The first and third photodimer had strong absorption in the infrared spectrum at 745 cm.$^{-1}$ (*cis*-disubstituted double bond[11]), while the second dimer (**4**) had bands of approximately equal intensity at 745 and at 845 and 805 cm.$^{-1}$ (trisubstituted double bond[11]).

**Thermal Rearrangement of Dimer 3.**—Aliquots of a solution of the major photodimer from α-phellandrene (29 mg., purified by preparative g.l.p.c.) and an internal standard (*cis*-1,9-octadecadiene, 7 μl.) in chloroform (45 μl.) were sealed in melting point capillaries and heated in an oil bath at 173 ± 3°. Samples were withdrawn and analyzed by g.l.p.c. on an XF 1150 column; the data for the disappearance of dimer **3** (six points) followed good first-order kinetics through two half-lives with $k_1 = 3.7 \times 10^{-5}$ sec.$^{-1}$. The thermal rearrangement of dimer **3** led to the second photodimer **4**, α-phellandrene, and other products having retention times appropriate for dimeric hydrocarbons.

(11) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p. 24.

## Deuterated Amino Acids. I. The Synthesis of Glycine-$d_5$ and Related Derivatives[1a]

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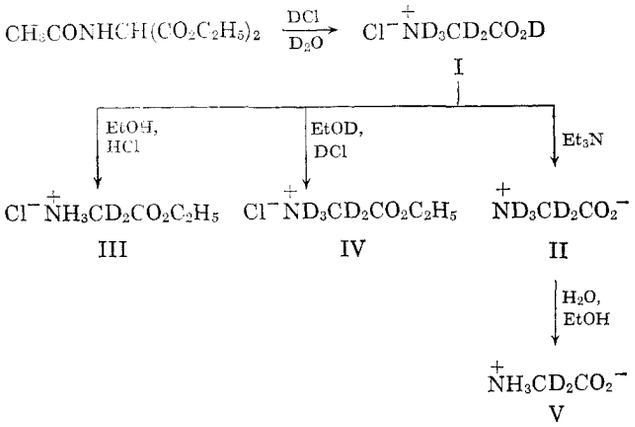
*Received August 31, 1965*

As part of a general research program concerned with the synthesis of deuterated amino acids and derived peptides, an inexpensive and efficient method for the preparation, in quantity, of glycine-$d_5$ and its ethyl ester hydrochloride was required. Examination of the literature revealed that the best preparations of glycine-$d_5$ were those which involved a standard exchange technique.[2] Since a thorough deuterium substitution of the nonlabile protons is both costly and time consuming owing to the necessity of performing several exchanges, the following synthetic scheme was devised.




When diethyl acetamidomalonate is refluxed in a DCl–$D_2O$ solution, prepared by the reaction of thionyl chloride with $D_2O$, glycine-$d_5$ deuteriochloride (I) is produced in 97% yield. The deuteriochloride salt I is quantitatively converted to glycine-$d_5$ (II) (97.1% isotopic purity) by treatment with triethylamine. Recrystallization of the amino acid II from water produced glycine-$d_2$ (V) which possesses >99% deuteration on the *α-carbon atom*. Glycine-2-$d_2$ ethyl ester hydrochloride (III), and the $d_5$ derivative IV are prepared in high yields from the salt I by Fischer esterification. A high degree of deuterium substitution on the α-carbon atom of salts I, III, and IV was indicated by n.m.r. (>95%) and substantiated by deuterium analysis[3] of V (99.7 atom % D). Deuterium analysis of salts I, III, and IV gave somewhat lower results (89–96 atom % D) than for compounds II and V owing to the hygroscopic nature[4] of the former substances.

