Synthesis of Condensed Tannins. Part 18.† Stilbenes as Potent Nucleophiles in Regio- and Stereo-specific Condensations: Novel Guibourtinidol–Stilbenes from *Guibourtia coleosperma*

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(*E*)-3,3′,4,5′-Tetrahydroxy- and 3′,4,5′-trihydroxy-stilbenes function as strong nucleophiles in regio- and stereo-specific condensations with carbenium ions generated from 2,3-*trans*- and 2,3-*cis*-flavan-3,4,4′,7-tetraols (leucoguibourtinidins) to generate those [4,2]-'dimeric' and [4,2:4,6]-'trimeric' proguibourtinidin oligomers which occur in *Guibourtia coleosperma*. Problems of structural analysis associated with dynamic rotational isomerism and exceptional energy requirements for the coalescence of ^{1}H n.m.r. resonances have been surmounted by synthesis. The requisite 3,3′,4,5′-tetrahydroxystilbene was prepared *via* a modified Reimann procedure.

Chromatographic recognition[1] of the yellow anthocyanidin generated under acid conditions from the heartwood extractives of *Guibourtia* spp. (Caesalpinioideae) as 3,4′,7-trihydroxyflavylium chloride (guibourtinidin)[2] provided the first indication of the still rare 4′,7-dihydroxy phenolic functionality of constituent condensed tannins (proguibourtinidins) and their associated flavan-3,4-diols (leucoguibourtinidins). Subsequent complete synthesis of racemic 2,3-*trans*-4′,7-dihydroxyflavan-3,4-*trans*-diol (2,3-*trans*-3,4-*trans*-flavan-3,4,4′,7-tetraol),[3] and also of the dimethyl ether diacetates of the four possible diastereoisomeric racemates,[4] permitted identification of a mixture of 2,3-*cis*-3,4-*trans*, 2,3-*trans*-3,4-*trans*, and 2,3-*trans*-3,4-*cis* isomers in *Guibourtia coleosperma* ('large false mopane') by paper ionophoresis and ^{1}H n.m.r. spectroscopy. However, neither these flavan-3,4-diols nor their derivatives were isolated. The methyl ethers of the oligomeric proguibourtinidin tannins range in mass up to 2 110 daltons.[3] Detailed examination of those present in *G. coleosperma* has now shown[5] that stilbenes, and 3,3′,4,5′-tetrahydroxystilbene (stilbene-3,3′,4,5′-tetraol) in particular, serve as potent nucleophiles. They, therefore, replace the ubiquitous catechins which normally initiate condensation sequences as, for example, in the 'conventional' [4,6]- and [4,8]-(+)-guibourtinidol–(+)-catechins and –(−)-epicatechins which occur (also as carboxylic acids) in *Acacia luederitzii*[6] (Mimosoideae) and in *Julbernardia globiflora* (Caesalpinioideae).[7] The present work provides spectrometric and synthetic proof of structure for the novel class of proguibourtinidin–stilbene condensed tannins (**9**), (**11**), (**13**), (**15**), and (**17**) from *Guibourtia coleosperma*.

One of the problems connected with structural assignments of one of the 'trimeric' proguibourtinidin–stilbenes is the combination of abnormally high temperatures and low magnetic field strengths required to provide sharp spectra (see ref. 8 for discussion of this relationship). Under these limiting conditions signal overlap in the aromatic region precludes assignment of aromatic bonding positions. For the remainder of this group high-temperature (150—180 °C) high-resolution (300 and 500 MHz) spectra are essential for unravelling complexity due to overlap of ethylenic and aromatic proton resonances. Apart from this problem, all oligomeric derivatives proved unstable; (*E*)–(*Z*) isomerism of their stilbene moieties occurring readily, even in indirect light.

The 500 MHz ^{1}H n.m.r. spectrum, in $(CD_3)_2SO$ ($[^2H_6]$DMSO) at 170 °C, of the hexamethyl ether acetate of the [4,2′]-2,3-*cis*-3,4-*trans*-guibourtinidol–stilbene (**12**),‡ which has the lowest temperature requirements for 'fast' rotation, exhibits two non-equivalent *meta*-coupled doublets at δ 6.757 [6′-H(D)] and δ 6.552 [4′-H(D)] in place of the A_2B-system (δ 6.737, d, 2-H + 6′-H; and δ 6.379, t, 4′-H in the same solvent) characteristic of 3,3′,4-5′-tetramethoxystilbene (**20**) (tetra-*O*-methylpiceatannol[9]). The non-equivalence of the doublets of the oligomer and their chemical shifts establishes flavanyl substitution at the 2′-position of the stilbene. A sharp 500 MHz spectrum ($[^2H_6]$DMSO) of the corresponding derivative of the 2,3-*trans*-3,4-*trans* isomer (**10**)‡ could not be obtained at the maximum permissible temperature (180 °C), but at 300 MHz the same *meta*-coupled AB-system could be discerned at δ 6.700 [6-H(D)] and 6.497 [4-H(D)] in spite of a degree of line-broadening under comparable conditions. The position of substitution in the 2,3-*cis*-3,4-*trans* isomer (**12**) was confirmed by n.O.e. difference spectroscopy (Figure 1), and the accessibility of the 2-position in the parent stilbene (**19**) established by bromination.

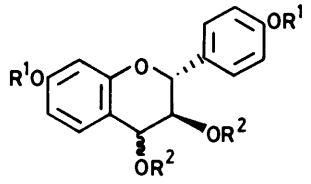
Among the 'trimers' the octamethyl ether diacetate (**18**) of the [4,2′:4,6′]-bi-[2,3-*cis*-3,4-*trans*-guibourtinidol]–stilbene provides a ^{1}H n.m.r. spectrum at 80 MHz (100 °C) similar to that of the 2,3-*cis*-3,4-*trans* 'dimeric' derivative (**12**). Complete overlap of aromatic, heterocyclic, methoxy, and acetoxy proton resonances attributable to identical substituent flavanyl units, and the chemical shift of the residual D-ring singlet [δ 6.662, 4-H(D)] in $[^2H_6]$DMSO (150 °C), indicate molecular symmetry resulting from substitution at C-2 and C-6 (D-ring) on the basis of presumed equivalence of these positions. This is attributable either to resonance, or to induced non-coplanarity of the remaining styryl system relative to the D-ring within the stilbene moiety due to steric hindrance. Substitution positions were confirmed by n.O.e. difference spectroscopy (Figure 1).

The remaining 'trimeric' isomers of 'mixed' stereochemistry, the [4,2′:4,6′]-2,3-*trans*-3,4-*trans*:2,3-*cis*-3,4-*trans*-biguibourtinidol–stilbenes (**13**) and (**15**), differing only as regards hydroxylation of the E-rings of the stilbene units,§ proved the most intractable as regards adequate resolution at high magnetic field strengths. Thus, although resolution of the heterocyclic region was attainable at 80 MHz (170 °C), the temperature limit of 180 °C at either 300 or 500 MHz proved

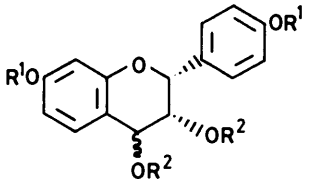
† Part 17, E. Young, E. V. Brandt, D. A. Young, D. Ferreira, and D. G. Roux, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1737.

‡ The stereochemistry of these 'dimers' [(**10**) and (**12**)] and also of the (trimers) [(**13**), (**15**), and (**17**)] is discussed at a later stage.

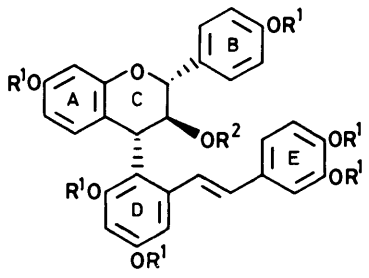
§ The stilbene units correspond to piceatannol[9] and resveratrol[10] in compounds (**13**) and (**15**) respectively.



