Halogenated Ketenes: Valuable Intermediates in Organic Synthesis[1]

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The preparation and 1,2-cycloaddition of halogenated ketenes with olefins and other unsaturated compounds is described. Many illustrations of the formation of α-halo- and α,α-dihalocyclobutanones and other 4-membered rings are given. The usefulness of halogenated ketenes in synthesis is demonstrated by some examples of the conversion of dihalo- and alkylhaloketene cycloadducts with cyclopentadiene to tropone derivatives. Further utility is shown by some ring contraction reactions of the cyclobutanones and cyclobutanols to cyclopropane derivatives.

In dieser Arbeit werden die Herstellung von halogenierten Ketenen und ihre 1,2-Cycloadditionsreaktionen mit Olefinen und anderen ungesättigten Verbindungen beschrieben. Anhand zahlreicher Beispiele wird die präparative Anwendbarkeit der halogenierten Ketene zur Synthese von 2-Halogen- und 2,2-Dihalogen-cyclobutanonen, von Tropon-Derivaten über die Cyclopentadien-Addukte und von Cyclopropan-Derivaten über Cyclobutanone und Cyclobutanole aufgezeigt.

Introduction

Ketenes have been known since the synthesis of diphenylketene by Staudinger in 1905[2]. This new class of compounds was extensively studied during the next twenty years. During these investigations, attempts were made to prepare some halogenated ketenes; dichloro-, ethylchloro-, methylbromo-, and ethylbromoketenes[4,5,6]. These ketenes could not be detected and were described as unstable compounds which polymerize readily even at very low temperatures.

Investigations in the two decades following Staudinger's initial studies resulted in the industrial development of the parent compound, ketene. This development resulted in a thorough study of the chemistry of ketene itself. Halogenated ketenes were unknown until just a few years ago. A comprehensive review on preparative ketene chemistry[3] including halogenated ketenes appeared in 1968.

This report reviews the developments of halogenated ketenes since the initial reports on difluoroketene in 1957 and dichloroketene in 1965–66 with particular emphasis on the use of these ketenes as intermediates in organic synthesis. The ketenes are divided into the following categories: dihaloketenes, aldohaloketenes, alkylhaloketenes, phenylhaloketenes, and some miscellaneous which are not easily classified. The ketenes are discussed within this framework followed by some applications to the synthesis of some important organic compounds.

[1] We define halogenated ketenes as ketenes which have a halogen atom directly attached to the ketene functionality.

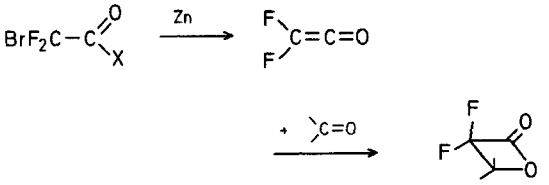
[2] H. STAUDINGER, Chem. Ber. **38**, 1735 (1905).

[3] D. BORRMANN, *Herstellung und Umwandlung von Ketenen*, in HOUBEN-WEYL, *Methoden der Organischen Chemie*, 4th ed., Eu. MÜLLER, editor, Vol. VII/4, Georg Thieme Verlag, Stuttgart, 1968, p. 65.

1. Halogenated Ketenes

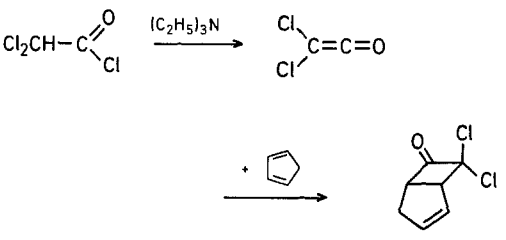
1.1. Dihaloketenes

The preparation of difluoroketene was reported in 1957 by the zinc dehalogenation of chlorodifluoroacetyl bromide[7]. However, several efforts to repeat this work have been unsuccessful[8]. More recently, difluoroketene has been prepared by the zinc dehalogenation of bromodifluoroacetyl halide and this elusive compound trapped with benzaldehyde or acetone to yield β-lactones.



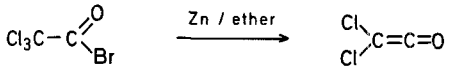
Difluoroketene exhibits an anomalous behavior as dissociation occurs readily at 35° to form carbon monoxide and tetrafluoroethylene[9].

The preparation of dichloroketene was independently reported[10,11,12] from three different laboratories in 1965–1966. The dehydrochlorination of dichloroacetyl chloride with triethylamine in the presence of cyclopentadiene produced the corresponding 1,2-cycloadduct.



[4] H. STAUDINGER, E. ANTHES, H. SCHNEIDER, Chem. Ber. **46**, 3539 (1913).

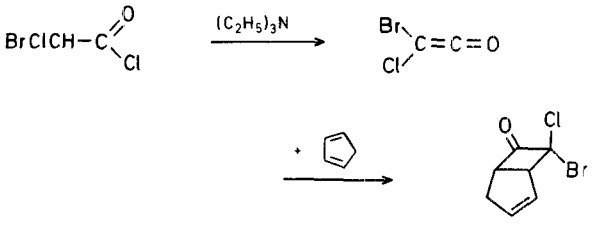
The dehalogenation of trichloroacetyl bromide with zinc was also found to be an effective method for the generation of dichloroketene in solution.



