THE STEREOCHEMISTRY AND MECHANISM OF
ALKYLHALOKETENE-OLEFIN
CYCLOADDITIONS

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THE STEREOCHEMISTRY AND MECHANISM OF ALKYLHALOKETENE-OLEFIN CYCLOADDITIONS

DISSERTATION

Presented to the Graduate Council of the North Texas State University in Partial Fulfillment of the Requirements

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By

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>LIST OF TABLES</th>
<th>iv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter</td>
<td></td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>II. EXPERIMENTAL</td>
<td>24</td>
</tr>
<tr>
<td>III. RESULTS AND DISCUSSION</td>
<td>55</td>
</tr>
<tr>
<td>BIBLIOGRAPHY</td>
<td>83</td>
</tr>
<tr>
<td>Table</td>
<td>Page</td>
</tr>
<tr>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td>I. Acid Halides Prepared from Commercially Available Acids</td>
<td>26</td>
</tr>
<tr>
<td>II. P.M.R. Spectral-Structural Correlations for Ketoketene Cyclopentadiene Adducts</td>
<td>46</td>
</tr>
<tr>
<td>III. Methylhaloketene Cycloadduct Isomer Distribution with Cyclopentene and Cyclopentadiene in Hexane</td>
<td>47</td>
</tr>
<tr>
<td>IV. Substituent and Solvent Effects on Isomer Distributions</td>
<td>48</td>
</tr>
<tr>
<td>V. Cyclopentadiene-Methylhaloketene Adduct Isomer Distributions in Various Solvents at 0-5°C</td>
<td>49</td>
</tr>
<tr>
<td>VI. The Effect of Temperature on Cyclopentadiene Unsymmetrical Ketoketene Adduct Isomer Distributions in Hexane</td>
<td>50</td>
</tr>
<tr>
<td>VII. P.M.R. Spectral-Structural Correlations for Methylchloroketene-Olefin Adducts</td>
<td>51</td>
</tr>
<tr>
<td>VIII. Methylchloroketene-Cyclopentadiene Adduct Isomer Distributions in Solvents of Different Polarity at 0-5°C</td>
<td>66</td>
</tr>
<tr>
<td>IX. Differences in the Free Energies of Solvation between Endo- and Exo-Alkyl Transition States</td>
<td>68</td>
</tr>
<tr>
<td>X. The Endo-/Exo-Alkyl Isomer Distributions of Alkylbromoketene-Cyclopentadiene Adducts in Hexane at 25°C vs. Taft's Steric Factors</td>
<td>71</td>
</tr>
<tr>
<td>XI. Comparison of Reported and Estimated Endo/Exo Isomer Distributions</td>
<td>72</td>
</tr>
</tbody>
</table>
CHAPTER I

INTRODUCTION

Ketenes are a family of organic compounds which have a functional group that contains both a carbon to carbon double bond and a carbon to oxygen double bond. In the ketene functionality, the double bonds are cumulative, and one of the carbon atoms is common to both double bond systems. Ketene is structurally the simplest member of this family.

\[
\text{C}==\text{C}==\text{O} \quad \text{H}\text{C}==\text{C}==\text{O} \\
\text{ketene functionality} \quad \text{ketone}
\]

Other members of the ketene family can be considered for the purpose of classification to have been derived from ketene by the substitution of one or more groups for the hydrogen substituents of ketene. If only one of the hydrogens is substituted by some group, the resulting unsymmetrical structure is known as an aldoketene; if both hydrogens are substituted by other groups, the resulting structure is known as a ketoketene. Ketoketenes may be symmetrical or unsymmetrical depending upon whether the substituted groups indicated by A and B are alike or different.

\[
\begin{align*}
\text{A} \text{C}==\text{C}==\text{O} & \quad \text{A} \text{C}==\text{C}==\text{O} \\
an \text{aldoketene} & \quad \text{a ketoketene}
\end{align*}
\]
Most ketenes are highly reactive substances which exist only fleetingly in the reaction systems in which they are produced. Only ketene, diphenylketene, dimethylketene, bis-(trifluoromethyl)ketene and a few others have been isolated and characterized in a pure state (18, 19, 48). Ketenes and ketene intermediates generated in a reaction system may combine with the reagents from which they are produced (10, 18, 41) or undergo dimerization or polymerization (24, 36, 57). The high degree of chemical reactivity of ketenes toward a variety of chemical substances makes this family of compounds of considerable interest in organic synthesis.

Ketenes may be generated by the pyrolysis of compounds which give rise to the desired ketene as a decomposition product: the dehalogenation of a 2-haloalkanoyl halide, the dehydrohalogenation of an acid halide which has at least one \( \alpha \)-hydrogen and a number of less well-known procedures (13, 15, 16, 38, 43). The method employed to generate a ketene depends upon the reactivity of the ketene and the intended use. Ketene reactivity is related to the structure, the method of generation and the media in which the ketene is generated (44). Ketene itself can be generated by the pyrolysis of a number of compounds which contain the acetyl group such as acetone, acetic acid, acetic anhydride or ethyl acetate. Ketene is conveniently prepared in the research laboratory by the pyrolysis of acetone (24).
Aldo- and ketoketenes have been generated by the pyrolysis of acids, acid anhydrides, ketones, esters, diazoketones and ketene dimers (24, 37, 44).

Aldo- and ketoketenes can also be prepared by the dehalogenation of a 2-haloalkanoyl halide by the use of zinc activated with copper as the dehalogenating agent (3, 8, 24, 44).

\[
\text{R-C-C-X} + \text{Zn(Cu)} \rightarrow \text{R=C=O} + \text{ZnX}_2
\]

One of the most commonly employed methods for generating aldo- and ketoketenes is the dehydrohalogenation of an acid bromide or chloride with a tertiary amine (24, 37, 44). An inert hydrocarbon, an ether or a chlorinated hydrocarbon solvent is usually employed (44). The tertiary amine must be a sufficiently strong base to be effective as a dehydrohalogenating agent. Pyridine and dimethylaniline, both weak bases, are reported to be ineffective as dehydrohalogenating agents (51). Triethylamine and other trialkylamines are the most widely employed. For example, triethylamine reacts with an acid halide which has at least one \(\alpha\)-hydrogen to produce the ketene and a triethylammonium halide salt (24, 37).

\[
\text{R-C-C-X} + (\text{C}_2\text{H}_5)_3\text{N} \rightarrow \text{R=C=O} + (\text{C}_2\text{H}_5)_3\text{NHX}
\]

The dehydrohalogenation of an acid halide is especially applicable as a method for generating some of the most reactive
ketenes known. Aldoketenes and the halogenated ketenes, which are extremely reactive ketenes, are easily generated in this manner (6, 7, 11, 14, 15, 37, 44, 56).

To take advantage of the great reactivity of ketenes as intermediates for organic synthesis, ketenes are generally intercepted in the reaction system in which they are generated. This type of reaction is known as an in situ reaction, and the substance employed to intercept the ketene is known as the ketenophile. Highly reactive ketenes are usually generated in the presence of a ketenophile, the result being that a product of the ketene and the ketenophile is formed. This product is called an adduct (44).

\[
\text{ketene} + \text{ketenophile} \rightarrow \text{adduct}
\]

In a mechanistic sense, a ketene acts as a powerful electrophilic reagent in its reactions with typical ketenophiles, while the ketenophile acts as a nucleophilic reagent (32, 61). The electrophilic or electron deficient site of a ketene is the carbon atom of the carbonyl group (61). This is illustrated by the valence-bond structure (I).

\[
\begin{align*}
I & : & \text{C}^+\text{C}=\text{O} \\
II & : & \text{C}=\text{C}=\text{O} \\
III & : & \text{C}^\ominus\text{C}=\text{C}^\ominus
\end{align*}
\]

The nucleophilic site of a ketenophile is an electron rich site that is capable of interacting with the electron deficient site of the ketene. Ketenophiles may be either dipolar substances or substances which have electron rich sites due to bond unsaturation. Ketenophiles having carbon to carbon
multiple bonds (2, 26, 40, 46), carbon to nitrogen double bonds (4, 43) and carbon to oxygen double bonds (35) are usually employed to intercept ketenes.

Olefins are the most common ketenophiles used to trap ketenes. Activated olefins such as cyclic conjugated dienes (12, 28, 35, 54, 56, 58), enol ethers (25, 34, 45) and enamines (27, 33, 47, 48, 49), which are more nucleophilic than ordinary olefins, are particularly well suited for trapping reactive ketenes to form adducts. The adducts formed from reactions of ketenes and olefins are cyclobutanones and are the result of a 1,2- or (2 + 2) cycloaddition.

\[
\text{C} = \text{C} = \text{O} + \text{C} = \text{C} \rightarrow \text{C} \equiv \text{C} = \text{O}
\]

Cyclopentadiene is the most widely used ketenophile for trapping highly reactive ketenes in situ. This olefin reacts rapidly and efficiently with ketenes to minimize the side reactions of ketenes generated in situ (41, 50). Cyclopentadiene-ketene adducts are cyclobutanones which are bicyclo-(3.2.0)hept-2-en-6-ones as illustrated by structure IV.

\[
\text{C} = \text{C} = \text{O} + \text{Cyclic} \rightarrow \text{IV} + \text{V}
\]

Structure IV is formed in preference to and to the exclusion of structure V. This has been verified for the bicyclo-(3.2.0)hept-2-en-6-ones derived from cyclopentadiene with diphenylketene (42, 52), dichloroketene (21),
methylchloroketene (6), methylbromoketene (7) and dimethylketene (46). The (2 + 4) Diels-Alder adduct, that is observed when an olefin reacts with a cis-diene, is not formed in the reaction of a ketene with cyclopentadiene (2, 17, 61).

In recent years, some extremely reactive ketenes have been generated and reacted in situ with cyclopentadiene. Among these ketenes are monoalkylketenes (5, 35, 43), monohaloketenes (5), dihaloketenes (3, 6, 56), alkylhaloketenes (6, 7, 11) and phenylhaloketenes (4, 10). Before 1965, these ketenes had not been detected although several attempts had been reported (55).

In a review of in situ ketene cycloadditions, Luknitskii and Vovsi have indicated that ketenes which have electron donating substituents are particularly reactive. Luknitskii and Vovsi noted that the method of ketene generation seems to be a factor which influences the reactivities of ketenes (44).

Recently, kinetic studies have been reported for reactions of diphenylketene (9, 32) and dimethylketene (33) with olefins. The activation parameters for the reactions of diphenylketene with 2,3-dihydropyran (9) and butyl vinyl ether (32) indicate that these reactions are characterized by relatively low enthalpies of activation and high negative entropies of activation. Relatively modest solvent effects have been reported for these reactions (9, 32). Kinetic isotope studies have been made utilizing the reactions of diphenylketene with cyclohexene (39) and styrene (1). It was concluded in these studies that the bond formation was not synchronous, and it was suggested
that the bond from the carbonyl carbon of the ketene to the olefin was formed slightly in advance of the second bond. The transition state was assumed to involve a parallel orientation of ketene and olefin with the sequence of bond formations as shown.

\[
\begin{array}{c}
\text{C} = \text{C} = \text{O} \\
+ \\
\text{C} = \text{C}
\end{array}
\rightarrow \left[ \begin{array}{c}
\text{C} \text{=} \text{C} \text{=} \text{O} \\
\text{2}
\end{array} \right] \rightarrow \boxed{\text{C}}
\]

Although the kinetic studies have aided in understanding some of the characteristics of ketene-olefin reactions, these studies have been limited by the lack of stable, yet sufficiently reactive, ketenes.

The stereochemistry of the products produced in ketene-olefin reactions has received some attention in the past few years. Diphenylketene and dimethylketene are reported to react with cis- and trans-enol ethers in a cis-stereospecific manner with respect to the olefin (25, 45). Ghosez and co-workers, studying the reaction of dichloroketene with cis- and trans-cyclooctene, also observed that dichloroketene adds cis-stereospecifically to cis- and trans-cyclooctene (21, 22).

Huisgen and Otto (33) have recently presented evidence which suggests that ketenes react with enamines, which are highly nucleophilic olefins, by competing concerted and stepwise processes. In the stepwise process a dipolar intermediate was suggested. The extent to which the two-step dipolar process operates was reported by Huisgen to be dependent upon the polarity of the solvent (33).
A recent extension of the principle of the conservation of orbital symmetry provides a basis for a better understanding of ketene-olefin reactions (30, 61). Although this principle is applicable to concerted processes, it is not necessarily applicable to two-step processes in which net orbital symmetry from reactants to products need not be conserved (30, 59, 60, 61). Hoffmann emphasizes the point that symmetry allowed processes need not follow the reaction path predicted by the principles of symmetry conservation. However, it has been emphasized that the conservation of orbital symmetry can be expected in each single step in a multiple-step process. The basic principle of a reaction proceeding by the lowest energy path is, according Hoffmann, of greater importance in determining the path of a reaction than the conservation of over-all reaction orbital symmetry. At present, the predictions which have been made on the basis of the conservation of orbital symmetry for ketene-olefin reactions are being experimentally tested by workers in various laboratories.

In a review of cycloaddition reactions involving polar intermediates, Gompper presents a case for not rejecting a priori the possibility for a two-step dipolar mechanism for ketenes and olefins (23). According to Gompper, theoretical calculations of the energy requirements for the transition states associated with concerted and two-step processes indicate that no large energy difference exists between the two reaction paths. In the case of the reactions of ketenes
with electron rich olefins such as the enamines, the calculations indicate that the energy requirement for the transition state associated with a two-step process is actually lower than for a one-step or concerted process (23). Thus, it would seem that a two-step process might be preferred in some ketene-olefin reactions.

