144. *Experiments on the Synthesis of Substances related to the Sterols Part XL.* (A) *The Preparation of* 2 : 7-*Dihydroxyphenanthrene and Certain Derivatives.* (B) *Further Observations on the Reduction of* 1-γ-*Ketobutyl*-2-*naphthol.*

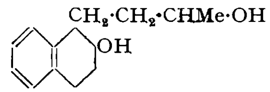
By J. W. Cornforth and Sir Robert Robinson.

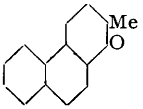
This interim report concerns two related topics in that the experiments with β-naphthol furnish a model for similar transformations of 2 : 7-dihydroxyphenanthrene or its monomethyl ether.

(A) A very satisfactory method of preparation of 2 : 7-dihydroxyphenanthrene and its methyl ethers has been devised, based on the synthesis of 2 : 3 : 6 : 7-tetra-acetoxydihydrophenanthrene from 3 : 4 : 3′ : 4′-tetramethoxydibenzyl by Erdtman (*Annalen*, 1933, **505**, 195). As a result this substance and its derivatives become readily accessible and a number of interesting developments are contemplated.

(B) (Compare McQuillin and Robinson, J., 1941, 586.) Pressure hydrogenation of 1-γ-ketobutyl-2-naphthol in the presence of copper chromite furnished the glycol (I), but satisfactory conditions for the oxidation of this substance to the desired diketone have not yet been found. When Raney nickel was used as the catalyst, the fully reduced chroman (II) was produced in good yield.

(I.)





(II.)

(A) 2 : 7-DIHYDROXYPHENANTHRENE (III, R = R′ = H) was first obtained by Fieser (*J. Amer. Chem. Soc.*, 1929, **51**, 2471) by alkali fusion of the corresponding disulphonic acid, isolated from a mixture produced by the sulphonation of phenanthrene-2-sulphonic acid. In an attempt to find a better procedure, Rapson and Robinson (J., 1935, 1533) applied the Pschorr synthesis, starting with 6-nitro-3-methoxybenzaldehyde and *m*-methoxyphenylacetic acid. 2 : 7-Dimethoxyphenanthrene was obtained in this way, but the major product of the ring-closure stage was 2 : 5-dimethoxyphenanthrene-9-carboxylic acid.

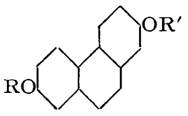
Of the two methods introduced by Erdtman (*loc. cit.*), that depending on a cyclisation by the Ullmann reaction was the more suitable for the purpose in view.

3 : 3′-Dimethoxydibenzyl had been prepared by Späth as a by-product (*Monatsh.*, 1913, **34**, 1999). It was obtainable from 3 : 3′-dimethoxybenzoin (Schönberg and Malchow, *Ber.*, 1922, **55**, 3746) by reduction according to Clemmensen and catalytic reduction of the product, which was found to be mixed with 3 : 3′-dimethoxystilbene. At this stage Erdtman's first method was tried; 3 : 3′-*dihydroxydibenzyl*, prepared by demethylation of its dimethyl ether, gave yellow resins on oxidation with ferric chloride and nothing definite could be isolated from them.

The iodination of 3 : 3′-dimethoxydibenzyl by means of iodine and mercuric acetate in acetic acid solution gave an almost theoretical yield of 6 : 6′-*di-iodo*-3 : 3′-*dimethoxydibenzyl* (IV) and cyclisation by means of copper bronze afforded a 70% yield of 2 : 7-*dimethoxy*-9 : 10-*dihydrophenanthrene*. Under some conditions dehydrogenation to 2 : 7-dimethoxyphenanthrene (III, R = R′ = Me) also occurred but this could be accomplished in any case by heating the dihydro-compound with sulphur.

Improvement of the preparation of dimethoxydibenzyl was found possible by a combination of excellent methods already described.

Following Woodward (*J. Amer. Chem. Soc.*, 1940, **62**, 1478), *m*-methoxybenzyl alcohol was obtained in 90% overall yield from *m*-hydroxybenzaldehyde. It was converted into its chloride in 91% yield (cf. Rapson and Robinson, *loc. cit.*, p. 1537) and then into 3 : 3′-dimethoxydibenzyl in 89% yield by an adaptation of the method of Michaelenko and Sassypkina (*J. Russ. Phys. Chem. Soc.*, 1921, **53**, 343).



