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Dissociation Constants of Pyridinepentacarboxylic Acid and Other Pyridinecarboxylic Acids

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By using the potentiometric titration method, with glass and calomel electrodes, the dissociation constants of pyridine, six substituted pyridines, and eight pyridinecarboxylic acids, including pyridinepentacarboxylic acid, have been measured at 25° C.

THE DISSOCIATION constants of a number of dicarboxylic acids have been measured. Those of some tricarboxylic acids are known—for example, citric acid (*2*) and isocitric acid (*9*)—but few polycarboxylic acids of higher degree have been studied. One of these is benzenehexacarboxylic acid (mellitic acid), the six dissociation constants of which have been elucidated by Maxwell and Partington (*11*). An analogous example is pyridinepentacarboxylic acid where the pyridinium ion affords the sixth stage of dissociation. The authors now have prepared this acid and studied its dissociation constants. In addition, a number of other pyridine derivatives have been made and their dissociation constants measured.

MATERIALS

The samples of pyridine, 2,6-dimethylpyridine, and 2,4,6-trimethylpyridine were obtained commercially and triply distilled to give fractions of b. p. 114–15°, 142–43°, and 162–64° C., respectively.

A sample of 3,5-dicyanopyridine was recrystallized three times from water to give thin flakes, m. p. 112–13° C.

The remaining compounds for this study were prepared by known methods and are described in Table I.

The criterion used for all compounds was chromatographic purity, using an ascending paper system (Whatman No. 3), developed with the upper phase of the mixture 1-butanol–acetic acid–water (4 : 1 : 5) and sprayed with bromocresol green (0.5% in 95% ethanol adjusted to pH 8.0–9.0 with 0.1N sodium hydroxide).

The analytical data for pyridinepentacarboxylic acid, given in Table I, are not in good agreement with the calculated values. The authors suspect this was due to difficulty in drying the compound. Therefore, the dipotassium salt was prepared. Calcd: C, 31.1; H, 1.1; N, 3.7%. Found: C, 31.3; H, 1.4; N, 3.7%. This was dissolved in water containing 2 moles of hydrochloric acid per mole of the dipotassium salt to give a solution for electrometric titration.

MEASUREMENTS

Values of pK were determined by potentiometric titration, using glass and calomel electrodes. The temperature of the system was maintained at 25° C. The glass electrode was standardized with aqueous 0.05 molal potassium tetraoxalate (pH 1.68), 0.05 molal potassium hydrogen phthalate (pH 4.01), and the equimolal mixture of 0.025 molal potassium dihydrogen phosphate and 0.025 molal disodium hydrogen phosphate (pH 6.86).

The results are given in Table II. The first seven entries refer to monobasic acids; thus, although pyridine is itself a base, the pK value quoted is that of the conjugate acid and the dissociation process is:

$$BH^+ \rightleftarrows H^+ + B$$

The pK value of the pyridinium ion, BH^+, is given by the equation:

$$pK = pH + \log m_1/m_2 + \log \gamma_{BH^+}/\gamma_B$$

where m_1 is the molality of pyridinium ion and m_2 that of pyridine at any stage in the titration of a solution of pyridinium hydrochloride with sodium hydroxide. γ designates an activity coefficient and, for the dilute solutions used in this work, it suffices to write:

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Table I. Pyridine Derivatives Prepared

Name	M.P., ° C.	Previously Reported M.P., ° C.	Calcd.		Found
3,5-Dicarbethoxy-2,6-dimethylpyridine	72–73	73(*16*)	C	62.12	62.45
			H	6.82	6.65
			N	5.58	5.62
3,5-Dicarbethoxy-2,4,6-trimethylpyridine[a]	...	...	C	63.38	62.88
			H	7.22	7.33
			N	5.28	5.68
2,3,5,6-Tetracarbmethoxy-pyridine	112–13	118–19(*3*)	C	50.16	50.73
			H	4.21	4.22
			N	4.50	4.55
Pyridine-2,4-dicarboxylic acid	237–38	248–50(*12*)	C	50.31	50.23
			H	3.02	3.16
			N	8.38	8.32
Pyridine-3,5-dicarboxylic acid	322–23[b]	322(*4*)	C	50.31	50.36
			H	3.02	3.10
			N	8.38	8.39
Pyridine-2,5-dicarboxylic acid	254–55	254(*10*)	C	50.31	50.07
			H	3.02	3.21
			N	8.38	8.36
2,6-Dimethylpyridine-3,5-dicarboxylic acid	315–16[b]	316(*17*)	C	55.38	55.55
			H	4.65	4.71
			N	7.18	6.91
2,4,6-Trimethylpyridine-3,5-dicarboxylic acid	324–25	...	C	55.04	55.00
			H	5.57	5.80
			N	6.42	6.31
Pyridine-3,4,5-tri-carboxylic acid	275–76	261(*15*)	C	45.51	45.84
			H	2.39	2.53
			N	6.64	6.72
Pyridine-2,3,5,6-tetra-carboxylic acid	150–55[c]	150(*7*)	C	39.57	39.61
			H	2.58	2.64
			N	5.13	4.65
Pyridinepentacarboxylic acid	190–95[c]	200[c](*6*)	C	37.86	37.28
			H	2.23	2.99
			N	4.42	4.41

[a] B.p. 120–21° C. at 0.3–0.4 mm., density 1.080 at 25°; literature value (*5*) 1.087 at 150° C. [b] Sealed. [c] Decomposed.

