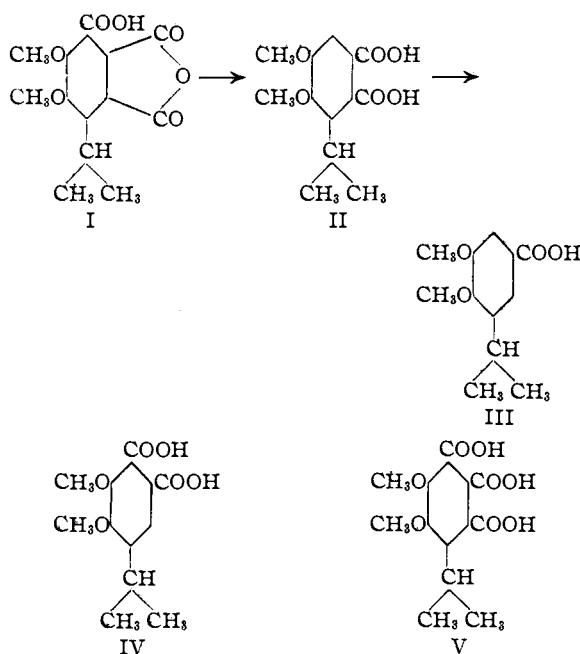


[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Structure of Gossypol. XXI.¹ Synthesis of 1,2-Dimethoxy-3-isopropyl-4-benzoic Acid and of Apogossypolic Acid

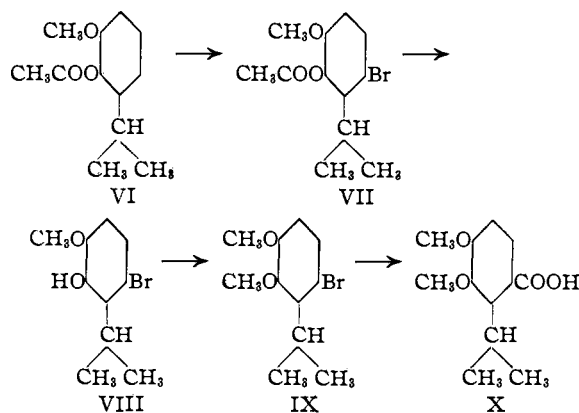
BY ROGER ADAMS AND B. R. BAKER

The establishment of 1,2-dihydroxy-3-isopropyl-5-benzoic acid as the compound obtained by the action of hydrobromic acid on gossic (I) or apogossypolic acid (II) suffices to narrow the

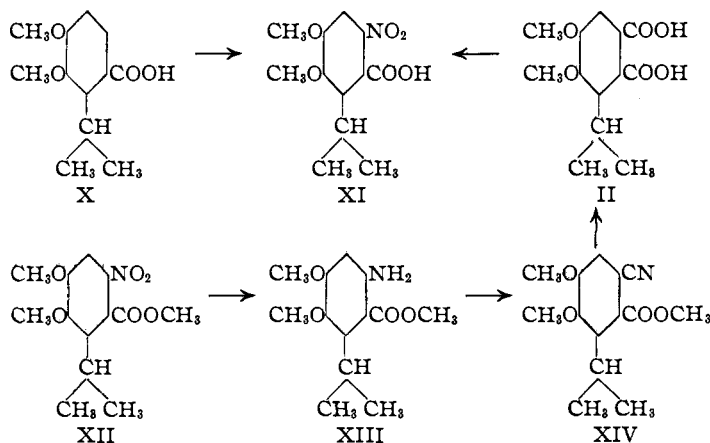


possible formulas for apogossypolic acid to that shown in II and to the 5,6-dicarboxylic acid (IV). Although the latter is impossible on the basis of the suggested formulas for gossypol and apogossypol, nevertheless complete proof of formula II can be obtained only by synthesis. This has now been accomplished.

