Free-radical Substitution in Aliphatic Compounds. Part XIV.[1] The Halogenation of Esters of Butan-1-ol

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The chlorination of n-butyl formate, acetate, and trifluoroacetate, and the bromination of n-butyl acetate and trifluoroacetate have been studied in the gas phase by use of a static system. Chlorination is appreciably deactivated at the 1-position and slightly in the 2-position. Bromination is activated at the 1-position and slightly deactivated at the 2-position. From halogenations at a range of temperatures approximate Arrhenius parameters have been calculated for attack at each site. The difference in reactivity of different positions is principally determined by differences in activation energy although the pre-exponential factors for the substituted position are invariably lower than for the 4-position. The results are considered in terms of current theories.

COMPARED with the literature on the atomic halogenation of carboxylic acid derivatives,[2] very little has been reported on the reactivity of alcohol derivatives. The atomic halogenation of free alcohols yields a variety of compounds as a result of the instability of α-halogeno-alcohols

$$\mathrm{R{\cdot}CH_2OH + X{\cdot} \longrightarrow R{\cdot}\dot{C}HOH + HX}$$

$$\mathrm{R{\cdot}\dot{C}HOH + X_2 \longrightarrow R{\cdot}CHXOH + X{\cdot}}$$

$$\mathrm{R{\cdot}CHXOH \longrightarrow R{\cdot}CHO + HX}$$

The first product is the aldehyde but this reacts further in the presence of the hydrogen halide. Halogenation of esters of long-chain alcohols has received very little study. Brown and Ash report the liquid-phase chlorination of n-propyl acetate both with sulphuryl chloride and direct photochlorination.[3] An earlier report by Waddle and his co-workers on the chlorination of propyl and butyl trichloroacetate is also of interest.[4] The most extensive work is that of Bruylants and his co-workers who reported that there was no attack at the 1-position in propyl acetate and no attack at either the 1- or the 2-position in n-butyl acetate.[5] Brown and Ash's work in the solution phase was not completely satisfactory because of fairly extensive overchlorination, and dependence on fractionation for separation of their products. Nonetheless their reported isomer distribution of 23% of 1-, 42% of 2-, and 35% of 3- seems more probable than the Belgian work. The early work of Waddle suggests a very low rate of attack at the 1-position in trichloroacetate esters.

In view of the paucity and slightly contradictory nature of previous work further studies on the atomic halogenation of the esters of long-chain alcohols was clearly desirable. The present work used derivatives of butan-1-ol in order that the results would be directly comparable with those of our previous halogenations.

EXPERIMENTAL

The method has been described.[2]

Reactants.—n-Butyl acetate, formate, and trifluoroacetate were prepared by standard methods. The esters were fractionally distilled and the purity checked by gas chromatography.

Authentic Halogeno-esters for Identification.—The following esters were prepared according to methods described in the literature: n-butyl chloroformate,[6] 4-chlorobutyl formate,[7] 4-chlorobutyl acetate,[8] 1-chlorobutyl acetate,[9] n-butyl chloroacetate,[10] 4-chlorobutyl trifluoroacetate,[11] n-butyl bromoacetate,[10] and 4-bromobutyl acetate.[8] 1-Chlorobutyl trifluoroacetate and 1-bromobutyl acetate

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[1] Part XIII, H. Singh and J. M. Tedder, preceding Paper.

[2] H. Singh and J. M. Tedder, *J. Chem. Soc.*, 1964, 4737.

[3] H. C. Brown and A. B. Ash, *J. Amer. Chem. Soc.*, 1955, **77**, 4019.

[4] C. W. Gaylord and H. M. Waddle, *J. Amer. Chem. Soc.*, 1941, **63**, 3358; cf. also H. M. Waddle and H. Adkins, *ibid.*, 1939, **61**, 3361.

[5] A. Bruylants, M. Tits, and R. Danby, *Bull. Soc. chim. belges*, 1949, **58**, 310; A. Bruylants, M. Tits, C. Dieu, and R. Gauthier, *ibid.*, 1952, **61**, 366.

