393. *Synthesis of Derivatives of Quinol related to Dihydroflavoglaucin.*

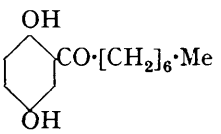
By J. H. Cruickshank and Robert Robinson.

In view of the possibility that dihydroflavoglaucin is an alkyl (amyl or isomeric chains in a block or distributed) derivative of 2 : 5-dihydroxyoctophenone, this substance and some related ketones have been synthesised. Considerable variations have been experienced in the results of applying similar procedure to closely related substances. This applies to the relative yields of dihydroxy-ketones and their ethers and monomethyl ethers in the Friedel–Crafts syntheses and also to the behaviour of the various ketones towards aluminium bromide.

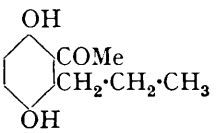
2 : 5-*Dihydroxyoctophenone* (I) resembles dihydroflavoglaucin in colour and in its reactions; 6-*propylquinacetophenone* (II) is, however, colourless and its carbonyl group is inert (that of dihydroflavoglaucin is readily brought into reaction).

2 : 5-*Dihydroxy*-4-n-*amyloctophenone* (III) has a paler yellow colour than (I), but otherwise is very like dihydroflavoglaucin. The outcome of this investigation has been to confirm the correctness of the views expressed in the preceding communication.

Unfortunately 2 : 5-dihydroxy-3-*n*-amyloctophenone has not been obtained. Its *monomethyl* ether (IV) was found to break down on attempted demethylation.



(I.)



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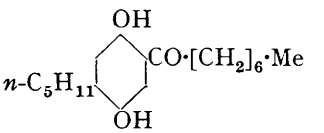
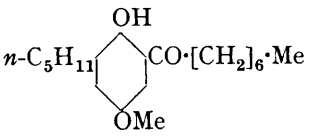


(III.)

QUINOL dimethyl ether and *n*-octoyl chloride in the presence of aluminium chloride afford 2-*hydroxy*-5-*methoxyoctophenone* (V), which may be further demethylated by means of aluminium bromide with formation of (I). It was thought that the 5-n-*amyl* ether of (I) might undergo a migration process involving the amyl group when it was treated with aluminium halides, but in these circumstances the dihydroxyoctophenone was regenerated.



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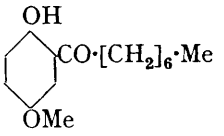

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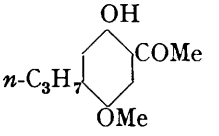
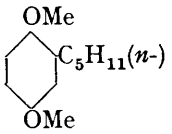


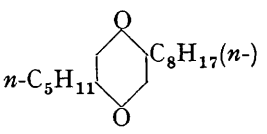
(VI.)

Friedel–Crafts acetylation of *n*-propylquinol dimethyl ether gave the *monomethyl* ether (VI) of 2 : 5-*dihydroxy*-4-n-*propylacetophenone* and this was demethylated by the action of aluminium chloride or bromide; a considerable proportion of the ketone was converted into *n*-propylquinol in these operations.

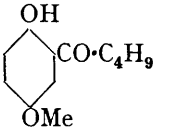
2 : 5-*Dimethoxy*-n-*amylbenzene* (VII) has been prepared by the *n*-valerylation of quinol dimethyl ether, followed by Clemmensen reduction of the product (IX) (which is mono-demethylated) and finally by methylation. These stages were used in other cases of a similar nature. *n*-Octoylation of (VII) was accompanied by mono-demethylation and in



(VII.)



(VIII.)



(IX.)

this case the second methyl group could be removed without difficulty and with formation of 2 : 5-dihydroxy-4-*n*-amyloctophenone (III). Successive reduction of the intermediate monomethyl ether by Clemmensen's method, methylation, and oxidation by nitric acid in acetic acid solution gave 2-n-*amyl*-5-n-*octylbenzoquinone* (VIII). The experiment was made in order to determine whether such a heavily alkylated quinol dimethyl ether could be nitrated and for comparison with the behaviour of a reduced and methylated flavoglaucin derivative towards nitric acid.

As the dihydroxy-4-*n*-amyloctophenone (III) resembled dihydroflavoglaucin apart from its much paler yellow colour, we desired to examine the corresponding *iso*amyl ketone in order to find out what effect, if any, the branching of the alkyl chain has on the intensity of colour in this series of compounds.

2 : 5-*Dihydroxy*-4-iso*amyloctophenone* was accordingly prepared by a method similar to that already described for the isomeride and it also was a pale yellow substance. Accordingly the 1 : 2 : 4 : 5-arrangement of substituents in flavoglaucin appears to be excluded unless there is an additional substituent as, for example, in a 2 : 5-dihydroxy-3 : 4-dialkyloctophenone.

