preparation of the alkyl mercuric chloride derivative[9] (found m. p. 140–3°; reported[10a,b,c] m. p. 140°, 143°, 147°).

After removal of the excess carbon tetrachloride, there was obtained a fraction of 15 g. distilling constantly at 119–120° which was identified as ethyl *n*-butyrate by hydrolysis and identification of *n*-butyric acid as the *p*-toluidide and ethyl alcohol as the 3,5-dinitrobenzoate.

The black residue remaining in the distillation flask after removal of the volatile products was extracted with ethyl alcohol. Twenty-five grams of hexachloroethane, m. p. 184°, was obtained.

Decomposition of Isobutyryl Peroxide.—The decomposition of isobutyryl peroxide in carbon tetrachloride was carried out in the same manner. A yield of 24 g. of isopropyl chloride, b. p. 35–36°, was obtained. Its identity was established by the preparation of the alkylmercuric chloride, m. p. 92–94°; a mixture with an authentic sample of isopropylmercuric chloride melted at 93–94°.

After removal of the more volatile fractions containing the alkyl chloride and carbon tetrachloride, there was obtained 14 g. of ethyl isobutyrate, b. p. 109°. The identification of the ester was confirmed by the isolation of ethyl alcohol and isobutyric acid upon hydrolysis. Extraction of the residue yielded 21 g. of hexachloroethane.

(9) Shriner and Fuson, "Identification of Organic Compounds," 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 158.

(10) (a) Marvel, Gauerke and Hill, THIS JOURNAL, **47**, 3009 (1925); (b) Goret, *Bull. sci. pharmacol.*, **29**, 297 (1922); (c) Slotta and Jacobi, *J. prakt. Chem.*, **120**, 249 (1929).

Summary

n-Butyryl peroxide reacts with carbon tetrachloride to form as primary products *n*-propyl chloride and hexachloroethane. Similarly isobutyryl peroxide forms isopropyl chloride and hexachloroethane. The formation of the *pure* alkyl chloride in each case is advanced as evidence that isomerization of free radicals does not occur in the course of reactions involving these intermediates.

The isolation of ethyl *n*-butyrate and ethyl isobutyrate from the action of ethyl ether on the corresponding peroxides is interpreted as indicating that the decomposition of the alkyl peroxides proceeds at least partially through the production of free alkoxy radicals.

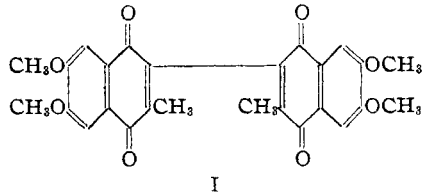
CHICAGO, ILLINOIS RECEIVED NOVEMBER 19, 1940

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

Structure of Gossypol. XXIV. Attempts to Prepare Desapogossypolone Tetramethyl Ether[1]

BY ROGER ADAMS, T. A. GEISSMAN, B. R. BAKER AND H. M. TEETER

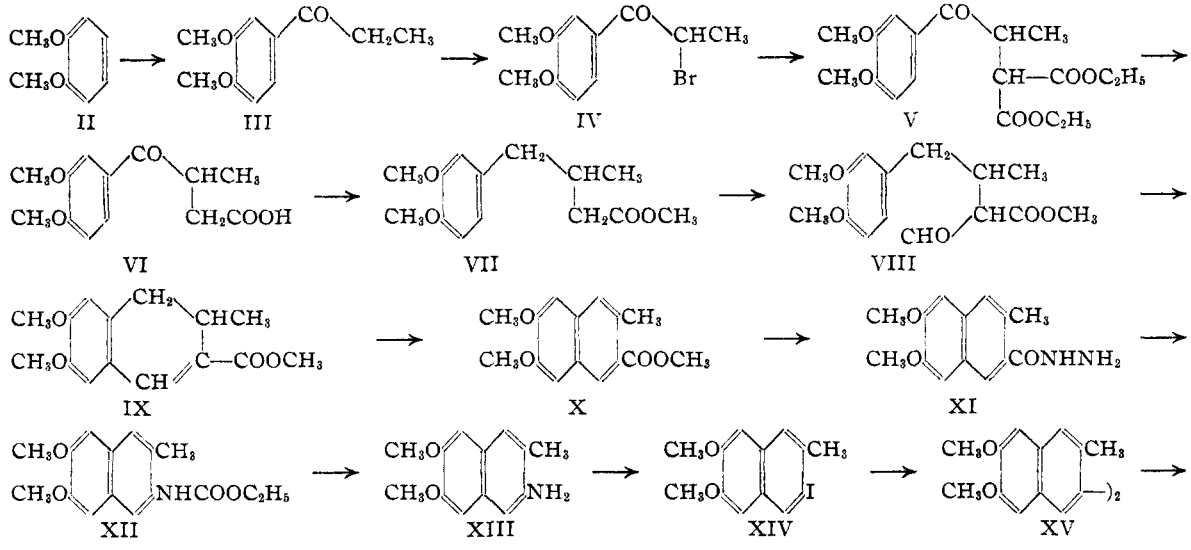
In the previous paper the desirability of synthesizing desapogossypolone tetramethyl ether (I) in order to establish directly the presence of a binaphthyl nucleus in gossypol was explained and an unsuccessful approach to the problem was described. A second method of synthesis now has been devised and studied but failure of the next to the last step prevented its completion. The projected series of reactions are shown by formulas II–XV.