Dibromoketene was also prepared by this method as well as by the dehydrohalogenation of dibromoacetyl chloride with triethylamine and subsequent *in situ* trapping with cyclopentadiene to yield the isolable 1,2-cycloadduct[13]. I.R. absorption bands were reported for dichloro- and dibromoketenes at 1940 and 1970 cm^{-1}, respectively. However, later studies reveal these assignments are incorrect and perhaps represent the corresponding dimers.

Chlorofluoroketene has been prepared by the triethylamine dehydrochlorination of chlorofluoroacetyl chloride in the presence of cyclopentadiene to produce the cycloadduct[14].

Also, bromochloroketene has been generated *in situ* by the dehydrochlorination of bromochloroacetyl chloride and trapped with cyclopentadiene to yield the 1,2-cycloadduct. Interestingly, it appears that only the *endo*-bromo isomer was produced. This is certainly the isomer expected to predominate as will be discussed later[15].



7-Bromo-7-chloro-6-oxobicyclo[3.2.0]hept-2-ene[15]**:** Bromochloroacetyl chloride (15 g, 0.078 mol) was slowly added at room temperature with vigorous stirring to a solution of triethylamine (8.6 g, 0.085 mol) and cyclopentadiene (16 g, 0.25 mol) in hexane (200 ml). After the addition was complete, stirring was continued for 3 hr. The amine salt was removed by filtration and the filtrate concentrated using a rotatory evaporator. The residue was distilled in vacuo; yield: 10 g (60%); b.p. 62–63°/0.15 mm. I.R.: 1805 (C=O), 1610 cm^{-1} (C=O).

Since the initial reports on dichloroketene, many papers have appeared on halogenated ketenes and unfortunately, these reactive compounds have not been isolated but generated and reacted *in situ* as illustrated above. Halogenated ketenes are very susceptible to polymerization and most reactions involving these compounds are accompanied by the formation of significant amounts of tarry material.

While many methods for the preparation of particular ketenes are reported in the literature only the two methods cited above have been successfully employed for the preparation of halogenated ketenes:

- the dehydrohalogenation of an appropriately substituted acid halide,
- the zinc dehalogenation of an appropriately substituted acid halide.

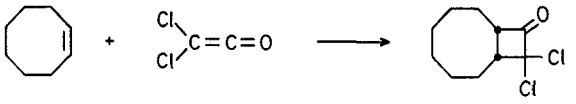
The most common olefin for trapping the elusive halogenated ketenes has been cyclopentadiene and although a 1,4-cycloaddition is possible, the cycloaddition occurs exclusively in a 1,2-manner. This conjugated diene is an unusually reactive cycloaddition partner in ketene cycloaddition reactions. Many other olefins have been investigated and the result is activated or nucleophilic olefins are much more reactive (as evidenced by much higher yields of adducts) than unactivated olefins and deactivated or electrophilic olefins do not undergo cycloaddition or do so in very poor yield. A rather definitive report on dichloroketene has recently appeared which describes in detail the ability of dichloroketene to enter into cycloaddition reactions with various types of olefins[16]. This unusually reactive ketene is inert toward electrophilic olefins such as methyl methacrylate or methyl fumarate. Strained olefins such as norbornene and norbornadiene react sluggishly with dichloroketene. Also, tri- and tetrasubstituted ethylenes are very unreactive toward cycloaddition, i.e., isobutylene undergoes cycloaddition in very low yield and 2,3-dimethyl-2-butene yielded no isolable adduct[15].

The cycloadditions of several derivatives of cyclopentadiene with dichloroketene have been studied and the yields of cycloadducts are generally quite good, e.g., 6,6-dimethylfulvene, 6,6-diphenylfulvene, 1-*t*-butylcyclopentadiene, indene, and methylcyclopentadiene[15–20]. The 1,2-cycloadducts of dichloroketene and the following olefins have also been reported but the yields are generally lower than with cyclopentadiene and derivatives: cyclohexene, cyclopentene, 1-pentene, styrene, 1,5-cyclooctadiene, 1,3-cyclohexadiene, 1,3-butadiene, methylenecyclobutane, ethyl vinyl ether, and dihydropyran[16,21,22].

[5] E. Ott, Liebigs Ann. Chem. **401**, 159 (1914).
[6] H. Staudinger, H. Schneider, Helv. Chim. Acta **6**, 304 (1923).
[7] N.N. Yarovenko, S.P. Motornyi, L.I. Kirenskaya, Zh. Obshch. Khim. **27**, 2796 (1957); Engl. Edit., p. 2832.
[8] a) R.E. Banks, R.N. Haszeldine, D.R. Taylor, J. Chem. Soc. **1965**, 5602, refer to some unpublished work by J.M. Birchall, R.N. Haszeldine, and M. Jefferies, who were unable to repeat this preparation of difluoroketene.
b) Efforts in this laboratory to prepare difluoroketene by this method have also been unsuccessful.
[9] D.C. England, C.G. Krespan, J. Org. Chem. **33**, 816 (1968).
[10] H.C. Stevens, D.A. Reich, D.R. Brandt, K.R. Fountain, E.J. Gaughan, J. Amer. Chem. Soc. **87**, 5257 (1965).
[11] L. Ghosez, R. Montaigne, P. Mollet, Tetrahedron Lett. **1966**, 135.
[12] W.T. Brady, H.G. Liddell, W.L. Vaughn, J. Org. Chem. **31**, 626 (1966).
[13] W.T. Brady, J. Org. Chem. **31**, 2676 (1966).
[14] Y.A. Cherburkow, A.M. Platoshkin, I.L. Knunyants, Dokl. Akad. Nauk SSSR **173**, 1117 (1967); as seen in C.A. **67**, 53761 (1967).

