326. *Synthesis of* 3-*Hydroxy*isoquinolines *and* 2-*Hydroxy*-1 : 4-*naphthaquinones from Esters of* 2-*Acyl*-4 : 5-*dimethoxyphenylacetic Acids.*

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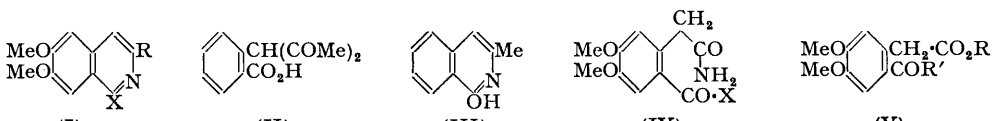
Esters of 2-acetyl- and 2-benzoyl-4 : 5-dimethoxyphenylacetic acids are hydrolysed normally to the corresponding acids by aqueous sodium hydroxide, and are converted by ammonia into 3-hydroxy*iso*quinolines. With sodium hydroxide and also with aqueous ammonia, however, methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate and methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate are converted in good yield into 2-hydroxy-1 : 4-naphthaquinones.

In the course of a search for new syntheses of papaverine (I; R = H) we have devoted some attention to the possibility of preparing 3-substituted *iso*quinolines and in particular the compounds (I; R = OH and Cl).

1 : 3-Dichloro*iso*quinoline has been obtained by the action of phosphorus oxychloride on homophthalimide (Gabriel, *Ber.*, 1886, **19**, 1653, 2354) and partial dehalogenation of the former is stated to give 3-chloro*iso*quinoline; 1-chloro-3-hydroxy*iso*quinoline is also obtained by partial reaction of homophthalimide (Gabriel, *loc. cit.*). Apart from these

examples, so far as we are aware, 3-chloro- and 3-hydroxy-*iso*quinolines have not been described. A possible route to the 3-hydroxy*iso*quinolines was suggested by the work of Hurtley (*J.*, 1929, 1870) who showed that evaporation of an aqueous solution of the ammonium salt of the keto-acid (II) gave 1-hydroxy-3-methyl*iso*quinoline (methyl*iso*-carbostyril) (III). With the ultimate object of effecting a synthesis of papaverine *via* 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetamide (IV) a general study of the preparation and properties of derivatives of 2-acyl-4 : 5-dimethoxyphenylacetic acids (V; R = H) was undertaken.



(I) (II) (III) (IV) (V)

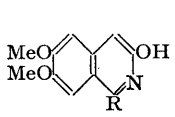
[X = 3 : 4 : 1-$(MeO)_2C_6H_3 \cdot CH_2 \cdot$]

In preliminary experiments, ethyl homoveratrate and acetyl chloride were found to react smoothly with aluminium chloride in carbon disulphide, to give ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (V; R = Et, R′ = Me). By using methyl homoveratrate the corresponding methyl ester was obtained. The orientation of the acetyl group in these two esters was established by oxidation with sodium hypochlorite which in each case gave 2-carboxy-4 : 5-dimethoxyphenylacetic acid (V; R = H, R′ = OH). Previous application of the Friedel–Crafts ketone synthesis to the phenylacetic acid series is confined to ethyl phenylacetate itself which with chloroacetyl chloride gives ethyl *p*-chloroacetylphenylacetate (Kunckell, *Ber.*, 1905, **38**, 2610). Ethyl and methyl 2-acetyl-4 : 5-dimethoxyphenylacetates (V; R = Et and Me; R′ = Me) are hydrolysed normally by aqueous sodium hydroxide to the acid (V; R = H, R′ = Me). Each of the esters reacts with aqueous ammonia to give, in good yield, a product $C_{12}H_{13}O_3N$, apparently by formation of the corresponding amide followed by loss of the elements of water. Attempts to isolate the intermediate amide were unsuccessful. This compound has been shown to be 3-hydroxy-6 : 7-dimethoxy-1-methyl*iso*quinoline (VI; R = Me) and the alternative formulation as 3-amino-6 : 7-dimethoxy-1-naphthol (VII) has been excluded by the following facts. The compound forms a crystalline picrate and hydrochloride and gives an intense red-violet ferric chloride colour; it does not react with nitrous acid and is converted by acetic anhydride into a monoacetate which, since it does not give a ferric chloride colour, is an *O*-acetate. The 3-hydroxy*iso*quinoline structure is confirmed by preparation of 3-hydroxy-6 : 7-dimethoxy-1-phenyl*iso*quinoline (VI; R = Ph) from methyl 2-benzoyl-4 : 5-dimethoxyphenylacetate (V; R = Me, R′ = Ph). The last-named compound is also hydrolysed normally by aqueous sodium hydroxide but fails to react with aqueous ammonia at ordinary temperatures. It is converted into 3-hydroxy-6 : 7-dimethoxy-1-phenyl*iso*quinoline (VI; R = Ph) by ethanolic ammonia at 130—140°; in this case, cyclisation by the alternative route to give an aminophenol is excluded.

