247. *Steric Inhibition of Resonance. Part III. The Basic Strengths of Some Dimethyl-substituted Aromatic Primary and Tertiary Amines.*

By George Thomson.

The pK_a values of a series of methyl-substituted anilines and dimethylanilines have been measured at 25° in aqueous-alcoholic solution. Dimethyl-*m*-2-xylidine is found to differ little in strength from dimethyl-*m*-5-xylidine in such solutions. Doubt is expressed as to whether resonance plays so large a part as has been attributed to it in determining the strength of aromatic tertiary bases.

The value of the molecular refractivity of dimethyl-*p*-xylidine is found to be in accordance with views expressed in Part II of this series (*J.*, 1944, 408).

It has been suggested (Baddeley, *Nature*, 1939, **144**, 444; Branch and Calvin, "The Theory of Organic Chemistry," New York, 1941, 260; Wheland, "The Theory of Resonance," New York 1944, 189) that the higher basicity of dimethyl-*o*-toluidine than of its *m*- and *p*-isomerides (Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469; Davies and Addis, *J.*, 1937, 1622) is due to steric inhibition by the *o*-methyl substituent of the resonance of the dimethylamino-group with the benzene nucleus. If this explanation is well founded, intro-

duction of a second methyl group ortho to the dimethylamino-group would be expected to result in a considerable increase in basic strength: Hampson and Ingham (*J.*, 1939, 981) have shown from dipole-moment measurements that in dimethylmesidine and nitrodimethylaminodurene resonance of the dimethylamino-group with the benzene nucleus is almost completely suppressed, and in Part II of this series (*loc. cit.*) it was shown that the atomic refractivity of the nitrogen atom in *N*-dimethyl-*m*-2-xylidine approximates to that observed in aliphatic tertiary amines. But Davies and Addis (*loc. cit.*) found that in 50% aqueous alcohol at 20° dimethylmesidine (pK_a* 5·15) was only a slightly stronger base than dimethyl-*o*-toluidine (pK_a 5·07). It was therefore decided to measure the basic strengths of some *N*-dimethylxylidines and of the parent xylidines; for comparison, measurements were made under similar conditions on aniline, dimethylaniline, *o*-toluidine, and dimethyl-*o*-toluidine. The method adopted was measurement of the pH values of a series of mixtures of base and standard hydrochloric acid solution, a glass electrode being used with a saturated potassium chloride–calomel half-cell as reference electrode. Because of the low solubility in water of the tertiary amines, solutions in 50% and in 75% aqueous ethyl alcohol were used and, in view of uncertainty as to the value of K_w in those alcoholic solutions, the results are expressed as pK_a for the conjugate acids (calculated by means of the simple Henderson equation $pK_a = pH + \log [salt]/[base]$).

Discussion of Results.—The results are summarised in Table I. All measurements are at 25°.

TABLE I.

	In 50% alcohol. Mean p*K*.	In 75% alcohol. Mean p*K*.		In 50% alcohol. Mean p*K*.	In 75% alcohol. Mean p*K*.
Aniline	4·25	3·98	Dimethylaniline	4·26	3·84
o-Toluidine	3·98	—	Dimethyl-*o*-toluidine	5·07	4·47
m-2-Xylidine	3·42	3·19	Dimethyl-*m*-2-xylidine	4·69	4·26
m-4-Xylidine	4·61	4·35	Dimethyl-*m*-4-xylidine	5·28	4·76
m-5-Xylidine	4·48	4·30	Dimethyl-*m*-5-xylidine	4·48	4·11
p-Xylidine	4·17	4·00	Dimethyl-*p*-xylidine	5·19	4·62

