Synthesis and ^{1}H N.M.R. Spectroscopic Analysis of Some 3,7-Dioxabicyclo-[3.3.0]octane Lignans

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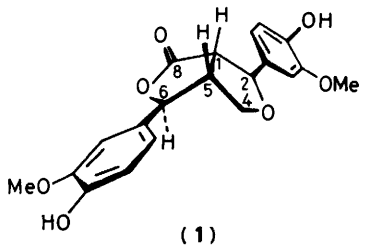
Within the framework of a synthetic project towards the preparation of the natural germination inhibitor 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane, several molecules with the same bicyclic skeleton were prepared and their ^{1}H n.m.r. spectra are described in detail. For the symmetrical systems particularly, the spectra exhibited second-order features and were interpreted analytically or, when necessary, by computer simulation. These n.m.r. data enabled a conformational analysis of the ring system.

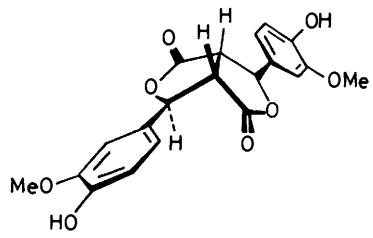
The monoepoxylignanolide (**1**) isolated from the seed dispersal units of *Aegilops ovata* L. was found to exhibit germination inhibition activity under specific conditions.[1–4] In order to develop a study on structure–activity relationships with respect to this inhibitory characteristic, larger quantities of compound (**1**) and some analogues were required. To this end, a synthetic program was worked out, using two different approaches for the synthesis of the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octan-8-one system characteristic of compound (**1**). The first approach produced a number of bicyclo[3.3.0]octanes which could be resolved only through repeated chromatography. It involved the coupling reaction between ferulic acid and coniferyl alcohol in the presence of ferric chloride and oxygen, a reaction known to produce the expected monoepoxylignanolide (**1**), together with the dilactone (**2**), and pinoresinol (**3a**).[3] A detailed re-examination of this reaction allowed a revision of the yields and also led to the isolation and identification of a second monoepoxylignanolide (**4a**). This new compound is described below.

In the second approach, a bicyclo[3.3.0]octane skeleton was used as the starting material which, through appropriate modifications, could be used for preparation of compound (**1**). With this in mind, the dilactone (**2**) was subjected to a selective reduction of one of the carbonyl functions with di-isobutyl-aluminium hydride (DIBAL), producing the key asymmetric intermediate (**5**); when an excess of this reagent was used, compound (**6a**) was isolated. In order to complete our spectroscopic studies, this dilactol (**6a**) was converted into its tetra-acetate (**6b**) and ditosylate (**6c**). Attempts are being made to use the tosylation procedure, as well as other possibilities, on the asymmetric lactone-lactol (**5**) to reach the desired level of oxidation, as in (**1**). Recently, and independently, a similar sequence was used and described for the synthesis of 4,8-dihydroxysesamin.[5]

A full description and detailed ^{1}H n.m.r. analysis of compound (**5**), together with n.m.r. analyses of compounds (**2**), (**3**), and (**6**), are given here.



(**1**)



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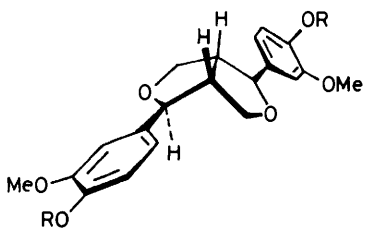


