

XXXII.—*Preparation, Hydrolysis and Reduction of the Fluoro-, Chloro-, and Bromo-benzyl Bromides.*

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IN previous communications (J., 1922, **121**, 1392; 1923, **123**, 2828; 1924, **125**, 1312, 2278) an account was given of the manner in which the reactivity of halogen atoms in various halogenated benzenoid derivatives is influenced by oxygen and by the hydrogen of a methyl group. The investigations have been continued with a view to discovering the effect of fluorine, chlorine, and bromine in such compounds. From the point of view of the principle of induced alternate polarities the halogens, except fluorine, appear to act as weakly negative "key-atoms" (as pointed out by Lapworth, *Mem. Manchester Phil. Soc.*, 1920, **64**, No. 3). The present investigation has shown that (1) fluorine is capable of inducing differences of reactivity very similar to, but smaller than those met with in the cases of the methoxybenzyl bromides (J., 1922, **121**, 1392) and the ω -bromoxylenes (J., 1924, **125**, 2278) and (2) chlorine and bromine induce still smaller differences, and the chloro- and bromo-benzyl bromides provide the first examples encountered in this series, in

which a change of reagent does not cause a change in the order of reactivity.

The order of ease with which the bromides lose their bromine as bromidion in solution in aqueous alcohol is: (1) *p*-fluorobenzyl bromide > benzyl bromide > *o*-fluoro- > *m*-fluoro-; (2) benzyl bromide > *p*-chloro- > *o*-chloro- > *m*-chloro-; (3) benzyl bromide > *p*-bromo- > *o*-bromo- > *m*-bromo-. The order of ease of reduction by hydriodic acid is: (1) *o*-fluoro- > *m*-fluoro- > benzyl bromide > *p*-fluoro-; (2) *o*-chloro- > *p*-chloro- > *m*-chloro- > benzyl bromide; and (3) *o*-bromo- > *p*-bromo- > *m*-bromo- > benzyl bromide. The differences of ease of hydrolysis are quite marked. Those of ease of reduction are small, but several repetitions of the experiments led to the same order of reactivity and, as is seen from the above, the order of ease of reduction of the chloro- and bromo-compounds is not analogous to that discovered in the cases of the methoxybenzyl bromides, the ω -bromoxylenes, and the fluorobenzyl bromides.

A series of experiments was undertaken to see if this non-reversal of the order of reactivity is due to any of the following causes: (a) removal of halogen from the nucleus, (b) liberation of iodine as follows: (1) $R \cdot C_6H_4 \cdot CH_2Br + HI \rightarrow R \cdot C_6H_4 \cdot CH_2I + HBr$. (2) $2R \cdot C_6H_4 \cdot CH_2I \rightarrow R \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot C_6H_4R$ (compare Silberrad, J., 1924, **125**, 2196), and (c) the more rapid formation of the iodide in the case of the para-isomerides and subsequent reduction of the iodides by hydriodic acid. The bromides were reduced for a long time, but the slight elimination of nuclear halogen then noted was not sufficient to reverse the discovered order of reactivity when correction was made for it. Reaction (2) is a photochemical one and does not take place in a dark thermostat such as was used in these experiments. In order to test (c), the bromobenzyl iodides were prepared; they were reduced by hydriodic acid at the same rate as the corresponding bromides. Thus it appears as if the conversion of the bromide into iodide is due to a mass-action effect and, owing to the concentration of hydriodic acid used, goes almost equally rapidly in all cases. Some of the iodides lose iodine more rapidly than their isomerides, and when a change in order of reactivity with change of reagent takes place alternating polar influences are very strong, *e.g.*, in the methoxybenzyl bromides.

An approximate estimate of the magnitude of the three influences which affect the reactivity of the bromine atom in the bromides, namely, the general (represented by *g*), the alternating (represented by *a*), and the so-called steric influence (represented by *s*), may be arrived at from considerations similar to those put forward by Flürscheim (J., 1909, **95**, 726). A comparison by means of reaction velocities, which is the most satisfactory method, is impossible,

because only during the hydrolysis of *o*- and *m*-fluorobenzyl bromides and also of the isomeric nitrobenzyl bromides (Shoesmith and Hetherington, J., 1924, **125**, 1316) were the reactions slow enough to give monomolecular velocity coefficients. The reduction of the bromides, moreover, is not the simple bimolecular reaction investigated by West in the case of bromomalonyl compounds (J., 1924, **125**, 710). The reciprocals of the times taken for half-completion of the reaction in the various cases may be used to obtain the necessary comparison.

