Free-radical Substitution in Aliphatic Compounds. Part XXVIII.[1] The Gas-phase Bromination of Halogenocyclohexanes and Halogenocyclopentanes in a Fast Flow Reactor

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The bromination of fluoro-, chloro-, and bromo-cyclohexane and chloro- and bromo-cyclopentane has been investigated in the gas phase using a flow system. Unlike previous work in solution and in a static gas phase apparatus, normal directive effects were observed, and no olefinic products were obtained. These results suggest that the high yields of 1,2-dibromoalkanes reported previously in solution phase experiments are not due to ' anchimeric assistance ' although ' bridging ' by the substituent may be an important factor.

In 1961 Fredricks and Tedder [2] reported that the principal products from the bromination of the 2-halogenobutanes were 2-bromo-2-halogenobutanes. These experiments were performed using a flow reactor in which contact times were less than a minute and in which hydrogen bromide and unchanged bromine were removed before the other products and unchanged halogenoalkanes were condensed out of the gas stream. Earlier studies by Fredricks and Tedder [3] of the chlorination of 1-bromobutane had shown that elimination of bromine atoms from 1-bromo-2-butyl radicals was very fast at moderate temperatures. At the same time in the bromination of 1-halogenobutanes no evidence was obtained for particularly high rates of attack at the 2-position.

Thaler,[4] in 1963, reported very high yields of 1,2-dibromoalkanes from the bromination of monobromoalkanes in solution, but he found that the bromination of monochloroalkanes in solution gave results virtually identical with those Fredricks and Tedder had obtained for the gas phase. Thaler explained his abnormal bromination results in terms of ' neighbouring group participation ', or more specifically as due to ' bridging ' by the substituent bromine. It is very important to appreciate there are two separate suggestions here, (i) that the substituent bromine in some way interacts with a half-filled orbital at the adjacent carbon atom (' bridging ') and (ii) that this ' bridging ' results in accelerated attack at the 2-position. We believe that the distinction between ' bridging ' on the one hand and ' anchimeric assistance ' on the other is vital. No explanation was offered by Thaler as to why ' anchimeric assistance ' was observed in solution, but not in the gas phase.

The whole question of ' bridging ' and ' anchimeric assistance ' has become one of considerable controversy.[5-9] Opponents of the ' anchimeric assistance ' hypothesis have suggested that in solution the reversible nature of bromination [reactions (1), (−1)] is important. The alkyl radical and hydrogen bromide are likely to be held in a solvent cage long enough for the reverse reaction to become important, and various ingenious experiments

$$RH + Br\cdot \underset{k_{-1}\,(-1)}{\overset{k_1\ (1)}{\rightleftharpoons}} HBr + R\cdot$$

have been performed in attempts to remove hydrogen bromide. However the reproducibility of some of the experiments has been questioned. The crux of the problem remains: is the 2-position in a bromoalkane unexpectedly reactive to bromine atom attack as Thaler suggested, or are the other positions *apparently* less reactive because in solution the reverse reaction is favoured?

In a previous paper [1] we have reported that elimination of hydrogen halide and the formation of *trans*-1,2-dibromocyclohexane occurs in the bromination of halogenocyclohexanes (even fluorocyclohexane) in the gas phase in a *static* system. We also found that the extent of these ' unexpected ' reactions was increased by the addition of hydrogen bromide and by increasing the surface : volume ratio of the reactor. The present paper reports the investigation of the gas phase bromination of fluoro-, chloro-, and bromo-cyclohexane and of chloro- and bromo-cyclopentane in the *flow reactor* originally used by Fredricks and Tedder in their study of the halogenation of halogenobutanes. In the flow reactor the reactants and products are in contact with the walls of the vessel and with the product hydrogen bromide for a very short time (<50 s). It was anticipated that by leading the product flow directly through a tube of Carbosorb to remove hydrogen bromide, and by a judicious choice of flow rates, the heterogeneous elimination reaction with hydrogen bromide could be avoided.