The two 3-hydroxy*iso*quinolines described above are high-melting yellow compounds with phenolic properties: they are soluble in aqueous sodium hydroxide, give violet ferric chloride colours, and form red azo-derivatives with benzenediazonium chloride solution. It has not been possible to replace the 3-hydroxyl group by chlorine by using phosphorus oxychloride (cf. Gabriel, *loc. cit.*; Gabriel and Colman, *Ber.*, 1900, **33**, 985). 3-Hydroxy*iso*quinolines are thus more truly phenolic than are 1-hydroxy*iso*quinolines and resemble 3-hydroxy-pyridines and -quinolines rather than the formally analogous 2-hydroxy-derivatives.

In attempts to extend these reactions to the phenylacetyl series, methyl homoveratrate reacted smoothly also with phenylacetyl chloride, giving methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) which was not hydrolysed normally in aqueous sodium hydroxide and did not yield a 3-hydroxy*iso*quinoline with ammonia. Both of these reagents convert the keto-ester smoothly and in good yield into bright-red 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone (VIII; R = Ph) [neither the carboxylic acid (V; R = H; R′ = CH_2Ph) nor the corresponding amide could be isolated].

This quinone gives a monoacetate, a monobenzoate, and a monomethyl ether, and on reductive acetylation furnishes the corresponding triacetoxynaphthalene derivative. Similarly treatment of methyl homoveratrate with homoveratroyl chloride gives methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate [V; R = Me, R′ = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$] which with either aqueous sodium hydroxide or ammonia gives 2-hydroxy-6 : 7-dimethoxy-3-(3 : 4-dimethoxyphenyl)-1 : 4-naphthaquinone [VIII; R = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$]. Although ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (V; R = Et,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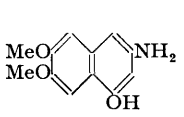
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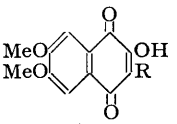
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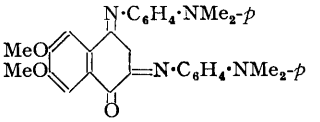
(IX)

R′ = Me) reacts normally with aqueous sodium hydroxide to give the corresponding carboxylic acid and does not yield a naphthaquinone under these conditions, the ketone is rapidly converted into 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (VIII; R = H) in good yield by ethanolic sodium ethoxide with free access to air.

The formation of 2-hydroxynaphthaquinones from alkyl 2-acylphenylacetates proceeds by intramolecular loss of ethanol or water to give a 1 : 3-dihydroxynaphthalene, atmospheric oxidation of which will proceed rapidly in alkaline solution to give the corresponding hydroxynaphthaquinone (cf. Volhard, *Annalen*, 1897, **296**, 14; Soliman and Latif, *J.*, 1944, 55). In support of this view, treatment of methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) with sodium ethoxide and ethanol with complete exclusion of oxygen gave a colourless amorphous phenolic product which oxidised rapidly to the corresponding red hydroxynaphthaquinone on exposure to the air.