(**3**)
a; R = H
b; R = Ac

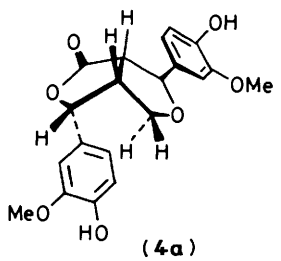
Results and Discussion

Following the first synthetic approach, ferulic acid and coniferyl alcohol were coupled to obtain the 2,6-diaryl-dioxabicyclo-[3.3.0]octan-8-one (**1**). During the purification of this product a new crystalline compound (**4a**), m.p. 131—133 °C, was obtained. The presence of a γ-lactone was detected by the 1 755 cm^{-1} band in the i.r. spectrum. From the high resolution mass analysis, the formula $C_{20}H_{20}O_7$ was deduced, showing the compound to be isomeric with the natural germination inhibitor (**1**). Oxidative coupling of ferulic acid and coniferyl alcohol can, in principle, lead to 2,4- and/or 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane derivatives. However, the existence of 2,4-diaryl-3,7-dioxabicyclo[3.3.0]octane structures has not been reported so far in nature,[1,2,6,7] and laboratory oxidative coupling experiments leading to furofuranoid lignans invariably give the 2,6-diaryl derivatives. 2,4-Diaryl derivatives can only be prepared through a different and tedious synthetic procedure.[4] Assuming, therefore, 2,6-diaryl substitution, three isomeric structures (**4a**—**c**) must be considered. The drawings of the formulae (**4a**—**c**) are schematic, and the stereochemical constraints are best seen using the appropriate molecular models. Thus, it can be seen that while a possible interaction between the two *endo*-aryl groups in (**4b**) can be easily relieved

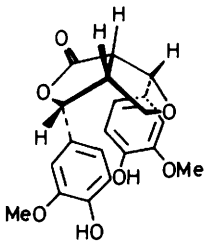
Table 1. ^{1}H N.m.r. data (δ) of relevant protons in compounds (**1**), (**4a**), and (**5**) [a]

Compound	δ/p.p.m. 1-H	2-H	*endo*-4-H	*exo*-4-H	5-H	6-H	CH_3O
(**1**)	3.40 (dd, 9, 3.5)	5.28 (d, 3.5)	4.15 (dd, 9, 4.5)	4.30 (dd, 9, 6.5)	3.18 (m)	5.27 (d, 3.5)	3.78 (s)
(**4a**)	*ca.* 3.5 (m) [2.98]	5.32 (d, 1.5) [5.48]	*ca.* 3.5 (m) [3.12]	3.88 (m) [3.22]	*ca.* 3.5 (m) [3.47]	5.74 (d, 5) [5.81]	3.90 (s), 3.92 (s) [3.51]
(**5**)	3.53 (dd, 8.7, 5.9)	5.21 (d, 5.9)	5.51 (d, *ca.* 1)		3.16 (dd, 8.7, 6.7)	5.36 (d, 6.7)	3.79 (s), 3.77 (s)

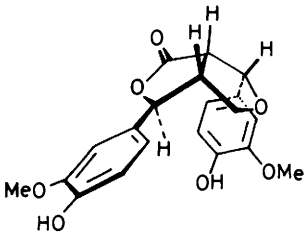
[a] $CDCl_3$ as solvent except for the data in square brackets which are for C_6D_6. Tetramethylsilane as internal standard. Data in parentheses are: multiplicity, coupling constant (Hz).



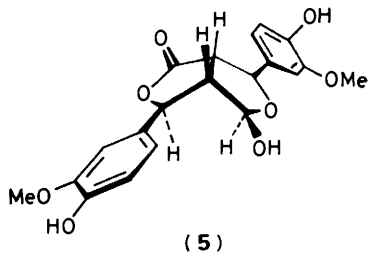
(**4a**)



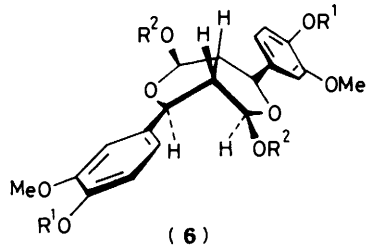
(**4b**)



(**4c**)



(**5**)



