

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<sup>3</sup> 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<sub>2</sub>O<sub>2</sub> applied) of the latter.

SHELL DEVELOPMENT CO.  
EMERYVILLE, CALIF.

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### Basicity and Ionization Constants of Some Pyrazine Derivatives

DONALD A. KEYWORTH

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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.

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

where

[R<sub>3</sub>NH<sup>+</sup>] is the molar concentration of the protonated amine ion,

[OH<sup>-</sup>] is the molar concentration of the hydroxide ion,  
[R<sub>3</sub>N] 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 pH of the aqueous solution can be measured using the glass electrode, calibrated with reference buffers. From the pH, and the ionic strength, [OH<sup>-</sup>] can be estimated using the activity coefficients of Kortüm and Bockris<sup>1</sup> to obtain [OH<sup>-</sup>] in units of moles per liter. These measured quantities are sufficient to calculate from Equation 1 ionization constants for each derivative.

#### EXPERIMENTAL

Purified pyrazine derivatives were dissolved in various concentrations of hydrochloric acid, and in 0.1M 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	pK	Ionic Strength
1	Pyrazine	$1.3 \times 10^{-13}$	12.9	0.001
2	2-Methylpyrazine	$3.0 \times 10^{-13}$	12.5	0.001
3	2,5-Dimethylpyrazine	$1.1 \times 10^{-12}$	11.9	0.001
4	2,6-Dimethylpyrazine	$4.4 \times 10^{-12}$	11.5	0.001
5	2,3,5,6-Tetramethylpyrazine	$6.7 \times 10^{-12}$	11.2	0.01

#### DISCUSSION

Pyrazine is a weak organic base, with a pK 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.

RESEARCH DIVISION  
WYANDOTTE CHEMICALS CORPORATION  
WYANDOTTE, MICH.

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### Ionization Constants for Some Piperazine Derivatives

DONALD A. KEYWORTH

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