Structure and Synthesis of the Aryltetralin Lignans Hypophyllanthin and Nirtetralin

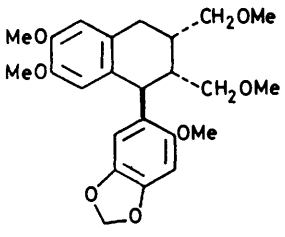
By Gail E. Schneiders and Robert Stevenson,* Department of Chemistry, Brandeis University, Waltham, Massachusetts 02254

Structures previously suggested for hypophyllanthin, the major aryltetralin lignan constituent of *Phyllanthus niruri* are shown to be incorrect. The structure *r*-1-(3,4-dimethoxyphenyl)-6-methoxy-*t*-2,*c*-3-bismethoxymethyl-7,8-methylenedioxy-1,2,3,4-tetrahydronaphthalene (5) now proposed is confirmed by an unambiguous synthesis. Synthesis of the congener, nirtetralin, is also described.

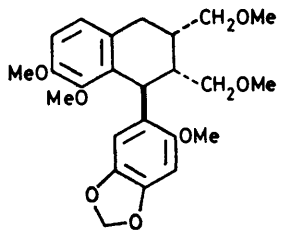
FROM the plant *Phyllanthus niruri* Linn. (Euphorbiaceae), extracts of which have been used medicinally [1] (notably in the treatment of asthma, jaundice, and bronchial infections), two unidentified compounds, named phyllanthin and hypophyllanthin were isolated [2] in 1946. In a series of papers between 1964 and 1979, Row and his colleagues have described the extraction of six lignans from this source and established that two (phyllanthin and niranthin) are dibenzylbutanes and four (hypophyllanthin, nirtetralin, phyltetralin, and lintetralin) are aryltetralins.

The structural elucidation of the principal aryltetralin, hypophyllanthin, has been particularly fraught with uncertainty. The molecular formula originally proposed [2] ($C_{19}H_{22}O_6$) was corrected by Row *et al.*[3] to $C_{24}H_{30}O_7$ and the nature of the functional groups was established. These workers suggested, principally on the basis of the 60 MHz ^{1}H n.m.r. spectrum, that hypophyllanthin was a phenyltetralin lignan of structure (1A), a conclusion supported by the claimed identification of metahemipinic acid and 2-methoxy-4,5-methylenedioxybenzoic acid as oxidative degradation products. In 1970, a revised structure (1B), based on interpretation of a 220 MHz ^{1}H n.m.r. spectrum, was presented.[4] A year later, attention was drawn to the fact that alternative structures were compatible with the existing data and, on evidence based upon proton magnetic double resonance and mass spectral fragmentation, the structure (1C) was proposed.[5] Most recently, a fourth structure (1D) has been forwarded on the basis of the ^{13}C n.m.r. spectrum.[6]

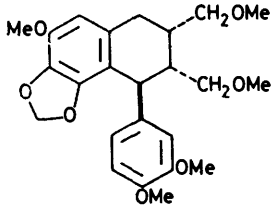
For several reasons, we considered each of these structures to be suspect. Firstly, our earlier work [7] on the constitution of otobain (2) revealed that the methylenedioxy-group in ring A gave a highly distinctive ^{1}H n.m.r. signal because of the non-equivalence of the two protons. The close correspondence in both spin–spin coupling and chemical shifts reported for this group in hypophyllanthin placed, in our view, the location of a methylenedioxy-group at C-7 and -8. Secondly, the close correspondence in chemical shift for the methylenedioxy-group in compound (2) and hypophyllanthin implied the same quasi-equatorial nature of the pendant ring-C. This conformation would be favoured, rather than the quasi-axial disposition (which would minimize the C-8 peri-interaction), if the substituent at C-3 also had an equatorial conformation, *i.e.* the C-1, -3, substituents should have a *cis*-relationship. Thirdly, we



