Synthesis of 5-*p*-Hydroxybenzyl-5,6-dihydro-2-naphthol, (±)-Sequirin D

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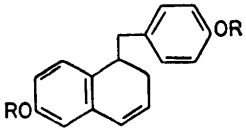
A high-yield six-step synthesis of sequirin D (1a), a naturally occurring norlignan, is described. Michael addition of deoxyanisoin (2) to acrylonitrile gives a ketonitrile (3), which on Wolff–Kishner reduction is reduced and hyrolysed *in situ* to 4,5-bis-*p*-methoxyphenylpentanoic acid (4). Cyclodehydration of (4) with polyphosphoric acid, followed by borohydride reduction and dehydration furnishes di-*O*-methylsequirin D (1b) which affords on demethylation sequirin D (1a) in an overall yield from (2) of 60%. The key synthon (4) has also been prepared by three other routes.

An unusual norlignan naphthol, 5-*p*-hydroxybenzyl-5,6-dihydro-2-naphthol (1a) [(±)-sequirin D], a constituent of *Sequoia sempervirens*,[1] attracted our interest because of our earlier syntheses [2] of various naturally occurring naphthols. After starting our work on the synthesis of the phenolic naphthol (1a) we came across Whiting's interesting communication [3] on the synthesis of (±)-di-*O*-methylsequirin D (1b) and its absolute configuration. However, in view of the biogenetic novelty of the norlignan [1,3-5] (1a), the possible contribution of the free

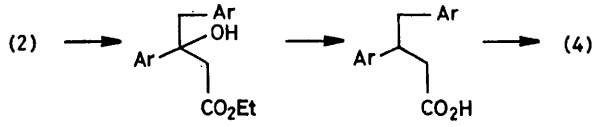


(1) a; R = H
b; R = Me

phenolic naphthol to the fungal resistance and durability of the wood,[6] coupled with the estrogenic and antigonatropic activity of a closely related compound,[7] and finally the non-availability [3] of the synthetic natural product itself, we pursued our project and communicate here a high-yield synthesis of (±)-sequirin D (1a) (60%) as well as its di-*O*-methyl ether (1b) (73%) [*cf.* the reported [3] synthesis of (1b) which gives an overall yield of only 7%]. Additionally, 4,5-bis-*p*-methoxyphenylpentanoic acid (4), the key intermediate in the present work as well as in that of Whiting,[3] has been secured by us *via* four independent routes (Schemes 1—4), one of which provided access to the acid (4) in large quantities and very high yield.

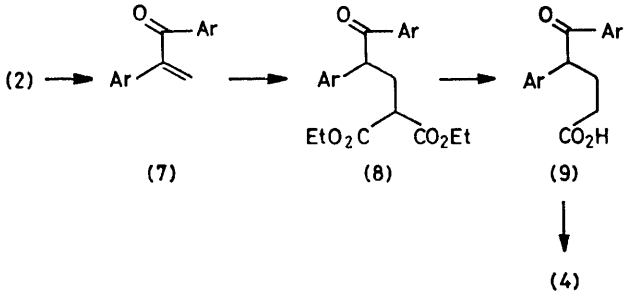
Michael addition of deoxyanisoin (2) to acrylonitrile [8] (2) gave the ketonitrile (3) in quantitative yield. Wolff–Kishner reduction [9] of (3), accompanied by *in situ* hydrolysis, afforded the required bis-*p*-methoxyphenylpentanoic acid (4) as a crystalline solid in 97% yield (Scheme 1).

Arndt–Eistert homologation of the known bis-*p*-methoxyphenylbutanoic acid [10] (6) gave the pentanoic acid (4). The yield of the butanoic acid (6), prepared earlier,[10] has now been very much increased by hydrogenolysis of the β-hydroxy-ester obtained from deoxyanisoin (2) by Reformatsky reaction (Scheme 2).