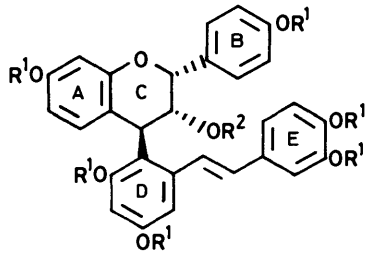
(1) § ≡ ⋮ $R^1 = R^2 = H$
(2) § ≡ ⋮ R^1 = Me, R^2 = H
(3) § ≡ ▲ $R^1 = R^2 = H$
(4) § ≡ ▲ R^1 = Me, R^2 = H



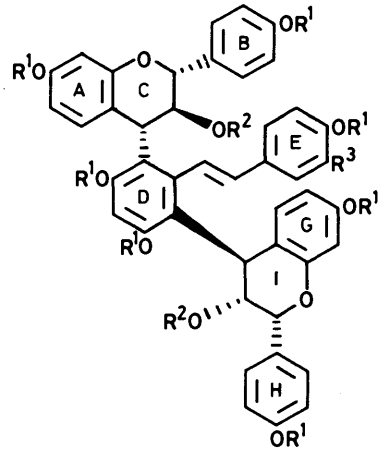
(5) § ≡ ⋮
(6) § ≡ ⋮
(7) § ≡ ▲
(8) § ≡ ▲



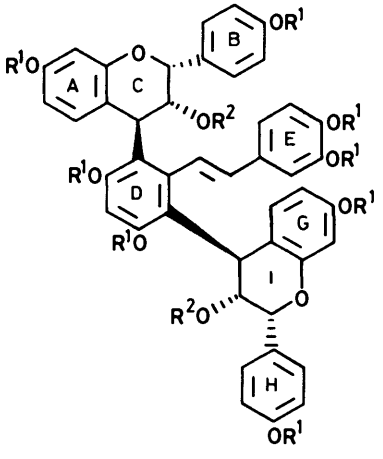
(9) $R^1 = R^2 = H$
(10) R^1 = Me, R^2 = Ac



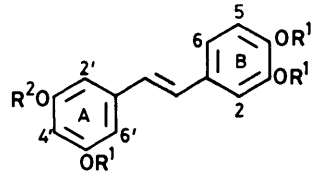
(11) $R^1 = R^2 = H$
(12) R^1 = Me, R^2 = Ac



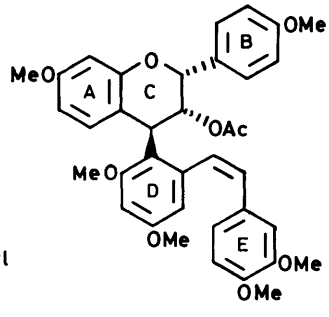
(13) $R^1 = R^2 = H$, R^3 = OH
(14) R^1 = Me, R^2 = Ac, R^3 = OMe
(15) $R^1 = R^2 = R^3 = H$
(16) R^1 = Me, R^2 = Ac, R^3 = H



(17) $R^1 = R^2 = H$
(18) R^1 = Me, R^2 = Ac



(19) $R^1 = R^2 = H$
(20) $R^1 = R^2$ = Me
(21) $R^1 = H$, R^2 = β-glycosyl



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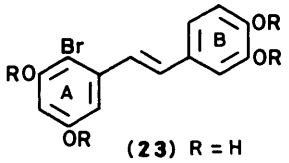
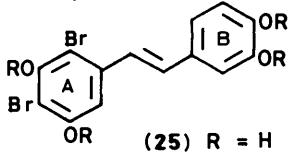


(23) R = H
(24) R = Me



(25) R = H
(26) R = Me

inadequate for interpretation of the points of aromatic bonding and also of the *E* or *Z* configuration of the stilbene unit, due to excessive line-broadening. These difficulties were overcome by condensation of the predominant of the four flavan-3,4-diol isomers 2,3-*cis*-3,4-*trans*-3,4,4′,7-tetrahydroxyflavan (**7**) with [4,2′]-2,3-*trans*-3,4-*trans*-guibourtinidol-(*E*)-3,3′,4,5′-tetrahydroxystilbene (**9**), and also independent condensation of a mixture of 2,3-*trans*-3,4-*trans*-(**1**) and 2,3-*trans*-3,4-*cis*-3,4,4′,7-tetrahydroxyflavan (**3**) with [4,2′]-2,3-*cis*-3,4-*trans*-guibourtinidol-(*E*)-3,3′,4,5′-tetrahydroxystilbene (**11**); both affording a single product, [4,2:4,6]-2,3-*trans*-3,4-*trans*:2,3-*cis*-3,4-*trans*-biguibourtinidol-(*E*)-3,3′,4,5′-tetrahydroxystilbene (**13**). This proved the substitution positions at C-2′ and C-6′ of the stilbene moiety beyond doubt. The chemical shifts and coupling

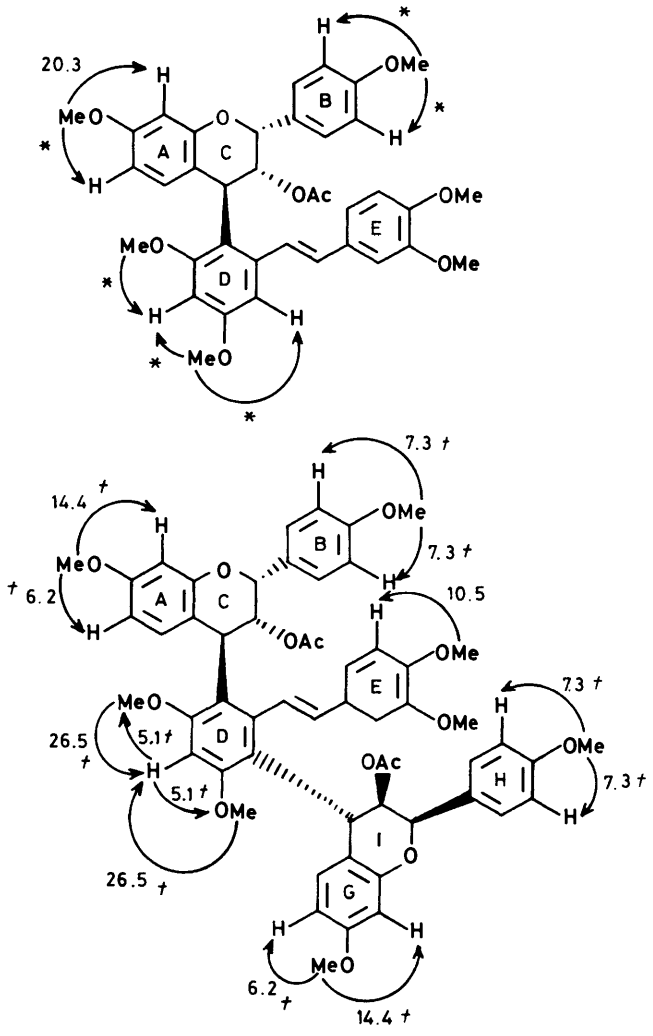


Figure 1. Percentage n.O.e. enhancements and n.O.e. associations in 2,3-*cis*-3,4-*trans*-guibourtinidol–stilbenes

* Percentage n.O.e. enhancements not available owing to partial signal overlap.

† Percentage n.O.e. enhancements reflect multiple effects due to the magnetic equivalence of protons of the ABC and GHI flavanoid systems.

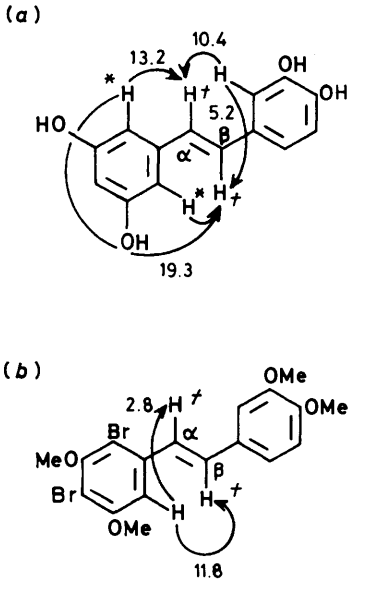


Figure 2. Percentage n.O.e. enhancements of α and β protons of (a) 3,3′,4,5′-tetrahydroxystilbene (in [$^2H_6$]acetone) and (b) 2′,4′-dibromo-3,3′,4,5′-tetramethoxystilbene ($CDCl_3$) on irradiation of (a) 2, 2′, and 6′ and (b) 6′ protons

* Multiple effects due to magnetically equivalent protons.