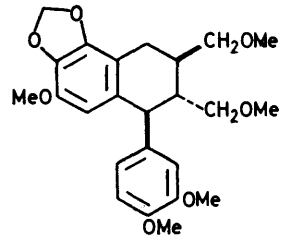
(1A)



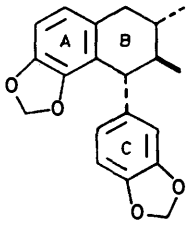
(1B)



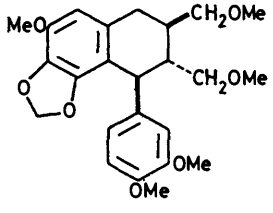
(1C)



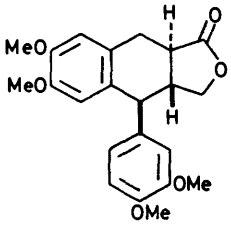
(1D)



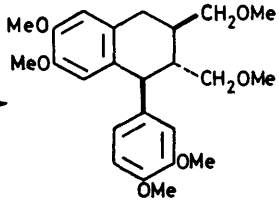
(2)



(5)



(3)



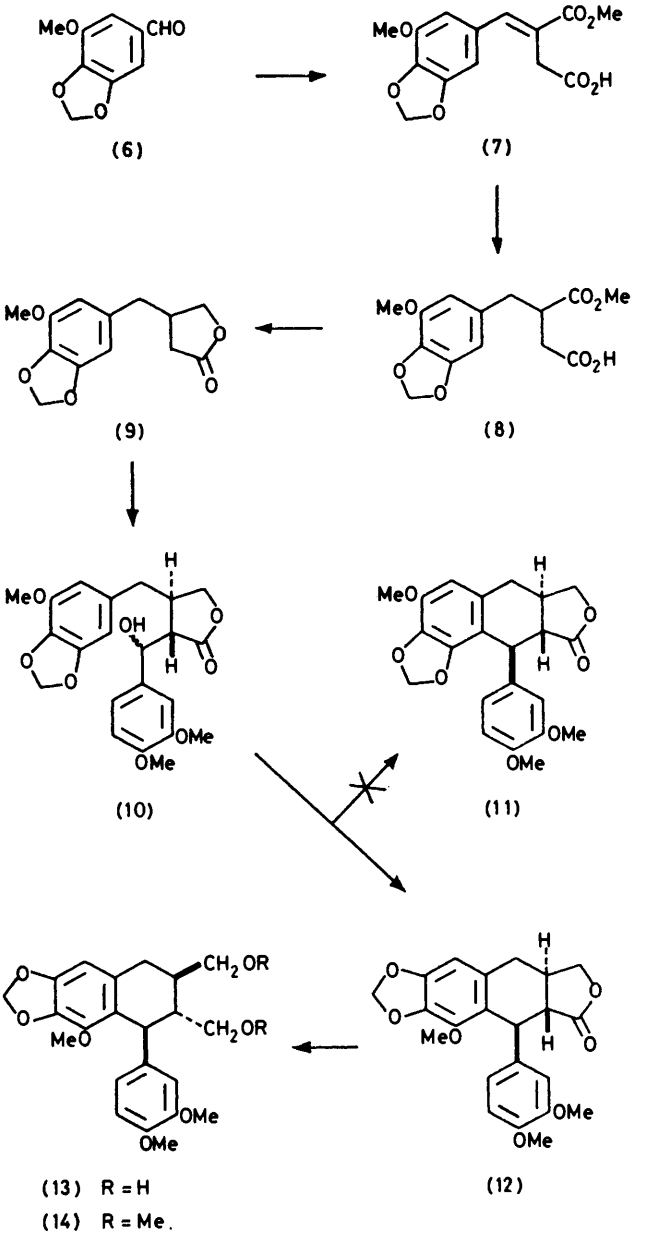
(4)

have established the constitution of the congeneric aryltetralin, phyltetralin, by conversion of α-conidendrin (3) into (−)-phyltetralin (4).[8] Since similar chemical-shifts are reported for the ring-B substituents in all four *Phyllanthus* aryltetralins, this points to *trans–trans*-C-1, -2, -3, substitution in hypophyllanthin. These considerations lead to a rejection of structures (1A)—(1D), and to the proposal of another structure (5) which we considered consistent with all the reported spectroscopic data. This work reports the confirmation of this conclusion by an unequivocal synthesis of (±)-hypophyllanthin (5),[9] the structure of which has also been reached independently by an *X*-ray structural analysis.[10]

