BROMOCHLORINATION
OF
UNSATURATED
HYDROCARBONS

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CONTENTS

CHAPTER 1

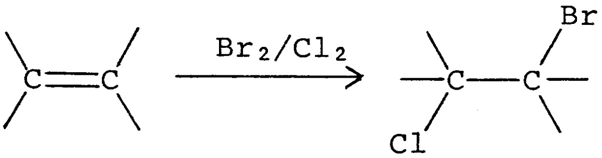
GENERAL INTRODUCTION

Bromine chloride (BrCl) has been reported to be obtained by direct combination of bromine and chlorine.1–4) This bromine chloride was characterized by spectrophotometric or pressure measurements,5–7) but is a rather unstable compound, and so has not been obtained in the pure state. It is highly dissociated in the vapor phase and in solution, while the dissociation constant for the following reaction (Scheme 1) in carbon tetrachloride solution was shown to be 0.145±0.006.5)

$$2BrCl \rightleftharpoons Br_2 + Cl_2$$

Scheme 1

Such a high instability of bromine chloride (the heat of formation of bromine chloride has been estimated as 0.3 kcal/mol5)) provides some difficulties in studying its chemical reactions. Nonetheless, bromine chloride has been used as an bromochlorinating agent of alkenes and alkynes. As with the other electrophilic additions to alkenes, the reaction of alkenes with a mixture of bromine and chlorine can occur to give the bromo chloro compounds (Scheme 2).



Scheme 2

White et al.[8)] have established the third order kinetics (first order in alkene and second order in bromine chloride) for the addition of a mixture of bromine and chlorine (within the initial concentration range 0.4—0.8 mol dm^{-3} of BrCl in acetic acid solution) to alkenes such as cinnamic and crotonic acids, as follows:

$$\text{Rate}=k[\text{alkene}][\text{BrCl}]^2$$

They have also reported the order of reactivity of the interhalogens and bromine to alkene as follows:

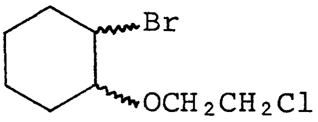
$$I_2 \ll \text{IBr} < Br_2 < \text{ICl} < \text{BrCl}$$

The kinetic studies have shown further that bromine chloride adds to alkenes 4×10^2 times faster than bromine.

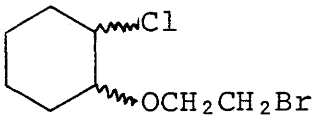
Hanson et al.[9)] reported the kinetics of BrCl and Br_2 addition to substituted cinnamic acids to be second order, first order in alkenes and first order in BrCl in carbon tetrachloride or chloroform as the solvents. The rate of BrCl addition has been reported to be much larger than that of Br_2 addition. Such an enhancement of rate of BrCl addition may be largely due to the existence of a permanent dipole moment (μ=0.57 D)[7)] in the molecule, in which bromine is positively polarized, thus greatly facilitating the electrophilic attack to alkene.

The rate of addition of a mixture of bromine and chlorine (with the total concentration of halogens constant) to cis-cinnamic acid in carbon tetrachloride-acetic acid solution was greatest when $[Br_2]/[Cl_2]$ was unity.8) The kinetic form of the reaction was the same as that for the other interhalogens (ICl and IBr) and for bromine, but not for chlorine. These results show that the reaction of a mixture of bromine and chlorine involves a different attacking reagent (BrCl), not bromine and chlorine alone.

The reaction of a mixture of bromine and chlorine to cyclohexene in the presence of ethylene oxide has been reported to give 1-bromo-2-(2-chloroethoxy)cyclohexane (1), whereas that to ethylene in the presence of cyclohexene oxide gave only 1-(2-bromoethoxy)-2-chlorocyclohexane (2).10)



(1)

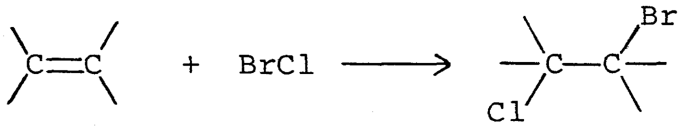


(2)

In this reaction the bromine atom adds to the carbon atom of the alkene, while the chlorine atom adds to the carbon atom of the epoxide. These results show that the bromine chloride is an attacking reagent to alkene, but not bromine or chlorine. Similar results have been found in the reaction of propene and 2-methylpropene with a mixture of bromine and chlorine in the presence of ethylene oxide.[11)]

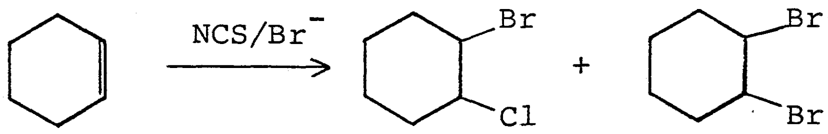
Meanwhile, the reaction of alkenes with a mixture of N-bromoacetamide and hydrogen chloride (or N-chloroacetamide and hydrogen bromide) has been known to proceed by prior formation of bromine chloride which adds subsequently to alkenes.[12,13)]

$$\mathrm{AcNHBr} + \mathrm{HCl} \rightleftarrows \mathrm{AcNH_2Br^+} + \mathrm{Cl^-} \rightleftarrows \mathrm{AcNH_2} + \mathrm{BrCl}$$



Scheme 3.

Similarly, Wilbur et al.[14)] have reported that cyclohexene gives bromochlorinated adducts upon the reaction of bromine chloride prepared in situ from the reaction of N-chlorosuccinimide and bromide ion (Scheme 4).



Scheme 4.

A mixture of bromine and antimony (III or V) chloride was shown to react with alkenes to give the bromo chloro compounds (Scheme 5).[15)]

$$SbCl_5 + Br_2 \rightleftharpoons BrCl + SbCl_4Br$$

$$SbCl_4Br \rightleftharpoons BrCl + SbCl_3$$

$$C_6H_{10} + BrCl \longrightarrow C_6H_{10}BrCl$$

Scheme 5.

Crystalline bromine chloride complexes such as pyridine bromine chloride complex[16–18] and polyhalide ions (Br_2Cl^- or $BrCl_2^-$)[19,20] may be used as bromochlorinating agents to alkenes. It has been reported that these reagents can be readily prepared in stable forms under the normal conditions. Pyridine bromine chloride complex (3) was reported to be prepared from bromine chloride and excess pyridine.[16] Dichlorobromate(1-) ion (4) can be prepared from the reaction of chlorine and bromide ion.[20] Chlorodibromate(1-) ion (5) was also reported to be prepared by treating bromine with chloride ion.[19]

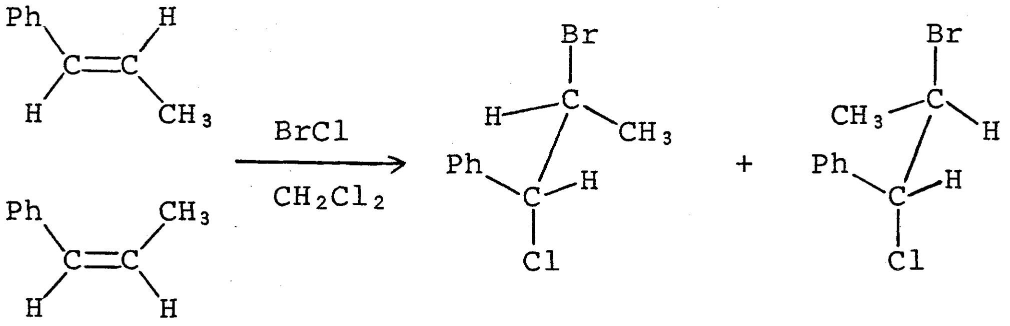
$C_5H_5N{-}BrCl$	$(CH_3)_4NBrCl_2$	$(CH_3)_4NBr_2Cl$
(3)	(4)	(5)

The structure of polyhalide ion such as 4 has been confirmed from vibrational spectroscopy[21,22] and reported to be a linear and symmetrical ion, similar to tribromide ion.

$$[Cl{-}Br{-}Cl]^-$$

As has been described, there are numerous methods to prepare bromine chloride and the reaction of alkenes with bromine chloride has been reported in the literatures.[15,19,23–26)

Walden[23) has reported in 1897 that the reactions of fumaric and maleic acids with bromine chloride give the corresponding bromo chloro compounds, i.e., meso- and dl-2-bromo-3-chlorosuccinic acids, respectively, in an anti stereospecific manner. Buckles et al.[24) reported that the addition reaction of bromine chloride (prepared in situ from the reaction of bromine and chlorine) to cyclohexene and trans-stilbene took place in an anti stereospecific manner, but, that to cis-stilbene gave a mixture of dl- and meso-1-bromo-2-chloro-1,2-diphenylethane in a stereoselective manner. Similarly, the reaction of cis- and trans-1-phenylpropenes with bromine chloride gave a mixture of threo- and erythro-2-bromo-1-chloro-1-phenylpropanes (Scheme 6).[19)

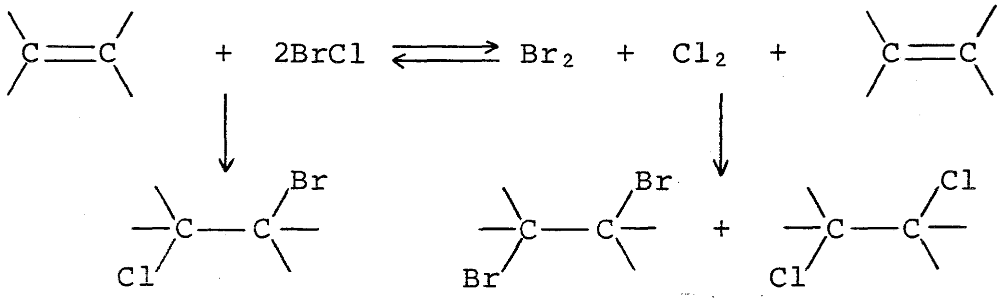


trans-alkene	91.5%	8.5%
cis-alkene	21.0%	79.0%

Scheme 6.

Thus, the stereochemistry of addition of bromine chloride to alkenes is considered to be dependent on the structures of alkenes employed.

Table 1 shows the product composition of addition to some alkenes with bromine chloride, prepared in situ from the reaction of bromine and chlorine. The isolated yields appeared to be somewhat low due to the contamination of dichloro- and dibromoalkanes. The formation of these by-products is undoubtedly due to the attack of both bromine and chlorine which are formed in an equilibrium with bromine chloride (Scheme 7).[5)]



Scheme 7.

Unsymmetrical alkenes such as styrene, trans-cinnamic acid, and 1-phenylpropenes give the Markownikoff adducts by the reaction with bromine chloride in a regiospecific manner. On the other hand, the reaction of 1-hexene, methyl crotonate, and methyl isocrotonate with bromine chloride afforded the regioselective Markownikoff adduct, while that of methyl acrylate gave the regioselective anti-Markownikoff adduct. These results show that the regiochemistry of addition to

Table 1. Product Distributions for the Addition of Bromine Chloride to Some Alkenes.

Alkene	Solvent	%M[a)]	%aM[a)]	Yield/%	Ref.
$CH_2=CH_2$	CH_2Cl_2			39	24
$C_4H_9CH=CH_2$	CCl_4	61	39	96[b)]	25
cyclohexene	$CHCl_3$			56[c)]	24
$C_6H_5CH=CH_2$	$CHCl_3$	100	0	67	24
(t)PhCH=CHPh	$CHCl_3$			52[d)]	24
(c)PhCH=CHPh	$CHCl_3$			73.5[e)]	24
(t)$PhCH=CHCH_3$	CH_2Cl_2	100	0	60[f)]	19
(c)$PhCH=CHCH_3$	CH_2Cl_2	100	0	60[g)]	19
(t)$PhCH=CHCO_2H$	$CHCl_3$	100	0	31[h)]	24
$CH_2=CHCOOCH_3$	CH_2Cl_2	17	83	89[b)]	26
(c)$CH_3CH=CHCOOCH_3$	CH_2Cl_2	93	7	85[b,i)]	26
(t)$CH_3CH=CHCOOCH_3$	CH_2Cl_2	70	30	91[b,j)]	26

a) M=Markownikoff adduct. aM=anti-Markownikoff adduct. b) Yields were determined by ^1H NMR analysis. c) trans. d) erythro. e) a mixture of 68% of threo- and 5.5% of erythro-bromo chloro adducts. f) a mixture of 91.5% of erythro- and 8.5% of threo-bromo chloro adducts. g) a mixture of 21% of erythro- and 79% of threo-bromo chloro adducts. h) erythro. i) threo. j) erythro.

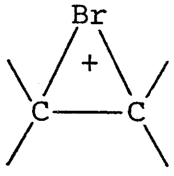
alkenes with bromine chloride is dependent on the structures of alkenes employed.

Similar results have been reported for the bromoclorination of alkenes with bromine chloride prepared in situ from the reaction of $SbCl_5$ and Br_2 (or $SbCl_3$ and Br_2) in CCl_4.15)

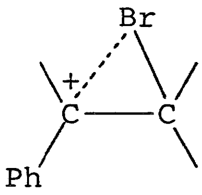
Meanwhile, there are several studies on the stereochemistry of bromination of alkenes with molecular bromine. Rolston et al.27) found that the addition to cis- and trans-2-butenes with bromine in various solvents is in an anti stereospecific manner, while the addition to cis- and trans-1-phenylpropenes is in a nonstereospecific manner although anti stereospecific addition product was formed mainly. A similar stereochemistry has been observed by Fahey et al.29) for the bromination of trans-anethole. Buckles et al.30) also reported that the reaction of trans-stilbene with bromine took place in an anti stereospecific manner, while the addition to cis-stilbene took place in an stereoselective manner.

These results show that the stereochemistry of the addition is the same for both bromine and bromine chloride (Table 1). It is quite reasonable to consider that the reaction intermediate is nearly the same for both bromine and bromine chloride addition. Thus, the study of the addition of bromine chloride to alkenes would give a further insight into the addition mechanisms which could not be observed in the reaction of symmetrical electrophiles such as bromine.

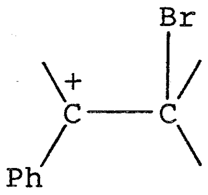
The mechanism of the electrophilic addition of bromine to alkenes has been widely investigated from both the kinetic and the stereochemical points of view.[31,32] It is well known that the nature of the reaction intermediate of addition varies with the structure of the alkene and the reaction medium,[27,28] namely ranging from a strongly bridged bromonium ion of type (6) originally postulated by Roberts et al.[33] to a weakly bridged ion of the type (7) or an open carbonium ion like intermediate (8).



(6)



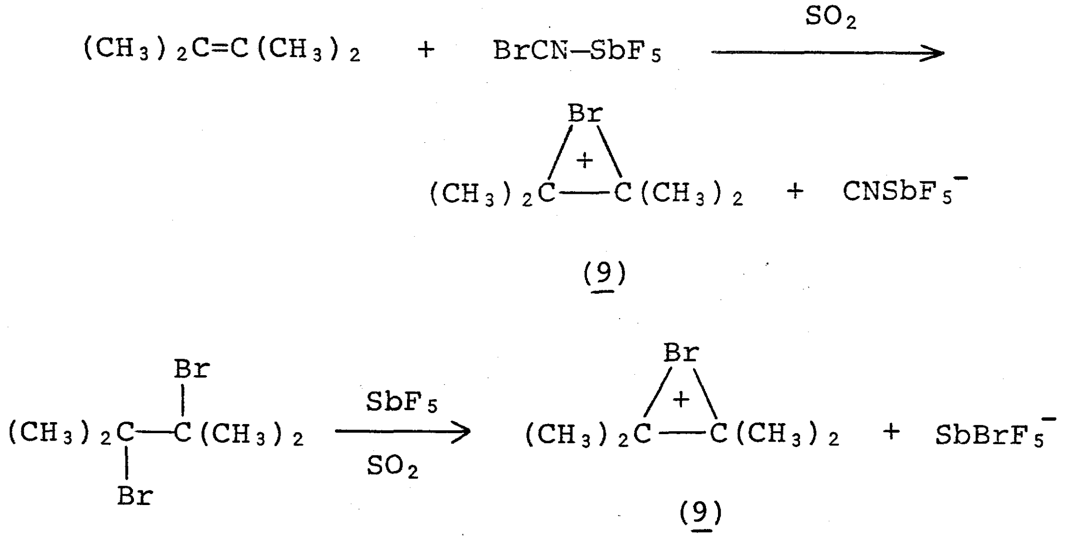
(7)



(8)

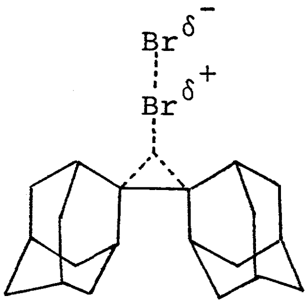
An intermediate of type (6) is believed to be involved in the bromination of alkyl-substituted ethylenes, which gives only the anti stereospecific product irrespective of the reaction medium,[27] while in the reaction of phenyl-substituted ethylenes, the unsymmetrical bridged ion (7) or open carbonium ion (8) must be involved in order to rationalize the nonstereospecific course of the addition, which leads to syn as well as to anti-adducts and depends on the reaction medium.[28]

The existence of a bridged ion (6) and its structure are well supported by stereochemical data,[31,32] kinetic data[34] and theoretical calculations.[35] Furthermore, there is direct evidence for the existence of halonium ions such as those which are involved in the chlorination, bromination, and iodination reactions of alkenes. Olah et al.[36–39] have reported the data of ^{1}H and ^{13}C NMR spectra for some three-membered cyclic bromonium ions. The addition of the highly-polarized complex, BrCN-SbF$_5$, in SO$_2$ to 2,3-dimethyl-2-butene gives a bridged ion (9),[39] whose ^{1}H NMR spectrum is identical with the ion prepared by the ionization of 2,3-dibromo-2,3-dimethylbutane (Scheme 8).[36] These results are consistent with the idea that a bridged bromonium ion (9) is formed in the reaction of 2,3-dimethyl-2-butene with bromine.



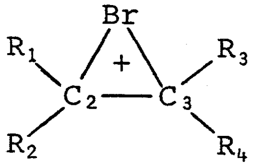
Scheme 8.

The isolation of the stable adamantylideneadamantane alkonium type π-complex (10) has also been reported in the reaction of adamantylideneadamantane with bromine in CCl$_4$, SO$_2$, HF-SO$_2$ or FSO$_3$H-SO$_2$ solution.[39]

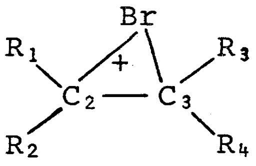


(10)

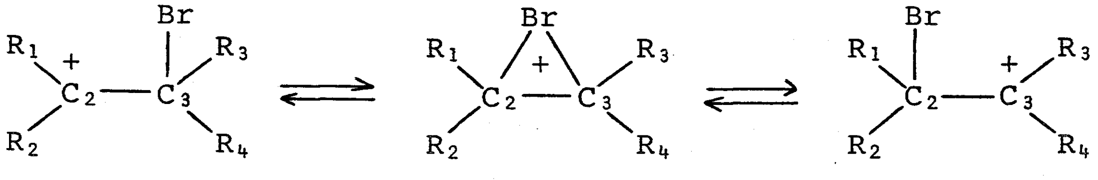
The ^{1}H and ^{13}C NMR spectra of several alkyl-substituted ethylene bromonium ions have shown several structural possibilities for the bromonium ion which is dependent on the alkyl-substituent as follows: the static symmetrical bridged ion in which the C_2-Br bond length is equal to the C_3-Br bond length (10); the static unsymmetrical bridged ion in which the C_2-Br bond length is not equal to the C_3-Br bond length (11); the bromonium ion in equilibrium with a pair of open-chain bromoalkenium ions (12).[40]



(10)

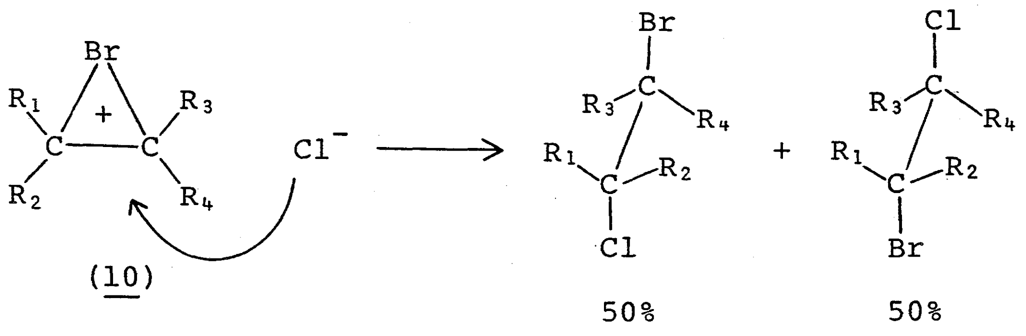


(11)



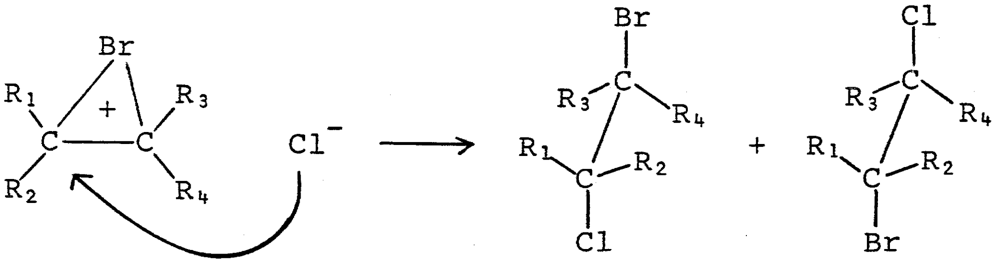
(12)

Meanwhile, the regio- and stereochemistries of the products formed by electrophilic addition of bromine chloride (or the other interhalogens) to alkenes are dependent on the structure of intermediate at the product-determining step, thus in turn depend on the structure of the cationic intermediates immediately preceding the product-determining step. If the intermediate has a symmetrical bridged structure such as (10), nucleophilic attack of chloride ion can occur only on the face opposite to the electrophile. Such a backside attack of nucleophile is analogous to the S_N2 type mechanism and consequently the addition product is formed in an anti stereospecific manner. The additions are in a non-regiospecific manner since the attack of nucleophile can occur at both carbon atoms of the bridged intermediate (10) (Scheme 9).



Scheme 9.

If the intermediate has an unsymmetrical bridged structure (11), nucleophilic attack of chloride ion can occur only at the opposite to the electrophile similar to the attack on 10. The addition is in a regioselective manner since the attack of nucleophile on 11 can occur predominantly at the carbon atom bearing a more positive charge development (Scheme 10).



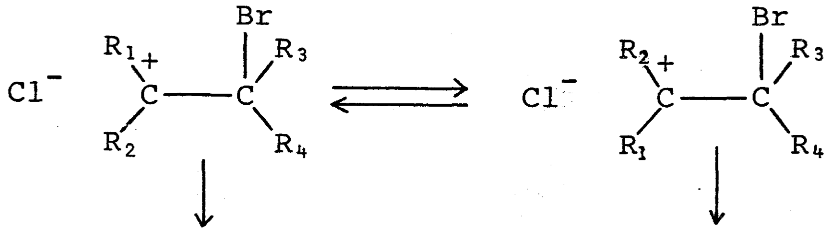
(11)

major

minor

Scheme 10.

If the intermediate has an open carbonium ion-like structure (12), nucleophilic attack of chloride ion can occur at both faces and hence both syn and anti addition products are expected (Scheme 11).



(12)

syn and anti adducts

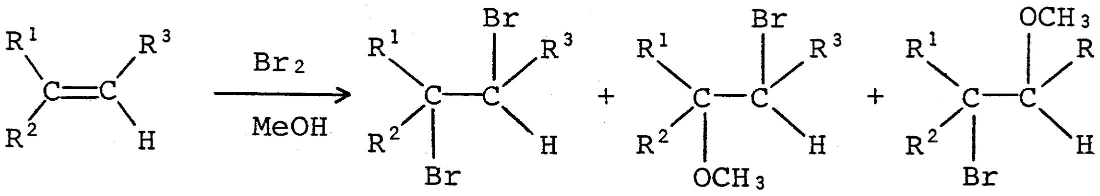
syn and anti adducts

Scheme 11.

The addition is in a regiospecific Markownikoff manner since the attack of nucleophile on 12 can occur only at the carbon atom bearing a positive charge.

Thus, in order to gain further information in more detail on the electrophilic addition of bromine chloride (and bromine) to alkenes, it is necessary to have more experimental data on the regio- and stereochemistries of the addition products.

Dubois et al.41) have reported that the product distribution on the addition of several methyl-substituted ethylenes with bromine in methanol (Scheme 12).

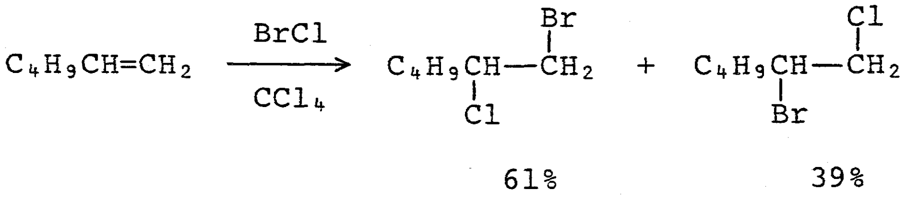


$R^1=CH_3$, $R^2=R^3=H$	39.3	49.4	11.3
$R^1=R^2=CH_3$, R =H	15.3	84.7	0
$R^1=R^2=R^3=CH_3$	18.6	81.4	0

Scheme 12.

These results show that the regiochemistry of the addition is dependent on the methyl-substituent, therefore methyl-substituent affects the structure of a cationic intermediate. It has also been reported that the bromochlorination of propene with bromine chloride in aqueous hydrochloric acid gives 1-bromo-2-chloropropane and 2-bromo-1-chloropropane in the proportion of 54 : 46.42) Thus, the intermediate formed in the reaction of propene has been shown to be nearly symmetrical bromonium ion-like (10), whereas that of 2-methylpropene or 2-methyl-2-butene is an unsymmetrical bromonium ion-like (11) or an open carbonium ion-like (12).

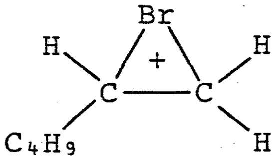
As shown in Table 1, Heasley et al.[25] reported that the addition of bromine chloride to 1-hexene in CCl_4 gives a mixture of 1-bromo-2-chloro- and 2-bromo-1-chlorohexanes (Scheme 13).



$$C_4H_9CH{=}CH_2 \xrightarrow[CCl_4]{BrCl} \underset{61\%}{C_4H_9\underset{Cl}{CH}{-}\overset{Br}{CH_2}} + \underset{39\%}{C_4H_9\underset{Br}{CH}{-}\overset{Cl}{CH_2}}$$

Scheme 13.

Such nonregiospecific addition also suggests that the intermediate of the reaction of 1-hexene with bromine chloride in CCl_4 is a nearly symmetrical bridged bromonium ion-like (13).

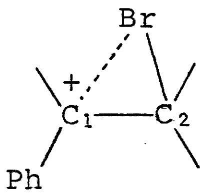


(13)

However, only very few systematic studies have been carried out on the regiochemistry of the reaction of alkyl-substituted ethylenes with bromine chloride.

Data on the regiochemistry of bromochlorination of phenyl-substituted ethylenes with bromine chloride are also very limited. Buckles et al.[24] found that the addition of bromine chloride to styrene occurs in a regiospecific manner, giving

2-bromo-1-chloro-1-phenylethane (Table 1). The addition of bromine chloride to 1-phenylpropenes was also found to take place in regiospecific and stereoselective manners.19) The bromochlorination of styrene with a mixture of $SbCl_5$ and Br_2 (or $SbCl_3$ and Br_2) gave only the regiospecific Markownikoff product, 2-bromo-1-chloro-1-phenylethane.15) These reports show that the intermediate from the reaction of styrene derivatives with bromine chloride is an unsymmetrically weakly bridged benzylic bromonium ion-like (14) or an open carbonium ion-like (15).



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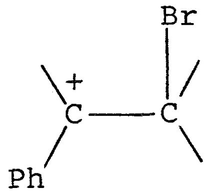
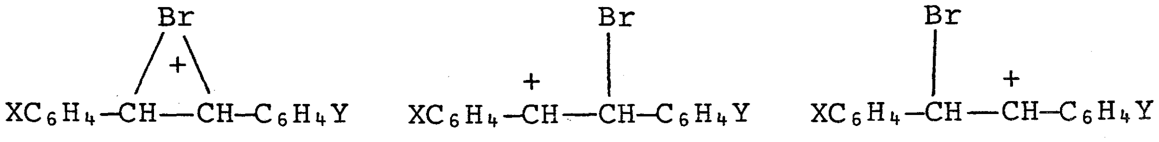


(15)

Meanwhile, Ruasse et al.43,46) have measured the rates of bromination of several trans-stilbene derivatives in methanol and reported that the reaction proceeds via one, two, or all three intermediates, dependent on the substituents and the solvents (Scheme 14).



Scheme 14

Rolston et al.[44)] have measured the rate of bromine addition to some styrene derivatives in acetic acid. Correlation with Hammett's σ^+ substituent constants gave ρ of -4.21. This value shows that the rate-determining transition state has an unsymmetrical charge distribution, most of the charge being developed at phenyl-substituted carbon C_1 with little delocalization on C_2 or bromine atom (14). This conclusion is supported by the very small secondary isotope effect ($k_H/k_D=0.98\pm0.01$) observed in the bromination of trans-1-phenylpropene-α-d_1 in acetic acid.[45)]

However, answers to the structure of the reaction intermediate may await further work for the regiochemistry of addition.

There are several literatures on the regio- and stereochemistries for the addition products of unsymmetrical electrophilic reagents such as interhalogens (BrF, IF, ICl, and IBr),[47)] pseudohalogens (XNCO: X=Cl, Br, or I; XN_3: X=Cl, Br, or I),[47)] sulphenyl chloride (PhSCl),[48)] and selenenyl chloride (PhSeCl)[48)] to alkenes. All these results available in the literature for the reactions of a variety of unsymmetrical reagents with some alkenes are summarized in Table 2. These data were carefully selected from studies, in which the product proportions appeared to be under kinetic control.

It is apparent that the reaction of alkenes with these electrophiles proceeds via formation of a positively charged

Table 2. Product Distributions for the Addition of Some Unsymmetrical Electrophilic Reagents to Alkenes in CH_2Cl_2

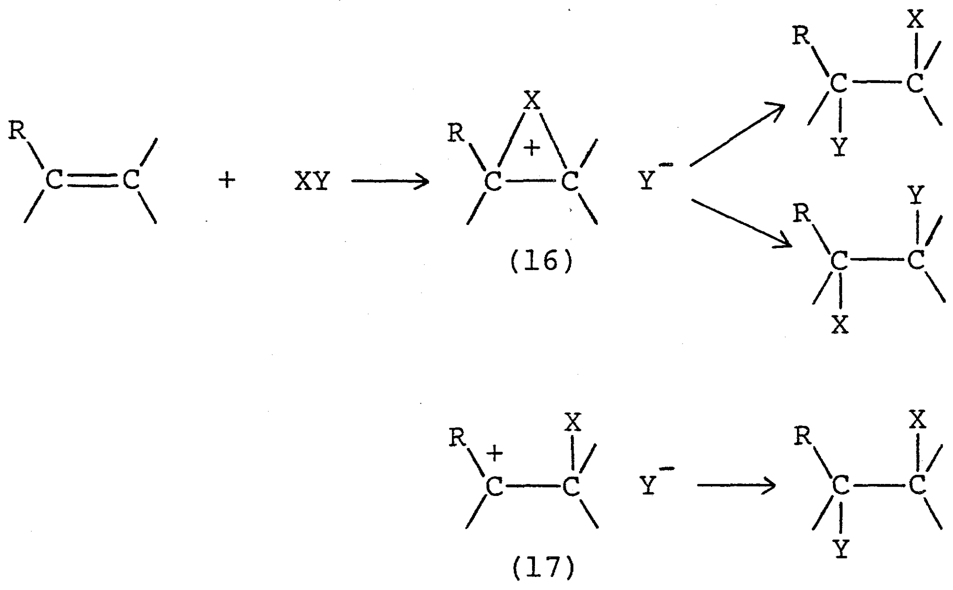
Alkene	%M[a)]	%aM[b)]	Configuration
	Addition of ICl[c)]		
$CH_3CH=CH_2$	65	35	
i-PrCH=CH_2	30	70	
t-BuCH=CH_2	0	100	
(Z)-$C_2H_5CH=CHCH_3$	33	67	threo
(E)-$C_2H_5CH=CHCH_3$	36	64	erythro
(Z)-$C_6H_5CH=CHCH_3$	100	0	threo
(E)-$C_6H_5CH=CHCH_3$	100	0	erythro
	Addition of IBr[d)]		
$CH_3CH=CH_2$	65	35	
$C_2H_5CH=CH_2$	45	55	
i-PrCH=CH_2	15	85	
t-BuCH=CH_2	0	100	
(Z)-$C_2H_5CH=CHCH_3$	40	60	threo
(E)-$C_2H_5CH=CHCH_3$	45	65	erythro
(Z)-$C_6H_5CH=CHCH_3$	100	0	threo
(E)-$C_6H_5CH=CHCH_3$	100	0	erythro
$C_6H_5CH=CH_2$	100	0	
(Z)-anethole	100	0	mixture[e)]
(E)-anethole	100	0	mixture[e)]

Table 2 (continued)

Alkene	%M[a]	%aM[b]	Configuration
	Addition of C_6H_5SCl[f]		
$CH_3CH=CH_2$	32	68	
$C_2H_5CH=CH_2$	25	75	
i-$PrCH=CH_2$	0	100	
t-$BuCH=CH_2$	0	100	
(Z)-$C_2H_5CH=CHCH_3$	36	64	threo
(E)-$C_2H_5CH=CHCH_3$	32	68	erythro
	Addition of 4-ClC_6H_4SCl[g]		
$C_6H_5CH=CH_2$	83	17	
(Z)-$C_6H_5CH=CHCH_3$	66	34	threo
(E)-$C_6H_5CH=CHCH_3$	100	0	erythro
	Addition of 2,4-$(NO_2)_2C_6H_3SCl$[h]		
(Z)-anethole	100	0	mixture[i]
(E)-anethole	100	0	mixture[j]

a) M=Markownikoff adduct. b) aM=anti-Markownikoff adduct. c) Ref. 47. d) Ref. 47. e) The ratio of threo and erythro adduct was not reported. f) Ref. 48. g) Ref. 48. h) Ref. 49. In 1,1,2,2-tetrachloroethane as the solvent. i) threo : erythro=70 : 30. j) threo : erythro=5 : 95.

intermediate to give addition products (Scheme 15).



Scheme 15.