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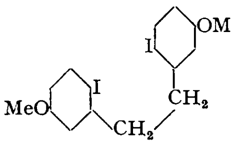

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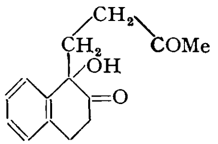

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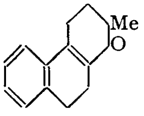

(VI.)

Demethylation of 2 : 7-dimethoxyphenanthrene is facile and conditions of methylation have been worked out which afford the dimethyl ether and 2-*hydroxy*-7-*methoxyphenanthrene* (III, R = H, R′ = Me) in about equal amount with little loss. This is an improvement on an earlier process in which the monobenzoate was prepared, methylated and hydrolysed. An indication has been obtained that this monomethyl ether can be γ-ketobutylated but the 2-hydroxyphenanthrenes are not analogous to β-naphthol in all respects. For instance, 2 : 7-dihydroxyphenanthrene is not convertible into its methyl ethers by the action of methyl-alcoholic hydrogen chloride, under conditions that succeed with β-naphthol.

Pressure hydrogenation of 2-hydroxy-7-methoxyphenanthrene in the presence of copper chromite gave a mixture of the non-phenolic 1 : 2 : 3 : 4-*tetrahydro*-derivative, which was isolated by means of its picrate, and more fully hydrogenated products, among which the 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8-octahydro-derivative was probably present.

2 : 7-*Dihydroxy*-9 : 10-*dihydrophenanthrene* and its *monomethyl ether* have been prepared and converted into a *dicarboxylic acid* and a *monocarboxylic acid*, respectively, by the Kolbe reaction. Arguing from analogy the carboxyl groups will occupy the symmetrical positions 3 and 6. The yields of these acids were inferior and the projected reduction to pimelic acid derivatives (Einhorn) and subsequent cyclisation was abandoned.

According to Shah and Laiwalla (J., 1938, 1828) a modified Gattermann synthesis enables the formyl group to be introduced into position 3 of methyl β-resorcylate. The Robinson–Schlittler synthesis might be shortened if the *m*-methoxyphenylacetyl group could be similarly introduced. A model experiment with phenylacetyl chloride, however, gave a product that could be converted into 4-phenylethylresorcinol. Accordingly reduction of this to a dihydroresorcinol (the R.–S. type of intermediate) (cf. Hofmann La Roche, E.P. 427,297 of 1937) was not attempted. The Hoesch synthesis using phenylacetonitrile and methyl β-resorcylate did not succeed and the *m*-methoxyphenylacetyl derivative of methylumbelliferone could not be made to undergo a Fries rearrangement (cf. Limaye, *Ber.*, 1932, **65**, 376; Baker, J., 1934, 1954; Russell, Frye, and Mauldin, *J. Amer. Chem. Soc.*, 1940, **62**, 1441, for successful preparations of 2-substituted resorcinols by this method).

2 : 5 : 3′-*Trimethoxydibenzyl* has been prepared in poor yield, but the demethylation of this substance gave tars.

(B) The glycol (I, see above) is a derivative of β-tetralol and it is therefore not surprising that we have been unable to prepare the diketone corresponding to (I). No neutral products were obtained by the use of bromine water or permanganate, though in both cases oxidation was rapid in the cold. Mild treatment with chromic acid gave unidentified ketonic substances. Excess of chromic acid gave a neutral *substance*, probably

(V). Oxidation by the Oppenauer method gave a *substance*, $C_{14}H_{16}O$, the properties of which are best explained by means of the structure (VI).

In another experiment the desired diketone was among the products because a *bisdinitrophenylhydrazone* could be isolated. Attempted dehydrogenation of (I) by means of Raney nickel led to dehydration instead and the dihydro-derivative of (VI) was produced. The same substance resulted from the hydrogenation of 1-γ-ketobutyl-2-benzyloxynaphthalene diethyl ketoacetal.

An attempt to open the heterocyclic ring of (II) by means of acetic anhydride and zinc chloride furnished an unsaturated acetoxy-compound.

EXPERIMENTAL.