The general pathway adopted involved the cyclization of an appropriate β-benzyl-α-hydroxybenzylbutyrolactone followed by the requisite functional group modification. This procedure appeared particularly attractive in view of much recent work, notably by Brown and his co-workers [11,12] and Ziegler and Schwarz [13,14] on aryltetralin and bisbenzocyclo-octene lignans, which extended earlier observations and promise of general applicability.[15]

The required starting β-benzylbutyrolactone was obtained in three steps from the benzaldehyde (6) [16] by Stobbe condensation with dimethyl succinate in methanol, which contained sodium methoxide, to give the benzylidene half-ester (7). This was followed by catalytic hydrogenation, which proceeded quantitatively, to give the benzyl half-ester (8) and reduction with calcium borohydride to give the butyrolactone (9) in 86% yield. Treatment of the enolate of compound (9), prepared with lithium di-isopropylamide (LDA) in tetrahydrofuran (THF) gave the expected mixture of the epimeric alcohols (10) which, without separation, was subjected to cyclization by acidification at room temperature with trifluoroacetic acid. Ample precedent exists for this procedure which yielded the all-*trans*-aryltetralin lactone. A distinction between the two possible products (11) [*i.e.* the desired intermediate for hypophyllanthin of the postulated structure (5)] and (12) was clearly and immediately made from the ^{1}H n.m.r. spectrum of the product, easily isolated by direct crystallization. It was anticipated that the spectrum of compound (12) would exhibit *one* highly shielded aryl methoxy-group signal (δ *ca.* 3.3) and a normal (δ *ca.* 5.8—6.0) methylenedioxy-signal, whereas compound (12) would have normal (δ *ca.* 3.8—3.9) methoxy-signals and the highly characteristic and shielded OCH_2O signal [*cf.* otobain (2)]. The presence of the former and absence of the latter spectroscopic features clearly indicated structure (12) for the product of cyclization. The availability of compound (12), however, did permit the completion of a synthesis of (±)-nirtetralin, whose isolation was reported in 1973 [17] and for which the structure (14) was forwarded in 1979.[6] As outlined in Scheme 1, reduction of the lactone (12) with lithium aluminium hydride gave the diol (13) which, on methylation with methyl iodide in dimethyl sulphoxide, gave (±)-nirtetralin (14), identified by direct spectral comparison (^{1}H n.m.r., i.r., and mass) with authentic natural nirtetralin.

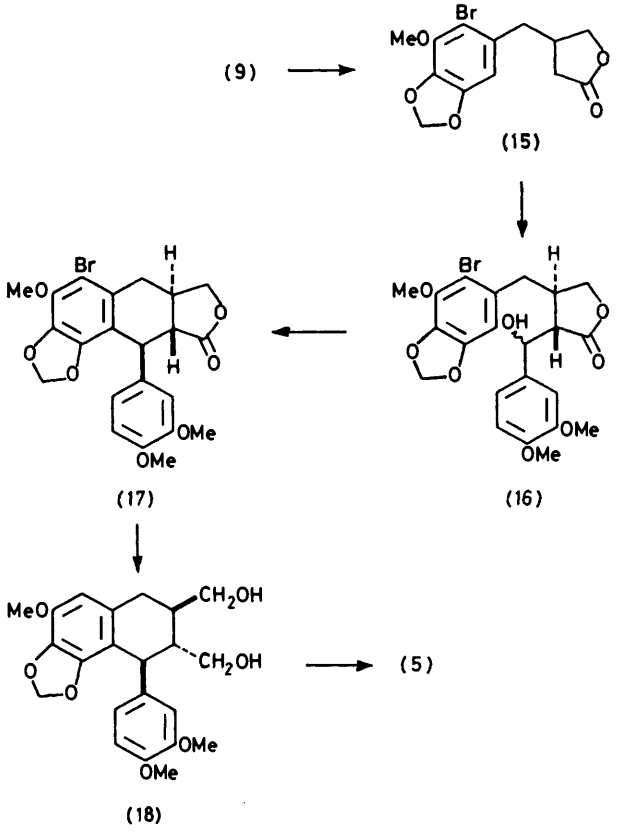
The necessary modification of this approach to a synthesis of (±)-hypophyllanthin is formulated in



