THE STEREOCHEMISTRY OF THE CYCLOADDITION
OF UNSYMMETRICAL PHENYL KETENES
TO CYCLOPENTADIENE:

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THE STEREOCHEMISTRY OF THE CYCLOADDITION
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TO CYCLOPENTADIENE

DISSERTATION

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By

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CHAPTER I

INTRODUCTION

Ketenes have been known since the beginning of the century, but recently have received renewed attention in the literature. Staudinger first noted the preparation (44) and cycloaddition (45) of ketenes before 1910. For general purposes, ketenes are classified as either aldoketenes or ketoketenes depending on the nature of the substitution. The simplest member of the family, ketene itself, is illustrated below. The aldoketenes as a class arise from the substitution of any group for one and only one of the hydrogen atoms. If both of the hydrogens are replaced, the result is a ketoketene. Aldoketenes as a group are much less stable and therefore have been much less studied than ketoketenes. In addition, ketenes are frequently classified as symmetrical or unsymmetrical, or as halo or non-halo depending on the desired context. Most of the work in the literature has been with the non-halo-, symmetrical ketoketenes, such as dimethylketene or diphenylketene.

Ketenes are prepared by a variety of different methods, the most notable being pyrolysis of certain compounds,
dehalogenation of an α-haloacid halide and dehydrohalogena-
tion of appropriately substituted acid halides. Pyrolysis
of a variety of compounds leads to the formation of specific
ketenes (29, 31, 46, 52). The pyrolysis method is usually

\[
\begin{align*}
\text{CH}_3\text{C}_2\text{H}_5\text{C}_2\text{H}_5 & \xrightarrow{\Delta} \text{CH}_3=\text{C}=0 + \text{CO}_2 \\
\text{CH}_3\text{CH}_2\text{C}_2\text{H}_5 & \xrightarrow{\Delta} \text{CH}_3=\text{C}=0 + \text{CH}_3\text{CH}_2\text{C}_2\text{H}_5
\end{align*}
\]

restricted to relatively stable, low molecular weight ketenes.

The dehalogenation of α-haloacid halides has been known
since 1905 when diphenylchloroacetyl chloride was dechlo-
nated with zinc by Staudinger to give diphenylketene (44).

\[
\text{C}_6\text{H}_5\text{C}_2\text{H}_5\text{Cl} + \text{Zn} \xrightarrow{\Delta} \text{C}_6\text{H}_5=\text{C}=0 + \text{ZnCl}_2
\]

Perhaps the most common method for the generation of a
ketene is the dehydrohalogenation of an acid halide with a
tertiary amine. Some sporadic mechanistic work has been done on this elimination. The earlier work indicated that perhaps the acid halide underwent substitution to produce an acyl-

ammonium salt (1, 34, 40) which then possessed an α-hydrogen of enhanced acidity, which could be abstracted by another amine molecule. Recent evidence, however, indicates that the dehydrohalogenation may proceed through the ElcB mechanism (14, 20, 21, 32), which requires that the α-proton be lost in the first step producing a resonance stabilized
carbanion which may then lose a halide ion to yield the ketene. The evidence presented here suggests that perhaps even an E1cB mechanism does not adequately describe the elimination process for some acid halides, but rather a combination of the two proposed mechanisms gives a more complete picture of the elimination reaction.

Perhaps the most common reaction of ketenes is the reaction with themselves to form either dimers or polymers. The stability of any particular ketene is largely related to a tendency to undergo dimerization or polymerization.

Aldoketenes are usually more susceptible to these two reactions and therefore not isolated, but trapped by in situ reactions. Haloketenes, either keto- or aldo-, have stabilities comparable to the non-halo aldoketenes. The isolable ketenes usually take the form of ketoketenes; for example, diphenylketene (44), dimethylketene (31), di-t-butylketene (38) and phenylmethylketene (50), although some aldoketenes have been isolated, for example, methylketene (34). No halo-ketene has been isolated to date, however solutions of halogenated ketenes have been observed by an infrared absorption near 2000 cm\(^{-1}\) (17).

Another general reaction of ketenes is a nucleophilic addition reaction, as illustrated by the following equation.
One of the most interesting reactions of ketenes is cycloaddition to unsaturated compounds. The unsaturated compounds may take the form of carbon-oxygen, carbon-nitrogen, carbon-carbon multiple bonds and others. Carbonyl cycloadditions with ketenes produce β-lactones as illustrated below

\[
\begin{align*}
\text{Y} \quad \text{C=O} & \quad + \quad \text{X} \\
& \quad \text{R-C-H} \quad \rightarrow \quad \text{R-C-O} \\
\end{align*}
\]

(6, 7). Both ketones and aldehydes have been successfully used in this reaction.

Both imines (22, 25) and carbodiimides (8) will undergo cycloaddition with ketenes to produce β-lactams.

\[
\begin{align*}
\text{Y} \quad \text{C=O} & \quad + \quad \text{R-} \quad \text{C=N-R''} \\
& \quad \text{R-C} \quad \rightarrow \quad \text{R-C-N-R''} \\
\end{align*}
\]

Cycloadditions with olefins have occupied the majority of the work in the literature concerning ketenes. The olefins used have included simple olefins (45), acetylenic compounds (23, 30), conjugated dienes (36) and vinyl ethers (47). Cyclobutanone derivatives are the product of ketene-olefin cycloadditions. That is, ketenes undergo 1,2-cycloaddition almost exclusively. Even with conjugated dienes which have a predominant "cisoid" conformation, where 1,4-cycloaddition might be expected, the observed products can be accounted for
on the basis of 1,2-cycloaddition. The lack of Diels-Alder or 1,4-cycloaddition has been interpreted to mean that the ketene always acts in an antarafacial manner in cycloaddition reactions (53).

In the majority of cases of ketene cycloadditions, there exists the possibility of structural isomers from either an unsymmetrical olefin or a difunctional olefin and geometrical isomers from an unsymmetrical ketene. Consider the following example in which two structural isomeric products would be expected. Only one isomer has ever been observed for cycloadditions involving an unsymmetrical olefin and a symmetrical ketene.

A large volume of data in the literature indicates that the mechanism of ketene-olefin cycloadditions is "near-concerted with some charge separation in the transition state" (3, 13, 26, 28, 35). The ether portion of the
cycloadducts (A and B in the example above) would be expected to stabilize the two transition states differently. In the present example, transition state B' should be more stable, and indeed cycloadduct B is the exclusive product of the cycloaddition. The same type of data and reasoning is used with unsymmetrical dienes like cyclopentadiene. Isomer C constitutes 100 per cent of the observed product in cyclopentadiene cycloadditions (5, 18, 19, 33, 42). Careful analysis of the cycloadducts indicated that in every case
very effective stereospecificity in the sense of syn (suprafacial) addition to the olefin is observed (4, 35, 37).

Equally interesting is the very strong preference for 1,2-cycloaddition over 1,4-cycloaddition when both paths appear possible. The recent extension of the Woodward-Hoffmann rules for the conservation of orbital symmetry in concerted cycloaddition reactions (24, 53, 54, 55) provides a very adequate explanation for the lack of 1,4-cycloaddition. Conservation of orbital symmetry considerations indicate that the ketenes prefer to assume the role of the antarafacial reaction partner, while the olefin assumes the suprafacial role. A 1,4-cycloaddition would require the formation of an antibonding π-orbital in the cyclohexenone. The limited number of examples of 1,4-cycloadditions involving ketenes are examples of unusual ketenes which probably do not assume this antarafacial role (43, 48).

