at −70°, m.p. 48–50°. This melting point was not depressed when mixed with dibromo ketone XIb.

Recrystallization of *fraction b* from petroleum ether at −70° gave monobromo ketone Xa, m.p. 67–69°.

Fraction c, after recrystallization from petroleum ether and sublimation *in vacuo* yielded yellow crystals, m.p. 50–53°. Reported for carbocamphenilone (VI), m.p. 58–59°,[32] 56–59°.[4]

The reaction of I *with potassium t-butoxide.* Potassium *t*-butoxide, 8.2 g., was added to 350 ml. of toluene and 100 ml. of toluene was removed by distillation. Compound I, 7.4 g., was added slowly to the resulting clear solution, a precipitate formed immediately. After heating for 4 hr., the mixture was allowed to cool and was filtered. The toluene solution was washed with water and then the toluene was removed. Distillation afforded 7.0 g. of XIX and XX, b.p. 46.5–47° (0.3 mm.), n_D^{20} 1.4730, λ_{max} 6.05 μ.

Anal. Calcd. for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.39; H, 11.34.

One gram of the enol ether mixture was treated with Brady's reagent[9] affording 1.58 g. of an orange solid, m.p. 125–127°. A portion of this solid, 229 mg., was chromatographed on silica gel and afforded the following fractions: (*a*) 57.2 mg. of the 2,4-dinitrophenylhydrazone of ketone IIb, m.p. 117–119° from ethanol; (*b*) 5.0 mg. of the 2,4-dinitrophenylhydrazone of aldehyde V; and (*c*) 125.5 mg. of the 2,4-dinitrophenylhydrazone of ketone IIa, m.p. 136–138° from ethanol.

2-Butyne. To a solution of 19.5 g. of potassium *t*-butoxide, dried at 170° *in vacuo*, in 150 ml. of *p*-cymene heated to 160° was added 18.5 g. of 1,2-dibromo-2-methylpropane at such a rate that the exothermic reaction which ensued did not cause *t*-butyl alcohol to distill from the system. A volatile product, 3 g., crystallizing as long white needles, was collected in a Dry Ice–trichloroethylene cooled trap. There followed the distillation of a colorless liquid, b.p. 80–82°, whose infrared spectrum was identical with that of *t*-butyl alcohol. The infrared spectrum of the volatile product, in a gas cell, displayed all the maxima characteristic of 2-butyne. In addition, a weak band at 5.10 μ and a strong band at 11.20 μ suggested the presence of a small amount of 1,2-butadiene.

Addition of bromine to the volatile product afforded a white solid, m.p. 228–230° from petroleum ether. Reported for 2,2,3,3-tetrabromobutane, m.p. 230°,[33] 237°.[34]

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LAFAYETTE, IND.

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[CONTRIBUTION FROM THE DEPARTAMENTO DE QUÍMICA, FACULDADE DE FILOSOFIA, CIENCIAS E LETRAS,
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Synthesis of 6,8-Diphenoxyoctanoic Acid

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6,8-Diphenoxyoctanoic acid has been synthesized from the γ-butyrolactone by two different routes.

In our studies of homologation of the fatty acids chain[1a,1b] we were looking for substituting groups would emerge unaltered from the intermediate reactions. Dibenzylthio groups proved to be unsuitable for this purpose, since it was observed that 3,5-dibenzylthiopentanoic acid failed to undergo the Kolbe reaction and that the use of 2,4-dibenzylthiobutyric acid afforded secondary products in several steps of the chain homologation reactions.[2] Phenoxy groups which are less reactive deserved our attention. This paper describes a synthesis of 6,8-diphenoxyoctanoic acid.

γ-Butyrolactone was converted into 2,4-dibromobutyric acid by the modified Plieninger procedure.[3,4]

In order to avoid the elimination of hydrogen bromide which would lead to the formation of α-bromo-γ-butyrolactone, the crude reaction product was converted immediately into the corresponding methyl ester by treatment with methanol saturated with hydrogen chloride. The reaction of methyl 2,4-dibromobutyrate with sodium phenolate yielded methyl 2,4-diphenoxybutyrate. This compound was reduced to 2,4-diphenoxybutanol with lithium aluminium hydride in cold tetrahydrofuran, which by treatment with phosphorus tribromide gave 1-bromo-2,4-diphenoxybutane. The condensation of the latter compound with methyl sodiomalonate, followed by alkaline hydrolysis and decarboxylation, produced 4,6-diphenoxyhexanoic acid, which was characterized by conversion into the *S*-benzylisothiouronium salt. When the ethyl sodiomalonate was used, difficulties were found during the purification of the intermediate diethyl ester.

