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LIGNANS, NEOLIGNANS AND NORNEOLIGNANS FROM *KRAMERIA CYSTISOIDES**

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Key Word Index—*Krameria cystisoides*; Krameriaceae; new lignans, neolignans and norneolignans.

Abstract—The hexane extract from the roots of *Krameria cystisoides* yielded besides conocarpan, licarin A, eupomatenoids 6 and 13, and ratanhiaphenol I 16 hitherto unknown lignans, neolignans and norneolignans, among them toltecol and olmecol. Structural elucidation was based mainly on spectroscopic investigations, especially ^{13}C NMR.

INTRODUCTION

Krameria cystisoides is a shrub growing in Central and South-west Mexico. The root is used for various medicinal purposes, including the treatment of stomach and bowel cancer [1]. Chemical investigation of root extracts resulted in the isolation of 21 compounds of the lignan, neolignan and norneolignan type. Among these are 16 hitherto unknown natural products.

RESULTS AND DISCUSSION

Repeated chromatography of the non-polar components from the methanolic root extract yielded the known compounds **2**, **4**, **7**, **8**, **11** and the new neolignans **1**, **3**, **5**, **6**, **9**, **10**, **12**–**21**.

Dihydrobenzofuranes (1–6)

The *trans*-2-aryl-3-methyl-2,3-dihydro-benzofuran system can easily be recognized in these compounds from ^{1}H NMR [2–4] [δ5.03 (*d*, J = 9 Hz; H-2), δ3.35 (*m*, H-3), δ1.36 (*d*, J = 6.7 Hz, Me-3)] as can the *trans*-propenyl group in **1**–**4** and the 3-hydroxypropyl group in **5** and **6**. Key fragments in the mass spectra give information on the kind of substituents at phenyl ring A and the correct positions were deduced from the ^{13}C NMR data observed for the isolated compounds and the shift of NMR signals on acetylation. Recently published ^{13}C NMR values [5–7] easily allowed us to identify one of the isolated compounds as licarin A (**2**) and helped us in the assignment of ^{13}C signals (Table 1), which were used to establish the positions of the substituents.

5 and **6** exhibited in their NMR spectra the characteristic features of a 3-hydroxypropyl-substituent [8].

1–**4** all show positive Cotton effects at 260 nm and, therefore, have the 2*R*,3*R* configuration [2, 9–14]. However, the CD curves of **5** and **6** exhibit a negative Cotton effect at 281 nm and a positive one at 233 nm. The same behaviour is observed with the hydrogenation product of **4**, which gives evidence that the configuration in **5** and **6** must also be 2*R*,3*R*.

Benzofurans (7–16)

The 2-aryl substituted benzofuran system could be established from the electron spectra and NMR data. The ^{13}C NMR data are shown in Tables 2 and 3. Comparison of spectroscopic and physicochemical data show **7** to be identical with ratanhiaphenol II [15] (= eupomatenoid 6 [16]) and **8** with kachirachirol A [17] (= eupomatenoid 13 [18]). Treatment of the naturally occurring aldehyde **9** with sodium borohydride yields the corresponding primary alcohol. In consequence of the anisotropic effect [19] of the aldehyde group at C-3 on the neighbouring aromatic proton, in ^{1}H NMR this reduction causes a significant up-field shift of H-4 [δH-4 7.72 (in **9**) → 7.26 (in alcohol)].

A general feature of benzofurans **10**–**15** is the 'missing' carbon substituent at C-3. Therefore, these compounds belong to the norneolignan series. The assignment of substituents R^2 and R^3 at ring A—as in **11** and **12** (=toltecol)—is based on the characteristic NMR shifts observed after acetylation. **11** is ratanhiaphenol I, which has recently been described from *Krameria triandra* [15]. The structure of olmecol (**16**) was easily deduced from its spectroscopic data and comparison with the hydrogenation product of **7**.

1-*Aryl*-2-*phenoxy*-1-*propanols* (17, 18)

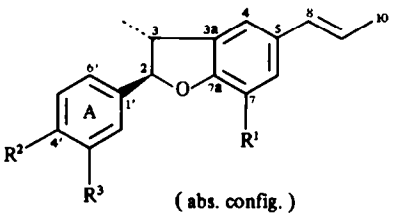
In contrary to the above mentioned compounds, **17** and **18** exhibit $[M]^+$ ions of rather weak intensity in their mass spectra. From ^{1}H NMR and ^{13}C NMR data (see Table 4) most details of the structure of **17**—including the *erythro*-configuration [20–23]—could be established;

*Synonyms found in the literature include *cysticioides*, *cytisoides*, *cytissoides*.

Table 1. ^{13}C NMR data of **1–6**, acetylation products of **1** and **3** and the hydrogenation product of **4**

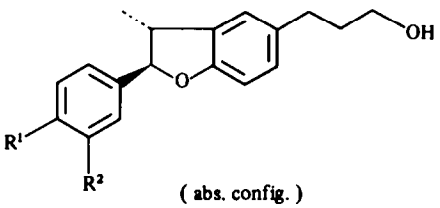
	1*	1 Ac*	2	3	3 Ac	4	4 hyd	5	6
C-2	93.02	92.37	94.02	93.61	92.83	93.12	93.29	93.19	93.47
C-3	45.27	45.46	46.25	46.14	46.63	45.53	46.21	46.14	46.11
C-3a	132.54†	132.11†	134.56†	134.41†	134.19†	133.13†	133.11†	133.08†	133.28†
C-4	120.79	120.86	114.43	114.39	114.48	121.45	124.47	124.43	124.40
C-5	131.40†	131.55†	133.00†	132.79†	133.18†	131.63†	135.60	135.39	135.45
C-6	126.28	126.35	111.41	111.30	111.46	126.73	128.78	128.72	128.69
C-7	109.27	109.31	145.10	144.98	145.14	109.40	109.41	109.41	109.41
C-7a	158.33	158.28	147.86‡	147.75	147.68	159.02	158.49‡	158.25‡	158.35
C-8	130.91†	130.84†	132.12	132.04†	132.04†	131.63†	38.25	35.90	35.93
C-9	122.91	122.81	123.31	123.20	123.46	122.72	25.74	32.35	32.35
C-10	18.28	18.27‡	18.48§	18.37‡	18.53‡	18.34	14.00	61.91	61.84
C-1′	132.38†	139.78	132.94†	132.50†	139.42	132.35†	132.89†	132.89†	133.08†
C-2′	108.78	110.15	110.83	128.46	127.85	128.21	128.48	128.43	110.74
C-3′	146.87	151.42	148.44	116.08	122.64	115.93	116.15	116.14	148.42
C-4′	145.89	138.78	147.60‡	158.15	151.74	157.80	158.36‡	158.38‡	147.55
C-5′	114.37	123.07	115.67	116.08	122.64	115.93	116.15	116.14	115.65
C-6′	119.58	118.32	120.26	128.46	127.85	128.21	128.48	128.43	120.14
CH_3-3	17.76	18.14‡	18.03§	18.11‡	18.37‡	17.92	18.23	18.18	17.98
CH_3O	55.97	55.99	56.43 56.53	56.41	56.51				56.38
COO		168.78			169.46				
CH_3-Ac		20.55			20.91				

*In acetone-d_6; in $CDCl_3$.
†,‡,§Similar values within a column may be interchanged.



(abs. config.)

	R¹	R²	R³
1	H	OH	OMe
2	OMe	OH	OMe
3	OMe	OH	H
4	H	OH	H



(abs. config.)

	R¹	R²
5	OH	H
6	OH	OMe

Scheme 1.

characteristic fragments in the mass spectrum showed that the phenoxy group is placed at C-8 [24].

18 has NMR data identical with those reported for the ring B system of surinamensin [20]. Final evidence for **18** was achieved by synthesis of 1-(4-methoxyphenyl)-2-(2-methoxy-4-propenylphenoxy)-1-propanol, which proved to be identical with the methyl ether of **18**.

Tetrahydrofurans (**19–21**)

NMR signals and mass spectral fragmentation showed **19** to belong to a group of 2,5-diaryl-3,4-dimethyl-tetrahydrofurans with low symmetry [25–28]. Comparison of the ^{1}H NMR with published data [25, 28–30] allowed us to establish the structure, which also is in agreement with ^{13}C NMR.

20 carries an additional methoxy group. Its position was determined as follows: ^{13}C NMR of **19** shows slightly different sets of shifts for all carbons in the two aryl substituents. Because of its interaction with the *cis*-standing methyl group, the resonances at higher field were assigned to the aryl ring at C-5 [26] (Table 5). In the ^{13}C NMR of **20** the set of signals at higher field was unchanged in comparison with **19**. Therefore, the additional OMe substituent had to be placed at the phenyl at C-2 and there in the *m*-position to correspond with the resonances in **1**, **2** and **6**.

