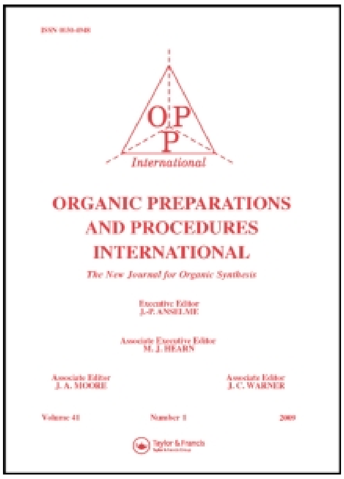

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DL-4-ACETAMIDO-4-HYDROXY-2-BUTENOIC ACID γ-LACTONE

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DL-4-ACETAMIDO-4-HYDROXY-2-BUTENOIC ACID γ-LACTONE[1]

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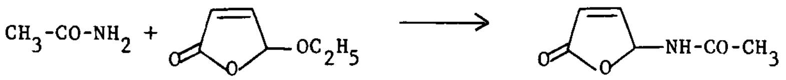

1 2

The title compound (2) has been isolated from Fusarium molds[2,3] and implicated as a causative agent in "fescue foot" of cattle.[2] The method described here is based on the reported small-scale synthesis from acetamide and malealdehydic acid in dilute hydrochloric acid,[3,4] but has several significant differences. Malealdehydic acid was replaced by its pseudo ester 1 and concentrated hydrochloric acid was used instead of dilute acid. These modifications made larger scale synthesis feasible. Although malealdehydic acid could be an intermediate, it is not isolated.

Experimental

4-Ethoxy-4-hydroxy-2-butenoic Acid γ-Lactone.-- This compound was prepared photochemically from furfural, oxygen, and ethanol in the presence of eosin and vanadium pentoxide, by the method of Schenck.[5] Crude product was found to be best removed from the reaction mixture by distillation in a rotary evaporator at 0.2 to 0.5 mm from a water bath at 75° and with the receiver immersed in ice water. Three redistillations through a Vigreux column gave pure pseudo ester 1, bp 54-6° at 0.4 mm.

The pseudo ester (85 g, 0.67 mole) was dissolved in 25 ml of 12N hydrochloric acid. Acetamide (60 g, 1.02 mole) was added, and the mixture was heated on a steam bath for 15 min, whereupon it turned black. Tlc [acetone/CCl_4 (1/2)] indicated about 50% conversion with only a small amount of malealdehydic acid present. More acetamide (50 g, 0.85 mole) and 5 ml of water were added and the mixture warmed again until tlc showed no ester remaining. Tetrahydrofuran was added to the reaction mixture and an inorganic precipitate filtered off.[6] The filtrate was evaporated, and the residue was chromatographed on a total of 1200 g of Florisil. Ether eluted an oil. Ethyl acetate then eluted a mixture of acetamide and **2**, which was dissolved in chloroform. Addition of 2-3 volumes of ether precipitated fine crystals which were filtered and subjected to sublimation at 75° and 0.5 mm to remove acetamide. The residue was recrystallized from chloroform to give 24 g of **2**, mp 115.0-5.5° (reported[2] mp 115.5-7.5°), with infrared, nuclear magnetic resonance, and ultraviolet spectra identical to those reported.[2,3]

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1. This work was carried out under a contract with the Northern Utilization Research and Development Division, Agricultural Research Service, United States Department of Agriculture.
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6. This is presumably NH_4Cl from hydrolysis of acetamide.
7. We thank Dr. Ivan Wolff for a sample of genuine **2**.

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