Having seen that only one of the possible structural isomers is formed from either an unsymmetrical olefin or a difunctional olefin, an examination of the effect of an
unsymmetrical ketene upon the stereochemistry of the products is in order. Two geometrical isomers are possible when unequally substituted ketenes are employed. Until recently, very little work had been done concerning the stereochemistry of ketene cycloadditions (11, 12, 27, 34, 37). A renewed interest in cycloadduct isomers has occurred (9, 10, 15, 16, 17) as a consequence of the recent Woodward-Hoffmann rules. Built into the rules is a theoretical explanation of the isomer distribution which needs experimental verification. A particular type of unsymmetrical ketene, namely where one substituent is halogen, has been the subject of several reports in the past few years. An extension of the methods of preparation of ketenes to include halogenated ketenes is partly responsible for the renewed interest, as well as the synthesis of tropolone and substituted tropones from halogenated cycloadducts with cyclopentadiene (2, 49, 51).
As a consequence of the previous renewal of interest in unsymmetrical ketene cycloadditions and in haloketene cycloadditions, it was deemed desirable to synthesize a new class of ketenes utilizing the interesting features of both types of ketenes. Arylhaloketenes represent a new class of ketenes which is at the same time both halo- and unsymmetrical. Therefore a study involving the synthesis and chemistry of arylhaloketenes and cyclopentadiene cycloadducts, and a study of the cycloadduct isomer distribution was begun. In the interest of completeness, several of the arylalkylketenes and their cycloadducts with cyclopentadiene would be necessary. Two obvious difficulties with such a study are immediately apparent. The actual synthesis of the desired compounds may present some problems, but more important is the realization that the validity of the entire project is dependent upon a very reliable method for assigning the stereochemistry of the cycloadducts. The problem of structural assignment was solved by the observation of the nmr spectrum of each isomer for several similar types of cycloadducts and observing some reoccurring effects (15, 16, 17, 41). Once a table of nmr spectra was produced for both isomers of a number of cycloadducts, the stereochemical assignments could be made merely with the aid of the nmr spectrum of the compound.

The problem, as described here, was twofold:
1. the synthesis and study of an unknown class of ketenes with emphasis on cycloadducts with cyclopentadiene; and,
2. the study of the isomer distribution in these cycloadducts, and any others which may be necessary to help solve the problem of understanding the isomer distribution.
CHAPTER BIBLIOGRAPHY


CHAPTER II

EXPERIMENTAL

Infrared spectral data were obtained on Perkin-Elmer Models 237 and 700 Grating Infrared Spectrophotometers. Fixed thickness sodium chloride cells (0.5 mm thickness) or thin films between sodium chloride discs were run. Nuclear magnetic resonance (nmr) spectra were obtained on Varian A-60, Varian A-60A, Varian T-60 and Joel Minimar-60 Nuclear Magnetic Resonance Spectrometers. Tetramethysilane was used as an internal standard for all spectra, which were run at room temperature. Vapor phase chromatography separations were accomplished with an Aerograph AP-49 or a Varian Model 1525-B instrument, using thermal conductivity detectors. Separations were achieved using a 10 ft. x ¼ in. column packed with 15 percent Ucon 50HB 2000 Polar and 2 per cent Cronite NIW on Chromosorb W (DMCS) 60/80 mesh or, a 10 ft. x ¼ in. column packed with 10 per cent QF-1 on Chromosorb W (acid washed) 60/80 mesh. Elemental analyses were performed by analysts in the Chemistry Department of North Texas State University, Denton, Texas, and C. F. Geiger, Ontario, California.

Preparation of Reagents

Solvents (hexane, acetonitrile, tetrahydrofuran) and commercially available reagents were dried and purified by
distillation from calcium hydride or lithium aluminum hydride and were subsequently stored over calcium hydride or molecular sieves-4A. Trichloroacetyl chloride was distilled immediately before use. Other commercially available acid halides which were used without further purification include 2-phenoxypyropanoyl chloride (Pfaltz and Bauer, Inc., Flushing, New York), phenylacetyl chloride (Aldrich Chemical Co., Gardena, California), 2-chlorobutanoyl bromide (Chemtech Co., Dallas, Texas) and 2-chloropropanoyl bromide (Chemtech Co., Dallas, Texas). Cyclopentadiene was obtained from the commercially available dimer by thermal cracking at about 140°. The monomer was stored at -10° for no more than five days.

2-Chloro-2-phenylethanoyl chloride was prepared according to the method of Walden (9). Thus, 100 g (0.48 mol) of

\[
\text{C}_6\text{H}_5-\text{CH-C-OH} + 2 \text{PCl}_5 \rightarrow \text{C}_6\text{H}_5-\text{CH-C-Cl} + 2 \text{POCl}_3 + 2 \text{HCl}
\]

phosphorous pentachloride was placed in a one-neck flask equipped with a condenser. Over this solid was placed 40 g (0.263 mol) of mandelic acid. The mixture was heated at the boiling point of phosphorous oxychloride (107°) until the hydrogen chloride vapors ceased to be evolved. The phosphorous oxychloride was distilled under an aspirator vacuum, and the acid halide distilled at 66° at 0.9 mm to give 69 g (76 per cent) of the product.

2-Phenylpropanoic acid was prepared by the silver oxide oxidation of the commercially available hydratropaldehyde.
(2-phenylpropanal) according to the procedure described in Organic Synthesis (6).

A 150 g (0.88 mol) portion of silver nitrate dissolved in 300 ml of water was added with stirring to a solution of 70 g (1.75 mol) of sodium hydroxide in 300 ml of water. The mixture was cooled in an ice bath and 58 g (0.425 mol) of hydratropaldehyde was added slowly with stirring. The reduced silver was filtered and washed with hot water. The water washings and the filtrate were combined, acidified with concentrated hydrochloric acid, and the acid extracted with several portions of ether. The ether extracts were dried with magnesium sulfate, evaporated and distilled to yield 33 g (52 per cent) of the acid boiling at 145° at 15 mm; ir (CDCl₃) 1704 cm⁻¹ (C=O) and 1597 cm⁻¹ (C=C); nmr (25 per cent v/v solution of the acid in chloroform-d) δ1.47 (doublet, 3H, J = 7.0 Hz), δ3.70 (quartet, 1H, J = 7.0 Hz), δ7.25 (singlet, 5H) and δ11.76 (singlet, 1H).

**Acid Chlorides**

All of the acid chlorides in Table I were prepared from the corresponding acids and thionyl chloride. The preparations were achieved by placing the acid in a one-neck flask equipped with a reflux condenser and a drying tube, and introducing the thionyl chloride from the top of the condenser. The solutions were refluxed, where necessary, and then distilled through a 24 inch vigreaux column.
Synthesis of α-Halovinyl Esters (Enol Esters of Acid Halides)

**General Preparation**

To a stirred solution of 0.2 mol of the acid halide in 200 ml of hexane at room temperature was added with stirring a solution of 0.1 mol of triethylamine in 50 ml of hexane. Stirring was continued for three hours before filtration of the triethylammonium halide. Concentration of the filtrate on a rotary evaporator followed by a vacuum distillation afforded the α-halovinyl esters.

**Specific Esters**

1-Chloro-2-bromopropenyl 2-bromopropanoate (I).— A 45 per cent yield of (I) was obtained boiling at 60° at 0.15 mm; ir (neat) 1788 cm⁻¹ (C=O) and 1661 cm⁻¹ (C=C); nmr (CCl₄) 61.90 (doublet, 3H, J = 7.3 Hz), 62.27 and 62.40 (singlet, two isomers, 3H total), 64.45 (quartet, 1H, J = 7.3 Hz).