I

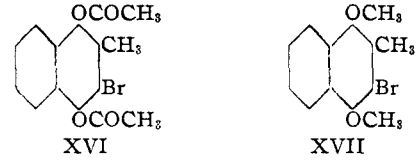
Veratrol (II) was converted to propioveratrone (III) by means of propionyl chloride in the presence of aluminum chloride. This, in turn, was brominated in chloroform to the α-bromopropioveratrone (IV) which was condensed with sodio-malonic ester in benzene to compound V. This substance (V) was not isolated but was saponified in a crude state and the corresponding malonic acid heated to cause decarboxylation to β - methyl - β - (3,4 - dimethoxybenzoyl) - propionic acid (VI). Clemmensen reduction of this last product gave β-methyl-γ-(3,4-dimethoxyphenyl)-butyric acid which was esterified without purification to the methyl ester (VII). Condensation of the methyl β-methyl-γ-(3,4-dimethoxyphenyl)-butyrate with ethyl formate in presence of sodium ethoxide gave methyl α-formyl-β-methyl-γ-(3,4-dimethoxyphenyl)-butyrate (VIII). Cyclization of compound VIII proceeded readily with a mixture of phosphoric and sulfuric acids to give the ester of 1,2-dihydro-2-methyl-6,7-dimethoxy-3-naphthoic acid (IX). In actual practice sometimes ethyl formate, sometimes amyl formate was used in preparing the formyl derivative. As a consequence, some *trans*-esterification

(1) For previous paper in this series see Adams and Geissman, THIS JOURNAL, **61**, 2083 (1939).



took place so that the product VIII consisted of a mixture of esters. Cyclization of this mixture consequently gave a mixture of cyclic esters. Upon saponification of the mixed cyclic esters, however, the pure acid was isolated and re-esterified with methanol to give the pure methyl ester (IX). Dehydrogenation of ester IX proceeded best with sulfur to form methyl 2-methyl-6,7-dimethoxy-3-naphthoate (X). Hydrazine hydrate converted the naphthoic ester (X) to the corresponding hydrazide (XI) which with ethyl nitrite and hydrochloric acid in ethanol was transformed to the corresponding urethan, 2-methyl-6,7-dimethoxy-3-naphthyl urethan (XII). Methanolic potassium hydroxide saponified the urethan with formation of 2-methyl-6,7-dimethoxy-3-naphthylamine (XIII). The amine group was readily diazotized and replaced by iodine to 2 - methyl - 3 - iodo - 6,7 - dimethoxynaphthalene (XIV). All attempts to couple two molecules of compound XIV to compound XV by means of the Ullmann reaction failed. The binaphthyl (XV) which was to be oxidized to desapogossypolone tetramethyl ether (XVI) was not obtained. Lack of material prevented a study of the diazotization of the amine (XIII) and coupling to compound XV according to a reaction which has been successful with some aromatic amines.

The use of the Ullmann reaction for synthesizing a binaphthyl which could be oxidized to desapogossypolone tetramethyl ether was given further trial in certain type reactions. A superior method of preparation of 2-methyl-3-bromo-1,4-naphthoquinone by direct bromination of 2-methyl-1,4-naphthoquinone in the presence of sodium acetate and glacial acetic acid was found. From this compound both 1,4-diacetoxy-2-methyl-3-bromonaphthalene (XVI) and 1,4-dimethoxy-2-methyl-3-bromonaphthalene (XVII) were readily synthesized.

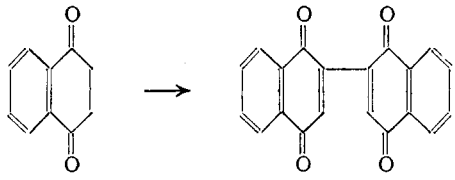


It was considered that these molecules, unlike the 2-methyl-3-iodo-6,7-dimethoxynaphthalene (XIV) contain no hydrogens in the 1- or 4-positions which might have been the complicating factor in the Ullmann reaction with compound XIV. However, no positive results were obtained. At lower temperatures, only starting material was recovered, at higher temperatures complete decomposition occurred. The bromine atom is too unreactive. Moreover, a methyl group *ortho* to a halogen is known to hinder the Ullmann reaction.

Another approach to the synthesis of desapogossypolone tetramethyl ether consisted in taking advantage of the reaction of Pummerer[2] who

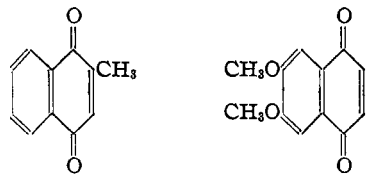
(2) Pummerer, *Ber.*, **72**, 1623 (1939); Rosenbauer, Braun, Pummerer and Riegelbauer, *ibid.*, **70**, 2287 (1937).

demonstrated that α-naphthoquinone could be converted readily by means of quinoline and acetic acid in ethanol to 2,2′-biquinones. Thus α-naphthoquinone (XVIII) gave 2,2′-bi-(1,4-naphthoquinone) (XIX).



