NOTES

Ethyl Formylaminomalonate: An Intermediate in the Synthesis of Amino Acids

By Alexander Galat

Several acyl derivatives of aminomalonic ester have been employed as intermediates in the synthesis of amino acids, but there appears to be no record of the use for this purpose of the simplest and perhaps the most accessible member of this series, formylaminomalonic ester.

Ethyl formylaminomalonate was readily prepared in an over-all yield of 55% by nitrosation of ethyl malonate with sodium nitrite and acetic acid, followed by reduction with zinc and formic acid, according to the procedure of Conrad and Schulze.[1] When the nitrosation was carried out with butyl nitrite[2] the over-all yield was 63%. Since ethyl formylaminomalonate can thus be prepared in a substantially higher yield than ethyl acetylaminomalonate (40%)[3] and, unlike the latter, does not require the use of a catalytic reduction under pressure, this ester offers definite advantages as a convenient intermediate in the synthesis of amino acids.

Ethyl formylaminomalonate was condensed with benzyl chloride, ethyl chloroacetate and acrylonitrile under the general conditions described for acetylaminomalonic ester,[4] and the condensation products were subjected, without isolation, to acid hydrolysis, thus yielding *dl*-phenylalanine (60%), *dl*-aspartic acid (55%) and *dl*-glutamic acid (57%), respectively. Other amino acids may undoubtedly be synthesized by the same method and the use of formylaminomalonic ester may be considered a convenient variation of the Sörensen method.

Experimental

Ethyl Formylaminomalonate.—To a mixture of 30.4 ml. (0.2 mole) of ethyl malonate and 34 ml. (0.6 mole) of glacial acetic acid was added a solution of 38 g. (0.55 mole) of sodium nitrite in 55 ml. of water. The mixture was stirred during the addition of the nitrite and maintained at below 20°. After the addition had been completed, the mixture was stirred for an additional four and one-half hours at room temperature, extracted with chloroform and the solvent removed *in vacuo* on a water-bath. The residue, a yellow oil weighing about 38 g., was dissolved in 160 ml. of technical formic acid (a 90% acid was used without detriment instead of the less readily available 99–100% acid recommended by Conrad and Schulze), and the mixture was transferred into a three-neck flask provided with a thermometer, a stirrer and a reflux condenser. A small amount of technical zinc dust was added and the mixture was stirred and heated until the reaction started. There usually was an induction period of several minutes after which the reaction proceeded with violence, unless only a small amount of zinc was present at this stage. Thirty grams of zinc dust was then added through the condenser at such a rate that the temperature was maintained at 75–80° without external heating. After the addition of zinc had been completed (fifteen to twenty minutes), the mixture was filtered hot, the filter-cake of zinc formate thoroughly washed with formic acid and the filtrate evaporated *in vacuo* on a water-bath. The residue, which was an oil containing a small amount of zinc formate, was fractionally distilled *in vacuo* and the fraction boiling between 130 and 132° at 2–3 mm. of mercury was collected. It solidified into a white crystalline mass which had a setting point of 48–49°; yield, 22.2 g. (54.7%).

Anal. Calcd. for $C_8H_{13}O_5N$: C, 47.3; H, 6.4; N, 6.9. Found: C, 47.6; H, 6.6; N, 7.1.

***dl*-Aspartic Acid.**—To a solution of 1.2 g. (0.052 mole) of sodium in 100 ml. of absolute alcohol was added 10.15 g. (0.05 mole) of ethyl formylaminomalonate. To the resulting solution was added 5.4 ml. (0.052 mole) of dry ethyl chloroacetate (Dow) and a few crystals of sodium iodide. The mixture was allowed to stand at room temperature for two days during which much sodium chloride precipitated. It was then heated for two and one-half hours on the water-bath, sodium chloride removed by filtration and the filtrate evaporated *in vacuo* to dryness. There remained a brown sirup containing some crystals. This mixture was treated with 75 ml. of concentrated hydrochloric acid and refluxed for three hours. The brown solution was then evaporated *in vacuo* to dryness, the residue dissolved in 30 ml. of water, treated hot with charcoal and filtered, yielding a colorless filtrate. Concentrated ammonia was added until a *p*H of 3, the solution evaporated to a small volume and chilled for twenty-four hours. *dl*-Aspartic acid which crystallized was collected by filtration, washed with cold water and alcohol and recrystallized from a small amount of water; yield, 3.55 g. (54.7%). The material decomposed above 300°, gave a hydrochloride which melted at 180–185° (dec.) and the N-benzoyl derivative melting at 160–162°.

Anal. Calcd. for $C_4H_7O_4N$: C, 36.1; H, 5.27; N, 10.53. Found: C, 36.3; H, 5.30; N, 10.3.

Galat Chemical Development, Inc.
61 So. Broadway
Yonkers, N. Y.

Received December 2, 1946

(1) Conrad and Schulze, *Ber.*, **42**, 733 (1909).

(2) Redemann and Dunn, *J. Biol. Chem.*, **130**, 345 (1939).

(3) Snyder and Smith, This Journal, **66**, 350 (1944).

(4) Albertson and Archer, *ibid.*, **67**, 308 (1945). Snyder, Skeleton and Lewis, *ibid.*, **67**, 310 (1945).

Methylcyclopropane: Infrared Absorption Spectrum and Synthesis from *i*-Butyl Chloride

By Francis E. Condon and Dan E. Smith

Cyclopropanes have been obtained from the reaction of sodium or sodium alkyls with neoalkyl chlorides.[1] The present work extends this reaction to *i*-butyl chloride.

From 117.5 g. of *i*-butyl chloride and 10.2 g. of sodium (*cf.* ref. 1a) there was obtained 3.1 g. of methylcyclopropane; other products were 8.8 g. of *i*-butane, 4.7 g. of *i*-butylene and 5.5 g. of 2,5-dimethylhexane; 78 g. of *i*-butyl chloride was recovered. The reaction of 80.7 g. of *i*-butyl chloride, 146.5 g. of dipropylmercury and 22.5 g. of sodium in 218.3 g. of *n*-heptane (*cf.* ref. 1c) resulted in 9.6 g. of methylcyclopropane; lower-boiling products were

(1) (a) Whitmore, Popkin, Bernstein and Wilkins, This Journal, **63**, 124 (1941); (b) Whitmore and Carney, *ibid.*, **63**, 2633 (1941); (c) Whitmore and Zook, *ibid.*, **64**, 1783 (1942); (d) Whitmore, Weisberger and Shabica, *ibid.*, **65**, 1469 (1943).