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SUBSTITUENT AND NEIGHBOURING GROUP EFFECTS IN THE BROMINATION OF OLEFINS

by

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(Hatfield College)

A thesis submitted for the Degree of Doctor of
Philosophy in the University of Durham

1973

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The receipt of a Science Research Council award is gratefully acknowledged.

- TO HELEN -

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1968 and October 1971.

This work has not been submitted for any other degree and is the original work of the author except where acknowledged by reference.

Part of this work has been published:

S.R. Hooley and D.L.H. Williams, J. Chem. Soc. (Perkin II), 1973, in the press.

ABSTRACT

Second-order rate constants have been determined for the bromination of the series $CH_2=C(X)CH_2Cl$ (for -X = -H, -F, -Cl and -Br) in 50% by volume methanol-water and trifluoroacetic acid solvents. 2-Halo substitution caused deactivation with respect to the unsubstituted allyl chloride, but enhanced reactivity was observed for the 2-fluoro substituted olefin compared to the 2-chloro and 2-bromo substituted compounds.

The above data were compared with the rate coefficients for the addition of trifluoroacetic acid to a series of 2-halopropenes. The difference in the scale of rate enhancement for the 2-fluoro substituted olefins in the two reactions is discussed in terms of the relative contributions of the cyclic bromonium ion structure and of the classical open carbonium ion structure to the transition state for electrophilic addition to olefins.

Second-order rate constants have been measured for the addition of bromine to allyl chloride and bromide and benzyl chloride and bromide in acetic acid-water and trifluoroacetic acid solvents. The relative rate enhancement for addition to allyl bromide in trifluoroacetic acid compared to allyl chloride was discussed in terms of solvent enhancement of the inductive effects of the halo substituents by hydrogen bonding, and compared to the rates of electrophilic substitution of bromine into the analogous aromatic compounds.

The second-order rate constants for bromination of the two series $CH_2=CH(CH_2)_{n-2}OH$ and $CH_2=CH(CH_2)_{n-2}Br$ (where n = 3 to 6) were measured in acetic acid-water and trifluoroacetic acid solvents. Neighbouring group participation was not observed in the bromo-substituted series of olefins.

This was compared to the observed participation by the substituent bromine atom in the addition of trifluoroacetic acid to 5-bromopent-1-ene and discussed in terms of the relative contributions of the cyclic bromonium ion structure and of the classical open carbonium ion structure in the transition states of the two reactions.

Participation by the hydroxy substituent was observed in the bromination of 4-penten-1-ol in the acetic acid-water solvent but not in trifluoroacetic acid solvent. This was discussed in terms of substituent-solvent hydrogen bonding which modified the effectiveness of the hydroxy group as an internal nucleophile.

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A. Substituent Effects

B. Neighbouring Group Effects

CHAPTER 1

ELECTROPHILIC ADDITION[1,2]

1.1 Classification of Reagents

In the discussion of chemical systems it is useful and convenient to draw into groups and categories reagents and reactions bearing common characteristics. It should be borne in mind, however, that whatever the criteria chosen for the classification, there will always be examples which exhibit a certain degree of overlap.

The most generally applicable categorisation of reactions is that done by Ingold[3] into homolytic and heterolytic divisions.

(a) Homolytic

In this type of reaction between reagents X and Y, the two electrons required to form a single bond between them are supplied equally by both of them

$$X^{\bullet} + Y^{\bullet} \underset{\text{homolysis}}{\overset{\text{colligation}}{\rightleftharpoons}} X{:}Y \tag{1.1}$$

This type of reaction normally occurs between free-radicals or odd-electron entities, which because of their extreme reactivity are generally produced in situ, by thermal, photolytic or electrolytic means.

Although free-radical brominations do occur, this study is confined to bromination under polar conditions where free-radical mechanisms have not generally been observed.

(b) Heterolytic

Here, the electrons for a single covalent bond between reagents X and Y are supplied by one reagent only. Both reagents are usually even-electron species, and reactions of this type

$$X{:} + Y \underset{\text{heterolysis}}{\overset{\text{co-ordination}}{\rightleftharpoons}} X{:}Y \tag{1.2}$$

form the largest class of reactions in organic chemistry. Electrons previously under exclusive control of one reagent become shared by formation of a new bond.

This conveniently leads to a means of defining the roles played by reagents in these reactions. Reagents which act by acquiring electrons, or a share in electrons previously controlled by the other are termed electrophiles. The reagents providing the electrons are termed nucleophiles. Extension of the terms 'acid' and 'base' as used by Lewis[4] in the discussion of co-ordination would give the same correlation.

It is, however, purely arbitrary convention which designates the attacking species in these heterolytic reactions of which the following are examples of the main types.[3]

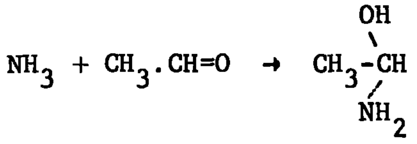
(i) Nucleophilic substitution: S_N

$OEt^- + CH_3\text{-}I \rightarrow CH_3\text{-}OEt + I^-$ 1.3

(ii) Electrophilic substitution: S_E

$NO_2^+ + Ph\text{-}H \rightarrow Ph\text{-}NO_2 + H^+$ 1.4

(iii) Nucleophilic addition: Ad_N



$NH_3 + CH_3.CH{=}O \rightarrow CH_3\text{-}\underset{NH_2}{\overset{OH}{CH}}$ 1.5

(iv) Electrophilic addition: Ad_E

$HCl + CH_3.CH{=}CH_2 \rightarrow CH_3.CHCl\text{-}CH_3$ 1.6

(v) Elimination reactions: E_1 (or E_N)

$OEt^- + (CH_3)_2CHBr \rightarrow EtOH + CH_3\text{-}CH{=}CH_2 + Br^-$ 1.7

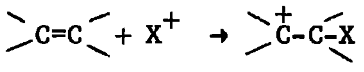
$OH^- + HO\text{-}C(CH_3)_2\text{-}CN \rightarrow H_2O + (CH_3)_2C{=}O + CN^-$ 1.8

Reactions carried out in this study have been concerned with type (iv) - electrophilic addition.

1.2 Halogenation as an Electrophilic Addition Reaction

The bromination of all unsaturated compounds considered was carried out in solution. In the absence of radical initiation, additions are favoured by a polar environment suggesting reaction by a heterolytic rather than a homolytic pathway.

Potentially, olefins can exhibit both nucleophilic or electrophilic behaviour forming either carbonium ions or carbanion entities.



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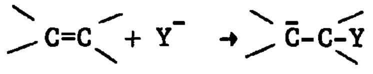
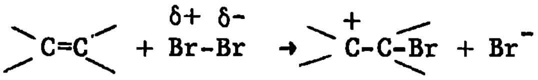


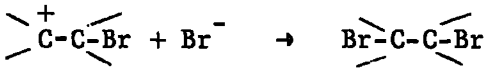
1.10

Theoretically, carbonium ions are considered to be the more stable of the two species, and nucleophilic attack by negatively charged ions on the ethylenic carbon atoms would be expected to be retarded by the π electronic system of the olefinic double bond,[2] suggesting that the olefin would be more susceptible to electrophilic than nucleophilic attack.

An early review by Williams[5] summarised the demonstration by Ingold et al.[6] that for a series of simple olefins electron-donating substituents such as -Ph and -Me increase the rate of addition, whereas electron-attracting substituents such as -Br, $-CO_2H$ and $-NMe_3^+$ retard addition.[3] The addition of ICl, considered to be polarised I^+Cl^-, was used to illustrate initial attack by an electrophilic species.[7] Electron-donating groups (-Ph and -Me) promoted Markownikoff orientation, whilst electron-withdrawing groups ($-CO_2H$, $-SO_3H$) favoured anti-Markownikoff addition. It was shown[8] that the rate of bromination of the acrylate ion was faster than that of the undissociated acid, again an observation consistent with electrophilic attack.

For addition in polar solvents, a two-stage mechanism was suggested,[6a] consisting of a rate-determining electrophilic attack by the positively-polarised end of the bromine molecule ($Br^{\delta+} \ldots Br^{\delta-}$) to form a positively-charged intermediate, which then rapidly reacted with bromide ion to give the dibromide product.

Step 1.  1.11

Step 2.  1.12

Polarisation of the type $Me \rightarrow CH\overset{\frown}{=}\overset{\delta-}{C}H_2$ by electron-donating substituents thus explained the increased rate of addition by the polarised bromine molecule.

Evidence for the existence of the second step was provided by the incorporation in the products of the anions of salts added to the reaction mixture.[9] e.g.

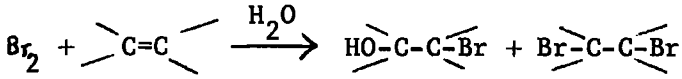
$$Br_2 + CH_2{=}CH_2 \xrightarrow{aq.NaCl} CH_2ClCH_2Br + CH_2BrCH_2Br \qquad 1.13$$

$$Br_2 + CH_2{=}CH_2 \xrightarrow{aq.NaNO_3} CH_2(NO_3)CH_2Br + CH_2BrCH_2Br \qquad 1.14$$

$$I_2 + CH_2{=}CH_2 \xrightarrow{aq.NaCl} CH_2ClCH_2I + CH_2ICH_2I \qquad 1.15$$

The incorporation of the nucleophilic solvent molecules has also been observed. It was shown[10] that the products of bromination of stilbene in methanol included the methoxy bromide, the quantity of which was depressed by added bromide ion. The observation that the rate was independent of acidity ruled out the possibility of bromination by the methoxy bromide species. Formation of halohydrins from the reaction of aqueous halogen solutions has long been known.

$$Br_2 + CHPh{=}CHPh \xrightarrow{MeOH} CHPh(OMe)CHPhBr + CHPhBrCHPhBr \qquad 1.16$$


1.17

It thus appears that the halogenation reaction involves initial attack by an electrophilic species on the olefinic double bond, placing it in a large group of reactions which are considered to use an electrophilic addition mechanism.

Table 1.1[3]

Electrophilic Addition Reactions

Reagent	Substrate	Addition Product
MnO_4^-, H_2O	$R_2C{=}CR_2$	R_2COHCR_2OH
H_3O^+	$R_2C{=}CR_2$	R_2CHCR_2OH
H_2SO_4	$R_2C{=}CR_2$	$R_2CHCR_2(OSO_3H)$
Hal_2	$R_2C{=}CR_2$	$R_2CHalCR_2Hal$
Hal_2,ROH	$R_2C{=}CR_2$	$R_2CHalCR_2OH$
HOHal, H_3O^+	$R_2C{=}CR_2$	$R_2CHalCR_2OH$
HHal	$R_2C{=}CR_2$	R_2CHCR_2Hal
NOHal	$R_2C{=}CR_2$	$R_2C(NO)CR_2Hal$

1.3 Kinetics of Halogenation

The kinetics of halogen addition to olefins present a complicated picture which is sometimes difficult to interpret. Early rate data for the bromination of simple olefins in water,[8,11] methanol[10] and aqueous acetic acid[8] all showed second-order kinetics, first-order in olefin and first-order in bromine.

$$\text{Rate} = k_2[\text{olefin}][\text{Br}_2] \tag{1.18}$$

The kinetic form of chlorination reactions is almost always second-order as above. Added ions affect the rate only slightly through a salt effect. In acetic acid,[12] electrolytes enhanced addition and for chloride catalysis the modified kinetic equation has been proposed.[13]

$$\text{Rate} = k_2[\text{olefin}][\text{Cl}_2][\text{Cl}^-] \tag{1.19}$$

The kinetics of iodination are often complicated and vary with reaction conditions.

In aprotic solvents such as carbon disulphide and carbon tetrachloride, a fourth-order reaction was dominant.[14]

$$-\frac{d[\text{I}_2]}{dt} = k_4[\text{olefin}][\text{I}_2]^3 \tag{1.20}$$

In acetic acid and nitrobenzene,[15] third-order kinetics were also identified.

$$-\frac{d[\text{I}_2]}{dt} = k_3[\text{olefin}][\text{I}_2]^2 \tag{1.21}$$

The situation is further complicated by the reversible nature[17] of many iodine addition reactions since the reaction is only just exothermic (10 kcal for ethylene)[16] and has an unfavourable entropy change.

This precludes the direct observation of a second-order reaction at low concentrations. Robertson,[17] however, has suggested a composite rate equation combining equations 1.20 and 1.21. The higher-order term was considered to be dominant in solvents where iodine was not strongly polarised by solvation (violet solutions), and the lower-order term was observed in solvents capable of effective solvation (brown solutions).

Although, the kinetic observations for bromination are not as simple as for chlorination they are far less complicated than for iodination. As stated previously, bromination reactions are generally second-order, although Robertson et al have found[8a,18] that for more concentrated bromine solutions (> M/40) in acetic acid, reaction proceeded by a third-order rate law.

$$-\frac{d[Br_2]}{dt} = k_3[\text{olefin}][Br_2]^2 \qquad 1.22$$

The above observation has not been made for solvents more polar than acetic acid. Dilution, increase of temperature and addition of water tended to cause a reversion to second-order kinetics. Substituent effects were similar for third-order and second-order reactions, which implied no fundamental change in mechanism.

Table 1.2[19]

Effect of Substituents on the Relative Rate of Third-order Bromination

Olefin	Relative Rate		
	R = CH_2Cl	R = Hal	R = CO_2H
CMe_2=CHR	-	0.5	0.15
trans-CHPh=CHR	77	0.1	0.017
CH_2=CHR	1.6	0.001	-

White and Robertson[20] suggested that for third-order bromination the initial bromine molecule co-ordinated reversibly to the olefin, which was then susceptible to attack by a further bromine molecule. This view has been supported more recently by Dubois[21] who has shown the existence of transitory charge transfer complexes (CTCE) by means of a spectrokinetic method, (Chapter 2).

In contrast with the previously mentioned slight anion catalysis in chlorination reactions, anion catalysis in bromination reactions was considerably more marked. Added lithium chloride catalysed the rates of addition of bromine to allyl chloride and vinyl bromide in acetic acid solution[22] according to equation 1.23.

$$-\frac{d[Br_2]}{dt} = k[\text{olefin}][Br_2][Cl^-] \qquad 1.23$$

Generally, bromide ions also catalysed reactions which were enhanced by chloride ions but structural effects on rates were complicated and no simple interpretation could be made. Interference by salt effects of unknown magnitude has made correlation difficult. It can be seen in Table 1.3 that catalysis or inhibition by added bromide ions is also dependent on solvent.

In connection with reactions containing added bromide ions, it should be noted that equilibrium (1.24) would reduce the effective concentration of free bromine.

$$Br^- + Br_2 \overset{K}{\rightleftharpoons} Br^-_3 \qquad 1.24$$

If bromine was the only brominating agent then added bromide ions would be expected to reduce the rate of addition. However, anion catalysis would be kinetically indistinguishable from attack at the

Table 1.3[23]

Effect of Added Bromide Ions on the Rate of Bromination of Olefins in Solution

Solvent	[MBr] mole l^{-1}	$[Br_2]$ mole l^{-1}	Rate increase/decrease	Reference
MeOH	10^{-2} to 5×10^{-1}	10^{-3}	decrease	10
H_2O	5×10^{-2} to 2×10^{-1}	10^{-3}	decrease	24
H_2O	10^{-2} to 5×10^{-1}	10^{-5}	decrease	25
MeOH	10^{-4} to 5×10^{-1}	10^{-5} to 10^{-3}	decrease	26
AcOH	5×10^{-2} to 10^{-1}	10^{-2}	increase	27
AcOH	5×10^{-2} to 10^{-1}	10^{-2}	increase	28

double bond by tribromide ion. The interaction of ions Br_3^-, Br_2Cl^-, Br_2OAc^- was suggested for the catalysed bromination of olefins of the type $CH_2=CHX$, where -X was a strongly electron-attracting group such as $-SO_2Me$.[29]

More recently, separated rate constants for bromination by both bromide and tribromide have been elucidated by means of studying the variation of rate with bromide ion concentration using equation 1.25.

$$k_{obs} = \frac{k_{Br_2} + k_{Br_3^-}K[Br^-]}{1 + K[Br^-]} \qquad 1.25$$

Since K was measured independently by spectroscopic means, k_{Br_2} and $k_{Br_3^-}$ were obtained by plotting $k_{obs}(1 + K[Br^-])$ against $K[Br^-]$. Atkinson and Bell[30] have measured the separated rate constants for a series of olefins in water at 25°C.

Table 1.4

Rate constants of Bromination in Water at 25°C

Olefin	k_{Br_2} (l mole^{-1}sec^{-1})	$k_{Br_3^-}$(l mole^{-1}sec^{-1})	$k_{Br_3^-}/k_{Br_2}$
propene	4.5×10^6	3.2×10^6	0.7
stilbene	7.8×10^5	-	small
allyl alcohol	6.7×10^5	6.9×10^4	0.10
ethylene	3.94×10^5	2.0×10^4	0.05
allyl cyanide	440	100	0.23
ethyl acrylate	1.06×10^{-1}	6.7×10^{-2}	0.63

The k_{Br_2} values above fell steadily as did the $k_{Br_3^-}$ values on passing to olefins containing more electron-withdrawing substituents, suggesting electrophilic behaviour by the attacking bromine and tribromide ion. As would be expected, bromine appeared to be a more effective brominating agent than the tribromide ion, although this was not always the case as will be shown later. It is a matter of conjecture whether the attack by tribromide ion be regarded as electrophilic or nucleophilic.

Although nearly all bromine additions to olefins are regarded as electrophilic, it has been suggested[28] that in the acid-catalysed bromination of α,β- unsaturated aldehydes[31] and ketones,[18b] reaction involved nucleophilic attack by bromine on the ion produced by addition of a proton to the group conjugated with the double bond thus allowing delocalisation of the positive charge onto the carbon atom under attack by the bromine, e.g.

$$\mathrm{R\text{-}CH{=}CH\text{-}CHO} + \mathrm{H^+} \rightleftharpoons [\mathrm{R\text{-}CH{=}CH\text{-}\overset{+}{C}HOH} \leftrightarrow \mathrm{R\overset{+}{C}H\text{-}CH{=}CHOH}] \xrightarrow{\mathrm{Br_2}} \text{products} \qquad 1.26$$

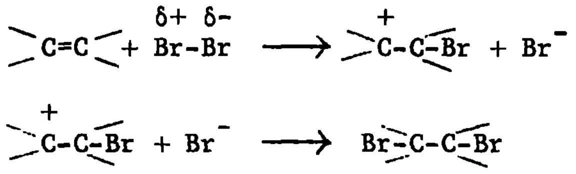
This suggestion was borne out by the high rate of addition to the α,β-unsaturated aldehydes and ketones compared with addition to the corresponding acids.[32]

Thus, kinetic data provide valuable, if at times confusing, information into the mechanism of halogenation, particularly from the effect of substituent atoms or groups. This has not been discussed in detail since it forms the basis of Chapter 2.

1.4 Nature of the Intermediate

During the discussion of the kinetic behaviour of halogenation, no reference was made to the nature of the intermediate involved in the two-step mechanism. Equation 1.11, as written, included a positively-charged carbonium ion as an intermediate, but was merely meant to indicate that a positively-charged species was involved.

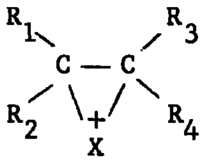
As a consequence of their early studies, Ingold and Ingold[6a] suggested that initial attack on the olefinic double bond was made by the positively-polarised bromine molecule to form a carbonium ion intermediate, which was then open to attack by the bromide ion liberated in the first step.



1.27

1.28

The above intermediate was regarded as a positively-charged free cation, with the charge localised on the carbon atom shown. This was then susceptible to attack by any nucleophilic species, whether bromide ions, added salts,[9] or solvent. The above view was supported by Bartlett and Tarbell[10,33] in their studies of the bromination of stilbene, dimethylmaleic and dimethylfumaric acids. This was called into question by Ogg[34] on the grounds that analysis of the products of halogenation reactions in general showed predominantly trans addition. This could not be expected from the carbonium ion intermediate in equation 1.27, since free rotation about the carbon-carbon bond would be possible, which would lead to equal quantities of cis and trans addition products. Roberts and Kimball,[35] however, argued that rotation about the carbon-carbon bond would not be expected since in the carbonium ion intermediate one of the 'p' orbitals on the positively-charged carbon atom would be empty and the added halogen would contain three orbitals occupied by lone-pairs. Thus, a co-ordinate link would "almost certainly" be formed, producing a cyclic halonium ion intermediate (1.1) compared with the isoelectronic ethylene oxide type.

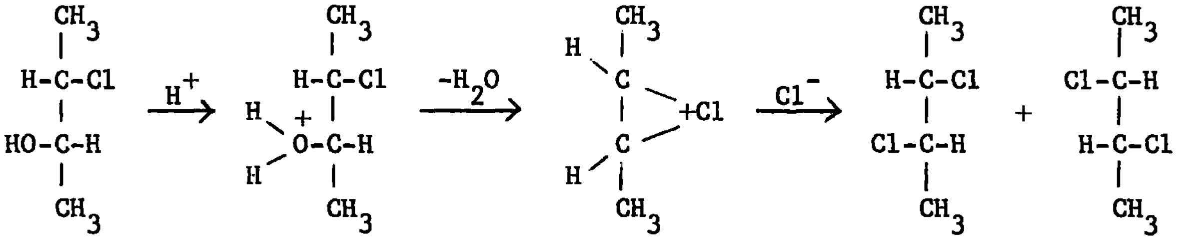


(1.1)

For a cyclic intermediate, (1.1), the second stage of reaction, attack by halide ion or other nucleophile in situ, would take place from the side opposite to the side of initial attack. The carbon-X^+ bond would be synchronously broken and a trans-adduct would result. The rider was added that in cases where the olefin contained similarly-charged groups such as $-COO^-$ (in positions R_1 and R_3 or R_2 and R_4) there might be sufficient repulsion between these groups to enable rotation about the double-bond and the adoption of the opposite configuration could take place before attack by the nucleophile. This would explain the predominantly trans addition to maleic acid, fumaric acid[36] and fumarate ion, and also the cis addition to maleate ion.[37]

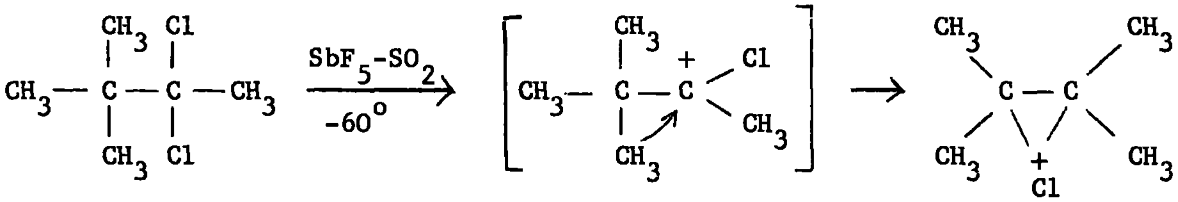
The observation[40] that addition of bromine and chlorine to cyclohexene systems lead to predominantly diaxial products, was consistent with a halonium ion intermediate, although it was noted that bromination appeared to be more stereospecific than chlorination.

The existence of positively-charged three-membered cyclic intermediates has since been postulated in other reactions such as the conversion of 3-chloro-2-butanols to 2:3-dichlorobutanes.[38]



1.29

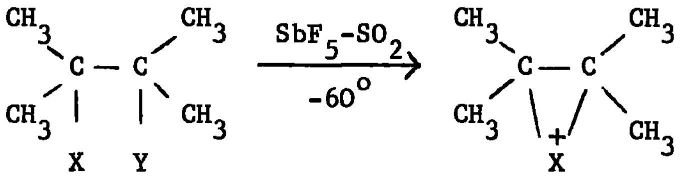
Further evidence[39] has recently been obtained by n.m.r., which has shown the following ionisation of 2,2-dichloro-3,3-dimethylbutane.



1.30

It was not possible to observe the equivalent behaviour for 2,3-diiodo-2,3-dimethylbutane because of its instability.

On grounds of size and polarisability the most easily formed halonium ion would be the iodonium ion. Extended Huckel calculations[41] predict the stability of the symmetrical cyclic ions to be greater for bromine than chlorine. The recent n.m.r. data [39] also indicated that the trend in ability to bear positive charge was I > Br > Cl. It was shown that a series of 2,3-dihalo-2,3-dimethylbutanes ionised thus in antimony pentafluoride-sulphur dioxide solutions at -60°C.

