428.   *The Mechanism of Aromatic Side-chain Reactions with Special Reference to the Polar Effects of Substituents. Part IV. The Mechanism of Quaternary Salt Formation.*

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Certain features of the results described in Part III (this vol., p. 519) suggested the desirability of extending the investigation of the effect of unipolar * substituents on the velocity of interaction of benzyl bromides with pyridine, and this paper records data obtained for an extended series of *p*-alkyl substituents, and for the 2 : 4-dinitro-compound. The latter was included because, in dry acetone, a single *p*-nitro-substituent had been found to exert an almost negligible retarding effect upon the reaction.† The results are summarised in Table I, which should be regarded as an extension of Table IV in Part III (*loc. cit.*), the various columns having the same significance as therein.

These additional data show that the small retarding influence of a *p*-nitro-substituent is replaced by an accelerating effect when a second nitro-group is introduced into the 2-position.   In dry acetone the velocity of interaction of the 2 : 4-dinitrobenzyl bromide with pyridine is greater even than that of the *p*-methyl compound.   Hence, in a series of sub-

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* In these papers the term " unipolar " is applied to groups, the polar effect of which is solely one either of electron-release or of electron-attraction.   The term " ambipolar " is applied to groups, *e.g.*, the halogens ($-I$, $+T$), which may permit opposing polar effects, one of electron-release, the other of electron-attraction.

† The interest attaching to this point was suggested by Professor Ingold in the course of private discussion upon the earlier results.

TABLE I.

Kinetic data for the interaction of $R \cdot C_6H_4 \cdot CH_2Br$ *with pyridine in dry acetone*
$(c_a = c_p = 0.025M)$.

R.	Temp.	$k_p \times 10^4$ (g.-mol./ l./sec.).	E. cals.	$P \times 10^6$.	$Z \times 10^{-11}$.	R.	Temp.	$k_p \times 10^4$ (g.-mol./ l./sec.).	E. cals.	$P \times 10^6$.	$Z \times 10^{-11}$.
p-Me	20°	2·020 ⎫	12,510*	1·50*	2·87	p-Buγ	20°	1·652 ⎫	12,500	1·08	3·11
p-Me	40	7·983*⎭				p-Buγ	30	3·357 ⎬			
p-Et	20	1·811 ⎫				p-Buγ	40	6·467 ⎭			
p-Et	30	3·517 ⎬	12,210	0·75	3·02	2 : 4-Me₂	20	6·287 ⎫	12,200	2·61	3·02
p-Et	40	6·733 ⎭				2 : 4-Me₂	30	12·48 ⎬			
p-Prβ	20	1·633 ⎫	12,570	1·28	3·03	2 : 4-Me₂	40	24·05 ⎭			
p-Prβ	40	6·500 ⎭				2 : 4-(NO₂)₂	20	2·288 ⎫	12,400	1·38	2·94
						2 : 4-(NO₂)₂	30	4·700 ⎬			
						2 : 4-(NO₂)₂	40	8·960 ⎭			

* Revised values from redeterminations. The value at 20° was confirmed.

stituent groups arranged in order of decreasing $+ I$ or increasing $- I$ effects, a minimum velocity is found with the *p*-nitro-compound :

$$2 : 4\text{-Me}_2 > \{p\text{-Bu}^\gamma < p\text{-Pr}^\beta < p\text{-Et} < p\text{-Me}\} > H > p\text{-NO}_2 \ll 2 : 4\text{-(NO}_2)_2$$
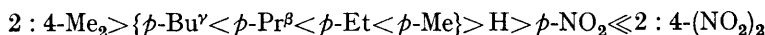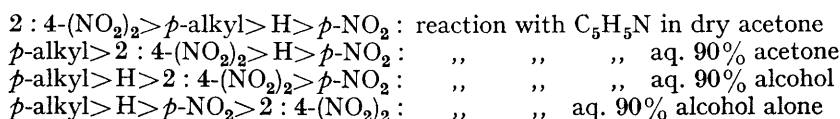
Ingold and Hughes (this vol., p. 244; with Gleave, *ibid.*, p. 236) have already noted the occurrence of a minimum velocity in such a graded polar series consequent upon a change in reaction kinetics from a bi- to a uni-molecular reaction. The position of the 2 : 4-dinitro-group in the above series now illustrates a new phenomenon, *viz.*, the occurrence of a minimum velocity in a graded polar series without change in reaction kinetics. The interaction of the 2 : 4-dinitrobenzyl bromide with pyridine is strictly bimolecular, the velocity co-efficient in dry acetone at 40° being independent of the concentration, as shown by the following data, which eliminate any suggestion that the velocity increase is due to catalysis by the highly polar dinitrobenzyl bromide (cf. *Chem. and Ind.*, 1935, **54**, 490) :