The mass spectra of **20** and **21** are almost identical; from the ^{1}H NMR of **21** the relative configuration of the four substituents at the tetrahydrofurans ring can be deduced [20, 27, 29].

Major constituents of *K. cystisoides* were found to be

Table 2. ^{13}C NMR data of **7–9**, **16**, the hydrogenation product of **7** and the acetylation product of **8**

	7	7 hyd.	8	8 Ac	9	16*
C-2	152.42†	152.21†	152.26	151.67†	166.56	152.62†
C-3	110.02	109.82	110.28†	112.57	120.79	110.02
C-3a	132.31‡	132.30	134.66	134.99	137.11	132.72
C-4	117.00	119.24	109.89†	110.15	112.19	119.30
C-5	133.72	137.55	133.95	133.72	132.12	137.41
C-6	122.95	125.39	105.84	106.37	106.77	125.47
C-7	111.16	110.87	145.89	146.09	145.97	111.10
C-7a	153.76†	153.10†	142.96	143.31	143.12	153.57†
C-8	132.48‡	38.68	132.54	132.48	132.12	36.06
C-9	124.48	25.87	124.51	124.84	126.00	33.13
C-10	18.51	14.04	18.41	18.44	18.51	62.40
C-1′	123.80	123.85	123.77	129.60	128.44	124.40
C-2′	129.02	129.02	128.95	128.34	131.84	129.21
C-3′	116.55	116.58	116.49	122.98	117.06	116.56
C-4′	158.43	158.60	158.36	151.08†	161.26	158.61
C-5′	116.55	116.58	116.49	122.98	117.06	116.56
C-6′	129.02	129.02	128.95	128.34	131.84	129.21
R-3	9.40	9.40	9.50	9.56	186.82	9.43
CH_3O			56.46	56.50	56.45	
COO				169.46		
CH_3-Ac				20.95		

*In CD_3OD.

†,‡Similar values within a column may be interchanged.

Table 3. ^{13}C NMR data of **10–15** and the acetylation product of **11**

	10	11	11 Ac	12	13	14	15
C-2	157.76	154.51*	154.43	154.32	157.54	154.80	154.64
C-3	100.18	104.54	104.35	104.87	100.46	104.11*	104.34*
C-3a	130.90	131.21	130.59	132.74*	132.41*	131.23	132.76†
C-4	118.58	118.61	119.03	111.72†	111.43	118.48	111.49‡
C-5	134.28	134.04	134.41	134.99	135.19	133.89	134.90
C-6	122.85*	122.68	123.49	105.55	105.58	122.45	105.35
C-7	111.43	111.13†	111.49	145.96	146.05	111.04†	145.83
C-7a	154.83	153.89*	153.40	143.12	144.06	153.73	142.93
C-8	132.20	132.28	132.14	132.54*	132.41*	132.24	132.50†
C-9	124.73	124.48	124.98	124.55	124.71	124.37	124.43
C-10	18.47	18.47	18.51	18.41	18.41	18.47	18.40
C-1′	123.03*	111.72†	117.08	111.59†	123.05	110.68†	110.71‡
C-2′	127.35	156.63	149.79	156.57	127.29	156.75	156.69
C-3′	116.69	102.94	110.55	102.91	116.65	104.01*	104.08*
C-4′	159.13	162.02	161.71	161.98	159.02	159.68	159.69
C-5′	116.69	106.73	113.09	106.73	116.65	108.53	108.53
C-6′	127.35	128.47	129.29	128.43	127.29	128.56	128.53
CH_3O		55.65	56.13	55.65, 56.46	56.43		56.41
COO			169.30				
CH_3-Ac			21.30				

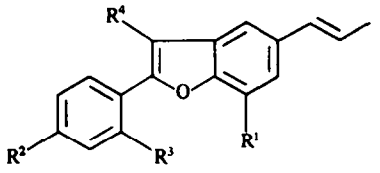
*,†,‡Similar values within a column may be interchanged.

conocarpan (**4**) [8], olmecol (**16**) and **3**. All other isolated compounds were minor components.

EXPERIMENTAL

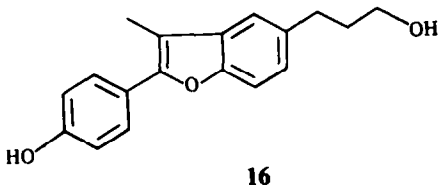
Plant material. Roots were collected in Vaumave, Tamaulipas in March 1984; a voucher specimen is kept at the herbarium of the Department of Biology, Monterrey (Reg. No. 7814).

Extraction and chromatography. The concd MeOH extract (20 g from 120 g air dried roots) was diluted with H_2O and extracted first with petrol (60–70°) and then with CCl_4. Both extracts (2.5 g from petrol, 3.7 g from CCl_4) were concd and repeatedly chromatographed over silica gel using CH_2Cl_2, $CHCl_3$, $CHCl_3$–MeOH mixtures and cyclohexane–EtOAc mix-



	R^1	R^2	R^3	R^4
7	H	OH	H	Me
8	OMe	OH	H	Me
9	OMe	OH	H	CHO
10	H	OH	H	H
11	H	OMe	OH	H
12	OMe	OMe	OH	H
13	OMe	OH	H	H
14	H	OH	OH	H
15	OMe	OH	OH	H

Scheme 2.



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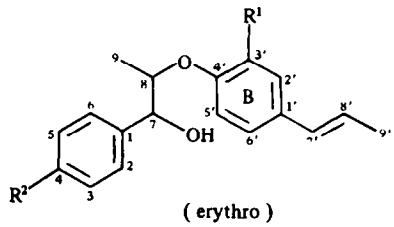
Scheme 3.

Table 4. ^{13}C NMR data of **17–18** and the methylation product of **18**

	17	**18**	**18***	**18** met.
C-1	131.52†	133.72†	133.74†	134.76†
C-2	128.72	128.55	127.66	128.56
C-3	115.62	115.57	115.14	114.17
C-4	157.43	157.35	155.07	159.87
C-5	115.62	115.57	115.14	114.17
C-6	128.72	128.55	127.66	128.56
C-7	79.21	81.86	82.27	81.75
C-8	75.66	75.09	73.91	75.03
C-9	14.76	14.39	13.40	14.46
C-1′	134.02	133.59†	132.01†	133.73†
C-2′	127.72	111.28	109.81	111.27
C-3′	117.12	152.41	151.46	152.39
C-4′	158.18	147.57	145.87	147.52
C-5′	117.12	119.64‡	119.11‡	119.62‡
C-6′	127.72	119.73	119.76‡	119.73‡
C-7′	131.78†	131.77	130.58	131.75
C-8′	123.65	124.51	124.89	124.55
C-9′	18.40	18.39	18.25	18.39
MeO		56.46	55.96	55.45
				55.50

*In $CDCl_3$.

†,‡Similar values within a column may be interchanged.



(erythro)

	R^1	R^2
17	H	OH
18	OMe	OH

Scheme 4.

Table 5. ^{13}C NMR data of **19–21**

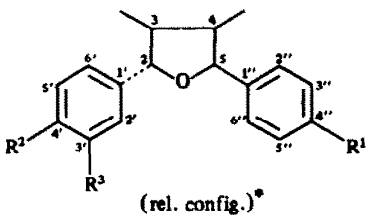
	19	**20**	**21**
C-2	86.16*	86.36*	88.17*
C-3	44.06†	44.02†	45.35†
C-4	48.38†	48.32†	45.65†
C-5	85.19*	85.12*	87.95*
C-1′	135.42	136.07	135.28
C-2′	128.24	110.65	111.03
C-3′	115.88	148.33	148.30
C-4′	157.60	146.80	146.89
C-5′	115.88	115.39	115.48
C-6′	128.24	119.84	119.95
C-1″	132.85	132.85	134.44
C-2″	127.97	127.94	128.53
C-3″	115.55	115.56	115.91
C-4″	157.01	156.97	157.71
C-5″	115.55	115.56	115.91
C-6″	127.97	127.94	128.53
CH_3-3	12.06	12.16	12.95‡
CH_3-4	9.72	9.75	13.12‡
CH_3O		56.38	56.35

*,†,‡Similar values within a column may be interchanged.

tures as eluents. Thus from the petrol extract were isolated **1–4**, **7**, **8**, **10–13**; the CCl_4 extract gave **5**, **6**, **9**, **14–21**.

