Formation of Acetylenes by Ring-Opening of 1,1,2-Trihalocyclopropanes

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This review describes studies into the conversion of substituted 1,1,2-trihalocyclopropanes into acetylenic acetals and acetylenic ketals by application of alcohols or alkoxides under basic conditions. The acetal/ketal ratio turned out to depend both on the substituents attached to the ring and on the reaction conditions prevailing during the reaction. Under the right conditions, however, completely regioselective ring-opening occurs to give either acetylenic acetals or acetylenic ketals, with formation of either no or only minor amounts of other products. The reactions are thought to involve cyclopropene intermediates, which are consumed by nucleophilic attack of alcohol or alkoxide. In some cases, the cyclopropene intermediates rearrange to the corresponding vinyl carbenes, which undergo insertion reactions with protic species present in the reaction mixture and give various 2-propenal derivatives as by-products.

Introduction

Substituted cyclopropanes are valuable compounds in organic synthesis because they are easily available and can be converted into a number of other compounds possessing a variety of useful structural features. Some of these conversions are fairly general and rather insensitive to the nature of the substituents present, e.g. thermal ring-opening,[1−4] allene formation,[5−8] and reductive dehalogenation,[9−11] whereas other transformations are more sensitive to the interplay between the reaction conditions and the chemical reactivity of the molecule. A reaction of the latter kind is base-induced elimination from halogenated cyclopropanes using alkoxides. When such cyclopropanes contain one or more cyclopropyl hydrogen atoms, the primary reaction is usually β elimination to furnish the corresponding cyclopropene,[12−22] a reaction which is facilitated by electron-withdrawing substituents on the ring.[18,19,23−25]

However, quite frequently *the isolated product is not a cyclopropene*. This is fairly common when cyclopropanes with one or more hydrogen atoms adjacent to the ring are treated with a base that is strong, but not nucleophilic. In such cases, migration of the carbon−carbon double bond takes place and provides alkylidenecyclopropanes.[26−33] Such prototropic reactions occur, for example, when alkyl-substituted 1,1-dichlorocyclopropanes[29,30] and bicyclic compounds possessing a *gem*-dichlorocyclopropane moiety[31−33] are exposed to potassium *tert*-butoxide in dimethyl sulfoxide. Even cyclopropabenzenes and cyclopropanaphthalenes have been prepared in this way.[34−36] Furthermore, when halogenated cyclopropanes are treated with alkoxides that are more nucleophilic than *tert*-butoxide, the initially obtained cyclopropenes are not usually isolated due to subsequent addition of the base to the highly strained carbon−carbon double bond. As a result, alkoxy-substituted cyclopropanes are produced[13,28,37,38] (even from halocyclopropanes that undergo ring-opening with *tert*-butoxide under the same conditions[32]).

The general pattern outlined above clearly implies that, unless an electron-withdrawing group is attached to the ring, ring-opening of halogenated cyclopropanes under basic conditions requires a strong base. We were therefore surprised by what we found when we tried to prepare 1,1,2-tribromo-2-methylcyclopropane from 2-bromopropene using Makosza's method[39] (alkene, haloform [1−2 equivalents], 50% aqueous sodium hydroxide [2−6 equivalents], and a small amount of TEBA; two-phase conditions) in the presence of a rather large amount of ethanol (*added by*

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MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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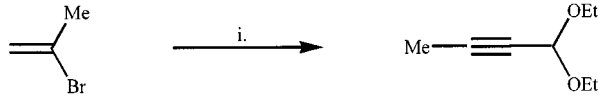
accident). One compound, 1,1-diethoxy-2-butyne, obtained in low yield and assumed to result from ring-opening of the tribromide, was the only product detected after workup, which had included evaporation of solvent at somewhat elevated temperature under vacuum (Scheme 1).[40] This serendipitous discovery led us to investigate more closely the synthesis and ring-opening of a variety of 1,1,2-trihalocyclopropanes, and the progress so far in our work in this field is described in this review.