Analysis: Calculated for C₆H₇Br₂C₁O₂: C, 23.5; H, 2.28. Found: C, 24.0; H, 2.23.

1,2-Dichloro-1-butenyl 2-chlorobutanoate (II).— Compound (II) was prepared in a 41 per cent yield boiling at 59° at 0.45 mm; ir (neat) 1788 cm⁻¹ (C=O) and 1653 cm⁻¹ (C=C); nmr (CCl₄) 61.16 (two triplets, 6H), 62.30 (multiplet, 4H), and 64.28 (pair of triplets, 1H, J = 6.2 Hz).

Analysis: Calculated for C₈H₁₁Cl₂O₂: C, 39.1; H, 4.47. Found: C, 39.2; H, 4.40.
1-Bromo-2-chloro-1-butenyl 2-chlorobutanoate (III).— A 31 per cent yield was obtained for compound (III); bp 69° at 0.1 mm; ir (neat) 1780 cm\(^{-1}\) (C=O) and 1648 cm\(^{-1}\) (C=C); nmr (CCl\(_4\)) \(\delta 1.20\) (two triplets, 6H), \(\delta 2.22\) (multiplet, 4H) and \(\delta 4.30\) (pair of triplets, 1H, \(J = 6.3\) Hz). Treatment of (III) with methanol gave a compound which was chromatographically identical with and had an infrared spectrum identical to an authentic sample of methyl 2-chlorobutanoate.

1-Bromo-2-chloropropenyl 2-chloropropanoate (IV).— A 43 per cent yield of (IV) was obtained boiling at 52° at 0.17 mm; ir (neat) 1786 cm\(^{-1}\) (C=O) and 1653 cm\(^{-1}\) (C=C); nmr (CCl\(_4\)) \(\delta 1.75\) (doublet, 3H, \(J = 7.3\) Hz), \(\delta 2.09\) and 2.25 (two singlets, two isomers, 3H total) and \(\delta 4.51\) (quartet, 1H, \(J = 7.3\) Hz). Treatment of (IV) with methanol have a compound which was chromatographically identical with and had an infrared spectrum identical to an authentic sample of methyl 2-chloropropanoate.

1-Chloro-2,2-dibromovinyl dibromoethanoate (V).— An 11 per cent yield of compound (V) was obtained with a boiling point of 100° at 0.15 mm; ir (neat) 1786 cm\(^{-1}\) and 1600 cm\(^{-1}\) (C=O) and (C=C) respectively; nmr (CCl\(_4\)) \(\delta 5.92\) (singlet).

Analysis: Calculated for C\(_4\)HBr\(_4\)ClO\(_2\): C, 10.99; H, 0.229. Found: C, 10.64; H, 0.376. A sample weighing 0.00766 g produced 0.01557 g of silver halide by the Carius method. The theoretical weight of silver halide for that
weight of sample is 0.01569 g.

1,2-Dichloropropenyl trichloroethanoate (VI).-- To a stirred solution of 31 g (0.24 mol) of α-chloropropionyl chloride in 200 ml of hexane at -78° was added dropwise a solution of 23.2 g (0.23 mol) of triethylamine in 50 ml of hexane. Stirring was continued for one hour at this temperature. A 45.5 g (0.25 mol) portion of trichloroacetyl chloride was then added to the reaction mixture and stirring continued as the mixture warmed to room temperature overnight. The salt was filtered and the filtrate was concentrated and vacuum distilled at 50° at 0.1 mm to yield 42 g (67 per cent) of (VI); ir (neat) 1799 cm⁻¹ (C=O) and 1661 cm⁻¹ (C=C); nmr (CCl₄) δ 2.16 and δ 2.29 (singlets, two isomers with areas indicating the isomer distribution to be 1.85/1).

Analysis: Calculated for C₅H₅ClO₂: C, 22.0; H, 1.10; Cl, 65.14. Found: C, 21.7; H, 1.30; Cl, 64.93.

1,2-Dichloro-2-phenylvinyl 2-chloro-2-phenylethanoate (VII).-- To a well stirred solution of 36.2 g (0.19 mol) of 2-chloro-2-phenylethanoyl chloride in 200 ml of hexane, was added dropwise a solution of 9.7 g (0.096 mol) of triethylamine in 25 ml of hexane at room temperature. Stirring was continued for two days and the salt was filtered and washed with two 100 ml portions of dry ether. The hexane filtrate was combined with the ether washings and evaporated. The resulting oil was recrystallized from ether to yield 18.7 g
(54 per cent) of (VII); mp 59-60\(^\circ\); ir (neat) 1792 cm\(^{-1}\) (C=O) and 1626 cm\(^{-1}\) (C=C); nmr (CCl\(_4\)) \(\delta\) 5.19 (singlet, 1H), \(\delta\) 7.18 (singlet, 5H), and \(\delta\) 7.25 (singlet, 5H).

Analysis: Calculated for C\(_{16}\)H\(_{11}\)Cl\(_2\)O\(_2\): C, 56.2; H, 3.22. Found: C, 56.2; H, 3.34.

**Ketene Cycloadditions**

The product of a ketene-cyclopentadiene cycloaddition is a substituted bicyclo[3.2.0]hept-2-en-6-one. For reference to nmr spectra, the following numbering system will be used:

![Numbering System](image)

**General Method for in situ Cycloadditions**

A 0.2 mole portion of triethylamine in 50 ml of dry hexane was added dropwise and with stirring to a solution containing 0.2 mole of the acid halide and 0.9-1.0 mole of fresh cyclopentadiene in 250 ml of hexane at room temperature. After one hour stirring at room temperature, the reaction mixture was refluxed for six hours before filtration of the salt. Concentration of the filtrate and vacuum distillation of the residue afforded the substituted bicyclo[3.2.0]hept-2-en-6-ones. All cycloadditions were also run in acetonitrile to check isomer distribution in a polar solvent. In no case
was the isomer distribution changed, but in most cases about a ten per cent increase in the yield was noted.

Specific Cycloadducts

7-exo-Chloro-7-endo-phenylbicyclo[3.2.0]hept-2-en-6-one (VIII).— An 80 per cent yield of (VIII) boiling at 113° at 0.9 mm could be obtained; ir (neat) 1784 cm⁻¹ (C=O) and 1600 cm⁻¹ (C=C); nmr (CCl₄) δ2.55 (H₄, multiplet, 2H), δ4.05 (H₁, multiplet, 1H), δ4.35 (H₅, three doublets, 1H), δ5.35 (H₃, multiplet, 1H), δ5.70 (H₂, multiplet, 1H), δ7.40 (phenyl, multiplet, 5H).

Analysis: Calculated for C₁₃H₁₁ClO: C, 71.4; H, 5.08. Found: C, 71.3; H, 5.07.

7-exo-Bromo-7-endo-phenylbicyclo[3.2.0]hept-2-en-6-one (IX).— Compound (IX) was prepared in a 53 per cent yield; bp 110° at 0.8 mm; ir (neat) 1801 cm⁻¹ (C=C) and 1610 cm⁻¹ (C=C); nmr (CCl₄) δ2.55 (H₄, multiplet, 2H), δ4.05 (H₁, multiplet, 1H), δ4.36 (H₅, three doublets, 1H), δ5.41 (H₂ or H₃, multiplet, 1H), δ5.78 (H₃ or H₂, multiplet, 1H), and δ7.40 (phenyl, multiplet, 5H).

Analysis: Calculated for C₁₃H₁₁BrO: C, 59.4; H, 4.18. Found: C, 59.7; H, 4.08.

