Rates of Reaction of Benzylamines with 1-Chloro-2,4-dinitrobenzene and with Toluene-*p*-sulphonyl Chloride

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Rates of reaction of several 3- and 4-substituted benzylamines with 1-chloro-2,4-dinitrobenzene in azeotropic ethanol at 45° and with toluene-*p*-sulphonyl chloride in benzene at 45° have been measured.

WE recently reported the dissociation constants of substituted benzylamines.[1] Like the dissociation reaction, the reactions studied in the present work, *viz.*, reaction with 1-chloro-2,4-dinitrobenzene and with toluene-*p*-sulphonyl chloride, were expected to lead to substituent constants ($\bar{\sigma}$) in good agreement with Taft's $\bar{\sigma}^\circ$ values which measure the inductive effect of substituted phenyl groups.[2]

EXPERIMENTAL

Benzylamines.—3-Cyanobenzylamine, b. p. 112°/0·5 mm., was prepared by reaction of 3-cyanobenzyl bromide with anhydrous ammonia in an autoclave at 24°. The hydrochloride had m. p. 221° (lit.,[3] 222°). Preparation and physical constants of the other benzylamines have been described previously.[1]

Reagents.—1-Chloro-2,4-dinitrobenzene was recrystallised four times from ether, m. p. 51°. Toluene-*p*-sulphonyl chloride was recrystallised twice from ether, m. p. 69°. Benzene (AnalaR) was dried over sodium and distilled. It was then frozen and the container evacuated, flushed with nitrogen (to remove carbon dioxide), and protected with soda-lime guard tubes. Commercial ethanol (96%) was distilled from sulphuric acid (1% of 4M) to remove basic impurities. Aqueous sodium hydroxide (5% of 0·1M) was added and the ethanol fractionated through a 5-ft. column packed with helices. Immediately before use the ethanol was freed from carbon dioxide. It was cooled to −72° and the container evacuated. The ethanol, under reduced pressure in the closed flask, was allowed to come to room temperature so that the dissolved gas could escape. This process was repeated five times.

Kinetics.—Arylation reaction. An ampoule of the benzylamine was broken under 100 ml. of CO_2-free ethanol, and the solution (*ca.* 0·1M) placed in the thermostatted water-bath at 44·9°. Samples (5 ml.) of the solution were titrated with standard hydrochloric acid (Methyl Red–Bromocresol Green). A solution of 1-chloro-2,4-dinitrobenzene of exactly half the molarity of the benzylamine was prepared, and to each of three aliquot portions (20 ml.) at 44·9° benzylamine solution (20 ml.) was added. At seven intervals of 1—2 hr. a sample (5 ml.) of each reaction mixture was quenched by adding it to a known excess amount of standard hydrochloric acid, and, after allowing the precipitate to coagulate, the excess of acid was titrated with standard 0·01M-sodium hydroxide. The ethanolic solution of 4-nitrobenzylamine was prepared by adding an excess of the hydrochloride to a standard solution of sodium hydroxide in ethanol.

From the reaction

$$2ArCH_2{\cdot}NH_2 + (NO_2)_2C_6H_3Cl \longrightarrow ArCH_2{\cdot}NH{\cdot}C_6H_3(NO_2)_2 + ArCH_2{\cdot}NH_3^+Cl^-$$

and the assumption of a first-order rate-dependence on each reactant, the following rate equation may be derived:[4]

$$x/[A(A - x)] = 2kt \qquad (1)$$

where A is the initial concentration of 1-chloro-2,4-dinitrobenzene and x the concentration of product at t. Excellent linear plots of $1/(A - x)$ against t were obtained. Reactions were followed to between 50 and 70%. After about 40% reaction the *N*-(2,4-dinitrophenyl)benzylamine began to crystallise from the reaction mixture. Such crystallisation was without effect on the rate of the reaction, as judged from the linearity of the plots of $1/(A - x)$ against t. At the completion of the set of runs on each compound, the reaction mixture remaining was set aside overnight. The

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[1] L. F. Blackwell, A. Fischer, I. J. Miller, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, 1964, 3588.

