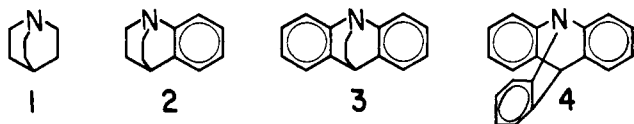# pKa of Azatriptycene

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The pKa of azatriptycene (9H-9,10(1′,2′)-benzenoacridine) (4) is measured and found to be 2.1. This value is obtained by potentiometric titration of 4 at 25° with $HClO_4$ in anhydrous HOAc and is related to the aqueous system through the relationship of Wegmann and Simon. The inductive effect of adding benzo-substituents to 1 reduces the basicity an average of 2.8 pK units per substituent.

Aryl amines are approximately six orders of magnitude less basic than aliphatic amines. This decrease in basicity is attributed to both resonance and inductive effects. Van der Krogt and Wepster (*9, 11*) have measured the basicities of quinuclidine (**1**), benzoquinuclidine (**2**), and dibenzoquinuclidine (**3**) (pKa's 10.58, 7.79, and 4.46, respectively, at 25°C). Since the nitrogen lone pairs in these compounds are orthogonal to the pi systems, resonance effects are minimal, and the ΔpKa's of ~3 pK units which Wepster observed are attributed solely to the inductive effects of the phenyl rings. We have now measured the pKa of the final compound in this series, azatriptycene (*12*) [9H-9,10(1′,2′)-benzenoacridine] (**4**), and report the change in basicity for the addition of the third benzo substituent to quinuclidine.

The insolubility of azatriptycene and its salts in water precluded the direct measurement of the pKa in this solvent. The measurement was therefore carried out in acetic acid (HOAc) and referred back to the aqueous system through the relationship of Wegmann and Simon (*10*).

Kolthoff and Bruckenstein (*2-4, 7, 8*) have developed equations defining a pH scale in HOAc. Wegmann and Simon (*10*) have measured apparent pKa's of a number of bases by potentiometric titration of them with anhydrous perchloric acid ($HClO_4$) in HOAc. The apparent pKa's were defined as equal to the pH at half-neutralization:

$$pK'_{HOAc} = pH \text{ half-neutralization} =$$

$$9.18 - \frac{(E_{NaOAc} - E_{Base})}{59.16} \quad (1)$$

The reference point of 9.18 corresponds to the theoretical pH of a $0.003M$ solution of sodium acetate (NaOAc) in anhydrous HOAc at half-neutralization as calculated using the equations of Kolthoff and Bruckenstein. The potentials in Equation 1 are measured potentials of $0.003M$ NaOAc and base at half-neutralization.

Potentiometric titrations of NaOAc and azatriptycene in HOAc with anhydrous $HClO_4$ in HOAc were carried out at 25°C with a glass electrode and a modified calomel electrode similar to that used by Wegmann and Simon (*10*). Sample titration curves are shown in Figure 1. The measured potentials for NaOAc and azatriptycene at half-neutralization are −296 and −406 mV, respectively. The pK'$_{HOAc}$ for azatriptycene, as calculated from Equation 1, is 7.32.

As a check, the pK'$_{HOAc}$ for diphenylamine (pK'$_{HOAc}$ = 6.22 at 25°C) was also measured by this method. This corresponds well with the value obtained previously by Wegmann and Simon (*10*) (pK'$_{HOAc}$ = 6.09 at 25°C).

Wegmann and Simon (*10*) have also shown that for amines there exists a good linear relationship between the pK'$_{HOAc}$ and the corresponding pKa in aqueous solution. By use of this relationship, it is possible to estimate the aqueous pKa for azatriptycene to be 2.1. This is in excellent agreement with an earlier estimate of 2.0 which we obtained using *o*- and *m*-chloroaniline for calibration, an aqueous combination pH electrode, and utilizing an earlier relationship between pK'$_{HOAc}$ and pKa aqueous derived by Hall (*6*).

By obtainment of a value for the pKa of azatriptycene, it is evident that for the series of compounds **1, 2, 3,** and **4,** the inductive effects for the successive benzo substitutions of qui-
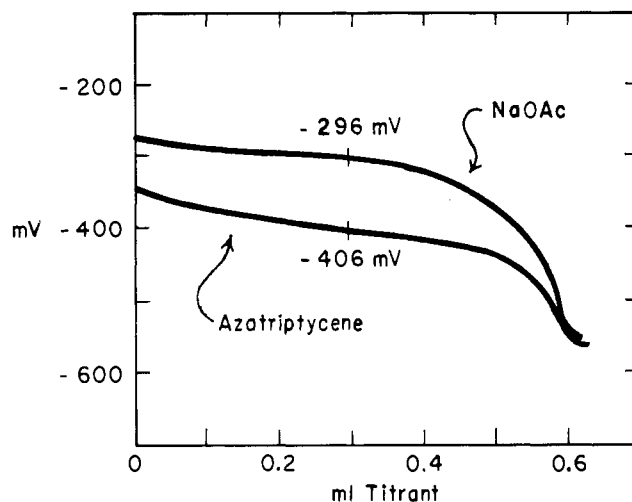

