Tetrahedron Vol. 37, No. 17, pp. 2949 to 2966, 1981
Printed in Great Britain.

0040-4020/81/172949-18$05.00/0
Pergamon Press Ltd

TETRAHEDRON REPORT NUMBER 113

SYNTHETIC APPLICATIONS INVOLVING HALOGENATED KETENES

WILLIAM T. BRADY

Department of Chemistry, North Texas State University, Denton, TX 76203, U.S.A.

(*Received in the U.S.A.* 16 *March* 1981)

INTRODUCTION

We wrote a review on halogenated ketenes as valuable intermediates in organic synthesis in 1970[1] and since that time numerous examples of the synthetic utility of halogenated ketenes, particularly dichloroketene, have been published. Recently, two volumes have been published on *The Chemistry of Ketenes, Allenes, and Related Compounds.*[2]

This review of halogenated ketenes will focus on reports since the review of 1970 and also attention will be directed to the halogenated ketene cycloaddition products rather than the ketenes themselves. The section on the preparation of halogenated ketenes briefly surveys the different halogenated ketenes and the sections that follow describe the synthetic applications of the halogenated ketenes, particularly dichloroketene.

Early attempts to prepare halogenated ketenes (defined as ketenes with a halogen atom directly bonded to the ketene functionality) were unsuccessful and it was concluded that these ketenes were possibly formed but were unstable and polymerized under the reaction conditions.[3-6] However, in recent years it has been demonstrated that while halogenated ketenes are unstable these ketenes can be generated and trapped *in situ* with unsaturated compounds to yield a wide variety of synthetically useful cycloaddition products. Halogenated ketenes are quite susceptible to polymerization and reactions involving these labile compounds are often accompanied by the formation of tarry polymerization products.

There are essentially four general reactions which ketenes undergo, cycloaddition, nucleophilic addition, dimerization and polymerization. These latter two reactions are usually considered undesirable and efforts are made to minimize dimerization and polymerization. Although ketenes undergo nucleophilic addition reactions to yield acylation products, there are usually simpler routes to these compounds and therefore ketene acylation reactions are generally not synthetically useful. Clearly the most synthetically useful reaction of ketenes is the (2+2) cycloaddition reaction to form compounds with four-membered rings. This reaction constitutes one of the few routes to synthetically versatile four-membered rings. The developments in the past few years involving halogenated ketenes have greatly widened the scope and utility of this important synthetic reaction. The halogenated ketenes are generally more reactive in cycloaddition reactions than alkyl- or arylketenes. The cycloaddition products from halogenated ketenes are useful synthetic intermediates because the halogen atom(s) is easily replaced by

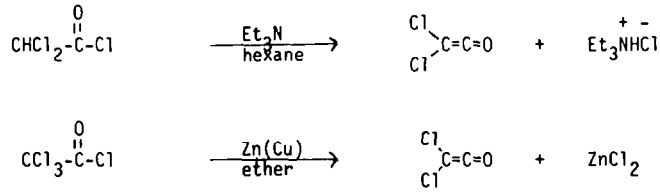
hydrogen and also, since the halogen is a good leaving group, substitution and ring contraction reactions of the ketene cycloadducts become important. Another significant consideration is that the starting materials for the preparation of halogenated ketenes are inexpensive and readily available.

It is interesting to note that halogenated ketenes do not undergo dimerization to cyclobutanediones or 2-oxetanones as most all other ketenes do.

Although several halogenated ketenes are known, the large majority of synthetic applications of these ketenes is with dichloroketene. The availability of this ketene by two different methods, the reactivity and generally good to excellent yields and ease of removal of the halogens are responsible for this wide applicability. Dichloroketene is more reactive in ketene-olefin cycloaddition reactions than nonhalogenated ketenes. The reactivity of dichloroketene with unactivated olefins such as cyclopentene,[7] cyclohexene,[8] 1-methylcyclohexene,[9] and 2,3-dimethyl-2-butene[9,10] contrasts sharply with the relative inertness of ketene, alkyl- or even aryl substituted ketenes under the same mild experimental conditions. The reactivity of olefinic compounds in ketene cycloaddition reactions parallels the nucleophilicity of the olefin. Both activated olefins and unactivated olefins readily enter into cycloaddition reactions with the electrophilic dichloroketene but deactivated olefins such as acrylonitrile do not undergo cycloaddition even with dichloroketene.[8]

Preparation of halogenated ketenes

The two most widely used methods for the preparation of ketenes are (a) the dehalogenation of an appropriately substituted α-haloacid halide with activated zinc;[11-13] and (b) the triethylamine dehydrohalogenation of an acid halide.[14-16] Most of the halogenated ketenes are generated by one of these two methods and both methods have been widely used for the *in situ* generation of dichloroketene as illustrated. However, there are certain limitations to each of these two methods. Tertiary amines and/or



ammonium salts are known to catalyze the polymerization of particularly low molecular weight ketenes.[8] The zinc dehalogenation method is applicable only for olefins that are not susceptible to cationic polymerization. The zinc halide etherate formed in the reaction catalyzes the polymerization of olefins such as ethyl vinyl ether, styrene, furan, enol ethers, cyclopentadiene and other conjugated dienes.[7-9]

The preparation of dichloroketene was independently reported from three different laboratories in 1965–66 by both the dehydrohalogenation and the dehalogenation methods.[7,17,18] The dehydrohalogenation method of generating dichloroketene has been more widely used in recent years but the recent report of two improved procedures for the dehalogenation method may result in a more widespread use of this method.[9,10] The essential feature of one improved method involves formation of the reactive dichloroketene so as to deter polymerization of the ketene in favor of the cycloaddition process. This is accomplished by effecting the *in situ* cycloadditions at a higher dilution and a slower rate of addition of the acid halide to the zinc slurry. The results of this improved procedure were rather remarkable in that heretofore *in situ* cycloadditions with tetrasubstituted olefins had been largely unsuccessful and are now possible in good yield. The scope of the reaction of the cycloaddition of dichloroketene with olefins was significantly broadened by this report.[9]

The other improved procedure reports that the addition of phosphorus oxychloride to the reaction mixture of zinc, trichloroacetyl chloride and the olefin facilitates product isolation and leads to improved yields of dichloroketene cycloaddition products. The role of the phosphorous oxychloride appears to be that of complexing the zinc chloride.[10]

The preparation of difluoroketene was first reported in 1957 but several attempts to repeat this work have been unsuccessful.[19,20] However, difluoroketene has been successfully prepared by the dehalogenation of bromodifluoroacetyl halides with zinc.[21]

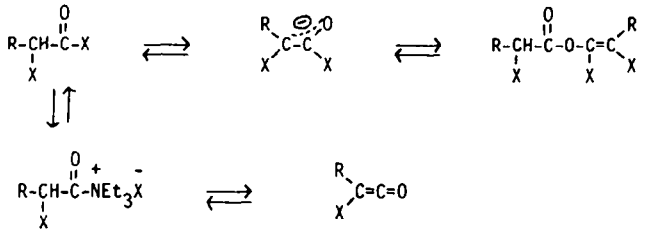
Dibromoketene has been prepared by both of the above described methods and also by treatment of the trimethylsilyl ester of tribromoacetic acid with triphenylphosphine.[22,23]

Chlorofluoroketene has been prepared by the triethylamine dehydrohalogenation of

chlorofluoroacetyl chloride in the presence of cyclopentadiene to yield the (2+2) cycloaddition product.[24] Also, bromochloroketene has been generated by the dehydrochlorination of bromochloroacetyl chloride and trapped with cyclopentadiene.[25]

The dehydrohalogenation of haloacetyl halides in the presence of cyclopentadiene produces the corresponding (2+2) cycloadducts of fluoro-, chloro-, and bromoketenes.[26,27] These haloketenes have also been prepared by the dehalogenation of appropriately substituted dihaloacetyl halides.

The triethylamine dehydrohalogenation of α-haloacid halides yields alkylhaloketenes which have been trapped *in situ* by olefinic compounds.[28] There is another reaction which competes with ketene formation and results in the formation of an α-halovinyl ester.[29-31] The α-halovinyl esters are likely formed by acylation of an intermediate enolate ion.[32] The formation of the α-halovinyl ester can be



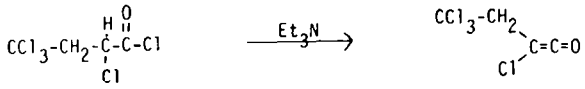
minimized or even eliminated if the acid halide is slowly added to triethylamine which prevents the formation of the enolate ion in an excess of the acid halide. The formation of the enolate ion is reversible and it is clear that a complex series of equilibria are involved in the dehydrohalogenation of α-haloacid halides and that the order and rate of addition of the reagents is very important.

Phenylbromo- and phenylchloroketenes have been prepared by the dehydrochlorination of α-bromo- and α-chlorophenylacetyl chlorides.[33-35] The ketenes are unstable but have been trapped with olefins to yield the (2+2) cycloaddition products.

