and chloroacetate buffers for the range 2.0 to 3.5. The ionic strength was maintained constant at 0.02 *M* by addition of sodium chloride, the final concentration of the amine being 0.001 *M*. Spectral absorption curves were determined with a Cary recording spectrophotometer (model 11), the ratio RNH_3^+/RNH_2 being determined at intervals of 5 mμ over suitable regions of the absorption curves, and the cell compartment being held at 25 ± 0.2°. *p*H measurements of the buffer solutions were determined with a Cambridge *p*H meter, the glass electrode being initially tested for linearity, and calibrated with a saturated solution of potassium hydrogen tartrate (3.57). Readings were taken on the buffer solutions at 25° before and after the spectrophotometric measurements with repeated recalibrations.

Precision of pK_a Results.—In this paper relating to substituted anilines, and in subsequent papers dealing with substituted naphthylamines and heterocyclic bases, the technique of pK_a measurement was standarized, and an estimate of the precision can be made from consideration of the equation used, *viz.*, $pK_a = pH + \log RNH_3^+/RNH_2$. The quantity $\log RNH_3^+/RNH_2$ was obtained from the relation $RNH_3^+/RNH_2 = (A_b - A/(A - A_a)$ where A_a, A_b and A are the absorbances of the acid, base and buffered solutions. Matched 1-cm. cells were used, the blank differing from the absorbing solution only in the absence of amine. Spectrophotometric measurements were taken in the range 250–400 mμ in which for most systems there is at least one isobestic point, and in which absorbances of the acid species are frequently negligible. In the case of aniline the values of $\log RNH_3^+/RNH_2$ for the buffers 4.74 and 4.25 were $-0.07_7 \pm 0.005$ and $0.40_0 \pm 0.009$ (10 results) giving pK_a values of 4.66 and 4.65. With a correction of −0.06 for ionic strength, the figure of 4.59_5 is obtained with a precision which, allowing ±0.02 for the *p*H measurements and ±0.01 for the log ratios, may be given as within ±0.03 unit. Measurements were rejected unless log ratios were consistent and pK_a values were within 0.03.

Infrared measurements were made with a Perkin–Elmer model 112 recording infrared spectrophotometer using a LiF prism. Spectra were determined in approximately 0.005 *M* solutions of the amines in dried and freshly distilled carbon tetrachloride, gaseous ammonia spectra being interpolated between the records of successive amines. Assignment of frequencies was made by reference to the ammonia bands 3396 and 3472 cm.$^{-1}$, the accuracy being considered to be ±1 cm.$^{-1}$.

Acknowledgments.—The author is indebted to Mr. I. Reece for taking the ultraviolet and infrared spectral absorption curves, and to Drs. M. S. Carpenter, B. M. Wepster and Messrs. Light and Co. for gifts of chemicals.

Appendix.—The probability that the sets of data for the −M and +M groups of substituents lie on separate regression lines can be determined by evaluating the variance ratio $F = s^2_{a+b}/s^2$ where s^2 is the residual variance for all 16 substituents with 14 degrees of freedom, and s^2_{a+b} is the combined residual variance of the two separate groups calculated from the equation

$$s^2_{a+b} = \frac{6s^2_a + 4s^2_b}{10}$$

where the number of degrees of freedom is 10. The residual variances are calculated by the equation

$$s^2 = \frac{(I - r^2)\ \Sigma(\Delta pK_a)^2 - \dfrac{(\Sigma\Delta pK)^2}{n}}{n - 2}$$

r being the correlation coefficient and *n* the sample number.[20] Values of 0.00277 and 0.00409 for s^2 and s^2_{a+b} give $F_{10,14} = s_{a+b}/s^2 = 1.5$ corresponding to a significance level of about 0.25. Such a high level indicates that there is little difference between the probabilities of the ΔpK_a values lying on a single line or being accommodated on two separate lines.

(20) K. A. Brownlee, "Industrial Experimentation," H. M. Stationary Office, London, pp. 32, 59. C. A. Bennett and N. L. Franklin, "Statistical Analysis in Chemistry and the Chemical Industry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 223.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF NEW SOUTH WALES, SYDNEY, AUSTRALIA]

The Effects of Substituents on the pK_a Values and N–H Stretching Frequencies of 1- and 2-Naphthylamines

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The pK_a values and N–H stretching frequencies of 44 naphthylamines substituted in various ring positions by the groups NO_2, CN, $COOCH_3$, Cl, Br, I, OH, OCH_3 and NH_2 have been measured, interest being devoted chiefly to the compounds in which the groups are in non-quinonoid positions. The results reveal characteristic differences between the effects of substituents in *m*-substituted anilines, 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines, the most noteworthy feature being shown by the 3-substituted 1-naphthylamines where substituents group themselves into two classes depending on their mesomeric +M or −M characteristics. Similar but smaller effects are observable in the 4-substituted 2-naphthylamines. The σ-values derived satisfy equations of the type $\sigma = a\sigma_I + b\sigma_R$ where σ_I and σ_R are the Taft constants, and the extent of the polar and mesomeric contributions to the substituent effect in *m*-anilines, 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines can be inferred, and the observed behavior explained. An attempt is made to correlate the results with electronic structure. Relations for compounds with the substituents in the second ring are less clearly defined, but the distinction between the 7-substituted 1-naphthylamines and the 5-substituted 1-naphthylamines is interpreted to indicate smaller intergroup conjugation in the latter. Unexpected relations are shown between pK_a values and N–H frequencies, these being characterized by the non-conformity of the parent amines with the lines given by the various positional series.

Previous communications[1] have described the effects of the groups NO_2 and SO_3^- on the pK_a values of 1- and 2-naphthylamines substituted in the available ring positions, and a tentative interpretation has been offered[2] for these effects in terms of structural changes in the base components of the systems. This theory as applied to the 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines, for instance, assumed that the inductive effect of the substituent NO_2 on the NH_3^+ pole of the acid was the same as in the similarly constituted *m*-nitroaniline, and that the burden of changes in substitutional effects lay in influences affecting the delocalization of the electrons in the

(1) A. Bryson, *Trans. Faraday Soc.*, **45**, 257 (1949); **47**, 522 (1951).

(2) A. Bryson, *ibid.*, **47**, 528 (1951).

amino group of the base. It was clear that this contention could only be maintained on much more experimental evidence, and a more systematic investigation therefore has been carried out, using in addition to the NO_2 group, the substituents Cl, Br, I, OH, OCH_3, CN, $COOCH_3$, CH_3 and NH_2 placed at suitable ring positions. The pK_a values and N–H stretching frequencies of these substituted naphthylamines have been measured, and it is now possible to compare the behavior of the various positional series over an adequate range of substituents. From the picture graphically revealed by Hammett plots, it now has become clear that the previous contention no longer can be maintained, and that the acid–base relations in the various series are distinctive, and appear to be determined by influences which reflect the importance of the mesomeric moment of the substituent. The relations between pK_a values and N–H frequencies are also distinctive, and reveal a pattern which is difficult to interpret.

Experimental

Melting points are not corrected. Substituted naphthylamines were prepared in most cases from the appropriate nitronaphthylamines by the diazo reaction. Preparation of the mononitronaphthylamines closely followed the literature instructions (a summary of methods has been published,[3] and no account will be given of these methods except in the case of 3-nitro-1-naphthylamine and 4-nitro-2-naphthylamine where a modified procedure gives an improved separation of these isomers).

