

2-Bromo-3',5-diacetaminobiphenyl (XI).—A solution containing 3 g. of 2-bromo-3'-nitro-5-acetaminobiphenyl and 6.5 g. of hydrated stannous chloride in 100 cc. of alcohol was refluxed for ten hours. After removal of alcohol, sodium hydroxide was added, and the base extracted with ether. After removal of the ether, the crude base was acetylated, yielding 1.9 g. of a product which melts at 265–266° when crystallized from glacial acetic acid.

*Anal.* Calcd. for  $C_{16}H_{13}N_2O_2Br$ : Br, 23.03. Found: Br, 22.84.

The above product melted unchanged when mixed with the bromo diacetamino derivative obtained from IX by a similar method.

2-Bromo-5-nitroiodobenzene.—A hot solution of 36 g. of 2-bromo-5-nitroaniline<sup>9</sup> in 400 cc. of glacial acetic acid was quickly cooled to room temperature. It was then diazotized by adding it to 13 g. of sodium nitrite in 91 cc. of concd. sulfuric acid, keeping the temperature below 40°. The diazonium solution was added to a solution of 98 g. of potassium iodide and 200 g. of anhydrous sodium acetate in 1100 cc. of ice water. After standing overnight the precipitated crystals were washed and crystallized from methanol; yield, 31 g., m. p. 95–96°. The pure product melts at 97–98°.

*Anal.* Calcd. for  $C_6H_4NO_2IBr$ : N, 4.27. Found: N, 4.41.

2-Bromo-3',4',5-trinitrophenyl (XII).—This was prepared by Ullmann's reaction on a mixture of 3,4-dinitro-

(9) Wheeler, *Am. Chem. J.*, **17**, 899 (1895).

iodobenzene and 2-bromo-5-nitroiodobenzene. After repeated crystallization from alcohol-acetone a product melting at 222–223° was obtained.

*Anal.* Calcd. for  $C_{12}H_6N_3O_6Br$ : Br, 21.72. Found: Br, 21.44.

This product melted unchanged when mixed with the trinitrophenyl obtained by treating IX with fuming nitric acid (sp. gr. 1.59).

Oxidation of XII with chromic anhydride in acetic acid in presence of vanadium oxide yielded 2-bromo-5-nitrobenzoic acid, m. p. 177°.

### Summary

1. The nitration of 2-chlorobiphenyl according to Mascarelli is shown to yield 2-chloro-4',5-dinitrophenyl.

2. The nitration of 2-bromo-2'-nitro-2-bromo-4'-nitro-, and 2-bromo-3'-nitrophenyl with ethyl nitrate forms in every case a 2-bromo-5-nitro derivative.

3. The further nitration of the above dinitro products yields in the first two cases 2-bromo-2',4',5-trinitrophenyl and in the last case 2-bromo-3',4',5-trinitrophenyl.

4. Proof of the structures of the nitration products is given.

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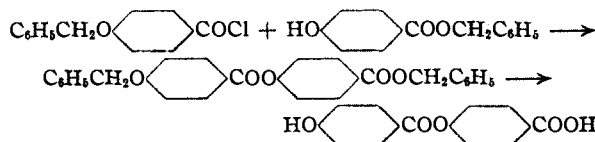
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF WINTHROP CHEMICAL COMPANY, INC.]

## Synthesis of Phenolic Acid Esters. I. Depsides<sup>1</sup>

BY CHESTER J. CAVALLITO AND JOHANNES S. BUCK

The preparation of depsides by the method of E. Fischer<sup>2</sup> involves several disadvantages, notably differential saponification to remove the protecting group, anhydride formation, and migration of certain acyl groups.

Other methods of preparation, such as those of Currie and Russell,<sup>3</sup> and Pepe,<sup>4</sup> yield only the methyl ethers of the depsides.



The present authors have found that, by causing the benzyl ether of a phenolic acid chloride to react with the benzyl ester of a phenolic acid, there is obtained smoothly and in good yield the benzyl ether-benzyl ester of a didepside. This is readily converted by hydrogenolysis under mild conditions into the didepside. By this method,

(1) Presented before the Division of Organic Chemistry at the 106th meeting of the American Chemical Society, Pittsburgh, Pennsylvania, Sept. 8, 1943.