(A) 3 : 3'-*Dimethoxydibenzyl*.—(1) *m*-Methoxybenzaldehyde (total, 470 g.) was converted into 3 : 3'-dimethoxybenzoin in the known manner and this was purified only by removal of unchanged and acidic material. A mixture of the crude product (50 g. portions), water (400 c.c.), concentrated hydrochloric acid (400 c.c.), toluene (50 c.c.), and amalgamated zinc (200 g.) was refluxed for 5 hours. The fraction of the product, b. p. 160—190°/2 mm., partly solidified (110 g., total) and by crystallisation of a small part from light petroleum (b. p. 60—80°), 3 : 3'-dimethoxystilbene, m. p. 99°, was isolated (Kopp, *Annalen*, 1893, **277**, 358, gives m. p. 99—100°). The mixed material was hydrogenated in alcohol (800 c.c.), Raney nickel being used at the ordinary temperature and atmospheric pressure. The product (107 g. or 25% overall) solidified to a mass, m. p. 33—35°, raised to the correct m. p., 39—40° on recrystallisation from alcohol.

(2) Schönberg and Malchow (*loc. cit.*) oxidised 3 : 3'-dimethoxybenzoin by means of Fehling's solution. The method of Clarke and Dreyer (*Organic Syntheses*, 1926, **6**, 6) for the oxidation of benzoin has been adapted for work on a larger scale. Crude dimethoxybenzoin (54 g.) was added to a hot solution of hydrated copper sulphate (100 g.) in pyridine (100 g.) and water (40 g.). After stirring for 2 hours at 90—100° the mixture was cooled, and the cake of dimethoxybenzil separated, washed, and dried (45 g., m. p. 78—82°). Crystallisation from aqueous alcohol or benzene gave yellow prisms, m. p. 84° (lit. m. p. 83°). The crude substance was reduced exactly as in (1), including the necessary final catalytic hydrogenation, and 3 : 3'-dimethoxydibenzyl (25 g., or 33% overall) obtained.

(3) Rapson and Robinson (*loc. cit.*) state the method of preparation of *m*-methoxybenzyl chloride but give no details.

Thionyl chloride (148 g.) was gradually added to *m*-methoxybenzyl alcohol (170 g.) and pyridine (100 g.), stirred during 2½ hours below 30°. After ½ hour more, the product was isolated in the known manner; it had b. p. 112—115°/10 mm. (178 g. or 91%).

A mixture of the chloride (100 g.), ether (300 c.c.), and magnesium (8 g.) was gently heated under reflux until ebullition occurred; anhydrous ferric chloride (2·5 g.) was at once added with good stirring. The vigorous reaction that soon set in was controlled by cooling until it subsided (about 15 minutes). The mixture was then stirred and refluxed for an hour. The product was isolated and on distillation methoxybenzyl chloride (4 g.) was recovered. The main fraction (66 g.) had b. p. 203—205°/10 mm., m. p. 38—39° (yield, 89% or 80% from *m*-methoxybenzaldehyde).

6 : 6'-*Di-iodo*-3 : 3'-*dimethoxydibenzyl* (IV).—A solution of 3 : 3'-dimethoxydibenzyl (110 g.) in acetic acid (1000 c.c.) was stirred at 50° and mercuric acetate (160 g.) and powdered iodine (233 g.) were added alternately in small quantities during 1½ hours. The solution was decolorised by means of a little sodium bisulphite, and potassium iodide (200 g.) added. After stirring for 15 minutes, the mixture was poured into water, and the solid product collected. The moist cake was boiled with alcohol (2 l.), the hot solution decanted and cooled, the crystals collected, and the mother-liquor used for another extraction until all the product had been recrystallised in this way. The substance so obtained was already pure, m. p. 113—114°, unaffected by further crystallisation (210 g. or 93%) (Found: C, 38·6; H, 3·2. $C_{16}H_{16}O_2I_2$ requires C, 38·9; H, 3·2%).

2 : 7-*Dimethoxy*-9 : 10-*dihydrophenanthrene*.—A mixture of 6 : 6'-di-iodo-3 : 8'-dimethoxydibenzyl (50 g.) and copper bronze (42 g.) was heated to 230°. An exothermic reaction set in, and was kept under control by occasional removal from the oil-bath, the temperature of which was meanwhile raised to 260°. After about 20 minutes the reaction was allowed to complete itself spontaneously, the internal temperature sometimes rising as high as 280—290°. It was found that if the reaction was controlled too much the yield was inferior. Finally, the mixture was heated for ½ hour at 260°, cooled, and triturated with acetone. The copper residues were removed, the acetone evaporated, and the product distilled, b. p. 180—190°/0·5 mm. (17 g. or 70%). This product was sufficiently pure for the next stage; crystallisation from benzene afforded large, colourless rhombs, m. p. 108—109° (Found : C, 80·1; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%).