Scheme 1. Formation of 1,1-diethoxy-2-butyne from 2-propene under Makosza conditions with a large excess of ethanol; reagents: i. $CHBr_3$, 50% aq. NaOH, TEBA, EtOH (large excess)

Synthesis of 1,1,2-Trihalocyclopropanes

1,1,2-Trihalocyclopropanes have been, and still are, most practically prepared by addition of dihalocarbene to the corresponding vinyl halides. Although studies have shown that dihalocarbene species usually react more slowly with such alkenes than with their halogen-free analogues,[41–43] the corresponding trihalocyclopropanes have been obtained in reasonable yields from a variety of vinyl halides.[40,44–46]

Most of the 1,1,2-trihalocyclopropanes known when we started our work had been synthesised under ordinary, two-phase conditions[47–50] using triethylbenzylammonium chloride (TEBA) or hexadecyltrimethylammonium bromide (Cetrimide) as catalyst, and we therefore decided to adopt the same method in our preparation of the starting materials for the ring-opening reactions. A range of trihalocyclopropanes was indeed formed under these conditions, but the yields varied considerably: from 69% in the case of 2-bromo-1,1-dichloro-2,3-dimethylcyclopropane, to 10% when 2-bromoheptene was converted into 2-bromo-1,1-dichloro-2-pentylcyclopropane (Table 1).[44,46,51] Other reactions competing with cyclopropane formation were generally insignificant, and so it was no surprise that the product mixtures contained considerable amounts of unchanged alkene, which could be recovered, giving a material balance of better than 90% in most reactions.

Table 1. Selected 1,1,2-trihalocyclopropanes prepared by addition of dihalocarbene to vinyl halides under different conditions

R^1	R^2	X	Y	Yield (%) Makosza	Ultrasound	Seyferth
H	H	Br	Br	30[a]	–	–
H	Me	Br	Br	50[a]	–	–
H	Me	Cl	Br	51[a]	–	–
H	Ph	Br	Br	38[a]	–	–
H	Propyl	Br	Br	46[b]	77[b]	–
H	Cyclohexyl-CH_2	Br	Br	40[b]	75[b]	–
H	Cyclohexyl-CH_2	Br	Cl	20[b]	56[b]	–
H	Pentyl	Br	Br	10[b]	57[b]	–
H	*t*Bu	Br	Cl	–	50[b]	–
H	4-$ClC_6H_4OCH_2$	Br	Br	28[c]	–	84[c]
H	4-$O_2NC_6H_4OCH_2$	Br	Br	10[c]	–	79[c]
Me	Me	Br	Cl	69[a]	–	–

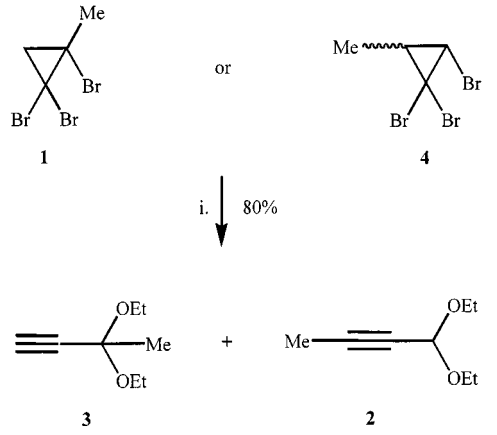
[a] From ref.[44]. – [b] From ref.[51]. – [c] From ref.[46].

When the dihalocarbene addition to a vinyl halide was inefficient, we found we could increase the yield of the corresponding trihalocyclopropane by adding some haloform to the crude product mixture from the first reaction and repeating the cyclopropanation under standard Makosza conditions. This indicated that the low yield in the first reaction was partly caused by undesired interactions or reactions with the water present, and it was therefore anticipated that the cyclopropane syntheses could be improved by generating the dihalocarbene and performing the reaction under less aqueous, or anhydrous, conditions. And indeed, by taking appropriate measures, significant improvements were made. When 50% aqueous sodium hydroxide and vigorous stirring were replaced with finely ground, solid NaOH and ultrasound irradiation as described by Xu and Brinker,[52] the yield more than doubled in some cases (Table 1). Even better results were obtained when dibromocarbene was generated by thermal decomposition of phenyl(tribromomethyl)mercury (Seyferth's method);[53] thus, the yield of 1,1,2-tribromo-2-(4-nitrophenoxy)methylcyclopropane was increased eight times by switching from Makosza's to Seyferth's method (Table 1).

It is therefore concluded that 1,1,2-trihalocyclopropanes are available in good yields from simple starting materials and, as such, are useful starting materials for ring-opening reactions.

