PREPARATION AND REARRANGEMENT OF SUBSTITUTED BICYCLO[2.2.1]HEPT-2-ENE-ANTI-7-OLS

by

Dale Francis Regelman

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I hereby recommend that this dissertation prepared under my direction by Dale Francis Regelman entitled Preparation and Rearrangement of Substituted Bicyclo(2.2.1)hept-2-ene-anti-7-ols be accepted as fulfilling the dissertation requirement for the degree of Doctor of Philosophy.

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SIGNED: [Signature]
To My Parents
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ABSTRACT

The acid-catalyzed rearrangements of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol and 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol were studied.

The bicyclic alcohols were prepared from 2,2-dimethylbicyclo[2.2.1]hept-5-ene-7-one. The intermediate bicyclic ketone was prepared from the Diels-Alder adduct of methacrolein and 1,1-diethoxy-2,3,4,5-tetrachlorocyclopentadiene by reduction of the formyl group, dechlorination and generation of the C\textsubscript{7} keto group with dilute aqueous acid.

Treatment of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol in refluxing aqueous acetic acid gave only the anti-C\textsubscript{7} acetate and starting material. Analogous treatment of 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol afforded 2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene, 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene and starting material. The bicyclic ether was identified by $^1$HMR, $^{13}$CMR, ir and mass spectral analysis. Treatment of 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol in a deuterated rearrangement reaction mixture gave analogous partially deuterated products in comparable percentages. Refluxing 2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene in aqueous
acetic acid afforded 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene and starting material.

A mechanism consistent with the isolated rearrangement products was proposed.
INTRODUCTION

Photolysis of eucarone, \( \lambda \), in 95% ethanol gives two isomeric bicyclic ketones, \( \kappa \) and \( \lambda \) (1). Treatment of each ketone with methylmagnesium iodide gives the tertiary alcohols \( \kappa \) and \( \lambda \) (Figure 1). Refluxing \( \lambda \) in aqueous acetic acid affords the bicyclic rearrangement products \( \epsilon \), \( \eta \), and \( \zeta \) (2). Analogous treatment of \( \kappa \) gives two isomeric aldehydes, \( \iota \) and \( \lambda \) (2).

Figure 2 was published by Jones and Jones (2) in 1971 to account for the rearrangement products of \( \lambda \). Protonation and dehydration of \( \lambda \) gives the tertiary cation \( \upsilon \). Migration of the \( C_1-C_7 \) bond from \( C_1 \) to \( C_2 \) gives \( \chi \).
Figure 1. Photolysis of eucarvone.
Figure 2. Rearrangement of substituted bicyclo(2.2.1)hept-5-ene-anti-7-ols via protonation of the C_5-C_6 double bond.
Proton loss from $\text{C}_1$ gives the diene $\text{C}_7$; hydration gives the $\text{C}_7$ anti-alcohol $\text{C}_6$. Protonation of the $\text{C}_5$-$\text{C}_6$ double bond gives the secondary cation $\text{C}_6$. Migration of the $\text{C}_1$-$\text{C}_2$ bond gives the tertiary monocyclic carbonium ion $\text{C}_2$. Nucleophilic attack by the alcohol forms the bicyclic ether $\text{C}_8$.

Migration of the $\text{C}_1$-$\text{C}_2$ bond to stabilize the $\text{C}_6$ cation is a bond rearrangement that has not been generally observed.

Structures $\text{C}_0$ and $\text{C}_2$ illustrate delocalization of the cation $\text{C}_0$ through participation of neighboring sigma bonds (3). Formation of $\text{C}_2$ from $\text{C}_0$ is analogous to the formation of $\text{C}_2$ from $\text{C}_1$ in Figure 2.

Relative solvolysis rates show that incorporation of a $\text{C}_1$ methyl group gives a 50 fold rate enhancement substantiating the viability of structure $\text{C}_1$ (4). Incorporating geminal methyl groups at $\text{C}_6$ gives a 25 fold rate deceleration (4).
Treating $\mathcal{Z}_0$ in trifluoroacetic acid gave the trifluoroacetate products $\mathcal{Z}_2$ and $\mathcal{Z}_4$ in equivalent amounts. The intermediate cation $\mathcal{Z}_1$, which could be stabilized by a structure analogous to $\mathcal{Z}_2$, is not formed preferentially (5).

Figure 2, if operative, would constitute an unusual carbonium ion rearrangement.
It was recognized that an alternative pathway, Figure 3, could also explain the rearrangement products. As in Figure 2 the diene $\mathcal{G}$ and the alcohol $\mathcal{H}$ arise from the $C_7$ cation $\mathcal{I}$. The bicyclic ether $\mathcal{J}$ can also arise from the same $C_7$ cation. Migration of the $C_1$-$C_2$ bond to $C_1$-$C_7$ gives the cyclopentadienyl system $\mathcal{K}$. Hydration of the tertiary cation affords the alcohol $\mathcal{L}$. Protonation of the cyclopentaienyl ring gives the allylic cation $\mathcal{M}$; attack by the alcohol affords the bicyclic ether.

The stability of the $C_7$ bicyclo[2.2.1]hept-2-enyl cation and the stereospecificity of its reactions have been well documented (6). Structures $\mathcal{A}_1$ and $\mathcal{A}_2$ illustrate delocalization of the $C_7$ cation by participation of the pi electrons from the $C_5$-$C_6$ double bond. Structure $\mathcal{A}_3$ incorporates the various resonance forms giving the bishomocyclopropenyl cationic compound (6).

Solvolysis rate data indicate that the stability of substituted bicyclo[2.2.1]heptyl and heptyl cations depends both on the nature of the $C_7$ cation and the presence or absence of the double bond. Compound $\mathcal{A}_5$, capable of
Figure 3. Rearrangement of substituted bicyclo[2.2.1]hept-5-ene-anti-7-ols via migration of the C1-C2 bond.
forming an intermediate bishomocyclopropenyl cation, solvolyses $10^{10}$ times faster than the saturated analog \( \text{44} \) (7). Compound \( \text{46} \), capable of forming an intermediate tertiary cation, reacts $10^8$ times faster than does \( \text{44} \) (7). Incorporation of both a C\(_7\) methyl and a C\(_2\)–C\(_3\) double bond, \( \text{47} \) gives a $10^{14}$ fold rate enhancement (7).

\[
\begin{align*}
\text{44} & : \quad \text{H} \quad \text{OTs} \\
& : \quad \text{1.00} \\
\text{46} & : \quad \text{CH}_3 \quad \text{OTs} \\
& : \quad 1 \times 10^8 \\
\text{45} & : \quad \text{H} \quad \text{OTs} \\
& : \quad 1.8 \times 10^{10} \\
\text{47} & : \quad \text{CH}_3 \quad \text{OTs} \\
& : \quad 1.3 \times 10^{14}
\end{align*}
\]

To investigate the viability of Figure 2 compound \( \text{50} \) was prepared. Figure 2 requires the geminal methyl functionality at C\(_2\), the C\(_5\)–C\(_6\) double bond and the anti-C\(_7\) alcohol. The absence of methyl groups at C\(_4\) and C\(_7\) should not affect the course of the rearrangement.

\[
\begin{align*}
\text{50} & : \quad \text{H} \quad \text{OH} \quad \text{CH}_3 \\
& \quad \text{CH}_3 \quad \text{CH}_3 \\
\text{51} & : \quad \text{CH}_3 \quad \text{OH} \\
& \quad \text{CH}_3 \quad \text{CH}_3
\end{align*}
\]
To study the role of the C_7 cation in the rearrangement of \( \mathcal{A} \) compound \( 51 \) was prepared. If Figure 3 is operative the nature of the C_7 cation becomes critical. With the introduction of the C_7 methyl group \( 51 \) should parallel the rearrangement of \( \mathcal{A} \) if Figure 3 constitutes the reaction pathway.
RESULTS

Preparation of Starting Materials

Gassman and Pape (8) reported the preparation of bicyclo[2.2.1]hept-2-ene-anti-7-ol from bicyclo[2.2.1]hept-2-ene-7-one in 52% yield. The desired rearrangement starting materials, 2,2-dimethyl bicyclo[2.2.1]hept-5-ene-anti-7-ol, compound $\text{5}_0$, and 2,2,7-trimethyl bicyclo[2.2.1]hept-5-ene-anti-7-ol, compound $\text{5}_1$, were prepared in an analogous fashion from 2,2-dimethyl bicyclo[2.2.1]hept-5-ene-7-one, compound $\text{5}_0$.

A Diels-Alder reaction was envisioned as the most efficient route to assemble the bicyclic carbon structure with the necessary functionality to give, eventually, compound $\text{6}_0$. Figure 4 summarizes the successful and unsuccessful Diels-Alder reactions performed. Reaction between cyclopentadienone, compound $\text{5}_2$ and isobutylene would give compound $\text{6}_0$ directly. Because of its reactivity as both diene and dienophile, cyclopentadienone cannot be prepared and isolated as a monomer. Attempts to trap the reactive monomeric dienone with other reactive dienophiles have also failed; only the dimer of compound $\text{1}_t$ is isolated in good yield (9).

Successful Diels-Alder reactions of 1,1-diethoxy-cyclopentadiene, compound $\text{5}_3$, have been reported. Eaton
Figure 4. Successful and unsuccessful Diels-Alder reactions attempted.
(10) reported reactions of \( \text{ compound } \) with tetracyanoethylene, maleic anhydride and benzoquinone in yields of 76%, 70%, and 60% respectively. Eaton (10) also reported successful addition of acrolein to give a mixture of adducts with no yield being given.

The preparation and reactions of compound \( \text{ compound } \) are summarized in Figure 5. Although compound \( \text{ compound } \) dimerizes less readily than does compound \( \text{ compound } \), it must be used directly after preparation with a large excess of dienophile to avoid dimerization. 1,1-Diethoxycyclopentane, \( \text{ compound } \), was prepared from cyclopentanone using triethylorthoformate in anhydrous ethanol. Eaton (10) reported the preparation of the dibromo-ketal, \( \text{ compound } \), by treating the ketal with two equivalents of pyridinium bromide perbromide (PBP) in ethanol "just below room temperature." Treatment of \( \text{ compound } \) with two equivalents of pyridinium bromide perbromide in ethanol at 18°C for one hour gave a back tar on work-up. Treatment of \( \text{ compound } \) in an analogous reaction mixture for thirty minutes gave a yellow oil which on attempted purification by either column chromatography or vacuum distillation decomposed into a black viscous tar. The desired dibromo ketal was subsequently prepared by stirring the ketal, \( \text{ compound } \), and two equivalents of PBP in ethanol at 15°C until no visible unreacted, orange PBP remained. This reaction time was usually about twenty-five minutes. The product was used directly after work-up without further purification.
Figure 5. Preparation and reactions of 1,1-diethoxycyclopentadiene.
Compound $\text{C}$ was prepared by treating the crude dibromoketal with a four-fold excess of potassium t-butoxide in dimethyl sulfoxide at room temperature. The crude diene was added to an excess of dienophile and the resulting reaction mixture was stirred overnight at room temperature.

Freshly distilled methacrolein was first used to trap the reactive diene. After removing solvent and excess methacrolein $^1$HMR showed no aldehydic protons; the only product seen was the dimer of $\text{C}$, compound $\text{D}$. In an attempt to duplicate Eaton's work, acrolein was used to trap the freshly prepared 1,1-diethoxycyclopentadiene. Once again no desired adduct was isolated, only the dimer of $\text{C}$ was observed.

In a private communication Eaton (11) advised that the preparation of the 2,5-dibromo ketal was actually done at 6°C, not at the somewhat higher temperature published. Eaton advised also that "these ketals dimerize very readily" and suggested that if anything other than "very reactive dienophiles" were used successful reactions were unlikely (11). 1,1-Dimethoxytetrachlorocyclopentadiene, compound $\text{E}$, was suggested as an alternate choice when working with less reactive dienophiles.

Hoch (12) reported successful Diels-Alder reactions between compound $\text{E}$ and ethylene, propylene and methyl-acrylate in 60%, 50%, and 86% yields. Reaction of $\text{E}$ with
isobutylene has not been reported but would give compound \( \text{55} \), which in two additional steps would give compound \( \text{60} \).

1,1-Dimethoxy-tetrachlorocyclopentadiene was prepared by the method of Newcomer and McBee (13) in 75\% yield. Attempts to prepare compound \( \text{55} \) from \( \text{54} \) and isobutylene were unsuccessful. Condensing an excess of isobutylene at -78°C and adding it to \( \text{54} \) at room temperature afforded no reaction at all. Adding the condensed isobutylene to \( \text{54} \) at higher temperatures gave unreacted diene and a thick viscous tar, presumably polyisobutylene.

Employing Hoch's reaction conditions, compound \( \text{54} \) and methyl methacrylate gave the Diels-Alder adduct, compound \( \text{55} \), in 86\% yield (Figure 6). Only the exo carbono-methoxy adduct was obtained. The observation that reaction of unsaturated dienophiles with cyclopentadiene usually gives the endo adduct was rationalized by Alder and Stein (14) in 1937 as a result of the principle of "maximum accumulation of unsaturation." Numerous deviations from the "endo rule" are known. Steric and/or inductive effects have been reported to favor exo addition in certain cases. Kobuke (15) reported that the rule of endo addition is of minor importance in predicting the stereoselectivities of methyl substituted dienophiles. Berson, Hamlet, and Mueller (16) reported that in Diels-Alder reactions with cyclopentadiene, methyl acrylate obeys the endo rule in all solvents but methyl methacrylate violates the endo rule in
all solvents. Berson et al. (16) stated further that other α-methyl substituted dienophiles are intermediate in their stereoselectivities, giving a mixture of exo and endo adducts.

Figure 6 summarizes the preparation and reactions of compound 55. Reaction of 55 with a four fold excess of lithium aluminum hydride gave the alcohol, compound 70, in 61% yield. Treatment of 70 with a two fold excess of p-toluenesulfonyl chloride in pyridine gave the tosylate, compound 71, in 50% yield. Analogous treatment of 70 with methanesulfonyl chloride in pyridine gave the mesylate, compound 72, in 65% yield.

Conversion of 71 to 2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene, compound 58, was not successful. Reaction of the tosylate, 71, with a five fold excess of lithium aluminum hydride in either room temperature or refluxing anhydrous ether for twenty-four hours gave unchanged starting material. Treatment in refluxing dry tetrahydrofuran gave a 20% conversion of vinyl chloride to alkene but no displacement of the tosyl group. Refluxing in di-nbutyl ether for twenty-four hours gave unchanged starting material.

