

*Anal.* Calcd. for  $C_{18}H_{11}N_3O_8$ : C, 54.41; H, 2.79; N, 10.58. Found: C, 54.24; H, 3.10; N, 10.73.

The trinitrobenzene compound melted at 137–138° after three crystallizations from methanol.

*Anal.* Calcd. for  $C_{18}H_{11}N_3O_7$ : C, 56.70; H, 2.91; N, 11.02. Found: C, 56.48; H, 3.24; N, 11.18.

**Ethyl Glyoxylate and Related Compounds.**—Oxalic acid was reduced to glyoxylic acid as follows.<sup>19</sup> Zinc powder (30 g.), 47.5 g. of sodium and 700 g. of mercury were fused to a melt under dry nitrogen, and the cooled amalgam was crushed to small lumps. The amalgam was added during 2 hr. to a solution of 130 g. of oxalic acid dihydrate and 450 g. of concd. hydrochloric acid in 1200 cc. of water, the mixture being kept at 8–12°. The solution was brought to pH 3–4 by addition of 30% alkali, and was evaporated almost to dryness in an air stream. The glyoxylic acid was extracted from the inorganic salts with absolute ethanol in a Soxhlet for 3 days. The extract (1.5 l.) was dried over calcium sulfate, saturated with hydrogen chloride and refluxed for 3 hr. The solvent was removed through a 2-ft. Vigreux column, and the residue was taken up in ether, washed with ice-cold 5% carbonate solution, ammonium chloride solution and distilled. The principal fractions were 7.9 g., b.p. 132–134° (1 atm.),  $n_D^{20}$  1.4306, apparently ethyl glyoxylate or its ethyl hemiacetal<sup>19b</sup> and 48.6 g., b.p. 186–189° (1 atm.),  $n_D^{20}$  1.4160, the diethyl acetal.<sup>19b</sup> Hydrolysis of the latter with 2 *N* hydrochloric acid in the cold gave ethyl glyoxylate.

**Condensation of Ethyl Glyoxylate with Tetralone Forming XVI.**—Ethyl glyoxylate (0.25 g.) and 0.365 g. of  $\alpha$ -tetralone were dissolved in 2 cc. of acetic anhydride containing 1 drop of concd. sulfuric acid; the mixture was stirred under nitrogen for 16 hr. at room temperature, and was then heated on the steam-bath for 4 hr. The acetic anhydride was decomposed with a little boiling water, and the mixture was then cooled and brought to pH 6 with 10% carbonate. From the dried ether extract of this mixture, a yellow oil (0.49 g.) was obtained which did not crystallize; it was hydrolyzed by refluxing 4.5 hr. with 5 cc. of concd. hydrochloric acid. The hydrolysis mixture, worked up by the usual procedure, yielded 0.229 g. (46%) of bicarbonate-

soluble crystalline material, which melted at 186.5–187.5° after four crystallizations from ethyl acetate, and gave no depression on mixed m.p. with XVI obtained by periodate oxidation of II. The two samples were also compared through the crystalline ethyl esters XVII, again proving identity of the material obtained by synthesis and oxidation.

Condensation of  $\alpha$ -tetralone with ethyl glyoxylate with sodium hydride gave a poor yield of XVI.

**Condensation of Isopropoxymethylenetetralone with Malonic Ester to Form XXI.**—Malonic ester (1.6 g.) was converted to the sodio compound with 0.25 g. of powdered sodium in dry ether and was cooled to 0°; to this was added 2.16 g. of the isopropoxy compound in 10 cc. of dry ether under nitrogen. The mixture was stirred for 10 min. at 0°, 30 min. at room temperature, and was refluxed for 1 hr. Ice-water was added, and the mixture was extracted with ether; the latter was extracted thoroughly with 5% carbonate and then with water. Yellow prisms, m.p. 144–146° (0.75 g.) were obtained by digesting the residue from the neutral portion with ether, and, after four crystallizations from benzene-cyclohexane, they melted at 150°.

*Anal.* Calcd. for  $C_{16}H_{14}O_4$  (XXI): C, 71.10; H, 5.22. Found: C, 71.16; H, 5.17.

The compound dissolved slowly in hot 10% alkali; it gave no carbonyl derivatives and no color with ferric chloride.

The combined basic extracts from the reaction mixture were acidified with mineral acid, and extracted with ether-benzene. The organic layer was again extracted with 5% carbonate, acidified and taken up in ether-benzene. Evaporation of the dried solution and addition of ether caused the separation of 0.16 g. of yellow needles, m.p. 197–199°. The m.p. was raised to 200° by three crystallizations from benzene.

*Anal.* Calcd. for  $C_{14}H_{10}O_4$  (XXII): C, 69.42; H, 4.16. Found: C, 69.42; H, 4.17.

Alkaline hydrolysis of the ester XXI gave the acid XXII.

**Spectra.**—Infrared spectra were taken by Mr. Carl Whiteman on a Perkin-Elmer spectrograph, using Nujol suspensions. Ultraviolet spectra were taken on a Beckman instrument, and methylene chloride was used as solvent for compounds I and II because they reacted with alcohol.

ROCHESTER, N. Y.

(19) (a) W. Mohrschulz, *Z. Elektrochem.*, **32**, 451 (1926); (b) W. Traube, *Ber.*, **40**, 4953 (1907).

## NOTES

### A Synthesis of Valine

By P. T. ADAMS AND B. M. TOLBERT<sup>1</sup>

RECEIVED JUNE 9, 1952

In the preparation of radioactive compounds it is often of interest to explore syntheses which, although not involving novel methods, have not been previously reported and which offer special advantages in availability of intermediates or position of label. Thus the preparation of aliphatic amino acids by the reduction of the corresponding oxazolone has been described only twice before<sup>2,3</sup> and in both cases with either poor or no reported yields. In fact, most authors consider this an unsatisfac-

tory method for the preparation of aliphatic amino acids.<sup>3,4</sup>

This method has, however, been applied to the synthesis of valine with unexpectedly good results. Starting with 10 millimoles of glycine, 2-phenyl-4-isopropylidene oxazolone-5 has been prepared through the intermediate hippuric acid by the method of Ramage and Simonsen<sup>5</sup> in 57% yield with 24% recovery of unused glycine or 75% yield based on glycine used. The oxazolone was then reduced in 75% yield to valine using red phosphorus and hydrogen iodide.<sup>6</sup> It is possible that part of the increased applicability of this method is due to the use of newer and more efficient methods (ion

(1) The work described in this paper was sponsored by the U. S. Atomic Energy Commission.

(2) E. Erlenmeyer and J. Kunlin, *Ann.*, **316**, 145 (1901).

(3) H. E. Carter, P. Handler and D. B. Melville, *J. Biol. Chem.*, **129**, 359 (1939).

(4) "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 206, 208.

(5) G. R. Ramage and J. L. Simonsen, *J. Chem. Soc.*, 534 (1935).

(6) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 489.

- (3) C. Willgerodt, *Ber.*, **24**, 592 (1891); *J. prakt. Chem.*, [2] **45**, 145 (1892).