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PART I  ANTI-TRICYCLO[3.1.1.0²⁴]HEPTYL AND RELATED SYSTEMS

PART II  REDUCTIVE CLEAVAGE OF SUCCINIC ESTERS UNDER ACYLOIN CONDITIONS

DISSERTATION
Presented in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy in the Graduate School of The Ohio State University

BY
Xavier Creary, B.S.

* * * * *

The Ohio State University
1975

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Department of Chemistry
To Betsy
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VITA

Xavier Creary, the son of Herman B. and Thelma A. Creary, was born on September 27, 1946 in Montclair, New Jersey, where he received his primary and secondary education. In September, 1964, he entered Seton Hall University, South Orange, New Jersey where he received his B.S. in Chemistry in June, 1968. In September, 1968 he entered The Graduate School of The Ohio State University where he held the positions of Teaching Assistant, Goodyear Fellow, and Research Associate. On January 27, 1973 he married Elizabeth Ann McCaw of Cuyahoga Falls, Ohio. In June, 1973 he received his Ph.D. in Organic Chemistry from The Ohio State University.
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<td>S. Winstead, E. Grunewald, and L.L. Ingraham, ibid., 70, 821 (1948)</td>
<td>138</td>
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</table>
15. Spectra were supplied by Dr. T.J. Atkins................. 141
20. M.S. Morgan, R.S. Tipson, A. Lowry and W.E. Baldwin, ibid., 66, 404 (1944)................................................ 156
22. H. Bowde, Chem. Ber., 70, 1167 (1937)....................... 156

XXV
PART I  ANTI-TRICYCLO[3.1.1.0²⁴]HEPTYL AND RELATED SYSTEMS

PART II  REDUCTIVE CLEAVAGE OF SUCCINIC ESTERS UNDER ACYLOIN CONDITIONS

By:

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The tosylate derivative of endo-anti-tricyclo[3.1.1.0²⁴]heptan-6-ol was prepared in sixteen steps from norbornadiene and solvolyzed in buffered acetic acid and aqueous diglyme containing sodium borohydride. Kinetic data and reaction products implied a stepwise rearrangement process involving a series of equilibrating cations, each of which was potentially bishomoantiaromatic. Direct generation of each of these cationic intermediates solvolytically from different precursors showed that these cations do not possess any special instability as a result of antiaromatic character. The rate retarding effect of a non-participating homoallylic double bond in these systems was found to be as small as a factor of 1.56 and as large as a factor of 1.65 x 10³. This polar effect may be a field effect rather than an inductive effect through bonds. The lack of any observable bishomoantiaromaticity could be rationalized in terms of available lower energy pathways for reaction.

-1-
The p-nitrobenzoate derivative of \textit{exo-anti}-tricyclo[3.1.1.0^{2,4}]heptan-6-ol was prepared and its solvolytic reactivity was determined. Extensive cyclopropyl participation resulted in large rate enhancements over model systems and in structurally rearranged products. Rate enhancements attributable to cyclopropyl participation were estimated to be substantially greater than in the less strained p-nitrobenzoate derivative of \textit{exo-anti}-tricyclo[3.2.1.0^{2,4}]octan-8-ol, consistent with the increased demand for participation at the more strained incipient cationic center.

As an approach to the \textit{trans}-bicyclo[4.1.0]heptyl ring system, \textit{trans}-1,2-dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester was subjected to the acyloin condensation. Under heterogeneous conditions, with added chlorotrimethylsilane, ring closure occurred, followed by thermal rearrangement of the initially formed \textit{trans}-cyclobutene derivative. Under homogeneous conditions, using sodium in liquid ammonia, reductive cleavage occurred to produce dimethylsuberic acid dimethyl ester. The mechanism, scope, and synthetic utility of this cleavage reaction was investigated using a series of 1,2-diesters which were subjected to both heterogeneous and homogeneous acyloin conditions. The reductive cleavage reaction of these diesters was found to be very solvent dependent. Cleavage occurred readily in liquid ammonia when the ester functions could become coplanar. Ring closure occurred preferentially in toluene with added chlorotrimethylsilane with reductive cleave occurring only when strain precluded ring formation. The different behavior of 1,2-diesters under the two sets of conditions sug-
gested that the mechanism of the acyloin condensation might be different in the two solvents with differences arising from the rates of electron transfer in the two solvent systems.
PART I

ANTI-TRICYCLO[3.1.1.0²⁴]HEPTYL AND RELATED SYSTEMS

CHAPTER I

a) Historical

Neighboring group participation, as defined by Winstein,¹ is the phenomenon in which a molecular substituent that is not directly attached to a reaction center interacts with that center by becoming bonded or partially bonded to it during a chemical reaction. In the study of solvolytic displacement reactions, this phenomenon has been a topic of considerable interest with many substituents being capable of this type of participation. Neighboring group participation by a substituent will usually manifest itself in terms of large reaction rate enhancements which is termed anchimeric assistance. Substituents which are capable of neighboring group participation in solvolytic reactions include neighboring halogen, amine, amide, ether, thioether, ester, and ketone.²

Perhaps the most widely studied participation is that of neighboring carbon, which can be divided into two classes; carbon–carbon

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2. For a review of the various types of participation see B. Capon, Quart. Revs., 18, 45 (1964).
multiple bond participation and carbon-carbon sigma bond participation.

Carbon-Carbon Multiple Bond Participation

Participation by neighboring aryl groups in solvolytic reactions may be considered a type of $\pi$ participation as is allylic participation leading to allylic cations. These types of carbon-carbon multiple bond participations will not be considered at present.

One of the first examples of neighboring group participation involving a carbon-carbon double bond (other than aryl or allylic) was that involving the double bond in cholesteryl p-toluenesulfonate and chloride. Evidence for participation of the double bond with formation of ion 2 include for formation of acetate 3 with retained configuration and a rate enhancement by a factor of forty over the saturated analogue.

\[ \text{TsO} \quad 1 \rightarrow \quad 2 \rightarrow \quad \text{AcO} \quad 3 \]

3. For leading references, see footnote 2.


Even larger rate enhancements due to homoallylic participation can be seen in tosylate 1 and brosylate 2 with rate accelerations due to anchimeric assistance being approximately $10^3$ and $10^4$.

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_2-\text{OTs} & \text{CH}_3 & \quad \text{CH}_2 \\
\text{CH}_3 & \quad & & \\
& \quad & & \\
& \quad & & \\
& \quad & & \\
\end{align*}
\]

The 7-norbornenyl cation, 3, provides one of the most interesting examples of homoallylic participation. In terms of rate enhancements, anti-norborn-2-en-7-yl p-toluenesulfonate, 4, solvolyzes $10^{11}$ faster than the saturated analogue 7-tosyloxynorbornane, 5.

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_2-\text{OTs} & \text{CH}_3 & \quad \text{CH}_2 \\
\text{CH}_3 & \quad & & \\
& \quad & & \\
& \quad & & \\
& \quad & & \\
\end{align*}
\]


Some controversy has arisen concerning the exact nature of the intermediate in the solvolysis of $\mathcal{O}$ with one school favoring delocalized ion $10^{10}$ and the other$^{11}$ favoring a pair of rapidly equilibrating ions $10a$ and $10b$. However, nmr studies$^{12}$ of alcohol $11$ in strong acid shows the equivalence of protons on C$_2$ and C$_3$ even at $-60^\circ$. This implies a delocalized ion or an improbable, extremely rapid equilibrium even at $-60^\circ$. In addition, Gassman$^{13}$ has shown that the accelerative effects of methyl groups in p-nitrobenzoates $12$ and $13$ are not additive but multiplicative. This is also consistent with

the representation of the intermediate formed in solvolysis of \( \text{8} \) as bishomocyclopropenyl cation \( \text{10, 14} \).

Participation by more remote double bonds is also possible and has been postulated to occur in solvolysis of \( \text{14, 15, 16, 18, 17} \) and \( \text{20, 18} \) with the formation of ions \( \text{15, 17, 19, and 21} \), respectively.

![Diagram](image)

Carbon-Carbon Sigma Bond Participation

Carbon-carbon σ-bond participation can be divided into two classes; participation by relatively unstrained σ bonds, such as in the solvolysis of exo-2-norbornyl tosylate, and participation by neighboring small rings, cyclopropyl in particular. The nature of the rate acceleration in the solvolysis of exo-2-norbornyl tosylate and related compounds have been subject to extensive debate and will not be discussed here.

A cyclopropyl group situated adjacent to a developing cationic center in a solvolysis reaction is capable of accelerating the rate of that reaction. This is, in all probability, due to the unusual nature of the bonding in the cyclopropane ring.

Solvolysis of cyclopropylmethyl benzenesulfonate, $^{21}$, in ethanol is faster than either 3-butenyl, $^{22}$, or allyl benzenesulfonate $^{23}$

by factors of $10^3$ and $10^4$, respectively. $^{21}$ It was suggested that this enhanced reactivity is due to a highly delocalized transition state represented by a combination of resonance hybrids. Subsequently, numerous cyclopropyl carbonyl systems have been prepared and solvoly-

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zed with the intention of elucidating the exact nature of the intermediate(s) involved in the reaction. Many delocalized structures have been considered, with structures receiving recent support.


Although the nature of the charge delocalization remains unresolved, certain geometrical requirements appear necessary for stabilization of an adjacent cationic center by a cyclopropyl group. The nmr spectrum of cation 28 in SO₂-SbF₅ has been interpreted in terms of a symmetrical species with the vacant p orbital parallel to the plane of the cyclopropane ring. This conformation, 29, is preferred over the unsymmetrical conformation 30 or the symmetrical conformation 31. Hence, the solvolysis 32 is not assisted by cyclopropyl participation due to the unfavored geometry in 33.
One of the first examples of more remote cyclopropyl participation was observed by Winstein in the solvolysis of cis tosylate. Evidence for the delocalized nature of the intermediate included a rate acceleration over the corresponding trans tosylate, statistical scrambling of the methylene groups in labeled \( \text{24} \), and the isolation of only cis acetate \( \text{36} \) as the acetylsis product. The nature of cation \( \text{25} \) has also been discussed in terms of a homocyclopropenyl species, analogous to the aromatic cyclopropenyl cation, \( \text{37} \).


One of the largest rate accelerations due to cyclopropyl participation is seen in the solvolysis of p-nitrobenzoate $3\tilde{8}$. In terms of rate, $3\tilde{8}$ is $10^1$ to $10^3$ times faster than the unsaturated p-nitrobenzoate $39$. If one can extrapolate p-nitrobenzoate rates to tosylate rates, $3\tilde{8}$ becomes $10^{12}$ to $10^{14}$ times as reactive as the saturated analogue $40$. The intermediate in the solvolysis of $3\tilde{8}$ is analogous to cation $10$ and can be represented by $41$. The large rate acceleration is due to the very favorable geometry for interaction of the developing cationic center with the bent bond of the cyclopropane ring.

Further examples of remote participation to the edge of a cyclopropane ring can be seen in the solvolyses of \( \text{h}_2^{32} \) and \( \text{h}_4^{33} \) which yield cations \( \text{h}_3^2 \) and \( \text{h}_5^5 \), respectively.

\[ \begin{array}{c}
\text{H} \quad \text{OPNB} \\
\text{h}_2 \\
\to \\
\text{h}_3 \\
\end{array} \]

\[ \begin{array}{c}
\text{OTs} \\
\text{h}_4 \\
\to \\
\text{h}_5 \\
\end{array} \]


b) The Problem

The degree of anchimeric assistance by a neighboring group in a unimolecular solvolysis reaction should be a function of both the ability of that group to stabilize a cationic center and also the demand of that cationic center. This premise is borne out in the solvolysis of tosylates $\text{H}^6$ and $\text{H}^8$ and the methoxyacetate $\text{H}^4$.

Rate enhancements attributable to the double bond increase as the strain at the developing cationic center increases. The increasing demand for participation as the cationic center changes from a cyclohexyl in $\text{H}^6$ to cyclobutyl in $\text{H}^7$ results in an increase in anchimeric assistance.

Cyclopropyl participation should also be a function of the demand of the cationic center. As previously discussed, it is also very dependent on molecular geometry. It would, therefore, be of interest to prepare and solvolyze derivatives of exo-anti-tricyclo-$[3.1.1.0^{2,4}]$heptan-6-ol, $\text{H}^8$, in view of the geometry of the system.

and the increased demand for participation relative to 38. It would also be of interest to prepare epimeric derivative 49 in view of the cyclopropyl carbinyl systems conceptually derived by solvolysis of this system.
CHAPTER II

SYNTHESIS OF TRICYCLO[3.1.1.0²⁴]HEPTANE RING SYSTEMS

The synthetic approach to the tricyclo[3.1.1.0²⁴]heptane ring system involved the ring contraction of the exo-tricyclo[3.2.1.0²⁴]-octane ring system. The construction of the initial tricyclo-

[3.2.1.0²⁴]octane ring system was achieved by a Simmons-Smith reaction on norbornadiene. The methylene transfer reagent was prepared using the Sawada-Inouye modification³⁶ which involved prior reaction of ethyl zinc iodide with methylene iodide. This method gave moderate, though reproducible, yields of exo-tricyclo[3.2.1.0²⁴]octene, ⁵₀ ³⁷ in contrast to the normal Simmons-Smith procedure using zinc-copper and methylene iodide.

The immediate synthetic goal was the conversion of olefin 50 to an $\alpha$-diazoketone which could be ring contracted. Olefin 50 was, therefore, converted to ketone 51 by a hydroboration-oxidation scheme. However, all attempts to convert ketone 51 to $\alpha$-diazoketone 52 directly were unsuccessful. Attempts to oxidize 51 to the diketone 52 or to convert to the formyl derivative, both of which are in principle easily converted to an $\alpha$-diazoketone, were also unsuccessful. $\alpha$-Diazoketone 52 was, therefore, approached in an alternate manner as shown below. Ozonolysis of olefin 50 followed by oxidative workup and esterification of the crude diacid gave a 64% yield of diester 54. In what was considered one of the key steps in the reac-

ion sequence, diester 54 was successfully cyclized using the acyloin condensation. The critical factor was the introduction of chlorotrimethylsilane into the reaction mixture which allowed the trapping of the intermediate enediolate as the bistrimethylsilyl ether 55 in 84% yield. This was considered a conversion of major importance since upon hydrolysis, silyl ether 55 gave α-hydroxyketone 56, which

should, in principle, have been readily oxidizable to the $\alpha$-diketone $52$. However, all oxidative attempts to produce the diketone were unsuccessful.

Diketone $52$ could, however, be produced in excellent yield by the addition of bromine in carbon tetrachloride to bistrimethylsilyl ether $55$ at $-25^\circ$. Unfortunately, the yield and purity of monotosylhydrazone $57$, produced by the reaction of diketone $52$ with tosylhydrazine in methanol was poor. Diketone $52$ is probably unstable to protic solvents as evidenced by the disappearance of its bright yellow color when dissolved in methanol. The fate of diketone $52$ in protic solvents was not investigated in view of a more attractive approach to the ring contracted tricyclo[3.1.1.0$^{2,4}$]heptane ring system.

This approach grew out of the observed thermal reactivity of lithium salt $64$, prepared as shown in Scheme I. Ozonolysis-oxidation of norbornene $41$ followed by esterification of the crude 1,3-cyclopentadecarboxylic acid gave diester $58$. Acyloin condensation of this diester $42$ using sodium in toluene with added chlorotrimethylsilane gave bistrimethylsilyl ether $59$. Methanolation of $59$ followed by

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH

Scheme I

1) O₃
2) H₂O₂
3) CH₃OH
ketalization of the α-hydroxyketone and Sarett oxidation gave ketal-ketone 62 in 76% overall yield from silyl ether 59. Treatment of ketal-ketone 62 with tosylhydrazine in methanol gave tosylhydrazone 63 which could be converted to its lithium salt by treatment with butyl lithium in tetrahydrofuran. The dry lithium salt was pyrolyzed under vacuum according to the procedure of Shechter.43 The product of this pyrolysis in 60% yield was the dimethylketal of nortricyclanone, 67, identified by spectral comparison with an authentic sample.44 This product can be explained in terms of loss of nitrogen from the intermediate diazoketal 65 with the resulting carbene,

\[ \text{Diagram showing chemical structures and reaction} \]


44. Spectra were provided by Dr. J. MacMillan.
inserting intramolecularly into a carbon-hydrogen bond.

The analogous lithium salt in the tricyclo[3.2.1.0²⁵⁸]octane system was prepared in an analogous manner as shown in Scheme II. It

Scheme II

\[
\begin{array}{c}
\text{56} \xrightarrow{\text{CH₃OH/H}^+} \text{68} \xrightarrow{\text{CrO}_3} \text{69} \\
\text{70} \xleftarrow{\text{NH₂NHTs}} \xrightarrow{\text{CH₃OH}} \\
\text{72} \xrightarrow{100^\circ} \text{71} \xrightarrow{\text{BuLi}} \\
\text{73} \xrightarrow{\text{H₂NHTs}} \text{74}
\end{array}
\]
was hoped that thermal ring contraction of lithium salt \( \text{71} \) could be achieved in view of the highly strained nature of the tricyclic product, \( \text{74} \), that would result from an intramolecular carbene insertion. However, when pyrolized, \( \text{71} \) gave no ring contracted olefin, \( \text{75} \). In-

\[
\begin{align*}
\text{72} & \quad \xrightarrow{\text{\textit{\( / \)}}} \quad \text{75} \\
\text{76} & \quad \xrightarrow{\text{\textit{\( H_3O^+ \)}}} \quad \text{77} \\
\text{68} & \quad 1) \text{NaH} \quad \xrightarrow{\text{\textit{\( 2) \CH_3I \)}}} \quad \text{78}
\end{align*}
\]
stead, the only isolable product was the vinyl ether 76 which arose presumably through methoxy group migration to the carbenic center of 72.

Although numerous examples of alkoxy group migration to photochemically generated carbenoid centers have been reported, such migrations to thermally generated carbenes are rare. Shechter and Straus have discussed the reasons for the lack of alkoxy group migration to thermally generated carbone centers in terms of the high energy intermediate 72 or transition state 80 by which the lowest singlet state of a carbene must rearrange. Even in the case of photolytic generation of carbenes from diazoalkanes, it has been noted

\[ \begin{array}{c}
\text{R} \quad \text{RC} \quad \text{CR}_2 \\
\downarrow \quad \downarrow \\
\text{O} \quad \text{R}
\end{array} \quad \begin{array}{c}
\text{R} \quad \text{RC} \quad \text{CR}_2 \\
\downarrow \quad \downarrow \\
\text{O} \quad \text{R}
\end{array} \]

that 'the alkoxy group is not particularly prone to migrate but rather that a β-alkoxy group tends to promote migration of other β-substituents'. For these reasons, the formation of alkoxy


migration product 76 was considered unusual.

The structure of 76 was based on spectroscopic as well as chemical evidence. The nmr spectrum showed absorptions at $\tau$ 6.33 (6H, s), 7.30 (2H, m), and 8.40-9.30 (6H, m). Treatment with dilute hydrochloric acid gave keto-ether 77 which was identical in all respects to a sample prepared independently by methylation of hydroxy-ketal 68 with sodium hydride and methyl iodide followed by acid catalyzed hydrolysis of the resultant ketal-ether 78.

Additional evidence for the structure of 76 was obtained from its ozonolysis in methanol, which gave the expected diester 24 in addition to ketal-ketone 69 in a 48:52 ratio, respectively. The formation of 69 was unusual in that an oxidation had occurred, but carbon-carbon bond cleavage had not. A study was, therefore, undertaken to elucidate the mechanism of the formation of 69 in the ozonolysis of 76.

In terms of current mechanistic thinking, ozonolysis can involve a multistep process with recent support being given to the

---

intermediacy of peroxy epoxides, $\text{81}$, and Staudinger molozonides, $\text{82}$. Considering these intermediates in the ozonolysis of $\text{76}$, the formation of $\text{69}$ could arise via at least two alternate routes. The first would involve the formation of peroxy epoxide $\text{83}$ or zwitterion $\text{84}$. The loss of oxygen and concerted intramolecular endo methoxyl group migration would give ketal-ketone $\text{69}$ directly.

This possibility was ruled out by carrying out the ozonolysis in methanol-$d_4$. In this case, the ketal-ketone isolated had incorporated a deuterated methoxyl group stereospecifically in the exo position. The necessary controls were carried out to insure that undeuterated ketal-ketone $\text{69}$ did not exchange under the reaction conditions.
An alternate mechanism to account for the stereospecific incorporation of a deuterated methoxyl group in the exo position of 88 is given in Scheme III. Loss of oxygen from peroxo epoxide 83 could produce epoxide 85. Epoxide 85 could open under the reaction conditions, incorporate solvent by exo attack on 86, with the eventual formation of deuterated ketal-ketone 88.