(**6**)
a; $R^1 = R^2 = H$
b; $R^1 = R^2 = Ac$
c; R^1 = tosyl, $R^2 = H$

by a slight twist of the molecule, there is no apparent way of eliminating severe crowding between the carbonyl at C(8) and a C(2)-*endo*-aryl substituent. Therefore, the formation of isomers (**4b**) and (**4c**) is unlikely, and (**4a**) is the most probable structure. This *exo*-arylepoxide-*endo*-aryl-lactone structure (**4a**) is well supported by the ^{1}H n.m.r. spectrum. The chemical shift values and coupling constants are presented in Table 1, where they can be compared to those of compound (**1**). All the assignments are based on decoupling experiments involving all the protons (including the aromatic ones, to detect benzylic coupling to 2-H and 6-H). In compound (**4a**), the protons at C(5) and C(6) are deshielded, whereas those at C(4) are shielded relative to their counterparts in compound (**1**). Indeed, an *endo*-aryl substituent at C(6) will bring both protons at C(5) and C(6) into the deshielding region of the benzene ring, if it is assumed that there is a preferred conformation of the ring about the C(6) aryl bond (as suggested by models). In contrast, the *endo*-proton at C(4) will be shielded by the C(6) aryl substituent. Gaudemer[8] discusses the difficulty of the assignment of stereochemistry in pentacycles through the analysis of vicinal coupling constants; however, in our more rigid fused systems a correlation is possible. Indeed, in compound (**4a**) the two benzylic protons at C(2) and C(6) have different coupling constants with the vicinal bridgehead hydrogens (*J* 1.5 and 5 Hz, respectively), while in compound (**1**) they are identical (*J* 3.5 Hz). For compound (**4a**), the smaller coupling constant (*J* 1.5) falls safely in the range for *trans* interacting protons[8] (1-H and 2-H), whereas the higher value (*J* 5 Hz) is due to *cis* hydrogens at C(5) and C(6). Spin-spin decoupling experiments carried out in deuteriated chloroform and benzene confirm the chemical shift assignments for compound (**4a**). As expected, the benzene solvent molecules are oriented by the dipole of the lactone carbonyl,[9,10] so that the protons neighbouring the ring are shifted upfield. Finally, the variation of the different chemical shifts observed when compound (**1**) is compared to (**4a**) are very close to those described for eudesmin (an *exo*-diaryldiepoxide) and epi-eudesmin (an *endo*-aryl-*exo*-aryldiepoxide).[11]

Following the second synthetic approach, compounds (**5**) and (**6**) were formed. Intermediate (**5**) possessing both a lactol and a lactone function was considered as a key intermediate for the synthesis of the monoepoxylignan (**1**). It was obtained in good yield by reducing selectively one of the lactone functions present in compound (**2**). By using equimolar quantities of DIBAL, compounds (**2**), (**5**), and (**6**) were identified in the reaction mixture, (**5**) being the major product. Following column chromatography, compound (**5**) crystallized from acetone, m.p. 194—195 °C; $\nu_{max.}$ 1 755 cm^{-1} for the γ-lactone. The *exo*-orientation of the hydroxy group of the lactol ring was deduced from the ^{1}H n.m.r. data. Indeed, a very narrow doublet (*J ca.* 1 Hz) was observed for 4-H, a value requiring a dihedral angle between 4-H and 5-H of about 90°, the 4-H being *endo*.

Table 2. ^{1}H N.m.r. signals (δ) of relevant protons in compounds possessing an AA'XX' system

Compound	Solvent	1,5-H	2,6-H	*endo*-4,8-H	*exo*-4,8-H	CH_3O	CH_3CO
(2)	$CDCl_3$	3.56	5.86			3.91	
	$(CD_3)_2CO$	4.09	5.78			3.87	
	$(CD_3)_2SO$	4.20	5.73			3.80	
(3a)	$CDCl_3$	3.02	4.66	3.78	4.17	3.83	
(3b)	$CDCl_3$	3.06	4.78	3.92	4.27	3.84	2.30
(6a)	$(CD_3)_2SO$	2.77	4.75	5.39		3.77	
(6b)	$CDCl_3$	3.25	5.23	6.51		3.87	2.03, 2.32
(6c)	$(CD_3)_2SO$	2.74	4.87	5.55		3.53	