Ring-Opening of 1,1,2-Trihalocyclopropanes Under Phase-transfer Conditions

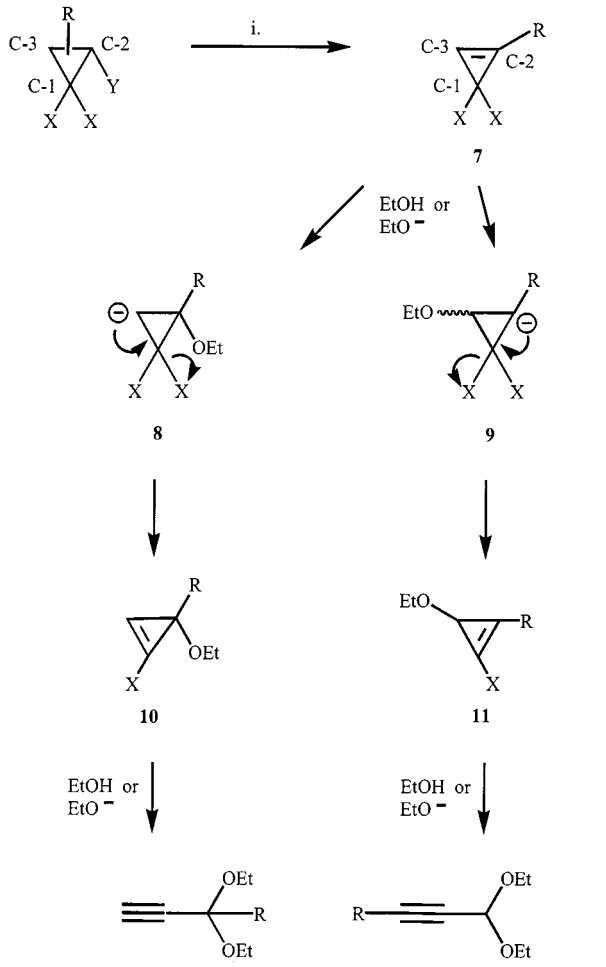
The systematic study of the ring-opening of 1,1,2-trihalocyclopropanes began with our repeating the synthesis of 1,1,2-tribromo-2-methylcyclopropane (**1**) under standard Makosza conditions (no ethanol, but haloform [1–2 equivalents], 50% aqueous sodium hydroxide [4 equivalents], and a small amount of TEBA). When 2-bromopropene was treated with dibromocarbene under these conditions, **1** was formed, but no ring-opening occurred. However, when **1** was exposed to 50% aqueous sodium hydroxide (8 equivalents) in the presence of ethanol (4 equivalents), some dichloromethane and a small amount of TEBA [these conditions will be referred to as "phase-transfer conditions" = PTC throughout] in a subsequent reaction, the trihalide suffered ring-opening and was completely converted into a 50:50 mixture of 1,1-diethoxy-2-butyne (**2**) and 3,3-diethoxy-1-butyne (**3**) (Scheme 2). (Compound **3**, found in this case but not in the initial experiment, proved much more volatile than the isomeric acetal **2**[44] and so in the first experiment had obviously disappeared during the workup, which had included solvent stripping under vacuum at elevated temperature.) Careful workup gave **2** and **3** in 80% combined yield, which indicated that acetylenic acetals and acetylenic ketals (referred to simply as "acetals" and "ketals" throughout) may easily be obtained in good combined yield from substituted 1,1,2-trihalocyclopropanes. The fate of a variety of such trihalides under PTC was therefore investigated.



Scheme 2. Ring-opening of methyl-substituted 1,1,2-tribromocyclopropanes; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, EtOH (4 equivalents), CH_2Cl_2, room temperature (referred to as "phase-transfer conditions" = PTC)

Most of the 1,1,2-trihalocyclopropane derivatives reacted smoothly when the reaction mixture was well stirred, and underwent ring-opening to afford, in most cases, mixtures of a ketal and the corresponding acetal in fair to excellent total yields. It was noted that the ketal/acetal ratio was sensitive to the nature of the substituents attached to the ring (vide infra). It was also noteworthy that the product mixtures from **1** and from a mixture of *cis*- and *trans*-1,1,2-tribromo-3-methylcyclopropane (**4**) were identical (Scheme 2), which indicated that the same intermediate was involved in the two reactions. Another important observation was the complete inertness of 1,1,2-tribromo-3,3-dimethylcyclopropane (**5**) and 1,1-dibromo-2-chloro-3,3-dimethylcyclopropane (**6**) under PTC; both compounds were recovered almost quantitatively even after stirring at elevated temperatures for a long period of time.