† α-H and β-H assignments are based on spin-decoupling experiments.

constants of heterocyclic ring protons of the corresponding derivative of the remaining stilbene-type 'trimer' (**16**) are virtually identical with those of the octamethyl ether diacetate (**14**) of the aforementioned stereochemically 'mixed' 'trimer'. Differences amount to the introduction of an additional AA_1BB_1 aromatic system coupled with reduction of the number of methoxy-proton resonance signals to seven. This indicates that 3′,4,5′-trihydroxystilbene (resveratrol[10]) serves as nucleophilic substrate during condensations in place of piceatannol.[9]

The relatively elevated energy requirements of methyl ether acetates of [4,2′]- or [4,2′:4,6′]-oligomers involving stilbenes, compared with those based on 6- and 8-substitution of catechin units,[6,7] may be ascribed to additional steric hindrance contributed by the 'rigid' α-methine proton of the vinylene system of stilbenes. This also implies that such steric hindrance induces non-coplanarity of the stilbene unit, thus raising its ground-state energy level, and ensuring equivalence of substituents at C-2′ and C-6′ as in the symmetrical [4,2′:4,6′]-bi-(2,3-*cis*-3,4-*trans*)-stilbene derivative (**18**). The same argument is apparently valid for 3,3′,4,5′-tetrahydroxystilbene and its tetra-*O*-methyl derivative where interaction between the α-methine proton and the 2- and 6-proton is presumably sufficient to promote non-coplanarity and hence magnetic equivalence of the latter pair. Nuclear Overhauser enhancement (n.O.e.) difference spectroscopy (Figure 2) in conjunction with conformational analysis using Van der Walls radii (Dreiding models) supports this notion through association of β-H with both 2-H(A) and 6-H(A), and α-H with both 2-H(B) and 6-H(B). This arrangement is possible if the α- and β-protons occupy an out-of-plane conformation relative to the aromatic A- and B-ring.

Additional steric effects contributed by flavanyl substituents on the stilbene are indicated by a gradational increase in both hypsochromic shifts and hypochromic effects indicative of progressive reduction in conjugation of stilbene units with increasing molecular complexity reflected in the sequence: stilbene tetramethyl ether (**20**) ($\lambda_{max.}$ 330 nm, log ε 4.34), stilbene-based 'dimeric' (**10**) ($\lambda_{max.}$ 319 nm, log ε 4.26), and 'trimeric' derivatives (**14**) and (**18**) ($\lambda_{max.}$ 307, 306 nm; log ε 4.09, 4.02 respectively). Similarly the greater dynamic mobility about 'interflavanyl' bonds in derivatives of the 'dimer' and 'trimer' of exclusive 2,3-*cis*-3,4-*trans* configuration [(**12**) and (**18**) respectively] compared with those isomers which incorporate 2,3-*trans*-3,4-*trans* units [(**10**) and (**14**)] must conceivably be due to the axial-3-acetoxy function of the former pair, compared with an equatorial orientation of the same functionality in the latter which would enhance steric interaction with the stilbene unit.

The remarkable rate of condensation of the flavan-3,4,4′,7-tetraols with (*E*)-stilbene-3,3′,4,5′-tetraol (**19**) is reflected, for example, in the synthesis of the [4,2′]-2,3-*trans*-3,4-*trans*-guibourtinidol–stilbene 'dimer' (**9**), the reaction running to completion in *ca.* 1 h compared with the *ca.* 8 h required for analogous condensation of (+)-mollisacacidin [(+)-2,3-*trans*-3,4-*trans*-3′,4′,7-trihydroxyflavan-3,4-diol] with (+)-catechin under strictly comparable conditions. This effect is attributed to the enhanced 'nucleophilicity' of the A-ring of the stilbene due

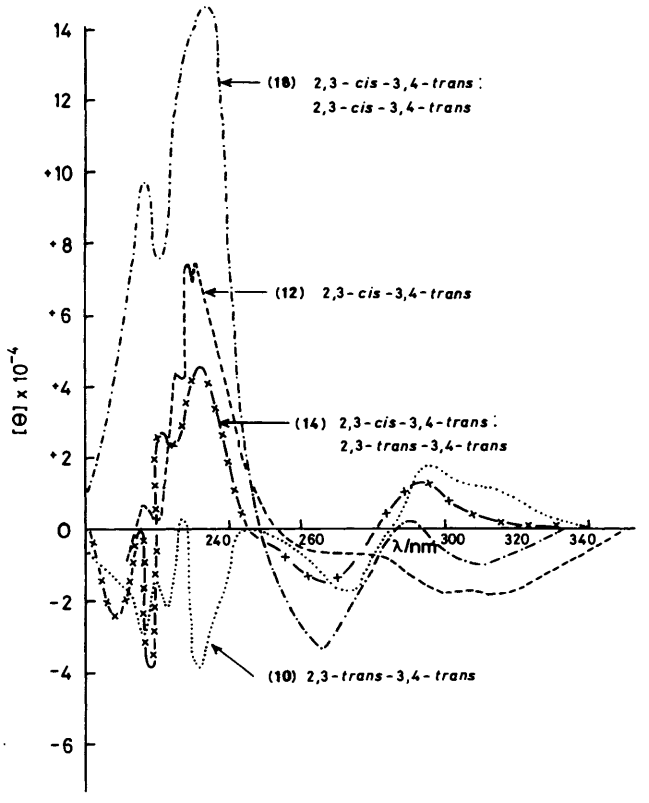
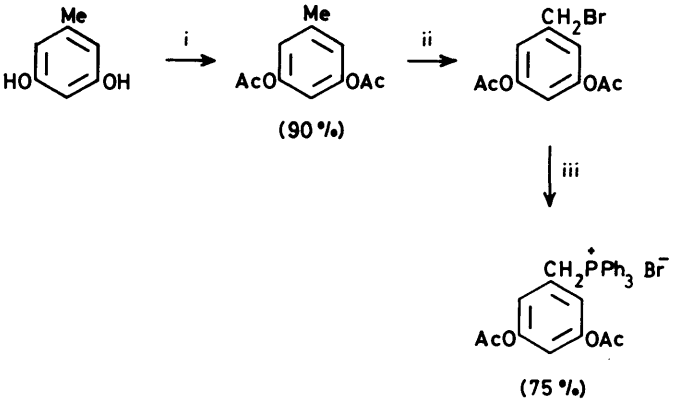


Figure 3. C.d. spectra of the hexamethyl ether acetates of [4,2′]-guibourtinidol–stilbenes (**10**) and (**12**) and octamethyl ether diacetates of [4,2′:4,6′]-biguibourtinidol–stilbenes (**14**) and (**18**) in methanol



Scheme. *Reagents*: i, Ac_2O, pyridine; ii, NBS, benzoyl peroxide, CCl_4; iii, PPh_3, benzene

to conjugation with the 4-OH function of the B-ring *via* the vinylene group. This results in efficient stabilization of the transition state during electrophilic attack in a reaction analogous (as regards 1,3,5-trisubstitution of each) to the rapid condensation with phloroglucinol.[11]

The relative 2,3-*cis*-3,4-*trans* stereochemistry of the flavanyl substituents on the stilbenes is based on the coupling constants of their heterocyclic protons: $J_{2,3}$ 3.0; $J_{3,4}$ 6.0 Hz for the 'dimer' (**12**) and $J_{2,3}$ 3.5, 4.0; $J_{3,4}$ 6.0, 6.5 Hz for the 'trimers' (**14**) and (**18**) respectively. Similarly, 2,3-*trans*-3,4-*trans* configurations ($J_{2,3}$ 9.80, 9.75; $J_{3,4}$ 9.80, 9.75 Hz) were allocated to the appropriate flavanyl substituents of the 'dimer' (**10**) and 'trimers' (**14**) and (**16**). The absolute configurations of these units as (2*R*,3*R*,4*R*) and (2*R*,3*S*,4*S*) respectively are accordingly defined by the method of synthesis from the flavan-3,4,4′,7-tetraols of known (2*R*) absolute configuration. The absolute stereochemistry of substituent units at C-4 was confirmed by positive Cotton effects at low wavelengths[11,12] for *cis-trans* compounds (**12**) and (**18**) and negative effects for the *trans-trans* compound (**10**) (Figure 3). 'Trimers' with flavanyl units of 'mixed' stereochemistry, (**14**) and (**16**), exhibit couplets in this region. Coupling constants for the oligomeric vinylene systems (*J* 16.0 Hz), where discernible, indicate a *trans* configuration for the stilbene system, confirmation being available for all oligomers *via* synthesis. Mass spectra of the 'dimeric' derivatives (**10**) and (**12**) show a fragment ion at *m/z* 283 representing typical methylene loss from the stilbene ion-radical (*m/z* 297).

