Structure and Synthesis of Gymnopusin, a Novel Phenanthrenediol from the Orchid *Bulbophyllum gymnopus*

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By the synthesis of 5,6,7-trimethoxyphenanthrene-2,10-diol (**14**) the structure originally proposed for gymnopusin is shown to be erroneous. Reinterpretation of the spectroscopic data for gymnopusin led to the proposal of a revised structure 3,4,9-trimethoxyphenanthrene-2,7-diol (**31**) which was confirmed by synthesis. The key step in the synthesis of these 9(10)-oxygenated phenanthrenes was a Pummerer rearrangement.

In continuation of our interest in the synthesis of phenanthrenoid natural products [1] we were attracted to the synthesis of gymnopusin, a phenanthrenediol recently isolated from the Indian orchid *Bulbophyllum gymnopus*.[2] This compound was assigned structure (**14**) (Scheme 1) by Majumder and Banerjee [2] on the grounds of its spectroscopic properties and those of its diacetate and its di-*O*-methyl ether. It is the first naturally occurring phenanthrene with an oxygen substituent at the 9(10)-position.

Our synthetic strategy for gymnopusin (**14**) depended on the Pummerer rearrangement and subsequent cyclization of the β-oxo sulphoxide (**11**).[3] In order to synthesize this biphenyl derivative we commenced with the acetoxy compound (**1**) which on bromination smoothly afforded one bromo compound assigned structure (**2**) since on hydrolysis it furnished the known bromophenol (**3**).[4,5] This compound on isopropylation furnished the ether (**4**) which was caused to react with copper(I) cyanide thereby supplying the nitrile (**5**). Hydrolysis of the nitrile (**5**) gave the carboxylic acid (**6**) which was converted into the oxazoline (**7**) by the standard method.[6] The oxazoline (**7**) was allowed to react with the Grignard reagent derived from 1-bromo-2,3,4-trimethoxybenzene.[7] In this reaction the methoxy group in the position *ortho* to the oxazoline ring was displaced [6] and a good yield of the biphenyl (**8**) was secured. Deprotection of this last-mentioned compound afforded the carboxylic acid (**9**) which was converted into its methyl ester (**10**). Treatment of this compound with sodium methylsulphinylmethanide afforded the β-oxo sulphoxide (**11**) which on treatment with trifluoroacetic anhydride underwent Pummerer rearrangement and cyclization to give the phenanthrol (**12**). This compound was not isolated but was immediately treated with an excess of W-2 Raney nickel in ethanol at room temperature. This reaction achieved smooth desulphurization and yielded the phenanthrol (**13**). This compound was deisopropylated by brief reaction with boron trichloride and gave the phenanthrenediol (**14**). This compound and its diacetate (**15**) had different spectroscopic properties and melting points to those reported for gymnopusin and its diacetate.[2] However the di-*O*-methyl ether (**16**) had identical spectroscopic properties to those recorded for di-*O*-methylgymnopusin so that the structure (**16**) is correct.

We now considered alternative structures for gymnopusin. In the ^{1}H n.m.r. spectrum of gymnopusin the signals for the 8- and 9-protons were assigned by Majumder and Banerjee to two singlets at δ 6.94 and 7.08 which are shifted to δ 6.86 and 7.26 in the diacetate. We reasoned that these data could be explained by structure (**18**), or by structure (**31**) (Scheme 3) if these assignments were reversed.

Methylation of the phenanthrol (**13**) gave the methyl ether (**17**). We expected that treatment of this compound with boron trichloride would cause deisopropylation and demethylation of the methoxy group at the 6-position since this is the most sterically hindered.[8] Treatment of compound (**17**) with boron trichloride gave a mixture of two products which was acetylated and separated by radial chromatography. One product proved to be a diacetate and it was assigned structure (**19**) by the use of n.O.e. difference spectroscopy. This technique showed strong interactions between methoxy groups and the 4-, 8-, and 9-protons as expected for structure (**19**). The spectroscopic properties and melting point of this compound, however, were different from those of gymnopusin diacetate. The other product isolated proved to be a triacetate and this was assigned structure (**20**) since n.O.e. difference spectroscopy showed strong interactions between methoxy groups and the 8- and 9-protons.