EXPERIMENTAL

The gas-phase flow reactor was similar to that described previously.[10] The reactant halogenocycloalkane was carried in a metered flow of nitrogen from a storage trap into the reaction vessel *via* a pre-heating spiral. A similar metered

[1] Part XXVII, D. S. Ashton, A. Nechvatal, I. K. Stoddart, J. C. Walton, and J. M. Tedder, *J.C.S., Perkin I*, 1973, 846.
[2] P. S. Fredricks and J. M. Tedder, *J. Chem. Soc.*, 1961, 3520.
[3] P. S. Fredricks and J. M. Tedder, *J. Chem. Soc.*, 1960, 144.
[4] W. Thaler, *J. Amer. Chem. Soc.*, 1963, **85**, 2607.
[5] P. S. Skell and P. D. Readio, *J. Amer. Chem. Soc.*, 1964, **86**, 3334; P. S. Skell and K. J. Shea, *Israel J. Chem.*, 1972, **10**, 493.
[6] J. G. Traynham and W. G. Hines, *J. Amer. Chem. Soc.*, 1968, **90**, 5208.
[7] D. D. Tanner, D. Darwish, M. W. Mosher, and N. J. Bunce, *J. Amer. Chem. Soc.*, 1969, **91**, 7398.
[8] D. D. Tanner, H. Yabuuchi, and E. V. Blackburn, *J. Amer. Chem. Soc.*, 1971, **93**, 4802; D. D. Tanner, M. W. Mosher, N. C. Dass, and E. V. Blackburn, *ibid.*, p. 5846.
[9] C. Ronneau, J. P. Soumillion, P. Dejaifve, and A. Bruylants, *Tetrahedron Letters*, 1972, 317.
[10] P. C. Anson, P. S. Fredricks, and J. M. Tedder, *J. Chem. Soc.*, 1959, 918.

flow of bromine was arranged to enter the reaction vessel *via* a jet directly opposed to that of the halogenocycloalkane. The light source was 2 × 150 W tungsten lamps. From the reaction vessel (82 cm^3) the products were taken through a large heated tube containing carefully dried Carbosorb which removed bromine and hydrogen bromide. They were then collected in a trap cooled in liquid nitrogen. Analysis of the products was carried out on a Griffin and George D6 gas density balance chromatograph using a 6 ft × $\frac{3}{16}$ in column packed with 15% tritolyl phosphate on Embacel. The results are tabulated as relative selectivities ($RS^{1,x}_{1,1}$), *i.e.* the rate of attack at any position *cis* or *trans* relative to the rate of attack at the 1-position.

Reagents.—Commercially available bromocyclopentane, bromocyclohexane, chlorocyclopentane, and chlorocyclohexane were purified by spinning band column distillation and preparative g.l.c. to give material boiling at 137° and 758 mmHg, 163° and 760 mmHg, 114° and 760 mmHg, and 142° and 760 mmHg respectively. Each compound showed only one peak by analytical g.l.c. Fluorocyclohexane was prepared by the slow addition of hydrogen fluoride to cyclohexene at −50°.[11] Final purification was by preparative g.l.c. to give material, b.p. 62° at 180 mmHg, which showed only one peak by analytical g.l.c.

Identification of Isomeric Bromohalogenocycloalkanes.—The bromination of bromocyclohexane gave six isomeric dibromocyclohexanes while the bromination of bromocyclopentane gave four isomeric dibromocyclopentanes. The bromination of chlorocyclohexane gave seven isomeric bromochlorocyclohexanes while the bromination of chlorocyclopentane gave five isomeric bromochlorocyclopentanes. This was shown by g.l.c.–mass spectroscopy of the reaction mixtures. The order of elution of the isomeric bromochloro-, dibromo-, and dichloro-cycloalkanes on tritolyl phosphate is now well established:[12] 1,1-dihalogeno; *trans*-1,2; *trans*-1,3; *trans*-1,4; *cis*-1,3; *cis*-1,4; and *cis*-1,2-isomers.