The acetyl derivative of 1-methoxy-2-hydroxy-3-isopropylbenzene (VI) was brominated. As the methoxyl has a greater orientating power than the acetoxy, the bromine enters the 4-position (VII). This orientation has previously been demonstrated.² Deacetylation gave the compound 1-methoxy-2-hydroxy-3-isopropyl-4-bromobenzene (VIII) and subsequent methylation 1,2-dimethoxy-3-isopropyl-4-bromobenzene (IX) which on



forming the Grignard reagent and treatment with carbon dioxide gave 1,2-dimethoxy-3-isopropyl-4-benzoic acid (X). This acid, which is analogous to veratric acid and its homologs,³ should and does nitrate in the open position para to the 2-methoxyl giving 1,2-dimethoxy-3-isopropyl-5-nitro-4-benzoic acid (XI), which proved to be identical with the product of nitration of apogossypolic acid (II). The methyl ester of the synthetic nitro compound (XII) and that derived from the nitrated apogossypolic acid also proved to be the same. Upon reduction, the methyl 1,2-dimethoxy-3-isopropyl-5-



nitro-4-benzoate gave the corresponding amine (XIII) which was diazotized and the nitrile (XIV) which was diazotized and the nitrile

(1) For previous paper see Adams, Hunt and Baker, *THIS JOURNAL*, **61**, 1134 (1939).

(2) Hindmarsh, Knight and Robinson, *J. Chem. Soc.*, **111**, 941 (1917).

(3) Heinisch, *Monatsh.*, **15**, 230 (1894); Ziucke and Franke, *Ann.*, **293**, 189 (1895).

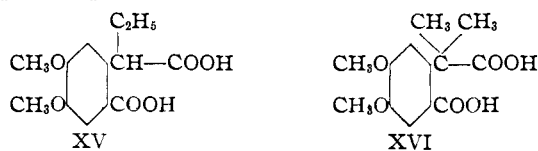
group introduced (XIV). By saponification, 1,2-dimethoxy-3-isopropyl-4,5-dicarboxybenzene (II) resulted which proved to be identical with apogossypolic acid. The synthetic nitro compound (XI) upon reduction and sublimation gave 1,2-dimethoxy-3-isopropyl-5-aminobenzene which has been synthesized previously.⁴

It is of interest that, as an intermediate in the synthesis just described, 1,2-dimethoxy-3-isopropyl-4-benzoic acid (X) was prepared. This is the dimethyl ether of the third possible 1,2-dihydroxy-3-isopropylbenzoic acid discussed in the previous paper.¹

With the formula of apogossypolic acid proven, the structure of gossic acid, except for the establishment of which two carboxyls take part in the formation of the anhydride linkage, is defined (I). Gossic acid in hydrated form (V) differs from apogossypolic acid (II) merely by an additional carboxyl group. Since only one position is available for that group, the relative positions of this carboxyl group and the isopropyl group are fixed as para.

Gossic and apogossypolic acids are obtained by analogous procedures from gossypol hexamethyl ether and apogossypol hexamethyl ether, respectively. The essential difference between these two latter compounds lies in the presence of two aldehyde groups in the gossypol derivative which are replaced by hydrogens in the apogossypol derivative. It follows, therefore, that the carboxyl group in gossic acid which is not found in apogossypolic acid corresponds to one of the aldehyde groups in gossypol. Thus, each of the aldehyde groups in gossypol is proved to be para to an isopropyl group. Since the two hydroxyls and the isopropyl have been shown previously to be orientated 1,2-dihydroxy-3-isopropyl, the groups in the gossypol molecule must be 1-aldehydro-2,3-dihydroxy-4-isopropyl. This verifies what has been proposed as the placement of groups in the naphthalene nuclei of gossypol.

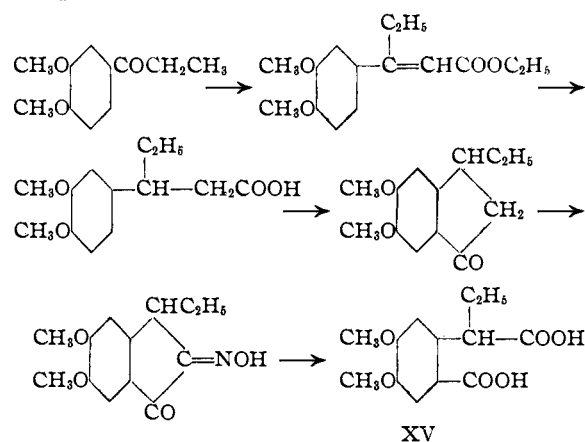
Before it was recognized that an isopropyl group was present in the ring in these benzene degradation products, it was postulated that apogossypolic acid might have the structure XV



(4) Adams, Hunt and Morris, *THIS JOURNAL*, **60**, 2972 (1938).

or XVI. An investigation was under way to synthesize these molecules but was incomplete when evidence became available that these formulas could not be the correct ones for the compounds in hand. Opportunity is taken here to describe the experimental results which led to the preparation of 1,2-dimethoxy-4,5- α -ethyl homophthalic acid (XV) and the corresponding α -methyl compound which, however, was not successfully methylated further to give a compound of structure XVI.