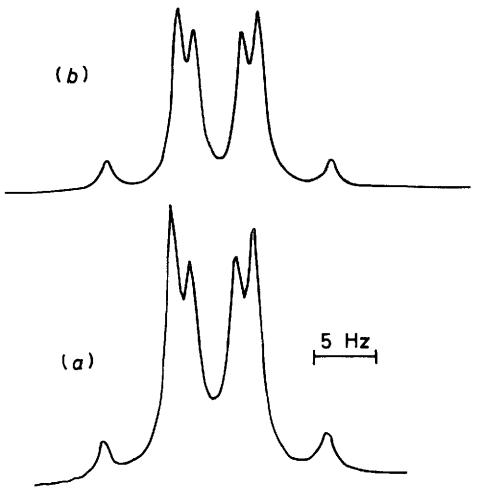


Figure 1. 1,5-H Signal in compound (**6b**): (*a*) experimental, and (*b*) calculated

Otherwise, most of the values recorded for compound (**5**) are closely related to those of (**1**). Indeed, inspection of a model indicates that the 4-*exo*-hydroxy group points away from the neighbouring protons.

The ^{1}H n.m.r. spectra of compounds (**2**), (**3**), and (**6**) (Table 2) exhibit second-order features. The symmetry of these molecules implies that while 1-H and 5-H, for instance, have the same chemical shift (chemical equivalence), they are magnetically *inequivalent* and therefore the aliphatic ring protons of (**2**) have to be interpreted as an AA'XX' system. In the case of compounds (**6a**) and (**6b**), 4-H and 8-H appear as a sharp singlet owing to a *ca.* 90° dihedral angle with 5-H and 1-H respectively, similar to the lactol proton in (**5**) (*vide supra*); therefore, the remaining aliphatic ring protons also constitute an AA'XX' system. The 1-H/5-H multiplet for (**6b**) is shown in Figure 1(*a*); the 2-H/6-H signal has the same shape, but is somewhat broadened owing to benzylic coupling (irradiation of the aromatic protons results in line sharpening). The expected 10-line system is reduced to 6 lines owing to the very small value of $J_{2,6}$; otherwise, the analysis is well documented [12] and produces the coupling constants shown in Table 3. Figure 1(*b*) shows the computed spectrum using these values which is in excellent agreement with Figure 1(*a*). Compound (**6a**) generates a similar multiplet, and therefore has coupling constants close to those for (**6b**) (see Table 3). For the dilactone (**2**), the small value of $J_{1,2}$ (or $J_{5,6}$) results in closely spaced central lines and a small outer pair,* necessitating very good spectral resolution; however, the analysis is again unambiguous.

* In ref. 4, p. 844, there is a printing error in the coupling constants of this compound [(**14**) in that paper].

Table 3. Values (in Hz), of coupling constants observed in different AA'XX' systems

	(2)	(3b)	(6a)	(6b)
$J_{1,2}$	2.5	5.5	8.0	7.5
$J_{1,4\text{-}endo}$		−0.4	0	0
$J_{1,4\text{-}exo}$		−0.4		
$J_{1,5}$	9.7	9.7	6.6	7.2
$J_{1,6}$	−0.3	−0.9	−1.2	−0.9
$J_{1,8\text{-}endo}$		4.0	0	0
$J_{1,8\text{-}exo}$		7.3		
$J_{2,8}$		0	0	0
$J_{4\text{-}endo,4\text{-}exo}$		9.1		