3-Nitro-1-naphthylamine and 4-nitro-2-naphthylamine were prepared by the reduction of 1,3-dinitronaphthalene with sodium sulfide in boiling methanol as described by Hodgson and Birtwell,[4] and the filtered solution on cooling deposited practically pure 3-nitro-1-naphthylamine. The filtrate was diluted with water and the mixture of 3-nitro-1-naphthylamine and 4-nitro-2-naphthylamine removed next day. Hodgson and Birtwell[4] recorded the difficulty of separating these isomers, but the following method based on the relative insolubility of 4-nitro-2-naphthylammonium nitrate proved satisfactory. To the solution of the mixed amines in 0.1 *N* hydrochloric acid was added one-third of the volume of saturated potassium nitrate solution whereupon a cream precipitate of 4-nitro-2-naphthylammonium nitrate was produced. Re-solution in dilute hydrochloric acid and precipitation with further potassium nitrate followed by basification gave 4-nitro-2-naphthylamine which after crystallization from aqueous alcohol had m.p. 98° (lit.[4] m.p. 98.5°).

Chloronaphthylamines were prepared from the appropriate nitronaphthylamines by diazotization at 5° with sodium nitrite and pouring into cuprous chloride solution. After purification, reduction of the chloronitronaphthalene was effected with stannous chloride or by hydrogen over Raney nickel. Bromo and iodo compounds were prepared in analogous fashion.

Hydroxy- and methoxy-naphthylamines.—The author is indebted to Imperial Chemical Industries Ltd. for the gift of a number of these dyestuff intermediates. Compounds not available from this source were prepared as illustrated for 4-methoxy-2-naphthylamine. 3-Nitro-1-naphthol (5 g. from 3-nitro-1-naphthylamine) was dissolved in 10% sodium hydroxide (15 ml.) and dimethyl sulfate (10 g.) added. The mixture was warmed on a water-bath for 30 minutes when yellow crystals of 4-methoxy-2-nitronaphthalene separated. Crystallization from ethanol gave yellow needles, m.p. 105°, and reduction with stannous chloride gave 4-methoxy-2-naphthylamine, m.p. 59–60° (lit.[5] m.p. 57.5–58.5°).

***O*-Methylation of Aminonaphthols**.—The aminonaphthol (2 g.) was dissolved in pyridine (5 ml.) and acetic anhydride (3 ml.) added. The mixture was heated on the water-bath for 15 minutes, producing a precipitate of the acetaminonaphthol acetate. After crystallization from alcohol, the substance was added to 5 *N* sodium hydroxide (20 ml.), and warmed to hydrolyze the acetate group as shown by complete solubility. To this warm solution at 50° was added dimethyl sulfate (2 ml.) after which the acetaminomethoxynaphthalene separated. The mixture was heated for a further 15 minutes, water added and the precipitate removed. Hydrolysis of the acetamino group was effected by refluxing with hydrochloric acid and alcohol for 30 minutes.

3-Methyl-1-naphthylamine was prepared as described by Marion and McRae.[6]

4-Amino-2-naphthol was prepared by the Raney reduction of 4-nitro-2-naphthol. The filtered alcoholic solution was evaporated in a stream of nitrogen and the residue crystallized from water in an atmosphere of nitrogen giving white needles rapidly darkening in air. The melting point determined in an evacuated capillary was 207°. Literature values are conflicting; *e.g.*, 185°,[7] 198°[8] and 211°,[9] the last being in CO_2.

4-Amino-2-naphthonitrile was supplied by the courtesy of Professor J. Cason. The compound was hydrolyzed to 4-amino-2-naphthoic acid as described by this author,[10] and converted to the methyl ester by refluxing a methanolic solution in the presence of hydrochloric acid.

Methyl 4-amino-2-naphthoate, not previously described, forms colorless needles of m.p. 87° from petroleum ether. *Anal.* Calcd. for $C_{13}H_9NO_2$: C, 71.6; H, 5.51; N, 6.96. Found: C, 71.75; H, 5.41; N, 6.90.

3-Amino-1-naphthonitrile, not previously described, was prepared by the reduction with iron and acetic acid of 3-nitro-1-naphthonitrile m.p. 178°, prepared by the Sandmeyer reaction on 3-nitro-1-naphthylamine. It crystallizes from cyclohexane in pale yellow needles of m.p. 116–117°. *Anal.* Calcd. for $C_{11}H_8N_2$: C, 78.55: H, 4.78; N, 16.67. Found: C, 78.35; H, 4.53; N, 16.15.

7-Methoxy-1-naphthylamine, not previously reported, is prepared by the methylation of 7-hydroxy-1-naphthylamine and has m.p. 81°.

3-Amino-1-naphthoic acid[11] was esterified by refluxing a methanolic solution through which hydrogen chloride was passed. **Methyl 3-amino-1-naphthoate** has m.p. 72° (lit.[11] m.p. 72–73°).

1- and 2-naphthylacetic acids were commercial products and were purified by recrystallization from aqueous alcohol.

***pK*$_a$ Determinations**.—With the exception of those nitronaphthylamines with pK_a values less than 1.0, all measurements were made by the spectrophotometric method previously described for *m*-substituted anilines, the concentrations of the amines being 0.0005 to 0.001 *M* at an ionic strength of 0.02. As in the case of the substituted anilines, the accuracy and precision of the results are dependent on the errors involved in the measurements of the *p*H of the buffer solutions used, the ratios RNH_3^+/RNH_2, and the correction term for ionic strength. In general, for any given experiment, two buffers were used close to the expected pK_a' values, and measurements were rejected and the experiment repeated if the two pK_a' values were not within 0.03 unit. Replicate experiments were carried out on a number of halogen substituted naphthylamines with the following results (after correction for ionic strength): 3-chloro-1-naphthylamine, 2.69, 2.69; 2.67, 2.66; 2.64, 2.64; mean 2.66_5, std. dev. 0.02; 3-chloro-1-naphthylamine (I.C.I. sample), 2.70, 2.72, mean 2.71; 3-bromo-1-naphthylamine, 2.71, 2.68; 2.66, 265, mean 2.67_5, std. dev. 0.03; 4-chloro-2-naphthylamine, 3.41, 3.39; 3.37, 3.39; 3.36, 3.36; mean, 3.38, std. dev. 0.03; 4-bromo-2-naphthylamine, 3.41, 3.42, 3.42; 3.39, 3.38; mean, 3.40, std. dev. 0.02; 4-iodo-2-naphthylamine, 3.41, 3.40; 3.38, 3.39; mean, 3.39_5, std. dev. 0.01. These figures were obtained with a Uvispek spectrophotometer, mark II, in which the range of absorbance measurements is inferior to that possible with the Cary

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TABLE I

pK_a VALUES (H_2O AT 25° UNLESS SPECIFIED) AND N–H STRETCHING FREQUENCIES OF SUBSTITUTED NAPHTHYLAMINES (TOGETHER WITH 1- AND 2-NAPHTHYLACETIC ACIDS)