SCHEME 1

Scheme 2. The reaction of compound (10) to give compound (12) indicated that the site *ortho*- to the methoxy-group of ring-A (as compared with the site *ortho*- to the methylenedioxy-group) was the more susceptible to electrophilic substitution, and that this order of reactivity would also pertain to the lactone (9). Treatment of compound (9) with bromine in acetic acid did yield, in fact, the monobromo-substitution product (15), the ^{1}H n.m.r. spectrum of which reveals a methoxy-group downfield shift comparable with that found in the con-

version of anisole into *o*-bromoanisole. As for the previous case, α-hydroxybenzylation of compound (15) with veratraldehyde yielded the epimeric alcohol mixture (16) which underwent ready cyclization to the bromoaryltetralin lactone, which gave a ^{1}H n.m.r. spectrum fully consistent with structure (17). Treatment of



SCHEME 2

compound (17) with lithium aluminium hydride resulted both in reductive debromination and lactone reduction to yield the diol (18), methylation of which gave (±)-hypophyllanthin (5), with spectra identical with authentic natural hypophyllanthin.

The specific rotation values reported for the natural aryltetralins are: hypophyllanthin $[\alpha]_D$ +4°, nirtetralin $[\alpha]_D$ +14°, and phyltetralin $[\alpha]_D$ +17.5° and the same absolute configuration seems most likely. Since structure (4) is that of (−)-phyltetralin, the natural dextrorotatory forms of hypophyllanthin and nirtetralin should most probably be represented, respectively, by the enantiomers of structures (5) and (14).

EXPERIMENTAL

M.p.s were determined with a Fisher–Johns apparatus and are uncorrected. Varian A-60A, Perkin-Elmer R-32, and Bruker FT (90 MHz) spectrometers were employed for determination of ^{1}H n.m.r. spectra, with tetramethylsilane (TMS) as internal reference.

3-Methoxycarbonyl-4-(3-methoxy-4,5-methylenedioxyphenyl)but-3-enoic Acid (7).—To a solution of sodium methoxide (2.48 g) in methanol (20 ml) was added, while being stirred, a hot solution of 3-methoxy-4,5-methylenedioxybenzaldehyde (6) (3.30 g) and dimethyl succinate (2.68 g) in methanol (10 ml). The mixture was heated under reflux for 90 min, then concentrated to half the volume, cooled, and acidified with 6M hydrochloric acid. The diethyl ether extract (3 × 50 ml) was washed with saturated sodium hydrogen carbonate solution (3 × 50 ml). Evaporation of the dried diethyl ether phase gave unchanged starting materials from which the aldehyde (6) (900 mg) was recovered by crystallization from methanol. The aqueous sodium hydrogen carbonate layer was acidified, extracted with $CHCl_3$, and the washed and dried extract was evaporated. The residual oil was crystallized from CCl_4–CH_2Cl_2 to yield the benzylidene half-ester (7) as short *needles* (1.51 g), m.p. 147.5—148 °C (Found: C, 57.15; H, 4.85. $C_{14}H_{14}O_7$ requires C, 57.14; H, 4.80%); δ_H [$(CD_3)_2CO$] 3.59 (s, CH_2), 3.79 (s, CO_2Me), 3.91 (s, ArOMe), 6.05 (s, OCH_2O), 6.70br (s, ArH), 6.81br (s, ArH), and 7.78 (s, vinyl H).

