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ACID-CATALYZED AND THERMAL REARRANGEMENTS OF OBTUSAQUINOL AND RELATED 3,3-DIARYLPROPENES

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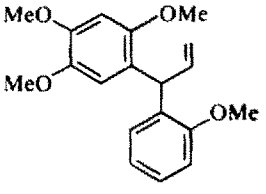
Abstract—Thermal rearrangement of the natural neoflavanoid, (±)-obtusaquinol, yields (±)-obtusafuran. In aqueous acid media obtusaquinol, latifolin and related phenolic 3,3-diarylpropenes rearrange to the isomeric 2-cinnamylphenols. The acid-catalyzed transformations involve initial elimination of a cinnamyl cation. 3-Cinnamylflavans are formed as minor products in these reactions.

3,3-Diarylpropenes (neoflavanoids) frequently co-occur with cinnamylphenols and 2-phenyl-3-methyldihydrobenzofurans in *Dalbergia* species.[1,2] Of the various biogenetic theories advanced to account for the formation of these substances, two are particularly plausible on phytochemical and mechanistic grounds, viz. (a) that compounds of all three classes result from the direct alkylation of a phenolic unit by cinnamyl pyrophosphate,[3] or (b) that 3,3-diarylpropenes, which may be derived by reduction of initially formed 4-arylcoumarins,[2,4] are the precursors of natural cinnamylphenols and, possibly, dihydrobenzofurans.[5]

The mechanistic feasibility of the first proposal was demonstrated by the observation[6] that protonated cinnamyl alcohol condenses readily with phenols in aqueous acetic or citric acid solutions to yield both cinnamylphenols and isomeric 3,3-diarylpropenes. Extending these studies on acid-catalyzed condensations as biogenetic models, Ollis and his associates[7] further noted that the composition of the condensation products varied with the organic acid used, viz. (a) in aqueous formic acid neoflavanoid formation is suppressed, both *cis* and *trans* cinnamylalcohols giving *trans* cinnamylphenols as the major products, and (b) in aqueous propionic acid 1-phenylallylalcohol yields mainly neoflavanoids with lesser or only trace amounts of cinnamylphenols. They suggested[1,7] that the above results exclude the possibility that the same mesomeric 1-phenylallyl cation ($Ph-\overset{\oplus}{C}H-CH=CH_2 \leftrightarrow Ph-\overset{\oplus}{C}H-CH=CH_2$) is involved as an intermediate in both cases, and that the reaction of these alcohols with phenols involves reaction mechanisms having some S_N2 character.

In support of the second biogenetic proposal, it was demonstrated that di-O-methyl latifolin (**1**) forms a cyclopropane derivative on irradiation,[8] and slowly (4 days) isomerizes to the cinnamyl compound (**2**) in the presence of boron trifluoride,[9] a cyclic, intramolecular mechanism being proposed[9] for this reaction. This isomerization establishes the feasibility of neo-flavanoid-cinnamylphenol rearrangements, although as a biogenetic model this particular conversion may not be unequivocal, since it requires anhydrous media and BF_3 as a specific catalyst.



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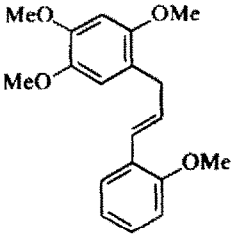

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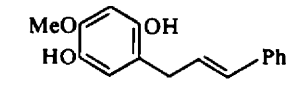
We have now investigated the acid-catalyzed and thermal rearrangements of obtusaquinol (**4**), latifolin (**18**), and the related 3,3-diarylpropene (**9**). The results establish (a) the feasibility of neoflavanoid-cinnamylphenol isomerization under relatively mild, aqueous conditions, (b) clarify the observed effects of formic and other organic acids on the course of phenol-cinnamyl alcohol condensation reactions, and (c) demonstrate the thermal rearrangement of (±)-obtusaquinol to the racemic form of the natural 2-phenyl-3-methyldihydrobenzofuran, obtusafuran. Communication of these results was particularly prompted by the recent report of Schmid *et al.*[11] on the acid-catalyzed and thermal rearrangements of 2-(1′-phenylallyl)phenol (**14**) and similar 3,3-diarylpropenes to yield phenylmethyldihydrobenzofurans. The acid-catalyzed behavior of the natural 3,3-diarylpropenes now examined differs markedly from that of the 3,3-diaryl-propenes investigated by Schmid.

As previously reported,[12,13] cinnamyl alcohol reacts with methoxy quinol in aqueous citric acid solution to yield crystalline 2-cinnamyl-5-methoxyquinol (**3**), (**4**), and (±)-obtusafuran (**5**), (**5**) being isolated by distillation of the crude, condensation mixture. In this earlier work the significance of the distillation step was not recognized. Chromatographic re-examination of the alkylation reaction mixture has now revealed that obtusafuran is *not* formed during the acid condensation reaction, e.g., by protonation of an intermediate ether of type **6**, but is formed by thermal rearrangement of one of the condensation products during the purification procedure. Pure obtusaquinol (**4**), heated to 225° under reduced pressure, partially isomerizes to yield crystalline obtusafuran, indicating that 3,3-diarylpropenes, rather than ethers of type **6**, are the source of the dihydrobenzofurans produced in this synthetic alkylation procedure. The thermal rearrangement of **4** to **5** via the cyclic intermediate **7** is in accord with Schmid's observations[11] on the thermal rearrangement of 2-(1′-phenylallyl)phenol.