	M.p., °C.		Substituent			N–H stretching frequencies	
	Exptl.	Lit.	X	pK_a	ΔpK_a		
1-Naphthylacetic acid	134	134–135		4.23		..	..
2-Naphthylacetic acid	142	142		4.30		..	..
1-Naphthylamine	50	50		3.92[c]		3396	3477
2-Naphthylamine	112	112		4.16[c]		3399	3485
I, 1-NH_2, 3-X	135.5	136	NO_2	2.07(2.22)[a]	1.85	3405	3489
	123–124	125–126	CN	2.26	1.66	3405	3489
	68–69[d]	62	Cl	2.66	1.26	3403	3486
	71	71.5	Br	2.67	1.25	3402	3486
	88–89[d]	84	I	2.82	1.10	3401	3484
	87	..	$COOCH_3$	3.12	0.80	3398	3481
	..	..[f]	OCH_3	3.26	.66	3400	3482
	207	211	OH	3.30	.62	..[k]	..[k]
	51	51–52	CH_3	3.96	− .04	3395	3477
	67–68[e]	62	Cl	2.71	1.21	3402	3486
II, 2-NH_2, 4-X	98	98.5	NO_2	2.43(2.63)[a]	1.73	3403	3493
	116–117	..	CN	2.66	1.50	3402	3491
	69	68	Cl	3.38	0.78	3400	3487
	71.5	72	Br	3.40	.76	3400	3487
	84[d]	76	I	3.41	.75	3399	3486
	72	72–73	$COOCH_3$	3.38	.78	3399	3484
	59–60	58–59	OCH_3	4.05	.11	3395	3481
III, 1-NH_2, 6-X	166	167	NO_2	2.89(3.15)[a]	1.03	3400	3482
	64	63–64	Cl	3.48	0.44	3398	3480
	74–75	73–74	OCH_3	3.90	.02	3396	3476
	189	190.5	OH	3.97	− .05	3395	3475
IV, 2-NH_2, 5-X	144	146	NO_2	3.01(3.13)[a]	1.15	3405	3495
	201	199	OH	4.07	0.09	3398	3481
V, 2-NH_2, 7-X	184	184	NO_2	3.10(3.13)[a]	1.06	3405	3494
	123–124	120–121	Cl	3.71(23°)	0.43	3401	3494
	143	143	OCH_3	4.19	− .03	3397	3484
	201	201	OH	4.25	− .09	3397	3484
	160	161	NH_2	4.66[b](18°)	− .50	3395	3483
VI, 1-NH_2, 5-X	118.5	119	NO_2	2.73(2.80)[a]	1.19	3398	3480
	85	85	Cl	3.34	0.58	3399	3480
	Dec.	Dec.	OH	3.96	− .04	3397	3479
	188	189	NH_2	4.21[b]	− .29	3398	3479
VII, 1-NH_2, 7-X	134	134	NO_2	2.55(2.83)[a]	1.37	3406	3489
	45–46	46	Cl	3.48	0.44	3396	3477
	81	..[g]	OCH_3	4.07	− .15	3387	3464
	206	206	OH	4.20	− .28	3385	3464
VIII, 2-NH_2, 6-X	203	203	NO_2	2.62(2.75)[a]	1.54	3408	3501
	139	139	OCH_3	4.64	−0.48	3390	3474
IX, 2-NH_2, 8-X	105	104–105	NO_2	2.73(2.86)[a]	1.43	3408	3500
X, 1-NH_2, 4-X	191	191	NO_2	.. (0.54)[a]	3.38	3419	3509
	102	102	Br	3.21	0.71	3400	3482
XI, 1-NH_2, 2-X	144	144	NO_2	−1.74(−1.6)[a]	5.66	3365	3522
XII, 1-X, 2-NH_2	127	127	NO_2	−0.85(−1.0)[a]	4.95	3390	3541
XIII, 2-NH_2, 3-X	..	115–116[h]	NO_2	1.48	2.62	3407	3515
XIV, 1-NH_2, 8-X	97.5	97	NO_2	.. (2.79)[a]	1.13	3347	3456

[a] Values determined by Spekker absorptiometer and reported previously.[1] [b] Dissociation exponents pK_1 and pK_2 for symmetrical naphthylenediamines in 50% methanol have been published,[13] only the results for the 1,5- and 2,7-diamines being of interest in the present context. The values are:

	pK_2	pK_1
1,5-Naphthylenediamine	4.07 (20°)	1.74 (20°)
2,7-Naphthylenediamine	4.55 (18°)	2.18 (18°)

Log 2 must be subtracted from pK_2 and added to pK_1 to eliminate the statistical effect of the two NH_2 groups, and a correction of −0.50 unit applied to convert the values from 50% methanol to water.[14,15,16] Using the temperature correction recommended by Hall and Sprinkle[17] we obtain final pK_2 values of 4.21 and 4.66 for 1,5- and 2,7-naphthylenediamine at 25°. [c] The experimental values for 1- and 2-naphthylamine agree with those previously published, *viz.*, 3.92[17,18] and 4.11,[17] 4.27,[18] respectively. [d] Literature values for the melting points of 3-chloro-1-naphthylamine, 3-iodo-1-naphthylamine and 4-iodo-2-naphthylamine are appreciably lower than those found in the present investigation. [e] A sample of 3-chloro-1-naphthylamine supplied by Imperial Chemical Industries confirmed the previous measurements of melting point, pK_a value and N–H frequencies. [f] 3-Methoxy-1-naphthylamine was characterized by its acetyl derivative, m.p. 178° (lit.[9] m.p. 179°). [h] Sample supplied by Professor P. E. Verkade. [k] Sample too insoluble in carbon tetrachloride.

recording instrument used for most of the remaining determinations. The precision of the pK_a' values can be taken as of the order of ±0.03. A standard correction of 0.06 for ionic strength is therefore justified. The values for the nitronaphthylamines are lower by amounts of 0.05 to 0.20 than those previously published,[1] and can be regarded as more accurate, for the latter were obtained in unbuffered solutions, and the ratios RNH_3^+/RNH_2, measured with a filter photometer, are subject to greater uncertainty than those obtained with a spectrophotometer.

The very weak bases 2-nitro-1-naphthylamine and 1-nitro-2-naphthylamine required the following special method illustrated for the former compound. Solutions containing 86%, 30.3% and 0.1 N sulfuric acid were prepared, and to equal volumes of these were added equal weights of the amine to give a final concentration of 20 mg. per liter, the assumption being made that in 86% sulfuric acid the amine is entirely in the acid form, while in 0.1 N acid it is present as the free base. The absorbances of the solutions at wave lengths 430, 440 and 450 mμ were measured, from which the ratio log $R_{NH_3^+}/R_{NH_2}$ in the 30.3% sulfuric acid was determined as −0.20. The Hammett acidity function H_0 for acid of this concentration is −1.54, hence the (apparent) pK_a value for 2-nitro-1-naphthylamine is −1.74. In similar fashion the value for 1-nitro-2-naphthylamine was found to be −0.85.

The pK_a values of the 1- and 2-naphthylacetic acids were determined by potentiometric titration at concentrations of 0.002 M in boiled-out distilled water, 0.05 N alkali being added from a microburet. The pK_a values were calculated by the equation

$$pK_a' = pH + \log \frac{C_A - (C_{H^+} + C_{Na^+})}{C_{H^+} + C_{Na^+}}$$

where C_A is the total acid concentration, C_{Na^+} is the added sodium hydroxide and C_{H^+} is the estimated hydrogen ion concentration. The ionic correction term was taken as +0.02.

Infrared Measurements.—N–H stretching frequencies were determined in 0.001 to 0.005 M solutions of the amines in freshly distilled carbon tetrachloride as in the previous article. The author is indebted to Dr. R. L. Werner for the determination of the frequencies of a considerable number of the compounds and to Mr. I. Reece for recording the spectra of the remainder.

Experimental Results

A summary of the experimental results together with relevant data from the literature is shown in Table I. For economy of space no detailed references are given for the recorded melting points of the compounds. All data and references are, however, included in Elsevier's "Encyclopaedia of Organic Chemistry," Vol. 12B, where these summaries are to be found: halogenonaphthylamines, p. 708; mononitronaphthylamines, p. 745; naphthylenediamines, p. 805; aminonaphthols, p. 1633; aminonaphthoic acids, p. 4183.

