Nitrofuraldoximes. Separation of Isomers by Urea Complex Formation

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The separation of various types of isomers by complex formation with urea is a rapidly expanding field of investigation. Most of the work to date has been in the separation of straight chain aliphatic compounds from branched chain compounds.[1] The separation of isomers of aromatic and heterocyclic compounds has also been reported.[2] The examples of separation of stereoisomers are quite rare. Priewe[3] reported the separation of the *cis-trans* isomers of estradiol, and the separation of oleic acid from elaidic acid has been carried out utilizing urea complex formation.[4]

It is the purpose of this paper to report the separation of the *syn* and *anti* forms of 5-nitro-2-furaldoxime by means of urea complex formation. The two isomeric oximes were first reported by Gilman,[5] the *syn* form melting at 121° and the *anti* at 153°. Raffauf[6] reported the melting points as 121° and 159–161°, respectively.

When 5-nitro-2-furaldehyde diacetate was reacted with hydroxylammonium sulfate in the presence of sulfuric acid, a mixture of the isomeric oximes was obtained. Since the *anti* form is much less soluble in methanol than the *syn* it was not difficult to isolate the former from the mixture by recrystallization. Also, the mixture could be completely converted to the *anti* form by treatment of the hydrochlorides of the mixture of oximes with sodium carbonate.[5]

In order to isolate the *syn* form, the applicability of urea complex formation was investigated. An available sample of relatively pure *syn* oxime was treated with urea in methanolic solution and found to form a (1:1) complex. Under identical conditions the *anti* isomer did not form a complex. Decomposition of the *syn* oxime-urea complex with cold water regenerated the pure *syn* oxime.

Taking advantage of the above findings, it was found that a mixture of the two forms could be separated into its two components. Treatment of a 60:40 (*syn*:*anti*) mixture with urea and methanol resulted in a 77% recovery of the pure *syn* form and a 53% recovery of the pure anti form.

The physical constants for the syn oxime were significantly different from those previously reported.[5,6] The melting point was found to be 129–130° compared to 121° and the ultraviolet absorption data in water showed ϵ values of 13,400 and 13,200 at 232.5 mμ and 349 mμ, respectively, compared to 11,900 and 12,500 at 230 mμ and 345 mμ reported by Raffauf.[6]

A melting point curve[7] of varying mixtures (in 10% increments) of the two pure isomers revealed that mixtures containing from 10% to 70% of the *syn* form had a melting point range of about 118–150°. However, mixtures containing 80% or 90% of the *syn* form were completely melted at 119–123° and 119–124°, respectively.

EXPERIMENTAL[8]

syn-5-Nitro-2-furaldoxime-urea Complex (I). To a solution of 98 g. of 5-nitro-2-furaldoxime (m.p. 117–118°) in 400 cc. of methanol was added 60 g. of urea. The mixture was stirred for one hour at 25° and the resulting precipitate filtered and air dried to yield 66.7 g. of yellow crystals, m.p. 123–125°.

Anal. Calcd. for $C_6H_8N_4O_5$: C, 33.34; H, 3.73; N, 25.92. Found: C, 33.45; H, 3.84; N, 25.97.

Attempted preparation of anti-5-nitro-2-furaldoxime (II)–*urea complex.* A mixture of 10 g. of *anti*-5-nitro-2-furaldoxime, 40 cc. of methanol, and 6 g. of urea was stirred at 25° for 15 hr. No complex formed.

Regeneration of syn-5-nitro-2-furaldoxime (III) *from its urea complex.* A suspension of 30 g. of I in 750 cc. of water was stirred for 2 hr. The mixture was filtered and the solid washed with two 50-cc. portions of water. After drying there was obtained 18.6 g., 85%, of III, m.p. 129–130°.

Anal. Calcd. for $C_5H_4N_2O_4$: C, 38.47; H, 2.58; N, 17.95. Found: C, 38.6; H, 2.44; N, 17.59.

Conversion of this material to the urea complex, followed by regeneration of the oxime, gave no further change in properties.

Separation of syn and anti forms of 5-nitro-2-furaldoxime. A solution of 100 g. of a mixture of the isomers of 5-nitro-2-furaldehyde oximes (m.p. 118–145°, ϵ = 11,600 at 232.5 mμ) in 500 cc. of methanol was stirred with 75 g. of urea for one hour at 25°. The mixture was filtered to yield 43 g. of the complex (I). The filtrate was evaporated to dryness and the residue slurried with 300 cc. of water to yield 65 g. of a mixture of II and III. This mixture was recrystallized from 250 cc. of methanol (cooling only to 20°) to yield 11.6 g. of II, m.p. 157–160°. The methanolic filtrate was then stirred with 35 g. of urea for one hour at 25° to yield 18.7 g. of I. The filtrate was evaporated to dryness and the above procedure repeated. A total of 71.7 g. of I, 21.3 g. of II, and 14 g. of unseparated material was obtained. The 71.7 g. of I were stirred with 400 cc. of water for one hour. The solid was removed by filtration, washed with cold water, and dried at 60° to yield 46.2 g. of pure III.

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(1) Two review articles which discuss this aspect and contain many references to the literature are F. Cramer, *Rev. Pure and Appl. Chem. (Australia)*, **5**, 143 (1955); and K. Kobe and W. Domask, *Petroleum Refiner*, **31**, No. 3, 106 (1952).

(2) See H. Schotte, U.S. Patent **1,830,859** (Nov. 10, 1931); L. Fetterly, U. S. Patent **2,613,204** (Oct. 7, 1952); G. Reithol, U.S. Patent **2,295,606** (Sept. 15, 1942).

(3) H. Priewe, U. S. Patent **2,300,134** (Oct. 27, 1942).

(4) British Patent **671,563** (May 7, 1952).

(5) H. Gilman and G. Wright. *J. Am. Chem. Soc.*, **52**, 2553 (1930).

(6) R. Raffauf, *J. Am. Chem. Soc.*, **68**, 1765 (1946).

(7) I am indebted to Mr. B. Stevenson for preparing a pure sample of *anti*-5-nitro-2-furaldoxime and obtaining these melting point data.

(8) Microanalyses were carried out by Messrs. G. Ginther and A. Mayer of these laboratories. The ultraviolet absorption data were obtained by Mr. C. Eaton using a Beckman DU spectrophotometer. Melting points were taken on the Fisher-Johns apparatus and are corrected.