[2] R. W. Taft and I. C. Lewis, *J. Amer. Chem. Soc.*, 1959, **81**, 5343; R. W. Taft, *J. Phys. Chem.*, 1960, **64**, 1805.

[3] F. Ehrlich, *Ber.*, 1901, **34**, 3367.

[4] J. J. Blanksma and H. H. Schreinmachers, *Rec. Trav. chim.*, 1933, **52**, 428.

precipitate (yellow needles) was then filtered off, washed with water to remove traces of reaction solution and amine salt product, dried, and analysed. When two sets of three runs on 4-nitrobenzylamine were carried out using independent solutions of amine and 1-chloro-2,4-dinitrobenzene, the mean rate constants for each set differed by less than 0·5%.

TABLE 1

Melting points and analyses for *N*-(X-benzyl)-2,4-dinitroanilines

X	M. p.	C	H	N	C	H	N
H[a]	113·5°	57·4	4·3	15·0	57·2	4·0	15·4
3-Br ...	124[b]	22·2[c]		11·3	22·8[c]		11·9
4-Br ...	159	22·8[c]		11·7	22·8[c]		11·9
3-Cl......	131	11·8[d]		—	11·5[d]		—
4-Cl......	146·5	50·9	3·9	—	50·8	3·3	—
3-CN ...	147	56·6	3·4	18·6	56·4	3·4	18·8
4-CN ...	196	56·5	3·6	18·3	56·4	3·4	18·8
3-F ...	129	53·7	3·7	14·0	53·5	3·4	14·4
4-F ...	147	—	—	14·5	—	—	14·4
3-OMe	126	—	—	13·6	—	—	13·9
4-OMe	95·5	55·6	4·4	14·0	55·5	4·3	13·9
3-Me ...	117·5	—	—	14·3	—	—	14·7
4-Me ...	109	—	—	14·9	—	—	14·7
3-NO_2	169	—	—	17·5	—	—	17·6
4-NO_2	187	48·9	3·5	17·1	49·2	3·2	17·6

[a] M. p. 116°.[5] [b] A second crystalline form (hexagonal) had m. p. 112°. [c] % Br. [d] % Cl.

Sulphonamide formation. An ampoule of the purified amine was broken under 100 ml. of CO_2-free benzene. Aliquot portions of this solution (2 ml.) were added to acetic acid and titrated with standard perchloric acid (0·02M) in acetic acid using Crystal Violet indicator. A solution of toluene-*p*-sulphonyl chloride of exactly half the molarity of the amine solution was prepared and brought to 44·9°. To each of three 25-ml. aliquots of the toluene-*p*-sulphonyl chloride solution, 25 ml. of the amine solutions, also at 44·9° were added. At intervals, 5-ml. samples of each reaction mixture were withdrawn, using pipettes fitted with glass-wool filters to prevent the ingress of precipitated amine salt, added to acetic acid (10 ml.) to quench the reaction, and the unreacted amine titrated with standard perchloric acid. The analytical method was checked by preparing accurately by weight a standard solution of benzylamine in benzene and determining the concentration by perchloric acid titration, and also by adding an excess of standard hydrochloric acid and back-titrating with standard sodium hydroxide. The concentrations obtained by the three methods agreed to ±0·2%.

From the reaction

$$2ArCH_2{\cdot}NH_2 + Cl{\cdot}SO_2{\cdot}C_6H_4{\cdot}CH_3 \longrightarrow ArCH_2{\cdot}NH{\cdot}SO_2{\cdot}C_6H_4{\cdot}CH_3 + ArCH_2{\cdot}NH_3{}^+Cl^-$$

