205. *The Mechanism of Aromatic Side-chain Reactions with Special Reference to the Polar Effects of Substituents. Part II. Kinetic Studies of the Interaction of Benzyl Bromides with* (1) *Pyridine,* (2) *Aqueous Alcohol, and* (3) *Silver Nitrate.*

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IN Part I * (Baker, J., 1933, 1128) the suggestion was made that the anomalies frequently observed in the effect of ambipolar substituents on the velocity of aromatic side-chain

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* The communication cited is regarded as Part I because the views relating to reaction mechanism therein put forward form the basis of the series.

reactions may possibly be explained on the basis of a dual mechanistic control, the formation of the ultimate reaction product(s) requiring the consummation of two (or more) processes of opposite polar requirements (electron accession or recession), and the view was expressed that the first essential is a more detailed analysis of the reaction mechanisms of simple side-chain reactions. The present series of investigations is a contribution to this aspect of the problem, and preliminary results have supplied evidence which supports the suggestions made.

In this paper are described the reactions named in the title, which were carried out at 30° in 90% alcohol (by wt.), and in dry acetone, in some cases. The effects of unipolar substituents on the velocities are found to vary widely.

I. *The Pyridine Reaction.*—Earlier results have already shown (*a*) that the reaction

$$R{\cdot}C_6H_4{\cdot}CH_2Br + C_5H_5N \longrightarrow R{\cdot}C_6H_4{\cdot}CH_2{\cdot}\overset{\oplus}{N}C_5H_5\}\overset{\ominus}{Br} \quad \text{(I.)}$$

is facilitated by electron-accession towards the side chain (Baker, J., 1932, 2361), and (*b*) that its velocity is dependent on the concentration of the pyridine (Part I, *loc. cit.*).

A more detailed study of the effects of solvent, of concentration, and of added salts on the velocity of this reaction has revealed the fact that the velocity of hydrolysis of the benzyl bromide by the solvent is not negligible in relation to the velocity of reaction (I) : hence the initial velocity of such solvent reaction (v_s) has been separately determined in each set of experiments. On the assumption that the two reactions proceed simultaneously without mutual interference, the true value of the initial velocity of the pyridine reaction (v_p) has then been determined from the relationships $k_p = v_p/c_a c_p = (v_e - v_s)/c_a c_p$, where k_p is the bimolecular velocity coefficient for the pyridine reaction, v_e the observed (experimental) initial velocity ($= k_e c_a c_p$, where k_e is the apparent bimolecular coefficient), and c_a and c_p are the initial concentrations of the benzyl bromide and pyridine, respectively, in g.-mols. per litre. Time, throughout, is in minutes.

Data have, so far, been obtained in 90% alcohol (by wt.) and in dry acetone, and the results, summarised in Tables I and V, indicate that, in acetone, the solvent reaction is almost negligible, and hence this solvent will be a suitable one for a more detailed study of reaction (I). The data in 90% alcohol are, however, required for purposes of comparison with the silver nitrate reaction, which is more readily studied in alcoholic solution owing to the very small solubility of silver nitrate in dry acetone; k_s is the pseudo-unimolecular velocity coefficient.

TABLE I.

Interaction of benzyl bromide with solvents at 30° ± 0·02°.

No.	c_a.	Solvent.	$k_s \times 10^4$.	$v_s \times 10^6$.	No.	c_a.	Solvent.	$k_s \times 10^4$.	$v_s \times 10^6$.
1	0·0125	90% EtOH	1·9 ± 0·1	2·4	5	0·05	90% EtOH	3·2 ± 0·5	16·0
3	0·025	,,	1·9 ± 0·1	4·8	6	0·025	$COMe_2$	0·097 ± 0·003	0·24
4	0·025	90% EtOH + 0·0025*M*-salt*	2·3 ± 0·3	5·8					

* Benzylpyridinium nitrate, see below.

Salt effects. Before the effect of concentration on reaction (I) was investigated, the possible influence of the resultant quaternary salt on the velocity was determined. In order to avoid introduction of unnecessary foreign ions, or of large amounts of bromide (which would reduce the accuracy of the titrations), benzylpyridinium nitrate was employed (concentration, c_s). This salt is extremely hygroscopic, but can be conveniently used as a standard solution in 90% alcohol. The results (Table II) are corrected for the solvent reaction as indicated above.

TABLE II.

Effect of added benzylpyridinium nitrate on reaction (I) *in* 90% EtOH *at* 30°.

