 5.323 (dd, 1H, d,  $J = 10.08, 1.38$  Hz), 4.765 (d, 1H, e,  $J = 7.34$  Hz), 4.647 (d, 1H, e,  $J = 7.34$  Hz), 4.615 (br, 1H, f), 3.730 (dd, 1H, g,  $J = 6.87, 4.59$  Hz), 3.400 (s, 3H, h), 2.840 (d, 1H, i,  $J = 16.7$  Hz), 2.594 (d, 1H, i,  $J = 16.7$  Hz), 2.567 (m, 1H, j), 2.3-2.42 (m, 2H, j), 1.849 (m, 1H, j)

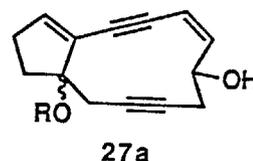


the [1,2]-rearrangement product 27a

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 3% *i*-PrOH in hexane, 3.4 mL/min);

Rt=18-19 min

$^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ); 6.28 (t, 1H,  $J=2.9$  Hz), 5.96 (dd, 1H,  $J=10.9, 6.7$  Hz), 5.71 (d, 1H,  $J=10.9$  Hz), 5.0-5.1 (m, 1H), 4.84 (d, 1H,  $J=7.4$  Hz), 4.78 (d, 1H,  $J=7.4$  Hz), 3.47 (s, 3H), 2.8 (m, 1H), 2.2-2.7 (m, 6H), 1.7 (m, 1H)



**1-*t*-butyldimethylsilyloxy-6-vinylbicyclo[7.3.0]dodec-9-ene-3,7-diyn-5-ol (26b)**

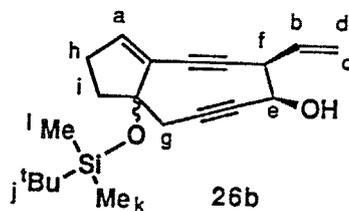
HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 5% ethyl acetate in hexane, 3.4 mL/min); Rt=8.7-9.5 min

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.959 (t, 1H, a,  $J = 2.56$  Hz), 5.847 (ddd, 1H, b,  $J = 17.1, 9.83, 5.99$  Hz), 5.424 (ddd, 1H, c,  $J = 17.1, 2.99, 1.28$  Hz), 5.272 (ddd, 1H, d,  $J = 9.83, 2.99, 1.28$  Hz), 4.451 (brdd, 1H, e,  $J = 10.26, 4.70$  Hz), 3.790 (brdd, 1H, f,  $J = 5.99, 4.70$  Hz), 2.685 (d, 1H, g,  $J = 16.7$  Hz), 2.569 (m, 1H, h), 2.494 (dd, 1H, g, 16.7, 1.29 Hz), 2.415 (m, 1H, h), 2.094 (ddd, 1H, i,  $J = 14.10, 8.98, 3.42$  Hz), 1.934 (ddd, 1H, i,  $J = 14.10, 8.98, 5.56$  Hz), 0.898 (s, 9H, j), 0.135 (s, 3H, k or l), 0.109 (s, 3H, l or k)

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  134.4, 132.5, 130.8, 118.8, 96.5, 96.4, 90.6, 87.9, 86.2, 67.8, 49.1, 38.3, 34.3, 30.2, 25.8, 18.3, -3.0, -3.2.

IR (neat) 3000, 2920, 2850, 2180, 1460, 1385, 1250, 1215, 1080, 1010, 985, 920, 830, 750, 660.

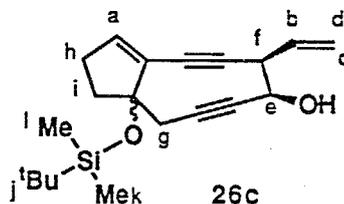
MS(FD);  $m/z$  328 ( $\text{M}^+$ )



**the [2,3]-rearrangement product 26c**

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 5% ethyl acetate in hexane, 3.4 mL/min); Rt=14.5-15.3 min

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.95 (m, 1H, a), 5.89 (ddd, 1H, b,  $J = 15, 9.5, 5.6$  Hz), 5.44 (ddd, 1H, c,  $J = 15$  Hz), 5.26 (ddd, 1H, d,  $J = 9.5$  Hz), 4.24 (m, 1H, e), 3.72 (brdd, 1H, f,  $J = 5.6, 4.6$  Hz), 2.64 (d, 1H, g,  $J = 16.4$  Hz), 2.53 (dd, 1H, g,  $J = 16.4, 1.0$  Hz), 1.8-2.5 (m, 4H, h), 0.17 (s, 9H, i)



**preparation of ESP-CAL model 28 and Bergman cyclization of 28**

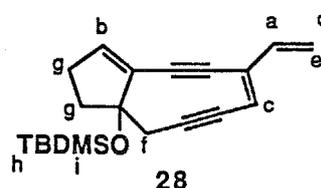
A mixture of the alcohol 26b (20 mg, 0.06 mmol), dichloromethane (2 mL) and DMAP (100 mg, 0.82 mmol) was added dropwise distilled mesyl chloride (0.02 mL, 0.25 mmol) at -20 °C. After being stirred for 30 min at 0 °C, the reaction mixture was poured into water. The aqueous layer was extracted with pentane and the combined

organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After the solution was concentrated to 1 mL *in vacuo*, the residue was passed through the short pad of silica gel eluted with petroleum ether to give the solution of 28. After the solution of 28 was concentrated to 0.5 mL *in vacuo* at 0 °C, the residue was immediately diluted with degassed benzene (30 mL) and the resulting solution was standing in the presence of hydroquinone (1 g) at room temperature for 24 h to give the cyclized product 30 (10 mg, 0.03 mmol) in 50% yield.

**1-*t*-butyldimethylsilyloxy-6-vinylbicyclo[7.3.0]dodeca-5,9-diene-3,7-diyne (28)**

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with hexane, 2.0 mL/min);  
Rt=16-17 min

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.38 (dd, 1H, a, J = 16.3, 9.9 Hz), 6.06 (t, 1H, b, J = 2.6 Hz), 5.98 (br, 1H, c), 5.71 (d, 1H, d, J = 9.9 Hz), 5.69 (d, 1H, e, J = 16.3 Hz), 2.88 (d, 1H, f, J = 18 Hz), 2.85 (d, 1H, f, J = 18 Hz), 1.8 -2.7 (m, 4H, g), 0.89 (s, 9H, h), 0.06 (s, 6H, i)



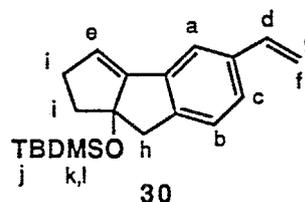
**2,3,3a,4-tetrahydro-3a-*t*-butyldimethylsilyloxy-7-vinylcyclopent[a]indene (30)**

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with hexane, 2.0 mL/min);  
Rt=10.7-11.2 min

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.47 (br, 1H, a), 7.24 (d, 1H, b or c, J = 6.1 Hz), 7.18 (d, 1H, c or b, J = 6.1 Hz), 6.72 (dd, 1H, d, J = 17.8, 10.5 Hz), 5.93 (dd, 1H, e, J = 3.5, 1.7 Hz), 5.76 (dd, 1H, f, J = 17.8, 1.1 Hz), 5.20 (dd, 1H, g, J = 10.5, 1.1 Hz), 2.92 (brs, 2H, h), 1.8 -2.8 (m, 4H, i), 0.74 (s, 9H, j), -0.11 (s, 3H, k or l), -0.28 (s, 3H, l or k)

IR (CHCl<sub>3</sub>) 2920, 2850, 1060, 1010.

MS(EI); m/z 312(M<sup>+</sup>, 5.9%), 255(33.7%), 181(11.6%), 75(100%)



**6-oxabicyclo[10.3.0]pentadec-1,8,12-triene-3,10-diyne (31)**

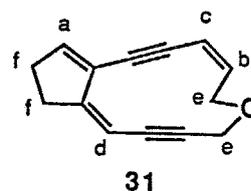
To a solution of the alcohol 24 (30 mg, 0.14 mmol) in dichloromethane (2 mL) and DMAP (100 mg, 0.82 mmol) was added dropwise distilled mesyl chloride (0.02 mL, 0.25 mmol) at 0 °C. After being stirred for 1 h at the same temperature, the

reaction mixture was poured into water. The aqueous layer was extracted with ether and the combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 10 : 1) to give the dehydrated product **31** (14 mg, 0.07 mmol, 50%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.54 (br 1H, a), 6.00 (dd, 1H, b,  $J = 10.3, 7.0$  Hz), 5.95 (d, 1H, c,  $J = 10.3$  Hz), 5.42 (br, 1H, d), 4.2-4.7 (m, 4H, e), 2.4-2.8 (m, 4H, f)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 148.8, 137.4, 126.9, 117.1, 98.2, 90.2, 89.9, 86.1, 85.3, 63.9, 56.6, 31.1, 31.0

IR (neat) 3010, 2920, 2860, 2180, 1700, 1440, 1360, 1215, 1060, 920, 745, 660

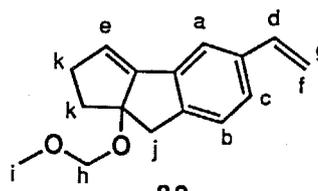


### 2,3,3a,4-tetrahydro-3a-methoxymethoxy-7-vinylcyclopent[a]indene (**32**)

To a mixture of dry dimethyl sulfoxide (0.06 mL, 0.84 mmol) and dry dichloromethane (1.5 mL) was added distilled oxalyl chloride (0.03 mL, 0.35 mmol) at  $-78$  °C. After 1 h, a solution of **26a** (10 mg, 0.05 mmol) in dry dichloromethane (1.5 mL) was added to the mixture at the same temperature. After 1 h, dry triethylamine (0.6 mL) was added to the reaction mixture at  $-78$  °C. After being stirred for 30 min at room temperature, the reaction mixture was poured into water and the aqueous layer was extracted with ether. The combined organic layer was washed with saturated copper sulfate, saturated sodium bicarbonate, brine and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 20 : 1) to give the cyclized product **32** (3 mg, 0.015 mmol, 30%).

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 0.5% *i*-PrOH in hexane, 3.3 mL/min);  $R_t$ =5.2-5.8 min

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 (br, 1H, a), 7.26 (d, 1H, b or c,  $J = 5.4$  Hz), 7.20 (d, 1H, c or b,  $J = 5.4$  Hz), 6.70 (dd, 1H, d,  $J = 18.0, 10.0$  Hz), 6.12 (br, 1H, e), 5.76 (d, 1H, f,  $J = 18.0$  Hz), 5.24 (d, 1H, g,  $J = 10.0$  Hz), 4.66 (d, 1H, h,  $J = 7.3$  Hz), 4.61 (d, 1H, h,  $J = 7.3$  Hz), 3.24 (s, 3H, i), 3.22 (d, 1H, j,  $J = 16$  Hz), 2.84 (d, 1H, j,  $J = 16$  Hz), 1.8-2.1 (m, 4H, k)



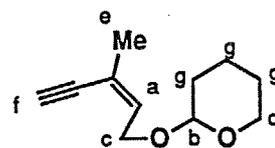
**tetrahydro-2-[(Z)-(3-methyl-2-penten-4-ynyloxy)]-2H-pyran (34)**

To a mixture of commercially available 3-methyl-2-penten-4-yn-1-ol (33) (15.0 g, 156 mmol), dry dichloromethane (120 mL), and a catalytic amount of *p*-toluenesulfonic acid was added dihydropyran (15.7 mL, 172 mmol) at 0 °C. After the addition was complete, the mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with ether and the combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ether = 10 : 1) to give the ether 34 (28.0 g, 155 mmol, quant.).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.90 (brt, 1H, a, J = 6.8 Hz), 4.61 (br, 1H, b), 4.0 -4.5 (m, 2H, c), 3.3 -4.0 (m, 2H, d), 3.13 (brs, 1H, e), 1.88 (dt, 3H, f, J = 1.3, 1.3 Hz), 1.3 -1.8 (m, 6H, g)

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 135.4, 120.2, 98.5, 82.0, 65.8, 62.2, 30.7, 25.5, 23.0, 19.6.

IR (neat) 3280, 2930, 2860, 1440, 1380, 1355, 1320, 1260, 1205, 1120, 1080, 1055, 1025, 910, 870, 870, 815, 640



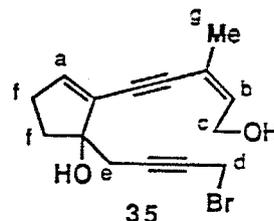
34

**1-(4-bromo-2-butynyl)-2-[(Z)-5-hydroxy-3-methyl-3-penten-1-ynyl]-2-cyclopenten-1-ol (35)**

To a mixture of palladium acetate (3 mol%, 88 mg), triphenylphosphine (12 mol%, 476 g), CuI (6 mol%, 173 mg) and *t*-butylamine (3.2 mL, 30 mmol) in benzene (32 mL) was added a solution of alkenyl bromide 17 (3.5 g, 15.2 mmol) in benzene (16 mL) and a solution of the enyne 34 (3.27 g, 18.1 mmol) in benzene (16 mL) at room temperature. After being stirred for 3.5 h at the same temperature, the reaction mixture was diluted with ethyl acetate and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution and 1N HCl. The aqueous layer was extracted with ethyl acetate twice and the combined organic layer was washed with saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ethyl acetate = 3 : 2) to give the coupling product (4.38 g, 13.3 mmol, 87%).

To a mixture of the coupling product (3.8 g, 11.5 mmol) and pyridine (0.94 mL, 11.6 mmol) in dry acetonitrile (80 mL) was added tetrabromomethane (1.01 eq, 3.84 g) and triphenylphosphine (1.01 eq, 3.04 g) in several portions at -40 °C. The mixture was stirred for 2 h at the -20 °C, methanol (1 mL) was added to the clear solution at the same temperature. Then the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with ethyl acetate and the combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was dissolved by pentane (40 mL), ether (20 mL), ethyl acetate (2 mL), and water (1 mL) with vigorous stirring. After decantation, the residue was washed with five portions of pentane (20 mL), ether (10 mL), and water (0.5 mL) with vigorous stirring. The combined filtrate was washed with saturated copper sulfate, saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue (6.12 g) was diluted with methanol (50 mL). A catalytic amount of pyridinium *p*-toluenesulfonate (90 mg) was added to the solution at room temperature. After being stirred for 15 h, the reaction mixture was concentrated to 10-20 mL under reduced pressure at 20 °C. The concentrated solution was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the residue was purified by the column chromatography on silica gel (elution with hexane : ethyl acetate = 1: 1) to give the bromo alcohol **35** (2.50 g, 8.1 mmol, 70%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.20 (t, 1H, a, J = 2.8 Hz), 5.89 (tq, 1H, b, J = 6.8, 1.6 Hz), 4.28 (dd, 2H, c, J = 6.8, 0.9 Hz), 3.91 (t, 2H, d, J = 2.5 Hz), 2.70 (dt, 1H, e, J = 16.6, 2.5 Hz), 2.65 (dt, 1H, e, J = 16.6, 2.5 Hz), 1.9-2.6 (m, 4H, f), 1.93 (dt, 3H, g, J = 1.6, 0.9 Hz)  
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 140.0, 136.0, 129.6, 120.9, 91.2, 88.2, 85.1, 83.9, 77.2, 66.0, 61.2, 36.9, 30.5, 23.1, 15.2  
 IR (neat) 3354, 3052, 2920, 2846, 2310, 2230, 2186, 1728, 1435, 1206, 1062, 1003, 959, 736, 696, 608, 541

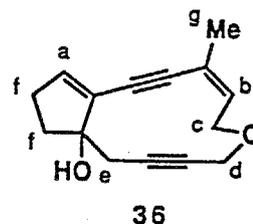


### 9-methyl-6-oxabicyclo[10.3.0]pentadec-8,12-diene-3,10-diyn-1-ol (**36**)

To a suspension of NaH (55%, 280 mg), which was already washed with dry hexane (5 mL X3), in dry THF (65 mL), dry HMPA (0.5 mL, 2.2 mmol), and ethanol

(0.03 mL) was slowly added a solution of the bromo alcohol **35** (207 mg, 0.67 mmol) in dry THF (65 mL) dropwise over 32 h using microfeeder at 20 °C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into ice-cooled saturated ammonium chloride and the aqueous solution was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ethyl acetate = 8 : 1) to give the cyclic ether **36** (134 mg, 0.59 mmol, 88%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.18 (t, 1H, a, J = 2.9 Hz), 5.85 (tq, 1H, b, J = 7.9, 1.6 Hz), 4.30 (brd, 2H, c, J = 7.9 Hz), 4.15 (t, 2H, d, J = 2.1 Hz), 2.69 (dt, 1H, e, J = 17, 2.1 Hz), 2.64 (dt, 1H, e, J = 17, 2.1 Hz), 1.8 -2.6 (m, 4H, f), 1.97 (d, 3H, g, J = 1.6 Hz)  
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 139.3, 131.1, 130.6, 127.2, 91.9, 89.3, 83.5, 83.0, 80.4, 65.1, 56.4, 38.5, 31.9, 29.8, 22.7.  
 IR (neat) 3416, 2936, 2848, 2280, 2218, 2192, 1733, 1625, 1446, 1353, 1258, 1056, 924, 892, 804, 734, 714, 588.

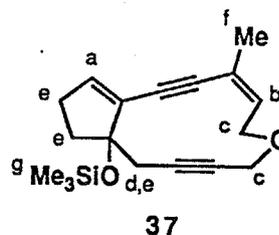


### protection of the alcohol **36**

To a mixture of the alcohol **36** (134 mg, 0.59 mmol), dry triethylamine (0.35 mL, 3 mmol), and dry dichloromethane (3 mL) was added trimethylsilyl trifluoromethanesulfonate (0.19 mL, 0.98 mmol) dropwise at 0 °C. After being stirred for 18 h at 20 °C, the reaction mixture was diluted with ether. The solution was washed with saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 20 : 1) to give the ether **37** (123 mg, 0.41 mmol, 70%). When this reaction was carried out at 30 °C, **39** was also obtained (~10%).

**1-trimethylsilyloxy-9-methyl-6-oxabicyclo[10.3.0]pentadec-8,12-diene-3,10-diyne (37)**  
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.10 (t, 1H, a, J = 2.8 Hz), 5.78 (m, 1H, b), 3.8 -4.3 (m, 4H, c), 2.56 (dt, 1H, d, J = 13, 2.6 Hz), 1.8 -2.54 (m, 5H, e), 1.95 (brs, 3H, f), 0.20 (s, 9H, g)  
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 137.8, 132.2, 131.5, 126.9, 91.8, 90.6, 85.9, 85.0, 78.6, 61.6, 55.9, 40.0, 33.1, 29.8, 22.6, 2.1

IR (neat) 2950, 2896, 2848, 2284, 2198, 1624, 1450, 1352, 1320, 1250, 1181, 1123, 1090, 1059, 988, 927, 894, 842, 756

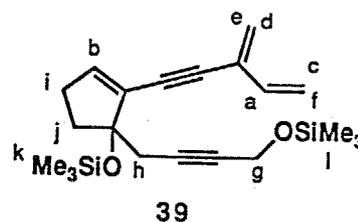


**1-(4-trimethylsilyloxy-2-butynyl)-2-(3-methylene-4-penten-1-ynyl)-2-cyclopenten-1-yl trimethylsilyl ether (39)**

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.368 (dd, 1H, a,  $J = 17.0, 10.1$  Hz), 6.205 (t, 1H, b,  $J = 2.75$  Hz), 5.702 (dd, 1H, c,  $J = 17.0, 0.92$  Hz), 5.520 (s, 1H, d), 5.433 (d, 1H, e,  $J = 0.92$  Hz), 5.256 (ddd, 1H, f,  $J = 10.1, 0.92, 0.92$  Hz), 4.252 (t, 1H, g,  $J = 2.29$  Hz), 2.671 (dt, 1H, h,  $J = 16.5, 2.92$  Hz), 2.655 (dt, 1H, h,  $J = 16.5, 2.29$  Hz), 2.5-2.6 (m, 1H, i), 2.3-2.47 (m, 2H, i,j), 1.97-2.07 (m, 1H, j), 0.152 (s, 3H, k or l), 0.124 (s, 3H, l or k)

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  139.9, 136.0, 130.6, 130.3, 123.4, 117.9, 89.1, 87.8, 86.9, 82.1, 79.6, 51.3, 36.8, 31.8, 30.9, 1.9, -0.3

IR ( $\text{CHCl}_3$  solution) 3026, 3008, 2956, 2440, 2396, 1602, 1252, 1176, 1145, 1122, 1082, 997, 923, 895, 864, 844



**1-hydroxy-6-methyl-6-vinylbicyclo[7.3.0]dodec-9-ene-3,7-diyn-5-yl acetate (40)**

To a solution of the protected cyclic ether **37** (74 mg, 0.25 mmol) in dry THF (7 mL) was added *t*-butyllithium (1.93 N, 1.2 eq, 0.20 mL) dropwise at  $-78$  °C. After 10 min, 3 mL of saturated ammonium chloride was added to the reaction mixture in one portion at the same temperature. After being stirred for 10 min at room temperature, the mixture was diluted with ether. The organic layer was washed with saturated ammonium chloride, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the crude **38** was used for the next reaction without further purification.

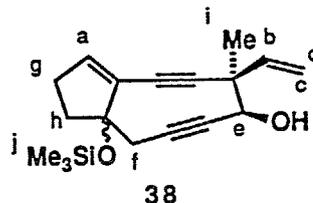
A mixture of the crude alcohol **38**, dichloromethane (2 mL) and pyridine (0.18 mL, 2.2 mmol) was added acetyl chloride (0.08 mL, 1.1 mmol) dropwise at  $0$  °C. After being stirred for 15 min at the same temperature, the reaction mixture was poured into water. The organic layer was washed with saturated copper sulfate, the aqueous layer was extracted with ether. The combined organic layer was washed

with saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, acetic acid, THF and water (4:1:1, 3 mL) was added to the residue at 20 °C. After being stirred for 1 h at the same temperature, the reaction mixture was diluted with ether. The solution was washed with saturated sodium bicarbonate several times and brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 5 : 1) to give the alcohol **40** (46 mg, 0.17 mmol, 68% from the cyclic ether **37**).

### 38

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 0.5% *i*-PrOH in hexane, 3.3 mL/ min);  
Rt=6.5-7.2 min

<sup>1</sup>H NMR of **38** (500 MHz, CDCl<sub>3</sub>) δ 5.945 (t, 1H, a, J = 2.75 Hz), 5.839 (dd, 1H, b, J = 16.95, 10.08 Hz), 5.502 (dd, 1H, c, J = 16.95, 1.38 Hz), 5.230 (dd, 1H, d, J = 10.08, 1.38 Hz), 4.037 (d, 1H, e, J = 9.16 Hz), 2.670 (d, 1H, f, J = 16.96 Hz), 2.564 (dddd, 1H, g, J = 18.3, 8.71, 5.50, 2.75 Hz), 2.482 (d, 1H, f, J = 16.96 Hz), 2.403 (dddd, 1H, g, J = 18.3, 9.16, 4.13, 2.75 Hz), 2.218 (ddd, 1H, h, J = 13.6, 8.71, 4.13 Hz), 1.941 (ddd, 1H, h, J = 13.6, 9.16, 5.50 Hz), 1.359 (s, 3H, i), 0.161 (s, 9H, j)



### 40

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.979 (t, 1H, a, J = 2.75 Hz), 5.671 (dd, 1H, b, J = 17.0, 10.1 Hz), 5.524 (dd, 1H, c, J = 17.0, 1.37 Hz), 5.165 (dd, 1H, d, J = 10.1, 1.37 Hz), 5.295 (brs, 1H, e), 2.679 (d, 1H, f, J = 17.0 Hz), 2.640 (dd, 1H, f, J = 17.0, 1.37 Hz), 2.616 (dddd, 1H, g, J = 18.3, 9.17, 5.50, 2.75 Hz), 2.422 (dddd, 1H, g, J = 18.3, 8.7, 4.13, 2.75 Hz), 2.180 (ddd, 1H, h, J = 13.7, 9.17, 4.13 Hz), 1.924 (ddd, 1H, h, J = 13.7, 8.7, 5.50 Hz), 2.041 (s, 3H, i), 1.417 (s, 3H, j)

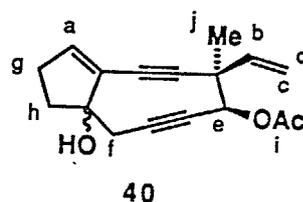
<sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) δ 5.654 (dd, 1H, c, J = 17.0, 1.84 Hz), 5.642 (t, 1H, a, J = 2.75 Hz), 5.595 (dd, 1H, b, J = 17.0, 9.62 Hz), 5.506 (brs, 1H, e), 5.002 (dd, 1H, d, J = 9.62, 1.84 Hz), 2.425 (d, 1H, f, J = 17.0 Hz), 2.153 (dddd, 1H, g, J = 17.9, 8.70, 5.04, 2.75 Hz), 2.109 (dd, 1H, f, J = 17.0, 1.5 Hz), 2.007 (ddd, 1H, h, J = 13.8, 8.70, 4.12 Hz), 1.840 (dddd, 1H, g, J = 17.9, 8.70, 4.12, 2.75 Hz), 1.520 (s, 1H, i), 1.393 (ddd, 3H, h, J = 13.8, 8.70, 4.12, 2.75 Hz), 1.279 (s, 3H, j)

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 170.0, 136.8, 134.6, 129.8, 116.9, 100.1, 93.2, 87.4, 87.0, 84.5, 72.9, 51.6, 36.5, 32.8, 30.2, 26.2, 20.9

$^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  169.4, 137.6, 134.2, 130.8, 116.7, 100.5, 93.9, 88.4, 87.2, 85.2, 73.2, 52.3, 36.7, 33.0, 30.3, 26.4, 20.3

IR (neat) 3440, 2930, 2850, 2352, 2210, 1742, 1453, 1370, 1228, 1149, 1063, 1023, 927, 850, 759.

MS(FD)  $m/z$  270 ( $\text{M}^+$ )



### 6-methyl-6-vinylbicyclo[7.3.0]dodeca-1,9-diene-3,7-diyn-5-yl acetate (41)

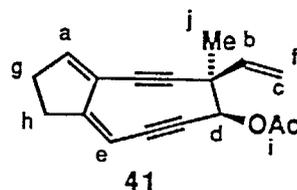
To a solution of the alcohol 40 (15 mg, 0.056 mmol) in dichloromethane (2 mL) and DMAP (100 mg, 0.82 mmol) was added dropwise distilled mesyl chloride (0.02 mL, 0.25 mmol) at 0 °C. After being stirred for 20 min at 20 °C, the reaction mixture was poured into water. The aqueous layer was extracted with ether and the combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . After concentration of the resulting solution to 1 mL, the residue was passed rapidly through a short pad of silica gel (Kieselgel 100, Art. 10185, Merck, elution with hexane : ether = 5 : 1). After removal of the solvent at -20 °C, thus obtained pure 41 (12 mg, 0.048 mmol, 86%) was dissolved with  $\text{C}_6\text{D}_6$  and immediately examined by NMR spectroscopy at room temperature. The labile 41 was easily decomposed in  $\text{CDCl}_3$  within three hours.

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  6.347 (m, 1H, a), 5.684 (dd, 1H, b,  $J = 16.95, 10.08$  Hz), 5.500 (dd, 1H, c,  $J = 16.95, 1.37$  Hz), 5.384 (dd, 1H, d,  $J = 1.38$  Hz), 5.282 (br, 1H, e), 5.161 (dd, 1H, f,  $J = 10.08, 1.37$  Hz), 2.718 (m, 2H, g or h), 2.587 (m, 2H, h or g), 2.039 (s, 3H, i), 1.452 (s, 3H, j)

$^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  5.926 (dt, 1H, a,  $J = 1.83, 3.0$  Hz), 5.69 - 5.71 (m, 3H, b,c,d), 5.108 (br, 1H, e), 5.079 (dd, 1H, f,  $J = 6.88, 4.58$  Hz), 2.08 - 2.12 (m, 2H, g), 1.88 - 1.92 (m, 2H, h), 1.640 (s, 3H, i), 1.385 (s, 3H, j)

$^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ , 0.06 M)  $\delta$  164.9, 161.1, 140.6, 136.6, 130.5, 117.6, 105.2, 101.4, 100.5, 98.7, 92.7, 79.9, 60.4, 42.0, 41.5, 37.6, 32.6

IR ( $\text{CCl}_4$  soln.) 2956, 2926, 2854, 2184, 1742, 1369, 1228, 1122, 1071, 1018, 975, 926.

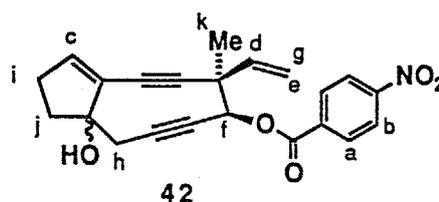


**1-hydroxy-6-methyl-6-vinylbicyclo[7.3.0]dodec-9-ene-3,7-diyn-5-yl *p*-nitrobenzoate (42)**

A mixture of the alcohol **38** (39 mg, 0.13 mmol), dichloromethane (2 mL) and pyridine (0.2 mL, 2.5 mmol) was added *p*-nitrobenzoyl chloride (72 mg, 0.39 mmol) dropwise at 0 °C. After being stirred for 4 h at room temperature, the reaction mixture was poured into water. The organic layer was washed with saturated copper sulfate, the aqueous layer was extracted with ether. The combined organic layer was washed with saturated copper sulfate, saturated sodium bicarbonate, brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, a mixture of acetic acid, THF and water (4:1:1, 5 mL) was added to the residue at 20 °C. After being stirred for 30 min at the same temperature, the reaction mixture was diluted with ether. The solution was washed with ice-cooled saturated sodium bicarbonate several times and brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 5 : 1) to give the alcohol **42** (28 mg, 0.074 mmol, 57%).

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 8.272 (d, 1H, a or b, J = 9.2 Hz), 8.156 (d, 1H, b or a, J = 9.2 Hz), 6.034 (t, 1H, c, J = 2.75 Hz), 5.376 (dd, 1H, d, J = 17.0, 10.1 Hz), 5.594 (dd, 1H, e, J = 17.0, 1.38 Hz), 5.480 (s, 1H, f), 5.154 (dd, 1H, g, J = 10.1, 1.38 Hz), 2.707 (d, 1H, h, J = 17.4 Hz), 2.690 (d, 1H, h, H = 17.4 Hz), 2.638 (dddd, 1H, i, J = 18.3, 8.9, 5.0, 2.75 Hz), 2.452 (dddd, 1H, i, J = 18.3, 8.7, 4.1, 2.75 Hz), 2.187 (ddd, 1H, j, J = 14.2, 8.9, 4.1 Hz), 1.950 (ddd, 1H, j, J = 14.2, 8.7, 5.0 Hz), 1.503 (s, 3H, k)

<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) δ 163.7, 150.8, 136.7, 135.05, 135.02, 130.9, 129.7, 123.7, 117.4, 99.7, 94.2, 87.9, 87.1, 84.0, 74.6, 51.9, 36.6, 32.9, 30.3, 26.3

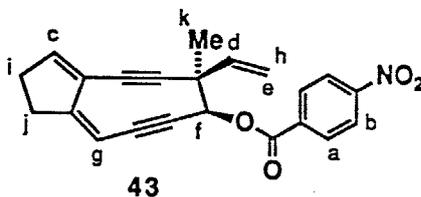


**6-methyl-6-vinylbicyclo[7.3.0]dodec-1,9-diene-3,7-diyn-5-yl *p*-nitrobenzoate (43)**

To a solution of the alcohol **42** (7 mg, 0.018 mmol) in dichloromethane (1 mL) and DMAP (100 mg, 0.82 mmol) was added dropwise distilled mesyl chloride (0.02 mL, 0.25 mmol) at -20 °C. After being stirred for 1 h at 10 °C, the reaction mixture was poured into water. The aqueous layer was extracted with ether and the combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 10 : 1) to give the dehydrated product **43** (3 mg, 0.008 mmol, 42%).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.260 (d, 1H, a or b,  $J = 8.5$  Hz), 8.178 (d, 1H, b or a,  $J = 8.5$  Hz), 6.396 (s, 1H, c), 5.760 (dd, 1H, d,  $J = 17.0, 10.1$  Hz), 5.572 (d, 1H, e,  $J = 17.0$  Hz), 5.536 (s, 1H, f), 5.299 (s, 1H, g), 5.163 (d, 1H, h,  $J = 10.1$  Hz), 2.7-2.8 (m, 2H, i or j), 2.58-2.65 (m, 2H, j or i), 1.531 (s, 3H, k)

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  165.8, 163.8, 150.7, 143.2, 136.7, 135.2, 131.0, 127.4, 123.5, 116.9, 101.2, 97.2, 95.3, 95.0, 87.8, 75.0, 51.4, 31.3, 30.7, 26.0



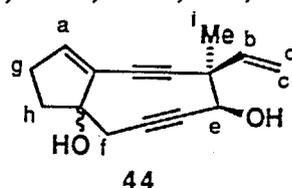
**6-methyl-6-vinylbicyclo[7.3.0]dodec-9-ene-3,7-diyne-1,5-diol (44)**

To a solution of the protected cyclic ether **37** (60 mg, 0.20 mmol) in dry THF (6 mL) was added *t*-butyllithium (1.93 N, 1.5 eq, 0.16 mL) dropwise at  $-78$  °C. After 10 min, 2 mL of saturated ammonium chloride was added to the reaction mixture in one portion at the same temperature. After being stirred for 10 min at room temperature, the mixture was diluted with ether. The organic layer was washed with saturated ammonium chloride, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, acetic acid, THF and water (4:1:1, 3 mL) was added to the crude **38** at  $20$  °C. After being stirred for 2 h at the same temperature, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with dichloromethane. The combined organic layer was washed with saturated sodium bicarbonate and brine, and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 2 : 1) to give the diol **44** (32 mg, 0.14 mmol, 70%).

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.990 (t, 1H, a,  $J = 2.75$  Hz), 5.800 (dd, 1H, b,  $J = 16.5, 10.1$  Hz), 5.523 (d, 1H, c,  $J = 16.5$  Hz), 5.237 (d, 1H, d,  $J = 10.1$  Hz), 4.071 (s, 1H, e), 2.698 (d, 1H, f,  $J = 17.0$  Hz), 2.603 (d, 1H, f,  $J = 17.0$  Hz), 2.57-2.67 (m, 1H, g), 2.388 (dddd, 1H, g,  $J = 17.9, 8.70, 3.67, 2.75$  Hz), 2.142 (ddd, 1H, h,  $J = 13.8, 8.25, 3.67$  Hz), 1.897 (ddd, 1H, h,  $J = 13.8, 8.70, 5.95$  Hz), 1.366 (s, 3H, i)

$^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  137.9, 135.1, 129.8, 116.9, 100.8, 91.4, 87.5, 87.4, 86.6, 73.2, 53.13, 37.3, 32.5, 30.1, 26.1

IR( $\text{CHCl}_3$ , solution) 3406, 2928, 2854, 2204, 1602, 1528, 1283, 1069, 1038, 1014, 924, 849



**methyl (7-methyl-6-oxo-7-vinyl-1,2,3,5,6,7-hexahydro-1*S*-indacenylthio)acetate (47)**

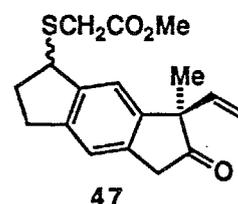
To a mixture of dry dimethyl sulfoxide (0.40 mL, 5.6 mmol) and dry dichloromethane (3 mL) was added distilled oxalyl chloride (0.24 mL, 2.8 mmol) at -78 °C. After 30 min, a solution of the diol 44 in dry dichloromethane (3 mL) was added to the mixture at the same temperature. After 1 h, dry triethylamine (2 mL) was added to the reaction mixture at -78 °C. After the suspension was stirred for 30 min at -30 °C, methyl thioglycolate (0.1 mL) was added dropwise to the resulting solution of 45 at the same temperature. After being stirred for 30 min at -30 °C, the reaction mixture was poured into water and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 12 : 1) to give a 1 : 1 mixture of diastereomers 47 (24 g, 0.076 mmol, 54%).

PLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, 10% ethyl acetate in hexane, 3 L/min); Rt=20-22 min

<sup>1</sup>H NMR (500 MHz, CD<sub>2</sub>Cl<sub>2</sub>); see attached spectra.

IR (neat); 2954, 2926, 2854, 1743, 1601, 1436, 1286, 1262, 1126, 1009, 930, 809

MS (FD); m/z 316 (M<sup>+</sup>)

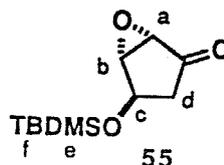


**(1*S*,3*R*,4*R*\*)-4-(*t*-butyldimethylsilyloxy)-2,3-epoxycyclopentanone (55)**

To a mixture of 2-(*t*-butyldimethylsilyloxy)-3-cyclopentenone (54) (13.4 g, 63.6 μmol) in dichloromethane (200 mL) and tetrabutylammonium hydrogensulfate (1.3 g, 3.8 mmol) was added 10% aqueous solution of sodium hypochlorite (33 mL, 445 μmol) dropwise at 0 °C. After being stirred for 24 h at room temperature, the reaction mixture was poured into an aqueous solution of saturated sodium bisulfate. The aqueous layer was extracted with ether and combined organic layer was washed with saturated ammonium chloride and brine. The organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 85: 15) to give the epoxide 55 (10.3 g, 45.2 μmol, 71%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  4.60 (brd, 1H, c,  $J = 5.7$  Hz), 3.79 (d, 1H, a,  $J = 2.1$  Hz), 3.40 (brd, 1H, b,  $J = 2.1$  Hz), 2.61 (dd, 1H, d,  $J = 18.0, 5.7$  Hz), 1.93 (dd, 1H, d,  $J = 18.0$  Hz), 0.89 (s, 9H, f), 0.12 (s, 6H, e)

IR(neat) 2930, 2856, 1756, 1470, 1396, 1347, 1258, 1161, 1084, 1006, 977, 902, 782, 669, 433

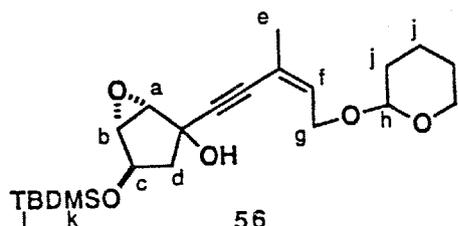


(2*S*\*,3*R*\*,4*R*\*)-4-(*t*-butyldimethylsilyloxy)-1-[(*Z*)-5-(tetrahydro-2*H*-pyran-2-yloxy)-3-methyl-3-penten-1-ynyl]-2,3-epoxycyclopentanol (56)

To a solution of (*Z*)-1-(tetrahydro-2*H*-pyran-2-yloxy)-3-methyl-2-penten-4-yne (34) (1.04 g, 5.78 mmol) in dry THF (20 mL) was added dropwise a solution of butyllithium (1.84 N, 2.9 mL, 5.33 mmol) at  $-78$  °C. After 1 h, a solution of the ketone 55 (1.01 g, 4.4 mmol) in dry THF (10 mL) was added dropwise at the same temperature. The temperature gradually rose up to  $-50$  °C. The reaction mixture was poured into an aqueous solution of saturated ammonium chloride, and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 2 : 1) to give the 1,2-adduct 56 (1.37 g, 3.33 mmol, 75%).

$^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  5.83 (dd, 1H, f,  $J = 7.41, 6.59$  Hz), 4.69 (m, 1H, h), 4.45 (d, 1H, c,  $J = 5.29$  Hz), 4.28 (d, 1H, g,  $J = 7.41$  Hz), 4.25 (m, 1H, g), 3.79-3.93 (m, 1H, i), 3.56 (d, 1H, a,  $J = 2.36$  Hz), 3.44-3.58 (m, 1H, i), 3.38 (dd, 1H, b,  $J = 2.36$  Hz), 2.06 (d, 1H, d,  $J = 13.9$  Hz), 1.89 (dd, 1H, d,  $J = 13.9, 5.29$  Hz), 1.83 (s, 3H, e), 1.4-1.8 (m, 6H, j), 0.845 (s, 9H, l), 0.04 (s, 6H, k)

IR(neat) 3422, 2946, 2242, 1632, 1384, 1253, 1121, 1020, 908, 838, 733, 429

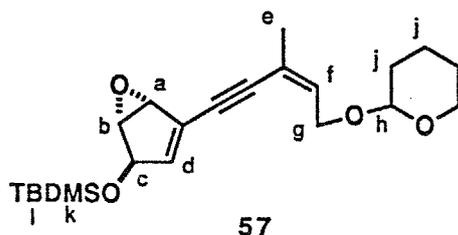


**(3*R*\*,4*R*\*,5*R*\*)-3-(*t*-butyldimethylsilyloxy)-1-[(*Z*)-5-(tetrahydro-2*H*-pyran-2-yloxy)-3-methyl-3-penten-1-ynyl]-4,5-epoxy-1-cyclopentene (57)**

To a solution of the alcohol **56** (1.53 g, 3.75 mmol) in freshly distilled dry dichloromethane (30 mL) was added 2,6-lutidine (1.30 mL, 11.25 mmol) and trifluoromethanesulfonic acid anhydride (0.63 mL, 3.75 mmol) dropwise at -78 °C. After being stirred for 20 min at the same temperature, the reaction mixture was poured into water. The aqueous layer was extracted with ether and combined organic layer was washed with saturated copper sulfate, sodium bicarbonate, and brine. The organic solution was dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 10 : 1) to give the diene monoxide **57** (786 mg, 2.02 mmol, 54%).

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 6.12 (m, 1H, d), 6.10 (m, 1H, f), 4.61 (m, 2H, c,h), 4.34-4.10 (m, 2H, g), 3.94-3.78 (m, 3H, a,b,i), 3.44-3.58 (m, 1H, j), 1.85 (m, 3H, e), 0.90 (m, 9H, l), 0.12 (m, 6H, k)

IR(neat) 2948, 2192, 1632, 1593, 1460, 1202, 1024, 834, 671

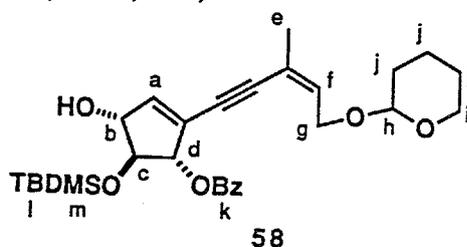


**1*S*\*,2*S*\*,3*R*\*)-2-(*t*-butyldimethylsilyloxy)-5-[(*Z*)-5-(tetrahydro-2*H*-pyran-2-yloxy)-3-methyl-3-penten-1-ynyl]-3-hydroxy-4-cyclopentenyl benzoate (58)**

A mixture of palladium acetate (50.6 mg, 20 mol%, 0.226 mmol), triphenylphosphine (237 mg, 0.904 mmol), and benzoic acid (415.3 mg, 3.4 mmol) was stirred for 1 h at room temperature. To the mixture was added a solution of diene monoxide **57** (442.6 mg, 1.13 mmol) in THF (5 mL) dropwise at 0 °C. After being stirred for 24 h at room temperature, the reaction mixture was filtered through Celite with hexane. The filtrate was washed with saturated sodium bicarbonate and brine. The organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 1 : 1) to give the benzoate **58** (515 mg, 1.0 mmol, 89%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 8.31-7.26 (m, 5H, k), 6.21 (m, 1H, a), 5.85 (m, 2H, f,d), 4.79 (m, 1H, b), 4.70-4.40 (m, 2H, c,h), 4.30-3.20 (m, 2H, g,i), 1.70 (m, 3H, e), 2.0-1.2 (m, 6H, j), 0.86 (m, 9H, l), 0.05 (m, 6H, m)

IR(neat) 3436, 2950, 2194, 1727, 1602, 1452, 1265, 1115, 1025, 838, 712



(2*S*\*,3*R*\*)-2-(*t*-butyldimethylsilyloxy)-3-(tetrahydro-2*H*-pyran-2-yloxy)-5-[(*Z*)-5-(tetrahydro-2*H*-pyran-2-yloxy)-3-methyl-3-penten-1-ynyl]-4-cyclopentenone (61)

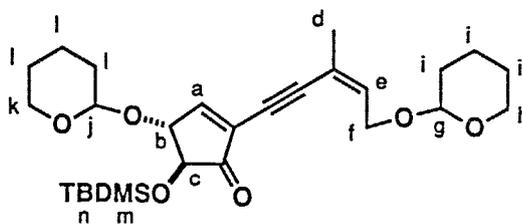
To a solution of the alcohol **58** (837 mg, 1.63 mmol) and dihydropyran (0.22 mL, 2.42 mmol) in dichloromethane (10 mL) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. The reaction mixture was stirred for 20 min at room temperature. To the organic solution was added large excess of triethylamine and the mixture was concentrated *in vacuo*. The residue was used for the next reaction without further purification.

To a solution of the crude ether **59** in methanol was added potassium carbonate (2.0 g, 14.4 mmol) at room temperature. After being stirred for 24 h at the same temperature, the reaction mixture was filtered through Celite with hexane. The filtrate was washed with brine and the organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was used for the next reaction without further purification.

To a solution of the crude **60** in dichloromethane (15 mL) was added pyridinium chlorochromate (1.05 g, 4.89 mmol) at room temperature. After being stirred for 8 h at the same temperature, the reaction mixture was diluted with dichloromethane. The organic solution was passed through florisil and the filtrate was washed with saturated sodium bicarbonate, brine, and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with benzene : ethyl acetate = 75 : 1) to give the enone **61** (463 mg, 0.95 mmol, 58%)

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.44 (d, 1H, a, *J* = 2.2 Hz), 4.86 (m, 1H, e), 3.4-5.0 (m, 10H, b,c,f,g,i,j,k), 1.91 (d, 3H, d, *J* = 1.1 Hz), 1.2-2.0 (m, 6H, h,l), 0.91 (m, 9H, n), 0.17 (m, 6H, m)

IR(neat) 3456, 2932, 2202, 1738, 1463, 1256, 1120, 1033, 839, 782, 733

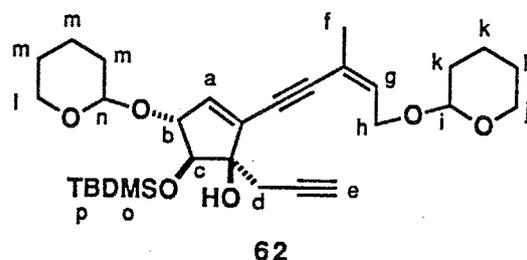


61

**(2S\*,3R\*)-2-(*t*-butyldimethylsilyloxy)-1-(2-pentynyl)-3-(tetrahydro-2H-pyran-2-yloxy)-4-[(Z)-5-(tetrahydro-2H-pyran-2-yloxy)-3-methyl-3-penten-1-ynyl]-4-cyclopentenol (62)**

To a solution of the enone **61** (45.1 mg, 0.092 mmol) in dry ether (2 mL) was added an ether solution of propargylmagnesium bromide (1.2 N, 0.20 mL, 0.22 mmol) dropwise at 0 °C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into ice-cooled saturated ammonium chloride with vigorous stirring. The aqueous layer was extracted with ether. Then the combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with benzene : ethyl acetate = 15 : 1) to give the alcohol **62** (39.0 mg, 0.074 mmol, 80%).

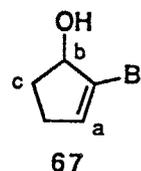
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.17 (m, 1H, a), 6.02, (m, 1H, g), 4.0-4.8 (m, 6H, b,c,h,i,n), 3.4-4.0 (m, 4H, j,l), 2.5 (m, 2H, d), 2.0 (m, 1H, e), 1.85 (m, 3H, f), 1.4-2.0 (m, 12H, m), 0.93 (m, 9H, p), 0.17 (m, 6H, o)



**2-bromo-2-cyclopenten-1-ol (67)**

To a mixture of 2-bromo-2-cyclopenten-1-one (**15**) (5.9 g, 37 mmol), cerium(III) chloride heptahydrate (13.6 g, 37 mmol), and methanol (90 mL) was added sodium borohydride (1.4 g, 37 mmol) portionwise at 0 °C. After being stirred for 1 h, the reaction mixture was poured into 1 N HCl solution. The aqueous layer was extracted with dichloromethane and the organic layer was washed with saturated sodium bicarbonate and brine. The resultant organic solution was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was column chromatographed on silica gel (elution with hexane : ether = 6 : 1) to give the alcohol **67** (3.4 g, 21 mmol, 57%).

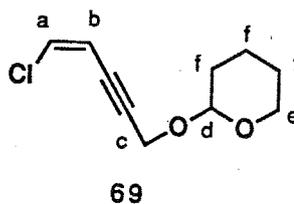
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.04 (m, 1H, a), 4.5-4.8 (br, 1H, b), 2.0-2.6 (m, 4H, c)  
IR(neat) 3250-3500, 2920, 2850, 1620, 1430, 1320, 1160, 1040, 1020, 980, 920, 900, 810



**tetrahydro-2-[(Z)-5-chloro-4-penten-2-ynyloxy]-2H-pyran (69)**

To a mixture of palladium acetate (3 mol%, 44 mg), triphenylphosphine (12 mol%, 240 mg), CuI (6 mol%, 80 mg) and *t*-butylamine (1.5 mL, 14.3 mmol) in benzene (14 mL) was added (Z)-1,2-dichloroethylene (68) (2.7 mL, 35.7 mmol) and a solution of tetrahydro-2-(2-propynyloxy)-2H-pyran (18) (1.0 g, 7.14 mmol) in benzene (10 mL) at 20 °C. After being stirred for 2 h at the same temperature, the reaction mixture was diluted with hexane and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution, 1N HCl, saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 13 : 1) to give the enyne 69 (1.13 g, 5.64 mmol, 79%).

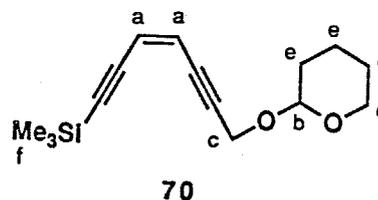
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.40 (d, 1H, a, J = 7.5 Hz), 5.90 (dt, 1H, b, J = 7.5, 2.0 Hz), 4.88 (brs, 1H, d), 4.46 (d, 2H, c, J = 2.0 Hz), 3.36-4.0 (m, 2H, e), 1.4-2.1 (m, 6H, f)  
IR(neat) 3080, 3020, 2940, 2860, 1590, 1450, 1440, 1340, 1260, 1200, 1180, 1120, 1080, 1060, 1020, 940, 900, 870, 790, 760, 720, 640



**tetrahydro-2-[(Z)-7-trimethylsilyl-4-heptene-2,6-diynyloxy]-2H-pyran (70)**

To a mixture of palladium acetate (3 mol%, 47 mg), triphenylphosphine (12 mol%, 254 mg), CuI (6 mol%, 91 mg) and *t*-butylamine (1.7 mL, 16 mmol) in benzene (15 mL) was added a solution of alkenyl chloride 69 (1.6 g, 8 mmol) in benzene (5 mL) and a solution of trimethylsilylacetylene (3.4 mL, 24 mmol) in benzene (5 mL) at 5 °C. After being stirred for 2 h at room temperature, the reaction mixture was diluted with hexane and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution, 1N HCl, saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 20 : 1) to give the enediyne 70 (3.5 g, 13.3 mmol, 89%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.84 (brs, 2H, a), 4.87 (br, 1H, b), 4.46 (brs, 2H, c), 3.4-4.0 (m, 2H, d), 1.4-2.0 (m, 6H, e), 0.215 (s, 9H, f)  
IR(neat) 2940, 2130, 1440, 1390, 1250, 1120, 1080, 1050, 1020, 940, 900, 840, 790, 760, 630



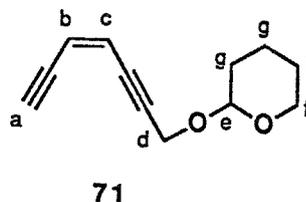
**tetrahydro-2-[(Z)-4-heptene-2,6-diynoxy]-2H-pyran (71)**

To a solution of **70** (3.5 g, 13.0 mmol) in THF (25 mL) was added tetrabutylammonium fluoride (1.0 g) in several portions at 0 °C. After being stirred for 10 min, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ether = 10 : 1) to give the deprotected enediyne **71** (2.4 g, 12.7 mmol, 95%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.94 (ddt, 1H, c, J = 11.0, 0.4, 1.5 Hz), 5.84 (dd, 1H, b, J = 11.0, 1.9 Hz), 4.90 (brs, 1H, e), 4.47 (d, 2H, d, J = 1.5 Hz), 3.4-4.0 (m, 2H, f), 3.33 (d, 1H, a, J = 1.9 Hz), 1.4-2.0 (m, 6H, g)

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 121.2, 118.7, 97.2, 96.8, 93.7, 84.7, 80.6, 62.1, 54.7, 30.4, 25.5, 19.2

IR(neat) 3280, 2940, 2860, 1200, 1120, 1020, 900, 870, 790

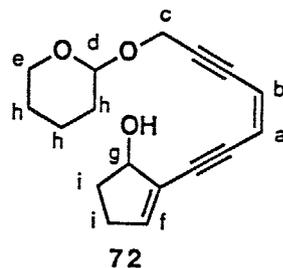


**2-[(Z)-7-(tetrahydro-2H-pyran-2-yloxy)-3-heptene-1,5-diynyl]-2-cyclopenten-1-ol (72)**

To a mixture of palladium acetate (3 mol%, 34 mg), triphenylphosphine (12 mol%, 182 mg), CuI (6 mol%, 66 mg) and *t*-butylamine (1.2 mL, 10.5 mmol) in benzene (12 mL) was added a solution of alkenyl bromide **67** (940 mg, 5.77 mmol) in benzene (5 mL) and a solution of enediyne **71** (993 mg, 5.23 mmol) in benzene (5 mL) at 5 °C. After being stirred for 2 h at room temperature, the reaction mixture was diluted with hexane and filtered by cotton. The filtrate was washed with ammonia-ammonium chloride pH 8 buffer solution, 1N HCl, saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 10 : 1) to give the enediyne **72** (495 mg, 1.82 mmol, 35%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.24 (br, 1H, f), 5.94 (d, 1H, a,  $J = 10.7$  Hz), 5.84 (dt, 1H, b,  $J = 10.7, 1.8$  Hz), 4.93 (br, 1H, d), 4.6-4.9 (br, 1H, g), 4.45 (d, 2H, c,  $J = 1.8$  Hz), 3.3-4.0 (m, 2H, e), 2.0-2.4 (m, 4H, i), 1.3-2.0 (m, 6H, h)

IR(neat) 3400-3500, 2950, 2850, 2190, 1200, 1120, 1020, 900, 870, 820, 740



### 2-[(Z)-7-bromo-3-heptene-1,5-diynyl]-2-cyclopenten-1-ol (76)

To a solution of the alcohol **72** (495 mg, 1.82 mmol) in pyridine (3 mL) was added acetic anhydride (0.6 mL, 6 mmol) at 0 °C. After being stirred for 6 h at room temperature, the reaction mixture was diluted with ether. The solution was washed with ice-cooled 1N HCl and saturated sodium bicarbonate and brine. The organic layer was dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

To the crude acetate **73** in methanol (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid at room temperature. After being stirred for 3 h at the same temperature, the reaction mixture was poured into an aqueous solution of saturated sodium bicarbonate. The aqueous layer was extracted with dichloromethane and organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

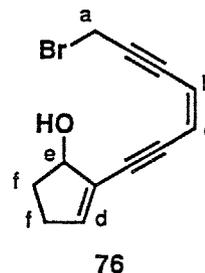
To a solution of the crude alcohol **74** in dry acetonitrile (18 mL) was added tetrabromomethane (1.5 eq, 900 mg) and triphenylphosphine (1.5 eq, 710 mg) in one portion at 0 °C. After being stirred for 30 min at the same temperature, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with ether and the combined organic layer was washed with brine three times and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

To a solution of crude bromide **75** in methanol (20 mL) was added potassium carbonate (1.0 g) at the room temperature. After being stirred for 3 h, the reaction mixture was filtered with Celite and the filtrate was concentrated *in vacuo*. After the removal of the solvent, the residue was purified by the column chromatography on silica gel (elution with hexane : ether = 10: 1) to give the bromo alcohol **76** (240 mg, 0.96 mmol, 53% from **72**).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.28 (m, 1H, e), 5.97 (d, 1H, c,  $J = 10.8$  Hz), 5.86 (dt, 1H, b,  $J = 10.8, 1.9$  Hz), 4.7-4.95 (m, 1H, e), 4.16 (d, 2H, a,  $J = 1.9$  Hz), 2.1-2.7 (m, 4H, f)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  141.5, 128.2, 121.1, 118.2, 93.2, 92.1, 89.5, 84.2, 78.8, 32.8, 31.4, 15.0

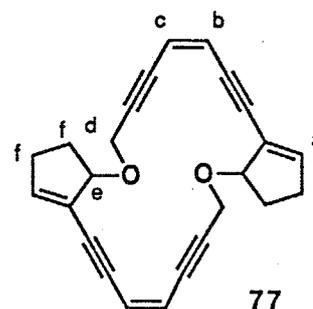
IR(neat) 3300-3400, 3040, 2920, 2840, 2170, 1040, 920, 740, 600



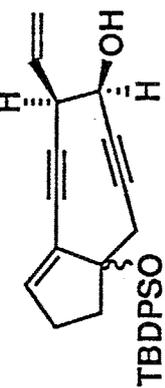
### O-alkylation of 76

To a suspension of KH (20 mg, 0.5 mmol) washed with dry hexane (3 mL X 3) and 18-crown-6 (30 mg) in dry THF (10 mL) was slowly added a solution of the bromo alcohol **76** (26 mg, 0.10 mmol) in dry THF (10 mL) dropwise over 3.5 h at  $-78$  °C. After being stirred for 6 h at  $-20$  °C, the reaction mixture was poured into saturated ammonium chloride and the aqueous solution was extracted with ether. The combined organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ether = 10 : 1) to give the cyclic ether **77** (7 mg, 0.04 mmol, 40%).

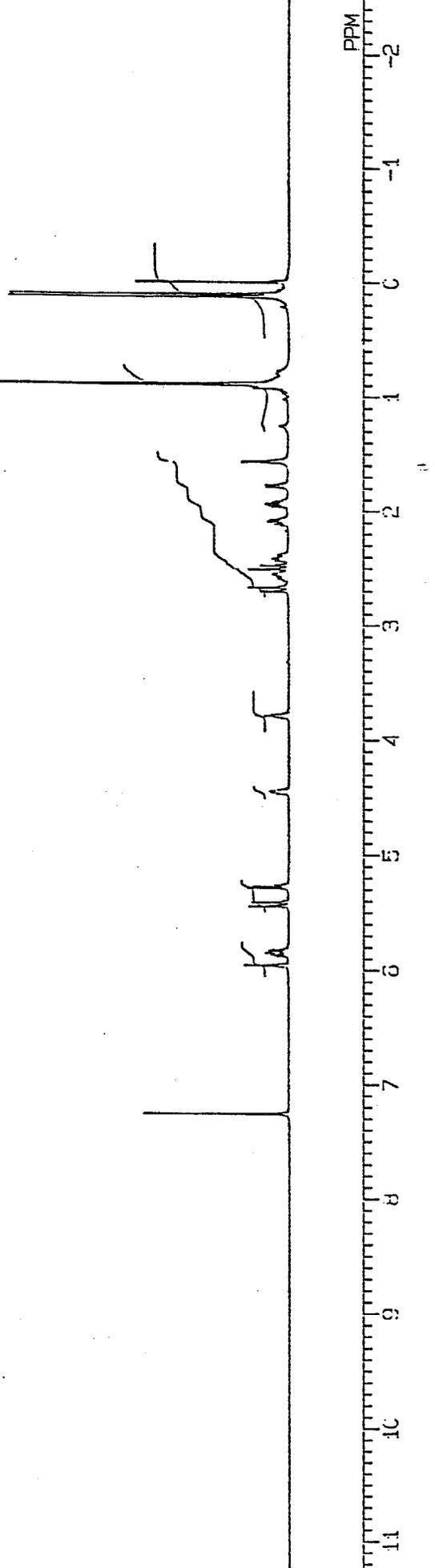
$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.34 (t, 1H, a,  $J = 2.9$  Hz), 5.94 (d, 1H, b,  $J = 9.0$  Hz), 5.88 (d, 1H, c,  $J = 9.0$  Hz), 4.81 (brs, 2H, d), 4.6-4.8 (m, 1H, e), 1.7-2.6 (m, 4H, f)



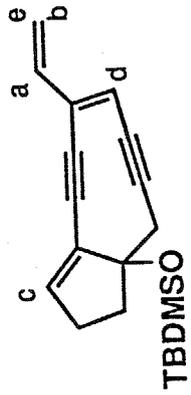
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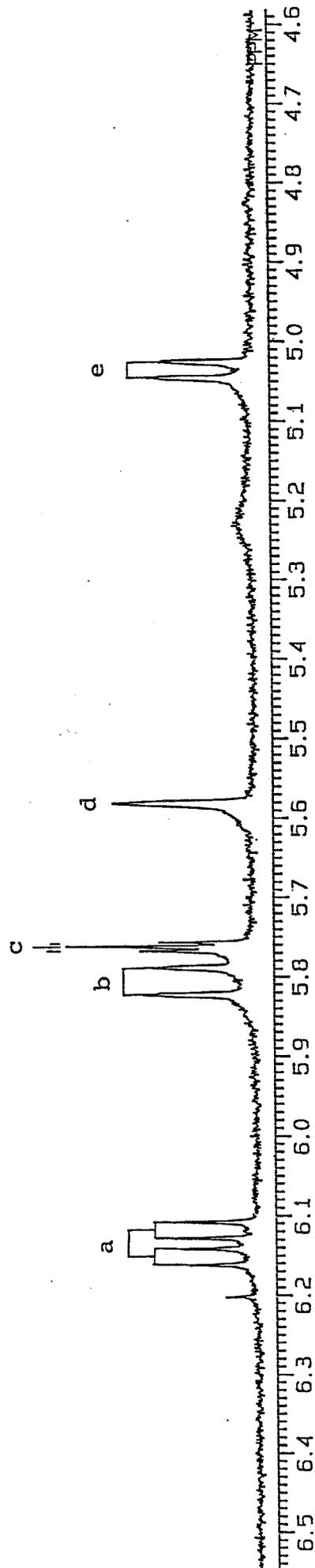
26b (CDCl<sub>3</sub>)

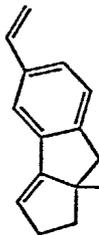


partial  $^1\text{H}$  NMR spectrum



28 ( $\text{C}_6\text{D}_6$ )





TDDMSO

30 (CDCl<sub>3</sub>)

NUCLEUS

OBS. (MHz)

<sup>13</sup>C (125.05 (122.5) (115.03))

<sup>1</sup>H (199.60 (189.00) (159.80))

□ ( ) □ ( ) □ ( ) □ ( )

LOCK

<sup>2</sup>D/<sup>1</sup>I

IRR.

SOLVENT

CONCENTRATION

REFERENCE

TEMPERATURE

OFFSET

OBS.(AF)

IRR.

PULSE

WIDTH (PW)

INTERVAL (PI)

REPETITION (PR)

DATA POINTS (FID)

WINDOW EX-

NO. OF PULSES

SPECTRAL WIDTH

AMPLITUDE

DECOUPLING

LINEAR COM. CORR.

NOISE

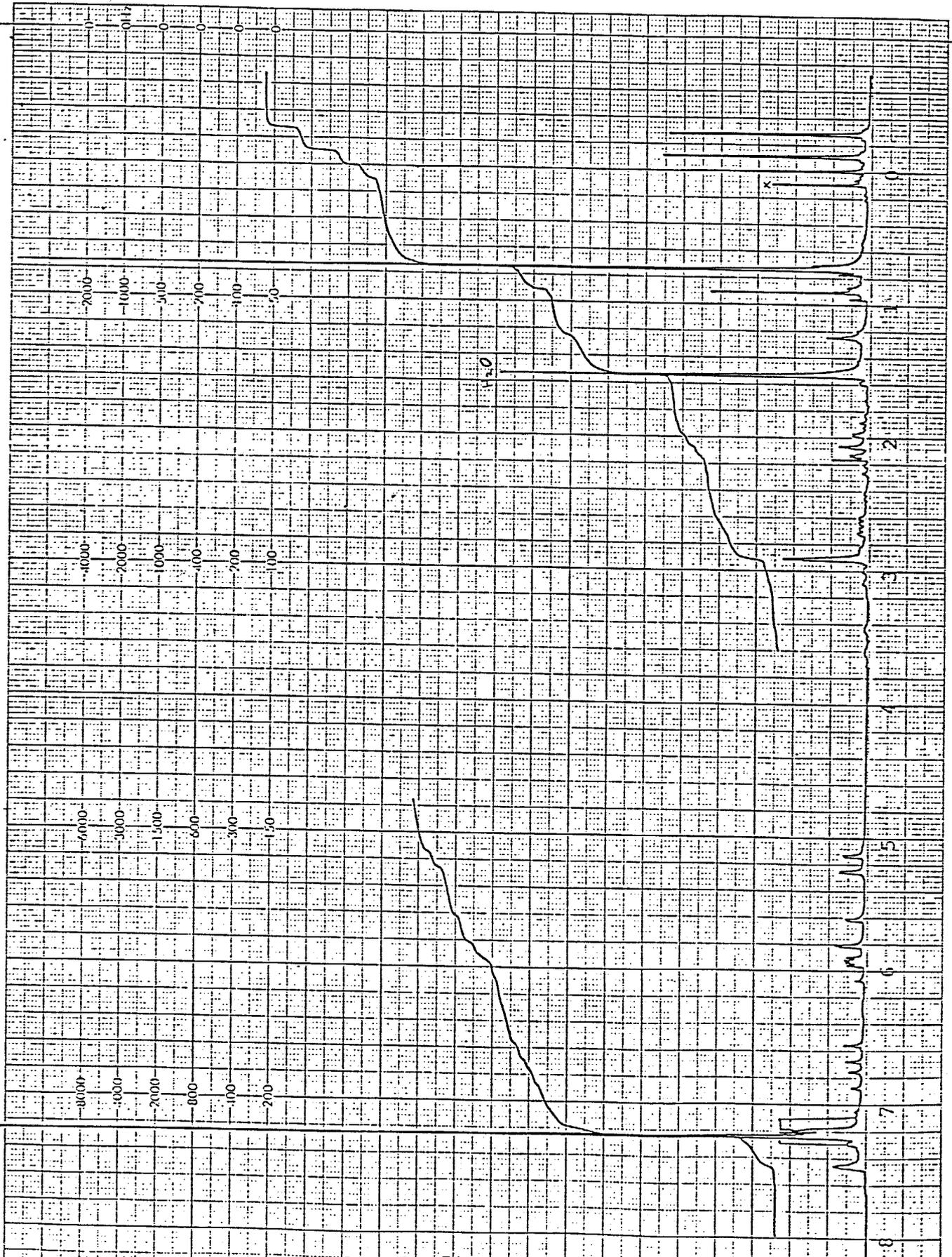
DATE

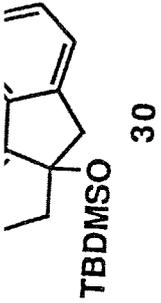
OPERATOR

REMARKS: ADRES

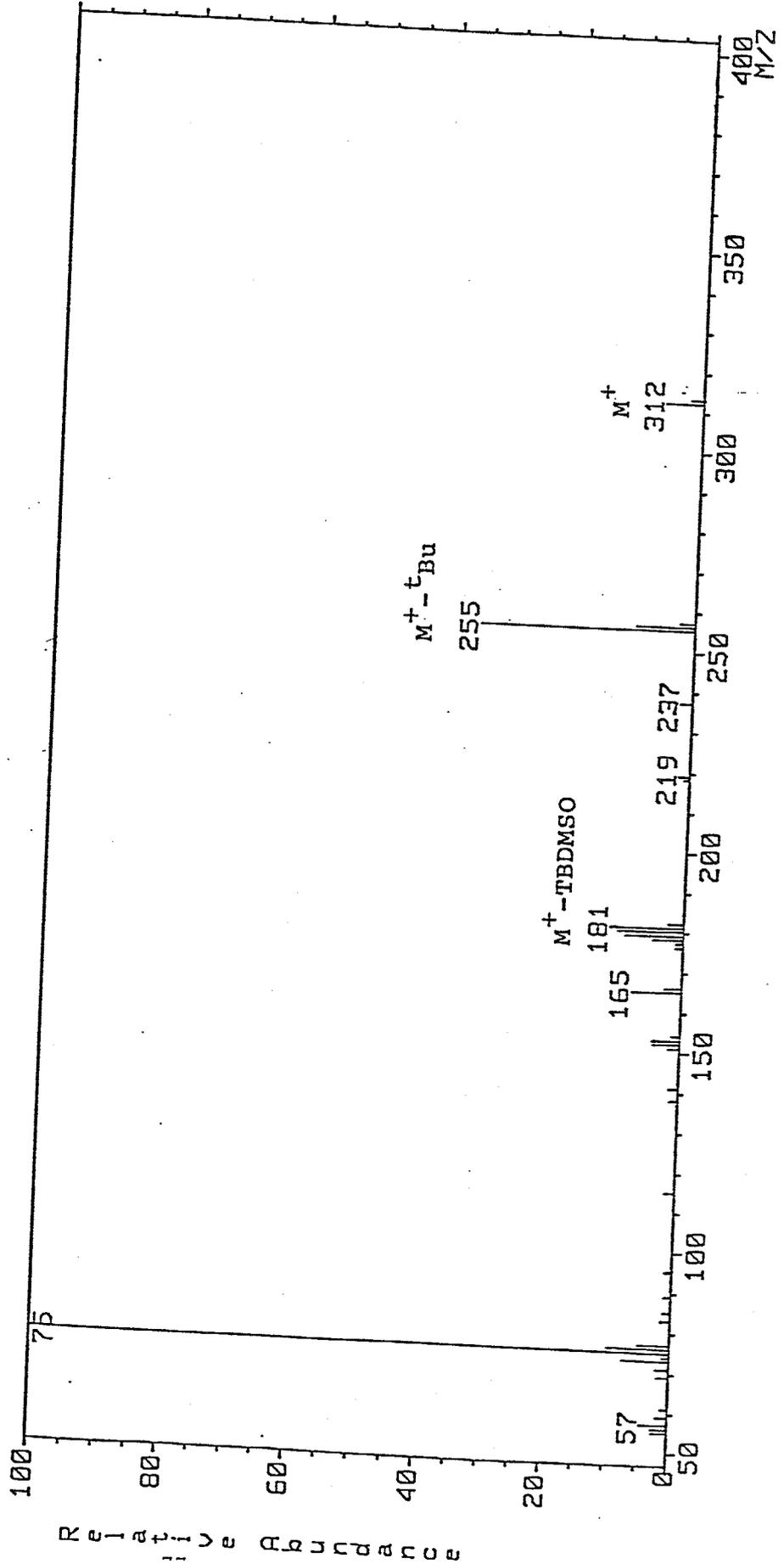
AMOUNT

NOISE





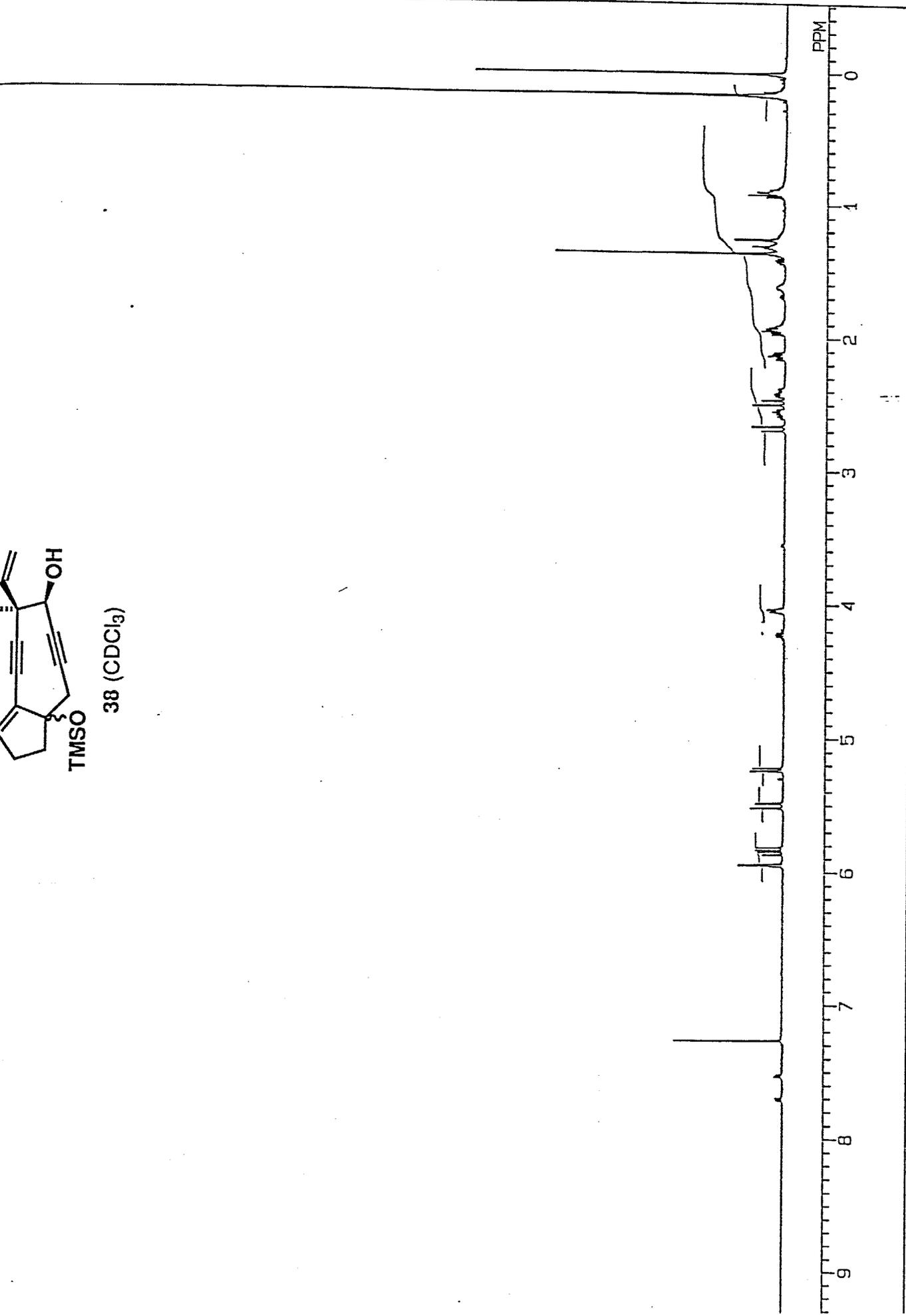
MASS SPECTRUM  
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Scan# (655)



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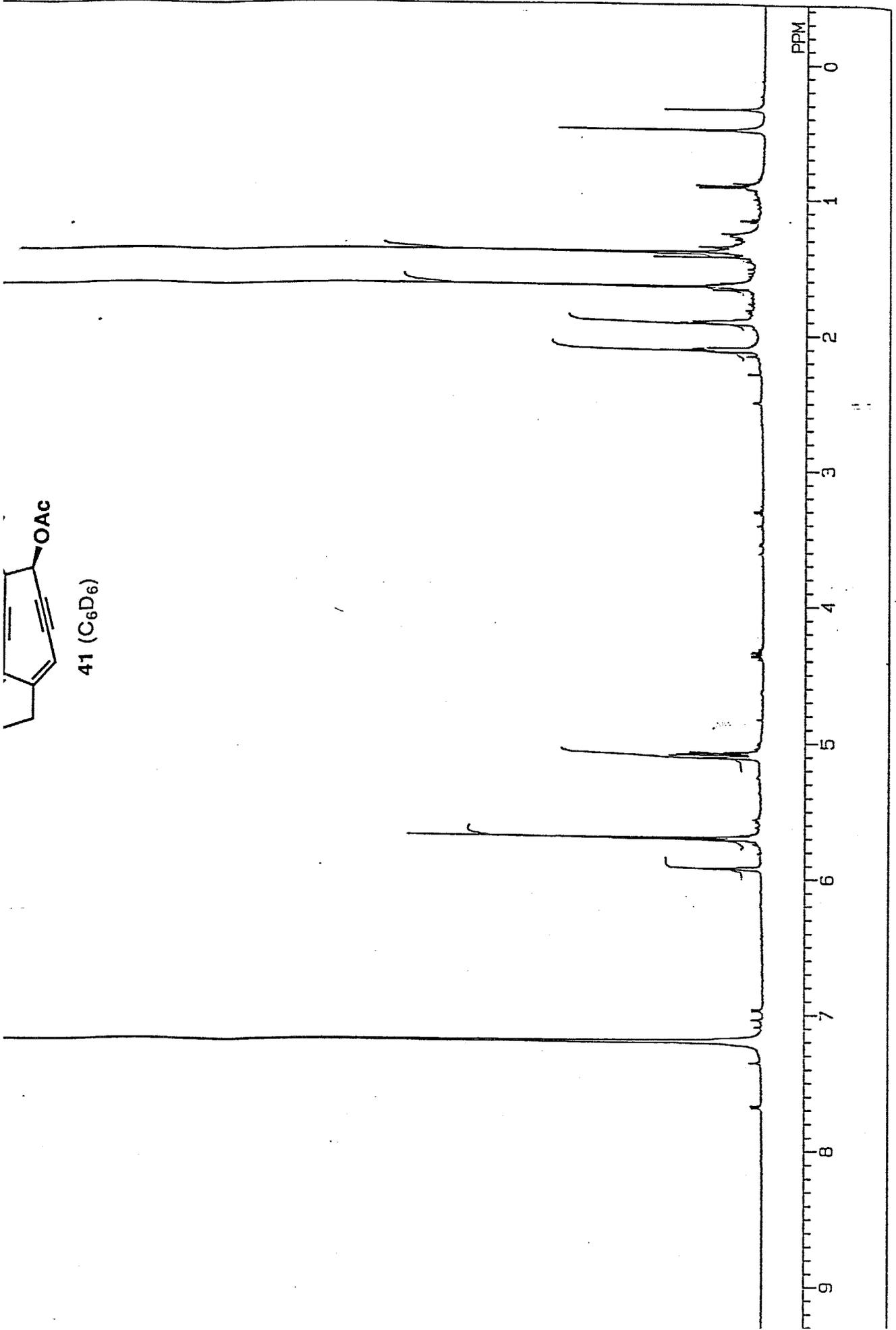


38 (CDCl<sub>3</sub>)



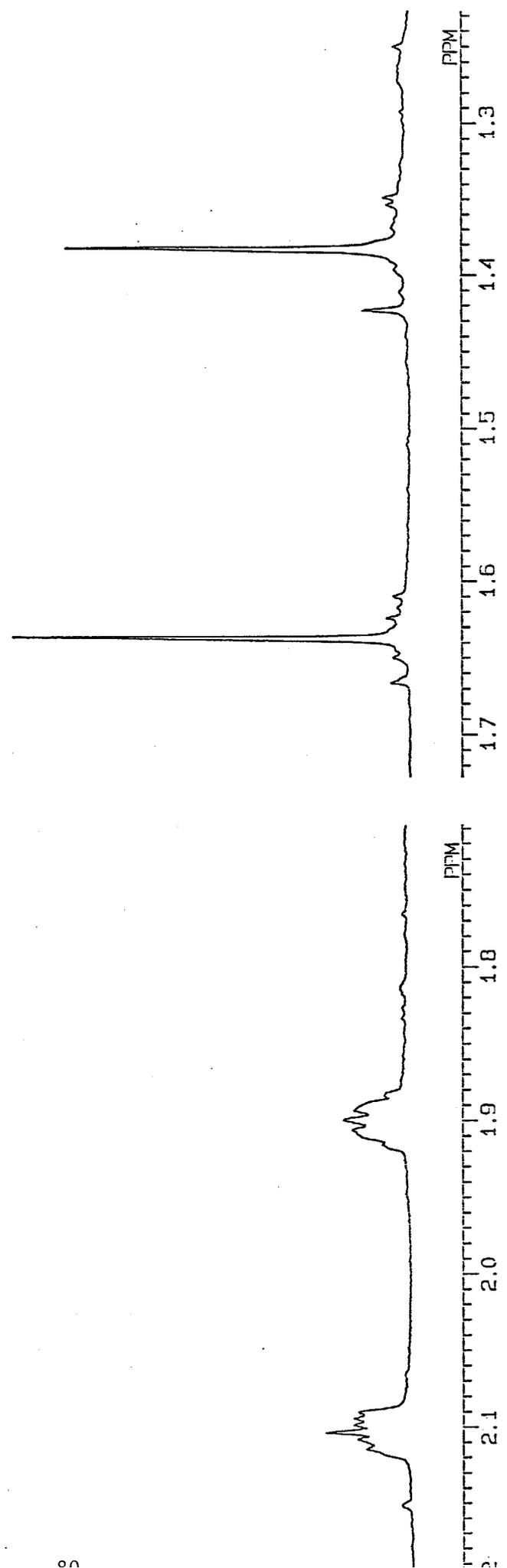
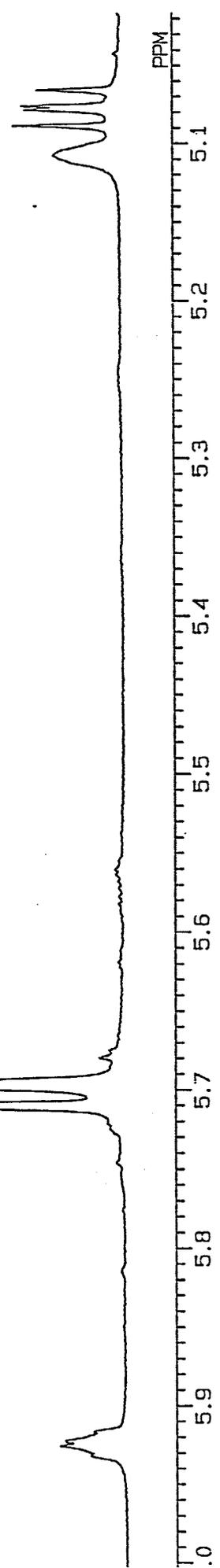


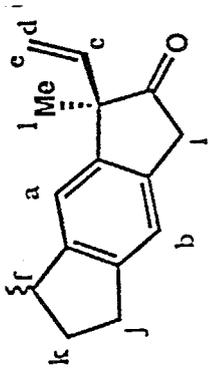
41 (C<sub>6</sub>D<sub>6</sub>)





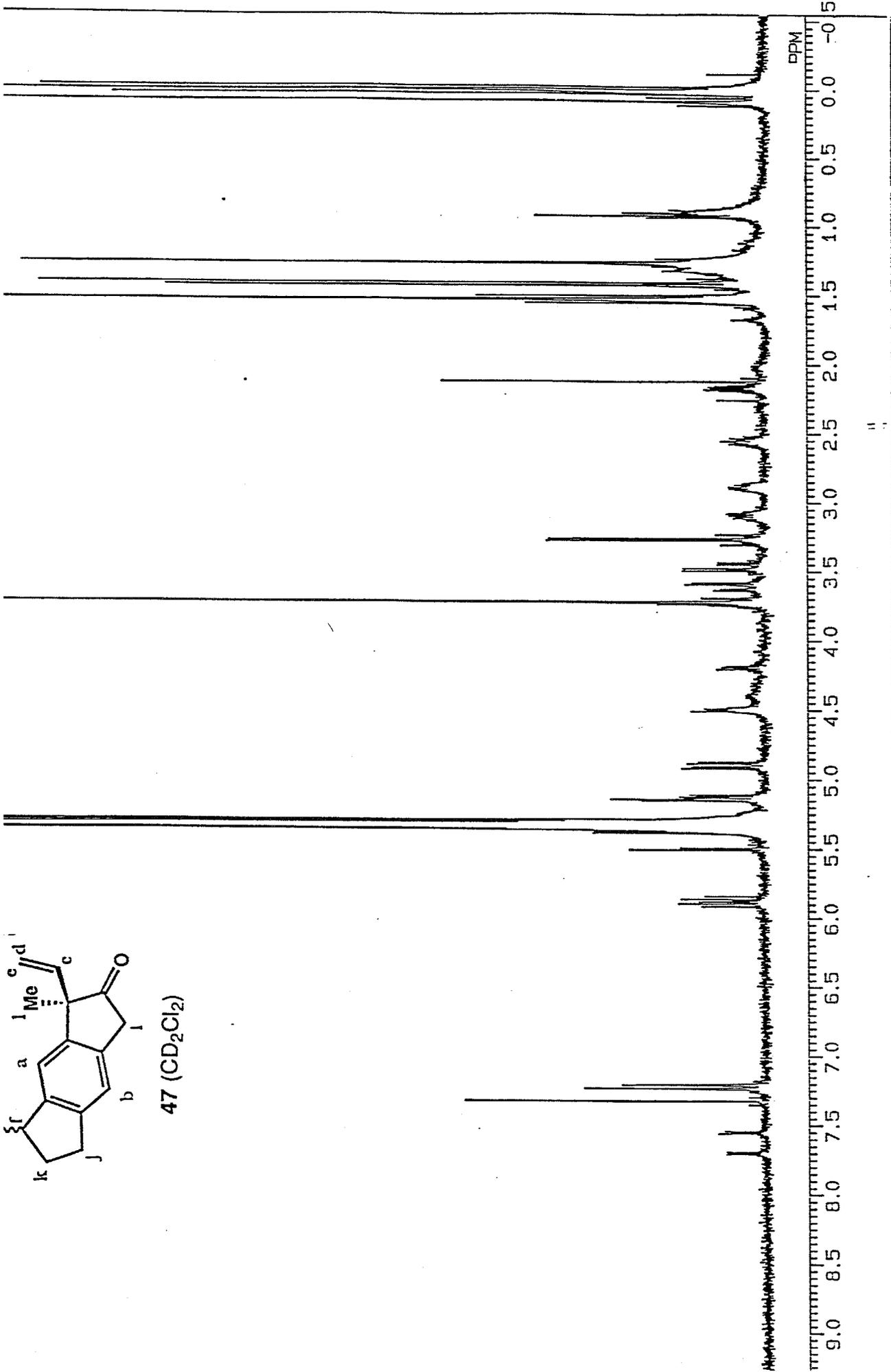
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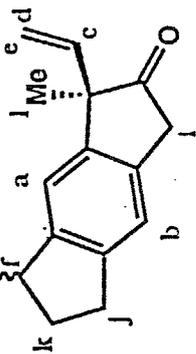
47 (CD<sub>2</sub>Cl<sub>2</sub>)

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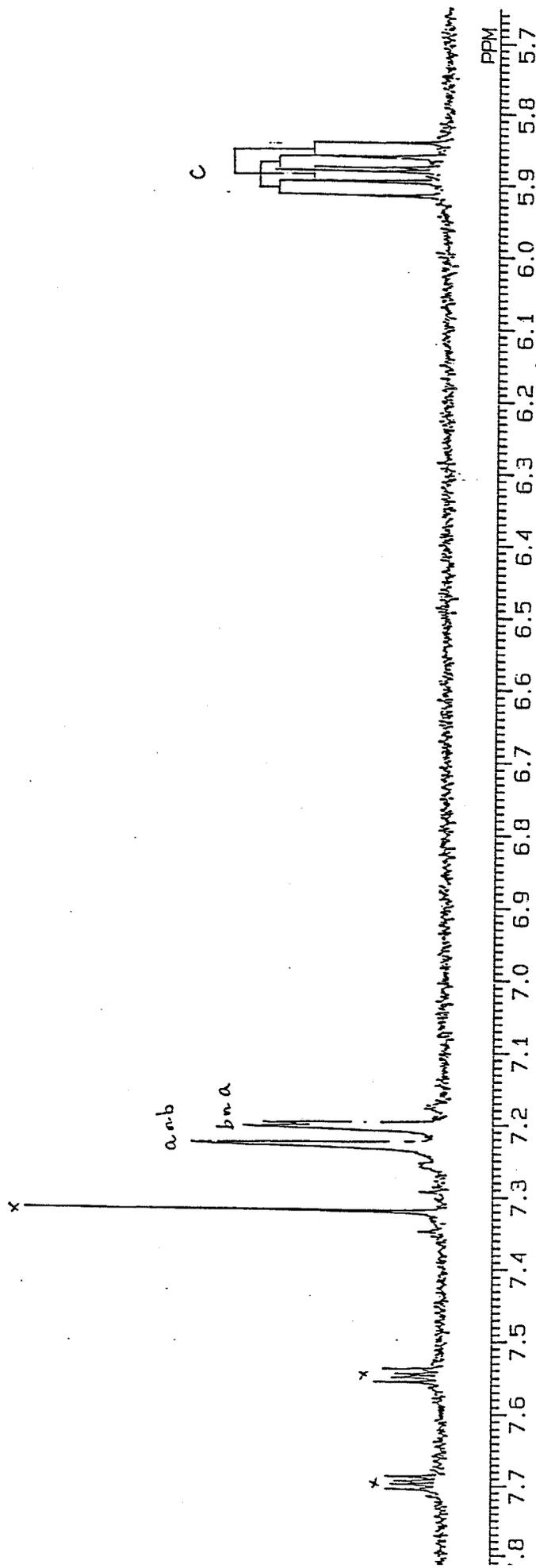
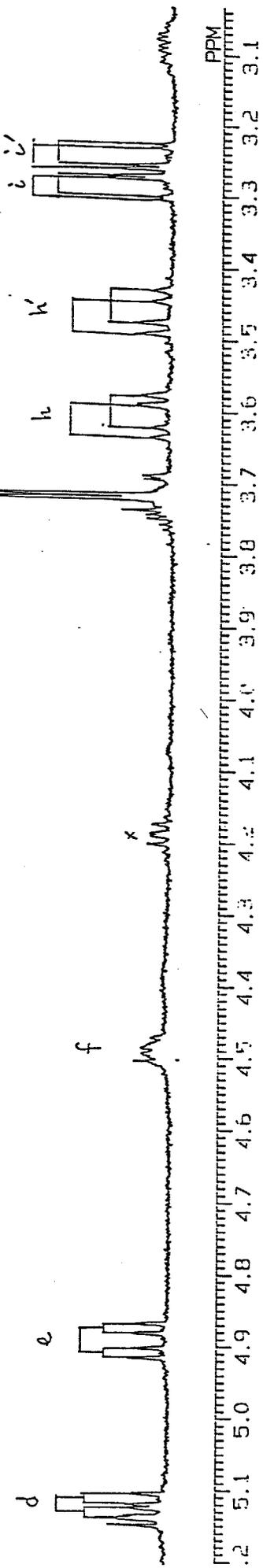


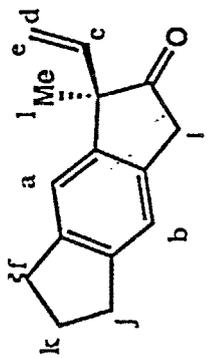
11

SCH<sub>2</sub>CO<sub>2</sub>Me

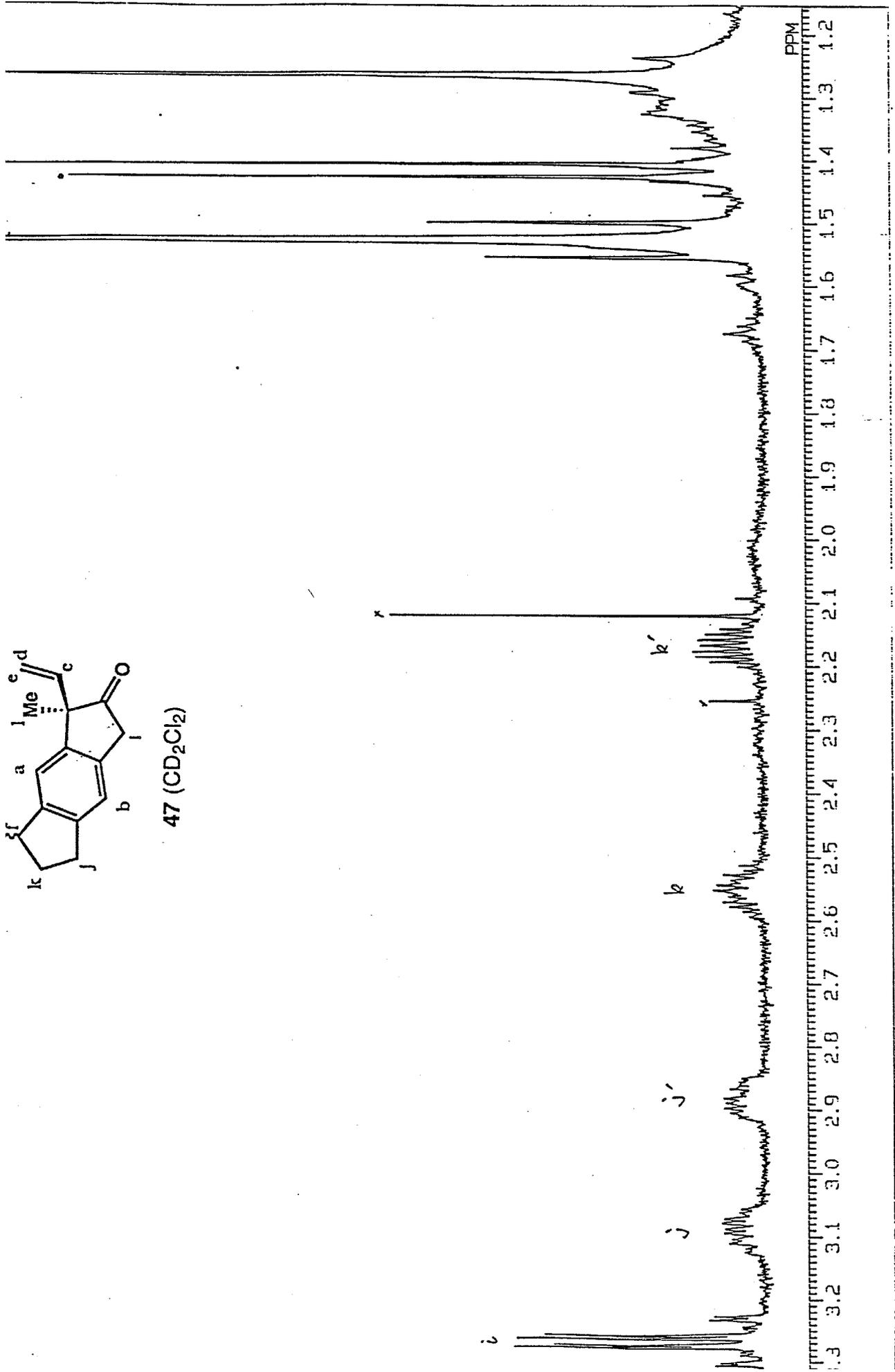


47 (CD<sub>2</sub>Cl<sub>2</sub>)

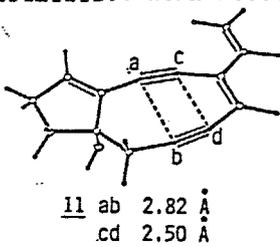




47 (CD<sub>2</sub>Cl<sub>2</sub>)



The structure 11 was calculated using the MacroModel implementation of the MM2 molecular mechanics force field.