Additional confirmation was obtained by injecting into the chromatographic apparatus authentic samples of the appropriate *trans*-1,2-bromohalogenocycloalkane.

trans-1,2-Dibromocycloalkanes were prepared from the cycloalkene and bromine while the *trans*-1-bromo-2-chlorocycloalkane was prepared from the cycloalkene, *N*-bromosuccinimide, and hydrogen chloride.[13] The isomeric bromochlorocyclopentanes were prepared by overchlorination of bromocyclopentane, were separated by preparative g.l.c., and their n.m.r. spectra were determined. The spectra closely resembled those published by Russell.[14] A similar overbromination of bromocyclopentane enabled the n.m.r. spectra of *cis*- and *trans*-1,3-dibromocyclopentane to be obtained. *cis* and *trans*-1,4-dibromocyclohexane were synthesised from cyclohexane-1,4-diol and hydrogen bromide.[15]

TABLE 1

Identification of isomeric bromohalogenocycloalkanes

System	Isomer						
	1,1-	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3	*trans*-1,4	*cis*-1,4
BrC_6Br	M.s.	Synth M.s. N.m.r.		M.s.	M.s.	Synth. M.s. N.m.r.	Synth. M.s. N.m.r.
ClC_6Br	M.s.	Synth. M.s. N.m.r.	M.s.	M.s.	M.s.	M.s.	M.s.
FC_6Br	M.s.	Synth. M.s. N.m.r.		M.s.	M.s.	Synth. M.s.	Synth. M.s.
BrC_5Br	M.s.	Synth. M.s. N.m.r.	M.s.	M.s. N.m.r.	M.s. N.m.r.		
ClC_5Br	M.s. N.m.r.	Synth. M.s. N.m.r.	M.s. N.m.r.	M.s. N.m.r.	M.s. N.m.r.		

Since the fluorohalogenocyclohexanes are eluted in a different order from the other dihalogenocycloalkanes, attempts were made to synthesise *trans*-1,2-; *trans*-1,4-; and *cis*-1,4-bromofluorocyclohexane. In general, the appropriate isomeric dibromocyclohexane was added to a vigorously stirred solution of potassium fluoride in Digol maintained at 150°. A mixture of products was obtained in each experiment. All components of the mixture were analysed by g.l.c.–mass spectroscopy. The peak identified by retention time corresponding to the appropriate peak in the reaction mixture of bromofluorocyclohexanes was separated by preparative g.l.c. and its n.m.r. spectrum was determined. Table 1 summarises the mode of identification employed for each isomeric bromohalogenocyclohexane.

Gas-phase Bromination of Bromocyclohexane in a Flow Reactor.—Metered flows of bromocyclohexane (9 parts) and bromine (1 part) were allowed to react in the flow reactor; the respective flow rates enabling a contact time between reactants of <50 s. Removal of excess of bromine and hydrogen bromide formed in the reaction was effected by passing the gaseous products through a tube packed with dry Carbosorb and the products then immediately condensed into a tube immersed in liquid nitrogen. Injections were made directly into the chromatography apparatus, a

[11] S. M. McElvain and J. W. Langston, *J. Amer. Chem. Soc.*, 1944, **66**, 1759.
[12] D. S. Ashton, J. M. Tedder, and J. C. Walton, *J. Chromatography*, 1972, **72**, 269.
[13] H. L. Goering and L. L. Sims, *J. Amer. Chem. Soc.*, 1955, **77**, 3465.
[14] A. Ito and G. A. Russell, *J. Amer. Chem. Soc.*, 1963, **85**, 2983; A. Ito, Ph.D. Thesis, Iowa State University, Ames, Iowa.
[15] E. Havinga, W. Kwestroo and F. A. Meijer, *Rec. Trav. chim.*, 1954, **73**, 721.

6 ft × $\frac{3}{16}$ in column packed with 15% tritolyl phosphate on Embacel (60—100) mesh at 150° was used for the analysis. The results are shown in Table 2.