	Concn., g.-mol./l.						
No.	c_a.	c_p.	c_s.	$k_e \times 10^4$.	$v_e \times 10^6$.	$v_p \times 10^6$.	$k_p \times 10^4$.
10	0·0125	0·0125	—	336 ± 5	5·25	2·85	183
11	0·0125	0·0125	0·0125	459 ± 26	7·17	4·67	299
12	0·025	0·025	—	323 ± 6	20·19	15·39	245
13	0·025	0·025	0·0025	339 ± 20	21·19	15·44	247

Addition of an equimolecular proportion of the salt (No. 11) causes a considerable increase in the velocity, but the increase caused by addition of only 0·1 equimolecular proportion (No. 13) is within the experimental error. Since the evaluation of the bimolecular velocity coefficient was usually restricted to the first 10—20% of the reaction, the effect of the quaternary bromide formed may, as a first approximation, be neglected. The standard conditions, for comparison of velocities, adopted throughout, however, are $c_a = c_p = c_s = 0{\cdot}0125$.

Effect of concentration. The effect of the concentration of both the benzyl bromide (c_a) and the pyridine (c_p) on the reaction velocity is summarised in Table III. The correction for the solvent reaction, with acetone as solvent, is only about 2% of the total velocity, whereas in 90% alcohol it may exceed 25% : hence the data in acetone are probably of a much greater degree of accuracy. The probable error in k_e (mean deviation from the mean) is given in each case.

TABLE III.

Effect of concentration on reaction (I) *at* 30° *in* (a) 90% EtOH (*by wt.*) ; (b) *dry* $COMe_2$.

No.	c_a.	c_p.	$k_e \times 10^4$.	$v_e \times 10^6$.	$k_p \times 10^4$.	No.	c_a.	c_p.	$k_e \times 10^4$.	$v_e \times 10^6$.	$k_p \times 10^4$.
(*a*) 10	0·0125	0·0125	336±5	5·25	(183)*	(*b*) 16	0·0122	0·0122	135±6	2·01	(127)*
12	0·025	0·025	323±6	20·19	245	17	0·025	0·025	139±3	8·66	135
14	0·025	0·50	275±9	344·4	272	18	0·025	0·125	139±3	43·46	138
15	0·050	0·050	343±9	85·75	279	19	0·025	0·250	132±3	82·74	132
						20	0·050	0·025	150±3	18·75	146
						21	0·050	0·025	150±3		

* In such dilute solutions the correction for the velocity of the solvent reaction is a large proportion of the whole, and the values of k_p are, in consequence, probably subject to rather large errors.

The essentially bimolecular character of reaction (I) would seem to be established, since with equimolar concentrations of the reactants or with a moderate excess of pyridine, the velocity is directly proportional to the product $c_a c_p$. With excess of benzyl bromide (Nos. 20, 21) the higher value of k_e suggests that under such conditions the velocity increases rather more rapidly than required by direct proportionality with the concentrations. This effect, which may be due to a resultant alteration in the nature of the medium, is being investigated more fully. For the purpose of the argument developed below, the essential feature is that, with equimolar concentrations (0·0125—0·025*M*) of the reactants, reaction (I) is a true bimolecular reaction, the velocity of which is directly proportional to the concentration of each.

Effect of unipolar substituents. The effect of the *unipolar* substituents of opposite polar types (Me, $+I$; NO_2, $-I-T$) in the para-position, on the reaction velocity under the standard conditions is given in Table IV.

TABLE IV.

Effect of p-*substituents* (R) *on the velocity of reaction* (I) *in* 90% EtOH *at* 30°.

($c_a = c_p = c_s =$ 0·0125 g.-mol./l.)

No.	R.	$k_e \times 10^4$.	$v_e \times 10^6$.	$v_s \times 10^6$.	$k_p \times 10^4$.	$(k_p)_R/(k_p)_H$.
11	H	459±26	7·17	2·5	299	(1·0)
22	Me	1422±27	22·22	10·24	958	3·2
23	NO_2	87±2·5	1·36	0·25	71	0·24
*24	NO_2	68±3	4·25	(0·5)	60·4	(0·25) †

* $c_a = c_p = 0{\cdot}025$; $c_s = 0$. † Comparison with No. 12, Table II.

Thus, under the standard conditions, the effect of the uniquely electron-repelling methyl group is to increase the velocity three-fold, whereas introduction of the uniquely electron-attracting nitro-group reduces the velocity to one-quarter.

II. *The Reaction with Alcohol.*—The velocities of interaction of the various benzyl bromides with 90% alcohol (by wt.) alone, determined primarily as solvent corrections, provide subsidiary data relative to the effect of unipolar substituents on the velocity of alcoholysis :

$$R{\cdot}C_6H_4{\cdot}CH_2Br + EtOH \longrightarrow R{\cdot}C_6H_4{\cdot}CH_2{\cdot}OEt + HBr \quad \text{(II.)}$$

Similar data have been obtained by Olivier (*Rec. trav. chim.*, 1922, **41**, 310) for the hydrolysis of various benzyl chlorides in 48% alcohol, the combined data being given in Table V.