The pK_a value (4·26) found for dimethylaniline in 50% alcohol is a little higher than would be expected from Davies and Addis's value (*loc. cit.*) (4·21 at 20°), since Hall and Sprinkle (*loc. cit.*) found the temperature coefficient of pK_a to be negative; the same is true of the value found for dimethyl-*o*-toluidine, which is identical with that found by Davies and Addis (*loc. cit.*). These differences, however, are not serious and may possibly be due to slight differences in the solvents. Change of solvent from 50% to 75% alcohol affects the pK_a values for the primary amines much less than those for the tertiary amines; if the pK_a values are plotted against vol.-% of alcohol and the points for each substance are joined by straight lines, it is found that the slopes of the lines for the tertiary amines are all similar but steeper than those for the primary amines, which in turn are similar (cf. Wynne-Jones, *Proc. Roy. Soc.*, 1933, *A*, **140**, 440). The relative pK_a values for the primary bases in the two solvents are closely parallel: the ratio pK_a xylidine/pK_a aniline which varies from xylidine to xylidine has for any given xylidine much the same value (within 2—3%) in 50% alcohol and in 75% alcohol, and the same holds true for the tertiary bases (taking for them the ratio pK_a tertiary amine/pK_a dimethylaniline). It will be noticed that dimethylaniline, which in aqueous solution is a stronger base than aniline (Hall, *J. Amer. Chem. Soc.*, 1930, **52**, 5115; Hall and Sprinkle, *loc. cit.*), appears in 50% alcohol to be identical in strength with aniline but in 75% alcohol to be weaker; also that dimethyl-*m*-5-xylidine in 50% alcohol appears identical in strength with *m*-5-xylidine whereas the latter is the stronger in 75% alcohol. It would, therefore, appear valid to compare among themselves basic strengths of nuclear-substituted anilines or nuclear-substituted dimethylanilines in any one solvent [cf. Bennett, Brooks, and Glasstone (*J.*, 1935, 1821), who concluded that " the strength of a series of acids or bases *of the same type* should be in the same order in all solvents provided there be no complicating side reactions of a purely chemical nature "]; on the other hand, arguments based on comparisons between basic strengths of primary and tertiary amines seem of questionable validity in view of the uncertainty that the dissociation constant of the base in any solvent—even in water—is a true measure of the intrinsic strength of the base, that is, of its tendency to gain a proton.

From the data in Table I it is evident that introduction into dimethylaniline of one methyl group in the *o*-position results in an increase of pK_a but that introduction of a second methyl group in the other *o*-position as in dimethyl-*m*-2-xylidine results, not in a further increase, but in a decided decrease in pK_a; introduction of the second nuclear methyl group para to the dimethylamino-group as in dimethyl-*m*-4-xylidine, or meta to the dimethylamino-group and para to the first nuclear methyl group as in dimethyl-*p*-xylidine, results in an increase of pK_a, slightly greater in the first case than in the second but in each case of the same order of magnitude as the decrease resulting from the introduction of the second methyl group in the *o*-position.

Further, the astonishing fact emerges that dimethyl-*m*-5-xylidine, in which both nuclear methyl groups are meta to the dimethylamino-group and no question of steric inhibition of resonance can arise, does not have a pK_a value widely different from that of dimethyl-*m*-2-xylidine. The evidence of other properties suggests that there can be little doubt that substitution of two methyl groups ortho to a dimethylamino-group does almost completely suppress resonance between that group and the benzene nucleus, but the closeness of the values of pK_a for dimethyl-*m*-2- and -*m*-5-xylidine raises doubt whether resonance plays so large a part as has been

* Throughout this paper bases are compared by reference to the pK_a values for their conjugate acids.

attributed to it in determining the strength of aromatic tertiary bases: if it did, one would expect a difference of at least 3 or 4 logarithmic units (*i.e.*, a difference approaching in magnitude the difference in pK_a between an aromatic and an aliphatic tertiary base) instead of the observed difference of less than 0·3 logarithmic unit. Doubt is strengthened by the data of Table II.

TABLE II.

	pK_a.		pK_a.
o-Toluidine	4·39 *	*o*-Anisidine	4·49 *
p-Toluidine	5·12 *	*p*-Anisidine	5·29 *
Dimethyl-*o*-toluidine	5·86 *	Dimethyl-*o*-toluidine	5·07 †
Dimethyl-*p*-toluidine	5·50 *	Dimethyl-*p*-toluidine	4·77 †
Diethyl-*o*-toluidine	7·18 *	Dimethyl-*o*-anisidine	5·49 †
Diethyl-*p*-toluidine	7·09 *	Dimethyl-*p*-anisidine	5·16 †

* In water at 25° (Hall and Sprinkle, *loc. cit.*).
† In 50% alcohol at 20° (Davies and Addis, *loc. cit.*).