Chlorocyanoketene has been prepared by the thermal cleavage of β-azido-α-chloro-γ-methoxy-$\Delta^{\alpha,\beta}$-crotonolactone. This ketene is not stable but has been trapped in solution with dicyclohexylcarbodiimide.[36]

Trifluoromethylfluoroketene has been prepared and trapped *in situ* by the dehydrochlorination of 2,3,3,3-tetrafluoropropanoyl chloride in the presence of cyclopentadiene.[24]

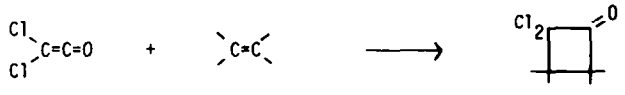
Chlorotrichloroethylketene has recently been prepared by the dehydrochlorination of 2,4,4,4-tetrachlorobutanoyl chloride in the presence of isobutylene. The 2-chlorocyclobutanone is a key intermediate



in the synthesis of an important precursor to a pyrethroid acid.[37]

Cyclobutanones

Dichloroketene readily undergoes a (2+2) cycloaddition with various olefinic compounds to yield 2,2-dichlorocyclobutanones. Some examples of the wide variety of olefinic compounds which undergo

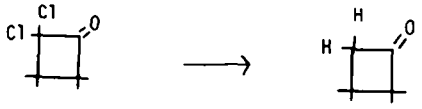


this cycloaddition reaction include cyclopentadiene,[17] indene,[38] cyclohexene,[8] styrene,[8] 1-pentene,[8] 1,5-cyclooctadiene,[8] ethyl vinyl ether,[8] steroid olefins,[39] diphenylfulvene,[40] diphenylbenzofulvene,[40] *cis*- and *trans*-cyclooctene,[41] norbornene,[42] norbornadiene,[42] dimethylfulvene,[44] 1-t-butylcyclopentadiene,[45] 2-methylcyclopentadiene,[25] trimethylsilylcyclopentadiene,[46] 2,3-dimethyl-2-butene,[9] 1-methylcyclohexene,[9] 2-methyl-2-butene,[9] α-pinene[9] and bicyclopropylidene.[47]

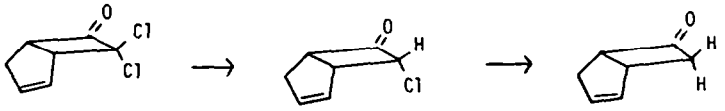
Dichloroketene reacts with unsymmetrical olefins in a regiospecific manner, i.e. the most nucleophilic carbon atom of the olefin is always bonded to the sp hybridized carbon atom of the ketene molecule. The reaction is rather general and the yields moderate to good. Dichloroketene generation and subsequent

cycloaddition reactions require only mild experimental conditions. Since the precursors to the ketene, dichloroacetyl chloride and trichloroacetyl chloride, are so readily available, this has become an increasing attractive method for the synthesis of cyclobutanone derivatives.

The chlorine atoms may be easily removed from the 2,2-dichlorocyclobutanones by zinc in acetic acid or tri-*n*-butyltin hydride in near quantitative yields.[26,42,48] The 2,2-dichlorocyclobutanones may even be selectively reduced to the monochlorocyclobutanones, i.e. 7,7-dichlorobicyclo(3.2.0)-hept-2-en-6-one

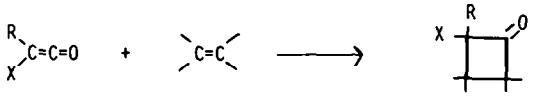


preferentially reduces to yield only the *endo*-chloro isomer.[26,48] The resultant nonhalocyclobutanones possess the same structure as would be obtained by the cycloaddition of ketene itself with the olefin.

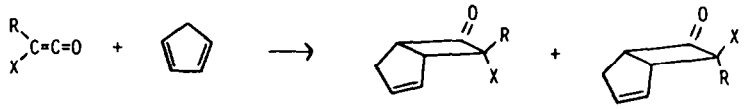


The advantage of dichloroketene over ketene is the much greater reactivity of the ketene. Hence, the use of dichloroketene followed by the reductive halogen removal described significantly broadens the scope of cyclobutanone synthesis.

Alkylhaloketenes also react with a wide variety of olefinic compounds under mild conditions to yield 2-halo-2-alkylcyclobutanones. The yields are generally as good as cycloadditions with dichloroketene.



Cycloaddition with cyclic olefins produces both *endo*- and *exo*-halo-1,2-cycloadducts. The isomer

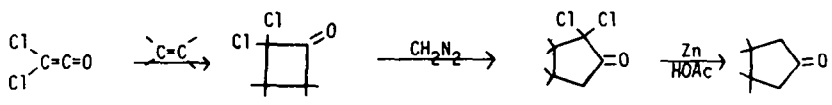


distributions are dependent upon the nature of the substituents on the alkylhaloketene, the solvent media, and the reaction temperature.[49-51]

The monohaloketenes will undergo *in situ* cycloaddition reactions with olefinic compounds to yield 2-halocyclobutanones but the yields are lower than the corresponding dichloroketene cycloadditions and in most instances there are no synthetic advantages to these ketenes.

Cyclopentanones

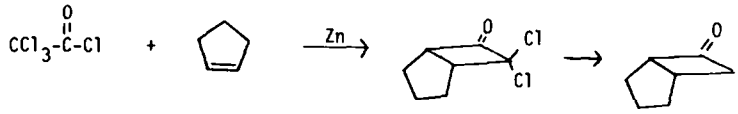
A three-carbon annelation process has been reported which utilizes three known reactions of dichloroketene and cycloaddition products. This report demonstrates the synthesis of cyclopentanones and various cyclopentanone derivatives from olefins.[52] The 2,2-dichlorocyclobutanones, readily available from dichloroketene cycloadditions, cleanly undergo a highly regiospecific one-carbon ring expansion with diazomethane to yield the corresponding 2,2-dichlorocyclopentanones. These ring expanded products are then readily dechlorinated to yield the substituted cyclopentanones. The overall yields from the olefins are generally quite good.



The widespread presence of the cyclopentane ring in many classes of natural products, particularly prostaglandins, should make this three-carbon annelation an attractive synthetic route to many natural products.

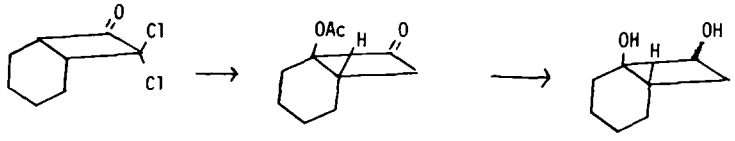
Bicyclo[n.2.0]alkane derivatives

Bicyclo[*n*.2.0]alkanones have become increasingly important as intermediates in a wide variety of synthetic schemes. The regiospecific cycloaddition of ketenes to cyclic olefins makes these bicyclic compounds easily assessible from readily available starting compounds. A representative preparation is illustrated with dichloroketene and cyclopentene to yield the bicyclo[3.2.0]heptanone followed by reductive removal of the chlorine atoms.[7]



Bicyclo[3.2.0]hept-2-en-6-one is readily obtained in good yield by the cycloaddition of dichloroketene and cyclopentadiene followed by the removal of the chlorine atoms as described above. This bicyclic compound has been found to be a versatile intermediate in prostaglandin synthesis[53-57] and also has been used to achieve a short high yield synthesis of *cis*-jasmone.[58] There are numerous other examples involving the use of bicyclo[3.2.0]heptan-6-ones in synthetic schemes leading to compounds of chemical and/or biological interest. An excellent review on these bicyclic compounds has appeared in the literature.[59] Also, the cycloaddition product from dichloroketene and *endo*-dicyclopentadiene has been reportedly used as the starting material for the preparation of prostanoids.[60]

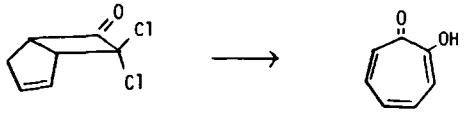
The synthesis of bicyclo[*n*.2.0]alkanediols has been described utilizing the cycloaddition of dichloroketene to a cycloalkene.[61,62] Cyclohexene was treated with dichloroketene to give the corresponding cycloadduct which was treated with triethylammonium acetate and chromium dichloride to give the ketoacetate which was reduced with lithium aluminum hydride to give the bicyclooctanediol. Bicyclo-



heptanediol was similarly prepared.

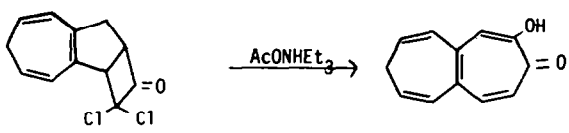
Tropolones and tropones

One of the most interesting synthetic applications of halogenated ketenes is the synthesis of tropolones and 2-alkyltropones from readily available starting materials. Tropolone can be obtained in good yield simply by hydrolysis of the dichloroketene-cyclopentadiene adduct, 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one.[17,63] The cycloaddition products of dibromo- and bromochloroketenes with

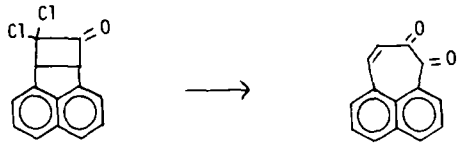


cyclopentadiene have also been solvolyzed to tropolone and these proceed as smoothly as the dichloroketene cycloadduct.[25] In a similar fashion the hydrolysis of the cycloaddition product of dichloroketene and 1-t-butylcyclopentadiene affords β-t-butyltropolone and hydrolysis of the dichloroketene and 1-methylcyclopentadiene cycloaddition product yields 4-methyltropolone.[25,45] The cycloaddition product of dichloroketene and indene has been solvolyzed to 4,5-benzotropolone.[38] The hydrolysis of the cycloadducts of dichloroketene with 1- and 2-isopropylcyclopentadienes afforded thujaplicin (isopropyltropolones).[64] Also, this reaction has been utilized in an elegant synthetic route to an established colchicine precursor.[65] Solvolysis of the cycloadduct of dichloroketene and 6,6-dimethylfulvene yields α-dolabrin (3-isopropenyltropolone) in excellent yield.[44]