Although reactions which are stereospecific would seem to be the logical consequence of a concerted cycloaddition, stereospecificity is not necessarily the final criterion for distinguishing between a concerted and a dipolar two-step process (23). In a two-step process, the stereochemistry is determined by the relative rates of ring closure in the second step and of the internal rotation in the dipolar intermediate (23, 29, 33). Thus, reactions may be highly stereoselective and approach being stereospecific without being concerted processes. Examples of two-step processes involving dipolar intermediates which are highly stereoselective have been reported (23, 50).

One approach that has been suggested for aiding in distinguishing between a concerted process and a two-step process involves changing the substituents of the reacting structures (23). According to Gompper, substituents which are charge stabilizing would give rise to greatly increased reaction rates in the case of dipolar two-step processes (23). There are no reports of ketene-olefin reactions in which the structure of the ketene and the polarity of the solvent have been varied. The lack of suitably substituted ketenes has precluded kinetic studies of unsymmetrically substituted ketenes with olefins.
A recent report on the differences in the reactivities of substituted olefins with diphenylketene indicates that a two-step process may be operative when olefins with good charge stabilizing groups react with diphenylketene (32, 33). By analogy, ketenes with good charge stabilizing groups might be expected to participate in a dipolar two-step ketene-olefin reaction. Reactions which involve a dipolar intermediate and are stereoselective would be expected to show a varying response to solvent polarity and, in particular, a varying degree of stereoselectivity with solvent polarity (23, 50).

The first report in which cyclobutanone isomers from the (2 + 2) cycloaddition of an unsymmetrical ketoketene with an olefin were detected was by Martin, Gott, Goodlett and Hasek (46). The unsymmetrical ketene, butylethylketene, was reported to react with 1,3-butadiene, alkyl-substituted butadienes, 1,3-butadienylmethyl ether, cyclopentadiene, indene, cyclohexene, cyclooctene, 1,3-cyclooctadiene and a variety of other alkyl substituted alkenes. An analysis of the reaction mixtures by i.r., v.p.c. and p.m.r. revealed that mixtures of cyclobutanone isomers were produced in several of the olefin systems. Although it was assumed that isomeric cyclobutanones were formed in these reactions, the stereochemistry of these isomers was not established.
Shortly after the report of Martin and co-workers, Jaz and Denis prepared the (2 + 2) cyclopentadiene cycloadducts of a series of monosubstituted alkylketenes (35). Although this series of unsymmetrical ketenes would have been expected to yield endo- and exo-alkyl cyclobutanone isomers, no mention of isomers was reported.

The first study in which the stereochemistry of cyclobutanone isomers from the (2 + 2) cycloaddition of an unsymmetrical ketene with an olefin was elucidated was made by Brady and Holifield (6). Methylchloroketene generated by the dehydrohalogenation of 2-chloropropanoyl bromide with triethylamine in the presence of cyclopentadiene was reported to produce a mixture of endo-methyl and exo-methyl isomers. An analysis of the reaction products by a combination of instrumental and chemical methods revealed the mixture of endo- and exo-methyl cycloadducts to be in a 3:1 ratio.
Brady and Holifield, in a later study, reported that methylbromoketene also reacted with cyclopentadiene to yield a mixture of endo- and exo-methylcyclobutanone isomers but in a ratio of 1:2 (7).

The isomer distributions of the cyclobutanones formed in the reaction of cyclopentadiene with methylchloroketene (3:1 endo to exo) and with methylbromoketene (1:2 endo to exo) were completely unexpected by these workers. At that time, ketene-olefin reactions were assumed to occur by a thermally concerted or "near-concerted" process that involved a four-center transition state. In this transition state, the ketene and olefin were visualized to approach one another in parallel planes with respect to their carbon to carbon double bond systems (6, 7).

In terms of a parallel orientation of ketene and olefin in the transition state, Brady and Holifield were unable to explain the observed isomer distributions because the transition state considered would have been expected to give rise to a 1:1 endo-to exo-cyclobutanone isomer ratio when either methylchloroketene or methylbromoketene reacted with cyclopentadiene by a concerted process. Based on an examination of molecular models for the assumed transition states of these systems (19, 39), it was suggested by Brady and Holifield that the residual double bond in cyclopentadiene might be interacting with the halogen group of these methylhaloketenes and, thus, be an influence in determining the ratios of isomer products produced. Specifically, it was suggested that the bromine substituent might be large enough to interact with the residual $\pi$-electron system.
of cyclopentadiene (6, 7). The interaction which was suggested to occur favoring formation of the exo-methyl adduct is illustrated by showing methylbromoketene and cyclopentadiene in an orientation approaching the transition state. In this illustration, the ketene is arbitrarily drawn above the plane of cyclopentadiene, and the orientation of the bromine group is nearest to the π-system of the olefin.

Another possibility considered by Brady and Holifield to account for the puzzling isomer distributions observed was that methylchloroketene and methylbromoketene might be reacting with cyclopentadiene by a two-step dipolar process rather than by a concerted process. It was suggested that if a two-step reaction mechanism were operative, the initial attack on cyclopentadiene by the ketene would not necessarily determine the isomer distributions. The isomer distributions might then be determined by two separate ring closing steps (6).
Following the studies of the methylchloroketene and methylbromoketene cycloaddition reactions with cyclopentadiene, Brady and Holifield generated ethylchloro- and ethylbromo-ketenes in the presence of cyclopentadiene (7). Endo and exo isomers were produced in both systems as evidenced by v.p.c. analysis of the reaction mixtures; however, these workers did not establish the stereochemistry of the cycloadducts. The instrumental and chemical methods, which had been employed in deriving the configurational assignments at carbon-7 of the endo- and exo-methyl cycloadducts produced in the reactions of cyclopentadiene with methylchloro- and methylbromoketenes, were not suitable for the ethylbromo- and ethylchloroketene-cyclopentadiene adducts.

Whereas the endo- and exo-methyl cyclopentadiene cycloadducts of methylchloro- and methylbromoketenes could be distinguished rather easily on the basis of characteristic p.m.r. spectral differences between non-equivalent endo- and exo-methyl groups, no corresponding simplification in the spectral properties of the cyclopentadiene-ethylhaloketene adducts was noted (7).

A reaction involving an unsymmetrical halogenated ketene with an olefin other than cyclopentadiene was also described by Brady and Holifield (7). The reaction of methylchloroketene
with ethyl vinyl ether was reported to yield a mixture of cyclo-
butanone isomers in a ratio of 3:1; however, the stereochemical
assignments for these isomers were not reported.

Perhaps the most significant question raised by the work
of Brady and Holifield in the studies of unsymmetrical halo-
genated ketoketenes cycloadditions was whether these ketenes
were reacting with cyclopentadiene in a concerted or a stepwise
manner (6, 7). To answer this question, the conjectures of
Brady and Holifield had to be experimentally tested. Classical
kinetic studies were not feasible because of the instability of
halogenated ketoketenes (44). The experimentally measurable
quantities which appeared the most appropriate for answering
the question raised by Brady and Holifield were isomer distrib-
utions. Isomer distributions had to be determined for the
cycloadducts of variously substituted alkylhaloketenes and
olefins having different structures and reactivities.

A major problem in obtaining meaningful isomer distri-
butions in this study was to establish the structures of the
isomer products which would be new compounds. Since unam-
biguous group configurations had to be assigned, methods had
to be devised to make these assignments.

That unsymmetrical halogenated ketoketenes are uniquely
suited to aid in answering this question is brought out by
the fact that only alkylhaloketenes have been observed to
react with cyclopentadiene to produce both endo- and exo-alkyl
isomers. The only other unsymmetrical ketenes which have been
observed to produce cyclobutanone isomers with cyclopentadiene have either produced isomers which are reported to be indistinguishable or have produced only a single isomer (5, 46). In previous reports by Brady, Hoff and co-workers, aldoketenes are reported to react with cyclopentadiene to yield, within the limits of detection, only the exo-hydrogen isomer (5).

\[
\begin{align*}
R &= F, Cl, Br, CH_3 \\
\text{Recently, Brady, Parry and co-workers reported that phenylchloro-, phenylbromo- and phenylmethylketenes react stereospecifically, within the limits of detection, with cyclopentadiene to give only the endo-phenyl isomers (10).}
\end{align*}
\]

\[
\begin{align*}
C_6H_5 &= C\equiv C\equiv O \\
\text{Although the reaction of these ketenes with cyclopentadiene to produce single isomers is extremely important from a synthetic point of view, these ketenes are less suitable in elucidating the mechanism of ketene-olefin reactions than are ketenes which give more than a single isomer. Hence, the objectives of this research problem was to employ alkylhaloketene-olefin isomer }
\end{align*}
\]
distributions to aid in understanding the stereochemistry and mechanism of alkylhaloketene-olefin cycloadditions.
CHAPTER BIBLIOGRAPHY


CHAPTER II

EXPERIMENTAL

Proton nuclear magnetic resonance (p.m.r.) spectra were taken at room temperature with a Varian Associates A-60 Analytical Spectrometer. Carbon tetrachloride and chloroform were the solvents employed, and tetramethysilane (T.M.S.) was the internal standard (chemical shift = 0.00 p.p.m.).

Infrared spectra (i.r.) were taken with a Perkin-Elmer Model 237 Grating Infrared Spectrometer using both neat and solution samples. Sodium chloride discs or fixed thickness cells, which were appropriate to sample concentrations, were employed.

Analytical and small-scale preparative vapor phase chromatography (v.p.c.) was done on an F and M Scientific Model 700 instrument employing a thermal conductivity detection system. Separations were achieved using columns 10 ft. by ¼ in. packed with either 2 per cent Silicone Fluid FS-1265-QF-1 on Chromosorb G or with 15 per cent Ucon and 2 per cent Dronite NIW on Chromosorb W (DMCS) 60/80 mesh.

Elemental analyses were performed by the Analytical Services Section of the Chemistry Department of North Texas State University, Denton, Texas, and by C. F. Geiger and Associates, of Ontario, California.
Preparation of Reagents

All solvents were commercially available. Acetonitrile was refluxed in contact with potassium hydroxide prior to distillation in order to remove acrylonitrile, a common impurity. The acetonitrile was distilled through a 24 in. Vigreaux column and stored in contact with Linde 4A molecular sieves. All hydrocarbon solvents were pretreated by shaking with Linde 4A molecular sieves prior to their further purification by fractional distillation from calcium hydride or lithium aluminum hydride. These solvents were stored in contact with Linde 4A molecular sieves. Other solvents were shaken with Linde 4A molecular sieves, fractionally distilled through a 24 in. Vigreaux column and stored in contact with Linde 4A molecular sieves. Commercially available triethylamine was stored over molecular sieves and distilled prior to use.

Commercially available dicyclopentadiene was thermally cracked at about 140° C. and slowly fractionated through a 24 in. Vigreaux column by distillation at atmospheric pressure. Cyclopentadiene was collected at 40-40.5° C. and was stored at -10° C. The cyclopentadiene was redistilled immediately before use. Cyclopentene, cyclohexadiene, cyclohexene and cyclooctene were dried over molecular sieves and purified by fractional distillation immediately before use. Ethyl vinyl ether and 2,3-dihydropyran were purified by fractional distillation immediately before use.

The acid halides were prepared by reacting the acids with appropriate halogenating agents. Acid bromides were prepared
by the use of phosphorous tribromide, and acid chlorides were prepared by the use of either phosphorous trichloride or phosphorous pentachloride. The parent acids, with the exception of 2-chloro-3-methylbutanoic acid and 2-bromo-3,3-dimethyl-butanoic acid, were commercially available. The structures of these acid halides were confirmed by an analysis of their p.m.r. spectra as well as by the agreement of their observed boiling points with those found in the literature. The yields of acid halides were comparable to those cited in the reference indicated in Table I.

TABLE I

ACID HALIDES PREPARED FROM COMMERCIALLY AVAILABLE ACIDS

<table>
<thead>
<tr>
<th>Acid Halide</th>
<th>Boiling Range (°C.)</th>
<th>Yield (%)</th>
</tr>
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<tbody>
<tr>
<td>2-Chloropropanoyl chloride (10)</td>
<td>110-112</td>
<td>63</td>
</tr>
<tr>
<td>2-Chloropropanoyl bromide (10)</td>
<td>126-127</td>
<td>88</td>
</tr>
<tr>
<td>2-Chlorobutanoyl chloride (11)</td>
<td>129-131</td>
<td>79</td>
</tr>
<tr>
<td>2-Chloro-3-methylbutanoyl chloride (10)</td>
<td>149-150</td>
<td>41</td>
</tr>
<tr>
<td>2-Bromopropanoyl chloride (4)</td>
<td>131-132</td>
<td>73</td>
</tr>
<tr>
<td>2-Bromopropanoyl bromide (4)</td>
<td>154-155</td>
<td>67</td>
</tr>
<tr>
<td>2-Bromo-3-methylbutanoyl chloride (5)</td>
<td>59 (15 mm.)</td>
<td>61</td>
</tr>
<tr>
<td>2-Bromobutanoyl chloride (3)</td>
<td>150-152</td>
<td>72</td>
</tr>
<tr>
<td>2-Methylpentanoyl chloride (8)</td>
<td>45-47 (15 mm.)</td>
<td>81</td>
</tr>
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</table>
2-Chloro-3-methylbutanoyl chloride

2-Chloro-3-methylbutanoyl chloride was prepared by a two-step procedure that consisted of the conversion of 3-methylbutanoic acid to 2-chloro-3-methylbutanoic acid followed by the conversion of the latter acid to the desired acid halide, 2-chloro-3-methylbutanoyl chloride. In the first step of this procedure, a 102 g. portion (1.0 mole) of 3-methylbutanoic acid and 10 ml. of phosphorous trichloride were placed in a 500 ml. two-necked flask equipped with a gas tube and a reflux condenser. The porous fritted glass end of the gas tube extended into liquid acid. By means of the gas tube, 82 g. (1.16 mole) of chlorine gas from a previously weighed gas cylinder was slowly bubbled into the acid over a 6 hr. period. This reaction was accomplished under an efficient fume hood; heating was not required. After the addition of the chlorine gas, the acid mixture was purged with dry nitrogen gas to remove the residual chlorine and hydrogen chloride gases. In the second step of this procedure, the reaction mixture was cooled in an ice bath and treated with 220 g. (1.06 mole) of phosphorous pentachloride. After this addition, the reaction mixture was fractionally distilled at atmospheric pressure. The product acid chloride distilled at 147-149° C. (literature value, 149-150° C.). There was obtained 63 g. (0.41 mole) of product, corresponding to a yield of 41 per cent.

