

**2-Benzyl-4-chloro-6-dimethylaminomethylphenol.**—Using 219 g. (1.0 mole) of 2-benzyl-4-chlorophenol, 190 ml. of aqueous dimethylamine and 80 ml. of formalin, the Mannich reaction was carried out as above. On neutralization of the acid extracts, the Mannich base separated as a solid. It was extracted into benzene (its solubility in ether was very low), and the benzene solution dried by shaking with saturated sodium chloride and filtering through anhydrous sodium sulfate. The benzene was evaporated and the crude product crystallized from methanol, giving 209 g. (76% yield) of 2-benzyl-4-chloro-6-dimethylaminomethylphenol, m.p. 84.5–86.5°. Repeated recrystallization from methanol sharpened the m.p. to 85.5–86.5°.

*Anal.* Calcd. for  $C_{16}H_{18}ClNO$ : C, 69.7; H, 6.6. Found: C, 69.7; H, 6.7.

RESEARCH DIVISION  
BRISTOL LABORATORIES, INC.  
SYRACUSE 1, NEW YORK

### The Acidity Constant, Solubility Product and Solubility of Dithioöxamide<sup>1</sup>

BY RUTH POWERS YAFFE AND ADOLF F. VOIGT

RECEIVED FEBRUARY 4, 1952

Dithioöxamide, frequently called rubeanic acid, is a well-known complexing agent of the platinum group metals. It is readily soluble in alkaline solutions and forms salts which have been called rubeanates. Although the acidic behavior of dithioöxamide is well known, no determination of its acidity constant has been reported.

The method followed for this determination was the potentiometric titration procedure for acids of limited solubility given by Back and Steenberg.<sup>2</sup>

The potentiometric titrations were made with a Beckman Model G pH meter equipped with a #1190-E High pH Glass Electrode. A known quantity of dithioöxamide was dissolved in a known excess volume of standard base. This solution was then titrated with a standard acid. At the beginning of the titration the weak acid was in the form of its soluble salt in a slight excess of base. After this excess base was neutralized, a known concentration,  $C_s$ , of titrating acid was added and the pH measured. This process was repeated with about five additions of acid before flocculation occurred. From each of these measurements a value of  $pK_a$  was calculated by means of equation (1)

$$pK_a = pH + \log \left\{ \frac{C_s + C_{OH} - C_H}{C_a + C_H - C_s - C_{OH}} \right\} + \frac{0.5 \sqrt{\mu}}{1 + \sqrt{\mu}} \quad (1)$$

where  $C_a$  is the total concentration of the weak acid  $[HA + A^-]$ . The titration was continued through the stage of flocculation, about five more measurements being obtained before salting out of the dithioöxamide at the reference electrode caused the results to be inconsistent. These data were used in equation (2) to calculate the solubility product.

$$pK_{sp} = pH - \log \{ C_a + C_H - C_s - C_{OH} \} + \frac{0.5 \sqrt{\mu}}{1 + \sqrt{\mu}} \quad (2)$$

The solubility of the acid is given by the relation

$$S = K_{sp}/K_a \quad (3)$$

(1) Contribution No. 171 from the Institute for Atomic Research and the Department of Chemistry, Iowa State College, Ames, Iowa. Work performed in the Ames Laboratory of the Atomic Energy Commission.

(2) E. Back and B. Steenberg, *Acta Chem. Scand.*, **4**, 810 (1950).

It was found that the dithioöxamide behaved as a monobasic acid. Equations (1) and (2) give the thermodynamic constants since they contain an expression for the activity coefficient of the acid ion, and the hydrogen ion activity is determined directly. The values of  $\mu$  used in the equations were calculated for each point and were approximately 0.01. In each titration, 5 or 6 individual determinations of  $K_a$ ,  $K_{sp}$  and  $S$  were obtained. In all, five complete titrations were carried out. The over-all averages of these 25 to 30 determinations and their standard deviations are: for the acidity constant,  $K_a$ ,  $(1.28 \pm 0.04) \times 10^{-11}$ , for the solubility product,  $K_{sp}$ ,  $(3.94 \pm 0.12) \times 10^{-14}$  and for the solubility,  $S$ ,  $(3.07 \pm 0.04) \times 10^{-3}$  mole per liter.

In addition to these thermodynamic constants, the non-thermodynamic constants at an ionic strength of 1.0 were desired. Sodium perchlorate, made by dissolving sodium carbonate in perchloric acid, was used as the inert electrolyte. Three complete titrations were made, and the results averaged. The non-thermodynamic constants may be summarized as follows:  $k_a = (3.78 \pm 0.04) \times 10^{-11}$ ;  $k_{sp} = (6.27 \pm 0.14) \times 10^{-14}$ ;  $s = (1.66 \pm 0.03) \times 10^{-3}$  mole per liter.

AMES LABORATORY  
IOWA STATE COLLEGE  
AMES, IOWA

## NEW COMPOUNDS

### Derivatives of *p*-Aminosalicylic Acid<sup>1,2</sup>

Two derivatives of *p*-aminosalicylic acid have been prepared.

**Methyl N-(2-Hydroxyethyl)-*p*-aminosalicylate.**—To a vigorously stirred solution of 33.4 g. (0.2 mole) of methyl *p*-aminosalicylate (prepared from commercial *p*-aminosalicylic acid<sup>3</sup>) and 700 ml. of anhydrous ether in a one-liter flask surrounded by an ice-bath were added simultaneously over a period of 30 minutes 61 ml. (0.1 mole) of a 10% solution of ethylene oxide in anhydrous ether and 40 ml. of a 2% solution of boron trifluoride etherate in anhydrous ether. After two hours of additional stirring, the ice-bath was removed and stirring continued for 30 minutes. The mixture was then heated at reflux temperature for one hour, transferred to a separatory funnel and extracted quickly with three 150-ml. portions of 10% sodium hydroxide solution. The extracts were combined, treated with carbon dioxide, and filtered at intervals to obtain the precipitate in several fractions. These were dried in a vacuum desiccator, dissolved in anhydrous ether, filtered from any carbonates, and the ether evaporated. Each fraction was a mixture of methyl *p*-aminosalicylate (I) and methyl N-(2-hydroxyethyl)-*p*-aminosalicylate (II), the latter being present in increasing proportions in successive fractions. By fractional sublimation at 0.02–0.05 mm. pressure 24.1 g. of I and 2.9 g. (37%) of II were obtained. From a mixture of benzene and petroleum ether II was obtained as a white crystalline solid, m.p. 90°.

*Anal.* Calcd. for  $C_{10}H_{12}NO_4$ : N, 6.63. Found: N, 6.53.

**N-(2-Hydroxyethyl)-*p*-aminosalicylic Acid.**—In a pear-shaped 25-ml. flask a mixture of 0.75 g. (0.0036 mole) of methyl N-(2-hydroxyethyl)-*p*-aminosalicylate and 4.27 ml. (0.0106 mole) of 10% sodium hydroxide solution were re-

(1) From the M. S. thesis of E. Kenneth Brakebill, June, 1951.

(2) This work was supported in part by a Research Corporation Grant-in-Aid.

(3) J. J. Schaefer and Leonard Doub, *THIS JOURNAL*, **71**, 3564 (1949).