c_a	0·05	0·025	0·0125
c_p	0·025	0·025	0·025
$k_p \times 10^4$	9·07	8·96	8·91

Data previously obtained (Part III, *loc. cit.*) have shown that the relative effects of substituents on the velocity are dependent upon the solvent employed. Since it was found that the (almost negligible) retarding effect of a *p*-nitro-substituent in dry acetone is greatly increased in aqueous media, determination of the velocity of reaction of the 2 : 4-dinitro-derivative in such media is obviously important. The data obtained for the reaction between 2 : 4-dinitrobenzyl bromide and (i) pyridine in aqueous 90% acetone, (ii) pyridine in aqueous 90% alcohol, and (iii) 90% alcohol alone (the solvent reaction) are given below :

$(c_a = c_p = 0.025M.)$

Reaction.	Temp.	$k_p \times 10^4$.	
(i)	30°	5·222 ⎫	$E = 14400, P = 43.54 \times 10^{-6}$
(i)	40	11·27 ⎭	
(ii)	30	1·297	(corrected for solvent reaction, iii)
(iii)	30	0·0025	

The accelerating effect of the 2 : 4-nitro-groups observed in dry acetone is almost absent in aqueous 90% acetone ($k_p^H \times 10^4 = 10.47$ at 40°), and becomes a retarding influence in aqueous 90% alcohol ($k_p^H \times 10^4 = 3.075$ at 30°). If reaction (iii) is included, a (solvent) series is obtained in which the position of the 2 : 4-dinitro-compound gradually changes from that of maximum to that of minimum velocity :

$2 : 4\text{-(NO}_2)_2 > p\text{-alkyl} > H > p\text{-NO}_2$:	reaction with C_5H_5N in dry acetone
$p\text{-alkyl} > 2 : 4\text{-(NO}_2)_2 > H > p\text{-NO}_2$:	,, ,, ,, aq. 90% acetone
$p\text{-alkyl} > H > 2 : 4\text{-(NO}_2)_2 > p\text{-NO}_2$:	,, ,, ,, aq. 90% alcohol
$p\text{-alkyl} > H > p\text{-NO}_2 > 2 : 4\text{-(NO}_2)_2$:	,, ,, aq. 90% alcohol alone

In the following discussion of these results, alkyl substituents are considered collectively : their relative effects amongst themselves constitute a separate problem (see Part V).

The experimental results recorded in this and previous papers lead to the following conclusions. (1) The reaction between benzyl halides and tertiary bases in non-aqueous media is strictly bimolecular * and involves a simultaneous addition and dissociation denoted by the electron-cycle $C_5H_5N^b$ $Ar\!-\!{}^aBr \rightarrow C_5H_5\overset{+}{N}Ar\}\overset{-}{Br}$. (2) The Arrhenius energy of activation E is, within experimental error, unaffected by substituents and is closely related to the energy changes involved in the electron-cycle as a *whole*; it is not possible to separate the energy requirements of the two stages (a) and (b). (3) The velocity of the reaction, as affected by substituent groups in the aryl bromide, is determined mainly by some factor which is incorporated in the P term of the equation $k_p = PZe^{-E/RT}$. (4) Electron accession towards the side chain ($+ I$ effect) increases the reaction velocity; up to a point (at p-NO_2), decrease of electron-availability in the side chain decreases the velocity, but greater electron-recession [in $2 : 4$-$(NO_2)_2$] from the side chain to the nucleus reverses this effect and greatly increases the velocity.