It is interesting to note that the generation of dichloroketene by the dehalogenation method in the presence of 4-*t*-butylcyclohexene produced the expected 1,2-cycloadduct but generation of the ketene by the dehydrohalogenation method yielded no cycloadduct[23].

The stereochemistry of the cycloaddition of dichloroketene with olefins has been determined by an examination of the cycloaddition of this ketene with *cis*- and *trans*-cyclooctene[24]. The cycloaddition with *cis*-cyclooctene produces *cis*-10,10-dichloro-9-oxobicyclo[6.2.0]decane and the cycloaddition with *trans*-cyclooctene yields the *trans*-isomer. The addition of dichloroketene to olefins is therefore considered to be a *cis* stereospecific cycloaddition.

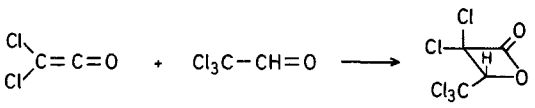


Dichloroketene has been generated by the dehalogenation method in the presence of some steroid olefins (5α-cholest-1-, -2-, and -3-enes) and the corresponding 1,2-cycloadducts isolated[25]. In cycloadditions with cyclohexene systems, dichloroketene cycloadditions are not only stereospecific but highly regioselective, i.e., the newly formed bond of the carbonyl carbon will prefer to be axial with respect to the 6-membered ring (chair conformation)[26,27].

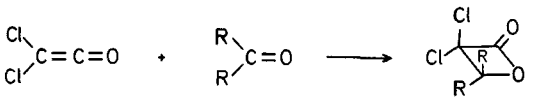
Dichloroketene has also been found to be quite susceptible to undergoing cycloaddition with unsaturated systems other than olefins:

Alkynes. The triethylamine dehydrochlorination of dichloroacetyl chloride in the presence of 2-butyne produced 3,3-dichloro-1,2-dimethyl-4-oxocyclobutene[28].

Carbonyl Compounds. Dichloroketene is effectively trapped when generated by the dehydrohalogenation process with activated carbonyl compounds such as chloral to yield the 2-oxetanones.



Simple ketones such as acetone, cyclohexanone, and acetophenone would not cycloadd to the ketene under these conditions[29,30]. However, cycloaddition will occur with a variety of simple ketones when the ketene is generated by the dehalogenation method. Apparently, the $Zn/ZnX_2 \cdot (C_2H_5)_2O$ activates the ketones to cycloaddition.



[15] W. T. Brady, J. P. Hieble, unpublished results.

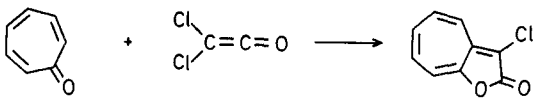
[16] L. Ghosez, R. Montaigne, A. Roussel, H. Vanlierde, P. Mollet, Tetrahedron **27**, 615 (1971).

Unfortunately, simple aldehydes will not undergo cycloaddition under these conditions as trimerization and polymerization of the aldehyde occurs[31]. As indicated earlier, difluoroketene adducts of acetone and benzaldehyde have been reported[9].

Activation of Zinc[12]:
Hydrated copper sulfate (14 g, 0.016 mol) was dissolved in water (150 ml), and this solution was added to zinc dust (60 g, 0.92 g-atom). This mixture was stirred for 2 hr. The zinc dust was removed by filtration and washed several times with acetone. The zinc was dried in a vacuum oven at 100° prior to use in the dehalogenation reaction.

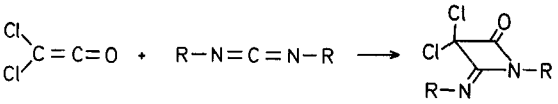
3,3-Dichloro-1-oxaspiro[3.5]nonan-2-one:
Trichloroacetyl chloride (20 ml, 182 mmol) in ether (50 ml) was added dropwise to rapidly stirred zinc (15 g in 200 ml of ether containing 25 ml of cyclohexanone). The reaction temperature was maintained at 30° with a water bath. Filtration after 6 hr showed 90% of the theoretical amount of zinc had been consumed. The filtrate was concentrated and extracted with hexane. Removal of the hexane and distillation of the residue afforded a 51% yield of the 2-oxetanone; b.p. 62°/0.2 mm.
I.R.: 1850 cm^{-1} (C=O).