The structures assigned to the 2-hydroxynaphthaquinones (VIII; R = H and Ph) have been confirmed by unambiguous syntheses which also serve to establish the assumed orientation of the substituent groups in methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (V; R = Me, R′ = CH_2Ph) and hence, by analogy, that of the groups in the keto-ester [V; R = Me, R′ = 3 : 4 : 1-$(MeO)_2C_6H_3{\cdot}CH_2$]. Condensation of 6 : 7-dimethoxy-1-tetralone with *p*-nitrosodimethylaniline gives the anil (IX), hydrolysis of which gives 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (VIII; R = H) identical with the specimen obtained by the route described above (cf. Pfeiffer and Hesse, *J. pr. Chem.*, 1941, **158**, 315). Treatment of the last compound with benzenediazonium chloride (cf. Neunhoeffer and Weise, *Ber.*, 1938, **71**, 2705) gave 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone identical with the compound obtained as described above.

Experimental

**Ethyl 2-Acetyl-4 : 5-dimethoxyphenylacetate.*—Dry, finely powdered aluminium chloride (12·0 g., 1 mol.) and acetyl chloride (6·4 ml., 1 mol.) were added to a cooled solution of ethyl homoveratrate (20·0 g., 1 mol.) in dry carbon disulphide (120 ml.). The mixture was boiled under reflux for 1 hour, then cooled, and the solvent decanted from the dark complex which was decomposed with ice-water. The product was collected by means of ether, and the ethereal extract washed with saturated aqueous sodium hydrogen carbonate and then with water, dried, and evaporated, to give *ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate* (12·0 g., 51%) which crystallises from light petroleum (b. p. 60—80°) as silky needles, m. p. 94° (Found: C, 63·3; H, 6·6. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%), and gives a red *2 : 4-*dinitrophenylhydrazone*, rhombs (from ethyl acetate), m. p. 171° (Found: C, 53·6; H, 4·9. $C_{20}H_{22}O_8N_4$ requires C, 53·8; H, 5·0%).

Methyl 2-Acetyl-4 : 5-dimethoxyphenylacetate.—This *ester* (3·5 g., 30%) was obtained similarly from methyl homoveratrate (9·5 g.), acetyl chloride (3·5 g.), and aluminium chloride (6·0 g.) in carbon disulphide (60 ml.) and after crystallisation from ether–light petroleum (b. p. 60—80°) formed needles, m. p. 114° (Found: C, 61·7; H, 6·7. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4%). The 2 : 4-*dinitrophenylhydrazone* separated as red needles, m. p. 194°, from ethyl acetate (Found: N, 13·7. $C_{19}H_{20}O_8N_4$ requires N, 13·0%).

* We are grateful to Professor Sir Robert Robinson, F.R.S., for permission to include a description of the compounds thus marked, which were first made in the Oxford laboratory (H. R. Bentley, Thesis, 1947).

*2-*Acetyl*-4 : 5-*dimethoxyphenylacetic Acid.*—Hydrolysis of the methyl and the ethyl ester with aqueous sodium hydroxide (5%), by either shaking overnight at room temperature or boiling for 15 minutes under reflux followed by acidification, gave 2-*acetyl*-4 : 5-*dimethoxyphenylacetic acid* which crystallised from ethanol as needles, m. p. 175° (Found: C, 60·3; H, 6·1. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%).

2-*Carboxy*-4 : 5-*dimethoxyphenylacetic Acid.*—Methyl 2-acetyl-4 : 5-dimethoxyphenylacetate (150 mg.) was hydrolysed by aqueous sodium hydroxide (10%, 10 ml.) at 80° during 15 minutes. Sodium hypochlorite solution [6·0 ml.; from aqueous sodium hydroxide (20%) saturated with chlorine] was added dropwise with stirring during 30 minutes to the cooled alkaline solution which was finally boiled under reflux for 15 minutes. After cooling of the solution and acidification, the precipitated solid was collected and crystallised from water, to yield 2-carboxy-4 : 5-dimethoxyphenylacetic acid as needles, m. p. 216° (Found: C, 55·3; H, 5·3. Calc. for $C_{11}H_{12}O_6$: C, 55·0; H, 5·0%) (Perkin and Robinson, *J.*, 1907, **91**, 1082, give m. p. 215°).