XVIII XIX

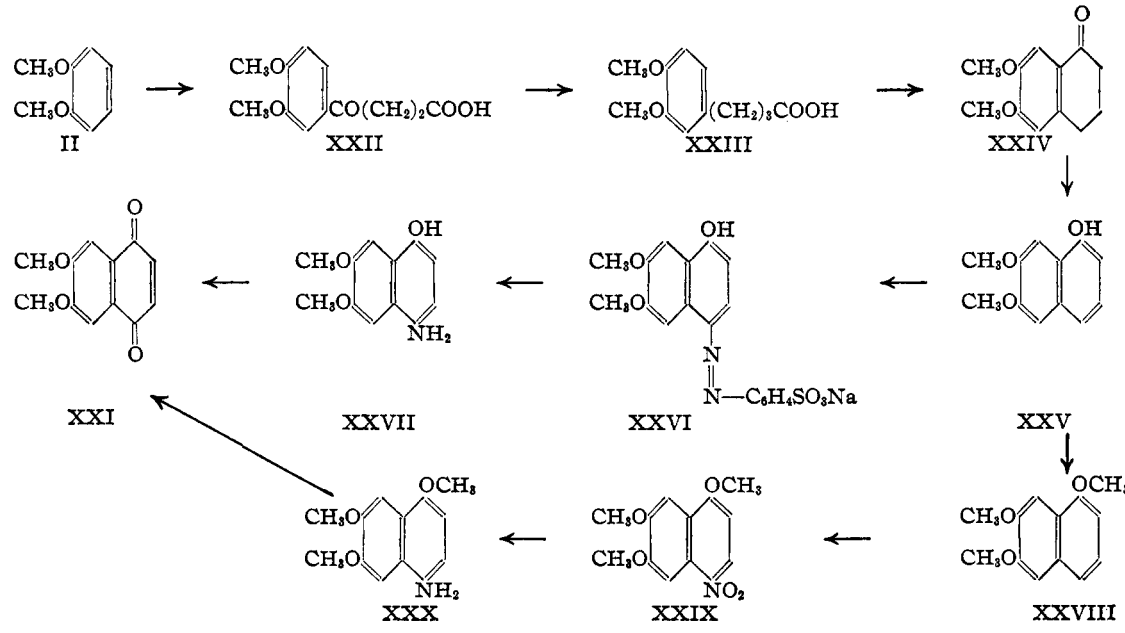
Pummerer's synthesis could be repeated satisfactorily and consequently attempts to apply it as a type reaction to 2-methyl-1,4-naphthoquinone (XX) and to 6,7-dimethoxy-1,4-naphthoquinone (XXI) were made.



XX XXI

Neither of these products could be oxidized under the conditions used to the corresponding biquinone. It is not surprising that the presence of the methyl group in the methyl naphthoquinone (XX) prevented the coupling through the hindered 3-position. The 6,7-dimethoxy-1,4-naphthoquinone was so insoluble that only starting material was recovered when Pummerer's highly specific conditions were used. Variations of the conditions resulted primarily in amorphous products or recovery of the original quinone. Possibly by a more extensive study, this reaction might be applicable to the synthesis of the desired binaphthoquinone. Lack of success in converting 2-methyl-1,4-naphthoquinone by an analogous procedure to the corresponding binaphthoquinone led us to abandon further study of the method.

The preparation of 6,7-dimethoxy-1,4-naphthoquinone used in these experiments involves an interesting synthesis. Veratrol (II) was converted to β-(3,4-dimethoxybenzoyl)-propionic acid (XXII). This latter product was reduced by the method of Clemmensen to γ-(3,4-dimethoxyphenyl)-butyric acid (XXIII). Concentrated sulfuric acid or preferably acetic anhydride and zinc chloride closed the ring to the corresponding tetralone (XXIV). Upon dehydrogenation of the tetralone with sulfur, 6,7-dimethoxy-1-naphthol (XXV) resulted. Two methods of conversion of this product to 6,7-dimethoxy-1,4-naphthoquinone were employed, both of which left something to be desired in respect to yield. The first consisted in coupling the 6,7-dimethoxy-1-naphthol with diazotized sulfanilic acid and reduction of the azo compound (XXVI) with stannous chloride followed by oxidation of the aminophenol (XXVII) to the quinone (XXI) by means of potassium dichromate. The second involved the methylation of the 6,7-dimethoxy-1-naphthol to



II XXII XXIII XXIV XXV XXVI XXVII XXI XXVIII XXIX XXX

the known 1,6,7-trimethoxynaphthalene (XXVIII) followed by nitration to 4-nitro-1,6,7-trimethoxynaphthalene (XXIX). The nitro compound was then catalytically reduced and the resulting amine (XXX) oxidized to the quinone (XXI).