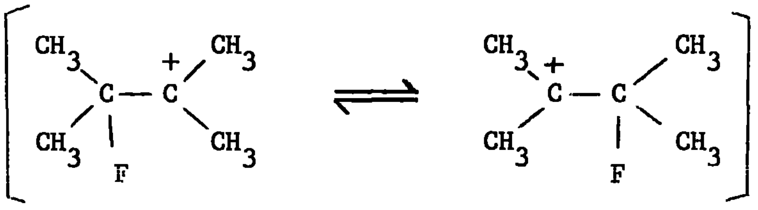


1.31

where X = Cl   X = Br   X = I

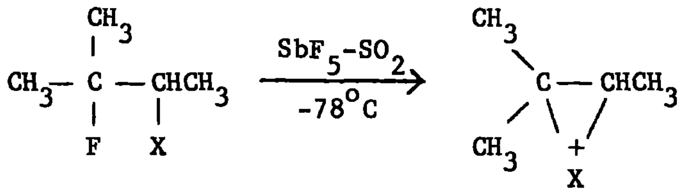
Y = F, Cl   Y = F, Br   Y = F

It was not possible to illustrate the formation of a cyclic fluoronium ion even at lower temperatures. The spectra were consistent with a rapidly equilibrating β-fluorocarbonium ion of type (1.2).



(1.2)

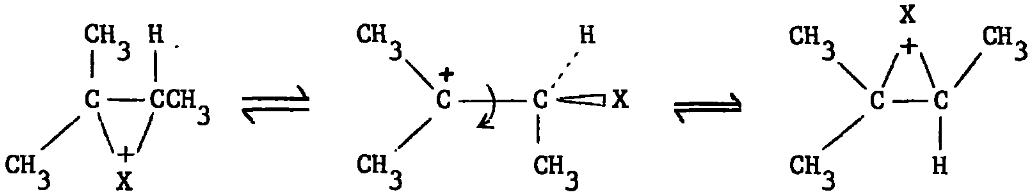
Further studies,[42] involving 2-fluoro-3-halo-2-methylbutane illustrated the formation of unsymmetrical ions, 1.32,



1.32

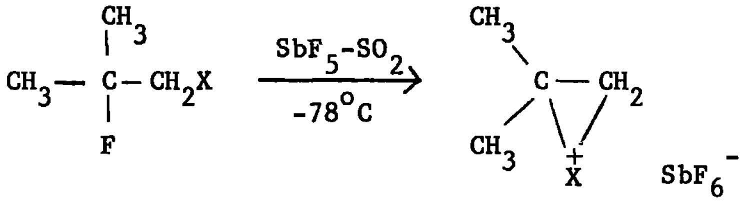
where X = I, Br, Cl.

The unsymmetrical nature of the carbon-halogen bond was illustrated by the deshielding differences for the single methyl compared to the geminal methyl groups. The equivalence of the geminal methyl groups in the bromonium and chloronium ions suggested the possibility of a rapid equilibrium, 1.33.



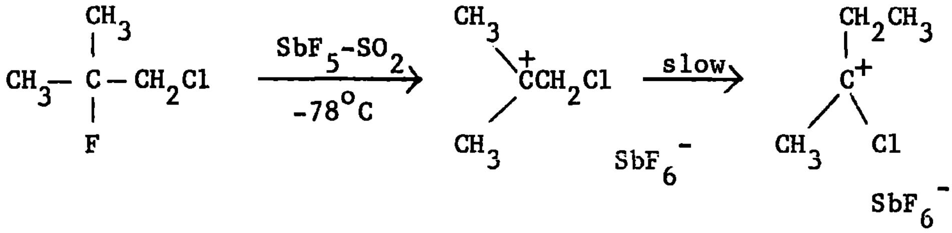
1.33

The stability order I > Br > Cl >> F was further illustrated by a series of 1-halo-2-fluoro-2-methylpropanes



1.34

X = Br or I

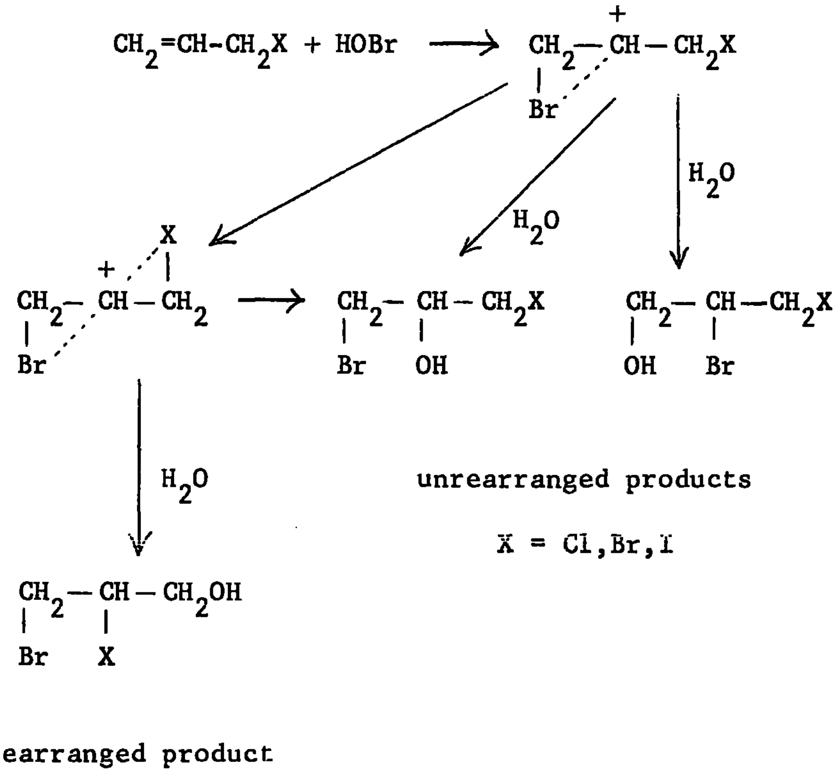


1.35

Direct evidence of halonium ions has been provided by the addition of bromine to the highly-hindered adamantylideneadamantane in carbon tetrachloride to give a bromonium ion bromide solid which was able to be isolated.[43]

It should, however, be noted that although the existence of the three-membered cyclic halonium species has been illustrated, it does not establish their participation as intermediates in halogen addition reactions.

Other electrophilic addition reactions to olefins have provided kinetic and product data which are consistent with a cyclic halonium ion intermediate. The addition of water to allyl bromide has been shown[44] to produce 10% of 2-bromopropan-1-ol in addition to 1-bromopropan-2-ol. Also the addition of hypobromous acid to allyl chloride,[45] bromide[45] and iodide[46] produced 0.8%, 28% and 48% of rearranged product respectively according to Scheme (1.36).



1.36

Once again the stability order I > Br > Cl was illustrated.

In contrast with the evidence for the existence of cyclised halonium ion species, the assumption has been questioned[47] that internal rotation about the carbon-carbon bond ion a positively-charged carbonium ion intermediate was fast in comparison to attack by the nucleophilic species. If the assumption was not correct and nucleophilic attack was faster than internal rotation, stereospecific addition would occur whether or not formation of a cyclic halonium ion took place.

Thus, the postulated cyclic halonium ion intermediate was, and has remained, a subject of controversy. It would appear that the open bromocarbonium ion intermediate and the cyclic bromonium ion intermediate represent the two possible extremes in the mechanism of bromine addition. There is much evidence in the literature indicating tendencies to one or other reaction pathway under certain reaction conditions, but no conclusive evidence for the preference of one to the exclusion of the other in all circumstances has yet been found.

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CHAPTER 2

SUBSTITUENT EFFECTS

2.1 Introduction

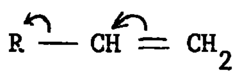
From the earliest kinetic studies of the halogenation of unsaturated compounds, the effects on the rates and products of varying substituents have provided valuable data for the elucidation of the mechanism of reaction. It was Ingold's observation that substituents which attracted electronic charge reduced the rates of bromination, whilst substituents which repelled electronic charge enhanced the rates of bromination.

Table 2.1[2]

Second-order Rate Constants for Chlorination in Acetic Acid

Olefin	k_2 (l.mole^{-1}min^{-1})
$CH(CO_2H)=CHCO_2H$	0.00011
$CH_2=CHCO_2H$	0.018
trans-$CHMe=CHCO_2H$	0.62
trans-$CHPh=CHCO_2H$	4.9
$CMe_2=CHCO_2H$	51.0

The above behaviour was explained in terms of electron-withdrawing groups reducing the electronic charge associated with the double bond and thus reducing its susceptibility to electrophilic attack.



$R-CH=CH_2$

(2.1)

Qualitative inspection of the rate data indicated cumulative effects of added substituents, e.g. two methyl groups were more activating than one.

This applied in general, although there were notable exceptions where special effects occurred. An example of this was the behaviour of substituent phenyl groups.

Table 2.2[3]

Second-order Rate Constants for Bromination (M/80) in Acetic Acid at 24°C

Olefin	k_2
$CHPh{=}CH_2$	$\sim 11 \times 10^3$
$CH_2{=}CH_2$	~ 84
$CHPh{=}CHPh$	18

This deactivating behaviour of multi-substituted phenyl olefins was noted by Ingold[1] for tetraphenylethylene, and explained in terms of the electronic charge supplied by one phenyl group being absorbed by another, the overall effect resulting in reduction in electronic charge associated with the double bond for the more phenyl-substituted olefins.

A list of the chlorination and bromination reactions carried out by Robertson et al in acetic acid has been made.[3]

2.2 Stereochemical Effects of Substituents

The majority of the early evidence in favour of a cyclic halonium ion intermediate in halogenation reactions was of a stereochemical nature. The addition of bromine[4,5] to neat cis and trans 2-butene at -15°C yielded 95% of trans addition product. Addition of bromine to cyclohexene,[6] 1-bromocyclohexene,[7] and 4-t-butylcyclohexene[8] illustrated the preference for trans diaxial attack, which was also shown for cholestene systems.[9] Earlier work had indicated that trans attack was predominant in bromine addition to maleic and fumaric acids.[10,11] Data for the chlorination of some olefins was tabulated by Fahey.[12]

Table 2.3 indicates that simple olefinic derivatives undergo polar additions in a highly stereospecific manner, which is consistent with the cyclic halonium ion acting as an intermediate.

However, it has been observed that not all halogenation reactions are completely stereospecific. The addition of bromine to cis and trans stilbenes[13,14] in relatively non-polar solvents exhibited approximately 90-100% trans stereospecificity. On increasing the polarity of the solvent the stereospecificity became less until in solvents with a dielectric constant of 35 or higher, the reaction became almost non-stereospecific, both isomers giving 80-100% mesodibromide. Added bromide ions improved the stereospecificity somewhat. It should be added that stilbene dibromides have been known to isomerise in the presence of bromine.[15]

Heublein[16] considered that in non-polar solvents the halonium ion was stabilised by partial intramolecular charge redistribution, whilst in more polar solvents the carbonium ion became more stabilised by solvation allowing free rotation. The end-product of addition was regarded as being determined by the sterically most favourable conformation of the intermediate.

The addition of bromine in acetic acid to ten ring and side-chain substituted styrenes[17] was found to proceed in a non-stereospecific manner, although trans-addition was favoured. Addition to cis and trans 2-butenes was completely stereospecifically trans and gave almost exclusively the dibromide as product. The percentage of trans addition product formed in

Table 2.3

Stereochemistry of Alkene Chlorination

Olefin	Solvent	% trans addition			% other products
		DiCl	2Cl3OR	3Cl2OR	
2-butene					
trans	Neat	98	-	-	2 (3-chloro-butene)
trans	HOAc	74	24	-	2 "
cis	Neat	97	-	-	3 "
cis	HOAc	54	43	-	3 "
cyclohexene	Neat	80	-	-	20 (3-chloro-cyclohexene)
Di-t-butylethylene					
trans	CCl_4	54	-	-	46 (4-chloro-2,3,5,5-tetramethyl-1-hexene)
cis	CCl_4	100	-	-	-
2-pentene					
trans	HOAc	76	10	13	1 (3-chloro-1-pentene)
trans	MeOH	16	35	49	0.5
trans	CF_3COOH	91	4	5	-
cis	HOAc	53	12	32	3
cis	CF_3COOH	83	7	10	-

the bromination of cis and trans β-methylstyrenes was shown to be solvent dependent.[18] The solvents used varied in polarity between dioxan and nitrobenzene, and the greatest variation in the stereochemistry of addition occurred for the cis olefin which ranged from 73% trans addition in acetic acid to 80% cis addition in dioxan. Again, the cis and trans 2-butenes formed exclusively dibromides stereospecifically and trans. It would therefore appear that bridged bromonium ions participated in the aliphatic systems but that weakly bridged (rather than open benzylic carbonium) ions participated in these aryl systems.

It has been suggested[19] that the solvation of cationic intermediates from alkylolefins was stronger than for the delocalised intermediates of arylolefins. This was reflected in the greater solvent incorporation in the products for the former. This viewpoint conflicts with the observations of Yates above.

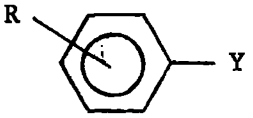
It has been shown that the bromination of cis and trans 1-phenylpropenes and trans anethole in carbon tetrachloride was also non-stereospecific.[20] Previously, the chlorination of cis and trans 1-phenylpropenes,[21] and trans methyl cinnamate[22] had been interpreted as forming resonance-stabilised benzylic cations as intermediates, which despite the greater ability of bromine to act as a neighbouring group also appeared to be involved in the bromination reactions.

Consequently, although a good deal of the stereochemical evidence indicated the existence of cyclic intermediates, there were a number of observations which suggested otherwise. It was because of these (and later the development of the potentiometric technique for measuring the fasterrates of bromination) that attempts were made to provide evidence of a non-stereochemical nature for the existence or otherwise of cyclic intermediates. A number of direct observations of cyclised species were described in Chapter 1, which, although indicating the existence of ring-closed structures, did not illustrate their participation as intermediates in the addition of halogens to olefins.

2.3 Kinetic Effects of Substituents

Since 1960 (before which it was only possible to measure the rates of halogenation of the slower-reacting olefins), several attempts have been made to correlate on a more quantitative basis the relationships between observed experimental reactivity and the structural effects of varied substituents which produce them.

In the 1930's Hammett[23] proposed a method of relating the effects of substituents R on the reactivity of a side-chain Y in benzene derivatives of the type 2.1, to the strengths of the corresponding substituted and unsubstituted benzoic acids. The relationshsip suggested was



2.1

$$\log(k/k_o) = \sigma\rho \qquad 2.2$$

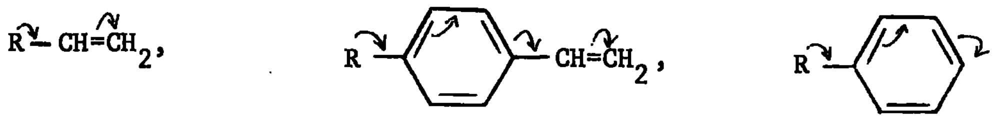
where k and k_o are rate or equilibrium constants for substituted and unsubstituted compounds respectively. σ is a substitution constant ($\equiv \log K/K_o$ where K_o and K are the acid dissociation constants of benzoic acid and the substituted acid) and ρ is the reaction constant, depending on the reaction concerning the side-chain Y.

Due to the limited application of the Hammett equation, particularly in the reactions of compounds with hyperconjugated substituents, Brown[24] proposed a new electrophilic substituent constant σ^+ in a modified Hammett equation.

$$\log k/k_o = \rho\sigma^+ \qquad 2.3$$

On the Hammett scale, reactions involving compounds with para substituents which exhibit hyperconjugation show a poor correlation, indicative of the degree of interaction between the para substituent and the electron-deficient reaction centre. Meta substituents, however, are in general well represented by the Hammett equation, and thus σ_M and σ_M^+ values agree. Hence, values of ρ are available, which in turn lead to values of σ_P^+.

It was noticed by de la Mare that a treatment of the above type could be applied to olefinic systems, since substituents behaved in similar ways in both olefinic and aromatic compounds, e.g. an electron-donating substituent.

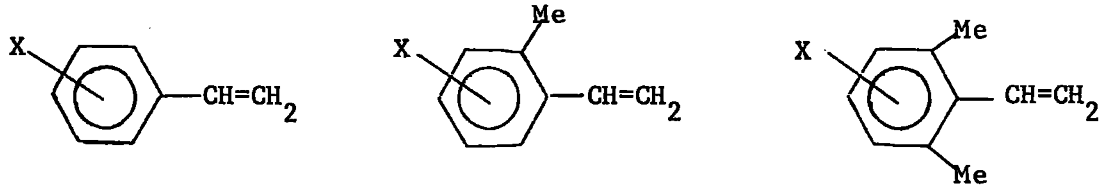


(2.2)

He[25] attempted a reactivity-structure correlation for the addition of chlorine to (a) β-substituted acrylic acids ($RR'C{=}CHCO_2H$) and (b) substituted trans cinnamic acids ($RC_6H_4CH{=}CHCO_2H$). Plotting $\log_{10}\frac{k_2\ \text{subst}}{k_2\ \text{unsubst}}$ against $\Sigma\sigma^+$ for (a) gives a good fit for only RR' = Me_2, MeH and HH, which had a slope of $\rho \approx -5.5$

De la Mare concluded that σ^+ constants provided very limited predictive information when extended from aromatic to structurally related olefinic systems.

Dubois et al, however, have since carried out extensive investigations into the bromination kinetics of olefins using their potentiometric[26] method of measurement. They have used several of the linear free energy relationships to correlate reactivity with structure. Early work[27] was concerned with the second-order rate constants for the addition of bromine in the presence of excess bromide ions to a series of substituted styrenes of the type:



(a) (b) (c)

(2.3)

Using the equation

$$\log k/k_o = \rho\,\Sigma\sigma^+ \tag{2.4}$$

reaction constants of -4.30 for all three types of compound for -X = -F, -Me, -OMe were obtained. This compared with the ρ value of -3.90 for the chlorination of substituted cinnamic acids.[25]

For the bromination of substituted 1,1-diphenylethylenes,[28] Brown's σ^+ values were found to overcorrect for resonance interactions and the plot of log k/σ^+ curved downwards, p-methoxy and p-methyl groups being more reactive than predicted. It was found that the Yukawa-Tsuno relationship[29] for reactions involving resonance stabilisation of a positive charge provided a good correlation.

$$\log k = \rho(\sigma + r\Delta\sigma^{+}_{R}) + \log k_{o} \tag{2.5}$$

where r = reaction constant indicative of the degree of resonance in the transition state

$\Delta\sigma^{+} = \sigma^{+}-\sigma$ (which..for 'well behaved meta substituents is zero)

A value of $\rho = -3.61$ was obtained which implied that less charge development occurred in the transition state for 1,1-diphenylethylenes than for 1-phenylethylenes. The low value of $r = 0.415$ indicated the reduced resonance interaction in the transition state relative to the bromination of styrene. This was believed to be due to the steric interference of the ortho hydrogens which was relieved by their twisting out of the plane of the double bond. Further investigations,[30] with substituents in the ortho position of one ring suggested that in the transition state, the unsubstituted ring favoured a position with a high degree of coplanarity with the carbon-carbon reaction centre.

Yates and Wright[31] studied the bromination of certain ring substituted styrenes in acetic acid by a spectrophotometric method. Their second-order rate constants showed a good correlation using σ substituent constants,[32] but were corrected later,[33] due to an oversight involving the spectrophotometric method of measurement. The corrected values gave a ρ value of -4.71 using σ^{+} constants,[24] as opposed to the former value of -2.24. Comparing the higher value with the ρ values for a series of reactions involving carbonium ions as intermediates whose ρ values were in the region of -4.2, the inference was made that the intermediate in the bromination reaction more resembled an open-ended carbonium ion than a cyclic bromonium ion.

The observed rate-constants of bromination of side-chain methyl-substituted styrenes in the presence of bromide ions using a potentiometric technique[34] indicated that there was no simple dependence of rate-constants on the number of methyl groups attached to the double bond which contrasted with the ethylenic systems. α-methyl substitution gave significant rate enhancement whilst β-substitution produced little effect, further indicating an unsymmetrical charge distribution in the transition state for bromine addition.

Meta and para substituted styrenes were also investigated. Separating the relative contributions of bromination by bromine and tribromide ion it was found that both k_{Br_2} and $k_{Br_3^-}$ correlated better with σ^+ than σ giving values of $\rho_{Br_2} = -4.21$, $\rho_{Br_3^-} = -2.02$. This was again regarded as an indication that in the transition state the majority of the charge was being developed at C_α in direct conjugation with the phenyl group. The lower ρ value for attack by the tribromide ion was consistent with its decreased electrophilicity and less cationic charge was developed at C_α in the transition state.

It was expected that highly deactivated styrenes would not permit easy dispersal of the charge developed on the α carbon atom and thus might require assistance from the neighbouring bromine. This was indicated by a ρ value of -4.5 for 3-fluoro, 3-chloro, 3-bromo-, and 3,4-dichlorostyrenes but $\rho = -2.0$ for 3-nitro- and 4-nitrostyrenes. Variation of charge distribution from styrene to styrene was thus illustrated.

A number of studies concerning the relative reactivities of bromine and tribromide ion as brominating agents have been carried out. In aqueous media, Kanyäev[35] reported that the ratio $k_{Br_3^-}/k_{Br_2}$ decreased as olefin reactivity increased. This was not observed by Bell,[36] who found no particular correlation. Dubois[37] examined ten alkenes and alkenols in methanol and water and found that for $16 \leq Q < \infty$ in methanol and $1.5 \leq Q < \infty$ in water (where $Q = k_{Br_2}/k_{Br_3^-}$), the overall rate constant k_{obs} was proportional to k_{Br_2} to within an uncertainty of 0.5 log units.

In certain instances it has been observed that the ratio $k_{Br_3^-}/k_{Br_2}$ was greater than unity, e.g. for the more deactivated styrenes,[34] diethyl fumarate and isobutene.[36] This is hard to understand if it is accepted that reaction occurs by electrophilic attack by bromine and tribromide to give the same positively-charged intermediate. It is difficult to envisage that the tribromide ion would be a stronger electrophile than the bromine molecule, which is the implication of the above observation.

As an alternative for reactions in water, Kanyaev[35] linked the proportions of dibromide and bromohydrin in the products, supposing that the former was formed by reaction with tribromide ion and the latter by reaction with the bromine molecule.

Hence the following relationship should hold

$$\frac{[SBr_2]}{[S(OH)Br]} = \frac{k_{Br_3^-}[Br_3^-]}{k_{Br_2}[Br_2]} = \frac{K.k_{Br_3^-}[Br^-]}{k_{Br_2}} \qquad 2.6$$

However, the product ratio predicted by the above equation and the observed ratio did not agree for the deactivated styrenes,[34] allyl alcohol, propene, diethyl fumarate,[36] and for the bromination of stilbene.[38]

More recently, it has been suggested by Dubois[39] that in bromination reactions in the presence of bromide ions there exist two competing mechanisms associated with the bromide ions, namely

(a) electrophilic attack by tribromide ion on the substrate

(b) slow nucleophilic attack by bromide ion on the charge transfer complex between bromine and the olefin.

The reaction scheme was expressed as,

$$>C=C< + Br_2 \xrightarrow{k_{Br_2}} \text{products} \tag{2.7}$$

$$>C=C< + Br_2 + Br^- \xrightarrow{k_{Br^-}} \text{products} \tag{2.8}$$

the overall rate constant was expressed by,

$$- k_{obs} \frac{(1 + K[Br^-])}{k_{Br_2}} = 1 + B[Br^-] \tag{2.9}$$

where B - the 'catalytic coefficient' - was expressed by

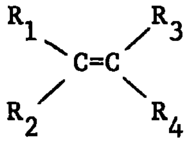
$$B_{Br^-} = a + \frac{k_{Br^-}}{k_{Br_2}} \tag{2.10}$$

where a = coefficient of the exponential of the primary salt effect on k_{Br_2}.

Plotting k_{Br_2} against B resulted in a curve of positive slope for the more reactive olefins studied which became negative for the less reactive olefins. The inversion of the slope was interpreted as illustrating that at high reactivity mechanism (a) predominated whilst at low reactivity mechanism (b) took over. Thus at low reactivity the assistance effect of bromide ions was more important than the electrophilic addition of both bromine and tribromide ion, with the tribromide ion always being less reactive than the bromine molecule.