Discussion

The Inductive Effect of the Naphthalene Ring.—As part of the general survey of the effects of substituents in the naphthalene ring, the pK_a values of 1- and 2-naphthylacetic acids were determined, since in these compounds the aromatic ring is isolated from the carboxylic group by a methylene group and may be expected to act purely inductively. In the absence of mesomeric interaction with the side chain, the inductive effect of the ring at the 1- and 2-positions should be determined by the electronegativities of the ring carbon atoms at these positions. The values found, *viz.*, 4.23 (4.24) for 1-naphthylacetic acid and 4.30 (4.26) for 2-naphthylacetic acid, agree with those (in brackets) previously published,[12] and indicate that the inductive effects at the 1- and 2-positions differ only slightly from one another and from that of the phenyl group in phenylacetic acid (4.31). In agreement with the above, it is found that the dissociation constants K_a are in the same order as the electronegativities derived from molecular orbital considerations by Jaffé,[19] and 'indices of free valence' defined by Daudel and Pullman[20] and Coulson.[21]

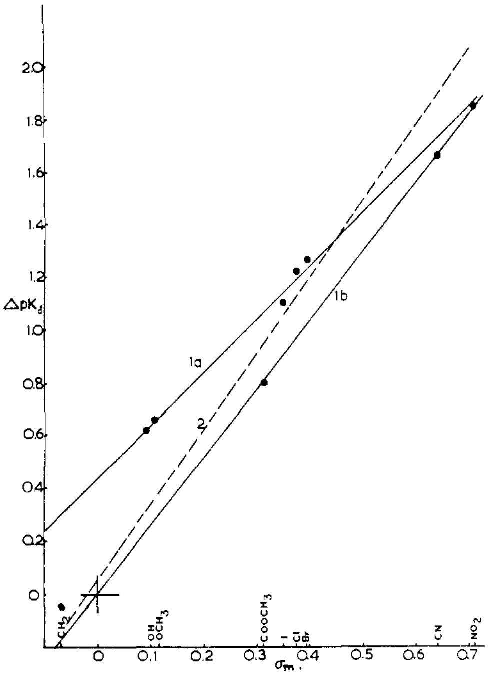

Fig. 1.—1a, 3-substituted-1-naphthylamines +M; 1b, 3-substituted-1-naphthylamines −M; 2, m-substituted anilines.

Graphical Representation of Results.—Graphical representations of the effects of substituents in various ring positions are shown in Figs. 1, 2, 3 and 4 by plotting ΔpK_a values ($\Delta pK_a = \log K/K_0$ where K_0 is the constant for the parent naphthylamine) against the appropriate Hammett m-substituent constants. The interpretation of this presentation, *viz.*, that substituent constants at all ring positions have the same σ-value, and that reaction constants ρ vary from series to series is scarcely plausible, and it is more realistic to consider that the reaction constant for all positions is equal to that for m-substituted anilines. The appropriate substituent constants σ then can be readily evaluated by drawing intercepts to the aniline line. The values so found are shown in Table II.

This information is supplementary to the table of substituent constants recently published by Wells and Ward,[22] and enables a comparison with the figures evaluated from other reactions.

Analysis of ΔpK_a–σ_m Graphs.—Apart from the question of interpretation, Figs. 1, 2, 3 and 4

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(21) C. A. Coulson, "Valence," Oxford University Press, New York, N.Y., 1952, p. 253.

(22) P. R. Wells and E. R. Ward, *Chemistry & Industry*, 528 (1958).

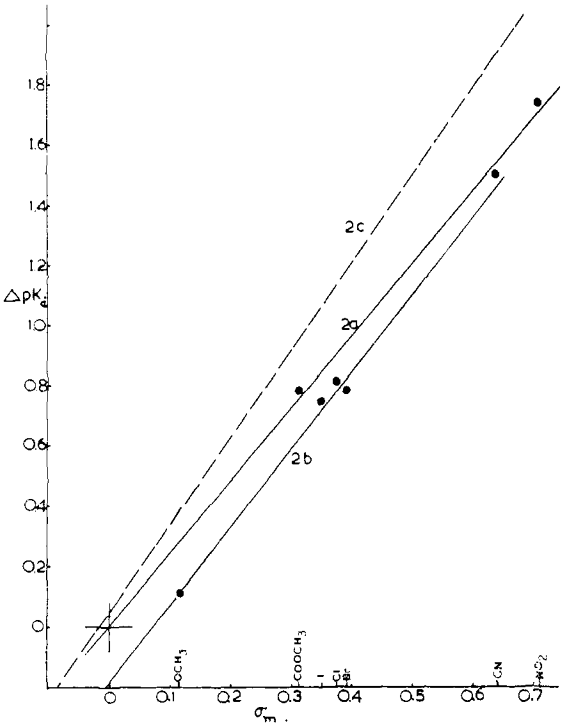

Fig. 2.—2a, 4-substituted-2-naphthylamines −M; 2b, 4-substituted-2-naphthylamines +M; 2c, *m*-substituted anilines.

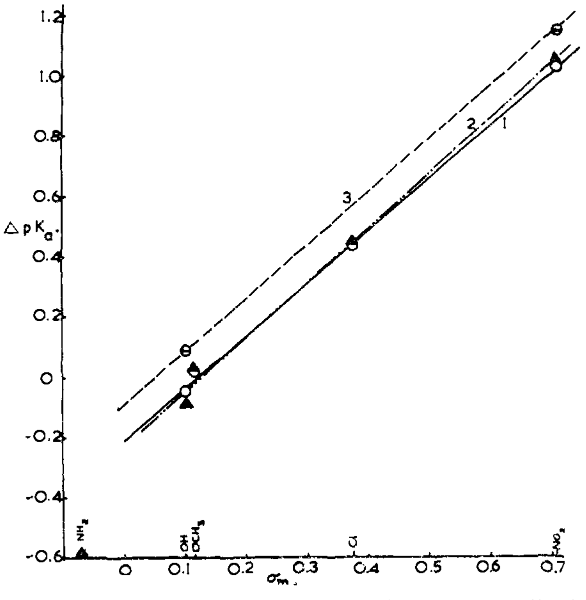

Fig. 3.—1, 6-substituted-1-naphthylamines; 2, 7-substituted-2-naphthylamines; 3, 5-substituted-2-naphthylamines.

can most simply be regarded as comparisons of the effects of substituents in various naphthalene ring positions with those in the corresponding *m*-substituted benzoic acids, and the distinctive features of the individual series readily can be recognized.

1. Compounds Formally Analogous to *m*-Substituted Anilines (Figs. 1 and 2, series I and II, Table I).—In 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines the amino and substituent groups are in the same relative positions as in *m*-substituted anilines. Mesomeric interaction between groups should therefore be at a minimum, and the substituent effect predominantly inductive. It could therefore be expected that the Hammett graphs would show regression lines of similar slopes passing through the origin. Figure 1, however, reveals an unexpected pattern for the 3-substituted 1-naphthylamines in which the substituents fall into two classes, those with −I, −M character such as NO_2, CN, $COOCH_3$ which appear to fall on a line through the origin, and those with −I, +M character such as the halogens, OCH_3 and OH which lie on a line passing approximately through the point representing the NO_2 group, and cutting the axis at a positive value of ΔpK_a. The point for 3-CH_3 appears to lie slightly above the former line. Figure 2 shows the behavior of the 4-substituted 2-naphthylamines and in this case all the substituents except 4-$COOCH_3$ appear to lie on a line approximately 0.35 unit lower than the aniline line. However, it is equally plausible to regard the points representing the NO_2, CN and $COOCH_3$ groups as colinear with a line passing through the origin, the substituents Cl, Br, I, OCH_3 lying on the lower line. Such behavior is consistent with that of the 3-substituted 1-naphthylamines and this interpretation will be adopted.