 <p>11 ab 2.82 Å cd 2.50 Å</p>	<pre>***** * * * * * * * *****</pre>	<p>TOTAL MM2            ENERGY IS            23.442 kcal/mol</p> <p>Van der Waals            6.271            Stretch            0.957</p> <p>Torsion            0.839            Bend            15.871</p> <p>Improper Torsion            0.016            Stretch-Bend            -0.197</p> <p>Hydrogen-Bond            0.000            Electrostatic            -0.314</p>
		<p>Energy minimization RMS            =    0.0009 kcal/Å-mol</p>

Connection Table

Atomic Charges, Coordinates and Connectivity

- single bond, = doble bond, % triple bond

Atom Type	Number	Charge	Coordinates			Residue	Attached Atoms & Bonds			
			X	Y	Z					
C2	( 1)	-0.042	6.6773	8.6388	0.5337	0	2-	5=	15-	
C3	( 2)	0.042	5.3495	7.9941	0.2495	0	1-	3-	16-	17-
C3	( 3)	0.000	5.7501	6.8607	-0.7182	0	2-	4-	18-	19-
C3	( 4)	0.107	7.2352	6.5288	-0.4188	0	3-	5-	26-	14-
C2	( 5)	-0.042	7.6939	7.8565	0.1603	0	4-	1=	6-	
C1	( 6)	0.000	9.0872	8.1188	0.3573	0	5-	7%		
C1	( 7)	0.000	10.3108	8.1066	0.3843	0	6%	8-		
C2	( 8)	0.000	11.6907	7.7617	0.1825	0	7-	9=	10-	
C2	( 9)	0.000	11.8487	6.7191	-0.6554	0	8=	12-	20-	
C2	( 10)	0.000	12.8043	8.4624	0.8296	0	8-	11=	21-	
C2	( 11)	0.000	12.6288	9.4978	1.6628	0	10=	22-	23-	
C1	( 12)	0.000	10.6232	6.1868	-1.1820	0	9-	13%		
C1	( 13)	-0.107	9.4497	5.9850	-1.4672	0	12%	14-		
C3	( 14)	0.107	7.9880	6.0023	-1.6612	0	13-	24-	25-	4-
H1	( 15)	0.000	6.7796	9.6163	1.0341	0	1-			
H1	( 16)	0.000	4.9240	7.5959	1.2009	0	2-			
H1	( 17)	0.000	4.6302	8.7089	-0.2163	0	2-			
H1	( 18)	0.000	5.0732	5.9755	-0.6588	0	3-			
H1	( 19)	0.000	5.6737	7.2611	-1.7580	0	3-			
H1	( 20)	0.000	12.8293	6.3008	-0.9345	0	9-			
H1	( 21)	0.000	13.8339	8.1232	0.6214	0	10-			
H1	( 22)	0.000	11.6284	9.8862	1.9127	0	11-			
H1	( 23)	0.000	13.4928	9.9991	2.1297	0	11-			
H1	( 24)	0.000	7.8037	6.6739	-2.5305	0	14-			
H1	( 25)	0.000	7.6360	4.9811	-1.9348	0	14-			
O3	( 26)	0.313	7.2912	5.5428	0.5924	0	4-	27-	28-	29-
H2	( 27)	0.246	6.7570	4.8096	0.3401	0	26-			
Lp	( 28)	-0.312	7.8380	5.2985	0.5637	0	26-			
Lp	( 29)	-0.312	6.9752	5.7524	1.0577	0	26-			
Total charge on system =			0.000							



Connection Table

Atomic Charges, Coordinates and Connectivity

- single bond, = doble bond, % triple bond

13A

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds				
Type	Number		X	Y	Z						
C3	( 1)	0.172	9.6900	3.7816	-9.0787	0	2-	9-	18-	19-	
O3	( 2)	0.494	9.4834	3.4584	-10.4455	0	1-	3-	20-	21-	
C3	( 3)	0.107	8.2689	4.0155	-10.9730	0	2-	4-	22-	23-	
C2	( 4)	-0.042	8.2982	5.5257	-11.0174	0	3-	5=	24-		
C2	( 5)	0.000	7.5415	6.3252	-10.2503	0	4=	6-	25-		
C1	( 6)	0.000	6.6355	5.8077	-9.2709	0	5-	7%			
C1	( 7)	0.000	5.8999	5.3331	-8.4204	0	6%	17-			
C2	( 8)	-0.042	3.8478	5.1643	-7.1211	0	14-	17=	26-		
C1	( 9)	-0.107	8.6083	3.3996	-8.1570	0	1-	10%			
C1	(10)	-0.107	7.6892	3.1215	-7.4159	0	9%	11-			
C3	(11)	0.107	6.5461	2.8245	-6.5408	0	10-	12-	27-	28-	
C3	(12)	0.107	5.7270	4.0783	-6.2078	0	11-	13-	15-	17-	
C3	(13)	0.000	4.4897	3.7764	-5.3285	0	12-	14-	29-	30-	
C3	(14)	0.042	3.4424	4.8424	-5.7092	0	13-	8-	31-	32-	
O3	(15)	0.313	6.5633	4.9886	-5.5249	0	12-	16-	33-	34-	
H2	(16)	0.246	6.0564	5.7420	-5.2747	0	15-				
C2	(17)	-0.042	5.0834	4.7378	-7.4079	0	7-	8=	12-		
H1	(18)	0.000	9.8805	4.8769	-8.9831	0	1-				
H1	(19)	0.000	10.6171	3.2522	-8.7537	0	1-				
Lp	(20)	-0.312	9.9238	3.7494	-10.7390	0	2-				
Lp	(21)	-0.312	9.3872	2.8626	-10.4492	0	2-				
H1	(22)	0.000	8.1890	3.6418	-12.0210	0	3-				
H1	(23)	0.000	7.4131	3.6044	-10.4174	0	3-				
H1	(24)	0.000	8.9979	5.9893	-11.7350	0	4-				
H1	(25)	0.000	7.6174	7.4210	-10.3449	0	5-				
H1	(26)	0.000	3.1915	5.7081	-7.8212	0	8-				
H1	(27)	0.000	5.9106	2.0730	-7.0635	0	11-				
H1	(28)	0.000	6.9323	2.3592	-5.6047	0	11-				
H1	(29)	0.000	4.0842	2.7740	-5.6090	0	13-				
H1	(30)	0.000	4.7138	3.7516	-4.2354	0	13-				
H1	(31)	0.000	2.4022	4.4420	-5.6543	0	14-				
H1	(32)	0.000	3.5291	5.7601	-5.0808	0	14-				
Lp	(33)	-0.312	6.6771	4.7415	-4.9892	0	15-				
Lp	(34)	-0.312	6.9321	5.2269	-5.9328	0	15-				
Total charge on system =		0.000									



## 13C

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.172	9.3600	4.2932	-9.3706	0	2-	9-	18-	19-
O3	( 2)	0.494	10.6898	4.1572	-8.8894	0	1-	3-	20-	21-
C3	( 3)	0.107	10.8795	4.7300	-7.6026	0	2-	4-	22-	23-
C2	( 4)	-0.042	10.8015	6.2367	-7.5917	0	3-	5=	24-	
C2	( 5)	0.000	9.7650	6.9690	-7.1571	0	4=	6-	25-	
C1	( 6)	0.000	8.5352	6.4247	-6.6648	0	5-	7%		
C1	( 7)	0.000	7.4417	6.0107	-6.3092	0	6%	17-		
C2	( 8)	-0.042	5.0991	6.3816	-6.3615	0	14-	17=	26-	
C1	( 9)	-0.107	8.3301	3.8001	-8.4413	0	1-	10%		
C1	( 10)	-0.107	7.5595	3.4486	-7.5725	0	9%	11-		
C3	( 11)	0.107	6.7257	3.0851	-6.4194	0	10-	12-	27-	28-
C3	( 12)	0.107	5.6767	4.1402	-6.0498	0	11-	13-	15-	17-
C3	( 13)	0.000	4.5082	4.2173	-7.0595	0	12-	14-	29-	30-
C3	( 14)	0.042	3.9012	5.6184	-6.8555	0	13-	8-	31-	32-
O3	( 15)	0.313	5.1548	3.7542	-4.7933	0	12-	16-	33-	34-
H2	( 16)	0.246	4.4647	4.3441	-4.5430	0	15-			
C2	( 17)	-0.042	6.1127	5.5929	-5.9750	0	7-	8=	12-	
H1	( 18)	0.000	9.2866	3.7146	-10.3219	0	1-			
H1	( 19)	0.000	9.1617	5.3664	-9.6038	0	1-			
Lp	( 20)	-0.312	10.7608	3.5642	-8.8027	0	2-			
Lp	( 21)	-0.312	11.0204	4.5050	-9.2559	0	2-			
H1	( 22)	0.000	10.1794	4.2674	-6.8682	0	3-			
H1	( 23)	0.000	11.9028	4.4369	-7.2631	0	3-			
H1	( 24)	0.000	11.6838	6.7678	-7.9914	0	4-			
H1	( 25)	0.000	9.8238	8.0692	-7.2029	0	5-			
H1	( 26)	0.000	5.1267	7.4846	-6.3469	0	8-			
H1	( 27)	0.000	6.2374	2.1042	-6.6231	0	11-			
H1	( 28)	0.000	7.4288	2.9444	-5.5658	0	11-			
H1	( 29)	0.000	4.9240	4.1556	-8.0945	0	13-			
H1	( 30)	0.000	3.7620	3.3953	-6.9445	0	13-			
H1	( 31)	0.000	3.5019	6.0394	-7.8087	0	14-			
H1	( 32)	0.000	3.1047	5.6267	-6.0746	0	14-			
Lp	( 33)	-0.312	4.8478	3.2468	-4.8888	0	15-			
Lp	( 34)	-0.312	5.5773	3.8830	-4.3870	0	15-			

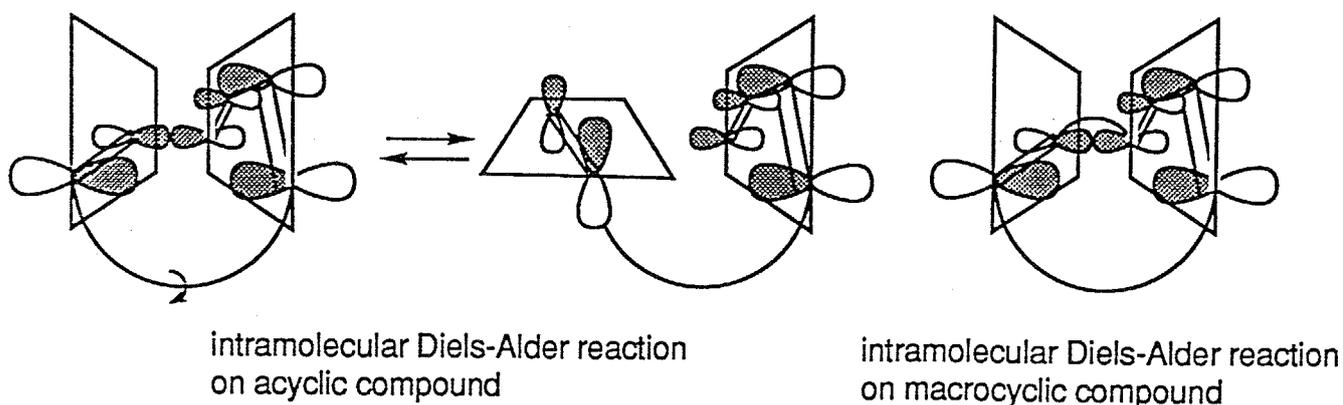
Total charge on system = 0.000

## 第四章 大員環内 Diels-Alder 反応

### 4-1 大員環内 Diels-Alder 反応の特徴

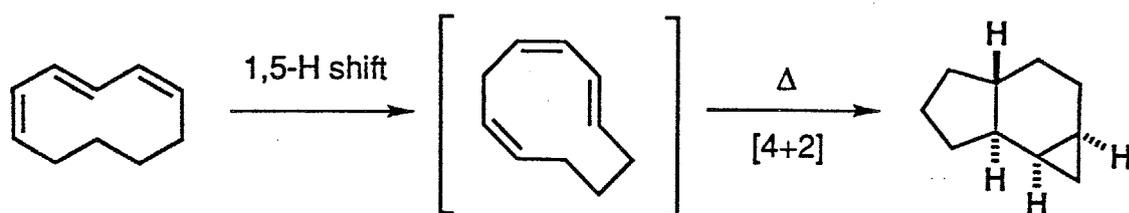
Diels-Alder 反応は最もよく知られている6員環骨格構築法の1つであり、その分子内反応の例も非常に多く報告されているものの<sup>76)</sup>、大員環内での反応例はほとんどない。しかし、大員環内 Diels-Alder 反応が進行するならば、一挙に3つの環と4つの不斉中心を構築することができ、新規骨格合成法及び、新規立体制御法として極めて意義が大きいと考えられる。

その特徴を次に述べる。従来の鎖状化合物の分子内 Diels-Alder 反応は反応部位は近くに存在するものの、反応に関与する二重結合の $\pi$ 軌道は方向は定まっていない。これに対し、大員環化合物の Diels-Alder 反応では、反応部位の両側が環の炭素鎖により規制されるので、反応部位がより近くに存在しエントロピ的に有利になる。さらに $\pi$ 軌道は環平面に対し水平方向を向くのが有利なため、環平面の内側を向いている $\pi$ 軌道は、反応に容易に関与できると考えられる。この点で鎖状化合物や5,6員環化合物と比べ大きく異なり、極めて高い反応性が期待できる。また大員環の立体配座を制御することにより、Diels-Alder 反応の立体化学制御が可能であると考えた。(Fig. 4-1)。



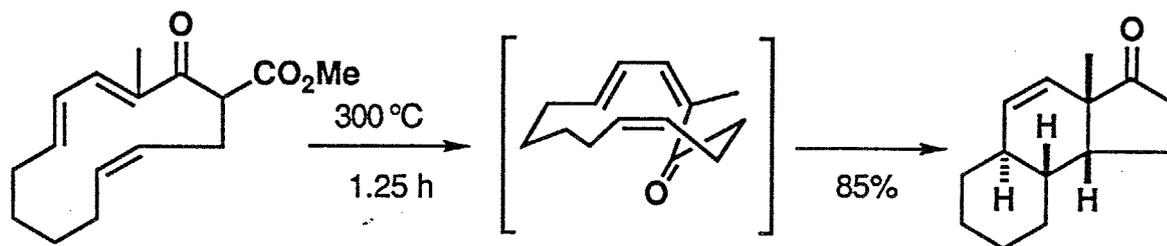
(Fig. 4-1)

Daubenらは1981年、10員環共役トリエンを熱処理すると、1,5-ヒドリド転位して生じるトリエンで分子内Diels-Alder反応が起こることを報告している<sup>77)</sup> (Scheme 4-1)。



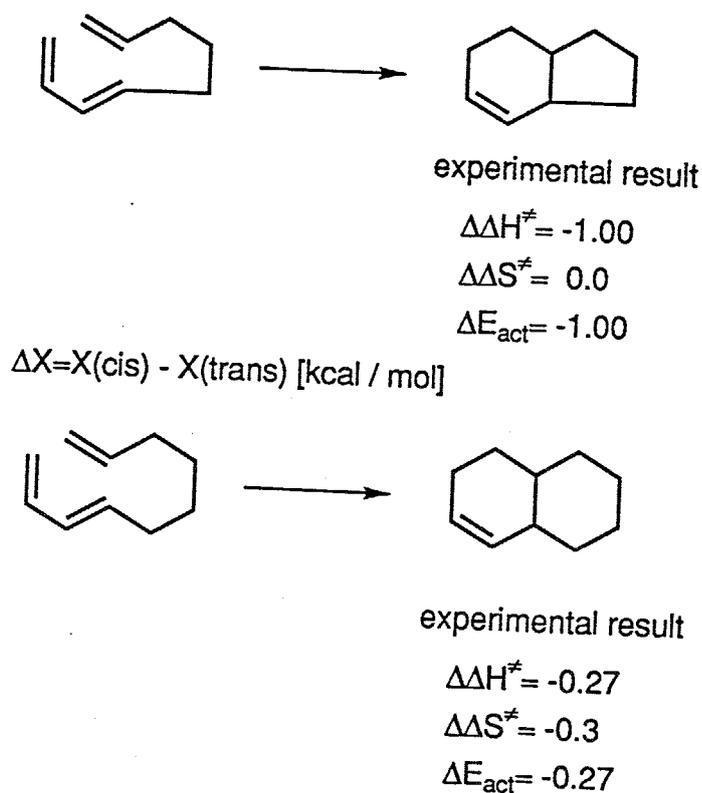
(Scheme 4-1)

Deslongchampsらは、1987年はじめて13員環内Diels-Alder反応により、6,6,5員環を構築することを報告し<sup>45)</sup>、1988年には14員環トリエンのオレフィン部分の幾何異性体について14員環内Diels-Alder反応の反応性および、立体選択性を報告している<sup>78)</sup> (Scheme 4-2)。



(Scheme 4-2)

ところで、Houkらは1985年ブタジエンとエチレンのDiels-Alder反応の遷移状態を *ab initio* 計算から求め、それを基にしたMM2遷移状態モデルを用いて1,3,8-ノナトリエンおよび1,3,9-デカトリエンの分子内Diels-Alder反応のエンド、エキソ選択性を定量的に説明することに成功している<sup>15)</sup> (Scheme 4-3)。



(Scheme 4-3)

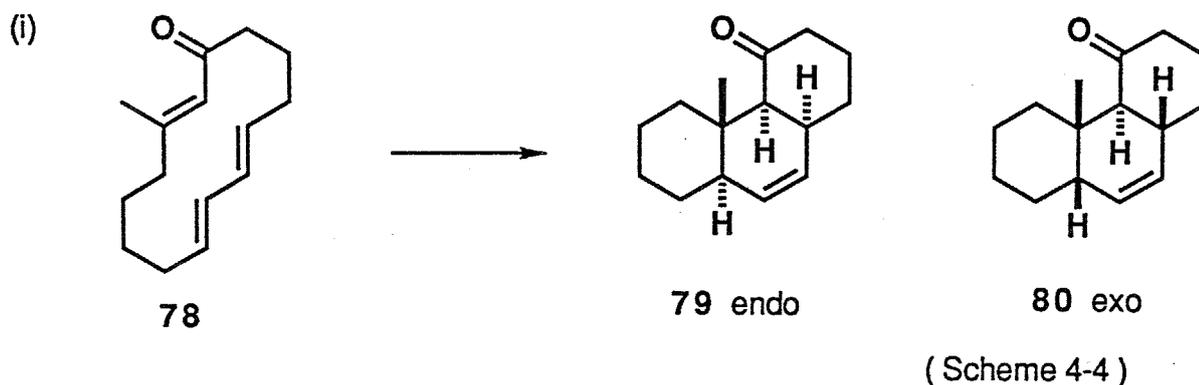
筆者は、14員環内Diels-Alder反応の立体選択性を *ab initio* 計算の結果を基にしたMM2 遷移状態モデルの計算から予測し、実際に実験を行い実験結果と計算結果の比較を行った。さらにこのMM2遷移状態モデル計算をステロイド骨格の新規合成法に応用したので以下に述べる。

## 4-2 共役ジエンとエノンを含む14員環内Diels-Alder反応

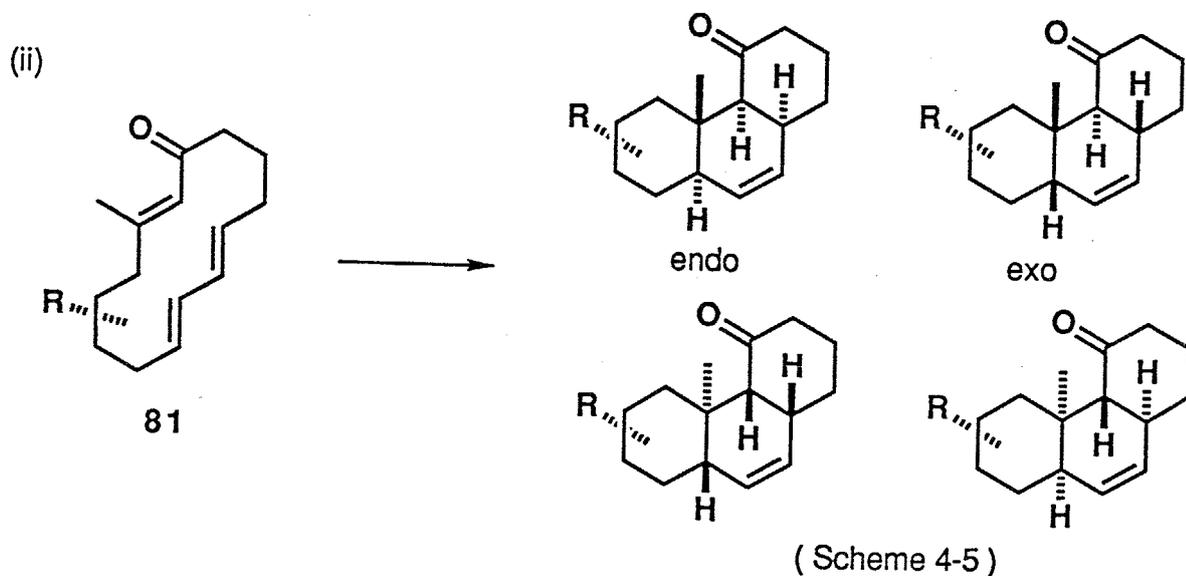
### 4-2-1 計画

次の3つの系を計画した。

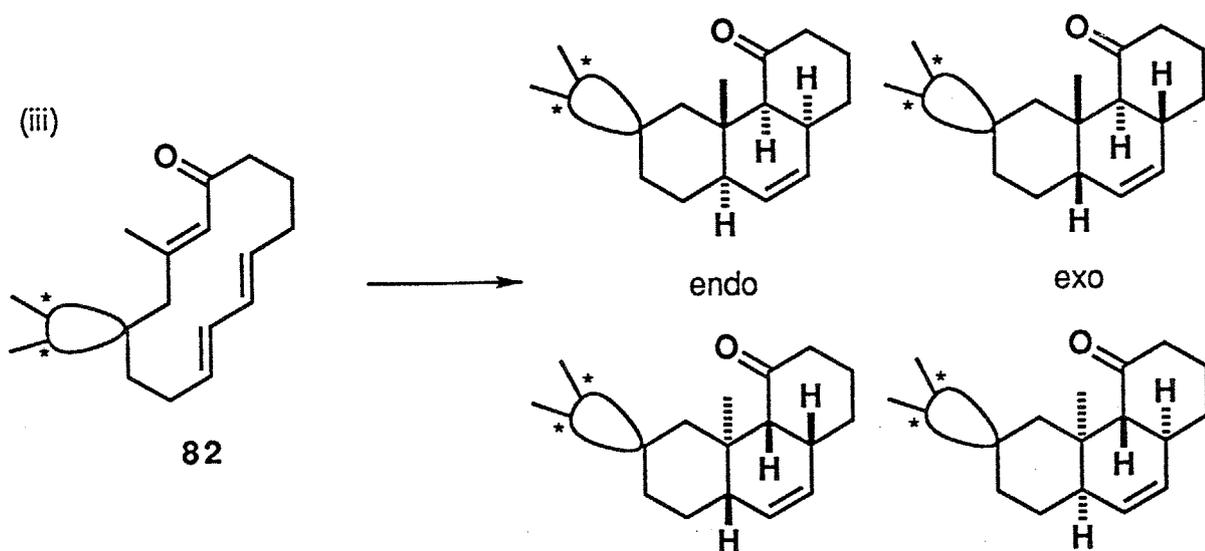
(i) 不斉中心のない14員環トリエノンのDiels-Alder反応 (Scheme 4-4)  
反応が進行すれば、エンドとエキソの遷移状態を経て2種の生成物(エンド体・エキソ体)が得られる可能性がある。この立体選択性を定量的に予測するために、遷移状態のエネルギー差をMM2遷移状態モデル計算から求める。しかし、MM2計算では遷移状態の電子的因子は含まれないので、エンド効果<sup>79)</sup>が期待されるこの系では特に計算結果がそのまま実験結果を再現できるとは予想しがたい。そこで(i)の反応でエンドとエキソの遷移状態のMM2遷移状態モデル計算と実験結果を比較し、実験結果を再現するように補正値を求めることを目的とする。



(ii) 14員環上の1つの置換基の不斉中心から遠隔立体制御が可能か (Scheme 4-5)。(i)で求める補正値を用い、MM2遷移状態モデル計算からその立体選択性を予測し、実験結果と比較する。



(iii) プロキラルな14員環上にキラルな修飾子を付けた場合、不斉誘起できるか (Scheme 4-6)。(ii)と同様に補正值を用いたMM2遷移状態モデルの計算から不斉誘起の選択性を予測し実験結果と一致するかどうかを調べる。もしキラルな修飾子とのジアステレオマーの一方が優先して生成するなら、修飾子を除去することによって光学活性体を合成できる。つまりこのジアステレオ選択性を予測することができるなら、目的の立体化学を得るために、どのようなキラルな修飾子をどの位置に、どの絶対構造を用いれば良いかを合成計画の際に選択できると考えられ、非常に有用になる。



(Scheme 4-6)

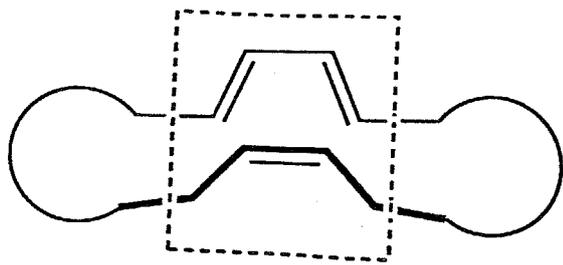
#### 4-2-2 計算結果と実験結果の検証

##### (i) - 1 MM2遷移状態モデルの計算

MM2遷移状態モデルの計算は次のように行った。

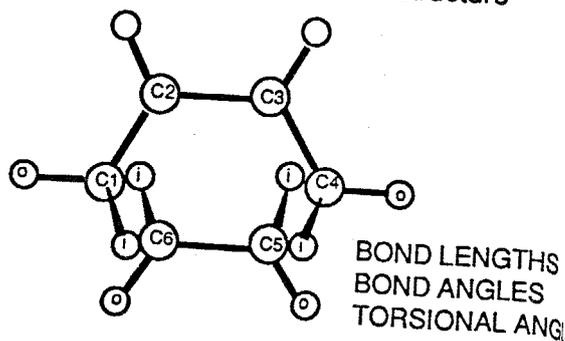
ジエンとジエノフィル部分は、Houkが報告しているブタジエンとエチレンのDiels-Alder反応の遷移状態構造<sup>15a)</sup> (Fig. 4-2)に固定した。残りの部分は、そこから炭素鎖をのぼし、MM2によるエネルギー極小化を行って、MM2遷移状態構造を求めた。(Fig. 4-3)

MM2 transition structure model



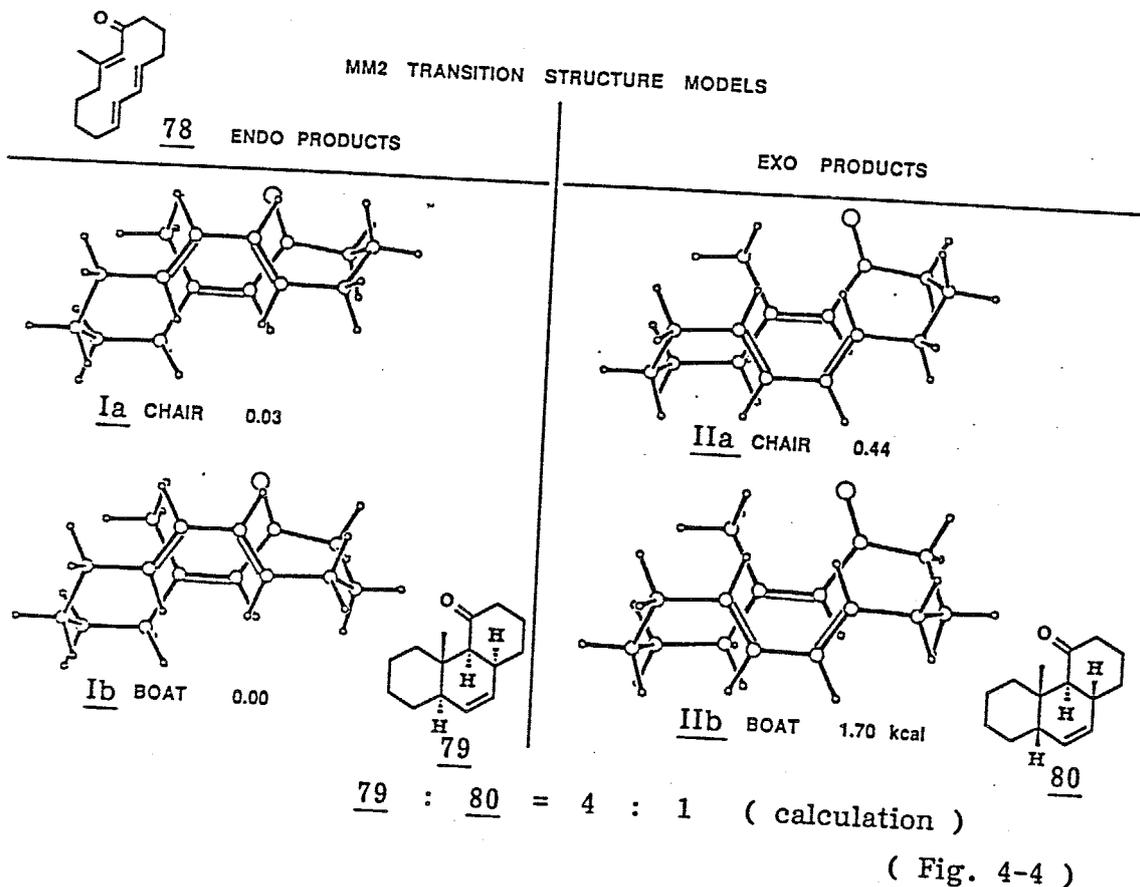
(Fig. 4-3)

STO-3G Diels-Alder transition structure



(Fig. 4-2)

Schere 4-4に示したDiels-Alder反応の計算を、エンドとエキソの遷移状態について、それぞれA環部はメチル基との反発を避けるいす型だけを考え、C環部はいす型とボート型<sup>80)</sup>を想定して行い、次の4つの計算結果を得た (Fig. 4-4)。この結果から単純にBoltzmann分布から20 °Cにおける立体選択性を計算するとエンド：エキソ=4：1となった。

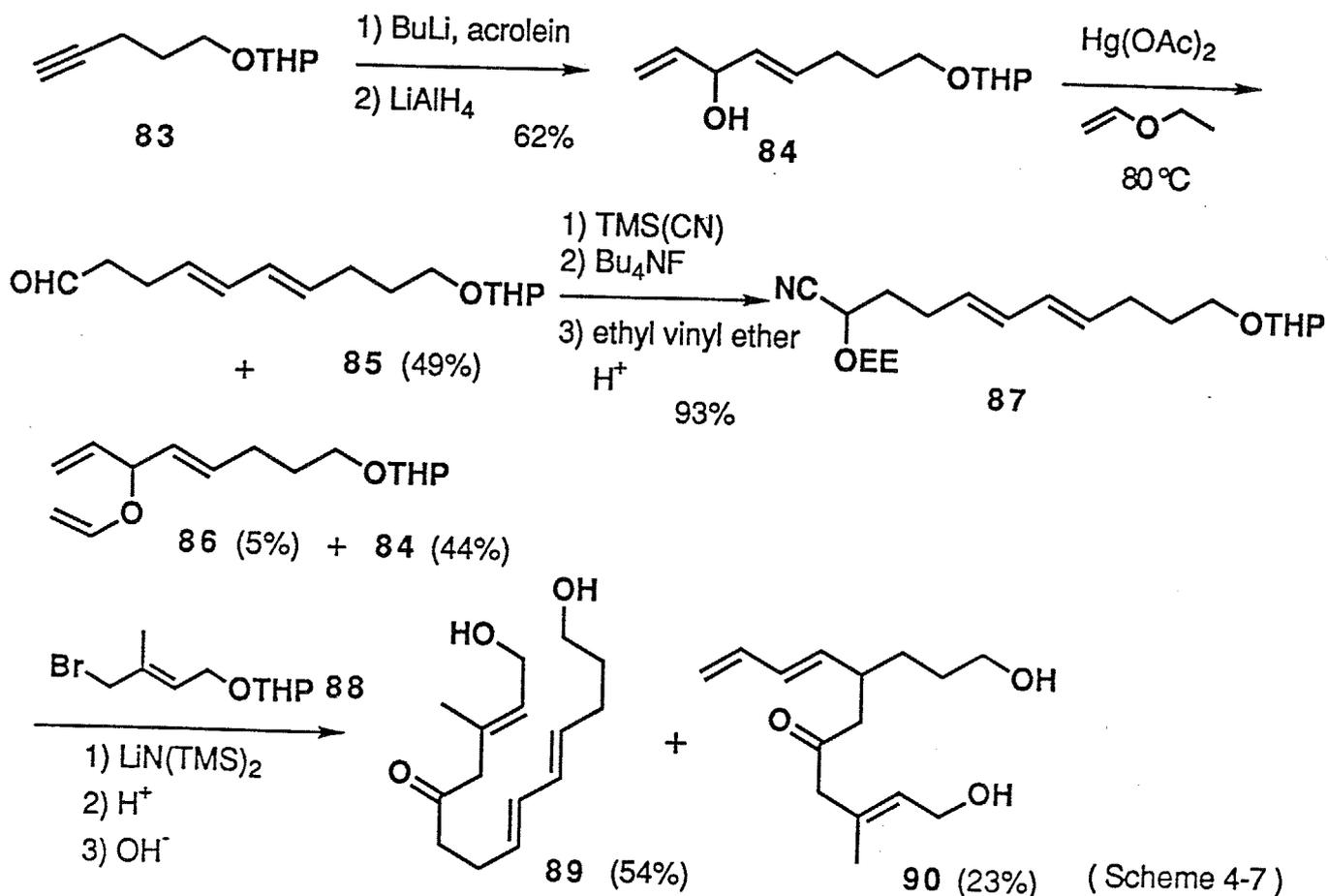


( i ) - 2 実験結果

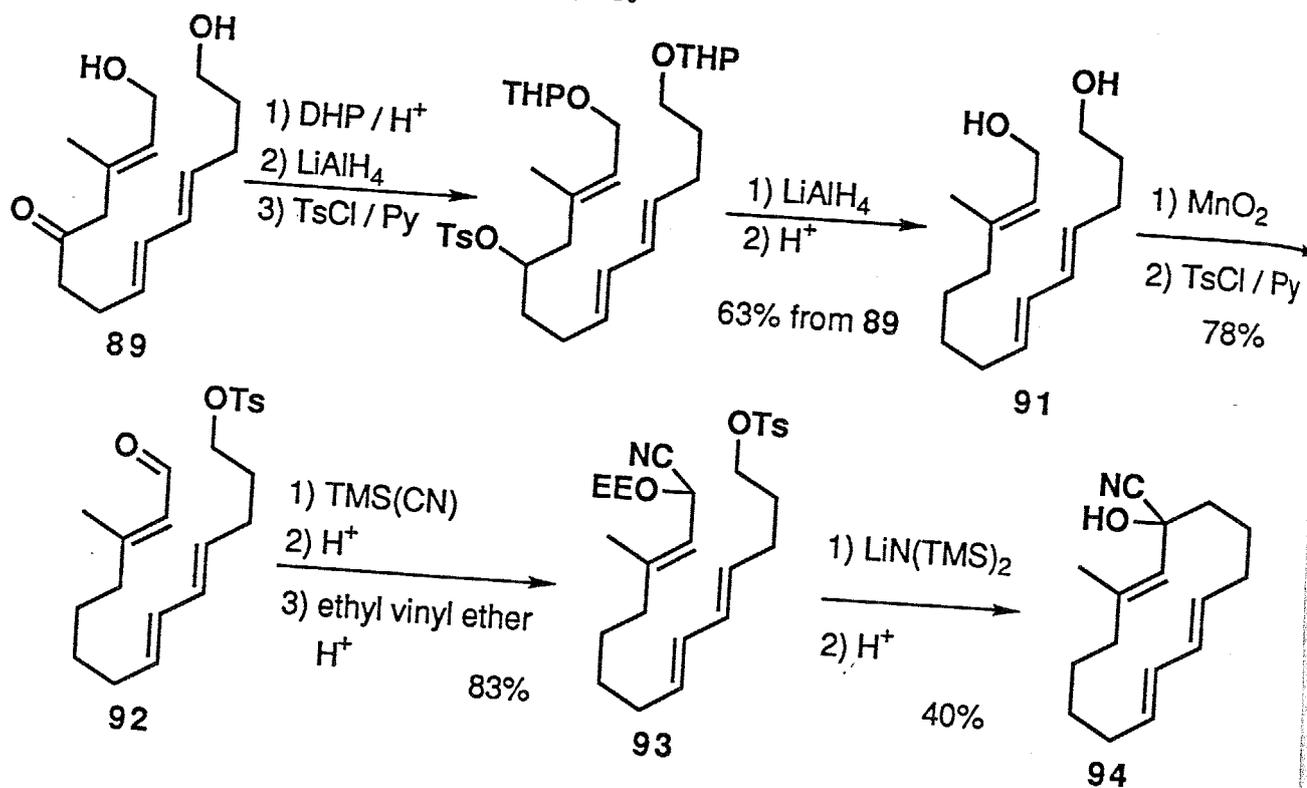
4-ペンテン-1-オール<sup>83)</sup>のTHPエーテル<sup>83)</sup>をBuLiで処理し、生じたアセチリドをアクロレインに1,2付加させた。得られたアルキニルアルコールをLiAlH<sub>4</sub>を

用いて (E)-アリルアルコール 84 へ還元した (61%, 2 steps)。続いて、エチルビニルエーテルでビニルエーテル化を行いながら、80 °Cで同時にクライゼン転位反応を行い、ビニルエーテル 86 を5%、転位生成物 85 を49%、原料 84 を44%回収した。この際、転位反応は、立体的に混んでいない末端側から優先して起こり、さらにいす型遷移状態を経て、(E,E)-ジエン 85 が得られた。この反応の位置異性体との比は約3:1であったが、ここでの分離は難しかったので混合物のまま次の反応を行った。

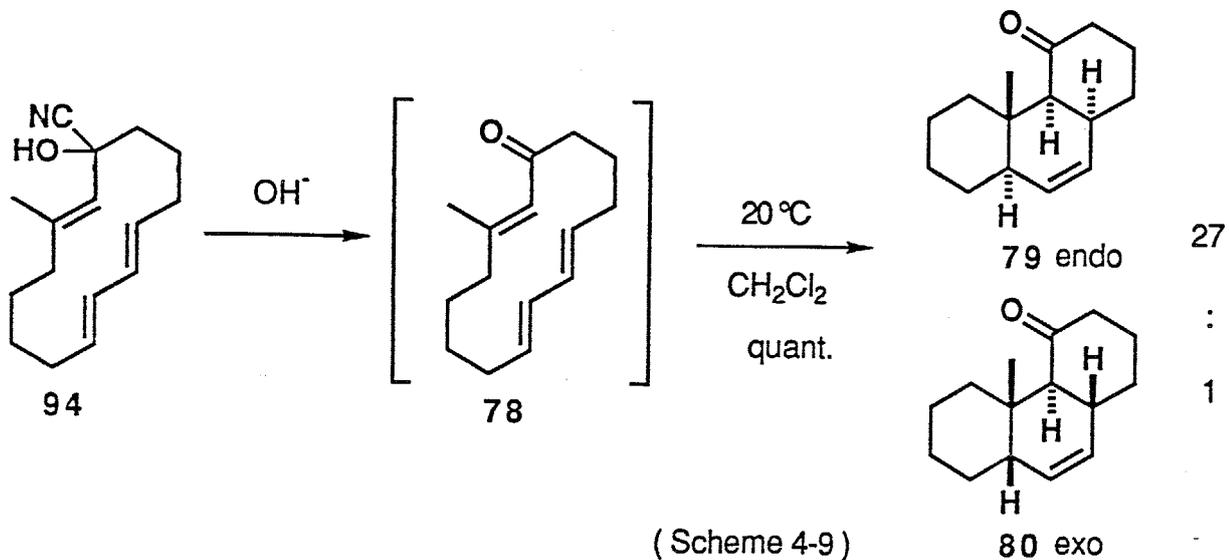
アルデヒド 85 にTMS(CN)を作用させ、TMS基を除去した後、水酸基をエチルビニルエーテルで保護した (93%)。この保護したシアノヒドリン 87 とブレンールから既知の方法で得られるアリルブロミド 88 との混合物を、塩基 (LiN(TMS)<sub>2</sub>) のTHF溶液中へ、60 °Cで滴下し、アルキル化を行った。つづいて、希酸、希塩基処理を行いアルキル化したケトンを受率77%で得た。ここで、先のクライゼン転位反応による位置異性体 90 とシリカゲルカラムで分離し、β, γ不飽和ケトン 89 を収率54%で単離した (Scheme 4-7)。



この際、89の $\alpha, \beta$ 不飽和ケトンへの異性化が起こっていないことは、IRスペクトル ( $1710 \text{ cm}^{-1}$ ) により確認した。また、ジエンの立体配置は、既知化合物とのスペクトルデータ<sup>63)</sup>との比較から (E,E)-体であることを決定し、 $^{13}\text{C}$  NMRにより純粋であることを確認した。



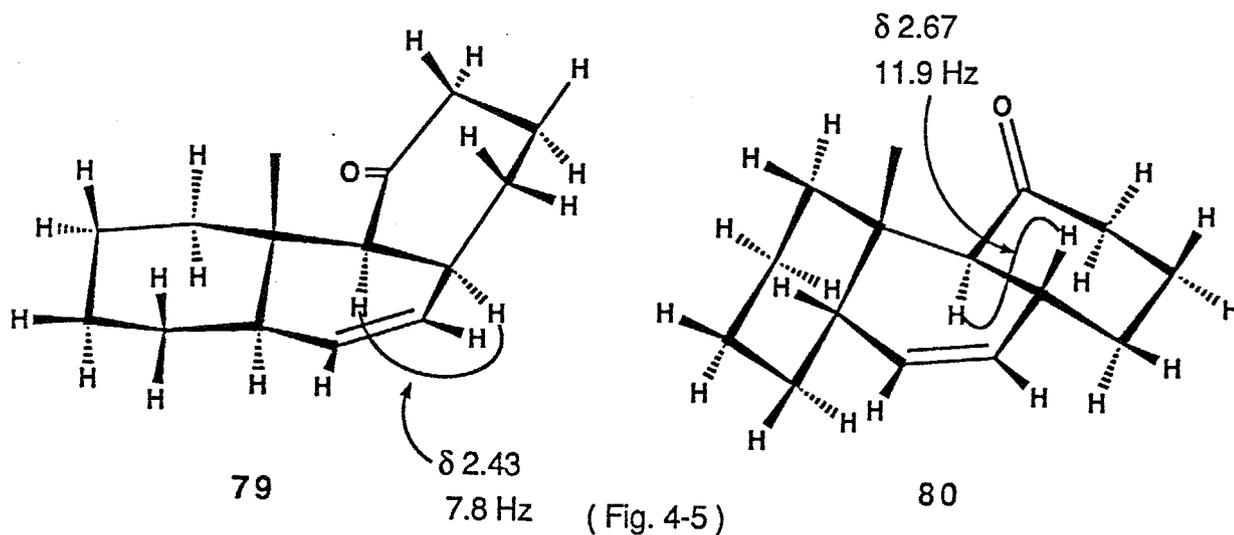
(Scheme 4-8)  
次にジオール 89 を DHP で保護した後、ケトン を  $\text{LiAlH}_4$  で還元し、得られた水酸基をトシル化した。続いて  $\text{LiAlH}_4$  を用いてトシラートを還元し、メチレンへ変換した後、THP 基を除去してジオール 91 を収率 63% で得た。さらに 91 のアリルアルコールのみ選択的に  $\text{MnO}_2$  を用いて酸化し、残った水酸基をトシル化してトシラート 92 へ収率 78% で導いた。次に、エナール 92 をシアノヒドリンに変換し、2つの水酸基は、エチルビニルエーテルで保護した (83%)。閉環反応は、 $\text{LiN}(\text{TMS})_2$  を塩基として使い、THF 溶媒中、 $60^\circ\text{C}$  で塩基中に 93 をゆっくり滴下して行った。反応は滴下と同時に終了し、続いて希酸処理して 14 員環のシアノヒドリン 94 を得た。閉環の際、10% 程度 Diels-Alder が進行した化合物も得られたので 94 を HPLC を用いて純粋に単離した (Scheme 4-8)。



シアノヒドリン 94 を分液ロート中で、2%の水酸化ナトリウム水溶液と0 °Cで3分間振り混ぜて、エノン 78 へ導き、後処理後CH<sub>2</sub>Cl<sub>2</sub>中20 °Cで放置したところ、30分でDiels-Alder反応が定量的に進行することが確認できた。得られた 79 と 80 の比は、HPLC分析により27:1であった (Scheme 4-9)。

### (i) - 3 構造決定

各々の、<sup>1</sup>H NMRを測定しケトンのα位のプロトンの結合定数を比べてみると 79 では、7.8 Hzとアキシャル-エクソトリアルルの結合定数を示したのに対し、80 では11.9 Hzとアキシャル-アキシャルの結合定数を示したことから 79 がエンド体、80 がエキソ体と決定した (Fig. 4-5)。



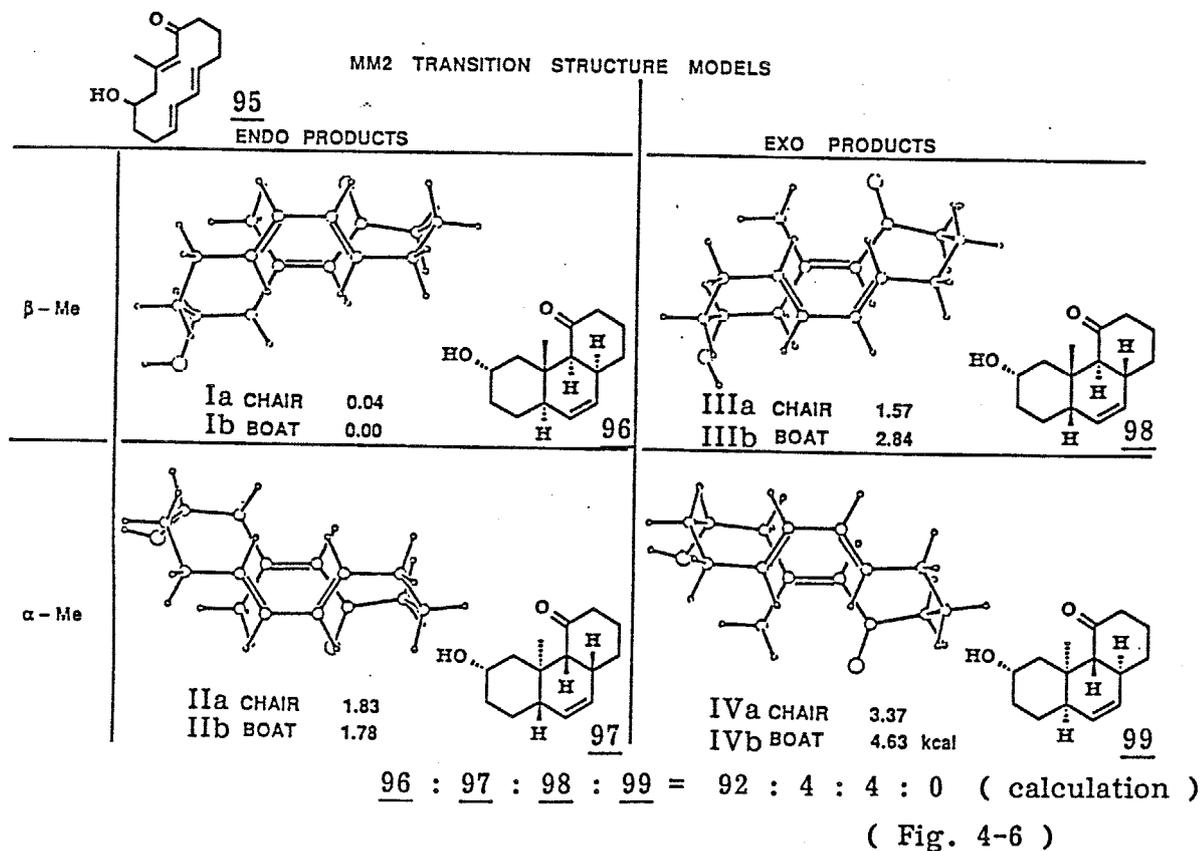
(i) - 4 結論

この計算結果と実験結果の差は、エンド効果などに代表されるMM2では計算に含まれない電子的な要因であると考え、この実験結果を再現できるように補正項を設けた。すなわちMM2遷移状態モデルのエネルギー値からエンドの遷移状態の場合は1.15 kcal/molを差し引けば実験結果を再現することが算出された。そこで、以後のエンドのMM2遷移状態モデルの計算は、この補正值を引いた値を用いた。

(ii) - 1 補正值を用いたMM2遷移状態モデルの計算

95のDiels-Alder反応を行ってジエノフィルのホモアリル位の水酸基の立体化学からDiels-Alder反応の遠隔立体制御が可能かについて検討することにした。

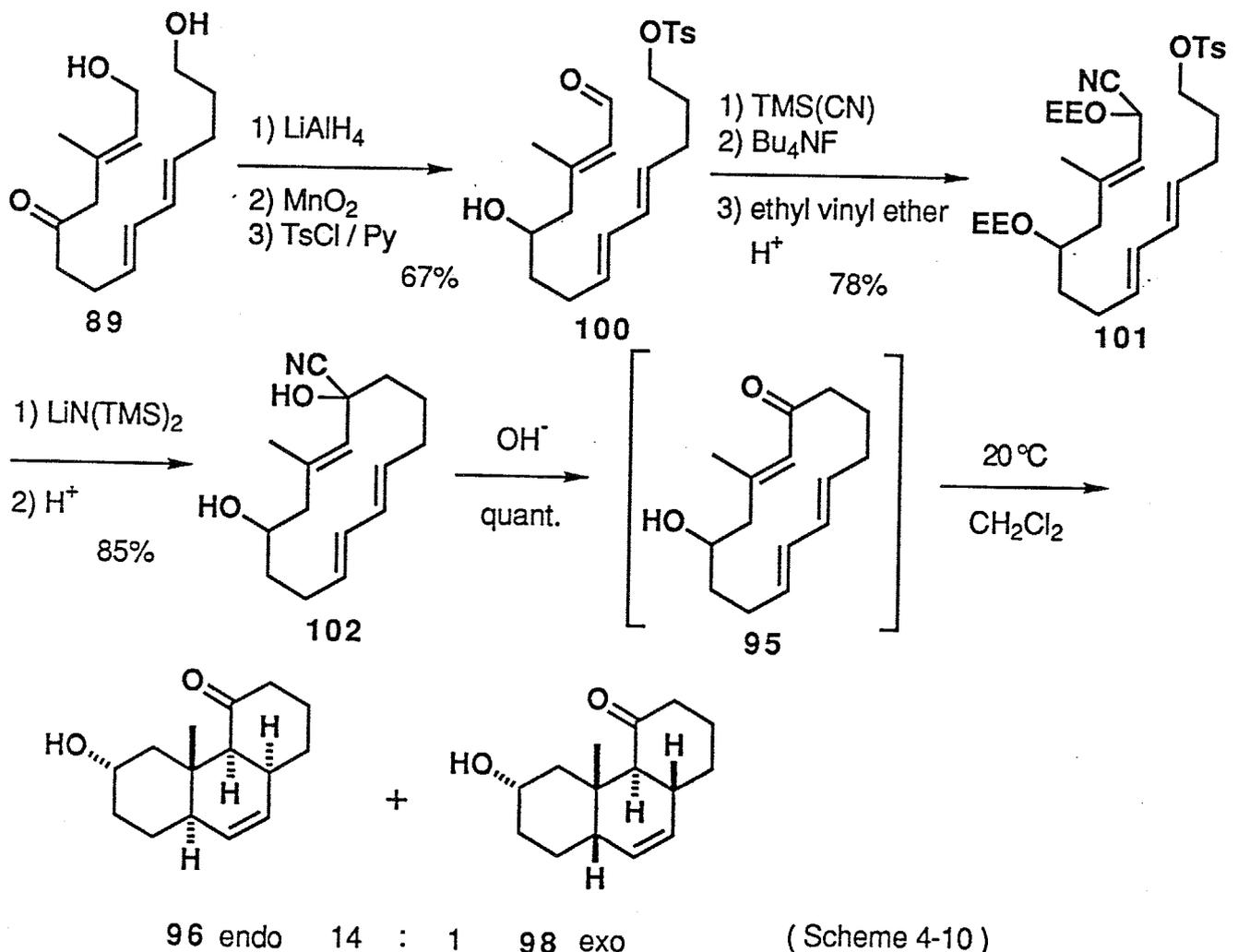
95のDiels-Alder反応では、4種類のジアステレオマー(96, 97, 98, 99)の生成する可能性がある。すなわち、エンド体とエキソ体及び、水酸基に対しメチル基が、トランス配置のものとシス配置のものである。それぞれのMM2遷移状態モデルをC環がいす型とボート型について、計8種の計算を行った。さらに(i)で得られた補正值を基にエンドのMM2遷移状態モデルのエネルギー値を補正した結果を下に示した(Fig. 4-6)。



この計算結果から Boltzmann 分布より 20 °C で  $96 : 97 : 98 : 99 = 92 : 4 : 4 : 0$  と予測した。すなわち、エンド体とエキソ体では (i) の場合と同様高くエンドに制御され、水酸基の立体配置からのメチル基の立体化学の誘起は、高くトランス配置に制御されると予想できる。

(ii) - 2 実験結果

Scheme 4-7 に示したケトン 89 を  $\text{LiAlH}_4$  で還元して得られたトリオールのアリルアルコールだけを二酸化マンガンを酸化し、続いて1級水酸基を選択的にトシル化しトシラート 100 を収率67%で得た。エナール 100 を  $\text{TMS}(\text{CN})$  で処理し、希酸で  $\text{TMS}$  基を除去した後、2つの水酸基をエチルビニルエーテルで保護し、収率78%で 101 へ導いた。先と同様に 70~80 °C でジオキサン中、 $\text{LiN}(\text{TMS})_2$

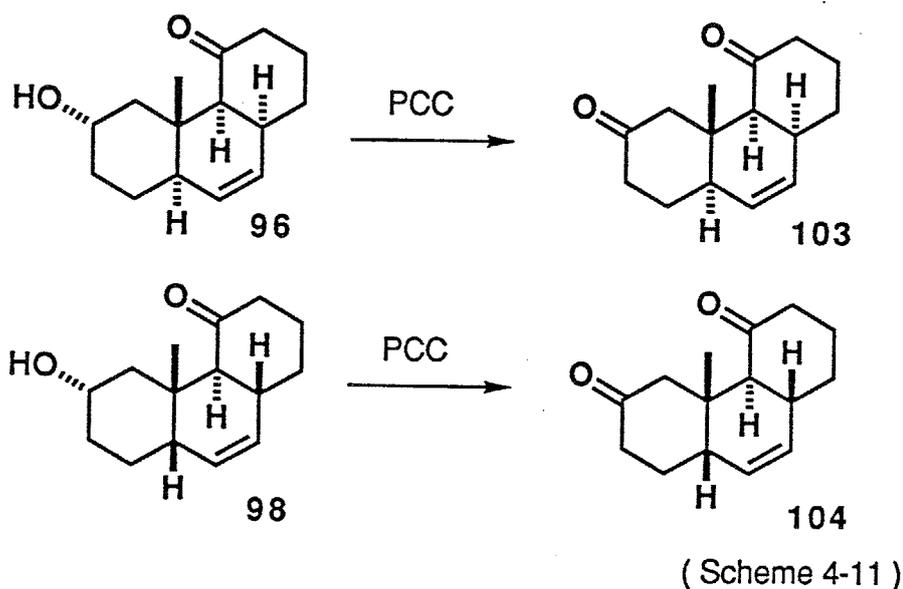


を塩基として閉環反応を行い、希酸でエトキシエチル基を除去して 102 を収率85%で得た。この閉環反応の時にDiels-Alder反応が進行した化合物が10%程度混合していたので、HPLCによりシアノヒドリン 102 を単離生成し、分液ロート中で、2%の水酸化ナトリウム水溶液と0 °Cで3分間振り混ぜて、エノン 95 へ導き、後処理後CH<sub>2</sub>Cl<sub>2</sub>中20 °Cで放置したところ、30分でDiels-Alder反応が定量的に進行した。HPLCで分析したところ 96 と 98 だけが確認され、その比は14:1であった (Scheme 4-10)。

### (ii) - 3 構造決定

まず、得られた 96 と 98 が水酸基の立体化学によるジアステレオマーか、あるいはエンド、エキソによるジアステレオマーかどうかを調べるために両方の水酸基を酸化した。もし水酸基によるジアステレオマーであれば、両者からは、同じ化合物が、生成するはずであり、一致しなければエンドとエキソ体であることがわかる。

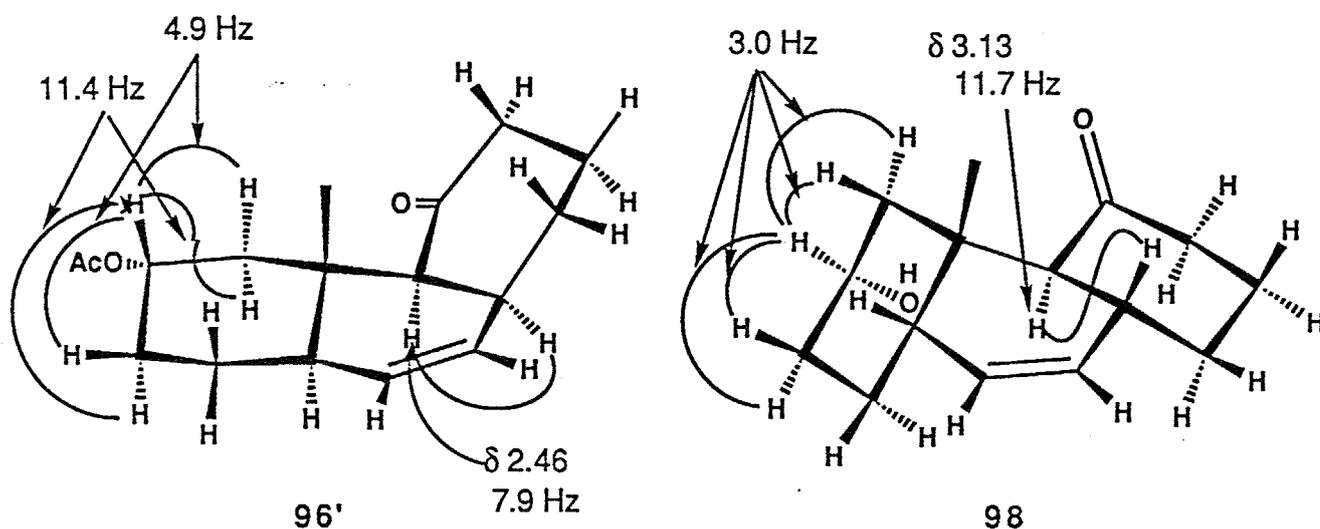
実際に、96 および 98 をPCCを用いて酸化したところ、それぞれケトン 103 と 104 を与え、両者は、TLCにおけるR<sub>f</sub>値、NMRスペクトルにおいて、異なるジケトンを与えることがわかった (Scheme 4-11)。つまり 96 と 98 は、エンドとエキソの異性体と決定した。



次に、96と98の立体化学を決定するために500 MHzの<sup>1</sup>H NMRスペクトルの解析を試みた。ただし、96は水酸基をアセチル基で保護した96'について行った (Fig. 4-7)。

96'のB, C環はケトンのα位が7.9 Hzとアキシール-エクソトリアル結合定数を示したことからシス結合して、エンド生成物であると決定した。またアセテートの付いている水素原子の分裂パターンから、11.4 Hzの結合定数で2つのプロトンと4.9 Hzの結合定数でさらに2つのプロトンとカップリングしていることがわかった。したがって、水素原子はアキシール-アキシール、アキシール-エクソトリアルのカップリングを有するアキシール配置をとっていることがわかる。つまり、水酸基とメチル基はトランス配置と決定した。

98のB, C環の縮環部位は11.7 Hzとアキシール-アキシールの結合定数を示したことからトランス結合しており、エキソ生成物であると決定した。また、水酸基の付いている水素原子の分裂パターンから、3.0 Hzの結合定数で4つのプロトンとカップリングしていることがわかった。これを満たすのは、水素原子がエクソトリアルするときである。すなわち、水酸基とメチル基はトランス配置をとっていると決定した。



(Fig. 4-7)

(ii) - 4 結論

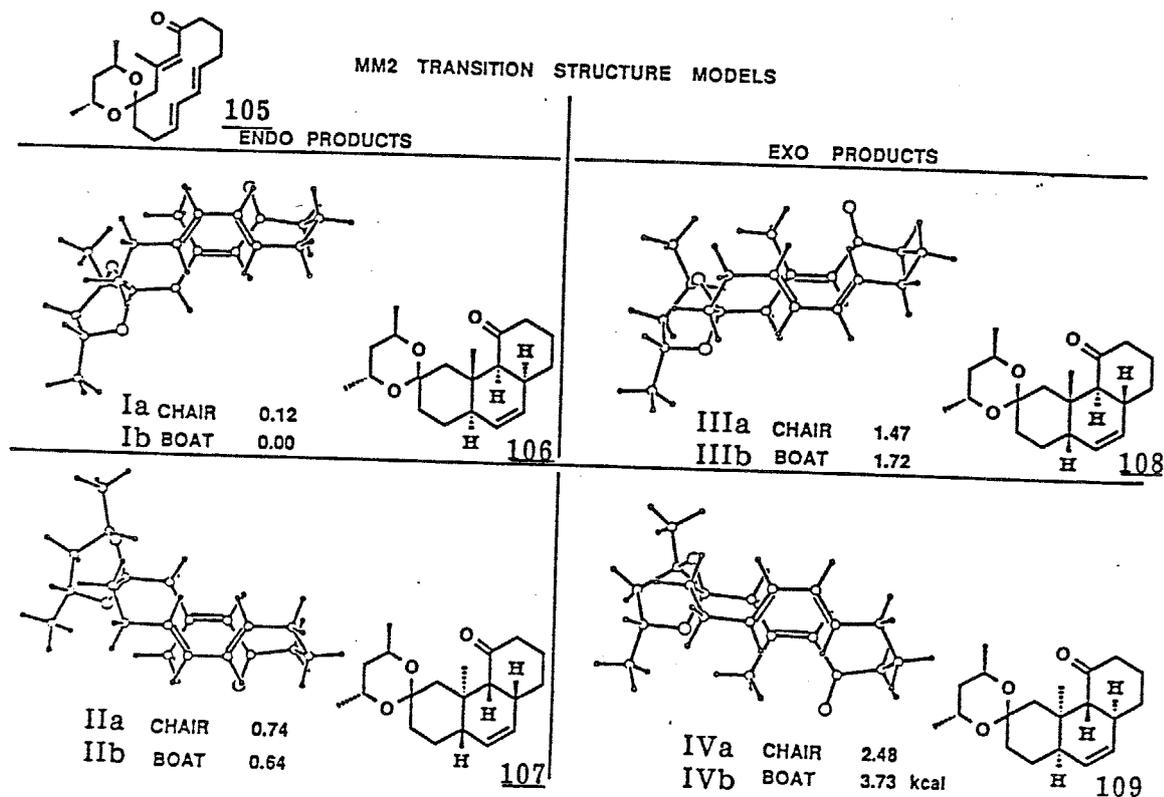
計算結果の  $\underline{96} : \underline{97} : \underline{98} : \underline{99} = 92 : 4 : 4 : 0$  と

実験結果  $\underline{96} : \underline{97} : \underline{98} : \underline{99} = 93 : 0 : 7 : 0$  を比較すると

非常に良く一致していることがわかる。 $\underline{97}$ と $\underline{99}$ は確認できず、計算結果どおりメチル基の立体配置が水酸基の立体配置から高度に遠隔立体化学制御されていることがわかった。つまり、 $\beta$ -メチル基を得たいときは、 $\alpha$ の立体化学を有する水酸基を原料とすれば良いことが、あらかじめ予測可能であり、合成計画の際に非常に有効な手段になる。

(iii) - 1 補正值を用いたMM2遷移状態モデルの計算

光学活性のアセタールから不斉が誘起できるかどうかを検討することにした。光学活性アセタールとして、 $(2R, 4R)$ -2,4-ペンタンジオールを用いた場合の  $\underline{105}$  の可能な8種のMM2遷移状態モデル (エンド, エキソ;  $\beta$ -メチル,  $\alpha$ -メ



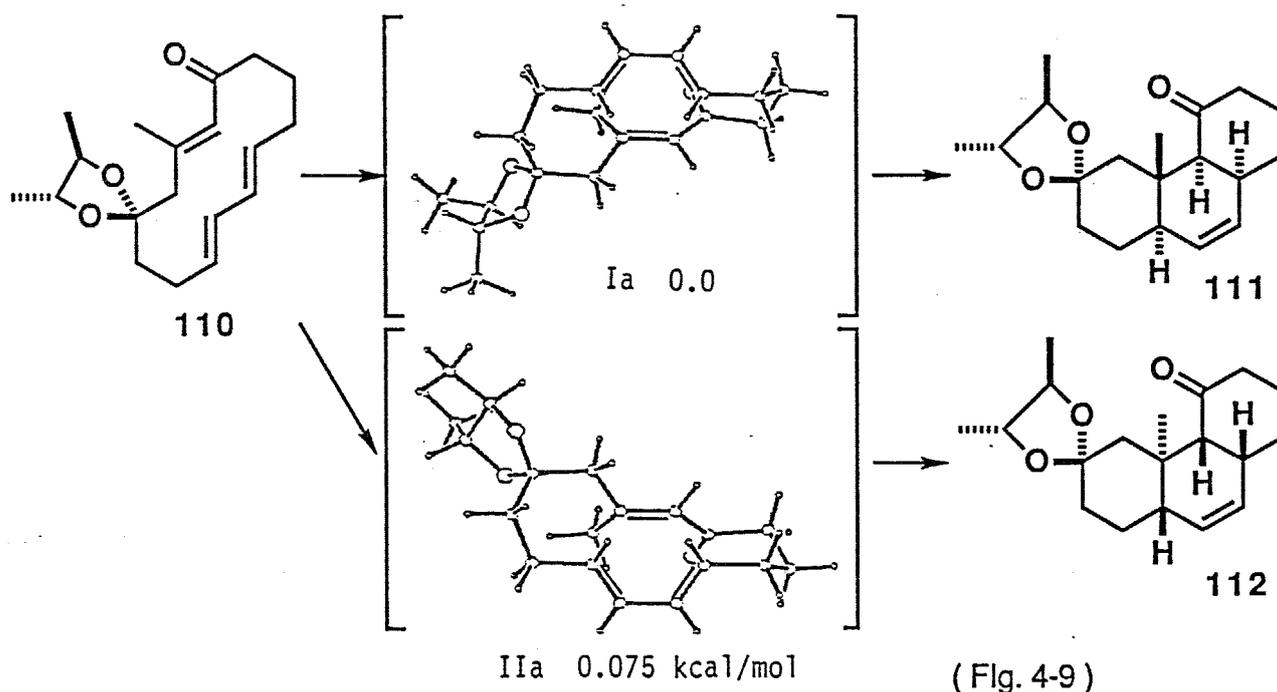
$$\underline{106} : \underline{107} : \underline{108} : \underline{109} = 70 : 24 : 5 : 1 \text{ ( calculation )}$$

( Fig. 4-8 )

テル; C環がいす型, ボート型)の計算を行った。この際、6員環のアセタール部分は最も有利な立体配座を用いた。(ii)の場合と同様にエンドの遷移状態モデルのエネルギー値を補正した結果をFig. 4-8に示した。

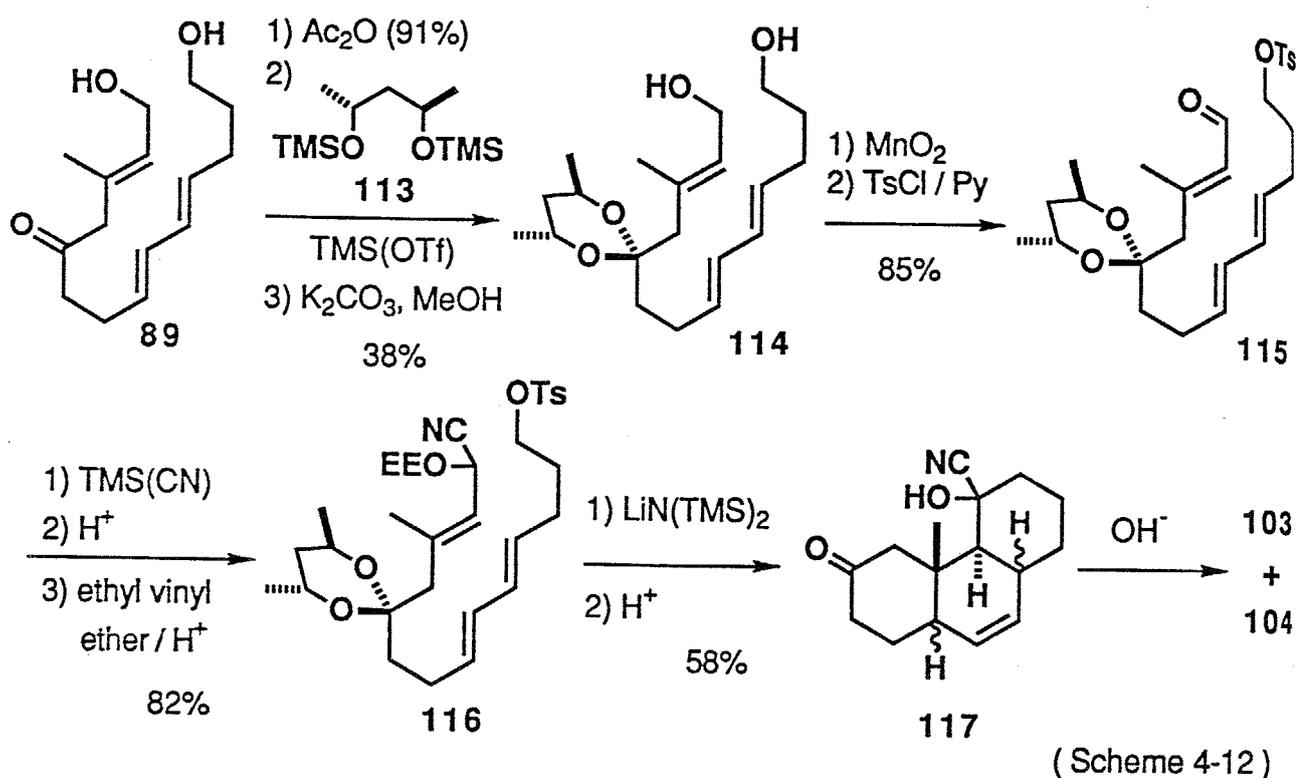
計算結果からBoltzmann分布より20 °Cで106:107:108:109=70:24:5:1と予測できる。すなわち、計算結果からエンド生成物が優先し、光学活性なアセタールからはβ-メチル体が優先して得られると予想される。

また同様にして光学活性アセタールとして(2R,3R)-2,3-ブタンジオールを用いた110の計算も行ったが、β-メチル111とα-メチル112の遷移状態にさしたるエネルギー差は見られなかったため、光学活性なペンタンジオールを用いた6員環の光学活性アセタールについて実際の実験を行った(Fig. 4-9)。



### (iii) - 2 実験結果

89の2つの水酸基をアセテートで保護した後、TMS(OTf)を用いて(2R,4R)-2,4-ペンタンジオールジシリルエーテル(113)でアセタール化し<sup>84)</sup>、続いてアセテートを除去してジオール114を収率38%で得た。114のアリルアルコールだけを二酸化マンガンを酸化し、残った水酸基はトシル化し115へ



収率85%で導いた。次に常法に従ってエチルビニルエーテルで保護したシアノヒドリン **116** を収率82%で得た。閉環反応を種々の塩基 ( $\text{LiN(TMS)}_2$ あるいは  $\text{NaN(TMS)}_2$ ) を用いて60~80 °Cで検討したが、いずれの場合も閉環と同時に Diels-Alder反応が進行し、望む14員環化合物は得られなかった。このことは、生成物を強い酸で脱保護すると3環性の化合物 **117** が得られ、さらに希塩基処理すると **103** と **104** に導かれることから確認した。そこで低温での閉環反応 (0~20 °C) を検討したが、今度は閉環反応が進行しなかった。現在までのところ純粋な14員環化合物が得られていない (Scheme 4-12)。

### (iii) - 3 結論

従来の分子内のDiels-Alder反応では活性化されていないジエノフィルの場合、高温・長時間が必要なことと比較すると、この14員環化合物は異常に反応性が良い。つまり14員環上にアセタールが存在することにより、14員環の炭素鎖の

立体配座がDiels-Alderに都合の良い方向に規制され、異常に反応性に富む結果になったと考えられる。

#### 4-2-3 今後の展望

以上ジエノフィル部位に活性基を有する14員環トリエンの渡環的 Diels-Alder反応について述べてきた。このように電子的効果が働く場合も補正項を用いたMM2遷移状態モデルの計算を行うことにより、その立体選択性を予測することができることを示した。しかし、置換基が異なるごとに補正項を考慮することは限界があるので、より一般的なMM2遷移状態モデルの計算が望まれる。その一つの解決法としては、Diels-Alder反応に直接関与する部位をab initio計算で得られた構造に固定するのではなく、その構造をMM2計算で再現できるようにパラメータ化することである。これが実現すれば様々な置換基を有するDiels-Alder反応の立体選択性を補正項を用いることなく定量的に評価することが可能になると考えられる。

4-3 14員環内Diels-Alderを用いた新規ステロイド骨格合成への応用<sup>85)</sup>

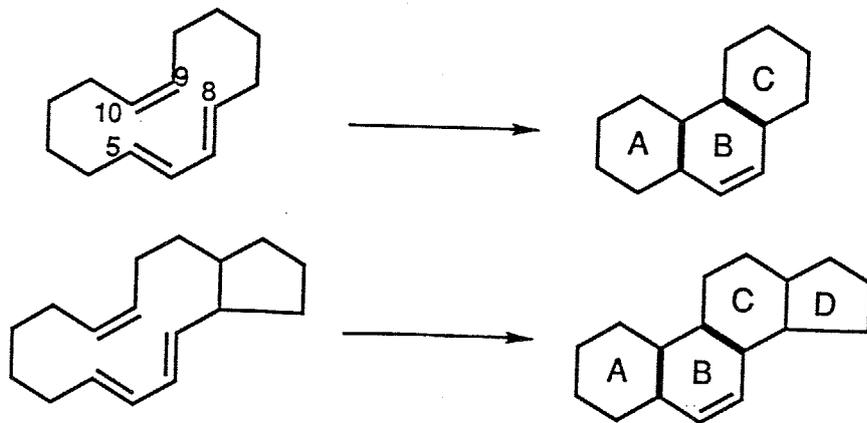
4-3-1 ステロイド骨格合成

従来のステロイド骨格合成はTable 4-1に示すように類別されている<sup>86)</sup>。

( Table 4-1 ) Total syntheses of the Most Important Natural Steroids

name of steroid	Type of synthesis	Authers and year
Equilenin	AB→C→D	Bachmann, 1939
	AB→D→C	Hughes, Smith, 1960
Estrone	AB→C→D	Anner, Miescher, 1948
	AB→CD	Johnson, Robins, 1958
	AB→D→C	Windholz; Crispin, Whitehurst; Miki; Smith; Trogov, 1963
	AC→B→D	Johnson, Christiansen, 1951
	AD→BC	Smith, 1960
	BC→D→A	Velluz, 1960
	CD→A→B	Smith, Hughes, 1963
Androsterone, testosterone	CD→B→A	Velluz, 1963
	BC→A→D	Robinson, 1951
	BC→D→A	Velluz, 1960
	CD→B→A	Stork, 1958
Pregnanolone, progesterone	BC→A→D	Nagata, 1963
	BC→D→A	Velluz, 1961
	CD→B→A	Nagata, 1960
Cortisone	BC→A→D	Sarett, 1952
	BC→D→A	Velluz, 1960
	CD→B→A	Woodward, 1951
Aldosterone	BC→A→D	Wettstein; Reichstein; Szpilfogel, 1955-1960
	CD→B→A	Johnson, 1958
Conessine	BC→A→D	Nagata, 1963
	BC→D→A	Stork, 1962
	CD→B→A	Johnson, 1962

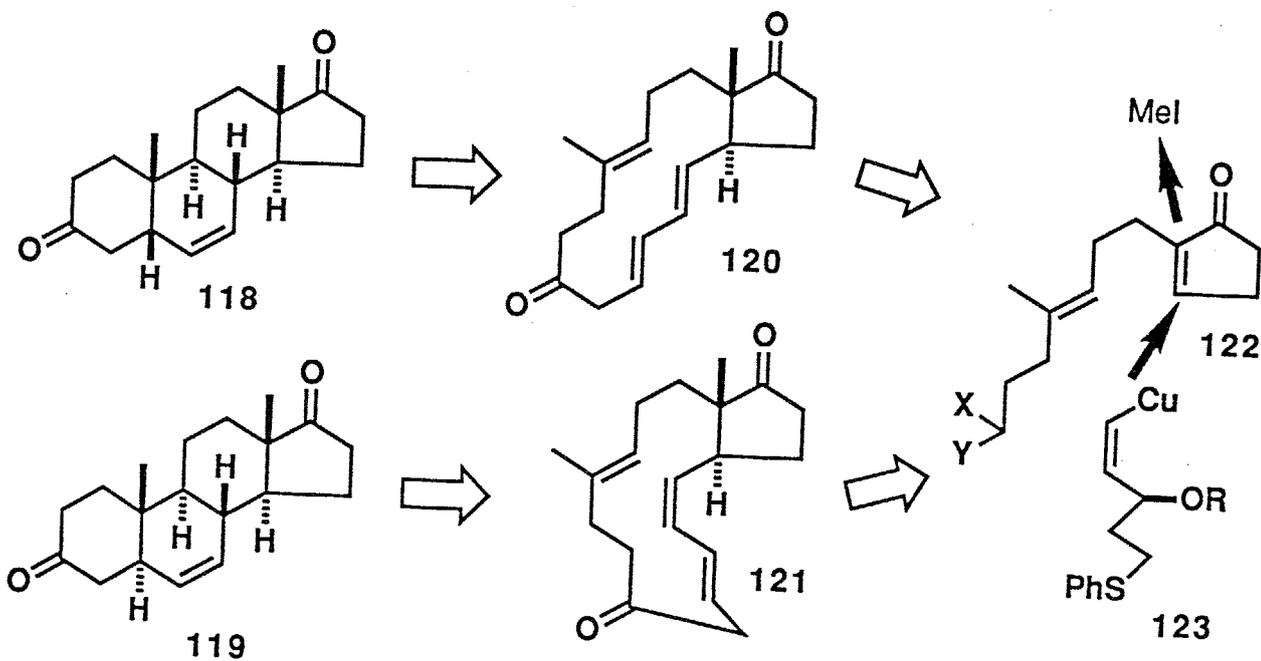
これに対し、大員環内Diels-Alderでは、例えばFig. 4-10のようにC<sub>5</sub>-C<sub>10</sub>, C<sub>8</sub>-C<sub>9</sub>を同時に結び、ABC環を一挙に構築できる。従って、あらかじめD環を用意しておけば、D→ABCという従来にない、新しいタイプのステロイド骨格合成が可能である。



(Fig. 4-10)

#### 4-3-2 合成計画

6,5(β)-Androstene-3,17-dione (118) および5(α)-体 (119) の合成を次のように計画した (Scheme 4-13)。



(Scheme 4-13)

118は、(E,E,E)-トリエンを有する14員環化合物120の分子内Diels-Alder反応により得られ、119は、(Z,E,E)-トリエンを有する121から同様にして得られると考えた。

120および121の合成は、次のように計画した。

エノン122に、シスビニル銅試薬123を面選択的に共役付加させ、生成するエノラートを、共役した基と同じ側から優先してメチル化を行ってC13位のメチル基とC14位の水素とのトランスの立体化学を得、続いて側鎖のアリルアルコールとスルフィドを使って、(Z,E)-あるいは、(E,E)-ハロゲン化ジエニルへ導き、さらにX,Yを利用したアシルアニオンの分子内閉環反応で合成できると考えた。

この際、メチル化が共役付加した基と同じ側から優先して起こることは、既に当研究室で確かめられている。筆者はこのメチル化の選択性について、計算による説明を試みたので4-4で述べる。

実際の合成については、当研究室の清水克也氏が行い、すでに修士論文において詳細に述べている。

筆者は、計算による考察を行ったので以下に述べる。

#### 4-3-3 MM2計算による考察

まず、14員環化合物120、121の大員環内Diels-Alder反応が、進行しやすいかどうかを予想するため、次のような計算を行った。

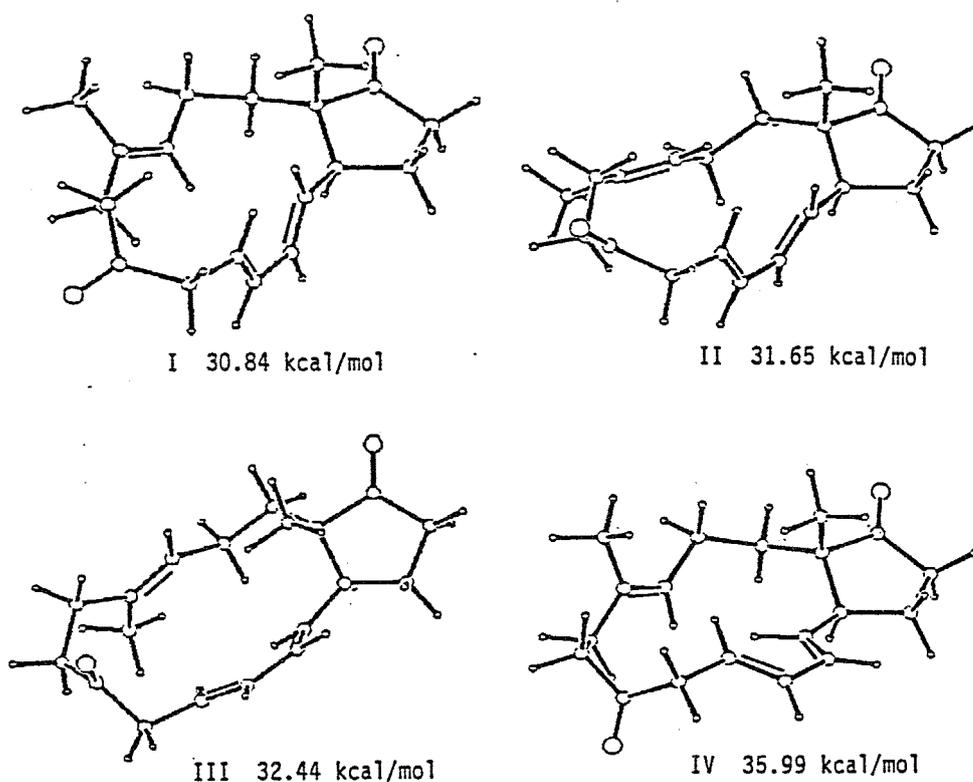
Diels-Alder反応は、ジエン部位がS-シスで進行することが知られているので、14員環化合物のジエン部分がS-シスの配座異性体を、MMRSとMM2により求めた。そしてこの配座異性体から、Diels-Alder反応の反応性がある程度予想できると考えた。なぜなら、大員環化合物は、渡環的立体反発を避けるため、 $\pi$ 軌道が環平面に対して水平方向を向いた方が有利である。したがって、ジエン部分をS-シスにしてあれば、Diels-Alder反応が進行する形を擬似することができる。そこで、この配座異性体でジエンとジエノフィルの距離及び、 $\pi$ 軌道の重なり具合から反応性を予想することにした。

まず、(E,E,E)-トリエン 120 についてジエン部分をS-シスにして検討した。

MMRSにより次の条件で

dihedral angle resolution	45°
closure distance	1.0-3.0 Å
transannular contact	2.4 Å

11種の初期入力座標を得、MM2により構造最適化を行ったところ4つの配座異性体が得られた (Fig. 4-11)。



( Fig. 4-11 )

IVを除けば、いずれもジエンとジエノフィルの距離は近く、 $\pi$ 軌道の重なりも良い。したがって、120のDiels-Alder反応は、非常に容易に進行することが予想された。

(Z,E,E)-トリエン 121 についても同様に行った。

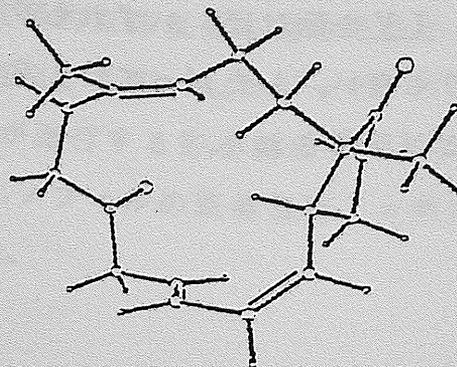
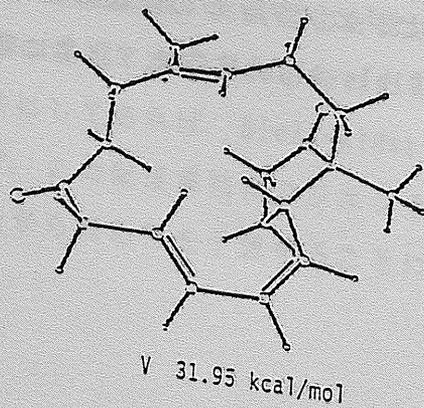
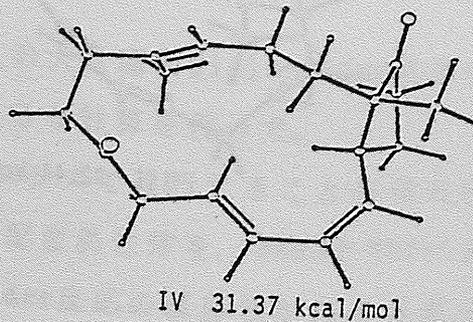
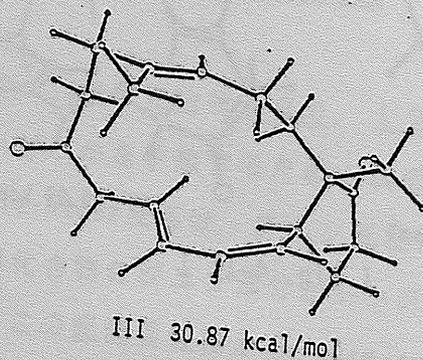
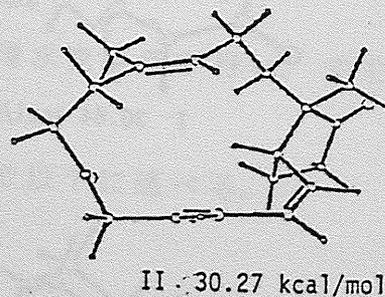
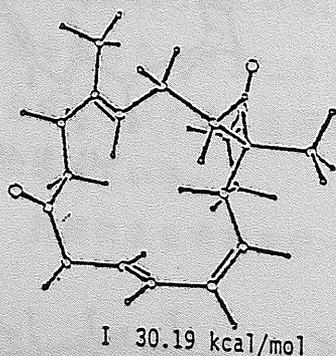
MMRSにより次の条件で

dihedral angle resolution  $45^\circ$

closure distance 1.0-3.0 Å

transannular contact 2.4 Å

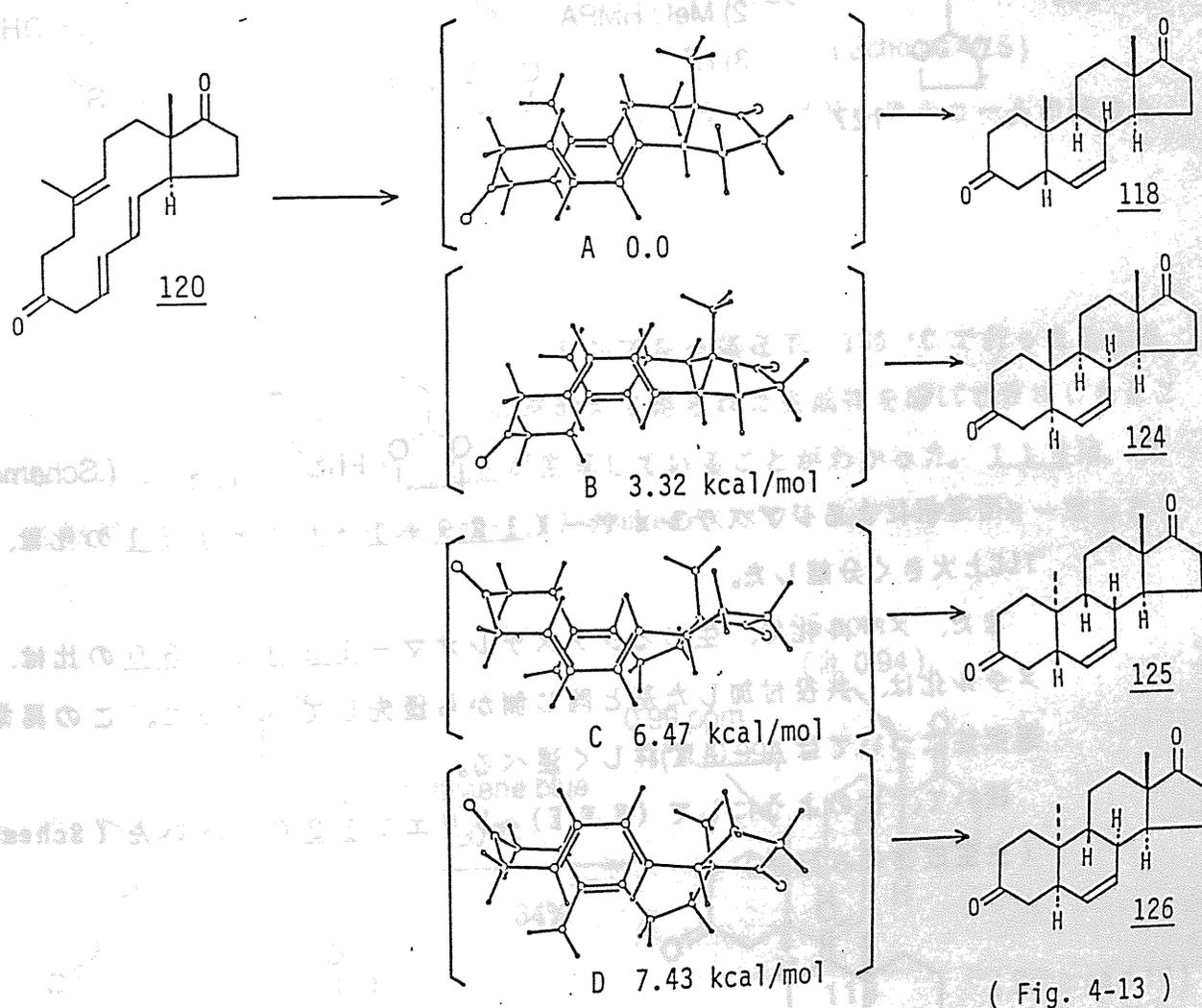
25種の初期入力座標を得、MM2で構造最適化を行い6つの配座異性体が得られた。いずれの場合もジエンとジエノフィルの距離が遠く、 $\pi$ 軌道が互いに向き合っていないので、Diels-Alder反応が進行するためには、かなり分子が歪まなければならないことがわかった。したがって、121からDiels-Alder反応が進行するためには、(E,E,E)-トリエン 120 よりもかなり高いエネルギーが必要と考えられた (Fig. 4-12)。



( Fig. 4-12 )

次に、反応がスムーズに進行すると予想された (E,E,E)-トリエン120の分子内 Diels-Alder反応について、その立体選択性を予測するためにMM2遷移状態モデルを計算した。

4-2と同様にジエンおよびジエノフィル部分を ab initio 遷移状態構造に固定し、そこから残りの炭素鎖をつなげ、MM2により構造最適化し、次の4つのMM2遷移状態モデルを得た (Fig. 4-13)。



遷移状態構造 A は、他よりも 3.3 kcal 以上有利であるから、

Boltzmann分布より 180 °C で、

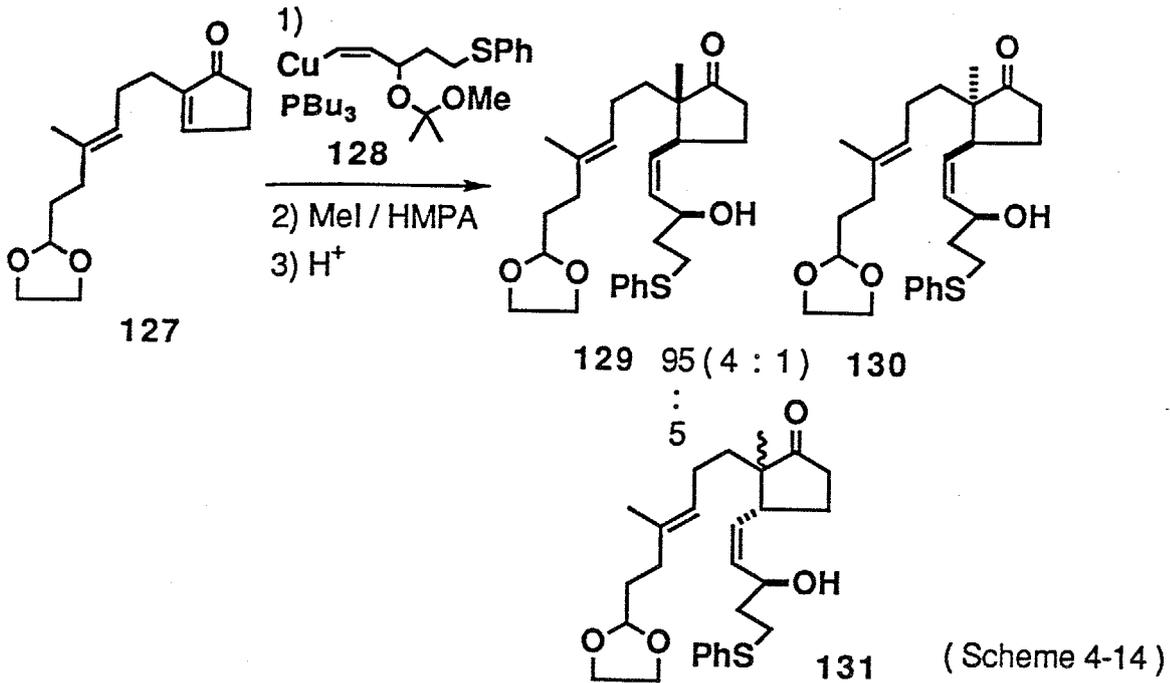
$118 : 124 : 125 : 126 = 40 : 1 : <1 : <1$  と、求められる。

したがって、A から優先して反応は進行し、高立体選択的に求める 118 が、得られると予測できる。

4-3-4 合成

実際の合成は、簡単に述べる。

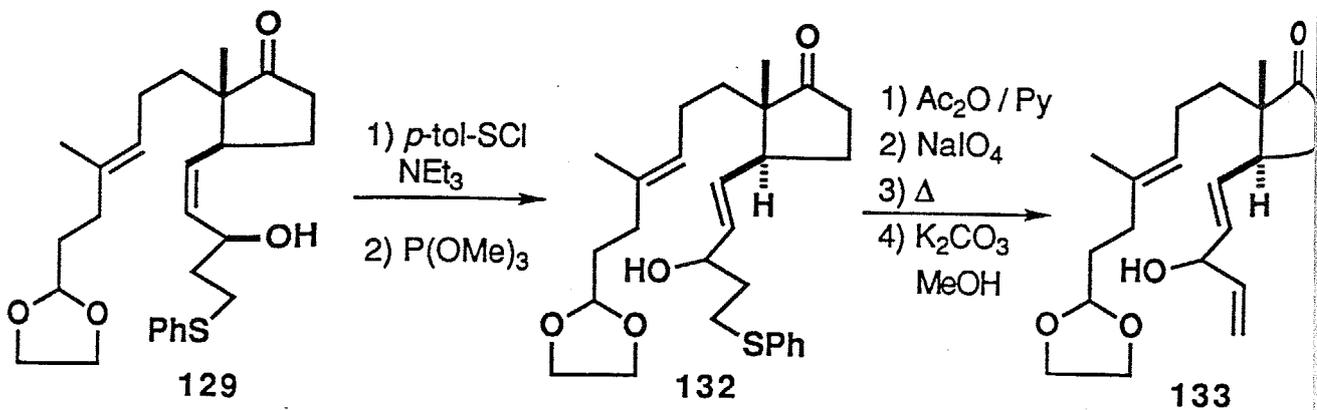
エノン 127 への 128 の共役付加-メチル化 (Scheme 4-14)