Since his initial work on the bromination of arylolefins, Dubois has published a considerable quantity of material dealing mainly with the application of linear free energy relationships to olefinic systems in general, of which only a sample will be mentioned.

For a series of compounds



where R = alkyl or H

(2.4)

Dubois[40] illustrated the absence of hyperconjugative effects by use of the Ingold-Taft[41] relationship, separating inductive and steric effects

$$\log k = \log k_o + \rho^* \Sigma\sigma^* + \delta\ \Sigma\ E_s \qquad 2.11$$

where ρ^* is the reaction polar constant and $\sigma^*$is the reaction steric constant.

Using the overall rate constants (k_{obs}), all thirteen substituents showed a good fit and values of $\rho^* = -5.299$ and $\delta = 0.914$ were obtained, illustrating the absence of conjugative effects.

The above treatment was also used to examine the difference in rates between cis and trans isomers of the type $R_1CH{=}CHR_2$, where R = alkyl.[42] The separation of the polar and steric effects in both the ground and transition states was discussed.

An appraisal of the work on 72 olefins[43] of the above type lead to the conclusion that additivity of the effects of simple substituents applied, but that large interactions occurred if polar or steric effects were present together. In general, trans isomers were less reactive than cis isomers due to steric twisting, and steric interactions were very important for gem-disubstituted compounds.

The investigation of the effects of hetero-atoms was extended from aromatic species[27,44] to aliphatic systems of the type CH_2=CH-CHXX'.[45] The reactions were carried out in methanol and the overall rate constants were used in the relationship.[41]

$$\log k = \log k_o + \rho^* \sigma^* \qquad 2.12$$

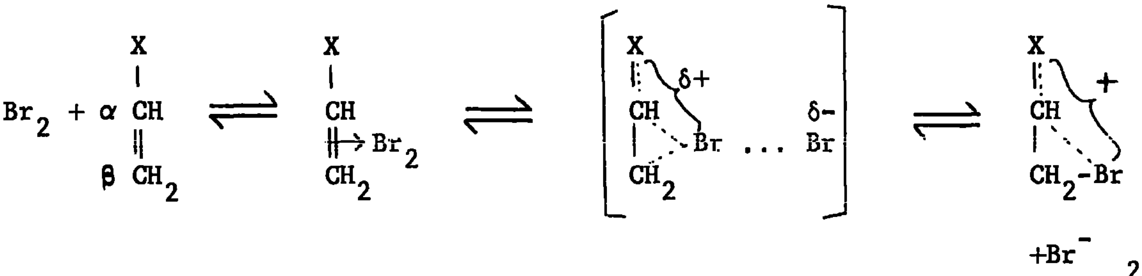
It was noted that the substituents -OH, -$OCOCH_3$, and -CN did not fit into the above treatment due to interaction with the solvent, probably by hydrogen bonding which modified the inductive effect of the substituent. A new set of substituent constants (σ^*_{MeOH}) were proposed based on work by Taft,[46] taking into account the effect of hydrogen bonding on the substituent. A much better correlation resulted, giving a reaction constant value of -2.9 as opposed to -2.4 using the unmodified substituent constants.

A number of other authors have discussed the effects of β-heteropolar groups. The second-order rate constants for the addition of bromine, k_{Br_2} and $k_{Br_3^-}$ have been determined for acrylamide, methyl acrylate, methyl methacrylate and methyl crotonate in water.[47] The overall rates of reaction were in the order methacrylate > crotonate > acrylate, which concurred with the values obtained by Bell for ethyl acrylate and crotonate.[36] As expected for an electrophilic reaction, the methyl group enhanced reaction for addition by both bromine and tribromide ion, being slightly more effective in the α-position than the β-position indicating an unsymmetrical transition state. Acrylamide was found to be faster than methyl acrylate, the above order being supported by the observed activation energies. The third-order rate constants in acetic acid[48] exhibited the same behaviour, methacrylamide > acrylamide >> n-butylmethacrylate > crotonic acid.

The bromination of acrylic and crotonic acids[49] was examined at 25°C in water. Rate constants for attack by bromine and tribromide ion on both the undissociated acid and the anionic forms were calculated and althagh crotonic acid reacted more rapidly, no reaction was detected between either anion and the tribromide ion, or between the undissociated acrylic acid and either brominating agent.

Table 2.4 is a summary of the rate constants measured by Bell[50] at 25°C in aqueous solution. The $\Sigma\sigma^*$ values were used to show an approximate correlation, since a number of the compounds exhibited resonance and steric effects.

Investigations concerning the effect of directly conjugated substituents in compounds of the type $CH_2{=}CH{-}X$ were performed to look into the charge distribution in the transition state.[51] For an activating group conjugated to the double bond, the reaction path expected was,



2.13

The effects of substituent α- and β- methyl groups were investigated, since the charge densities at C_α and C_β were expected to be different, due to the directly conjugated -X group. It was observed that the effect of a β-methyl group was much less than the effect of an α-group supporting the postulate of a large unsymmetrical charge distribution.

Table 2.4[50]

Second-order Rate Constants for the Bromination of Olefins in Aqueous Solution at 25°C

Olefin	k_{Br_2} (l.mole^{-1}sec^{-1})	$k_{Br_3^-}$ (l.mole^{-1}sec^{-1}	$\Sigma\sigma^*$
Diethyl fumarate	3.40×10^{-5}	3.72×10^{-4}	(4.98)
Diethyl maleate	3.60×10^{-5}	5.20×10^{-5}	4.98
3,3-dichloroallyl alcohol	6.5×10^{-3}	-	4.97
Ethyl acrylate	1.06×10^{-1}	6.7×10^{-2}	3.47
Ethyl crotonate	2.76	1.04	2.98
cis-3-chloroallyl alcohol	3.01	0.15	3.50
trans-3-chloroallyl alcohol	3.08	0.31	3.50
2-chloroallyl alcohol	65	9.9	3.50
Ethyl cinnamate	220	23	3.58
Allyl cyanide	440	100	2.77
Ethylene	3.9×10^{5}	2.0×10^{4}	1.96
Allyl alcohol	6.7×10^{5}	6.9×10^{4}	2.03
Propene	4.5×10^{6}	3.2×10^{5}	1.47

However, for -X = -OEt the effects of both α- and β-methyl groups were very weak, indicating remoteness from the charge centre, which was difficult to appreciate.

2.4 Effects of Solvent Variation

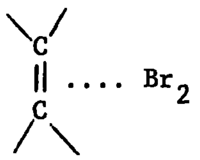
The examination of the effect of solvents on the rates of bromination of olefinic species has provided varied and valuable information.

The effect of solvent on the bromination of a number of branched and unconjugated alkenes and β-heteropolar compounds was investigated for a large range of reactivity in methanol and water[52] solvents. The structural effects were almost independent of solvent except for substituent groups $-CH_2OH$ and $-CH(OCOCH_3)$ where considerable solvent-substituent interaction was observed. Earlier work,[53] had been confined to a series of unhindered compounds containing no heteroatoms in water, methanol and methanol-water mixtures. The absence of solvent-substituent interaction was illustrated by the approximately equal reaction constants in the different solvents.

For the reactions in methanol, use of σ^*_{MeOH} parameters provided a good fit. The greater rate of reaction in water than methanol is consistent with the generally accepted mechanism which would predict the greater solvent stabilisation of the transition state for the more polar solvent. In the compounds containing substituents which exhibited solvent-substituent interaction ($-CH_2OH$, $-CH(OCOCH_3)$), the electron-attracting effect was greater in water than methanol, probably due to the greater strength of the hydrogen bonding and not to the variation of the field effect by the influence of the dielectric constant.

It was concluded that the solvent modified the sensitivity of the double bond to substituents attached to the double bond very little.

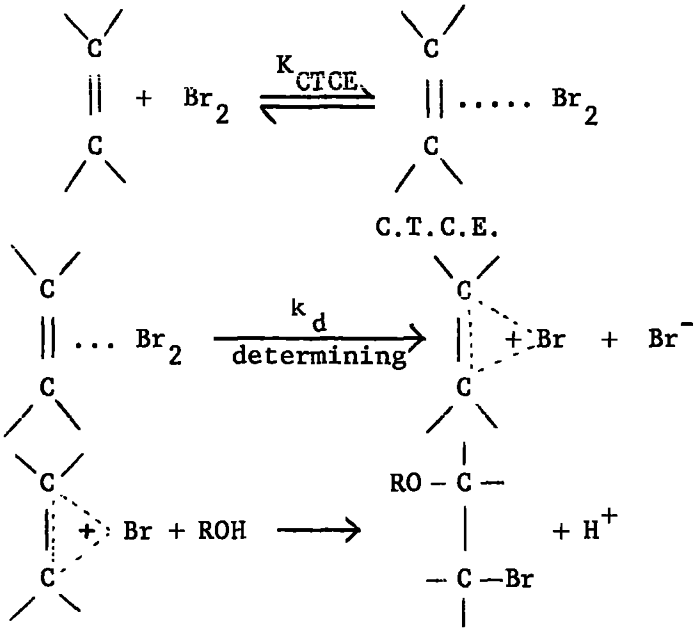
The variation of the rate of bromination of pent-1-ene in a series of solvents has been used to illustrate[54] the mode of reaction of transitory charge transfer complexes,



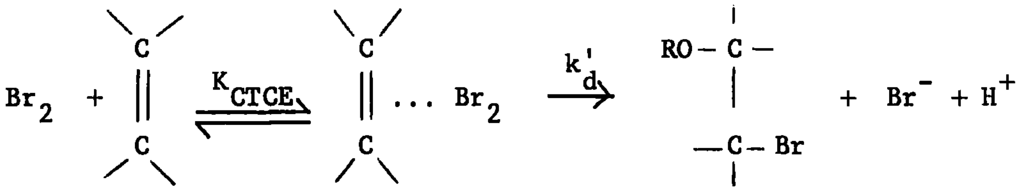
2.14

Dubois has put forward evidence[55] for the intermediacy of transitory charge transfer complexes by means of a spectrokinetic method which enabled consideration of the variation of the parameter Γ (the energy of interaction of the complex in the fundamental state), explaining the variable stability of the complexes.

It was observed that the rate of bromination of pent-1-ene was markedly dependent on the ionising power of the solvent. This was interpreted as indicative of a unimolecular ionisation (2.15) similar to that found in S_N1 reactions, as opposed to the simultaneous rupture of the bromine-bromine bond and attack by a nucleophile (2.16).



2.15



$$Br_2 + \begin{matrix}\diagdown\ \diagup\\ C\\ \|\\ C\\ \diagup\ \diagdown\end{matrix} \underset{}{\overset{K_{CTCE}}{\rightleftharpoons}} \begin{matrix}\diagdown\ \diagup\\ C\\ \|\\ C\\ \diagup\ \diagdown\end{matrix}\cdots Br_2 \xrightarrow{k_d'} \begin{matrix}|\\ RO-C-\\ |\\ -C-Br\\ |\end{matrix} + Br^- + H^+ \qquad 2.16$$

C.T.C.E.

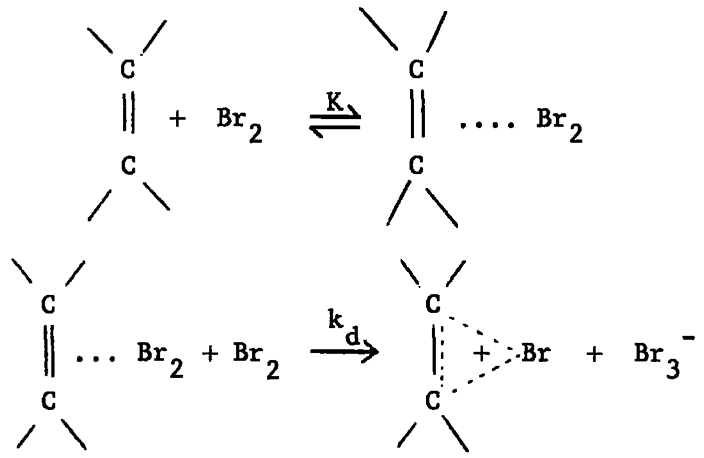
$$k_{2(obs)} = K_{CTCE} \times k_d \ (k_d') \qquad 2.17$$

The equilibrium constant K_{CTCE} was regarded as almost insensitive to solvent effects, and any variation was considered to be due to the solvent sensitivity of k_d (or k_d'). It was expected that the transition state in the S_N1 type unimolecular ionisation would be less bulky and more polarised than the bimolecular transition state, and therefore more sensitive to solvation. The plot of log $k_{2(obs)}/Y$ (the ionising power of the solvent) gave a slope of 1.16, whereas S_N1 and S_N2 reactions are known to give slopes of ~ 1 and ~ 0.3 respectively.[56]

Hence the unimolecular mechanism (2.15) was considered more probable.

In discussing the effects of solvent on the rates of bromination of olefins, it is appropriate to note the effect of bromide ions in acetic acid solvent. Bromide ions in water and methanol[35,50,57] were observed to decrease the rate of reaction. However, bromide ions catalysed the reaction in acetic acid.[58] Since the dissociation constant of acetic acid is 7.2×10^{-7},[59] very few free ions will be present, the majority being in the form of ion pairs. It has been suggested,[60] that attack by tribromide ions, significant in water and methanol, would be negligible in acetic acid because the formation of tribromide ions would be restricted by the bromide ions being involved in ion pairs. Calculations suggested that a large salt effect superimposed itself and displaced the tribromide equilibrium. It was also considered possible that the speed of nucleophilic attack could be slowed to such an extent to become rate-determining.

The observation of several authors that at higher bromine concentrations than M/40 in acetic acid, the reaction was second-order in bromine, has been commented upon by Dubois,[62] suggesting that the second molecule was involved in assisting the formation of the charge-transfer complex in the rate-determining step.



2.18

In conclusion, it should be stated that although a more quantitative investigation into the role of substituents has provided valuable and meaningful information, there have been serious difficulties in applying a general reactivity-structure correlation for halogen additions to all olefins. In simple systems where complicating hyperconjugative, steric and solvent effects are negligible, the treatments performed convey useful data. However, in the more complicated systems, where much is based on reasoned assumption, the applicability of the conclusions must be regarded with more caution.

Although substituent effects have not provided conclusive evidence for any one particular mechanism, they have shown that there exist considerable differences in the form of the intermediates produced in addition reactions. The interpretations are, however, only qualitative, but the unsymmetrical nature of the transition state has been illustrated in a number of cases.

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CHAPTER 3

NEIGHBOURING GROUP PARTICIPATION[1]

3.1 Introduction

In the previous chapter the effects of substituent groups or atoms on the reactivity of certain olefins have been considered. The variation of the rates of halogenation was discussed in terms of the electronic influence of the substituents on the double bond and on the stability of any intermediate as a result of this polar nature.

However, systems have been investigated in which substituents affect the kinetics, products and stereochemistry of reactions by becoming bonded or partially bonded to the reaction centre in the transition state and sometimes as intermediates. These reactions exhibit neighbouring group participation sometimes termed intramolecular catalysis.

In reactions where the rate is enhanced by bond formation in the transition state, partial or otherwise, the participating substituent is said to afford anchimeric assistance to the reaction. The effect of bond formation is to stabilise the transition state and thus facilitate the rate of reaction. Substituents which stabilise transition states other than the one involved in the rate determining step may affect the composition of the products but not the rate of reaction.

Although evidence for the existence of neighbouring group participation has been conveniently detected by means of enhanced kinetics and the formation of cyclised or rearranged products, it is often difficult to measure quantitatively the amount of participation, because of problems in estimating what the behaviour of the reaction would be if participation did not occur. Estimates have been made using the unsubstituted reactant, but care must be taken to separate the effect which the substituent exerts because of its polarity from its effect via anchimeric assistance. This separation has been attempted for several systems by means of one of the linear free energy relationships devised by Hammett, Brown, Taft or Yukawa-Tsuno, depending on the reaction involved.

In his studies into participation by methoxyl groups in solvolysis reactions, Winstein[2] utilised three rate constants, k_Δ the rate constant for the anchimerically assisted ionisation, k_s the rate constant for the anchimerically unassisted ionisation and k_c the rate constant for an idealised reaction involving neither anchimeric assistance nor solvent participation.

3.2 Neighbouring Group Participation by Oxygen and Halogen Atoms in Solvolysis and Addition Reactions

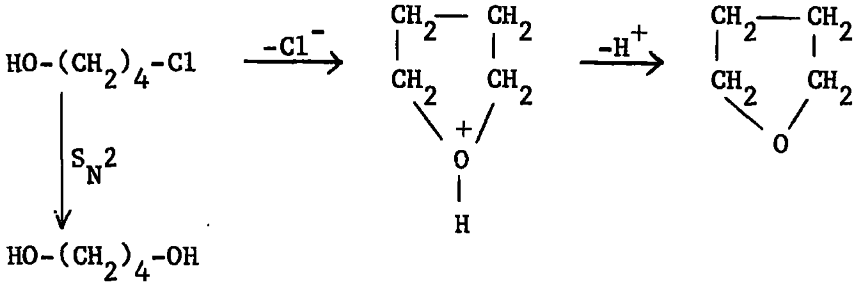
Although participation by neighbouring groups has been observed for a number of types of reaction, the most common occurrence is the neighbouring group acting as an intramolecular nucleophile. One of the first reactions which was found to react in this manner was the hydrolysis in water of a series of w-hydroxyalkyl halides $Cl(CH_2)_nOH$.[3]

Table 3.1

Rates of Hydrolysis of the Series $Cl(CH_2)_nOH$ in Aqueous Solution at 70.5°C

n	2	3	4	5
10^5k (min^{-1})	1.82	7.79	1710	70

Analysis of the products found that for ethylene chlorohydrin and propylene chlorohydrin, no ethylene oxide nor propylene oxide was formed. The products were entirely the respective glycols indicating that the reaction was consistent with an S_N2 attack by water as previously proposed.[4] For the hydrolysis of butylene chlorohydrin, a 73% yield of tetrahydrofuran was obtained further supporting the kinetic evidence for the participation of the hydroxyl group in the formation of the transition state through a cyclic intermediate.



3.1

Accompanying thermodynamic data suggested that the entropy of activation for n = 4 was greater than for n = 2. This was attributed to the lower degree of solvation of the cyclic transition state by water molecules in comparison with the solvation of the transition state containing a free hydroxyl group.

Examples of participation involving cyclisation have been observed most readily for reactions where the formation of five-membered rings containing an oxygen atom has been possible. In general terms, the factors affecting ring closure are interdependent. The entropy loss on cyclisation becomes greater as the length of the carbon chain increases. Enthalpy factors are also affected by the length of the carbon chain due to variation in the strain energy involved in ring closure. The strain decreases progressively in going from three- to six-membered rings, increases for seven-, eight- and nine-membered rings and decreases for those of larger size. It should be mentioned that the participating group can affect the behaviour of the leaving group. Usually, both the participating and leaving groups are electron-attracting and have the effect of reducing the nucleophilicity of each other. This effect becomes much less important as the length of the carbon chain increases. It has been found that preferential formation of five-membered rings occurs, particularly for those involving intramolecular attack on a saturated carbon atom by an oxygen or nitrogen atom. There are, however, cases where participation of six-membered rings has been observed, such as the solvolysis of 5-methoxy-1-pentyl p-bromobenzenesulphonate in acetic acid and formic acid.[5] Participation involving three-membered cyclic systems is, however, far less common.

Winstein[6] has studied the role of a number of neighbouring groups in replacement reactions. Having discussed qualitatively the effects of α- and β-methyl substitution, a semi-quantitative treatment was proposed which enabled the calculation of the free energy of activation contribution of the neighbouring group to the overall free energy of activation taking into account the inductive effect of the substituents. This was regarded as the driving force of neighbouring group participation (λ_o).

Table 3.2

Values of Driving Force λ_o for Neighbouring Groups in β-Substituted Ethyl Compounds

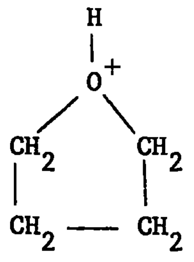
Neighbouring Groups	$-CH_2CH_2OH$	-I	$-NH_2$	$-O^-$	-Br	$-OH, -OCH_3$
λ_o (kcal/mole)	13	8.7	8	6	4.5	1.3

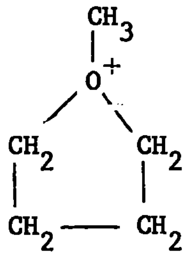
Several examples of participation by oxygen containing groups have been illustrated in the literature, in addition to the hydrolysis of w-hydroxyalkyl halides. These included oxygen atoms contained in acid, ester and amide groups.[7]

More recently, the role of participation by oxygen in reactions involving cyclisation has been questioned.[8] It has generally been accepted that the oxygen-containing entity participates in the reactions under consideration but whether cyclic intermediates or cyclic transition states are formed has been a subject for discussion.

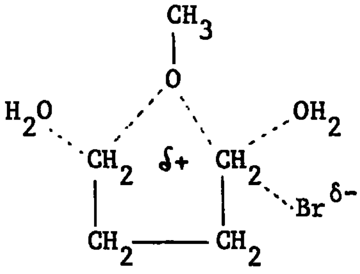
A Bronsted catalysis law plot[9] for the formation of tetrahydrofuran from 4-chlorobutanol in the presence of three different bases - water, borate ion, hydroxyl ion - indicated that the transfer of the alcoholic proton was about 25% complete in the transition state.

However, although tetrahydrofuran was the sole product of the hydrolysis of 4-chloro-1-butanol,[8] the absence of a primary deuterium isotope effect when the reaction was performed in deuterated water was inferred to indicate that the oxygen-hydrogen bond did not undergo significant rupture during the activation process. The absence of methanol and tetrahydrofuran products in the hydrolysis of 4-bromo-butyl methyl ether was quoted in support of the above, and casting doubt on the role of intermediates (3.1) and (3.2).


(3.1)


(3.2)

However, the hydrolysis of 4-methoxy[1-^{13}C] butyl bromide yielded 4-methoxybutanol with the label scrambled equally between C_1 and C_4. It was inferred that at some stage a symmetrical transition state such as (3.3) was involved which could collapse to form either oxygen-methylene bond.



(3.3)

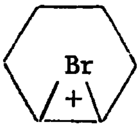
It would appear that the bromide ion was sufficiently removed in the transition state so that it afforded no protection to attack by water. If such protection were important, methoxyl migration would be expected to be greater than 50%. Thus it was concluded that for hydrolysis in water an ionic intermediate was not a necessary concomitant of anchimeric assistance.

In a less nucleophilic solvent, acetic acid, the existence of ion pairs becomes more significant. For the acetolysis of 4-methoxy-1-pentyl- and 5-methoxy-2-pentyl-p-bromobenzene sulphonates[10] two varieties of o-methyl-2-methyltetrahydrofuranium ion pairs as well as the dissociated ion were identified as common intermediates. It was considered that the amount of product resulting from the intimate ion pairs was unimportant, the majority being formed from the solvent-separated species.

Thus, although there is general acceptance that neighbouring groups do play a significant role in the above reactions, there is some difference of opinion concerning the precise nature of the mechanism.

It is of interest to mention the involvement of substituent halogens in reactions exhibiting neighbouring group participation. Reactions have been postulated to proceed via three-, four-, five- and six-membered rings due mainly to the observed enhancement of rates and the configuration of some of the products.

1,2 participation[11] was invoked to explain the differences in rates of acetolysis of cis and trans 2-bromocyclohexyl p-bromobenzenesulphonate. The rate of reaction of the trans isomer was noticeably faster than for the cis isomer, which was regarded as being unassisted. The trans isomer also deviated from the $\sigma^+\rho^+$ correlation for cyclohexyl p-bromobenzene sulphonates.[12] Intermediates of the type (3.4) were considered to be



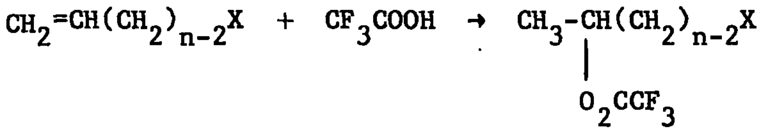
(3.4)

involved. It should be added that trans 2-chlorocyclohexyl p-bromobenzene sulphonate did not react abnormally fast in acetic acid, again illustrating the greater tendency of bromine to be involved in cyclisation reactions.