7-endo-Methyl-7-exo-phenoxylbicyclo[3.2.0]hept-2-en-6-one (X).— Compound (X) was prepared in a 69 per cent yield; bp 118° at 0.2 mm; ir (neat) 1776 cm⁻¹ (C=O) and 1597 cm⁻¹
(C=C); nmr (CCl₄) δ1.26 (singlet, 3H), δ2.53 (H₆, multiplet, 2H), δ3.68 (H₁, multiplet, 1H), δ4.05 (H₅, three doublets, 1H), δ5.83 (H₂ and H₃, multiplet, 2H), and δ7.10 (phenyl, multiplet, 5H).

Analysis: Calculated for C₁₄H₁₄O₂: C, 78.5; H, 6.54. Found: 78.68; H, 6.85.

Bromine was added slowly, cautiously and dropwise from a small syringe to a 30 per cent solution of (X) in carbon tetrachloride in an nmr tube. This addition was done inter- mittently and was continued until the nmr spectra showed no resonance for the vinyl protons. It was observed that during the addition of bromine the methyl singlet at δ1.26 began to decrease in intensity and a new singlet at δ1.56 began to appear. At the end of the experiment, only the new methyl resonance remained at δ1.56.

7-endo-Phenoxybicyclo[3.2.0]hept-2-en-6-one (XI) -- A 17.2 g (0.17 mol) portion of triethylamine in 50 ml of dry hexane was added dropwise with stirring to a solution of 30 g (0.176 mol) of phenoxyacetyl chloride, 66 g (1.0 mol) of fresh cyclopentadiene, and 250 ml of dry hexane. Upon completion of the addition at room temperature, the mixture was refluxed for six hours before filtration of the amine salt. Concentration of the filtrate and recrystallization from hexane afforded a 65 per cent yield of (XI); mp 55.5-56°; ir (neat) 1789 cm⁻¹ (C=O) and 1597 cm⁻¹ (C=C); nmr (CCl₄) δ2.66 (H₄, multiplet, 1H), δ3.48 (H₁, multiplet, 1H), δ5.48 (H₂ and H₃, multiplet, 2H).
1H), 65.19 (H7, two doublets, $J_{H_1-H_7} = 8.0$ Hz, $J_{H_5-H_7} = 3.0$ Hz), 65.76 (H2 and H3, multiplet, 2H), 67.00 (phenyl, multiplet, 5H).

Analysis: Calculated for C13H12O2: C, 78.00; H, 6.00.
Found: C, 78.12; H, 6.06.

General Method for Cycloadditions using Free Ketenes

A 0.2 mole portion of the ketene in 50 ml of dry hexane was added dropwise to a 0.8 mole portion of fresh cyclopentadiene in 200 ml of hexane. After the addition was complete, the reaction mixture was heated to reflux until the yellow color of the ketene had disappeared (six to ten hours). Concentration and recrystallization from ether afforded the pure cycloadducts.

Specific Cycloadducts

7-exo-Methyl-7-endo-phenylbicyclo[3.2.0]hept-2-en-6-one (XII).— Compound (XII) was prepared in an 85 per cent yield; mp 29-30°; ir (neat) 1773 cm⁻¹ (C=O) and 1603 cm⁻¹ (C=C); nmr (CCl₄) 61.61 (singlet, 3H), 62.52 (H₄, multiplet, 2H), 63.49 (H₁, multiplet, 1H), 63.93 (H₅, three doublets, 1H), 65.52 (H₂ and H₃, multiplet, 2H) and 67.28 (phenyl, multiplet, 5H).

Analysis: Calculated for C₁₃H₁₂O₂: C, 84.85; H, 7.13.
Found: C, 84.9; H, 7.16.

Bromine was added slowly, cautiously and dropwise from a small syringe to a 30 per cent solution of (XII) in carbon
tetrachloride in an nmr tube. The addition was done inter-
mittently and was continued until the nmr spectra showed no
resonance for the vinyl protons. On an expanded portion of
the spectrum, the methyl resonance at δ1.61 could be seen to
disappear and a new singlet appear at δ1.63. This change
went undetected in the normal spectrum.

7-exo-Ethyl-7-endo-phenylbicyclo[3.2.0]hept-2-en-6-one
(XIII).— An 82.5 per cent yield of (XIII) could be obtained
with a melting point of 43.5-44°C; ir (neat) 1761 cm⁻¹ (C=O)
and 1592 cm⁻¹ (C=C); nmr (CCl₄) δ0.75 (triplet, 3H), δ2.00
(quartet, 2H), δ2.45 (H₁, multiplet, 2H), δ3.50 (H₁, multi-
plet, 1H), δ3.86 (H₂, three doublets, 1H), δ5.46 (H₂ and H₃,
multiplet, 2H), and δ7.21 (phenyl, multiplet, 5H).

Analysis: Calculated for C₁₅H₁₆O: C, 84.9; H, 7.55.
Found: C, 85.2; H, 7.67.

Preparation of Pure Ketenes

General Method for Ketene Preparations

A solution of 0.2 mole of triethylamine in 50 ml of
benzene was added dropwise to 0.2 mole of acid halide in
200 ml of dry benzene at room temperature. After two hours
of stirring at room temperature, the salt was removed by fil-
tration, the solvent evaporated and the ketene distilled as
rapidly as possible. Once the ketene has been removed from
the residual salt and polymer, it is reasonably stable and
may be fractionated carefully before use.
Specific Ketenes

Phenylmethylketene (XIV).— A 70 per cent yield of the pure ketene was prepared boiling at 58° at 2.5 mm; ir (neat) 2117 cm\(^{-1}\); nmr (CCl\(_4\)) \(\delta 1.87\) (singlet, 3H) and \(\delta 7.12\) (multiplet, 5H).

Phenylethylketene (XV).— A 64 per cent yield of (XV) with a boiling point of 62° at 0.1 mm could be prepared; ir (neat) 2110 cm\(^{-1}\); nmr (CCl\(_4\)) \(\delta 1.18\) (triplet, 3H), \(\delta 2.38\) (quartet, 2H) and \(\delta 7.13\) (multiplet, 5H).


CHAPTER III

RESULTS AND DISCUSSION

Phenylchloroketene was chosen for the first part of the study of arylhaloketene cycloadditions because of the availability of starting materials. \( \alpha \)-Chloro-\( \alpha \)-phenylacetic acid and \( \alpha \)-chloro-\( \alpha \)-phenylacetyl chloride were commercially available, but prohibitively expensive. Therefore, the starting acid halide was synthesized from mandelic acid and phosphorus pentachloride. Since no previous workers had succeeded in the isolation of any haloketenes, \textit{in situ} trapping experiments appeared more promising. The dehydrochlorination of \( \alpha \)-chloro-\( \alpha \)-phenylacetyl chloride in the presence of fresh cyclopentadiene afforded a good yield of the 1,2-cycloadduct. However, when the experimental conditions were systematically varied to optimize the yield, an unexpected result was obtained. A crystalline, non-cycloadduct product was formed when there was a deficiency of amine in the reaction mixture. This side product could be produced in as much as fifty-five per cent yield when the ratio of acid halide to amine to olefin was 2:1:0. The optimum stoichiometry indicated that the solid had the elemental composition of a ketene-acid halide adduct. A ketene-acid halide adduct seemed logical in view of the fact that ketenes are known to react with acid halides to produce \( \beta \)-ketoacid halides (18).
Since the reaction of a ketene with an acid halide is not a well-known reaction of ketenes, it seemed desirable to investigate the scope of the reaction. While the extension of the ketene-acid halide reaction was in progress, two reports appeared in the literature describing reactions with similar stoichiometry. Lavanish and co-workers (11) reported that a 2:1 ratio of dichloroacetyl chloride to triethylamine produced trichlorovinyl dichloroacetate. Dreiding and co-workers (9) reported similar results for the α-chloropropionyl chloride system.