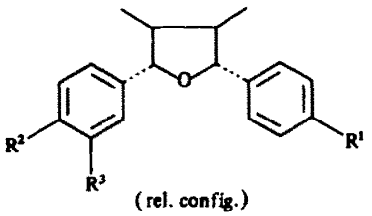
General procedures. TLC was performed on precoated plates (Nano plates Sil-20 UV, Macherey-Nagel), using the systems: S-1 = CH_2Cl_2 (at 7°); S-2 = cyclohexane–EtOAc (9:1); S-3 = cyclohexane–EtOAc (4:1); S-4 = $CHCl_3$–MeOH (49:1); S-5 = $CHCl_3$–MeOH (19:1); S-6 = $CHCl_3$; S-7 = $CHCl_3$–MeOH (99:1); S-8 = cyclohexane–EtOAc (19:1); S-9 = cyclohexane–EtOAc (99:1); detection: UV and anisaldehyde [31] followed by heating. IR spectra were recorded in KBr unless otherwise mentioned and UV in MeOH solns. Unless otherwise stated, ^{1}H NMR were recorded at 90 MHz and ^{13}C NMR at 22.5 MHz in acetone-d_6 solns; int. ref. TMS. Highfield NMR were measured at 400 and 100 MHz, respectively, in acetone-d_6. MS were obtained by EI at 70 eV.

(2R,3R)-2,3-*Dihydro*-2-(4-*hydroxy*-3-*methoxyphenyl*)-3-*methyl*-5-(E)-*propenylbenzofuran* (**1**). Colourless crystals (113 mg), mp 105–107°; TLC (S-1): R_f 0.41, grey with anisaldehyde; $[\alpha]_D^{21}$ +94° (*c* 1.10; MeOH); CD nm ($\Delta\varepsilon$): 300 (+0.32), 260 (+6.55), 225 (−5.70); IR ν_{max} cm^{-1}: 3380 (OH), 1610; UV λ_{max} (log ε): 208 (4.53), 264 (4.36), 287 (3.95, sh), 305 (3.68);



(rel. config.)*

	R^1	R^2	R^3
19	OH	OH	H
20	OH	OH	OMe



(rel. config.)

	R^1	R^2	R^3
21	OH	OH	OMe

*Meanwhile the absolute configurations of **19** and **20** could be established by comparison of the CD curves with that of chicanine [32]

Scheme 5.

+ NaOH: 263 (4.43), 298 (4.06); ^{1}H NMR (400 MHz): δ1.37 (3H, *d*, J = 7.1 Hz, Me-3), 1.83 (3H, *dd*, J_1 = 6.4, J_2 = 2 Hz, Me-10), 3.35 (1H, *m*, H-3), 3.85 (3H, *s*, MeO), 5.08 (1H, *d*, J = 9.3 Hz, H-2), 6.10 (1H, *dq*, J_1 = 15.7, J_2 = 6.4 Hz, H-9), 6.38 (1H, *dd*, J_1 = 15.7, J_2 = 2 Hz, H-8), 6.70 (1H, *d*, J = 8.3 Hz), 6.84 (1H, *d*, J = 8.5 Hz), 6.91 (1H, *dd*, J_1 = 8.5, J_2 = 2 Hz), 7.09 (1H, *d*, J = 2 Hz), 7.13 (1H, *dd*, J_1 = 8.3, J_2 = 1.5 Hz), 7.24 (1H, *br s*), 7.65 (1*H*, *s*, OH); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 296 (100, [M]$^+$), 281 (15), 267 (2), 253 (5), 171 (4), 159 (2), 151 (4), 150 (5), 137 (10), 131 (4), 115 (4), 103 (2), 91 (4).

Acetylation of **1**. **1** (35.7 mg) was dissolved in a mixture of 1.5 ml Ac_2O and 1.5 ml pyridine and stirred at room temp. for 24 hr. The solvent was evapd and the residue purified by CC (3 g silica gel, S-8) yielding 38.4 mg colourless crystals, mp 98–102°; TLC (S-2): R_f 0.20, grey with anisaldehyde; $[\alpha]_D^{21}$ + 65° (*c* 0.29; MeOH); CD nm ($\Delta\varepsilon$): 310 (+0.29), 265 (+7.35), 223 (−7.13); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765 (C=O); UV λ_{max} (log ε): 264 (4.37), 271 (4.34, sh), 305 (3.68); ^{1}H NMR: δ1.40 (3H, *d*, J = 6.8 Hz, Me-3), 1.85 (3H, *d*, J = 5 Hz, Me-10), 2.29 (3H, *s*, Me–Ac), 3.20–3.56 (1H, *m*, H-3), 3.80 (3H, *s*, MeO), 5.10 (1H, *d*, J = 8.8 Hz, H-2), 5.92–6.21 (1H, *m*, H-9), 6.35 (1H, *br d*, J = 16 Hz, H-8), 6.72–6.89 (2H, *m*), 6.95–7.16 (4H, *m*); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 338 (41, [M]$^+$), 297 (21), 296 (100), 281 (15), 267 (2), 253 (5), 235 (2), 178 (3), 172 (9), 171 (7), 159 (4), 151 (7), 137 (17), 123 (15), 115 (10), 103 (5), 91 (8), 77 (9).

(2R,3R)-2,3-*Dihydro*-2-(4-*hydroxy*-3-*methoxyphenyl*)-7-*methoxy*-3-*methyl*-5-(E)-*propenylbenzofuran* (**2**) (= *licarin A* [2]). Colourless crystals (84 mg), mp 102–104°; TLC (S-1): R_f 0.28, pale violet with anisaldehyde; $[\alpha]_D^{21}$ + 52° (*c* 0.79. MeOH); CD nm ($\Delta\varepsilon$): 275 (+5.06), 222 (−4.04); IR ν_{max} cm^{-1}: 3370 (OH), 1610; UV λ_{max} (log ε): 219 (4.30), 273 (4.06), 315 (3.21); + NaOH: 268 (4.16), 300 (3.81); ^{1}H NMR: δ1.33 (3H, *d*, J = 6.8 Hz, Me-3), 1.81 (3H, *br d*, J = 5.1 Hz, Me-10), 3.38 (1H, *m*, H-3), 3.81 (6H, *s*, 2 × MeO), 5.05 (1H, *d*, J = 9.3 Hz, H-2), 5.89–6.26 (1H, *m*, H-9), 6.31 (1H, *br d*, J = 16 Hz, H-8), 6.77–7.07 (5H, *m*), 7.56 (1H, *s*, OH); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 326 (100, [M]$^+$), 311 (6), 297 (< 1), 283 (1), 202 (5), 189 (2), 163 (4), 151 (4), 137 (6).

(2R,3R)-2, 3-*Dihydro*-2-(4-*hydroxyphenyl*)-7-*methoxy*-3-*methyl*-5-(E)-*propenylbenzofuran* (**3**). Colourless crystals (229 mg), mp 100–103°; TLC (S-1): R_f 0.10, violet with anisaldehyde; $[\alpha]_D^{21}$ + 57° (*c* 0.67; MeOH); CD nm ($\Delta\varepsilon$): 295 (+1.36), 270 (+5.30), 220 (−4.63); IR ν_{max} cm^{-1}: 3460 (OH), 1610, 1600; UV λ_{max} (log ε): 223 (4.57), 269 (4.40), 302 (3.66); + NaOH: 252 (4.46), 270 (4.44), 302 (4.03); ^{1}H NMR: δ1.34 (3H, *d*, J = 6.8 Hz, Me-3), 1.83 (3H, *br d*, J = 5.1 Hz, Me-10), 3.37 (1H, *m*, H-3), 3.83 (3H, *s*, MeO), 5.09 (1H, *d*, J = 8.8 Hz, H-2), 5.94–6.27 (1H, *m*, H-9), 6.33 (1H, *br d*, J = 16 Hz, H-8), 6.80–6.97 (4H, *m*), 7.30 (2H, *dm*, J = 8.5 Hz, H-2'; H-6'); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 296 (100, [M]$^+$), 281 (5), 267 (1), 253 (1), 202 (5), 189 (2), 165 (1), 121 (7), 119 (5), 107 (8).

Acetylation of **3**. **3** (40.5 mg) was acetylated in the usual manner. CC (3 g silica gel, S-8) yielded 36.8 mg oily product. TLC (S-2): R_f 0.46, violet with anisaldehyde; $[\alpha]_D^{21}$ + 14.8° (*c* 0.78; MeOH); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 (C=O); UV λ_{max} (log ε): 217 (4.56), 267 (4.17), 277 (4.16, sh), 300 (3.60), 314 (3.46); ^{1}H NMR: δ1.39 (3H, *d*, J = 6.8 Hz, Me-3), 1.81 (3H, *br d*, J = 5.1 Hz, Me-10) 2.24 (3H, *s*, Me–Ac), 3.37 (1H, *m*, H-3), 3.84 (3H, *s*, MeO), 5.20 (1H, *d*, J = 8.6 Hz, H-2), 5.94–6.28 (1H, *m*, H-9), 6.33 (1H, *br d*, J = 16 Hz, H-8), 6.83 (1H, *br d*, J = 1 Hz), 6.87 (1H, *br d*, J = 1 Hz), 7.13 (2H, *dm*, J = 8 Hz, H-3', H-5'), 7.47 (2H, *dm*, J = 8 Hz, H-2', H-6'); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 338 (71, [M]$^+$), 296 (100), 281 (7), 202 (13), 189 (4), 165 (4), 131 (4), 121 (8), 119 (7), 115 (7), 107 (12).