Masamune, Rossy, and Bates (17) reported a method for removal of mesyloxy groups and halides in high yield. Two equivalents of lithium trimethoxyaluminum hydride in THF are added to one equivalent of dry CuI to form "some
Figure 6. Preparation of 1,4,5,6-tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene.
Cu(I) species." The authors call the reactive species "reagent I." Lithium trimethoxyaluminum hydride was prepared using Brown and Weismann (18) method; this was then added to CuI duplicating Masamune et al.'s preparation of "reagent I." Treatment of compound with the freshly prepared reagent failed to give the desired geminal dimethyl compound. A 33% conversion of vinyl chloride to alkene was, however, obtained.

In a United States Patent abstract Hamb (19) reported a successful Diels-Alder reaction between compound and 2-butenal giving the substituted 2-formyl-3-methyl-5-norbornenyl compound. Reaction of with freshly distilled commercial methacrolein gave 1,4,5,6-tetrachloro-2-formyl-2-methyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene, compound in 40% yield. The product mixture distilled over a wide temperature range (bp 120-140/1.5 mm). HMR indicated a 2.7:1 ratio of exo/endo formyl group adducts. After receiving Hamb's complete patent application it was learned that compound had previously been prepared in 57% yield. Later repetition of the synthetic scheme required the preparation of methacrolein. Formerly available at low cost, methacrolein had become a custom synthesis item. Nagai and Nakajima's (20) procedure was used to prepare methacrolein from propanal via an acid-catalyzed Aldol reaction. A 2:1 mixture of methacrolein/propanal was
obtained. Using this mixture in the Diels-Alder reaction with \( \text{5}_4 \) gave a 2.5:1 exo/endo product mixture of \( \text{5}_6 \) in 67\% yield.

Reduction of \( \text{5}_6 \) to compound \( \text{5}_8 \) proved to be a difficult task. The hydrazone of \( \text{5}_6 \), compound \( \text{7}_3 \), was prepared in 88\% yield using Zelinsky and Kasansky's (21) procedure. The product mixture contained both the syn and anti hydrazones from both the exo and endo formyl groups. Attempted crystallization of the crude product from hot ethanol gave a tan, sticky solid. Because of the difficulty in handling and transferring the hydrazone product, a Huang-Minion modification of the Wolff-Kishner reduction was employed. The Huang-Minion (22) procedure prepares the hydrazone in situ at 115°C in the presence of potassium hydroxide. The reaction mixture is then heated to higher temperature, typically 195-210°C for several hours. Treatment of \( \text{5}_6 \) with the normal Huang-Minion reaction conditions lead to degradation of the molecule.

Cram and Sahyan (23) have reported a number of Wolff-Kishner reductions done in dimethyl sulfoxide at room temperature. Augustine (24, p. 177) reports, however, that "the necessity of preparing pure hydrazones and maintaining anhydrous conditions while these are slowly (author's emphasis) added to the basic reaction medium must count as serious disadvantages." The problems encountered in
handling compound 73 precluded use of the room temperature procedure.

Brown and Garg (25) reported the partial reduction of aliphatic and aromatic nitriles to the corresponding aldehydes in 68-90% using lithium triethoxyaluminum hydride in ether. The preparation of \( \text{56} \) from the corresponding nitrile, compound \( \text{57} \), was attractive for two reasons. The preparation of \( \text{56} \) from \( \text{54} \) and methacrolein was initially a low yield reaction. The preparation of \( \text{56} \) from \( \text{54} \) via \( \text{57} \) could lead to an increase in overall per cent yield. Secondly, the Diels-Alder reaction of acrylonitrile with \( \text{54} \) might afford a more favorable exo/endo adduct ratio, i.e., methyl methacrylate which gave only the exo-carbomethoxy epimer of \( \text{55} \). This greater stereoselectivity could give, eventually, a more easily crystallized and workable hydrazone, compound \( \text{58} \). A pure, easily workable hydrazone could allow the use of Cram's low temperature procedure.

Compound \( \text{57} \), 1,4,5,6-tetrachloro,2-methyl,2-cyano-7,7-dimethoxybicyclo[2.2.1]hept-5-ene, was prepared from \( \text{54} \) and methacrylonitrile using the usual Diels-Alder reaction conditions in 85% yield. The product mixture contained a 4:1 mixture of exo/endo cyano adducts. Using Brown and Garg's procedure, conversion to the aldehyde was accomplished in 15% yield. \(^1\)HMR showed the product mixture to be a 2.5:1 ratio of exo/endo formyl groups. The preparation of \( \text{56} \) via the nitrile, \( \text{57} \), affords the same ratio of epimeric
products as did the direct synthesis from 54 and metha-
crolein. The yield of the partial reduction of the nitrile
was not maximized because of the unfavorable exo/endo
product mixture.

The inability to prepare crystalline, pure
hydrazones coupled with the degradation of compound 56 at
high reaction temperatures, necessitated the use of a low
temperature Huang-Minlon-type reduction. Gates and Tschudi
(26) reported the extensive demethylation of a dimethoxy
compound when employing the usual Huang-Minlon reactions
conditions. Lowering the reaction temperature to 150°C and
the reaction time to three hours gave the desired reduced
product without demethylation. Gates and Tschudi's reaction
conditions resulted again in degradation of 56 with no
desired product, 58, isolated.

Throughout the Wolff-Kishner type reactions no
residual aldehyde could be detected in the product mixture.
The problems encountered in these reductions reflect the
sensitivity of the entire molecule to the vigorous
reaction conditions employed.

Heating 56 with a five fold excess of hydrazine and
a six fold excess of potassium hydroxide in diethylene
glycol at 120°C for one hour gave the desired product,
1,4,5,6-tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo-
[2.2.1]hept-5-ene, 58, in 53% yield. Lowering the reaction
temperature to 100°C for one hour gave 58 in 30% yield.
Figure 7 summarizes the preparation of the 2,2-dimethylbicyclo[2.2.1]hept-5-ene-7-one, \(^{6}\), from \(^{5}\). Dechlorination of \(^{5}\) to give 2,2-dimethyl-7,7-dimethoxy-bicyclo[2.2.1]hept-5-ene, compound \(^{6}\), was accomplished using a five fold excess of cubed sodium and a two fold excess of t-butyl alcohol in dry tetrahydrofuran under an Argon atmosphere. Gassman and Pape (8) recommend vigorous stirring and the use of sufficient heat to promote a gentle reflux for eight hours. It was found that, regardless of how vigorously the heterogeneous reaction mixture is stirred, at temperatures necessary to give even a gentle reflux, the sodium cubes form one large aggregate. The available surface area of the large sodium ball is much less than the total area of the smaller cubes necessitating a longer reaction time. Sixteen to twenty hours were needed to consume all the tetrachloro starting material. Under these reaction conditions a 6:1 ratio of alkene/alkane products was obtained in a total yield of 45%. Using a reaction temperature of 45-50°C with vigorous did not cause accumulation of sodium into one large mass. The heterogeneous reaction mixture was vigorously stirred for eight hours at this reaction temperature giving the product, compound \(^{6}\), in 53% yield. No undesired alkane side products were seen by \(^{1}\)HMR under these conditions.

Table 1 summarizes the \(^{1}\)HMR chemical shifts observed for the substituted bicyclo[2.2.1]hept-5-enes and
Figure 7. Preparation of 2,2-dimethyldicyclo[2.2.1]hept-5-ene-7-one.
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bicyclo[2.2.1]heptanes. Figure 8 shows the vicinal and geminal coupling constants reported and observed for the bicyclo ring systems (27). The couplings observed in the substituted compounds compare well with the reported values. The \( \text{C}_4 \) bridgehead hydrogen splits the \( \text{C}_3 \) exo hydrogen with a four Hertz coupling constant. The \( \text{C}_4 \) hydrogen does not couple with the \( \text{C}_3 \) endo hydrogen. The \( \text{C}_3 \) hydrogens split each other with a geminal coupling constant of twelve Hertz. Jackman and Sternhell (27, p. 275) report the "geminal coupling constants in five-membered rings are not appreciably different from those in six-membered rings or freely rotating systems." Their reported geminal coupling constant for cyclohexane is 12.6 Hertz (27). Jones and Jones (2) reported twelve Hertz geminal coupling between the \( \text{C}_3 \) hydrogens in compound 6 (Figure 8). Because of the multiple couplings, the \( \text{C}_1', \text{C}_4', \text{and} \text{C}_7 \) hydrogens are observed as broad singlets. The \( \text{C}_5 \) and \( \text{C}_6 \) vinyl hydrogens appear as multiplets.

Treatment of compound \( \text{5}_0 \) with 5% sulfuric acid solution for twenty hours gave 2,2-dimethylbicyclo[2.2.1]-hept-5-ene-7-one, \( \text{5}_0 \), in 91% yield. Figure 9 summarizes the preparation of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, compound \( \text{5}_0 \), and 2,2,7-trimethylbicyclo[2.2.1]-hept-5-ene-anti-7-ol, compound \( \text{5}_1 \), from \( \text{6}_0 \).

Using Gassman and Pape's (8) reaction conditions, compound \( \text{5}_1 \) was prepared from \( \text{6}_0 \) in 52% yield. The crude
$J_{1,2}(H_2 \text{ exo})$ 3-4 Hertz  
$J_{1,2}(H_2 \text{ endo})$ 0-2 Hertz  

$J_{5,6}$ 5.1-6.0 Hertz  
$J_{1,6}$ 2.3-3.3 Hertz  
$J_{1,7}$ 0-3.5 Hertz

Literature vicinal couplings (27)

$J_{3,3}$ 12 Hertz

Literature geminal coupling (2)

$J_{3,4}(H_3 \text{ exo})$ 4 Hertz  
$J_{3,4}(H_3 \text{ endo})$ 0 Hertz  
$J_{3,3}$ 12 Hertz

Observed couplings

Figure 8. $^1$HMR coupling constants for substituted bicyclo-[2.2.1]heptenes and bicyclo[2.2.1]heptanes.
Figure 9. Reactions of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-7-one.
The orientation at C7 of 50 was determined by the chemical shift of the C7 hydrogen. Franzus and Snyder (28) reported the chemical shifts for both syn- and anti-bicyclo[2.2.1]hept-5-ene-7-ol. The configuration of the anti-epimer places the C7 hydrogen above the C5-C6 double bond. The chemical shift of this hydrogen is affected by long-range, diamagnetic anisotropic shielding and is therefore shifted upfield with respect to the syn epimer. The chemical shifts of the C7 hydrogens were reported as δ3.53 in the anti-alcohol and δ3.75 in the syn-alcohol (28).

The C7 hydrogen in compound 50 should experience a similar long-range shielding effect if the desired anti alcohol was prepared. Hydrogenation of 50 using a 10% palladium on carbon catalyst in ethanol under one atmosphere of hydrogen gave 2,2-dimethylbicyclo[2.2.1]heptan-7-ol, compound 78, in 72% yield. Figure 9 summarizes the reactions and rearrangements of 50.

The C7 hydrogen is observed at 3.70 in the alkene, 50, and at 4.07 in the alkane, 78. The 1HMR spectrum of 78 shows an upfield shift for all signals except those for the C7 hydrogen and the C2 endo methyl group. The C7 hydrogen exhibits long-range shielding in the alkene which is absent in the alkane and must, therefore, exist in the anti alcohol
configuration. The entire $^1$HMR spectrum is summarized in Table 1.

The infrared spectrum shows bands at 3600 cm$^{-1}$ and 3400 cm$^{-1}$ for O-H bond stretches. A band for olefinic C-H stretching is seen at 3030 cm$^{-1}$. Mass spectral data of $\text{5}_0$ is summarized in Table 2.

2,2,7-Trimethylbicyclo[2.2.1]hept-5-ene-anti-7-01, compound $\text{5}_1$, was prepared in 83% yield from $\text{6}_0$ by treatment with methyl magnesium iodide in ether at room temperature followed by workup with saturated ammonium chloride solution (Figure 9). The crude product mixture was separated and purified by gas chromatography. Five fractions were collected in 18%, 3%, 5%, 1%, and 73% respectively of the product mixture. Fractions 2 and 4 were determined by $^1$HMR not to be norbornyl derivatives and were not further identified. 2,2-Dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene, compound $\text{7}_5$, was isolated as fraction 1. The $^1$HMR chemical shifts observed for $\text{7}_5$ are summarized in Table 1. The infrared spectrum shows absorbances at 3050 cm$^{-1}$ for olefinic C-H stretches, 1660 cm$^{-1}$ for C=C double bond stretches and at 880 cm$^{-1}$ for C-H bending of the terminal methylene. The mass spectrum shows the parent ion peak at m/e=136. Compound $\text{7}_5$ is the dehydration product of the desired tertiary alcohol $\text{5}_1$.

2,2,7-Trimethyl-anti-7-methoxy-bicyclo[2.2.1]hept-5-ene, $\text{7}_4$, was isolated as fraction 3. The $^1$HMR spectrum of
Table 2. Mass spectral data of selected bicyclo[2.2.1]-heptenes prepared.

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</tbody>
</table>
shows a peak at 3.17 for the C7 anti methoxyl group, the entire \(^1\)HMR data for \(\mathcal{A}\) are summarized in Table 1. The infrared spectrum shows absorbances at 1135 cm\(^{-1}\) and 1060 cm\(^{-1}\) for C-O bond stretches. The mass spectral data for \(\mathcal{A}\) are summarized in Table 2.

The desired tertiary alcohol, \(\mathcal{A}\), was isolated as fraction 5. \(^1\)HMR chemical shifts are given in Table 1. The infrared spectrum shows absorbances at 3600 cm\(^{-1}\) for O-H bond stretching and at 3030 for olefinic C-H bond stretches. Mass spectral data are given in Table 2.

The configuration at C7 of compounds \(\mathcal{A}\) and \(\mathcal{A}\) can again be determined by \(^1\)HMR chemical shifts. Compound \(\mathcal{A}\) arises from reaction of the intermediate tertiary magnesium alkoxide with excess magnesium iodide used in the preparation of the methyl Grignard reagent. The configuration of \(\mathcal{A}\) and \(\mathcal{A}\), either syn or anti oxygen functionalities, should be identical. Comparison of the chemical shift of the methoxyl group in \(\mathcal{A}\) with the shifts for the syn and anti methoxyl groups in compound \(\mathcal{A}\) should establish the configuration at C7. The signal in \(\mathcal{A}\) is observed at δ3.17; the syn-methoxyl of \(\mathcal{A}\) appears at δ3.08, the anti- at δ3.17. The chemical shift in \(\mathcal{A}\) compares favorably with the anti-methoxyl group in \(\mathcal{A}\). Literature \(^1\)HMR spectra for the series of compounds \(\mathcal{A}\) and \(\mathcal{A}\) (see below) report the methoxyl signals at δ3.10 and δ3.11 respectively (29, 30). Little change in the chemical shifts of the methoxyl
hydrogens with replacement of methyl groups for methoxyl groups is seen.