4,6-Diphenoxyhexanoic acid was submitted to electrolysis in the presence of an excess of benzyl hydrogen succinate. The benzyl ester, then formed by crossed coupling, could be either separated from the methyl ester of the starting acid by fractional

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distillation or, without isolation, be converted into the required acid by hydrogenolysis.[5]

Using the first procedure we obtained the 6,8-diphenoxyoctanoic acid in 32.4% yield. It was characterized by conversion into the *S*-benzylisothiouronium salt. Of the two expected products of symmetrical coupling, only the benzyl adipate was identified. This is the first case of homologation of a fatty acid chain containing a phenoxy group. To our knowledge, only the symmetrical Kolbe reaction with phenoxyacetic acid has been described.[6]

6,8-Diphenoxyoctanoic acid was also obtained by the following reactions: The 4,6-diphenoxyhexanoic acid was first converted into the corresponding methyl ester by the use of methanol saturated with hydrogen chloride. The methyl 4,6-diphenoxyhexanoate was reduced to the corresponding alcohol with lithium aluminium hydride in tetrahydrofuran and the 4,6-diphenoxyhexanol treated with phosphorus tribromide. 1-Bromo-4,6-diphenoxyhexane, obtained in this way, was not fully characterized, but when condensed with methyl sodiomalonate, afforded, after alkaline hydrolysis and decarboxylation, the 6,8-diphenoxyoctanoic acid. Its *S*-benzylisothiouronium salt was identical with that obtained from the electrolysis product. The over-all yield of the 6,8-diphenoxyoctanoic acid obtained from the 4,6-diphenoxyhexanoic acid, by the sequence of reactions described above, was 29.3% which was only slightly lower than that obtained by direct anodic synthesis.

Transformation of 6,8-diphenoxyoctanoic acid into 6,8-dibromooctanoic acid which may be easily converted into α-lipoic acid[7,8] is being studied.

EXPERIMENTAL

Methyl 2,4-dibromobutyrate. One ml. of phosphorus tribromide was added to 49.5 g. of γ-butyrolactone and the reaction mixture was heated to 100°. The mixture was stirred while 28 ml. of bromine was added dropwise beneath the surface of the liquid. The temperature was maintained at 110–115° by the rate of bromine addition. When the rate of bromine uptake decreased, 0.25 ml. of phosphorus tribromide was added and heat was applied to maintain reaction temperature. The addition of bromine was continued until hydrogen bromide evolution was evident. Then the product was stirred and cooled to room temperature and finally cooled in an ice bath. To this crude product 240 ml. of absolute methanol was added and the resulting solution was saturated with dry hydrochloric acid. The reaction mixture was allowed to stand at room temperature for 22 hr. and the methanol was removed *in vacuo*. The residue was extracted with ether. The ether extract was washed with 3% sodium bicarbonate solution to remove unchanged acid and then dried over anhydrous sodium sulfate. The solvent was removed and the residue distilled under reduced pressure. A fraction was collected boiling at 68–70°/2 mm., weight 130.2 g. (86.8%).

Anal. Calcd. for $C_5H_8O_2Br$: C, 23.1; H, 3.1. Found: C, 23.5; H, 3.1.

Methyl 2,4-diphenoxybutyrate. Sodium, 63.36 g., was dissolved in 1.870 ml. of absolute ethanol. To this solution was added with stirring 288 g. of phenol and slowly, 360 g. of the methyl 2,4-dibromobutyrate. Sodium bromide immediately began to separate. The mixture was refluxed for about 5 hr. and the alcohol distilled. After addition of water the reaction product was extracted with ether and washed with dilute sodium hydroxide to remove an excess of phenol. Afterwards it was washed with water. The ethereal solution was evaporated *in vacuo* and the solid residue recrystallized from ethanol. The yield of product was 134 g. (40.0%), m.p. 91–92°.

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.3; H, 6.3. Found: C, 71.2; H, 6.6.

2,4-Diphenoxybutanol. To a stirred suspension of 7.0 g. of lithium aluminium hydride in 90 ml. of anhydrous tetrahydrofuran, cooled in an ice-salt bath, was added, dropwise, a solution of 30 g. of methyl 2,4-diphenoxybutyrate in 160 ml. of anhydrous tetrahydrofuran. The reaction mixture was stirred for 2 hr. at room temperature and then water was added dropwise to decompose an excess of lithium aluminium hydride. The mixture was stirred with 200 ml. of 10% sulfuric acid and extracted with ether. The ether extract was washed with water, dried over anhydrous sodium sulfate and the solvent removed *in vacuo*. The residue was distilled to yield 28 g. (96.4%) of a liquid, b.p. 190°/1 mm.

