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Partition Studies. VI. Partition Coefficients and Ionization Constants of Methyl-substituted Anilines

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The partition coefficients of aniline and 12 methyl-substituted derivatives have been measured in 2 immiscible solvent pairs, cyclohexane–water and cyclohexane–aqueous citrate, phosphate buffer. In the latter system, the logarithms of the observed partition coefficients of each aniline were directly proportional to the *p*H of the buffer. Approximate ionization constants of the anilines were calculated by a previously derived equation that relates partition coefficients and ionization constants. Calculated values were in excellent agreement with values obtained by other methods. The application of this information to the separation of isomeric anilines is discussed.

Polar constituents of coal—hydrogenation oil, like those of coal tar—comprise two broad classes, phenols and organic bases. A thorough characterization of the phenolic portion of coal–hydrogenation oil has been completed recently.[1] In this work, the classical methods of organic chemistry were supplemented by extensive use of infrared and ultraviolet spectroscopy, by precise fractional distillation, and by countercurrent distribution techniques. In preparation for a similar characterization of the basic portion of coal–hydrogenation oil, fundamental spectroscopic and partition data on appropriate model compounds are being compiled. Golumbic and Orchin[2] have recently measured the partition coefficients of a large number of alkyl-substituted pyridines and quinolines in systems suitable for countercurrent distribution and have shown how these data may be employed in estimating base strength. The present communication presents similar information on methyl-substituted anilines.

The immiscible solvent systems employed for distribution were cyclohexane–water and cyclohexane–aqueous citrate, phosphate buffer. The partition coefficients (*k* values) of aniline and 10 methyl-substituted derivatives, measured in the former system, are recorded in Table I. These values are expressed as the ratio of concentration in the organic phase to concentration in the aqueous phase. The initial concentration of base was 0.5 mg./ml.; at this concentration, association effects are either absent or negligible (see Experimental part).

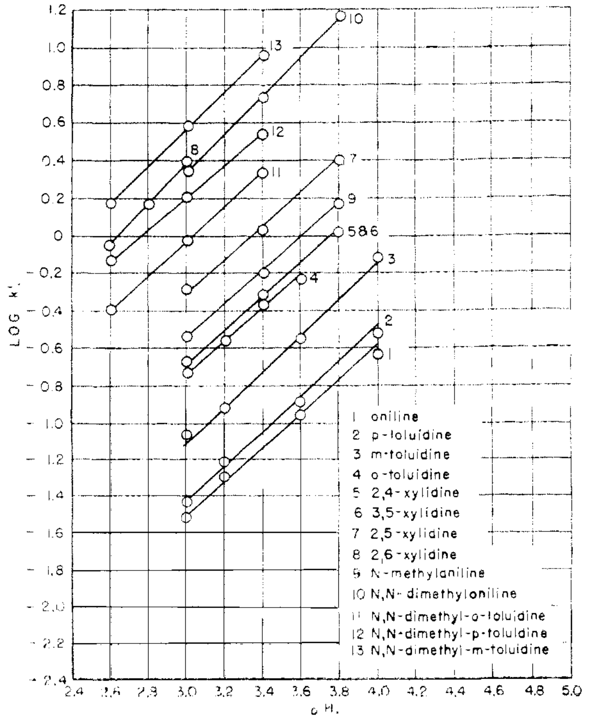

Fig. 1.—Effect of *p*H on partition coefficient of anilines.

TABLE I

PARTITION COEFFICIENTS AND IONIZATION CONSTANTS OF ANILINES AT 25°

Compound	*k*-(H_2O)[a]	*k'*(*p*H 3.0)[b]	*m*	*p*Ka This work	*p*Ka Literature
Aniline	1.04	0.03	0.94	4.6	4.62[c]
o-Toluidine	4.68	.19	.93	4.5	4.43[c]
m-Toluidine	4.32	.09	.97	4.8	4.71[c]
p-Toluidine	3.76	.04	.96	5.1	5.12[c]
2,6-Xylidine	22.2	2.49	1.04	4.1	3.42[d]
2,5-Xylidine	16.7	0.51	0.94	4.6	4.17[d]
3,5-Xylidine	15.1	.21	.92	4.9	4.48[d]
2,4-Xylidine	16.8	.21	.97	5.0	4.61[d]
N-Methylaniline	16.9	.29	.91	4.8	4.78[d]
N,N-Dimethylaniline	295	2.21	1.05	5.1	5.1[c]
N,N-Dimethyl-*o*-toluidine	890	0.94	.97	6.0	5.86,[e] 5.96[f]

[a] Solvent system: cyclohexane and water. [b] Solvent system: cyclohexane and aqueous citrate, phosphate buffer. [c] N. F. Hall, THIS JOURNAL, **52**, 5115 (1930). [d] Ref. 4. [e] N. F. Hall and M. R. Sprinkle, *ibid*,, **54**, 3469 (1932). [f] H. Ley and R. Grau, *Ber.*, **58B**, 1765 (1925).