### Experimental Section[5]

**Glycine-$d_5$ Deuteriochloride** (I).—Diethyl acetamidomalonate (21.7 g., 0.1 mole) was hydrolyzed[6] by refluxng overnight in an acidic solution prepared by carefully adding 30 ml. (0.413 mole) of redistilled thionyl chloride to 126 g. of 99.7% $D_2O$ at 0° in a dry atmosphere. The reaction mixture was concentrated to a semisolid at reduced pressure, and 400 ml. of tetrahydrofuran was added to precipitate the product. The mixture was chilled, filtered, and washed with absolute ether to give 11.42 g. (97%) of compound I as crystalline white needles. The product is slightly hygroscopic and should be protected from moisture at all times. Infrared analysis showed $\lambda_{max}^{KBr}$ 3.35, 4.18–4.62, 5.83, and 7.34 μ. Analysis by n.m.r. ($D_2O$) revealed no signal for the compound. The amino acid gave a single spot on paper chromatography, $R_f$ 0.63.

*Anal.* Calcd. for $C_2D_6ClNO_2$: C, 20.43; H, 5.72; Cl, 30.16; N, 11.91. Found: C, 20.79; H, 5.44; Cl, 30.13; N, 12.15.

The hydrogen analysis was based on 10.28% deuterium such that the calculated percentage of hydrogen obtained by routine analysis is 5.72%.

*Anal.* Calcd. for $C_2D_6ClNO_2$: D, 100 atom %. Found: D, 88.5 atom %.

**Glycine-$d_5$** (II).—The conversion of the salt I to the amino acid II was carried out in a nitrogen atmosphere (glove bag) in the following manner. The deuteriochloride I (2.00 g., 0.017 mole) was dissolved in 2 ml. of 99.7% $D_2O$, treated with 2.7 ml. (0.0193 mole) of freshly distilled triethylamine, and stirred magnetically for 10 min. Dry acetone (25 ml.) was added and the mixture was stirred an additional 10 min. The slurry of compound I and triethylamine deuteriochloride was filtered and washed with 10 ml. of acetone, three 10-ml. portions of chloroform, and finally with anhydrous ether to give 1.36 g. (100%) of compound II. Recrystallization from deuterium oxide afforded an analytical sample: $\lambda_{max}^{KBr}$ 4.16–4.78, 6.26, 7.10, 8.50, and 11.43 μ. Analysis by n.m.r. (DCl, $D_2O$) showed no absorption bands. Paper chromatography indicated a single spot, $R_f$ 0.64.

*Anal.* Calcd. for $C_2D_5NO_2$: C, 29.99; H, 7.00; N, 17.49. Found: C, 30.21; H, 6.74; N, 17.14.

The deuterium analysis accounts for 12.58% deuterium such that the calculated percentage of hydrogen as obtained by a routine analysis is 7.00%.

*Anal.* Calcd. for $C_2D_5NO_2$: D, 100 atom %. Found: D, 97.1 atom %.

(1) (a) This study was supported in part by the National Science Foundation, Grant No. G-18902; (b) Esso Education Foundation Fellow, 1964–1965; (c) National Institutes of Health Molecular Biology Training Grant Postdoctoral Fellow, 1965.

(2) (a) A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Interscience Publishers, Inc., New York, N. Y., 1958; (b) S. Suzulci, T. Shimanovchi, and M. Tsuboi, *Spectrochim. Acta*, **19**, 1195 (1963); (c) P. Neelakantan, R. S. Krishnan, and Y. Iitaka, *Proc. Indian Acad. Sci.*, **58**, 275 (1963).

(3) Unless otherwise stated, all deuterium analyses were performed by the falling-drop technique.

(4) The true degree of deuteration of these salts is difficult to ascertain, since they are unavoidably exposed to the atmosphere just prior to analysis.

(5) Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill. Deuterium analyses were carried out by Josef Nemeth, Urbana, Ill. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer, proton magnetic resonance spectra on a Varian Associates 60-Mc., Model A-60 instrument. Paper chromatography was performed by the ascending technique on Whatman No. 1 paper employing the solvent system ethanol–water (1:1) and ninhydrin as developer. Diethyl acetamidomalonate was obtained from the Aldrich Chemical Co., Inc., and recrystallized from absolute ethanol before use.

(6) For a related synthesis of tritiated glycine, see H. R. V. Arnstein and J. C. Crawhill, *Biochem. J.*, **67**, 180 (1957).