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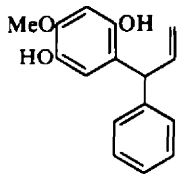

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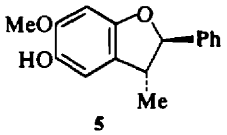

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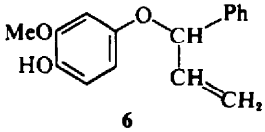

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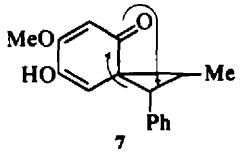

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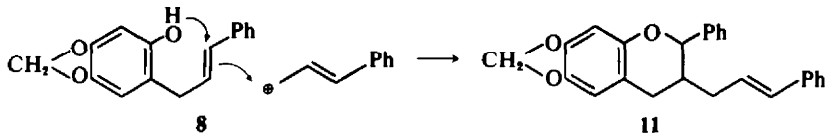
(±)-Obtusaquinol occurs in the heartwood of *Dalbergia retusa* Hemsley.[14] The authors have briefly reported[13] that (distillation of) oily extracts of the wood also yield (±)-obtusafuran. With the recognition of the facile, thermal rearrangement of **4**, the natural occurrence of **5** in the wood became doubtful. The absence of obtusafuran was confirmed by chromatographic re-examination of petroleum ether extracts prior to distillation.

The observation that formic acid catalysis of phenol-cinnamyl alcohol condensations tends to increase[7] yields of cinnamyl phenols relative to 3,3-diarylpropenes has generally been confirmed in this investigation. However, comparison of the reaction of cinnamyl alcohol and of (±)-1-phenylallyl alcohol with methoxyquinol (and other phenols) in aqueous propionic acid under the same conditions did not reveal significant differences in the nature of the product. Both of these alcohols give **3** (major product), **4**, and after distillation, **5**, in essentially identical amounts. In this connection it was also noted that 1-phenyl-allyl alcohol is completely converted into the cinnamyl isomer (and polymer) when it is warmed in aqueous propionic acid. Distillation of the product gave a mixture of cinnamyl alcohol and cinnamyl propionate (2·5 : 1), the NMR spectrum of the crude distillate confirming the absence of any 1-phenyl-allyl alcohol or of its propionate.

2-Cinnamyl-5-methoxyquinol is stable in warm, aqueous citric and formic acids. Obtusaquinol (**4**) is also stable to prolonged heating with aqueous citric acid. With aqueous formic acid, however, **4** rapidly formed a complex mixture of products, which on chromatography appeared to be identical with those produced in the aqueous formic acid catalyzed condensation of methoxyquinol with cinnamyl alcohol. The major product formed from obtusaquinol readily crystallized (m.p. 108°), and proved to be identical with authentic[12] 2-cinnamyl-5-methoxyquinol. A minor product of this reaction was chromatographically identical (on cellulose and on silicic acid) with methoxyquinol. Treated with cinnamoyl chloride and pyridine it formed a crystalline dicinnamate, identified as methoxyquinol dicinnamate by its NMR spectrum and by direct comparison with an authentic specimen prepared by cinnamoylation of methoxyquinol. Obtusafuran was not formed in this acid degradation of **4**.

Further information on the acid-catalyzed transformations of neoflavanoids was provided by reactions of methylenedioxy analogs. Thus, sesamol was condensed with cinnamyl alcohol in aqueous formic acid. A colorless compound, $C_{25}H_{22}O_3$, m.p. 131–132°, readily crystallized from the crude reaction mixture. Distillation and subsequent crystallization of the reaction residue gave 2-cinnamylsesamol (**8**), m.p. 83°, 2-(1′-phenylallyl)-4,5-methylenedioxyphenol (**9**), m.p. 116–117° and the dihydrobenzofuran (**10**), m.p. 74–75°. Structures were assigned to **8**, **9** and **10** on the basis of their NMR spectra, which closely agreed with those of the corresponding methoxyquinol derivatives.

The product, $C_{25}H_{22}O_3$, results from the condensation of two cinnamyl units with sesamol. It does not contain a phenolic OH group, and its 100 MHz NMR spectrum in $CDCl_3$ shows the presence of a methylene and a methine group as a 3H multiplet at δ1·78–δ2·42, a methylene group as a 2H multiplet at δ2·44–δ2·90, a methine proton 1H doublet (J–7·0 Hz) at δ4·71, the methylenedioxy group as a 2H singlet at δ5·82, two vinylic protons as a 1H sextet at δ6·10 and 1H doublet (J–16·0 Hz) at δ6·34, two para-coupled aromatic protons as singlets at δ6·45 and δ6·48, and two phenyl rings as a 10H multiplet



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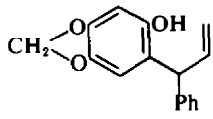

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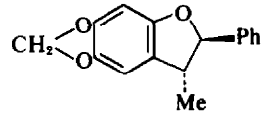

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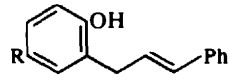
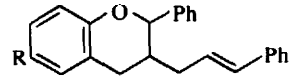
at δ7·10–δ7·50. On the basis of this spectrum the product is considered to be 3-cinnamyl-6,7-methylenedioxyflavan (**11**), and to be formed by the further condensation of 2-cinnamylsesamol with a cinnamyl cation (or protonated cinnamyl alcohol). This was confirmed by the synthesis of **11** by brief reaction of 2-cinnamylsesamol with excess cinnamyl alcohol in aqueous formic acid. As with obtusaquinol, the 3,3-diarylpropene (**9**) proved to be unstable in warm, aqueous formic acid, its acid degradation yielding the crystalline flavan (**11**) and 2-cinnamylsesamol (**8**).