2-Bromo-3,3-dimethylbutanoyl chloride

2-Bromo-3,3-dimethylbutanoyl chloride was made from commercially available 3,3-dimethylbutanoic acid by a two-step
procedure similar to the procedure for the preparation of 2-
chloro-3-methylbutanoyl chloride. In the first step of this
procedure, a 116 g. portion (1.0 mole) of 3,3-dimethylbutanoic
acid and 10 ml. of phosphorus trichloride were placed in a
500 ml. two-necked flask equipped with a dropping funnel and a
reflux condenser. By means of the dropping funnel, a 55 ml.
portion (1.0 mole) of bromine was added to the acid mixture;
the reaction was accomplished under an efficient fume hood.
The reaction mixture was heated at 70-80°C. until the reaction
mixture no longer showed the red color of unreacted bromine;
this required approximately 24 hours. After the completion of
the bromination, the reaction mixture was purged with dry nitro-
gen gas to remove residual bromine and hydrogen bromide. In
the second step of this procedure, the reaction mixture was
cooled in an ice bath and treated with a 208 g. portion (1.0
mole) of phosphorus pentachloride. After this addition, the
reaction mixture was heated at reflux for two hours, and then
it was fractionally distilled. The acid chloride product
distilled at 106-110°C. at 30 mm. There was obtained 138 g.
of product, corresponding to a yield of 61 per cent. The
p.m.r. spectrum of 2-bromo-3,3-dimethylbutanoyl chloride in
carbon tetrachloride solution showed resonances at 4.42 p.p.m.
(singlet, 1H) for the single proton on the 2-carbon and 1.18
p.p.m. (singlet, 9H) for the methyl protons of the tertiary
butyl group.
General Procedure for In Situ Ketene-Olefin Cycloadditions

To a 500 ml. three-necked flask equipped with a dropping funnel, a sealed stirrer and a drying tube, was added a solution containing 0.2 mole of triethylamine and 0.5 mole of an olefin in 200 ml. of solvent. A 0.2 mole portion of the acid halide in 25 ml. of solvent was placed in the dropping funnel. The reaction flask and its contents were brought to the desired temperature for the reaction by means of either an ice bath or a heated oil bath. The acid halide solution was added dropwise to the olefin solution over a period of about one hour. Efficient stirring was maintained during the addition of the acid halide solution. After the addition of the acid halide, the cooling or heating baths were removed, and the reaction mixture was stirred an additional two hours. The triethylammonium salt was removed by filtration and was washed with three 50 ml. portions of the solvent. The filtrate was concentrated without heating by vacuum rotoevaporation. The concentrated reaction mixture was analyzed for endo- and exo-alkyl isomers by i.r., v.p.c. and p.m.r. The concentrated mixture was vacuum distilled through a 12 in. Vigreaux column at a reduced pressure. Yields were based on total endo- and exo-alkyl isomers in the fractional distillation. Low boiling impurities and the distillation residue were discarded. The endo- and exo-alkyl isomers were separated by preparative v.p.c. utilizing either a QF-1 column or a Ucon-Cronite
column. Infrared and p.m.r. spectra of the individual endo- and exo-alkyl isomers were taken in a carbon tetrachloride solution. Elemental analyses were obtained for mixtures of endo- and exo-alkyl isomers.

7-Chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one

To a mixture of 20 g. (0.20 mole) of triethylamine, 33 g. (0.50 mole) of cyclopentadiene and 200 ml. of dry hexane at 0-5° C., 25 g. (0.20 mole) of 2-chloropropanoyl chloride in 25 ml. of dry hexane was added dropwise over a period of approximately one hour. After the addition of the acid halide was complete, the mixture was stirred for two additional hours as it was allowed to warm to room temperature. The amine salt by-product of the reaction was removed by filtration and was washed with hexane and dried. There was obtained a theoretical amount of triethylammonium chloride salt. The filtrate was concentrated by means of solvent evaporation at room temperature employing a rotary evaporator. A v.p.c. analysis of the concentrated reaction mixture by peak area integrations indicated an endo-methyl to exo-methyl isomer distribution of 4.3. A p.m.r. analysis of the same concentrated reaction mixture by calculation of the ratio of the peak integrations of the methyl proton resonances of the endo-methyl isomer (1.77 p.p.m.) and the exo-methyl isomer (1.47 p.p.m.) gave identical endo-methyl to exo-methyl isomer distributions of 4.3. The p.m.r. spectral data for the endo- and exo-methyl isomers is summarized in Table II. Vacuum distillation through a 12 in. Vigreaux column
at 70-82° C. and 5 mm. produced 24.2 g. of mixture of endo- methyl and exo-methyl isomers which corresponded to a 77 per cent yield. Analytical data was the same as that reported in the literature (1).

The endo-methyl to exo-methyl isomer distributions were found to be unchanged upon reflux for 4 hours at simulated distillation conditions; the oil bath temperature was 145° C., and a pressure of 5 mm. was maintained.

Following a procedure identical to the one described for the preparation of the endo-methyl and exo-methyl isomers, isomer distributions were determined periodically during the additions of reagents. Portions of the reaction mixture were quenched with an aqueous sodium bicarbonate solution. The cyclobutanone isomers were extracted from the resulting aqueous mixture with diethyl ether. The ether solution containing the cycloadducts was dried over anhydrous magnesium sulfate and then filtered; the ether was evaporated, and the isomer distributions were determined by v.p.c. The isomer distributions determined periodically during the addition of the reagents were found to be identical to the isomer distributions determined upon completion of the addition of the reagents.

**Hydrogenation of 7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one.**—To 50 ml. of ethanol and 0.5 g. of palladium black was added 5 g. (0.03 mole) of 7-chloro-7-methylbicyclo(3.2.0)-hept-2-6-one isomers in a ratio of 0.59 endo- to exo-methyl. Hydrogenation was affected at room temperature at near
atmospheric pressure until a theoretical amount of hydrogen was consumed. The hydrogenation apparatus employed was identical to that described by Vogel (12). The catalyst was removed by filtration, and the solvent was evaporated by a rotary evaporator. Vacuum distillation afforded 3.5 g. (70 per cent) of the endo- and exo-methyl isomers of 7-chloro-7-methylbicyclo(3.2.0)heptan-6-one at 47-58°C at 1.0 mm. with an isomer distribution of 0.5 endo- to exo-methyl. The i.r. absorption of both isomers at 1796 cm.\(^{-1}\) indicated the presence of a carbonyl group. An absorption at 1605 cm.\(^{-1}\), indicative of a carbon to carbon double bond, was not detected.

Approximately 0.25 ml. of the endo-methyl isomer of 7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one was separated by preparative v.p.c. from a mixture of the unsaturated isomers. The unsaturated endo- isomer was hydrogenated as previously described and then purified by preparative v.p.c.

The v.p.c. retention times and p.m.r. spectra of the hydrogenated endo- and exo-methyl isomers of 7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one were identical to the corresponding endo- and exo-methyl isomers of 7-chloro-7-methylbicyclo(3.2.0)heptan-6-one.

**7-Bromo-7-methylbicyclo(3.2.0)hept-2-en-6-one**

A mixture of endo- and exo-methyl isomers of methylbromo-ketene and cyclopentadiene was prepared according to the procedure reported in the literature (2). This procedure differed from the one previously described for the preparation of
7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one in that the acid halide employed was 2-bromopropanoyl bromide. A v.p.c. and a p.m.r. analysis of the reaction mixture gave identical endo-methyl to exo-methyl isomer distributions of 0.71. The p.m.r. spectral data for the endo- and exo-methyl isomers is summarized in Table II.

It was demonstrated that the isomer distribution did not change during the course of the reaction and that the isomer distributions were heat stable at reflux at simulated distillation conditions.

Hydrogenation of 7-bromo-7-methylbicyclo(3.2.0)hept-2-en-6-one.—The endo- and exo-methyl isomers of 7-bromo-7-methylbicyclo(3.2.0)hept-2-en-6-one were hydrogenated, isolated and characterized in the same manner as the hydrogenated endo- and exo-methyl isomers of 7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one. The hydrogenated endo- and exo-methyl isomers corresponded exactly to the corresponding endo- and exo-methyl isomers obtained from the reaction of methylbromoketene with cyclopentene.

Methylbromoketene cycloaddition with cyclopentadiene.—A hexane solution of methylbromoketene was slowly added to a solution of 30 ml. of cyclopentadiene in 150 ml. of hexane at room temperature. After one hour of efficient stirring, the solution was concentrated by rotoevaporation of the solvent at room temperature. The isomer distribution was determined by v.p.c. and p.m.r. and found to be 0.84 endo- to exo-methyl.
Methylbromoketene was prepared by the dropwise addition of 8.1 g. (0.08 mole) of triethylamine in 25 ml. of hexane to a well stirred solution of 21.6 g. (0.1 mole) of 2-bromopropanoyl bromide in 150 ml. of hexane at -78° C. Upon warming to room temperature with stirring, a yellow color developed in the solution. An aliquot of the solution was placed in a fixed thickness infrared absorption cell. The infrared spectra revealed an asymmetrical bond stretching at 2125 cm.⁻¹ and a symmetric bond stretching at 1120 cm.⁻¹. Stirring was continued at room temperature, and the reaction mixture was periodically monitored by following the characteristic ketene absorptions at 2125 cm.⁻¹ and 1120 cm.⁻¹. When the ketene absorptions reached a maximum, the mixture was cooled in a dry ice-acetone bath, and the amine salt was removed by filtration under a nitrogen atmosphere to yield a hexane solution of methylbromoketene.

7-Chloro-7-methylbicycle(3.2.0)heptan-6-one

A v.p.c. and a p.m.r. analysis of the concentrated reaction mixture indicated two major products with methyl proton resonances at 1.43 p.p.m. and at 1.70 p.p.m. The ratio of these products by the appropriate v.p.c. and p.m.r. area integrations was 4.5. A distillation at reduced pressure gave 15.2 g. of the cycloadducts at 48-58° C. at 1 mm. corresponding to a 48 percent yield of cycloadducts; i.e. (neat), both isomers, 1796 cm.⁻¹ (C =O); p.m.r. (CCl₄), endo-methyl isomer, 1.43 p.p.m. (singlet, 3H) methyl protons, 1.7 p.p.m. (H₂, H₃, H₄ multiplet)
6H protons, 3.03 p.p.m. (H\textsubscript{1} multiplet, 1H), 4.03 p.p.m. (H\textsubscript{5} multiplet, 1H); p.m.r. (CCl\textsubscript{4}), \textit{exo}-methyl isomer, 1.70 p.p.m. (singlet, 3H), 1.7 p.p.m. (H\textsubscript{2}, H\textsubscript{3}, H\textsubscript{4} multiplet, 6H), 2.09 p.p.m. (H\textsubscript{1} multiplet, 1H) and 3.76 p.p.m. (H\textsubscript{5} multiplet, 1H).

Analysis calculated for C\textsubscript{8}H\textsubscript{11}ClO: C, 60.57; H, 6.94. Found: C, 60.30; H, 7.01.

7-Bromo-7-methylicyclo(3.2.0)heptan-6-one

A vacuum distillation yielded 15 g. or 37 per cent of the cycloadduct isomers at 60-80° C. at 1.0 mm.; i.r. (neat), both isomers, 1800 cm\textsuperscript{-1} (C =0); p.m.r. (CCl\textsubscript{4}), \textit{endo}-methyl isomer, 3.98 p.p.m. (H\textsubscript{5} multiplet, 1H), 2.87 p.p.m. (H\textsubscript{1} multiplet, 1H), 1.58 p.p.m. (singlet, 3H), 1.6 p.p.m. (H\textsubscript{2}, H\textsubscript{3}, H\textsubscript{4} multiplet, 6H); p.m.r. (CCl\textsubscript{4}), \textit{exo}-methyl isomer, 3.79 p.p.m. (H\textsubscript{5} multiplet, 1H), 2.83 p.p.m. (H\textsubscript{1} multiplet, 1H), 1.87 p.p.m. (singlet, 3H) and 1.6 p.p.m. (H\textsubscript{2}, H\textsubscript{3}, H\textsubscript{4} multiplet, 6H).

Analysis calculated for C\textsubscript{8}H\textsubscript{11}BrO: C, 47.23; H, 5.42. Found: C, 47.41; H, 5.53.

7-Chloro-7-ethylcyclo(3.2.0)hept-2-en-6-one

The \textit{endo}- and \textit{exo}-ethyl cycloadducts of ethylchloroketene and cyclopentadiene were prepared according to the procedure of Brady and Holifield (2). The \textit{endo}-/\textit{exo}-ethyl isomer distribution was 5:3. Isomer distributions were determined by v.p.c. peak area integrations and were checked with synthetic mixtures of the purified isomers. The purified \textit{endo}- and \textit{exo}-ethyl isomers were obtained by repeated fractional distillation and
preparative v.p.c. Both isomers showed the characteristic carbonyl absorptions at 1800 cm$^{-1}$ and carbon-carbon unsaturation at 1607 cm$^{-1}$. That portion of the p.m.r. spectrum not recorded in Table II for the endo- and exo-ethyl isomers consisted of proton resonances at: 1.8 p.p.m. (multiplet, 2H) for methylene protons of the ethyl groups and 1.1 p.p.m. (multiplet, 3H) for the methyl protons of the ethyl groups. The p.m.r. and i.r. spectra of the endo- and exo-ethyl isomers corresponded respectively to the p.m.r. isomers previously described as low and high boiling isomers (2). The endo- and exo-ethyl isomers were related to the endo- and exo-methyl isomers of 7-chloro-7-methylbicyclo(3.2.0)hept-2-en-6-one by the coincidence of corresponding methinyl proton resonances shown in Table II.