Anal. Calcd. for $C_{16}H_{18}O_3$: C, 74.4; H, 7.0. Found: C, 73.8; H, 7.2.

1-Bromo-2,4-diphenoxybutane. 2,4-Diphenoxybutanol, 13.3 g., was maintained below 0° while 5.4 g. (15% excess) of phosphorus tribromide was added dropwise with stirring. Stirring was continued for 5 hr. at 0° and the reaction mixture was allowed to stand at room temperature overnight. The reaction mixture was poured into cold water and extracted with ether. The ether extract was washed with water and dried over anhydrous sodium sulfate. The solvent was removed and the residue distilled under reduced pressure. The main fraction was collected, 10.8 g. (65.4%), b.p. 184–186°/1 mm.

Anal. Calcd. for $C_{16}H_{17}O_2Br$: C, 59.8; H, 5.3. Found: C 60.4; H, 5.4.

4,6-Diphenoxyhexanoic acid. Sodium, 9.4 g., was dissolved in 340 ml. of absolute ethanol. To this solution 81 g. of methyl malonate and 131 g. of 1-bromo-2,4-diphenoxybutane were added with stirring. The mixture was refluxed for about 28 hr. until the reaction was complete. Most of the alcohol was removed by distillation from a steam bath and water was added to dissolve the sodium bromide. The ester layer was extracted with ether and dried over anhydrous sodium sulfate. The ether was removed and the residue distilled under reduced pressure to give, as the main fraction, a liquid, 127.8 g., b.p. 200–230°/1 mm. This impure product was refluxed with 176 ml. of 30% sodium hydroxide for 32 hr. The solution was then cooled and separated from the unchanged ester by several extractions with ether. The aqueous solution was acidified with concentrated hydrochloric acid and the separated acid was extracted with ether which was dried over anhydrous sodium sulfate and removed under reduced pressure. The residue which weighed 73.3 g., was heated in a metal bath at 190° until the evolution of carbon dioxide had ceased. The remaining material was distilled under reduced pressure. The acid was collected at 224°/0.7 mm.; yield 54.6 g. (44.6%).

Anal. Calcd. for $C_{18}H_{20}O_4$: equiv. 300. Found: equiv. 303.7.

S-Benzylisothiouronium salt of 6,8-diphenoxyhexanoic acid. A concentrated solution of the neutral salt of the 6,8-diphenoxyoctanoic acid was added rapidly with stirring to a slight excess of a 15% solution of *S*-benzylthiouronium chloride in hot ethanol solution. Upon cooling the solid product

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separated. This was crystallized from dilute ethanol, m.p. 107–109°.

Anal. Calcd. for $C_{26}H_{30}O_4N_2S$: C, 67.0; H, 6.4; N, 6.0; S, 6.8. Found: C, 67.6; H, 7.0; N, 5.6; S, 6.3.

Methyl 4,6-diphenoxyhexanoate. A solution of 40.8 g. of 4,6-diphenoxyhexanoic acid in 60 ml. of absolute methanol was saturated with dry hydrochloric acid. The reaction mixture was allowed to stand at room temperature for 24 hr. and methanol was removed *in vacuo*. The residue was extracted with ether which was washed with 3% sodium bicarbonate solution to remove unchanged acid and then dried over anhydrous sodium sulfate. After the remotion of the solvent, the residue was distilled under reduced pressure giving 39 g. (91.3%) of the ester collected at 203–205°/1 mm.

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.1; H, 7.0. Found: C, 72.1; H, 6.8.

4,6-Diphenoxyhexanol. To a stirred suspension of 9.0 g. of lithium aluminium hydride in 115 ml. of anhydrous tetrahydrofuran, cooled in an ice-salt bath, was added dropwise a solution of 39.0 g. of methyl 4,6-diphenoxyhexanoate in 150 ml. of anhydrous tetrahydrofuran. The reaction mixture was worked up as described for preparation of 2,4-diphenoxybutanol. The yield of product, b.p. 215°/1 mm., was 32.9 g. (88%).

Anal. Calcd. for $C_{18}H_{22}O_3$: C, 75.6; H, 7.7. Found: C, 76.0; H, 8.2.

1-Bromo-4,6-diphenoxyhexane. Phosphorus tribromide, 11.6 g., was treated with 30.5 g. of 4,6-diphenoxyhexanol by the procedure described for the preparation of 1-bromo-2,4-diphenoxybutane. Distillation of the residue gave 30.6 g. (82%) of a liquid boiling at 197–200°/1 mm.