The comparison of the signals in compounds $5\alpha$ and $7\alpha$ indicate an anti-methoxy orientation in $7\alpha$. The alcohol, $5\beta$, having arisen from the same alkoxide intermediate as $7\alpha$, should also possess the anti configuration.

Rearrangement of 2,2-Dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol and Related Compounds

Forty milligrams for glc-purified 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol were refluxed for ten minutes in a mixture of 1.0 ml of distilled glacial acetic acid, 0.5 ml of water and one drop of concentrated sulfuric acid. Figure 10 summarizes the reactions of glc separation of the crude rearrangement product mixture gave 2 fractions. Fraction 1 constituted 75% of the product mixture. 2,2-Dimethylbicyclo[2.2.1]hept-5-ene-anti-7-acetate, compound $7\alpha$, was isolated as the first fraction. The $^1$HMR spectrum shows a loss of the hydroxyl proton at $\delta 1.70$ (ref. 50) and a new signal at $\delta 2.07$ for the acetyl methyl group. Complete
Figure 10. Reactions of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol.
\textsuperscript{1}HMR chemical shift data are given in Table 1. The infrared spectrum shows the absence of absorptions at 3600 cm\(^{-1}\) and 3400 cm\(^{-1}\) (ref. \textsuperscript{56}); new bands are seen at 1725 cm\(^{-1}\) for the C-O double bond ester stretch and at 1240 cm\(^{-1}\) for the "acetate band" - C-O bond stretch. The mass spectrum shows a small parent peak, m/e = 180, and a large \textit{P}-acetic acid peak, m/e = 120. Fraction 2 was identified as unchanged starting material.

Hydrogenation of \textsuperscript{79} using a 10\% palladium on carbon catalyst in ethanol at room temperature under one atmosphere of hydrogen gave 2,2-dimethylbicyclo[2.2.1]heptane-7-acetate, compound \textsuperscript{80}. Examination of the \textsuperscript{1}HMR chemical shifts of the C\(_7\) hydrogens in compounds \textsuperscript{79} and \textsuperscript{80} indicates the orientation at C\(_7\). The chemical shifts observed are \(\delta 4.33\) in \textsuperscript{79} and \(\delta 4.80\) in \textsuperscript{80}. The upfield shift in the alkene, \textsuperscript{79}, results from long-range shielding from the C\(_5\)-C\(_6\) double bond. This shielding effect, present in the alkene but absent in the alkane, confirms the \textit{anti} acetate orientation in \textsuperscript{79}.

Treatment of compound \textsuperscript{78} with similar rearrangement conditions also gave two fractions, in 68\% and 32\% of the product mixture. Fraction 1 was identified as 2,2-dimethylbicyclo[2.2.1]heptane-7-acetate, compound \textsuperscript{80}. Fraction 2 was identified as unchanged starting material. The \textsuperscript{1}HMR of \textsuperscript{80} obtained from \textsuperscript{78} was identical with that of \textsuperscript{80} obtained from the hydrogenation of \textsuperscript{78}.
Rearrangement of 2,2,7-Trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol and Related Compounds

Figure 11 summarizes the rearrangement products of \( \text{L} \) in \( \text{H}^+ \) and \( \text{D}^+ \) catalyzed reactions. Refluxing forty milligrams of \( \text{L} \) in 1.0 ml of distilled glacial acetic acid, 0.5 ml water and one drop of concentrated sulfuric acid for ten minutes gave four fractions on glc separation of the crude reaction product mixture. Increasing the reaction time gave the same products in differing amounts. Table 3 summarizes the rearrangement results, the glc retention times for the four fractions are given for comparison. The volatility of fractions 1 and 2 dictated a change in the experimental procedure, noted in Table 3 as Method B. Reflux was done using two condensers (double height) with circulating cold water throughout the reaction. The reaction mixture was cooled to 0°C before and during neutralization. Concentration of the final crude product mixture was done at room temperature. The percentages of fraction 1 reported in Table 3 for the ten and twenty minute rearrangements are somewhat lower than the actual percentages produced. A comparison of the twenty-five minute rearrangements indicates that Method B minimizes loss of the more volatile components, fractions 1 and 2, during the reflux period.
Figure 11. Reactions of 2,2,7-trimethylbicycle[2.2.1]hept-5-ene-anti-7-ol.
Table 3. Rearrangement products of 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol.

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Compound</th>
<th>GLC retention time</th>
<th>10 min</th>
<th>20 min</th>
<th>25 min</th>
<th>Method B 25 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fraction 1</td>
<td>$^{17}$</td>
<td>2.0 min</td>
<td>6%</td>
<td>44%</td>
<td>58%</td>
<td>73%</td>
</tr>
<tr>
<td>Fraction 2</td>
<td>$^{29}$</td>
<td>3.0 min</td>
<td>7.6%</td>
<td>33%</td>
<td>29%</td>
<td>23%</td>
</tr>
<tr>
<td>Fraction 3</td>
<td></td>
<td>6.5 min</td>
<td>1.4%</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Fraction 4</td>
<td>$^{15}$</td>
<td>8.8 min</td>
<td>85%</td>
<td>19%</td>
<td>13%</td>
<td>4%</td>
</tr>
</tbody>
</table>
Fraction 1 was identified as the previously characterized dehydration product of \( \text{5}_\ell \), 2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene, compound \( \text{7}_\ell \). Fraction 3, absent after the longer rearrangement periods, was not obtained in sufficient quantities to identify. Fraction 4 was identified as the starting alcohol, \( \text{5}_\ell \).

Fraction 2 was identified as 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene, compound \( \text{8}_\ell \).

![Chemical Structure](image)

The \( ^1\text{HMR} \) spectrum shows singlets at \( \delta 1.25 \) and \( \delta 1.28 \) for three and six hydrogens. The first is assigned to the \( C_5 \) methyl group. This assignment is confirmed by deuteration studies. The second signal is assigned to the geminal methyl groups at \( C_3 \). The \( C_4 \) methylene hydrogens appear as a singlet at \( \delta 1.83 \). The beta hydrogens of tetrahydrofuran are reported at \( \delta 1.79 \). The \( C_6 \) allylic hydrogens are observed as doublets centered at \( \delta 2.17 \) and \( \delta 2.40 \) with an 18 Hertz geminal coupling constant. Each doublet is further split by numerous small couplings into five Hertz broad multiplets. The \( C_1 \) hydrogen is an eight Hertz broad singlet.
at $\delta$4.60. The vinyl hydrogens appear as a six Hertz broad singlet centered at $\delta$5.77. Double irradiation $^1$HMR experiments indicate multiple, small couplings between the C$_1$, C$_6$, C$_7$ and C$_8$ hydrogens. Irradiation at the vinyl signal sharpens the C$_1$ signal to a six Hertz broad singlet; the C$_6$ signals narrow to four Hertz wide multiplets. Irradiation at the C$_1$ signal sharpens the vinyl signal to a four Hertz broad singlet; the C$_6$ multiplets narrow to three Hertz. The signals for the C$_6$ methylene hydrogens are too broad to allow decoupling studies; however, partial incorporation of one deuterium into either allylic position, compound $\mathcal{A}_6$, narrows the C$_1$ hydrogen singlet and the vinyl singlet to four Hertz wide signals. The vicinal olefinic C-H to allylic CH$_2$ coupling constant in cyclopentene is reported to be 0.5 Hertz (31). Allylic couplings, -CH=CH-CH$_2$-, are reported in the range of 0-3 Hertz (32). Homoallylic couplings, -CH-CH=CH-CH$_2$-, in the range of 0-1.6 Hertz have been reported (32). The observed multiple, small couplings in $\delta_6$ are consistent with the literature values.

The infrared spectrum shows a sharp band at 3050 cm$^{-1}$, 1110 cm$^{-1}$, 1040 cm$^{-1}$ and 1010 cm$^{-1}$ for C-O bond stretching. A sharp band is seen at 730 cm$^{-1}$ for the cis-disubstituted double bond.

Table 4 summarizes the $^{13}$CMR data obtained for compound $\mathcal{A}_6$. The chemical shifts were obtained from the
Table 4. $^{13}$CMR Shifts of 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene.

<table>
<thead>
<tr>
<th></th>
<th>C1</th>
<th>C3</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
<th>C7</th>
<th>C8</th>
<th>C3</th>
<th>C3</th>
<th>C5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical shift, ppm</td>
<td>95.0</td>
<td>82.1</td>
<td>48.6</td>
<td>49.4</td>
<td>54.2</td>
<td>132.4</td>
<td>132.9</td>
<td>29.8</td>
<td>29.3</td>
<td>27.6</td>
</tr>
<tr>
<td>Multiplicity (# H's on C)</td>
<td>d(1)</td>
<td>s(0)</td>
<td>t(2)</td>
<td>s(0)</td>
<td>t(2)</td>
<td>d(1)</td>
<td>d(1)</td>
<td>q(e)</td>
<td>q(3)</td>
<td>q(3)</td>
</tr>
</tbody>
</table>
broad band spectrum, the couplings, standard abbreviations used, were obtained from the off resonance spectrum.

The vinyl carbons, C\textsubscript{7} and C\textsubscript{8}, should have the largest chemical shifts. C\textsubscript{1} and C\textsubscript{2}, both attached to oxygen, should have the largest shifts of the aliphatic carbons. Because it is also allylic, C\textsubscript{1} should be downfield from C\textsubscript{3}. C\textsubscript{6} should have the next largest shift since it is an allylic carbon. C\textsubscript{5} and C\textsubscript{4} should have similar shifts since both are beta to the oxygen; C\textsubscript{5}, beta to the double bond also, should be a little further downfield from C\textsubscript{4}. The chemical shifts and multiplicities observed fit the structure of \( \text{8} \) exactly.

Figure 12 illustrates a possible mass spectrum fragmentation pattern for compounds \( \text{8} \), \( \text{8}_1 \), and \( \text{8}_4 \). Data for \( \text{8} \) are from the literature (2). Table 5 summarizes the peaks observed and relative intensities recorded in the mass spectra of \( \text{8} \), \( \text{8}_1 \), and \( \text{8}_4 \). The relative intensity of the peak at m/e = 137, P-15, for \( \text{8}_1 \) is shown in Table 5 as 55.5%. The spectrum obtained on a different spectrometer shows this peak with a relative intensity of 100.0%. The reported spectra of \( \text{8}_1 \) and \( \text{8}_4 \) were obtained from the same instrument.

Refluxing 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, 51, in a mixture of 1.0 ml of D\textsubscript{4}-acetic acid (ca. 70% acidic D), 0.5 ml of D\textsubscript{2}O and one drop of concentrated sulfuric acid under the usual rearrangement
Figure 12. Mass spectral fragmentation patterns of substituted 2-oxabicyclo-[3.3.0]octenes prepared.
Table 5. Mass spectral data for substituted 2-oxabicyclo[3.3.0]octenes prepared.

<table>
<thead>
<tr>
<th></th>
<th>Parent peak</th>
<th>P-CH₃⁺</th>
<th>P-[CH₃⁺ &amp; CH₃CCH₃]</th>
</tr>
</thead>
<tbody>
<tr>
<td>8₁</td>
<td>m/e 152</td>
<td>137</td>
<td>79</td>
</tr>
<tr>
<td></td>
<td>int. 0.0</td>
<td>55.5%</td>
<td>100.0%</td>
</tr>
<tr>
<td>8₄</td>
<td>m/e 154 153 152</td>
<td>139 138 137</td>
<td>81 80 79</td>
</tr>
<tr>
<td></td>
<td>int. 0.0 0.0 0.0</td>
<td>21.7% 38.9% 33.9%</td>
<td>41.3% 100.0% 89.3%</td>
</tr>
<tr>
<td>8</td>
<td>m/e 166</td>
<td>151</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>int. 3%</td>
<td>100%</td>
<td>90%</td>
</tr>
</tbody>
</table>
conditions (twenty-five minutes—Method B) followed by the standard work-up gave three products on glc analysis.

Deuterio-2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene, compound 3, was isolated as 61% of the product mixture. $^1$HMR shows a small deuterium incorporation into the exocyclic double bond. Deuterio-3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-5-ene, compound 4, was isolated as 33% of the mixture. $^1$HMR shows deuterium incorporation into two places. The C$_5$ methyl group integrates for 1.5 hydrogens; the allylic hydrogens at C$_6$ integrate for a total of one hydrogen. The mass spectrum of 4, summarized in Table 5, shows mono- and di-deuterio products.

Treatment of approximately twenty milligrams of 2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene, 5, in 0.5 ml of CDCl$_3$ with the standard $^1$H$^+$ rearrangement conditions and work-up gave only unchanged diene on glc analysis. Treatment of thirteen milligrams of 5 without organic solvent gave two fractions on glc analysis (bottom reaction in Figure 11). Unchanged 5 was isolated as 82% of the product mixture; 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene, 6, was isolated as 18% of the rearrangement products. Identification of 6 was made using the glc retention time (identical with an authentic sample) and the $^1$HMR spectrum.
DISCUSSION

Jones and Jones (2) reported the rearrangement of 2,2,4,7-tetramethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, \( \alpha \), in refluxing acqueous acetic acid. Five rearrangement products were obtained; three were identified. Figure 2 shows the products identified and the percentages in which these products were obtained. Refluxing \( \gamma \) in acqueous acetic acid gave the same products in comparable percentages. Treatment of \( \delta \) with refluxing acqueous acetic acid did not afford either \( \delta \) or \( \gamma \).

It was recognized that an alternate pathway, Figure 3, would also account for the products obtained. Both mechanisms propose the formation of the diene \( \gamma \) from the starting alcohol, via the C7 cationic intermediate \( \eta \). The mechanisms differ in the pathway followed from the starting alcohol to the bicyclic ether \( \iota \).

Figure 2 proposes protonation of the double bond giving the secondary carbonium ion \( \kappa \); cleavage of the \( C_1-C_2 \) bond giving the tertiary cation \( \lambda \) and finally ring closure affording the ether \( \iota \).

Figure 3 proposes cleavage of the \( C_1-C_2 \) bond of the cationic intermediate \( \eta \) giving the tertiary carbonium ion \( \theta \). Hydration of \( \theta \) gives the neutral compound \( \mu \) which on protonation affords the allylic cation \( \nu \). Nucleophilic
attack of the alcohol followed by proton loss gives the bicyclic ether \( \overset{\beta}{\phi} \). The neutral compound \( \overset{\alpha}{\gamma} \) was not found in the rearrangement product mixture.