Three-membered cyclic halonium ions have been postulated in the conversion of 3-chloro-2-butanol to 2,3-dichlorobutanes,[13] and in the formation of 1,2-dibromocyclohexanes from various starting materials.[14] These interpretations quickly followed the original postulate of cyclic halonium ion intermediates in the addition of halogens to olefins.[15]

An extensive series of investigations has been performed by Peterson and co-workers into the addition of various solvents to a number of branched, unbranched and cyclic olefinic compounds, acetylenes and also some branched and unbranched alkyl tosylates and brosylates. The majority of the work has involved the addition of acetic, formic and trifluoroacetic acids. Evidence for the participation of halogens resulted mainly from kinetic and product studies.

The reactions carried out in trifluoroacetic acid have provided surprising data concerning the inductive effects of added substituents. Substituents separated from the reaction centre by as many as ten carbon atoms have been postulated to affect the rates of reaction[16] for the addition of trifluoroacetic acid to a series of substituted olefins $CH_2{=}CH(CH_2)_{n-2}X$.



$$CH_2{=}CH(CH_2)_{n-2}X + CF_3COOH \rightarrow \underset{\displaystyle O_2CCF_3}{CH_3{-}CH}(CH_2)_{n-2}X \qquad 3.2$$

where n = 4 → 11

It is illustrated (Table 3.3) that the deactivating effect of the substituent -X (= $-O_2CCF_3$, -CN and -Cl) influenced the reaction centre even when n = 11. The rate of addition to the substituted olefin containing eleven carbon atoms was less than the rate of addition to the corresponding unsubstituted olefin. This behaviour was attributed to the solvent enhancement of the inductive effect via hydrogen bonding which was particularly evident in trifluoroacetic acid.

Inspection of the above data also revealed the enhanced rate of reaction in the chloro-substituted olefin for n = 5. This was attributed to participation by the chlorine atom, enabling the formation of a five-membered cyclised transition state.

Table 3.3

Rates of Addition of Trifluoroacetic Acid to Alkenes

$CH_2=CH(CH_2)_{n-2}X$ at 60°C

	$k \times 10^6 sec^{-1}$					
n/X	-H	$-O_2CCF_3$	-CN	$-O_2CCH_3$	-Cl	$-OCH_3$
4	1200	0.263	-	2.62	2.85	4.57
5	1140	7.30	5.33	29.1	217	185
6	1470	45.6	23.8	90.0	175	205
7	1540	166	110	249	308	293
8	1680	377	298	582	708	568
9	1640	655	-	-	853	951
10	1840	1030	-	-	-	-
11	1590	1060	983	-	1250	-

In his treatment illustrating participation, Peterson assumed that for compounds showing no participation, the inductive effect fell off by a constant factor (ϵ) per methylene group between the substituent and the reaction centre.

The inductive effect was defined as

$$\log k_H - \log k_x = \Delta \log k \qquad 3.3$$

where k_H = rate constant for the unsubstituted alkene

k_x = rate constant for the substituted alkene

For comparison of olefins of different chain lengths

$$\Delta \log k_n = \epsilon^{n-m}(\Delta \log k_m) \qquad 3.4$$

where n and m are the number of carbon atoms in each of the two chains.

Taking logs

$$\log \Delta \log k_n = (n-m) \log \varepsilon + \log \Delta \log k_m \qquad 3.5$$

Plotting $\log \Delta \log k_n$ against (n-m) or the number of carbon atoms in the chain, ε was determined from the slope. Plots of this nature were also an indication of the degree of substituent participation.

Reactions involving participation usually exhibited rates much faster than the above procedure predicted, thus providing an estimate of the difference between the observed rate of reaction and that expected if participation did not occur.

Early interest in the behaviour of reactions in trifluoroacetic acid had been stimulated by the observed unreactivity of 5-hexen-2-yl trifluoroacetate to trifluoroacetic acid. A study[17] of the first-order rate constants for the addition of trifluoroacetic acid to a series of 5-substituted 1-hexenes showed large rate decelerations with acetoxy, trifluoroacetoxy and cyano substituents and relatively small rate effects of approximately equal magnitude for chloro, bromo, iodo and methoxy substituents.

The large rate decelerations for acetoxy, trifluoroacetoxy and cyano groups indicated that inductive effects were larger than expected. These were attributed to the strong hydrogen bonding between the trifluoroacetic acid solvent and the substituents.

The strong interaction of trifluoroacetic acid with the substituents leading to enhanced inductive effects was supported by the n.m.r. studies of Taft.[18] The modified shifts of m-substituted fluorobenzenes in trifluoroacetic acid were used to form a new series of electrophilic substitution constants in which the values for oxygen and nitrogen containing substituents were much increased.

Table 3.4

Rates of Addition of Trifluoroacetic Acid to 5-substituted-1-hexenes

Substituent	35°C $k \times 10^6$, sec^{-1}	60°C $k \times 10^6$, sec^{-1}	35°C k_H/k_x
-H	235	1470	1
-Cl	60.3	356	3.90
-Br	73.3	439	3.21
-I	72.2	420	3.26
$-OCH_3$	63.0	502	3.75
$-O_2CCH_3$	5.60	45.1	42.0
$-O_2CCF_3$	1.12	8.79	192
-CN	0.39	4.72	602

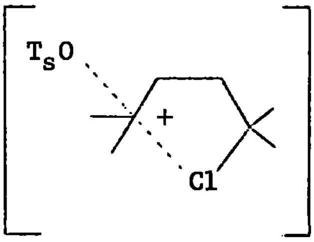
The observation of rate effects of a similar order for chloro, bromo and iodo substituents forming five-membered rings contrasted with that for the acetolysis of trans-2-halocyclohexyl brosylates[12] where the reaction was postulated to proceed via a three-membered cyclic intermediate and the order of reactivity was I >> Br >> Cl.

There have been several other examples of participation via cyclised five-membered halonium ion species. 1,4 chlorine shifts have been observed in the addition of trifluoroacetic acid to 5-chloro-1-pentyne[19,20] and 5-chloro-1-hexene-5-d,[21] and in the solvolysis of 5-chloro-2-hexyl tosylate,[22] 5-chloro-1-hexyl nosylate[23] and 4-chloro-1-pentyl nosylate[24] in trifluoroacetic acid. 1,4 bromine participation has been observed in the solvolysis of 4-bromobutyl-1,1-d_2 nosylate[24] in acetic acid.

More recently, an example of 1,3 participation has been cited[25] in the solvolysis of 3-halo-1-butyl trifluoromethanesulphonates in trifluoroacetic acid. Participation tendencies decreased in the sequence I > Br > Cl, that for the chloro substituent being very small.

Peterson and Bopp[26] also claimed the existence of fluoronium ion intermediates in the reaction of trifluoroacetic acid with 5-fluoropentyne and 5-fluoro-2-pentyl tosylate. The latter was based on a value of 2.4 for k_{Δ}/k_{s}, the ratio of the rate constants for the participation reaction and the estimated unassisted reaction.

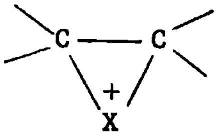
The observed reactivity for participation involving five-membered rings was found to be $F \leq Cl \cong Br \cong I$. It was suggested[22] that in ions such as (3.5) the weak C...X-R interaction could be regarded as analogous



(3.5)

to hydrogen bonding of the type H...X-R, where the stability order is F >> Cl > Br > I. This would indicate that fluorine should participate more rapidly than any of the other halogens. Inspection of models indicated that the short carbon-fluorine bond would fail to come within a covalent bonding distance of the incipient carbon atom in an ion such as (3.5). This latter factor was expected to be overriding and would explain the slight participation by fluorine.

In contrast, reactions exhibiting 1,2 halogen shifts were thought[22] to preclude weak participation and to form transition states approaching the form (3.6).



(3.6)

These were considered more energetically feasible for the larger, more polarisable halogen atoms.

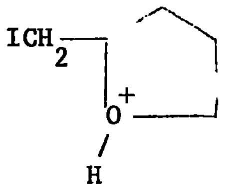
By means of a treatment similar to that of Peterson, Williams et al have investigated the electrophilic addition of halogens (bromine and iodine) to a series of olefins in methanol and water solvents. The initial work concerned the iodination[27] of a series of alcohols $CH_2=CH(CH_2)_nOH$ in aqueous potassium iodide solution at 0°C. Measurement of initial rate coefficients showed a greatly enhanced rate of addition for n = 3 and a smaller rate enhancement for n = 4. Subsequent product analysis for n = 3 showed that the ring-closed species 2-iodomethyltetrahydrofuran was the sole product.

Table 3.6

Second-order Rate Coefficients for the Iodination of the Series $CH_2=CH(CH_2)_nO$ in Potassium Iodide Solution at 0°C

n	1	2	3	4
k_2 ($l.mole^{-1}min^{-1}$)	0.011	0.023	2.2	0.38

The above data suggested hydroxyl participation via intermediates (3.7) and (3.8).



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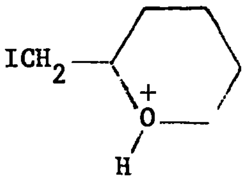
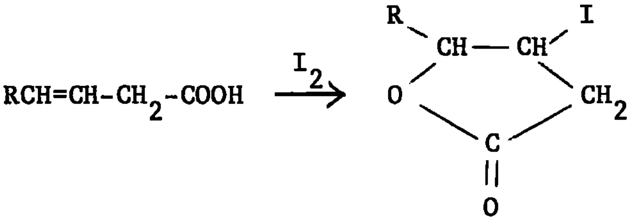


(3.8)

Previous evidence from product analyses has illustrated the formation of cyclic products in addition reactions, e.g.

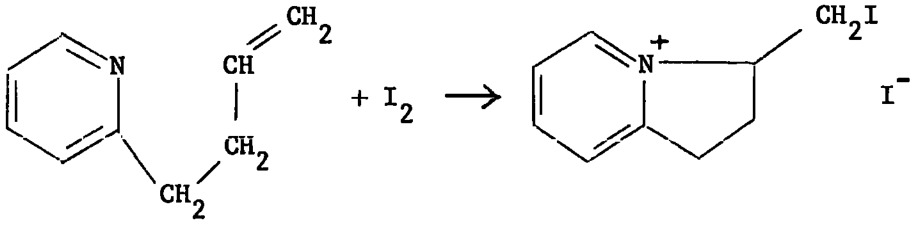
(i) the formation of iodolactones from olefinic acids[28]



3.6

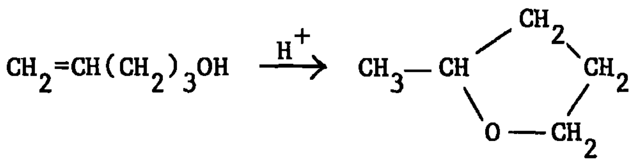
and also their sodium salts.[29] Chloro- and bromo- β-lactones have been formed from maleic acid,[30]

(ii) in the reaction of the following mono-substituted pyridine.[31]



3.7

(iii) in the reaction of strong acid with unsaturated alcohols.[32]



3.8

Participation to a lesser degree was also illustrated by kinetic and product data for the bromination in the presence of sodium bromide of the series of alcohols $CH_2=CH(CH_2)_nOH$ in both water and methanol solvents at 25°C.[33]

Table 3.7

Rate Coefficients for Bromination of Olefinic Alcohols[33]

k_2 (l.mole^{-1}min^{-1})

Olefin	(MeOH)	(H_2O)
$CH_2=CHCH_2OH$	284 ± 4	1.36×10^7
$CH_2=CH(CH_2)_2OH$	525 ± 4	$6.9 \times 10^7 \pm 0.2 \times 10^7$
$CH_2=CH(CH_2)_3OH$	2630 ± 50	$31 \times 10^7 \pm 1.4 \times 10^7$
$CH_2=CH(CH_2)_4OH$	1730 ± 30	$37 \times 10^7 \pm 1.5 \times 10^7$

Analysis of the products showed the presence of ring-closure for the alcohols where n = 3 and 4.

Table 3.8[33]

Proportion of Ring-closed Product Detected (%)

Olefin	(MeOH)	(H_2O)
$CH_2=CH-CH_2OH$	None	None
$CH_2=CH(CH_2)_2OH$	None	-
$CH_2=CH(CH_2)_3OH$	50-60	50-60
$CH_2=CH(CH_2)_4OH$	5-10	-

The bromination reactions were carried out at different bromide ion concentrations, thus enabling the individual contributions of bromine and tribromide ion to the overall rate of bromination to be calculated.

Table 3.9[33]

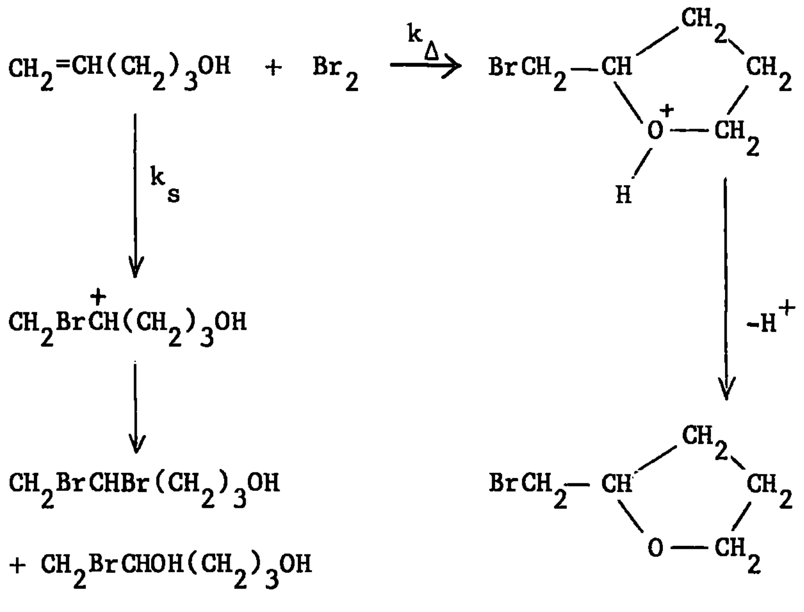
Individual Rate Constants for the Bromination of

Olefinic Alcohols $CH_2=CH(CH_2)_nOH$ at 25°C

	n = 1	n = 2	n = 3	n = 4
k_{Br_2} $(l.mole^{-1}min^{-1})$	3.95×10^3	6.74×10^3	5.09×10^4	2.31×10^4
$k_{Br_3^-}$ $(l.mole^{-1}min^{-1})$	1.89×10^2	3.51×10^2	1.28×10^3	1.12×10^3

Participation by the hydroxyl group, illustrated by inspection of the kinetic data, was demonstrated by means of the treatment used by Peterson[22] which assumed a linear fall-off of the inductive effect of the substituent with distance from the reaction centre. Using the overall rate constant k_2 to calculate $\log(\Delta \log k_n)$, the resulting graph indicated that the rate constant observed for n = 3 and 4 was much larger than that expected on grounds of the linear diminishing of the inductive effect with distance.

It was proposed that the data could be interpreted in terms of a concurrent reaction by both assisted and unassisted pathways, where k_Δ was the rate coefficient for the assisted reaction and k_s was the rate coefficient for the unassisted reaction.


3.9

Although the intermediate in the unassisted reaction was written as a bromocarbonium ion, it was not meant to indicate a preference for that ion over a cyclic bromonium ion intermediate.

Using a value of ε calculated for the equivalent bromide series,[35] a value of k_Δ/k_s = 1.53 (predicting 60% ring-closed product) was calculated for the bromination of 4-penten-1-ol in methanol, whereas k_Δ/k_s = 0.16 (predicting 14% ring closure) was calculated for the bromination of 5-hexen-1-ol in the same solvent. This compared with observed values of 50-60% and 5-10% respectively.

For the bromination in water, a value of ε = 0.58 was calculated from the first two alcohols giving no assistance, an indication that the inductive effects were less rapidly attenuated in the more polar solvent of higher dielectric. This led to a prediction of 42% ring-closed product, compared with the 50-60% observed.

In contrast, the degree of participation exhibited for the bromination (in methanol) and iodination (in water) of the series $CH_2=CH(CH_2)_nBr$ for n = 1 → 4 was much less than for the corresponding alcohols.[35]

An attenuation plot for the bromination reaction showed that there was no rate enhancement over that expected on polar grounds. Although no attenuation plot was done for the iodination reaction because of the unavailability of rate data for the unsubstituted compounds, the rate maximum when n = 3 indicated some degree of assistance by the neighbouring bromine atom.

The attenuation plot for the bromination reaction used the rate coefficient k_{Br_2} as opposed to the observed composite rate coefficient k_2, since the ratio

$$Q = \frac{k_{Br_2}}{k_{Br_3^-}}$$

was not always between the limits $\infty > Q > 16$,[34] rendering k_2 unreliable as an individual rate constant.

Table 3.10

Variation of Rate Coefficients for Bromination of Olefins

$CH_2{=}CH(CH_2)_nBr$ in Methanol at 25°C

	n = 1	n = 2	n = 3	n = 4
k_{Br_2} $(l.mole^{-1}min^{-1})$	7.03	594	5710	15700
$k_{Br_3^-}$ $(l.mole^{-1}min^{-1})$	1.23	58.8	362	763
Q	5.7	10	16	21

Plotting log Δ log k/n as described by Peterson,[26] a good straight line was obtained indicating the absence of participation, the slope of which yielded a value of ϵ = 0.43. Use of the composite rate coefficients gave a value of ϵ = 0.42.

Inspection of Table 3.11 indicated the slight participation via neighbouring bromine in the iodination of 5-bromopent-1-ene.

Table 3.11

Second-order Rate Coefficients for the Iodination of $CH_2{=}CH(CH_2)_nBr$ in Aqueous Potassium Iodide Solution (7.7 x 10^{-3}M) at 20°C

n	k_2 ($l.mole^{-1}min^{-1}$)
1	$4.2 \times 10^{-2} \pm 0.2 \times 10^{-2}$
2	$6.8 \times 10^{-1} \pm 0.1 \times 10^{-1}$
3	3.3 ± 0.15
4	2.3 ± 0.1

However, the participation by bromine in both bromination and iodination reactions involving five- and six-membered ring systems was much less marked than for the corresponding alcohols. As commented previously, the expected order of stability for intermediates of the three-membered halonium ion ring type was OH, OR >> I >> Br >> Cl >> F, and this would appear to be true for five- and six-membered ring systems for halogenation reactions in hydroxylic systems. This observation is in contrast with that of Peterson,[22] where the observed order of participation for the addition of trifluoroacetic acid was Cl $\sim$ Br $\sim$ OR.

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CHAPTER 4

THE PRESENT WORK

A. Substituent Effects

4.1 Introduction

The considerable quantity of work by a great number of researchers - Chapter 2 - has provided invaluable data on the rates of addition to olefins with as yet no complete picture of the detailed mechanism of reaction. The majority of these data have been based on the effect of substituent groups on either the kinetics or products of the reactions involved.

In studying the kinetic effects of substituents the behaviour of halogens has been shown to influence reactions by both the electron-withdrawing -I effect and the electron-releasing +M effect depending largely on the position of the substituent halogen.

The above effects are illustrated by the observed partial rate factors in which the halo-substituent is in a position para to the position of attack in electrophilic aromatic substitution reactions. Although halogen substitution in the aromatic molecule reduces the rate of electrophilic substitution with respect to the unsubstituted aromatic substrate, it can be seen from Table 4.1 that for bromination, chlorination, acetylation and mercuration reactions, a substituted fluorine atom activates the position para to the substituent to electrophilic attack.

The deactivating -I effect of halo substituents on olefinic compounds involved in electrophilic addition reactions is illustrated by comparison of the second-order rate constants for the addition of bromine to the chloro-substituted olefins in Table 4.2.[2,3]

Table 4.1[1]

Kinetic and Product Data for Electrophilic Substitution Reactions of Halobenzenes

	Fluorobenzene		Chlorobenzene		Bromobenzene	
	$k_{subst}/k_{unsubst}$	p_f^F	$k_{subst}/k_{unsubst}$	p_f^{Cl}	$k_{subst} / k_{unsubst}$	p_f^{Br}
Bromination	-	4.62	-	0.145	-	0.618
Chlorination	0.737	3.93	0.10	0.406	0.07	0.310
Acetylation	0.252	1.51	0.02	0.125	0.01	0.084
Nitration	0.14	0.77	0.03	0.13	0.03	0.103
Mercuration	0.70	2.98	0.10	0.36	0.09	0.27

Table 4.2

Second-Order Rate Constants for Bromination at 25°C in Methanol containing added Bromide ion (0.2N)

Olefin	k_2 l.mole^{-1}min^{-1}
$CH_2=CH-CH_3$	1840
$CH_2=CH-CH_2Cl$	2.20
trans-$ClCH_2-CH=CH-CH_2Cl$	8.67×10^{-2}

The effects of α-halo substituents in olefinic reactions, however, are less well documented. The overall deactivating effect of chloro substituents is demonstrated by the addition of bromine to several chloro-substituted allyl alcohols in water.

Table 4.3[2,4]

Second-Order Rate Constants for Bromination at 25°C in Aqueous Solution containing added Bromide ion (0.2N)

Olefin	k_2 l.mole^{-1}min^{-1}
allyl alcohol	1.36×10^{7}
2-chloroallyl alcohol	2.32×10^{-1}
trans-3-chloroallyl alcohol	9.75×10^{-1}
cis-3-chloroallyl alcohol	8.33×10^{-1}
3,3-dichloroallyl alcohol	1.54×10^{-3}

More recently, Peterson[5] (Table 4.4) has reported the considerable activation of 2-fluoropropene with respect to the other 2-halo-substituted propenes in the addition of trifluoroacetic acid. This he attributed to the stabilisation of the 2-fluoropropyl cation by 2p-2p overlap. The thermodynamic stability order F > H > Cl > Br was also indicated by gas phase mass spectroscopic studies.[6]

Table 4.4

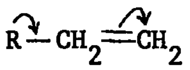
First-Order Rate Coefficients for Addition of Trifluoroacetic Acid at 25°C

Olefin	10^5 k_1 $\sec^{-1}$	Rel. rate coefficient
Propene	4.81	1
2-fluoropropene	340	71
2-chloropropene	1.70	0.35
2-bromopropene	0.395	0.082

Since the addition of both trifluoroacetic acid and bromine to olefins is believed to commence by initial, rate-determining electrophilic attack on the olefinic double bond and pass through a positively-charged reaction intermediate, the bromination of the series $CH_2=C(X)-CH_2Cl$ for X = H, F, Cl, Br has been carried out in two solvent systems to establish whether the behaviour observed by Peterson is a general feature of electrophilic addition reactions.

As an indirect consequence of the studies carried out on the allyl chloride series and on the bromination of the bromide series $CH_2=CH(CH_2)_{n-2}Br$ for n = 3 → 6 in Section B of Chapter 4, a comparison of the relative deactivating effects of the β-substituted halogens was possible.

Comparisons of similar effects of substituents on reaction rates and orientation of the products for electrophilic addition and aromatic substitution reactions have often been noticed.[6(a)] This is attributed to the ability of the π-electronic configurations of both olefinic and aromatic systems to be conjugated with electron-attracting or electron donating substituents.



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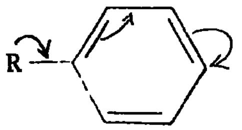

(4-1)

(4-2)

In this study, comparisons are drawn between the rates of addition of bromine to allyl bromide and allyl chloride, and the rates of electrophilic substitution of bromine into benzyl bromide and benzyl chloride.

4.2 Principles of Rate Measurement

As is described in Chapter 5, second-order rate constants for the bromination of the olefins considered were obtained by following the change in e.m.f. generated by a rotating platinum electrode with time. The e.m.f. was measured with reference to a glass or calomel electrode.

For

$$\text{olefin} + Br_2 \rightarrow \text{products} \qquad 4.1$$

the reaction is first-order in olefin and first-order in bromine.

$$v = -\frac{d[Br_2]}{dt} = k_2[Br_2][\text{olefin}] \qquad 4.2$$

Since a large excess of olefin was used in the reactions, first-order kinetics were observed, the first-order rate constant being given by

$$-\frac{d[Br_2]}{dt} = k_1[Br_2] \qquad 4.3$$

where $k_1 = k_2[\text{olefin}]$

On integration

$$k_1 t = \ln\frac{[Br_2]_o}{[Br_2]_t} \qquad 4.4$$

However, the reaction at the platinum electrode is expressed by

$$\tfrac{1}{2}Br_2 + e^- \rightleftharpoons Br^- \qquad 4.5$$

therefore

$$E = E^o + \frac{RT}{F}\ln\frac{[Br_2]^{\frac{1}{2}}}{[Br^-]} \qquad 4.6$$

The reactions were carried out in solutions containing a large excess of bromide ion (c.f. the bromine concentration), and the concentration of bromide ion could be regarded as constant.

