The Reaction of Pyrrolealdehyde with Rhodanine and Hydantoin[1]

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In attempts to prepare β-2-pyrrolealanine, 2-pyrrolealdehyde was condensed with compounds containing active methylene groups. Unexpected products were obtained from the reaction of 2-pyrrolealdehyde with diketopiperazine and 2-acetyl-3-thiohydantoin. To elucidate the structures of these products will require further investigation. Likewise, the reaction of the aldehyde with hippuric acid appears to be more complex than reported.[3] Rhodanine and hydantoin, however, condensed with pyrrolealdehyde to give the expected compounds.

We wish to report at this time the reaction of 2-pyrrolealdehyde with rhodanine and hydantoin, and the hydrolysis of pyrrolalrhodanine to 2-pyrrolethiopyruvic acid. The reaction of 2-pyrrolealdehyde with hydantoin in acetic anhydride in the presence of sodium acetate gave a very small yield of what is believed to be pyrrolalacetylhydantoin. An analogous product was obtained by Barger and Easson[4] in the synthesis of β-2-thienylalanine.

Experimental

2-Pyrrolalrhodanine.—A finely ground mixture of 7 g. of pyrrolealdehyde,[5] 10 g. of rhodanine and 7 g. of anhydrous sodium acetate was refluxed with 40 ml. of glacial acetic acid for twenty minutes. It was cooled and filtered; the reddish-brown product was thoroughly washed with water to remove acetic acid. Dilution of the filtrate with water produced more pyrrolalrhodanine. The combined material was recrystallized from alcohol; by working up the mother liquors, a total of 6.5 g. (42%) was obtained, m. p. 286° on a Dennis melting point bar. The ochre plates were soluble in ethanol, acetone, ethyl acetate, partially soluble in ether, benzene and carbon tetrachloride and insoluble in water.

Anal. Calcd. for $C_8H_6N_2OS_2$: N, 13.32. Found: N, 13.11.

2-Pyrrolethiopyruvic acid.—Six grams of the preceding compound was powdered and suspended in 120 ml. of water containing 30 g. of barium hydroxide. The mixture was heated on the steam-bath until solution of the red material was complete. The solution was filtered and the filtrate cooled in an ice-bath. It was then carefully neutralized with dilute hydrochloric acid until precipitation was complete. The yellow product was filtered, washed with water and dried in a vacuum desiccator. The yield was 3.5 g., m. p. 130° (dec.). When exposed to air it decomposed rapidly. Attempts to recrystallize or reprecipitate it were unsuccessful, so that the crude material was used for the analysis.

Anal. Calcd. for $C_7H_7NO_2S$: N, 8.28; neut. equiv., 169. Found: N, 9.05; neut. equiv., 175–180.

The neutral equivalent could not be determined with accuracy because of the color of the solution.

Reaction of 2-Pyrrolealdehyde with Hydantoin.—A finely ground mixture of 1.7 g. of pyrrolealdehyde, 1.7 g. of hydantoin, and 1.7 g. of anhydrous sodium acetate was refluxed with 10 ml. of acetic anhydride for two and one-half hours. After cooling and extracting with water, a blackish-green residue remained. It was extracted with 50 ml. and again with 25 ml. of hot ethanol. The combined ethanol extracts, which showed a violet fluorescence, were treated with charcoal, evaporated to 25 ml., again treated with charcoal and evaporated to a volume of 15 ml. On chilling, 0.13 g. of light-green needles, m. p. 184–185°, separated. The compound was partially soluble in ether and cold ethanol and soluble in hot ethanol, water and acetic acid. The product imparted a violet fluorescence to its solutions.

Anal. Calcd. for $C_{10}H_9N_3O_3$: N, 19.17. Found: N, 19.18.

Fusion of the aldehyde, hydantoin and sodium acetate by the method of du Vigneaud and co-workers[6] at various temperatures resulted in tars only. Pyrrolealdehyde heated with hydantoin in absolute ethanol in the presence of catalytic amounts of methylamine hydrochloride and sodium carbonate led to tarry materials and recovery of unreacted hydantoin. When equivalent amounts of aldehyde and hydantoin in piperidine were heated at reflux for two minutes only unidentified compounds were isolated.

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[3] Asahina and Mitsunaga, *J. Pharm. Soc. Japan*, 986 (1917).

[4] Barger and Easson, *J. Chem. Soc.*, 2100 (1938).

[5] Fischer and Orth, "Die Chemie des Pyrrols," Vol. I, Akademische Verlagsgesellschaft, Leipzig, 1934, p. 152.

[6] du Vigneaud, McKennis, Simmonds, Dittmer and Brown, *J. Biol. Chem.*, **159**, 385 (1945).