From these results it is evident that the ring-opening reaction involves several steps, including dehydrohalogenation, formal substitution of halogen atoms by ethoxy groups, and eventually ring-opening. In the absence of ethanol no reaction took place, and so ethoxide is presumed to be the active base. Furthermore, since **5** and **6** are completely unreactive under the reaction conditions, it is assumed that the ring-opening is initiated by abstraction of a hydrogen from C-3 and expulsion of one of the halogen atoms. In addition, since identical product mixtures were obtained when 2-alkyl-substituted and 3-alkyl-substituted 1,1,2-trihalocyclopropanes reacted (e.g., both **1** and **4** gave a 50:50 mixture of the corresponding acetylenic ketal and acetal in 80% combined yield), it is the halogen atom at C-2 that is expelled, resulting in formation of the corresponding 3,3-dihalocyclopropene (**7**) (Scheme 3). Cyclopropenes like **7** are known to react with nucleophiles,[54−57] and attack of ethoxide and/or ethanol at either end of the carbon−carbon double bond results in the formation of cyclopropyl anions **8** and **9**. These anions are unstable and collapse to cyclopropenes **10** and **11**, respectively, which react with ethoxide and/or ethanol to provide ketals and acetals, respectively, as the final products (Scheme 3).[20,54,57−59]



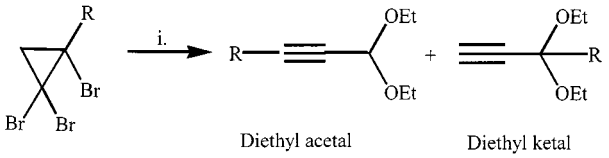
Scheme 3. Conceivable mechanism for formation of acetals and ketals; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, EtOH (4 equivalents), CH_2Cl_2, room temperature

From the reaction pathways presented in Scheme 3, it is reasonable to expect that the course of reaction should be sensitive to the electronic and leaving-group properties of the halogen atoms, and such an influence has indeed been observed. This is illustrated by the data in Table 2, which show several notable features. Thus, the larger the number of chlorine atoms attached to the ring, the lower the acetal yield. This is nicely reflected in the results obtained from the reaction of 1,1,2-trihalo-2-methylcyclopropanes under PTC; the total yield of acetylenic products drops 10−15% for each chlorine atom introduced at the expense of a bromine atom. In similar fashion, the yield of 3,3-diethoxy-1-propyne dropped significantly when the starting material was changed from 1,1,2-tribromocyclopropane to 2-bromo-1,1-dichlorocyclopropane. It is also noteworthy that the isomer composition is halogen-dependent. Thus, when **1** is allowed to react under PTC, **2** and **3** are formed in a 1:1 ratio, a result in sharp contrast to the product mixture obtained under the same conditions from 1,1,2-trichloro-2-methylcyclopropane, which contains **3** almost exclusively (**3/2** > 20, Table 2).

Table 2. Selected examples of formation of 3-alkyl-3,3-diethoxy-1-propyne (ketal) and 1-alkyl-3,3-diethoxy-1-propyne (acetal) from 2-alkyl-1,1,2-trihalocyclopropanes under PTC (from ref.[44])

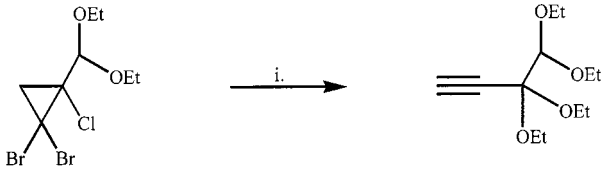
Alkyl	X	Y	Ketal/Acetal	Total yield[c] (%)
H	Br	Br	[b]	70
H	Br	Cl	[b]	57
Me	Br	Br	1.0	80
Me	Br	Cl	> 9	50
Me	Cl	Br	1.0	64
Me	Cl	Cl	> 20	40

[a] Total isolated yield of ketal and acetal. – [b] Only one product possible. – [c] Total isolated yield of ketal and acetal.