Hydrogen bonding between the amine group of the anilines and water molecules undoubtedly must play a major role in these distributions. The importance of this effect in determining the actual values of the partition coefficients is apparent from the much larger partition coefficients of the N-methyl substituted isomers. Steric effects of ortho substituents, which were so pronounced with alkyl phenols in the same system,[3] are apparent but less striking in the aniline series. This may be merely the result of the somewhat weaker hydrogen bonding tendency of the amino group in comparison with the phenolic hydroxyl group.

For the distributions of aniline and twelve of its alkyl derivatives in the system cyclohexane–aqueous citrate, phosphate buffer, the observed partition coefficients (*k'* values) were related to the *p*H of the buffer in the acidic range (*p*H 2–4); plots of the logarithms of the *k'* values *vs.* *p*H, presented in Fig. 1, are straight lines with slopes (*m*) very close to

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(1) E. O. Woolfolk, C. Golumbic, R. A. Friedel, M. Orchin and H. H. Storch, Bureau of Mines Bulletin 487, 56 (1950).

(2) C. Golumbic and M. Orchin, THIS JOURNAL, **72**, 4145 (1950).

(3) C. Golumbic, M. Orchin and S. Weller, *ibid.*, **71**, 2624 (1949).

1 (Table I). These results show that the simple relationship previously developed for the equilibria involved in the distribution of weak acids and bases in an immiscible system comprising a non-polar and an ionizing solvent applies not only to phenols[3] and heterocyclic bases,[2] but also to anilines. This relationship is

$$\log k' = p\mathrm{H} + \log k - pK_a \qquad (1)$$

where k' is the partition coefficient in pH regions in which ionization of the base is essentially complete, k is the partition coefficient of the un-ionized base, and pK_a is the acidic ionization constant.

An approximate ionization constant for each base was calculated by means of this equation. The calculated values, recorded in Table I, are in excellent agreement with previously reported data. No measurements of pK_a values of the xylidines in water solution appear to have been made previously. The calculated values decrease in the same order as those determined by Thomson[4] in 50% alcohol solution.

N-Methyl as well as meta- and para-methyl substituents caused a significant increase in the base strength of aniline, probably because of the inductive and/or hyperconjugative effect of the methyl group. The base-weakening action of ortho-methyl constituents is exceptional and has been explained as a -I effect.[5] Brown and Cahn[6] have recently given a more satisfactory interpretation in terms of the steric requirements of the anilinium ion: Steric strain arising from the presence of ortho-methyl groups opposes the formation of this ion, thereby decreasing the base strength. In N-dimethyl-*o*-toluidine, the ortho-methyl substituent exerts the usual base-strengthening action. Here, apparently, steric inhibition of resonance is the major factor, although (according to Brown and Cahn) the magnitude of the increase in base strength is less than anticipated, because steric strain in the anilinium ion is still operative in some degree.

When aqueous buffer solutions are used as one phase of a solvent pair, the application of fractional distribution schemes, such as countercurrent distribution, to the separation of acidic and basic compounds is greatly facilitated.[7] Since at any given acidic pH, isomeric and homologous alkyl anilines show significant relative differences in their partition coefficients (see Table I), separation of mixtures of these compounds by countercurrent distribution should be feasible.

Experimental

Materials and Procedure.—All the aromatic bases were Eastman Kodak Co. highest-purity grade. These were subjected to a 1- to 2-plate fractionation, and the constant-boiling fraction was used for partition measurements. The solvent employed for the organic phase was spectrographic-grade cyclohexane. The aqueous buffers were McIlvaine's standard phosphate–citrate mixture.[8] Salting-out effects were absent or negligible with this buffer system, similar to the observation made when the same buffer was used for the distribution of heterocyclic bases.[2]

The procedure for measuring the partition coefficients was the same as that previously employed for pyridines and quinolines[2]; the ultraviolet absorption of the cyclohexane solution of the aniline was measured before and after equilibration with the aqueous phase. In order to obtain a significant change in absorption when compounds with high partition coefficients were used, repeated extraction of the organic phase was required. It might be pointed out that the recently devised technique of "interchange extraction"[9] would yield more precise values for the large partition coefficients.

Constancy of the partition ratios in the concentration range involved in this work was indicated by the close agreement between experimental and theoretical countercurrent distribution curves of toluidines and xylidines; these results will be reported in detail elsewhere.

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[4] G. Thomson, *J. Chem. Soc.*, 1113 (1946).

[5] G. M. Bennett and A. N. Mosses, *J. Chem. Soc.*, 2367 (1930).

[6] H. C. Brown and A. Cahn, THIS JOURNAL, **72**, 2939 (1950).

[7] C. Golumbic, *ibid.*, **71**, 2627 (1949).

[8] W. M. Clark, "The Determination of Hydrogen Ions," The Williams and Wilkins Co., Baltimore, Md., 1927, p. 116.

[9] C. Golumbic and S. Weller, *Anal. Chem.*, **22**, 1418 (1950).