**Glycine-$d_2$ (V).**—Two recrystallizations of the amino acid II from water–ethanol effected exchange of the labile protons, producing glycine-$d_2$ in high yield: $\lambda_{max}^{KBr}$ 3.15–3.74, 4.45–4.70, 6.24, 6.64, 7.15, and 11.44 $\mu$. Analysis by n.m.r. (DCl, $D_2O$) showed only absorption due to the exchangeable protons. Paper chromatography indicated a single spot, $R_f$ 0.64.

*Anal.* Calcd. for $C_2H_3D_2NO_2$: C, 31.16; H, 6.83; N, 18.17. Found: C, 31.12; H, 6.65; N, 18.13.

The hydrogen analysis accounts for 3.92% hydrogen and 5.23% deuterium such that the calculated percentage of hydrogen as obtained by a routine analysis is 6.83%.

*Anal.* Calcd. for $C_2H_3D_2NO_2$: D, 40.00 atom %. Found: D, 39.9 atom % (99.7%).

**Glycine-2-$d_2$ Ethyl Ester Hydrochloride (III).**—Freshly distilled thionyl chloride (3.2 ml., 0.0455 mole) was carefully added to 25 ml. of absolute ethanol. When evolution of sulfur dioxide had ceased, the salt I (5.00 g., 0.0425 mole) was added and the solution was refluxed for 3 hr. After refrigeration, the solid was filtered, washed with anhydrous ether, and dried to afford 5.77 g. (96%) of the ester III. Four recrystallizations from absolute ethanol (30 ml. each) effected complete exchange of hydrogen for deuterium at the labile positions on nitrogen to give 5.06 g. (84%) of the ester III: m.p. 147.5–148°; $\lambda_{max}^{KBr}$ 3.30, 4.14–4.58, 5.72, 7.58, 8.35, and 11.67 $\mu$. Analysis by n.m.r. ($D_2O$) showed only signals due to the exchangeable protons and the ethyl moiety.

The ester III was homogeneous as indicated by paper chromatography, $R_f$ 0.82.

*Anal.* Calcd. for $C_4H_8D_2ClNO_2$: C, 33.93; H, 7.28; Cl, 25.04; N, 9.89. Found: C, 34.19; H, 7.27; Cl, 25.21; N, 10.02.

The hydrogen analysis accounts for 5.69% hydrogen and 2.85% deuterium such that the calculated percentage of hydrogen as obtained by a routine analysis is 7.28%.

*Anal.* Calcd. for $C_4H_8D_2ClNO_2$: D, 20.00 atom %. Found: D, 19.10 atom % (95.5%).

**Glycine-$d_4$ Ethyl Ester Deuteriochloride (IV).**—This material was prepared in 89% yield, m.p. 143–144.5°, by the same procedure as used for compound III except that ethanol-*d* was used as solvent.[7] Recrystallization from this solvent afforded an analytical sample: m.p. 145.5–146.5°; $\lambda_{max}^{KBr}$ 3.33, 4.37–4.60 5.72, 7.57, 8.43, and 11.67 $\mu$. Analysis by n.m.r. ($D_2O$) showed only signals due to the ethyl group.

Paper chromatography indicated one spot, $R_f$ 0.82, and a faint trace at $R_f$ 0.63 (glycine).

*Anal.* Calcd. for $C_4H_5D_5ClNO_2$: C, 33.22; H, 7.36; Cl, 24.52; N, 9.69. Found: C, 32.94; H, 7.08; Cl, 24.32; N, 9.81.

The hydrogen analysis accounts for 3.48% hydrogen and 6.97% deuterium such that the calculated percentage of hydrogen as obtained by a routine analysis is 7.36%.

*Anal.* Calcd. for $C_4H_5D_5ClNO_2$: D, 50.00 atom %. Found: D, 46.5 atom % (93.0%).

(7) A. Streitwieser, Jr., L. Verbit, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).