Modifying equation 4.6

$$E = E' + \frac{RT}{2F} \ln[Br_2] \qquad 4.7$$

$$\text{where } E' = E^o - \frac{RT}{F} \ln[Br^-]$$

Differentiating equations 4.4 and 4.7 w.r.t. time

$$\frac{dE}{dt} = \frac{RT}{2F} \frac{d \ln[Br_2]}{dt} \qquad 4.8$$

$$k_1 = - \frac{d \ln[Br_2]}{dt} \qquad 4.9$$

Therefore

$$\underline{k_1 = - \frac{2F}{RT} \cdot \frac{dE}{dt}} \qquad 4.10$$

Thus, with the olefin in large excess, first-order kinetics were observed, k_1 being proportional to the rate of decrease of the observed e.m.f.

Second-order rate constants were given by

$$\underline{k_2 = - \frac{2F}{RT} \cdot \frac{dE}{dt} \cdot \frac{1}{[\text{olefin}]}} \qquad 4.11$$

4.3 Results and Discussion

(a) Substituent Effects of α-halo Atoms

As confirmation of the reliability of the method of measurement, the rate of bromination of allyl chloride was measured in methanol solutions containing a range of bromide ion concentrations.

Table 4.5

Second-order Rate Constants for the Bromination of Allyl Chloride at 25°C in Methanol Solution containing Sodium Bromide

$[Br^-]$	k_2 ($l.mole^{-1}min^{-1}$)
0.2N	2.23
0.1N	2.45
0.05N	2.97
0.02N	3.75

The above values agree well with those reported by Dubois.[7]

Since the reactions were carried out in the presence of excess bromide ions, tribromide ions were present in solution as a result of equilibrium (4.12)

$$Br^- + Br_2 \rightleftharpoons Br_3^- \qquad 4.12$$

$$K = \frac{[Br_3^-]}{[Br^-][Br_2]} \qquad 4.13$$

For simultaneous bromination by both bromine and the tribromide ion, the individual rate constants k_{Br_2} and $k_{Br_3^-}$ can be estimated.

Let Br_2^* be the total concentration of bromine present

Br_2 be the concentration of free bromine present

Br_3^- be the concentration of tribromide ion present

By definition,

$$[Br_2^*] = [Br_2] + [Br_3^-] \qquad 4.14$$

$$= [Br_2].\{1 + K[Br^-]\} \qquad 4.15$$

For simultaneous bromination

$$k_2[Br_2^*] = k_{Br_2}[Br_2] + k_{Br_3^-}[Br_3^-] \qquad 4.16$$

$$k_2[Br_2]\{1 + K[Br^-]\} = k_{Br_2}[Br_2] + k_{Br_3^-}K[Br^-][Br_2] \qquad 4.17$$

$$k_2 = \frac{k_{Br_2} + k_{Br_3^-}K[Br^-]}{\{1 + K[Br^-]\}} \qquad 4.18$$

From Fig.4.1, (using K = 177 $l.mole^{-1}$)[8]

k_{Br_2} = 10.8 $l.mole^{-1}min^{-1}$ (cf. 10.0 $l.mole^{-1}min^{-1}$)[7]

$k_{Br_3^-}$ = 2.0 $l.mole^{-1}min^{-1}$ (cf. 1.98 $l.mole^{-1}min^{-1}$)[7]

The data achieved above verified the response of the equipment being used.

The second-order rate coefficients for the bromination of the series $CH_2=C(X)-CH_2Cl$, (X = H,F,Cl,Br) were measured both in 50% by vol methanol-water and trifluoroacetic acid solvents at 25°C. The results are tabulated below (Table 4.6).

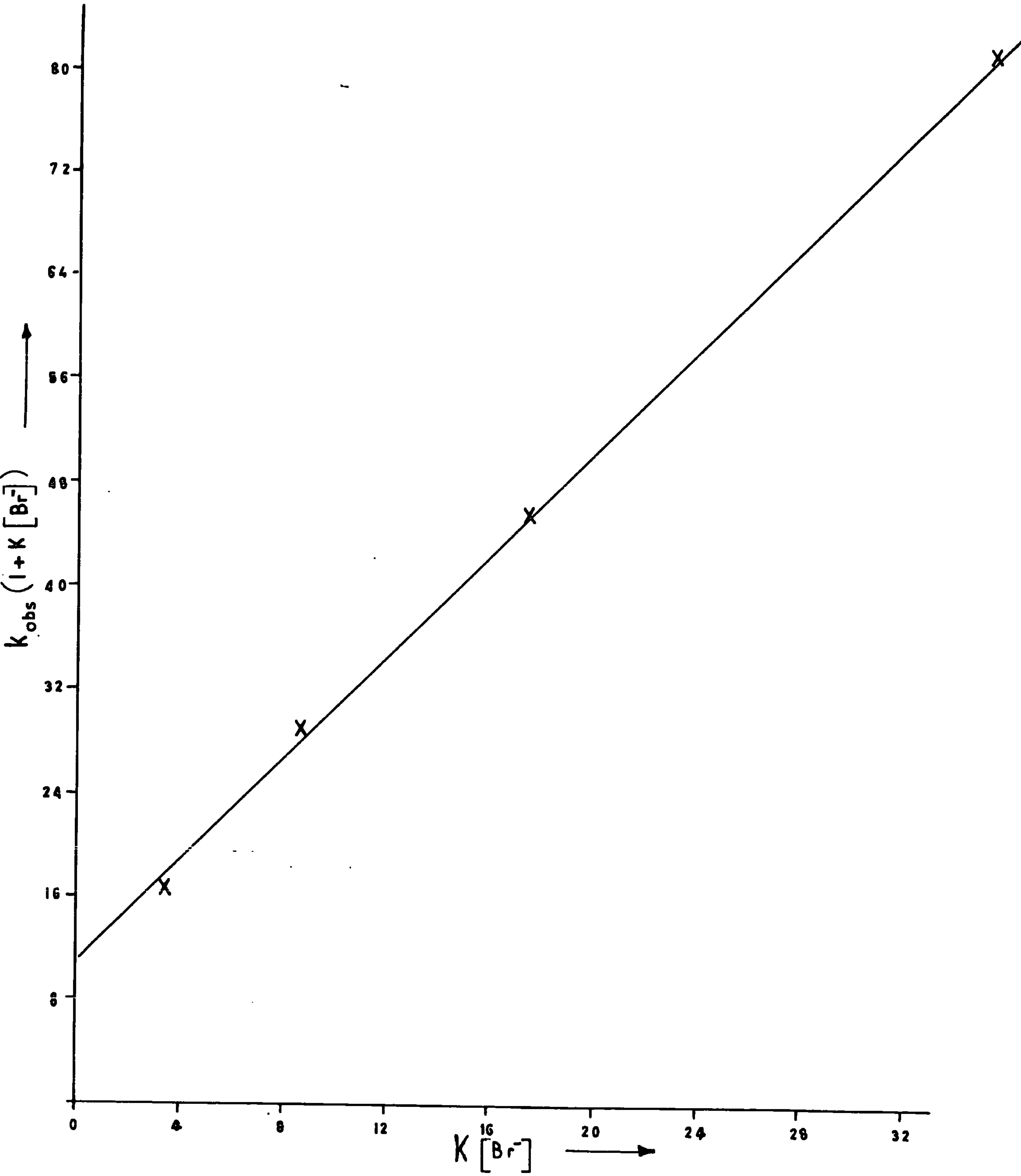

FIG. 4 - 1. PLOT OF $k_{obs}(1+K[Br^-])$ AGAINST $K[Br^-]$ FOR THE BROMINATION OF ALLYL CHLORIDE IN METHANOL.

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Table 4.6

Second-order Rate Constants for the Bromination of the Series $CH_2=C(X)-CH_2Cl$ at 25°C

Olefin	50% methanol-water* k_2 $l.mole^{-1}min^{-1}$	Trifluoroacetic Acid** k_2 $l.mole^{-1}min^{-1}$
$CH_2=CH-CH_2Cl$	1440 ± 40	1020 ± 20
$CH_2=CF-CH_2Cl$	5.3 ± 0.3	0.56 ± 0.03
$CH_2=CCl-CH_2Cl$	0.27 ± 0.01	0.11 ± 0.005
$CH_2=CBr-CH_2Cl$	0.34 ± 0.01	-

* containing 0.2N NaBr

** containing 0.01N NaBr

The above are mean values of at least three determinations and the error quoted is the maximum variation from the mean of these determinations. This applies to all the rate data quoted in this chapter except where stated. Fig.4.2 shows a typical trace obtained for the bromination of allyl chloride in 50% methanol-water solvent, linearity being observed for 60 mV, greater than 97% of the reaction, thus illustrating the first-order nature of the reaction.

The results quoted are the composite rate coefficients involving contributions from bromination via both bromine and the tribromide ion species. Because of the low solubility of sodium bromide in trifluoroacetic acid, individual rate constants have not been determined. Dubois[9] measured the equilibrium constant for equation (4.12) in trifluoroacetic acid containing lithium bromide by a spectrophotometric method and found

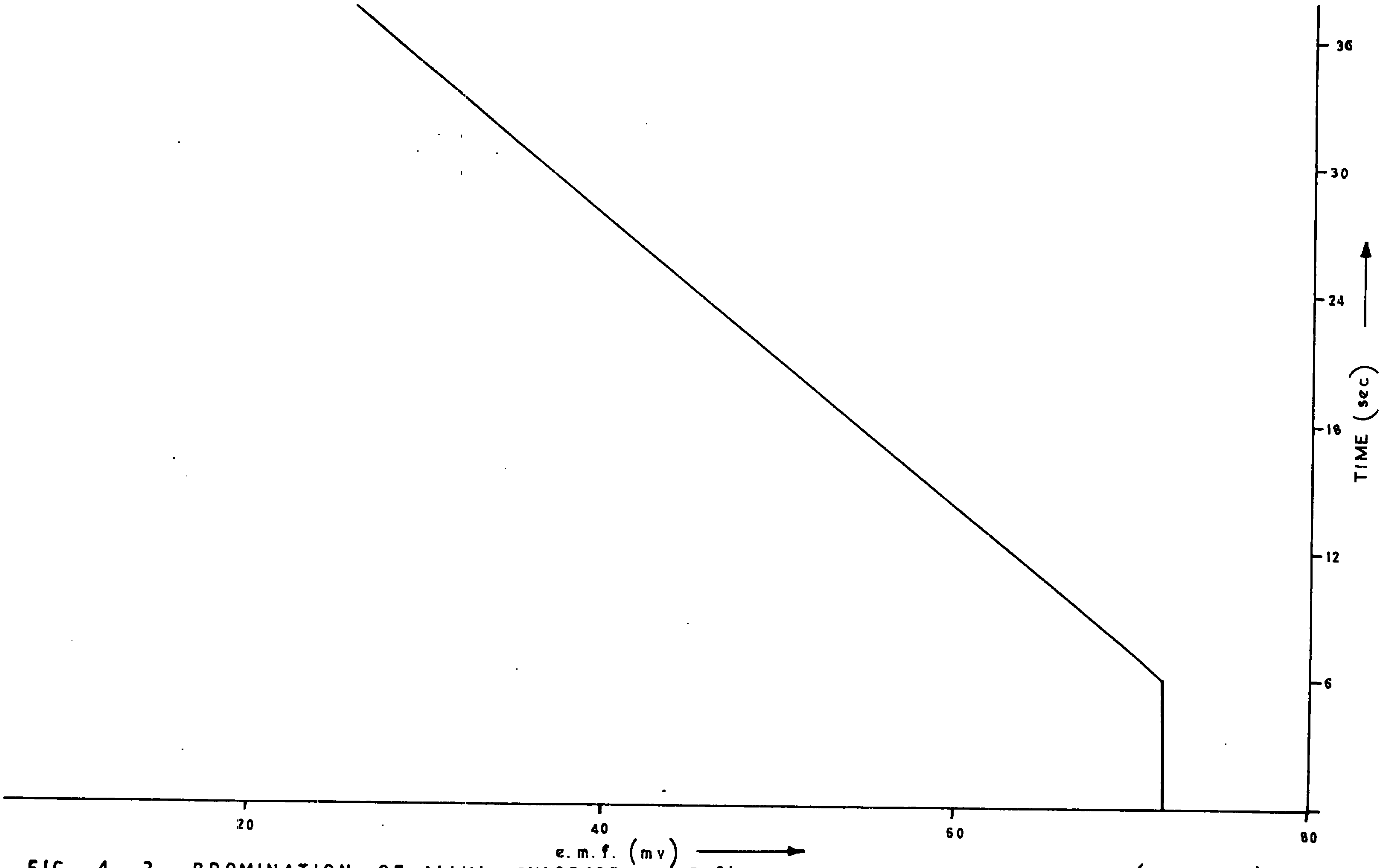


FIG. 4 – 2. BROMINATION OF ALLYL CHLORIDE IN 50% METHANOL - WATER SOLVENT (0·2Na Br) – DECREASE OF e.m.f. WITH TIME.

the low value (cf. methanol and acetic acid) of $K < 0.9$ l.mole^{-1}. He thus considered it acceptable to use the composite rate coefficients as a first approximation in the discussion of molecular structure correlations in trifluoroacetic acid solutions at low bromide ion concentrations. It has also been shown that the composite rate coefficients are sufficiently precise to permit their use as a measure of the reactivity of the olefin without recourse to finding k_{Br_2} in both methanol[10] and water[2(a)] solvents.

It is apparent in Table 4.6 that substitution of halogens in the 2-position of allyl chloride causes overall deactivation by means of the electron-withdrawing -I effect in both solvent systems. However, if only the inductive effect was operative the expected effectiveness of deactivation (cf. X = H) would be X = F > Cl > Br as indicated by the electrophilic substitution constants (σ and σ^+).[11]

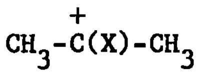
However, the 2-fluoroallyl chloride has been shown to be significantly more reactive than the 2-chloro or 2-bromo compounds. This is consistent with the interpretation that a contribution from the electron-releasing +M effect is being observed, the expected magnitude of which would decrease in the order F > Cl > Br. A combination of these two effects acting in competition would lead to the observed order of reactivity of X = H > F > Cl ~ Br. This observation is analogous to the relative rates of electrophilic substitution of halobenzenes (cf. benzene) shown in Table 4.1.

The influence of the electron-releasing +M effect is also illustrated in electrophilic aromatic substitution reactions by the orientation of substitution. The halobenzenes generally undergo substitution in the ortho and para positions with deactivation as a result of the dominant -I inductive effect. However, in the case of fluorobenzene the para position is activated towards electrophilic attack by the dominant +M effect of the fluoro substituent, resulting in largely para products for electrophilic substitution reactions.

The 2-halo substituents of the allyl chloride series have been shown to exert a similar influence on the products.[12] The addition of bromine to allyl chloride in the 50% by vol. methanol-water solvent gave approximately 30% 1-bromo-3-chloropropan-2-ol and 70% 2-bromo-3-chloropropanol, whereas for the substituted series Markownikoff addition was observed, 1-bromo-3-chloroacetone being the dominant product in each case.

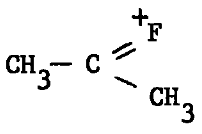
Comparison of Tables 4.6 and 4.4 shows that whilst the addition of both bromine and trifluoroacetic acid exhibit greater reactivity for the 2-fluoro olefin than that expected from the contribution of the inductive effect alone, the scale of rate enhancement for the bromination reaction is much less. The 2-fluoro olefin reacts twenty times faster in the methanol-water solvent and five times faster in trifluoroacetic acid than the 2-chloro compound for bromination. The 2-fluoro compound is also twenty-five times slower in methanol-water and two thousand times slower in trifluoroacetic acid than the unsubstituted chloride. (The differences in the relative rates of bromination in the two solvents may reflect some degree of solvent enhancement of the inductive effect of the 2-halo substituents by hydrogen bonding in the trifluoroacetic acid solvent). The above figures compare with 2-fluoropropene being two hundred times faster than 2-chloropropene and seventy times faster than unsubstituted propene for the addition of trifluoroacetic acid.[5]

The difference in the scale of the rate-enhancement for the fluoro-substituted olefin between the two reactions may well be due to a different form of positively-charged species in the transition state. The addition of trifluoroacetic acid is believed to pass through a transition state resembling the classical carbonium ion, (4-3) which is stabilised



$CH_3\text{-}\overset{+}{C}(X)\text{-}CH_3$

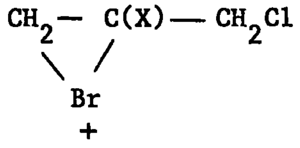
(4-3)



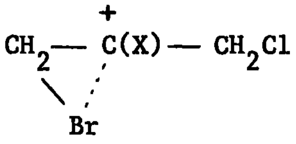
(4-4)

most effectively in the substituted propene series for the 2-fluoropropyl cationic species (4-4) by 2p-2p overlap. This leads to a predicted reactivity sequence of X = F > Cl > Br > H.

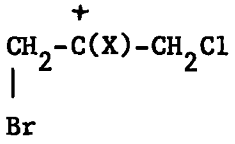
For bromination reactions, however, positively-charged species of types (4-5) to (4-7) have been proposed in the literature[13] as intermediates.



(4-5)



(4-6)



(4-7)

In the series of reactions studied, the ground states of the halo-substituted olefins would be stabilised with respect to the unsubstituted allyl chloride by the electron-withdrawing (-I) inductive effect. This would be progressively larger in the order X = H < Br < Cl < F, but the overall magnitude of the effect would be relatively small.

However, in the transition state, a species resembling an ion of type (4-7) would be destabilised by the -I inductive effect of the substituent halogens but also stabilised by all the halogens by 2p-p overlap. The order of effectiveness would be X = F >> Cl > Br, with the overlap of the 2p orbitals of carbon and fluorine being particularly significant. This order has been confirmed by non-empirical L.C.A.O., M.O. and S.C.F. calculations for the classical halogen substituted ethyl cations.[14]

It can be inferred from Table 4.6 that this stabilisation in the transition state is much less for the bromination reaction than for the addition of trifluoroacetic acid. This would indicate a degree of delocalisation of the positive charge away from the 2-carbon atom, and that the transition state more resembles a species of type (4-5). However, it is unlikely that the transition state completely resembles the bridged bromonium ion (4-5) since this would be destabilised by all the 2-halo substituents by the -I inductive effect, predicting an order of reaction H > Br > Cl > F.

It is therefore suggested that the transition state resembles a species similar to (4-6) where there is significant delocalisation of the positive charge towards the additive bromine atom by ion-dipole interaction, explaining the observed reactivity sequence H > F > Cl ~ Br.

On the other hand, the kinetic and product[12] data suggest that the intermediate for the bromination of allyl chloride is the bromonium ion since significant quantities of both Markownikoff and anti-Markownikoff addition products are formed. The predominance of Markownikoff addition products for the 2-halo substituted olefins suggested the existence of the classical carbonium ion intermediate stabilised by the electron-donating +M effect of the substituent halogens.

(b) Substituent Effects of β-halo Atoms

Second-order rate coefficients were determined at 25°C for the bromination of the series $CH_2=CH-CH_2X$ (where X = Cl and Br) in acetic acid-water and trifluoroacetic acid solvents.

Table 4.7

Second-order Rate Constants for the Bromination of $CH_2=CH-CH_2X$ at 25°C in Solutions containing 0.01N Sodium Bromide

Olefin	Acetic acid-water* k_2 ($l.mole^{-1}min^{-1}$)	Trifluoroacetic Acid k_2 ($l.mole^{-1}min^{-1}$)
allyl chloride	12.9	1020
allyl bromide	12.35	1230

* Acetic acid containing 1% by vol. of water.

The rate of bromine addition to allyl chloride was greater than that for allyl bromide in the acetic acid-water mixture, but the order was reversed in trifluoroacetic acid. As previously, the above are all composite rate coefficients of the two concurrent reactions involving simultaneous attack by bromine and tribromide ion.

The results for bromination in acetic acid compare with the observations of Robertson,[15] who reported the second-order rate constants for the bromination of the series $CH_2=CH-CH_2X$ for X = Cl, Br, CN in a 20% acetic acid-water mixture at 25°C.

Table 4.8[15]

Second-order Rate Constants for the Bromination of the Series $CH_2=CH-CH_2X$ in 20% Acetic Acid-Water Solvent

	k_2
$CH_2=CHCH_2Cl$	1.6
$CH_2=CHCH_2Br$	1.1
$CH_2=CHCH_2CN$	0.23

The electrophilic substitution constants (σ and σ^+)[11] for chloro and bromo substituents lead to the prediction that both the $-CH_2Cl$ and $-CH_2Br$ substituents exert an electron-withdrawing -I effect on the olefinic double bond, thus reducing its susceptibility to electrophilic attack. The substitution constants suggest that the deactivating effect of a β-chloro substituent would be greater than that of a β-bromo substituent thus predicting an order of reactivity, allyl bromide > allyl chloride.

However, the activating effects of substituted methyl groups by hyperconjugation are well known.[16] Activation is attributed to the overlap of the in-plane electrons of the carbon-hydrogen bonds of the methyl group with the π electrons of the double bond, thus increasing the susceptibility of the double bond to electrophilic attack.

For the $-CH_2Cl$ and $-CH_2Br$ substituents the unexpected order of reactivity is attributable to the decreased contribution via hyperconjugation for the $-CH_2Br$ substituent, because of movement of the in-plane carbon-hydrogen bonds out of plane by the larger bromine atom, to such an extent that the difference of the inductive effects of chloro and bromo substituents is outweighed by the difference in hyperconjugation contributions of the two substituents.

In trifluoroacetic acid, however, it would appear that the order of reactivity follows that expected on inductive grounds, suggesting the possibility of solvent enhancement of the inductive effect. F^{19} n.m.r. measurements[17] indicate that the halogen substituents exhibit relatively small changes in substituent-solvent interaction in passing from acetic acid to trifluoroacetic acid solvent.

In this case, however, the differences in reactivity of the two olefins are small when considering the large difference in rate between bromination in trifluoroacetic acid and acetic acid solvent. The enhanced rate of reaction for allyl bromide in comparison to allyl chloride in trifluoroacetic acid may be indicative of a degree of enhancement of the inductive effect via hydrogen bonding, which will be greater for the more electronegative chloro substituent.

In order to examine whether any variation of the inductive effect of the substituent halogens would be exhibited by the aromatic compounds analogous to the allyl halides in electrophilic substitution reactions in the acetic acid-water and trifluoroacetic acid solvents, the rates of bromination of benzyl chloride and bromide were measured in the presence of added sodium bromide.

The reaction of bromine with benzyl bromide was measured at 48.37°C in an acetic acid solution containing 1% by vol. of water and 0.01N sodium bromide. Because of the low initial bromine concentration, high temperature and presence of water, the second-order contibution of bromine[18] was reduced. First-order kinetics were observed because the benzyl bromide concentration was in large excess and could be regarded as constant throughout the reaction.

Thus, the following rate expression could be used,

$$k_2 = \frac{2.303}{t.b} \log \frac{a}{a-x} \qquad 4.19$$

where

t = time (mins)

a = initial bromine concentration

b = initial benzyl bromide concentration

x = bromine concentration at time t.