There now existed another possible structure for the ketene-acid halide adduct of the α-chloro-α-phenylacetyl chloride system. The significance of this side reaction would be enhanced tremendously if the product were an α-halovinyl ester. Enol esters of acid halides as a class of compounds are unknown and investigations into the scope of the reaction would be in order. A few reports of α-halovinyl esters are
in the literature, but each has been made by an individual procedure and no general preparative method exists for this type of compound (8). The structure determination was facilitated by the fact that the unknown compound possessed only one carbonyl in the infrared, although it was closer to the acid halide region than to the ester region. The nmr spectrum was consistent with both structures as was the elemental analysis. If a carbon-carbon double bond existed, it would have been masked by the aromatic absorption in the same region of the infrared. When a similar compound was prepared which had no aromatic substituent, the presence of a carbon-carbon double bond in the infrared confirmed the \( \alpha \)-halovinyl ester structure.

The problem of defining the scope of the vinyl ester-forming reaction was approached by the attempted synthesis of \( \alpha \)-halovinyl esters from a variety of acid halides. Table II lists the results. It became apparent very early in the investigation that the formation of \( \alpha \)-halovinyl esters is not a general reaction of acid halides and tertiary amines. The synthesis of vinyl esters from the \( \alpha \)-halopropionyl and \( \alpha \)-halobutyryl systems posed no problems, however the non-halogenated acid halides could not be made to yield vinyl esters. The reaction appears to require an \( \alpha \)-proton of enhanced acidity as evidenced by the necessity of an \( \alpha \)-halogen. However, the presence of an \( \alpha \)-halogen does not insure the formation of \( \alpha \)-halovinyl esters. For example, repeated
attempts to synthesize the α-halovinyl ester from chloroacetyl chloride resulted in total failure.

An examination of some of the literature reports for this type of reaction revealed some interesting features. Some 1:1 adducts of tertiary amines and acid halides have been reported and are assumed to have the structure of an acylammonium ion (1, 13). An intermediate acylammonium ion would very adequately explain the catalytic effect tertiary amines have on the acylating ability of acid halides (7, 17). A positively charged nitrogen attached to a carbonyl would render the carbon of the carbonyl much more electrophilic than a normal acid halide carbonyl, and therefore would be expected to enhance the reactivity of the acid halide in acylation reactions.

However, in order to explain the formation of the α-halovinyl esters, it is necessary to devise a mechanism which involves an oxyanion, since the product appears to be the result of an enolate anion being acylated by the acid halide from which it is produced. The most obvious elimination mechanism available is known as the E1cB mechanism. The first step would be the abstraction of an α-hydrogen to give the desired enolate ion which could then eject a halide ion to yield the ketene, or be acylated by another acid.
halide molecule to yield the α-halovinyl ester. Thus, an E1cB mechanism would be able to account for nearly all of the experimental results, and was in fact proposed by the two original workers (9, 11). Such a mechanism could not explain, however, the failure of the chloroacetyl chloride system; nor is it very consistent with the work already in the literature.

Perhaps a more plausible mechanism would be as shown in the following reaction sequence. The three intermediates
between the acid halide and ketene are, for discussion purposes, labeled A, B and C. If this mechanism is accurate, then the initial reaction between the amine and the acid halide involves a nucleophilic attack on the carbon of the carbonyl resulting in the zwitterionic species A. Intermediate A would be expected to be relatively short-lived and decay to either B or C rapidly. The formation of B from A would involve the loss of a halide ion and the formation of an acyl quaternary ammonium chloride. Alternately, if species A decomposes to intermediate C to get to the ketene, and oxyanion C is long-lived enough, acylation by another acid halide molecule may occur giving rise to the observed α-halo-vinyl esters. Thus, the above mechanism has accounted for the isolation of the several ammonium salts in the literature already, as well as for the isolation of the several α-halo-vinyl esters described here. What remains to be seen is what factors affect the mode of decay of intermediate A. Since the transition from A to C involves the loss of a proton and a triethylamine moiety, it would seem logical that the acidity of the α-proton of the starting acid halide would be an important factor. Indeed such acidity may be the driving force for the A → C pathway; that is, with a relatively acidic α-hydrogen, the activation energy from A to C may be sufficiently lower than that for the A to B process. All the data seems to fit the mechanism very concisely except the lack of formation of an α-halovinyl ester from the
h haloacetyl halide systems. Apparently, if the oxyanion \( C \) is formed for these systems, it does not have a sufficiently long lifetime to permit acylation.

In an effort to obtain a qualitative idea of the lifetime of an oxyanion intermediate, stoichiometric amounts of triethylamine and \( \alpha \)-chloropropionyl chloride were mixed over a period of one hour at \(-78^\circ\) and then allowed to stir for an additional hour. Trichloroacetyl chloride was then added and the mixture allowed to warm to room temperature. A sixty-seven per cent yield of the "mixed" vinyl ester, resulting from acylation of an oxyanion by a foreign acid halide, was isolated.

\[
\begin{align*}
\text{CH}_3\text{CH}-\text{C}-\text{Cl} + (\text{C}_2\text{H}_5)_3\text{N} &\rightarrow \left[ \begin{array}{c}
\text{CH}_3 \\
\text{Cl}
\end{array} \right] + (\text{C}_2\text{H}_5)_3\text{N}^+ \\
\text{CCl}_3-\text{C}-\text{O}-\text{C}=\text{C}-\text{CH}_3 &\rightarrow \left[ \begin{array}{c}
\text{H} \\
\text{Cl}
\end{array} \right] \text{CCl}_3-\text{C}-\text{O}-\text{C}=\text{C}-\text{CH}_3 (\text{VI}) + (\text{C}_2\text{H}_5)_3\text{NCl}
\end{align*}
\]

Additional support for the proposed mechanism is found in the difference between the acid chloride and acid bromide of the same acid. The latter invariably produces an extremely difficult system with which to work, the net result being a poorer yield of \( \alpha \)-halovinyl ester. With the bromide ion being a better leaving group than a chloride ion, the intermediate \( C \) could be expected to have a longer lifetime when derived from an acid chloride. Conversely, the bromide counterpart of oxyanion \( C \) would be expected to go more
readily to the ketene which then could polymerize and result in a lower yield of the trapped intermediate. Indeed for several of the acid bromide systems, an absorption for the free ketene in the infrared has been observed (6, 16).

With the investigation of the scope of the α-halovinyl ester-forming reaction complete, it was desirable to return to the original problem, namely cycloaddition and isomer distribution from the phenylhaloketene systems. The most pressing problem to be faced was that of isomer distinction. Without a reliable method for assigning the stereochemistry at carbon-7, the results would be meaningless. The numbering system used for these bicyclic compounds is illustrated below.

It has been known for some time that in the nmr spectrum of a ketene-cyclopentadiene adduct, a methyl group in the exo position on C$_7$ is different by about 0.36 from a methyl group in the endo position. A determination of the nmr spectrum of 7,7-dimethylbicyclo[3.2.0]hept-2-en-6-one revealed two singlets at 0.936 and 1.286 (12). Brady and Hollifield (4) have shown by bromination for both isomers of the methylchloroketene-cyclopentadiene cycloadduct and both isomers of the methylbromoketene-cyclopentadiene cycloadduct that the endo-methyl resonates about 0.36 farther upfield.
than does the exo-methyl. Bromination of the carbon-carbon double bond results in a downfield shift of about 0.36 for

\[
\begin{align*}
\text{(XVII)} & \quad \text{CH}_3 (1.776) \\
\text{(XVIII)} & \quad \text{CH}_3 (1.476)
\end{align*}
\]

the endo-methyl while the shift for the exo-methyl is almost negligible. Several workers have used the difference in chemical shifts of methyl groups for isomer distinction (2, 3, 4, 5, 14, 15).