In a more recent synthetic application utilizing dichloroketene, cycloaddition with 1,6-dihydroazulene occurred in good yield and hydrolysis with triethylammonium acetate in acetone–water resulted in the formation of 8H-cyclohepta(*d*)tropolone in excellent yield.[66]

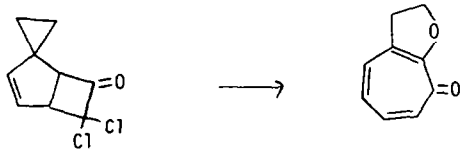


The hydrolysis of the cycloadduct of dichloroketene with acenaphthylene yields pleiadiene-7,8-dione.[67]

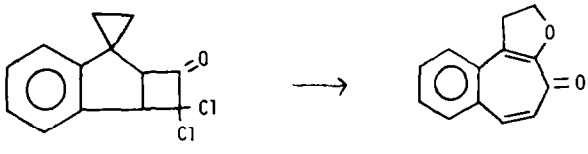


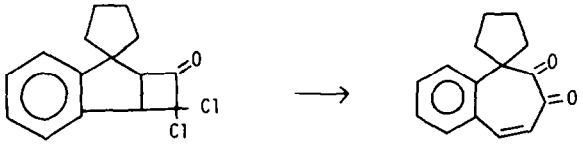
The cycloadduct of dichloroketene and acenaphthylene has also been converted to 1,2-dihydrocyclohepta(*de*)naphthalen-2-ol by ring cleavage and reduction.[68]

Hydrolysis of the cycloaddition product of 5,5-dimethylene-1,3-cyclopentadiene and dichloroketene

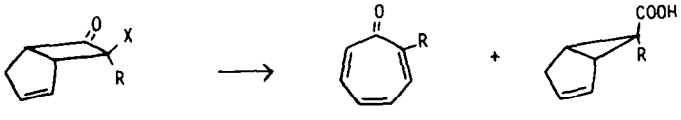


gave a dihydrofurotropone. Similarly, hydrolysis of the following cycloadducts of dichloroketene and some cyclopentadiene derivatives gave the tropone derivatives indicated.[69]





The solvolysis of the cycloadducts of dichloroketene with cyclopentadiene and cyclopentadiene derivatives has been extended to include the adducts of alkylhaloketenes and cyclopentadiene resulting in the development of a new general method for the preparation of 2-alkyltropones. It is quite noteworthy that only the *exo* - 7 - halo - *endo* - 7 - alkylbicyclo[3.2.0]hept - 2 - en - 6 - ones undergo conversion to the 2-alkyltropones. There is a competing Favorskii-type ring contraction reaction which accompanies these solvolysis reactions yielding 6 - alkyl - 6 - carboxybicyclo[3.1.0]hex - 2 - enes. The



relative amounts of 2-alkyltropones and ring contraction produced are strongly dependent on both the nature of the halogen and the steric size of the alkyl substituent on the alkylhaloketene. The *exo*-alkyl isomers of the alkylhaloketene–cyclopentadiene cycloadducts undergo only the ring contraction reaction under the reaction conditions to produce 2-alkyltropones as will be discussed later.[70,71]

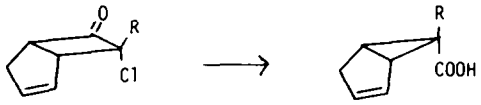
Also, the solvolysis of the cycloadducts of methylchloroketene and 1-methylcyclopentadiene and isopropylchloroketene and 1-methylcyclopentadiene (the *exo*-halo isomers) yield 2,5-dimethyltropone and 2-isopropyl-5-methyltropone respectively.[25]

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

Cyclopropane derivatives

The ring contraction of α-halocyclobutanones with aqueous base to yield cyclopropane derivatives has been known for many years.[72] The cycloadducts of halogenated ketenes and olefinic compounds provides an excellent synthesis of α-halocyclobutanones from readily available starting materials. Consequently, halogenated ketenes become pertinent intermediates in the synthesis of cyclopropane derivatives.

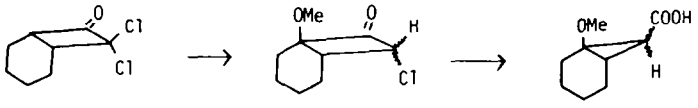
The cycloadducts of cyclopentadiene and alkylhaloketenes, 7 - halo - 7 - alkylbicyclo[3.2.0]hept - 2 - en - 6 - ones, undergo a stereospecific base catalyzed ring contraction reaction to yield 6 - alkyl - 6 -



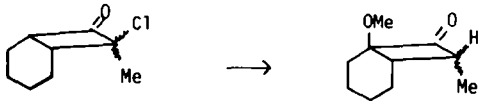
R = Me, Et, n-Pr, i-Pr, n-Bu

carboxybicyclo[3.1.0]hex - 2 - enes.[71,73–76] The *endo*-chloroketones yield the corresponding *endo*-acids and the *exo*-chloro ketones the *exo*-acids. The *exo*-halo isomers also yield 2-alkyltropones as previously mentioned. Because of conformational effects in the cyclobutanone ring, 7 - *exo* - chloro - 7 - *endo* - isopropylbicyclo[3.2.0]hept - 2 - en - 6 - one rearranges abnormally on base treatment and gives three hydroxycyclohexenecarboxylic acids.[77]

In the presence of strong base the cycloadduct of dichloroketene and cyclopentadiene undergoes a ring opening reaction in contrast to the ring contraction with the monochloro cycloadducts.[7,42,63,78] However, the cycloadduct of dichloroketene and cyclohexene upon treatment with sodium methoxide in methanol undergoes substitution and then ring contraction.[79]

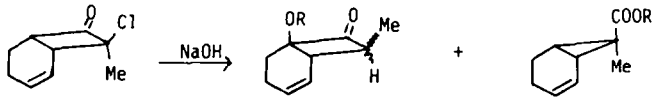


Treatment of the cycloadduct of methylchloroketene and cyclohexene with sodium methoxide in refluxing methanol yields only the substitution product since a second leaving group is not present for ring contraction as in the dichloroketene case. The adducts of methylchloro- and methylbromoketenes



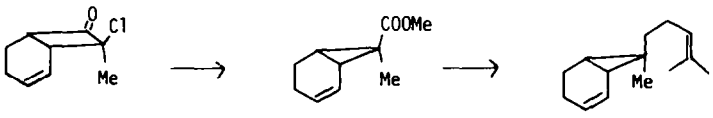
and cyclopentadiene also yield substitution at C-5 when treated with sodium methoxide in methanol at 0–5°. However, treatment of these adducts with sodium methoxide in refluxing methanol afforded ring contraction rather than substitution.[71]

The isomeric *endo*- and *exo*-chlorobicyclic ketones obtained from the cycloaddition of methylchloroketene and 1,3-cyclohexadiene were separately treated with various bases.[80] A stereospecific ring contraction and an allylic substitution involving the enol form of the bicyclic ketone were found to be dependent on the base.

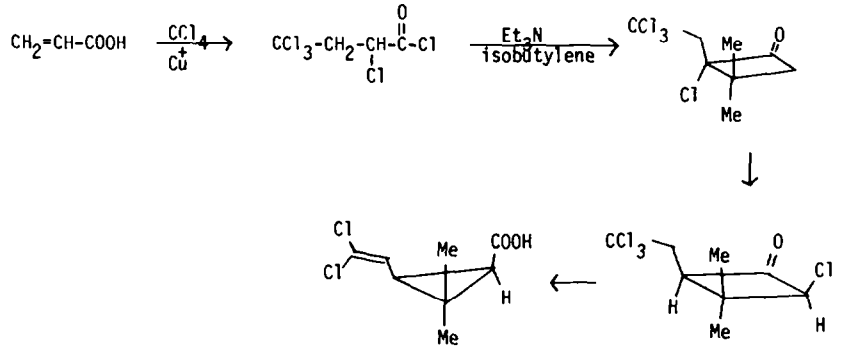


The endo-methyl isomer of the cycloadduct of methylchloroketene and 1,3-cyclohexadiene has been used as a key intermediate in the synthesis of demethylsesquicarene, an analog of natural products. The *endo*-methyl isomer was stereospecifically ring contracted cleanly by refluxing in methanolic silver nitrate

for 24 hr. The ring contracted product was then converted to the demethylsesquicarene.[81]

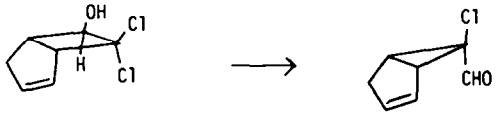


The (2+2) cycloaddition of the new 2,2,2-trichloroethylchloroketene with isobutylene yields a chlorocyclobutanone which is a valuable intermediate in a new synthesis of insecticidal pyrethroids.[37] The triethylamine dehydrochlorination of 2,4,4,4-tetrachlorobutanoyl chloride in the presence of isobutylene yields the expected chlorocyclobutanone. The tetrachloroacid chloride is readily obtained by the copper(I)-catalyzed free radical addition of chloroform to acrylic acid.[82] Treatment of the cycloadduct with a catalytic amount of triethylamine results in a novel cine rearrangement forming the *cis* isomer by a 95/5 ratio. The base induced stereospecific Favorskii rearrangement ring contraction of this rearrangement product and dehydrochlorination yielded the *cis* - 3 - (2,2-dichlorovinyl) - 2,2 - dimethylcyclopropanecarbocylic acid.[83] Esters of this acid are the most promising insecticides due to their



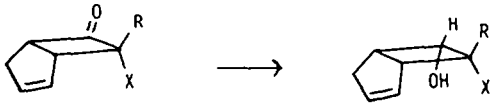
extraordinarily high potency and considerably increased photostability compared with those of the esters of the naturally occurring chrysanthemic acid.