Table 4.9

Rate Data for the Bromination of Benzyl Bromide in Acetic Acid containing 1% by vol of Water and 0.01N Sodium Bromide

t(min)	titre(ml)	$\frac{a}{a-x}$	$\log \frac{a}{a-x}$	$k_2 \times 10^3$ $l.mole^{-1}min^{-1}$
0	7.25	1	0	-
60	7.10	1.021	0.0091	1.83
183	6.85	1.058	0.0244	1.61
306	6.52	1.112	0.0461	1.82
449	6.35	1.142	0.0577	1.55
561	6.15	1.179	0.0715	1.54
754	5.65	1.283	0.1082	1.73
1406	4.75	1.526	0.1835	1.57
1772	4.05	1.790	0.2529	1.73
2194	3.65	1.986	0.2980	1.64
2749	3.05	2.377	0.3760	1.65

$b = 1.905 \times 10^{-1}$ mole.l^{-1}

Temp = 48.37 ± 0.02°C

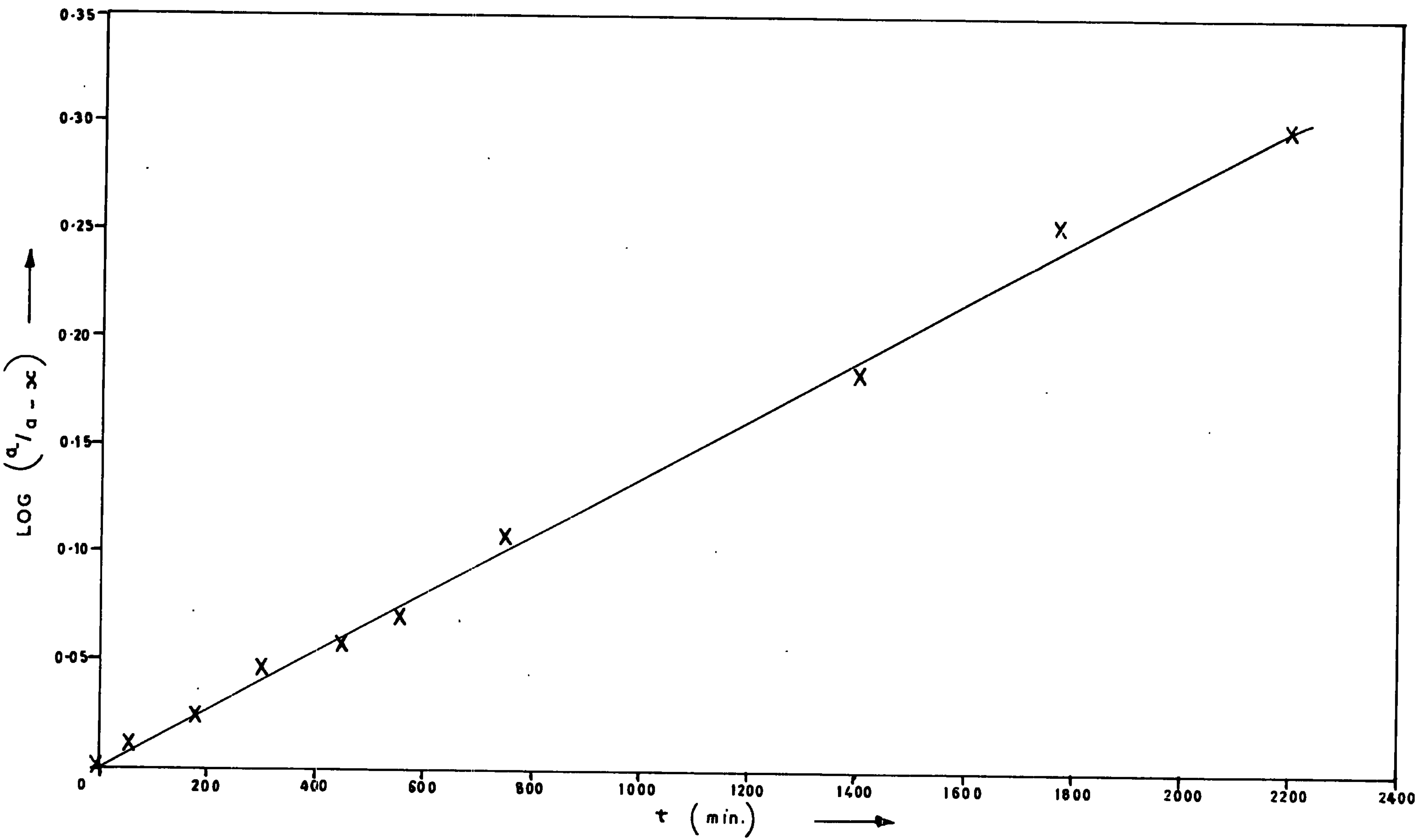


FIG. 4-3. PLOT OF LOG $\left({}^{a}/_{a-x}\right)$ AGAINST t (time) FOR THE BROMINATION OF BENZYL BROMIDE IN ACETIC ACID — WATER SOLVENT (0·01N Na Br.)

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From Fig.4.3

$$\text{Slope} = \frac{0.310}{2300} = 1.348 \times 10^{-4}$$

$$k_2 = \underline{1.63 \times 10^{-3}}\ \text{l.mole}^{-1}\text{min}^{-1}$$

A repeat run gave

$$k_2 = \underline{1.78 \times 10^{-3}}\ \text{l.mole}^{-1}\text{min}^{-1}$$

The procedure was repeated for benzyl chloride and the results are shown in Table 4.10. All rate constants are the mean of two measurements.

Table 4.10

Second-order Rate Constants for Bromination in Acetic Acid containing 1% by vol of Water

	0.01N NaBr k_2 (l.mole^{-1}min^{-1})	0.1N NaBr k_2 (l.mole^{-1}min^{-1})
benzyl chloride	5.6×10^{-3}	9.3×10^{-4}
benzyl bromide	1.7×10^{-3}	3.8×10^{-4}

Temperature = 48.37°C

The rates of bromination of benzyl chloride and bromide were also measured in trifluoroacetic acid with added sodium bromide. The reactions were measured at 25°C and exhibited second-order kinetics obeying the following equation

$$k_2 = \frac{2.303}{t(a-b)} \log \frac{b}{a}\frac{(a-x)}{(b-x)} \qquad 4.20$$

where t = time (mins)

a = initial benzyl chloride concentration

b = initial bromine concentration

x = bromine concentration at time t

Table 4.11

Rate Data for the Bromination of Benzyl Chloride in Trifluoroacetic Acid containing 0.01N Sodium Bromide at 25°C

t (min)	(b-x) (mls)	(a-x) (mls)	$\frac{(a-x)}{(b-x)}$	$\log \frac{(a-x)}{(b-x)}$
0	8.80	13.92 (calc)	1.582	0.1993
16	8.80	13.92	1.582	0.1993
183	7.85	12.97	1.652	0.2180
305	7.90	13.02	1.648	0.2170
438	7.20	12.32	1.711	0.2330
571	6.30	11.42	1.813	0.2584
663	6.10	11.22	1.839	0.2646
759	5.20	10.32	1.985	0.2978
1051	5.05	10.17	2.014	0.3040
1334	4.40	9.52	2.164	0.3353
1646	3.75	8.87	2.365	0.3738
2209	2.80	7.92	2.828	0.4514

a = 3.481×10^{-2} mole/litre

b = 2.200×10^{-2} mole/litre

From Fig.4.4:

$$\text{Slope} = \frac{0.390 - 0.199}{1800} = 1.061 \times 10^{-4}$$

$$\underline{k_2 = 1.91 \times 10^{-2} \text{ l.mole}^{-1}\text{min}^{-1}}$$

The procedure was repeated for benzyl bromide.

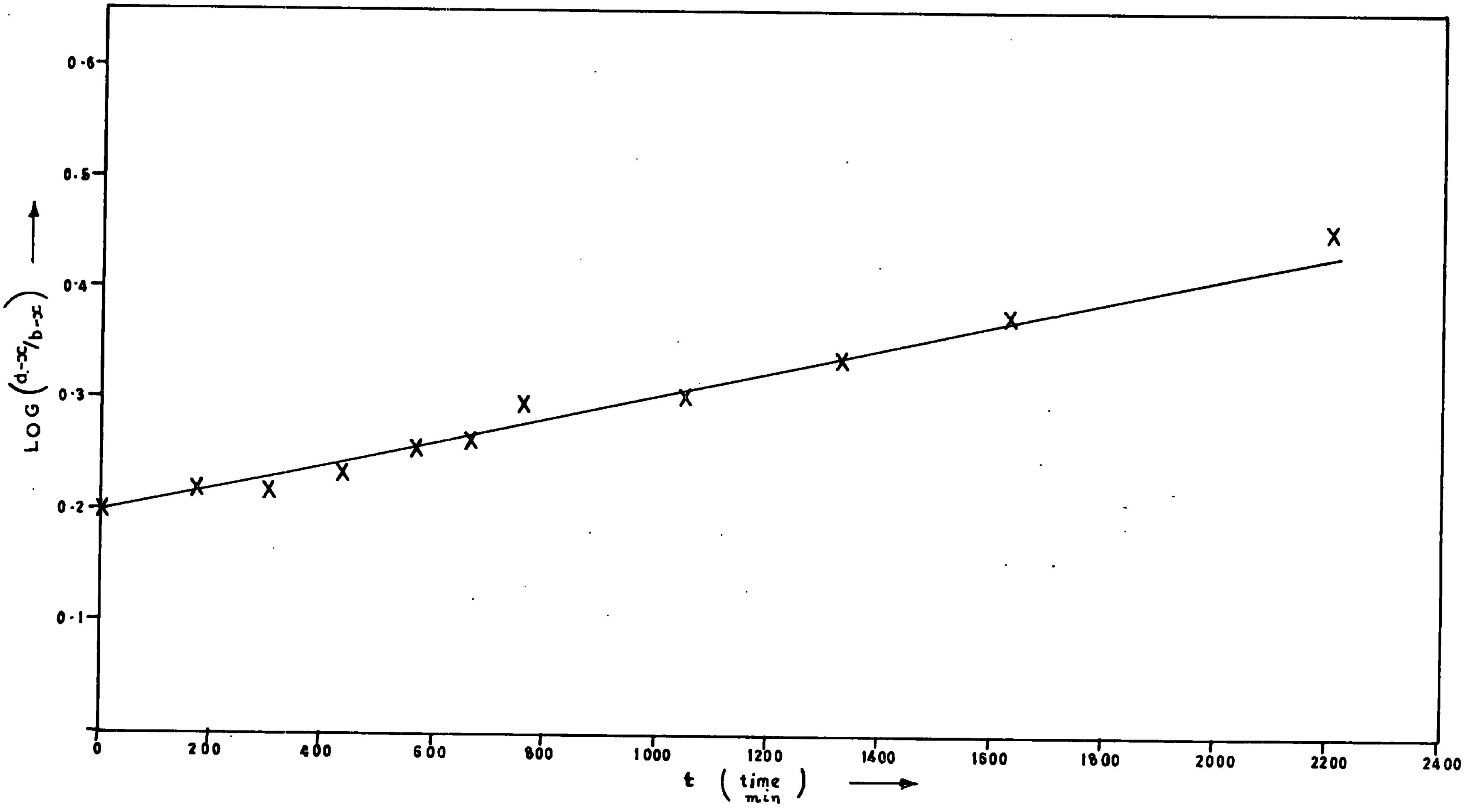

FIG. 4-4. PLOT OF LOG$\left(^{a-x}/_{b-x}\right)$ AGAINST t(time) FOR BROMINATION OF BENZYL CHLORIDE IN TRIFLUOROACETIC ACID (0·01N NaBr.)

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Table 4.12

Second-order Rate Constants for Bromination in Trifluoroacetic Acid at 25°C

	0.01N NaBr k_2 (1.mole^{-1}min^{-1})
benzyl chloride	1.91×10^{-2}
benzyl bromide	6.84×10^{-3}

Comparison of Tables 4.10 and 4.12 show that there is a slight decrease in the relative reactivity of benzyl chloride with respect to benzyl bromide in passing from the acetic acid-water solvent to trifluoroacetic acid. However, the effect is so small that because of the degree of experimental error, confirmation of the enhanced inductive effect of the chloro substituent with respect to the bromo substituent cannot be inferred.

It would be expected, however, that the same degree of modification of the inductive effect of the halo-substituents in trifluoroacetic acid in comparison with acetic acid would have a much less marked effect on the rate of electrophilic bromine substitution in the aromatic halides than on the rate of bromine addition to the allyl halides because of the larger hyperconjugative contribution of the α carbon-hydrogen bond electrons in the former case. This is illustrated by the small overall deactivating effect of the $-CH_2X$ substituents (X = Cl,Br) with respect to toluene.[15]

It is therefore suggested that the observed rate enhancement of allyl bromide with respect to allyl chloride in trifluoroacetic acid may be attributable to a slight modification of the substituent-solvent interaction by hydrogen bonding in the non-aqueous solvent, as has been suggested by Peterson[3] for the addition of trifluoroacetic acid to the $CH_2=CH(CH_2)_{n-2}Cl$

It was also hoped to make a comparison of the products of bromination of the allyl and benzyl halides. However, it did not prove possible using the g.l.c. equipment available to identify positively the isomers of the bromobenzyl halides produced.

The presence of monobrominated products was indicated by infra-red spectroscopy, but the separation of ortho, meta and para bromobenzyl halides from a mixture made up from commercial samples was not sufficiently precise to draw a definite conclusion as to which isomers were found in the bromination reaction.

B. Neighbouring Group Effects

4.4 Introduction

As described in Chapter 3, earlier work by Williams et al[2] dealt with the neighbouring group effects of the substituent hydroxyl and bromo groups in bromination and iodination reactions to olefins in methanol and water solvents.

The data provided evidence for the involvement of cyclic five- and six-membered oxonium ion intermediates in the reactions of bromine and iodine with the series $CH_2=CH(CH_2)_nOH$ when n = 3 and 4.

However, the failure to observe any detectable participation by the bromo substituent in the bromination of the series $CH_2=CH(CH_2)_nBr$, and the indication that participation was a possibility for the iodination reaction involving the more selective and polarisable electrophilic reagent, suggested that participation might be greater in a less nucleophilic solvent where competition from solvent nucleophiles for the positively-charged intermediate would be correspondingly less.

This was supported by the reported kinetic[3] and product[19] data for the addition of trifluoroacetic acid to the series $CH_2=CH(CH_2)_nX$, (where $-X = -H, -O_2CCF_3, -CN, -O_2CCH_3, -Cl, -OCH_3$) which illustrated participation by the group -X (for-X = -OMe, -Cl) in five-membered cyclic intermediates. Also published [3] were the rate-constants for addition of trifluoroacetic acid to three bromo-alkenes - Table 4.13.

Table 4.13

Rates of Addition of Trifluoroacetic Acid at 60°C

	$k_1 \times 10^6$ (sec^{-1})
4-bromobut-1-ene	2.80
5-bromopent-1-ene	177
6-bromohex-1-ene	156

Furthermore, the work of Peterson provided interesting data on the influence of substituents remote from the reaction centre at the olefinic double bond. He reported the very low fall-off of the inductive effect of substituent groups in the addition of trifluoroacetic acid to the series $CH_2=CH(CH_2)_nX$ as above. This was interpreted in terms of solvent enhancement of the inductive effect by hydrogen bonding.

As stated previously, the similarities between the electrophilic addition of protic acids and halogens are well established, It was therefore considered worthwhile to investigate whether any of the features reported for the trifluoroacetic acid addition reactions were present in electrophilic bromination reactions.

4.5 Results and Discussion

(a) Bromination in Acetic Acid containing 1% by vol. of Water

Bromination of the series $CH_2=CH(CH_2)_{n-2}OH$ was carried out in a solution of acetic acid containing 1% by volume of water in the presence of added bromide ions. The water was added because at bromine concentrations of about $10^{-3}M$, interference from kinetic orders above unity for bromine begins to become significant.[20] The first-order nature of the reaction was illustrated by the linear decrease of e.m.f. over 97% of the reaction.

$$k_2 = -\frac{RT}{2F} \cdot \frac{dE}{dt} \cdot \frac{1}{[\text{olefin}]} \qquad 4.21$$

The following second-order rate constants were calculated using equation (4.21), the figures quoted being the mean of at least three measurements.

Table 4.14

Second-Order Rate Constants for Bromination of the Series $CH_2=CH(CH_2)_{n-2}OH$ in Acetic Acid containing 1% by vol. Water with added Bromide Ions

	k_2 (l.mole^{-1}min^{-1})			
	n = 3	n = 4	n = 5	n = 6
0.01N NaBr	222 ± 4	500 ± 10	4080 ± 30	1910 ± 30
0.1N NaBr	251 ± 1	594 ± 6	4020 ± 20	1595 ± 25

The second-order rate constants for the unsubstituted olefins pent-1-ene and hex-1-ene were also measured, but because of difficulties with vapour loss under similar experimental conditions, the corresponding unsubstituted olefins for n = 3 and 4 were not measured.

Table 4.15

Second-order Rate Constants for Bromination in Acetic Acid containing 1% by vol. Water with added Bromide Ions

	k_2 (l.mole^{-1}min^{-1})	
	pent-1-ene	hex-1-ene
0.01N NaBr	4040 ± 60	3620 ± 150
0.05N NaBr	2080 ± 100	2670 ± 40
0.1N NaBr	1730 ± 60	2050 ± 100

The rate constants in Tables 4.14 and 4.15 are composite rate coefficients of the two concurrent reactions involving electrophilic attack by bromine and tribromide ion. Because of the low solubility of sodium bromide in acetic acid, it was not possible to investigate the effect of added bromide ions on the rates of bromination for a range large enough to elucidate the individual rate constants for bromination by bromine and tribromide. However, Dubois[21] investigated the effect of the more soluble lithium bromide and found that the observed overall rate constant k_2 and the extrapolated value achieved for k_{Br_2} varied by approximately 0.1 log units, and thus considered it acceptable to use the composite rate coefficient in discussions of reactions in this medium.

Inspection of Table 4.14 shows a quite marked maximum for n = 5, far greater than any expected by the reduction of influence of the inductive effect with increasing distance of the substituent hydroxyl group from the reaction centre. It is noted that the figure of k_2 = 4080 $1.mole^{-1}min^{-1}$ is marginally greater than that for the corresponding unsubstituted olefin, pent-1-ene.

Since the rate data for the lower unsubstituted olefins were not available, a complete treatment of the inductive effect in the manner described by Peterson[3] was not possible. However, assuming that the rate coefficients for the unsubstituted olefins were constant around 4000 $1.mole^{-1}min^{-1}$, an approximate attenuation plot could be carried out. It was noted that the variation of the second-order rate constants for the unsubstituted olefins was only slight[2] in both water and methanol solvents.

Using equation 4.22, (for the derivation see Chapter 3, equations 3.3 to 3.5), the data in Table 4.16 may be calculated, and in Fig.4.5,

$$\log \Delta \log k_n = \log \varepsilon\,(n-m) + \log \Delta \log k_m \qquad 4.22$$

where n and m are the nos. of carbon atoms in the chain (n > m)

log Δ log k_n was plotted against n (the number of carbon atoms in the chain).

From Fig.4.5, the slope lead to a value of ε = 0.51 on the assumption that there was no neighbouring group participation for the compounds in which n = 4 and 6. The modification of the inductive effect for allyl alcohol by solvent interaction[22,23] was again illustrated by the high value of ε = 0.70, if it was assumed that no anchimeric assistance occurred for the compounds in which n = 3 and 4.

For the reaction involving neighbouring group participation for n = 5, the following scheme was suggested.[2]

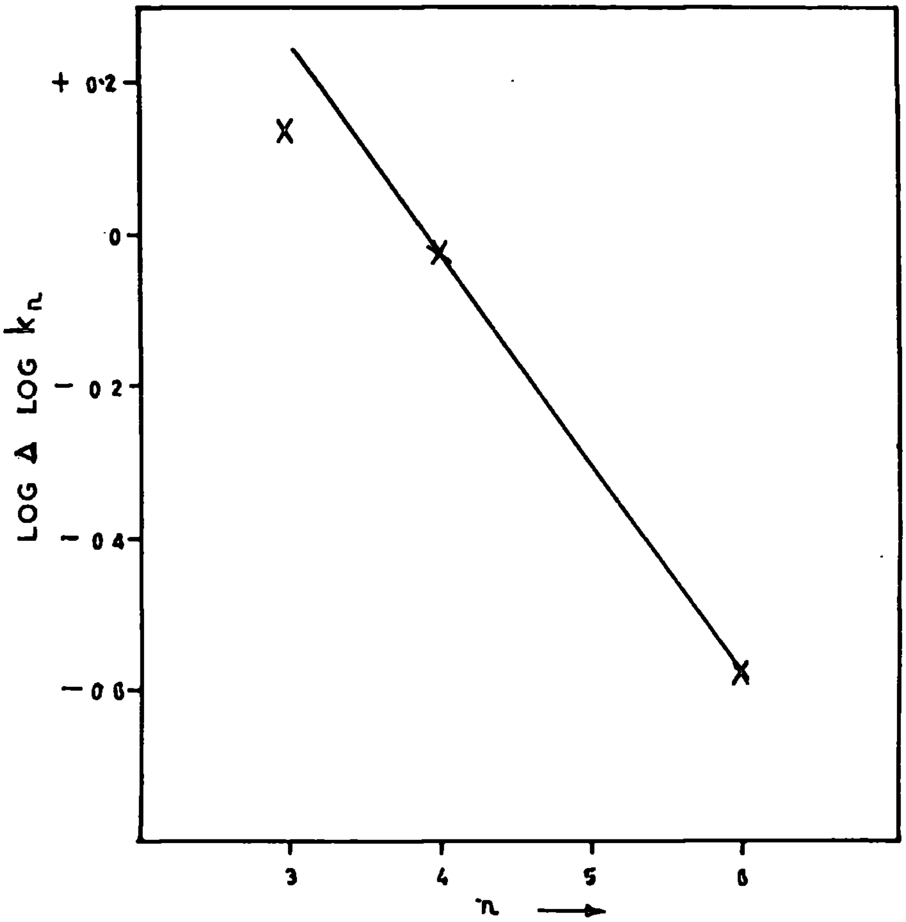
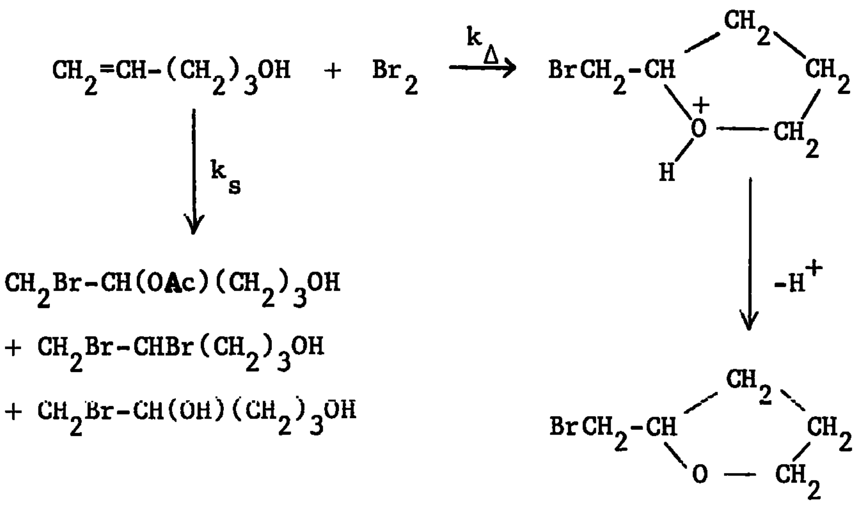


FIG. 4 - 5. PLOT OF LOG Δ LOG k_n AGAINST n FOR BROMINATION OF THE SERIES $CH_2=CH(CH_2)_{n-2}OH$ IN ACETIC ACID – WATER SOLVENT.

Table 4.16

Estimate of Inductive Effects - Bromination in Acetic Acid Solvent containing 1% by vol. Water

Olefin	k_2(l.mole^{-1}min^{-1})	$\Delta \log k_n$	$\log \Delta \log k_n$	n
allyl alcohol	222	1.379	0.1396	3
3-buten-1-ol	500	0.951	-0.0218	4
4-penten-1-ol	4080	0	$-\infty$	5
5-hexen-1-ol	1910	0.277	-0.5575	6



4.23

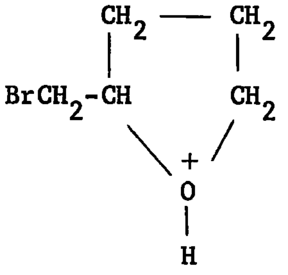
The overall rate constant k_{obs} is given by

$$k_{obs} = k_\Delta + k_s \tag{4.24}$$

However, using the value of $\epsilon = 0.51$ and assuming no participation for the compound where $n = 4$, k_s for $n = 5$ was calculated to be 1300 $1.mole^{-1}min^{-1}$. Hence k_Δ/k_s was estimated to be approximately 2, predicting that 65% of the product should be the ring-closed species.

The above prediction compared with 35% of ring-closed product detected for the bromination of 4-penten-1-ol and 8% for 5-hexen-1-ol. The presence of ring-closed product in the mixture resulting from the bromination of 5-hexen-1-ol would indicate that the figure of $\epsilon = 0.51$ was a little high. However, participation to such a low extent would only slightly affect the rate data.