Experimental

Propioveratrone (III).—This substance was prepared by Haworth and Woodcock[3] using nitrobenzene as a solvent for the condensation of the propionyl chloride and veratrol. The removal of the nitrobenzene is tedious and, consequently, an attempt was made with benzene as a solvent. The reactions proceeded very satisfactorily in a much shorter time.

To a mixture of 138 g. of veratrol, 160 g. of aluminum chloride and 500 cc. of benzene was added slowly with stirring 92 g. of anhydrous aluminum chloride at such a rate as to cause gentle refluxing and the solution was refluxed for thirty minutes after all the acid chloride had been added. The reaction mixture was decomposed with iced sulfuric acid, steam distilled to remove benzene and unchanged veratrol and the product extracted with ether: b. p. 158–160° (3 mm.); yield 163 g. The product solidified on cooling and was advantageously recrystallized from a mixture of ether–petroleum ether (b. p. 30–60°) with ice cooling. A pure dry white product, m. p. 59–60°, was thus obtained.

α-Bromopropioveratrone.—This was made by Haworth and Woodcock's[3] procedure. Using pure dry crystalline propioveratrone, a 90% yield of product resulted, m. p. 85–86°.

β-Methyl-β-(3,4-dimethoxybenzoyl)-propionic Acid (VI).—The method of synthesis of this acid was essentially identical to that described by Haworth and Woodcock.[3] From 144 g. of α-bromopropioveratrone and 147 g. of malonic ester divided into two individual runs about 80 g. of crude acid resulted.

Methyl β-Methyl-γ-(3,4-dimethoxyphenyl)-butyrate (VII).—A mixture of 80 g. of crude β-methyl-β-(3,4-dimethoxybenzoyl)-propionic acid, 200 g. of amalgamated zinc, 125 cc. of water, 250 cc. of concentrated hydrochloric acid and 200 cc. of toluene was refluxed vigorously for forty-four hours, six 50-cc. portions of concentrated hydrochloric acid being added at equal intervals throughout this period. After cooling, the toluene layer was separated and the aqueous layer extracted with ether. The combined toluene and ether solutions were treated with a liter of *N* aqueous sodium hydroxide and the mixture distilled until all the solvents were removed. To the hot alkaline solution was then added 60 cc. of dimethyl sulfate in small portions and after it had reacted, the solution was cooled, acidified and extracted with chloroform.

The chloroform was removed by distillation; the residual oil was refluxed with 450 cc. of methanol and 50 cc. of concentrated sulfuric acid for six hours, allowed to stand overnight, poured into water and extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate, then water, dried and distilled. The product when pure was obtained as an almost colorless oil, b. p. 171–172° (2 mm.); $n^{24}D$ 1.5122; d^{20}_2 1.090.

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.61; H, 7.94. Found: C, 65.90; H, 7.68.

p-Bromophenacyl Ester of β-Methyl-γ-(3,4-dimethoxyphenyl)-butyric Acid.—A sample of the methyl β-methyl-γ-(3,4-dimethoxyphenyl)-butyrate just described was saponified with aqueous ethanolic potassium hydroxide and the acid isolated, after acidification, by ether extraction. The oily acid was dissolved in 10% aqueous sodium hydroxide and the solution made faintly acid by careful addition of hydrochloric acid. A solution of 0.5 g. of *p*-bromophenacyl bromide in 5 cc. of ethanol was then added and the mixture refluxed for one hour.

The solution was poured into water, extracted with ether, the ether solution washed with aqueous sodium bicarbonate, then water and dried. The oily product, after removal of solvent, crystallized on scratching its ether–petroleum ether (b. p. 30–60°) solution and was then purified by crystallization from the same solvent; colorless flat needles, m. p. 69–71°.

Anal. Calcd. for $C_{21}H_{23}O_5Br$: C, 57.93; H, 5.29 Found: C, 57.88; H, 5.29.

Methyl α-Formyl-β-methyl-γ-(3,4-dimethoxyphenyl)-butyrate (VIII).—A suspension of dry sodium ethoxide was prepared by allowing 11.5 g. of absolute ethanol to react overnight with 5.75 g. of powdered sodium under 60 cc. of dry ether. The suspension was cooled to 0° and a mixture of 65 g. of methyl β-methyl-γ-(3,4-dimethoxyphenyl)-butyrate and 22 g. of ethyl formate was added. The mixture was allowed to stand for four hours at 0° and two days at room temperature. Finally, cracked ice was added and the aqueous layer was separated. The ether layer was washed with several portions of ice water which were then added to the first aqueous layer and these combined aqueous portions then extracted with ether. From the ether solutions 56 g. of unreacted ester was recovered.

Upon acidification of the aqueous solution with ice-cold dilute sulfuric acid, an oil resulted which was extracted with ether. The crude formyl derivative weighed 8.5 g. Numerous runs with new and recovered ester gave essentially the same results. The conversion averages around 10–15% but recovered ester was used over and over again.

