Participation by Neighbouring Groups in Addition Reactions. Part III.[1] Bromination in Acetic Acid and Trifluoroacetic Acid Solvents

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Rate measurements and product analyses for bromination of $CH_2=CH[CH_2]_nOH$ (for n = 1—4) in acetic acid indicated substantial participation by the neighbouring hydroxy-group for n = 3 and a smaller but still significant participation for n = 4. The general pattern of behaviour was very similar to that observed previously for reactions in methanol and water solvents. However, in trifluoroacetic acid solvent the extent of such hydroxy-participation was drastically reduced (there being only 4% ring-closed product for n = 3). The effect is attributed to hydrogen-bonding between the solvent and the hydroxy-substituent, which reduces the nucleophilicity (and hence its effectiveness as a neighbouring group) of the hydroxy-substituent. As for the methanol reactions, there was no kinetic indication of any participation by neighbouring bromine in the bromination of $CH_2=CH[CH_2]_nBr$ in either acetic acid or trifluoroacetic acid solvent.

PARTS I and II [1,2] discuss the extent of participation by the neighbouring groups OH and Br, particularly *via* five- and six-membered transition states, in the bromination and iodination of $CH_2=CH[CH_2]_nOH$ (for $n = 1$—4), and the corresponding bromoalkenes, in methanol and water solvents. Both rate measurements and product analyses showed that 5-OH, and to a lesser extent 6-OH participation, occurred in the bromination and iodination of the alcohols. In iodination the reaction leading to ring-closed products completely dominated the normal addition reaction for $n = 3$ and 4, whereas for bromination both the assisted and the non-assisted reactions were detected. Indeed there was reasonable agreement between the observed yields of ring-closed products and those estimated from the rate measurements. There was no kinetic evidence whatsoever for substituent bromine participation in the bromination of the series $CH_2=CH[CH_2]_nBr$ and only a suggestion of a small degree of participation in the iodination of 5-bromopent-1-ene. It was thought to be of interest to extend the work to reactions in solvents of low nucleophilicity, where it might be expected that the neighbouring group, acting as an internal nucleophile, would play a more prominent part in the reaction. This paper describes the results of measurements on the same hydroxy- and bromo-alkenes in acetic acid and trifluoroacetic acid solvents.

Substantial rate enhancements have, of course, been observed in solvolyses proceeding by way of a carbonium ion, for a variety of neighbouring groups.[3] Quantitative work of the extent of participation in addition reactions is much less well documented; the most notable contributions are from the work of Peterson and his co-workers,[4] based on the addition of trifluoroacetic acid to alkenes. Here a large range of neighbouring groups have been studied (CN, O_2CCF_3, O_2CMe, Cl, OMe, *etc.*) and there is much evidence [5] from rate measurements, and from the identification of various rearrangement products, for the involvement particularly of five- and six-membered cyclic intermediates. Relatively little information is available which demonstrates neighbouring group participation in electrophilic halogenation, apart from a number of cyclic product identifications, *e.g.* the formation of iodolactones from iodine and carboxylic acids.[6]

Tables 1 and 2 give the experimental second-order rate constants determined for the bromination of the hydroxy- and bromo-alkene series in various solvents. The results for methanol are taken from our earlier work,[1,2] and are included here for comparison purposes.

TABLE 1

Variation of k_2 with n for bromination of $CH_2=CH[CH_2]_nOH$ in methanol, acetic acid, and trifluoroacetic acid

	k_2 l mol^{-1} min^{-1}		
Alkene	MeOH *	CH_3CO_2H †	CF_3CO_2H ‡
$CH_2=CHCH_2OH$	284	251	3480
$CH_2=CH[CH_2]_2OH$	525	594	17000
$CH_2=CH[CH_2]_3OH$	2630	4020	38900
$CH_2=CH[CH_2]_4OH$	1730	1595	51500
$CH_2=CH[CH_2]_3H$	2090	1730	101000

* Containing 0·2M-NaBr. † Containing 0·1M-NaBr. ‡ Containing 0·01M-NaBr.