Probably non-polar factors are also involved, but this series of investigations is concerned more especially with the polar effects of substituent groups, and under the experimental conditions employed, it is reasonable to assume that any such unknown factors have been maintained sensibly constant. Ultimately, these results will probably be best interpreted on an energetical basis (cf. Ingold, *Chem. and Ind.*, 1935, **54**, 1008), but the present state of our knowledge renders such formulation difficult. For this reason the Arrhenius equation has been adopted as the basis of discussion, and the following mechanistic picture is tentatively proposed.

Although the formation of the quaternary salt requires the completion of the electron-cycle denoted above, it is suggested that the *initiation* of this cycle may depend on either (a) the incipient anionisation of the bromine or (b) the incipient electrostriction of the tertiary base. The electronic structure of the aryl halide determines the probability of initiation by either (a) or (b). Since its electronic structure is altered by introduction of substituent groups into the aryl bromide, such substitution will alter the balance of probability of initiation of the electron-cycle by either (a) or (b). There will thus be a critical point in the structure of the aryl bromide at which occurs a transition from initiation (a) to (b) as the *major* probability. The introduction of uniquely electron-repelling alkyl groups into the unsubstituted benzyl bromide—the standard of reference—causes an increase in velocity which is greater the larger the number of suitably oriented alkyl substituents. Hence it appears that the electronic structure of the unsubstituted parent is such that initiation (a) is the more probable.† Introduction of alkyl groups merely increases this pre-existent probability. Hence the velocity of reaction is also increased by such substitution. Introduction of an electron-attracting p-nitro-group, however, so alters the electronic structure of the aryl bromide that the probability of this initiation is reduced—but not beyond the critical point—hence the reaction velocity is also reduced. Entry of a second nitro-group (into the 2-position) may now be assumed further to decrease the probability of this initiation beyond the critical point, the electronic structure of the $2 : 4$-dinitro-compound now favouring initiation (b). This will be greatly facilitated by the positive character of the α-carbon atom, induced by the now-powerful electron-attraction originating from the two nitro-groups in the o- and p-positions to the side chain, and a considerably increased reaction velocity results. Further introduction of electron-attracting groups should, therefore, continue to increase the velocity.

Such a view of the mechanism also accommodates, at least qualitatively, the observed effect of the solvent upon the reaction. Increase in the ionising power of the medium (such as presumably occurs in partly aqueous solvents) would be expected to increase the tendency of the bromide towards ionisation, *i.e.*, to alter the position of the critical point further in favour of initiation (a). In such solvents, therefore, (i) the retarding effects of electron-attracting substituents will be greater than in dry acetone, and (ii) more powerful electron-attraction will be necessary in order to reduce the probability of initiation (a)

* See p. 1844.

† The essential feature of this idea was contained in an earlier statement (Baker, J., 1932, 2634; 1933, 1129), that the benzyl bromide is " predisposed " to react by anionisation of the halogen.

beyond the critical point. Thus, in aqueous acetone, the retarding effect of a *p*-nitro-substituent is enhanced, whilst the accelerating effect of the 2 : 4-nitro-groups has almost vanished. In aqueous alcohol the position of the critical point is such that, even in the 2 : 4-dinitro-compound, initiation (*a*) is still the major probability, so that a retarding influence is observed in this medium. On the basis of this theory it would be anticipated that the effect of substituents upon velocity would be revealed mainly in the *P* term of the Arrhenius equation, a deduction in accord with experimental observations.

