682. *Free-radical Substitution in Aliphatic Compounds. Part III.*[1] *Halogenation of the 2-Halogenobutanes.*

By P. S. FREDRICKS and J. M. TEDDER.

The 2-halogenobutanes have been fluorinated, chlorinated, and brominated in the gas phase. The hydrogen atom most readily replaced by chlorine or bromine is that situated on the same carbon atom as the substituent halogen. Substitution of the hydrogen atoms attached to the adjacent carbon atoms is retarded for all halogenations. These results are in excellent accord with predictions based on previous study of the n-butyl halides.[1] Both the expected 2,3-dihalogenobutanes are formed in the chlorination and fluorination of these compounds, but the amounts of the two stereoisomers are not equal. A possible explanation of this observation is given.

THE halogenation of the secondary alkyl halides has received less study than the analogous reaction with the primary compounds. Two chlorinations of secondary alkyl chlorides [2,3] and the bromination of some secondary alkyl chlorides and bromides [4] comprise all the work that has been reported. The present study is a direct continuation of previous work [5,1] and has proved valuable in confirming ideas put forward on the basis of earlier results.

EXPERIMENTAL

As previously, the greatest problem was the correct identification of the products separated by gas chromatography.[1] The situation was more complicated in that there were now five dihalogenobutanes compared with the four obtained from the halogenation of the n-butyl halides. The principal method of identification was still the individual addition of the known dihalides to the reaction mixture. However, all such identifications were confirmed by elution of the material of each separate peak on the chromatogram and obtaining the infrared spectrum of the material causing each individual peak which was then compared with the infrared spectrum of the authentic material. Infrared spectra were also used to determine the relative proportions of two components which could not be completely resolved by chromatography. Spectra were obtained of the two authentic components and of synthetic mixtures of them, as well as of the unresolved mixture from the chromatogram. From these spectra the relative concentrations of the two components could readily be calculated. In two cases where the authentic compounds could not be synthesised the materials corresponding to the peaks were eluted from the chromatography column and their nuclear magnetic resonance spectra examined.

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[1] Part II, Fredricks and Tedder, *J.*, 1960, 144.
[2] Tischenko and Churbakov, *Z. obshchei Khim.*, 1937, **7**, 663.
[3] Rust and Vaughan, *J. Org. Chem.*, 1941, **6**, 479.
[4] Kharasch, Zimmt, and Nudenberg, *J. Org. Chem.*, 1955, **20**, 1430.
[5] Anson, Fredricks, and Tedder, *J.*, 1959, 918.

Preparation of Authentic Dihalides for Identification.—The preparation of 1,2-dichlorobutane, 1,3-dichlorobutane, and 1,3-difluorobutane has been described previously.[1] 2,2-Dichlorobutane [6] was prepared from ethyl methyl ketone by treatment with phosphorus pentachloride. Racemic and *meso*-2,3-dichlorobutane [7] were prepared by the addition of chlorine to but-2-ene.[8] 2-Chloro-2-fluorobutane [9] and 2,2-difluorobutane [6] were prepared from 2,2-dichlorobutane by treatment with antimony trifluoride containing 5% of bromine. The 2-chloro-3-fluorobutanes and 2,3-difluorobutanes were prepared from 2,3-dichlorobutane by treatment with mercuric oxide and hydrogen fluoride. The products were characterised by their infrared spectra and retention times. It was assumed that the *erythro*-derivatives were eluted first by analogy with the 2,3-dichlorobutanes. 1-Chloro-3-fluorobutane was prepared from 1,3-dichlorobutane by the same method; none of the isomeric 3-chloro-1-fluorobutane was formed.

Apparatus and Experimental Techniques.—These were identical with those described previously.[1, 5]

Chlorination of 2-Chlorobutane.—Results for an initial mixture of 2-chlorobutane (11 parts), chlorine (1 part), and nitrogen (360 parts) were:

Temp.	No. of runs	CH_3—	—CHCl—	—CH_2— (*meso*) (±)	—CH_3
35°	7	4·1 ± 0·7	26·3 ± 0·7	51·0 ± 0·5 (36·4 ± 1·1) (14·6 ± 0·6)	18·6 ± 0·9
78	6	4·3 ± 0·9	26·2 ± 1·1	49·8 ± 1·3 (35·0 ± 1·2) (14·8 ± 0·6)	19·7 ± 0·8

Identification of products. There were five peaks on the chromatogram and these were identified by the individual addition of the authentic dihalides to the reaction products.