(2R,3R)-2,3-*Dihydro*-2-(4-*hydroxyphenyl*)-3-*methyl*-5-(E)-*propenylbenzofuran* (**4**) (= *conocarpan* [8]). Colourless crystals (293 mg), mp 133–135°; TLC (S-1): R_f = 0.18, grey with anisaldehyde; $[\alpha]_D^{21}$ + 122° (*c* 1.03; MeOH); CD nm ($\Delta\varepsilon$): 300 (+0.46), 260 (+11.45), 225 (−9.97); IR ν_{max} cm^{-1}: 3380 (OH), 1610, 1603; UV λ_{max} (log ε): 227 (4.29), 264 (4.33), 303 (3.65); + NaOH: 262 (4.40), 305 (3.90); ^{1}H NMR: δ1.28 (3H, *d*, J = 6.8 Hz, Me-3), 1.78 (3H, *br d*, J = 5 Hz, Me-10), 3.30 (1H, *m*, H-3), 5.00 (1H, *d*, J = 8.8 Hz, H-2), 5.89–6.20 (1H, *m*, H-9), 6.30 (1H, *br d*, 16 Hz, H-8), 6.67 (1H, *d*, 7.8 Hz), 6.78 (2H, *dm*, J = 9 Hz, H-3', H-5'), 6.90–7.14 (2H, *m*), 7.27 (2H, *dm*, J = 8.5 Hz, H-2', H-6'), 8.45 (1H, *s*, OH); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 266 (100, [M]$^+$), 265 (7), 251 (12), 237 (2), 223 (7), 171 (3), 159 (3), 131 (5), 121 (6), 119 (9), 107 (8), 91 (3), 77 (4).

Hydrogenation of **4**. **4** (12 mg) was hydrogenated at 14° with PtO_2 as catalyst in MeOH soln. Hydrogen uptake was completed within 20 min. The mixture was filtered and the solvent evapd to obtain 12 mg oily product. TLC (S-3): R_f 0.28, grey-blue with anisaldehyde; $[\alpha]_D^{21}$ + 39° (*c* 0.98; MeOH); CD nm ($\Delta\varepsilon$): 281 (−2.0), 233 (+13.8); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1610, 1603; UV λ_{max} (log ε): 229 (4.26), 277 (3.64, sh), 284 (3.70), 296 (3.52, sh); + NaOH: 245 (4.25), 289 (3.82); ^{1}H NMR: δ0.92 (3H, *t*, J = 7.4 Hz, Me-10), 1.32 (3H, *d*, J = 6.8 Hz, Me-3), 1.47–1.81 (2H, *m*, H-9), 2.54 (2H, *t*, J = 7.5 Hz, H-8), 3.35 (1H, *m*, H-3), 5.04 (1H, *d*, J = 8.9 Hz, H-2), 6.61–7.11 (5H, *m*), 7.29 (2H, *dm*, J = 8.5 Hz, H-2', H-6'); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 268 (100 [M]$^+$), 253 (7), 240 (9), 239 (53), 221 (5), 145 (24), 121 (5), 115 (7), 107 (13).

(2R,3R) 2,3-*Dihydro*-2-(4-*hydroxyphenyl*)-5-(3-*hydroxypropyl*)-3-*methylbenzofuran* (**5**). Colourless crystals (46mg), mp 123–125°. TLC (S-4): R_f 0.10, grey-green with anisaldehyde;

$[\alpha]_D^{21}$ +4.1° (*c* 0.56; MeOH); CD nm (Δε): 281 (−0.37), 233 (+2.20); IR ν_{max} cm^{-1}: 3610 (OH), 3540 (OH); UV λ_{max} (log ε): 229 (4.16), 285 (3.67), 296 (3.51, sh); +NaOH: 245 (4.14), 288 (3.72); ^{1}H NMR (400 MHz): δ 1.36 (3H, *d*, *J* = 6.6 Hz, Me-3), 1.77–1.83 (2H, *m*, H-9), 2.64 (2H, *t*, *J* = 7.7 Hz, H-8), 3.35 (1H, *m*, H-3), 3.53 (< 1H, *t*, *J* = 5.0 Hz, OH-10), 3.56 (2H, *m*, H-10), 5.05 (1H, *d*, *J* = 8.9 Hz, H-2), 6.68 (1H, *d*, *J* = 8.1 Hz, H-7), 6.87 (2H, *dm*, *J* = 8.0 Hz, H-3', H-5'), 6.99 (1H, *dd*, J_1 = 8.1, J_2 = 1.5 Hz, H-6), 7.05 (1H, *br s*, H-4), 7.30 (2H, *dm*, *J* = 8.0 Hz, H-2',H-6'), 8.42 (1H, *s*, OH); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 284 (100, [M]$^+$), 269 (4), 240 (6), 239 (35), 223 (8), 165 (5), 145 (22), 133 (10), 131 (11), 121 (9), 120 (5), 119 (9), 115 (13), 107 (22), 91 (10).

(2R,3R)-2,3-*Dihydro*-2-(4-*hydroxy*-3-*methoxyphenyl*)-5-(3-*hydroxypropyl*)-3-*methylbenzofuran* (**6**). Oil (53 mg). TLC (S-4): R_f 0.29, grey with anisaldehyde: $[\alpha]_D^{21}$ +37° (*c* 0.76; MeOH); CD nm (Δε) 285 (−1.61), 233 (+5.14); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620 (OH), 3540 (OH); UV λ_{max} (log ε): 231 (4.21), 285 (3.84); +NaOH: 236 (4.11), 252 (4.11), 291 (3.93); ^{1}H NMR: δ 1.35 (3H, *d*, *J* = 6.8 Hz, Me-3), 1.67–1.94 (2H, *m*, H-9), 2.65 (2H, *t*, *J* = 7.7 Hz, H-8), 3.17–3.69 (3H, *m*, H-10, H-3), 3.83 (3H, *s*, MeO), 5.04 (1H, *d*, *J* = 9.3 Hz, H-2), 5.59 (< 1H, *s*, OH), 6.62–7.05 (6H, *m*), 7.63 (1H, *s*, OH); ^{13}C NMR: see Table 1; MS *m/z* (rel. int.): 314 (100, [M]$^+$) 299 (10), 281 (< 1), 269 (12), 253 (4), 251 (4), 165 (4), 145 (12), 137 (12), 131 (6), 123 (4), 115 (8), 91 (7).

2-(4-*Hydroxyphenyl*)-3-*methyl*-5-(E)-*propenylbenzofuran* (**7**) (= *eupomatenoid* 6 [16]; *ratanhiaphenol II* [15]). Colourless crystals (90 mg), mp 148–151°; TLC (S-1): R_f 0.33, grey-blue with anisaldehyde; IR ν_{max} cm^{-1}: 3320 (OH); UV λ_{max} (log ε): 226 (3.96), 256 (4.21), 294 (4.11), 320 (4.02, sh); +NaOH: 238 (4.12), 261 (4.08), 332 (4.20); ^{1}H NMR: δ 1.85 (3H, *br d*, *J* = 5.0 Hz, Me-10), 2.39 (3H, *s*, Me-3), 6.01–6.39 (1H, *m*, H-9), 6.52 (1H, *br d*, *J* = 16.8 Hz, H-8), 7.02 (2H, *dm*, *J* = 8.8 Hz, H-3',H-5'), 7.32 (2H, *m*), 7.48 (1H, *br s*), 7.68 (2H, *dm*, *J* = 8.8 Hz, H-2', H-6'), 8.67 (1H, *s*, OH); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 264 (100, [M]$^+$), 263 (17), 247 (2), 237 (5), 235 (2), 221 (4), 202 (2), 189 (2), 178 (2), 165 (3), 143 (1), 141 (2), 132 (6), 121 (5), 107 (2).

Hydrogenation of **7**. **7** (21.5 mg) was hydrogenated in the usual manner with PtO_2 as catalyst to obtain 21.5 mg colourless crystals, mp 101–103°; TLC: (S-3): R_f 0.27, grey-blue with anisaldehyde; IR ν_{max} cm^{-1}: 3400 (OH); UV λ_{max} (log ε): 221 (4.20, sh), 242 (3.87), 280 (4.29, sh), 310 (4.46), 325 (4.22, sh); +NaOH: 254 (3.75), 283 (3.66, sh), 323 (4.51); ^{1}H NMR: δ0.94 (3H, *t*, *J* = 7.3 Hz, Me-10), 1.48–1.89 (2H, *m*, H-9), 2.41 (3H, *s*, Me-3), 2.69 (2H, *t*, *J* = 7.5 Hz, H-8), 7.00 (2H, *dm*, *J* = 8.5 Hz, H-3',H-5'), 7.13 (1H, *d*, *J* = 1.7 Hz), 7.30–7.41 (2H, *m*), 7.67 (2H, *dm*, *J* = 8.9 Hz, H-2',H-6'); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 266 (100, [M]$^+$), 238 (15), 237 (80), 121 (1), 119 (8), 107 (2).

