Neutron Activation Analysis of *l*-Ephedrine and Norephedrine Silver Complexes

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Silver complex pyridinates of *l*-ephedrine and norephedrine were prepared and analyzed by neutron activation. The analytical results have established satisfactory correlations between theoretical and experimental values for percent silver in the two compounds.

DURING THE PAST several years neutron activation analysis (NAA) has become a sensitive, powerful analytical tool effective for approximately two-thirds of the elements. NAA provides an analytical method without destruction of the sample. Activation is carried out by placing the sample in a neutron field; *i.e.*, in a nuclear reactor or a neutron howitzer, where thermal neutrons present create radioactive nuclides through an (n,γ) nuclear reaction. Analysis is usually achieved by measuring the radioactivity of the product nuclides by direct γ-ray spectrometry with a scintillation detector and a γ-ray spectrometer or a multichannel analyzer.

Quantitative measurements are made either by comparison of the sample with a standard or by mathematical calculations based on the knowledge of the neutron flux (1) as well as the efficiency and geometry of the γ-ray detector (2). Sometimes the actual measurement must be preceded by a radiochemical separation procedure. Basic principles and application of NAA are described in the literature as well as in the excellent reference books (3–6).

This paper presents an analytical procedure for the determination of silver in *l*-ephedrine and norephedrine silver complex pyridinates by neutron activation utilizing the $^{109}Ag(n,\gamma)^{110}Ag$ nuclear reaction and equipment available to educational and manufacturing facilities, and requiring a minimum of shielding.

EXPERIMENTAL

Both *l*-ephedrine and norephedrine silver complex pyridinates were prepared according to the method reported by Nakatsuka in 1936 (7) for the synthesis of argentic 8-hydroxyquinolinate.

Neutron Activation Analysis—Solid samples of the silver complex and a standard sample ($AgNO_3$) of approximately the same, but accurately known, weight were placed in separate 2-ml. volumetric flasks, and introduced into the irradiation ports of a neutron howitzer[1] containing 3 Ci of plutonium-beryllium. After 20 min. both the sample and the standard were removed and counted for 10 sec. The counting system consisted of a commercial shielded well scintillation detector with 4.4 × 5 cm. ($1^3/_4 \times 2$ in.) NaI(Tl) crystal.[2] The detector output was fed into a γ-ray spectrometer[3] set on the ^{110}Ag photopeak (0.663 Mev.) and using a 20-Kev. window. Since the irradiation time was sufficiently long to achieve saturation, and the time between the removal of the material from the howitzer and the beginning of counting was maintained constant for both the sample and the standard, no decay correction was necessary.

The silver content was calculated as follows:

$$\% \text{ silver in sample} = \frac{\text{g. of standard} \times \% \text{ silver in standard}}{\text{g. of sample}} \times \frac{\text{c.p.m. (sample)}}{\text{c.p.m. (standard)}}$$

RESULTS AND DISCUSSION

Table I summarizes the results of NAA *l*-ephedrine and norephedrine silver complex pyridinates. The data for the samples and the standards are the averages of 15 determinations.

The activity of the samples (A) was calculated from the relationship

$$A = \bar{n} \pm S_m$$

where $\bar{n}$ is the average count rate and S_m is the standard deviation of the mean (8). Chauvenet's criterion was applied to each set of data in order to determine whether or not any values should be rejected as not being representative of the Poisson distribution. The chi-square test (9) indicated that the counting equipment was operating properly. Because of the short half-life of the radionuclide produced (^{110}Ag), no time was required for any products to decay before counting as noted previously by some authors (10).

The results of this study have established satisfactory correlation between theoretical and experimental values for percent silver in the two compounds as indicated by 1.90 and 1.35% error for *l*-ephedrine and norephedrine silver complex pyridinates, respectively. This investigation primarily demonstrated the usefulness of NAA as a method for the determination of silver content of compounds having pharmaceutical interest. It also showed that by selecting suitable metals for complexation with some organic compounds, NAA can be carried out using isotopic neutron sources. The radioactive product is not excessively active and may be easily handled by laboratory technicians trained in the handling of radioactive isotopes.