TABLE 2

Gas-phase bromination of bromocyclohexane in a flow reactor

$RS^{1,x}_{1,1}$

Temp. (°C)	1,1	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3	*trans*-1,4	*cis*-1,4
			Isomer				
78	1	0·93		0·38	0·16	0·37	0·16
111	1	1·24		0·40	0·30	0·40	0·22
146	1	1·70		0·48	0·31	0·69	0·28
162	1	2·40		0·60	0·48	1·19	0·37
204	1	2·72		0·75	0·67	1·78	0·29

Error of each value is *ca.* ±10%.

Gas-phase Bromination of Chlorocyclohexane in a Flow Reactor.—Metered flows of chlorocyclohexane (11 parts) and bromine (1 part) reacted in the flow reactor. The products were collected and analysed in the sequence described; the analysis temperature for the isomeric bromochlorocyclohexanes was 125°.

TABLE 3

Gas-phase bromination of chlorocyclohexane in a flow reactor

$RS^{1,x}_{1,1}$

Temp. (°C)	1,1	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3	*trans*-1,4	*cis*-1,4
			Isomer				
78	1	0·51	0·03	0·35	0·16	0·25	0·19
111	1	0·73	0·04	0·47	0·21	0·31	0·22
146	1	0·81	0·04	0·55	0·26	0·34	0·23

Error of each value is *ca.* ±10%.

Gas-phase Bromination of Fluorocyclohexane in a Flow Reactor.—Metered flows of fluorocyclohexane (6 parts) and bromine (1 part) reacted in the flow reactor. To obtain complete resolution of the isomeric bromofluorocyclohexanes, two chromatographic columns were employed; the 15% tritolyl phosphate column at 110° eluted 1,1-bromofluorocyclohexane; *trans*-1,2; *trans*-1,3; *cis*-1,3; and *trans*-1,4 + *cis*-1,4 while a 30 ft × $\frac{3}{8}$ in column of silicone oil on Perkin-Elmer Chromosorb G (80—100 mesh) at 90° eluted 1,1-bromofluorocyclohexane; *trans*-1,2 + *trans*-1,3; *cis*-1,3; *trans*-1,4; and *cis*-1,4. Combination gave the results in Table 4.

TABLE 4

Gas-phase bromination of fluorocyclohexane in a flow reactor

$RS^{1,x}_{1,1}$

Temp. (°C)	1,1	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3	*trans*-1,4	*cis*-1,4
			Isomer				
78	1	1·44		0·93	1·00	1·34	0·40
111	1	1·42		1·08	0·74	0·92	0·44
146	1	1·53		1·30	1·23	1·49	0·85

Error of each value is *ca.* ±10%.

Gas-phase Bromination of Bromocyclopentane in a Flow Reactor.—Metered flows of bromocyclopentane (10 parts) and bromine (1 part) reacted in the flow reactor. The products were collected and analysed in sequence described; the analysis temperature for the isomeric dibromocyclopentanes was 115°.

TABLE 5

Gas-phase bromination of bromocyclopentane in a flow reactor

$RS^{1,x}_{1,1}$

Temp. (°C)	1,1	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3
		Isomer			
78	1	0·444		0·204	0·125
111	1	0·621		0·317	0·218
146	1	0·817		0·419	0·364

Error of each value is *ca.* ±10%.

Gas-phase Bromination of Chlorocyclopentane in a Flow Reactor.—Metered flows of chlorocyclopentane (8 parts) and bromine (1 part) reacted in the flow reactor. The products were collected and analysed at 115°.