The formation of the bicyclic ether \( \overset{\beta}{\phi} \) via Figure 2 is dependent on the anti orientation of the \( C_7 \) alcohol but should not be affected by the absence of the \( C_7 \) syn-methyl group. The geminal dimethyl groups at \( C_2 \) are necessary to stabilize the cationic intermediate \( \overset{\gamma}{\lambda} \); the \( C_4 \) methyl group in compound \( \overset{\lambda}{\delta} \) should not play a role in the formation of \( \overset{\delta}{\phi} \).

2,2-Dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, \( \overset{\gamma}{\delta} \), possesses the necessary orientation at \( C_7 \) and the methyl groups at \( C_2 \) to allow rearrangement via Figure 2 giving 3,3-dimethyl-2-oxa bicyclo[3.3.0]oct-5-ene, \( \overset{\delta}{\gamma} \). Compound \( \overset{\delta}{\delta} \) could rearrange via Figure 3 also, giving the same bicyclic ether \( \overset{\delta}{\gamma} \) as the expected product. Rearrangement would proceed through the \( C_7 \) cation \( \overset{\gamma}{\gamma} \). Figure 13 summarizes the results expected from the acid catalyzed rearrangement of \( \overset{\gamma}{\gamma} \). The initial cationic intermediates for each mechanism are shown also. The bottom reaction in Figure 13 gives the actual results of the acid catalyzed rearrangement of \( \overset{\gamma}{\gamma} \). Other than starting material, only the anti-\( C_7 \) acetate of the starting alcohol was isolated; none of the expected bicyclic ether \( \overset{\delta}{\gamma} \) was obtained.

Figure 14 summarizes Winstein's (33) results from the acetolysis of bicyclo[2.2.1]hept-2-ene-7-toluene-sulfonates. The anti-tosylate, \( \overset{\gamma}{\delta} \), gave only the
Figure 13. Predicted and isolated rearrangement products of 2,2-dimethylbicyclo-[2.2.1]hept-5-ene-anti-7-ol.
Figure 14. Solvolysis of syn- and anti-7-tosylbicyclo[2.2.1]hept-2-ene.
anti-acetate \(_{\text{90}}\). The resonance stabilized bishomocyclopropenyl cation \(_{\text{43}}\) was the proposed intermediate (33). Numerous studies have substantiated the stability of \(_{\text{43}}\) and the stereospecificity of its subsequent reactions (6).

Winstein (33) also reported the acetolysis of the syn-tosylate, \(_{\text{94}}\). The only product isolated from the solvolysis of this epimer was the bicyclo[3.2.0]hept-3-ene-2-acetate, \(_{\text{93}}\). The proposed bicyclo[3.2.0]heptenyl allylic cation intermediate, \(_{\text{92}}\), is also shown in Figure 14.

The absence of the expected rearrangement product \(_{\text{86}}\) implies that initial protonation of the C\(_{5}\)-C\(_{6}\) double bond, if it occurs, does not cause bond cleavage leading to rearranged products. Exclusive formation of the anti-acetate implies that the C\(_{7}\) cation \(_{\text{87}}\), shown in the bottom reaction of Figure 11, as the delocalized bishomocyclopropenyl cation, is the only reaction intermediate formed that leads to isolated products.

To investigate the relationship between the nature of the intermediate C\(_{7}\) carbonium ion formed and the formation of bicyclic ether rearrangement products 2,2,7-trimethyl bicyclo[2.2.1]hept-5-ene-anti-7-ol, \(_{\text{55}}\), was subjected to the Jones and Jones (2) reaction conditions. Figure 15 summarizes the expected and isolated rearrangement products. Both Figures 2 and 3 predict the formation of the dehydration product \(_{\text{75}}\). Both figures also predict, via different pathways, the formation of a bicyclic ether
Figure 15. Predicted and isolated rearrangement products of 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol.
product \( g_4 \). Rearrangement of \( 5_1 \) in refluxing aqueous acetic acid did give the diene \( 7_5 \) as a reaction product. The anticipated ether \( 9_4 \) was not obtained; however, an isomeric compound \( 3,3,5\text{-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene, } 8_1 \), was isolated as a product. Neither Figure 2 nor 3 can explain the formation of \( 8_1 \) and the absence of \( 9_4 \).

An alternate pathway, Figure 16, can account for all the products formed. The initial equilibria between \( 5_1, 9_5, \) and \( 7_5 \) parallel the initial steps in Figure 3. Rearrangement of \( 5_1 \) in a partially deuterated reaction mixture, Figure 11, gave \( 8_2 \), partially deuterated starting material. One-half of the hydrogens in the \( C_7 \) methyl group of \( 8_2 \) were replaced by deuterium atoms. Incorporation of deuterium into the \( C_7 \) methyl group establishes the equilibrium of starting material \( 5_1 \) with the diene product \( 7_5 \). The exclusive formation of the anti epimeric deuterated alcohol implies the equilibrium proceeds via the resonance stabilized cation \( 11b \). Treatment of thirteen milligrams of \( 7_5 \) with refluxing acetic acid for twenty-five minutes gave an 82:18 mixture of \( 7_5 \) and \( 8_1 \). No alcohol, \( 5_1 \), was isolated or detected.

Wagner-Meerwein-type migration of the \( C_3-C_4 \) bond gives the allylic cation \( 9_6 \) analogous to \( 9_2 \) (Figure 14) reported by Winstein (33). Cleavage of the cyclobutane gives the tertiary cation \( 3_6 \). Intermediate \( 3_6 \) (R=methyl)
Figure 16. Rearrangement of substituted bicyclo[2.2.1]hept-5-ene-anti-7-ols via migration of the C$_3$-C$_4$ bond.
appears in Figure 3. Formation of the bicyclic ether parallels Figure 3.

Migration of the more highly substituted carbon, C₂, rather than C₃ might be expected. Movement of the C₁-C₂ bond analogous to the C₃-C₄ migration shown in Figure 16 would give intermediate cation 97.

Models indicate that the C₁ methyl and one of the C₇ geminal methyls must be eclipsed in 97. Steric crowding caused by the eclipsed methyl groups prevents the formation of 97.

Gassman and Pascone (7) reported the acetolysis of 7-hydroxy,7-methyl bicyclo[2.2.1]hept-2-ene derivatives. Figure 17 summarizes the reported results. Gassman and Pascone (7) noted that ample precedent exists for this type of ion interconversion of structures 98 and 99. Bond migration in 98 gives the bicyclo[3.2.0]heptenyl allylic cation 101. Compound 101 affords two acetate products, 102 and 103. Gassman and Pascone (7) concluded that the exclusive exo stereochemistry of the acetate function (in 102 and 103) implies that this allylic cation (101) must be interacting with the cyclobutane ring.
Figure 17. Solvolysis of syn- and anti-7-methyl-7-tosylbicyclo[2.2.1]hept-2-enes.
Interaction between the allylic cation and the cyclobutane ring in \( \text{96} \) (Figure 16), coupled with the relief of ring strain and the formation of the conjugated cyclopentadienyl system can account for the bond cleavage of \( \text{96} \) giving the tertiary cation \( \text{96} \).

Figure 18 examines possible resonance structures for the \( \text{C}_7 \) carbonium ions \( \text{lla} \) and \( \text{llb} \). In analogy to Gassman's studies, \( \text{lla} \) and \( \text{llb} \) can delocalize two different ways. Participation of the double bond gives the bishomocycloproenyl cations \( \text{107a} \) and \( \text{107b} \). Cations \( \text{107a} \) and \( \text{107b} \) give the dienes \( \text{7} \) and \( \text{7f} \) and the alcohols \( \text{6} \) and \( \text{5f} \) in equilibrium reactions.

Participation of the \( \text{C}_3-\text{C}_4 \) bond with the \( \text{C}_7 \) cation gives structures \( \text{105a} \) and \( \text{105b} \) which, after bond migration, afford the allylic bicyclo[3.2.0]heptenyl cations \( \text{106a} \) and \( \text{106b} \). The bicyclic ethers \( \text{8} \) and \( \text{8f} \) are formed from \( \text{106a} \) and \( \text{106b} \) via a non-equilibration pathway.

Gassman and Pascone (7) reported the following relative rates of acetolysis for the following compounds:

\[
\begin{array}{ccc}
\text{H} & \text{OTs} & \text{CH}_3 & \text{OTs} \\
\includegraphics[width=0.3\textwidth]{figure1.png} & 1 & 1.8 \times 10^{-10} & 1.3 \times 10^{14}
\end{array}
\]
Figure 18. Rearrangement products of the C₇ 2,2,7-trimethylbicyclo[2.2.1]hept-5-enyl cation.
Gassman and Pascone concluded that the relatively meager effect of the methyl group in the 7 position on the relative rates of solvolysis demonstrates the powerful stabilizing influence of the anti-double bond.

The product-determining ability of the C7 methyl group may very well be steric and not inductive in origin. The C7 methyl in structure 11 might facilitate bicyclic ether formation by sterically hindering the anti-side of the molecule enough to preclude acetate attack. Intermediates 87 and 89 lack the C7 and C2 methyls respectively, and do afford acetate products.

The presence or absence of the C7 methyl determines which products are formed from the acid-catalyzed rearrangements. The presence or absence of the C4 methyl may determine how much of each product is formed. The stabilities of cations 105a, 105b, 106a, and 106b would be expected to influence the amounts of bicyclic ethers formed. Cation 105, delocalized as shown in Figure 17, places some cationic character at C4. Cation 105a, having a C4 methyl group, should be more stable than the non-methylated cation 105b. Similarly, the tertiary allylic structure 106a should be more stable than the secondary allyl carbonium ion 106b.

The enhanced stabilities of 105a and 106a might be expected to translate into 8 comprising a greater percentage of the reaction products than does 81. Subjecting 8 to the rearrangement conditions for ten minutes gives 8 as 63% of
the reaction products; treatment of $\text{5}_1$ for twenty-five
minutes affords $\text{8}_1$ as only 23% of the isolated products.

The rearrangements of $\text{6}$ and $\text{5}_1$ in deuterated reac-
tion mixtures shed no light on the operative mechanism.
Figure 19 illustrates that Figures 2, 3, and 16 all
incorporate deuterium into the same site, $\text{C}_6$, of the
bicyclic ethers predicted.

The absence of $\text{37}_a$ and $\text{37}_b$ as rearrangement products
can be explained by examining literature models, Figure 20.
Slabey and Wise (34) treated $\text{10}_8$ with concentrated sulfuric
acid to obtain the dehydration product $\text{10}_9$. An unwanted
side product 2,2-dimethyl tetrahydrofuran, $\text{11}_0$, was also
obtained. Treatment of $\text{10}_8$ with one part concentrated
sulfuric acid and two parts water gave $\text{11}_0$ exclusively. The
intermediate, neutral unsaturated carbinol $\text{11}_1$ was not
isolated as a produce in either reaction (34).

The preparation of $\text{11}_3$ from the diol $\text{11}_2$ was
catalyzed using only a "granule" of iodine to minimize
formation of $\text{11}_0$ (35). Even under these mild conditions
only a 40% of $\text{11}_3$ was obtained; $\text{11}_0$ was obtained in 60%
yield. Unreacted, residual $\text{11}_2$ was not found (35).

The isolation of 2,2-dimethyl tetrahydrofurans as
acid-catalyzed rearrangement products with little or none of
the intermediate unsaturated alcoholic precursors being
isolated is not unprecedented.
Figure 19. Predicted and isolated rearrangement products of 2,2,7-trimethylbicyclo[2,2,1]hept-5-ene-anti-7-ol in a deuterated reaction mixture.
Figure 20. Acid catalyzed preparation of 2,2-dimethyltetrahydrofuran.
General

Proton nuclear magnetic resonance (NMR) spectra were recorded on a 60 MHz Varian Associates T-60 spectrometer. Chemical shifts are given in $\delta$ (ppm) relative to tetramethylsilane (TMS, $(\text{CH}_3)_4\text{Si}, \delta=0$) internal standard. Peak multiplicity is indicated as s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet. Coupling constants (J) are given in Hertz; relative integrated areas are given in number of hydrogens. Carbon nuclear magnetic resonance spectra were recorded on a Bruker WH-90 FT spectrometer. Chemical shifts, in ppm (reference TMS), were obtained from broad band spectra. Peak multiplicities, identified as in $^1$HMR spectra, were determined from off resonance spectra.

Infrared spectra (ir) were recorded on Perkin Elmer models 137 or 337 spectrometers, calibrated at the 1601 and/or 1028 lines of polystyrene. Absorptions are reported in wavenumbers (cm$^{-1}$). Spectra were determined using neat samples between sodium chloride plates, potassium bromide pellets or in matching sodium chloride solution cells.

Mass spectra were obtained with a Hewlett Packard model 5930-A mass spectrometer. Spectra were determined at 70 eV unless otherwise noted. All melting and boiling points are uncorrected. Melting points were determined with a Mel-Temp capillary apparatus. Gas chromatography was performed on a Varian Aerograph model 90-P chromatograph. All separations were done using a 10 foot column packed with
5% Carbowax 20M absorbed on 60/80 mesh Chromosorb W. Column chromatography was carried out on Silica gel Woelm (0.063-0.2 mm, ICN Pharmaceuticals, Inc.). Columns were prepared by first making a slurry of the silica gel in the solvent to be used for elution, then pouring the slurry into a standing column of the same solvent in the chromatography column.

Solvents were removed on a Büchi Rotovapor R rotary evaporation device.

Preparation of 1,1-Diethoxy-cyclopentane

A solution of 9 ml (8.56 g, 0.10 moles) of freshly distilled cyclopentanone, 20 ml (17.82 g, 0.12 moles) of triethylorthoformate, 7 ml of anhydrous ethanol and one drop of concentrated sulfuric acid were stirred at room temperature for five hours.

One g of anhydrous sodium carbonate was added and the suspension stirred at room temperature for five minutes. The solid was removed by filtration and excess ethanol removed by distillation. Vacuum distillation of the residue afforded 13.8 g (87%) of produce: bp 60-62°C/12 mm; NMR (CDCl₃) δ1.17(t,3H, J=12 Hz), δ1.70(broad s, 4H), δ3.47(q, 2H, J=12Hz).
Preparation of 1,1-Diethoxy-2,5-dibromo-cyclopentane

A solution of 4.0 g (0.025 moles) of 1,1-diethoxycyclopentane, 20 g of 80% pyridinium bromide perbromide (16 g, 0.050 moles), and 50 ml of absolute ethanol were stirred at 15°C for twenty-five minutes (until no visible traces of unreacted orange pyridinium bromide perbromide remain); 100 ml of ether were added and the suspension filtered. The ethereal solution was added to 300 ml of 5% sodium bicarbonate solution with stirring. The ethereal fraction was separated and washed once with water. After drying over anhydrous magnesium sulfate the ether was removed. Distillation of the residue caused decomposition; therefore the resulting yellow oil was used without further purification: NMR (CDCl₃) δ1.00-1.47 (multiplet, 3H), δ2.00-2.66 (multiplet, 2H), δ3.37-3.93 (multiplet, 2H), δ4.01-4.50 (multiplet, 1H).

