

*Amino Acid Synthesis from Nitromalonic Ester. III¹⁾.
Note on the Synthesis of Glutamic Acid*

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Several amino acids have been prepared by means of the addition reaction of diethyl nitromalonate with α,β -unsaturated compounds such as acrylonitrile²⁾ and acrolein¹⁾. If the similar type of reaction could occur between nitromalonic and acrylic esters, an approach to the synthesis of glutamic acid would be possible. Both the esters have been found to react in the presence of a catalytic amount of triethylamine in alcoholic solution to give 2-carbomethoxyethyl-nitromalonic ester in a good yield. Elimination of one α -ester group of the substituted nitromalonic ester and subsequent hydrogenation³⁾ gave pyrrolidonecarboxylic ester, which was easily converted into DL-glutamic acid monohydrate. The overall yield was

about 50%. Direct reduction of 2-carbomethoxyethyl-nitromalonic ester with Raney nickel in alcoholic solution gave 2-carbomethoxyethyl-malonic ester, indicating the hydrogenolysis occurred during the reaction¹⁾.

Experimental

Diethyl 2-Carbomethoxyethyl-nitromalonate.—Forty-four grams of diethyl nitromalonate and 22 g. of methyl acrylate in 70 ml. of absolute alcohol were heated under reflux in the presence of 3 ml. of triethylamine for 7 hr. and after the concentration of the reaction mixture the residue was dissolved in 400 ml. of ether. The ether solution was extracted with cold aqueous sodium bicarbonate, washed with water and dried. Evaporation of ether gave 55 g. of crude product. When the crude product was distilled in vacuo, there was obtained 49 g. of the pure material boiling at 120–150°C/2 mmHg.

Anal. Found: C, 45.74; H, 6.07; N, 4.83. Calcd. for $C_{11}H_{17}O_5N$: C, 45.36; H, 5.84; N, 4.81%.

1) Paper II of this series; T. Okuda, *This Bulletin*, **30**, 358 (1957).

2) S. Akabori, Y. Izumi and T. Okuda, *J. Chem. Soc. Japan, Pure Chem. Sec. (Nippon Kagaku Zasshi)*, **77**, 490 (1956).

3) D. I. Weisblat and D. A. Lyttle, U. S. Pat., 2,606,921 (1952).

4) D. I. Weisblat and D. A. Lyttle, *J. Am. Chem. Soc.*, **71**, 3079 (1948).

Ethyl 2-Carbomethoxyethyl-nitroacetate^{3,5)}.—A solution of 51 g. of crude diethyl 2-carbomethoxyethyl-nitromalonate in 450 ml. of dry ether was treated with 4.10 g. of sodium dissolved in 100 ml. of absolute alcohol at 0°C as already reported in the preceding papers^{1,2)}. The resulting slurry was transferred to a separatory funnel, 150 ml. of ether and 70 ml. of cold 10% hydrochloric acid were added and vigorous shaking was applied. The ether layer was separated and the aqueous layer was extracted with ether. The ether solutions were combined, washed with water and dried. Concentration and vacuum-distillation gave 34 g. of the product of b.p. 115~128°C/2 mmHg.

Anal. Found: C, 43.10; H, 5.95; N, 6.18. Calcd. for $C_8H_{13}O_6N$: C, 43.83; H, 5.98; N, 6.39%.

Ethyl Pyrrolidonecarboxylate.—The pressure-hydrogenation of 34 g. of 2-carbomethoxyethyl-nitroacetate was carried out using 150 ml. of ethanol and 4 g. of Raney nickel. The catalyst was filtered off, and the ethanol was evaporated. Crude ethyl pyrrolidonecarboxylate thus obtained

weighed 22 g. This can be purified either by recrystallization from ether-petroleum ether or by distilling at 2 mm., m.p. 48~50°C, b.p. 153°C/2 mmHg.

Anal. Found: C, 53.80; H, 7.14; N, 8.99. Calcd. for $C_7H_{11}O_3N$: C, 53.49; H, 7.05; N, 8.91%.

The ester was converted into DL-glutamic acid monohydrate by acid hydrolysis. The overall yield with respect to diethyl nitromalonate was about 50%.

Anal. Found: C, 36.59; H, 6.62; N, 8.92. Calcd. for $C_5H_{11}O_5N$: C, 36.36; H, 6.71; N, 8.48%.

Diethyl 2-Carbomethoxyethylmalonate.—Twelve grams of diethyl 2-carbomethoxyethyl-nitromalonate was reduced in alcohol with 2 g. of Raney nickel. After the removal of the catalyst and the alcohol the residue was distilled. There was obtained 8 g. of diethyl 2-carbomethoxyethylmalonate boiling at 125~130°C/2 mmHg.

Anal. Found: C, 53.23; H, 7.73. Calcd. for $C_{11}H_{19}O_6$: C, 53.66; H, 7.32%.

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5) N. Kornblum and J. H. Eeicher, *ibid.* 78, 1499 (1956).