3-Methoxycarbonyl-4-(3-methoxy-4,5-methylenedioxyphenyl)butanoic Acid (8).—A solution of the butenoic acid (7) (294 mg) in ethyl acetate (30 ml) was stirred with palladium–charcoal (10%, 100 mg) at room temperature under H_2 for 2.5 h. Filtration and evaporation gave a residue which crystallized from Et_2O–EtOAc to yield the benzyl half-ester (8) as fine *needles* (291 mg), m.p. 153.5—154 °C (Found: C, 56.95; H, 5.5. $C_{14}H_{16}O_7$ requires C, 56.75; H, 5.44%); δ_H [$(CD_3)_2CO$)] 2.55—3.28 (m, 2-, 3-, 4-H), 3.65 (s, CO_2Me), 3.90 (s, ArOMe), 5.96 (s, OCH_2O), 6.44br (s, ArH), and 6.50br (s, ArH).

The use of MeOH as the hydrogenation solvent was less desirable since some dimethyl ester was also formed.

3-(3-Methoxy-4,5-methylenedioxybenzyl)butyrolactone (9).—Ethanolic KOH solution was added as drops to a solution of the half-ester (8) (1.25 g) in EtOH (30 ml) until this solution became basic to phenolphthalein. The solvent was then removed under reduced pressure to yield the residual potassium salt. Powdered, anhydrous $CaCl_2$ (1.0 g) was dissolved in anhydrous EtOH (20 ml) and cooled to −10 °C. A solution of $NaBH_4$ (900 mg) in anhydrous EtOH (35 ml) was added as drops, while being stirred, for 15 min and the mixture was then stirred for a further 30 min. A solution of the potassium salt in anhydrous EtOH (40 ml) was then added during 30 min, at −10 °C, and continuously stirred at this temperature for 3 h, and then at room temperature for a further 2 h. Work-up by aqueous dilution, acidification with dilute HCl, concentration, and extraction with Et_2O yielded, on evaporation of the washed and dried extract the lactone (9) as a pale yellow *oil* (904 mg) (Found: C, 62.7; H, 5.75. $C_{13}H_{14}O_5$ requires C, 62.39; H, 5.64%); ν 1 790 cm^{-1} (lactone); δ_H ($CDCl_3$) 2.25—2.95 (m, 2-, 3-H and $ArCH_2$), 3.91 (s, OMe), 4.06—4.35 (m, 4-H), 5.95 (s, OCH_2O), and 6.35 (s, Ar 2- and 6-H).

trans-2-(α-Hydroxy-3,4-dimethoxybenzyl)-3-(3-methoxy-4,5-methylenedioxybenzyl)butyrolactone (10).—A solution of the lactone (9) (500 mg) in tetrahydrofuran (THF) (5 ml) was added as drops during 2 min to a stirred solution of $LiN(CHMe_2)_2$ [prepared from $(Me_2CH)_2NH$ (0.42 ml) and Bu^nLi (2.58M, 1.17 ml)] in THF (3 ml) at −78 °C under N_2. The mixture was stirred at this temperature for 15 min, then a solution of 3,4-dimethoxybenzaldehyde (332 mg) in THF (5 ml) was added during 5 min, the mixture was stirred for 30 min, and hydrochloric acid (1M, 5 ml) added. After being warmed to room temperature, the layers were separated.

The washed and dried organic layer was evaporated to give the epimeric hydroxybenzyl lactones (10) as a pale yellow oil [δ_H ($CDCl_3$) 4.84 (d, *J* 7 Hz), and 5.30 (d, *J* 3.5 Hz) which correspond to ArC*H*OH] which was used directly for cyclization.