Attempted Preparation of 2-Formyl-7,7-diethoxybicyclo[2.2.1]hept-5-ene

A solution of 1.6 g (0.0050 moles) of 1,1-diethoxy-2,5-dibromo-cyclopentane, 2.24 g (0.020 moles) of potassium t-butoxide and 12 ml of dry dimethyl sulfoxide were stirred at room temperature for 80 minutes. The reaction mixture was poured onto 20 g of ice. The aqueous solution was extracted twice with a total of 30 ml of pentane. The combined pentane extracts were dried over anhydrous
magnesium sulfate; 5 ml (4.3 g, 0.077 moles) of freshly distilled acrolein were added to the stirred pentane solution. The reaction mixture was stirred overnight at room temperature. Pentane and unreacted acrolein were removed leaving a dark viscous oil. NMR of the residue showed no aldehydic protons.

Preparation of 1,1 Dimethoxy-2,3,4,5-tetrachlorocyclopentadiene

A solution of 29.4 g (0.525 moles) of potassium hydroxide dissolved in 130 ml of methanol was added drop-wise to a stirred solution of 32.0 ml (54.46 g, 0.20 moles) of hexachlorocyclopentadiene in 170 ml of methanol. The reaction mixture was stirred at room temperature for twenty-four hours; 100 ml of water were added and the phases were separated. Additional water was added to dissolve all insoluble salts and the resulting aqueous solution extracted twice with a total of 150 ml of ether. The combined organic fractions were dried over anhydrous magnesium sulfate. Distillation afforded 39.1 g (75%) of product: \[ \text{bp} - 78^\circ \text{C}/1 \text{mm} \ (\text{Lit. } 108-110^\circ \text{C}/1 \text{mm}) ; \text{NMR (CDCl}_3), \delta 3.43(\text{singlet}). \]

Preparation of 1,4,5,6-Tetrachloro-2-carbomethoxy-2-methyl-7,7-dimethoxy-bicyclo[2.2.1]hept-5-ene

A solution of 34.1 g (0.13 moles) of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene, 13.8 ml (13.0 g, 0.13
moles) of methyl methacrylate and 0.05 g hydroquinone were refluxed for twenty-four hours.

The dark reaction mixture was distilled affording 40.8 g (86%) of product: bp 143-147°C/1.5 mm. The addition of 1 ml of ether induced crystallization: mp 94-95°C NMR (CDCl₃), δ1.6 (s, 3H), δ2.17 (d, 1H, J=13 Hz, C₃ endo proton), δ2.92 (d, 1H, J=13 Hz, C₃ exo proton), δ3.50, 3.57, 3.63 (s, 9H, O-CH₃); ir, thin film, 2950 cm⁻¹, 2850 cm⁻¹, 1740 cm⁻¹, 1625 cm⁻¹, 770 cm⁻¹.

Preparation of 1,4,5,6-Tetrachloro-2-methylcarbinol-2-methyl-7,7-dimethoxy(-5-norbornene)bicyclo[2.2.1]hept-5-ene

A solution of 10.4 g (0.029 moles) of 1,4,5,6-tetrachloro-2-carbomethoxy-2-methyl-7,7-dimethoxybicyclo-[2.2.1]hept-5-ene in 20 ml dry tetrahydrofuran were added dropwise to a stirred solution of 1.08 g (0.029 moles) of lithium aluminum hydride in 20 ml of dry tetrahydrofuran at room temperature. After addition was complete the reaction mixture was stirred at room temperature for thirty minutes and then refluxed for two hours.

After cooling to room temperature, 1.5 ml of ethyl acetate were added dropwise with stirring. Ten ml of water were added slowly to the stirred solution. The two phase liquid system was filtered and the phases were separated. The aqueous phase was extracted once with ether. The combined organic fractions were washed once with 5% sodium
bicarbonate solution and then dried over anhydrous magnesium sulfate.

Ether and tetrahydrofuran were removed by distillation. The crude product consisted of a 3:2 mixture of product and starting material (by NMR). Crystallization from methanol gave 5.9 g (61%) of product (a yellow, highly viscous oil at room temperature). NMR (CDCl₃) δ1.6 (s, 3H, C₂ methyl), δ2.13-2.27 (multiplet, 2H, C₃ endo proton and hydroxy proton), δ2.97 (d, 1H, J=13 Hz, C₂ endo proton), δ3.50-3.63 (multiplet, 8H, syn and anti O-CH₃ and -CH₂OH); ir, thin film, 3400 cm⁻¹, 2950 cm⁻¹, 2870 cm⁻¹, 1740 cm⁻¹ (residual ester), 1600 cm⁻¹.

Preparation of 1,4,5,6-Tetrachloro-2-methyl-2-methylene p-Toluene-sulfonate-7,7-dimethoxybicyclo[2.2.1]hept-5-ene

A solution of 3.36 g (0.010 moles) of 1,4,5,6-tetrachloro-2-methyl-2-methylcarbinol-7,7-dimethoxybicyclo[2.2.1]hept-5-ene dissolved in 6 ml dry pyridine was cooled to 8°C in an ice bath; 3.4 g (0.020 moles) of p-toluene-sulfonyl chloride were added in portions with stirring to maintain reaction temperature below 12°C. After addition was complete the reaction mixture was stored overnight in the freezer.

The brown suspension was poured into 20 ml of ice water. The aqueous suspension was diluted with 20 ml of ether and filtered. After separating phases the aqueous
fraction was extracted twice with a total of 50 ml ether. The combined ethereal fractions were washed once with water, twice with 15% hydrochloric acid solution and once again with water. After drying over anhydrous magnesium sulfate the solvent was removed leaving 2.3 g (50%) of product. Stirring the yellow oil in ligroin overnight afforded light yellow crystals: mp 126-128°C; NMR (CDCl₃), δ1.40 (s, 3H, C₂ methyl), δ1.73 (d, 1H, J=13 Hz, C₂ endo proton), δ2.18 (d, 1H, J=13Hz, C₂ exo proton), δ2.45 (s, 3H, Ar-CH₃), δ3.47 (s, 3H, syn O-CH₃), δ3.53 (s, 3H, anti O-CH₃), δ3.67 (s, 2H, -CH₂-OSO₂Ar), δ7.33 (d, 2H, J=8 Hz, C₃ and C₅ aromatic protons), δ7.75 (d, 2H, J=8 Hz, C₂ and C₆ aromatic protons); ir, 10% CHCl₃, 3030 cm⁻¹, 2980 cm⁻¹, 2950 cm⁻¹, 2850 cm⁻¹, 1600 cm⁻¹, 1350 cm⁻¹, 1300 cm⁻¹, 1100-1200 cm⁻¹.

Preparation of 1,4,5,6-Tetrachloro-2-methyl-2-methylene Methyl Sulfonate-7,7-dimethoxybicyclo[2.2.1]hept-5-ene

A solution of 3.4 g (0.010 moles) of 1,4,5,6-tetrachloro-2-methyl-2-methyl carbinol-7,7 dimethoxybicyclo[2.2.1]hept-5-ene dissolved in 10 ml dry pyridine was cooled to 5°C and 1.6 ml (2.30 g, 0.020 moles) of freshly distilled methane-sulfonyl chloride were added dropwise not allowing the reaction temperature to exceed 10°C. The resulting suspension was stored overnight in the freezer. Twenty g of ice water were poured onto the brown reaction mixture. Ether was added and the phases were
separated. The aqueous layer was extracted twice with a total of 100 ml of ether.

The combined ethereal fractions were washed once with 50 ml of water, twice with 25 ml of 15% hydrochloric acid solution and once again with 50 ml of water. The ethereal solution was dried over anhydrous magnesium sulfate and the ether was removed. The resulting thick, viscous oil was dissolved in 150 ml of petroleum ether at room temperature and cooled slowly with scratching to -78°C to induce crystallization. The isolated yellow solid melted on warming to room temperature. Stirring the recovered yellow oil in 20 ml of petroleum ether overnight at room temperature gave 2.7 g (65%) of light tan crystals, mp 95-97°C. NMR (CDCl₃) δ 1.53 (s, 3H, C₂ methyl), δ 1.92 (d, 1H, J=13 Hz, C₃ endo proton), δ 2.33 (d, 1H, J=13 Hz, C₃ exo proton), δ 3.00 (s, 3H, OSO₃CH₃), δ 3.53 (s, 3H, syn OCH₃), δ 3.62 (s, 3H, anti OCH₃), δ 3.85 (s, 2H, -CH₂-OSO₂-).

Attempted Preparation of 1,4,5,6-Tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]-hept-5-ene

A solution of 2.0 g (0.0041 moles) of 1,4,5,6-tetrachloro-2-methyl-2-methylene p-toluenesulfonate-7,7-dimethoxybicyclo[2.2.1]hept-5-ene in 5 ml dry ether were added dropwise to 0.20 g (0.0055 moles) of lithium aluminum hydride in 10 ml of dry ether. The reaction mixture was
stirred at room temperature for twenty-four hours and then refluxed for one hour.

After cooling to 0°C in an ice/salt bath water was added dropwise to decompose excess lithium aluminum hydride. After filtering the phases were separated. The aqueous phase was extracted twice with ether. The combined ethereal fractions were washed with 10% sodium bicarbonate solution and once with water. After drying over anhydrous magnesium sulfate the solvent was removed. NMR of the crude product indicated only unchanged starting material.

The analogous reaction done in refluxing tetrahydrofuran for twenty-four hours gave no conversion of tosylate to methyl but did afford a 20% conversion of vinyl chloride to alkene.

Treatment in refluxing di-n butyl ether gave only unchanged tosylate.

Preparation of "Reagent I"

A suspension of 0.55 g (0.015 moles) of lithium aluminum hydride was stirred in 16 ml dry tetrahydrofuran under a dry argon atmosphere. The stirred suspension was cooled in an ice bath and 1.75 ml (1.38 g, 0.043 moles) of dry methanol were added dropwise. After addition was complete the gray lithium trimethoxy aluminum hydride solution was allowed to warm to room temperature and was then added dropwise to 1.37 g (0.0072 moles) dry cuprous
iodide under an argon atmosphere at 0°C. Additional tetrahydrofuran was added to facilitate stirring. After addition was complete the black solution was stirred for thirty minutes at 0°C before use.

Attempted Preparation of 1,4,5,6-Tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene

A solution of 1.5 g (0.0036 moles) of 1,4,5,6-tetrachloro-2-methyl-2-methylene methyl sulfonate-7,7-dimethoxybicyclo[2.2.1]hept-5-ene in 10 ml of dry tetrahydrofuran were added dropwise to 0.0072 moles of freshly prepared "Reagent I" at 0°C with stirring. After 15 minutes a gel had formed requiring the addition of 40 ml of tetrahydrofuran to facilitate stirring. The ice bath was removed and the reaction mixture allowed to warm to room temperature. The black reaction mixture was stirred at room temperature for four hours.

Six ml of methanol were added dropwise. The black solution was diluted with ether and filtered through celite. The ethereal solution was washed once with saturated ammonium chloride solution and dried over anhydrous magnesium sulfate. Ether was removed leaving a yellow oil. Stirring overnight in petroleum ether failed to induce crystallization. NMR of the yellow oil indicated 67% unchanged starting mesylate and 33% 1,4-dichloro-2-methyl-2-methylene methyl sulfonate-7,7-dimethoxy-5-norbornene (NMR
identical with starting material with addition of singlet at \( \delta 6.00 \) for vinyl protons).

Preparation of 1,4,5,6-Tetrachloro-2-methyl-2-cyano-7,7-dimethoxybicyclo-[2.2.1]hept-5-ene

A solution of 38.7 g (0.147 moles) of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene, 12.3 ml (9.86 g, 0.147 moles) of methacrylonitrile and 0.05 g of hydroquinone were refluxed for twenty hours. The resulting viscous black liquid was vacuum distilled affording 41.5 g (85%) of a 4:1 mixture of exo-endo cyano group products: bp 134-145°C/1.2 mm; NMR \((\text{CDCl}_3)\), exo isomer, \( \delta 1.33 (s, 3H, C_2 \text{ endo methyl group}) \), \( \delta 1.90 (d, 1H, J=13 \text{ Hz}, C_3 \text{ endo proton}) \), \( \delta 2.93 (d, 1H, J=13 \text{ Hz}, C_3 \text{ exo proton}) \), \( \delta 3.53 (s, 3H, \text{ syn O-CH}_3) \), \( \delta 3.66 (s, 3H, \text{ anti O-CH}_3) \); endo isomer—only different peak—\( \delta 1.77 (s, 3H, C_2 \text{ exo methyl group}) \); ir, thin film, 2990 cm\(^{-1}\), 2950 cm\(^{-1}\), 2850 cm\(^{-1}\), 2250 cm\(^{-1}\), 1600 cm\(^{-1}\).

Preparation of Methacrolein

To a mixture of 23.2 g paraformaldehyde, 4.5 ml 98% sulfuric acid, and 50 ml water at 95°C was added a mixture of 49 g (60.7 ml, 0.85 moles) of freshly distilled propanal and 68 ml of 37% aqueous formaldehyde solution (27.25 g, 0.91 moles) dropwise with stirring over ninety minutes. After addition was complete the reaction mixture was heated and stirred for an additional thirty minutes.
Propanal, methacrolein and water were distilled from the reaction mixture until the distilling temperature reached 90°C. The phases were separated and the organic phase dried over anhydrous magnesium sulfate and redistilled; 29.8 g of a 2:1 (by NMR) mixture of methacrolein: propanal (19.67 g methacrolein, 33% yield) were obtained: bp 50-68°C.

Preparation of 1,4,5,6-Tetrachloro-2-formyl-2-methyl-7,7-dimethoxybicyclo-[2.2.1]hept-5-ene

Method A. A solution of 17.48 g (0.066 moles) of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene, 5.6 ml (4.63 g, 0.066 moles) of freshly distilled methacrolein (commercial sample) and 0.022 g of hydroquinone were heated at 65°C for seventy-two hours.