(2) E. Fischer, "Untersuchungen über Depside und Gerbstoffe," J. Springer, Berlin, 1919.

(3) T. Currie and A. Russell, *J. Chem. Soc.* 2263 (1932); 140 (1933).

(4) R. O. Pepe, *J. prakt. Chem.*, **126**, 241 (1930); *Chem. Abs.*, **34**, 3426 (1940); **37**, 2723 (1943).

differential saponification, anhydride formation and migration are all avoided. The method is capable of considerable extension. The properties of the compounds involved are listed in the table.

### Experimental

**Benzyl Esters of *o*-, *m*- and *p*-Hydroxybenzoic Acids.**—Fourteen grams (0.1 mole) of the hydroxybenzoic acid was dissolved in 150 cc. of 95% ethanol. To this 100 cc. of 1 *N* sodium hydroxide solution and 13 cc. (0.11 mole) of benzyl chloride were added and the mixture refluxed for two hours, then distilled to about one-third of its volume. Water was added to the residue and the whole chilled until the oily product which first separated became crystalline. The meta and para derivatives were recrystallized from 70% ethanol and the ortho isomer was distilled under reduced pressure.

**Benzyl 2,4-Dihydroxybenzoate.**—To 31 g. (0.2 mole) of *β*-resorcylic acid was added 250 cc. of 95% ethanol, 50 cc. of 4 *N* potassium hydroxide solution and 25 cc. (0.21 mole) of benzyl chloride. The whole was refluxed for two hours. After cooling, the water insoluble layer was separated and extracted with sodium bicarbonate solution. The oily insoluble residue was distilled under reduced pressure to yield a waxy crystalline solid.

**Benzyl 4-Benzoyloxybenzoate.**—To a solution of 14 g. (0.1 mole) of *p*-hydroxybenzoic acid in 125 cc. of 95% ethanol was added 67 cc. of 3 *N* sodium hydroxide solution and 25 cc. (0.21 mole) of benzyl chloride. The mixture was refluxed for three hours, then cooled. The crystals formed were filtered off, washed with sodium carbonate solution and recrystallized from 95% ethanol.