The assignment of stereochemistry in 88 is based on its nmr spectrum. Whereas 82 showed proton absorbances at δ 6.67 and 6.60, deuterated analogue, 88, showed only the latter absorbance.
Since exo-methyl groups generally appear at higher field in the nmr spectra of ketals of norcamphor and related compounds, the deuterated methoxyl group of 88 was initially assigned to the exo-position. This stereochemical assignment was confirmed by conversion of deuterated ketone 88 to the corresponding endo-methyl ether, 82, by sodium borohydride reduction followed by methylation with sodium hydride and methyl iodide. Deuterated ketal-ether 89 showed methyl signals at $\tau$ 6.67 and 6.56 in the nmr. The corresponding undeuterated ketal-ether 78 showed methyl signals at $\tau$ 6.79, 6.67, and 6.56. Upon treatment with p-toluenesulfonic acid in methanol-$d_4$, the upfield methoxyl signal disappeared rapidly. The signal at intermediate field

slowly decreased and the downfield signal underwent no change. On the basis of the extensive studies of Traylor and Perrin50 on exchange rates, the signals were assigned as shown. The absence of the signal at $\gamma 6.79$ in the deuterated ketal-ether 89 shows the deuterated methoxy group of 88 must have been in the exo-position. These studies implicate epoxide 85 as an intermediate in the formation of 88. Epoxide formation can be a major process in the ozonolysis of hindered olefins.51 The electron rich double bond of vinyl ether 76 also appears to be susceptible to this type of reaction. Hoffmann and Schneider52 also obtained evidence for the formation of an epoxide in the auto-oxidation of the electron rich olefin tetramethoxyethylene. In contrast to our results, the epoxide appears to rearrange in inert solvents by an intramolecular process to give dimethyl carbonate and methyl trimethoxy acetate. Ozonolysis led to similar products but the mechanistic implications of this reaction were not investigated.

If epoxide 85 is actually an intermediate in the formation of 69, then epoxidation of olefin 76 in methanol should also yield 69. When 76 was treated with m-chloroperbenzoic acid in methanol buffered with sodium carbonate, no trace of epoxide 85 could be found. Instead, ketal-ketone 69 was isolated, attesting to the reactivity of the postulated epoxide intermediate in methanol.

51. For leading references, see: P.S. Bailey, Chem. Revs., 58, 925 (1958).
Although the pyrolysis of lithium salt 74 led to an interesting methoxyl migration with resultant formation of an olefin of unusual reactivity, the desired thermal ring contraction was not achieved. It would appear that strain was a major factor in the failure of ring contraction to occur to the carbene center of 72. Hence, a more conventional ring contraction procedure was pursued.

Ketal-tosylhydrazone 70 was hydrolyzed in aqueous tetrahydrofuran to the monotosylhydrazone 57. Treatment of 57 with aqueous sodium hydroxide gave the desired α-diazoketone 52. Photolysis of a methanol solution of the α-diazoketone gave a 35% yield of a mixture of ring contracted esters 90. Also produced in about 5% yield was keto-ether 77 which arises presumably via insertion of the intermediate carbene 91 into methanol. Keto-ether 77 was also formed as the only product in the reaction of α-diazoketone 52 with silver oxide in methanol.

Treatment of the mixture of esters, 90, with sodium methoxide in methanol gave no change in the ir or nmr spectrum of the mixture. Saponification of the mixture followed by reesterification also gave the same mixture of esters as produced in the photolysis of 52.
Apparently, the mixture of esters produced photolytically is a thermodynamic mixture. Since endo-epimer 90a appears to be the most stable
for steric reasons, the major epimer was tentatively assigned this stereochemistry. These results contrast with those of other workers\textsuperscript{53} in which kinetic control is seen in the addition of solvent to hindered ketenes with the predominance of the less stable epimer in the isolated product. Apparently the stereochemistry of addition to relatively unhindered ketenes will be controlled by thermodynamic factors, while addition to form the least stable product will occur only when large steric factors predominate. This type of thermodynamic control was also seen in the addition of methanol to the analog of ketene 92 which does not contain the cyclopropyl group.\textsuperscript{54a}

Similar behavior is seen in the hydride reduction of ketones to alcohols. In the reduction of a number of ketones with a series of hydride reducing agents, Brown has observed that "the direction of reduction is controlled by the stability of the product in flexible, relatively unhindered ketones, and by the steric factor in rigid sterically congested ketones".\textsuperscript{54b}

The completion of the synthetic sequence was relatively straightforward. Saponification of the mixture of esters, \textsuperscript{92}, followed by treatment of the corresponding acids, \textsuperscript{92}, with two equivalents of methyl lithium gave methyl ketones \textsuperscript{94}. Baeyer-Villiger oxidation of


of $24$ with m-chloroperbenzoic acid in methylene chloride gave acetates $25$. Cleavage of the mixture of acetates with either methyl lithium or lithium aluminum hydride gave an 86:14 mixture of endo and exo-alcohols, $26$ and $27$, respectively. This confirmed the

\[
\begin{align*}
&\text{CO}_2\text{CH}_3 \\
&\xrightarrow{1) \text{KCH}} \xrightarrow{2) \text{KHSO}_4} \text{CO}_2\text{H} \\
&\xrightarrow{2 \text{ CH}_3\text{Li}} \text{COCH}_3
\end{align*}
\]

$H$-bonded ($\nu_{\text{CH}} = 3580 \text{ cm}^{-1}$)

$H$ (\(\tau 5.98\), quartet, 
\(J = 2.2 \text{ Hz}\))

$\text{CH}_3\text{Li}$

$26$ (major)

$27$ (minor)
original stereochemical assignments of esters 90a and 90b. The overall yield of alcohols 96 and 97 in fifteen steps from norbornadiene was 1.6%.

The stereochemistry of alcohols 96 and 97 was based on nmr as well as hydrogen bonding studies in the infra-red. endo-Alcohol 96 shows a quartet, $J = 2.2 \text{ Hz}$, at $\tau 5.98$ in the nmr. The additional splitting results from long range coupling to the unique cyclopropane proton. Very pure samples of alcohol 96 show the carbonyl proton as a broad, poorly resolved doublet, coupled with the hydroxyl proton, indicative of a non-exchanging intramolecularly hydrogen bonded hydroxyl proton.

The infra-red spectrum of endo-alcohol 96 in dilute carbon tetrachloride solution shows only a sharp band in the hydroxyl region of the spectrum at $3580 \text{ cm}^{-1}$. This is again indicative of a strongly intramolecularly hydrogen bonded hydroxyl proton. No free hydroxyl stretching band could be seen even when the solution was made more dilute, consistent with complete hydrogen bonding to the edge of the cyclopropane ring.

The nmr spectrum of exo-alcohol 97 showed a doublet at $\tau 5.93$


$J = 7 \text{ Hz}$, consistent with the expected $\nu$-coupling of the carbinyl proton. The infra-red spectrum in dilute carbon tetrachloride solution shows only a relatively broad hydroxyl stretching band at $3650 \text{ cm}^{-1}$, consistent with the expected free hydroxyl stretching frequency.
CHAPTER III

SOLVOLYSIS OF DERIVATIVES OF endo-TRICYCLO [3.1.1.0\(^{2,4}\)]HEPTAN-6-OL AND RELATED SYSTEMS

endo-Tricyclo[3.1.1.0\(^{2,4}\)]heptan-6-ol, 96, was converted to the corresponding tosylate by treatment with p-toluenesulfonyl chloride in pyridine. Tosylate 98 proved to be very reactive for a cyclobutyl tosylate, undergoing solvolysis in buffered acetic acid at room temperature. The results of kinetic studies are given in Table I. In terms of rate, tosylate 98 is 12 times less reactive than tosylate 102.\(^{58}\) This corresponds to a slight electron withdrawing effect of the \(\beta\)-cyclopropyl group.\(^{59}\) However, tosylate 102 undergoes solvolysis with a large rate acceleration due to \(\sigma\)-participation. Hence, tosylate 98 must also solvolyze with a large amount of anachimetric assistance. The magnitude of this assistance will be considered in Chapter IV.


Table I. Rates of Solvolysis in Acetic Acid -0.10 M NaOAc

<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp. (± 0.03°C)</th>
<th>k (sec⁻¹)</th>
<th>ΔH⁺ (kcal/mol)</th>
<th>ΔS⁺ (eu)</th>
<th>k_rel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TsO</td>
<td>16.7</td>
<td>(7.70±0.02) x 10⁻⁵</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.0</td>
<td>(2.27±0.01) x 10⁻⁴</td>
<td>21.8±0.1</td>
<td>-2.1±0.2</td>
<td>1.0 x 10⁷</td>
</tr>
<tr>
<td></td>
<td>33.8</td>
<td>(6.82±0.01) x 10⁻⁴</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TsO</td>
<td>25.0</td>
<td>2.64 x 10⁻³ b</td>
<td></td>
<td></td>
<td>5.6 x 10⁸</td>
</tr>
<tr>
<td>OTs</td>
<td>25.0 a</td>
<td>2.24 x 10⁻¹¹ b</td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
</tbody>
</table>

a) Extrapolated from higher temperatures. (b) Ref. 58
The major product of the acetolysis of tosylate 98 in 52% yield was cycloheptatriene, identified by infra-red spectral comparison with an authentic sample. In addition to this hydrocarbon product, two acetates were produced. The major acetate could be catalytically hydrogenated to cycloheptyl acetate and the minor to an isomeric acetate. In order to further simplify identification of the acetate products, they were reduced with lithium aluminum hydride to the corresponding alcohols which were separable by gas chromatography.

\[
\begin{array}{c}
\text{TsO} \\
\text{H}
\end{array}
\xrightarrow{1) \text{HAc}}
\begin{array}{c}
\text{Cycloheptatriene} \\
+ \\
\text{Cycloheptadienol}
\end{array}
\xrightarrow{2) \text{LiAlH}_4}
\begin{array}{c}
\text{Cycloheptadienylacetate} \\
+ \\
\text{Norcaranol}
\end{array}
\]

The two alcohols produced were cycloheptadienol 101 and trans-norcaranol 100. The structure of the cycloheptadienol, 101, was based on its nmr spectrum which shows an olefinic 4H multiplet at \( \tau \) 4.25, a 1H multiplet at \( \tau \) 5.60, a doubly allylic 2H multiplet at \( \tau \) 7.16 and an allylic 2H multiplet at \( \tau \) 7.51 superimposed on an exchangeable 1H singlet at \( \tau \) 7.51.

The structure of norcaranol 100 was based on its nmr spectrum as well as independent synthesis. Addition of dibromocarbene to 1,4-cyclohexadiene\(^\text{60}\) gave 7,7-dibromonorcar-3-ene, 102. Silver

---

assisted solvolysis in acetic acid\textsuperscript{61} gives a mixture of bromoacids, 1\textsuperscript{03}, along with 3-bromocyclohexatriene, 1\textsuperscript{04}. 7,7-Dibromonorcar-3-ene is substantially less reactive than the saturated analogue, 7,7-
dibromonorcarane. This reactivity will be discussed.

Mechanistically, bromoacetates can arise via homoallylic rearrangement of the initially formed allyl cation, while 3-bromocycloheptatriene, can result from proton loss from either cation or . Saponification of bromoacetates followed by dehalogenation with sodium-t-butanol in tetrahydrofuran gave a mixture of alcohols and , which were separable by gas chromatography. The major alcohol was identical in all respects to the minor alcohol produced in the solvolysis of tosylate . The stereochemistry of the major alcohol (5%) was assigned on the basis of its hydrogenation to trans-2-methylcyclohexanol. The minor alcohol (4%)
could be partially hydrogenated to cis-norcan-2-ol\textsuperscript{62} or fully hydrogenated to cis-2-methylcyclohexanol.

Both rate data and products obtained in the solvolysis of tosylate \textsuperscript{28} indicated that the driving force is the rearrangement of the four membered ring presumably to yield cation \textsuperscript{112}. Stepwise cyclopropylcarbiny1-homoallylic rearrangements would give cations \textsuperscript{113} and \textsuperscript{114}, respectively. The intermediacy of cations \textsuperscript{113} and \textsuperscript{114} would account for the formation of alcohols \textsuperscript{100} and \textsuperscript{101}, respectively. Proton loss from either ion would give the major product of the reaction, cycloheptatriene.

![Diagram of chemical reactions]

The postulated first intermediate cation \textsuperscript{112} is the bishomo analog of the cyclopentadienyl cation\textsuperscript{63} and as such is potentially bishomoantiaromatic. Gajewski\textsuperscript{64} has generated the trans-analog of \textsuperscript{112} solvolytically from the corresponding p-nitrobenzoate \textsuperscript{115a}.


\textsuperscript{63} R. Breslow and J.M. Hoffman, Jr., \textit{ibid.}, \textbf{94}, 2110 (1972); R. Breslow and S. Mazur, \textit{ibid.}, \textbf{95}, 584 (1973).

Unrearranged alcohol 117a was the only product produced. However, no conclusions were drawn concerning the potential bishomoantiaromatic nature of cation 116a.

One might raise the question as to whether cis-cation 112 is actually produced in the solvolysis of 98, or whether the rearrangement is a concerted process producing cation 113 directly. If cation 112 is actually produced, one might ask whether it possesses any antiaromatic character which causes it to rearrange in contrast to cation 116.

The first of these questions was answered by the actual trapping of cation 112 under solvolytic conditions. When treated with sodium borohydride in aqueous diglyme, 98 gave an 11% yield of tricyclic hydrocarbon 115 along with 13% 2-norcarene, 116, 35% 99.

1,4-cycloheptadiene 117, and 1,3-cycloheptatriene, 99. The structures of hydrocarbons 115, 116, and 99 were based on comparison of infra-red spectra with authentic samples, while the structure of diene 117 was based on nmr spectroscopy. Diene 117 showed an olefinic 4H multiplet at $\tau$ 4.20, a doubly allylic 2H multiplet at $\tau$ 7.10, and an allylic 4H multiplet at $\tau$ 7.72.

This trapping supports the existence of an intermediate with substantial positive charge on the carbon atom that was originally the bridgehead carbon of tosylate 98. Such an intermediate is cation 112. The inability of the less nucleophilic acetic acid to trap cation 112 implies a rapid rearrangement with such a process precluding the existence of 112. This evidence, along with least motion considerations, argues against concerted rearrangement of tosylate 98 to cation 113 and strongly implicates cation 112 as a discrete intermediate with a lifetime long enough to be trapped. These results, along with the inability of cation 112 to be trapped when cation 114 is generated directly, render very improbable a single delocalized ion to account for the observed products. In addition, the rate of solvolysis of tosylate 98 is predictable on the basis of the inductive effect of a $\beta$-cyclopropyl group and without considering antiaromatic destabilization of the initially formed cation 112 and argues against any such antiaromatic character in this cation.

Cation 112 probably owes its ease of rearrangement to steric reasons. Interaction between geminal methylene hydrogens would increase the rate of rearrangement relative to the trans-analog 116a.
Support for this postulate is seen in the stereochemistry of the addition of methylene to cyclopentadiene in which the trans-diadduct predominates over the cis-adduct.

In view of the lack of evidence for antiaromatic character in cation 112, cations 113 and 114, which are also potentially bishomointeriomatic, should be of interest. In an attempt to prepare these two cations directly, the corresponding p-nitrobenzoates, 118, 119, and 120 were prepared and solvolyzed in 70% aqueous acetone buffered with triethylamine. Solvolysis of all three p-nitrobenzoates gave
cycloheptatriene as the major product along with cycloheptadienol 101 as the major alcohol with norcarenol 100 being the minor alcohol product. The similarity of the products produced with those produced in the solvolysis of tosylate 98 implies that a similar set of cationic intermediates are involved. The alcohol ratio changes somewhat due in part to their slow conversion to cycloheptatriene under the reaction conditions with norcarenol 100 being converted to cycloheptatriene at a faster rate than cycloheptadienol 100. However, the alcohol product ratios are in line with incomplete equilibration of the cationic intermediates with p-nitrobenzoates 118 and 119 producing more of alcohol 100 than p-nitrobenzoate 120. The equilibration of the intermediate cations 112, 113 and 114 is very probable in view of the sodium borohydride trapping experiments previously described which also implies incomplete cation equilibration. It should also
be noted that the bridged analogues of cations $112$, $113$, and $114$
capture solvent in accord with discrete ions which do not completely
equilibrates.$^{59}$

A kinetic study was done to evaluate the effect of the homo-
allylic double bond on the initially formed cations in the solvoly-
sis of p-nitrobenzoates $118$, $119$, and $120$. The results of this
study are given in Table II. Unsaturated p-nitrobenzoates $118$ and
$119$ solvolyzed respectively $17$ and $13$ times slower than the satu-
ted analogs $121$ and $122$, consistent with a small inductive destabil-
ilizing effect of the homoallylic double bond.$^{67}$ This implies that
the primary stabilization in cation $113$ is due to the cyclopropyl
group, with no evidence for antiaromatic character in this cation.

Diene p-nitrobenzoate $120$ solvolyzed $1.56$ times slower than the
monoene analog $123$. The rate retarding effect of the homoallylic
double bond therefore appears to be less than in either $118$ or $119$.
This might be due to some homoallylic participation in the formation

$^{67.}$ The inductive effect of a double bond has been used to explain
effects similar in magnitude. See M. Hanack and W. Keberle,
Chem. Ber., 96, 2937 (1963); M. Hanack and H.J. Schneider,
Angew. Chem. Int. Ed. Engl., 6, 674 (1967); P.D. Bartlett, W.D.
Closson, and T.J. Cogdell, J. Amer. Chem. Soc., 87, 1508 (1965);
C.H. DePuy, I.A. Ogawa, and J.C. McDaniel, ibid., 83, 1668
(1961); E.N. Peters and H.C. Brown, ibid., 94, 5899 (1972); C.F.
Wilcox, Jr., and H.D. Banks, ibid., 94, 8231 (1972); P.G. Gass-
man, J. Seter and F.J. Williams, ibid., 93, 1673 (1971); W.D.
Closson, J.L. Jernow, and D. Gray, Tet. Letters, 1141 (1970);
J.B. Lambert, H.G. Smith, Jr., and A.J. Javonovich, ibid., 25,
Table II. Rates of Solvolysis in 70% Aqueous Acetone

<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp. (± 0.03°C)</th>
<th>( k (\text{sec}^{-1}) )</th>
<th>( \Delta H^\ddagger ) ( \text{(kcal/mol)} )</th>
<th>( \Delta S^\ddagger ) ( \text{(eu)} )</th>
<th>( k_{rel} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Structure 1]</td>
<td>100.0</td>
<td>((3.50\pm0.03) \times 10^{-5})</td>
<td>24.8±0.3</td>
<td>-12.9±0.8</td>
<td>3.90</td>
</tr>
<tr>
<td>[Structure 2]</td>
<td>120.0</td>
<td>((2.04\pm0.02) \times 10^{-4})</td>
<td>26.7±0.2</td>
<td>-12.5±0.5</td>
<td>4.34</td>
</tr>
<tr>
<td>[Structure 3]</td>
<td>80.0</td>
<td>((9.31\pm0.02) \times 10^{-5})</td>
<td>23.8±0.0</td>
<td>-9.9±0.1</td>
<td>67.8</td>
</tr>
<tr>
<td>[Structure 4]</td>
<td>100.0</td>
<td>((6.08\pm0.01) \times 10^{-4})</td>
<td>26.8±0.2</td>
<td>-12.5±0.5</td>
<td></td>
</tr>
<tr>
<td>Compound</td>
<td>Temp. (± 0.03°C)</td>
<td>$k$(sec)$^{-1}$</td>
<td>$\Delta H^\ddagger$ (kcal/mol)</td>
<td>$\Delta S^\ddagger$ (eu)</td>
<td>$k_{rel}$</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------</td>
<td>-----------------</td>
<td>-------------------------------</td>
<td>------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>[Structure Image]</td>
<td>80.0</td>
<td>$(7.32\pm0.02) \times 10^{-5}$</td>
<td>24.6±0.1</td>
<td>-8.1±0.4</td>
<td>56.6</td>
</tr>
<tr>
<td>[Structure Image]</td>
<td>100.0</td>
<td>$(5.08\pm0.04) \times 10^{-4}$</td>
<td>5.49±0.03</td>
<td>-13.5±0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>[Structure Image]</td>
<td>120.0</td>
<td>$(2.81\pm0.04) \times 10^{-4}$</td>
<td>8.97 x 10$^{-6}$</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[Structure Image]</td>
<td>140.0</td>
<td>$(1.02\pm0.01) \times 10^{-4}$</td>
<td>1.40 x 10$^{-5}$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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a) extrapolated value
of cation 114. However, the major stabilization is probably allylic in nature and one sees no evidence for homoantiaromatic character in cation 114.

These results contrast with those of Winstein, Sakai, and Diaz in the solvolysis of p-nitrobenzoates 124, 125, and 126.

\[
\begin{align*}
\text{rel rate} & \quad 0.0041 & 0.0043 & 1 \\
124 & \quad \text{OPNB} & \quad \text{OPNB} & \quad \text{OPNB} \\
125 & \quad \text{H} & \quad \text{OPNB} & \\
126 & \quad \text{H} & \quad \text{OPNB} & 
\end{align*}
\]

The presence of the second double bond in p-nitrobenzoates 124 and 125 caused these esters to be only 0.0041 and 0.0043 times as reactive as the monoene analog 126. This rate retarding effect was considered too large to be an inductive effect of the second double bond and is "in line with the antihomoaromatic designation for the first intermediate cation formed in the solvolysis of the diene p-nitrobenzoates".

In view of the contrasting results in the formation of potentially homoantiaromatic cations 112, 113, and 114, it would be of value to determine the true polar effect of a double bond in the absence of homoallylic participation. The term polar effect is used to imply that this effect might be very dependent on the alignment of the double bond in a structurally rigid system, i.e., the effect might
be a field effect.