[6] C. E. Slimowicz and E. F. Degering, *J. Amer. Chem. Soc.*, 1949, **71**, 1043.

[7] E. Szarvasi, *Bull. Soc. chim. France*, 1949, 649.

[8] J. B. Cloke and F. J. Pilgrim, *J. Amer. Chem. Soc.*, 1939, **61**, 2667.

[9] E. Späth and H. Schmidt, *Ber.*, 1940, **73**, 243.

[10] A. I. Vogel, *J. Chem. Soc.*, 1948, 644.

[11] W. A. T. Macy, *J. Phys. Chem.*, 1960, **64**, 254.

were prepared by adaption of the method described by Ulich and Adams.[12]

Chlorination of n-Butyl Formate.—Mixtures of n-butyl formate (10 parts) and chlorine (1 part) at a total pressure of 25 mm. were irradiated by a 200w tungsten lamp for 1·5 hr. The results (Table 1) are expressed as per cent of each isomer; the errors represent standard deviations as in Tables 2—5. The reaction mixture was analysed on a 6 ft. column packed with 25% tritolyl phosphate on Celite (60—100 mesh). The resulting chromatogram showed five product peaks in addition to that for unchanged butyl formate. The first and last product peaks were identified by the addition of authentic material and found to be butyl chloroformate and 4-chlorobutyl formate. The remaining peaks were assumed to be 1-chloro-, 2-chloro-, and 3-chloro-butyl formate eluted in that order. As expected 1-chlorobutyl formate was unstable and decomposed during analysis.

Chlorination of n-Butyl Acetate.—Mixtures of n-butyl acetate (10 parts) and chlorine (1 part) at a total pressure of 25 mm. were irradiated by a 200w tungsten lamp for 2 hr. (Table 2). The mixture was analysed on a 6 ft. column of 25% tritolyl phosphate on Celite. In addition to the starting material there were four product peaks; the third had a prominent shoulder just behind it and was due to n-butyl chloroacetate. The first peak proved to be 1-chlorobutyl acetate and the fourth 4-chlorobutyl acetate. The second and third peaks were assumed to be due to 2-chloro- and 3-chloro-butyl acetates eluted in that order.

Chlorination of n-Butyl Trifluoroacetate.—Mixtures of n-butyl trifluoroacetate (10 parts) and chlorine (1 part) at a total pressure of 29 mm. were irradiated by a 150w tungsten lamp for 2 hr. (Table 3). The mixture was analysed on a 6 ft. column of 30% tritolyl phosphate on Celite. Apart from starting material there were only four peaks on the chromatogram. The first and last product peaks were due to 1-chloro and 4-chloro-butyl trifluoroacetate, respectively. The remaining two peaks were assumed to be due to 2-chloro- and 3-chloro-butyl trifluoroacetates eluted in that order.

TABLE 1

Temp.	No. of runs	HCO·O —	—CH_2—	—CH_2—	—CH_2—	—CH_3
40°	9	1·98 ± 0·08	—	19·43 ± 0·26	58·71 ± 0·49	19·89 ± 0·43
98	5	1·85 ± 0·01	—	20·02 ± 0·43	57·22 ± 0·55	20·19 ± 0·33
150	8	1·56 ± 0·03	—	18·64 ± 0·37	57·74 ± 0·56	22·07 ± 0·30

TABLE 2

Temp.	No. of runs	$CH_3CO{\cdot}O$ —	—CH_2—	—CH_2—	—CH_2—	—CH_3
40°	5	Traces	0·88 ± 0·02	27·27 ± 0·62	53·28 ± 0·57	18·58 ± 0·32
100	8	1·19 ± 0·09	1·54 ± 0·19	27·24 ± 0·68	50·70 ± 0·67	19·24 ± 0·27
145	6	Traces	0·83 ± 0·09	27·93 ± 0·52	50·01 ± 1·04	20·19 ± 0·24
160	8	Traces	1·35 ± 0·14	28·12 ± 0·40	49·92 ± 0·59	20·61 ± 0·39