Since the crude formyl product obviously contained both methyl and ethyl esters due to *trans*-esterification, no attempt was made to purify it but it was cyclized directly. In some runs amyl formate was substituted for ethyl formate with essentially the same results.

1,2-Dihydro-2-methyl-3-carbalkoxy-6,7-dimethoxynaphthalene.—To a mixture of 40 cc. of 85% phosphoric acid and 10 cc. of concentrated sulfuric acid cooled to −5 to −10° was dropped in slowly with stirring 5 g. of the crude formyl derivative just described. Stirring was continued for two hours with the temperature maintained at −5° and the reaction mixture was then poured onto ice. The product was extracted with ether, the ether solution treated with aqueous sodium carbonate to remove any unchanged formyl derivative, dried and distilled. The residual oil consisting of mixed esters was not purified but saponified directly to the acid. From 27.0 g. of crude formyl esters (combination of four runs)

(3) Haworth and Woodcock, *J. Chem. Soc.*, 811 (1938).

was obtained 19 g. of dihydronaphthalene esters, b. p. 205–230° (4 mm.).

1,2 - Dihydro - 2 - methyl - 6,7 - dimethoxy - 3 - naphthoic Acid.—A mixture of 19 g. of the distilled mixture of dihydronaphthalene esters just described, a solution of 10 g. of potassium hydroxide in 10 cc. of water and 100 cc. of methanol was refluxed for thirty minutes. After addition of 200 cc. of water, the methanol was removed by distillation, the residual solution treated with Norite and filtered. Acidification gave 12 g. of acid. It was purified by crystallization from ethyl acetate–petroleum ether (b. p. 60–110°), dilute ethanol and finally acetic acid; tiny white needles, m. p. 198–200°.

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.71; H, 6.45; neut. equiv., 248. Found: C, 67.57; H, 6.67; neut. equiv., 247.

Methyl 1,2-Dihydro-2-methyl-6,7-dimethoxy-3-naphthoate (IX).—A solution of 13.6 g. of 1,2-dihydro-2-methyl-6,7-dimethoxy-3-naphthoic acid in 100 cc. of methanol and 5 cc. of concentrated sulfuric acid was refluxed for four hours, poured into water and extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate. The product formed a very viscous, pale yellow oil, b. p. 193–195° (1 mm.); yield 13.0 g. It solidified and could be recrystallized from methanol; tiny white prisms, m. p. 119–120° (cor.).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.70; H, 6.88. Found: C, 68.57; H, 7.01.

Methyl 2-Methyl-6,7-dimethoxy-3-naphthoate (X).—A mixture of 10.6 g. of methyl 1,2-dihydro-2-methyl-6,7-dimethoxy-3-naphthoate and 1.3 g. of powdered sulfur was placed in a small sausage flask (v. Braun type) and immersed in a metal-bath at 235°. The flask was shaken gently until the globule of sulfur had dissolved and the temperature was then raised to 245–250° and held there for thirty minutes. The pressure was reduced and the contents of the flask distilled. The distillate which solidified in the receiver was removed with chloroform and after removal of the solvent, crystallized from methanol: white needles, m. p. 126–127° (cor.); yield 8.5 g.

Anal. Calcd. for $C_{15}H_{16}O_4$: C, 69.23; H, 6.15. Found: C, 69.12; H, 6.21.

2-Methyl-6,7-dimethoxy-3-naphthoic Acid.—A small sample of the corresponding ester was saponified with methanolic-aqueous sodium hydroxide. Isolated in the usual way, the acid was then purified by crystallization from dilute methanol; tiny white needles, m. p. 224–225° (cor.).

Anal. Calcd. for $C_{14}H_{14}O_4$: C, 68.29; H, 5.69. Found: C, 68.39; H, 5.92.

2-Methyl-6,7-dimethoxy-3-naphthohydrazide (XI).—A mixture of 7.8 g. of methyl 2-methyl-6,7-dimethoxy-3-naphthoate, 15 cc. of 85% hydrazine hydrate and enough methanol (about 50 cc.) to bring about complete solution of the solid was refluxed for three hours. The condenser water was then shut off and heating continued, allowing methanol to escape through the condenser until the volume of the reaction mixture was reduced to 25 cc. Upon resumption of refluxing for an hour, crystals began to separate from the solution. The mixture was allowed to cool and the solid collected and washed with dilute methanol and water. The crude dried product (7.75 g.) was purified by boiling with 200 cc. of xylene in which the hydrazide is only slightly soluble. The suspension was cooled and 5.35 g. of substance obtained. After recrystallization from benzene it formed tiny white leaflets, m. p. 226–228° (cor.).

Anal. Calcd. for $C_{14}H_{16}O_3N_2$: C, 64.61; H, 6.15; N, 10.76. Found: C, 64.41; H, 6.14; N, 10.88.