An interesting ring contraction of cyclobutanols, obtained by the sodium borohydride reduction of adducts of halogenated ketenes and cyclopentadiene, has been reported.[84,85] The reduction of the dichloroketene cyclopentadiene adduct gave two epimeric alcohols in a ratio of 4:1 with the 6-*endo*-alcohol assigned as the predominate isomer. The *exo*-alcohol of the adduct of dichloroketene and



cyclopentadiene, 7,7-dichlorobicyclo[3.2.0]hept-2-en-7-*exo*-ol upon treated with base yielded the *endo*-carboxaldehyde which could be easily oxidized to the corresponding acid. The *endo*-alcohol analogously produced the *exo*-aldehyde. This stereospecific base catalyzed ring contraction involves the chlorine atom *trans* to the hydroxy group.

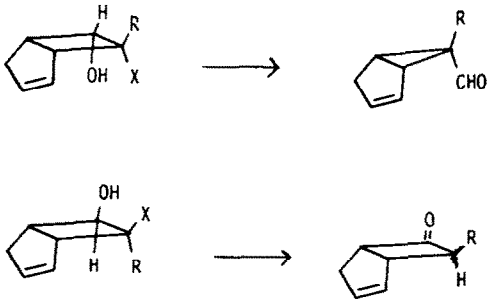
The lithium aluminum hydride or sodium borohydride reduction of the 7 - *endo* - halo - 7 - alkylbicyclo[3.2.0]hept - 2 - en - 6 - ones proceeded stereospecifically to give the corresponding 7 - *endo* -



halo - 7 - alkylbicyclo[3.2.0]hept - 2 - en - 6 - *endo* - ols. No evidence for even small amounts of the *exo* alcohols could be found. Conversely, the *exo*-haloketenes gave a mixture of 6 - *exo* and 6-*endo* alcohols.

The 7 - *endo* - halo - 7 - alkylbicyclo[3.2.0]hept - 2 - en - 6 - *endo* - ols upon treatment with base gave the bicyclo[3.1.0]hex - 2 - en - 6 - *endo* - carboxaldehydes. However, the base treatment of the 7 - *exo* - chloro - 6 - *exo* - alcohol produced no aldehyde. A hydride shift was demonstrated to have occurred,

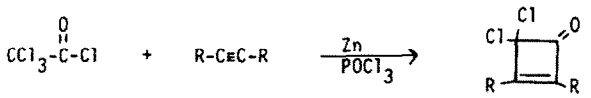
thus producing the ketone. Ring contraction, the normally favored reaction course, is not observed because



the required conformation produces a bad interaction between the 7-*endo*-alkyl and C-4 hydrogen atom.[86-88]

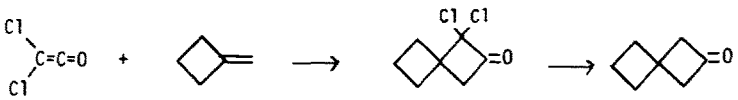
Cyclobutenones

The *in situ* cycloaddition of dichloroketene with 2-butyne was originally reported to occur in very low yield.[89,90] However, more recently the generation of dichloroketene from trichloroacetyl chloride using zinc and phosphorous oxychloride in the presence of alkynes has recently been reported to occur in substantially improved yields. 1-Hexyne, 2-hexyne, diphenylacetylene, and 2-butyne have all been reported to undergo this cycloaddition reaction.[91]



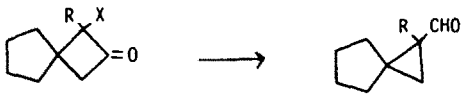
Spiro[3.n] *and spiro* [2.n] *compounds*

The cycloaddition of ketenes with methylenecycloalkanes yields spiro [3.*n*] ketones. Dichloroketene undergoes cycloaddition with methylenecyclobutane to yield the dichloro spiro[3.3]heptanone which can be dechlorinated to yield the spiro[3.3]heptanone.[92]



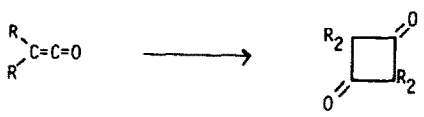
The cycloaddition of dichloroketene with methylenecyclohexane and subsequent dechlorination yields the spiro(3.5)nonanone.[93]

The cycloaddition of methylchloroketene with methylenecyclohexane, methylenecyclobutane, β-pinene and 5-methyl-2-norborene yields the corresponding spiro(3.5) and spiro(3.3) ketones in moderate to good yields under the appropriate conditions.[94] The halogenated ketenes give much better yields of cycloadducts than the nonhalogenated ketenes. The sodium borohydride reduction of the halo spiro ketones to the corresponding alcohols and subsequent base-catalyzed ring contraction occurs smoothly to the spiroaldehydes thus yielding spiro[2.*n*] compounds as illustrated with the cycloadduct of methylenecyclopentane.[92,95]

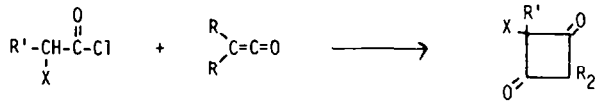


1,3-*Cyclobutanediones and derivatives*

1,3-Cyclobutanediones are readily available by the dimerization of dialkylketenes. A wide variety of tetraalkylcyclobutanediones have been prepared by the triethylamine dehydrohalogenation of appropriately substituted acid halides.

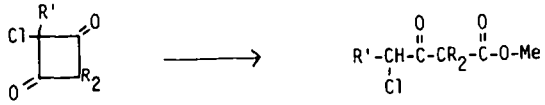


Numerous efforts to homodimerize halogenated ketones to 1,3-cyclobutanediones have been unsuccessful. However, halogenated ketenes will undergo mixed dimerization with nonhalogenated ketenes to yield halo-1,3-cyclobutanediones. The alkylhaloketenes have been generated *in situ* in the presence of dialkylketenes to yield the unsym-1,3-cyclobutanediones.[97-99] Also, the mixed dimers have been prepared



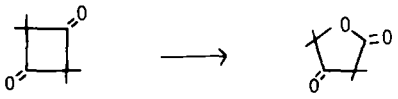
by the simultaneous generation of the two ketenes from their respective acid halides. A wide variety of these compounds have been prepared in this manner.[98]

Tetraalkyl-1,3-cyclobutanediones undergo ring opening reactions in the presence of base to yield β-ketoesters.[100] The chlorotrialkyl-1,3-cyclobutanediones also undergo ring opening reactions to yield β-ketoesters. Although two β-ketoesters are possible, only the expected γ-chloro-β-ketoesters were found.



The chlorotrialkyl-1,3-cyclobutanediones react with tri-n-butyltin hydride to yield the corresponding trialkyl-1,3-cyclobutanediones which exist as the dione in the solid state, but the enol form is the predominant form in solution.[101]

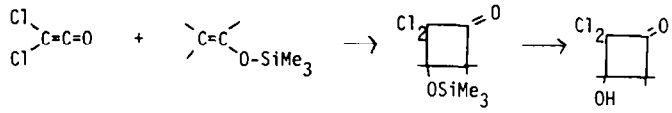
The peracid oxidation of tetramethyl-1,3-cyclobutanedione occurs smoothly and in good yield to the expected lactone, 2,4-furandione.[102,103] This Baeyer–Villiger oxidation of chlorotrialkyl-1,3-cyclo-



butanedione gives the ring expanded product as shown. No other ring expansion products were detected.[101]

3-Functionalized cyclobutanones

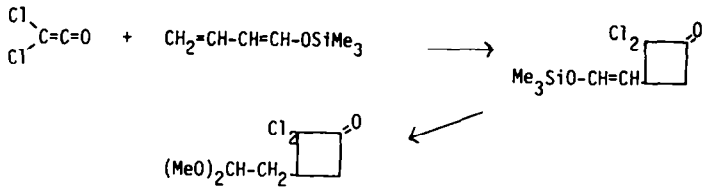
The cycloaddition of dichloroketene with the readily available trimethylsilyl enol ethers occur regiospecifically to give good yields of 3-siloxycyclobutanones which are readily hydrolyzed to the



3-hydroxycyclobutanones. The initial reports described the generation of dichloroketene by the dehalogenation method but more recently it has been found that the dehydrohalogenation method for generating dichloroketene may be used successfully.[106]

The cycloaddition of methylchloroketene with the silyl enol ether derived from cyclopentanone yielded both the *endo*-methyl and *exo*-methyl isomers. The cycloaddition of phenylchloroketene and this silyl enol ether afforded only the *endo*-phenyl isomer as expected.[107]