Accordingly, tosylates 130 and 131 were prepared. Using the procedure of Schollkopf, 1,4-cyclohexadiene was converted to a mixture of chloroethyl ethers, 127, by treatment with dichloromethyl chloroethyl ether and methyl lithium containing methyl iodide. The epimer ratio was 2:1 with the endo-epimer predominating. Treatment of chloroethyl ethers 127 with n-butyl lithium gave a mixture of endo and exo-alcohols 128 and 129 which are separable by gas chromatography. Tosylate 130 was prepared in the usual manner and solvolyzed

---


### Table III. Solvolysis Rates in Acetic Acid Containing 0.1M Sodium Acetate.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp. (±0.03°C)</th>
<th>k (sec⁻¹)</th>
<th>ΔH⁺ (kcal)</th>
<th>ΔS⁺ (eu)</th>
<th>k_rel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TsO</td>
<td>150.0</td>
<td>(2.40±0.03) x 10⁻⁵</td>
<td>30.9±0.4</td>
<td>-7.2±0.9</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>170.0</td>
<td>(1.31±0.01) x 10⁻⁴</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>130</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TsO</td>
<td>100</td>
<td>7.39 x 10⁻⁴</td>
<td></td>
<td></td>
<td>1.65 x 10⁻³</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>3.96 x 10⁻⁵⁸</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) Ref. 70.

in buffered acetic acid. Results of kinetic studies are given in Table III.

Tosylate 130 was very unreactive when compared to the saturated analog 132.⁷⁰ This reactivity is in line with the decreased reactivity seen in the silver assisted solvolysis of 7,7-dibromonorcar-3-ene, 102. One may attribute this to the polar effect of the double bond in this system which has a relatively rigid transition state in

---

which the double bond is not capable of homoallylic participation. The polar effect causes a rate deceleration of $1.65 \times 10^3$. Homo-
antiaromatic character in the transition state, 133, can be ruled
out since orbital alignment in this transition state is very un-
favorable for any 1-3 interactions. Hence, the polar effect of a
double bond in a rigid system can be quite large. If effects simi-
lar in magnitude are operative in the solvolysis of diene p-nitro-
benzoates 124 and 125, then there is no need to invoke homoanti-
aromaticity to explain their decreased reactivity relative to monoene
p-nitrobenzoate 126.

Due to the high temperatures required for the solvolysis of tosylate
130, product studies were done using the triflate derivative\textsuperscript{71} of al-
cohol 128 prepared by reaction with trifluoromethanesulfonic anhy-
dride in pyridine. Solvolysis at $80^\circ$ in buffered acetic acid followed
by lithium aluminum hydride reduction of the acetate products, gave
the same products, 99, 100, and 101, produced in the solvolysis of

tosylate 98 and p-nitrobenzoates 118, 119, and 120. As expected, these correspond to the symmetry allowed concerted ring opening process of triflate 132 to give allylic cation 114 followed by rearrangement to cyclopropylcarbinyl cation 115.

The finite rate of this rearrangement process is borne out by the reaction of triflate 134 with sodium borohydride in aqueous diglyme. The only products isolated were cycloheptatriene and cycloheptadiene, consistent with the proposed equilibration scheme which involves interception of cation 114 before equilibration to 113.

The lack of any demonstrable antiaromatic character in the intermediates formed in the solvolyses of tosylate 98, p-nitrobenzoates 118, 119, 120, 121, or 125 implies a fundamental difference between antiaromaticity and homoantiaromaticity. This difference
might best be seen by considering possible energy-reaction coordinate
diagrams representing the formation of aromatic, antiaromatic, homo-
antiaromatic and homoaromatic systems.

In the aromatic system, Figure 1, the localized ion, $\text{a}_1$, is not
an energy minimum. One can bypass the higher energy, localized sys-
tem, $\text{b}_1$. Hence, a transition state will show aromatic character. In
the antiaromatic system, Figure II, the localized ion, $\text{c}_1$, is not an
energy minimum, although its energy should be lower than the anti-
aromatic ion, $\text{d}_1$. The difference between antiaromaticity and homo-
antiaromaticity lies in the nature of the localized intermediates.
In the homoantiaromatic system, Figure III, the 'localized' ions
$\text{112}_1$, $\text{113}_1$, and $\text{114}_1$, lie at an energy minimum. One may therefore bypass
the homoantiaromatic ion $\text{e}_1$. This is in contrast to the antiaromatic
system in which the antiaromatic cation $\text{d}_1$ cannot be bypassed since
the localized ion $g$ possesses no finite lifetime, being simply a point along a reaction coordinate. This may be the difference between destabilizing $1,2$ and destabilizing $1,3$ interactions. In the homoaromatic system, Figure IV, similar energetic considerations explain the existence of homoaromatic stabilization $^{14}$ in contrast to the lack of existence of homoanticaromatic destabilization. Homoaromatic ion $f$ will be formed eventually, whether directly or indirectly through localized ion $g$. Localized ion $g$ may or may not represent an energy minimum depending on whether the opening of the cyclopropane ring (retro $1,3$ interaction) requires an activation energy. The aromatic cation $f$ will eventually be produced regardless of the mechanism of its formation.
Figure I. Formation of an aromatic cation

Figure II. Formation of an antiaromatic cation
Figure III. Formation of a homoantiaromatic cation

Figure IV. Formation of a homocaromatic cation
CHAPTER IV

SOLVOLYSIS OF DERIVATIVES OF exo-TRICYCLO[3.1.1.0^2,6]HEPTAN-6-OL

exo-Alcohol 27 was converted to the corresponding exo-p-nitrobenzoate 135 by treatment with p-nitrobenzoyl chloride in pyridine. Solvolytic product studies were carried out in 70% aqueous acetone buffered with triethyl amine. The major alcohol product, in 61% yield, was tricyclic alcohol, 136, identified by spectral comparison with an authentic sample.\(^72\) Rearranged p-nitrobenzoate 137 amounted to 28% of the product. Lithium aluminum hydride reduction of p-nitrobenzoate 137 gave 136.

\[
\begin{align*}
\text{H} & \quad \text{OPNB} \\
\text{70% aqueous acetone} & \quad \downarrow \quad \text{H} \\
\text{135} & \quad \rightarrow \quad \text{H} \\
& \quad \text{OH} \\
& \quad \text{OPNB} \\
\text{136} & \quad + \quad \text{H} \\
\text{137} & \\
\end{align*}
\]

A kinetic study was carried out to determine the anchimeric assistance attributable to the cyclopropyl group in p-nitrobenzoate 135. The results are given in Table IV. exo-p-Nitrobenzoate 135

Table IV. Rates of Solvolysis in 70% Aqueous Acetone

<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp. (±0.03°C)</th>
<th>k (sec⁻¹)</th>
<th>ΔH⁺ (kcal/mole)</th>
<th>ΔS⁺ (eu)</th>
<th>k_{rel}</th>
</tr>
</thead>
<tbody>
<tr>
<td>OPNB</td>
<td>105.0</td>
<td>(1.67±0.02) x 10⁻⁵</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>120.0</td>
<td>(7.50±0.02) x 10⁻⁵</td>
<td>27.9±0.2</td>
<td>-7.2±0.5</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>135.0</td>
<td>(2.75±0.01) x 10⁻⁴</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>90.2</td>
<td>3.54 x 10⁻⁸</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.0</td>
<td>6.31 x 10⁻¹⁰</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H^OPNB</td>
<td>150.0</td>
<td>(8.67±0.01) x 10⁻⁶</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>160.2</td>
<td>(1.83±0.01) x 10⁻⁵</td>
<td>26.4±0.1</td>
<td>-19.9±0.3</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>170.0</td>
<td>(3.75±0.01) x 10⁻⁵</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.0</td>
<td>1.15 x 10⁻¹¹</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNBO</td>
<td>90.2</td>
<td>1.35 x 10⁻⁴ᵃ</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) Ref. 31. (b) Extrapolated value.
is only 38 times less reactive than the corresponding tricyclo-
[3.2.1.0^{2,4}]octyl system 132, despite the smaller bond angle at the
developing cationic center. Since p-nitrobenzoate 132 undergoes sol-
volysis with a rate enhancement estimated at $10^{12}$ in 70% aqueous
acetone, the rate of solvolysis of p-nitrobenzoate 135 must also be
greatly accelerated by the anti-cyclopropyl group. This rate accele-
ration, along with the rearranged products produced in the solvolysis,
implies delocalized cation 140 is the initially formed cationic inter-
mediate. Reaction with water from the endo-side of delocalized ion

\[ H \text{OPNB} \rightarrow ^+ \]

135 \quad 140

\[ H \text{OPNB} + H \text{OPNB OH} \rightleftharpoons + \]

137 \quad 136 \quad 140, or internal return of p-nitrobenzoate ion gives the observed
solvolysis products.

Lustgarten\textsuperscript{72} has generated cation 140 independently from the
corresponding tosylate of alcohol 136 and has obtained evidence that
it undergoes a degenerate rearrangement under the solvolysis conditions. The tosylate labeled in the methylene position or the carbinyl position underwent solvolysis with extensive scrambling of the labeled positions.

The task of estimating the rate enhancement in \( \text{135} \) attributable to cyclopropyl participation becomes difficult since no good model exists for estimating the unassisted rate of solvolysis of \( p \)-nitrobenzoate \( \text{135} \). Therefore the rate of acetolysis of tosylate \( \text{142} \) was estimated by determining the rate difference between exo-\( p \)-nitrobenzoate \( \text{135} \) and endo-\( p \)-nitrobenzoate \( \text{138} \). As can be seen in Table
IV, at 25°C, exo-p-nitrobenzoate 135 is 55 times as reactive as the endo-epimer 138. By assuming this reactivity difference will be the same for the corresponding tosylates, one may estimate a rate of acetolysis of tosylate 142 by multiplying this factor by the rate of acetolysis of tosylate 28 at 25°C. The estimated rate is given in Table V.

Bicyclic tosylate 103 does not represent a suitable model for predicting the unassisted rate of solvolysis of exo-tosylate 142. The solvolysis of 103 occurs 3 x 10³ faster than 7-norbornyl tosylate, 2, even though the smaller bond angle at the incipient cationic center in 103 requires a slower unassisted solvolysis rate. Hence, 103 solvolyzes with substantial anchimeric assistance.

Since no good model is readily available for predicting the unassisted solvolysis rate of tosylate 142, brosylate 144 was chosen in an attempt to evaluate the amount of anchimeric assistance in the solvolysis of tosylate 142. The solvolysis of brosylate 144 does

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Table V. Rates of Acetolysis at 25°C of Tosylates

<table>
<thead>
<tr>
<th>Compound</th>
<th>$k_{25°C}$ (sec$^{-1}$)</th>
<th>$k_{rel}$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Compound 1" /></td>
<td>$1.25 \times 10^{-2}$</td>
<td>$5.6 \times 10^8$</td>
</tr>
<tr>
<td><img src="image2.png" alt="Compound 2" /></td>
<td>$2.24 \times 10^{-11}$a</td>
<td>1.0</td>
</tr>
<tr>
<td><img src="image3.png" alt="Compound 3" /></td>
<td>$2.4 \times 10^{-15}$b</td>
<td>1.1 $\times 10^{-4}$</td>
</tr>
<tr>
<td><img src="image4.png" alt="Compound 4" /></td>
<td>$6.4 \times 10^{-15}$c</td>
<td>2.9 $\times 10^{-4}$</td>
</tr>
</tbody>
</table>

a) ref. 58.  b) ref. 73.  c) ref. 9.
not involve any participation of the cyclopropane ring other than a small ring retarding inductive effect which should be similar in magnitude to the inductive effect in tosylate $\text{142}$. The C$_1$-C$_6$-C$_5$ bond angle$^{74}$ in brosylate $\text{144}$ is $97^\circ$ while the corresponding C$_1$-C$_7$-C$_5$ bond angle in p-bromobenzoate $\text{145}$ $^{75}$ is $82^\circ$. However, tosylate $\text{142}$, with a bond angle approximately $15^\circ$ smaller at the developing cationic center, solvolyzes $5.2 \times 10^{12}$ faster than tosylate $\text{143}$. Hence, the rate acceleration due to cyclopropyl participation in exo-tosylate $\text{142}$ must be much greater than $5.2 \times 10^{12}$.

To determine the true magnitude of the rate enhancement, one must know the rate retarding effect of contracting an incipient cationic center approximately $15^\circ$. This effect may be roughly estimated

\[
\begin{array}{c}
\text{H} & \text{OTs} \\
\text{146} & \text{109.5}^\circ \\
\end{array}
\]

\[
\begin{array}{c}
\text{H} & \text{OTs} \\
\text{2} & \text{95}^\circ \\
\end{array}
\]

\[
\text{rel rate} \quad 10^{5.8} \quad 1.0
\]


by considering a similar bond angle contraction in secondary tosylates \( 1^{-67} \) and 2. The effect of a \( 14^0 \) bond angle contraction at the reaction cite is a rate decelerating effect of \( 10^{5.8} \). If similar angle contraction effects are operative in the solvolyses of tosylates \( 1^{42} \) and \( 1^{43} \), then the rate acceleration can be determined by multiplying this effect by the rate of \( 1^{42} \) relative to \( 1^{43} \).

This gives a crudely estimated rate enhancement in \( \text{exo-tosylate} \) \( 1^{42} \) of \( 10^{18} \). This compares to the \( 10^{12} \) value in 70% aqueous acetone obtained for the less strained tricyclo[3.2.1.0\(^2\)\(^7\)]octyl system, 132. Hence, the degree of participation by a cyclopropyl group is largely a function of strain at the incipient cationic center. It is largely dependent on geometry with very subtle factors being able to influence the amount of anchimeric assistance. Coates 77 has recently prepared

\[
\begin{align*}
\text{H} & \quad \text{OTs} \\
\text{147} & \\
\text{rel rate} & \quad 1.0 \\
\text{H} & \quad \text{OTs} \\
\text{142} & \\
\text{rel rate} & \quad 6.1 \times 10^2
\end{align*}
\]


a bridged analog of $\frac{14}{2}$. The rate acceleration is less than in the parent tosylate $\frac{14}{2}$. In the bridged system, $\frac{14}{7}$, the bridging methylene group appears to constrain the participating cyclopropyl group thus destabilizing the resulting trishomocyclopropenyl cation intermediate.
PART II

REDUCTIVE CLEAVAGE OF SUCCINIC ESTERS UNDER ACYLOIN CONDITIONS

CHAPTER I

a) Historical

Strained polycyclic molecules have intrigued chemists since Baeyer first introduced the concept of ring strain in 1885.¹ Of the methods used to introduce strain into polycyclic molecules, the acyloin condensation has been of recent importance.²³ A brief survey of this reaction would therefore be of value before a discussion of its applications to the synthesis of strained polycyclic molecules.

The acyloin condensation⁴ involves the condensation of two ester molecules with the eventual formation of an α-hydroxy ketone (acyloin) via an intermediate enediolate. Prior to 1964, the conditions

\[
2 \text{RCOO}_2\text{R'} + 4 \text{Na} \rightarrow \text{R}-\text{C} = \text{C}-\text{R} \rightarrow \text{R}-\text{CH} = \text{C}-\text{R}
\]

---

4. For a review of the acyloin condensation prior to 1948, see: S.M. McElvain, Organic Reactions, 4, 256 (1948).
usually employed involved the use of sodium in liquid ammonia (homogeneous) or sodium in some inert solvent such as ether, xylene or toluene (heterogeneous) as the condensing reagent. A study of the reaction of a number of esters of aliphatic and aromatic acids$^5$ led to the suggestion that mechanistically, the reaction proceeded via coupling of two diradical anions followed by loss of alkoxide and a subsequent two electron reduction of the resultant diketone. Production of the enediolate followed by ketonization would produce the $\alpha$-hydroxyketone.

These conclusions from the homogeneous sodium-liquid ammonia medium do not require that the same mechanism be operative in the very dissimilar heterogeneous reaction in inert hydrocarbon solvents

in which one of the reactants and the products are insoluble. However careful product analysis, in two cases, has indicated that a radical reaction is also probably involved in the heterogeneous (hydrocarbon solvent) acyloin condensation. The hydrocarbon products obtained from the reaction of ester \( \overset{1}{\text{1}} \) with sodium in toluene are best explained in terms of the loss of sodium ethoxide and carbon monoxide from radical anion \( \overset{2}{\text{2}} \), and subsequent dimerization of radical \( \overset{3}{\text{3}} \). In an attempt to demonstrate a similar mechanistic pathway in a purely aliphatic system, ester \( \overset{5}{\text{5}} \) was subjected to the heterogeneous acyloin conditions. Ester \( \overset{5}{\text{5}} \) reacted in a manner analogous to ester \( \overset{1}{\text{1}} \), losing 68% of the theoretical amount of carbon monoxide.

These experiments provide evidence that a radical mechanism is operative in the heterogeneous as well as in the homogeneous acyloin condensation. It should be noted, however, that detailed mechanistic studies on the acyloin condensation are still limited. Our understanding of the reaction remains inadequate and subject to a certain amount of speculation.

When the acyloin condensation is carried out on a diester, an intramolecular reaction may occur with resultant ring formation.⁸

---

⁸ For a review of the acyloin condensation as a cyclization method, see: K.T. Finley, Chem. Revs., 64, 573 (1964).
This intramolecular reaction has the potential for the introduction of ring strain. For the preparation of large rings\(^9\) \((n > 11)\), the intramolecular acyloin condensation is an excellent method, giving good yields when high dilution techniques are employed. It is the method of choice for the preparation of medium rings\(^{10}\) \((n = 8-10)\).

Five, six and seven membered rings can also be prepared in low to moderate yields using either homogeneous or heterogeneous conditions. In the case of these normal rings, the Dieckmann condensation can be a major competing reaction, lowering the yield of acyloin product.

Prior to 1967, there were only two published accounts of the production of a four-membered ring by the acyloin condensation. Treatment of cis-1,2-dicarboethoxy cyclohexane, \(2\), under a variety

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \text{Na} \\
\text{CO}_2\text{Et} & \quad \text{cyclo}
\end{align*}
\]

\[10\]


\[10. \quad \text{V. Prelog, L. Frenkiel, M. Kobelt, and P. Barman, ibid., 30, 1741 (1947).}\]
of conditions\textsuperscript{11} gave a maximum yield of 12\% of the cyclized product 10. Bloomfield and Irelan\textsuperscript{12} could obtain moderate to good yields of cyclized product treatment of diester 11 with the reactive sodium-potassium alloy in benzene while sodium in toluene failed to effect cyclization. However, the formation of four membered rings via the acyloin condensation remained far from a general reaction.

![Chemical structure](image)

Perhaps the most significant advance in the area of acyloin condensations since its discovery was the work of Schrapler and Ruhlmann.\textsuperscript{13,14} They demonstrated that the introduction of chlorotrimethylsilane into the heterogeneous reaction allowed the trapping of the intermediate enediolate as a bistrimethylsilyl ether. Chloro-

\[
\begin{align*}
2 R-C-OR' & \overset{4 \text{ Na}}{\longrightarrow} R-CO_2^- + 2 R'O^- \\
& \overset{\text{ClSi(CH}_3)_3}{\longrightarrow} R-COSi(CH}_3)_3 + 2 R'Osisi(CH}_3)_3
\end{align*}
\]

\textsuperscript{14} U. Schrapler and K. Ruhlmann, \textit{ibid.}, \textbf{97}, 1383 (1964).
trimethylsilyl was also an effective scavenger for the alkoxide produced in the reaction. Excellent yields of bistrimethylsilyl ethers could be obtained using both monesters\textsuperscript{13} and diesters.\textsuperscript{14} The trimethylsilyl ethers could also be easily hydrolyzed to the acyloins.

Bloomfield\textsuperscript{15} demonstrated the importance of chlorotrimethylsilane as a base scavenger in the acyloin reaction in which Claisen and Diekmann condensations are major competing reactions or the acyloin condensation is slow. Diesters 13 and 15 could be successfully cyclized in 87\% and 75\% yields, respectively, using chlorotrimethylsilane as a base scavenger. In the absence of chlorotrimethylsilane,

13 gave only Diekmann products\textsuperscript{16,17} while 15 gave a mixture of Diekmann and acyloin products.

The use of chlorotrimethyllumsiline in the acyloin condensation permits the isolation of excellent yields of cyclobutene bistri­methyllumsilyl ethers by the cyclization of 1,2-diester.s\textsuperscript{3} The yield of cyclized product in the acyloin condensation of diester 2 is increased from 12\% to 89\% by use of chlorotrimethyllumsiline as a base scavenger. The unsubstituted cyclobutene system can be generated in 76\% yield by cyclization of diethyl succinate,\textsuperscript{18}.

\begin{align*}
\begin{array}{c}
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Et}
\end{array} \\
\text{Na/toluene} \\
\text{ClSi(\text{CH}_3)_3}
\end{array}
\rightarrow
\begin{array}{c}
\begin{array}{c}
\text{OSi(\text{CH}_3)_3} \\
\text{OSi(\text{CH}_3)_3}
\end{array}
\end{array}
\end{align*}

\begin{align*}
\begin{array}{c}
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Et}
\end{array} \\
\text{Na/toluene} \\
\text{ClSi(\text{CH}_3)_3}
\end{array}
\rightarrow
\begin{array}{c}
\begin{array}{c}
\text{OSi(\text{CH}_3)_3} \\
\text{OSi(\text{CH}_3)_3}
\end{array}
\end{array}
\end{align*}


b) The Problem

Gassman, Seter and Williams\(^2\) have used the acyloin condensation as one of the key steps in the synthesis of the \textit{trans-bicyclo[5.1.0]-octyl} ring system.\(^{16}\) The acyloin condensation, therefore, appears to be capable of introducing a certain amount of strain into a molecule. In addition, once formed, the \(\alpha\)-hydroxy ketone allows for straightforward functionalization which can lead to ring contraction and the introduction of increased strain.