2-(4-*Hydroxyphenyl*)-7-*methoxy*-3-*methyl*-5-(*E*)-*propenylbenzofuran* (**8**) (=*eupomatenoid* 13 [18]; *kachirachirol A* [17]). Colourless crystals (50 mg), mp 193–196°; TLC (S-1): R_f 0.18, grey with anisaldehyde; IR ν_{max} cm^{-1}: 3400 (OH), 1610, 1590; UV λ_{max} (log ε): 228 (4.16), 266 (4.73), 295 (4.32); +NaOH: 237 (4.25), 272 (4.28), 320 (4.37); ^{1}H NMR: δ 1.85 (3H, *br d*, *J* = 5.1 Hz, Me-10), 2.38 (3H, *s*, Me-3), 3.99 (3H, *s*, MeO), 6.09–6.40 (1H, *m*, H-9), 6.45 (1H, *br d*, *J* = 16 Hz, H-8), 6.92–7.09 (4H, *m*), 7.68 (2H, *dm*, *J* = 8.8 Hz, H-2',H-6'), 8.65 (1H, *s*, OH); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 294 (100, [M]$^+$), 293 (10), 267 (4), 251 (3), 235 (3), 165 (2), 147 (6), 121 (4), 107 (2).

Acetylation of **8**. **8** (25 mg) was acetylated in the usual manner. CC (3 g silica gel, S-1) yielded 24 mg colourless crystals, mp 131–134°; TLC (S-1): R_f 0.80, grey with anisaldehyde; IR ν_{max} cm^{-1}: 1745 (C=O); UV λ_{max} (log ε): 226 (3.87), 265 (4.49), 273 (4.46, sh), 295 (4.36); ^{1}H NMR: δ 1.86 (3H, *br d*, *J* = 5.2 Hz, Me-10), 2.29 (3H, *s*, Me-Ac), 2.44 (3H, *s*, Me-3), 4.02 (3H, *s*, MeO), 6.10–6.43 (1H, *m*, H-9), 6.48 (1H, *br d*, *J* = 16 Hz, H-8), 6.98 (1H, *d*, *J* = 1.4 Hz), 7.12 (1H, *d*, *J* = 1.4 Hz), 7.27 (*dm*, *J* = 9 Hz, H-3',H-5'), 7.85 (2H, *dm*, *J* = 9 Hz, H-2', H-6'); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 336 (27, [M]$^+$), 294 (62), 293 (10), 251 (1), 235 (2), 189 (1), 178 (5), 121 (1), 43 (100).

3-*Formyl*-2-(4-*hydroxyphenyl*)-7-*methoxy*-5-(*E*)-*propenylbenzofuran* (**9**). Yellow solid (20 mg), mp 258–261°; TLC (S-4): R_f 0.22, fluorescence at 366 nm (yellow), grey with anisaldehyde; IR ν_{max} cm^{-1}: 3370 (OH) 1650 (C=O); UV λ_{max} (log ε): 250 (4.43), 292 (4.06), 332 (4.11); +NaOH: 260 (4.42), 380 (4.28); ^{1}H NMR: δ 1.89 (3H, *d*, *J* = 5 Hz, Me-10), 4.05 (3H, *s*, MeO), 6.16–6.66 (2H, *m*, H-8, H-9), 7.02–7.14 (3H, *m*, H-3', H-5', H-6), 7.72 (1H, *d*, *J* = 1.5 Hz, H-4), 7.88 (2H, *dm*, *J* = 8.5 Hz, H-2',H-6'), 9.14 (< 1H, *s*, OH) 10.30 (1H, *s*, H-aldehyde); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 308 (100, [M]$^+$), 307 (13), 293 (6), 278 (13), 265 (1), 251 (3), 237 (3), 221 (7), 207 (4), 194 (3), 178 (5), 165 (8), 152 (4), 121 (15), 115 (5), 107 (2).

Acetylation of **9**. **9** (12.9 mg) was acetylated in the usual manner. CC (silica gel, S-3) yielded 5 mg colourless crystals, mp 112–115°; TLC (S-3): R_f 0.31, fluorescence at 366 nm, grey with anisaldehyde; IR ν_{max} cm^{-1}: 1750 (C=O), 1670 (C=O); UV λ_{max} (log ε) 247 (4.22), 287 (3.94), 327 (3.85); ^{1}H NMR: δ 1.89 (3H, *d*, *J* = 5.0 Hz, Me-10), 2.33 (3H, *s*, Me-Ac), 4.06 (3H, *s*, MeO), 6.13–6.62 (2H, *m*, H-8,H-9) 7.12 (1H, *d*, *J* = 1.5 Hz, H-6), 7.42 (2H, *dm*, *J* = 8.5 Hz, H-3',H-5'), 7.71 (1H, *d*, 1.5 Hz, H-4), 8.06 (2H, *dm*, *J* = 8.5 Hz, H-2',H-6') 10.35 (1H, *s*, H-aldehyde); MS *m/z* (rel. int.): 350 (46, [M]$^+$), 309 (18), 308 (100), 307 (11), 293 (5), 277 (3), 221 (3), 207 (3), 189 (2), 178 (5), 165 (6), 152 (3), 121 (7), 115 (2), 58 (5), 43 (35).

3-*Hydroxymethyl*-2-(4-*hydroxyphenyl*)-7-*methoxy*-5-(E)-*propenylbenzofuran by reduction of* **9**. A soln of **9** (5 mg, 0.0162 mmol) in 2 ml EtOH was gradually added to a stirred soln of $NaBH_4$ (20 mg) in 1 ml EtOH. The mixture was stirred for 20 hr at room temp. H_2O (20 ml) and some drops of HOAc were then added and the mixture extracted with *t*-butyl Me ether (4 × 20 ml). The combined extracts were dried (Na_2SO_4) and evapd. CC (silica gel, S-5) produced 2.9 mg colourless crystals, mp 221–223°; TLC (S-4): R_f = 0.11, brown with anisaldehyde, no fluorescence; IR ν_{max} cm^{-1}: 3520, 3430, 3250, 1610, 1595; UV λ_{max} (log ε): 225 (4.37), 266 (4.61), 274 (4.58, sh), 295 (4.48); +NaOH: 238 (4.46), 273 (4.42), 317 (4.54); ^{1}H NMR: δ 1.87 (3H, *br d*, *J* = 5.0 Hz, Me-10), 4.02 (3H, *s*, MeO), 4.20, (1H, *t*, *J* = 5.5 Hz, $CH_2\underline{O}H$), 4.84 (2H, *d*, *J* = 5.5 Hz, $C\underline{H}_2OH$), 6.13–6.60 (2H, *m*, H-8,H-9), 6.95–7.08 (3H, *m*, H-3',H-5',H-6), 7.26 (1H, *d*, *J* = 1.3 Hz), 7.79 (2H, *dm*, *J* = 8.8 Hz, H-2',H-6'), 8.73 (1H, *s*, OH); MS *m/z* (rel. int.): 310 (100, [M]$^+$) 309 (3), 294 (8), 293 (16), 280 (5), 261 (3), 221 (3), 207 (3), 189 (2), 178 (3), 165 (5), 121 (20), 115 (3), 107 (2).

2-(4-*Hydroxyphenyl*)-5-(E)-*propenylbenzofuran* (**10**). Colourless crystals (14 mg), mp 208–211°; TLC (S-6): R_f 0.20, grey with anisaldehyde; IR ν_{max} cm^{-1}: 3420 (OH), 1610, 1595; UV λ_{max} (log ε): 225 (4.23), 254 (4.31), 290 (4.30), 305 (4.31), 319 (4.27), 332 (4.19, sh); +NaOH: 235 (4.31), 260 (4.17), 335 (4.39); ^{1}H NMR: δ 1.85 (3H, *d*, *J* = 5.1 Hz, Me-10), 6.00–6.37 (1H, *m*, H-9), 6.50 (1H, *br d*, *J* = 16 Hz, H-8), 6.89–6.98 (3H, *m*), 7.2–7.4 (2H, *m*), 7.53 (1H, *br s*), 7.77 (2H, *dm*, *J* = 9.0 Hz, H-2',H-6'), 8.70 (1H, *s*, OH); ^{13}C NMR: see Table 3; MS *m/z* (rel.int.): 250 (100, [M]$^+$), 249 (10), 231 (3), 223 (10), 221 (11), 202 (5), 189 (2), 178 (4), 165 (6), 149 (8), 128 (5), 121 (12), 107 (4).