7-Bromo-7-ethylbicyclo(3.2.0)hept-2-en-6-one

The endo- and exo-ethylcycloadducts of ethylbromoketene and cyclopentadiene were prepared according to the procedure of Brady and Holifield (2). The endo- exo-ethyl isomer distribution was 1.6. Isomer distributions were determined by v.p.c. peak area integrations and were checked with synthetic mixtures of the purified isomers. The purified endo- and exo-ethyl isomers were obtained by repeated fractional distillation and preparative v.p.c. Both isomers showed the characteristic carbonyl absorption at 1800 cm$^{-1}$ and carbon-carbon unsaturation at 1607 cm$^{-1}$. That portion of the p.m.r. spectrum not recorded in Table II for the endo- and exo-ethyl isomers cor-
isomers previously described as low and high boiling isomers (2). The endo- and exo-ethyl isomers were related to the endo- and exo-methyl isomers of 7-bromo-7-methylbicyclo(3.2.0)hept-2-en-6-one by the coincidence of corresponding methinyl proton resonances shown in Table II.

7-Chloro-7-(2-propyl)-bicyclo(3.2.0)hept-2-en-6-one

A v.p.c. analysis of the concentrated reaction mixture revealed an endo-/exo-isopropyl isomer distribution of 10. Distillation yielded 26 g. or 71 per cent of crude product at 66-74° C. at 0.2 mm. The isomers were separated by v.p.c. Both isomers showed characteristic carbonyl absorptions in the i.r. at 1600 cm.\(^{-1}\) and carbon-carbon unsaturation at 1607 cm.\(^{-1}\), (C = C); that portion of the p.m.r. spectrum not recorded in Table II showed resonances for the endo-isopropyl isomer at 2.1 p.p.m. (multiplet, 1H), 0.97 p.p.m. (doublet, 3H) and 1.08 p.p.m. (doublet, 3H) and resonances for the exo-isopropyl isomer at 2.0 p.p.m. (multiplet, 1H), 0.95 p.p.m. (doublet, 3H) and 1.10 p.p.m. (doublet, 3H).

Analysis calculated for \(\text{C}_{10}\text{H}_{13}\text{OCl}\): C, 65.0; H, 7.1.
Found: C, 64.75; H, 6.91.

7-Bromo-7-(2-propyl)-bicyclo(3.2.0)hept-2-en-6-one

The v.p.c. analysis of the concentrated reaction mixture revealed an endo-/exo-isopropyl isomer distribution of 2.8. Distillation yielded 37 g. or 78 per cent of crude product at 0.1 mm. The isomers were separated by v.p.c. The isomers
showed the characteristic carbonyl absorptions in the i.r. at 1800 cm\(^{-1}\) and carbon-carbon unsaturation at 1607 cm\(^{-1}\). That portion of the p.m.r. spectrum not recorded in Table II showed resonances for the endo-isopropyl isomer at 1.9 p.p.m. (multiplet, 1H), 1.0 p.p.m. (doublet, 3H) and 1.1 p.p.m. (doublet, 3H) and resonances for the exo-isopropyl isomer at 1.9 p.p.m. (multiplet, 1H), 1.0 p.p.m. (doublet, 3H) and 1.1 p.p.m. (doublet, 3H).

Analysis calculated for C\(_{10}\)H\(_{13}\)OBr: C, 52.24; H, 5.77. Found: C, 52.30; H, 5.67.

7-Bromo-7-(2-methyl-2-propyl)bicyclo(3.2.0)hept-2-en-6-one

Distillation yielded 26 g. or 54 per cent of product at 66-67° C. at 0.4 mm. The i.r. spectra indicated a carbonyl absorption at 1800 cm\(^{-1}\) and a carbon to carbon double bond absorption at 1607 cm\(^{-1}\). That portion of the p.m.r. spectrum not recorded in Table II showed a resonance at 1.12 p.p.m. (singlet, 9H) for the methyl protons of the tertiary butyl groups. Only one isomer, the endo-t-butyl isomer, was obtained as evidenced by the p.m.r. and v.p.c. analysis of the concentrated reaction solution prior to distillation.

Analysis calculated for C\(_{12}\)H\(_{15}\)OBr: C, 54.3; H, 6.17. Found: C, 54.54; H, 6.19.

7-Methyl-7-(propyl)bicyclo(3.2.0)hept-2-en-6-one

The v.p.c. and p.m.r. analysis of the concentrated reaction mixture revealed an endo-/exo-n-propyl isomer distribution of 1.4. Distillation yielded 27 g. or 81 per cent of
product at 95-98°C at 2.5 mm. The i.r. spectra of both isomers showed the characteristic carbonyl absorption at 1800 cm.\(^{-1}\) and a carbon to carbon double bond absorption at 1609 cm.\(^{-1}\). The p.m.r. spectra not recorded in Table II showed resonances of 1.4 p.p.m. (multiplet, 4H) for the methylene protons of the n-propyl group and 1.05 p.p.m. (multiplet, 3H) for the methyl protons of the n-propyl group.

Analysis calculated for C\(_{11}\)H\(_{16}\)O: C, 80.4; H, 9.80.
Found: C, 80.2; H, 10.17.

**8-Chloro-8-methylbicyclo(4.2.0)oct-2-en-7-one**

A 2.5 g. (0.02 mole) portion of 2-chloropropanoyl chloride in 25 ml. of hexane was added dropwise over a one hour period to a solution of 2.3 g. (0.02 mole) of triethylamine, 4.0 g. (0.05 mole) of 1,3-cyclohexadiene and 50 ml. of dry hexane at room temperature. After the addition was complete, the mixture was stirred an additional 3 hours and allowed to stand for 24 hours. After the removal of the amine salt by filtration, the solvent was evaporated. The endo- to exo-methyl isomer distribution was 4:9 as indicated by v.p.c. and p.m.r. The yield of cycloadducts was estimated by v.p.c. to be 50 ± 10 per cent. The isomers were separated by v.p.c.; i.r. (neat), both isomers, 1800 cm.\(^{-1}\) (C = O) and 1607 cm.\(^{-1}\) (C = C); p.m.r. (CCl\(_4\)), endo-methyl isomer, 5.95 p.p.m. (H\(_2\), H\(_3\) multiplet, 2H), 4.23 p.p.m. (H\(_6\) multiplet, 1H), 3.71 p.p.m. (H\(_1\) multiplet, 1H), 2.6 to 1.6 p.p.m. (H\(_4\), H\(_5\) broad multiplet, 4H) and 1.47 p.p.m. (singlet, 3H). The p.m.r. spectrum obtained in CCl\(_4\) for the
exo-methyl isomer revealed a resonance at 1.77 p.p.m. (singlet, 3H). The complete p.m.r. spectrum for the exo-methyl isomer was not obtained.

Analysis calculated for $C_9H_{11}ClO$: C, 63.34; H, 6.45.
Found: C, 63.51; H, 6.53.

8-Bromo-8-methylbicyclo(4.2.0)oct-2-en-7-one

A 3.4 g. (0.02 mole) portion of 2-bromopropanoyl chloride in 25 ml. of hexane was added dropwise over a one hour period to a solution of 2.3 g. (0.02 mole) of triethylamine, 4.0 g. (0.05 mole) of 1,3-cyclohexadiene and 50 ml. of dry hexane at room temperature. After the addition was complete, the mixture was stirred an additional 3 hours and allowed to stand for 24 hours. After the removal of the amine salt by filtration, the solvent was evaporated. The endo- to exo-methyl isomer distribution was 0.53 as indicated by v.p.c. and p.m.r. The yield of cycloadducts was estimated by v.p.c. to be $40 \pm 10$ per cent.

The isomers were separated by v.p.c.; i.r. (neat), both isomers, 1800 cm.$^{-1}$ (C = O) and 1607 cm.$^{-1}$ (C = C); p.m.r. ($CCl_4$), exo-methyl isomer, 5.95 p.p.m. ($H_2$, $H_3$ multiplet, 2H), 4.05 p.p.m. ($H_6$ multiplet, 1H), 3.6 p.p.m. ($H_1$ multiplet, 1H), 2.6 to 1.6 p.p.m. ($H_4$, $H_5$ broad multiplet, 4H) and 1.92 p.p.m. (singlet, 3H) for the methyl protons of the exo-methyl group. The p.m.r. spectrum obtained in $CCl_4$ for the endo-methyl isomer revealed a resonance at 1.59 p.p.m. (singlet, 3H) for the methyl protons of the endo-methyl group. The complete p.m.r. spectrum for the endo-methyl isomer was not obtained.
Analysis calculated for $C_9H_{11}BrO$: C, 50.23; H, 5.12.
Found: C, 50.34; H, 5.25.

8-Chloro-8-methylbicyclo(4.2.0)octan-7-one

The endo-/exo-methyl isomer distribution in the concentrated reaction mixture was 4.5 as indicated by v.p.c. and p.m.r. Distillation yielded 9 g. or 26 per cent of the crude product at 55-67° C. at 1.0 mm. Successive fractionations of the isomer mixture through a 6 in. Vigreaux column yielded a fraction at 57-58° C. at 1.0 mm. that had an endo- to exo-isomer distribution of greater than 10; i.r. (neat), both isomers, 1800 cm.$^{-1}$ (C =O); p.m.r. ($CCl_4$), endo-isomer, 4.1 p.p.m. ($H_6$ multiplet, 1H), 2.8 p.p.m. ($H_1$ multiplet, 1H), 1.8 p.p.m. ($H_2$, $H_3$, $H_4$, $H_5$ broad multiplet, 8H) and 1.45 p.p.m. (singlet, 3H). A singlet at 1.72 p.p.m. was attributed to the exo-methyl isomer. The higher boiling fractions were contaminated by unidentified side reaction products.

Analysis calculated for $C_9H_{13}ClO$: C, 62.60; H, 7.55.
Found: C, 62.37; H, 7.41.

10-Chloro-10-methylbicyclo(6.2.0)decan-9-one

The endo-/exo-methyl isomer distribution in the concentrated reaction mixture was 5.1 as evidenced by v.p.c. and p.m.r. Distillation yielded 6 g. or 15 per cent of crude product at 122-129° C. at 0.5 mm. Careful fractionation through a 6 in. Vigreaux column yielded a fraction at 122-124° C. at 0.5 mm. that had an endo- to exo- isomer ratio of greater than 10; i.r. (neat), both isomers, 1800 cm.$^{-1}$ (C =O); p.m.r.
\[ (\text{CCl}_4), \text{endo isomer}, 3.6 \text{ p.p.m.} (H_6 \text{ multiplet, 1H}), 2.8 \text{ p.p.m.} (H_4 \text{ multiplet, 1H}), 1.7 \text{ to 1.2 p.p.m.} (H_2, H_3, H_5, H_6, H_7 \text{ broad multiplet, 12H}) \text{ and 1.43 p.p.m.} (\text{singlet, 3H}). \] A singlet at 1.72 p.p.m. was attributed to the \textit{exo}-methyl isomer. The higher boiling fractions were contaminated by unidentified side reaction and decomposition products. The product was contaminated by decomposition products and for that reason, a 2,4-dinitrophenylhydrazone derivative was prepared.

Analysis calculated for C_{11}H_{17}N_{4}O_{4}Cl: C, 53.60; H, 5.52; N, 14.72. Found: C, 53.34; H, 5.64; N, 14.51.

**8-Chloro-8-methyl-2-oxabicyclo(4.2.0)octan-7-one**

The \textit{endo-}/\textit{exo}-methyl isomer distribution in the concentrated reaction mixture was 5.0 as indicated by v.p.c. and p.m.r. Distillation yielded 14 g. or 40.1 per cent of crude product at 56-57° C. at 0.8 mm. Successive fractionations of the isomer mixture through a 6 in. Vigreaux column yielded a fraction at 56-57° C. at 0.8 mm. which had an \textit{endo}- to \textit{exo}-methyl isomer distribution of greater than 20, and a fraction at 66-67° C. which had an \textit{endo}- to \textit{exo}-methyl isomer distribution of less than 0.1; i.r. (neat), both isomers, 1800 cm. \(^{-1}\) (C =0); p.m.r., \textit{endo} isomer, 4.28 p.p.m. (H, doublet, 1H), 3.9 p.p.m. (H\textsubscript{6} multiplet, 1H), 3.5 p.p.m. (H\textsubscript{3} multiplet, 2H) for the methylene protons adjacent to ether linkage, 1.6 p.p.m. (H\textsubscript{4}, H\textsubscript{5} multiplet, 4H) and 1.51 p.p.m. (singlet, 3H); p.m.r. \textit{exo}-isomer, 3.98 p.p.m. (H, doublet, 1H), 3.7 p.p.m. (H\textsubscript{6}
8-Bromo-8-methyl-2-oxabicyclo(4.2.0)octan-7-one

The endo-/exo-methyl isomer distribution in the concentrated reaction mixture was 0.6 as indicated by v.p.c. and p.m.r. Distillation yielded 11 g. or 50.2 per cent of crude product at 75-88° C. at 1.0 mm. Successive fractionations of the isomer mixture through a 6 in. Vigreaux column yielded a fraction at 76-77° C. at 1.0 mm. which had an endo- to exo-methyl isomer distribution of greater than 10 and a fraction at 86-88° C. at 10 mm. which had an endo- to exo-methyl isomer distribution of less than 0.2; i.r. (neat), both isomers, 1800 cm.⁻¹ (C = O); p.m.r., endo isomer, 4.35 p.p.m. (H₁ doublet, 1H), 3.9 p.p.m. (H₆ multiplet, 1H), 3.5 p.p.m. (H₃ multiplet, 2H), 1.6 p.p.m. (H₄, H₅ multiplet, 4H) and 1.60 p.p.m. (singlet, 3H); p.m.r., exo-isomer, 4.03 p.p.m. (H₁ doublet, 1H), 3.7 p.p.m. (H₆ multiplet, 1H), 3.5 p.p.m. (H₃ multiplet, 2H), 1.6 p.p.m. (H₄, H₅ multiplet, 4H) and 1.85 p.p.m. (singlet, 3H).

