28. *Free-radical Substitution in Aliphatic Compounds. Part II.*[1] *Halogenation of the* n-*Butyl Halides.*

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The n-butyl halides have been fluorinated, chlorinated, and brominated in the gas phase. The effect of the halogen already present in the molecule is to retard substitution at a β-carbon atom, the effectiveness of the halogens being in the order F > Cl > (Br); fluorine slightly deactivates the γ-position. The halogen already present also affects substitution at the α-carbon atom, but to an extent and manner which varies greatly with the nature of the attacking radical. The selectivity of the radicals is in the same order as found before,[1] Br ⋙ Cl > F, but the nature of the selectivity is no longer similar. At the β-carbon atom bromination is *relatively* the least affected by the halogen already present, fluorination the most. At the α-carbon atom fluorination appears to be appreciably, and chlorination is slightly, retarded by the substituent halogens in the order Br > Cl ≃ F, but bromination is activated. These results are explained in terms of the relative strengths of the bonds broken and formed, and the polarity of the hydrogen halide produced.

The halogenation of the alkyl halides,[2–8] usually by the same halogen, has received considerable study and the generalisation that the halogen already in the molecule directs attack away from itself [2] has been accepted [8] in spite of the fact that the results available show that this is a poor approximation of the truth. The present investigation has been carried out under exactly similar conditions to those used for the previous study of the halogenation of n-butane and isobutane.[1] Fluorine has been used both as substituent and halogenating agent for the first time in such investigations.

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Experimental

The halogenations were performed as described previously,[1] a flow apparatus being used and the products separated by gas-phase chromatography. The greatest problem was the correct identification of the isomers formed. When dihalides of known structure were available the procedure was to chromatograph the product and then add the individual dihalides one at a time to the reaction product and see which peak had been enlarged. By this means the peak on the original chromatogram could be identified unequivocally. However, in many cases synthesis of the dihalides would have been extremely tedious; for instance, no satisfactory synthesis of unsymmetrical 1,2-dihalides is known. Another method was to halogenate a 2-halogenobutane and compare the retention times of the products; *e.g.*, chlorination of n-butyl fluoride yielded four dihalide peaks. The retention times of two of these peaks were identical with the retention times of two of the peaks on the chromatogram obtained from the fluorination of 2-chlorobutane. These peaks must therefore be due to 2-chloro-1-fluorobutane and 3-chloro-1-fluorobutane. It was possible in some cases to identify peaks by analogy, *e.g.*, chlorination of n-butyl fluoride and n-butyl chloride yielded chromatograms of identical shape, differing only slightly in their relative areas. All the peaks from the chlorination of butyl chloride had been identified by the addition of known compounds. The final peak from butyl fluoride, which corresponded to the 1,4-dichlorobutane peak, was identified as due to 1-chloro-4-fluorobutane by the same means. The reasonable assumption was therefore that the other peaks from butyl fluoride corresponded with those from butyl chloride similarly. In a few cases it was possible to collect sufficient of an isomer eluted from the column to attempt chemical identification but this never proved very satisfactory. In one case a single isomer was collected in this fashion and its structure deduced from its nuclear magnetic resonance spectrum.

Preparation of Authentic Dihalides for Identification.—1,1-Dichlorobutane,[9] 1,3-dichlorobutane,[10] 1,4-difluorobutane,[11] and 1-chloro-4-fluorobutane [12] were prepared as described in the literature. 1,4-Dichlorobutane and 1,2-dibromobutane were available commercially. The following were prepared by adaptions of well-known methods: 1,2-dichlorobutane by addition of chlorine to but-1-ene; [13] 1-chloro-1-fluorobutane and 1,1-*difluorobutane* from 1,1-dichlorobutane by treatment with mercuric oxide and anhydrous hydrogen fluoride [14] (Found: C, 51·4; H, 8·5. $C_4H_8F_2$ requires C, 51·1; H, 8·6%); 1,3-*difluorobutane* from 1,3-dibromobutane by a similar method (Found: C, 50·7; H, 8·6%); 1-*bromo*-3-*chlorobutane* from 1-bromo-3-hydroxybutane [15] by treatment with thionyl chloride (b. p. 34—36·3°/15 mm.) (Found: C, 28·3; H, 4·8. C_4H_8ClBr requires C, 28·0; H, 4·7%); 1-bromo-4-chlorobutane from 4-chlorobutan-1-ol by treatment with concentrated hydrobromic acid and sulphuric acid; [16] 1,3-dibromobutane from butane-1,3-diol by the same method; 1,4-dibromobutane from tetrahydrofuran and hydrogen bromide.

