Chemistry of Heterocyclic Compounds, Vol. 34, No. 9, 1998

REACTION OF THE SODIUM SALT OF 2-OXO-4-(2-THIENYL)BUTENOIC ACID WITH HYDROXYLAMINE

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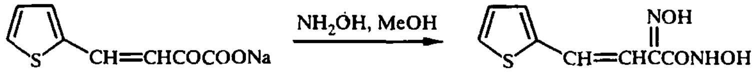
The reaction of salts and esters of 4-substituted 2-oxobutenoic and the corresponding 2-oxobutanoic acids with hydroxylamine has been little studied even though the oximes obtained are valuable intermediates in the synthesis of modified amino acids. Hydroxamic acids are important, biologically active compounds [1]. We have found that the reaction of the ethyl ester of 2-oxo-4-phenylbutanoic acid with hydroxylamine in neutral solution (pH 7) and in acid medium (pH 1) gives mainly the ethyl ester of 2-hydroxyimino-4-phenylbutanoic acid but in basic medium gives the corresponding hydroxamate of 2-oxo-4-phenylbutanoic acid [2]. The hydroxamic acid oxime was not found in the reaction products.

When treating the sodium salt of 2-oxo-4-(2-thienyl)butenoic acid with hydroxylamine in methanol solution the basic reaction product was the hydroxamic acid oxime:



The increased reactivity of the sodium salt of 2-oxo-4-(2-thienyl)butenoic acid when compared with ethyl 2-oxo-4-phenylbutanoate in reaction with hydroxylamine is evidently related to the presence of conjugated double bonds in the starting molecule and the presence of the thienyl group. It may also be proposed that, in reaction with hydroxylamine, α-oxoacid salts have a higher reactivity than their esters.

Synthesis of 2-Hydroxyimino-4-(2-thienyl)butenehydroxamic Acid. Sodium methylate (prepared from sodium (0.18 g) dissolved in methanol (3.08 ml)) was added to a suspension of hydroxylamine hydrochloride (0.84 g) in methanol (5 ml). The sodium chloride formed was filtered off.

Hydroxylamine (2.5 equivalents in methanol solution prepared as described above) was added with cooling to the sodium salt of 2-oxo-4-(2-thienyl)butenoic acid (0.5 g, $2.12 \cdot 10^{-3}$ mole) and the mixture was held for 12 h at room temperature. The precipitate (0.33 g, purity 70%) was filtered off.

The 2-hydroxyimino-4-(2-thienyl)butenehydroxamic acid content was determined using HPLC on a Du Pont 850 chromatograph with a Silasorb C18 filled column (3.9 × 150 mm), an eluent of CH_3CN (20%), 0.1 M KH_2PO_4, H_3PO_4 (80%), pH 2.5, and ultraviolet detection at 220 nm. The flow rate was 1.0 ml/min. According to HPLC, the filtrate contained the starting material (0.09 g). The yield was 51.8% calculated on reacted starting material. The precipitate was purified by recrystallization from butanol to give 0.12 g of finely crystalline, white product with mp 180°C. 1H NMR spectrum, ppm (DMSO-D_6): 6.68 (1H, d, α-CH); 7.02 (1H, dd, 4-CH); 7.22 (1H, d, 3-CH); 7.49 (1H, d, 5-CH); 7.64 (1H, d, β-CH). IR spectrum, cm^{-1}: 1650 (C=O); 3180 (NH); 3280 (NH). The product gave a characteristic violet coloration when treated with $FeCl_3$ solution. Found, %: C 41.31; H 4.02; N 11.77. $C_8H_8SO_3N_2 \cdot H_2O$. Calculated, %: C 41.73; H 4.38; N 12.17.

The work was financed by the Latvian science council (grant No. 709).

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Latvian Institute of Organic Synthesis, Riga LV-1006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1266-1267, September, 1998. Original article submitted September 10, 1998.

0009-3122/98/3409-1088$20.00