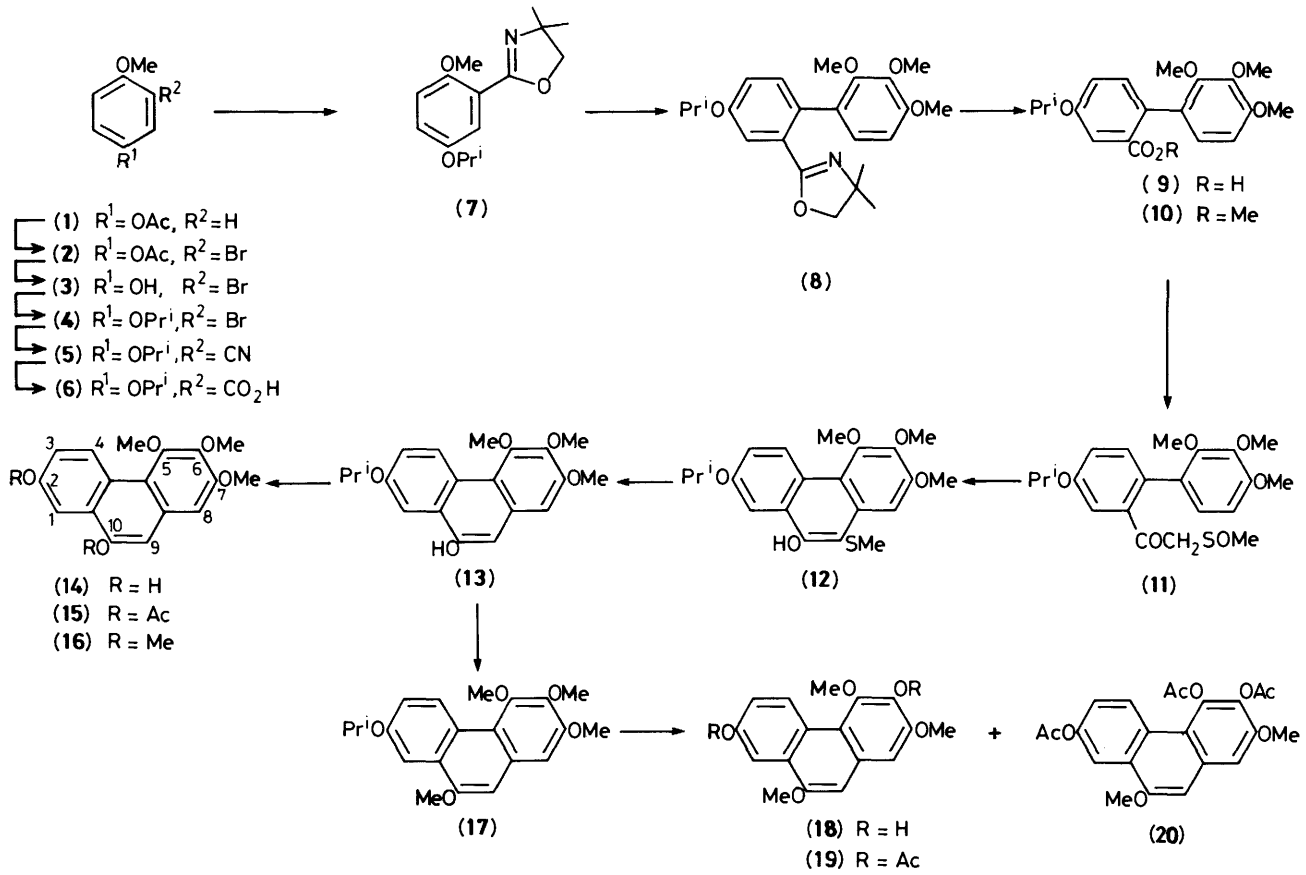
In order to synthesize compound (**31**) we required 1-bromo-4-isopropoxy-2,3-dimethoxybenzene (**24**) (Scheme 2). This compound has been synthesized by bromination of 1-isopropoxy-2,3-dimethoxybenzene and separation of the two isomers thereby produced.[9] In an attempt to simplify this synthesis we investigated the bromination of the acetate (**21**). This reaction produced only one bromo compound which was assigned structure (**22**) by comparison with an authentic sample obtained by acetylation of the bromophenol (**23**).[9]

The synthesis of the phenanthrol (**29**) now followed closely the previous method and proceeded *via* the intermediates (**25**)—(**28**). Methylation of compound (**29**) gave the methyl ether (**30**) which on treatment with boron trichloride underwent deisopropylation and provided the diol (**31**). This compound proved to be identical with an authentic sample of gymnopusin by all the usual criteria so that gymnopusin possesses structure (**31**).

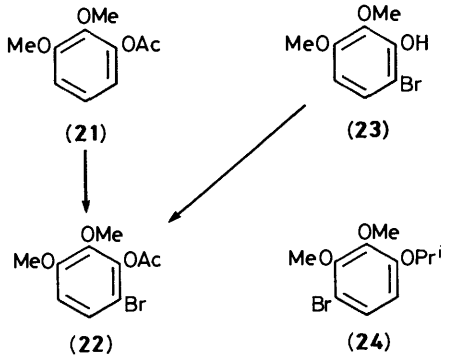
Experimental

General directions have been given previously.[9]

3-Bromo-4-methoxyphenyl Acetate (**2**).—A solution of bromine (38.0 g) in acetic acid (70 ml) was added dropwise with stirring to a solution of 1-acetoxy-4-methoxybenzene (**1**) (33.0 g) in acetic acid (70 ml) containing anhydrous sodium acetate (31.0 g). After 18 h a further quantity of bromine (3.0 g) in acetic acid (10 ml) was added and the whole was stirred for a further 18 h. The mixture was poured into water and the crude product was isolated by extraction with ethyl acetate. The extract was washed in turn with water, saturated sodium hydrogen carbonate solution, and finally with saturated brine. The crude product was distilled under diminished pressure and was obtained as an oil (45.3 g, 93%), b.p. 115 °C at 0.03 mmHg,



Scheme 1.



Scheme 2.

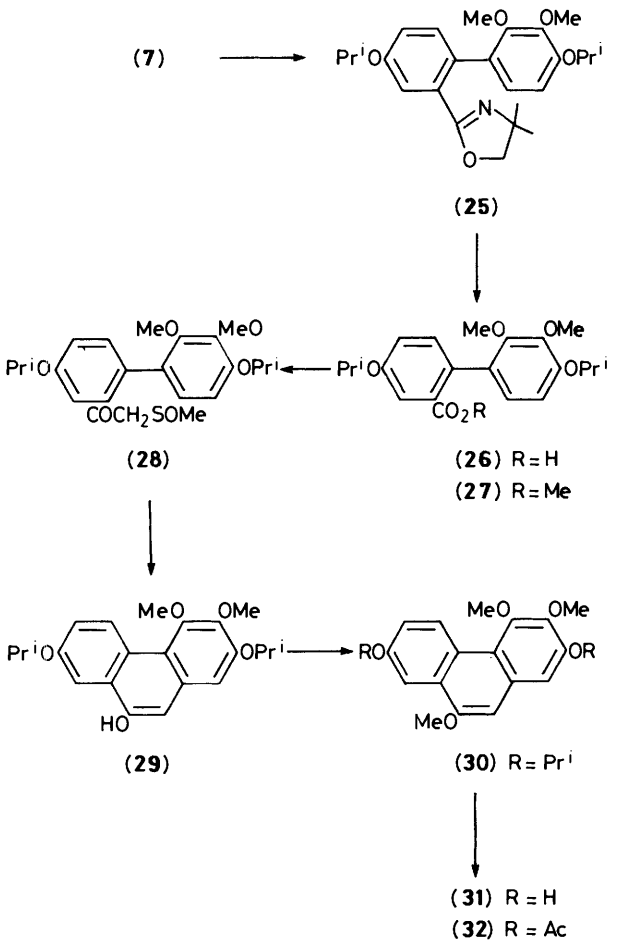
which eventually solidifed to give *compound* (**2**) as needles (from dichloromethane–light petroleum), m.p. 51—52 °C (Found: C, 44.25; H, 3.65; Br, 32.75%; M^+, 244/246. $C_9H_9BrO_3$ requires C, 44.1; H, 3.7; Br, 32.6%; *M*, 244/246); δ_H(80 MHz) 2.26 (3 H, s, OAc), 3.86 (3 H, s, OMe), 6.95 (2 H, m, ArH), and 7.31 (1 H, m, ArH).