2-(2-*Hydroxy*-4-*methoxyphenyl*)-5-(E)-*propenylbenzofuran* (**11**) (=*ratanhiaphenol I* [15]). Colourless crystals (77 mg), mp 182–184°; TLC (S-1): R_f 0.59, brown-yellow with anisaldehyde; IR ν_{max} cm^{-1}: 3500 (OH, sharp), 1620, 1595; UV λ_{max} (log ε): 233 (4.36), 255 (4.34), 275 (4.26), 288 (4.25), 313 (4.37, sh), 320 (4.44), 327 (4.37), 335 (4.39); +NaOH: 245 (4.49), 282 (4.16), 293 (4.13), 350 (4.37); ^{1}H NMR: δ 1.85 (3H, *dd*, J_1 = 5.9, J_2 = 1.0 Hz, Me-10), 3.80 (3H, *s*, MeO), 6.00–6.38 (1H, *m*, H-9), 6.48 (1H, *br d*, *J* = 16 Hz, H-8), 6.54–6.68 (2H, *m*), 7.20–7.54 (4H, *m*), 7.89 (1H, *dm*,

J = 9.0 Hz), 9.25 (1H, *s*, OH); ^{13}C NMR: see Table 3; MS *m/z* (rel. int.): 280 (100, [M]$^+$), 265 (35), 253 (1), 251 (4), 237 (1), 209 (1), 181 (1), 165 (4), 151 (4), 140 (7).

2-(2-*Hydroxy*-4-*methoxyphenyl*)-7-*methoxy*-5-(E)-*propenyl benzofuran* (**12**) (= *toltecol*). Colourless crystals (20.3 mg), mp 101–102°; TLC (S-6): R_f 0.40, grey-green with anisaldehyde; IR ν_{max} cm^{-1}: 3500 (OH, sharp), 1630, 1595; UV λ_{max} (log ε): 232 (4.29), 267 (4.38), 289 (4.26), 316 (4.34), 324 (4.30, sh), 331 (4.26); + NaOH; 245 (4.43), 280 (4.28), 290 (4.17), 342 (4.30); ^{1}H NMR: δ1.85 (3H, *br d*, J = 5.0 Hz, Me-10), 3.80 (3H, *s*, MeO), 4.03 (3H, *s*, MeO), 6.00–6.55 (2H, *m*, H-8,H-9), 6.57–6.68 (2H, *m*), 6.92 (1H, *d*, J = 1.5 Hz), 7.12 (1H, *d*, J = 1.5 Hz), 7.24 (1H, *s*), 7.88 (1H, *br d*, J = 9.4 Hz), 9.26 (1H, *s*, OH); ^{13}C NMR: see Table 3; MS *m/z* (rel. int.): 310 (100, [M]$^+$), 295 (12), 281 (1), 267 (1), 251 (3), 178 (3), 165 (9), 151 (9), 115 (9), 77 (7).

2-(4-*Hydroxyphenyl*)-7-*methoxy*-5-(E)-*propenylbenzofuran* (**13**). Colourless crystals (25 mg), mp 177–179°; TLC (S-6): R_f 0.26, grey with anisaldehyde; IR ν_{max} cm^{-1}: 3330 (OH), 1610, 1595; UV λ_{max} (log ε): 225 (4.34), 266 (4.47), 295 (4.45), 305 (4.45), 317 (4.29, sh), + NaOH: 232 (4.39), 273 (4.31), 322 (4.49); ^{1}H NMR: δ1.85 (3H, *br d*, J = 5.0 Hz, Me-10), 4.02 (3H, *s*, MeO), 5.98–6.30 (1H, *m*, H-9), 6.45 (1H, *br d*, J = 16 Hz, H-8), 6.91–7.07 (5H, *m*), 7.75 (2H, *dm*, J = 8.8 Hz, H-2′,H-6′), 8.69 (1H, *s*, OH); ^{13}C NMR: see Table 3; MS *m/z* (rel. int.): 280 (100, [M]$^+$), 279 (8), 265 (1), 253 (4), 237 (4), 221 (10), 207 (3), 194 (5), 165 (12), 121 (9), 115 (12), 107 (1).

2-(2,4-*Dihydroxyphenyl*)-5-(E)-*propenylbenzofuran* (**14**). Colourless crystals (90 mg), mp 181–184°; TLC (S-4): R_f = 0.07, brown-yellow with anisaldehyde; IR ν_{max} cm^{-1}: 3350 (OH), 1630, 1600; UV λ_{max} (log ε): 233 (4.47), 256 (4.46), 275 (4.39), 288 (4.37), 314 (4.44, sh), 320 (4.48), 328 (3.98, sh), 335 (4.48); + NaOH: 240 (4.52), 256 (4.44, sh), 280 (4.29), 295 (4.27), 345 (4.53); ^{1}H NMR: δ1.83 (3H, *br d*, J = 5.1 Hz, Me-10), 5.99–6.50 (2H, *m*, H-8,H-9), 6.52–6.64 (2H, *m*), 7.11–7.51 (4H, *m*), 7.81 (1H, *d*, J = 8.1 Hz), 8.63 (1H, *s*, OH), 9.17 (1H, *s*, OH); ^{13}C NMR: see Table 3. MS *m/z* (rel. int.): 266 (100, [M]$^+$), 265 (5), 251 (1), 237 (10), 223 (2), 197 (2), 181 (1), 165 (6), 152 (3), 137 (7), 128 (3), 123 (1), 115 (4).

2-(2,4-*Dihydroxyphenyl*)-7-*methoxy*-5-(E)-*propenylbenzofuran* (**15**). Colourless crystals (72 mg), mp 172–174°; TLC (S-7): R_f 0.21, grey-green with anisaldehyde; IR ν_{max} cm^{-1}: 3440 (OH), 3330 (OH), 1620, 1595; UV λ_{max} (log ε): 232 (4.39), 266 (4.45), 290 (4.36), 317 (4.43), 332 (4.36, sh); + NaOH: 239 (4.44), 275 (4.34), 342 (4.45); ^{1}H NMR: δ1.84 (3H, *br d*, J = 4.9 Hz, Me-10), 4.02 (3H, *s*, MeO), 5.99–6.39 (1H, *m*, H-9), 6.42 (1H, *br d*, J = 16 Hz, H-8), 6.52–6.61 (2H, *m*), 6.90 (1H, *d*, J = 1.5 Hz), 7.11 (1H, *d*, J = 1.5 Hz), 7.22 (1H, *s*, H-3), 7.83 (1H, *d*, J = 8.5 Hz, H-6′), 8.61 (1H, *s*, OH), 9.15 (1H, *s*, OH); ^{13}C NMR: see Table 3; MS *m/z* (rel. int.): 296 (100, [M]$^+$), 295 (5), 281 (2), 267 (3), 253 (5), 237 (7), 223 (1), 197 (1), 165 (3), 152 (4), 137 (6), 115 (4).

2-(4-*Hydroxyphenyl*)-5-(3-*hydroxypropyl*)-3-*methylbenzofuran* (**16**) (=*olmecol*). Colourless crystals (203 mg), mp 161–162°; TLC (S-5): R_f 0.46, grey with anisaldehyde; IR ν_{max} cm^{-1}: 3420 (OH), 3130 (OH); UV λ_{max} (log ε): 242 (3.85), 280 (4.25, sh), 309 (4.37), 326 (4.18, sh); + NaOH: 323 (4.41); ^{1}H NMR (CD_3OD): δ1.62–2.03 (2H, *m*, H-9), 2.35 (3H, *s*, Me-3), 2.76 (2H, *br t*, J = 7.8 Hz, H-8), 3.60 (2H, *t*, J = 6.4 Hz, H-10), 4.84 (*s*, *br*, OH), 6.91 (2H, *dm*, J = 9.0 Hz, H-3′,H-5′), 6.99–7.10 (1H, *m*), 7.25–7.34 (2H, *m*), 7.61 (2H, *dm*, J = 9.0 Hz, H-2′,H-6′); ^{13}C NMR: see Table 2; MS *m/z* (rel. int.): 282 (100, [M]$^+$), 251 (1), 238 (73), 237 (51), 223 (8), 207 (3), 195 (4), 194 (3), 178 (3), 165 (10), 152 (3), 131 (2), 121 (2), 119 (4), 115 (4), 107 (2).

Erythro-1-(4-*hydroxyphenyl*)-2-[4-(E)-*propenylphenoxy*]-*propan*-1-*ol* (**17**). Oily substance (8.8 mg). TLC (S-6): R_f 0.13, grey-violet with anisaldehyde; $[\alpha]_D^{21}$ −6.4° (*c* 0.44; MeOH); CD nm (Δε): 275 (−0.46), 222 (+1.20); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1615, 1595; UV λ_{max} (log ε): 218 (4.25, sh), 227 (4.06, sh), 260 (4.38), 269 (4.30, sh), 285 (3.67, sh), 297 (3.47, sh), 309 (3.27, sh); + NaOH: 259 (4.41) 269 (4.30, sh), 295 (3.67, sh), 309 (3.27, sh); ^{1}H NMR: δ1.22 (3H, *d*, J = 6.4 Hz, H-9), 1.81 (3H, *br d*, J = 4.9 Hz, H-9′), 4.29 (1H, *d*, J = 4.0 Hz, OH-7), 4.49 (1H, *dq*, J_1 = 6.4, J_2 = 4.0 Hz, H-8), 4.78 (1H, *dd*, J_1 = J_2 = 4.0 Hz, H-7), 5.85–6.20 (1H, *m*, H-8′), 6.31 (1H, *br d*, J = 16 Hz, H-7′), 6.69–6.93 (4H, *m*), 7.18–7.38 (4H, *m*), 8.16 (1H, *s*, OH); ^{13}C NMR: see Table 4; MS *m/z* (rel. int.): 284 (13, [M]$^+$), 162 (13), 161 (13), 134 (100), 133 (27), 123 (38), 115 (13), 105 (6), 91 (9), 77 (8).