The Alcohols $CH_2=CH[CH_2]_nOH$.—Mere inspection of the rate constants in Table 1 show that the substituent effects in acetic acid parallel those for methanol very closely. In particular there is a sudden increase from but-3-en-1-ol to pent-4-en-1-ol followed by a drop to hex-5-en-1-ol. Kinetic evidence of a maximum rate constant value at some point along a series of this kind is usually ascribed to participation by a neighbouring group. This case is strengthened when it is seen that for bromination in both methanol and acetic acid the rate constants for pent-4-en-1-ol exceed that for the unsubstituted pent-1-ene. Similar rate maxima

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[1] Part II, E. Bienvenüe-Goetz, J. E. Dubois, D. W. Pearson, and D. L. H. Williams, *J. Chem. Soc.* (*B*), 1970, 1275.

[2] D. L. H. Williams, E. Bienvenüe-Goetz, and J. E. Dubois, *J. Chem. Soc.* (*B*), 1969, 517.

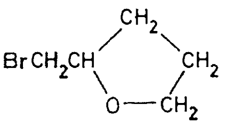
[3] B. Capon, *Quart. Rev.*, 1964, **18**, 45, and references therein.

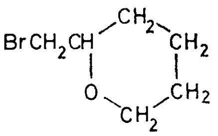
[4] P. E. Peterson and G. Allen, *J. Amer. Chem. Soc.*, 1963, **85**, 3608; P. E. Peterson, C. Casey, E. V. P. Tao, A. Agtarap, and G. Thompson, *ibid.*, 1965, **87**, 5163; P. E. Peterson and E. V. P. Tao, *ibid.*, 1964, **86**, 4503; P. E. Peterson, R. J. Bopp, D. M. Chevli, E. L. Curran, D. E. Dillard, and R. J. Kamat, *ibid.*, 1967, **89**, 5902.

[5] P. E. Peterson, *Accounts Chem. Res.*, 1971, 407.

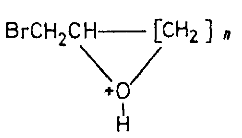
[6] E. E. van Tamelen and M. Shamma, *J. Amer. Chem. Soc.*, 1954, **76**, 2315.

have been observed [7] for example in the solvolysis of the series $Cl[CH_2]_nOH$. Further, we have found that the ring closed products (I) and (II) are among the products of the reactions in acetic acid of pent-4-en-1-ol and hex-5-en-1-ol respectively (together with the normal addition products, the dibromide and the bromoacetoxy-compound) to the extent of 35 and 8%.


(I)


(II)

It is possible to estimate the rate constant for reaction *without* participation by the neighbouring group, and hence get a measure of the degree of assistance, if it is assumed that the inductive effect falls off along a carbon chain by a constant factor ε per CH_2 group. This procedure [8] has been used extensively by Peterson, and by us in our earlier work; there has in general been good agreement between the calculated and observed yields of ring-closed products. In this case the method yields values of 1033 and 1380 l mol^{-1} min^{-1} for the unassisted rate constants for the bromination of pent-4-en-1-ol and hex-5-en-1-ol respectively, in acetic acid solvent. These values predict 70 and 14% ring-closed products as compared with the 35 and 8% observed. The agreement is much less good than for the corresponding reactions in methanol and water, and although the method is somewhat approximate it may well suggest that a significant fraction of the assisted reaction finally gives the normal addition products, instead of the ring-closed product. This could arise either by ring-opening of the intermediate (III) by nucleophilic attack by bromide ion or the solvent (which competes with proton loss), or, more probably if the structure of the intermediate resembles (IV) rather than (III), *i.e.* where the positive charge lies mostly on the carbon atom and the carbon–oxygen bond is not a fully developed covalent bond. Competition between nucleophilic attack at carbon and proton loss from oxygen could then more readily be understood. Structures like (IV) have in fact been postulated by Robertson and his co-workers [9] as intermediates in solvolysis reactions, in order to explain the observed ^{13}C scrambling which occurs between C-1 and -4 in the hydrolysis of 4-methoxy[1-^{13}C]butyl bromide.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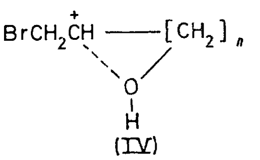
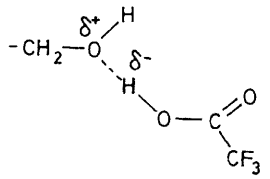

(IV)

The acetic acid results, which show much greater participation for pent-4-en-1-ol than for hex-5-en-1-ol again illustrate the now well known [10] order of stability of the cyclic intermediates, where the five-membered ring containing oxygen is favoured over the six-membered ring.