R	Diethyl acetal : Diethyl ketal
Me	1.0
Ph	1.0
Octyl	2.0
Propyl	2.5
Cyclohexyl-CH_2	2.5
t-Bu	10.0

Scheme 4. Ring-opening of alkyl-substituted 1,1,2-tribromocyclopropanes; examples taken from refs. 44 and 51; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, EtOH (4 equivalents), CH_2Cl_2, room temperature



Scheme 5. Regiospecific ring-opening of 1,1-dibromo-2-chloro-2-diethoxymethylcyclopropane; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, EtOH (4 equivalents), CH_2Cl_2, room temperature

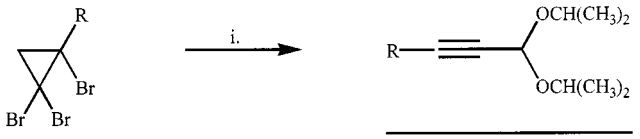
It also turned out that the ketal/acetal distribution was sensitive to the amount of ethanol present during the reaction. When **1** was allowed to react under modified PTC, with 35 equivalents of ethanol instead of 4 and with an ethanol/base ratio of 35 instead of 0.5, the products were identical to those (**2** and **3**) obtained under our standard conditions, but the large excess of ethanol caused the ketal/acetal ratio (**3**/**2** ratio) to decrease to 0.25, compared to 1.0 under standard PTC. This clearly suggests that *acetal formation results from ethanol addition to the intermediate cyclopropene*, whereas *ketal formation is predominantly due to ethoxide attack on the same intermediate*. Consequently, intermediate **7** is preferentially attacked at C-2 by ethoxide and at C-3 by ethanol.

The trends summarised above were mainly based on experiments with methyl- and phenyl-substituted 1,1,2-trihalocyclopropanes, and it was therefore of interest to examine reactions of 1,1,2-trihalocyclopropane derivatives containing at least one substituent with greater steric bulk and higher polarity. When such reactions were carried out with a number of such compounds, a slightly different picture emerged. Acetylenic ketals and acetals were still formed, but the ketal/acetal ratios deviated considerably from the 1.0 ratio obtained with the 2-methyl and 2-phenyl analogues. Deviations in both directions were observed. Thus, formation of acetal at the expense of ketal was observed when the steric bulk of R was increased and made the attack of **7** at C-2 more difficult: when R was changed from methyl to *tert*-butyl, the ketal/acetal ratio dropped from 1.0 to 0.1 (Scheme 4). However, when a polar substituent was attached at C-2, attack of **7** at C-2 was obviously facilitated, because ketal formation was heavily predominant. This was particularly so when the C-2 substituent was (diethoxy)methyl; this reaction was completely regiospecific and furnished 3,3,4,4-tetraethoxy-1-butyne as the only product (Scheme 5).[60]

The preference for ketals in cases when a polar substituent is attached to C-2 is significant, because from a steric point of view, acetal predominance should have been expected in these cases as well. Since acetal formation is due to ethanol attack on **7** at C-3, ketal preference clearly suggests that *the polar substituents redirect the ethanol attack from C-3 to C-2. It is therefore believed that the regioselective ring-opening observed with some 1,1,2-trihalocyclopropanes under phase-transfer conditions is due to hydrogen bonding*.

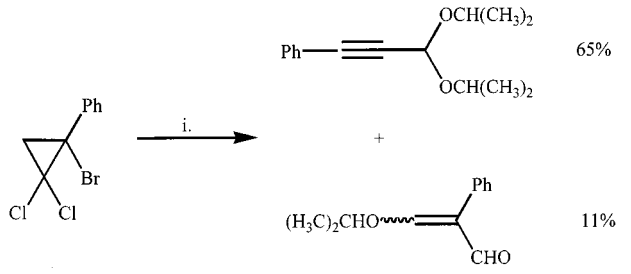
On the basis of the mechanistic aspects described above, two measures were believed to improve the regioselectivity of the ring-opening. If the reaction was performed under phase-transfer conditions *in the presence of an alcohol less acidic than ethanol and whose corresponding alkoxide was less nucleophilic than ethoxide*, nucleophilic attack of **7** at C-3 should become relatively more favourable and give a higher relative yield of the acetal. On the other hand, if the reaction was carried out using as reagent an excess of ethoxide in an inert solvent, the ethanol concentration would be low and formation of ketal should be favoured. In order to achieve the first goal, a number of 1,1,2-trihalides were allowed to react under the standard phase-transfer conditions in the presence of 2-propanol. Replacement of ethanol with the less acidic 2-propanol lowers the alkoxide concentration and makes alkoxide attack on **7** less likely, relative to alcohol attack, thus favouring formation of acetal at the expense of the corresponding ketal. Such a change did indeed take place, but it was surprising to find that *ketal formation was completely suppressed*. However, the outcome of the suppression with respect to the yield was substrate-dependent. Thus, the 2-alkyl-1,1,2-tribromocyclopropanes exposed to PTC in the presence of isopropyl alcohol gave the corresponding 3-alkyl-1,1-diisopropoxy-2-alkyne in medium to good yields (Scheme 6), whereas 1,1-dichloro-2-halocyclopropanes gave considerable amounts of several by-products. This was particularly the case with 1,1,2-trichloro-2-methylcyclopropane and 2-bromo-1,1-dichloro-2-methylcyclopropane, which afforded intractable reaction