Such ideas, although deduced from a detailed study of only one exchange reaction, are probably of general application to all such reactions. If this be admitted, it will be observed that a logical extension of the argument must postulate an extreme case where the electronic structure of the halide and the ionising power of the medium are such that the probability of initiation (*a*) is overwhelmingly large. The reaction may then become of the unimolecular type, $Ar–Br \longrightarrow Ar^{\cdot} + Br'$ (Baker, *J.*, 1933, 1130), postulated and experimentally verified by Hughes (this vol., p. 255).*

<div align="center">EXPERIMENTAL.†</div>

Preparation of Materials.—2 : 4-*Dinitrobenzyl bromide.* Attempted nitration of *p*-nitro-benzyl bromide with a mixture of nitric (*d* 1·45) and concentrated sulphuric acids was unsatis-factory, bromine being evolved even at low temperatures. 2 : 4-Dinitrobenzyl chloride (11 g.) was therefore prepared by similar nitration of *p*-nitrobenzyl chloride (cf. Beilstein, 4th edtn., V, 344) and was converted into the bromide by refluxing with an excess of sodium bromide (12 g.) in 100 c.c. of aqueous 90% acetone for 3 hours. After evaporation of the acetone, the bromide, isolated as usual by ether extraction, and crystallised from ether–ligroin (b. p. 40—60°), had m. p. 43·5° (Found : Br, 30·2. Calc. for $C_7H_5O_4N_2Br$: Br, 30·6%). Repeated crystallis-ation from the same solvent gave a sample of constant m. p. 46·4° (Davies and Oxford, *J.*, 1931, 220, give m. p. 46—47°). With pyridine it forms 2 : 4-*dinitrobenzylpyridinium bromide*, m. p. 196° (decomp.), after crystallisation from dry methyl alcohol (Found : Br, 23·3. $C_{12}H_{10}O_4N_3Br$ requires Br, 23·5%).

p-Alkylbenzyl bromides. The corresponding chlorides were usually prepared by Sommelet's method (*Compt. rend.*, 1913, **157**, 1445), and were converted into the bromides by refluxing with an aqueous-acetone solution of sodium bromide. The following is a typical procedure. A solution of 43·4 g. of ethylbenzene (sodium-dried) and 32·2 g. of chloromethyl methyl ether in 2—3 vols. of carbon tetrachloride was cooled to − 10°, and 25·8 g. of anhydrous stannic chloride were added dropwise with rapid mechanical stirring, the temperature being maintained at − 10°. After addition was complete, stirring was continued for 1 hour, the mixture was decomposed with ice, and steam-distilled. The distillate was extracted with the distilled carbon tetra-chloride, the aqueous liquor again extracted with ether, and the combined extracts dried with calcium chloride. Fractional distillation of the residue after removal of the solvents gave 21 g. of the chloride, b. p. 100—104°/9 mm. This was refluxed with 50 g. of sodium bromide in about 50 c.c. of aqueous 90% acetone for 18 hours, the product isolated in the usual manner, and again refluxed with sodium bromide. Complete purification of the alkylbenzyl bromides by distillation alone is difficult. Repeated fractionation, using a Claisen flask with a column and a carefully controlled bath, gave a fraction of b. p. 83—85°/0·8 mm. This crystallised in a freezing mixture and was drained on porous porcelain below 0°; the molten solid was then dried in a vacuum over calcium chloride. Redistillation of the dried material gave pure *p-ethylbenzyl bromide*, b. p. 84°/0·8 mm., m. p. 14·5—15·2° (Found : Br, 40·3. $C_9H_{11}Br$ requires Br, 40·2%).

* The suggestion (Bodendorf and Böhme, *Annalen*, 1935, **516**, 1) that an intermediate, "heteropolar" form $\overset{+}{R}\overset{-}{Cl}$ may intervene in the ionic dissociation of an alkyl halide, expresses the connexion between the true bimolecular reaction which we have observed and the unimolecular reaction observed by Hughes (*loc. cit.*). Thus, as the electron-release capacity of the group R is continually increased, the true bimolecular reaction $RCl + C_5H_5N \longrightarrow$ products is replaced by the reaction sequence $RCl \underset{\text{fast}}{\overset{\longrightarrow}{}} \overset{+}{R}\overset{-}{Cl}$, and $\overset{+}{R}\overset{-}{Cl} + C_5H_5N \xrightarrow{\text{slow}}$ products, and finally by the unimolecular reaction $RCl \longrightarrow \overset{+}{R} + \overset{-}{Cl}$, followed by $\overset{+}{R} + C_5H_5N \underset{\text{instantaneous}}{\overset{\longrightarrow}{}} R\overset{+}{N}C_5H_5$. In the series of substituted benzyl halides investigated, these three stages *may* be exemplified by the *p*-NO_2, 2 : 4-Me_2, and *p*-OMe (Baker, *loc. cit.*) derivatives respectively.