The new dicinnamylation reaction leading to 3-cinnamylflavans is similar to the novel BF_3 catalyzed diprenylation of phenolic ketones recently reported by Seshadri *et al.*[15] The dicinnamylation reaction appears to be quite general and crystalline 3-cinnamylflavans have been isolated in a number of other phenol-cinnamyl alcohol condensations, e.g., 4-methoxyphenol yields **12a** and **13a**, the structure of **13a** being independently confirmed by its synthesis from **12a**. 4-Ethylphenol and 4-t.butylphenol similarly yield the 2-cinnamylphenols (**12b**, **12c**) and the 3-cinnamylflavans (**13b**, **13c**).

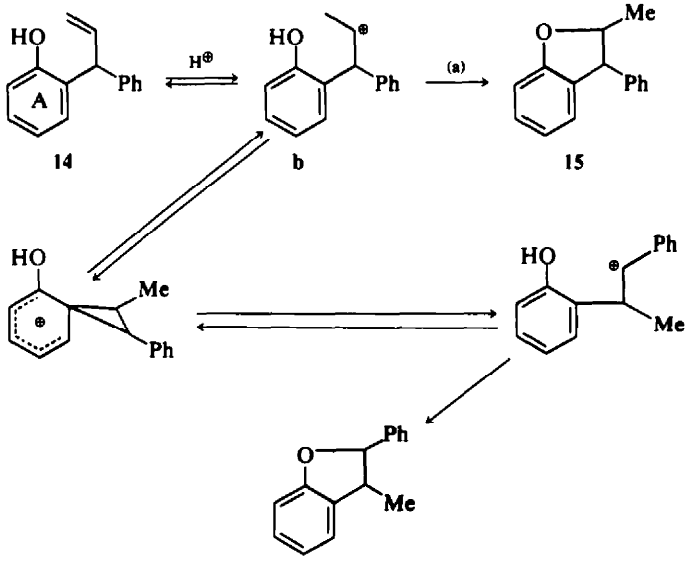


12a: R = OMe
b: R = Et
c: R = CMe_3



13a: R = OMe
b: R = Et
c: R = CMe_3

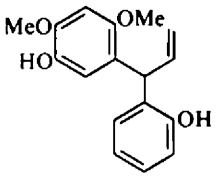
Schmid and his associates[11] have established that the acid catalyzed (HBr-acetic acid) rearrangement of **14** gives high yields of mixtures of *cis* and *trans* 2-methyl-3-phenyl- and 3-phenyl-2-methyldihydrobenzofurans of types **15** and **16**. This rearrangement involves initial protonation of the ethylenic double bond of **14**, and subsequent cyclization reactions of type (**a**) and of type (**b**), in which intermediate phenonium ions participate:



14 b 15

16

The acid-catalyzed reactions of **4** and **9** indicate that in these 3,3-diarylpropenes the nucleophilicity of the A ring is enhanced by the high degree of oxygenation and that it is protonated preferentially to the ethylenic double bond. Elimination of the cinnamyl cation from the intermediate protonated species, e.g., **17**, would yield methoxyquinol, which may then recombine with the cinnamyl cation to give stable 2-cinnamyl-5-methoxyquinol (**3**) and other minor products, identical with those formed in the direct alkylation of methoxyquinol with protonated cinnamyl alcohol:



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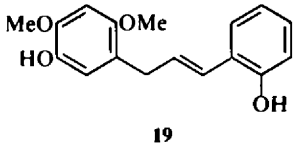

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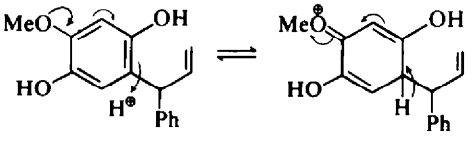
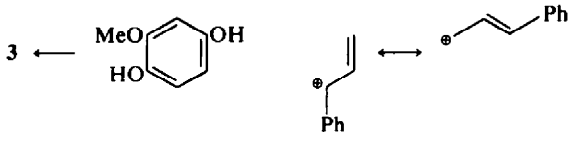
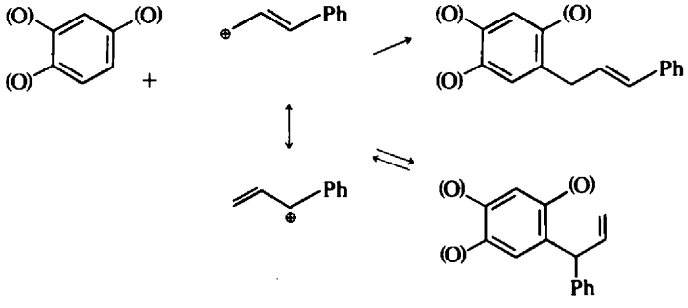


4 **17**



Fission of the phenolic A ring–phenylallyl C—C bond in this acid rearrangement is substantiated by the isolation of methoxyquinol from **4**, and elimination of cinnamyl cation (or incipient cinnamyl carbonium ion if a bimolecular displacement process is involved) is indicated by the formation of the 3-cinnamylflavan (**11**) from **9**. This was further confirmed by treating obtusaquinol (**4**) with aqueous formic acid in the presence of excess of pyrogallol.