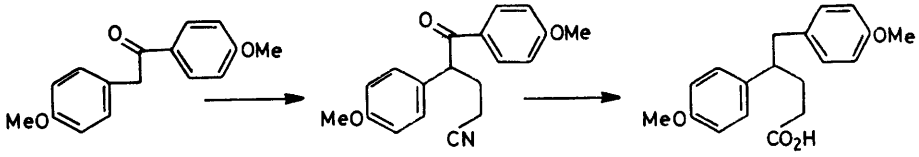
Scheme 2 Ar = C_6H_4OMe-*p*

Michael addition of diethyl malonate to α-methylenedeoxyanisoin [11] (7) gave the keto-diester (8). Saponification of (8), followed by decarboxylation gave the keto-acid (9) which on Wolff–Kishner reduction furnished the required pentanoic acid (4) (Scheme 3).



Scheme 3 Ar = C_6H_4OMe-*p*

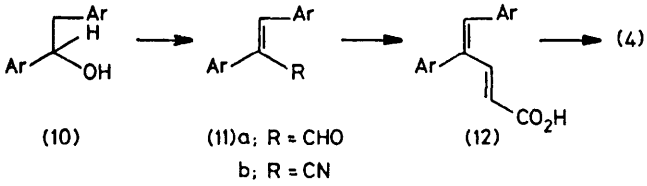
Vilsmeier formylation [12] of deoxydihydroanisoin [13] (10) gave the anisylcinnamaldehyde (11a) which was elaborated to the dienoic acid (12) (*EZ*-mixture) by condensation with malonic acid. Reduction of (12) with nickel–aluminium alloy [14] gave the pentanoic acid (4) (Scheme 4). The cinnamaldehyde (11a) was also obtained by tin(II) chloride reduction [15] of *p*-methoxy-α-*p*-methoxy-



Scheme 1

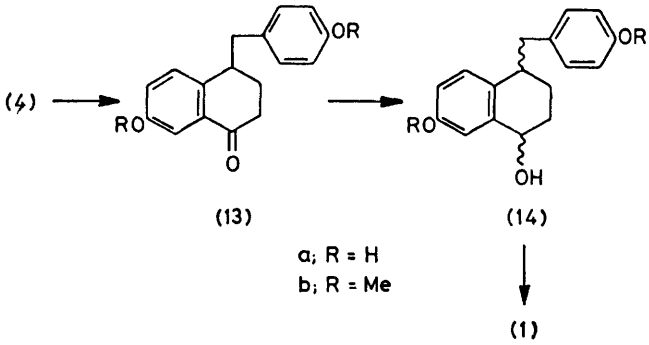
phenylcinnamonitrile (11b), prepared in high yield by condensation of *p*-anisaldehyde with *p*-methoxyphenylacetonitrile.[16]

Cyclodehydration of the bis-*p*-methoxyphenylpentanoic acid (4) with polyphosphoric acid [17] (PPA) gave the



SCHEME 4 Ar = C_6H_4OMe-*p*

dimethoxytetralone (13b) in 84% yield. Reduction of (13b) with sodium borohydride gave in 97% yield the dimethoxytetralol (14b), which was smoothly dehydrated in 92% yield to di-*O*-methylsequirin D (1b), m.p. 108—109 °C (lit.,[1,4] 107.5—109 °C). Demethyl-



ation of (1b) with pyridine hydrochloride [18] afforded the natural product, sequirin D (1a) in 83% yield. In a related, though comparatively less satisfactory approach, the dimethoxytetralone (13b) was demethylated to the dihydroxytetralone (13a). Reduction with borohydride gave the dihydroxytetralol (14a) which on dehydration gave sequirin D (1a).

EXPERIMENTAL

Solvent extracts of reaction products were appropriately washed and dried (Na_2SO_4) before removal of solvent. The instruments used for recording of spectra are (i) for i.r., Perkin-Elmer model 397 or 700, (ii) for u.v., Beckman model 26, and (iii) for ^1H n.m.r., Varian T-60 or Brucker 270 MHz spectrometers, the last with $SiMe_4$ as internal standard. B.t. refers to bath temperature during short-path distillations. For t.l.c. separations, Acme silica gel was used.

