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NEOLIGNANS AND *NOR*-NEOLIGNANS FROM *KRAMERIA LANCEOLATA**

HANS ACHENBACH, JOHANN GROß, PETER BAUEREIß, XORGE A. DOMINGUEZ,† HUMBERTO SANCHEZ VEGA,† JULIA VERDE STAR† and CARLOS ROMBOLD‡

Institute of Pharmacy and Food Chemistry, Department of Pharmaceutical Chemistry, Universität Erlangen, D-8520 Erlangen, F.R.G.; †Departamento de Quimica, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, N.L. 64849, Mexico; ‡CIDESON, Hermosillo, Son., Mexico

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Key Word Index—*Krameria lanceolata*; Krameriaceae; 8.3′-neolignans.

Abstract—From the hexane extract of the roots of *Krameria lanceolata*, five new phenylpropanoids were isolated, besides 13 neolignans/*nor*-neolignans already known from other Krameriaceae.

INTRODUCTION

Krameria lanceolata Torr. forms a perennial herb from woody stocks and is widespread in the Mexican States of Coahuila and Chihuahua. It also grows in Texas [2]. A tea prepared from *K. lanceolata* has been used in folk medicine to cure dysentery and to heal stomach and intestinal cancers [3].

Chemical investigation of the root extracts resulted in the isolation of 18 compounds, all of the neolignan or *nor*-neolignan type. Of these compounds, 13 have already been isolated from other Krameriaceae species, whereas five constituents represent hitherto unknown natural products.

RESULTS AND DISCUSSION

Repeated chromatography of the non-polar components from the roots of *Krameria lanceolata* yielded the known compounds **1**–**13** and the new neolignans **14**–**18**.

The deduced structures are mainly the result of spectroscopic investigations. In particular ^{1}H and ^{13}C NMR experiments and correlations with recently isolated compounds from other Krameriaceae species [4–8] served to establish the structures. The absolute configurations of **14** and **17** were determined by gas chromatography [9] according to Horeau's method [10]. Table 1 presents a synopsis of the neolignans and *nor*-neolignans isolated from *K. lanceolata* and their occurrence in other analysed *Krameria* species.

An oxidized β-position in the C_3-side chain obviously represents a characteristic structural feature of some neolignans in *K. lanceolata*. This moiety is rare in lignans/neolignans and according to our knowledge has only been described from a *Eupomatia* species [11].

We suggest the name zapotecol for **14** and, correspondingly, zapotecone for **15**.

EXPERIMENTAL

Plant material. Krameria lanceolata was collected around Saltillo, Coah. (Mexico), in July 1986 and June 1987. Botanical identification by H. Sanchez V.; voucher specimens are kept at the ITESM herbarium (Reg. No. 7863) in Monterrey, N.L. (Mexico).

Extraction and chromatography. Dried roots (400 g) of *K. lanceolata* were extracted successively with hexane and MeOH to yield 6.0 g hexane extract and 78 g MeOH extract. 2.8 g of the hexane extract were repeatedly chromatographed on silica gel using $CHCl_3$, CH_2Cl_2 and cyclohexane–EtOAc as eluents to yield **1**–**18**.

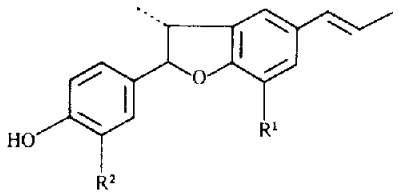
General. TLC was performed on ready made plates using the solvent system cyclohexane–EtOAc (7:3) unless otherwise stated, with detection by UV and anisaldehyde [12] followed by heating. IR spectra were recorded in $CHCl_3$ solns and KBr pellets, respectively. UV were recorded in MeOH. ^{1}H NMR and ^{13}C NMR spectra were recorded in Me_2CO-d_6 at 90 and 22.5 MHz, respectively, unless otherwise stated; int. standard TMS. MS were run at 70 eV using the direct inlet system.

Identification of **1**–**5** and **7**–**12** is based on the chromatographic and spectroscopic properties of the isolated compounds and their comparison with authentic substances [4–6]. Ratanhiaphenol III (**6**) was identified by comparison of spectroscopic data with reported data [7, 8].

