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.

(1) This work was taken from a thesis presented to the Graduate School of the University of Southern California by Earl Frieden in partial fulfillment of the requirements for the degree of Master of Science.

(2) We wish to acknowledge the support of this work by grants from the National Research Council Committee on Research in Endocrinology and from the Eli Lilly Company, and to thank the Hancock Foundation for providing laboratory facilities.

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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-

tion of benzyl cyanide in the presence of sodamide[1] and (2) the conversion of β-methyl-β-phenylglycidate through the aldehyde and oxime[2] are either long or subject to difficulties, an attempt was made to convert α-chloroethylbenzene into the desired nitrile.

Our first attempt was to treat α-chloroethylbenzene with an alcoholic solution of sodium cyanide by the procedure used in preparing benzyl cyanide from benzyl chloride.[3] Instead of the expected nitrile, there was obtained only ethyl (α-phenylethyl) ether,[4] b. p. 67° (11 mm.); micro b. p. 183° (745 mm.) with decomposition; $n^{20}D$ 1.4848; d^{20}_4 0.9212.

Inasmuch as the ether was formed in preference to the nitrile, it appeared desirable to carry out the reaction in the absence of alcohol. Consequently α-chloroethylbenzene was heated with cuprous cyanide in the manner of the von Braun nitrile synthesis. Runs were made with and without potassium iodide[5] and copper sulfate[6] as catalysts. When the reaction mixture was heated in an oil-bath at 130°, a vigorous reaction set in, accompanied by the evolution of hydrogen cyanide. It was found best to chill the reaction flask after fifteen minutes and to extract the reaction mixture with benzene. A colorless oil distilled at 134–135° (*ca.* 1 mm.), micro b. p. 311° (737 mm.); $n^{20}D$ 1.5939; d^{20}_4 0.9968. This product contained neither nitrogen nor chlorine, but decolorized bromine in cold carbon tetrachloride. These physical[7] and chemical properties approximate those of the diphenylbutenes (distyrenes).

The position of unsaturation was determined by treating the liquid with a solution of hydrogen peroxide in *t*-butyl alcohol in the presence of osmium tetroxide.[8] After removal of the solvent under diminished pressure, benzaldehyde distilled. No other homogeneous fraction was isolated. The benzaldehyde was characterized as the 2,4-dinitrophenylhydrazone.

Benzaldehyde should be obtained by the cleavage of either 1,3-diphenyl-1-butene (I) or 1,3-diphenyl-2-methyl-1-propene (II). The latter should also yield methyl benzyl ketone, whereas the hydratropaldehyde of the former might be easily oxidized further. Failure to isolate a second degradation product from the hydroxylation mixture indicated I as the more probable structure of our compound.

A liquid distyrene of formula I has been described by numerous investigators. From it Stobbe and Posnjak[9] obtained a dibromide melting at 102°. This product is described by Stoermer and Kootz[10] and Marion[11] as a mixture of racemic dibromides which are derived from the *cis* form of I. The *trans* isomer of I is a solid melting at 47°.[11]

Bromination of our liquid hydrocarbon by the procedure of Stobbe and Posnjak[9] gave a white crystalline compound melting at 102°. When this was mixed with an authentic sample of the dibromo derivative of *cis*-1,3-diphenyl-1-butene obtained from cinnamic acid by the method of Stoermer and Kootz,[10] no melting point depression was observed. Our hydrocarbon is thus shown to be *cis*-1,3-diphenyl-1-butene.

Experimental

α-Chloroethylbenzene was prepared by a modification of the procedure of Kharasch and Kleiman.[12] Five hundred twenty grams (5 moles) of styrene containing its inhibitor was placed in a 1-liter three-necked flask equipped with a mercury-sealed stirrer, an inlet tube and an exit tube immersed in a reservoir of mercury. The flask was immersed in an ice–salt-bath and dry hydrogen chloride gas was passed in under a pressure of 50 to 75 mm. Saturation of the styrene with hydrogen chloride required eight to twelve hours. Distillation of the reaction mixture under diminished pressure gave α-chloroethylbenzene in yields of 80–90%.

Preparation of 1,3-Diphenyl-1-butene (I).—This preparation was carried out in a hood. One hundred seventy-five grams (1.25 moles) of α-chloroethylbenzene was added to 112 g. of commercial cuprous cyanide (dried and undried material gave identical results) in a 500-ml., three-necked flask equipped with an effective mercury-sealed stirrer, a thermometer and an uncooled reflux condenser. A glass tube connected the top of the condenser to a coil and receiver packed in an ice–salt-bath. The reaction flask was heated in an oil-bath. At a temperature of 130° a vigorous evolution of hydrogen cyanide occurred. After 40 to 45 ml. of hydrogen cyanide was condensed in the coil and receiver, the temperature in the flask rose suddenly and the reaction proceeded more vigorously. The condenser was now flooded with water. After ten minutes, the oil-bath was replaced by a cold water-bath. The cold reaction mixture was extracted with four 100-ml. portions of benzene.

The benzene was removed and the crude product fractionated under reduced pressure through a one-foot column packed with glass helices. A colorless oil, distilling at 134–135° (*ca.* 1 mm.), was obtained; yield, 41%.

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Complete Chlorination of Methyltrichlorosilane[1]

BY PHILIP A. DI GIORGIO,[2] LEO H. SOMMER AND FRANK C. WHITMORE

Prior publications[3,4] on the synthesis and properties of chloromethyl silicon compounds have

(1) Paper XX in a series on organosilicon compounds. For paper XIX see THIS JOURNAL, **70**, 2876 (1948).

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