No further attempt was made at purification but this product was used at once for the next preparation.

6,8-Diphenoxyoctanoic acid. (a). *From 1-bromo-4,6-diphenoxyhexane.* The general procedure used was that described for the preparation of 4,6-diphenoxyhexanoic acid. The quantities used were: 20 g. of sodium, 73 ml. of absolute ethanol, 17.25 g. of methyl malonate and 30.4 g. of 1-bromo-4,6-diphenoxyhexane. The distillation under reduced pressure gave the main fraction boiling at 205–240°/1 mm., weight 25 g. Hydrolysis of this impure product with 43 ml. of 30% sodium hydroxide, followed by decarboxylation gave a residue which boiled at 243–245°/1 mm.; yield 12.8 g. (44.7%).

Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.2; H, 7.3; neut. equiv. 328. Found: C, 73.0; H, 7.8; neut. equiv. 325.

S-Benzylisothiouronium salt of 6,8-diphenoxyoctanoic acid. The procedure used was that described for the preparation of the *S*-benzylisothiouronium salt of 6,8-diphenoxyhexanoic acid. The m.p. of the solid product was 130–131°.

Anal. Calcd. for $C_{28}H_{34}O_4N_2S$: C, 67.9; H, 6.8; N, 7.6; S, 6.4. Found: C, 67.6; H, 6.7; N, 7.8; S, 5.9.

(b) *From 4,6-diphenoxyhexanoic acid.* A mixture of 4,6-diphenoxyhexanoic acid (9.8 g.) and benzyl hydrogen succinate (17.2 g.) in methanol (90 ml.), which contained 0.08 g. of sodium, was electrolyzed (0.8 amp., faradays passed *ca.* 1.5 times theoretical). A considerable amount of a colorless polymer began to separate from the electrolyte at an early stage in the electrolysis. After the electrolysis the alkaline cell contents were acidified and then evaporated. The residue was separated in the usual way into acidic and neutral fractions. Distillation of the latter gave three fractions: (i) A liquid (2.6 g.) b.p. 70–90°/0.3 mm. (ii) A fraction (2.65 g.) b.p. 150–180°/0.3 mm. which partly solidified. (iii) A liquid (7.4 g.) b.p. 210–250°/0.3 mm. Fraction (iii) and sodium hydroxide (4.0 g.) in water (8 ml.) and methanol (26 ml.) were boiled under reflux for 10 hr. An excess of alkali was then neutralized by 2*N* hydrochloric acid, the methanol was distilled off and the aqueous solution was extracted with ether. Evaporation of ether extract yielded a resinous product (1 g.). The ether insoluble material was treated with an excess of 30% hydrochloric acid and the resulting acid was extracted with ether. The residue left on evaporation of ether was distilled, giving 2.5 g. (32.4%) of 6,8-diphenoxyoctanoic acid, b.p. 234°/0.4 mm. Its *S*-benzylisothiouronium salt prepared as in (a) melted at 130–131° undepressed on admixture with a sample of the *S*-benzylisothiouronium salt prepared in (a). Fraction (ii), crystallized from petroleum ether (b.p. 50–70°), had m.p. 39°, undepressed on admixture with a specimen of benzyl adipate.

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[CONTRIBUTION FROM THE B. F. GOODRICH RESEARCH CENTER AND GOODRICH-GULF CHEMICALS, INC.]

Deuterio 1,3-Butadienes Derived by Reductive Dechlorination

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1,3-Butadiene-d_6, 1,3-butadiene-2,3-d_2, 1,3-butadiene-2-d_1 and 1,3-butadiene-1-d_1 have been prepared. The method of synthesis involves the reduction of mono-, di- and hexachloro-1,3-butadienes, and 1,4-dichloro-2-butyne with zinc and deuterium oxide. The reduction is catalyzed by cupric chloride as well as by sodium iodide. It was also applied to three dichlorobutenes. Dioxane, as previously reported, is a convenient solvent for the reaction but actually no solvent other than water is required. The use of maleic anhydride and gas phase chromatography (propylene carbonate column) for the analysis of 1,3-butadiene is described.

As part of an extensive program in these laboratories for the preparation of a variety of deuterated polymers, interest was recently focused on the preparation and stereospecific polymerization of several deuterio 1,3-butadiene monomers, *viz.*, butadiene-2-d_1, butadiene-2,3-d_2, and butadiene-d_6. This paper is concerned with the preparation of these monomers. The stereoregular polymerization[1a] of the monomers and the infrared spectra[1b] of the polymers will be presented elsewhere.

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