4,5-Bis-p-methoxyphenyl-5-oxopentanenitrile (3).—To a solution of potasium t-butoxide [from potassium (50 mg) and t-butyl alcohol (60 ml)] was added with stirring deoxyanisoin (2) (3 g). Acrylonitrile (0.75 g) was added dropwise and the stirring was continued for 4 h. After heating the solution at 40 °C for 2 h, most of the t-butyl alcohol was removed, the residue was poured into water (100 ml) and the product was extracted with ether (3 × 40 ml). Removal of solvent afforded the *ketonitrile* (3) (3.62 g, 100%), b.t. 190 °C at 3 mmHg; $\nu_{max.}$ (film) 2 250 (C≡N) and 1 675 cm^{-1} (C=O); δ (CCl_4) 2.2 (4 H, m, 2 × CH_2), 3.7 (3 H, s, 4-aryl OCH_3), 3.77 (3 H, s, 5-aryl OCH_3), 4.52 (1 H, t, *J* 8 Hz, CH), 6.73 (2 H, d, *J* 9 Hz, 4-aryl H-3 and H-5), 6.77 (2 H, d, *J* 9 Hz, 5-aryl H-3 and H-5), 7.12 (2 H, d, *J* 9 Hz, 4-aryl H-2 and H-6), and 7.83 (2 H, d, *J* 9 Hz, 5-aryl H-2 and H-6) (Found: C, 74.0; H, 6.6; N, 4.6. $C_{19}H_{19}NO_3$ requires C, 73.8; H, 6.2; N, 4.5%).

4,5-Bis-p-methoxyphenylpentanoic Acid (4).—A mixture of the ketonitrile (3) (1.75 g), potassium hydroxide (1.75 g), and hydrazine hydrate (2.5 ml) in diethylene glycol (25 ml) was heated to reflux for 6 h. After cooling to room temperature, aqueous potassium hydroxide (30% w/v; 30 ml) was added and the refluxing was continued for 5 h The mixture was diluted with water (30 ml) and washed with ether (2 × 30 ml), the aqueous phase was neutralized with dilute hydrochloric acid, and the liberated organic acid was extracted with ether. Work-up of the extract gave the *pentanoic acid* (4) (1.72 g, 97%), m.p. 115—116 °C (from ethanol); $\nu_{max.}$ (Nujol) 1 700 (C=O) and 1 615 cm^{-1} (C=C); δ ($CDCl_3$) 2.13 (4 H, m, 2-CH_2 and 3-CH_2), 2.81 (3 H, m, 4-CH and 5-CH_2), 3.78br (6 H, s, 2 × OCH_3), 6.9 (8 H, m, 8 × ArH), and 9.56br (1 H, s, CO_2H) (Found: C, 72.2; H, 7.1; $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.1%).

3,4-Bis-p-methoxyphenylbutanoic Acid (6).—A solution of the hydroxy-ester [19] (5) (6 g) in glacial acetic acid (35 ml) and perchloric acid (0.5 ml) was shaken with palladium–carbon (10%; 0.3 g) and hydrogen at atmospheric pressure. After the absorption of hydrogen had ceased (17 h) the catalyst was filtered off and most of the acetic acid was removed under reduced pressure. Usual work-up gave the hydrogenolysed ester, $\nu_{max.}$ (OH peak absent) 1 725 cm^{-1} (ester C=O). Without further purification the ester was saponified with aqueous ethanolic potassium hydroxide (10% w/v; 100 ml) to give the butanoic acid (6) (5 g, 96%), m.p. 168—169 °C (from ethanol) (lit.,[10] 173 °C); $\nu_{max.}$ (Nujol) 1 700 cm^{-1} (C=O of CO_2H); δ ($CDCl_3$) 2.65 and 2.85 (4 H, 2d, *J* 7 Hz, 2-CH_2 and 4-CH_2), 3.1—3.53 (1 H, m, 3-H), 3.77 (6 H, s, 2 × OCH_3), 6.77 (2 H, d, *J* 9 Hz, 2 × ArH), 6.82 (2 H, d, *J* 9 Hz, 2 × ArH), 7.0 (2 H, d, *J* 9 Hz, 2 × ArH), 7.07 (2 H, d, *J* 9 Hz, 2 × ArH), and 9.53br (1 H, CO_2H).