If K_o , K_m , K_p and K_u represent the reciprocals of the times taken for half-completion of the reactions for the ortho-, meta-, para- and unsubstituted compounds, respectively, the manner in which the velocities of the reactions are affected by the three influences mentioned above may be expressed by the following equations : *

$$\log_{10} K_o = \log_{10} K_u + g + a + s.$$

$$\log_{10} K_m = \log_{10} K_u + g - a.$$

$$\log_{10} K_p = \log_{10} K_u + g + a,$$

and hence

$$g = \frac{1}{2}(\log_{10} K_m + \log_{10} K_p - 2 \log_{10} K_u),$$

$$a = \frac{1}{2}(\log_{10} K_p - \log_{10} K_m),$$

and $s = \log_{10} K_o - \log_{10} K_p.$

Obtained from graphs plotted from observations recorded in this and previous communications, the reciprocals of the various times taken for half-hydrolysis (x) and half-reduction (y) at the temperatures stated are summarised in Table I, on which the following remarks are based :

The general effect. The order in which the atoms or groups affect the reactivity of the bromine (a) towards hydrolysing agents in a general way is OMe, Me, F, Cl, Br, CO₂H, NO₂, ranging from the strongly enhancing methoxy-group to the strongly retarding nitro-group, and (b) towards hydrogen iodide is OMe and Me, Cl, Br, CO₂H, and F. In the latter case, only the methoxy- and the methyl-group have an appreciable general influence on the reduction velocity. The strong general influence of the methoxy-group is noteworthy.

The alternating effect. The order in which alternation towards hydrolysing agents is produced is similar to that given above (a); in this case, however, the magnitudes of the effect may be compared. The order is OMe > F > Me > Cl > Br > CO₂H > NO₂. The differences observed in the first five cases, *i.e.*, negative groups, have positive values, whilst in the last two, *i.e.*, positive groups, they have negative values. For reduction, the order is OMe and Me > CO₂H > F, Cl,

* Logarithms are used in order that the expressions shall finally involve a product or a quotient as the case may be.

TABLE I.

Compounds.	K_e		K_m		K_p		g		a		s	
	x .	y .	x .	y .	x .	y .	Hyd.	Red.	Hyd.	Red.	Hyd.	Red.
Methoxybenzyl bromides.	<33.3 (60°)	0.107 (25°)	0.47	12.5	>33.3*	0.00	>1.54	+∞	0.92	-∞	nil	∞
ω -Bromoxylenes.	2.17 (60°)	>0.00 (25°)†	0.77	0.15	2.78	0.00	0.68	+∞	0.28	-∞	-0.11	∞
Fluorobenzyl bromides.	0.28 (60°)	0.00 (25°)	0.20	0.00	0.91	0.00	-0.39	—	0.33	—	-0.51	—
Fluorobenzyl bromides.	1.0 (76°)	0.27 (101°)	0.71	0.22	4.0	0.18	-0.22	0.00	0.37	-0.05	-0.6	0.18
Chlorobenzyl bromides.	0.85 (76°)	0.36 (101°)	0.65	0.24	1.8	0.31	-0.60	0.27	0.22	+0.05	-0.32	0.07
Bromobenzyl bromides.	0.84 (76°)	0.36 (101°)	0.71	0.23	1.43	0.29	-0.67	0.22	0.15	+0.05	-0.23	0.09
Nitrobenzyl bromides.	0.29 (76°)	—	0.33	—	0.29	—	-1.69	—	0.028	—	nil	—
ω -Bromotoluic acids.	—	—	—	0.72 (76°)	0.56	0.65	-1.07	+0.06	0.055	+0.19	—	—

Benzyl bromide $x = 0.67$ (60°), 2.17 (76°). $y = 0$ (25°), 0.20 (101°), 0.39 (110°).

* The extraordinary rapidity with which *p*-methoxybenzyl bromide is hydrolysed in aqueous alcoholic solution suggests that this figure should be much greater and hence *g* and *a* for hydrolysis approach those for reduction, *i.e.*, ∞

† ω -Bromo-*o*-xylene is definitely but very slowly reduced at 25°. A definite value for $K_e(y)$ cannot be given, but *s* (red.) must be large on account of the stability of ω -iodo-*p*-xylene at 25° in presence of hydrogen iodide.

