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PART II. ACYLATION OF MEDIUM RING OLEFINS.

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Part I. Studies in the Synthesis of 5,8-Dimethylene-1,3,6-cyclooctatriene Derivatives

Part II. Acylation of Medium Ring Olefins

By

Burt L. Strasser

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

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To my

mother and father.
PART I
INTRODUCTION

The nature and origin of aromatic character has fascinated organic chemists since Kekule\(^1\) first applied the term aromatic, from an odor description, to derivatives of benzene. Shortly after Kekule's proposal Erlenmeyer suggested that the term aromatic should encompass those compounds which had similar chemical properties rather than similar structural features. Later, the empirical theory of the "aromatic sextet" was introduced by Armit and Robinson.\(^3\) This theory stated that any compound which had six electrons in a concentric system could be expected to exhibit benzene-like properties. This explained the aromatic character of non-benzenoid heterocycles, such as thiophene and pyrrole, and carbocycles, such as the cyclopentadienide anion.

It, however, became evident that aromatic character was not present to the same extent in these new "sextet" compounds or even in the benzenoid compounds.\(^4\) Thiophene and pyrrole undergo electrophilic substitution like benzene, but at a faster rate. Pyrogallol, although a benzene derivative, is easily oxidized, even by air. Physical properties such as bond length also vary; for example, the 1,2 and 2,3 bond lengths in naphthalene differ. Thus chemical reactivity was not a reliable criterion of aromatic character and a broader definition of the term was necessary.

The basic electronic and structural principle underlying our present-day concepts of aromaticity was proposed by Hückel in 1931.\(^5\) Considering unsaturated and aromatic compounds from a quantum mechanical standpoint he concluded that any planar, fully conjugated, monocyclic olefin possessing \((4n + 2)\) \(\pi\)-electrons, where \(n\) is any integer, would
have enhanced electronic stability. This theory not only encompassed the existing aromatic species but predicted that many other compounds possessing other than six electrons would have aromatic character.

Hückel's rule stimulated numerous synthetic and theoretical investigations which sought to substantiate, disprove, modify, and discover the limits of his theory.⁴

The degree of aromatic character, according to Hückel's rule, is a function of the ground state electronic structure, i.e., the extent of π-electron delocalization. Physical quantities which can be correlated with the extent of delocalization include dipole moment, changes in bond length, the strength of the π-electrons' ring current as measured by nmr techniques, and heats of combustion.⁴

It should be noted that these methods often give numbers which do not accurately portray the degree of delocalization, but reflect other structural effects also, such as strain. The early criterion of aromatic character, chemical reactivity, was limiting since it considered the energy content of the molecules' excited state, and the transition states of reactions. If the free energy difference between the molecules' ground state and the transition state of a particular reaction is small, the compound is reactive irrespective of its absolute ground state energy.⁶,⁷ Thus, the possession of a delocalized π-electron system does not automatically result in the thermodynamic stability and the relative chemical inertness exhibited by benzene derivatives.

Recent investigations of aromaticity have centered on non-benzenoid cyclic conjugated compounds.⁸ Indeed, these studies have shown that possession of strong electron delocalization according to Hückel's rule does not guarantee benzenoid properties. This further substantiates the difference between the aromatic character of the ground state and the
aromatic stability and reactivity. The stabilization due to \( \pi \)-delocalization can also be cancelled in some circumstances. Many cyclic conjugated systems fit the Hückel rule, but possess structural features or a geometry that inhibits delocalization. The correlation of reactivity and stability of cyclic conjugated systems with structure is thus a matter of great interest.

In this connection a class of compounds which are isomeric with benzene and its derivatives, called fulvenes (\( \mathfrak{F} \)), are of special importance.\(^9\) The nature of the bonding in fulvenes can be described qualitatively as a resonance hybrid of two contributing structures, one being completely covalent \( \mathfrak{F}a \) and the other dipolar \( \mathfrak{F}b \).

\[
\begin{align*}
\mathfrak{F}a & \leftrightarrow \mathfrak{F}b \\
\end{align*}
\]

The extent of polarization in the ground state has been determined by dipole moment measurements. When \( R = \) alkyl or aryl, the fulvenes have a dipole moment of 1.3-1.5 D\(^{10}\); thus, structure \( \mathfrak{F}b \) contributes only 10-15% to the net structure. The contribution is greater in the excited state and is responsible for a decrease in the energy difference between the ground and excited states. This accounts for the fact that fulvenes absorb light at a longer wave length than do benzenoid compounds. Dialkyl and diarylfulvenes are of a yellow to red color, in contrast to their colorless benzenoid isomers.

The resonance energy calculated\(^{11}\) for fulvene by simple MO methods is considerably greater than that obtained experimentally from heats of
combustion and hydrogenation. The discrepancy is eliminated if a correction for ring strain is included in the calculated resonance energy. A value of ca 12 kcal per molecule or ~2 kcal per π-electron for the delocalization energy of the fulvene ring system indicates that fulvene lies on the borderline between cyclic polyenes (DE = 3-5 kcal or <2 kcal per π-electron) and true aromatic substances such as benzene (DE = 36 kcal or 4-6 kcal per π-electron).

The nmr spectra of fulvenes also indicate their small degree of aromatic character. In the case of fulvene itself, the ring protons appear at τ 3.56 and τ 3.69 and the exocyclic protons at τ 4.22. These chemical shifts increase to τ 3.61 and τ 3.90 for the ring protons in 6,6-diphenylfulvene. Comparing these values with that given for cyclopentadiene (τ 3.58) one concludes that the ring current must be almost negligible.

Fulvenes were first prepared by Thiele in 1900 by condensing cyclopentadiene with aldehydes and ketones in the presence of base. The parent hydrocarbon is a very unstable yellow oil which decomposes rapidly. It will last for a week if stored in vacuo or under nitrogen. Other modes of preparation include reaction of cyclopentadienyl magnesium bromide and the appropriate ketones or reaction of the cyclopentadienide anion with various Meerwein reagents.

The great chemical reactivity of most fulvenes, as seen in their readiness to add halogens, to undergo the Diels-Alder reaction, both as dienes and dienophiles, and to form peroxides, has been described. However, fulvenes can, under certain conditions, substitute bromine and undergo the Wilsmeier reaction. This can be attributed to some benzenoid stability and further indicates that fulvenes' aromatic character lies between that of olefinic and benzenoid compounds.
The degree of aromaticity in fulvenes may vary depending on substituents at C-6. The parent hydrocarbon is exceedingly unstable with little or no aromatic character as indicated by dipole moment and nmr experiments. With increasing electron-donating character of substituents at C-6 the charge-delocalized structure of \( \text{\text{I}} \) becomes more important; 6,6-dialkoxylfulvenes and 6,6-bis(dialkylamino)fulvenes possess significantly higher dipole moments (3.5-5.0 D.) and show chemical stability closer to true aromatic compounds (e.g. lack of Diels-Alder reactivity and stability to air and light) than do the hydrocarbon fulvenes.\(^{17,18}\) The nmr evidence regarding the presence of a ring current and the degree of hindrance to rotation along the electron-releasing C-N bond further substantiates increased delocalization.\(^{19}\)

A new class of compounds which are somewhat analogous to the fulvenes is the dimethylenecyclooctatrienes, 2 and 3.

Structure 2 has the same relationship to the cyclooctatetraene dianion as fulvene has to the cyclopentadiene anion. The trivial names of "1,4-octafulvene" and "1,2-octafulvene" will be used to designate 5,8-dimethylene-1,3,6-cyclooctatriene (2) and 7,8-dimethylene-1,3,5-cyclooctatriene (3) respectively.
Resonance energy calculations performed in these laboratories by the Hückel molecular orbital method indicated that 2 would have an overall delocalization energy of 42 kcal. This value is reduced to 20 kcal when a correction for the strain involved in a planar eight-membered ring is included. 1,4-octafulvenes, like fulvene, possess ~2 kcal per π-electron delocalization energy and should exhibit properties intermediate between benzenoid and olefinic compounds. Similarly, the degree of delocalization could vary depending upon the nature of the substitution at the exocyclic carbon atoms. Derivatives with electron donating groups for R would have increased contribution from structure 2b and thus might exhibit more aromatic character.

An interesting possibility which is not present in the fulvene system is that the polyene structure 2a, due to the angle strain of a planar eight-membered ring, may not be planar, but instead may be tub-like 2c.

\[ \text{2c} \]

Orbital overlap is almost impossible in this folded structure and no significant degree of delocalization could be expected from this geometry. Thus, if the electronic stabilization of planar 2 is not greater than the angle strain involved in a planar 8-membered ring, then the molecule may prefer to exist only as the completely localized tub form. The linear conjugated polyene 1,2-octafulvene has been prepared by Sondheimer and coworkers via the zinc debromination of 1,2-bis(bromo-
methyl)cyclooctatetraene (eq 1).

\[
\begin{align*}
\text{Br} & \\
\text{Zn} & \quad \text{DMF} \\
\text{Br} & \\
\end{align*}
\]

This gives the parent 1,2-octafulvene as an unstable yellow oil which exhibits chemical and physical properties characteristic of a polyene, rather than a delocalized aromatic species.

To date, no examples of 1,4-octafulvene systems have been reported. In fact, except for the cyclooctatetraene dianion and its benzo-derivatives, few examples of non-benzenoid cyclic conjugated systems with eight-membered rings are known. There have been, however, two previous attempted syntheses of the 1,4-octafulvene systems. Murray and Kaplan reported\textsuperscript{21} in 1966 that condensation of the cyclooctatetraene dianion with tropylidium bromide did not yield the expected 1,4-adducts, but 7,7-tropyli. Later Cantrell and Shechter\textsuperscript{22} reported dehydration of various 5,8-bis(\alpha-hydroxyalkyl)-1,3,6-cyclooctatrienes to give tricyclic ethers, not substituted 1,4-octafulvenes.

Preparation of certain derivatives of 1,4-octafulvenes and investigation of their spectra, stability, and reactivity would greatly enhance our knowledge of the chemistry of eight-membered ring non-benzenoid aromatic compounds and of the nature of aromaticity.

The investigation of several synthetic pathways to 1,4-octafulvene derivatives is discussed in the remainder of Part I.
DISCUSSION AND RESULTS

Several synthetic pathways were explored in attempts to synthesize derivatives of 5,8-dimethylene-1,3,6-cyclooctatriene (2) for study. The first synthetic sequence involved the hexahydro and tetrahydro derivatives of 1,4-octafulvene 4 and 5 as key intermediates. Stepwise introduction of the remaining unsaturations via allylic halogenation (with N-bromosuccinimide) followed by dehalogenation should afford the desired compound 2 (eq 2 and 3).

\[
\begin{align*}
4 & \xrightarrow{3 \text{ NBS}} \xrightarrow{\text{Base}} 2 \\
5 & \xrightarrow{2 \text{ NBS}} \xrightarrow{\text{Base}} 2
\end{align*}
\] (2)

The first approach to synthesis of compound 2 employed the Emmons-Wadsworth modification of the Wittig reaction as its key step.\textsuperscript{23}
Pommer reported the conversion of 1,4-dibromo-2-butene to the bisphosphonate ester and subsequent condensation with ketones in the presence of strong base to afford conjugated trienes. Thus, treatment of 3,8-dibromocyclooctene (6) with triethyl phosphite and condensation of the resulting bisphosphonate with carbonyl compounds such as acetone, benzophenone and benzaldehyde should yield trienes of the general structure 2 (eq 4).

\[
\begin{align*}
\text{Br} & \quad \text{Br} \\
\text{O} & \quad \text{P(OEt)}_2 \\
\text{O} & \quad \text{P(OEt)}_2 \\
\text{R} & \quad \text{R} \\
\text{2} & \quad \text{NaOEt}
\end{align*}
\]

\[
\begin{align*}
\text{6} & \quad \text{7}
\end{align*}
\]

In our hands, compound 6, which is available via allylic bromination of cyclooctene, did not form the bisphosphonate but decomposed to give hydrocarbons and triethyl phosphite. Evidently the very reactive allylic secondary halogen functions have been eliminated to give the triene which subsequently decomposes.

A more broadly applicable approach to the hexahydro derivative involves the Wittig reaction itself. With the variety of Wittig reagents available many derivatives of octafulvene could be prepared. Reaction of 1,4-cyclooctanedione \(^{25}\) (7) with two moles of Wittig reagents such as benzylidene triphenylphosphorane was expected to yield compound 8 (eq 5).
The requisite starting material $\mathcal{L}$ is obtained via hydroxylation of cis-cyclooctene with performic acid, followed by hydrolysis with aqueous formic acid of cis-cyclooctene oxide. Oxidation of the 1,4-diol with NBS-acetone-water gave a good yield of 1,4-cyclooctane dione ($\mathcal{L}$).

Benzyltriphenylphosphonium chloride prepared from standard procedures was treated with butyllithium in ethyl ether. To the red solution of benzylidenetriphenylphosphorane thus formed was added a solution of dione $\mathcal{L}$. Precipitation of triphenylphosphine oxide occurred as expected, but in no case was any diolefin isolated. Only the known intramolecular aldol condensation product of dione $\mathcal{L}$, bicyclo[3.3.0]-1-(5)-octene-2-one, identified by its infrared spectrum ($\text{ir } 1685$, and $1620 \text{ cm}^{-1}$) was detected.

Attempts to reduce the intramolecular condensation reaction by altering reaction conditions, i.e., lower temperature, and by using the Corey method of generating the phosphorane (dimethyl sulfoxide in DMSO) were of no avail.

The reaction of dione $\mathcal{O}$ with a more reactive Wittig reagent such as isopropylidenetriphenylphosphorane also gave intramolecular aldol product.

The failure of this system to undergo the Wittig reaction is attributed to its particular liability to undergo aldol condensation
catalyzed by the basic yield. It had previously been noted that base-catalyzed condensations of the carbonyl compound seriously interfered in some reactions with Wittig reagents.  

Milder methods of generating Wittig reagents were considered, but with successful results coming from a third route, the Wittig scheme was abandoned.

The final attempt to prepare compound 5 is outlined in eqs 6 and 7.
The reaction of cyclooctatetraene dianion with benzophenone is known to give, as the major product, 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene (2). The partial hydrogenation of this trienediol (2) and dehydration of the resulting enediol 10 should afford triene 11. The triene diol 2 was prepared according to the procedure of Cantrell and Shechter. Due to the oxygen sensitivity of compound 2 it was hydrogenated without purification directly in ethyl acetate using 10% palladium-on-charcoal catalyst. The rate of hydrogenation was observed to decrease greatly after the uptake of 1-1.5 moles and addition of a further amount of catalyst was necessary for the consumption of the full two moles of hydrogen. Evaporation of the solvent after filtration of the catalyst left a yellow glass. The infrared spectrum of this material showed no carbon-carbon double bond stretching band at 1650 cm\(^{-1}\) in contrast to its precursor 2. The nmr of the product 10 exhibited two vinyl hydrogens and eight aliphatic hydrogens indicating that two double bonds had been reduced. Although a definite assignment of the position of the remaining double bond could not be made, it was tentatively assigned the 6,7 position.

The belief that the C1-C2 and C3-C4 double bonds of 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene were preferentially reduced was based on the reasonable hypothesis that the 6,7 double bond would be quite hindered due to the presence of the very bulky (α-hydroxybenzhydryl) substituents at C5 and C8.

Indeed, treatment of compound 10 with trace amounts of p-toluene-sulfonic acid in benzene for 14 hours at 50° gave a fair yield of the expected conjugated triene 11. The structure of 3,8-bis(benzhydrylidene)cyclooctene (11) was deduced from its analysis, its ultraviolet absorption maximum at 320 mμ (ε 14,580), and its nmr spectrum which
included a two vinyl proton singlet at \( \tau 3.86 \). This indicates a symmetrical environment for the vinyl protons in agreement with structure 11. The lack of splitting due to allylic hydrogens is also evident from structure 11. This definite assignment of compound 11 corroborates the position of the double bond in compound 10.

With the desired tetrahydro-1,4-octafulvene intermediate 11 in hand, we proceeded with the final two steps of the synthesis in the hope that allylic halogenation followed by dehydrohalogenation would afford the desired tetraphenyl-1,4-octafulvene 13 (eq 8).

![Chemical structure](image)

Treatment of compound 11 with NBS gave only an uncharacterizable yellow solid which decomposed rapidly. Repeated attempts to convert this material to 13 by dehydrohalogenation without purification yielded only polymeric material. It would appear that introduction of the remaining two elements of unsaturation at this last stage will be difficult, due to the great reactivity of the octafulvene system. A synthesis designed to incorporate the dehydration of the exocyclic methylene as the final step may be more effective. Thus the synthesis of 1,4-octafulvene derivatives using compounds of the general structure...
(4 and 5) as the key intermediate was abandoned.

The second route explored involved compound 2 since considerable quantities were available from the previous synthetic scheme. It is well-known\textsuperscript{30} that 1,3-cyclooctadienes undergo photochemical electrocyclic closure to give bicyclo[4.2.0]octene. These bicyclo compounds can reopen by a thermal non-Woodward-Hoffmann process to the starting material. Thus, photolysis of compound 2 to compound 14, followed by dehydration and thermal reopening should give the desired 1,4-octafulvene (eq 9).
In fact, photolysis of 2 yielded only viscous yellow oils which could not be clearly characterized. In the infrared spectrum of the oil, the strong absorption at 1650 cm\(^{-1}\) present in the spectrum of the starting material had disappeared. The nmr spectrum indicated that the number of vinyl hydrogens was less than that expected in 1,4.