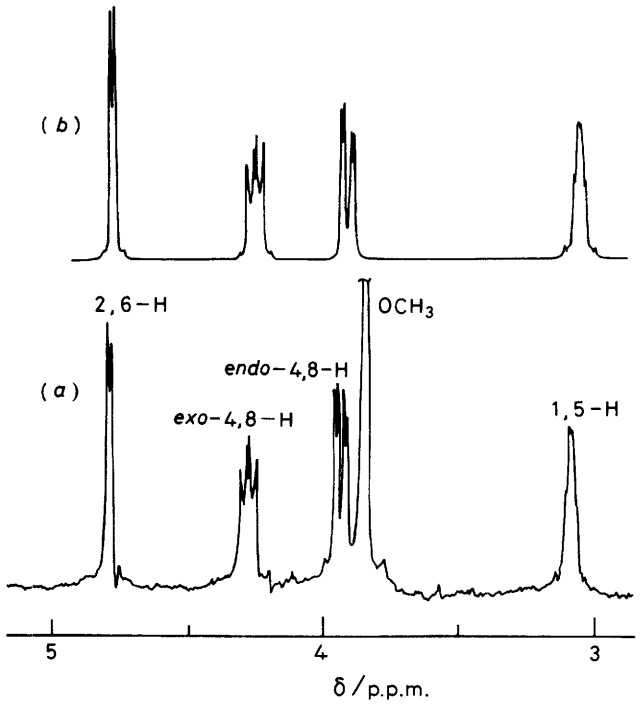


Figure 2. Partial ^{1}H n.m.r. spectrum of pinoresinol acetate (**3b**): (*a*) experimental, and (*b*) calculated

The ^{1}H n.m.r. spectrum of pinoresinol (**3a**) has been the subject of an early first-order analysis.[13] However, it is actually a fairly complex system [see Figure 2(*a*) for the spectrum of the diacetate (**3b**)] and the two fused pentacycles support eight protons which are again chemically (but not magnetically) equivalent in pairs. In this case an analytical approach is not feasible, and the extraction of coupling constants from the spectrum necessitated the fitting of computed to experimental line shapes, to some extent by trial and error. The fit between the calculated [Figure 2(*b*)] and experimental [Figure 2(*a*)] spectra

is good enough to warrant a confidence range of at least ±0.5 Hz for the coupling constants presented in Table 3.

An attempt can be made to rationalize the information contained in Table 3 in terms of a conformational analysis of the bicyclo[3.3.0]octane system. In both compounds (**2**) and (**3b**), $J_{1,5}$ is of the order of 10 Hz, indicating that the two bridgehead protons are essentially eclipsed. The values of $J_{1,2}$ are very different [2.6 Hz for (**2**) and 5.5 Hz for (**3b**)], since the dihedral angle between these two hydrogens falls in a region of the Karplus curve where the vicinal coupling constant is extremely sensitive to the angle (135 ± 10°). For compound (**3b**), the methylene is oriented in such a way that the bridgehead proton nearly eclipses the *exo*-hydrogen ($J_{1,8\text{-}exo}$ 7.3 Hz) and makes an angle of *ca.* 120° with the *endo*-hydrogen ($J_{1,8\text{-}endo}$ 4.0 Hz). These dihedral angles are in good agreement with the *X*-ray structure of the closely related syringaresinol.[14] The fact that both the dilactone and the diether share a similar conformation suggests this is the lowest-energy form of the ring system.

The introduction of 4- and 8-*exo*-oxy substituents [compounds (**6**)] seems to introduce some strain, and the ring system reacts by slightly rotating around the central 1,5-bond ($J_{1,5}$ decreases to *ca.* 7 Hz); this simultaneously increases the 1-H/2-H dihedral angle, and therefore the coupling constant, and at the same time leads to nearly a perpendicular relationship between the C(1)-H and C(8)-H(*endo*) bonds, reducing the coupling constant between the two protons to almost zero.

The 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes exhibit a characteristic mass fragmentation pattern, which has been reviewed in detail.[15] For most of our compounds, the main ionic fragments have structures I, II, or III and/or result from the gain or loss of a hydrogen atom thereof.