Synthesis of the requisite 3,3′,4,5′-tetrahydroxystilbene (**19**) was carried out using a simplified Reimann[13] procedure, thus overcoming difficulties in arriving at 3,5-diacetoxybenzyl bromide required for formation of the phosphorus ylide in the sequence leading to the Wittig reaction. Orcinol (5-methylresorcinol) is used instead of α-resorcylic acid[13] as starting material in two simple steps (Scheme), isolation of the benzyl bromide intermediate being unnecessary. This modification should find general application in the synthesis of 3,5-dihydroxystilbenes, also on account of satisfactory yields.

Considering that the C-2 and C-6 positions on the resorcinol A-ring of the stilbene (**19**) involved in electrophilic aromatic substitution by flavanyl units are both subject to considerable steric hindrance, attempts were made to confirm the apparent lack of involvement of C-4 by bromination. However, reaction of molar equivalents of *trans*-3,3′,4,5′-tetrahydroxystilbene (**19**) and pyridinium bromide perbromide under 'controlled' conditions gave 2′-bromo- (**23**) and 2′,4′-dibromo-stilbene (**25**) derivatives and unchanged stilbene in almost equivalent amounts. The position of substitution for the 2′-bromo derivative was obvious from conversion of the *meta*-coupled A_2B aromatic proton A-ring system of piceatannol (two proton doublet and triplet) to a *meta*-coupled AB-system in the derivative; and also from equivalence of the 3′- and 5′-methoxy resonances in the unsubstituted tetramethyl ether to their non-equivalence in the 2′-bromo tetramethyl ether derivative (**24**). Similar observation as regards the non-equivalence of the four methoxy-proton resonances in the 2′,4′-dibromotetramethoxy derivative (**26**) is conclusive in defining asymmetric substitution on the A-ring. However, its hydrogenation to the corresponding dihydrostilbene enabled demonstration of long-range coupling between 6′-H(A) and the α CH_2 group in full support of the structural allocation.

This result provides strong evidence of preferential substitution at C-2′ of the A-ring of the stilbene. Presumed sequential entry of the second bromine at C-4′ in contrast to [2′,6′]-biflavanyl substitution most likely results from lack of selectivity during offering of bromine on a molar equivalent basis due to a fast reaction rate, as indicated by the substantial recovery of unbrominated stilbene. By contrast slower 2′,6′-disubstitution using two molar equivalents of the bulky flavanyl 4-carbocation may be the product of greater regioselectivity.

Some of the putative participants in the formation of proguibourtinidin–stilbenes are in evidence in the heartwood of *G. coleosperma* as a complete series of 2,3-*trans*- [(**1**) and (**3**)], and 2,3-*cis*- [(**5**) and (**7**)] flavan-3,4,4′,7-tetraols, which were isolated for the first time (*cf.* ref. 4). The ^1H n.m.r. spectra of their dimethyl ether diacetates were in exact agreement with those of the synthetic racemates.[4] By contrast the predominant 3,3′4,5′-tetrahydroxystilbene 'nucleophilic substrate' occurs in the sapwood as the 3′-*O*-glucoside (**21**), but is absent from the heartwood. Its quantitative removal during condensation in the latter environment is to be anticipated considering demon-

stration of its high reactivity during *in vitro* synthesis. The proportion in which 2,3-*cis*- and 2,3-*trans*-flavanyl units occur in the guibourtinidol–stilbene oligomers is reflected in the relative occurrence of flavan-3,4-diols of corresponding stereochemistry, the 2,3-*cis*-3,4-*trans* isomer being predominant. Stereospecificity, as reflected in 2,3-*cis*-3,4-*trans*- and 2,3-*trans*-3,4-*trans*-flavanyl substituents in the oligomers, may be rationalized in terms of neighbouring group participation (*via* the axial 3-OH) in condensations involving 2,3-*cis*-flavanyl carbenium ions, and heightened stereocontrol contributed by the bulk of the stilbene substrate at the point of substitution (repulsive effect of the axial 2-H) when involving 2,3-*trans*-flavanyl carbenium ions.

Conversions which occur very readily in (*E*)-stilbene oligomers on access of indirect light was illustrated by exposure of the [4′,2′]-guibourtinidol–stilbene hexamethyl ether acetate (**12**) to direct sunlight, which resulted in a 1:1 equilibrium mixture of *E* and *Z* (**22**) isomers.

Experimental

^{1}H N.m.r. spectra were recorded on Bruker WP-80 FT, AM-300, and WM-500 spectrometers in $CDCl_3$ and $(CD_3)_2SO$ ([$^2H_6$]DMSO) as solvents with Me_4Si as internal standard. Tubes were firmly stoppered to avoid solvent loss where spectra were recorded above (100 °C) the boiling point of $CDCl_3$. Mass spectra were obtained with a Varian CH-5 instrument and c.d. data in methanol on a Jasco J-20 spectropolarimeter. T.l.c. was performed on precoated Merck plastic sheets (silica gel 60 PF_{254}, 0.25 mm) and were sprayed with H_2SO_4–HCHO (40:1 v/v) after development. Preparative plates (p.l.c.), 20 × 20 cm, Kieselgel PF_{254} (1.0 mm) were air-dried and used without prior activation. Where R_F differences were small, efficient p.l.c. separation was obtained on Merck DC-Fertigplatten Kieselgel 60 F_{254}, 0.25 mm. Two-way paper chromatograms on Whatman No. 1 paper (28.5 × 46 cm) were developed successively in butan-2-ol and 2% acetic acid. After drying, components were located under u.v. light or with the aid of spray reagents. Separations on Sephadex LH-20 columns (2.6 and 5 × 125 cm) were in ethanol applying *ca.* 2.0 g or 20 g respectively depending on the complexity of the phenolic mixture. Fractions (25 ml each) were collected on a rotary fraction collector, starting with the first emergence of phenolic material.

Alkali fusions were performed under anhydrous conditions. Methylations were with an excess of diazomethane in methanol–diethyl ether over 48 h at −15 °C while acetylations were in acetic anhydride–pyridine at room temperature. Evaporations were done under reduced pressure at *ca.* 60 °C in a rotary evaporator. N.m.r. spectra (300 and 500 MHz) provided criteria of purity of the various diastereoisomers.

Isolation of Flavan-3,4,4′,7-tetraols

Air-dried drillings (660 g) of the heartwood of *Guibourtia coleosperma* were extracted with methanol in a Soxhlet apparatus. After evaporation the solid extractives (85 g, 12.8% yield) were redissolved in methanol (300 ml) and extracted with hexane (4 × 300 ml). The dewaxed extract (2 × 20 g) was separated on two columns (5 × 125 cm) with Sephadex LH-20 as substrate and ethanol as eluant. Fractions were collected as follows at a flow rate of 25 ml/30 min: Fractions 1—42 (1.68 g), 43—72 (1.85 g), 73—100 (1.00 g), and 101—126 (0.60 g). The grouped fraction 43—72 gave, after p.l.c. separation in benzene–acetone–methanol (7:2:1 by vol.), the sub-fractions at R_F 0.42 (427 mg), 0.33 (77 mg), 0.28 (464 mg), and 0.14 (117 mg).

(2R,3S,4S)-2,3-cis-3,4-trans-3,4-*Diacetoxy*-4′,7-*dimethoxyflavan* (**8**).—Methylation of the R_F 0.28 fraction (464 mg) and p.l.c. separation of the product in benzene–acetone (8:2 v/v) gave a single prominent compound at R_F 0.34 (278 mg). Acetylation followed by crystallization from ethanol gave the 2,3-*cis*-3,4-*trans* dimethyl ether diacetate (**8**) (289 mg) as prisms, m.p. 108—109 °C (lit.,[4] 109—110 °C for the racemate), with ^{1}H n.m.r. spectrum identical with that of the synthetic racemate;[4] c.d. spectrum $[\theta]_{220}$ +1 000, $[\theta]_{203}$ +2 700, $[\theta]_{204}$ + 2 400, $[\theta]_{227}$ +5 900, $[\theta]_{228}$ +5 100, $[\theta]_{231}$ +7 800, $[\theta]_{234}$ +5 200, $[\theta]_{236}$ +6 300, $[\theta]_{245}$ 0, $[\theta]_{266}$ −2 900, and $[\theta]_{290}$ 0.