2 : 7-*Dimethoxyphenanthrene* (I, R = R' = Me).—Dimethoxydihydrophenanthrene (50 g.) was heated with sulphur (7·5 g.) at 220—230° until the evolution of hydrogen sulphide had ceased (about 3 hours). The product was distilled, and the fraction, b. p. 170—200°/0·2 mm., dissolved in hot benzene. On cooling, nearly pure dimethoxyphenanthrene, m. p. 166—168° (30 g. or 60%), separated in colourless crystals. The m. p. was raised to 169—170° by recrystallisation from benzene.

2 : 7-*Dihydroxyphenanthrene* (I, R = R' = H).—A solution of 2 : 7-dimethoxyphenanthrene (22 g.) in acetic acid (60 c.c.) was boiled, and hydriodic acid (60 c.c., *d* 1·7) added dropwise during 20 minutes. The mixture was boiled until the precipitate obtained on dilution with water dissolved completely in aqueous sodium hydroxide (about ½ hour), and then poured into sodium bisulphite solution (800 c.c. of 1%). The product was dried at 100° (19 g.). Crystallisation from acetic acid gave colourless prisms, m. p. 264° with previous softening. This material (5 g.) in methyl alcohol (50 c.c.) was saturated with hydrogen chloride with cooling in ice; a large proportion of the phenanthrenediol crystallised during this process. After 3 days unchanged 2 : 7-dihydroxyphenanthrene was isolated and no methylation had occurred. The same result followed if the mixture was refluxed for 8 hours. This is a striking contrast with the behaviour of β-naphthol.

2-*Hydroxy*-7-*methoxyphenanthrene* (I, R = H, R' = Me).—(i) 2 : 7-Dihydroxyphenanthrene and benzoyl chloride were heated at 260° for ½ hour. The product insoluble in alcohol consisted of the *dibenzoate* of 2 : 7-dihydroxyphenanthrene, and crystallised from acetic acid, or better from nitrobenzene, in colourless leaflets, m. p. 252—253° (Found : C, 80·0; H, 4·5. $C_{28}H_{18}O_4$ requires C, 80·4; H, 4·3%).

The crude monobenzoate, soluble in alcohol, was methylated and hydrolysed in the usual way. The phenolic product was sublimed at 250°/10 mm. and crystallised from benzene containing a little alcohol, forming colourless leaflets, m. p. 170—171° (Found : C, 80·7; H, 5·7. $C_{15}H_{12}O_2$ requires C, 80·4; H, 5·4%).

(ii) The following is a better method. Aqueous sodium hydroxide (20 c.c. of 10%) was added to an ice-cooled and well-stirred mixture of 2 : 7-dihydroxyphenanthrene (10·5 g.), acetone (100 c.c.), and methyl sulphate (5·4 c.c.) during 1 hour. An excess of dilute aqueous sodium hydroxide was then added, and the acetone distilled. 2 : 7-Dimethoxyphenanthrene (5 g.) was collected and the filtrate on acidification afforded material from which 2-hydroxy-7-methoxyphenanthrene (4·5 g.) was extracted (Soxhlet, 8 hours) by benzene–light petroleum (b. p. 60—80°, 1 : 1). It had m. p.

171—173°, with softening from 167°, and, purified by sublimation at 230°/15 mm., m. p. 173—174° (4 g.). About 0·8 g. of a less pure product was obtained on continuing the extraction for 8 hours, and 0·6 g. of 2 : 7-dihydroxyphenanthrene insoluble in benzene–light petroleum was also obtained.

2-*Hydroxy*-7-*methoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*.—A mixture of 2-hydroxy-7-methoxyphenanthrene (5 g.), alcohol (150 c.c.), and copper chromite (1·5 g.) was stirred and heated at 170—175° for 6 hours under hydrogen at 100 atm. The product was a viscous oil, b. p. 195—200°/0·1 mm. When it was treated with nearly saturated alcoholic picric acid, a crystalline precipitate was thrown down; this was collected after the mixture had been kept for a few hours below 0°. The derivative was decomposed by means of aqueous ammonia and ether. The oil after evaporation of the ether solidified and the *substance* (1·0 g.) crystallised from benzene–light petroleum in small, flat, colourless needles, m. p. 123—124° (Found : C, 78·5; H, 7·1. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·0%).