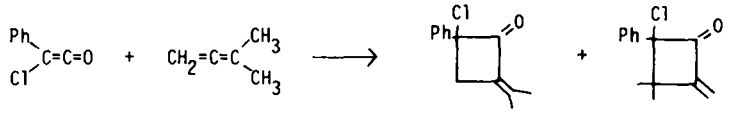
The cycloaddition of conjugated silyl enol ethers with both dichloroketene and methylchloroketene also occurred regiospecifically to yield the (2 + 2) cycloaddition products. The cycloaddition of the silyl enol ether derived from crotonaldehyde and dichloroketene yielded 2,2-dichloro-3-(2-trimethylsiloxyethenyl)cyclobutanone which upon methanolysis formed the dimethyl acetal.[108]



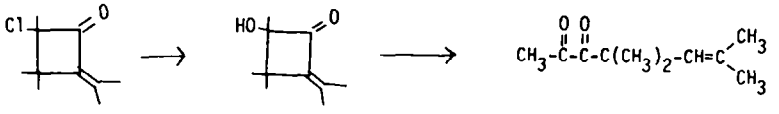
Alkylidenecyclobutanones

The cycloaddition of halogenated ketenes with allenes occurs in a regiospecific manner to yield halogenated alkylidenecyclobutanones. Tetramethylene allene and 1,2-cyclononadiene exhibit unusual reactivity in such cycloadditions.[109,110]

The reaction of an excess of *unsym*-dimethylallene with phenylchloroketene yielded the two 2-alkylidenecyclobutanones indicated in a ratio of 5 with the 2-isopropylidenecyclobutanone predominating.

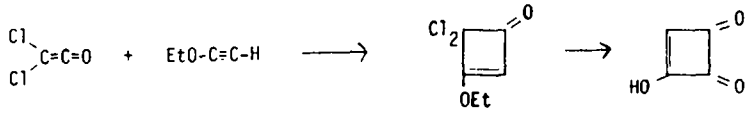


The reaction of the cycloadduct of methylchloroketene and tetramethylallene with base resulted in the formation of the α-hydroxy compound which underwent an unusual ring opening reaction to yield an α,β-dione.[112]

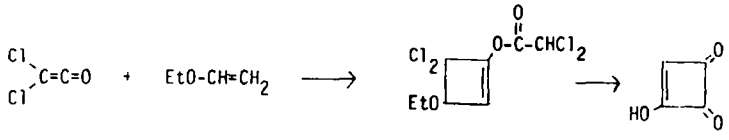


Squaric acid, semisquaric acid and derivatives

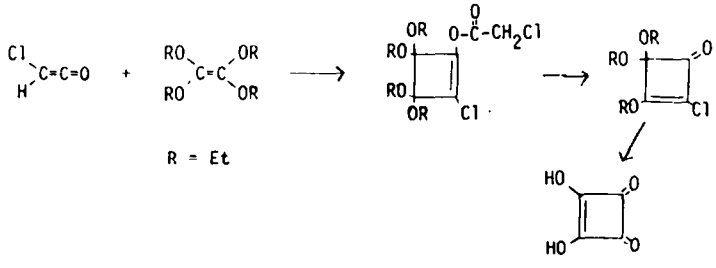
Squaric acid and semisquaric acid, 3,4-dihydroxy-3-cyclobuten-1,2-dione and 3-hydroxy-3-cyclobuten-1,2-dione respectively, have recently been synthesized in an elegant manner utilizing cycloaddition reactions involving dichloroketene and chloroketene. The *in situ* cycloaddition of dichloroketene with ethoxyacetylene yields the expected (2+2) cycloaddition product which upon hydrolysis forms semisquaric acid.[113]



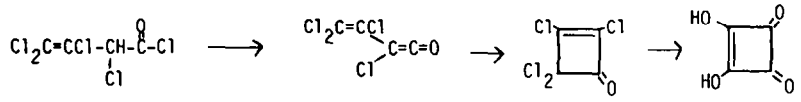
The *in situ* cycloaddition of dichloroketene with ethyl vinyl ether affords an enol ester which upon bromination and hydrolysis yield semisquaric acid.[114,115]



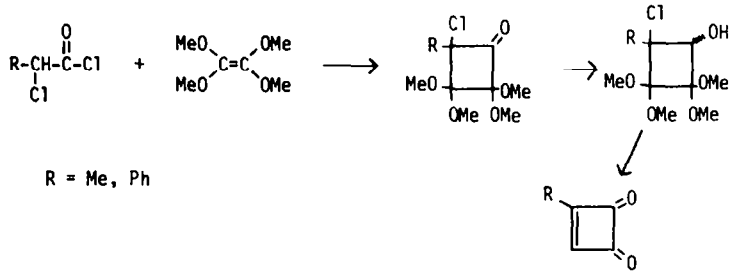
The cycloaddition of tetraethoxyethylene with chloroketene yields the cyclobutenol ester which upon treatment with silica gel/triethylamine provided the cyclobutenone. Hydrolysis of this product yielded squaric acid.[116,117]



Squaric acid has also been synthesized by the hydrolysis of the product of cyclization of perchlorovinylchloroketene. This ketene was generated by the dehydrochlorination of 2,3,4,4-tetrachloro-3-butenoyl chloride.[115,118,119]



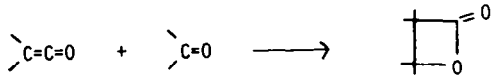
The cycloaddition of methylchloroketene and phenylchloroketene generated *in situ* by the dehydrochlorination of α-chloropropionyl chloride and α-chlorophenylacetyl chloride respectively with tetramethoxyethylene occur in high yields to produce the 2-chlorotetramethoxycyclobutanones. The sodium borohydride reduction of the cyclobutanones yields the 2-chlorotetramethoxycyclobutanols which upon hydrolysis yield the 2-substituted derivatives of semisquaric acid.[120]



R = Me, Ph

2-Oxetanones and olefins

The preparation of 2-oxetanones (β-lactones) by the cycloaddition of ketenes and carbonyl compounds dates back to the early investigations of Staudinger. The addition of simple carbonyl compounds to diphenylketene did not normally proceed unless elevated temperatures were employed. Since the high

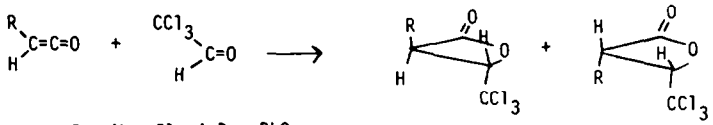


temperature required for cycloadditions polymerized aldoketenes or monosubstituted ketenes and lower ketoketenes, early investigations were mostly limited to diphenylketene.[121]

Later the cycloaddition of ketene to aldehydes was found to proceed smoothly in ether in the presence of mild Friedel–Crafts-type catalysts.[122] Ketones, however, required much stronger catalysts and more vigorous conditions to react with ketene.[123]

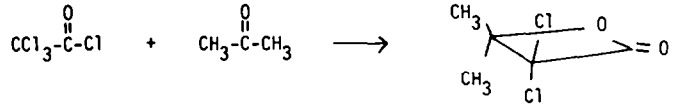
It has been more recently reported that the cycloaddition of simple ketoketenes and carbonyl compounds is possible when the carbonyl compound is activated by electronegative substituents on the α-carbon atom.[124] Thus, the cycloaddition of several ketenes to chloral to yield the corresponding 2-oxetanones were accomplished. The 2-oxetanone derived from dichloroketene and chloral was prepared by the *in situ* preparation of dichloroketene and subsequent trapping of this ketene with chloral.[125] However, under these conditions it was found that dichloroketene would not react with simple ketones such as acetone, cyclohexanone, and acetophenone.

The reaction of methyl-, chloro-, isopropyl-, and phenoxyketenes with chloral yields both *cis*- and *trans*-2-oxetanones in approximately equal amounts.[126,127]



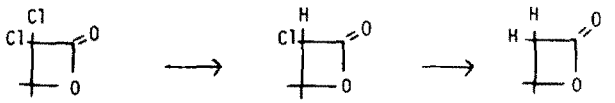
R = Me, Cl, i-Pr, PhO

The generation of dichloroketene by the zinc dehalogenation of trichloroacetyl chloride in the presence of acetone and cyclohexanone afforded these 2-oxetanones. Zinc, apparently activates the carbonyl group, thus increasing the reactivity of these simple ketones with dichloroketene.[127]

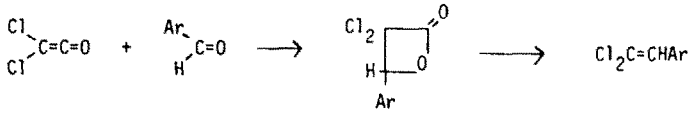


The cycloaddition of methylchloro- and methylbromoketenes with chloral, o-chlorobenzaldehyde and *sym*-dichlorotetrafluoroacetone reveals that activation of the carbonyl group is necessary for cycloaddition.[128]

The 3,3-dichloro-2-oxetanones may be selectively reduced with tri-n-butyltin hydride to the corresponding monochloro-2-oxetanones. The reduction may also be effected to produce the non-halogenated 2-oxetanones.[129]

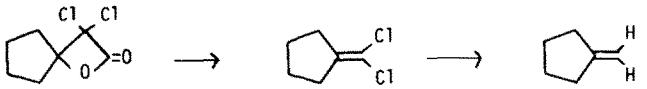


The generation of dichloroketene from dichloroacetyl chloride in the presence of monosubstituted benzaldehydes gave 3,3-dichloro-4-aryl-2-oxetanones. Benzaldehydes substituted with electron-with-