Chlorination of 2-Fluorobutane. Products from an initial mixture of 2-fluorobutane (10 parts), chlorine (1 part), and nitrogen (400 parts) were:

Temp.	No. of runs	2-Cl,2-FC_4H_8	(±)-2-Cl,3-FC_4H_8 (*erythro*) (*threo*)	1-Cl,2-F- + 1-Cl,3-FC_4H_8
35°	10	35·6 ± 2·1	41·6 ± 1·3 (24·7 ± 0·9) (16·9 ± 0·9)	22·8 ± 1·5
78	11	33·0 ± 1·7	40·6 ± 2·2 (24·2 ± 1·8) (16·4 ± 1·3)	26·4 ± 3·1

Identification of products. There were only four peaks on the chromatogram. The first three materials eluted were identified as 2-chloro-2-fluorobutane, and the two racemic 2-chloro-3-fluorobutanes by addition of authentic material to the products. This was checked by comparing the infrared spectra of the components of the product with those of authentic materials. Because the synthesis of the two " authentic " 2-chloro-3-fluorobutanes was not completely unambiguous the materials corresponding to the second and third peaks from the reaction mixture were eluted and their nuclear magnetic resonance spectra examined. The proton spectra were observed for both compounds. The majority of protons in the molecules had similar chemical shifts, *i.e.*, there were two methyl groups. Besides the intense group of lines due to the methyl groups there were two less intense groups due to the 2- and 3-hydrogen atoms. These facts together with the fine details of the spectra indicated that the two peaks on the chromatogram were in fact the two racemates of 2-chloro-3-fluorobutane. The final peak on the chromatogram had a retention time corresponding to that due to 1-chloro-2-fluoro- plus 1-chloro-3-fluoro-butane obtained from the fluorination of 1-chlorobutane.[1] Judged from the amount of 1,2-dichlorobutane produced in the chlorination of 2-chlorobutane (see above) it would be expected that the amount of 1-chloro-2-fluorobutane produced in the present experiment would be very small. This was confirmed by examination of infrared spectra; the spectrum corresponding to the peak due to 1-chloro-2-fluoro- plus 1-chloro-3-fluoro-butane from the present experiment was compared with that of authentic 1-chloro-3-fluorobutane to which it was very similar. It was also compared with the spectrum of the material of the

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[6] Henne, Renoll, and Leicester, *J. Amer. Chem. Soc.*, 1934, **61**, 938.

[7] Lucas and Gould, *J. Amer. Chem. Soc.*, 1941, **63**, 2541.

[8] Davis, *J. Amer. Chem. Soc.*, 1928, **50**, 2779.

[9] Henne and Hinkamp, *J. Amer. Chem. Soc.*, 1945, **67**, 1194.

analogous peak from the fluorination of n-butyl chloride which showed several extra absorption bands due to the 1-chloro-2-fluorobutane.

Fluorination of 2-Fluorobutane.—A mixture of 2-fluorobutane (10 parts), fluorine (2 parts), and nitrogen (400 parts) gave the following products:

Temp.	No. of runs	*meso*-2,3-$F_2C_4H_8$	(±)-2,3- + 1,3-$F_2C_4H_8$	1,2-$F_2C_4H_8$
21°	7	19·2 ± 1·9	56·9 ± 1·2	23·9 ± 0·9

Identification of products. There were only three peaks on the chromatogram. Addition of authentic 2,2-difluorobutane showed that this isomer would be eluted with the unchanged butyl fluoride. The first of the three peaks was shown to be due to 2,3-difluorobutane by addition of authentic material. It was assumed to be the *meso*-isomer by analogy with the dichlorides. The final peak was identified as due to 1,2-difluorobutane on the basis of retention time and infrared spectrum compared with those of 1,2-difluorobutane from the fluorination of n-butyl fluoride. The middle peak was shown to contain both 2,3-difluorobutane [assumed to be (±)] and 1,3-difluorobutane by addition of authentic materials. The infrared spectrum of this mixture was compared with those of mixtures containing the authentic 1,3-difluorobutane and (±)-2,3-difluorobutane of known concentration. By using an absorption band at 848 cm.$^{-1}$ for 1,3-difluorobutane where there was no absorption from (±)-2,3-difluorobutane, and bands at 1178 cm.$^{-1}$ and 933 cm.$^{-1}$ for (±)-2,3-difluorobutane where there was only moderate absorption from 1,3-difluorobutane, it was possible to calculate the proportions of the two isomers in the product. From four synthetic mixtures the ratio of [1,3-$C_4H_8F_2$]/[(±)-2,3-$C_4H_8F_2$] was estimated to be 3·58 : 1.