The cycloaddition of dichloroketene with tropone appears to be novel in that a 1,3-cycloaddition apparently occurs.



This is probably the result of a nucleophilic attack by the oxygen of tropone on the ketene to yield a dipolar intermediate which undergoes ring closure followed by loss of hydrogen chloride to yield the observed product[32].

Carbodiimides. Dibromo- and dichloroketenes readily cycloadd to dialkylcarbodiimides to yield the azetidinones (β-imino-β-lactams)[33,34,35].



Imines. Imines cycloadd to dichloroketene in nearly quantitative yield to produce α,α-dihalo-β-lactams which are considered potential precursors of various functionally substituted β-lactams[36]. α,β-Unsaturated imines yield both 1,2- and 1,4-cycloadducts. This is possible in these systems because cycloaddition across the C=N is well established to be a two-step process via a dipolar intermediate[37-40].

[17] T. Asao, T. Machiguchi, T. Kitamura, Y. Kitahara, Chem. Commun. **1970**, 89.

[18] R. E. Harmon, W. D. Barta, S. K. Gupta, G. Slomp, Chem. Commun. **1970**, 935.

[19] R. W. Turner, T. Seden, Chem. Commun. **1966**, 399.

[20] P. D. Bartlett, T. Ando, J. Amer. Chem. Soc. **95**, 7518 (1970).

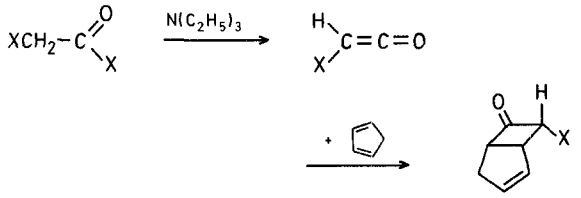
[21] W. T. Brady, O. H. Waters, J. Org. Chem. **32**, 3703 (1967).

[22] P. R. Brook, J. G. Griffiths, Chem. Commun. **1970**, 1344.

[23] A. Hassner, V. R. Fletcher, D. P. G. Hamon, J. Amer. Chem. Soc. **93**, 264 (1971).

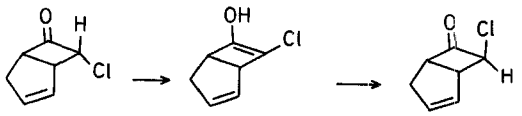
1.2. Aldohaloketenes

The dehydrohalogenation of haloacetyl halides in the presence of cyclopentadiene produces the corresponding 1,2-cycloadducts of fluoro-, chloro-, and bromoketenes. Since aldoketenes (monosubstituted ketenes) are by nature unsymmetrical, the possibility exists for the formation of two stereomers in the cycloaddition reaction as illustrated with cyclopentadiene. These unsymmetrical aldohaloketenes undergo cycloaddition stereospecifically to yield only the *endo*-halo isomer[41-44].

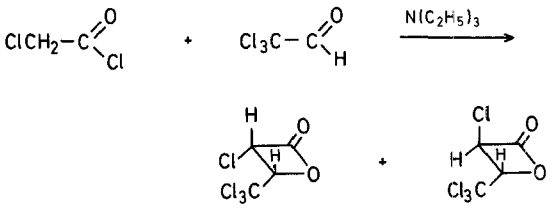


The cycloadduct of chloroketene and 6,6-dimethylfulvene has also been prepared by this method[17].

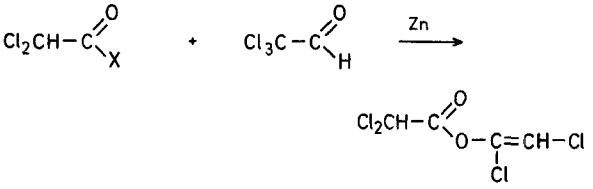
endo-7-Chloro-6-oxobicyclo[3.2.0]hept-2-ene has been isomerized to some extent to the *exo*-chloro isomer by treatment with triethylamine[45]. If the *in situ* cycloaddition of chloroketene and cyclopentadiene is conducted in an excess of amine, some of the *exo*-chloro isomer is produced[15]. This formation of the *exo*-chloro isomer is probably a result of isomerization through the enol form of the ketone.



When chloroketene is prepared by the dehydrohalogenation method in the presence of chloral, a mixture of *cis*- and *trans*-4-trichloromethyl-2-oxetanones are produced.



However, the preparation of chloroketene by the dehalogenation of dichloroacetyl chloride yields only α,β-dichlorovinyl dichloroacetate[46,47].

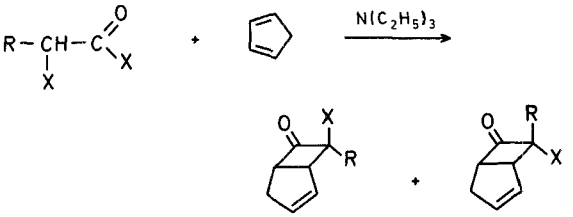


Chloro- and fluoroketenes have also been trapped with diisopropylcarbodiimide to yield the β-imino-β-lactams[34].

