ice-cold solution of 30 ml. of concentrated sulfuric acid in 150 ml. of water. The liberated monoperphthalic acid was extracted into the ether and removed completely from the water by 3 more 150-ml. portions of ether. The combined ether extracts were washed with a 200-ml. portion of 40% ammonium sulfate solution and dried overnight in the cold over 50 g. of anhydrous magnesium sulfate. Analyses[3] for both hydrogen peroxide and for monoperphthalic acid indicated the presence of less than 0.02 mole of the former and 0.39 mole (78% yield based on phthalic anhydride or 65% on H_2O_2 applied) of the latter.

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Basicity and Ionization Constants of Some Pyrazine Derivatives

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Received March 11, 1959

Pyrazine and the methyl derivatives of pyrazine are such weak bases that aqueous potentiometric titrations fail. However these bases are readily titrated in glacial acetic acid with perchloric acid. Under these conditions only one of the pyrazine nitrogens will be titrated. The ionization constant for the pyrazine derivatives is expressed as the classical concentration constant by Equation 1. The ratio of the protonated amine to free amine in aqueous solutions was determined spectrophotometrically.

$$K = \frac{[R_3NH^+]\,[OH^-]}{[R_3N]} \qquad (1)$$

where

$[R_3NH^+]$ is the molar concentration of the protonated amine ion,
$[OH^-]$ is the molar concentration of the hydroxide ion,
$[R_3N]$ is the molar concentration of the free amine.

The spectrum of 0.0002 mole of 2,5-dimethylpyrazine in a liter of tenth molar sodium hydroxide shows a broad unsymmetrical absorption peak in the region of 300 to 250 millimicrons, with an adsorption maximum at 275 millimicrons. The spectrum obtained when 0.0002 mole of the amine is dissolved in a liter of one molar hydrochloric acid shows a symmetrical peak for the same region, with an absorption maximum at 284 millimicrons. If 0.0002 mole of the amine is dissolved in a liter of tenth normal perchloric acid where glacial acetic acid is the solvent the spectrum corresponds to that obtained for the amine in the one molar hydrochloric acid. Therefore in one molar hydrochloric acid the amine is monoprotonated. When the amine is dissolved in more dilute hydrochloric acid solutions, the spectra obtained are intermediate between the two extremes. In tenth molar sodium hydroxide the spectrum is characteristic of the unprotonated amine. Using the appropriate spectra, the molar absorbancy index for the free amine and for the protonated amine can be calculated. The *p*H of the aqueous solution can be measured using the glass electrode, calibrated with reference buffers. From the *p*H, and the ionic strength, $[OH^-]$ can be estimated using the activity coefficients of Kortüm and Bockris[1] to obtain $[OH^-]$ in units of moles per liter. These measured quantities are sufficient to calculate from Equation I ionization constants for each derivative.

EXPERIMENTAL

Purified pyrazine derivatives were dissolved in various concentrations of hydrochloric acid, and in 0.1*M* sodium hydroxide. Spectral measurements were made using the Perkin-Elmer Spectracord 4000. These spectra were analyzed using the procedure above to calculate the constants in Table I.

TABLE I

IONIZATION CONSTANTS FOR PYRAZINE AND ITS METHYL DERIVATIVES (t = 25°C.)

No.	Compound	K	*p*K	Ionic Strength
1	Pyrazine	1.3×10^{-13}	12.9	0.001
2	2-Methylpyrazine	3.0×10^{-13}	12.5	0.001
3	2,5-Dimethylpyrazine	1.1×10^{-12}	11.9	0.001
4	2,6-Dimethylpyrazine	4.4×10^{-12}	11.5	0.001
5	2,3,5,6-Tetramethylpyrazine	6.7×10^{-12}	11.2	0.01

DISCUSSION

Pyrazine is a weak organic base, with a *p*K of 12.9. Substitution of a methyl group into the 2 position of the pyrazine ring approximately doubles the basicity. Introduction of another methyl group in the five position causes approximately a tenfold increase in basicity, but when the second methyl group is introduced into the six position the basicity is increased more than thirty-fold. Introduction of four methyl groups into all available positions on the pyrazine ring results in a fifty-fold increase in basicity. In summary, the basicity of the pyrazine nitrogen increases with the number of ring hydrogens replaced by methyl groups. For disubstitution the increase is greater if the two methyl groups are substituted on carbon atoms adjacent the same nitrogen.

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Ionization Constants for Some Piperazine Derivatives

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Received March 11, 1959

A potentiometric titration method has been used to determine ionization constants for piperazine

TABLE I

IONIZATION CONSTANTS FOR PIPERAZINE AND DERIVATIVES (t = 25°c.)