Although Cantrell and Schecter had unsuccessfully tried to dehydrate compound 2 directly to the 1,4-octafulvene system with various reagents,\(^{22}\) the dehydration may be possible using non-acidic reagents such as phenyl isocyanate. Oroshnik reported\(^{31}\) dehydration of a tertiary alcohol in the final step of a Carotenoid synthesis using phenyl isocyanate. However, application of the Oroshnik procedure to compound 2 led only to intractable gums and starting material as indicated by ir. No further investigation of synthetic pathways involving 5,8-bis-(\(\alpha\)-hydroxybenzhydryl)-1,3,6-cyclooctatriene was performed.

The final synthetic investigation was based on the recent reports that the reaction of cyclopentadienide anion with trialkoxycarbonium, alkoxybis(dialkylamine)carbonium, tris(alkythio)carbonium ion salts or with the carbonium immomium methosulfate complexes yield fulvenes substituted at the exocyclic carbon by alkoxy, thioalkoxy and amino groups\(^{17,32,33,19}\) (eqs 10, 11, and 12).

\[
\begin{align*}
\text{2} & \quad + \quad (\text{RO})_3\text{C}^+\text{BF}_4^- \quad \rightarrow \quad \text{RO} \quad \text{OR} \quad \text{RO} + \text{OR} \\
\text{NR}_2 & \quad + \quad (\text{R}_2\text{N})_2\text{C}^+\text{BF}_4^- \quad \rightarrow \quad \text{NR}_2 \quad \text{NR}_2
\end{align*}
\]
The fulvenes of this type exhibit greater stability and are generally less reactive than the simple hydrocarbon fulvenes, since the electron-donating C₆-substituents increase the contribution of the dipolar resonance structures. Thus, cyclooctatetraene dianion might condense with the substituted carbonium ion tetrafluoroborate or dimethylsulfate complexes to yield the corresponding 1,4-octafulvenes (eq 13). It seemed likely that the electron-donating substituents on the exocyclic carbon would result in more stable examples of the octafulvene system.

Thus, cyclooctatetraene dianion was treated with dimethylsulfate complex of N-methylpyrrolidone according to the procedure Crabtree and Bartelli¹⁹ used with cyclopentadienide anion. Once again, only polymeric material was isolated. The reaction of cyclooctatetraene dianion with bisdimethylaminoethoxy carbonium fluoroborate, analogously to the Hafner procedure¹⁷ using cyclopentadienide anion gave only non-characterizable red oils.
It would appear, as mentioned previously, that the 1,4-octafulvene system exists in a non-conjugated tub-like structure, $\mathcal{Z}_c$, in which resonance with the necessarily planar dipolar structure is not possible. The tub-like form would be expected to exhibit properties characteristic of a polyolefin, including high chemical reactivity. This may account for the lack of success in the chemical syntheses thus far explored.
EXPERIMENTAL*

Benzyltribenzyolphosphonium Chloride. According to the procedure of Friedrich and Henning, triphenylphosphine (26.1 g, 0.1 mole) was dissolved in neat benzyl chloride (20.2 g, 0.16 mole). The stirred solution was heated until the phosphonium salt precipitated (10 min). The mixture was cooled in order to obtain additional crystalline salt, then filtered, and the salt was washed with ether. Recrystallization from ethanol gave 29.1 g (75%) of white prisms, mp 316-317° (lit. mp 317-318°).

Wittig Reaction with 1,4-Cyclooctanedione, Method A (Using Butyl Lithium in Ether). The reaction was carried out according to the procedure of Wittig and Hogg. To a 250 ml 3-neck round-bottomed flask equipped with stirrer, reflux condenser, and charged with benzylidene-triphenylphosphorane (11.6 g, 0.029 mole) [prepared from 1.84 g, 0.029 mole] butyl lithium and (11.2 g, 0.029 mole) benzyltribenzyolphosphonium chloride mixed in 50 ml of dry ether] in 100 ml of dry ether under nitrogen atmosphere was added dropwise a solution of (2.0 g, 0.14 mole) 1,4-cyclooctanedione in 20 ml of ether. Disappearance of the phosphorane was accompanied by a color change from a deep orange to a pale yellow suspension. The mixture was stirred at room temperature for 4 hrs and refluxed overnight. The resulting cream colored slurry was cooled, filtered (to remove triphenylphosphine oxide and unreacted phosphonium

* All melting points and boiling points are reported uncorrected. Infrared spectra were taken on a Beckmann-IR 8. Nuclear magnetic resonance spectra were taken on a Varian A-60 or a Varian A-56/60 spectrometer using tetramethylsilane as an internal standard. Ultraviolet spectra were taken on a Bausch and Lomb Spectronic 505 or a Cary Model 14 instrument. Elemental analyses were done by commercial analytical laboratories.
salt, dried (magnesium sulfate), and concentrated to give 4.3 g (50%) of a yellow oil; ir (film) 1685, 1630, 1440, 1388, 1185, 1120, 720, and 700 cm\(^{-1}\). The infrared spectrum indicated the presence of a conjugated carbonyl and triphenylphosphine oxide. In no case was any 7,8-dibenzylidene-1,3,6-cyclooctatriene isolated. Alumina chromatography of the reaction yielded only triphenylphosphonium oxide, mp 155\(^{0}\) [lit\(^{34}\) mp 155-156\(^{0}\)].

Although isolation and identification of the unsaturated ketone was not attempted, its structure appeared to be bicyclo[3.3.0]-1(5)-octen-2-one considering the known susceptibility of the dione to intramolecular aldolization.\(^{27}\)

**Wittig Reaction with 1,4-Cyclooctanediene, Method B (Using Sodium in Dimethyl Sulfoxide).** The reaction was carried out according to the procedure of Corey, Greenwald and Chaykovsky.\(^{35}\) Sodium hydride (1.24 g, 0.03 mole, as a 55% dispersion in mineral oil) in a 200 ml three-necked flask was washed with several portions of n-pentane to remove the mineral oil. Under a nitrogen atmosphere, 20 ml of dimethyl sulfoxide was added via syringe and heated at 75-80\(^{0}\) for 45 min or until the evolution of hydrogen ceased. The resulting solution was cooled in an ice-water bath and a solution of benzyltriphenylphosphonium chloride (11.6 g, 0.03 mole) in 60 ml of dimethyl sulfoxide was added. After the resulting dark red solution was stirred for 30 min, a solution of 1,4-cyclooctanediene (2.0 g, 0.014 mole) in 10 ml of DMSO was added and stirred for 3 hrs at room temperature. The reaction mixture was poured into water and extracted with n-pentane; the combined pentane extracts were washed with water, dried (sodium sulfate), and evaporated to give a white solid. The solid was collected by filtration and washed with
cold pentane to yield 7 g of triphenylphosphine oxide identified by its mp [155-156°; lit[24] mp 155-156°] and its ir spectrum (CCl₄) which was identical with a published spectrum. The ir spectrum (film) of the filtrate (1685 and 1630 cm⁻¹) indicated the presence of conjugate ketone and was not further investigated.

Preparation of 5,8-Bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene (2). To an ether solution of diliithium cyclooctatraenide was added benzophenone according to the procedure of Cantrell and Schechter.22 Workup gave, besides the solid 1,1,10,10-tetraphenyldecatetraene-1,10-diol, 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene in 50% yield as a yellow syrup. The nmr and infrared spectra were in good agreement with the published results.

Hydrogenation of 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene (2). A solution of crude 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene (10.0 g) in ethyl acetate was shaken with 10% palladium on charcoal under 1 atm of hydrogen until there had been an uptake of 2 moles of hydrogen. It was necessary to add fresh catalyst, as consumption of hydrogen had become quite slow after the uptake of ca 1.5 moles. Alternatively, use of very large quantities of catalyst usually gave complete reduction without the addition of a fresh batch. The reaction was filtered, dried (magnesium sulfate), and the solvent evaporated yielding 7.6 g of a pale yellow glassy solid, mp 65-71°: ir (Kbr) 3550, 3100, 3065, 3040, 1601, 750, and 697 cm⁻¹; nmr (CCl₄) τ 4.5 (2 H, multiplet, olefinic H), τ 6.45 (2 H, multiplet, allylic H), τ 7.3 (2 H, broad singlet, OH), and complex absorption at τ 7.95-9.0 (8 H, aliphatic).
Dehydration of 3,8-(α-hydroxybenzhydryl)-1-cyclooctene (10).
A solution of 3,8-(α-hydroxybenzhydryl)-1-cyclooctene (10) in 50 ml of benzene was flushed with nitrogen for 0.5 hrs. p-Toluenesulfonic acid (200 mg) was added and the solution was stirred for 14 hrs at 50°. The dark brown reaction mixture was poured into water, extracted twice with sodium bicarbonate, dried, and evaporated. The viscous tan oil, after standing overnight, crystallized. The residue was filtered and further crystals were obtained by triturating the benzene mother liquor with 1:1 etherethanol. Recrystallization from acetone gave a fluffy white solid, mp 172-174°, (1.1 g, 40%): ir (KBr) 3098, 3080, 3033, 1595, 778, 762, and 703 cm⁻¹; uv (hexane) max 320 mp (ε 14,580); nmr (CDCl₃) τ 2.8 (2 H, multiplet, phenyl H), τ 3.86 (2 H, singlet, vinyl H), τ 7.40 (4 H, multiplet, allylic H), τ 8.46 (4 H, multiplet, aliphatic H).

Anal: Calcd for C₃₄H₃₀: C, 93.11; H, 6.89. Found: C, 92.59; H, 7.41.

Bromination of Triene (11). To a solution of triene 11 (200 mg, 0.4 mmole) in 5 ml of carbon tetrachloride flushed with nitrogen was added N-bromosuccinimide (170 mg, 0.9 mole) and a catalytic amount of benzoylperoxide. After refluxing for 3 hrs, the reaction mixture was cooled and filtered to remove succinimide; the orange filtrate was dried and concentrated to give 180 mg of a glassy yellow solid which decomposed on standing at room temperature. In subsequent experiments, preparation of the dibromide was followed immediately by dehydrohalogenation, with no attempt at purification.
Attempted Dehydrohalogenation of Dibromotriene 12 with 1,5-
Diazobicyclo[4.3.0]-5-nonene. To an excess of 1,5-diazobicyclo-
[4.3.0]-5-nonene(DBN) (10 ml) in 20 ml of benzene was added a
solution of freshly prepared dibromotriene 12 (0.4 g) in 10 ml of
benzene. The resulting dark red reaction mixture was warmed to 60°
for 1 hr, cooled, and poured into a slurry of ice-dilute sulfuric
acid. The organic layer was separated, washed with dilute sulfuric
acid until neutral, dried, and concentrated to give 0.3 g of viscous
black-green oil. Trituration with carbon tetrachloride gave a dark
green solid polymer. The infrared spectrum indicated a strong
absorption at 1650 cm⁻¹ (C=O) in addition to 3050 cm⁻¹ (aryl). The
nmr (CCl₄) except for phenyl absorption at τ 2.8 was a featureless
broad blur.

Photolysis of 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclo-
octatriene (9). A solution of crude 5,8-bis(α-hydroxybenzhydryl)-
1,3,6-cyclooctatriene (4.7 g) in 200 ml of dry ether was placed in
a water cooled, concentric reaction vessel, flushed with nitrogen,
and irradiated for 10 hrs through a Vycor filter with 450 w Hanovia
medium-pressure mercury lamp. The course of the reaction was
followed by tlc. After 13 hrs almost all of the starting material
had been consumed. Evaporation of solvent yielded 4.5 g of a yellow
glass. The ir (CCl₄) indicated that the strong double bond absorption
of the starting material trienediol at 1660 cm⁻¹ was absent. The
olefinic region of the nmr spectrum contained an uncharacterizable
broad multiplet (τ 3.8-4.6) whose integral was not in agreement with
the expected product.

Attempted treatment of the crude reaction mixture with
p-toluenesulfonic acid in benzene gave only an uncharacterizable red gum. Thus this synthetic procedure was abandoned.

**Dehydration of 5,8-bis(α-hydroxybenzhydryl)-1,3,6-cyclooctatriene (2) with Phenyl Isocyanate.** To phenyl isocyanate (2 ml) was added, according to the procedure of Oroshnik, trienediol (3.3 g, 7.0 mmoles) and several drops of a solution of methyl magnesium bromide in tetrahydrofuran as catalyst. Several more drops of Grignard catalyst were added since no precipitation of diphenyl urea appeared. The red reaction mixture was stirred under nitrogen at 95° for 3 hrs. Excess phenyl isocyanate was removed under vacuum to give 3 g of a red paste. The infrared spectrum (CCl₄) with peaks at 3600 and 2245 cm⁻¹ indicated the presence of only starting material.

**Attempted Preparation of Compound 16 Using the Dimethyl Sulfate Complex.** The reaction was carried out according to the Crabtree and Bertelli procedure for the preparation of 1-methyl-2-cyclopentadienylidene-2,3,4,5-tetrahydropyrrole. To a solution of cyclooctatetraene (10 g, 0.1 mole) in 200 ml of dry tetrahydrofuran in a 500 ml 3-neck round-bottomed flask flushed with nitrogen was added potassium metal (8 g, 0.2 mole) in small pieces over a 0.5 hr period. The black-green solution was stirred overnight in order to completely dissolve all the potassium. A mixture of N-methyl-2-pyrroli-done (19.8 g, 0.2 mole) and dimethyl sulfate (25.2 g, 0.2 mole) was heated for 20 min on the steam bath. The resulting red complex was added dropwise to the dipotassium cyclooctatetraenide solution which was cooled to -5° in an ice-salt bath. After the resulting black-red mixture had stirred ca 2 hrs, the suspension was filtered under
nitrogen and the filtrate was concentrated to give a dark-brown polymeric solid. The infrared spectrum (film) exhibited, except for a peak at 1610 cm⁻¹ (unreacted N-methylpyrrrolidone), indistinguishable blurs, rather than sharp bands.

**Attempted Preparation of Compound 16 Using the Fluoroborate Salt.** The reaction was carried out according to the procedure of Hafner, et al.¹⁷ To a solution of dipotassium cyclooctatetraenide (0.84 g, 8 mmoles, prepared as described previously) in 50 ml of dry tetrahydrofuran was added bisdimethylaminooxy carbonium fluoroborate (3.7 g, 16 mmoles, mp 81-82°, prepared as described by H. Meerwein, et al.¹⁸) and stirred for 4 hrs at room temperature. The dark red reaction mixture was filtered to remove sodium fluoroborate and then concentrated to give a red tacky mass. Tlc indicated a complex mixture, whose nmr spectrum (CCl₄) possessed a signal at τ 4.3 (cyclooctatetraene), N-methyl signals at τ 7.3 and uncharacterizable blurs.
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PART II
INTRODUCTION

The alkylation and acylation of unsaturated compounds in the presence of Lewis acid catalysts comprise a broad class of reactions, collectively known as Friedel-Crafts reactions.\(^1\,^2\) This group of transformations is extremely useful synthetically and has been an important part of organic chemistry since the initial report by C. Friedel and J. M. Crafts almost 90 years ago.\(^3\) The most common versions of the Friedel-Crafts reaction are those with aromatic compounds as substrate and involving electrophilic attack by species produced from alkylation agents, usually an alkyl halide or acid anhydride, and a metal halide catalyst. The product formed is an alkyl or acyl aromatic, the net result of substitution into the ring (eq 1).

\[
\begin{align*}
\text{C} & \quad + \quad \text{RX} & \quad \xrightarrow{\text{MX}} & \quad \text{C} & \quad \text{RCO}\quad \text{(eq 1)}
\end{align*}
\]

A short time after Friedel and Crafts introduced aromatic alkylation and acylation, I. L. Kondakov in 1892 extended acylation to aliphatic systems.\(^4\) The reagents involved are similar to those in the aromatic cases. Reaction of the olefin with the electrophilic species gives a mixture of β-haloketones and unsaturated ketones. Yields range up to 60%, but frequently are quite low due to rearrangement of the products, polymerization, and polyacylation of the olefin. Distillation of the crude product mixture from base or refluxing in base usually results in formation of an \(\alpha,\beta\)-unsaturated ketone (eq 2).
\[ \text{RHC=CHR} + \text{R'}\text{COX} \xrightarrow{\text{MC}_{n}} \text{RXC=CHR-COR'} + \text{RHC=CR-COR'} \] (2)

\( X = \text{halogen or OCOR'} \)

\[ \text{Base} \]

\[ \text{RHC=CR-COR'} \]

The most detailed mechanistic examination of the acylation reaction has been carried out in the aromatic series so as to limit the number of competing reactions and products.\(^5\) The basic mechanism can be briefly represented as follows (eq 3):

\[ \text{RCOX} + \text{MX}_3 \xrightleftharpoons{} (\text{RCO}^+\text{MX}_4^-) \] (3)

\[ \xrightarrow{} \text{COR} \quad \text{COR} \quad + \text{H}^+\text{(MX}_4^-) \]

\[ \text{H}^+\text{(MX}_4^-) \xrightleftharpoons{} \text{HCl} + \text{MX}_3 \]

The role of the catalyst is to activate the acid halide in some way and produce a more powerful electrophilic species. Controversy still exists as to whether the attacking species is an addition complex \( \_1 \), a free acylium ion \( \_2 \), or an ion pair \( \_3 \).

\[ \begin{array}{c}
\text{R} \\
\text{C}=\text{O}^+\text{AlCl}_3 \\
\text{Cl} \\
\_1
\end{array} \quad \begin{array}{c}
\text{R-C}=\text{O}^+\text{AlCl}_4^- \\
\_2
\end{array} \quad \begin{array}{c}
\text{R-C}=\text{O}^+\text{AlCl}_4^- \\
\_3
\end{array} \]

Many addition compounds between Lewis acids and acid chlorides have been isolated and characterized as 1:1 complexes,\(^5\) although formation of an isolable addition compound is not necessary for these to function as acylating species.\(^6\) The ionic nature of these addition compounds has been established by dipole moment\(^7\) and conductimetric measurements.\(^8\)
However, the extent of ionization is still uncertain.