The resulting dark viscous liquid was distilled giving 8.9 g unchanged ketal, bp 77-100°C/1 mm and 8.8 g (40%) of a 2.7:1 mixture of exo:endo (formyl group) adducts: bp 120-140°C/1.5 mm; NMR (CDCl₃) exo formyl isomer, δ1.0 (s, 3H, endo methyl), δ1.63 (d, 1H, J=13 Hz, C₃ endo proton), δ2.83 (d, 1H, J=13 Hz, C₃ exo proton), δ3.45 (s, 3H, C₇ syn O-CH₃), δ3.53 (s, 3H, C₇ anti O-CH₃), δ9.87 (s, 1H, formyl proton); ENDO FORMYL ISOMER, δ1.47 (s, 3H), δ2.07 (d, 1H, J=12 Hz, C₃ endo proton), δ2.70 (d, 1H, J=12 Hz, C₃ exo proton), δ3.53 (s, 3H, C₇ syn O-CH₃), δ3.58 (s, 3H, C₇ anti O-CH₃), δ9.43 (s, 1H, formyl proton); ir,
2950 cm\(^{-1}\), 2850 cm\(^{-1}\), 1725 cm\(^{-1}\), 1600 cm\(^{-1}\); Mass Spectrum, m/e (relative intensity), 301(32.8), 299(98.9), 297(100.0), 271 (13.0), 269(35.9), 267(39.2), 239(22.9), 237(28.7), 235(25.5), 233(38.7), 221(24.0), 161(20.3), 160(34.4), 123(26.6), 59(33.0).

**Method B.** A solution of 58 g (0.22 moles) of 1,1-dimethoxy-2,3,4,5-tetrachlorocyclopentadiene, 29.9 g of a 2:1 mixture of methacrolein/propanal (19.7 g, 0.28 moles methacrolein) and 0.10 g of hydroquinone were gently refluxed for sixty-five hours. Distillation of the yellow reaction mixture gave 49.3 g (67%) of a 2.5:1 mixture of exo formyl/endo formyl group product mixture; bp 120-130°C/0.5 mm.

**Method C.** A suspension of 0.38 g (0.010 moles) of lithium aluminum hydride was stirred in 10 ml dry ether. This suspension was cooled to 0°C and 1.47 ml (1.32 g, 0.015 moles) of ethyl acetate were added dropwise with stirring; 3.31 g (0.010 moles) of 1,4,5,6-tetrachloro-2-cyano-2-methylbicyclo[2.2.1]hept-5-ene in 5 ml of dry ether were added dropwise to the cooled lithium triethoxy aluminum hydride solution with stirring. After addition was complete the reaction mixture was stirred for one hour at room temperature.

Ten ml of 5% sulfuric acid solution were added dropwise and the resulting two phase system was diluted with
ether and separated. The aqueous layer was extracted three times with a total of 75 ml ether. The combined ethereal fractions were washed once with 50 ml of 5% sodium bicarbonate solution and three times with 50 ml of water. After drying over anhydrous magnesium sulfate the solvent was removed. Distillation of the residue gave 1.4 g of a 36:64 mixture of aldehyde:nitrile (0.50 g product, 2.5:1 exo/endo formyl adducts, 15% yield), bp 125-130°C/1 mm.

Preparation of 1,4,5,6-Tetrachloro-2-formyl-2-methyl-7,7-dimethoxybicyclo-[2.2.1]hept-5-ene Hydrazone

A solution of 8.8 g (0.026 moles) of 1,4,5,6-tetrachloro-2-formyl-2-methyl-7,7-dimethoxybicyclo[2.2.1]-hept-5-ene, 0.83 ml (0.86 g, 0.026 moles) of hydrazine and 10 ml anhydrous n-butanol were refluxed for two hours.

The dark viscous reaction mixture was distilled to remove n-butanol and excess hydrazine. The remaining viscous oil was dissolved in hot ethanol. The hot ethanolic solution was treated with Norite, filtered, and stored in the freezer overnight. Eight g (88%) of a tan sticky solid were obtained.

Preparation of 1,4,5,6-Tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo-[2.2.1]hept-5-ene

A solution of 10 g (0.031 moles) of 1,4,5,6-tetrachloro-2-formyl-2-methyl-7,7-dimethoxybicyclo[2.2.1]-hept-5-ene, 5 ml (5 g, 0.155 moles) of hydrazine, 10.4 g
(0.186 moles) of potassium hydroxide and 80 ml of diethylene glycol were stirred at 120°C for one hour.

After cooling to room temperature the dark viscous reaction mixture was extracted three times with 50 ml of ether. Two hundred fifty ml of water were added to the diethylene glycol solution and the resulting aqueous emulsion extracted twice with a total of 200 ml of ether. The combined ethereal fractions were washed once with 100 ml of 5% hydrochloric acid solution and once with 100 ml of water. After drying over anhydrous magnesium sulfate the solvent removed and the residue distilled giving 5.1 g (53%) of product: bp 95-100°C/1 mm; NMR (CDCl₃), δ0.87 (s, 3H, C₂ endo methyl), δ1.33 (s, 3H, C₂ exo methyl), δ1.70 (d, 1H, J=12 Hz, C₃ endo proton), δ2.27 (d, 1H, J=12 Hz, C₃ exo proton), δ3.50 (3, 3H, syn O-CH₃), δ3.56 (s, 3H, anti O-CH₃); Mass Spectrum, m/e (relative intensity), 287(5.9), 285(26.6), 283(27.1), 133(10.0), 45(100.0).

Preparation of 2,2-Dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene

A solution of 1.0 g (0.0031 moles) of 1,4,5,6-tetrachloro-2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene, 13 ml of dry tetrahydrofuran and 3.26 ml (2.56 g, 0.035 moles) of t-butyl alcohol were stirred under an argon atmosphere at room temperature; 1.70 g (0.074 moles) of cubed sodium were added and the reaction mixture gently refluxed and vigorously stirred for eight hours.
After cooling to room temperature 14 ml of methanol were added slowly. The reaction mixture was poured over 50 g of ice and the phases were separated. The aqueous phase was extracted three times using a total of 150 ml of ether. The combined ethereal fractions were washed twice with 50 ml of water and once with 50 ml of saturated sodium chloride solution. The ethereal solution was dried over anhydrous magnesium sulfate and solvents removed by distillation. Vacuum distillation of the remaining brown oil gave 0.3 g (53%) of product: bp 75-80°C/8 mm; NMR (CDCl₃), δ0.83 (s, 3H, C₂ endo methyl), δ0.90 (d, 1H, J=12 Hz, C₃ endo proton), δ1.30 (s, 3H, C₂ exo methyl), δ1.73 (d, 1H, J=12 Hz, further split into a doublet, J=4 Hz, C₃ exo proton), δ2.33 (broad s, 1H, C₁ bridgehead proton), δ2.78 (broad s, 1H, C₄ bridgehead proton), δ3.08 (s, 3H, syn O-CH₃), δ3.17 (s, 3H, anti O-CH₃), δ5.77-6.27 (multiplet, 2H, C₅ and C₆ vinyl protons); ir (thin film) 3030 cm⁻¹, 2950 cm⁻¹, 2870 cm⁻¹, 1650 cm⁻¹; Mass Spectrum, m/e (relative intensity) 182 (2.1), 167 (2.8), 110 (14.0), 93 (27.2), 43 (27.3), 41 (73.2), 39 (100.0).

Preparation of 2,2-Dimethylbicyclo-[2.2.1]hept-5-ene-7-one

A mixture of 4.5 g (0.025 moles) of 2,2-dimethyl-7,7-dimethoxybicyclo[2.2.1]hept-5-ene and 17 ml of 5% aqueous sulfuric acid solution were rapidly stirred at 40°C for twenty hours.
After cooling to room temperature the reaction mixture was extracted three times with a total of 60 ml of pentane. The combined organic fractions were dried over anhydrous magnesium sulfate and the pentane removed; 3.1 g (91%) of product remained and was used without further purification. NMR (CDCl₃) δ0.9(s, 3H, C₂ endo methyl), δ1.08(broad s, 4H, C₂ exo methyl and C₃ endo proton), δ1.63(d, 1H, J=12 Hz further split into a doublet J=4 Hz, C₃ exo proton), δ2.37(broad s, 1H, C₁ bridgehead proton), δ2.73(broad s, C₄ bridgehead proton), δ6.30-6.60(multiplet, 2H, C₅ and C₆ vinyl protons); ir (thin film). 3050 cm⁻¹, 2950 cm⁻¹, 2879 cm⁻¹, 1750 cm⁻¹, 1650 cm⁻¹; Mass Spectrum, m/e (relative intensity), 108(22.7), 93(33.6), 41(62.2), 39(100.0).

Preparation of 2,2-Dimethylbicyclo-[2.2.1]hept-5-ene-anti-7-d

A solution of 2.85 g (0.075 moles) of lithium aluminum hydride in 25 ml of dry ether were added dropwise to a stirred solution of 0.5 g (0.0037 moles) of 2,2-dimethylbicyclo[2.2.1]hept-5-ene-7-one in 40 ml of dry ether at 0°C under an argon atmosphere. After addition was complete the gray reaction mixture was stirred in an ice bath for an additional three hours.

Twelve ml of water were carefully added dropwise over forty-five minutes to decompose excess lithium aluminum hydride. The resulting white suspension was filtered and
the white solid washed twice with a total of 50 ml of ether. The combined filtrate and washings were dried over anhydrous magnesium sulfate and concentrated; 0.3 g (59%) of product were obtained. The alcohol was purified by GLC (column temperature 150°C, flow rate 50 ml/min): mp 55-60°C, NMR (CDCl₃) δ0.70(s, 3H, C₂ endo methyl), δ1.10(d, 1H, J=12 Hz, C₃ endo proton), δ1.33(s, 3H, C₂ exo methyl), δ1.70(s, 1H, not present in D₂O/CDH₃ hydroxyl proton), δ1.86(d, 1H, J=12 Hz further split into a doublet J=4 Hz, C₃ exo proton), δ2.10(broad s, 1H, C₁ bridgehead proton), δ2.53(broad s, 1H, C₄ bridgehead proton), δ3.70(broad s, 1H, C₇ proton), δ5.93-6.17(multiplet, 2H, C₅ and C₆ vinyl protons); ir, 10% CDCl₃ solution, 3600 cm⁻¹, 3400 cm⁻¹, 3030 cm⁻¹, 2950 cm⁻¹, 2850 cm⁻¹, 1060 cm⁻¹; Mass Spectrum, m/e (rel. int.) 138(2.3), 123(9.1), 120(9.7), 107(42.6), 105(100.0), 93 (88.0), 91(71.2), 83(27.6), 82(74.5), 81(45.1), 80(87.0), 79(52.1), 78(19.8), 77(63.8), 67(31.1), 65(19.7), 59(29.8).

Preparation of 2,2-Dimethylbicyclo-[2.2.1]heptane-7-ol

Forty milligrams of GLC-purified 2,2-dimethylbicyclo-[2.2.1]hept-5-ene-anti-7-ol were hydrogenated with 10% palladium on carbon catalyst in ethanol for four hours at room temperature under one atmosphere of hydrogen. After filtering and concentrating, the ethanolic solution was separated by GLC (column temperature 130°C, flow rate
40 ml/min). Thirty milligrams (72%) were collected: NMR (CDCl₃) δ1.00 (s, 3H), δ1.20 (s, 3H), δ1.27-2.00 (multiplet, 9H), δ4.07 (s, 1H).

Rearrangement of 2,2-Dimethylbicyclo-[2.2.1]heptane-7-ol

Thirty milligrams of GLC-purified 2,2-dimethylbicyclo[2.2.1]heptane-7-ol, 1 ml of distilled glacial acetic acid, 0.5 ml of water and one drop of concentrated sulfuric acid were refluxed with vigorous stirring for ten minutes.

After cooling to room temperature, the reaction mixture was diluted with ether and sufficient 10% aqueous sodium carbonate solution added to raise the pH of the aqueous layer to 8 (by indicator paper). The layers were separated and the aqueous layer extracted once with ether. The combined ether fractions were dried over anhydrous magnesium sulfate, concentrated and separated by GLC (column temperature 130°C, flow rate 35 ml/min). Two components were collected: Fraction I (retention time 3 min 55 sec)—68%, Fraction II (retention time 11 min)—32%. Fraction II was identical in all respects with the starting alcohol (NMR, IR, GLC retention time). Fraction I was identified as the C₇ acetate of the starting alcohol: NMR (CDCl₃) δ1.06, δ1.12 (s, 6H, C-CH₃), δ1.23-2.00 (multiplet, 8H, C₁, C₃, C₄, C₅, C₆ protons), δ2.07 (s, 3H, acetate methyl), δ4.8 (broad s, 1H, C₇ proton): ir, 10% CDCl₃, 2950 cm⁻¹, 2850 cm⁻¹, 1740 cm⁻¹, 1240 cm⁻¹.
Rearrangement of 2,2-Dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol

Forty milligrams of GLC-purified 2,2-dimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, 1 ml of distilled glacial acetic acid, 0.5 ml of water and 1 drop of concentrated sulfuric acid were refluxed with vigorous stirring for ten minutes.

After cooling to room temperature the reaction mixture was diluted with ether and sufficient 10% sodium carbonate solution added to raise the pH of the aqueous layer to 8 (by indicator paper). The ethereal layer was separated and the aqueous layer extracted once with ether. The combined ethereal fractions were dried over anhydrous magnesium sulfate, concentrated, and separated by GLC (column temperature 130°C, flow rate 40 ml/min).

Two components were collected: Fraction I (retention time 5 min 55 sec)—75%, Fraction II (retention time 9 min 40 sec)—25%. Fraction II was identical in all respects with starting material (by GLC retention time, m.p. NMR and IR). Fraction I was identified as the C₇-acetate of starting material: NMR (CDCl₃) δ 0.88 (s, 3H, C₂ endo methyl), δ 1.10 (s, 1H, C₃ endo proton), δ 1.23 (s, 3H, C₂ exo), δ 1.75 (d, 1H, J=12 Hz—further split into a doublet J=4 Hz, C₃ exo proton), δ 2.07 (s, 3H, acetate methyl), δ 2.33 (broad s, 1H, C₁ bridgehead proton), δ 2.70 (broad s, 1H, C₄ bridgehead proton), δ 4.33 (broad s, 1H, C₇ proton), δ 5.90–6.23 (multiplet,
2H, C₅ and C₆ vinyl protons); ir, 10% CDCl₃, 3030 cm⁻¹, 2950 cm⁻¹, 2850 cm⁻¹, 1725 cm⁻¹, 1240 cm⁻¹, 1040 cm⁻¹; Mass Spectrum m/e (rel. int.) 180(1.2), 120(26.3), 105(85.9), 93(19.0), 91(25.1), 83(32.4), 82(100.0), 77(25.5), 67(19.4), 43(50.6).