Apparatus and Procedure for Halogenations.—These were as before.[1] The butyl halides were introduced into the gas stream by passing nitrogen through a trap containing the compound. The trap was surrounded by a constant-temperature bath. The concentration of the butyl halide in the gas stream was controlled by the temperature of this bath, and the actual concentration determined from a vapour-pressure curve which was measured in the conventional way beforehand.

Gas-phase Chromatography.—The apparatus has been described.[1] The analysis depends on the assumption that the thermal conductivity of the isomeric dihalogenobutanes is very similar. All the data at present available indicate that any variations in the thermal conductivity of isomers of this type would be extremely small. In the chlorination of butyl chloride the validity of this assumption was checked by analysing identical runs on both our chromatography column and on a Pye Argon Chromatograph. The results were the same within experimental error.

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[11] Hoffman, *J. Org. Chem.*, 1949, **14**, 105.
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Halogenations.—The degree of substitution at the four positions of a butyl halide (%) are shown in Table 1, with relevant details.

Identificaton of Halogenation Products.—Chlorination of n-butyl chloride. These were identified by the individual addition of the authentic dihalide to the reaction products.

Chlorination of n-butyl fluoride. 1-Chloro-4-fluoro- and 1-fluoro-1-chloro-butane were identified by the addition of authentic materials. The shape of the chromatogram was identical with that from chlorinated butyl chloride. Fluorination of 2-chlorobutane yielded a mixture, the chromatogram of which had two peaks which coincided with two of the peaks on the chromatogram from the above results; these were therefore due to 2-chloro-1-fluoro- and 3-chloro-1-fluoro-butane.

Chlorination of n-butyl bromide. There were five peaks on the chromatogram. The first eluted was of 1,2-dichlorobutane. The fourth and the fifth were identified as due to 1-bromo-3-chlorobutane and 1-bromo-4-chlorobutane respectively, by the addition of authentic material. The second peak was established as due to 1-bromo-1-chlorobutane by comparison with the products from the bromination of butyl chloride. The third and smallest (less than 3%) was therefore due to 1-bromo-2-chlorobutane.

Bromination of n-butyl chloride. The very small peak which was the last to be eluted was identified as due to 1-bromo-4-chlorobutane by addition of authentic material. The first peak was identified as due to 1-bromo-1-chlorobutane by comparison with the chromatograms from the chlorination of n-butyl bromide. The remaining two peaks were therefore of 2-bromo-1-chlorobutane and 3-bromo-1-chlorobutane and were assumed to be eluted in this order by analogy with the dichlorobutanes.

Bromination of n-butyl fluoride. There were only three peaks on the chromatogram and the third and largest was collected and submitted to nuclear magnetic resonance spectroscopy. Both the ^{1}H and ^{19}F spectra were examined. The proton spectrum clearly established the presence of a methyl group adjacent to a $-CHX-$ group. This means that the peak must have been due to 3-bromo-1-fluorobutane and all the other details of the spectra confirmed this. The remaining peaks were assumed to be due to 1-bromo-1-fluorobutane and 2-bromo-1-fluorobutane eluted in this order by analogy with the results described above.

Bromination of n-butyl bromide. Bromination of butyl bromide was strongly inhibited by some product of the reaction, and when conditions similar to those described for the bromination of butyl chloride and butyl fluoride were employed, a large portion of the bromine failed to react and the sides of the vessel became coated with a brown film. We believe this to be due to the formation of olefinic material by loss of bromine from some of the intermediate radicals ($-\dot{C}H-CHBr- \longrightarrow -CH=CH-$). Runs were attempted at both 78° and 146°; the chromatogram only showed one large peak which was found to be due to 1,3-dibromobutane by the addition of authentic material. There were other very small and badly defined peaks; two of these were identified as due to 1,2 and 1,4-dibromobutane, but there remained other low-boiling compounds which could not be identified.