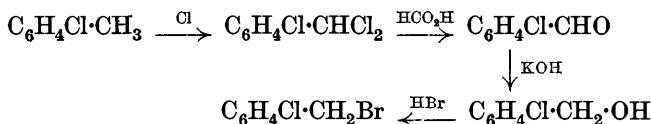
and Br. Here the differences in the cases of the OMe, Me and F compounds have positive values and in the other cases negative values. According to the principle of induced alternate polarities the sign of the difference is determined by the positive or negative character of the substituents, and the reduction of the chloro- and bromo-benzyl bromides is the only case so far met with in this series in which the sign of the difference is other than was expected.

The steric effect. The values obtained for s show that this effect in some cases diminishes and in other cases increases the reactivity, the former being observed in the hydrolyses, the latter in the reductions. Therefore the retarding of the reactions cannot be due to steric hindrance as normally conceived, and the results justify the conclusion that there is a disturbing factor governing the reactivity of ortho-compounds (see Lapworth and Shoesmith, J., 1922, **121**, 1394).

The influence of atoms or groups of atoms having the same electronic shell may be compared also, since the manner in which the methyl and the methoxy-group and the fluorine atom each affect the reactivity of the bromine atom of the $-C_6H_4 \cdot CH_2Br$ group has been investigated. The order of potency is $OMe > Me > F$, except in the case of alternation of hydrolysis, for which the order is $OMe > F > Me$.

EXPERIMENTAL.

Preparation of the Isomeric Chlorobenzyl Bromides.—The most reliable method of preparing the ortho- and para-isomerides is indicated by the scheme :



The appropriate chlorotoluene, mixed with 5% of its weight of phosphorus pentachloride, was chlorinated at 160° until the required increase in weight had taken place. The oil thus obtained was boiled with twice its bulk of 98% formic acid (d 1.20) for $\frac{1}{2}$ hour, the mixture poured into an excess of cold water, and the oil separated, dissolved in ether, washed twice with water, and once with aqueous sodium hydroxide. The aldehyde was precipitated as the bisulphite compound, which was carefully washed with ether, dissolved in water, and the pure aldehyde liberated by the addition of excess of sodium carbonate. It was converted into the alcohol (*o*-, m. p. 70°; *p*-, m. p. 72°) by treatment with 25% alcoholic potassium hydroxide, and this into the bromide by means of hydrogen bromide in benzene solution.

o-Chlorobenzyl Bromide is an oil, b. p. $102^{\circ}/9$ mm. (Found: Br, 39.05. C_7H_6ClBr requires Br, 38.9%). *p*-Chlorobenzyl bromide has m. p. 51° (compare Jackson and Field, *Ber.*, 1878, **11**, 905) (Found: Br, 38.7%).

m-Chlorobenzyl Bromide.—*m*-Nitrobenzaldehyde was converted into *m*-chlorobenzaldehyde (Erdmann and Schwechten, *Annalen*, 1890, **260**, 59), b. p. 213 — 214° , and this was reduced to the alcohol in alcoholic potassium hydroxide. The alcohol had b. p. 242° , not 234° as stated by Mettler (*Ber.*, 1905, **38**, 1749), and from it *m*-chlorobenzyl bromide, an oil of b. p. $109^{\circ}/10$ mm. (Found: Br, 38.8%), was obtained as before.

The Isomeric Bromobenzyl Bromides.—Each of these compounds was prepared by passing a stream of air through a weighed quantity of bromine into the appropriate, boiling bromotoluene. The product was distilled under diminished pressure, the portion passing over between 120° and $140^{\circ}/12$ — 16 mm. being collected, cooled, and when solid recrystallised from alcohol. The bromides thus obtained had m. p.'s: *o*-, 31° ; *m*-, 40° ; and *p*-, 63° [Found: hydrolysable Br, (*o*-) 32.1, (*m*-) 31.8, (*p*-) 31.8. Calc. for $C_7H_7Br_2$, hydrolysable Br, 32.0%] (compare Jackson, *Ber.*, 1876, **9**, 932).