o-Anisidine has a pK_a value comparable with that for *o*-toluidine, yet the pK_a value for dimethyl-*o*-anisidine exceeds that for dimethyl-*o*-toluidine by rather more than the amount by which the pK_a value for the latter exceeds that for dimethyl-*p*-toluidine; the latter difference has been attributed to inhibition of resonance in dimethyl-*o*-toluidine. The enhanced basicity of dimethyl-*o*-anisidine can hardly be attributed to the steric effect of the methoxyl group, an effect which has been shown to be considerably less than that of methyl [cf., *e.g.*, the work of Adams and his co-workers (*J. Amer. Chem. Soc.*, 1940, **62**, 2191; 1941, **63**, 2859) on restricted rotation in arylamines]. It appears significant also that the difference in pK_a between diethyl-*o*- and -*p*-toluidine should be so much smaller than that between the corresponding dimethyl compounds; greater steric incompatibility would be expected between the diethylamino-group and an *o*-methyl group than between the dimethylamino-group and an *o*-methyl group.

The nuclear methyl-substituted anilines present a marked contrast to the dimethylanilines: introduction of *o*-methyl groups leads to a progressive reduction of pK_a, and we have aniline > *o*-toluidine > *m*-2-xylidine, whereas in the *N*-dimethyl derivatives the order is dimethyl-*o*-toluidine > dimethyl-*m*-2-xylidine > dimethylaniline.

Further work on disubstituted aromatic bases is in progress.

Note on the Molecular Refractivity of Dimethyl-p-*xylidine.*—The molecular refractivity of dimethyl-*p*-xylidine for sodium yellow is found to be 49·61 c.c. Landolt and Jahn (*Z. physikal. Chem.*, 1892, **10**, 289) found for *p*-xylene $[R_L]_D$ 35·95 c.c. The difference, 13·66 c.c., is in close agreement with the difference, 13·62 c.c., between dimethyl-*m*-4-xylidine and *m*-xylene recorded in Part II of this series (*loc. cit.*) and corroborates the conclusion there reached that, whenever methyl or chlorine is substituted ortho to the dimethylamino-group, the group refraction of the latter group suffers a reduction of approximately 1 c.c.

EXPERIMENTAL.

The specimens of dimethylaniline, *m*-2- and *m*-4-xylidines and their *N*-dimethyl derivatives, and *N*-dimethyl-*m*-5-xylidine were those used in the work described in Part II (*loc. cit.*). They were redistilled before use. *m*-5-Xylidine was a fresh specimen prepared by Haller and Adams's method (*J. Amer. Chem. Soc.*, 1920, **42**, 1840). Aniline was prepared by hydrolysis of a pure specimen of acetanilide. *p*-Xylidine, prepared from the hydrochloride (Eastman Kodak Company), had b. p. 215·4°/749 mm., $d_4^{25°}$ 0·97140, $n_D^{25°}$ 1·55752, $n_{5461}^{25°}$ 1·56282; $[R_L]_D$ is therefore 40·13 (Brühl, *Z. physikal. Chem.*, 1895, **16**, 193, gives 39·95). *N*-Dimethyl-*p*-xylidine, prepared by methylation with methyl sulphate (Evans and Williams, *J.*, 1939, 1199), had b. p. 202—202·2°/756 mm., $d_4^{25°}$ 0·91406, $n_D^{25°}$ 1·52073, $n_{5461}^{25°}$ 1·52503, whence $[R_L]_D$ 49·61, $[R_L]_{5461}$ 49·95 (Brown, Widiger, and Letang, *J. Amer. Chem. Soc.*, 1939, **61**, 2597, give b. p. 199°/745 mm., $n_D^{20°}$ 1·5223). Dimethyl-*o*-toluidine (B.D.H.) was treated with *p*-toluenesulphonyl chloride to remove any primary or secondary base; it had b. p. 183·4°/757 mm. *o*-Toluidine (from aceto-*o*-toluidide) had b. p. 199°/759 mm.

pH values were measured by using a Marconi–Ekco pH meter.

Solutions were prepared as follows: in " 50% alcohol " by dissolving *w* g. of base in rather less than 50 ml. of ethyl alcohol, adding 50 ml. of 0·01N-aqueous hydrochloric acid, and making the volume up to 100 ml. with ethyl alcohol in a standard flask; in " 75% alcohol " by a similar procedure but using only 25 ml. of 0·01N-acid.