*3-*Hydroxy*-6 : 7-*dimethoxy*-1-*methyl*isoquinoline.*—Finely powdered ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (1·0 g.) was shaken for 16 hours with aqueous ammonia (*d* 0·88; 30 ml.); the yellow solid (0·5 g., 60%) was collected and crystallised from ethanol, giving 3-*hydroxy*-6 : 7-*dimethoxy*-1-*methyl*isoquinoline as yellow prisms, m. p. 286° (decomp.) (Found: C, 65·7; H, 6·0; N, 6·6. $C_{12}H_{13}O_3N$ requires C, 65·7; H, 5·9; N, 6·4%). This does not react with nitrous acid, but in ethanol yields a *picrate* which crystallises from ethanol as yellow prisms, m. p. 236—239° (Found: C, 48·3; H, 3·4. $C_{12}H_{13}O_3N,C_6H_3O_7N_3$ requires C, 48·2; H, 3·6%). Addition of excess of hydrochloric acid to a solution of the base in aqueous sodium hydroxide gives a *hydrochloride*, crystallising from aqueous dioxan as pale yellow needles, m. p. 250° (decomp.) after softening from 240° (Found: C, 52·7; H, 5·8; N, 5·4. $C_{12}H_{13}O_3N,HCl,H_2O$ requires C, 52·65; H, 5·9; N, 5·1%); the base is recovered from the hydrochloride by treatment with aqueous sodium hydrogen carbonate. The base (0·1 g.) and boiling acetic anhydride (3·0 ml.) give in 1 hour a *monoacetate*, crystallising from light petroleum (b. p. 60—80°)–benzene as needles, m. p. 139—140° (Found: C, 64·6; H, 5·7; N, 5·8. $C_{14}H_{15}O_4N$ requires C, 64·35; H, 5·8; N, 5·4%).

Methyl 2-*Benzoyl*-4 : 5-*dimethoxyphenylacetate.*—Dry, finely powdered aluminium chloride (9·0 g., 1·3 mols.) and benzoyl chloride (9·4 g., 1·3 mols.) were added to methyl homoveratrate (10·0 g., 1·0 mol.) in dry carbon disulphide (150 ml.), and the mixture was boiled under reflux for 2 hours. Solvent was then decanted from the dark complex which was allowed to decompose for several hours in contact with ice-water. The product was isolated with ether, the ethereal solution washed with saturated sodium carbonate solution, and the dried solution evaporated. The residue crystallised partly after several hours in the refrigerator. The solid was collected (5·1 g., 34%) by using a small volume of cold ethanol, and crystallised from benzene–light petroleum (b. p. 60—80°), giving *methyl* 2-*benzoyl*-4 : 5-*dimethoxyphenylacetate* as stout needles, m. p. 107° (Found: C, 68·8; H, 5·6. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%).

Hydrolysis for 30 minutes in boiling aqueous sodium hydroxide (10%) followed by acidification gave the *acid* which crystallised from aqueous ethanol as long needles, m. p. 163° (Found: C, 67·6; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%).

3-*Hydroxy*-6 : 7-*dimethoxy*-1-*phenyl*isoquinoline.*—A mixture of methyl 2-benzoyl-4 : 5-dimethoxyphenylacetate (1·0 g.) and saturated ethanolic ammonia (30 ml.) was heated at 130—140° for 4 hours in the autoclave. Evaporation of the solvent gave a partly crystalline product which was collected with ethanol. 3-*Hydroxy*-6 : 7-*dimethoxy*-1-*phenyl*isoquinoline (550 mg., 61%) crystallised from ethanol as yellow prisms, m. p. 243° (decomp.) after softening from 230° (Found: C, 72·2; H, 5·5; N, 5·3. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·4; N, 5·0%).

Methyl 4 : 5-*Dimethoxy*-2-*phenylacetylphenylacetate.*—A mixture of methyl homoveratrate (20·0 g.), dry powdered aluminium chloride (12·8 g., 1 mol.) and phenylacetyl chloride (14·8 g., 1 mol.) in dry carbon disulphide (120 ml.) was boiled under reflux for 1 hour, then cooled, and the solvent decanted from the dark complex which was then decomposed with ice-water. The product was collected by means of ether, giving *methyl* 4 : 5-*dimethoxy*-2-*phenylacetylphenylacetate* (10·0 g., 32%) which crystallised from chloroform–light petroleum (b. p. 60—80°) as needles, m. p. 94° (Found: C, 69·8; H, 6·2. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%), and gave a 2 : 4-*dinitrophenylhydrazone* crystallising from ethanol as red needles, m. p. 148° (Found: N, 10·8. $C_{25}H_{24}O_8N_4$ requires N, 11·0%).