The grouped fraction 73—100 when subjected to p.l.c. separation in benzene–acetone–methanol (7:2:1 by vol.) gave sub-fractions at R_F 0.52 (50.5 mg), 0.43 (568 mg), 0.30 (31.8 mg), and 0.22 (37.8 mg). Methylation of the R_F 0.43 sub-fraction (568 mg) gave a product which, after p.l.c. in benzene–acetone (17:3 v/v), gave two compounds at R_F 0.33 (95 mg) and 0.27 (140 mg).

(2R,3R,4S)-2,3-trans-3,4-cis-3,4-*Diacetoxy*-4′,7-*dimethoxyflavan* (**4**).—Acetylation of the R_F 0.33 methyl ether (95 mg), which crystallized from ethanol as needles, m.p. 143 °C (lit.,[14] 144 °C), gave the 2,3-*trans*-3,4-*cis* dimethyl ether diacetate (**4**) as a non-crystalline solid, with ^{1}H n.m.r. spectrum identical with that of the synthetic racemate;[4] c.d. spectrum $[\theta]_{220}$ +1 200, $[\theta]_{222}$ +1 050, $[\theta]_{231}$ +8 200, $[\theta]_{232}$ +7 900, $[\theta]_{236}$ +11 000, $[\theta]_{250}$ +600, $[\theta]_{266}$ +1 100, and $[\theta]_{282}$ 0.

(2R,3R,4R)-2,3-trans-3,4-trans-3,4-*Diacetoxy*-4′7-*dimethoxyflavan* (**2**).—Acetylation of the R_F 0.27 methyl ether (140 mg), which crystallized from aqueous ethanol as needles, m.p. 75 °C (lit.,[14] 75 °C), followed by crystallization of the product from ethanol gave the 2,3-*trans*-3,4-*trans* dimethyl ether diacetate (**2**) as needles (144 mg), m.p. 105 °C (lit.,[14] 106 °C), with ^{1}H n.m.r. spectrum identical with that of the synthetic racemate;[4] c.d. spectrum $[\theta]_{225}$ 0, $[\theta]_{231}$ −16 300, $[\theta]_{233}$ −10 500, $[\theta]_{234}$ −11 900, $[\theta]_{248}$ −1 500, $[\theta]_{268}$ −3 850, and $[\theta]_{290}$ 0.

The grouped fraction 101—126, on p.l.c. separation in benzene–acetone–methanol (6:3:1 by vol.), gave sub-fractions at R_F 0.53 (40 mg), 0.47 (118 mg), 0.41 (60 mg), and 0.31 (38 mg). Methylation of the R_F 0.43 sub-fraction (118 mg) yielded a product which, after p.l.c. in benzene–acetone (8:2 v/v), gave two compounds at R_F 0.50 (12 mg) and 0.42 (49 mg).

(2R,3S,4R)-2,3-cis-3,4-cis-3,4-*Diacetoxy*-4′,7-*dimethoxyflavan* (**6**).—Acetylation of the R_F 0.42 compound (49 mg) followed by crystallization from ethanol gave the 2,3-*cis*-3,4-*cis* dimethyl ether diacetate as needles, m.p. 142—143 °C [lit.,[4] m.p. 143—144 °C (racemate)]; c.d. spectrum $[\theta]_{200}$ −5 530, $[\theta]_{207}$ −11 430, $[\theta]_{210}$ 0, $[\theta]_{213}$ +3 130, $[\theta]_{215}$ +740, $[\theta]_{222}$ +11 800, $[\theta]_{225}$ 0, $[\theta]_{227}$ −4 600, $[\theta]_{231}$ −600, $[\theta]_{233}$ −1 400, $[\theta]_{248}$ −300, $[\theta]_{270}$ −400, and $[\theta]_{290}$ 0.

Isolation of Oligomeric Flavanoids with a Stilbene as 'Nucleophile'

Air-dried drillings (3 kg) from the heartwood of *G. coleosperma* were extracted exhaustively with water-saturated EtOAc at ambient temperature. After removal of the solvent the crude extract (100 mg, 3.3% yield) was dissolved in methanol (2 × 300 ml portions) and each portion was extracted with hexane (4 × 300 ml). The recovered dewaxed phenols (98 g) were dissolved in the lower phase (500 ml) of a mutually saturated water–butan-2-ol–n-hexane mixture (5:3:2 by vol.) and the solution was introduced into the first ten tubes (50 ml each) of a 150-tube Craig countercurrent apparatus. After 150 transfers the contents of the tubes were grouped as follows: Tubes 35—75 (5.6 g), 76—110 (17.8 g), 111—115 (7.9 g), 116—135 (56.6 g), and 136—150 (4.3 g).

Fraction 116—135 was separated on 8 columns (2.5 × 125 cm) (7 g per column) with Sephadex LH-20 as substrate and ethanol as eluant. Sub-fractions (25 ml each) were collected as follows from each and were combined: Sub-fractions 98—146 (3.5 g), 147—235 (7.5 g), and 236—270 (6.2 g). The sub-fraction 147—235 gave, after p.l.c. separation in benzene–acetone–methanol (6:3:1 by vol.), phenolic fractions at R_F 0.47 (1.056 g), 0.41 (586 mg), 0.37 (1.02 g), and 0.30 (832 mg).

Methylation of the phenolic fraction R_F 0.47 yielded a major component at R_F 0.36 (192 mg) after p.l.c. in benzene–acetone (9:1 v/v). After acetylation of the methyl ether, p.l.c. of the product in benzene–acetone (98:2 v/v, × 3) gave two fractions, at R_F 0.45 (61 mg) and 0.35 (52 mg).

(E)-2-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4'7-*dimethoxyflavan*-4-*yl*]-3,3',4',5-*tetramethoxystilbene* (**12**).—The R_F 0.45 hexamethyl ether acetate (**12**) was isolated as a *solid* (Found: C, 70.6; H, 6.0%; M^+, 626.2513. $C_{37}H_{38}O_9$ requires C, 70.9; H, 6.1%; *M*, 626.2516); δ([$^2H_6$]DMSO; 500 MHz; 170 °C) 7.253 [d, *J* 8.5 Hz, 2-H(B) + 6-H(B)], 6.995 (br d, *J* 15.7 Hz, α-H), 6.949 [br s, 2-H(E)], 6.893 [d, *J* ~8.5 Hz, 5-H(E)], 6.879 [d, *J* 8.5 Hz, 3-H(B) + 5-H(B)], 6.866 [dd, *J* 1.5 and ~8.5 Hz, 6-H(E)], 6.824 (d, *J* 15.7 Hz, β-H), 6.753 [d, *J* 2.2 Hz, 6-H(D)], 6.618 [d, *J* 8.5 Hz, 5-H(A)], 6.550 [d, *J* 2.2 Hz, 4-H(D) + 8-H(A)], 6.439 [dd, *J* 2.2 and 8.5 Hz, 6-H(A)], 5.600 [dd, *J* 3.0 and 6.0 Hz, 3-H(C)], 5.466 [d, *J* 2.0 Hz, 2-H(C)], 4.605 [d, *J* 6.0 Hz, 4-H(C)], 3.860, 3.810 (× 2), 3.770, 3.760, and 3.590 (each s, 6 × OMe), and 1.820 [s, 3-OAc(C)]; c.d. spectrum (Figure 3).