The substance is insoluble in aqueous sodium hydroxide and the formation of a picrate indicates that it is a naphthalene derivative.

No definite product could be obtained from the residual oily material that did not form a picrate, but treatment with hot hydriodic acid gave largely non-phenolic substances.

3 : 3′-*Dihydroxydibenzyl*, prepared by demethylation of its dimethyl ether in the manner described above, crystallised from water in long needles, m. p. 139—140° (Found : C, 78·3; H, 6·7. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%).

2 : 7-*Dihydroxy*-9 : 10-*dihydrophenanthrene*.—The dimethyl ether (5 g.) was demethylated with hydriodic acid (15 c.c., *d* 1·7) in acetic acid (15 c.c.), as described for 2 : 7-dimethoxyphenanthrene. The product (4·2 g.) crystallised from aqueous acetic acid in colourless leaflets, m. p. 206—208° (Found : C, 78·8; H, 5·5. $C_{14}H_{12}O_2$ requires C, 79·2; H, 5·7%). The *substance* gave a green coloration with aqueous or alcoholic ferric solution.

2-*Hydroxy*-7-*methoxy*-9 : 10-*dihydrophenanthrene*.—Dihydroxydihydrophenanthrene (4·5 g.) was heated with benzoyl chloride (2·5 c.c.) at 210—220° for ½ hour. The product was cooled, powdered, and extracted thrice with boiling alcohol. The residue consisted of 2 : 7-*dibenzoyloxy*-9 : 10-*dihydrophenanthrene*, which crystallised from acetic acid in colourless, slender needles, m. p. 208—210° (Found : C, 80·2; H, 4·9. $C_{28}H_{20}O_4$ requires C, 80·0; H, 4·8%). The filtrate, on concentration, deposited the crude monobenzoate (3·5 g.).

Sodium hydroxide solution (10 c.c. of 50%) was added to the crude monobenzoate (38 g.) dissolved in a mixture of acetone (200 c.c.) and methyl sulphate (11·4 c.c.), and on shaking and heating the reaction was soon completed. An excess of aqueous sodium hydroxide was added, and the mixture refluxed for 1 hour; water was added, and the acetone removed. Neutral material was extracted with ether, and the phenol liberated, collected by means of ether, and distilled, b. p. 215—220°/1—2 mm. (19 g.). The product appeared to contain a trace of dihydroxy-compound, as indicated by its weak green ferric reaction. Extraction of a portion with hot light petroleum and crystallisation of the extract from benzene–light petroleum and finally from benzene gave colourless crystals, m. p. 118—120° (Found : C, 79·5; H, 6·3. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·2%).

2-*Hydroxy*-7-*methoxy*-9 : 10-*dihydrophenanthrene*-3-*carboxylic Acid*.—The sodio-derivative of the above monomethyl ether was prepared in alcoholic solution, and dried by evaporation under diminished pressure. The powdered solid (10 g.) was heated with carbon dioxide at 210—220°/20 atms. for 6 hours. The product was dissolved in dilute alkali, and the solution acidified and extracted with ether. The ethereal solution was shaken with sodium bicarbonate solution, which was then acidified. The crystalline precipitate (1·5 g.) was collected and recrystallised from benzene, then from alcohol–benzene, and finally twice from alcohol. The *acid* formed light brown rhombs, m. p. 225—226° (decomp.) (Found : C, 71·3; H, 5·7. $C_{16}H_{14}O_4$ requires C, 7·11; H, 5·2%). The ferric reaction was deep blue.

2 : 7-*Dihydroxy*-9 : 10-*dihydrophenanthrene*-3 : 8-*dicarboxylic Acid*.—2 : 7-Dihydroxy-9 : 10-dihydrophenanthrene (5 g.) was converted into its disodio-derivative as above. The dry, powdered solid was heated at 200°/5 atms. with carbon dioxide for 7 hours. The acidified product was extracted with ethyl acetate, and the extract shaken with sodium bicarbonate solution; acidification gave the *acid*, which crystallised from methanol in colourless, microscopic rods, m. p. 305° (decomp.) (Found : C, 64·1; H, 4·4. $C_{16}H_{12}O_6$ requires C, 64·0; H, 4·0%).