Methyl 4 : 5-*Dimethoxy*-2-(3 : 4-*dimethoxyphenylacetyl*)*phenylacetate.*—Homoveratroyl chloride (7·0 g.) was added to an ice-cold solution of powdered aluminium chloride (7·0 g.) in nitrobenzene (50 ml.), and methyl homoveratrate (10·0 g.) was added dropwise with stirring during 1 hour. The mixture was stirred overnight at room temperature, ether (100 ml.) was added and sufficient

crushed ice to decompose the complex. The ethereal layer was separated, washed with dilute hydrochloric acid, saturated sodium hydrogen carbonate solution, and water, and freed from solvents by steam-distillation. The product was collected by means of benzene and crystallised from benzene–light petroleum (b. p. 60—80°), to give *methyl* 4 : 5-*dimethoxy*-2-(3 : 4-*dimethoxyphenylacetyl*)*phenylacetate* (1·7 g., 13%) as rosettes of prisms, m. p. 132° (Found: C, 65·2; H, 6·5. $C_{21}H_{24}O_7$ requires C, 64·9; H, 6·2%). The 2 : 4-*dinitrophenylhydrazone* crystallises from ethanol as red needles, m. p. 150° (Found: C, 57·3; H, 5·2. $C_{27}H_{28}O_{10}N_4$ requires C, 57·0; H, 5·0%).

2-*Hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone*.—Methyl 4 : 5-dimethoxy-2-phenylacetylphenylacetate (200 mg.) was shaken with sodium hydroxide solution (5%; 10 ml.) or with aqueous ammonia (*d* 0·88; 10 ml.) during 2 days. The deep violet solution was acidified and the precipitated solid (100 mg., 53%) crystallised from methanol–chloroform, to give 2-*hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone* as long red needles, m. p. 255° (Found: C, 70·0; H, 4·8. $C_{18}H_{14}O_5$ requires, C, 69·7; H, 4·5%). This gives a red-brown colour (not intense) with ferric chloride in ethanol and a dark-green colour with concentrated sulphuric acid. With acetic anhydride in pyridine it forms a *monoacetate* which crystallises from chloroform–methanol as microscopic yellow prisms, m. p. 218—220° (Found: C, 68·2; H, 4·8. $C_{20}H_{16}O_6$ requires C, 68·2; H, 4·6%). With benzoyl chloride in pyridine a *monobenzoate* is obtained which crystallises from chloroform–methanol as orange prisms, m. p. 232° (Found: C, 72·4; H, 4·6. $C_{25}H_{18}O_6$ requires C, 72·4; H, 4·4%). With an excess of ethereal diazomethane the 2-hydroxynaphthaquinone gives 2 : 6 : 7-*trimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone* which crystallises from chloroform–methanol as microscopic yellow prisms, m. p. 214° (Found: C, 70·0; H, 5·1. $C_{19}H_{16}O_5$ requires C, 70·4; H, 5·0%). A solution of the quinone (300 mg.) in acetic anhydride (5 ml.) containing zinc dust (300 mg.) and sulphuric acid (*d* 1·84; 0·1 ml.) was boiled under reflux for 20 minutes; the solution was decanted from solid and decomposed with water. The solid product (250 mg., 60%) separating overnight was collected and crystallised from ethanol, to give 1 : 2 : 4-*triacetoxy*-6 : 7-*dimethoxy*-3-*phenylnaphthalene* as clusters of stout needles, m. p. 175—177° (Found: C, 66·0; H, 5·1. $C_{24}H_{22}O_8$ requires C, 65·75; H, 5·1%).