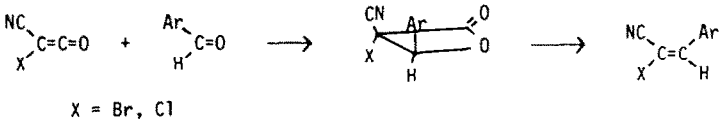


drawing groups led to higher yields than benzaldehydes bearing electron-donating substituents. Thermolysis of the β-lactones gave the corresponding β,β-dichlorostyrenes in good yields. Electron donating groups enhance the rate of decarboxylation.[130]

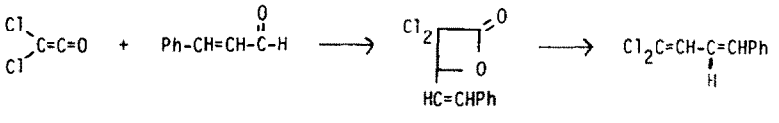
Exocyclic olefins are generally prepared by the Wittig reaction but aside from this well-known reaction, little information on other methods is available in the literature. The cycloadduct resulting from the cycloaddition of dichloroketene and cyclic ketones, 3,3-dichloro-2-oxetanones, are easily decarboxylated upon heating, yielding dichloromethylenecycloalkanes. The dechlorination of this exocyclic olefin with sodium in liquid ammonia affords the methylenecycloalkanes in near quantitative yield as illustrated with the 2-oxetanone from dichloroketene and cyclopentanone.[131]



The reaction of halocyanoketenes with aromatic aldehydes reportedly gives exclusively the *E*-isomers of the corresponding β-lactones. The β-lactones stereospecifically decarboxylate under the reaction conditions to yield the corresponding olefins.[132] This stereoselective conversion of an aldehyde into an alkene is certainly of synthetic note. These reactions provide a convenient stereoselective route to *E*-1-halo-1-cyano-2-arylethenes.



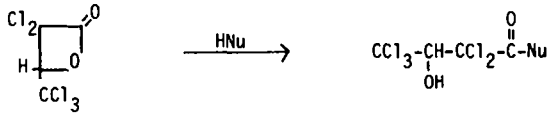
The generation of dichloroketene by the zinc dechlorination of trichlaroacetyl chloride in the presence of *E*-cinnamaldehyde and subsequent workup and distillation resulted in the formation of 1,1-dichloro-4-phenyl-1,3-butadiene. The *in situ* cycloaddition of dichloroketene and α-methylcin-



namaldehyde gave a similar result, yielding 1,1-dichloro-3-methyl-4-phenyl-1,3-butadiene.[133] The zinc halide etherate produced as a byproduct in the dehalogenation presumably functions as a catalyst for these cycloadditions. Apparently, in these cycloadditions with the cinnamaldehydes, the 2-oxetanones undergo decarboxylation during distillation to yield the highly conjugated systems.

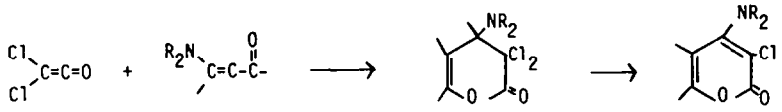
Halogenated 2-oxetanones are much more reactive towards nucleophiles such as water, methanol, dimethylamine etc., than nonhalogenated 2-oxetanones. Nucleophilic addition to halogenated 2-

oxetanones yields only acyl-oxygen cleavage products.[134]



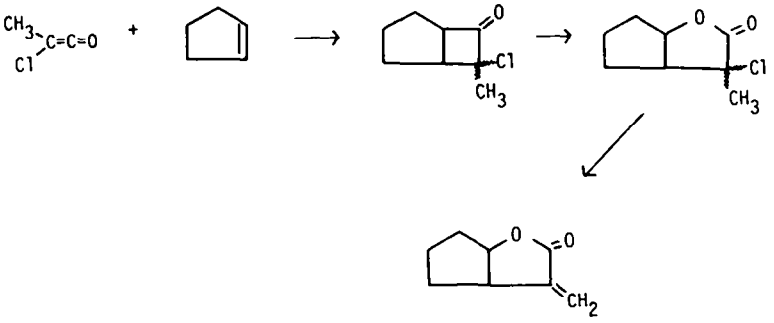
Other lactones

Dichloroketene undergoes a polar 1,4-cycloaddition with N,N-disubstituted vinyl ketones to give δ-lactones or 2-pyrone derivatives. The synthetic utility of this unusual 1,4-addition reaction of a ketene



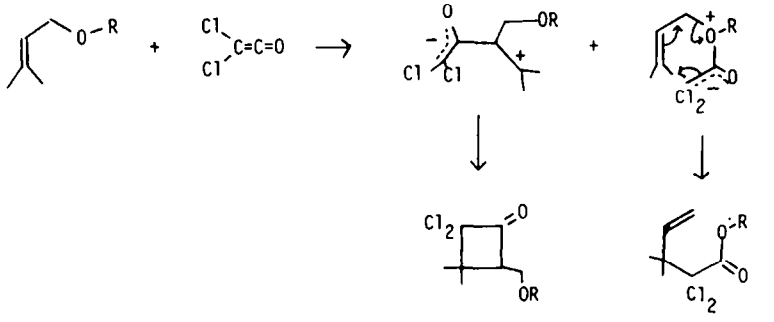
has been well demonstrated by the synthesis of a wide variety of 2-pyrones.[135–139] Dehydrochlorination of the cycloaddition product readily occurs to yield the corresponding chloropyranones.

The *in situ* prepararation of methylchloroketene from α-chloropropionyl chloride and triethylamine in the presence of cyclic olefins yields the expected (2+2) cycloaddition products as illustrated with cyclopentene.[140] Baeyer-Villiger oxidation of the cyclobutanones yields the corresponding lactones. Base catalyzed dehydrochlorination of the lactones yields α-methylene- γ-lactones.



This is a facile transformation of cyclic olefins into *cis*-fused α-methylene- γ-butyrolactones in three steps and should have wide applicability in the synthesis of a number of biologically active naturally occurring compounds containing these functionality.

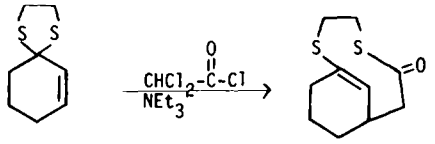
The *in situ* reaction of dichloroketene, generated by the zinc dehalogenation of trichloroacetyl chloride, with allyl ethers occurs in two competing pathways. Besides the expected (2+2) cycloaddition product a (3,3)-sigmatropic (Claisen) rearrangement *via* a 1,3-dipolar intermediate takes place.[141] This rearrangement leads to esters of α, α-dichloro-γ, δ-unsaturated acids. Apparently, the nucleophilic oxygen atom in the allylic starting compound competes successfully with the double bond for the electrophilic



dichloroketene. The 1,3-dipolar intermediate thus formed is ideally suited for a (3,3)-rearrangement leading to the ester. This reaction has also been demonstrated to occur with allyic *S*- and Se-ethers.

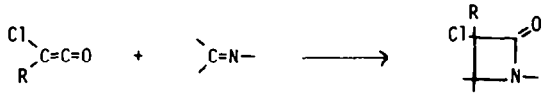
A very facile synthesis of the naturally occurring macrolides (±)-phoracantholide I and (±)-phoracantholide J exemplifies the applicability of this new rearrangement for the transformation of cyclic, n-membered, α-vinyl-substituted ethers into unsaturated (n + 4)-membered lactones.[141]

This reaction has recently been extended whereby cyclic thioketals of α,β-cycloenones undergo a four-carbon cycloenlargement of 1,3-dithia-n-membered ring by reaction with dichloroketene to give 1,7-dithiacycloalk-5-en-2-one derivatives in good yield as illustrated with the thioketal of 2-cyclohexenone.[142]

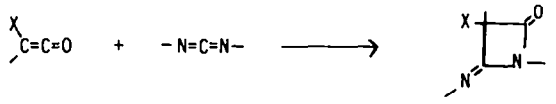


2-Azetidinones

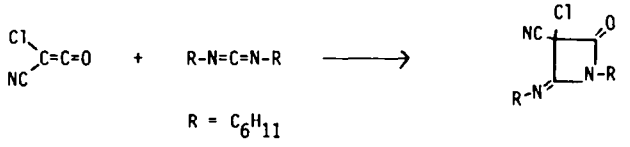
There are many examples in the literature of the formation of 2-azetidinones (β-lactams) by the cycloaddition of a ketene and an imino compound. The synthesis of 3-chloro-2-azetidinones, 3,3-dichloro-2-azetidinones, and 3-chloro-3-methyl-2-azetidinones which are potential precursors of various functionally substituted 2-azetidinones is possible by the cycloaddition of chloro-, dichloro- and methylchloroketenes with imines.[143–145]



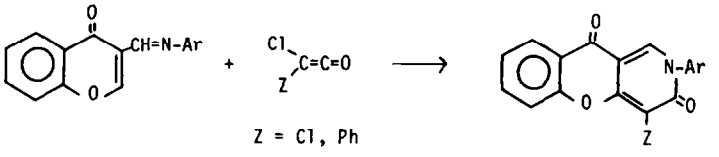
3-Halo-4-imino-2-azetidinones are available through halogenated ketenes by cycloaddition with carbodiimides. Various types of halogenated ketenes have been shown to undergo cycloaddition with the aliphatic carbodiimides, dicyclohexyl-and diisopropylcarbodiimides.[146–148]



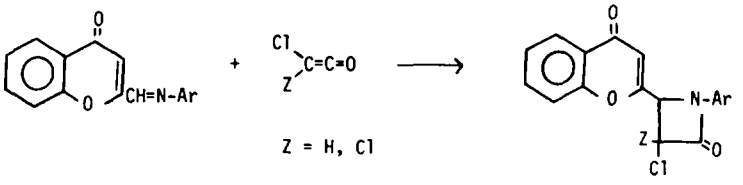
Chlorocyanoketene has recently been prepared and allowed to undergo cycloaddition with dicyclohexylcarbodiimide to yield the α-chloro-α-cyano-β-imino-β-lactam. It appears that a variety of functionally substituted β-lactams are possible by this new method.