Preparation of 2,2,7-Trimethylbicyclo-[2.2.1]hept-5-ene-anti-7-ol

A solution of 2.84 ml (6.47 g, 0.046 moles) of freshly distilled methyl iodide in 30 ml of dry ether were added dropwise to a stirred suspension of 1.2 g (0.050 moles) magnesium in 20 ml of dry ether at room temperature; 3.1 g (0.023 moles) of 2,2-dimethyl-5-norbornene-7-one in 30 ml of ether were added dropwise to the above methyl grignard solution at room temperature. The reaction mixture was stirred at room temperature for one hour after addition was complete.

Saturated ammonium chloride solution was added dropwise to the stirred reaction mixture until the initial cloudy solution turned clear and a large cake of solid was deposited. The ethereal solution was decanted and the solid precipitate was washed once with ether. The combined ethereal fractions were concentrated giving 2.9 g (83%) of crude product (by NMR). The alcohol was purified by GLC (column temperature 100°C, flow rate 40 ml/min). Five components were collected:
<table>
<thead>
<tr>
<th>Fraction</th>
<th>Ret. Time</th>
<th>% Collected</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>2 min 26 sec</td>
<td>18%</td>
<td>(2,2)-dimethyl-7-methylenebicyclo([2.2.1])hept-5-ene</td>
</tr>
<tr>
<td>II</td>
<td>3 min 40 sec</td>
<td>3%</td>
<td>unknown</td>
</tr>
<tr>
<td>III</td>
<td>4 min 40 sec</td>
<td>5%</td>
<td>(2,2)-dimethyl-7-methoxybicyclo([2.2.1])hept-5-ene</td>
</tr>
<tr>
<td>IV</td>
<td>7 min 20 sec</td>
<td>1%</td>
<td>unknown</td>
</tr>
<tr>
<td>V</td>
<td>12 min 28 sec</td>
<td>73%</td>
<td>(2,2,7)-trimethylbicyclo([2.2.1])-hept-5-ene-anti-7-ol</td>
</tr>
</tbody>
</table>

Fraction I: NMR (CDCl\(_3\)) \(\delta 0.90\) (s, 3H, \(C_2\) endo methyl), \(\delta 0.93\) (d, 1H, \(J=12\) Hz, \(C_3\) endo proton), \(\delta 1.10\) (s, 3H, \(C_2\) exo methyl), \(\delta 1.50\) (d, 1H, \(J=12\) Hz further split into doublets J=4 Hz, \(C_3\) exo proton), \(\delta 2.43\) (broad s, 1H, \(C_1\) bridgehead proton), \(\delta 2.93\) (broad s, \(C_4\) bridgehead proton), \(\delta 4.23\) (broad s, 2H, exocyclic methylene), \(\delta 6.16-6.23\) (multiplet, 2H, \(C_5\) and \(C_6\) vinyl protons); ir, 10% CDCl\(_3\), 3050 cm\(^{-1}\), 2950 cm\(^{-1}\), 2850 cm\(^{-1}\), 1660 cm\(^{-1}\), 880 cm\(^{-1}\); Mass Spectrum, m/e (rel. int.) 136(30.5), 92(41.0), 91(100.0), 79(95.7), 77(81.6), 39(52.6). 

Fraction III: NMR (CDCl\(_3\)) \(\delta 0.83\) (s, 3H, \(C_2\) endo methyl), \(\delta 0.87\) (d, 1H, \(J=12\) Hz, \(C_3\) endo proton), \(\delta 1.28\) (s, 3H, \(C_7\) methyl), \(\delta 1.35\) (s, 3H, \(C_2\) exo methyl), \(\delta 1.85\) (d, 1H, \(J=12\) Hz further split into doublets J=4 Hz, \(C_3\) exo proton), \(\delta 2.10\) (broad s, 1H, \(C_1\) bridgehead proton), \(\delta 2.60\) (broad s, 1H, \(C_4\) bridgehead proton), \(\delta 3.17\) (s, 3H, \(O-CH_3\)), \(\delta 3.18\) (s, 3H, \(O-CH_3\)).
δ5.77-6.30 (multiplet, 2H, C₅ and C₆ vinyl protons); ir, 10% CDCl₃, 3030 cm⁻¹, 2950 cm⁻¹, 2870 cm⁻¹, 1135 cm⁻¹, 1060 cm⁻¹.

Fraction V: NMR (CDCl₃) δ0.83 (s, 3H, C₂ endo methyl), δ0.90 (d, 1H, J=12 Hz, C₃ endo proton), δ1.37 (s, 3H, C₇ syn methyl), δ1.40 (s, 3H, C₂ exo methyl), δ1.50 (s, 1H, not present in D₂O--hydroxyl proton), δ1.83-2.17 (multiplet, 2H, C₁ bridgehead and C₃ exo proton), δ2.37 (broad s, 1H, C₄ bridgehead proton), δ5.83-6.20 (multiplet, 2H, C₅ and C₆ vinyl protons); ir, 10% CDCl₃, 3600 cm⁻¹, 3030 cm⁻¹, 2950 cm⁻¹, 2850 cm⁻¹, 1250 cm⁻¹; Mass Spectrum (75 eV), m/e (rel. int.) 152 (1.7), 137 (3.8), 134 (4.0), 119 (19.1), 109 (39.6), 94 (11.4), 43 (100.0), Mass Spectrum (10 eV), m/e (rel. int.) 152 (1.8), 137 (0.7), 134 (9.2), 119 (12.4), 109 (61.8), 94 (100.0).

Preparation of 2,2,7-Trimethylbicyclo-[2.2.1]heptane-7-ol

Thirty milligrams of GLC-purified 2,2,7-trimethyl-5-norbornene-7-ol were hydrogenated over 10% palladium on carbon catalyst in ethanol for four hours at room temperature under one atmosphere of hydrogen. After filtering and concentrating, the ethanolic solution was separated by GLC (column temperature 130°C, flow rate 40 ml/min. Two components were collected: Fraction I (retention time--6 min)--21%, Fraction II (retention time--7 min 21 sec)--79%. Fraction I was identified as the starting alkene; Fraction II, 15 milligrams (49%), was identified as desired
product: NMR (CDCl3) δ1.00, 1.27, 1.40 (s, 9H, C–CH₃), δ1.50–2.16 (multiplet, 9H).

Rearrangement of 2,2,7-Trimethylbicyclo-[2.2.1]heptane-7-ol

Thirteen milligrams of GLC-purified 2,2,7-trimethyl-7-norbornanol were refluxed in a mixture of 1.0 ml distilled glacial acetic acid, 0.5 ml of water and one drop of concentrated sulfuric acid for ten minutes with vigorous stirring.

After cooling to room temperature the reaction mixture was diluted with ether and sufficient 10% sodium carbonate solution added to raise the pH to 8 (by indicator paper). The layers were separated and the aqueous layer was extracted once with ether. The combined ethereal fractions were dried over anhydrous magnesium sulfate, concentrated and separated by GLC (column temperature 130°C, flow rate 40 ml/min). Two components were collected: Fraction I (retention time 4 min)--2%; Fraction II (retention time 7 min 20 sec)--98%. Insufficient amounts of Fraction I were collected to identify it; Fraction II was identical by GLC retention time and NMR with the starting saturated alcohol.
Rearrangement of 2,2,7-Trimethylbicyclo-[2.2.1]hept-5-ene-anti-7-ol

**Method A.** Forty milligrams of 2,2,7-trimethyl-bicyclo 2.2.1 hept-5-ene-anti-7-ol were refluxed with vigorous stirring in a solution of 1.0 ml of distilled glacial acetic acid, 0.5 ml of water and one drop of concentrated sulfuric acid for ten minutes.

After cooling to room temperature, the reaction mixture was diluted with ether and sufficient 10% sodium carbonate solution added to raise the pH of the aqueous layer to 8 (by indicator paper). The layers were separated and the aqueous layer extracted once with ether. The combined ethereal fractions were dried over anhydrous magnesium sulfate, concentrated and separated by GLC (column temperature 110°C, flow rate 40 ml/min). Four components were collected: Fraction I (ret. time—2 min)—6%, Fraction II (ret. time—3 min)—7.6%, Fraction III (ret. time—6 min 30 sec)—1.4%, Fraction IV (ret. time—8 min 50 sec)—85%.

Refluxing forty milligrams of the starting alcohol for longer periods of time gave the same products in different ratios:

<table>
<thead>
<tr>
<th>Fraction</th>
<th>10 min</th>
<th>20 min</th>
<th>25 min</th>
<th>25 min—Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>6%</td>
<td>44%</td>
<td>58%</td>
<td>73%</td>
</tr>
<tr>
<td>II</td>
<td>7.6%</td>
<td>33%</td>
<td>29%</td>
<td>23%</td>
</tr>
<tr>
<td>III</td>
<td>1.4%</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>IV</td>
<td>85%</td>
<td>19%</td>
<td>13%</td>
<td>4%</td>
</tr>
</tbody>
</table>
**Method B.** Forty milligrams of alcohol were treated in an analogous reaction mixture using two condensers (double height) with circulating ice water throughout the reflux. Before neutralization the reaction mixture was cooled to 0°C in an ice bath. Neutralization with 10% sodium carbonate was done at 0°C and the final, dry ethereal solution was concentrated at room temperature.

Fraction I was identified as 2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene. The NMR, ir, GLC retention time and mass spectrum were all identical with the previously characterized diene. Fraction II was identified as 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene:

\[
\text{HMR (CDCl}_3\text{), } \delta 1.25(s, 3H, C_5 \text{ methyl group}), \delta 1.28(s, 6H, C_3 \text{ methyl groups}), \delta 1.83(s, 2H, C_4 \text{ protons}), \delta 2.17(d, 1H, J=18 Hz further split into multiplets by small, long range coupling, C_6 \text{ proton}), \delta 2.40(d, 1H, J=18 Hz further split into multiplets by small, long range coupling, C_6 \text{ proton}), \delta 4.60(broad s, 1H, C_1 \text{ proton}), \delta 5.77(broad s, 2H, C_7 \text{ and C_8 \text{ vinyl hydrogens; CMR (CDCl}_3\text{), } \delta 132.9(d, C_8 \text{), } \delta 132.4(d, C_7 \text{), } \delta 95.0(d, C_1 \text{), } \delta 82.1(s, C_3 \text{), } \delta 54.2(t, C_6 \text{), } \delta 49.4(s, C_5 \text{), } 48.6(t, C_4 \text{), } \delta 29.8(q, CH_3 \text{), } \delta 29.3(q, CH_3 \text{), } \delta 27.6(q, CH_3 \text{); ir, 10\% CDCl}_3, 3050 \text{ cm}^{-1}, 2950 \text{ cm}^{-1}, 2870 \text{ cm}^{-1}, 1160 \text{ cm}^{-1}, 1040 \text{ cm}^{-1}, 1020 \text{ cm}^{-1}; \text{ir, thin film, } 3050, 2990, 2950, 2870, (1010-1160, 730, 110C10, 1110, 1160), 1160, 1110, 1040, 1010, \]

730; Mass Spectrum, m/e (rel. int.), 137(100.0), 109(25.3), 95(52.1), 94(20.5), 79(46.3), 43(57.8). Fraction III was not isolated in sufficient quantities to allow identification. Fraction IV was identified as starting alcohol (identical NMR, ir, and GLC retention time).

Rearrangement of 2,2,7-Trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol in Deuterium Oxide-Deuterioacetic Acid Solution

Fifty-two milligrams of GLC-purified 2,2,7-trimethylbicyclo[2.2.1]hept-5-ene-anti-7-ol, 1 ml of deuterioacetic acid (ca. 70% acidic D), 0.5 ml of D_2O and one drop of concentrated sulfuric acid were refluxed (double condenser—cold water) for twenty-five minutes.

After cooling in an ice bath the reaction mixture was diluted with ether. Sufficient 10% sodium carbonate solution was added to raise the pH of the aqueous layer to 8 (by indicator paper). The layers were separated and the aqueous fraction extracted once with ether. The combined ethereal fractions were dried over anhydrous magnesium sulfate, concentrated and separated by GLC (column temperature 100°C, flow rate 40 ml/min). Three components were collected: Fraction I (ret. time 2 min 20 sec) 61%, Fraction II (ret. time 4 min) 33%, Fraction III (ret. time 13 min) 6%. Fraction I was identified as deuterio-2,2-dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene. NMR indicated incorporation of deuterium into the exo-cyclic double
bond, δ4.23 (s, 1.5H, partially deuterated exocyclic methylene). All other NMR parameters were unchanged. The ir and GLC retention time were identical with non-deuterated material. Fraction II was identified as poly-deuterated 3,3,5-trimethyl-2-oxabicyclo[3.3.0]oct-7-ene: NMR (CDCl₃) δ1.25 (s, 1.5H, partially deuterated CH₃), δ1.28 (s, 6H, CH₃), δ1.83 (s, 2H), δ2.13-2.50 (multiplet, 1H—partially deuterated C₆ position), δ4.63 (s, 1H), δ5.78 (s, 2H); mass spectrum—non-deuterated reference sample—m/e (rel. int.) 139 (0.0), 138 (11.8), 137 (55.5), 97 (0.0), 96 (11.3), 95 (53.6), 79 (100.0), 77 (51.6), 69 (17.8), 68 (11.9), 67 (30.3); deuterated sample 139 (21.7), 138 (38.9), 137 (33.9), 97 (27.0), 96 (50.8), 95 (51.6), 81 (41.3), 80 (100.0), 79 (89.3), 78 (49.1), 77 (61.2), 69 (36.0), 68 (44.1), 67 (58.3). The ir and GLC retention times were identical with the nondeuterated sample.

Fraction III was identified as partially deuterated starting material. The C₇ methyl group integrated for 1.5 protons; all other NMR parameters were identical with nondeuterated material. The GLC retention time and ir were unchanged.

Rearrangement of 2,2-Dimethyl-7-methylenebicyclo[2.2.1]hept-5-ene in Acqueous Acetic Acid

Thirteen milligrams of 2,2-dimethyl-7-methylene-bicyclo[2.2.1]hept-5-ene were refluxed in a mixture of 1.0 ml of distilled glacial acetic acid, 0.5 ml of water and one drop of concentrated sulfuric acid for twenty-five
minutes. Two condensers (double height) were used with circulating ice water throughout the reflux.

The reaction mixture was cooled in an ice bath and diluted with ether. Sufficient 10% sodium carbonate solution was added to the cooled two phase mixture to raise the pH of the aqueous layer to 8 (by indicator paper). The layers were separated and the aqueous layer extracted once with ether. The combined ethereal fractions were dried over anhydrous magnesium sulfate, concentrated at room temperature and separated by GLC (column temperature 95°C, flow rate 40 ml/min). Two components were collected: Fraction I (retention time 2 min 30 sec)--82%, Fraction II (retention time 4 min 10 sec)--18%. Fraction was identified by NMR and GLC retention time as the starting diene; Fraction II was identified by NMR and GLC retention time (identical with an authentic sample) as 3,3,5-trimethyl-2-oxabicyclo[3,3,0]oct-7-ene.