Whether a bridged intermediate (16) or a carbonium ion-like intermediate (17) is involved in the addition of these reagents, depends primarily on the structures of alkenes. Generally, the addition of these reagents to alkyl-substituted ethylenes proceeds in nonregiospecific and anti stereospecific manners. Phenyl-substituted ethylenes have been shown to react with these reagents to yield a mixture of regio- and stereochemical isomers dependent on both the structures of alkenes and the electrophiles employed. As shown in Table 2, the reaction of cis- and trans-1-phenylpropenes with ICl and IBr occurs in a regiospecific manner, while the reaction of styrene and cis-1-phenylpropene with 4-chlorophenylsulphenyl chloride proceeds in a nonregiospecific manner. The reaction of anetholes with IBr and 2,4-dinitrophenylsulphenyl chloride takes place in a nonstereospecific manner although the anti addition product is formed mainly.

Thus, the reaction of aliphatic systems with electrophiles normally goes through a bridged ion intermediate (16), but that of phenyl-substituted ethylenes is in a borderline case (16 or 17). When the phenyl ring has an electron releasing substituent such as methoxy group, there is sufficient stabilization to permit formation of carbonium ion (17), giving a regiospecific but nonstereospecific product.

Table 2 shows that the amount of product of the Markownikoff orientation decreases as the size of substituent increases from ethyl, isopropyl to t-butyl. Thus, the regiochemistry of addition of electrophiles to alkyl-substituted ethylenes depends on the steric effect of the substituents.

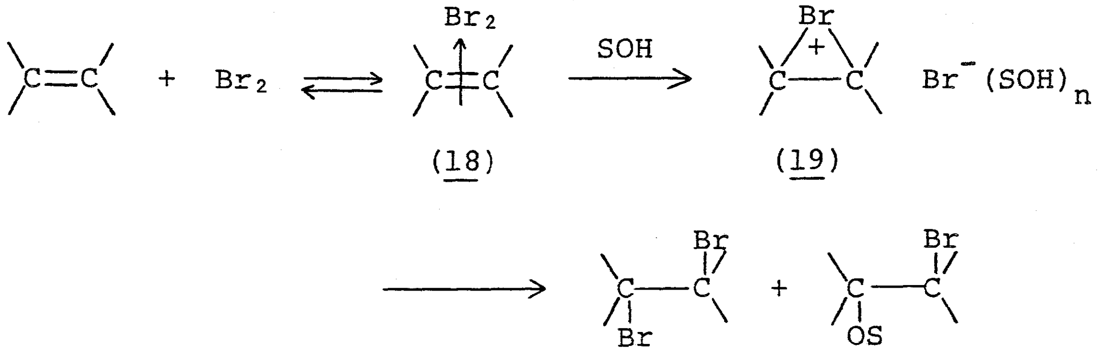
Depending on the reaction conditions, the rate law for the ionic bromination of alkenes is expressed by the whole or a part of equation as follows:50)

$$\frac{-d[Br_2]}{dt} = k_2[Br_2][A] + k_3[Br_2]^2[A] + k_3'[Br_3^-][A]$$

$$[A]=[Alkene]$$

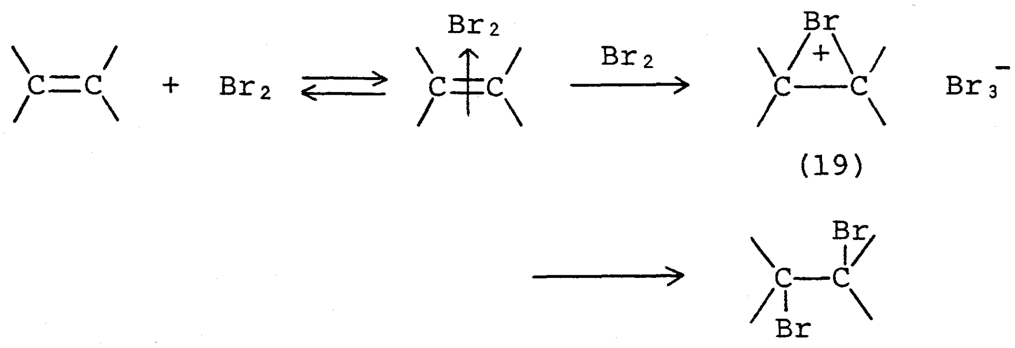
Equation 1.

In aqueous media, methanol, or acetic acid as solvent, at low bromine concentration (less than 3×10^{-3} mol dm^{-3}) and in the absence of a bromide ion, only the first term ($k_2[Br_2][A]$) in equation (1) makes a significant contribution to the observed rate. The first term represents the reversible formation of charge-transfer complex (18) followed by rate-determining solvent-assisted bromine-bromine bond cleavage ($AdEC_1$ type mechanism) (Scheme 16). Evidence for such a specific role of solvent is available from the work of Dubois et al.$^{51)}$ who found a large solvent deuterium-isotope effect for the bromination of 1-pentene in methanol.



Scheme 16.

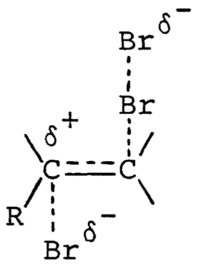
In solvents incapable of such solvent assistance, the second term ($k_3[Br_2]^2[A]$) in equation (1) becomes dominant even at low bromine concentration.$^{52)}$ Under such reaction conditions, the second bromine molecule may assist the bromine-bromine bond cleavage by forming both cationic intermediate (19) and tribromide ion (Scheme 17).



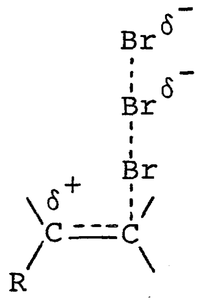
Scheme 17.

Yates et al.53) reported the rates of ring-substituted styrenes under both dominant second-order ($k_2[Br_2][A]$) and diminant third-order ($k_3[Br_2]^2[A]$) conditions in acetic acid. The given ρ values (vs. σ^+) for each process are very similar (for k_2, $\rho=-4.8$; for k_3, $\rho=-4.6$). Such results suggest that a similar cationic intermediate (19) is involved in both reactions (k_2 and k_3 process).

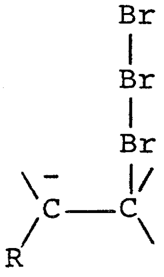
The mechanistic explanation for the third term ($k_3'[Br_3^-][A]$) in equation (1) is still not entirely settled. The relative reactivities of the reaction of bromine and tribromide ion with a variety of alkenes in protic solvent have been studied by the groups of Bell,54) Yates,27) Dubois,55) and Buckles56) and a number of mechanisms have been proposed. These are following: catalysis by bromide ion (20); electrophilic addition of tribromide ion (21); nucleophilic addition of tribromide ion (22).



(20)



(21)



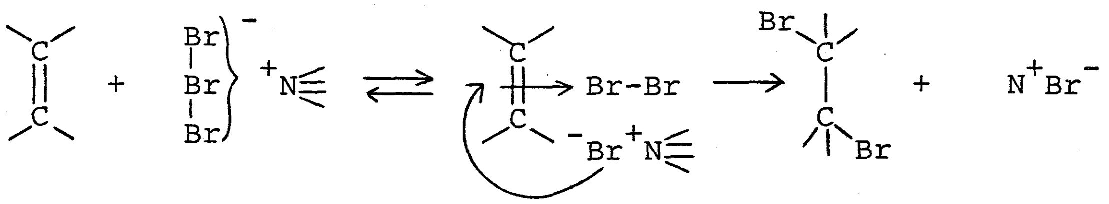
(22)

Dubois et al.55) have found that the plots of the ratio k_{Br^-}/k_{Br_2} versus the reactivities of several substituted ethylenes are curved dependent on the substituents, and interpreted this result in terms of two competing mechanisms. One involves nucleophilic attack of tribromide ion on the unreactive alkenes (22), while the other undergoes via a slow attack of bromide ion on the charge-transfer complex (20).

Buckles et al.30) reported that the bromination of cis-stilbene with bromine in dichloromethane gives a mixture of threo- and erythro-1,2-dibromo-1,2-diphenylethane, whereas the reaction of bromine in the presence of bromide ion gives only one component in an anti stereospecific manner. These results are consistent with the assumption that the bromination of alkenes with tribromide ion occurs by a bromide ion catalyzed mechanism (20).

The kinetic of the reaction of cyclohexene with tetrabutylammonium tribromide in 1,2-dichloroethane has been investigated by Bellucci et al.57) They have reported the

the difference between the reaction of tribromide ion and that of molecular bromine. The latter reaction proceeds through a cationic intermediate formed in the rate-determining step (Scheme 17), whereas the former involves the rate- and product-determining nucleophilic attack on the charge transfer complex (23) with little charge development in the transition state ($AdEC_2$-type mechanism) (Scheme 18).

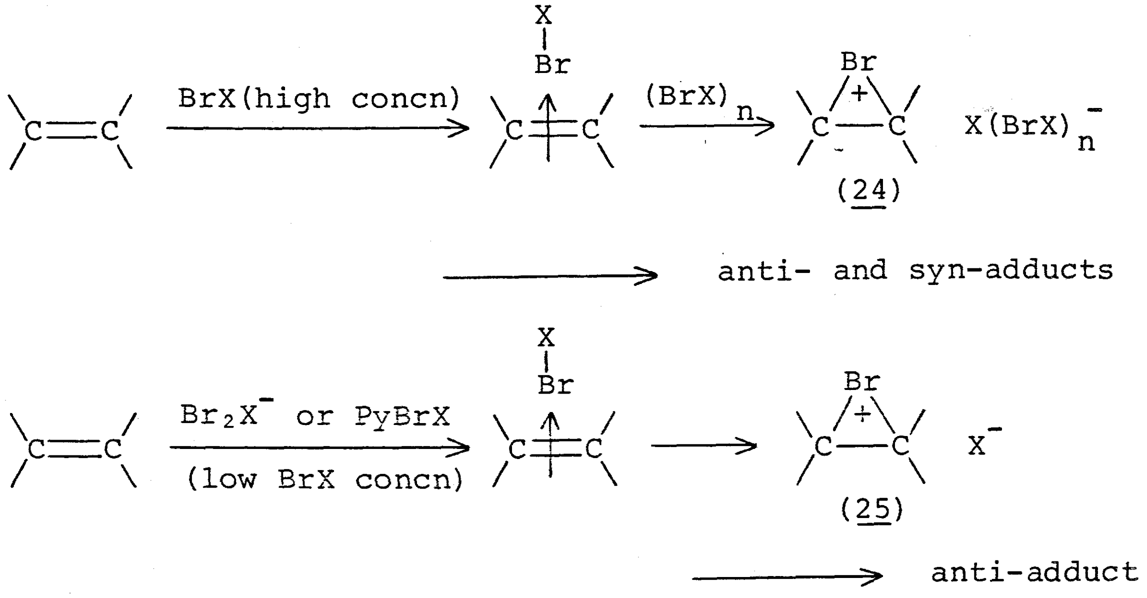


(23)

Scheme 18.

Similarly, Bellucci et al.[57)] also carried out a kinetic study on the reaction of cyclohexene with pyridine bromine complex in 1,2-dichloroethane and found that the reaction of this reagent involves a rate- and product-determinig nucleophilic attack on the charge-transfer complex (23) as shown in Scheme 18. A similar $AdEC_2$-type mechanism has also proposed in the reaction of substituted cyclohexenes with pyridine dibromide or pyridine hydrobromide dibromide ($PyHBr_3$).[58)]

Heasley et al.[19)] have reported the reaction of 1-phenylpropenes with various brominating (or bromochlorinating) reagents such as Br_2, $PyHBr_3$, $PyBr_2$, BrCl, PyBrCl, and Me_4NBr_2Cl in dichloromethane. The addition of halogen complexes to 1-phenylpropenes proceeds nearly in an anti stereospecific manner, whereas that of molecular bromine (or bromine chloride) was found to proceed in a nonstereospecific manner, although the anti addition product was mainly formed. They have discussed the differences of the mechanism between the reaction of molecular halogens and halogen complexes as follows: one possible explanation for these differences is a fundamental mechanistic change, involving a type $AdEC_1$ mechanism (Scheme 17) with the molecular halogens and a type $AdEC_2$ mechanism with the complexes (Scheme 18). They presented another possible explanation for the results obtained with these reagents. The differences between the reaction of molecular halogens and the halogen complexes result from the fact that with molecular halogens two or more halogen molecules participate in the transtion state (second order), whereas the reactions with halogen complexes limit the availability of halogen and impose a first-order mechanism. In other words, the function of the complexes would be to limit the concentration of free halogen. The two mechanisms are shown in Scheme 19.



Scheme 19.

They have suggested that the structures of the anions in the intermediates constitute the real differences between the two mechanisms. While the anion in the reaction of BrX would be a trihalide (or polyhalide) ion (24), the anion in the reaction of halogen complex would be a simple halide ion (25). Therefore, ion pair 25 should be much less stable than ion pair 24 and would quickly collapse to the anti-adduct before opening of the brominium ion could occur. The greater stability of the anion in 24 would result in an ion pair of a longer lifetime, thus permitting bromonium ion ring opening and accompanying syn-adduct.

As described above, the stereochemistry of the bromination (or bromochlorination) reaction of alkenes would be dependent on the brominating (or bromochlorinating) reagents and the reaction conditions. However, definite answers to the mechanistic questions (or structures of the reaction intermediates) may await further stereochemical and regiochemical investigations, since the systematic studies of the reactions of various alkenes have not been carried out.

Furthermore, the bromochlorination of alkenes with above reagents usually gives the bromo chloro compounds with a considerable amount of by-products (particularly in the reaction with molecular bromine chloride) (Table 1). It is very interesting to find a new bromochlorinating reagent to alkenes.

Meanwhile, Wilbur et al.14) reported that the reaction of cyclohexene with NCS and bromide ion in aprotic solvents yields two major addition products (1-bromo-2-chlorocyclohexane and 1,2-dibromocyclohexane) (Scheme 4). The yield of the bromo chloro adduct was reported to increase with the increase of the amount of added chloride ions. From this result, they suggested that bromine chloride prepared in situ from the reaction of NCS and bromide ion is stabilized by an association of the added chloride ions in solution (Scheme 20). However, the mechanistic approach of addition of $BrCl_2^-$ was not carried out.

$$2BrCl \rightleftharpoons Br_2 + Cl_2$$

$$BrCl + Cl^- \rightleftharpoons BrCl_2^-$$

$$BrCl + Br^- \rightleftharpoons Br_2Cl^-$$

$$Br_2Cl^- \rightleftharpoons Br_2 + Cl^-$$

Scheme 20

Similar evidence for such stabilization of BrCl by the added chloride ion can be obtained from an investigation by de la Mare et al.[59)] They have reported the reaction 3-β-substituted cholest-5-enes with bromine chloride in deuteriochloroform gives bromo chloro compounds with a considerable amount of both dibromo and dichloro adducts, whereas the reaction in tetraphenylarsonium chloride gives only bromo chloro compounds indicating no formation of dibromo and dichloro adducts. This result suggests the presence of dichlorobromate(1-) ion ($BrCl_2^-$). A dichlorobromate(1-) ion was also suggested to be involved in the bromochlorination of propene with bromine chloride in hydrochloric acid.[42)]

Thus, dichlorobromate(1-) ion would be very effective bromochlorinating reagent to alkenes. However, no chemical reaction with stable quaternary ammonium dichlorobromate(1-) has been carried out although such dichlorobromate(1-) ion has been accepted as an intermediate of the bromochlorination of alkenes.[14,42,59)]

The reaction of alkenes with R_4NBrCl_2 may proceed via BrCl as a possible intermediate on assuming the following equilibrium (Scheme 21).

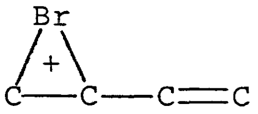
$$R_4N^+Br^- \; + \; Cl_2 \rightleftarrows R_4N^+BrCl_2^- \rightleftarrows R_4N^+Cl^- \; + \; BrCl$$

Scheme 21.

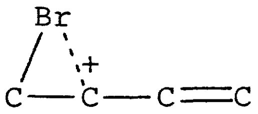
Addition to Conjugated Dienes.

As with the addition of the general electrophilic reagents to conjugated dienes, addition of bromine (or bromine chloride) to conjugated dienes can occur to give a mixture of 1,2- and 1,4-addition products.[60–63)]

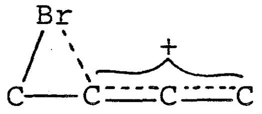
In the addition of bromine (or bromine chloride) to 1,3-butadiene, at least three reaction intermediates having different charge distributions may be considered to be involved. The possible intermediates are as follows:



(26)



(27)



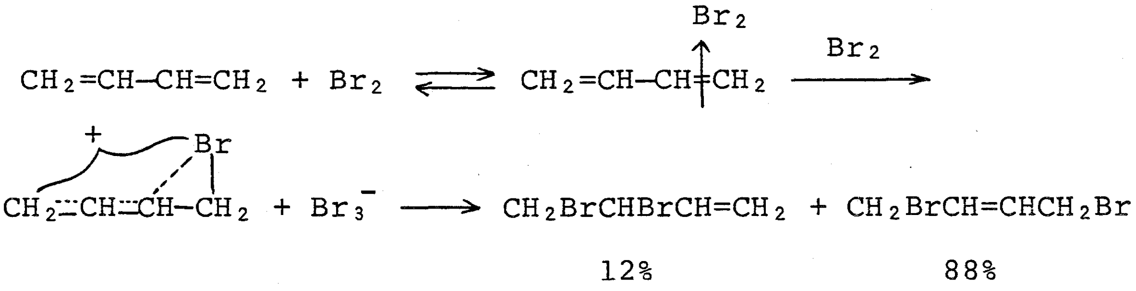
(28)

Intermediate (26) is a bromonium ion with symmetrical bridging. Intermediate (27) shows the charge as essentially localized on the secondary carbonium ion. Intermediate (28) represents the charge as highly delocalized across the bromine atom and the adjacent allylic system.

Bellucci et al.[64)] have established the third-order kinetics (first-order in 1,3-butadiene and second-order in bromine) of addition to 1,3-butadiene with molecular bromine in 1,2-dichloroethane and dichloromethane (Equation 2).

$$\frac{-d[Br_2]}{dt} = k[\text{diene}][Br_2]^2 \qquad \text{Equation 2.}$$

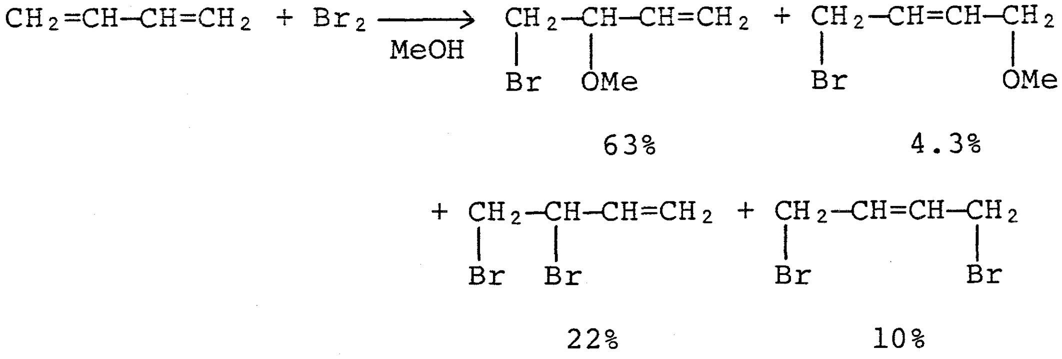
These results fit well into the general mechanism of bromination of alkenes in aprotic solvents of low polarities (Scheme 22).



Scheme 22.

The second order dependence on bromine in equation 2 indicates the intervention of a second molecule of bromine at the rate-determining transition state. This rate-determining transition state probably consists of a bromine-assisted heterolytic fisson of the Br–Br bond in an initially formed diene-bromine charge-transfer complex to give an ion pair involving a covalent, cationic intermediate and a stable Br_3^- ion. It is suggested that the moderate increase in rate constant on passing from dichloromethane to the slightly more polar 1,2-dichloroethane as solvent is consistent with the ionic intermediate of this process (Scheme 22). The predominance of the 1,4-adduct over the 1,2-adduct is considered to suggest a delocalized carbonium ion (28) than a bromonium ion intermediate (26 or 27).

Meanwhile, Heasley et al.61) reported that the bromination of 1,3-butadiene in methanol gives 4-bromo-3-methoxy-1-butene as the principal product (Scheme 23).



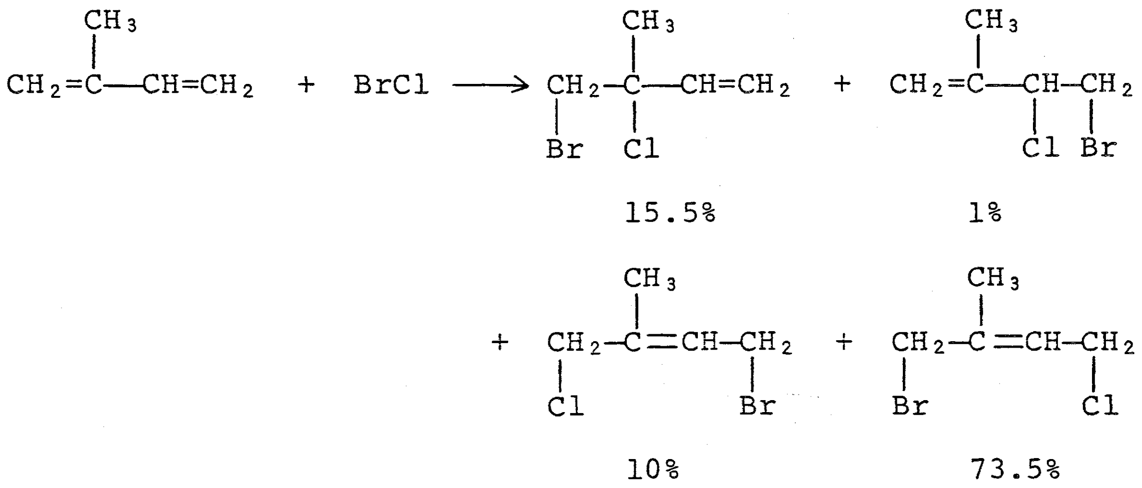
$$CH_2{=}CH{-}CH{=}CH_2 + Br_2 \xrightarrow[MeOH]{} \underset{63\%}{\underset{Br}{CH_2}{-}\underset{OMe}{CH}{-}CH{=}CH_2} + \underset{4.3\%}{\underset{Br}{CH_2}{-}CH{=}CH{-}\underset{OMe}{CH_2}}$$

$$+ \underset{22\%}{\underset{Br}{CH_2}{-}\underset{Br}{CH}{-}CH{=}CH_2} + \underset{10\%}{\underset{Br}{CH_2}{-}CH{=}CH{-}\underset{Br}{CH_2}}$$

Scheme 23.

No anti-Markownikoff adduct (3-bromo-4-methoxy-1-butene) was obtained. From these results, they suggested that the intermediate in the bromination of butadiene in methanol is best described by 27 with slight delocalization of the charge across the allylic system. Such a partially bridged intermediate (27) was suggested for the reaction of conjugated dienes with N-bromosuccinimide in moist dimethyl sulfoxide, where the 1,2-addition product was obtained mainly.65) For example, the reaction of 2-methyl-1,3-butadiene with NBS in moist dimethyl sulfoxide gave only one compound (1-bromo-2-methyl-but-4-en-2-ol) in 94% yield.

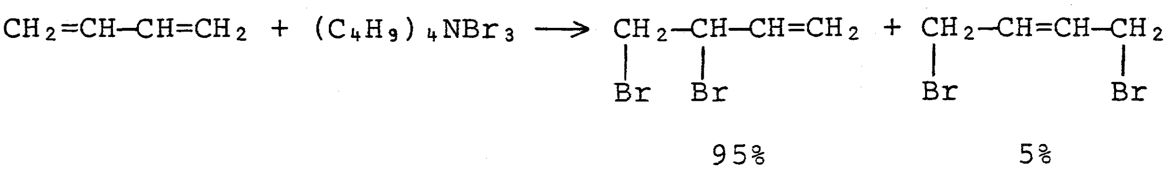
The product distribution in the reaction of molecular bromine chloride (BrCl) with cyclopentadiene, 2-methyl-1,3-butadiene, cis-and trans-1,3-pentadienes in dichloromethane was reported by Heasley et al.[19,66]. The reaction of BrCl to dienes was reported to give very complicated products. For example, the ionic bromochlorination of 2-methyl-1,3-butadiene with BrCl in dichloromethane gave four products along with considerable amounts of dichloro and dibromo adducts (Scheme 24).



Scheme 24.

Such a predominant formation of 1,4-addition products (1,4-adduct : 1,2-adduct=84 : 16) shows that the reaction intermedaite in the bromochlorination with BrCl is similar to that of bromination with Br_2 (Scheme 22).

Meanwhile, the product distribition can be shifted to favor the 1,2-addition products by use of such milder brominating agents as the pyridine-bromine complex or tribromide ion (and pyridine-bromine chloride complex as the bromochlorinating agent).[19,58,67] When tetrabutylammonium tribromide is used as the brominating agent in 1,2-dichloroethane, the 1,2-addition product was obtained in 95% yield (Scheme 25).[58]

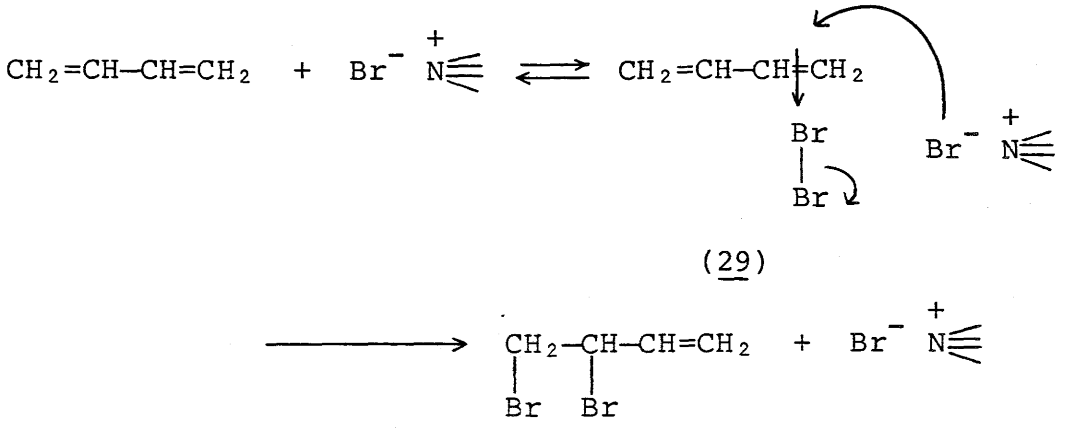


$$CH_2=CH-CH=CH_2 + (C_4H_9)_4NBr_3 \longrightarrow \underset{95\%}{\underset{Br}{CH_2}-\underset{Br}{CH}-CH=CH_2} + \underset{5\%}{\underset{Br}{CH_2}-CH=CH-\underset{Br}{CH_2}}$$

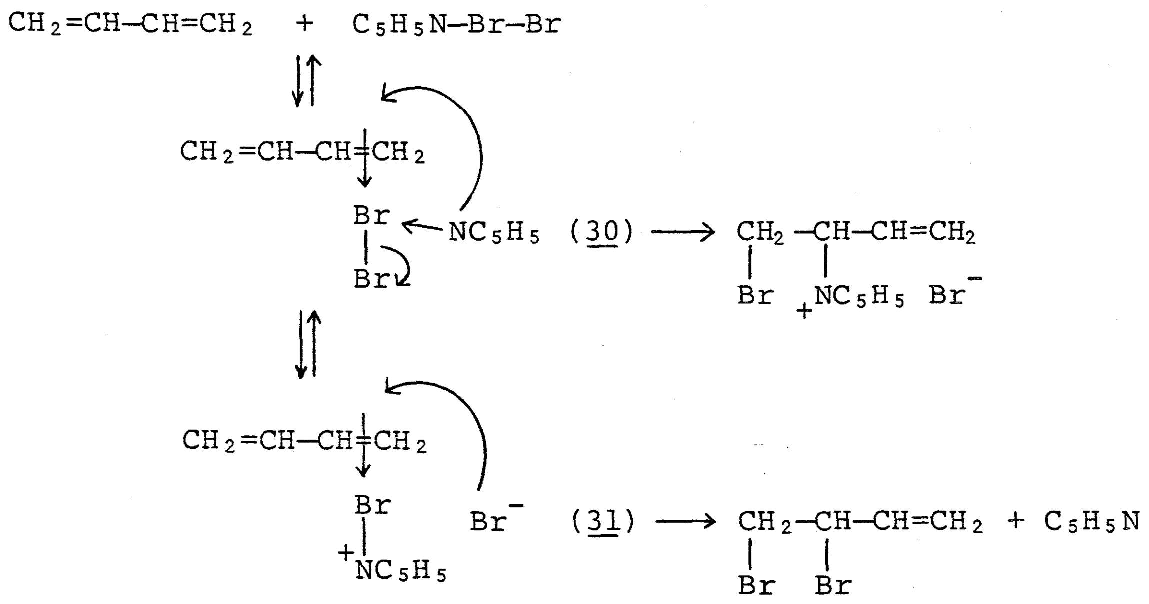
Scheme 25.

Similarly, the reaction of 1,3-butadiene with bromine in the presence of excess pyridine in 1,2-dichloroethane was reported to give a mixture of 3,4-dibromo-1-butene and 1,4-dibromo-2-butene (1,2-adduct : 1,4-adduct=87 : 13) with a considerable amount of N-(4-bromo-1-butene-3-yl)pyridinium bromide (41%).[64]

Bellucci et al.[64] suggested that the kinetic behavior and the product distribution observed in the bromination of butadiene, in the presence of tetrabutylammonium bromide (or in the presence of pyridine), can be explained on the basis of the mechanism as shown in Schemes 26 and 27. These two mechanisms involve rate- and product-determining nucleophilic attack on the charge transfer (<u>29</u>, <u>30</u>, or <u>31</u>) with little charge development in the transition states ($AdEC_2$-type mechanism), similar to that proposed for the bromination of cyclohexene under the same conditions.

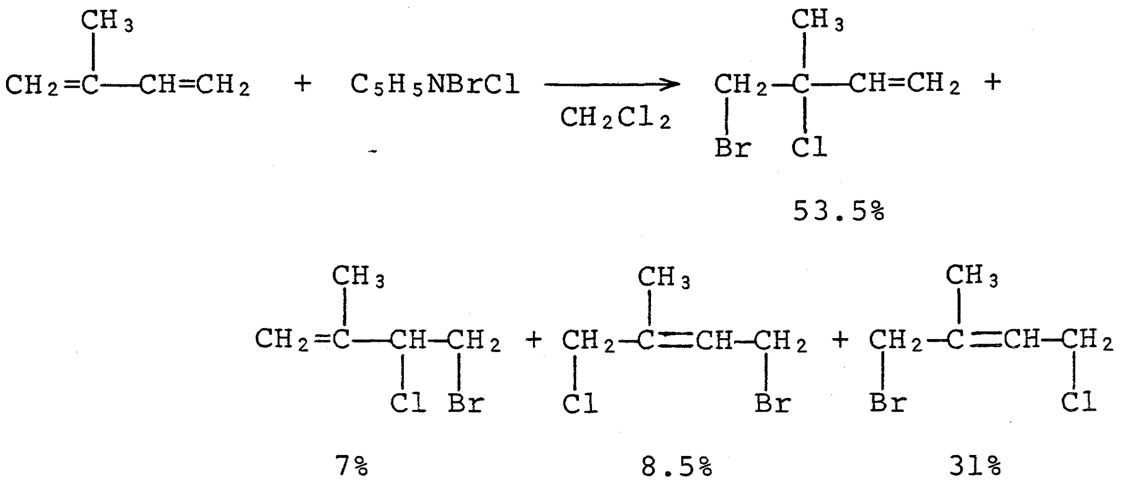


Scheme 26.



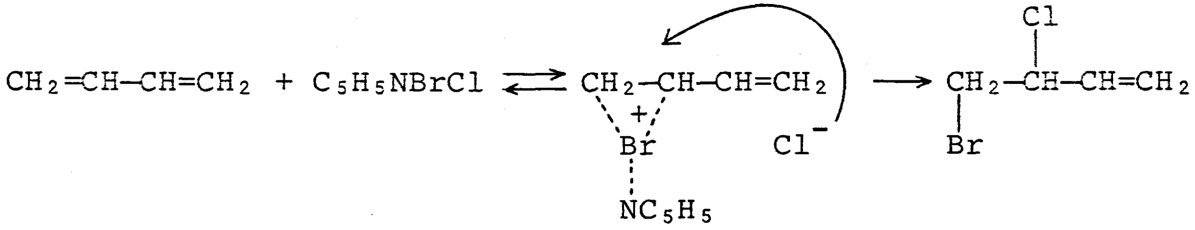
Scheme 27.

As with the reaction of bromine, the bromochlorination of dienes with pyridine bromine chloride complex gave predominantly 1,2-addition products.[16, 66] For example, the reaction of 2-methyl-1,3-butadiene with pyridine bromine chloride complex in the presence of excess pyridine in dichloromethane gave a mixture of 1,2-adduct (60%) and 1,4-adducts (40%) (Scheme 28).[19]



Scheme 28.

Such a predominant formation of 1,2-addition products is explained on the basis of the mechanism involving slow attack of chloride ion on the charge transfer complex (32) as shown in Scheme 29, similar to the addition of pyridine bromine complex to dienes (Scheme 27).[19,66]

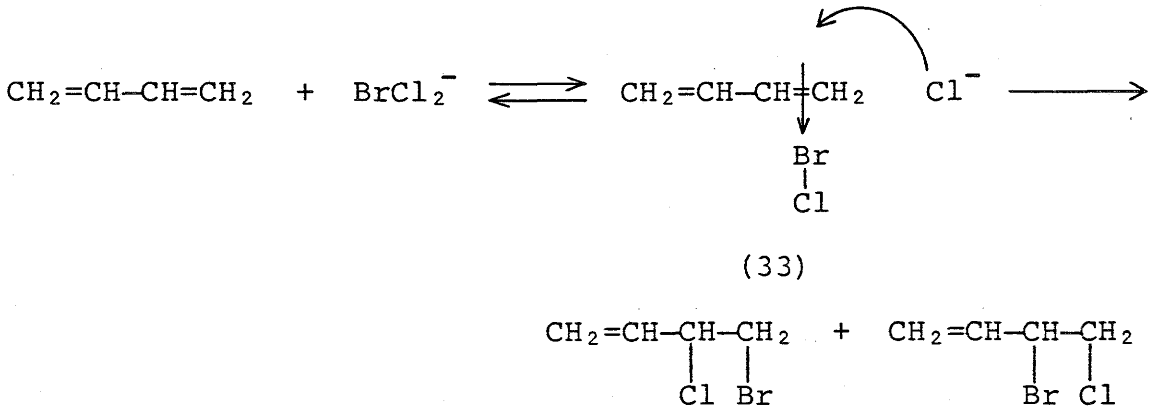


(32)

Scheme 29.

As described above, the product distribution (the ratio of 1,2-adduct to 1,4-adduct) from the bromochlorination (or bromination) of conjugated dienes is considered to be dependent on the bromochlorinating (or brominating) reagents and the reaction conditions. However, definite answers to the mechanistic (or the structures of the reaction intermediates) questions have to await further regiochemical investigations for the reaction products, since the regiochemical studies on the bromine chloride addition have not been carried out.