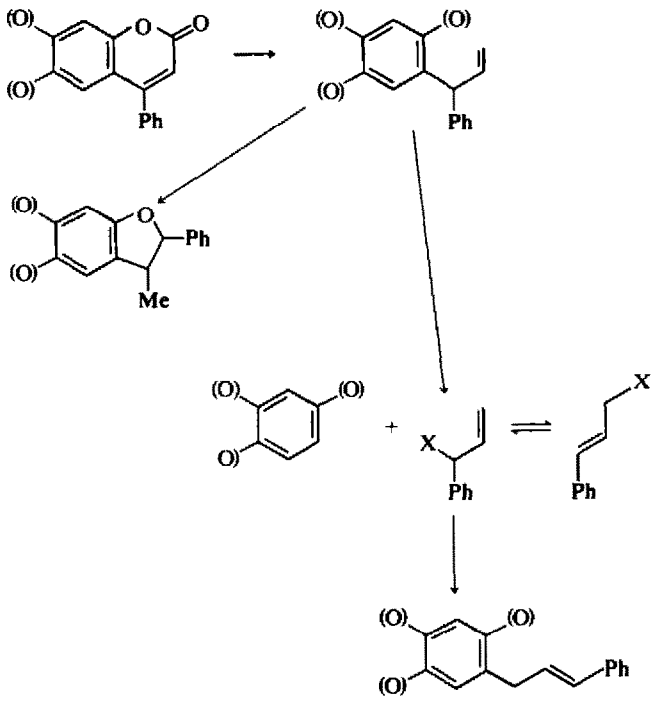


The major reaction product, $C_{15}H_{14}O_3$, was identical with authentic[6] 2-cinnamylpyrogallol.

On the basis of the proposed mechanism the ease of this type of rearrangement should be determined by H^+ concentration, by the nucleophilicity of ring A, *and* by the stability of the potential cinnamyl cation. From this last consideration it would be anticipated that latifolin (**18**), which could give rise to the very stable 0-hydroxycinnamyl cation, should rearrange even more readily than **4** or **9**. It has now been established that latifolin rearranges even in dilute aqueous citric acid (which is without effect on obtusaquinol) to give the crystalline isomer **19**, m.p. 133–134° and a number of minor products. The separation of these other products is currently being investigated.

The acid-instability of 3,3-diarylpropenes indicates that the observed effect of formic acid on phenol-cinnamyl alcohol condensations arises from the reversibility of the alkylation reaction leading to these neoflavanoids:

The rearrangements which have been described also clearly provide significant chemical support for Seshadri's theory that natural 3,3-diarylpropenes play a central biosynthetic role. It is noteworthy, however, that our proposed mechanism for the acid transformation of 3,3-diarylpropenes does involve subsequent alkylation reactions similar to those in the Ollis-Gottlieb biogenetic theory. A modified combination of both of these



theories, therefore, could be suggested to account for the formation and natural co-occurrence of neoflavanoids, cinnamyl phenols, and dihydrobenzofurans.

EXPERIMENTAL

Reaction of methoxyquinol with cinnamyl alcohol and with 1-phenylallyl alcohol

(a) A mixture of methoxyquinol (100 g), *trans* cinnamyl alcohol (100 g), ascorbic acid (8·0 g), and 1% aq. citric acid soln (2 l.) was boiled under reflux for 20 hr. The oily product was separated by decantation, washed well with water, dissolved in warm benzene, and the dried soln treated with about one-third of its volume of Skelly solve F. 2-Cinnamyl-5-methoxyquinol (3) crystallized (64·0 g). The pure product crystallized from ether-Skelly solve F as colorless needles, m.p. 108° (diacetate, m.p. 103–104°).

TLC on silicic acid of the residue in the benzene-Skelly solve F filtrate from 3 showed no trace of (±)-obtusafuran. Distillation of the residue gave an oil (A), b.p. 205–210°/1·0 mm (54·88 and an oil (B), b.p. 215–225°/1·0 mm (25·0 g). The NMR spectrum of (A) indicated the presence of obtusaquinol (3 parts), obtusafuran (1 part) and only traces of 3 and other minor products. The NMR spectrum of (B) showed the presence of 3 (approximately 3 parts), obtusaquinol (1 part) and obtusafuran (1 part). The oil (A), dissolved in warm benzene and treated with Skelly solve F, deposited crystalline (±)-obtusaquinol (m.p. and m.m.p. 99–100°) on cooling (11·0 g). The filtrate was evaporated to an oil, which was dissolved in warm MeOH (200 ml) and treated with water (50 ml). (±)-Obtusafuran crystallized (11·5 g). The aq. MeOH filtrate was diluted with excess of water and the oily product was acetylated. Crystallization of the crude acetate from MeOH gave a further quantity of obtusaquinol as its diacetate (15·0 g; m.p. 104°). Fractional crystallization of oil (B) from benzene-Skelly solve F gave 3 (6·5 g; m.p. 107–108°) and obtusafuran (2·1 g; m.p. 121°).