2-*Hydroxy*-6 : 7-*dimethoxy*-3-(3 : 4-*dimethoxyphenyl*)-1 : 4-*naphthaquinone*.—Treatment of methyl 4 : 5-dimethoxy-2-(3 : 4-dimethoxyphenylacetyl)phenylacetate with aqueous sodium hydroxide or ammonia as described above gives 2-*hydroxy*-6 : 7-*dimethoxy*-3-(3 : 4-*dimethoxyphenyl*)-1 : 4-*naphthaquinone* which crystallises from methanol as long red needles, m. p. 226° (Found: C, 65·0; H, 5·1. $C_{20}H_{18}O_7$ requires C, 64·9; H, 4·9%). The *monobenzoate* was obtained as orange prisms, m. p. 206°, from chloroform–methanol (Found: C, 68·3; H, 4·4. $C_{27}H_{22}O_8$ requires C, 68·3; H, 4·7%).

2-*Hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone*.—(*a*) Solutions of 6 : 7-dimethoxy-1-tetralone (5·2 g., 1 mol.) in ethanol (50 ml.) and *p*-nitrosodimethylaniline (7·5 g., 2 mols.) in ethanol (100 ml.) together with aqueous sodium hydroxide (10%; 5 ml.) were mixed and set aside at room temperature. Next day the precipitate (5·5 g., 46%) was collected and crystallised from ethyl acetate, to give 1 : 2 : 3 : 4-*tetrahydro*-1-*keto*-6 : 7-*dimethoxy*-2 : 4-*bis*-p-*dimethylanilonaphthalene* as small permanganate-coloured needles, m. p. 230° (decomp.) (Found: C, 71·2; H, 6·2; N, 11·9. $C_{28}H_{30}O_3N_4$ requires C, 71·5; H, 6·4; N, 11·9%). A mixture of the anil (10·0 g.) and sulphuric acid (20% w/v; 300 ml.) was boiled under reflux for 1 hour, then cooled, and the solid product was collected, dried *in vacuo*, and extracted (charcoal) with boiling benzene (2 × 500 ml.). Concentration of the combined extracts gave 2-*hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone* (800 mg., 16%), which was obtained after recrystallisation from benzene and sublimation (10^{-3} mm.) as microscopic orange needles, m. p. 212° (decomp.) (Found: C, 61·4; H, 4·5. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%).

(*b*) Solutions of ethyl 2-acetyl-4 : 5-dimethoxyphenylacetate (1·0 g.) in ethanol (30 ml.) and of sodium (0·18 g., 2 atoms) in ethanol (5 ml.) were mixed and the mixture was boiled under reflux for 20 minutes and set aside at room temperature with free access to air. Next day the red solid was collected, washed with ethanol, dried, and dissolved in water (50 ml.). Acidification of the aqueous solution gave an orange-brown precipitate (700 mg., 80%) which was collected, washed with water and ethanol, dried, and crystallised from benzene, giving 2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone as small orange needles, m. p. 212° (decomp.) alone or mixed with the specimen described above.

2-*Hydroxy*-6 : 7-*dimethoxy*-3-*phenyl*-1 : 4-*naphthaquinone from* 2-*Hydroxy*-6 : 7-*dimethoxy*-1 : 4-*naphthaquinone*.—Aniline (290 mg.) in water (12 ml.) and hydrochloric acid (*d* 1·18; 0·36 ml.) was diazotised at 0° with sodium nitrite (250 mg.) in water (5 ml.) and hydrochloric acid (*d* 1·18; 0·36 ml.). The solution was added dropwise with stirring during 5 minutes to a solution of

2-hydroxy-6 : 7-dimethoxy-1 : 4-naphthaquinone (560 mg.) in potassium hydroxide solution (5%; 24 ml.) kept at 45°. After a further 20 minutes' stirring at 45° the mixture was adjusted to pH 6·0 with dilute acetic acid and filtered. The filtrate was acidified with hydrochloric acid, and the yellow precipitate collected, washed, and dried (150 mg.). Crystallisation from ethanol gave a red-orange solid (50 mg.), m. p. 240°, which after chromatography on calcium carbonate with benzene as solvent gave 2-hydroxy-6 : 7-dimethoxy-3-phenyl-1 : 4-naphthaquinone (20 mg.), crystallising from methanol–chloroform as red needles, m. p. 255°, alone or mixed with a sample prepared by the alternative route.

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