**4-Benzoyloxybenzoic Acid.**—This could be prepared by saponification of the previously described compound or

TABLE I

No. <sup>a</sup>	Compound	Appearance	Yield, %	M. p., °C.	Formula	Analyses, % <sup>b</sup>			
						Carbon		Hydrogen	
						Calcd.	Found	Calcd.	Found
1	Benzyl 4-hydroxybenzoate	Prisms	40	111	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	...	...	...	...
2	Benzyl 3-hydroxybenzoate	Large granular crystals	35	70	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	73.69	73.83	5.27	5.39
3	Benzyl 2-hydroxybenzoate	Colorless liquid		B. p. (3 mm.) 158	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	...	...	...	...
4	Benzyl 2,4-dihydroxybenzoate	Waxy crystals	30	60 <sup>c</sup>	C <sub>14</sub> H <sub>12</sub> O <sub>4</sub>	68.85	69.10	4.92	5.15
5	Benzyl 4-(benzyloxy)-benzoate	Needles	56	115	C <sub>20</sub> H <sub>18</sub> O <sub>3</sub>	79.24	79.26	5.66	5.65
6	4-(Benzyloxy)-benzoic acid	Elongated plates	90+ from no. 5	188	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	73.69	73.31	5.27	5.26
7	2-(Benzyloxy)-benzoic acid	Plates	50 from salicylic acid	70	C <sub>14</sub> H <sub>12</sub> O <sub>3</sub>	73.69	73.90	5.27	5.07
8	2,4-Bis-(benzyloxy)-benzoic acid	Granular crystals	5 <sup>±</sup> from β-resor-cyclic acid	180	C <sub>20</sub> H <sub>18</sub> O <sub>4</sub>	75.45	75.80	5.39	5.45
9	3,4,5-Tris-(benzyloxy)-benzoic acid	Long, fibrous needles	30 from gallic acid	189	C <sub>26</sub> H <sub>24</sub> O <sub>4</sub>	76.36	76.43	5.45	5.63
10	4-(Benzyloxy)-benzoyl chloride	Needles	90+ from 6	110	C <sub>14</sub> H <sub>11</sub> O <sub>2</sub> Cl		Cl,	14.40	14.0
11	3,4,5-Tris-(benzyloxy)-benzoyl chloride	Needles	80 from 9	115	C <sub>26</sub> H <sub>23</sub> O <sub>2</sub> Cl		Cl,	7.74	7.3
12	Benzyl 4-(4-(benzyloxy)-benzyloxy)-benzoate	Plates	90+ from 1 and 10	166	C <sub>28</sub> H <sub>24</sub> O <sub>4</sub>	76.71	76.83	5.02	4.89
13	Benzyl 3-(4-(benzyloxy)-benzyloxy)-benzoate	Cryptocrystalline	90+ from 2 and 10	107	C <sub>28</sub> H <sub>24</sub> O <sub>4</sub>	76.71	76.65	5.02	5.08
14	Benzyl 2-(4-(benzyloxy)-benzyloxy)-benzoate	Very small needles	70 from 3 and 10	73	C <sub>28</sub> H <sub>24</sub> O <sub>4</sub>	76.71	77.00	5.02	4.80
15	Benzyl 4-(2-(benzyloxy)-benzyloxy)-benzoate	Cryptocrystalline	75 from 1 and 7	71	C <sub>28</sub> H <sub>24</sub> O <sub>4</sub>	76.71	76.69	5.02	5.11
16	4-(4-Hydroxybenzyloxy)-benzoic acid	Granular crystals	90+ from 12	270 <sup>±</sup>	C <sub>14</sub> H <sub>10</sub> O <sub>4</sub>	65.11	65.40	3.87	4.12
17	3-(4-Hydroxybenzyloxy)-benzoic acid	Wedge-shaped crystals	90+ from 13	247	C <sub>14</sub> H <sub>10</sub> O <sub>4</sub>	65.11	65.01	3.87	4.01
18	2-(4-Hydroxybenzyloxy)-benzoic acid	Prisms	90+ from 14	180	C <sub>14</sub> H <sub>10</sub> O <sub>4</sub>	65.11	65.19	3.87	3.85
19	4-(2-Hydroxybenzyloxy)-benzoic acid	Granular crystals	90 from 15	210	C <sub>14</sub> H <sub>10</sub> O <sub>4</sub>	65.11	65.30	3.87	3.85
20	Benzyl 4-(3,4,5-tris(benzyloxy)-benzyloxy)-benzoate	Needles	60 from 1 and 11	107	C <sub>44</sub> H <sub>34</sub> O <sub>7</sub>	77.53	77.60	5.23	5.13
21	4-(3,4,5-Trihydroxybenzyloxy)-benzoic acid	Rhombs	90+ from 20	255-260	C <sub>14</sub> H <sub>10</sub> O <sub>7</sub>	57.93	58.02	3.45	3.51
22	Benzyl 2,4-dis-(4-benzyloxy-benzyloxy)-benzoate	Cryptocrystalline	60 <sup>±</sup> from 4 and 10	111	C <sub>42</sub> H <sub>32</sub> O <sub>8</sub>	75.90	75.74	4.82	4.96
23	2,4-Dis-(4-hydroxybenzyloxy)-benzoic acid	Very small granular crystals	80-90 from 22	210 <sup>±</sup>	C <sub>14</sub> H <sub>10</sub> O <sub>8</sub>	63.96	63.61	3.55	3.57

<sup>a</sup> Nos. 1 and 3 are available from Eastman Kodak Co. Others have been prepared previously by different methods: 6, Bacon, *Chem. Zentr.*, 79, II, 945 (1908); 7, Perkin, *Ann.*, 148, 27 (1868); 9, Schöpf and Winterhalter, *ibid.*, 544, 62 (1940); 10, Cohen and Dudley, *J. Chem. Soc.*, 97, 1746 (1910); 16, Beilstein, 4th ed., Vol. X, p. 162; 17, Lepsius, *Ann.*, 406, 16 (1914); 21, E. Fischer, *Ber.*, 41, 2876, 2888 (1908). <sup>b</sup> The authors wish to thank Miss E. Bass and Miss H. Hutchinson for the microanalyses. <sup>c</sup> B. p., 2 mm., 215°.

directly as follows: 138 g. (1 mole) of *p*-hydroxybenzoic acid was dissolved in 1 liter of 95% ethanol and 500 cc. of 2 *N* sodium hydroxide solution. To this solution was added 346 cc. (3 moles) of benzyl chloride and the whole was then refluxed. One liter of 5 *N* sodium hydroxide solution was added dropwise over a period of two hours. After heating for an additional hour, the solvent was distilled off until one-half the original volume was reached and 2 liters of water was then added. The warm aqueous solution was acidified with hydrochloric acid to precipitate the product which was recrystallized from 95% ethanol.