TABLE 3

Temp.	No. of runs	$CF_3CO{\cdot}O$—	—CH_2—	—CH_2—	—CH_2—	—CH_3
51°	8	—	2·79 ± 0·12	19·51 ± 0·14	56·53 ± 0·28	21·18 ± 0·29
106	9	—	3·13 ± 0·18	19·93 ± 0·25	54·35 ± 0·40	22·58 ± 0·53
184	8	—	3·56 ± 0·07	20·20 ± 0·31	52·90 ± 0·29	23·35 ± 0·43

TABLE 4

Temp.	No. of runs	$CH_3CO{\cdot}O$ —	—CH_2—	—CH_2—	—CH_2—	—CH_3
150°	5	Traces	15·78 ± 0·93	23·04 ± 1·86	59·96 ± 1·90	1·22 ± 0·04

TABLE 5

Temp.	No. of runs	$CF_3CO{\cdot}O$—	—CH_2—	—CH_2—	—CH_2—	—CH_3
23°	5	—	2·06 ± 0·17	4·90 ± 0·54	92·50 ± 0·15	0·44 ± 0·02
88	5	—	2·12 ± 0·08	6·57 ± 0·09	90·36 ± 0·34	0·95 ± 0·08
153	6	—	2·78 ± 0·18	9·14 ± 0·36	86·15 ± 0·40	1·95 ± 0·08
244	5	—	1·97 ± 0·17	12·24 ± 0·27	82·25 ± 0·32	3·53 ± 0·06

Bromination of n-Butyl Acetate.—A mixture of butyl acetate (10 parts) and bromine (1 part) at a total pressure of 23 mm. was irradiated by a 200w lamp for 2–5 hr. (Table 4). The mixture was analysed on a 6 ft. column of 30% tritoyl phosphate on Celite. Apart from starting material, there were four product peaks. The third had a shoulder, preceding it; this was due to n-butyl bromoacetate. The first and last peaks were shown to be due to 1-bromo- and 4-bromo-butyl acetates. The remaining two peaks were assumed to be due to 2-bromo- and 3-bromo-butyl acetates eluted in that order.

Bromination of n-Butyl Trifluoroacetate.—Mixtures of n-butyl trifluoroacetate (10 parts) and bromine (1 part) at a total pressure of 25 mm. were irradiated by a 200w lamp for 3·5 hr. (23°), 2 hr. (88 and 153°), and 1 hr. (244°)

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[12] L. H. Ulich and R. Adams, *J. Amer. Chem. Soc.*, 1921, **43**, 660.

(Table 5). The mixture was analysed on a 6 ft. column of 30% tritolyl phosphate on Celite. There were only four product peaks and these were assumed to be eluted in the order 1-, 2-, 3-, 4-bromo-butyl trifluoroacetates, by analogy with previous results.

DISCUSSION

The chlorination results at 100° are summarised in Table 6. The 1-chloro-derivative of n-butyl formate was too unstable to be estimated accurately. The relative selectivities for the H–CO– and CH_3CO– groups are also given in Table 6. The results show that the 1-position is appreciably deactivated and the 2-position slightly deactivated in all three esters. Neither positions are as deactivated as Bruylants suggested [5] and it seems probable that the Belgians did not succeed in completely separating their isomers. The present results show greater deactivation at the 1-position than Ash and Brown observed in their liquid-phase study,[3] although too close comparison of gas- and liquid-phase results is questionable. Contrary to the suggestions made by Brown and Ash [3] on the basis of Waddle's earlier work,[4] the 1-position in n-butyl trifluoroacetate is less deactivated than the 1-position in n-butyl acetate. On the other hand the deactivation of the 2-position is in the order trifluoroacetate slightly more deactivated than formate, more deactivated than acetate, *i.e.*, extent of deactivation follows the electron-withdrawing ($-I\sigma$) properties of the acyl group. This is in accord with all our previous results, which show that the extent of deactivation of halogenation at a position β to a subtituent correlates very well with the electron-withdrawing properties of the substituent, whereas the reactivity of the position α to a substituent depends on a number of factors of which the electron-withdrawing properties of the substituent is by no means always predominant.[13-15]