Arndt–Eistert Homologation of Butanoic Acid (6).—An ethereal solution (15 ml) of the acid chloride of (6) [from the butanoic acid (6) (3 g) and thionyl chloride (6 ml)] was added dropwise to an ice-cold ethereal solution (40 ml) of diazomethane [prepared from *N*-nitrosomethyl urea (9 g)]. After allowing the reaction mixture to stand overnight, the excess of diazomethane and ether were removed under reduced pressure at 30 °C (water-bath) to afford an orange diazoketone, $\nu_{max.}$ (film) 2 140 cm^{-1} ($COCHN_2$). A solution of the diazoketone in dioxan (35 ml) was added dropwise over 15 min to a mechanically stirred suspension of silver oxide (2.6 g) in aqueous sodium thiosulphate (3.8 g, 130 ml), maintained at 65—70 °C. Stirring at this temperature was continued for 2 h. It was cooled, potassium hydroxide was added to ensure alkalinity, and the solids were filtered off through neutral alumina. The filtrate was acidified with dilute hydrochloric acid and the liberated organic acid was purified through reprecipitation from aqueous sodium hydrogencarbonate with dilute hydrochloric acid to afford the homologated acid (2.54 g, 81%), m.p. 114—115 °C (from benzene), identified (mixed m.p.) as the *acid* (4) obtained according to Scheme 1.

Ethyl 2-Ethoxycarbonyl-4,5-bis-p-methoxyphenyl-5-oxopentanoate (8).—α-Methylenedeoxyanisoin (7) (1.3 g) in ether (10 ml) was added during 30 min to a mixture of diethyl malonate (1.6 g) and ethanolic potassium hydroxide

[0.2 g in ethanol (95%; 1.5 ml)] in ether (10 ml) at 15 °C. After having been stirred at room temperature for 2 h it was poured into ice–water, extracted with ether, and purified by column chromatography (silica gel, benzene) to afford the *keto-diester* (8) (1.82 g, 88%), $\nu_{max.}$ 1 725 (ester C=O) and 1 670 (ketone C=O); δ (CCl_4) 1.17 (3 H, t, *J* 7 Hz, OCH_2CH_3), 1.25 (3 H, t, *J* 7 Hz, OCH_2CH_3), 2.03—2.73 (2 H, m, $CHCH_2CH$), 3.15 [1 H, t, *J* 7.5 Hz, $CH(CO_2Et)_2$], 3.63 (3 H, s, 4-aryl OCH_3), 3.7 (3 H, s, 5-aryl OCH_3), 3.87—4.37 (4 H, m, 2 × $CO_2CH_2CH_3$), 4.5 (1 H, t, *J* 7 Hz, CHCO), 6.63 (2 H, d, *J* 9 Hz, 4-aryl H-3 and H-5), 6.68 (2 H, d, *J* 9 Hz, 5-aryl H-3 and H-5), 7.05 (2 H, d, *J* 9 Hz, 4-aryl H-2 and H-6), and 7.77 (2 H, d, *J* 9 Hz, 5-aryl H-2 and H-6) (Found: C, 66.7; H, 6.6. $C_{24}H_{28}O_7$ requires C, 67.3; H, 6.6%).