Addition compounds are also known between ketones and Lewis acids. Some are 1:1 complexes, for example, aluminum chloride and zinc chloride, whereas stannic chloride and ferric chloride form 2:1 complexes. Indeed, prolonged exposure of the ketone to Lewis acids will result in self-condensation; Calloway and Green reported that the major product of aluminum chloride acetylation of benzene was not acetophenone but \( \alpha \)-methylstyrlyl phenyl ketone.

By analogy of the known ability of aluminum chloride to coordinate with the oxygen atom in ketones and ethers, Pfeiffer in 1927 proposed structure \( 1 \) for the acylating species.

\[
\begin{align*}
\text{R} & \quad \text{C}=\text{O} \quad \text{AlCl}_3 \\
\text{Cl} & \quad \text{AlCl}_3
\end{align*}
\]

This was largely ignored and structure \( 2 \) as proposed by Meerwein was generally accepted. Several other structures have been proposed over the years, but the majority of the evidence favors these two. It may be that the exact nature of the acylating species depends on the various reaction conditions.

From the above sequence (eq 3), it would appear that only a catalytic amount of metal halide is needed. However, experimentally somewhat more than one equivalent is necessary to obtain good conversion of the starting material. This is due to the basic nature of the product ketone which can coordinate with the metal halide. Baddeley and Voss have reported that the ionization of acyl halide is not prevented by adding ketones to Friedel-Crafts reaction mixtures, implying that ketones are less strongly coordinated to metal halides that are acyl halides. The observation,
mentioned above, that more than one mole of metal halide is necessary for complete reaction, is best explained by complex formation of one molecule of product ketone with one of the "acylating species" (whatever its nature); thus preventing its attacking the substrate. It may be concluded that, in the absence of substantial amounts of catalyst, the action of the acylum ion, rather than that of the catalyst, is blocked. The competition between the ketone and substrate for the acylum ion may be represented as follows (eq 4).

\[
\begin{align*}
R\text{C}=O\text{AlCl}_3 & \rightleftharpoons R\text{C}=O\text{AlCl}_4^- \\
\text{ArH} & \rightleftharpoons \text{Ar}\text{C}=O\text{AlCl}_3 + \text{HCl} \\
\text{ArCOR} & + \text{AlCl}_4^- \\
\end{align*}
\]

(coordination of ArCOR with AlCl₃ inhibits above)

From this data, it would appear that the favored form of the acylating species is the acylum ion, but this may not be so in some cases. Kaye¹² has shown that anisole acylates in the presence of acid halides and iodine. This surely acylates via RCIC=O:IC₂ rather than RC=O ClI₂.

Since ClI₂ is unstable under the reaction conditions.

The halogen exchange experiments of Fiarbrother¹³ favor acylum ion formation (eq 5):

\[
\begin{align*}
\text{RCOOCl} + \text{AlCl}_3 & \rightarrow \text{R}^+\text{C}=O\text{AlCl}_4^- \\
\text{R}^+\text{C}=O\text{AlCl}_4^- & \rightarrow \text{RCOCl}^* + \text{AlCl}_2\text{Cl} \\
\end{align*}
\]

Cl* indicates radioactive Chlorine
However, one could argue that a species such as $\frac{1}{2}$, which results from the direct addition of aluminum chloride across the carbonyl, accounts for the exchange. A more convincing halogenation exchange experiment was performed by Addeley and Voss.\textsuperscript{10} 1,3,5-trihalobenzoylchloride and aluminum chloride exchanged halides and reacted with aromatic hydrocarbons in the normal way. Large steric hindrance would be encountered if structure $\frac{2}{2}$ had been involved.

The numerous infrared studies of addition complexes have been summarized by Olah.\textsuperscript{14} The structures, either acylium salts or oxonium ions, vary depending on conditions employed. In the solid state the aluminum chloride and acetyl chloride complex exists as an acylium salt,\textsuperscript{15} in chloroform as the oxonium salt,\textsuperscript{16} and in nitrobenzene as a mixture of both.\textsuperscript{16}

The majority of the kinetic investigations of acylation have been obtained from aluminum halide-catalyzed benzoylations.\textsuperscript{5} Yet even in this one case, various kinetic expressions were obtained depending on the solvents used. Brown and coworkers\textsuperscript{17} obtained some of the more significant kinetic data from the aluminum chloride-catalyzed benzoylation in benzoyl chloride as solvent. Previous experiments\textsuperscript{18} with nitrobenzene as solvent have complicated kinetics because aluminum chloride complexes with nitrobenzene.
The reaction followed simple second order kinetics; first order in the aromatic substrate and first order in the acylating species, if one assumes a 1:1 complex between acid halide and catalyst.

\[ \text{Rate} = k_2 \left[ \text{ArCOCl} \right] \left[ \text{AlCl}_3 \right] \left[ \text{ArH} \right] \]

The kinetic evidence indicates that the rate of acylation is dependent on the concentration and nature of the aromatic hydrocarbon; thus if an acylium ion or ion pair is involved, the rate determining step cannot be its formation. Kinetic experiments to establish the relationship of the rate of exchange to the rate of acylation have not been done. Establishing these relationships would unambiguously determine the mechanism.

Since the energy difference between the acylium ion salt and the addition complex (eq 6) is small, making the predominance of either dependent on conditions employed, two mechanisms for acylation can be written. The acylium ion mechanism (A) is shown in (eqs 6-8).

\[ \text{RC-Cl} + \text{AlCl}_3 \rightarrow (\text{RC}^+\text{O AlCl}_4^-) \]  

(6)

\[ \text{RC}^+\text{O} + \text{ArH} \rightarrow \text{RC-ArH} \]  

(7)

\[ \text{RC-ArH} + \text{AlCl}_4^- \rightarrow \text{RC-Ar} + \text{HCl} \]  

(8)

The rate controlling step can be eq 7 or, if the acylium ion exists as an ion pair, eq 6 could be rate controlling. The oxonium ion mechanism (B)\(^\text{10}\) is shown below (eqs 9 and 10).
Kinetic isotope studies are ambiguous and the increase in rate with the increase in polarity of the solvent can be explained with various steps of either mechanism being rate controlling.\textsuperscript{19} It may be that the rate determining step is solvent dependent.

Acylation of olefins proceeds via the same electrophilic species as discussed in aromatic acylation. However, a variety of products are obtained depending upon how the incipient carbonium ion reacts (Scheme I):

**SCHEME I**

\[ R'\text{CH}_2\text{CH}==\text{CHR}'' + \text{RCOCl}--\text{AlCl}_3 \]

Path A \[ \xrightarrow{\text{Z}} \]

\[ R'\text{CH}_2\text{CH}==\text{CHR}''--\text{COR} \]

Path B \[ \xrightarrow{\theta} \]

\[ R'\text{CH}_2\text{CH}==\text{CHR}''--\text{COR} \]

Path C \[ \xrightarrow{\theta} \]

\[ R'\text{CHCl}_2\text{CH}==\text{CHR}'--\text{COR} \]

Path D \[ \xrightarrow{\theta} \]

\[ R'\text{CH}_2\text{CH}==\text{CHR}'--\text{COR} \]

\[ \xrightarrow{\theta} \]

\[ R'\text{CHCl}_2\text{CH}==\text{CHR}'--\text{COR} \]

\[ \xrightarrow{\theta} \]

\[ R'\text{CH}_2\text{CH}==\text{CHR}'--\text{COR} \]

\[ \xrightarrow{\theta} \]

\[ R'\text{CHCl}_2\text{CH}==\text{CHR}'--\text{COR} \]

Carbonium ion $\theta$ which is formed by the Markownikov addition of the acyl group can add a halide ion to form $\zeta$, eliminate in two directions forming $\theta$ and $\gamma$, and undergo hydride transfer.
Several mechanisms for the subsequent reaction of species Ḟ have been proposed. Path A represents addition of the anion and later dehydrohalogenation. Path B represents a formal direct substitution. Satchell\textsuperscript{18} has reported that a decrease in the addition product with an increase of Lewis acid strength favors Path B. However, Taylor\textsuperscript{20} reports substitution which definitely occurs via addition; this could be accounted for by the reversal of Path A followed by Path B. Halides could also be formed if Path B were reversible. This step has been demonstrated by carbon-14 labeling\textsuperscript{21} and cleavage experiments\textsuperscript{22} to be reversible.

Diacylation of unsaturated ketones has indicated the possibility of a cyclic mechanism. Pyrylium salts, which are the subsequent products of diacylation, usually result when olefin acylations are run for extended periods of time with excess catalyst, or if the unsaturated ketones themselves are treated with strong Bronsted acid and an anhydride (eq 11).

\begin{equation}
\begin{array}{c}
\text{O} \\
\text{\text{CH}$_3$}
\end{array}
\xrightarrow{\text{R-}\text{C=O}}
\begin{array}{c}
\text{R}
\end{array}
\xrightarrow{\text{H}^+}
\begin{array}{c}
\text{R}
\end{array}
\xrightarrow{\text{+H$, -H$_2$O}}
\begin{array}{c}
\text{R}
\end{array}
\end{equation}

What is unusual is that the major olefin isomer is the non-conjugated, thermodynamically less stable one. This has been explained by a mechanism involving a cyclic transition state\textsuperscript{23} (eq 12).

\begin{equation}
\begin{array}{c}
\text{H}
\end{array}
\xrightarrow{\text{+}}
\begin{array}{c}
\text{R}
\end{array}
\xrightarrow{\text{H}}
\begin{array}{c}
\text{R}
\end{array}
\xrightarrow{\text{\text{HO}}}$
\text{R} \rightleftharpoons
\begin{array}{c}
\text{R}
\end{array}
\end{equation}
Normal olefin acylation also gives mixtures of unsaturated ketone isomers. This was first reported by Harries\textsuperscript{24} in his study of the acylation of isobutylene. With care, the $\beta,\gamma$-unsaturated ketone could be separated;\textsuperscript{25} the conjugated isomer was the major product. The olefin isomers can vary with the catalyst used as was shown by Arnaud.\textsuperscript{26}

Deno and Chafetz\textsuperscript{27} found that when the acylation of methylcyclohexene in acetic anhydride and zinc chloride was conducted with the careful exclusion of base in the workup procedure, the major product was the non-conjugated isomer. A cyclic mechanism or trans-addition of the acylating species with accompanying trans-elimination can explain these results.

With the use of anhydrides as acylating agents many workers reported cleaner reactions;\textsuperscript{28} this is attributed to the lack of haloketone formation. Contrarily, Belov\textsuperscript{29} has found $\beta$-haloketone formation in anhydride acylation although no trace of acid chloride is present. The following cyclic mechanism is proposed (eq 13):

\[
\begin{align*}
\text{AcO} &+ \text{CH}_3 \rightarrow \\
\text{OMX}_3 &\rightarrow \text{OAc} \rightarrow \\
\text{CH}_3 &+ \text{AcOMCl}_2
\end{align*}
\]

Hydride transfer is the third mode of reaction possible for the intermediate carbonium. It is the most interesting, since skeletal rearrangements may occur. Nenitzescu and Gavat\textsuperscript{30} first observed this reaction in 1935 when the acylation product of cyclohexene and acetyl chloride was reacted with benzene in the presence of aluminum chloride. The expected 1-acetyl-2-phenylcyclohexane was not obtained; instead
the product was 1-acetyl-3-phenylcyclohexane. Similarly 1-acetyl-3-phenylcyclopentane was obtained from cyclopentene. This explains why some traces of chloro compounds remain even after treatment of the mixture of haloketone and unsaturated ketone with base. The stability of δ-haloketones to base was proven when Steven and Farkas\textsuperscript{31} unambiguously synthesized 4-chloro-1-benzoylcyclohexane and were unable to effect dehydrohalogenation with sodium ethoxide. This compound was also isolated in 3-5% yield from the benzoylation of cyclohexene. Treatment of the ϒ-haloketone with aluminum chloride in carbon disulfide isomerised it to the δ-haloketone.

In 1953 Nenitzescu\textsuperscript{32} reported a comparative study of the acylation of C\textsubscript{5}-C\textsubscript{8} cycloolefins. An 86% yield of ϒ-chloroketone was found with cyclopentene plus small amounts of the β-chloro isomer and unsaturated ketone. In the higher olefins, δ-haloketone predominated over the ϒ- and γ-halo isomers with the major product being the unsaturated ketone. In certain instances Nenitzescu found haloacetylcyclohexane products from the acylation of cycloheptene and cyclooctene.

Baddeley\textsuperscript{32c} also showed that chlorocyclohexane reacts with aluminum chloride and acetyl chloride in nitrobenzene solvent to yield acetylcyclohexene. Using ethylene dichloride as solvent 2-methyl-1-acetylcyclopentene is obtained.

The variety of products from the acylation of olefins is dependent upon the attacking species and the subsequent reaction of the carbonium ion generated. All these possibilities can be modified depending on what type of systems are used. The wide variations possible in catalysts, acylating agents, and solvent make generalization somewhat difficult. However, evaluation of reaction conditions deserve some consideration.\textsuperscript{33}
The mode of addition most often employed is the addition of the olefin to a solution of the catalyst and acylating agent. This is most convenient with aluminum chloride and acid halides in methylene chloride solvent. However, if the ketone product is subject to polyacylation the acyl derivative is added to a mixture of olefin and catalyst. Polymerization of the olefin by the catalyst is kept to a minimum by addition of the catalyst to a mixture of olefin and acylating agent.

The acylating agents most commonly employed are acid halides and anhydrides. The relative reactivity of the acid halides usually follows the electronegativity of the halide, i.e., I > Br > Cl > F.\textsuperscript{34,35}

The nature of the acylating agent can cause several anomalies. A highly branched acylating agent like trimethylacetyl chloride can decarbonylate\textsuperscript{36} (eq 14).

\[
\begin{align*}
\text{COCl--AlCl}_3 & \rightarrow \text{+ CO} \rightarrow \text{+ CO + AlCl}_4 \rightarrow \text{Benzene (14)} \\
& \downarrow \\
\text{Ar + CO + HCl + AlCl}_3
\end{align*}
\]

Others could give products which are susceptible to cyclization\textsuperscript{37} (eq 15).

\[
\begin{align*}
\text{R}_2-\text{C}==\text{C-R}_2 + \begin{array}{c}
\text{Cl} \\
\text{O}
\end{array} & \xrightarrow{\text{AlCl}_3} \text{Pheny} + \text{C}==\text{C} + \text{C}==\text{C} \text{(15)}
\end{align*}
\]

The choice of reaction medium can also play an important role.
in the course of acylation. Common reaction media are: carbon
disulfide, nitrobenzene, methylene chloride, halogenated solvents,
hydrocarbons, or no solvent at all.

Non-polar solvents such as carbon disulfide and the halogenated
solvents are most often used. Carbon disulfide usually promotes
dehydrohalogenated products. Methylene chloride gives better yields
of both halogenated and unsaturated ketones. Methylene chloride is
favored over carbon disulfide when using aluminum chloride since the
acylating complex is soluble in methylene chloride and not in carbon
disulfide. The acylating complex can then be decanted from the excess
aluminum chloride.²⁰

Hydrocarbon solvents promote hydride transfers and are used in
preparation of saturated ketones. Many acylations, especially when
anhydrides are used, are run without solvent. These conditions favor
unsaturated ketone products although some haloketones have been reported.

The relative effectiveness of the most common metal halides,
aluminum chloride, stannic chloride, and zinc chloride in catalyzing
acylation reactions follows their Lewis acid strength. Zinc chloride,
the mildest of the three catalysts, is usually used without solvent in
excess anhydride.⁴⁷²⁷ These conditions favor unsaturated ketone formation,
thus avoiding the dehydrohalogenation stage. The mild conditions permit
determination of the true isomer ratio of the unsaturated ketones.²⁷ In the
case of the more highly substituted anhydrides, e.g. propionic and
benzoic, the acid chlorides were found to give better yields.

Stannic chloride is used with both anhydrides and acid chlorides,
similar to zinc chlorides, but is most often used with acid chlorides.
Being of intermediate reactivity, stannic chloride has a multitude of
uses. It gives the best yield in acylation of cyclohexene in comparison with zinc chloride or aluminum chloride.\textsuperscript{38} Favorable results have been reported using one equivalent or less of the catalyst. Stannic chloride has advantages over aluminum chloride in that it does not cause rearrangement of the haloacetone products or destruction of sensitive acid chlorides.\textsuperscript{39}

Aluminum chloride, is one of the most powerful acylation catalysts.\textsuperscript{41} It may lead to product rearrangement if care is not taken. Lower reaction temperatures and polar solvents such as nitrobenzene are usually used.