mixtures containing only minor amounts of 1,1-diisopropoxy-2-butyne, and from which no pure compound could be easily isolated in significant quantities.[45] The reaction mixture from 2-bromo-1,1-dichloro-2-phenylcyclopropane was less complex and allowed the isolation of two products: 3,3-diisopropoxy-1-phenyl-1-propyne in 65% yield and 3-isopropoxy-2-phenyl-2-propenal in 11% yield (Scheme 7).[45] The aldehyde formation is discussed later.



R	Yield (%)
Me	82
Ph	79
Propyl	50
Cyclohexyl-CH_2	52

Scheme 6. Ring-opening of alkyl-substituted 1,1,2-tribromocyclopropanes; examples taken from refs.[45] and [51]; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, *i*PrOH (4 equivalents), CH_2Cl_2, room temperature



Scheme 7. Ring-opening of 2-bromo-1,1-dichloro-2-phenylcyclopropane; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, *i*PrOH (4 equivalents), CH_2Cl_2, room temperature

Ring-Opening of 1,1,2-Trihalocyclopropanes Under Nonaqueous Conditions

In order to facilitate alkoxide attack on **7**, the substrates were treated with a suspension of sodium ethoxide, prepared from sodium and extremely dry ethanol, in absolutely dry tetrahydrofuran (THF). Under these conditions, a number of trihalocyclopropanes reacted cleanly and gave acetylenic diethyl ketals in good to excellent isolated yields on a multigram scale (Table 3). None of the trihalocyclopropanes gave even traces of the corresponding acetals, and in no case were any functionalised alkenes detected. Consequently, it is evident that the double bond in the cyclopropene intermediate is attacked by ethoxide regiospecifically at the most substituted carbon atom (C-2) and affords cyclopropene **10**, which undergoes ring-opening by attack of another ethoxide ion at the carbon atom attacked in the first step, to give the corresponding ketal (Scheme 3).

Table 3. Selected examples of formation of 3-alkyl-3,3-diethoxy-1-propyne (ketal) by treating 2-alkyl-1,1,2-trihalocyclopropanes with dry sodium ethoxide in dry THF

Alkyl	X	Y	Yield (%)
Me	Br	Br	79[a]
Me	Cl	Br	72[a]
Ph	Br	Br	81[a]
Pr	Br	Br	65[b]
Cyclohexyl-CH_2	Br	Br	64[b]
Pentyl	Br	Cl	52[b]

[a] From ref.[44]. – [b] From ref.[51].

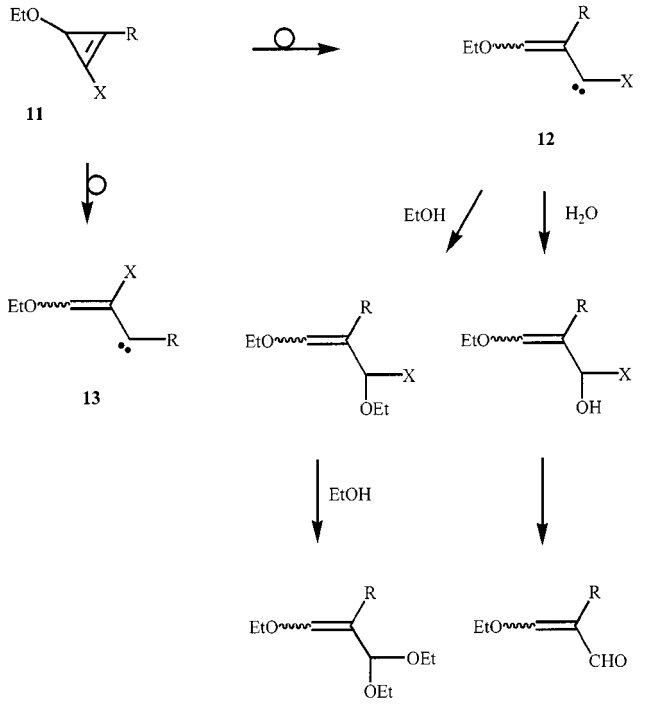
If reactions were performed with sodium ethoxide prepared from sodium and ethanol containing traces of water, small amounts (less than 3%) of α,β-unsaturated aldehydes were formed (vide infra). It is also noteworthy that the use of several commercial samples of so-called dry sodium ethoxide in dry THF led to considerably less efficient and/or less regiospecific reactions than those reported in Table 3. These results indicate that the ethoxide reactivity is influenced by the presence of sodium hydroxide.