3-*Bromo*-4-*methoxyphenol* (**3**).—A solution of potassium hydroxide (11.8 g) in water (100 ml) was added dropwise to a stirred solution of the foregoing acetate (**2**) (48.6 g) in methanol (750 ml) under an atmosphere of argon. The solution was stirred at room temperature for 45 min and then diluted with water and acidified. The crude phenol (**3**) was isolated by extraction with dichloromethane. It formed cubes (38.7 g, 96%) from benzene, m.p. 76—77 °C (lit.,[4,5] 77—78 °C, 74—76 °C).

3-*Bromo*-4-*methoxyphenyl Isopropyl Ether* (**4**).—The foregoing phenol (**3**) (38.7 g), anhydrous potassium carbonate (43.0 g), and 2-bromopropane (23.3 ml) were stirred together in *N*,*N*-dimethylformamide (DMF) (190 ml) under an argon atmosphere for 18 h. The mixture was next poured into water and the crude product was isolated with ethyl acetate in the usual way. The *ether* (**4**) (38.8 g, 83%) was isolated as an oil, b.p. 100 °C at 0.55 mmHg (Found: C, 48.95; H, 5.4; Br, 32.95%; M^+, 244/246. $C_{10}H_{13}BrO_2$ requires C, 49.0; H, 5.35; Br, 32.6%; *M*, 244/246); δ_H(80 MHz) 1.28 (6 H, d, 2 × Me), 3.81 (3 H, s, OMe), 4.39 (1 H, septet, CH), 6.79 (2 H, m, ArH), and 7.11 (1 H, m, ArH).

3-*Cyano*-4-*methoxyphenyl Isopropyl Ether* (**5**).—A solution of the foregoing bromo compound (**4**) (29.0 g) in anhydrous DMF (180 ml) was heated and stirred under reflux with copper(I) cyanide (15.9 g) under an atmosphere of argon for 4 h. The cooled reaction mixture was poured into an excess of aqueous ethylenediamine and the crude product was isolated by extraction with ethyl acetate. The *ether* (**5**) was distilled under reduced pressure and was obtained as an oil (21.8 g, 96%), b.p. 75 °C at 0.02 mm Hg (Found: C, 69.0; H, 6.6%; M^+, 191. $C_{11}H_{13}NO_2$ requires C, 69.1; H, 6.85%; *M*, 191); δ_H(300 MHz) 1.30 (6 H, d, 2 × Me), 3.87 (3 H, s, OMe), 4.42 (1 H, septet, CH), and 6.90—7.09 (3 H, m, ArH); $\nu_{max.}$(film) 2 220 cm^{-1}.

3-(4,5-*Dihydro*-4,4-*dimethyloxazol*-2-*yl*)-4-*methoxyphenyl Isopropyl Ether* (**7**).—The foregoing nitrile (**5**) (25.8 g) was boiled under reflux with potassium hydroxide (38.0 g), water (100 ml), and methanol (500 ml) for 6.5 days. The bulk of the methanol was removed by distillation and the residue was diluted with water and next extracted with ether; this extract was discarded. The aqueous phase was acidified and the crude acid was isolated by extraction with ethyl acetate. The oily acid



Scheme 3.

(**6**) (25.1 g), so obtained, was stirred in tetrachloromethane (120 ml) with thionyl chloride (29.0 ml) for 18 h. The solvent and excess thionyl chloride were removed *in vacuo*, finally by azeotroping with benzene. The crude acid chloride, so obtained, was stirred with 2-amino-2-methylpropan-1-ol (34.3 g) in tetrachloromethane (120 ml) for 5 h. The precipitate was filtered off and washed with a little tetrachloromethane. The filtrate was washed with water and with saturated brine. The oily amide (32.8 g), so obtained, was stirred with thionyl chloride (85 ml) in tetrachloromethane (140 ml) for 3 h and then poured onto ice. The organic phase was washed with water and the aqueous washings were basified and extracted with dichloromethane. The *oxazoline* (**7**) (25.4 g, 82%) was obtained as an oil, b.p. 135 °C at 0.15 mmHg (Found: C, 68.55; H, 8.15%; M^+, 263. $C_{15}H_{21}NO_3$ requires C, 68.4; H, 8.05%; M^+, 263); δ_H(80 MHz) 1.26 (6 H, d, Me_2CH), 1.36 (6 H, s, Me_2), 3.78 (3 H, s, OMe), 4.04 (2 H, s, CH_2), 4.43 (1 H, septet, CH), 6.87 (2 H, m, ArH), and 7.30 (1 H, m, ArH).