TABLE 6

Gas-phase bromination of chlorocyclopentane in a flow reactor

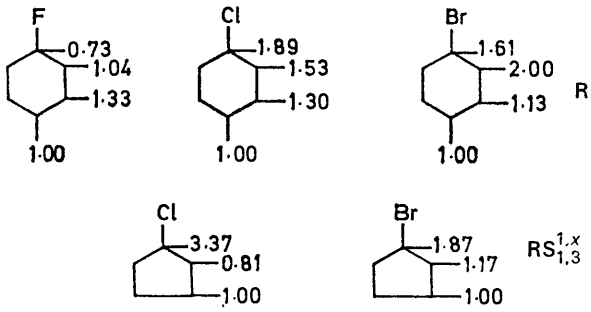
$RS^{1,x}_{1,1}$

Temp. (°C)	1,1	*trans*-1,2	*cis*-1,2	*trans*-1,3	*cis*-1,3
		Isomer			
78	1	0·171	0·007	0·157	0·074
111	1	0·233	0·009	0·202	0·095
146	1	0·321	0·012	0·276	0·131
162	1	0·418	0·012	0·345	0·148

Error of each value is *ca.* ±10%.

DISCUSSION

The bromination of the halogenocycloalkanes gave only the expected bromohalogenocycloalkane isomers. Unlike the reactions in a static system no measurable amount of bromocycloalkane or *trans*-1,2-dibromocycloalkane was detected. The present results are



SCHEME Relative selectivities for photobromination of bromofluoro-, and chloro-cyclohexane and chloro- and bromocyclopentane in a flow reactor at 110° (contact time 50 s).

summarised in the Scheme. In the absence of competitive experiments, the position remote from the substituent has been taken as standard since it has been found in linear compounds that a substituent has little effect at the 3-position and virtually no effect beyond the 3-position. The similarity of the $RS^{1,3}_{1,4}$ values for each halogenocyclohexane suggests this is a reasonable approximation. The results show that in contrast

to the solution-phase work there is no significant activation of the 2-position in either bromocyclohexane or bromocyclopentane; at lower temperatures, the 1-position is more reactive in the bromo- and chloro-cycloalkanes studied. In chlorocyclopentane the 2-position is the least reactive site in the molecule. Unfortunately data do not exist for the gas-phase brominations of linear bromoalkanes under exactly the same conditions. However the data of Fredricks and Tedder [2,3] for the bromination of 1-fluoro- and 1-chloro-butane (at a higher temperature) and the chlorination of 2-fluoro- and 2-chloro-butane are shown in Table 7. Bromination of

TABLE 7

Halogenation of halogenobutanes in a flow reactor

(a) Bromination RS_4^z at 142°

$$\underset{10}{F}-\underset{9}{CH_2}-\underset{82}{CH_2}-\underset{1}{CH_3}$$

$$\underset{34}{Cl}-\underset{32}{CH_2}-\underset{82}{CH_2}-\underset{1}{CH_3}$$

(b) Chlorination RS_{40}^z at 78° [a]

$$\underset{<0\cdot1}{CH_3}-\underset{3\cdot2}{CHF}-\underset{2\cdot1}{CH_2}-\underset{0\cdot7}{CH_3}$$

$$\underset{0\cdot2}{CH_3}-\underset{3\cdot0}{CHCl}-\underset{2\cdot9}{CH_2}-\underset{0\cdot8}{CH_3}$$

[a] 4° Primary position in 1-chlorobutane.

the 2-halogenobutanes yielded predominately the 2-bromo-2-halogenobutanes as in the corresponding chlorinations where the most reactive site was also that carrying the substituent halogen.[3] When the results in Table 7 are considered together with the present work a very consistent overall picture is obtained.

The *trans* : *cis* ratio, for the 1,2-dihalogenocycloalkanes obtained in the bromination reaction is very high and in some cases no *cis*-isomer was detected. Table 8 gives

TABLE 8

Halogenation of halogenocycloalkanes. *trans* : *cis* Ratios for 1,2-isomers and 1,3-isomers at 100°

	Compound	1,2-Isomer	1,3-Isomer
Bromination	Cyclo-FC_6	>[40]	1·3
	Cyclo-ClC_5	25·7	2·1
	Cyclo-ClC_6	20·1	2·2
	Cyclo-BrC_5	>[58]	1·5
	Cyclo-BrC_6	>[52]	1·3
Chlorination	Cyclo-FC_6	40·5	1·0
	Cyclo-ClC_5	15·5	1·7
	Cyclo-ClC_6	10·5	2·0