2-*Hydroxy*-5-*methoxy*-3-n-*amyloctophenone* (IV) has been synthesised from the *n*-valerylation product of quinol dimethyl ether, namely, the monomethyl ether (IX). The corresponding *hydroxymethoxy*-n-*amylbenzene* was obtained by Clemmensen's method of reduction and the *n*-octoate of this was submitted to a Fries migration. The ketone (IV) might well have proved to be identical with dihydroflavoglaucin monomethyl ether, but it is not so, although the resemblance is close. We were unable to effect the demethylation of this substance and all attempts in this direction led to decomposition with formation of *n*-amylquinol.

Unexpected difficulties were encountered in the attempted preparation of the *iso*amyl analogue of (IV). Thus the 5-*benzyl* ether of 2 : 5-*dihydroxy*iso*valerophenone* did not form a semicarbazone under the usual conditions; in the presence of pyridine the *ketazine* was produced. Again the *iso*valerylation of quinol dimethyl ether proceeded abnormally, giving only a poor yield of partly demethylated product, and the *semicarbazone* of

2-*hydroxy*-5-*methoxy*isovalerophenone was converted into a *ketazine* under the conditions of the Wolff–Kishner process. Experiments along these lines will be continued.

6-Allylquinacetophenone and some of its derivatives have already been prepared by Baker and Lothian (J., 1936, 279); the dimethyl ether gives the iodoform reaction and affords a flavylium salt when condensed with *o*-vanillin in the presence of hydrogen chloride. Moreover its styryl derivative has been oxidised with permanganate, and the product identified as 3 : 6-dimethoxyphthalic anhydride; therefore the constitution attributed to the allyl ketone by Baker and Lothian is undoubtedly correct.

In order to exclude ambiguity due to the unsaturated side chain, 6-allylquinacetophenone has been catalytically reduced to 6-n-*propylquinacetophenone* (II). The two 6-substituted quinacetophenones are colourless and do not form semicarbazones or dinitrophenylhydrazones. This is clearly due to *o*-hindrance and, as flavoglaucin readily reacts with reagents for the carbonyl group, we may be sure that the 6-position is not substituted in the molecule of that colouring matter.

Experimental.

4-*Methoxyphenyl Valerate*.—*n*-Valeryl chloride (16 g., b. p. 126—127°) was added to a mixture of quinol monomethyl ether (16 g.), pyridine (20 c.c.), and ether (100 c.c.). After 2 hours, the solution was washed with dilute hydrochloric acid and then with aqueous sodium hydroxide, the ether evaporated, and the residue distilled, b. p. 150—152°/10 mm. (21 g.) (Found: C, 69·2; H, 7·7; MeO, 14·2. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7; 1MeO, 14·9%).

2-*Hydroxy*-5-*methoxy*-n-*valerophenone* (IX).—(A) Rosenmund and Lohfert (*Ber.*, 1928, **61**, 2601) claimed that good yields of ketones could be obtained from phenolic esters by the use of aluminium chloride in nitrobenzene solution. Stoughton, Baltzly, and Bass (*J. Amer. Chem. Soc.*, 1934, **56**, 2007) prefer to use higher temperatures without nitrobenzene, and report poor yields by the other method. In the present example the migration did not occur in nitrobenzene solution.

A mixture of 4-methoxyphenyl valerate (47 g.) and aluminium chloride (40 g.) was heated on the steam-bath for 6 hours. The resulting dark brown oil deposited yellow crystals after 2 hours, and later set to a dark brown, porous mass. The solid was decomposed with ice and hydrochloric acid, and the product isolated by means of ether as a dark brown oil, which was extracted with light petroleum. The solvent-free yellow oil which dissolved had b. p. 146—154°/0·2 mm. (23 g.); it solidified on cooling. The *substance* crystallised from light petroleum in large, pale yellow needles, m. p. 62°, or from alcohol in thin, very pale yellow needles (Found: C, 69·0; H, 8·1; MeO, 15·2. $C_{12}H_{16}O_3$ requires C, 69·2; H, 7·7; 1MeO, 14·9%). The ferric reaction in alcoholic solution was a persistent green coloration and a yellow colour was developed in alcoholic sodium hydroxide. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–chloroform in deep red needles, m. p. 186° (Found: C, 55·4; H, 5·3. $C_{18}H_{20}O_6N_4$ requires C, 55·7; H, 5·2%).