3-(4,5-*Dihydro*-4,4-*dimethyloxazol*-2-*yl*)-4-(2,3,4-*trimethoxyphenyl*)*phenyl Isopropyl Ether* (**8**).—The Grignard reagent was prepared in the usual way from 1-bromo-2,3,4-trimethoxybenzene[7] (13.6 g), magnesium (1.5 g), and dry tetrahydrofuran (THF) (70 ml) under argon. This was added dropwise to a solution of the foregoing oxazoline (**7**) (14.15 g) in dry THF (80 ml) and the mixture was stirred at room temperature for 2 h and then heated under reflux for 2 h. A further quantity of Grignard reagent prepared from the bromo compound (6.2 g) was next added to the cooled solution which was stirred at room temperature for 2 h and then heated under reflux for 2 h. The cooled solution was poured into water and the crude product was extracted with ethyl acetate and the oxazoline was isolated in acid in the usual way. The crude product was purified by radial chromatography with 30% ethyl acetate–light petroleum as eluant. The *oxazoline* (**8**) (13.2 g, 61%) formed prisms (from di-isopropyl ether–light petroleum), m.p. 71—73 °C (Found: C, 69.05; H, 7.6; N, 3.65. $C_{23}H_{29}NO_5$ requires C, 69.15; H, 7.3; N, 3.5%); δ_H(80 MHz) 1.27 (6 H, s, Me_2), 1.35 (6 H, d, Me_2CH), 3.80 (2 H, s, CH_2), 3.53, 3.88, and 3.90 (each 3 H, s, OMe), 4.64 (1 H, septet, CH), 6.66 and 6.92 (2 H, AB, $J_{5',6'}$ 8.5 Hz, 5'- and 6'-H), and 6.92—7.38 (3 H, m, 2-, 5-, and 6-H).

3-*Carboxy*-4-(2',3',4'-*trimethoxyphenyl*)*phenyl Isopropyl Ether* (**9**).—A solution of the foregoing oxazoline (**8**) (13.2 g) and iodomethane (18.0 ml) in nitromethane (40 ml) was stirred and heated at 70 °C for 22 h. The solvents were removed under reduced pressure and the resultant methiodide was stirred and heated under reflux with methanol (370 ml) and aqueous potassium hydroxide (20%; 370 ml) for 44 h. The cooled reaction mixture was extracted with ether and this extract was discarded. The aqueous phase was acidified and the crude acid was isolated by extraction with ethyl acetate. The *biphenylcarboxylic acid* (**9**) (9.5 g, 83%) crystallized from di-isopropyl ether–light petroleum as prisms, m.p. 119—120 °C (Found: C, 65.8; H, 6.7%; M^+, 346. $C_{19}H_{22}O_6$ requires C, 65.9; H, 6.4%; *M*, 346).

The *methyl ester* (**10**) (95%) (iodomethane–potassium carbonate–DMF–room temperature) formed prisms (from dichloromethane–light petroleum), m.p. 82 °C (Found: C, 66.9; H, 7.05%; M^+, 360. $C_{20}H_{24}O_6$ requires C, 66.65; H, 6.7%; *M*, 360); δ_H(300 MHz) 1.35 (6 H, d, 2 × Me), 3.53, 3.65, 3.86, and 3.88 (each 3 H, s, OMe), 4.61 (1 H, septet, CH), 6.70 and 6.90 (2 H, AB, $J_{5',6'}$ 8.55 Hz, 5'- and 6'-H), 7.03 (1 H, dd, $J_{6,2}$ 2.7 Hz, $J_{6,5}$ 8.5 Hz, 6-H), 7.22 (1 H, d, $J_{5,6}$ 8.5 Hz, 5-H), and 7.40 (1 H, d, $J_{2,6}$ 2.7 Hz, 2-H); $\nu_{max.}$(KBr) 1 725 cm^{-1}.

3-*Methylsulphinylacetoxy*-4-(2',3',4'-*trimethoxyphenyl*)-*phenyl Isopropyl Ether* (**11**).—Sodium hydride in oil (55%; 1.0 g) was washed under argon with pentane and then anhydrous dimethyl sulphoxide (10 ml) was added. The stirred mixture was heated at 70 °C (bath) under argon for 1 h. It was then cooled to 0 °C and anhydrous THF (15 ml) was added followed by the dropwise addition of a solution of the foregoing ester (**10**) (3.17 g) in THF (15 ml). The solution was stirred at room temperature for 1 h and next diluted with a slight excess of cold dilute hydrochloric acid. The crude *sulphoxide* (**11**), isolated by extraction with dichloromethane and work-up, crystallized from dichloromethane–light petroleum as needles (2.78 g, 77%), m.p. 101—102 °C (Found: C, 62.0; H, 6.65; S, 7.95%; M^+, 406. $C_{21}H_{26}O_6$ requires C, 62.05; H, 6.45; S, 7.9%; *M*, 406); δ_H(80 MHz) 1.38 (6 H, d, 2 × Me), 2.66 (3 H, s, Me), 3.51 (2 H, s, CH_2), 3.90 (9 H, s, 3 × OMe), 4.63 (1 H, septet, CH), 6.77 and 6.99 (2 H, AB, $J_{5',6'}$ 8.6 Hz, 5'- and 6'-H), and 6.99—7.32 (3 H, m, ArH); $\nu_{max.}$(KBr) 1 690 and 1 040 cm^{-1}.

2-*Isopropoxy*-5,6,7-*trimethoxyphenanthren*-10-*ol* (**13**).—A solution of the sulphoxide (**11**) (1.0 g) in dichloromethane (15 ml) was treated with trifluoroacetic anhydride (378 μl) and then stirred at room temperature for 15 min. After this it was poured into water and the crude product (**12**) was isolated by extraction with dichloromethane. The extract was washed in turn with water, saturated aqueous sodium hydrogen carbonate and finally with saturated brine. A solution of the crude product in ethanol (100 ml) was stirred at room temperature with W-2 Raney nickel (5.0 g) for 30 min. The nickel was separated by filtration through Celite and the cake was washed with ethanol. The solvent was removed from the filtrate and the residue was

purified by radial chromatography with 20% ethyl acetate–light petroleum as eluant. The *phenanthrol* (**13**) (589 mg, 70%) crystallized from dichloromethane–light petroleum as prisms, *m.p. 170—172* °C (Found: C, 70.55; H, 6.7%; M^+, 342. $C_{20}H_{22}O_5$ requires C, 70.15; H, 6.5%; *M*, 342); δ_H(80 MHz) 1.39 (6 H, d, 2 × Me), 3.82 (3 H, s, OMe), 4.00 (6 H, s, 2 × OMe), 4.76 (1 H, septet, CH), 6.66 (1 H, s, 8- or 9-H), 6.78 (1 H, s, 8- or 9-H), 7.26 (1 H, dd, $J_{3,4}$ 9.4, $J_{3,1}$ 2.8 Hz, 3-H), 7.77 (1 H, d, $J_{1,3}$ 2.8 Hz, 1-H), and 9.40 (1 H, d, $J_{4,3}$ 9.4 Hz, 4-H).