2-Methyl-6,7-dimethoxy-3-naphthylurethan (XII).—To a solution of 5.25 g. of 2-methyl-6,7-dimethoxy-3-naphthohydrazide in 250 cc. of boiling absolute ethanol cooled to 45–50° was added a solution of 1.1 g. of hydrogen chloride in 8 cc. of absolute ethanol (prepared from dry hydrogen chloride and ethanol followed by titration of the solution). By cooling rapidly to 0–5° with stirring, the hydrazide hydrochloride separated. A solution of 1.85 g. of ethyl nitrite in 5.5 cc. of absolute ethanol was added in small portions with continued stirring and cooling. Stirring was continued at 0° for two hours and the flask was then stoppered and allowed to stand at 0° for sixteen hours. The reaction mixture was now heated on a steam cone until nitrogen evolution had ceased and a clear solution resulted; it was then concentrated by distillation to 150 cc., whereupon the product crystallized upon cooling. The compound was purified from ethanol: white prisms, m. p. 177–178° (cor.); yield 5.58 g. (95%).

Anal. Calcd. for $C_{16}H_{19}O_4N$: C, 66.40; H, 6.60; N, 4.84. Found: C, 66.07; H, 6.81; N, 4.91.

2-Methyl-6,7-dimethoxy-3-naphthylamine (XIII).—A solution of 2-methyl-6,7-dimethoxy-3-naphthylurethan in 75 cc. of 20% methanolic potassium hydroxide was refluxed for twenty minutes. About 20 cc. of water was added and refluxing was continued for thirty minutes longer, during which time a heavy precipitate of white crystals separated.

The suspension was cooled and 3 *N* hydrochloric acid was added until a clear solution resulted (about 70 cc.). A brisk evolution of carbon dioxide occurred as the substance dissolved and the final solution was perfectly clear and nearly colorless. After filtration, the solution was made basic with aqueous ammonia whereupon the amine separated as a gelatinous precipitate. It was extracted with chloroform. The product was purified from ethanol: colorless leaflets, m. p. 200–201°; yield 89%.

Anal. Calcd. for $C_{13}H_{15}O_2N$: C, 71.89; H, 6.91; N, 6.45. Found: C, 71.30; H, 7.66; N, 6.60.

2-Methyl-3-iodo-6,7-dimethoxynaphthalene (XIV).—A solution of 3.2 g. of the 3-methyl-6,7-dimethoxy-3-naphthylamine in a warm mixture of 6 cc. of concentrated sulfuric acid and 30 cc. of water was cooled to 0° with stirring and the resulting paste of amine sulfate was diazotized by addition of a solution of 1.05 g. of sodium nitrite in a few cubic centimeters of water over a period of an hour. Stirring at 0° was continued for one hour longer.

A solution of 6 g. of potassium iodide in 5 cc. of water was then added and stirring continued for twenty hours, allowing the mixture to come gradually to room temperature. A few cubic centimeters of benzene was added to reduce foaming. The flask was then surrounded by hot water and warmed to 70–80° while small portions of sodium bisulfite were added until the color of the iodine had disappeared. Upon cooling the product formed a brown granular mass.

It was dissolved in chloroform and the resulting solution washed with aqueous sodium bisulfite, dilute alkali and water. The product was then purified by crystallization from ethanol; buff platelets, m. p. 161–162° (cor.).

Anal. Calcd. for $C_{13}H_{13}O_2I$: C, 47.58; H, 3.96. Found: C, 47.97; H, 4.16.

Attempts to cause the iodo compound to condense with copper powder under a variety of conditions in order to obtain the binaphthyl all resulted in failure.

2-Methyl-3-bromo-1,4-naphthoquinone.—The methods[4] previously described for preparation of this compound proved unsatisfactory in our hands. To a solution of 5.5 g. of 2-methyl-1,4-naphthoquinone, 11 g. of freshly fused, powdered sodium acetate in 50 cc. of glacial acetic acid, cooled to incipient crystallization was added 2 cc. (10% excess) of dry bromine. The flask was stoppered and allowed to stand in the dark for three days. A yellow crystalline mass separated. The entire contents was added to 300 cc. of water and the precipitate filtered. It was purified by recrystallization from methanol; bright yellow needles, m. p. 151–152° (cor.); yield, 6.1 g. (76%). Madinaveitia reports m. p. 150°; Fries and Lohmann, m. p. 151°.

Anal. Calcd. for $C_{11}H_7O_2Br$: C, 52.69; H, 2.79. Found: C, 53.0; H, 2.90.

1,4-Diacetoxy-2-methyl-3-bromonaphthalene (XVI).—To a refluxing solution of 2.58 g. of 2-methyl-3-bromo-1,4-naphthoquinone in 50 cc. of acetic anhydride was added gradually powdered zinc at such a rate that a little excess was always present. When the solution was colorless, addition of zinc was stopped, 3 g. of anhydrous sodium acetate added and refluxing continued for fifteen minutes. The solution was filtered, the residue washed with acetone, the filtrate and washings combined and poured onto ice. An oil separated which slowly crystallized: colorless needles, m. p. 209° (cor.); yield, 2.28 g. (66%). The product agrees in properties with that reported by Fries and Lohmann.