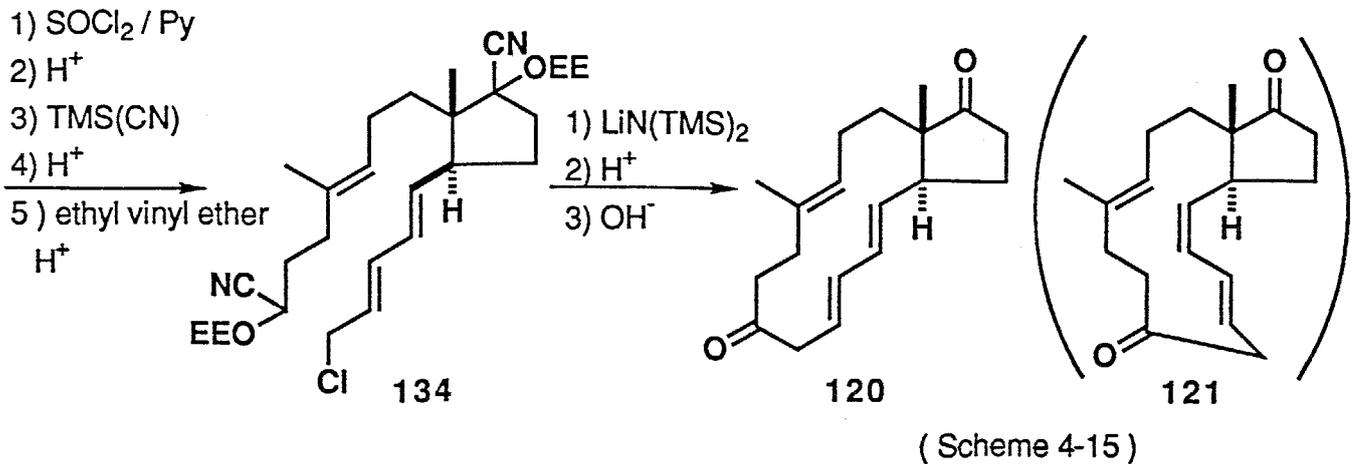


面選択によるジアステレオマー (129 + 130) と 131 の比は、95 : 5 で TLC 上大きく分離した。

また、メチル化で、生じるジアステレオマー 129 と 130 の比は、4 : 1 でメチル化は、共役付加した基と同じ側から優先しておこった。この異常な立体選択性については 4-4 で詳しく述べる。

続いて、次のようにして (E,E,E)-トリエン 120 へ導いた (Scheme 4-15)。(主生成物のみ記述)

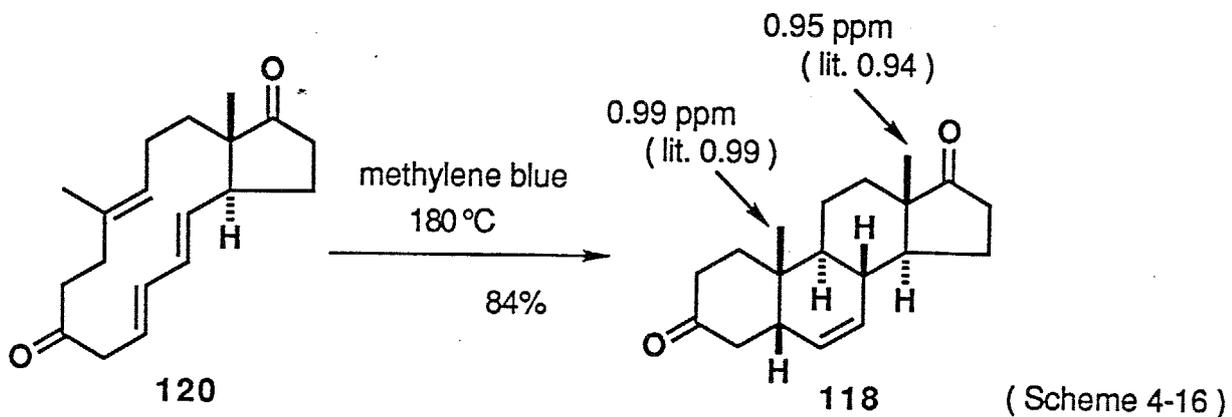




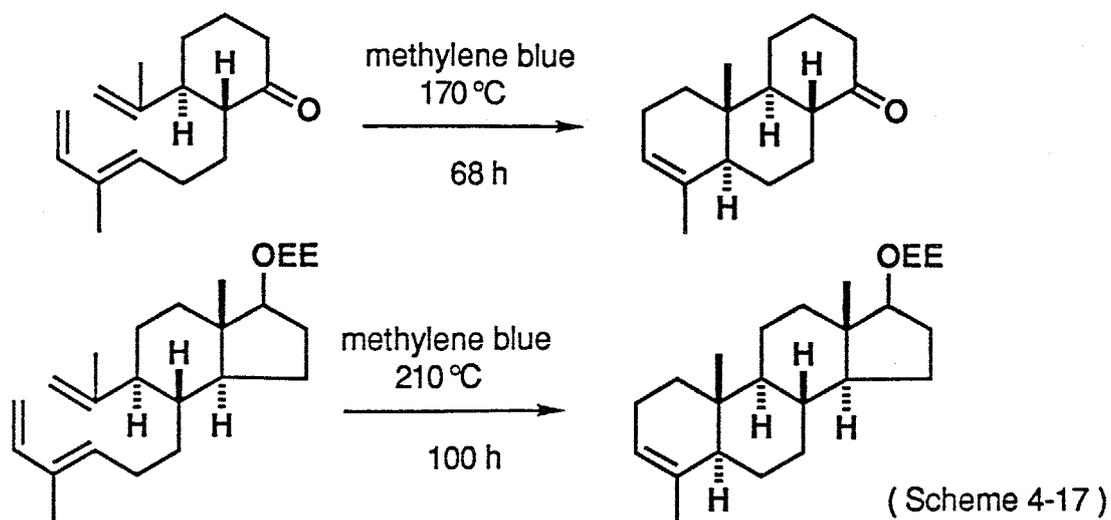
また、(Z,E,E)-トリエン 121 は、129 からアリルアルコールの転位を行わず、同様にして得られた。

#### 4-3-5 実験結果

120 の Diels-Alder 反応をメチレンブルー存在下、180 °C で行ったところ反応は1時間以内に完結した。収率84%で得られた生成物をHPLCで分析したところ、90%以上の選択性で 118 が生成していることがわかった。118 は、文献記載の 6,(5β)-Androstene-3,17-dione のスペクトルデータ<sup>87)</sup> と一致した ( Scheme 4-16 )。

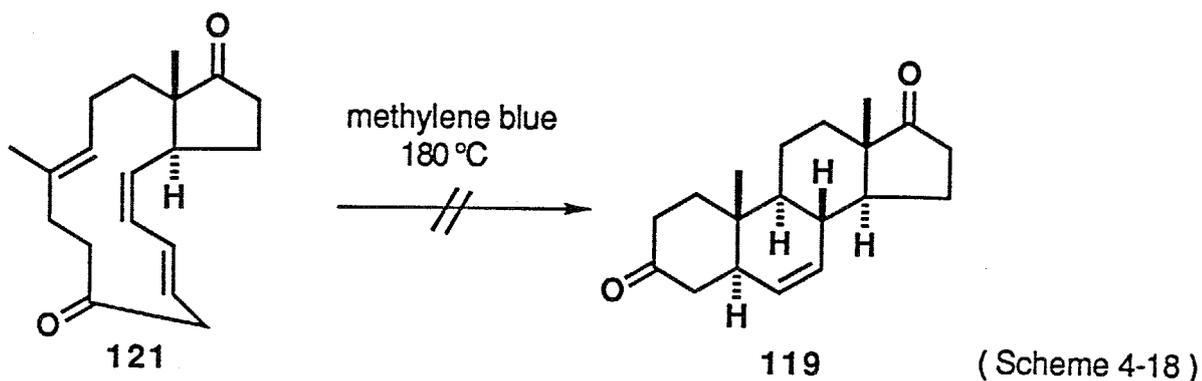


これまでの類似の鎖状の分子内 Diels-Alder 反応<sup>88)</sup> は、数十時間を必要とする ( Scheme 4-17 ) ことから 120 の大員環内 Diels-Alder 反応は、これらに比べはるかに速いことがわかる。反応時間が短いことは、副反応を抑えるために重要なことである。これは、Fig. 4-1 に示したように大員環化合物の渡環反応がエントロピー的に有利なことと、π軌道の重なりが良さが、好結果につながったと考えられる。



さらに90%以上の立体選択性は、Fig. 4-12に示したMM2遷移状態モデルの計算から予測した結果とよく一致した。

一方、(Z,E,E)-トリエン 121 の大員環内Diels-Alder反応を 120 と同じ条件で行ったが、TLC上に多くのスポットが現れた (Scheme 4-18)。



これは、121 がDiels-Alder反応に適した配座を取ることが難しく、反応が進行しにくいという、Fig. 4-11に示した立体配座解析から予想された結果と一致する。

#### 4-3-6 結論

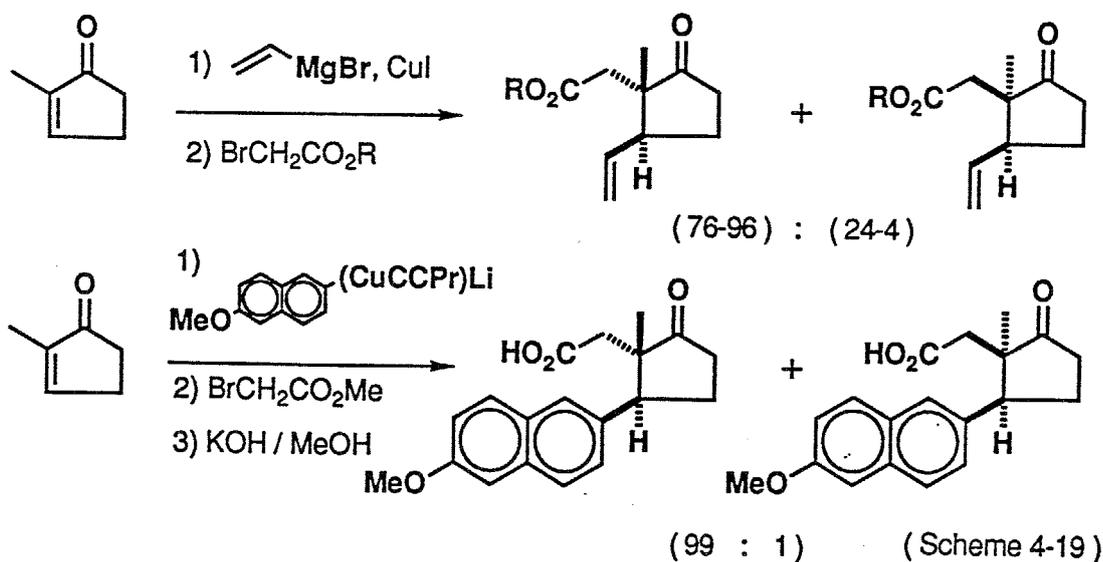
4-3-5の結果から、ジエンの幾何異性体で求める渡環的Diels-Alder反応がスムーズに進行したり、全く進行しないことがわかった。中・大員環化合物の分子内渡環反応が本質的にエントロピー的に有利であっても、立体配座の規制により反応の遷移状態構造を取りにくい場合は、反応が起こりにくくなる。つまり中間体のデザイン次第で極めて大きな反応性の差が生じることは注意しなければならない点である。筆者は、基底状態の立体配座解析を行うことでこの反応性を予想することができることについて述べた。さらにMM2遷移状態モデルの計算から、大員環化合物の渡環的Diels-Alder反応の立体選択性を予測し、D環→ABC環という新しいタイプのステロイド骨格合成への応用に成功し、MM2遷移状態モデルの計算による立体選択性の予測が、分子設計に十分利用できることを示した。

#### 4-4 $\alpha$ 位に長鎖のアルキル基を有する5員環エノンへの共役付加-メチル化の立体選択性

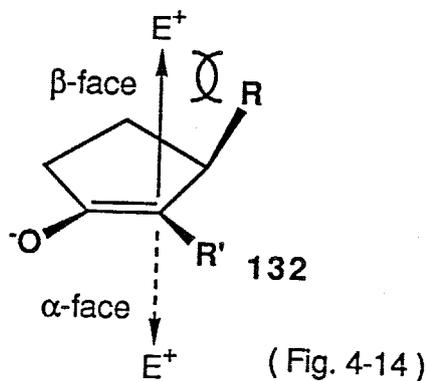
##### 4-4-1 5員環エノラートのアルキル化

ケトンの $\alpha$ 、 $\beta$ 位に異なる置換基を位置および立体選択的に導入することは、有機合成上非常に重要である。この一つの解決法としてエノンへの共役付加-アルキル化が挙げられる。

特に $\alpha$ 位にメチル基を有する5員環エノンに対し、共役付加-アルキル化が行われた例をScheme 4-19に示した<sup>89)</sup>。この際のアシル化は、共役付加した基

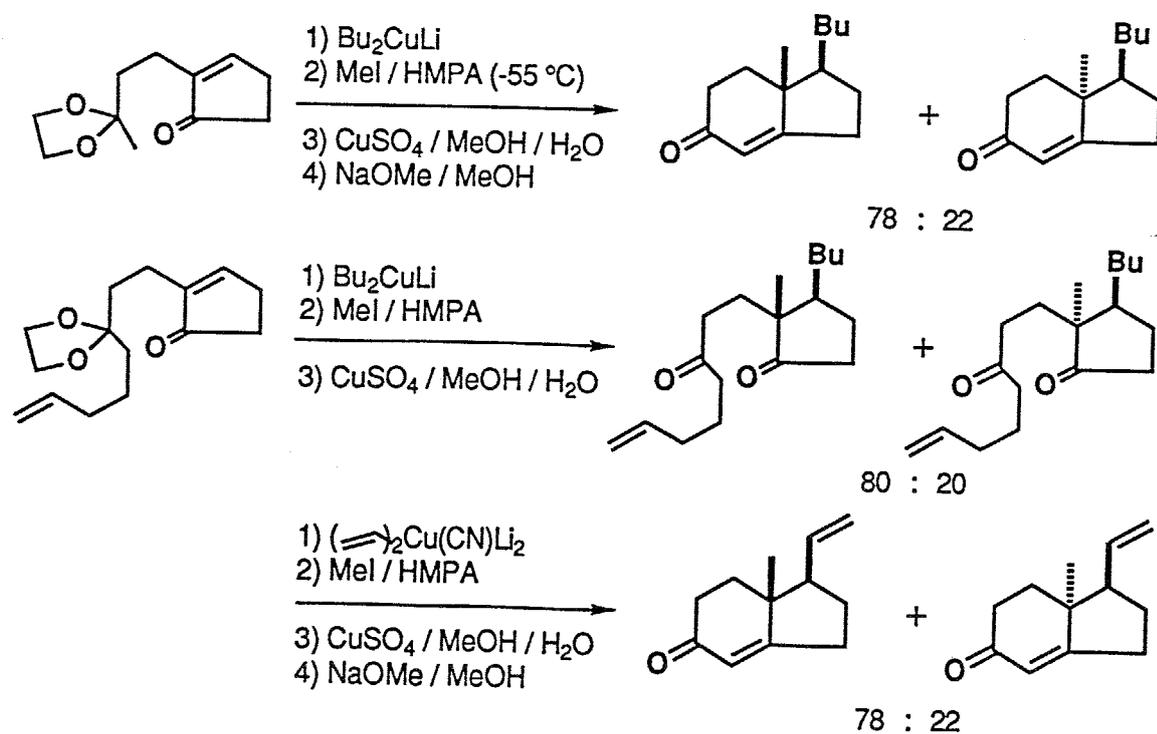


と反対側から進行している。このことはエノラート 132 を考えた場合、 $\beta$ 側からの攻撃がR基により妨げられ、立体障害がない $\alpha$ 側から起こるためと説明されている (Fig. 4-14)。



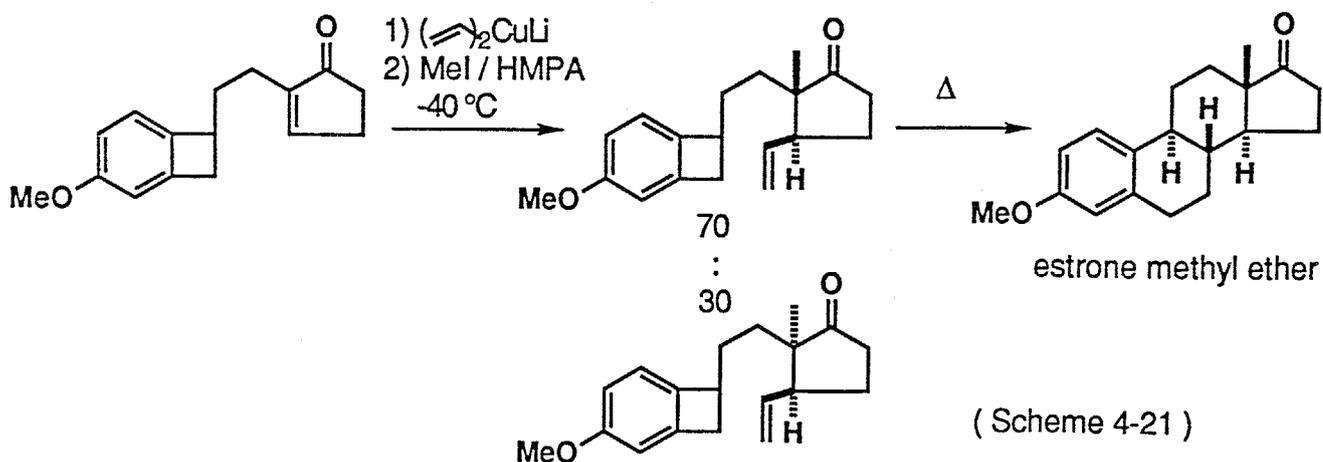
しかし、これらの例は $\alpha$ 位にメチル基を有している場合だけで、 $\alpha$ 位に長鎖の置換基がある系での報告例はなかった。

これに対し、当研究室の清水らは $\alpha$ 位に長鎖の置換基を有する5員環エノンに対し、共役付加-メチル化を行い、その結果共役付加した基と同じ側からのメチル化が優先することを報告した<sup>92)</sup> (Scheme 4-20)。すなわちScheme 4-19の例とは逆の立体選択性を示している。



(Scheme 4-20)

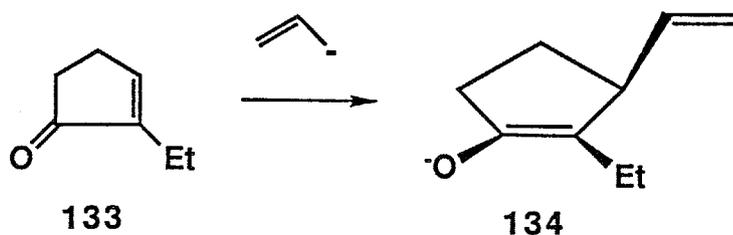
さらに、 $\alpha$ 位に長鎖の置換基を有する5員環エノンへの共役付加-メチル化反応を行って、Oppolzer-亀谷ルート<sup>93)</sup>の合成中間体を合成し、エストロンメチルエーテルへ導くことに成功した<sup>91)</sup> (Scheme 4-21)。



この従来の"less hindered side attack"では説明できないメチル化の立体選択性を、MM2計算を用いて解析した。

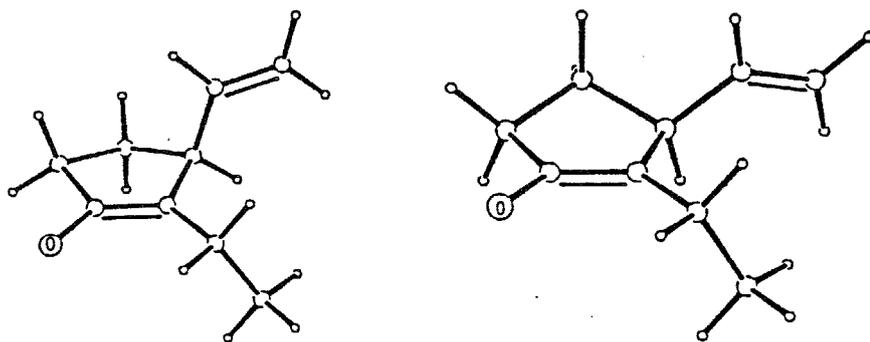
#### 4-4-2 MM2計算

単純化した計算モデルとして、 $\alpha$ 位に長鎖のかわりにエチル基を有するエノン133に対し、ビニル基が共役付加して生成するエノラート134を考えた (Scheme 4-22)。



(Scheme 4-22)

まず134の配座異性体を求めた。5員環の立体配座について、 $\beta$ 位のビニル基が擬アキシアルに向く場合と擬エカトリアルに向く場合の2種類と、 $\alpha$ 位のエチル基のメチル部分が自由回転してできる3種類を考え、計6つの立体配座のMM2計算を行ったところ、次の2つの配座異性体I, IIが最も安定であった (Fig. 4-15)。



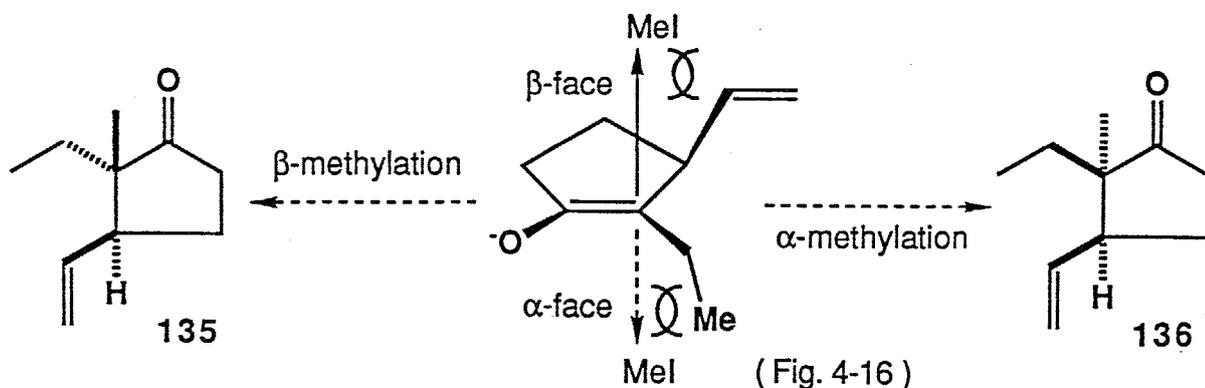
I 10.84 kcal/mol

II 10.61 kcal/mol

( Fig. 4-15 )

アルキル化が早期遷移状態で進行すると仮定し、これらの配座異性体からメチル化が起こると考えると、 $\beta$ 面は $\beta$ 位のビニル基により妨げられており、 $\alpha$

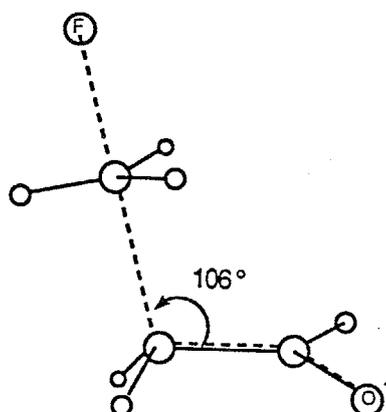
面はエテル基のメチル部分により遮られていることがわかった (Fig. 4-16)。このことから、Scheme 4-19に示した例のように、 $\alpha$ 位がメチル基の場合には $\alpha$ 面の立体障害がないことに比べ、 $\alpha$ 位が長鎖の場合は自由回転できるアルキル基が $\alpha$ 面を遮断するためにメチル化の立体選択性が大きく異なると説明できる。



では、 $\alpha$ 面側も $\beta$ 面側も共に立体障害が生じるこのメチル化反応では、どちら側からの反応がより有利なのか。このことを視覚的に説明することは不可能なので、遷移状態を仮定したMM2遷移状態モデルの計算を行った。

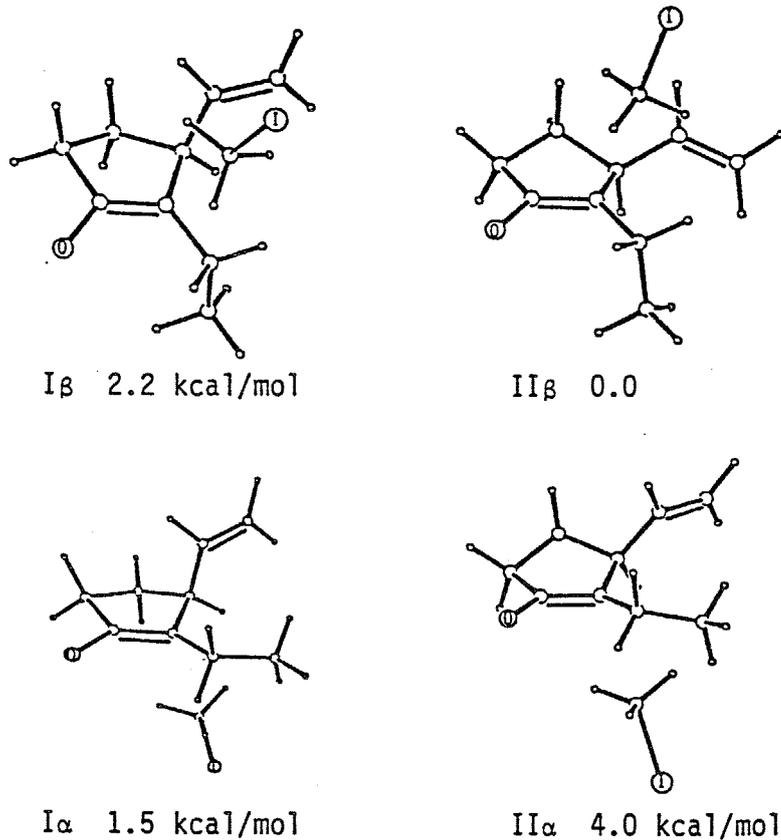
#### 4-4-3 MM2遷移状態モデル計算

エノラートとフッ化メチルのアルキル化反応の遷移状態構造は、Houkらによって *ab initio* 計算から Fig. 4-17に示すように報告されている<sup>12)</sup>。ただし、詳細な遷移状態構造は、発表されていない。



(Fig. 4-17)

そこで、ヨウ化メチルをエノラートに対し鉛直方向に $106^\circ$ の角度で $3.0 \text{ \AA}$ の位置に一直線に固定し、メチル化の遷移状態と仮定した。このように仮定した遷移状態構造を用い、先に示した配座異性体I, IIについて $\beta$ 面と $\alpha$ 面からのメチル化においてそれぞれMM2遷移状態モデルの計算を行った結果を示す (Fig. 4-18)。



計算の結果、 $\beta$ 面からのメチル化が $\alpha$ 面からに比べて $1.5 \text{ kcal/mol}$ 有利であることがわかった。このエネルギー差は実験結果に比べて大きな値を示しているが、 $\beta$ 面からの攻撃が有利である点は一致している。このように溶液中のエノラートの集合体を見捨てた単純なモデルではあるが、視覚的にはわからない問題を解決でき、非常に有効であると考えられる。

#### 4-4-4 結論

従来無視されていたエノラートの $\alpha$ 位の側鎖が、アルキル化の立体選択性に大きく関与していることを、MM2遷移状態モデルの計算から定性的ではあるが説明することができた。この概念は $\beta$ 位の置換基だけが立体障害に関与するとされていた通例を覆す新しい問題提起である<sup>92)</sup>。

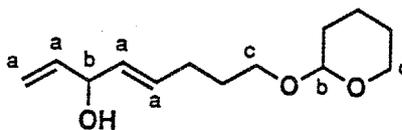
## EXPERIMENTAL SECTION

### (4*E*)-8-(tetrahydro-2*H*-pyran-2-yloxy)-1,4-octadien-3-ol (84)

To a solution of the alkyne **83** (29.8 g, 177 mmol) in dry THF (300 mL) was added a hexane solution of butyllithium (1.60 N, 110 mL, 176 mmol) dropwise over 30 min at -76 °C under nitrogen. The mixture was stirred for 30 min each at -40 °C, -20 °C, and 0 °C. To the solution was added dropwise a solution of acrolein (15 mL) in dry THF (100 mL) at -78 °C. After being stirred for 2 h at -40 °C and for 1 h at 0 °C, the reaction mixture was poured into cold saturated ammonium chloride. The aqueous layer was extracted with 7:3 ether:hexane and the organic layer was washed with saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue (49 g) was used for the next reaction without further purification.

To a suspension of lithium aluminum hydride (8.7 g, 0.22 mol) in dry THF (300 mL) was added dropwise a solution of the crude alkynyl alcohol in dry THF (200 mL) at 0 °C. After being stirred for 6 h at room temperature, the mixture was diluted with ether (500 mL) at 0 °C. To the solution was added dropwise saturated sodium sulfate at the same temperature until white solid was precipitated. After decantation of the reaction mixture, the solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was chromatographed on silica gel (elution with 2:1 hexane:ether) to give the (*E*)-allylic alcohol **84** (24.7 g, 109 mmol, 62% from the alkyne **83**).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.0 -6.14 (m, 5H, a), 4.4 -4.6 (br, 2H, b), 3.2 -4.0 (m, 4H, c),



**84**

### (4*E*,6*E*)-10-(tetrahydro-2*H*-pyran-2-yloxy)-4,6-decadienal (85)

A mixture of the allylic alcohol **84** (1.88 g, 8.32 mmol), Hg(OAc)<sub>2</sub> (160 mg, 0.5 mmol), AcONa (50 mg, 0.6 mmol), and ethyl vinyl ether (25 mL, large excess) was heated in an autoclave at 80 °C for 20 h. Then the reaction mixture was cooled to 0 °C. Potassium carbonate (500 mg, 3.6 mmol) was added to the solution. After being stirred for 1 h, the mixture was diluted with ether and passed through a short pad of Celite. After removal of the solvent, the residue was chromatographed on silica gel (elution with 5:1 hexane:ether) to give the vinyl ether **86** (100 mg, 0.4 mmol,

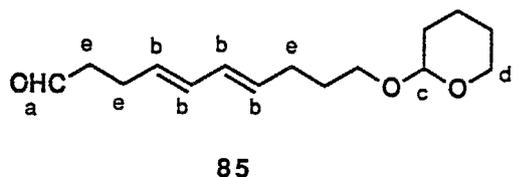
4.8%), the aldehydes **85** (1.03 g, 4.09 mmol, 49%), and the allylic alcohol **84** (830 mg, 3.67 mmol, 44%).

The aldehydes **85** were 3:1 mixture of regioisomers, which were used for the next reaction without further purification.

The aldehyde **85** (major isomer)

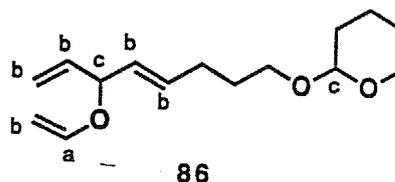
$^1\text{H NMR}$  (90 MHz,  $\text{CDCl}_3$ )  $\delta$  9.76 (t, 1H, a,  $J = 1.3$  Hz), 4.9 -6.4 (m, 4H, b), 4.4 -4.6 (br, 1H, c), 3.2 -4.0 (m, 4H, d), 2.0 -2.7 (m, 6H, e)

IR (neat) 2925, 2860, 2700, 1725, 1440, 1350, 1260, 1200, 1140, 1120, 1080, 1030, 990, 900, 870, 810, 735



The vinyl ether **86**

$^1\text{H NMR}$  (60 MHz,  $\text{CCl}_4$ )  $\delta$  6.15 (dd, 1H, a,  $J = 7, 14$  Hz), 4.9 -6.5 (m, 7H, b), 4.3-4.5 (br, 2H, c)



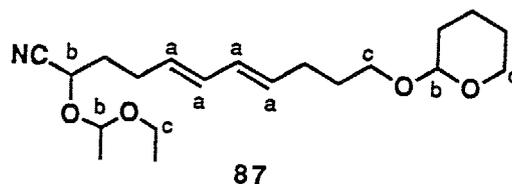
### (5*E*,7*E*)-2-(1-ethoxyethyloxy)-11-(tetrahydro-2*H*-pyran-2-yloxy)-5,7-dodecadienenitrile (**87**)

A mixture of the aldehydes **85** (10.3 g, 40.9 mmol), trimethylsilyl cyanide (5.5 mL, 40.9 mmol), and a catalytic amount of DC-18-CR-6 was stirred for 2 h at 0 °C. The mixture was diluted with THF (50 mL) and tetrabutylammonium fluoride (2.0 g) was added to the solution at 0 °C. After being stirred for 1 h at the same temperature, the reaction mixture was poured into ice-cooled 1N HCl (20 mL). The aqueous layer was extracted with ether twice and the organic layer was washed with brine twice and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue (14 g) was used for the next reaction without further purification.

To a mixture of the crude cyanohydrin in dry dichloromethane (100 mL) and ethyl vinyl ether (4.7 mL, 50 mmol) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After the reaction mixture was stirred for 15 min at the same temperature, triethylamine (0.1 mL, large excess) was added to the solution.

After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with 1:1 hexane:ether) to give the protected cyanohydrin **87** (13.4 g, 93% from the aldehydes **85**).

$^1\text{H NMR}$  (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.3 -6.4 (m, 4H, a), 4.5 -5.2 (m, 3H, b), 3.2 -4.2 (m, 6H, c)



(*2E,8E,10E*)-1,14-dihydroxy-3-methyl-2,8,10-tetradecatrien-5-one (**89**)

To a solution of  $\text{NH}(\text{TMS})_2$  (4.6 mL, 22 mmol) in dry THF (46 mL) was added dropwise a hexane solution of butyllithium (1.6 N, 12.5 mL, 20 mmol) at 0 °C and the reaction mixture was stirred for 30 min. A mixture of the protected cyanohydrin **87** (1.32 g, 3.75 mmol), the allylic bromide **88** (1.5 g, 6.0 mmol), and dry THF (30 mL) was added to the solution of  $\text{LiN}(\text{TMS})_2$  dropwise over 1 h at 60 °C under argon. After the addition was complete, the reaction mixture was poured into cold saturated ammonium chloride with vigorous stirring. The aqueous layer was extracted with 7:3 ether:hexane. The organic layer were washed with saturated sodium bicarbonate, brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

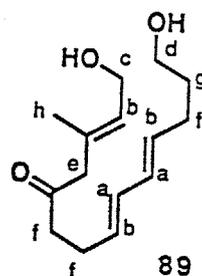
To a solution of the crude alkylated product in methanol (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After the mixture was stirred for 3 h at room temperature, triethylamine (0.1 mL, large excess for acid) was added dropwise to the reaction mixture at 0 °C. The solution was poured into ice-cooled saturated sodium bicarbonate. The mixture was vigorously shaken for 5 min in a separatory funnel. Then the aqueous layer was extracted with three portions of ethyl acetate. The organic layer were washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with 1:3 hexane:ethyl acetate) to give the ketone **89** (700 mg, 2.8 mmol, 54%) and the mixture of the ketone **89** and more polar product **90** (300 mg, 23%) which is a regioisomer obtained by the Claisen rearrangement of the allylic alcohol **84**.

The ketone **89**

$^1\text{H NMR}$  (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.8 -6.2 (m, 2H, a), 5.3 -5.75 (m, 3H, b), 4.17 (d, 2H, c,  $J = 6.8$  Hz), 3.64 (t, 2H, d,  $J = 6.3$  Hz), 3.10 (s, 2H, e), 2.0 -2.7 (m, 6H, f), 1.4 -2.0 (m, 2H, g), 1.66 (d, 3H, f,  $J = 0.7$  Hz)

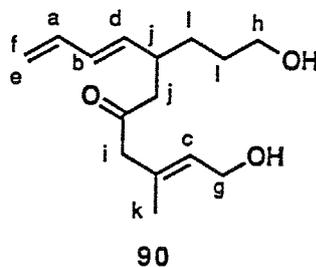
$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  208.8 (C=O), 132.4, 131.8, 131.3, 130.4, 123.0, 129.0 (olefin), 61.8, 58.7, 53.5, 41.6, 32.2, 28.8, 26.7, 16.7

IR (neat) 3050-3650, 2920, 1710, 1440, 1060, 995, 910, 735



The isomer 90

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.29 (ddd, 1H, a,  $J = 15.5, 10.1, 9.2$  Hz), 6.02 (dd, 1H, b,  $J = 10.1, 10.1$  Hz), 5.50 (t, 1H, c,  $J = 6.8$  Hz), 5.3 -5.6 (m, 1H, d), 5.10 (dd, 1H, e,  $J = 15.5, 2.0$  Hz), 4.98 (dd, 1H, f,  $J = 9.2, 2.0$  Hz), 4.16 (d, 2H, g,  $J = 6.8$  Hz), 3.60 (t, 2H, h,  $J = 6.5$  Hz), 3.06 (s, 2H, i), 2.3 -2.8 (m, 3H, j), 1.66 (brs, 3H, k), 1.3 -1.6 (m, 4H, l)



(2*E*,8*E*,10*E*)-3-methyl-2,8,10-tetradecatrien-1,14-diol (91)

To a solution of the diol 89 (2.0 g, 7.93 mmol) in dichloromethane (50 mL) containing a catalytic amount of *p*-toluenesulfonic acid was added dihydropyran (1.52 mL, 16.6 mmol) at 0 °C. After being stirred for 15 min at the same temperature, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with dichloromethane and the combined organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

To a solution of the crude ketone in THF (70 mL) were added several portions of lithium aluminum hydride (300 mg, 7.93 mmol) at 0 °C. After the addition was complete, ether (50 mL) was added to the reaction mixture. To the mixture was added saturated sodium sulfate dropwise at 0 °C until white solid was precipitated. After decantation with several portions of ether, the solution was dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was purified by short column chromatography on silica gel (elution with hexane : ether = 2 : 1) to give the alcohol (2.97 g), which was used for the next reaction without further purification.

To a solution of the alcohol (2.97 g, 7.03 mmol) in chloroform (7 mL) which was passed through a plug of alumina, was added pyridine (2.27 mL, 28.1 mmol) at

0 °C. Several portions of *p*-toluenesulfonyl chloride (2.68 g, 14.1 mmol) and a catalytic amount of 4-(*N,N*-dimethylamino)pyridine were added to the solution at 0 °C. After being stirred for 9 h at room temperature, the reaction mixture was poured into water. The aqueous layer was extracted with 7 : 3 mixture of ether and hexane, and the combined organic layer was washed with ice-cooled 1N HCl solution twice, saturated sodium bicarbonate, and brine. The organic solution was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

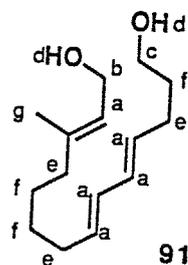
To a solution of lithium aluminum hydride (1.07 g, 28.1 mmol) in THF (50 mL) was added dropwise a solution of the crude tosylate in THF (70 mL) at 0 °C. After being stirred for 1.5 h at 65 °C, the reaction mixture was diluted with ether (100 mL) at 0 °C. To the solution was added dropwise saturated sodium sulfate at the same temperature until white solid was precipitated. After decantation with several portions of ether, the organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue (4.2 g) was used for the next reaction without further purification.

To a solution of the crude protected diol in methanol (140 mL) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After stirring for 3 h at room temperature, triethylamine (0.5 mL, large excess for acid) was added dropwise to the reaction mixture at 0 °C. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 2 : 1) to give the diol **91** (1.19 g, 4.99 mmol, 63% from **89**).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.2-6.2 (m, 5H, a), 4.11 (d, 2H, b, J = 7.0 Hz), 3.6 (t, 2H, c, J = 6.4 Hz), 2.4-2.95 (m, 2H, d), 1.85-2.4 (m, 6H, e), 1.1-1.85 (m, 6H, f), 1.63 (s, 3H, g)

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 139.3, 132.4, 131.2, 130.9, 130.3, 123.4, 62.1, 59.2, 39.3, 32.4, 32.3, 28.9, 28.8, 27.2, 16.1

IR(neat) 3270, 2910, 1665, 1435, 1050, 990, 630



(4*E*,6*E*,12*E*)-13-formyl-12-methyl-4,6,12-tridecatrienyl *p*-toluenesulfonate (**92**)

To a solution of the diol **91** (120 mg, 0.50 mmol) in dry dichloromethane (2 mL) was added several portions of manganese(IV) oxide (0.66 g, 7.5 mmol) at room temperature. After being vigorously stirred for 15 h at room temperature, the

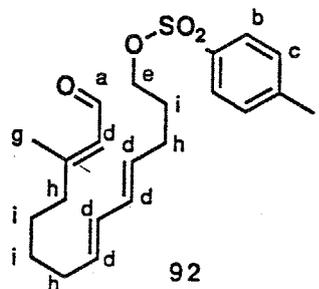
reaction mixture was diluted with ethyl acetate. To the solution was added florisil (0.67 g) with vigorous stirring. The mixture was filtered through Celite, which was washed with ethyl acetate (300 mL). After removal of the solvent without heating, the residue was used for the next reaction without further purification.

To a solution of the crude alcohol in chloroform (1 mL) which was passed through a plug of alumina, was added dry pyridine (0.12 mL, 1.5 mmol) at 0 °C. To the solution was added several portions of *p*-toluenesulfonyl chloride (145 mg, 0.76 mmol) at the same temperature. After being stirred for 2 h at 0 °C, the reaction mixture was poured into water. The aqueous layer was extracted with three portions of 7 : 3 mixture of ether and hexane. The organic layer was washed with ice-cooled 1N HCl twice, saturated sodium bicarbonate, and brine. The organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent without heating, the residue was column chromatographed on silica gel (elution with 2:1 hexane:ether) to give the tosylate **92** (154 mg, 0.39 mmol, 78% from **91**).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 9.96 (d, 1H, a, J = 8.4 Hz), 7.77 (d, 2H, b, J = 8.1 Hz), 7.33 (d, 2H, c, J = 8.1 Hz), 5.0-6.1 (m, 5H, d), 4.01 (t, 2H, e, J = 5.9 Hz), 2.44 (s, 3H, f), 2.14 (s, 3H, g), 1.85-2.65 (m, 6H, h), 1.04-1.85 (m, 6H, i)

IR(neat) 2920, 2850, 1665, 1600, 1440, 1360, 1175, 1100, 990, 960, 920, 815, 660, 575, 555

<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 191.1, 164.0, 144.6, 133.1, 132.3, 131.6, 130.4, 129.8, 127.8, 127.2, 69.8, 40.3, 32.2, 28.7, 28.4, 28.2, 26.5, 21.6, 17.5



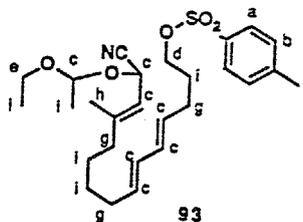
(*4E,6E,12E*)-14-cyano-14-(1-ethoxyethoxy)-12-methyl-4,6,12-tetradecatrienyl *p*-toluenesulfonate (**93**)

A mixture of the enal **92** (189 mg, 0.48 mmol), TMS(CN) (0.1 mL, 0.75 mmol) and a catalytic amount of DC-18-CR-6 was stirred for 15 min at 0 °C. After the reaction mixture was diluted with THF (2 mL), 0.1 N HCl (0.3 mL) was added to the solution at 0 °C. After being stirred for 15 min at the same temperature, the reaction mixture was poured into ice-cooled 1N HCl. The aqueous layer was extracted with ether and the combined organic layer was washed with brine twice, and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue (222 mg) was used for the next reaction without further purification.

To a mixture of the crude cyanohydrin in dry benzene (3.6 mL) and ethyl vinyl ether (0.07 mL, 0.7 mmol) was added a catalytic amount of *p*-toluenesulfonic acid at 4 °C. After stirring for 10 min at the same temperature, triethylamine (0.1 mL, large excess for acid) was added dropwise to the reaction mixture. The mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with 5:1 hexane:ether) to give the protected cyanohydrin **93** (198 mg, 0.40 mmol, 83%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.79 (d, 2H, a, J = 8.1 Hz), 7.34 (d, 2H, b, J = 8.1 Hz), 4.65-6.3 (m, 7H, c), 4.03 (t, 2H, d, J = 6.2 Hz), 3.2-3.8 (m, 2H, e), 2.45 (s, 3H, f), 1.9-2.5 (m, 6H, g), 1.73 (d, 3H, h, J = 1.1 Hz), 1.05-1.9 (m, 12H, i)

IR (neat) 2930, 1660, 1600, 1440, 1365, 1190, 1180, 930-1150, 815, 660, 575, 555

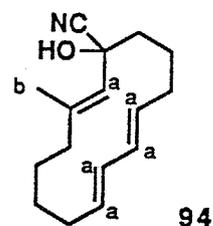


**(2*E*,8*E*,10*E*)-1-hydroxy-3-methyl-2,8,10-cyclotetradecatrienylcarbonitrile (94)**

A solution of the protected cyanohydrin **93** (38 mg, 0.078 mmol) in dry THF (5 mL) was added to a solution of NaN(TMS)<sub>2</sub> (0.66 N benzene solution, 1.18 mL, 0.78 mmol) and dry THF (3 mL) dropwise over 1 h at 60 °C. After the addition was complete, the reaction mixture was poured into ice-cooled ammonium chloride with vigorous stirring. The aqueous layer was extracted with ether and the combined organic layer was washed with saturated sodium bicarbonate and brine. The organic layer was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was dissolved in methanol (2.5 mL). To the solution was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was diluted with ether. The organic solution was washed with brine twice and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel to give a mixture (7.6 mg, 0.03 mmol, 40%) of 14-membered ring compound and diastereomers of Diels-Alder product. The cyanohydrin **94** was isolated by HPLC.

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 1% *i*-PrOH in hexane, 3.35 mL / min); Rt=14.2-16.8 min

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.2-6.3 (m, 5H, a), 1.94 (d, 3H, b,  $J = 1.3$  Hz), 0.8-2.4 (m, 15H)



### Diels-Alder reaction of 94

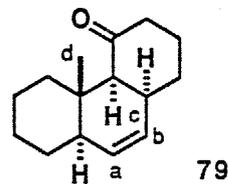
A mixture of the cyanohydrin **94** (5.3 mg), dichloromethane (15 mL), and ice-cooled 2% NaOH was vigorously shaken for 3 min in a separatory funnel. The aqueous layer was extracted with dichloromethane and the combined organic layer was washed with brine. The organic solution was dried over  $\text{MgSO}_4$ . After filtration, the solution of the enone **78** was kept at 20 °C for 12 h. After removal of the solvent, 14 : 1 mixture of the Diels-Alder adducts of **79** and **80** was obtained quantitatively.

#### *cis-transoid-trans-rel*-(4a*S*,4b*S*,8a*R*,10a*S*)-4b-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthren-4-one (**79**)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 2% ethyl acetate in hexane, 2.39 mL / min);  $R_t$ =19.1-21.7 min

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.58 (ddd, 1H, a or b,  $J = 10.1, 3.2, 3.2$  Hz), 5.33 (dm, 1H, b or a,  $J = 10.1$  Hz), 2.56 (m, 1H), 2.47 (dm, 1H,  $J = 14.7$  Hz), 2.43 (d, 1H, c,  $J = 7.8$  Hz), 2.30 (ddd, 1H,  $J = 14.3, 14.3, 5.6$  Hz), 2.05 (ddd, 1H,  $J = 12.5$  Hz, 6.1, 2.9 Hz), 1.91 (dm, 1H,  $J = 13.3$  Hz), 1.2-1.8 (m, 11H), 0.98 (s, 3H, d)

IR ( $\text{CHCl}_3$  solution) 2928, 2858, 1687, 1601, 1094, 933, 631

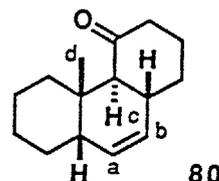


#### *trans-transoid-cis-rel*-(4a*S*,4b*S*,8a*S*,10a*R*)-4b-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthren-4-one (**80**)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 2% ethyl acetate in hexane, 2.39 mL / min);  $R_t$ =10.2-11.2 min

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.61 (ddd, 1H, a or b,  $J = 9.6, 5.0, 2.8$  Hz), 5.39 (brd, 1H, b or a,  $J = 9.6$  Hz), 2.67 (d, 1H, c,  $J = 11.9$  Hz), 2.53 (dm, 1H,  $J = 14.7$  Hz), 2.37 (ddd, 1H,

$J = 13.2, 13.2, 6.4$  Hz), 2.24-2.32 (m, 2H), 2.06-2.13 (m, 1H), 1.96 (dm, 1H,  $J = 11.5$  Hz), 1.60-1.83 (m, 3H), 1.47-1.60 (m, 2H), 1.39-1.47 (m, 1H), 0.98-1.39 (m, 4H), 1.08 (s, 3H, d) IR (CHCl<sub>3</sub> solution) 2926, 2854, 1706, 1601, 1453, 665



**(4E,6E,12E)-13-formyl-10-hydroxy-12-methyl-4,6,12-tridecatrienyl *p*-toluenesulfonate (100)**

To a solution of the ketone **89** (1.0 g, 4.0 mmol) in dry THF (70 mL) were added several portions of lithium aluminum hydride (320 mg, 8 mmol) at 0 °C. After the addition was complete, ether (100 ml) was added to the reaction mixture. To the mixture was added saturated sodium sulfate dropwise at 0 °C until white solid was precipitated. After decantation with several portions of ethyl acetate, the solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue (1.18 g) was used for the next reaction without further purification.

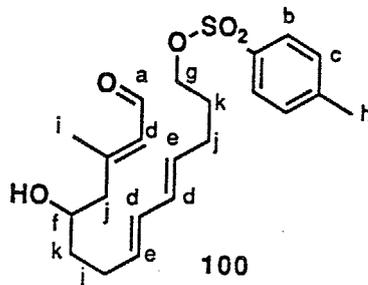
To a solution of the crude triol in dry dichloromethane (8 mL) was added several portions of manganese(IV) oxide (3.6 g, 41 mmol) at 10 °C. After being vigorously stirred for 5 h at room temperature, the reaction mixture was diluted with ethyl acetate. To the solution was added florasil (4 g) with vigorous stirring. The mixture was filtered through Celite, which was washed with ethyl acetate (300 mL). After removal of the solvent without heating, the residue was roughly purified by short column chromatography on silica gel (elution with 1:3 hexane:ethyl acetate) to give the enal (950 mg), which was used for the next reaction without further purification.

To a solution of the diol (690 mg, 2.74 mmol) in chloroform (2.8 mL) which was passed through a plug of alumina, was added dry pyridine (0.44 mL, 5.4 mmol) at 0 °C. To the solution was added several portions of *p*-toluenesulfonyl chloride (780 mg, 4.1 mmol) at the same temperature. After being stirred for 1 h at 0 °C, the reaction mixture was poured into ice-cooled 2 N HCl solution. The aqueous layer was extracted with three portions of ethyl acetate. The organic layer were washed with brine, saturated sodium bicarbonate, and brine, then dried over MgSO<sub>4</sub>. After removal of the solvent at 10 °C, the residue was column chromatographed on silica gel (elution with 1:1 hexane:ethyl acetate) to give the mono-tosylate **100** (790 mg, 1.95 mmol, 71% from the ketone **89**), which was used for the next reaction immediately.

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  9.96 (d, 1H, a,  $J = 7.9$  Hz), 7.77 (d, 2H, b,  $J = 8.2$  Hz), 7.34 (d, 2H, c,  $J = 8.2$  Hz), 5.7 -6.2 (m, 3H, d), 5.2 -5.7 (m, 2H, e), 3.6 -4.3 (m, 1H, f), 4.02 (t, 2H, g,  $J = 6.2$  Hz), 2.45 (s, 3H, h), 2.20 (s, 3H, i), 1.9 -2.5 (m, 6H, j), 1.4 -1.9 (m, 4H, k)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  190.9 (C=O), 160.9, 144.7, 133.3, 131.8, 131.4, 130.7, 130.1, 129.8, 129.2, 127.8, 69.8, 69.1, 48.6, 37.1, 28.7, 28.6, 28.2, 21.6, 18.0

IR (neat) 3350-3450, 3020, 2930, 2870, 1660, 1440, 1380, 1270, 1200, 1130, 1060, 995, 740, 700



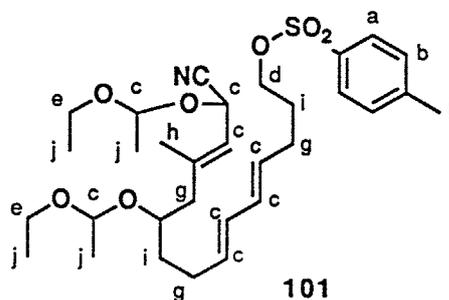
**(4E,6E,12E)-14-cyano-10,14-bis(1-ethoxyethoxy)-12-methyl-4,6,12-tetradecatrienyl *p*-toluenesulfonate (101)**

A mixture of the enal 100 (790 mg, 1.95 mmol), TMS(CN) (0.55 mL, 4.1 mmol) and a catalytic amount of DC-18-CR-6 was stirred for 1 h at 0 °C. After the reaction mixture was diluted with THF (10 mL), tetrabutylammonium fluoride (500 mg) was added to the solution at 0 °C. After being stirred for 50 min at the same temperature, the reaction mixture was poured into ice-cooled 1N HCl solution. The aqueous layer was extracted with dichloromethane and the combined organic layer were washed with brine twice, and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

To a mixture of the crude cyanohydrin in dry benzene (6 mL) and ethyl vinyl ether (0.75 mL, 8 mmol) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After being stirred for 1 h at 0 °C and additional 4 h at room temperature, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate and the organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with 1:1 hexane:ether) to give the protected cyanohydrin 101 (990 mg, 1.54 mmol, 78%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 (d, 2H, a,  $J = 8.2$  Hz), 7.33 (d, 2H, b,  $J = 8.2$  Hz), 5.0 -6.1 (m, 8H, c), 4.02 (t, 2H, d,  $J = 6.2$  Hz), 3.3 -3.9 (m, 5H, e), 2.45 (s, 3H, f), 1.9 -2.4 (m, 6H, g), 1.79 (brs, 3H, h), 1.44-1.9 (m, 4H, i), 1.04-1.44 (m, 12H, j)

IR (neat) 2980, 2930, 1600, 1440, 1360, 1190, 1180, 930-1140, 840, 820, 740, 710, 690, 660, 580, 560



**(2E,8E,10E)-1,5-dihydroxy-3-methyl-2,8,10-cyclotetradecatrienylcarbonitrile (102)**

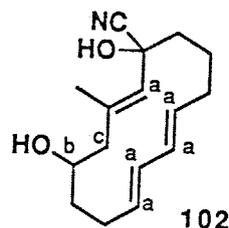
To a solution of  $\text{NH}(\text{TMS})_2$  (1.3 mL, 6.1 mmol) in dry dioxane (20 mL) was added dropwise a hexane solution of butyllithium (1.76 N, 3.0 mL, 5.3 mmol) at 10 °C and the mixture was stirred for 30 min. A solution of the protected cyanohydrin 101 (500 mg, 0.87 mmol) in dry dioxane (40 mL) was added to the solution of  $\text{LiN}(\text{TMS})_2$  dropwise over 4 h at 70 °C. After the addition was complete, the reaction mixture was poured into ice-cooled saturated ammonium chloride with vigorous stirring. The aqueous layer was extracted with 7:3 ether:hexane. Then the organic layer was washed with saturated sodium bicarbonate, brine and dried over  $\text{MgSO}_4$ .

After removal of the solvent, the residue was dissolved in THF (10 mL). To the solution was added 3 N HCl (3 mL) dropwise at 0 °C. After being stirred for 1 h, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with three portions of ether and the organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was purified by short column chromatography on silica gel to give a mixture (ca. 200 mg, ca. 85%) of diastereomers of the 14-membered ring product and diastereomers of Diels-Alder product.

As one of the diastereomers of the 14-membered ring product, the cyanohydrin 102 was isolated by HPLC.

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 10% *i*-PrOH in hexane, 2.53 mL / min);  $R_t=14.0-14.8$  min

$^1\text{H NMR}$  (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.3 -6.2 (m, 5H, a), 3.4 -3.8 (m, 1H, b), 2.08 (d, 3H, c,  $J = 1.3$  Hz)



## Diels-Alder reaction of 95

A mixture of the cyanohydrin 102 (10 mg), ether (10 mL) and ice-cooled 2% NaOH was vigorously shaken for 3 min in a separatory funnel. The aqueous layer was extracted with dichloromethane and the organic layer was washed with brine and dried over MgSO<sub>4</sub>. After the filtration, the solution of the enone 95 was kept at 20 °C for 30 min. After removal of the solvent, 14 : 1 mixture of Diels-Alder adducts of 96 and 98 was obtained quantitatively.

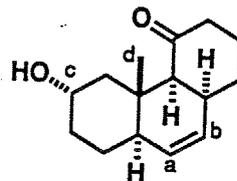
### *cis-transoid-trans-rel*-(4a*S*,4b*S*,6*R*,8a*R*,10a*S*)-6-hydroxy-4b-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthren-4-one (96)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 10% *i*-PrOH in hexane, 2.53 mL / min); Rt=15.1-16.7 min

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 5.60 (ddd, 1H, a or b, J = 10.0, 2.6, 2.6 Hz), 5.37 (ddd, 1H, a or b, J = 10.0, 1.6, 1.6 Hz), 3.5 -4.1 (m, 1H, c), 0.9 -2.7 (m, 15H), 0.95 (s, 3H, d)

IR (CHCl<sub>3</sub> solution) 2930, 2860, 1690, 1020

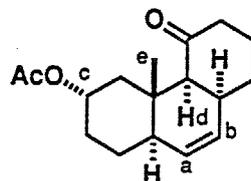
<sup>13</sup>C NMR (22.5 MHz, CDCl<sub>3</sub>) δ 212.6, 129.6, 128.9, 67.1, 60.6, 47.0, 45.2, 43.1, 38.6, 36.0, 35.8, 29.2, 26.0, 24.7, 16.5



96

### The acetate 96'

<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 5.62 (ddd, 1H, a or b, J = 10.0, 3.0, 3.0 Hz), 5.37 (ddd, 1H, a or b, J = 10.0, 1.8, 1.8 Hz), 4.96 (dddd, 1H, c, J = 11.4, 11.4, 4.9, 4.9 Hz), 2.46 (d, 1H, d, J = 7.9 Hz), 2.00 (s, 3H, e), 1.02 (s, 3H, f)



96'

### *trans-transoid-cis-rel*-(4a*S*,4b*S*,6*R*,8a*S*,10a*R*)-6-hydroxy-4b-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthren-4-one (98)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 10% *i*-PrOH in hexane, 2.53 mL / min); Rt=9.0-9.5 min

<sup>1</sup>H N

or a,

Hz),

IR(C

<sup>13</sup>C N

40.5,

The d

mL)

temp

7:3 e

remo

ether

*trans*

dode

HPLC

mL /

<sup>1</sup>H N

or a,

IR(C

*cis-tr*

dode

HPLC

mL /

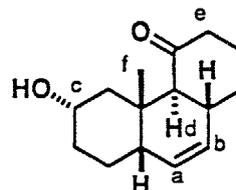
<sup>1</sup>H N

10.3

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.63 (ddd, 1H, a or b,  $J = 9.9, 4.3, 2.4$  Hz), 5.44 (dd, 1H, b or a,  $J = 9.9, 1.7$ ), 4.09 (dddd, 1H, c,  $J = 3.0, 3.0, 3.0, 3.0$  Hz), 3.13 (d, 1H, d,  $J = 11.7$  Hz), 2.77 (dm, 1H, e,  $J = 15.0$  Hz), 1.1-2.5 (m, 13H), 1.05 (s, 3H, f)

IR ( $\text{CHCl}_3$  solution) 2900, 2850, 1700, 940

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  197.1, 131.4, 128.6, 109.1, 67.3, 53.8, 45.5, 43.6, 41.9, 40.5, 32.8, 32.4, 37.1, 35.7, 23.6



98

#### The diketone 103 (104)

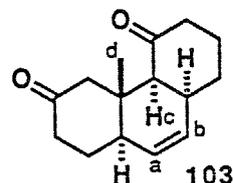
To a solution of the alcohol 96 (98) (8 mg, 0.03 mmol) in dry dichloromethane (1 mL) was added pyridinium chlorochromate (30 mg, 0.08 mmol) at room temperature. After being stirred for 30 min, the reaction mixture was diluted with 7:3 ether:hexane. The solution was passed through a short pad of Celite. After removal of the solvent, the residue was chromatographed on silica gel (elution with ether:hexane 2:1) to give the diketone 103 (104) (5 mg, 60%).

#### *trans-transoid-cis-rel*-(4a*S*,4b*S*,6*R*,8a*S*,10a*R*)-4a-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthrene-3,5-dione (103)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 5% *i*-PrOH in hexane, 2.53 mL / min);  $R_t$ =7.8-8.3 min

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.70 (ddd, 1H, a or b,  $J = 10.0, 2.6, 2.6$  Hz), 5.38 (d, 1H, b or a,  $J = 10.0$  Hz), 2.26 (d, 1H, c,  $J = 5.3$  Hz), 0.91 (s, 3H, d)

IR ( $\text{CHCl}_3$  solution) 2930, 2860, 1710, 1680

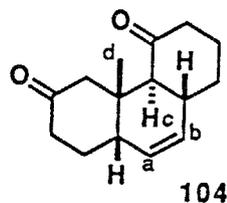


#### *cis-transoid-trans-rel*-(4a*S*,4b*S*,6*R*,8a*R*,10a*S*)-4a-methyl-1,2,3,4,4a,4b,5,6,7,8,8a,10a-dodecahydrophenanthrene-3,5-dione (104)

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 5% *i*-PrOH in hexane, 2.53 mL / min);  $R_t$ =6.3-7.2 min

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.70 (dm, 1H, a or b,  $J = 10.3$  Hz), 5.40 (d, 1H, b or a,  $J = 10.3$  Hz), 2.84 (d, 1H, c,  $J = 14.6$  Hz), 1.13 (s, 3H, d)

IR (CHCl<sub>3</sub> solution) 2930, 2860, 1710



### preparation of diol 114

To a solution of the diol 89 (3.73 g, 14.8 mmol) in dichloromethane (80 mL) was added pyridine (7.17 mL, 88.7 mmol) at 0 °C. To the solution was added acetyl chloride (3.15 mL, 44.3 mmol) at the same temperature. After being stirred for 5 min at 0 °C, the reaction mixture was poured into water. The aqueous layer was extracted with 7 : 3 mixture of ether and hexane, and the combined organic layer was washed with ice-cooled 1 N HCl twice, saturated sodium bicarbonate, and brine. The organic solution was dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane : ether = 3 : 1) to give the diacetate (4.54 g, 13.5 mmol, 91%).

To a mixture of the ketone (1.06 g, 3.15 mmol) and (2R,4R)-2,4-bis(trimethylsilyloxy)-pentane (1.57 g, 6.32 mmol) in freshly distilled dichloromethane (2.5 mL) was added trimethylsilyl trifluoromethanesulfonate (0.024 mL, 0.12 mmol) at -78 °C. The reaction mixture was warmed from -78 °C to -10 °C over 3 h. After stirring for 3 h at -10 °C and additional 1 h at room temperature, pyridine (0.3 mL) was added dropwise to the mixture at 0 °C. The reaction mixture was poured into ice-cooled 1 N HCl and the aqueous layer was extracted with ether. The combined organic layer was washed with saturated sodium bicarbonate and brine. The organic solution was dried over 1 : 1 mixture of Na<sub>2</sub>SO<sub>4</sub> and Na<sub>2</sub>CO<sub>3</sub> and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

To a solution of the crude diacetate in methanol (50 mL) was added potassium carbonate (131 mg, 0.95 mmol) at 0 °C. After being stirred for 3 h at room temperature, the reaction mixture was diluted with ether. After removal of the solvent without heating, the residue was diluted with dichloromethane and the solution was poured into water. The aqueous layer was extracted with dichloromethane and the combined organic layer was washed with saturated ammonium chloride, brine, and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent without heating, the residue was column chromatographed on silica gel (elution

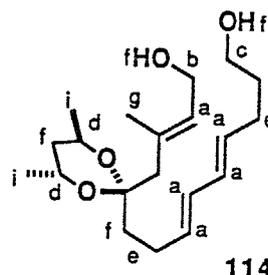
with hexane : ethyl acetate = 1 : 1) to give the diol **114** (404, mg, 1.19 ,mmol, 38% from the ketone), which was used for the next reaction immediately.

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.3-6.2 (m, 5H ,a), 4.15 (d, 2H, b,  $J = 6.6$  Hz), 3.63 (t, 2H, c,  $J = 6.4$  Hz), 3.4-4.3 (m, 2H, d), 1.95-2.65 (m, 6H, e), 1.4-1.95 (m, 8H, f), 1.74 (s, 3H, g), 1.17 (d, 6H, i,  $J = 6.2$  Hz)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  135.4, 132.3, 131.3, 130.9, 130.0, 128.0, 102.5, 62.7, 62.6, 62.3, 59.3, 44.6, 41.1, 35.0, 32.3, 28.9, 27.0, 21.8, 21.6, 17.5

IR(neat) 3340, 2924, 1662, 1444, 950-1400, 915, 829, 734, 615, 435.

$[\alpha]_{\text{D}}^{25} = -16.4^\circ$  (c 2.01,  $\text{CHCl}_3$ )



#### preparation of tosylate **115**

To a solution of the diol **114** (157 mg, 0.46 mmol) in dry dichloromethane (2 mL) was added several portions of manganese(IV) oxide (800 mg, 0.92 mmol) at room temperature. After being vigorously stirred for 17 h at the same temperature, the reaction mixture was diluted with ethyl acetate. To the solution was added florisil (4 g) with vigorous stirring. The mixture was filtered through florisil and the filtrate was concentrated *in vacuo*. The residue was used for the next reaction without further purification.

To a solution of the crude alcohol in dichloromethane (1 mL) which was passed through a plug of alumina, was added dry pyridine (0.11 mL, 1.39 mmol) at 0 °C. To the solution was added several portions of *p*-toluenesulfonyl chloride (138 mg, 0.72 mmol) at the same temperature. After being stirred for 3 h at 0 °C, the reaction mixture was poured into ice-cooled 1 N HCl solution. The aqueous layer was extracted with three portions of ether. The organic layer were washed with brine, saturated sodium bicarbonate, and brine, then dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with 3:1 hexane:ethyl acetate) to give the mono-tosylate **115** (180 mg, 0.39 mmol, 85% from **114**)

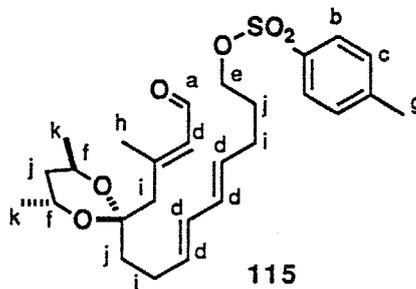
$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  10.00 (d, 1H, a,  $J = 8.4$  Hz), 7.78 (d, 2H, b,  $J = 8.1$  Hz), 7.33 (d, 2H, c,  $J = 8.1$  Hz), 5.1-6.1 (m, 5H, d), 4.01 (t, 2H, e,  $J = 6.2$  Hz), 3.7-4.25 (m, 2H, f),

2.45 (s, 3H, g), 2.26 (d, 3H, h,  $J = 0.88$  Hz), 1.9-2.75 (m, 6H, i), 1.45-1.9 (m, 6H, j), 1.18 (d, 6H,  $J = 6.6$  Hz)

$^{13}\text{C}$  NMR (22.5 MHz,  $\text{CDCl}_3$ )  $\delta$  190.9, 159.9, 144.6, 133.1, 132.1, 131.6, 130.7, 130.0, 129.8, 127.9, 127.8, 101.9, 69.8, 63.0, 62.8, 46.2, 40.6, 35.7, 28.5, 28.2, 26.9, 21.8, 21.6, 21.5, 18.8

IR(neat) 2968, 2928, 1670, 1629, 1598, 1445, 1361, 880-1320, 815, 764, 664, 574, 555

$[\alpha]_{\text{D}}^{25} = -6.34^\circ$  (c 3.88,  $\text{CHCl}_3$ )



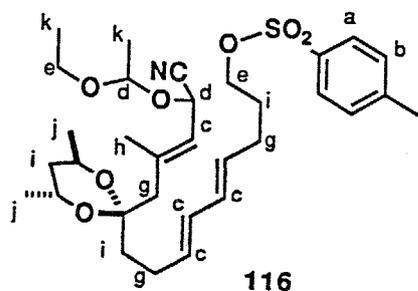
### preparation of the protected cyanohydrin ether 116

A mixture of the enal **115** (157 mg, 0.34 mmol), TMS(CN) (0.05 mL, 0.37 mmol) and a catalytic amount of DC-18-CR-6 was stirred for 1 h at 0 °C. After the reaction mixture was diluted with THF (2 mL), 0.1 N HCl (0.3 mL) was added to the solution at 0 °C. After being stirred for 5 min at the same temperature, the reaction mixture was poured into brine. The aqueous layer was extracted with ether and the combined organic layer was washed with brine twice, and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the residue was used for the next reaction without further purification.

To a mixture of the crude cyanohydrin in dry benzene (4 mL) and ethyl vinyl ether (0.2 mL, 2.1 mmol) was added a catalytic amount of pyridinium *p*-toluenesulfonate at 4 °C. After stirring for 1 h at room temperature, triethylamine (0.1 mL, large excess for acid) was added dropwise to the reaction mixture. The mixture was poured into ice-cooled saturated sodium bicarbonate and the aqueous layer was extracted with ether. The combined organic layer was washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with 4:1 hexane:ether) to give the protected cyanohydrin **116** (157 mg, 0.28 mmol, 82%).

$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d, 2H, a,  $J = 8.1$  Hz), 7.34 (d, 2H, b,  $J = 8.1$  Hz), 5.25-6.1 (m, 5H, c), 4.7-5.25 (m, 2H, d), 3.3-4.15 (m, 6H, e), 2.45 (s, 3H, f), 1.9-2.5 (m, 6H, g), 1.83 (d, 2H, h,  $J = 1.3$  Hz), 1.45-1.9 (m, 6H, i), 1.17 (d, 6H, j,  $J = 6.4$  Hz), 1.0-1.45 (m, 6H, k)

IR(neat) 2970, 2928, 2232, 1662, 1597, 1445, 1362, 900-1200, 815, 664, 575, 555

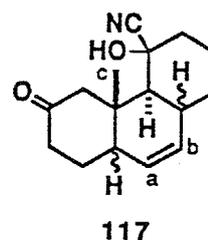


### ring closure reaction of 116

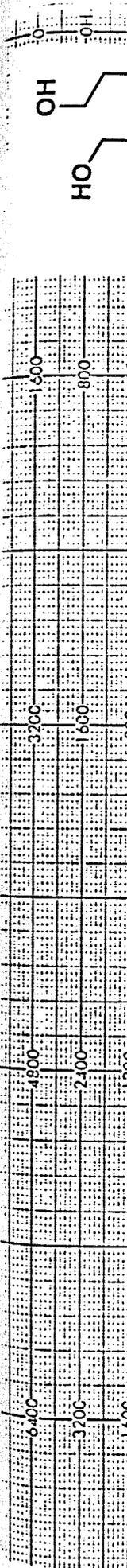
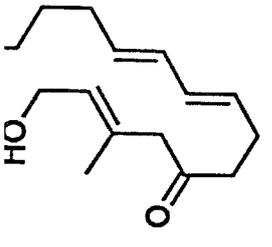
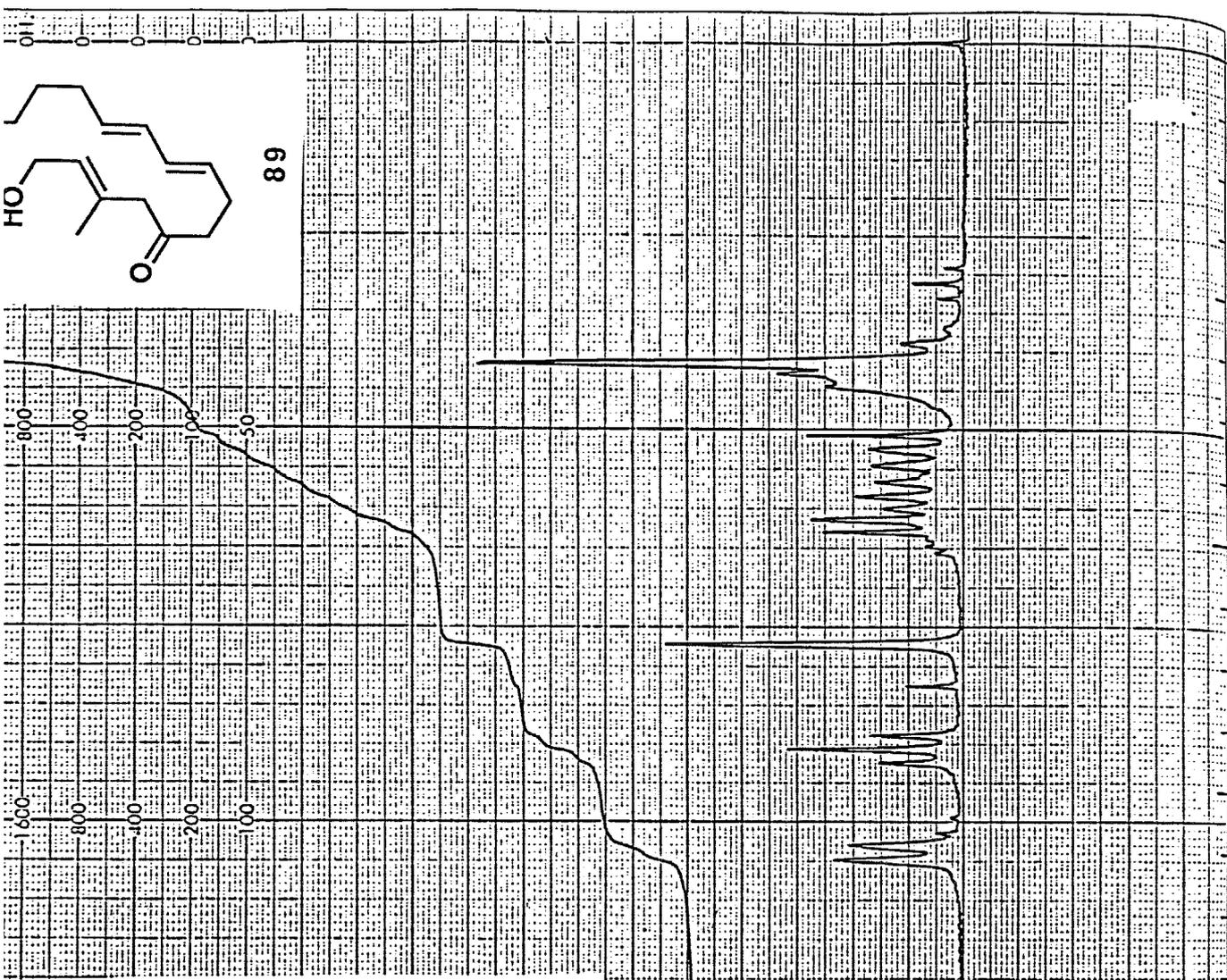
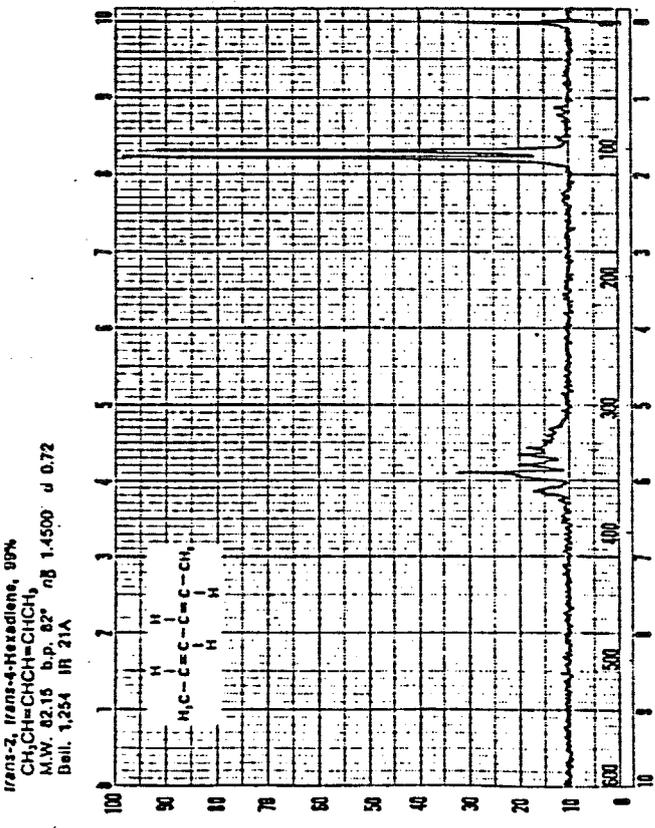
To a solution of  $\text{NH}(\text{TMS})_2$  (0.26 mL, 1.2 mmol) in dry dioxane (8 mL) was added dropwise a hexane solution of butyllithium (1.69 N, 0.59 mL, 1.0 mmol) at 10 °C and the mixture was stirred for 30 min. A solution of the protected cyanohydrin **116** (70 mg, 0.12 mmol) in dry dioxane (8 mL) was added to the solution of  $\text{LiN}(\text{TMS})_2$  dropwise over 3 h at 60-80 °C. After the addition was complete, the reaction mixture was poured into ice-cooled saturated ammonium chloride with vigorous stirring. The aqueous layer was extracted with ether. Then the combined organic layer was washed with saturated sodium bicarbonate, brine and dried over  $\text{Na}_2\text{SO}_4$ .

After removal of the solvent, the residue was passed through a short pad of silica gel (elution with hexane : ether = 10 : 1) to obtain only Diels-Alder adduct (19.5 mg). A mixture of this product and methanol (2 mL) and a catalytic amount of p-toluenesulfonate was stirred at room temperature for 1 h. The reaction mixture was poured into water and the aqueous layer was extracted with ether. The organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue passed through a short pad of silica gel to give **117** (19 mg, 0.07 mmol, 58%), which was led to a mixture of diketone **103** and **104** with weak base treatment.

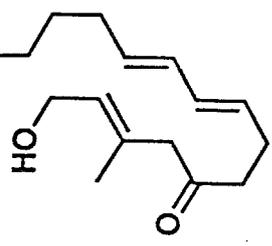
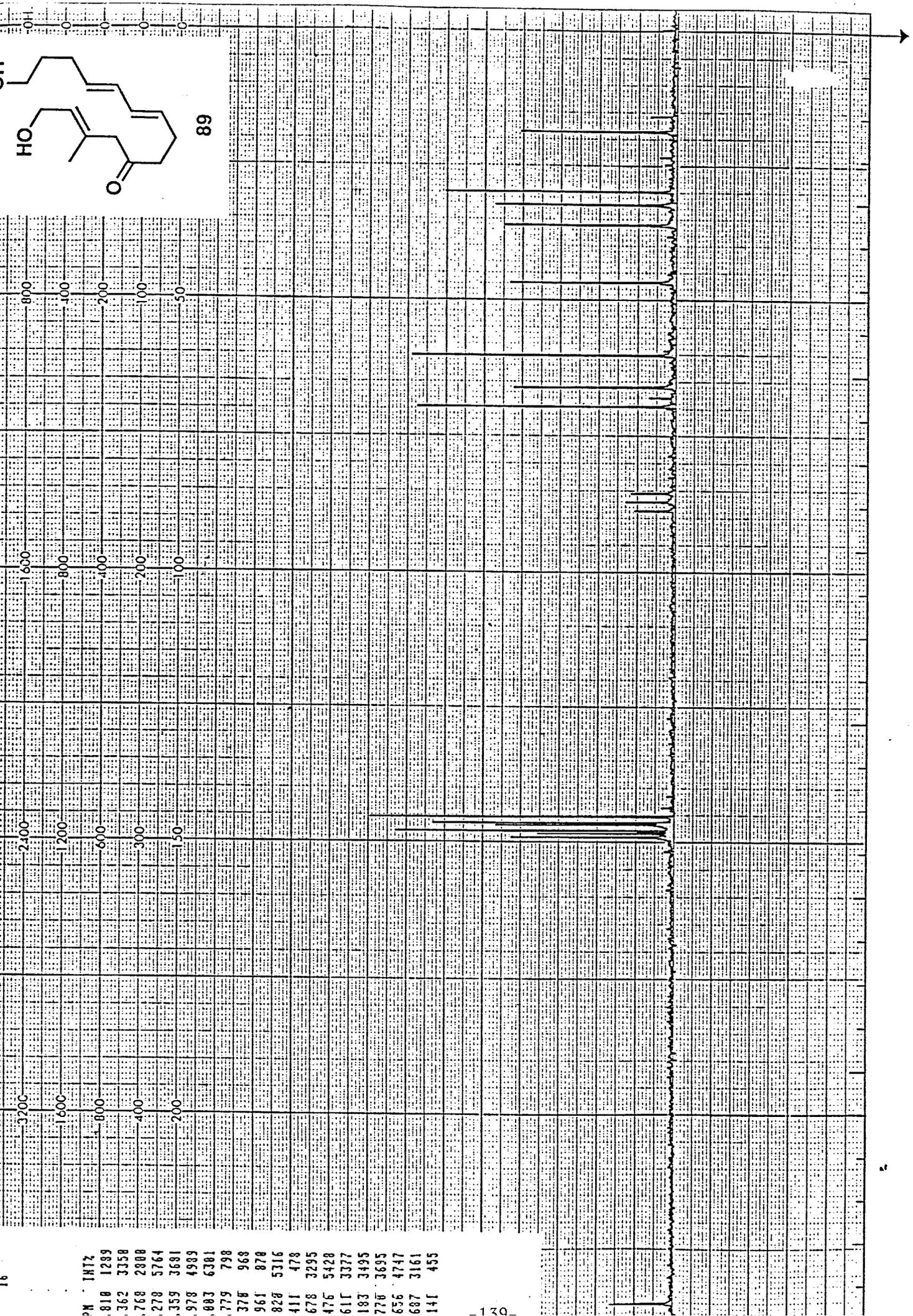
$^1\text{H}$  NMR (90 MHz,  $\text{CDCl}_3$ )  $\delta$  5.56 (ddd, 1H, a or b,  $J = 7.4, 4.6, 2.6$  Hz), 5.38 (dd, 1H, b, or a,  $J = 7.4, 2.0$  Hz), 1.2-2.6 (m, 15H), 1.25 (s, 3H, c)



*trans*-2, *trans*-4-Hexadiene, 99%  
 $\text{CH}_3\text{CH}=\text{CH}-\text{CH}=\text{CH}_2$   
 M.W. 82.15 b.p. 82° n<sub>D</sub> 1.4500 d 0.72  
 Dens. 1.254 IR 21A



8.8800  
 1.3574  
 16

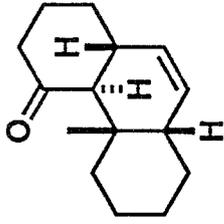


89

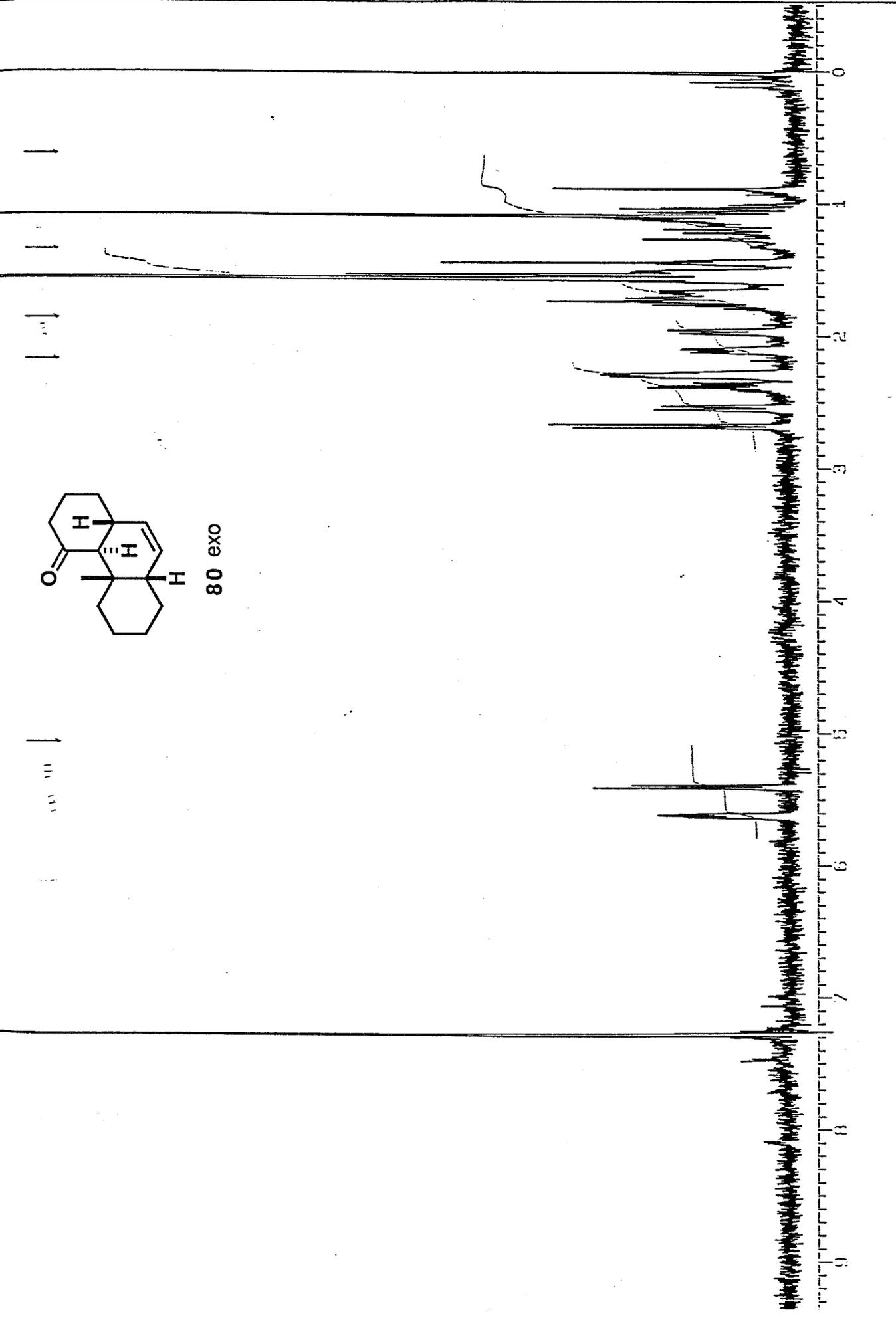
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2.78	5764
3.59	3681
9.78	4989
8.83	6381
7.79	798
3.78	968
9.61	878
8.28	5316
4.11	478
6.78	3295
4.76	5428
6.11	3377
1.83	3495
7.78	3695
6.56	4747
6.87	3161
1.41	455

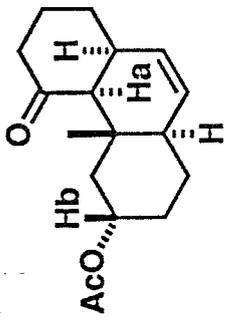
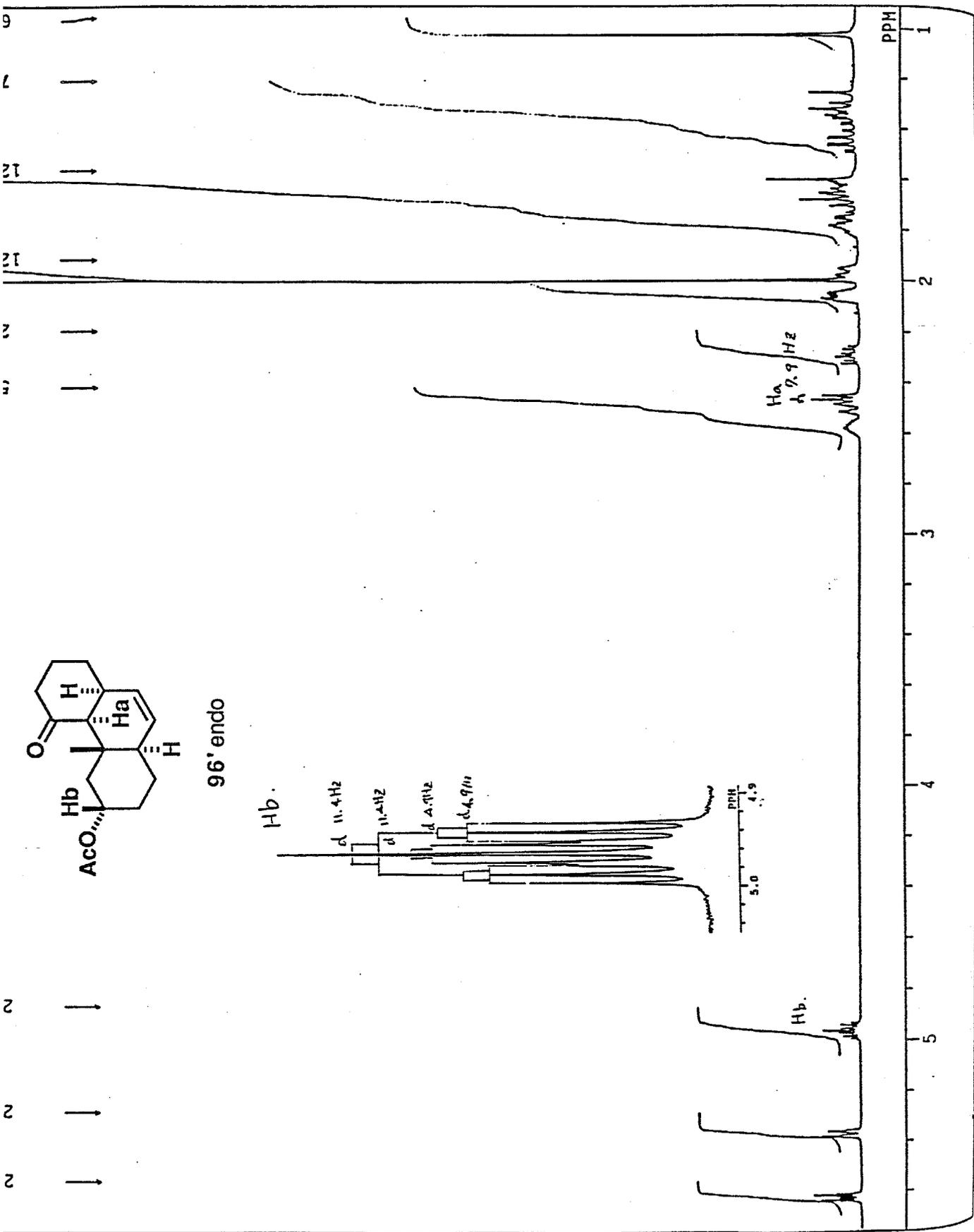


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80 exo

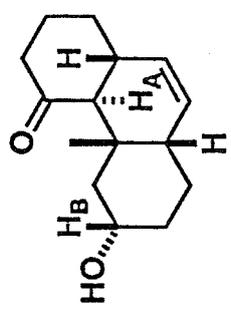




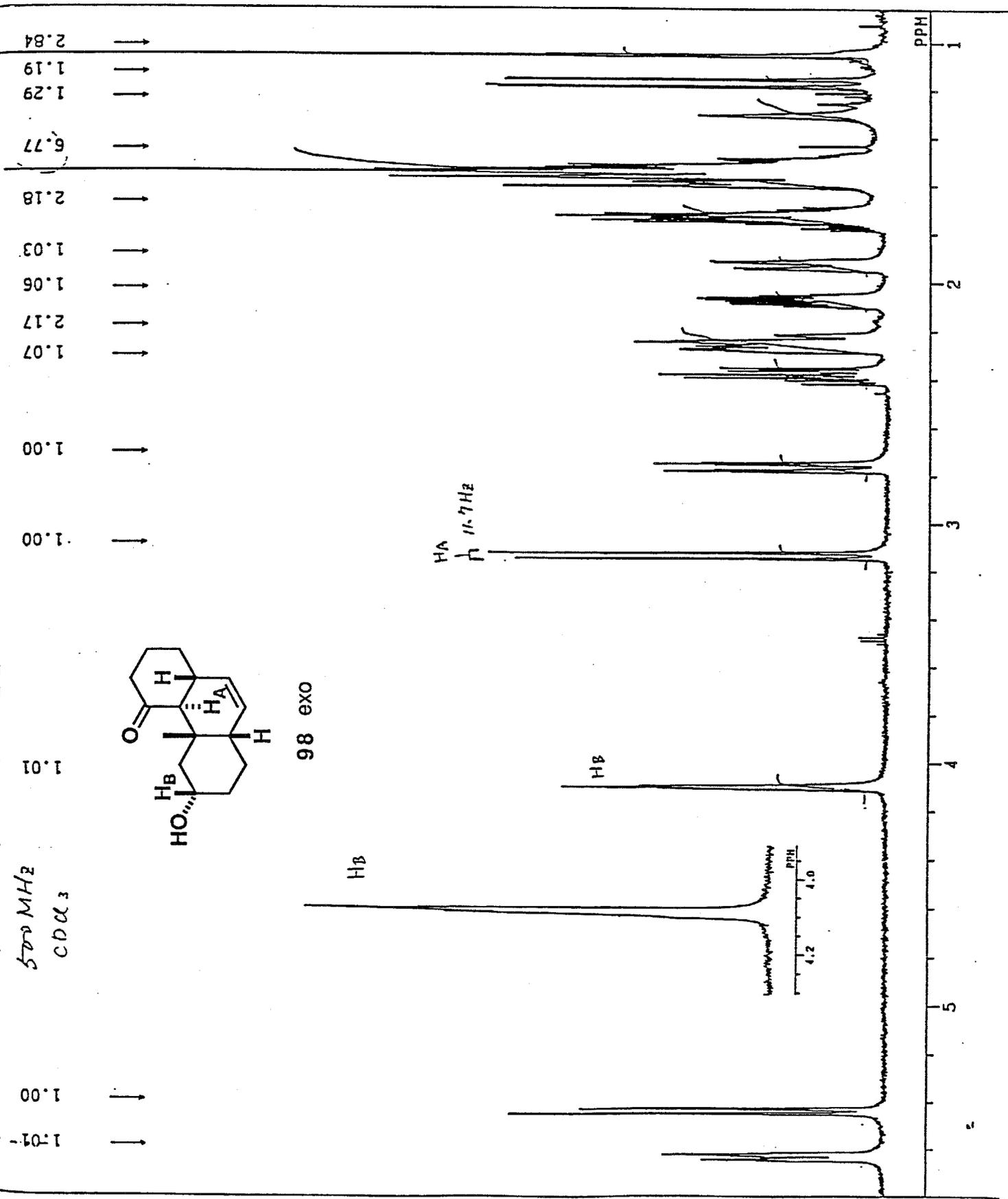
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1707 10.22

500 MHz  
CDCl<sub>3</sub>



98 exo



MM2 transition structure models of transannular Diels-Alder reaction on 78

MM2 transition structure models of Diels-Alder reaction on 78 were obtained as follows. Houk's synchronous STO-3G transition structure of the butadiene-ethylene reaction was used as the partial structure of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens, and resulting conformations were obtained by using MM2 force field.

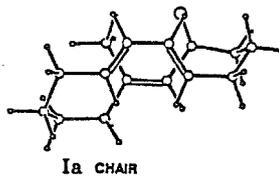
"a" means the transition state of chair-boat-chair like confirmation.

"b" means the transition state of chair-boat-boat like confirmation.

Ia

FINAL STERIC ENERGY IS 66.7310 KCAL.

COMPRESSION	1.8862		
BENDING	6.1127		
STRETCH-BEND	.2028		
VANDERWAALS			
1,4 ENERGY	10.9612		
OTHER	27.1394		
TORSIONAL	20.8754		
DIPOLE	-.4466	DIPOLE MOMENT	2.632 D

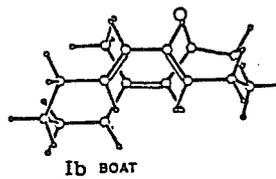


-----  
END OF DA666HMO ENDO CHAIR CHAIR TRANSITION STATE

Ib

FINAL STERIC ENERGY IS 66.6970 KCAL.

COMPRESSION	1.9101		
BENDING	6.3881		
STRETCH-BEND	.2338		
VANDERWAALS			
1,4 ENERGY	11.1254		
OTHER	27.8309		
TORSIONAL	19.6334		
DIPOLE	-.4247	DIPOLE MOMENT	2.638 D

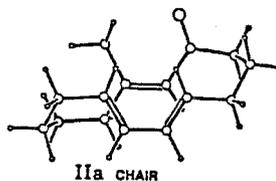


-----  
END OF DA666HMO ENDO CHAIR BOAT TRANSITION STATE

Iia

FINAL STERIC ENERGY IS 67.1402 KCAL.

COMPRESSION	1.9135
BENDING	5.7655
STRETCH-BEND	.2261
VANDERWAALS	
1,4 ENERGY	10.8455
OTHER	27.3838
TORSIONAL	21.4367
DIPOLE	-.4308



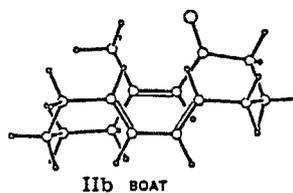
DIPOLE MOMENT 2.673 D

END OF DA66HMO EXO CHAIR CHAIR TRANSITION STATE

Iib

FINAL STERIC ENERGY IS 68.4027 KCAL.