In view of Bloomfield's success\(^3\) in the formation of the \textit{bicyclo[4.2.0]octyl} system \textit{via} the acyloin condensation using chlorotrimethylsilane, this technique could be a key reaction in the construction of strained \([4.1.0]\) systems. Of particular interest would be the construction of the \textit{trans-bicyclo[4.1.0]heptyl} system, in view of the highly strained "twist bent" bond\(^{16}\) that would result in such a system. Such a system might be constructed by ring contraction of a \textit{trans-bicyclo[4.2.0]octyl} system, potentially avail-

able from the acyloin condensation. The formation of this "trans-norcarane" system was, therefore, approached in this manner.
CHAPTER II

a) Results and Discussion

The trans-bicyclo[4.1.0]heptyl system was approached by way of the acyloin condensation for construction of the precursor trans-bicyclo[4.2.0]octyl system. The use of trans-1,2-dicarbomethoxy-cyclohexane, \(23\), as a starting diester was decided against since the eventual trans-bicyclic systems are less stable than the cis-fused systems and are expected to be acid or base labile.\(^{19}\) Instead, the

\[
\begin{align*}
\text{CO}_2\text{CH}_3 & \quad \text{---} \quad \text{CO}_2\text{CH}_3 \\
\text{23} & \quad \rightarrow \\
\end{align*}
\]

Immediate synthetic target was the methyl substituted diester, 27, in which the eventual problem of trans- to cis-ring fusion epimerization would be avoided due to the presence of methyl groups.

\[
\text{trans-Diester } 27 \text{ was prepared as shown in Scheme I. Diels-Alder addition of citraconic anhydride to butadiene}^{20} \text{ gave the unsaturated anhydride, } 29. \text{ Catalytic hydrogenation followed by esterification gave cis-diester } 31. \text{ Diester } 31 \text{ could be alkylated by conversion to the enolate anion using triphenylmethyl sodium followed by treatment with methyl iodide. The alkylated diester consisted of a mixture of two stereoisomers as indicated by the wide melting point range (50°) of the diacids produced on saponification. Diesters } 27 \text{ and } 28 \text{ were inseparable by gas chromatography. However, reduction to the corresponding diols followed by methylation with sodium hydride and methyl iodide gave a mixture of methyl ethers separable by gas chromatography. The diester ratio analyzed in this manner was 55:45 with trans-diester } 27 \text{ being the predominant isomer.}

The separation of the two isomeric diacids, 32 and 34, presented considerable difficulty. The mixture of diacids could be con-

Scheme I

\[
\begin{align*}
\text{CH}_3\text{CH}_3 + \text{GO}_2\text{CH}_3 & \xrightarrow{130^\circ} \text{CH}_3\text{CH}_3 \text{GO}_2\text{CH}_3 \xrightarrow{\text{H}_2/\text{PtO}_2} \\
\hline
\text{CH}_3\text{CH}_3 \xrightarrow{\Phi_3\text{C}^-\text{Na}^+} \xrightarrow{\text{CH}_3\text{I}} \text{CH}_3\text{CH}_3 \xrightarrow{\text{KOH}} \\
\text{CH}_3\text{CH}_3 & \xrightarrow{\text{HCl}} \xrightarrow{210^\circ} \\
\hline
\text{CH}_3\text{CH}_3 \xrightarrow{1) \text{KOH}} \xrightarrow{2) \text{HCl}} \text{CH}_3\text{CH}_3 & \xrightarrow{210^\circ} \text{no reaction}
\end{align*}
\]
verted to a mixture of anhydrides by treatment with acetyl chloride. However, both the cis- and the trans-fused anhydrides were of comparable reactivity and were converted to diacids upon treatment with aqueous potassium carbonate. Both anhydrides proved to be unreactive with aqueous potassium bicarbonate.

Separation was finally achieved by thermal conversion of the cis-isomer to the anhydride 32 by heating the mixture of diacids to 210°. The trans-diacid 34 did not react under these conditions. Separation of the cis-anhydride 32 and the trans-diacid 34 was achieved by extraction with aqueous potassium bicarbonate solution. Diazomethane esterification of pure diacid 34 gave the desired trans-diester 27.

Pure cis-diester 28 could be prepared by basic hydrolysis of anhydride 32 followed by diazomethane esterification of the resultant diacid. Alternately, cis-diester 28 could be produced as shown in Scheme II. Addition of dimethyl maleic anhydride21 to butadiene22

followed by hydrogenation, hydrolysis, and esterification gave diester 28, identical in all respects to the cis-diester obtained in the methylation of diester 31.

Although this Diels-Alder approach to cis-diester 28 was successful, similar approaches to trans-diester 27 were unsuccessful.

trans-Diester 27 was subjected to heterogeneous acyloin conditions using sodium in refluxing toluene with added chlorotrimethylsilane. The product isolated was not the expected cyclobutene 36, but the cyclooctadiene 37. Diene 37 is the expected product from
the thermally allowed\textsuperscript{23} conrotatory ring opening of cyclobutene \textsuperscript{36,24}


\textsuperscript{24} Bloomfield has reported the thermal isomerization of a related cyclobutene derivative. See reference 3.
The structure of 27 was based on its nmr spectrum which shows a 6H singlet at τ 8.35, consistent with olefinic methyl groups and inconsistent with structure 26. In addition, the reaction product is thermally stable, being recovered unchanged after heating for one hour at 205°.

Since 27 is the apparent thermal isomerization product of the desired product 26, the condensation was rerun at 25° using sodium-potassium alloy in benzene with added chlorotrimethylsilane. Solvents were removed at room temperature. Again the only product obtained was the diene.

This observed thermal isomerization was unusual in view of the fact that cyclobutene 30, reported by Bloomfield, was stable at room temperature. Temperatures of greater than 100° were required to cause its rearrangement.

\[
\begin{align*}
\text{CH}_3 & \quad \text{OSi(CH}_3)_3 \\
\text{OSi(CH}_3)_3 & \quad \xrightarrow{100°} \text{CH}_3 \\
\text{OSi(CH}_3)_3 & \quad \text{OSi(CH}_3)_3
\end{align*}
\]

In terms of energy differences, if one conservatively estimates a half-life of one hour at 25° for the isomerization of 26 to 27, the difference in activation free energies for the rearrangements of 26 and 28 is a minimum of 6 kcal/mole. This corresponds to a least
at $10^4$ to $10^5$ rate difference at $25^\circ$.\textsuperscript{25}

Increased product stability can account for a small portion of this rate difference. The extra methyl substitution in diene \textsuperscript{37} should increase its stability by approximately 1.7 kcal/mole relative to triene \textsuperscript{39}. The remainder of the rate increase must be due to increased ground state strain in cyclobutene \textsuperscript{36} relative to cyclobutene \textsuperscript{38}. A portion of this increased strain is probably due to the extra axial methyl group in \textsuperscript{36}. This increases ground state energy by approximately 1.5 to 1.9 kcal/mole as determined by con-

![Diagram]

formational free energy differences.\textsuperscript{26} A closer look at \textsuperscript{38} reveals

\textsuperscript{25} This assumes a normal activation energy for the conversion of \textsuperscript{38} to \textsuperscript{39} of about 27 kcal/mole. Activation energies of this magnitude have been found for similar cyclobutene-butadiene rearrangements. See R. Criege and H.G. Reinhardt, Chem. Ber., \textsuperscript{101}, 102 (1968).

the absence of methyl group-axial hydrogen interactions, while four such interactions are present in \(26\). These ground state differences, along with product stability differences are consistent with the observed faster rate of isomerization of \(26\) and can account for at least part of the rate difference.

The structure of diene \(27\) was further demonstrated by its facile hydrolysis in methanol which gave a mixture of keto and enol tautomers \(4la\) and \(4lb\). In order to attain complete keto-enol, cis-trans-methyl isomer equilibrium, prolonged reflux with aqueous tetrahydrofuran-hydrochloric acid was required.

Diketone \(4lb\) could be prepared alternately as shown in Scheme III. Dimethylsuberic acid dimethyl ester, \(42\), prepared from the corresponding diacid, \(27\) was cyclized via the acyloin condensation and the resultant bistrimethylsilyl ether, \(43\), oxidized with bromine

---

according to the procedure of Wynberg. Upon distillation, the intermediate ditromide, 44 gave diketone 41b. When refluxed with acidic aqueous tetrahydrofuran, the same keto-enol, cis-trans-methyl isomer mixture was observed as that obtained by acid catalyzed equilibration of 41a. Once again, attainment of equilibrium was not the facile process that is observed in simple acyclic systems.

Scheme III

The behavior of cis-diester $28$ under heterogeneous acyloin conditions with added chlorotrimethylsilane was as expected. The bis-

$28$
trimethylsilyl ether, \( \text{CH}_{3}\text{Si} \), was stable thermally since the allowed thermal ring opening process is probably too slow to be observed at the temperature of refluxing toluene. Evidence for the structure of \( \text{CH}_{3}\text{Si} \) was based on nmr spectroscopy which showed a 6H singlet at \( \tau \) 9.00 consistent with the tertiary methyl groups of \( \text{CH}_{3}\text{Si} \).

In order to avoid the thermal ring opening which the desired bistrimethylsilyl ether \( \text{CH}_{3}\text{Si} \) underwent, the feasibility of carrying out the ring closure under homogeneous conditions in liquid ammonia at \(-78^\circ\) was investigated. cis-Diester \( \text{CH}_{3}\text{Si} \) reacted with sodium under these conditions to give a 70% yield of the cyclized \( \alpha \)-hydroxy ketone \( \text{CH}_{3}\text{Si} \), directly. The same \( \alpha \)-hydroxy ketone was produced by the methanolysis of silyl ether \( \text{CH}_{3}\text{Si} \).

\[
\text{CH}_3\text{CO}_2\text{CH}_3 \quad \text{Na}/\text{NH}_3 \quad \text{CH}_3\text{CO}_2\text{CH}_3
\]

\[
\text{47}
\]

In contrast to the reaction of cis-diester \( \text{CH}_{3}\text{Si} \) with sodium in liquid ammonia, trans-diester \( \text{CH}_{3}\text{Si} \) under the same conditions, gave only

\[
\text{CH}_3\text{CO}_2\text{CH}_3 \quad \text{Na}/\text{NH}_3 \quad \text{CH}_3\text{CO}_2\text{CH}_3
\]

\[
\text{42}
\]
dimethylsuberic acid dimethyl ester, \( \text{42} \), identical to a sample prepared by esterification of the known dimethylsuberic acid.\(^{27}\) The attempt to prepare a trans-bicyclo[4.1.0]heptyl ring system using the acyloan condensation as a key transformation, appears doomed to failure due to the unexpected ring opening of the bistrimethylsilyl ether \( \text{36} \) obtained under heterogeneous acyloan conditions, and the unusual reduction which occurred under homogeneous conditions.

The formation of \( \text{42} \) requires the reductive cleavage of a carbon-carbon \( \sigma \) bond of the succinic ester function. Although a few isolated samples of reductive cleavages occurring under acyloan conditions are known,\(^{29,30}\) the mechanistic aspects, the generality, solvent dependency and synthetic utility have not been investigated. Therefore, a more detailed investigation of this unusual reductive cleavage was undertaken.

b) Mechanistic Aspects

When either cis-1,2-dicarbomethoxy cyclopropane, \( \text{48} \), or trans-

\[
\begin{align*}
\text{ cis-1,2-dicarbomethoxy cyclopropane (48)} & \xrightarrow{\text{Na, NH}_3} \text{ trans-1,2-dicarbomethoxy cyclopropane (50)} \\
\text{trans-1,2-dicarbomethoxy cyclopropane (48)} & \xrightarrow{\text{Na, NH}_3} \text{ cis-1,2-dicarbomethoxy cyclopropane (50)} \\
\end{align*}
\]

\[\text{48} \quad \text{49} \]

\[\text{50} \]

---

1,2-dicarbomethoxy cyclopropane, \( \text{I} \), was treated with sodium in liquid ammonia at \(-78^\circ\), dimethyl glutarate was produced in 25\% and 22\% yields, respectively. Apparently the same type of reductive cleavage reaction that produced diester \( \text{I} \) was occurring. Mechanistically, the cleavage appears to proceed via a two electron transfer to produce the diradical dianion commonly postulated as an intermediate in the acyloin condensation. Cleavage of diradical dianion \( \text{II} \) would result in the formation of bis-alkoxy enolate \( \text{III} \). Protonation of such an enolate anion would produce the reductively cleaved diester.

\[
\begin{align*}
\text{CO}_2\text{CH}_3 & \quad \text{CO}_2\text{CH}_3 \\
\text{CO}_2\text{CH}_3 & \quad \text{CO}_2\text{CH}_3 \\
\text{ClSi(\text{CH}_3)}_3 & \\
\text{H}_2\text{O} & \\
\text{CH}_3\text{OH} & \\
\text{OSi(\text{CH}_3)}_3 & \\
\text{OSi(\text{CH}_3)}_3 & \\
\text{CO}_2\text{CH}_3 & \\
\text{CO}_2\text{CH}_3 & \\
\end{align*}
\]

As evidence for such a mechanism, bis-alkoxy enolate \( \text{III} \) could be trapped under heterogeneous conditions with chlorotrimethylsilane with the production of bis-ketene ketal \( \text{IV} \). (Diester \( \text{I} \) was chosen in an attempt to trap such an intermediate since ring closure under
heterogeneous conditions would be a difficult process). This strongly implicates dienolate 52 as an intermediate in the reductive cleavage.

The structure of bis-ketene ketal 53 arises from exact high resolution mass spectrometry, its facile hydrolysis in methanol to dimethyl glutarate, and its independent synthesis from dimethyl glutarate. Stepwise silation of the enolate produced from dimethyl glutarate and lithium hexamethyilsilazide31 in tetrahydrofuran at -78° produced 53, albeit in only 4.5% yield.

c) Solvent Dependency and Generality

In order to test the generality of the reductive cleavage of 1,2-diesters with sodium in liquid ammonia, diester 55 was treated under these conditions at -78°. cis-Cyclopent-2-ene-1,3-diacetic acid dimethyl ester, 56, was produced in 72% yield. The same diester was produced in 33% yield by treatment of trans-diester 57 under the same conditions. Table I summarized the yields of reductive cleavage products in this and in other cases.

Diester 56 could be saponified to give cis-cyclopent-2-ene.
Table I. Reaction of 1,2-Diesters with Sodium

<table>
<thead>
<tr>
<th>Starting Ester</th>
<th>Product</th>
<th>Conditions</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Structure 1" /></td>
<td><img src="image2" alt="Structure 2" /></td>
<td>Na/liq NH₃</td>
<td>54%</td>
</tr>
<tr>
<td><img src="image3" alt="Structure 3" /></td>
<td><img src="image4" alt="Structure 4" /></td>
<td>Na/liq NH₃</td>
<td>25%</td>
</tr>
<tr>
<td><img src="image5" alt="Structure 5" /></td>
<td><img src="image6" alt="Structure 6" /></td>
<td>Na/liq NH₃</td>
<td>22%</td>
</tr>
<tr>
<td><img src="image7" alt="Structure 7" /></td>
<td><img src="image8" alt="Structure 8" /></td>
<td>Na/liq NH₃</td>
<td>72%</td>
</tr>
</tbody>
</table>
Table I. (Cont)

<table>
<thead>
<tr>
<th>Starting Ester</th>
<th>Product</th>
<th>Conditions</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="51" /></td>
<td><img src="image" alt="56" /></td>
<td>Na/liq NH₃</td>
<td>33%</td>
</tr>
<tr>
<td><img src="image" alt="52" /></td>
<td><img src="image" alt="60" /></td>
<td>Na/liq NH₃</td>
<td>52%</td>
</tr>
<tr>
<td><img src="image" alt="61" /></td>
<td><img src="image" alt="60" /></td>
<td>Na/liq NH₃</td>
<td>20%</td>
</tr>
<tr>
<td><img src="image" alt="62" /></td>
<td><img src="image" alt="60" /></td>
<td>Na/toluene ClSi(CH₃)₃</td>
<td>38%</td>
</tr>
</tbody>
</table>
Table I. (Cont.)

<table>
<thead>
<tr>
<th>Starting Ester</th>
<th>Product</th>
<th>Conditions</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO_2CH_3</td>
<td>Na/toluene ClSi(CH_3)_3</td>
<td>low (difficult to purify)</td>
<td></td>
</tr>
<tr>
<td>CH_3 CO_2CH_3</td>
<td>Na/toluene ClSi(CH_3)_3</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>CH_3 CO_2CH_3</td>
<td>Na/toluene ClSi(CH_3)_3</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>CH_3 CO_2CH_3</td>
<td>Na/toluene ClSi(CH_3)_3</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>Starting Ester</td>
<td>Product</td>
<td>Conditions</td>
<td>Yield</td>
</tr>
<tr>
<td>---------------</td>
<td>---------</td>
<td>----------------</td>
<td>-------</td>
</tr>
<tr>
<td><img src="image1.png" alt="Structure" /></td>
<td><img src="image2.png" alt="Structure" /></td>
<td>Na/liq NH₃</td>
<td>70%</td>
</tr>
<tr>
<td><img src="image3.png" alt="Structure" /></td>
<td><img src="image4.png" alt="Structure" /></td>
<td>Na/toluene ClSi(CH₃)₃</td>
<td>86%</td>
</tr>
</tbody>
</table>
1,3-diacetic acid, \(^{58}\). Catalytic hydrogenation gave \textit{cis-}

cyclopentane-1,3-diacetic acid dimethyl ester, which could also be
produced by the reductive cleavage of saturated diesters \(^{59}\) and \(^{61}\).
Saponification of \(^{60}\) gave the known cyclopentane-1,3-diacetic acid,
\(^{62}\). \(^{32}\) This reductive cleavage reaction represents the best method
for the preparation of \(^{62}\), previously available in low yield only
through Arndt-Eistert homologation of 1,3-cyclopentane dicarboxylic
acid.

The widely divergent behavior of \textit{trans-}diester \(^{27}\) as reaction
conditions are changed from heterogeneous to homogeneous suggests
that the reaction is extremely solvent dependent. To test this
premise, \textit{cis-}diester \(^{55}\), which cleaves in 72\% yield in liquid ammonia,
was subjected to sodium in toluene with added chlorotrimethylsilyl
ether. The only product isolated in 86\% yield was the cyclobutene
bis-tri-

methyldisilyl ether \(^{63}\). \(^{33}\) The reductive cleavage in liquid ammonia

\[ \begin{align*}
\text{55} & \xrightarrow{\text{Na/toluene}} \text{ClSi(CH}_3\text{)}_3 \\
\text{62} & \xrightarrow{\text{ClSi(CH}_3\text{)}_3} 
\end{align*} \]


\(^{33}\) Miller and Dolce have prepared \(^{63}\) although no experimental
details were given. See R.D. Miller and D. Dolce, \textit{Tetrahedron
therefore appears to be a function of solvent and not ring strain in the potential cyclobutene formed by ring closure. This solvent dependency will be discussed in more detail.

d) Stereochemical Requirements

The dihedral angle between carbomethoxy groups in the 1,2-diester also appears to be critical in determining the amount of cleavage product formed. A 0° or 180° angle appears preferable. In the rigid norbornyl system, the yield of cleavage product decreases substantially as the angle deviates from 0° in the cis-diesters 55 and 59, to approximately 120° in the trans-diesters 57 and 61.

![Dihedral Angles](image)

Although a 0° dihedral angle between carbomethoxy groups cannot be attained in diester 27, a trans-diaxial configuration is quite feasible due to electrostatic interactions. In this conformation, cleavage can occur as shown in either 63a or 64 depending on the configuration of the carbonyl group. In both processes, the bond which cleaves does so in a single plane. The process represented by 63a can be defined as symmetrical mode II and 64 as symmetrical mode I. Diester 55 can also cleave in a symmetrical process represented
by 63b while trans-diester 27 cannot. Table II summarizes the types of cleavages which 1,2-diesters can undergo in terms of preferred modes for stabilizing the transition state leading to the dienolate dianion.

**Table II. Modes of Cleavage of 1,2-Diesters**

<table>
<thead>
<tr>
<th>Starting Ester</th>
<th>Side view of bond being cleaved</th>
<th>Mode of Cleavage</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Symmetrical mode I" /></td>
<td><img src="image2" alt="Symmetrical mode I" /></td>
<td>symmetrical mode I (in plane defined by four carbon atoms)</td>
</tr>
<tr>
<td><img src="image3" alt="Symmetrical mode II" /></td>
<td><img src="image4" alt="Symmetrical mode II" /></td>
<td>symmetrical mode II (perpendicular to plane defined by four carbon atoms)</td>
</tr>
<tr>
<td><img src="image5" alt="Dissymmetrical" /></td>
<td><img src="image6" alt="Dissymmetrical" /></td>
<td>dissymmetrical (in two planes)</td>
</tr>
</tbody>
</table>
The cleavage mode for diester 57 involves cleavage of the bond in two planes and is termed dissymmetrical. (One plane is perpendicular to that defined by C1C2C3 while the other is perpendicular to that defined by C2C3C4). It appears that the disrotatory symmetrical and the conrotatory symmetrical processes are more efficient and will lead to higher yields of cleavage products than the dis-symmetrical process.