2-Methyl-3-bromo-1,4-naphthohydroquinone.—To the paste obtained by cooling rapidly a solution of 15 g. of 2-methyl-3-bromo-1,4-naphthoquinone in 200 cc. of 95% ethanol, was added 41.5 g. of stannous chloride in 41.5 cc. of concentrated hydrochloric acid. The hydroquinone was precipitated by addition of 170 cc. of water; by heating it dissolved and the solution was allowed to cool slowly: white needles, not melting under 250°; yield, 14 g. (93%). It agrees in properties with the substance described by Fries and Lohmann.

1,4-Dimethoxy-2-methyl-3-bromonaphthalene (XVII).—To a suspension of 13 g. of 2-methyl-3-bromo-1,4-naphthohydroquinone in 68.5 cc. of dimethyl sulfate with vigorous stirring and in a nitrogen atmosphere was added in 1-cc. portions a solution of 110 g. of potassium hydroxide in 220 cc. of water. After each addition a transitory dark reddish-violet color appears which fades in a few seconds. At the end of the addition, the solution should be pale orange in color and consequently if the dark color does fail to fade out more dimethyl sulfate should be used. The reaction mixture was heated on a steam-bath for one hour and then allowed to cool. It was diluted to 2 liters with water and extracted with a liter of ether in 200-cc. portions. The ether solution was washed with 5% aqueous sodium hydroxide, with water and then dried. The product was purified by crystallization from methanol: white plates, m. p. 84–85° (cor.); yield, 10 g. (69%).

Anal. Calcd. for $C_{13}H_{13}O_2Br$: C, 55.5; H, 4.63. Found: C, 55.3; H, 4.73.

β-(3,4-Dimethoxybenzoyl)-propionic Acid (XXII).—The preparation of this substance, its reduction and cyclization to the corresponding tetralone have been described by Haworth.[5] Since his procedures were considerably improved, additional data on the synthesis are included here.

Haworth reported high yields on the preparation of β-(3,4-dimethoxybenzoyl)-propionic acid and his results were duplicated. The quantities of reactants used were small. The same conditions are not satisfactory if larger amounts of product in a single run are desired.

To a mixture of 110 g. of succinic anhydride, 160 g. of veratrol and 1 liter of nitrobenzene, cooled in an ice-salt-bath and efficiently stirred was added 300 g. of anhydrous aluminum chloride at such a rate that the temperature always remained below 25°. The reaction mixture was allowed to come very slowly to room temperature and stirred for eighteen hours. It was then poured into iced hydrochloric acid, allowed to stand four hours and the product filtered. It was purified by dissolving in dilute aqueous sodium hydroxide, washing with benzene, treating with Norite and acidifying. Crystallization from ethanol gave white crystals m. p. 159–161°, which coincides with that reported by Haworth; yield, 135 g. (50%).

The ethyl ester from absolute ethanol and concentrated sulfuric acid by the usual procedure was distilled, b. p. 190–200° (2 mm.). It solidified and formed white needles from methanol, m. p. 62°.

6,7-Dimethoxy-1-tetralone (XXIV).—The yield of γ-(3,4-dimethoxyphenyl)-butyric acid (XXIII) by Clemmensen reduction of β-(3,4-dimethoxybenzoyl)-propionic acid was 40%. Haworth's directions were used. However, it was found that the over-all yield was much better if the product after reduction was extracted with benzene, the benzene evaporated and the crude product used without further purification.

The crude γ-(3,4-dimethoxyphenyl)-butyric acid obtained from reduction of 20 g. of β-(3,4-dimethoxybenzoyl)-propionic acid was refluxed with a mixture of 125 cc. of acetic acid, 85 cc. of acetic anhydride and 12 g. of zinc chloride for one hour. The solution was then poured into 1 liter of hot water and the product extracted with benzene. The benzene extracts were washed with 10% aqueous sodium hydroxide and the solvent then removed. The black residue was extracted with boiling petroleum ether (b. p. 60–110°), the solution allowed to cool with scratching and successively decanted from the oil until crystals separated. The separated oil was returned to the original black residue and extraction was continued until no more crystals were obtained. The product was purified by

(4) Madinaveitia, *Anales soc. espan. fis. quim.*, **31**, 750 (1933); Fries and Lohmann, *Ber.*, **54**, 2912 (1921).

(5) Haworth and Mavin, *J. Chem. Soc.*, 1487 (1932).

recrystallization from the same solvent: white crystals, m. p. 98–99°, identical with that reported by Haworth; yield, 6 g. (39%).

6,7-Dimethoxy-1-naphthol (XXV).—In a two-bulbed flask designed for distilling solids[6] was placed an intimate mixture of 2.45 g. of sulfur and 15.3 g. of 6,7-dimethoxytetralone which was heated in a bath at 240–250° for forty minutes. At this time, the evolution of hydrogen sulfide had ceased. The product was distilled at 2 mm.; it crystallized in the receiver after standing. It was purified by recrystallization from toluene: white prisms, m. p. 168–169° (cor.); yield, 6.8 g. (45%).

Anal. Calcd. for $C_{12}H_{12}O_3$: C, 70.55; H, 5.93. Found: C, 71.00; H, 6.29.