2 : 5 : 3′-*Trimethoxydibenzyl*.—A mixture of *m*-methoxyphenylacetyl chloride (70·4 g.), quinol dimethyl ether (53 g.), and carbon disulphide (200 c.c.) was added to a suspension of aluminium chloride (48 g.) in carbon disulphide (200 c.c.), and the whole refluxed gently with stirring for 10 hours. Next day the product was decomposed with water, and the carbon disulphide removed. The residue was extracted with ether, and the ether shaken with aqueous sodium bicarbonate and then with water. The ether was removed, and the residue distilled in steam, quinol dimethyl ether (17 g.) being recovered. The residue was boiled with amalgamated zinc (250 g.), concentrated hydrochloric acid (500 c.c.), and water (500 c.c.) for 8 hours. The oily product (77 g.) was isolated by means of ether and was largely phenolic. It was methylated by means of sodium hydroxide (200 c.c. of 10%) and methyl sulphate (48 c.c.), acetone (100 c.c.) being added to assist solution. After the first reaction was over, sodium hydroxide (20 g.) and methyl sulphate (30 c.c.) were used in a further methylation. The neutral, oily product was collected by means of ether, freed from solvent, and extracted twice with light petroleum (400 c.c., b. p. 60—80°). The evaporated extract was distilled; the main fraction had b. p. 205—220°/8 mm. The residues from the petroleum extraction were digested with benzene, filtered, and also distilled. The combined distillates were fractionated at a lower pressure; a main fraction (16 g.), b. p. 175—185°/1 mm., and a smaller one (5·5 g.), b. p. 210—220°/1 mm., were then obtained. Most of the product was a resin. The lower fraction was redistilled, giving a nearly colourless oil with a faint blue fluorescence, b. p. 177—180°/0·4 mm. (Found : C, 75·3; H, 7·3. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·3%).

Condensation of Phenylacetyl Chloride with Methyl β-Resorcylate.—Methyl β-resorcylate (5 g.) was suspended in carbon disulphide (45 c.c.), and aluminium chloride (8 g.) added. The solution was cooled and stirred while phenylacetyl chloride (4·6 g.), dissolved in a little carbon disulphide, was added gradually; after 2 hours the mixture was heated gently to complete the reaction. The isolated product, probably *methyl* 2-*hydroxy*-4-*phenylacetoxybenzoate*, crystallised from light petroleum (b. p. 40—60°) in flattened needles, m. p. 53—54° (Found : C, 67·1; H, 5·0. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%).

On hydrolysis with alkali β-resorcylic and phenylacetic acids were obtained.

The condensation was therefore carried out in nitrobenzene solution. Powdered aluminium chloride (16 g.) was gradually added to a mixture of methyl β-resorcylate (8·4 g.), phenylacetyl chloride (7·7 g.), and nitrobenzene (45 g.) at 30—40°. After ½ hour the temperature was raised to 50—60°, which was maintained for a further ½ hour. The cooled product was decomposed with dilute hydrochloric acid. The organic layer was diluted with benzene and washed with concentrated sodium carbonate solution, and the solvents removed in steam. The residue, on crystallisation from benzene, gave prisms which on recrystallisation had m. p. 150—151° (Found : C, 67·3; H, 5·1. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%). The alcoholic solution gave a blood-red coloration with ferric chloride. From what follows it is clearly *methyl* 2 : 4-*dihydroxy*-5-*phenylacetylbenzoate*. A mixture of the substance (2 g.), alcohol (40 c.c.), amalgamated zinc dust (27 g.), concentrated hydrochloric acid (300 c.c.), water (30 c.c.), and a layer of benzene was refluxed for 4 hours with occasional additions of hydrochloric acid. The zinc residues were collected and washed with benzene. On evaporation of the solvent an oil remained which quickly solidified. Recrystallised from benzene, the substance formed colourless prisms, m. p. 114—115° (Found: C, 70·3; H, 5·9. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). The ferric reaction in alcohol was a deep blue coloration.

Apparently the methyl ester was not hydrolysed ($C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%) and the substance is probably *methyl* 2 : 4-*dihydroxy*-5-*phenylethylbenzoate*. The substance (0·5 g.) was heated for 2 hours on the steam-bath with alcohol (15 c.c.) and aqueous sodium hydroxide (5 c.c. of 10%). After removal of most of the alcohol and addition of water the solution was acidified and extracted thrice with ethyl acetate. The extract was evaporated, and the residue refluxed with water (50 c.c.) for 3 hours. After cooling, the product was collected and crystallised twice from water, forming colourless platelets, m. p. 137—138° alone or mixed with authentic 4-phenylethylresorcinol.