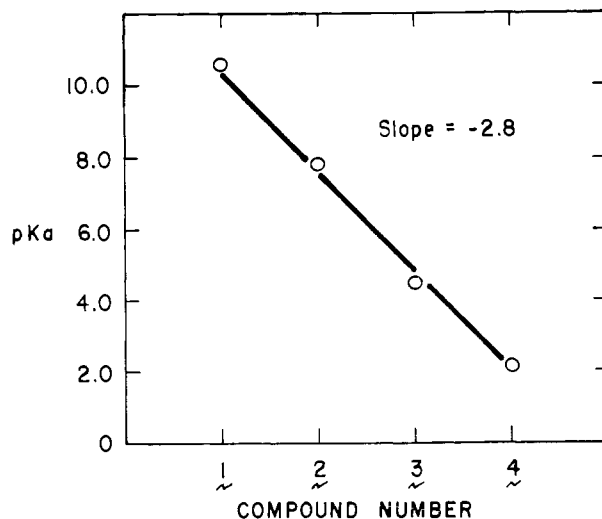Figure 1. Sample titration curves for NaOAc and azatriptycene

Figure 2. Relationship between pKa and degree of benzo substitution for quinuclidine and its benzo derivatives

nuclidine are approximately additive and lead to an average reduction in pKa of 2.8 pK units per benzo substitution. This relationship is shown in Figure 2.

Experimental

Anhydrous HOAc was prepared by distillation from triacetyl borate following Eichelberger and LaMer (5). Analysis of the distillate by the method of Bruckenstein (1) revealed no detectable H_2O. The ~0.1N $HClO_4$ titrant in anhydrous HOAc was prepared by adding 5.1 ml acetic anhydride to 2.2 ml of 70% $HClO_4$ in 70 ml HOAc. The mixture was then diluted to 250 ml with HOAc and allowed to stand for several days before use. The NaOAc was dried at 110°C for 24 hr prior to the preparation of the standard solution.

The titrations were carried out in a constant temperature bath at 25° ± 0.5°C using a Leeds and Northrup Model 7403-A2 pH meter. A Leeds and Northrup #1199-72 glass electrode was used as the indicating electrode, and the reference electrode was a modified calomel electrode containing a saturated solution of NaCl, $NaClO_4$, and Hg_2Cl_2 in anhydrous HOAc (4).

Samples containing ~0.06 meq base in 20 ml HOAc were titrated with the $HClO_4$ titrant using a 10-ml microburet. Prepurified N_2, dried by passing through a Drierite drying tower and saturated with HOAc by bubbling through anhydrous HOAc, was passed over the solutions throughout the titrations.

The preliminary experiment was run in anhydrous HOAc with a Sargent S-300072-15 combination electrode. The o- and m-chloroaniline, used as references, were purified by distillation.

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Synthesis of Certain l-Menthol Compounds

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Several new optically active l-menthol derivatives are synthesized by several different techniques. The index of refraction, boiling or melting points, optical rotatory dispersion, infrared spectrum identification, and percent yield are reported.

l-Menthoxy compounds are of considerable interest because of their utility as monodentate probes in the determination of vicinal and chromophoric effects on the induced Cotton effect of the cobalt (III) d-d transitions (3). Several new l-menthoxy ligands have been synthesized and are reported herein. The synthesis and structural determination of transition-metal complexes of these ligands are presently being investigated in this laboratory.

Experimental

l-Menthoxypropanenitrile (I) was prepared by alkaline condensation of l-menthol with acrylonitrile using trimethyl benzyl ammonium hydroxide according to the method of Bruson (1). The colorless oil had a bp 108-110°/2 torr (lit bp 149°/10 torr). l-Menthoxybutanenitrile (II) was prepared from l-menthol and allyl cyanide by the same procedure as for (I). The colorless oil had a bp of 122-125°/2 torr. l-Menthoxypropanoic acid (III) was prepared by acid hydrolysis of (I) according to the general method for hydrolysis of alkoxypropanenitriles (4).

The colorless oil had a bp of 130-133°/2.7 torr. l-Menthoxybutanoic acid (IV) could not be prepared by general methods of either alkaline (2) or acid (4) hydrolysis for alkoxynitriles. Instead, it was prepared by the reactions of sodium l-menthoxide and 4-chlorobutanoic acid according to the method used for the synthesis of l-menthoxyacetic acid (5). The straw-colored oil had a bp of 134-137°/2 torr. l-Menthoxyacetamide (V) was prepared by conversion of l-menthoxyacetic acid (Aldrich Co.) to the acetyl chloride with thionyl chloride (6) and subsequent conversion to the amide by bubbling ammonia gas through an ethereal solution of the acetyl chloride for 4 hr. The solid product was twice recrystallized from hot water and subsequently sublimed, mp (uncorrected) 71-72°. l-Menthoxyethylamine (VI) was prepared by reduction of (V) with lithium aluminum hydride (7). The colorless oil had a bp of 126-130°/6 torr. Physical properties of Compounds I-VI are shown in Table I.

Melting points were determined on a Hoover mp apparatus. IR spectra were measured from thin films of the neat liquid (a melt of the solid acetamide) between NaCl plates. Continuous ORD spectra from 580 to 210 nm were measured from 3.22 mg/l. ethanolic solutions on a Cary 60 spectropolarimeter using 1-cm quartz cells. All of the ligands exhibited plain negative Drude ORD spectra over these regions. Optical rotations at 578, 546, 436, 365, and 313 nm were rechecked on a Perkin Elmer 241 spectropolarimeter, using larger quartz cells (1 dm) at the same ligand concentrations. Specific rotations agreed with ±0.2% for both instrumental measurements. Satisfactory elemental analyses were obtained for all new compounds (Huffman Labs, Wheatridge, Colo., and Schwarzkopf Labs, New York, N.Y.).

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