(B) *n*-Valeryl chloride (40 g.) was added to a suspension of powdered aluminium chloride (40 g.) in carbon disulphide (100 c.c.), and the mixture heated on the steam-bath until all the solid had dissolved. A solution of quinol dimethyl ether (50 g.) in carbon disulphide (200 c.c.) was then gradually added and after 4 hours the carbon disulphide was decanted from the oily reaction product. Decomposition with ice and hydrochloric acid, and working up as before, gave yellow needles, m. p. 62° (35 g.); 2 : 4-dinitrophenylhydrazone, m. p. 186°, identical with the product obtained under (A). The yield could be improved by cooling the solution in ice during the addition of the quinol dimethyl ether and then allowing the mixture to heat spontaneously.

2-*Hydroxy*-5-*methoxy*-n-*amylbenzene*.—The original method of Clemmensen (*Ber.*, 1913, **46**, 1837; 1914, **47**, 51) was employed. The modification used by Stoughton, Baltzly, and Bass (*loc. cit.*) gave poor yields (10%) in their hands when used for the reduction of 2 : 5-dihydroxy-*n*-valerophenone.

A mixture of 2-hydroxy-5-methoxy-*n*-valerophenone (35 g.), amalgamated zinc (120 g.), and hydrochloric acid (200 c.c. of 20%) was boiled for 4 hours with frequent shaking and addition of concentrated hydrochloric acid (125 c.c.) in portions from time to time. The products were isolated by the use of ether, and separated by distillation into a low-boiling fraction possessing a fruity odour and one (18 g.) of b. p. 138—140°/0·1 mm. This slowly solidified on keeping and the *substance* crystallised from light petroleum in colourless needles, m. p. 44° (Found:

C, 74·4; H, 9·3. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). It quickly coloured on exposure to the air; the ferric reaction in alcoholic solution was a very transient green coloration.

4-*Methoxy*-2-n-*amylphenyl Octoate*.—2-Hydroxy-5-methoxy-*n*-amylbenzene (6 g.) and *n*-octoyl chloride (6 g., b. p. 193—195°/750 mm.) were added successively to an ice-cold mixture of pyridine (10 c.c.) and ether (50 c.c.), well shaken for 5 minutes, and kept overnight. The ethereal solution was washed with dilute hydrochloric acid, then with aqueous sodium hydroxide, dried, and evaporated; the residual oil had b. p. 167—171°/0·1 mm. (9 g.) (Found: C, 75·3; H, 9·7. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·0%). The ferric reaction was negative; there was no coloration with sodium hydroxide in acetone, and no coupling with *p*-nitrobenzenediazonium salts was observed.

2-*Hydroxy*-5-*methoxy*-3-n-*amyloctophenone* (IV).—The above ester (8 g.) was added to powdered aluminium chloride (3·5 g.) under hydrogen, and the mixture heated on the steam-bath. After 12 hours, the dark brown mass was decomposed with ice and hydrochloric acid; the isolated product had b. p. 180—190°/0·1 mm. (5 g., 2·5 g. below 180°). It was a discoloured oil which could not be crystallised; the ferric reaction was an intense permanent green coloration, and a deep yellowish-brown colour was developed with alcoholic sodium hydroxide. The substance was characterised as its 2 : 4-*dinitrophenylhydrazone*, which crystallised from alcohol in long, deep red needles, m. p. 103° (Found: C, 62·3; H, 7·5; N, 11·3; MeO, 5·9. $C_{26}H_{36}O_6N_4$ requires C, 62·4; H, 7·2; N, 11·2; 1MeO, 6·4%). The derivative was moderately readily soluble in alcohol.

Reaction of the hydroxy-ketone with aluminium bromide (cf. Pfeiffer, *J. pr. Chem.*, 1933, **136**, 125; 1937, **147**, 293) led to decomposition. The ketone (1 g.), dissolved in dry benzene (10 c.c.), was added slowly at room temperature to a solution of aluminium bromide (3 g.) in benzene (20 c.c.). After heating on the steam-bath for 4 hours, the yellow crystalline precipitate originally formed changed to a thick black oil. The mixture was decomposed with dilute hydrochloric acid, the benzene layer evaporated, and the residual dark tar extracted with hot light petroleum (b. p. 40—60°). The cooled extracts deposited colourless needles, which were recrystallised from a little benzene; m. p. 86°. Stoughton, Baltzly, and Bass (*loc. cit.*) ascribe the m. p. 85—86° to *n*-amylquinol (Found: C, 73·2; H, 8·9. Calc. for $C_{11}H_{16}O_2$: C, 73·3; H, 8·9%).

The colourless needles rapidly coloured in the air, gave a deep brown alkaline solution, and a very transient green ferric reaction.