I

II

III

Experimental

M.p.s were taken on a Fischer-Johns apparatus. I.r. spectra were recorded on a Perkin-Elmer 467 grating spectrophotometer and refer to KBr pellets; u.v. spectra were recorded on a Cary 118 instrument for solutions in ethanol; ^{1}H and ^{13}C n.m.r. spectra were determined on Bruker WH-270 and WH-90 (at 22.63 MHz) instruments respectively. T.l.c. was carried out on chromatoplates (E. Merck, 200 × 200 mm, silica gel F_{254}). Preparative chromatoplates of 2-mm thickness were used (200 × 200 mm, silica gel F_{254}) for mixture separations. Mass spectra were taken under the direction of Dr. Z. Zaretskii with a Varian MAT 731 HR instrument and an improved Atlas CH4 instrument. Ether refers to diethyl ether.

Synthesis of Compounds (**1**), (**2**), (**3a**), *and* (**4a**).—A solution of coniferyl alcohol (698 mg, 3.88 × 10^{-3}M) (see below) and ferulic acid (402 mg, 2.59 × 10^{-3}M) in methanol (40 ml) was added in small portions to a solution of ferric chloride (6.31 g, 38.9 × 10^{-3}M) in water (100 ml) while oxygen was blown through vigorously. The flow of oxygen was then continued at room temperature for 17 h. The mixture containing the rust-coloured precipitate was warmed and agitated at 75 °C (internal temperature) for 5 min, cooled, diluted with water (300 ml), and extracted twice with ether (300 and 200 ml)* to afford an orange gum (471 mg). Chromatography over silica gel (60 g) with elution with benzene–ethyl acetate (1:1 by vol) yielded the required products as a yellow gum (147 mg) which on t.l.c. (benzene–ethyl acetate, 1:2) showed essentially only two spots, of R_F 0.69 for the dilactone (**2**) and R_F 0.62 for compounds (**1**) and (**4a**). This mixture was further purified on two preparative chromatoplates eluting with benzene–ethyl acetate (1:2 by vol). Recovery of the mixture of (**1**) and (**4a**) from the appropriate band (u.v. inspection) by elution with acetone gave a gum (50 mg) which on t.l.c., as before, showed a very strong spot at R_F 0.63 with the typical yellow colour after exposure to iodine vapour, and a very faint indication of a trace of a higher spot.

This mixture (260 mg from several runs) was further separated by preparative t.l.c. on two plates as before by eluting with chloroform–methanol (19:1). A strong band at R_F 0.48 yielded 107 mg of a gum which after three crystallizations from concentrated solutions in ethyl acetate gave pure compound (**4a**) (10 mg), m.p. 131—133 °C to a clear melt on being heated at 4 °C/min. The mother-liquors of these crystallizations were shown to contain (**1**) as well as pinoresinol (**3a**) by ^{1}H n.m.r. analysis. The following products were obtained. 2,6-*exo*-Bis-(4-hydroxy-3-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octan-8-one (**1**) (monoepoxylignanolide, MEL), m.p. 190—192 °C, spectroscopic data in excellent agreement with those found for the naturally occurring lignan.[4]

2,6-exo-*Bis*(4-*hydroxy*-3-*methoxyphenyl*)-3,7-*dioxabicyclo*-[3.3.0]*octane*-4,8-*dione* (**2**), m.p. 207—208 °C;[4] $\lambda_{max.}$ 234 and 280 nm (ε 15 623 and 8 271); $\nu_{max.}$ 1 770, 1 220, and 1 170 cm^{-1}; *m/z* (%) 386.1007 (92) (M^+ for $C_{20}H_{18}O_8$), 342.1107 (75) ($M^+ - CO_2$), 298.1199 (11) ($M - 2 \times CO_2$), 190.0632 (57) (ion type I − H, $C_{11}H_{10}O_3$), 152.0456 (30) (ion II, $C_8H_8O_3$), 151.0390 (100) (ion II − H, $C_8H_7O_3$), and 124.0515 (23) (ion III, $C_7H_8O_2$).