5,6,7-*Trimethoxyphenanthrene*-2,10-*diol* (**14**).—A solution of boron trichloride (290 mg) in dichloromethane (1.0 ml) was added at −10 °C to a stirred solution of the foregoing phenanthrol (**13**) (400 mg) in dichloromethane (15 ml). The solution was stirred at −10 °C for 0.5 h and then poured into water. The crude product was isolated by extraction with dichloromethane and next subjected to radial chromatography with 40% ethyl acetate–light petroleum as eluant. The *diol* (**14**) (274 mg, 78%) crystallized from chloroform–light petroleum as needles, m.p. 178—180 °C (Found: C, 67.8; H, 5.45. $C_{17}H_{16}O_5$ requires C, 68.0; H, 5.35%); δ_H[80 MHz; $CDCl_3$, $(CD_3)_2SO$], 3.95, 3.96, and 3.97 (each 3 H, s, OMe), 5.82 (2 H, b, OH), 6.87 (1 H, s, 8-H), 6.93 (1 H, s, 9-H), 7.11 (1 H, dd, $J_{3,4}$ 9.3 Hz, $J_{3,1}$ 2.8 Hz, 3-H), 7.73 (1 H, d, $J_{1,3}$ 2.8 Hz, 1-H), and 9.29 (1 H, d, $J_{4,3}$ 9.3 Hz, 4-H); δ_C[75.5 MHz; $CDCl_3$, $(CD_3)_2SO$] 55.72 (6-OMe), 60.09 and 61.20 (each OMe), 103.45, 105.86, and 106.24 (each Ar*C*H), 114.56 (ArC), 117.28 (Ar*C*H), 124.59 and 127.73 (each ArC), 128.17 (Ar*C*H), 129.88, 140.22, 150.32, 151.52, 151.58, and 154.64 (each ArC); *m/z* 301 (19%), 300 (M^+, 100), 286 (13), 285(60), 257 (21), 242 (63), 213 (13), 199 (18), 171 (32), and 150 (20); $\lambda_{max.}$(MeOH) 213, 229, 255, 261, 271infl, 286, 343, and 360 nm (log ε 4.25, 4.24, 4.68, 4.69, 4.49, 4.20, 3.37, and 3.40 respectively); $\nu_{max.}$(KBr) 3 420, 1 612, 1 578, 1 212, 1 090, 840, 825 cm^{-1}.

The *diacetate* (**15**) formed needles (from dichloromethane–light petroleum), m.p. 103—103.5 °C (Found: C, 66.0; H, 5.55%; M^+, 384. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.25%; *M*, 384); δ_H(300 MHz) 2.35 and 2.46 (each 3 H, s, MeCO), 3.93 (3 H, s, OMe), 4.00 (6 H, s, 2 × OMe), 7.01 (1 H, s, 8-H), 7.41 (1 H, dd, $J_{3,4}$ 9.35, $J_{3,1}$ 2.54 Hz, 3-H), 7.45 (1 H, s, 9-H), 7.65 (1 H, d, $J_{1,3}$ 2.54 Hz, 1-H), and 9.59 (1 H, d, $J_{4,3}$ 9.35 Hz, 4-H); δ_C(75.5 Hz) 21.13 and 21.22 (each CO*Me*), 55.82 (6-OMe), 60.34 and 61.26 (each OMe), 105.22 and 112.92 (each Ar*C*H), 117.30 (ArC), 118.37 and 121.50 (each Ar*C*H), 127.08 (ArC), 128.64 (Ar*C*H), 129.06, 129.08, 142.85, 144.07, 148.45, 152.14, and 152.81 (each ArC), and 169.24 and 169.52 (each C=O); $\lambda_{max.}$(MeOH) 222, 260, 287infl, 306, 340, and 356 nm (log ε 4.41, 4.86, 4.20, 3.99, 2.15, and 3.03 respectively); $\nu_{max.}$(KBr) 1 770, 1 615, 1 497, 855, and 830 cm^{-1}.

The *dimethyl ether* (**16**) formed prisms (from dichloromethane–light petroleum), m.p. 130—130.5 °C (lit.,[2] 122 °C) (Found: C, 69.3; H, 6.45. $C_{19}H_{20}O_5$ requires C, 69.5; H, 6.15%); δ_H(80 MHz) 3.95 and 3.96 (each 3 H, s, OMe), 3.99 (6 H, s, 2 × OMe), and 4.03 (3 H, s, OMe), 6.86 and 6.96 (each 1 H, s, 8- and 9-H), 7.26 (1 H, dd, $J_{3,4}$ 9.4, $J_{3,1}$ 2.9 Hz, 3-H), 7.73 (1 H, d, $J_{1,3}$ 2.9 Hz, 1-H), and 9.40 (1 H, d, $J_{4,3}$ 9.4 Hz, 4-H); δ_C(20.1 MHz) 55.11 (2 × OMe), 55.62, 60.01, and 61.04 (each OMe), 102.51 (2 × ArC), 104.22 (Ar*C*H), 114.86 (ArC), 117.17 (Ar*C*H), 125.18 and 127.43 (ArC), 128.16 (Ar*C*H), 129.60, 140.97, 151.79, 151.97, 152.81, and 157.25 (each ArC); *m/z* 329 (20%), 328 (M^+, 100), 313 (60), 285 (16), 270 (66), 255 (22), 227 (28), 199 (25), 184 (10), 164 (19), 156 (10), and 135 (19); $\lambda_{max.}$(MeOH) 213, 230, 259, 270infl, 283, 308infl, 339, and 355 nm (log ε 4.26, 4.31, 4.80, 4.62, 4.26, 3.83, 3.32, and 3.38 respectively); $\nu_{max.}$(KBr) 1 610, 1 465, 850, 840, and 820 cm^{-1}.