Condensation of m-*Methoxyphenylacetyl Chloride with Methyl β-Resorcylate.*—The acid chloride (22 g.) and the ester (20 g.) were dissolved in nitrobenzene (80 g.) and treated at 30° with powdered aluminium chloride (40 g.). The mixture was occasionally shaken and gently heated during 4 hours. Next day it was worked up as before and, on concentration of a benzene solution of the product, crystals of unchanged resorcyclic ester (7 g.) were deposited. The mother-liquors were further concentrated, boiled with alcohol (charcoal), filtered, and concentrated to a small volume. After several days crystals separated and were collected (3 g.) after addition of a little benzene. After repeated crystallisation from benzene, a colourless product was obtained, m. p. 165° with softening from 150°, unchanged by further recrystallisation. Some demethylated product was present (ferric reaction, blood-red).

The crude product was hydrolysed to the corresponding acid by means of aqueous alcoholic sodium hydroxide. The acid, so obtained, crystallised from ethyl acetate in nodules, m. p. 237—240°. It was heated at 240° until carbon dioxide was no longer evolved, and the product dissolved in dilute alkali. The solution was shaken with ether, acidified, and again extracted with ether. The extract was shaken with sodium bicarbonate solution and evaporated. The residual oil solidified, and was crystallised twice from a little acetic acid, then taken up in benzene, and the solution filtered. The filtrate was evaporated, and the residue taken up in a few drops of acetic acid. On keeping, colourless leaflets were deposited. The substance had m. p. 109—110° and gave a blood-red ferric reaction (Found: C, 69·9; H, 5·2. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·4%). Taking the results of the phenylacetylation (above) into consideration, this substance is 4-m-*methoxyphenylacetylresorcinol*.

m-Methoxyphenylacetyl chloride was heated with methylumbelliferone at 140° for ½ hour. Aluminium chloride was then added, and the mixture heated slowly to 170° and maintained at that temperature for an hour. No new product could be isolated from this or a similar experiment in which zinc chloride was employed.

(B) 1-(γ-*Hydroxybutyl*)-2-*hydroxy*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (I)—1-γ-Ketobutyl-2-naphthol (20 g.) in alcohol (400 c.c.) was hydrogenated at 155°/75 atms., in the presence of copper chromite (2·5 g.) for 4 hours. The solution was filtered and evaporated under diminished pressure. The residue on distillation gave 18 g., b. p. 200—220°/10 mm., of a colourless, glassy mass. A portion crystallised from benzene–light petroleum gave a *substance*, m. p. 111—112°, which was evidently one of the stereoisomeric forms of the glycol (Found: C, 76·3; H, 9·1. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%). The mother-liquors from the crystallisation were evaporated, and the residue distilled, b. p. 215—220°/10 mm. (Found: C, 76·1; H, 9·0%), showing that the hydrogenation product consisted entirely of the glycol. When the hydrogenation was carried out above 170°, the yield was much lower owing to formation of a chroman derivative.

Oxidation Experiments.—(i) The crude glycol (4 g.) in benzene (30 c.c.) was stirred with an equal volume of water and a mixture of potassium dichromate (4·5 g.), sulphuric acid (6 g.), and water (70 c.c.) was slowly added. When oxidation was complete the benzene solution was separated, washed with sodium carbonate solution, and evaporated. The residue, on distillation, gave a small fraction, b. p. 170—200°/10 mm., and a resinous residue. The distillate was partly ketonic, but no definite product could be obtained from it.

(ii) The glycol (5 g.) in benzene (20 c.c.) was added slowly to a stirred solution of potassium dichromate (30 g.), glacial acetic acid (25 c.c.), sulphuric acid (25 c.c.), and water (150 c.c.). The stirring was continued for 6 hours, with occasional addition of benzene to replace losses by evaporation. Finally the benzene solution was separated, washed with dilute sodium carbonate solution, then with water, and evaporated. The residue on distillation afforded a fraction (1·2 g.), b. p. 150°/0·1 mm., which gave an immediate precipitate with Brady's reagent. The substance crystallised from light petroleum in well-formed, colourless prisms, m. p. 79—80° (Found: C, 72·7; H, 7·0. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). This must be a hydroxy-derivative of the desired diketone, and most probably it is 1-*hydroxy*-1-γ-*ketobutyl*-2-*keto*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (V).