r-1-(3,4-*Dimethoxyphenyl*)-c-3-*hydroxymethyl*-8-*methoxy*-6,7-*methylenedioxy*-1,2,3,4-*tetrahydronaphthalene*-t-2-*carboxylic Acid Lactone* (12).—To a stirred solution of F_3C–CO_2H (4 ml) in CH_2Cl_2 (30 ml) at room temperature under N_2 was added a solution of the epimeric lactone mixture (10) (700 mg) in CH_2Cl_2 (5 ml). After being stirred for 3 h, the mixture was washed with H_2O, dried, and evaporated. Crystallization of the residue from CH_2Cl_2–MeOH gave the all-*trans*-lactone (12), as *needles* (320 mg), m.p. 223—224 °C (Found: C, 66.1; H, 5.65. $C_{22}H_{22}O_7$ requires C, 66.3; H, 5.55%); δ_H ($CDCl_3$) 2.51 (m, 2- and 3-H), 2.90 (m, 4-H), 3.30 (s, 8-OMe), 3.85 and 3.90 (s, 3'- and 4'-OMe), 3.98 (m, CH_2O), 4.40 (m, 1-H), 5.90 (OCH_2O), 6.44 (s, 5-H), 6.68 (dd, *J* 9, 1 Hz, 6'-H), 6.80 (d, *J* 9 Hz, 5'-H), and 6.99 (d, *J* 1 Hz, 2'-H).

r-1-(3,4-*Dimethoxyphenyl*)-t-2,c-3-*bishydroxymethyl*-8-*methoxy*-6,7-*methylenedioxy*-1,2,3,4-*tetrahydronaphthalene* (13).—To a stirred suspension of $LiAlH_4$ (150 mg) in THF (10 ml) was added as drops a solution of the lactone (12) (290 mg) in THF (35 ml), while being stirred under N_2. The mixture was stirred at room temperature for 3 h, then EtOAc added, followed by saturated NH_4Cl until the inorganic constituents coagulated, whereupon the organic layer was decanted off. Evaporation of the dried extract gave a residue which crystallized after several days from CCl_4 to give the diol (13) as irregular *prisms*, m.p. 143.5—145 °C (Found: M^+, 402.1682. $C_{22}H_{26}O_7$ requires M^+, 402.1678); δ_H ($CDCl_3$) 1.6—2.1 (m, 2- and 3-H), 2.3—2.75 (m, 4-H), 3.65—4.2 (m, 1-H and 2- and 3-C*H*$_2$OH), 3.37 (s, 8-OMe), 3.82 (s, 3'- and 4'-OMe), 5.85 (s, OCH_2O), 6.39 (s, 5-H), and 6.68 (m, 2'-, 5'-, and 6'-H).

(±)-*Nirtetralin* (14).—MeI (0.6 g) was added to a stirred solution of the diol (13) (140 mg) in dry dimethyl sulphoxide (DMSO) (10 ml). NaH (0.9 g in 57% oil dispersion) was washed twice with dry diethyl ether, covered with DMSO, and this added as portions during 5 min to the diol solution, followed by more MeI (0.5 ml). After being stirred at room temperature for 2.5 h, the product was isolated in the usual way by careful addition of water and diethyl ether extraction. Evaporation of the washed and dried extract yielded *r*-1-(3,4-dimethoxyphenyl)-8-methoxy-*t*-2,*c*-3-bismethoxymethyl-6,7-methylenedioxy-1,2,3,4-tetrahydronaphthalene (14) as an *oil* (129 mg) (Found: M^+, 430.2019. $C_{24}H_{30}O_7$ requires M^+, 430.1992); δ_H ($CDCl_3$) 1.7—2.2 (m, 2- and 3-H), 2.66 (m, 4-H), 3.29 (s, CH_2OMe), 3.34 (s, 3-CH_2OMe), 3.49 (s, 8-OMe), 3.82 (s, 3'- and 4'-OMe), 3.0—3.5 (m, 2 × C*H*$_2$OMe), 4.29 (d, *J* 6 Hz, 1-H), 5.87 (s, OCH_2O), 6.41 (s, 5-H), 6.54 (dd, *J* 8, 2 Hz, 6'-H), 6.69 (d, *J* 3 Hz, 2'-H), and 6.72 (d, *J* 8 Hz, 5'-H). It was identified by comparison of spectra (^1H n.m.r., i.r.) with those of authentic (+)-nirtetralin.