and the assumption of a first-order rate-dependence on each reactant, rate equation (1) may be derived, where A is now the initial concentration of toluene-*p*-sulphonyl chloride. Most of the rate plots $1/(A - x)$ against t showed increasing curvature after 15% reaction. This was also the stage at which precipitation of amine salt became apparent, and it is possible that the precipitated salt acts as a catalyst for the reaction. Rate constants were therefore extracted from the initial slopes of the run plots, and are subject to substantial errors. The rate acceleration was not caused by incursion of side-reactions. In a few cases the identity of the products was confirmed. The precipitate was filtered off from the reaction mixture and its m. p. determined. The benzene filtrate was evaporated to dryness and the residue recrystallised from 60% ethanol. The precipitate from reaction of 3-chlorobenzylamine had m. p. 227° (3-chlorobenzylamine hydrochloride, m. p.[6] 225°) and the recrystallised residue, N-(3-*chlorobenzyl*)*toluene*-p-*sulphonamide*, white needles, m. p. 82° (Found: N, 4·6. $C_{14}H_{14}ClNO_2S$ requires N, 4·8%). The precipitate from reaction of 4-chlorobenzylamine had m. p. 262° (4-chlorobenzylamine hydrochloride, m. p.[7] 261·5°) and the recrystallised residue, N-(4-*chlorobenzyl*)*toluene*-p-*sulphonamide*, white needles, m. p. 105·5° (Found: N, 4·4%). The precipitate from reaction of 3-fluorobenzylamine had m. p. 272° (3-fluorobenzylamine hydrochloride, m. p.[8] 268°), and the recrystallised residue white needles, m. p. 87°. The precipitate from reaction of 4-fluorobenzylamine had m. p. 257° (4-fluorobenzylamine hydrochloride, m. p.[9] 268°), and the recrystallised residue white needles, m. p. 103·5°. All four sulphonamide products exhibited medium to strong i.r. absorption in the 7·3—7·7 and 8·5—8·8 μ regions, characteristic of sulphonamides.[10]

RESULTS AND DISCUSSION

Rate constants for reaction of benzylamines with 1-chloro-2,4-dinitrobenzene in azeotropic ethanol and initial rate constants for reaction with toluene-*p*-sulphonyl chloride in benzene are shown in Table 2. For reaction with 1-chloro-2,4-dinitrobenzene, rate constants are estimated to be accurate to ±3%, but for reaction with toluenesulphonyl chlorides errors may be as much as ±30%.

TABLE 2

Rate constants (l. mole^{-1} sec.$^{-1}$) for reaction at 45° of X-benzylamines with 1-chloro-2,4-dinitrobenzene in azeotropic ethanol (k'), and with toluene-*p*-sulphonyl chloride in benzene (k'')

X	$10^4k'$	$10^4k''$	σ
H	18·8	14	0·00
3-Br	9·3	4	+0·40
4-Br	11·6	4	+0·27
3-Cl	10·1	4	+0·35
4-Cl	11·0	4	+0·30
3-CN...........	6·4	2	+0·61
4-CN...........	5·9	0·5	+0·66
3-F	9·7	4	+0·37
4-F	14·4	8	+0·15
3-OMe	17·3	30	+0·04
4-OMe	25·4	30	−0·17
3-Me	22·8	19	−0·11
4-Me	23·3	40	−0·12
3-NO_2	5·6	2	+0·69
4-NO_2	5·4	—	+0·71

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[5] N. M. Cullinane, O. E. Embrey, and D. R. Davies, *J. Chem. Soc.*, 1932, 2363.

[6] J. v. Braun, M. Kühn, and J. Weismantel, *Annalen*, 1926, **449**, 249.

[7] K. Kindler, *Arch. Pharm.*, 1927, **265**, 389.

[8] L. F. Blackwell, Thesis, University of New Zealand, 1962.

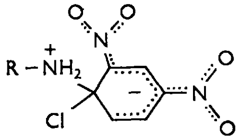
[9] S. Saijo, *J. Pharm. Soc. Japan*, 1952, **72**, 1009.

[10] L. J. Bellamy, "The Infra-Red Spectra of Complex Molecules," Methuen, London, 1958, p. 363.