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[1] Neutron-Pac, Irradiator-Howitzer, NAC-64, Nuclear Materials and Equipment Corp., Apollo, Pa.

[2] Model 810B, Baird-Atomic, Inc., Cambridge, Mass.

[3] Model 530, Baird-Atomic, Inc., Cambridge, Mass.

TABLE I—RESULTS OF NEUTRON ACTIVATION ANALYSIS OF *l*-EPHEDRINE AND NOREPHEDRINE SILVER COMPLEX PYRIDINATES

Compound	Sample Wt., g.	Amount Ag, g.	Activity, C.p.m.	% Ag (Exptl.)	% Ag (Theor.)	%[a] Error
l-Ephedrine-Ag pyridinate $(C_{20}H_{27}N_2O_2)Ag(C_5H_5N)$	0.5393	0.0541	38 ± 2	20.6	21.0	1.90
Standard $AgNO_3$	0.5393	0.1665	114 ± 3	—	63.5	—
Norephedrine-Ag-pyridinate $(C_{18}H_{23}N_2O_2)Ag(C_5H_5N)$	0.3918	0.0491	39 ± 2	22.0	22.3	1.35
Standard $AgNO_3$	0.3929	0.1215	113 ± 3	—	63.5	—

[a] $\frac{[\text{Percent Ag (Exptl.)} - \text{Percent Ag (Theor.)}]}{\text{Percent Ag (Theor.)}} \times 100$.

The use of this procedure in a manufacturing facility would provide a convenient analytical method for compounds of this nature.

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Keyphrases

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Identification of Aliphatic Amines from Rates of Cinnamoylation

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The second-order rate constants for reaction between *trans*-cinnamic anhydride and 26 aliphatic amines in acetonitrile solution are reported. The rate constant for this reaction is a discriminating criterion of identity.

EARLIER PAPERS in this series have described the identification of alcohols from rates of alkaline hydrolysis of their 3,5-dinitrobenzoate esters (1) and of sugars from their rates of oxime formation (2). Kinetic studies provide a powerful approach to the characterization of organic compounds because of the marked sensitivity of reaction rate to structure of the reactants. Because of its potential for distinguishing between closely related compounds, and its advantages of sensitivity, simplicity, and speed, rate measurement (actually rate constant measurement) should become a useful adjunct to spectroscopy and to conventional chemical methods of qualitative analysis.[1]

A procedure for the determination of amines has recently been described in which the amine is quantitatively converted to the corresponding cinnamide by acylation with *trans*-cinnamic anhydride (3). During the development of the method some cinnamoylation rates were measured, and it was noted that the acylation rate constant is dependent upon the amine structure. In the present paper this dependence is exploited to provide a new method for the characterization of primary and secondary aliphatic amines.

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[1] An incidental benefit of this approach is the accumulation of extensive collections of rate data for related compounds under common conditions; such data may be put to valuable mechanistic use, and may also provide guidance in the development of quantitative analyses.

EXPERIMENTAL

Materials—*Trans*-cinnamic anhydride (J. T. Baker Chemical Co.) was recrystallized three times from benzene; m.p. 134–136°. Acetonitrile (Fisher Scientific Co., catalog No. A-21) was refluxed over phosphorus pentoxide and then distilled from phosphorus pentoxide through a packed column (4); b.p. 81–81.5°. Amines were purified by distillation.

Apparatus—Spectral measurements were made with a Cary model 14 recording spectrophotometer fitted with a thermostated cell compartment.

Procedure—Acetonitrile solutions of cinnamic anhydride (approximately 4×10^{-6} *M*) and of an amine (5.0×10^{-6} to 2.5×10^{-2} *M*, depending upon