(E)-2'-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*Acetoxy*-4',7-*dimethoxyflavan*-4-*yl*]-3,3',4,5'-*tetramethoxystilbene* (**10**).—The R_F 0.35 methyl ether acetate (**10**) was isolated as a *solid* (Found: C, 70.7; H, 6.25%; M^+, 626.2477); δ([$^2H_6$]DMSO; 300 MHz; 180 °C) 7.290 [d, *J* 8.75 Hz, 2-H(B) + 6-H(B)], 6.943 (br d, *J* ~15.5 Hz, α-H), 6.845 [d, *J* 8.75 Hz, 3-H(B) + 5-H(B)], 6.788 (br d, *J* ~15.5 Hz, β-H), 6.700 [d, *J* 2.3 Hz, 6-H(D)], 6.573 [d, *J* 8.5 Hz, 5-H(A)], 6.497 [br d, *J* 2.3 Hz, 4-H(D)], 6.443 [d, *J* 2.3 Hz, 8-H(A)], 6.408 [dd, *J* 2.3 and 8.5 Hz, 6-H(A)], 5.683 [t, *J* 9.8 Hz, 3-H(C)], 5.000 [br d, *J* 9.8 Hz, 4-H(C)], 4.972 [d, *J* 9.8 Hz, 2-H(C)], 3.812 (× 2), 3.797, 3.766, and 3.689 (× 2) (each s, 6 × OMe), and 1.531 [s, 3-OAc(C)]; c.d. spectrum (Figure 3).

Mass fragmentation spectra of compounds (**12**) and (**10**) were respectively: *m/z* 626 (M^+ 66, 51%), 584 (71, 2.3), 5.66 (51, 38), 445 (74, 55), 434 (85, 98), 415 (76, 69), 414 (67, 40), 403 (36, 29), 299 (4.9, 3.3), 297 (14.6, 9.2), 296 (9.7, 3.6), 283 (60, 14.6), 282 (100, 4.8), 267 (15.4, 9.9), 192 (2.2, 2.0), 151 (79, 55), 150 (34, 24), and 121 (90, 100).

Methylation of the free phenolic fraction R_F 0.37 from the 147—235 fraction from the Sephadex column gave a mixture of methyl ethers, which after p.l.c. in benzene–acetone (8:2 v/v, × 2) gave three products, at R_F 0.45 (126 mg), 0.42 (112.8 mg), and 0.40 (104 mg).

(E)-2'-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4',7-*dimethoxyflavan*-4-*yl*]-6'-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*acetoxy*--4',7-*dimethoxyflavan*-4-*yl*]-3,4,5'-*trimethoxystilbene* (**16**).—Acetylation of the R_F 0.45 methyl ether (126 mg) followed by p.l.c. in benzene–acetone (98:2 v/v, × 4) gave three sub-fractions: R_F 0.49 (21.9 mg), 0.31 (4.5 mg), and 0.29 (3.6 mg). Repurification of the R_F 0.49 component in hexane–acetone–ethyl acetate (65:20:15 by vol., × 4) yielded the 'trimeric' derivative (**16**), R_F 0.53 (16.5 mg) as a *solid* (Found: M^+, 922.3557. $C_{55}H_{54}O_{13}$ requires *M*, 922.3564); δ([$^2H_6$]DMSO; 80 MHz; 170 °C) 7.39—6.31 (m, 19 × ArH + α- and β-H), 5.88 [t, *J* 9.75 Hz, 3-H(C)], 5.78 [dd, *J* 3.75 and 6.75 Hz, 3-H(I)], 5.47 [d, *J* 3.75 Hz, 2-H(I)], 4.94 [br d, *J* 9.75 Hz, 4-H(C)], 4.86 [d, *J* 9.75 Hz, 2-H(C)], 4.58 [d, *J* 6.75 Hz, 4-H(I)], 3.82, 3.81, 3.77, 3.74 (× 2), 3.66, and 3.61 (each s, 7 × OMe), 1.75 [s, 3-OAc(I)], and 1.63 [s, 3-OAc(C)]; *m/z* 922 (M^+, 5.1%), 862 (21), 802 (49), 730 (35), 699 (13.5), 639 (5.8), 535 (2.9), 268 (4.4), 267 (17.1), 192 (0.8), 150 (16.7), and 121 (100); c.d. spectrum $[\theta]_{200}$ −10 000, $[\theta]_{213}$ −50 000, $[\theta]_{217}$ −37 000, $[\theta]_{218}$ −41 000, $[\theta]_{222}$ 0, $[\theta]_{230}$ +33 000, $[\theta]_{243}$ 0, $[\theta]_{264}$ −12 000, $[\theta]_{280}$ 0, $[\theta]_{286}$ +10 000, and $[\theta]_{327}$ 0.

(E)-2',6'-*Bis*-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*acetoxy*-4',7-*dimethoxyflavan*-4-*yl*]-3,3',4,5'-*tetramethoxystilbene* (**18**).—Acetylation of the R_F 0.42 methyl ether fraction (112.8 mg) followed by p.l.c. in benzene–acetone (95:5 v/v) gave two compounds, at R_F 0.52 (80 mg) and 0.39 (10 mg). Further purification by p.l.c. in dichloromethane–acetone (99:1 v/v, × 8) of the R_F 0.52 fraction yielded the *title product* (**18**), R_F 0.55 (70 mg), as a *solid* (Found: C, 70.5; H, 6.0%; M^+, 952.3686. $C_{56}H_{56}O_{14}$ requires C, 70.6; H, 5.9%; *M*, 952.3670); δ([$^2H_6$]DMSO; 500 MHz; 150 °C) 7.186 [d, *J* 8.5 Hz, 2-H(B), 6-H(B), 2-H(H), +6-H(H)], 6.820 [d, *J* 8.5 Hz, 5-H(E)], 6.732 [d, *J* 8.5 Hz, 3-H(B), 5-H(B), 3-H(H), +5-H(H)], 6.662 [s, 4-H(D)], 6.642 [br d, *J* ~1.0 Hz, 2-H(E)], 6.604 [br d, *J* ~16 Hz, α-H], 6.545 [br d, *J* 8.5 Hz, 6-H(E)], 6.509 [d, *J* 8.5 Hz, 5-H(A) + 5-H(G)], 6.468 [d, *J* 2.5 Hz, 8-H(A) + 8-H(G)], 6.425 [dd, *J* 2.5 and 8.5 Hz, 6-H(A) + 6-H(G)], and 6.185 [d, *J* 16.0 Hz, β-H]; δ($CDCl_3$; 80 MHz; 100 °C) 5.82 [dd, *J* 3.5 and 5.75 Hz, 3-H(C) + 3-H(I)], 5.53 [d, *J* 3.5 Hz, 2-H(C) + 2-H(I)], 4.58 [d, *J* 5.75 Hz, 4-H(C) + 4-H(I)], 3.84, 3.80, 3.75 (× 2), 3.70 (× 2), and 3.50 (× 2) (each s, 8 × OMe), and 1.75 [s, 3-OAc(C) + 3-OAc(I)]; c.d. spectrum (Figure 3).

(E)-2'-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4',7-*dimethoxyflavan*-4-*yl*]-6'-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*acetoxy*-4',7-*dimethoxyflavan*-4-*yl*]-3,3',4,5'-*tetramethoxystilbene* (**14**).—Acetylation of the R_F 0.40 methyl ether fraction (104 mg) followed by p.l.c. in benzene–acetone (95:5 v/v, × 3) gave the substituted stilbene of 'mixed' stereochemistry (**14**) as a *solid*, R_F 0.33 (100 mg) (Found: C, 70.5; H, 6.1%; M^+, 952.3695); δ([$^2H_6$]DMSO; 80 MHz; 170 °C) 7.39—6.31 (m, 18 × ArH + α- and β-H), 5.89 [t, *J* 9.75 Hz, 3-H(C)], 5.77 [dd, *J* 3.75 and 6.75 Hz, 3-H(I)], 5.45 [d, *J* 3.75 Hz, 2-H(I)], 4.95 [br d, *J* ~9.75 Hz, 4-H(C)], 4.88 [d, *J* 9.75 Hz, 2-H(C)], 4.59 [d, *J* 6.75 Hz, 4-H(I)], 3.81, 3.78, 3.77, 3.74 (× 2), 3.71, 3.69, and 3.59 (each s, 8 × OMe), 1.72 [s, 3-OAc(I)], and 1.60 [s, 3-OAc(C)], c.d. spectrum (Figure 3).

Mass fragmentation spectra of compounds (**18**) and (**14**) were respectively: *m/z* 952 (M^+, 15.2, 14.2%), 892 (48, 41), 832 (68, 10.4), 760 (55, 60), 729 (49, 29), 669 (18.8, 14.7), 565 (11.6, 7.9), 298 (4.5, 1.6), 267 (53, 63), 192 (3.7, 3.6), 150 (49, 52), and 121 (100, 100).