† This section includes also the experimental data of Part V (following paper).

p-iso*Propylbenzyl bromide*, similarly prepared through the chloride, b. p. 108—109°/14 mm., from *iso*propylbenzene, could not be induced to crystallise, but repeated fractionation afforded a liquid, b. p. 75°/0·4 mm., which still contained a small trace of hydrocarbon impurity (Found : Br, 36·2. $C_{10}H_{13}Br$ requires Br, 37·5%).

p-tert.-*Butylbenzyl bromide* was prepared by direct bromination of *p-tert.*-butyltoluene obtained by Verley's method (*Bull. Soc. chim.*, 1898, **19**, 67). Repeated fractionation and crystallisation as above gave the bromide, b. p. 99°/0·3 mm., m. p. 15·1° (Found : Br, 35·3. $C_{11}H_{15}Br$ requires Br, 35·7%).

2 : 4-*Dimethylbenzyl bromide* was prepared from the chloride (Sommelet, *loc. cit.*) by reaction with sodium bromide. Repeated fractional distillation and crystallisation gave the pure bromide, b. p. 79°/1·2 mm., m. p. 15° (Found : Br, 40·0. $C_9H_{11}Br$ requires Br, 40·2%). It does not keep well, and this sample was used for the velocity determinations immediately after the final distillation.

Velocity Determinations.—The technique was essentially that described in Part III (*loc. cit.*), except that it was developed on the micro-scale, all quantities previously used being reduced to one-tenth of their earlier values. For instance, 10 c.c. of a $N/20$-solution of pyridine in dry acetone were mixed at the temperature of the thermostat with 10 c.c. of a similar solution of the aryl bromide, 2-c.c. samples were withdrawn, the aryl bromide removed, and the bromide ion determined by addition of 1 c.c. of $N/20$-silver nitrate, the excess of which was titrated with $N/20$-ammonium thiocyanate from a 2-c.c. microburette, graduated in 0·01 c.c. All apparatus was carefully calibrated against N.P.L. standards. Calibration of the pipettes used for making up the acetone solutions and removal of samples was carried out using this solvent, since, on the micro-scale, the volume delivered is slightly different for aqueous and for acetone solutions. A carefully standardised technique was employed throughout. The accuracy of the method was established in two ways. (1) Redeterminations of velocity constants already determined by the earlier method were consistent : *e.g.*, p-Me·C_6H_4·CH_2Br at 20°, $k_p \times 10^4 = 2·02$ (previous value 2·02) ; 2 : 4-$(NO_2)_2C_6H_3$·CH_2Br at 40°, $k_p \times 10^4 = 8·82$ (former value, 8·96). (2) When values of $x/(a - x)$ obtained in simultaneous determinations by both methods were plotted against time, all the points fell on the same straight line. The main advantage of the new method is the economy in pure acetone, the large-scale preparation of which (Part III) is expensive and tedious.

In Part III it was noted that a slight upward drift in the bimolecular velocity coefficient sometimes occurred towards the end of the reaction. This was traced to two main causes : (1) the small reaction between the acetone and the aryl bromide and (2) loss of small amounts of acetone (resulting in a slight increase in the concentration of the solution) condensed upon the stopper of the reaction flask when it was removed to take the samples. Both faults have been eliminated, the former by still further purification of the acetone, and the latter by use of special reaction tubes so constructed that the stopper could be completely immersed in the thermostat. With such improvements in technique, the bimolecular velocity coefficient remained constant over the whole reaction range.

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