Trifluoroacetic anhydride reacts with acetic acid to form a mixed anhydride which favors unsaturated ketone formation since the intermediate $\mathbf{12}$,

\[
\begin{array}{c}
\text{Ac} \\
\text{OOCCF}_3 \\
\end{array}
\]

is very easily eliminated. Perchloric acid must be used with caution since diacylation may result.

Cyclic olefins containing six to eight carbons undergo a wide variety of processes when treated with acylating agents. Cyclohexene usually gives normal products, i.e., $\beta$-haloketone and $\alpha$-$\beta$ unsaturated ketones and small amounts of $\gamma$- or $\delta$-haloketone as mentioned previously.\textsuperscript{32,33}

Cycloheptene gave 1-acetyl-cycloheptene when treated with aluminum chloride in carbon disulfide according to Taub and Szmuszkovic.\textsuperscript{42} This was confirmed by Rosenfielder and Ginsburg.\textsuperscript{43} Jones, Taylor, and Rudd used aluminum chloride-acid halide complexes in methylene chloride and reported the isolation of 1-acetyl-cycloheptene. In contrast, Friess and
Pinson\textsuperscript{45} obtained 3- and 4-methyl-1-acetylcyclohexane in cyclohexane solution; using either cyclohexane or carbon disulfide as solvents. Nenitzescu, Pogany, and Mihai found only rearranged 6-membered ring ketones.\textsuperscript{32}

Conflicting results have been reported for the acylation of cyclooctene. Ruzicka\textsuperscript{46} first reported that 1-acetylcyclooctene was obtained using stannic chloride in carbon disulfide. Later Jones, Taylor, and Rudd,\textsuperscript{44} using the aluminum chloride-acetyl chloride complex in methylene chloride, also reported 1-acetylcyclooctene. However, Nenitzescu reported rearrangement to 6-membered ring ketones.\textsuperscript{32} Brief reinvestigation, in these laboratories, of cyclooctene acylations under the reaction conditions of Jones, Taylor, and Rudd gave different results, which were similar to those of Nenitzescu. Rearranged haloketones and ring contractions products containing six and seven-membered rings were found.\textsuperscript{47}

Nenitzescu proposed successive 1,2-hydride shifts to account for halogen migration and 1,2-bond shifts for skeletal contractions.

However, in medium ring compounds (C\textsubscript{8}-C\textsubscript{11}) which are very prone to hydride transfer, the hydride shifts are not 1,2 but transannular.\textsuperscript{48} The chemistry of medium ring compounds has only recently been intensively investigated, owing to their lack of synthetic availability. The first example of a transannular hydride shift was reported by Cope, Fenton, and Spencer in 1952.\textsuperscript{49} Formolysis of cyclooctene oxide with subsequent hydrolysis gave some of the normal 1,2-diol; however, the major product was 1,4-cyclooctanediol (eq 16).
This can be explained by a 1,3- or 1,5-hydride transfer followed by attack of a formate ion. Later, Cope demonstrated the reaction proceeded to the extent of 61% by 1,5-hydride shift and 39% by 1,3-hydride shift.\textsuperscript{50}

In the acylation of olefins, transannular hydride transfers due to the proximity effect of the medium ring could account for the rearranged haloketones. The inherent reactivity of medium rings due to Pitzer strain, Baeyer strain, and proximity interactions would favor contraction to rings where this strain is absent.\textsuperscript{51}

Thus, a systematic investigation of the acylation of C-8 and C-9 olefins under various conditions in order to resolve the conflicting reports of cyclooctene acylation seemed attractive. The remainder of Part II of this dissertation describes the results of our investigations of these reactions.
DISCUSSION AND RESULTS

A. Cyclooctene

An initial investigation in these laboratories reported\textsuperscript{47} that acylation of cyclooctene using aluminum chloride-acetyl chloride complex in methylene chloride at -15°C according to the procedure\textsuperscript{44} of Jones, Taylor and Rudd gave no 1-acetylcylooctene but instead a mixture of 1-acetyl-4-chloro-4-ethylyclohexane (\textsuperscript{13}, 50%), trans-1-acetyl-4-methylcycloheptane (\textsuperscript{14}, 14%) and a small amount of acetylchlorocyclooctane (5%) subsequently identified as 1-acetyl-4-chlorocyclooctane \textsuperscript{15} (eq 17).

\[
\begin{align*}
&\text{CH}_2\text{COCl} \\
&\text{AlCl}_3-\text{CH}_2\text{Cl}_2 \to \begin{array}{c}
\text{Ac} \\
\text{C}_2\text{H}_5\text{Cl} \\
\text{CH}_3
\end{array} + \begin{array}{c}
\text{Ac} \\
\text{C}_2\text{H}_5 \\
\text{CH}_3
\end{array} + \begin{array}{c}
\text{Cl} \\
\text{Ac}
\end{array}
\end{align*}
\]

During the course of the writing of this dissertation a paper by Jones and Groves appeared, describing a reinvestigation of cyclooctene acylation,\textsuperscript{52} and concluding that their results using the above-mentioned conditions were erroneous. They now report that either compound \textsuperscript{13} or compound \textsuperscript{15} may be obtained, depending upon the purity of the aluminum chloride used. Since formation of compound \textsuperscript{13} and \textsuperscript{14} may be envisaged.

As proceeding via rearrangement of 4-acetylcylooctyl cation (\textsuperscript{16})
in the presence of especially active aluminum chloride, the use of a milder catalyst might be expected to yield compound 15 as the major product.

In the present investigation we find that acetylation of cyclooctene in the presence of stannic chloride in methylene chloride at -15°C provides 1-acetyl-4-chlorocyclooctane (15, 70%) and an unresolved mixture of 1-acetylcyclooctene (18) and 4-acetylcyclooctene (19) in 18% yield (eq 18).

\[ \text{CH}_3\text{COCl} \rightarrow \text{Cl} \]  
\[ \text{SnCl}_3 \text{ CH}_2\text{Cl}_2 \]  

Compound 15, 1-acetyl-4-chlorocyclooctane isolated as a mixture of cis and trans-isomers was identified by analytical and spectral data, its lack of reactivity toward base and by chemical degradation to 4-chlorocyclooctanone identical with an authentic sample. The isolation of only one chlorocyclooctanone in the degradation suggests but does not prove that no other positional isomers are formed in the acylation.
In the degradation sequence shown (Scheme II), Baeyer-Villiger oxidation of 15 gave the acetate 21 in high yield; separation of 21 from unreacted 15 was accomplished by treatment with Girard's reagent T. Lithium aluminum hydride reduction of 21 followed by oxidation with Jones reagent gave 4-chlorocyclooctanone (23) identical with an authentic sample. \(^{53}\)

Treatment of compound 15 with sodium methoxide in refluxing methanol gave essentially unchanged starting material (ir, glc). However, the cis:trans ratio changed from 55:47 to 65:35. The major component was tentatively assigned the cis structure by comparison of the glc retention time of the crude acylation reaction mixture (in which 15 appears as one unresolved peak at retention time of 8 min) to the glc of the isomer mixture from base treatment in which the major component has an identical retention time. It is also known\(^ {48}\) that substituents produced by transannular hydride transfers in eight-membered rings usually possess cis stereochemistry.

The formation of compound 15 can be accounted for on the basis of the well documented\(^ {48}\) 1,3 or 1,5-hydride transfer in medium rings (Scheme III).
The intermediate carbonium ion $\mathbf{17}$ may undergo simple addition of chloride anion or transannular hydride transfer to give 4-acetylcyclooctyl cation $\mathbf{16}$. Subsequent loss of a proton from $\mathbf{16}$ or chloride anion addition affords either compound $\mathbf{19}$ or the chloroketone $\mathbf{15}$. Compound $\mathbf{20}$ easily undergoes dehydrohalogenation to give 1-acetylcyclooctene whereas $\mathbf{15}$ if more stable to base.

Acylations using carbon disulfide as solvent have been reported$^{40,42}$ to give better yields of dehydrohalogenated products. Jones and Groves reported$^{52}$ acetylation of cyclooctene with stannic chloride in carbon disulfide at room temperature for 6 hrs gave 1-acetylcyclooctene (18, 38%) and 1-acetyl-4-chlorocyclooctene (15, 25%). In our hands, acetylation of cyclooctene with stannic chloride in carbon disulfide at -10° gave a reaction mixture showing an identical pattern on glc to that obtained using methylene chloride as solvent (eq 19). The infrared spectrum of the two mixtures were identical. Distillation from sodium
carbonate did give a slightly larger portion of elimination product. Analytical glc indicated a 30% mixture of compound 19 and 18 and 60% chloroketone 15.

\[
\begin{align*}
\text{CS}_2 & \xrightarrow{-5^\circ} \text{Cl-SnCl}_4 \xrightarrow{\text{O}} \text{Ac} \\
\text{Ac} & + \quad \text{Ac} \\
15 & \quad 18 & \quad 19
\end{align*}
\]

In a private communication, Groves ascribes the formation of 1-acetylcyclooctene (18) as the major product to a medium effect; a medium of low polarity prevents hydride transfer in cation 17 and gives rise to the β-chloroketone which is easily dehydrohalogenated.

On the basis of our results, we believe the critical factor is not the medium but rather the temperature used. Since cation 17 does undergo 1,3- or 1,5-hydride transfer the products obtained by Jones and Groves might arise by chloride abstraction form the 4-chloroketone 15 by the catalyst at high temperature. Indeed, when the 4-chloroketone 15 and an excess of stannic chloride were stirred in carbon disulfide for 6 hrs at room temperature the major products obtained were 1-acetylcyclooctene (19) and 4-acetylcyclooctene (18) (glc, ir, nmr) in yields of 25% and 15% plus minor amounts of unreacted compound 15 and three minor components of short glc retention time; these probably are ring contraction products but were not identified.

With the considerable quantities of 1-acetyl-4-chlorocyclooctane (15) on hand, it became feasible to examine how the ring contraction
products 13 and 14 are formed. These may arise from direct Wagner-Meerwein rearrangement of the 4-acetylcylooctyl cation (16) and subsequent ionization of chloroketone 15 by catalyst. In fact, treatment of 4-chloroketone 15 with excess aluminum chloride in methylene chloride for 2 hrs at -15° gave unchanged 4-chloroketone 15. However, using a freshly opened bottle of reagent aluminum chloride, we did obtain ring contraction products. Gas chromatography of the crude reaction mixture indicates no 4-chloroketone remained, but only products of considerably shorter glc retention time, probably not containing chlorine. The nmr spectrum showed no >CH-Cl signal; it did however possess C-methyl and C-ethyl signals at τ 8.7-9.1 characteristic of ring contraction products. These results testify to the ability of the catalyst to abstract the chlorine and the effect of catalyst purity on its ionizing power.

Thus, the six and seven membered ring products may arise from rearrangement of compound 15, but equally likely, or more so, the 4-acetylcylooctyl cation (16) proceeds to rearrange without a chlorine becoming attached and later being removed.

Acylation of olefins with stannic chloride-acetic anhydride without solvent as mentioned earlier gives cleaner reactions, i.e., less darkening of products due to chlorine-containing compounds. Using this procedure, one avoids the dehydrohalogenation stage and the unsaturated ketone is formed directly.27,28 The lack of chloroketone product has been used as evidence against the formation of any acetyl chloride during the acylation. Others report finding traces of β-haloketone which they ascribe to being formed by a cyclic mechanism.29

Acylation of cyclooctene using stannic chloride-acetic anhydride
without solvent according to a modified procedure of Royals and Hendry\textsuperscript{28} gave a mixture of products in poor yield. The major product (\sim 70\% of the total area) was a 1:1 mixture of 1-acetylcylooctene (18) and 4-acetylcylooctene (19) (identified by ir and glc); minor amounts (\sim 30\%) of substitution products (compound \textit{15} and acetylcyclooctyl acetate) were also obtained (eq 20).

\[ \text{Ac}_2\text{O} \xrightarrow{\text{SnCl}_4} 15 + 16 + 19 + \text{Ac}_2\text{O} \quad (20) \]

Stannic chloride was added to a mixture of cylooctene and acetic anhydride (in quantities sufficient to ensure an excess anhydride) in contrast to the procedure of Royals and Hendry, but only minor amounts of substitution products were detected. The low yield results from polyacylation of the elimination product in the presence of excess acetic anhydride, as was noted by Royals and Hendry. They ascribed the lack of residual chlorine containing product in the stannic chloride-acetic anhydride acylation of cyclohexene to the fact that acetyl chloride is not an intermediate in the reaction. They proposed that the intermediate 2-acetyl-cyclohexyl cation is attacked by acetate ion rather than the chloride ion since it is a more powerful nucleophile to give 2-acetylcyclohexyl acetate as a transient intermediate which undergoes elimination during workup. But in cylooctene, the 2-acetylcyclooctyl cation possess sufficient life time to allow transannular hydride transfer. Therefore, the 4-acetylcyclooctyl cation might have time to capture acetate ion and would be expected according to Royals and Hendry to yield substantial
amounts of acetate substitution. However, this is not observed.

Acylation of cyclooctene using acetic acid-trifluoroacetic anhydride without solvent according to the procedure of Henne and Tedder gave a mixture of elimination product and trifluoroacetoxycyclooctane. Refluxing the mixture in alcoholic sodium hydroxide afforded us the major product 4-acetylcylooctene (95\%, identified by ir and glc).

Jones and Groves also report isolation of 4-acetylcylooctene as the major product when cyclooctene was acylated using acetic anhydride in the presence of zinc chloride, again without solvent.

When cyclooctene was acylated using acetic anhydride-stannic chloride in a non-polar solvent (methylene chloride) the major product was 1-acetyl-4-chlorocylooctane (15, 70\% identified by ir and glc) along with minor amounts of 4-acetylcylooctene (19, 18\%) and acetylcyclooctyl acetate 24 (7\%). Even in the presence of excess acetic anhydride the chloroketone 15 is the major substitution product, rather than the acetate.

Compound 19, 4-acetylcylooctene was identified by the following spectral data including infrared bands at 3040 and 1710 cm\(^{-1}\) which indicated no conjugated carbonyl absorption, its nmr spectrum which exhibited signals at \(\tau\) 4.28 (a vinyl hydrogen multiplet of relative area 2), \(\tau\) 7.75 (an allylic hydrogen multiplet of relative area 4), \(\tau\) 7.91 (an acetyl methyl singlet), \(\tau\) 8.2-8.5 (a broad aliphatic hydrogen multiplet of relative area 6), and a lack of absorption at \(\tau\) 6.8 which eliminates the \(\beta,\gamma\) unsaturated isomer, and its conversion to a semicarbazon and a 2,4-dinitrophenylhydrazone whose melting points were identical to the reported values.

Compound 24 possessed both ketonic and ester absorption in its ir
and nmr spectrum. The position of the acetate and acetyl groups were not established but in lieu of the previous acylation results the product is probably 4-acetylcyclooctyl acetate.

Thus, the nature of the acylation products using Lewis acid-acetic anhydride is dependent upon the polarity of the medium.

B. 1,3-Cyclooctadiene

Acylation of 1,3-cyclooctadiene with acetyl chloride-aluminum chloride in methylene chloride at -60° afforded a mixture of products which rapidly decomposed before they could be characterized. Rapid chromatography on silica gel did give an orange material whose ir spectrum indicated the presence of both saturated and unsaturated ketone moieties; this material decomposed on standing. It would appear that aluminum chloride is too active for successful acylation of 1,3-cyclooctadiene. Either the starting diene or the products themselves are too labile in the strongly acidic medium.

Reaction of 1,3-cyclooctadiene using stannic chloride as catalyst under the above conditions afforded 1-acetyl-1,3-cyclooctadiene (25) and 1-acetyl-4-chlorocyclooctene (27) in yields of 40% and 12%, along with several minor products (~ 8% each, one of which was identified as 2-acetyl-1,3-cyclooctadiene (26) (eq 21).

\[
\begin{align*}
\text{AcCl} & \quad \text{SnCl}_4 \\
\text{CH}_2\text{Cl}_2 & \quad \text{Ac} \\
\text{25} & \quad \text{26} \\
\text{27} & \quad \text{Cl}
\end{align*}
\]
Compound 25 was initially identified by its spectral data including infrared bands at 1660 and 1610 cm\(^{-1}\) indicative of a doubly conjugated ketone, its ultraviolet spectrum [\(\lambda_{\max}^{\text{EtOH}} 276 \text{ mu (}\epsilon 10,000)\)] which favors a linear conjugated ketone rather than the cross conjugated ketone 26, and the nmr spectrum, which exhibits an acetyl methyl singlet at \(\tau 7.74\), a multiplet of four aliphatic hydrogens at \(\tau 8.3-8.8\), a one hydrogen apparent triplet at \(\tau 3.06\), \(J = 2.0 \text{ Hz}\), whose chemical shift is indicative of a vinyl hydrogen \(\beta\) to a carbonyl, a two hydrogen multiplet at \(\tau 4.17\) indicative of a vinyl hydrogens \(\gamma, \delta\) to a carbonyl and a multiplet of four allylic hydrogens at \(\tau 7.5-7.7\). These spectra do not conclusively identify the dienone as the linearly conjugated ketone 25: the cross conjugated structure 26 also possesses a vinyl hydrogen \(\beta\) to a carbonyl which should appear as a triplet. However, several literature examples of the nmr spectra of substituted 1,3-cyclooctadienes indicates that the coupling constant between vinyl and allylic protons (\(J\) between the protons on C-1 and C-8 in compound 26) is 7-8 Hz in contrast to our observed coupling constant of 2 Hz. This small splitting is consistent, however, with the expected \(J_{2,3}\) for a twisted 1,3-diene such as 1,3-cyclooctadiene. \(J_{2,4}\) should be of the same magnitude, leading to the apparent triplet observed for the hydrogen at C-2 in the linear conjugated dienone 25.