In an attempt to facilitate exclusive ethanol addition to cyclopropene **7** at C-3, some 1,1,2-trihalocyclopropanes were dissolved in dry ethanol and subsequently treated with selected bases which do not act as nucleophiles. The most successful base in this respect was 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). When 1,1,2-trihalocyclopropanes were refluxed in DBU/ethanol mixtures containing 2 equivalents of DBU (relative to trihalide), regiospecific ring-opening and formation of the corresponding acetal were observed. Thus, it is evident that ethanol regiospecifically attacks the double bond in **7** at the least substituted carbon atom (C-3) and gives cyclopropene **11**. This is in turn attacked by another ethanol molecule, at the carbon atom attacked in the first step, and suffers subsequent ring-opening to give the acetal. The acetals were isolated in rather moderate yields (50−67%) because of incomplete consumption of the starting material; this was the case even when a large excess of DBU was used. In no case was any of the corresponding ketal formed, but some 1,1,2-trihalides, not unexpectedly, gave minor amounts of the corresponding 2-substituted 3-ethoxy-2-propenal diethyl acetal as a by-product (vide infra).[45]

Mechanistic Aspects Related to By-product Formation

As frequently mentioned above, ring-opening of some of the 1,1,2-trihalocyclopropanes gave minor amounts (typically 2−5%, but in some cases as high as 10%) of either a 2-substituted α,β-unsaturated aldehyde (under PTC) or the corresponding 2-substituted α,β-unsaturated aldehyde diethyl acetal (in ethanol/DBU). The aldehydes were isolated by flash chromatography and subsequently converted into the respective 4-substituted isoxazoles by treatment with hydroxylamine.[44] Similar aldehydes have been obtained from

other halogenated cyclopropanes under comparable conditions,[61] by a reaction sequence involving a cyclopropene−vinylcarbene rearrangement.[54,62−65] Such a rearrangement may very well occur in these cases as well and convert cyclopropene **11** to vinyl carbene **12**, which can react by insertion with either water, to afford α,β-unsaturated aldehyde, or with ethanol, to give substituted α,β-unsaturated aldehyde diethyl acetal (Scheme 8). The alternative rearrangement (**11**→**13**), which has literature precedence,[48,66] would require an unprecedented and complex rearrangement to give the unsaturated by-products and is therefore regarded as a very unlikely reaction pathway. Several experiments aiming at trapping carbene **12** (by performing the ring-opening in the presence of a reactive alkene) were unsuccessful, but then so were a number of similar experiments designed to trap similar carbene intermediates.[62,67−69] The lifetime of carbene **12** is therefore deemed to be short.

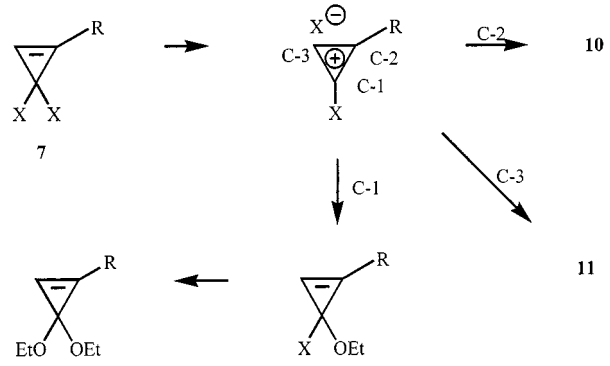


Scheme 8. Formation of by-products from cyclopropene **7** by rearrangement to vinyl carbenes

It is interesting to note that all the olefinic by-products isolated are 2-substituted 3-alkoxy-2-propenal derivatives; in no case was the corresponding 3-substituted analogue detected. This means that the by-product precursor must be cyclopropene **11** and *not* **10** (Scheme 3). A corollary of this is that the latter intermediate is unable to undergo the cyclopropene-vinyl carbene rearrangement before it is consumed in other reactions (e.g. nucleophilic attack). This reluctance of **10** to rearrange is in accordance with the results of similar reactions studied by Müller and Pautex,[61] but the reason for this unwillingness to react is not evident. Further studies will hopefully clarify this problem.