Fluorination of 2-Chlorobutane.—The mixture, 2-chlorobutane (10 parts), fluorine (5 parts), and nitrogen (400 parts) gave the following products:

Temp.	No. of runs	(±)-*erythro*-2-Cl, 3-FC_4H_8	(±)-*threo*-2-Cl, 3-F- + 2-Cl, 1-F-C_4H_8	3-Cl, 1-FC_4H_8
21°	4	17·0 ± 0·9	16·3 ± 0·2	66·6 ± 0·8

Identification of products. There were only three chlorofluorobutane peaks on the chromatogram. The first of these was not completely resolved from the unchanged 2-chlorobutan- when the normal proportions of the reactants were used. By increasing the extent of fluorine ation it was possible to inject less material into the column and so resolve the first peak previously obtained. It was found to be a (±)-2-chloro-3-fluorobutane by the addition of authentic material. The last peak to be eluted was similarly shown to be due to 3-chloro-1-fluorobutane. The centre peak was shown to contain the other (±)-2-chloro-3-fluorobutane, by addition of authentic material, and 2-chloro-1-fluorobutane, by comparison with the chromatogram of chlorinated 1-fluorobutane. All these identifications were confirmed by examination of the infrared spectra of the materials of the individual peaks. The proportions of the second racemic 2-chloro-3-fluorobutane and 2-chloro-1-fluorobutane corresponding to the centre peak were estimated from the infrared spectrum by using synthetic mixtures made up from the authentic 2-chloro-3-fluorobutane racemate and 2-chloro-1-fluorobutane from the chlorination of n-butyl fluoride. The spectrum of 2-chloro-1-fluorobutane had a strong band at 845 cm.$^{-1}$ in which region racemic 2-chloro-3-fluorobutane did not absorb; similarly 2-chloro-3-fluorobutane had a strong band at 895 cm.$^{-1}$ in which region 2-chloro-1-fluorobutane was completely transparent. The ratio of the isomers so obtained was [$CH_2F{\cdot}CHCl{\cdot}C_2H_5$]/[$CH_3{\cdot}CHCl{\cdot}CHF{\cdot}CH_3$] = 0·9 : 1. The infrared spectra and the chromatogram showed that the more extensive fluorination had resulted in the formation of small amounts of trihalogenobutanes and the results of these experiments are likely therefore to be less accurate than the others.

Bromination of 2-Fluorobutane.—Reaction of 2-fluorobutane (10 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146°. There was only one large dihalide peak on the chromatogram, although two small subsequent peaks were just discernible. The material of the main peak was examined by nuclear magnetic resonance spectroscopy; both proton and fluorine-19 spectra were observed and they clearly showed that the product was 2-bromo-2-fluorobutane. By injecting large samples into the chromatograph it was possible to make the very small second and third peaks large enough for their relative areas to be estimated. It seems probable that these two peaks were the two racemic 2-bromo-3-fluorobutanes in proportions 64·3% of *erythro* and 35·7% of *threo.* The two isomers represented less than 8% of the detected bromofluorobutane.

Bromination of 2-*Bromobutane*.—Reaction of 2-bromobutane (10 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146° and, unlike the bromination of n-butyl bromide, proceeded smoothly. There was only one large product peak on the chromatogram and this was shown by nuclear magnetic resonance spectroscopy to be due to 2,2-dibromobutane. There were two very small, badly defined peaks subsequent to the 2,2-dibromobutane peak which may have been due to the two 2,3-dibromobutanes but the concentrations were too small to permit any further investigation.

Bromination of 2-*Chlorobutane*. Reaction of 2-chlorobutane (11 parts), bromine (1 part), and nitrogen (400 parts) was carried out at 146°. The chromatogram had only one large peak in addition to that due to unchanged 2-chlorobutane. By analogy with the preceding two experiments this single product was assumed to be 2-bromo-2-chlorobutane.