Similar behavior of diradicals is observed in ketone photochemistry in competition between cyclization and photoelimination in the Norris type 2 reaction. Substituents β to the carbonyl group decrease the amount of elimination (cleavage) products. This is interpreted in terms of steric interference of the conformation necessary for cleavage of a biradical. Wagner suggests that

the preferred conformation for such a reaction requires the four carbon atoms to be in a plane and arranged for maximum overlap between both radical $p$ orbitals and the developing $p$ orbitals from the $\sigma$ bond being cleaved. Conformational effects can greatly decrease the yield of cleavage product as in the case of phenyl cyclobutyl ketone which gives mostly cyclization products.\(^{37}\) It appears likely that the diradical dianions produced in the acyloin condensation are subject to the same stereochemical requirements for cleavage as are biradicals produced in ketone photochemistry.

\textit{cis}-Diester \(^{48}\) gives an unusually low yield (27\%) of reduced product for one which is capable of cleaving in a symmetrical mode. This might be rationalized by the fact that the bent bond of the cyclopropane ring which must cleave is not in the plane in which cleavage must occur. Cleavage should be preferred in the plane of the cyclopropane ring and not in the plane perpendicular to the $C_1C_2C_3C_4$ plane which is normally the preferred plane for the syn-

metrical mode II cleavage. In this case, cleavage might not be the expected facile process relative to competing reactions.

e) Discussion

The very dissimilar heterogeneous and homogeneous reactions which 1,2-diesters can undergo under acyloin conditions demands an explanation. Ring strain is precluded as the major determining factor since, under heterogeneous conditions, disters 27 and 55 give quite strained cyclobutene derivatives. Also, on the basis of strain, one would expect trans-diesters in general, to be cleaved more effectively than cis-diesters. However, this is not always the case.

A change in the mechanism of the acyloin condensation of 1,2-diesters offers an explanation of why reaction pathways of certain diesters change as solvent is changed from liquid ammonia to toluene. The following mechanisms are proposed to explain the dichotomy of behavior. In liquid ammonia, initial electron transfer to the diester is probably rapid. A second electron transfer could also occur rapidly under the homogeneous conditions to give the postulated diradical dianion. This is illustrated below in the case of diester 55. Cleavage is rapid relative to the electrostatically unfavorable coupling of the diradical dianion 65. Support for the intermediacy of diradical 65 in liquid ammonia comes from the similar behavior of biradicals generated in the Norrish type 2 cleavage of ketones.
Mechanism in Liquid Ammonia

In toluene, a second electron transfer under the heterogeneous conditions to give dianion $65$ is probably slow. Evidence for this premise is the relatively slow rate of cyclization of aliphatic diesters to form medium and large rings.\textsuperscript{14,15} In addition, when diradical dianion $65$ is produced, albeit in liquid ammonia, it cleaves to give bis-alkoxy enolate $66$. Alternately, radical anion $64$ might cyclize to produce $68$, which could undergo further electron transfer to produce eventually the observed bistrimethylsilyl ether $62$.

These different mechanisms can account for the change in
Mechanism in Toluene

reaction products with the change in solvent, with the major difference being the rate at which a second electron addition will occur in the different solvents.

In the case of the reaction of cis-diester 68 with sodium in liquid ammonia, the mechanism must be modified to account for the observed ring closed product. Apparently cleavage of diradical 69
is slow, due to previously discussed geometrical requirements, relative to coupling to produce dianion \( \text{70} \). This rate phenomenon would be in accord with the observed products in liquid ammonia.

Certain factors are evident when one attempts to predict whether ring cleavage or ring closure will occur in the acyloin reaction of 1,2-diesters. Reductive cleavage will occur preferentially with sodium in liquid ammonia when the ester functions can become coplanar. Ring closure will occur preferentially with sodium in toluene with added chlorotrimethylsilane when the potential bistrimethylsilyl ether is not prohibitively strained. To date, bistrimethylsilyl ether, \( \text{72} \), which contains the bicyclo[2.2.0]hexyl
nucleus is the most strained system generated by the acyloin condensation. This system probably represents the limit of strain which can be introduced directly by the acyloin condensation in a cis-fused system. In this system, some reductive cleavage occurs. Apparently, reductive cleavage will occur under heterogeneous conditions only when ring closure is slow or impossible as in the case of diesters \(^{48}\) and \(^{49}\). In these systems, one of the processes which radical anion \(^{75}\) can undergo under heterogeneous conditions is further electron transfer and eventual ring cleavage.
In summary, reductive cleavage of diesters under acyloin conditions is very solvent dependent. Cleavage will occur readily in liquid ammonia if the ester satisfies certain geometrical requirements. In toluene, ring closure is found to be the preferred pathway, with reductive cleavage occurring only when strain precludes ring formation. The different behavior of 1,2-diesters under the two sets of conditions suggests that the mechanism of the acyloin condensation may be different in the two solvents. Conclusive proof for this suggestion remains to be demonstrated.
EXPERIMENTAL

Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 137 Infracord as neat liquids, in solution in carbon tetrachloride or as powdered solids in potassium bromide discs. Nuclear magnetic resonance spectra were obtained on a Varian Associates A60-A Spectrometer and reported in tau (τ) units relative to tetramethylsilane (τ = 10.00) as the internal standard. Exact mass determinations were obtained on an MS-9 High Resolution Mass Spectrometer.
Zinc-copper couple. Zinc-copper couple was prepared using a modification of the procedure of LeGoff. Zinc dust (70 g) was added to a rapidly stirred solution of 8.0 g cupric acetate dihydrate in 200 ml acetic acid at 55°. The mixture was stirred for one minute, collected on a fritted disc funnel and washed repeatedly with dry ether.

exo-Tricyclo[3.2.1.02,4]octene (50). A solution of ethyl zinc iodide was prepared in a 5-l, three-necked flask from 312 g of ethyl iodide, zinc-copper couple (prepared from 140 g zinc dust and 16 g of cupric acetate dihydrate), and 1500 ml of anhydrous ether. Methylene iodide (268 g) was added over a 5 min period, and the mixture was refluxed for 10 hr. Water was carefully added, followed by one liter of ammonium chloride solution. The organic phase was separated, washed with 10% potassium hydroxide solution, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the ether solution was distilled through a glass helice packed column. The fraction boiling between

123° and 130° was collected. The yield was 39.9 g (38%).

Ozonolysis of exo-tricyclo[3.2.1.0^2.4]octene (50). A solution of 60 g of exo-tricyclo[3.2.1.0^2.4]octene (0.54 mol) in 500 ml of absolute methanol was ozonized exhaustively at -78°. Methanol was removed under vacuum and 200 ml of glacial acetic acid was added to the glassy residue. A solution of 8.6 g of concentrated sulfuric acid in 150 ml of water and 136 g of 30% hydrogen peroxide was then added. The mixture was heated to approximately 90° at which temperature the reaction became exothermic. Cooling in ice was necessary. If the reaction became too exothermic, yields were decreased. Reflux was continued for two hours. Solvents were removed under reduced pressure (following neutralization of the sulfuric acid with sodium hydroxide) to give a light yellow semi-crystalline residue.

The crude diacid was converted directly to the diester by addition of 250 ml of absolute methanol, 150 ml of acetone dimethylacetal and 3 ml of concentrated sulfuric acid. This mixture was refluxed for one hour, poured into 500 ml of water, and extracted with three 400-ml portions of ether. The combined ether extracts were washed with water, 10% aqueous potassium bicarbonate, and saturated sodium chloride solution, and then dried over sodium sulfate. After filtration, the ether was removed on a steam bath and the residue was distilled to give 69.5 g (62%) of diester δ₄, bp 90° (0.20 mm), n_D^25 = 1.4650. Diester δ₄ had the following spectral properties:

\[
\text{ir (neat) } \nu = 5.72 \mu; \ \text{nmr (CDCl}_3/\text{TMS}) = 6.30 (6H, s), 7.0-7.4 (2H,} \]
Acyloin Condensation of Diester 50. Sodium (9.3 g, 0.404 mol) was dispersed in 500 ml of refluxing dry toluene and chlorotrimethylsilane (53 g, 0.49 mol) was added. A solution of 15.95 g (0.081 mol) of diester 52 in 200 ml of toluene was added dropwise over a three hour period using a Hirshberg addition funnel. Refluxing was continued for ten hours. The mixture was then filtered through celite. Toluene was removed from the filtrate at 60° by distillation at reduced pressure. The residue was then distilled to give 19.0 g (64%) of the bistrimethylsilyl ether 55, bp 70-73° (0.1 mm).

Bistrimethylsilyl ether 55 had the following spectral properties:

\[ \text{nmr (CDCl}_3\right): 7.57 (2H, t, J = 2 Hz), 8.4-9.3 (8H, m), 9.85 (18H, s). \]

**Anal.** Calcd for C\(_{14}H_26O_2Si_2\): C, 59.51; H, 9.28.

**Found:** C, 59.32; H, 9.30.

Methanolysis of 6,7-di(trimethylsiloxy)-exo-tricyclo[3.2.1.0\(^{2,4}\)]oct-6-ene (55). To 100 ml of dry methanol under nitrogen was added 13.23 g (0.049 mol) of bistrimethylsilyl ether 55. The mixture was refluxed for 20 hours and the methanol was removed under vacuum. The residue was then dissolved in 10 ml of methanol and 7 ml of trimethylorthoformate. Toluenesulfonic acid (0.01 g) was added and
the mixture was stirred at room temperature for one hour. The
toluene sulfonic acid was neutralized with sodium methoxide and ex-
cess solvents were removed under vacuum. The residue was distilled
to give 7.78 g (90%) of hydroxyketal 68, bp 65\(^\circ\) (0.1 mm), \(n^25_D = 1.4875\). The nmr spectrum (CDCl\(_3\)/TMS) showed \(\tau\) 6.20 (1H, t, \(J = 5\) Hz),
6.58 (3H, s), 6.77 (3H, s), 7.58 (2H, m), 8.6-9.6 (5H, m), 9.78 (1H, t, \(J = 6.5\) Hz).

**Anal.** Calcd for C\(_{10}\)H\(_{16}\)O\(_3\): C, 65.19; H, 8.75.
Found: C, 65.10; H, 8.81.

Oxidation of 68. Sarett reagent was prepared from 13.0 g of chromium
trioxide in 130 ml of pyridine. Hydroxyketal 68 (7.78 g, 0.042 mol)
was added and stirring was continued for 20 hours at room tempera-
ture. The mixture was then poured into 600 ml of water and ex-
tracted with three 150-ml portions of ether. The combined ether
extracts were washed with water, carefully with dilute hydrochloric
acid, 10% aqueous potassium bicarbonate, and saturated sodium chlo-
ride solution, respectively. The ether was then dried over anhy-
drous sodium sulfate, filtered, and the solvent evaporated on a
steam bath. The residue was distilled to give 6.05 g (80%) of ketal-
ketone 69, bp 66\(^\circ\) (0.16 mm), \(n^25_D = 1.4843\). Ketal-ketone 69 had the
following spectral properties: ir (neat) C=O 5.64 \(\mu\), nmr (CDCl\(_3\)/TMS)
\(\tau\) 6.60 (3H, s), 6.67 (3H, s), 7.40 (2H, m), 8.50-9.8 (6H, m).

**Anal.** Calcd for C\(_{10}\)H\(_{14}\)O\(_3\): C, 65.91; H, 7.74.
Found: C, 65.75; H, 7.94.
Preparation of 70. To a solution of 5.11 g (0.0274 mol) of tosylhydrazine in 25 ml of dry methanol was added 5.00 g (0.0274 mol) of ketal-ketone 69. The mixture was left standing at room temperature for three hours (until crystallization was complete). The crystals were collected and air dried to give 8.4 g (85%) of 70, mp 160-165° (dec). An analytical sample was obtained by recrystallization from methanol, mp 169-170° (dec).

Anal. Calcd for C_{17}H_{22}N_{2}O_{4}S: C, 58.27; H, 6.33; N, 7.99; S, 9.15.

Found: C, 58.23; H, 6.40; N, 7.94; S, 9.00.

Hydrolysis of 70. Tosylhydrazone 70 (6.0 g, 0.017 mol) was dissolved in 60 ml of tetrahydrofuran and 25 ml of 1 M hydrochloric acid was added. The mixture was stirred at 35° for two hours. After one hr the mixture became homogeneous. Upon continued stirring, a precipitate formed. The solvents were removed under vacuum and cold methanol was added. The crystals of tosylhydrazone 57 were collected, washed with cold methanol, and dried, mp 195-196° (dec). The yield was 4.65 g (89%).

Anal. Calcd for C_{15}H_{16}N_{2}O_{3}S: C, 59.19; H, 5.30; N, 9.20; S, 10.53.

Found: C, 58.92; H, 5.29; N, 9.22; S, 10.44

Formation of 53. To a one liter, round bottomed flask was added 56 g (0.118 mol) of monotosylhydrazone 57. A solution of 5.4 g of
sodium hydroxide in 260 ml of water was added followed by 350 ml of pentane. The mixture was stirred for 30 min and the pentane decanted. Fresh pentane (350 ml) was added and stirring was continued for one hr. The pentane was again decanted. This procedure was repeated until a total of two liters of pentane had been used. The combined pentane extracts were dried over anhydrous sodium sulfate, filtered, and the pentane was removed from the filtrate by distillation under reduced pressure. The residue consisted of 11.24 g (64%) of a yellow solid, mp 45-47°. The crude diazoketone was used directly in the next step.

**Anal.** Calcd % for C₇H₈N₂O: 148.0637.

Found (obs. m/e): 148.0694.

Photolysis of 52 in Methanol. A solution of 4.92 g (0.0332 mol) of diazoketone 52 in 100 ml of methanol (distilled from magnesium) and 65 ml of THF (distilled from lithium aluminum hydride) was irradiated (base washed apparatus) using a Hanovia lamp with quartz probe and a corex D filter for three hr. Solvents were remove at reduced pressure and the residue was distilled to give 1.92 g (38%) of a product boiling at 65-73° (1.3 mm). Gas chromatography shows 10% impurity identified as ketone 77. Ring contracted esters 90 had the following spectral properties: ir (neat) C=O 5.74 μ; nmr (CDCl₃/TMS) τ 6.31 (3H, s), 6.99 (1H, m), 7.3 (2H, m), 8.3-9.6 (6H, m). An analytical sample of ester 90 was prepared by diazomethane esterification of acid 92.
Anal. Calcd for CsH12O2: C, 71.02; H, 7.95.
Found: C, 70.56; H, 7.97.
Calcd. m/e : 152.0847.
Found : 152.0838.

Saponification of 90. To 86 ml of methanol was added 10.5 g of the mixture of esters 90. A solution of 9.45 g (0.145 mol) of potassium hydroxide in 66 ml of water was added and the mixture was heated at 80° for 2½ hr. Most of the methanol was then distilled off and 90 ml of water was added. The total volume was reduced to approximately 75 ml by distillation at reduced pressure. The aqueous solution was then extracted with 100 ml of pentane to remove neutral material. The aqueous phase was then acidified with a solution of 20.1 g (0.147 mol) of potassium bisulfate in water. The mixture was then extracted with three 70-ml portions of ether and the combined ether extracts were dried over anhydrous sodium sulfate. After filtration, the solvents were removed on a steam bath and the crude acid 93 was distilled to give 7.54 g (87%) of acid 93, bp 82-85° (0.1 mm).

Anal. Calcd m/e for CsH10O2: 138.0681
Found: 138.0682

Preparation of 94. To a solution of 7.39 g of acid 93 in 200 ml of anhydrous ether was added dropwise 53 ml of 2.13 M (0.113 mol) methyl lithium (diluted to 100 ml with anhydrous ether). After the
addition was complete, the mixture was allowed to stand at room
temperature for 30 min. Acetone (5 ml) was added followed by 150
ml of 10% ammonium nitrate solution. The organic phase was sepa-
rated and washed with ammonium nitrate solution, water, and satu-
rated sodium chloride solution. The ether phase was then dried
over anhydrous sodium sulfate. After filtration, the ether was
removed on a steam bath and the ketone 24 was distilled to give 6.92
g (92%), bp 80-85° (9 mm). Ketone 24 had the following spectral
properties: ir (neat) C=0, 5.82 μ; nmr (CDCl3/TMS) τ 6.4-7.1 (1H, ... m), 7.22 (2H, m), 7.9 (3H, m), 8.2-8.8 (4H, m), 8.9-9.6 (2H, m).

Found: C, 79.68; H, 8.88.

Baeyer-Villiger Oxidation of 24. m-Chloroperbenzoic acid (17.1 g)
was dissolved in 90 ml of methylene chloride and 5.5 g of ketone
24 was added. The mixture was allowed to stand at room temperature
for three days. The precipitated m-chlorobenzoic acid was removed
by filtration. The filtrate was washed thoroughly with a sodium
sulfite-potassium bicarbonate mixture and then dried over sodium
sulfate. The drying agent was removed by filtration and the solvent
was removed by distillation through a Vigreux column. The residue
was distilled to give 4.2 g (68%) of acetates, 25, bp 43-45° (0.4
mm). Pure endo-acetate 25 could be prepared by treatment of pure
alcohol 26 with acetyl chloride in ether containing 2 equivalents
of pyridine and had the following spectral properties: ir (neat)
C=0, 5.72 μ; nmr (CDCl₃/TMS) δ 5.35 (1H, q, J = 2 Hz), 7.36 (2H, m), 7.94 (3H, s), 8.40 (1H, m), 8.5-8.9 (2H, m), 9.0-9.5 (3H, m).

**Anal.** Calcd for C₉H₁₂O₂: C, 71.02; H, 7.95.

**Found:** C, 70.81; H, 7.98.

Cleavage of 95 with Methyllithium. A mixture of acetates 95 (4.2 g) was dissolved in 20 ml of anhydrous ether and 30 ml of 2.13 M methyllithium in ether was added dropwise while the mixture was cooled in an ice bath. Upon completion of the addition, the mixture was allowed to stir at room temperature for 45 min. The mixture was then carefully decomposed with water. The ether phase was separated, washed once with water and then dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the solvent was removed by distillation through a Vigreux column. The residue was distilled to give a mixture of alcohols 96 and 97, bp 43-50° (0.9 mm).

**Anal.** Calcd for C₇H₁₀O: C, 76.32; H, 9.15.

**Found:** C, 76.04; H, 9.17.

The mixture of alcohols could be separated by preparative gas chromatography on a 6 ft 5% XF-1150 on 45/60 Chrom W column. Pure endo alcohol 96 showed the following nmr (CDCl₃/TMS): δ 5.98 (1H, q, J = 2.2 Hz), 6.96 (1H, s), 7.66 (2H, m), 8.40 (1H, m), 8.5-8.85 (2H, m), 8.9-9.35 (2H, m), 9.4-9.75 (1H, m). Pure exo-alcohol 97 showed the following nmr spectrum: (CDCl₃/TMS) δ 5.93 (1H, d, J = 7 Hz), 7.03 (1H, s), 7.70 (2H, m), 8.5-9.1 (5H, m), 9.58 (1H, t, J = 7 Hz).
Preparation of 98. Alcohol 96 (413 mg) was dissolved in 1.5 ml of pyridine and the mixture was cooled in an ice bath. A solution of 821 mg of p-toluenesulfonyl chloride in 3 ml of pyridine was added to the cooled solution. The mixture was stored at 0° for 18 hr. The mixture was poured into ice water and extracted with two 30-ml portions of ether. The combined ether extracts were washed rapidly with cold water, sodium bisulfate solution, potassium bicarbonate solution, and saturated sodium chloride solution. The organic phase was then dried over anhydrous sodium sulfate, filtered, and the solvent was removed at less than 0° on a rotary evaporator. The crude tosylate 98 (981 mg, 92%) melted sharply at 92° with immediate decomposition upon melting. After storage for two weeks at 0°, the melting point decreased to 86°. Tosylate 98 had the following spectral properties: nmr (CDCl₃/TMS) τ 2.40 (4H, doublet of doublets), 5.57 (1H, q, J = 2.2 Hz), 7.54 (5H, s), 8.35-8.6 (1H, m), 8.6-8.9 (2H, m), 8.9-9.6 (3H, m).

Preparation of 138. Alcohol 96 (500 mg) was dissolved in 3 ml of pyridine and the mixture was cooled in an ice bath. A solution of 845 mg of p-nitrobenzoyl chloride in 10 ml of pyridine was added to the cooled solution. The mixture was stored at 0° for 2½ days with occasional swirling. The mixture was then poured into 50 ml of water and extracted with three 30-ml portions of ether. The combined ether extracts were washed with water, dilute sodium bisulfate solution, potassium bicarbonate solution, saturated sodium chloride
solution, and then dried over anhydrous sodium sulfate. After filtration, the ether was removed on a rotary evaporator to give 1.00 g (85%) of p-nitrobenzoate 138. Recrystallization from pentane gave an analytical sample, mp 87-89°. p-Nitrobenzoate 138 had the following spectral properties: nmr (CDCl3/TMS) \( \tau \) 1.81 (4H, s), 5.10 (1H, q, \( J = 2.3 \) Hz), 7.26 (2H, m), 8.15-8.5 (1H, m), 8.55-8.9 (2H, m), 8.9-9.5 (3H, m).

Anal. Calcd for C14H13NO2: C, 64.86; H, 5.05; N, 5.40.
Found: C, 64.96; H, 5.18; N, 5.42.