(E)-*Stilbene*-3,3',4,5'-*tetraol* (*Piceatannol*) (**19**)

Synthesis.—The stilbene was synthesized according to the general method for free-phenolic stilbenes developed by Reimann,[13] but modified as regards the route leading to 3,5-dihydroxybenzyl(triphenyl)phosphonium bromide (see Scheme).

3,5-*Diacetoxytoluene*. Anhydrous orcinol (5-methylresorcinol) (10.3 g) was acetylated to give the diacetate (15.17 g, 90.5% yield).

3,5-*Diacetoxybenzyl bromide*. 3,5-Diacetoxytoluene (15 g) was dissolved in dry tetrachloromethane (300 ml). After addition of freshly recrystallized *N*-bromosuccinimide (NBS) (12.8 g) and catalytic amounts of benzoyl-peroxide, the mixture was refluxed for 3 h. After the mixture had cooled, the succinimide was removed by filtration, and the solvent was removed under reduced pressure. The residual 3,5-diacetoxybenzyl bromide was taken up directly in dry benzene and treated with triphenylphosphine (18.91 g) in dry benzene (100

ml) under reflux for 6 h, during which time 3,5-diacetoxybenzyl-(triphenyl)phosphonium bromide precipitated as a white salt. After being washed with benzene the salt (32.52 g, 75%), m.p. 247 °C (lit.,[13] 249—251 °C) was used directly[13] in the synthesis of 3,5-dihydroxybenzyl(triphenyl)phosphonium bromide (80% yield), and its condensation with 3,4-bis(trimethylsiloxy)-benzaldehyde to form the desired stilbene (**19**) (5.3 g, 51%) as needles from water, m.p. 229 °C (lit.,[13] 229 °C); δ[$(CD_3)_2CO$; 300 MHz; 30 °C] 7.082 [d, *J* 2.1 Hz, 2-H(B)], 6.958 (d, *J* 16.6 Hz, α-H), 6.912 [dd, *J* 2.1 and 8.1 Hz, 6-H(B)], 6.825 (d, *J* 16.6 Hz, β-H), 6.810 [d, *J* 8.1 Hz, 5-H(B)], 6.532 [d, *J* 2.2 Hz, 2-H(A) + 6-H(A)], and 6.266 [t, *J* 2.2 Hz, 4-H(A)].

Isolation.[15]—Air-dried drillings from the heartwood of *Pericopsis angolensis* were ground to a fine mesh size, dried at 60 °C for 24 h, and extracted in a Soxhlet apparatus successively with diethyl ether and methanol to give a pale yellow oil (11 g) and a brown solid (9 g) respectively after removal of the solvents. P.l.c. of the solid in benzene–acetone–methanol (6:3:1 by vol.) gave a single prominent fraction at R_F 0.45 (2 g). Crystallization from water gave stilbene-3,3′,4,5′-tetraol (**19**) as pale yellow needles, m.p. 225—226 °C (lit.,[15] 225—227 °C).

Selective Bromination of (E)-*Stilbene*-3,3′,4,5′-*tetraol* (**19**)

(*E*)-Stilbene-3,3′,4,5′-tetraol (300 mg) was dissolved in methanol (10 ml) and the solution was cooled to 0 °C. A solution of pyridinium bromide perbromide (393 mg) in methanol (10 ml) was added dropwise during 20 min, after which the mixture was allowed to come to room temperature gradually. After removal of the methanol under reduced pressure the product was subjected to p.l.c. in trichloromethane–methanol (9:1 v/v). Three fractions were obtained, at R_F 0.53 (69 mg), 0.43 (77 mg), and 0.36 (80 mg); the R_F 0.36 fraction representing unchanged stilbenetetraol.

(E)-2′,4′-*Dibromo*-3,3′,4,5′-*tetramethoxystilbene* (**26**).—Methylation of the R_F 0.53 fraction followed by p.l.c. of the product in benzene–acetone (9:1 v/v) afforded the dibromostilbene derivative (**26**), R_F 0.53 (35 mg), which crystallized from methanol as *pale yellow needles*, m.p. 142 °C (Found: M^+, 457.9573. $C_{18}H_{18}{}^{79}Br^{81}BrO_4$ requires *M*, 457.9553); δ(C_6H_6; 80 MHz; 30 °C) 7.55 (d, *J* 16.25 Hz, α-H), 7.10 [d, *J* 2.25 Hz, 2-H(B)], 7.09 [dd, *J* 2.25 and 9.0 Hz, 6-H(B)], 6.97 (d, *J* 16.25 Hz, β-H), 6.75 [s, 6-H(A)], 6.60 [d, *J* 9.0 Hz, 5-H(B)], and 3.75, 3.48, 3.44, and 3.30 (each s, 4 × OMe); *m/z* 460 (M^+, 28%), 458 (M^+, 54), 456 (M^+, 29), 298 (100), 283 (9.9), 268 (13.6), 150 (4.1), and 148 (11.7).

2′,4′-*Dibromo*-3,3′,4,5′-*tetramethoxydihydrostilbene.*—Hydrogenation (PtO_2, ethanol) of the dibromostilbene tetramethyl ether (**26**) (35 mg) followed by p.l.c. of the product in benzene–acetone (9:1 v/v) gave the title dihydrostilbene as a *pale yellow solid* (Found: M^+, 459.9741. $C_{18}H_{20}{}^{79}Br^{81}BrO_4$ requires *M*, 459.9711); δ($CDCl_3$; 300 MHz; 19 °C) 6.80 [d, *J* 8.25 Hz, 5-H(B)], 6.723 [dd, *J* 1.75 and 8.25 Hz, 6-H(B)], 6.692 [d, *J* 1.75 Hz, 2-H(B)], 6.449 [s, 6-H(A)], 3.890, 3.867, 3.857, and 3.793 (each s, 4 × OMe), 3.013 (m, α-H_2), and 2.848 (m, β-H_2).

(E)-2′-*Bromo*-3,3′,4,5′-*tetramethoxystilbene* (**24**).—Methylation of the R_F 0.43 fraction followed by p.l.c. of the product in benzene–acetone (9:1 v/v) gave the monobromo derivative (**24**), R_F 0.52 (62 mg), as *pale yellow needles*, m.p. 112 °C (from methanol) (Found: M^+, 380.0432. $C_{18}H_{19}{}^{81}BrO_4$ requires *M*, 380.0447); δ($CDCl_3$; 300 MHz; 19 °C) 7.393 (d, *J* 16.5 Hz, α-H), 7.103 [d, *J* 2.0 Hz, 2-H(B)], 7.103 [dd, *J* 2.0 and 9.0 Hz, 6-H(B)], 6.966 [d, *J* 16.5 Hz, β-H], 6.873 [d, *J* 9.0 Hz, 5-H(B)], 6.797 [d, *J* 2.75 Hz, 6-H(A)], 6.423 [d, *J* 2.75 Hz, 4-H(A)], and 3.967, 3.917, 3.900, and 3.870 (each s, 4 × OMe); *m/z* 380 (M^+, 28%), 378 (25), 299 (100), 284 (43), 269 (16.5), 268 (42), 150 (5.2), and 149 (23).

Synthesis of Oligomeric Flavonoids with Stilbene as Nucleophile

Acid-catalysed Condensation of (2R,3R,4S)-2,3-cis-3,4-trans-*flavan*-3,4′,7-*tetraol* (**7**) *with* (E)-*stilbene*-3,3′,4,5′-*tetraol* (**19**).—A solution of the 2,3-*cis*-3,4-*trans*-flavan-3,4-diol (**7**) (352 mg) in aqueous 0.1M-HCl (50 ml) was added dropwise to a stirred aqueous solution of (*E*)-stilbene-3,3′,4,5′-tetraol (**19**) (940 mg). After 1 h the reaction mixture was extracted with ethyl acetate and the extract was dried (Na_2SO_4). The residue (1.2 g) remaining after removal of the solvent under reduced pressure was subjected to column (6 × 60 cm) chromatography on Sephadex LH-20 with ethanol as solvent. Fractions (25 ml) obtained on introduction of the product were combined as follows: fractions 13—23 (570 mg) and 29—52 (415 mg). Fraction 13—23 consisted of unchanged stilbene (**19**). Fraction 29—52 was methylated, the product giving a single compound, R_F 0.38 (197 mg), on p.l.c. in benzene–acetone (97:3 v/v, × 2). (E)-2′-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4′,7-*dimethoxy*-*flavan*-4-*yl*]-3,3′,4,5′-*tetramethoxystilbene* (**12**). Acetylation of the R_F 0.38 (197 mg) methyl ether gave the acetate as a solid, with 500 MHz ^{1}H n.m.r., mass fragmentation, and c.d. spectrometric properties identical with those of the hexamethyl ether acetate derived from *G. coleosperma*.