4,5-*Bis*-p-*methoxyphenyl*-5-*oxopentanoic Acid* (9).—A mixture of the keto-diester (8) (4 g) and aqueous ethanolic potassium hydroxide (10%, 100 ml) was heated to reflux for 12 h. Most of the ethanol was removed and the residue was diluted with water. The keto-acid liberated by neutralization with dilute hydrochloric acid was heated (100 °C, 2 h) and purified by extraction with ether (3 × 40 ml), followed by re-extraction with aqueous sodium hydrogencarbonate. Acidification of the hydrogencarbonate phase with dilute hydrochloric acid gave the pure *keto-acid* (9) (1.87 g, 61%) as a viscous gum, b.t. 230 °C at 2 mmHg; $\nu_{max.}$ (film) 1 705 (acid C=O) and 1 670 cm^{-1} (ketone C=O); δ ($CDCl_3$) 2.33 (4H, m, 2 × CH_2), 3.70 (3 H, s, 4-aryl OCH_3), 3.77 (3 H, s, 5-aryl OCH_3), 4.53 (1 H, t, *J* 7.5 Hz, $ArCHCO$), 6.73 (2 H, d, *J* 9 Hz, 4-aryl H-3 and H-5), 6.78 (2 H, d, *J* 9 Hz, 5-aryl H-3 and H-5), 7.13 (2 H, d, *J* 9 Hz, 4-aryl H-2 and H-6), 7.87 (2 H, d, *J* 9 Hz, 5-aryl H-2 and H-6), and 9.1br (1 H, s, CO_2H) (Found: C, 69.7; H, 5.8. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.1%).

Wolff–Kishner Reduction of the Keto-acid (9).—A solution of the keto-acid (9) (2 g) in butane-1,4-diol (20 ml) containing sodium hydroxide (1 g), hydrazine hydrate (85%; 1 ml), and water (1 ml) was heated to reflux for 6 h. The reaction mixture was then heated slowly, without using a condenser, until the temperature rose to 200 °C. The cooled solution was poured into a mixture of concentrated hydrochloric acid (5 ml) and ice (50 g) and the precipitated acid (1.57 g, 82%), m.p. 114—115 °C (from benzene–hexane) was identified (mixed m.p.) as the *acid* (4) obtained according to Scheme 1.

p-*Methoxy*-α-p-*methoxyphenylcinnamaldehyde* (11a).—(a) *By Vilsmeier reaction from deoxydihydroanisoin* (10). To a solution of (10) (2.6 g) in dimethylformamide (20 g) was added phosphorus oxychloride (9 g) dropwise with stirring and the reaction mixture was heated at 100 °C for 14 h. The iminium complex was decomposed with aqueous sodium acetate [27 g in water (70 ml)] and the product was extracted with ether (3 × 30 ml). Removal of the solvent afforded the *aldehyde* (11a) (2.65 g, 98%), m.p. 120 °C (from benzene–hexane); $\nu_{max.}$ (Nujol) 2 850 (*H*–*C*=O) and 1 675 cm^{-1} (H–*C*=*O*); $\lambda_{max.}$ (ethanol) 233 (log ε 4.25) and 323 nm (4.27); δ ($CDCl_3$) 3.73 (3 H, s, α-aryl OCH_3), 3.80 (3 H, s, β-aryl OCH_3), 6.63—7.23 (9 H, m, 8 × ArH and vinylic H), and 9.63 (1 H, s, CHO) (Found: C, 75.9; H, 6.2. $C_{17}H_{16}O_3$ requires C, 76.0; H, 6.0%).

(b) *By tin*(II) *chloride reduction of* p-*methoxy*-α-p-*methoxyphenylcinnamonitrile* (11b). To a well stirred mixture of *p*-methoxyphenylacetonitrile (5.4 g) and *p*-anisaldehyde (5.2 g) was added dropwise a solution of sodium ethoxide in ethanol (20%; 5 ml). The reaction mixture was heated on a boiling water-bath and stirred for 1 h, then diluted with water. The solid was filtered off to afford the *cinnamonitrile* (11b) (9 g, 92%), m.p. 108—109 °C (from ethanol); $\nu_{max.}$ (Nujol) 2 225 cm^{-1} (conj. C≡N); $\lambda_{max.}$ (ethanol) 234 (log ε 4.24) and 335 nm (4.33); δ (CCl_4) 3.80 (3 H, s, α-aryl OCH_3), 3.83 (3 H, s, β-aryl OCH_3), 6.85 (2 H, d, *J* 8.5 Hz, α-aryl H-3 and H-5), 6.88 (2 H, d, *J* 8.5 Hz, β-aryl H-3 and H-5), 7.30 (1 H, s, vinylic *H*), 7.53 (2 H, d, *J* 8.5 Hz, α-aryl H-2 and H-6), and 7.80 (2 H, d, *J* 8.5 Hz, β-aryl H-2 and H-6) (Found: C, 76.8; H, 5.5; N, 5.3. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%). Finely powdered anhydrous tin(II) chloride (5 g) was suspended in dry ether and dry hydrogen chloride gas was passed through the suspension till saturation, when two layers separated. The cinnamonitrile (11b) (2 g) was added with vigorous stirring and the stirring was continued for 6 h. The reaction mixture was left overnight. The salt formed was filtered off and hydrolysed with warm water and the liberated cinnamaldehyde was extracted with ether (2 × 30 ml). Removal of solvent gave the *cinnamaldehyde* (11a) (0.425 g, 21%), identical with the specimen obtained from Vilsmeier reaction of (10).