Preparation of 135. exo-Alcohol 27, (158 mg) was dissolved in 4 ml of pyridine and the mixture was cooled in an ice bath. p-Nitrobenzoyl chloride (293 mg) was added in small portions with stirring. The mixture was stored at 0° for 2 days. The mixture was then poured into water and extracted with two 20-ml portions of ether. The combined ether extracts were washed with water, dilute sodium bisulfate solution, potassium bicarbonate solution, saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After filtration, the ether was removed on a rotary evaporator. The entire residue was recrystallized from pentane to give 229 mg (62%) of p-nitrobenzoate 135, mp 85-86°. A second recrystallization from pentane gave an analytical sample, mp 85.5-86.5°. p-Nitrobenzoate 135 had the following spectral properties: nmr (CDCl3/TMS) \( \tau \) 1.70 (4H, s), 5.12 (1H, d, \( J = 7.5 \) Hz), 7.30 (2H, m), 7.70-8.10 (1H, m), 8.4-9.0 (4H, m), 9.36 (1H, t, \( J = 7 \) Hz).
Analy. Calcd for C_{14}H_{13}NO_2: C, 64.86; H, 5.05; N, 5.40.

Found: C, 64.83; H, 5.19; N, 5.42.

**Acylcin condensation of 1,3-cyclopentane dicarboxylic acid dimethyl ester, 58.** The procedure used was a modification of that of Russell and Holland. Sodium (45 g) was dispersed in 2-l of dry toluene. Chlorotrimethylsilane (248 g) was added. A solution of 70.8 g of diester 58 was added dropwise over a 6 hr period to the refluxing solution. Refluxing was continued for an additional 8 hr. The toluene solution was cooled and then filtered through celite. The solvent was removed from the filtrate by distillation at reduced pressure. The residue was distilled to give 91.6 g (89%) of bistrimethylsilyl ether 59, \(^2\) bp 65-68°C (0.1 mm).

**Methanolysis of bistrimethylsilyl ether 59.** Bistrimethylsilyl ether 59 (4 g) was refluxed with 20 ml of dry methanol under a nitrogen atmosphere for 2 hr. The solvents were then removed by distillation at reduced pressure and 10 ml of methanol, 8 ml of trimethyl orthoformate and 0.01 g \(p\)-toluenesulfonic acid was added. The mixture was stirred at room temperature for 30 min. Solvents were removed by distillation at reduced pressure. The residue was distilled to give 2.55 g (94%) of hydroxyketal 61, bp 50°C (0.14 mm).

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Hydroxyketal 61 had the following spectral properties: nmr (CDCl₃/TMS) τ 6.23 (1H, d, J = 5 Hz), 6.72 (3H, s), 6.82 (3H, s), 7.12 (1H, broad s), 7.65 (2H, broad s), 8.2-8.9 (6H, m).

Anal. Calcd m/e for CsH₁₄O₃: 172.1099
Found: 172.1102

Sarett oxidation of 61. Chromium trioxide (23 g) was added to 230 ml of cold pyridine. After stirring for 20 min. 12.9 g of hydroxyketal 61 was added. The mixture was stirred at room temperature for 18 hr. The mixture was then poured into 1 liter of water and extracted with three 200-ml portions of ether. The combined ether extracts were washed with dilute hydrochloric acid to remove the pyridine. Care was taken not to let the mixture become acidic. The organic phase was then washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. After filtration, the ether was removed on a steam bath and the residue was distilled to give 10.3 g (61%) of ketal-ketone 62, bp 50-51 ° (0.2 mm). Ketal-ketone had the following spectral properties: ir (neat) C=O, 5.73μ; nmr (CDCl₃/TMS) τ 6.65 (6H, s), 7.34 (2H, m), 7.80-8.65 (6H, m).

Anal. Calcd for CsH₁₄O₃: C, 63.51; H, 8.29.
Found: C, 63.54; H, 8.40.

Formation of 63. Tosylhydrazine (5.47 g) was partially dissolved in 26 ml of dry methanol. Ketal-ketone 62 (5.00 g) was added and the mixture was warmed to 40 ° until the remaining tosylhydrazine dis-
solved. The mixture was left standing at room temperature for 4 hr during which time the product crystallized. The solution was then cooled to 0° and tosylhydrazone 63 was collected on a fritted disc funnel. The yield of 63 was 8.9 g (89%), mp 125-126°. An analytical sample was prepared by recrystallization from methanol and contains 1 mole of methanol of crystallization.

Anal. Calcd for C17H26O5N2S: C, 54.88; H, 7.07; N, 7.56; S, 8.65.

Found: C, 54.52; H, 7.04; N, 7.78; S, 8.89.

Pyrolysis of 64. Tosylhydrazone 63 (7.0 g) was partially dissolved in 60 ml of dry tetrahydrofuran. Butyllithium (13.5 ml), 1.6 N in hexane, was added dropwise with stirring to the cooled solution. The mixture became homogeneous. The solvents were removed at reduced pressure. The last traces of solvent were removed under a vacuum of 0.1 mm. The lithium salt 64 was then slowly heated to 105° under a pressure of 0.1 mm. An orange liquid distilled at approximately 105° and was condensed in a trap at -78°. The temperature was raised to 120° and the remainder of the volatile material distilled. The ir spectrum of the crude distillate shows the presence of diazoketal 65 (C=N, 4.80 μ). The distillate was heated to 120° at atmospheric pressure. The orange color disappeared with evolution of nitrogen gas. The residue was then distilled to give 1.90 g (60%) of ketal 67, bp 99° (90 mm). The spectral properties
(ir and nmr) of the product were identical to those of an authentic sample of nortricyclanone dimethyl ketal, $^6$.^3

Pyrolysis of $^7$. Tosylhydrazone $^7$ (30 g) was dissolved in 200 ml of dry tetrahydrofuran and 53.3 ml of 15.1\% n-butyllithium in hexane was added at 0°. The solvents were removed under vacuum with the last traces being removed at 0.1 mm. The dry lithium salt could be collected and stored. Thirty grams of the dried salt was heated with stirring to 110° under a vacuum of 0.1 mm. An orange liquid distilled into the collection flask cooled in a dry ice bath. The ir of the crude distillate shows the presence of diazoketal $^8$ (C=N, 4.82 μ). The distillate was heated to 100° at atmospheric pressure, and then distilled to give 2.6 g (19\%) of $^6$, bp 74° (2 mm). Olefin $^6$ had the following spectral properties: ir (neat) C=C, 5.99 μ; nmr (CDCl₃/TMS) τ 6.33 (6H, s), 7.30 (2H, m), 8.40-9.30 (6H, m). Olefin $^6$ was unstable and polymerized on standing at 0°.

Hydrolysis of $^6$. To 10 ml of 0.1 N hydrochloric acid in water was added 0.2 g of olefin $^6$. The mixture was stirred at room temperature for 2 hr. The mixture was extracted with ether and dried over anhydrous sodium sulfate. After filtration, the ether was removed by distillation. The crude residue (106 mg, 57\%) was subjected to molecular distillation. The ir and the gas chromatographic reten-

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3. Spectra were provided by Dr. J. MacMillan.
tion times on column A and column B on column B were identical to an authentic sample of ether-ketone \( \text{CCH}_3 \), prepared independently as described below.

Methylation of \( \text{CCH}_3 \). Alcohol \( \text{CCH}_3 \) (2.9 g) was added to a mixture of 1.0 g of sodium hydride in 25 ml of tetrahydrofuran. The mixture was heated at reflux for 1 hr, excess methyl iodide was added, and the mixture was refluxed for an additional 2 hr. Most of the solvent was removed by distillation and 30 ml of ether was added. Water was then carefully added to decompose the excess sodium hydride. The organic phase was then separated and the aqueous phase was extracted with an additional 30-ml portion of ether. The combined ether extracts were washed with two portions of water, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. After filtration, the solvents were removed on a steam bath. The residue was distilled to give 2.35 g (82\%) of ketal-ether \( \text{CCH}_3 \), bp 80° (1.1 mm). Ketal-ether \( \text{CCH}_3 \) had the following spectral properties: nmr (CDCl3/TMS) \( \delta 6.56 \) (5H, s), \( \delta 6.67 \) (5H, s), \( \delta 6.79 \) (5H, s), \( \delta 7.50 \) (2H, m), \( 8.6-9.1 \) (4H, m), \( 9.3-9.9 \) (2H, m).

**Anal.** Calcd for C\(_{11}\)H\(_{16}\)O\(_3\): C, 66.64; H, 9.15. 
Found: C, 66.71; H, 9.22

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4. Column A; 6 ft 5% XF-1150 on 45/60 Chrom W. Column B; 6 ft SE-30 Silicone Rubber. Column C; 6 ft 3% SE-30 on Diaport S. Column D; 20 ft 20% DC Silicone fluid #200 on 60/80 Chrom P.
Hydrolysis of 76. Ketal-ether 78 was dissolved in 10 ml of tetra-
hydrofuran and 8 ml of 1 M hydrochloric acid was added. The mix-
ture was stirred for 3.5 hr at room temperature, poured into water
and extracted with two 20-ml portions of ether. The combined ether
extracts were washed with water, dilute potassium bicarbonate solu-
tion, saturated sodium chloride solution, and dried over anhydrous
sodium sulfate. After filtration, the ether was removed on a
steam bath. The residue was distilled to give 1.1 g (72%) of
ether-ketone 77, bp 76° (1.1 mm). Ether-ketone 77 had the follow-
ing spectral properties: ir (neat) C=O 5.77 μ; nmr (CDCl₃/TMS)
τ 6.38 (1H, m), 6.47 (5H, s), 7.20 (1H, m), 7.40 (1H, m), 8.40
9.25 (5H, m), 9.48 (1H, t, J = 7.5 Hz).

Anal. Calcd for C₉H₁₂O₂:  C, 71.02; H, 7.95.
Found:    C, 70.85; H, 8.06

Ozonolysis of 76 in methanol. Olefin 76 (500 mg) was dissolved in
6 ml of dry methanol and the mixture was ozonized exhaustively. The
solution was then added to a solution of 2 g of sodium iodide in 20ml
of acetic acid containing a small amount of zinc dust. The mixture
was then poured into water and extracted with two 20-ml portions
of ether. The combined ether extracts were washed with water, di-
lute sodium hydroxide solution and dried over anhydrous sodium
sulfate. After filtration, the ether was removed by distillation
through a Vigreux column. The products were separated by prepara-
tive vpc on column B at 120°. The two products, ester 7k, and
ketal-ketone 69, were identified by comparison of ir spectra with those of authentic samples.

Ozonolysis of 76 in Methanol-d$_4$. Olefin 76 (300 mg) was dissolved in 4 ml of methanol-d$_4$ (distilled from sodium) and the mixture was ozonized exhaustively. The solution was then added to 1.0 g of sodium iodide in 5 ml of acetic acid containing a small amount of zinc dust. The mixture was then poured into water and extracted with two 15-ml portions of ether. The combined ether extracts were washed with water, dilute sodium hydroxide solution and dried over anhydrous sodium sulfate. After filtration, the ether was removed by distillation. The two products, diester 54 and ketal-ketone 88, were separated by preparative vpc on column C at 120°. The nmr spectrum of ketal-ketone 88 was identical to that of ketal-ketone 69 except for the absence of the methyl signal at $\tau$ 6.67.

The mass spectrum of 88 shows m/e = 157, indicative of loss of carbon monoxide from the parent ion. The mass spectrum of 69 showed m/e = 154, also indicative of the loss of carbon monoxide from the parent ion. Neither ketal-ketone 69 or 88 gave a parent ion in the mass spectrum.

Epoxidation of 76 in Methanol. m-Chloroperbenzoic acid (175 mg), sodium acetate (52 mg) and sodium carbonate (65 mg) were added to a 5 ml flask equipped with a magnetic stirring bar. One ml of dry methanol was added and the mixture was cooled in an ice bath. A
solution of 50 mg of olefin 76 in 1.5 ml of dry methanol was added dropwise. Stirring was continued at 0° for 30 min. The mixture was then stirred at room temperature for 2 hr, poured into water, and extracted with ether. The ether extract was washed with sodium thiosulfate solution, sodium hydroxide solution, and dried over anhydrous sodium sulfate. After filtration, the solvent was removed by distillation through a Vigreux column. The product was isolated by preparative vpc on column C at 110°. The yield of ketal-ketone 69 was 21 mg (34%) and was identical to an authentic sample of 69 by comparison of ir spectra and gc retention times on column A and column B.4

Formation of 89. Deuterated ketal-ketone 88 (45 mg) was added to a solution of 100 mg of sodium borohydride in 1 ml of methanol containing a small amount of sodium hydroxide. The mixture was allowed to stand at room temperature for 8 hr. The mixture was then poured into dilute sodium hydroxide solution and extracted with ether. The ether extract was washed with dilute sodium hydroxide solution and dried over anhydrous sodium sulfate. After filtration, the ether was removed by distillation. The crude deuterated hydroxy-ketal was added to 100 mg of sodium hydride in 3 ml of tetrahydrofuran. The mixture was refluxed for 1 hr and excess methyl iodide was added. Refluxing was continued for 2 hr. Water was carefully added to the mixture to decompose the excess sodium hydride. The mixture was then extracted with pentane and the pentane extract was washed
with water. The organic phase was dried over anhydrous sodium sulfate, filtered, and the solvent was removed by distillation. The nmr spectrum of the crude residue was identical to that of ketalether 76 except for the absence of the methoxyl signal at $\tau$ 6.79.

Silver assisted solvolysis of 102. A mixture of 15 g of 7,7-dibromonorcarene, 102, 25 g of silver acetate and 150 ml of glacial acetic acid was stirred under reflux for 92 hr. The mixture was filtered to remove the precipitated silver bromide and the unreacted silver acetate, diluted with 300 ml of ether and then refiltered. The filtrate was washed successively with three 100-ml portions of water, dilute sodium hydroxide solution, dilute potassium bicarbonate solution, and saturated sodium chloride solution. The ether phase was then dried over anhydrous sodium sulfate and filtered. The solvent was removed on a steam bath and the residue was distilled through a Vigreux column and collected in 3 fractions. Fraction 1: 2.1 g, bp 44-56° (1.6 mm); Fraction 2: 1.9 g, bp 56-99° (1.6 mm); Fraction 3, 4.6 g, bp 99-106° (1.6 mm). Fraction 1 was redistilled through a Vigreux column to give 1.6 g of product, bp 80-82° which was shown to be identical by nmr to 3-bromocycloheptatriene. 5 The total yield of 3-bromocycloheptatriene 101 from fractions 1 and 2 was 3.4 g (34%). Fraction 3 contains bromoacetates 103. The total yield of bromoacetates 103 from fractions 2 and 3 was 5.1 g (37%).

acetates 103 had the following spectral properties: ir (neat) C=O, 5.72; nmr (CDCl₃/TMS) ν 4.10-4.80 (2H, m), 7.2-8.0 (5H, m containing a sharp singlet at 7.95), 8.05-8.50 (2H, m), 8.6-9.4 (2H, m). Bromoacetates 103 were relatively unstable and were used immediately in the next step.

Saponification of 103. Potassium hydroxide (1.60 g) was dissolved in 2 ml of water and a solution of 4.20 g of bromoacetates 103 in 15 ml of methanol was added. The mixture became warm and turned black. Stirring was continued at room temperature for 12 hr. The mixture was then poured into 40 ml of water and extracted with three 30-ml portions of ether. The combined ether extracts were washed with 2 portions of water, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. After filtration, the ether was removed on a steam bath. The residue was distilled to give 2.78 g (81%) of a mixture of bromoalcohols 105, bp 82-85° (0.5 mm). Bromoalcohols 105 had the following spectral properties: nmr (CDCl₃/TMS) ν 4.33 (1H, m), 5.67 (1H, m), 7.75 (2H, m), 8.05 (1H, s), 8.25 (2H, m), 8.55-9.35 (2H, m).

Anal. Calcd for C₇H₉OBr: C, 44.47; H, 4.80; Br, 42.27.

Found: C, 44.31; H, 4.91; Br, 41.91.

Debromination of 105. Sodium (5.0 g) was cut into small pieces and added to 50 ml of dry tetrahydrofuran. t-Butyl alcohol (5.0 g) was added. The mixture was brought to reflux as 2.5 g of bromoalcohols
was added. After 30 min the sodium clumped together and refluxing was continued for an additional 3 hr. The excess sodium was removed by filtration through a wire screen and washed thoroughly with ether and methanol. Ether (100 ml) was added followed by 70 ml of water. The organic phase was separated, and the aqueous phase was extracted with another 100 ml of ether. The combined ether extracts were washed with two 100-ml portions of water, saturated sodium chloride solution and dried over anhydrous sodium sulfate. After filtration, the solvents were removed by distillation through a Vigreux column. The residue was distilled to give 0.95 g (66%) of a mixture of alcohols 100 and 106, bp 65-68° (3.5 mm).

The two alcohols could be separated by preparative vpc on column A at 75°. The major alcohol, 100, (54%) had the following spectral properties: nmr (CDCl3/MeS) τ 3.65-4.05 (1H, m), 4.50-4.90 (1H, m), 5.50-5.90 (1H, m), 7.70-8.10 (2H, m), 7.72 (IH, s, exchanges with D2O), 8.30-9.60 (4H, m).

Anal. Calcd m/e for C7H10O: 110.07316.
Found: 110.07326.

The minor alcohol, 106, (46%) had the following spectral properties: nmr (CDCl3/MeS) τ 3.85-4.20 (1H, m), 4.50-4.90 (1H, m), 5.60-6.00 (1H, m), 7.3-8.7 (4H, m), 7.67 (1H, m, exchanges with D2O), 9.00-9.40 (2H, m).

Anal. Calcd m/e for C7H10O: 110.07316.
Found: 110.07326.
Hydrogenation of 100 with Pd/C. Alcohol 100 (64 mg) was dissolved
in 15 ml of ether and 60 mg of 1/2 palladium on carbon was added.
The mixture was hydrogenated at 68 psi for 1 hr. The catalyst was
removed by filtration through celite and the solvent was removed from
the filtrate by distillation through a Vigreux column. The residue
consisted of 58 mg (91%) of trans-2-methylcyclohexanol, 107, identi-
fied by comparison of the ir spectrum with that of an authentic sam-
ple.6 The product contained no cis-isomer, 109, by vpc analysis on
column A.

Hydrogenation of 106 with Pd/C. Alcohol 106 (54 mg) was dissolved
in 15 ml of ether and 70 mg of 1/2 Pd on charcoal was added. The
mixture was hydrogenated at 68 psi for 1 hr. The catalyst was re-
moved by filtration through celite and the solvent was removed by
distillation through a Vigreux column. The product was isolated by
preparative vpc on column A, and consisted of 17 mg (32%) of cis-2-
methylcyclohexanol, 109, identified by comparison of the ir spectrum
with that of an authentic sample of 109.7 The product contained no
trans isomer 107 by vpc on column A.

Hydrogenation of 106 with platinum oxide. Alcohol 106 (45 mg) was

dissolved in 15 ml of ether containing 25 mg of platinum oxide
which had been previously reduced by shaking for 4 hr under a hy­
drogen pressure of 70 psi. The mixture was hydrogenated at 65 psi
for 3 hr. The catalyst was removed by filtration through celite
and the solvent was removed by distillation through a Vigreux column.
The product (12 mg, 27%) was isolated by preparative vpc on column
C and was shown to be identical to cis-2-hydroxybicyclo[4.1.0]hep­
tane, 108, by ir spectral comparison with an authentic sample.8

Preparation of p-Nitrobenzoate esters—general procedure. The
appropriate alcohol was dissolved in pyridine and the mixture was
cooled to 0°. p-Nitrobenzoyl chloride (1.05 equivalents) was added
in small portions with stirring. After storing at 0° for 2 days,
the mixture was poured into water and extracted with ether. The
ether extract was washed with water, dilute potassium bisulfate
solution, dilute potassium bicarbonate solution, and then dried over
anhydrous sodium sulfate. After filtration, the solvent was removed
on a rotary evaporator to give the crude p-nitrobenzoate ester.

Preparation of 118. Alcohol 100 (280 mg) gave 624 mg (98%) of crude
p-nitrobenzoate 118, mp 45-48°. Recrystallization from pentane gave
an analytical sample, mp 66-67°. The nmr of \( ^{118} \) (CDCl3/MS) showed:

   (1963).
\[ \tau 1.85 (4H, m), 3.60-3.95 (1H, m), 4.10-4.35 (1H, m), 4.40-4.80 (1H, m), 7.50-7.85 (2H, m), 8.17-8.66 (2H, m), 8.70-9.45 (2H, m). \]

**Anal.** Calcd for C\(_{14}H_{13}NO_2\): C, 64.86; H, 5.05; N, 5.40.

Found: C, 65.05; H, 5.06; N, 5.47.

Preparation of 119. Alcohol 106 (297 mg) gave 639 mg (92\%) of crude p-nitrobenzoate 119, mp 92-94°. Recrystallization from pentane gave an analytical sample, mp 95-96°. The nmr of 119 (CDCl\(_3\)/TMS) showed: \( \tau 1.81 (4H, m), 3.70-4.10 (1H, m), 4.20-4.80 (2H, m), 7.10-8.10 (2H, m), 8.35-8.60 (2H, m), 8.85-9.20 (2H, m). \)

**Anal.** Calcd for C\(_{14}H_{13}NO_2\): C, 64.86; H, 5.05; N, 5.40.

Found: C, 64.91; H, 5.04; N, 5.43.