TABLE 6

The gas-phase chlorination of n-butyl formate, acetate, and trifluoroacetate at 100° expressed in relative selectivities RS_p^x

	XCO·O·CH_2—	CH_2——	CH_2——	CH_3
X = H *	—	1·45	4·09	1
X = CH_3 †	0·1	2·13	3·95	1
X = CF_3	0·2	1·33	3·61	1

* $RS_p^X = 0{\cdot}3$. † $RS_p^X = 0{\cdot}06$

Table 7 shows that bromination is also appreciably deactivated at the 2-position. The extent of deactivation is very different for the two esters. The 1-position is activated in comparison with the terminal primary position (4) although it is deactivated compared to position 3. Unfortunately bromination of butyl acetate was accompanied by decomposition and it was not possible to study this reaction over an extensive temperature range. There is no previous work with which to compare the bromination results.

TABLE 7

Gas-phase bromination of n-butyl acetate and trifluoroacetate at 150° expressed as relative selectivites RS_p^x

	XCO–OCH_2—	CH_2——	CH_2——	CH_3
X = CH_3*	19	29·5	73	1
X = CF_3	2	7	66	1

* Trace only.

The combined results of the chlorinations of butyl formate (at 40, 98, and 150°), butyl acetate (at 40, 100, 145, and 160°), butyl trifluoroacetate (at 51, 106, and 183°) together with the combined results of the bromination of butyl trifluoroacetate (23, 88, 153, and 224°) have been used to calculate approximate Arrhenius parameters for each reaction. The present results only provide relative rates but in order to put the figures on an absolute scale it has been assumed that the 3-position in all the esters behaves exactly as a secondary position in n-butane. The values in Table 8 for position 3 in each ester are taken from Knox and Nelson [16] for chlorination and from Fettis, Knox, and Trotman-Dickenson [17] for bromination and the values for the other positions calculated accordingly.

Current theories assume that the difference in attack by halogen atoms at different sites is principally due to differences in activation energy.[18] These theories have been extremely successful in correlating experiments but sufficient accurate data over suitable temperature ranges have been lacking. Although the results in Table 8 must be regarded as approximate it is very satisfactory to find that the activation energy for attack by chlorine atoms is greater at position 2 than position 3 and greatest of all at position 1. This is in accord with the idea that chlorination is very sensitive to polar effects and not so sensitive to the strength of the C–H bond. The C–H bond in position 1 should be slightly weakened because the incipient radical can be stabilised by resonance. In chlorination this effect will be more

$$RCH{-}O{\cdot}COX \longleftrightarrow R\overset{-}{C}H{-}\overset{+}{O}COX$$

than offset by the electronegativity of the COX group. Unfortunately the scatter in the results for the 1-position in butyl acetate is too large for a comparison with the 1-position in butyl trifluoroacetate to have much meaning. It is noticeable that the deactivation of the 1-position in both molecules is partly due to low values of A_2. Thus the basic concepts of the theory are correct but changes in the pre-exponential factors in the rate expression do affect the observed reactivity.

The importance of the pre-exponential factor is even

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[13] P. S. Fredricks and J. M. Tedder, *J. Chem. Soc.*, 1960, 144; 1961, 3520.

[14] I. Gabba, J. M. Tedder, and R. A. Watson, *J. Chem. Soc.*, 1964, 1321.

[15] H. Singh and J. M. Tedder, *J. Chem. Soc.*, 1964, 4737.

[16] J. H. Knox and R. L. Nelson, *Trans. Farday Soc.*, 1959, **55**, 937.