2,6-*exo*-Bis(4-hydroxy-3-methoxyphenyl)-3,7-dioxabicyclo-[3.3.0]octane (**3a**) and its diacetate (**3b**). Pinoresinol (**3a**) is a well-known compound;[16] for its diacetate (**3b**) see ref. 4.

2-exo,6-endo-*Bis*(4-*hydroxy*-3-*methoxyphenyl*)-3,7-*dioxa-bicyclo*[3.3.0]*octan*-8-*one* (**4a**) (*iso-MEL*), m.p. 131—133 °C; $\nu_{max.}$ 3 430 (OH) and 1 755 cm^{-1} (γ-lactone); *m/z* (%) 372.1191 (92) (M^+ for $C_{20}H_{20}O_7$), 354.1074 (18) ($M - H_2O$, $C_{20}H_{18}O_6$), 152.0446 (26) (ion II, $C_8H_8O_3$), and 151.0388 (100) (ion II − H, $C_8H_7O_3$).

Improved Synthesis of Coniferyl Alcohol.[17]—Methyl acetoferulate [m.p. 120—121 °C (lit.,[18] 124 °C); 3.01 g, 12.0 × 10^{-3}M] in anhydrous ether (360 ml) was added dropwise during 75 min ($CaCl_2$ tube protection) to a stirred suspension of lithium aluminium hydride (1.4 g, 37 × 10^{-3}M) in anhydrous ether (80 ml) and the internal temperature of the mixture was kept at −13 to −11 °C by cooling it in ice–salt. The mixture was then allowed to warm to room temperature while being stirred overnight. After being cooled again, to −6 °C, the excess of hydride was destroyed by careful addition of ethyl acetate (5 ml) in ether (10 ml), followed by ammonium carbonate (7 g) in water (120 ml). Extraction with ether afforded a yellowish syrup (2.19 g) which crystallized on standing. It was chromatographed over silica gel (150 g) and the product (1.97 g) eluted with benzene–ethyl acetate (1:1 by vol). It crystallized (Craig tube) from ethyl acetate (1.5 ml) and benzene (4.5 ml) to afford coniferyl alcohol (1.40 g), m.p. 74—75.5 °C; concentration of the mother-liquor yielded a further 0.08 g of coniferyl alcohol, m.p. 72—75 °C (total yield 68%). It was recrystallized in the same way to a constant m.p. 76.5—77 °C; δ (270 MHz; $CDCl_3$) 6.92—6.87 (3 H, m, ArH), 6.53 (1 H, d, *J* 16 Hz, 3-H), 6.22 (1 H, dt, *J* 16 and 6 Hz, 2-H), 5.68 (1 H, s, ArOH), and 4.32 (2 H, d, *J* 6 Hz, 1-H); $\nu_{max.}$ 3 420 and 3 190 (OH), 1 570, and 1 490 cm^{-1} (aromatic).

* The aqueous layer was treated with concentrated hydrochloric acid (40 ml) and again extracted with ether (400 and 200 ml) to afford only 62 mg of gum which contained mainly compounds more polar (by t.l.c.) than the required coupling products.