3-(2-*Bromo*-3-*methoxy*-4,5-*methylenedioxybenzyl*)*butyrolactone* (15).—A solution of bromine (176 mg) in AcOH (4.3 ml) was added to a solution of the lactone (9) (280 mg) in the same solvent (10 ml). The mixture was stirred at room temperature for 30 min, the solvent was then removed under reduced pressure, and the residue crystallized from methanol to give the bromobenzyl lactone (15) as fine *needles* (226 mg), m.p. 113—114 °C (Found: C, 47.85; H, 3.8. $C_{13}H_{13}BrO_5$ requires C, 47.45; H, 4.0%); δ_H ($CDCl_3$) 2.10—2.91 (m, 2-, 3-H, and $ArCH_2$), 4.02—4.38 (m, 4-H), 4.06 (s, OMe), 6.00 (s, OCH_2O), and 6.48 (s, 6-H).

5-*Bromo*-r-1-(3,4-*dimethoxyphenyl*)-c-3-*hydroxymethyl*-6-*methoxy*-7,8-*methylenedioxy*-1,2,3,4-*tetrahydronaphthalene*-t-2-*carboxylic Acid Lactone* (17).—A solution of the bromobenzyl lactone (15) (160 mg) in THF (4 ml) was added as drops to a solution of $LiN(CHMe_2)_2$ [prepared from $(Me_2CH)_2NH$ (0.14 ml) and Bu^{n}Li (2.58M, 0.39 ml) in THF (2 ml)] and treated with 3,4-dimethoxybenzaldehyde (81 mg) in THF (4 ml), as for the analogous α-hydroxylactones (10). Work-up as before gave a mixture of the epimeric hydroxybenzyl lactones (16) as a yellow oil (220 mg) [δ_H ($CDCl_3$) 4.86 (d, *J* 7 Hz) and 5.24 (d, *J* 3 Hz)] which was dissolved in CH_2Cl_2 (3 ml) and added as drops during 5 min to CH_2Cl_2 (13 ml) and F_3C–CO_2H (2 ml). The mixture was stirred for 3 h and, after work-up as before, the product was crystallized from CH_2Cl_2–MeOH to give the bromoaryl lactone (17) as fine *needles* (90 mg), m.p. 217.5—218 °C (Found: C, 55.15; H, 4.65. $C_{22}H_{21}BrO_7$ requires C, 55.36; H, 4.44%); δ_H ($CDCl_3$) 2.3—2.8 (m, 2-, 3-, and 4-H), 3.85 (s, 3'- and 4'-OMe), 4.02 (s, 6-OMe), 4.17 (m, 1-H), 4.45 (m, CH_2O), 5.61 and 5.74 (dd, *J* 1 Hz, OCH_2O), and 6.78 (m, 2'-, 5'-, and 6'-H).

r-1-(3,4-*Dimethoxyphenyl*)-t-2,c-3-*bishydroxymethyl*-6-*methoxy*-7,8-*methylenedioxy*-1,2,3,4-*tetrahydronaphthalene* (18).—To a stirred suspension of $LiAlH_4$ (100 mg) in THF (10 ml) was added a solution of the bromoaryl lactone (17) (60 mg) in THF (15 ml) with treatment and work-up as for compound (13). Solvent evaporation gave the solid residual product (50 mg); δ_H [$CDCl_3$–$(CD_3)_2CO$] 1.6—2.0 (m, 2- and 3-H), 2.6—3.2 (m, 4-H and 2 × OH), 3.76, 3.80, and 3.86 (each s, 6-, 3'-, and 4'-OMe), 3.5—4.2 (m, 1-H and 2- and 3-C*H*$_2$OH), 5.62 and 5.72 (dd, *J* 1 Hz, OCH_2O), 6.40 (s, 5-H), and 6.60—6.86 (m, 2'-, 5'-, and 6'-H) which was used directly for methylation.