The same type of effect would be expected for hydrogens on carbon-7, and indeed, private communications with Dreiding* have indicated that an exo-hydrogen is about 0.56 farther downfield than an endo-hydrogen.

An interesting feature was observed in the nmr spectrum of the above four compounds. The chemical shift of \(H_5\) (see Table III) for (XVII) did not agree with the \(H_5\) resonance

*Professor Andre Dreiding, University of Zurich in Switzerland, private communications on the nmr spectra of similar bicyclic compounds.
in (XVIII). Since the difference between (XVII) and (XVIII) was only a difference in stereochemistry, a significant difference between the resonances of H₅ was not expected. Moreover, the differences which did exist between the two isomers seemed sufficiently far removed from H₅ that similar chemical shifts were expected. A completely analogous situation was observed for the isomers of the methylbromoketene-cyclopentadiene cycloadduct. In each case, the endo-methyl isomer possessed a more deshielded resonance for H₅ by 0.25-0.35 ppm. The cycloadducts from other alkylhaloketene-cyclopentadiene systems were synthesized, the isomers separated, and their individual nmr spectra recorded (15). Comparison with the spectra for (XVII) through (XX) revealed the same differences in the chemical shift of H₅ for any pair of isomers.

It was hoped that the cross-ring deshielding by an exo-halogen on carbon-7 would be a general method for isomer distinction. The only prerequisite seemed to be the separation of isomers and the determination of the nmr spectrum for each isomer. Of special interest were those systems where stereospecific cycloaddition was observed. In the case of the chloroketene-cyclopentadiene cycloadduct, in which the stereochemistry was independently assigned (3), the H₅ resonance was found to be where it would have been expected for the endo-chloro isomer.

Recognition of the cross-ring deshielding effect was facilitated by, and possibly the result of a lack of
cross-ring coupling \((\Delta H^5-H_2=0=\Delta H^5-H_5)\). The result is a pattern of three doublets which can be identified even when the resonance for \(H_1\) is not far removed. If the cross-ring coupling constants were not zero, a multiplet for \(H_5\) would result, which would frequently be indistinguishable from \(H_1\).

The observation of three doublets for \(H_5\) (which are overlapping and appear as two triplets) requires a system of coupling constants defined by \(\Delta H^5-H_1 \neq \Delta H^5-H_4_{\text{exo}} > \Delta H^5-H_4_{\text{endo}}\). The result would appear as in the following diagram. As the

\[
H_5
\]

\[
\begin{align*}
a &= J_{H_1-H_5} \\
b &= J_{H_4_{\text{exo}}-H_5} \\
c &= J_{H_4_{\text{endo}}-H_5}
\end{align*}
\]

difference between \(\Delta H^5-H_1\) and \(\Delta H^5-H_4_{\text{exo}}\) approaches and exceeds one Hz, the splitting pattern begins to degenerate into a multiplet. If a multiplet had resulted, recognition of the cross-ring deshielding effect may not have occurred.

Dreiding and co-workers indicate that when similar spectra are obtained using a 100 MHz nmr, and decoupling, it is possible to determine \(\Delta H^5-H_1\) and \(\Delta H^5-H_4_{\text{exo}}\) as well as
However, it is apparent that Dreiding failed to observe the cross-ring deshielding effect of halogen (14).

α-Chloro-α-phenylacetyl chloride was dehydrochlorinated with triethylamine in the presence of cyclopentadiene to yield 7-chloro-7-phenylbicyclo[3.2.0]hept-2-en-6-one. By adjusting the stoichiometry so as to eliminate the α-halovinyl ester, the cycloadduct could be obtained in as much as an eighty per cent yield. An nmr spectrum on the reaction mixture proved to be identical to that of the distilled cycloadduct, so it was concluded that the isomer distribution was relatively temperature stable. Only one resonance for $H_5$ was observed and it was found to be considerably deshielded from the $H_5$ absorption in non-halogenated cycloadducts (see Table III). The conclusion was, therefore, that the cycloaddition was stereospecific to yield only the endo-phenyl isomer. A peculiarity in the vinyl region of the spectrum was noticed. Instead of the symmetrical multiplet which is normally obtained for ketene-cyclopentadiene adducts, two identical multiplets appeared, each of which was symmetrical about its midpoint. The chemical shifts of the multiplets
were 5.358 and 5.708, the midpoint of which, 5.526, is considerably upfield from most vinyl resonances for these cycloadducts. Several possible factors could have caused this unusual pattern. The first of which, an impurity, was discarded on the basis of the integrated areas, the symmetries of the two multiplets and a correct elemental analysis. The absorption could be the result of a normal AB pattern with a somewhat greater than usual separation between the two multiplets. A third possibility was that the two vinyl protons were sufficiently different to resonate 0.358 apart. The latter explanation would be a unique situation for ketene cycloadducts except for the cyclopentadiene adduct with diphenylketene (see Table III). Nmr decoupling experiments were needed to distinguish between the two possibilities. Decoupling at the frequency of the $H_4$ resonance, collapsed the upfield portion of the vinyl group into a doublet of about 6.5 Hz; while the downfield portion became a pair of doublets of 6.5 and 2.0 Hz. It seemed obvious then, that each absorption represented one proton. Moreover, with the coupling to $H_4$ removed and no cross-ring coupling with $H_5$, $H_3$ should be a doublet and $H_2$ should be a pair of doublets. It was therefore apparent that $H_2$ was responsible for the downfield portion of the total vinyl resonance, while the upfield portion was due to $H_3$. The coupling constants $J_{H_2-H_3}$ and $J_{H_1-H_2}$ could be seen to be 6.5 and 2.0 Hz respectively.
The decoupling results indicated that $H_2$ absorbed in the general region of vinyl protons while $H_3$ was considerably shielded. Before a reason could be given for either of the unexpected results (the stereochemistry or the shielding of $H_3$) for the phenylchloroketene system, other closely related cycloadducts would have to be studied. The most obvious choice was the phenylbromoketene-cyclopentadiene system. When the nmr spectrum of 7-bromo-7-phenylbicyclo[3.2.0]hept-2-en-6-one was obtained, it appeared remarkably similar to the analogous chloro compound (see Table III). The $H_5$ absorption again indicated only one isomer with an exo-halogen and the vinyl portion of the spectrum was split into two identical multiplets at 5.416 and 5.786. The results of decoupling from the phenylchloroketene system were extended to the vinyl protons of the phenylbromoketene cycloadduct. The stereo-specificity was still unexplainable; however, the peculiar resonance for the vinyl protons appeared to be the result of an endo-phenyl. A shielded absorption for $H_3$ was common to only three cycloadducts, each of which possessed a phenyl group in the endo position. An examination of models led to the prediction of restricted rotation about the $C_7$-phenyl bond.
If the rotation of the phenyl group was sufficiently restricted, \( \text{H}_2 \) could be seen to be more nearly in the center of the aromatic shielding cone than was \( \text{H}' \).