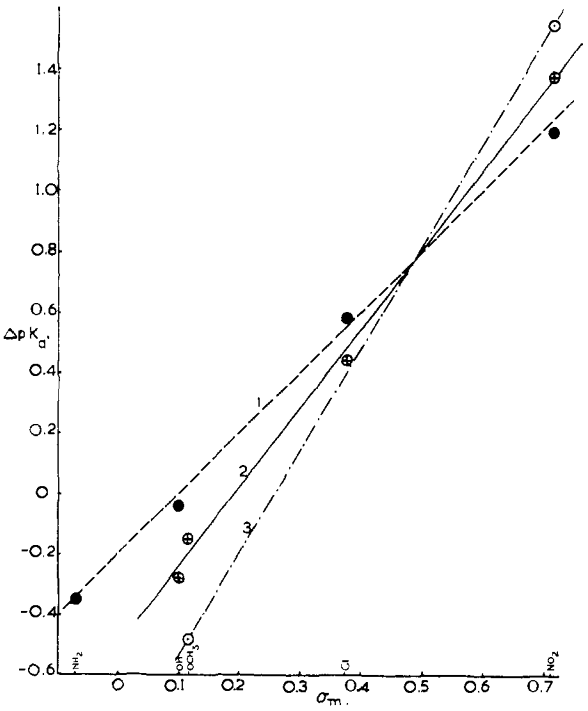

Fig. 4.—1, 5-substituted-1-naphthylamines; 2, 7-substituted-1-naphthylamines; 3, 6-substituted-2-naphthylamines.

Considerable clarification of this behavior becomes possible if we apply modifications of the equation proposed for *m*-substituted benzene compounds by Taft,[23] *viz.*

$$\sigma_m = \sigma_I + 0.33\sigma_R \qquad (1)$$

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(23) R. W. Taft, Jr., "Steric Effects in Organic Chemistry," ed. M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, Chap. 13; also *Ann. Rev. Phys. Chem.*, **9**, 292 (1958).

TABLE II

SUBSTITUENT CONSTANTS σ FOR POSITIONS IN THE NAPHTHALENE RING

Substituent	Ring positions									
	3α	4α	5α	6α	7α	4β	5β	6β	7β	8β
NO_2	0.625	1.21	0.39	0.34	0.44	0.58	0.37	0.52	0.34	0.48
CN	.56	..	..	..	..	.50	..	..	..	..
Cl	.41	..	.18	.13	.13	.25	..	..	.13	..
Br	.40	0.21	..	..	..	.24	..	..	..	..
I	.36	..	..	..	..	.24	..	..	..	..
$COOCH_3$	.26	..	..	..	..	.25	..	..	..	..
OCH_3	.21	..	..	− .01	− .08	.02	..	− .18	− .01	..
OH	.20	..	− .03	− .04	− .18	..	.01	..	− .08	..
CH_3	− .04	..	..	..	..	..	..	..	..	..

TABLE III

COMPARISON BETWEEN CALCULATED AND EXPERIMENTAL VALUES OF SUBSTITUENT CONSTANTS σ FOR "*meta*" ANILINES AND NAPHTHYLAMINES

Substituent	σ_I[a]	σ_R[a]	σ					
			m-Anilines		3-X-1-Naphthylamines		4-X-2-Naphthylamines	
			Calcd.	Exptl.[b]	Calcd.	Exptl.	Calcd.	Exptl.
NO_2	0.63	0.16	0.71	0.71	0.62	0.62	0.55	0.58
CN	.58	.10	.64	.62	.56	.56	.49	.50
$COOCH_3$	.26[c]	.15	.32	.33	.26	.26	.26	.25
CH_3	− .05	− .11	− .09	− .07	− .06	− .04	..	..
Cl	.47	− .24	.41	.37	.42	.41	0.27	0.25
Br	.45	− .22	.40	..	.40	.40	.26	.24
I	.39	− .11	.37	..	.36	.36	.26	.24
OCH_3	.26[c]	− .51	$.10_5$	.11	$.18_6$	.21	.00	.02
OH	.26[c]	− .60	$.07_5$	.10	$.17_5$	.20	..	..
NH_2	.17[d]	− .76	− .07	− .05	..	..	..	..

[a] Ref. 23. [b] Ref. 36, values calculated from regression equation $\Delta pK_a = 2.82\,\sigma + 0.08_0$. [c] Value of 0.26 gives better agreement for all methoxy, hydroxy and carbomethoxy compounds examined than the Taft values. [d] This value gives better concordance for anilines, pyridines, quinolines and isoquinolines than the Taft value 0.10.

based on the experimental work of Roberts and Moreland.[24] In eq. 1, σ_I, which is a polar constant evaluated from bicyclic saturated carboxylic acids and adjusted to apply to substituted benzoic acids, constitutes the component of the total σ_m effect due to the substituent dipole, while σ_R is the mesomeric component effective at the *p*-position, and multiplied by 0.33 to give the effect at the *m*-position. Writing the equation in the form $\sigma = a\sigma_I + b\sigma_R$ where *a* and *b* are adjustable parameters, it is possible by successive approximations to obtain satisfactory calculated and experimental agreement by a suitable choice of these parameters, the equations being

$$m\text{-anilines},\ \sigma = 1.05\sigma_I + 0.33\sigma_R \quad (2)$$

$$\text{3-substd.-1-naphthylamines},\ \sigma = 0.95\sigma_I + 0.12\sigma_R \quad (3)$$

$$\text{4-substd.-2-naphthylamines},\ \sigma = 0.78\sigma_I + 0.40\sigma_R \quad (4)$$

The relevant values are shown in Table III. I am indebted to one of the referees for pointing out the close correlation between the σ-values for the 3-substituted 1-naphthylamines and the Taft σ_I-values.

It will be shown in a further paper that similar equations are capable of reproducing the experimental σ-values of "*meta*" substituted pyridines, quinolines and isoquinolines, and these applications coupled with the fact that the substituents cover a wide range, encourages the belief that the parameters *a* and *b* have a degree of quantitative significance, and may be used to infer the relative importance of the polar and mesomeric components of the inductive effects of substituents in different ring systems.

Since the reaction constant is the same in each case, the ΔpK_a values of the *m*-anilines, 3-X-1-naphthylamines and 4-X-2-naphthylamines are in the ratio: $1.05\sigma_I + 0.33\sigma_R : 0.95\sigma_I + 0.12\sigma_R : 0.78\sigma_I + 0.40\sigma_R$, and it therefore follows that as compared with their effects in anilines: (1) *m*-substituents show decreased polar effects in both the 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines, the decrease being more notable in the latter series; (2) the mesomeric components of the inductive effect are considerably less in the 3-substituted 1-naphthylamines, and somewhat greater in the 4-substituted 2-naphthylamines; and (3) the ΔpK_a–σ_m graphs shown in Figs. 1 and 2 show distinctive regression lines for the −I, −M and −I, +M groups of substituents. This behavior arises from the circumstance that in the latter group the M and I influences have an inverse relation and oppose one another, whereas in the former they are in direct relation and reinforce one another, and this coupled with the characteristic values of *a* and *b* leads to the distinctive relations noted. Where the values of *a* and *b* are similar as in all reaction series involving a common benzene ring, such differences must be small, and as has been shown for *m*-anilines in the preceding paper, they are incapable of clear resolution. It is to be expected that comparisons of other ring systems using parameters based on benzene compounds will reveal behavior analogous to that shown by the naphthalene ring.

2. Compounds with the Substituents in Non-conjugated Positions in the Second Ring.—Three series of compounds are of interest here, *viz.*, III,

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[24] J. D. Roberts and W. T. Moreland, THIS JOURNAL, **75**, 2167 (1953).