COMPRESSION	1.9227
BENDING	6.3467
STRETCH-BEND	.2580
VANDERWAALS	
1,4 ENERGY	11.0808
OTHER	28.4061
TORSIONAL	20.8245
DIPOLE	-.4362



DIPOLE MOMENT 2.661 D

END OF DA66HMO EXO CHAIR BOAT TRANSITION STATE

Ia

0 DA666HMO ENDO CHAIR CHAIR TRANSITION STATE

21,14,22,29,29, 2, 1.359, 1.421, 121.2,

2, 2, 9,11, .

1, 1, 3, 7,

2, 4, 4, 8,

1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,

2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,

3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,

4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,

1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,

3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,

2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6,20, 0, 0,0,
1, 6, 5,14, 1,9,1.080,120.2, 101.0,	5, 0, 0, 0,0,
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6, 0, 0, 0,0,
1, 6, 5,16,32,9,1.500,120.3, -104.1,	5,17,19,19,0,
6, 5,16,17, 2,9,1.500,120.0, 180.0,	16,18, 0, 0,0,
5,16,17,18, 2,9,1.540,109.5, -100.0,	12,17, 0, 0,0,
6, 5,16,19,14,9,1.400,120.0, 0.0,	16,16, 0, 0,0,
5, 6,13,20, 2,9,1.540,109.5, 180.0,	13,21, 0, 0,0,
6,13,20,21, 2,9,1.540,109.5, -110.0,	11,20, 0, 0,0,

DA666HMO ENDO CHAIR CHAIR TRANSITION STATE

38 1 11 0 1 500.

3				0	22	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	--
6	15														
16	19														
1	9	2	7	3	8	4	10	5	14	11	22	11	23	12	24
12	25	13	26	13	27	15	28	15	29	15	30	17	31	17	32
18	33	18	34	20	35	20	36	21	37	21	38				
.00000	.00000	.00000		2		1.35900		.00000		.00000		.00000		29	2
2.09512	1.21547	.00000		29		1.46550		2.41982		.00000		.00000		2	4
.26504	2.29020	1.85935		2		-.44129		1.12391		1.85935		.24633		2	6
1.88923	-.91163	.24633		5		3.14866		1.16793		.24633		.49556		5	8
-.54276	.78999	-.49556		5		.51395		2.53482		-.49556		.02832		5	10
-.81218	-1.27382	.00705		1		2.25500		3.71585		.02832		1.59737		1	12
-1.93969	1.20590	1.56573		1		-.21986		3.21898		1.59737		2.62541		5	14
.00738	-.00244	2.78541		1		1.53807		2.46974		2.62541		1.31234		3	16
2.16434	3.85580	2.55104		1		3.06563		3.93559		1.31234		1.34654		1	18
2.11335	1.63588	3.28676		7		-2.70590		-.11486		1.34654		.80932		1	20
-2.30950	-.93602	.10808		1		-.48700		-1.97398		.80932		2.62294		5	22
-.63242	-1.80016	-.96073		5		1.54335		4.56955		-.07702		2.62294		5	24
2.92318	3.75083	-.86469		5		-2.13650		1.89564		.71117		2.62294		5	26
-2.39057	1.69716	2.46083		5		1.05693		-.33082		2.62294		3.84463		5	28
-.59380	-.92909	2.70347		5		-.11567		.31948		3.84463		2.51914		5	30
2.76259	4.04283	3.47445		5		1.37776		4.64558		2.51914		1.38969		5	32
3.56270	4.93499	1.27463		5		3.88098		3.17768		1.38969		2.25494		5	34
-3.79133	.13255	1.24999		5		-2.65050		-.75766		2.25494		-.80429		5	36
-2.89532	-1.88695	.09600		5		-2.62028		-.37179		-.80429				5	LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011114111

14	5	1	8						
2	2	3	1	0.15	2.091	0.0			
2	2	3	7	0.91	2.091	0.0			

5	2	3	1	0.0	2.091	0.0
5	2	3	7	0.0	2.091	0.0
1	1	2	29	-0.44	0.24	0.06
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	3	6.370		1.4767		
2	2	9.444		1.366		
2	29	9.444		1.359		
5	29	4.60		1.09		
29	29	6.115		1.421		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

Ib

0 DA66HMO ENDO CHAIR BOAT TRANSITION STATE  
21,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,  
1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,  
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,

1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,  
 6, 5,16,17, 2,9,1.500,120.0, 180.0, 16,18, 0, 0,0,  
 5,16,17,18, 2,9,1.540,109.5, -30.0, 12,17, 0, 0,0,  
 6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,  
 5, 6,13,20, 2,9,1.540,109.5, 180.0, 13,21, 0, 0,0,  
 6,13,20,21, 2,9,1.540,109.5, -110.0, 11,20, 0, 0,0,

DA66HMO ENDO CHAIR BOAT TRANSITION STATE

38 1 11 0 1 500.

3				0	22	0	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1		
6	15															
16	19															
1	9	2	7	3	8	4	10	5	14	11	22	11	23	12	24	
12	25	13	26	13	27	15	28	15	29	15	30	17	31	17	32	
18	33	18	34	20	35	20	36	21	37	21	38					
.00000	.00000	.00000		.00000		2		1.35900	.00000	.00000		.00000		29	2	
2.09512	1.21547	.00000		.00000		29		1.46550	2.41982	.00000		.00000		2	4	
.26504	2.29020	1.85935		2				-.44129	1.12391	1.85935		2		6		
1.88923	-.91163	.24633		5				3.14866	1.16793	.24633		5		8		
-.54276	.78999	-.49556		5				.51395	2.53482	-.49556		5		10		
-.81071	-1.27471	.00904		1				2.29562	3.69330	.03819		1		12		
-1.94036	1.20112	1.57232		1				-.21986	3.21898	1.59737		5		14		
.02140	.00747	2.78961		1				1.54370	2.51002	2.60081		3		16		
2.09099	3.93365	2.54934		1				1.91665	4.63202	1.19121		1		18		
2.16519	1.68238	3.22735		7				-2.70031	-.12392	1.35880		1		20		
-2.30823	-.94030	.11602		1				-.48179	-1.97424	.81038		5		22		
-.63347	-1.80041	-.95954		5				2.18365	4.22320	-.93772		5		24		
3.38082	3.45505	.13666		5				-2.14268	1.88842	.71711		5		26		
-2.38932	1.69223	2.46844		5				1.07756	-.30157	2.63280		5		28		
-.56494	-.92885	2.70771		5				-.10593	.33379	3.84695		5		30		
3.18219	3.88826	2.77928		5				1.60993	4.52862	3.36100		5		32		
.87373	5.00329	1.05536		5				2.55922	5.54526	1.16110		5		34		
-3.78802	.11674	1.27131		5				-2.63186	-.76724	2.26596		5		36		
-2.89201	-1.89250	.10404		5				-2.62391	-.37418	-.79346		5		LAST		

IIa

0 DA66HMO EXO CHAIR CHAIR TRANSITION STATE

21,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
 2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
 3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
 4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,

1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6, 0, 0, 0,0,
1, 6, 5,14,32,9,1.500,120.2, 101.0,	5,17,19,19,0,
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6,20, 0, 0,0,
1, 6, 5,16, 1,9,1.080,120.3, -104.1,	5, 0, 0, 0,0,
6, 5,14,17, 2,9,1.500,120.0, 180.0,	14,18, 0, 0,0,
5,14,17,18, 2,9,1.540,109.5, 100.0,	12,17, 0, 0,0,
6, 5,14,19,14,9,1.400,120.0, 0.0,	14,14, 0, 0,0,
5, 6,15,20, 2,9,1.540,109.5, 180.0,	15,21, 0, 0,0,
6,15,20,21, 2,9,1.540,109.5, 90.0,	11,20, 0, 0,0,

DA66HMO EXO CHAIR CHAIR TRANSITION STATE

38 1 11 0 1 500.

3				0	22	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1	
6	13														
14	19														
1	9	2	7	3	8	4	10	5	16	11	22	11	23	12	24
12	25	13	26	13	27	13	28	15	29	15	30	17	31	17	32
18	33	18	34	20	35	20	36	21	37	21	38				
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29		2	
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2		4	
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935		1.85935		2		6	
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633		.24633		5		8	
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556		-.49556		5		10	
-.71043	-1.33467	.07810		1		2.29272	3.68604	.09534		.09534		1		12	
-1.94838	1.18755	1.62221		1		-.33332	3.62071	1.51987		1.51987		3		14	
.05751	.00769	2.77743		1		1.14559	2.39394	2.47600		2.47600		5		16	
.61416	4.80832	1.64637		1		1.45207	4.94247	.36810		.36810		1		18	
-1.46430	3.83933	1.15045		7		-.59412	-1.38370	2.65586		2.65586		1		20	
-.34089	-2.13238	1.33816		1		-.45683	-1.92277	-.83585		-.83585		5		22	
-1.81448	-1.19232	.04044		5		2.83379	3.82051	-.87153		-.87153		5		24	
3.06231	3.57301	.89513		5		-2.23952	1.70420	.68142		.68142		5		26	
-2.43434	1.70115	2.48293		5		-2.44214	.19744	1.56445		1.56445		5		28	
-.14070	.36753	3.81529		5		1.16474	-.09789	2.69751		2.69751		5		30	
1.27542	4.69277	2.53679		5		.02089	5.73853	1.81474		1.81474		5		32	
.77452	5.13456	-.49846		5		2.12438	5.83014	.45384		.45384		5		34	
-1.68957	-1.32196	2.85000		5		-.20033	-2.02184	3.48440		3.48440		5		36	
.72906	-2.44334	1.30121		5		-.92343	-3.08549	1.34343		1.34343		5		LAST	

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011116111

14 5 1 8

2	2	3	1	0.15	2.091	0.0
2	2	3	7	0.91	2.091	0.0
5	2	3	1	0.0	2.091	0.0
5	2	3	7	0.0	2.091	0.0
1	1	2	29	-0.44	0.24	0.06
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	3	6.370		1.4767		
2	2	9.444		1.366		
2	29	9.444		1.359		
5	29	4.60		1.09		
29	29	6.115		1.421		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

IIb

0 DA66HMO EXO CHAIR BOAT TRANSITION STATE  
21,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,

1, 6, 5, 14, 32, 9, 1.500, 120.2,	101.0,	5, 17, 19, 19, 0,
4, 5, 6, 15, 2, 9, 1.500, 120.3,	104.1,	6, 20, 0, 0, 0,
1, 6, 5, 16, 1, 9, 1.080, 120.3,	-104.1,	5, 0, 0, 0, 0,
6, 5, 14, 17, 2, 9, 1.500, 120.0,	180.0,	14, 18, 0, 0, 0,
5, 14, 17, 18, 2, 9, 1.540, 109.5,	40.0,	12, 17, 0, 0, 0,
6, 5, 14, 19, 14, 9, 1.400, 120.0,	0.0,	14, 14, 0, 0, 0,
5, 6, 15, 20, 2, 9, 1.540, 109.5,	180.0,	15, 21, 0, 0, 0,
6, 15, 20, 21, 2, 9, 1.540, 109.5,	100.0,	11, 20, 0, 0, 0,

DA66HMO EXO CHAIR BOAT TRANSITION STATE

3				0	22	0	0	0	0	0	0	38	1	11	0	1	500.
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1			
6	13																
14	19																
1	9	2	7	3	8	4	10	5	16	11	22	11	23	12	24		
12	25	13	26	13	27	13	28	15	29	15	30	17	31	17	32		
18	33	18	34	20	35	20	36	21	37	21	38						
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29	2				
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2	4				
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935		2	6						
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633		5	8						
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556		5	10						
-.71159	-1.33310	.08573		1		2.27820	3.70395	.03333		1	12						
-1.94735	1.18809	1.61819		1		-.32053	3.62063	1.50136		3	14						
.05875	.01366	2.78215		1		1.14559	2.39394	2.47600		5	16						
.61583	4.82038	1.60730		1		2.09386	4.52040	1.31980		1	18						
-1.45486	3.83225	1.13711		7		-.59331	-1.37693	2.66427		1	20						
-.33831	-2.12634	1.34751		1		-.46094	-1.92479	-.82672		5	22						
-1.81566	-1.19080	.04996		5		1.99508	4.32720	-.84817		5	24						
3.36503	3.48315	-.08913		5		-2.23706	1.69721	.67285		5	26						
-2.43357	1.71025	2.47359		5		-2.44358	.19872	1.57011		5	28						
-.13850	.37706	3.81896		5		1.16588	-.09264	2.70117		5	30						
.49969	5.26587	2.62339		5		.27221	5.58602	.87153		5	32						
2.65495	5.48252	1.23366		5		2.56417	3.98695	2.17906		5	34						
-1.68878	-1.31538	2.85830		5		-.19926	-2.01359	3.49384		5	36						
.73214	-2.43551	1.31065		5		-.91866	-3.08078	1.35513		5	LAST						

MM2 transition structure models of transannular Diels-Alder reaction on 95

MM2 transition structure models of Diels-Alder reaction on 95 were obtained as follows. Houk's synchronous STO-3G transition structure of the butadiene-ethylene reaction was used as the partial structure of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens, and resulting conformations were obtained by using MM2 force field.

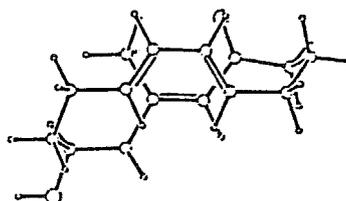
"a" means the transition state of chair-boat-chair like confirmation.

"b" means the transition state of chair-boat-boat like confirmation.

Ia

FINAL STERIC ENERGY IS 67.1483 KCAL.

COMPRESSION	1.8823
BENDING	5.9550
STRETCH-BEND	.2070
VANDERWAALS	
1,4 ENERGY	11.2125
OTHER	26.9887
TORSIONAL	21.4244
DIPOLE	-.5216



DIPOLE MOMENT 2.104 D

-----  
END OF DAOHAMO ENDO CHAIR CHAIR TRANSITION STATE

Ib

FINAL STERIC ENERGY IS 67.1109 KCAL.

COMPRESSION	1.9002
BENDING	6.2786
STRETCH-BEND	.2364
VANDERWAALS	
1,4 ENERGY	11.3761
OTHER	27.6329
TORSIONAL	20.1859
DIPOLE	-.4992

DIPOLE MOMENT 2.127 D

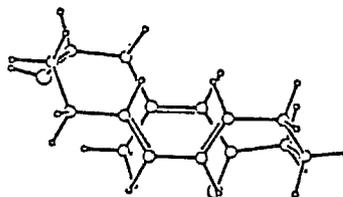
-----  
END OF DAOHAMO ENDO CHAIR BOAT TRANSITION STATE

Ila

FINAL STERIC ENERGY IS 68.9411 KCAL.

COMPRESSION 1.9061  
BENDING 7.0201  
STRETCH-BEND .2724  
VANDERWAALS  
1,4 ENERGY 11.2137  
OTHER 27.4049  
TORSIONAL 21.5146  
DIPOLE -.3906

DIPOLE MOMENT 3.311 D



-----  
END OF DAHBMO ENDO CHAIR CHAIR TRANSITION STATE

Iib

FINAL STERIC ENERGY IS 68.8882 KCAL.

COMPRESSION 1.9281  
BENDING 7.3571  
STRETCH-BEND .3015  
VANDERWAALS  
1,4 ENERGY 11.3726  
OTHER 28.0636  
TORSIONAL 20.2290  
DIPOLE -.3638

DIPOLE MOMENT 3.343 D

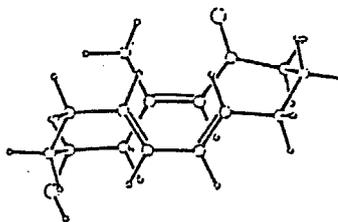
-----  
END OF DAHBMO ENDO CHAIR BOAT TRANSITION STATE

IIIa

FINAL STERIC ENERGY IS 67.5295 KCAL.

COMPRESSION 1.8464  
BENDING 5.5738  
STRETCH-BEND .2226  
VANDERWAALS  
1,4 ENERGY 11.1450  
OTHER 27.2682  
TORSIONAL 21.9840  
DIPOLE -.5105

DIPOLE MOMENT 2.167 D



-----  
END OF DAHAMO EXO CHAIR CHAIR TRANSITION STATE

IIIb

FINAL STERIC ENERGY IS 68.7963 KCAL.

COMPRESSION	1.9112		
BENDING	6.2540		
STRETCH-BEND	.2592		
VANDERWAALS			
1,4 ENERGY	11.3279		
OTHER	28.1424		
TORSIONAL	21.4117		
DIPOLE	-.5101	DIPOLE MOMENT	2.153 D

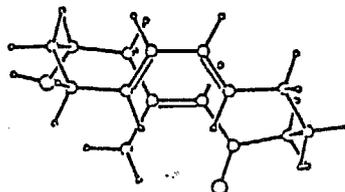
-----

END OF DAOHAMO EXO CHAIR BOAT TRANSITION STATE

IVa

FINAL STERIC ENERGY IS 69.3288 KCAL.

COMPRESSION	1.8714		
BENDING	6.6512		
STRETCH-BEND	.2858		
VANDERWAALS			
1,4 ENERGY	11.1265		
OTHER	27.7566		
TORSIONAL	22.0137		
DIPOLE	-.3764	DIPOLE MOMENT	3.332 D



-----

END OF DAOHBMO EXO CHAIR CHAIR TRANSITION STATE

IVb

FINAL STERIC ENERGY IS 70.5923 KCAL.

COMPRESSION	1.9337		
BENDING	7.3452		
STRETCH-BEND	.3220		
VANDERWAALS			
1,4 ENERGY	11.3015		
OTHER	28.6163		
TORSIONAL	21.4501		
DIPOLE	-.3764	DIPOLE MOMENT	3.323 D

-----

END OF DAOHBMO EXO CHAIR BOAT TRANSITION STATE

Ia

0 DAOHAMO ENDO CHAIR CHAIR TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,		
2, 2, 9,11,		
1, 1, 3, 7,		
2, 4, 4, 8,		
1, 2, 3, 4,22,9,1.359,121.2, 0.0,	3, 3,10,12,0,	
2, 1, 4, 5,22,9,2.217, 70.7, -117.3,	6, 6,14,16,0,	
3, 4, 1, 6,22,9,2.217, 70.7, 117.3,	5, 5,13,15,0,	
4, 3, 2, 7, 1,9,1.083,117.8, -165.1,	2, 0, 0, 0,0,	
1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,	
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,	
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,	
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,	
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,	
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6,20, 0, 0,0,	
1, 6, 5,14, 1,9,1.080,120.2, 101.0,	5, 0, 0, 0,0,	
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6, 0, 0, 0,0,	
1, 6, 5,16,32,9,1.500,120.3, -104.1,	5,17,19,19,0,	
6, 5,16,17, 2,9,1.500,120.0, -178.0,	16,18, 0, 0,0,	
5,16,17,18, 2,9,1.540,109.5, -87.0,	12,17, 0, 0,0,	
6, 5,16,19,14,9,1.400,120.0, 0.0,	16,16, 0, 0,0,	
5, 6,13,20, 2,9,1.540,109.5, 171.0,	13,21,22, 0,0,	
6,13,20,21, 2,9,1.540,109.5, -65.0,	11,20, 0, 0,0,	
6,13,20,22, 4,9,1.450,109.5, 174.0,	20,23, 0, 0,0,	
13,20,22,23,21,9,0.940,106.9, -174.0,	22, 0, 0, 0,0,	

DAOHAMO ENDO CHAIR CHAIR TRANSITION STATE

39 1 11 0 1 500.

4				0	22	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	
6	15														
16	19														
20	22														
1	9	2	7	3	8	4	10	5	14	11	24	11	25	12	26
12	27	13	28	13	29	15	30	15	31	15	32	17	33	17	34
18	35	18	36	20	37	21	38	21	39	22	23				
.00000	.00000	.00000		2		1.35900		.00000		.00000		.00000		29	2
2.09512	1.21547	.00000		29		1.46550		2.41982		.00000		.00000		2	4
.26504	2.29020	1.85935		2		-.44129		1.12391		1.85935		1.85935		2	6
1.88923	-.91163	.24633		5		3.14866		1.16793		.24633		.24633		5	8
-.54276	.78999	-.49556		5		.51395		2.53482		-.49556		-.49556		5	10
-.80736	-1.27653	.00113		1		2.25599		3.71513		.02307		.02307		1	12
-1.93891	1.19940	1.56146		1		-.21986		3.21898		1.59737		1.59737		5	14
.00965	-.00279	2.78392		1		1.53835		2.47355		2.62402		2.62402		3	16
2.16521	3.85931	2.54454		1		3.06713		3.93683		1.30625		1.30625		1	18

2.11336	1.64205	3.28857	7	-2.70001	-.12409	1.34304	1	20
-2.30503	-.94145	.10224	1	-4.06965	.20764	1.21618	6	22
-4.58252	-.58156	1.26077	21	-.48161	-1.97810	.80199	5	24
-.62548	-1.79918	-.96825	5	1.54517	4.56929	-.08428	5	26
2.92385	3.74681	-.87032	5	-2.13647	1.88820	.70667	5	28
-2.39256	1.68799	2.45618	5	1.06168	-.32487	2.62507	5	30
-.58546	-.93284	2.69627	5	-.11930	.31575	3.84345	5	32
2.76312	4.04917	3.46759	5	1.37865	4.64900	2.51047	5	34
3.56459	4.93597	1.26677	5	3.88207	3.17865	1.38514	5	36
-2.64535	-.76216	2.25605	5	-2.88774	-1.89389	.08994	5	38
-2.61719	-.37506	-.80779	5					

LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011114111

14	5	1	8						
2	2	3	1	0.15	2.091	0.0			
2	2	3	7	0.91	2.091	0.0			
5	2	3	1	0.0	2.091	0.0			
5	2	3	7	0.0	2.091	0.0			
1	1	2	29	-0.44	0.24	0.06			
1	2	29	29	0.0	9.415	0.0			
5	2	29	29	0.0	9.415	0.0			
5	1	2	29	0.0	0.0	-0.24			
2	29	29	2	0.0	2.23	0.80			
1	2	29	5	0.0	9.415	0.0			
2	29	29	5	0.0	2.23	0.0			
5	2	29	5	0.0	9.415	0.0			
3	1	2	29	0.0	0.0	0.10			
5	29	29	5	0.0	2.23	0.0			
2	3	6.370		1.4767					
2	2	9.444		1.366					
2	29	9.444		1.359					
5	29	4.60		1.09					
29	29	6.115		1.421					
	29	0.044		1.940					
2	29	29		0.43	120.0				
5	29	29		0.36	120.0				
	29	29		0.050					
5	29	2		0.36	120.0				
	29	2		0.05					
1	2	29		0.55	121.4				
5	2	29		0.36	120.0				
	2	29		0.05					

Ib

0 DAOHAMO ENDO CHAIR BOAT TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,		
2, 2, 9,11,		
1, 1, 3, 7,		
2, 4, 4, 8,		
1, 2, 3, 4,22,9,1.359,121.2, 0.0,	3, 3,10,12,0,	
2, 1, 4, 5,22,9,2.217, 70.7, -117.3,	6, 6,14,16,0,	
3, 4, 1, 6,22,9,2.217, 70.7, 117.3,	5, 5,13,15,0,	
4, 3, 2, 7, 1,9,1.083,117.8, -165.1,	2, 0, 0, 0,0,	
1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,	
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,	
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,	
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,	
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,	
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6,20, 0, 0,0,	
1, 6, 5,14, 1,9,1.080,120.2, 101.0,	5, 0, 0, 0,0,	
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6, 0, 0, 0,0,	
1, 6, 5,16,32,9,1.500,120.3, -104.1,	5,17,19,19,0,	
6, 5,16,17, 2,9,1.500,120.0, -175.0,	16,18, 0, 0,0,	
5,16,17,18, 2,9,1.540,109.5, -38.0,	12,17, 0, 0,0,	
6, 5,16,19,14,9,1.400,120.0, 0.0,	16,16, 0, 0,0,	
5, 6,13,20, 2,9,1.540,109.5, 171.0,	13,21,22, 0,0,	
6,13,20,21, 2,9,1.540,109.5, -65.0,	11,20, 0, 0,0,	
6,13,20,22, 4,9,1.450,109.5, 174.0,	20,23, 0, 0,0,	
13,20,22,23,21,9,0.940,106.9, -174.0,	22, 0, 0, 0,0,	

DAOHAMO ENDO CHAIR BOAT TRANSITION STATE

4				0	22	0	0	0	0	0	0	0	0	0	39	1	11	0	1	500.
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1						
6	15																			
16	19																			
20	22																			
1	9	2	7	3	8	4	10	5	14	11	24	11	25	12	26					
12	27	13	28	13	29	15	30	15	31	15	32	17	33	17	34					
18	35	18	36	20	37	21	38	21	39	22	23									
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29	2							
2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4												
.26504	2.29020	1.85935	2	-.44129	1.12391	1.85935	2	6												
1.88923	-.91163	.24633	5	3.14866	1.16793	.24633	5	8												
-.54276	.78999	-.49556	5	.51395	2.53482	-.49556	5	10												
-.80684	-1.27688	.00469	1	2.29628	3.69275	.03376	1	12												
-1.93952	1.19600	1.56849	1	-.21986	3.21898	1.59737	5	14												
.02382	.00830	2.78927	1	1.54328	2.51726	2.59877	3	16												
2.08413	3.94351	2.54225	1	1.91160	4.63611	1.18087	1	18												

2.16785	1.69334	3.22711	7	-2.69498	-.13138	1.35692	1	20
-2.30464	-.94477	.11223	1	-4.06754	.19220	1.24171	6	22
-4.57524	-.60007	1.29058	21	-.47719	-1.97741	.80490	5	24
-.62820	-1.79974	-.96518	5	2.18752	4.21782	-.94512	5	26
3.38114	3.45521	.13763	5	-2.14225	1.88170	.71244	5	28
-2.39069	1.68549	2.46396	5	1.08276	-.29331	2.63693	5	30
-.55582	-.93174	2.70200	5	-.11011	.33198	3.84660	5	32
3.17468	3.90393	2.77625	5	1.59798	4.53979	3.34991	5	34
.86797	5.00369	1.04041	5	2.55197	5.55082	1.14854	5	36
-2.62748	-.76937	2.26917	5	-2.88550	-1.89835	.10069	5	38
-2.62185	-.37692	-.79513	5					LAST

IIa

0 DAOHBMO ENDO CHAIR CHAIR TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,		
2, 2, 9,11,		
1, 1, 3, 7,		
2, 4, 4, 8,		
1, 2, 3, 4,22,9,1.359,121.2, 0.0,	3, 3,10,12,0,	
2, 1, 4, 5,22,9,2.217, 70.7, -117.3,	6, 6,14,16,0,	
3, 4, 1, 6,22,9,2.217, 70.7, 117.3,	5, 5,13,15,0,	
4, 3, 2, 7, 1,9,1.083,117.8, -165.1,	2, 0, 0, 0,0,	
1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,	
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,	
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,	
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,	
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,	
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6,20, 0, 0,0,	
1, 6, 5,14, 1,9,1.080,120.2, 101.0,	5, 0, 0, 0,0,	
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6, 0, 0, 0,0,	
1, 6, 5,16,32,9,1.500,120.3, -104.1,	5,17,19,19,0,	
6, 5,16,17, 2,9,1.500,120.0, -178.0,	16,18, 0, 0,0,	
5,16,17,18, 2,9,1.540,109.5, -87.0,	12,17, 0, 0,0,	
6, 5,16,19,14,9,1.400,120.0, 0.0,	16,16, 0, 0,0,	
5, 6,13,20, 2,9,1.540,109.5, 171.0,	13,21,22, 0,0,	
6,13,20,21, 2,9,1.540,109.5, -65.0,	11,20, 0, 0,0,	
6,13,20,22, 4,9,1.450,109.5, 61.0,	20,23, 0, 0,0,	
13,20,22,23,21,9,0.940,106.9, 60.0,	22, 0, 0, 0,0,	

DAOHBMO ENDO CHAIR CHAIR TRANSITION STATE

39 1 11 0 1 500.

4				0	22	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1
6	15													
16	19													
20	22													



6, 5, 16, 19, 14, 9, 1.400, 120.0, 0.0, 16, 16, 0, 0, 0,  
 5, 6, 13, 20, 2, 9, 1.540, 109.5, 171.0, 13, 21, 22, 0, 0,  
 6, 13, 20, 21, 2, 9, 1.540, 109.5, -65.0, 11, 20, 0, 0, 0,  
 6, 13, 20, 22, 4, 9, 1.450, 109.5, 61.0, 20, 23, 0, 0, 0,  
 13, 20, 22, 23, 21, 9, 0.940, 106.9, 60.0, 22, 0, 0, 0, 0,

DAOHMO ENDO CHAIR BOAT TRANSITION STATE

39 1 11 0 1 500.

4				0	22	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	
6	15														
16	19														
20	22														
1	9	2	7	3	8	4	10	5	14	11	24	11	25	12	26
12	27	13	28	13	29	15	30	15	31	15	32	17	33	17	34
18	35	18	36	20	37	21	38	21	39	22	23				
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29		2	
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2		4	
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935				2		6	
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633				5		8	
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556				5		10	
-.80643	-1.27729	.00137		1		2.29638	3.69263	.03188				1		12	
-1.94111	1.19564	1.57203		1		-.21986	3.21898	1.59737				5		14	
.03548	.00892	2.78283		1		1.54218	2.52343	2.59961				3		16	
2.07997	3.95084	2.53839		1		1.90788	4.63913	1.17491				1		18	
2.16706	1.70734	3.23774		7		-2.73069	-.10283	1.30099				1		20	
-2.30520	-.94526	.08721		1		-2.75227	-.92798	2.44533				6		22	
-3.16411	-.46554	3.15520		21		-.48618	-1.97983	.80316				5		24	
-.61588	-1.80276	-.96488		5		2.18996	4.21468	-.94888				5		26	
3.38100	3.45561	.13939		5		-2.13162	1.90853	.73522				5		28	
-2.39436	1.66960	2.47463		5		1.10437	-.26377	2.64821				5		30	
-.50807	-.94733	2.66466		5		-.12958	.31209	3.84186				5		32	
3.17036	3.91463	2.77381		5		1.59169	4.54879	3.34353				5		34	
.86370	5.00408	1.03163		5		2.54657	5.55495	1.14066				5		36	
-3.80316	.17510	1.14684		5		-2.88961	-1.89670	.07675				5		38	
-2.60359	-.39531	-.83802		5											LAST

IIIa

0 DAOHMO EXO CHAIR CHAIR TRANSITION STATE

23, 14, 22, 29, 29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9, 11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4, 22, 9, 1.359, 121.2, 0.0, 3, 3, 10, 12, 0,  
 2, 1, 4, 5, 22, 9, 2.217, 70.7, -117.3, 6, 6, 14, 16, 0,  
 3, 4, 1, 6, 22, 9, 2.217, 70.7, 117.3, 5, 5, 13, 15, 0,

4, 3, 2, 7, 1,9,1.083,117.8, -165.1,	2, 0, 0, 0,0,
1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6, 0, 0, 0,0,
1, 6, 5,14,32,9,1.500,120.2, 101.0,	5,17,19,19,0,
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6,20, 0, 0,0,
1, 6, 5,16, 1,9,1.080,120.3, -104.1,	5, 0, 0, 0,0,
6, 5,14,17, 2,9,1.500,120.0, 177.0,	14,18, 0, 0,0,
5,14,17,18, 2,9,1.540,109.5, 84.0,	12,17, 0, 0,0,
6, 5,14,19,14,9,1.400,120.0, 0.0,	14,14, 0, 0,0,
5, 6,15,20, 2,9,1.540,109.5, -172.0,	15,21,22, 0,0,
6,15,20,21, 2,9,1.540,109.5, 67.0,	11,20, 0, 0,0,
6,15,20,22, 4,9,1.450,109.5, -173.0,	20,23, 0, 0,0,
15,20,22,23,21,9,0.940,106.9, 174.0,	22, 0, 0, 0,0,

DAOHAMO EXO CHAIR CHAIR TRANSITION STATE

												39	1	11	0	1	500.
4				0	22	0	0	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1			
6	13																
14	19																
20	22																
1	9	2	7	3	8	4	10	5	16	11	24	11	25	12	26		
12	27	13	28	13	29	13	30	15	31	15	32	17	33	17	34		
18	35	18	36	20	37	21	38	21	39	22	23						
.00000	.00000	.00000		2		1.35900		.00000		.00000		.00000		29	2		
2.09512	1.21547	.00000		29		1.46550		2.41982		.00000		.00000		2	4		
.26504	2.29020	1.85935		2		-.44129		1.12391		1.85935		1.85935		2	6		
1.88923	-.91163	.24633		5		3.14866		1.16793		.24633		.24633		5	8		
-.54276	.78999	-.49556		5		.51395		2.53482		-.49556		-.49556		5	10		
-.71134	-1.33347	.07763		1		2.29578		3.68327		.09579		.09579		1	12		
-1.94742	1.18836	1.61911		1		-.33197		3.62113		1.52183		1.52183		3	14		
.05955	.00809	2.77450		1		1.14559		2.39394		2.47600		2.47600		5	16		
.61909	4.80582	1.64637		1		1.45525		4.93966		.36711		.36711		1	18		
-1.46655	3.84297	1.16577		7		-.59814		-1.37913		2.65392		2.65392		1	20		
-.34108	-2.12910	1.33850		1		-.08314		-2.17287		3.70585		3.70585		6	22		
-.58921	-2.96522	3.76862		21		-.45736		-1.92232		-.83574		-.83574		5	24		
-1.81539	-1.19144	.03918		5		2.83811		3.81688		-.87050		-.87050		5	26		
3.06422	3.56963	.89662		5		-2.23641		1.70770		.67910		.67910		5	28		
-2.43489	1.69983	2.48023		5		-2.44213		.19896		1.55786		1.55786		5	30		
-.13545	.36791	3.81260		5		1.16589		-.10063		2.69037		2.69037		5	32		
1.28129	4.68954	2.53601		5		.02825		5.73741		1.81571		1.81571		5	34		
.77708	5.13131	-.49907		5		2.12769		5.82734		.45186		.45186		5	36		

-1.69299 -1.31236 2.85543 5 .72884 -2.43884 1.30400 5 38  
 -.92449 -3.08128 1.34384 5 LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011116111

14	5	1	8					
2	2	3	1	0.15	2.091	0.0		
2	2	3	7	0.91	2.091	0.0		
5	2	3	1	0.0	2.091	0.0		
5	2	3	7	0.0	2.091	0.0		
1	1	2	29	-0.44	0.24	0.06		
1	2	29	29	0.0	9.415	0.0		
5	2	29	29	0.0	9.415	0.0		
5	1	2	29	0.0	0.0	-0.24		
2	29	29	2	0.0	2.23	0.80		
1	2	29	5	0.0	9.415	0.0		
2	29	29	5	0.0	2.23	0.0		
5	2	29	5	0.0	9.415	0.0		
3	1	2	29	0.0	0.0	0.10		
5	29	29	5	0.0	2.23	0.0		
2	3	6.370		1.4767				
2	2	9.444		1.366				
2	29	9.444		1.359				
5	29	4.60		1.09				
29	29	6.115		1.421				
	29	0.044		1.940				
2	29	29		0.43	120.0			
5	29	29		0.36	120.0			
	29	29		0.050				
5	29	2		0.36	120.0			
	29	2		0.05				
1	2	29		0.55	121.4			
5	2	29		0.36	120.0			
	2	29		0.05				

IIIb

0 DAOHAMO EXO CHAIR BOAT TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
 2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
 3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
 4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
 1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,

3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,
1, 6, 5,14,32,9,1.500,120.2, 101.0, 5,17,19,19,0,
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6,20, 0, 0,0,
1, 6, 5,16, 1,9,1.080,120.3, -104.1, 5, 0, 0, 0,0,
6, 5,14,17, 2,9,1.500,120.0, 178.0, 14,18, 0, 0,0,
5,14,17,18, 2,9,1.540,109.5, 31.0, 12,17, 0, 0,0,
6, 5,14,19,14,9,1.400,120.0, 0.0, 14,14, 0, 0,0,
5, 6,15,20, 2,9,1.540,109.5, -172.0, 15,21,22, 0,0,
6,15,20,21, 2,9,1.540,109.5, 67.0, 11,20, 0, 0,0,
6,15,20,22, 4,9,1.450,109.5, -173.0, 20,23, 0, 0,0,
15,20,22,23,21,9,0.940,106.9, 169.0, 22, 0, 0, 0,0,

DAOHAMO EXO CHAIR BOAT TRANSITION STATE

39 1 11 0 1 500.

4				0	22	0	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1		
6	13															
14	19															
20	22															
1	9	2	7	3	8	4	10	5	16	11	24	11	25	12	26	
12	27	13	28	13	29	13	30	15	31	15	32	17	33	17	34	
18	35	18	36	20	37	21	38	21	39	22	23					
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29		2		
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2		4		
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935		1.85935		2		6		
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633		.24633		5		8		
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556		2.53482		5		10		
-.71153	-1.33330	.07861		1		2.27972	3.70303	.03058		3.70303		1		12		
-1.94677	1.19132	1.61607		1		-.31302	3.62489	1.50687		3.62489		3		14		
.05695	.00907	2.77675		1		1.14559	2.39394	2.47600		2.39394		5		16		
.63225	4.81733	1.62070		1		2.10754	4.51246	1.32311		4.51246		1		18		
-1.44585	3.84360	1.14225		7		-.60080	-1.37799	2.65509		-1.37799		1		20		
-.34168	-2.12810	1.34015		1		-.08791	-2.17174	3.70803		-2.17174		6		22		
-.59443	-2.96385	3.77009		21		-.45751	-1.92286	-.83429		-1.92286		5		24		
-1.81556	-1.19103	.04004		5		1.98883	4.33105	-.84498		4.33105		5		26		
3.36512	3.48180	-.10328		5		-2.23363	1.70996	.67506		1.70996		5		28		
-2.43380	1.70679	2.47505		5		-2.44370	.20286	1.55697		.20286		5		30		
-.13991	.36969	3.81422		5		1.16339	-.10011	2.69433		-.10011		5		32		
.52381	5.25241	2.64213		5		.28948	5.59291	.89503		5.59291		5		34		
2.67241	5.47258	1.23944		5		2.58072	3.97125	2.17593		3.97125		5		36		
-1.69601	-1.31074	2.85445		5		.72853	-2.43699	1.30686		-2.43699		5		38		
-.92437	-3.08072	1.34525		5												LAST

IVa

0 DAOHBMO EXO CHAIR CHAIR TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,		
2, 2, 9,11,		
1, 1, 3, 7,		
2, 4, 4, 8,		
1, 2, 3, 4,22,9,1.359,121.2,	0.0,	3, 3,10,12,0,
2, 1, 4, 5,22,9,2.217, 70.7,	-117.3,	6, 6,14,16,0,
3, 4, 1, 6,22,9,2.217, 70.7,	117.3,	5, 5,13,15,0,
4, 3, 2, 7, 1,9,1.083,117.8,	-165.1,	2, 0, 0, 0,0,
1, 2, 3, 8, 1,9,1.083,117.8,	165.1,	3, 0, 0, 0,0,
3, 2, 1, 9, 1,9,1.079,120.2,	32.1,	1, 0, 0, 0,0,
2, 3, 4,10, 1,9,1.079,120.2,	-32.1,	4, 0, 0, 0,0,
3, 2, 1,11, 2,9,1.500,121.1,	-172.6,	1,21, 0, 0,0,
2, 3, 4,12, 2,9,1.500,121.1,	172.6,	4,18, 0, 0,0,
4, 5, 6,13, 2,9,1.500,120.2,	-101.0,	6, 0, 0, 0,0,
1, 6, 5,14,32,9,1.500,120.2,	101.0,	5,17,19,19,0,
4, 5, 6,15, 2,9,1.500,120.3,	104.1,	6,20, 0, 0,0,
1, 6, 5,16, 1,9,1.080,120.3,	-104.1,	5, 0, 0, 0,0,
6, 5,14,17, 2,9,1.500,120.0,	177.0,	14,18, 0, 0,0,
5,14,17,18, 2,9,1.540,109.5,	84.0,	12,17, 0, 0,0,
6, 5,14,19,14,9,1.400,120.0,	0.0,	14,14, 0, 0,0,
5, 6,15,20, 2,9,1.540,109.5,	-172.0,	15,21,22, 0,0,
6,15,20,21, 2,9,1.540,109.5,	67.0,	11,20, 0, 0,0,
6,15,20,22, 4,9,1.450,109.5,	-59.0,	20,23, 0, 0,0,
15,20,22,23,21,9,0.940,106.9,	-60.0,	22, 0, 0, 0,0,

DAOHBMO EXO CHAIR CHAIR TRANSITION STATE

4	0	22	0	0	0	0	0	0	0	0	0	39	1	11	0	1	500.
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1			
6	13																
14	19																
20	22																
1	9	2	7	3	8	4	10	5	16	11	24	11	25	12	26		
12	27	13	28	13	29	13	30	15	31	15	32	17	33	17	34		
18	35	18	36	20	37	21	38	21	39	22	23						
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29		2			
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2		4			
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935		1.85935		2		6			
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633		.24633		5		8			
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556		-.49556		5		10			
-.71217	-1.33320	.08032		1		2.29762	3.68223	.09210		.09210		1		12			
-1.94452	1.19540	1.60790		1		-.32757	3.62422	1.52437		1.52437		3		14			
.05816	.01079	2.77991		1		1.14559	2.39394	2.47600		2.47600		5		16			
.62797	4.80577	1.64706		1		1.45920	4.93942	.36484		.36484		1		18			

-1.46369	3.85445	1.17873	7	-0.53279	-1.40840	2.66639	1	20
-.32946	-2.13915	1.33053	1	-1.90642	-1.41037	2.98832	6	22
-2.01963	-1.10251	3.87139	21	-.46736	-1.91627	-.83929	5	24
-1.81654	-1.19499	.04945	5	2.83718	3.81446	-.87594	5	26
3.06835	3.56858	.89075	5	-2.22594	1.74030	.68039	5	28
-2.44123	1.68016	2.47917	5	-2.43741	.21035	1.50356	5	30
-.15040	.36602	3.81687	5	1.16832	-.06639	2.70759	5	32
1.29336	4.68626	2.53389	5	.04099	5.73909	1.82036	5	34
.77817	5.13126	-.49904	5	2.13269	5.82655	.44709	5	36
-.06625	-2.04150	3.46187	5	.73548	-2.46204	1.26288	5	38
-.91729	-3.08856	1.34184	5					LAST

IVb

0 DAOHBMO EXO CHAIR BOAT TRANSITION STATE

23,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, -3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,  
1, 6, 5,14,32,9,1.500,120.2, 101.0, 5,17,19,19,0,  
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6,20, 0, 0,0,  
1, 6, 5,16, 1,9,1.080,120.3, -104.1, 5, 0, 0, 0,0,  
6, 5,14,17, 2,9,1.500,120.0, 178.0, 14,18, 0, 0,0,  
5,14,17,18, 2,9,1.540,109.5, 31.0, 12,17, 0, 0,0,  
6, 5,14,19,14,9,1.400,120.0, 0.0, 14,14, 0, 0,0,  
5, 6,15,20, 2,9,1.540,109.5, -172.0, 15,21,22, 0,0,  
6,15,20,21, 2,9,1.540,109.5, 67.0, 11,20, 0, 0,0,  
6,15,20,22, 4,9,1.450,109.5, -59.0, 20,23, 0, 0,0,  
15,20,22,23,21,9,0.940,106.9, -60.0, 22, 0, 0, 0,0,

DAOHBMO EXO CHAIR BOAT TRANSITION STATE

4				0	22	0	0	0	0	0	0	0	0	0	0	0	39	1	11	0	1	500.
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1								
6	13																					
14	19																					
20	22																					

1	9	2	7	3	8	4	10	5	16	11	24	11	25	12	26
12	27	13	28	13	29	13	30	15	31	15	32	17	33	17	34
18	35	18	36	20	37	21	38	21	39	22	23				
.00000	.00000	.00000	.00000	2				1.35900	.00000	.00000		29	2		
2.09512	1.21547	.00000	29					1.46550	2.41982	.00000		2	4		
.26504	2.29020	1.85935	2					-.44129	1.12391	1.85935		2	6		
1.88923	-.91163	.24633	5					3.14866	1.16793	.24633		5	8		
-.54276	.78999	-.49556	5					.51395	2.53482	-.49556		5	10		
-.71233	-1.33310	.07989	1					2.28127	3.70192	.02806		1	12		
-1.94376	1.19858	1.60436	1					-.30846	3.62835	1.51098		3	14		
.05501	.01083	2.78131	1					1.14559	2.39394	2.47600		5	16		
.64171	4.81730	1.62307	1					2.11543	4.50867	1.32274		1	18		
-1.44301	3.85626	1.15757	7					-.53660	-1.40796	2.66595		1	20		
-.33046	-2.13873	1.33055	1					-1.91110	-1.40884	2.98415		6	22		
-2.02642	-1.10084	3.86689	21					-.46692	-1.91634	-.83945		5	24		
-1.81668	-1.19475	.04848	5					1.98728	4.33168	-.84521		5	26		
3.36585	3.47980	-.11097	5					-2.22263	1.74454	.67675		5	28		
-2.44055	1.68560	2.47432	5					-2.43875	.21457	1.49984		5	30		
-.15555	.36629	3.81778	5					1.16527	-.06701	2.71102		5	32		
.53670	5.25264	2.64476	5					.30009	5.59436	.89842		5	34		
2.68304	5.46724	1.23980	5					2.58866	3.96394	2.17329		5	36		
-.07259	-2.04148	3.46257	5					.73485	-2.46070	1.26455		5	38		
-.91760	-3.08857	1.34108	5												

LAST

MM2 transition structure models of transannular Diels-Alder reaction on 105

MM2 transition structure models of Diels-Alder reaction on 105 were obtained as follows. Houk's synchronous STO-3G transition structure of the butadiene-ethylene reaction was used as the partial structure of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens, and resulting conformations were obtained by using MM2 force field.

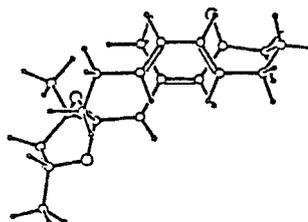
"a" means the transition state of chair-boat-chair like confirmation.

"b" means the transition state of chair-boat-boat like conformation.

Ia

FINAL STERIC ENERGY IS 82.1879 KCAL.

COMPRESSION	2.4720
BENDING	9.7232
STRETCH-BEND	.5332
VANDERWAALS	
1,4 ENERGY	16.8709
OTHER	25.5100
TORSIONAL	27.8618
DIPOLE	-.7832



DIPOLE MOMENT 2.643 D

-----  
END OF DA666KE6MO ENDO CHAIR CHAIR TRANSITION STATE D

Ib

FINAL STERIC ENERGY IS 82.0698 KCAL.

COMPRESSION	2.4953
BENDING	10.0987
STRETCH-BEND	.5449
VANDERWAALS	
1,4 ENERGY	16.8790
OTHER	26.5238
TORSIONAL	26.2903
DIPOLE	-.7624

DIPOLE MOMENT 2.617 D

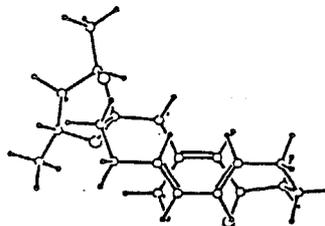
-----  
END OF DA666KE6MO ENDO CHAIR BOAT TRANSITION STATE 1

IIa

FINAL STERIC ENERGY IS 82.8075 KCAL.

COMPRESSION 2.4975  
BENDING 9.9212  
STRETCH-BEND .5181  
VANDERWAALS  
1,4 ENERGY 16.6835  
OTHER 26.2508  
TORSIONAL 27.7049  
DIPOLE -.7685

DIPOLE MOMENT 2.621 D



-----  
END OF DA666KA6MO ENDO CHAIR CHAIR TRANSITION STATE 4

IIb

FINAL STERIC ENERGY IS 82.7074 KCAL.

COMPRESSION 2.4895  
BENDING 10.3135  
STRETCH-BEND .5471  
VANDERWAALS  
1,4 ENERGY 16.9175  
OTHER 26.6495  
TORSIONAL 26.5316  
DIPOLE -.7412

DIPOLE MOMENT 2.681 D

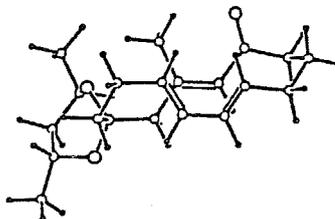
-----  
END OF DA666KA6MO ENDO CHAIR BOAT TRANSITION STATE 1C

IIIa

FINAL STERIC ENERGY IS 82.3880 KCAL.

COMPRESSION 2.3969  
BENDING 9.2020  
STRETCH-BEND .5310  
VANDERWAALS  
1,4 ENERGY 16.7511  
OTHER 26.1218  
TORSIONAL 28.1574  
DIPOLE -.7721

DIPOLE MOMENT 2.623 D



-----  
END OF DA666KA6MO EXO CHAIR CHAIR TRANSITION STATE 1

IIIb

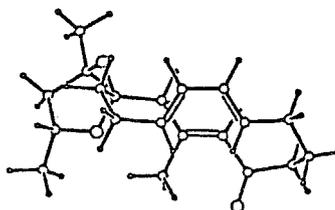
FINAL STERIC ENERGY IS 83.6426 KCAL.

COMPRESSION	2.4534		
BENDING	9.9080		
STRETCH-BEND	.5646		
VANDERWAALS			
1,4 ENERGY	16.9320		
OTHER	26.9280		
TORSIONAL	27.6259		
DIPOLE	-.7693	DIPOLE MOMENT	2.618 D

-----  
END OF DA666KA6MO EXO CHAIR BOAT TRANSITION STATE 1IVa

FINAL STERIC ENERGY IS 83.3952 KCAL.

COMPRESSION	2.4352		
BENDING	9.7398		
STRETCH-BEND	.5091		
VANDERWAALS			
1,4 ENERGY	16.6481		
OTHER	26.6551		
TORSIONAL	28.1641		
DIPOLE	-.7562	DIPOLE MOMENT	2.549 D

-----  
END OF DA666KE6MO EXO CHAIR CHAIR TRANSITION STATE 1IVb

FINAL STERIC ENERGY IS 84.6468 KCAL.

COMPRESSION	2.4928		
BENDING	10.4376		
STRETCH-BEND	.5430		
VANDERWAALS			
1,4 ENERGY	16.8287		
OTHER	27.4605		
TORSIONAL	27.6376		
DIPOLE	-.7534	DIPOLE MOMENT	2.544 D

-----  
END OF DA666KE6MO EXO CHAIR BOAT TRANSITION STATE 1

Ia

0 DA666KE6MO ENDO CHAIR CHAIR TRANSITION STATE D

28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
 2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
 3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
 4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
 1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
 3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
 2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
 3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
 2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
 4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,  
 1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,  
 4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,  
 1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,  
 6, 5,16,17, 2,9,1.500,120.0, 180.0, 16,18, 0, 0,0,  
 5,16,17,18, 2,9,1.540,109.5, -87.0, 12,17, 0, 0,0,  
 6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,  
 5, 6,13,20, 2,9,1.540,109.5, 171.0, 13,21,22,25,0,  
 6,13,20,21, 2,9,1.540,109.5, -65.0, 11,20, 0, 0,0,  
 6,13,20,22, 4,9,1.450,109.5, 60.0, 20,23, 0, 0,0,  
 13,20,22,23, 2,9,1.450,109.5, 130.0, 22,24,28, 0,0,  
 20,22,23,24, 2,9,1.540,109.5, 175.0, 23, 0, 0, 0,0,  
 6,13,20,25, 4,9,1.450,109.5, 180.0, 20,26, 0, 0,0,  
 13,20,25,26, 2,9,1.450,109.5, 175.0, 25,27,28, 0,0,  
 20,25,26,27, 2,9,1.540,109.5, 170.0, 26, 0, 0, 0,0,  
 20,22,23,28, 2,9,1.540,109.5, 55.0, 23,26, 0, 0,0,

DA666KE6MO ENDO CHAIR CHAIR TRANSITION STATE D

53 1 11 0 1 995.

6				0	30	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	
6	15														
16	19														
20	22	23	28	26	25	20									
23	24														
26	27														
1	9	2	7	3	8	4	10	5	14	11	29	11	30	12	31
12	32	13	33	13	34	15	35	15	36	15	37	17	38	17	39
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47
26	48	27	49	27	50	27	51	28	52	28	53				
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000	29	2			

2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4
.26504	2.29020	1.85935	2	-.44129	1.12391	1.85935	2	6
1.88923	-.91163	.24633	5	3.14866	1.16793	.24633	5	8
-.54276	.78999	-.49556	5	.51395	2.53482	-.49556	5	10
-.81958	-1.26596	.00721	1	2.25682	3.71452	.02078	1	12
-1.93858	1.20219	1.54791	1	-.21986	3.21898	1.59737	5	14
.01612	.00259	2.78526	1	1.53476	2.48210	2.62837	3	16
2.16015	3.86819	2.54088	1	3.06546	3.93922	1.30484	1	18
2.10549	1.66104	3.30932	7	-2.77635	-.08008	1.29245	1	20
-2.31618	-.91379	.07577	1	-2.74512	-.93914	2.42013	6	22
-3.72556	-.63769	3.39150	1	-3.45903	-1.51017	4.62352	1	24
-4.09215	.39695	1.02274	6	-5.11449	-.54421	1.28754	1	26
-6.44804	.06172	.83261	1	-5.10985	-.88791	2.78301	1	28
-.51234	-1.96848	.81394	5	-.62596	-1.79871	-.95456	5	30
1.54702	4.56898	-.09086	5	2.92665	3.74294	-.87125	5	32
-2.10055	1.89886	.69194	5	-2.38348	1.73059	2.42152	5	34
1.07952	-.29059	2.64965	5	-.53873	-.94653	2.66842	5	36
-.15175	.30527	3.84406	5	2.75556	4.06519	3.46408	5	38
1.37285	4.65683	2.50000	5	3.56472	4.93736	1.26273	5	40
3.87879	3.17983	1.38863	5	-2.87758	-1.87655	.04122	5	42
-2.60008	-.36121	-.85185	5	-3.60961	.43253	3.68641	5	44
-4.21740	-1.32005	5.41752	5	-2.45291	-1.29513	5.05259	5	46
-3.49158	-2.59375	4.36621	5	-4.91779	-1.45306	.67114	5	48
-7.29052	-.64289	1.02156	5	-6.43184	.28871	-.25853	5	50
-6.66404	1.01282	1.37146	5	-5.85711	-.27648	3.34129	5	52
-5.41225	-1.95452	2.90595	5					LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011114111

14	5	1	8					
2	2	3	1	0.15	2.091	0.0		
2	2	3	7	0.91	2.091	0.0		
5	2	3	1	0.0	2.091	0.0		
5	2	3	7	0.0	2.091	0.0		
1	1	2	29	-0.44	0.24	0.06		
1	2	29	29	0.0	9.415	0.0		
5	2	29	29	0.0	9.415	0.0		
5	1	2	29	0.0	0.0	-0.24		
2	29	29	2	0.0	2.23	0.80		
1	2	29	5	0.0	9.415	0.0		
2	29	29	5	0.0	2.23	0.0		
5	2	29	5	0.0	9.415	0.0		
3	1	2	29	0.0	0.0	0.10		
5	29	29	5	0.0	2.23	0.0		
2	3	6.370		1.4767				
2	2	9.444		1.366				

2	29	9.444	1.359	
5	29	4.60	1.09	
29	29	6.115	1.421	
	29	0.044	1.940	
2	29	29	0.43	120.0
5	29	29	0.36	120.0
	29	29	0.050	
5	29	2	0.36	120.0
	29	2	0.05	
1	2	29	0.55	121.4
5	2	29	0.36	120.0
	2	29	0.05	

Ib

0 DA666KE6MO ENDO CHAIR BOAT TRANSITION STATE 1

28,14,22,29,29, 2, 1.359, 1.421, 121.2,

2, 2, 9,11,

1, 1, 3, 7,

2, 4, 4, 8,

1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,

2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,

3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,

4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,

1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,

3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,

2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,

3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,

2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,

4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,

1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,

4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,

1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,

6, 5,16,17, 2,9,1.500,120.0, -175.0, 16,18, 0, 0,0,

5,16,17,18, 2,9,1.540,109.5, -38.0, 12,17, 0, 0,0,

6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,

5, 6,13,20, 2,9,1.540,109.5, 171.0, 13,21,22,25,0,

6,13,20,21, 2,9,1.540,109.5, -61.0, 11,20, 0, 0,0,

6,13,20,22, 4,9,1.450,109.5, 60.0, 20,23, 0, 0,0,

13,20,22,23, 2,9,1.450,109.5, 86.0, 22,24,28, 0,0,

20,22,23,24, 2,9,1.540,109.5, -173.0, 23, 0, 0, 0,0,

6,13,20,25, 4,9,1.450,109.5, -179.0, 20,26, 0, 0,0,

13,20,25,26, 2,9,1.450,109.5, -156.0, 25,27,28, 0,0,

20,25,26,27, 2,9,1.540,109.5, -175.0, 26, 0, 0, 0,0,

20,22,23,28, 2,9,1.540,109.5, 65.0, 23,26, 0, 0,0,

DA666KE6MO ENDO CHAIR BOAT TRANSITION STATE 1												53	1	11	0	1	800.
6				0	30	0	0	0	0	0	0	0	0	0	0	0	
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1			
6	15																
16	19																
20	22	23	28	26	25	20											
23	24																
26	27																
1	9	2	7	3	8	4	10	5	14	11	29	11	30	12	31		
12	32	13	33	13	34	15	35	15	36	15	37	17	38	17	39		
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47		
26	48	27	49	27	50	27	51	28	52	28	53						
.00000	.00000	.00000		.00000		2		1.35900		.00000		.00000		29	2		
2.09512	1.21547	.00000		.00000		29		1.46550		2.41982		.00000		2	4		
.26504	2.29020	1.85935		1.85935		2		-.44129		1.12391		1.85935		2	6		
1.88923	-.91163	.24633		.24633		5		3.14866		1.16793		.24633		5	8		
-.54276	.78999	-.49556		-.49556		5		.51395		2.53482		-.49556		5	10		
-.82033	-1.26803	-.00217		-.00217		1		2.29652		3.69249		.02771		1	12		
-1.94237	1.17292	1.57641		1.57641		1		-.21986		3.21898		1.59737		5	14		
.06305	.01599	2.77918		2.77918		1		1.54052		2.54258		2.59737		3	16		
2.05985	3.97694	2.52799		2.52799		1		1.89333		4.64985		1.15627		1	18		
2.17732	1.74287	3.24420		3.24420		7		-2.73832		-.14501		1.38132		1	20		
-2.31806	-.93172	.12029		.12029		1		-2.58942		-1.02610		2.48323		6	22		
-3.40289	-.70708	3.59379		3.59379		1		-3.01934		-1.64262		4.74675		1	24		
-4.09326	.25390	1.20282		1.20282		6		-5.02723		-.70198		1.66559		1	26		
-6.43158	-.23363	1.26646		1.26646		1		-4.87417		-.84850		3.18445		1	28		
-.48710	-1.99333	.77368		.77368		5		-.65349		-1.77274		-.98386		5	30		
2.20011	4.20436	-.95943		-.95943		5		3.37999		3.45729		.14988		5	32		
-2.13650	1.83911	.70334		.70334		5		-2.38524		1.72065		2.43878		5	34		
1.14837	-.19711	2.67875		2.67875		5		-.39720		-.97547		2.61744		5	36		
-.15770	.28556	3.83719		3.83719		5		3.14811		3.95798		2.77511		5	38		
1.55564	4.57615	3.32233		3.32233		5		.84781		5.00595		1.00079		5	40		
2.52650	5.56926	1.11671		1.11671		5		-2.88167		-1.89272		.06999		5	42		
-2.63446	-.34816	-.77726		-.77726		5		-3.17233		.33937		3.90424		5	44		
-3.64189	-1.43883	5.64824		5.64824		5		-1.95057		-1.50664		5.03252		5	46		
-3.15889	-2.71098	4.46279		4.46279		5		-4.81848		-1.67106		1.15198		5	48		
-7.20617	-.95311	1.61885		1.61885		5		-6.52363		-.14848		.15895		5	50		
-6.66391	.76518	1.70222		1.70222		5		-5.47147		-.07495		3.72207		5	52		
-5.28490	-1.84011	3.48766		3.48766		5										LAST	

IIa

0 DA666KA6MO ENDO CHAIR CHAIR TRANSITION STATE 4  
 28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,

2, 4, 4, 8,  
 1, 2, 3, 4, 22, 9, 1.359, 121.2, 0.0, 3, 3, 10, 12, 0,  
 2, 1, 4, 5, 22, 9, 2.217, 70.7, -117.3, 6, 6, 14, 16, 0,  
 3, 4, 1, 6, 22, 9, 2.217, 70.7, 117.3, 5, 5, 13, 15, 0,  
 4, 3, 2, 7, 1, 9, 1.083, 117.8, -165.1, 2, 0, 0, 0, 0,  
 1, 2, 3, 8, 1, 9, 1.083, 117.8, 165.1, 3, 0, 0, 0, 0,  
 3, 2, 1, 9, 1, 9, 1.079, 120.2, 32.1, 1, 0, 0, 0, 0,  
 2, 3, 4, 10, 1, 9, 1.079, 120.2, -32.1, 4, 0, 0, 0, 0,  
 3, 2, 1, 11, 2, 9, 1.500, 121.1, -172.6, 1, 21, 0, 0, 0,  
 2, 3, 4, 12, 2, 9, 1.500, 121.1, 172.6, 4, 18, 0, 0, 0,  
 4, 5, 6, 13, 2, 9, 1.500, 120.2, -101.0, 6, 20, 0, 0, 0,  
 1, 6, 5, 14, 1, 9, 1.080, 120.2, 101.0, 5, 0, 0, 0, 0,  
 4, 5, 6, 15, 2, 9, 1.500, 120.3, 104.1, 6, 0, 0, 0, 0,  
 1, 6, 5, 16, 32, 9, 1.500, 120.3, -104.1, 5, 17, 19, 19, 0,  
 6, 5, 16, 17, 2, 9, 1.500, 120.0, 180.0, 16, 18, 0, 0, 0,  
 5, 16, 17, 18, 2, 9, 1.540, 109.5, -100.0, 12, 17, 0, 0, 0,  
 6, 5, 16, 19, 14, 9, 1.400, 120.0, 0.0, 16, 16, 0, 0, 0,  
 5, 6, 13, 20, 2, 9, 1.540, 109.5, 180.0, 13, 21, 22, 25, 0,  
 6, 13, 20, 21, 2, 9, 1.540, 109.5, -110.0, 11, 20, 0, 0, 0,  
 6, 13, 20, 22, 4, 9, 1.450, 109.5, 10.0, 20, 23, 0, 0, 0,  
 13, 20, 22, 23, 2, 9, 1.450, 109.5, 90.0, 22, 24, 28, 0, 0,  
 20, 22, 23, 24, 2, 9, 1.540, 109.5, -150.0, 23, 0, 0, 0, 0,  
 6, 13, 20, 25, 4, 9, 1.450, 109.5, 130.0, 20, 26, 0, 0, 0,  
 13, 20, 25, 26, 2, 9, 1.450, 109.5, -55.0, 25, 27, 28, 0, 0,  
 20, 25, 26, 27, 2, 9, 1.540, 109.5, -150.0, 26, 0, 0, 0, 0,  
 20, 22, 23, 28, 2, 9, 1.540, 109.5, -30.0, 23, 26, 0, 0, 0,

DA666KA6MO ENDO CHAIR CHAIR TRANSITION STATE 4 53-1 11 0 1 800.

6				0	30	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	
6	15														
16	19														
20	22	23	28	26	25	20									
23	24														
26	27														
1	9	2	7	3	8	4	10	5	14	11	29	11	30	12	31
12	32	13	33	13	34	15	35	15	36	15	37	17	38	17	39
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47
26	48	27	49	27	50	27	51	28	52	28	53				
.00000	.00000	.00000		.00000		2		1.35900		.00000		.00000		29	2
2.09512	1.21547	.00000		.00000		29		1.46550		2.41982		.00000		2	4
.26504	2.29020	1.85935				2		-.44129		1.12391		1.85935		2	6
1.88923	-.91163	.24633				5		3.14866		1.16793		.24633		5	8
-.54276	.78999	-.49556				5		.51395		2.53482		-.49556		5	10
-.83152	-1.26145	.02364				1		2.25826		3.71377		.01249		1	12

-1.94400	1.20368	1.58298	1	-.21986	3.21898	1.59737	5	14
.04255	.00470	2.77753	1	1.53738	2.49106	2.62291	3	16
2.15640	3.87991	2.52940	1	3.06520	3.94629	1.29591	1	18
2.11625	1.67849	3.30715	7	-2.76846	-.09383	1.37713	1	20
-2.32532	-.90633	.13835	1	-2.66406	-.88260	2.55102	6	22
-3.77773	-1.71853	2.79055	1	-3.44464	-2.62011	3.98532	1	24
-4.11689	.28283	1.11301	6	-4.89674	.48199	2.27680	1	26
-6.26547	1.02421	1.84745	1	-5.00972	-.84219	3.04228	1	28
-.50682	-1.97950	.80936	5	-.66912	-1.78376	-.94955	5	30
1.54958	4.56824	-.10612	5	2.92939	3.73551	-.87875	5	32
-2.14043	1.89479	.72995	5	-2.34481	1.72121	2.48349	5	34
1.11466	-.25617	2.64726	5	-.46906	-.96585	2.64415	5	36
-.14077	.29004	3.83861	5	2.74827	4.08511	3.45310	5	38
1.36637	4.66539	2.48142	5	3.56321	4.94487	1.24961	5	40
3.87913	3.18813	1.38503	5	-2.91394	-1.84943	.06314	5	42
-2.61376	-.32239	-.76854	5	-3.93048	-2.36514	1.89428	5	44
-4.29874	-3.29422	4.22591	5	-3.21209	-2.01755	4.89330	5	46
-2.55630	-3.25721	3.76753	5	-4.39658	1.25637	2.90523	5	48
-6.92176	1.19405	2.73196	5	-6.78428	.31478	1.16253	5	50
-6.15920	1.99513	1.31042	5	-5.12677	-.61668	4.12838	5	52
-5.91861	-1.41003	2.73319	5					LAST

## Iib

0 DA666KA6MO ENDO CHAIR BOAT TRANSITION STATE 1C  
28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,  
1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,  
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,  
1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,  
6, 5,16,17, 2,9,1.500,120.0, -175.0, 16,18, 0, 0,0,  
5,16,17,18, 2,9,1.540,109.5, -38.0, 12,17, 0, 0,0,  
6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,  
5, 6,13,20, 2,9,1.540,109.5, 171.0, 13,21,22,25,0,

6,13,20,21,	2,9,1.540,109.5,	-63.0,	11,20, 0, 0,0,
6,13,20,22,	4,9,1.450,109.5,	60.0,	20,23, 0, 0,0,
13,20,22,23,	2,9,1.450,109.5,	126.0,	22,24,28, 0,0,
20,22,23,24,	2,9,1.540,109.5,	-177.0,	23, 0, 0, 0,0,
6,13,20,25,	4,9,1.450,109.5,	-178.0,	20,26, 0, 0,0,
13,20,25,26,	2,9,1.450,109.5,	-69.0,	25,27,28, 0,0,
20,25,26,27,	2,9,1.540,109.5,	-169.0,	26, 0, 0, 0,0,
20,22,23,28,	2,9,1.540,109.5,	-55.0,	23,26, 0, 0,0,

DA666KA6MO ENDO CHAIR BOAT TRANSITION STATE 1C 53 1 11 0 1 800.

6				0	30	0	0	0	0	0	0	0	0	0	
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1	
6	15														
16	19														
20	22	23	28	26	25	20									
23	24														
26	27														
1	9	2	7	3	8	4	10	5	14	11	29	11	30	12	31
12	32	13	33	13	34	15	35	15	36	15	37	17	38	17	39
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47
26	48	27	49	27	50	27	51	28	52	28	53				
.00000	.00000	.00000		2		1.35900		.00000		.00000		29		2	
2.09512	1.21547	.00000		29		1.46550		2.41982		.00000		2		4	
.26504	2.29020	1.85935		2		-.44129		1.12391		1.85935		2		6	
1.88923	-.91163	.24633		5		3.14866		1.16793		.24633		5		8	
-.54276	.78999	-.49556		5		.51395		2.53482		-.49556		5		10	
-.82772	-1.26291	.03092		1		2.29633		3.69271		.03081		1		12	
-1.94286	1.20830	1.58019		1		-.21986		3.21898		1.59737		5		14	
.04494	.01605	2.78788		1		1.54267		2.53030		2.59687		3		16	
2.07083	3.96141	2.53500		1		1.90168		4.64360		1.16808		1		18	
2.17569	1.71860	3.23250		7		-2.77298		-.08223		1.36016		1		20	
-2.32177	-.90819	.13342		1		-2.68852		-.87353		2.53325		6		22	
-3.84264	-1.64722	2.78773		1		-3.54127		-2.57420		3.97122		1		24	
-4.11543	.29720	1.06861		6		-4.90776		.56557		2.20996		1		26	
-6.27812	1.05945	1.72933		1		-5.01403		-.70085		3.06961		1		28	
-.50666	-1.96969	.82826		5		-.65826		-1.79610		-.93513		5		30	
2.19426	4.21080	-.95250		5		3.38047		3.45639		.14457		5		32	
-2.13555	1.90709	.73254		5		-2.34076		1.71823		2.48617		5		34	
1.11774	-.24236	2.65789		5		-.47515		-.95260		2.66992		5		36	
-.12948	.31828	3.84573		5		3.16007		3.93373		2.77682		5		38	
1.57385	4.55849	3.33546		5		.85702		5.00505		1.01943		5		40	
2.53818	5.56086	1.13202		5		-2.90803		-1.85411		.07177		5		42	
-2.60613	-.33716	-.78299		5		-4.05103		-2.27574		1.88926		5		44	
-4.42922	-3.19785	4.22487		5		-3.25640		-1.99250		4.87787		5		46	
-2.69673	-3.26153	3.73295		5		-4.42479		1.39168		2.78296		5		48	

-6.94440	1.28855	2.59280	5	-6.78287	.29471	1.09527	5	50
-6.17708	1.98836	1.12160	5	-5.03434	-.40357	4.14456	5	52
-5.96573	-1.24725	2.87055	5					LAST

IIIa

0 DA666KA6MO EXO CHAIR CHAIR TRANSITION STATE 1  
 28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
 2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
 3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
 4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
 1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
 3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
 2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
 3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
 2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
 4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,  
 1, 6, 5,14,32,9,1.500,120.2, 101.0, 5,17,19,19,0,  
 4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6,20, 0, 0,0,  
 1, 6, 5,16, 1,9,1.080,120.3, -104.1, 5, 0, 0, 0,0,  
 6, 5,14,17, 2,9,1.500,120.0, 177.0, 14,18, 0, 0,0,  
 5,14,17,18, 2,9,1.540,109.5, 84.0, 12,17, 0, 0,0,  
 6, 5,14,19,14,9,1.400,120.0, 0.0, 14,14, 0, 0,0,  
 5, 6,15,20, 2,9,1.540,109.5, -172.0, 15,21,22,25,0,  
 6,15,20,21, 2,9,1.540,109.5, 67.0, 11,20, 0, 0,0,  
 6,15,20,22, 4,9,1.450,109.5, -57.0, 20,23, 0, 0,0,  
 15,20,22,23, 2,9,1.450,109.5, -86.0, 22,24,28, 0,0,  
 20,22,23,24, 2,9,1.540,109.5, 173.0, 23, 0, 0, 0,0,  
 6,15,20,25, 4,9,1.450,109.5, 180.0, 20,26, 0, 0,0,  
 15,20,25,26, 2,9,1.450,109.5, 156.0, 25,27,28, 0,0,  
 20,25,26,27, 2,9,1.540,109.5, 175.0, 26, 0, 0, 0,0,  
 20,22,23,28, 2,9,1.540,109.5, -65.0, 23,26, 0, 0,0,

DA666KA6MO EXO CHAIR CHAIR TRANSITION STATE 1 53 1 11 0 1 800.  
 6 0 30 0 0 0 0 0 0 0 0 0 0 0  
 1 2 3 4 12 18 17 14 5 6 15 20 21 11 1  
 6 13  
 14 19  
 20 22 23 28 26 25 20  
 23 24  
 26 27  
 1 9 2 7 3 8 4 10 5 16 11 29 11 30 12 31

12	32	13	33	13	34	13	35	15	36	15	37	17	38	17	39
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47
26	48	27	49	27	50	27	51	28	52	28	53				
.00000	.00000	.00000		2		1.35900	.00000	.00000		.00000		29	2		
2.09512	1.21547	.00000		29		1.46550	2.41982	.00000		.00000		2	4		
.26504	2.29020	1.85935		2		-.44129	1.12391	1.85935				2	6		
1.88923	-.91163	.24633		5		3.14866	1.16793	.24633				5	8		
-.54276	.78999	-.49556		5		.51395	2.53482	-.49556				5	10		
-.70032	-1.33843	.09627		1		2.30216	3.67970	.08600				1	12		
-1.94079	1.21876	1.58415		1		-.31558	3.63232	1.53256				3	14		
.03775	.00022	2.77579		1		1.14559	2.39394	2.47600				5	16		
.65124	4.80501	1.65560		1		1.47141	4.93980	.36673				1	18		
-1.45137	3.88174	1.19961		7		-.62247	-1.39895	2.70269				1	20		
-.33881	-2.12257	1.36981		1		-2.03236	-1.33740	2.84803				6	22		
-2.47186	-1.18048	4.18204		1		-3.99373	-.99174	4.15980				1	24		
-.01589	-2.16401	3.73815		6		-.88095	-3.13229	4.29791				1	26		
-.07029	-3.99512	5.27202		1		-2.04273	-2.41086	4.99148				1	28		
-.42713	-1.93594	-.80602		5		-1.80505	-1.21529	.03231				5	30		
2.83429	3.81075	-.88631		5		3.07916	3.56338	.87818				5	32		
-2.20079	1.81448	.68279		5		-2.45312	1.65615	2.47131				5	34		
-2.44481	.25460	1.38967		5		-.08897	.38757	3.81223				5	36		
1.13948	-.12529	2.66246		5		1.32342	4.67524	2.53583				5	38		
.07394	5.74230	1.83981		5		.78401	5.13604	-.49109				5	40		
2.14914	5.82403	.44549		5		.73550	-2.41780	1.34769				5	42		
-.90206	-3.08507	1.34339		5		-2.01259	-.24968	4.59110				5	44		
-4.39464	-.87072	5.19248		5		-4.50139	-1.86545	3.69030				5	46		
-4.27595	-.08482	3.57656		5		-1.25491	-3.78455	3.47211				5	48		
-.71446	-4.76961	5.74846		5		.38153	-3.37633	6.08098				5	50		
.75966	-4.51931	4.74409		5		-2.88550	-3.13136	5.11152				5	52		
-1.75075	-2.08302	6.01692		5											LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011116111

14	5	1	8												
2	2	3	1	0.15	2.091	0.0									
2	2	3	7	0.91	2.091	0.0									
5	2	3	1	0.0	2.091	0.0									
5	2	3	7	0.0	2.091	0.0									
1	1	2	29	-0.44	0.24	0.06									
1	2	29	29	0.0	9.415	0.0									
5	2	29	29	0.0	9.415	0.0									
5	1	2	29	0.0	0.0	-0.24									
2	29	29	2	0.0	2.23	0.80									
1	2	29	5	0.0	9.415	0.0									
2	29	29	5	0.0	2.23	0.0									
5	2	29	5	0.0	9.415	0.0									

3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	3	6.370		1.4767		
2	2	9.444		1.366		
2	29	9.444		1.359		
5	29	4.60		1.09		
29	29	6.115		1.421		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

### IIIb

0 DA666KAMO EXO CHAIR BOAT TRANSITION STATE 1

28,14,22,29,29, 2, 1.359, 1.421, 121.2,		
2, 2, 9,11,		
1, 1, 3, 7,		
2, 4, 4, 8,		
1, 2, 3, 4,22,9,1.359,121.2, 0.0,	3, 3,10,12,0,	
2, 1, 4, 5,22,9,2.217, 70.7, -117.3,	6, 6,14,16,0,	
3, 4, 1, 6,22,9,2.217, 70.7, 117.3,	5, 5,13,15,0,	
4, 3, 2, 7, 1,9,1.083,117.8, -165.1,	2, 0, 0, 0,0,	
1, 2, 3, 8, 1,9,1.083,117.8, 165.1,	3, 0, 0, 0,0,	
3, 2, 1, 9, 1,9,1.079,120.2, 32.1,	1, 0, 0, 0,0,	
2, 3, 4,10, 1,9,1.079,120.2, -32.1,	4, 0, 0, 0,0,	
3, 2, 1,11, 2,9,1.500,121.1, -172.6,	1,21, 0, 0,0,	
2, 3, 4,12, 2,9,1.500,121.1, 172.6,	4,18, 0, 0,0,	
4, 5, 6,13, 2,9,1.500,120.2, -101.0,	6, 0, 0, 0,0,	
1, 6, 5,14,32,9,1.500,120.2, 101.0,	5,17,19,19,0,	
4, 5, 6,15, 2,9,1.500,120.3, 104.1,	6,20, 0, 0,0,	
1, 6, 5,16, 1,9,1.080,120.3, -104.1,	5, 0, 0, 0,0,	
6, 5,14,17, 2,9,1.500,120.0, 178.0,	14,18, 0, 0,0,	
5,14,17,18, 2,9,1.540,109.5, 31.0,	12,17, 0, 0,0,	
6, 5,14,19,14,9,1.400,120.0, 0.0,	14,14, 0, 0,0,	
5, 6,15,20, 2,9,1.540,109.5, -172.0,	15,21,22,25,0,	
6,15,20,21, 2,9,1.540,109.5, 67.0,	11,20, 0, 0,0,	
6,15,20,22, 4,9,1.450,109.5, -57.0,	20,23, 0, 0,0,	
15,20,22,23, 2,9,1.450,109.5, -86.0,	22,24,28, 0,0,	
20,22,23,24, 2,9,1.540,109.5, 173.0,	23, 0, 0, 0,0,	
6,15,20,25, 4,9,1.450,109.5, 180.0,	20,26, 0, 0,0,	



Iva

0 DA666KE6MO EXO CHAIR CHAIR TRANSITION STATE 1  
 28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
 2, 2, 9,11,  
 1, 1, 3, 7,  
 2, 4, 4, 8,  
 1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
 2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
 3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
 4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
 1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
 3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
 2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
 3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
 2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
 4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,  
 1, 6, 5,14,32,9,1.500,120.2, 101.0, 5,17,19,19,0,  
 4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6,20, 0, 0,0,  
 1, 6, 5,16, 1,9,1.080,120.3, -104.1, 5, 0, 0, 0,0,  
 6, 5,14,17, 2,9,1.500,120.0, 177.0, 14,18, 0, 0,0,  
 5,14,17,18, 2,9,1.540,109.5, 84.0, 12,17, 0, 0,0,  
 6, 5,14,19,14,9,1.400,120.0, 0.0, 14,14, 0, 0,0,  
 5, 6,15,20, 2,9,1.540,109.5, -172.0, 15,21,22,25,0,  
 6,15,20,21, 2,9,1.540,109.5, 65.0, 11,20, 0, 0,0,  
 6,15,20,22, 4,9,1.450,109.5, -59.0, 20,23, 0, 0,0,  
 15,20,22,23, 2,9,1.450,109.5, -152.0, 22,24,28, 0,0,  
 20,22,23,24, 2,9,1.540,109.5, -173.0, 23, 0, 0, 0,0,  
 6,15,20,25, 4,9,1.450,109.5, 180.0, 20,26, 0, 0,0,  
 15,20,25,26, 2,9,1.450,109.5, 86.0, 25,27,28, 0,0,  
 20,25,26,27, 2,9,1.540,109.5, -174.0, 26, 0, 0, 0,0,  
 20,22,23,28, 2,9,1.540,109.5, 64.0, 23,26, 0, 0,0.

DA666KE6MO EXO CHAIR CHAIR TRANSITION STATE 1 53 1 11 0 1 800.  
 6 0 30 0 0 0 0 0 0 0 0 0 0 0  
 1 2 3 4 12 18 17 14 5 6 15 20 21 11 1  
 6 13  
 14 19  
 20 22 23 28 26 25 20  
 23 24  
 26 27  
 1 9 2 7 3 8 4 10 5 16 11 29 11 30 12 31  
 12 32 13 33 13 34 13 35 15 36 15 37 17 38 17 39  
 18 40 18 41 21 42 21 43 23 44 24 45 24 46 24 47  
 26 48 27 49 27 50 27 51 28 52 28 53  
 .00000 .00000 .00000 2 1.35900 .00000 .00000 29 2

2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4
.26504	2.29020	1.85935	2	-.44129	1.12391	1.85935	2	6
1.88923	-.91163	.24633	5	3.14866	1.16793	.24633	5	8
-.54276	.78999	-.49556	5	.51395	2.53482	-.49556	5	10
-.70024	-1.33966	.09616	1	2.30348	3.67897	.08409	1	12
-1.93994	1.22038	1.57286	1	-.31275	3.63354	1.53156	3	14
.03013	.00299	2.78702	1	1.14559	2.39394	2.47600	5	16
.65588	4.80476	1.65543	1	1.47456	4.93995	.36576	1	18
-1.44779	3.88670	1.19886	7	-.63009	-1.39609	2.70266	1	20
-.33176	-2.11463	1.37151	1	-2.02228	-1.22637	2.91126	6	22
-2.73938	-2.39682	3.24784	1	-4.19994	-1.98199	3.47091	1	24
-.02643	-2.18849	3.71725	6	-.82359	-2.31038	4.87777	1	26
-.01755	-3.07960	5.93098	1	-2.11447	-3.03982	4.49321	1	28
-.42342	-1.93797	-.80444	5	-1.80589	-1.22598	.03442	5	30
2.83423	3.80918	-.88909	5	3.08163	3.56230	.87510	5	32
-2.19383	1.82980	.67911	5	-2.46123	1.64252	2.46228	5	34
-2.44310	.26080	1.35341	5	-.16069	.38878	3.81541	5	36
1.13644	-.11169	2.71107	5	1.32893	4.67311	2.53471	5	38
.08018	5.74268	1.84149	5	.78642	5.13719	-.49124	5	40
2.15329	5.82344	.44423	5	.75191	-2.37243	1.35551	5	42
-.83312	-3.10907	1.34456	5	-2.71137	-3.08619	2.37153	5	44
-4.83290	-2.86401	3.72272	5	-4.62516	-1.50911	2.55532	5	46
-4.28471	-1.24413	4.30173	5	-1.03946	-1.28519	5.26667	5	48
-.60763	-3.21067	6.86709	5	.91881	-2.53439	6.19218	5	50
.27086	-4.09036	5.56138	5	-1.89604	-4.11326	4.28185	5	52
-2.81665	-3.01819	5.35912	5					LAST

IVb

0 DA666KEMO EXO CHAIR BOAT TRANSITION STATE 1  
28,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6, 0, 0, 0,0,  
1, 6, 5,14,32,9,1.500,120.2, 101.0, 5,17,19,19,0,  
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6,20, 0, 0,0,

1, 6, 5,16, 1,9,1.080,120.3, -104.1,	5, 0, 0, 0,0,
6, 5,14,17, 2,9,1.500,120.0, 178.0,	14,18, 0, 0,0,
5,14,17,18, 2,9,1.540,109.5, 31.0,	12,17, 0, 0,0,
6, 5,14,19,14,9,1.400,120.0, 0.0,	14,14, 0, 0,0,
5, 6,15,20, 2,9,1.540,109.5, -172.0,	15,21,22,25,0,
6,15,20,21, 2,9,1.540,109.5, 65.0,	11,20, 0, 0,0,
6,15,20,22, 4,9,1.450,109.5, -59.0,	20,23, 0, 0,0,
15,20,22,23, 2,9,1.450,109.5, -152.0,	22,24,28, 0,0,
20,22,23,24, 2,9,1.540,109.5, -173.0,	23, 0, 0, 0,0,
6,15,20,25, 4,9,1.450,109.5, 180.0,	20,26, 0, 0,0,
15,20,25,26, 2,9,1.450,109.5, 86.0,	25,27,28, 0,0,
20,25,26,27, 2,9,1.540,109.5, -174.0,	26, 0, 0, 0,0,
20,22,23,28, 2,9,1.540,109.5, 64.0,	23,26, 0, 0,0,

DA666KE6MO EXO CHAIR BOAT TRANSITION STATE 1 53 1 11 0 1 800.

6				0	30	0	0	0	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	14	5	6	15	20	21	11	1			
6	13																
14	19																
20	22	23	28	26	25	20											
23	24																
26	27																
1	9	2	7	3	8	4	10	5	16	11	29	11	30	12	31		
12	32	13	33	13	34	13	35	15	36	15	37	17	38	17	39		
18	40	18	41	21	42	21	43	23	44	24	45	24	46	24	47		
26	48	27	49	27	50	27	51	28	52	28	53						
.00000	.00000	.00000			2		1.35900	.00000		.00000		.00000		29	2		
2.09512	1.21547	.00000			29		1.46550	2.41982		.00000		.00000		2	4		
.26504	2.29020	1.85935			2		-.44129	1.12391		1.85935		1.85935		2	6		
1.88923	-.91163	.24633			5		3.14866	1.16793		.24633		.24633		5	8		
-.54276	.78999	-.49556			5		.51395	2.53482		-.49556		-.49556		5	10		
-.70063	-1.33939	.09681			1		2.28457	3.69989		.02335		.02335		1	12		
-1.93896	1.22535	1.56980			1		-.28890	3.63905		1.51729		1.51729		3	14		
.02637	.00373	2.78931			1		1.14559	2.39394		2.47600		2.47600		5	16		
.67745	4.81367	1.64770			1		2.14462	4.49307		1.32897		1.32897		1	18		
-1.41809	3.89303	1.16483			7		-.63545	-1.39441		2.70315		2.70315		1	20		
-.33331	-2.11335	1.37310			1		-2.02821	-1.22277		2.90628		2.90628		6	22		
-2.74755	-2.39219	3.24163			1		-4.20916	-1.97659		3.45611		3.45611		1	24		
-.03679	-2.18769	3.71998			6		-.83744	-2.30600		4.87848		4.87848		1	26		
-.03624	-3.07569	5.93503			1		-2.12925	-3.03262		4.49163		4.49163		1	28		
-.42337	-1.93854	-.80310			5		-1.80622	-1.22530		.03448		.03448		5	30		
1.97628	4.33910	-.83805			5		3.36571	3.47632		-.13838		-.13838		5	32		
-2.18990	1.83796	.67753			5		-2.45982	1.64898		2.45875		2.45875		5	34		
-2.44479	.26756	1.34836			5		-.16642	.39048		3.81696		3.81696		5	36		
1.13269	-.11229	2.71555			5		.58578	5.22884		2.67905		2.67905		5	38		

.34066	5.61063	.94262	5	2.72164	5.44639	1.25060	5	40
2.62157	3.93243	2.16706	5	.75070	-2.36983	1.35941	5	42
-.83360	-3.10832	1.34575	5	-2.71503	-3.08354	2.36704	5	44
-4.84353	-2.85789	3.70684	5	-4.62953	-1.50592	2.53715	5	46
-4.29813	-1.23664	4.28463	5	-1.05178	-1.27973	5.26534	5	48
-.62929	-3.20404	6.86964	5	.90069	-2.53237	6.19813	5	50
.25080	-4.08765	5.56765	5	-1.91379	-4.10758	4.28498	5	52
-2.83448	-3.00541	5.35490	5					LAST

MM2 transition structure models of transannular Diels-Alder reaction on 110

MM2 transition structure models of Diels-Alder reaction on 110 were obtained as follows. Houk's synchronous STO-3G transition structure of the butadiene-ethylene reaction was used as the partial structure of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens, and resulting conformations were obtained by using MM2 force field.

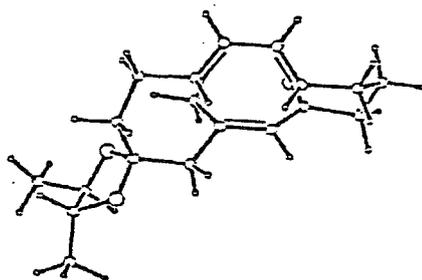
"a" means the transition state of chair-boat-chair like confirmation.

Ia

FINAL STERIC ENERGY IS 77.2282 KCAL.

COMPRESSION	2.1108
BENDING	8.7098
STRETCH-BEND	.3043
VANDERWAALS	
1,4 ENERGY	12.8932
OTHER	25.2187
TORSIONAL	28.6961
DIPOLE	-.7046

DIPOLE MOMENT 2.612 D



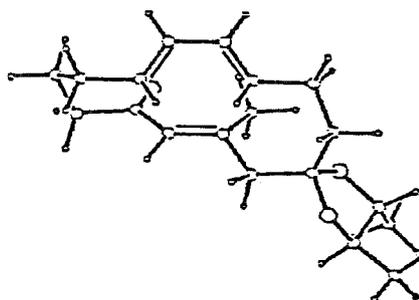
-----  
END OF DA666KE5MO ENDO CHAIR CHAIR TRANSITION STATE 2

IIa

FINAL STERIC ENERGY IS 77.3035 KCAL.

COMPRESSION	2.1052
BENDING	8.6660
STRETCH-BEND	.3031
VANDERWAALS	
1,4 ENERGY	12.8707
OTHER	25.2782
TORSIONAL	28.7800
DIPOLE	-.6996

DIPOLE MOMENT 2.616 D



-----  
END OF DA666KA5MO ENDO CHAIR CHAIR TRANSITION STATE

Ia

0 DA666KE5MO ENDO CHAIR CHAIR TRANSITION STATE 2  
27,14,22,29,29, 2, 1.359, 1.421, 121.2,  
2, 2, 9,11,  
1, 1, 3, 7,  
2, 4, 4, 8,  
1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,  
2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,  
3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,  
4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,  
1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,  
3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,  
2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,  
3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,  
2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,  
4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,  
1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,  
4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,  
1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,  
6, 5,16,17, 2,9,1.500,120.0, 180.0, 16,18, 0, 0,0,  
5,16,17,18, 2,9,1.540,109.5, -100.0, 12,17, 0, 0,0,  
6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,  
5, 6,13,20, 2,9,1.540,109.5, 180.0, 13,21,22,25,0,  
6,13,20,21, 2,9,1.540,109.5, -110.0, 11,20, 0, 0,0,  
6,13,20,22, 4,9,1.450,109.5, 10.0, 20,23, 0, 0,0,  
13,20,22,23, 2,9,1.450,109.5, 115.0, 22,24,26, 0,0,  
20,22,23,24, 2,9,1.540,109.5, 155.0, 23, 0, 0, 0,0,  
6,13,20,25, 4,9,1.450,109.5, 130.0, 20,26, 0, 0,0,  
13,20,25,26, 2,9,1.450,109.5, -130.0, 23,25,27, 0,0,  
20,25,26,27, 2,9,1.540,109.5, 155.0, 26, 0, 0, 0,0,

DA666KE5MO ENDO CHAIR CHAIR TRANSITION STATE 2 50 1 11 0 1 800.  
6 0 28 0 0 0 0 0 0 0 0 0 0 0  
1 2 3 4 12 18 17 16 5 6 13 20 21 11 1  
6 15  
16 19  
20 22 23 26 25 20  
23 24  
26 27  
1 9 2 7 3 8 4 10 5 14 11 28 11 29 12 30  
12 31 13 32 13 33 15 34 15 35 15 36 17 37 17 38  
18 39 18 40 21 41 21 42 23 43 24 44 24 45 24 46  
26 47 27 48 27 49 27 50  
.00000 .00000 .00000 2 1.35900 .00000 .00000 29 2  
2.09512 1.21547 .00000 29 1.46550 2.41982 .00000 2 4

.26504	2.29020	1.85935	2	-.44129	1.12391	1.85935	2	6
1.88923	-.91163	.24633	5	3.14866	1.16793	.24633	5	8
-.54276	.78999	-.49556	5	.51395	2.53482	-.49556	5	10
-.81186	-1.27453	-.00548	1	2.25836	3.71365	.01302	1	12
-1.94260	1.18614	1.57932	1	-.21986	3.21898	1.59737	5	14
.04308	.00116	2.77264	1	1.53655	2.49094	2.62439	3	16
2.15671	3.87924	2.53007	1	3.06544	3.94518	1.29652	1	18
2.11295	1.67921	3.31167	7	-2.72600	-.12353	1.33803	1	20
-2.31017	-.94401	.10502	1	-2.66067	-.96328	2.47879	6	22
-3.89049	-.84554	3.15495	1	-4.16993	-2.12869	3.93733	1	24
-4.08759	.24772	1.15526	6	-4.85590	-.56862	2.01105	1	26
-6.13217	.16799	2.41726	1	-.48176	-1.99322	.77777	5	28
-.63590	-1.78432	-.98283	5	1.54982	4.56830	-.10509	5	30
2.92944	3.73570	-.87826	5	-2.14344	1.88709	.73545	5	32
-2.38965	1.66775	2.48023	5	1.11736	-.25367	2.64878	5	34
-.46305	-.97042	2.62650	5	-.15002	.27783	3.83427	5	36
2.74887	4.08441	3.45361	5	1.36715	4.66520	2.48212	5	38
3.56414	4.94342	1.25042	5	3.87887	3.18647	1.38550	5	40
-2.88991	-1.89767	.08788	5	-2.62231	-.38009	-.80646	5	42
-3.80177	.03220	3.83986	5	-5.15714	-2.07094	4.44998	5	44
-3.38889	-2.29817	4.71389	5	-4.18131	-3.01690	3.26492	5	46
-5.09293	-1.50016	1.44225	5	-6.76483	.38834	1.52682	5	48
-5.89747	1.13543	2.91742	5	-6.73553	-.44767	3.12276	5	LAST

11

1111 2111 3111 4111 5111 6111 7111 8111 91111011114111

14	5	1	8			
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5	2	3	1	0.0	2.091	0.0
5	2	3	7	0.0	2.091	0.0
1	1	2	29	-0.44	0.24	0.06
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	3	6.370		1.4767		
2	2	9.444		1.366		
2	29	9.444		1.359		
5	29	4.60		1.09		
29	29	6.115		1.421		

	29	0.044	1.940	
2	29	29	0.43	120.0
5	29	29	0.36	120.0
	29	29	0.050	
5	29	2	0.36	120.0
	29	2	0.05	
1	2	29	0.55	121.4
5	2	29	0.36	120.0
	2	29	0.05	

IIa

0 DA666KA5MO ENDO CHAIR CHAIR TRANSITION STATE

27,14,22,29,29, 2, 1.359, 1.421, 121.2,

2, 2, 9,11,

1, 1, 3, 7,

2, 4, 4, 8,

1, 2, 3, 4,22,9,1.359,121.2, 0.0, 3, 3,10,12,0,

2, 1, 4, 5,22,9,2.217, 70.7, -117.3, 6, 6,14,16,0,

3, 4, 1, 6,22,9,2.217, 70.7, 117.3, 5, 5,13,15,0,

4, 3, 2, 7, 1,9,1.083,117.8, -165.1, 2, 0, 0, 0,0,

1, 2, 3, 8, 1,9,1.083,117.8, 165.1, 3, 0, 0, 0,0,

3, 2, 1, 9, 1,9,1.079,120.2, 32.1, 1, 0, 0, 0,0,

2, 3, 4,10, 1,9,1.079,120.2, -32.1, 4, 0, 0, 0,0,

3, 2, 1,11, 2,9,1.500,121.1, -172.6, 1,21, 0, 0,0,

2, 3, 4,12, 2,9,1.500,121.1, 172.6, 4,18, 0, 0,0,

4, 5, 6,13, 2,9,1.500,120.2, -101.0, 6,20, 0, 0,0,

1, 6, 5,14, 1,9,1.080,120.2, 101.0, 5, 0, 0, 0,0,

4, 5, 6,15, 2,9,1.500,120.3, 104.1, 6, 0, 0, 0,0,

1, 6, 5,16,32,9,1.500,120.3, -104.1, 5,17,19,19,0,

6, 5,16,17, 2,9,1.500,120.0, 180.0, 16,18, 0, 0,0,

5,16,17,18, 2,9,1.540,109.5, -100.0, 12,17, 0, 0,0,

6, 5,16,19,14,9,1.400,120.0, 0.0, 16,16, 0, 0,0,

5, 6,13,20, 2,9,1.540,109.5, 180.0, 13,21,22,25,0,

6,13,20,21, 2,9,1.540,109.5, -110.0, 11,20, 0, 0,0,

6,13,20,22, 4,9,1.450,109.5, 10.0, 20,23, 0, 0,0,

13,20,22,23, 2,9,1.450,109.5, 85.0, 22,24,26, 0,0,

20,22,23,24, 2,9,1.540,109.5, -95.0, 23, 0, 0, 0,0,

6,13,20,25, 4,9,1.450,109.5, 130.0, 20,26, 0, 0,0,

13,20,25,26, 2,9,1.450,109.5, -85.0, 23,25,27, 0,0,

20,25,26,27, 2,9,1.540,109.5, -145.0, 26, 0, 0, 0,0,

DA666KA5MO ENDO CHAIR CHAIR TRANSITION STATE

50 1 11 0 1 500.