(Z)-2′-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4′,7-*dimeth*-*oxyflavan*-4-*yl*]-3,3′,4,5′-*tetramethoxystilbene* (**22**).—The (*E*)-isomer (**12**) (100 mg) in ethanol (25 ml) was exposed to direct sunlight for 48 h, after which the isomeric mixture was separated by p.l.c. in benzene–acetone (97:3 v/v, × 2). Two fractions, R_F 0.38 (50 mg) and R_F 0.36 (30 mg), representative of the (*E*)- and (*Z*)-isomer respectively, were isolated, the latter as a solid.

The purity of the product, and *Z* stereochemistry of its stilbene moiety, were established by high-temperature high-resolution n.m.r. spectroscopy; δ([$^2H_6$]DMSO; 300 MHz; 180 °C) 7.145 [d, *J* 9.0 Hz, 2-H(B) + 6-H(B)], 6.823 [d, *J* 9.0 Hz, 3-H(B) + 5-H(B)], 6.767 [d, *J* 8.0 Hz, 5-H(E)], 6.713 [d, *J* 2.25 Hz, 2-H(E)], 6.685 [dd, *J* 2.25 and 8.0 Hz, 6-H(E)], 6.516 [d, *J* 2.75 Hz, 6-H(D)], 6.488 [dd, *J* 1.0 and 8.5 Hz, 5-H(A)], 6.473 [d, *J* 2.50 Hz, 8-H(A)], 6.365 [d, *J* 2.75 Hz, 4-H(D)], 6.357 (d, *J* 12.0 Hz, α-H), 6.307 [dd, *J* 2.50 and 8.50 Hz, 6-H(A)], 6.292 (d, *J* 12.0 Hz, β-H), 5.547 [dd, *J* 3.0 and 5.5 Hz, 3-H(C)], 5.360 [d, *J*3.0 Hz, 2-H(C)], 4.428 [d, *J* 5.5 Hz, 4-H(C)], 3.767, 3.763, 3.737, 3.673, 3.573, and 3.543 (each s, 6 × OMe), and 1.675 [s, 3-OAc(C)].

(E)-2′,6′-*Bis*-[(2R,3S,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4′,7-*dimethoxyflavan*-4-*yl*]-3,3′,4,5′-*tetramethoxystilbene* (**18**).—The 2,3-*cis*-3,4-*trans*-flavan-3,4-diol (**7**) (394 mg) and the tetrahydroxystilbene (**19**) (175 mg) were condensed under the conditions described above. After 3 h the reaction mixture (560 mg) was separated on a Sephadex LH-20 column with ethanol as eluant, to give combined fractions 6—14 (10 mg), 58—72 (24 mg), and 74—84 (390 mg). Fraction 6—14 consisted of unchanged flavan (**7**), and fraction 58—72 was the 2,3-*cis*-3,4-*trans*-flavan-4-ylstilbene 'dimer'.

Methylation of fraction 74—84 followed by p.l.c. in benzene–acetone (9:1 v/v) gave a single product, R_F 0.29 (310 mg). Acetylation of the methyl ether gave the octamethyl ether diacetate (**18**) of the 2,6-bis-(2,3-*cis*-3,4-*trans*-flavan-4-yl)stilbene as a solid, with ^{1}H n.m.r., mass, and c.d. spectra identical with those of the corresponding derivative derived from *G. coleosperma*.

Acid-catalysed Condensation of the (2R,3S)-2,3-trans-*Flavan*-3,4,4′,7-*tetraol Isomeric Mixture* (**1**) *and* (**3**) *with* (E)-*Stilbene*-

3,3′,4,5′-*tetraol* (**19**).—Condensation of the 2,3-*trans*-flavan-3,4-diols (350 mg) and the tetrahydroxystilbene (935 mg) for 1 h under conditons described above gave free-phenolic material (1.27 g). Fractionation on a Sephadex LH-20 column (ethanol as eluant) gave two combined fractions 23—29 (680 mg) and 57—80 (330 mg). The first of these represented unchanged stilbene (**19**), and methylation of the second fraction followed by p.l.c. in benzene–acetone (9:1 v/v) yielded a single product, R_F 0.45 (190 mg).

(E)-2′-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*Acetoxy*-4′,7-*dimethoxyflavan*-4-*yl*]-3,3′,4,5′-*tetramethoxystilbene* (**10**). Acetylation of the R_F 0.45 methyl ether (190 mg) followed by p.l.c. in hexane–acetone–ethyl acetate (65:20:15 by vol., × 2) gave two products, at R_F 0.62 (8 mg) and R_F 0.57 (110 mg), of which the R_F 0.57 fraction represented the hexamethyl ether acetate (**10**) of the 2-(2,3-*trans*-3,4-*trans*-flavan-4-yl)stilbene, isolated as a solid. Its 300 MHz ^{1}H n.m.r., mass, and c.d. spectra were identical with those of the corresponding hexamethyl ether acetate derived from *G. coleosperma*.

Acid-catalysed Condensation of (E)-2′-[(2R,3R,4R)-2,3-cis-3,4-trans-3,4′,7-*Trihydroxyflavan*-4-*yl*]- *and* (E)-2′-[(2R,3S,4S)-2,3-trans-3,4-trans-3,4′,7-*Trihydroxyflavan*-4-*yl*]*stilbene*-3,3′,4,5′-*tetraol* (**11**) *and* (**9**) *with* (2R,3S,4R)-2,3-trans-3,4-trans- *and* (2R,3R,4S)-2,3-cis-3,4-trans-*Flavan*-3,4,4′,7-*tetraol* (**1**) *and* (**7**) *respectively*.—Condensation of the two flavan-3-ol–stilbene 'dimers' (335 mg) with the respective flavan-3,4-diols (202 mg) in reactions similar to those above gave phenolic material (*ca.* 520 mg) in both instances. Fractionation of each product by similar methods on Sephadex LH-20 columns (ethanol as eluant) at the same flow rate gave combined fractions 41—72 (90 mg and 82 mg, respectively) and 73—100 (265 mg and 272 mg, respectively) in each instance.

The first mentioned fractions contained the respective unchanged flavan-3-ol–stilbene 'dimers'. Methylation of the latter fractions followed by p.l.c. in benzene–acetone (17:3 v/v) gave a single product in both instance, R_F 0.42 (245 mg and 248 mg).

(E)-2′-[(2R,3R,4R)-2,3-cis-3,4-trans-3-*Acetoxy*-4′,7-*dimethoxyflavan*-4-*yl*]-6′-[(2R,3S,4S)-2,3-trans-3,4-trans-3-*acetoxy*-4′7-*dimethoxyflavan*-4-*yl*]-3,3′,4,5′-*tetramethoxystilbene* (**14**). Acetylation of the R_F 0.42 methyl ethers followed by p.l.c. in benzene–acetone (9:1 v/v) gave a single product in both instances as a solid with identical 80 MHz ^{1}H n.m.r., mass, and c.d. spectra, also in complete agreement with those of the methyl ether acetate derived from *G. coleosperma*.

Acknowledgements

Support by the South African Foundation for Research Development, Pretoria, and the Sentrale Navorsingsfonds of this University is acknowledged. 500 MHz ^{1}H N.m.r. spectra were recorded by Mr. I. Antonowitz, National Chemical Research Laboratory, C.S.I.R., Pretoria, and mass spectra by Dr. J. M. Steyn, Department of Pharmacology of this University and Mr. U. Nordhoff, National Chemical Research Laboratory, C.S.I.R., Pretoria. Wood specimens of *G. coleosperma* and *P. angolensis* were supplied by the Zimbabwe Forestry Commission, Bulawayo.

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Received 10*th June* 1986; *Paper* 6/1162