Attempted demethylations with aluminium bromide in boiling carbon disulphide, hydrobromic acid in acetic acid solution, hydriodic acid in acetic acid, and ice-cold acetic anhydride saturated with dry hydrogen bromide, gave amylquinol as the only isolable product.

2 : 5-*Dimethoxy*-n-*amylbenzene* (VII).—2-Hydroxy-5-methoxy-*n*-amylbenzene (18 g.) in acetone (50 c.c.) was refluxed for 1 hour at a time with two portions each of methyl sulphate (5 c.c.) and aqueous sodium hydroxide (10 c.c. of 20%). An excess of sodium hydroxide was added, most of the acetone removed in a vacuum, and the product isolated with ether as a colourless oil, b. p. 144—146°/12 mm. (16 g.) (Found: MeO, 29·4. $C_{13}H_{20}O_2$ requires 2MeO, 29·8%).

2-*Hydroxy*-5-*methoxy*-4-n-*amyloctophenone*.—*n*-Octoyl chloride (12·2 g., b. p. 193—195°/750 mm.) and powdered aluminium chloride (10 g.) were completely dissolved in carbon disulphide (100 c.c.) by refluxing and the solution was then cooled in ice. A solution of 2 : 5-dimethoxy-*n*-amylbenzene (15 g.) in carbon disulphide (100 c.c.) was slowly introduced and the mixture was kept in the ice-bath for 2 hours, allowed to reach room temperature during 1 hour, and then refluxed for 8 hours. The supernatant viscous dark oil was separated and decomposed with ice and hydrochloric acid. The product was isolated by extraction with light petroleum and concentration of the solution, which, on cooling in a freezing mixture, deposited pale yellow needles (19 g.), m. p. 42°; after recrystallisation from light petroleum or alcohol, m. p. under water 42° (Found: C, 74·9; H, 9·9; MeO, 9·0. $C_{20}H_{32}O_3$ requires C, 75·0; H, 10·0; 1MeO, 9·7%).

The substance gave a deep yellow coloration with sodium hydroxide in acetone and a permanent green coloration with ferric chloride in alcoholic solution. The 2 : 4-*dinitrophenylhydrazone* formed dark red plates, m. p. 117°; it was sparingly soluble in alcohol, and best crystallised from chloroform–ethyl alcohol (Found: N, 11·4. $C_{26}H_{36}O_6N_4$ requires N, 11·3%).

2 : 5-*Dihydroxy*-4-n-*amyloctophenone* (III).—With aluminium bromide under the same conditions as were employed in attempted demethylation of the 3-*n*-amyl isomeride, 2-hydroxy-5-methoxy-4-*n*-amyloctophenone was almost quantitatively demethylated. The resultant benzene solution was evaporated, and the product taken up in light petroleum. The cooled

extracts deposited pale yellow needles, which were recrystallised from light petroleum or aqueous alcohol; m. p. 94°; m. p. under water, 85° (Found: C, 74·3; H, 10·1. $C_{19}H_{30}O_3$ requires C, 74·5; H, 9·8%).

The substance was much paler yellow than the isomeric dihydroflavoglaucin, but closely resembled it in respect of the ferric reaction (green changing to reddish-brown), and the behaviour with sodium hydroxide in acetone (deep yellow coloration changing to reddish-brown on shaking in air).

The 2 : 4-dinitrophenylhydrazone was readily soluble in alcohol and crystallised from methyl alcohol in purple needles, m. p. 112°; the colour of the derivative changed to brick-red at about 90°.

The dihydroxyketone and its monomethyl ether were recovered unchanged after treatment with zinc dust and acetic acid under the conditions which effected the complete reduction of dihydroflavoglaucin.

2-n-*Amyl*-5-n-*octylbenzoquinone* (VIII).—2-Hydroxy-5-methoxy-4-*n*-amyloctophenone (3 g.) and amalgamated zinc (20 g.) were boiled with hydrochloric acid (50 c.c. of 20%) for 2 hours. The product was isolated by means of ether as a pale yellow oil. Without further purification, acetone (25 c.c.), aqueous sodium hydroxide (4 c.c. of 10%), and methyl sulphate (1 c.c.) were added and, after shaking for 5 minutes, the mixture was heated on the steam-bath for ½ hour. The oily product, doubtless 2-*n*-amyl-5-*n*-octylquinol dimethyl ether, was isolated in the usual way.

Attempted oxidations of this material to a terephthalic acid were unsuccessful, but the corresponding *quinone* was formed when the dimethyl ether was dissolved in acetic acid (2 vols.) and treated with nitric acid (1 vol.) at room temperature. Yellow crystals appeared immediately; after ½ hour these were taken up in ether, freed from acid by washing with aqueous sodium carbonate, and, after evaporation of the solvent, crystallised from alcohol, being obtained in yellow needles, m. p. 65° (Found: C, 78·4; H, 10·2. $C_{19}H_{30}O_2$ requires C, 78·6; H, 10·3%).