In situ reactions of the aldohaloketenes involve the formation of more polymeric material and lower yields of adducts than the dihaloketenes. However, this is perhaps as expected since aldoketenes are well known to be less stable than ketoketenes.

1.3. Alkylhaloketenes

The dehydrohalogenation of 2-haloalkanoyl halides with triethylamine produces alkylhaloketenes. Unfortunately, isolation of these ketenes has not yet been possible and the elusive intermediates were trapped *in situ* with cycloaddition partners in an analogous fashion as described above. Methylchloro-, methylbromo-, ethylchloro-, and ethylbromoketenes were first prepared and trapped with cyclopentadiene to produce the isolable adducts[48,49]. These unsymmetrical ketenes yield a distribution of *endo*-alkyl and *exo*-alkyl 1,2-cycloadducts as illustrated with cyclopentadiene.



The isomer distributions are strongly dependent upon the polarity of the solvent, the nature of the ketene substituents, and the reaction temperature[50,51]. When the alkyl portion of the alkylhaloketenes is systematically increased from methyl to *t*-butyl, the amount of the *endo*-alkyl isomer produced increases, i.e., the larger substituent has a greater tendency to accept the *endo*-position in the adduct[44,51,52]. This is consistent with a concerted cycloaddition involving an orthogonal approach of the ketene and olefin as dictated by the principle of orbital-symmetry conservation[53].

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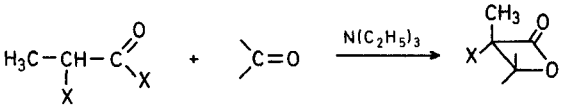
[24] R. MONTAIGNE, L. GHOSEZ, Angew. Chem. **80**, 194 (1968); Angew. Chem., Internat. Edit. **7**, 221 (1968).
[25] G. M. L. CRAGG, J. Chem. Soc. [C] **1970**, 1829.
[26] A. HASSNER, J. Org. Chem. **33**, 2684 (1968).
[27] V. R. FLETCHER, A. HASSNER, Tetrahedron Lett. **1970**, 1071.
[28] H. KNOCHE, Liebigs Ann. Chem. **722**, 232 (1969).
[29] D. BORRMANN, R. WEGLER, Chem. Ber. **99**, 1245 (1966).
[30] D. BORRMANN, R. WEGLER, Chem. Ber. **100**, 1575 (1967).
[31] W. T. BRADY, A. PATEL, J. Heterocyclic Chem., in press.
[32] J. CIABATTONI, H. W. ANDERSON, Tetrahedron Lett. **1967**, 3377.
[33] R. HULL, J. Chem. Soc. [C] **1967**, 1154.
[34] W. T. BRADY, E. D. DORSEY, F. H. PARRY, J. Org. Chem. **34**, 2846 (1969).
[35] C. METZGER, J. KURZ, Chem. Ber. **104**, 50 (1971).
[36] F. DURAN, L. GHOSEZ, Tetrahedron Lett. **1970**, 245.
[37] A. GOMES, M. M. JOULLIE, Chem. Commun. **1967**, 935.
[38] H. B. KAGAN, J. L. LUCHE, Tetrahedron Lett. **1968**, 3093.

The cycloaddition of methylchloroketene with cyclopentene, cyclohexene, 1,3-cyclohexadiene, cyclooctene, dihydropyran, ethyl vinyl ether, methylcyclopentadiene, 6,6-dimethylfulvene, and indene has also been reported. The *endo-/exo*-methyl isomer ratios were found to vary only slightly. The isomer ratios for the cycloaddition of methylbromoketene with 1,3-cyclohexadiene, dihydropyran, ethyl vinyl ether, and cyclopentadiene were also nearly constant. The synthesis of some other alkylhaloketenes led to the development of a quantitative relationship (log *endo-/exo-* $= 1.5\,\Delta E_s$) utilizing Taft's substituent constants (E_s) for the ketene substituent which reveals that the strong preference for *endo* or *cis* selectivity is due to the size of the larger substituent on the ketene molecule[54].

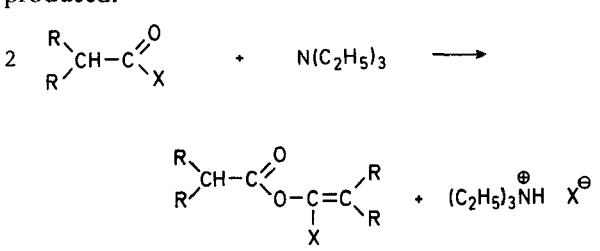
Since alkylhaloketenes cycloadd to cyclopentadiene usually yielding both isomers with a predominance of that isomer with the larger substituent on the ketene in the *endo*-position, a study was made to detail the effect of removing the steric bulk from the ketene functionality. The cycloaddition of cyclohexylbromo-, cyclohexylmethylbromo-, and 2-cyclohexylethylbromoketenes with cyclopentadiene produced both *endo*- and *exo*-bromo isomers. The isomer distributions were found to be dependent upon the polarity of the solvent in which the cycloadditions were effected as had been previously noted for other systems[50,51]. As expected, the *exo-/endo*-bromo isomer ratios decreased as the cyclohexyl moiety was removed from the reaction site. This decrease in isomer distribution further reflects the steric control in these cycloadditions[55,56].