To verify the shielding hypothesis and also to determine whether a halogen influences the stereochemistry of the cycloaddition, the adduct from phenylmethylketene was desired. The commercially available hydratropaldehyde was oxidized with silver oxide to give 2-phenylpropanoic acid, and the acid chloride was prepared. Dehydrochlorination of the acid halide produced the ketene which was purified before cycloaddition with cyclopentadiene. The cycloadduct was observed to be stereospecific as evidenced by only one singlet in the nmr for the methyl group at 1.615. It was not immediately obvious which isomer was responsible for this resonance, but the chemical shift of the methyl group strongly suggested an exo-methyl (4). To confirm the stereochemical assignment, bromination of the cycloadduct in an nmr tube was in order. A change in the chemical shift of the methyl group of 0.025 was observed upon bromination. Clearly then, the isomer formed must have been the exo-methyl isomer. It was extremely disappointing to see a vinyl region which consisted
of one multiplet for a cycloadduct with an endo-phenyl group, although it appeared to be split slightly into two multiplets. However, the total multiplet was symmetrical and was shielded considerably when compared to cycloadducts without aromatic substituents (see Table III). It seemed plausible at this point that a slight amount of rotation of the phenyl could cause the two vinyl protons to be equivalent, giving rise to one shielded absorption.

Attention was now turned to establishing the reason for the surprising stereochemistry of the cycloadditions of unsymmetrical phenyl ketenes. Three unsymmetrical ketenes had been reacted with cyclopentadiene and each produced only the sterically unfavored isomer. Phenylethylketene was synthesized in an effort to determine the effect on the stereochemistry of increasing the size of the non-aromatic portion of the ketene. Stereospecific cycloaddition was again observed as evidenced by only one quartet for the exocyclic methylene group, as well as only one deshielded multiplet for the vinyl protons (see Table III). The chemical shift for a methylene group on C₇ was totally uninformative as to the stereochemistry of the cycloadduct, since no correlations
for model compounds had been made. However, an _exo-ethyl group would still be expected to have a more deshielded methylene resonance than would the methylene group of an _endo-ethyl group. The only means of stereochemical assignment was the chemical shift of the vinyl protons, which was consistent with what had been observed for cycloadducts known to have an _endo-phenyl (compare XIII with an _endo-ethyl adduct XXI). Apparently then, the increase in size of the alkyl portion of the ketene from methyl to ethyl had no effect on the steric course of the cycloaddition with cyclopentadiene.

In order to determine the exact nature of the importance of substituent size on the stereochemistry of these cycloadducts, the distance between the bulky aromatic ring and the ketene functionality was increased. 2-Phenoxypropanoyl chloride was dehydrochlorinated in the presence of cyclopentadiene to yield 7-methyl-7-phenoxybicyclo[2.2.3]hept-2-en-6-one. One methyl singlet in the nmr indicated that a stereo-

\[
\begin{align*}
\text{O} & \quad \text{C}_6\text{H}_5 \\
\text{CH}_3 & \\
\text{(X)}
\end{align*}
\]

specific cycloaddition had occurred. A chemical shift of 1.266 was very indicative of an _endo-methyl isomer, as was a vinyl multiplet centered at 5.836 (see Table III). However,
bromination of the cycloadduct would serve as unequivocal proof of the stereochemistry. The brominated cycloadduct revealed only one methyl singlet, but it was located at 1.56δ which verified that the methyl group of the original cycloadduct was in the endo position.

Such a complete reversal in the stereochemistry of the cycloadduct was very surprising. The possibility of some interaction between an oxygen and either the cumulative or the conjugated double bond systems had to be investigated. Therefore phenoxyacety chloride was dehydrochlorinated to give the aldoketene, phenoxyketene, which was reacted in situ with cyclopentadiene to yield the substituted cyclobutanone.

\[
\begin{align*}
&\text{(XI)} \\
&\text{(XI)}
\end{align*}
\]

An nmr on the concentrated reaction mixture revealed a pair of doublets for \(H_7\) centered at 5.19δ with coupling constants which could only be reconciled with a system of three \(\text{cis}\)-protons on the four membered ring (see Table III). The absence of any absorption about 0.56 farther upfield indicated a stereospecific cycloaddition, which was expected from the results of other workers (3, 10) with aldoketenes. The coupling constants were 8.0 Hz and 3.0 Hz respectively. While a 3.0 Hz cross-ring coupling is probably consistent
with either isomer of the cycloadduct, the vicinal coupling of 8.0 Hz could only be the result of two protons which were very nearly in the same plane.

For the cycloadducts of unsymmetrical phenyl ketenes, the only isomer produced was sterically the least favored one, with the exception of the phenoxyethyl system. That is, an endo-phenyl or phenoxy isomer was the only observed product with the one exception. The very timely extension of the Woodward-Hoffmann Rules (principle of conservation of orbital symmetry), gives a very complete explanation for the observed stereochemistry from these systems, and conversely, the stereochemistry described is among the first experimental verification of the untested Woodward-Hoffmann Rules (19).

Woodward and Hoffmann have revised the original rules so as to achieve a maximum orbital overlap and yet conserve orbital symmetry. The original parallel approach (the reacting ketene and olefin molecules lie in planes parallel to each other) has been replaced by an approach in which the
plane of the olefin is perpendicular to the plane of the ketene molecule, and the plane of the orbitals of the carbon-carbon double bond of the ketene is perpendicular to the plane of the orbitals of the carbon-carbon double bond of the olefin. An interaction between the nucleophilic olefin and the carbon of the ketene carbonyl (which is quite electrophilic due to the vinylium cation character of the ketene, $\text{C}^+\text{C}^-\text{O}$) can promote such an orientation even when the two reactants are still relatively far apart. The initial interaction at long distances leads to a transition state in which the two reacting carbon-carbon double bonds lie one on top of the other. The interesting feature of the Woodward-Hoffmann Rules is that the predicted transition state has a very definite geometry. An examination of the possible transition states can lead to a prediction of which one would predominate.

For an unsymmetrical ketene and an unsymmetrical olefin (like cyclopentadiene), there are four possible transition state geometries, as shown below. It should be apparent that orientation $D'$ and $E'$ are much less favorable from a steric point of view than either $F'$ or $G'$. Moreover, when "X" is
the larger group, one would expect G* to predominate over F*.

In cases where there is a considerable difference between the
size of the two substituents, orientation G* might be expected
to be populated exclusively. With respect to the z-axis, it
is apparent that the ketene molecule must rotate 90° clock-
wise before bonding can occur. In addition, a twisting must
occur about the carbon-carbon bond of the ketene in order to
achieve the requirements for σ-bond formation. When the
required rotation and twisting is performed with models on
orientation G*, it is apparent that the isomer with "X" (the
larger group) in the endo position of the cycloaddition
product will result. Orientation F* would result in an
isomer with "X" in the exo position. In accordance with the Woodward-Hoffmann Rules, then, the sterically preferred transition state leads to that isomer of the cycloadduct with the larger group in the endo position.

For the cases presently under investigation, the steric bulk of a phenyl group is sufficiently greater than the bulk of any of the other groups and the result is only one isomer. Similar reasoning can be used for the phenoxyketene-cyclopentadiene cycloaddition. However, it is all too clear that the cycloaddition picture is in need of some modification if it is to explain the results with the phenoxyethylketene system. There is some evidence suggesting that the steric bulk is not the only factor involved in the prediction of isomer distribution (6, 14). In the case of methylpropylketene (where the two substituents are considerably different in size), the exo-/endo-methyl isomer distribution is about 1.5/1.

