DL-5-Hydroxy-2-methyltryptophan.—A solution of 16.5 g. (0.0705 mole) of crude (m.p. 248–250°) DL-5-benzyloxy-2-methyltryptophan in 250 ml. of 0.5 *N* NaOH was hydrogenated [initial pressure 4.22 kg./cm.^{2} (60 lb./p.s.i.)] in the presence of 10 g. of 10% palladium on charcoal.[10] Hydrogenation stopped after 0.268 kg./cm.^{2} of hydrogen had been absorbed (theoretical uptake, 0.288 kg./cm.^{2}). The solution was filtered and evaporated *in vacuo*, and the residue was dissolved in water. The resulting solution was adjusted, to pH 5.86 with 6 *N* HCl, filtered to remove SiO_2, and evaporated to dryness. The residue was slurried twice with ice water (5-ml. portions) and recrystallized from 50% ethanol; yield 3.07 g. (15.8%), m.p. 292–293°.

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.03; N, 11.96.

(10) This procedure was developed by J. Koo, S. Avakian, and G. J. Martin, *J. Org. Chem.*, **42**, 279 (1959), for the hydrogenolysis of 5-benzyloxytryptophan to 5-hydroxytrytophan.

The Synthesis of Disalicyl Alcohols

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Salicyl alcohol is used as an antipyretic and as a local anesthetic.[1] It is possible that the related compounds which we report might possess similar potential uses. Clemmensen and Heitman[2] have shown that 5,5′-methylenedisalicylic acid can be prepared by the condensation of formaldehyde and salicylic acid. In this investigation, the dimethyl ester of this acid has been reduced to its corresponding alcohol with $LiAlH_4$. It is shown that the efficiency of the reduction is related to the nature of the bridging group. A significant increase in yield was realized when a modification of the procedure was used to synthesize 5,5′-isopropylidenedisalicyl alcohol.

Experimental[3,4]

5,5′-Isopropylidenedisalicylic Acid.—A mixture of 32 g. (0.23 mole) of salicylic acid, 7.73 g. (0.133 mole) of acetone, and 180 g. of 60% sulfuric acid was heated under gentle reflux for 10–12 hr. with constant stirring. It was then allowed to cool and was filtered, and the residue was washed with cold water and air dried. Unchanged salicylic acid was removed by adding the powdered product to boiling water, with constant stirring, filtering while hot, and allowing the residue to dry in air. Purification was effected by dissolving the crude product in an excess of hot 95% ethanol, treating with Norit, filtering, and reprecipitating with cold water. The tan material was dried in a vacuum desiccator ($CaCl_2$); yield 11 g. (30.2%), m.p. 287–289°.

Anal. Calcd. for $C_{17}H_{16}O_6$: C, 64.60; H, 5.07. Found: C, 64.90; H, 5.35.

Dimethyl 5,5′-Isopropylidenedisalicylate.—This dimethyl ester was prepared by the Fischer–Speier[5] method. The product was isolated in the usual manner and recrystallized from absolute methanol. Fifty grams of acid gave 18 g. (33.3%) of pure ester, m.p. 98–99°.

5,5-Isopropylidenedisalicyl Alcohol.—A solution of 4.0 g. (0.1 mole) of $LiAlH_4$ in 225 ml. of absolute ether was made by stirring the slurry for 4 hr. The reaction mixture was protected from atmospheric moisture by attaching $CaCl_2$ tubes to all openings. Then a solution of 12.0 g. (0.035 mole) of dimethyl 5,5′-isopropylidenedisalicylate in 120 ml. of absolute ether was added through the dropping funnel at a rate which produced gentle reflux. After the addition, the reaction was gently heated at reflux temperature for 12 hr. and allowed to cool. The excess $LiAlH_4$ was decomposed by the cautious addition of water. The contents of the reaction flask were then added to a mixture of crushed ice and concentrated H_2SO_4, stirred for 10 min., and filtered. This residue was combined with the residue obtained by evaporating the dried ether layer of the filtrate. These solids were then repeatedly recrystallized from hot water until long white needles of the desired pure alcohol were obtained; yield 5.0 g. (25%), m.p. 146–147°.

Anal. Calcd. for $C_{17}H_{20}O_4$: C, 70.83; H, 6.94. Found: C, 70.85; H, 6.79.

5,5′-Methylenedisalicyl Alcohol.—This alcohol was prepared by the $LiAlH_4$ reduction of its dimethyl ester according to the procedure outlined above for the isopropylidene alcohol. The crude product was recrystallized from hot water to give glistening, pale gray plates; yield 2.0 g. (8%), m.p. 166–167°.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.23; H, 6.15. Found: C, 69.25; H, 6.20.

(1) C. O. Wilson and T. E. Jones, "The American Drug Index," J. B. Lippincott Co., Philadelphia, Pa., 1956, p. 419.

(2) E. Clemmensen and H. C. Heitman, *J. Am. Chem. Soc.*, **33**, 737 (1911).

(3) Microanalyses by Drs. Weiler and Strauss, Microanalytical Laboratory, Oxford, England.

(4) Melting points were determined in a standard capillary melting point bath with a calibrated thermometer.

(5) E. Fischer and A. Speier, *Ber.*, **28**, 3252 (1895).

Aromatic Fluorine Compounds. XIII. Substituted N-Phenylglycine Ethyl Esters and Hydrazides[1]

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Data on the herbicidal and medicinal properties of halogenated N-arylglycine esters and hydrazides are limited to a few compounds. In 1949 when the plant growth regulating properties of maleic hydrazide[2] were reported, N-(2,4-dichlorophenyl)-glycine[3] was found also to have herbicidal properties. The first biological data on fluorinated arylglycine derivatives appeared about a decade later. Tuberculostatic tests[4] were reported on N-(4-fluorophenyl)glycine, its ethyl ester, and its hydrazide. Tomato leaf curvature data[5] appeared in 1959 on N-(3-trifluoromethylphenyl)glycine and N-(3-trifluoromethyl-4-chlorophenyl)-glycine and their amides.

A large number of fluorine, other halogen, and methyl derivatives of N-phenylglycine was prepared as part of a program[6] on the synthesis of fluorinated herbicides and medicinals. Tables I and II summarize the physical data on 31 glycine ethyl esters and 28 glycine hydrazides, respectively.

Experimental[7]

N-Phenylglycine Ethyl Esters.—These compounds with substitution in the phenyl group were prepared by condensing the appropriately substituted primary anilines with ethyl chloroacetate.[4,8]

To a well-stirred mixture of 114 g. (0.75 mole) of sodium acetate trihydrate and 50–75 ml. of ethanol was added 0.5 mole of the appropriate aniline and 62 g. (0.5 mole) of ethyl chloroacetate. The reaction mixture was refluxed gently with stirring for 24–48

(1) This research was supported in part by contract with the U. S. Army Biological Laboratories, Fort Detrick, Frederick, Md., through the University of Illinois. The research was the responsibility of the Illinois State Geological Survey.

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(7) All melting points were taken in a capillary tube and are corrected (ASTM-specification thermometer).

(8) W. Baker, W. D. Ollis, and V. D. Poole, *J. Chem. Soc.*, 307 (1949).