1,6,7-Trimethoxynaphthalene (XXVIII).—To a suspension of 1.0 g. of 6,7-dimethoxy-1-naphthol in 20 cc. of methanol and 3 cc. of dimethyl sulfate was added 10% methanolic potassium hydroxide slowly with stirring until the solution was permanently basic to litmus. Dimethyl sulfate was then added until the solution was acid to litmus. The treatment with alkali and dimethyl sulfate was repeated once more. Upon dilution with water, the desired product separated: white crystals, m. p. 128° (cor.), yield, 0.95 g. (90%). Friedländer and Silberstein[7] report m. p. 127–128°.

1,6,7-Trimethoxy-4-nitronaphthalene (XXIX).—To a solution of 6.6 g. of 1,6,7-trimethoxynaphthalene in 100 cc. of acetic acid was added portionwise a solution of 2 cc. of fuming nitric acid (sp. gr. 1.5) in 25 cc. of glacial acetic acid. The temperature was maintained below 20° during the nitration by cooling. The product separated; more was obtained from the filtrate by dilution with water. It was purified by recrystallization from acetic acid: yellow plates, m. p. 170° (cor.); yield, 4.8 g. (61%).

Anal. Calcd. for $C_{13}H_{13}NO_5$: N, 5.32. Found: N, 5.16.

6,7-Dimethoxy-1,4-naphthoquinone (XXI).—A. To a solution of 0.52 g. of sulfanilic acid and 0.18 g. of sodium carbonate in 5 cc. of water was added 0.19 g. of sodium nitrite. This solution was poured onto 4 g. of ice and 1 cc. of concentrated hydrochloric acid, whereupon the diazonium salt separated. This suspension was poured into an ice cold solution of 0.50 g. of 6,7-dimethoxy-1-naphthol in 4 cc. of 10% aqueous sodium hydroxide. After the magenta colored solution had stood overnight, to it was added 2 g. of stannous chloride in 3 cc. of concentrated hydrochloric acid and the mixture heated on a steam-bath for ten minutes. The red solid which had separated thus dissolved to give an orange-brown solution and this was treated with Darco. After addition of 2 cc. of concentrated sulfuric acid, the solution was poured into 30 cc. of water containing 3 g. of potassium dichromate. The product was removed by filtration after an hour, air-dried and sublimed at 160° (2 mm.). It was recrystallized from ethanol: orange needles, m. p. 236–237° (cor.) with decomposition; yield, 0.22 g. (41%).

B. A suspension of 4.5 g. of 1,6,7-trimethoxy-4-nitronaphthalene in 100 cc. of acetone was shaken with hydrogen at 2–3 atm. pressure in presence of Raney nickel for twenty-four hours. The resulting solution was filtered into a flask containing a crystal of stannous chloride and a drop of concentrated hydrochloric acid. The solvent was evaporated and the residue dissolved in 100 cc. of water containing 5 cc. of concentrated sulfuric acid. This was poured in a thin stream with stirring into a solution of 3.5 g. of potassium dichromate in 50 cc. of water. A dark precipitate formed immediately. It was filtered, air-dried and sublimed at 180° (3 mm.). It was further purified by recrystallization from glacial acetic acid: orange needles, m. p. 236–237° (cor.) with decomposition; yield, 1.2 g. (32%).

Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05; H, 4.58. Found: C, 65.80; H, 4.45.

1,4-Diacetoxy-6,7-dimethoxynaphthalene.—To a boiling solution of 0.14 g. of 6,7-dimethoxy-1,4-napthoquinone and 0.1 g. of fused sodium acetate in 4 cc. of acetic anhydride and 1 cc. of acetic acid was added a pinch of zinc dust. The mixture was refluxed for thirty minutes and then decanted from unreacted zinc into hot water. The product which separated was purified by crystallization from methanol; white plates, m. p. 185° (cor.).

Anal. Calcd. for $C_{16}H_{16}O_6$: C, 63.13; H, 5.29. Found: C, 63.48; H, 5.34.

(6) Fieser, "Experiments in Org. Chem.," D. C. Heath and Co., New York, N. Y., 1935, p. 246.

(7) Friedländer and Silberstein, *Monatsh.*, **23**, 530 (1902).

Summary

1. 2 - Methyl - 3 - iodo - 6,7 - dimethoxynaphthalene was prepared by a series of reactions starting from veratrol. Conversion of this product to a binaphthyl by means of the Ullmann reaction was unsuccessful.

2. Both 1,4 - diacetoxy - 2 - methyl - 3 - bromonaphthalene and 1,4-dimethoxy-2-methyl-3-bromonaphthalene were prepared from 2-methyl-3-bromo-1,4-naphthoquinone but neither could be condensed to a binaphthyl.

3. Oxidations of 2-methyl-1,4-naphthoquinone and 6,7-dimethoxy-1,4-naphthoquinone to biquinones by means of quinoline and acetic acid as described by Pummerer were unsuccessful. The latter compound was prepared by a series of reactions from veratrol through γ-(3,4-dimethoxyphenyl)-butyric acid and 6,7-dimethoxy-1-naphthol.

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