The cycloaddition of dichloroketene and phenylchloroketene with 2-(aryliminomethyl)chromones presumably occurs in a dipolar 1,4-cycloaddition process to yield the corresponding lactams.[149]



The 3-(aryliminomethyl)chromones react with both dichloroketene and chloroketene to yield the (2 + 2) cycloadduct, the azetidinones. It is likely that this cycloaddition also occurs through a dipolar intermediate.



REFERENCES

[1]W. T. Brady, *Synthesis* 8, 415 (1971).
[2]S. Patai, *The Chemistry of Ketenes, Allenes and Related Compounds*. Interscience, New York (1980).
[3]H. Staudinger, E. Anthes and H. Schneider, *Chem. Ber* **46**, 3539 (1913).
[4]E. Ott, *Liebigs Ann. Chem.* **401**, 159 (1914).
[5]H. Staudinger and H. Schneider, *Helv. Chim. Acta* **6**, 304 (1923).
[6]D. Borrmann *Houben-Weyl Methoden der Organischen Chemie*, (Edited by E. Muller) 4th Edn. Vol. VII/4, p. 65, George Thieme Verlag, Stuttgart (1968).
[7]L. Ghosez, R. Montaigne, and P. Mollet, *Tetrahedron Letters* 135 (1966).
[8]W. T. Brady and O. H. Waters, *J. Org. Chem.* **32**, 3703 (1967).
[9]W. T. Brady and D. A. Bak, *Ibid.* **44**, 107 (1979).
[10]A. Hassner and L. R. Krepski, *Ibid* **43**, 2879 (1978).
[11]H. Staudinger, *Chem. Ber.* **38**, 1735 (1905).
[12]C. W. Smith and D. G. Norton, *Organic Syntheses Coll. Vol. IV*, 348 (1963).
[13]C. C. McCarney and R. S. Ward, *J. Chem. Soc., Perkin I* 1600 (1975).
[14]J. C. Sauer, *J. Am. Chem. Soc.* **69**, 2444 (1947).
[15]E. C. Taylor, A. McKillop and G. H. Hawks, *Organic Syntheses* **52**, 36 (1972).
[16]W. T. Brady and G. A. Scherubel, *J. Org. Chem.* **39**, 3790 (1974).
[17]H. C. Stevens, D. A. Reich, D. R. Brandt, K. R. Fountain and E. J. Gaughan, *J. Am. Chem. Soc.* **87**, 5257 (1965).
[18]W. T. Brady, H. G. Liddell and W. L. Vaughn, *J. Org. Chem.* **31**, 626 (1966).
[19]N. N. Yarovenko, S. P. Motornyi and L. I. Kirenskaya, *Zh. Obshch. Khim.* **27**, 2796 (1957).
[20]R. E. Banks, R. N. Haszeldine and D. R. Taylor, *J. Chem. Soc.* 5602 (1965).
[21]D. C. England and C. G. Krespan, *J. Org. Chem.* **33**, 816 (1968).
[22]W. T. Brady, *Ibid.* **31**, 2676 (1966).
[23]T. Okada and R. Okawara, *Tetrahedron Letters* 2801 (1971).
[24]Yu. A. Chebrukov, A. M. Platoshkin and I. L. Knuyants, *Dokl. Akad. Nauk. SSSR* **173**, 1117 (1967).
[25]W. T. Brady, J. P. Hieble, unpublished results.
[26]W. T. Brady and E. F. Hoff, Jr., R. Roe, Jr. and F. H. Parry, III, *J. Am. Chem. Soc.* **91**, 5679 (1969).
[27]W. T. Brady and T. C. Cheng, *J. Org. Chem.* **42**, 732 (1977).
[28]W. T. Brady and B. M. Holifield, *Tetrahedron Letters* 5511 (1966).
[29]W. T. Brady and R. Roe, *Ibid* 1977 (1968).
[30]R. Giger, M. Rey and A. S. Dreiding, *Helv. Chim. Acta.* **51**, 1466 (1968).
[31]J. M. Lavanish, *Tetrahedron Letters* 6003 (1968).
[32]W. T. Brady, F. H. Parry, R. Roe, E. F. Hoff and L. Smith, *J. Org. Chem.* **35**, 1515 (1970).
[33]W. T. Brady, E. D. Dorsey and F. H. Parry, *Ibid.* **34**, 2846 (1969).
[34]W. T. Brady, F. H. Parry, R. Roe and E. F. Hoff, *Tetrahedron Letters* 819 (1970).
[36]D. M. Kunert, R. Chambers, F. Mercer, L. Hernandez, Jr. and H. W. Moore, *Tetrahedron Letters* 929 (1978).
[37]D. Bellus, P. Martin and H. Greuter, *J. Am. Chem. Soc.* **101**, 5853 (1979).
[38]R. W. Turner and T. Seden, *Chem. Commun.* 399 (1966).
[39]G. L. M. Cragg, *J. Chem. Soc.* (*C*) 1829 (1970).
[40]R. E. Harmon, W. D. Barta, S. K. Gupta, K. Surendra and G. Slomp, *J. Chem. Soc.* (*D*) *Chem. Comm.* 935 (1970).
[41]R. Montaigne and L. Ghosez, *Angew. Chem. Int. Ed. Engl.* **7**, 221 (1968).
[42]L. Ghosez, R. Montaigne, A. Roussel, H. Vanlierde and P. Mollet, *Tetrahedron* **27**, 615 (1971).
[43]L. Ghosez, R. Montaigne, H. Vanlierde and F. Dumay, *Angew. Chem. Int. Ed. Engl.* **7**, 643 (1968).
[44]T. Asao, T. Machiguchi, T. Kitamura and Y. Kitahara, *J. Chem. Soc.* (*D*). *Chem. Comm* 89. (1970).
[45]P. D. Bartlett and T. Ando, *J. Am. Chem. Soc.* **92**, 7518 (1970).
[46]I. Fleming, *Chem. & Ind.* (*London*) 449 (1975).
[47]W. Weber, I. Erden and A. deMeijere, *Angew. Chem. Int. Ed. Engl.* **19**, 387 (1980).
[48]M. Rey, U. A. Huber and A. S. Dreiding, *Tetrahedron Letters* 3585 (1968).
[49]W. T. Brady and R. Roe, Jr., *J. Am. Chem. Soc.* **92**, 4618 (1970).
[50]W. T. Brady, R. Roe, E. F. Hoff and F. H. Parry, *Ibid.* **92**, 146 (1970).
[51]W. T. Brady and R. Roe, *Ibid.* **93**, 1662 (1971).
[52]A. E. Greene and J. P. Depres, *Ibid.* **101**, 4003 (1979).
[53]E. J. Corey and R. Noyori, *Tetrahedron Letters* 311 (1970).
[54]E. J. Corey, K. C. Nicolaou and D. J. Beames, *Ibid.* 2439 (1974).
[55]E. J. Corey and J. Mann, *J. Am. Chem. Soc.* **95**, 6832 (1973).
[56]J. J. Partridge, N. K. Chadha and M. R. Uskokovic, *Ibid.* **95**, 7171 (1973).
[57]E. J. Corey, Z. Arnold and J. Hutton, *Tetrahedron Letters* 307 (1970).
[58]P. A. Grieco, *J. Org. Chem.* **37**, 2363 (1972).
[59]S. M. Ali, T. V. Lee and S. M. Roberts, *Synthesis* 155 (1977).
[60]J. B. Wiel and F. Rouessac, *Bull. Soc. Chim. Fr.* 273 (1979).
[61]K. E. Harding, J. W. Trotter and L. May, *Syn. Commun.* **4**, 231 (1972).
[62]K. E. Harding, J. W. Trotter and L. M. May, *J. Org. Chem.* **42**, 2715 (1977).
[63]H. C. Stevens, J. K. Rinehart, J. M. Lavanish and G. M. Trenta, *Ibid.* **36**, 2780 (1971).
[64]K. Tanaka and A. Yoshikashi, *Tetrahedron* **27**, 4889 (1971).
[65]M. Kato, F. Kido, M.D. Wu and A. Yoshikashi, *Bull. Chem. Soc. Japan* **47**, 1516 (1974).
[66]S. Kuroda and T. Asao, *Tetrahedron Letters* 285 (1977).
[67]J. Tsunetsugu, M. Sato, M. Kanda, M. Takahashi and S. Ebine, *Chem. Letters* 885 (1977).
[68]G. Ashworth, D. Berry and D. C. Smith, *J. Chem. Soc. Perkin Trans. I* 2995 (1979).
[69]J. Tsunetsugu, M. Asai, H. Uchiyama, Y. Kurata, A. Mori, M. Sato and *S. Ebine, Koen Yoshishu-Hibenzenkei Hokozoku Kagaku Toronkai (Oyobi) Kozo Yuki Kagaku Toronkai, 12th*, 49 (1979).
[70]W. T. Brady and J. P. Hieble, *Tetrahedron Letters* 3205 (1970).
[71]W. T. Brady and J. P. Hieble, *J. Am. Chem. Soc.* **94**, 4278 (1972).