Fluorination of n-butyl fluoride. There were only three difluoride peaks. Addition of authentic 1,1-difluorobutane to the products showed that this isomer would not be separated from the unchanged butyl fluoride. The first difluorobutane peak on the chromatogram was found to be due to 1,3-difluorobutane and the third to 1,4-difluorobutane, both by addition of authentic material. The second difluoride peak was therefore due to 1,2-difluorobutane. Because of the impossibility of separating the 1,1-difluorobutane from the unchanged butyl fluoride we sought another method of analysis. Dr. J. R. Majer examined our products on the mass spectrometer. The calculation of results from the mass-spectra proved considerably more difficult than expected; the large excess of unchanged butyl fluoride again greatly complicated the problem. The products from two runs having identical conditions to those described in Table 1 (except that the amount of nitrogen was increased to 400 parts) were analysed and the results (%) were as follows:

unchanged C_4H_9F	1,1-	1,2-	1,3-	1,4-$C_4H_8F_2$
92·2	<0·5	1·3	3·5	3·0
92·0	<0·5	1·0	4·9	2·1

The agreement between the mass-spectra results and those obtained by gas chromatography is very good (the relative proportions of the 1,2- and the 1,4-isomer are identical by both methods,

and the mass-spectra indicate the presence of slightly more of the 1,3-isomer). The mass-spectra clearly show the 1,1-isomer to be present in the smallest proportion.

TABLE 1.

BuX (parts)	Y_2 (parts)	N_2 (parts)	Temp.	No. of runs	CH_2X—	—CH_2—	—CH_2—	—CH_2
Chlorination of n-butyl chloride (X = Y = Cl)								
10	1	400	35°	10	8·1 ± 0·6	25·8 ± 0·6	48·6 ± 1·1	17·5 ± 1·2
,,	,,	,,	78	,,	9·6 ± 0·8	26·1 ± 1·1	45·7 ± 1·0	18·6 ± 1·0
,,	,,	,,	146	8	9·6 ± 1·1	22·5 ± 1·2	47·1 ± 0·8	20·8 ± 2·0
,,	,,	,,	,,	5	8·2 ± 0·7	22·1 ± 1·6	47·5 ± 1·8	22·2 ± 3·1
Chlorination of n-butyl fluoride (X = F; Y = Cl)								
10	1	100	0	10	9·7 ± 0·6	20·8 ± 0·6	52·5 ± 1·8	17·0 ± 1·5
,,	,,	,,	35	10	10·7 ± 0·8	20·8 ± 0·5	48·6 ± 0·7	19·9 ± 0·9
10	1	400	78	7	11·4 ± 0·7	21·8 ± 0·4	47·4 ± 0·4	19·4 ± 0·9
,,	,,	,,	146	7	12·7 ± 0·8	21·5 ± 0·8	45·4 ± 0·5	20·4 ± 1·4
Chlorination of n-butyl bromide (X = Br; Y = Cl) (at 252 mm. Hg)								
4	4	200	35	4	8·0 ± 0·7	Trace	66·8 ± 1·5	25·2 ± 1·9
,,	,,	,,	78	6	7·8 ± 0·5	,,	64·9 ± 1·7	27·3 ± 2·0
Bromination of n-butyl chloride (X = Cl; Y = Br)								
10	1	400	146	9	23·0 ± 2·0	21·7 ± 0·9	55·3 ± 2·4	Trace
Bromination of n-butyl fluoride (X = F; Y = Br)								
10	2	400	146	5	10·0 ± 0·5	8·9 ± 0·5	81·1 ± 0·6	Not detected
Fluorination of n-butyl fluoride (X = Y = F)								
5	1	100	21	10	—	23·8 ± 1·8	30·5 ± 1·4	45·7 ± 1·6
Fluorination of n-butyl chloride (X = Cl; Y = F)								
5	1	100	21	5	—	52·3 ± 1·6		47·7 ± 1·6

* Analysed on a Pye Argon Chromatograph, Cat. 12,000.

Fluorination of n-butyl chloride. There were only two peaks. The second was established as due to 1-chloro-4-fluorobutane by addition of authentic material. Comparison with the chromatogram of chlorinated butyl fluoride showed that 1-chloro-1-fluorobutane would not have been separated from the unchanged butyl chloride. In the chlorination of n-butyl fluoride, the chlorofluorobutanes were eluted in the order 1,1-, 1,2-, 1,3-, and 1,4-. In the fluorination of butyl fluoride the elution order of the 1,2- and the 1,3-difluoride was inverted. This suggested that in the fluorination of butyl chloride the 1-chloro-2-fluoro- and 1-chloro-3-fluorobutane would have very similar retention times. The size of the first peak actually obtained indicated that the retention times of the two products were so similar that only one large peak appeared on the chromatogram. This was confirmed by careful comparison with the chromatogram from the chlorination of 2-fluorobutane.

