maining after removal of the dibromide gave a 3.71 g. fraction, b.p. *ca.* 110° at 1.2 mm., which crystallized and was identified as succinimide; thus, in this experiment, essentially all of the succinimido portion of the original NBS has been accounted for as succinimide and N-phenylsuccinimide.

In another experiment, 3.0 g. of cyclobutene, 8.1 g. of NBS and 34 ml. of carbon tetrachloride were heated in a sealed tube at 75° for ninety minutes with occasional shaking; there was isolated, *inter alia*, 0.30 g. of a viscous pale brown oil, b.p. 107–109° at 1 mm. This oil contained halogen (Beilstein test), was insoluble in cold 48% hydrobromic acid and dissolved in this solvent on heating; the analysis indicated the presence of the 1:1 adduct[14] of cyclobutene and NBS.

Anal. Calcd. for $C_8H_{10}BrNO_2$: C, 41.40; H, 4.34; N, 6.04. Found: C, 40.62; H, 4.91; N, 5.84.

(14) An analogous product was obtained[5] under similar conditions from methylenecyclobutane and NBS; *cf.* ref. 5, footnote 8.

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The Synthesis of the Glycine Homolog of Thyroxine[1]

BY EARL FRIEDEN[2] AND RICHARD J. WINZLER

In a search for compounds which might prove to be competitive inhibitors of thyroxine, and to elucidate further the structural requirements for thyroxine-like activity, we have synthesized the glycine homolog of thyroxine, a compound having a glycine instead of an alanine side chain. This was accomplished, though in poor yield, by the application of a Strecker synthesis to the aldehyde, 3,5-diiodo-4-(4′-methoxyphenoxy)-benzaldehyde, prepared essentially by the method of Harington and Barger[3] and Niemann and Redemann.[4] The resulting amino acid (I) was treated with hydroiodic acid to give the 3,5-diiodo-DL-thyronine homolog (II), which was iodinated to produce 3,5-diiodo-4-(3′,5′-diiodo-4′-hydroxyphenoxy)-DL-phenylglycine. This compound has proved to be approximately one-third as active as DL-thyroxine in accelerating amphibian metamorphosis and 1/500 as active as DL-thyroxine in preventing the increase of the thyroid weights of mice fed thiouracil.[5]

Experimental

3,5-Diiodo-4-(4′-methoxyphenoxy)-DL-phenylglycine (I).—To a solution of 2.7 g. of 3,5-diiodo-4-(4′-methoxyphenoxy)-benzaldehyde in ethanol was added 15 ml. of an aqueous solution containing 1.25 g. sodium cyanide and 1.62 g. ammonium chloride. The mixture was shaken for eighteen to twenty hours at room temperature, then diluted with water and extracted with three 30-ml. portions of 6 *N* hydrochloric acid. The combined acid extracts were washed once or twice with ether. The acid solution was then heated to the boiling point for several hours while being subjected to a very gentle suction to concentrate the solution and to reduce the hydrochloric acid concentration. After filtration and cooling, a white crystalline solid, the hydrochloride of I, appeared. Neutralization of the acid mother liquor gave free I. The two fractions were dissolved in warm, dilute ammonium hydroxide, the solution filtered, and I obtained in 5–10% yield by the addition of acetic acid. I gave a positive ninhydrin reaction but a negative Folin phenol test. For elementary analysis a sample was repeatedly recrystallized as the hydrochloride from 1% hydrochloric acid. The free acid, obtained by isoelectric precipitation, was then employed for analysis. Under the microscope, it appeared as flat, rectangular crystals, m.p. 186–189°.

Anal. Calcd. for $C_{15}H_{13}O_4NI_2$ (525): C, 34.3; N, 2.7; I, 48.4. Found: C, 34.3; N, 2.8; I, 48.2.

3,5-Diiodo-4-(4′-hydroxyphenoxy)-DL-phenylglycine (II).—I, 250 mg., was dissolved in 8 ml. of glacial acetic acid and refluxed for ninety minutes with 2 ml. freshly distilled 50% hydriodic acid. The mixture was then evaporated to dryness on a water-bath, water added, and again distilled to dryness. The residue was dissolved in 15 ml. of warm dilute hydrochloric acid, filtered, and washed several times with ethyl ether. Neutralization of the aqueous fraction to *p*H 6 precipitated II in 60% yield. Since II gave a strongly positive Folin phenol test and caused an appreciable depression of melting point when mixed with an equal quantity of I, an elementary analysis was not deemed necessary. It melted at 192–194°.

3,5-Diiodo-4-(3,5′-diiodo-4′-hydroxyphenoxy)-DL-phenylglycine, (III), the Glycine Homolog of DL-Thyroxine.—When II was iodinated with iodine monochloride according to the method of Block and Powell,[6] no product could be isolated. However, iodination was effected by the method of Datta and Prosad.[7] II, 100 mg., dissolved in 3 ml. 7 *N* ammonium hydroxide, was cooled in an ice-bath, and 0.9 ml. 1 *N* potassium triiodide slowly added. The rapid decolorization of the solution indicated absorption of iodine. After allowing the mixture to stand in the cold for thirty minutes, the excess iodine was destroyed with sodium bisulfite. Neutralization of the solution with acetic acid gave crude III, as needles, in 50% yield. III was recrystallized by acidifying a dilute ammoniacal solution of the amino acid. III gave positive ninhydrin, Folin phenol tests and a red positive Kendall test for *o*-diiodophenols. III melted with decomposition at 167–170°.

Anal. Calcd. for $C_{14}H_9O_4NI_4$ (763): C, 22.0; I, 66.5; H, 1.2. Found: C, 21.7; I, 64.2; H, 1.4.

The somewhat low iodine and carbon analyses and the high hydrogen analysis can be accounted for by assuming at least partial hydration of compound III, a well known property of *o*-diiodo phenols.

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A Synthesis of *cis*-1,3-Diphenyl-1-butene

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In the course of an investigation in this laboratory, it became necessary to prepare hydratroponitrile (α-phenylpropionitrile). Inasmuch as the preparative methods involving (1) the methyla-