Sodium borohydride reduction of acetyl-cyclooctadiene (later shown to be an 80:20 mixture of dienones 25 and 26, \textit{vide infra}) gave the dienols 28 and 29 (still in an ca. 85:15 ratio), which were irradiated in either solution in order to effect electrocyclic ring closure to bicyclo [4.2.0] oct-7-ene derivatives (Scheme IV).
The linear dienone 25 would afford structure 30 which possesses two vinyl protons whereas the bicyclic carbinol 31 derived from the cross conjugated dienone 26 would possess only one vinyl proton.

Irradiation through Vycor of an ether solution of the dienol mixture gave a mixture of two products, contaminated with the unchanged dienols 28 and 29. The nmr spectrum of this mixture exhibited two one hydrogen quartets at \( \tau \ 5.85 \) and \( \tau \ 6.35 \). The low field position of the first signal suggests a methine hydrogen which is both allylic and \( \alpha \) to an OH group. The quartet splitting pattern is, of course, caused by an adjacent methyl. The proton at \( \tau \ 6.35 \) is evidently a methine which is no longer allylic, but is \( \alpha \) to an OH and still split by an adjacent methyl. These two adjacent methyls appear as a pair of partly overlapping three hydrogen doublets at \( \tau \ 8.7 \) and \( \tau \ 8.72 \). The upfield shift of the hydrogen \( \alpha \) to the secondary alcohol indicates ring closure has occurred and the mixture contains compound 30. The other signal at \( \tau \ 5.85 \) results from either compound 31 or the dienols (28 and 29).
However, the number of vinyl hydrogens could not be accurately determined from the nmr spectrum of the mixture. Attempts to isolate pure components were unsuccessful. This scheme was abandoned and the structure was established by other nmr work.

Double resonance experiments on compound 25 substantiated the assignment of the linear conjugated structure. The apparent triplet at $\tau 3.06, J = 2$ Hz, was actually a special case of the X part of an ABX system.

Before Double Irradiation  
After Irradiation  

Irradiation of the vinyl protons at $\tau 4.17$ (H at C-3 and C-4) while simultaneously sweeping the low field vinyl triplet (H at C-2) caused the triplet to collapse to a singlet. In the cross conjugated system 26 this would not occur since the vinyl proton at C-1 ($\tau 3.02$) would be coupled to the allylic protons at C-8 rather than the C-3 and C-4 vinyl protons.

The nmr spectrum of a sample of compound 25 which stood for an extended period of time exhibited a second acetyl singlet at $\tau 7.78$ and a second low field vinyl absorption at $\tau 3.26$ (1 H, triplet, $J = 7$ Hz). Repeated gas chromatography indicated the material to be an 80:20 mixture of 25 and 26 which possess very similar retention times. As mentioned previously coupling constants of $J = 7$ Hz in substituted 1,3-cyclooctadienes are characteristic of vicinal vinyl-allylic coupling. In compound 26 the vinyl proton $\beta$ to the carbonyl is adjacent to allylic
protons, leading us to assign the cross conjugated diene structure to the minor component. Comparing the glc pattern on several columns of the original acylation reaction mixture to the diene mixture indicates that compound 26 was indeed originally present in ca. 8% yield. Compound 25 apparently undergoes isomerization, either thermally or on catalysis by a trace of hydrochloric acid produced from decomposition of small amounts of chloroketone present. In general, linear conjugated dienones are more stable than the corresponding cross conjugated diene. However, in 1,3-cyclooctadiene systems the diene moiety is in an almost orthogonal configuration and any electronic advantage of conjugation is greatly diminished. The non-planarity of the diene moiety of 1,3-cyclooctadiene is manifested in the lowering of the extinction coefficient and a shift to shorter wave length of its ultraviolet absorption maximum \[ \lambda_{\text{max}} \text{EtOH} = 228 \ (\epsilon \ 5,600) \] in comparison to 1,3-cyclohexadiene and 1,3-cycloheptadiene which show \[ \lambda_{\text{max}} \text{Hexane} = 256 \ (\epsilon \ 7,940) \] and \[ \lambda_{\text{max}} \text{Isocetane} = 248 \ (\epsilon \ 7,400) \] respectively.\(^{58}\)

Compound 25 which possesses a uv absorption maximum at 273 mu \( (\epsilon \ 10,000) \) has a lower extinction coefficient than 1-acetylcyclooctene \[ \lambda_{\text{max}} \text{EtOH} = 240 \ (\epsilon \ 11,600) \].\(^{59}\) Linear dienones, as compared with simple enones, exhibit ultraviolet absorption with an increased extinction coefficient at a somewhat longer wave length, i.e., 3,5-heptadien-2-one exhibits \[ \lambda_{\text{max}} \text{EtOH} = 273 \ (\epsilon \ 24,550) \] in comparison to 3-penten-2-one \[ \lambda_{\text{max}} \text{EtOH} = 220 \ (\epsilon \ 10,700) \].\(^{60}\) In compound 25 extended conjugation has lowered the extinction coefficient rather than increased it. Therefore, the linear diene 25 is almost certainly not planar and the stability of compound 25 does not appear to be much greater than compound 26 although the actual difference in stabilities is not known.
Compound 27, 1-acetyl-4-chlorocyclooctene was identified by analytical and spectral data:

![Diagram of compound 27](image)

The infrared spectrum shows bands at 3010, 1668, and 1639 cm$^{-1}$ indicating only a singly conjugated carbonyl; the nmr spectrum displays a triplet at $\tau$ 3.35 (area 1, $J = 8$ Hz, hydrogen on C-2), a triplet of triplets at $\tau$ 5.82 (area 1, hydrogen on C-4), a doublet at $\tau$ 7.19 (area 1, $J = 8$ Hz, $H_B$ on C-3), a doublet of doublets at $\tau$ 7.28 (area 1, $J = 8$ Hz, $J' = 2$ Hz, $H_A$ on C-3), a multiplet at $\tau$ 7.55 (area 2, hydrogens on C-8), a methyl singlet at $\tau$ 7.72 (area 3, CH$_3$CO), a multiplet from $\tau$ 8.15-8.6 (area 6, hydrogens on C-5, C-6 and C-7).

The chlorine cannot be at C-5 or C-6 since (a) this would surround the methine group with two chemically equivalent methylenes and the triplet of triplets splitting pattern observed indicates an unsymmetrical environment, (b) one of the two allylic methylene appears at a lower than normal chemical shift, i.e., $\tau$ 7.19 and 7.28 in comparison to $\tau$ 7.5-8.0. The presence of a chlorine adjacent to the allylic methylene would account for such a perturbation of the chemical shift.

The C-8 and C-3 positions can be eliminated since in these structures the splitting pattern could not be a triplet of triplets and the signal would appear at a much lower chemical shift than $\tau$ 5.85 due to the adjacent double bond.

A decision as to whether the chlorine is at C-4 or C-7 is possible on the basis of a mechanistic argument which will be discussed later and
the following nmr analysis.

The low field allylic methylene hydrogens are actually non-equivalent; one hydrogen $H_A$ exists as a doublet of doublets ($J_{AC} = 8$ Hz, $J_{AD} = 2$ Hz) at $\tau 7.19$. $H_A$ is first split by $H_C$, $J = 8$ Hz and is further split by coupling to $H_D$, $J = 2$ Hz. The signal of the second allylic hydrogen $H_B$ is a doublet, $J_{BC} = 8$ Hz at $\tau 7.29$. The lack of additional splitting by $H_D$ is due to a dihedral angle between $H_B$ and $H_D$ of ca. $90^\circ$. This type of splitting pattern for the allylic protons with an adjacent chlorine would not be possible with the chlorine at C-7. The allylic protons would not be vicinally coupled to the vinyl proton but allylically coupled. This should result in a coupling constant of $\leq 3$ Hz, not $8$ Hz.

Attempted dehydrohalogenation of the chloroenone 27 by distillation from sodium carbonate gave no reaction. But distillation from 1,5-diazabicyclo[4.3.0]-5-nonene, (DBN) did give an 85:15 mixture of 25 and 26 (glc, column A, at 155$^\circ$), even though compound 27 appeared to be $> 95\%$ pure by glc analysis. Gas chromatography of a sample of 25 which has been stored for several weeks indicated that it had partially isomerized and was now also an 85:15 mixture of 25 and 26. Glc on several different columns of an admixture of the dehydrohalogenation mixture and the partially isomerized "authentic" 25 showed the two mixtures to be of identical composition. Comparison of the infrared spectrum showed them to be indistinguishable, except for a trace of saturated carbonyl absorption.

The yield of compound 25 stated earlier was for isolated material after spinning band distillation. Initial distillation of the crude acylation reaction mixtures resulted in an exotherm, with a rapid thermal elimination of hydrogen chloride. The resultant distillate was composed mostly of the acetyl dienes 25 and 26 as mentioned earlier. Glc analysis
of the crude reaction mixture prior to the exothermic distillation indicated two major peaks comprising 30% (retention time 3 min) and 61% (retention time 8 min) of the total area. The infrared spectrum of this mixture indicated the presence of both saturated (1715 cm\(^{-1}\)) and unsaturated ketones (1664, and 1613 cm\(^{-1}\)). GLC of the mixture after redistillation showed the area ratio of the two major peaks had changed to 70% (retention time 3 min):20% (retention time 8 min). The infrared spectrum of the mixture contained only a trace of saturated carbonyl absorption and strong bands due to a singly conjugated (1668, and 1639 cm\(^{-1}\)) and doubly conjugated ketone (1660, and 1613 cm\(^{-1}\)). In addition, in certain acylation reaction mixtures, which were not allowed to warm slowly to 0\(^0\), but poured directly into ice-dilute acid mixture, the infrared spectrum of the crude unstable reaction mixture indicated only saturated ketone. The nmr spectrum exhibited a pair of non-conjugated acetyl singlets of equal intensity at \(\tau 7.82\) and \(\tau 7.87\) and a multiplet at \(\tau 4.3\) indicative of vinyl protons. These data suggest that 36 and 32 (Scheme V), or both are present; the chloroketone 27 is an artifact obtained from double bond isomerization of compound 36. From the preceding evidence, the following conclusions regarding the various mechanistic pathways by which the products are formed may be reached.

Acylation of 1,3-cyclooctadiene involves the generation of an allylic carbonium ion in a medium-ring diene. The medium-ring system which is capable\(^{48}\) of undergoing 1,3 and 1,5-hydride transfers presents a multitude of reaction paths (Scheme V).

The major product compound 25 can be formed by either 1,2-addition and subsequent 1,2-elimination of the \(\beta\)-haloketone (path A) or by conjugate addition followed by 1,4-elimination (path F). The relative minor formation of compound 26 either represents the small percentage to
transannular hydride transfer mechanism (path D) or is only an artifact arising from isomerization of compound 25. The liability of the chloroketones 26 and 27 is seen by their thermal dehydrohalogenation during distillation. However, since the only chloroketone identified was compound 27, it appears that compound 26 may undergo double bond isomerization as well as 1,4-elimination. The relative amounts of the unstable chloroketone 26 and 27 cannot be accurately determined since they are not well resolved by gas chromatography. However, the nmr spectrum of the unstable reaction mixture does indicate two non-conjugated acetyl methyl singlets of intensities ca. 55:45 suggesting that both may be formed.

Chloroketone 33 (path B) could also be part of the unstable non-conjugated chloroketone mixture. Loss of hydrogen chloride from compound 33 would afford compound 37 which could be identified by its six allylic protons in the nmr. Since the dehydrohalogenation product is an 85:15 mixture of 26 and 25 which possess only four allylic protons either compound 37 is not formed or it isomerizes to compound 26 under the reaction conditions. This particular question has not been resolved.

It was previously mentioned that the position of the chlorine in compound 27 could not be at C-7 according to the nmr evidence. Mechanistically, a chlorine at C-7 is unlikely since there is no simple path available to generate a positive charge there. Only a further 1,2-hydride shift subsequent to transannular hydride transfer (paths D and E) could account for such a product. Considering the small amount of transannular hydride transfer products, substitution of a chlorine at C-7 appears unlikely.

The infrared spectrum of the dienone mixture obtained by
dehydrohalogenation of compound 27 with DBN contained a trace of saturated carbonyl absorption (IR). This is attributed to a small percentage of compound 38 arising from compound 37 (path C). The fraction boiling between compound 25 and 27 also contained some saturated carbonyl absorption (IR) but could not be separated on GLC columns available and was not further investigated.

The formation of diene 39 appears unlikely since the NMR spectrum of the acetylcylooctadienes possess only 4 allylic protons, whereas the diene 39 produced by path E would exhibit 8.

In general, the high reactivity of 1,3-cyclooctadiene favors formation of the "normal" acylation products rather than the transannular products as were obtained with cyclooctene. Transannular hydride transfer in 1,3-cyclooctadiene acylation represents an uphill energy process since the initially generated allylic carbenium ion is considerably more stable than a secondary carbenium ion. In other words, the carbenium ion has been stabilized at the C-2 and C-4 positions and these positively charged carbon atoms capture the chloride anion before hydride transfer can occur.

C. Cyclononene

Extending the systematic investigation of medium ring olefins to cyclononene, one might expect cyclononene, the medium ring with the most severe transannular interactions to give bridged products as well as those formed via ring contraction. The limitations of most synthetic methods of obtaining cyclononene has curtailed the study of the chemistry of this olefin. However, Garnes and Narayana have recently reported a convenient synthesis of cyclononene from commercially available cyclooctene
by addition of dibromocarbene, conversion of the gem-dibromobicyclo-
nonane to 1,2-cyclononadiene, and partial catalytic readduction of the
allene. Prelog and coworkers\textsuperscript{63} have reported that formoylation of cis-
cyclononene oxide gave a mixture of stero-isomeric 1,5-diols arising via
1,5-hydride transfer as with cyclooctene. To our knowledge, no
investigations of the acylation of cyclononenes have yet been reported.

The initial acylation reaction was conducted using the milder
stannic chloride-acetylchloride in methylene chloride at -15\degree. This
would by analogy with cyclooctene, favor the formation of transannular
substitution products, with ring contraction and bridging being
suppressed.

Thus, acetylation of \textit{cis}-cyclononene in the presence of stannic
chloride in methylene chloride at -15\degree, gave as the major product 1-acetyl-
5-chlorocyclononane (4\textsubscript{1}, 40-50\% by glc); there were also formed smaller
amounts of elimination products [acetylcyclononene (4\textsubscript{2}) and 5- or
6-acetylcyclononene (4\textsubscript{3}, 20\%) and a mixture of chlorohydrocarbons
(4\textsubscript{2}, 5-10\%) (eq 22). These yields also vary depending on the purity of

\[
\begin{align*}
\text{CH}_3\text{COCl} & \quad \text{SnCl}_4 \quad \text{CH}_2\text{Cl}_2 \\
\text{Ac} & \quad \text{Ac} \\
4\textsubscript{3} & \quad 4\textsubscript{1} \quad 4\textsubscript{2} \quad 4\textsubscript{4} \\
\end{align*}
\]
stannic chloride used.

The absence of ring contraction products was confirmed by conversion of the acylation reaction mixture to methyl cyclononanecarboxylate, which was identified by comparison with an authentic sample (Scheme VI).

SCHEME VI

\[
\begin{align*}
\text{Ac} & \quad \text{NaBH}_4 & \quad \text{OH} & \quad \text{Na} & \quad \text{OH-THF} & \quad \text{Jones} \\
\text{Cl} & \quad \rightarrow & \quad \text{Cl} & \quad \rightarrow & \quad \rightarrow \\
\text{L} & \quad \text{L} & \quad \text{L} & \quad \text{L} & \quad \text{L} \\
\text{45} & \quad \text{46} & \quad \text{47} \\
\end{align*}
\]

Treatment of this acylation reaction mixture with sodium borohydride gave a mixture of chloroalcohols \( \text{45} \), which was dechlorinated using sodium in a t-butyl alcohol-tetrahydrofuran solution to give crude methyl cyclononylnyl carbinol (\( \text{46} \)). Oxidation of compound \( \text{46} \) gave acetylcyclononane (\( \text{47} \), \( \sim 90\% \) pure by glc). Oxidation of acetylcyclononane under the haloform conditions and subsequent treatment with diazomethane yielded methyl cyclononanecarboxylate (\( \text{48} \)). This was identical to an authentic sample independently synthesized from cyclodecanone (\( \text{49} \)) according to the procedure of Schenuker and Prelog.\(^{64}\)
The chlorohydrocarbons 42 exhibited an ir spectrum characteristic of a hydrocarbon with no carbonyl absorption. The nmr spectrum showed no acetyl methyl group, but only a one hydrogen quintet at 7.58 for the -CHCl and a broad aliphatic proton multiplet at 7.84.

The presence of compounds 42 and 43 in the chlorine-free fraction was inferred from the following spectral data on the mixture. The presence of both conjugated and non-conjugated carbonyl groups was indicated by infrared bands at 1660 and 1708 cm\(^{-1}\). The nmr spectrum exhibited a characteristic olefinic triplet at 3.11(=CH=CH=COO), a vinyl proton absorption at 4.3 and both conjugated (7.71) and non-conjugated (7.89) acetyl methyl groups.