**2-Benzyloxybenzoic Acid.**—This was prepared by the above procedure from salicylic acid. The product obtained was heated to 120° under reduced pressure (2 mm.) to remove salicylic acid, then recrystallized from 70% ethanol.

**2,4-Bis-(benzyloxy)-benzoic Acid.**—To 20 g. (0.1 mole) of β-resorcylic acid (trihydrate) dissolved in 200 cc. of 95% ethanol was added 100 cc. of 1 *N* sodium hydroxide solution and 58 cc. (0.5 mole) of benzyl chloride. While refluxing the solution, 100 cc. of 5 *N* sodium hydroxide solution was added over forty-five minutes. After refluxing for an additional hour, 50 cc. of 5 *N* sodium hydroxide solution was added and the whole heated for one hour. The solvent was distilled off until one-half the original volume was reached and the solution was then cooled and acidified. The precipitate which formed was recrystallized from 95% ethanol. The yield was poor.

**3,4,5-Tris-(benzyloxy)-benzoic Acid.**—To 170 g. of gallic acid (or 188 g. of monohydrate or 1 mole) dissolved in 2 liters of 95% ethanol was added 1 liter of 1 *N* sodium

hydroxide solution and 750 cc. (825 g. or 6.5 moles) of benzyl chloride. The solution was refluxed, and 1.1 liters of 5 *N* sodium hydroxide solution was added over a period of ninety minutes. After refluxing for an additional hour, 200 cc. of 40% potassium hydroxide solution was added and the whole heated for a further hour. After cooling, the upper aqueous layer was separated and hydrochloric acid was added to precipitate the product, which was then recrystallized from 95% ethanol.

**Acid Chlorides of the Phenolic Acid Benzyl Ethers.**—The phenolic acid benzyl ethers were dissolved by heating for fifteen to thirty minutes in an excess of thionyl chloride on a steam-bath. Excess thionyl chloride was distilled off under reduced pressure. If the product was solid, it could be recrystallized from hot Skellysolve C or Skellysolve-benzene mixture.

The gallic acid tribenzyl ether was more conveniently converted to the acid chloride by means of phosphorus pentachloride in benzene. Skellysolve was then added, the acid chloride precipitating on cooling.

To avoid tar formation in preparing the acid chloride, the gallic acid tribenzyl ether should be recrystallized until perfectly white.

**Depside Benzyl Ethers-Benzyl Esters.**—The desired benzyl ether acid chloride and benzyl ester of the phenolic acid were dissolved in pyridine and mixed in molar proportions. The pyridine solution was heated on a steam-bath for one and one-half to two hours, cooled and diluted with water to precipitate the product. Recrystallization was carried out from 95% ethanol or ethanol-dioxane mixture.

Attempts to esterify phenolic acid benzyl esters by means

of 2,4-bis-(benzyloxy)-benzoyl chloride resulted in the formation of tarry amorphous products. Since tarry products resulted from warming the acid chloride alone in pyridine, it appears that the compound is capable of reacting with itself. The use of alkali bases instead of pyridine resulted in the same behavior.

**Free Depsides.**—The depside benzyl ethers—benzyl esters were dissolved in dioxane and reduced at 50° with spongy palladium catalyst<sup>5</sup> under about 40 lb. pressure. After thirty to sixty minutes, the hydrogenolysis was complete as measured by the hydrogen absorption. The catalyst was filtered off, the dioxane distilled off under

reduced pressure and the depside recrystallized from 70% ethanol.

### Summary

Simple depsides have been prepared by treating benzyloxybenzoyl chlorides with benzyl esters of phenolic acids to form the benzyl ethers—benzyl esters of depsides which are then catalytically hydrogenolyzed to form the free depsides. The synthesis has been used to prepare ortho, meta and para depsides.