2-*n*-Amyl-5-*n*-octylquinol was prepared by reduction of the quinone with sodium hyposulphite in 50% alcohol. It formed white needles, rapidly darkening in the air, and gave a very transient green ferric reaction. It developed an intense dark brown coloration in alcoholic sodium hydroxide; this faded only slowly, so that diazo-coupling reactions could not be observed. It was almost insoluble in cold aqueous sodium hydroxide.

*Quinol Di*isov*alerate*.—*iso*Valeryl chloride (48 g.) was added slowly to a stirred suspension of quinol (22 g.) in pyridine (20 c.c.) and ether (150 c.c.) cooled in ice-water. Stirring was continued for 15 minutes, and the mixture kept overnight. Water was then added, and the ethereal layer extracted with dilute hydrochloric acid and 5% aqueous sodium hydroxide. Evaporation of the solvent left a partly crystalline oil, which was distilled. After rejection of a small first fraction, the distillate solidified and crystallised from alcohol in colourless rods, m. p. 55° (50 g.) (Found: C, 68·9; H, 8·0. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%).

2 : 5-*Dihydroxy*iso*valerophenone*.—The yields obtained in the following experiment agree with the findings of Stoughton, Baltzly, and Bass (*loc. cit.*) for quinacetophenone, and do not bear out the claims of Rosenmund and Lohfert (*loc. cit.*). A mixture of quinol di*iso*valerate (28 g.), quinol (11 g.), and powdered aluminium chloride (30 g.) was cautiously heated to 150—160° (oil-bath), and maintained at that temperature for 1 hour; a long and wide condenser was found to be necessary. Decomposition with dilute hydrochloric acid liberated a dark brown oil, which solidified almost completely (22 g.). It contained a quantity of quinol, which was separated by solution in hot benzene. The *substance* (15 g.) crystallised from benzene in yellow plates and from light petroleum (b. p. 60—80°) in stout yellow needles, m. p. 110° (Found: C, 68·2; H, 7·0. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

2-*Hydroxy*-5-*benzyloxy*iso*valerophenone*.—A mixture of alcoholic sodium ethoxide (from 1·8 g. of sodium and 100 c.c. of alcohol), benzyl chloride (10 g.), and 2 : 5-dihydroxy*iso*valerophenone (13 g.) was refluxed on the steam-bath for 8 hours; the alcohol was then removed in a vacuum, and the product isolated by means of ether and distilled. The fraction, b. p. 160—170°/2 mm. (12 g.), solidified on cooling and crystallised from alcohol in pale yellow rhombs, m. p. 60° (10·4 g.) (Found: C, 76·2; H, 7·1. $C_{18}H_{20}O_3$ requires C, 76·1; H, 7·0%).

No semicarbazone of this substance could be isolated in any of a large number of attempts; the conditions which gave a small yield of the semicarbazone of the monomethyl ether failed completely with the monobenzyl ether. The following procedure led to the formation of the *ketazine*. A mixture of 2-hydroxy-5-benzyloxy*iso*valerophenone (1 g.), semicarbazide hydrochloride (0·7 g.), and pyridine (15 c.c.) was heated on the steam-bath for 4 hours. The resulting deep yellow solution, diluted with water, deposited a yellow crystalline precipitate (0·7 g.).

Recrystallisation from aqueous pyridine gave deep yellow needles, m. p. 174°, almost insoluble in alcohol and in benzene (Found : C, 76·4; H, 7·0; N, 5·2. $C_{36}H_{40}O_4N_2$ requires C, 76·6; H, 7·1; N, 5·0%).

An attempt to prepare the hydrazone, using a very large excess (20 mols.) of hydrazine hydrate in acetic acid solution, gave the same product, m. p. 174°.

Staudinger and Kepfer (*Ber.*, 1911, **44**, 2205) reduced ketazines to hydrocarbons by heating with an excess of hydrazine hydrate at 200°. In this case, the ketazine (2 g.) was heated with hydrazine hydrate (10 c.c.) at 200° for 24 hours in a sealed tube. The product was a dark tar, from which only a trace of a colourless oil could be distilled, and the only substance that could be isolated was the unchanged ketazine, m. p. 174°.