The homophthalic acid derivative (XV) and its methyl homolog were synthesized by the following procedure.



Experimental

1-Methoxy-2-acetoxy-3-isopropylbenzene (VI).—A solution of 20 g. of crude 1-methoxy-2-hydroxy-3-isopropylbenzene⁴ in 40 cc. of acetic anhydride was refluxed for three hours and then poured into water. The acetyl derivative was extracted with ether: colorless liquid, b. p. 118–120° (3 mm.); n_D^{20} 1.5023; d_{20}^{20} 1.057; yield, 22 g. (80%).

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.23; H, 7.69. Found: C, 69.08; H, 7.61.

1-Methoxy-2-acetoxy-3-isopropyl-4-bromobenzene (VII).—To a solution of 19 g. of 1-methoxy-2-acetoxy-3-isopropylbenzene in 30 cc. of carbon tetrachloride kept below 0° was added dropwise with stirring over a period of an hour 5.2 cc. of bromine in 20 cc. of carbon tetrachloride. After removal of the solvent, the residue was fractionally distilled: yellowish oil, b. p. 157–168° (10 mm.); n_D^{20} 1.5370; d_{20}^{20} 1.500; yield, 24 g. (92%).

Anal. Calcd. for $C_{12}H_{15}O_3Br$: C, 50.17; H, 5.23. Found: C, 49.87; H, 5.24.

1,2-Dimethoxy-3-isopropyl-4-bromobenzene (IX).—A solution of 16.5 g. of 1-methoxy-2-acetoxy-3-isopropyl-4-bromobenzene and 20 g. of potassium hydroxide in 75 cc. of ethanol and 20 cc. of water was refluxed for two hours. The ethanol was evaporated on the steam-bath and the residue diluted with water and acidified. The phenol was extracted with ether and the solvent evaporated. It was then dissolved in 25 cc. of methanol, 15 cc.

of dimethyl sulfate was added and 20% aqueous potassium hydroxide was introduced slowly until the solution was permanently alkaline to litmus. This procedure was repeated with two 5-cc. portions of dimethyl sulfate. Finally, the mixture was heated for thirty minutes on a steam-bath. The cooled solution was extracted with ether. The product was a colorless liquid, b. p. 122–125° (3 mm.); n_D^{20} 1.5413; d_4^{20} 1.326; yield, 9.5 g. (63%).

Anal. Calcd. for $C_{11}H_{16}O_2Br$: C, 51.00; H, 5.79. Found: C, 51.04; H, 5.87.

1,2-Dimethoxy-3-isopropyl-4-benzoic Acid (X).—To 9.5 g. of 1,2-dimethoxy-3-isopropyl-4-bromobenzene in 150 cc. of dry ether was added 1 g. of magnesium followed by the gradual addition of 12 cc. of ethyl bromide. The mixture was refluxed for sixteen hours on a steam-bath, then the solution was decanted from the excess magnesium and carbonated by the addition of dry ice. After standing for an hour, the solution was poured into dilute hydrochloric acid. The ether layer was separated and extracted with 10% aqueous sodium hydroxide. Upon acidification of the alkaline solution and cooling, the product was filtered; yield, 5 g. (60%). It was purified by crystallization from a mixture of benzene and petroleum ether (b. p. 60–110°); white crystals, m. p. 119–121° (corr.).

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.30; H, 7.14. Found: C, 64.16; H, 6.99.

1,2-Dimethoxy-3-isopropyl-5-nitro-4-benzoic Acid (XI).—A suspension of 0.5 g. of 1,2-dimethoxy-3-isopropyl-4-benzoic acid in 20 cc. of water and 5 cc. of nitric acid (sp. gr., 1.42) was refluxed an hour. Complete solution took place. Upon cooling, fine white needles separated; yield, 0.52 g. (95%). It was purified by crystallization from dilute ethanol, m. p. 157–159° (corr.).