2-*Isopropoxy*-5,6,7,10-*tetramethoxyphenanthrene* (**17**).—The phenanthrol (**13**) (245 mg) was methylated with dimethyl sulphate and potassium carbonate in DMF at room temperature under argon in the usual way. The crude product was purified by radial chromatography to yield a *viscous oil* (**17**) (223 mg, 87%) (Found: C, 71.1; H, 6.8. $C_{21}H_{24}O_5$ requires C, 70.75; H, 6.9%); δ_H(80 MHz) 1.40 (6 H, d, Me_2), 3.94 (9 H, s, 3 × OMe), 3.99 (3 H, s, OMe), 4.77 (1 H, septet, CH), 6.83 and 6.95 (each 1 H, s, 8- and 9-H), 7.25 (1 H, dd, $J_{3,4}$ 9.4, $J_{3,1}$ 2.8 Hz, 3-H), 7.76 (1 H, d, $J_{1,3}$ 2.8 Hz, 1-H), and 9.40 (1 H, d, $J_{4,3}$ 9.40 Hz, 4-H); *m/z* 357 (24%), 356 (M^+, 100), 341 (23), 314 (29), 313 (12), 300 (15), 299 (83), 271 (22), 256 (53), 241 (12), and 213 (17).

Dealkylation of 2-*Isoproxpoxy*-5,6,7,10-*tetramethoxyphenanthrene* (**17**).—A solution of boron trichloride (106 mg) in dichloromethane (0.3 ml) was added to a stirred solution of the substrate (**17**) (147 mg) in dichloromethane (5.0 ml) at 0 °C under argon. The solution was stirred at 0 °C for 0.5 h and then at room temperature for 1 h; it was then poured into water. The crude product was isolated by extraction with ethyl acetate and then acetylated by treatment with acetic anhydride and pyridine at room temperature during 18 h. Work-up gave a crude product which was subjected to radial chromatography with 30% ethyl acetate–light petroleum as eluant. The band of higher R_F gave 2,6-*diacetoxy*-5,7,10-*trimethoxyphenanthrene* (**19**) which crystallized from dichloromethane–light petroleum as beige prisms (61 mg, 38%), m.p. 169—171 °C (Found: C, 65.75; H, 5.5%; M^+, 384. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.25%; *M*, 384); δ_H(300 MHz) 2.36 and 2.44 (each 3 H, s, COMe), 3.89, 3.94, and 4.01 (each 3 H, s, OMe), 6.89 (1 H, s, 8-H), 7.03 (1 H, s, 9-H), 7.37 (1 H, dd, $J_{3,4}$ 9.3, $J_{3,1}$ 2.6 Hz, 3-H), 8.04 (1 H, d, $J_{1,3}$ 2.6 Hz, 1-H), and 9.40 (1 H, d, $J_{4,3}$ 9.3 Hz, 4-H); $\lambda_{max.}$(MeOH) 219, 259, 335, and 352 nm (log ε 4.39, 4.79, 3.09, and 3.00 respectively); $\nu_{max.}$ 1 760 and 1 610 cm^{-1}.

The band of lower R_F gave 2,5,6-*triacetoxy*-7,10-*dimethoxyphenanthrene* (**20**) which crystallized from dichloromethane–light petroleum as cream plates (55 mg, 32%), m.p. 218—220 °C (Found: C, 64.05; H, 4.3%; M^+, 412. $C_{22}H_{20}O_8$ requires C, 64.05; H, 4.9%; *M*, 412); δ_H(300 MHz) 2.35, 2.37, and 2.49 (each 3 H, s, MeCO), 3.92 and 3.96 (each 3 H, s, OMe), 6.85 (1 H, s, 9-H), 7.12 (1 H, s, 8-H), 7.35 (1 H, dd, $J_{3,4}$ 9.3, $J_{3,1}$ 2.7 Hz, 3-H), 8.04 (1 H, d, $J_{1,3}$ 2.7 Hz, 1-H), and 8.91 (1 H, d, $J_{4,3}$ 9.3 Hz, 4-H); $\lambda_{max.}$(MeOH) 220, 258, 335, and 352 nm (log ε 4.29, 4.76, 3.21, and 3.19 respectively); $\nu_{max.}$ 1 775, 1 760, and 1 635 cm^{-1}.

2-*Bromo*-5,6-*dimethoxyphenyl Acetate* (**22**).—2,3-Dimethoxyphenol[9] was acetylated with acetic anhydride and pyridine in the usual way. The acetate (**21**) was obtained as an oil, b.p. 140 °C at 0.4 mmHg (Kugelrohr). This acetate (347 mg) and anhydrous sodium acetate (400 mg) were stirred together in acetic acid (3.0 ml) and treated dropwise with bromine (283 mg) in acetic acid (9.0 ml). After the addition of the bromine the mixture was stirred for a further 10 min and then poured into saturated aqueous sodium hydrogen carbonate. The crude product *compound* (**22**), isolated by extraction with ethyl acetate, was obtained as an *oil*, b.p. 170 °C at 0.5 mmHg (Kugelrohr) (Found: C, 43.7; H, 3.95; Br, 29.05. $C_{10}H_{11}BrO_4$ requires C, 43.65; H, 4.05; Br, 29.05%); δ_H(60 MHz) 2.32 (3 H, s, MeCO), 3.79 (6 H, s, 2 × OMe), and 6.64 and 7.18 (2 H, AB, *J* 8 Hz, ArH). This material was identical with a sample prepared by the acetylation of 2-bromo-5,6-dimethoxyphenol (**23**).[9]

4,5-*Dihydro*-2-(4,4′-*di-isopropoxy*-2′,3′-*dimethoxybiphenyl*-2-*yl*)-4,4-*dimethyloxazole* (**25**). The Grignard reagent was prepared from 1-bromo-4-isopropoxy-2,3-dimethoxybenzene (**24**)[9] (5.51 g) and this was allowed to react at room temperature during 21 h with the oxazoline (**7**) (5.26 g) in a manner similar to that described above. The crude product was purified by radial chromatography with 30% ethyl acetate–light petroleum as eluant. The oxazoline (**25**) (6.30 g, 74%) was obtained as an oil;

δ_H(80 MHz) 1.35 and 1.39 (each 6 H, d, Me_2CH), 1.28 (6 H, s, 2 × Me), 3.54 and 3.89 (each 3 H, s, OMe), 3.80 (2 H, s, CH_2), 4.60 (2 H, septet, Me_2CH), 6.66 and 6.89 (2 H, AB, $J_{5',6'}$ 8.5 Hz, 5'- and 6'-H), 6.97 (1 H, dd, $J_{5,6}$ 8.3 Hz, $J_{5,3}$ 2.6 Hz, 5-H), 7.25 (1 H, d, $J_{6,5}$ 8.3 Hz, 6-H), and 7.35 (1 H, d, $J_{3,5}$ 2.6 Hz, 3-H); *m/z* 396 (M^+).