Table II. Dissociation Constants of Pyridine and Some of Its Derivatives at 25° C.[a]

Pyridine	5.22	Pyridine-2,4-dicarboxylic acid	K_2 2.17
2,6-Dimethylpyridine	6.64		K_3 5.17
2,4,6-Trimethylpyridine	7.25	Pyridine-3,5-dicarboxylic acid	$K_1 \sim 1.1$
3,5-Dicyanopyridine	1.31		K_2 2.72
3,5-Dicarbethoxy-2,6-dimethylpyridine in			K_3 4.62
water	(2.96)[b]	Pyridine-2,5-dicarboxylic acid	K_2 2.49
30% methanol	2.66		K_3 5.12
40% methanol	2.54	2,6-Dimethylpyridine-3,5-dicarboxylic acid	K_1 1.72
50% methanol	2.45		K_2 2.81
60% methanol	2.35		K_3 6.16
70% methanol	2.25	2,4,6-Trimethylpyridine-3,5-dicarboxylic acid	K_2 1.77
3,5-Dicarbethoxy-2,4,6-trimethylpyridine in			K_3 6.57
water	(3.08)[b]	Pyridine-3,4,5-tricarboxylic acid	K_2 2.01
20% methanol	2.88		K_3 3.69
30% methanol	2.79		K_4 5.48
40% methanol	2.68	Pyridine-2,3,5,6-tetracarboxylic acid	$K_2 \sim 1.2$
50% methanol	2.57		K_3 2.52
60% methanol	2.48		K_4 4.16
2,3,5,6-Tetracarbmethoxypyridine in			K_5 5.58
water	1.99	Pyridinepentacarboxylic acid	$K_2 \sim 0.5$
40% methanol	1.95		K_3 1.97
50% methanol	1.92		K_4 3.46
60% methanol	1.89		K_5 4.91
			K_6 6.43

[a] Values quoted are those of pK (= − log K). [b] Values in parentheses are for aqueous solutions and have been obtained by extrapolation of pK values measured in water-methanol solvent mixtures.

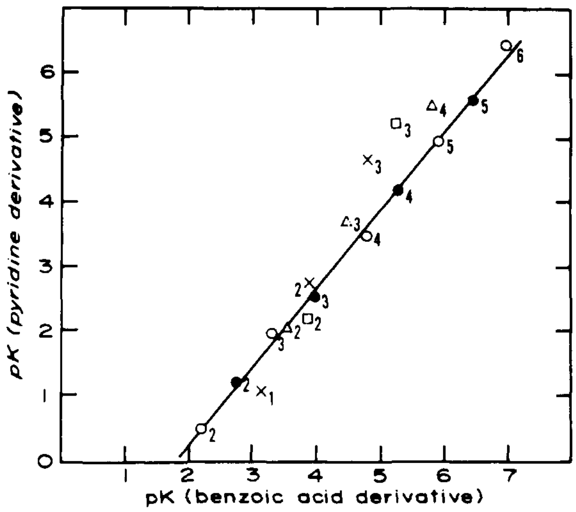

Figure 1. pK of a benzenepolycarboxylic acid vs. pK of a pyridine–polycarboxylic acid

○ Benzenehexacarboxylic acid–pyridinepentacarboxylic acid
● Benzenepentacarboxylic acid–pyridine-2,3,5,6-tetracarboxylic acid
△ Benzene-1,2,3,5-tetracarboxylic acid–pyridine-3,4,5-tricarboxylic acid
□ Benzene-1,2,4-tricarboxylic acid–pyridine-2,4-dicarboxylic acid
X Benzene-1,3,5-tricarboxylic acid–pyridine-3,5-dicarboxylic acid

The figure beside each point refers to the stage of dissociation. Thus, ○6 indicates the final stages of dissociation of benzene hexacarboxylic acid and pyridinepentacarboxylic acid.

$$-\log \gamma_{BH^+}/\gamma_B = AI^{1/2}/(1 + I^{1/2})$$

where A is the parameter of the Debye-Hückel equation (0.5108 kg.$^{1/2}$ mole$^{-1/2}$ for water at 25° C.) and I is the ionic strength of the solution.

The calculations become much more tedious in the case of a polycarboxylic acid with overlapping dissociation constants. The treatment in such cases has been outlined (*14*). Of the compounds listed in Table II, two were insufficiently soluble in water to enable meaningful titrations to be made. Measurements were, therefore, made in a number of water-methanol solvents. A small correction could be made to the data reported to allow for the liquid junction potential at the interface between the water-methanol solution and the aqueous calomel electrode (*13*). The data in Table II have not been corrected because the purpose of these titrations was to obtain extrapolated values in aqueous solution, and both corrected and uncorrected pK values led to the same extrapolated values for methanol-free solvent.

Accurate pK values are difficult to obtain by potentiometric titration if the pK value is small, of the order of 2 or less. Such values in Table II should, therefore, be taken as indicating only an approximation.

DISCUSSION

The value of pK = 5.22 for pyridine itself agrees with an earlier determination (*1, 8*), but the value of 6.64 for 2,6-dimethylpyridine is not in such good agreement with the earlier value (*1, 8*) of 6.72.

Perhaps the most interesting feature of these results is illustrated in Figure 1, where the pK values of a number of benzenepolycarboxylic acids are plotted against those of the corresponding pyridinecarboxylic acids. Thus, the point at the top right-hand corner represents the pK value for the last stage of the dissociation of benzenehexacarboxylic acid and that for the last stage of the dissociation of pyridinepentacarboxylic acid. There is an approximately linear relation between the points in Figure 1—i.e., the benzenepolycarboxylic acids and the pyridinecarboxylic acids have a kind of Hammett rule relation. The correlation is particularly good for the five points for benzenehexacarboxylic acid and the four points for benzenepentacarboxylic acid.

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