6				0	28	0	0	0	0	0	0	0	0	0
1	2	3	4	12	18	17	16	5	6	13	20	21	11	1

6	15																		
16	19																		
20	22	23	26	25	20														
23	24																		
26	27																		
1	9	2	7	3	8	4	10	5	14	11	28	11	29	12	30				
12	31	13	32	13	33	15	34	15	35	15	36	17	37	17	38				
18	39	18	40	21	41	21	42	23	43	24	44	24	45	24	46				
26	47	27	48	27	49	27	50												
.00000	.00000	.00000		.00000		2		1.35900		.00000		.00000		29	2				
2.09512	1.21547	.00000		.00000		29		1.46550		2.41982		.00000		2	4				
.26504	2.29020	1.85935		2				-.44129		1.12391		1.85935		2	6				
1.88923	-.91163	.24633		5				3.14866		1.16793		.24633		5	8				
-.54276	.78999	-.49556		5				.51395		2.53482		-.49556		5	10				
-.81551	-1.27267	.00156		1				2.25833		3.71369		.01287		1	12				
-1.94260	1.19215	1.58274		1				-.21986		3.21898		1.59737		5	14				
.04324	.00166	2.77334		1				1.53706		2.49057		2.62365		3	16				
2.15694	3.87904	2.52989		1				3.06554		3.94538		1.29626		1	18				
2.11434	1.67834	3.30959		7				-2.72999		-.11531		1.34669		1	20				
-2.31343	-.94039	.11654		1				-2.66432		-.93123		2.50446		6	22				
-3.98397	-1.28369	2.84839		1				-4.07383		-1.51437		4.35693		1	24				
-4.09278	.24411	1.15068		6				-4.78121		-.09326		2.33433		1	26				
-6.24424	-.39634	2.01128		1				-.48383		-1.99086		.78451		5	28				
-.64391	-1.78504	-.97522		5				1.54972		4.56829		-.10520		5	30				
2.92930	3.73574	-.87849		5				-2.14462		1.89284		.73894		5	32				
-2.38235	1.67425	2.48696		5				1.11688		-.25484		2.64740		5	34				
-.46470	-.96949	2.63016		5				-.14679		.28020		3.83505		5	36				
2.74912	4.08395	3.45346		5				1.36726		4.66490		2.48222		5	38				
3.56395	4.94377	1.25020		5				3.87918		3.18688		1.38507		5	40				
-2.89612	-1.89208	.09924		5				-2.62466		-.37784		-.79613		5	42				
-4.22811	-2.21517	2.28271		5				-5.11853		-1.75746		4.65735		5	44				
-3.75307	-.60975	4.92264		5				-3.42037		-2.36134		4.66899		5	46				
-4.69545	.78333	3.02107		5				-6.75231		.50082		1.58859		5	48				
-6.79582	-.70211	2.92947		5				-6.33064		-1.22034		1.26647		5	LAST				

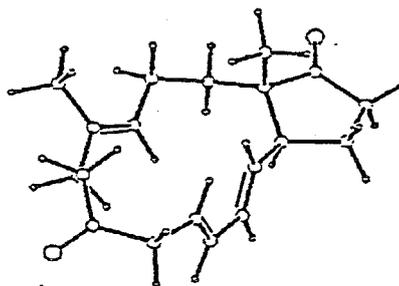
Conformational analysis of the 14-membered (E,E,E)-triene 120

The starting geometries which were constructed to be a s-cis form of E,E-diene, were generated using MMRS at 45° dihedral angle resolution and with a closure distance range of 1.0-3.0 Å, and with a transannular contact of 2.4 Å. Structures of 11 conformations obtained were optimized by MM2 to get 4 conformations (HITAC).

I

FINAL STERIC ENERGY IS 30.8400 KCAL.

COMPRESSION	1.7215		
BENDING	7.4259		
STRETCH-BEND	0.2687		
VANDERWAALS			
1,4 ENERGY	11.4939		
OTHER	-3.4280		
TORSIONAL	12.2384		
DIPOLE	1.1196	DIPOLE MOMENT	2.426 D



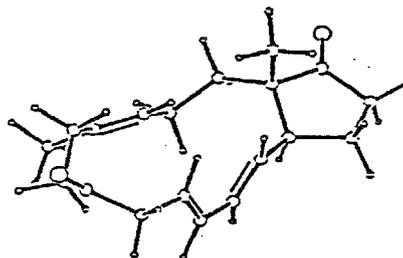
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END OF

TOTAL ELAPSED TIME IS 24.64 SEC.

II

FINAL STERIC ENERGY IS 31.6504 KCAL.

COMPRESSION	1.7339		
BENDING	7.7819		
STRETCH-BEND	0.2777		
VANDERWAALS			
1,4 ENERGY	11.9545		
OTHER	-4.0935		
TORSIONAL	12.8461		
DIPOLE	1.1498	DIPOLE MOMENT	3.678 D



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END OF

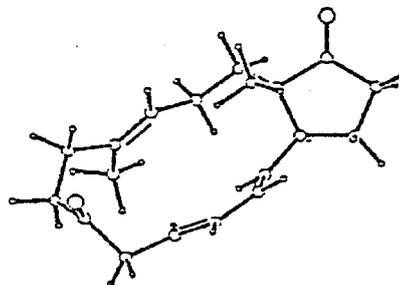
TOTAL ELAPSED TIME IS 19.55 SEC.

III

FINAL STERIC ENERGY IS 32.4429 KCAL.

COMPRESSION	1.6778
BENDING	9.0685
STRETCH-BEND	0.3035
VANDERWAALS	
1,4 ENERGY	11.0820
OTHER	-3.7170
TORSIONAL	12.7747
DIPOLE	1.2535

DIPOLE MOMENT 4.972 D



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END OF

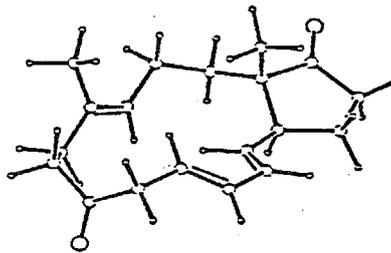
TOTAL ELAPSED TIME IS 41.03 SEC.

IV

FINAL STERIC ENERGY IS 35.9935 KCAL.

COMPRESSION	1.8162
BENDING	9.4735
STRETCH-BEND	0.3624
VANDERWAALS	
1,4 ENERGY	11.5849
OTHER	-2.8522
TORSIONAL	14.4425
DIPOLE	1.1663

DIPOLE MOMENT 2.309 D



-----  
END OF

TOTAL ELAPSED TIME IS 38.08 SEC.

0 E,E s-cis DIENE 14MEMBERED RING

21 14 2 22 22 1 1.50 1.34 120.0 1 0 45 1.0 3.0 100 1.2

2 14 0 0

1 3 3 0

2 2 4 19

1 2 3 4 2 1 1.50 120.0 180.0 3 5 0 0 0

2 3 4 5 2 0 1.54 109.5 0.0 4 6 0 0 0

3 4 5 6 32 0 1.50 109.5 0.0 5 7 20 20 0

4 5 6 7 2 0 1.50 120.0 0.0 6 8 0 0 0

5 6 7 8 22 0 1.50 109.5 0.0 7 9 9 0 0

6 7 8 9 2922 0 1.34 120.0 0.0 8 8 10 0 0

7 8 9 10 2922 1 1.50 120.0 180.0 9 11 11 0 0

8 9 10 11 22 1 1.34 120.0 0.0 10 10 12 0 0

9 10 11 12 2 1 1.50 120.0 180.0 11 13 15 0 0

10 11 12 13 2 0 1.54 109.5 0.0 12 14 17 18 0

11 12 13 14 2 1 1.54 109.5 240.0 13 1 0 0 0

10 11 12 15 2 2 1.54 109.5 120.0 12 16 0 0 13

13 12 15 16 2 1 1.54 108.0 0.0 15 17 0 0 0

15 12 13 17 32 1 1.50 108.0 0.0 13 16 21 21 0

11 12 13 18 2 1 1.54 109.5 0.0 13 0 0 0 0

1 2 3 19 2 1 1.50 120.0 0.0 3 0 0 0 0

4 5 6 20 14 2 1.40 120.0 180.0 6 6 0 0 7

12 13 17 21 14 1 1.40 120.0 180.0 17 17 0 0 0

47 4 0 0 1 500.

6

26

1

1 2 3 4 5 6 7 8 9 10 11 12 13 14 1

12 15 16 17 13

13 18

3 19

6 20

17 21

1 22 1 23 2 24 4 25 4 26 5 27 5 28 7 29

7 30 8 31 9 32 10 33 11 34 12 35 14 36 14 37

15 38 15 39 16 40 16 41 18 42 18 43 18 44 19 45

19 46 19 47

10 3 1 8

1 1 2 29 -0.44 0.24 0.06

1 2 29 29 0.0 9.415 0.0

5 2 29 29 0.0 9.415 0.0

5 1 2 29 0.0 0.0 -0.24

2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	29	9.444		1.340		
5	29	4.60		1.09		
29	29	6.115		1.470		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

I

NO4 ENERGY = 30.8400

-.4100	-.1604	.4248	1	1.0896	-.0237	.3740	2
1.7751	1.1334	.2958	2	3.2917	1.1430	.2478	1
3.9248	2.0317	1.3336	1	5.3485	1.6056	1.6722	3
5.5775	.6368	2.8294	1	4.4035	-.2899	3.0198	2
4.3056	-1.4907	2.4195	29	3.0782	-2.3157	2.3768	29
1.8653	-1.9180	2.8080	2	.6153	-2.7351	2.6058	1
-.7071	-1.9629	2.3602	1	-.9430	-1.5306	.8910	1
.3576	-3.6398	3.8228	1	-1.0765	-4.1332	3.6086	1
-1.7117	-3.0594	2.7456	3	-.9676	-.8062	3.3435	1
1.1164	2.4907	.2220	1	6.2822	2.0232	1.0241	7
-2.8703	-3.0972	2.4007	7	-.7660	.0089	-.6196	5
-.8579	.6470	1.0470	5	1.6505	-.9705	.3602	5
3.6142	1.4977	-.7591	5	3.6819	.1045	.3391	5
3.3207	2.0103	2.2688	5	3.9316	3.0963	1.0003	5
5.7510	1.2212	3.7624	5	6.5033	.0501	2.6257	5
3.5612	.1211	3.5977	5	5.1614	-1.8477	1.8436	5
3.1509	-3.2780	1.8669	5	1.7419	-.9541	3.3195	5
.7782	-3.4164	1.7358	5	-2.0451	-1.4783	.7248	5
-.5791	-2.3267	.1999	5	.4187	-3.0440	4.7642	5
1.0916	-4.4772	3.9018	5	-1.6314	-4.2655	4.5668	5
-1.0872	-5.0894	3.0346	5	-1.9899	-.3868	3.1996	5
-.2517	.0343	3.2088	5	-.8940	-1.1284	4.4066	5
.0190	2.4474	.0499	5	1.5444	3.0749	-.6237	5
1.2861	3.0592	1.1637	5	.0000	.0000	.0000	0

II

NO10 ENERGY = 31.6504

.1913	-.7500	-.0853	1	1.5351	-.1345	.2082	2
1.9000	1.1484	.0221	2	3.3247	1.5898	.3063	1
4.0718	2.0183	-.9709	1	5.5173	1.5374	-.9909	3
5.8465	.3058	-1.8277	1	4.8102	-.7717	-1.6218	2
3.8747	-1.0743	-2.5431	29	2.7056	-1.9487	-2.3063	29
2.5568	-2.7792	-1.2576	2	1.2769	-3.5215	-.9613	1
.7220	-3.3156	.4692	1	-.1531	-2.0518	.6677	1
1.4477	-5.0400	-1.1343	1	.2197	-5.6232	-.4261	1
-.1482	-4.5727	.6050	3	1.7730	-3.4615	1.5910	1
.9804	2.2299	-.4928	1	6.3702	2.1086	-.3492	7
-1.0375	-4.7140	1.4124	7	.1410	-.9320	-1.1832	5

-.6062	-.0080	.1505	5	2.3088	-.8254	.5644	5
3.8888	.7674	.8036	5	3.3066	2.4251	1.0450	5
4.0536	3.1287	-1.0765	5	3.5687	1.6183	-1.8804	5
6.8506	-.0928	-1.5529	5	5.8942	.6280	-2.8934	5
4.7887	-1.2273	-.6189	5	3.9005	-.5380	-3.4934	5
1.8820	-1.8644	-3.0175	5	3.3814	-2.9229	-.5439	5
.4822	-3.2100	-1.6811	5	-.2321	-1.8239	1.7567	5
-1.1895	-2.3080	.3410	5	2.3775	-5.3873	-.6248	5
1.5131	-5.3461	-2.2057	5	.4287	-6.6083	.0528	5
-.6360	-5.7254	-1.1340	5	1.2901	-3.5035	2.5943	5
2.4911	-2.6155	1.6278	5	2.3746	-4.3927	1.4886	5
-.0366	1.8709	-.7604	5	1.3994	2.6973	-1.4116	5
.8650	3.0247	.2782	5	.0000	.0000	.0000	0

### III

N05 ENERGY = 32.4429

.0717	-.1518	-.3019	1	1.5399	-.0517	.0410	2
2.1667	1.0599	.4767	2	3.6213	1.0308	.9180	1
4.5437	2.1426	.3821	1	5.2026	1.8472	-.9576	3
4.7971	2.6592	-2.1803	1	3.4971	2.0914	-2.6793	2
3.4249	1.1874	-3.6743	29	2.2234	.3844	-3.9891	29
1.0358	.5186	-3.3688	2	-.1028	-.4714	-3.4359	1
.0659	-1.6787	-2.4801	1	-.3964	-1.4290	-1.0254	1
-.3940	-1.0699	-4.8228	1	-1.3254	-2.2461	-4.5065	1
-.8769	-2.6987	-3.1298	3	1.4674	-2.3169	-2.5270	1
1.4477	2.3739	.6900	1	6.0400	.9770	-1.0504	7
-1.2473	-3.7251	-2.6087	7	-.2708	.7421	-.8678	5
-.4606	-.1161	.6787	5	2.1123	-.9913	-.0010	5
4.0855	.0394	.7069	5	3.5867	1.1153	2.0300	5
5.3936	2.2625	1.0956	5	4.0399	3.1348	.3649	5
5.5938	2.5800	-2.9561	5	4.6899	3.7383	-1.9238	5
2.6148	2.3566	-2.0802	5	4.3469	.9219	-4.1950	5
2.3726	-.4470	-4.6774	5	.8832	1.3478	-2.6638	5
-1.0342	.0750	-3.1477	5	-.1463	-2.3148	-.3949	5
-1.5121	-1.3793	-1.0428	5	.5286	-1.4711	-5.3012	5
-.8519	-.3324	-5.5244	5	-1.2503	-3.0695	-5.2550	5
-2.3849	-1.9061	-4.4304	5	1.5226	-3.2275	-1.8877	5
2.2571	-1.6215	-2.1697	5	1.7484	-2.6322	-3.5573	5
.3422	2.3038	.6011	5	1.7836	3.1390	-.0439	5
1.6517	2.7579	1.7150	5	.0000	.0000	.0000	0

IV

NO1 ENERGY = 35.9935

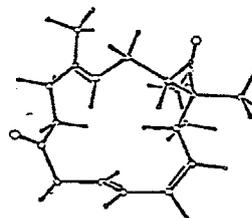
- .3811	- .1097	.4721	1	1.0852	.0516	.1455	2
1.8096	1.1821	.2731	2	3.2582	1.2506	- .1870	1
4.2533	2.0212	.7059	1	5.2171	1.1508	1.5023	3
4.9903	.9803	2.9984	1	3.8120	.0667	3.1888	2
3.8807	-1.1628	3.7337	29	2.7177	-2.0745	3.7344	29
1.8537	-2.0561	2.7032	2	.6199	-2.8943	2.5108	1
- .6588	-2.0421	2.3043	1	- .8722	-1.5221	.8584	1
.2914	-3.8806	3.6430	1	-1.1460	-4.3038	3.3254	1
-1.7360	-3.0801	2.6510	3	- .7947	- .9228	3.3546	1
1.2145	2.4839	.7596	1	6.1512	.6079	.9550	7
-2.9174	-2.9618	2.4209	7	- .8983	.1754	- .4754	5
- .7224	.6251	1.2329	5	1.5690	- .8328	- .3010	5
3.2113	1.7619	-1.1776	5	3.6609	.2322	- .3952	5
3.7512	2.7458	1.3840	5	4.9043	2.6480	.0510	5
4.7952	1.9700	3.4717	5	5.9080	.5577	3.4694	5
2.8561	.4520	2.7982	5	4.8141	-1.5074	4.1819	5
2.6210	-2.8082	4.5348	5	2.0575	-1.3765	1.8680	5
.7941	-3.5076	1.5936	5	-1.9753	-1.4796	.6975	5
- .5055	-2.2695	.1169	5	.3089	-3.3691	4.6340	5
.9935	-4.7473	3.6830	5	-1.7215	-4.5897	4.2369	5
-1.1625	-5.1447	2.5930	5	-1.7577	- .3754	3.2349	5
.0315	- .1804	3.2792	5	- .7740	-1.3157	4.3961	5
.1071	2.5288	.6778	5	1.5910	3.3353	.1486	5
1.4835	2.6590	1.8256	5	.0000	.0000	.0000	0

Conformational analysis of the 14-membered Z,E,E-triene 121

The starting geometries which were constructed to be a s-cis form of Z,E-diene, were generated using MMRS at 45° dihedral angle resolution and with a closure distance range of 1.0-3.0 Å, and with a transannular contact of 2.4 Å. Structures of 25 conformations obtained were optimized by MM2 to get 11 conformations within 2.0 kcal/mol from the lowest energy conformation.

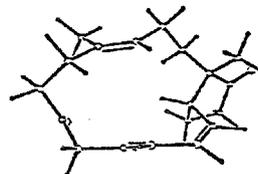
I NO= 2 ENERGY= 30.1936

ST= 1.66 BD= 8.71 SB= .31 14= 10.62  
OT= -3.90 T= 11.54 DP= 1.25 DM= 4.36D



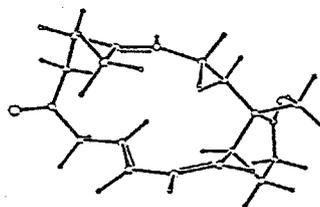
II NO= 20 ENERGY= 30.2730

ST= 1.58 BD= 7.24 SB= .26 14= 11.06  
OT= -4.58 T= 13.62 DP= 1.10 DM= 4.37D



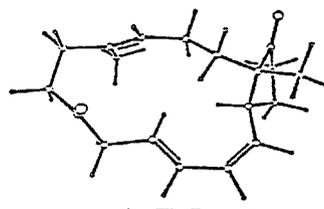
III NO= 6 ENERGY= 30.8681

ST= 1.64 BD= 8.59 SB= .15 14= 11.23  
OT= -5.30 T= 13.52 DP= 1.05 DM= 1.93D



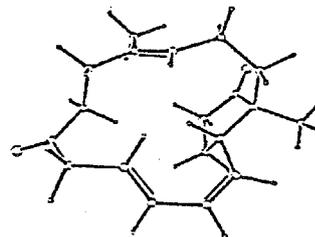
IV NO= 17 ENERGY= 31.3679

ST= 1.67 BD= 10.43 SB= .13 14= 11.44  
OT= -4.85 T= 11.08 DP= 1.47 DM= 5.16D



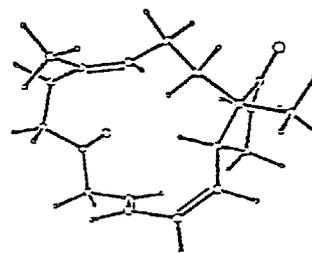
V NO= 22 ENERGY= 31.9488

ST= 1.71 BD= 8.95 SB= .31 14= 11.10  
OT= -5.13 T= 13.87 DP= 1.14 DM= 2.48D



VI NO= 14 ENERGY= 32.1007

ST= 1.53 BD= 8.34 SB= .27 14= 11.18  
OT= -5.01 T= 14.75 DP= 1.05 DM= 5.13D



ENERGY: FINAL STERIC ENERGY, ST: COMPRESSION, BD: BENDING, SB: STRETCH-BEND,  
14: VAN DER WAALS\_1,4 ENERGY, OT: VAN DER WAALS\_OTHER, T: TORSIONAL, DP: DIPOLE,  
DM: DIPOLE MOMENT [ KCAL/MOL ]

0 Z,E s-cis DIENE 14MEMBERED RING

21 14 2 22 22 1 1.50 1.34 120.0 1 1 45 1.0 3.0 100 1.2  
 2 14 0 0  
 1 3 3 0  
 2 2 4 19  
 1 2 3 4 2 1 1.50 120.0 180.0 3 5 0 0 0  
 2 3 4 5 2 0 1.54 109.5 0.0 4 6 0 0 0  
 3 4 5 6 32 0 1.50 109.5 0.0 5 7 20 20 0  
 4 5 6 7 2 0 1.50 120.0 0.0 6 8 0 0 0  
 5 6 7 8 22 0 1.50 109.5 0.0 7 9 9 0 0  
 6 7 8 9 2922 0 1.34 120.0 0.0 8 8 10 0 0  
 7 8 9 10 2922 1 1.50 120.0 180.0 9 11 11 0 0  
 8 9 10 11 22 1 1.34 120.0 0.0 10 10 12 0 0  
 9 10 11 12 2 1 1.50 120.0 0.0 11 13 15 0 0  
 10 11 12 13 2 0 1.54 109.5 0.0 12 14 17 18 0  
 11 12 13 14 2 1 1.54 109.5 240.0 13 1 0 0 0  
 10 11 12 15 2 2 1.54 109.5 120.0 12 16 0 0 13  
 13 12 15 16 2 1 1.54 108.0 0.0 15 17 0 0 0  
 15 12 13 17 32 1 1.50 108.0 0.0 13 16 21 21 0  
 11 12 13 18 2 1 1.54 109.5 0.0 13 0 0 0 0  
 1 2 3 19 2 1 1.50 120.0 0.0 3 0 0 0 0  
 4 5 6 20 14 2 1.40 120.0 180.0 6 6 0 0 7  
 12 13 17 21 14 1 1.40 120.0 180.0 17 17 0 0 0

47.4 0 0 1 500.

6 26 1  
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 1  
 12 15 16 17 13  
 13 18  
 3 19  
 6 20  
 17 21  
 1 22 1 23 2 24 4 25 4 26 5 27 5 28 7 29  
 7 30 8 31 9 32 10 33 11 34 12 35 14 36 14 37  
 15 38 15 39 16 40 16 41 18 42 18 43 18 44 19 45  
 19 46 19 47  
 10 3 1 8  
 1 1 2 29 -0.44 0.24 0.06  
 1 2 29 29 0.0 9.415 0.0  
 5 2 29 29 0.0 9.415 0.0  
 5 1 2 29 0.0 0.0 -0.24

2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	29	9.444		1.340		
5	29	4.60		1.09		
29	29	6.115		1.470		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

I

- .5824	1.3735	1.6467	1	.6492	1.1302	.8125	2
1.2612	1.9983	-.0140	2	2.5022	1.6470	-.8181	1
2.7506	.1573	-1.1054	1	3.2597	-.6754	.0623	3
3.1511	-2.1902	-.0552	1	1.7095	-2.6253	-.1534	2
1.0142	-3.1637	.8652	29	-.4009	-3.5752	.7500	29
-1.4101	-2.8456	.2315	2	-1.3397	-1.4163	-.2594	1
-2.2113	-.3938	.5153	1	-1.5235	.1592	1.7867	1
-1.7428	-1.2678	-1.7352	1	-1.9330	.2457	-1.8937	1
-2.4537	.6799	-.5409	3	-3.5931	-.9713	.8908	1
.8044	3.4263	-.2155	1	3.7365	-.1625	1.0501	7
-3.0264	1.7319	-.3454	7	-1.1691	2.2445	1.2839	5
-.2153	1.6491	2.6640	5	1.0875	.1335	.9511	5
3.3918	2.1100	-.3311	5	2.3912	2.1432	-1.8115	5
3.5347	.0647	-1.8937	5	1.8186	-.2830	-1.5274	5
3.6384	-2.6576	.8317	5	3.7126	-2.5316	-.9553	5
1.2157	-2.4806	-1.1285	5	1.5354	-3.3883	1.7972	5
-.6535	-4.5486	1.1767	5	-2.4083	-3.3134	.2038	5
-.2937	-1.0571	-.1936	5	-.9881	-.6784	2.2931	5
-2.3185	.4756	2.5031	5	-2.7091	-1.7916	-1.9276	5
-.9782	-1.6797	-2.4362	5	-2.6373	.5052	-2.7182	5
-.9551	.7559	-2.0611	5	-4.2719	-.1822	1.2887	5
-3.5071	-1.7490	1.6834	5	-4.1105	-1.4255	.0153	5
.0358	3.7726	.5076	5	.3871	3.5513	-1.2404	5
1.6673	4.1208	-.1006	5	.0000	.0000	.0000	0

II

-.6231	-2.4360	-.2024	1	.6323	-1.7826	-.7290	2
1.8491	-1.7547	-.1518	2	3.0327	-1.1528	-.8912	1
3.9641	-.2572	-.0608	1	3.3059	1.0192	.4354	3
3.0322	2.1258	-.5733	1	1.5516	2.2714	-.8075	2
.9625	2.1594	-2.0126	29	-.4908	2.3277	-2.2268	29
-1.4727	1.8214	-1.4535	2	-1.2864	.9101	-.2576	1
-2.2103	-.3337	-.2685	1	-1.5982	-1.5051	.5409	1
-1.6347	1.6706	1.0356	1	-3.1475	1.4941	1.1927	1
-3.4310	.1776	.4993	3	-2.6669	-.7986	-1.6623	1
2.1583	-2.3851	1.1862	1	3.0489	1.1760	1.6083	7
-4.5071	-.3734	.5260	7	-.3606	-3.2849	.4681	5
-1.1352	-2.9373	-1.0560	5	.5210	-1.3036	-1.7159	5

2.6963	-.5841	-1.7894	5	3.6295	-2.0135	-1.2751	5
4.8457	.0396	-.6766	5	4.3885	-.8203	.8025	5
3.5769	1.9210	-1.5232	5	3.4290	3.0854	-.1683	5
.9476	2.5114	.0825	5	1.5932	2.0268	-2.8932	5
-.7823	2.8751	-3.1241	5	-2.5146	2.0627	-1.7233	5
-.2310	.5657	-.2244	5	-2.4365	-2.1493	.8996	5
-1.0993	-1.1220	1.4614	5	-1.3268	2.7427	1.0143	5
-1.1183	1.1945	1.9032	5	-3.7022	2.2973	.6535	5
-3.4691	1.4718	2.2603	5	-3.2404	-1.7519	-1.6036	5
-1.8002	-.9582	-2.3419	5	-3.3384	-.0618	-2.1579	5
1.2917	-2.8758	1.6772	5	2.5079	-1.6139	1.9075	5
2.9548	-3.1545	1.0715	5	.0000	.0000	.0000	0

III

-.2275	-1.7367	-.4703	1	1.1206	-1.8107	.2019	2
2.3104	-1.5069	-.3489	2	3.5483	-1.4767	.5234	1
3.5609	-.2054	1.3914	1	3.6370	1.0840	.5870	3
2.5131	2.1038	.7232	1	1.2889	1.6661	-.0450	2
.9784	2.1337	-1.2693	29	-.1101	1.6686	-2.1613	29
-1.3375	1.1805	-1.8806	2	-2.0074	1.0200	-.5357	1
-2.4421	-.4173	-.1442	1	-1.3130	-1.2443	.5071	1
-3.3021	1.8540	-.4699	1	-4.0284	1.3127	.7668	1
-3.5250	-.1121	.8943	3	-3.1258	-1.2080	-1.2743	1
2.5173	-1.1090	-1.7916	1	4.5750	1.2924	-.1500	7
-3.9169	-.8852	1.7374	7	-.4943	-2.7441	-.8674	5
-.1761	-1.0415	-1.3328	5	1.1031	-2.1018	1.2655	5
4.4726	-1.5438	-.0965	5	3.5530	-2.3746	1.1860	5
4.4496	-.2254	2.0653	5	2.6633	-.1811	2.0522	5
2.8772	3.0875	.3457	5	2.2596	2.2513	1.7982	5
.6985	.8620	.4133	5	1.6771	2.8485	-1.7080	5
.1109	1.7829	-3.2255	5	-1.9736	.9139	-2.7420	5
-1.3555	1.4329	.2661	5	-1.7310	-2.1342	1.0347	5
-.8575	-.6126	1.3049	5	-3.9293	1.6760	-1.3754	5
-3.1051	2.9510	-.4055	5	-5.1382	1.3447	.6617	5
-3.7228	1.8701	1.6832	5	-3.4924	-2.1925	-.9032	5
-2.4324	-1.4182	-2.1185	5	-4.0038	-.6682	-1.6953	5
1.6174	-1.2289	-2.4321	5	3.3044	-1.7507	-2.2477	5
2.8503	-.0507	-1.8685	5	.0000	.0000	.0000	0

IV

-.2677	1.4420	.3244	1	1.2069	1.5071	.6330	2
2.2075	1.6283	-.2584	2	3.6494	1.5334	.1979	1
4.2458	.1789	-.2189	1	3.4065	-.9918	.2773	3
2.7929	-1.9527	-.7320	1	1.2864	-2.0090	-.6104	2
.6196	-3.1200	-.2422	29	-.8361	-3.3654	-.0872	29
-1.9363	-2.5923	-.2236	2	-2.0786	-1.1300	-.5848	1
-2.2822	-.1772	.6240	1	-.9537	.3654	1.1882	1
-3.3029	-.8750	-1.4876	1	-3.5260	.6382	-1.3888	1
-3.1306	.9491	.0405	3	-3.0994	-.8300	1.7564	1
2.0059	1.7802	-1.7480	1	3.2190	-1.1557	1.4625	7
-3.4408	1.9603	.6259	7	-.4335	1.2195	-.7507	5
-.7153	2.4426	.5283	5	1.4646	1.4041	1.7003	5
3.7270	1.6398	1.3055	5	4.2379	2.3756	-.2356	5
5.2724	.0699	.2038	5	4.3585	.1351	-1.3264	5
3.2589	-2.9512	-.5660	5	3.0447	-1.6521	-1.7744	5
.7627	-1.0757	-.8508	5	1.2454	-3.9890	-.0294	5
-1.0580	-4.3960	.2037	5	-2.9002	-3.0905	-.0192	5
-1.2025	-.8083	-1.1851	5	-.2781	-.5108	1.3246	5
-1.1097	.7922	2.2072	5	-4.2045	-1.3969	-1.0870	5
-3.1454	-1.2188	-2.5379	5	-4.5800	.9338	-1.6017	5
-2.8362	1.1900	-2.0696	5	-3.3462	-.0966	2.5580	5
-2.5326	-1.6584	2.2391	5	-4.0657	-1.2428	1.3867	5
.9919	2.1391	-2.0279	5	2.1864	.8130	-2.2680	5
2.7154	2.5341	-2.1572	5	.0000	.0000	.0000	0

V

-1.5531	1.6279	1.5406	1	-.0650	1.4377	1.4154	2
.7766	1.9648	.5066	2	2.2441	1.5766	.5239	1
2.5607	.6162	-.6350	1	3.7030	-.3478	-.3518	3
3.5487	-1.3862	.7537	1	2.1214	-1.8164	.9949	2
1.5997	-2.9890	.5916	29	.2167	-3.4198	.8912	29
-.9269	-2.7273	.7039	2	-1.0746	-1.3827	.0241	1
-2.3702	-.5679	.2808	1	-2.3414	.3009	1.5610	1
-1.0019	-1.5453	-1.5058	1	-1.5079	-.2053	-2.0494	1
-2.4722	.2799	-.9859	3	-3.6398	-1.4482	.3004	1
.3822	2.9101	-.6026	1	4.7082	-.3207	-1.0270	7
-3.2217	1.2163	-1.1382	7	-1.9681	2.3072	.7668	5
-1.7186	2.1546	2.5106	5	.3555	.7642	2.1799	5

2.5031	1.0990	1.4959	5	2.8818	2.4893	.4648	5
2.7806	1.2002	-1.5597	5	1.6750	-.0123	-.8803	5
3.9695	-.9676	1.6968	5	4.1713	-2.2716	.4874	5
1.4940	-1.1232	1.5742	5	2.2617	-3.7138	.1148	5
.1159	-4.4487	1.2449	5	-1.8605	-3.2560	.9505	5
-.2147	-.7433	.3031	5	-1.9851	-.3350	2.4055	5
-3.3933	.5765	1.8128	5	-1.6843	-2.3642	-1.8355	5
.0249	-1.7916	-1.8682	5	-2.0064	-.3053	-3.0418	5
-.6747	.5306	-2.1246	5	-4.5657	-.8307	.2443	5
-3.7171	-2.0381	1.2415	5	-3.6766	-2.1573	-.5575	5
-.6968	3.1703	-.6266	5	.6318	2.4744	-1.5953	5
.9440	3.8654	-.4970	5	.0000	.0000	.0000	0

VI

-.7651	-2.2107	.1213	1	.5862	-1.6861	.5402	2
1.7537	-1.9602	-.0712	2	3.0840	-1.5229	.5119	1
3.6108	-.2161	-.0972	1	3.0160	1.0423	.5129	3
3.0018	2.2965	-.3455	1	1.5932	2.4685	-.8458	2
1.1908	2.1504	-2.0884	29	-.2117	2.2935	-2.5257	29
-1.3046	1.8967	-1.8426	2	-1.3484	1.1383	-.5299	1
-2.2671	-.1132	-.5066	1	-1.5403	-1.4080	-.9385	1
-1.8579	2.0222	.6234	1	-2.1981	1.0163	1.7277	1
-2.7345	-.1651	.9469	3	-3.5465	.0592	-1.3558	1
1.8619	-2.7617	-1.3488	1	2.5516	1.0638	1.6307	7
-3.4608	-1.0113	1.4143	7	-1.3791	-2.3789	1.0346	5
-.6119	-3.2458	-.2639	5	.6019	-1.0777	1.4598	5
3.8192	-2.3431	.3358	5	3.0163	-1.4342	1.6211	5
3.4533	-.2173	-1.2004	5	4.7095	-.1416	.0802	5
3.7317	2.1996	-1.1818	5	3.3033	3.1825	.2601	5
.8645	2.8436	-.1102	5	1.9356	1.8508	-2.8276	5
-.3642	2.7294	-3.5158	5	-2.2784	2.1318	-2.3012	5
-.3260	.7893	-.2588	5	-.8843	-1.1883	-1.8130	5
-2.3191	-2.1085	-1.3231	5	-2.7849	2.5601	.3119	5
-1.1186	2.7850	.9617	5	-2.9467	1.4113	2.4537	5
-1.2805	.6904	2.2715	5	-4.2703	-.7708	-1.1855	5
-3.3176	.0556	-2.4459	5	-4.0860	1.0030	-1.1124	5
.8892	-2.9431	-1.8549	5	2.3276	-3.7516	-1.1412	5
2.4976	-2.2260	-2.0889	5	.0000	.0000	.0000	0

MM2 transition structure models of transannular Diels-Alder reaction on 120

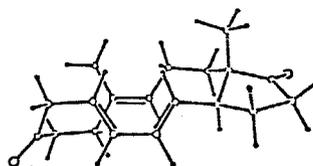
MM2 transition structure models of Diels-Alder reaction on 120 were obtained as follows. Houk's synchronous STO-3G transition structure of the butadiene-ethylene reaction was used as the partial structure of the reactive diene and dienophile in the macrocycle. Connecting saturated carbon chains were substituted for appropriate hydrogens, the macroring was constructed by using the MMRS program, and the resulting conformations were optimized by MM2 to get 4 possible transition structure models of A, B, C, and D.

A

FINAL STERIC ENERGY IS 72.9373 KCAL.

COMPRESSION	2.5598
BENDING	9.0714
STRETCH-BEND	.0461
VANDERWAALS	
1,4 ENERGY	12.2415
OTHER	24.1377
TORSIONAL	23.6747
DIPOLE	1.2062

DIPOLE MOMENT 1.788 D



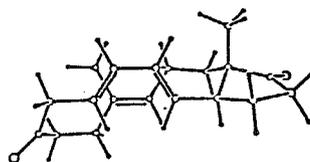
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END OF TRANSITION STRUCTURE MODEL A

B

FINAL STERIC ENERGY IS 76.2609 KCAL.

COMPRESSION	2.6498
BENDING	11.1768
STRETCH-BEND	.0698
VANDERWAALS	
1,4 ENERGY	12.7130
OTHER	24.6082
TORSIONAL	23.8286
DIPOLE	1.2148

DIPOLE MOMENT 2.043 D

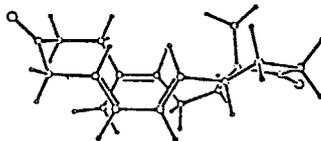


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END OF TRANSITION STRUCTURE MODEL B

C

FINAL STERIC ENERGY IS 79.4030 KCAL.

COMPRESSION	2.7885
BENDING	11.4341
STRETCH-BEND	.1616
VANDERWAALS	
1,4 ENERGY	13.8216
OTHER	25.4787
TORSIONAL	24.5349
DIPOLE	1.1836



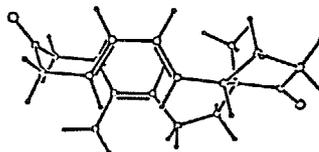
DIPOLE MOMENT 1.438 D

-----  
END OF TRANSITION STRUCTURE MODEL C

D

FINAL STERIC ENERGY IS 80.3702 KCAL.

COMPRESSION	2.8190
BENDING	12.2276
STRETCH-BEND	.1655
VANDERWAALS	
1,4 ENERGY	13.6899
OTHER	25.8222
TORSIONAL	24.4593
DIPOLE	1.1868



DIPOLE MOMENT 1.490 D

-----  
END OF TRANSITION STRUCTURE MODEL D

A

0 D-A TRANSITION STRUCTURE OF DIELS-ALDER A

21 50, 22, 22, 22, 2, 1.359, 1.421, 121.2, 0, 1, 45, 1.0, 2.3, 3,,

2, 2, 13, 0,

1, 1 3, 0,

2, 4, 4, 0,

1	2	3	4	22	9	1.359	121.2	0.0	3	3	7	0	0
2	3	4	5	22	9	2.217	101.4	59.67	6	6	10	18	0
3	2	1	6	22	9	2.217	101.4	-59.67	5	5	11	0	0
2	3	4	7	2	9	1.50	121.1	180.0	4	8	0	0	0
3	4	7	8	32	9	1.50	109.0	-60.0	7	9	19	19	0
4	7	8	9	2	9	1.65	109.0	-60.0	10	8	0	0	0
1	6	5	10	2	9	1.65	109.5	-110.0	5	9	0	0	0
2	1	6	11	2	9	1.50	91.8	180.0	6	12	0	0	0
1	6	11	12	2	9	1.54	109.5	80.0	11	17	0	0	0
3	2	1	13	2	9	1.50	121.1	-170.0	1	14	17	0	0
2	1	13	14	2	9	1.54	109.5	-90.0	13	15	0	0	0
1	13	14	15	2	9	1.54	98.0	-130.0	14	16	0	0	0
13	14	15	16	32	9	1.50	98.0	0.0	15	17	20	20	0
2	1	13	17	2	9	1.54	109.5	150.0	12	13	16	21	0
11	6	5	18	2	9	1.50	120.2	0.0	5	0	0	0	0
4	7	8	19	14	9	1.40	120.0	120.0	8	8	0	0	0
14	15	16	20	14	9	1.40	120.0	-130.0	16	16	0	0	0
1	13	17	21	2	9	1.50	109.5	60.0	17	0	0	0	0

TRANSITION STRUCTURE MODEL A

47 4 1 0 1 500.

5						26													
4	3	2	1	13	17	12	11	6	5	18									
5	10	9	8	7	4														
8	19																		
13	14	15	16	17	21														
16	20																		
1	22	2	23	3	24	4	25	6	26	7	27	7	28	9	29				
9	30	10	31	10	32	11	33	11	34	12	35	12	36	13	37				
14	38	14	39	15	40	15	41	18	42	18	43	18	44	21	45				
21	46	21	47																
.00000	.00000	.00000	2				1.35900	.00000	.00000	.00000	29	2							
2.09512	1.21547	.00000	29				1.46550	2.41982	.00000	.00000	2	4							
.28991	2.29972	1.87581	2				-.43821	1.09745	1.87581	1.87581	2	6							
2.31657	3.66503	.02501	1				3.19096	3.67377	1.26471	1.26471	3	8							
2.49557	3.53676	2.60757	1				1.55696	2.32429	2.73293	2.73293	1	10							
-1.95693	1.05458	1.77082	1				-2.58466	-.35082	1.69534	1.69534	1	12							
-.76767	-1.28000	.20548	1				-.62910	-2.36445	-.87190	-.87190	1	14							
-1.77201	-3.33918	-.52772	1				-2.71249	-2.54083	.36318	.36318	3	16							
-2.28363	-1.07730	.37515	1				-.49774	3.59711	1.76585	1.76585	1	18							
4.39137	3.80909	1.18307	7				-3.62876	-3.00900	.99696	.99696	7	20							
-3.01051	-.42011	-.81643	1				-.56251	.83441	-.44254	-.44254	5	22							
1.89080	-.91936	.25291	5				3.16995	1.16283	.18541	.18541	5	24							
.45442	2.55042	-.41982	5				.04237	.24274	2.38584	2.38584	5	26							
1.69749	4.59006	.02545	5				2.94190	3.70198	-.89750	-.89750	5	28							

3.28764	3.45135	3.38950	5	1.96104	4.48925	2.82575	5	30
2.14709	1.38590	2.61317	5	1.19284	2.31142	3.78794	5	32
-2.33430	1.68255	.93430	5	-2.33722	1.52676	2.70766	5	34
-3.69132	-.26518	1.81159	5	-2.22671	-.95967	2.55920	5	36
-.37103	-1.73845	1.14505	5	.37155	-2.85869	-.86158	5	38
-.77576	-1.92005	-1.88412	5	-1.39224	-4.21007	.05628	5	40
-2.30427	-3.70433	-1.43687	5	-1.27248	3.57440	.96849	5	42
.13386	4.48040	1.54003	5	-.99920	3.80948	2.73714	5	44
-2.86703	-.97421	-1.77086	5	-2.68731	.62572	-1.00739	5	46
-4.10871	-.38665	-.63231	5					

LAST

6

1111 2111 3111 4111 5111 6111

14	5	1	8			
2	2	3	1	0.15	2.091	0.0
2	2	3	7	0.91	2.091	0.0
5	2	3	1	0.0	2.091	0.0
5	2	3	7	0.0	2.091	0.0
1	1	2	29	-0.44	0.24	0.06
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	1	2	29	0.0	0.0	0.10
5	29	29	5	0.0	2.23	0.0
2	3	6.370		1.4767		
2	2	9.444		1.366		
2	29	9.444		1.359		
5	29	4.60		1.09		
29	29	6.115		1.421		
	29	0.044		1.940		
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
	29	29		0.050		
5	29	2		0.36	120.0	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		

B

0 D-A TRANSITION STRUCTURE OF DIELS-ALDER B

21 50, 22, 22, 22, 2, 1.359, 1.421, 121.2, 0, 1, 45, 1.0, 2.3, 3.,,

2, 2, 13, 0,

1, 1 3, 0,

2, 4, 4, 0,

1	2	3	4	22	9	1.359	121.2	0.0	3	3	7	0	0
2	3	4	5	22	9	2.217	101.4	-59.67	6	6	10	18	0
3	2	1	6	22	9	2.217	101.4	59.67	5	5	11	0	0
2	3	4	7	2	9	1.50	121.1	180.0	4	8	0	0	0
3	4	7	8	32	9	1.50	109.0	135.0	7	9	19	19	0
4	7	8	9	2	9	1.65	109.0	-60.0	10	8	0	0	0
1	6	5	10	2	9	1.65	109.5	-80.0	5	9	0	0	0
2	1	6	11	2	9	1.50	91.8	60.0	6	12	0	0	0
1	6	11	12	2	9	1.54	109.5	80.0	11	17	0	0	0
3	2	1	13	2	9	1.50	121.1	180.0	1	14	17	0	0
2	1	13	14	2	9	1.54	109.5	80.0	13	15	0	0	0
1	13	14	15	2	9	1.54	98.0	-130.0	14	16	0	0	0
13	14	15	16	32	9	1.50	98.0	0.0	15	17	20	20	0
2	1	13	17	2	9	1.54	109.5	-50.0	12	13	16	21	0
11	6	5	18	2	9	1.50	120.2	0.0	5	0	0	0	0
4	7	8	19	14	9	1.40	120.0	120.0	8	8	0	0	0
14	15	16	20	14	9	1.40	120.0	-130.0	16	16	0	0	0
1	13	17	21	2	9	1.50	109.5	60.0	17	0	0	0	0

.00000	.00000	.00000	2	1.35900	.00000	.00000	29	2
2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4
.28991	2.29972	-1.87581	2	-.43821	1.09745	-1.87581	2	6
2.23033	3.71826	.03518	1	1.27574	4.88432	-.16574	3	8
.35413	4.86898	-1.37430	1	-.47459	3.58585	-1.56545	1	10
-.12722	-.07119	-2.80167	1	-.98739	-1.33979	-2.61440	1	12
-.83881	-1.24834	-.10029	1	-.83173	-2.21131	1.09341	1	14
-1.59687	-3.43148	.54202	1	-1.61186	-3.23264	-.96854	3	16
-.62702	-2.12738	-1.34519	1	1.45453	2.40333	-2.84984	1	18
1.26670	5.81403	.61045	7	-2.32726	-3.82773	-1.73956	7	20
.72060	-2.85954	-1.50921	1	-.55114	.84774	.43925	5	22
1.91230	-.92111	-.16821	5	3.16925	1.17806	-.19191	5	24
.47406	2.49519	.46962	5	-1.48807	1.17575	-1.53762	5	26
3.05106	3.75435	-.71575	5	2.70060	3.81447	1.04172	5	28
-.35293	5.72635	-1.26905	5	.96249	5.09776	-2.27883	5	30
-1.16742	3.44999	-.70159	5	-1.13299	3.75660	-2.45035	5	32
.95259	-.33227	-2.78365	5	-.33600	.30512	-3.83123	5	34
-.85065	-2.01136	-3.49521	5	-2.06630	-1.05590	-2.60548	5	36
-1.89094	-.87208	-.16979	5	-1.31786	-1.77235	1.99714	5	38
.21409	-2.48369	1.36780	5	-2.65042	-3.44431	.90748	5	40
-1.10922	-4.39460	.80455	5	2.10101	1.49894	-2.85897	5	42
2.13979	3.24929	-2.63987	5	1.06196	2.56503	-3.87925	5	44
1.06658	-3.35564	-.57518	5	1.54326	-2.20218	-1.86051	5	46
.63530	-3.65846	-2.28129	5					

LAST

C  
 0 D-A TRANSITION STRUCTURE OF DIELS-ALDER C  
 21 50, 22, 22, 22, 2, 1.359, 1.421, 121.2, 0, 1, 45, 1.0, 2.3, 3.,

2,	2,	13,	0,
1,	1	3,	0,
2,	4,	4,	0,
1 2 3 4 22 9	1.359	121.2	0.0
2 3 4 5 22 9	2.217	101.4	59.67
3 2 1 6 22 9	2.217	101.4	-59.67
2 3 4 7 2 9	1.50	121.1	180.0
3 4 7 8 32 9	1.50	109.0	-135.0
4 7 8 9 2 9	1.65	109.0	60.0
1 6 5 10 2 9	1.65	109.5	80.0
2 1 6 11 2 9	1.50	91.8	-60.0
1 6 11 12 2 9	1.54	109.5	-80.0
3 2 1 13 2 9	1.50	121.1	180.0
2 1 13 14 2 9	1.54	109.5	-120.0
1 13 14 15 2 9	1.54	98.0	-130.0
13 14 15 16 32 9	1.50	98.0	0.0
2 1 13 17 2 9	1.54	109.5	120.0
11 6 5 18 2 9	1.50	120.2	0.0
4 7 8 19 14 9	1.40	120.0	-120.0
14 15 16 20 44 9	1.40	120.0	-130.0
1 13 17 21 2 9	1.50	109.5	60.0

.00000	.00000	.00000	2	1.35900	.00000	.00000	29	2
2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4
.28991	2.29972	1.87581	2	-.43821	1.09745	1.87581	2	6
2.23100	3.71770	-.05334	1	1.29157	4.88782	.18744	3	8
.41475	4.86653	1.42809	1	-.45006	3.60534	1.59746	1	10
-.20521	-.14967	2.69946	1	-1.38688	-1.14274	2.56226	1	12
-.68298	-1.34552	.14044	1	-1.18483	-2.01641	-1.14450	1	14
-2.00207	-3.20515	-.59919	1	-2.29585	-2.84636	.85266	3	16
-1.86970	-1.40081	1.11653	1	1.46859	2.34618	2.83613	1	18
1.25970	5.82304	-.58142	7	-2.76134	-3.60473	1.67043	7	20
-3.11209	-.57998	.69761	1	-.61412	.81114	-.42402	5	22
1.92119	-.91148	.21284	5	3.17069	1.17954	.18429	5	24
.46606	2.48445	-.45636	5	-1.47747	1.26655	1.56706	5	26
2.66653	3.81780	-1.07499	5	3.07785	3.74906	.66833	5	28
1.06263	5.03632	2.31821	5	-.26368	5.75150	1.37716	5	30
-1.09858	3.77381	2.49002	5	-1.14808	3.50399	.73302	5	32
-.13551	.15283	3.77099	5	.76701	-.63598	2.45830	5	34
-2.24819	-.78626	3.17431	5	-1.05993	-2.10220	3.02843	5	36
.07106	-2.05802	.55780	5	-.35111	-2.33846	-1.81304	5	38
-1.83249	-1.31252	-1.71810	5	-1.39870	-4.14301	-.61117	5	40
-2.94714	-3.36578	-1.16858	5	2.00142	1.37201	2.90917	5	42
1.10127	2.61196	3.85320	5	2.23989	3.09689	2.56897	5	44
-3.62877	-.99868	-.19545	5	-2.89460	.47199	.42086	5	46
-3.87436	-.56688	1.50946	5					

LAST

D

0 D-A TRANSITION STRUCTURE OF DIELS-ALDER D

21 50, 22, 22, 22, 2, 1.359, 1.421, 121.2, 0, 1, 45, 1.0, 2.3, 3.,

2, 2, 13, 0,

1, 1 3, 0,

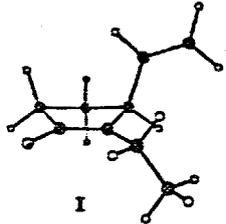
2, 4, 4, 0,

1	2	3	4	22	9	1.359	121.2	0.0	3	3	7	0	0
2	3	4	5	22	9	2.217	101.4	-59.67	6	6	10	18	0
3	2	1	6	22	9	2.217	101.4	59.67	5	5	11	0	0
2	3	4	7	2	9	1.50	121.1	180.0	4	8	0	0	0
3	4	7	8	32	9	1.50	109.0	60.0	7	9	19	19	0
4	7	8	9	2	9	1.65	109.0	60.0	10	8	0	0	0
1	6	5	10	2	9	1.65	109.5	80.0	5	9	0	0	0
2	1	6	11	2	9	1.50	91.8	180.0	6	12	0	0	0
1	6	11	12	2	9	1.54	109.5	-70.0	11	17	0	0	0
3	2	1	13	2	9	1.50	121.1	170.0	1	14	17	0	0
2	1	13	14	2	9	1.54	109.5	30.0	13	15	0	0	0
1	13	14	15	2	9	1.54	98.0	-130.0	14	16	0	0	0
13	14	15	16	32	9	1.50	98.0	0.0	15	17	20	20	0
2	1	13	17	2	9	1.54	109.5	-90.0	12	13	16	21	0
11	6	5	18	2	9	1.50	120.2	0.0	5	0	0	0	0
4	7	8	19	14	9	1.40	120.0	-120.0	8	8	0	0	0
14	15	16	20	14	9	1.40	120.0	-130.0	16	16	0	0	0
1	13	17	21	2	9	1.50	109.5	60.0	17	0	0	0	0

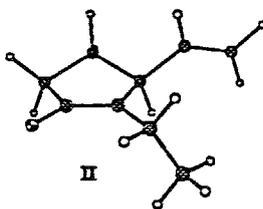
.00000	.00000	.00000	2	1.35900	.00000	.00000	29	2
2.09512	1.21547	.00000	29	1.46550	2.41982	.00000	2	4
.28991	2.29972	-1.87581	2	-.43821	1.09745	-1.87581	2	6
2.32181	3.66277	-.01216	1	3.17436	3.70184	-1.26573	3	8
2.45102	3.59996	-2.59636	1	1.54969	2.36245	-2.73868	1	10
-1.92878	.88576	-1.72385	1	-2.32482	-.58567	-2.00473	1	12
-.89636	-1.22065	.00982	1	-.42074	-2.50463	.70273	1	14
-1.52675	-3.51035	.32389	1	-2.20715	-2.90471	-.89739	3	16
-1.42954	-1.67079	-1.36080	1	-.53604	3.56820	-1.73204	1	18
4.37640	3.83261	-1.20385	7	-3.22494	-3.32427	-1.39619	7	20
-.35843	-2.25865	-2.31056	1	-.50703	.88220	.41743	5	22
1.89367	-.93253	-.18516	5	3.17066	1.16273	-.18098	5	24
.45738	2.56374	.42100	5	.09458	.30450	-2.41402	5	26
2.96402	3.67683	.89936	5	1.70757	4.59063	.02036	5	28
1.87760	4.54062	-2.76160	5	3.22522	3.56958	-3.39990	5	30
1.18170	2.35301	-3.79235	5	2.16597	1.43957	-2.62953	5	32
-2.44357	1.52940	-2.47571	5	-2.30717	1.22512	-.73222	5	34
-2.35629	-.75539	-3.10642	5	-3.37623	-.70783	-1.65210	5	36
-1.78974	-.90663	.60740	5	-.31142	-2.38191	1.80672	5	38
.56280	-2.83637	.29666	5	-2.28441	-3.59483	1.13791	5	40
-1.11908	-4.52191	.09176	5	-1.38413	3.44662	-1.02156	5	42
-.95787	3.84545	-2.72462	5	.04608	4.44312	-1.37622	5	44
.04106	-3.23783	-1.96218	5	.54186	-1.62174	-2.43160	5	46
-.77992	-2.44818	-3.32381	5					LAST

Conformation analysis of enolate 134

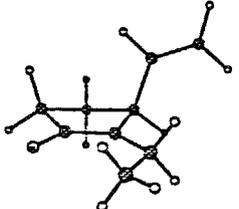
6 possible conformers of 134 were calculated using the MacroModel implementation of the MM2 molecular mechanics force field.

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*****
*                                     *
*  *
*                                     *
* I *
*                                     *
*****
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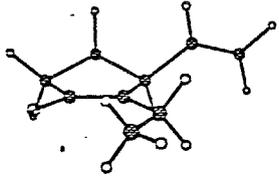
TOTAL MM2	ENERGY IS	10.839 kcal/mol	
Van der Waals	1.761	Stretch	0.549
Torsion	1.933	Bend	9.454
Improper Torsion	0.004	Stretch-Bend	-0.152
Hydrogen-Bond	0.000	Electrostatic	-2.711
Energy minimization RMS		= 0.0011 kcal/Å-mol	

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*****
*                                     *
*  *
*                                     *
* II *
*                                     *
*****
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TOTAL MM2	ENERGY IS	10.607 kcal/mol	
Van der Waals	1.747	Stretch	0.512
Torsion	1.483	Bend	9.763
Improper Torsion	0.008	Stretch-Bend	-0.135
Hydrogen-Bond	0.000	Electrostatic	-2.772
Energy minimization RMS		= 0.0010 kcal/Å-mol	

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*                                     *
*  *
*                                     *
* III *
*                                     *
*****
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TOTAL MM2	ENERGY IS	11.011 kcal/mol	
Van der Waals	2.225	Stretch	0.529
Torsion	0.997	Bend	10.058
Improper Torsion	0.003	Stretch-Bend	-0.152
Hydrogen-Bond	0.000	Electrostatic	-2.650
Energy minimization RMS		= 0.0015 kcal/Å-mol	

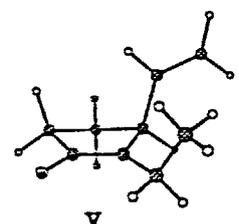
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*****
*                                     *
*  *
*                                     *
* IV *
*                                     *
*****
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TOTAL MM2	ENERGY IS	11.093 kcal/mol	
Van der Waals	2.463	Stretch	0.492
Torsion	0.644	Bend	10.328
Improper Torsion	0.007	Stretch-Bend	-0.125
Hydrogen-Bond	0.000	Electrostatic	-2.715
Energy minimization RMS		= 0.0008 kcal/Å-mol	

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*****
TOTAL MM2      ENERGY IS      10.897 kcal/mol
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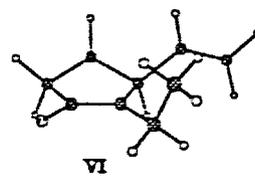
V

Van der Waals	1.740	Stretch	0.567
Torsion	1.792	Bend	9.676
Improper Torsion	0.001	Stretch-Bend	-0.164
Hydrogen-Bond	0.000	Electrostatic	-2.715
Energy minimization RMS		=	0.0013 kcal/Å-mol

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*****
TOTAL MM2      ENERGY IS      11.441 kcal/mol
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*
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*
*****

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VI

Van der Waals	1.854	Stretch	0.514
Torsion	2.032	Bend	9.939
Improper Torsion	0.010	Stretch-Bend	-0.124
Hydrogen-Bond	0.000	Electrostatic	-2.784
Energy minimization RMS		=	0.0013 kcal/Å-mol

Connection Table

Atomic Charges, Coordinates and Connectivity

- single bond, = double bond, % triple bond

I

Atom Type	Number	Charge	Coordinates			Residue	Attached Atoms & Bonds			
			X	Y	Z					
C3	( 1)	0.083	3.7826	4.4842	0.4357	UNK 0	2-	5-	8-	19-
C3	( 2)	0.000	5.0786	5.0084	1.1041	UNK 0	1-	3-	9-	10-
C3	( 3)	0.042	6.2638	4.3257	0.3858	UNK 0	2-	4-	11-	12-
C2	( 4)	0.114	5.5744	3.1000	-0.1165	UNK 0	3-	5=	7-	
C2	( 5)	-0.369	4.2315	3.1474	-0.0968	UNK 0	4=	1-	6-	
C3	( 6)	0.042	3.2902	2.0852	-0.5861	UNK 0	5-	13-	14-	15-
OM	( 7)	-0.870	6.3559	2.1109	-0.5438	UNK 0	4-			
H1	( 8)	0.000	2.9704	4.3677	1.1922	UNK 0	1-			
H1	( 9)	0.000	5.1513	6.1221	1.1228	UNK 0	2-			
H1	(10)	0.000	5.0829	4.6622	2.1677	UNK 0	2-			
H1	(11)	0.000	6.6236	4.9326	-0.4783	UNK 0	3-			
H1	(12)	0.000	7.1095	4.0982	1.0774	UNK 0	3-			
C3	(13)	0.000	2.4422	1.5041	0.5512	UNK 0	6-	16-	17-	18-
H1	(14)	0.000	3.8690	1.2616	-1.0671	UNK 0	6-			
H1	(15)	0.000	2.6312	2.5263	-1.3706	UNK 0	6-			
H1	(16)	0.000	1.7794	0.6893	0.1767	UNK 0	13-			

H1	( 17)	0.000	3.0879	1.0758	1.3530	UNK	0	13-		
H1	( 18)	0.000	1.7868	2.2784	1.0122	UNK	0	13-		
C2	( 19)	-0.042	3.3504	5.3571	-0.7154	UNK	0	20=	21-	1-
C2	( 20)	0.000	2.0876	5.7652	-0.9029	UNK	0	19=	22-	23-
H1	( 21)	0.000	4.1241	5.6551	-1.4446	UNK	0	19-		
H1	( 22)	0.000	1.8159	6.3958	-1.7653	UNK	0	20-		
H1	( 23)	0.000	1.2841	5.4817	-0.2046	UNK	0	20-		

Total charge on system = -1.000

## II

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds				
Type	Number		X	Y	Z						
C3	( 1)	0.042	7.5217	4.6994	-0.0966	UNK	0	2-	5-	8-	12-
C3	( 2)	0.000	6.3225	5.5138	-0.6316	UNK	0	1-	3-	9-	10-
C3	( 3)	0.083	5.0488	4.7588	-0.1796	UNK	0	2-	4-	11-	19-
C2	( 4)	-0.369	5.5456	3.3405	-0.0746	UNK	0	3-	5=	7-	
C2	( 5)	0.114	6.8887	3.3483	-0.0206	UNK	0	4=	1-	6-	
OM	( 6)	-0.870	7.7120	2.3125	0.1234	UNK	0	5-			
C3	( 7)	0.042	4.6514	2.1409	0.0484	UNK	0	4-	13-	14-	15-
H1	( 8)	0.000	8.4013	4.7319	-0.7827	UNK	0	1-			
H1	( 9)	0.000	6.3348	6.5830	-0.3109	UNK	0	2-			
H1	( 10)	0.000	6.3752	5.4987	-1.7480	UNK	0	2-			
H1	( 11)	0.000	4.7606	5.0876	0.8480	UNK	0	3-			
H1	( 12)	0.000	7.8161	5.0308	0.9272	UNK	0	1-			
H1	( 13)	0.000	5.2659	1.2098	0.0488	UNK	0	7-			
C3	( 14)	0.000	3.8115	2.1929	1.3299	UNK	0	7-	16-	17-	18-
H1	( 15)	0.000	3.9866	2.0930	-0.8458	UNK	0	7-			
H1	( 16)	0.000	3.1711	1.2850	1.4238	UNK	0	14-			
H1	( 17)	0.000	4.4627	2.2451	2.2334	UNK	0	14-			
H1	( 18)	0.000	3.1365	3.0798	1.3401	UNK	0	14-			
C2	( 19)	-0.042	3.8967	4.9209	-1.1359	UNK	0	20=	21-	3-	
C2	( 20)	0.000	2.7052	5.4284	-0.7906	UNK	0	19=	22-	23-	
H1	( 21)	0.000	4.0584	4.5966	-2.1787	UNK	0	19-			
H1	( 22)	0.000	1.8929	5.5245	-1.5296	UNK	0	20-			
H1	( 23)	0.000	2.4999	5.7629	0.2387	UNK	0	20-			

Total charge on system = -1.000

## III

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds				
Type	Number		X	Y	Z						
C3	( 1)	0.083	3.7826	4.1971	0.7479	UNK	0	2-	5-	8-	19-
C3	( 2)	0.000	5.0786	4.3168	1.5888	UNK	0	1-	3-	9-	10-

C3 ( 3)	0.042	6.2638	4.0847	0.6255	UNK	0	2-	4-	11-	12-
C2 ( 4)	0.114	5.5744	3.2744	-0.4224	UNK	0	3-	5=	7-	
C2 ( 5)	-0.369	4.2315	3.3056	-0.3817	UNK	0	4=	1-	6-	
C3 ( 6)	0.042	3.2902	2.6303	-1.3365	UNK	0	5-	13-	14-	15-
OM ( 7)	-0.870	6.3559	2.6315	-1.2870	UNK	0	4-			
H1 ( 8)	0.000	2.9704	3.7179	1.3448	UNK	0	1-			
H1 ( 9)	0.000	5.1513	5.2719	2.1619	UNK	0	2-			
H1 ( 10)	0.000	5.0829	3.4852	2.3368	UNK	0	2-			
H1 ( 11)	0.000	6.6236	5.0423	0.1805	UNK	0	3-			
H1 ( 12)	0.000	7.1095	3.5419	1.1107	UNK	0	3-			
C3 ( 13)	0.000	4.0373	1.7889	-2.3776	UNK	0	6-	16-	17-	18-
H1 ( 14)	0.000	2.6726	3.3967	-1.8619	UNK	0	6-			
H1 ( 15)	0.000	2.5902	1.9873	-0.7527	UNK	0	6-			
H1 ( 16)	0.000	3.3254	1.3288	-3.1021	UNK	0	13-			
H1 ( 17)	0.000	4.7553	2.4147	-2.9572	UNK	0	13-			
H1 ( 18)	0.000	4.6084	0.9587	-1.9020	UNK	0	13-			
C2 ( 19)	-0.042	3.3504	5.5286	0.1875	UNK	0	20=	21-	1-	
C2 ( 20)	0.000	2.0876	5.9757	0.2291	UNK	0	19=	22-	23-	
H1 ( 21)	0.000	4.1241	6.1512	-0.2950	UNK	0	19-			
H1 ( 22)	0.000	1.8159	6.9531	-0.2025	UNK	0	20-			
H1 ( 23)	0.000	1.2841	5.3811	0.6921	UNK	0	20-			
Total charge on system = -1.000										

#### IV

Atom Type Number	Charge	Coordinates			Residue	Attached Atoms & Bonds
		X	Y	Z		
C3 ( 1)	0.042	7.5216	4.3538	0.5422	UNK 0	2- 5- 8- 12-
C3 ( 2)	0.000	6.3223	5.2242	0.9798	UNK 0	1- 3- 9- 10-
C3 ( 3)	0.083	5.0487	4.4551	0.5521	UNK 0	2- 4- 11- 19-
C2 ( 4)	-0.369	5.5457	3.6550	-0.6237	UNK 0	3- 5= 7-
C2 ( 5)	0.114	6.8887	3.6122	-0.5898	UNK 0	4= 1- 6-
OM ( 6)	-0.870	7.7121	2.9696	-1.4148	UNK 0	5-
C3 ( 7)	0.042	4.6516	2.9486	-1.6011	UNK 0	4- 13- 14- 15-
H1 ( 8)	0.000	8.4012	4.9643	0.2273	UNK 0	1-
H1 ( 9)	0.000	6.3345	5.4811	2.0662	UNK 0	2-
H1 ( 10)	0.000	6.3749	6.1834	0.4085	UNK 0	2-
H1 ( 11)	0.000	4.7605	3.7296	1.3506	UNK 0	3-
H1 ( 12)	0.000	7.8160	3.6329	1.3412	UNK 0	1-
H1 ( 13)	0.000	4.0255	3.6932	-2.1472	UNK 0	7-
C3 ( 14)	0.000	5.4596	2.1281	-2.6132	UNK 0	7- 16- 17- 18-
H1 ( 15)	0.000	3.9536	2.2857	-1.0379	UNK 0	7-
H1 ( 16)	0.000	4.7869	1.6295	-3.3496	UNK 0	14-
H1 ( 17)	0.000	6.1656	2.7771	-3.1820	UNK 0	14-

H1 ( 18)	0.000	6.0538	1.3302	-2.1106	UNK 0	14-			
C2 ( 19)	-0.042	3.8966	5.3643	0.2142	UNK 0	20=	21-	3-	
C2 ( 20)	0.000	2.7055	5.3197	0.8271	UNK 0	19=	22-	23-	
H1 ( 21)	0.000	4.0580	6.1046	-0.5886	UNK 0	19-			
H1 ( 22)	0.000	1.8932	6.0078	0.5408	UNK 0	20-			
H1 ( 23)	0.000	2.5004	4.5962	1.6321	UNK 0	20-			

Total charge on system = -1.000

### V

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3 ( 1)	0.083	3.7769	4.1888	0.7287	UNK 0	2-	5-	8-	19-	
C3 ( 2)	0.000	5.0471	4.3236	1.6039	UNK 0	1-	3-	9-	10-	
C3 ( 3)	0.042	6.2547	4.1184	0.6642	UNK 0	2-	4-	11-	12-	
C2 ( 4)	0.114	5.6066	3.2934	-0.4001	UNK 0	3-	5=	7-	--	
C2 ( 5)	-0.369	4.2619	3.2999	-0.3903	UNK 0	4=	1-	6-		
C3 ( 6)	0.042	3.3011	2.6203	-1.3245	UNK 0	5-	13-	14-	15-	
OM ( 7)	-0.870	6.4403	2.6683	-1.2280	UNK 0	4-				
H1 ( 8)	0.000	2.9532	3.6955	1.2991	UNK 0	1-				
H1 ( 9)	0.000	5.0904	5.2763	2.1839	UNK 0	2-				
H1 ( 10)	0.000	5.0475	3.4868	2.3460	UNK 0	2-				
H1 ( 11)	0.000	6.6029	5.0843	0.2277	UNK 0	3-				
H1 ( 12)	0.000	7.1022	3.5950	1.1675	UNK 0	3-				
C3 ( 13)	0.000	2.3884	3.5487	-2.1326	UNK 0	6-	16-	17-	18-	
H1 ( 14)	0.000	2.6702	1.9260	-0.7206	UNK 0	6-				
H1 ( 15)	0.000	3.8999	1.9968	-2.0297	UNK 0	6-				
H1 ( 16)	0.000	-1.7187	2.9592	-2.8018	UNK 0	13-				
H1 ( 17)	0.000	1.7334	4.1572	-1.4667	UNK 0	13-				
H1 ( 18)	0.000	2.9788	4.2368	-2.7812	UNK 0	13-				
C2 ( 19)	-0.042	3.3468	5.5184	0.1614	UNK 0	20=	21-	1-		
C2 ( 20)	0.000	2.0895	5.9791	0.2199	UNK 0	19=	22-	23-		
H1 ( 21)	0.000	4.1190	6.1310	-0.3361	UNK 0	19-				
H1 ( 22)	0.000	1.8212	6.9560	-0.2149	UNK 0	20-				
H1 ( 23)	0.000	1.2873	5.3972	0.7010	UNK 0	20-				

Total charge on system = -1.000

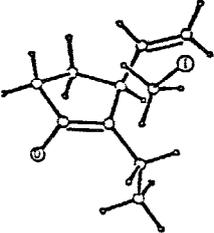
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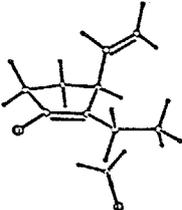
Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3 ( 1)	0.042	7.5089	4.3607	0.5928	UNK 0	2-	5-	8-	12-	
C3 ( 2)	0.000	6.2940	5.2162	1.0112	UNK 0	1-	3-	9-	10-	
C3 ( 3)	0.083	5.0412	4.4377	0.5445	UNK 0	2-	4-	11-	19-	

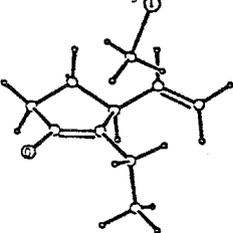
C2	( 4)	-0.369	5.5692	3.6506	-0.6293	UNK	0	3-	5=	7-	
C2	( 5)	0.114	6.9125	3.6244	-0.5636	UNK	0	4=	1-	6-	
OM	( 6)	-0.870	7.7837	3.0115	-1.3614	UNK	0	5-			
C3	( 7)	0.042	4.6558	2.9671	-1.6079	UNK	0	4-	13-	14-	15-
H1	( 8)	0.000	8.3908	4.9825	0.3076	UNK	0	1-			
H1	( 9)	0.000	6.2776	5.4612	2.1003	UNK	0	2-			
H1	( 10)	0.000	6.3511	6.1816	0.4509	UNK	0	2-			
H1	( 11)	0.000	4.7401	3.6989	1.3260	UNK	0	3-			
H1	( 12)	0.000	7.7903	3.6340	1.3911	UNK	0	1-			
H1	( 13)	0.000	4.0113	2.2553	-1.0404	UNK	0	7-			
C3	( 14)	0.000	3.7572	3.8899	-2.4381	UNK	0	7-	16-	17-	18-
H1	( 15)	0.000	5.2922	2.3636	-2.2977	UNK	0	7-			
H1	( 16)	0.000	3.1185	3.2972	-3.1342	UNK	0	14-			
H1	( 17)	0.000	3.0723	4.4836	-1.7892	UNK	0	14-			
H1	( 18)	0.000	4.3585	4.5914	-3.0619	UNK	0	14-			
C2	( 19)	-0.042	3.8882	5.3422	0.1958	UNK	0	20=	21-	3-	
C2	( 20)	0.000	2.6873	5.2842	0.7881	UNK	0	19=	22-	23-	
H1	( 21)	0.000	4.0583	6.0921	-0.5964	UNK	0	19-			
H1	( 22)	0.000	1.8757	5.9702	0.4949	UNK	0	20-			
H1	( 23)	0.000	2.4732	4.5519	1.5828	UNK	0	20-			
Total charge on system =			-1.000								

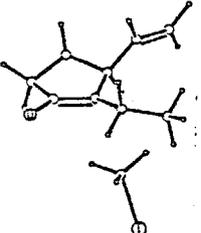
MM2 transition structure models in the methylation of enolate 134

MM2 transition structure models in  $\alpha$ - and  $\beta$ -methylations of the enolate 134I and 134II were calculated, respectively. In these calculations, the distance (3.0 Å) and the attacking angle (106 °) of the methyl iodide to the enolate, and the two  $sp^2$  hybridized carbons of the enolate were fixed and the geometry for the rest of molecule was optimized by MM2.

*****		TOTAL MM2	ENERGY IS	13.246 kcal/mol
*		*		
*		*	Van der Waals	0.896
*		*	Stretch	0.794
*		*	Torsion	4.821
*		*	Bend	9.545
*		*	Improper Torsion	0.211
*		*	Stretch-Bend	-0.174
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.847
*		*	Energy minimization RMS	= 0.7642 kJ/A-mol
*****				

*****		TOTAL MM2	ENERGY IS	12.488 kcal/mol
*		*		
*		*	Van der Waals	0.099
*		*	Stretch	0.683
*		*	Torsion	4.096
*		*	Bend	10.297
*		*	Improper Torsion	0.166
*		*	Stretch-Bend	-0.137
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.715
*		*	Energy minimization RMS	= 0.1593 kJ/A-mol
*****				

*****		TOTAL MM2	ENERGY IS	11.021 kcal/mol
*		*		
*		*	Van der Waals	-0.154
*		*	Stretch	0.624
*		*	Torsion	3.048
*		*	Bend	10.326
*		*	Improper Torsion	0.171
*		*	Stretch-Bend	-0.130
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.863
*		*	Energy minimization RMS	= 0.8283 kJ/A-mol
*****				

*****		TOTAL MM2	ENERGY IS	14.997 kcal/mol
*		*		
*		*	Van der Waals	1.209
*		*	Stretch	0.758
*		*	Torsion	4.796
*		*	Bend	10.931
*		*	Improper Torsion	0.157
*		*	Stretch-Bend	-0.071
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.782
*		*	Energy minimization RMS	= 1.7439 kJ/A-mol
*****				

Connection Table

Atomic Charges, Coordinates and Connectivity

LB

Atom Type	Number	Charge	Coordinates			Residue	Attached Atoms & Bonds			
			X	Y	Z					
C3	( 1)	0.083	2.8041	4.3187	-0.9358	UNK 0	2-	5-	8-	19-
C3	( 2)	0.000	4.0959	4.1641	-0.0917	UNK 0	1-	3-	9-	10-
C3	( 3)	0.042	5.2759	4.2925	-1.0774	UNK 0	2-	4-	11-	12-
C2	( 4)	0.114	4.6030	3.7782	-2.3071	UNK 0	3-	5-	7-	
C2	( 5)	-0.369	3.2583	3.8082	-2.2893	UNK 0	4-	1-	6-	
C3	( 6)	0.042	2.3617	3.0420	-3.2233	UNK 0	5-	13-	14-	15-
OM	( 7)	-0.870	5.3741	3.1134	-3.1646	UNK 0	4-			
H1	( 8)	0.000	2.0024	3.6600	-0.5244	UNK 0	1-			
H1	( 9)	0.000	4.1594	4.8675	0.7728	UNK 0	2-			
H1	(10)	0.000	4.1159	3.1277	0.3295	UNK 0	2-			
H1	(11)	0.000	5.5727	5.3565	-1.2325	UNK 0	3-			
H1	(12)	0.000	6.1589	3.6861	-0.7641	UNK 0	3-			
C3	(13)	0.000	2.1500	1.6030	-2.7334	UNK 0	6-	16-	17-	18-
H1	(14)	0.000	2.8210	3.0058	-4.2392	UNK 0	6-			
H1	(15)	0.000	1.3751	3.5531	-3.3080	UNK 0	6-			
H1	(16)	0.000	1.5040	1.0326	-3.4411	UNK 0	13-			
H1	(17)	0.000	3.1194	1.0590	-2.6477	UNK 0	13-			
H1	(18)	0.000	1.6546	1.5777	-1.7355	UNK 0	13-			
C2	(19)	-0.042	2.3511	5.7550	-0.9397	UNK 0	20-	21-	1-	
C2	(20)	0.000	1.0727	6.1317	-0.7962	UNK 0	19-	22-	23-	
H1	(21)	0.000	3.1246	6.5309	-1.0725	UNK 0	19-			
H1	(22)	0.000	0.7897	7.1971	-0.8100	UNK 0	20-			
H1	(23)	0.000	0.2676	5.3910	-0.6668	UNK 0	20-			
C3	(24)	0.126	2.4596	6.1035	-4.0565	0	25-	26-	27-	28-
H1	(25)	0.000	1.5509	5.8337	-3.4789	0	24-			
H1	(26)	0.000	3.3020	6.4617	-3.4263	0	24-			
H1	(27)	0.000	2.7887	5.2924	-4.7410	0	24-			
IO	(28)	-0.126	1.8888	7.7445	-5.3197	0	24-			

Total charge on system = -1.000

Constrained Interaction Energies

4 Constrained Interactions Present

Constrained Distances Specified

Number = 1

Atom Numbers		Force Const	Distance Constr	Energy (kJ/mol) Actual	
5	24	2.2000	3.0000	3.0343	1.455

Constrained Three Atom (A-B-C) Angles Specified

Number = 2

Atom Numbers			Force Consts		Angle		Energy (kJ/mol)
			KBnd1	KBnd2	Constr	Actual	
4	5	24	99.9000	0.0000	105.9998	105.9603	0.014
5	24	28	99.9000	0.0000	179.9997	179.9998	0.000

Constrained Four Atom (A-B-C-D) Angles Specified

Number= 1

Atom Numbers				Force Consts			Angle		Energy (kJ/mol)
				V1	V2	V3	Constr	Actual	
7	4	5	24	-956.023	0.000	0.000	-90.0000	-89.3802	-5.824

Iα

Atom Type	Number	Charge	Coordinates			Residue	Attached Atoms & Bonds			
			X	Y	Z					
C3	( 1)	0.083	3.5311	4.0987	1.6064	UNK 0				
C3	( 2)	0.000	4.9747	4.0469	2.1657	UNK 0	2-	5-	8-	19-
C3	( 3)	0.042	5.9158	4.1094	0.9429	UNK 0	1-	3-	9-	10-
C2	( 4)	0.114	4.9954	3.5708	-0.1028	UNK 0	2-	4-	11-	12-
C2	( 5)	-0.369	3.7046	3.4448	0.2563	UNK 0	3-	5=	7-	
C3	( 6)	0.042	2.5966	3.1727	-0.7263	UNK 0	4=	1-	6-	
OM	( 7)	-0.870	5.5395	3.2902	-1.2844	UNK 0	5-	13-	14-	15-
H1	( 8)	0.000	2.8281	3.5355	2.2633	UNK 0	4-			
H1	( 9)	0.000	5.1846	4.8347	2.9281	UNK 0	1-			
H1	( 10)	0.000	5.1213	3.0583	2.6669	UNK 0	2-			
H1	( 11)	0.000	6.1950	5.1601	0.6928	UNK 0	2-			
H1	( 12)	0.000	6.8319	3.4862	1.0759	UNK 0	3-			
C3	( 13)	0.000	1.2037	2.9706	-0.1167	UNK 0	3-			
H1	( 14)	0.000	2.8703	2.2978	-1.3617	UNK 0	6-	16-	17-	18-
H1	( 15)	0.000	2.5426	4.0577	-1.4044	UNK 0	6-			
H1	( 16)	0.000	0.4472	2.7956	-0.9169	UNK 0	6-			
H1	( 17)	0.000	1.1595	2.0954	0.5672	UNK 0	13-			
H1	( 18)	0.000	0.8724	3.8672	0.4552	UNK 0	13-			
C2	( 19)	-0.042	3.0833	5.5298	1.4282	UNK 0	13-			
C2	( 20)	0.000	2.0204	6.0593	2.0500	UNK 0	20=	21-	1-	
H1	( 21)	0.000	3.6806	6.1708	0.7564	UNK 0	19=	22-	23-	
H1	( 22)	0.000	1.7366	7.1129	1.8931	UNK 0	19-			
H1	( 23)	0.000	1.3987	5.4605	2.7346	UNK 0	20-			
C3	( 24)	0.126	3.4211	0.6642	1.3575	UNK 0	20-			
H1	( 25)	0.000	2.7804	1.3107	1.9927	0	25-	26-	27-	28-
						0	24-			

H1 ( 26)	0.000	4.4964	0.9390	1.4336	0	24-
H1 ( 27)	0.000	3.0844	0.6174	0.2999	0	24-
IO ( 28)	-0.126	3.2186	-1.3236	2.1447	0	24-

Total charge on system = -1.000

Constrained Interaction Energies

4 Constrained Interactions Present

Constrained Distances Specified

Number = 1

Atom Numbers		Force Const	Distance		Energy (kJ/mol)
			Constr	Actual	
5	24	2.2000	3.0000	3.0243	0.745

Constrained Three Atom (A-B-C) Angles Specified

Number = 2

Atom Numbers			Force Consts		Angle		Energy (kJ/mol)
			KBnd1	KBnd2	Constr	Actual	
4	5	24	99.9000	0.0000	105.9998	105.9542	0.019
5	24	28	99.9000	0.0000	179.9997	179.9800	0.004

Constrained Four Atom (A-B-C-D) Angles Specified

Number= 1

Atom Numbers				Force Consts			Angle		Energy (kJ/mol)
				V1	V2	V3	Constr	Actual	
7	4	5	24	-956.023	0.000	0.000	90.0000	90.0983	-6.406

II B

Atom Type	Charge	Coordinates			Residue	Attached Atoms & Bonds			
Number		X	Y	Z					
C3 ( 1)	0.042	7.0271	4.8136	-0.3517	UNK 0	2-	5-	8-	12-
C3 ( 2)	0.000	5.8240	5.4883	0.3433	UNK 0	1-	3-	9-	10-
C3 ( 3)	0.083	4.5728	4.7376	-0.1706	UNK 0	2-	4-	11-	19-
C2 ( 4)	-0.369	5.0028	4.3171	-1.5572	UNK 0	3-	5=	7-	
C2 ( 5)	0.114	6.3478	4.2980	-1.5786	UNK 0	4=	1-	6-	
OM ( 6)	-0.870	7.1344	3.7513	-2.5024	UNK 0	5-			
C3 ( 7)	0.042	4.1218	3.5956	-2.5398	UNK 0	4-	13-	14-	15-
H1 ( 8)	0.000	7.8480	5.5335	-0.5818	UNK 0	1-			
H1 ( 9)	0.000	5.9044	5.4950	1.4568	UNK 0	2-			
H1 ( 10)	0.000	5.7819	6.5512	0.0019	UNK 0	2-			
H1 ( 11)	0.000	4.4511	3.7967	0.4191	UNK 0	3-			
H1 ( 12)	0.000	7.4171	3.9577	0.2484	UNK 0	1-			
H1 ( 13)	0.000	4.5893	3.6304	-3.5522	UNK 0	7-			
C3 ( 14)	0.000	3.9181	2.1309	-2.1322	UNK 0	7-	16-	17-	18-
H1 ( 15)	0.000	3.1320	4.1005	-2.6136	UNK 0	7-			

H1 ( 16)	0.000	3.2808	1.5957	-2.8743	UNK	0	14-		
H1 ( 17)	0.000	4.8912	1.5903	-2.0696	UNK	0	14-		
H1 ( 18)	0.000	3.4167	2.0496	-1.1402	UNK	0	14-		
C2 ( 19)	-0.042	3.2937	5.5252	-0.0841	UNK	0	20=	21-	3-
C2 ( 20)	0.000	2.0851	4.9617	0.0530	UNK	0	19=	22-	23-
H1 ( 21)	0.000	3.3587	6.6234	-0.1655	UNK	0	19-		
H1 ( 22)	0.000	1.1713	5.5767	0.0966	UNK	0	20-		
H1 ( 23)	0.000	1.9685	3.8686	0.1239	UNK	0	20-		
C3 ( 24)	0.126	4.1889	6.8100	-3.0203	0		25-	26-	27- 28-
H1 ( 25)	0.000	3.2434	6.3523	-2.6618	0		24-		
H1 ( 26)	0.000	4.8573	7.1236	-2.1889	0		24-		
H1 ( 27)	0.000	4.7208	6.1637	-3.7529	0		24-		
I0 ( 28)	-0.126	3.6071	8.5929	-4.0667	0		24-		

Total charge on system = -1.000

### Constrained Interaction Energies

4 Constrained Interactions Present

#### Constrained Distances Specified

Number = 1

Atom Numbers		Force Const	Distance		Energy (kJ/mol)
			Constr	Actual	
4	24	2.2000	3.0000	3.0252	0.799

#### Constrained Three Atom (A-B-C) Angles Specified

Number = 2

Atom Numbers			Force Consts		Angle		Energy (kJ/mol)
			KBnd1	KBnd2	Constr	Actual	
5	4	24	99.9000	0.0000	105.9998	105.9621	0.013
4	24	28	99.9000	0.0000	179.9997	179.9998	0.000

#### Constrained Four Atom (A-B-C-D) Angles Specified

Number = 1

Atom Numbers				Force Consts			Angle		Energy (kJ/mol)
				V1	V2	V3	Constr	Actual	
6	5	4	24	-956.023	0.000	0.000	-90.0000	-89.7019	-6.280

### II $\alpha$

Atom Type	Number	Charge	Coordinates			Residue	Attached Atoms & Bonds			
			X	Y	Z					
C3 ( 1)		0.042	7.1590	4.1721	1.1394	UNK 0	2-	5-	8-	12-
C3 ( 2)		0.000	5.9060	4.8938	1.6739	UNK 0	1-	3-	9-	10-
C3 ( 3)		0.083	4.6732	4.1014	1.1637	UNK 0	2-	4-	11-	19-
C2 ( 4)		-0.369	5.2209	3.3095	-0.0020	UNK 0	3-	5=	7-	
C2 ( 5)		0.114	6.5537	3.4914	-0.0421	UNK 0	4=	1-	6-	

OM	( 6)	-0.870	7.3989	3.0921	-0.9895	UNK	0	5-			
C3	( 7)	0.042	4.4352	2.8151	-1.1920	UNK	0	4-	13-	14-	15-
H1	( 8)	0.000	7.9795	4.8784	0.8678	UNK	0	1-			
H1	( 9)	0.000	5.9136	5.0255	2.7826	UNK	0	2-			
H1	( 10)	0.000	5.8965	5.9162	1.2224	UNK	0	2-			
H1	( 11)	0.000	4.3299	3.4010	1.9578	UNK	0	3-			
H1	( 12)	0.000	7.5298	3.4048	1.8594	UNK	0	1-			
H1	( 13)	0.000	5.0124	2.0094	-1.7046	UNK	0	7-			
C3	( 14)	0.000	2.9942	2.3377	-0.9716	UNK	0	7-	16-	17-	18-
H1	( 15)	0.000	4.3918	3.6747	-1.9026	UNK	0	7-			
H1	( 16)	0.000	2.5006	2.1349	-1.9510	UNK	0	14-			
H1	( 17)	0.000	2.9325	1.3885	-0.3996	UNK	0	14-			
H1	( 18)	0.000	2.3703	3.0956	-0.4489	UNK	0	14-			
C2	( 19)	-0.042	3.5651	5.0507	0.7835	UNK	0	20=	21-	3-	
C2	( 20)	0.000	2.4418	5.2075	1.4977	UNK	0	19=	22-	23-	
H1	( 21)	0.000	3.7139	5.6653	-0.1216	UNK	0	19-			
H1	( 22)	0.000	1.6660	5.9260	1.1862	UNK	0	20-			
H1	( 23)	0.000	2.2591	4.6244	2.4143	UNK	0	20-			
C3	( 24)	0.126	4.7869	0.6998	1.4238	0	0	25-	26-	27-	28-
H1	( 25)	0.000	3.8567	1.2826	1.5874	0	0	24-			
H1	( 26)	0.000	5.6691	1.1862	1.8966	0	0	24-			
H1	( 27)	0.000	4.9799	0.4563	0.3561	0	0	24-			
IO	( 28)	-0.126	4.4769	-1.1654	2.4427	0	0	24-			

Total charge on system = -1.000

Constrained Interaction Energies

4 Constrained Interactions Present

Constrained Distances Specified

Number = 1

Atom Numbers		Force Const	Distance		Energy (kJ/mol)
			Constr	Actual	
4	24	2.2000	3.0000	3.0308	1.180

Constrained Three Atom (A-B-C) Angles Specified

Number = 2

Atom Numbers			Force Consts		Angle		Energy (kJ/mol)
			KBnd1	KBnd2	Constr	Actual	
5	4	24	99.9000	0.0000	105.9998	105.9408	0.032
4	24	28	99.9000	0.0000	179.9997	179.9800	0.004

Constrained Four Atom (A-B-C-D) Angles Specified

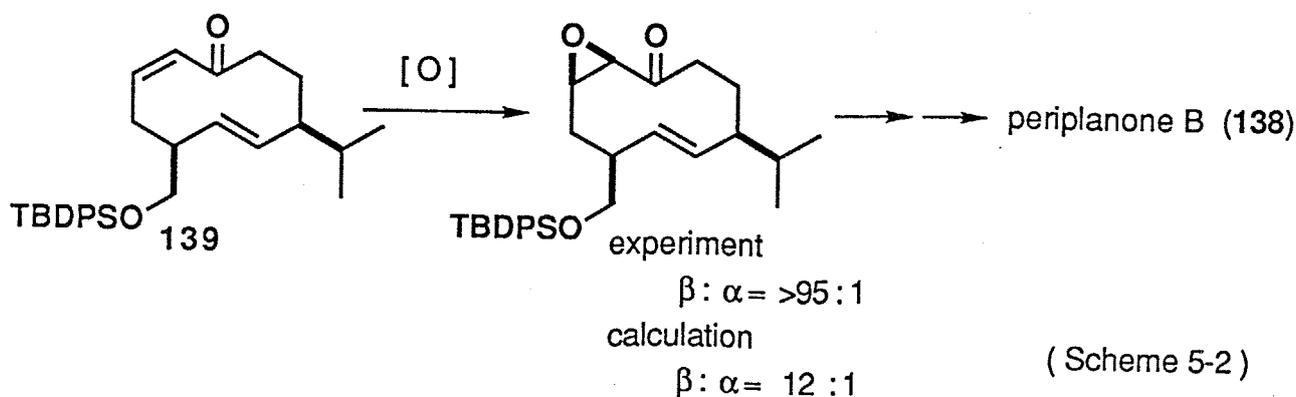
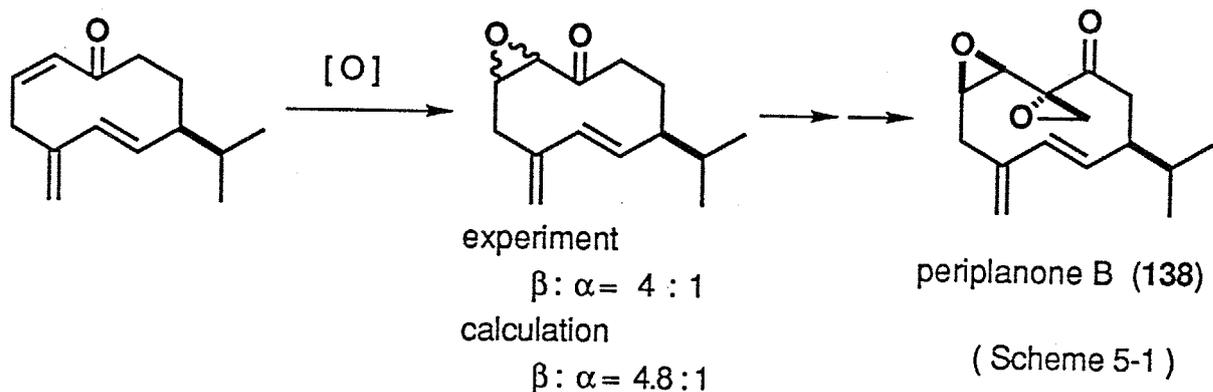
Number = 1

Atom Numbers				Force Consts			Angle		Energy (kJ/mol)
				V1	V2	V3	Constr	Actual	
6	5	4	24	-956.023	0.000	0.000	90.0000	90.1179	-6.399

## 第五章 ペリプラノンAの合成研究

### 5-1 ペリプラノン

ペリプラノンA (以下PAと略す, 137), ペリプラノンB (PB, 138) は、共にワモンゴキブリの性フェロモンとして知られているゲルマクラン型セスキテルペンである。ワモンゴキブリの性フェロモンの研究は<sup>93)</sup>、1950年以後その強い活性物質をめぐる多くのグループにより活発に行われてきた。しかし、この活性物質の単離は、天然から超微量しか得られないこと、また活性が強いために生物活性試験を指標にしての単離が技術的に難しかったことから困難を極めた。1974年、Persoonsらは、ワモンゴキブリの雌75,000匹から2つの活性物質PA, PBをそれぞれ20  $\mu\text{g}$ , 200  $\mu\text{g}$ 単離し<sup>94)</sup>、PBの平面構造式を提出した<sup>95)</sup>。1979年Stillは合成 (Scheme 1-8) によりPBの構造を絶対配置も含め138と決定した<sup>23, 96)</sup>。その後Schreiber<sup>97)</sup>, Hauptmann<sup>98)</sup>, 高橋<sup>43)</sup>, 北原<sup>99)</sup>らによってそれぞれPBの全合成が報告されている。特に当研究室では10員環エノンのMM2立体配座解析を行い、すべての配座異性体からの活性化エネルギーが等しく、配座異性体の存在比がそのまま生成比に反映すると仮定して、エポキシ化の立体選択性の予測が可能であることを報告している。すなわちSchreiberらの中間体のエポキシ化の立体選択性が4:1であること (Scheme 5-1)、高橋らの中間体からのエポキシ化は $\beta$ 体だけであること (Scheme 5-2) はMM2の計算結果とよく一致している。