If the intermediate is a alkene-bromine chloride charge transfer complex (33) with little development of positive charge on the carbon, nucleophilic attack of chloride ion can be on either side of carbon atoms of the intermediate in the reaction of conjugated dienes with dichlorobromate(1-) ion (Scheme 30).



Scheme 30.

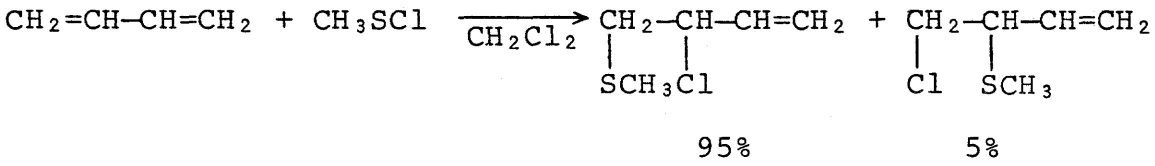
There are a few works on the reactions of conjugated dienes with the other unsymmetrical electrophilic reagents such as interhalogens, pseudohalogenes and sulphenyl chlorides.[47,48] Ingold et al.[68] reported that the reaction of iodine bromide (IBr) with 1,3-butadiene in dichloromethane at -35 °C afforded predominantly the 1,4-adduct, 1-chloro-4-iodo-2-butene, together with some 1,2-adduct, 3-chloro-4-iodo-1-butene.

No anti-Markownikoff adduct, 4-chloro-3-iodo-1-butene was obtained. Reaction of iodine isocyanate (INCO) with conjugated dienes was reported to give only the 1,4-addition product.69) The reaction of 4-chlorophenylsulphenyl chloride with conjugated dienes at 25 °C in 1,1,2,2,-tetrachloroethane was reported to give predominantly the Markownikoff 1,2-adduct.49) For example, the reaction of 1,3-butadiene with this reagent gave 1,2-adduct in 100% yield (Scheme 31).

$$CH_2{=}CH{-}CH{=}CH_2 \quad + \quad 4\text{-}ClC_6H_4SCl \longrightarrow ClC_6H_4SCH_2{-}CHClCH{=}CH_2$$

Scheme 31.

Muller et al.70) studied the reaction of conjugated dienes with methane- and phenylsulphenyl chlorides in dichloromethane. The reactions of both reagents with dienes also gave predominantly 1,2-addition products. They found that the reaction of 1,3-butadiene with methanesulphenyl chloride gave a small amount of the anti-Markownikoff adduct (Scheme 32).



$$CH_2{=}CH{-}CH{=}CH_2 + CH_3SCl \xrightarrow[CH_2Cl_2]{} \underset{SCH_3}{CH_2}{-}\underset{Cl}{CH}{-}CH{=}CH_2 + \underset{Cl}{CH_2}{-}\underset{SCH_3}{CH}{-}CH{=}CH_2$$

95% 5%

Scheme 32.

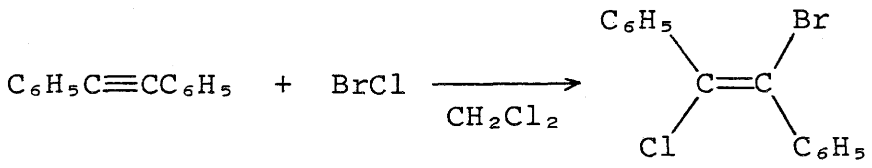
Addition to Alkynes

The reaction of bromine chloride (BrCl) to alkynes can occur to give bromo chloro compounds (Scheme 33).

$$-C\equiv C- \quad + \quad BrCl \longrightarrow -CCl=CBr-$$

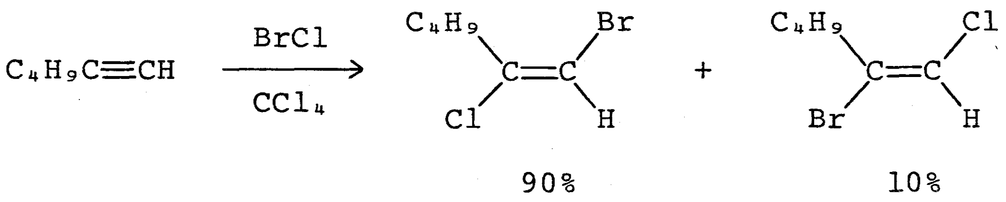
Scheme 33.

Buckles et al.[24)] reported that the reaction of diphenylacetylene with a mixture of bromine and chlorine gave 1-bromo-2-chloro-1,2-diphenylethene in a low yield (Scheme 34).

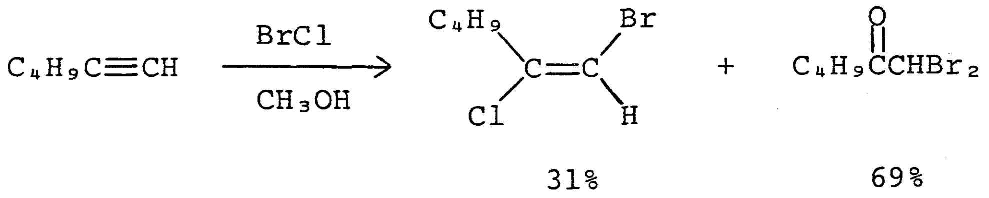


Scheme 34.

The reaction of 1-hexyne and bromine chloride in carbon tetrachloride was shown to give a mixture of (E)-1-bromo-2-chloro- and (E)-2-bromo-1-chloro-1-hexenes (Scheme 35), whereas the reaction in methanol gave regiospecific Markownikoff adduct, (E)-1-bromo-2-chloro-1-hexene along with a considerable amount of 1,1-dibromo-2-hexanone (Scheme 36).[25)]

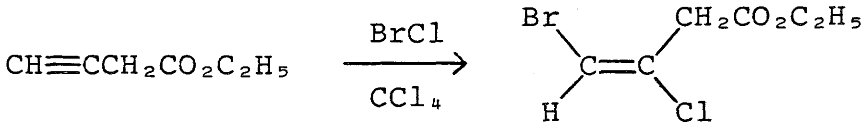


Scheme 35.



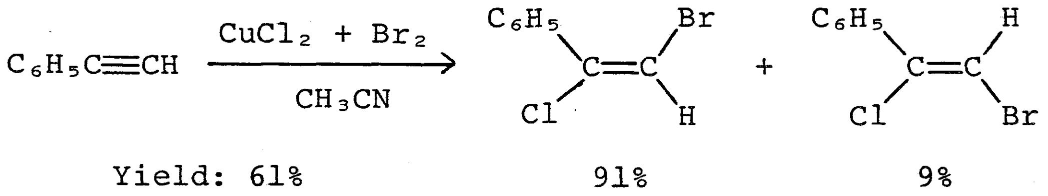
Scheme 36.

The treatment of bromine chloride with ethyl 3-butynoate in CCl_4 was reported to give the regiospecific Markownikoff adduct in a stereospecific manner (Scheme 37).71)



Scheme 37.

The reaction of phenylacetylene with a mixture of copper(II) chloride and bromine in CH_3CN was shown to give a mixture of (E)-2-bromo-1-chloro- and (Z)-2-bromo-1-chloro-1-phenylethenes along with a large amount of dibromo and dichloro adducts (Scheme 38).72)



Scheme 38.

All these results show that the regio- and stereochemistries of the addition of bromine chloride to alkynes are dependent both on the structure of alkyne and on the reaction medium employed. However, the data for the bromochlorination of alkynes with bromine chloride are rather meager.

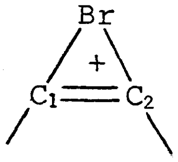
Meanwhile, the addition of bromine to alkynes can be found in standard text books. While the dibromo adducts are usually formed as products in the bromination in aprotic solvent, bromination in hydroxylic solvent such as methanol or acetic acid results in the formation of solvent-incorporated products (Scheme 39). Bromoalkynes are sometimes formed in the bromination of terminal acetylenes.

$$\mathrm{R{-}C{\equiv}CH} + \mathrm{Br_2} \xrightarrow[\mathrm{SOH}]{} \mathrm{R{-}C(Br){=}CHBr} + \mathrm{R{-}C(OS){=}CHBr}$$

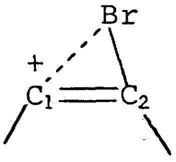
$$+ \ \mathrm{R{-}C{\equiv}CBr}$$

Scheme 39.

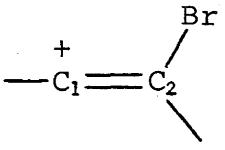
The mechanism of the electrophilic addition of bromine to alkynes has been widely investigated both from the kinetic and stereochemical points of view.73) It is well known that the structure of the addition intermediate depends both on the structure of the alkyne and on the reaction medium, and at least three reaction intermediates having different charge distributions can be involved.73) The possible intermediates are as follows:



34



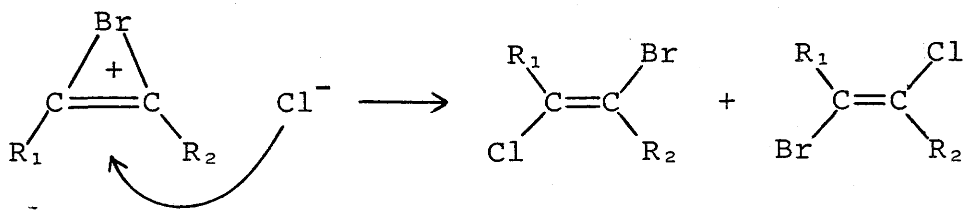
35



36

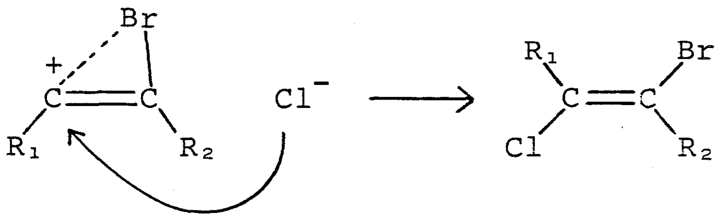
Intermediate (34) is a symmetrical bridged bromonium ion in which the C_1-Br bond length is equal to the C_2-Br bond length; Intermediate (35) illustrates an unsymmetrical weakly bridged ion in which the charge is localized mainly on one carbon; Intermediate (36) is an open vinyl cation.

Meanwhile, the regio- and stereochemistries of the electrophilic addition of bromine chloride (or the other interhalogens) to alkynes are dependent on the structure of the product-determining transition states which in turn depends on the structure of the cationic intermediate formed immediately before the product-determining step. If the intermediate has a symmetrical bridged structure such as 34, nucleophilic attack of chloride ion can occur only on the face opposite to the electrophile. Consequently, the product is formed by anti stereospecific addition. The addition is completely in a nonregiospecific manner since the attack of chloride ion can occur on both carbon atoms of the bridged intermediate (34) (Scheme 40).



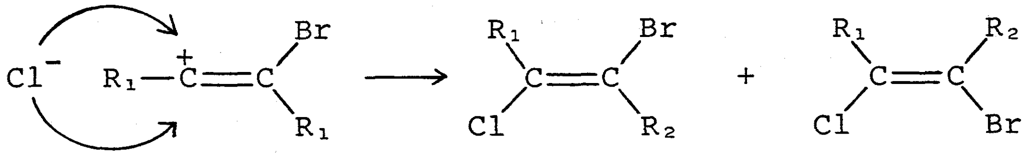
Scheme 40.

If the intermediate has a weakly bridged structure such as 35, nucleophilic attack of chloride ion can occur only from the opposite side to the electrophile similar to the attack on 34. The addition is in a regiospecific manner since the attack of chloride ion on 35 can occur predominantly only on one carbon atom with the more positive charge development (Scheme 41).



Scheme 41.

If the intermediate has an open vinyl cation-like structure (36), nucleophilic attack of chloride ion can occur at both faces and hence both syn and anti addition products are expected (Scheme 42). The addition occurs in a regiospecific manner.



Scheme 42.

Meanwhile, Pincock et al.[74)] reported that the rate law for the ionic bromination of alkynes can be correlated with the whole or a part of equation (3) depending on the reaction conditions.

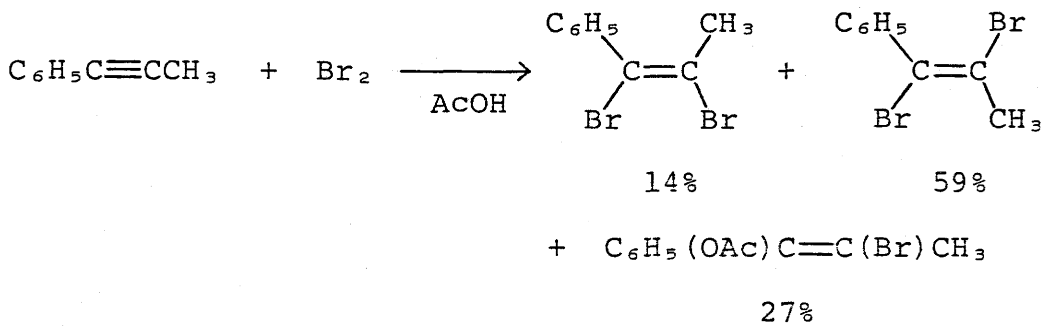
$$\frac{-d[Br_2]}{dt} = k_2[Br_2][A] + k_3[Br_2]^2[A] + k_3'[Br_3^-][A]$$

[A]=alkyne

Equation 3.

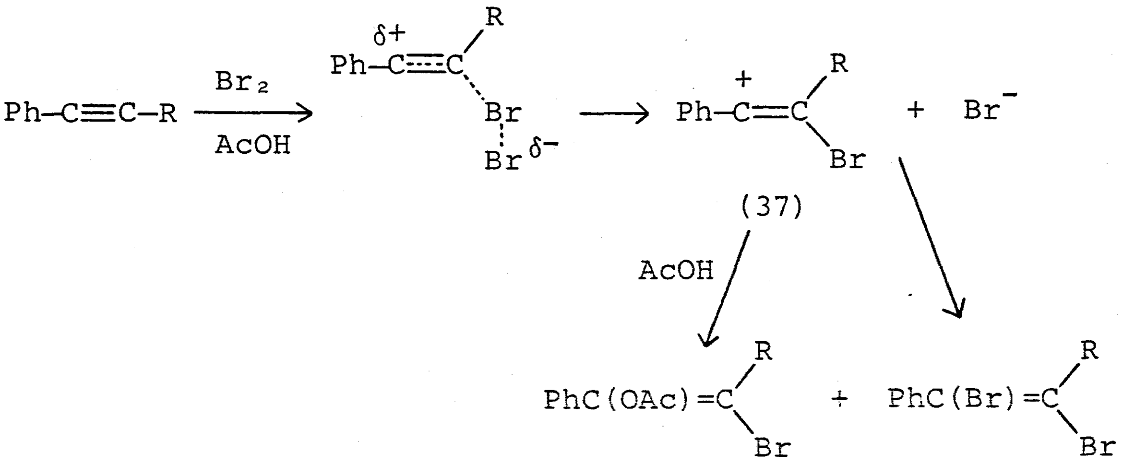
In acetic acid as the solvent, at low concentration (less than 3×10^{-4} mol dm^{-3}) and in the absence of a bromide ion, only first term ($k_2[Br_2][A]$) in equation (3) makes a significant contribution to the observed rate. At a bromine concentration of approximately 1×10^{-2} mol dm^{-3}, both the k_2 and k_3 terms contribute to the overall rate equation. In the presence of added bromide ion, the third term ($k_3'[Br_3^-][A]$) becomes important.

Under conditions where overall second-order kinetics are followed, Pincock et al.[74)] have studied the effect of the structures of alkynes on the rate of bromination in acetic acid. The rates for the ring-substituted phenylacetylenes are correlated well with σ^+ values, giving ρ value of -5.17. This data clearly suggest that the bromination of phenylacetylenes in acetic acid is an electrophilic reaction. Furthermore, they have reported that the reaction of phenylacetylene, 4-methylphenylacetylene, and 1-phenylpropyne with bromine in acetic acid gives nonstereospecific dibromoalkenes and regiospecific solvent-incorporated products with Markownikoff orientation. For example, the reaction of 1-phenylpropyne with bromine in acetic acid gave (Z)- and (E)-1,2-dibromo-1-phenylpropenes and 1-acetoxy-2-bromo-1-phenylpropene (Scheme 43).



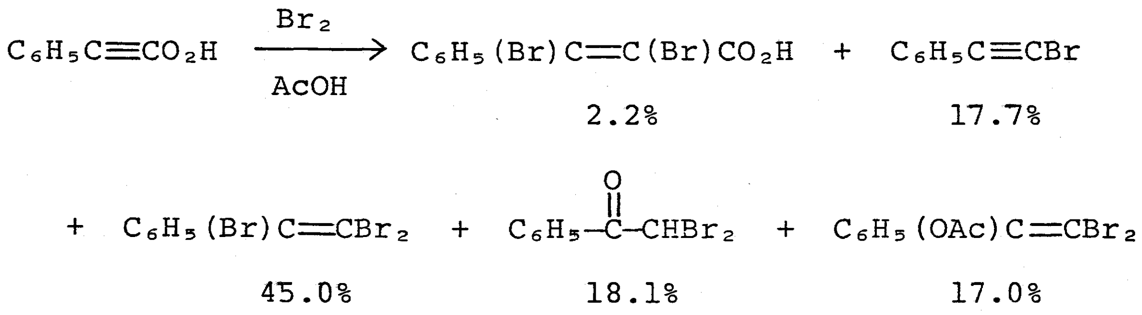
Scheme 43.

Thus, both the rate and the product data for the addition of bromine to phenyl-substituted acetylenes are consistent with an Ad_E2 type mechanism involving a vinyl cationic intermediate (37) as shown in Scheme 44.



Scheme 44.

Ehrlich et al.[75)] studied the kinetics of the addition of bromine to phenylpropiolic acid, its anion, and its ethyl ester in 75% aqueous acetic acid. The reaction of the acid is characterized by the first term ($k_2[Br_2][A]$) in equation (3). The reaction of phenylpropiolic acid and its anion with bromine gave small amounts of cis- and trans-α,β-dibromocinnamic acids and extensive decarboxylation products, as well as products formed by solvent incorporation (Scheme 45).

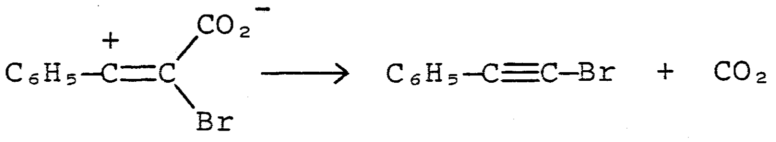


$$C_6H_5C{\equiv}CO_2H \xrightarrow[AcOH]{Br_2} \underset{2.2\%}{C_6H_5(Br)C{=}C(Br)CO_2H} + \underset{17.7\%}{C_6H_5C{\equiv}CBr}$$

$$+ \underset{45.0\%}{C_6H_5(Br)C{=}CBr_2} + \underset{18.1\%}{C_6H_5{-}\overset{O}{\overset{\|}{C}}{-}CHBr_2} + \underset{17.0\%}{C_6H_5(OAc)C{=}CBr_2}$$

Scheme 45.

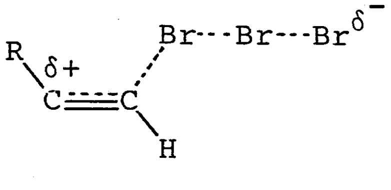
They have suggested that the bromination of phenylpropiolic acid and its anion involves the electrophilic attack of bromine on the alkynes and proceeds through an open vinyl cationic intermediate (38) as follows:



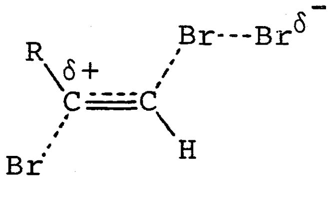
(38)

Meanwhile, the reaction of 1-hexyne or 3-hexyne with bromine in acetic acid was shown to give the anti stereospecific adducts.[74)] No solvent-incorporated product was observed. These results suggest that the intermediate in the reaction of alkyl-substituted acetylenes with bromine is a cyclic bromonium ion-like (34).

The mechanistic explanation for the third term ($k_3'[Br_3^-][A]$) in equation (3) has still not been settled. Two mechanisms have been proposed to explain the k_3' term. One involves the electrophilic attack of tribromide ion (39), while the other is a bromide ion catalyzed process (40).[74–76)]

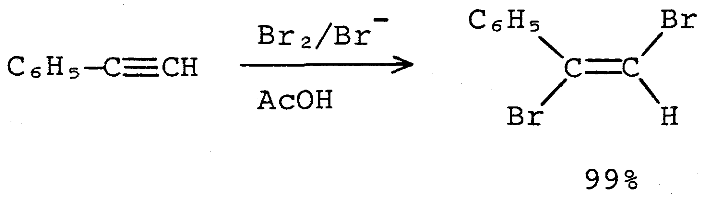


(39)

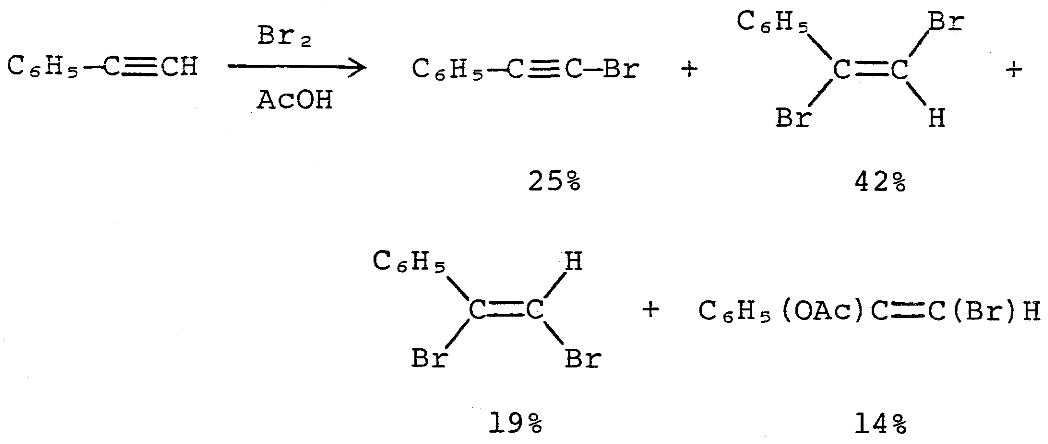


(40)

When the bromination of phenylacetylene, 4-methylphenylacetylene, and 1-phenylpropene with bromine in the presence of added bromide ion was carried, the anti stereospecific product was formed predominantly.74) For example, the reaction of phenylacetylene with bromine in the presence of excess lithium bromide in acetic acid gave one compound, (E)-1,2-dibromo-1-phenylethene in an anti stereospecific manner (Scheme 46), whereas the reaction in the absence of lithium bromide gave a mixture of (E)- and (Z)-dibromoalkenes (Scheme 47).



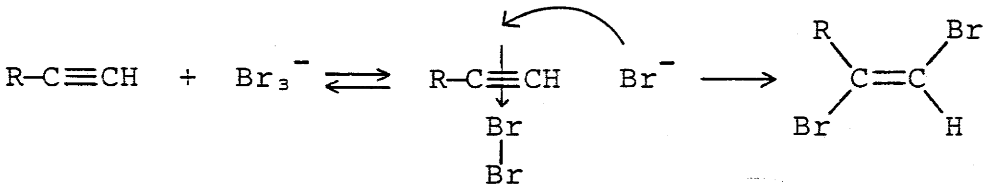
Scheme 46.



Scheme 47.

Based on the marked decrease of the bromoacetate and the increase of anti addition product (Scheme 46) it was suggested that the bromination of phenyl-substituted acetylenes in the presence of bromide ion involves a bromide ion catalyzed Ad_E3 type mechanism, proceeding through a transition state like 40.[74) Ehrlich et al.[75) also concluded that the bromination of alkynes in the presence of bromide ion occurs by a bromide ion catalyzed mechanism.

These product distributions formed in the reaction of alkynes with bromine in the presence of bromide ion also may be rationalized on the basis of alternative mechanism, involving the rate- and product-determining attack of bromide ion on a π-complex such as 41 (Scheme 48).

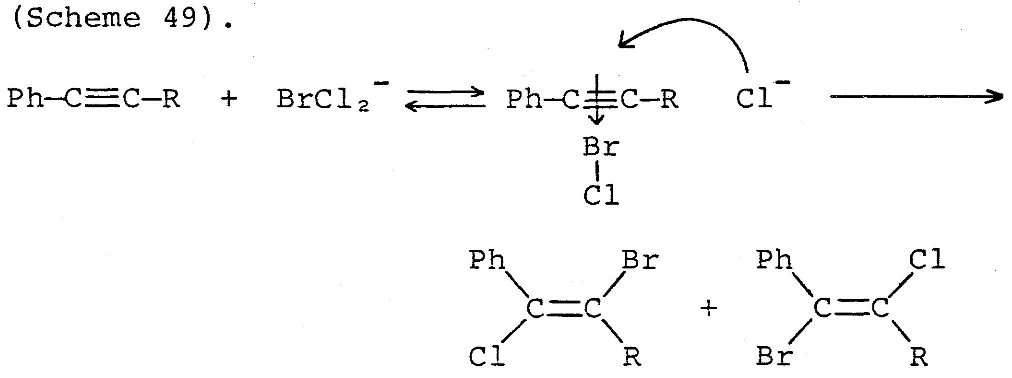


(41)

Scheme 48.

As described above, the product distribution (regio- and stereochemistries) in the bromination (or bromochlorination) of alkynes is considered to be dependent both on the structure of alkynes and on the brominating (presumably including bromochlorinating) reagent employed. However, definite answers to the mechanistic (or the structures of the reaction intermediates) questions may have to await further regio- and stereochemical works for the addition products, since only a few systematic studies have been carried out on the reaction of alkynes with bromine chloride under various conditions.

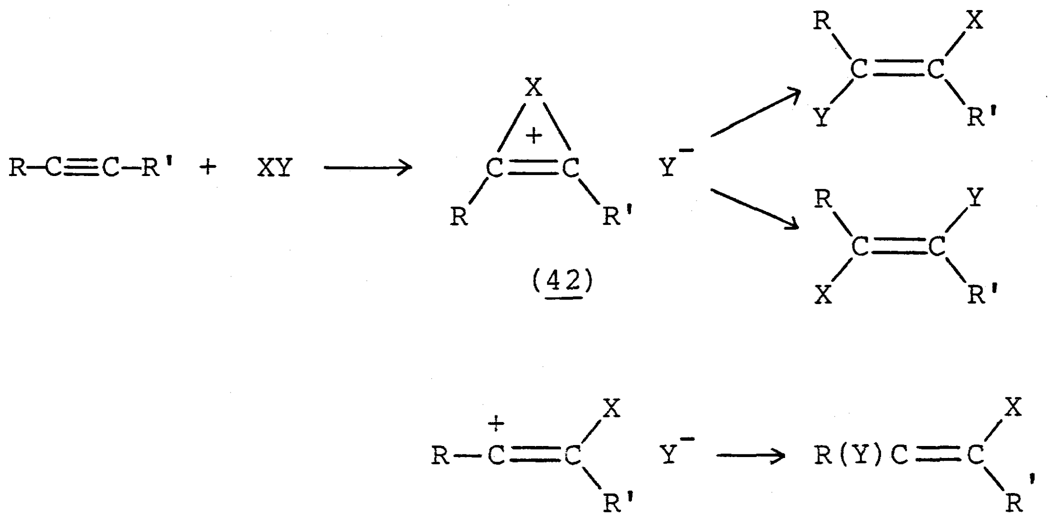
If the intermediate is a π-complex (41) with little charge development on the carbon, nucleophilic attack of chloride ion can occur on both carbon atoms of the intermediate in the reaction of phenyl-substituted alkynes with dichlorobromate(1-) ion (Scheme 49).



Scheme 49.

There have been a few studies on the regio- and stereochemistries for the addition products of unsymmetrical electrophilic reagents such as interhalogens (BrF, ICl, and IBr),77) pseudohalogens (INCO and IN_3),77) sulphenyl halides,78) and selenenyl halides78) to alkynes.

It is apparent that the reaction of alkynes with these electrophiles proceeds via a positively charged intermediate to give addition products (Scheme 50).



(42)

(43)

Scheme 50.

Whether a bridged intermediate (42) or an open vinyl cation-like intermediate (43) is involved in the addition of these reagents, depends both on the structure of alkyne and on the electrophile employed.

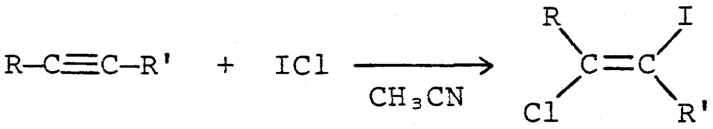
Dear[79)] has studied the addition of bromine fluoride (prepared in situ from the reaction of anhydrous hydrogen fluoride and N-bromoacetamide) to 1-hexyne, 3-hexyne, 1,4-dichloro-2-butyne, and phenylacetylene. In the case of terminal alkynes, the addition of BrF occurred in the regiospecific Markownikoff manner (Scheme 51).

$$\mathrm{R{-}C{\equiv}CH} \; + \; \mathrm{BrF} \longrightarrow \mathrm{R(F)C{=}C(Br)H}$$

Scheme 51.

The reaction of phenylacetylene and 1,4-dichloro-2-butyne was in the anti stereospecific manner, whereas that of 1-hexyne and 3-hexyne gave a mixture of the (E)- and (Z)-isomers in an anti stereoselective manner. For example, the addition of BrF to 1-hexyne gave 95% of (E)-1-bromo-2-fluoro-1-hexene and 5% of (Z)-1-bromo-2-fluoro-1-hexene.

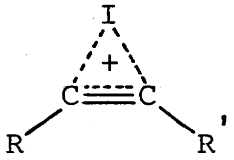
Tendil et al.71) reported that the addition of iodine chloride (ICl) to ethyl 3-butynoate gives only the regiospecific Markownikoff adduct, whereas the addition of iodine bromide (IBr) gives a mixture of Markownikoff and anti-Markownikoff adducts. Addition of ICl to 1-octyne, phenylacetylene, and alkylphenylacetylenes in acetonitrile has been reported to occur regio- and stereospecifically to give (E)-iodo chloro adducts (Scheme 52).80)



R=Ph, R'=alkyl or H; R=alkyl, R=H'.

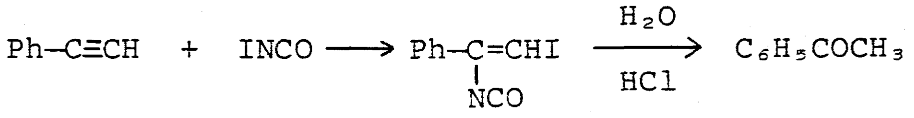
Scheme 52.

The high anti stereospecificity of the addition of IBr has been interpreted as evidence for the formation of a cyclic iodonium ion intermediate (44).



(44)

The addition of iodine isocyanate (INCO) to phenylacetylene was shown to occur in tetrahydrofuran.81) However, the addition product was not isolated, but the work-up of the addition product with hydrochloric acid yielded acetophenone (Scheme 53).



$$\text{Ph—C}\equiv\text{CH} + \text{INCO} \longrightarrow \text{Ph—}\underset{\text{NCO}}{\text{C}}\text{=CHI} \xrightarrow[\text{HCl}]{\text{H}_2\text{O}} \text{C}_6\text{H}_5\text{COCH}_3$$

Scheme 53.

This result indicates that the addition of INCO to phenylacetylene gives the Markownikoff adduct. The reactions of diphenylacetylene, 2-octyne, and 4-octyne with INCO were shown to give addition product.69)

The addition of iodine azide (IN_3) to 1-phenylpropyne and phenyl(1-hydroxycyclopentyl)ethyne was shown to give the regiospecific anti-Markownikoff adducts (Scheme 54).82)

$$C_6H_5C\equiv CR + IN_3 \longrightarrow C_6H_5CI{=}C(N_3)R$$

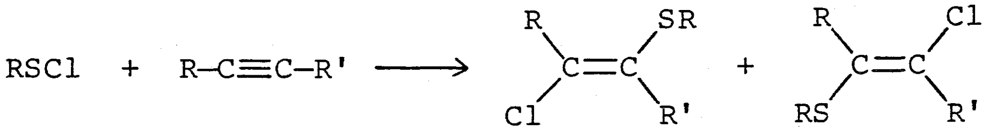
$R=CH_3$ or R=1-hydroxycyclopentyl

Scheme 54.

Thus, the regiochemistry of addition of IN_3 is opposite to that normally found for the addition of other pseudohalogens and interhalogens.77)

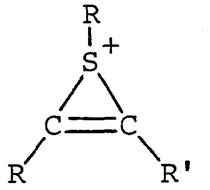
Sulphenyl chlorides react with alkynes to give a mixture of Markownikoff and anti-Markownikoff adducts, dependent both on the structure of alkyne and on the reaction medium.83–87)

Generally, the addition of sulphenyl chlorides to alkynes takes place in the anti stereospecific manner (Scheme 55).



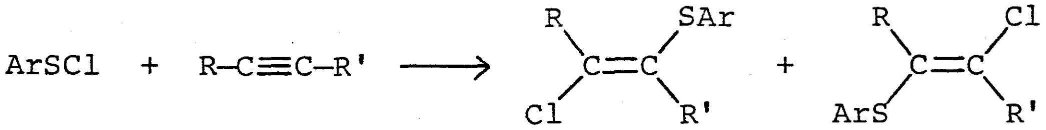
Scheme 55.

This reaction has been well rationalized on the basis of Ad_E2 mechanism involving a thiirenium ion intermediate (45).[88]



(45)

Schmid et al.[83,84] have reported the product distribution for the addition of 4-chlorophenylsulphenyl chloride to unsymmetrical alkynes in 1,1,2,2-tetrachloroethane (Scheme 56).



Ar=4-ClC$_6$H$_4$.

(46)

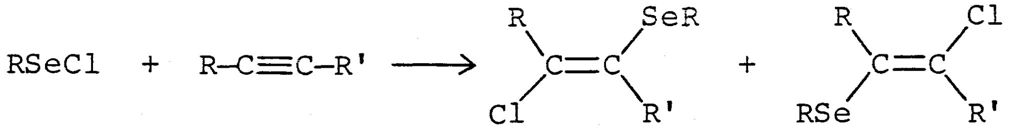
(47)

Scheme 56.

Their results show that the orientation of addition is dependent on both the steric and electronic effects of the substituent. Thus, the reaction of alkyl-substituted acetylenes (R=alkyl, R'=H) gave the regioselective anti-

Markownikoff adduct (47), whereas the reaction of phenyl-substituted acetylenes (R=phenyl, R'=H or alkyl) gave the regioselective Markownikoff adduct (46).