Synthesis of Compounds (**5**), (**6a**), (**6b**), *and* (**6c**).—The dilactone (**2**) was dissolved in dry tetrahydrofuran and the solution was cooled to −40 °C under nitrogen. A solution of di-isobutylaluminium hydride in hexane (4 equiv.) was slowly added. The cooling bath was removed and the mixture was stirred at room temperature for 1 h. After being cooled to 0 °C, water was added and the products extracted with ethyl acetate. Compounds (**2**), (**5**), and (**6a**) were separated on a silica gel column. 2,6-exo-*Bis*(4-*hydroxy*-3-*methoxyphenyl*)-4-exo-*hydroxy*-3,7-*dioxabicyclo*[3.3.0]*octan*-8-*one* (**5**), m.p. 194—195 °C; $\lambda_{max.}$ 233 and 275 nm (ε 23 711 and 11 676); $\nu_{max.}$ 3 400, 1 755, 1 600, 1 500, 1 230, and 1 020 cm^{-1}; *m/z* (%) 388.1180 (42) (M^+ for $C_{20}H_{20}O_8$), 326.1160 (100) ($M - CO_2 - H_2O$), 190.0613 (18) (ion I − H, $C_{11}H_{10}O_3$), 153.0555 (66) (ion II + H, $C_8H_9O_3$), 152.0486 (32) (ion II, $C_8H_8O_3$), 151.0391 (49) (ion II − H, $C_8H_7O_3$), and 124.0509 (27) (ion III, $C_7H_8O_2$).

2,6-exo-*Bis*(4-*hydroxy*-3-*methoxyphenyl*)-4,8-exo-*dihydroxy*-3,7-*dioxabicyclo*[3.3.0]*octane* (**6a**), m.p. 219—221 °C; $\lambda_{max.}$ 230 and 280 nm (ε 26 325 and 10 432); $\nu_{max.}$ 3 400, 1 600, 1 510, 1 430, and 1 280 cm^{-1}; *m/z* (%) 390.1280 (26) (M^+ for $C_{20}H_{22}O_8$), 192.0773 (26) (ion I + H, $C_{11}H_{12}O_3$), 153.0549 (38) (ion II + H, $C_8H_9O_3$), 152.0462 (82) (ion II, $C_8H_8O_3$), and 151.0388 (100) (ion II − H, $C_8H_7O_3$).

2,6-exo-*Bis*(4-*acetoxy*-3-*methoxyphenyl*)-4,8-exo-*diacetoxy*-3,7-*dioxabicyclo*[3.3.0]*octane* (**6b**). Compound (**6a**) was acetylated overnight with acetic anhydride and pyridine. After the usual work-up, the mixture was purified on preparative chromatoplates and the tetra-acetate (**6**) was crystallized from ethyl acetate, m.p. 189—190 °C; $\lambda_{max.}$ 220 and 270 nm (ε 39 060 and 25 110); $\nu_{max.}$ 1 745, 1 725, 1 590, and 1 200 cm^{-1}; *m/z* (%) 558 (7) (M^+), 516 (22) ($M - CH_2CO$), and 474 (17) ($M - 2 \times CH_2CO$).

2,6-exo-*Bis*(3-*methoxy*-4-*tosyloxyphenyl*)-4,8-exo-*dihydroxy*-3,7-*dioxabicyclo*[3.3.0]*octane* (**6c**). Compound (**6a**) was dissolved in pyridine and cooled to 0 °C; then toluene-*p*-sulphonyl chloride was added and the mixture was stirred overnight. After the usual work-up, compound (**6c**) was crystallized from ethyl acetate; m.p. 180—181 °C; $\lambda_{max.}$ 223 and 275 nm (ε 9 140 and 39 885); $\nu_{max.}$ 3 400, 1 590, 1 390, and 1 170 cm^{-1}; *m/z* (%) 306 (33) (ion II), 151 (32) (ion II − tosyl), 155 (62) (tosyl), and 91 (100) (C_7H_7, tropylium ion).

Acknowledgements

We thank Dr. R. Poupko for providing the computer program used in the simulation of the ^1H n.m.r. spectra, and Dr. R. J. Highet, National Heart and Lung Institute, N.I.H., Bethesda, Md, for very well-resolved ^1H n.m.r. spectra of the dilactone (**2**). F. S. would like to thank the Royal Society for the award of a visiting Professorship in the Israel Academy Program during the summer of 1981.

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Received 27*th July* 1983; *Paper* 3/1297