Anal. Calcd. for $C_{12}H_{13}NO_6$: C, 53.55; H, 5.58; N, 5.22. Found: C, 53.20; H, 5.56; N, 5.11.

This product proved to be identical with the nitration product of apogossypolic acid⁵ as shown by melting points and mixed melting points.

Methyl 1,2-Dimethoxy-3-isopropyl-5-nitro-4-benzoate (XII).—To a dry ether solution of 0.15 g. of the nitro acid was added an ether solution of diazomethane (excess). After standing overnight, the ether was evaporated and the residue sublimed at 115° (3 mm.). The product formed light yellow prisms, m. p. 89–91° (corr.); yield, 0.15 g.

Anal. Calcd. for $C_{13}H_{17}O_6N$: C, 55.12; H, 6.00; N, 4.95. Found: C, 55.28; H, 5.92; N, 4.96.

The methyl ester of nitrated apogossypolic acid was prepared in a similar manner. It had the same crystalline form and melting point. A mixed melting point gave no depression.

Anal. Calcd. for $C_{13}H_{17}O_6N$: N, 4.95. Found: N, 5.16.

Methyl 1,2-Dimethoxy-3-isopropyl-5-amino-4-benzoate Hydrochloride (XIII).—A solution of 0.4 g. of nitro ester in ethanol was reduced with hydrogen at 2.5 atm. and Raney nickel. The product after removal of the alcohol was dissolved in absolute ether and the amine hydrochloride precipitated by passing in dry hydrogen

chloride. It was purified by recrystallization from a mixture of absolute ethanol and dry ether; white crystals, m. p. 181–182° with decomposition (corr.); yield, 0.31 g. (75%).

Anal. Calcd. for $C_{13}H_{20}O_4NCl$: N, 4.83. Found: N, 4.94.

Anhydride of 1,2-Dimethoxy-3-isopropyl-4,5-dicarboxybenzene (II).—To a suspension of 0.21 g. of methyl 1,2-dimethoxy-3-isopropyl-5-amino-4-benzoate hydrochloride in 4 cc. of water and 1 cc. of concentrated hydrochloric acid well-cooled in an ice-bath was added a solution of sodium nitrite until a positive test with starch-iodide paper appeared. Excess nitrous acid was destroyed with urea. Sodium carbonate was then added until the solution was basic to litmus paper. The reaction mixture was now added to a hot solution of 0.2 g. of cuprous cyanide and 0.4 g. of potassium cyanide in 4 cc. of water. After heating for twenty minutes on a steam-bath, the dark oil which separated was extracted with ether. The product was distilled onto a cold finger at 120° (3 mm.). The oil, methyl 1,2-dimethoxy-3-isopropyl-5-cyano-4-benzoate, thus obtained did not solidify. It was refluxed with 3 cc. of 10% aqueous sodium hydroxide for sixteen hours, during which time ammonia was liberated. The brown solution was treated with Norite, acidified, saturated with ammonium sulfate and extracted with ether. After drying the ether extracts over anhydrous sodium sulfate, the ether was evaporated and the residue sublimed at 140° (3 mm.); yield, 0.06 g. The product was recrystallized from petroleum ether (b. p. 60–110°), m. p. 92–93° (corr.).

Anal. Calcd. for $C_{13}H_{14}O_6$: C, 62.40; H, 5.60. Found: C, 62.89; H, 5.93.

The melting point and crystalline form were the same as those of apogossypolic acid anhydride. A mixed melting point showed them to be identical.

1,2-Dimethoxy-3-isopropyl-4,5-dicarboxybenzene (Apogossypolic Acid) (II).—A solution of 0.03 g. of the anhydride just described in a little 10% aqueous sodium hydroxide was cooled and acidified. The solid acid which separated was filtered and recrystallized from a mixture of ether and petroleum ether (b. p. 60–110°); m. p. 169–170° with decomposition (corr.).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.2; H, 5.97. Found: C, 57.96; H, 6.07.

1,2-Dimethoxy-3-isopropyl-5-aminobenzene.—An ethanol solution of 0.5 g. of 1,2-dimethoxy-3-isopropyl-5-nitro-4-benzoic acid containing potassium hydroxide in excess over that necessary to form the potassium salt was reduced with hydrogen at 2.5 atm. and Raney nickel. The solution obtained was evaporated to dryness, the residue dissolved in 5 cc. of water and the solution carefully neutralized to congo red. The amino acid was filtered and washed with water and then dried and sublimed at 100° (15 mm.); white crystals, m. p. 74–75°; yield, 0.17 g. (48%).