4,5-*Bis*-p-*methoxyphenylpenta*-2,4-*dienoic acid* (12).—A solution of the cinnamaldehyde (11a) (2 g), malonic acid (4 g), and piperidine (3 drops) in pyridine (4 ml) was heated on a steam-bath for 10 h and then refluxed for 4 h. The reaction mixture was cooled and poured into ice (80 g) and concentrated hydrochloric acid (20 ml). The ether extract (3 × 40 ml) was shaken with aqueous sodium hydrogencarbonate (10% w/v; 3 × 25 ml). Neutralization of the aqueous layer with dilute hydrochloric acid, followed by re-extraction with ether (3 × 30 ml) and usual work-up of the ethereal extract gave the *dienoic acid* (12) (0.463 g, 20%) as a viscous gum (*EZ*-mixture); $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1} (acid C=O); δ ($CDCl_3$) 3.77 (6 H, 2 peaks, 2 × OCH_3), 6.6—7.8 (11 H, m, 8 × ArH and 3 × vinylic H), and 9.0 (1 H, broad hump, CO_2H) (Found: C, 74.0; H, 6.2. $C_{19}H_{18}O_4$ requires C, 73.5; H, 5.9%).

Nickel–Aluminium Alloy Reduction of (12).—A solution of the dienoic acid (12) (350 mg) in aqueous sodium hydroxide (10% w/v; 30 ml) was treated at 80 °C with nickel–aluminium alloy powder (4 g) in small portions under vigorous but controlled stirring to avoid frothing over. After completion of addition, heating was continued at 80 °C for 2 h. The metallic powder was filtered off and the filtrate neutralized with dilute hydrochloric acid to liberate the reduced acid (223 mg, 63%), m.p. 116 °C (from ethanol), identified (mixed m.p.) as the acid (4) obtained according to Scheme 1.

7-*Methoxy*-4-p-*methoxybenzyl*-3,4-*dihydronaphthalen*-1(2H)-*one* (13b).—The pentanoic acid (4) (1.5 g) was stirred with polyphosphoric acid [from phosphorus pentaoxide (16 g) and phosphoric acid (10 ml)] at 85 °C for 1½ h. The reaction mixture was decomposed with crushed ice and the product was extracted with ether (2 × 40 ml). Usual processing of the ethereal extract gave the *tetralone* (13b) (1.19 g, 84%), m.p. 93—94 °C (from carbon tetrachloride); $\nu_{max.}$ (Nujol) 1 680 (C=O) and 1 610 cm^{-1} (C=C); δ (CCl_4) 1.53—2.23 (2 H, m, 2 × H-3), 2.27—3.2 (5 H, m, 2 × H-2, H-4, and benzylic CH_2), 3.78 (3 H, s, OCH_3), 3.83 (3 H, s, OCH_3), 6.77 (2 H, d, *J* 9 Hz, H-3′ and H-5′), 7.0br (2 H, s, H-5 and H-6), 7.03 (2 H, d, *J* 9 Hz, H-2′ and H-6′), and 7.47br (1 H, s, H-8) (Found: C, 76.7; H, 6.9. $C_{19}H_{20}O_3$ requires C, 77.0; H, 6.8%).