4,4'-*Di-isopropoxy*-2',3'-*dimethoxybiphenyl*-2-*carboxylic Acid* (**26**).—Deprotection of the oxazoline (**25**) by a method similar to that described above gave the *acid* (**26**) (94%) which crystallized from di-isopropyl ether–light petroleum as needles, m.p. 113—114 °C (Found: C, 67.35; H, 7.3%; M^+, 374. $C_{21}H_{26}O_6$ requires C, 67.35; H, 7.0%; *M*, 374); δ_H(300 MHz) 1.37 and 1.39 (each 6 H, d, Me_2), 3.57 and 3.83 (each 3 H, s, OMe), 4.59 (2 H, septet, 2 × CH), 6.68 and 6.88 (2 H, AB, $J_{5',6'}$ 8.7 Hz, 5'- and 6'-H), 7.06 (1 H, dd, $J_{5,6}$ 8.5, $J_{5,3}$ 2.7 Hz, 5-H), 7.21 (1 H, d, $J_{6,5}$ 8.5 Hz, 6-H), and 7.43 (1 H, d, $J_{3,5}$ 2.7 Hz, 3-H); $\nu_{max.}$(KBr) 1 690 and 1 600 cm^{-1}.

The methyl ester (**27**) (83%) was obtained as an oil; δ_H(300 MHz) 1.37 and 1.39 (each 6 H, d, Me_2), 3.54, 3.66, and 3.88 (each 3 H, s, OMe), 4.57 and 4.63 (each 1 H, septet, CH), 6.70 and 6.88 (2 H, AB, $J_{5',6'}$ 8.6 Hz, 5'- and 6'-H), 7.03 (1 H, dd, $J_{5,6}$ 8.5, $J_{5,3}$ 2.7 Hz, 5-H), 7.23 (1 H, d, $J_{6,5}$ 8.5, $J_{5,3}$ 2.7 Hz, 5-H), and 7.38 (1 H, d, $J_{3,5}$ 2.7 Hz, 3-H); *m/z* 388 (M^+).

4,4'-*Di-isopropoxy*-2',3'-*dimethoxy*-2-(*methylsulphinyl*)-*acetoxybiphenyl* (**28**).—This was prepared from the foregoing ester (**27**) by a method similar to that described above. Crystallization from dichloromethane–light petroleum yielded *compound* (**28**) as prisms (90%), m.p. 112—113 °C (Found: C, 63.9; H, 7.3; S, 7.0%; M^+, 434. $C_{23}H_{30}O_6S$ requires C, 63.55; H, 6.95; S, 7.4%; *M*, 434); δ_H(300 MHz) 1.38 and 1.40 (each 6 H, d, Me_2), 2.66 (3 H, s, SOMe), 3.51 and 3.88 (each 3 H, s, OMe), 3.86 and 4.05 (2 H, AB, *J* 14.2 Hz, CH_2), 4.61 (2 H, septet, CH), 6.77 and 6.96 (2 H, AB, $J_{5',6'}$ 8.7 Hz, 5'- and 6'-H), 7.07 (1 H, d, $J_{5,6}$ 8.5, $J_{5,3}$ 2.6 Hz, 5-H), 7.18 (1 H, d, $J_{3,5}$ 2.6 Hz, 3-H), and 7.27 (1 H, d, $J_{6,5}$ 8.5 Hz, 6-H); $\nu_{max.}$(KBr) 1 685, 1 600, 1 055, and 1 040 cm^{-1}.

2,7-*Di-isopropoxy*-3,4-*dimethoxyphenanthrene*-9-*ol* (**29**).—Ring-closure and subsequent desulphurization of compound (**28**) by a method similar to that described above gave the *phenanthrol* (**29**) (94%) which crystallized from dichloromethane–light petroleum as blades, m.p. 144—146 °C (Found: C, 71.0; H, 7.4%; M^+, 370. $C_{22}H_{26}O_5$ requires C, 71.35; H, 7.05%; *M*, 370); δ_H(300 MHz) 1.39 and 1.41 (each 6 H, d, Me_2), 3.98 and 4.00 (each 3 H, s, OMe), 4.59 and 4.79 (each 1 H, septet, CH), 6.75 and 6.79 (each 1 H, s, 1- and 10-H), 7.26 (1 H, dd, $J_{6,5}$ 9.4, $J_{6,8}$ 2.8 Hz, 6-H), 7.72 (1 H, d, $J_{8,6}$ 2.8 Hz, 8-H), and 9.39 (1 H, d, $J_{5,6}$ 9.4 Hz, 5-H); $\nu_{max.}$(KBr) 1 620 and 1 610 cm^{-1}.

2,7-*Di-isopropoxy*-3,4,9-*trimethoxyphenanthrene* (**30**).—Methylation of the phenanthrol (**29**) in a manner similar to that described above the phenanthrene (**30**) (74%) as a gum; δ_H(300 MHz) 1.40 and 1.43 (each 6 H, d, Me_2), 3.97, 4.00, and 4.01 (each 3 H, s, OMe), 4.69 and 4.78 (each 1 H septet, CH), 6.83 and 6.98 (each 1 H, s, 1- and 10-H), 7.24 (1 H, dd, $J_{6,5}$ 9.4, $J_{6,8}$ 2.9 Hz, 6-H), 7.75 (1 H, d, $J_{8,6}$ 2.9 Hz, 8-H), and 9.40 (1 H, d, $J_{5,6}$ 9.4 Hz, 5-H); *m/z* 385 (29%), 384 (M^+, 100), 342 (17), 327 (12), 300 (20), and 285 (26).