Semicarbazone of 2-*Hydroxy*-5-*methoxy*iso*valerophenone*.—The Friedel–Crafts reaction between *iso*valeryl chloride (48 g.) and quinol dimethyl ether was carried out exactly as for 2-hydroxy-5-methoxy-*n*-valerophenone. The product was a dark oil, which on distillation gave a fraction (8 g.), b. p. 100—130°/2 mm., and another (31 g.), b. p. 120—155°/0·02 mm. The latter contained the desired product mixed with 2 : 5-dimethoxy*iso*valerophenone. The pure monomethyl ether was isolated in the form of its sodium salt (cf. Baker and Lothian, J., 1936, 279). An ethereal solution of the fraction was shaken with 25% aqueous sodium hydroxide; the dark-coloured aqueous solution then became filled with yellow needles. The solid was collected, washed with a little ether, and then with light petroleum. The sodium salt was decomposed with hydrochloric acid, giving an almost colourless oil which still could not be crystallised, and the semicarbazone was prepared for further purification.

Nothing was deposited from an aqueous alcoholic solution of the oily material, semicarbazide hydrochloride, and sodium acetate in 4 days. On addition of a few c.c. of pyridine, however, and keeping for some hours, there was a copious separation of long needles, but even so no more than 40—50% of the oil could be converted into the *semicarbazone*. Recrystallised from alcohol, it formed very pale yellow needles, m. p. 171° (Found : C, 59·0; H, 7·3; N, 15·6. $C_{13}H_{19}O_3N_3$ requires C, 58·9; H, 7·2; N, 15·9%).

Ketazine of 2-*Hydroxy*-5-*methoxy*iso*valerophenone*.—It was anticipated that a Wolff–Kishner reduction of the above semicarbazone would proceed smoothly to give 2-hydroxy-5-methoxy-*iso*amylbenzene, but this did not prove to be the case. The semicarbazone (3 g.) was heated at 180—185° with alcoholic sodium ethoxide (from 0·4 g. of sodium and 10 c.c. of alcohol) for 36 hours in a sealed tube. The product, which solidified on cooling, was washed with alcohol. The washings were evaporated, and distillation of the residue gave only a trace of a colourless oily distillate. The solid product (2·5 g.) was recrystallised from aqueous pyridine and obtained in deep yellow needles, m. p. 144°, only slightly soluble in alcohol (Found : C, 69·7; H, 7·6; N, 6·7. $C_{24}H_{32}O_4N_2$ requires C, 69·7; H, 7·8; N, 6·8%).

2 : 5-*Dimethoxy*iso*valerophenone*.—The product from the above preparation of 2-hydroxy-5-methoxy*iso*valerophenone consisted of a mixture of the mono- and the di-methyl ether. A homogeneous product was obtained by methylation.

The combined distillates (25 g.) were dissolved in acetone (100 c.c.) and refluxed for 20 minutes at a time with five successive additions of aqueous sodium hydroxide (10 c.c. of 10%) and methyl sulphate (2·5 c.c.). The product was worked up in the usual way, and 2 : 5-*dimethoxy*iso*valerophenone* (24 g.) isolated as a colourless oil, b. p. 124—126°/1 mm. (Found : C, 70·4; H, 8·2. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%).

2 : 5-*Dimethoxy*iso*amylbenzene*.—2 : 5-Dimethoxy*iso*valerophenone, submitted to the Clemmensen process, gave a slightly poorer yield of reduced product than that obtained from 2-hydroxy-5-methoxy-*n*-valerophenone. Exactly the same conditions being used, the ketone (23 g.) gave 2 : 5-*dimethoxy*iso*amylbenzene* (10 g.) as a colourless oil, b. p. 100—102°/2 mm. (Found : C, 75·2; H, 9·8. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·6%).

2 : 4-*Dinitrophenylhydrazone of* 2-*Hydroxy*-5-*methoxy*-4-iso*amyloctophenone*.—A solution of 2 : 5-dimethoxy*iso*amylbenzene (7·5 g.) in carbon disulphide (50 c.c.) was added to one of *n*-octoyl chloride (6 g.) and aluminium chloride (5 g.) in carbon disulphide (75 c.c.). The reaction was carried out, and the product isolated, by the methods used for the corresponding *n*-amyl compound. The product was a dark oil (8 g.), exhibiting a permanent green ferric coloration, and a deep yellowish-brown coloration in aqueous alcoholic sodium hydroxide. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–chloroform in deep red needles, m. p. 146° (Found : C, 62·6; H, 7·4; N, 11·1. $C_{26}H_{36}O_6N_4$ requires C, 62·4; H, 7·2; N, 11·2%).

A small quantity of the oil was demethylated with aluminium bromide. The pale yellow solid produced was a hydroxy-ketone (reaction with Brady's reagent, and ferric reaction), whose colour was no more intense than that of the analogous 2 : 5-dihydroxy-4-*n*-amyloctophenone.