Analysis calculated for C₉H₁₁BrO₂: C, 43.84; H, 5.02. Found: C, 43.71; H, 5.14.

8,8-Dimethyl-2-oxabicyclo(4.2.0)octan-7-one

There was obtained 8 g. or 52 per cent of distilled product at 65-67° C. at 1.8 mm. (literature value, 65-66° C. at
2-Chloro-2-methyl-3-ethoxycyclobutanone

A mixture of cis and trans isomers of 2-chloro-2-methyl-3-ethoxycyclobutanone in a 4:1 ratio was obtained by following the procedure of Brady and Holifield (2). The p.m.r. spectrum of the cis isomer in which the methyl group is cis with respect to the ethoxy group revealed resonances at 4.3 p.p.m. (multiplet, 1H) for the methinyl proton, 3.6 p.p.m. (quartet, 2H) for the methylene protons of the ethoxy group, 3.2 p.p.m. (two doublets, 2H) for the ring methylene protons, 1.58 p.p.m. (singlet, 3H) for the methyl protons of the cis-methyl group on the ring and 1.25 p.p.m. (triplet, 3H) for the methyl protons of the ethoxy group. The p.m.r. spectrum of the trans-methyl isomer revealed a resonance at 1.64 p.p.m. (singlet, 3H) for the methyl protons of the trans-methyl group.

2-Bromo-2-methyl-3-ethoxycyclobutanone

The cis and trans isomer distribution in the concentrated reaction mixture was 0.59 as indicated by v.p.c. and p.m.r. Distillation yielded 16 g. or 38.6 per cent of crude product at 39-45°C at 0.4 mm. Some decomposition occurred upon distillation. An analysis of fractions from successive
distillations indicated that the adducts were unstable to heat. One of the decomposition products was identified as the starting vinyl ether. A rapid vacuum distillation afforded a fraction at 39-40° C. at 0.4 mm. that had a cis to trans isomer ratio of 0.9 as evidenced by v.p.c. and p.m.r. The starting vinyl ether which appeared as a decomposition product in the distilled fraction was removed by rotoevaporation prior to submitting the sample for elemental analysis. The i.r. (neat), both isomers, showed characteristic carbonyl absorptions at 1800 cm\(^{-1}\). The p.m.r. spectrum of a mixture of the cis and trans isomers revealed resonances at: 4.3 p.p.m. (multiplet, 1H) for the methinyl proton, 3.6 p.p.m. (quartet, 2H) for the methylene protons of the ethoxy group, 3.2 p.p.m. (multiplet, 2H) for the ring methylene protons, 1.73 p.p.m. (singlet, 3H) for the methyl protons of the cis isomer, 1.80 p.p.m. (singlet, 3H) for the methyl protons of the trans isomer and 1.25 p.p.m. (triplet, 3H) for the methyl protons of the ethoxy group.

Analysis calculated for C\(_7\)H\(_{11}\)BrO\(_2\): C, 40.51; H, 5.32. Found: C, 40.37; H, 5.34.

P.M.R. Spectra of Ketoketene Cyclopentadiene Adducts

The p.m.r. spectral data not previously described is presented in Table II. P.m.r. spectra were taken in carbon tetrachloride solutions of adducts. The adduct concentrations were about 20 per cent by volume. Chemical shifts are given in p.p.m. with respect to T.M.S.
<table>
<thead>
<tr>
<th>Z</th>
<th>Y</th>
<th>( H_1 )</th>
<th>( H_2 ) and ( H_3 )</th>
<th>( H_4 )</th>
<th>( H_5 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>Cl</td>
<td>4.08</td>
<td>5.9</td>
<td>2.68</td>
<td>4.25</td>
</tr>
<tr>
<td>( CH_3 )(1.28)</td>
<td>( CH_3 )(0.93)</td>
<td>3.15</td>
<td>5.8</td>
<td>2.52</td>
<td>3.95</td>
</tr>
<tr>
<td>( CH_3 )(1.77)</td>
<td>Cl</td>
<td>3.62</td>
<td>5.9</td>
<td>2.65</td>
<td>3.95</td>
</tr>
<tr>
<td>Cl</td>
<td>( CH_3 )(1.47)</td>
<td>3.65</td>
<td>5.9</td>
<td>2.64</td>
<td>4.28</td>
</tr>
<tr>
<td>( CH_3 )(1.91)</td>
<td>Br</td>
<td>3.55</td>
<td>5.8</td>
<td>2.60</td>
<td>4.03</td>
</tr>
<tr>
<td>Br</td>
<td>( CH_3 )(1.58)</td>
<td>3.75</td>
<td>5.8</td>
<td>2.62</td>
<td>4.26</td>
</tr>
<tr>
<td>( C_2H_5 )</td>
<td>Cl</td>
<td>3.60</td>
<td>5.9</td>
<td>2.63</td>
<td>3.94</td>
</tr>
<tr>
<td>Cl</td>
<td>( C_2H_5 )</td>
<td>3.70</td>
<td>5.9</td>
<td>2.62</td>
<td>4.27</td>
</tr>
<tr>
<td>( C_2H_5 )</td>
<td>Br</td>
<td>3.54</td>
<td>5.8</td>
<td>2.60</td>
<td>3.90</td>
</tr>
<tr>
<td>Br</td>
<td>( C_2H_5 )</td>
<td>3.70</td>
<td>5.8</td>
<td>2.60</td>
<td>4.26</td>
</tr>
<tr>
<td>i-C(_3)H(_7)</td>
<td>Cl</td>
<td>3.65</td>
<td>5.9</td>
<td>2.65</td>
<td>3.95</td>
</tr>
<tr>
<td>Cl</td>
<td>i-C(_3)H(_7)</td>
<td>3.64</td>
<td>5.9</td>
<td>2.60</td>
<td>4.20</td>
</tr>
<tr>
<td>i-C(_3)H(_7)</td>
<td>Br</td>
<td>3.66</td>
<td>5.8</td>
<td>2.68</td>
<td>3.97</td>
</tr>
<tr>
<td>Br</td>
<td>i-C(_3)H(_7)</td>
<td>3.76</td>
<td>5.9</td>
<td>2.58</td>
<td>4.27</td>
</tr>
<tr>
<td>Br</td>
<td>t-C(_4)H(_9)</td>
<td>3.90</td>
<td>5.9</td>
<td>2.61</td>
<td>4.39</td>
</tr>
<tr>
<td>( CH_3 )(1.28)</td>
<td>n-C(_3)H(_7)</td>
<td>3.15</td>
<td>5.8</td>
<td>2.50</td>
<td>3.95</td>
</tr>
<tr>
<td>n-C(_3)H(_7)</td>
<td>( CH_3 )(0.95)</td>
<td>3.15</td>
<td>5.8</td>
<td>2.50</td>
<td>3.95</td>
</tr>
</tbody>
</table>
All proton resonances other than methyl proton resonances appeared as multiplets. The centers of multiplets indicated were reproducible ± 0.05 p.p.m.

The p.m.r. spectra of 7,7-dichlorobicyclo(3.2.0)hept-2-en-6-one (6) and 7,7-dimethylbicyclo(3.2.0)hept-2-en-6-one (9) have been previously reported.

Cycloadditions of Methylhaloketenes with Cyclopentene and Cyclopentadiene

Methylchloroketene (MCK) and methylbromoketene (MBK) were generated and reacted in situ with cyclopentene (CP) and cyclopentadiene (CPD) to produce the corresponding cyclobutanones. Table III shows the endo-/exo-methyl isomer distributions obtained.

**TABLE III**

METHYLHALOKETENE CYCLOADDUCT ISOMER DISTRIBUTION WITH CYCLOPENTENE AND CYCLOPENTADIENE IN HEXANE

<table>
<thead>
<tr>
<th>Ketene</th>
<th>Olefin</th>
<th>Temp., °C.</th>
<th>% Yield</th>
<th>Endo-/Exo-Methyl Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCK</td>
<td>CPD</td>
<td>0-5</td>
<td>75</td>
<td>4.3</td>
</tr>
<tr>
<td>MCK</td>
<td>CPD</td>
<td>40</td>
<td>61</td>
<td>4.5</td>
</tr>
<tr>
<td>MCK</td>
<td>CP</td>
<td>0-5</td>
<td>35</td>
<td>4.2</td>
</tr>
<tr>
<td>MCK</td>
<td>CP</td>
<td>40</td>
<td>48</td>
<td>4.2</td>
</tr>
<tr>
<td>MBK</td>
<td>CPD</td>
<td>40b</td>
<td>69</td>
<td>1.3</td>
</tr>
<tr>
<td>MBK</td>
<td>CP</td>
<td>40</td>
<td>37</td>
<td>1.2</td>
</tr>
</tbody>
</table>
All of the isomer distributions reported in Table III were
determined by v.p.c. and further verified by p.m.r.

Cycloadditions of Unsymmetrical Ketoketenes with

Cyclopentadiene in Hexane and Acetonitrile

Unsymmetrical ketoketenes were generated and reacted in situ with cyclopentadiene at 0-5° C. in hexane (H) and aceto-
nitrile (AN) to produce the endo-/exo-alkyl isomer distrib-
utions shown in Table IV.

<table>
<thead>
<tr>
<th>Ketene</th>
<th>Solvent</th>
<th>Yield (%)</th>
<th>Endo-/Exo-Alkyl Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCK</td>
<td>H</td>
<td>75</td>
<td>4.3</td>
</tr>
<tr>
<td>ECK</td>
<td>H</td>
<td>77</td>
<td>5.3</td>
</tr>
<tr>
<td>i-PCK</td>
<td>H</td>
<td>71</td>
<td>10</td>
</tr>
<tr>
<td>MCK</td>
<td>AN</td>
<td>62</td>
<td>0.59</td>
</tr>
<tr>
<td>ECK</td>
<td>AN</td>
<td>77</td>
<td>1.1</td>
</tr>
<tr>
<td>i-PCK</td>
<td>AN</td>
<td>55</td>
<td>1.1</td>
</tr>
<tr>
<td>MBK</td>
<td>H</td>
<td>63</td>
<td>0.71</td>
</tr>
<tr>
<td>EBK</td>
<td>H</td>
<td>70</td>
<td>1.6</td>
</tr>
<tr>
<td>i-PBK</td>
<td>H</td>
<td>78</td>
<td>2.8</td>
</tr>
<tr>
<td>t-BBK</td>
<td>H</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td>MBK</td>
<td>AN</td>
<td>60</td>
<td>0.14</td>
</tr>
<tr>
<td>EBK</td>
<td>AN</td>
<td>54</td>
<td>0.27</td>
</tr>
<tr>
<td>i-PBK</td>
<td>AN</td>
<td>49</td>
<td>0.56</td>
</tr>
<tr>
<td>t-BBK</td>
<td>AN</td>
<td>54</td>
<td>100</td>
</tr>
<tr>
<td>M-n-PK</td>
<td>H</td>
<td>8</td>
<td>1.4</td>
</tr>
<tr>
<td>M-n-PK</td>
<td>AN</td>
<td>81</td>
<td>1.4</td>
</tr>
</tbody>
</table>
Alkylhaloketenes are abbreviated in Table IV as follows: methyl-, ethyl- and isopropylchloroketenes as MCK, ECK and i-PCK respectively; methyl-, ethyl-, isopropyl- and tertiary-butylbromoketenes as MBK, EBK, i-PBK and t-BBK respectively and methyl-n-propylketene, M-n-PK.

Cycloadditions of Methylchloroketene with Cyclopentadiene in Solvents of Different Polarity at 0-5° C.

Methylchloroketene was generated in situ and reacted in situ with cyclopentadiene in solvents of different polarity to produce the corresponding cyclobutanones. Table V shows the endo-/exo-methyl isomer distributions obtained.

**TABLE V**

**CYCLOPENTADIENE-METHYLHALOKETENE ADDUCT ISOMER DISTRIBUTIONS IN VARIOUS SOLVENTS AT 0-5° C.**

<table>
<thead>
<tr>
<th>X</th>
<th>Solvent</th>
<th>Per Cent Yield</th>
<th>Endo-/Exo-Methyl Isomer Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>Hexane</td>
<td>75</td>
<td>4.3</td>
</tr>
<tr>
<td>Cl</td>
<td>Triethylamine</td>
<td>32</td>
<td>2.2</td>
</tr>
<tr>
<td>Cl</td>
<td>Benzene</td>
<td>60</td>
<td>1.9</td>
</tr>
<tr>
<td>Cl</td>
<td>Chloroform</td>
<td>40</td>
<td>1.6</td>
</tr>
<tr>
<td>Cl</td>
<td>Methylene Chloride</td>
<td>52</td>
<td>1.2</td>
</tr>
<tr>
<td>Cl</td>
<td>Acetonitrile</td>
<td>62</td>
<td>0.59</td>
</tr>
<tr>
<td>Br</td>
<td>Hexane</td>
<td>63</td>
<td>0.71</td>
</tr>
<tr>
<td>Br</td>
<td>Triethylamine</td>
<td>53</td>
<td>0.28</td>
</tr>
<tr>
<td>Br</td>
<td>Acetonitrile</td>
<td>60</td>
<td>0.14</td>
</tr>
</tbody>
</table>

In Table V cycloadditions with methylchloroketene are indicated by $X = Cl$, and those with methylbromoketene are indicated by
X = Br. All of the isomer distributions reported in Table V were determined by v.p.c. and further verified by p.m.r.