[72]J. M. Conia and J. R. Salaun, *Accts. Chem. Res.* **5**, 33 (1972).
[73]P. R. Brook, J. M. Harrison and A. J. Duke, *J. Chem. Soc.* (*D*) *Chem. Comm.* 589 (1970).
[74]W. T. Brady and J. P. Hieble, *J. Org. Chem.* **36**, 2033 (1971).
[75]D. L. Garin and K. L. Cammack, *J. Chem. Soc. Chem. Commun.* 333 (1972).
[76]P. R. Brook and A. J. Duke, J. M. Harrison and K. Hunt, *J. Chem. Soc. Perkin I* 927 (1974).
[77]P. R. Brook and J. M. Harrson, *J. Chem. Soc. Chem. Commun* 997 (1972).
[78]P. R. Brook and A. J. Duke, *J. Chem. Soc.* (*C*) 1764 (1971).
[79]V. R. Fletcher and A. Hassner, *Tetrahedron Letters* 1071 (1970).
[80]W. T. Brady and P. L. Ting, *J. Chem. Soc. Perkin I* 456 (1975).
[81]K. E. Harding and J. W. Trotter, *J. Org. Chem.* **42**, 4157 (1977).
[82]D. Bellus, P. Martin and H. Greuter, *Pestic. Sci.* **11**, 141 (1980).
[83]D. Bellus, P. Martin, and E. Steiner, *Helv. Chim. Acta* **63**, 1947 (1980).
[84]P. R. Brook, *J. Chem. Soc.* (*D*) *Chem. Comm.* 565 (1968).
[85]P. R. Brook and A. J. Duke, *J. Chem. Soc. Perkin I* 1013 (1973).
[86]P. R. Brook and A. J. Duke, *Ibid.* (*D*) *Chem. Comn.* 652 (1970).
[87]A. S. Dreiding, *Helv. Chim. Acta.* **60**, 1528 (1977).
[88]P. R. Brook, A. J. Duke, J. G. Griffiths, S. M. Roberts, M. Rey and A. S. Dreiding, *Ibid.* **60**, 1528 (1977).
[89]E. V. Dehmlow, *Chem. Ber.* **100**, 3829 (1967).
[90]H. Knoche, *Justus Liebigs Ann. Chem.* **722**, 232 (1969).
[91]A. Hassner and J. Dillion, *Synthesis* **9**, 689 (1979).
[92]P. R. Brook and J. G. Griffiths, *J. Chem. Soc.* (*D*) *Chem. Comm* 1344 (1970).
[93]J. R. Wiseman and H. F. Chan, *J. Am. Chem. Soc.* **92**, 4749 (1970).
[94]W. T. Brady and A. D. Patel, *J. Org. Chem.* **38**, 4106 (1973).
[95]R. Maruic and M. Bertrand, *Bull. Soc. Chim. Fr.* 998 (1970).
[96]D. Bellus, P. Martin, H. Greuter and E. Steiner, *Chimia* **34**, 238 (1980).
[97]W. T. Brady and P. L. Ting, *Tetrahedron Letters* 2619 (1974).
[98]W. T. Brady and P. L. Ting, *J. Org. Chem.* **40**, 3417 (1975).
[99]W. T. Brady and P. L. Ting, *Ibid.* **41**, 2336 (1976).
[100]E. U. Elam and R. G. Nations, *U.S. Patent* 3, 412, 461.
[101]W. T. Brady and T. C. Cheng, *J. Org. Chem.* **41**, 2036 (1976).
[102]P. Y. Johnson and J. Yee, *Ibid.* **37**, 1058 (1972).
[103]D. H. Gilson and J. T. Joseph, *Tetrahedron Letters* 3483 (1972).
[104]A. Hassner and L. R. Krepski, *J. Org. Chem.* **43**, 3173 (1978).
[105]A. Hassner, H. W. Pinnick and J. M. Ansell, *Ibid.* **43**, 1774 (1978).
[106]W. T. Brady and R. M. Lloyd, *Ibid.* **44**, 2560 (1979).
[107]W. T. Brady and R. M. Lloyd, *Ibid.* **45**, 2025 (1980).
[108]W. T. Brady and R. M. Lloyd, *Ibid.* **46**, 000 (1981).
[109]J. C. Martin, P. G. Gott, V. W. Goodlett and R. H. Hasek, *Ibid.* 30, 4175 (1965).
[110]W. T. Brady, J. D. Stockton and A. D. Patel, *Ibid.* **39**, 236 (1974).
[111]P. R. Brook, J. M. Harrison and K. Hunt, *J. Chem. Soc.* (*D*) *Chem. Comm.* 33 (1973).
[112]W. T. Brady and A. D. Patel, *J. Org. Chem.* **39**, 1949 (1974).
[113]J. P. Springer, J. Clardy, R. J. Cole, J. W. Kirksey, R. K. Hill, R. M. Carlson, and J. L. Isidor, *J. Am. Chem. Soc.* **96**, 2267 (1974).
[114]D. Bellue, H. Fischer, H. Greuter and P. Martin, *Helv. Chim. Acta.* **61**, 1984 (1978).
[115]D. Bellus, *Oxocarbons* 1980, (Edited by R. West). Academic Press, New York, (1980).
[116]D. Bellus, *J. Am. Chem. Soc.* **100**, 8026 (1978).
[117]D. Bellus, *J. Org. Chem.* **44**, 1208 (1979).
[118]G. Maahs, *Ann. Chem.* **686**, 55 (1965).
[119]D. Bellus, P. Martin and H. Greuter, *Helv. Chim. Acta.* **64**, 000 (1981).
[120]W. T. Brady and R. D. Watts, *J. Org. Chem.* **45**, 3525 (1980).
[121]R. N. Lacey, in *The Chemistry of Alkenes*, (Edited by S. Patai). Interscience, New York (1968).
[122]F. E. Kung, *U. S. Patent* 2, 356, 459 (1944).
[123]H. E. Zaugg, *Org. Reactions* **8**, 314 (1954).
[124]D. Borrman and R. Wegler, *Chem. Ber.* **99**, 1245 (1966).
[125]D. Borrman and R. Wegler, *Ibid.* **102**, 64 (1969).
[126]W. T. Brady and L. Smith, *Tetrahedron Letters* 2963 (1970).
[127]W. T. Brady and L. Smith, *J. Org. Chem.* **36**, 1637 (1971).
[128]W. T. Brady and A. D. Patel, *J. Heterocyclic Chem.* **8**, 739 (1971).
[129]W. T. Brady and A. D. Patel, *J. Org. Chem.* **37**, 3536 (1972).
[130]H. O. Krabbenhoft, *Ibid.* **43**, 1305 (1979).
[131]W. T. Brady and A. D. Patel, *Synthesis* 565 (1972).
[132]H. W. Moore, F. Mercer, D. Kunert and P. Albaugh, *J. Am. Chem. Soc.* **101**, 5435 (1979).
[133]W. T. Brady and K. Saidi, *J. Org. Chem.* **44**, 733 (1979).
[134]W. T. Brady and A. D. Patel, *J. Heterocyclic Chem.* **10**, 239 (1973).
[135]L. Mosti, P. Schenone and G. Menozzi, *Ibid.* **15**, 181 (1978).
[136]A. Bargagna, F. Evangelisti and P. Schenone, *Ibid.* **16**, 93 (1979).
[137]L. Mosti, P. Schenone and G. Menozzi, *Ibid.* **16**, 913 (1979).
[138]A. Bargagna, P. Schenone and F. Bondavalli, *Ibid.* **17**, 33 (1980).
[139]L. Mosti, P. Schenone and G. Menozzi, *Ibid.* **17**, 61 (1980).
[140]A. Hassner, H. W. Pinnick and J. M. Ansell, *J. Org. Chem.* **43**, 1774 (1978).
[141]D. Bellus and R. Malherbe, *Helv. Chim. Acta.* **61**, 3096 (1978).
[142]G. Rosini, G. G. Spineti, E. Foresti and G. Pradella, *J. Org. Chem.* **46**, 000 (1981).
[143]F. Duran and L. Ghosez, *Tetrahedron Letters* 245 (1970).
[144]D. A. Nelson, *Ibid.* 2543 (1971).

[145]J. P. Luttringer and J. Streigh, *Ibid.* 4163 (1973).
[146]R. Hull, *J. Chem. Soc.* (*C*) 1154 (1967).
[147]W. T. Brady and E. F. Hoff, *J. Am. Chem. Soc.* **90**, 6256 (1968).
[148]W. T. Brady and E. D. Dorsey, *J. Org. Chem.* **34**, 2846 (1969).
[149]A. O. Fitton, J. R. Frost, P. G. Houghton and H. Suschitzky, *J. Chem. Soc. Perkin Trans I* 1450 (1977).