[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

2-Nitro-4-methoxyacetoacetanilide[1]

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2-Nitro-4-methoxyacetoacetanilide was prepared by the reaction of either ethyl acetoacetate or diketene with 2-nitro-*p*-anisidine. Misani and Bogert[3] have reported failure to obtain a condensation of ethyl acetoacetate with this amine. The product was assigned the anilide structure rather than that of ethyl 2-nitro-4-methoxy-β-anilinocrotonate on the basis of its synthesis involving diketene and its elementary analysis.

Several attempts to effect the cyclization of 2-nitro-4-methoxyacetoacetanilide to produce 6-methoxy-8-nitro-2-lepidol according to the method of Knorr–Conrad–Limpach failed, although several variations of the conditions of Mikhailov[4] were studied. The only reaction observed was, in some cases, the cleavage to form 2-nitro-*p*-anisidine. This failure was somewhat surprising in view of the conversion of 3-nitro-4-acetoacetaminoveratrole to 6,7-dimethoxy-8-nitro-2-lepidol by Frisch and Bogert.[5]

Experimental

2-Nitro-4-methoxyacetoacetanilide. (A) From Ethyl Acetoacetate.—Eighty milliliters (0.6 mole) of ethyl acetoacetate was heated with stirring to 160° and stirring was continued while 24 g. (0.14 mole) of recrystallized 2-nitro-*p*-anisidine,[6] m. p. 125–127°, was added during a period of twenty minutes. The mixture was held at 160° for four hours after the addition of the amine, then was cooled and agitated with 1000 ml. of 1% aqueous sodium hydroxide. The solid, unreacted amine which was removed by filtration at this point weighed 11.3 g. (47%), m. p. 119–123°. Acidification of the alkaline filtrate precipitated the anilide as an orange-brown solid; yield, 12.7 g. (35% on the total starting amine, but 67% on the basis of amine actually consumed), m. p. 71–73°. Several recrystallizations from petroleum ether (b. 30–60°)-alcohol gave orange-red crystals, m. p. 74.5–75.5°.

Anal. Calcd. for $C_{11}H_{12}N_2O_5$: C, 52.39; H, 4.80; N, 11.11. Found[7]: C, 52.54, 52.42; H, 5.36, 5.25; N, 11.26, 11.25.

A red by-product weighing 0.5 g., m. p. 246–248° (dec.), was isolated during the recrystallization; it was insoluble in the mixture of solvents. Its structure was not determined.

(B) From Diketene.—While a solution of 6.0 g. (0.036 mole) of 2-nitro-*p*-anisidine in 65 ml. of thiophene-free benzene was gently boiled under reflux, 3 g. (0.036 mole) of diketene[8] was added dropwise during five minutes. The solution was boiled under reflux for five and one-half hours, the solvent was removed under reduced pressure, and the residual liquid was agitated, when cool, with 220 ml. of 1% sodium hydroxide solution. Unreacted 2-nitro-*p*-anisidine (1.4 g., 23%) was filtered. Acidification of the filtrate gave 5.4 g. of anilide, m. p. 67–71°; yield, 60% based upon starting amine, or 78% based upon amine which actually reacted. A trace of the red by-product, m. p. 246–248° (dec.), was isolated.

Attempts to Cyclize 2-Nitro-4-methoxyacetoacetanilide.—One gram of 2-nitro-4-methoxyacetoacetanilide and 1 ml. of sulfuric acid (d. 1.84) were heated together at 95° for ten minutes. Some gas was evolved. The mixture was cooled to 60° and poured into a large excess of water, causing the precipitation of 0.5 g. of 3-nitro-4-aminoanisole, m. p. 122–124°. When 100% sulfuric acid was used in a similar experiment, no water-insoluble product was formed.

Summary

2-Nitro-4-methoxyacetoacetanilide was prepared. Attempts to cyclize this compound to 6-methoxy-8-nitro-2-lepidol failed.

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[3] Misani and Bogert, *J. Org. Chem.*, **10**, 347 (1945).

[4] Mikhailov, *J. Gen. Chem.* (U. S. S. R.), **6**, 511 (1936); *C. A.*, **30**, 6372 (1936).

[5] Frisch and Bogert, *J. Org. Chem.*, **9**, 348 (1944).

[6] Supplied by the National Aniline and Film Corporation.

[7] Analyses by Dr. Carl Tiedcke, Laboratory of Microchemistry, New York, N. Y.

[8] Williams and Krynitsky, *Org. Syn.*, **21**, 64 (1941).