Competitive Chlorination of n-Butane and n-Butyl Chloride.—Approximately equal concentrations of butane (5 parts) and butyl chloride (5 parts) in nitrogen (100 parts) were mixed with chlorine (1 part) in nitrogen (100 parts). The method was exactly as above, and the yields of 2-chlorobutane and 1,3-dichlorobutane were compared. To do this the gas phase chromatography apparatus had to be calibrated with synthetic mixtures of 2-chlorobutane and 1,3-dichlorobutane (there was no reason to suppose the thermal conductivity of these two compounds to be the same). The relative rates per hydrogen atom in two sets of runs were 2-chlorobutane/1,3-dichlorobutane = 1·07 and 1·21. These results are unity within experimental error, as very accurate measurement of the flow rates of butane and butyl chloride was not possible.

DISCUSSION

The experimental results are shown in Table 2 as Relative Selections (RS_p^x), *i.e.*, relative reactivities per hydrogen atom at each carbon atom, the primary hydrogen atoms in n-butane being taken as unity:

$$RS_p^x = \tfrac{3}{2}[1,x\text{-Dihalogenobutane}]/[1,4\text{-Dihalogenobutane}]$$

TABLE 2. *Halogenation of n-butyl halides*, RS_p^x.

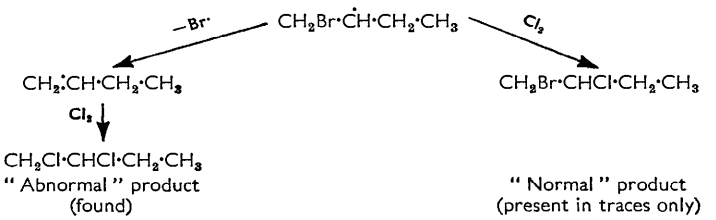
Temp.	X	CH_2X—CH_2—CH_2—CH_3			
		(*a*) Fluorination			
20°	H	1	1·3	1·3	1
20	F	<0·3	0·8	1·0	1
21	Cl	?	1·7		1
		(*b*) Chlorination			
0	H	1	4·3	4·3	1
35	,,	1	$3·9_5$	$3·9_5$	1
78	,,	1	3·6	3·6	1
146	,,	1	3·3	3·3	1
0	F	0·9	1·8	(4·6)	1
35	,,	0·8	1·6	3·7	1
78	,,	0·9	1·7	3·7	1
146	,,	0·9	1·6	3·2	1

Temp.	X	CH_2X—CH_2—CH_2—CH_3			
		(*b*) Chlorination			
35°	Cl	0·7	2·2	4·2	1
78	,,	0·8	2·1	3·7	1
146	,,	0·7	1·6	3·4	1
35	Br	0·5	—	4·0	1
78	,,	0·4	—	3·6	1
		(*c*) Bromination			
146	H	1	82	82	1
146	F	10	9	82	1 *
146	Cl	34	32	82	1 *

* RS_p^3 is assumed to be 82 and the RS_p^2 and RS_p^1 are calculated accordingly.

The results are presented together with previous ones for the halogenation of n-butane [1] for comparison. The validity of this comparison has been checked in the chlorination of butyl chloride, by competitive chlorination with n-butane. The similarity of the RS_p^3 values in all cases confirms that the rate of attack on $C_{(4)}$ in these compounds is the same as on the terminal carbon atoms in butane. The present results are in reasonable agreement with such previous work as is available (*e.g.*, chlorination of butyl chloride [2,3,4,8] and bromination of butyl chloride [7]). The chlorinations carried out at more than one temperature show that in these examples the differences in reactivity of the different hydrogen atoms are mainly due to differences in the energies of activation.

The first generalisation that can be made about these results is that halogen atoms already present in an aliphatic hydrocarbon retard hydrogen abstraction from a β-carbon atom, and the extent of this retardation follows the electronegativity of the substituent halogen, F > Cl > (Br). Fluorine exerts a slight influence on the γ-carbon atom, as shown by the fluorination results. Data about substitution β to a bromine atom have been hard to obtain because of the instability of the intermediate radical $CH_2Br–\dot{C}H–CH_2–CH_3$. Rust and Vaughan [4] found previously that above 200° apparent rate of chlorination at the β-carbon atom in butyl chloride decreased with increasing temperature until at 320° practically no 1,2-dichloride occurred in the reaction products. Ash and Brown have suggested that this " vicinal effect " is due to the instability of the intermediate radical ($CH_2Cl–\dot{C}H–C_2H_5$) at high temperatures.[8] Our results confirm this suggestion, for, although we have not attempted halogenation at very high temperatures, the corresponding bromobutyl radical breaks down at quite moderate temperatures and we have found 1,2-dichlorobutane in place of the expected 1-bromo-2-chlorobutane. Our results also indicate that at 146° the breakdown of the butyl chloride radical occurs slightly.