50% Alcohol.			75% Alcohol.		
w.	pH.	p*K.*	*w.*	pH.	p*K.*
Dimethylaniline.					
0·3378	4·79	4·24	0·1709	4·43	3·87
0·2581	4·56	4·27	0·2580	4·64	3·87
	Mean	4·26	0·1771	4·45	3·88
				Mean	3·87
Dimethyl-*m*-2-xylidine.					
0·1188	4·43	4·66	0·1993	4·86	4·22
0·0827	3·78	4·74	0·1125	4·56	4·26
0·1133	4·40	4·68	0·0807	4·35	4·28
0·1102	4·36	4·68	0·1608	4·81	4·29
	Mean	4·69	0·1098	4·55	4·25
				Mean	4·26

50% Alcohol.			75% Alcohol.		
w.	pH.	p*K.*	*w.*	pH.	p*K.*
Dimethyl-*m*-4-xylidine.					
0·0989	4·78	5·27	0·1700	5·35	4·80
0·1143	5·02	5·29	0·1184	5·08	4·74
0·0979	4·76	5·26	0·0976	4·95	4·74
0·1481	5·30	5·30	0·1811	5·31	4·72
	Mean	5·28	0·1365	5·22	4·80
			0·0987	5·00	4·78
				Mean	4·76
Dimethyl-*m*-5-xylidine.					
0·1273	4·32	4·47	0·1500	4·59	4·11
0·1093	4·14	4·47	0·1654	4·62	4·08
0·1456	4·43	4·45	0·1078	4·40	4·12
	Mean	4·46	0·0732	4·11	4·12
			0·2196	4·83	4·14
				Mean	4·11

50% Alcohol.			75% Alcohol.		
w.	pH.	p*K*.	*w.*	pH.	p*K*.
		Dimethyl-*p*-xylidine.			
0·1938	5·40	5·18	0·3100	5·47	4·61
0·1184	4·97	5·19	0·2507	5·37	4·61
0·1714	5·30	5·19	0·1701	5·18	4·63
0·0998	4·73	5·20	0·1393	5·07	4·63
	Mean	5·19		Mean	4·62
		Dimethyl-*o*-toluidine.			
0·2980	5·58	5·05	0·2610	5·30	4·47
0·4615	5·85	5·08	0·3929	5·52	4·49
0·2097	5·39	5·07	0·4994	5·60	4·46
0·4199	5·79	5·07	0·5850	5·67	4·46
	Mean	5·07		Mean	4·47
		Aniline.			
0·3758	5·11	4·26	0·2968	5·03	3·98
0·2987	4·95	4·24	0·4134	5·20	3·98
0·5212	5·28	4·27	0·2357	4·95	3·99
	Mean	4·26		Mean	3·98
		m-2-Xylidine.			
0·2185	3·82	3·40	0·1717	3·84	3·17
0·2612	3·95	3·43	0·2351	4·06	3·23
0·3045	4·00	3·40	0·3293	4·20	3·21
0·3801	4·15	3·43	0·2123	3·92	3·14
	Mean	3·42		Mean	3·19

50% Alcohol.			75% Alcohol.		
w.	pH.	p*K*.	*w.*	pH.	p*K*.
		m-4-Xylidine.			
0·2486	5·09	4·60	0·2612	5·25	4·37
0·3393	5·27	4·61	0·2154	5·12	4·33
	Mean	4·61	0·3267	5·25	4·36
				Mean	4·35
		m-5-Xylidine.			
0·2988	5·07	4·47	0·2335	5·12	4·29
0·4401	5·28	4·48	0·3825	5·39	4·32
0·2116	4·90	4·50	0·5297	5·52	4·30
	Mean	4·48		Mean	4·30
		p-Xylidine.			
0·2569	4·70	4·19	0·3811	5·07	4·01
0·2943	4·76	4·17	0·3208	4·97	3·99
0·3637	4·85	4·15		Mean	4·00
0·5342	5·06	4·17			
	Mean	4·17			
		o-Toluidine.			
0·4531	4·85	3·98			
0·5249	4·92	3·97			
0·2241	4·48	3·98			
	Mean	3·98			

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