## The Preparation of 9-D-Mannofuranosyladenine[1]

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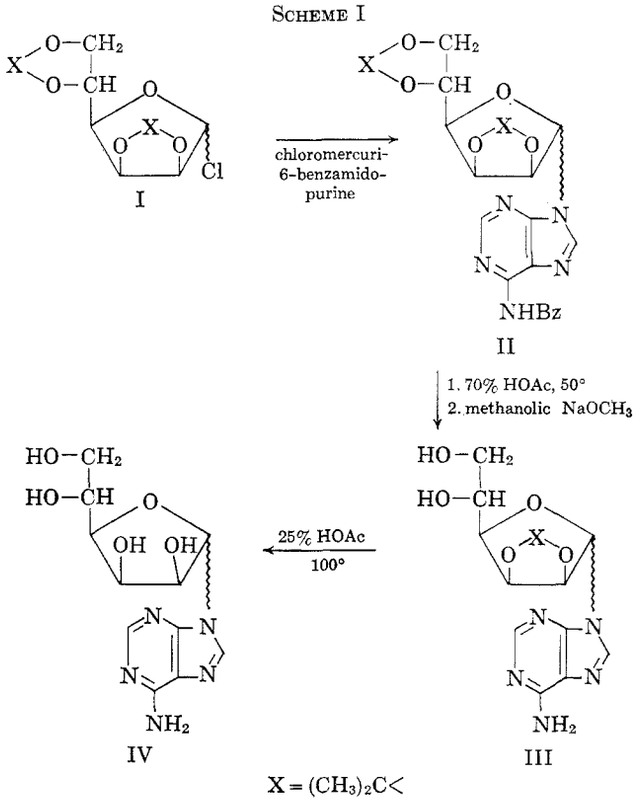
*Received July 19, 1965*

In recent years there has been an interest in the synthesis of hexofuranosyl nucleosides. From the laboratory of the authors has come a general procedure[2] for obtaining furanose derivatives of aldohexoses by using γ-lactones as starting materials. In the pathway, which capitalizes on the presence of the furan ring in γ-lactones, the hydroxyl groups are blocked by acylation and the lactone is reduced to a hemiacetal with bis(3-methyl-2-butyl)borane (disiamylborane). The anomeric hydroxyl group is then acylated, and an acylglycosyl halide is prepared and coupled with the base, from which hexofuranosyl nucleosides are obtained by removal of the blocking acyl groups.

Prior to this, special methods have been required to obtain furanose derivatives of the hexoses. Wolfrom, *et al.*,[3] proceeded by way of dithioacetal formation and furanose thioglycosides to effect the synthesis of gluco- and galactofuranosyl nucleosides. Isopropylidene derivatives of glucose[4] and a number of 6-deoxyhexoses[5] have been used as a means of obtaining furanose rings of six-carbon sugars in order to prepare nucleosides. Before nucleosides were prepared from these derivatives, however, it was necessary to block the 5-hydroxyl, remove the acetone blocking group, acylate the free hydroxyls, and prepare an acylglycosyl halide.

In the present report a synthetic pathway is described (Scheme I) for the preparation of a mannofuranosyl nucleoside which utilizes 2,3:5,6-diisopropylidenemannofuranose as the source of the furanose. It is unique in that the isopropylidene derivative is converted directly to a glycosyl halide and condensed with chloromercuri-6-benzamidopurine to yield a nu-

SCHEME I




(1) (a) Taken in part from a thesis submitted by L. M. Lerner to the University of Illinois Graduate College in partial fulfillment of the requirements for the Ph.D. degree. (b) Supported in part by Grant P-161 from the American Cancer Society and by Training Grant GM-471 from the Division of General Medical Sciences of the U. S. Public Health Service.

(2) P. Kohn, R. H. Samaritano, and L. M. Lerner, *J. Am. Chem. Soc.*, **86**, 1457 (1964).

(3) M. L. Wolfrom, P. McWain, R. Pagnucco, and A. Thompson, *J. Org. Chem.*, **29**, 454 (1964); M. L. Wolfrom and P. McWain, *ibid.*, **30**, 1099 (1965).

(4) E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1958 (1958).

(5) B. R. Baker and K. Hewson, *ibid.*, **22**, 966 (1957); E. J. Reist, R. R. Spencer, and B. R. Baker, *ibid.*, **23**, 1753; 1757 (1958); E. J. Reist, L. Goodman, R. R. Spencer, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 3962 (1958); E. J. Reist, L. Goodman, and B. R. Baker, *ibid.*, **80**, 5775 (1958).