The *isomeric bromobenzyl iodides* were prepared by boiling aqueous acetone solutions of the corresponding bromides with rather more than the calculated quantity of potassium iodide for $\frac{1}{2}$ hour. The mixture was then poured into water, and the iodide recrystallised from light petroleum. *o*-Bromobenzyl iodide crystallises in shining, white needles, m. p. 47° (Found: I, 42.75. C_7H_6BrI requires I, 42.7%). *m*-Bromobenzyl iodide crystallises in white, six-sided prisms, m. p. 42° (Found: I, 42.8%). *p*-Bromobenzyl iodide crystallises in white needles, m. p. 73° (Hantzsch and Schultze, *Ber.*, 1896, **29**, 2253, give 80 — 81°) (Found: I, 42.9%).

[With R. H. SLATER.]

Preparation of the Isomeric Fluorotoluenes.—A solution of the requisite toluidine (25 g.) in a mixture of 30 c.c. of concentrated sulphuric acid and 80 c.c. of water was cooled to -5° and diazotised with 20 g. of sodium nitrite dissolved in 50 c.c. of water, the temperature being kept below 5° . The solution of the diazotised base was added to about 400 c.c. of commercial hydrofluoric acid (50—60%) in a 1,500 c.c. brazed spun-copper flask surrounded by ice, after which the flask was fitted, by means of a cork, with a copper reflux condenser and very carefully warmed on a water-bath for about an hour (alternatively, the mixture may be left at room temperature for about 16 hours). The condenser was then reversed and the flask heated directly. The mixture of fluorotoluene, hydrofluoric acid,

and cresol that distilled was collected in a copper beaker containing 300 c.c. of 30% aqueous sodium hydroxide solution surrounded by a good freezing mixture. When all the fluorotoluene had distilled, the *alkaline* mixture in the beaker was extracted thrice with ether, the combined extracts were de-emulsified by saturated ammonium sulphate solution and dried over anhydrous sodium sulphate, and the ether was evaporated. In each case the fluorotoluene distilled at 113–118° and the yield was 15–16 g. (65%) (compare Holleman and Beekman, *Rec. trav. chim.*, 1904, **23**, 238).

Preparation of the Isomeric Fluorobenzyl Bromides.—Each fluorotoluene (80 g. in four lots) was brominated by volatilising bromine (30 g.) in a slow stream of dry air and passing the vapour into the boiling fluorotoluene (20 g.); by using small quantities nuclear substitution was avoided. The brominated oil was boiled with formic acid (*d* 1.20; *ca.* 2 vols.) for 6 hours, fluorobenzotribromide and fluorobenzylidene bromide being thus converted into fluorobenzoic acid and fluorobenzaldehyde, respectively, and some of the fluorobenzyl bromide into fluorobenzyl alcohol. The mixture was poured into a large excess of water, and the oil was separated, and washed in ethereal solution with 10% aqueous sodium hydroxide until free from fluorobenzoic and formic acids. After complete removal of the fluorobenzaldehyde with freshly prepared sodium bisulphite solution—the aldehydes and the benzyl bromides form constant-boiling mixtures—the ethereal solution was dried over anhydrous sodium sulphate, and the ether distilled. The residual oil was saturated in benzene solution with dry hydrogen bromide to convert any fluorobenzyl alcohol into the bromide, and after the removal of the benzene the fluorobenzyl bromide was fractionally distilled in a vacuum in the apparatus described by Widmer (*Helv. Chim. Acta*, 1924, **7**, 52). *o*-Fluorobenzyl bromide had b. p 84–85°/15 mm.; *m*-fluorobenzyl bromide, 77°/12 mm.; and *p*-fluorobenzyl bromide, 85°/15 mm. [Found: Br, 42.4 (*o*-); 42.0 (*m*-); 42.1 (*p*-). C_7H_6FBr requires Br, 42.3%].

Hydrolysis of the Bromides.—Twenty c.c. of a standard solution (105 c.c.) of the bromide in absolute alcohol were placed in a standard 25 c.c. flask, 5 c.c. of water added, and the volume was made exactly 25 c.c. by adding absolute alcohol. The whole was thoroughly mixed, immersed in the vapour of boiling carbon tetrachloride for a definite time, and then poured into a large volume of water. The liberated hydrobromic acid was titrated directly with standard aqueous sodium hydroxide and methyl-red. The results are in Table II, where *w* represents the total weight of benzyl bromide used, *x* the percentage changed, and *t* the time of hydrolysis in hours.

TABLE II.