The chloroacetylclononane 44 was initially characterized by its analysis, its ir spectrum which showed a band at 1710 cm\(^{-1}\) characteristic of a saturated carbonyl group, and its nmr spectrum which indicated, inter alia, the presence of a one hydrogen multiplet attributable to the hydrogen on a chlorine-bearing carbon at 7.85 and methyl singlet at 7.85 for the acetyl group.

Distillation of compound 44 from DBN gives unchanged starting material (ir, glc). However, 44 does undergo thermal elimination. It darkens on storage more rapidly than the analogous eight-ring compound, 15. Distillation causes loss of hydrogen chloride and attempted isolation of 44 via preparative glc gave only products of elimination (ir, glc).

The positions of the chlorine and acetyl groups were established by effecting an intramolecular alkylation, resulting in ring closure to methyl cis-hexahydroindan-3a-yl ketone (50) identical with an authentic sample prepared by an unambiguous synthesis (Scheme VII).
Treatment of 1-acetyl-5-chlorocyclononane with sodium hydride in dimethoxyethane afforded a chlorine-free product which showed no olefinic absorption in the nmr or ir spectrum. The absence of cyclopropyl protons in the nmr precluded a bicyclo[5.1.0]nonane structure. The infrared spectrum of the product was superimposable with a sample of compound 50 independently synthesized according to a modified procedure of Becker and Kronenthal.\textsuperscript{65}

Ring closure of the chloroketone 41 with potassium t-butoxide in refluxing t-butanol gave a 70:30 mixture of two products with almost identical glc retention times. The smaller fraction was identified as compound 50 by preparative glc and comparison of its ir spectrum with
that of authentic compound 50. The larger component which possesses a similar ir spectrum to 50 has no vinyl protons in the nmr and is probably the trans isomer, i.e., methyl trans-hexahydroindan-3a-yl ketone.

The 1,5-transannular eliminations observed here are most likely concerted processes. Since only methyl cis-hexahydroindan-3a-yl ketone is afforded, using sodium hydride, it appears that a direct cyclization of the chloroacetylcyclononane has occurred. Potassium t-butoxide, on the other hand, effects prior epimerization of the acetylchlorocyclononane to a mixture of cis and trans isomers, which eventually undergo the concerted 1,5-elimination to give both methyl cis- and trans-hexahydroindan-3a-yl ketone.

Acylation of cyclononene with acetic acid-trifluoroacetic anhydride without solvent gave a mixture of elimination product and trifluoroacetoxyacetylcyclononane (ir, glc). Attempted acid hydrolysis of the reaction mixture afforded the elimination product 5- or 6-acetylcyclononene (glc > 90% pure). The non-conjugated ketone displayed the following spectral data: the ir spectrum, possesses absorption at 3010 and 1710 cm\(^{-1}\); nmr studies, inter alia, indicate the presence of a pair of vinyl protons as a multiplet at \(\tau\) 4.3 and a non-conjugated acetyl methyl group as a singlet at \(\tau\) 7.9. By analogy with the position of the chlorine atom in compound 41 we believe the non-conjugated ketone to be the 5- or 6-acetylcyclononene 43. Glc analysis on several columns of an admixture of the above non-conjugated ketone and that obtained in the stannic chloride-acetyl chloride acylation of cyclononene indicates they were identical.

Preliminary studies in the acetylation of cyclononene using aluminum
chloride catalyst indicates that extensive rearrangement has occurred. The nmr spectrum of the reaction mixture does display signals characteristic of C-methyl and C-ethyl groups. At the time of this writing, others in these laboratories are engaged in degradation of the product mixture to dechlorinated ring ketones.

In conclusion, the conflicting reports in the acylation of medium ring olefins can be attributed to the various reaction conditions employed. Not only is the choice of catalyst critical, but also the purity of the catalysis, the temperature, and the polarity of the medium. Each of these factors can easily influence the mode of reaction of a system which is so prevalent to rearrange. The results obtained are summarized in Table I.
Table I

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Catalyst</th>
<th>Acylating Agent</th>
<th>Solvent</th>
<th>Temp</th>
<th>Products and Yields</th>
</tr>
</thead>
<tbody>
<tr>
<td>cis-cyclooctene</td>
<td>SnCl$_4$</td>
<td>AcCl</td>
<td>CH$_2$Cl$_2$</td>
<td>-5$^\circ$C</td>
<td>15 (70%), 18 + 19 (20%)</td>
</tr>
<tr>
<td></td>
<td>AlCl$_3$</td>
<td>AcCl</td>
<td>CH$_2$Cl$_2$</td>
<td>-10$^\circ$C</td>
<td>13 (45%), 14 (4%), 15 (5%)</td>
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<tr>
<td></td>
<td>SnCl$_4$</td>
<td>AcCl</td>
<td>CS$_2$</td>
<td>-10$^\circ$C</td>
<td>15 (60%), 18 + 19 (30%)</td>
</tr>
<tr>
<td></td>
<td>SnCl$_4$</td>
<td>Ac$_2$O</td>
<td>-</td>
<td>27$^\circ$C</td>
<td>15 (10%), 18 + 19 (70%) [1:1], 24 (20%)</td>
</tr>
<tr>
<td></td>
<td>SnCl$_4$</td>
<td>Ac$_2$O</td>
<td>CH$_2$Cl$_2$</td>
<td>-5$^\circ$C</td>
<td>15 (70%), 19 (18%), 24 (7%)</td>
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<tr>
<td></td>
<td>CF$_3$COOH</td>
<td>(CF$_3$CO)$_2$O</td>
<td>-</td>
<td>27$^\circ$C</td>
<td>19 (90%)</td>
</tr>
<tr>
<td>1,3-cyclooctadiene</td>
<td>AlCl$_3$</td>
<td>AcCl</td>
<td>CH$_2$Cl$_2$</td>
<td>-55$^\circ$C</td>
<td>polymer</td>
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<tr>
<td></td>
<td>SnCl$_4$</td>
<td>AcCl</td>
<td>CH$_2$Cl$_2$</td>
<td>-55$^\circ$C</td>
<td>25 (40%), (25) (~8%), 27 (12%)</td>
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<tr>
<td>cis-cyclononene</td>
<td>SnCl$_4$</td>
<td>AcCl</td>
<td>CH$_2$Cl$_2$</td>
<td>-15$^\circ$C</td>
<td>41 (45%), 42 + 15 (20%) [2:1], 44 (~5%)</td>
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<tr>
<td></td>
<td>CF$_3$COOH</td>
<td>(CF$_3$CO)$_2$O</td>
<td>-</td>
<td>27$^\circ$C</td>
<td>43 (95%)</td>
</tr>
<tr>
<td>1-acetyl-1,4-chlorocyclooctane</td>
<td>xs SnCl$_4$</td>
<td>-</td>
<td>CS$_2$</td>
<td>25$^\circ$C</td>
<td>15 (15%), 18 + 19 (55%) [2:1]</td>
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<tr>
<td></td>
<td>xs AlCl$_3^*$</td>
<td>-</td>
<td>CH$_2$Cl$_2$</td>
<td>-10$^\circ$C</td>
<td>15 (60%), 18 + 19 (20%)</td>
</tr>
<tr>
<td></td>
<td>xs AlCl$_3$</td>
<td>-</td>
<td>CH$_2$Cl$_2$</td>
<td>-10$^\circ$C</td>
<td>18 + 19 (20%), 13 +15 (70%)</td>
</tr>
</tbody>
</table>

*deactivated
EXPERIMENTAL *

Acylation of cis-Cyclooctene with Acetyl Chloride Using Stannic Chloride as Catalyst. To a solution of stannic chloride (26 g, 0.1 mole) in 50 ml of methylene chloride at -5° was added dropwise a solution of acetyl chloride (7.8 g, 0.1 mole) and cyclooctene (11.0 g, 0.1 mole) in 30 ml of methylene chloride over a period of one-half hour. The reaction mixture was stirred at -5° for one hour, allowed to warm to 0° and then the red-orange solution was poured into a slurry of ice-dilute hydrochloric acid. The methylene chloride layer was washed with water until neutral, dried (sodium sulfate), and concentrated under reduced pressure to give a crude yellow oil (15.1 g, 80%). The ir spectrum (film) of the crude product indicated a saturated carbonyl band at 1710 cm⁻¹. Analytical gc on column B at 160° indicated a mixture of four products, containing 77% of 1-acetyl-4-chlorocyclooctane and 23% of three shorter retention time products. Distillation of the reaction mixture gave two fractions: (I) bp 35-90 (0.5 mm) contained mostly short retention time products (gc); (II) was predominantly 1-acetyl-4-chlorocyclooctane (15), bp 95-100 (0.5 mm), 7.5 g, (> 80% pure by gc). Conversion of compound 15 to a semicarbazone was accomplished using a standard procedure. The derivative was obtained after recrystallization from aqueous ethanol as white flakes mp 151-152°.

*Gas chromatographic analyses were performed on a Varian Aerograph Model 202-1B Gas Chromatograph (thermal conductivity detector) utilizing the following columns: Column A, 20% SE-30 on Chromosorb P, 5 ft x 1/4 in; Column B, 10% QF-1 fluorosilicone rubber on Chromosorb W, 6 ft x 1/4 in; Column C, 15% Carbowax 20-M on Chromosorb P, 5 ft x 1/4 in; Column D, 20% Diethyleneglycol succinate on Chromosorb W, 5 ft x 1/4 in. The remaining general information is similar to that reported in the experimental of Part I.

The nmr spectrum (film) exhibited signals at τ 5.85 (1 H, quintet, J = 5 Hz, HC-Cl), τ 7.55 (1 H, multiplet, H-COO), τ 7.93 (3 H, singlet, H₃COO), and τ 8.3-8.6 (12 H, broad multiplet, aliphatic protons).

Distillation of the crude reaction mixture from sodium carbonate gave mostly unchanged 1-acetyl-4-chlorocyclooctane (15) and a slight increase in the amount of elimination product (glc, column B); ir (film) 1710 and 1660 cm⁻¹.

A mixture of the acylation reaction products and the dehydrohalogenation products was analyzed on column B and exhibited identical spectra except for an increase in one of the short retention time products (2 min at 160⁰) in the sodium carbonate-treated material. Collection of this short retention component from column B gave a mixture of conjugated ketone (ir [film] 1660 and 1630 cm⁻¹) and non-conjugated ketone (1710 cm⁻¹). The non-conjugated ketone and 4-acetylcyclooctene had identical glc retention times on several columns. The conjugated ketone was believed to be 1-acetylcyclooctene.

Refluxing 1-acetyl-4-chlorocyclooctane (15) in methanol with an excess of sodium methoxide gave, after work-up, a liquid which showed no vinyl hydrogens, and only saturated carbonyl absorption in its nmr and ir spectrum. Glc analysis on column B at 160⁰ indicates a 38:62 mixture of spimers with no short retention time peaks characteristic of elimination products.

Careful glc analysis of the original distilled acylation reaction indicated the peak attributed to 1-acetyl-4-chlorocyclooctane (15) was actually two peaks in a 55:45 ratio. The two components are believed to be cis and trans-1-acetyl-4-chlorocyclooctane 15. Degradation of the
mixture gave only 4-chlorocyclooctanone (vide infra) and no other positional isomer, indicating 15 was a mixture of geometric isomers.

**Bayer Villiger Oxidation of 15.** Trifluoroperacetic acid was prepared by dropwise addition of 3.8 ml (0.02 mole) of trifluoroacetic anhydride to a suspension of 0.74 ml (0.02 mole) of 90% hydrogen peroxide in 20 ml of cold methylene chloride. This was added to vigorously stirred solution of crude ketone 15 (5.0 g, 0.026 mole) and disodium phosphate (22 g) in methylene chloride (70 ml). The solution was stirred and refluxed overnight. The solid was filtered, washed twice with methylene chloride; the combined methylene chloride solutions were washed three times with water, dried (sodium sulfate), and concentrated to yield a colorless liquid (5.2 g, 95% yield). Analytical glc on column B at 175° indicate a 70% conversion to ester: ir (film), 1732, 1710, and 1245 cm⁻¹.

The ketonic product was removed via Girard's reagent T according to the procedure of Fieser.⁶⁷ A mixture of 4.7 g of the crude chloroketone-ester mixture, 4.7 g of Girard's reagent T and 5 ml of acetic acid was refluxed in 50 ml of ethanol for 1 hr. The reaction mixture was cooled, poured into water and extracted with ether. The ether extracts were washed with 10% sodium carbonate solution and saturated salt solution, dried (magnesium sulfate), and concentrated under reduced pressure to give 2.7 g of almost 90% pure chloroester 21 (glc): ir (film), 1733 and 1240 cm⁻¹.

**Reduction of 1-Acetoxy-4-chlorocyclooctane (21).** To a slurry of 0.5 g of lithium aluminum hydride in 25 ml of absolute ether was added dropwise compound 21 (2.7 g, 0.013 mole) in 10 ml ether over a half-hour period. The reaction was stirred at room temperature for an additional
three hours; the excess lithium aluminum hydride was destroyed with ethanol and the solution was poured into a solution of cold aqueous ammonium chloride. The ether layer was separated, washed twice with water, dried (sodium sulfate), and concentrated under reduced pressure to give a poor yield of 4-chloro-cyclooctanol: ir (film), 3460 and 1045 cm⁻¹; no carbonyl absorption was present; glc analysis indicated the alcohol was > 80% pure.

Oxidation of 4-Chlorocyclooctanol (22). A solution of 0.27 g of crude chlorocyclooctanol 22 in 25 ml of acetone at 0° was treated drop-wise with Jones reagent⁶⁹ until further reagent was not decolorized. The solution was poured into water, extracted twice with ether, back washed with water, dried (sodium sulfate), and evaporated to give 4-chlorocyclooctanone (0.25 g, 95%): ir (film) 1703 and 670 cm⁻¹; glc analysis indicate compound 22 to be > 85% pure. The 2,4-dinitrophenylhydrazone prepared in the usual manner, crystallized from ethanol-ethyl acetate as orange needles, mp 151-152°, undepressed on admixture with 2,4-dinitrophenylhydrazone of authentic 4-chlorocyclooctanone.⁵³ The infrared spectrum (CCl₄) of the two 2,4-dinitrophenylhydrazones were superimposable. Glc on column B of the mixture of the degraded specimen and the authentic sample showed only one peak.

Acetylation of Cyclooctene Using Stannic Chloride Catalyst and Carbon Disulfide as Solvent. To a solution of stannic chloride (26 g, 0.1 mole) in 50 ml of carbon disulfide at -10° was added over a period of one-half hour a mixture of acetyl chloride (7.85 g, 0.1 mole) and cyclooctene (11 g, 0.1 mole). The brown solution was stirred for 15 min at -10°, let warm to 0°, and worked up in the manner described for the acetylation of cyclooctene using methylene chloride as solvent.
Evaporation of the carbon disulfide gave 19 g of a yellow oil; the infrared spectrum [(film) 1710 and 660 cm\(^{-1}\)] was identical to the ir of material obtained using methylene chloride as solvent. Analytical glc on column B at 175\(^\circ\) of an admixture of the methylene chloride reaction mixture and carbon disulfide reaction mixture showed no additional peaks.

Distillation from sodium carbonate gave mostly 1-acetyl-4-chlorocyclooctane (1/5) bp 93-105\(^\circ\) (0.3 mm): ir (film), 1710 and 1660 cm\(^{-1}\). Analytical glc on column B at 160\(^\circ\) of the reaction mixture showed that it was identical to starting material except for a slight increase in the peak attributable to elimination products.

Treatment of 1-Acetyl-4-chlorocyclooctane (1/5) with Stannic Chloride. A mixture of 1-acetyl-4-chlorocyclooctane (0.2 g) and excess stannic chloride (1 g) in 50 ml of carbon disulfide was stirred at room temperature for 6 hrs. The black solution was poured into dilute hydrochloric acid-ice slurry and worked up in the usual manner to give an orange oil (0.1 g). Analytical glc on column C at 160\(^\circ\) indicate one major component (ca 2.5 min retention time) comprising 55% of the total area and two minor components comprising 36%. The first minor component was a mixture of three peaks (18%), retention time 1-2 min. The second minor component was unreacted compound (1/5), identified by glc. The major component was a 2:1 mixture of conjugated ketone [probably 1-acetylcyclooctene (1/9)] and 4-acetylcyclooctene (glc peak identical on admixture with known compound 1/5 prepared by acetylation of cyclooctene with trifluoroacetic anhydride - acetic acid). The infrared spectrum (film) of the mixture showed bands for conjugated (1660 and 1615 cm\(^{-1}\)) and non-conjugated ketone (1710 cm\(^{-1}\)). The nmr spectrum
(CCl₄) exhibited signals at τ 3.12 (triplet, J = 8 Hz, indicative of
-CH=CCO), τ 4.32 (broad multiplet, non-conjugated vinyl protons), τ 7.73
(singlet, conjugated acetyl methyl), τ 7.88 (singlet, saturated acetyl
methyl), and τ 8.2-8.8 (broad multiplet, aliphatic proton and C-methyl
singlet).