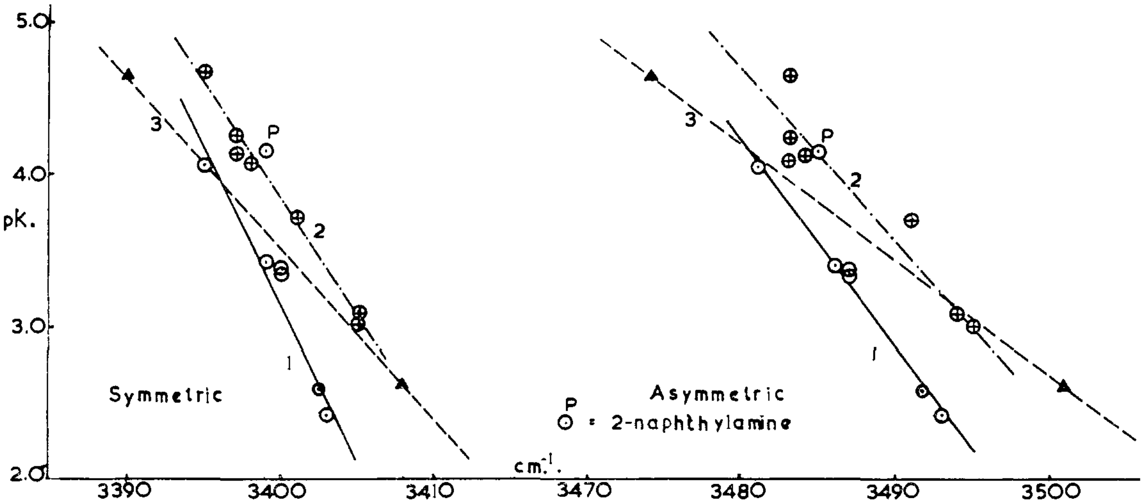

Fig. 5.—Relations between pK_a and N–H stretching frequencies: 1, —⊙—⊙—, 4-substituted-2-naphthylamines; 2, —·—·⊕ —·—·—⊕—·— 5- and 7-substituted-2-naphthylamines; 3, —▲—▲—, 6-substituted-2-naphthylamines.

IV and V in Table I (*peri* compounds show proximity effects and are discussed separately). The ΔpK_a–σ_m relationships are demonstrated in Fig. 3 and show lines of similar slope for the three series. The range of substituents is limited to NO_2, Cl, OCH_3 and OH, and the σ-values for the 6-X-1-naphthylamines and the 7-X-2-naphthylamines in Table II are reproduced reasonably well by the equation

$$\sigma = 0.44\sigma_I + 0.28\sigma_R \qquad (4)$$

Although the coefficients *a* and *b* are subject to some uncertainty, eq. 4 indicates considerable mesomeric contributions to the ΔpK_a values, and may indicate the extent to which conjugation of the substituent with the ring is effective in the second ring.

3. **Compounds with the Substituent in Quinonoid Positions in the Second Ring.**—Four series of compounds are included in this group, *viz.*, VI, VII, VIII and IX (Table I), and the graphical relations are shown in Fig. 4 where four points are available for VI and VII and define the behavior of the +M substituents. Comparison of the slopes of the lines in Figs. 3 and 4 shows that the ΔpK_a values are enhanced by the nitro group and diminished by the methoxy group in the case of the 6,2-, 7,1- and possibly 8,2-compounds. The increased effects of the nitro group probably are due to intergroup conjugation, but the decreased effects of the methoxy group cannot be attributed to this cause and presumably are due to mesomeric influences similar to those acting in the non-quinonoid compounds. This trend is not shown by the 5,1-compounds and coupled with the unexpected behavior revealed in the pK_a–ν graph (Fig. 5) indicates that 5-substituted 1-naphthylamines are somewhat anomalous in their properties. Elderfield[25] has remarked on a similar anomaly in 5-substituted as compared with 7-substituted quinolines. The data are insufficient to permit the application of the Taft equation.

4. ***ortho* and *para* Type Compounds.**—Only two 4-substituted 1-naphthylamines were available and their behavior was found to be very similar to *p*-substituted anilines. Among the *ortho* type compounds only the 1,2-nitronaphthylamines were examined, the bases being found to be weaker than *o*-nitroaniline. In the case of 3-nitro-2-naphthylamine a correction is to be noted. The pK_a value of this substance was given previously as 2.93,[1] the compound having been prepared by the method of Hodgson and Turner,[26] a confirmatory sample having been obtained from the authors. Subsequently this method was shown to produce a mixture of 5- and 8-nitro-2-naphthylamine,[27,28] and an authentic sample of 3-nitro-2-naphthylamine from Professor Verkade gave a pK_a value of 1.48.[29] This contrasts with the values of −1.75 and −0.85 for 2-nitro-1-naphthylamine and 1-nitro-2-naphthylamine and indicates that 3-nitro-2-naphthylamine is more than 200 times stronger as a base than 1-nitro-2-naphthylamine. A similar difference has been found in the rates of deacylation of 3-nitro-2-acetoaminonaphthalene and 1-nitro-2-acetoaminonaphthalene, the rate constants determined by Verkade, *et al.*,[30] being 0.014 and 2.20 min.$^{-1}$, respectively. These differences undoubtedly are due to the lower order of the C_2–C_3 bond in the naphthalene ring.

Correlation of pK_a Values with Electronic Structure.—The conclusions drawn from the application of the Taft equation to the 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines are sufficiently novel to invite speculations as to their cause, and an attempt will be made to describe a mechanism of substituent action in aromatic bases. With the preliminary assumption usually made that pK_a values are proportional to potential energy changes produced by the substituent, we can nominate four factors as significant in the control of acid–base equilibria in such systems.

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(25) R. C. Elderfield, "Heterocyclic Compounds," Vol. 4, John Wiley and Sons, Inc., New York, N. Y., 1952, p. 6.

(26) H. H. Hodgson and S. Turner, *J. Chem. Soc.*, 689 (1943).

(27) Van Rij, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.*, **70**, 236 (1951).

(28) E. R. Ward and T. M. Coulson, *Chemistry & Industry*, 542 (1953).

(29) A. Bryson and R. L. Werner, *ibid.*, 947 (1955).

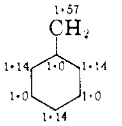
(30) L. H. Krol, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.* **71**, 545 (1952).

1. **Applying to the Acid RNH_3^+.**—The most important term is the interaction between the substituent dipole and the positive pole of the acid usually described by the Bjerrum–Eucken equation. Since the dipole moments of most substituents except alkyls have their positive poles toward the aromatic ring, this interaction term which may be designated I_a results in an increase in energy with consequent destabilization of the acid. The second, and quite significant, term is an interaction between the positive pole of the acid and the mesomeric moment of the substituent. This moment arises from the conjugation of the substituent with the ring, and involves the donation or withdrawal of electrons at the quinonoid positions creating a charge separation which although small, is compensated by the appreciable distance between the charges. This term may be designated M_a and called the mesomeric effect. For $-M$ substituents such as NO_2, CN and $COOCH_3$, M_a will be positive and acid destabilizing. (The inconsistency of sign results from the viewpoint adopted, *i.e.*, whether attention is focused on the substituent or the functional group.) For $+M$ substituents such as Cl, OH and NH_2, M_a will be negative, and in these cases the mesomeric effect will oppose the polar effect of the substituent. This term should apply to all substituents in quinonoid and nonquinonoid positions except those in which intergroup conjugation occurs such as *p*-nitroaniline.

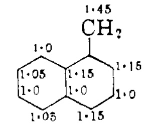
2. **Applying to the Base RNH_2.**—These are considered to be of significance only where they concern the delocalization of the electrons of the amino group, for the interaction of the substituent and functional dipoles may be regarded as of second order. The first effect is an interaction between the substituent dipole and the delocalized electrons which is not present in the unsubstituted compound. This term is designated I_b and is negative for all substituents except alkyls. The second effect which may be designated M_b is analogous to M_a and describes the effect of the mesomeric moment on the delocalization process of the NH_2 lone pair electrons. It is probably of limited significance in acid–base reactions.