(±)-Obtusaquinol (4) separated from ether-Skelly solve F as colorless needles, m.p. 99–100° (diacetate, m.p. 104°), identical with the product previously prepared by hydrolysis of the diacetate.

(±)-Obtusafuran (5), recrystallized from aq. AcOH and from ether-Skelly solve F, was obtained as glistening, colorless needles, m.p. 123°. (Found: C, 75·2; H, 6·32; MeO—, 12·0. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·29; 1 MeO—, 12·1%.) 100 MHz NMR spectrum in $CDCl_3$: 5H, S, δ7·38; 1H, S δ6·72; 1H, S, δ6·50; 1H (OH), S, δ5·23; 1H, d, δ5·12, $J = 8·2$ Hz; 1H, m, δ3·10–δ3·60, $J = 8·2$, 7·0 Hz; 3H, S, δ3·86; 3H, d δ1·37, $J = 7·0$ Hz. Obtusafuran shows a characteristic color reaction with $AgNO_3$ on silicic acid chromatograms (R_F 0·88 in benzene/ethanol, 9:1 v/v, 0·77 in EtOAc-Skelly solve F, 1:4 v/v). The spot first becomes intensely white and then slowly (5–10 min) darkens with reduction of the $AgNO_3$. It forms a *monoacetate*, colorless plates ex methanol, m.p. 119–120°. (Found: C, 72·5; H, 6·08. Calc. for $C_{18}H_{18}O_4$: C, 72·5; H, 6·08%.) 100 MHz NMR spectrum in $CDCl_3$: 3H, d, δ1·37, $J = 7·0$ Hz; 3H, S, δ2·29; 1H, m, δ3·20–δ3·60; 3H, S δ3·80; 1H, d δ5·16, $J = 8·4$ Hz; 1H, S, δ6·55; 1H, S, δ6·79; 5H, S, δ7·38 (b) A soln of methoxyquinol (20 g) and cinnamyl alcohol (20 g) in 50% aq. propionic acid (160 ml) was boiled under reflux for 5 hr, diluted with water (400 ml) and cooled. The oily product, dissolved in benzene (100 ml) (dried) and treated with Skelly solve F (50 ml) deposited crystalline 2-cinnamyl-5-methoxyquinol, m.p. 107° (4·8 g). Distillation of the residue from 3 gave an oil, b.p. 190–210°/1·0 m (7·6 g). A soln of this oil in AcOH (40 ml) and water (30 ml) gave crystalline obtusafuran, m.p. and m.m.p. 123° (1·51 g). The aq. AcOH filtrate gave an oil with excess of water. This was acetylated and the crude acetate crystallized from MeOH to give obtusaquinol diacetate, m.p. and m.m.p.

103° (1·35 g). (c) A soln of methoxyquinol (20 g) and (±)-1-phenylallyl alcohol (20 g) in 50% aq. propionic acid (160 ml) was heated under reflux for 5 hr and the oily product was worked up exactly as described in (b). It gave crystalline 2-cinnamyl-5-methoxyquinol (6·0 g; m.p. and m.m.p. with authentic **3**, 108°; mixed with obtusaquinol (m.p. 99–100°) it melted at 78–84°), (±)-obtusafuran (m.p. 123°, 1·53 g), and (±)-obtusaquinol diacetate, m.p. and m.m.p. 103° (1·1 g).

Thermal rearrangement of obtusaquinol

Compound **4** (1·0 g) was heated to 225° under reduced pressure (0·35 mm) for 30 min. The oily product partially crystallized from aqueous MeOH. Recrystallized from aq. MeOH and from ether-Skelly solve F (±)-obtusafuran was obtained as colorless needles, m.p. and m.m.p. 123° (0·14 g).

Rearrangement of obtusaquinol in aqueous formic acid

A soln of **4** (1·0 g) in 60% aq. formic acid (5·0 ml) was heated on a steam-bath for 4 hr and diluted with water (25 ml). A soln of the oily product in benzene (dried)-Skelly solve F deposited cream-colored needles on cooling (0·33 g, m.p. 105–106°). Recrystallized from benzene-Skelly solve F pure **3** was obtained as cream-colored needles, m.p. and m.m.p. 108°. Mixed with obtusaquinol (m.p. 99–100°) the product melted at 85–90°. (Found: C, 75·1; H, 6·34. Calc. for $C_{16}H_{16}O_3$: C, 75·0; H, 6·29%.) The product formed a diacetate, m.p. and m.m.p. with 2-cinnamyl-5-methoxyquinol diacetate, 103–104°; m.m.p. with obtusquinol diacetate (m.p. 104°), 90°. (Found: C, 70·6; H, 6·00. Calc. for $C_{20}H_{20}O_5$: C, 70·6; H, 5·92%.)