Treatment of 1-Acetyl-4-chlorocyclooctane (15) with "Active" Aluminum
Chloride. A mixture of compound 15 (0.2 g) and an excess of aluminum
chloride (from a freshly opened container) in 50 ml of methylene chloride
was stirred for 1 hr at -10⁰. The reaction was worked up in the usual
manner to give a yellow oil. Analytical glc on column A indicated the
reaction mixture was composed of three components whose retention times
were all considerably shorter than the starting chlorocompound 15. The
nmr spectrum showed no -CHCl signals; the singlets at τ 7.85-7.8 attribu-
table to acetyl groups, and C-methyl and C-ethyl signals at τ 8.7-9.1
indicated the presence of ring contraction products. The retention time
of all glc peaks of this material were shorter than that of 1-acetyl-4-
chloro-4-ethylcyclohexane (13).

Treatment of 1-Acetyl-4-chlorocyclooctane with "Deactivated"
Aluminum Chloride. A mixture of crude 1-acetyl-4-chlorocyclooctane (1 g)
and an excess of aluminum chloride (from an old bottle) in 50 ml of
methylene chloride was stirred for one hour at -10⁰. The reaction was
worked up in the usual manner to give 0.9 g of recovered 1-acetyl-4-
chlorocyclooctane; their spectrum and the glc pattern were identical with
that of starting material.

Acylation of Cyclooctene Using Stannic Chloride-Acetic Anhydride
without Solvent. To a mixture of cyclooctene (10 g, 0.1 mole) and
acetic anhydride (10 g, 0.1 mole) was added stannic chloride (26 g, 0.1
mole) at room temperature. The reaction vessel was cooled with ice-bath
to maintain a reaction temperature at 25-30°. After stirring for 1 hr at 25°, the viscous black syrup was poured into water, and extracted with ether; the combined ether extracts were washed several times with saturated sodium chloride, dried (magnesium sulfate), and concentrated to yield 7 g of a red oil: ir (film) 3005, 1710, 1660, and 745 cm⁻¹; analytical glc on column A at 185° indicated a major component of > 70% of the total area was a mixture of acetylcyclooctene isomers (1β and 19) identified by glc and two minor components (20%) identified as 1-acetyl-4-chlorocyclooctane (15) and acetylcyclooctyl acetate, also by glc and ir.

Acetylation of Cyclooctene Using Trifluoroacetic Anhydride and Acetic Acid. To a mixture of trifluoroacetic anhydride (10 g, 0.05 mole) and acetic acid (3.0 g, 0.05 mole) was added cyclooctene (5.0 g, 0.05 mole) over a period of 15 min at 27°. The reaction was stirred at 27° for an additional 1.5 hr, poured into water-ether solution and the layers separated. The ether layer washed with saturated sodium chloride solution until neutral, dried (magnesium sulfate), and concentrated to give a brown oil (6 g): ir (film), 3010, 1780, (CF₃COO⁻), 1708, 1260, and 760 cm⁻¹. Analytical glc (on column A at 178°) indicated two components; (A) non-conjugated acetylcyclooctene (56% of the total area) and (B) trifluoroacetoxyacetylcyclooctane (44%).

The crude reaction mixture was heated under reflux with aqueous methanolic sodium hydroxide for two hours. The reaction mixture was poured into water and extracted with ether; the combined ether extracts were washed with water, dried (sodium sulfate), and the solvent removed to afford 4-acetylcyclooctene (19) as a pale yellow oil (~95% pure, glc). Distillation of the above oil yielded two fractions: fraction I,
4-acetylcylooctene, [bp 67-75° (0.7 mm), 5.1 g, 90%] was identified by its glc retention time and its ir and nmr spectrum; fraction II, acetylcylooctanol [bp 125-150° (0.7 mm), 0.5 g], exhibited strong ir (CCl₄) absorption bands at 3600 and 1710 cm⁻¹.

**Acylation of Cylooctene with Acetic Anhydride-Stannic Chloride in Methylene Chloride.** To a mixture of cylooctene (10 g, 0.1 mole) and acetic anhydride (10 g, 0.1 mole) in 150 ml of methylene chloride cooled to -5° was added stannic chloride (26 g, 0.1 mole) in 50 ml of methylene chloride over 15 min, then stirred for an additional hour at -5°. The dark red solution was poured into a dilute hydrochloric acid-ice slurry, and worked up in the usual manner to give 16.0 g of a crude orange oil; analytical glc on column A at 185° indicated three peaks which were identified as follows: (1) 4-acetylcylooctene (19, 4.0 min, 17% of total area), (2) 1-acetyl-4-chlorocylooctane (15, 10 min, 75%), and (3) acetoxyacetylcylooctane (14, 16.5 min, 7%). Fractional distillation of the crude reaction mixture gave three fractions: fraction I, 4-acetylcylooctene (19) [bp 60-65° (0.5 mm)] was obtained as a pale yellow oil (2.5 g, glc indicated ~ 95% pure): ir (film), 3080 and 1710 cm⁻¹; nmr (CCl₄), τ 4.28 (2H, multiplet, vinyl protons), τ 7.75 (4H, multiplet, allylic protons), τ 7.91 (3H, singlet, CH₃CO), and τ 8.2-8.5 (6H, broad multiplet, aliphatic protons); no nmr signals at ca τ 6.7 for allylic protons which are β to a carbonyl group. A 2,4-dinitrophenylhydrazone, mp 103-104° (lit 103-104°) and a semicarbazone, mp 176-177.5° (lit 177-178°) were prepared.

Fraction II, 1-acetyl-4-chlorocylooctane (15) [bp 110-112° (1 mm), 9.5 g] was identical (ir and glc) to compound 15 isolated and identified previously.
Fraction III bp $135^\circ$ (1 mm), 1.4 g, appeared to be acetyl-cyclooctyl acetate $2^\frac{1}{2}$: ir (film), 1706, 1720, and 1250 cm$^{-1}$; the nmr (CCl$_4$) spectrum displayed a singlet at $\tau$ 7.91 and $\tau$ 8.04 attributable to acetyl methyl and acetoxy groups. The position of the acetate and acetyl groups were not established but in lieu of previous acylation result the product is probably 4-acetyl-cyclooctyl acetate.

Various modes of addition, i.e., olefin to catalyst and anhydride, catalyst to olefin and anhydride, anhydride to olefin and catalyst in a non-polar solvent gave generally the same product mixtures discussed above.

Acylation of 1,3-Cyclooctadiene with Acetyl Chloride-Aluminum Chloride Complex. A solution of 1,3-cyclooctadiene (21.6, 0.2 mole) in methylene chloride was added to a stirred solution of aluminum chloride (28.4 g, 0.2 mole) and acetyl chloride (15.7 g, 0.2 mole) in methylene chloride at $-50^\circ$ to $-60^\circ$. After the addition was completed (0.5 hr), the resultant red solution was stirred for an additional one-half hour, warmed to $0^\circ$, and poured onto crushed ice-dilute hydrochloric acid slurry. The black methylene chloride solution was washed with water and 5% sodium bicarbonate solution until neutral, dried (magnesium sulfate), and concentrated under reduced pressure, to give a black viscous oil. Attempted distillation of the black oil gave no distillable product. Rapid chromatography on silica gel gave a dark orange oil, ir (film), 1707, 1664, and 1610 cm$^{-1}$, which rapidly decomposed on standing.

Acylation of 1,3-Cyclooctadiene with Acetyl Chloride Using Stannic Chloride as Catalyst. A solution of 1,3-cyclooctadiene (21.6 g, 0.2 mole) in methylene chloride was added to a solution of stannic chloride (52 g, 0.2 mole) and acetyl chloride (28.4, 0.2 mole) in methylene chloride over
a period of 0.5 hr at -50° to -60°. The reaction was stirred for one-half hour, warmed to 0°, and then poured into crushed ice-dilute hydrochloric acid slurry. The methylene chloride solution was washed with water and 5% aqueous sodium bicarbonate until neutral and then with saturated sodium sulfate, dried (magnesium sulfate), and concentrated under reduced pressure to give 15.8 g of crude yellow oil. Distillation of the crude reaction product which had turned black on standing overnight at 0°, gave 15 g of yellow liquid, bp 71-79° (0.2 mm); analytical glc on column B at 155° showed five peaks corresponding to relative amounts (of total area) of 1% (2.2 min), 28% (2.8 min), 7% (3.5 min), 2% (6 min), 62% (8 min). The infrared spectrum (CCl₄) of the distilled reaction mixture exhibited bands at 3010, 1713, 1664 and 1613 cm⁻¹. Isolation of the two major components by collection from column A at 155° gave colorless oils, both of which possessed conjugated carbonyl bands in the ir spectrum: ir (film), 1661, 1613 cm⁻¹ for the short retention time product (5 min), and ir (film), 1671, 1620 cm⁻¹ for the long retention time product (8 min). Initial fractional distillation produced a thermal dehydrohalogenation. Glc of this crude mixture on column B at 155° indicated that the two major peaks had changed in area ratio to 70% (2.8 min), and 20% (8 min): ir (film) 1668, 1660, 1639 and 1613 cm⁻¹, and a trace of saturated carbonyl absorption at 1710 cm⁻¹. Redistillation of a 9 g portion on a spinning band column gave the following fractions: Fraction I, 1-acetyl-1,3-cyclooctadiene (26) was obtained as a colorless oil, bp 46-50° (0.3 mm) (6.1 g, 60%): ir (film), 3015, 1661, 1613, and 695 cm⁻¹; nmr (CCl₄), τ 3.06 (1H, apparent triplet, J = 2.0 Hz, which is the X portion of an ABX pattern, -CH=CCOCH₃) τ 4.17 (2H, multiplet, AB portion of the ABX multiplet, vinyl protons), τ 7.72 (3H, singlet, -CH₃CO), τ 7.5-7.7 (4H, multiplet, allylic protons), and τ 8.5
(4H, multiplet, aliphatic protons); uv (ethanol) max 276 mu (ε 10,000); a Beilstein test for halogen was negative. A semicarbazone of 25 prepared in the standard manner, crystallized from aqueous ethanol as white leaflets, mp 204-205°. 

Anal. Calcd for C_{11}H_{17}ON_3: C, 63.77; H, 8.21. Found: C, 63.79; H, 8.24.

Glc analysis of fraction I on column B at 162° indicated it to be 95% pure (retention time 1.9 min) with a small impurity compound (26) (retention time 2.1 min). Upon standing the ratio of pure compound 25 to compound 26 increased to 80:20. Nmr (CCl₄) examination of this mixture showed that it contained not only the previously mentioned signals due to compound 25, but additional signals at τ 4.15 (increased multiplicity), and τ 7.78 (acetyl singlet). These spectral data were consistent for 2-acetyl-1,3-cyclooctadiene (26).

Fraction II, [bp 53-72° (0.4 mm), 0.9 g] was complex mixture of six components including compounds 25 and 26 as indicated by glc analysis on column B and was not further investigated: ir (film) 1715, 1665, and 1612 cm⁻¹ indicated both saturated and conjugated carbonyl groups.

Fraction III, [bp 75-77 (0.4 mm) 1.2 g] was identified as 1-acetyl-4-chlorocyclooctene (27), a yellow oil which darkened on standing: ir (film), 3010, 1668, and 1639 cm⁻¹, indicated only a singly conjugated ketone in contrast to fraction I; uv (ethanol) max 240 mu (ε 11,100); nmr (CCl₄), τ 3.26 (1H, triplet, J = 8 Hz, vinyl proton, H₀ on C-2), τ 5.82 (1H, triplet of triplets, -CHCl), τ 7.19 (1H, doublet, J = 8 Hz, H₅ on C-3), τ 7.29 (1H, a doublet of doublets, Jₐc = 8 Hz, Jₐd = 2 Hz, H₆ on C-3), τ 7.72 (3H, singlet, acetyl methyl) and τ 8.15-8.6 (6H, multiplet, aliphatic hydrogens); a Beilstein test was positive. The semicarbazone was obtained from aqueous ethanol as white flakes, mp
210-211.5°C.

**Anal.** Calcd for C_{11}H_{18}ClN_{3}O: C, 54.33; H, 7.39. Found: C, 54.68; H, 7.74.

Distillation of compound 27 from sodium carbonate gave only starting material (glc and ir analysis). However, distillation of compound 27 from an equivalent amount of 1,5-diazabicyclo[4.3.0]-5-nonene (DBN) gave a mixture of compound 25 and 26 in a ratio of 85:15; glc of an admixture of the dehydrohalogenation mixture and "authentic" fraction one gave only two peaks, identical to pure fraction one from the acylation reaction. The infrared spectrum (CCl₄) of the two mixtures was identical except for a very weak band due to saturated carbonyl at 1700 cm⁻¹.

In certain acylation reactions of 1,3-cyclooctadiene, the reaction mixtures were not allowed to warm slowly to 0°C, but poured directly into ice-dilute hydrochloric acid slurry. The infrared spectrum (film) of the crude reaction mixture showed bands at 3015, and 1712 cm⁻¹ indicative of only unsaturated non-conjugated ketone; the nmr spectrum (CCl₄) consisted, _inter alia_, of two non-conjugated acetyl methyl singlets at 7.82 and 7.87 and a multiplet at 4.3 (vinyl hydrogens).

Reduction of Acetylcy clooctadienones (25 and 26). To a stirred solution of fraction I (an ~ 80:20 mixture of dienones 25 and 26) from the acetylation of cyclooctadiene (0.9 g, 6.1 mmole) in 40 ml of methanol cooled at 0°C was added dropwise an excess of sodium borohydride (0.5 g, 13 mmole) in 20 ml of methanol. After addition was complete (30 min), the reaction was stirred for an additional hour at 0°C. The crude reaction mixture was concentrated under reduced pressure to give a grey residue. This residue was dissolved in water and extracted three times with ether; the combined ether extracts were washed with saturated sodium
sulfate, dried (sodium sulfate), and evaporated to give a colorless oil (0.8 g, 95%) whose infrared spectrum (film) 3600, 3400, 3005, 1650, and 695 cm\(^{-1}\) indicated complete reduction of the ketones. Glc analysis on column A, at 165\(^{\circ}\) gave one major peak (retention time 7.8 min) and an incompletely resolved minor peak of retention time (7.5 min) in a ratio of 88:12, assigned to compound 28 and 29. The nmr spectrum (CCl\(_4\)) of the mixture exhibited signals at \(\tau\) 4.15 (1 H, multiplet, vinyl proton), \(\tau\) 4.32 (2 H, multiplet, vinyl protons), \(\tau\) 5.84 (1 H, quartet, \(J = 7\) Hz, methine hydrogen adjacent to an alcohol and allylic) \(\tau\) 7.09 (1 H, broad singlet, OH), \(\tau\) 7.82 (4 H, multiplet, aliphatic methylenes), \(\tau\) 8.75 (3 H, doublet, \(J = 7\) Hz, aliphatic methyl). Tlc (silica gel) gave only one spot using various solvents for elution.

Photolysis of the Dienols (28 and 29). The crude ~80:20 mixture of dienols 28 and 29 (0.71 g) in 200 ml of dry ether was placed in a water-cooled, concentric reaction vessel, flushed with nitrogen and irradiated for 13 hr through a Vycor filter by a Hanovia Type L medium pressure 450-W mercury arc lamp. The course of the reaction was followed by glc. Evaporation of the solvent and short-path distillation of the residue gave 0.15 g of a pale yellow oil bp 98-115 (bath temperature, 0.3 mm). Glc analysis on column A at 145\(^{\circ}\) indicated four components with very similar retention times. The two major components were of shorter retention times than the minor components whose retention times were similar to the starting dienols. The nmr spectrum (CCl\(_4\)) of the mixture displayed signals at \(\tau\) 6.1-6.5 (complex vinyl proton multiplet), \(\tau\) 5.85 (quartet, \(J = 7\) Hz, HO-CH\(_2\)C=CH\(_2\)), \(\tau\) 6.4 (quartet, \(J = 8\) Hz, HOCH\(_3\)), \(\tau\) 6.8 (broad singlet, OH), and \(\tau\) 8.85 and 8.80 (a pair of doublets, \(J = 7\) Hz, aliphatic methyl). The number of vinyl hydrogens could not
be accurately determined. The two major components were isolated by preparative glc on column A at 135°. Glc analysis of the isolated components indicated that they were still mixtures; analysis on several columns failed to give complete resolution. Tlc on silica gel indicated two spots. Isolation of the major spot and glc analysis indicated the same mixture of four products.

**Synthesis of Cyclononene.** Cyclononene was prepared according to a modified procedure of Gordon and Narayana. Cyclooctene (100 g, 0.9 mole) was treated with potassium t-butoxide (1.2 moles) and bromoform (1.0 mole) to afford after distillation 81 g (30% of 9,9-dibromobiclo[6.1.0]nonane, bp 70-72° (0.3 mm) [lit. 82 bp 45° (0.15 mm)].

A solution of 9,9-dibromobiclo[6.1.0]nonane (80 g, 0.3 mole) in 150 ml of dry ether was added dropwise to a one liter, three neck flask, equipped with a stirrer, and two connected condensers, which contained 36 g (1.5 mole) of magnesium turnings in 400 ml of dry ether. The double condenser apparatus was necessary due to the initial very rapid rate of reaction. After the initial rapid reaction has started the rate of addition was adjusted to give a steady reflux. After the addition was complete, the mixture was stirred under reflux for 3 hrs, cooled and then an ice water mixture was cautiously added to the cloudy brown solution. Filtration of the white suspension gave a milk white ether-water filtrate. The two layers were separated and water layer was extracted with ether; the combined ether solution was washed with water (3 times) and dried (sodium sulfate). A major portion of the ether was removed by an atmospheric distillation through a Vigreux column and then transferred to a smaller distillation apparatus. After the remaining ether was removed under reduced pressure (200 mm),
distillation of the clear residue gave 1,2-cyclononadiene (18 g, 80%), bp 45-50°(0.5 mm) [lit.62 bp 94° (44 mm)] which was > 98% pure from glc analysis on column B at 140°.