Anal. Calcd. for $C_{11}H_{17}NO_2$: C, 67.70; H, 8.72; N, 7.18. Found: C, 67.90; H, 8.49; N, 7.44.

The crystalline form and melting point of this substance were the same as of the substance obtained from apogossypolic acid. A mixed melting point showed them to be identical. The diacetyl derivative of the amine was

(5) Adams and Butterbaugh. *THIS JOURNAL*, **60**, 2174 (1938).

prepared (m. p. 84–85°) and proved to be the same compound as that described previously.

1,2-Dimethoxy-4,5- α -methylhomophthalic Acid.—The 2-isonitroso-3-methyl-5,6-dimethoxyindanone used in this preparation was made by the series of reactions described by Perkin.⁶ The reagents, however, were modified in several instances with improvement in yields. (1) 1,2-Dimethoxy-4-acetophenone was condensed with zinc and ethyl bromoacetate to ethyl β -methyl-3,4-dimethoxycinnamate, b. p. 169–170° (4 mm.) (Perkin reports 195–196° (10 mm.)); yield 72%. (2) Saponification of this ester with aqueous alkali and reduction of the alkaline solution thus obtained by means of Raney nickel and hydrogen at 2–3 atm. pressure gave 3,4-dimethoxy- β -methylhydrocinnamic acid, m. p. 80–82° (corr.) (Perkin used sodium amalgam and reports a m. p. of 84–85°); yield, 60%. (3) Closure of the ring to 5,6-dimethoxy-3-methylindanone was effected by means of phosphorus pentoxide in benzene, m. p. 88–90° (Perkin reports m. p. of 90–91°); yield, 85%. (4) The indanone, by means of a large excess of butyl nitrite and concentrated hydrochloric acid in methanol solution, gave the 2-isonitroso-3-methyl-5,6-dimethoxyindanone, m. p. 223–224° (corr.) with decomposition (Perkin reports m. p. of 225–226°); yield, 83%.

To a suspension of 3 g. of 2-isonitroso-3-methyl-5,6-dimethoxyindanone in 30 cc. of dry ether was added slowly with stirring 5 cc. of purified thionyl chloride. Solution was complete in about thirty minutes, after which time the reaction mixture was poured carefully into water, the ether removed by warming on the steam-bath and the resulting oil extracted with ether. After evaporation of the solvent the residue was refluxed for six hours with 20 cc. of 10% aqueous sodium hydroxide, at the end of which time no more ammonia was evolved. Decolorization with Norite and addition of hydrochloric acid gave the product which was purified by recrystallization from water; colorless plates, m. p. 173–175° (corr.) with decomposition; yield, 1.5 g.

Anal. Calcd. for C₁₂H₁₄O₆: C, 56.70; H, 5.52. Found: C, 57.00; H, 5.63.

1,2-Dimethoxy-4,5- α -methylhomophthalic Anhydride.—By sublimation of the corresponding acid at 10 mm. and the bath at 140°, white crystals were obtained, m. p. 126–127° (corr.).

Anal. Calcd. for C₁₂H₁₂O₅: C, 61.03; H, 5.08. Found: C, 61.28; H, 5.04.

Dimethyl-1,2-dimethoxy-4,5- α -methylhomophthalate.—From 6.5 g. of acid, 30 cc. of methanol and 2 cc. of concentrated sulfuric acid refluxed for twelve hours, the product was obtained in the usual way. It was first an oil which slowly solidified. It was purified by crystallization from ether-petroleum ether (b. p. 30–60°) followed by sublimation at 20 mm. with bath at 120°; white crystals, m. p. 57–58° (corr.).

Anal. Calcd. for C₁₄H₁₈O₆: C, 59.60; H, 6.38. Found: C, 59.59; H, 6.37.

Ethyl 3,4-dimethoxy- β -ethylcinnamate.—This was prepared from 1,2-dimethoxy-4-propiofenone and ethyl α -bromopropionate according to the general procedure of

Perkin. The product when pure had a b. p. of 165° (4 mm.); yield, 78%.

Anal. Calcd. for C₁₅H₂₀O₄: C, 68.18; H, 7.58. Found: C, 68.15; H, 7.53.