7-*Methoxy*-4-p-*methoxybenzyl*-1,2,3,4-*tetrahydro*-1-*naphthol* (14b).—Sodium borohydride (70 mg) was added to a solution of the dimethoxytetralone (13b) (1 g) in ethanol (15 ml)

and the reaction mixture was left overnight. Most of the ethanol was distilled off *in vacuo*, the residue was poured into water (15 ml), and the product was extracted with ether (3 × 25 ml). Usual processing of the ethereal extract gave the *dimethoxytetralol* (14b) (0.976 g, 97%), m.p. 100—101 °C (from benzene–hexane); $\nu_{max.}$ (Nujol) 3 420 cm^{-1} (OH); δ ($CDCl_3$) 1.68 and 1.8—2.0 (5 H, 2 m, OH, 2 × H-2 and 2 × H-3), 2.56—2.7 and 2.8—3.10 (3 H, 2 m, H-4 and benzylic CH_2), 3.80 and 3.81 (6 H, 2 s, 2 × OCH_3), 4.70 (1 H, t, *J* 6.5 Hz, *H*COH), 6.81 (1 H, dd, *J* 9 and 3 Hz, H-6), 6.84 (2 H, dd, *J* 9 Hz, H-3′ and H-5′), 7.04 (1 H, d, *J* 3 Hz, H-8), 7.10 (2 H, dd, *J* 9 Hz, H-2′ and H-6′), and 7.17 (1 H, d, *J* 9 Hz, H-5) (Found: C, 76.1; H, 7.6. $C_{19}H_{22}O_3$ requires C, 76.5; H, 7.4%).

6-*Methoxy*-1-p-*methoxybenzyl*-1,2-*dihydronaphthalene* (*Di-O-methylsequirin D*) (1b).—A solution of the dimethoxytetralol (14b) (0.8 g) in benzene (20 ml) was heated to reflux with toluene-*p*-sulphonic acid (*ca.* 10 mg) for 12 h. The solution was washed with aqueous sodium hydrogencarbonate (10% w/v; 20 ml). The solvent was removed and the residue purified by preparative t.l.c. (silica gel, benzene) to afford di-*O*-methylsequirin D (1b) (0.66 g, 92%), m.p. 108—109 °C (from n-hexane) (lit.,[1,4] 107.5—109 °C), $\nu_{max.}$ (Nujol) 1 605 cm^{-1} (C=C); $\lambda_{max.}$ (ethanol) 230 (log ε, 4.36) and 265 nm (3.61); δ ($CDCl_3$) 2.26 (2 H, m, allylic CH_2), 2.55—2.83 (3 H, m, benzylic CH_2 and H-1), 3.79 (6 H, s, 2 × OCH_3), 5.9 (1 H, m, vinylic H-3), 6.44br (1 H, d, *J* 11 Hz, vinylic H-4), 6.5—6.9 (3 H, m, H-5, H-7, and H-8), 6.73 (2 H, d, *J* 9 Hz, H-3′ and H-5′), and 6.95 (2 H, d, *J* 9 Hz, H-2′ and H-6′) (Found: C, 81.0; H, 7.2. $C_{19}H_{20}O_2$ requires C, 81.4; H, 7.2%).

5-p-*Hydroxybenzyl*-5,6-*dihydro*-2-*naphthol* [(±)-*Sequirin D* (1a)].—A mixture of di-*O*-methylsequirin D (1b) (0.3 g) and pyridine hydrochloride (3 g) was heated to reflux for 2 h under nitrogen. After cooling to room temperature, the reaction mixture was diluted with water (10 ml) and extracted with ether (3 × 20 ml). Removal of solvent from the extract furnished the demethylated product which was purified by t.l.c. to afford *sequirin D* (1a) (0.224 g, 83%), m.p. 184—185 °C (from aqueous methanol); $\nu_{max.}$ (Nujol) 3 380 cm^{-1} (OH); $\lambda_{max.}$ (ethanol) 230 (log ε 4.60), 266 (3.86), and 275 nm (3.89); δ [$CDCl_3$ + $(CD_3)_2SO$] 2.20 (2 H, m, allylic CH_2), 2.62 (3 H, m, benzylic CH_2 and H-5), 5.82 (1 H, m, vinylic H-7), 6.31br (1 H, d, *J* 10 Hz, vinylic H-8), and 6.34—6.9 (7 H, m, 7 × ArH) (Found: C, 81.2; H, 6.6. $C_{17}H_{16}O_2$ requires C, 80.9; H, 6.4%).