3,4,9-*Trimethoxyphenanthrene*-2,7-*diol* (*Gymnopusin*) (**31**).—A solution of the foregoing phenanthrene (**30**) (232 mg) in anhydrous dichloromethane (5 ml) was stirred and cooled to −10 °C and then treated with boron trichloride (180 mg) in dichloromethane (0.5 ml) and stirred under argon at −10 °C for 10 min. The solution was then poured into water and next extracted with dichloromethane. Work-up gave a crude product which was purified by radial chromatography with 20% ethyl acetate–light petroleum as eluant. *Gymnopusin* (**31**) (171 mg, 95%) crystallized from ethyl acetate–light petroleum as prisms, m.p. 202—204 °C, undepressed on admixture with an authentic sample which had m.p. 197—200 °C (lit.,[2] 192 °C) (Found: C, 65.9; H, 5.75. $C_{17}H_{16}O_5 \cdot 0.5H_2O$ requires C, 66.05; H, 5.55%); δ_H(300 MHz) 4.07, 4.03, and 3.96 (each 3 H, s, OMe), 5.95 (2 H, D_2O exchangeable OH), 6.81 (1 H, s, 10-H), 7.07 (1 H, s, 1-H), 7.19 (1 H, dd, $J_{6,5}$ 9.25, $J_{6,8}$ 2.9 Hz, 6-H), 7.69 (1 H, d, $J_{8,6}$ 2.9 Hz, 8-H), and 9.35 (1 H, d, $J_{5,6}$ 9.25 Hz, 5-H); δ_C(75.5 MHz) 55.42, 59.73, and 61.32 (each OMe), 102.48, 106.05, and 106.98 (each Ar*C*H), 114.66 (ArC), 116.70 (Ar*C*H), 125.30 and 127.67 (each ArC), 128.35 (Ar*C*H), 130.15, 138.88, 147.72, 150.63, 152.57, and 153.20 (each ArC); *m/z* 301 (21%), 300 (M^+, 100), 286 (13), 285 (65), 271 (6), 270 (5), 257 (11), 242 (40), 227 (14), 199 (14), 185 (7), 171 (5), and 150 (16); $\lambda_{max.}$(MeOH) 210, 229, 260, 285, 342, and 359 nm (log ε 4.20, 4.18, 4.63, 4.08, 3.20, and 3.27 respectively); $\nu_{max.}$(KBr) 3 360, 1 613, 1 578, 1 511, 860, 828 cm^{-1}; it exhibited identical R_F values with an authentic sample on t.l.c. in three different solvent systems.

The *diacetate* (**32**) crystallized from dichloromethane–light petroleum as plates, m.p. 126.5—127 °C (lit.,[2] 113 °C) (Found: C, 65.85; H, 5.15. $C_{21}H_{20}O_7$ requires C, 65.6; H, 5.25%); δ_H(300 MHz) 2.33 and 2.37 (each 3 H, s, MeCO), 3.95, 3.97, and 3.98 (each 3 H, s, OMe), 6.81 (1 H, s, 10-H), 7.23 (1 H, s, 1-H), 7.39 (1 H, dd, $J_{6,5}$ 9.35 Hz, $J_{6,8}$ 2.64 Hz, 6-H), 8.06 (1 H, d, $J_{8,6}$ 2.64 Hz, 8-H), and 9.56 (1 H, d, $J_{5,6}$ 9.35 Hz, 5-H); δ_C(75.5 MHz) 20.72 and 21.15 (each *Me*CO), 55.40, 59.99, and 61.10 (each OMe), 102.54, 114.05, and 115.81 (each Ar*C*H), 118.82 (ArC), 121.39 (Ar*C*H), 128.12 and 128.47 (each ArC), 128.65 (Ar*C*H), 130.23, 142.88, 143.47, 148.89, 152.47, and 152.83 (each Ar*C*), 169.19 and 169.55 (each Me*C*O); *m/z* 385 (25%), 384 (M^+, 100), 342 (20), 300 (26), and 285 (35); $\lambda_{max.}$(MeOH) 217, 257, 300, 310, 339, and 356 nm (log ε 4.35, 4.62, 3.83, 3.82, 3.06, and 3.03 respectively); $\nu_{max.}$(KBr) 1 750, 1 610, and 1 215 cm^{-1}.

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References

1 C. F. Carvalho and M. V. Sargent, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1913; M. V. Sargent and E. Stanojevic, *ibid.*, 1984, 1919; C. F. Carvalho, M. V. Sargent, and E. Stanojevic, *Aust. J. Chem.*, 1984, **37**, 2111.
2 P. L. Majumder and S. Banerjee, *Phytochemistry*, 1988, **27**, 245.
3 *Cf.* Y. Oikawa and O. Yonemitsu, *Tetrahedron*, 1974, **30**, 2653; I. A. Blair, L. N. Mander, and P. H. C. Mundill, *Aust. J. Chem.*, 1981, **34**, 1235.
4 F. M. Irvine and J. C. Smith, *J. Chem. Soc.*, 1927, 74.
5 D. R. Henton, K. Anderson, M. J. Manning, and J. S. Swenton, *J. Org. Chem.*, 1980, **45**, 3422.
6 A. I. Meyers, R. Gabel, and E. D. Mihelich, *J. Org. Chem.*, 1978, **43**, 1372.
7 J. M. Bruce and F. K. Sutcliffe, *J. Chem. Soc.*, 1955, 4435.
8 C. F. Carvalho, A. V. Russo, and M. V. Sargent, *Aust. J. Chem.*, 1985, **38**, 777.
9 M. V. Sargent, *J. Chem. Soc., Perkin Trans. 1*, 1987, 2553.

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