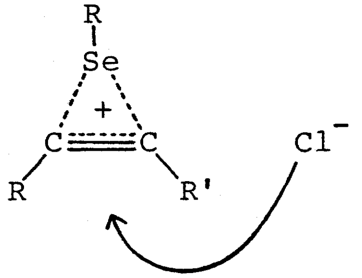
As with the addition of sulphenyl chlorides, the addition of selenenyl chlorides to alkynes gave a mixture of two regioisomers (48 and 49), dependent both on the structure of alkynes and on the reaction medium (Scheme 57).[78]



(48) (49)

Scheme 57.

Generally, the addition of selenenyl chlorides occurs in an anti stereospecific manner. Both the kinetic data and product analysis seem to suggest that the addition reaction involves a product-determining attack of chloride ion on a bridged selenirenium ion intermediate (50).[78]



(50)

With the background of all accumulated works on electrophilic additions of various electrophiles to alkenes, dienes, and alkynes bearing various substituents in different media, the author has carried out a systematic study on the bromochlorination of alkenes, conjugated dienes, and alkynes with dichlorobromate(1-) ion and molecular bromine chloride.

In the second chapter, the author describes the details of the products obtained from the addition of dichlorobromate(1-) ion and molecular bromine chloride to various alkenes, also the mechanistic aspects of these reactions.

In the third chapter, the author describes the bromochlorination of conjugated dienes with dichlorobromate(1-) ion.

In the fourth chapter, the author describes the bromochlorination of various alkynes with dichlorobromate(1-) ion and molecular bromine chloride.

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CHAPTER 2

BROMOCHLORINATION OF ALKENES WITH DICHLOROBROMATE(1-) ION AND MOLECULAR BROMINE CHLORIDE

2. 1. Synthetic Utility for Bromochlorination of Alkenes with Dichlorobromate(1-) Ion

In the general introduction, it was shown that quaternary ammonium dichlorobromate(1-) (R_4NBrCl_2) is prepared by treatment of quaternary ammonium bromide with chlorine.[1) No chemical reaction with R_4NBrCl_2, however, has been tried although a dichlorobromate(1-) ion has been accepted as an intermediate of the bromochlorination of alkenes.[2,3)

The reaction of alkenes with R_4NBrCl_2 may proceed via BrCl as a possible intermediate, on assuming the following equilibrium (Scheme 1):

$$R_4N^+Br^- + Cl_2 \rightleftarrows R_4N^+BrCl_2^- \rightleftarrows R_4N^+Cl^- + BrCl$$

Scheme 1.

The author investigated the reaction of styrene with chlorine in the presence of tetrabutylammonium bromide and the addition of R_4NBrCl_2 to alkenes. The author describes here the details of the reaction products obtained from the reaction with styrene, the synthetic utility for the bromochlorination, and also the mechanistic aspects of this reaction.

Results and Discussion

A solution of an excess amount of styrene (1a) in chloroform was treated at 15 °C with a chloroform solution of chlorine containing various amounts of tetrabutylammonium bromide. The reaction mixture was directly subjected to GLC analysis. The reaction products were a mixture of 1-chloro-2-phenylethylene (2), 1,2-dichloro-1-phenylethane (3), 2-bromo-1-chloro-1-phenylethane (4a), and 1,2-dibromo-1-phenylethane (5) with recovery of 1a (Scheme 2).

$$\underset{\text{1a}}{C_6H_5CH{=}CH_2} \xrightarrow{Cl_2/Br^-} \underset{\text{2}}{C_6H_5CH{=}CHCl} + \underset{\text{3}}{C_6H_5CHClCH_2Cl}$$

$$+ \underset{\text{4a}}{C_6H_5CHClCH_2Br} + \underset{\text{5}}{C_6H_5CHBrCH_2Br}$$

Scheme 2.

As was expected, the formation of the bromo chloro adduct (4a) was markedly dependent on the amount of a bromide ion added (Table 1). The amount of 4a increased proportionally with the increase of bromide ions until the number of bromide ions reached that of chlorine. Further addition of bromide ions moderately decreased the amount of 4a with the formation of the dibromoalkane (5). Consequently, it is apparent that almost all the added bromide ions were incorporated into the adduct up to the equimolar amount of bromide ions to that of chlorine. It is important to note that the ratios of 2 to 3 were nearly constant regardless of the numbers of bromide ions,

Table 1. The Product Distribution in the Reaction of Styrene (1a) with Chlorine in the Presence of a Bromide Ion[a] in $CHCl_3$ (50 ml) at 15 °C

Entry	Added salt	Mol. ratio	%Composition[b]			
	mmol	Br^-/Cl_2	2	3	4a	5
1	no		45.7	54.3		
2	0.55	0.17	35.2	49.3	15.5	
3	0.80	0.25	34.4	42.5	23.1	
4	1.28	0.40	23.5	36.0	40.5	
5	1.95	0.61	14.1	23.1	62.8	
6	2.88	0.90	2.50	5.20	92.3	
7	3.22	1.01			100	
8	4.73	1.48			83.7	16.3

a) Tetrabutylammonium bromide. b) Determined by GLC analysis. Values are not corrected for TCD response factors. Percentages are normalized to 100%.

and pretty close to that of the addition product of chlorine in the absence of bromide ions (Entry 1, Table 1).4) In addition, only the bromo chloro adduct (4a) was formed in a regiospecific manner without contamination with 1-bromo-2-chloro-1-phenylethane, regardless of the number of bromide ions. The structure of the adduct (4a) was identified by comparison of its ^{13}C and ^{1}H NMR spectra with those of an authentic sample prepared from 1,2-dibromo-1-phenylethane and $SnCl_4$.5)

If the bromochloroalkane (4a) was formed by the initial attack of chlorine, giving dichloride (3), and followed by either subsequent attack of a bromide ion on 3 or a 2-chloro-1-phenylethyl cation6) as an intermediate, the ratios of 2 to 3 would be dependent on the amount of ammonium bromide. The present observations are inconsistent with the above mechanism and strongly suggest that the formation of 4a is through a quite different mechanism from that of the process giving 2 and 3. The most plausible process giving 4a would involve an electrophilic attack of BrCl or dichlorobromate(1-) ion ($BrCl_2^-$) instead of chlorine. In fact, the reaction of BrCl to the same alkene has been found to yield only 4a in a regiospecific manner.7)

On the other hand, it is well known that the addition of molecular BrCl to alkene gives bromochloroalkane together with considerable amounts of dibromo and dichloro adducts formed by the attacks of bromine and chlorine, which are in equilibrium with bromine chloride.[7,8] No dibromo and dichloro adducts were found in the present reaction by using an equimolar mixture of chlorine and bromide ion (Entry 7, Table 1). The results suggest that this reaction involves a different attacking species, not molecular bromine chloride. A similar result was also observed for the reaction of 3-β-trifluoroacetoxy-5-cholestene with BrCl in the presence of tetraphenylarsonium chloride, which gave the bromo chloro adducts in good yields without any formation of the dibromo and dichloro adducts.[9] In addition, the kinetic data for the addition reaction of bromine to alkenes in the presence of a chloride ion have suggested a dichlorobromate(1-) ion as the reacting species.[3] Thus, a dichlorobromate(1-) ion would be the reactant and bromine chloride would not be involved in the process giving 4a. A dichlorobromate(1-) ion was also suggested to be involved in the bromochlorination of cyclohexene with NCS and a bromide ion.[2]

As mentioned above, an equimolar mixture of chlorine and bromide ions would be a very effective and convenient bromochlorinating agent. Further, several quaternary ammonium dichlorobromates(1-) were found to be easily isolable. The bromochlorinations of alkenes were also tried with the isolated salts. The reaction of styrene (1a) with tetrabutylammonium dichlorobromate(1-) (6) in chloroform completed within a few minutes at 0 °C, giving 4a in a nearly quantitative yield (Scheme 3).

$$\underset{\underline{1a}}{C_6H_5CH{=}CH_2} \quad + \quad \underset{\underline{6}}{BrCl_2^-} \xrightarrow{CHCl_3} \underset{\underline{4a}}{C_6H_5CHClCH_2Br} \quad + \quad Cl^-$$

Scheme 3

Tetramethylammonium and phenyltrimethylammonium dichlorobromates(1-) (7 and 8) were also useful for the bromochlorination of alkenes, regardless of their lower solubilities. The reaction of 1a with 6 was examined in several different solvents with a wide variety of polarities. Reactions in dioxane, carbon tetrachloride, ethyl acetate, dichloromethane, 1,2-dichloroethane, and acetic anhydride gave 4a in similar yields. Thus, the usual aprotic solvents can be employed as the reaction medium. Meanwhile, the reaction of 1a in acetic acid gave 4a (65%) and 1-acetoxy-2-bromo-1-phenylethane (9, 35%). In methanol, the major product was 2-bromo-1-methoxy-1-phenylethane (10, 80%).

In order to study the synthetic merit and the mechanism of the addition of dichlorobromate(1-) ion to alkenes, the reactions of 6 with a variety of alkenes were examined. The results are given in Table 2. In analogy with the reaction of 1a, the reactions with methyl trans-cinnamate (1b), indene (1c), and vinyl acetate (1d) in chloroform gave the corresponding regiospecific Markownikoff adducts in good yields. Addition to methyl acrylate (1e) gave regiospecific

Table 2. Bromochlorination of Alkenes with 6 in $CHCl_3$ [a]

Alkenes	Temp/°C	Configuration	Products	Yield /% [b]
$C_6H_5CH{=}CH_2$ (1a)	0		$C_6H_5CHClCH_2Br$ (4a)	85(97)
1a	15		4a	84(98) [c]
1a	15		4a	86(95) [d]
(t)$C_6H_5CH{=}CHCO_2Me$ (1b)	70	erythro	$C_6H_5CHClCHBrCO_2Me$ (4b)	85
indene (1c)	0	trans	C_9H_8BrCl (4c)	95
$CH_2{=}CHOCOCH_3$ (1d)	-5		$CH_2BrCHClOCOCH_3$ (4d)	82
$CH_2{=}CHCO_2CH_3$ (1e)	40		$CH_2ClCHBrCO_2CH_3$ (4e)	79
$CH_3CH{=}CH_2$ (1f)	0		$CH_2BrCHClCH_3$ (4f)	85 [e]
			$CH_2ClCHBrCH_3$ (4f')	
$CH_2{=}CHCH_2Cl$ (1g)	50		$CH_2BrCHClCH_2Cl$ (4g)	82 [f]
			$CH_2ClCHBrCH_2Cl$ (4g')	
$CH_2{=}CHCH_2CN$ (1h)	20		$CH_2BrCHClCH_2CN$ (4h)	78 [g]
			$CH_2ClCHBrCH_2CN$ (4h')	
cyclohexene (1i)	0	trans	$C_6H_{10}BrCl$ (4i)	85

Table 2 (continued)

Alkenes	Temp/°C	Configuration	Products	Yield/%[b)]
(c) $CH_3CH=CHCH_3$ (1j)	-10	threo	$CH_3CHBrCHClCH_3$ (4j)	84
(t) $CH_3CH=CHCH_3$ (1j')	-10	erythro	$CH_3CHBrCHClCH_3$ (4j')	85
(c) $C_6H_5CH=CHC_6H_5$ (1k)	20	threo	$C_6H_5CHBrCHClC_6H_5$ (4k)	95
(t) $C_6H_5CH=CHC_6H_5$ (1k')	20	erythro	$C_6H_5CHBrCHClC_6H_5$ (4k')	97
(c) $EtO_2CCH=CHCO_2Et$ (1ℓ)	70	erythro	$EtO_2CCHBrCHClCO_2Et$ (4ℓ')	66
(t) $EtO_2CCH=CHCO_2Et$ (1ℓ')	70	erythro	$EtO_2CCHBrCHClCO_2Et$ (4ℓ')	71
(c) $MeO_2CCH=CHCO_2Me$ (1m)	70	erythro	$MeO_2CCHBrCHClCO_2Me$ (4m')	69
(t) $MeO_2CCH=CHCO_2Me$ (1m')	70	erythro	$MeO_2CCHBrCHClCO_2Me$ (4m')	73

a) Reactions were carried out with 30 mmol of 6, 30 mmol of alkene, and 100 ml of $CHCl_3$. b) Isolated yield. Values in parentheses represent product yields determined by ^1H NMR before isolation using ethylbenzene as the internal standard. c) 7 as bromochlorinating agent. d) 8 as bromochlorinating agent. e) 4f : 4f'=56 : 44. f) 4g : 4g'=31 : 69. g) 1h : 1h'=39 : 61.

anti-Markownikoff adduct (4e) (Scheme 4).

$$\underset{\mathbf{1e}}{CH_2{=}CHCOOCH_3} \xrightarrow[CHCl_3]{6} \underset{\mathbf{4e}}{CH_2ClCHBrCOOCH_3}$$

Scheme 4.

Meanwhile, addition of 6 to such alkenes as propene (1f), 3-chloropropene (1g), and allyl cyanide (1h) gave both Markownikoff and anti-Markownikoff adducts (4 and 4') (Scheme 5).

$$\underset{\mathbf{1}}{CH_2{=}CHCH_2X} \xrightarrow[CHCl_3]{6} \underset{\mathbf{4}}{CH_2BrCHClCH_2X} + \underset{\mathbf{4'}}{CH_2ClCHBrCH_2X}$$

f: X=H g: X=Cl h: X=CN

Scheme 5.

Although attempts to separate two regioisomers (4 and 4') were unsuccessful, the orientation of halogen atoms was elucidated on the basis of chemical shifts of the carbon bearing bromine and chlorine atoms in ^{13}C NMR, since it has been observed that the carbon atom bearing a chlorine atom is deshielded relative to the one bearing a bromine atom.10) The structures of two regioisomers (4 and 4') have been determined by comparison of their ^{13}C NMR spectra with those of the corresponding dibromo and dichloro compounds. Selected ^{13}C NMR spectra of dihaloalkanes are listed in Table 3. The two regioisomers from the reaction of 3-chloropropene (1g) were identified by comparison of their ^{13}C NMR spectra with those of the authentic samples.

Table 3. ^{13}C Chemical Shifts for 1,2-Dihaloalkanes in $CDCl_3$ (δ value)

$C^1H_2XC^2HYCH_3$

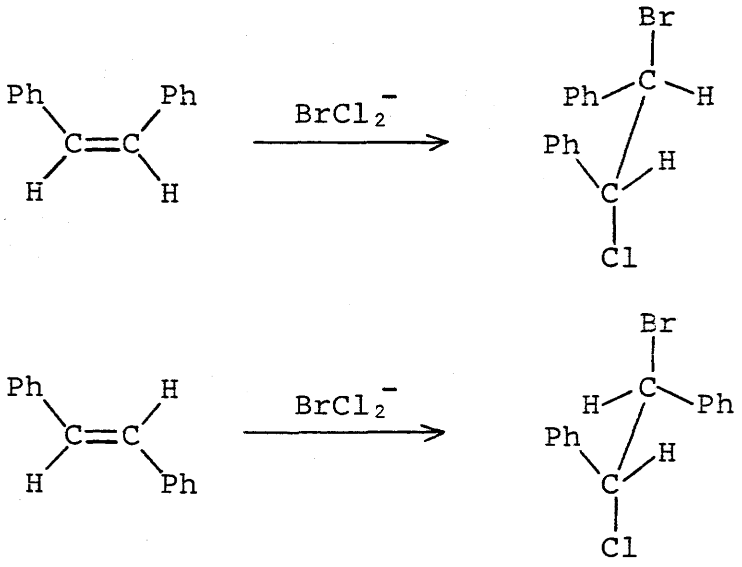
X	Y	C^1	C^2
Br	Br	37.6	45.7
Cl	Cl	49.5	55.8
Br	Cl	37.5	55.4
Cl	Br	49.6	46.3

$C^1H_2XC^2HYCH_2CN$

X	Y	C^1	C^2
Br	Br	34.2	42.5
Cl	Cl	45.9	53.3
Br	Cl	33.5	53.0
Cl	Br	46.1	42.1

The reason for the formation of anti-Markownikoff adducts is uncertain; however, it may be attributed to the combined effects of polar and steric effects. A similar orientation has also been found in the reactions of these alkenes with other bromochlorinating agents.11,12)

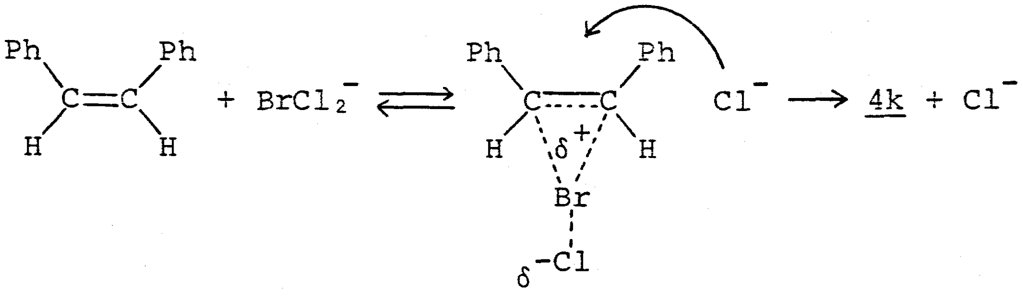
Additions to methyl trans-cinnamate (1b), indene (1c), cyclohexene (1i), cis- and trans-2-butenes (1j and 1j') with 6 in $CHCl_3$ gave anti stereospecific products. Similarly, anti stereospecific products, threo- and erythro-1-bromo-2-chloro-1,2-diphenylethanes (4k and 4k') were obtained from cis- and trans-stilbenes (1k and 1k'), respectively (Table 2 and Scheme 6).



Scheme 6.

The solvent effect on anti stereospecific addition was examined. The reactions of 1k in dichloromethane, 1,2-dichloroethane, acetic anhydride, and nitromethane gave threo isomer (1k) free from erythro isomer (4k'). In contrast, it has previously been reported that the addition of molecular bromine chloride to 1k' in chloroform is anti stereospecific, while that of 1k gives considerable amounts of 4k'.[7)] Furthermore, the stereochemistry of bromine addition to 1k has been known to be dependent on the solvents.[13)] Thus, the mode of the reaction is very different in the additions to 1k with 6 and with BrCl (and Br_2). Therefore, the present results cannot be explained on the basis of any accepted mechanism for the additions of bromine and bromine chloride.[13,14)]

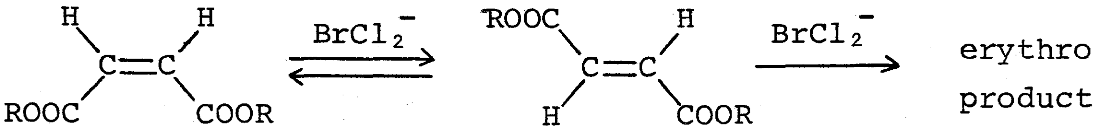
The completely anti stereospecific addition with 6 can be explained by assuming an $AdEC_2$-type mechanism involving a rate- and product-determining attack of a chloride ion to a three-center bound π-complex intermediate (11),[15)] as shown in Scheme 7: a similar mechanism has been suggested for the additions of Br_3^- and Br_2Cl^- to alkenes and dienes.[14,16)]



11

Scheme 7

The product obtained from diethyl maleate (1ℓ) and fumarate (1ℓ') was the same compound, diethyl erythro-2-bromo-3-chlorosuccinate (4ℓ'). Similar results were also observed for the reaction of dimethyl maleate (1m) and fumarate (1m') with 6 in chloroform (Table 2). The reactions with these electron-deficient alkenes proceeded only on heating and the maleate was found to isomerize to the fumarate under the reaction conditions (Scheme 8).



Scheme 8.

On the other hand, fumaric and maleic acids have been known to react with BrCl, yielding erythro- and threo-2-bromo-3-chlorosuccinic acids, respectively.17) The difference of such stereochemistry of addition would be additional evidence to support the assumption that the reactant in the reaction of 6 is not BrCl but $BrCl_2^-$.

When compared with other bromochlorinating agents, the merits of quaternary ammonium dichlorobromate(1-) become evident (Table 4). Although the formation of bromochloroalkanes by the use of a mixture of bromine and chlorine has been well known,7) the yields appeared to be relatively low due to the contamination of dichloro- and dibromoalkanes. Certain olefinic substances with BrCl prepared in situ from N-bromoacetamide and hydrogen chloride also give undesired by-products,5) as was the case for a mixture of N-chlorosuccinimide (NCS) and a bromide ion.2) Although pyridine-BrCl complex14,18) and a mixture of Br_2 and $SbCl_5$(or $SbCl_3$)11) were reported to be effective bromochlorinating agents, the products were usually complex. Tetraalkylammonium dichlorobromate(1-) can be handled easily and can be used as a very convenient bromochlorinating agents. Simple purification of the product provides pure bromochloroalkane in nearly quantitative yields.

Table 4. Yields of Bromochloroalkanes from Various Methods[a)]

Bromochlorinating agent	Bromochloroalkanes(%) from Styrene,	cyclohexene,	trans-stilbene,	cis-stilbene
$BrCl_2^-$ [b)]	85	85	97	95
NBA and HCl[c)]	36–44		67	
NCS, LiBr, and LiCl[d)]		86[e)]		
Br_2 and Cl_2 [f)]	67	56	52	74[g)]
$SbCl_5$(or $SbCl_3$) and Br_2 [h)]	87	96[e)]	74	

a) Isolated yield. b) This work. c) Ref. 5. d) Ref. 2. e) Determined by GLC. f) Ref. 7. g) A mixture of threo- and erythro-bromochloroalkanes. h) Ref. 11.

Experimental

All the melting points and boiling points are uncorrected. NMR spectra were recorded on a JEOL JNM FX-60Q spectrometer, using TMS as the internal standard. Mass spectra were recorded on a JMS-D-300 Mass spectrometer. The GLC analyses were performed on a Yanako GCG-550T with a Silicone DC 550 (25%)-Celite 545 (2 m) column (A) or Yanako G-180 gas chromatograph with a High vacuum silicone grease (25%)-Celite 545 (2 m) column (B). All the organic starting materials, including the solvents, were distilled or recrystallized before use. Chlorine was passed through water and sulfuric acid.

Synthesis of Quaternary Ammonium Dichlorobromates(1-). Quaternary ammonium dichlorobromates(1-) were prepared by the known procedure.1) To a suspension of tetrabutylammonium bromide (32.2 g, 100 mmol) in carbon tetrachloride (200 ml) was added 120 mmol of chlorine in the same solvent (200 ml) at 0–5 °C with stirring. The crystalline tetrabutylammonium dichlorobromate(1-) (6) was filtered and washed with CCl_4 (500 ml). Yield 38.5 g (98%); mp 66–67 °C. Further purification was unnecessary for the subsequent experiments, but small amounts could be recrystallized from acetic acid to give a product of mp 66.5–67 °C. This salt has been already reported, but melting point was not recorded.19) Similarly, tetramethylammonium dichlorobromate(1-) (7) was prepared by the treatment of tetramethylammonium bromide with chlorine in acetic acid. Yield 85%; mp 162–163 (lit,[1)] 160–163 °C). Phenyltrimethylammonium dichlorobromate(1-) (8) was prepared from phenyltrimethylammonium bromide and chlorine in chloroform. Yield 90%; mp 106–108 °C.

The Reaction of Styrene (1a) with Chlorine in the Presence of Tetrabutylammonium Bromide. Experiments were carried out by adding 20 ml of chlorine solution in chloroform (0.16 mol dm^{-3}) in the presence of various amounts of tetrabutylammonium bromide (0.55–4.73 mmol) to 6.4 mmol of 1a (in 30 ml of the same solvent) at 15 °C with stirring for 10 min. After the reaction completed, the mixture was washed with aq Na_2CO_3 and water, and dried over $MgSO_4$. The solvent was removed by evaporation. The relative amounts of products were determined by measuring the peak areas of GLC on the column (A) at 100 °C with hydrogen as a carrier gas (50 ml/min). Retention times (in minutes) were: 1a, 1; 2, 3.2; 3, 7.8; 4a, 12.8; 5, 14. The results are given in Table 1.

The Reaction of Styrene (1a) with 6. General Procedure: To a solution of 1a (3.12 g, 30 mmol) in chloroform (100 ml) was added 6 (11.8 g, 30 mmol) at 0 °C over 20 min with stirring. The mixture was stirred for an additional 10–20 min, then washed with five 100-ml portions of water to remove the ammonium salt, dried over Na_2SO_4, and the solvent was evaporated. Distillation afforded 5.6 g (85%) of pure 4a: bp 80–81 °C

/1 mmHg (lit,[5)] 106–107 °C/6 mmHg; ^{1}H NMR ($CDCl_3$) δ=3.82, 3.83 (2H, 2d, J=8.3 and 6.6 Hz, CH_2Br), 5.03 (1H, q, J=8.3 and 6.6 Hz, CHCl), and 7.36 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=35.9, 61.3, 127.2, 128.6, 129.0, and 138.3; MS M^+ at m/z= 218, 220, and 222 (100 : 129 : 34); Found: m/z 217.9494. Calcd for C_8H_8BrCl: M, 217.9499. Yields in other aprotic solvents were: in dioxane, 78%; CCl_4, 80%; $CH_3COOC_2H_5$, 79%; CH_2Cl_2, 85%; CH_2ClCH_2Cl, 83%; $(CH_3CO)_2O$, 80%.

In Acetic Acid as the Solvent. To a solution of 1a (1.04 g, 10 mmol) in acetic acid (30 ml) was added 6 (3.93 g, 10 mmol) at 20 °C over 5 min with stirring. The product was isolated by pouring the reaction mixture into cold saturated aq NaCl, followed by extraction with ether (200 ml) and washing with aq $NaHCO_3$ and water. The ethereal extract was dried over $MgSO_4$ and concentrated. The residue (2.00 g) was analyzed by GLC and ^{1}H NMR. The composition analyzed by GLC was: 4a, 65.4 and 1-acetoxy-2-bromo-1-phenylethane (9), 34.6%. ^{1}H NMR shows 67 : 33 mixture of 4a and 9, respectively (by integration of methine protons). The ^{1}H NMR spectrum of 9 corresponds well with that reported in the literature.[20)]

In Methanol as the Solvent. To a solution of 1a (1.04 g, 10 mmol) in methanol (30 ml) was added 6 (3.93 g, 10 mmol) at 0 °C over 5 min with stirring. The solvent was removed by evaporation, and ether (150 ml) was added to the residue. The ethereal solution was washed with aq $NaHCO_3$ and water.

The ethereal extract was dried over $MgSO_4$ and concentrated. ^1H NMR spectrum of the residue shows a 80 : 20 mixture of 2-bromo-1-methoxy-1-phenylethane (10) and 4a, respectively (by integration of methine protons). Column chromatography of the residual oil (1.85 g) on silica gel with hexane as the eluent gave 1.10 g of pure 10 and 0.2 g of 4a. The data for 10 are as follows: bp 65–66 °C/2 mmHg (lit,$^{21)}$ 57 °C/0.4 mmHg); ^1H NMR ($CDCl_3$) δ=3.32 (3H, s, CH_3), 3.49, 3.50 (2H, 2d, J= 5.7 and 7.0 Hz, CH_2Br), 4.37 (1H, approx. triplet, CH), and 7.35 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=36.2, 57.2, 83.4, 126.7, 128.4, 128.6, and 139.0; MS M^+ at m/z=214 and 216 (100 : 96); Found: m/z 213.9981. Calcd for $C_9H_{11}BrO$: M, 213.9994.

Syntheses of Bromochloroalkanes by 6 in Chloroform. The procedure was the same as that described for that of 1a except for the reaction temperature and period. The results are given in Table 2.

Methyl erythro-2-bromo-3-chloro-3-phenylpropanate (4b). Mp 118–120 °C (from pentane); ^1H NMR ($CDCl_3$) δ=3.89 (3H, s, CH_3), 4.62 (1H, d, J=11.3 Hz, CHBr), 5.27 (1H, d, J=11.3 Hz, CHCl), and 7.39 (5H, s, C_6H_5); Found: C, 43.51; H, 3.37%. Calcd for $C_{10}H_{10}BrClO_2$: C, 43.27; H, 3.63%.

trans-2-Bromo-1-chloroindane (4c). After the usual work-up procedure, column chromatography of the residue on silica gel with hexane as the eluent gave a pure 4c: ^1H NMR ($CDCl_3$) δ=3.23 (1H, d of d, J=3.4 and 17.1 Hz) 3.82 (1H, d of d, J=

5.9 and 17.1 Hz), 4.70 (1H, approx. q), 5.47 (1H, d, J=2.4 Hz), and 7.30–7.45 (4H, m); ^{13}C NMR ($CDCl_3$) δ=41.4, 53.9, 67.9, 125.0, 125.4, 127.8, 129.6, 139.9, and 140.2; MS M^+ at m/z=230, 232, and 234 (100 : 130 : 32).

1-Acetoxy-2-bromo-1-chloroethane (4d). Bp 80–81 °C/25 mmHg (lit,[11)] 64–65 °C/10 mmHg); ^1H NMR ($CDCl_3$) δ=2.17 (3H, s, CH_3), 3.70 (2H, d, J=6.0 Hz, CH_2Br), and 6.53 (1H, t, J=6.0 Hz, CHCl); ^{13}C NMR ($CDCl_3$) δ=20.6, 32.7, 80.0, and 168.0.

Methyl 2-Bromo-3-chloropropionate (4e). Bp 60–63 °C/25 mmHg; ^1H NMR ($CDCl_3$) δ=3.4–4.4 (3H, m, CH_2Cl and CHBr) and 3.80 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$) δ=43.8, 53.4, 54.8, and 167.5. The ^1H NMR spectrum of 4a corresponds well with that reported in the literature.[22)]

1-Bromo-2-chloropropane (4f) and 2-Bromo-1-chloropropane (4f'). Gaseous propene (1f) from a cylinder was passed through the chloroform solution of 6 at 0 °C until the yellow color disappeared. After the usual work-up, mixed bromochloroalkanes (4f and 4f') were obtained: bp 53–55 °C/70 mmHg. ^1H NMR shows a 56 : 44 mixture of 4f and 4f'. ^1H NMR ($CDCl_3$) (an asterisk indicates 4f) δ=1.65* (d, J=6.35 Hz, CH_3), 1.79 (d, J=6.34 Hz, CH_3), and 3.3–4.4 (m). ^{13}C NMR ($CDCl_3$) (an asterisk indicates 4f) δ=23.2, 37.5,* 46.3, 49.6, and 55.4*. Although attempts to separate two regioisomers were unsuccessful, these assignments were supported for dibromo and dichloro analogs.[23]

1-Bromo-2,3-dichloropropane (4g) and 2-Bromo-1,3-dichloropropane (4g′). A mixture of two isomeric bromodichloropropanes (4g and 4g′) was obtained from 3-chloropropene (1g): bp 60–62 °C/22 mmHg. ^{13}C NMR shows a 31 : 69 mixture of 4g and 4g′, respectively. The ratio was obtained by comparison of the spectra of the pure samples as follows: 4g, ^{13}C NMR (CDCl$_3$) δ=33.1, 46.0, and 57.9; 4g′, ^{13}C NMR (CDCl$_3$) δ=45.2 and 49.1.

4-Bromo-3-chlorobutyronitrile (4h) and 3-Bromo-4-chlorobutyronitrile (4h′). A mixture of 4h and 4h′ was obtained from vinyl cyanide (1h): bp 67–68 °C/2 mmHg. ^{13}C NMR shows a 39 : 61 mixture of 4h and 4h′, respectively. ^{13}C NMR (CDCl$_3$) (an asterisk indicates 4h) δ=25.2, 25.7,* 33.5,* 42.1, 46.1, 53.0,* 115.3,* and 115.6. These assignments were supported for dibromo and dichloro analogs as follows: 3,4-dibromobutyronitrile, ^{13}C NMR (CDCl$_3$) δ=26.1, 34.2, 42.5, and 115.9; 3,4-dichlorobutyronitrile, ^{13}C NMR (CDCl$_3$) δ=24.7, 45.9, 53.3, and 117.0.

trans-1-Bromo-2-chlorocyclohexane (4i). Bp 91–92 °C/18 mmHg (lit,[11] 90–95 °C/17 mmHg); ^{1}H NMR (CDCl$_3$) δ=1.10–2.69 (8H, m) and 4.03–4.41 (2H, m); ^{13}C NMR (CDCl$_3$) δ=22.5, 23.3, 32.8, 33.3, 55.5, and 62.9; MS M^{+} at m/z=196, 198, and 200 (100 : 129 : 32); Found: m/z 195.9640. Calcd for $C_6H_{10}BrCl$: M, 195.9655. The ^{1}H NMR spectrum corresponds well with that reported in the literature.[24]

threo-2-Bromo-3-chlorobutane (4j). Bp 45–48 °C/30 mmHg (lit,[25] 50–52 °C/30 mmHg; ^{1}H NMR ($CDCl_3$) δ=1.60 (3H, d, J=6.6 Hz, CH_3), 1.74 (3H, d, J=6.6 Hz, CH_3), and 4.0–4.8 (2H, m, CHCl and CHBr); ^{13}C NMR ($CDCl_3$) δ=20.3, 20.4, 52.5, and 60.5; MS M^+ at m/z=170, 172, and 174 (100 : 129 : 31); Found: m/z 169.9490. Calcd for C_4H_8BrCl: M, 169.9498.

erythro-2-Bromo-3-chlorobutane (4j'). Bp 51–52 °C/50 mmHg (lit,[25] 50–52 °C/51 mmHg); ^{1}H NMR ($CDCl_3$) δ=1.65 (3H, d, J=6.3 Hz, CH_3), 1.80 (3H, d, J=6.5 Hz, CH_3), and 4.0–4.3 (2H, m, CHBr and CHCl); ^{13}C NMR ($CDCl_3$) δ=23.5, 53.8, and 61.8; MS M^+ at m/z=170, 172, and 174 (100 : 131 : 33); Found: m/z 169.9495. Calcd for C_4H_8BrCl: M, 169.9498.

threo-1-Bromo-2-chloro-1,2-diphenylethane (4k). Mp 102.5–103 °C (from 95% ethanol) (lit,[7] 99–100 °C); ^{1}H NMR ($CDCl_3$) δ=5.34 (2H, s, CHBr and CHCl) and 7.18 (10H, s, 2 C_6H_5); MS M^+ at m/z=294, 296, and 298 (100 : 127 : 32); Found: m/z 293.9819. Calcd for $C_{14}H_{12}BrCl$: M, 293.9811.

erythro-1-Bromo-2-chloro-1,2-diphenylethane (4k'). Mp 218–221 °C (from ligroine) (lit,[7] 220–221 °C); ^{1}H NMR ($CDCl_3$) δ=5.32 (2H, s, CHBr and CHCl) and 7.40–7.44 (10H, m, 2 C_6H_5); MS M^+ at m/e=294, 296, and 298 (100 : 132 : 34); Found: m/z 293.9809. Calcd for $C_{14}H_{12}BrCl$: M, 293.9811.