No.	Compound	pK_1	pK_2	K_1[a]	K_2[b]
1	Piperazine	3.97	8.34	1.07×10^{-4}	3.6×10^{-9}
2	2-Methylpiperazine	4.10	8.54	8.0×10^{-5}	2.9×10^{-9}
3	2,5-Dimethylpiperazine (*cis*)	4.02	8.77	9.5×10^{-5}	1.7×10^{-9}
4	2,5-Dimethylpiperazine (*trans*)	4.16	8.66	6.9×10^{-5}	2.2×10^{-9}
5	2,6-Dimethylpiperazine	4.14	8.60	7.2×10^{-5}	2.5×10^{-9}
6	1,2,4-Trimethylpiperazine	5.64	10.06	2.3×10^{-6}	8.6×10^{-11}
7	1,4-Bis(2-hydroxypropyl)-2-methylpiperazine	5.85	10.37	1.4×10^{-6}	4.3×10^{-11}
8	1,4-Bis(3-dimethylaminopropyl)-*trans*-2,5-dimethylpiperazine[c]	4.57	4.57	2.7×10^{-5}	2.7×10^{-5}
9	2,3,5,6-Tetramethylpiperazine	4.06	8.89	8.7×10^{-5}	1.3×10^{-9}

[a] ionic strength, $\mu = 2.5 \times 10^{-2}$. [b] ionic strength, $\mu = 7.5 \times 10^{-2}$. [c] $K_3 = 2.1 \times 10^{-1}$; $pK_3 = 8.68$; ionic strength, $\mu = 1.3 \times 10^{-1}$.

and some of its derivatives. Classical concentration constants were calculated for a specified ionic strength.

EXPERIMENTAL

The purity of the amines selected for these studies was determined by titration, and assayed 98 ± 2% in all cases on a dry weight basis. Where the amines were dibasic the two titration breaks were equal. Purity was further substantiated by boiling point or melting point data, and gas chromatography.

About 0.005 mole of amine was dissolved in 100 ml. of distilled water and titrated with 0.5*N* hydrochloric acid. Potentiometric titrations were performed at 25°. The electrode system was standardized before and after each titration using *p*H 4.00, 7.00, and 10.00 reference buffers. The activity coefficient of Kortüm and Bockris was used to calculate hydroxide ion concentration.[1] At least two titrations meeting all the specified conditions were performed for each amine.

The results are summarized in Table I.

DISCUSSION

All *p*K values for the bases considered were calculated for the buffer region where effect of impurities is slight. Maximum deviation from the average *p*K values was ± 0.05 *p*K units. Average deviation was ± 0.03 *p*K units.

The values in Table I show that the addition of one to four methyl groups in the 2,3,5 and/or 6 ring positions decreases the basicity of the amine only slightly. However substitution in the 1,4 position, so that the amine is changed from a secondary amine to a tertiary amine, causes a larger decrease in basicity. In the case of 1,4-bis(3-dimethylaminopropyl)-*trans*-2,5-dimethylpiperazine both side chain amine nitrogens titrate in water as one end point. Only one of the ring nitrogens is titrated, and this nitrogen is a very weak base. Comparison of compounds number 6, and 7 suggests that the 2-hydroxypropyl group is a stronger electron attracting group than the methyl group, thereby reducing the electron density of the amine nitrogen and rendering it less basic. In summary, the basicity of the piperazine nitrogen decreases with methyl substitution of the ring hydrogens, and the decrease in basicity is greater for disubstitution and greatest for trisubstitution.

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Oxidation of Hindered Phenols. IX. Equilibria between Phenoxy Radicals

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Received March 11, 1959

In 1926 Conant suggested[1] that a hydrogen atom may be reversibly removed from a phenolic hydroxyl group. This suggestion, which formed part of the basis for Conant's apparent oxidation potential scale, seems eminently reasonable, and has received support from Fieser's measurements of critical oxidation potentials[2] and recently through molecular orbital calculations.[3] During our work on stable phenoxy radicals, equilibria between such radicals and their parent phenols have frequently been observed.[4]

Thus, if a small amount of 2,6-di-*t*-butyl-4-*t*-butyoxyphenol is added to a solution of the blue 2,4,6-tri-*t*-butylphenoxy (I), the red color of 2,6-di-*t*-butyl-4-*t*-butoxyphenoxy (II) immediately appears. On addition of 2,4,6-tri-*t*-butylphenol to this solution the color changes to purple and, if enough of the tri-*t*-butylphenol is added, goes back to blue. Obviously, a mobile equilibrium exists; hence, we undertook the evaluation of the equilibrium constant. Since a relatively large number of

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