It can be reasonably assumed that I_a and I_b, both of which are due to the substituent dipole, are jointly proportional to $a\sigma_I$, while M_a and M_b are likewise proportional to $b\sigma_R$. Since the reaction constants ρ are equal for *m*-anilines, 3-substituted 1-naphthylamines and 4-substituted 2-naphthylamines, it follows that the polar components of the ΔpK_a values are proportional to $1.05\sigma_I$, $0.95\sigma_I$ and $0.78\sigma_I$, and if σ_I is identified with the substituent dipole, the remaining factors indicate the efficiencies with which the dipole actions are transmitted to the reaction site. Likewise, the terms $0.33\sigma_R$, $0.12\sigma_R$ and $0.40\sigma_R$ are identified with the action of the mesomeric moment, and should be correlated with the electron densities in the various ring systems.

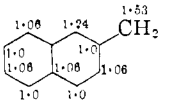
Unfortunately, accurate values of π-electron densities are not known, and therefore we use the model proposed by Longuet-Higgins,[31] in which approximate π-electron densities are calculated for alternant hydrocarbons or ions derived from these by very simple calculations.



I



II

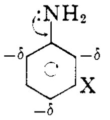


III

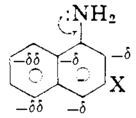
The values for the three carbanions I, II and III are shown and reveal characteristic π-electron densities that are relevant to the problem in hand, since the group $-CH_2^-$ is isoelectronic with NH_2, OH and Cl. It may confidently be expected that the π-electron densities in anilinium and naphthylammonium ions substituted by these groups will be similar to those shown in I, II and III, although modified by the different coulomb integrals of the groups concerned and by the presence of the NH_3^+ pole. In the same way, the unsubstituted bases themselves will have density patterns similar to I, II and III, and substituents will tend to impose their own pattern upon these.

There are two significant features in the patterns shown by I, II and III, *viz.*, the similarity between I and II, and the comparatively low π-electron densities at positions 3 and 10 in III.

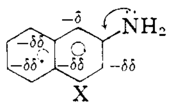
Consider now the factors that may affect the polar term $a\sigma_I$. Of these by far the most important is I_a and this might be expected to be equal for the three series since as shown in VII, VIII and IX the substituent and NH_3^+ groups are in spatially equivalent positions. Variations could be caused by any of the following: (1) the intrinsic dipole moments of the substituents may be smaller in the naphthylamines, (2) dielectric constants may be smaller in the naphthylamines or (3) in the case of the 4-substituted 2-naphthylamines the dipole vector may be deflected by the steric effect of the *peri* CH group. There is evidence from dipole measurements that this is so; *cf.*, for example, the discussion on dimethoxynaphthalenes by Sutton.[32] The third of these possibilities seems the most likely. The second factor I_b relates to the base, and inspection of IV, V and VI and comparison with I, II and III shows that this effect should be in the order IV ≈ V > VI, *i.e.*, least for the 4-substituted 2-naphthylamines. Both factors combine in the expected direction to produce a polar constant a having the lowest value for the 4-substituted 2-naphthylamines.



IV



V



VI

Coming to the factors that may influence the mesomeric component $b\sigma_R$, we have postulated the most important as the term M_a measuring the interaction of the NH_3^+ pole with the mesomeric moment of the substituent. Inspection of VII, VIII and IX, and comparison with I, II and III shows

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[31] H. C. Longuet-Higgins, *Proc. Roy. Soc.* (*London*), **A207**, 121 (1951).

[32] L. E. Sutton, "Determination of Organic Structures by Physical Methods," ed. E. A. Braude and F. E. Nachod, Academic Press, Inc., New York, N. Y., 1954, p. 395.

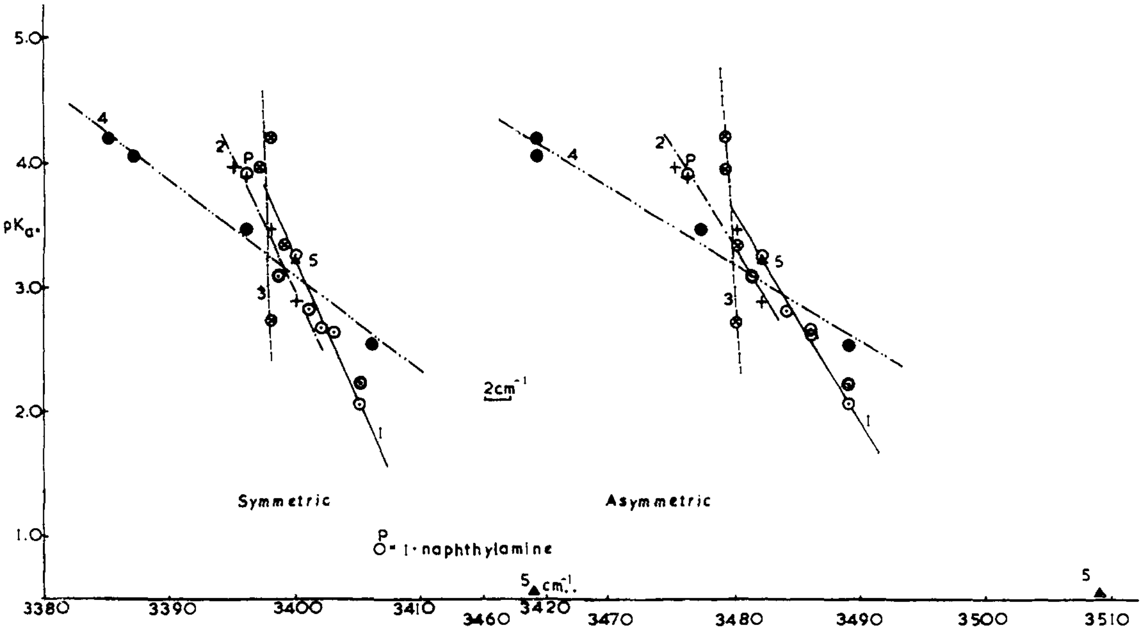
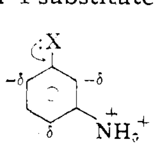
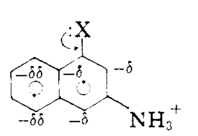


Fig. 6.—Relation between pK_a and N–H stretching frequencies: 1, —⊙—⊙—, 3-substituted-1-naphthylamines; 2, -·⊙·-⊙·, 6-substituted-1-naphthylamines; 3, ····⊗····⊗·-, 5-substituted-1-naphthylamines; 4, -·-·-·●-··●-, 7-substituted-1-naphthylamines; 5, ▲, 4-substituted-1-naphthylamines.

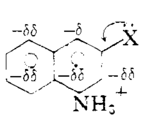
that where X is Cl, OH or NH_2, this effect should be in the order VIII ≈ VII > IX, *i.e.*, the values of $b\sigma_R$ should be approximately equal for *m*-anilines and 4-substituted 2-naphthylamines, and least for the 3-substituted 1-naphthylamines. The order is confirmed in the experimental values, the low value for the 3-substituted 1-naphthylamines being noteworthy and giving the impression that the substituent effects are wholly polar.



VII



VIII



IX

N–H Stretching Frequencies.—The relations between pK_a values and N–H frequencies are shown graphically in Figs. 5 and 6 and reveal the distinctive features: (1) Where the data are sufficiently extensive, linear relations appear to hold for both symmetric and asymmetric modes. (2) The most striking feature of Figs. 5 and 6 is the position of the parent naphthylamine in relation to the various substituted series. Since hydrogen is but one of a number of substituents, on the assumption of proportionality between pK_a and ν-values, the parent compound should fall into line with the members of any given series; hence, since no preference applies to any of these, all lines relating to 1-naphthylamine for example should be co-linear or concurrent with the point representing the parent amine. This is clearly not the case. It is perhaps not without significance that the points representing the parent amines fall very close to the lines for the non-quinonoid compounds with the substituents in the second ring.