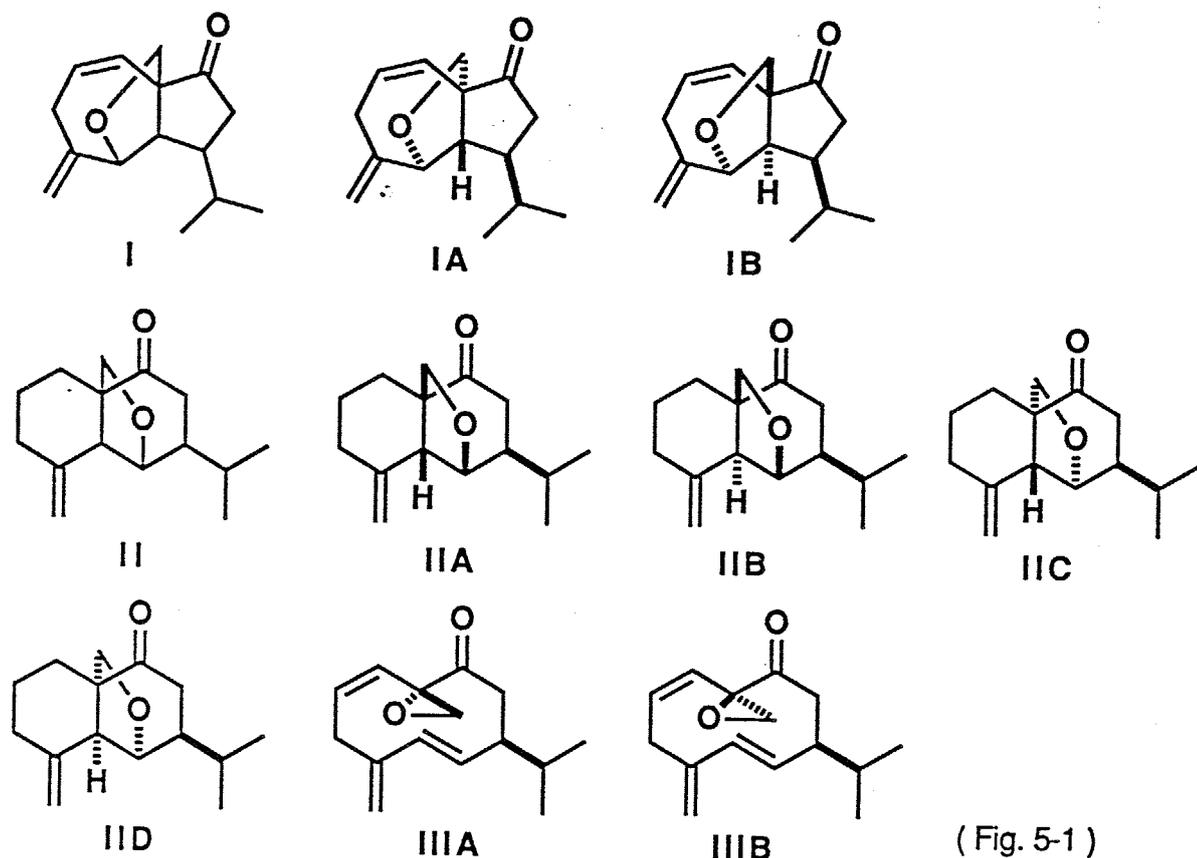


Persoonsらは1982年、P AとしてFig.5-1に示すIの平面構造式を提出し<sup>100)</sup>、これが徐々に分解して安定な生物活性のないIIAになると報告した。志津里らは1987年IAおよびIBを合成したが、Persoonsらの報告しているスペクトルとは異なっていた<sup>101)</sup>。

Macdonaldらは1987年、IIIBとIIBを合成し、IIIBの構造をP Aと提唱し、その活性は $10^{-13}$ - $10^{-14}$  g/mLでP Bと同じ程度であると報告している<sup>102)</sup>。時を同じくHauptmannらは1986年IIIAをワモンゴキブリから単離し、その合成も行い、合成物の生物活性試験からIIIAが高い生物活性を有することを報告した。しかし、これらの化合物のNMRスペクトルは、Persoonsの報告とは全く異なっていた<sup>103)</sup>。

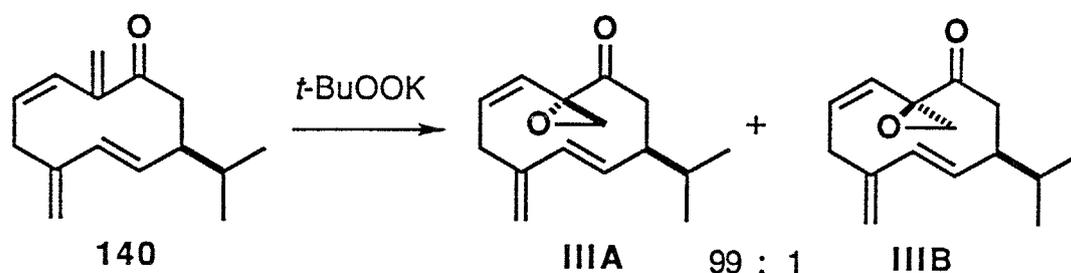
またMacdonaldら<sup>102)</sup>と志津里ら<sup>104)</sup>は独自に1987年合成物とNMRスペクトルの比較からIICがPersoonsらのP Aの分解物と提唱した。さらに志津里らは、分子力場計算を用いたNMRスペクトルの解析からPersoonsらのP Aの推定構造をIIDと報告した<sup>104)</sup>。

The proposed structures of periplanone A (137)



当時、筆者はHauptmannらの合成中間体 140 が P A, P B の生合成における共通の中間体で、酸化度の違いで IIIA と P B ( 138 ) ができると考え、Persoonsらの単離した化合物は、IIIA が酸により渡環反応して生成したのではないかと推測し、真の P A を求めて研究を行った。

Hauptmannらはエノン 140 に対し共役付加的エポキシ化を行って 99 : 1 の立体選択性で IIIA を得たと報告している<sup>103)</sup> (Scheme 5-3)。



(Scheme 5-3)

しかし 140 と類似の構造をしたSchreiberらの中間体 (Scheme 5-1) は、立体配座解析から非常に多くの配座異性体が存在することから、140 から高い選択性でエポキシ化が進行しているHauptmannらの結果に疑問をもった。またMacdonaldらが提出している IIIB のエポキシ基の立体化学は推測にすぎず、Hauptmannらの提出している IIIA も多くの立体配座が存在する中員環の立体化学を立体配座解析を行わずNOEから決定しており問題があると考えた。

そこでHauptmannらの合成中間体 140 の立体配座解析を行った。

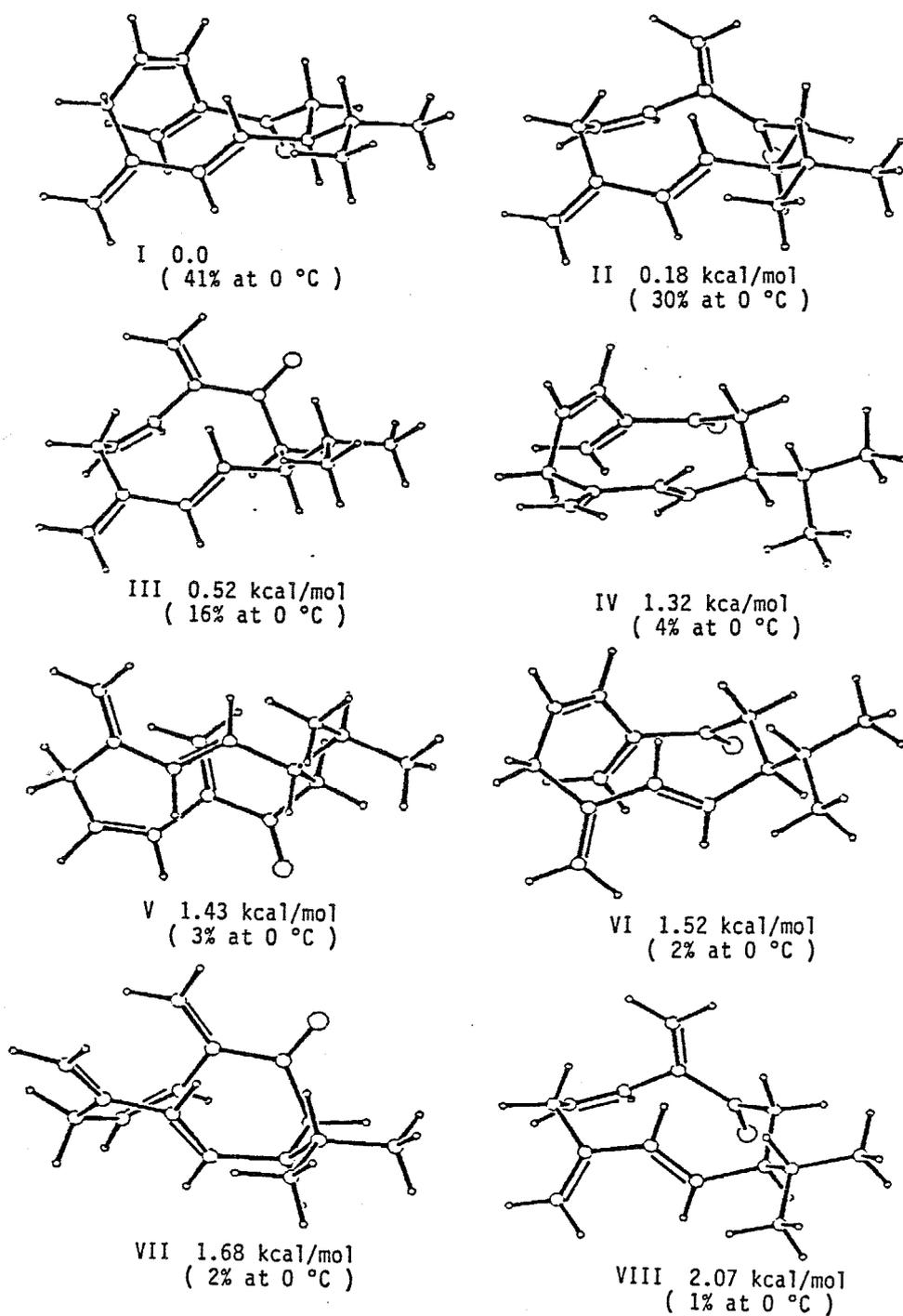
## 5-2 MM2を用いた立体配座解析

140の全ての立体配座を求めめるため、MMRSを用いて初期座標を発生させ、生じた60個の立体配座をMM2によって構造最適化を行ったところ、2.0 kcal/mol以内に8つの配座異性体が存在した。(Fig. 5-2)。

dihedral angle resolution 30 deg

closure distance 1.0-2.4 A

transannular contact 2.4 A

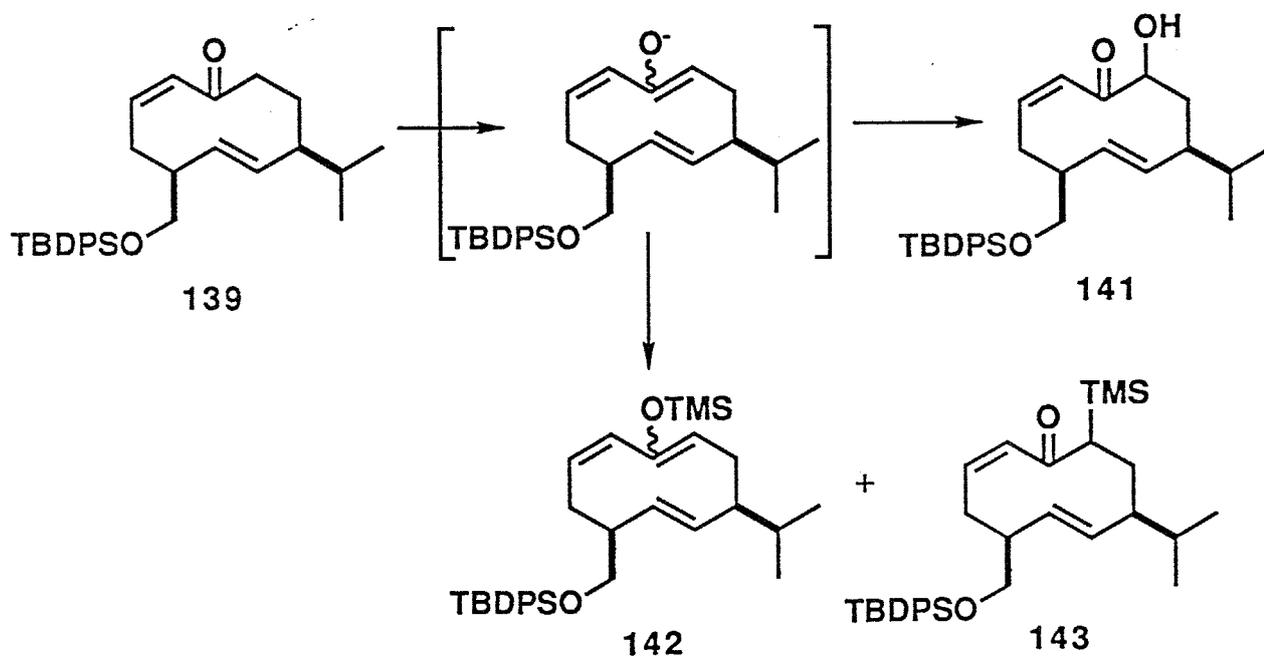


( Fig. 5-2 )

当研究室で既に報告しているPB合成のときと同様に<sup>43)</sup>各配座異性体からのエポキシ化の活性化エネルギーが等しいと仮定し、配座異性体の存在比がそのまま生成物の比に反映されるとすると、Scheme 5-3に示すエポキシ化の立体選択性はBoltzmann分布から0 °CでIIIA: IIIB = 48: 52と予測された。この計算結果はHauptmannらの実験結果とは全く異なっており、計算結果が正しいかどうかを確認するためにこのエポキシ化反応を実際に行った。またこの計算結果が正しいなら、立体化学の疑問なIIIAとIIIBを同時に得られるので、両ジアステレオマーの構造決定および生物活性試験の際に比較することができ有効であると考えた。

### 5-3 実験結果<sup>185)</sup>

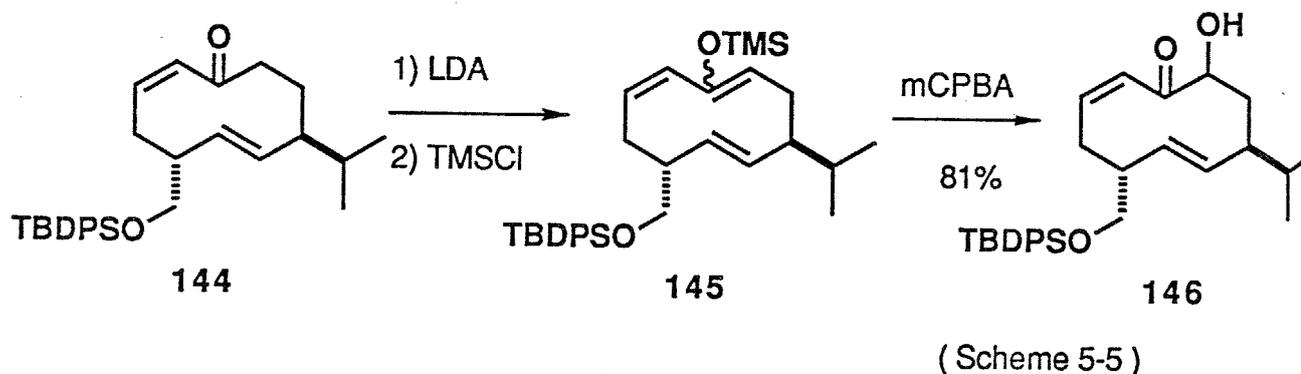
当研究室ですでに報告しているPB合成中間体139<sup>43)</sup>に対し、ケトンの $\alpha'$ 位への水酸基の導入を検討した。LDAを用いてケトンの $\alpha'$ 位に選択的にエノレートを発生させ、酸素、 $\text{MoO}_5 \cdot \text{HMPA} \cdot \text{Py}$ 等で直接水酸基の導入を試みたが満足する収率で求める141が得られなかったのでシリルエノールエーテルのエポキシ化を検討した。



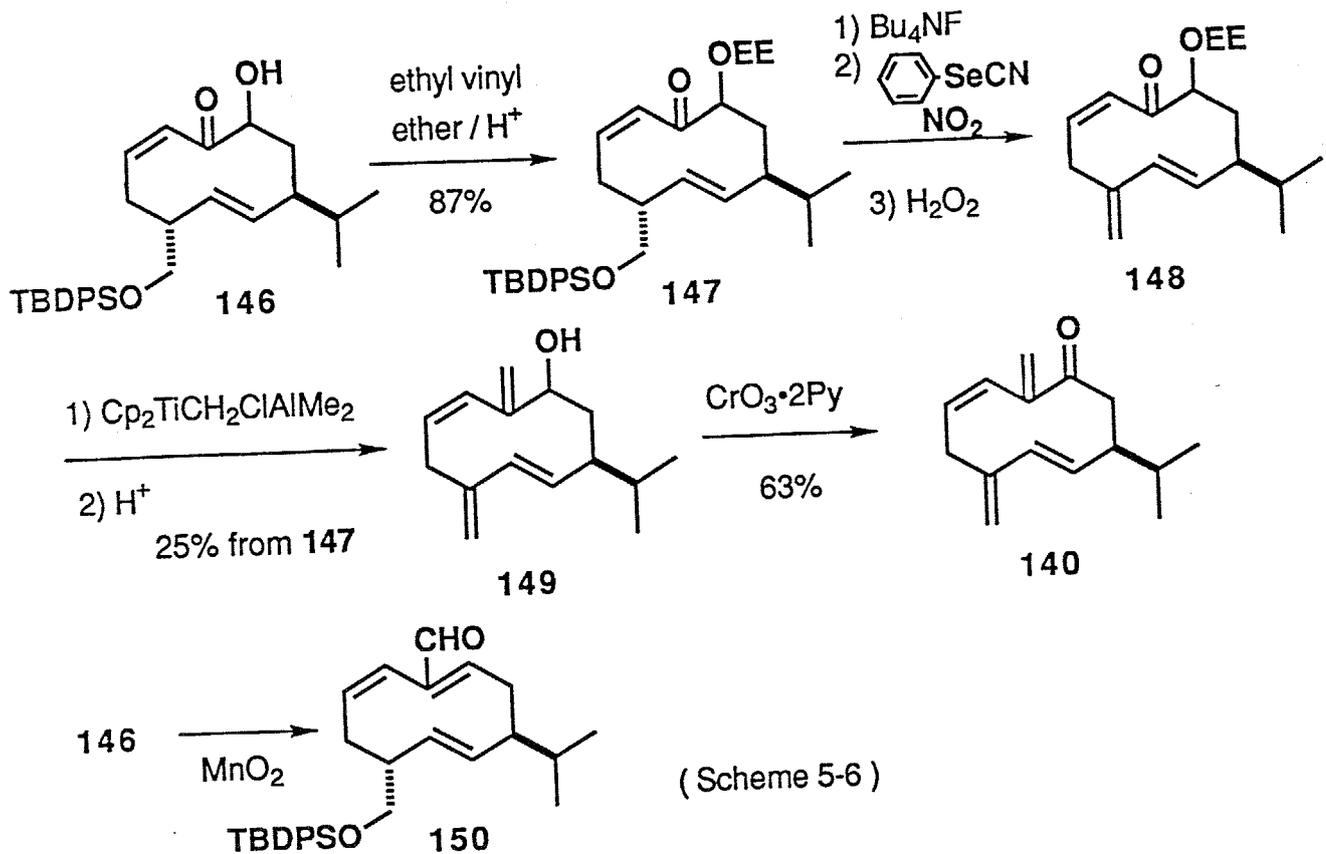
(Scheme 5-4)

LDAで発生したエノレートをTMSClで捕捉したところ、通常の鎖状分子では考えられないC-シリル化が進行し、143が得られた。これはアルコキシメチル基により10員環の立体配座が制御され、トリエン構造142をとりにくいためではないかと考えた (Scheme 5-4)。

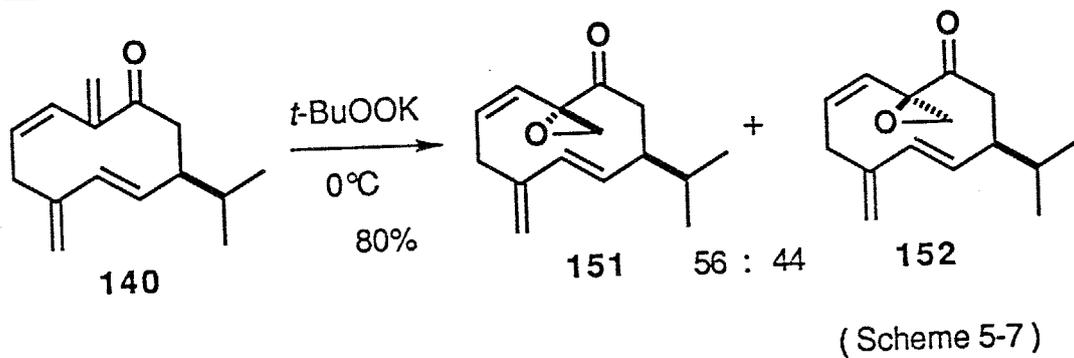
そこで139とアルコキシメチル基のエピマーである144で検討した。LDAを用いてケトンの $\alpha'$ 位にエノレートを発生し、TMS基で捕捉して145だけを得ることができた。145はシリカゲルに安定で、カラムで生成することができたが、そのままmCPBAでエポキシ化し、後処理を行うと同時に加水分解が起こり、求める $\alpha'$ -ヒドロキシケトン146を収率81%で得ることができた (Scheme 5-5)。



続いて、146の水酸基をエチルビニルエーテルで保護して147とし、*t*-ブチルジフェニルシリル基を除去した後、セレン化して酸化すると、 $\beta$ 脱離反応を経て148が得られた。さらに $\text{Cp}_2\text{TiCH}_2\text{ClAlMe}_2$ を用いてケトンエキソメチレンへ変換し、保護基を除去して147から収率25%で149へ導いた。149をCollins酸化してHauptmannらの中間体140を収率63%で得た。なお146を二酸化マンガンを酸化すると、転位を伴って酸化が起こった150が得られた (Scheme 5-6)。



エノン 140 を  $0^\circ\text{C}$  でカリウム *t*-ブチルペルオキシドにより処理したところ、求めるエポキシ化物 151、152 が収率 80% で得られた。HPLC による分析の結果、151 : 152 = 56 : 44 であることがわかった (Scheme 5-7)。



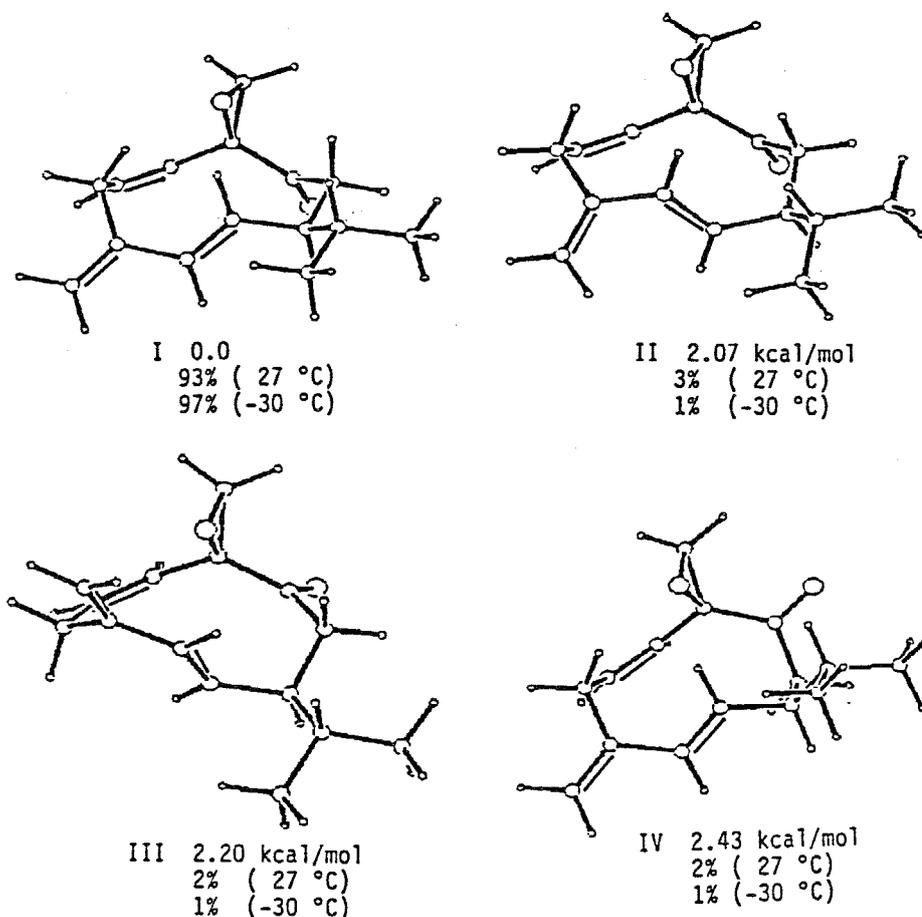
この実験結果は Hauptmann らの報告<sup>103)</sup> とは異なり、計算結果とよく一致した。

#### 5-4 構造決定

151と152の構造決定を行うためにはそれらの立体配座を調べることが不可欠と考え、MM2を用いた立体配座解析を行った。

151の全ての立体配座を求めるため、MMRSを用いて初期座標を発生させ、生じた88個の立体配座をMM2によって構造最適化を行ったところ、3.0 kcal/mol以内に4つの配座異性体が存在した (Fig. 5-3)。

dihedral angle resolution	30 deg
closure distance	1.0-2.7 Å
transannular contact	2.24 Å



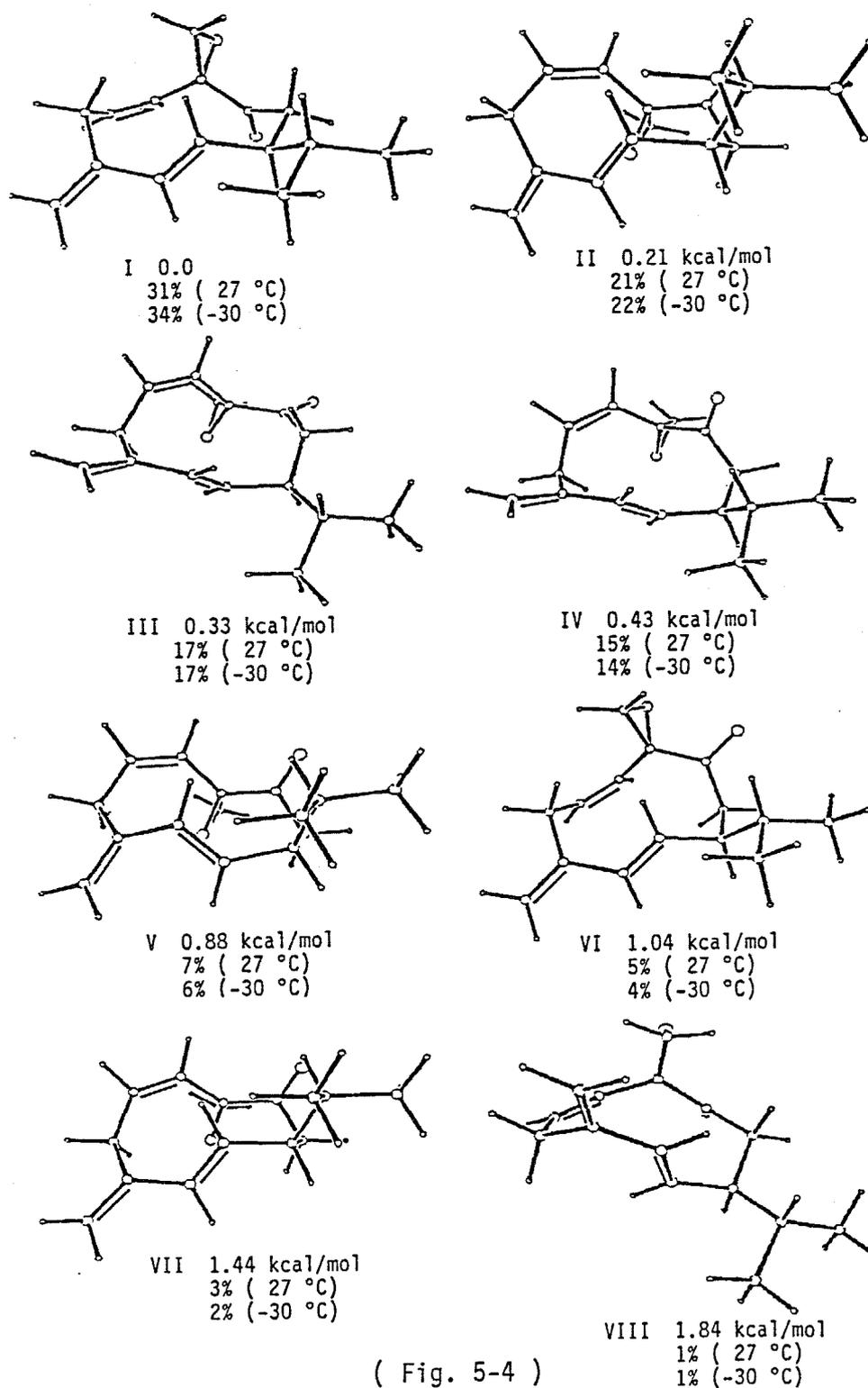
( Fig. 5-3 )

一方、152の全ての立体配座を求めるため、MMRSを用いて初期座標を発生させ、生じた80個の立体配座をMM2によって構造最適化を行ったところ、2.0 kcal/mol以内に8つの配座異性体が存在した (Fig. 5-4)。

dihedral angle resolution            30 deg

closure distance                    1.0-2.7 Å

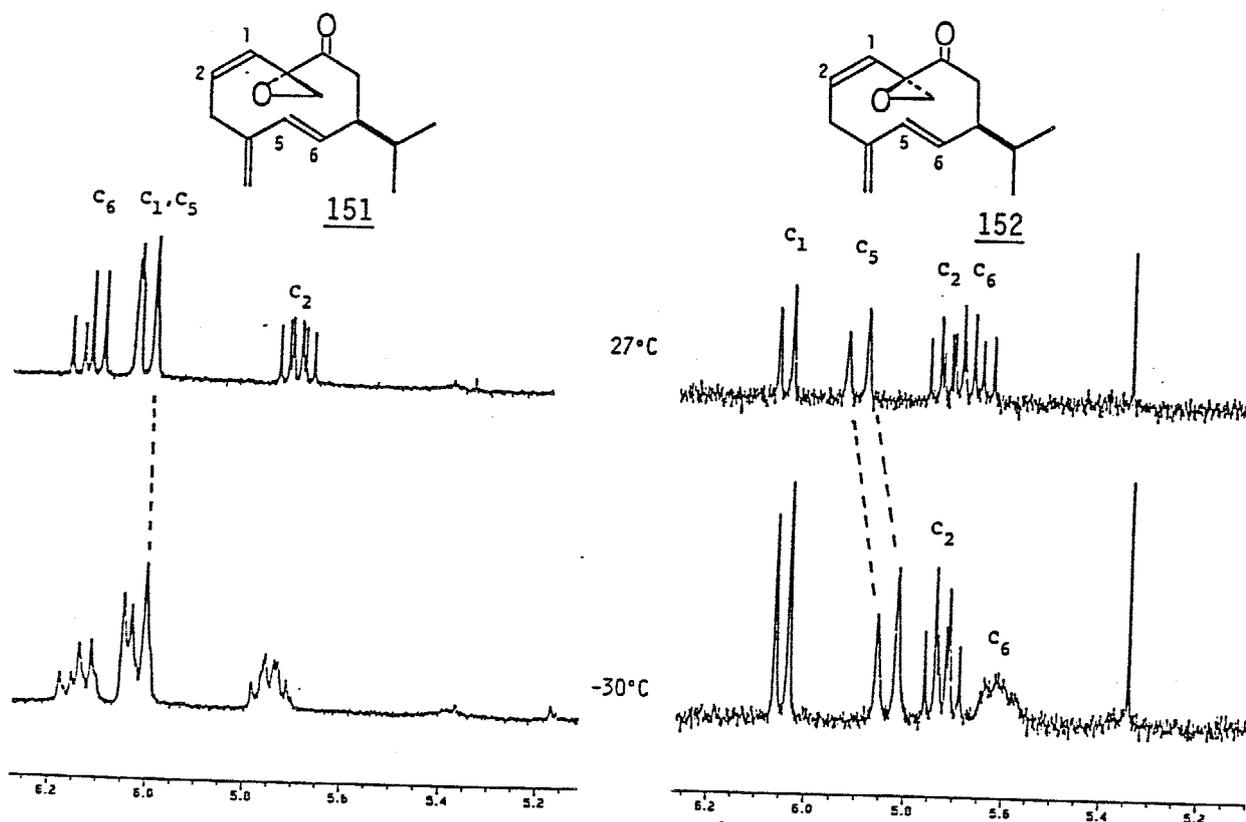
transannular contact                2.24 Å



( Fig. 5-4 )

これらの結果から、151は、ほとんど1つの配座異性体だけが存在していると予想される。そこで151のNMRスペクトルはIの立体配座が測定されたものと考えられる。これに対し、多くの配座異性体が存在していると予想される152のNMRスペクトルは、配座異性体の平均として測定されると考えられる。したがって1つの配座異性体しかない151のスペクトルは低温測定においても変化せず、152では多くの配座異性体間の変換が低温になることにより遅くなり、いくつかの配座異性体に基づくピークへの分裂や、配座異性体の存在比が変化することによる化学シフトの変化などが起こるはずである<sup>20)</sup>。

そこで実際にNMRの低温測定を行った。Fig. 5-5に27 °Cと-30 °Cの結果を示した。



( Fig. 5-5 )

その結果、151ではNMRの低温測定によるピークの分裂あるいは化学シフトの変化がほとんど見られなかったのに対し、152ではC-6のプロトンがブロードし、C-5のジエンのプロトンは高磁場にシフトした。したがって151は1つの配座異性体の存在が、152は少なくとも2つ以上の配座異性体の存在が考えられ、計算結果と比較して151、152の立体化学を図のように決定した。

151のNMRスペクトルはHauptmannらのIIIAと、152はMacdonaldらのIIIBと一致したことから彼らの提唱した立体化学が正しいことが決定できた。

#### 5-5 生物活性試験<sup>105)</sup>

生物活性試験は、実際にワモンゴキブリの性フェロモンの単離を行っている、京都大学の高橋正三教授と共同で行った。ゴキブリの雄の、性フェロモンに対する反応性は、雄の状態、環境の条件付けなどの要因に、かなり敏感なことが知られており、次に示す厳密な条件下ワモンゴキブリ (*Periplaneta americana*)、ヤマトゴキブリ (*Periplaneta japonica*)、トビイロゴキブリ (*Periplaneta brunnea*)、トウヨウゴキブリ (*Blatta orientalis*)、コワモンゴキブリ (*Periplaneta australasia*)、クロゴキブリ (*Periplaneta fuliginosa*) について活性試験を行った (Table 5-1,2)。

##### <条件>

- ≡ 検定用に用いる雄成虫は、予め雌成虫から一ヶ月以上隔離した。
- ≡ 生物検定は、12L-12Dの光条件の暗期に行った (19:00 on/5:00 off)。
- ≡ 生物検定を行った部屋は、25 °C ± 2 °C に調節した。

##### <方法>

一定量の試料を 2 cm平方のガラス板の上に付け、雄のシェルターの前 5 cmの所に置く。雄はシェルターから出てきてガラス板に対して交尾行動 (羽を左右にひろげてふるわせ、いわゆる dragonfly posture をとったり、腹部末端を突き出すなどの行動) をとる。30秒-1分間にガラスのまわりに集まってきた雄の数を調べる。反応の程度を表すために次の基準を設け、(-)(+)(++)(+++)の4段階表示を行った。

(-) 集まらないとき

(+) 1分以内に10匹以下の雄が集まったとき。

(++) 30秒以内に10匹以上の雄が集まったとき。

(+++) 試料のついたガラス板を置くとすぐに30匹以上の雄が集まったとき。

< 検定結果 >

Table 5-1 Behavioral responses of six species to synthetic 151

Male	Dose (g)					Behavior observed
	$4 \times 10^{-11}$	$4 \times 10^{-10}$	$4 \times 10^{-9}$	$4 \times 10^{-8}$	$4 \times 10^{-7}$	
<i>P. americana</i>	++	++	+++	+++	+++	Attracted to the source
<i>P. japonica</i>	-	-	-	+	+	Walking around the source, not attracted, a few raised wings
<i>P. brunnea</i>	-	-	-	+	++	Slowly attracted
<i>B. orientalis</i>	-	-	-	+	++	Running around
<i>P. australasiae</i>	-	±	+	++	++	Running around, not attracted, a few raised wings and short flight
<i>P. fuliginosa</i>	-	-	-	-	-	Antennal waving

Table 5-2 Behavioral responses of six species to synthetic 152

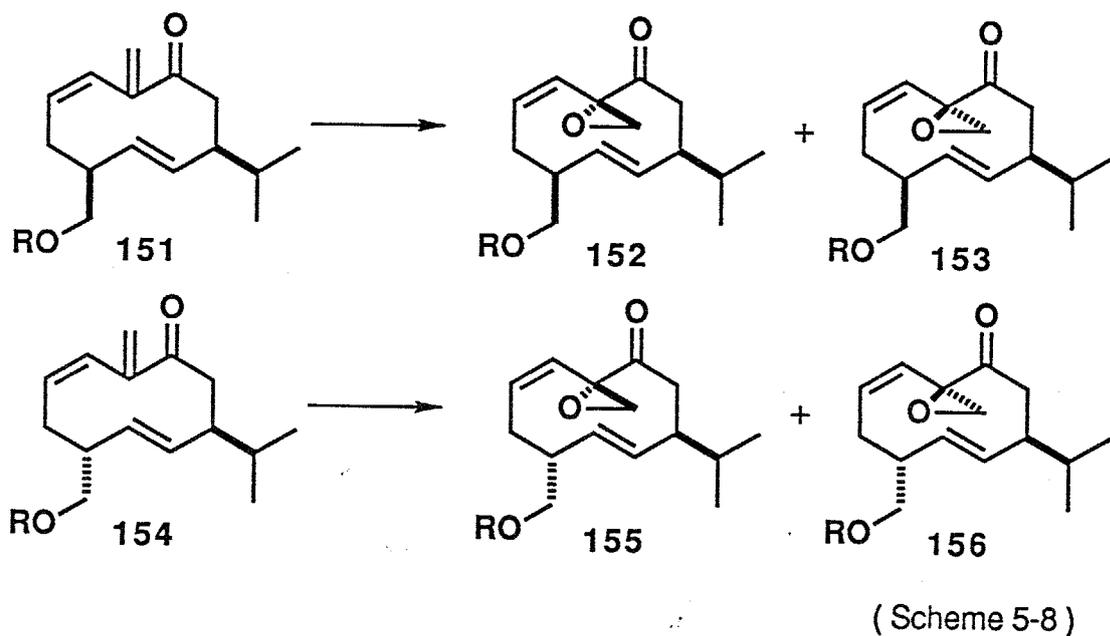
Male	Dose (g)					Behavior observed
	$4 \times 10^{-10}$	$4 \times 10^{-9}$	$4 \times 10^{-8}$	$4 \times 10^{-7}$	$4 \times 10^{-6}$	
<i>P. americana</i>	-	+	++	++	+++	Attracted to the source
<i>P. japonica</i>	-	-	-	-	+	Walking around, a few raised wings
<i>P. brunnea</i>	-	-	-	-	+	Slowly attracted, a few raised wings
<i>B. orientalis</i>	-	-	-	-	+	Running around
<i>P. australasiae</i>	-	-	-	±	+	Running around, a few raised wings
<i>P. fuliginosa</i>	-	-	-	-	-	Antennal waving

この結果、ワモンゴキブリに対し 151 は 152 の1000倍の活性があることがわかり、Hauptmannらの単離した IIIA が真のPAと考えられた。また 151, 152 は他のヤマトゴキブリ, トビイロゴキブリ, コワモンゴキブリ, トウヨウゴキブリの雄にもフェロモン活性があった。

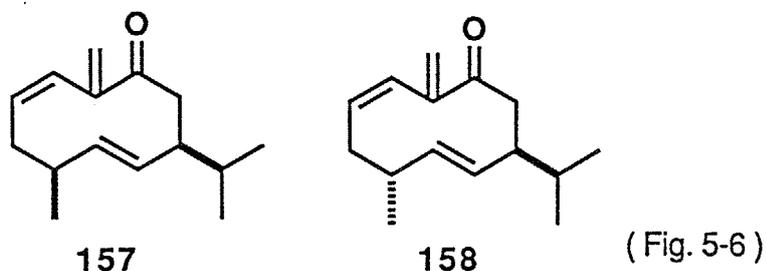
5-6 合成中間体の設計

エノン140は、分子力場計算の結果からわかるように、多くの立体配座をとることができるため、エポキシ化の立体選択性がないものと考えられる。

そこで、エポキシ化の立体化学を制御するために140の官能基を変えることによって立体配座を規制しようと考えた。すなわち、次に示す中間体151, 154を考えた (Scheme 5-8)。



これら中間体のエポキシ化の立体選択性を予測するためMM2による立体配座解析を行った。ただし計算は簡略化のためアルコキシメチル基をメチル基とした157, 158で行った (Fig. 5-6)。



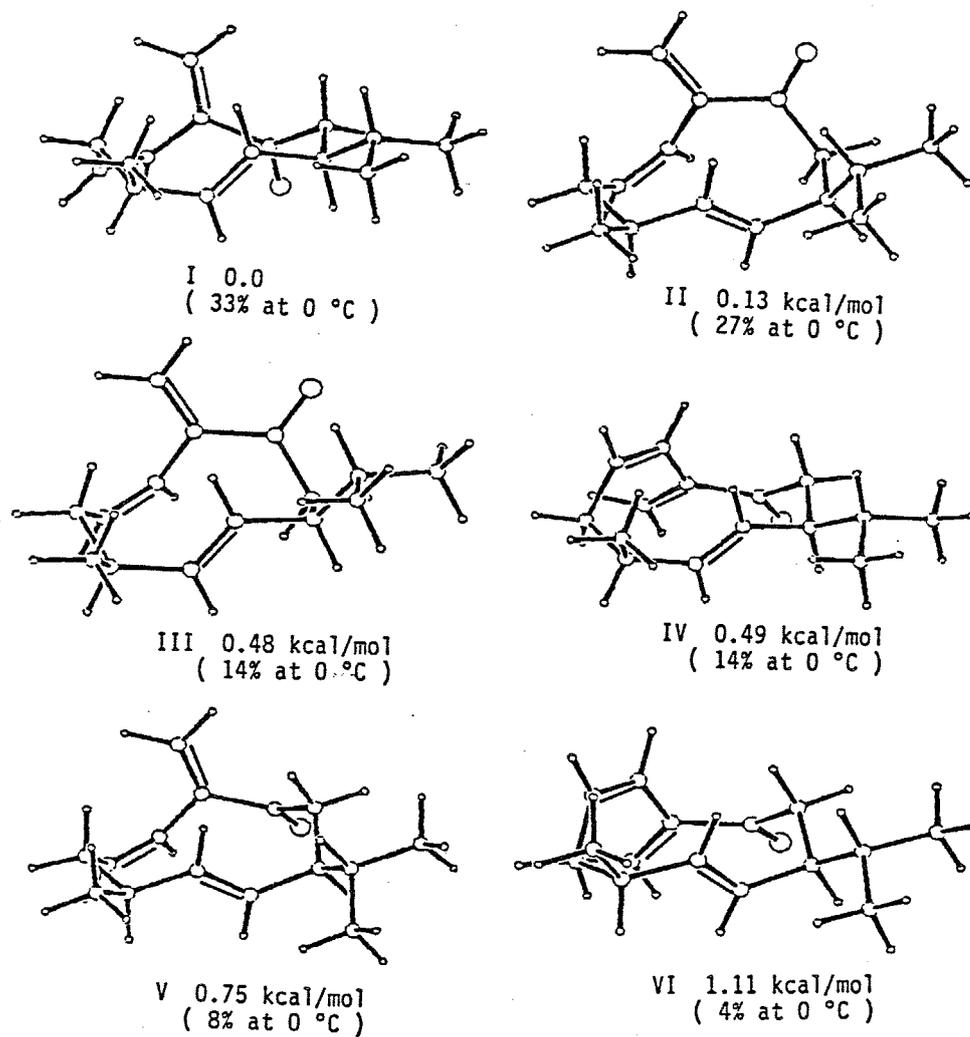
157について MMR Sを用いて次の条件で

dihedral angle resolution 30 deg

closure distance 1.0-2.4 A

transannular contact 2.4 A

61個の初期入力座標を得、MM2で構造最適化を行ったところ、2.5 kcal以内に6つの配座異性体の存在がわかった (Fig. 5-7)。



( Fig. 5-7 )

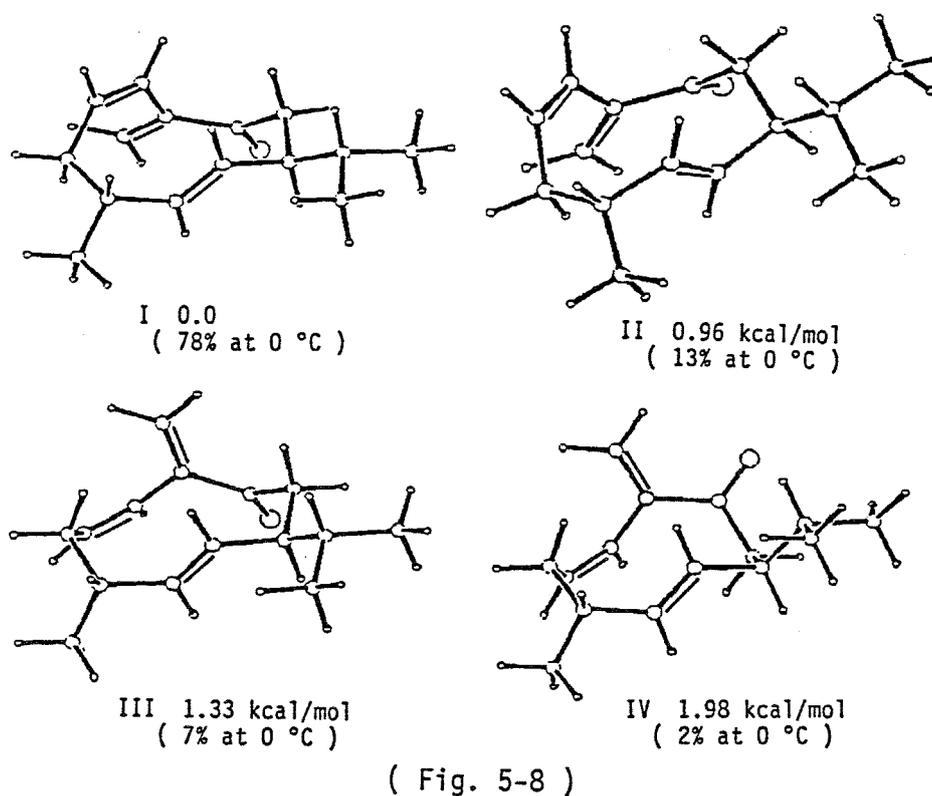
158について同様にMMRSを用いて次の条件で

dihedral angle resolution 30 deg

closure distance 1.0-2.4 A

transannular contact 2.4 A

60個の初期入力座標を得、MM2により構造最適化を行ったところ 2 kcal以内  
に、4つの配座異性体の存在がわかった (Fig. 5-8)。



この結果、先の計算と同様に、立体配座の存在比が単純に生成物の立体化学に  
反映すると仮定し、Boltzmann分布から0 °Cで次のような予測を得た。

157 → エポキシ化  $\beta : \alpha = 1 : 5$

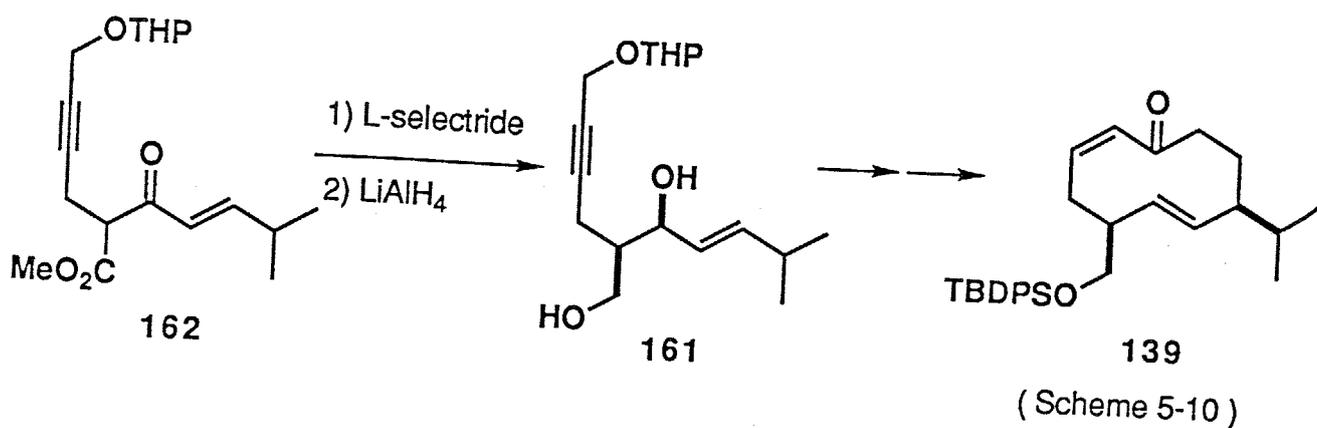
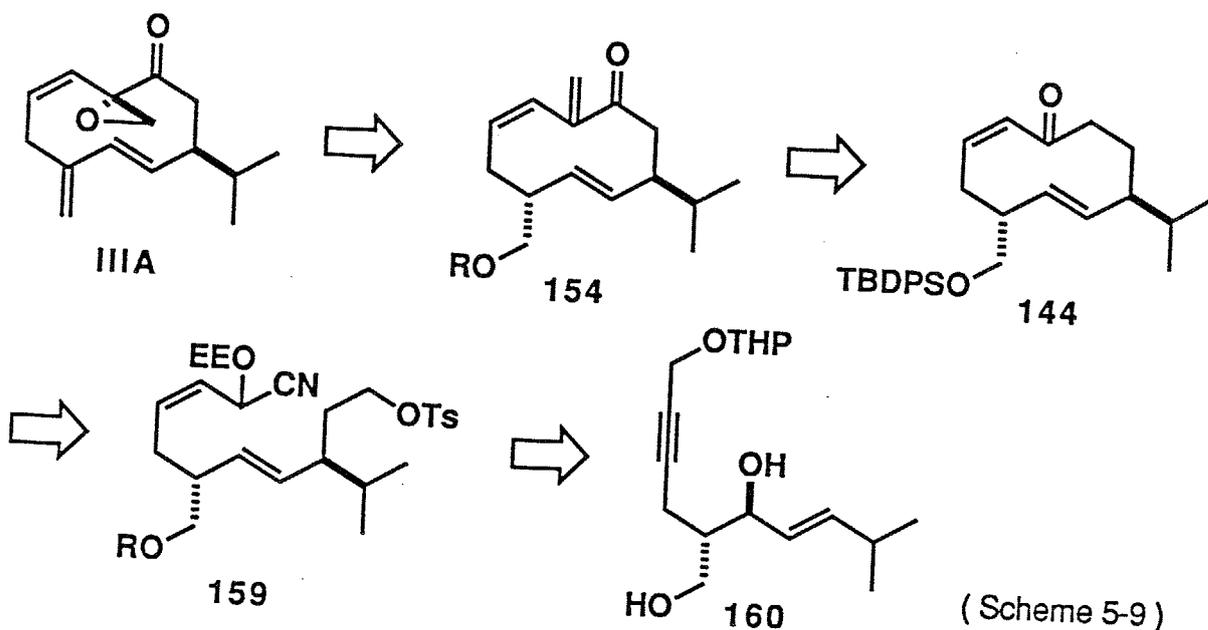
158 → エポキシ化  $\beta : \alpha = 10 : 1$

したがって、158と154では環の立体配座がほとんどかわらないと考えら  
れるので、154を中間体とすれば $\beta$ -エポキシ体155が合成上十分高い立体  
選択性で得られると考えられる。

5-7 IIIAの立体選択的な合成の計画

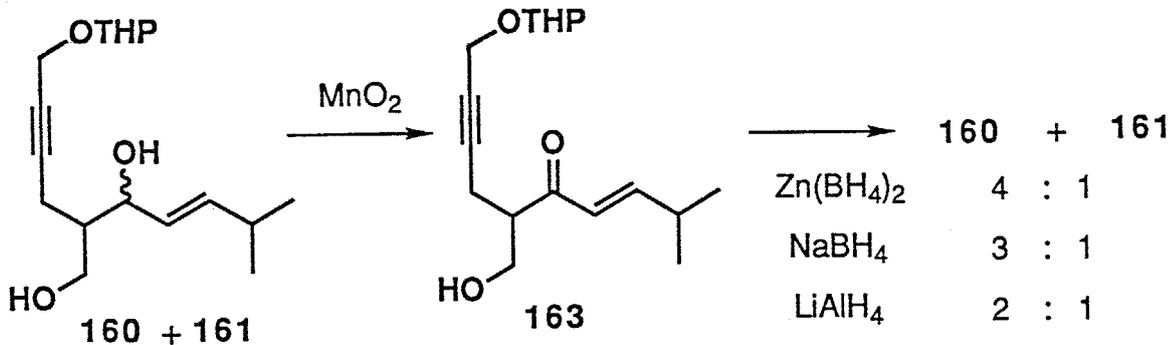
合成計画をScheme 5-9に示した。

IIIAはエノン154に対しエポキシ化した後、脱保護して得られる水酸基を脱離することにより導く。154はエノン144の $\alpha'$ 位に酸素官能基を導入した後、カルボニル基をエキソメチレンへ変換して導く。エノン144は保護したシアンヒドリン159の分子内アルキル化反応により導く。159はアリルアルコール160のJohnson-Claisen転位反応で必要な炭素鎖、トランス二重結合、およびアルコキシメチル基とイソプロピルの立体化学を一挙に構築できる。当研究室で既に報告しているPBの合成では、160のトレオ異性体161を $\beta$ -ケトエステル162のL-Selectrideを用いた還元反応で選択的に得、139へ導いていることから<sup>43)</sup> (Scheme 5-10)、エリトロ体160が得られるなら144を選択的に合成できると考えた。



## 5-8 実験結果

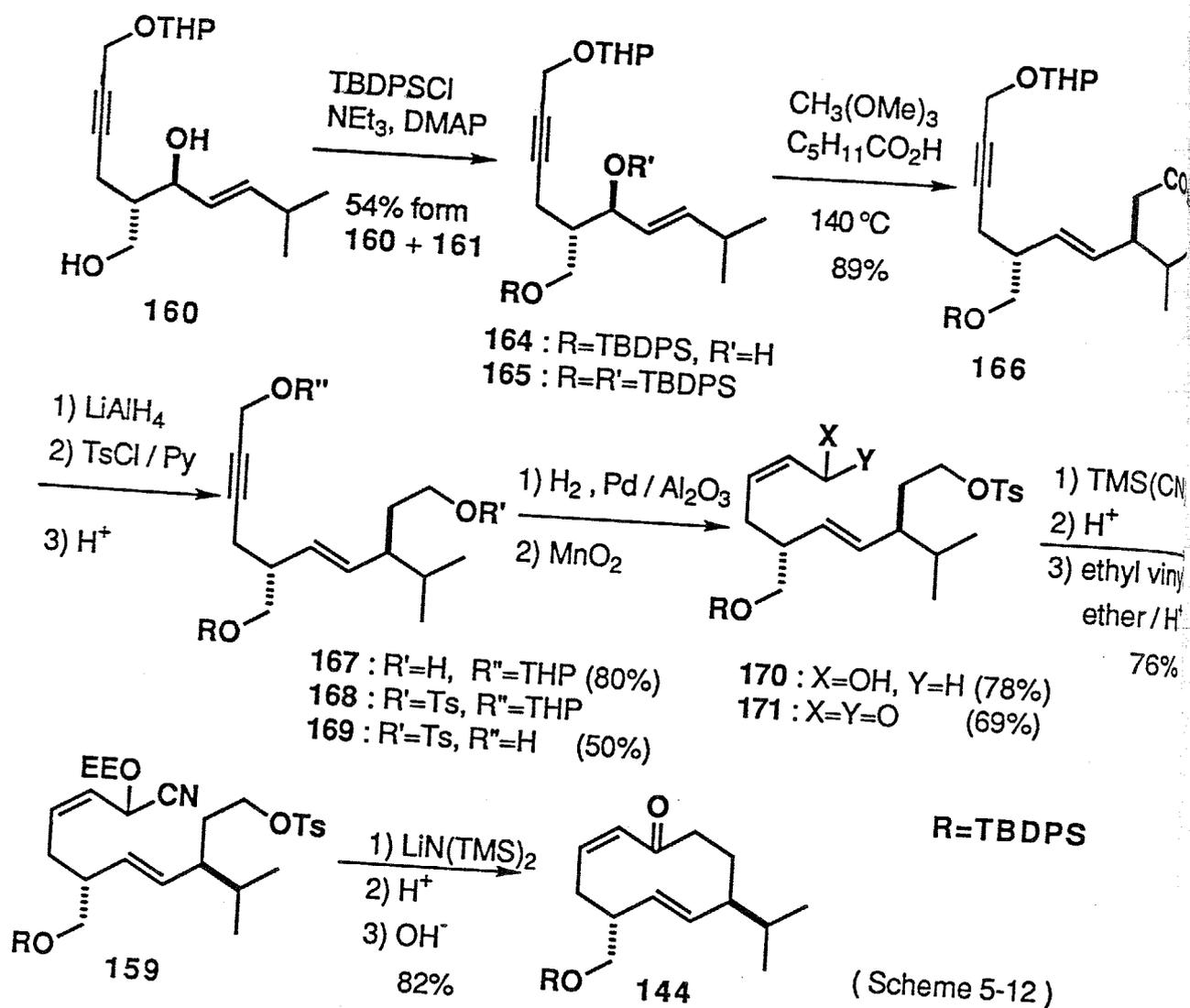
160, 161の混合物をMnO<sub>2</sub>で一度エノン163に変換した後、Zn(BH<sub>4</sub>)<sub>2</sub>を用いて0℃で還元すると160:161=4:1で得られた(Scheme 5-11)。この異性体の比は生成物を酸性条件下で処理して得られるトリオールについてHPLC分析を行い、PB合成の際の結果と比較することにより決定した。



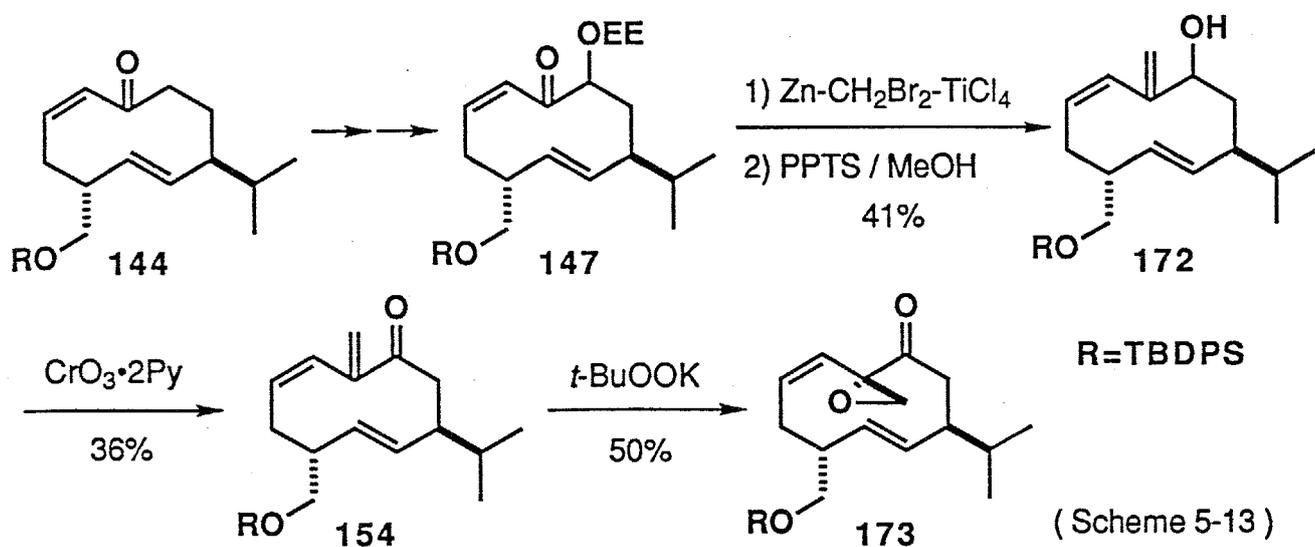
(Scheme 5-11)

なお163をNaBH<sub>4</sub>で還元したときは3:1, LiAlH<sub>4</sub>では2:1比で求める160を主生成物として与えた。この段階で160と161の分離は行わず合成を進めた。(以下主生成物だけを示す。)

まず、ジオール160の1級アルコールだけを保護した。(t-BuPh<sub>2</sub>SiCl/DMAP / Et<sub>3</sub>N, 0℃, 54%)。このシリル化はイミダゾール, DMF中で行うとジシリル体165を与える。得られたシリルエーテル164を用いJohnson-Claisen転位反応を行い(CH<sub>3</sub>C(OMe)<sub>3</sub>/H<sup>+</sup>, 140℃)、エステル166へ収率89%で導いた。このときC-5位のC-O不斉をC-C不斉へと誘起している。166のエステルを還元し、アルコール167とした(LiAlH<sub>4</sub>, 0℃, 80%)。この時副生物として三重結合が還元されたと思われる生成物も得られた。167をトシル化(TsCl/Py)した後、168のTHPを除去し(p-TsOH/MeOH)、アルコール169へ収率50%で導いた。さらに169の三重結合をLindlar触媒を用いて水素雰囲気下、シスの二重結合へ還元し(78%)、続いて170の水酸基をMnO<sub>2</sub>で酸化してエナール171を収率69%で得た。171は常法に従い、保護したシアニドリン159へ収率76%で変換した。閉環反応はLiN(TMS)<sub>2</sub>のジオキサン溶液中に80℃で159を滴下して行った。生成物を単離することなく、希酸, 希塩基処理を行って、目的の10員環エノン144へ収率82%で導いた(Scheme 5-12)。



エノン 144 は Scheme 5-5, 6 に従い 147 へ変換した。エノン 147 に Zn- $\text{CH}_2\text{Br}_2\text{-TiCl}_4$  (106) を  $0^\circ\text{C}$  で反応させてエキソメチレンを構築し、続いて PPTS/MeOH 条件下で脱保護して、アリルアルコール 172 を収率 41% で得た。172 を Collins 酸化し ( $\text{CrO}_3 / 2\text{ eq Py}$ , 36%)、鍵中間体 154 を得ることができた。エポキシ化反応は  $t\text{-BuOOH}$  を THF 溶媒中 KH で処理して生じたアニオン溶液中に、 $-20^\circ\text{C}$  でエノン 154 を滴下して行った。その結果エポキシド 173 が収率 50% で得られ、HPLC の分析では異性体を見いだすことが出来なかった (Scheme 5-13)。



#### 5-9 まとめ (Fig. 5-9)

1988年西野らによってHauptmannと同様にIIIAがワモンゴキブリから単離された<sup>107)</sup>。さらに志津里らはHauptmannらの中間体140からIIIA, IIIBの合成を行い、筆者らと同様の結果 (IIIA: IIIB = 53: 37, -23 °C) を得、IIIAは  $5 \times 10^{-10}$  g/mLで活性を示したもののIIIBは  $10^{-6}$  g/mLでも活性を示さなかったと報告している<sup>108)</sup>。そこでHauptmannらの単離したIIIAが真のPAで、PersoonsらのPAは単離の際転位反応が進行したartefactの可能性が高まった。

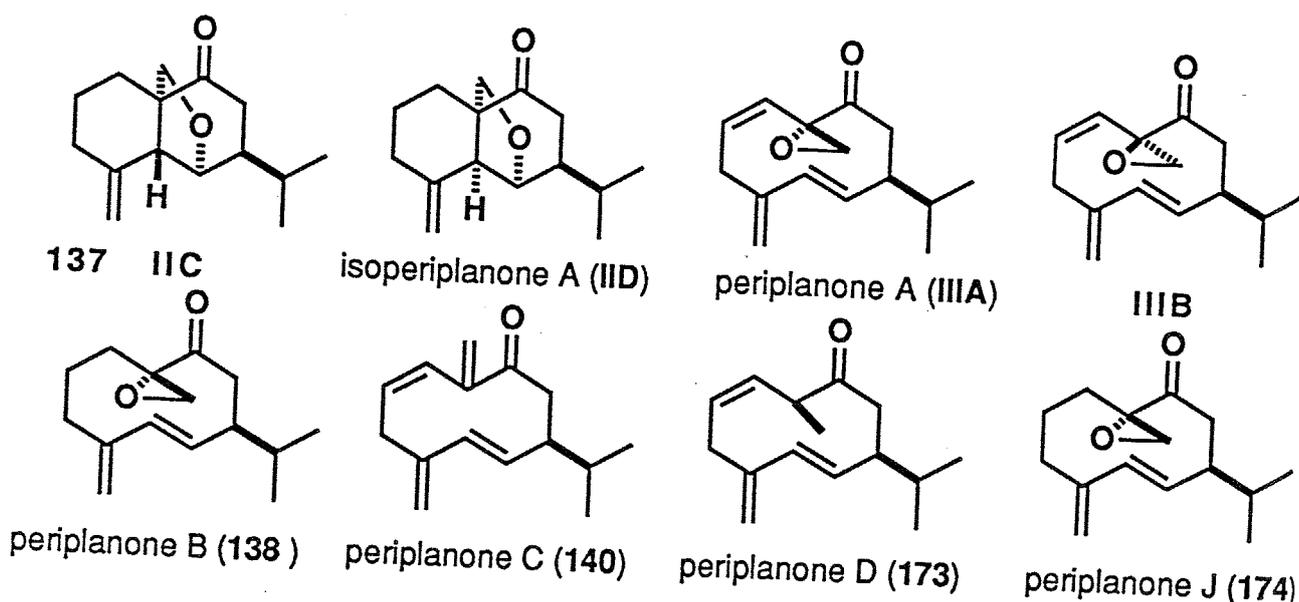
1989年森らによりIICが合成され、PersoonsらのPAの転位生成物と一致することが報告された<sup>109)</sup>。

1990年志津里らは彼らの提唱していたIIDの合成を行い、PersoonsらのPAのスペクトルと比較したが一致しなかったと報告した<sup>110)</sup>。

桑原らは1990年、光学活性体のIIIAを合成し、X線結晶解析から絶対配置を含めIIIAの立体構造を完全に決定した<sup>111)</sup>。さらにPersoonsらのPAは、HauptmannらのPA (IIIA) の熱転位生成物であると考え、IIIAの220 °Cのガスクロマトグラフィーから転位生成物IIDを得、その誘導体のX線結晶解析から立体構造を決定した。IIDのMS, IR, NMRのスペクトルデータはPersoonsらのPAと完全に一致した。IIDには生物活性はなくPersoonsらのPAはartefactであることがわかった。

1990年、Persoons, Ritter, Verwiel, Hauptmann, 森らは<sup>112)</sup> IIIAをペリプラノンAとし、IIDをイソペリプラノンAと提出した。さらにBiendlらによって単離された2つの活性物質<sup>113)</sup>をペリプラノンC (140) およびペリプラノンD (173) とすることを報告した。

また1990年、京都大学の高橋正三らによりヤマトゴキブリの性フェロモンとして単離されたペリプラノンJ (174) は<sup>114)</sup>、微量でNMRスペクトルがないことから、その推定構造が提出されているにすぎず、当研究室でその立体構造の決定のために合成を行っている。



(Fig. 5-9)

### 5-10 今後の展開

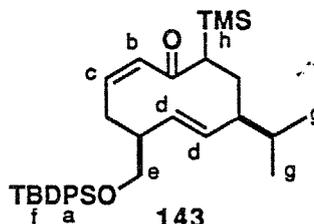
ペリプラノンA (IIIA) の立体構造はペリプラノンB (138) のX線の構造に非常に類似している。これに対しIII Bはこれらと同じ立体配座をとる配座異性体の確率が低く、活性発現のためにはPA, PBと同じ3次元構造が必要であると考えられる。さらに、活性発現のためにどの置換基がどの位置にあることが不可欠であるかを3次元構造解析と合成品による生物活性試験との比較から明らかにすれば、活性の高い類縁体の創作にもつながる。MM2を用いる立体配座の解析は、立体選択性の予測や中間体の設計としてだけでなく、生物活性と3次元構造の関係を明らかにする第一歩としても意義が大きいと考える。

## EXPERIMENTAL SECTION

### C-silylation of 139

In a dried two-necked flask were placed dry THF (1 mL) and diisopropylamine (0.037 mL, 0.26 mmol) under nitrogen. To this solution was added butyllithium (1.57 N, 0.16 mL, 0.25 mmol) dropwise at 0 °C. After 5 min, the solution was cooled to -78 °C. The enone 139<sup>43)</sup> (30 mg, 0.065 mmol) was added dropwise to that solution which became yellowish. After the mixture was stirred for 15 min at -78 °C, trimethylsilyl chloride (0.025 mL, 0.22 mmol) was added to the reaction mixture. After being stirred for 15 min at -15 °C, the reaction mixture was poured into an aqueous solution of saturated sodium bicarbonate. The aqueous layer was extracted with pentane and the combined organic layer was washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel to give the C-silylated product 143 (15 mg, 0.027 mmol, 41%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.2-7.7 (m, 10H, a), 6.14 (d, 1H, b, J = 12.0 Hz), 5.64 (ddd, 1H, c, J = 9.8, 9.8, 12 Hz), 4.8-5.3 (m, 2H, d), 3.4-3.8 (m, 2H, e), 1.2-2.6 (m, 8H), 1.02 (s, 9H, f), 0.84 (d, 3H, g, J = 6.5 Hz), 0.76 (d, 3H, g, J = 6.5 Hz), 0.05 (s, 9H, h)



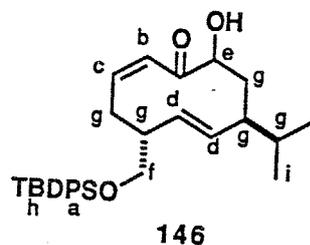
(4*S*\*,7*R*\*)-(5*E*,9*Z*)-7-(*t*-butyldiphenylsilyloxy)methyl-2-hydroxy-4-isopropyl-5,9-cyclodecadien-1-one (146)

In a dried two-necked flask were placed dry THF (1 mL) and diisopropylamine (0.042 mL, 0.3 mmol) under nitrogen. To this solution was added butyllithium (1.68 N, 0.17 mL, 0.29 mmol) dropwise at 0 °C. After 5 min, the solution was cooled to -78 °C. The enone 144<sup>43)</sup> (35 mg, 0.074 mmol) was added dropwise to that solution which became yellowish. After the mixture was stirred for 45 min at -30 °C, trimethylsilyl chloride (0.025 mL, 0.22 mmol) was added to the reaction mixture. After 15 min, the reaction mixture was poured into saturated sodium bicarbonate. The aqueous layer was extracted with pentane and the combined organic layer was washed with brine and dried over MgSO<sub>4</sub>. After

removal of the solvent, the residue was used for the next reaction without further purification.

To a mixture of mCPBA (34 mg, 0.15 mmol) and hexane (8 mL) which was stirred for 30 min at room temperature was added the solution of the silyl enol ether 145 in hexane (5 mL) at -20 °C. After being stirred for 30 min, the reaction mixture was poured into an aqueous solution of sodium thiosulfate. The aqueous layer was extracted with ether, and the organic layer was washed with saturated sodium bicarbonate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was chromatographed on silica gel (elution with 1:9 hexane:ethyl acetate) to give the hydroxyketone 146 (27 mg, 0.06 mmol, 81%).

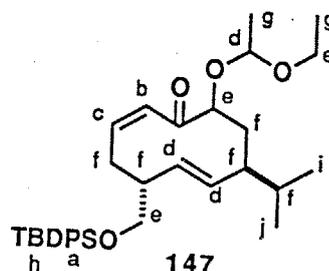
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.2 -7.7 (m, 10H, a), 6.56 (d, 1H, b, J = 11.6 Hz), 5.90 (ddd, 1H, c, J = 9.0, 9.0, 11.6 Hz), 4.7 -4.9 (m, 2H, d), 3.84-4.1 (br, 1H, e), 3.7 (dd, 1H, f, J = 6.2, 10.3 Hz), 3.56 (dd, 1H, g, J = 6.9, 10.3 Hz), 1.6 -2.6 (m, 7H, g), 1.04 (s, 9H, h), 0.91 (d, 3H, i, J = 4.6 Hz), 0.82 (d, 3H, j, J = 4.6 Hz)



(4*S*\*,7*R*\*)-(5*E*,9*Z*)-7-(*t*-butyldiphenylsilyloxy)methyl-2-(1-ethoxyethoxy)-4-isopropyl-5,9-cyclodecadien-1-one (147)

To a mixture of the alcohol 146 (41 mg, 0.086 mmol) in dichloromethane and ethyl vinyl ether (0.06 mL, 0.6 mmol) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After being stirred for 30 min at the same temperature, the reaction mixture was poured into saturated sodium bicarbonate. The aqueous layer was extracted with ether and the organic layer was washed with brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was column chromatographed on silica gel to give the ether 147 (41 mg, 0.075 mmol, 87%).

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 7.2 -7.8 (m, 10H, a), 6.58,6.62 (d, 1H, b, J = 11.6 Hz), 5.7 -6.1 (m, 1H, c), 4.4 -4.9 (m, 3H, d), 3.2 -4.0 (m, 5H, e), 1.5 -2.8 (m, 5H, f), 1.1 -1.35 (m, 6H, g), 1.04 (s, 9H, h), 0.89 (d, 3H, i, J = 3.1 Hz), 0.82 (d, 3H, j, J = 3.1 Hz)



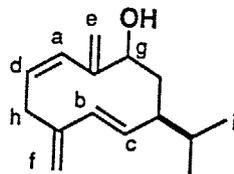
**(3Z,7E)-9-isopropyl-2,6-divinylidene-3,7-cyclodecadien-1-ol (149)**

To a solution of the silyl ether 147 (204 mg, 0.37 mmol) in THF (5 mL) was added tetrabutylammonium fluoride (200 mg, 0.74 mmol) at room temperature. After being stirred for 1 h at the same temperature, the reaction mixture was poured into brine and extracted with ether. The combined organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*.

A mixture of the residue and *o*-nitrophenyl selenocyanate (359 mg, 1.58 mmol) in THF (5 mL) was treated with tributylphosphine (0.4 mL, 1.58 mmol) at room temperature. After 30 min, 35% hydrogen peroxide (1 mL) was added to the mixture at 0 °C, and the reaction mixture was stirred for 10 h at room temperature. Then the solution was poured into an aqueous solution of sodium thiosulfate. The aqueous layer was extracted with ether, and the combined extracts were washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was purified by short column chromatography on silica gel to give the diene 148.

To a solution of the enone 148 in dry THF (5 mL) was added a benzene solution of  $\text{Cp}_2\text{TiCH}_2\text{ClAlMe}_2$  (0.176 N, 6.5 mL, 1.14 mmol) at room temperature. The mixture was stirred for 1 h at the same temperature, and 2% NaOH was added dropwise to the reaction mixture at 0 °C. The aqueous layer was extracted with ether and the combined organic layer were washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was dissolved in methanol (4 mL) and dichloromethane (1 mL). A catalytic amount of pyridinium *p*-toluenesulfonate was added to the solution at room temperature. After being stirred for 3 h at the same temperature, the reaction mixture was poured into ice-cooled saturated sodium bicarbonate. The aqueous layer was extracted with ether and the organic layer was washed with brine and dried over  $\text{MgSO}_4$ . After removal of the solvent, the residue was column chromatographed on silica gel (elution with hexane:ether 4:1) to give the alcohol 149 (20 mg, 0.092 mmol, 25% from the ether 147).

$^1\text{H NMR}$  (90 MHz,  $\text{CDCl}_3$ )  $\delta$  6.0 (d, 1H, a,  $J = 12.0$  Hz), 5.7 (d, 1H, b,  $J = 16.0$  Hz), 5.48 (dd, 1H, c,  $J = 3.9, 16.0$  Hz), 5.44 (ddd, 1H, d,  $J = 7.2, 8.2, 12.0$  Hz), 5.28 (s, 1H, e), 5.02 (s, 1H, e), 4.87 (s, 1H, f), 4.70 (s, 1H, f), 3.8-4.0 (m, 1H, g), 3.28 (dd, 1H, h,  $J = 8.2, 13.0$  Hz), 2.73 (dd, 1H, f,  $J = 7.2, 13.0$  Hz), 0.92 (d, 3H, i,  $J = 6.4$  Hz), 0.84 (d, 3H, i,  $J = 6.4$  Hz)



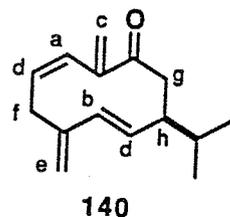
149

**(3Z,7E)-9-isopropyl-2,6-divinylidene-3,7-cyclodecadien-1-one (140)**

To a solution of pyridine (0.42 mL, 5.4 mmol) and dichloromethane (1.5 mL) was added chromium oxide (245 mg, 2.45 mmol) at 0 °C. After the mixture was stirred for 30 min, a solution of the alcohol 149 (16 mg, 0.07 mmol) was added to the solution at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was diluted with 7:3 ether:hexane. This solution was passed through a short pad of florisil and concentrated *in vacuo*. The residue was purified by short column chromatography on silica gel to give the enone 140 (10 mg, 63%).

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 1% ethyl acetate in hexane, 2.67 mL / min); Rt=26.5-28.5 min

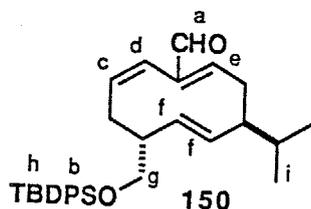
<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 6.2 (d, 1H, a, J = 11.3 Hz), 5.82 (d, 1H, b, J = 15.4 Hz), 5.73 (s, 1H, c), 5.36-5.72 (m, 2H, d), 5.44 (s, 1H, c), 4.90 (s, 1H, e), 4.70 (s, 1H, e), 3.40 (dd, 1H, f, J = 9.8, 10.3 Hz), 3.00 (dd, 1H, f, J = 10.3, 10.3 Hz), 2.58 (dd, 1H, g, J = 6.9, 13.0 Hz), 2.37 (dd, 1H, g, J = 7.7, 13.0 Hz), 1.9 -2.2 (m, 1H, h), 0.95 (d, 3H, i, J = 6.7 Hz), 0.84 (d, 3H, i, J = 6.7 Hz)



**oxidation of 146 with manganese(IV) oxide**

A mixture of the alcohol 146 (10 mg, 0.02 mmol) and manganese(IV) oxide (50 mg, 0.57 mmol) in hexane (1 ml) was stirred at room temperature for 12 h. The reaction mixture was filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was column chromatographed on silica gel to give the enal 150 (5 mg, 0.01 mmol, 50%)

<sup>1</sup>H NMR (90 MHz, CDCl<sub>3</sub>) δ 8.85 (d, 1H, a, J = 1.3 Hz), 7.3-7.7 (m, 10H, b), 5.70 (ddd, 1H, c, 9.0, 10.3, 11.6 Hz), 5.25 (d, 1H, d, J = 11.6 Hz), 5.10 (m, 1H, e), 4.5-5.0 (m, 2H, f), 3.4-3.8 (m, 2H, g), 1.2-2.4 (m, 7H), 1.04 (s, 9H, h), 0.93 (d, 3H, i, J = 3.8 Hz), 0.85 (d, 3H, 3.8 Hz)



## epoxidation of 140

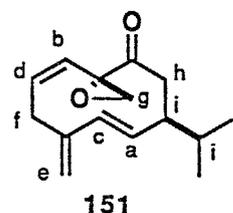
To a suspension of potassium hydride (40 mg, 1 mmol) which was washed with dry hexane, in THF (5 mL) was added anhydrous TBHP (3.4 M, 0.3 mL, 1 mmol) at -20 °C. After 15 min, a solution of the enone **140** (4 mg, 0.018 mmol) was added dropwise to 1 mL of above solution at 0 °C. The reaction mixture was stirred for 30 min at the same temperature, and then poured into cold-water. The aqueous layer was extracted with ether and the combined organic layer was washed with saturated sodium thiosulfate, brine and dried over MgSO<sub>4</sub>. After removal of the solvent, the residue was purified by short column chromatography on silica gel to give a mixture (3.3 mg, 0.014 mmol, 80%) of epoxide **151** and **152**. The epoxides were separated by HPLC leading to **151** (1.3 mg) and **152** (1.1 mg), respectively.

### 151

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 2% ethyl acetate in hexane, 2.67 mL / min); Rt=18.0-21.0 min

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 6.08 (dd, 1H, a, J = 8.0, 16.0 Hz), 5.96 (d, 1H, b, J = 6.0 Hz), 5.95 (d, 1H, c, J = 8.0 Hz), 5.66 (ddd, 1H, d, J = 7.2, 8.8, 12.4 Hz), 4.92 (s, 1H, e), 4.77 (s, 1H, e), 3.74 (dd, 1H, f, J = 8.8, 12.0 Hz), 2.87 (d, 1H, g, J = 4.0 Hz), 2.82 (d, 1H, g, J = 4.0 Hz), 2.66 (dd, 1H, h, J = 8.0, 11.6 Hz), 2.56 (dd, 1H, f, J = 7.2, 12.0 Hz), 2.01 (dd, 1H, h, J = 8.0, 14.0 Hz), 1.5 -1.7 (m, 2H, i), 0.87 (d, 3H, j, J = 6.0 Hz), 0.84 (d, 3H, j, J = 6.0 Hz)

MS(EI); m/z 232 (M<sup>+</sup>)

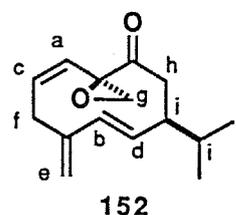


### 152

HPLC (Silica gel 60-5 mm, 7.5 o.d. x 300 mm, elution with 2% ethyl acetate in hexane, 2.67 mL / min); Rt=30.0-35.0 min

<sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 6.00 (d, 1H, a, J = 11.6 Hz), 5.85 (d, 1H, b, J = 16.0 Hz), 5.65 (ddd, 1H, c, J = 8.0, 8.0, 11.6 Hz), 5.59 (dd, 1H, d, J = 8.8, 16.0 Hz), 4.93 (s, 1H, e), 4.79 (s, 1H, e), 3.0 -3.1 (m, 1H, f), 2.88 (d, 1H, g, J = 7.2 Hz), 2.82 (d, 1H, g, J = 7.2 Hz), 2.51 (dd, 1H, h, J = 10.4, 15.2 Hz), 2.48 (dd, 1H, h, J = 10.4, 12.8 Hz), 2.23 (dd, 1H, f, J = 8.0, 8.0 Hz), 1.5 -1.7 (m, 2H, i), 0.92 (d, 3H, j, J = 6.8 Hz), 0.87 (d, 3H, j, J = 6.8 Hz)

MS(EI); m/z 232 (M<sup>+</sup>)

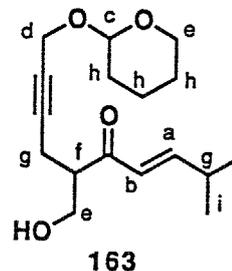


**(E)-2-[4-(tetrahydro-2H-pyran-2-yloxy)-2-butynyl]-1-hydroxy-6-methyl-4-hepten-3-one (163)**

A mixture of the diol 160 and 161<sup>43)</sup> (4.2 g, 14 mmol) and manganese(IV) oxide (12 g, 140 mmol) in dichloromethane (30 mL) was stirred at room temperature for 3 days. The reaction mixture was filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was used for the next reaction without further purification.

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 6.92 (dd, 1H, a, J= 6.4, 15.8 Hz), 6.15 (dd, 1H, b, J= 1.3, 15.8 Hz), 4.77 (brs, 1H, c), 4.22 (brs, 2H, d), 3.35-4.00 (m, 4H, e), 3.13 (t, 1H, f, J= 5.7 Hz), 2.20-2.65 (m, 3H, g), 1.35-1.90 (m, 6H, h), 1.01 (d, 6H, i, J= 6.4 Hz)

IR (neat) 3450, 2950, 1690, 1670, 1630, 1440, 1360, 1270, 1220, 900, 870, 820, 740

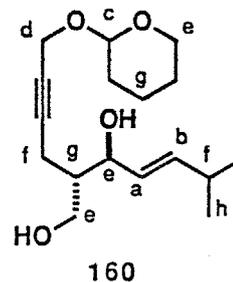


**(2S\*,3S\*)-(E)-2-[4-(tetrahydro-2H-pyran-2-yloxy)-2-butynyl]-6-methyl-4-heptene-1,3-diol (160)**

To a mixture of the crude enone 163 (10 g) in ether (100 mL) was added zinc borohydride (0.397 N in ether, 72 mL) at 0 °C. The mixture was stirred for 30 min. The reaction mixture was quenched with 1 N HCl. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate and brine. The organic mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 5.73 (dd, 1H, a, J= 5.9, 15.7 Hz), 6.15 (dd, 1H, b, J= 6.7, 15.7 Hz), 4.80 (brs, 1H, c), 4.25 (brs, 2H, d), 3.40-4.10 (m, 5H, e), 2.05-2.45 (m, 3H, f), 1.25-2.00 (m, 7H, g), 1.02 (d, 6H, h, J= 6.7 Hz)

IR (neat) 3350, 2950, 1440, 1200, 1120, 1020, 900, 870, 820

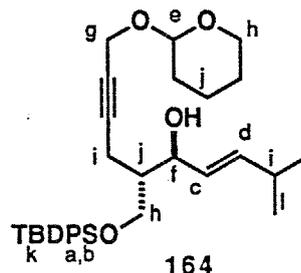


**(5*S*\*,6*S*\*)-(*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-2-methyl-10-(tetrahydro-2*H*-pyran-2-yloxy)-3-decen-8-yn-5-ol (164)**

To a mixture of crude diol **160** (10 g), triethylamine (14 mL) and 4-dimethylaminopyridine (150 mg) in dichloromethane (30 mL) was added dropwise *t*-butylchlorodiphenyl silane (11.1 mL, 41 mmol) at 0 °C. The mixture was stirred for 1 h. The reaction mixture was quenched with 1 N HCl. The aqueous layer was extracted with ether. The organic layer was washed with saturated sodium bicarbonate and brine. The organic mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:5 ether:hexane) to give the alcohol **164** (10 g, 18.6 mmol, 54% from the mixture of alcohol **160** and **161**).

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.60-7.80 (m, 4H, a), 7.30-7.55 (m, 6H, b), 5.73 (dd, 1H, c, J= 5.9, 15.7 Hz), 5.37 (dd, 1H, d, J= 6.7, 15.7 Hz), 4.76 (brs, 1H, e), 4.30-4.45 (m, 1H, f), 4.20 (brs, 2H, g), 3.35-4.00 (m, 4H, h), 2.20-2.55 (m, 3H, i), 1.40-1.90 (m, 7H, j), 1.08 (s, 9H, k), 0.98 (d, 6H, l, J= 6.7 Hz)

IR (neat) 3400, 2950, 2850, 1590, 1470, 1430, 1390, 1360, 1260, 1200, 1110, 1020, 820, 700

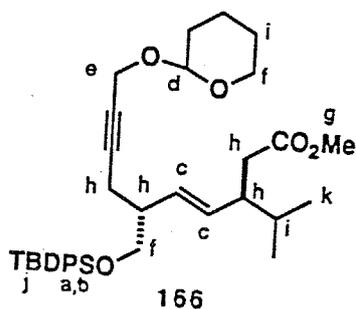


**methyl (3*S*\*,6*R*\*)-(*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-10-(tetrahydro-2*H*-pyran-2-yloxy)-3-isopropyl-4-decen-8-ynoate (166)**

A mixture of the allylic alcohol **164** (12 g, 22.3 mmol) trimethyl orthoacetate (8.5 mL, 67.2 mmol) and a catalytic amount of heptanoic acid in xylene (40 mL) was heated at 140 °C for 2 h with continuous removal of methanol. The reaction mixture was quenched with saturated sodium bicarbonate. The aqueous layer was extracted with ether. The organic layer was washed with brine. The organic mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:10 ether:hexane) to give the ester **166** (11.8 g, 20.0 mmol, 89%).

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.55-7.80 (m, 4H, a), 7.30-7.50 (m, 6H, b), 5.30-5.50 (m, 2H, c), 4.76 (brs, 1H, d), 4.20 (brs, 2H, e), 3.40-3.95 (m, 4H, f), 3.60 (s, 3H, g), 2.20-2.55 (m, 6H, h), 1.40-1.85 (m, 7H, i), 1.04 (s, 9H, j), 0.70-0.95 (m, 6H, k)

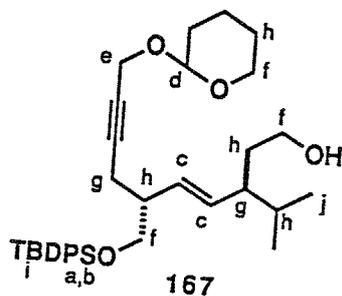
IR (neat) 2950, 2850, 1740, 1590, 1430, 1270, 1200, 1150, 1020, 910, 740, 700



(3*S*\*,6*R*\*)-(*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-3-isopropyl-10-(tetrahydro-2*H*-pyran-2-yloxy)-4-decen-8-yn-1-ol (166)

To a suspension of LiAlH<sub>4</sub> (90 mg, 2.2 mmol) in dry THF was added a solution of the ester 166 (900 mg, 1.5 mmol) in dry THF at 0 °C. After being stirred for 1 h, the reaction mixture was quenched with an aqueous solution of saturated sodium sulfate. The mixture was filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:5 ether:hexane) to give the alcohol 167 (680 mg, 1.2 mmol, 80%).

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.55-7.75 (m, 4H, a), 7.25-7.50 (m, 6H, b), 5.20-5.35 (m, 2H, c), 4.77 (brs, 1H, d), 4.20 (brs, 2H, e), 3.35-3.95 (m, 6H, f), 2.10-2.50 (m, 3H, g), 1.50-1.95 (m, 10H, h), 1.06 (s, 9H, i), 0.75-0.95 (m, 6H, j)  
 IR (neat) 3350, 2950, 2850, 1590, 1470, 1430, 1380, 1250, 1120, 1030, 980, 910, 790, 700, 510

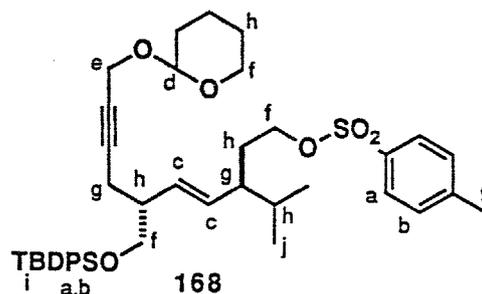


(3*S*\*,6*R*\*)-(*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-3-isopropyl-10-(tetrahydro-2*H*-pyran-2-yloxy)-4-decen-8-ynyl *p*-toluenesulfonate (168)

To a solution of the alcohol 167 (680 mg, 1.2 mmol) in dry pyridine (3 mL) was added *p*-toluenesulfonyl chloride (915 mg, 4.8 mmol) at 0 °C. The mixture was stirred for 3 h. The reaction mixture was quenched with 1 N HCl. The aqueous layer was extracted with ether. The organic layer was washed with saturated sodium bicarbonate and brine. The resulting mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

$^1\text{H NMR}$  ( $\text{CDCl}_3$  90 MHz)  $\delta$  7.55-7.85 (m, 6H, a), 7.30-7.50 (m, 8H, b), 5.10-5.20 (m, 2H, c), 4.77 (brs, 1H, d), 4.19 (brs, 2H, e), 3.40-4.05 (m, 6H, f), 2.20-2.50 (m, 6H, g), 1.40-1.90 (m, 9H, h), 1.05 (s, 9H, i), 0.65-0.85 (m, 6H, j)

IR (neat) 2950, 2850, 1590, 1460, 1420, 1360, 1170, 1110, 1020, 810, 750, 700, 660, 550

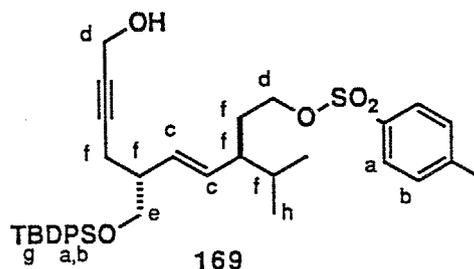


(3*S*\*,6*R*\*)-(*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-10-hydroxy-3-isopropyl-4-decen-8-ynyl *p*-toluenesulfonate (169)

A mixture of the crude tosylate 168 and a catalytic amount of *p*-toluenesulfonic acid in methanol (5 mL) was stirred at room temperature for 1 h. The reaction mixture was quenched with saturated sodium bicarbonate. The aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine. The organic mixture was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:2 ether:hexane) to give the alcohol 169 (390 mg, 0.6 mmol, 50% from the alcohol 167).

$^1\text{H NMR}$  ( $\text{CDCl}_3$  90 MHz)  $\delta$  7.55-7.90 (m, 6H, a), 7.20-7.50 (m, 8H, b), 5.10-5.25 (m, 2H, c), 3.90-4.30 (m, 4H, d), 2.55-2.65 (m, 2H, e), 1.20-2.45 (m, 10H, f), 1.06 (s, 9H, g), 0.70-0.86 (d, 3H, h,  $J = 3.8$  Hz), 0.76 (d, 3H, h,  $J = 3.8$  Hz)

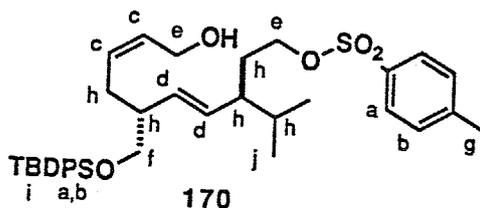
IR (neat) 3550, 2950, 2850, 1600, 1460, 1430, 1360, 1180, 1110, 960, 780, 700, 660



(3*S*\*,6*R*\*)-(4*E*,8*Z*)-6-(*t*-butyldiphenylsilyloxy)methyl-10-hydroxy-3-isopropyl-4,8-decadienyl *p*-toluenesulfonate (170)

A mixture of the alkyne 169 (100 mg, 0.16 mmol) and 10%  $\text{Pd}/\text{Al}_2\text{O}_3$  (20 mg) in methanol was stirred at room temperature for 2 h under a hydrogen atmosphere. The reaction mixture was filtered through florisil. The filtrate was concentrated *in vacuo* to give the allylic alcohol 170 (78 mg, 0.12 mmol 78%).

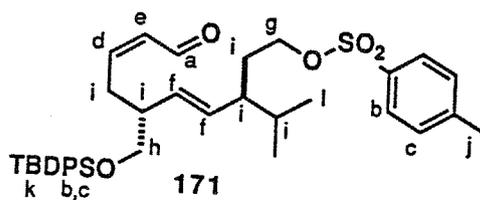
$^1\text{H NMR}$  ( $\text{CDCl}_3$  90 MHz)  $\delta$  7.50-7.85 (m, 6H, a), 7.25-7.50 (m, 8H, b), 5.30-5.70 (m, 2H, c), 5.00-5.20 (m, 2H, d), 3.80-4.20 (m, 4H, e), 3.40-3.90 (m, 2H, f), 2.30-2.45 (m, 3H, g), 1.30-2.30 (m, 7H, h), 1.06 (brs, 9H, i), 0.70-0.95 (m, 6H, j)  
 IR (neat) 3400, 2950, 1740, 1600, 1460, 1360, 1180, 1100, 970, 910, 820, 700, 660, 550, 500



**(3S\*,6R\*)-(4E,8Z)-6-(*t*-butyldiphenylsilyloxy)methyl-3-isopropyl-9-formyl-4,8-nonadienyl *p*-toluenesulfonate (171)**

A mixture of the allylic alcohol 170 (100 mg, 0.16 mmol) and manganese (IV) oxide (137 mg, 1.5 mmol) in hexane (2 mL) was stirred at room temperature for 2 h. The reaction mixture was filtered through florisil. The filtrate was concentrated *in vacuo* to give the enal 171 (69 mg, 0.11 mmol 69%).

$^1\text{H NMR}$  ( $\text{CDCl}_3$  90 MHz)  $\delta$  10.02 (d, 1H, a,  $J = 7.9$  Hz), 7.50-7.80 (m, 6H, b), 7.10-7.50 (m, 8H, c), 6.51 (dt, 1H, d,  $J = 7.7, 11.5$  Hz), 5.92 (dd, 1H, e,  $J = 7.9, 11.5$  Hz), 5.00-5.25 (m, 2H, f), 3.90-4.00 (m, 2H, g), 3.45-3.65 (m, 2H, h), 1.30-3.05 (m, 7H, i), 2.39 (s, 3H, j), 1.03 (s, 9H, k), 0.65-0.85 (m, 6H, l)  
 IR (neat) 2950, 2850, 1680, 1600, 1460, 1430, 1190, 1180, 1110, 970, 910, 780, 700, 660, 560, 500



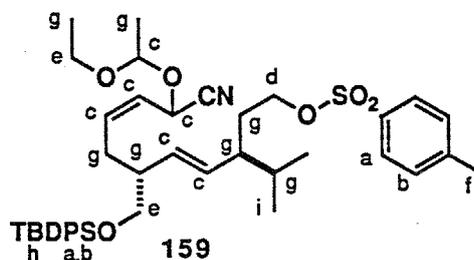
**(3S\*,6R\*)-(4E,8Z)-6-(*t*-butyldiphenylsilyloxy)methyl-10-cyano-10-(1-ethoxyethoxy)-3-isopropyl-4,8-decadienyl *p*-toluenesulfonate (159)**

A mixture of the enal 171 (1.7 g, 2.69 mmol), trimethyl silyl cyanide (0.8 mL, 6 mmol) and a catalytic amount of DC-18-CR-6 KCN was stirred at 0 °C for 30 min. To the mixture was added dry THF (15 mL) and 0.1 N HCl (2 mL). The reaction mixture was stirred at room temperature for 1 h. The organic mixture was washed with brine. The aqueous layer was extracted with ether. The organic layer was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

To a mixture of the cyanohydrin and ethyl vinyl ether (0.36 mL, 4 mmol) in dry benzene (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. After being stirred for 20 min, the reaction mixture was quenched with saturated sodium bicarbonate. The aqueous layer was extracted with ether. The organic layer was washed with brine. The organic mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:10 ether:hexane) to give the protected cyanohydrin **159** (1.5 g, 2.04 mmol, 76% from the enal **171** ).