Other alkylhaloketenes which have been formed *in situ* and trapped with cyclopentadiene and other olefins include methyliodo-, propylbromo-, isopropylchloro-, isopropylbromo-, butylbromo-, butylchloro-, *t*-butylbromo-, and octylbromoketenes[51,54,55].

Methylchloroketene has also been trapped in solution with dicyclohexylcarbodiimide to yield the expected β-imino-β-lactam[34]. Methylchloro- and methylbromoketenes, generated by the dehydrohalogenation method, cycloadd to chloral, 2-chlorobenzaldehyde, and *sym*-dichlorotetrafluoroacetone yielding the 2-oxetanones. With the unsymmetrical carbonyl compounds, both isomers were produced in approximately equal amounts. The carbonyl group must be activated as propanal, benzaldehyde, acetone, and butanone do not undergo cycloaddition with these ketenes under these conditions[31].



In an effort to prepare and isolate the dimer of methylchloroketene, the triethylamine dehydrochlorination of 2-chloropropanoyl chloride was conducted in the absence of a cycloaddition partner. When the order of addition was such that the amine was slowly added to the acid halide, a compound was isolated which was originally considered to be a 1:1 adduct of methylchloroketene and 2-chloropropanoyl chloride[57]. However, this compound was not an adduct of the ketene and acid halide but rather 1,2-dichloropropenyl 2-chloropropanoate[58]. Similar results were obtained with dichloroacetyl chloride and triethylamine to produce trichlorovinyl dichloroacetate[59]. The reaction of triethylamine with a variety of acid halides has been studied and a number of these α-halovinyl esters (enol esters of acid halides) produced.



This is not a general reaction but occurs for disubstituted acid halides when at least one of the substituents is halogen. The α-halovinyl esters are considered to be the result of acylation of an intermediate enolate ion[60].

The formation of α-halovinyl esters can be a very serious competing reaction in the generation of halogenated ketenes *in situ*. This side reaction will occur in the formation of most alkylhalo-, dihalo-, and phenylhaloketenes if the order of addition is amine to acid halide. The reaction can be minimized or eliminated if the acid halide is slowly added to the amine.

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1.4. Phenylhaloketenes

Phenylchloro- and phenylbromoketenes have been prepared by the dehydrochlorination of α-chloro- and α-bromophenylacetyl chlorides at room temperature[34,61]. Numerous attempts to isolate phenylchloroketene resulted in a tarry polymer of the ketene. However, the ketenes could be trapped by heating the dehydrohalogenation mixtures with cyclopentadiene or 1-methylcyclopentadiene to yield the isolable cycloadducts in good yield. Only the *endo*-phenyl isomer was detected in each system. This stereochemical result is consistent with the pattern as described above whereby the larger substituent on the ketene sterically prefers the *endo*-position and when there is a large difference in the size of the ketene substituents this isomer is formed to the exclusion of the other[45,61,62].

Phenylchloroketene has also been trapped with dicyclohexylcarbodiimide to produce the β-imino-β-lactam[34].

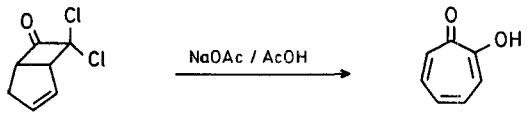
1.5. Miscellaneous Halogenated Ketenes

Some other halogenated ketenes which do not readily correspond to the above categories have also been prepared and trapped *in situ* with cyclopentadiene, i.e., trifluoromethylfluoro-, bromoethylbromo-, vinylbromo-, and isopropenylbromoketenes[14,15].

2. Applications of Halogenated Ketenes in Synthesis

2.1. Tropolones and 2-Alkyltropones

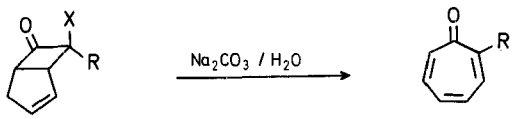
The initial report on dichloroketene described the conversion of the dichloroketene-cyclopentadiene adduct into tropolone by hydrolysis with sodium acetate in aqueous acetic acid[10].



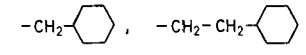
An improved method for effecting this conversion has recently appeared which utilizes acetate ion in water as the medium for the conversion. Triethylammonium acetate in aqueous acetone will also convert the adduct to tropolone but sodium methoxide or aqueous carbonate opens the 4-membered ring. The adducts of dibromo- and bromochloroketenes with cyclopentadiene have also been solvolyzed to tropolone and these solvolyses proceed as smoothly as with the dichloroketene adduct[55]. In a similar fashion, the hydrolysis of the adduct of dichloroketene and 1-*t*-butylcyclopentadiene affords β-*t*-butyltropolone and hydrolysis of the adduct of dichloroketene and 1-methylcyclopentadiene yields 4-methyltropolone[20,55]. The adduct of dichloroketene and indene has been solvolyzed to 4,5-benzotropolone[19]. Solvolysis of the adduct of dichloroketene and 6,6-dimethylfulvene by triethylammonium acetate in aqueous acetone yields α-dolabrin (3-isopropenyltropolone), whereas solvolysis of the chloroketene-6,6-dimethylfulvene adduct under various conditions has been reported to not yield any tropone[17]. However, the solvolysis of the chloroketene-cyclopentadiene adduct to tropone has been indicated in two separate reports in low yield but no details whatever were given[17,63].