	Ortho-compounds.			Meta-compounds.			Para-compounds.		
F :	$w = 0.5218$ g.			0.5456 g.			0.5102 g.		
Cl :	0.5600 ,,			0.5441 ,,			0.5418 ,,		
Br :	0.6702 ,,			0.6600 ,,			0.6693 ,,		
	x .			x .			x .		
t .	F.	Cl.	Br.	F.	Cl.	Br.	F.	Cl.	Br.
$\frac{1}{2}$	25	25	24	24	21	21	68	45	40
1	51	46	44	41	38	39	88	69	62
2	76	68	66	63	58	60	96	88	85
4	94	88	87	86	80	82	98	96	95
8	95	96	96	94	92	95	99	98	98

In Table III are results obtained in a similar manner in order to compare the hydrolysis of benzyl bromide, *m*-methoxybenzyl bromide,* the fluorobenzyl bromides, and the ω -bromoxylenes at 60.5° (b. p. of chloroform).

TABLE III.

	Fluorobenzyl bromides.			<i>m</i> -Methoxybenzyl bromide.	Benzyl bromide.
w .	o .	m .	p .	0.543	0.4610
	0.5240	0.5252	0.5102		
t .	x .			x .	x .
$\frac{1}{2}$	9	7	26.5	14	22
1	20	11	48	29	39
2	33	23	69	49	59
4	56	41	90	72	80
8	76	63	95	88	88
16	91	81	96	—	—

Reduction of the Bromides.—Reduction at 25° under the conditions described by Lapworth and Shoemith and by Shoemith and Slater (*loc. cit.*) being so slow that satisfactory results could not be obtained, the bromides were reduced in a thermostat at 101°. Ten c.c. of a standard solution of the bromide in 50 c.c. of glacial acetic acid were placed in the 25 c.c. standard flask, 10 c.c. of freshly distilled hydriodic acid (d 1.680) added, the volume was made up to 25 c.c. with glacial acetic acid, and the whole thoroughly mixed, and kept in the thermostat for a definite time. The percentage reduction was then estimated as in previous cases.

The concentration of the hydriodic acid and the amount of iodine in it both influence the rate of reduction, and therefore a series of reductions was carried out on the same day with the same hydriodic acid. The results are in Table IV, t and x having the same significance as before.

* At all temperatures, in aqueous alcoholic solution, *p*-methoxybenzyl bromide is completely, and the *o*-compound almost completely, hydrolysed in 2½ minutes.

TABLE IV.

<i>t.</i>	Ortho-compounds.			Meta-compounds.			Para-compounds.		
	<i>x.</i>			<i>x.</i>			<i>x.</i>		
	F.	Cl.	Br.	F.	Cl.	Br.	F.	Cl.	Br.
1½	29.5	32	30 (31)	23	23	23 (21)	22.5	28	26 (27)
3	45	53	53 (54)	37	43	43 (41)	34	49	47 (47)
6	65	76	74 (76)	63	64	61 (60)	57	68	64 (65)

Benzyl bromide : $x = 25, 38,$ and 61 for $t = 1\frac{1}{2}, 3,$ and $6,$ respectively.

The figures in brackets represent the reduction of the bromobenzyl iodides. In Table V are the results of reductions of the bromides made at a higher temperature (110°) in order to determine the amount of nuclear halogen eliminated.

TABLE V.

<i>t.</i>	Ortho-compounds.		Meta-compounds.		Para-compounds.	
	<i>x.</i>		<i>x.</i>		<i>x.</i>	
	Cl.	Br.	Cl.	Br.	Cl.	Br.
2	76	77	57	57	70	72
4	91	91	81	79	88	88
8	102	100	97	97	98	97
18	104	103	100	100	101	101

p-Chlorobenzyl iodide (m. p. 65°) was isolated from the reaction of *p*-chlorobenzyl bromide and hydrogen iodide in glacial acetic acid at 25° (compare Shoesmith and Slater, *loc. cit.*), but, owing to the dilution at which the reductions had to be carried out, end-products in the other cases could not be separated. The figures obtained, however, show that the reaction in the cases of the meta- and para-isomerides was quite normal in that it first involved conversion of the bromide into iodide and subsequent reduction of this to the halogenated toluene.

The iodobenzyl bromides have not been examined, since in a former communication we showed that hydrogen iodide reduces iodo-toluene to toluene.

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