Thus, participation by the neighbouring -OH group was confirmed for 4-penten-1-ol in acetic acid solvent in addition to that previously found[2] in methanol and water solvents. Since the above treatment is approximate, it is difficult to draw any firm conclusions about the relative degrees of participation in the three solvents, water, methanol and acetic acid. It would be expected that on decreasing the nucleophilicity of the solvent, the effectiveness of internal nucleophilic attack by the hydroxyl group would be facilitated. The kinetic data is consistent with greater assistance by the neighbouring hydroxyl group in passing from a more to a less nucleophilic solvent. The observed difference between the predicted value of 65% ring-closed product and the detected 35% may suggest the possibility that the ring-closed intermediate of type (4-8)



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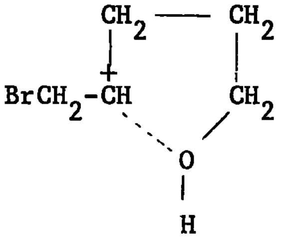


(4-9)

is not fully developed and more resembles ion (4-9),[24] thus allowing straight chain products to result from the reaction pathway involving participation.

The small quantity of ring-closed product detected for the bromination of 5-hexen-1-ol again emphasises the greater stability of the five- compared with the six-membered ring species.

Bromination of the series $CH_2=CH-(CH_2)_{n-2}Br$ was also carried out in the less nucleophilic (compared with water and methanol) acetic acid solvent containing 1% by vol. of water and gave the second-order rate constants shown in Table 4.17.

Table 4.17

Second-order Rate Constants for Bromination of the Series $CH_2=CH(CH_2)_{n-2}Br$ in Acetic Acid containing 1% by vol of Water with added Bromide Ions

	k_2(l.mole^{-1}min^{-1})			
	n = 3	n = 4	n = 5	n = 6
0.01N NaBr	12.35 ± 0.05	96.3 ± 3	517 ± 4	3280 ± 50
0.1N NaBr	-	97.2 ± 2	522 ± 5	2655

Inspection of Table 4.17 shows a steady increase in magnitude of k_2 with increasing distance of the bromo substituent from the olefinic double bond. This is consistent with the gradual attenuation of the inductive effect with distance from the reaction centre. For 5-bromopent-1-ene, the marked jump in rate observed in Table 4.14 for 4-penten-1-ol is absent indicating the lack of any detectable participation by the substituent bromine atom.

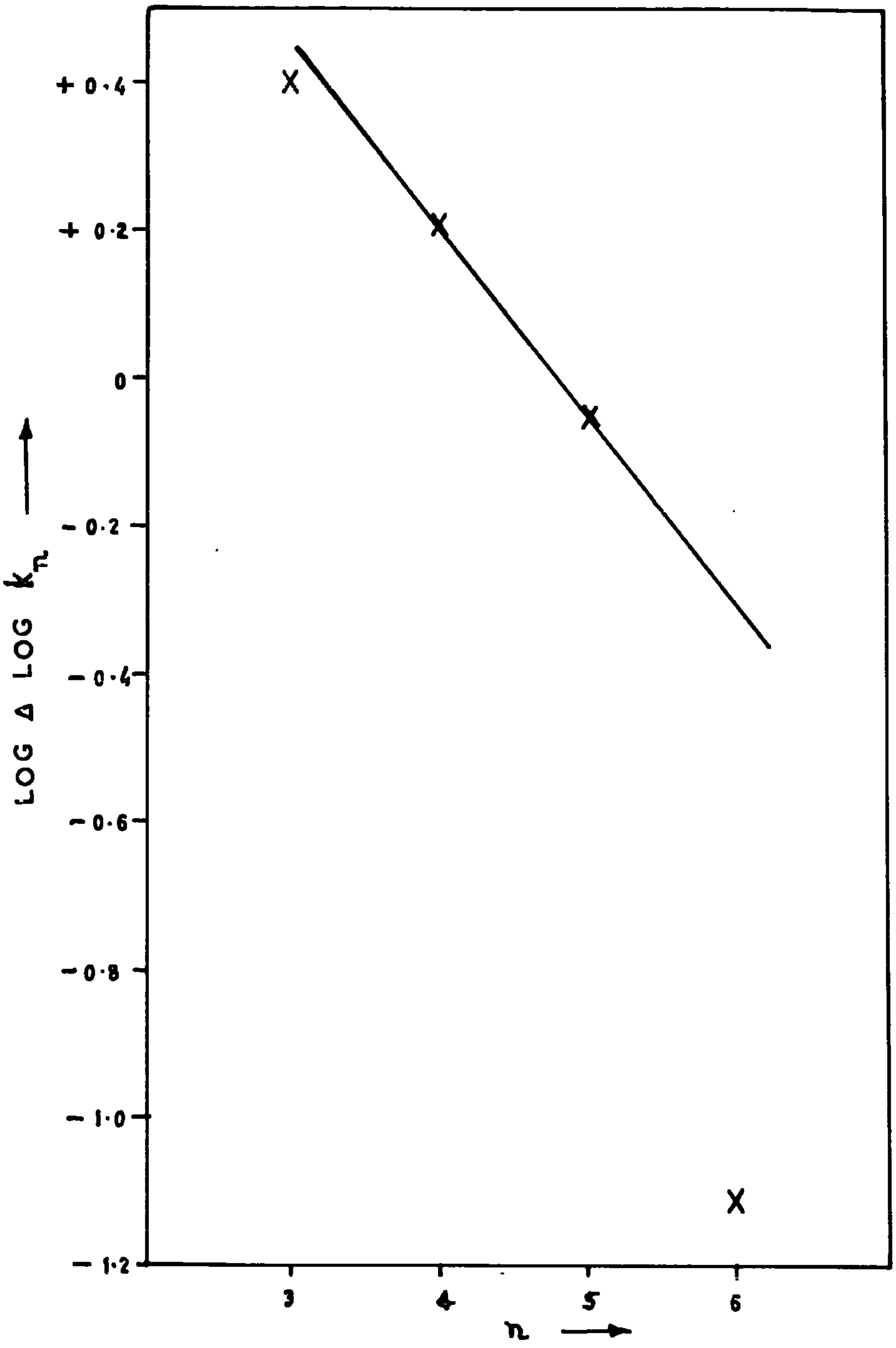


FIG. 4-6. PLOT OF LOG Δ LOG k_n AGAINST n FOR BROMINATION OF THE SERIES $CH_2=CH(CH_2)_{n-2}Br$ IN ACETIC ACID - WATER SOLVENT.

Again on the assumption that the rate constants for the unsubstituted olefins were constant around 4000 $\mathrm{l.mole^{-1}min^{-1}}$, an approximate attenuation plot of log Δ log k_n against n was calculated, Fig.4-6.

Table 4.18

Estimate of Inductive Effects - Bromination in Acetic Acid containing 1% by vol. of Water

Olefin	$k_2(\mathrm{l.mole^{-1}min^{-1}})$	Δ log k_n	log Δ log k_n	n
allyl bromide	12.35	2.5284	0.4028	3
4-bromobut-1-ene	96.3	1.6185	0.2090	4
5-bromopent-1-ene	517	0.8886	-0.0513	5
6-bromohex-1-ene	3280	0.0862	-1.0645	6

The above treatment produced a reasonably linear plot for n = 3 to 5 giving a value of ε=0.55, which is similar to that found for the alcohol series. The second-order rate constant for 6-bromohex-1-ene was regarded as spurious because of difficulties with re-purification of the previously made sample.

The rate data, however, suggest that there is no participation by the substituent bromine atom in any of the bromo-olefins of the above series. This observation is similar to that made for the bromination of the same series in methanol and gives no indication whether participation would occur in a less nucleophilic solvent than acetic acid.

(b) Bromination in Trifluoroacetic Acid

The bromination of the series $CH_2=CH(CH_2)_{n-2}OH$ was carried out in trifluoroacetic acid solvent at 25°C. All reactions were first-order with respect to both olefin and bromine and second-order rate constants were calculated using equation 4.11.

Table 4.19

Second-order Rate Constants for Bromination of the Series $CH_2=CH(CH_2)_{n-2}OH$ in Trifluoroacetic Acid containing 0.01N Sodium Bromide at 25°C

Olefin	k_2(l.mole^{-1}min^{-1})
allyl alcohol	$3.48 \times 10^3 \pm 100$
3-buten-1-ol	$1.70 \times 10^4 \pm 500$
4-penten-1-ol	$3.89 \times 10^4 \pm 1000$
5-hexen-1-ol	$5.15 \times 10^4 \pm 2000$

The above are the mean values of at least three measurements and are the composite rate coefficients involving addition by both bromine and tribromide ion. As previously, the low solubility of sodium bromide in trifluoroacetic acid prevented a comprehensive study of the effect of varying the bromide ion concentration in order to determine the individual rate constants k_{Br_2} and $k_{Br_3^-}$.

Inspection of Table 4.19 shows the gradual increase in rate with distance of the substituent hydroxyl group from the reaction centre, which is consistent with the attenuation of the inductive effect. However, there was no marked jump in rate for 4-penten-1-ol as was observed for bromination in acetic acid and also in methanol and water solvents.[2] This was most surprising in view of the expected enhancement of participation in trifluoroacetic acid compared with the more nucleophilic solvents, and also the observation of participation for the addition of trifluoroacetic acid to certain substituted olefins.[3]

In addition to the above series of substituted olefins, the rates of bromination of pent-1-ene and hex-1-ene were measured. As before the rates of bromination of the corresponding lower unsubstituted olefins were not measured because of vapour loss difficulties.

Table 4.20

Second-order Rate Constants for Bromination in Trifluoroacetic Acid containing 0.01N Sodium Bromide at 25°C

Olefin	k_2(l.mole^{-1}min^{-1})
pent-1-ene	100,000
hex-1-ene	110,000

On the assumption that the rate constants for the unsubstituted olefins were constant around 10^5 l.mole^{-1}min^{-1}, an attenuation plot was calculated as described for the reactions in acetic acid.

Fig.4.7 shows that rates of bromination of the series $CH_2{=}CH(CH_2)_{n-2}OH$ in trifluoroacetic acid are very similar to those predicted on the assumption of a linear attenuation of the inductive effect with distance from the reaction centre. The value for 4-penten-1-ol suggests marginal rate enhancement, but because of the approximate nature of the plot this cannot be interpreted as evidence of participation by the substituent hydroxy

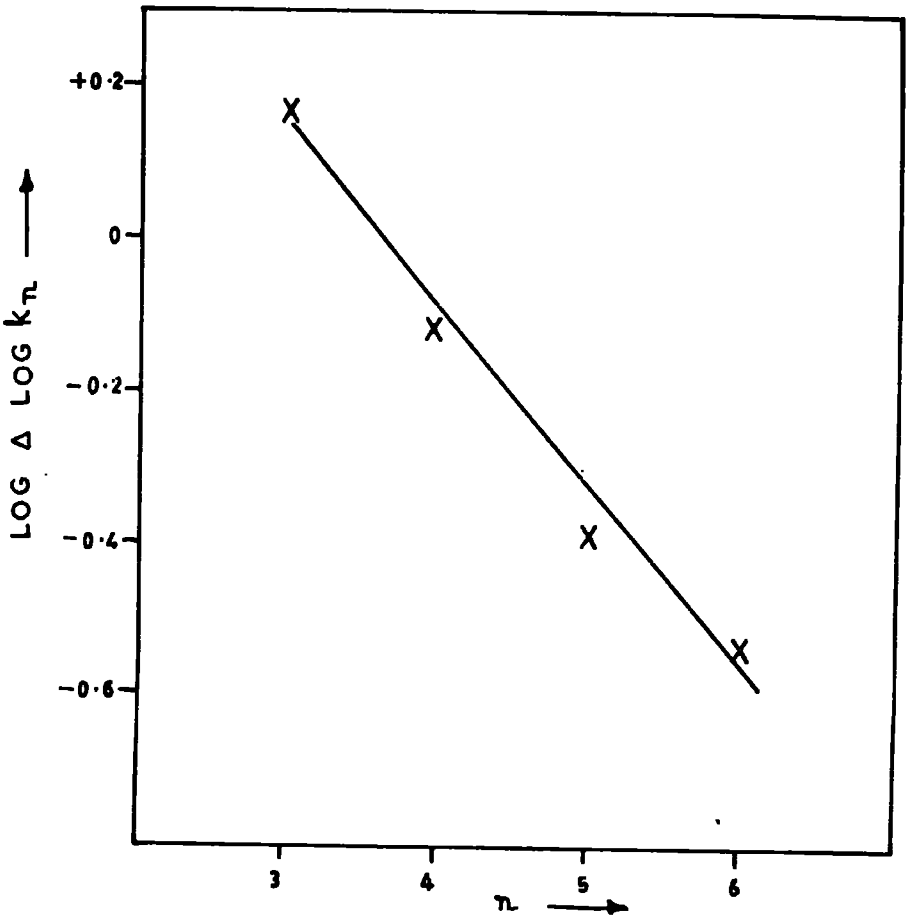


FIG. 4–7. PLOT OF LOG Δ LOG k_n AGAINST n FOR BROMINATION OF THE SERIES $CH=CH(CH_2)_{n-2}OH$ IN TRIFLUOROACETIC ACID.

Table 4.21

Estimate of Inductive Effects - Bromination in Trifluoroacetic Acid

Olefin	k_2(l.mole^{-1}min^{-1})	Δ log k_n	log Δ log k_n	n
allyl alcohol	3,480	1.4584	0.1637	3
3-buten-1-ol	17,000	0.7696	-0.1138	4
4-penten-1-ol	38,900	0.4101	-0.3871	5
5-hexen-1-ol	51,400	0.2882	-0.5403	6

group. Analysis of the product mixtures for the bromination of 4-penten-1-ol and 5-hexen-1-ol found only4.7% and 7.6% of ring-closed product respectively. This confirmed that participation by the substituent hydroxyl group was not significant for any of the above series of olefinic alcohols.

The slope of Fig.4.7 lead to a value of ϵ = 0.59 which is slightly larger than that obtained for bromination of the same series in acetic acid.

The rates of bromination of the bromide series, $CH_2{=}CH(CH_2)_{n-2}Br$ were also measured under similar conditions. The composite second-order rate constants are shown in Table 4.22.

Table 4.22

Second-order Rate Constants for Bromination of the Series $CH_2{=}CH(CH_2)_{n-2}Br$ in Trifluoroacetic Acid containing 0.01N Sodium Bromide at 25°C

Olefin	k_2(l.mole^{-1}min^{-1})
allyl bromide	$1.23 \times 10^3 \pm 20$
4-bromobut-1-ene	$3.22 \times 10^4 \pm 1200$
5-bromopent-1-ene	$6.83 \times 10^4 \pm 1200$
6-bromohex-1-ene	$9.05 \times 10^4 \pm 2500$

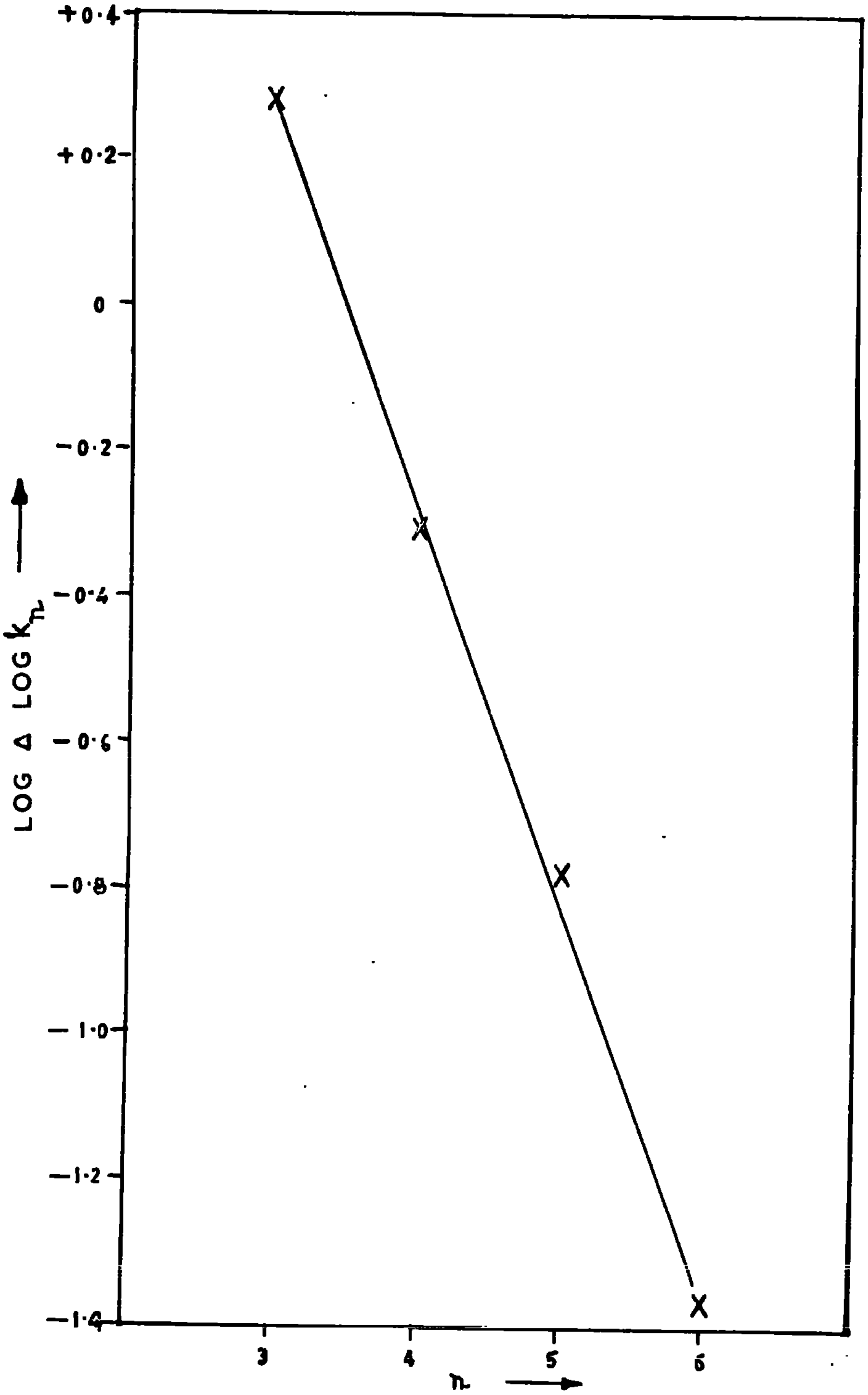


FIG. 4 - 8. PLOT OF LOG Δ LOG k_n AGAINST n FOR BROMINATION OF THE SERIES $CH_2{=}CH(CH_2)_{n-2}Br$ IN TRIFLUOROACETIC ACID.

The above are the mean values of at least three measurements and the errors quoted are the maximum variance from the mean.

Inspection of Table 4.22 indicates that only the previously observed increase in rate due to the fall-off of the inductive effect with distance from the reaction centre is illustrated. Using the same treatment as described for the alcohol series, Fig.4.8 was drawn.

Table 4.23

Estimate of Inductive Effects - Bromination in Trifluoroacetic Acid

Olefin	k_2(l.mole^{-1}min^{-1})	Δ log k_n	log Δ log k_n	n
allyl bromide	1,230	1.9101	0.2810	3
4-bromobut-1-ene	32,200	0.4921	-0.3079	4
5-bromopent-1-ene	68,300	0.1656	-0.7809	5
6-bromohex-1-ene	90,500	0.0434	-1.3625	6

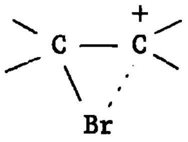
Fig.4.8 confirms the visual inspection that there is no participation by the substituent bromine atom in any of the olefins above. This is in agreement with the observations for bromination in methanol[2] and acetic acid solvents. The slope gives a value of ϵ = 0.28, indicating a low degree of substituent-solvent interaction by hydrogen bonding.

(c) Conclusions

Several features emerge from the data presented in Tables 4.14 to 4.23.

The postulate that participation by the bromo substituent in the series $CH_2{=}CH(CH_2)_{n-2}Br$ might be observed in the weakly nucleophilic solvent, trifluoroacetic acid, was not supported by experiment. This provided further evidence of significantly different behaviour between the addition of trifluoroacetic acid to olefins as measured by Peterson[3] and the addition of bromine to olefins in trifluoroacetic acid.

As suggested in Section A of this chapter, the difference in behaviour may well be due to the different form of the positively-charged species in the transition state. The bromination of the 2-halo substituted allyl chlorides indicated that the transition state more resembled a partially delocalised species of type (4-10) rather than a classical carbonium ion of type (4-11), which is generally considered to be involved in the addition of trifluoroacetic acid.



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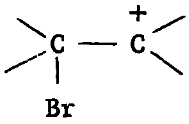


(4-11)

For the addition of trifluoroacetic acid to 5-bromopent-1-ene, it was postulated that the weakly nucleophilic bromine substituent stabilised the transition state by interaction with the positively-charged carbonium ion centre forming a species approximating to a five-membered ring.

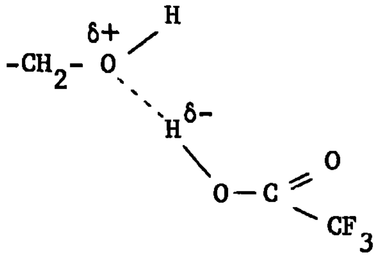
In the addition of bromine, however, the positive charge in the transition state is partially delocalised towards the additive bromine atom, thus presenting a less electrostatically attractive site to the 5-bromo atom. This delocalisation of charge away from the 2-carbon atom coupled with the steric hindrance afforded by the additive bromine and the solvating trifluoroacetic acid molecules may be sufficient to reduce the susceptibility of the positively-charged 2-carbon atom to nucleophilic attack by the substituent bromine, thus making the formation of a cyclic five-membered intermediate energetically less favourable.

The observation of quite significant participation for the bromination of 4-penten-1-ol in the acetic acid-water solvent and the corresponding lack of participation in trifluoroacetic acid is less easy to reconcile. The observation of participation by the substituent hydroxyl group has been made for the bromination of 4-penten-1-ol in methanol and water solvents;[2] and participation has also been observed by the methoxy substituent in the addition of trifluoroacetic acid to 5-meth oxypent-1-ene.[3] It is therefore surprising that participation by the substituent hydroxyl group did not occur for bromination in trifluoroacetic acid.

A possible explanation may lie in an examination of which mode of hydrogen bonding is dominant in the solvent systems concerned. The failure to observe any participation by the substituent hydroxyl group in bromination reactions in trifluoroacetic acid may be attributable to the reduced nucleophilicity of the hydroxyl group by hydrogen bonding to the trifluoroacetic acid solvent.

The hydroxyl substituent can hydrogen bond by both proton loss and proton gain in the hydroxylic solvents used in this study. The F^{19} n.m.r. data published by Taft[23] shows that in methanol and methanol-water solvents (and by inference in acetic acid-water solvent) hydrogen bonding by proton donation of the hydroxyl substituent is dominant, exhibited by the observed shift to higher field strength. Hydrogen bonding by proton donation has the effect of increasing the nucleophilicity of the substituent.

However, almost all basic substituents exhibit a downfield shift in trifluoroacetic acid, the magnitude of which is dependent on the basicity of the substituent. This evidence suggests that the dominant mode of hydrogen bonding by the substituent hydroxyl group in trifluoroacetic acid is proton gain - Scheme (4-12) - thus reducing the nucleophilicity of the substituent and its effectiveness as an internal nucleophile. The



(4-12)

reduction of nucleophilicity in trifluoroacetic acid compared with the solvent enhancement of the nucleophilicity of the substituent in methanol may be sufficient to explain the lack of participation by the hydroxyl group in bromination reactions in trifluoroacetic acid.

It is noted that the 5-methoxy substituent also exhibits hydrogen bonding by proton gain but still provides anchimeric assistance in the addition of trifluoroacetic acid to 5-methoxypent-1-ene. However, in this case internal nucleophilic attack is directed towards a classical carbonium ion centre of type (4-11) and not a partially delocalised species (4-10). The observation of participation in this reaction is not inconsistent with the postulate explaining the lack of participation in the bromination reaction.

The investigation of the bromination of the series $CH_2=CH(CH_2)_{n-2}OMe$ may provide further evidence of the differing forms of the transition state for addition of bromine and trifluoroacetic acid.

