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.[19] 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 *p*H 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.), $n^{14}D$ 1.4306, apparently ethyl glyoxolate or its ethyl hemiacetal[19b] and 48.6 g., b.p. 186–189° (1 atm.), $n^{18}D$ 1.4160, the diethyl acetal.[19b] Hydrolysis of the latter with 2 *N* hydrochloric acid in the cold gave ethyl glyoxylate.

Condensation of Ethyl Glyoxylate with Tetralone Forming XVI.—Ethyl glyoxalate (0.25 g.) and 0.365 g. of α-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 *p*H 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 α-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[1]

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[2,3] and in both cases with either poor or no reported yields. In fact, most authors consider this an unsatisfactory method for the preparation of aliphatic amino acids.[3,4]

This method has, however, been applied to the synthesis of valine with unexpectedly good results. Starting with 10 millimoles of glycine, 2-phenyl-4-isopropylidine oxazolone-5 has been prepared through the intermediate hippuric acid by the method of Ramage and Simonsen[5] in 57% yield with 24% recovery of unused glycine or 75% yield based on glycine used. The oxazalone was then reduced in 75% yield to valine using red phosphorus and hydrogen iodide.[6] 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).

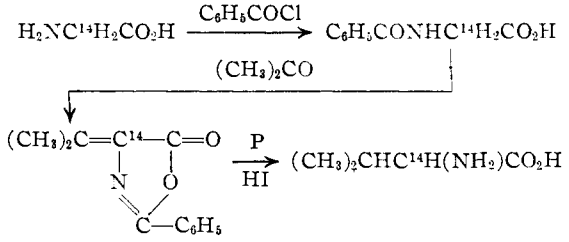
(4) "Organic Reactions," Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1946, pp. 206, 208.

(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.

exchange resins) for the purification of products, a particularly important point in many small scale radiochemical syntheses.

In the preparation described in this paper, glycine-2-C^{14} was used as the starting material, so that labeled valine was obtained.



Experimental

2-Phenyl-4-isopropylidine-(oxazalone-4-C^{14})-5.—Glycine-2-C^{14} (120 μc., 0.76 g., 10.1 millimoles) was converted to hippuric-2-C^{14} acid by reaction with benzoyl chloride.[7] The product was ground to a fine powder with 0.6 g. of freshly fused sodium acetate and dissolved in 35 ml. of dry acetone. Acetic anhydride (5 ml.) was added dropwise and the mixture heated under reflux for 15 hours.[8] The hot solution was poured onto crushed ice and diluted to 250 ml. with water. The precipitate was collected by filtration and dried *in vacuo*. The oxazalone (m.p. 98–100°) weighed 1.16 g. (5.77 millimoles, 57% yield from glycine) and contained 71 μc. or 59% of the initial radioactivity. Thus, the specific activity was correct within the limits of accuracy of the activity determinations (±5%). The filtrate contained 36 μc. (30% of the glycine activity), of which 28 μc. (23%) was recovered as 0.27 g. (2.42 millimoles, 23.9%) of glycine hydrochloride.

Valine-2-C^{14}.—The oxazalone was mixed with 2.0 g. of red phosphorus and 12.5 ml. of acetic anhydride. Hydroiodic acid (12.5 ml., specific gravity 1.7) was added and the solution was heated under reflux for 20 hours. The reaction mixture was filtered and the filtrate evaporated to dryness *in vacuo*. The residue, dissolved in 100 ml. of 70% ethanol, was poured through a glass column containing 60 ml. of Dowex-50 cation exchange resin (50–100 mesh) in the acid form. The amino acid remained quantitatively on the resin, while all anions were removed by rinsing with 100 ml. of 70% ethanol followed by 250 ml. of water.

The amino acid was eluted from the resin with 250 ml. of 2 *N* ammonium hydroxide followed by 250 ml. of water. The eluate was evaporated to dryness on a steam-bath *in vacuo*. The resulting valine-2-C^{14} (50 μc., 0.504 g., 4.3 millimoles) was shown to be free from radioactive or amino acid contaminants by two-dimensional paper chromatography and radioautography.[8] The yield was 74.5% by weight from the oxazalone (70.5% radioactivity recovery), or 56% by weight (54% of the radioactivity) from unrecovered glycine-2-C^{14}.

Acknowledgment.—The authors wish to thank Prof. M. Calvin for his interest and assistance in this work.

(7) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 328.

(8) A. A. Benson, *et al.*, THIS JOURNAL, **72**, 1710 (1950).

RADIATION LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY 4, CALIFORNIA

The Reduction of Picryl Chloride to 1,3,5-Trinitrobenzene[1]

BY A. H. BLATT AND E. W. TRISTRAM

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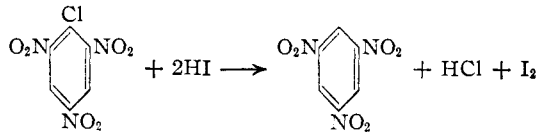
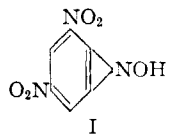
As part of a study that will be reported at another time it was necessary to replace the halogen atom in a heterocyclic nitro aryl halide by hydrogen. The usual methods of replacing halogen by hydrogen could not be used because they would also reduce the nitro groups. It occurred to us that the reduction of α-halo ketones by acidified potassium iodide, the second step in the Kurt Meyer indirect titration of enols, might be suitable provided the reaction did not involve the carbonyl group as such but depended rather upon the proper location of the halogen atom with respect to electron-attracting groups.

$$CH_3COCH_2Br + 2HI \longrightarrow CH_3COCH_3 + HBr + I_2$$

Picryl chloride was an ideal model compound for testing this possibility; not only because of its ready availability and structural similarity to the heterocyclic compound in which we were interested, but also because the reduction of picryl chloride to trinitrobenzene has been the object of of so much study. A review of the literature[2] did not reveal any attempts to carry out the reduction in the way we had in mind, so we undertook the necessary experiments and found that picryl chloride can be readily reduced to trinitrobenzene by sodium iodide in formic acid at the temperature of the steam-bath, or in acetic acid at the temperature of the steam-bath or at the boiling point, or in acetone containing some acetic acid at room temperature. The yield of crude trinitrobenzene varies between 70 and 100% depending on the experimental conditions; the yield of pure product averages 55–60%. Since the method of purification permits a maximum recovery of 80% of the trinitrobenzene present in the crude product, the yield of pure product corresponds to a yield of about 70% in the reaction.



After these experiments had been completed we reviewed the relevant literature again and found that the reaction had been done before, but the results were incorrectly interpreted, the product was listed as a substance of unknown structure, and the reaction had accordingly been overlooked for nearly 60 years. Willgerodt[3] had reported that a solution of picryl chloride and potassium iodide in acetic acid or formic acid or ethanol gave on boiling under reflux a product which he formulated originally as a dinitrosonitrophenol of unspecified orientation and later as the dinitro-*o*-phenylenehydroxylamine (I). The properties reported by Willgerodt for his product, including even the formation of addition products with



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(1) This note is based on work done under Contract DA-19-020-ORD-12 with the Office of the Chief of Ordnance and has been approved for publication by the Public Information Division, National Military Establishment.

(2) L. Desvergnes, *Chimie & Industrie*, **25**, 291 (1931); Roger Adams and C. S. Marvel, OSRD-312, December, 1941. A later reference is W. T. Smith, Jr., THIS JOURNAL, **71**, 2855 (1949).

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