(±)-*Hypophyllanthin* (5).—The above diol (18) (50 mg) was treated with MeI–DMSO as for the preparation of nirtetralin (14), and the product was crystallized from light petroleum to give *r*-1-(3'-4'-dimethoxyphenyl)-6-methoxy--*t*-2,*c*-3-bismethoxymethyl-7,8-methylenedioxy-1,2,3,4-tetrahydronaphthalene (5) as fine *needles* (28 mg), m.p. 109—109.5 °C (Found: C, 66.75; H, 7.1. $C_{24}H_{30}O_7$ requires C, 66.96; H, 7.02%); δ_H ($CDCl_3$) 1.7—2.2 (m, 2- and 3-H), 2.77br (d, 4-H), 3.0—3.5 (m, 2 × C*H*$_2$OMe), 3.31 (s, 2-CH_2OMe), 3.33 (s, 3-CH_2OMe), 3.80, 3.85, and 3.87 (each s, 6-, 3'-, and 4'-OMe), 4.11 (d, *J* 8 Hz, 1-H), 5.65 and 5.73 (dd, *J* 1.5 Hz, OCH_2O), 6.33 (s, 5-H), 6.62br (d, *J* 8 Hz, 6'-H), 6.68 (d, *J* 3 Hz, 2'-H), and 6.75 (d, *J* 8 Hz, 5'-H).

We wish to thank the National Institutes of Health (General Medical Sciences) for a research grant and Dr. R. S. Ward (University College, Swansea) for kindly providing authentic specimens of the natural lignans.

[1/971 *Received*, 17*th June*, 1981]

REFERENCES

[1] L. M. Perry, 'Medicinal Plants of East and Southeast Asia,' The MIT Press, Cambridge, Massachusetts, 1980, pp. 83, 150, 281, 292.

[2] G. V. Krishnamurty and T. R. Seshadri, *Proc. Ind. Acad. Sci.*, 1946, **24**, 357.

[3] L. R. Row, C. Srinivasulu, M. Smith, and G. S. R. Subba Rao, *Tetrahedron Lett.*, 1964, 1557.

[4] L. R. Row, P. Satyanarayana, and C. Srinivasulu, *Tetrahedron*, 1970, **26**, 3051.

[5] G. Subba Rao and R. Bramley, *Tetrahedron Lett.*, 1971, 3175.
[6] R. S. Ward, P. Satyanarayana, L. R. Row, and B. V. Gopala Row, *Tetrahedron Lett.*, 1979, 3043.
[7] N. S. Bhacca and R. Stevenson, *J. Org. Chem.*, 1963, **28**, 1638.
[8] R. Stevenson and J. R. Williams, *Tetrahedron*, 1977, **33**, 2913.
[9] P. A. Ganeshpure, G. E. Schneiders, and R. Stevenson, *Tetrahedron Lett.*, 1981, 393, incorporates this work in preliminary communication form.
[10] M. M. Bhadbhade, G. S. R. Subba Rao, and K. Vankatasan, *Tetrahedron Lett.*, 1980, 3097.
[11] E. Brown, J.-P. Robin, and R. Dhal, *J. Chem. Soc., Chem. Commun.*, 1978, 566, and references cited therein.
[12] E. Brown, M. Loriot, and J.-P. Robin, *Tetrahedron Lett.*, 1979, 1389.
[13] F. E. Ziegler and J. A. Schwartz, *Tetrahedron Lett.*, 1975, 4643.
[14] F. E. Ziegler and J. A. Schwartz, *J. Org. Chem.*, 1978, **43**, 985, and references cited therein.
[15] M. Kuhn and A. von Wartburg, *Helv. Chim. Acta*, 1967, **50**, 1546.
[16] G. E. Schneiders and R. Stevenson, *Chem. Ind.*, 1980, 538; *J. Org. Chem.*, 1981, **46**, 2969.
[17] A. S. R. Anjaneyulu, K. J. Rao, L. R. Row, and C. Subrahmanyam, *Tetrahedron*, 1973, **29**, 1291.