Competitive Chlorination of 1-*Chloro- and* 2-*chloro-butane*.—A mixture (10 parts) of 1- and 2-chlorobutane was placed in a trap surrounded by a constant-temperature bath at 0°, and a vapour mixture was entrained into the reactor by bubbling nitrogen (in all 400 parts) through the liquid. The relative concentrations of the two components in the vapour entering the reactor was determined by diverting the gas stream through a second trap in which the butyl halides were recondensed. By this means, samples of the reactants could be obtained at intervals while the chlorination (by 1 part of chlorine) was in progress. The ratio of the two butyl chlorides varied only very slightly during the chlorination provided the quantity of liquid mixture in the initial trap was fairly large. The chlorinated products were collected and analysed as before:

		Reactants	Products % ($C_4H_8Cl_2$)	
Temp.	No. of runs	2-ClC_4H_9 : 1-ClC_4H_9	1,3-	1,4-
35°	6	$0{\cdot}99 \pm 0{\cdot}03$	$77{\cdot}8 \pm 1{\cdot}9$	$22{\cdot}2 \pm 1{\cdot}9$
78	7	$0{\cdot}95 \pm 0{\cdot}09$	$76{\cdot}3 \pm 2{\cdot}1$	$23{\cdot}7 \pm 2{\cdot}1$

DISCUSSION

It is important that the present results should be related to the previous work on the halogenation of butane and the n-butyl halides. It seems reasonable to assume that the 2-position of 2-halogenobutanes will be affected in a similar fashion to the 1-position in the 1-halogenobutanes. The chlorination results in Table 1 have been calculated on this assumption, the validity of which was checked by the competitive chlorination of 1-chlorobutane and 2-chlorobutane. The relative proportions of 1,3- and 1,4-dichlorobutane formed as a result of the chlorination of 1-chlorobutane were already known so that the rate of chlorination of carbon atom 4 in 2-chlorobutane could be compared with rate of chlorination of carbon atom 4 in 1-chlorobutane by competitive chlorination. The results gave RS_p^4 for 2-chlorobutane as $0{\cdot}76 \pm 0{\cdot}4$ (calc. 0·8; cf. Table 1) at 35°, and as $0{\cdot}82 \pm 0{\cdot}38$ (calc. 0·8) at 78°. The striking feature of the above results is that the most reactive site in 2-halogenobutanes is the one bearing the substituent halogen. This is in agreement with the results of Rust and Vaughan [3] and emphasises how misleading was the previously accepted generalisation that the substituent halogen directs attack away from itself.[10] Comparison of the present results with the previous work on n-butyl halides confirms the importance of hyperconjugation in determining the reactivity of a particular hydrogen atom.[11] For instance, the hydrogen atoms on carbon atom 1 in 2-chlorobutane, carbon atom 2 in 1-chlorobutane, and carbon atom 3 in 2-chlorobutane are all the same distance

TABLE 1. *The chlorination of* 2-*halogenobutanes;* RS_p^x.

Temp.	X	CH_3—	—CHX—	—CH_2—	—CH_3
35°	H	1	$3{\cdot}9_5$	$3{\cdot}9_5$	1
78	H	1	3·6	3·6	1
35	Cl	0·2	3·2	3·1	0·8
78	Cl	0·2	3·0	2·9	0·8
35	F	<0·1	3·6	2·1	0·7
78	F	<0·1	3·2	2·0	0·7

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[10] Brown and Ash, *J. Amer. Chem. Soc.*, 1955, **77**, 4019.

[11] Fredricks and Tedder, *Chem. and Ind.*, 1959, 490.

from the substituent chlorine, yet their reactivities *relative to the corresponding sites in unsubstituted butane* are approximately 0·2, 0·6, and 0·8, respectively. The extent of deactivation due to the inductive effect of the substituent halogen must be the same for each position, but the change in hyperconjugation at each position due to the substituent is very different.