Cycloadditions of Unsymmetrical Ketoketenes with Cyclopentadiene in Hexane at Different Temperatures

Unsymmetrical ketoketenes were generated and reacted in situ with cyclopentadiene at 0-5° C., 25° C. and 40° C. The effect of temperature on the endo-/exo-alkyl isomer distributions is shown in Table VI.

### TABLE VI

THE EFFECT OF TEMPERATURE ON CYCLOPENTADIENE UNSYMMETRICAL KETOKETENE ADDUCT ISOMER DISTRIBUTIONS IN HEXANE

<table>
<thead>
<tr>
<th>Ketene</th>
<th>Temperature (° C.)</th>
<th>Endo-/Exo-Alkyl Isomer Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCK</td>
<td>0-5</td>
<td>4.3</td>
</tr>
<tr>
<td>MCK</td>
<td>25</td>
<td>4.5</td>
</tr>
<tr>
<td>MCK</td>
<td>40</td>
<td>4.7</td>
</tr>
<tr>
<td>MBK</td>
<td>0-5</td>
<td>0.71</td>
</tr>
<tr>
<td>MBK</td>
<td>25</td>
<td>1.1</td>
</tr>
<tr>
<td>MBK</td>
<td>40</td>
<td>1.4</td>
</tr>
<tr>
<td>EBK</td>
<td>0-5</td>
<td>1.6</td>
</tr>
<tr>
<td>EBK</td>
<td>25</td>
<td>1.7</td>
</tr>
<tr>
<td>EBK</td>
<td>40</td>
<td>1.8</td>
</tr>
<tr>
<td>i-PBK</td>
<td>0-5</td>
<td>2.8</td>
</tr>
<tr>
<td>i-PBK</td>
<td>25</td>
<td>6.7</td>
</tr>
<tr>
<td>i-PBK</td>
<td>40</td>
<td>7.4</td>
</tr>
<tr>
<td>M-n-PK</td>
<td>0-5</td>
<td>1.4</td>
</tr>
<tr>
<td>M-n-PK</td>
<td>40</td>
<td>1.6</td>
</tr>
</tbody>
</table>
P.M.R. Spectral-Structural Correlations for Methylchloroketene-Olefin Adducts

The p.m.r. spectral data employed in distinguishing the cycloadduct isomers produced in the reactions of methylchloroketene with various olefins is shown in Table VII.

**TABLE VII**

P.M.R. SPECTRAL-STRUCTURAL CORRELATIONS FOR METHYLCHLOROKETENE-OLEFIN ADDUCTS

<table>
<thead>
<tr>
<th>Olefin</th>
<th>Z</th>
<th>Y</th>
<th>H_A</th>
<th>H_B</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPD (9)</td>
<td>Me (1.28)</td>
<td>Me (0.93)</td>
<td>3.95</td>
<td>3.15</td>
</tr>
<tr>
<td>CPD (6)</td>
<td>Cl</td>
<td>Cl</td>
<td>4.25</td>
<td>4.08</td>
</tr>
<tr>
<td>CPD (1)</td>
<td>Me (1.77)</td>
<td>Cl</td>
<td>3.95</td>
<td>3.62</td>
</tr>
<tr>
<td>CPD (1)</td>
<td>Cl</td>
<td>Me (1.47)</td>
<td>4.28</td>
<td>3.65</td>
</tr>
<tr>
<td>CP (6)</td>
<td>Cl</td>
<td>Cl</td>
<td>4.08</td>
<td>3.39</td>
</tr>
<tr>
<td>CP</td>
<td>Me (1.70)</td>
<td>Cl</td>
<td>3.76</td>
<td>2.89</td>
</tr>
<tr>
<td>CP</td>
<td>Cl</td>
<td>Me (1.43)</td>
<td>4.03</td>
<td>3.03</td>
</tr>
<tr>
<td>CHD</td>
<td>Me (1.77)</td>
<td>Cl</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CHD</td>
<td>Cl</td>
<td>Me (1.47)</td>
<td>4.23</td>
<td>3.71</td>
</tr>
<tr>
<td>CH</td>
<td>Me (1.72)</td>
<td>Cl</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CH</td>
<td>Cl</td>
<td>Me (1.45)</td>
<td>4.1</td>
<td>2.8</td>
</tr>
<tr>
<td>CO</td>
<td>Me (1.72)</td>
<td>Cl</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>CO</td>
<td>Cl</td>
<td>Me (1.43)</td>
<td>3.6</td>
<td>2.8</td>
</tr>
<tr>
<td>DHP</td>
<td>Me (1.68)</td>
<td>Cl</td>
<td>3.7</td>
<td>3.98</td>
</tr>
<tr>
<td>DHP</td>
<td>Cl</td>
<td>Me (1.51)</td>
<td>3.9</td>
<td>4.28</td>
</tr>
<tr>
<td>EVE (2)</td>
<td>Me (1.64)</td>
<td>Cl</td>
<td>3.6</td>
<td>4.3</td>
</tr>
<tr>
<td>EVE (2)</td>
<td>Cl</td>
<td>Me (1.58)</td>
<td>3.6</td>
<td>4.3</td>
</tr>
<tr>
<td>PPE (7)</td>
<td>Me (1.24)</td>
<td>Me (1.12)</td>
<td>3.4</td>
<td>3.8</td>
</tr>
</tbody>
</table>
The olefins indicated in Table VII are abbreviated as follows: cyclopentadiene, CPD; cyclopentene, CP; 1,3-cyclohexadiene, CHD; cyclohexene, CH; cis-cyclooctene, CO; 2,3-dihydropyran, DHP; ethyl vinyl ether, EVE and cis-1-propenyl propyl ether, PPE. The methyl substituent of methylchloroketene is abbreviated "Me". The p.m.r. data expressed in Table VII is in terms of p.p.m. with respect to T.M.S. (chemical shift = 0.00 p.p.m.).
CHAPTER BIBLIOGRAPHY


CHAPTER III

RESULTS AND DISCUSSION

The unexpected and unexplained observations of Brady and Holifield of a reversal in the endo-/exo-methyl isomer ratios in the in situ reactions of methylchloro- and methylbromo-ketenes with cyclopentadiene (3, 4) prompted a further examination of alkylhaloketene-olefin reactions. The predominance of the endo-methyl isomer VI for the 2-chloropropanoyl chloride-triethylamine-cyclopentadiene system and a predominance of the exo-methyl IX isomer for the 2-bromopropanoyl bromide-triethylamine-cyclopentadiene system were reported (3, 4).

\[
\begin{align*}
\text{VI} & \quad \text{VII} & \quad \text{VIII} & \quad \text{IX} \\
\begin{array}{c}
\text{O} & \text{Cl} & \text{Cl} & \text{O} \\
\text{O} & \text{CH}_3 & \text{CH}_3 & \text{O} \\
\text{Cl} & \text{CH}_3 & \text{Br} & \text{Br} \\
\text{O} & \text{Br} & \text{Br} & \text{O} \\
\end{array}
\end{align*}
\]

The conjecture that a secondary \( \pi^- \)-system interaction between the bromine substituent of methylbromoketene and the residual \( \pi^- \)-system of cyclopentadiene was the cause for the predominance of IX was experimentally tested. Cycloadditions with methylchloro- and methylbromoketenes with cyclopentene were accomplished as illustrated.
The results in Table III, p. 47 show that in both reactions the \textit{endo-} and \textit{exo-}methyl isomers were produced in essentially the same distributions as the \textit{endo-} and \textit{exo-}methyl isomers produced in the corresponding cyclopentadiene-methylhaloketene cycloadditions.

The cyclopentadiene adducts VI-IX were separated by preparative v.p.c. and differentiated by p.m.r. Hydrogenation of VI and VII produced X and XI, respectively, as evidenced by corresponding identical i.r. and p.m.r. spectra and v.p.c. retention times. Isomers XII and XIII were similarly related to the hydrogenated isomers of VII and IX, respectively. Since the dehydrohalogenation of 2-chloro- and 2-bromopropanoyl halides with triethylamine in the presence of cyclopentene produced the same distribution of \textit{endo-}methyl and \textit{exo-}methyl 1,2-cycloadducts as cyclopentadiene, it was concluded that the isomer distributions were not influenced by the residual double bond in cyclopentadiene (7).

The possibility that the observed \textit{endo-}/\textit{exo-}methyl isomer distributions might arise from the reaction of some specie
other than the free ketene with cyclopentadiene was investiga-
gated. Methylbromoketene was generated in hexane by the
dehydrobromination of 2-bromopropanoyl bromide with triethyl-
amine in the absence of cyclopentadiene. The reaction mixture
was filtered under a nitrogen atmosphere to yield a hexane
solution of methylbromoketene which was treated with cyclopen-
tadiene at 0-5°C. The cycloadducts obtained from this system
had an endo-/exo-methyl ratio of 0.84 which corresponded to
the respective in situ reaction ratio of 0.79 at 0-5°C. Since
the reaction of free methylbromoketene with cyclopentadiene in
hexane gave essentially the same endo-/exo-methyl isomer distri-
bution as the in situ dehydrohalogenation, the possibility of
isomer distributions being determined by some species other than
the free ketene was considered unlikely (7).

A major problem encountered in utilizing endo- and exo-
alanyl isomer distributions to elucidate the stereochemistry
and the mechanism of alkylhaloketene-cyclopentadiene reactions
was that of distinguishing between the endo- and exo-7,7-disub-
stituted bicyclo(3.2.0)hept-2-en-6-one isomers. Prior to the
present study, a general method for distinguishing between the
endo- and exo-alkyl isomers produced in alkylhaloketene-cyclo-
pentadiene cycloadditions had not been devised. Although Brady
and Holifield had prepared the cyclopentadiene adducts of
ethylchloro- and ethylbromoketenes, they did not distinguish
between the respective endo- and exo-ethyl isomers. When the
cyclopentadiene adducts of isopropylchloro-, isopropylbromo-
and \textit{t}-butylbromoketenes were prepared, the respective \textit{endo}- and \textit{exo}-alkyl isomers had to be distinguished. Although the isomer distributions produced in these systems were determined by employing v.p.c. peak area ratios and were verified by the v.p.c. analysis of synthetic mixtures, the isomer distributions were of no value if the stereochemical structures were known.

The first general observation made after the series of alkylhaloketene-cyclopentadiene adducts shown in Table IV, p. 48 had been prepared was that the ratio of the lower to higher boiling isomer increased in the series of alkylbromoketene-cyclopentadiene adducts as the steric bulk of the alkyl substituent of the ketene increased from methyl, ethyl to isopropyl. When the alkyl substituent of the alkyl bromoketene was the \textit{t}-butyl group, the product ratio estimated by v.p.c. became $>100$. Since Brady and Holifield had established that the lower boiling isomers produced in the reactions of methylbromo- and methylchloroketenes with cyclopentadiene were the \textit{endo}-methyl isomers (4), it was tentatively assumed that the lower boiling isomer in each adduct pair was the \textit{endo}-alkyl isomer. In order to test this assumption, the individual adducts from each system were separated by the successive fractional distillation of adduct mixtures and by preparative v.p.c. The p.m.r. spectra of each isomer was determined and examined very carefully for the presence of some common spectral feature which would make possible the assignment of stereochemical structures.
An examination of the p.m.r. spectra of the lower boiling isomer of each pair of isomers revealed that the $H_5$ methinyl proton appeared as three doublets centered at 4.3 ± 0.1 p.p.m. as compared to the $H_5$ methinyl proton of the higher boiling isomer which was centered at 3.95 ± 0.05 p.p.m. Thus, as had been initially assumed, the lower boiling isomer in each adduct pair was the endo-alkyl isomer. An inspection of the molecular models of the endo- and exo-alkyl adducts, especially those with large alkyl substituents, reveals that the exo-alkyl isomers are less sterically hindered than the endo-alkyl isomers. Since a more sterically hindered isomer of an isomer pair is often observed to have a lower boiling point than the less sterically hindered isomer, the above assumption seemed to be a reasonable empirical relationship.

The assignment of group configuration about carbon-7 was established by relating the structures of low boiling and high boiling alkyl isomers of unknown configuration about carbon-7 to structurally similar endo- and exo-7,7-disubstituted bicyclo (3.2.0)hept-2-en-6-ones of known configuration about carbon-7. An examination of the p.m.r. data in Table II, p. 46 reveals a characteristic difference in the chemical shift of $H_5$ in endo- and exo-alkyl cycloadducts. When the halogen substituent is endo, the center of the $H_5$ absorption varies from 3.9 to 4.0 p.p.m., and when the halogen substituent is exo, the center of the $H_5$ absorption varies from 4.2 to 4.4 p.p.m. The $H_5$ methinyl proton resonance appears as three doublets due to the coupling of $H_5$ with $H_1$ and the methylene protons on carbon-4. The
difference in the chemical shift of $H_5$ in the endo- and exo-alkyl isomers results from cross ring deshielding of $H_5$ by the exo-halogen substituent. This was established by a comparison of the spectra of the cyclopentadiene adduct of dichloroketene with that of dimethylketene. When the halogen is exo as in the dichloroketene adduct, the chemical shift of $H_5$ is 4.25 p.p.m., whereas for an exo-methyl as in the dimethylketene adduct, the chemical shift of $H_5$ is 3.95 p.p.m.

