# Derivatives of Some Alkoxybenzoic Acids

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EARLIER STUDIES have described the preparation and characterization of a number of isomeric alkoxybenzoic acids (*1*) and local anesthetic activity of the hydrochlorides of some dialkylaminoethyl esters of these alkoxybenzoic acids (*2*). Some amide and anilide derivatives of these alkoxybenzoic acids have the type structure

$ROCH_2CH_2O$-  $-CO-NH_2$(or $-NHC_6H_5$)

where R = $CH_3$, $C_2H_5$, and $C_6H_5$.

Alkoxybenzoyl chloride was prepared from alkoxybenzoic acid and excess thionyl chloride, then alkoxybenzoyl chloride was reacted with concentrated ammonium hydroxide to form the amide or with aniline to form the anilide.

The alkoxybenzamides and some of their properties are listed in Table I, and the alkoxybenzanilides are listed in Table II. The composition of these new derivatives has been verified by chemical and infrared spectral analysis.

## EXPERIMENTAL PROCEDURE

**Alkoxybenzoyl Chlorides.** In a 250-ml. round-bottomed flask equipped with a reflux condenser were placed 0.15 mole of the alkoxybenzoic acid and 47.6 grams (0.4 mole) of thionyl chloride. The mixture was refluxed gently on a steam bath for 45 minutes or until no more hydrogen chloride was evolved. The excess thionyl chloride was then removed under reduced pressure, and the crude alkoxybenzoyl chloride was purified by vacuum distillation. It was found later that the crude alkoxybenzoyl chloride could be converted into the alkoxybenzamide or alkoxybenzanilide just as satisfactorily as the purified alkoxybenzoyl chloride.

**Alkoxybenzamides.** In a 500-ml. three-necked flask equipped with a dropping funnel, mechanical stirrer, and reflux condenser was placed 250 ml. of concentrated ammonium hydroxide. The flask was immersed in an ice-salt bath and the solution was throughly chilled. If the alkoxybenzoyl chloride was a solid at room temperature, it was warmed gently in order to liquefy it, and 0.15 mole of the alkoxybenzoyl chloride was placed in a warmed dropping funnel. With vigorous stirring the alkoxybenzoyl chloride was added by drops to the cold ammonium hydroxide, the rate of addition being such that no product was lost from the condenser. After all of the alkoxybenzoyl chloride had been added, the temperature was raised to 40° C. and held constant for 2 hours. Upon cooling, the alkoxybenzamide precipitated, was filtered and dried. The alkoxybenzamide was recrystallized from aqueous ethanol (Table I) until a constant melting point was obtained.

**Alkoxybenzanilides.** In a 500-ml. three-necked flask equipped with a dropping funnel, mechanical stirrer, and reflux condenser was placed 5.6 grams (0.06 mole) of aniline. Alkoxybenzoyl chloride (0.02 mole in 75 ml. of benzene) was then added slowly from dropping funnel to aniline with stirring. After all of the alkoxybenzoyl chloride had been added, the reaction mixture was refluxed gently on a stream bath for 30 minutes. The solution was cooled, the precipitate of aniline hydrochloride filtered, and the benzene

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Table I. Preparation of R-  $-CONH_2$

| R | M.P., ° C. | Yield, % | Formula | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|
| *p*-(2-Butoxyethoxy)- | 111-112 | 70 | $C_{13}H_{19}NO_3$ | 5.90 | 5.82*T* |
| *m*-(2-Ethoxyethoxy)- | 103.5-105 | 35 | $C_{11}H_{15}NO_3$ | 6.69 | 6.70 |
| *o*-(2-Ethoxyethoxy)-[a] | 70-71.5 | 39 | $C_{11}H_{15}NO_3$ | 6.69 | 6.52 |
| *p*-(2-Ethoxyethoxy)- | 132.5-133.5 | 68 | $C_{11}H_{15}NO_3$ | 6.69 | 6.67 |
| *m*-(2-Methoxyethoxy)-[b] | 79.5-80.5 | 30 | $C_{10}H_{13}NO_3$ | 7.18 | 7.09 |
| *p*-(2-Methoxyethoxy)- | 153-154.5 | 83 | $C_{10}H_{13}NO_3$ | 7.18 | 7.08 |
| *p*-(2-Phenoxyethoxy)-[c] | 203.5-204 | 62 | $C_{15}H_{15}NO_3$ | 5.57 | 5.57 |

[a] Amide recrystallized from 95% ethanol. [b] Amide recrystallized from petroleum ether (30°-60° C.). [c] Amide recrystallized from dioxane.