[17] G. C. Fettis, J. H. Knox, and A. F. Trotman-Dickenson, *J. Chem. Soc.*, 1960, 4177.

[18] J. M. Tedder, *Quart. Rev.*, 1960, **14**, 336.

more striking in brominations. The low rate of bromination at positions α to a substituent has always been somewhat of an embarrassment to the theory because bromination, unlike chlorination, is endothermic and should therefore be very sensitive to changes in the strength of the C–H bond. As most substituents tend to weaken the adjacent C–H bond we would expect activation rather than deactivation of bromination of the 1-position. In our previous study on the bromination of methyl pentanoate we suggested that the low reactivity of the α-position might be due to low *A* factors rather than a higher activation energy, but the results were insufficiently accurate for us to be certain.[15] The present bromination results show that for butyl esters, the activation energy for attack at the 1-position is within experimental error the same as for attack at the 3-position. The low reactivity of this 1-position is almost entirely due to a low *A* factor. Thus chlorination is retarded at the 1-position because the polar effect largely swamps the importance of C–H bond strength; in bromination the polar effect and C–H bond strength balance each other but the actual rate of attack is lower because $\Delta S^{\ddagger}$ is lower.

TABLE 8

Approximate values for the Arrhenius parameters for the chlorination of n-butyl formate, acetate, and trifluoroacetate and for the bromination of n-butyltrifluoroacetate

(log A_2 in mole^{-1} cm.^{3} sec.$^{-1}$; E in kcal. mole^{-1})

$$\mathrm{RH + Cl\cdot\ (Br\cdot) \xrightarrow{k_2} R\cdot + HCl\ (HBr)}$$

	$\mathrm{XCO{\cdot}O{\cdot}CH_2}$		$\mathrm{CH_2}$		$\mathrm{CH_2}$		$\mathrm{CH_3}$	
	log A_2	E_2	log A_2	E_2	log A_2	E_2	log A_2	E_2
Chlorination								
X = H	—	—	12·8	0·3	*13·3*	*0·3*	12·9	0·6
= $\mathrm{CH_3}$	12·0	0·9	13·2	0·5	*13·3*	*0·3*	12·9	0·7
= $\mathrm{CF_3}$	12·5	1·0	13·0	0·5	*13·3*	*0·3*	13·0	0·7
Bromination								
= $\mathrm{CF_3}$	12·1	10·4	13·4	11·6	*13·6*	*10·2*	13·4	13·3

The results show, as predicted, that the deactivation of the 2-position represents a higher activation energy due to the polar effect. It would need experiments of far greater precision than are at present possible to be able to compare the activation energies for attack at the 2-position in different molecules. Probably the lower $RS_p{}^2$ for the chlorination of the butyl trifluoroacetate than of the acetate is due to a greater activation energy but we cannot be certain. Finally the consistent values obtained for the Arrhenius parameters of position 4 and their closeness to the known values for the primary positions in n-butane gives some idea of the reliability of the results and shows we are justified in assuming that the 3-position is unaffected by the substituent.

It is not our intention to compare in detail the directive effects of different types of substituent but a direct comparison of n-butyl acetate and methyl pentanoate (see Table 9) provides some measure of the influence of the $\mathrm{O{\cdot}COCH_3}$ group.

TABLE 9

$RS_p{}^x$ for the halogenation of n-butyl acetate and methyl n-pentanoate.[15]

Chlorination at 100°				
$\mathrm{CH_3}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CO{\cdot}OCH_3}$
1	3·4	2·4	0·4	0·09
$\mathrm{CH_3}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{O{\cdot}COCH_3}$
1	3·9	2·1	0·1	0·06
Bromination at 150°				
$\mathrm{CH_3}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CO{\cdot}OCH_3}$
1	77	35	41	trace
$\mathrm{CH_3}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{CH_2}$	$\mathrm{O{\cdot}COCH_3}$
1	73	29	19	trace

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