Prior to the present study, the chemical shift of $H_5$ in the endo- and exo-methyl isomers derived from methylchloro- and methylbromoketenes with cyclopentadiene had not been recognized. The structures of the methylhaloketene-cyclopentadiene adducts were established previously by observing the shift in the endo-methyl resonance upon bromination and hydrogenation of the carbon-carbon double bond in the cycloadduct (7). Other structural correlations appear when the p.m.r. spectra of other ketoketene-cyclopentadiene adducts in Table II, p. 46 are examined. For example, endo-methyl groups are more shielded than exo-methyl groups, and $H_1$ is more deshielded by exo-halogen substituents than by endo-halogen substituents. From these structural correlations with the chemical shift of $H_5$, the structures of other alkylhaloketene-cyclopentadiene adduct isomers were distinguished by determining the chemical shift of $H_5$. Cycloadducts produced by the reaction of a ketoketene which has a methyl substituent are distinguished by determining the chemical shifts of the endo- and exo-methyl groups.
An application of the p.m.r. spectral-structural correlations was made in determining the endo or cis and exo or trans isomers of methylchloro- and methylbromoketenes with several olefins other than cyclopentadiene. The endo or cis methyl isomers were distinguished from the exo or trans methyl isomers on the basis of the position of the chemical shifts of the methyl proton resonances and the resonances of the protons indicated as $H_A$ and $H_B$ in Table VII, p. 51. The relevant portions of the p.m.r. spectra of several related dimethyl- and dichloroketene-olefin cycloadducts as well as literature references are included in Table VII.

The suggestion of Brady and Holifield that a two-step dipolar reaction mechanism as previously described on p. 13 might be responsible for the endo-/exo-methyl isomer distributions observed in the reactions of methylchloro- and methylbromoketenes with cyclopentadiene (4) was tested indirectly by employing endo-/exo-alkyl isomer distributions. The endo-/exo-alkyl isomer distributions obtained in the reactions of a variety of alkylhaloketenes with cyclopentadiene were analyzed. The reactions of cyclopentadiene with alkylhaloketenes in which the alkyl substituents of the ketenes were systematically varied in size from methyl to t-butyl were studied in solvents of different polarity and at several reaction temperatures.

Table IV, p. 48 shows that as the alkyl portion of the alkylhaloketene was systematically varied from methyl, ethyl, isopropyl to t-butyl, the endo-/exo-alkyl isomer distribution
increased. As the steric bulk of the alkyl group was increased, the amount of the isomer having the larger substituent in the \textit{endo} position increased. If a two-step mechanism as suggested by Brady and Holifield (4) were responsible for determining the \textit{endo}/\textit{exo}-alkyl isomer distribution, a decrease in the \textit{endo}/\textit{exo}-alkyl isomer distribution would have been expected as the steric bulk of the alkyl substituent was increased. In a two-step mechanism in which the second or ring closing step determined the stereoisomers formed, the amount of isomer having the larger group in the \textit{exo} position would have been expected since larger groups would experience more steric hinderance than smaller groups.

An inspection of Fisher-Hirschfelder-Taylor atom models leads to the prediction that the isomer having the larger group in the \textit{exo} position would be more thermodynamically stable than the isomer in which the larger group is in the \textit{endo} position. If a concerted process were operative in which the ketene and olefin approached one another with respect to their carbon to carbon double bonds, a decrease in the \textit{endo}/\textit{exo}-alkyl isomer would be expected as the steric bulk of the alkyl substituent was increased. Thus, it was concluded that alkylhaloketene-cyclopentadiene cycloadditions were not determined by a two-step process in which the second step was rate determining and that a concerted process involving a parallel orientation of ketene and olefin in the transition state was inconsistent with observed stereoisomer ratios.
The possibility of a dipolar two-step mechanistic or competing mechanistic pathway was further tested by determining the stereoisomer product ratios produced in the cycloadditions of alkylhaloketenes with cyclopentadiene in solvents of different polarity. If a distinct dipolar intermediate were formed in the first step of the reaction, some freedom of rotation of groups within the dipolar intermediate might be possible as illustrated.

In polar solvents the lifetimes of the dipolar intermediates would be expected to be longer than in non-polar solvents. The stereochemical consequence that would be predicted for a relatively long lived alkylhaloketene-cyclopentadiene dipolar intermediate in a polar media would be a decrease in the endo-/exo-alkyl isomer distribution as the steric bulk of the alkyl substituent increased.

When endo-/exo-alkyl isomer distributions for alkylhaloketene-cyclopentadiene cycloadducts were determined in solvents of different polarity, a stereoselective response to solvent polarity was observed as shown in Table IV, p. 48 and in Table V, p. 49. The effect of solvent polarity is dramatically illustrated by the endo-/exo-alkyl isomer distributions produced in hexane and acetonitrile. For example, the endo-/exo-methyl isomer distribution produced in the reaction of
methylchloroketene with cyclopentadiene in hexane at 0-5°C. is 4.3, whereas in acetonitrile, the distribution is 0.59; the endo-/exo-methyl isomer distribution produced in the reaction of methylbromoketene with cyclopentadiene in hexane at 0-5°C. is 0.71, whereas in acetonitrile, the distribution is 0.14. With the exception of the t-butylbromoketene-cyclopentadiene reaction which was observed to be stereospecific, corresponding endo-/exo-alkyl isomer distributions were lower in acetonitrile than in hexane.

An examination of the data in Table IV, p. 48 reveals that endo-/exo-alkyl isomer distributions increase with an increase in the steric bulk of the alkyl substituent of the alkylhaloketene. This trend exists in the isomer ratios in the polar solvent, acetonitrile, as well as in the non-polar solvent, hexane. For example, the endo-/exo-alkyl isomer distributions in the alkylbromoketene-cyclopentadiene adduct series in acetonitrile increase as the steric bulk of the alkyl group increases. The endo-/exo-alkyl isomer distributions show just the opposite response to solvent polarity to what would have been expected if a two-step dipolar mechanism as proposed by Brady and Holifield were operative.

The observation that the endo-/exo-n-propyl isomer distributions produced from cyclopentadiene and methyl-n-propylketene shown in Table IV, p. 48 were not affected by a change in solvent from hexane to acetonitrile was taken as evidence against a distinctly different mechanism being operative in solvents of different polarity (6). The endo-/exo-n-propyl isomer
distribution of 1.4 was interpreted to mean that the reaction was kinetically, rather than thermodynamically, controlled since a greater amount of the more sterically hindered isomer was produced.

The solvent dependency of the endo-/exo-alkylhaloketene isomer distributions was interpreted to mean that the unsymmetrical alkylhaloketene were forming non-equivalent transition states which were unequally solvated. Non-equivalent alkylhaloketene-cyclopentadiene transition states would be expected a priori to differ in their dipole moments and in their geometries and, thus, interact differently with the solvent. The unequal solvation was assumed to be due primarily to the halogen substituent of the alkylhaloketene.

A similar effect of solvent on the ratio of endo and exo product ratios produced in the (2 + 4) Diels-Alder reactions of cyclopentadiene with several dienophiles was reported by Berson, Hamlet and Mueller (1). The ratios of the endo(N) to exo(X) Diels-Alder adducts were interpreted as being equivalent to the ratios of reaction rate constants, $k_N/k_X$, of the competing concerted reactions. The logarithms of the rate constants, log $k_N/k_X$, was assumed to be linearly related to the free energy difference between the transition states which gave rise to the endo- and exo-adducts. The effect of solvent on the endo-/exo-Diels-Alder adduct ratios was interpreted by Berson and co-workers to mean that the transition states which gave rise to the endo and exo adducts were non-equivalent and were
solvated differently. The observation was made that the logarithm of the \textit{endo-}/\textit{exo-} adduct isomer distribution showed a monotonic response to solvent polarity (1).

The interpretation of Berson and co-workers that the ratio of \textit{endo-}/\textit{exo-} Diels-Alder adducts could be interpreted to represent the ratio of the rate constants of competing concerted reactions can be employed in an explanation of the effect of solvent on the \textit{endo-}/\textit{exo-} alkyl isomer distribution produced in alkylhaloketene-cyclopentadiene reactions. In Table V, p. 49 the \textit{endo-}/\textit{exo-} methyl isomer distributions produced in the reaction of methylchloroketene with cyclopentadiene in solvents of different polarity is shown. In Table VIII \textit{endo-}/\textit{exo-} methyl isomer distributions and $E^s(30)$ solvent polarity values (9) are shown.

\begin{table} [H]
\centering
\begin{tabular}{|l|c|c|}
\hline
Solvent & Solvent Polarity $E^s(30)$ Values & $\text{Endo}(N)/\text{Exo}(X)$ \\
\hline
Hexane & 30.9 & 4.3 \\
Benzene & 34.5 & 1.9 \\
Chloroform & 40.0 & 1.6 \\
Methylene chloride & 41.1 & 1.2 \\
Acetonitrile & 46.0 & 0.59 \\
\hline
\end{tabular}
\caption{METHYLCHLOROKETENE-CYCLOPENTADIENE ADDUCT ISOMER DISTRIBUTIONS IN SOLVENTS OF DIFFERENT POLARITY AT 0-5° C.}
\end{table}
A plot of the logarithms of the \textit{endo}(N)-/\textit{exo}(X)-methyl isomer distributions vs. \(E_T^\prime(30)\) solvent polarity values indicates a linear monotonic decrease in the \textit{endo}(N)-/\textit{exo}(X)-methyl isomer distribution with increasing solvent polarity. This is interpreted to mean that the free energy difference between the transition states giving rise to the \textit{endo}- and \textit{exo}-methyl isomers is dependent upon solvent polarity. In hexane the \textit{endo}-methyl transition state is favored, whereas in acetonitrile, the \textit{exo}-methyl transition state is favored. The change in the \textit{endo}/\textit{exo}-methyl isomer distribution with a change in solvent from hexane to acetonitrile must then be attributed to the difference in the free energy solvation of the \textit{endo}- and \textit{exo}-methyl transition states.

The free energy of solvation difference, \(\Delta \Delta G_s\), between the \textit{endo}(N)- and \textit{exo}(X)-methyl transition states may be estimated by application of the linear free energy relationship,
\[
\log \frac{N}{X} = \frac{(\Delta G^+_X - \Delta G^+_N)}{2.303RT},
\]
where \(\Delta G^+_X\) and \(\Delta G^+_N\) are the free energies of activation of the transition states leading to the \textit{endo}(N)- and \textit{exo}(X)-methyl isomers; \(R\) is the universal gas constant; \(T\) is the absolute temperature and 2.303 is a constant associated with the conversion of natural logarithms to common logarithms.

In hexane the \textit{endo}/\textit{exo}-methyl ratio if 4.3 at 0-5\(^\circ\) C. which corresponds to a difference in transition state free energies of about 0.8 kcal/mole; in acetonitrile the \textit{endo}-/\textit{exo}-methyl isomer distribution is 0.59 which corresponds to
a difference in transition state free energies of -0.3 kcal/mole. The free energy of solvation difference between the transition states which give rise to the endo- and exo-methyl isomers must then be approximately 1.1 kcal/mole. Since the corresponding endo- and exo-alkyl transition states of other alkylhaloketenes with cyclopentadiene are structurally similar to the methylchloroketene-cyclopentadiene adducts, approximately the same free energy of solvation differences between the transition states giving rise to endo- and exo-alkyl isomers would be expected in changing from hexane to acetonitrile. Table IX shows the results of the calculation of the differences in free energies of solvation, $\Delta \Delta G_s$, of the endo- and exo-alkyl transition states between hexane and acetonitrile at 0-5°C.

**TABLE IX**

**DIFFERENCES IN THE FREE ENERGIES OF SOLVATION BETWEEN END0- AND EXO-ALKYL TRANSITION STATES**

<table>
<thead>
<tr>
<th>R</th>
<th>X</th>
<th>N/X (Hexane)</th>
<th>N/X (Acetonitrile)</th>
<th>$\Delta \Delta G_s$ (kcal/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃</td>
<td>Cl</td>
<td>4.3</td>
<td>0.59</td>
<td>1.1</td>
</tr>
<tr>
<td>C₂H₅</td>
<td>Cl</td>
<td>5.3</td>
<td>1.1</td>
<td>0.96</td>
</tr>
<tr>
<td>i-C₃H₇</td>
<td>Cl</td>
<td>10</td>
<td>1.1</td>
<td>1.3</td>
</tr>
<tr>
<td>CH₃</td>
<td>Br</td>
<td>0.71</td>
<td>0.14</td>
<td>0.89</td>
</tr>
<tr>
<td>C₂H₅</td>
<td>Br</td>
<td>1.6</td>
<td>0.27</td>
<td>0.96</td>
</tr>
<tr>
<td>i-C₃H₇</td>
<td>Br</td>
<td>2.8</td>
<td>0.56</td>
<td>0.87</td>
</tr>
<tr>
<td>i-C₄H₉</td>
<td>Br</td>
<td>&gt;100</td>
<td>&gt;100</td>
<td>---</td>
</tr>
</tbody>
</table>
Since the difference in the free energy of solvation between hexane and acetonitrile for the endo- and exo-alkyl transition states are essentially the same, it was concluded that a change in mechanism with a change in solvent was unlikely and that the transition states leading to endo- and exo-alkyl isomers were probably not solvated differently in hexane.

Since the linear free energy relationship between the logarithms of the ratios of the endo- to exo-alkyl isomer products and the free energy differences between transition states led to an adequate explanation of the effect of solvent upon isomer distributions, additional applications of this relationship were sought. A more detailed examination of the free energy relationship on p. 67 shows that the free energy of activation difference term, $\Delta A_G^\ddagger$, is made up of an enthalpy of activation difference term, $\Delta A_H^\ddagger$, and an entropy of activation difference term, $\Delta A_S^\ddagger$. By incorporating the $\Delta A_H^\ddagger$ and $\Delta A_S^\ddagger$ terms which are related by $\Delta A_S^\ddagger = \Delta A_H^\ddagger - T \Delta A_S^\ddagger$ into the expression on p. 67, the linear relationship,

$$\log \frac{N}{X} = \frac{\Delta A_H^\ddagger}{2.303RT} + \frac{\Delta A_S^\ddagger}{2.303R}$$

is obtained. Assuming that the difference in the entropies of activation between the endo(N) and exo(X) transition states determined the product ratios, the linear free energy expression reduces to

$$\log \frac{N}{X} = \frac{\Delta A_S^\ddagger}{2.303R}$$. A similar expression, $\log \frac{k}{k_o} = \delta E_S$, has been employed by Taft (17) in evaluating the steric effects in a series of sterically controlled reactions. In this expression, $k_o$ is the rate constant of a reference reaction, $k$ is the rate constant of a similar reaction in which a
substituent change has been made in the vicinity of the reaction center, $S$ is a reaction constant related to the steric requirements of substituents and $E_s$ is a steric factor which is a measure of the total steric effect associated with a given substituent relative to a standard of comparison.