Preparation of 2-Methyl-4-ethoxalycyclopentane-1,3,5-trione

A solution of 12.5 g (0.50 moles) of sodium in 160 ml of absolute ethanol was prepared with stirring. The stirred sodium ethoxide solution was cooled to 5°C and a cold mixture of 22.35 ml (18.0 g, 0.55 moles) of freshly distilled 2-butanone and 74.5 ml (80.33 g, 0.55 moles) of diethyl oxalate were added over thirty minutes. The
stirred, orange reaction mixture was allowed to warm to room temperature and was then refluxed for thirty minutes. After cooling to 0°C, 28 ml of 50% sulfuric acid solution was added in portions. The sodium sulfate formed was removed by filtration and washed with ethanol. The combined filtrate and washings were concentrated at room temperature for three days; 46.2 g (83%) of crude product were filtered, washed with cold water and air dried. The product was used without further purification.

Preparation of 2-Methylcyclopentanone-1,3,5-trione Hydrate

A solution of 40 g (0.179 moles) of 2-methyl-4-ethoxalylcyclopentane-1,3,5-trione, 20 ml of 85% phosphoric acid and 182 ml of water were refluxed for four hours. The reaction mixture was cooled to -5°C and the precipitated oxalic acid-product mixture was collected by suction filtration. The filtrate was extracted eight times with ether. The solid mixture was treated with refluxing ether for two hours. The combined ethereal fractions were dried over anhydrous magnesium sulfate and the ether removed; 23.6 g (78%) of product were obtained: mp 74-76°C (lit. 76-78°C).

Preparation of 2-Methylcyclopentane-1,3,5-trione-5-semicarbazone

A solution of 9.0 g (0.063 moles) of 2-methylcyclopentane-1,3,5-trione hydrate in 32 ml of water
and 62.5 ml of ethanol was prepared. A solution of 9.4 g (0.115 moles) of sodium acetate in 13 ml of water was added to the stirred ethanolic solution to raise the pH to 5.0 (by indicator paper). The precipitate formed was removed by filtration. The solution was warmed to 45°C and a mixture containing 7.0 g (0.063 moles) of semicarbazide hydrochloride and 9.4 g (0.115 moles) of sodium acetate in 16 ml of water was added over thirty minutes with vigorous stirring. After addition was complete the reaction mixture was stirred at 45°C for an additional hour.

The cream-colored product was collected by suction filtration and dried at 100°C; 10.0 g (86%) of product were obtained.

Preparation of 2-Methylcyclopentane-1,3-dione

Method A. A solution of 10 g (0.18 moles) of potassium hydroxide dissolved in 100 ml of ethylene glycol was heated to 130°C and 1 ml of water was added. Ten g (0.055 moles) of 2-methylcyclopentane-1,3,5-trione-5-semicarbazone were added in portions over a thirty minute period. The reaction temperature was raised to 155°C for thirty minutes and then increased to 170°C for two hours.

After cooling to room temperature the ethylene glycol was removed at 78°C/4 mm. The residue was dissolved in 20 ml of water and cooled to 0°C. The brown solution was made
acidic to Congo Red indicator paper by slow addition of concentrated hydrochloric acid. Eight g of crude, brown product were collected by suction filtration. The crude solid was recrystallized twice from 50% aqueous ethanol using decolorizing carbon. Four (64%) of purified product were obtained: mp 211-212°C (Lit. 213-215°C); NMR (d₆-DMSO) δ1.50 (s, 3H, C₂ methyl—enol tautomer), δ2.33 (s, 4H, C₄ and C₅ methylenes—enol tautomer).

Preparation of 2-Methyl-1,3-cyclopentanone

Method B. To 10 ml of anhydrous nitromethane was added 8.8 g (0.066 moles) of aluminum chloride in portions at room temperature; 2.6 g (0.022 moles) of succinic acid were added in portions to the stirred nitromethane solution; 6.5 ml (6.1 g, 0.066 moles) of propionyl chloride were added dropwise to the stirred reaction mixture. After evolution of gas stopped the reaction mixture was heated to 85°C for three hours.

The black reaction mixture was poured over 15 g of ice and stored overnight in the freezer. The crude product was filtered and washed with saturated sodium chloride solution. The brown solid was recrystallized from water using decolorizing carbon. One g (41%) of white solid was obtained: mp 215-216°C.
Method C. Thirty-four milliliters of dry nitromethane was added to 35.9 g (0.27 moles) of aluminum chloride with cooling; 16.7 ml (16.6 g, 0.23 moles) of propionic acid were added to the cooled nitromethane solution; 17.4 g (0.12 moles) of succinyl chloride were added slowly to the stirred, cooled reaction mixture. The stirred, black solution was allowed to warm to room temperature and was then heated at 80°C for three hours.

The black reaction mixture was poured over 50 g of ice and stored in the freezer overnight. The crude product was collected by suction filtration, washed with saturated sodium chloride solution and recrystallized from water using decolorizing carbon. Four g of a first crop, mp 214-215°C and 0.3 g of a second crop, mp 213-215°C were combined (32%).

Preparation of 3-Iodopropene

A solution of 17.3 ml (24.2 g, 0.20 moles) of 3-bromopropene and 37.5 g (0.25 moles) of sodium iodide in 34 ml of acetone was refluxed for eighteen hours. The reaction mixture was poured into 160 ml of water. The aqueous solution was extracted three times using a total of 250 ml of ether. The ethereal solution was dried over anhydrous magnesium sulfate, concentrated and distilled through a vigreux column; 23.5 g (70%) of product were
obtained: bp 95°C (Lit. 102-103°C); NMR (CCl₄) δ3.90(d, 2H, J=7 Hz), δ5.00-6.00(multiplet, 3H).

Preparation of 3-Iodopropyne

A solution of 7.5 ml (11.9 g, 0.10 moles) of 3-bromopropyne and 18.75 g (0.125 moles) of sodium iodide in 18 ml of dry acetone was stirred at -15°C for four days. The reaction mixture was diluted with 50 ml of water and the phases separated. The aqueous layer was extracted twice using 50 ml of ether each time. The combined organic fractions were washed with 20 ml of 10% sodium thiosulfate solution and dried over anhydrous magnesium sulfate. Distillation gave 4.7 g (28%) of desired product: bp 110°C (Lit, 115°C1; NMR (CDCl₃) δ2.20(t, 1H, J=3 Hz), δ3.50(d, 2H, J=3 Hz).

Preparation of Ethyl Iodoacetate

A solution of 5.0 ml (6.28 g, 0.050 moles) of ethyl chloroacetate and 11.2 g (0.075 moles) of sodium iodide in 100 ml of dry acetone were stirred at room temperature for twenty hours. The reaction mixture was cooled in an ice bath and filtered. Fifty ml of ether were added to the filtrate. The organic solution was washed once with 40 ml of 10% sodium thiosulfate solution and once with 50 ml of water. The ethereal solution was dried over anhydrous magnesium sulfate, concentrated and distilled; 7.8 g (73%) of product were collected: bp 75°C/15 mm (Lit, 73°C/16 mm);
NMR (CDCl₃) δ1.17(t, 3H, J=7 Hz), δ3.57(s, 2H), δ4.00(q, 2H, J=7 Hz).

Preparation of the Thallium(I) Salt of 2-Methyl-1,3-cyclopentanedione

A suspension of 0.084 g (0.0075 moles) of 2-methyl-1,3-cyclopentanedione were stirred in 50 ml of dry tetrahydrofuran under a nitrogen atmosphere at room temperature; 0.5 ml (1.75 g, 0.0070 moles) of thallous ethoxide were added dropwise. The reaction mixture was stirred for thirty minutes at room temperature and then cooled in an ice bath. The solid product was recrystallized from absolute ethanol. One g of first crop and 0.7 g of second crop were combined (73%): mp > 250°C (d).

Preparation of 2-Methyl-2(3-propynyl)-1,3-cyclopentanedione

A solution of 0.7 g (0.0022 moles) of the thallium salt of 2-methyl-1,3-cyclopentanedione and 0.21 ml (0.42 g, 0.0025 moles) of 3-iodo propyne in 5 ml of dry benzene were stirred at 55°C for six days. After cooling to room temperature the yellow solid (thallous iodide) was removed by filtration and the filtrate concentrated. Three-tenths g of crude product were chromatographed on a 12 mm diameter column containing 10 g of silica gel in chloroform; 0.04 g (12%) of desired product were obtained: NMR (CDCl₃) δ1.10(s, 3H), δ2.00(t, 1H, J=3 Hz), δ2.45(d, 2H, J=3 Hz), δ2.82(s, 4H).
Preparation of 2-Methyl-2-(3-propenyl)-1,3-cyclopentanenedione

**Method A.** A solution of 1.0 g (0.0031 moles) of the thallium salt of 2-methyl-1,3-cyclopentanenedione and 0.27 ml (0.50 g, 0.0030 moles) of 3-iodopropene in 5 ml of dry benzene were stirred at 62°C for five days. Thallium iodide was removed by filtration and the filtrate was concentrated. Distillation of the resulting amber liquid gave 0.18 g (40%) of product: bp 55-65°C/1 mm; NMR (CDCl₃) δ1.02 (s, 3H), δ2.22 (d, 2H, J=7 Hz), δ2.70 (s, 4H), δ4.73-6.00 (multiplet, 3H).

**Method B.** A solution of 6.15 g of 40% Triton B/methanol solution (2.46 g, 0.015 moles N-benzyltrimethyl ammonium hydroxide) and 1.68 g (0.015 moles) of 2-methyl-1,3-cyclopentanenedione in 24 ml of anhydrous methanol was stirred at room temperature. To this mixture was added 2.0 ml (2.94 g, 0.024 moles) of 3-bromopropene and the reaction mixture refluxed for twenty-four hours.

Methanol was removed and the residue was dissolved in 10 ml of water. The aqueous solution was extracted three times with a total of 60 ml of chloroform. The combined chloroform fractions were washed once with 25 ml of 5% sodium bicarbonate solution and once with 25 ml of water. After drying over anhydrous magnesium sulfate the solvents were removed.
Distillation of the resulting amber liquid affords a mixture of C- and O- alkylated products; bp 55-80°C/1 mm. Two g of distilled product mixture were separated on a 12 mm diameter column containing 50 g of silica gel in chloroform; 1.16 g (51%) of desired product were obtained.

Preparation of 2-Methyl-2(1-ethanoic acid, ethyl ester)-1,3 Cyclopentanedione

A solution of 4.1 g of a 40% N-benzyltrimethyl-ammonium hydroxide/methanol solution (1.64 g, 0.010 moles hydroxide) and 1.12 g of 2-methyl-1,3-cyclopentanedione in 16 ml of anhydrous methanol was stirred at room temperature. To this mixture was added 1.57 ml (2.51 g, 0.015 moles) of ethyl bromoacetate and the reaction mixture refluxed for twenty-four hours.

Methanol was removed and the residue dissolved in 20 ml of water. The aqueous solution was extracted three times using a total of 60 ml of chloroform. The combined organic fractions were washed with 30 ml of 5% sodium bicarbonate solution and then with 30 ml of water.

After drying over anhydrous magnesium sulfate the solvents were removed; 2.5 g of crude product were separated on a 20 mm diameter column containing 50 g of silica gel in chloroform; 0.36 g (18%) of desired product were obtained:

NMR (CDCl₃) δ1.13 (s, 3H), δ1.25 (t, 3H, J=7 Hz), δ2.95 (broad s, 6H), δ4.10 (q, 2H, J=7 Hz); mass spectrum m/e (rel. int.)
198 (100.0), 170 (85.2), 152 (36.9), 125 (50.5), 124 (77.4),
88 (44.0).
APPENDIX A

PREPARATION OF SUBSTITUTED CYCLOPENTADIENES

Compounds \( 110_{a} \) and \( 110_{b} \) appear in Figure 16. Neither compound was isolated as a rearrangement product. The preparation of \( 110_{a} \) and \( 110_{b} \) was undertaken to study their reactions, if any, in refluxing aqueous acetic acid.

\[ \text{CH}_3 \quad \text{CH}_2-\text{C}-\text{OH} \]

\( 110 \quad a \ R = \text{CH}_3 \)

\( b \ R = \text{H} \)

The dione \( 130 \) was prepared for use as a synthetic precursor to \( 110_{a} \) and \( 110_{b} \). Figure 21 illustrates the preparation of \( 130 \) from 2-butanone and diethyl oxalate (36). Figure 22 details the preparation of \( 130 \) from succinic acid and propionic acid derivatives under Friedel-Crafts conditions (37, 38).

Kessar et al. (39) attempted to alkylate \( 130 \) at the \( C_2 \) position via a variety of reaction conditions. No \( C \)-alkylated products were obtained; only \( O \)-alkylated products were isolated.

100
Figure 21. Preparation of 2-methyl-1,3-cyclopentanedione.
Figure 22. Preparation of 2-methyl-1,3-cyclopentanedione via Friedel-Crafts reactions.
Corey and Sachder (40) reported successful C-alkylation of \( \text{I} \) via the thallium(I) salt \( \text{II} \). Figure 23 illustrates the successful alkylations of \( \text{III} \); \( \text{IV} \) was prepared from \( \text{V} \) and thallous ethoxide. The crystalline salt was re-crystallized from ethanol. Reaction of \( \text{III} \) and 3-iodopropyne in benzene gave \( \text{VI} \) in 12% yield. Analogous reaction with 3-iodo-1-propene gave \( \text{VII} \) in 40% yield.

Crispin, Vanstone, and Whitehurst (41) reported C-alkylation of \( \text{V} \) using N-benzyl-trimethylammonium hydroxide (Triton B) in methanol. Treatment of \( \text{V} \) using Crispin et al.'s conditions with 3-bromo-1-propene gave \( \text{VIII} \) in 51% yield (Figure 23). Analogous reaction with ethyl bromoacetate gave the ester \( \text{IX} \) in 18% yield.

Figure 24 illustrates the possible preparation of \( \text{XI}_a \) and \( \text{XI}_b \) from \( \text{IX} \). These reactions have not been completed.
Figure 23. Alkylations of 2-methyl-1,3-cyclopentanedione.
Figure 24. Possible synthetic routes to 1-methyl-1-(2-methyl-2-propanol)-cyclopentadiene and 1-methyl-1-(2-methyl-2-propanol)-2-methylcyclopentadiene.
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34. Slabey, V. A., and P. H. Wise, Chemical Abstracts, 45, 7532b