Strangely, in trifluoroacetic acid, the pattern of rate constants is different. There is no rate maximum at pent-4-en-1-ol, neither is there any evidence of an abnormally large increase along the series. In no case does the rate constant for the alcohol exceed that of the unsubstituted alkene. Indeed the attenuation plot [2,3] gives a quite good straight line for *n* 1—4 suggesting that there is no significant rate enhancement in the series over and above that expected on polar grounds, *i.e.* that there is no hydroxy-participation. This is borne out by the product analyses where only 4 and 7% of the tetrahydrofuran (I) and tetrahydropyran (II) derivatives were identified in the reaction mixtures. This result was, at first, somewhat unexpected in light of the very large effects found for neighbouring group participation for reactions in trifluoroacetic acid solvent.[3,11] A probable explanation of our result is that extensive hydrogen bonding develops between the hydroxy-substituent and the solvent, which would reduce the effective nucleophilicity of the substituent markedly. The hydroxy-group in alcohols can in principle become hydrogen bonded to hydroxylic solvents either by proton loss or by gain. The ^{19}F n.m.r. data of Taft and his co-workers [12] show that in methanol and methanol–water solvents (and also by inference in acetic acid), hydrogen bonding occurs by proton donation from the hydroxy-group to the solvent, as detected by the shift to higher field strength. This has the nett effect of increasing the nucleophilicity of the substituent, and has been taken [2,13] as the explanation of the apparent enhanced reactivity of allyl alcohol towards bromination in methanol. However almost all basic substituents exhibit a downfield shift for trifluoroacetic acid, the magnitude of which depends on the basicity of the substituents. This suggests strongly that in trifluoroacetic acid the dominant mode of hydrogen bonding is that of proton gain by the substituent [see (V)]. This would have the effect of


(V)

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[7] H. W. Heine, A. D. Miller, W. H. Barton, and R. W. Greiner, *J. Amer. Chem. Soc.*, 1953, **75**, 4778.

[8] J. McGowan, *J. Appl. Chem.*, 1960, **10**, 312; H. Klootsterziel, *Rec. Trav. chim.*, 1963, **82**, 508.

[9] M. J. Blandamer, H. S. Golonkin, and R. E. Robertson, *J. Amer. Chem. Soc.*, 1969, **91**, 2678.

[10] Ref. 3, pp. 105—109.

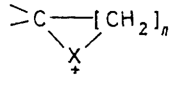
[11] See for example, J. E. Nordlander and W. G. Deadman, *J. Amer. Chem. Soc.*, 1968, **90**, 1590.

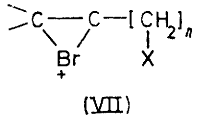
[12] R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davies, *J. Amer. Chem. Soc.*, 1963, **85**, 709.

[13] J. E. Dubois and E. Goetz, *Tetrahedron Letters*, 1965, **5**, 303.

reducing the nucleophilicity of the oxygen and hence reduce its effectiveness as an internal nucleophile in neighbouring group participation. This would also explain the apparently low reactivity towards bromination of allyl alcohol in trifluoroacetic acid, where the value of k_2 is 3% that of the unsubstituted alkene, whereas for methanol and acetic acid solvents k_2 is 15% that of the values of the unsubstituted alkenes in the appropriate solvents. We have used in this comparison the value of k_2 for pent-1-ene for that of propene (which we did not measure); there is expected to be very little variation in k_2 along the series propene–hex-1-ene (see ref. 2).

The Bromides $CH_2{=}CH[CH_2]_nBr$.—No neighbouring bromine participation was observed for bromination in methanol, and inspection of the rate data for acetic acid and trifluoroacetic acid solvents (Table 2) also shows the absence of a rate maximum anywhere in the series, and also the absence of any unusually large values over and above those expected from a normal fall off of the inductive effect of the bromine substituent, as n is increased. Attenuation plots are shown in Figures 1 and 2, and confirm the general absence of any rate enhancements attributable to neighbouring group participation. In these plots of log Δlog k against n, $\Delta\log k = \log k_2 - \log k_{\text{H}}$, and is a measure of the inductive effect of the substituent. Again we have used k_2 for pent-1-ene as k_{H} throughout the series. The measured value for hex-1-ene is very close to that of pent-1-ene. The only evidence available for any degree of bromine participation in electrophilic halogenations is the small maximum at 5-bromopent-1-ene for iodination in water.[1] Generally much bigger effects are found in iodination reactions than in bromination. The existence of cyclic halogenonium ions has been demonstrated on a number of occasions recently;[14] they appear to be reasonably stable in solvents of very low nucleophilicity and high ionising power, such as SbF_5–SO_2. It appears also, from Peterson's[5] work with trifluoroacetic acid, both from the attenuation plots and from product analyses (where 1,4-halogen shifts have been observed) that cyclic halogenonium intermediates are important in these reactions. An explanation of why these structures are not, apparently, so important in halogenation reactions lies in the probable different structures of the intermediate carbonium ions. Solvolysis and proton transfer to an alkene are thought to involve intermediates of type (VI) where a suitably placed neighbouring group, X, has interacted with what was formally the carbonium ionic centre. Bromination, on the other hand may involve intermediates with substantial contribution from bridged structures