(5) Willstätter, *Ber.*, **54**, 123 (1921).

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## Unsaturated Synthetic Glycerides. I. Unsymmetrical Monoöleo-Disaturated Triglycerides<sup>1</sup>

BY B. F. DAUBERT, H. H. FRICKE AND H. E. LONGENECKER

Much of the investigation concerning synthetic glycerides has been focused on the establishment of adequate methods of synthesis for glycerides containing only saturated acids from intermediates of proved configuration and structure. The saturated rather than unsaturated glycerides have occupied the attention of many workers primarily because of the availability of saturated acids of high purity and the comparative simplicity of obtaining crystalline products of relatively high melting point and purity. On the basis of the comprehensive work done on the synthesis of glycerides during the past few years, it seems reasonably certain that satisfactory methods are now available for the preparation of mixed triglycerides.

Relatively little attention has been devoted to the synthesis of glycerides containing unsaturated acids. Kreis and Hafner<sup>2</sup> heated symmetrical distearin with oleic acid under reduced pressure and reported a small yield of 2-oleo-1,3-distearin. Grün and co-workers<sup>3,4</sup> reported the preparation of the same compound by heating distearin with oleic anhydride. The isomeric 1-oleo-2,3-distearin was prepared by Amberger and Bromig<sup>5</sup> from 1-monoölein and stearyl chloride.

In view of the fact that an oleic acid of satisfactory purity has been prepared by simplified methods, only recently, by Wheeler and Riemenschneider,<sup>6</sup> Brown and Shinowara<sup>7</sup> and others, it is doubtful whether the earlier investigators had available an oleic acid of sufficient purity to warrant its use in the synthesis of glycerides.

In 1937, Bömer and Kappeller<sup>8</sup> reported the preparation of several mixed triglycerides con-

taining elaidic acid. The synthesis of 1-mono-linolein by debromination of 1-mono-(9,10,12,13-tetrabromo)-stearin has been reported by Black and Overley.<sup>9</sup>

The nomenclature of the fatty acid derivatives of glycerol, used in past literature references, has been somewhat inconsistent, Greek letters and numbers both being used to designate the carbons in the glycerol molecule. Since Greek letters are used to differentiate the geometrical isomers of unsaturated fatty acids, polymorphism in glycerides, etc., we have chosen to adopt the numerical nomenclature for the purpose of avoiding possible confusion. In this and succeeding publications from this Laboratory, alpha monoglycerides will be referred to as 1-monoglycerides, beta monoglycerides as 2-monoglycerides, symmetrical and unsymmetrical diglycerides as 1,3- and 1,2-diglycerides, respectively. The same nomenclature will be applied to symmetrical and unsymmetrical mixed triglycerides and to those mixed triglycerides containing three fatty acids.

Glycerides containing unsaturated acids are an important group of naturally occurring components of fats and oils. Because of the paucity of information concerning unsaturated synthetic glycerides, there is an evident necessity of obtaining physical and chemical data for this group of compounds. The postulated structures of those triglycerides isolated from natural sources will need to be checked against the evidence and data provided by synthesis.

The purpose of the present paper is to report the physical and chemical data for a series of unsymmetrical monoöleo-disaturated triglycerides. Data on the symmetrical isomers will be reported at a later date.

### Experimental

**Fatty Acids.**—All saturated fatty acids, including capric, lauric, myristic, palmitic, and stearic, were obtained by careful purification of crude acids.

(1) The authors are indebted to Swift and Company and to the Buhl Foundation for grants in support of this investigation.

(2) Kreis and Hafner, *Ber.*, **36**, 1123 (1903).

(3) Grün and Schacht, *ibid.*, **40**, 1778 (1907).

(4) Grün and Theimer, *ibid.*, **40**, 1792 (1907).

(5) Amberger and Bromig, *Biochem. Z.*, **130**, 252 (1922).

(6) Wheeler and Riemenschneider, *Oil and Soap*, **16**, 207 (1939).

(7) Brown and Shinowara, *THIS JOURNAL*, **59**, 6 (1937).

(8) Bömer and Kappeller, *Fette u. Seifen*, **44**, 340 (1937).

(9) Black and Overley, *THIS JOURNAL*, **61**, 3051 (1939).