

Bifunctional Amines and Ammonium Compounds. VII*

Base Strengths of Some *Tert.* Amino Alkyl Ethers

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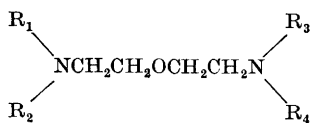
It was thought that information concerning the role of charge distribution in the structure-activity relations of a series of biologically active bis-quaternary ammonium salts of aliphatic ethers currently being studied in these laboratories could be had by determining the dissociation constants of the tertiary precursors of these ammonium compounds. The values found are recorded here.

Method. The freshly distilled tertiary amines were estimated by perchloric acid titration. A quantity sufficient to give 100 ml of a 0.0025 M solution was dissolved by addition of the equivalent amount of 0.1 N HCl. This solution was backtitrated according to Marshall¹ (cf. also Gero and Markham² and Campbell, Fatora and Campbell³).

The values for pK obtained with an observed $pH > 9$ are corrected for contribution of hydroxyl ions present thus:

$$pK = pH - \log \frac{C_B - C_{OH^-}}{C_{BH^+} + C_{OH^-}}$$

The pK values are plotted in Fig. 1 against the number of methyl substituents in the amino groups (lower tracing pK_1 , upper tracing pK_2).



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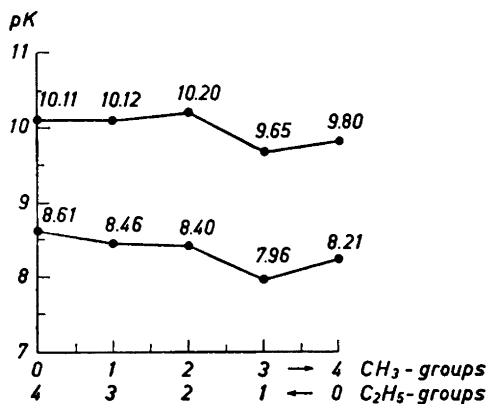


Fig. 1

The ionization constants do not differ very much within the series although both the first and second ionization constant pass through a minimum obtained with the bis-(2-diethyl-amino-2'-ethylmethyl-amino)-ethyl ether.

The interpolation of an ether oxygen between the two nitrogen atoms ought to enhance the inductive mutual hindrance of basic action between them. Thus these amino ethers should be weaker bases than the corresponding polymethylene diamines. No values are recorded for *N*-alkylsubstituted polymethylene-diamines, but Gero⁴ has reported the pK_1 and pK_2 values for the unsubstituted pentamethylene-diamine to be 9.13 and 10.25, respectively.

1. Marshall, P. B. *Brit. J. Pharmacol.* **10** (1955) 270.
2. Gero, A. and Markham, J. J. *J. Org. Chem.* **16** (1951) 1835.
3. Campbell, K. N., Fatora, F. C. jr. and Campbell B. K. *J. Org. Chem.* **17** (1952) 1141.
4. Gero, A. *J. Am. Chem. Soc.* **76** (1954) 5159.

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