(VI)


(VII)

like (VII) where no such interaction by X could occur. This would reduce the effectiveness of X in assisting

TABLE 2

Variation of k_2 with n for bromination of $CH_2{=}CH[CH_2]_nBr$ in methanol, acetic acid, and trifluoroacetic acid

	k_2 l mol^{-1} min^{-1}		
Alkene	MeOH *	CH_3CO_2H †	CF_3CO_2H †
$CH_2{=}CHCH_2Br$	1·39	12·4	1230
$CH_2{=}CH[CH_2]_2Br$	73·5	96·3	32,000
$CH_2{=}CH[CH_2]_3Br$	503	517	68,300
$CH_2{=}CH[CH_2]_4Br$	1170	980	90,500
$CH_2{=}CH[CH_2]_3H$	2090	1730	101,000

* Containing 0·2M-NaBr. † Containing 0·1M-NaBr.

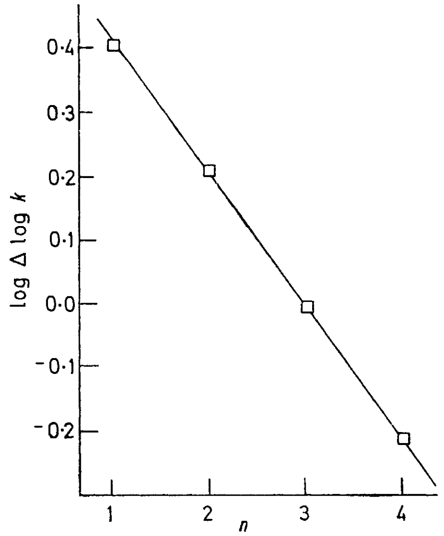


FIGURE 1 Attenuation plot for the bromination of $CH_2{=}CH[CH_2]_nBr$ in acetic acid

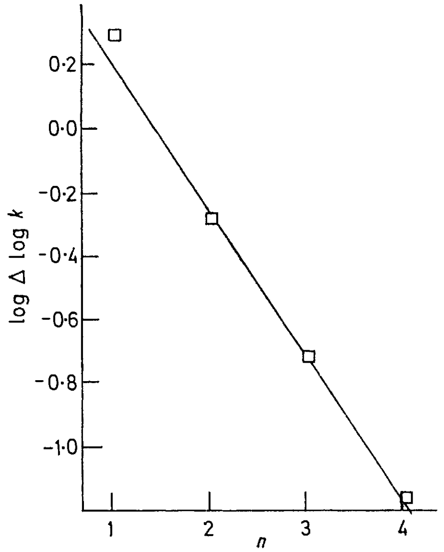


FIGURE 2 Attenuation plot for the bromination of $CH_2{=}CH[CH_2]_nBr$ in trifluoroacetic acid

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[14] G. A. Olah and P. E. Peterson, *J. Amer. Chem. Soc.*, 1968, **90**, 4675; G. A. Olah, *Science*, 1970, **168**, 1298.

such a reaction. The acetic acid results confirm that in the bromination of alkenes, participation by hydroxy is an order of magnitude greater than corresponding Br partitipation.