The aqueous formic acid reaction filtrate was extracted with ether. After washing with water and saturated Na_2CO_3aq the ether extract was evaporated to an oil. TLC of the oil showed the presence of a single, $AgNO_3$-reducing spot, identical in R_F values with methoxyquinol (on cellulose, R_F 0·61 in 1% aq. AcOH; on silicic acid, R_F 0·18 EtOAc-Skelly solve F, 1:4 v/v, R_F 0·26 in benzene-EtOH, 9:1 v/v). The oil was warmed with pyridine (1·0 ml) and cinnamoyl chloride (0·5 ml). The solid obtained on adding water crystallized from acetone-MeOH to give colorless needles, m.p. 177–178°, identical (m.m.p., NMR spectrum, TLC) with authentic methoxyquinol dicinnamate.

Methoxyquinol dicinnamate was prepared by treating methoxyquinol (1·40 g) in pyridine (6·0 g) with cinnamoyl chloride (4·0 g). It crystallized from acetone-MeOH as colorless needles, m.p. 177–178°. (Found: C, 75·1; H, 5·07. Calc. for $C_{25}H_{20}O_5$: C, 75·0; H, 5·03%.)

A suspension of obtusaquinol (2·0 g) in 5% aq. citric acid (25 ml) was heated for 20 hr. Crystallization of the product from benzene-Skelly solve gave unchanged obtusaquinol (1·06 g; m.p. and m.m.p. 99–100°).

Reaction of obtusaquinol with pyrogallol

A mixture of **4** (1·0 g), pyrogallol (2·0 g), HCOOH (2·0 ml) and water (1·0 ml) was heated on a steam-bath for 3 hr and diluted with excess water. A soln of the oily product in benzene deposited cream-colored crystals on adding Skelly solve F. Recrystallized from benzene 2-*cinnamylpyrogallol* was obtained as cream-colored needles, m.p. and m.m.p. 106–107° (0·40 g). (Found: C, 73·8; H, 5·86. Calc. for $C_{15}H_{14}O_3$: C, 74·4; H, 5·83%.) With authentic 2-cinnamylpyrogallol the product migrates as a single species on silicic acid TLC (R_F 0·34 in benzene-EtOH, 9:1 v/v; 0·31 in $CHCl_3$-MeOH, 10:1 v/v). The product formed a *triacetate*, colorless needles ex MeOH, m.p. and m.m.p. with 2-cinnamylpyrogallol triacetate, 110–111°. (Found: C, 68·5; H, 5·41. Calc. for $C_{21}H_{20}O_6$: C, 68·5; H, 5·47%.)

Compound **3**, heated in aq. formic or oxalic acids, alone or with added pyrogallol, was recovered unchanged (m.p. and m.m.p. 108°).

Reaction of sesamol with cinnamyl alcohol

Cinnamyl alcohol (100 g) was added in portions to a warm soln of sesamol (104 g) in formic acid (300 ml) and water (100 ml). The mixture was boiled under reflux for 40 min, an oil separating rapidly (5 min). Excess of water was added and the oily product was dissolved in boiling MeOH (400 ml). On cooling, colorless crystals separated (16·2 g). Recrystallized from acetone-MeOH and from ether 3-*cinnamyl*-6,7-*methylenedioxy-flavan* (**11**) separated as colorless needles, m.p. 131–132°. (Found: C, 80·9; H, 6·00. Calc. for $C_{25}H_{22}O_3$: C, 81·0; H, 5·99%.) 100 MHz NMR spectrum in $CDCl_3$: 3H, m, δ1·78–δ2·42; 2H, m, δ2·44–δ2·90; 1H, d, δ4·71, J = 7·0 Hz; 2H, S, δ5·82; 1H sextet, δ6·10; 1H, d, δ6·34, J = 16·0 Hz; 1H, S, δ6·45; 1H, S, δ6·48; 10H, m, δ7·10–δ7·50.

The MeOH filtrate from the crystallization of **11** was evaporated and distilled to give an oil, b.p. 210–230°/1·0 mm (116 g). This partially crystallized from ether-Skelly solve F to give cream-colored crystals (60 g). Recrystallized from benzene-Skelly solve F 2-*cinnamylsesamol* (**8**) was obtained as colorless, glistening prisms, m.p. 83°. (Found: C, 75·7; H, 5·99. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·55%.) 100 MHz NMR spectrum in $CDCl_3$: 2H, d, δ3·43, J = 6·0 Hz; 1H, S, δ4·87; 2H, S, δ5·86; 1H, m, δ6·28; 1H, S. δ6·41; 1H, d, δ6·48; 1H, S, δ6·64; 5H, m, δ7·14–δ7·32.

The benzene-Skelly solve F filtrate from **8** was extracted with 5% NaOH in 50% aq. MeOH (3 × 70 ml). Residual benzene-Skelly solve F layer was evaporated to an oil which partially crystallized on keeping. It was dissolved in boiling MeOH. On cooling 2-*phenyl*-3-*methyl*-5,6-*methylenedioxy-dihydrobenzofuran* (**10**) crystallized (10·0 g). Recrystallized from MeOH, **10** formed colorless prisms, m.p. 74–75°. (Found: C, 75·8; H, 5·53. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·55%.) 100 MHz NMR spectrum in $CDCl_3$: 3H, d, δ1·35, J = 7·0 Hz; 1H, m, δ3·16–δ3·50, J = 8·0, 7·0 Hz; 1H, d, δ5·14, J = 8·0 Hz; 2H, S, δ5·88; 1H, S, δ6·44; 1H, S, δ6·58; 5H, S, δ7·37.