TABLE V.

Hydrolysis of p-$R{\cdot}C_6H_4{\cdot}CH_2X$ *in aqueous alcohol at* 30°.

	X = Br.			X = Cl (Olivier).	
	$c_a = c_s =$ 0·0125 in 90% EtOH.			$c_a =$ 0·0125 in 48% EtOH.	
No.	R.	$k \times 10^4$.	k_R/k_H.	$k \times 10^4$.	k_R/k_H.
2	H	2·0 ±0·1	(1·0)	1·11	(1·0)
7	NO_2	0·21 ±0·008	0·1	0·0491	0·044
8*	NO_2	0·21 ±0·008	—	—	—
9	Me	8·19 ±0·75	4·1	10·38	9·4

* In presence of 0·0125*M*-HNO_3.

Olivier found that the reaction is unimolecular and the velocity is unaffected by hydrion concentration, conclusions which are confirmed by the present data (cf. Nos. 7 and 8). It is probable that the reaction is really a pseudo-unimolecular one, the water (or alcohol) molecules acting as a base:

$$R{\cdot}C_6H_4{\cdot}CH_2X + \text{solvent} \longrightarrow \overset{\ominus}{Br} + R{\cdot}C_6H_4{\cdot}\overset{\oplus}{C}H_{2\,\text{solvated}} \longrightarrow R{\cdot}C_6H_4{\cdot}CH_2{\cdot}OR + \overset{\oplus}{H}_{\text{solvated}},$$

the more important consideration thus being the anionisation of the bromine. The accelerating (4—9 times) effect of an electron-repelling methyl substituent and, more especially, the retarding effect (0·1—0·04) of the electron-attracting nitro-group are relatively larger in this reaction than in the definitely bimolecular reaction with pyridine.

III. *The Silver Nitrate Reaction.*—Burke and Donnan (J., 1904, **85**, 555; *Z. physikal. Chem.*, 1909, **69**, 148) have shown that the interaction of alcoholic silver nitrate with alkyl halides is represented by the simultaneous reactions:

$$\begin{cases} RBr + AgNO_3 + EtOH \longrightarrow AgBr + HNO_3 + R{\cdot}OEt & \text{(IIIA.) (70\%)} \\ RBr + AgNO_3 \longrightarrow AgBr + R{\cdot}O{\cdot}NO_2 & \text{(IIIB.)} \end{cases}$$

The *bimolecular* velocity coefficient, which remains moderately constant throughout any one experiment, is, however, increased by increasing the initial concentration of the silver nitrate, and, to a lesser extent, by decreasing that of the alkyl halide.

So far as the final products are concerned, the aryl bromide also reacts in accordance with equations (IIIA) and (IIIB) (76% in accordance with IIIA), but this reaction gives a good *unimolecular* constant throughout the whole course of the reaction; this constant, however, is also subject to vagaries similar to those observed by Burke and Donnan in the bimolecular coefficient in the corresponding reaction with alkyl halides. Moreover, the reaction is definitely and strongly catalysed by the precipitated silver bromide (cf. Senter, J., 1910, **97**, 346). This heterogeneous catalysis is being further studied in an endeavour to elucidate the reaction mechanism. The very much larger effects of the unipolar substituents (Me and NO_2) on this reaction [which, like (I) and (II), also requires anionisation of the bromine] are, however, significant.

The values of the initial velocity of the silver nitrate reaction under the standard conditions are summarised in Table VI. Whereas a *p*-methyl group only increases the velocity of the pyridine reaction 3-fold, it increases that of the silver nitrate reaction more than 60-fold. Conversely, the velocity of the reaction of *p*-nitrobenzyl bromide with

TABLE VI.

Velocity of interaction of p-$R{\cdot}C_6H_4{\cdot}CH_2Br$ *with silver nitrate in* 90% EtOH.

($c_a = c_{Ag} = c_s =$ 0·0125 g.-mol./l.)

No.	R.	Temp.	$v_e \times 10^6$.*	$(v_e)_R/(v_e)_H$.	No.	R.	Temp.	$v_e \times 10^6$.*	$(v_e)_R/(v_e)_H$.
25	H	30°	1350	1	27	Me	0°	*ca.* 8000	65
26	H	0	124	1	28	NO_2	30	26	0·02

* The relative velocity of the silver nitrate reaction is so great that the velocity of the solvent reaction falls well within the experimental error and may be neglected.

pyridine is 25% of that of the unsubstituted parent, but in the silver nitrate reaction it is only 2%.