4-Methyltropolone[20,55]:
To a solution of glacial acetic acid (50 g), water (60 g), triethylamine (100 g), and acetone (~300 ml) was added 0.08 mol of the cycloadduct of dichloroketene and 1-methylcyclopentadiene. This solution was refluxed for 1 hr. After cooling to room temperature, the reaction solution was extracted with ether (2×500 ml). The combined ether extracts were evaporated on a rotatory evaporator and the residue added to benzene (300 ml) and the remaining water removed by azeotropic distillation. The benzene is evaporated and the residue distilled in vacuo; yield: 70%; b.p. 95–100°/0.1 mm. The tropolone solidified upon cooling; m.p. 74–75°, after sublimation m.p. 75° (Ref.[64], m.p. 75°).

The solvolysis of the cycloadducts of dichloroketene and cyclopentadiene (and cyclopentadiene derivatives) has been extended to include the adducts of alkylhaloketenes and cyclopentadiene with the result being the development of a new general method for the preparation of 2-alkyltropones. The initial report described the solvolysis in 70% aqueous acetic acid containing sodium acetate but an improved method involves solvolysis in refluxing 20% aqueous sodium carbonate. The following 2-alkyltropones have been prepared by this method[55,65]:



R = CH_3, C_2H_5, i-C_3H_7, n-C_4H_9, n-C_8H_{17}, 



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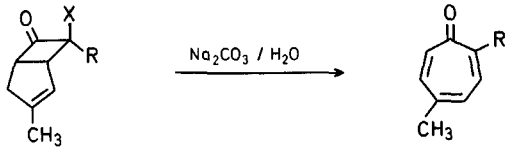
It is very noteworthy that only the *exo*-7-halo-*endo*-7-alkyl-6-oxobicyclo[3.2.0]hept-2-enes undergo conversion to the 2-alkyltropones. There is a competing rearrangement reaction which accompanies these solvolysis reactions which is discussed below. The solvolysis of the chloroketene-cyclopentadiene adduct to tropone, as mentioned above, probably occurs only from the *exo*-chloro isomer. Since this isomer has been difficult to obtain, the preparation of tropone by this method has been impeded.

The solvolysis of the adducts of methylchloroketene and 1-methylcyclopentadiene and isopropylchloroketene and 1-methylcyclopentadiene (the *exo*-halo isomers) yield 2,5-dimethyltropone and 2-isopropyl-5-methyltropone, respectively[55].

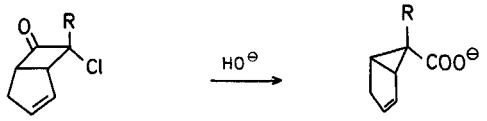


R = CH_3, i-C_3H_7

The preparations cited above represent the first convenient synthesis of tropone derivatives from easily available and inexpensive starting materials.

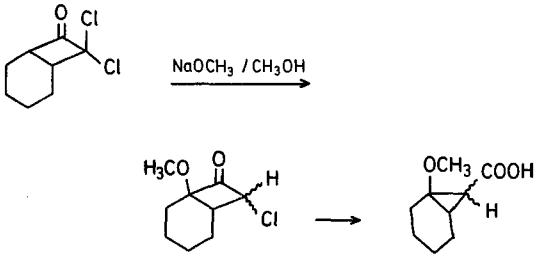
2.2. Cyclopropane Derivatives

The cycloadducts of cyclopentadiene and alkylhaloketenes undergo a stereospecific base-catalyzed ring-contraction reaction.

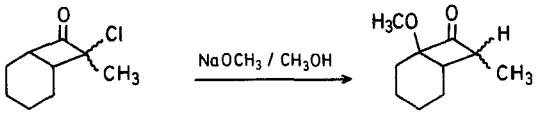


R = CH_3, C_2H_5, n-C_3H_7, n-C_4H_9, i-C_3H_7, H

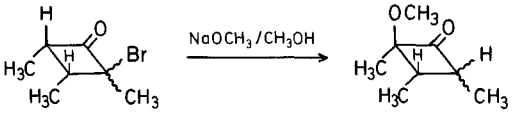
The *endo*-chloroketones yield the corresponding *endo*-acids and the *exo*-chloroketones the *exo*-acids[52]. The adduct of dichloroketene and cyclohexene undergoes this same type of ring contraction but substitution precedes the rearrangement[27].



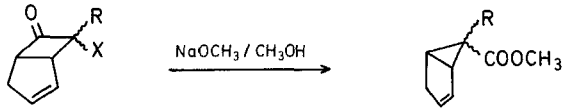
Treatment of the adduct of methylchloroketene and cyclohexene with sodium methoxide in refluxing methanol yields only the substitution product since a second leaving group is not present for ring contraction as in the dichloroketene case.



The adduct of methylbromoketene and *cis*-2-butene also undergoes just this substitution reaction.