The alkaline extract was acidified and extracted with benzene. Addition of Skelly solve F slowly precipitated colorless crystals (8·5 g). Recrystallized from ether-Skelly solve F 2-(1′-*phenylallyl*)-4,5-*methylene-dioxyphenol* (**9**) separated as colorless, glistening plates, m.p. 116–117°. (Found: C, 75·3; H, 5·57. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·55%.) 100 MHz NMR spectrum in $CDCl_3$: 1H (OH), S, δ4·62; 1H, sextet, δ4·84, J = 6·5, 1·5, 1·5 Hz; 1H, sextet, δ5·00, J = 17·0, 1·5, 1·5 Hz; 1H sextet, 5·28; J = 10·5, 1·5, 1·5 Hz; 2H, S, δ5·87; 1H, octet, δ6·31, J = 17·0, 6·5, 1·5 Hz; 1H, S, δ6·42; 1H, S, δ6·52; 5H, m, δ7·10–δ7·36.

3-*Cinnamyl*-6,7-*methylenedioxyflavan* (**11**)

2-Cinnamylsesamol (1·0 g) and cinnamyl alcohol (2·0 g) were heated in HCOOH (5 ml) and water (2·0 ml) for 10 min, and diluted with excess of water. A soln of the product in MeOH deposited colorless crystals. Recrystallized from acetone-MeOH 3-cinnamyl-6,7-methylenedioxyflavin was obtained as colorless needles, m.p. and m.m.p. 131–132° (0·34 g).

Reactions of 2-(1′-*phenylallyl*)-4,5-*methylenedioxyphenol in aq. formic acid*

Compound **9** (2·0 g) was heated on a steam-bath with 80% HCOOHaq acid (6·0 ml) for 1·5 hr and treated with water (50 ml). The oily product was dissolved in warm MeOH (5·0 ml). On cooling, colorless crystals separated (0·26 g). Recrystallization from acetone-MeOH gave pure **11**, m.p. and m.m.p. 131–132°. (Found: C, 81·3; H, 6·00. Calc. for $C_{25}H_{22}O_3$: C, 81·05; H, 5·99%.)

The MeOH filtrate from **11** was evaporated to an oil which was dissolved in ether and extracted with 5% NaOH in 50% aq. MeOH (2 × 15 ml). Acidification of the NaOH extract gave an oil, which partially crystallized from CCl_4 (0·31 g). Recrystallized from CCl_4 (**8**) was obtained, m.p. and m.m.p. 83°.

2-*Cinnamyl*-4-*ethylphenol* (**12b**) *and* 3-*cinnamyl*-6-*ethylflavan* (**13b**).

A soln of 4-ethylphenol (100 g) and cinnamyl alcohol (100 g) in HCOOH (400 ml) and H_2O (100 ml) was heated under reflux for 1 hr and diluted in water (1 l.). The product was distilled to give an oil, b.p. 193–196°/2 mm (77·0 g) and a residue (70·0 g).

The distillate crystallized from Skelly solve F (52·5 g). Recrystallized from Skelly solve F 2-*cinnamyl*-4-*ethylphenol* (**12b**) was obtained as colorless needles, m.p. 66–67°. (Found: C, 85·6; H, 7·76. Calc. for $C_{17}H_{18}O$: C, 85·7; H, 7·61%.) 100 MHz NMR spectrum in $CDCl_3$: 3H, t, δ1·09, J = 8·0 Hz; 2H, q, δ2·57, J = 8·0 Hz; 2H, d, δ3·42, J = 6·0 Hz; 1H (OH), S, δ5·00; 2H, m, δ6·16–δ6·62; 3H, m, δ6·62–δ7·04; 5H, m, δ7·10–δ7·44.

The nondistilled reaction residue was dissolved in boiling MeOH (200 ml) and cooled. The crystalline product (24·7 g; m.p. 131–132°) was recrystallized from acetone-MeOH to give 3-*cinnamyl*-6-*ethylflavan* (**13b**) as colorless needles, m.p. 132–133°. (Found: C, 87·8; H, 7·42. Calc. for $C_{26}H_{26}O$: C, 88·1; H, 7·39%.) 100 MHz NMR spectrum in $CDCl_3$: 3H, t, δ1·10, J = 8·0 Hz; 7H, m, δ1·76–δ3·04; 1H, d, δ4·78, J = 7·5 Hz; 1H, m, δ5·88–δ6·22; 1H, d, δ6·34, J = 16·0 Hz; 3H, m, δ6·72 0 δ7·04; 10H, m, δ7·14–δ7·46.

2-Cinnamyl-4-ethylphenol (1·2 g) and cinnamyl alcohol (1·34 g) were heated in formic acid (5 ml) and H_2O (1 ml) for 5 min. The oily product was dissolved in acetone-MeOH. On cooling, 3-cinnamyl-6-ethyl-flavan, m.p. and m.m.p. 132–133°, separated (0·36 g).

2-*Cinnamyl*-4-*methoxyphenol* (**12a**) *and* 3-*cinnamyl*-6-*methoxyflavan* (**13a**).