3,4-Dimethoxy- β -ethylhydrocinnamic Acid.—The ester just described was saponified with 15% aqueous potassium hydroxide. The alkaline solution thus obtained was reduced with hydrogen at 2–3 atm. pressure and Raney nickel. The product was an oil which was distilled, b. p. 185–186° (4 mm.). Upon standing it solidified and was recrystallized first from benzene-petroleum ether (60–110°) and then from petroleum ether; white crystals, m. p. 73° (corr.).

Anal. Calcd. for C₁₃H₁₈O₄: C, 65.54; H, 7.57. Found: C, 65.71; H, 7.68.

5,6-Dimethoxy-3-ethylindanone.—To a suspension of 40 g. of phosphorus pentoxide in 200 cc. of benzene was added rapidly with stirring 10 g. of 3,4-dimethoxy- β -ethylhydrocinnamic acid in 50 cc. of benzene. The mixture was refluxed for three hours with occasional breaking up of the lumps, then added to ice. The benzene solution was washed with aqueous alkali, dried and evaporated. On purification by crystallization from petroleum ether (b. p. 60–110°) the product gave white crystals, m. p. 92° (corr.); yield, 7.5 g. (80%).

Anal. Calcd. for C₁₃H₁₆O₃: C, 70.95; H, 7.56. Found: C, 71.06; H, 7.58.

5,6-Dimethoxy-3-ethyl-2-isonitrosoindanone.—To a solution of 4 g. of 5,6-dimethoxy-3-ethylindanone in 25 cc. of methanol was added 0.5 cc. of concentrated hydrochloric acid and 4 cc. of butyl nitrite and the mixture warmed on the steam-bath. Within ten minutes the product had separated and was filtered. The filtrate, after treatment with 2 cc. of butyl nitrite, yielded additional material: yellow plates, m. p. 218° (corr.) with decomposition; yield, 3.5 g. (78%). No solvent was found for recrystallization.

Anal. Calcd. for C₁₃H₁₅O₄N: N, 5.63. Found: N, 5.48.

1,2-Dimethoxy-4,5- α -ethylhomophthalic Acid.—This acid was prepared similarly to 1,2-dimethoxy-4,5- α -methylhomophthalic acid. It formed white crystals, m. p. 157–158° (corr.) with decomposition.

Anal. Calcd. for C₁₃H₁₆O₆: C, 58.22; H, 5.98. Found: C, 58.27; H, 6.17.

1,2-Dimethoxy-4,5- α -ethylhomophthalic Anhydride.—By sublimation of the acid at 20 mm. with the bath at about 135°, the anhydride was obtained. It was resublimed and recrystallized from benzene-petroleum ether (b. p. 60–110°); white needles, m. p. 85–86° (corr.).

Anal. Calcd. for C₁₃H₁₄O₅: C, 62.40; H, 5.60. Found: C, 62.50; H, 5.63.

1,2-Dihydroxy-4- α -ethylphenylacetic Acid.—A solution of 0.2 g. of 1,2-dimethoxy-4,5- α -ethylhomophthalic acid in 12 cc. of 42% aqueous hydrobromic acid was refluxed for two hours in an atmosphere of nitrogen. It was then neutralized with sodium carbonate to Congo red, saturated with ammonium sulfate and extracted with ether. The product, oily at first, solidified on standing. It was purified by recrystallization from benzene-petroleum

(6) Perkin and Koepfli, *J. Chem. Soc.*, 2995 (1928).

ether (b. p. 60–110°); white crystals, m. p. 124–125° (corr.). It gives a green color with ferric chloride.

Anal. Calcd. for $C_{16}H_{12}O_4$: C, 61.22; H, 6.13. Found: C, 61.27; H, 5.87.

Summary

1. The synthesis of 1,2-dimethoxy-3-isopropyl-4-benzoic acid was accomplished by brominating 1-methoxy-2-acetoxy-3-isopropylbenzene to 1-methoxy-2-acetoxy-3-isopropyl-4-bromobenzene. Saponification of the acetyl group and methylation gave 1,2-dimethoxy-3-isopropyl-4-bromobenzene which through the Grignard reagent and carbon dioxide gave the product desired.

2. This acid upon nitration gave 1,2-dimethoxy-3-isopropyl-5-nitro-4-benzoic acid, which was identical with the substance obtained by nitrating

apogossypolic acid. The methyl esters were also identical.