The Reactions of Dialkyl Fumarate and Maleate with 6. The mixture of 6 (11.8 g, 30 mmol) and diethylfumarate (1ℓ') (

5.16 g, 30 mmol) in 100 ml of $CHCl_3$ was stirred at refluxing temperature for 50 h. The reaction mixture was washed with aq Na_2SO_3 and water. After the usual work-up, the solid residue was recrystallized from ligroine to give 6.15 g (71%) of diethyl erythro-2-bromo-3-chlorosuccinate(4ℓ'): mp 56–57 °C ; ^1H NMR (CCl_4) δ=1.38 (6H, t, J=7.5 Hz, $2CH_3$), 4.38 (4H, q, J=7.5 Hz, $2CH_2$), and 4.50–4.58 (2H, m, 2CH). ^1H NMR spectrum of 4ℓ' corresponds well with that reported in the literature.[11)]

In a similar way, analysis of the residue from the reaction of 1ℓ with 6 by ^1H NMR revealed a mixture of 4ℓ' and unreacted alkenes. The solid residue was recrystallized from ligroine to give 5.7 g (66%) of product (mp 56–57 °C) (not depressed on admixture with the product obtained from 1ℓ'). ^1H NMR analysis of the recovered alkene indicated 77% of 1ℓ' and 23% of 1ℓ on the basis of relative areas of the signals at δ=6.84 and 6.25 for olefinic protons, respectively.

As with the addition of 6 to 1ℓ and 1ℓ', the addition to dimethyl maleate (1m) and fumarate (1m') gave also the same compound, dimethyl erythro-2-bromo-3-chlorosuccinate (4m'): mp 35–36 °C (from pentane); ^1H NMR (CCl_4) δ=3.92 (6H, s, $2CH_3$) and 4.65–4.72 (2H, m, 2CH); MS M^+ at m/z=258, 260, and 262 (100 : 131 : 32); Found m/z 257.9295. Calcd for $C_6H_8O_4BrCl$: M, 257.9276.

Reaction of cis-Stilbene (1k) with 6 in Various Solvents.

The reactions were carried out by the addition of 2 mmol of 6 to 2 mmol of 1k in 50 ml of the solvent at 20 °C with stirring. After the yellow color disappeared, the reaction mixture was washed with water and dried over Na_2SO_4. The product of the reaction in acetic anhydride was isolated by extraction with ether. After the solvent was removed under reduced pressure, the residue was analyzed by GLC and ^1H NMR. Reactions in $CHCl_3$, CH_2Cl_2, CH_2ClCH_2Cl, $(CH_3CO)_2O$, and CH_3NO_2 gave threo isomer (4k) free from the erythro isomer (4k'). Yields in the solvents were: in $CHCl_3$, 95%; CH_2Cl_2, 98%; CH_2ClCH_2Cl, 96%; $(CH_3CO)_2O$, 95%; CH_3NO_2, 95%. The GLC analysis was performed on the column (B) at 150 °C with helium as the carrier gas (50 ml/min).

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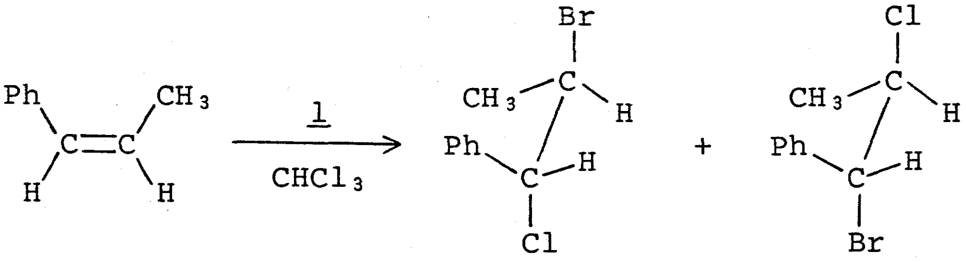
2. 2. Regio- and Stereochemistries for the Bromochlorination of 1-Phenylpropenes with Dichlorobromate(1-) Ion and Molecular Bromine Chloride

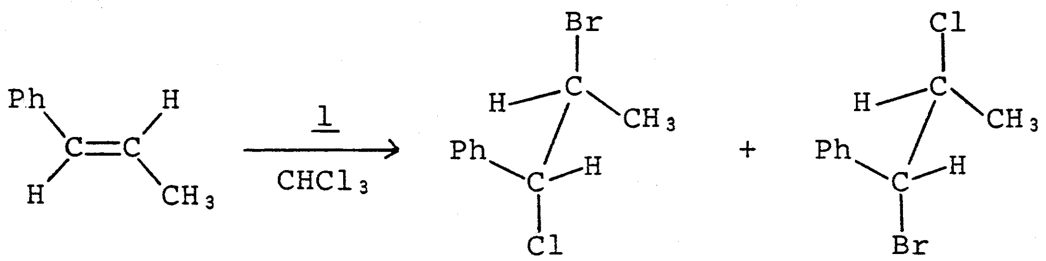
In the general introduction, it was shown that the stereochemistry of bromine addition to aryl-substituted alkenes is markedly dependent both on the brominating agents and on the solvents employed.1) The anti stereospecific additions were observed for the reaction with a tribromide ion2,3) or with pyridine-bromine complex3) as brominating agents. However, only a few systematic studies have been carried out on reaction with a dichlorobromate(1-) ion as a bromochlorinating agent. It has been reported that 1-phenylpropenes give bromochlorinated adducts by reaction with $(CH_3)_4NBr_2Cl$ and pyridine-bromine chloride in a trans manner, while addition of molecular bromine chloride gives significant amounts of cis-adduct.3) As described in the part of above section (2. 1), it has shown that tetrabutylammonium dichlorobromate(1-) reacted with various alkenes to give bromo chloro adducts in nearly quantitative yields, while the additions were in an anti stereospecific manner. In an attempt to gather more detailed information on bromochlorination with a dichlorobromate(1-) ion, the author has investigated the regio- and stereochemistries of the addition to 1-phenylpropenes in solvents with widely different polarities. The reactions of 1-phenylpropenes with molecular bromine chloride were also carried out for comparison with the reactions of a dichlorobromate(1-) ion. The author describes here reaction features of bromochlorination of 1-phenylpropenes with a dichlorobromate(1-) ion and molecular bromine chloride.

Results and Discussion

The reaction of tetrabutylammonium dichlorobromate(1-) (1) with cis-1-phenylpropene (2a) in chloroform gave a mixture of threo-2-bromo-1-chloro-1-phenylpropane (3a) and threo-1-bromo-2-chloro-1-phenylpropane (4a) in nearly quantitative yields. trans-1-Phenylpropene (2b) reacted with 1 to give a mixture of erythro-2-bromo-1-chloro and erythro-1-bromo-2-chloro adducts (3b and 4b, respectively) (Scheme 1).



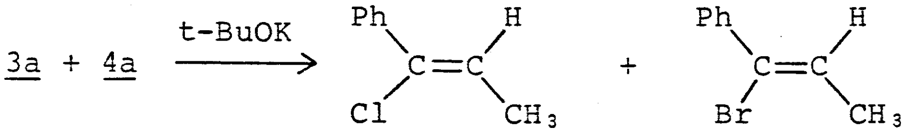
2a 3a, 76% 4a, 24%



2b 3b, 95% 4b, 5%

Scheme 1.

Structural assignments of the bromo chloro compounds 3a and 4a were deduced by dehydrohalogenation to haloalkenes (Scheme 2). When a mixture of 3a and 4a was treated with 0.78 equivalent of potassium t-butoxide in t-butyl alcohol, the alkene (5) with recovery of the unreacted bromo chloro compound (4a) was obtained in a good yield.



5 6

Scheme 2.

^{1}H NMR analysis of the reaction mixture revealed that one isomer (3a), which gives 5, was consumed faster than the other (4a); this isomer (4a), which gives 6, disappeared slowly. Thus, the more facile elimination of 3a (than that of 4a) would be due to either differences in eclipsing effect of the bulky substituents or in the ability of the leaving groups. The relative reactivities of 3a and 4a are in accordance with the usual reactivities of hydrogen halide elimination.[4)]

The structures of the major and minor products from 2a and 2b were also determined by comparisons of their ^{13}C and ^{1}H NMR spectra with those of the corresponding dibromo and dichloro adducts. Selected ^{13}C and ^{1}H NMR spectra of threo- and erythro-1,2-dihalo-1-phenylpropanes are listed in Tables 1 and 2, respectively.

Table 1. ^{13}C Chemical Shifts for threo- and erythro-1,2-Dihalo-1-phenylpropanes in $CDCl_3$ (δ value)

$C_6H_5C^1HXC^2HYCH_3$

X	Y	C^1	C^2	CH_3
threo				
Br	Br	58.9	52.7	22.3
Cl	Cl	67.4	61.2	21.6
Br	Cl	59.2	61.0	22.0
Cl	Br	67.4	53.0	22.4
erythro				
Br	Br	59.1	51.1	25.7
Cl	Cl	67.4	60.1	22.1
Br	Cl	58.8	59.6	24.0
Cl	Br	67.5	51.5	23.4

Table 2. ^{1}H Chemical Shifts for threo- and erythro-1,2-Dihalo-1-Phenylpropanes in $CDCl_3$ (δ value)

$C_6H_5CH_aXCH_bYCH_3$

X	Y	CH_3	H_a	H_b
threo				
Br	Br	1.67	5.22	4.59
Cl	Cl	1.44	5.00	4.38
Br	Cl	1.46	5.06	4.45
Cl	Br	1.62	5.06	4.47
erythro				
Br	Br	2.03	5.05	4.57
Cl	Cl	1.67	4.91	4.38
Br	Cl	1.80	—	—
Cl	Br	1.90	4.98	4.45

NMR analysis of the mixture of two regioisomers could be used to determine the amounts of each of these isomers.

The present addition reaction appeared to be stereospecific but not regiospecific. The lack of regiospecificity cannot be ascribed to the subsequent isomerization of the bromochloroalkanes, since prolonged reaction time did not cause a change of the isomer ratio of the products. Interconversions between two regioisomers (pure 3a or the mixed isomers; 3a :

4a=60 : 40) were examined. However, no isomerization was observed in chloroform at room temperature for 3 h by using either 2 equivalents of 1 or of tetrabutylammonium chloride. Another possibility for the formation of anti-Markownikoff adduct (4a or 4b) from the dichloro adducts of alkenes can also be excluded, since no dichloroalkane was found in the reaction products.

When the reaction was carried out in the presence of a free radical inhibitor, 2,6-di-t-butyl-4-methylphenol, the product composition did not change within experimental error. Moreover, the same product ratio was obtained under either an oxygen or nitrogen atmosphere. These results indicate that the reaction proceeds in an electrophilic process rather than in a free radical one.

When compared to the addition of other interhalogens to 1-phenylpropenes, the striking differences become evident. Product distributions for addition of interhalogens to cis-1-phenylpropene are summarized in Table 3. Thus, present results would be the first example of the formation of anti-Markownikoff adduct given in the interhalogen addition to 1-phenylpropenes.

Table 3. Regio- and Stereochemistries for Additions of Various Reagents to cis-1-Phenylpropene

Reagent	threo-M[a)]	threo-aM[b)]	erythro-M[a)]	Ref
$BrCl_2^-$	76	24	0	c
PyBrCl	100	0	0	d
BrCl	79	0	21	d
BrF	65	0	35	e
ICl	100	0	0	f
IBr	100	0	0	f

a) M=Markownikoff adduct. b) aM=anti-Markownikoff adduct. c) This work. d) Ref. 3. e) M, Zupan and A. Pollak, J. Chem. Soc., Perkin Trans. 1, 1976, 971. f) G. H. Schmid and D. G. Garratt,"The Chemistry of Double-Bonded Functional Groups," ed by Patai, John Wiley and Sons, London (1977), Supplement A, part 2, pp. 798–800.

The regio- and stereochemistries of the additions of 2a and 2b were investigated in solvents with widely different polarities in order to determine the mechanism of the reaction. Table 4 presents data for the effect of solvents on the regiochemistry of the addition to 2a and 2b. The reactions were completely anti stereospecific and nonregiospecific in all the aprotic solvents employed. No solvent effect on the regiochemistry has been observed (Table 4). A similar stereochemical

Table 4. Solvent Dependency of Regiochemistry of the Reactions of 2a and 2b with 1 at 0 °C

Solvent	Dielectric constant[a)]	Product composition/%[b)]			
		from 2a		from 2b	
		3a	4a	3b	4b
$CHCl_3$	4.81	76.0 (76.8)	24.0 (23.2)	94.5 (95.8)	5.5 (4.2)
$CH_3COOC_2H_5$	6.02	77.1	22.9	94.6	5.4
CH_2Cl_2	9.08	77.5 (77.9)	22.5 (22.1)	95.5 (93.9)	4.5 (6.1)
CH_2ClCH_2Cl	10.36	78.4	21.6	93.2	6.8
$(CH_3CO)_2O$	20.7	75.2 (75.9)	24.8 (24.1)	94.1 (94.6)	5.9 (5.4)
CH_3NO_2	35.87	78.0 (76.2)	22.0 (23.8)	92.2 (92.9)	7.8 (7.1)

a) J. A. Riddick and E. E. Toops,"Technique of Organic Chemistry," ed. by A. Weissberger, Interscience, New York (1955), Vol VII. b) Percentages are normalized to 100%. Determined by ^1H NMR analysis. Values in parentheses represent the product distributions determined by ^{13}C NMR analysis.

result has been shown for the reaction of cis-stilbene with 1 (above section).

In contrast to the present results, Heasley et al.$^{3)}$ have reported that the reactions of 2a and 2b with molecular bromine chloride (BrCl) in dichloromethane and carbon tetrachloride occurred in a nonstereospecific manner, although anti additions were favored. The author has reinvestigated the reaction of the same alkenes with BrCl in various solvents to compare the results with that of 1. Although the bromo chloro adducts were the major products in all cases, as expected, substantial amounts of dichloro and dibromo adducts were also found in the product. None of the anti-Markownikoff adducts were detected by ^1H and ^{13}C NMR analyses of the product mixtures in any of the solvents. The results are shown in Table 5.

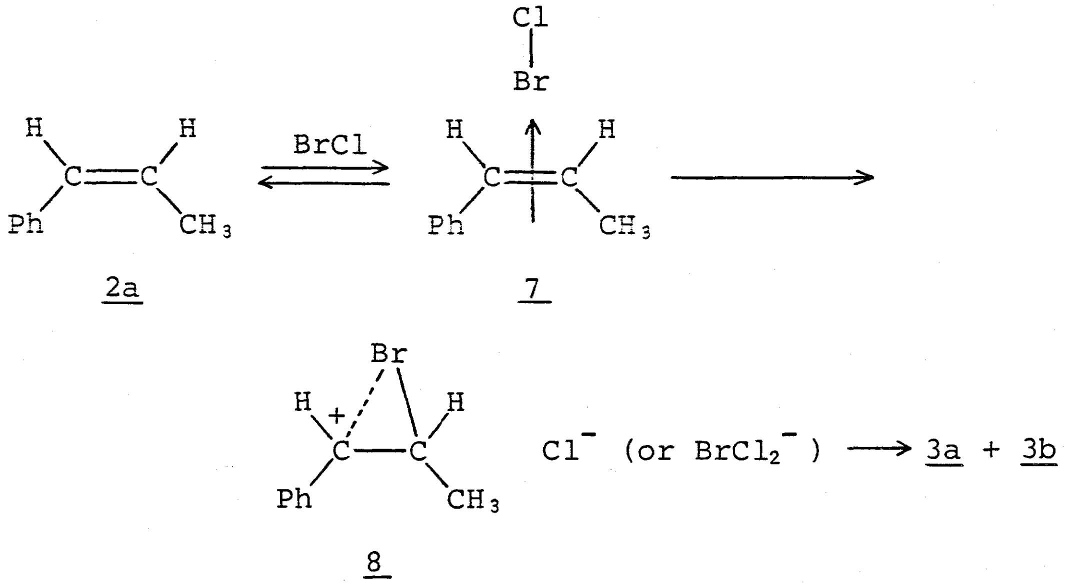
Table 5 shows that the stereochemistry of the addition to cis-alkene (2a) is dependent on the polarity of the solvent. The addition in acetic anhydride or in nitromethane was nonstereospecific. The results of trans-alkene (2b) showed a much smaller dependency on the nature of the solvent. All the additions of BrCl to 2b were found to be anti stereoselective. A similar stereochemistry has been observed for the addition of bromine to these alkenes.$^{1)}$ Since it is quite reasonable to consider that the process is the same for both molecular bromine and bromine chloride additions,$^{3,5)}$

Table 5. Solvent Dependency of Stereochemistry of Bromo Chloro Adducts Obtained from the Addition of Molecular Bromine Chloride to 2a and 2b at 0 °C

Solvent	Dielectric constant[b)]	Product composition/%[a)]			
		from 2a		from 2b	
		3a	3b	3a	3b
Dioxane[c)]	2.21	21.4	78.6	18.3	81.7
CCl_4	2.23	76.1 (75.5)[d)]	23.9 (24.5)[d)]	11.8	88.2
$CHCl_3$	4.81	75.2	24.8	9.8	90.2
CH_2Cl_2	9.08	75.7 (79)[d)]	24.3 (21)[d)]	6.3 (8.5)[d)]	93.7 (91.5)[d)]
$(CH_3CO)_2O$	20.7	51.4	48.6	14.5	85.5
CH_3NO_2	35.87	49.8	50.2	9.1	90.9

a) Based on the amount of bromo chloro adducts, as determined by GLC analysis. Values were not corrected for FID response factors. Percentages are normalized to 100%. Yields of bromo chloro adducts were found to be more than 70% in all runs. b) See footnote a in Table 4. c) At 20 °C. d) Data from Ref. 3.

a mechanism such as that illustrated in Scheme 3, similar to the bromine addition, would be involved in the addition with molecular bromine chloride.

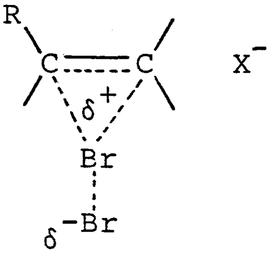


Scheme 3.

The solvent dependency of the stereochemistry and the regiospecific addition observed for the reaction with these alkenes are fully in accordance with the mechanism involving a very weakly bridged benzylic carbonium ion intermediate (8) prior to the product-determining step.$^{1)}$ The fact that the stereochemistry of the addition to 2a is more sensitive to solvent polarity than that of the addition to 2b gives strong evidence for the presence of the intermediate (8). The intermediate (8) for the reaction of 2a tends to take a more energetically favored conformation due to the eclipsing effect of the adjacent methyl and phenyl groups. Furthermore, the peculiarity of stereochemistry observed in dioxane is easily explained in terms of specific solvation for the carbonium ion intermediate.1)

As has been described above, the additions to alkenes appeared to be strikingly different in reactions with 1 and with molecular bromine chloride in all aprotic solvents employed. These marked differences in the reactions of 1 and BrCl suggest that these two reactions are quite different in their mechanisms. The formation of anti stereospecific and anti-Markownikoff adducts in the reaction with 1 rules out a weakly bridged benzylic-like ion intermediate (8), such as is shown in Scheme 3. If an intermediate such as 8 was involved, the complete formation of Markownikoff adduct would be expected.

The large differences in distributions of products obtained by the reaction with 1 are consistent with the previous proposal that this reagent is an independent electrophile rather than a precursor of BrCl as described in the above section. The reaction of $BrCl_2^-$ presently studied and that of Br_2Cl^- (or Br_3^-) reported by Heasley et al.3) seem to involve similar mechanisms. Two possible mechanisms hitherto being proposed by them involve the attack of a halide ion on a three-center bound π-complex (9)6) or on the bromonium ion intermediate (10).



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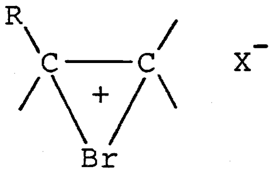

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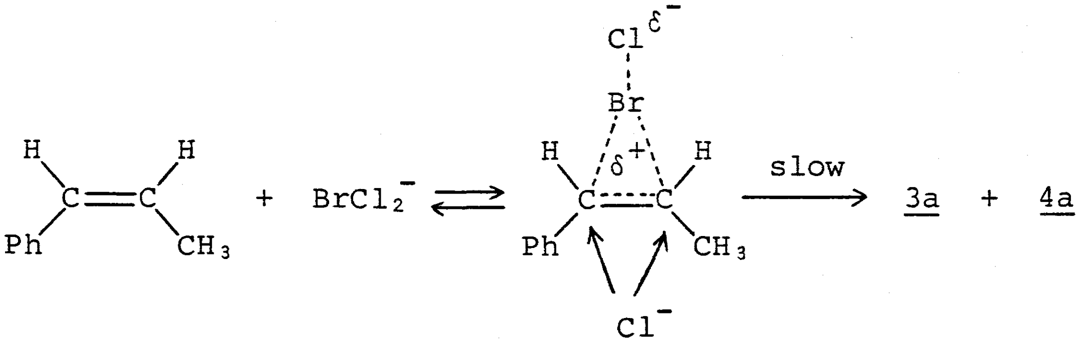
R=vinyl or phenyl

The bromonium ion intermediate (10), however, is hardly acceptable for the reaction of $BrCl_2^-$ since the present reaction gave nonregiospecific products. Thus, the AdEC_2 process involving an intermediate like 9 at the product-determining step would be applicable to the reaction of 1, as depicted in Scheme 4.



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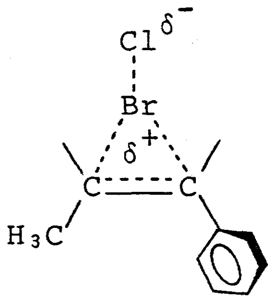
Scheme 4.

The regiochemistry of the reaction of 1 would be dependent on the electronic effect of the phenyl ring which stabilizes the developing cationic character on the carbon in the complex (11).

The cis- and trans-alkenes gave somewhat different regiochemical results. Markownikoff adducts were obtained mainly from both the cis- and trans-alkenes (2a and 2b) as given in Table 4. The cis-alkene gave less regioselectivity than the trans-alkene. The difference may be ascribed to the ability of stabilization of a cationic center by phenyl groups. The phenyl ring of the intermediate (12) formed from the cis-alkene would be skewed by the eclipsing effect.



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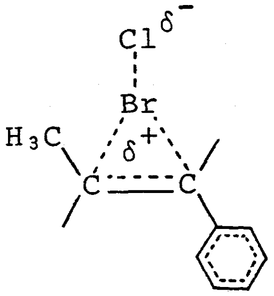

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The intermediate (13) formed from the trans-alkene would be free from such an eclipsing effect and the developing cationic character would be delocalized over the phenyl ring. This type of stabilization may develop the cationic character on the carbon adjacent to the phenyl ring. Thus, the attack of a chloride ion to the benzylic carbon atom would be more favored in the intermediate from the trans-alkene than in that from the cis-alkene.

Meanwhile, relative rates of the reactions of 2a and 2b with 1 were determined in chloroform relative to the rate of the reaction of styrene. Relative rates were measured at 0 °C by the competition method using ^{1}H NMR analysis. The results are listed in Table 6.

Table 6. Reactivity of $BrCl_2^-$ Addition to 2a and 2b Relative to Styrene in $CHCl_3$ at 0 °C

Alkene (mmol)		Styrene (mmol)	$BrCl_2^-$ (mmol)	k/k_s
2a,	1	2	0.6	1.21
	2	2	0.8	1.31
	2	1	0.6	1.28
				1.27[a)]
2b,	1	4	1.0	1.50
	2	2	0.8	1.53
	2	1	0.6	1.60
				1.54[a)]

a) Mean value

These results show that the trans-alkene (2b) reacts faster than the cis-alkene (2a), and suggest the assumption that the intermediate (13) formed from 2b is more stable than that (12) formed from 2a.

Experimental

Materials. All the organic starting materials, including the solvents, were distilled before use. Bromine chloride was prepared by adding an equimolar amount of bromine to a chlorine-carbon tetrachloride solution.

Reaction of cis-1-Phenylpropene (2a) with Tetrabutylammonium Dichlorobromate(1-) (1). Details of the reaction have been described in the above section. The mixture of 2a (5.90 g, 50 mmol) and 1 (19.7 g, 50 mmol) in 100 ml of $CHCl_3$ was stirred at 0 °C for 10 min. After the usual work-up, distillation afforded 9.3 g (80%) of a mixture of two isomeric bromochloroalkanes (3a and 4a): bp 90–91 °C/1 mmHg; MS M^+ at m/z=232, 234, and 236 (100 : 128 : 32); Found: m/z 231.9649. Cacld for $C_9H_{10}BrCl$: 231.9655. Although attempts to separate 3a and 4a by GLC were unsuccessful, ^1H NMR analysis (by integration of methyl protons) revealed the product composition to be 76% of 3a and 24% of 4a. The major product was characterized as 3a on the basis of the ^1H and ^{13}C NMR spectra of an authentic sample[3)] as follows: ^1H NMR ($CDCl_3$) δ=1.65 (3H, d, J=6.74, CH_3), 4.27–4.71 (1H, m, CHBr), 5.08 (1H, d, J=6.0 Hz, CHCl), and 7.36 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=22.4, 53.0, 67.4, 128.1, 128.2, 128.8, and 137.2.

Reaction of trans-1-Phenylpropene (2b) with 1. The reaction was carried out similarly to that of 2a.

Distillation afforded 9.6 g (82%) of mixed bromochloroalkanes (3b and 4b): bp 91–92 °C/1 mmHg; MS M^+ at m/z=232, 234, and 236 (100 : 128 : 32); Found: m/z 231.9648. Calcd for $C_9H_{10}BrCl$: M, 231.9655. ^1H NMR analysis established the product composition as 96% of 3b and 3% of 4b. The major product was also characterized as 3b on the basis of the ^1H and ^{13}C NMR spectra of an authentic sample$^{3)}$ as follows: ^1H NMR ($CDCl_3$) δ=1.91 (3H, d, J=6.4 Hz, CH_3), 4.21–4.67 (1H, m, CHBr), 4.98 (1H, d, J=8.54, CHCl), and 7.36 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=23.4, 51.5, 67.5, 127.5, 128.4, 128.7, and 139.3.

Dehydrohalogenation of Regioisomers (3a and 4a). To 2.34 g (10 mmol) of the mixture composed of 3a (76%) and 4a (24%) in t-butyl alcohol (50 ml) was added 6 ml (2.23 mmol) of potassium t-butoxide in t-butyl alcohol (0.372 mol dm^{-3}). The mixture was stirred at 20 °C. After 30 min, 1 ml of the solution was taken up, shaken with water, and extracted with pentane. The pentane layer was washed with dilute acid and dried over $MgSO_4$. Evaporation of pentane and analysis of the residue by ^1H NMR showed the composition to be: 3a, 53.3%; 4a, 25%; 5, 21.7 %; and 6, 0%. The reaction was carried out further by the addition of 15 ml (5.58 mmol) of potassium t-butoxide solution (0.372 mol dm^{-3}). The mixture was then stirred for 1h. The reaction mixture was then worked up in a fashion similar to that described above. Evaporation of pentane gave 1.58 g of the crude product. ^{1}H NMR showed the composition to be: 3a, 0.5%; 4a, 23%; 5, 76.5%; and 6, 0%. Column chromatography of this residue on silica gel with hexane as the eluent gave almost pure 4a (150 mg) and 5 (711 mg). The data for 4a are as follows: ^{1}H NMR ($CDCl_3$) δ=1.46 (3H, d, J=6.6 Hz, CH_3), 4.24–4.66 (1H, approx. quintet, CHCl), 5.06 (1H, d, J=6.1 Hz, CHBr), and 7.26–7.38 (5H, m, C_6H_5); MS M^+ at m/z=232, 234, and 236 (100 : 127 : 32); Found: m/z 231.9649. Calcd for $C_9H_{10}BrCl$: M, 231.9655. The data for 5 are as follows: ^{1}H NMR (CCl_4) δ=1.90 (3H, d, J= 6.7 Hz, CH_3), 6.31 (1H, d, J=6.7 Hz, CHCl), and 7.28–7.62 (5H, m, C_6H_5); MS M^+ at m/z=152 and 154 (100 : 32); Found m/z 153.0388. Calcd for C_9H_9Cl: M, 152.0393. The ^{1}H NMR spectrum for 5 corresponds well with that reported in the literature.7)

Dehydrochlorination of Pure Regioisomer (4a). To 120 mg (0.51 mmol) of 4a in t-butyl alcohol (5 ml) was added 2 ml (0.74 mmol) of potassium t-butoxide solution (0.372 mol dm^{-3}). This mixture was stirred at 20 °C. After 30 min, the reaction mixture was worked up as described above. Evaporation of pentane gave 75 mg of crude product 6 as a colorless oil: ^{1}H NMR (CCl_4) δ=2.00 (3H, d, J=7.5 Hz, CH_3), 6.40 (1H, d, J=7.5 Hz, CHBr), and 7.35–7.80 (5H, m, C_6H_5); MS M^+ at m/z=196 and 198 (100 : 97); Found: m/z 195.9898. Calcd for C_9H_9Br: M, 195.9888. The spectral patterns of this product were identical with those of a sample prepared by dehydrobromination of threo-1,2-dibromo-1-phenylpropane.

Reaction of 1 with 2a or 2b in Various Solvents. To 2 mmol of the alkene in 20 ml of the solvent was added 2 mmol of 1 at 0 °C over 5 min with stirring. After the yellow color disappeared, the mixture was washed with water and dried over Na_2SO_4. The product of the reaction in acetic anhydride was isolated by pouring the reaction mixture into water, followed by extraction with ether and washing with aq $NaHCO_3$ then water. After the solvent was removed under reduced pressure, the residues were analyzed by ^1H NMR and ^{13}C NMR in some cases. The relative amounts of products were determined from the ratio of the peak areas of the methyl protons of the bromo chloro compounds (3a and 4a or 3b and 4b), and also from the ratio of peak heights of aliphatic carbon (^{13}C NMR). The results are given in Table 4.

Reaction of Bromine Chloride with 2a or 2b in Various Solvents. To 2.1 mmol of the alkene in 20 ml of the solvent, was added 1.7 ml of BrCl solution in CCl_4 (1.2 mol dm^{-3}) at 0 °C with stirring. Products of the reactions in acetic anhydride and dioxane were isolated by extraction with ether as described above. Products of the reactions in carbon tetrachloride, chloroform, dichloromethane, and nitromethane were obtained by direct evaporation of the solvent. GLC analysis of the residue gave six peaks with retention times of 12.3, 13.7, 18.9, 21.1, 27.6, and 32.8 min. These were assigned to be erythro-1,2-dichloro-, threo-1,2-dichloro-, erythro-2-bromo-1-chloro-, threo-2-bromo-1-chloro-, erythro-1,2-dibromo-, and threo-1,2-dibromo-1-phenylpropanes, except for unreacted alkene, respectively. GLC analyses were performed on a High vacuum silicone grease(25%)-Celite 545 (2 m) column at 120 °C with helium as a carrier gas (35 ml/min). The results are given in Table 5.

The Reaction of 1 with 2a in the Presence of a Radical Inhibitor. When 2a was treated with 1 in chloroform as described above, O_2 was bubbled during the reaction. The product ratio of 76.5 : 23.5 was obtained by ^1H NMR analysis for 3a and 4a, respectively. The reaction was carried out with 1.18 g (10 mmol) of 2a, 3.93 g (10 mmol) of 1, and 0.70 g (0.3 mmol) of 2,6-di-t-butyl-4-methylphenol in $CHCl_3$ (30 ml). After the usual work-up, the product ratio of 77.8 : 22.2 was obtained by ^1H NMR analysis for 3a and 4a, respectively. ^{13}C NMR analysis also showed a 76.5 : 23.5 mixture of 3a and 4a, respectively.

Stability of the Bromo Chloro Compounds under the Reaction Conditions. To 1 mmol of the two regioisomers (3a and 4a) in $CHCl_3$ (10 ml) was added 2 mmol of 1 and allowed to stand for 3 h at room temperature with stirring. The mixture was shaken with aq sodium sulfite. The chloroform layer was separated, washed with water, and dried over $MgSO_4$. After the solvent was removed, the residue was analyzed by ^1H NMR spectrum. No interconversion was observed. Namely, the same isomer compositions were observed within experimental error: Starting from a 60 : 40 mixture of 3a and 4a recovered a 59 : 41 mixture of 3a and 4a, and only 3a was recovered from 3a without contamination with 4a.

Competitive Bromochlorination of 1-Phenylpropenes (2a and 2b) with 1. To the proper concentrations of 1-phenylpropene and styrene in 5 ml of chloroform, was added a limiting amount of 1 (required 20% conversion of alkenes) at 0 °C over 5 min with stirring. The mixture was stirred for an additional 5 min, then washed with three 15-ml portions of water, dried over Na_2SO_4, and chloroform layer was subjected to NMR analysis. The relative rates were determined relative to styrene by the competition method using NMR for product analysis, reported previously by Fahey et al.[8)] The results are given in Table 6.

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2. 3. Regiochemistry for the Bromochlorination of Styrene Derivatives with Dichlorobromate(1-) Ion and Molecular Bromine Chloride

In the above section, the author has described that the regiochemistry for the bromochlorination of alkenes with tetrabutylammonium dichlorobromate(1-) (1) is very sensitive to the alkene structures and the addition of 1 to 1-phenylpropenes is strikingly different from that of molecular bromine chloride (2). The author describes here the distinction of regiochemistry for the bromochlorination of styrene derivatives between 1 and 2.

Results and Discussion

The reaction of $(n\text{-}C_4H_9)_4NBrCl_2$ (1) with styrene derivatives (3a–c) in chloroform gave the corresponding bromo chloro compounds (4a–c) in nearly quantitative yields (Scheme 1).

$$\underset{3}{RC_6H_4CH{=}CH_2} \quad + \quad 1 \longrightarrow \underset{4}{RC_6H_4CHClCH_2Br}$$

a: R=H b: R=4-CH_3

c: R=4-F

Scheme 1.

On the other hand, the reaction of 3d–h with 1 gave a mixture of two regioisomers (4d–h and 5d–h), respectively (Scheme 2).

$$\underset{3}{RC_6H_4CH{=}CH_2} + 1 \longrightarrow \underset{4}{RC_6H_4CHClCH_2Br} + \underset{5}{RC_6H_4CHBrCH_2Cl}$$

d: R=4-Cl
e: R=3-Cl
f: R=2-Cl
g: R=4-Br
h: $R=3-NO_2$

Scheme 2.

All the results are summarized in Tbale 1.

The structures of two regioisomers (4d–h and 5d–h) were determined by comparisons of their ^{13}C NMR spectra with those of the corresponding dibromo and dichloro compounds. Selected ^{13}C NMR spectra of dihalo compounds are listed in Table 2. ^{13}C and ^{1}H NMR analyses of the mixture of two regioisomers could be used to determine the amounts of each of the isomers.

The lack of regiospecificity cannot be ascribed to the subsequent isomerization of the bromochloroalkanes, since prolonged reaction time did not cause a change of the isomer ratio of the products. In a control experiment, an isomer's mixture (4h : 5h=71 : 29) in chloroform was heated in the presence of two equivalents of tetrabutylammonium chloride. The same isomer ratio was found after heating at 30 °C for 3h.