1,2-Cyclononadiene (9.5 g, 80 mmole) was shaken (Parr hydrogenation) with a suspension of 150 mg of 10% palladium on charcoal and 250 ml of methanol under a pressure of 2 atm. After the theoretical quantity of hydrogen was absorbed (10 min), the catalyst was removed by filtration, water and methylene chloride added, and the layers separated. The water-methanol layer was extracted several times with methylene chloride; the combined methylene chloride solution was back washed with water, and dried. The two hydrogenation batches were combined and distilled; 300 ml of the total 400 ml of methylene chloride was removed by fractional distillation through a helix packed Vigreux column at atmospheric pressure. The remaining solution was transferred to small distilling apparatus, concentrated at reduced pressure and distilled to give cyclononene (15 g, 80%) as a colorless oil, bp 45-47° (5.9 mm) [lit.62 bp 85-86 (45 mm)]; the ir spectrum (film) exhibited strong bands at 3010 and 730 cm⁻¹ (cis C=C) and no absorption at 975 cm⁻¹ for the trans isomer.

Acylation of Cyclononene with Acetyl Chloride in the Presence of Stannic Chloride. To a solution of stannic chloride (12.5% 0.05 mole) in 30 ml of methylene chloride was added dropwise a solution of cyclononene (6 g, 0.05 mole) and acetyl chloride (4 g, 0.05 mole) in 20 ml of methylene chloride at -25° over one-half hr. The reaction was stirred at -15° for 1 hr, then allowed to warm to 0°, poured on to crushed ice, washed with dilute base until neutral, dried (magnesium sulfate), and concentrated to give a yellow oil (7.7 g). Glc analysis
of crude reaction mixture on column B at 174°C indicated seven components. These are, in order of retention times: (1) (0.5 min, 11% of total area) cyclononene, (2 and 3) [0.8 min, 13%], (4 and 5) [1.5 min, 20%] acetyl-
cyclononene isomers, (6) [4 min, 5%], (7) [5 min, 51%], 1-acetyl-5-
chlorocyclononane (4J) overall yield of 75%. Distillation of the
reaction mixture gave four fractions: (A) bp 25-29°C (0.3 mm), 0.8 g
(glcc indicated > 80% cyclononene); (B) bp 31-60°C (0.3 mm), 1.1 g,
(glcc indicated components 1-3); (C) bp 75-45°C (0.3 mm), 2.1 g, (glcc
indicated components 2-5), (D) bp 96-105°C (0.3 mm), 3.5 g (glcc
indicated components 4-7, > 70% of 7).

Fraction (B) appeared to be a mixture of chlorohydrocarbons and
cyclononene. The ir spectrum (film) possessed no carbonyl absorption.
The nmr (CCl₄) contained a quintet at τ 5.89 attributable to the hydrogen
on the chlorine-bearing carbon; a broad singlet at τ 8.4 due to aliphatic
protons; a small multiplet at τ 9.0 indicated the presence of a trace
of ring contraction products.

Fraction (C) exhibited spectral data indicative of acetyl-cyclo-
nonene isomers (4g and 4j); ir (film), 1710, 1660, and 1620 cm⁻¹; the
relative intensities of the bands at 1710 and 1660 cm⁻¹ showed that the
conjugated ketone was the major isomer.

Fraction (D) consisted mostly of 1-acetyl-5-chlorocyclononane (4l).
The semicarbazone of the mixture was prepared by the usual procedure, using equimolar amounts of semicarbazone hydrochloride and sodium
acetate in 50% ethanol. After three recrystallizations from ethanol the
white leaflets showed an mp 158-160°C.

Anal. Calc'd for C₁₂H₂₄O₂N₂Cl: C, 55.49%; H, 8.42. Found: C,
56.05; H, 8.79.
The spectral data for compound \(4\) includes: ir (film), 1710 (C=O) and 665 (C-Cl) cm\(^{-1}\); nmr (CCl\(_4\)), \(\tau\) 5.8 (1 H, quintet, \(J = 5.0\) Hz, -CHCl), \(\tau\) 7.85 (3 H, singlet, CH\(_2\)CO), \(\tau\) 7.6 (1 H, broad multiplet, -CHCO), \(\tau\) 8.3-8.7 (14 H, multiplet, aliphatic protons).

The distilled fraction 1-acetyl-5-chlorocyclononane (\(4\)) darkens slowly on standing at room temperature; the infrared spectrum (film) of aged material which showed both saturated and unsaturated carbonyl bands indicated that a mixture of chloroketone \(4\) and unsaturated ketone was present. This was further attested to by glc and nmr examination.

Distillation of crude reaction mixture gave mostly starting material with some increase in the amount of elimination products (ir, glc analysis).

Collection of a small portion of component (7) 1-acetyl-5-chlorocyclononane on column B at 160° gave a 4:1 mixture of nonconjugated and conjugated acetyl cyclononene (\(43\) and \(42\)). The nonconjugated acetyl component possessed identical glc retention time on several columns as compound (\(43\)) isolated in trifluoroacetic anhydride-acetic acid acylation of cyclononene.

Reduction of Cyclononene Acylation Mixture with Sodium Borohydride.

To the crude (glc indicated 75\% chloroketone \(4\) in this run* ) acylation reaction mixture (5.0 g, 0.26 mole) dissolved in 25 ml of methanol was added sodium borohydride (0.2 g, 55 mmole) in 30 ml of methanol over 15 min. The reaction mixture was stirred at room temperature for one hour, poured into water, and extracted with ether. The ether washing

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*This degradation was performed on an acylation mixture which contained ca. 20\% more chloroketone \(4\) then stated in the previous experimental section. The larger yield of chloroketone was obtained using deactivated stannic chloride i.e. catalyst which was not obtained from a freshly opened container.
was extracted twice with water, dried, and evaporated under reduced pressure to give (4.2 g, 84%) of crude 1-chloro-5-(α-hydroxyethyl)cyclononane (45) (glc indicated ca. 75% pure). The infrared spectrum (film) showed strong absorption for OH 3360 cm⁻¹ broad and no carbonyl absorption.

Dechlorination of 45. Sodium (10 g, 0.43 mole) was added in small pieces to a stirred, refluxing solution of the crude 1-chloro-5-(α-hydroxyethyl)cyclononane (45) (6 g, 0.03 mole) and t-butyl alcohol (100 ml) in tetrahydrofuran (400 ml). The reaction was stirred and refluxed until all the sodium had dissolved (overnight). The bulk of the solvent was removed under reduced pressure leaving an orange slurry which was poured into ice-water. The resulting mixture was extracted with ether; the ether extracts were then washed with water, dried, and concentrated. Distillation gave 1-cyclononyl ethanol (3.3 g, 58%) as a colorless oil, bp 93-95° (0.25 mm); ir (film), 3360, 1150 cm⁻¹, and no carbonyl absorption; glc analysis on column C indicated the alcohol to be ca. 90% pure.

Oxidation of the 1-cyclononyl ethanol (3.3 g) with Jones reagent gave acetylclzononane (3.0 g, 95%); ir (film), 1705 cm⁻¹, and no OH absorption. Glc analysis on column C showed the material to be ca. 90% pure.

Haloform Reaction on Acetylclzononane (47). To a solution of acetylclzononane (0.8 g, 3 mmole) in a 60% dioxane-water (200 ml) and 15 ml of 10% sodium hydroxide was added dropwise, with stirring, a 10% solution of iodine and potassium iodide until an excess of iodine was indicated (30 ml). After stirring overnight at room temperature, the reaction mixture was filtered to remove iodoform, acidified, and extracted three times with ether; the combined ether extracts were washed with a
20% sodium thiosulfate solution, dried (sodium sulfate), and concentrated to give 0.47 g of cyclononanecarboxylic acid; analytical glc on column A at 175° indicated one peak: ir (film), 3400-3100 (broad peak) and 1701 (broad peak) cm⁻¹.

**Esterification of Cyclononanecarboxylic Acid Using Diazomethane.**

To a 250 erlenmeyer flask was added a 40% solution of potassium hydroxide and ether. N-methyl-N-nitrosourea (10 g) was added slowly to the cooled solution 0°. The yellow ether layer containing diazomethane was decanted into a cooled ether solution of cyclononanecarboxylic acid (0.2 g). The solution was stirred at 0° for 30 min, then overnight at room temperature. Concentration at reduced pressure gave 0.11 g of methyl cyclononane carboxylate; ir (film), 1735, 1250 cm⁻¹, and no absorption at 3400. Glc analysis on column A at 180° indicated the material to be ca 95% pure. The infrared spectrum and glc retention time on column A and B were identical with those of authentic methyl cyclononanecarboxylate (synthesis described below).

**Independent Synthesis of Methyl Cyclononanecarboxylate.** To a refluxing carbon tetrachloride solution (15 ml) of cyclodecanone (0.86 g, 5.58 mmole) under irradiation by a 100-W bulb was added benzoylperoxide (10 mg) and N-bromosuccinimide (1.2 g) according to the procedure of Prelog and Schenuker⁸³. After 30 min, in which time the initial orange solution had turned pale yellow, the solution was cooled and filtered to remove succinimide. The filtrate was extracted with petroleum ether, dried (magnesium sulfate), and concentrated to give ca 1.2 g of a pale yellow oil.

The crude bromoketone (0.6 g) was added dropwise to an excess of sodium methoxide (0.5 g) in 3 ml of methanol at -20°. After addition was complete the reaction mixture was stirred overnight at room temperature;
25% potassium hydroxide solution was then added and the mixture was refluxed for one hr, poured into water, and extracted with ether. The water layer was acidified and extracted with ether; the combined ether extracts were dried (magnesium sulfate) and concentrated to give 0.1 g of crude cyclononanecarboxylic acid: IR (film), 3200 (broad) and 1710 (broad) cm\(^{-1}\).

Treatment with diazomethane in the manner described earlier gave 0.08 g of crude ester which was shown to be a mixture of three components by glc analysis (column D 140\(^{\circ}\)). Isolation of the major peak, which had the same retention time (7 min) as the degraded ester, by preparative gas chromatography on column D, at 140\(^{\circ}\) gave methyl cyclononanecarboxylate whose infrared spectrum (film) 1735 and 1248 cm\(^{-1}\) was superimposable with that of ester obtained by degradation of the acylation reaction mixture of cyclononene.

Treatment of 1-Acetyl-5-chlorocyclononane (\(\text{II}\)) with Sodium Hydride; Preparation of 3a-Acetylhydridlindane. To a suspension of excess sodium hydride (0.1 g) in (20 ml) dry dimethoxyethane (DME) under nitrogen atmosphere was added crude choroketone \(\text{II}\) (0.2 g) in 10 ml of dimethoxyethane. After an initial evolution of hydrogen (10 min), the reaction was stirred at room temperature for 1 hr. The dark orange DME solution was removed via syringe, added to water, and extracted twice with ether; the ether extracts were dried (magnesium sulfate) and concentrated to give 0.1 g of orange oil. In comparison to the glc pattern of the starting material (column D at 148\(^{\circ}\)) which indicated several minor short retention time time peaks and a major peak at 20 min (5-chloro-1-acetylcyclononane); the glc of the product exhibited a new major peak with a short retention time (4 min) [methyl cis-hexahydroindan-3a-yl ketone (59)] and an absence of the long retention time peak.
Ketone (50) was isolated by preparative glc on column D at 148°C. The nmr spectrum (CCl₄) indicated only one acetyl group at τ 8.02 (3 H, CH₃CO) and a signal at τ 8.25-8.8 (15 H, broad multiplet aliphatic H). The infrared spectrum (film) was identical to that of authentic methyl cis-hexahydroindan-3a-yl ketone, which was prepared by an unambiguous synthesis.

Treatment of 1-Acetyl-5-chlorocyclononane with Potassium t-butoxide.

To a refluxing solution of excess potassium t-butoxide (0.3 g) in 25 ml of t-butanol was added 5-chloroacetylclyclononanone (0.3 g). [the short retention time products were fractionally distilled away from chloro-ketone so as to have only 5-chloroacetylclyclononanone remain in the pot residue; glc analysis on column A indicated only one peak]. After the tan reaction mixture was refluxed for an hr, the excess t-butanol was removed under reduced pressure; water was added to the residue and the suspension was extracted with ether. The ether extracts were washed with water, dried (magnesium sulfate), and concentrated to give an orange oil which was distilled in a short path apparatus to give 0.15 g of a colorless oil, bp 55-70 (bath temperature, 0.2 mm): ir (film), 1704 (saturated carbonyl) cm⁻¹; nmr (CCl₄), two singlet at τ 7.93 and 7.99, (CH₃CO), a broad absorption at τ 8.2-8.6 (aliphatic H), and no olefinic hydrogen. The two singlets at τ 7.93 and 7.99 indicated a 30:70 mixture of acetyl compounds. This was verified by glc analysis on column C at 145°C, which showed two components: peak A (70%, retention time 11 min) and peak B (30%, retention time 12 min). The mixture was separated on column C and the ir spectrum (CCl₄) of peak B was identical to the ir spectrum of authentic methyl cis-hexahydroindan-3a-yl ketone (50, vide infra). The ir spectrum of peak A was similar to but not identical with that of 50; this component is probably methyl trans-
hexahydroindan-3a-yl ketone.

Preparation of Authentic Methyl cis-Hexahydroindan-3a-yl Ketone (50). Compound 50 was prepared according to a modified procedure of Kronenthal and Becker. A sealed steel lecture bottle containing 11 g (0.1 mole) of acetyl-cyclopentene [prepared according to the procedure of Jones and Taylor] bp 65-70 (0.5 mm) and 12 g (0.22 mole) of freshly distilled butadiene was heated at 180° for 15 hrs. Distillation of the black residue gave 3.0 g (20%) of methyl cis-3a,4,7,7a-tetrahydroindane-3a-yl ketone (51), bp 55-60 (0.5 mm) and a small high boiling fraction 85-150° (0.4 mm) in addition to an undistillable polymeric residue. Analytical gle on column A at 170° indicated compound 51 was > 95% pure with minor short retention time impurities probably vinylcyclohexene; ir (film), 3040 and 1705 cm⁻¹. The 2,4-dinitrophenylhydrazone was prepared and recrystallized from aqueous ethanol; the orange flakes thus obtained had a mp 131-132 (lit. mp 130.0-131).

A solution of compound 51 (1.8 g, 0.01 mole) and 10% palladium on charcoal (100 mg) in 250 ml of 95% ethanol was shaken under 2 atm. of hydrogen at room temperature until the uptake of hydrogen ceased (10 min.); a total of 0.01 mole was absorbed. Filtration of the catalyst, evaporation of the solvent, and distillation gave 1.4 g of methyl cis-hexahydroindan-3a-yl ketone (50) bp 52-55 (0.5 mm): ir (film), 1703 and no absorption at 3040 cm⁻¹; nmr (CDCl₃), δ 7.91 (3 H, singlet, CH₃CO), and δ 8.3-8.7 (15 H, broad multiplet, aliphatic protons).

Acylation of Cyclononene Using Trifluoroacetic Anhydride-Acetic Acid. To a mixture of trifluoroacetic anhydride (3.5 g) and acetic acid (1.0 g) was added dropwise cyclononene (2.0 g) over a period of 15 min at 27° according to the procedure of Henne and Tedder. The
black solution was stirred at 27°C for an additional 1.5 hr, poured into water and worked up in the same manner as described for cyclooctene to give 3.7 g of a yellow oil. The ir spectrum (film) showed absorption at 1710 cm⁻¹ for non-conjugated ketone and 1780, 1260 cm⁻¹ for trifluoroacetoxyacetylcyclononane.

The crude reaction mixture was stirred overnight at room temperature in aqueous acidic dioxane; the reaction mixture was neutralized and extracted with ether. The ether layers were dried (magnesium sulfate), concentrated, and distilled to give three fractions: (A) bp 68-80 (0.5 mm). 1.3 g, glc analysis on column A at 175°C showed one major peak > 75% corresponding to 5- or 6-acetylcyclononene 4/3 and three minor peaks of shorter retention time. (B) bp 90-100 (0.5 mm) 1.37 g, glc analysis on column A showed a peak for 5- or 6-acetylcyclononene composing over 90% of the total area: ir (film), 3025, 1710, and 730 cm⁻¹, with trace absorption at 1780 and 1260 cm⁻¹; nmr (CCl₄), τ 4.48 (2 H, multiplet, vinyl protons), τ 7.5-7.7 (5 H, multiplet, allylic hydrogens and -CHCO), τ 7.90 (3 H, singlet, CH₃CO), and τ 8.15-8.55 (8 H, broad multiplet, aliphatic protons). (C) bp 110-140 (0.5 mm), 0.3 g, glc analysis on column A showed a 1:3 mixture of compound 4/3 and a component of longer retention time, probably trifluoroacetoxyacetylcyclononane and hydrolized products: ir (film), 3500, 1780, 1710, and 1250 cm⁻¹.
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