There is no simple method for relating the results of the fluorination of the 2-halogenobutanes with those of previous work. However, the noticeable feature of Table 2 is the small proportions of 2-chloro-1-fluoro- and 2-chloro-3-fluoro-butane obtained by the fluorination of 2-chlorobutane. There is little doubt that this is the " vicinal effect " previously observed in the chlorination of 1-bromobutane and in 1-chlorobutane at high temperatures.[3,1] These results indicate that the intermediate chlorobutyl radical loses chlorine even at room temperature. This effect is probably masked in the chlorinations by the subsequent addition of chlorine to the butene so formed. Another explanation of the large vicinal effect in fluorination would be that the chlorobutyl radicals are relatively hot when formed in fluorination, but this seems less likely, for although the hydrogen abstraction step is very exothermic, most of this heat will be found in the hydrogen fluoride molecule rather than in the new radical.[12]

TABLE 2. *The fluorination (%) of the 2-halogenobutanes.*

Temp.	X	CH_3	CHX	CH_2	CH_3
20°	F	23·9	—	31·9	44·2
20	Cl	7·9	—	25·5	66·6

The almost exclusive attack at the 2-position by bromine atoms in the 2-halogenobutanes was expected. The bromination of n-butyl fluoride and chloride had shown that the substituent halogen accelerated substitution at the carbon atom to which it is attached by a factor of greater than ten, while at the same time reducing the reactivity of the adjacent positions by a factor of two or more.

The halogenation of the 2-halogenobutanes as expected yielded two 2,3-dihalogenobutanes. It is of considerable interest that the two 2,3-isomers are not formed in equal amounts (cf. Table 3; it has been assumed that the first 2,3-isomer to be eluted is invariably the *erythro*-compound). On the chromatogram from the bromination of 2-fluorobutane there were two small peaks eluted after the 2-bromo-2-fluorobutane, which was the major product. It seems probable that these small peaks were the 2-bromo-3-fluorobutanes. If this is so and the *erythro*-compound was eluted first, then the proportions of the two isomers were 64·3% *erythro* and 35·7% of *threo*.

TABLE 3. *The proportions of* erythro- *and* threo-2,3-*isomers formed during the halogenation of the* 2-*halogenobutanes.*

	Temp.	*erythro* (%)	*threo* (%)
(*a*) Chlorination of 2-chlorobutane:	35°	71·4	28·6
	75	70·3	29·7
(*b*) Chlorination of 2-fluorobutane:	35	59·4	40·6
	75	59·6	40·4
(*c*) Fluorination of 2-chlorobutane:	21	66·6	33·4
(*d*) Fluorination of 2-fluorobutane:	21	60·2	39·8

These results clearly imply that the reaction between the intermediate 2-halogeno-1-methylpropyl radicals ($CH_3{\cdot}CHX{\cdot}\dot{C}H{\cdot}CH_3$) and the halogen molecule is stereospecific. A possible explanation is that the two such radicals have preferred conformations both of which favour substitution from one direction. If it is assumed that the bonds about the tervalent carbon atom approximate to sp^2 and are nearly planar, then the other three bonds on the tetrahedral carbon can rotate relatively to this plane. However they can be expected to have a preferred conformation in which the methyl group of the tervalent carbon atom

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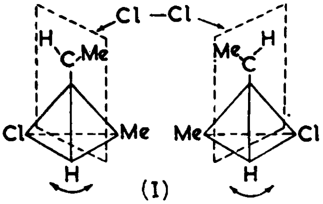
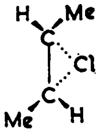
[12] Smith, *J. Chem. Phys.*, 1959, **31**, 1352; Polanyi, *ibid.*, p. 1338.

will be closely above the hydrogen atom of the tetrahedral carbon, slightly to either side (see the Figure). The incoming halogen molecule must approach approximately perpendicularly to the free-radical plane and this approach will be easier on the side away from the substituent halogen atom so that in both cases it will yield the *erythro*-compound. Table 3 shows that the size of the substituent halogen has a greater effect on the proportion of the two stereoisomers formed, than the reactivity of the attacking atom. This would agree with the suggested mechanism. An alternative explanation involving the bridged structure (II) which would occur most readily with the methyl groups in a "*trans*"-position, seems unlikely as no evidence for migration of halogen atoms has been observed during any of these halogenations.



(I)



(II)

Stereospecificity in free-radical reactions of the type reported here was previously observed by Kooyman and Vegter.[13] They halogenated norbornane (bicyclo[2,2,1]-heptane) in the gas and liquid phases and found that the 2 position was the most reactive. Of the two possible isomers the *exo*-compound predominated. The explanation offered by Kooyman and Vegter was essentially identical with that offered in the present paper.

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UNIVERSITY OF SHEFFIELD. [*Received, September* 28*th*, 1960.]

[13] Kooyman and Vegter, *Tetrahedron*, 1958, **4**, 382.