Another interesting point is the observation that the products formed from cyclopropene **11** depend on the nature of the halogen Y. When Y = Br and the reaction is performed so that the corresponding acetal is the only product formed, the analogous chloro derivatives (Y = Cl) generally give a 3-alkoxy-2-propenal derivative in addition to the acetal. One explanation for this difference might be that the former cyclopropene is attacked more readily than the latter by nucleophiles. It is also conceivable that **11** rearranges more easily to the corresponding vinyl carbene when Y = Cl than when Y = Br, although Baird[70] observed that 1-bromo-2-chloro-3,3-dimethylcyclopropene gave the corresponding vinyl carbenes bromo(1-chloro-2-methyl-1-propenyl)carbene and chloro(1-bromo-2-methyl-1-propenyl)carbene in a 1:1 ratio at room temperature. A firm conclusion must await additional studies.

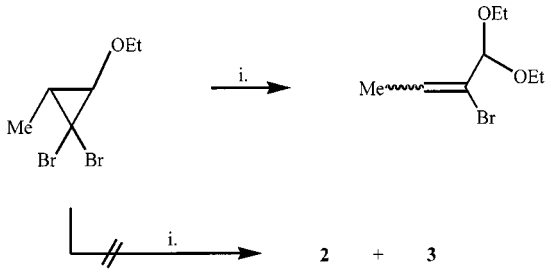
A different mechanism, involving a cyclopropenium intermediate (Scheme 9) and deviating from the favoured reaction scheme (Scheme 3) in the latter half, may also be imagined. Because of their stability,[71] cyclopropenium ions are easily generated from cyclopropenes like **7** by expulsion of a halide ion.[54,55] However, if such an intermediate were involved, one would, by analogy, expect products to be formed from nucleophilic attack at all three ring-carbon atoms.[54,55] Attack of the cation at C-2 and C-3 would give cyclopropenes **10** and **11**, respectively, and eventually ketal and acetal, respectively (Scheme 2), and these are indeed the main products from the trihalocyclopropanes. Attack at C-1, on the other hand, would afford the corresponding 1-substituted 3-chloro-3-ethoxycyclopropene intermediates, which would be expected to give the diethyl ketals of the corresponding cyclopropenones (Scheme 9).[55] Such diethyl ketals were not observed in any of our reactions (although such products might conceivably be stable under the reaction conditions[55]), and so this renders unlikely the intermediacy of a cyclopropenium cation.



Scheme 9. Expected products if the ring-opening involves a cyclopropenium intermediate

A comment regarding the fate of carbanions **8** and **9** under PTC is also appropriate. Under these conditions, abstraction of a proton and formation of the corresponding 2-ethoxy-1,1-dihalocyclopropanes derivatives prior to formation of cyclopropenes **10** and **11** may be envisaged. However, this possibility has been ruled out by experimentation. Thus, when 1,1-dibromo-2-ethoxy-3-methylcyclopropane, one of the two products that can be envisaged from reaction with **4**, was subjected to phase-transfer

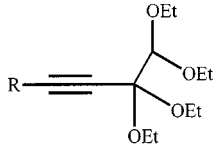
conditions, **2** and **3** were not obtained at all; the only product isolated was 2-bromo-1,1-diethoxy-2-butene, which upon hydrolysis under acidic conditions gave 2-bromo-2-butenal (Scheme 10).



Scheme 10. Ring-opening of 1,1-dibromo-2-ethoxy-3-methylcyclopropanes; reagents and conditions: i. 50% aq. NaOH (8 equivalents), TEBA, EtOH (4 equivalents), CH_2Cl_2, room temperature

Conclusions

1,1,2-Trihalocyclopropanes, which are easily available in large quantities, can, by choosing the right reaction conditions, be specifically transformed into either the corresponding acetylenic alkyl ketals or the corresponding acetylenic alkyl acetals. Both the ketals and the acetals are versatile building blocks in organic synthesis, as demonstrated by Katritzky and co-workers,[72−74] Faust et al.,[75] and others.[76] We are currently utilising these ring-opening reactions to prepare a variety of 1-alkyl-3,3,4,4-tetraethoxy-1-butyne derivatives (**14**), which are intended for use as starting materials for the synthesis of a variety of compounds, taking advantage of the reactivities of the acetal and ketal moieties, the triple bond and, when R = H, at the terminal carbon atom of the triple bond.



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