Preparation of 121. trans-2-Hydroxybicyclo[4.1.0]heptane (472 mg) gave 951 mg (87\%) of crude p-nitrobenzoate 121. Recrystallization from hexane gave 764 mg of 121, \(^9\) mp 85-87°.

Preparation of 122. cis-2-Hydroxybicyclo[4.1.0]heptane (2.238 g) gave 4.88 g (94\%) of crude p-nitrobenzoate 122. Recrystallization from hexane gave 4.29 g of 122, \(^9\) mp 83-85°.

Preparation of 120. Alcohol 101 (77.4 mg) gave 107 mg (54\%) of p-nitrobenzoate 120 as a light yellow oil which crystallized on

standing. Recrystallization from hexane gave an analytical sample of \( \text{120}\), mp 45-46.5\(^\circ\). The nmr (CDCl\(_3\)/TMS) of \( \text{120}\) showed: \( \tau \) 1.72 (4H, s), 4.10-4.80 (5H, m), 6.90-7.12 (2H, m), 7.20-7.50 (2H, m).

**Anal.** Calcd m/e for C\(_{14}\)H\(_{13}\)NO\(_2\): 259.0845.

Found: 259.0847.

**Preparation of 123.** Cyclohepten-3-ol\(^{10}\) (974 mg) gave 1.453 g (64\%) of p-nitrobenzoate \( \text{123}\) after recrystallization from hexane, mp 53-54\(^\circ\) (lit\(^{11}\) mp 53.1-53.3\(^\circ\)).

**Preparation of 127.** A mixture of 26.8 g of 1,4-cyclohexadiene and 6 g of dichloromethylchloroethyl ether was cooled in an ice-salt bath. Forty-four ml of 1.0 M methyllithium (prepared from lithium wire and methyl iodide in ether) was added over 2 min to the cooled solution. The mixture was allowed to stir for 1 hr at 0\(^\circ\) and then allowed to warm to room temperature. Water was carefully added and the mixture was transferred to a separatory funnel. The organic phase was washed with dilute sodium thiosulfate solution, water, and saturated sodium chloride solution, followed by drying over anhydrous sodium sulfate. After filtration, the solvent and unreacted 1,4-cyclohexadiene were removed by distillation through a Vigreux column. The residue was distilled to give 3.6 g (54\%) of a

10. A sample was supplied by Dr. E.A. Williams.

mixture of chloroethers 127, bp 73-76° (1.0 mm). Chloroethers 127 had the following spectral properties: nmr (CDCl₃/τMS) τ 4.20-4.60 (2H, m), 6.00-6.85 (5H, m), 7.55-7.90 (4H, m), 8.60-9.20 (2H, m).
The nmr indicated a mixture of isomers with the endo-isomer predominating in a ratio of 2:1.

Found: C, 62.46; H, 7.63; Cl, 20.41.

Preparation of alcohols 128 and 129. Chloroether 127 (6 g) was dissolved in 100 ml of ether and the mixture was cooled in an ice bath. A solution of 82 ml of n-butyllithium (1.9 M) in hexane was rapidly added to the cold solution. The mixture was allowed to warm to room temperature and stirring was continued for 2 hr. Water was carefully added and the mixture was transferred to a separatory funnel. The organic phase was separated, washed with water and saturated sodium chloride solution. After drying over anhydrous sodium sulfate and filtering, the solvent was removed by distillation through a Vigreux column. The residue was distilled to give 2.75 g (78%) of a mixture of alcohols 128 and 129, bp 55-58° (1 mm). The mixture of alcohols was unstable and, hence, was separated and converted to derivatives as soon as possible. Alcohols 128 and 129 were separable by preparative vpc on column A. The major alcohol, 128, mp 57-59°, had the following spectral properties: nmr (CDCl₃/τMS) τ 4.28 (2H, broad s), 6.50 (1H, t, J = 7.0 Hz), 7.50-7.85 (4H, m), 8.50 (1H, broad s, exchanges with D₂O), 8.85-9.15 (2H,
m). Alcohol 128 had the following spectral properties: nmr (CDCl₃/TMS) τ 4.50 (2H, m), 6.62 (1H, t, J = 2.5 Hz), 6.60-7.10 (1H, broad s), 7.60-7.75 (4H, m), 8.70-8.90 (2H, m).

The stereochemical assignments in alcohols 128 and 129 were based on the magnitude of coupling between the carbinyl proton and the protons at the ring fusion. For a cis relationship between these protons, the coupling constant will be approximately 7 Hz, whereas the trans coupling constant will be approximately 2.5 Hz. Hence, alcohol 128 with J = 7.0 Hz was assigned the endo configuration, and alcohol 129 with J = 2.5 Hz was assigned the exo-configuration.

Preparation of 130. endo-Alcohol 128 (58.6 mg) was dissolved in 0.5 ml of pyridine. A solution of 141 mg of p-toluenesulfonyl chloride in 2 ml of pyridine was added dropwise to the cooled solution. After storing at -5°C for 24 hr, the mixture was poured into water and extracted with two 20-ml portions of ether. The combined ether extracts were washed with water, dilute potassium bisulfate solution, dilute potassium bicarbonate solution, and saturated sodium chloride solution. The organic phase was dried over anhydrous sodium sulfate, filtered, and the solvent was removed on a rotary evaporator to give 130 mg (93%) of crude tosylate 130, mp

92-93°. Recrystallization from hexane gave an analytical sample, mp 96-97°. Tosylate 13 had the following spectral properties:
nmr (CDCl₃/TMS) τ 2.40 (1H, doublet of doublets), 4.47 (2H, broad s), 5.83 (1H, t, J = 7.0 Hz), 7.54 (3H, s), 7.65-8.05 (4H, m), 8.65-9.00 (2H, m).

Anal. Calc. for C₁₄H₁₆O₃S: C, 63.61; H, 6.10.
Found: C, 63.64; H, 6.20.

Preparation of 13. Trifluoromethanesulfonic anhydride 13 (324 mg) was placed in a 5 ml round bottom flask equipped with a magnetic stirrer. Two ml of pyridine was added to the cooled anhydride and the solid which formed was eventually dissolved. A solution of 84 mg of alcohol 128 in 1 ml of pyridine was added to the mixture at 0°. The mixture was stored at -5° for 18 hr and then poured into water, and extracted with two 15-ml portions of ether. The combined ether extracts were washed with water, dilute potassium bisulfate solution, dilute potassium bicarbonate solution, and saturated sodium chloride solution. The organic phase was dried over anhydrous sodium sulfate, filtered, and the solvent was removed on a rotary evaporator. The residue (168 mg, 94%) had the following spectral properties: nmr (CDCl₃/TMS) τ 4.35 (2H, broad s), 5.43 (1H, t, J = 7.0 Hz), 7.45-7.90 (4H, m), 8.50-8.85 (2H, m).

Kinetics in Anhydrous Acetic Acid

Reagents. Anhydrous acetic acid was prepared by refluxing a solution of acetic anhydride and sodium acetate in glacial acetic acid for 24 hr and subsequent fractional distillation in a dry atmosphere. Standard sodium acetate (0.10 M) was prepared by careful dilution of a mixture of 0.8203 g of reagent grade sodium acetate and 1.00 g of acetic anhydride to 100 ml with anhydrous acetic acid. The resulting solution contained 1% acetic anhydride. Standard perchloric acid in acetic acid was prepared by the addition of 70% perchloric acid to a mixture of anhydrous acetic acid and acetic anhydride such that 1% acetic anhydride remained after the water was removed, followed by standing at room temperature for 12 hr before use. The molarity of the standard perchloric acid in acetic acid was determined by potentiometric titration of an aliquot vs. potassium acid phthalate in anhydrous acetic acid.

Procedure. The kinetic procedure followed was essentially that of Winstein and coworkers. A known amount of a given tosylate was diluted to 10 ml with 0.10 M sodium acetate in anhydrous acetic acid containing 1% acetic anhydride. For each particular kinetic run, 1 ml aliquots were titrated at given time with perchloric acid in anhydrous acetic acid using a Metrohm E 436 automatic recording

titrator for the determination of the end point. All rate constants were determined using an infinity titer which agreed within 1% of the calculated value. Rate constants were calculated by the method of least squares as calculated by computer. Activation parameters were also calculated by computer. All solvolytic runs in buffered acetic acid gave excellent first order plots through greater than 75% reaction.

**Kinetics in 70% Aqueous Acetone**

Reagents. A solution of 70:30 v/v acetone:water was prepared by mixing 149.625 g of distilled water with 274.75 g of 99.5% reagent grade acetone. Solutions were prepared gravimetrically to permit greater reproducibility, independently of temperature. The mixture produced corresponds to a 70:30 v/v mixture at 25.0°C. Standard sodium hydroxide was prepared by dilution of a stock solution of carbonate free sodium hydroxide solution. The molarity of the standard solution was determined by titration vs potassium acid phthalate using phenolphthalein as an indicator.

Procedure. The kinetic procedure followed was essentially the same as in anhydrous acetic acid. A known amount of a given p-nitrobenzoate was dissolved in 10 ml of 70% aqueous acetone. For each particular kinetic run, 1 ml aliquots were titrated using a Methrohm E 436 automatic recording titrator with standard sodium hydroxide solution. All rates were determined using an infinity titer except
in the case of p-nitrobenzoate \( \text{In} \) were calculated infinity titers were used. In the case of p-nitrobenzoate, the observed infinity titer was only 72% of the calculated value, consistent with the observed internal return to produce unreactive p-nitrobenzoate.

Solvolyis of 98 in Anhydrous Acetic Acid--Product Analysis. TOSyorlate 98 (1.09 g) was dissolved in 25 ml of anhydrous acetic acid containing 0.379 g of sodium acetate. The mixture was allowed to stand at room temperature for 19 hr. The mixture was then poured into 60 ml of water and extracted with three 25-ml portions of ether. The combined ether extracts were washed with two portions of water, followed by dilute sodium hydroxide solution until the aqueous phase remained basic. The ether was then dried over anhydrous sodium sulfate and filtered. The filtrate was added dropwise to 0.50 g of lithium aluminum hydride in 20 ml of ether and the mixture was stirred at room temperature for 1 hr. Three ml of 10% sodium hydroxide was then carefully added and stirring was continued for 1 hr. The aluminum salts were removed by filtration and the solvent was separated from the filtrate by careful distillation. The products were isolated by preparative vpc on column A at 75°. The major product (52%) was identified as cycloheptatriene by ir comparison with an authentic sample. The major alcohol, 101, (3%) had the following spectral properties: nmr (CDCl3/TMS) \( \delta \) 4.25 \( (4H, m) \), 5.60 \( (1H, m) \), 7.16 \( (2H, m) \), 7.51 \( (2H, m) \), 7.51 \( (1H, s, \text{exchanges with } D_2O) \).
Anal. Calcd m/e for C7H10O: 110.0731.

Found: 110.0732.

The minor alcohol product, 100, (11%) was identical by ir and nmr comparison to the major alcohol produced in the dibromination of bromoalcohols 105. The yields given are vpc yields using column A at 70° with cyclohexanone as an internal standard to correct for gc detector response.

Solvolyis of 98 in Aqueous Diglyme Containing Sodium Borohydride.

A mixture of 1.637 g of tosylate, 98, 2.093 g of sodium borohydride, 0.491 g of sodium hydroxide, 19 ml of diglyme, and 8 ml of water was stirred at 30° for 5 hr. During this time the mixture became homogeneous. The mixture was then poured into water and extracted with two 25-ml portions of pentane. The combined pentane extracts were washed with three portions of cold water and then dried over anhydrous sodium sulfate. After filtration, the solvent was removed by careful distillation through a Vigreux column. The residue (422 mg, 72%) was analyzed on column B at 110°. The major product, 1,4-cycloheptadiene, 117, (35%) had the following spectral properties: nmr (CDCl3/TMS) τ 4.20 (4H, m), 7.10 (2H, m), 7.72 (4H, m).

The peak with the shortest retention time was cycloheptatriene, 99, (13%) which was identified by ir comparison with an authentic sample. Norcarene, 116, (13%) was identified by ir and nmr comparison with an authentic sample. The peak with longest retention

15. Spectra were supplied by Dr. T.J. Atkins.
time was identified as tricyclic hydrocarbon \( \text{115} \) (11\%) by comparison of the ir spectrum of authentic sample.

Solvolyis of p-Nitrobenzoates \( \text{118, 119, 120, 135} \). Product Analy-
sis—General Procedure. A given p-nitrobenzoate was dissolved in 70\% aqueous acetone containing 1.5 equivalents of triethylamine or 2,6-lutidine. The mixture was heated in a sealed tube at an appropriate temperature for approximately 10 half-lives, poured into water, and extracted with ether. The ether extract was washed with water, dilute potassium bisulfate solution, potassium bicarbonate solution, saturated sodium chloride solution, and dried over anhy-
drous sodium sulfate. After filtration, the solvent was removed by distillation through a Vigreux column. The products were separated by preparative vpc using column A and identified by spectral com-
parison with authentic samples. Yields were determined by vpc on column A using cyclohexanone as an internal standard. A control experiment showed that alcohols \( \text{100 and 106} \) were unstable under the reaction conditions, being slowly converted to cycloheptatriene with alcohol \( \text{100} \) converting at a faster rate than alcohol \( \text{106} \). This con-
version was slower when triethylamine was used as a buffer. Table VI gives the ratio of alcohols \( \text{101 and 100} \) produced in the solvoly-
sis of various esters.
Table I. Product Ratios in Solyolysis of Esters

<table>
<thead>
<tr>
<th>Starting Ester</th>
<th>Temperature</th>
<th>Ratio, 101/100</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="TsO" /></td>
<td>25°</td>
<td>3</td>
</tr>
<tr>
<td><img src="image" alt="OPNB" /></td>
<td>120°</td>
<td>15&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="OPNB" /></td>
<td>120°</td>
<td>4.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="OPNB" /></td>
<td>120°</td>
<td>13&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="OPNB" /></td>
<td>120°</td>
<td>4.2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="OPNB" /></td>
<td>120°</td>
<td>11.8&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="Tfo" /></td>
<td>80°</td>
<td>9.0</td>
</tr>
</tbody>
</table>

a) 2,6-lutidine buffer  (b) triethyl amine buffer.
PART II

REDUCTIVE CLEAVAGE OF SUCCINIC ESTERS UNDER ACYLOIN CONDITIONS

1-Methylcyclohexane-cis-1,2-dicarboxylic acid dimethyl ester (31).

A mixture of 7.0 g of saturated anhydride, 50 ml of methanol and 3 ml of concentrated sulfuric acid was refluxed for 8 hr. The mixture was poured into 200 ml of water and extracted with two 100-ml portions of ether. The combined ether extracts were washed with sodium carbonate solution and saturated sodium chloride solution. The organic phase was then dried over anhydrous magnesium sulfate, filtered and the solvent was removed on a rotary evaporator to give 6.8 g (78%) of diester 31, bp 85-87° (0.20 mm) [lit16 bp 98° (2 mm)]. Diester 31 had the following spectral properties: IR C=O 5.75; nmr (CDCl3/TMS) δ 6.33 (6H, s), 6.40 (1H, t, J = 6.5 Hz), 7.74-8.66 (8H, m), 8.70 (3H, s).

Alkylation of 1-Methyl-cis-1,2-dicarboxylic acid dimethyl ester (31).

Into a 3-necked 5-l flask fritter with a mechanical stirrer under a nitrogen atmosphere, was transferred 3600 ml of a 0.173 M solution

of trityl sodium\textsuperscript{17} in ether by means of nitrogen pressure. 1-Methyl-cis-1,2-dicarboxylic acid dimethyl ester (3\textsubscript{1}) (87 g) was added and the mixture was stirred for 3 hr at room temperature. Methyl iodide (125 ml) was added and the mixture was stirred for 3 hr at room temperature followed by reflux for 12 hr. Water (500 ml) was added and the mixture was poured into a 5-l separatory funnel. The organic phase was separated and dried over anhydrous sodium sulfate. The solution was filtered and the ether was removed on a steam bath.

The residue was distilled through a Vigreux column and the fraction boiling from 100\degree to 170\degree was collected. (The wide boiling point range was due to superheating caused by the large amounts of tri-phenylmethane produced in the reaction). Gas chromatographic analysis on column B showed the absence of any starting diester 3\textsubscript{1}. The yield of the mixture of diesters 27 and 28 was 35.0 g (58\%).

Saponification of the mixture of diesters 27 and 28. Sodium hydroxide (44 g) was dissolved in a mixture of 60 ml of water and 125 ml of absolute ethanol. The mixture of diesters 27 and 28 obtained from the alkylation (65.0 g) was added and the mixture was refluxed for 2 days. Most of the ethanol was removed by distillation and enough water was added to redissolve the residue. The mixture was then added to a solution of 140 ml of concentrated hydrochloric acid in 200 ml of water. Following completion of the acidification, the

mixture was warmed on a steam bath for 15 min. The precipitated solution was cooled in a refrigerator overnight. The mixture of diacids 32 and 34 was collected by filtration and air dried. The mixture of diacids obtained was 51.6 g (92%), mp 195-245°.

trans-1,2-Dimethylcyclohexane-1,2-dicarboxylic acid (34). A mixture of 5 g of cis- and trans-1,2-cyclohexane-1,2-dicarboxylic acids (32 and 34) obtained by saponification of the mixture of diesters 27 and 28, was placed in a 25 ml flask and heated at 205-210° for 15 min. The entire mixture was then transferred to a separatory funnel with 200 ml of ether and extracted with 10% potassium bicarbonate solution until no further reaction occurred. The aqueous extracts were filtered and added to excess 20% hydrochloric acid. The precipitated trans-diacid 34 was collected by filtration and air dried to give 2.5 g, mp 268° (dec with anhydride formation).

trans-1,2-Dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (27). Fifty ml of ether was added to 8.8 g of trans-diacid 34 and an ethereal solution of diazomethane was added until the yellow color persisted. The ether solution was filtered and the solvent removed on a steam bath. The residue was distilled to give 9.0 g (90%) of diester 27, bp 89° (0.20 mm). Diester 27 had the following spectral properties: ir (neat) C=O 5.75; nmr (CDCl3/TMS) δ 6.34 (6H, s), 7.85-8.60 (6H, m), 8.68 (6H, s).

Found: C, 62.86; H, 8.72.

cis-1,2-Dimethylcyclohexane-1,2-dicarboxylic acid anhydride (32).

Anhydride 32 was prepared by the method of Woodward and Loftfield.¹⁸

cis-1,2-Dimethylcyclohexane-1,2-dicarboxylic acid (32). cis-1,2-

Dimethylcyclohexane-1,2-dicarboxylic acid anhydride was dissolved in 100-ml of ether and 50-ml of 10% potassium carbonate solution was added. The mixture was stirred for 2 hr. The aqueous phase was separated and the organic phase was extracted with another 50 ml of 10% potassium bicarbonate solution for 2 hr. The combined aqueous phases were added to excess 10% hydrochloric acid with stirring, and the mixture was cooled in an ice bath. The product was collected by filtration and air dried to give 4.0 g (91%) of diacid 32, mp 191° (dec with anhydride formation) [lit¹⁸ mp 164-

168°]. Diacid 32 was prepared by Woodward and Loftfield by refluxing the anhydride with water. This was found in this laboratory to give a mixture of diacid and anhydride. The procedure described above is a superior method for preparing the pure diacid.

cis-1,2-Dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (28).

Diacid 32 (1.8 g) was dissolved in 20 ml of tetrahydrofuran and an

The ethereal solution of diazomethane was added until the yellow color persisted. The solvents were removed by distillation and the residue was distilled to give 1.7 g (86%) of diester 28, bp 72-73° (0.12 mm). Diester 28 had the following spectral properties: ir (neat) $\nu$=0 5.75 $\mu$; nmr (CDCl$_3$/TMS) $\tau$ 6.34 (6H, s), 7.80-8.64 (8H, m), 8.79 (6H, s).

**Anal.** Calcd for C$_{12}$H$_{20}$O$_4$: C, 63.13; H, 8.85.

Found: C, 63.01; H, 8.71.

Acyloin condensation of trans-1,2-dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (27) with sodium in toluene with added chlorotrimethylsilane. Sodium (4.6 g) was dispersed in 300 ml of dry toluene under nitrogen. Chloromethylsilane (24.5 g) was slowly added to the dispersion. A solution of 8.5 g of diester 27 in 100 ml of toluene was added dropwise to the refluxing solution over a 6 hr period. Reflux was continued for 11 hr. The solution was allowed to cool and then filtered through celite. The solvent was removed by distillation at 60° under reduced pressure. The residue was distilled to give 10.2 g (81%) of the cyclooctadiene 27, bp 62-65° (0.13 mm). The cyclooctadiene 27 had the following spectral properties: nmr (CDCl$_3$/CHCl$_3$) $\tau$ 7.85-8.20 (4H, m), 8.35 (6H, s), 8.60-9.25 (4H, m), 9.92 (18H, s).

**Anal.** Calcd for C$_{16}$H$_{32}$O$_2$Si$_2$: C, 61.48; H, 10.32.

Found: C, 61.35; H, 10.17.
Acyloin condensation of diester 27 with sodium-potassium alloy in benzene at room temperature with added chlorotrimethylsilane.