Variation of k$_2$ *with* [Br$^-$].—All the rate constants k_2 apply to equation (1) where [Br$_2$] refers to the total

$$-\mathrm{d}[\mathrm{Br}_2]/\mathrm{d}t = k_2[\mathrm{Br}_2][\mathrm{Alkene}] \qquad (1)$$

bromine concentration. Particularly in the presence of added bromide ions, significant quantities of the total bromine exist as the tribromide ion Br_3^-. The exact role of Br_3^- in addition reactions is still uncertain, though it has been argued that it also can act as an electrophilic reagent. The individual rate constants for bromination by the bromine molecule and also by the tribromide ion can readily be obtained from the variation of k_2 with added bromide ion, but it has been observed [2,15] that in general, the composite rate constant k_2 can be used reliably as a measure of reactivity, for example in the comparison of substituent effects. All our results for trifluoroacetic acid solvent refer to that solvent containing 0·01M-sodium bromide; no variation of bromide ion concentration was attempted because of the low solubility of sodium bromide. Dubois [16] has shown that (using the more soluble lithium salt) k_2 differs very little from the rate constant for attack by the bromine molecule. For the acetic acid reactions, we found for the bromination of the alcohols and bromides little variation of k_2 with added bromide ion (see Table 3). The differences are often within the experimental error of the measurements, so it seems reasonable to ignore any contribution by the tribromide ion species, so far as the general pattern of reactivity is concerned.

TABLE 3

Variation of k_2 with [NaBr] for a number of alkenes

	k_2/l mol^{-1} min^{-1}	
Alkene	0·01M-NaBr	0·1M-NaBr
$CH_2{=}CHCH_2OH$	222	251
$CH_2{=}CH[CH_2]_2OH$	500	594
$CH_2{=}CH[CH_2]_3OH$	4080	4020
$CH_2{=}CH[CH_2]_4OH$	1910	1595
$CH_2{=}CHCH_2Cl$	12·9	13·7
$CH_2{=}CH[CH_2]_2Br$	96·3	97·2
$CH_2{=}CH[CH_2]_3Br$	517	522

Bromination reactions, particularly in acetic acid have in the past [17] been complicated by kinetic terms with a second-order bromine dependence. We have avoided this in our work by using low bromine concentrations (1 × 10^{-4}M) and acetic acid solvent containing 1% added water. Good first-order behaviour was always observed.

EXPERIMENTAL

The preparation of materials has been described.[1,2] All the alkenes were purified by preparative g.l.c. immediately before use in the kinetic experiments. Trifluoroacetic acid was fractionally distilled from bromine, discarding the first 10% of each batch. Acetic acid was purified as described by Orton and Bradfield [18] adding the necessary amount of acetic anhydride to remove the water present initially.

Kinetic Measurements.—Rate coefficients were obtained by the potentiometric method,[19] noting the variation of the potential of the Pt,Br$_2$,Br$^-$ electrode relative to that of a glass electrode, with time, at 25°. The bromine was generated by electrolysis to a concentration of *ca.* 1 × 10^{-4}M, and the alkene (always in at least a 20-fold excess) added from a weighed syringe. Straight lines were obtained on a recorder (for the e.m.f. against time), for at least 60 mV, corresponding to *ca.* 95% reaction, and the rate constant obtained from the slope. All rate constants quoted are the mean values of at least three determinations, and were generally reproducible to ±2%. The method gave excellent agreement [20] with published rate data for the bromination of allyl chloride in methanol, over a range of added bromide ion concentration.

Product Analyses.—Bromine was added slowly over a period of time to a solution of the alkene in the appropriate solvent, keeping closely to the kinetic conditions. The solvent was removed and the residual product analysed by g.l.c. The yields of the ring-closed products 2-bromomethyl-tetrahydrofuran and -tetrahydropyran, were determined quantitatively with a gas density balance, using the authentic materials.[2]

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[15] J. E. Dubois and X. Q. Huynh, *Bull. Soc. chim. France*, 1968, 1436, and earlier papers.

[16] J. E. Dubois and M. Ropars, *J. Chim. Phys.*, 1968, **65**, 2000.

[17] P. W. Robertson, N. T. Clare, K. J. McNaught, and G. W. Paul, *J. Chem. Soc.*, 1937, 335; K. Yates and W. V. Wright, *Canad. J. Chem.*, 1967, **45**, 167.

[18] K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 1927, 983.

[19] J. R. Atkinson and R. P. Bell, *J. Chem. Soc.*, 1963, 3260; J. E. Dubois, R. Uzan, and P. Alcais, *Bull. Soc. chim. France*, 1968, 617.

[20] For details see S. R. Hooley, Ph.D. Thesis, Durham University, 1973; J. E. Dubois and E. Bienvenüe-Goetz, *Bull. Soc. chim. France*, 1968, 2086.