The adducts of methylchloro- and methylbromoketene and cyclopentadiene also yield substitution at C-5 when treated with sodium methoxide in methanol at 0–5°. However, treatment of these adducts with sodium methoxide in methanol at reflux affords ring contraction rather than substitution[66].



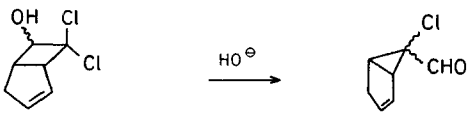
R = CH_3, H, $-CH{=}CH_2$
X = Cl, Br

This substitution probably involves attack of the methoxide ion on the enol form of the cyclobutanones. The enol form of the adducts of cyclohexene and 2-butene would be expected to be much more stable than the enol form of the cyclopentadiene adduct due to the increased amount of strain[66].

The cycloadducts derived from dichloroketene and olefinic compounds undergo a ring opening reaction in contrast to ring contraction in the presence of strong base[16,67].

6-Methoxycarbonyl-6-methylbicyclo[3.1.0]hex-2-ene:
A 150 ml portion of methanol to which 4 g of sodium had been added was vigorously refluxed while a solution of 10 g of the methylchloro- or methylbromoketene adduct of cyclopentadiene in 25 ml of methanol was added. There was an immediate precipitation of sodium halide. Refluxing was continued about 15 min. and then the mixture was added to 150 ml of water. This aqueous mixture was extracted with chloroform. Upon drying the combined extracts, the solvent was removed on a rotatory evaporator and the residue distilled at 60–62° at 2 mm; yield: 60%.

An interesting rearrangement of cyclobutanols, obtained by the sodium borohydride reduction of adducts of halogenated ketenes and cyclopentadiene, has been reported. The *endo*-alcohol of the adduct of dichloroketene and cyclopentadiene upon treatment with base yielded the *exo*-carboxaldehyde which could be easily oxidized to the corresponding acid.



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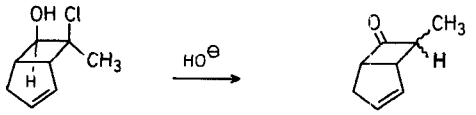
The *exo*-alcohol analogously produced the *endo*-aldehyde. This is a stereospecific base-catalyzed ring contraction involving the chlorine atom *trans* to the hydroxy group[68].

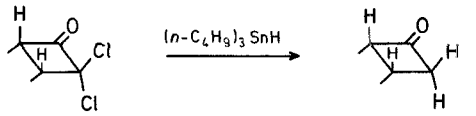
The cyclobutanols derived from chloro- and methylchloroketenes and cyclopentadiene behave in a similar fashion except for one notable exception. Base treatment of the 7-*exo*-chloro-6-*exo*-alcohol produced no aldehyde. A hydride shift was demonstrated to have occurred, thus producing the methyl ketone.



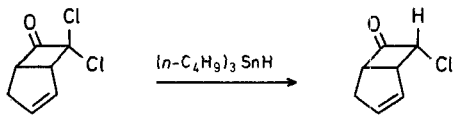
Ring contraction, the normally favored reaction course is not observed because the required conformation produces a bad interaction between the 7-*endo*-methyl and C-4 hydrogen atom[69].

2.3. Removal of Halogen from Cycloadducts

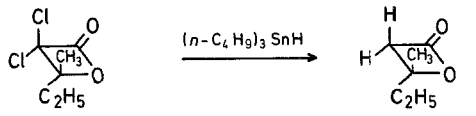
Halogenated ketene-olefin cycloadducts can be readily dehalogenated with tributyltin hydride or with zinc in acetic acid to the parent ketones[16,70].



This reduction may be done selectively with tributyltin hydride if the cycloadduct is present in excess, i.e., 7,7-dichloro-6-oxobicyclo[3.2.0]hept-2-ene is preferentially reduced to yield only the *endo*-chloro isomer[42].



The removal of one chlorine from the adduct of dichloroketene and butanone occurs readily with tributyltin hydride but the removal of both halogens appears to require the addition of a free radical source such as azobisisobutyronitrile[71].



The readiness with which the halogen(s) may be removed from the cycloadducts enables the easy accessibility of 4-membered ring compounds not readily available from non-halogenated ketene cycloadditions because of low reactivity, i.e., dichloroketene is a very reactive cycloaddition partner when compared to ketene and methylchloroketene is much more reactive than methylketene.

Conclusion

The cycloaddition of halogenated ketenes to olefins provides a useful and convenient source of α-halo- and α,α-dihalocyclobutanones from inexpensive readily available starting materials. Also, the cycloaddition of these ketenes with other unsaturated linkages such as carbonyl, imines, and carbodiimides provides easy access to functionally substituted β-lactones, β-lactams, and β-imino-β-lactams. The halogenated ketene cycloadducts provide an important substituent on the cycloadduct not found in other ketene cycloadducts: a good leaving group; hence, the solvolysis and rearrangement reactions. The synthetic possibilities offered by the halogenated ketenes and the corresponding cycloadducts will probably not be known for some time since new applications to organic syntheses are being discovered routinely.

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