Erythro-1-(4-*hydroxyphenyl*)-2-[2-*methoxy*-4-(E)-*propenylphenoxy*]-*propan*-1-*ol* (**18**). Oil (17 mg). TLC (S-4): R_f 0.08, grey-violet with anisaldehyde; $[\alpha]_D^{21}$ −11.6° (*c* 0.79; MeOH); CD nm (Δε): 300 (−0.65), 250 (−1.10), 228 (+3.1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 3500 (OH), 2950, 2870; UV λ_{max} (log ε): 221 (4.37, sh), 259 (4.20), 266 (4.18, sh), 284 (3.85, sh), 301 (3.71, sh); + NaOH: 249 (4.33), 267 (4.25, sh), 295 (3.97, sh); ^{1}H NMR (400 MHz): δ1.16 (3H, *d*, J = 6.4 Hz, H-9), 1.83 (3H, *dd*, J_1 = 6.6, J_2 = 1.4 Hz, H-9′), 3.84 (3H, *s*, MeO), 4.15 (1H, *d*, J = 4.0 Hz, OH-7), 4.40 (1H, *dq*, J_1 = 6.4, J_2 = 4.0 Hz, H-8), 4.80 (1H, *dd*, J_1 = J_2 = 4.0 Hz, H-7), 6.17 (1H, *dq*, J_1 = 15.7, J_2 = 6.6 Hz, H-8′), 6.35 (1H, *dq*, J_1 = 15.7, J_2 = 1.4 Hz, H-7′), 6.78 (2H, *dm*, J = 8.6 Hz, H-3,H-5), 6.85 (1H, *dd*, J_1 = 7.9, J_2 = 2.2 Hz, H-6′), 6.94 (1H, *d*, J = 7.9 Hz, H-5′), 7.04 (1H, *d*, 2.2 Hz, H-2′), 7.22 (2H, *dm*, J = 8.6 Hz, H-2,H-6), 8.19 (1H, *s*, OH); ^{13}C NMR: see Table 4; MS *m/z* (rel.int): 314 (10, [M]$^+$), 296 (5), 191 (6), 165 (11), 164 (100), 162 (8), 149 (10), 133 (8), 123 (8), 121 (6), 115 (7), 103 (9), 91 (10), 77 (12).

Methylation of **18**. To a soln of 1.4 mg **18** in dry Me_2CO was added 0.5 ml MeI and 25 mg dry K_2CO_3. The mixture was refluxed for 20 hr, the solvent evapd and the residue purified by CC (silica gel, S-3) to yield 0.9 mg oil. TLC (S-3): R_f 0.23, violet with anisaldehyde; $[\alpha]_D^{21}$ −35.5°, (*c* 0.09; MeOH); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500; UV λ_{max} (log ε): 221 (4.44, sh), 259 (4.28), 267 (4.25, sh), 283 (3.80, sh), 292 (3.70, sh); + NaOH: unchanged; ^{1}H NMR: δ1.16 (3H, *d*, J = 6.4 Hz, H-9), 1.82 (3H, *br d*, J = 5.1 Hz, H-9′), 3.76 (3H, *s*, MeO), 3.84 (3H, *s*, MeO), 4.19 (1H, *d*, J = 4.0 Hz, OH-7), 4.27–4.52 (1H, *m*, H-8), 4.82 (1H, *dd*, J_1 = J_2 = 4.0 Hz, H-7), 5.90–6.44 (2H, *m*, H-7′,H-8′), 6.80–6.98 (5H, *m*), 7.35 (2H, *dm*, J = 9.0 Hz, H-2,H-6); ^{13}C NMR: see Table 4, MS *m/z* (rel. int.): 328 (7, [M]$^+$), 191 (3), 165 (12), 164 (100), 149 (5), 137 (14), 91 (5).

1-(4-*Methoxyphenyl*)-2-*bromopropan*-1-*one*. *N*-Bromosuccinimide 1.24 g (0.007 mol) was added to a soln of 1.04 g (0.0063 mol) *p*-methoxypropiophenone (EGA No. M 2480-9) in dry CCl_4. After addition of a few mg of 2,2′-azobisisobutyronitrile the mixture was carefully heated until the reaction had started and then refluxed for 3 hr. The mixture was cooled, filtered and evapd. CC (silica gel, S-8) yielded 0.891 g (59%) colourless crystals, mp 66–67°; TLC (S-8): R_f 0.20, orange with 2,4-dinitrophenylhydrazine; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (C=O); ^{1}H NMR: δ1.83 (3H, *d*, J = 6.6 Hz, Me-9), 3.91 (3H, *s*, MeO), 5.61 (1H, *q*, J = 6.6 Hz, H-8), 7.06 (2H, *dm*, J = 9.0 Hz, H-3,H-5), 8.06 (2H, *dm*, J = 9.0 Hz, H-2,H-6); MS *m/z* (rel. int.): 244 (< 1), 242 (< 1, [M]$^+$), 136 (6), 135 (100), 107 (2), 92 (6), 77 (9).

1-(4-*Methoxyphenyl*)-2-[2-*methoxy*-4-(E)-*propenylphenoxy*]-*propan*-1-*one*. The Na salt of iso-eugenol (0.3 g, 1.60 mmol) was added to a stirred soln of 1-(4-methoxyphenyl)-2-bromopropan-1-one (0.34 g, 1.40 mmol) in dry DMF (3 ml). After being stirred for 28 hr at room temp. the mixture was diluted with H_2O (5 ml) and extracted with *t*-butyl Me ether (4 × 5 ml). The combined extracts were washed with 0.2 N aq. NaOH, H_2O, dried (Na_2SO_4) and evapd. CC (silica gel, S-8) yielded 0.412 g (90%) oily product. TLC (S-9): R_f 0.16, violet with anisaldehyde. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1685 (C=O); ^{1}H NMR: δ1.58 (3H, *d*, J = 6.6 Hz, Me-9), 1.80 (3H, *d*, J = 5.1 Hz, Me-9′), 3.82 (3H, *s*, MeO), 3.88

(3H, s, MeO), 5.58 (1H, q, J = 6.6 Hz, H-8), 5.82–6.17 (1H, m, H-8'), 6.28 (1H, br d, J = 16 Hz, H-7'), 6.75–6.77 (2H, m), 6.97–7.11 (3H, m), 8.13 (2H, dm, J = 9.3, J_2 = 2.0 Hz, H-2, H-6); MS m/z (rel. int.): 326 (54, $[M]^+$), 191 (39), 164 (26), 163 (29), 162 (16), 136 (9), 135 (100), 115 (6), 107 (10), 91 (10), 77 (14).

Erythro-1-(4-*methoxyphenyl*)-2-[2-*methoxy*-4-(E)-*propenylphenoxy*]-*propan*-1-*ol*. A soln of ketone (0.129 g, 0.396 mmol), in dry Et_2O (9 ml), was added dropwise to a stirred suspension of $LiAlH_4$ (0.220 g, 5.80 mmol) in 13 ml Et_2O. The mixture was then refluxed for 24 hr. Excess $LiAlH_4$ was carefully destroyed by addition of HOAc/ice and finally diluted with H_2O, acidified (10% HCl) and extracted with Et_2O. The combined Et_2O extracts were washed (1 N aq. NaOH; H_2O), dried (Na_2SO_4) and evaporated. CC (silica gel, S-7) afforded 27 mg oil. TLC, IR, UV, ^{1}H NMR, MS identical with methylation product of **18**. ^{13}C NMR: see Table 4.