2 : 5-*Dihydroxy*-6-n-*propylacetophenone* (II).—A solution of 2 : 5-dihydroxy-6-allylacetophenone (0·3 g., obtained by heating 2-hydroxy-5-allyloxyacetophenone, which could, however, be purified by distillation, b. p. 123—125°/2 mm.; Baker and Lothian, *loc. cit.*) in ethyl acetate (20 c.c.) was shaken with hydrogen under 2—3 atms. for 6 hours, a palladised strontium carbonate catalyst (0·2 g. of 2%) being used. Evaporation of the filtrate gave a solid residue, which crystallised from a little benzene in colourless needles, m. p. 88° (Found: C, 62·3; H, 7·4. $C_{11}H_{14}O_3,1H_2O$ requires C, 62·4; H, 7·5%. Found in material dried for 3 hours at 60° in a vacuum: C, 68·2; H, 7·0. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

Both this substance and the allyl precursor are colourless, and exhibit only a very transient green ferric coloration; they are recovered unchanged after attempts to form semicarbazones, hydrazones, and 2 : 4-dinitrophenylhydrazones. Addition of Brady's reagent to their alcoholic solutions produced no trace of a red colour.

Oxidation of **2 : 5-*Dimethoxy*-6-*allylphenyl Styryl Ketone***.—Potassium permanganate (11 g., 10 atoms O) was gradually added to a suspension of the unsaturated ketone (3 g.) in boiling water (100 c.c.) and aqueous sodium hydroxide (20 c.c. of 10%). When the solution became colourless, it was filtered, the manganese precipitate washed with hot water, and the filtrates acidified and concentrated to about 100 c.c. on the steam-bath. The solution was then heated under reflux on the steam-bath for 8 hours to complete the precipitation of 3 : 6-dimethoxyphthalic anhydride (Perkin and Weizmann, J., 1906, **89**, 1658). The solid was crystallised from acetic anhydride (0·5 g.; intensely blue fluorescent solution); m. p. 260° alone or mixed with an authentic specimen of m. p. 260° (Found: C, 57·8; H, 4·1. Calc. for $C_{10}H_8O_5$: C, 57·7; H, 3·8%).

2 : 5-*Dihydroxy*-n-*propylbenzene*.—The Friedel–Crafts reaction between quinol dimethyl ether and propionyl chloride gave an oily product, b. p. 140—190°/2 mm., consisting of a mixture of partially and completely demethylated ketones. The Clemmensen reduction product from this mixture gave a fraction (8 g.), b. p. 120—150°/2 mm., which partly crystallised on standing. The solid crystallised from benzene in colourless needles, m. p. 87° (Found: C, 71·3; H, 7·7. Calc. for $C_9H_{12}O_2$: C, 71·1; H, 7·9%). Johnson and Hodge (*J. Amer. Chem. Soc.*, 1913, **35**, 1020) describe colourless, microscopic needles, m. p. 86°.

2 : 5-*Dimethoxy*-n-*propylbenzene*.—The above mixture (6 g.) was converted into a homogeneous substance by methylation with methyl sulphate and sodium hydroxide; the product (6 g.) was a colourless oil, b. p. 128—130°/20 mm. (Found: C, 73·6; H, 8·8. Calc. for $C_{11}H_{16}O_2$: C, 73·3; H, 8·9%).

A portion of the distillate was stirred with nitric acid (4 vols. of 40%), and this resulted in the immediate formation of a solid derivative; it crystallised from aqueous alcohol in yellow needles, m. p. 64°. Thoms (*Ber.*, 1903, **36**, 857) prepared 3 : 6-dimethoxy-*n*-propylbenzene, b. p. 125°/20 mm., from dihydroasaron, and described the 4-nitro-derivative as yellow needles, m. p. 64°.

2 : 5-*Dihydroxy*-4-n-*propylacetophenone*.—2 : 5-Dimethoxy-*n*-propylbenzene (5 g.) was added to an ice-cold solution of acetyl chloride (2·5 g.) and aluminium chloride (4·5 g.) in carbon disulphide (50 c.c.). After being kept for 1 hour at room temperature, the mixture was heated on the steam-bath for 8 hours. Decomposition with ice and hydrochloric acid gave a dark oil, which was isolated and distilled, b. p. 150—155°/1 mm. (4 g.). This pale yellow product was nearly pure 2-hydroxy-5-methoxy-4-*n*-propylacetophenone; it gave a permanent green ferric reaction, and a well-crystallised 2 : 4-dinitrophenylhydrazone with Brady's reagent.