Following the procedure recommended by Taft and Lewis,[2] a regression line was fitted to the log k' against σ° data for the *meta*-substituted aryl groups containing the substituents H, Br, Cl, F, Me, NO_2: slope (ρ) $= -0{\cdot}786$; correlation coefficient (r) $= 0{\cdot}997$; intercept with the ordinate ($\log k'_0$) $= \bar{3}{\cdot}283$. Effective substituent constants ($\bar{\sigma}$) were then evaluated from the relationship $\bar{\sigma} = (\bar{3}{\cdot}283 - \log k')/0{\cdot}786$ for the fifteen substituted aryl groups. For the phenyl group and the 3-Br-, 4-Br-, 3-Cl-, 4-Cl-, 3-CN-, 3-F-, 4-F-, 3-Me-, 4-Me-, and 3-NO_2-phenyl groups, $\bar{\sigma}$ values did not deviate by more than $\pm 0{\cdot}04$ from the σ° values of Taft. Accordingly, a regression line was fitted to the log k' against σ° data for these aryl groups: $\rho = -0{\cdot}762$; $r = 0{\cdot}996$; standard deviation (s) $= 0{\cdot}019$; $s_{\rho} = 0{\cdot}023$; $\log k'_0 = \bar{3}{\cdot}272$. $\bar{\sigma}$ Values calculated from this regression line are shown in Table 2. The data for the 4-CN-, 3-OMe-, 4-OMe-, and 4-NO_2-benzylamines were not used in fitting the regression line because σ° values for the substituted phenyl groups are solvent-dependent. With a single exception, $\bar{\sigma}$ values for the other eleven substituted phenyl groups do not differ from σ° values by more than the standard deviation of the latter ($\pm 0{\cdot}03$). For *m*-tolyl the difference is 0·04. Thus, the present results provide further support for the generality and precision of Taft's σ° values.

For the substituents with solvent-dependent σ° values, $\bar{\sigma}$ values are more negative than the σ° values listed for pure aqueous solution. For the *m*- and *p*-anisyl and *p*-cyanophenyl substituents, $\bar{\sigma}$ values agree with the σ° values, for mixed aqueous organic solvents, within the precision of the latter. The $\bar{\sigma}$ value for *p*-nitrophenyl is 0·11 units lower than the σ° value for pure aqueous and mixed aqueous organic solvents, and is not significantly different from that for non-hydroxylic solvents.

The ratio of ρ(benzylamines) to ρ(anilines)[11] for 2,4-dinitrophenylation is $0{\cdot}76 : 3{\cdot}06 = 1 : 4$. The attenuation resulting from the introduction of the methylene group is much larger than the 1/2·8 factor for dissociation of the protonated amines.[1] This suggests that the nitrogen atom carries relatively less positive charge in the transition state for 2,4-dinitrophenylation of benzylamine than in the transition state for 2,4-dinitrophenylation of aniline. This conclusion can also be deduced from Hammond's postulate.[12] The mechanism of the 2,4-dinitrophenylation reaction should involve rate-determining intermediate complex (I) formation.[13]



(I)

Because of the greater basicity of benzylamine, its intermediate complex should be more stable, relative to the reactants, than that of aniline. The transition state for the aniline reaction will then resemble the corresponding intermediate complex more closely than does the transition state for the benzylamine reaction, a proposition which is an extension of Hammond's postulate. Hence, the aniline transition state should involve greater charge separation.

A regression line was fitted to the log k'' against σ° data for sulphonamide formation. $\rho = -1{\cdot}77$, $r = 0{\cdot}955$, $s = 0{\cdot}16$, $s_{\rho} = 0{\cdot}16$. Rate constants for sulphonamide formation are too inaccurate for any significance to be attached to the deviations of individual points from the Hammett plot. However, the slope of the plot indicates that the reaction is facilitated by electron accession from the aryl group of the benzylamine to the reaction site, and that the reaction is quite sensitive to the inductive effect of the aryl group. Sulphonamide formation is much more sensitive to these inductive effects than is the arylation reaction. At least part of this increase in susceptibility to electronic effects is to be attributed to the solvent change from ethanol for arylation to benzene for sulphonamide formation. In ethanol the charges separated at the transition state can be partly dispersed through solvation, and there is effectively less positive charge localised on the nitrogen atom than in benzene where solvation is much less efficient. For similar reasons, ρ for ion-pair formation of benzoic acids with 1,3-diphenylguanidine in benzene (2·24)[14] is greater than ρ for dissociation of benzoic acids in ethanol (1·89).[11]

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[11] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[12] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.

[13] J. F. Bunnett, *Quart. Rev.*, 1958, **12**, 1.

[14] M. M. Davis and H. B. Hetzer, *J. Res. Nat. Bur. Stand.*, 1958, **60**, 569.