In contrast to the reaction with 1, the bromochlorination of 3 with molecular bromine chloride (2) gave the regiospecific

Table 1. Bromochlorination of 3 with 1 in $CHCl_3$ [a)]

Alkenes 3	Product composition(%) [b)] 4	 5	Yield/% [c)]
3a	100(100)	0(0)	97.1
3b	100(100)	0(0)	97.2
3c	100(100)	0(0)	99.3
3d	93.5	6.5	99.5
3e	87.4(87.6)	12.6(12.4)	98.9
3f	66.4(64.0)	33.6(36.0)	
3g	93.2	6.8	97.2
3h	73.8(71.3)	26.2(28.7)	97.2

a) Reactions were carried out with 20 mmol of 1, 20 mmol of 3, and 50 ml of $CHCl_3$ at 0 °C. b) Determined by ^{13}C NMR analysis. Values in the parentheses represent the product compositions determined by ^1H NMR analysis. Percentages are normalized to 100%. c) Total product yields were determined by ^1H NMR using ethylbenzene as the internal standard.

Table 2. ^{13}C Chemical Shifts for 1,2-Dihalo Adducts in $CDCl_3$ (δ value) $R-C_6H_4C^1HXC^2H_2Y$

R	X	Y	C^1	C^2
4-Cl	Br	Br	49.5	34.7
	Cl	Cl	60.6	48.0
	Cl	Br	60.1	35.5
	Br	Cl	50.1	47.2
3-Cl	Br	Br	49.2	34.5
	Cl	Cl	60.5	47.9
	Cl	Br	60.1	35.4
	Br	Cl	49.9	47.2
2-Cl	Br	Br	45.4	33.5
	Cl	Cl	57.4	47.4
	Cl	Br	56.8	34.8
	Br	Cl	46.4	46.4
4-Br	Br	Br	49.5	34.5
	Cl	Cl	60.7	48.0
	Cl	Br	60.2	35.4
	Br	Cl	50.1	47.4
$3-NO_2$	Br	Br	48.0	34.2
	Cl	Cl	59.7	47.7
	Cl	Br	59.2	35.0
	Br	Cl	48.7	46.9

Markownikoff adduct (4) together with substantial amounts of the dichloro and dibromo adducts (Scheme 3).

$$\underset{\underline{3}}{\mathrm{RC_6H_4CH{=}CH_2}} + \underline{2} \longrightarrow \underset{\underline{4}}{\mathrm{RC_6H_4CHClCH_2Br}}$$

Scheme 3.

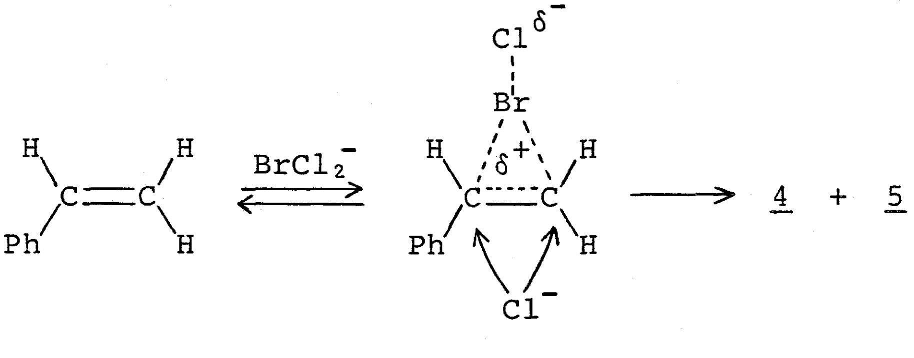
A small amount of anti-Markownikoff product (5h) alone was formed by the reaction of 3h. The results are shown in Table 3.

Table 3. Bromochlorination of 3 with 2 in $CHCl_3$[a)]

Alkenes 3	Product composition/%[b)] 4	 5	Yield/%[c)]
3a	100	0	69.3
3c	100	0	66.1
3d	100	0	76.6
3e	100	0	79.2
3f	100	0	81.2
3g	100	0	77.4
3h	98.1	1.9	79.8

a) Reactions were carried out with 3.2 mmol of 3, 3.2 mmol of 2, and 10 ml of $CHCl_3$ at 0 °C. b) Determined by ^{13}C NMR. Percentages are normalized to 100%. c) Determined by GLC analysis.

Tables 1 and 3 show that the regiochemistry of the addition to styrenes having electron-withdrawing groups is strikingly different in the reactions with 1 and with 2. The reaction with 1 can be best explained by assuming AdEC$_2$-type mechanism involving the attack of a chloride ion on a three-center bounded π-complex (6) as has been described in the above section (2. 2).



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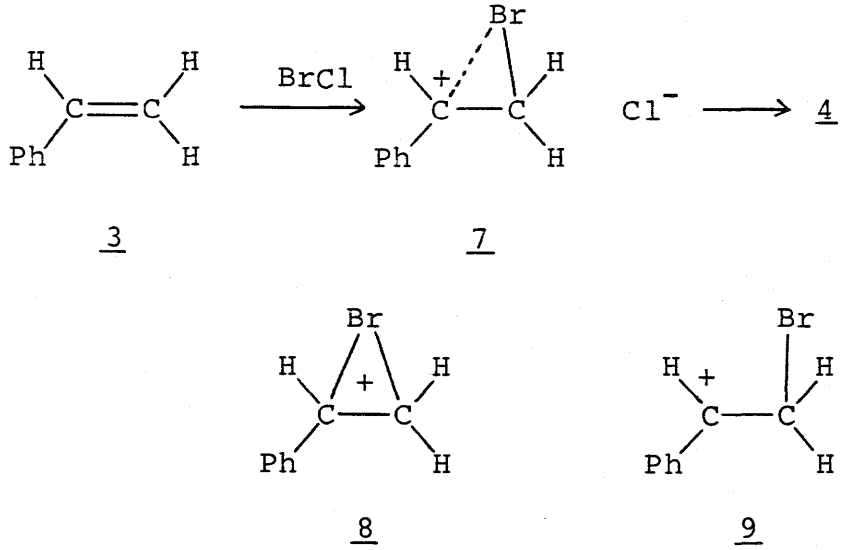
Scheme 4.

The data given in Table 1 show that all the styrene derivatives were attacked by a chloride ion mainly on the phenyl substituted carbon atom of the double bond. Furthermore, the regiochemistry of the addition with 1 would be dependent on the electronic effect of the substituent. The amount of anti-Markownikoff adduct (5) tends to increase with the increasing electron-withdrawing character of the ring substituent. These behaviors may be ascribed to the ability of stabilization of a cationic center by the substituent.

Meanwhile, Scheme 5 presents a possible mechanism which could account for the regiochemical data obtained in the reaction of 3 with 2: a similar mechanism has been suggested for the addition of bromine to alkenes.[1)] The structure of the cationic intermediate such as 7 has been extensively investigated from both kinetic and stereochemical points of view.[2,3)] It is well known that the structure of the intermediates depends on the electronic effect of the substituent, ranging from a bridged bromonium ion (8) to a weakly bridged benzylic-like ion (7) or open benzylic carbonium ion (9).



Ph=3-nitrophenyl

Scheme 5.

The present regiochemical results of the bromochlorination with 2 can be explained in terms of an intermediate (7) or (9), which gives only Markownikoff adduct. Whereas, the formation of anti-Markownikoff adduct (5h) for the reaction of 3h implicates a bridged bromonium ion (8). Similar intermediate (8) has been suggested for the bromination of 3- and 4-nitrostyrenes.$^{3)}$

Experimental

All the melting points and boiling points are uncorrected. All the organic starting materials, including the solvents were distilled before use. The reaction of 3a with 1 has been reported in the above section (2. 1).

Reaction of 3b–h with 1. General Procedure: Details of the reaction have been reported in the above section (2. 1). To a solution of 3 (30 mmol) in chloroform (50 ml) was added 1 (7.87 g, 20 mmol) at 0 °C over 20 min with stirring. After the usual work-up, the crude product was either recrystallized from an appropriate solvent or purified by distillation.

2-Bromo-1-chloro-1-(4-methylphenyl)ethanes (4b), yield 82%; bp 94–95 °C/5–7 mmHg; ^{1}H NMR ($CDCl_3$) δ=2.34 (3H, s, CH_3), 3.82, 3.84 (2H, 2d, J=8.5 and 6.6 Hz, CH_2Br), 5.02 (1H, q, J=8.5 and 6.6 Hz, CHCl), and 7.23 (4H, s, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=21.2, 35.9, 61.3, 127.1, 129.3, 135.3, and 139.0; MS M^+ at m/z=232, 234, and 236 (100 : 128 : 32).

2-Bromo-1-chloro-1-(4-fluorophenyl)ethanes (4c), yield 82%

mp 39.5–40 °C (from pentane); ^{1}H NMR ($CDCl_3$) δ=3.79, 3.82 (2H, 2d, J=9.5 and 6.3 Hz, CH_2Br), 5.03 (1H, q, J=9.5 and 6.3 Hz, CHCl), and 6.8–7.5 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ= 35.8, 60.3, 114.9, 116.4, 128.8, 129.3, 134.0, 134.2, 154.4, and 171.0; MS M^+ at m/z=236, 238, and 240 (100 : 130 : 32).

A Mixture of 2-Bromo-1-chloro- and 1-Bromo-2-chloro-1-(4-chlorophenyl)ethanes (4d and 5d), yield 80%; bp 105–106 °C/2 mmHg; ^{13}C NMR ($CDCl_3$) (an asterisk indicates *5d*) δ=35.5, 47.2,* 50.1,* 60.1, 128.6, 128.8, 134.8, and 136.7; MS M^+ at m/z=252, 254, 256, and 258 (100 : 159 : 73 : 11).

A Mixture of 2-Bromo-1-chloro- and 1-Bromo-2-chloro-1-(3-chlorophenyl)ethanes (4e and 5e), yield 84%; bp 108–110 °C/ 2–3 mmHg; ^{1}H NMR ($CDCl_3$) (an asterisk indicates *5e*) δ=3.59, 3.82 (2d, J=8.5 and 5.9 Hz, CH_2Br), 4.06,* 4.08,* (2d, J=9.0 and 6.6 Hz, CH_2Cl), 4.99 (q, J=8.5 and 5.9 Hz, CHCl and CHBr), and 7.25–7.40 (m, C_6H_4); ^{13}C NMR ($CDCl_3$) (an asterisk indicates *5e*) δ=35.4, 47.2,* 49.9,* 60.1, 125.5, 125.9,* 127.4, 127.9,* 129.2, 129.9, 134.5, and 140.9; MS M^+ at m/z= 252, 254, 256, and 258 (100 : 161 : 72 : 11).

A Mixture of 2-Bromo-1-chloro- and 1-Bromo-2-chloro-1-(2-chlorophenyl)ethanes (4f and 5f), yield 82%; bp 60–61 °C/1 mmHg; ^{1}H NMR ($CDCl_3$) (an asterisk indicates *5f*) δ=3.87 (d, J=7.3 Hz, CH_2Br), 4.15* (d, J=7.8 Hz, CH_2Cl), 5.64 (t, J=7.3 Hz, CHCl and CHBr), and 7.24–7.29 (m, C_6H_4); ^{13}C NMR ($CDCl_3$) (an asterisk indicates *5f*) δ=34.8, 46.4,* 56.8, 127.3, 127.4,* 128.3, 128.4,* 129.7, 129.9,* 130.0, 133.3, and 135.7; MS M^+ at m/z=252, 254, 256, and 258 (100 : 167 : 76 : 11).

A Mixture of 2-Bromo-1-chloro- and 1-Bromo-2-chloro-1-(4-bromophenyl)ethanes (4g and 5g), yield 80%; mp 30–32 °C (from pentane); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5g) δ=35.4, 47.1,* 50.1,* 60.2, 123.0, 128.9, 129.3,* 131.8, and 137.2; MS M^+ at m/z=296, 298, 300, and 302 (100 : 224 : 152 : 32).

A Mixture of 2-Bromo-1-chloro- and 1-Bromo-2-chloro-1-(3-nitrophenyl)ethanes (4h and 5h), yield 86%; mp 51.5–53 °C (from pentane); ^1H NMR ($CDCl_3$) (an asterisk indicates 5h) δ= 3.87, 3.90 (2d, J=9.1 and 5.1 Hz, CH_2Br), 4.13,* 4.15* (2d, J=8.8 and 5.9 Hz, CH_2Cl), 5.02–5.28 (br. q, CHCl and CHBr), and 7.44–8.31 (m, C_6H_4); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5h) δ=35.0, 46.9,* 48.7,* 59.2, 122.5, 122.8,* 123.9, 129.8, 133.4, 133.8,* 140.3, and 148.2; MS M^+ at m/z= 263, 265, and 267 (100 : 125 : 36).

Reaction of 3 with 2. Details of the reaction have been described in the above section (2. 2). To 3.2 mmol of 3 in 10 ml of chloroform was added 1 ml of BrCl (2) solution in carbon tetrachloride (3.2 mol dm^{-3}) at 0 °C with stirring. After the solvent was removed, the residue was subjected to GLC and ^{13}C NMR. The GLC analyses were performed on a High vacuum silicone grease (25%)-Celite 545 (2 m) column with helium as a carrier gas. The results are given in Table 3.

References

1) G. H. Schmid and D. G. Garratt,"The Chemistry of Double-Bonded Functional Groups," ed by S. Patai, John Wiley and Sons, London (1977), Supplement A, part 2, pp. 764–776.

2) R. C. Fahey and J.-J. Schneider, J. Am. Chem. Soc., 90, 4429 (1968).

3) J. H. Rolston and K. Yates, J. Am. Chem. Soc., 91, 1483 (1969).

2. 4. Regio- and Stereochemistries for the Bromochlorination of Styrene Derivatives and 1-Phenylpropenes with Dichlorobromate(1-) Ion in Protic Solvents

In the above section, the author has described that the regiochemistry for the bromochlorination of styrene derivatives with tetrabutylammonium dichlorobromate(1-) (1) is very sensitive to the substituent groups. Meanwhile, the regio- and stereochemistries for the reaction of 1-phenylpropenes with 1 have been shown to be independent of the solvent polarity when the reaction was carried out in aprotic solvents. As a continuation of these studies, the author describes here the effect of the protic solvent on the regio- and stereochemistries of the addition of 1 to styrene derivatives and 1-phenylpropenes.

Results and Discussion

The reaction of $(n\text{-}C_4H_9)_4NBrCl_2$ (1) with styrene derivatives (2a–f) in acetic acid gave the corresponding bromo chloro compounds (3a–f) along with substantial amounts of solvent-incorporated products (4a–f) in good yields (Scheme 1 and Table 1).

$$XC_6H_4CH{=}CH_2 + \underline{1} \longrightarrow XC_6H_4CHClCH_2Br + XC_6H_4CH(OCOCH_3)CH_2Br$$

2 3 4

a: X=H b: X=4-CH_3

c: X=4-F d: X=4-Cl

e: X=3-Cl f: X=4-Br

Scheme 1.

On the other hand, the reaction of 2-chloro- and 3-nitrostyrenes (2g–h) with 1 gave a mixture of two regioisomers (3g–h and 3g'–h') and 4g–h, respectively (Scheme 2 and Table 1).

$$XC_6H_4CH{=}CH_2 + \underline{1} \longrightarrow XC_6H_4CHClCH_2Br + XC_6H_4CHBrCH_2Cl$$

2 3 3'

$$+\ XC_6H_4CH(OCOCH_3)CH_2Br$$

4

g: X=2-Cl h: X=3-NO_2

Scheme 2.

The solvent-incorporated products (4) were found to be formed in a completely regiospecfic Markownikoff manner from all the styrene derivatives.

The reaction of trans-1-phenylpropene (2i) with 1 in acetic acid gave a mixture of erythro- and threo-2-bromo-1-chloro-1-phenylpropanes (3i and 3j, respectively) along with a substantial amount of erythro-1-acetoxy-2-bromo-phenylpropane (4i). When cis-1-phenylpropene (2j) was allowed to react with 1, a mixture of 3i, 3j, and threo-1-acetoxy-2-bromo-1-phenylpropane (4j) was obtained (Scheme 3 and Table 1).

$$\mathrm{PhCH{=}CHCH_3} + 1 \longrightarrow \mathrm{PhCHClCHBrCH_3} + \mathrm{PhCH(OCOCH_3)CHBrCH_3}$$

trans- (2i)	3i, 58.0% 3j, 6.8%	4i, 35.2%
cis- (2j)	3i, 7.7% 3j, 59.0%	4j, 33.3%

Scheme 3.

The formation of solvent-incorporated products (4) cannot be ascribed to the subsequent secondary reaction of the bromo chloro compounds (3) with acetic acid, since prolonged reaction did not cause any change in the isomer ratio of the products.

The author has shown that the reaction of 2d–h with 1 in chloroform occurred in a nonregiospecific manner, although the Markownikoff adducts were formed mainly (section 2. 3). The reactions of 1-phenylpropenes (2i and 2j) with 1 have been found to proceed in anti stereospecific and nonregiospecific manners in aprotic solvents in the above section (2. 2). As shown in Table 1, the regio- and stereochemistries for the reaction of 2 with 1 in acetic acid are very different from those of the reaction in aprotic solvents (see Table 4 in the section 2. 2 and Table 3 in the section 2. 3). Obviously, a different product-determining step must be involved in the reaction in acetic acid.

Table 1. Bromochlorination of 2 with 1 in Acetic Acid[a)]

Alkene	Product composition/%[b)]		
2	3	3'	4
2a	66.7 (65.4)	0	33.3 (34.6)
2b	72.2 (70.0)	0	27.8 (30.0)
2c	72.4 (71.4)	0	27.6 (28.6)
2d	69.8 (70.0)	0	30.2 (30.0)
2e	72.7 (71.2)	0	27.3 (28.8)
2f	72.9 (71.6)	0	27.1 (28.4)
2g	66.3	2.0	31.7
2h	71.8	6.8	21.4
2i	64.8[c)]	0	35.2
2j	66.7[d)]	0	33.3

a) Reactions were carried out with 10 mmol of 1, 10 mmol of 2, and 20 ml of acetic acid at 20 °C. b) Determined by ^{1}H NMR analysis. Values in parentheses represent the product compositions determined by GLC analysis. Percentages are normalized to 100%. Total yields were found to be more than 80% in all runs. c) A mixture of 3i (89.5%) and 3j (10.5%). d) A mixture of 3i (11.5%) and 3j (88.5%).

Furthermore, in order to determine the effect of solvent on the regiochemistry of the addition, the reactions of 2e and 2h with 1 have been investigated in various solvents. Table 2 presents the data on the effect of solvents on the regiochemistry of the bromo chloro adducts obtained from the reactions of 2e and 2h with 1. No change in the regiochemistry has been observed with the reactions in the aprotic solvents.

Meanwhile, the reaction of 3-chlorostyrene (2e) in methanol gave a solvent-incorporated product, 2-bromo-1-(3-chlorophenyl)-1-methoxyethane (5e, 78%) as the major product. In analogy with the reaction in acetic acid, the resulting bromo chloro adduct (3e, 22%) was found to be formed in a regiospecific Markownikoff manner. Similarly, the reaction of 3-nitrostyrene (2h) in methanol also gave 2-bromo-1-methoxy-1-(3-nitrophenyl)ethane (5h, 73%) along with a mixture of 3h and 3h' (3h : 3h'=93 : 7) (Table 2 and Scheme 4).

$$\underset{\underline{2}}{XC_6H_4CH{=}CH_2} + \underline{1} \xrightarrow{CH_3OH} \underset{\underline{3}}{XC_6H_4CHClCH_2Br} + \underset{\underline{3'}}{XC_6H_4CHBrCH_2Cl}$$

$$+ \underset{\underline{5}}{XC_6H_4CH(OCH_3)CH_2Br}$$

e: X=3-Cl h: $X=3\text{-}NO_2$

Scheme 4

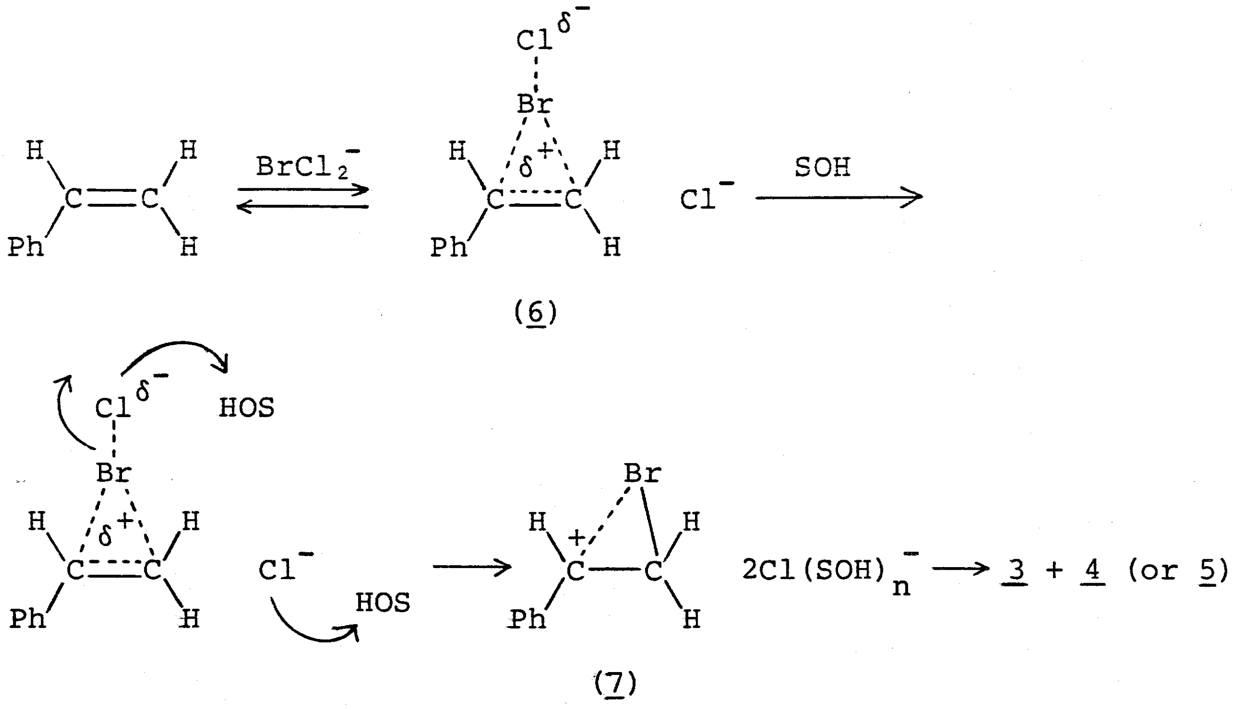
Table 2. Regiochemistry of Bromo Chloro Adducts Obtained from the Reactions of 2e and 2h with 1 in Various Solventsa)

Solvent	Dielectric constantc)	Product composition/%b)			
		from 2e		from 2h	
		3e	3e'	3h	3h'
$CHCl_3$	4.81	87.6	12.4	71.3	28.7
$CH_3COOC_2H_5$	6.02	87.2	12.8	69.1	30.9
CH_2Cl_2	9.08	87.0	13.0	71.7	28.3
$(CH_3CO)_2O$	20.7	87.7	12.3	70.0	30.0
CH_3COOHd)	6.19	100	0	91.3	8.7
CH_3OHe)	32.6	100	0	93.1	6.9

a) At 0 °C. b) Determined by ^{1}H NMR analysis. Percentages are normalized to 100%. c) J. A. Riddick and E. E. Toops, "Technique of Organic Chemistry," ed. by A. Weissberger, Interscience, New York (1955), Vol VII. d) At 20 °C. From the data of Table 1. e) The yield of 3e was 22%. The yield of a mixture of 3h and 3h' was 27%.

As shown in Table 2, the reaction in protic solvents proceeded in a more regioselective (or regiospecific) manner as compared with the reaction in aprotic solvents. The effect of protic solvent on the regiochemistry cannot be related to the dielectric constant of the medium, since in both acetic acid and ethyl acetate having similar dielectric constants, the regiochemistry was different, whereas chloroform and acetic anhydride have different dielectric constants but gave similar regiochemical results.

Two different mechanisms can account for the role of such protic solvents as acetic acid and methanol. They are indicated in Scheme 5 and 6



Scheme 5.

$$\underset{(\underline{1})}{\mathrm{BrCl_2^-}} \overset{\mathrm{SOH}}{\rightleftarrows} \underset{(\underline{8})}{\mathrm{Br{-}Cl{\cdots}HOS}} + \mathrm{Cl(SOH)_n^-}$$

Scheme 6.

According to Scheme 5, the major role of protic solvent is assumed to be the solvation of the external chloride ion ($\mathrm{Cl^-}$) in a three-center bound π-complex (6), and promoting the ionization of 6 by stabilizing the negatively polarized chlorine atom ($\mathrm{Br}^{\delta+}\cdots\mathrm{Cl}^{\delta-}$) via hydrogen bonding. The solvent molecule may then assist catalytically the bromine—chlorine bond cleavage, followed by the formation of the cationic intermediate (7). Evidence for such a specific role of the solvent has been observed by Dubois et al.1) for the bromination of 1-pentene in methanol.

In Scheme 6, the author assumes the initial formation of solvated BrCl (8) and chloride ion by the solvation of $\mathrm{BrCl_2^-}$ (1) in the protic solvent. The solvated BrCl (8) thus formed is assumed to react with alkene (2) to give the cationic intermediate (7), which in turn is attacked by chloride ion or solvent molecule to form a mixture of 3 and 4 (or 5). Although the author cannot decide by which mechanism the reactions proceed, the present results clearly show that the addition of 1 to alkenes in the protic solvent proceeds via a cationic intermediate (7) prior to the product-determining step.

The regiochemical results in protic solvents (Tables 1 and

2) show that all the styrene derivatives (except 2g and 2h) were attacked by chloride ion exclusively on the phenyl-substituted carbon atom of the double bond. Furthermore, the addition of 1-phenylpropenes (2i and 2j) was nonstereospecific, although the trans-addition product was formed mainly (Scheme 3). These results would be taken as evidence supporting that such a cationic intermediate resembles a weakly bridged benzylic carbonium ion intermediate (7).2) In the case of the reaction of 2h, the formation of anti-Markownikoff adduct (3h') would suggest that the intermediate resembles a fully bridged bromonium ion. A similar intermedaite has been suggested for the bromination of 3-nitro- and 4-nitrostyrenes in acetic acid.3) In the case of 2-chlorostyrene (2g), a small amount of anti-Markownikoff adduct (3g') was also isolated in the reaction in acetic acid (Table 1). Probably, the formation of this product is due to the combination of polar and steric effects.

Experimental

The GLC analyses were performed on a Yanako G-180 gas chromatograph with a Silicone SE-30(2.5%)-Chromosorb WAW DMCS (2 m) column with helium as the carrier gas. All the organic starting materials, including the solvents, were distilled before use.

Reaction of 2a–j with 1 in Acetic Acid. General Procedure: To a solution of 2 (10 mmol) in acetic acid (20 ml) was added 1 (3.93 g, 10 mmol) at 20 °C over 5 min with stirring. After the yellow color disappeared, the product was isolated by pouring the reaction mixture into a cold saturated aq NaCl solution, followed by extraction with ether (200 ml) and washing with aq $NaHCO_3$ and water. The ethereal extract was dried over $MgSO_4$ and concentrated. The crude products were subjected to GLC and NMR. All the results are given in Table 1. Furthermore, the crude products were separated by column chromatography (silica gel) with hexane–ether as the eluent. The structures of the bromo chloro adducts (3 and 3') were determined by comparison of their GLC and NMR spectra with those of the authentic samples prepared by the reaction of 1 with styrene derivatives (2) in chloroform (above sections 2. 2 and 2. 3). The spectral data of each of the bromo chloro adducts have been reported in the above sections (2. 2 and 2. 3). The structures of the acetoxy bromide (4) were determined by comparison of their GLC and NMR spectra with those of the authentic samples prepared by the reaction of 2 with bromine in acetic acid.4) The spectral data are as follows.

1-Acetoxy-2-bromo-1-phenylethane (4a): ^1H NMR ($CDCl_3$) δ= 2.12 (3H, s, $OCOCH_3$), 3.61, 3.62 (2H, 2d, J=5.9 and 7.0 Hz, CH_2Br), 5.97 (1H, approx. t, CH), and 7.34 (5H, s, C_6H_5);

^{13}C NMR ($CDCl_3$) $\delta=20.9$, 34.2, 74.7, 126.4, 128.5, 128.6, 137.5, and 169.6.

1-Acetoxy-2-bromo-(4-methylphenyl)ethane (4b): ^1H NMR ($CDCl_3$) $\delta=2.11$ (3H, s, $OCOCH_3$), 2.33 (3H, s, CH_3), 3.59, 3.60 (2H, 2d, J=5.9 and 7.3 Hz, CH_2Br), 5.95 (1H, approx. t, CH), and 7.26 (4H, s, C_6H_4); ^{13}C NMR ($CDCl_3$) $\delta=21.0$, 21.2, 34.2, 74.8, 126.5, 129.3, 134.7, 138.6, and 169.7.

1-Acetoxy-2-bromo-1-(4-fluorophenyl)ethane (4c): ^1H NMR ($CDCl_3$) $\delta=2.12$ (3H, s, $OCOCH_3$), 3.58, 3.59 (2H, 2d, J=6.1 and 7.2 Hz, CH_2Br), 5.94 (1H, approx. t, CH), and 6.9–7.6 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) $\delta=20.9$, 34.1, 74.1, 114.9, 116.4, 128.1, 128.7, 133.4, 133.6, 154.5, 169.6, and 170.9.

1-Acetoxy-2-bromo-1-(4-chlorophenyl)ethane (4d): ^1H NMR ($CDCl_3$) $\delta=2.12$ (3H, s, $OCOCH_3$), 3.57, 3.58 (2H, 2d, J=5.9 and 6.7 Hz, CH_2Br), 5.93 (1H, approx. t, CH), and 7.31 (4H, s, C_6H_4); ^{13}C NMR ($CDCl_3$) $\delta=20.8$, 33.8, 74.0, 127.9, 128.8, 134.6, 136.1, and 169.6.

1-Acetoxy-2-bromo-1-(3-chlorophenyl)ethane (4e): ^1H NMR ($CDCl_3$) $\delta=2.14$ (3H, s, $OCOCH_3$), 3.58 (2H, d, J=6.3 Hz, CH_2Br), 5.93 (1H, t, J=6.3 Hz, CH), and 7.28 (4H, br. s, C_6H_4); ^{13}C NMR ($CDCl_3$) $\delta=20.9$, 33.8, 74.0, 124.8, 126.6, 128.9, 129.9, 134.5, 139.6, and 169.5.

1-Acetoxy-2-bromo-1-(4-bromophenyl)ethane (4f): ^1H NMR ($CDCl_3$) $\delta=2.12$ (3H, s, $OCOCH_3$), 3.58 (2H, d, J=6.3 Hz, CH_2Br), 5.91 (1H, t, J=6.3 Hz, CH), and 7.13–7.68 (4H, m,

C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.8, 33.7, 74.0, 122.7, 128.2, 131.8, 136.6, and 169.4.

1-Acetoxy-2-bromo-1-(2-chlorophenyl)ethane (4g): ^1H NMR ($CDCl_3$) δ=2.17 (3H, s, $OCOCH_3$), 3.63, 3.68 (2H, 2d, J=6.9 and 4.4 Hz, CH_2Br), 6.36 (1H, q, 6.9 and 4.4 Hz, CH), and 7.20–7.70 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.8, 33.1, 71.4, 127.0, 127.4, 129.7, 132.2, 135.3, and 169.3.

1-Acetoxy-2-bromo-1-(3-nitrophenyl)ethane (4h): ^1H NMR ($CDCl_3$) δ=2.18 (3H, s, $OCOCH_3$), 3.65 (2H, d, J=6.2 Hz, CH_2Br), 6.04 (1H, t, J=6.2 Hz, CH), and 7.70–8.30 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=20.9, 33.5, 73.4, 121.5, 123.6, 129.6, 132.8, 139.6, 148.3, and 169.4.

erythro-1-Acetoxy-2-bromo-1-phenylpropane (4i): ^1H NMR ($CDCl_3$) δ=1.64 (3H, d, J=6.7 Hz, CH_3), 2.15 (3H, s, $OCOCH_3$), 4.15–4.57 (1H, m, CHBr), 5.95 (1H, d, J=5.3 Hz, CH), and 7.34 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=20.8, 20.9, 50.0, 78.2, 127.0, 128.3, 128.4, 137.1, and 169.5.

threo-1-Acetoxy-2-bromo-1-phenylpropane (4j): ^1H NMR ($CDCl_3$) δ=1.53 (3H, d, J=6.7 Hz, CH_3), 2.11 (3H, s, $OCOCH_3$), 4.08–4.56 (1H, m, CHBr), 5.82 (1H, d, J=7.8 Hz, CH), and 7.34 (5H, s, C_6H_5); ^{13}C NMR ($CDCl_3$) δ=21.0, 22.4, 50.5, 79.2, 127.1, 128.5, 128.6, 137.1, and 169.5.

Reaction of 2e and 2h with 1 in Aprotic Solvents. To a solution of the alkene (10 mmol) in the solvent (20 ml) was added 10 mmol of 1 at 0 °C over 5 min with stirring. After the yellow color disappeared, the mixture was washed with water and dried over Na_2SO_4. The product of the reaction in acetic anhydride was isolated by pouring the reaction mixture into water, followed by extraction with ether (200 ml) and washing with aq $NaHCO_3$, then with water. After the solvent was evaporated, the residues were analyzed by ^1H NMR. The relative amounts of products were determined from the ratio of the peak areas of the methylene protons of the bromo chloro adducts (3 and 3') as described in the above section (2. 3). The reuslts are given in Table 2.

Reaction of 2e and 2h with 1 in Methanol. To a solution of the alkene (10 mmol) in methanol (20 ml) was added 1 (10 mmol) at 0 °C over 5 min with stirring. The solvent was removed by evaporation and ether (200 ml) was added to the residue. The ethereal solution was washed with aq $NaHCO_3$ and water. The ethereal extract was dried over Na_2SO_4 and concentrated. In the case of 2e, ^1H NMR spectrum of the residue showed a 78 : 22 mixture of 5e and 3e (by integration of the methine protons). In the case of 2h, ^1H NMR spectrum of the residue showed a 73 : 27 mixture of 5h and 3h with a trace amount of 3h'.

Column chromatography of the residue (2.12 g) from the reaction of 2e on silica gel with hexane–ether as the eluent gave 1.50 g of 5e and 0.4 g of 3e. The spectral data for 2-bromo-1-(3-chlorophenyl)-1-methoxyethane (5e) are as follows: ^{1}H NMR ($CDCl_3$) δ=3.32 (3H, s, OCH_3), 3.46, 3.47 (2H, 2d, J=5.9 and 6.7 Hz, CH_2Br), 4.36 (1H, approx. t, CH), and 7.26–7.35 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=35.7, 57.4, 82.7, 125.0, 126.8, 128.6, 129.9, 134.6, and 141.1. The ^{1}H and ^{13}C NMR spectra of 5e correspond well with those of the authentic sample prepared by the reaction of 2e with N-bromosuccinimide (NBS) in methanol.5) The data for 2-bromo-1-chloro-1-(3-chlorophenyl)ethane (3e) have been reported in the above section (2. 3).