4-Methoxyphenol (124 g) and cinnamyl alcohol (134 g) heated in 60% aq. HCOOH (400 ml) for 1 hr as described above gave an oil, whose soln in hot MeOH (200 ml) deposited colorless crystals on cooling (18·0 g). Recrystallized from acetone-MeOH (**13a**) separated as colorless needles, m.p. 181°. An identical product was obtained by reaction of 2-cinnamyl-4-methoxyphenol with cinnamyl alcohol in aq. HCOOH. (Found: C, 84·5; H, 6·85; MeO—, 8·72. Calc. for $C_{23}H_{24}O_2$: C, 84·2; H, 6·79; 1 MeO—, 8·70). 100 MHz NMR spectrum in $CDCl_3$: 3H, m, δ1·72–δ2·44; 2H, m, δ2·44–δ3·04; 3H, S, δ3·74; 1H, d, δ4·76, J = 8·0 Hz; 1H, m, δ5·90–6·23; 1H, d, δ6·36, J = 16·0 Hz; 3H, m, δ6·54–δ6·91; 10H, m, δ7·06–δ7·48. Distillation of the residue from the MeOH filtrate gave an oil, b.p. 215–220°/1·0 mm (75·0 g). A soln of this in ether-Skelly solve F gave colorless needles of **12a** (47·0 g), m.p. 90°. (Found: C, 80·1; H, 6·79. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·71%.) 100 MHz NMR spectrum in $CDCl_3$: 2H, d, δ3·49, J = 6·0 Hz; 3H, S, δ3·72; 1H (OH), S, δ5·10; 2H, m, δ6·14–δ6·58; 3H, m, δ6·60–δ6·80; 5H, m, δ7·14–δ7·40.

2-*Cinnamyl*-4-*t*-*butylphenol* (**12c**) *and* 3-*cinnamyl*-6-*t*-*butylflavan* (**13c**)

A mixture of 4-t-butylphenol (60 g) and cinnamyl alcohol (54 g) in HCOOH (200 ml) and H_2O (25 ml) heated under reflux 1 hr and diluted in water gave an oil with excess water. This was dissolved in warm acetone-MeOH. On cooling colorless crystals separated (6·1 g). Recrystallized from acetone-MeOH 3-*cinnamyl*-6-*t*-*butylflavan* (**13c**) separated as colorless needles, m.p. 168°. (Found: C, 87·7; H, 7·91. Calc. for $C_{28}H_{30}O$: C, 87·9; H, 7·91%.) The MeOH filtrate from **16c** was evaporated and distilled to give an oil, b.p. 208–210°/2 mm (50·5 g). This crystallized from Skelly solve F to yield **12c** as colorless needles, m.p. 73° (42 g). (Found: C, 85·6; H, 8·45. Calc. for $C_{19}H_{22}O$: C, 85·7; H, 8·33%.)

Rearrangement of latifolin in aqueous citric acid

Latifolin (0·286 g, 1 mmole) was heated under reflux for 16 hr with 50 ml 5% aqueous citric acid. The cooled mixture was extracted with ether and the ethereal extract washed with water then dried over $MgSO_4$. After filtration, the solvent was removed leaving an oil which was chromatographed on a preparative TLC plate (Silica-gel; benzene/EtOH, 9:1) to give **19**, crystallized from benzene-Skelly solve F, m.p. 133–134°. (Found for $C_{17}H_{18}O_4$: m.w. 286·1219; Calc. for $C_{17}H_{18}O_4$; m.w. 286·1205). NMR spectrum in $CDCl_3$: 2H, d, δ3·45, J = 6 Hz; 3H, s, δ3·80; 3H, s, δ3·84; 1H, s, δ6·50; 1H, s, δ6·80; 2H, m, δ6·00–6·66; 4H, m, δ6·68–7·39.

REFERENCES

[1]O. R. Gottlieb, S. Mageswaran, W. D. Ollis, R. J. Roberts and I. O. Sutherland, *An. Acad. Brasil. Ciênc.* **42**, 417 (1970) Supplement

[2]T. R. Seshadri, *Phytochemistry* **11**, 881 (1972)

[3]W. D. Ollis and O. R. Gottlieb, *Chem. Commun.* 1396 (1968)

[4]J. Gautier, A. Cave, G. Kunesch and J. Polonsky, *Experientia* **28**, 759 (1972)

[5]S. K. Mukerjee, T. Saroja and T. R. Seshadri, *Indian J. Chem.* **8**, 21 (1970)

[6]L. Jurd, *Tetrahedron* **25**, 1407 (1969)

[7]S. Mageswaran, W. D. Ollis, R. J. Roberts and I. O. Sutherland, *Tetrahedron Letters* 2897 (1969)

[8]D. Kumari and S. K. Mukerjee, *Ibid.* 4169 (1967)

[9]D. Kumari, S. K. Mukerjee and T. R. Seshadri, *Ibid.* 1153, (1967)

[10]M. Gregson, W. D. Ollis, B. T. Redman and I. O. Sutherland, *Chem. Commun.* 1394 (1968)

[11]E. Schmid, Gy. Fráter, H. J. Hansen and H. Schmid, *Helv. Chim. Acta* **55**, 1625 (1972)

[12]L. Jurd, *Tetrahedron Letters* 2863 (1969)

[13]L. Jurd, K. Stevens and G. Manners, *Chem. Commun.* 992 (1972)

[14]L. Jurd, K. Stevens and G. Manners, *Tetrahedron Letters* 2149 (1972)

[15]B. S. Bajwa, P. L. Khanna and T. R. Seshadri, *Ibid.* 3371 (1972)