(iii) A mixture of the glycol (5 g.), acetone (120 g.), aluminium *tert.*-butoxide (12 g.), and benzene (250 c.c.) was refluxed for 10 hours. Water was then added, and the benzene layer washed with dilute sulphuric acid and with water, dried, and evaporated. The residue, distilled at 10 mm., gave two fractions, b. p. 155—170° and 185—200°. The higher fraction crystallised on rubbing with light petroleum, and separated from hot light petroleum (b. p. 60—80°) in colourless rosettes, m. p. 110°, undepressed by the crystalline form of the glycol. The lower fraction was a light yellow, mobile oil. It was redistilled, b. p. 156—158°/9 mm. (1·6 g.) (Found: C, 83·5; H, 8·0. $C_{14}H_{16}O$ requires C, 84·0; H, 8·0%). The *substance* gave an amorphous precipitate with Brady's reagent, and instantly decolorised a solution of bromine in carbon tetrachloride. After boiling with water for several hours, the oil decolorised bromine much more slowly. These facts indicate that the substance is the inner anhydride of a keto-alcohol. Such substances are known to react with reagents for ketones, and to be hydrolysed to keto-alcohols on heating with water. Since it is evident that the crystalline form of the glycol was less readily attacked than the other isomer, it is reasonable to assume that the oxidation involved the configuration-determining hydroxyl group and hence we prefer the structure (VI). The alternative in which the side-chain hydroxyl is oxidised and the β-tetralol group is unattacked is not excluded but is regarded as much less probable. Attempts further to oxidise this substance after boiling with water had no useful outcome.

(iv) A mixture of the glycol (6·5 g.), methyl ethyl ketone (10 g.), aluminium *tert.*-butoxide (10 g.), and benzene (250 c.c.) was refluxed for 36 hours. The fraction of the product, b. p. 175—200°/15 mm., was treated with alcoholic 2 : 4-dinitrophenylhydrazine sulphate. The amorphous precipitate was dissolved in the minimum quantity of ethyl acetate and the crystals that separated were collected after 24 hours and recrystallised from dioxan. The stout, four-sided, orange prisms had m. p. 212—213° (decomp.) (Found: N, 19·0. $C_{26}H_{24}O_8N_8$ requires N, 19·4%). Although the yield was unsatisfactory, this *substance* is doubtless a derivative of the diketone corresponding to the glycol.

(v) The glycol (3 g.) was heated under nitrogen at 150—160° for 6 hours with Raney nickel (*ca.* 2 g., washed with ether). On distillation, unchanged glycol was obtained along with a lower fraction, b. p. 156—170°/10 mm. This crystallised from alcohol in colourless prisms, m. p. 72—73°, and was identified with α-methyltetrahydro-5 : 6-benzochroman already described (McQuillin and Robinson, J., 1941, 589). The m. p. previously recorded was 68—69° but a mixture of the two specimens had m. p. 72°. The preparation from the above glycol establishes the constitution of this substance, for which two possibilities were considered.

This methyltetrahydrobenzochroman was also isolated when ketobutylnaphthol was first benzylated, then acetalised by means of ethyl orthoformate and alcoholic hydrogen chloride, and finally reduced in presence of Raney nickel at 100°/100 atms. The product had b. p. 165—180°/10 mm. and crystallised from alcohol in colourless prisms, m. p. 72—73°, alone or mixed with the specimen first obtained.

Perhydro-2-*methyl*-5 : 6-*benzochroman* (II).—A solution of ketobutylnaphthol (15 g.) in alcohol (400 c.c.) was boiled for 10 minutes with Raney nickel, filtered, and hydrogenated at 180°/125 atms. for 4½ hours in the presence of fresh Raney nickel (*ca.* 5 g.). The product was a colourless, mobile oil, b. p. 135—140°/11 mm. (13 g.). A redistilled fraction, b. p. 132—133°/9 mm., was analysed (Found : C, 80·7 ; H, 11·5. $C_{14}H_{24}O$ requires C, 80·8 ; H, 11·5%).

After this *perhydro*-compound had been heated in a sealed tube with an equal weight of acetic anhydride and a little zinc chloride (*ca.* 1% of its weight) at 200° for 6 hours, some unchanged material was recovered. There was also obtained a light yellow oil, b. p. 167—172°/9 mm. (Found : C, 75·5 ; H, 10·1%). The analysis indicates that this is chiefly an unsaturated monoacetate containing traces of the diacetate of the glycol of which the chroman is the anhydride.

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