Similarly, column chromatography of the residue (2.13 g) from the reaction of 2h gave 1.30 g of 5h and 0.45 g of the mixture of 3h and 3h'. The spectral data for 2-bromo-1-methoxy-1-(3-nitrophenyl)ethane (5h) are as follows: ^{1}H NMR ($CDCl_3$) δ=3.36 (3H, s, OCH_3), 3.53 (2H, d, J=5.9 Hz, CH_2Br), 4.51 (1H, t, J=5.9 Hz, CH), and 7.67–8.22 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ=35.3, 57.6, 82.1, 121.8, 123.4, 129.6, 132.8, 141.4, and 148.4. The ^{1}H and ^{13}C NMR spectra of 5h correspond well with those of the authentic sample prepared by the reaction of 2h with NBS in methanol.5) ^{1}H NMR spectrum of the isolated bromo chloro adducts showed a 93 : 7 mixture of 3h and 3h'. The data for 2-bromo-1-chloro- and 1-bromo-2-chloro-1-(3-nitrophenyl)ethanes (3h and 3h') have been shown in the above section (2. 3).

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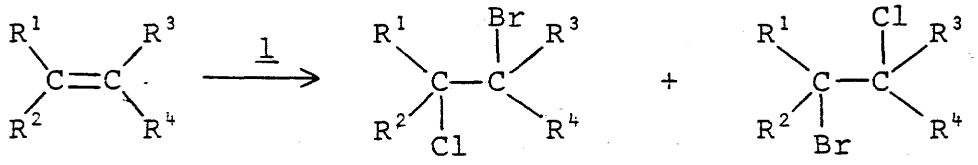
2. 5. Regiochemistry of Bromochlorination of Alkenes with Molecular Bromine Chloride and Dichlorobromate(1-) Ion

In the above sections (2. 2 and 2. 3), it has shown that the regioselectivity of bromochlorination of phenyl-substituted alkenes is markedly dependent both on the bromochlorinating agent and on the structure of alkene employed. There have been a few investigations on the regiochemistry of bromochlorinations of alkyl-substituted ethylenes with molecular bromine chloride and dichlorobromate(1-) ion, and the addition of BrCl to such alkenes as propene, 3-chloro-1-propene, and 1-hexene has been reported to give both Markownikoff and anti-Markownikoff adducts.[1,2] In the above section (2. 1), the author has also described that dichlorobromate(1-) ion reacted with propene, 3-chloropropene, and allyl cyanide to give two regioisomers. However, no systematic study has been carried out on the bromochlorination reaction of alkyl-substituted ethylenes. The author has carried out a study on the regiochemical effect of the alkyl substituent in the addition of molecular bromine chloride and dichlorobromate(1-) ion to various alkenes.

Results and Discussion

Reactions of a series of alkenes (3a–ℓ) with tetrabutylammonium dichlorobromate(1-) (1) in dichloromethane gave the corresponding bromo chloro compounds (4a–ℓ and 5a–ℓ) in good yields (Table 1 and Scheme 1).

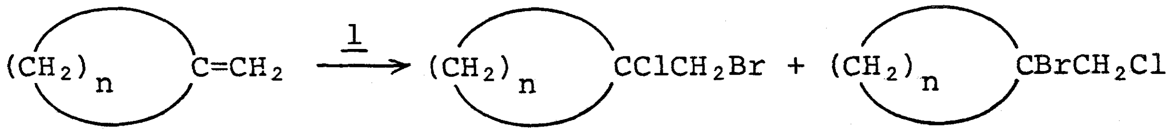


3 4 5

	R^1	R^2	R^3	R^4		R^1	R^2	R^3	R^4
a	Et	H	H	H	g	Et	H	Me	H
b	n-Pr	H	H	H	h	Me	Me	H	H
c	n-Bu	H	H	H	i	Et	Et	H	H
d	i-Pr	H	H	H	j	Me	Me	Me	H
e	t-Bu	H	H	H	k	Et	Me	H	Me
f	Et	H	H	Me	ℓ	Et	Me	Me	H

Scheme 1.

Similar reactions of methylenecycloalkanes (3m–n) with 1 also gave the corresponding bromo chloro compounds (4m–n and 5m–n) in good yields. (Table 1 and Scheme 2).



n=4:	3m	4m	5m
n=5:	3n	4n	5n

Scheme 2.

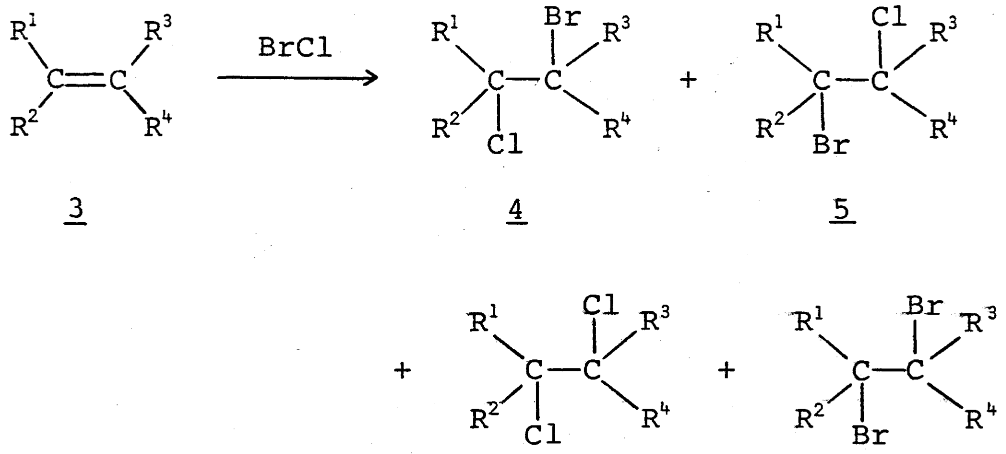
Table 1. Bromochlorination of Alkenes with 1 in CH_2Cl_2[a)]

Alkenes 3	Product composition/%[b)] 4	 5	Yield/%[c)]
3a	44	56	80
3b	43	57	82
3c	41	59	83
3d	24	76	78
3e	0	100	74
3f	40[d)]	60[d)]	82
3g	33[e)]	67[e)]	81
3h	69 (66)	31 (34)	78
3i	67 (68)	33 (32)	76
3j	71	29	79
3k	68[f)]	32[f)]	81
3ℓ	47[g)]	53[g)]	80
3m	92 (89)	8 (11)	75
3n	26 (25)	74 (75)	79

a) Reactions were carried out with 30 mmol of 1, 36 mmol of alkene, and 50 ml of CH_2Cl_2 at 0 °C. b) Percentages are normalized to 100%. Determined by ^{13}C NMR analysis. Values in parentheses represent the product distributions determined by ^{1}H NMR analysis. c) Isolated yield. Based on 1. d) erythro. e) threo. f) (RS, SR). g) (RS, RS).

The orientation of halogen atoms in all the addition products was elucidated mainly on the basis of chemical shifts of the carbon bearing bromine and chlorine atoms in ^{13}C NMR spectra, since it has been observed that the carbon atom bearing a chlorine atom is deshielded relative to the one bearing a bromine atom.$^{3)}$ Meanwhile, the structures of two regioisomers (4 and 5) have been determined by comparison of their ^{13}C NMR spectra with those of the corresponding dibromo and dichloro compounds. Selected ^{13}C NMR spectra of dihaloalkanes are listed in Table 2. Control experiments revealed that all the bromo chloro compounds are stable under the reaction conditions.

Treatments of a series of alkenes (3a–ℓ) with molecular bromine chloride (2) in dichloromethane also gave the corresponding bromo chloro compounds (4a–ℓ and 5a–ℓ) (Table 3 and Scheme 2).



Scheme 2.

Table 2. ^{13}C Chemical Shifts for Dihaloalaknes in $CDCl_3$ (δ value)

$C_2H_5C^1HXC^2H_2Y$

X	Y	C^1	C^2
Br	Br	54.3	35.6
Cl	Cl	62.6	47.8
Br	Cl	54.9	47.6
Cl	Br	62.1	35.8
$n\text{-}PrC^1HXC^2H_2Y$			
Br	Br	52.7	38.0
Cl	Cl	60.9	48.3
Br	Cl	53.2	48.3
Cl	Br	60.6	37.8
$n\text{-}BuC^1HXC^2H_2Y$			
Br	Br	53.0	36.3
Cl	Cl	61.2	48.2
Br	Cl	53.5	48.2
Cl	Br	60.8	36.5
$i\text{-}PrC^1HXC^2H_2Y$			
Br	Br	61.5	34.1
Cl	Cl	67.6	46.3
Br	Cl	61.8	46.1
Cl	Br	67.2	34.4

Table 2 (continued)

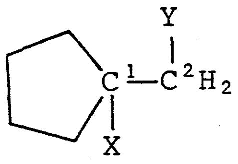
$t\text{-BuC}^1\text{HXC}^2\text{H}_2\text{Y}$			
X	Y	C^1	C^2
Br	Br	69.0	37.0
Cl	Cl	73.7	47.1
Br	Cl	68.8	47.6
Cl	Br	74.6	37.0
erythro-$C_2H_5C^1HXC^2HYCH_3$			
Br	Br	63.2	51.8
Cl	Cl	68.6	59.5
Br	Cl	63.0	59.7
Cl	Br	69.0	51.8
threo-$C_2H_5C^1HXC^2HYCH_3$			
Br	Br	62.1	52.2
Cl	Cl	67.9	59.7
Br	Cl	62.1	59.9
Cl	Br	68.2	52.2
$(CH_3)_2C^1XC^2H_2Y$			
Br	Br	62.1	44.7
Cl	Cl	67.6	54.6
Br	Cl	62.3	55.3
Cl	Br	67.1	43.7

Table 2 (continued)

$(C_2H_5)_2C^1XC^2H_2Y$

X	Y	C^1	C^2
Br	Br	75.3	38.2
Cl	Cl	76.1	48.5
Br	Cl	75.4	48.8
Cl	Br	75.8	37.7
$(CH_3)_2C^1XC^1HYCH_3$			
Br	Br	68.2	59.4
Cl	Cl	71.3	65.2
Br	Cl	67.9	66.1
Cl	Br	71.6	58.4
(RS, SR)-$C_2H_5C^1(CH_3)XC^2HYCH_3$			
Br	Br	74.9	56.2
Cl	Cl	75.8	62.5
Br	Cl	74.4	63.0
Cl	Br	76.1	55.6
(RS, RS)-$C_2H_5C^1(CH_3)XC^2HYCH_3$			
Br	Br	75.0	59.8
Cl	Cl	76.0	65.2
Br	Cl	74.7	66.0
Cl	Br	76.1	58.8

Table 2 (continued)



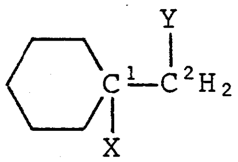
X	Y	C^1	C^2
Br	Br	74.9	41.4
Cl	Cl	79.0	51.9
Br	Cl	74.9	52.2
Cl	Br	79.2	41.2
			
Br	Br	72.3	44.7
Cl	Cl	73.2	54.6
Br	Cl	72.5	55.2
Cl	Br	72.7	44.3

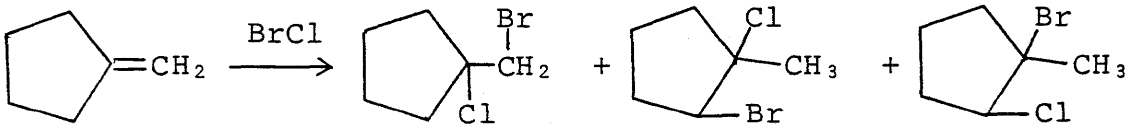
Table 3. Bromochlorination of Alkenes with 2 in CH_2Cl_2[a)]

Alkenes 3	Product composition/%[b)] 4	 5	Yield/%[c)]
3a	58	42	61
3b	55	45	72
3c	58	42	65
3d	41	59	69
3e	11	89	68
3f	48[d)]	52[d)]	72
3g	36[e)]	64[e)]	69
3h	86	14	72
3i	87	13	70
3j	86	14	71
3k	84[f)]	16[f)]	70
3ℓ	68[g)]	32[g)]	69
3m	100	0	11
3n	82	18	55

a) Reactions were carried out with 10 mmol of 2, 12 mmol of alkene, and 50 ml of CH_2Cl_2 at 0 °C. b) Percentages are normalized to 100%. Determined by ^{13}C NMR analysis. c) Determined by GLC analysis. d) erythro. e) threo. f) (RS, SR). g) (RS, RS).

The yields are lower than those in the reaction with 1 due to formation of dibromo- and dichloroalkanes. The formation of these by-products in the reaction is undoubtedly due to the attack of both bromine and chlorine, which are in equilibrium with bromine chloride, on alkenes.4)

On the other hand, the reaction of methylenecyclopentane (3m) with 2 gave a mixture of 2-bromo-1-chloro- and 1-bromo-2-chloro-1-methylcyclopentanes (4o and 5o, 54.5% yield by GLC analysis) as the major products. The expected bromo chloro compound (4m, 11.0% yield by GLC analysis) was a minor component (Scheme 4 and Table 3).



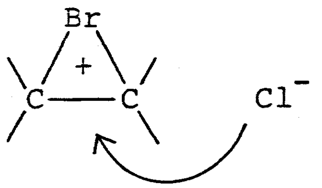
3m 4m 4o 5o

Scheme 4.

The formation of both 4o and 5o may be due to the competing allylic halogenation which produces hydrogen halide. The hydrogen halide thus formed is considered to isomerize the terminal alkene (3m) into a more stable internal alkene (3o, 1-methylcyclopentene), to which 2 is then presumed to add. In fact, the presence of 3o was confirmed by ^{1}H NMR analysis of the reaction mixture. Furthermore, the ratio of the two regioisomers (4o : 5o=86 : 14) is the same as that observed for the reaction of 3o with 2. A similar reaction has been reported for the addition of bromine to 3m.[5)] Similarly, a small amount of 2-bromo-1-chloro- and 1-bromo-2-chloro-1-methylcyclohexane (4p and 5p) was detected from the reaction of methylenecyclohexane (3n) with 2.

An inspection of the data in Tables 1 and 3 clearly reveals that the regiochemistry of the addition of 1 to alkenes is strikingly different from that of the reaction of 2. Therefore, the product-determining step must be different in these two reactions.

Regioselectivity of the Reaction of 3 with 2. The reaction with 2 can best be explained by the AdEC$_1$-type mechanism involving the attack of chloride ion to a bridged bromonium ion intermediate 6:[2,6)] a similar intermediate has also been suggested for the bromination of alkenes with molecular bromine.[7)]



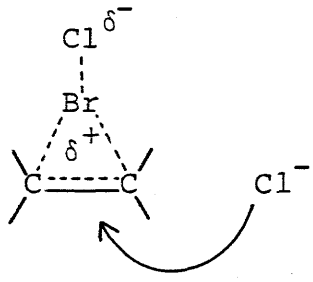
(6)

As shown in Table 3, the bromochlorination of the unsymmetrical alkenes, 1,2-dialkyl-(3f and 3g) and 1,1,2-trialkylethylenes (3k and 3ℓ), with 2 gave completely anti stereospecific adducts. This supports further the assumption that the intermediate in the bromochlorination of alkyl-substituted ethylenes with 2 resembles the bridged ion (6). These results are in marked contrast to the stereoselective addition of 2 to phenyl-substituted alkenes, which involves a very weakly bridged ion intermediate as shown in the above section (2. 2). Thus, the anti stereospecific addition of 2 to 3k and 3ℓ would rule out the possibility of carbonium ion-like intermediate which is considered to be involved in the bromination of these alkenes with bromine.7)

Both the steric and the electronic effects of the alkyl substituent on ethylene linkage would play a major role in the orientation of the approach of chloride ion on the bromonium ion intermediate (6). As shown in Table 3, nearly the same ratio of regioisomers is given for the reaction of 1-butene (3a), 1-pentene (3b), and 1-hexene (3c) with 2, which indicates the effects of linear alkyl substituents to be nearly the same. Meanwhile, replacement of one hydrogen on ethylene by isopropyl (3d) or t-butyl (3e) results in the formation of an increasing amount of the anti-Markownikoff adduct (5d or 5e). This reveals clearly that the addition of 2 can be influenced by steric factors of the bulky groups.

On the other hand, the additions of 2 to 1,1-disubstituted (3h and 3i) and 1,1,2-trisubstituted ethylenes (3j, 3k, and 3ℓ) or methylenecycloalkanes (3m and 3n) gave regioselective Markownikoff adducts (4) (Table 3). These results imply that the attack of chloride ion on the bromonium ion intermediate (6) occurs at the more substituted carbon atom. Thus, the orientation of bromochlorination with 2 would be due to the electronic effect of the 1,1-dialkyl substituent which stabilizes the developed cationic character on the more substituted carbon atom in the intermediate (6). A similar accumulative electronic effect of dialkyl substituent groups on the regiochemistry has previously been observed in the bromination of these alkenes in methanol.8)

Regioselectivity of the Reaction of 3 with 1. In the above sections, it has been suggested that the reaction of alkenes with 1 can be best explained by the AdEC$_2$-type mechanism involving the attack of chloride ion on the three-centered π-complex intermediate (7) with a very little charge development on the unsaturated carbon.



(7)

Therefore, there would be a relatively small demand for elctronic stabilization of the reaction center by alkyl substituents on the intermediate (7). As expected, the amount of the anti-Markownikoff adduct (5) in the addition of 1 (Table 1) is generally larger than that in the addition of 2 (Table 3). Thus, the addition of 1 to linear alkyl-substituted ethylenes (3a, 3b, and 3c) was found to be slightly more regioselective in an anti-Markownikoff manner than that in the addition of 2. Meanwhile, replacement of one hydrogen on ethylene by an isopropyl (3d) or a t-butyl group (3e) results in the formation of a larger amount of the anti-Markownikoff adduct (5) than that in the addition of 2. It is interesting to note that only the anti-Markownikoff adduct (5e) is obtained in the reaction of 3,3-dimethyl-1-butene (3e), as anticipated from the greater steric requirement of t-butyl group. The reaction of methylenecyclohexane (3n) with 1 also gives a regioselective anti-Markownikoff adduct (5n), where the opposite orientation results from that of the reaction with 2. All these results support that the steric effect outweighs the electronic effect of the alkyl substituent in the reaction with 1.

However, the reaction of 1 to 1,1-dialkyl-(3h and 3i) and 1,1,2-trialkylethylenes (3j and 3k) or methylenecyclopentane (3m) gave the regioselective Markownikoff adduct (4) (Table 1). As in the reaction with 2, the electronic effect of the 1,1-dialkyl groups would overcome partially the steric influence.

Experimental

All the organic starting materials, including the solvents, were distilled before use.

Reaction of Alkenes (3a–n) with 1. Details of the reaction have been reported in the above sections (2. 1 and 2. 2). To a solution of 3 (36 mmol) in CH_2Cl_2 (50 ml) was added 1 (11.8 g, 30 mmol) at 0 °C over 20 min with stirring. After the usual work-up, the products were purified by distillation. Although attempts to separate 4 and 5 were unsuccessful, these structures were determined by comparison of their ^{13}C NMR spectra with those of the corresponding dibromo and dichloro analogs.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chlorobutanes (4a and 5a) from 1-Butene (3a): Bp 82 °C/110 mmHg; MS M^+ at m/z=170, 172, and 174 (100 : 135 : 32); ^1H NMR ($CDCl_3$) δ= 1.04 (3H, t, J=6.5 Hz), 1.40–2.30 (2H, m), and 3.50–4.30 (3H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5a) δ=10.1, 11.1,* 28.4,* 28.8, 35.8, 47.6,* 54.9,* and 62.1. Although attempts to separate 4a and 5a were unsuccessful, these assignments were supported for dibromo and dichloro analogs as follows: 1,2-dibromobutane (8a), ^{13}C NMR ($CDCl_3$) δ=11.0, 29.0, 35.6, and 54.3; 1,2-dichlorobutane (9a), ^{13}C NMR ($CDCl_3$) δ=10.2, 28.2, 47.8, and 62.6.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chloropentanes (4b and 5b) from 1-Pentene (3b): Bp 70–72 °C/50 mmHg; MS M^+ at m/z=184, 186, and 188 (100 : 134 : 36); ^1H NMR ($CDCl_3$) δ= 0.83–2.30 (7H, m) and 3.33–4.35 (3H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5b) δ=13.3,* 13.4, 19.2, 20.2,* 36.5, 37.4,* 37.8, 48.3,*, 53.2,* and 60.6. These assignments were supported for dibromo and dichloro analogs as follows: 1,2-dibromopentane (8b), ^{13}C NMR ($CDCl_3$) δ=13.3, 20.1, 36.3, 38.0, and 52.7; 1,2-dichloropentane (9b), ^{13}C NMR ($CDCl_3$) δ= 13.5, 19.2, 37.1, 48.3, and 60.9.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chlorohexanes (4c and 5c) from 1-Hexene (3c): Bp 95–96 °C/50 mmHg; MS M^{+} at m/z=198, 200, and 202 (100 : 129 : 31); ^{1}H NMR ($CDCl_3$) δ= 0.93–2.40 (9H, m) and 3.50–4.30 (3H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5c) δ=13.9, 22.0,* 22.1, 28.0, 28.9,* 35.1,* 35.5, 36.5, 48.2,* 53.5,* and 60.8. These assignments were supported for dibromo and dichloro analogs as follows: 1,2-dibromohexane (8c), ^{13}C NMR ($CDCl_3$) δ=13.9, 21.9, 28.8, 35.7, 36.3, and 53.0; 1,2-dichlorohexane (9c), ^{13}C NMR ($CDCl_3$) δ=13.9, 22.1, 27.9, 34.7, 48.2, and 61.2.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chloro-3-methylbutanes (4d and 5d) from 3-Methyl-1-butene (3d): Bp 68–70 °C/50 mmHg; MS M^{+} at m/z=184, 186, and 188 (100 : 130 : 35); ^{1}H NMR ($CDCl_3$) δ=0.99 (6H, t, J=6.6 Hz), 2.00–2.57 (1H, m), and 3.63–4.33 (3H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5d) δ=15.1, 16.1,* 20.4, 21.4,* 29.6,* 30.8, 34.4, 46.1,* 61.8,* and 67.2. These assignments were supported for dibromo and dichloro analogs as follows: 1,2-dibromo-3-methylbutane (8d), ^{13}C NMR ($CDCl_3$) δ=15.5, 21.7, 29.9, 34.1, and 61.5; 1,2-dichloro-3-methylbutane (9d), ^{13}C NMR ($CDCl_3$)

δ=15.6, 20.2, 30.3, 46.3, and 67.6.

2-Bromo-1-chloro-3,3-dimethylbutane (5e) from 3,3-Dimethyl-1-butene (3e): Bp 95–100 °C/50 mmHg; MS M^+ at m/z=198, 200, and 202 (100 : 129 : 31); ^1H NMR ($CDCl_3$) δ=1.12 (9H, s) and 3.52–4.13 (3H, m); ^{13}C NMR ($CDCl_3$) δ=27.6, 36.3, 47.6, and 68.8. ^{13}C NMR spectra for dibromo and dichloro analogs are as follows: 1,2-dibromo-3,3-dimethylbutane (8e), ^{13}C NMR ($CDCl_3$) δ=27.6, 35.8, 37.0, and 69.0; 1,2-dichloro-3,3-dimethylbutane (9e), ^{13}C NMR ($CDCl_3$) δ=26.7, 36.2, 47.1, and 73.7.

A Mixture of erythro-2-Bromo-3-chloro- and 3-Bromo-2-chloropentanes (4f and 5f) from trans-2-Pentene (3f): Bp 71–72 °C/50 mmHg; MS M^+ at m/z=184, 186, and 188 (100 : 128 : 32); ^1H NMR ($CDCl_3$) δ=1.07 (3H, t, J=6.8 Hz), 1.33–2.26 (5H, m), and 3.78–4.40 (2H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5f) δ=10.5, 11.6,* 23.4, 23.5,* 29.1,* 29.4, 51.8, 59.7,* 63.0,* and 69.0. These assignments were supported for dibromo and dichloro analogs as follows: erythro-2,3-dibromopentane (8f), ^{13}C NMR ($CDCl_3$) δ=11.4, 25.2, 30.5, 51.8, and 63.2; erythro-2,3-dichloropentane (9f), ^{13}C NMR ($CDCl_3$) δ=10.4, 22.2, 28.3, 59.5, and 68.6.

A Mixture of threo-2-Bromo-3-chloro- and 3-Bromo-2-chloropentanes (4g and 5g) from cis-2-Pentene (3g): Bp 72–73 °C/50 mmHg; MS M^+ at m/z=184, 186, and 188 (100 : 132 : 35); ^1H NMR ($CDCl_3$) δ=1.07 (3H, t, J=6.9 Hz), 1.34–2.24 (5H, m), and 3.77–4.57 (2H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5g) δ=11.5, 12.6,* 21.3,* 21.5, 27.3,* 27.7, 52.2, 59.9,* 62.1,* and 68.2. These assignments were supported for dibromo and dichloro analogs as follows: threo-2,3-dibromopentane (8g), ^{13}C NMR ($CDCl_3$) δ=12.7, 21.6, 27.5, 52.2, and 62.1; threo-2,3-dichloropentane (9g), ^{13}C NMR ($CDCl_3$) δ=11.4, 20.8, 27.1, 59.7, and 67.9.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chloro-2-methylpropanes (4h and 5h) from 2-Methylpropene (3h): Bp 79–82 °C/90 mmHg; MS M^+ at m/z=170, 172, and 174 (100 : 132 : 34); ^{1}H NMR ($CDCl_3$) (an asterisk indicates 5h) δ=1.69, 1.83,* (6H, 2s), 3.63, and 3.83* (2H, 2s); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5h) δ=30.4, 31.0,* 43.7, 55.3,* 62.3,* and 67.1. These assignments were supported for dibromo and dichloro analogs as follows: 1,2-dibromo-2-methylpropane (8h), ^{13}C NMR ($CDCl_3$) δ=31.9, 44.7, and 62.1; 1,2-dichloro-2-methylpropane (9h), ^{13}C NMR ($CDCl_3$) δ=29.6, 54.6, and 67.6.

A Mixture of 1-Bromo-2-chloro- and 2-Bromo-1-chloro-2-ethylbutanes (4i and 5i) from 2-Ethyl-1-butene (3i): Bp 65–66 °C/19 mmHg; MS M^+ at m/z=198, 200, and 202 (100 : 130 : 35); ^{1}H NMR ($CDCl_3$) (an asterisk indicates 5i) δ=0.90–1.14 (6H, m), 1.66–2.11 (4H, m), 3.63, and 3.87* (2H, 2s); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5i) δ=8.2, 9.4,* 32.6, 32.9,* 37.7, 48.8,* 75.4,* and 75.8. These assignments were supported for dibromo and dichloro analogs as follows: 1,2-

dibromo-2-ethylbutane (8i), ^{13}C NMR ($CDCl_3$) δ=9.5, 33.8, 38.2, and 75.3; 1,2-dichloro-2-ethylbutane (9i) ^{13}C NMR ($CDCl_3$) δ= 8.2, 31.8, 48.5, and 76.1.

A Mixture of 3-Bromo-2-chloro- and 2-Bromo-3-chloro-2-methylbutanes (4j and 5j) from 2-Methyl-2-butene (3j): Bp 80–81 °C/70 mmHg; MS M^+ at m/z=184, 186, and 188 (100 : 134 : 35); ^{1}H NMR ($CDCl_3$) δ=1.67–1.98 (9H, m) and 4.13–4.46 (1H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5j) δ=21.9,* 22.1, 27.0, 27.9,* 32.5, 33.2,* 58.4, 66.1,* 67.9,* and 71.6. These assignments were supported for dibromo and dichloro analogs as follows: 2,3-dibromo-2-methylbutane (8j), ^{13}C NMR ($CDCl_3$) δ=23.5, 28.0, 34.9, 59.4, and 68.2; 2,3-dichloro-2-methylbutane (9j), ^{13}C NMR ($CDCl_3$) δ=20.6, 26.5, 31.1, 65.2, and 71.3.

A Mixture of (RS, SR)-2-Bromo-3-chloro- and 3-Bromo-2-chloro-3-methylpentanes (4k and 5k) from (E)-3-Methyl-2-pentene (3k): Bp 68–69 °C/48 mmHg; MS M^+ at m/z=198, 200, and 202 (100 : 134 : 28); ^{1}H NMR ($CDCl_3$) δ=0.93–1.18 (3H, m), 1.63–2.03 (8H, m), and 4.31 (1H, q, J=6.7 Hz); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5k) δ=8.6, 9.8,* 21.7, 21.8,* 24.6, 25.2,* 36.6, 36.9,* 55.6, 63.0,* 74.4,* and 76.1. These assignments were supported for dibromo and dichloro analogs as follows: (RS, SR)-2,3-dibromo-3-methylpenatne (8k), ^{13}C NMR ($CDCl_3$) δ=9.8, 23.2, 25.9, 38.4, 56.2, and 74.9; (RS, SR)-2,3-dichloro-3-methylpentane (9k), ^{13}C NMR ($CDCl_3$) δ=

8.4, 20.3, 23.8, 35.2, 62.5, and 75.8.

A Mixture of (RS, RS)-2-Bromo-3-chloro- and 3-Bromo-2-chloro-3-methylpentanes (4ℓ and 5ℓ) from (Z)-3-Methyl-2-pentene (3ℓ): Bp 70–71 °C/48 mmHg; MS M$^+$ at m/z=198, 200, and 202 (100 : 132 : 35); ^{1}H NMR (CDCl$_3$) δ=0.93–1.18 (3H, m), 1.61–2.20 (8H, m), and 4.08–4.52 (1H, m); ^{13}C NMR (CDCl$_3$) (an asterisk indicates 5ℓ) δ=8.8, 9.9,* 21.5,* 21.8, 27.8, 28.7,* 32.3, 32.7,* 58.8, 66.0,* 74.7,* and 76.1. These assignments were supported for dibromo and dichloro analogs as follows: (RS, RS)-2,3-dibromo-3-methylpentane (8ℓ), ^{13}C NMR (CDCl$_3$) δ= 10.0, 23.0, 30.3, 32.4, 59.8, and 75.0; (RS, RS)-2,3-dichloro-3-methylpentane (9ℓ), ^{13}C NMR (CDCl$_3$) δ=8.7, 20.4, 26.7, 31.8, 65.2, and 76.0.

A Mixture of 1-Bromomethyl-1-chloro- and 1-Bromo-1-(chloromethyl)cyclopentanes (4m and 5m) from Methylenecyclopentane (3m): Bp 42–43 °C/5 mmHg; MS M$^+$ at m/z=196, 198, and 200 (100 : 132 : 34); ^{1}H NMR (CDCl$_3$) (an asterisk indicates 5m) δ=1.52–2.26 (8H, m), 3.80, and 4.01* (2H, 2s); ^{13}C NMR (CDCl$_3$) (an asterisk indicates 5m) δ=23.8, 40.6, 41.2, 52.2,* 74.9,* and 79.2. These assignments were supported for dibromo and dichloro analogs as follows: 1-bromo-1-(bromomethyl)cyclopentane (8m), ^{13}C NMR (CDCl$_3$) δ=23.9, 41.3, 41.4, and 74.9; 1-chloro-1-(chloromethyl)cyclopentane (9m), ^{13}C NMR (CDCl$_3$) δ=23.6, 39.8, 51.9, and 79.0.

A Mixture of 1-Bromomethyl-1-chloro- and 1-Bromo-1-

(chloromethyl)cyclohexanes (4n and 5n) from Methylenecyclohexane (3n): Bp 41–42 °C/2 mmHg; MS M^+ at m/z=210, 212, and 214 (100 : 130 : 35); ^1H NMR ($CDCl_3$) (an asterisk indicates 5n) δ=1.40–2.00 (10H, m), 3.68, and 3.92* (2H, 2s); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5n) δ=22.1, 22.8,* 24.9, 37.3, 44.3, 55.2,* 72.5,* and 72.7. These assignments were supported for dibromo and dichloro analogs as follows: 1-bromo-1-(bromomethyl)cyclohexane (8n), ^{13}C NMR ($CDCl_3$) δ=23.0, 24.8, 38.0, 44.7, and 72.3; 1-chloro-1-(chloromethyl)cyclohexane (9n), ^{13}C NMR ($CDCl_3$) δ=21.8, 24.9, 36.4, 54.6, and 73.2.

Reaction of Alkenes (3a–n) with 2. To a solution of 3 (12 mmol) in CH_2Cl_2 (50 ml) was added 5.5 ml of BrCl solution in CCl_4 (1.8 mol dm^{-3}) at 0 °C over 5 min with stirring. After the solvent was removed under reduced pressure, the residues were analyzed by GLC and ^{13}C NMR. The results are given in Table 2. In all cases, GLC analyses showed the presence of 11–16% of dichloro adduct (9) and 13–19% of dibromo adduct (8) as by-products.

The reaction of 3,3-dimethyl-1-butene (3e) with 2 gave a mixture of 1-bromo-2-chloro- and 2-bromo-1-chloro-3,3-dimethylbutanes (4e and 5e). The product composition of 4e and 5e was determined by ^{13}C NMR analysis: ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5e) δ=26.8, 27.6,* 35.2, 36.3,* 37.0, 47.6,* 68.8,* and 74.6. These assignments were supported for the ^{13}C NMR data of dibromo and dichloro adducts (8e and

and 9e) as described above.

The reaction of methylenecyclopentane (3m) with 2 gave a mixture of 2-bromo-1-chloro- and 1-bromo-2-chloro-1-methylcyclopentanes (4o and 5o, 54.5%), 1-bromomethyl-1-chlorocyclopentane (4m, 11.0%), dichloro and dibromo adducts (25.5%), and unidentified products (9.0%) by GLC analysis. Although the isolation of 4o and 5o was not carried out, the retention time of GLC agreed with that of the sample prepared by the reaction of 1-methylcyclopentene (3o) with 1 as follows: bp 42—43 °C/5 mmHg; MS M^+ at m/z=196, 198, and 200 (100 : 131 : 32); ^1H NMR ($CDCl_3$) (an asterisk indicates 5o) δ=1.90, 1.96* (2s), 1.70—3.10 (m), and 4.44—4.62 (m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5o) δ=20.8, 21.0,* 28.5,* 28.6, 34.9,* 35.4, 39.3, 40.6,* 62.6, 70.9,* 75.1,* and 79.5. The ratio of 4o and 5o was shown to be 86 : 14 by ^{13}C NMR analysis. This product ratio is close to the product ratio (4o : 5o=83 : 17) for the reaction of 3o with 2 under the same reaction conditions.

^1H NMR analysis of the recovered alkenes from the reaction of 3m (20 mmol) with 2 (10 mmol) showed 67% of 1-methylcyclopentene (3o) and 33% of methylenecyclopentane (3m) as based on the relative areas of the signals at δ=5.30 and 4.83 for the olefinic protons, respectively.

The reaction of methylenecyclohexane (3n) with 2 also gave a mixture of 2-bromo-1-chloro- and 1-bromo-2-chloro-1-

methylcyclohexanes (4p and 5p, 7.5%), 4n and 5n (55.2%), dichloro and dibromo adducts (37.3%) by GLC analysis. Although the isolation of 4p and 5p was not carried out, the retention time agreed with that of the sample prepared by the reaction of 1-methylcyclohexene (3p) with 1 as follows: bp 41–42 °C/2 mmHg; MS M^+ at m/z=210, 212, and 214 (100 : 134 : 34); ^{1}H NMR ($CDCl_3$) (an asterisk indicates 5p) δ=1.75, 1.91,* (2s), 1.56–2.60 (m), and 4.35–4.70 (m).