The bimolecular character of the pyridine reaction confirms the previous suggestion (Baker, *loc. cit.*) that the formation of the final product (the quaternary bromide) involves the completion of *two* processes of opposite polar requirements, (*a*) the anionisation of the bromine, requiring electron-accession to the side chain, and (*b*) co-ordination of the unshared nitrogen electrons to the α-carbon, a process facilitated by electron-recession from the side chain. It is not considered possible to separate the energy requirements of these two processes, *i.e.*, the + *I* effect of a *p*-methyl substituent in lowering the energy potential required for the anionisation of the bromine is very largely counterbalanced by its effect in increasing the energy required for the co-ordination of the pyridine molecule, so that the resultant acceleration of the reaction velocity is relatively small. A similar, but converse, argument obviously applies to the effect of a *p*-nitro-substituent. Determination of the heats of activation of the reactions is important in this connexion, and this aspect of the problem is under investigation. The much greater effect of the same substituent groups on the velocity of the silver nitrate reaction does suggest that the anionisation of the bromine is at least an important part of whatever is being measured, even although the dynamics are complicated.

An urgent desideratum is some reaction in which the unimolecular ionisation of the halogen is definitely the *sole* process under examination, and such data may possibly be provided by the investigations on the hydrolysis of the series of aryl halides foreshadowed by Hughes and Ingold (*Nature*, 1933, **132**, 933). When the effects of unipolar substituents on the velocity of a reaction in which the sole polar requirement is electron-accession to the side chain are known, analysis of their effects on reactions of the pyridine type (involving conflicting polar requirements) may be rendered possible.

EXPERIMENTAL.

Materials.—The 90% alcohol (by wt.) was prepared by addition of the requisite weight of distilled water to carefully fractionated absolute alcohol dried over sodium. The acetone was purified through its sodium iodide compound.

The benzyl bromide was carefully fractionated in a vacuum, and each sample freshly redistilled (b. p. 85°/13 mm.) immediately before the commencement of a velocity measurement. The substituted benzyl bromides were purified as previously described (*loc. cit.*).

Benzylpyridinium nitrate. The corresponding bromide, prepared by direct addition of benzyl bromide to pyridine, was converted into the nitrate by double decomposition with an exactly equivalent quantity of aqueous silver nitrate. Evaporation of the aqueous solution gave the extremely hygroscopic nitrate (free from silver and bromide ions), which was washed with ether and dried for several weeks in a weighing bottle in a desiccator. A standard solution was prepared by quickly weighing out the salt into 90% alcohol and diluting the solution until 1 ml. contained 0·6382 g. of the salt. It was characterised as its *picrate*, m. p. 118°, after crystallisation from absolute alcohol (Found : C, 53·9; H, 3·6. $C_{18}H_{14}O_7N_4$ requires C, 54·3; H, 3·5%).

Velocity Measurements.—These were effected by titration of the bromide ion or unchanged silver nitrate by Volhard's method, 0·025*N*-solutions of ammonium thiocyanate and silver nitrate being used in the case of 0·0125*M*-solutions of the reactants, and 0·05*N*-solutions when higher concentrations were used, unchanged benzyl bromide being previously removed by extraction with ether. Only N.P.L. standard volumetric apparatus was used, under strictly standardised conditions.

The thermostat was electrically controlled, temperature variations, ± 0·02°, being observed on a Beckmann thermometer graduated in 0·01°, and the temperature of the bath being adjusted as nearly as possible to 30° as recorded on an N.P.L. standard thermometer. The experiments at 0° were conducted in a rapidly stirred bath of melting ice.

The aryl halide was weighed directly into the reaction flask, and 100 ml. of the solvent added. The second reactant (pyridine or silver nitrate) was weighed into a second flask, 10 ml. of the standard salt solution and 100 ml. of solvent added, and the solution left in the thermostat to regain the exact temperature; 100 ml. were then added to the aryl bromide solution. All solutions were sucked into pipettes at the constant thermostat temperature by suitable attachment to a filter-pump. The reaction mixture was mechanically stirred throughout.

In the pyridine and alcohol reactions, a 20 ml. sample was run into about 20 ml. of water and an equal volume of ether, and the soluble bromide, washed out by repeated extraction of the ethereal solution with water, was added to 10 ml. of the standard silver nitrate solution, acidified with halogen-free nitric acid, and the excess of silver nitrate titrated with standard ammonium thiocyanate solution from a 10 ml. burette graduated in 0·02 ml. In the silver nitrate reactions the unchanged silver nitrate, similarly freed from aryl bromide, was titrated directly with ammonium thiocyanate.

The values of the velocity coefficients given in Tables I—VI (except for the very rapid reactions) are all the mean of 6—8 concordant determinations, the mean deviation from the mean being recorded in each case.

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