2,3-Trans-3,4-cis-4,5-cis-2,5-bis-(4-*hydroxyphenyl*)-3,4-*dimethyltetrahydrofuran* (**19**). Colourless crystals (18 mg), mp 158–162°; TLC (S-4): R_f 0.05, bright violet with anisaldehyde; $[\alpha]_D^{21}$ +78° (c 0.142; MeOH); CD nm ($\Delta\varepsilon$): 230 (+10.9); IR ν_{max} cm^{-1}: 3360 (OH), 1620, 1600; UV λ_{max} (log ε): 228 (4.29), 277 (3.56), 283 (3.47, sh); +NaOH: 247 (4.37), 292 (3.64), 340 (3.20); ^{1}H NMR: δ0.57 (3H, d, J = 7.0 Hz, Me-4), 0.96 (3H, d, J = 6.6 Hz, Me-3), 2.20–2.83 (2H, m, H-3, H-4), 4.60 (1H, d, J = 9.3 Hz, H-2), 5.40 (1H, d, J = 4.1 Hz, H-5), 6.75–6.86 (4H, m), 7.13–7.32 (4H, m), 8.12 (1H, s, OH), 8.19 (1H, s, OH); ^{13}C NMR: see Table 5; MS m/z (rel. int.): 284 (5, $[M]^+$), 163 (11), 162 (100), 148 (7), 147 (71), 134 (7), 133 (9), 121 (9), 114 (3), 107 (10).

2,3-Trans-3,4-cis-4,5-cis-5-(4-*hydroxyphenyl*)-2-(4-*hydroxy*-3-*methoxyphenyl*)-3,4-*dimethyltetrahydrofuran* (**20**). Oil (40.4 mg). TLC (S-4): 0.16, violet with anisaldehyde; $[\alpha]_D^{21}$ +56° (c 0.358; MeOH); CD nm ($\Delta\varepsilon$): 230 (+4.64); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595 (OH), 3540 (OH), 1610, 1595; UV λ_{max} (log ε): 229 (4.33), 280 (3.78); +NaOH: 248 (4.48), 293 (4.05); ^{1}H NMR: δ0.57 (3H, d, J = 7.0 Hz, Me-4), 0.97 (3H, d, J = 6.3 Hz, Me-3), 2.22–2.67 (2H, m, H-3,H-4), 3.84 (3H, s, MeO), 4.61 (1H, d, J = 9.0 Hz, H-2), 5.43 (1H, d, J = 4.2 Hz, H-5), 6.74–6.95 (4H, m), 7.00–7.32 (3H, m), 7.39 (1H, s, OH), 8.13 (1H, s, OH); in $CDCl_3$: δ0.60 (3H, d, J = 6.8 Hz, Me-4), 0.98 (3H, d, J = 6.4 Hz, Me-3), 2.22–2.67 (2H, m, H-3,H-4), 3.84 (3H, s, MeO), 4.63 (1H, d, J = 9.0 Hz, H-2), 5.43 (1H, d, J = 4.2 Hz, H-5), 5.80 (< 1H, br s, OH), 6.68–6.93 (5H, m), 7.10–7.25 (2H, m); ^{13}C NMR: see Table 5; MS m/z (rel. int.): 314 (36, $[M]^+$), 229 (3), 192 (100), 177 (30), 164 (37), 163 (20), 162 (79), 161 (17), 160 (9), 151 (9), 148 (7), 147 (65), 146 (5), 145 (41), 137 (8), 134 (8), 133 (11), 132 (5), 131 (8), 129 (9), 124 (12), 121 (15), 117 (8), 107 (12).

2,3-Trans-3,4 cis-4,5-trans-5-(4-*hydroxyphenyl*)-2-(4-*hydroxy*-3-*methoxyphenyl*)-3,4-*dimethyltetrahydrofuran* (**21**). Oil (6.2 mg). TLC (S-4): R_f 0.08, grey-violet with anisaldehyde; $[\alpha]_D^{21}$ +3.7°, (c 0.54; MeOH); CD: no effect; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 3540 (OH), 1610; UV λ_{max} (log ε) = 228 (4.00), 277 (3.67), 310 (3.36, sh); +NaOH: 248 (4.07), 296 (3.70), 337 (3.66); ^{1}H NMR: δ0.95–1.05 (6H, m, Me-3,Me-4); 2.25 (2H, m, H-3,H-4), 3.85 (3H, s, MeO), 4.40 (2H, br d, J = 6.7 Hz, H-2,H-5); 6.69–6.98 (4H, m), 7.06 (1H, d, J = 1.5 Hz), 7.32 (2H, dm, J = 8.5 Hz); ^{13}C NMR: see Table 5; MS m/z (rel. int.): 314 (33, $[M]^+$), 193 (6), 192 (49) 177 (13), 164 (9), 163 (18), 162 (100), 161 (11), 148 (9), 147 (82), 145 (19), 137 (6), 134 (8), 133 (9), 129 (8), 124 (6), 121 (7), 107 (11).

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REFERENCES

1. Martinez, M. (1959) *Las Plantas Medicinales de Mexico*, 4th edn., p. 90. Ediciones Botas, Mexico.
2. Aiba, C. J., Campos Corrêa, R. G. and Gottlieb, O. R. (1973) *Phytochemistry* **12**, 1163.
3. Donnelly, B. J., Donnelly, D. M. X., O'Sullivan, A. M. and Prendergast, J. P. (1969) *Tetrahedron* **25**, 4409.
4. Gregson, M., Ollis, W. D., Redman, B. T., Sutherland, I. O. and Dietrichs, H. H. (1968) *Chem. Commun.* 1394.
5. Wenkert, E., Gottlieb, H. E., Gottlieb, O. R., da S. Pereira, M. O. and Formiga, M. D. (1976) *Phytochemistry* **15**, 1547.
6. Enriquez, R. G., Chavez, M. A. and Reynolds, W. F. (1984) *J. Nat. Prod.* **47**, 896.
7. Agrawal, P. K. and Thakur, R. S. (1985) *Magn. Reson. Chem.* **23**, 389.
8. Bremser, W., Ernst, L., Franke, B., Gerhards, R. and Hardt, A. (1981) *Carbon-13 Spectral Data*. Verlag Chemie, Weinheim.
9. Hayashi, T. and Thomson, R. H. (1975) *Phytochemistry* **14**, 1085.
10. Lima O. A., Gottlieb, O. R., Magalhães, M. T. (1972) *Phytochemistry* **11**, 2031.
11. Gottlieb, O. R., Mourão, J. C., Yoshida, M., Mascarenhas, Y. P., Rodrigues, M., Rosenstein, R. D. and Tomita, K. (1977) *Phytochemistry* **16**, 1003.
12. Fernandes, J. B., Gottlieb, O. R. and Maia, J. G. S. (1976) *Phytochemistry* **15**, 1033.
13. Aiba, C. J., Gottlieb, O. R., Pagliosa, F. M., Yoshida, M. and Magalhães, M. T. (1977) *Phytochemistry* **16**, 745.
14. de Alvarenga, M. A., Giesbrecht, A. M., Gottlieb, O. R. and Yoshida, M. (1977) *An. Acad. brasil. Ciênc.* **49**, 401.
15. Stahl, E. and Ittel, I. (1981) *Planta Med.* **42**, 144.
16. Bowden, B. F., Ritchie, E. and Taylor, W. C. (1972) *Aust. J. Chem.* **25**, 2659.
17. Ito, K., Ichino, K., Iida, T. and Lai, J. (1984) *Phytochemistry* **23**, 2643.
18. Read, R. W. and Taylor, W. C. (1979) *Aust. J. Chem.* **32**, 2317.
19. Kaouadji, M., Favre-Bonvin, J. and Mariotte, A.-M. (1978) *Phytochemistry* **17**, 2134.
20. Barata, L. E. S., Baker, P. M., Gottlieb, O. R. and Rúveda, E. A. (1978) *Phytochemistry* **17**, 783.
21. Wallis, A. F. A. (1973) *Aust. J. Chem.* **26**, 585.
22. Braga, A. C. H., Zacchino, S., Badano, H., Sierra, M. G. and Rúveda, E. A. (1984) *Phytochemistry* **23**, 2025.
23. Cavalcante, S. H., Yoshida, M. and Gottlieb, O. R. (1985) *Phytochemistry* **24**, 1051.
24. Isogai, A., Murakoshi, S., Suzuki, A. and Tamura, S. (1973) *Agric. Biol. Chem.* **37**, 1479.
25. Ahmed, R., Schreiber, F. G., Stevenson, R., Williams, J. R. and Yeo, H. M. (1976) *Tetrahedron* **32**, 1339.
26. Fonseca, S. F., Barata, L. E. S., Rúveda, E. A. and Baker, P. M. (1979) *Can. J. Chem.* **57**, 441.
27. Rao, K. V. and Alvarez, F. M. (1982) *J. Nat. Prod.* **45**, 393.
28. Lee, C. L. (1981) *Kó-Hsüeh-Fa-Chan* (*Yueh Kán*) **9**, 578.
29. Doskotch, R. W. and Flom, M. S. (1972) *Tetrahedron* **28**, 4711.
30. Sarkanen, K. V. and Wallis, A. F. A. (1973) *J. Heterocyclic Chem.* **10**, 1025.
31. Stahl, E. (1967) *Dünnschichtchromatographie*. Springer, Berlin.
32. Liu, J.-S., Huang, M.-F., Gao, Y.-L. and Findlay, J. A. (1981) *Can. J. Chem.* **59**, 1680.