Any analysis of N–H frequencies should take into account the possibility that a distinction might exist between the effects of +M and −M substituents in a manner similar to that demonstrated for the pK_a values of the 3-substituted 1-naphthylamines. If the differential effects of +M and −M substituents on pK_a values and N–H frequencies are proportional, it might be expected that all points relating to 3-substituted 1-naphthylamines, for example, would lie on a line passing through the point representing the parent amine. On the other hand, if these effects are not proportional, some distinction might exist between the pK_a–ν relations for the two groups of substituents. It previously has been suggested that this distinction exists in the pK_a–ν_s graph of *m*-substituted anilines (preceding paper), and an inspection of the values for the 3-substituted 1-naphthylamines in Fig. 6 shows that although all values except 3-$COOCH_3$ are accommodated on the line 1, it is equally plausible to regard the points for H, 3-$COOCH_3$, 3-CN and 3-NO_2 as forming one line, and those for the halogens, OCH_3 and OH as forming another. In the case of the 4-substituted 2-naphthylamines (Fig. 5, line 1), all substituents fall on one line which does not pass through the parent amine.[33]

While the interpretation given above for the "*meta*" series of compounds is necessarily speculative, there is no doubt as to the distinctive features shown by the quinonoid compounds. Of special interest are the 7- and 5-substituted 1-naphthylamines (Fig. 6, lines 3 and 4). In the former a considerable increase in frequency accompanies a change in the substituent from OH to NO_2, whereas in the latter virtually no alteration in NH fre-

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(33) It should be observed that recent values for the NH frequencies of 1- and 2-naphthylamine,[34] *viz.*, ν_s 3390 and 3390 cm.$^{-1}$, ν_a 3472 and 3475 cm.$^{-1}$, respectively, show considerable disagreement with the present values, and if used in Figs. 5 and 6 indicate an even greater lack of conformity with the various substitutional series.

(34) W. J. Orville-Thomas, A. E. Parsons and C. P. Ogden, *J. Chem. Soc.*, 1017 (1958).

quency occurs. The behavior of the 7-substituted 1-naphthylamines recalls the work of Califano and Moccia,[35] and Whetsel, Roberson and Krel,[36] found in the pK_a relations of substituted anilines that the substituents p-CH_3, p-OCH_3 and p-NH_2 lie on lines of slope different from those accommodating the substituents m-NO_2, m-CN, m-$COOCH_3$, m-Cl, m-OCH_3, p-NO_2 and p-Cl.

An interpretation of the varied behavior shown in the pK_a–ν graphs must remain a matter of difficulty until more is known of the mechanism of polar and mesomeric effects on NH bonds. The observation that the greatest divergences occur in quinonoid compounds when the substituents are π-electron-donating suggests that the balance of dipole and mesomeric effects in the bases is not the same as that exercised in the acid–base system where both components are affected.

Acknowledgments.—The author is indebted to Dr. E. Challen for microanalyses, to Dr. R. L. Werner and Mr. I. Reece for help with the spectrophotometric and infrared measurements, to Professors P. E. Verkade and J. Cason for samples of difficultly accessible compounds and finally to Imperial Chemical Industries Dyestuffs Research Laboratories for supplies of dyestuff intermediates.

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[35] S. Califano and R. Moccia, *Gazz. chim. ital.*, **86**, 1014 (1956).

[36] K. B. Whetsel, W. E. Roberson and M. W. Krell, *Anal. Chem.*, **30**, 1598 (1958).

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The Ionization Constants of 3-Substituted Pyridines, 3-Substituted Quinolines and 4-Substituted Isoquinolines

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Measurement of the pK_a values of 3-bromopyridine, 3-nitropyridine, 3-bromoquinoline, 3-nitroquinoline, 4-bromoisoquinoline and 4-nitroisoquinoline together with published data has enabled a survey to be made of the effects of substituents in the "*meta*" positions in these heterocyclic bases. A statistical analysis shows that 3-substituents in pyridine can be classified into those with $-M$ and $+M$ character, the former giving a regression line passing close to the origin, while the latter give a line cutting the ΔpK_a axis at a negative value, this indicating increased mesomeric effects of the substituents as compared with those in equivalent benzoic acids. The Hammett σ-values are reproduced satisfactorily by a modified Taft equation $\sigma = a\sigma_I + b\sigma_R$ and the parameters a and b can be correlated with electronic structures. The similarity of the behavior of the heterocyclic bases with m-substituted anilines and naphthylamines is demonstrated. The anomalous position of 4-hydroxy-isoquinoline is attributed to its zwitterion structure, and an estimate of the tautomeric constant confirms values found by other methods.

This paper records the determination of the dissociation constants of the heterocyclic bases pyridine, quinoline and isoquinoline substituted in the "*meta*" positions by the groups Br and NO_2. This information together with the published data for other substituents enables a comparison to be made of the effects of substituents in these bases and reveals the similarity between their effects in heterocyclic bases and the equivalent aromatic amines, aniline, 1-naphthylamine and 2-naphthylamine.

Experimental

3-Nitropyridine was prepared by the method of de-Hartog and Overhoff.[1] Toward the end of one run when the sulfuric acid had been largely converted to bisulfate, a violent explosion took place apparently as a result of overheating. 3-Nitropyridine was obtained in small yield (less than 5%), the colorless crystals from ether melting at 41° (lit.[1] m.p. 41°).

3-Bromoquinoline and 4-bromoisoquinoline were prepared by published methods,[2,3] and converted to 3-aminoquinoline and 4-aminoisoquinoline by ammonolysis as described by Craig and Cass.[3] 3-Hydroxyquinoline and 4-hydroxyisoquinoline are most easily made by the diazo reaction. The latter substance was prepared as follows: 4-aminoisoquinoline (2 g.) was dissolved in 5 N sulfuric acid (50 ml.), and diazotized with sodium nitrite (1 g.) in 5 ml. of water. The diazo solution was filtered and added to 150 ml. of 2 N sulfuric acid. The temperature was raised to 70° (evolution of nitrogen became vigorous) and held at this value for 15 minutes. The cooled solution was treated with 5 N sodium hydroxide until alkaline and filtered, the filtrate being acidified with acetic acid until precipitation was complete. The precipitate was crystallized from dilute alcohol as colorless crystals of 4-hydroxyisoquinoline, melting with decomposition at 233°, blackening at 200°.

Anal. Calcd. for C_9H_7NO: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.48; H, 4.74; N, 9.83.

3-Hydroxyquinoline prepared by the same method had m.p. 198°, (lit.[4] m.p. 198°).

3-Nitroquinoline was prepared by the condensation of o-aminobenzaldehyde with methazonic acid according to Schofield and Theobald.[5] 4-Nitroisoquinoline has not been reported previously and it was prepared as described: 4-aminoisoquinoline (3 g.) was dissolved in 2 N sulfuric acid (25 ml.), and diazotized with sodium nitrite (1.5 g.) in 5 ml. of water at 5°. The solution was neutralized with calcium carbonate and filtered, the filtrate being added to an aqueous solution of sodium nitrite (25 g.) in 100 ml. of water containing a suspension of 10 g. of cupro-cuproso sulfite and the mixture allowed to stand overnight. The solution was extracted with chloroform, the chloroform removed, and the residue crystallized from aqueous alcohol in pale yellow needles of m.p. 61–64°. Extraction of the material with 0.01 N hydrochloric acid to remove basic impurities and then recrystallization from alcohol gave pure 4-nitroisoquinoline, m.p. 64.5°.

Anal. Calcd. for $C_9H_6N_2O_2$: C, 62.06; H, 3.48; N, 16.09. Found: C, 62.41; H, 3.33; N, 15.98.

Determination of pK_a Values.—pK_a values were determined in all cases by the spectrophotometric method described in a previous paper,[6] acetate and chloroacetate buffers being used for pK_a values between 2 and 5. For the nitro-substituted compounds whose pK_a values lie between 1 and 1.5, the procedure was the same with the exception that the bases were converted to the acid form with

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