3. The methyl 1,2-dimethoxy-3-isopropyl-5-nitro-4-benzoate upon reduction to the corresponding amine, diazotization and replacement with a cyanide group and subsequent hydrolysis gave 1,2-dimethoxy-3-isopropyl-4,5-dicarboxybenzene, identical with apogossypolic acid.

4. The established structure of apogossypolic acid fixes the structure of gossic acid and thus indicates that the aldehyde groups in the gossypol molecule are para to the isopropyl groups. The character of the substituents in the 1-, 5-, 6-, 7- and 8-positions of the naphthalene nuclei of gossypol is thus verified.

URBANA, ILLINOIS

RECEIVED MARCH 6, 1939

[CONTRIBUTION FROM THE HENRY BAIRD FAVILL LABORATORY OF ST. LUKE'S HOSPITAL AND THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CHICAGO]

A Study of the Methods of Separation of Oleic Acid from Saturated Acids and Linoleic Acid with Observations on the Preparation of Oleic Acid

BY PAUL J. HARTSUCH¹

Several methods for the preparation of "pure" oleic acid have been reviewed by Brown and Shinowara.² The purity of the product obtained was calculated from the iodine and acid numbers and the melting point. These estimations in the presence of nearly equal amounts of saturated and linoleic acids do not demonstrate a purity exceeding 95%. Kaufmann³ improved the methods for estimating the components in mixtures of fatty acids by making determinations of both the iodine and the thiocyanogen numbers. Others have modified the Kaufmann procedure.⁴ In my investigations the procedure recommended by Irwin, *et al.*,^{4d} was used. The maximum purity of an oleic acid preparation purified by several methods was 97.8%.

(1) Seymour Coman Fellow in Medical Chemistry of the University of Chicago.

(2) J. B. Brown and G. Y. Shinowara, *THIS JOURNAL*, **59**, 6 (1937).

(3) (a) H. P. Kaufmann, *Arch. Pharm.*, **263**, 675 (1925); (b) H. P. Kaufmann, *Z. Untersuch. Lebensm.*, **51**, 15 (1926); (c) H. P. Kaufmann, *Z. angew. Chem.*, **41**, 19 (1928); (d) H. P. Kaufmann and M. Keller, *ibid.*, **42**, 20, 73 (1929).

(4) (a) G. S. Jamieson and W. F. Baughman, *Oil & Fat Industries*, **7**, 419, 437 (1930); (b) W. S. Martin and R. C. Stillman, *Oil & Soap*, **10**, 29 (1933) (gives many references to earlier articles); (c) H. N. Griffiths and T. P. Hilditch, *J. Soc. Chem. Ind.*, **53**, 75T (1934); (d) W. H. Irwin, *et al.*, *Ind. Eng. Chem., Anal. Ed.*, **8**, 233 (1936).

Experimental

The Separation of Saturated from Unsaturated Fatty Acids.—The method of Brown and Shinowara² was found to be the most efficient method for the separation of saturated from unsaturated fatty acids. Fifty grams of the mixed fatty acids of olive oil or of teaseed oil was dissolved in 500 ml. of acetone. The solution was cooled to -18 to -20° for four or five hours. The saturated acids which precipitated were separated from the solution by filtration on a jacketed Büchner funnel, cooled to -14° . In one experiment, a 50-g. sample of mixed fatty acids, of iodine no. 90.05, containing about 10.5% each of saturated acids and linoleic acid, was divided into a 5.3-g. precipitate of iodine no. 4.8, and a 44.0-g. filtrate of iodine no. 99.9. Only 1.0% of the saturated acids remained in the filtrate.

Three other methods were investigated for the separation of saturated acids from unsaturated fatty acids. The only one of these which compared favorably with the method of Brown and Shinowara was a recent modification of the Twitchell lead soap-alcohol method.^{4d} When a 50-g. sample of mixed fatty acids was separated by this method, the fatty acids recovered from the precipitate weighed 7.1 g. and had an iodine no. of 34.8, while the fatty acids recovered from the filtrate weighed 35.9 g. and had an iodine no. of 100.6. Only 1.0% of the fatty acids of the filtrate was saturated acids. However, the yield is not as great as with the Brown and Shinowara method, more oleic acid being lost with the precipitate, and more material being lost in transferring the sticky lead soaps from one container to another.