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CHAPTER 5

EXPERIMENTAL

5.1 Introduction.

Before the work of R.P. Bell[1] and J.E. Dubois[2] it had not been possible to measure the rather rapid rates of addition of bromine to a large number of olefins, since classical methods of analysis were far too slow.

The electrochemical technique described by them permitted the measurement of large second order rate constants by following the rate of disappearance of bromine by means of observing the change in the redox potential of a rotating platinum electrode in a solution containing both bromine and bromide ions. Dubois described two variations of the method:-

(a) The concentration of bromine in the reaction mixture was maintained at a constant level by means of electrolytic generation of bromine from bromide ions in situ. Consequently, the rate of disappearance of bromine in the reaction was given by the rate of generation of bromine necessary to maintain static conditions. This is the basis of the 'concentrostat' method, which Dubois and Mouvier[3] used to measure second-order rate constants of up to 3×10^7 $l.mole^{-1}$ min^{-1}.

(b) The decrease in the concentration of bromine in the reaction mixture was monitored continuously by following the change in e.m.f. generated by the rotating platinum electrode with reference to either a glass or calomel electrode.

In this study, the second method has been adopted. This was also the basis of Bell's measurements.

5.2 Method.

(a) Description

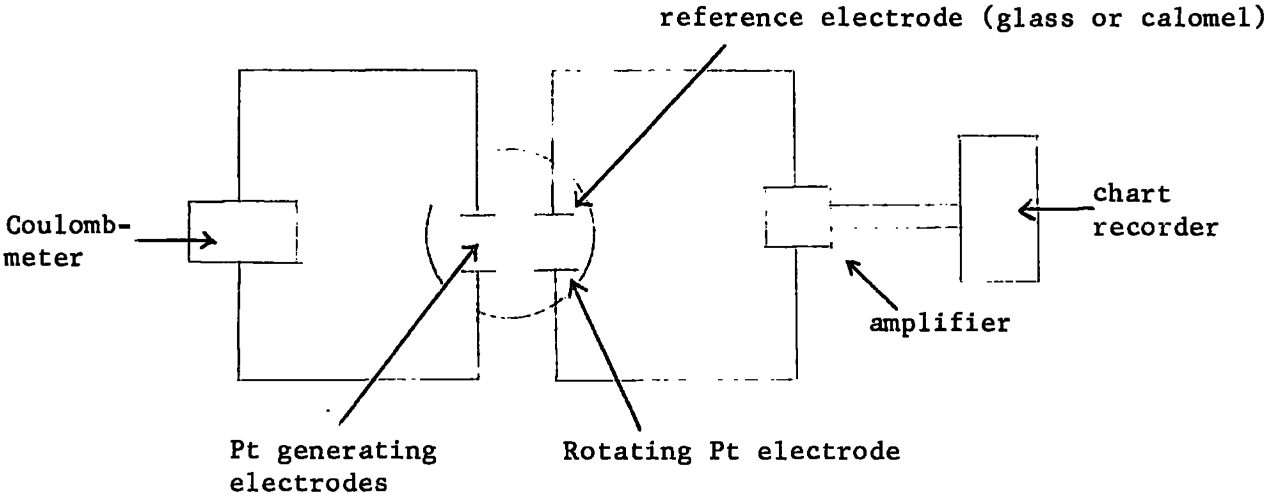

Fig. 5.1

The rates of bromination were measured using the apparatus shown schematically in Fig. 5.1. The reaction vessel, which was a Metrohm titration vessel, was cylindrical with a tapered base and had a total capacity of 200 mls. The vessel was fitted with a sealing P.T.F.E. head, containing five C14 inlets, one of which was central to accomodate the rotating platinum electrode.

The platinum electrode consisted of a uniform bore tube containing a copper wire. This wire was connected internally to a small piece of platinum wire which protruded through the glass. A glass sleeve terminating in a C14 cone provided the seal and located the electrode in the P.T.F.E. head. A paddle stirrer was added after insertion through the vessel head. The upper end of the copper wire was welded to a screw connector which joined the electrode to the motor spindle, the electrical take-off being effected via a silver stud onto a copper slip-ring mounted on the spindle. The electrode was rotated at a constant speed of 750r.p.m. The reference electrode (either glass or calomel) fitted into one of the other C14 inlets, and the e.m.f. resulting from the cell was amplified by an E.I.L. pH meter and fed into a Honeywell Electronik 15 chart recorder with drive speeds varying from 100 in/hr to 2,400 in/hr, and an 80 mV or 40 mV range.

The bromine generating electrode, consisting of two platinum plates sealed into glass, each of area 0.56 sq cms, fitted into a third C14 inlet in the P.T.F.E. vessel head. Accurately known quantities of bromine were generated by means of a Metrohm E.211A coulombmeter. It was possible to supply a range of currents from 0.03 mA to 20 mA for a precisely known time, since the switching mechanism also operated the electrical stop-clock incorporated in the coulombmeter.

The two other C14 inlets were stoppered, one of them being used for the injection of the olefin via a previously-weighed micro-syringe.

(b) Procedure.

Solutions of sodium bromide (recrystallised from water) were made up in the various solvents at 25°C. Known volumes of solution were pipetted into the reaction vessel, which was immersed in a thermostat at 25° ± 0.02°C. A precisely known quantity of bromine was generated in situ and the base line response of the analysing electrodes was checked to ensure that no bromine was lost through evaporation or reaction with the solvent. (It should be noted that it was not necessary to know the absolute emf of the system, but only the change in e.m.f. over a measured period of time). An excess of olefin was then injected into the reaction vessel via a weighed micro-syringe which was reweighed immediately after use. A linear decrease of e.m.f. with time was observed over approximately 60 mV representing about 97% of the reaction, which verified the first-order nature of the reaction under the experimental conditions.

5.3 Discussion.

The great advantages of this method were:-

(a) its ability to follow continuously the changing bromine concentration at high speed, the upper limit being determined by the speed of mixing of the reactants. In general the rate constant can be measured if the half-life of the reaction is greater than or equal to ten times the time taken for mixing.

(b) Its applicability to reactions carried out in very dilute solutions. Initial bromine concentrations of approximately 10^{-4}M have been used in this study, whereas Bell[4] et al have used initial bromine concentrations varying from 3×10^{-4}M to 3×10^{-6}M.

It should be noted, however, that the expected electrode response to a particular set of conditions was not always found. In a number of his publications,[5] Bell has commented upon unusual and irreproducible response by the potentiometric system. In this work, it was initially attempted to reproduce the values determined by Williams,[6] for the bromination of allyl alcohol and 4-penten-1-ol in a 0.2N solution of sodium bromide in methanol at 25°C. Initially, both rate constants were found to be approximately 30% high. Stringent purification of all reactants and checks on all the electrical equipment, (coulombmeter, amplifier, recorder) produced no change in this value. The possibility that the reference potential changed in the course of the reaction was tested using added sulphuric acid, but no change was produced. To reduce any polarisation of the platinum electrode, the methanol solvent was purged of any dissolved oxygen by passing through it a stream of nitrogen before making up the solutions - again this had no effect. The doubtful possibility of a contribution from a free radical mechanism was discounted since reactions carried out in a blackened vessel with or without any added sodium azide produced no change. Variation of the stirring speed between 500 and 1500 r.p.m. using a new motor also produced no effect.

Consequently, an investigation of the detailed response of the platinum electrode to known concentrations of bromine was carried out. Haissinsky[7] had found that potentials for solutions more dilute than 10^7M did not correspond to those calculated by the Nernst equation, an observation which was questioned by Bell and Pring.(5a) Plotting a graph of e.m.f. (mV) against log [Br_2] showed similar behaviour to that reported by Purdy et al.[8] However, it was observed that the linear dependance of the e.m.f. on log [Br_2] required by the Nernst equation did not occur until a concentration of bromine between 10^{-4}M and 10^{-5}M had been generated. Also it was noticed that even when this relationship did hold, a ten-fold change in bromine concentration produced a 39 mV change in e.m.f. instead of the 30 mV calculated. This observation thus explained the high rate constants for allyl alcohol and 4-penten-1-ol, and also the fact that the rates of reaction appeared to increase towards the end of the reaction. At lower bromine concentrations (on the S-part of the curve), the Nernst equation was not obeyed and a given decrease in the bromine concentration produced a much larger fall in e.m.f.

This problem was overcome by immersing the platinum electrode in hot, concentrated nitric acid[5(c),9] for about 30 minutes, and then in 10^{-2}M ferrous sulphate with a little added sulphuric acid, which would remove any possible oxide films.[10] It was then left in a moderately concentrated bromine/bromide solution in methanol for 24 hours. It was found that the polarographic S-shaped jump now appeared at a bromine concentration of approximately 10^{-7}M and that the final slope corresponded to 30 mV per ten-fold change in bromine concentration as required by the Nernst equation.

Following this treatment, the platinum electrode behaved more reliably, but on each day of operation this reliability of electrode response was checked by determining the rate of bromination of an olefin which had been measured previously. Periodic cleaning was found to be necessary.

5.4 Bromination of Allyl Chloride in Methanol.

The procedure of bromination was carried out as described in Section 5.2.

Allyl chloride - commercial reagent - was initially fractionally distilled, bpt 45°C, and then further purified by preparative g.l.c.

Sodium bromide was recrystallised from water, dried and kept in a dessicator. It was purified in this way for all the bromination experiments described.

Commercial grade methanol was dried by treatment with magnesium turnings and then fractionally distilled, b.pt. 65°C, the first 250 mls of any batch being discarded. Since, on trial runs, a slight drift of the base line was noticed, indicating reaction of bromine with solvent impurities, 300 ml batches of methanol were refluxed with 2 drops of bromine until the solution was completely colourless - about 15 mins. This oxidised any impurities still left in the solvent which might react with the bromine generated in the reaction vessel.

The rates of bromination were measured for solutions 0.2N, 0.1N, 0.05N, 0.02N, in sodium bromide using 75 mls of solution. The reaction was followed for a decrease in e.m.f. of 80 mV having used initial bromine concentrations of the order of 2.5×10^{-4}M and 10^{-1}M allyl chloride. These concentrations were varied from run to run without significant variation of the second-order rate constant.

5.5 Bromination of the Series $CH_2=C(X)-CH_2Cl$ in 50% by vol Methanol-Water Solvent.

The bromination of the series of olefins $CH_2=C(X)-CH_2Cl$ (where X = H, F, Cl, Br) was carried out in a 0.2N solution of sodium bromide in a 1:1 mixture by volume of methanol and water as solvent at 25°C. Solutions were made up in 250 ml batches by dissolving the sodium bromide in 125 mls of water and making up to volume with methanol. Methanol was purified as described previously, (Section 5.4) and the water was distilled from alkaline potassium permanganate.

Allyl chloride (b.pt. 45°C), 2-fluoro-3-chloroprop-1-ene (b.pt.55°C), 2:3-dichloroprop-1-ene (b.pt. 92°C) were purified by fractional distillation of commercial samples and then by preparative g.l.c. 2-bromo-3-chloroprop-1-ene was purified by preparative g.l.c.

All reactions were performed using 75 mls of solution and an initial bromine concentration of approximately 2.5×10^{-4}M. Olefin concentrations varied from 4.4×10^{-3}M to 0.2M. A glass electrode was used as a reference and the reactions were followed for 80 mV.

5.6 Bromination of the Series $CH_2 = C(X)-CH_2Cl$ in Trifluoroacetic Acid.

The bromination of the series $CH_2 = C(X)-CH_2Cl$ (where X = H, F, Cl) was carried out in 0.01N solutions of sodium bromide in trifluoroacetic acid at 25.00 ± 0.02°C. Because of the difficulty of dissolving the sodium bromide in trifluoroacetic acid, it was not possible to determine the rates of bromination at higher concentrations of bromide ions. At lower concentrations the excess of bromide ions over the bromine concentration would have been too small for the bromide ion concentration to have been considered constant throughout the reaction.

Before use, trifluoroacetic acid was fractionally distilled,[11] (b.pt. 72°C), and its purity checked by g.l.c. Trifluoroacetic acid was recovered by refluxing with added bromine until the liquid was colourless and then fractionating. The first 10% of every batch was discarded.

The olefins were purified as described in Section 5.5. All reactions were carried out using 100 mls of solution and the initial bromine concentration was approximately 10^{-4}M. Olefin concentrations varied from 3.4×10^{-3}M to 0.2M. Both glass and calomel electrodes were used as references and the reactions were followed for 80 mV.

5.7 Bromination of Allyl Chloride and Allyl Bromide in Acetic Acid containing 1% by vol of Water and Trifluoroacetic Acid.

Allyl chloride and allyl bromide were brominated in 0.01N solutions of sodium bromide in both trifluoroacetic acid, and acetic acid containing 1% by vol of water. Second-order rate constants were measured in both solvents. Initial concentrations of 10^{-4}M of bromine and between 1.2 x 10^{-2}M and 3.2 x 10^{-2}M of olefin in acetic acid - water solvent were used. 2 x 10^{-4}M of bromine and between 2.0 x 10^{-3}M and 3.5 x 10^{-3}M of olefin were used in trifluoroacetic acid and the reactions were followed for 80 mV in both solvents.

Allyl chloride (b.pt. 45°C) and allyl bromide (70-71°C) were purified by fractional distillation and then preparative g.l.c. Acetic acid solvent was purified as described by Orton and Bradfield.[12] The amount of water in each batch of acid was estimated by determination of the m.pt. Assuming a lowering of the m.pt. of 0.02°C for each 0.1% of water, a theoretical amount of acetic anhydride was added to each batch together with 2% of chromic oxide. The mixture was refluxed for approximately one hour and then fractionally distilled. The fraction boiling at 116°-118°C was collected, the first 10% being discarded.

The water was purified by distillation from alkaline potassium permanganate.

Trifluoroacetic acid was purified as described in Section 5.6.

5.8 Bromination of Benzyl Chloride and Benzyl Bromide in Acetic Acid containing 1% by vol of Water.

25 mls of a bromine solution, prepared by dissolving 100 µl of bromine in 100 mls of acetic acid solvent containing 1% by vol of water and 0.01N sodium bromide, were pipetted into a 50ml graduated flask. The acetic acid and water were purified as described in section 5.7. A known weight of benzyl halide was injected into the bromine solution, the flask was shaken vigorously and the solution decanted into a tube filler. All air drawn into the tube filler passed through a bubbler containing some of the same solution as in the filler. 2 ml aliquots were dispensed into clean, dry, drawn test tubes which were sealed immediately after filling.

The tubes were immersed in a thermostat bath at 48.37°C ± 0.02°C and withdrawn at intervals. The reaction was stopped by immersion in liquid air. The tubes were washed and broken under 50 mls of water containing 2 mls of potassium iodide solution (8.312 gms/litre). The iodine generated was titrated immediately with 0.01N sodium thiosulphate using 0.1% sodium starch glycollate as indicator.

Benzyl chloride (b.pt 61-63°C/9 mm) was purified by fractional distillation followed by preparative g.l.c. Benzyl bromide was purified by preparative g.l.c.

The reactions were repeated in solutions containing 0.1N sodium bromide.

5.9 Bromination of Benzyl Chloride and Benzyl Bromide in Trifluoroacetic Acid.

A solution of bromine in trifluoroacetic acid containing 0.1N sodium bromide was made up by dissolving 120 μl of bromine to give 100 mls of solution at 25°C. The flask was maintained at 25°C and a 25 ml aliquot was pipetted into a 50 ml graduated flask which was also maintained at 25°C. A known weight (100μl) of benzyl halide was injected from a previously weighed syringe into the 25 ml aliquot and the time noted. The solution was immediately shaken and transferred to the tube filler and 2 ml aliquots dispensed as quickly as possible. Each tube was sealed immediately and all tubes were immersed in the thermostat together. The tubes were withdrawn at intervals, quenched in liquid air and titrated immediately with sodium thiosulphate as before.

The initial bromine concentration was found by repeating the above procedure - without adding any benzyl halide - filling a number of tubes and titrating with sodium thiosulphate. Trial runs showed that all eleven tubes would be filled without any significant change in the titre, thus showing that bromine losses by evaporation had been eliminated. Blank runs were also done to check that there was no significant reaction of bromine solvent.

Benzyl chloride and benzyl bromide were purified as described in Section 5.8, and trifluoroacetic acid as in Section 5.6.

5.10 Determination of the Products of Bromination of Benzyl Chloride and Benzyl Bromide.

1.25 gms of benzyl chloride were dissolved in 50 mls of acetic acid solvent containing 1% by volume of water and 0.01M sodium bromide. An equivalent quantity of bromine was dissolved in a further 50 mls of acetic acid-water solvent. The benzyl chloride solution was placed in a thermostat at $48.37^{o} \pm 0.02^{o}$C. and the bromine solution added over three weeks.

The resulting solution was added to 150 mls of distilled water, neutralised with sodium carbonate and the organic products extracted twice with ether. The ether solution was dried over anhydrous $MgSO_4$, filtered and the ether removed on a rotary evaporator. The products were analysed by g.l.c. The presence of monobrominated product was illustrated, but the relative concentrations of the ortho-, meta- and para- bromobenzyl chlorides could not be determined since effective separation of the three isomers in the synthetic mixture did not prove possible.

The procedure was repeated for benzyl bromide with similar results.

Investigations carried out in trifluoroacetic acid for both compounds, again established the formation of monobrominated product.

5.11 Bromination of the Series $CH_2 = CH-(CH_2)_{n-2}OH$ in Acetic Acid containing 1% by vol of Water.

The bromination of the series of olefins $CH_2=CH-(CH_2)_{n-2}OH$ (where $n = 3 \rightarrow 6$) was carried out in solutions of sodium bromide in acetic acid containing 1% by volume of water. Second-order rate constants were determined in 0.1N and 0.01N solutions of sodium bromide using both the calomel and glass reference electrodes.

The acetic acid solvent was purified as described in Section 5.7. Water was purified by distillation from alkaline potassium permanganate. Allyl alcohol (b.pt 97°C), 3-buten-1-ol (b.pt 114°C), 4-penten-1-ol (b.pt 138-40°C), 5-hexen-1-ol (b.pt 56-58°C/15 mm) were purified by fractional distillation of commercial samples and preparative g.l.c.

75 mls of solution were used and the reactions were followed for 80 mV. The initial bromine concentration was 10^{-4}M. Initial olefin concentrations varied from 3.0 - 7.5 x 10^{-3}M.

5.12 Bromination of the Series $CH_2{=}CH\text{-}(CH_2)_{n-2}Br$ in Acetic Acid containing 1% by vol of Water.

The rates of bromination of the series $CH_2 = CH\text{-}(CH_2)_{n-2}Br$ (where n = 3 → 6) were measured in a solution of sodium bromide in acetic acid solvent containing 1% by vol of water. Conditions were as described previously (Section 5.11) except that the volume of solution used was 100 mls. Initial bromine concentrations were again 10^{-4}M, and initial olefin concentrations varied between 2.0 x 10^{-3}M and 2 x 10^{-2}M.

Allyl bromide, (b.pt. 70-71°C) and 4-bromobut-1-ene (b.pt 97-99°C) were purified by fractional distillation of commercial samples and preparative g.l.c.

5-bromopent-1-ene was prepared by the method described by LaForge et al.[13] 7.3 gms of 4-penten-1-ol and 1.9 gms of pyridine were placed in a flask immersed in an ethanol-carbon dioxide bath at a temperature of -25°C → -30°C. 9.5 gms of phosphorus tribromide were added dropwise over about 90 mins to the continuously stirred mixture in the flask. The product was then distilled using an oil bath until no more distillate was obtained. Care was taken to avoid the spontaneous ignition of escaping vapours, especially near the end of the operation. The distillate was washed twice with water, once with dilute caustic soda and dried over anhydrous calcium chloride. The final product, b.pt 127-129°C was purified by preparative g.l.c. before use.

6-bromohex-1-ene[14,15] was prepared by treating 5-hexen-1-ol with phosphorus tribromide in pyridine in the same molar proportions as for 5-bromopentene. The final product, b.pt 46-48°C at 11 mm, was purified by preparative g.l.c. before use.

5.13 Bromination of 1-pentene and 1-hexene in Acetic Acid containing 1% by vol of Water.

The rates of bromination of 1-pentene and 1-hexene were measured in 0.01N, 0.05N, 0.1N solutions of sodium bromide in acetic acid solvent containing 1% by volume of water. Newly-purchased samples of both olefins were purified by preparative g.l.c. before use. Initial concentrations were approximately 10^{-4}M of bromine and 3.0×10^{-3}M of olefin.

5.14 Bromination of the Series $CH_2=CH(CH_2)_{n-2}OH$ in Trifluoroacetic Acid.

The bromination of the series $CH_2=CH(CH_2)_{n-2}OH$ (where $n = 3 \rightarrow 6$) was carried out in 0.01N solutions of sodium bromide in trifluoroacetic acid at 25.00 ± 0.02°C. Due to the difficulty of dissolving the sodium bromide, it was not possible to determine the rates of bromination at higher concentrations of bromide ions.

Before use the trifluoroacetic acid was purified as described in Section 5.6. Both glass and calomel electrodes were used as references and the reactions were followed for 80 mV. The volume of each solution was 100 mls and the initial bromine concentration was approximately 10^{-4}M. Initial olefin concentrations varied between 2.0 - 6.0 x 10^{-3}M. The olefins were purified as described in section 5.11.

5.15 Bromination of the Series $CH_2=CH-(CH_2)_{n-2}Br$ in Trifluoroacetic Acid.

The bromination of the series $CH_2=CH(CH_2)_{n-2}Br$ (where n = 3 → 6) was carried out under conditions as in section 5.14. The compounds were prepared and purified as detailed in section 5.12. Initial concentrations of the olefins varied between 1.5 - 2.5 x 10^{-3}M.

5.16 Bromination of 1-pentene and 1-hexene in Trifluoroacetic Acid.

The bromination of 1-pentene and 1-hexene was carried out under conditions as described in section 5.14. The compounds were purified by preparative g.l.c. The initial concentrations of 1-pentene and 1-hexene were 1.3 x 10^{-3}M and 1.1 x 10^{-3}M respectively.

5.17 Determination of the Products of Bromination of 4-penten-1-ol in Acetic Acid containing 1% by vol of Water.

0.98 gms (1.1 x 10^{-2} moles) of 4-penten-1-ol were added to 100 mls of a 0.01N solution of sodium bromide in acetic acid containing 1% by vol of water. An equivalent quantity of bromine was dissolved in another 100 mls of acetic acid-water solvent. The resulting bromine solution was added dropwise to the solution of 4-penten-1-ol with continuous stirring over a period of three hours.

The solvent was removed from the product mixture on a rotary evaporator with the bath at a temperature of 52°C and at 17 mm Hg pressure.

The products were analysed by g.l.c. using two different columns - silicone grease and di-n-decylphthalate at 150°C. The ring-closed product, 2-bromomethyltetrahydrofuran, was identified by comparison with the retention time of an authentic sample which had previously been prepared by the bromination of tetrahydrofurfuryl alcohol with phosphorus tribromide.[6] This sample was fractionally distilled (b.pt 52°C at 9 mm) to effect purification. The purity and authenticity of the standard were checked by g.l.c. and infra-red spectroscopy.

The relative quantities of cyclised and straight chain products were evaluated by means of a gas density balance (G.D.B.) using a silicone grease column. The proportion of ring-closed products was found to be 35%.

5.18 Determination of the Products of Bromination of 5-hexen-1-ol in Acetic Acid containing 1% by vol of Water.

The procedure described in section 5.17 was repeated using 0.94gms of 5-hexen-1-ol. Comparison of the product mixture with a previously prepared sample of 2-bromomethyltetrahydropyran illustrated the presence of the ring-closed product. Analyses by G.D.B. showed that 8% of cyclised product was present.

5.19 Determination of the Products of Bromination of 4-penten-1-ol in Trifluoroacetic Acid.

The procedure described in section 5.17 was repeated using a 0.01N solution of sodium bromide in trifluoroacetic acid. The trifluoroacetic acid solvent was removed from the products at a bath temperature of 40°C and 40 mm pressure on a rotary evaporator; g.l.c. analysis again illustrated the presence of ring-closed product which the G.D.B. showed to be 4.7%.

5.20 Determination of the Products of Bromination of 5-hexen-1-ol in Trifluoroacetic Acid.

The procedure described in Section 5.17 was applied to 5 hexen-1-ol in trifluoroacetic acid containing 0.01N NaBr. G.l.c. analysis illustrated the presence of ring-closed product which the G.D.B. showed to be 7.6%.

5.21 Bibliography.

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