This oily product (2 g.) was added to a solution of aluminium bromide (8 g.) in benzene, and the mixture refluxed for 4 hours. After decomposition with water a dark-coloured solid product was isolated by means of ether, and this was extracted with hot benzene. The benzene solution deposited crystals on cooling, and the substance was again crystallised from benzene, forming colourless needles, m. p. 87° alone or mixed with *n*-propylquinol. The mother-liquors were evaporated, and the solid residue crystallised from carbon tetrachloride. It formed yellow, rectangular plates (50 mg.), m. p. 85° (Found: C, 67·9; H, 7·3. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%).

The monomethyl ketone was also demethylated by means of aluminium bromide, and the ketonic product isolated as the 2 : 4-dinitrophenylhydrazone; this crystallised from chloroform–alcohol in deep red needles, m. p. 216°.

2-*Hydroxy*-5-*methoxyoctophenone* (V).—A solution of quinol dimethyl ether (13·5 g.) in carbon disulphide (100 c.c.) was added to an ice-cooled solution of aluminium chloride (15 g.) and *n*-octoyl chloride (15·6 g.) in carbon disulphide (50 c.c.). After 2 hours, the mixture was allowed to reach room temperature (1 hour), and then refluxed for 10 hours on the steam-bath.

Decomposition as usual gave a dark oily product, which was almost completely soluble in hot light petroleum. The cooled solution deposited thick, pale yellow needles (16·2 g.), m. p. 45°, and a further quantity (4 g.) was obtained from the mother-liquor. Recrystallisation from light petroleum and alcohol did not raise the m. p., which was the same when taken under water (Found: C, 71·8; H, 9·1; MeO, 12·1. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8; 1MeO, 12·4%).

The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–chloroform in orange-red microscopic needles, m. p. 134° (Found: C, 58·7; H, 5·9; MeO, 7·5. $C_{21}H_{26}O_6N_4$ requires C, 58·6; H, 6·0; 1MeO, 7·2%).

2 : 5-*Dihydroxyoctophenone.*—A solution of aluminium bromide (52 g.) in benzene (100 c.c.) was slowly added at room temperature to one of the monomethyl ether (16 g.) in benzene (50 c.c.). After refluxing for 6 hours on the steam-bath, the mixture was decomposed with water and a yellow oil, which solidified, was isolated and crystallised from benzene, forming yellow needles (13 g.), m. p. 86° (m. p. under water, 75°) (Found: C, 70·7; H, 8·5. $C_{14}H_{20}O_3$ requires C, 71·1; H, 8·5%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–chloroform in red microscopic needles, m. p. 186° (Found: C, 57·7; H, 5·6; N, 13·5. $C_{20}H_{24}O_6N_4$ requires C, 57·7; H, 5·8; N, 13·5%). This *ketone* resembles dihydroflavoglaucin in its intensity of colour and it gives a similar ferric reaction (green fading to brown) and coloration with aqueous sodium hydroxide and acetone (deep yellow, slowly changing to reddish-brown on shaking in air). It is, however, readily soluble in aqueous sodium hydroxide.

2 : 4-*Dinitrophenylhydrazone of* 2-*Hydroxy*-5-n-*amyloxyoctophenone.*—2 : 5-Dihydroxyoctophenone (5 g.) in alcohol (20 c.c.) was mixed with a solution of sodium ethoxide (1 g. of sodium and 20 c.c. of alcohol) and with *n*-amyl bromide (6·6 g.). The brown solution was refluxed till the colour had all but disappeared (6 hours); the alcohol was then evaporated, and the residue taken up in ether. Evaporation and distillation gave an orange-coloured oil (2·5 g.), b. p. 190—195°/1·5 mm. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol in deep red, rhombic plates, m. p. 121° (Found: C, 61·6; H, 7·0; N, 11·7. $C_{25}H_{34}O_6N_4$ requires C, 61·7; H, 7·0; N, 11·5%).

Reaction with Aluminium Chloride (cf. Smith, *J. Amer. Chem. Soc.*, **1933**, **55**, 3718).—The amyl ether (2 g.) and aluminium chloride (2·2 g.) were mixed in carbon disulphide (20 c.c.) and kept at room temperature for 3 days. The product was an oil, which when stirred with light petroleum left a yellow microcrystalline precipitate (1·0 g.). Recrystallised from benzene, it formed yellow needles, m. p. 86° (2 : 4-dinitrophenylhydrazone, m. p. 186°) alone or in admixture with 2 : 5-dihydroxyoctophenone. The portion soluble in light petroleum was converted into the 2 : 4-dinitrophenylhydrazone (0·9 g.), which after one recrystallisation had m. p. 121°, undepressed by the dinitrophenylhydrazone of the original amyl ether.

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