Sodium-potassium alloy was prepared from 7.4 g of sodium and 12.8 g of potassium under benzene and transferred via syringe into 250 ml of dry benzene in a flask fitted with a vibromixer. A solution of 9.0 g of trans-diester 27 and 17.3 g of chlorotrimethylsilane in 150 ml of benzene was added dropwise over an 8 hr period. The reaction was left vibrating at room temperature for 22 hr. The mixture was then centrifuged and filtered through celite. The benzene was removed at approximately 20° using reduced pressure. The ir of the crude material was identical to that of 27. A 100 mg sample of the crude reaction product was sealed under nitrogen and heated at 200° for 1.5 hr. The ir of this material remained unchanged. The crude residue was then distilled to give 7.0 g (57%) of material with an identical ir and nmr to that of 27, bp 72° (0.2 mm).

Acyloin condensation of cis-1,2-dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (28) with sodium in toluene with added chlorotrimethylsilane. Sodium (5.8 g) was dispersed in 300 ml of dry toluene. Chlorotrimethylsilane (140.5 g) was added to this mixture. Reflux was continued as a solution of 11.3 g of cis-diester 28 in 140 ml of toluene was added dropwise over a 3 hr period. Reflux was continued for 8 hr. The mixture was then allowed to cool and was filtered through celite. Toluene was removed by distillation
at reduced pressure. The residue was distilled to give 13.8 g (88%) of bistrimethylsilyl ether \(\frac{45}{45}\), bp 68-70° (0.10 mm). Bistrimethylsilyl ether \(\frac{45}{45}\) had the following spectral properties: nmr (CDCl\(_3\)) \(\tau 8.55\) (8H, broad s), 9.00 (6H, s), 9.80 (18H, s).

**Anal.** Calcd for C\(_{16}\)H\(_{32}\)O\(_5\)Si\(_2\): C, 61.48; H, 10.32.

**Found:** C, 61.69; H, 10.14.

**Esterification of Dimethylsuberic acid.** Dimethylsuberic acid\(^{19}\) (12.2 g) was dissolved in 100 ml of dry methanol and 50 ml of acetone dimethyl ketal. Sulfuric acid (0.5 ml) was added and the mixture was refluxed for 2 hr and then allowed to stand at room temperature for 8 hr. The mixture was then poured into water and extracted with two portions of ether. The combined ether extracts were washed with water, potassium bicarbonate solution, saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. After filtration, the ether was removed on a steam bath and the residue was distilled to give 13.6 g (98%) of dimethylsuberic acid dimethyl ester, \(\frac{42}{42}\), bp 85-86° (0.3 mm). Diester \(\frac{42}{42}\) had the following spectral properties: ir (neat) C=O 5.72 \(\mu\); nmr (CDCl\(_3\)/TMS) \(\tau 4.32\) (6H, s), 7.58 (2H, m), 8.63 (8H, m), 8.85 (6H, d, J = 7 Hz).

**Anal.** Calcd C\(_{12}\)H\(_{22}\)O\(_4\): C, 62.58; H, 9.63.

**Found:** C, 62.56; H, 9.62.

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Acylloin condensation of dimethylsuberic acid dimethyl ester (42).

Sodium (6.5 g) was dispersed in 300 ml of refluxing toluene and 26.0 g of chlorotrimethylsilane was added. A solution of 10.0 g of diester 42 in 150 ml of toluene was added dropwise over an 8 hr period. Refluxing was continued for 18 hr. The mixture was then cooled and filtered through celite. Toluene was removed under reduced pressure. The residue was distilled to give 9.3 g (68%) of bistrimethylsilyl ether, \( \text{H}_3 \text{Si} \), bp 83-91°C (0.45 mm). Bistrimethylsilyl ether, \( \text{H}_3 \text{Si} \), had the following spectral properties: nmr (CDCl₃) \( \tau 7.40 \) (2H, m), 8.42 (8H, m), 8.80-9.06 (6H, doublet of doublets with doublet at 8.92, \( J = 7 \) Hz and doublet at 8.98 \( J = 7 \) Hz indicating a mixture of cis-trans-methyl group isomers), 9.76 (18H, d, separated by 1.5 Hz indicating a mixture of isomers).

**Anal. Calcd for \( \text{C}_{16}\text{H}_{34}\text{O}_{2}\text{Si} \): C, 61.08; H, 10.89.**

**Found: C, 61.31; H, 10.82.**

Bromination of bistrimethylsilyl ether, \( \text{H}_3 \text{Si} \). Bistrimethylsilyl ether, \( \text{H}_3 \text{Si} \) (3.0 g) was dissolved in 10 ml of carbon tetrachloride. The solution was cooled in a dry ice bath until the solvent began to freeze. A solution of 1.53 g of bromine in 5 ml of carbon tetrachloride was added dropwise with stirring to the freezing solution. Upon completion of the addition, the solvent was removed under vacuum as the mixture was allowed to warm to room temperature. The mixture was warmed at 35°C under vacuum of 25 mm for 3 hr. The residue was then distilled to give 1.4 g of diketone \( \text{H}_2 \text{Si} \) (87%).
bp 51-53° (0.3 mm). Diketone 4\(\text{lb}\) had the following spectral properties: nmr (CDCl\(_3\)/TMS) \(\tau\) 6.70-7.60 (2H, broad m), 7.70-8.74 (6H, m), 8.76-9.00 (6H, doublet of doublets containing a doublet at 8.85, \(J = 7 \text{ Hz}\), and a doublet at 8.93, \(J = 7 \text{ Hz}\) indicating a mixture of isomers). Approximately 5% of enol 4\(\text{la}\) was indicated by a weak singlet at \(\tau\) 8.05 (olefinic methyl group of 4\(\text{la}\)).

Anal. Calcd m/e for C\(_{10}\)H\(_{16}\)O\(_2\): 168.11502.

Found: 168.11527.

Acid catalyzed equilibration of diketone 4\(\text{lb}\). The keto-enol mixture, 4\(\text{lb}\), obtained by bromination of 4\(\text{l}\) (204 mg) was dissolved in 5 ml of tetrahydrofuran and 2 ml of 2 M hydrochloric acid was added. The mixture was refluxed for 14 hr, then poured into 15 ml of water and extracted with two 15-ml portions of ether. The combined ether extracts were washed with 10% potassium bicarbonate solution and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the ether by distillation. The residue was distilled to give 179 mg of product. The enol content had not changed substantially as indicated by nmr (weak singlet at \(\tau\) 8.05 remained unchanged). The major change that occurred was a reduction of the doublet at \(\tau\) 8.85, indicating methyl group equilibration. The nmr and ir of this mixture was now identical to that obtained after acid catalyzed equilibration of 4\(\text{la}\), obtained by methanolysis of bistrimethylsilyl ether 27.
Methanalysis of bistrimethylsilyl ether, 37. Bistrimethylsilyl ether, 37, 2.1 g was refluxed with 15 ml of methanol for 48 hr. The solvent was then removed by distillation at reduced pressure. The residue was distilled to give 1.0 g of 41a (90%), bp 53° (0.14 mm), showing the following nmr: (CDCl₃/TMS) δ 5.10 (0.35H, s, enol hydrogen which exchanges with D₂O), 6.70-7.60 (2H, broad m), 7.70-9.00 (12.6Hz, m, with singlet at 8.05 assigned to olefinic methyl group of enol form, 8.92, doublet, J = 7 Hz, assigned to methyl group of the enol form, 8.93, doublet, J = 7 Hz, assigned to the methyl groups of the keto form). Integration of the enolic hydrogen indicates approximately 35% enol content.

Anal. Calcd m/e for C₁₀H₁₈O₂: 168.11502.

Found: 168.11527.

Acid catalyzed equilibration of 41a. The keto-enol mixture, 41a, (204 mg) obtained by methanalysis of bistrimethylsilyl ether, 37, was dissolved in 5 ml of tetrahydrofuran and 2 ml of 2 M hydrochloric acid was added. The mixture was refluxed for 14 hr, then poured into 15 ml of water and extracted with two 15-ml portions of ether. The combined ether extracts were washed with 10% potassium bicarbonate solution and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the solvent by distillation. The residue was distilled to give 167 mg of product. The nmr indicated approximately 5% enol still remained. The peaks due to enol
at \( \tau 3.10, 8.05, \) and 8.92 had decreased substantially. A new doublet, \( J = 7 \text{ Hz} \), appeared at \( \tau 8.85 \) and was assigned to the methyl group(s) in one of the isomers of \( \text{H}_{11} \). The nmr and the ir of this mixture was now identical to that obtained after acid catalyzed equilibration of \( \text{H}_{11} \), obtained by bromination of tribromomethylsilylether, \( \text{H}_{13} \).

Reaction of cis-1,2-dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (28) with sodium in liquid ammonia. A solution of 2.9 g of diester 28 was added dropwise to a stirred solution of 2.0 g of sodium in 200 ml of liquid ammonia at dry ice temperature over a 4 hr period. Upon completion of the addition, the ammonia was allowed to evaporate. Ether (200 ml) was added followed by a solution of 10 g of ammonium chloride in 100 ml of water. The organic phase was then separated and the aqueous phase was extracted with another 100 ml of ether. The combined ether extracts were washed with water, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The ether was then filtered and solvent removed on a steam bath. The residue (1.8 g) was sublimed to give 1.5 g (70%) of \( \alpha \)-hydroxyketone \( \text{H}_{17} \). \( \alpha \)-Hydroxyketone \( \text{H}_{17} \) had the following spectral properties: ir (nujol) \( 0-H \ 2.90 \mu, \ C=O 5.62 \mu; \) nmr (CDCl\(_3\)/TMS) \( \tau 5.12 \) (1H, d, \( J = 7 \text{ Hz} \)), 6.11 (1H, d, \( J = 7 \text{ Hz} \)), 8.0-9.2 (1\( \alpha \)H, m containing singlets at \( \tau 8.68, 8.85, 8.98, \) and 9.10).

Anal. Calcd m/e for C\(_{10}\)H\(_{16}\)O\(_2\): 168.11502.
Found: 168.11527.
Hydrolysis of bistrimethylsilyl ether, $\text{H}_2$. A solution of 3.1 g of bistrimethylsilyl ether $\text{H}_2$ was refluxed with 20 ml of methanol for 5 hr. The solvent was removed under vacuum. The crude residue (1.50 g, 90%) was identical by ir and nmr to the product obtained by treatment of diester $\text{H}$ with liquid.

Reaction of trans-1,2-dimethylcyclohexane-1,2-dicarboxylic acid dimethyl ester (27) with sodium in liquid ammonia. Liquid ammonia (800 ml) was condensed in a 2 liter round bottomed flask. Sodium (4.78 g) was added with stirring and the mixture was cooled in a dry ice bath. A solution of 11.4 g of trans-diester, 27, in 450 ml of dry ether was added dropwise over a 6 hr period. Stirring was continued for 18 hr. A solution of 22 g of ammonia chloride in 100 ml of water was added slowly. The ammonia was then allowed to evaporate. After 24 hr, 500 ml of ether was added and the remaining ammonia was neutralized with dilute hydrochloric acid. The organic phase was then separated and dried over anhydrous sodium sulfate. The ether solution was filtered and the solvent was removed on a steam bath. The residue was distilled to give 6.1 g (53%) of diester $\text{H}2$, identical in all respects to an authentic sample prepared by esterification of dimethylsuccinic acid.

endo-cis-Norbornene-2,3-dicarboxylic acid dimethyl ester ($\text{H}2$).

cis-Diester $\text{H}2$, bp 86° (0.2 mm) was prepared by methanol esterification-
tion of the corresponding diacid, \([\text{lit}^{20} \text{ bp } 139^\circ (13 \text{ mm})]\).

**trans-Norbornene-2,3-dicarboxylic acid dimethyl ester (57).** trans-Diester 57, bp 82° (0.2 mm) was prepared by the Diels-Alder addition of dimethylfumarate to cyclopentadiene, \([\text{lit}^{21} \text{ bp } 132^\circ (9 \text{ mm})]\).

**endo-cis-Norbornane-2,3-dicarboxylic acid dimethyl ester (59).** cis-Diester 59, bp 82-85° (0.25 mm) was prepared by catalytic hydrogenation of unsaturated cis-diester 55, \([\text{lit}^{22} \text{ bp } 152^\circ (14 \text{ mm})]\).

**trans-Norbornane-2,3-dicarboxylic acid dimethyl ester (61).** trans-Diester 61, bp 75-77° (0.12 mm) was prepared by catalytic hydrogenation of unsaturated trans-diester 57, \([\text{lit}^{22} \text{ bp } 165^\circ (50 \text{ mm})]\).

**cis-Cyclopropane-1,2-dicarboxylic acid dimethyl ester (48).** cis-Diester 48, bp 69-71° (0.7 mm) was prepared by diazomethane esterification of the corresponding diacid, \([\text{lit}^{23} \text{ bp } 112^\circ (20 \text{ mm})]\).

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trans-Cyclopropane-1,2-dicarboxylic acid dimethyl ester (49).

trans-diesters bp 57-59° (0.8 mm) was prepared by diazomethane esterification of the corresponding diacid, [lit23 bp 103-104° (24 mm).

Reaction of 1,2-diester with sodium in liquid ammonia—General procedure. A solution of the appropriate 1,2-diester in anhydrous ether was added dropwise over a 3 to 4 hr period to a solution of sodium in liquid ammonia at dry ice temperature. Upon completion of the addition, the ammonia was allowed to evaporate. Ether was added to the solid residue, followed by a solution of ammonium chloride in water. The aqueous phase was separated and extracted with another portion of ether. The combined ether extracts were washed with water, saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the solvent was evaporated on a steam bath. The product was isolated by distillation of the residue.

Reaction of endo-cis-norbornene-2,3-dicarboxylic acid dimethyl ester (55) with sodium in liquid ammonia. cis-Diesters 55 (6.0 g) in 85 ml of ether was reacted with 3.0 g of sodium in 400 ml of liquid ammonia in the usual manner. Distillation of the residue gave 4.35 g (72%) of diester 58, bp 87° (25 mm). Diester 58 had the following spectral properties: ir (neat) C=0 5.72 µ; nmr (CDCl3/TMS) τ 4.30 (2H, s), 6.32 (6H, s), 6.92 (2H, q, J = 7 Hz), 7.25-7.80 (5H, m),
8.93 (1H, doublet of triplets, J = 13 Hz, J = 8 Hz).

Anal. Calcd for C_{11}H_{16}O_{4}: C, 62.25; H, 7.60.

Found: C, 62.05; H, 7.70.

Reaction of trans-norbornene-2,3-dicarboxylic acid dimethyl ester (57) with sodium in liquid ammonia. **trans-Diester 57 (6.0 g)** in 85 ml of ether was reacted with 3.0 g of sodium in 400 ml of liquid ammonia in the usual manner. Distillation of the residue gave 2.0 g (33%) of diester 58, bp 87° (0.25 mm). This material was identical in all respects to that obtained on treatment of diester 55 with sodium in liquid ammonia.

Hydrolysis of cis-1,4-cyclopent-2-ene diacetic acid dimethyl ester (56). **Diester 56 (2.0 g)** was added to a solution of 2.1 g of potassium hydroxide in 20 ml of methanol. The mixture was refluxed for 2 hr and most of the methanol was removed by distillation at reduced pressure. Water (30 ml) was added and the solution was extracted with 20 ml of ether. The aqueous phase was acidified with concentrated hydrochloric acid, filtered, and cooled in an ice bath. Crystallization occurred after 15 min. The product was collected by filtration, washed with cold water, and air dried to give 1.0 g (61%) of crude diacid 58, bp 124-126°. Recrystallization from water (85% recovery) gave an analytical sample, mp 127°-128°.

Anal. Calcd for C_{9}H_{12}O_{4}: C, 58.69; H, 6.57.

Found: C, 58.54; H, 6.64.
Hydrogenation of cis-1,4-cyclopent-2-ene diacetic acid dimethyl ester (56). Unsaturated diester 56 (1.0 g) was dissolved in 15 ml of ether and 60 mg of palladium on carbon was added. The mixture was hydrogenated at 65 psi for 6 hr. The mixture was then filtered through celite and the ether was removed by distillation. The residue (1.0 g, 99%) was identical in all respects to the diester obtained by treatment of diesters 52 and 61 with sodium in liquid ammonia.

Reaction of endo-cis-norbornane-2,3-dicarboxylic acid dimethyl ester (52) with sodium in liquid ammonia. cis-Diester 59 (6.0 g) in 85 ml of ether was reacted with 4.0 g of sodium in 400 ml of liquid ammonia in the usual manner. Distillation of the residue gave 3.1 g (52%) of diester 60, bp 91-95° (0.3 mm). Diester 60 had the following spectral properties: ir (neat) C=O 5.72 μ; nmr (CDCl₃/TMS) τ 6.35 (6H, s), 7.40-9.10 (12H, m).

Anal. Calcd for C₁₁H₁₆O₄: C, 61.66; H, 8.47.

Found: C, 61.53; H, 8.42.

Reaction of trans-norbornane-2,3-dicarboxylic acid dimethyl ester (61) with sodium in liquid ammonia. trans-Diester 61 (6.0 g) was reacted with 4.0 g of sodium in 400 ml of liquid ammonia in the usual manner. The yield of diester 60 was 1.2 g (20%), bp 91° (0.3 mm). The product was identical in all respects to the diester ob-
tained on treatment of cis-diester 59 with sodium in liquid ammonia.

Hydrolysis of cis-1,3-cyclopentane diacetic acid dimethyl ester (60).

Diester 60 (2.0 g) was added to a solution of 2.1 g of potassium hydroxide in 20 ml of methanol. The mixture was refluxed for 2 hr and most of the methanol was removed by distillation at reduced pressure. Water (30 ml) was added and the solution was extracted with 20 ml of ether. The aqueous phase was acidified with concentrated hydrochloric acid, filtered, and cooled in an ice bath. The crystals were collected by filtration, washed with water, and air dried to give 1.3 g (83%) of 1,3-cyclopentane diacetic acid 62, mp 137-139°. The product was recrystallized from 20 ml of water (90% recovery), mp 139-140° [lit24 mp 140-141°].

Reaction of cis-cyclopropane-1,2-dicarboxylic acid dimethyl ester (48) with sodium in liquid ammonia. cis-Diester 48 (6.0 g) in 85 ml of ether was reacted with 4.0 g of sodium in 400 ml of liquid ammonia. The residue was distilled to give 1.48 g (25%) of product, which was identical in all respects to an authentic sample of dimethyl glutarate.

Reaction of trans-cyclopropane-1,2-dicarboxylic acid dimethyl ester (49) with sodium in liquid ammonia. trans-Diester 49 (6.0 g) in 85

ml of ether was reacted with 4.0 g of sodium in 400 ml of liquid ammonia. The residue was distilled to give 1.35 g (22%) of product, which was identical in all respects to an authentic sample of dimethyl glutarate.

Reaction of cis-cyclopropane-1,2-dicarboxylic acid dimethyl ester (48) with sodium in toluene with added chlorotrimethylsilane.

Sodium (3.9 g) was dispersed in 200 ml of dry toluene and 18 g of chlorotrimethylsilane was added. A solution of 5.0 g of cis-diester 48 in 75 ml of toluene was added dropwise over a 5 hr period to the refluxing solution. Upon completion of the addition, refluxing was continued for 5 hr. The solution was then cooled, filtered through celite, and the solvent removed at 50°. The residue was distilled through a Vigreux column and collected in three fractions at 0.35 mm: fraction 1, bp 41-83°; fraction 2, bp 83-93 (2.7 g); fraction 3, bp 93-105° (1.8 g). Fraction 2 showed the following nmr: (CDCl3) τ 6.57 (6H, m with 6H, s at τ 6.57), 7.41 (2H, t, J = 7.5 Hz), 9.85 (18H, s). The product 52 was not pure by nmr.

Anal. Calcd m/e for C13H28O4Si2: 304.1526.

Found: 304.1530.

Methanolysis of bisketene ketal 52. Bisketene-ketal 53 (0.3997 g of combined fractions 2 and 3) was refluxed for 30 min with 5 ml of absolute methanol. The mixture was analyzed by gas chromatography using column A at 100° with naphthalene as an internal standard.
The yield of dimethyl glutarate was 0.1735 g (identified ir comparison with an authentic sample). Assuming a quantitative conversion of bisketene ketal \(^{52}\) to dimethyl glutarate, the purity of \(^{52}\) was 82.7\%. The yield of \(^{52}\) formed by cleavage of diester \(^{48}\) was, therefore, 38\%.

Acyloin condensation of endo-cis-norbornene-2,3-dicarboxylic acid dimethyl ester (\(^{55}\)) with sodium in toluene with added chlorotrimethylsilane. Sodium (5.0 g) was dispersed in 250 ml of dry toluene. Chlorotrimethylsilane (25 g) was added. A solution of 8.0 g of diester \(^{55}\) in 100 ml of toluene was added dropwise to the refluxing solution over a 7.5 hr period. Refluxing was continued for an additional 12 hr. The mixture was then cooled to room temperature and filtered through celite. The toluene was removed by distillation at reduced pressure. The residue was distilled to give 9.7 g (86\%) of bistrimethylsilyl ether, \(^{65}\), bp 91-95° (0.27 mm). Bistrimethylsilyl ether \(^{65}\) had the following spectral properties:

\[
\text{nmr (CDCl}_3\rangle \tau 4.11 (2H, t, J = 1.9 Hz), 7.20-7.57 (4H, m), 8.30 (2H, doublet of doublets), 9.88 (18H, s).}
\]

\text{Anal. Caled for } C_{15}H_{26}O_{2}Si_{2}: \text{ C, } 61.17; \text{ H, } 8.90.

\text{Found: C, 61.36; H, 9.02.}