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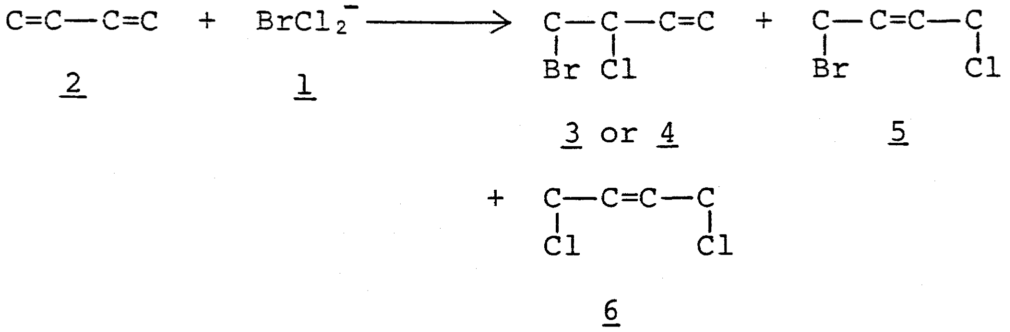
CHAPTER 3

BROMOCHLORINATION OF CONJUGATED DIENES WITH DICHLOROBROMATE(1-) ION.

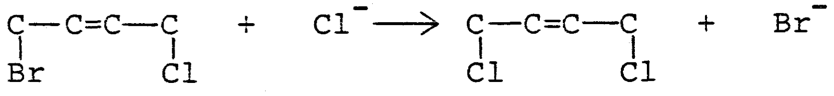
In the general introduction, it was shown that the ratio of 1,2- to 1,4-addition of bromine (and bromine chloride) to conjugated dienes is markedly dependent on the brominating (and bromochlorinating) agents employed.[1,2] The predominance of 1,2-addition was observed for the reaction with a tribromide ion.[1,2] However, no study has been carried out on the reaction with tetrabutylammonium dichlorobromate(1-) (1) as a bromochlorinating agent. In the chapter 2, the author described that the additions of 1 to alkenes are strikingly different from that of molecular bromine chloride (BrCl). In this chapter, the author describes the bromochlorination of some conjugated dienes with 1.

Results and Discussion

The reaction of 1 with 1,3-butadiene (2a), 2-methyl-1,3-butadiene (2b), cis- and trans-1,3-pentadienes (2c and 2d), and cyclopentadiene (2e) in dichloromethane gave the corresponding bromochloroalkenes (Scheme 1 and Table 1). In the cases of 2b and 2e, a small amount of 1,4-dichloro adduct (6) was isolated. Furthermore, in all cases, the yield of 1,4-bromochloro adduct (5) decreased by the prolonged reaction time. It was shown that 6 is also formed upon treatment of 5 with tetrabutylammonium chloride in dichloromethane. Therefore, it probably arises by the halogen-exchange reaction of 5 with generating chloride ions in the reaction system (Scheme 2).



Scheme 1.



Scheme 2.

A common characteristic of the present reaction is the highly selective formation of the 1,2-bromochloro adducts. Moreover, the addition to the 3,4-bond in 2c, 2d, and 2e gave anti stereospecific products (4c, 4d, and 3e).

In the case of 1,3-butadiene (2a), the reaction gave a mixture of 4-bromo-3-chloro-1-butene (3a) and 3-bromo-4-chloro-1-butene (3a') as the 1,2-adducts (Scheme 3).

Table 1. Reactions of Dienes with 1[a)]

Dienes	1,2-Adduct[b)]		1,4-adduct[b)]		Yield/%[c)]
	3	4	5	6	
2a	99.0[d)]		1.0		98
2b	78.6	11.0	9.2	1.2	98
2c	66.2	29.4	4.4		99
2d	87.1	5.1	7.8		99
2e	93.2		0.9	5.9[e)]	93

a) Reactions were carried out with 30 mmol of 1, 36 mmol of dienes, and 100 ml of CH_2Cl_2 at -12 °C. b) The products are identified as follows: from 2a, 4-bromo-3-chloro-1-butene (3a), 3-bromo-4-chloro-1-butene (3a'), trans-1-bromo-4-chloro-2-butene (5a); from 2b, 4-bromo-3-chloro-3-methyl-1-butene (3b), 4-bromo-3-chloro-2-methyl-1-butene (4b), 1-bromo-4-chloro-2-methyl-2-butene (5b), 1,4-dichloro-2-methyl-2-butene (6b); from 2c and 2d, cis- and trans-5-bromo-4-chloro-2-pentenes (3c and 3d), threo- and erythro-4-bromo-3-chloro-1-pentenes (4c and 4d), trans-1-bromo-4-chloro-2-pentene (5c=5d); from 2e, trans-4-bromo-3-chlorocyclopentene (3e), cis-3-bromo-5-chlorocyclopentene (5e'), cis- and trans-3,5-dichlorocyclopentenes (6e' and 6e). Percentages are normalized to 100%. c) Based on 1. Total bromochloroalkene yields determined by GLC. d) 3a : 3a'=84 : 16. e) 6e : 6e'=35 : 65.

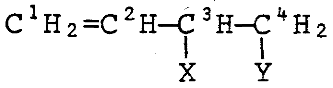
$$CH_2{=}CHCH{=}CH_2 + \underline{1} \longrightarrow CH_2BrCHClCH{=}CH_2 + CH_2ClCHBrCH{=}CH_2$$

$\underline{2a}$ $\underline{3a}$, 84% $\underline{3a'}$, 16%

Scheme 3.

Although attempts to separate two regioisomers ($\underline{3a}$ and $\underline{3a'}$) were unsuccessful, the orientation of halogen atoms were determined by comparisons of their ^{13}C NMR spectra with those of the dibromo and dichloro compounds. ^{13}C NMR spectra of 3,4-dihalo-1-butenes are listed in Table 2. ^{13}C NMR analysis of the mixture of two regioisomers could be used to determine the amounts of each isomer.

Table 2. ^{13}C Chemical Shifts for 3,4-Dihalo-1-butenes in $CDCl_3$ (δ Value)



$$C^1H_2{=}C^2H{-}\underset{X}{C^3}H{-}\underset{Y}{C^4}H_2$$

X	Y	C^1	C^2	C^3	C^4
Cl	Br	119.7	135.2	60.2	35.0
Br	Cl	119.7	135.5	51.1	47.0
Cl	Cl	119.7	134.8	60.1	47.3
Br	Br	119.8	136.0	50.5	34.5

When the reaction of $\underline{2a}$ with $\underline{1}$ was carried out in the presence of a free radical inhibitor, 2,6-di-t-butyl-4-methylphenol or oxygen, the product composition did not change within experimental error. This result indicates that the lack of regiospecificity cannot be ascribed to a radical process.[4)]

The regiochemistry of the reaction of 2a with 1 was investigated in solvents with widely different polarities in order to elucidate the mechanism of the reaction. Table 3 presents data for the effect of solvents on the regiochemistry of the addition to 2a.

Table 2. Solvent Dependency on Regiochemistry of the Reaction of 2a with 1 at -12 °C

Solvent	Dielectric constant[a)]	Product composition[b)]	
		% 3a	% 3a'
$CHCl_3$	4.81	85.9	14.1
CH_2Cl_2	9.08	84.3	15.7
CH_2ClCH_2Cl	10.36	84.4	15.6
$(CH_3CO)_2O$	20.7	84.2	15.8
CH_3NO_2	35.87	84.0	16.0

a) J. A. Riddick and E. E. Toops,"Technique of Organic Chemistry," ed. by A. Weissberger, Interscience, New York (1955), Vol. VII. b) Percentages are normalized to 100%. Determined by ^{13}C NMR analysis.

No solvent effect on the regiochemistry has been observed. The amount of 1,4-adduct was less than 2% in all the solvents.

A similar solvent independency on the regiochemistry has been shown for the reaction of 1-phenylpropenes with 1 (above chapter 2. 2).

In contrast to the present results, the high preference of 1,4-addition has been observed for the reaction of BrCl (and Br_2) with conjugated dienes.1,2,5) Furthermore, dependence of the 1,2- vs. 1,4-addition of bromine to 2a on solvent polarity has been reported.5) The author has also found that BrCl reacted with 2a to give a mixture of 3a and 5a with substantial amounts of dichloro and dibromo adducts (Scheme 4).

$$CH_2{=}CHCH{=}CH_2 \quad + \quad BrCl \longrightarrow CH_2BrCHClCH{=}CH_2 \; + \; CH_2BrCH{=}CHCH_2Cl$$

2a 3a, 27% 5a, 73%

Yield: 78.2%

Scheme 4.

None of the anti-Markownikoff adduct (3a') was detected by ^{13}C NMR analysis of the product mixture.

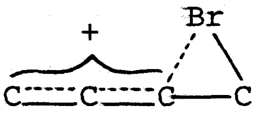
When compared to other reactions of 1,3-butadiene with interhalogens and pseudohalogens, the striking difference becomes evident. Product distributions for the additions of interhalogens and pseudohalogens to 1,3-butadiene are summarized in Table 4. Thus, present results would be the first example of the formation of anti-Markownikoff adduct given in the interhalogen addition to 1,3-butadiene.

Table 4. Product Distribution for Addition of Various Reagents to 1,3-Butadiene.

Reagent	1,2-Addition		1,4-Addition	Ref
	M[a)]	aM[a)]		
$BrCl_2^-$	84	16	trace	b
BrCl	27	0	73	b
ICl	22	0	78	c
INCO	0	0	100	d
BrOAc	83	0	17	e
ClOAc	71	0	29	e

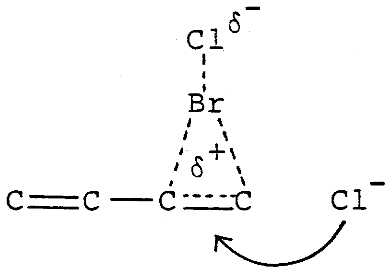
a) M=Markownikoff adduct. aM=anti-Markownikoff adduct. b) This work. c) C. K. Ingold and H. G. Smith, J. Chem. Soc., 1931, 2752. d) B. E. Grimwood and D. Swern, J. Org. Chem., 32, 3665 (1967). e) Ref. 5.

Thus, the addition to dienes appears to be very different in reactions with 1 and with BrCl. Therefore, the present reaction with 1 cannot be explained on the basis of any accepted mechanism involving a bromonium ion intermediate for the addition of BrCl (and Br_2).[2,3]



Cl^- (7)

The author would like to suggest another possible mechanism which involves the attack of chloride ions on a three-center bound π complex-type intermediate (8) with little delocalization of the positive charge across the allylic system: in the above chapter, a similar mechanism has been suggested for the addition of 1 to alkenes.



(8)

Experimental

The GLC analyses were performed on a Yanako G-180 gas chromatograph with a Silicone SE-30 (2.5%) (column A) or (5%) (column B)-Chromosorb WAW DMCS (2m) column with helium as a carrier gas. All the orgainc materials were distilled before use.

Reaction of 2a with 1. Details of the reaction have been reported in the above chapter. To a solution of 2a (3.0 ml, 36 mmol) in dichloromethane (100 ml) was added 1 (11.8 g, 30 mmol) at -12 °C over 20 min with stirring. After the usual work-up, distillation afforded 3.83 g (75.3%) of a mixture of 3a and 3a': Bp 46—48 °C/26 mmHg; MS M^+ at m/e (relative intensity)=168, 170, and 172 (100 : 132 : 35); Found: m/z

167.9330. Calcd for C_4H_6BrCl: M, 167.9342. ^{13}C NMR showed a 84 : 16 mixture of 3a and 3a', respectively. The structure of the minor 1,4-adduct (5a) was verified by comparison of the spectra of the sample prepared by the reaction of 2a with BrCl.[2)] 5a, ^1H NMR ($CDCl_3$) δ=3.90—4.10 (4H, m, CH_2Br and CH_2Cl), and 5.90—6.01 (2H, m, CH=CH); ^{13}C NMR ($CDCl_3$) δ=30.9, 43.5, and 130.3 (2C).

Reaction of 2b—e with 1. The reactions were carried out similarly to those of 2a. The relative amounts of the products were determined by measuring the peak areas of GLC (column A). The results are given in Table 1. All the reaction products were identified by comparing GLC and NMR spectra with the authentic samples prepared by the reaction of BrCl with these dienes.[1,2)] The ^1H NMR spectra of the products correspond well with those reported in the literature.[1,2)]

Reaction of 2a with 1 under Various Conditions. When 2a was treated with 1 in dichloromethane as described above, O_2 was bubbled during the reaction. ^{13}C NMR analysis of the residue showed a 85 : 15 mixture of 3a and 3a', respectively. The reaction was carried out with 12 mmol of 2a, 10 mmol of 1, and 3 mmol of 2,6-di-t-butyl-4-methylphenol in dichloromethane (50 ml). After the usual work-up, ^{13}C NMR analysis of the residue showed a 86 : 14 mixture of 3a and 3a', respectively.

To 12 mmol of 2a in 50 ml of the solvent ($CHCl_3$, CH_2Cl_2, CH_2ClCH_2Cl, $(CH_3CO)_2O$, and CH_3NO_2) was added 10 mmol of 1 at

-12 °C over 5 min with stirring. After the usual work-up, the residues were subjected to GLC and ^{13}C NMR analyses. In all cases, GLC analysis showed over 98% of the 1,2-adduct. The results are given in Table 3. The relative amounts of 3a and 3a' were determined by ^{13}C NMR analysis. GLC analyses of the residues were performed on the column B.

Reaction of 2a with Bromine Chloride. To 20 mmol of 2a in 100 ml of dichloromethane was added 4.5 ml of BrCl solution in CCl_4 (2.2 mol dm^{-3}) at -12 °C over 10 min with stirring. Evaporation of the solvent and analysis of the residue by GLC (column B) showed the composition to be: 3,4-dichloro-1-butene, 5.7%; 3a, 21.1%; trans-1,4-dichloro-2-butene, 6.2%; 3,4-dibromo-1-butene, 2.5%; 5a, 57.1%; trans-1,4-dibromo-2-butene, 7.4%.

Halogen Exchange Reaction. To 5 mmol of 5a in dichloromethane (25 ml) was added 10 mmol of tetrabutylammonium chloride and the mixture was allowed to stand for 24 h at 0 °C with stirring. After the usual work-up, GLC analysis (column B) showed the composition to be: 5a, 5%; trans-1,4-dichloro-2-butene (6a), 95%. A similar treatment of 5b–e and 5e' with chloride ions gave the corresponding 1,4-dichloro compounds in over 95% yield.

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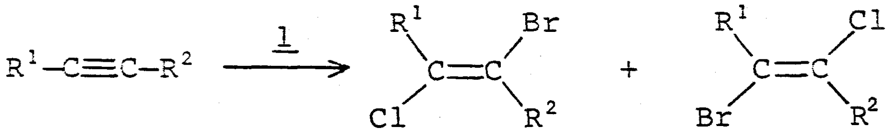
CHAPTER 4

REGIO- AND STEREOCHEMISTRIES OF BROMOCHLORINATION OF ALKYNES WITH MOLECULAR BROMINE CHLORIDE AND DICHLOROBROMATE(1-) ION

In the general introduction, it was shown that the stereochemistry of bromine addition to alkynes is markedly dependent both on the reaction conditions and on the structure of alkynes.1,2) However, only a few scattered data have been made available on the bromochlorination of alkynes. The reaction of diphenylacetylene,3) ethyl 3-butynoate,4) and 1-hexyne5) with molecular bromine chloride (2) has been reported to give the corresponding bromo chloro adducts in an anti stereospecific manner. In the chapter 2, the author has shown that tetrabutylammonium dichlorobromate(1-) (1) reacted phenyl- or alkyl-substituted ethylenes to give the bromo chloro adducts in nearly quantitative yields, and that the addition took place in an anti stereospecific manner, while the regio- and stereochemistries of the bromochlorination of alkenes (chapter 2) or dienes (chapter 3) with 1 are strikingly different from those with 2. As a continuation of the author's study, the author has studied on the regio- and stereochemistries of the reaction of 1 and 2 with various alkynes.

Results and Discussion

The reaction of 1-phenylpropyne (3a), 1-hexyne (3c), or 2-hexyne (3d) with tetrabutylammonium dichlorobromate(1-) (1) in CH_2Cl_2 gave a mixture of (E)-Markownikoff and (E)-anti-Markownikoff adducts (4a, 4c, and 4d and 5a, 5c, and 5d, respectively) in nearly quantitative yields (Scheme 1 and Table 1).



3 4 5

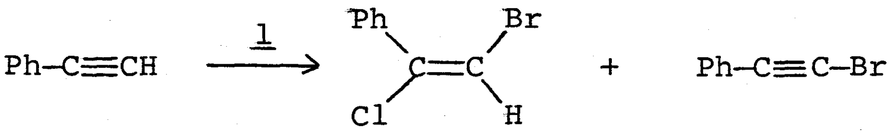
a: R^1=Ph, R^2=Me c: R^1=n-Bu, R^2=H

d: R^1=n-Pr, R^2=Me

Scheme 1.

Similarly, treatments of symmetrical alkynes such as diphenylacetylene (3e: R^1=R^2=Ph) and 3-hexyne (3f: R^1=R^2=Et) with 1 also gave the corresponding bromo chloro adducts (4e and 4f, respectively) in an anti stereospecific manner (Table 1).

On the other hand, the reaction of phenylacetylene (3b: R^1=Ph, R^2=H) with 1 gave a mixture of (E)-2-bromo-1-chloro-1-phenylethene (4b) and 1-bromo-2-phenylethyne (6b) (Scheme 2 and Table 1).



3b 4b 6b

Scheme 2.

Table 1. Regio- and Stereochemistries of the Bromochlorination of Alkynes with 1a)

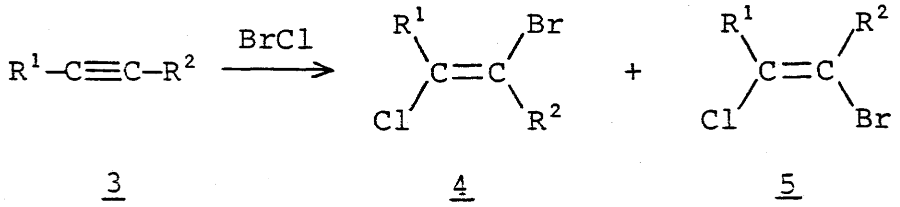
Alkynes	Product composition/%b)			Yield/%c)
	(E)-Md)	(E)-aMd)	(Z)	
3a	89.2	10.8	0	76 (97)
3b	100	0	0	42e)
3c	86.5	13.5	0	81 (97)
3d	50.2	49.8	0	81 (98)
	(E)	(Z)		
3e	100	0		93
3f	100	0		80 (96)

a) Reactions were carried out with 20 mmol of 1, 20 mmol of 3, and 50 ml of CH_2Cl_2 at 20 °C. b) Percentages are normalized to 100%. Determined by ^1H NMR analysis. c) Isolated yield. Yields in parentheses were determined by ^1H NMR using 1,2-dibromo-1-phenylethane as the internal standard. d) M=Markownikoff adduct (4). aM=anti-Markownikoff adduct (5). e) The other product was 1-bromo-2-phenylethyne (6b, 58%). Determined by GLC analysis.

The formation of 6b cannot be ascribed to the subsequent secondary reaction of 4b, since prolonged reaction time did not cause any change in the ratio of the products. Further, the bromo chloro adduct (4b) was stable under the reaction conditions. Formation of 1-bromo-2-phenylethyne (6b) has already been reported for the reaction of 3b with bromine.$^{2)}$

Although attempts to separate two regioisomers (4 and 5) were unsuccessful, the orientation of halogen atoms was elucidated mainly on the basis of the chemical shifts of the protons in the ^{1}H NMR spectra of the adducts. The structures of 4 and 5 have been determined by comparison of their ^{1}H NMR or ^{13}C NMR spectra with those of the corresponding dibromo and dichloro adducts. It has been known that the proton β to a bromine atom is deshielded relative to the one β to a chlorine atom, and that the proton α to a chlorine atom is deshielded relative to the one α to a bromine atom.$^{6)}$ Thus, the methyl protons of 4a give δ=2.56 but those of 5a δ=2.45, in agreement with the observation that the methyl protons (δ=2.60) of (E)-1,2-dibromo-1-phenylpropene are deshielded relative to those (δ=2.41) of (E)-1,2-dichloro-1-phenylpropene. Similarly, the methyl protons (=C–CH_3) of 4d give δ=2.38 but those of 5d δ=2.27 (Experimental). Control experiments revealed that all the bromo chloro adducts are stable under the reaction conditions.

Treatments of alkynes (3a and 3b) with molecular bromine chloride (2) in CH_2Cl_2 gave the corresponding (E)- and (Z)-Markownikoff adducts (4 and 4') in a regiospecific and nonstereospecific manner (Scheme 3 and Table 2).



a: R^1=Ph, R^2=Me   b: R^1=Ph, R^2=H

Scheme 3.

As with the reaction with 1, the reaction of alkyl-substituted acetylenes (3c and 3d) with 2 gave a mixture of (E)-Markownikoff and (E)-anti-Markownikoff adducts (4 and 5) in a nonregiospecific and anti stereospecific manner, and the reaction of 3-hexyne (3f) gave the anti stereospecific adduct (4f) (Table 2). The yields of the bromo chloro adducts were lower than those in the reaction of 1 because these dibromo- and dichloroalkenes were formed as by-products in every case.

Inspection of the data in Tables 1 and 2 clearly reveals that the regio- and stereochemistries of the bromochlorination of alkynes depend greatly both on the structure of alkynes and on the bromochlorinating agents employed. Therefore, the electronic structure of the intermediate in the product-forming step must depend both on the substituent on the

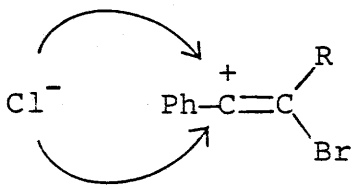
Table 2. Regio- and Stereochemistries of the Bromochlorination of Alkynes with 2a)

Alkynes	Product composition/%b)			Yield/%c)
	(E)-Md)	(Z)-Md)	(E)-aMd)	
3a	78.1 (77.9)	21.9 (22.1)	0	69
3b	62.8	37.2	0	70
3c	90.9	0	9.1	71
3d	47.5e)	0	52.5e)	73
	(E)	(Z)		
3e	100	0		20f)
3f	(100)	(0)		75

a) Reactions were carried out with 10 mmol of 2, 20 mmol of 3, and 50 ml of CH_2Cl_2 at 20 °C. b) Percentages are normalized to 100%. Determined by ^{1}H NMR analysis. Yields in parentheses were determined by GLC analysis. c) Determined by GLC analysis. d) M=Markownikoff adduct. aM=anti-Markownikoff adduct. e) Determined by ^{13}C NMR analysis. f) Ref. 3. Isolated yield.

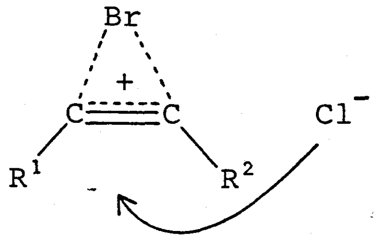
acetylene linkage and on the bromochlorinating agents.

Regio- and Stereochemistries of the Reaction of 3 with 2. As shown in Table 2, the addition of molecular bromine chloride (2) to phenyl-substituted alkynes such as 3a and 3b is nonstereospecific and regiospecific. This result can be explained on the basis of a mechanism involving the attack of chloride ion on an open vinyl cationic intermediate (7), in which the cationic character of the phenyl-substituted carbon atom is stabilized by overlap of p-orbitals of the phenyl group; a similar reaction intermediate has been suggested for the bromination of these alkynes with molecular bromine.1,2)



(7)

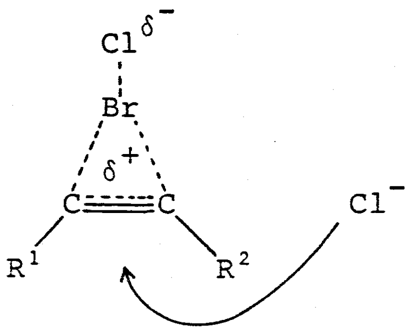
On the other hand, the addition of 2 to alkyl-substituted acetylenes (3c, 3d, and 3f) gave only trans-bromo chloro adducts (Table 2). Such an anti stereospecific addition of 2 to these alkynes are fully in accordance with the mechanism involving a bridged bromonium ion intermediate (8) as follows:2)



(8)

Meanwhile, the addition of 2 to monoalkyl-substituted acetylene (3c) gave the Markownikoff adduct (4c) as the major product. This implies that the attack of chloride ion on the intermediate (8) occurs at the alkyl-substituted carbon atom. Thus, the orientation of the addition of 2 would be due to the electronic effect of the alkyl substituent which stabilizes the developed cationic character on the alkyl-substituted carbon atom in the intermediate (8).5)

Regio- and Stereochemistries of the Reaction of 3 with 1. In contrast to the addition of 2 to alkynes, the addition of 1 is in an anti stereospecific manner irrespective of the substituents on the acetylene linkage (Table 1). Thus, the addition of 1 to phenyl-substituted alkynes (3a and 3b) gave only the anti stereospecific adducts. This result cannot be explained on the basis of the mechanism involving an open vinyl cationic intermediate (7) for the addition of 2 to 3a–b as described above. One may suggest another possible mechanism which involves the attack of chloride ion on a three-centered π-complex intermediate (9) in a product-forming step with a very little charge development on the unsaturated carbon; a similar intermediate has been suggested for the addition of 1 to alkenes and dienes (above chapters 2 and 3).



(9)

Meanwhile, the addition of 1 to phenylacetylene (3b) gave only the regiospecific Markownikoff adduct (4b). The addition to 1-phenylpropyne (3a) was in a regioselective Markownikoff manner. These results imply that the attack of chloride ion on the intermediate (9) occurs on the phenyl-substituted carbon atom. Thus, the orientation of the bromochlorination with 2 would depend on the electronic effect of phenyl substituent which stabilizes the developed cationic character on the phenyl-substituted carbon atom in the intermediate (9). The addition of 1 to 1-hexyne (3c) gave the regioselective Markownikoff adduct (4c). Thus, the orientation of addition of 1 can be influenced also by the electronic effect of the alkyl substituent.

Experimental

All the melting points and boiling points are uncorrected. All the organic starting materials, including the solvents, were distilled just before use.

Reaction of Alkynes with 1. General Procedure: To a solution of 3 (20 mmol) in dichloromethane (50 ml) was added 1 (7.87 g, 20 mmol) at 20 °C over 20 min with stirring. After the yellow color disappeared, the reaction mixture was washed with water and dried over Na_2SO_4. After the solvent was removed by evaporation, the products were purified by distillation. The results are shown in Table 1. Although attempts to separate 4 and 5 were unsuccessful, these structures were determined by a comparison of their ^1H NMR spectra (^{13}C NMR spectra in some cases) with those of the corresponding dibromo and dichloro analogs.

A Mixture of (E)-2-Bromo-1-chloro- and (E)-1-Bromo-2-chloro-1-phenylpropenes (4a and 5a) from 1-Phenylpropyne (3a): Bp 78–79 °C/2 mmHg; MS M^+ at m/z (rel intensity) 230, 232, and 234 (100 : 135 : 32). Found: m/z 229.9488. Calcd for C_9H_8BrCl: M, 229.9498. ^1H NMR ($CDCl_3$) (an asterisk indicates 5a) δ=2.45,* 2.56 (3H, s, CH_3), and 7.30–7.40 (5H, m, C_6H_5). These assignments were supported for the dibromo and dichloro analogs as follows: (E)-1,2-dibromo-1-phenylpropene, ^1H NMR ($CDCl_3$) δ=2.60 (3H, s, CH_3) and 7.20–7.40 (5H, m, C_6H_5); (E)-1,2-dichloro-1-phenylpropene, ^1H NMR ($CDCl_3$) δ=2.41 (3H, s, CH_3) and 7.20–7.50 (5H, m, C_6H_5).

(E)-2-Bromo-1-chloro-1-phenylethene (4b) and 1-Bromo-2-phenylethyne (6b) from Phenylacetylene (3b): 4b, bp

85–90 °C/6 mmHg; MS M^+ at m/z (rel intensity) 216, 218, and 220 (100 : 128 : 32). Found: m/z 215.9310. Calcd for C_8H_6BrCl: M, 215.9342. ^{1}H NMR ($CDCl_3$) δ=6.56 (1H, s, CH) and 7.30–7.67 (5H, m, C_6H_5). 6b, bp 76–78 °C/6 mmHg (lit,[7] bp 40–41 °C/0.1 mmHg; MS M^+ at m/z (rel intensity) 180 and 182 (100 : 100). Found: m/z 179.9550. Calcd for C_8H_5Br: M, 179.9575. ^{1}H NMR ($CDCl_3$) δ=7.28–7.53 (m, C_6H_5). The ^{1}H NMR spectrum of 4b corresponds well with that reported in the literature.[8]

A Mixture of (E)-1-Bromo-2-chloro- and (E)-2-Bromo-1-chloro-1-hexenes (4c and 5c): Bp 55–56 °C/25 mmHg; MS M^+ at m/z (rel intensity) 196, 198, and 200 (100 : 132 : 32). Found: m/z 195.9648. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^{1}H NMR ($CDCl_3$) (an asterisk indicates 5c) δ=0.75–1.10 (3H, br. t), 1.15–1.90 (4H, m), 2.40–2.80 (2H, m), 6.20, and 6.27* (1H, 2s); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5c) δ=13.8, 21.6, 21.7,* 28.5,* 29.2, 34.5, 34.9,* 101.1,* 114.8, 127.0, and 136.9.* The ^{1}H and ^{13}C NMR of a mixture (4c and 5c) correspond well with those reported in the literature.[5]

A Mixture of (E)-2-Bromo-3-chloro- and (E)-3-Bromo-2-chloro-2-hexenes (4d and 5d) from 2-Hexyne (3d): Bp 35–36 °C/5 mmHg; MS M^+ at m/z (rel intensity) 196, 198, and 200 (100 : 133 : 32). Found: m/z 195.9650. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^{1}H NMR ($CDCl_3$) (an asterisk indicates 5d) δ=0.93 (3H, t, J=7.3 Hz), 1.18–1.79 (2H, m), 2.27,* 2.38 (3H, 2s), and 2.43–2.74 (2H, m); ^{13}C NMR ($CDCl_3$) (an asterisk indicates 5d) δ=13.0,* 13.1, 20.3, 20.9,* 25.8,* 25.9, 39.6,* 40.1, 115.9, 121.7,* 125.4,* and 130.5. These assignments were supported for the dibromo and dichloro analogs as follows: (E)-2,3-dibromo-2-hexene: ^{1}H NMR ($CDCl_3$) δ=0.94 (3H, t, J= 6.7 Hz), 1.28–1.85 (2H, m), 2.41 (3H, s), and 2.65 (2H, t, J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ=13.0, 20.8, 28.8, 42.4, 115.2, and 121.8. (E)-2,3-dichloro-2-hexene: ^{1}H NMR ($CDCl_3$) δ=0.93 (3H, t, J=6.7 Hz), 1.26–1.88 (2H, m), 2.00 (3H, s), and 2.52 (2H, t, J=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ=13.1, 20.2, 23.2, 37.5, 124.9, and 129.9.

(E)-1-Bromo-2-chloro-1,2-diphenylethene (4e) from Diphenylacetylene (3e): Mp 170–172 °C (lit,3) 173–175 °C); ^{1}H NMR ($CDCl_3$) δ=7.30–7.66 (m, $2C_6H_5$); ^{13}C NMR ($CDCl_3$) δ= 117.7, 128.2, 128.8, 129.0, and 129.1.

(E)-3-Bromo-4-chloro-3-hexene (4f) from 3-Hexyne (3f): Bp 55–57 °C/25 mmHg; MS M^+ at m/z (rel intensity) 196, 198, and 200 (100 : 130 : 33). Found: m/z 195.9649. Calcd for $C_6H_{10}BrCl$: M, 195.9655. ^{1}H NMR ($CDCl_3$) δ=1.10 (6H, t, J=7.3 Hz) and 2.41–2.83 (4H, m); ^{13}C NMR ($CDCl_3$) δ=11.4, 12.2, 31.7, 32.2, 122.1, and 130.8.

Reaction of Alkynes (3) with Bromine Chloride (2). To a solution of 3 (20 mmol) in CH_2Cl_2 (50 ml) was added 5.5 ml of BrCl (2) solution in CCl_4 (1.8 mol dm^{-3}) at 20 °C over 5 min with stirring. After the reaction completed, the solvent and unreacted alkyne were removed under reduced pressure and the residues were analyzed by GLC and ^{1}H NMR or ^{13}C NMR. The results are given in Table 2. In all cases, GLC analyses showed the presence of 11–15% of the dichloro adduct and 12–17% of the dibromo adduct as by-products. GLC analyses were performed on a Yanako G-180 gas chromatograph with a Silicone SE-30(10%)-Chromosorb WAW DMCS (2 m) column, with helium as the carrier gas.

The reaction of 1-phenylpropyne (3a) with 2 gave a mixture of (E)-2-bromo-1-chloro- and (Z)-2-bromo-1-chloro-1-phenylpropenes (4a and 4a', 69%) (4a : 4a'=78 : 22) with dichloro and dibromo adducts (31%) by GLC analysis. After the bromo chloro adducts were separated by distillation, column chromatography (silica gel, with hexane as the eluent) of the mixture of 4a and 4a' gave almost pure 4a and 4a'. 4a: MS M^+ at m/z (rel intensity) 230, 232, and 234 (100 : 132 : 32). Found: m/z 229.9487. Calcd for C_9H_8BrCl: M, 229.9498. ^{1}H NMR ($CDCl_3$) δ=2.56 (3H, s, CH_3) and 7.30–7.40 (5H, m, C_6H_5). 4a': MS M^+ at m/z (rel intensity) 230, 232, and 234 (100 : 133 : 30). Found: m/z 229.9485. Calcd for C_9H_8BrCl: M, 229.9498. ^{1}H NMR ($CDCl_3$) δ=2.32 (3H, s, CH_3) and 7.30–7.40 (5H, m, C_6H_5).

The reaction of phenylacetylene (3b) with 2 gave a mixture of (E)-2-bromo-1-chloro- and (Z)-2-bromo-1-chloro-1-phenylethenes (4b and 4b', 70%) (4b : 4b'=63 : 37 by ^{1}H NMR analysis) with dichloro and dibromo adducts (26%) and a small amount of 1-bromo-2-phenylethyne (6b, 4%) by GLC analysis. Although the isolation of 4b and 4b' was not carried out, the retention time of GLC and the ^{1}H NMR (δ=6.56, vinyl proton of 4b and δ=6.82, vinyl proton of 4b') agreed with those of a sample prepared by the reaction of 3b with copper(II) chloride and bromine.$^{8)}$

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