Assuming that the polar and resonance effects in hexane are nearly constant in the transition states leading to endo- and exo-alkyl isomers, the logarithms of ratios of endo(N)- to exo(X)-alkyl isomer products would be expected to be linearly related to the steric factors proposed by Taft,

$$\log N/X = ES.$$  That this relationship is qualitatively applicable to an explanation of the endo-/exo-alkyl isomer distributions is revealed in Table X by the linear relationship between the logarithms of the endo-/exo-alkyl isomer distributions obtained from reactions of the alkylbromoketenes with cyclopentadiene at 25°C in hexane vs. the Taft steric factors for methyl, ethyl, isopropyl and t-butyl groups. The Taft steric factors listed in Table X were derived from acid catalyzed ester hydrolyses at 25°C in which the alkyl groups were adjacent to the reaction site. The reference substituent in the series below may be taken as the methyl or bromo group since both groups have $E_s$ values of 0.00 (17). A plot of the logarithms of the endo-/exo-alkyl ratios vs. the steric factors for the methyl, ethyl and isopropyl groups yields a linear relationship of the form $\log N/X = -1.5 E_s + 0.1$. Although this relationship is based on an insufficient number of
experimental points, it is, nevertheless, a useful semiquanti-
tative expression. On the basis of this relationship, the
endoe-endo-t-butyl isomer distribution would be expected to be
approximately 300.

**TABLE X**

<table>
<thead>
<tr>
<th>Alkylbromoketene</th>
<th>Endo-/Exo- Isomer Distribution</th>
<th>Steric Factors (E_s) for Alkyl Substituent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylbromoketene</td>
<td>1.2</td>
<td>0.00</td>
</tr>
<tr>
<td>Ethylbromoketene</td>
<td>1.7</td>
<td>-0.07</td>
</tr>
<tr>
<td>Isopropylbromoketene</td>
<td>6.7</td>
<td>-0.47</td>
</tr>
<tr>
<td>t-Butylbromoketene</td>
<td>100</td>
<td>-1.54</td>
</tr>
</tbody>
</table>

The observation that the endo-/exo-alkyl isomer distribu-
tions increase with temperature may be explained in a qual-
itative way through a consideration of the factors involved in
a determination of the steric substituent constants. According
to Taft, "Steric substituent constants, E_s, are determined by
both potential energy (strain) and by kinetic energy (hinder-
ances to motions) steric effects." (18) Since these quan-
tities are dependent upon the structure of substituents as well
as temperature, it is not surprising that reactions may be both
sterically controlled and temperature dependent. Since the
temperature dependent steric effects would probably be more
pronounced for an isopropyl group than for less complex alkyl
groups, an increase in endo-/exo-isopropyl isomer distribution might be expected.

The usefulness of the modified Taft expression, \( \log \frac{N}{X} \approx \delta \epsilon_s \), is further demonstrated in Table XI by a comparison of the endo/exo isomer distributions reported in the reactions of several unsymmetrical ketenes with cyclopentadiene with those estimated by use of the above relationship. In making estimations of other endo/exo isomer distributions, the \( \delta \) value, -1.5, obtained for the alkylbromoketene-cyclopentadiene series and the differences in \( \epsilon_s \) values between smaller and larger ketene substituents are employed (18).

**TABLE XI**

**COMPARISON OF REPORTED AND ESTIMATED ENDO/EXO ISOMER DISTRIBUTIONS**

<table>
<thead>
<tr>
<th>Larger Substituent ((L))</th>
<th>Smaller Substituent ((S))</th>
<th>Endo/Exo ((\text{Estimated}))</th>
<th>Endo/Exo ((\text{Reported}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \text{CH}_3 )</td>
<td>( \text{H} )</td>
<td>76</td>
<td>&gt;100 (2)</td>
</tr>
<tr>
<td>( \text{Cl} )</td>
<td>( \text{H} )</td>
<td>41</td>
<td>&gt;100 (2)</td>
</tr>
<tr>
<td>( \text{CH}_3 )</td>
<td>( \text{Cl} )</td>
<td>1.9</td>
<td>4.5 (7)</td>
</tr>
<tr>
<td>( \text{C}_2\text{H}_5 )</td>
<td>( \text{Cl} )</td>
<td>2.4</td>
<td>5.3 (6)</td>
</tr>
<tr>
<td>( \text{i-C}_3\text{H}_7 )</td>
<td>( \text{Cl} )</td>
<td>9.5</td>
<td>10 (6)</td>
</tr>
<tr>
<td>( \text{n-C}_3\text{H}_7 )</td>
<td>( \text{CH}_3 )</td>
<td>4.4</td>
<td>1.6 (6)</td>
</tr>
</tbody>
</table>
The estimates of endo/exo isomer distributions were made by taking differences in $E_s$ values between larger and smaller groups. The $E_s$ values employed were H, 1.24; C, 0.18; CH$_3$, 0.00; C$_2$H$_5$, 0.07; n-C$_3$H$_7$, -0.36 and i-C$_3$H$_7$, -0.47 (17).

An equivalent approach in estimating endo and exo product ratios was made on the basis of assumed entropy of activation differences between the transition states leading to endo and exo isomers. The endo(N) to exo(X) ratios were calculated on the basis of the free energy relationship, log $N/X = \Delta S^\ddagger / 2.303R$. This method was applied in calculating the expected endo-/exo-methyl isomer distribution for the methylketene-cyclopentadiene system and the expected endo-/exo-chloro isomer distribution for the chloroketene-cyclopentadiene system.

In these calculations, the assumption was made that the entropy of the ketene substituent closest to the reaction center was essentially frozen out (13). A similar assumption was made by Hammett and co-workers in explaining the effect of a substituent in the vicinity of the reaction center in a series of sterically controlled aldehyde and ketone reactions (13). The calculation of product ratios was simplified by the availability of the entropy values of substituents (16). In calculating the $N/X$ ratio, the entropy difference between the hydrogen and methyl substituents, 7.7 entropy units (16), was employed. Similarly, the difference in the entropies of the hydrogen and chloro substituents, 7.0 entropy units (16), was employed in calculating the $N/X$ ratios for the stereoisomer
products of chloroketene and cyclopentadiene. Previously, these reactions were reported to produce, within the limits of detection, only the endo cycloadducts in which the larger group was in the endo position (2). The ratios of endo to exo isomer, estimated on the basis of assumed entropy of activation differences between transition states, are 47.6 for the methylketene-cyclopentadiene adducts and 33.2 for the chloroketene-cyclopentadiene adducts. Recently, Dreiding and co-workers estimated the endo-/exo-methyl and chloro- isomer distributions produced in these reactions to be 49 and 32 respectively (10). Thus, it would appear that the product ratios produced in the reactions of unsymmetrical ketenes are highly dependent upon differences in entropies of activation.

The justification for employing entropies of activation to account for the production of product mixtures in sterically controlled reactions is formed in the relationship between entropy and probability (11). Since the entropy of activation of a reaction is related to the probability of molecular collisions having suitable orientations for forming a transition state, the Boltzman-Planck equation, \( S = 2.303R \log P \), which expresses a relationship between entropy, \( S \), and probability, \( P \), can be employed in expressing a relationship between the differences in entropy of activation between two transition states. If the probability of an unsymmetrical ketene and cyclopentadiene forming an endo(N) transition state is \( N \), and the probability of forming an exo(X) transition state is \( X \), it follows that
$$\log \frac{N}{X} = \frac{\left( \Delta^{\circ}_{N} - \Delta^{\circ}_{X} \right)}{2.303R}.$$ When there is a nullification or a cancellation of non-entropy factors, differences in the entropies of activation between the endo(N) and exo(X) transition states may be employed to qualitatively estimate N/X product ratios of kinetically controlled reactions.

Further evidence that endo-/exo-alkyl isomer distributions produced in the reactions of alkylhaloketenes with cyclopentadiene in hexane are sterically controlled is based on the results obtained in the reactions of alkylhaloketenes with other olefins. It was observed that endo-/exo-alkyl isomer distributions in the range of 4 to 6 are obtained in the reactions of methylchloroketene in hexane with cyclopentadiene, cyclopentene, cyclohexadiene, cyclohexene, cyclooctene, 2,3-dihydropyran and ethyl vinyl ether. The endo-/exo-alkyl isomer distributions produced in the reactions of methylbromoketene in hexane with cyclopentadiene, cyclopentene, cyclohexadiene, 2,3-dihydropyran and ethyl vinyl ether were observed to be in the range of 0.7 to 1.0. Since these olefins are structurally similar but differ greatly in their reactivities (15), it would seem that steric effects associated with entropy of activation differences in the transition states are of greater importance in determining the product ratios than are the differences in enthalpies of activation.

An additional indication that ketene-olefin reactions are sterically controlled due to entropy effects is contained in the activation parameters obtained in kinetic studies of the
reaction of diphenylketene with 2,3-dihydropyran (5). In this reaction, the enthalpy of activation was reported to be $9.1 \pm 0.1$ kcal/mole, and the entropy of activation was $43.5 \pm 2$ entropy units. An inspection of the rate expression, 

$$K = Qe^{-\Delta H^*/RT} + e^{\Delta S^*/R},$$

where $Q$ is a frequency factor, reveals that the exponential term containing the entropy of activation is smaller by approximately three powers of ten than the term containing the enthalpy of activation. If these exponential terms are interpreted to represent probabilities of collisions having sufficient energy and geometrical orientation (8) respectively, it is apparent that the probability of collisions having the proper orientation or entropy of activation is much less than the probability of collisions being of sufficient energy to produce a transition state. Hence, the rate of the reaction between diphenylketene and 2,3-dihydropyran would be expected to be sterically controlled.

The dependency of the endo-/exo-alkyl isomer distributions upon the nature of the substituents of the alkylhaloketene, is most easily understood by employing the ketene-olefin transition state model recently proposed by Woodward and Hoffmann (19). On the basis of this model and the principle of orbital symmetry conservation, ketene-olefin cycloadditions are concerted symmetry allowed processes at ordinary temperatures. The required transition state for concerted ketene-olefin reactions involves an orthogonal orientation of ketene and olefin as illustrated on p. 77.
As the ketene-olefin transition state is transformed into a cyclobutanone, maximum orbital overlap is maintained, and orbital symmetry is conserved as the reaction occurs by a relatively low energy path.

Concerted ketene-olefin reactions involving an orthogonal transition state require that the olefin plays a suprafacial role in which bonds made and broken lie on the same side of the reacting carbon-carbon double bonds as illustrated (19).

\[
\begin{array}{c}
\text{a suprafacial process}
\end{array}
\]

Cis-stereospecific addition of the ketene to the olefin is the consequence of an olefin acting in a suprafacial role. The ketene, in contrast to the olefin, plays an antarafacial role in which bonds made and broken lie on the opposite sides of the reacting carbon-carbon double bond as illustrated.

\[
\begin{array}{c}
\text{an antarafacial process}
\end{array}
\]

In order for the ketene to act in an antarafacial way, the carbon-carbon double bond is broken, and rotation occurs about the carbon to carbon double bond system of the ketene (19).
An application of the Woodward-Hoffmann model to alkyl-haloketene-cyclopentadiene cycloadditions leads to the prediction of four possible orthogonal transition states.

From an examination of molecular models as illustrated above with the ketene arbitrarily drawn in a position above the olefin, it is apparent that orientations (XIV) and (XV) are sterically preferred. As the size of the alkyl substituent increases, it would seem that geometry (XIV) would be preferred over (XV) because of steric interactions of the alkyl group with the olefin when the alkyl group is nearest to the olefin in (XV). In (XIV) the smaller substituent is toward the olefin, and the larger alkyl substituent is away from the olefin. Completion of the cycloaddition process in (XIV) leads to the alkyl group being endo. In (XV) the alkyl group becomes exo (14).
Transition state (XVII) which is sterically favored over (XVI) can not be responsible for determining the observed isomer distribution since a concerted process would lead to an increase in production of the exo-alkyl isomer as the steric bulk of the alkyl group increased. Thus, the observed increase in endo-/exo-alkyl isomer distributions when the alkyl substituent is increased may be interpreted as a stereochemical consequence of symmetry allowed concerted alkylketene-olefin cycloadditions.

The unexpected and previously unexplained isomer distributions observed by Brady and Holifield in the reactions of methylhaloketenes with cyclopentadiene have now been explained both in terms of a consequence of competing kinetically controlled reactions and in terms of the principle of the conservation of orbital symmetry.

Although the previously unexpected and unexplained isomer distributions observed by Brady and Holifield in the reactions of methylhaloketenes with cyclopentadiene have now been explained, and the stereochemistry and mechanism of
alkylhaloketene-cyclopentadiene cycloadditions have been elaborated by the application of isomer distributions, the larger significance of this work has not yet been mentioned. The significance of this work is that the orthogonal ketene-olefin transition state model recently proposed by Woodward and Hoffmann has been critically tested. Prior to this study, the predictions based on the orthogonal ketene-olefin transition state model had not been tested with unsymmetrical ketenes which yield detectable mixtures of isomer products. The interpretation of endo-/exo-alkyl isomer distributions as being equivalent to the ratios of rate constants of competing concerted reactions has led to the visualization of transition states which differ primarily in their activation parameters. Since orthogonal ketene-olefin transition states required for concerted ketene-olefin reactions meet the requirements for the observed isomer ratios which are consistent with concerted processes, ketene-olefin reactions are best interpreted as concerted processes. Thus, the two theoretical approaches merge and are consistent with one another. The concerted nature of ketene-olefin reactions is further verified.
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