<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.50-7.85 (m, 6H, a), 7.30-7.50 (m, 8H, b), 4.75-5.80 (m, 6H, c), 3.80-4.10 (m, 2H, d), 3.30-3.70 (m, 4H, e), 2.42 (s, 3H, f), 1.10-2.30 (m, 13H, g), 1.05 (s, 9H, h), 0.65-0.90 (m, 6H, i)

IR (neat) 2950, 2850, 2250, 1800, 1470, 1430, 1190, 1180, 1110, 1050, 910, 820, 740, 700, 660, 560, 500



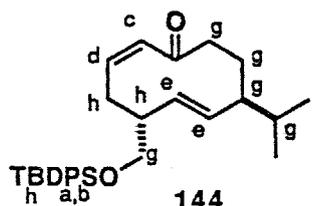
**(4*S*\*,7*R*\*)-(5*E*,9*Z*)-7-(*t*-butyldiphenylsilyloxy)methyl-4-isopropyl-5,9-cyclodecadien-1-one (**144**)**

To a solution of HN(TMS)<sub>2</sub> (3.2 mL, 15 mmol) in dry dioxane (50 mL) was added 1.65 N butyllithium (8.2 mL, 13.5 mmol) at 10 °C. After being stirred for 1 h, to the mixture was added dropwise a solution of the protected cyanohydrin **69** (1 g, 1.37 mmol) in dry dioxane (80 mL) for 6 h at 80 °C under a nitrogen atmosphere. The addition was complete, the reaction mixture was stirred at 80 °C for 30 min. The organic mixture was quenched with saturated ammonium chloride. The aqueous layer was extracted with ether. The organic layer was washed with brine and dried over MgSO<sub>4</sub>. The resulting mixture was concentrated *in vacuo*. The residue was used for the next reaction without further purification.

To a solution of the crude cyclic compound in methanol (20 mL) was added a catalytic amount of *p*-toluenesulfonic acid at 0 °C. The mixture was stirred for 1 h. The reaction mixture was diluted with ether. The organic mixture was quenched with 2% NaOH for 5 min. The aqueous layer was extracted with ether. The organic layer was washed with brine and dried over MgSO<sub>4</sub>. The resulting mixture was concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 10:1 hexane:ether) to give the cyclic enone **144** (520 mg, 1.13 mmol, 82%).

$^1\text{H}$  NMR ( $\text{CDCl}_3$  90 MHz)  $\delta$  7.55-7.70 (m, 4H, a), 7.25-7.45 (m, 6H, b), 6.26 (d, 1H, c,  $J=11.8$  Hz), 5.70 (dt, 1H, d,  $J=8.6, 11.8$  Hz), 4.70-4.85 (m, 2H, e), 3.50-3.80 (m, 2H, f), 1.25-2.60 (m, 9H, g), 1.02 (s, 9H, h), 0.70-0.95 (m, 6H, i)

IR (neat) 2950, 2850, 1690, 1620, 1590, 1460, 1430, 1390, 1110, 990, 820, 740, 700, 610, 500

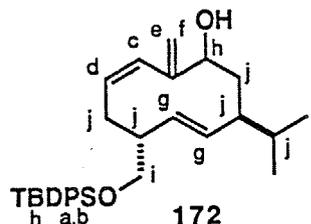


**(6*R*\*,9*S*\*)-(3*Z*,7*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-9-isopropyl-2-vinylidene-3,7-cyclodecadien-1-ol (172)**

To a solution of  $\text{Zn-CH}_2\text{Br}_2\text{-TiCl}_4$ <sup>106)</sup> (0.25 N, 2 mL, 0.5 mmol) in dichloromethane (0.7 mL) was added a solution of the ether 147 (100 mg, 0.18 mmol) in dichloromethane (0.5 mL) at 0 °C. The mixture was stirred for 1 h. The reaction mixture was quenched with saturated sodium bicarbonate. The aqueous layer was extracted with ether. The organic layer was washed with brine. The resulting mixture was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was used for the next reaction without further purification. To a solution of the diene in methanol (2 mL) was added a catalytic amount of pyridinium *p*-toluenesulfonate at 0 °C. The mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with saturated sodium bicarbonate. The aqueous layer was extracted with ether. The organic layer was washed with brine. The resulting mixture was dried over  $\text{MgSO}_4$  and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 1:5 ether:hexane) to give the allylic alcohol 172 (35 mg, 0.07 mmol, 41% from the ether 147).

$^1\text{H}$  NMR ( $\text{CDCl}_3$  90 MHz)  $\delta$  7.55-7.80 (m, 4H, a), 7.30-7.50 (m, 6H, b), 6.12 (d, 1H, c,  $J=12.0$  Hz), 5.35-5.75 (m, 1H, d), 5.13 (d, 1H, e,  $J=1.9$  Hz), 4.94 (brs, 1H, f), 4.70-4.90 (m, 2H, g), 3.95-4.20 (m, 1H, h), 3.55-3.70 (m, 2H, i), 1.40-2.50 (m, 7H, j), 1.02 (s, 9H, k), 0.75-0.95 (m, 6H, l)

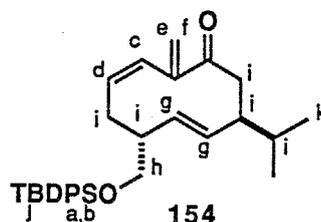
IR (neat) 3450, 2900, 1700, 1360, 1160, 960



**(6*R*\*,9*S*\*)-(3*Z*,7*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-9-isopropyl-2-vinylidene-3,7-cyclodecadien-1-one (154)**

To a solution of pyridine (0.43 mL, 5.4 mmol) in dichloromethane (1.5 mL) was added chromium oxide (250 mg, 2.50 mmol) at 0 °C. After being stirred for 1 h, to the mixture was added a solution of the alcohol 172 (15 mg, 0.03 mmol) in dichloromethane (1 mL). The reaction mixture was stirred for 15 min. The organic mixture was filtered through florisil. The filtrate was concentrated *in vacuo*. The residue was purified by HPLC to give the enone 154 (5.4 mg, 0.011 mmol, 36%).

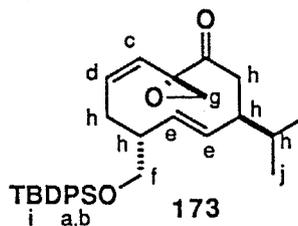
<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.50-7.75 (m, 4H, a), 7.25-7.45 (m, 6H, b), 6.50 (d, 1H, c, J= 11.9 Hz), 5.60-5.95 (m, 1H, d), 5.67 (d, 1H, e, J= 1.5 Hz), 5.30 (brs, 1H, f), 4.50-5.05 (m, 2H, g), 3.50-3.75 (m, 2H, h), 1.40-2.60 (m, 6H, i), 1.04 (s, 9H, j), 0.75-0.95 (m, 6H, k)

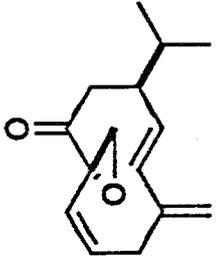


**(6*R*\*,9*S*\*)-(3*Z*,7*E*)-6-(*t*-butyldiphenylsilyloxy)methyl-9-isopropyl-2-epoxymethylene-3,7-cyclodecadien-1-one (173)**

To a suspension of KH (1.1 mg, 0.03 mmol) which was washed with dry hexane (0.2 mL) in THF (0.3 mL) was added dry *t*-butylhydroperoxide (3.491M in toluene, 0.008 mL) at -20 °C. After being stirred for 20 min, a solution of the enone 63 (4.5 mg, 0.01 mmol) in dry THF (0.3 mL) was added dropwise at -20 °C. After being stirred for 30 min, the reaction mixture was quenched with saturated sodium thiosulfate. The aqueous layer was extracted with ether. The organic layer was washed with brine. The resulting mixture was dried over MgSO<sub>4</sub> and concentrated *in vacuo*. The residue was chromatographed on silica gel (elution with 4: 1 hexane : ether) to give the epoxide 173 (2.2 mg, 0.005 mmol, 50%).

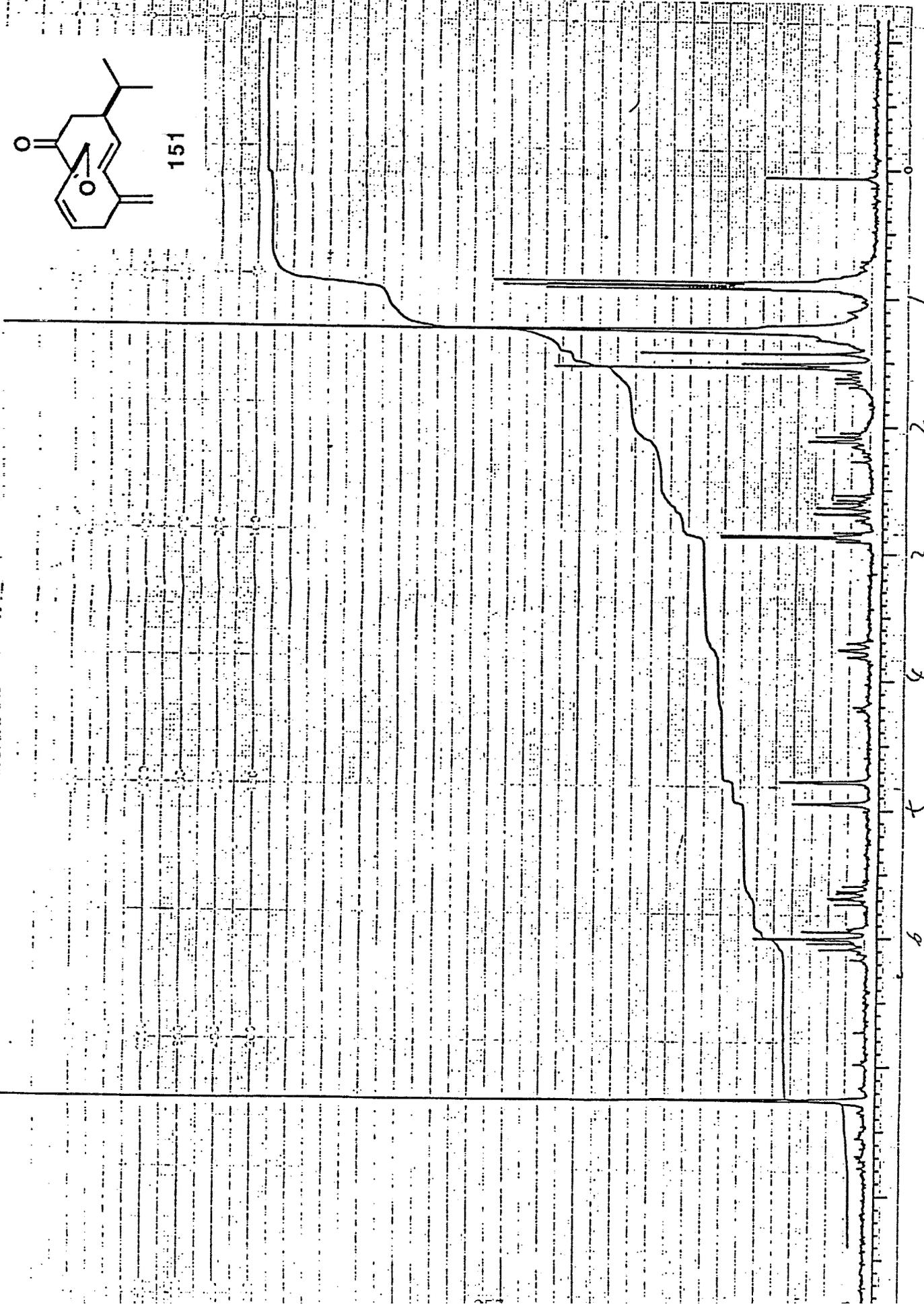
<sup>1</sup>H NMR (CDCl<sub>3</sub> 90 MHz) δ 7.50-7.70 (m, 4H, a), 7.25-7.45 (m, 6H, b), 5.30 (d, 1H, c, J= 8.1 Hz), 5.10-5.55 (m, 1H, d), 4.65-5.05 (m, 2H, e), 3.45-3.60 (m, 2H, f), 3.14 (d, 1H, g, J= 4.9 Hz), 2.86 (d, 1H, g, J= 4.9 Hz), 1.40-2.50 (m, 7H, h), 1.04 (s, 9H, i), 0.75-0.95 (m, 6H, j)



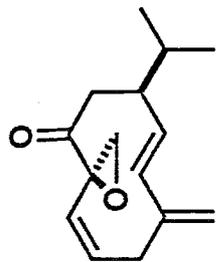


151

CONCENTRATION  
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 PREPARE  
 RECORDING  
 LOCK  
 DATE 62.9

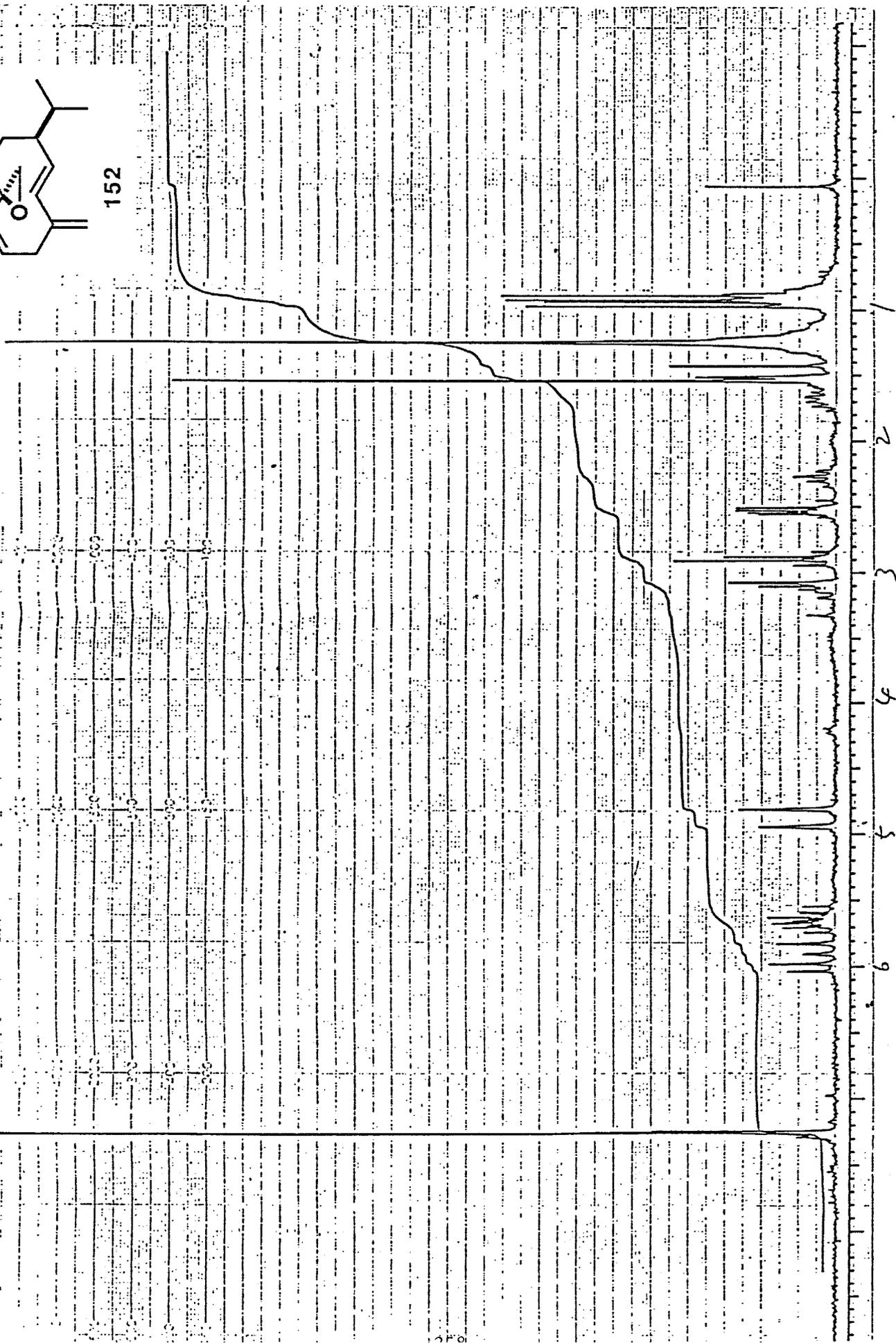


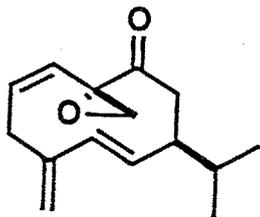
O



152

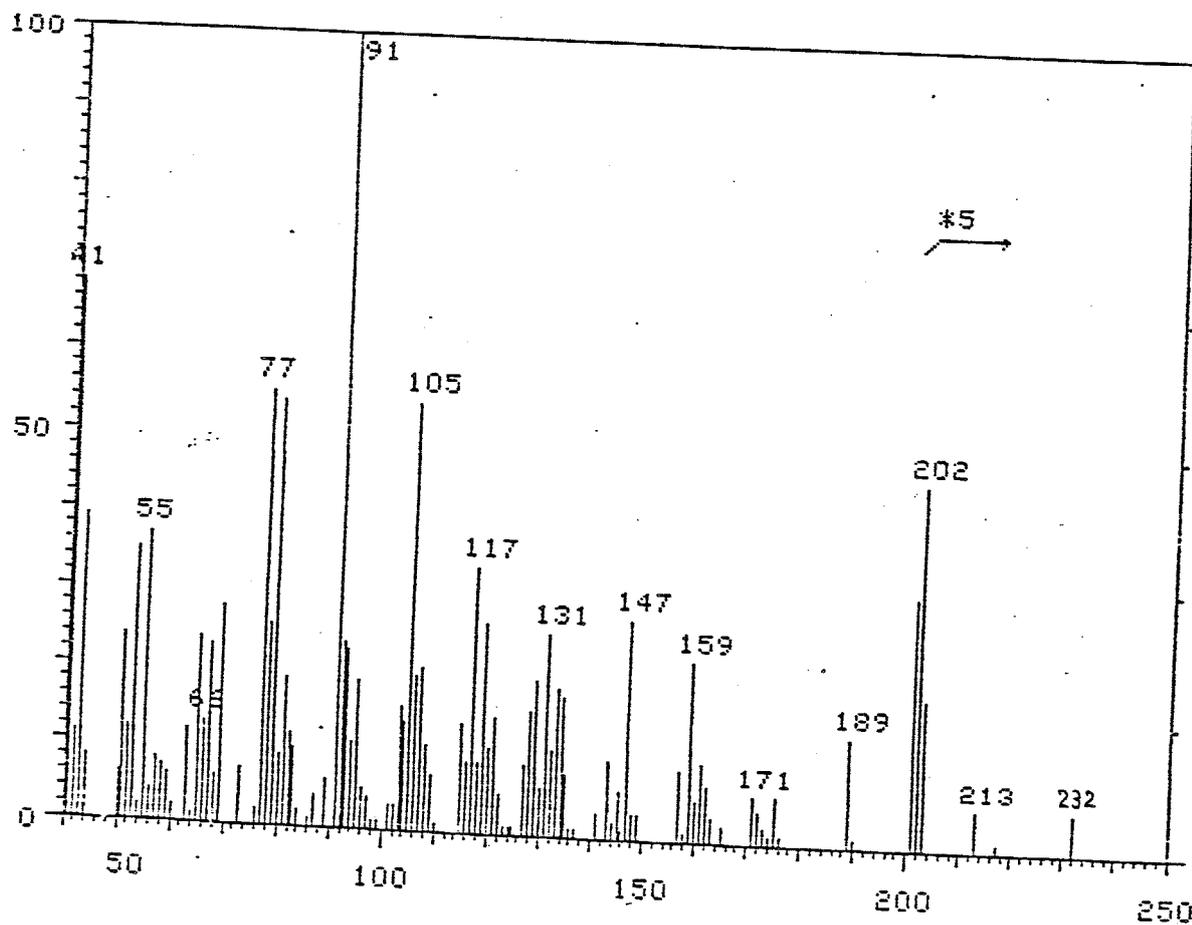
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SOLVENT  
CELL  
62.1

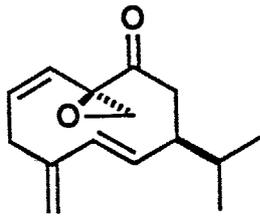




151

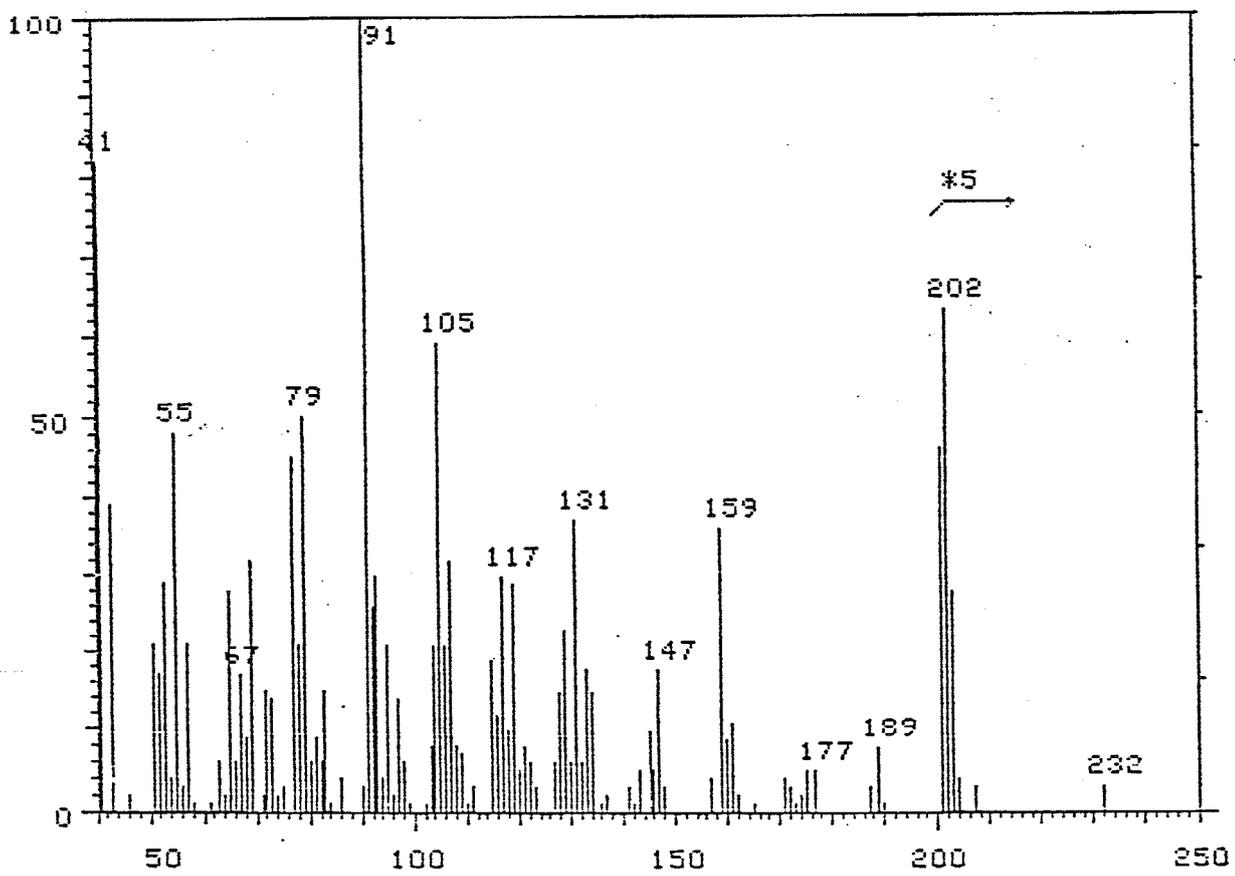
SAMPLE NO. : 6100 SCAN NO. : 457\*459-454 TIME(MIN): 10.3





152

SAMPLE NO. : 6100 SCAN NO. : 483\*486-481 TIME(MIN): 10.9



### Conformational analysis of the tetraenone 140

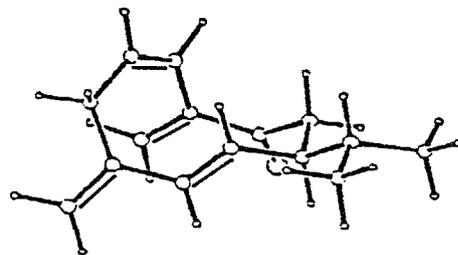
The starting geometries of 140 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.4 Å, and with a transannular contact of 2.4 Å. Structures of 60 conformations obtained were optimized by MM2 to get 8 conformers within 2.1 kcal/mol from the lowest energy conformer.

I

FINAL STERIC ENERGY IS 28.5012 KCAL.

COMPRESSION	1.5920
BENDING	4.8566
STRETCH-BEND	.0342
VANDERWAALS	
1,4 ENERGY	9.0231
OTHER	-.8966
TORSIONAL	13.8648
DIPOLE	.0272

DIPOLE MOMENT 2.631 D

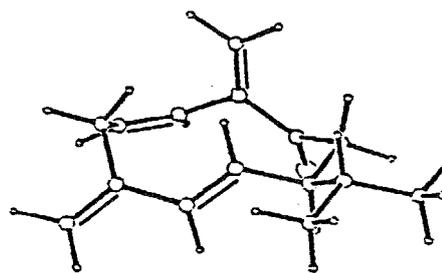


II

FINAL STERIC ENERGY IS 28.6765 KCAL.

COMPRESSION	1.2083
BENDING	2.9753
STRETCH-BEND	.0993
VANDERWAALS	
1,4 ENERGY	9.0996
OTHER	-2.0021
TORSIONAL	17.1604
DIPOLE	.1356

DIPOLE MOMENT 2.943 D

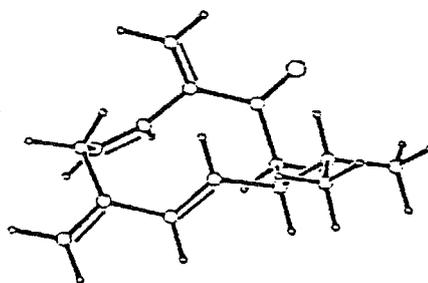


III

FINAL STERIC ENERGY IS 29.0197 KCAL.

COMPRESSION	1.2536
BENDING	3.4780
STRETCH-BEND	.1082
VANDERWAALS	
1,4 ENERGY	9.0538
OTHER	-2.0333
TORSIONAL	17.1221
DIPOLE	.0372

DIPOLE MOMENT 2.675 D

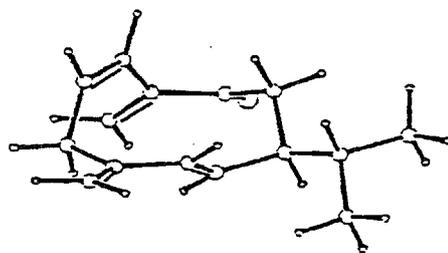


IV

FINAL STERIC ENERGY IS 29.8252 KCAL.

COMPRESSION	1.4197
BENDING	4.1042
STRETCH-BEND	.1211
VANDERWAALS	
1,4 ENERGY	8.9597
OTHER	-1.7627
TORSIONAL	16.9505
DIPOLE	.0327

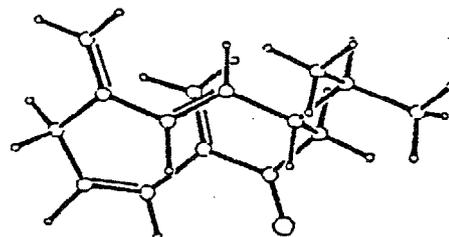
DIPOLE MOMENT 2.653 D

V

FINAL STERIC ENERGY IS 29.9327 KCAL.

COMPRESSION	1.5142
BENDING	4.9054
STRETCH-BEND	.0720
VANDERWAALS	
1,4 ENERGY	8.7365
OTHER	-1.1347
TORSIONAL	15.7002
DIPOLE	.1391

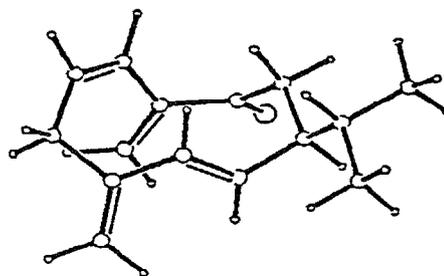
DIPOLE MOMENT 2.874 D

VI

FINAL STERIC ENERGY IS 30.0223 KCAL.

COMPRESSION	1.4411
BENDING	3.5574
STRETCH-BEND	.0847
VANDERWAALS	
1,4 ENERGY	9.2246
OTHER	-2.3076
TORSIONAL	17.9838
DIPOLE	.0382

DIPOLE MOMENT 2.732 D

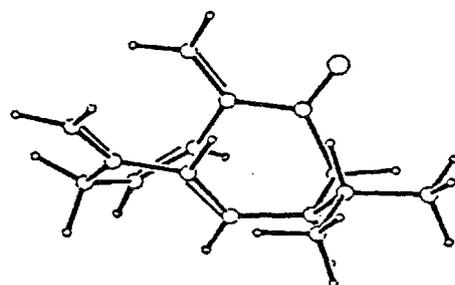


VII

FINAL STERIC ENERGY IS 30.1831 KCAL.

COMPRESSION	1.5759
BENDING	5.7200
STRETCH-BEND	.0912
VANDERWAALS	
1,4 ENERGY	8.8762
OTHER	-.5337
TORSIONAL	14.4284
DIPOLE	.0250

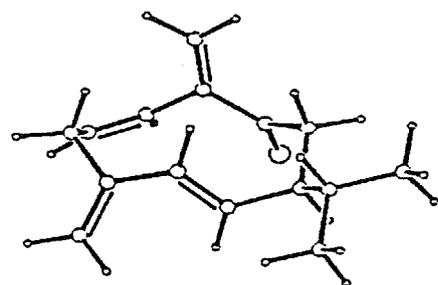
DIPOLE MOMENT 2.639 D

VIII

FINAL STERIC ENERGY IS 30.5716 KCAL.

COMPRESSION	1.1680
BENDING	2.9645
STRETCH-BEND	.1288
VANDERWAALS	
1,4 ENERGY	9.0462
OTHER	-2.5966
TORSIONAL	19.6785
DIPOLE	.1822

DIPOLE MOMENT 3.029 D



0 PA INTERMEDIATE

16	10	2	22	2922	1	1.50	1.34	120.0	1	1	30	1.0	2.4	0	1.2
2	10	0	0												
1	3	3	0												
2	2	4	0												
1	2	3	4	2922	1	1.50	120.0	0.0	3	5	12	12	0		
2	3	4	5	32	0	1.50	120.0	0.0	4	6	13	13	0		
3	4	5	6	2	0	1.50	120.0	0.0	5	7	0	0	0		
4	5	6	7	2	0	1.54	109.5	0.0	6	8	14	0	0		
5	6	7	8	22	0	1.50	109.5	0.0	7	9	9	0	0		
6	7	8	9	2922	0	1.34	120.0	0.0	8	8	10	0	0		
7	8	9	10	2922	1	1.50	120.0	180.0	1	9	11	11	0		
8	9	10	11	22	2	1.34	120.0	180.0	10	10	0	0	1		
2	3	4	12	22	2	1.34	120.0	180.0	4	4	0	0	5		
3	4	5	13	14	2	1.41	120.0	180.0	5	5	0	0	6		
5	6	7	14	2	2	1.54	109.5	240.0	7	15	16	0	8		
6	7	14	15	2	1	1.54	109.5	-60.0	14	0	0	0	0		
6	7	14	16	2	1	1.54	109.5	180.0	14	0	0	0	0		

36 4 0 0 1 500.

6					20				1						
1	2	3	4	5	6	7	8	9	10	1					
10	11														
4	12														
5	13														
7	14	15													
14	16														
1	17	1	18	2	19	3	20	6	21	6	22	7	23	8	24
9	25	11	26	11	27	12	28	12	29	14	30	15	31	15	32
15	33	16	34	16	35	16	36								
32	6	1	17												
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2	2	3	7	0.91		2.091		0.0							
5	2	3	1	0.0		2.091		0.0							
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2	2	1	29	0.10		0.0		0.50							
2	1	29	29	0.10		0.0		0.50							
2	1	29	2	0.10		0.0		0.50							
1	29	29	2	0.0		2.23		0.0							
1	29	29	5	0.0		2.23		0.0							
5	2	29	1	0.0		9.462		0.0							
29	1	2	5	0.0		0.0		0.60							
1	2	29	29	0.0		9.415		0.0							
5	2	29	29	0.0		9.415		0.0							
5	1	29	29	0.0		0.0		-0.24							

5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
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2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	29	29	5	0.0	2.20	0.0
5	29	29	5	0.0	2.23	0.0
2	29	3	7	0.91	1.540	0.91
29	29	3	7	0.91	1.540	0.91
2	29	29	3	0.0	2.20	0.0
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1	3	29	2	0.15	1.540	0.0
29	3	1	1	0.0	0.0	-0.330
29	3	1	5	0.0	0.0	0.0
29	2	1	29	0.10	0.0	0.500
29	29	3	1	0.15	1.540	0.0
2	29	9.444		1.340		
2	3	6.370		1.4767		
1	29	4.40		1.496		
5	29	4.60		1.09		
29	29	6.115		1.470		
3	29	6.290		1.480		
	29	0.044		1.940		
2	1	29		0.45	109.47	
5	1	29		0.36	109.39	
1	29	29		0.55	121.4	
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
3	29	29		0.43	117.0	
	29	29		0.050		
1	29	2		0.55	121.4	
5	29	2		0.36	120.0	
3	29	2		0.36	121.4	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		
7	3	29		0.43	122.5	
1	3	29		0.43	115.0	
	3	29		0.050		

I

-2.73430	-1.72532	-.71492	1	-2.25378	-.79630	-1.82247	2	2
-1.79741	.47174	-1.73754	29	-1.72329	1.31169	-.52188	29	4
-.40571	1.89567	-.11640	3	.90748	1.25144	-.57690	1	6
1.28452	-.01468	.23174	1	.09560	-.94146	.10637	2	8
-.90448	-.95899	1.00691	29	-2.25837	-1.48143	.70655	29	10
-3.10872	-1.66449	1.73575	2	-2.83710	1.51520	.20622	2	12
-.36601	2.85553	.62027	7	2.58797	-.69980	-.24015	1	14
3.81516	.22320	-.12319	1	2.85312	-1.98972	.56067	1	16
-2.39127	-2.75559	-.96768	5	-3.84731	-1.73383	-.77247	5	18
-2.28133	-1.24461	-2.83184	5	-1.41802	.92900	-2.65405	5	20
1.70688	2.01945	-.46568	5	.84978	1.01942	-1.66500	5	22
1.41568	.28461	1.29920	5	-.00480	-1.46921	-.85525	5	24
-.76143	-.42141	1.94633	5	-2.80870	-1.46937	2.77798	5	26
-4.13740	-2.02269	1.57180	5	-2.82263	2.11770	1.12829	5	28
-3.80452	1.08284	-.09636	5	2.47239	-.97954	-1.31630	5	30
4.75051	-.31286	-.40484	5	3.93910	.59681	.91889	5	32
3.74286	1.10315	-.80117	5	3.78593	-2.49380	.21797	5	34
2.02764	-2.72859	.44551	5	2.96459	-1.77011	1.64715	5	LAST

II

-2.98555	-1.01867	-.70994	1	-3.44915	.20528	.05141	2	2
-2.78746	1.37457	.17401	29	-1.51213	1.70543	-.49842	29	4
-.34127	1.89191	.41056	3	1.04743	1.42424	-.03022	1	6
1.26778	-.07935	.25395	1	.01743	-.79659	-.20460	2	8
-.80161	-1.47573	.61960	29	-2.17457	-1.87972	.23697	29	10
-2.75814	-2.89600	.89965	2	-1.46483	1.73737	-1.84237	2	12
-.49588	2.32639	1.52965	7	2.52508	-.66257	-.42689	1	14
3.80937	.06455	.00915	1	2.66455	-2.16723	-.12882	1	16
-2.39680	-.75300	-1.61342	5	-3.87713	-1.56195	-1.10064	5	18
-4.35167	.06220	.67160	5	-3.18119	2.11086	.87828	5	20
1.80618	2.03201	.51570	5	1.20080	1.64151	-1.11050	5	22
1.37928	-.20638	1.35750	5	-.24567	-.66002	-1.26476	5	24
-.48604	-1.64112	1.65124	5	-2.20816	-3.48618	1.65039	5	26
-3.80697	-3.17414	.70965	5	-.53990	1.95995	-2.39473	5	28
-2.37214	1.57096	-2.44511	5	2.41901	-.53979	-1.53304	5	30
4.71163	-.39968	-.45126	5	3.93607	.02773	1.11527	5	32
3.80921	1.13313	-.30366	5	3.56931	-2.59439	-.61932	5	34
1.79132	-2.74802	-.50420	5	2.75271	-2.35260	.96615	5	LAST

III

-3.23140	-.10107	-.50420	1	-3.03512	.87646	.63604	2	
-1.99653	1.71746	.82412	29	-.88465	1.97930	-.11647	29	
.51910	1.76049	.34860	3	.81475	.62133	1.32418	1	
.92498	-.76000	.63418	1	-.41258	-.97919	-.03500	2	
-1.43938	-1.65081	.51478	29	-2.82016	-1.46560	.01319	29	10
-3.73012	-2.43480	.22226	2	-1.14377	2.39234	-1.37058	2	12
1.42372	2.44073	-.07996	7	2.08603	-.88037	-.37874	1	14
3.46093	-.64758	.27288	1	2.07759	-2.26550	-1.05392	1	16
-2.64832	.16131	-1.41344	5	-4.30227	-.07274	-.81196	5	18
-3.76217	.77779	1.46169	5	-1.93832	2.23434	1.78459	5	20
.02039	.59376	2.10577	5	1.75091	.85415	1.88090	5	22
1.07309	-1.53207	1.42718	5	-.56221	-.43785	-.98133	5	24
-1.28296	-2.21771	1.43415	5	-3.44734	-3.39899	.67474	5	26
-4.78667	-2.29835	-.05768	5	-.33290	2.57758	-2.09300	5	28
-2.17584	2.56676	-1.71482	5	1.95196	-.11162	-1.17873	5	30
4.28585	-.80849	-.45866	5	3.62432	-1.34414	1.12665	5	32
3.57645	.39411	.64773	5	2.90469	-2.35962	-1.79470	5	34
1.12937	-2.45446	-1.60691	5	2.20117	-3.07848	-.30234	5	LAST

IV

-3.03694	1.09536	-.16629	1	-2.88374	.30267	1.11536	2	2
-2.24438	-.87540	1.27089	29	-1.69831	-1.72620	.19088	29	4
-.24690	-2.08476	.20398	3	.78234	-1.11207	.78808	1	6
1.20412	-.02837	-.23373	1	-.07612	.69896	-.59770	2	8
-.56379	1.79502	.01304	29	-1.98529	2.18564	-.12663	29	10
-2.32749	3.48074	.00557	2	-2.50952	-2.15961	-.79199	2	12
.13322	-3.11121	-.31337	7	2.36219	.88420	.23585	1	14
3.64550	.09485	.56240	1	2.70370	1.94078	-.83450	1	16
-4.07197	1.50692	-.20629	5	-2.91464	.47681	-1.08188	5	18
-3.21087	.82756	2.03049	5	-2.08010	-1.23075	2.29052	5	20
1.66299	-1.72292	1.08962	5	.39135	-.64196	1.71951	5	22
1.56705	-.53966	-1.15789	5	-.70174	.19135	-1.34922	5	24
.03940	2.33277	.74443	5	-1.56290	4.26614	.11950	5	26
-3.38217	3.79833	-.00233	5	-2.13220	-2.78324	-1.61803	5	28
-3.58285	-1.91020	-.80010	5	2.05658	1.40962	1.17265	5	30
4.48784	.78026	.81215	5	3.96476	-.53181	-.30150	5	32
3.51797	-.57021	1.44582	5	3.51664	2.61925	-.48740	5	34
1.83338	2.58806	-1.08428	5	3.04477	1.45815	-1.77884	5	LAST

## V

-3.52962	-1.05094	.57576	1	-3.55014	.43484	.90547	2	2
-2.77560	1.43105	.42407	29	-1.68415	1.32064	-.57157	29	4
-.37980	1.91421	-.14586	3	.94647	1.27480	-.56880	1	6
1.27921	-.02212	.20818	1	.14515	-.99074	-.05262	2	8
-.94428	-1.06969	.73478	29	-2.19711	-1.70493	.27061	29	10
-2.16573	-2.86541	-.41355	2	-1.88852	.67282	-1.73285	2	12
-.36125	2.87569	.58988	7	2.64045	-.65111	-.17554	1	14
3.82847	.29329	.08821	1	2.87556	-1.96922	.58924	1	16
-4.25373	-1.21086	-.25668	5	-3.92928	-1.59644	1.46271	5	18
-4.33874	.72781	1.62229	5	-2.93343	2.42146	.85813	5	20
1.74072	2.03416	-.38510	5	.95066	1.09136	-1.66730	5	22
1.30957	.22744	1.29604	5	.15812	-1.49714	-1.03215	5	24
-.98120	-.46045	1.63943	5	-1.22411	-3.39151	-.63758	5	26
-3.09667	-3.34535	-.75576	5	-1.09649	.56571	-2.48954	5	28
-2.87463	.25044	-1.98415	5	2.62891	-.88486	-1.26874	5	30
4.79988	-.21075	-.12253	5	3.84709	.63052	1.14981	5	32
3.80193	1.19600	-.56274	5	3.84908	-2.43330	.30804	5	34
2.08840	-2.72690	.37251	5	2.88893	-1.79713	1.68994	5	LAST

## VI

-3.07254	1.48153	.86692	1	-2.69845	.38234	1.84796	2	2
-2.12176	-.80686	1.56958	29	-1.80225	-1.34755	.22765	29	4
-.43916	-1.91007	-.02538	3	.78548	-1.23972	.60268	1	6
1.34170	-.10260	-.29060	1	.16298	.74216	-.72996	2	8
-.61297	1.39147	.15643	29	-2.00184	1.78824	-.15797	29	10
-2.31629	2.37754	-1.32699	2	-2.72390	-1.33337	-.75354	2	12
-.28712	-2.83650	-.78961	7	2.45818	.73608	.37321	1	14
3.67427	-.12278	.76751	1	2.92295	1.87374	-.55660	1	16
-3.23553	2.42492	1.43893	5	-4.04563	1.21911	.39178	5	18
-2.90137	.61107	2.90960	5	-1.82767	-1.42921	2.41809	5	20
1.56332	-2.02433	.75241	5	.53188	-.86033	1.61843	5	22
1.77565	-.56991	-1.20788	5	-.17478	.62096	-1.77366	5	24
-.31551	1.38827	1.20554	5	-1.55264	2.61471	-2.08491	5	26
-3.35641	2.66091	-1.55454	5	-2.49869	-1.72328	-1.75930	5	28
-3.74176	-.94812	-.58551	5	2.05961	1.19975	1.30827	5	30
4.49066	.50440	1.19452	5	4.08981	-.66284	-.11382	5	32
3.41719	-.87721	1.54518	5	3.72142	2.48718	-.07873	5	34
2.09148	2.57066	-.80935	5	3.33263	1.47078	-1.51111	5	LAST

VII

3.19260	-1.06631	-.64628	1	2.87363	.13824	-1.52166	2
2.11513	1.22237	-1.25177	29	1.43728	1.55304	.02137	29
-.04625	1.75484	.02316	3	-.90129	1.13273	-1.08267	1
-1.21024	-.36795	-.85559	1	.14612	-1.03495	-.73255	2
.80750	-1.18342	.43105	29	2.27217	-1.38616	.51571	29
2.79239	-1.77923	1.69475	2	2.16158	1.63541	1.15258	2
-.58378	2.37464	.91301	7	-2.20326	-.66004	.29492	1
-3.57662	.00389	.07477	1	-2.42142	-2.17660	.46609	1
4.24452	-.93408	-.30254	5	3.17977	-1.97181	-1.29656	5
3.33378	.09740	-2.52528	5	1.95792	1.93305	-2.06626	5
-.38323	1.26916	-2.05982	5	-1.84156	1.71892	-1.18897	5
-1.68828	-.77125	-1.78110	5	.67013	-1.22162	-1.68429	5
.28481	-.98584	1.36673	5	2.15509	-1.98733	2.56934	5
3.87781	-1.91316	1.82608	5	1.69180	1.85717	2.12396	5
3.25268	1.48094	1.14418	5	-1.79768	-.24989	1.25072	5
-4.29917	-.28982	.87062	5	-4.01599	-.29138	-.90535	5
-3.51839	1.11491	.10831	5	-3.11200	-2.39316	1.31337	5
-1.47379	-2.71938	.68122	5	-2.86246	-2.62404	-.45386	5

VIII

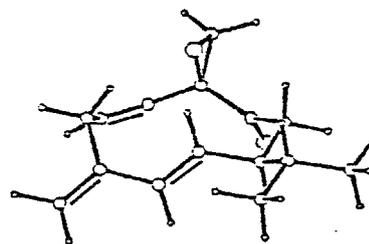
3.16841	-1.12655	.81939	1	3.57981	-.09142	-.20513	2
2.96043	1.08340	-.44403	29	1.80172	1.60852	.31266	29
.53841	1.74343	-.47235	3	-.79937	1.38324	.17689	1
-1.35953	.04256	-.35498	1	-.22216	-.95370	-.46783	2
.63793	-1.19498	.53793	29	1.94325	-1.84727	.30945	29
2.04192	-2.97778	-.41353	2	1.91680	1.85758	1.62935	2
.57225	2.00256	-1.65428	7	-2.52569	-.51887	.48810	1
-3.70152	.46985	.57962	1	-3.02779	-1.85779	-.08404	1
2.94949	-.64967	1.80058	5	4.01049	-1.83216	1.00911	5
4.37739	-.40167	-.90301	5	3.28340	1.65774	-1.31521	5
-1.51027	2.21530	-.03582	5	-.70344	1.33388	1.28368	5
-1.73861	.22879	-1.38915	5	-.02137	-1.36740	-1.47086	5
.48272	-.69366	1.49334	5	1.15064	-3.48918	-.81096	5
3.02318	-3.43280	-.62194	5	1.07737	2.24215	2.22816	5
2.87841	1.72566	2.15052	5	-2.15580	-.70865	1.52568	5
-4.55165	.03336	1.15261	5	-4.07845	.74047	-.43309	5
-3.41563	1.40921	1.10460	5	-3.86776	-2.26710	.52307	5
-2.22824	-2.63342	-.08969	5	-3.39313	-1.73540	-1.12931	5

## Conformational analysis of 151

The starting geometries of 151 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.7 Å, and with a transannular contact of 2.24 Å. Structures of 88 conformations obtained were optimized by MM2 to get 4 conformers within 3.0 kcal/mol from the lowest energy conformer.

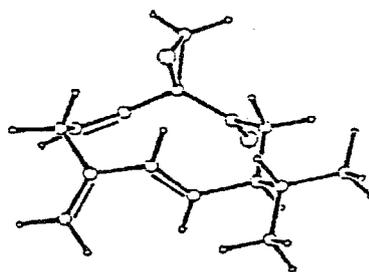
I NO= 22 ENERGY= 22.7942

ST= 1.03 BD= 4.74 SB= .17 14= 8.53  
OT= -2.92 T= 11.11 DP= .13 DM= 2.94D



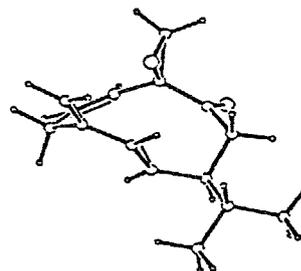
II NO= 23 ENERGY= 24.8600

ST= .98 BD= 4.43 SB= .20 14= 8.41  
OT= -3.68 T= 14.36 DP= .16 DM= 3.02D



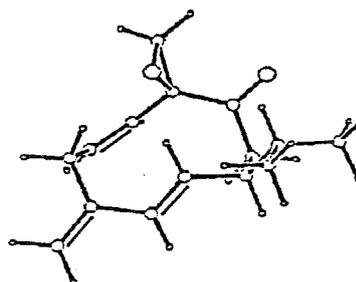
III NO= 31 ENERGY= 24.9894

ST= 1.16 BD= 8.50 SB= .20 14= 8.75  
OT= -1.72 T= 7.98 DP= .11 DM= 2.95D



IV NO= 27 ENERGY= 25.2268

ST= 1.12 BD= 5.76 SB= .23 14= 8.51  
OT= -2.23 T= 11.78 DP= .07 DM= 2.74D



ENERGY: FINAL STERIC ENERGY, ST: COMPRESSION, BD: BENDING, SB: STRETCH-BEND,  
14: VAN DER WAALS\_1,4 ENERGY, OT: VAN DER WAALS\_OTHER, T: TORSIONAL, DP: DIPOLE,  
DM: DIPOLE MOMENT [ KCAL/MOL ]

0 PA

19	10	2	22	22	2	1.50	1.34	120.0	1	1	30	1.0	2.7	0	1.12
2	10	0	0												
1	3	3	0												
2	2	4	0												
1	2	3	4	23	1	1.50	120.0	0.0	3	5	12	17	0		
2	3	4	5	32	0	1.50	120.0	0.0	4	6	13	13	0		
3	4	5	6	2	0	1.50	120.0	0.0	5	7	0	0	0		
4	5	6	7	2	0	1.54	109.5	0.0	6	8	14	0	0		
5	6	7	8	22	0	1.50	109.5	0.0	7	9	9	0	0		
6	7	8	9	2922	0	1.34	120.0	0.0	8	8	10	0	0		
7	8	9	10	2922	1	1.50	120.0	180.0	1	9	11	11	0		
8	9	10	11	22	2	1.34	120.0	180.0	10	10	0	0	1		
2	3	4	12	23	2	1.47	120.0	160.0	4	17	18	19	5		
3	4	5	13	14	2	1.41	120.0	180.0	5	5	0	0	6		
5	6	7	14	2	2	1.54	109.5	240.0	7	15	16	0	8		
6	7	14	15	2	1	1.54	109.5	-60.0	14	0	0	0	0		
6	7	14	16	2	1	1.54	109.5	180.0	14	0	0	0	0		
2	3	4	17	30	2	1.44	115.0	220.0	4	12	0	0	5		
3	4	12	18	1	1	1.10	120.0	0.0	12	0	0	0	0		
3	4	12	19	1	1	1.10	120.0	150.0	12	0	0	0	0		

37 4 0 0 1 500.

6					1	20			1										
1	2	3	4	5	6	7	8	9	10	1									
10	11																		
4	12	17	4																
5	13																		
7	14	15																	
14	16																		
12	18	12	19	1	20	1	21	2	22	3	23	6	24	6	25				
7	26	8	27	9	28	11	29	11	30	14	31	15	32	15	33				
15	34	16	35	16	36	16	37												
43	9	2	27																
7	3	22	22	1.5		0.0		0.0											
7	3	22	30	1.5		0.0		0.0											
7	3	22	5	0.0		0.0		0.001											
1	3	22	22	4.0		0.0		0.0											
1	3	22	30	-1.5		0.0		0.0											
1	3	22	5	0.0		0.0		0.001											
5	1	3	22	0.0		0.0		0.130											
5	22	30	22	0.0		0.0		0.167											
3	22	22	30	0.2		0.27		0.093											

3	22	22	5	0.0	0.0	0.120
5	22	22	30	0.0	0.0	0.167
3	22	30	22	0.2	0.27	0.093
1	3	22	2	0.0	0.0	0.0
2	2	22	3	0.0	0.0	0.0
5	2	22	3	0.0	0.0	0.0
1	2	2	22	-0.10	15.0	0.0
5	2	2	22	0.0	15.0	0.0
7	3	22	2	0.0	0.0	0.0
2	22	22	30	0.20	0.27	0.093
2	22	22	5	0.0	0.0	0.120
2	22	30	22	0.20	0.27	0.093
2	2	22	22	0.3	0.0	0.0
2	2	22	30	0.0	0.60	0.0
5	2	22	22	0.0	0.0	0.0
5	2	22	30	0.0	0.0	0.0
1	1	3	22	0.55	-0.18	0.40
1	1	2	29	-0.44	0.24	0.06
2	2	1	29	0.10	0.0	0.50
2	1	29	29	0.10	0.0	0.50
2	1	29	2	0.10	0.0	0.50
1	29	29	2	0.0	2.23	0.0
1	29	29	5	0.0	2.23	0.0
5	2	29	1	0.0	9.462	0.0
29	1	2	5	0.0	0.0	0.60
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	29	29	0.0	0.0	-0.24
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
5	1	29	2	0.0	0.0	-0.24
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
2	22	4.40		1.497		
3	22	4.40		1.497		
5	22	4.60		1.0868		
22	22	4.40		1.467		
22	30	5.36		1.400	1.377	
2	29	9.444		1.340		
1	29	4.40		1.496		
5	29	4.60		1.09		

	29	29	6.115	1.470	
		29	0.044	1.940	
		30	0.050	1.740	
	3	22	22	0.60	118.2
	3	22	30	0.90	115.0
	3	22	5	0.36	123.5
3	22	22	30	0.45	60.0
	5	22	30	0.36	124.5
	7	3	22	0.50	120.0
	1	3	22	0.40	116.6
		3	22	0.80	
3	22	30	22	0.77	60.0
	2	22	3	0.45	120.0
	2	22	22	0.60	118.2
	2	22	30	0.90	115.0
	2	2	22	0.55	121.4
	5	2	22	0.36	118.2
		2	22	0.05	
	2	1	29	0.45	109.47
	5	1	29	0.36	109.39
	1	29	29	0.55	121.4
	2	29	29	0.43	120.0
	5	29	29	0.36	120.0
		29	29	0.050	
	1	29	2	0.55	121.4
	5	29	2	0.36	120.0
		29	2	0.05	
	1	2	29	0.55	121.4
	5	2	29	0.36	120.0
		2	29	0.050	

## I

2.3367	-1.8282	.7759	1	3.0395	-.7994	-.0745	2
2.7143	.4924	-.2500	2	1.5803	1.2665	.3824	22
.3680	1.6067	-.4629	3	-1.0524	1.3835	.0470	1
-1.5862	-.0393	-.2210	1	-.5149	-.9877	.2581	2
.1041	-1.8861	-.5280	29	1.3528	-2.5606	-.1105	29
1.6900	-3.7268	-.6920	2	1.9666	2.2647	1.3855	22
.5628	2.0597	-1.5682	7	-2.9365	-.3397	.4662	1
-4.0492	.6175	.0034	1	-3.3765	-1.7929	.2065	1
1.3723	1.0693	1.7339	30	3.0267	2.4155	1.5758	5
1.3928	3.1874	1.4329	5	1.8415	-1.3663	1.6561	5
3.0936	-2.5224	1.2096	5	3.8908	-1.1864	-.6622	5
3.3341	1.0884	-.9414	5	-1.7094	2.1351	-.4486	5
-1.0794	1.6130	1.1372	5	-1.7200	-.1576	-1.3231	5
-.2082	-.8573	1.3066	5	-.2605	-2.0430	-1.5447	5
1.0155	-4.2327	-1.4016	5	2.6525	-4.2163	-.4739	5
-2.8096	-.2115	1.5696	5	-5.0274	.3527	.4666	5
-4.1767	.5806	-1.1026	5	-3.8393	1.6717	.2932	5
-4.3520	-2.0141	.6975	5	-2.6424	-2.5283	.6078	5
-3.4938	-1.9873	-.8842	5	.0000	.0000	.0000	0

## II

2.5131	-1.8876	.9151	1	3.1029	-.9850	-.1393	2
2.7712	.2914	-.3975	2	1.7527	1.1505	.3183	22
.4695	1.5126	-.4030	3	-.8955	1.3026	.2433	1
-1.6640	.0904	-.3280	1	-.7140	-1.0816	-.4350	2
.0249	-1.5076	.6037	29	1.1885	-2.3909	.4045	29
1.0881	-3.5282	-.3070	2	2.2896	2.1632	1.2327	22
.5570	1.9487	-1.5286	7	-2.9277	-.2790	.4808	1
-3.9307	.8862	.5537	1	-3.6264	-1.5147	-.1170	1
1.6806	1.0129	1.6909	30	3.3699	2.2666	1.3029	5
1.7674	3.1146	1.3015	5	2.3778	-1.3379	1.8734	5
3.2113	-2.7267	1.1423	5	3.8501	-1.4578	-.8008	5
3.2859	.7997	-1.2306	5	-1.4805	2.2367	.0769	5
-.7760	1.2122	1.3465	5	-1.9820	.3553	-1.3655	5
-.5365	-1.4950	-1.4426	5	-.0838	-1.0165	1.5706	5
.1222	-3.8716	-.7110	5	1.9727	-4.1556	-.4998	5
-2.6221	-.5321	1.5257	5	-4.8571	.5875	1.0961	5
-4.2285	1.2246	-.4649	5	-3.5136	1.7613	1.1014	5
-4.5388	-1.7837	.4635	5	-2.9658	-2.4116	-.1084	5
-3.9374	-1.3287	-1.1704	5	.0000	.0000	.0000	0

III

2.2382	-2.2019	-.6530	1	2.6470	-.8581	-1.2290	2
2.4167	.4109	-.8485	2	1.6527	.9821	.3244	22
.3598	1.7269	.0490	3	-.9909	1.2278	.5523	1
-1.5760	.0767	-.2944	1	-.4793	-.9506	-.4392	2
.0527	-1.5807	.6232	29	1.3641	-2.2628	.5789	29
1.7852	-2.9081	1.6843	2	2.4793	1.5254	1.4096	22
.4353	2.7413	-.6072	7	-2.8854	-.5231	.2645	1
-4.0188	.5167	.3286	1	-3.3461	-1.7230	-.5846	1
1.7779	.3458	1.5440	30	3.5603	1.4987	1.2932	5
2.1303	2.4203	1.9196	5	3.1878	-2.7554	-.4673	5
1.7115	-2.7732	-1.4525	5	3.2534	-.9642	-2.1471	5
2.8518	1.2014	-1.4843	5	-1.6928	2.0932	.5468	5
-.8771	.9280	1.6193	5	-1.7969	.4798	-1.3125	5
-.0152	-1.0314	-1.4354	5	-.4310	-1.4618	1.5938	5
1.1727	-2.9527	2.5993	5	2.7608	-3.4186	1.7171	5
-2.7057	-.8880	1.3049	5	-4.9704	.0548	.6787	5
-4.2098	.9671	-.6721	5	-3.7887	1.3408	1.0409	5
-4.2902	-2.1614	-.1870	5	-2.5909	-2.5419	-.5916	5
-3.5310	-1.4196	-1.6405	5	.0000	.0000	.0000	0

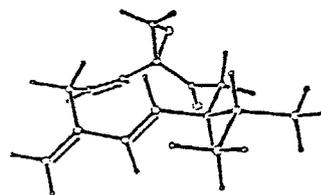
IV

-2.9248	-.9104	-.6958	1	-2.9770	.2317	.2924	2
-2.1166	1.2519	.4560	2	-.8616	1.5730	-.3245	22
.4727	1.5402	.3996	3	.8657	.3741	1.3011	1
1.2296	-.9465	.5869	1	-.0450	-1.4040	-.0762	2
-1.0097	-2.0920	.5587	29	-2.3910	-2.1268	.0312	29
-3.2055	-3.1361	.3909	2	-1.0342	2.5266	-1.4291	22
1.1981	2.5064	.3203	7	2.3959	-.8269	-.4190	1
3.6922	-.3302	.2459	1	2.6677	-2.1796	-1.1047	1
-.8295	1.1817	-1.6490	30	-2.0234	2.9525	-1.5806	5
-.2380	3.2326	-1.6512	5	-2.3155	-.6803	-1.5953	5
-3.9542	-1.0834	-1.0869	5	-3.8207	.1783	1.0033	5
-2.3272	1.9730	1.2640	5	.0253	.2065	2.0149	5
1.7191	.6933	1.9428	5	1.5163	-1.6934	1.3662	5
-.2213	-1.0198	-1.0897	5	-.8171	-2.4954	1.5544	5
-2.8381	-3.9837	.9917	5	-4.2657	-3.1505	.0923	5
2.1152	-.0893	-1.2106	5	4.5374	-.3150	-.4800	5
3.9865	-.9884	1.0950	5	3.5926	.7094	.6316	5
3.4995	-2.0992	-1.8419	5	1.7787	-2.5510	-1.6635	5
2.9498	-2.9574	-.3588	5	.0000	.0000	.0000	0

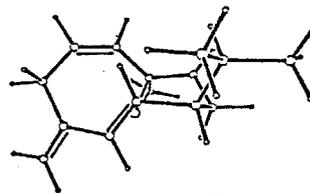
## Conformational analysis of 152

The starting geometries of 152 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.7 Å, and with a transannular contact of 2.24 Å. Structures of 54 conformations obtained were optimized by MM2 to get 8 conformers within 2.0 kcal/mol from the lowest energy conformer.

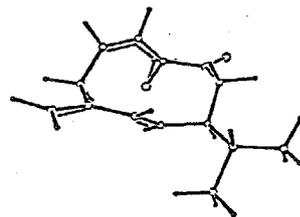
I NO= 21 ENERGY= 25.7129 ITER= 10  
ST= 1.04 BD= 5.35 SB= .20 14= 8.42  
OT= -2.89 T= 13.46 DP= .13 DM= 2.95D



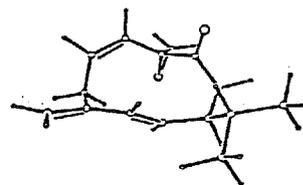
II NO= 51 ENERGY= 25.9252 ITER= 23  
ST= 1.25 BD= 8.64 SB= .21 14= 8.71  
OT= -1.48 T= 8.49 DP= .11 DM= 2.95D



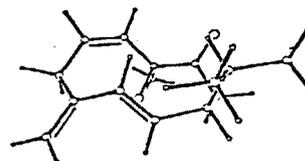
III NO= 44 ENERGY= 26.0383 ITER= 30  
ST= 1.15 BD= 6.05 SB= .25 14= 8.45  
OT= -1.78 T= 11.84 DP= .08 DM= 2.76D



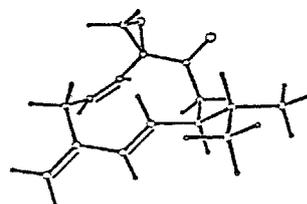
IV NO= 76 ENERGY= 26.1435 ITER= 12  
ST= 1.20 BD= 5.90 SB= .22 14= 8.46  
OT= -2.14 T= 12.37 DP= .13 DM= 2.94D



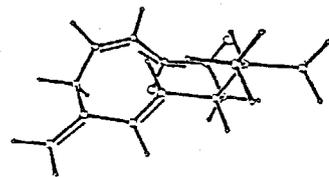
V NO= 55 ENERGY= 26.5896 ITER= 17  
ST= 1.14 BD= 5.53 SB= .23 14= 8.26  
OT= -2.50 T= 13.78 DP= .14 DM= 2.88D



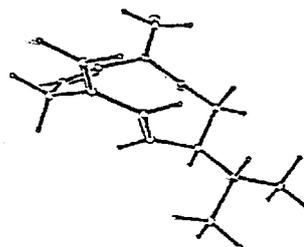
VI NO= 41 ENERGY= 26.7480 ITER= 8  
ST= 1.12 BD= 5.84 SB= .25 14= 8.96  
OT= -2.82 T= 13.38 DP= .03 DM= 2.67D



VII NO= 64 ENERGY= 27.1514 ITER= 5  
ST= 1.15 BD= 5.38 SB= .19 14= 7.94  
OT= -1.93 T= 14.31 DP= .12 DM= 2.93D



VIII NO= 33 ENERGY= 27.5553 ITER= 16  
ST= 1.13 BD= 8.99 SB= .24 14= 8.62  
OT= -2.51 T= 10.98 DP= .11 DM= 2.96D



ENERGY: FINAL STERIC ENERGY, ST: COMPRESSION, BD: BENDING, SB: STRETCH-BEND,  
14: VAN DER WAALS\_1,4 ENERGY, OT: VAN DER WAALS\_OTHER, T: TORSIONAL, DP: DIPOLE,  
DM: DIPOLE MOMENT [ KCAL/MOL ]



3	22	22	5	0.0	0.0	0.120
5	22	22	30	0.0	0.0	0.167
3	22	30	22	0.2	0.27	0.093
1	3	22	2	0.0	0.0	0.0
2	2	22	3	0.0	0.0	0.0
5	2	22	3	0.0	0.0	0.0
1	2	2	22	-0.10	0.0	0.0
5	2	2	22	0.0	15.0	0.0
7	3	22	2	0.0	15.0	0.0
2	22	22	30	0.0	0.0	0.0
2	22	22	5	0.20	0.27	0.093
2	22	30	22	0.0	0.0	0.120
2	2	22	22	0.20	0.27	0.093
2	2	22	22	0.3	0.0	0.0
5	2	22	30	0.0	0.60	0.0
5	2	22	22	0.0	0.0	0.0
1	1	3	30	0.0	0.0	0.0
1	1	2	22	0.55	0.0	0.0
2	2	1	29	-0.44	-0.18	0.40
2	1	1	29	0.10	0.24	0.06
2	1	29	29	0.10	0.0	0.50
2	1	29	2	0.10	0.0	0.50
1	29	29	2	0.0	0.0	0.50
1	29	29	5	0.0	2.23	0.0
5	2	29	1	0.0	2.23	0.0
29	1	2	5	0.0	9.462	0.0
1	2	29	29	0.0	0.0	0.60
5	2	29	29	0.0	9.415	0.0
5	1	29	29	0.0	9.415	0.0
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	0.0	-0.24
1	2	29	5	0.0	2.23	0.80
5	1	29	2	0.0	9.415	0.0
2	29	29	2	0.0	0.0	-0.24
5	2	29	5	0.0	2.23	0.0
2	22	4.40	5	0.0	9.415	0.0
3	22	4.40		1.497		
5	22	4.40		1.497		
22	22	4.60		1.0868		
22	22	4.40		1.467		
22	30	5.36		1.400		
2	29	9.444		1.340	1.377	
1	29	4.40		1.496		
5	29	4.60		1.09		

	29	29	6.115	1.470	
		29	0.044	1.940	
		30	0.050	1.740	
	3	22	22	0.60	118.2
	3	22	30	0.90	115.0
	3	22	5	0.36	123.5
3	22	22	30	0.45	60.0
	5	22	30	0.36	124.5
	7	3	22	0.50	120.0
	1	3	22	0.40	116.6
		3	22	0.80	
3	22	30	22	0.77	60.0
	2	22	3	0.45	120.0
	2	22	22	0.60	118.2
	2	22	30	0.90	115.0
	2	2	22	0.55	121.4
	5	2	22	0.36	118.2
		2	22	0.05	
	2	1	29	0.45	109.47
	5	1	29	0.36	109.39
	1	29	29	0.55	121.4
	2	29	29	0.43	120.0
	5	29	29	0.36	120.0
		29	29	0.050	
	1	29	2	0.55	121.4
	5	29	2	0.36	120.0
		29	2	0.05	
	1	2	29	0.55	121.4
	5	2	29	0.36	120.0
		2	29	0.050	

I

-2.4778	-1.5718	-.7180	1	-3.1405	-.4600	.0582	2
-2.7291	.8124	.1901	2	-1.4978	1.4482	-.4130	22
-.3057	1.6395	.5058	3	1.1346	1.3816	.0713	1
1.5754	-.0815	.2877	1	.4285	-.9391	-.1880	2
-.2652	-1.7681	.6127	29	-1.5736	-2.3379	.2219	29
-2.0247	-3.4335	.8610	2	-1.4004	1.5329	-1.8753	22
-.5320	2.0054	1.6376	7	2.8889	-.4503	-.4350	1
4.0659	.4276	.0253	1	3.2411	-1.9334	-.2155	1
-1.7838	2.6087	-1.1085	30	-2.1519	1.0212	-2.4709	5
-.4243	1.5222	-2.3494	5	-1.9222	-1.1818	-1.5965	5
-3.2638	-2.2309	-1.1549	5	-4.0474	-.7564	.6143	5
-3.3333	1.4869	.8209	5	1.7972	2.0641	.6530	5
1.2588	1.6755	-.9942	5	1.7229	-.2392	1.3830	5
.1268	-.7788	-1.2339	5	.0931	-1.9418	1.6289	5
-1.4073	-3.9630	1.6045	5	-3.0284	-3.8396	.6579	5
2.7479	-.2898	-1.5324	5	5.0152	.1221	-.4717	5
4.2189	.3497	1.1260	5	3.9076	1.5006	-.2264	5
4.1884	-2.2051	-.7354	5	2.4509	-2.6110	-.6120	5
3.3718	-2.1584	.8678	5	.0000	.0000	.0000	0

II

-2.5523	1.8166	.7118	1	-2.3060	.5735	1.5491	2
-1.8210	-.6467	1.2593	2	-1.3395	-1.2432	-.0424	22
.1384	-1.5512	-.1963	3	.9965	-.8311	-1.2282	1
1.4627	.5748	-.7854	1	.2086	1.2897	-.3413	2
-.7886	1.5675	-1.1993	29	-2.1704	1.8510	-.7522	29
-3.0988	2.1190	-1.6915	2	-2.2582	-2.1926	-.6823	22
.6191	-2.3848	.5376	7	2.5408	.5698	.3244	1
3.8071	-.2091	-.0774	1	2.9488	2.0085	.7000	1
-2.0463	-.9263	-1.1860	30	-3.1929	-2.4216	-.1757	5
-1.8308	-3.0533	-1.1916	5	-2.0178	2.6650	1.1992	5
-3.6374	2.0462	.8224	5	-2.5858	.7208	2.6083	5
-1.7530	-1.3631	2.0963	5	.4015	-.7709	-2.1688	5
1.8654	-1.4718	-1.4986	5	1.8840	1.1026	-1.6749	5
.0490	1.3753	.7443	5	-.6021	1.4336	-2.2665	5
-2.8498	2.1410	-2.7648	5	-4.1467	2.3267	-1.4233	5
2.1173	.0791	1.2351	5	4.6041	-.1098	.6949	5
4.2210	.1664	-1.0410	5	3.6167	-1.3009	-.1804	5
3.7088	2.0138	1.5149	5	2.0878	2.6120	1.0661	5
3.3870	2.5411	-.1748	5	.0000	.0000	.0000	0

III

-2.2818	-2.0531	.4759	1	-2.6582	-1.1084	-.6411	2
-2.4162	.2094	-.7496	2	-1.7353	1.1330	.2345	22
-.4533	1.8260	-.1866	3	.7526	1.0623	-.7304	1
1.4847	.1541	.2805	1	.5051	-.9386	.6393	2
.2058	-1.9801	-.1576	29	-1.0242	-2.7741	.0452	29
-1.0589	-4.0533	-.3711	2	-2.6370	1.8418	1.1539	22
-.4336	3.0369	-.1698	7	2.8479	-.3847	-.2156	1
3.8867	.7359	-.4168	1	3.4295	-1.4152	.7726	1
-1.8275	.8085	1.5738	30	-3.7063	1.6771	1.0426	5
-2.4004	2.8604	1.4507	5	-3.1275	-2.7593	.6453	5
-2.1363	-1.5393	1.4495	5	-3.1511	-1.5939	-1.5022	5
-2.7510	.7168	-1.6703	5	1.4608	1.8288	-1.1168	5
.4243	.4768	-1.6202	5	1.6890	.7479	1.2039	5
-.0621	-.7855	1.5692	5	.7862	-2.1601	-1.0631	5
-.1595	-4.5512	-.7681	5	-1.9863	-4.6457	-.3236	5
2.7056	-.8888	-1.2021	5	4.8779	.3186	-.7086	5
4.0317	1.3245	.5177	5	3.5999	1.4419	-1.2277	5
4.4138	-1.8021	.4217	5	2.7686	-2.3025	.8968	5
3.5821	-.9620	1.7788	5	.0000	.0000	.0000	0

IV

-2.5331	1.6751	-.6484	1	-2.9582	.7507	.4647	2
-2.5509	-.5114	.6781	2	-1.6028	-1.3263	-.1695	22
-.1559	-1.4663	.2652	3	.9781	-1.3610	-.7479	1
1.6076	.0472	-.8448	1	.4231	.9837	-.9857	2
-.0213	1.8538	-.0596	29	-1.3595	2.4794	-.1363	29
-1.5566	3.6699	.4604	2	-2.1858	-2.4836	-.8568	22
.0746	-1.6547	1.4379	7	2.6223	.3978	.2693	1
3.7223	-.6681	.4438	1	3.3152	1.7451	-.0246	1
-1.8523	-1.3248	-1.5284	30	-3.2316	-2.7168	-.6704	5
-1.5688	-3.3719	-.9708	5	-3.3882	2.3305	-.9348	5
-2.2802	1.1116	-1.5714	5	-3.6332	1.1983	1.2156	5
-2.9358	-1.0379	1.5680	5	.5780	-1.6565	-1.7456	5
1.7382	-2.1416	-.5245	5	2.1809	.0966	-1.8022	5
-.1656	.8357	-1.9052	5	.5525	2.0343	.8484	5
-.7242	4.2306	.9157	5	-2.5588	4.1246	.5089	5
2.0872	.4643	1.2470	5	4.5101	-.3236	1.1526	5
4.2193	-.8985	-.5262	5	3.3281	-1.6175	.8712	5
3.9843	2.0461	.8141	5	2.5951	2.5795	-.1745	5
3.9380	1.6817	-.9462	5	.0000	.0000	.0000	0

Y

-2.9725	-1.4759	-.4235	1	-2.7108	-.3100	-1.3513	2
-2.0589	.8326	-1.0743	2	-1.4050	1.2425	.2276	22
.0744	1.5750	.2150	3	1.0484	.9592	1.2119	1
1.6016	-.4328	.8359	1	.4332	-1.3928	.8920	2
-.4147	-1.5881	-.1329	29	-1.7420	-2.1993	.0750	29
-1.8631	-3.3426	.7753	2	-2.2401	1.9980	1.1656	22
.4625	2.3631	-.6176	7	2.4139	-.4691	-.4800	1
3.6407	.4618	-.4347	1	2.8902	-1.9002	-.7968	1
-1.9029	.6766	1.3847	30	-3.2513	2.2525	.8568	5
-1.7654	2.7814	1.7517	5	-3.6253	-2.2085	-.9536	5
-3.5569	-1.1054	.4498	5	-3.1074	-.4240	-2.3757	5
-1.9674	1.5796	-1.8810	5	.5465	.9154	2.2067	5
1.8912	1.6728	1.3578	5	2.3082	-.7528	1.6400	5
.1760	-1.7888	1.8893	5	-.2203	-1.0944	-1.0834	5
-.9849	-3.8808	1.1666	5	-2.8542	-3.7836	.9678	5
1.7731	-.1209	-1.3253	5	4.2497	.3720	-1.3635	5
4.3024	.2169	.4273	5	3.3516	1.5339	-.3558	5
3.4664	-1.9329	-1.7500	5	2.0411	-2.6108	-.9133	5
3.5501	-2.2912	.0111	5	.0000	.0000	.0000	0

VI

-2.9085	-.8263	-.5802	1	-2.9090	.1842	.5441	2
-2.1125	1.2526	.7234	2	-1.0034	1.7571	-.1680	22
.4419	1.6129	.2829	3	.8813	.5469	1.2810	1
1.2390	-.8098	.6320	1	-.0301	-1.2346	-.0620	2
-.9271	-2.0870	.4625	29	-2.3158	-2.1120	-.0444	29
-3.0771	-3.2017	.1651	2	-1.2872	2.0357	-1.5803	22
1.2590	2.4018	-.1381	7	2.4329	-.7729	-.3471	1
3.7368	-.3290	.3397	1	2.6478	-2.1541	-.9952	1
-1.2694	3.0331	-.6312	30	-2.2460	1.7429	-1.9992	5
-.4670	1.9240	-2.2854	5	-2.3507	-.4854	-1.4781	5
-3.9597	-.9667	-.9231	5	-3.6495	-.0203	1.3377	5
-2.2652	1.8569	1.6340	5	.0696	.4112	2.0333	5
1.7486	.9330	1.8638	5	1.4808	-1.5330	1.4478	5
-.2601	-.6891	-.9894	5	-.6819	-2.6466	1.3669	5
-2.6616	-4.1113	.6279	5	-4.1397	-3.2219	-.1244	5
2.2103	-.0444	-1.1647	5	4.5980	-.3700	-.3662	5
3.9781	-.9847	1.2072	5	3.6806	.7212	.7044	5
3.5041	-2.1378	-1.7080	5	1.7553	-2.4861	-1.5731	5
2.8628	-2.9295	-.2247	5	.0000	.0000	.0000	0

VII

-3.1016	-1.0240	-.1730	1	-2.4334	-.2447	-1.2829	2
-1.6368	.8334	-1.1770	2	-1.1637	1.5267	.0805	22
.3276	1.6042	.3256	3	.9972	.6439	1.2991	1
1.3427	-.7365	.6979	1	.0421	-1.3066	.1817	2
-.9016	-1.8381	.9770	29	-2.2838	-2.0999	.5201	29
-2.8822	-3.2220	.9629	2	-1.9920	2.6225	.5892	22
.9651	2.4325	-.2840	7	2.4251	-.7036	-.4065	1
3.7442	-.0712	.0733	1	2.7174	-2.1241	-.9291	1
-1.9446	1.3900	1.2102	30	-2.8711	2.9038	.0143	5
-1.4893	3.4745	1.0408	5	-4.0395	-1.4565	-.5930	5
-3.4493	-.3201	.6146	5	-2.6097	-.6384	-2.2997	5
-1.2303	1.2660	-2.1069	5	.3170	.5195	2.1738	5
1.9077	1.1285	1.7185	5	1.7164	-1.3867	1.5256	5
-.1563	-1.1784	-.8922	5	-.6706	-2.0009	2.0314	5
-2.3306	-3.9736	1.5507	5	-3.9423	-3.4307	.7483	5
2.0484	-.0908	-1.2622	5	4.5340	-.1423	-.7094	5
4.1258	-.5818	.9869	5	3.6325	1.0128	.3007	5
3.4787	-2.1070	-1.7426	5	1.8107	-2.6130	-1.3519	5
3.1062	-2.7780	-.1152	5	.0000	.0000	.0000	0

VIII

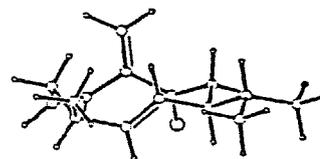
2.4273	-1.8610	-.8312	1	2.7617	-.4440	-1.2620	2
2.4431	.7642	-.7645	2	1.6058	1.1593	.4288	22
.2627	1.7990	.1342	3	-1.0620	1.1983	.5948	1
-1.5563	.0600	-.3223	1	-.3760	-.8572	-.5298	2
.2141	-1.5048	.4903	29	1.5668	-2.0914	.3898	29
2.0336	-2.8037	1.4341	2	1.9664	.6937	1.7726	22
.2690	2.8230	-.5121	7	-2.8074	-.6809	.1987	1
-4.0185	.2586	.3399	1	-3.1778	-1.8524	-.7301	1
2.3254	1.9385	1.3179	30	2.7380	-.0653	1.8684	5
1.1829	.5983	2.5190	5	3.4063	-2.3772	-.6984	5
1.9340	-2.3777	-1.6869	5	3.3959	-.4211	-2.1670	5
2.8437	1.6381	-1.3075	5	-1.8173	2.0176	.6177	5
-.9561	.8499	1.6468	5	-1.8149	.5059	-1.3133	5
.0846	-.8402	-1.5308	5	-.2675	-1.4864	1.4689	5
1.4284	-2.9692	2.3400	5	3.0413	-3.2483	1.4239	5
-2.5891	-1.1011	1.2106	5	-4.9267	-.3000	.6636	5
-4.2558	.7585	-.6269	5	-3.8451	1.0490	1.1046	5
-4.0786	-2.3934	-.3592	5	-2.3579	-2.6033	-.7984	5
-3.3984	-1.4926	-1.7610	5	.0000	.0000	.0000	0

# Conformational analysis of 157

The starting geometries of 157 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.4 Å, and with a transannular contact of 2.4 Å. Structures of 61 conformations obtained were optimized by MM2 to get 6 conformers within 2.5 kcal/mol from the lowest energy conformer.

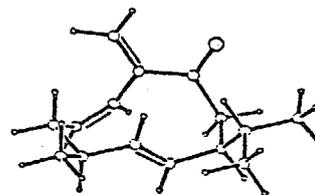
I NO= 20 ENERGY= 24.9586

ST= 1.21 BD= 2.58 SB= .18 14= 9.67  
OT= -3.24 T= 14.33 DP= .22 DM= 3.02D



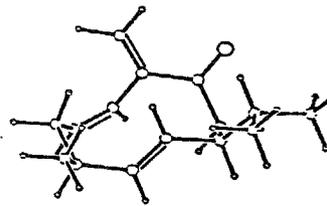
II NO= 29 ENERGY= 25.0846

ST= 1.36 BD= 3.75 SB= .20 14= 9.69  
OT= -2.53 T= 12.51 DP= .11 DM= 2.74D



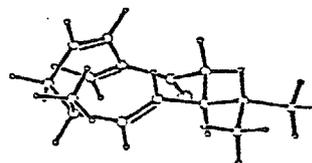
III NO= 17 ENERGY= 25.4336

ST= 1.30 BD= 2.78 SB= .17 14= 9.87  
OT= -3.34 T= 14.53 DP= .11 DM= 2.80D



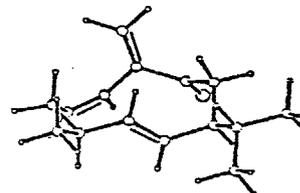
IV NO= 33 ENERGY= 25.4497

ST= 1.37 BD= 3.53 SB= .18 14= 9.77  
OT= -2.19 T= 12.68 DP= .11 DM= 2.70D



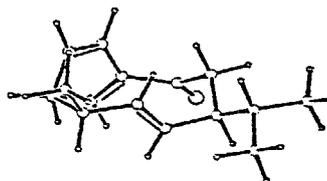
V NO= 15 ENERGY= 25.7109

ST= 1.18 BD= 2.66 SB= .18 14= 9.68  
OT= -3.55 T= 15.40 DP= .17 DM= 3.05D



VI NO= 38 ENERGY= 26.0660

ST= 1.33 BD= 2.81 SB= .16 14= 10.11  
OT= -3.14 T= 14.68 DP= .11 DM= 2.77D





5	2	29	1	0.0	9.462	0.0
29	1	2	5	0.0	0.0	0.60
1	2	29	29	0.0	9.415	0.0
5	2	29	29	0.0	9.415	0.0
5	1	29	29	0.0	0.0	-0.24
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
5	1	29	2	0.0	0.0	-0.24
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	29	29	5	0.0	2.20	0.0
5	29	29	5	0.0	2.23	0.0
2	29	3	7	0.91	1.540	0.91
29	29	3	7	0.91	1.540	0.91
2	29	29	3	0.0	2.20	0.0
3	29	2	5	0.0	9.415	0.0
1	3	29	2	0.15	1.540	0.0
29	3	1	1	0.0	0.0	-0.330
29	3	1	5	0.0	0.0	0.0
29	29	3	1	0.15	1.540	0.0
2	29	9.444		1.340		
2	3	6.370		1.4767		
1	29	4.40		1.496		
5	29	4.60		1.09		
29	29	6.115		1.470		
3	29	6.290		1.480		
	29	0.044		1.940		
2	1	29		0.45	109.47	
5	1	29		0.36	109.39	
1	29	29		0.55	121.4	
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
3	29	29		0.43	117.0	
	29	29		0.050		
1	29	2		0.55	121.4	
5	29	2		0.36	120.0	
3	29	2		0.36	121.4	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		
7	3	29		0.43	122.5	
1	3	29		0.43	115.0	
	3	29		0.050		

I

-3.0243	-.4132	-.3279	1	-3.1593	.8943	.4219	2
-2.3137	1.9645	.3252	29	-1.1762	2.0631	-.5376	29
.1305	2.2110	.1699	3	1.3613	1.4703	-.3520	1
1.4248	.0240	.1829	1	.0985	-.6356	-.1259	2
-.8417	-.8858	.7986	2	-2.2143	-1.4404	.4870	1
-2.1227	-2.7924	-.2383	1	-1.2969	1.9497	-1.8917	2
.2069	2.8384	1.2025	7	2.5934	-.8059	-.3956	1
3.9649	-.1724	-.1016	1	2.5705	-2.2439	.1575	1
-2.5390	-.2643	-1.3171	5	-4.0457	-.8048	-.5455	5
-3.9567	.9293	1.1846	5	-2.4740	2.7855	1.0277	5
2.2587	2.0424	-.0215	5	1.3860	1.4725	-1.4643	5
1.5591	.0781	1.2899	5	-.1044	-.8612	-1.1854	5
-.6378	-.6250	1.8508	5	-2.7430	-1.6164	1.4562	5
-1.5263	-3.5242	.3544	5	-1.6472	-2.6985	-1.2409	5
-3.1355	-3.2309	-.3927	5	-.4306	2.0095	-2.5671	5
-2.2855	1.8359	-2.3645	5	2.4740	-.8622	-1.5058	5
4.7949	-.8205	-.4656	5	4.1106	-.0182	.9920	5
4.0889	.8102	-.6103	5	3.4065	-2.8511	-.2595	5
1.6274	-2.7769	-.1023	5	2.6693	-2.2477	1.2672	5

II

-3.0972	.3105	.0487	1	-2.5507	1.1984	1.1471	2
-1.4245	1.9721	1.0731	29	-.5905	2.1786	-.0727	29
.8758	1.8932	.0297	3	1.4372	1.0482	1.1728	1
1.3475	-.4767	.9398	1	-.1171	-.8520	1.0059	2
-.9560	-.8942	-.0405	2	-2.4476	-1.0868	.1068	1
-2.9908	-2.0126	-.9911	1	-1.1119	2.6440	-1.2458	2
1.6400	2.3307	-.8012	7	2.0911	-.9847	-.3183	1
3.5903	-.6298	-.2952	1	1.9512	-2.5127	-.4668	1
-2.9146	.7539	-.9549	5	-4.2045	.2359	.1590	5
-3.0505	1.1060	2.1271	5	-1.0999	2.4510	1.9992	5
.9381	1.3235	2.1299	5	2.5006	1.3412	1.3307	5
1.8376	-.9837	1.8064	5	-.5315	-1.0113	2.0160	5
-.5873	-.6820	-1.0564	5	-2.6775	-1.5452	1.0996	5
-2.5024	-3.0135	-.9454	5	-2.8128	-1.5919	-2.0074	5
-4.0885	-2.1666	-.8767	5	-.4862	2.8033	-2.1383	5
-2.1793	2.9011	-1.3365	5	1.6554	-.5053	-1.2276	5
4.1209	-1.0625	-1.1744	5	4.0840	-1.0219	.6232	5
3.7640	.4688	-.3387	5	2.4710	-2.8789	-1.3820	5
.8894	-2.8350	-.5545	5	2.3929	-3.0427	.4078	5

III

-3.0076	.4457	-.2317	1	-2.6061	1.4689	.8094	2
-1.4456	2.1931	.8156	29	-.4426	2.2334	-.2051	29
.9644	1.8840	.1599	3	1.2202	.8275	1.2323	1
1.1486	-.6165	.6836	1	-.2387	-.7798	.1051	2
-1.3254	-1.0320	.8494	2	-2.7352	-.9768	.3039	1
-2.9762	-2.0506	-.7665	1	-.7479	2.5721	-1.4915	2
1.8968	2.3958	-.4176	7	2.2386	-.9675	-.3556	1
3.6641	-.7685	.1907	1	2.0868	-2.4250	-.8337	1
-2.4475	-.5978	-1.1803	5	-4.0869	.5746	-.4813	5
-3.2632	1.5309	1.6944	5	-1.2357	2.7793	1.7130	5
.4893	.9591	2.0633	5	2.2113	1.0194	1.7027	5
1.2617	-1.3147	1.5478	5	-.3603	-.5689	-.9697	5
-1.2067	-1.1912	1.9346	5	-3.4367	-1.1706	1.1525	5
-2.7837	-3.0700	-.3590	5	-2.3176	-1.9097	-1.6537	5
-4.0308	-2.0233	-1.1254	5	.0205	2.5889	-2.2809	5
-1.7740	2.8505	-1.7811	5	2.1195	-.3011	-1.2449	5
4.4288	-1.1083	-.5450	5	3.8184	-1.3456	1.1309	5
3.8892	.3016	.3984	5	2.8539	-2.6811	-1.6004	5
1.0934	-2.6133	-1.3007	5	2.2034	-3.1388	.0137	5

IV

-3.1091	.4564	.0215	1	-2.5340	-.0593	1.3239	2
-1.7022	-1.1373	1.4593	29	-1.3061	-2.0398	.4212	29
.1479	-2.2266	.1168	3	1.2182	-1.3092	.7129	1
1.4118	-.0056	-.0928	1	.1331	.7855	.0526	2
-.8349	.8394	-.8743	2	-2.1814	1.4913	-.6486	1
-2.1133	2.8140	.1315	1	-2.2466	-2.7388	-.2802	2
.5015	-3.1124	-.6294	7	2.6222	.8441	.3608	1
3.9633	.1068	.1905	1	2.6833	2.1711	-.4216	1
-4.1168	.8942	.2122	5	-3.2722	-.3816	-.6923	5
-2.7183	.5676	2.2135	5	-1.2663	-1.3063	2.4460	5
2.1645	-1.8956	.7109	5	1.0035	-1.0923	1.7841	5
1.5647	-.2783	-1.1644	5	-.0155	1.2747	1.0282	5
-.6930	.3006	-1.8264	5	-2.5968	1.7462	-1.6551	5
-1.4138	3.5302	-.3585	5	-1.7810	2.6801	1.1851	5
-3.1155	3.2999	.1716	5	-1.9741	-3.4382	-1.0863	5
-3.3198	-2.6433	-.0491	5	2.5005	1.0875	1.4451	5
4.8227	.7704	.4407	5	4.1002	-.2419	-.8586	5
4.0496	-.7753	.8636	5	3.5496	2.7927	-.0979	5
1.7724	2.7933	-.2674	5	2.7880	1.9861	-1.5152	5

V

3.1362	-.3529	.0574	1	2.9918	.8488	-.8515	2
2.1276	1.8965	-.6925	29	1.1934	2.0877	.3745	29
-.2213	2.2424	-.0707	3	-1.2719	1.3222	.5437	1
-1.5212	.0884	-.3503	1	-.1862	-.5079	-.7476	2
.7243	-.9552	.1303	2	2.0992	-1.4497	-.2565	1
2.4165	-2.7496	.5000	1	1.5424	2.0714	1.6929	2
-.5169	2.9808	-.9831	7	-2.4477	-.9678	.2941	1
-3.8281	-.3900	.6546	1	-2.6324	-2.1816	-.6364	1
3.0593	-.0639	1.1286	5	4.1687	-.7545	-.0717	5
3.5836	.8116	-1.7831	5	2.0751	2.6074	-1.5203	5
-2.2074	1.9157	.6648	5	-.9666	1.0022	1.5652	5
-2.0156	.4475	-1.2854	5	.0560	-.5255	-1.8238	5
.4988	-.9165	1.2084	5	2.1344	-1.6689	-1.3515	5
1.6556	-3.5345	.2821	5	2.4344	-2.5869	1.6023	5
3.4108	-3.1556	.2028	5	.7940	2.2134	2.4880	5
2.5928	1.9668	2.0063	5	-1.9751	-1.3312	1.2394	5
-4.5031	-1.1793	1.0582	5	-4.3238	.0546	-.2384	5
-3.7589	.3959	1.4401	5	-3.2991	-2.9466	-.1759	5
-1.6657	-2.6902	-.8548	5	-3.0861	-1.8771	-1.6072	5

VI

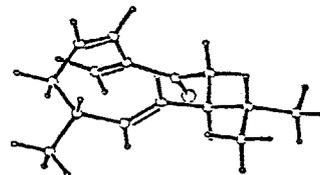
-2.9713	.1506	-.2423	1	-2.6478	-.4918	1.0899	2
-1.7501	-1.5059	1.2815	29	-1.0696	-2.2479	.2643	29
.4251	-2.2700	.2502	3	1.2202	-1.0938	.8166	1
1.4603	-.0035	-.2517	1	.1014	.4476	-.7432	2
-.7444	1.1868	-.0101	2	-2.1736	1.4622	-.4168	1
-2.7738	2.6201	.3957	1	-1.7687	-2.9271	-.6917	2
1.0192	-3.1895	-.2668	7	2.3454	1.1695	.2311	1
3.7669	.7139	.6105	1	2.4450	2.2655	-.8476	1
-4.0686	.3294	-.3241	5	-2.7077	-.5358	-1.0778	5
-3.0843	-.0071	1.9801	5	-1.5047	-1.7670	2.3131	5
2.1919	-1.5042	1.1737	5	.7161	-.6706	1.7149	5
1.9891	-.4720	-1.1167	5	-.2356	.0655	-1.7218	5
-.4358	1.5256	.9920	5	-2.1951	1.7554	-1.4954	5
-2.1874	3.5564	.2479	5	-2.7892	2.4002	1.4875	5
-3.8217	2.8291	.0795	5	-1.2609	-3.4925	-1.4891	5
-2.8707	-2.9410	-.6912	5	1.8865	1.6232	1.1429	5
4.4089	1.5823	.8851	5	4.2606	.1843	-.2360	5
3.7696	.0348	1.4924	5	3.0833	3.1127	-.5065	5
1.4501	2.6987	-1.0985	5	2.8887	1.8635	-1.7871	5

Conformational analysis of 158

The starting geometries of 158 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.4 Å, and with a transannular contact of 2.4 Å. Structures of 60 conformations obtained were optimized by MM2 to get 4 conformers within 2.0 kcal/mol from the lowest energy conformer.

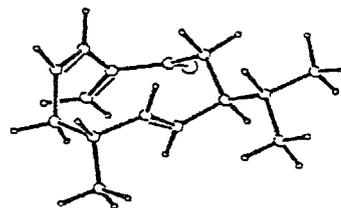
I NO= 32 ENERGY= 24.3818

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OT= -2.42 T= 12.42 DP= .11 DM= 2.70D



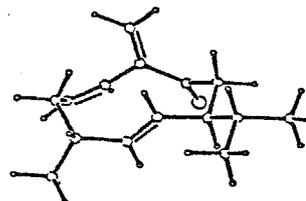
II NO= 37 ENERGY= 25.3402

ST= 1.32 BD= 2.96 SB= .16 14= 10.05  
OT= -3.25 T= 14.01 DP= .11 DM= 2.78D



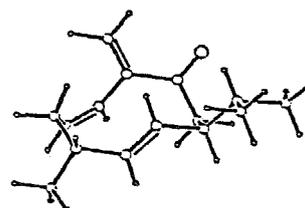
III NO= 20 ENERGY= 25.7107

ST= 1.21 BD= 2.59 SB= .19 14= 9.64  
OT= -3.06 T= 14.91 DP= .23 DM= 3.02D



IV NO= 18 ENERGY= 26.3662

ST= 1.32 BD= 2.75 SB= .18 14= 9.88  
OT= -3.11 T= 15.23 DP= .11 DM= 2.80D



ENERGY: FINAL STERIC ENERGY, ST: COMPRESSION, BD: BENDING, SB: STRETCH-BEND,  
14: VAN DER WAALS\_1,4 ENERGY, OT: VAN DER WAALS\_OTHER, T: TORSIONAL, DP: DIPOLE,  
DM: DIPOLE MOMENT [ KCAL/MOL ]

0 PA  $\alpha$ -methyl INTERMEDIATE

16	10	2	22	2922	1	1.50	1.34	120.0	1	1	30	1.0	2.4	0	1.2
2	10	0	0												
1	3	3	0												
2	2	4	0												
1	2	3	4	2922	1	1.50	120.0	0.0	3	5	12	12	0		
2	3	4	5	32	0	1.50	120.0	0.0	4	6	13	13	0		
3	4	5	6	2	0	1.50	120.0	0.0	5	7	0	0	0		
4	5	6	7	2	0	1.54	109.5	0.0	6	8	14	0	0		
5	6	7	8	22	0	1.50	109.5	0.0	7	9	9	0	0		
6	7	8	9	22	0	1.34	120.0	0.0	8	8	10	0	0		
7	8	9	10	2	1	1.50	120.0	180.0	1	9	11	0	0		
8	9	10	11	2	2	1.54	109.5	120.0	10	0	0	0	1		
2	3	4	12	22	2	1.34	120.0	180.0	4	4	0	0	5		
3	4	5	13	14	2	1.41	120.0	180.0	5	5	0	0	6		
5	6	7	14	2	2	1.54	109.5	240.0	7	15	16	0	8		
6	7	14	15	2	1	1.54	109.5	-60.0	14	0	0	0	0		
6	7	14	16	2	1	1.54	109.5	180.0	14	0	0	0	0		

38 4 0 0 1 500.