7-*Hydroxy*-4-p-*Hydroxybenzyl*-3,4-*dihydronaphthalen*-1(2H)-*one* (13a).—A mixture of the dimethoxytetralone (13b) (1 g), hydrobromic acid (48%; 18 ml), and glacial acetic acid (30 ml) was heated to reflux for 6 h. The reaction mixture was concentrated *in vacuo* to remove most of the acetic acid and the residue was diluted with water (40 ml). The product was extracted with ethyl acetate (2 × 30 ml) and the extract was worked up to afford the *dihydroxytetralone* (13a) (0.688 g, 76%), m.p. 200—202 °C (from ethyl acetate–hexane); $\nu_{max.}$ (Nujol) 3 300 (OH) and 1 665 cm^{-1} (C=O); δ [$CDCl_3$–$(CD_3)_2SO$] 2.01 (2 H, m, 2 × H-3), 2.53 (2 H, m, 2 × H-2), 2.8—3.1 (3 H, m, benzylic CH_2 and H-4), 6.73—7.23 (6 H, m, 6 × ArH), 7.5br (1 H, s, H-8), and 9.0br (2 H, 2 × OH) (Found: C, 75.6; H, 6.4. $C_{17}H_{16}O_3$ requires C, 76.1; H, 6.0%).

7-*Hydroxy*-4-p-*hydroxybenzyl*-1,2,3,4-*tetrahydro*-1-*naphthol* (14a).—Reduction of the dihydroxytetralone (13a) (0.4 g) with sodium borohydride (30 mg) as described for (13b) gave the *dihydroxytetralol* (14a) (0.363 g, 90%), m.p. 210 °C (from ethyl acetate–hexane); $\nu_{max.}$ 3 100—3 300 cm^{-1} (br, O*H*); δ [$(CD_3)_2SO$] 1.52br (2 H, s, 2 × H-3), 1.73br (2 H, s, 2 × H-2), 2.74—2.88 (3 H, m, benzylic CH_2 and H-4), 4.4 (1 H, m, *H*COH), 6.01 (1 H, d, *J* 6 Hz, HCO*H*), 6.57 (1 H, dd, *J* 8.5 and 2 Hz, H-6), 6.69 (2 H, d, *J* 8.5 Hz, H-3′ and H-5′), 6.87 (1 H, d, *J* 2 Hz, H-8), 7.02 (3 H, d, *J* 8.5 Hz, H-5, H-2′, and H-6′), and 9.09br and 9.19br (2 H, 2s, 2 × OH) (Found: C, 75.5; H, 6.7. $C_{17}H_{18}O_3$ requires C, 75.5; H, 6.7%).

Dehydration of the Dihydroxytetralol (14a).—Phosphorus oxychloride (1 ml) was added to a cooled and stirred solution of the dihydroxytetralol (14a) (200 mg) in pyridine (5 ml). The mixture was stirred for 4 h, poured onto crushed ice, and the product was extracted with ether (2 × 25 ml). Removal of the solvent followed by preparative t.l.c. (ethyl acetate–hexane; 3 : 7 v/v) afforded sequirin D (1a) (32 mg, 17%), identical (m.p. and mixed m.p.) with the specimen obtained from (1b) by demethylation.

One of us (M. P. R.) thanks the Council of Scientific and Industrial Research, New Delhi, for the award of a research fellowship.

[1/359 *Received*, 3rd *March*, 1981]

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