Square brackets denote the theoretical limit of detection, expressed as a *trans* : *cis* ratio.

the *trans* : *cis* ratios for the 1,2- and 1,3-compounds in the bromination of the halogenocycloalkanes studied. Where no *cis*-isomer was detected, the theoretical limit of detection is expressed as a *trans* : *cis* ratio (denoted by square brackets), *i.e.* the true *trans* : *cis* ratio is greater than this. The *trans* : *cis* ratios for the complimentary chlorinations of these molecules are also shown.

[16] D. S. Ashton and J. M. Tedder, *J. Chem. Soc.* (*B*), 1971, 1719; 1723.

The very high *trans* : *cis* ratio for the 1,2-dihalogenocycloalkanes from the bromination of these molecules is consistent with the picture we have proposed in previous chlorination studies; [16] of an interaction between the filled *p* atomic orbitals of the substituent halogen and the half-filled *p* orbital of the 2-halogenocycloalkyl radical leading to a preferred conformation. There has been increasing e.s.r. evidence [17] for this type of interaction. Although this interaction is unlikely to approach a 'bridging' situation when fluorine is the substituent, it may come closer to it when bromine is the substituent. However the complete absence of enhanced attack at the 2-position in the bromination of the bromocycloalkanes rules out anchimeric assistance.

The difference between the gas-phase and the liquid-phase reaction must be the reversible reaction promoted by the solvent cage, *i.e.* it is not enhanced attack at the 2-position but retarded reaction in solution (by reversibility) at the other positions. The orbital interaction between the substituent bromine and the radical site, which we have invoked to explain the predominance of the *trans*-isomer, also provides the explanation of why attack at the 2-position is not also retarded. We have proposed that this orbital interaction causes a particular conformation of the cycloalkyl radical to be preferred. Since this orbital interaction, to be effective, must be weakly bonding, it must also reduce the reactivity of the radical to such an extent that it inhibits reaction (−1) which is only *ca.* 10 kcal mol^{-1} exothermic but it is insufficient to inhibit reaction (2) which is >20 kcal mol^{-1} exothermic. A more electronegative substituent,

$$R\cdot + Br_2 \xrightarrow{(2)} RBr + Br\cdot$$

chlorine or fluorine, would enhance the rate of hydrogen transfer (−1). This picture explains the retention of optical activity in certain bromination experiments [18] and the observation that no exchange of bromine is involved in the bromination of 1-bromobutane.[9]

The difficulty in repeating some of the solution-phase work is not surprising. The course of the reaction depends on the time the incipient alkyl radical and the molecule of hydrogen bromide are held together in the solvent cage and this will in turn depend very much on the design of the apparatus.

The present results confirm unequivocally that there is no anchimeric assistance in the gas-phase bromination of bromocyclopentane and bromocyclohexane. On the other hand, previous papers [16] in this series have shown that there is good evidence for an orbital interaction of the 'bridging' type in these gas-phase reactions. The important difference between the gas-phase reaction and reaction in solution is that in the former situation the alkyl radical and the hydrogen bromide separate immediately. In solution the two products are held together in

[17] D. J. Edge and J. K. Kochi, *J. Amer. Chem. Soc.*, 1972, **94**, 6485; A. R. Lyons and M. C. R. Symons, *J. Amer. Chem. Soc.* 1971, **93**, 7330.

[18] P. S. Skell, D. L. Tuleen, and P. D. Readio, *J. Amer. Chem. Soc.*, 1963, **85**, 2489.

the solvent cage favouring the reverse reaction. Unfortunately experimental evidence for bridging has also been regarded as evidence for ' anchimeric assistance '. We hope the present results will convince protagonists on each side of this argument that bridging does occur and that the apparently high rate of bromination at the 2(β)-position in alkyl bromides in solution is attributable to the importance of the reverse reaction (−1) occurring in the solvent cage at all other positions.

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