6					22				1						
1	2	3	4	5	6	7	8	9	10	1					
10	11														
4	12														
5	13														
7	14	15													
14	16														
1	17	1	18	2	19	3	20	6	21	6	22	7	23	8	24
9	25	10	26	11	27	11	28	11	29	12	30	12	31	14	32
15	33	15	34	15	35	16	36	16	37	16	38				
31	6	1	17												
2	2	3	1	0.15		2.091		0.0							
2	2	3	7	0.91		2.091		0.0							
5	2	3	1	0.0		2.091		0.0							
5	2	3	7	0.0		2.091		0.0							
1	1	2	29	-0.44		0.24		0.06							
2	2	1	29	0.10		0.0		0.50							
2	1	29	29	0.10		0.0		0.50							
2	1	29	2	0.10		0.0		0.50							
1	29	29	2	0.0		2.23		0.0							
1	29	29	5	0.0		2.23		0.0							
5	2	29	1	0.0		9.462		0.0							
29	1	2	5	0.0		0.0		0.60							
1	2	29	29	0.0		9.415		0.0							

5	2	29	29	0.0	9.415	0.0
5	1	29	29	0.0	0.0	-0.24
5	1	2	29	0.0	0.0	-0.24
2	29	29	2	0.0	2.23	0.80
1	2	29	5	0.0	9.415	0.0
5	1	29	2	0.0	0.0	-0.24
2	29	29	5	0.0	2.23	0.0
5	2	29	5	0.0	9.415	0.0
3	29	29	5	0.0	2.20	0.0
5	29	29	5	0.0	2.23	0.0
2	29	3	7	0.91	1.540	0.91
29	29	3	7	0.91	1.540	0.91
2	29	29	3	0.0	2.20	0.0
3	29	2	5	0.0	9.415	0.0
1	3	29	2	0.15	1.540	0.0
29	3	1	1	0.0	0.0	-0.330
29	3	1	5	0.0	0.0	0.0
29	29	3	1	0.15	1.540	0.0
2	29	9.444		1.340		
2	3	6.370		1.4767		
1	29	4.40		1.496		
5	29	4.60		1.09		
29	29	6.115		1.470		
3	29	6.290		1.480		
	29	0.044		1.940		
2	1	29		0.45	109.47	
5	1	29		0.36	109.39	
1	29	29		0.55	121.4	
2	29	29		0.43	120.0	
5	29	29		0.36	120.0	
3	29	29		0.43	117.0	
	29	29		0.050		
1	29	2		0.55	121.4	
5	29	2		0.36	120.0	
3	29	2		0.36	121.4	
	29	2		0.05		
1	2	29		0.55	121.4	
5	2	29		0.36	120.0	
	2	29		0.05		
7	3	29		0.43	122.5	
1	3	29		0.43	115.0	
	3	29		0.050		

I

-3.0286	-.4363	-.5507	1	-2.3239	.2522	-1.7008	2
-1.4862	1.3284	-1.5941	29	-1.2019	2.0621	-.3987	29
.2115	2.1687	.0829	3	1.3369	1.3414	-.5431	1
1.4646	-.0707	.0695	1	.2073	-.8224	-.3005	2
-.8576	-.9603	.5034	2	-2.1579	-1.5696	.0298	1
-2.8740	-2.3002	1.1753	1	-2.2107	2.6669	.2953	2
.4857	2.9133	.9976	7	2.7163	-.8496	-.4000	1
4.0327	-.1518	-.0108	1	2.7236	-2.2773	.1815	1
-4.0047	-.8351	-.9141	5	-3.2691	.2830	.2631	5
-2.4079	-.2455	-2.6826	5	-.9496	1.6316	-2.4953	5
2.2747	1.9143	-.3652	5	1.2250	1.2890	-1.6500	5
1.5210	.0363	1.1792	5	.1528	-1.2086	-1.3321	5
-.8330	-.5315	1.5188	5	-1.9498	-2.3084	-.7825	5
-2.2341	-3.1118	1.5926	5	-3.8217	-2.7672	.8206	5
-3.1311	-1.6050	2.0073	5	-2.0247	3.2338	1.2212	5
-3.2529	2.6256	-.0600	5	2.6883	-.9301	-1.5147	5
4.9152	-.7756	-.2822	5	4.0780	.0384	1.0859	5
4.1694	.8189	-.5378	5	3.6187	-2.8481	-.1572	5
1.8338	-2.8667	-.1366	5	2.7365	-2.2553	1.2953	5

II

-2.9686	.4090	.2562	1	-2.5880	-.4717	1.4277	2
-1.7640	-1.5617	1.3663	29	-1.2329	-2.1678	.1837	29
.2484	-2.3033	.0355	3	1.1843	-1.2825	.6833	1
1.4004	-.0522	-.2263	1	.0360	.5523	-.4785	2
-.6501	1.2520	.4380	2	-2.0912	1.6784	.2698	1
-2.3055	2.5465	-.9781	1	-2.0586	-2.6135	-.8080	2
.7167	-3.1829	-.6520	7	2.4264	.9684	.3192	1
3.8394	.3683	.4453	1	2.4946	2.2165	-.5824	1
-4.0510	.6700	.3180	5	-2.8245	-.1226	-.7101	5
-2.9007	-.1083	2.4221	5	-1.4519	-2.0042	2.3148	5
2.1523	-1.8018	.8662	5	.8034	-.9776	1.6846	5
1.7942	-.4077	-1.2091	5	-.4446	.3100	-1.4409	5
-.1901	1.4476	1.4206	5	-2.3700	2.2926	1.1615	5
-1.6551	3.4512	-.9501	5	-3.3632	2.8914	-1.0429	5
-2.0796	1.9940	-1.9182	5	-1.6629	-3.0692	-1.7296	5
-3.1543	-2.5412	-.7146	5	2.1121	1.2951	1.3400	5
4.5767	1.1376	.7712	5	4.1913	-.0443	-.5278	5
3.8846	-.4459	1.2029	5	3.2334	2.9555	-.1956	5
1.5169	2.7464	-.6414	5	2.7978	1.9451	-1.6194	5

III

-2.9186	-.3283	-.8260	1	-3.1300	.8209	.1344	2
-2.2789	1.8759	.3130	29	-1.0658	2.1067	-.4104	29
.1714	2.0797	.4248	3	1.4446	1.4380	-.1255	1
1.4827	-.0795	.1527	1	.2036	-.6774	-.3927	2
-.8428	-1.0160	.3763	2	-2.1631	-1.5046	-.1744	1
-3.0001	-2.1980	.9121	1	-1.0646	2.2601	-1.7659	2
.1533	2.4775	1.5680	7	2.7188	-.7936	-.4403	1
4.0433	-.2145	.0886	1	2.6742	-2.3046	-.1413	1
-2.3504	.0101	-1.7206	5	-3.9085	-.6649	-1.2140	5
-4.0020	.7361	.8060	5	-2.5062	2.5633	1.1309	5
2.3064	1.9427	.3688	5	1.5559	1.6322	-1.2152	5
1.5083	-.2187	1.2602	5	.1237	-.7797	-1.4877	5
-.7736	-.8737	1.4673	5	-1.9466	-2.2609	-.9688	5
-2.4567	-3.0738	1.3367	5	-3.9639	-2.5725	.4967	5
-3.2403	-1.5097	1.7543	5	-.1409	2.4258	-2.3398	5
-2.0078	2.2666	-2.3354	5	2.7075	-.6610	-1.5503	5
4.9168	-.7913	-.2933	5	4.0790	-.2437	1.2016	5
4.1987	.8388	-.2367	5	3.5580	-2.8287	-.5724	5
1.7710	-2.7904	-.5757	5	2.6691	-2.4956	.9563	5

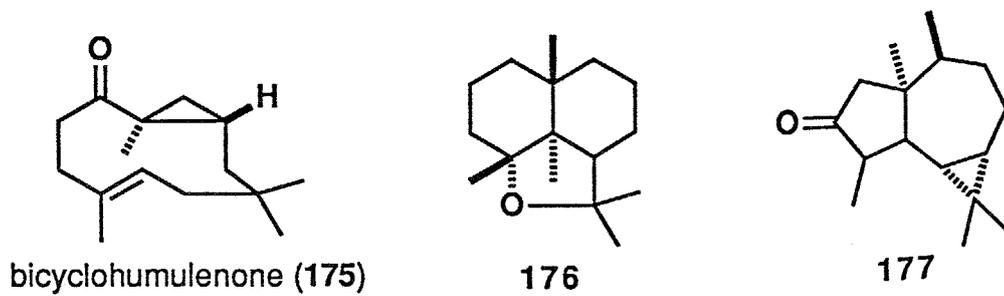
IV

-2.8927	.4936	-.6603	1	-2.6192	1.3407	.5638	2
-1.4694	2.0385	.8139	29	-.3533	2.2177	-.0646	29
1.0014	1.7979	.4067	3	1.1306	.5839	1.3231	1
1.1423	-.7542	.5481	1	-.1626	-.8220	-.2134	2
-1.3327	-1.1461	.3562	2	-2.6583	-1.0036	-.3569	1
-3.8050	-1.6119	.4663	1	-.5039	2.7550	-1.3102	2
1.9936	2.3815	.0328	7	2.3568	-.9443	-.3904	1
3.7015	-.8431	.3525	1	2.2876	-2.3077	-1.1064	1
-2.2282	.7983	-1.4992	5	-3.9336	.6723	-1.0172	5
-3.3777	1.2885	1.3637	5	-1.3693	2.4831	1.8065	5
.3011	.5907	2.0673	5	2.0532	.6894	1.9377	5
1.1586	-1.5807	1.2991	5	-.1562	-.4842	-1.2628	5
-1.3500	-1.4288	1.4218	5	-2.6025	-1.5620	-1.3237	5
-3.6320	-2.6974	.6519	5	-4.7769	-1.5174	-.0704	5
-3.9167	-1.1140	1.4563	5	.3532	2.8810	-1.9908	5
-1.4887	3.0912	-1.6725	5	2.3389	-.1457	-1.1721	5
4.5557	-1.0651	-.3277	5	3.7473	-1.5638	1.2005	5
3.8849	.1789	.7537	5	3.1499	-2.4453	-1.7986	5
1.3654	-2.4144	-1.7215	5	2.3049	-3.1465	-.3734	5

第六章 10員環エノンへの共役付  
 加的三員環形成反応の立体選択性の予測  
 : ビシクロフムレノンの合成<sup>115)</sup>

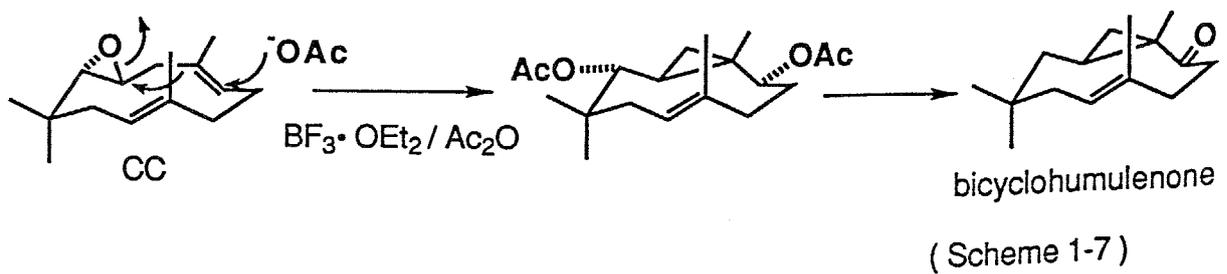
6-1 ビシクロフムレノン

(+)-ビシクロフムレノン (175) は1979年に松尾、野崎らによりハネゴケ科に属する日本原産のコハネゴケ (*Plagiochila acanthopylla* subsp. *japonica*) から(-)-maalioxide (176)、(+)-cyclocolorenone (177) と並んで単離されたセスキテルペンである<sup>116)</sup>。175はシダー臭、ショウノウ臭、花香様の混じったような独特の匂いをもっており、その匂いから香料として魅力的である (Fig. 6-1)。



(Fig. 6-1)

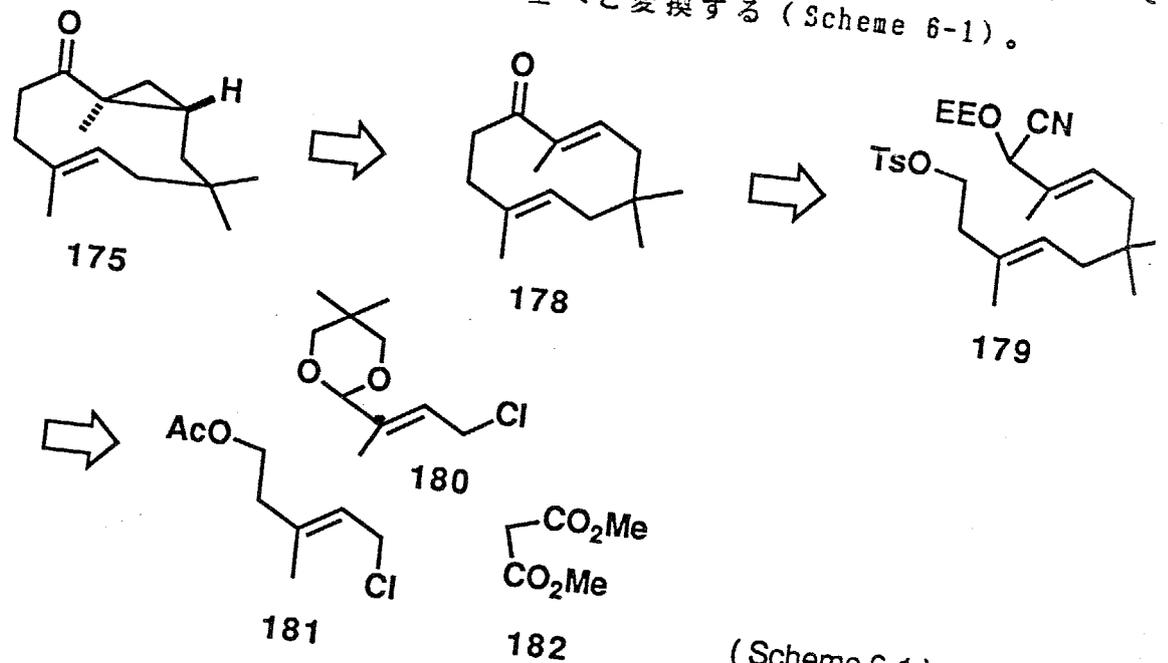
この化合物の合成は白浜、松本らによりフムレンエポキシド 178 より生合成類似反応によって行われているだけである<sup>37)</sup>。



(Scheme 1-7)

## 6-2 合成計画

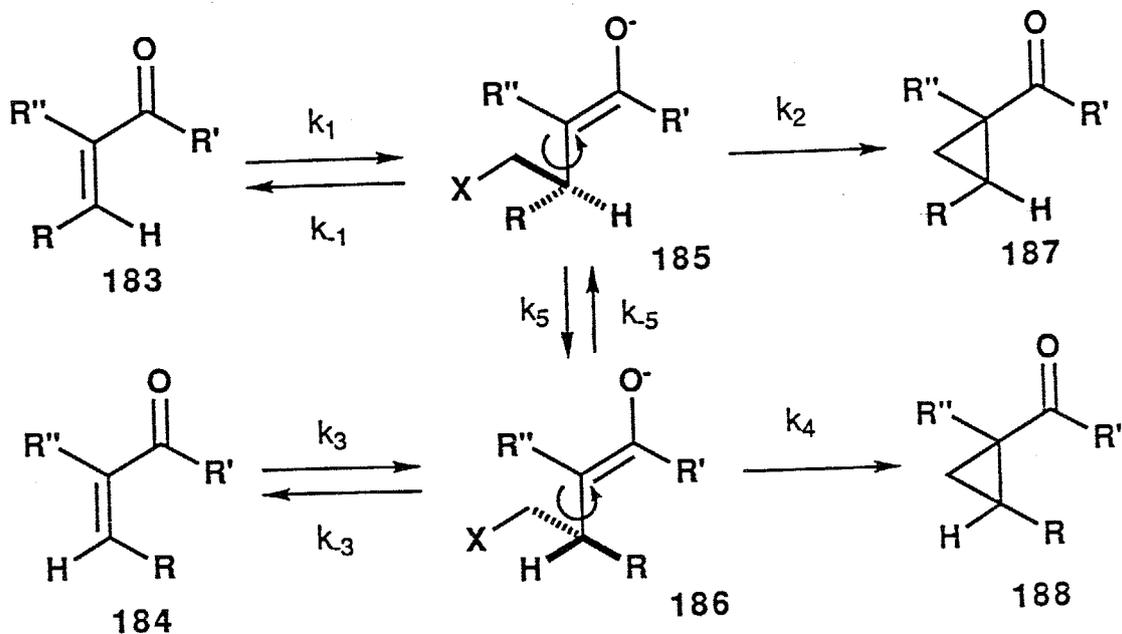
ビシクロフムレノン (175) の合成計画は次の通りである。175の3員環は、10員環エノン178への硫黄イリド<sup>(117)</sup>の共役付加-アルキル化で導入する。10員環エノンは保護したシアンヒドリン179の分子内アルキル化反応で構築する。179はマロン酸ジメチル182に(E)-アリルクロリド180と181を順次アルキル化し、必要な炭素鎖と官能基を導入する。さらにジエステルからC-5位のジメチル基へと変換する (Scheme 6-1)。



(Scheme 6-1)

## 6-3 シクロプロパン化の立体選択性

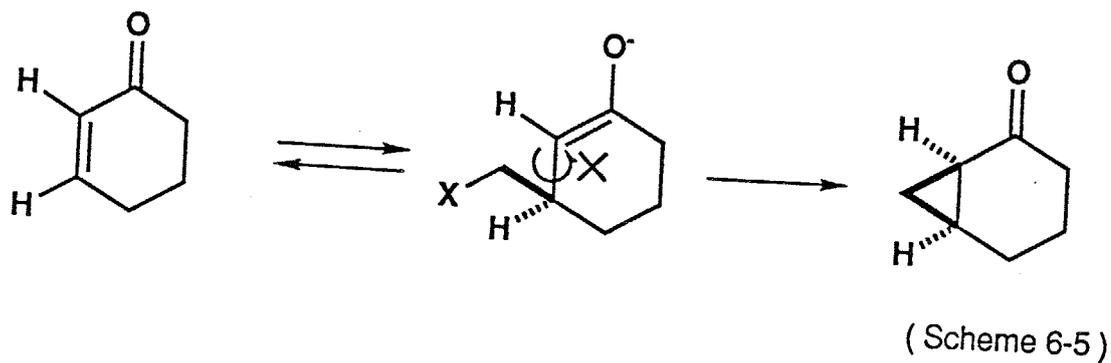
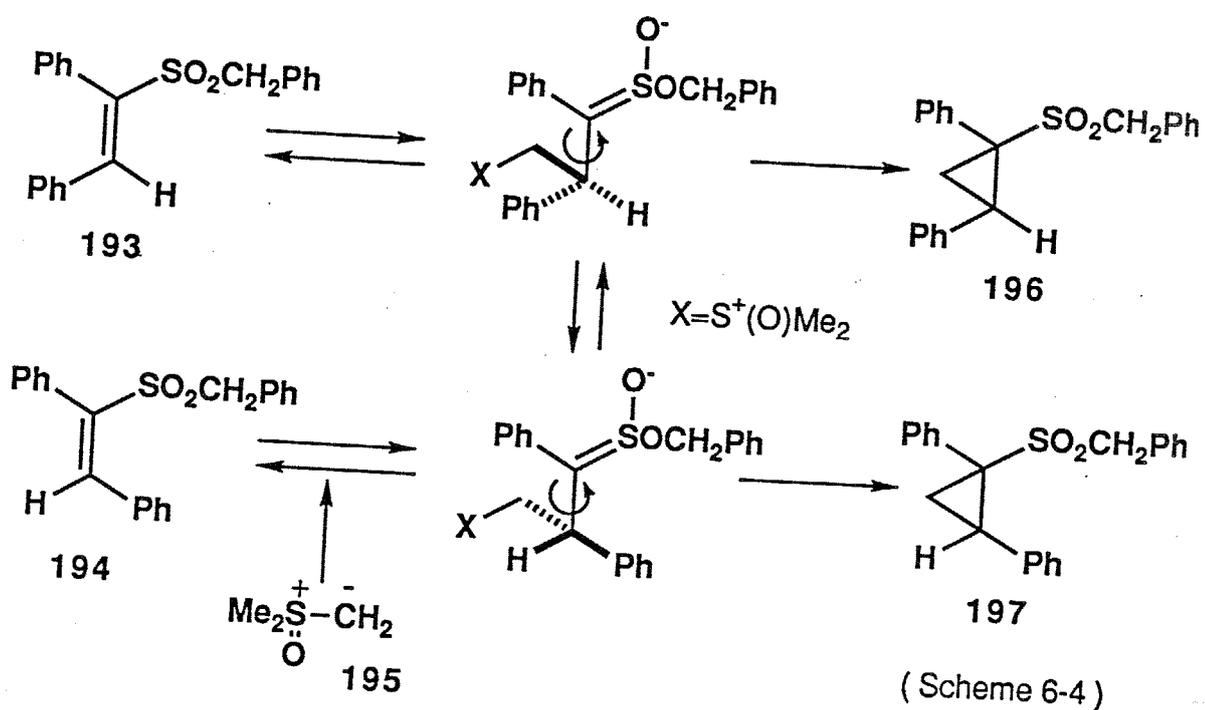
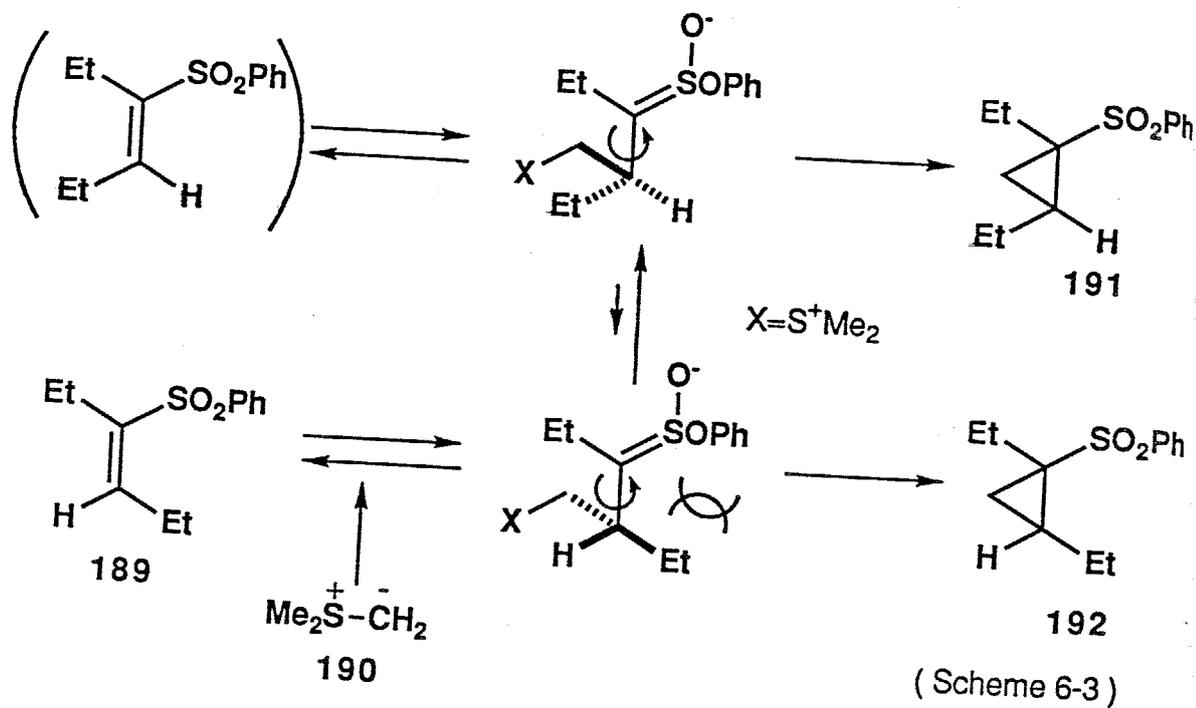
一般に、電子吸引基のついたオレフィン183に対し、硫黄イリドが共役付加すると、エノラート185が生成する。kはそれぞれの反応の速度定数とし、もし $k_2 > k_5$ ならば187のみが得られる。しかし $k_5 > k_2$ の場合、すなわち3員環形成反応よりも立体配座の変化の方が速いときは、エノラート186を經由し、186の生成が考えられる。同様に184についても $k_4 > k_{-5}$ の時は188だけが生成するのに対し、 $k_{-5} > k_4$ の場合はエノラート185を経て187が得られる (Scheme 6-2)。



(Scheme 6-2)

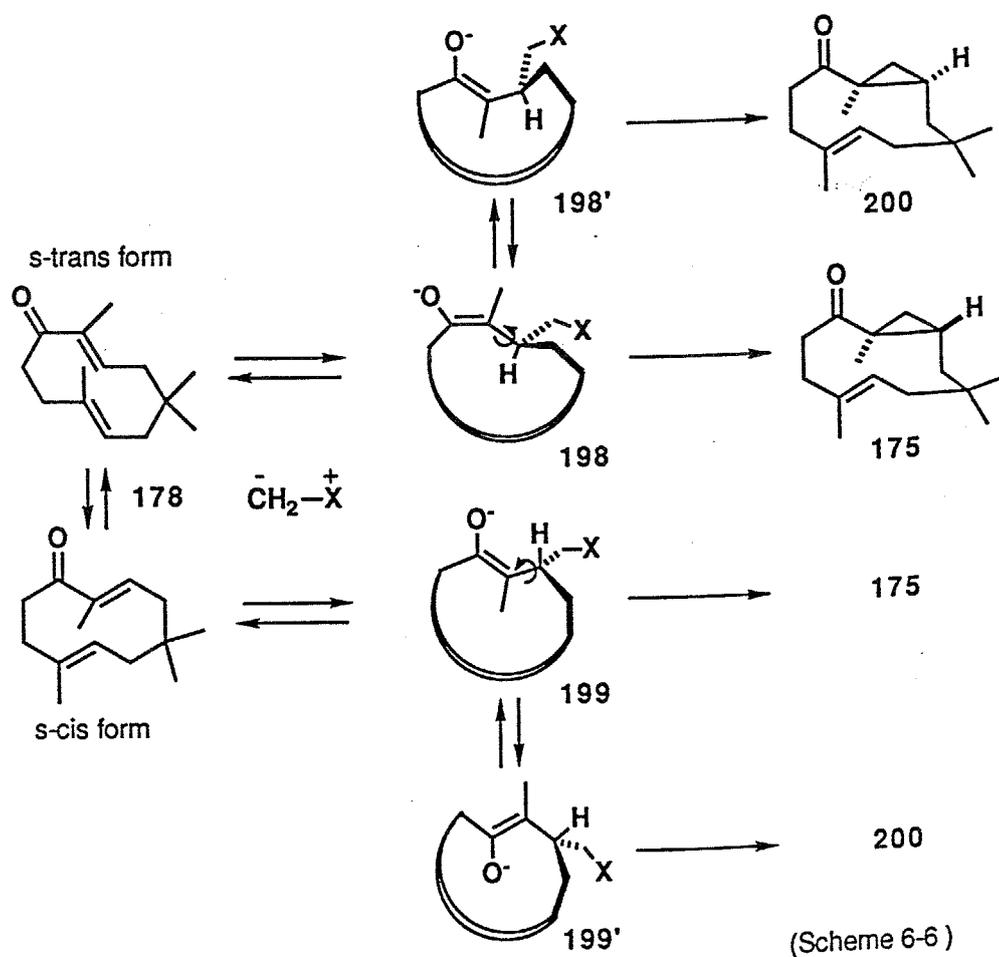
Scheme 6-3,4に鎖状化合物の例を示した。 $\alpha, \beta$ 不飽和スルホン 189 にジメチルスルホニウムメチリド (190) を反応させるとエノラートのアルキル化よりも自由回転で安定なエノラートになってからアルキル化が起こり 191: 192 が 7.5: 1 の比で得られることが報告されている<sup>118)</sup> (Scheme 6-3)。また 193 あるいは 194 とジメチルオキソスルホニウムメチリド (195) との反応ではいずれの場合も 196 と 197 を 1: 1 の比で与える<sup>119)</sup> ことからエノラートから3員環形成よりも速くエノラートの自由回転が起こっていることがわかる (Scheme 6-4)。

これに対し、5,6員環化合物の場合Scheme 6-2に示すエノラートの自由回転は起こり得ないので特異的に3員環が形成される (Scheme 6-5)。



一方鎖状分子のように自由ではないものの、5,6員環化合物とは異なり自由回転のできる中・大員環化合物ではどうであろうか。

10員環エノン 178 に硫黄イリドが付加する場合、エノン部分が *S*-トランスの配座異性体からは (*E*)-エノラート 198 が生成し、*S*-シスの配座異性体からは (*Z*)-エノラート 199 が生成すると考えられる。ここで環の立体配座変化 (198 → 198' あるいは 199 → 199') よりも3員環形成が速ければ 198 および 199 から 175 だけが得られる。しかし環の立体配座変化の方が速ければ、198' あるいは 199' を経て 200 が生成する可能性がある (scheme 6-6)。それぞれの配座異性体からの3員環生成の活性化エネルギーはほとんど等しいと仮定すると、198' あるいは 199' が有利に存在しえらば 200 が優先してできることになる。



そこでまずエノラート 198 と 199 の生成に重要なエノン 178 の立体配座についてMM2計算を用いて解析し、続いてエノラート 198 と 199 の立体配座解析を行った。

筆者は立体配座の計算を行い、実際の合成は当研究室の山下嘉郎氏が行った。

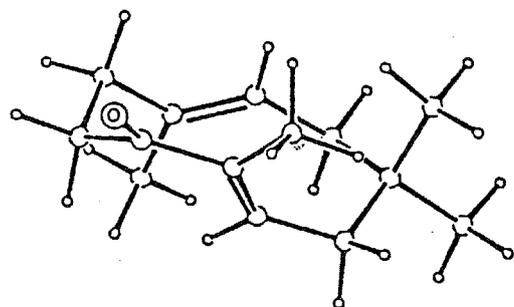
#### 6-4 計算予測

178 のすべての立体配座を得るため、MMRSを用いて初期座標を発生させ、75個の立体配座をMM2により構造最適化を行い、3.0 kcal/mol以内に4個の配座異性体の存在がわかった (Fig. 6-2)。

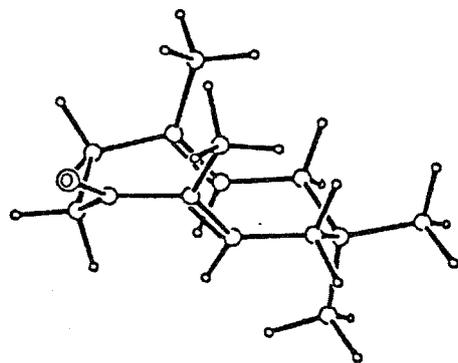
torsional angle resolution 30 deg

closure distance 1.0 - 2.7 Å

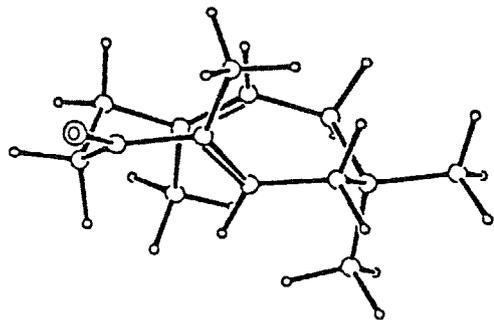
transannular contact 2.24 Å



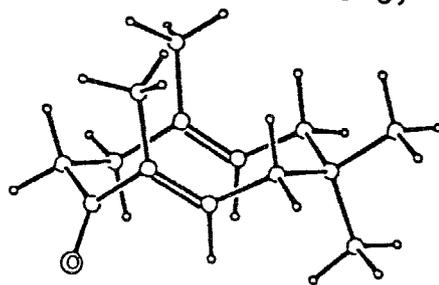
I 0.00 Kcal/mol  
45% (-30°C)



II 0.21 Kcal/mol  
30% (-30°C)



III 0.33 Kcal/mol  
23% (-30°C)



IV 1.53 Kcal/mol  
2% (-30°C)

( Fig. 6-2 )

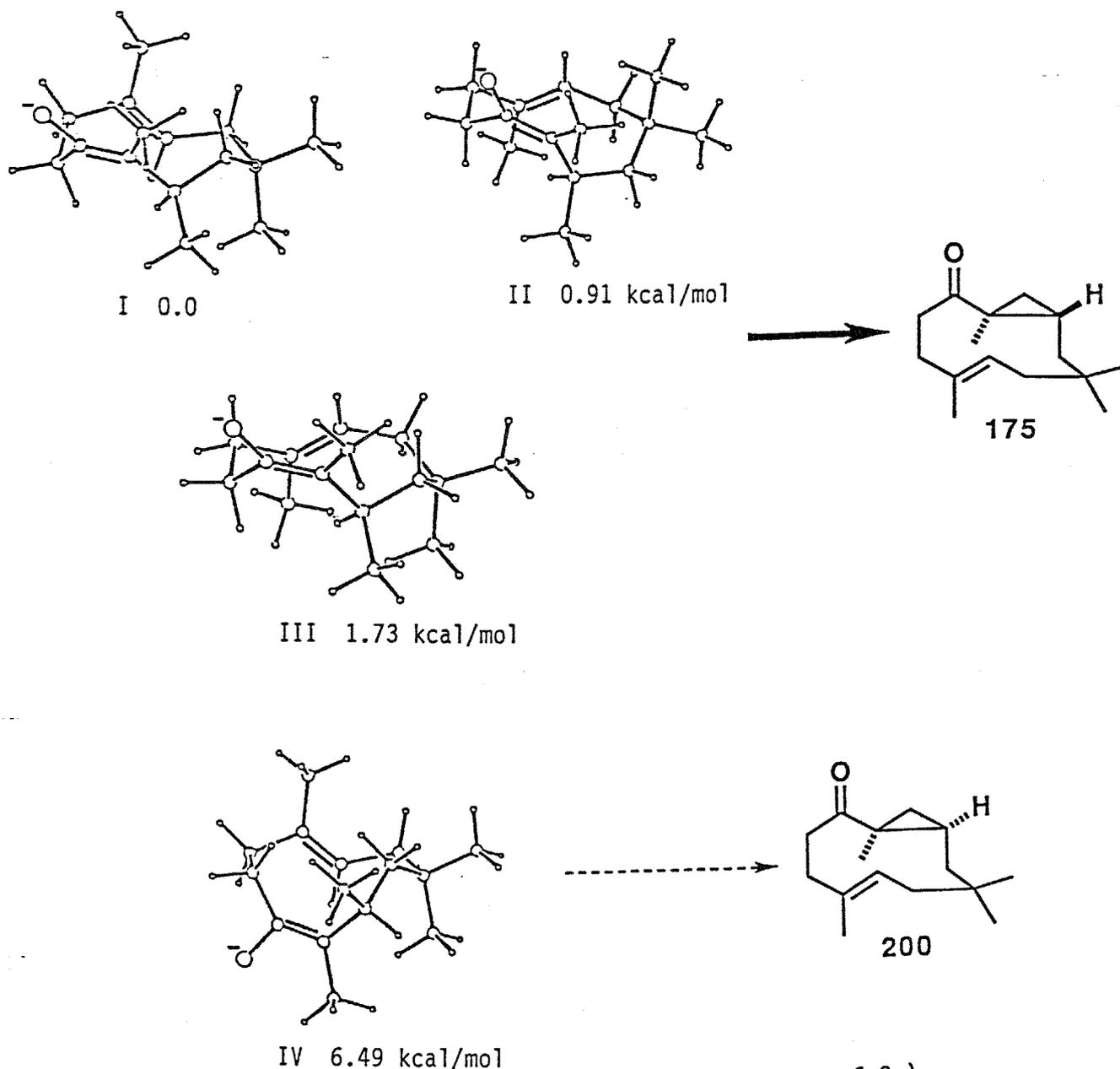
エノラートの分子力場計算は、計算簡略化のため共役付加した基をメチル基におきかえた(E)-エノラート 201、(Z)-エノラート 202 について行った。

201のすべての立体配座を得るため、MMRSを用いて初期座標を発生させ、66個の立体配座をMM2により構造最適化を行い、次に示す4個の配座異性体の存在がわかった (Fig. 6-3)。

torsional angle resolution 30 deg

closure distance 1.0 - 2.3 Å

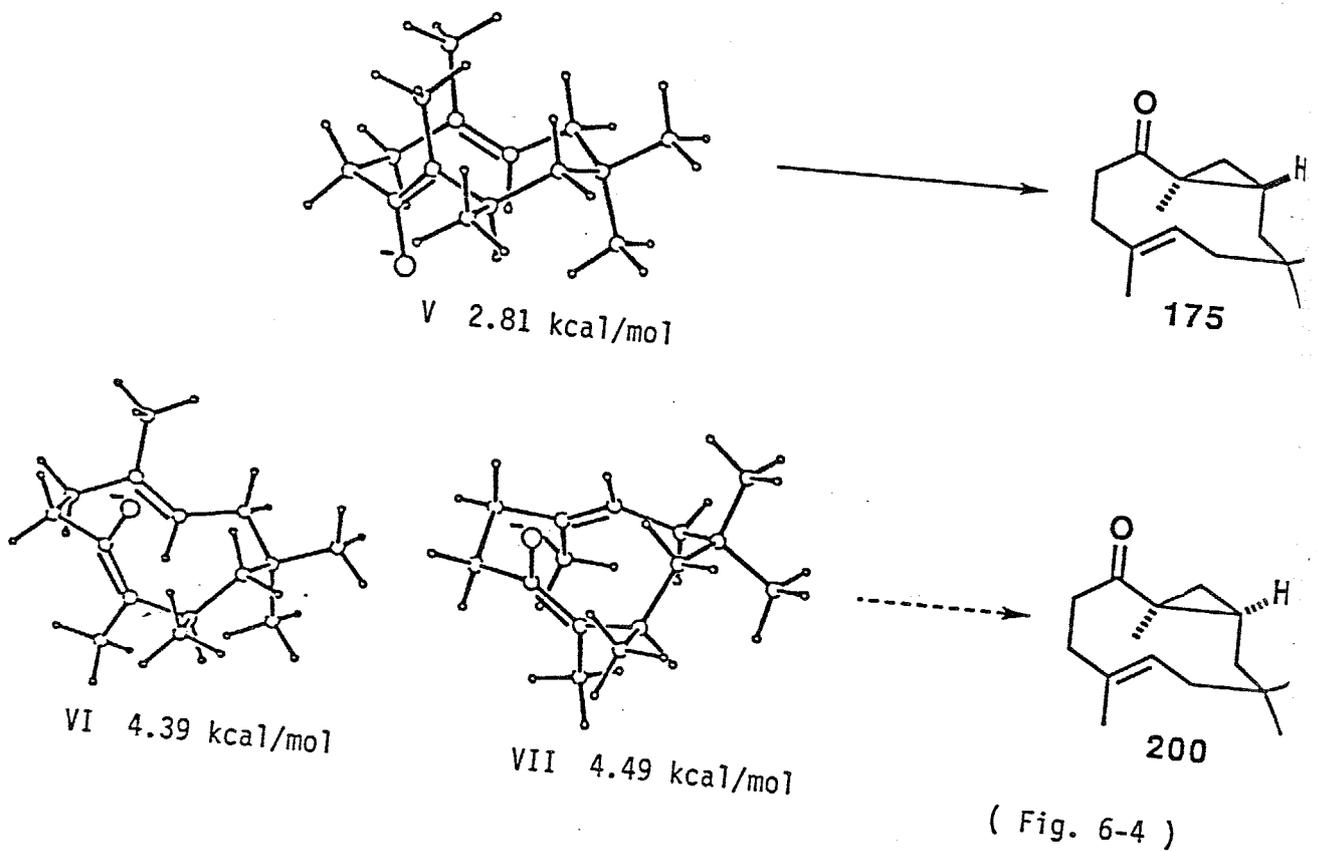
transannular contact 1.5 Å



( Fig. 6-3 )

202のすべての立体配座を得るため、MMRSを用いて初期座標を発生させ、116個の立体配座をMM2により構造最適化を行い、次に示す3個の配座異性体の在がわかった (Fig. 6-4)。

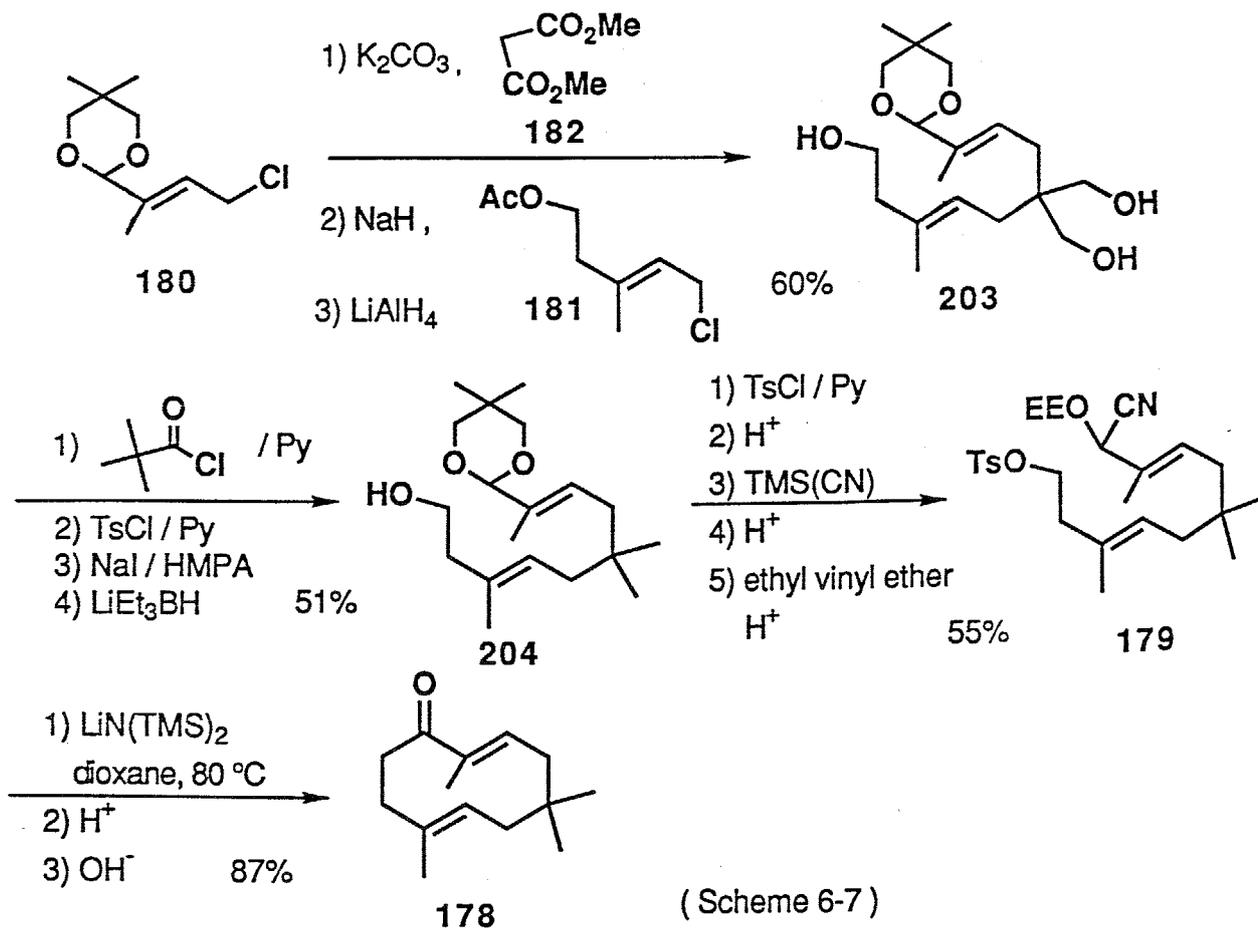
torsional angle resolution 30 deg  
 closure distance 1.0 - 2.3 Å  
 transannular contact 1.5 Å



これらの計算結果からすべての配座異性体からの3員環形成の活性化エネルギーがほぼ等しいと仮定すると、(E)-, (Z)-いずれのエノラートからも望むトランスの3員環を与えると予測される。

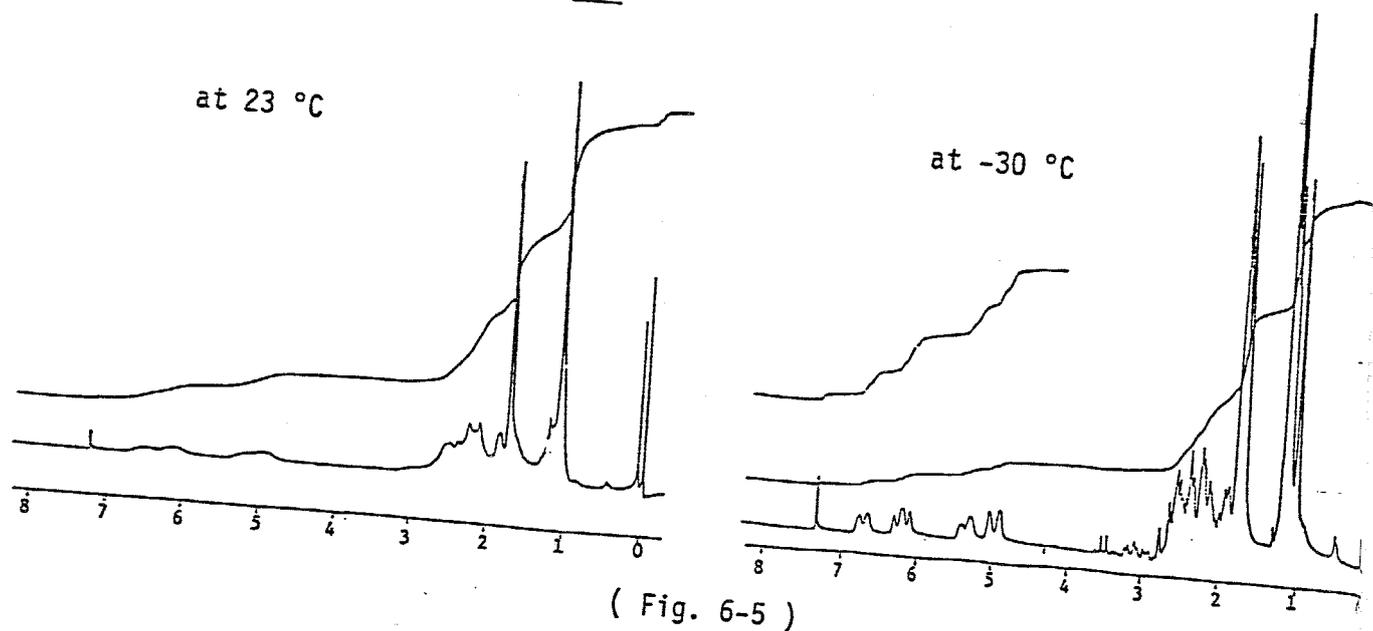
6-5 実験結果

実際の合成はScheme 6-7に示す通り178を得た。



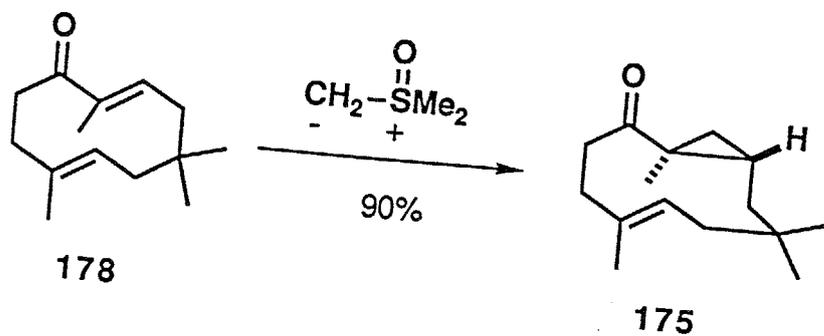
得られた10員環エノン178の $^1H$ -NMRは室温下非常にブロードしていたので、低温測定を行った。その結果Fig. 6-5のようにオレフィン部分のピークが $-30^\circ C$ で56:44の比の二つのピークに分かれた。これが178 II, 178 III, 178 Iからなっているすると、計算結果に基づくこれらの比を (II+III) : I = 53 : 45と考えるとNMRの測定結果とよく一致する。室温付近では配座異性体間の相互変換のスピードが NMRの測定速度とほぼ同じになったためにブロードしたと考えられる。

The NMR spectra of 178



( Fig. 6-5 )

次に鍵反応であるが、 $\text{Me}_3\text{SO}^+\text{I}^-$ をDMSO溶媒中 NaHで処理し、生じたジメチルオキソスルホニウムメチリド溶液中にエノン 178を加え反応させたところ収率90%で3員環生成物を与えた。反応粗製品のHPLC分析を行った結果、異性体は見いだせず単一生成物であった。生成物の NMRスペクトルは、徳島文理大学浅川義範教授より頂いた、天然より抽出されたピシクロフムレノン (175) の NMRスペクトルと一致した。この事から、分子力場計算による予測どおり、エノン 178 に対し立体選択的にトランス3員環が導入され、175 を与えたことが証明された。



( Scheme 6-8 )

今回、MM2計算により(E,E)-ジエンを有する10員環エノン 178 への硫黄イリドの求核付加、続く生成するエノラートの3員環形成反応によりトランス立体化学の3員環が立体選択的にできることを予測し、実際にビスクロムレノン(175)を立体選択的に合成することに成功した。この予測の際、エノラート配座異性体間の相互変換と3員環形成反応の速度を考え、どちらが速くともトランスの3員環を与えることを予想し、合成上 178 は理想の中間体であることがわかった。しかし、実際にどちらが速度が大きいかを調べることはできなかった。そこで次の系を考えればその関係が明らかになると考えられる。

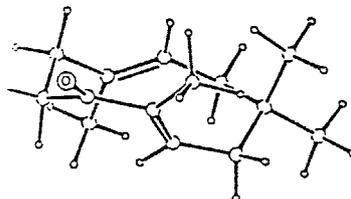
178 のエノンの二重結合の(Z)-体を用いて反応を行えば、生成するエノラートの3員環形成がその配座異性体間の自由回転よりも速ければシスの3員環 200 が得られるはずであり、逆に生成するエノラートの配座異性体間の自由回転が、3員環形成反応よりも速ければより有利な 198 や 199 を経てトランスの3員環 175 が得られると考えられる。このような3員環形成と配座異性体間の相互変換の速度の関係は、中員環化合物を合成中間体に用いる上で重要な問題であり、さらに詳細な研究が望まれる。

## Conformational analysis of 10-membered dienone 178

The starting geometries of 178 were generated using MMRS at 30° dihedral angle resolution and with a closure distance range of 1.0-2.3 Å, and with a transannular contact of 2.2 Å. Structures of 75 conformations obtained were optimized by MM2 to get 4 conformers within 3.0 kcal/mol from the lowest energy conformer.

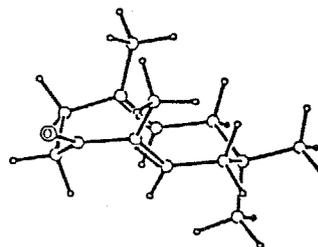
I NO= 17 ENERGY= 21.4983

ST= 1.97 BD= 5.64 SB= .39 14= 8.64  
OT= 1.11 T= 4.53 DP= -.79 DM= 2.95D



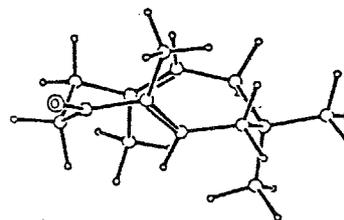
II NO= 19 ENERGY= 21.7086

ST= 1.97 BD= 4.58 SB= .37 14= 8.18  
OT= 1.22 T= 6.21 DP= -.81 DM= 2.76D



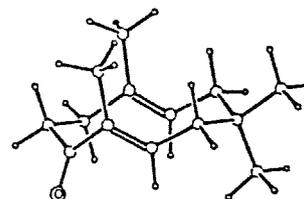
III NO= 52 ENERGY= 21.8329

ST= 1.84 BD= 5.04 SB= .38 14= 8.67  
OT= .18 T= 6.47 DP= -.73 DM= 2.98D



IV NO= 21 ENERGY= 23.0262

ST= 1.86 BD= 3.43 SB= .30 14= 8.13  
OT= -.38 T= 10.04 DP= -.36 DM= 3.38D



ENERGY: FINAL STERIC ENERGY, ST: COMPRESSION, BD: BENDING, SB: STRETCH-BEND,  
14: VAN DER WAALS\_1,4 ENERGY, OT: VAN DER WAALS\_OTHER, T: TORSIONAL, DP: DIPOLE,  
DM: DIPOLE MOMENT [ KCAL/MOL ]

0 JUINKAN TRANS ENONE

15	10	2	22	22	1	1.50	1.34	120.0	0	0	30	1.0	2.3	100	1.1
2	10	0	0												
1	3	3	11												
2	2	4	0												
1	2	3	4	2	1	1.50	120.0	180.0	3	5	0	0	0		
2	3	4	5	2	0	1.54	109.5	0.0	4	12	13	6	0		
3	4	5	6	2	0	1.54	109.5	0.0	5	7	0	0	0		
4	5	6	7	22	0	1.50	109.5	0.0	6	8	8	0	0		
5	6	7	8	22	0	1.34	120.0	0.0	7	7	9	14	0		
6	7	8	9	32	1	1.50	120.0	180.0	8	10	15	15	0		
7	8	9	10	2	0	1.54	109.5	0.0	1	9	0	0	0		
4	3	2	11	2	1	1.50	120.0	0.0	2	0	0	0	0		
3	4	5	12	2	2	1.54	109.5	240.0	5	0	0	0	6		
3	4	5	13	2	2	1.54	109.5	120.0	5	0	0	0	6		
6	7	8	14	2	1	1.50	120.0	0.0	8	0	0	0	0		
7	8	9	15	14	2	1.50	109.5	240.0	9	9	0	0	10		

37 4 0 0 1 500.

6					22				1						
1	2	3	4	5	6	7	8	9	10	1					
2	11														
5	12														
5	13														
8	14														
9	15														
1	16	1	17	3	18	4	19	4	20	6	21	6	22	7	23
10	24	10	25	11	26	11	27	11	28	12	29	12	30	12	31
13	32	13	33	13	34	14	35	14	36	14	37				
4	1	0	0												
2	2	3	1	0.15		2.091		0.0							
2	2	3	7	0.91		2.091		0.0							
1	2	3	1	0.0		2.091		0.0							
1	2	3	7	0.0		2.091		0.0							
2	3	6.370		1.4767											

I

-1.9880	-1.6122	-.7409	1				
.4492	-1.2014	-.9013	2	-.5507	-1.9310	-.3718	2
2.3586	.2407	-.0070	1	1.8949	-1.1720	-.4656	1
.0083	.5963	1.0162	2	1.4935	.8449	1.1394	1
-2.2975	.8120	.1808	3	-.9021	1.3185	.3395	2
-.3867	-2.9860	.6995	1	-2.6509	-.6741	.2923	1
2.4077	1.1974	-1.2201	1	3.8138	.1205	.5116	1
-3.1901	1.5832	-.0964	7	-.6020	2.6375	-.3337	1
-2.0593	-1.1371	-1.7479	5	-2.5508	-2.5708	-.8190	5
2.5191	-1.5238	-1.3193	5	.1792	-.4677	-1.6770	5
1.7089	1.9308	1.2540	5	2.0801	-1.8753	.3738	5
-.3215	-.3253	1.5172	5	1.8039	.3927	2.1102	5
-3.7534	-.7526	.1353	5	-2.4936	-1.0225	1.3384	5
-.9123	-3.9172	.3894	5	.6653	-3.2848	.8918	5
4.2105	1.1077	.8424	5	-.8248	-2.6543	1.6668	5
3.8869	-.5734	1.3801	5	4.4987	-.2689	-.2761	5
1.4103	1.3620	-1.6794	5	2.8057	2.1981	-.9356	5
.4340	3.0042	-.1722	5	3.0679	.8001	-2.0245	5
-.7674	2.5539	-1.4319	5	-1.2749	3.4318	.0616	5
				.0000	.0000	.0000	0

II

-1.7606	-1.9656	-.3084	1	-.5118	-1.6505	.4911	2
.6837	-1.5917	-.1254	2	1.9967	-1.1172	.4509	1
2.4873	.2294	-.1567	1	1.4450	1.3791	-.0225	1
.0796	1.0113	-.5489	2	-1.1167	1.2416	.0216	2
-2.3285	.5664	-.5305	3	-2.2037	-.7968	-1.2193	1
-.7491	-1.3499	1.9525	1	3.7654	.6571	.6067	1
2.8957	.0369	-1.6357	1	-1.3229	2.1094	1.2420	1
-3.4311	1.0425	-.3760	7	-2.5912	-2.2397	.3834	5
-1.5750	-2.8710	-.9335	5	.7098	-1.8483	-1.1975	5
2.7555	-1.9139	.2721	5	1.9332	-1.0103	1.5549	5
1.8013	2.2834	-.5678	5	1.3776	1.6424	1.0555	5
.1068	.4590	-1.4968	5	-3.1972	-1.0589	-1.6550	5
-1.5347	-.7119	-2.1052	5	.0667	-.7788	2.4447	5
-.8848	-2.3066	2.5054	5	-1.6784	-.7555	2.0914	5
4.1784	1.6117	.2076	5	4.5664	-.1132	.5264	5
3.5659	.8119	1.6918	5	3.3031	.9789	-2.0684	5
2.0516	-.2771	-2.2872	5	3.6858	-.7415	-1.7382	5
-.4092	2.6440	1.5794	5	-1.7051	1.5144	2.1004	5
-2.0717	2.9021	1.0167	5	.0000	.0000	.0000	0

III

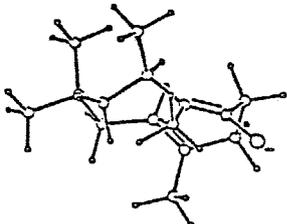
-1.6587	-1.8095	-.6464	1	-.1464	-1.7805	-.5326	2
.5647	-.8405	-1.1811	2	2.0329	-.5280	-1.0338	1
2.3610	.4586	.1253	1	1.2520	1.5216	.3664	1
-.1110	.9389	.6687	2	-1.2799	1.2469	.0775	2
-2.4856	.4302	.3882	3	-2.3651	-1.0890	.5233	1
.4444	-2.8014	.4103	1	2.6558	-.3051	1.4366	1
3.6688	1.2044	-.2424	1	-1.4792	2.3422	-.9434	1
-3.5814	.9423	.4503	7	-1.9801	-2.8765	-.6942	5
-1.9971	-1.3509	-1.6051	5	.0131	-.1436	-1.8349	5
2.3486	-.0838	-2.0064	5	2.6381	-1.4574	-.9397	5
1.2183	2.1712	-.5342	5	1.5356	2.1743	1.2242	5
-.1188	.1523	1.4382	5	-1.9146	-1.3485	1.5083	5
-3.4081	-1.4844	.5666	5	1.5552	-2.8120	.4207	5
.1292	-3.8245	.1051	5	.0922	-2.6301	1.4519	5
2.9463	.3916	2.2557	5	3.4934	-1.0283	1.3091	5
1.7831	-.8822	1.8070	5	3.9866	1.8999	.5679	5
3.5511	1.8145	-1.1672	5	4.5065	.4915	-.4196	5
-.5911	2.9872	-1.1117	5	-2.2965	3.0255	-.6197	5
-1.7646	1.8966	-1.9234	5	.0000	.0000	.0000	0

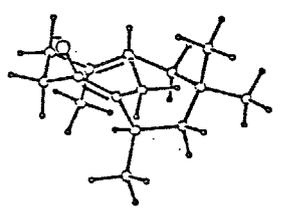
IV

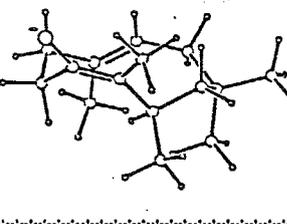
-2.1669	-1.3360	-.9454	1	-.8422	-1.7031	-.3009	2
.3010	-1.1657	-.7681	2	1.6870	-1.2404	-.1718	1
2.4498	.1177	-.1325	1	1.6673	1.2405	.6096	1
.2792	1.4409	.0523	2	-.8716	1.1475	.6845	2
-2.0903	1.1137	-.1682	3	-2.8778	-.1963	-.1810	1
-.9505	-2.6314	.8865	1	3.7806	-.1096	.6277	1
2.8271	.5730	-1.5611	1	-.9392	.7170	2.1273	1
-2.4297	2.0450	-.8627	7	-2.8169	-2.2411	-.9921	5
-2.0164	-1.0104	-2.0015	5	.2221	-.5576	-1.6821	5
2.2713	-1.9790	-.7676	5	1.6368	-1.6268	.8689	5
2.2173	2.2078	.5452	5	1.6215	.9741	1.6882	5
.2374	1.7436	-1.0073	5	-3.1038	-.5066	.8644	5
-3.8671	-.0034	-.6598	5	.0100	-2.8260	1.4089	5
-1.3274	-3.6199	.5398	5	-1.6741	-2.2501	1.6401	5
4.3874	.8235	.6766	5	4.4054	-.8886	.1336	5
3.6059	-.4438	1.6760	5	3.4290	1.5100	-1.5401	5
1.9446	.7748	-2.2057	5	3.4369	-.1991	-2.0833	5
-.2959	1.3599	2.7687	5	-.6144	-.3367	2.2601	5
-1.9716	.8291	2.5282	5	.0000	.0000	.0000	0

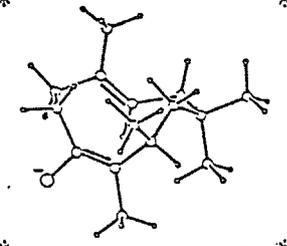
Conformational analysis of E-enolate 198

The starting geometries of 198 were generated using MULTIC submode of the MacroModel at 30° dihedral angle resolution and with a closure distance range of 1.0-2.3 Å, and with a transannular contact of 3.0 Å. Structures of 66 conformations obtained were subjected to block diagonal Newton-Raphson energy minimization using the MacroModel implementation of the MM2 molecular mechanics force field to get 4 conformers.

*****		TOTAL MM2	ENERGY IS	20.478 kcal/mol)
*		*		
*		*	Van der Waals	8.140
*		*	Stretch	1.921
*		*	Torsion	5.857
*		*	Bend	6.499
*		*	Improper Torsion	0.022
*		*	Stretch-Bend	0.479
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.440
*		*	Energy minimization RMS	= 0.0007 kcal/Å-mol
*****				

*****		TOTAL MM2	ENERGY IS	21.391 kcal/mol
*		*		
*		*	Van der Waals	8.473
*		*	Stretch	1.937
*		*	Torsion	4.004
*		*	Bend	8.480
*		*	Improper Torsion	0.080
*		*	Stretch-Bend	0.535
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.118
*		*	Energy minimization RMS	= 0.0009 kcal/Å-mol
*****				

*****		TOTAL MM2	ENERGY IS	22.209 kcal/mol
*		*		
*		*	Van der Waals	8.650
*		*	Stretch	1.902
*		*	Torsion	6.412
*		*	Bend	6.879
*		*	Improper Torsion	0.031
*		*	Stretch-Bend	0.519
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.185
*		*	Energy minimization RMS	= 0.0008 kcal/Å-mol
*****				

*****		TOTAL MM2	ENERGY IS	26.969 kcal/mol
*		*		
*		*	Van der Waals	9.493
*		*	Stretch	2.171
*		*	Torsion	7.251
*		*	Bend	9.607
*		*	Improper Torsion	0.126
*		*	Stretch-Bend	0.555
*		*	Hydrogen-Bond	0.000
*		*	Electrostatic	-2.233
*		*	Energy minimization RMS	= 0.0038 kJ/Å-mol
*****				

Connection Table

Atomic Charges, Coordinates and Connectivity  
 - single bond, = doble bond, % triple bond

I		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Atom Number		X	Y	Z		2-	10-	16-	17-
C3	( 1)	0.042	-2.9078	1.2113	-0.0112	0	2-	10-	16-	17-
C3	( 2)	0.042	-2.4072	0.1249	-0.9788	0	1-	3-	18-	19-
C2	( 3)	-0.083	-0.9213	-0.1213	-0.8118	0	2-	4=	13-	
C2	( 4)	-0.042	-0.0366	0.8033	-1.2282	0	3=	5-	20-	
C3	( 5)	0.042	1.4520	0.8068	-0.9957	0	4-	6-	21-	22-
C3	( 6)	0.000	1.9004	1.7318	0.1686	0	5-	7-	11-	12-
C3	( 7)	0.000	1.0363	1.5301	1.4457	0	6-	8-	23-	24-
C3	( 8)	0.042	-0.3394	2.2344	1.5303	0	7-	9-	37-	38-
C2	( 9)	-0.369	-1.4191	1.3286	2.1114	0	8-	10=	14-	
C2	( 10)	0.114	-2.5053	0.9228	1.4099	0	9=	1-	15-	
C3	( 11)	0.000	1.9298	3.2012	-0.2998	0	6-	25-	26-	27-
C3	( 12)	0.000	3.3602	1.3434	0.5187	0	6-	28-	29-	30-
C3	( 13)	0.042	-0.5754	-1.3962	-0.0759	0	3-	31-	32-	33-
C3	( 14)	0.042	-1.2260	0.8857	3.5450	0	9-	34-	35-	36-
OH	( 15)	-0.870	-3.4245	0.1184	1.9567	0	10-			
H1	( 16)	0.000	-2.5390	2.2124	-0.3285	0	1-			
H1	( 17)	0.000	-4.0193	1.2923	-0.0840	0	1-			
H1	( 18)	0.000	-2.9723	-0.8230	-0.8151	0	2-			
H1	( 19)	0.000	-2.6170	0.4326	-2.0312	0	2-			
H1	( 20)	0.000	-0.4311	1.7024	-1.7313	0	4-			
H1	( 21)	0.000	1.8069	-0.2277	-0.8024	0	5-			
H1	( 22)	0.000	1.9582	1.1011	-1.9447	0	5-			
H1	( 23)	0.000	0.9010	0.4308	1.5612	0	7-			
H1	( 24)	0.000	1.6218	1.8395	2.3420	0	7-			
H1	( 25)	0.000	0.9377	3.5622	-0.6489	0	11-			
H1	( 26)	0.000	2.2769	3.8758	0.5150	0	11-			
H1	( 27)	0.000	2.6311	3.3396	-1.1542	0	11-			
H1	( 28)	0.000	3.7902	2.0165	1.2959	0	12-			
H1	( 29)	0.000	3.4249	0.3026	0.9121	0	12-			
H1	( 30)	0.000	4.0254	1.4050	-0.3733	0	12-			
H1	( 31)	0.000	0.5083	-1.5572	0.0993	0	13-			
H1	( 32)	0.000	-1.0658	-1.4164	0.9230	0	13-			
H1	( 33)	0.000	-0.9392	-2.2736	-0.6568	0	13-			
H1	( 34)	0.000	-0.2223	0.4286	3.6906	0	14-			
H1	( 35)	0.000	-1.3215	1.7506	4.2381	0	14-			
H1	( 36)	0.000	-1.9700	0.1268	3.8750	0	14-			
C3	( 37)	0.000	-0.2826	3.5584	2.3151	0	8-	39-	40-	41-
H1	( 38)	0.000	-0.6430	2.5165	0.5041	0	8-			
H1	( 39)	0.000	-1.2881	4.0383	2.3614	0	37-			
H1	( 40)	0.000	0.0730	3.4133	3.3602	0	37-			
H1	( 41)	0.000	0.4060	4.2926	1.8406	0	37-			

Total charge on system = -1.000

II

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.042	-1.6432	-0.7171	-2.9495	0	2-	10-	16-	17-
C3	( 2)	0.042	-1.7907	-0.1908	-1.5111	0	1-	3-	18-	19-
C2	( 3)	-0.083	-0.4465	-0.2529	-0.8191	0	2-	4=	13-	
C2	( 4)	-0.042	0.4027	0.7755	-0.9832	0	3=	5-	20-	
C3	( 5)	0.042	1.8711	0.8186	-0.6586	0	4-	6-	21-	22-
C3	( 6)	0.000	2.7544	1.1505	-1.8890	0	5-	7-	11-	12-
C3	( 7)	0.000	2.7813	0.0300	-2.9693	0	6-	8-	23-	24-
C3	( 8)	0.042	1.4898	-0.6445	-3.4931	0	7-	9-	37-	38-
C2	( 9)	-0.369	0.4560	0.2544	-4.1519	0	8-	10=	14-	
C2	( 10)	0.114	-0.8682	0.1999	-3.8632	0	9=	1-	15-	
C3	( 11)	0.000	4.2083	1.3106	-1.3639	0	6-	25-	26-	27-
C3	( 12)	0.000	2.3757	2.5214	-2.4919	0	6-	28-	29-	30-
C3	( 13)	0.042	-0.1188	-1.5642	-0.1448	0	3-	31-	32-	33-
C3	( 14)	0.042	0.9371	1.1269	-5.2922	0	9-	34-	35-	36-
OM	( 15)	-0.870	-1.7409	0.9736	-4.5206	0	10-			
H1	( 16)	0.000	-1.1808	-1.7310	-2.9527	0	1-			
H1	( 17)	0.000	-2.6637	-0.8771	-3.3742	0	1-			
H1	( 18)	0.000	-2.1945	0.8494	-1.5319	0	2-			
H1	( 19)	0.000	-2.5289	-0.8008	-0.9387	0	2-			
H1	( 20)	0.000	0.0085	1.6672	-1.4938	0	4-			
H1	( 21)	0.000	2.0040	1.5992	0.1263	0	5-			
H1	( 22)	0.000	2.2307	-0.1371	-0.2214	0	5-			
H1	( 23)	0.000	3.3727	0.3958	-3.8399	0	7-			
H1	( 24)	0.000	3.3906	-0.8003	-2.5396	0	7-			
H1	( 25)	0.000	4.5726	0.3863	-0.8592	0	11-			
H1	( 26)	0.000	4.9209	1.5382	-2.1900	0	11-			
H1	( 27)	0.000	4.2910	2.1381	-0.6220	0	11-			
H1	( 28)	0.000	3.0960	2.8315	-3.2831	0	12-			
H1	( 29)	0.000	1.3664	2.5321	-2.9532	0	12-			
H1	( 30)	0.000	2.3814	3.3201	-1.7152	0	12-			
H1	( 31)	0.000	0.8464	-1.5657	0.4038	0	13-			
H1	( 32)	0.000	-0.9014	-1.8014	0.6107	0	13-			
H1	( 33)	0.000	-0.0920	-2.3969	-0.8827	0	13-			
H1	( 34)	0.000	1.8846	1.6551	-5.0589	0	14-			
H1	( 35)	0.000	1.1229	0.4991	-6.1921	0	14-			
H1	( 36)	0.000	0.2043	1.9121	-5.5835	0	14-			
C3	( 37)	0.000	1.8450	-1.7810	-4.4740	0	8-	39-	40-	41-
H1	( 38)	0.000	1.0278	-1.1557	-2.6227	0	8-			
H1	( 39)	0.000	0.9299	-2.3127	-4.8257	0	37-			
H1	( 40)	0.000	2.3831	-1.3985	-5.3711	0	37-			
H1	( 41)	0.000	2.5028	-2.5439	-3.9960	0	37-			

Total charge on system = -1.000

III

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z		2-	10-	16-	17-
C3	( 1)	0.042	-1.8996	-0.1738	-2.9662	0	2-	10-	16-	17-
C3	( 2)	0.042	-1.8283	-0.0538	-1.4340	0	1-	3-	18-	19-
C2	( 3)	-0.083	-0.4022	-0.1648	-0.9347	0	2-	4=	13-	
C2	( 4)	-0.042	0.3676	0.9351	-0.8772	0	3=	5-	20-	
C3	( 5)	0.042	1.8439	1.0116	-0.5853	0	4-	6-	21-	22-
C3	( 6)	0.000	2.7519	0.9656	-1.8465	0	5-	7-	11-	12-
C3	( 7)	0.000	2.0684	1.5993	-3.0892	0	6-	8-	23-	24-
C3	( 8)	0.042	1.0028	0.7603	-3.8384	0	7-	9-	37-	38-
C2	( 9)	-0.369	-0.2865	1.5269	-4.0990	0	8-	10=	14-	
C2	( 10)	0.114	-1.5003	1.0897	-3.6846	0	9=	1-	15-	
C3	( 11)	0.000	3.2332	-0.4730	-2.1324	0	6-	25-	26-	27-
C3	( 12)	0.000	4.0232	1.7948	-1.5270	0	6-	28-	29-	30-
C3	( 13)	0.042	0.0799	-1.5665	-0.6494	0	3-	31-	32-	33-
C3	( 14)	0.042	-0.1671	2.8121	-4.8908	0	9-	34-	35-	36-
OM	( 15)	-0.870	-2.6063	1.7998	-3.9390	0	10-			
H1	( 16)	0.000	-1.2957	-1.0377	-3.3277	0	1-			
H1	( 17)	0.000	-2.9482	-0.4305	-3.2531	0	1-			
H1	( 18)	0.000	-2.2937	0.9078	-1.1116	0	2-			
H1	( 19)	0.000	-2.4329	-0.8594	-0.9538	0	2-			
H1	( 20)	0.000	-0.1024	1.8942	-1.1560	0	4-			
H1	( 21)	0.000	1.9868	1.9780	-0.0474	0	5-			
H1	( 22)	0.000	2.1602	0.2394	0.1507	0	5-			
H1	( 23)	0.000	1.6340	2.5638	-2.7423	0	7-			
H1	( 24)	0.000	2.8482	1.8921	-3.8297	0	7-			
H1	( 25)	0.000	2.3989	-1.1834	-2.3131	0	11-			
H1	( 26)	0.000	3.8973	-0.5038	-3.0258	0	11-			
H1	( 27)	0.000	3.8166	-0.8838	-1.2768	0	11-			
H1	( 28)	0.000	4.7662	1.7482	-2.3562	0	12-			
H1	( 29)	0.000	3.7825	2.8708	-1.3644	0	12-			
H1	( 30)	0.000	4.5320	1.4226	-0.6079	0	12-			
H1	( 31)	0.000	1.1243	-1.6186	-0.2762	0	13-			
H1	( 32)	0.000	-0.5598	-2.0367	0.1311	0	13-			
H1	( 33)	0.000	0.0223	-2.1902	-1.5696	0	13-			
H1	( 34)	0.000	0.5075	3.5421	-4.3929	0	14-			
H1	( 35)	0.000	0.2350	2.6071	-5.9074	0	14-			
H1	( 36)	0.000	-1.1392	3.3336	-5.0354	0	14-			
C3	( 37)	0.000	1.5423	0.1643	-5.1515	0	8-	39-	40-	41-
H1	( 38)	0.000	0.7453	-0.1144	-3.2089	0	8-			
H1	( 39)	0.000	0.7664	-0.4555	-5.6587	0	37-			
H1	( 40)	0.000	1.8676	0.9523	-5.8678	0	37-			
H1	( 41)	0.000	2.4221	-0.4941	-4.9693	0	37-			

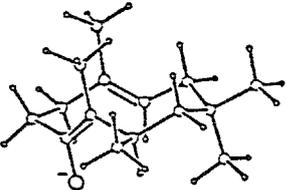
Total charge on system = -1.000

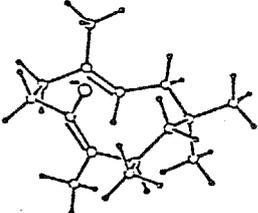
## IV

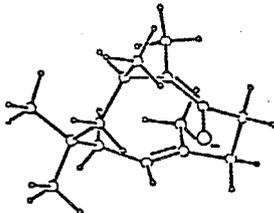
Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.042	-2.0727	1.6905	-0.4771	0	2-	10-	16-	17-
C3	( 2)	0.042	-1.8508	0.5451	-1.4847	0	1-	3-	18-	19-
C2	( 3)	-0.083	-0.6352	-0.2331	-1.0354	0	2-	4=	13-	
C2	( 4)	-0.042	0.5805	0.2889	-1.2744	0	3=	5-	20-	
C3	( 5)	0.042	1.8633	-0.0853	-0.5839	0	4-	6-	21-	22-
C3	( 6)	0.000	2.2564	1.0035	0.4550	0	5-	7-	11-	12-
C3	( 7)	0.000	1.0370	1.4350	1.3325	0	6-	8-	23-	24-
C3	( 8)	0.042	0.4769	2.8761	1.2733	0	7-	9-	37-	38-
C2	( 9)	-0.369	-0.1219	3.3913	-0.0298	0	8-	10=	14-	
C2	(10)	0.114	-1.1665	2.8678	-0.7167	0	9=	1-	15-	
C3	(11)	0.000	2.9381	2.1724	-0.2850	0	6-	25-	26-	27-
C3	(12)	0.000	3.3412	0.3790	1.3713	0	6-	28-	29-	30-
C3	(13)	0.042	-0.9315	-1.4201	-0.1480	0	3-	31-	32-	33-
C3	(14)	0.042	0.4545	4.7235	-0.4789	0	9-	34-	35-	36-
OM	(15)	-0.870	-1.6231	3.4872	-1.8137	0	10-			
H1	(16)	0.000	-1.9830	1.3130	0.5647	0	1-			
H1	(17)	0.000	-3.1268	2.0492	-0.5632	0	1-			
H1	(18)	0.000	-2.7363	-0.1331	-1.5101	0	2-			
H1	(19)	0.000	-1.7266	0.9370	-2.5219	0	2-			
H1	(20)	0.000	0.6420	1.1860	-1.9117	0	4-			
H1	(21)	0.000	1.7681	-1.0632	-0.0675	0	5-			
H1	(22)	0.000	2.6634	-0.2286	-1.3471	0	5-			
H1	(23)	0.000	0.2027	0.7109	1.2323	0	7-			
H1	(24)	0.000	1.3432	1.2918	2.3946	0	7-			
H1	(25)	0.000	2.2748	2.6147	-1.0572	0	11-			
H1	(26)	0.000	3.2638	2.9749	0.4142	0	11-			
H1	(27)	0.000	3.8527	1.8360	-0.8249	0	11-			
H1	(28)	0.000	3.7368	1.1240	2.1000	0	12-			
H1	(29)	0.000	2.9427	-0.4828	1.9554	0	12-			
H1	(30)	0.000	4.2091	0.0016	0.7826	0	12-			
H1	(31)	0.000	-0.0400	-2.0060	0.1576	0	13-			
H1	(32)	0.000	-1.4568	-1.0967	0.7788	0	13-			
H1	(33)	0.000	-1.5947	-2.1332	-0.6878	0	13-			
H1	(34)	0.000	0.2094	5.5060	0.2749	0	14-			
H1	(35)	0.000	1.5610	4.6890	-0.5803	0	14-			
H1	(36)	0.000	0.0649	5.0813	-1.4576	0	14-			
C3	(37)	0.000	-0.5253	3.1339	2.4176	0	8-	39-	40-	41-
H1	(38)	0.000	1.3479	3.5314	1.5141	0	8-			
H1	(39)	0.000	-0.8611	4.1972	2.4303	0	37-			
H1	(40)	0.000	-1.4332	2.4976	2.3333	0	37-			
H1	(41)	0.000	-0.0731	2.9256	3.4152	0	37-			
Total charge on system =			-1.000							

### Conformational analysis of Z-enolate 199

The starting geometries of 199 were generated using MULTIC submode of the MacroModel at 30° dihedral angle resolution and with a closure distance range of 1.0-2.3 Å, and with a transannular contact of 3.0 Å. Structures of 116 conformations obtained were subjected to block diagonal Newton-Raphson energy minimization using the MacroModel implementation of the MM2 molecular mechanics force field to get 3 conformers within 3.0 kcal/mol from the lowest conformer.

*****		TOTAL MM2	ENERGY IS	23.291 kcal/mol
*		*		
*		*	Van der Waals	9.088
*		*	Torsion	5.204
*		*	Improper Torsion	0.078
*		*	Hydrogen-Bond	0.000
*		*	Energy minimization RMS	= 0.0005 kcal/Å-mol
*****				

*****		TOTAL MM2	ENERGY IS	24.869 kcal/mol
*		*		
*		*	Van der Waals	8.586
*		*	Torsion	7.922
*		*	Improper Torsion	0.114
*		*	Hydrogen-Bond	0.000
*		*	Energy minimization RMS	= 0.0015 kcal/Å-mol
*****				

*****		TOTAL MM2	ENERGY IS	24.964 kcal/mol
*		*		
*		*	Van der Waals	9.141
*		*	Torsion	6.852
*		*	Improper Torsion	0.088
*		*	Hydrogen-Bond	0.000
*		*	Energy minimization RMS	= 0.0008 kcal/Å-mol
*****				

Connection Table

Atomic Charges, Coordinates and Connectivity

- single bond, = doble bond, % triple bond

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.042	-2.4510	-0.2714	-0.2358	0	2-	10-	16-	17-
C3	( 2)	0.042	-2.2670	0.7598	0.8991	0	1-	3-	18-	19-
C2	( 3)	-0.083	-0.9310	1.4645	0.7350	0	2-	4=	13-	
C2	( 4)	-0.042	0.1780	0.8732	1.2196	0	3=	5-	20-	
C3	( 5)	0.042	1.6160	1.2463	0.9797	0	4-	6-	21-	22-
C3	( 6)	0.000	2.6026	0.0593	0.7916	0	5-	7-	11-	12-
C3	( 7)	0.000	2.4342	-0.7423	-0.5330	0	6-	8-	23-	24-
C3	( 8)	0.042	1.2003	-1.6469	-0.7721	0	7-	9-	37-	38-
C2	( 9)	-0.369	-0.0834	-0.8829	-1.0605	0	8-	10=	14-	
C2	(10)	0.114	-1.2028	-1.1092	-0.3307	0	9=	1-	15-	
C3	(11)	0.000	2.5991	-0.8882	2.0121	0	6-	25-	26-	27-
C3	(12)	0.000	4.0204	0.6978	0.7418	0	6-	28-	29-	30-
C3	(13)	0.042	-0.9581	2.7306	-0.0849	0	3-	31-	32-	33-
C3	(14)	0.042	-0.0198	0.1453	-2.1675	0	9-	34-	35-	36-
OM	(15)	-0.870	-1.2428	-2.0403	0.6305	0	10-			
H1	(16)	0.000	-2.6623	0.2550	-1.1926	0	1-			
H1	(17)	0.000	-3.3441	-0.9126	-0.0418	0	1-			
H1	(18)	0.000	-3.1052	1.4957	0.9153	0	2-			
H1	(19)	0.000	-2.2998	0.2345	1.8834	0	2-			
H1	(20)	0.000	0.0320	-0.0257	1.8356	0	4-			
H1	(21)	0.000	1.7114	1.9201	0.1007	0	5-			
H1	(22)	0.000	1.9231	1.8352	1.8751	0	5-			
H1	(23)	0.000	2.5635	-0.0547	-1.3991	0	7-			
H1	(24)	0.000	3.3161	-1.4233	-0.5843	0	7-			
H1	(25)	0.000	1.6468	-1.4470	2.1336	0	11-			
H1	(26)	0.000	3.4030	-1.6551	1.9304	0	11-			
H1	(27)	0.000	2.7704	-0.3270	2.9591	0	11-			
H1	(28)	0.000	4.8224	-0.0688	0.6372	0	12-			
H1	(29)	0.000	4.1240	1.4006	-0.1169	0	12-			
H1	(30)	0.000	4.2490	1.2731	1.6685	0	12-			
H1	(31)	0.000	0.0341	3.2173	-0.1973	0	13-			
H1	(32)	0.000	-1.3649	2.5371	-1.1019	0	13-			
H1	(33)	0.000	-1.6211	3.4762	0.4089	0	13-			
H1	(34)	0.000	0.4102	-0.2968	-3.0924	0	14-			
H1	(35)	0.000	-1.0126	0.5390	-2.4684	0	14-			
H1	(36)	0.000	0.6074	1.0165	-1.8804	0	14-			
C3	(37)	0.000	1.4641	-2.6505	-1.9122	0	8-	39-	40-	41-
H1	(38)	0.000	1.0683	-2.2700	0.1422	0	8-			
H1	(39)	0.000	0.5712	-3.2920	-2.0980	0	37-			
H1	(40)	0.000	1.7256	-2.1413	-2.8671	0	37-			
H1	(41)	0.000	2.3108	-3.3330	-1.6658	0	37-			

Total charge on system = -1.000

## VI

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.042	-2.3663	0.3861	2.7844	0	2-	10-	16-	17-
C3	( 2)	0.042	-2.3624	0.2141	1.2469	0	1-	3-	18-	19-
C2	( 3)	-0.083	-1.1820	0.9837	0.6850	0	2-	4=	13-	
C2	( 4)	-0.042	0.0208	0.3799	0.6522	0	3=	5-	20-	
C3	( 5)	0.042	1.3564	1.0661	0.5650	0	4-	6-	21-	22-
C3	( 6)	0.000	2.4907	0.3561	1.3541	0	5-	7-	11-	12-
C3	( 7)	0.000	2.0976	-0.2772	2.7235	0	6-	8-	23-	24-
C3	( 8)	0.042	1.4537	0.5813	3.8381	0	7-	9-	37-	38-
C2	( 9)	-0.369	0.0195	1.0159	3.5738	0	8-	10=	14-	
C2	( 10)	0.114	-0.9778	0.1338	3.3182	0	9=	1-	15-	
C3	( 11)	0.000	3.6413	1.3700	1.5590	0	6-	25-	26-	27-
C3	( 12)	0.000	3.0454	-0.7867	0.4644	0	6-	28-	29-	30-
C3	( 13)	0.042	-1.4225	2.4425	0.3855	0	3-	31-	32-	33-
C3	( 14)	0.042	-0.1866	2.5123	3.6376	0	9-	34-	35-	36-
OM	( 15)	-0.870	-0.7790	-1.1893	3.3329	0	10-			
H1	( 16)	0.000	-2.7181	1.4086	3.0445	0	1-			
H1	( 17)	0.000	-3.1014	-0.3110	3.2536	0	1-			
H1	( 18)	0.000	-2.2715	-0.8696	0.9955	0	2-			
H1	( 19)	0.000	-3.3203	0.5626	0.7938	0	2-			
H1	( 20)	0.000	0.0615	-0.7021	0.8496	0	4-			
H1	( 21)	0.000	1.6325	1.1710	-0.5097	0	5-			
H1	( 22)	0.000	1.2539	2.0970	0.9665	0	5-			
H1	( 23)	0.000	1.4764	-1.1831	2.5551	0	7-			
H1	( 24)	0.000	3.0435	-0.6866	3.1501	0	7-			
H1	( 25)	0.000	3.3255	2.2393	2.1783	0	11-			
H1	( 26)	0.000	4.5182	0.9037	2.0636	0	11-			
H1	( 27)	0.000	3.9984	1.7782	0.5856	0	11-			
H1	( 28)	0.000	3.8952	-1.3149	0.9548	0	12-			
H1	( 29)	0.000	2.2661	-1.5502	0.2404	0	12-			
H1	( 30)	0.000	3.4239	-0.4067	-0.5122	0	12-			
H1	( 31)	0.000	-0.5319	2.9627	-0.0297	0	13-			
H1	( 32)	0.000	-2.2236	2.5318	-0.3823	0	13-			
H1	( 33)	0.000	-1.7609	2.9942	1.2888	0	13-			
H1	( 34)	0.000	0.3967	3.0336	2.8470	0	14-			
H1	( 35)	0.000	-1.2454	2.8313	3.5486	0	14-			
H1	( 36)	0.000	0.1600	2.8929	4.6251	0	14-			
C3	( 37)	0.000	1.5248	-0.1271	5.2044	0	8-	39-	40-	41-
H1	( 38)	0.000	2.0848	1.4962	3.9336	0	8-			
H1	( 39)	0.000	1.0885	0.5087	6.0099	0	37-			
H1	( 40)	0.000	0.9755	-1.0956	5.2008	0	37-			
H1	( 41)	0.000	2.5784	-0.3461	5.4956	0	37-			

Total charge on system = -1.000

## VII

Atom		Charge	Coordinates			Residue	Attached Atoms & Bonds			
Type	Number		X	Y	Z					
C3	( 1)	0.042	-2.4767	-0.4259	-0.8708	0	2-	10-	16-	17-
C3	( 2)	0.042	-2.2889	-0.1013	0.6278	0	1-	3-	18-	19-
C2	( 3)	-0.083	-1.1363	0.8755	0.7773	0	2-	4=	13-	
C2	( 4)	-0.042	0.1017	0.3906	0.9910	0	3=	5-	20-	
C3	( 5)	0.042	1.4104	1.1141	0.8334	0	4-	6-	21-	22-
C3	( 6)	0.000	2.4527	0.3844	-0.0629	0	5-	7-	11-	12-
C3	( 7)	0.000	1.9612	0.1179	-1.5184	0	6-	8-	23-	24-
C3	( 8)	0.042	1.2560	-1.2080	-1.9115	0	7-	9-	37-	38-
C2	( 9)	-0.369	-0.1426	-1.4110	-1.3542	0	8-	10=	14-	
C2	(10)	0.114	-1.1309	-0.5073	-1.5449	0	9=	1-	15-	
C3	(11)	0.000	2.9782	-0.8965	0.6174	0	6-	25-	26-	27-
C3	(12)	0.000	3.6658	1.3541	-0.1541	0	6-	28-	29-	30-
C3	(13)	0.042	-1.4604	2.3166	0.4652	0	3-	31-	32-	33-
C3	(14)	0.042	-0.3688	-2.7073	-0.6103	0	9-	34-	35-	36-
OM	(15)	-0.870	-0.9374	0.5988	-2.2723	0	10-			
H1	(16)	0.000	-3.0532	-1.3699	-1.0123	0	1-			
H1	(17)	0.000	-3.0914	0.3779	-1.3427	0	1-			
H1	(18)	0.000	-3.2239	0.3058	1.0799	0	2-			
H1	(19)	0.000	-2.0675	-1.0407	1.1864	0	2-			
H1	(20)	0.000	0.1997	-0.6779	1.2273	0	4-			
H1	(21)	0.000	1.2428	2.1274	0.4088	0	5-			
H1	(22)	0.000	1.8293	1.2590	1.8565	0	5-			
H1	(23)	0.000	1.3766	0.9982	-1.8663	0	7-			
H1	(24)	0.000	2.8778	0.1291	-2.1529	0	7-			
H1	(25)	0.000	2.1827	-1.6518	0.7852	0	11-			
H1	(26)	0.000	3.7721	-1.3816	0.0045	0	11-			
H1	(27)	0.000	3.4195	-0.6747	1.6159	0	11-			
H1	(28)	0.000	4.5239	0.9007	-0.7020	0	12-			
H1	(29)	0.000	3.3977	2.2977	-0.6836	0	12-			
H1	(30)	0.000	4.0466	1.6366	0.8545	0	12-			
H1	(31)	0.000	-0.6491	3.0253	0.7370	0	13-			
H1	(32)	0.000	-1.6947	2.4527	-0.6136	0	13-			
H1	(33)	0.000	-2.3510	2.6353	1.0523	0	13-			
H1	(34)	0.000	0.2945	-2.7959	0.2773	0	14-			
H1	(35)	0.000	-1.4145	-2.8393	-0.2586	0	14-			
H1	(36)	0.000	-0.1508	-3.5648	-1.2864	0	14-			
C3	(37)	0.000	1.2086	-1.3787	-3.4434	0	8-	39-	40-	41-
H1	(38)	0.000	1.8979	-2.0410	-1.5381	0	8-			
H1	(39)	0.000	0.7325	-2.3466	-3.7267	0	37-			
H1	(40)	0.000	0.6343	-0.5617	-3.9358	0	37-			
H1	(41)	0.000	2.2310	-1.3774	-3.8878	0	37-			
Total charge on system =			-1.000							

## 第七章 結論

本研究は中・大員環化合物を鎖状あるいは5,6員環化合物と同等に合成の鍵中間体として用い得ることを確立するために、従来この分野で問題となっていた立体選択性の予測、生成物の立体化学の証明の困難な点を分子力学計算(MM2)を用いる立体配座解析、あるいはMM2遷移状態モデルの計算に基づく反応の立体選択性の定量的な予測による解決を試みた。さらにこれらの計算が合成中間体の設計に応用しうることを明確にした。

第一章 序論では、分子力学計算(MM2)の合成反応の応用例、および中・大員環化合物を用いた立体化学制御の報告例を挙げ、それぞれの有用性を示し、本研究の目的を明らかにした。

第二章 MM2計算の方法：構造入力と出力分析では、分子力学計算(MM2)を配座異性体の多い中・大員環化合物の立体配座解析に用いる際の問題点を指摘し、本研究においてその解決策として用いた自動立体配座発生プログラム(MMRS, MULTIC)の原理、および出力される計算結果の処理について詳細に述べた。

第三章 ネオカルチノスタチンクロモフォアの合成研究および合成モデルを用いた天然物類似の渡環反応の研究では、MM2計算に基づいて設計した12員環化合物の渡環的[2,3]-Wittig転位反応を用いて、高歪で合成困難と考えられていた9員環化合物を効率よく合成することに成功した。この際の[2,3]-Wittig転位反応の反応性および立体選択性は計算による予測とよく一致した。本合成は大員環化合物を鍵中間体とする合成ルートの実用性を高め、その際に立体配座解析が不可欠であることを明確にした。さらにネオカルチノスタチンクロモフォアあるいはエスペラミシン・カリケミシンの合成モデルに導き、そのDNA切断試験、およびアポタンパクとの接合試験を行ったが活性は得られず、より高度な官能基の導入の必要性が示唆された。

第四章 大員環内Diels-Alder反応の研究では、 従来の鎖状化合物の分子内Diels-Alder反応との違いを指摘すると共にその立体選択性の予測をMM2遷移状態モデルを用いて行い、この計算の合成中間体設計における有用性を明確にした。この際、活性基のあるジエノフィルのDiels-Alder反応では立体電子的な効果を単純な系での実験と計算結果との比較から算出し、補正項を導入することにより解決した。また本反応を用いたステロイド骨格新規合成法の開発に成功し、MM2遷移状態モデルの計算の一般性を示した。

第五章 ペリプラノンAの合成研究では、 10員環化合物のエポキシ化から得られるペリプラノンAおよびその立体異性体の立体選択性を10員環化合物のMM2計算を用いた立体配座解析から予測し、実験結果とよく一致することを報告した。得られた化合物の立体配置の決定はその立体配座解析とNMRの低温測定の結果から行い、MM2計算を用いた立体配座解析が生成物の構造決定に有効であることを示した。さらに立体選択的なペリプラノンAの合成中間体の設計へ応用した。

第六章 10員環エノンへの共役付加的三員環形成反応の立体選択性の予測:  
ビシクロフムレノンの合成の研究では、 10員環化合物への硫黄イリドの共役付加、続く3員環形成反応の立体選択性をMM2計算に基づく立体配座解析から予測し、ビシクロフムレノンを立体選択的に合成することに成功した。この際、中員環化合物への共役付加-アルキル化反応において、共役付加反応で生成するエノラートの立体配座の変換速度とアルキル化の反応速度のどちらが大きいかにより、立体選択性の決まる律速段階が異なることを挙げ、いずれの場合も想定して、アルキル化反応の立体選択性の予測を行った。このことから中員環化合物では、立体配座の変換速度の大きい鎖状化合物や立体配座の変換が起こり得ない5,6員環化合物とは異なり、立体配座の変換が比較的遅いながら起こりうるために考えなければならない合成上の問題点を指摘し、中員環化合物を用いる反応においての問題意識を高めることができた。

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