It would seem likely that since the geometry of the transition state is fixed while the initial long-range interaction is taking place, only that portion of the substituents directly attached to the ketene functionality need be considered. Beyond a certain distance from the cumulative system, the steric bulk is unimportant, for linear type substituents. For methylpropylketene, the important factor would be a comparison of the size of a methylene and a methyl group. An isomer distribution of 1.5/1, when viewed in this
light is not surprising. For phenoxyalkylketene, the important feature would be a ratio of the sizes of a covalent oxygen to a methyl group. With a methyl group being much larger than an oxygen, it is not surprising that the methyl group is in the endo position of the cycloadduct. What is surprising is the completeness with which this stereochemical path is followed. One might justifiably expect a mixture of the two isomers and additional work on alkoxy- or phenoxyketene systems is necessary to fully understand the reason behind the stereochemistry of these systems.

It is relatively easy to see an experimental verification for the Woodward-Hoffmann Rules in the results presented here. The significance of this fact cannot be overemphasized. For five years the original Woodward-Hoffmann Rules were misinterpreted to forbid thermal, concerted (2+2)-cycloadditions of ketenes to olefins. The revised rules merely indicate how such cycloadditions can occur and the stereochemistry of the products provides a means of testing the rules. The cycloadducts from the phenylketenes and the aldoketenes (2, 5) which are formed stereospecifically, as well as the cycloadducts from alkylhaloketenes (4, 6) which are non-stereospecific, provide a very adequate verification of the theory of cycloaddition behind the Woodward-Hoffmann Rules.

A unique and extremely simple method of isomer distinction adds considerably to the significance of this work. In addition, the examination of a new reaction and the
synthesis of a new class of compounds, \( \alpha \)-halovinyl esters, and several new bicyclic compounds could prove extremely useful to the synthetic organic chemist.
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### TABLE I

**PREPARATION OF SOME ACID CHLORIDES**

\[
\begin{align*}
R-CH-C-Cl \\
\end{align*}
\]

<table>
<thead>
<tr>
<th>R</th>
<th>X</th>
<th>B.P.</th>
<th>% Yield</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH$_3$</td>
<td>Br</td>
<td>131</td>
<td>65</td>
<td>1</td>
</tr>
<tr>
<td>CH$_3$</td>
<td>Cl</td>
<td>110</td>
<td>72</td>
<td>2</td>
</tr>
<tr>
<td>C$_2$H$_5$</td>
<td>Cl</td>
<td>130</td>
<td>75</td>
<td>4</td>
</tr>
<tr>
<td>C$_2$H$_5$</td>
<td>C$_6$H$_5$</td>
<td>85 @ 4.0</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>Br</td>
<td>93 @ 1.0</td>
<td>61</td>
<td>3</td>
</tr>
<tr>
<td>C$_6$H$_5$</td>
<td>CH$_3$</td>
<td>60 @ 0.8</td>
<td>83</td>
<td>5</td>
</tr>
<tr>
<td>Br</td>
<td>Br</td>
<td>42 @ 10.0</td>
<td>76</td>
<td>7</td>
</tr>
</tbody>
</table>
TABLE II
Results of α-Halovinyl Ester Synthesis

\[
\begin{align*}
\text{R} & \quad \text{X'} \quad \text{X} \\
\text{CH}_3 & \quad \text{Br} \quad \text{Cl} \quad 45 \\
\text{C}_2\text{H}_5 & \quad \text{Cl} \quad \text{Cl} \quad 41 \\
\text{C}_2\text{H}_5 & \quad \text{Cl} \quad \text{Br} \quad 31 \\
\text{CH}_3 & \quad \text{Cl} \quad \text{Br} \quad 43 \\
\text{Br} & \quad \text{Br} \quad \text{Cl} \quad 11 \\
\text{C}_6\text{H}_5 & \quad \text{Cl} \quad \text{Cl} \quad 54 \\
\text{H} & \quad \text{H} \quad \text{Cl} \quad - \\
\text{H} & \quad \text{Cl} \quad \text{Cl} \quad - \\
\text{H} & \quad \text{CH}_3 \quad \text{Cl} \quad - \\
\text{CH}_3 & \quad \text{CH}_3 \quad \text{Cl} \quad - \\
\text{C}_6\text{H}_5 & \quad \text{C}_2\text{H}_5 \quad \text{Cl} \quad - \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \quad \text{Cl} \quad - \\
\text{CCl}_3\text{C}=\text{O}=\text{C} & \quad \text{Cl} \quad \text{CH}_3 \quad 67 \\
\end{align*}
\]
TABLE III
NMR Spectra for Some Cycloadducts

<table>
<thead>
<tr>
<th>Compound</th>
<th>A</th>
<th>B</th>
<th>H_1</th>
<th>H_2</th>
<th>H_3</th>
<th>H_4</th>
<th>H_5</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIII</td>
<td>Cl</td>
<td>C_6H_5</td>
<td>4.05</td>
<td>5.70</td>
<td>5.35</td>
<td>2.55</td>
<td>4.35</td>
</tr>
<tr>
<td>IX</td>
<td>Br</td>
<td>C_6H_5</td>
<td>4.05</td>
<td>5.78</td>
<td>5.41</td>
<td>2.55</td>
<td>4.36</td>
</tr>
<tr>
<td>XIV</td>
<td>C_6H_5</td>
<td>C_6H_5</td>
<td>4.23</td>
<td>5.71</td>
<td>5.45</td>
<td>2.67</td>
<td>3.78</td>
</tr>
<tr>
<td>X</td>
<td>C_6H_5-0</td>
<td>CH_3 (1.26)</td>
<td>3.86</td>
<td>5.83</td>
<td>2.53</td>
<td>4.05</td>
<td></td>
</tr>
<tr>
<td>XI</td>
<td>H* (5.19)</td>
<td>C_6H_5-0</td>
<td>3.48</td>
<td>5.76</td>
<td>2.53</td>
<td>3.86</td>
<td></td>
</tr>
<tr>
<td>XII</td>
<td>CH_3 (1.61)</td>
<td>C_6H_5</td>
<td>3.49</td>
<td>5.52</td>
<td>2.52</td>
<td>3.93</td>
<td></td>
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<tr>
<td>XIII</td>
<td>C_2H_5</td>
<td>C_6H_5</td>
<td>3.50</td>
<td>5.46</td>
<td>2.45</td>
<td>3.86</td>
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<tr>
<td>XV</td>
<td>Cl</td>
<td>Cl</td>
<td>4.08</td>
<td>5.9</td>
<td>2.68</td>
<td>4.25</td>
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</tr>
<tr>
<td>XVI</td>
<td>CH_3 (1.28)</td>
<td>CH_3 (0.93)</td>
<td>3.15</td>
<td>5.8</td>
<td>2.70</td>
<td>3.95</td>
<td></td>
</tr>
<tr>
<td>XVII</td>
<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>
<td></td>
</tr>
<tr>
<td>XVIII</td>
<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>
<td></td>
</tr>
<tr>
<td>XIX</td>
<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>
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<tr>
<td>XX</td>
<td>Br</td>
<td>CH_3 (1.58)</td>
<td>3.75</td>
<td>5.8</td>
<td>2.62</td>
<td>4.28</td>
<td></td>
</tr>
<tr>
<td>XXI</td>
<td>Cl</td>
<td>C_2H_5</td>
<td>3.70</td>
<td>5.9</td>
<td>2.62</td>
<td>4.27</td>
<td></td>
</tr>
<tr>
<td>XXII</td>
<td>C_2H_5</td>
<td>Cl</td>
<td>3.60</td>
<td>5.9</td>
<td>2.63</td>
<td>3.94</td>
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</tr>
</tbody>
</table>

* J_H_1-H_7 = 8.0 Hz; J_H_5-H_7 = 3.0 Hz
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