The second very noticeable feature of the present results is that the hydrogen atoms on the same carbon atom as the substituent halogen are comparatively easily abstracted by chlorine and bromine atoms. Ash and Brown adopt a far too naïve view of their own results,[8] which are reasonably in agreement with the present work, when they reassert

the generalisation that further substitution occurs preferentially at carbon–hydrogen bonds remote from the chlorine substituent. The reason for this mistake is hard to understand since Rust and Vaughan had previously drawn attention [4] to the high reactivity of the α-hydrogen atoms in chlorination. The hydrogen atoms on $C_{(1)}$ must be compared with those on the other terminal carbon atom (4) and not regarded as ordinary secondary hydrogen atoms to be compared with those at $C_{(2)}$ and $C_{(3)}$. On this basis the α-position in butyl chloride and fluoride is very slightly deactivated to chlorination, but is actually activated to bromination. With fluorination, however, the α-position in butyl fluoride is strongly deactivated and the evidence available suggests that it is also appreciably deactivated in butyl chloride, so that in fluorination further substitution really does occur preferentially at sites remote from the substituent halogen atom.

The third and perhaps most striking result of the present work is the very marked difference in the nature of the selectivity of the three different halogen atoms as hydrogen abstractors. Although the exact nature of these results could not in all probability have been predicted, they are readily explained on existing theory. We have already indicated our belief in the importance of resonance stabilisation of the incipient alkyl radical by conjugation or hyperconjugation in hydrogen abstraction reactions.[17] This readily explains the high reactivity of the α-position [cf. (I_A) and (I_B)]. The extent of the slight

$$(I_A)\ X\text{–}\dot{C}H\text{–}C_3H_7 \longleftrightarrow \cdot\overset{+}{X}\text{–}\bar{C}H\text{–}C_3H_7\ \ (I_B)$$

deactivation of the α-position to chlorination follows the order Br > Cl ≈ F so often observed with the halogens when the mesomeric effect ($+M$) is in opposition to the inductive effect ($-I$).[18] In bromination and with hydrogen abstraction by methyl radicals [19] the resonance stabilisation ($+M$) overcomes the inductive effect, and the hydrogen atoms on the same carbon atom as the substituent are activated. With methyl radicals the extent of this activation follows the mesomeric release of the halogens (*i.e.*, F > Cl > Br). The low reactivity of the β-position relative to the γ-position must be partly due to the reduced possibilities for hyperconjugation, and not solely to the inductive effect.

Several papers have discussed the difference in selectivity of different radicals,[20–23] but they have all suffered from insufficient data. The transition state in these hydrogen-abstraction reactions must have some of the characteristics of both reactants and products. In general the smaller D(C–H) and the larger D(H–X) the lower the activation energy. The breaking of the C–H bond will be greatly affected by the stability of the incipient alkyl radical, and the greater the resonance stabilisation of the alkyl radical the smaller is D(C–H).[24] However, we must also consider the bond being formed; unlike the breaking C–H bond, which is almost non polar, the H–X bond formed may be highly polar, usually in the direction $\overset{+}{H}\text{—}X$. The more polar HX, the more polar we may expect the transition state $\rangle\overset{+}{C}\cdots H\cdots X$. The ease with which such structures can be formed will be greatly affected by any polar properties of the organic compound, hindered by electron-withdrawing groups, and aided by electron-donating groups. We can therefore make the following predictions about the course of attack by a radical X· on an aliphatic compound. If HX has little polar character, that hydrogen atom which on abstraction yields the most stable alkyl radical will be removed preferentially. If HX is very polar then hydrogen abstraction will be favoured at the site which can most easily accommodate a positive charge. In

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both cases the selectivity of X· will depend mainly on the strength of the H–X bond being formed. The two effects can be in opposition, in which case the course of the reaction will be determined by the polarity of HX. Thus we can arrange the common radicals in the order Br > Me > Cl > OH > F for selectivity, but the extent to which they will be affected by polar substituents will be in the order F > OH > Cl > Br > Me. These predictions are well borne out by the present data.

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