Table II. Preparation of R-  $-CO-NH-C_6H_5$

| R | M.P., ° C. | Yield, % | Formula | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|
| *m*-(2-Ethoxyethoxy)- | 65.5-67 | 45 | $C_{17}H_{19}NO_3$ | 4.91 | 4.77 |
| *o*-(2-Ethoxyethoxy)- | 60-61.5 | 40 | $C_{17}H_{19}NO_3$ | 4.91 | 4.73 |
| *p*-(2-Ethoxyethoxy)- | 114.5-115 | 66 | $C_{17}H_{19}NO_3$ | 4.91 | 4.88 |
| *p*-(2-Phenoxyethoxy)-[a] | 193.5-195 | 58 | $C_{21}H_{19}NO_3$ | 4.20 | 4.23 |

[a] Anilide recrystallized from dioxane.

filtrate containing the alkoxybenzanilide saved. The precipitate was washed with two 10-ml. portions of benzene, and the washings were added to the benzene filtrate, which was washed successively with 20 ml. of water, 25 ml. of 5% hydrochloride acid to remove excess aniline, and 25 ml. of 5% sodium hydroxide. At this point some of the alkoxybenzanilide precipitated, and ether was added to redissolve it. The benzene-ether filtrate was finally washed with water, then dried over anhydrous potassium carbonate. Evaporation of the benzene and ether under vacuum left the crude alkoxybenzanilide, which was recrystallized from aqueous ethanol (Table II) until a constant melting point was obtained.

## LITERATURE CITED

(1) Bost, R.W., Winstead, M.B., *J. Am. Chem. Soc.*, **74**, 1821 (1952).

(2) Winstead, M.B., Wishnoff, S.H., Bost, R.W., *Ibid.*, **77**, 772 (1955).

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# Uranium Content of Uranyl Nitrate Solutions by Specific Gravity Measurement at Ambient Temperature

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SEVERAL ATTEMPTS have been made to correlate the specific gravity of aqueous solutions of uranyl nitrate with the corresponding uranium concentration of the solutions. An equation and nomograph have been reported (*5*) for uranium concentration determination from the specific gravity of uranyl nitrate solutions at 25° C. Also, specific gravity-uranium concentration data for uranyl nitrate solutions have been published (*1, 4*) for a temperature range of 10° to 90° C. with equations of correlation in terms of the specific gravity at 25° C.

Previously reported work does not provide an expression for obtaining the uranium concentration of a solution directly from a specific gravity reading made at temperatures of 10° to 50° C. Therefore, an effort was made to derive such an expression and to produce a nomograph based upon it capable of providing a rapid yet accurate means of uranium determination.

## DERIVATION OF EQUATION

The data and equations reported by Perkins (*4*) furnish a basis to derive an equation relating specific gravity of a uranyl nitrate solution with its uranium concentration directly at temperatures ranging from 10° to 50° C. The equation presented by Perkins is of the form

$$\rho^{25}_{4} = b_0 + b_1 C + b_2 N \tag{1}$$

where

$C$ = uranium concentration of an aqueous uranyl nitrate solution, grams per liter
$N$ = normality of free acid content in the solution
$b_0$, $b_1$, and $b_2$ = numerical constants at 25° C.

Inspection and analysis of Perkins' data show, however, that linear relationships exist between the following variables:

*a*. Constants $b_0$ and $b_1$ and the square of the temperature
*b*. Uranium concentration and constant $b_2$
*c*. Specific gravity and uranium concentration when the free acid content is zero

Substitution of relations *a* and *b* in Equation 1 results in an equation of the following general form to fit the experimental data:

$$\rho^{t}_{4} = x_0 + x_1 t^2 + (x_2 + x_3 t^2)\ C + (x_4 + x_5 C)\, N$$

or

$$\rho^{t}_{4} = x_0 + x_1 t^2 + x_2 C + x_3 C t^2 + x_4 N + x_5 C N \tag{2}$$

where

$t$ = temperature of the uranyl nitrate solution, ° C.
$x_1$, $x_2$, $x_3$, $x_4$, and $x_5$ = numerical constants at any temperature $t$

To test the thesis that Equation 2 satisfactorily fits the experimental data of Perkins, the data were related in a multiple regression analysis programmed on a LGP-30 digital computer. Computer analysis showed that Equation 2 has a 99.6% multiple correlation and is the best of 13 possible relationships investigated. Stated with the values obtained by multiple regression

$$\rho^{t}_{4} = 1.0042 + 1.345 \times 10^{-3} C - 5.98 \times 10^{-6} t^2 - 1.12 \times 10^{-8} C t^2 + 2.51 \times 10^{-2} N + 3.14 \times 10^{-5} C N \tag{3}$$

Rearranged to express uranium concentration as the dependent variable, Equation 3 becomes

$$C = \frac{\rho^{t}_{4} - 1.0042 + 5.98 \times 10^{-6} t^2 - 2.51 \times 10^{-2} N}{1.345 \times 10^{-3} - 1.12 \times 10^{-8} t^2 + 3.14 \times 10^{-5} N} \tag{4}$$

## EXPERIMENTAL EVALUATION

A limited amount of experimental work was performed to supplement the data of Burger and Perkins in the practical ranges of the variables and to test the reliability of Equation 4 (derived from Perkins' data) over these ranges. Several aqueous solutions of uranyl nitrate were compounded and tested. The methods of measurement duplicated normal procedures used in laboratory practice. Specific gravity measurements were made with glass hydrometers having a