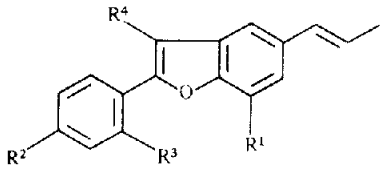
Ratanhiaphenol III (**6**) [8]. Colourless crystals (4 mg), mp 134–135°; R_f (CH_2Cl_2) 0.30 (grey with anisaldehyde); IR ν_{max}^{KBr} cm^{-1}: 3400 (*br*, OH); ^{1}H NMR: δ1.86 (3H, *br d*, J = 5 Hz, Me-10), 3.99 (3H, *s*, MeO), 6.00–6.40 (1H, *m*, H-9), 6.48 (1H, *br d*, J = 16 Hz, H-8), 6.50–6.70 (2H, *m*, H-3′, H-5′), 7.16 (1H, *s*, J = 1 Hz, H-3), 7.30 (1H, *dd*, J_1 = 8, J_2 = 2 Hz, H-6), 7.35 (1H, *dm*, J = 8 Hz, H-7), 7.55 (1H, *m*, H-4), 7.87 (1H, *dm*, $J \approx 9$ Hz, H-6′), 8.79 (1H, *s*, OH); ($CDCl_3$): δ1.90 (3H, *br d*, J = 5 Hz, Me-10), 3.97 (3H, *s*, MeO), 5.02 (1H, *br s*, OH), 6.00–6.38 (1H, *m*, H-9), 6.40–6.65 (3H, *m*, H-8, H-3′, H-5′), 7.14 (1H, *br s*, H-3), 7.22 (1H, *br dd*, J_1 = 8, J_2 = 2 Hz, H-6), 7.41 (1H, *br d*, J = 8 Hz, H-7), 7.47 (1H, *m*, H-4), 7.89 (1H, *dm*, $J \approx 9$ Hz, H-6′); ^{13}C NMR (100 MHz): δ18.52 (C-10), 55.86 (OMe), 100.24 (C-3′), 104.48 (C-3), 108.48 (C-5′), 111.09 (C-7), 112.05 (C-1′), 118.59 (C-4), 122.66 (C-6), 124.46 (C-9), 128.48 (C-6′), 131.28 (C-3a), 132.25 (C-8), 133.95 (C-5), 153.74 (C-2 or C-7a), 154.18 (C-7a or C-2), 159.14 (C-4′), 160.22 (C-1′); MS *m/z* (rel. int.): 280 (100, M$^+$), 265 (3), 237 (4), 134 (4).

Zapotecol (**14**). Colourless oil (15 mg); R_f 0.13 (brown with anisaldehyde); $[\alpha]_D^{21}$ +5° (MeOH; *c* 0.6); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH); UV λ_{max} nm (log ε): 322 (3.22), 277 (3.47); +NaOH: 341 (3.25), 284 (3.51), 236 (3.94); ^{1}H NMR (400 MHz, Me_2CO-d_6): δ1.04 (3H, *d*, J = 6 Hz, Me-9′), 2.50 (1H, *dd*, J_1 = 13, J_2 = 6 Hz, H_A-7′), 2.65 (1H, *dd*, J_1 = 13, J_2 = 6 Hz, H_B-7′), 3.44 (1H, *d*, J

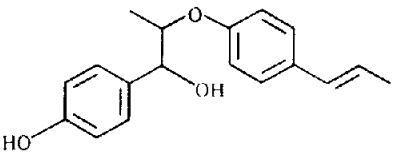
*Part 5 in the series 'Studies on Krameriaceae'. For part 4 see ref. [1].



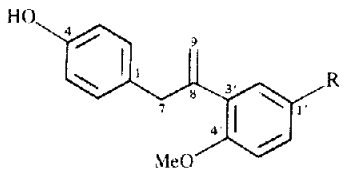
	R^1	R^2	
1	H	H	(Conocarpan)
2	H	OMe	
3	OMe	H	



	R^1	R^2	R^3	R^4	
4	H	OH	OH	H	
5	H	OMe	OH	H	(Ratanhiaphenol I)
6	H	OH	OMe	H	(Ratanhiaphenol III)
7	H	OH	OH	H	
8	OMe	OH	H	H	
9	H	OH	H	Me	(Eupomatenoid 6 = Ratanhiaphenol II)
10	OMe	OH	H	Me	(Eupomatenoid 13)
11	OMe	OH	H	CHO	



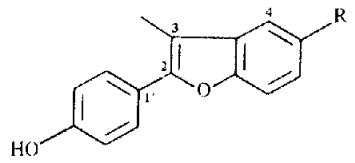
12 (rel. config.: erytho)



13 R = —CH=CH—Me (Hermosillol)

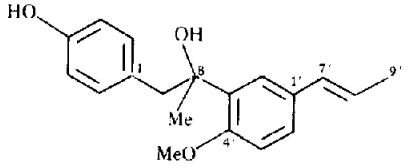
14 R = —CH_2—C(OH)(H)—Me

15 R = —CH_2—C(=O)—Me



17 R = —CH_2—C(OH)(H)—Me

18 R = —CH_2—C(=O)—Me



16 (rel. config.)

Table 1: Occurrence of neolignan/*nor*-neolignan-type compounds from *K. lanceolata* in other *Krameria* species

	K. cystisoides [4]	*K. ramosissima* [6]	*K. sonorae* [5]	*K. triandra* [7, 8]
1	+	—	+	—
2	+	—	+	—
3	+	—	—	—
4	+	—	—	–
5	+	+	+	+
6	–	—	—	+
7	+	—	—	—
8	+	—	—	—
9	+	—	+	+
10	+	—	+	—
11	+	—	—	—
12	—	—	+	—
13	—	+	+	—
14	—	—	–	
15	–	—	—	—
16	—	—	—	—
17	—	—	—	—
18	—	—	—	—

+: present.
—: not to be found.

$= 5$ Hz, OH), 3.69 (2H, *s*, H_2-7), 3.82 (3H, *s*, MeO), 3.8–3.9 (1H, *m*, H-8'), 5.00 (2H, *m*, H_2-9), 6.58 (2H, AA'BB'-system, H-3, H-5), 6.85 (1H, *d*, $J = 8$ Hz, H-5'), 6.90 (1H, *d*, $J = 2$ Hz, H-2'), 6.96 (2H, AA'BB'-system, H-2, H-6), 7.05 (1H, *dd*, $J_1 = 8$, $J_2 = 2$ Hz, H-6'), 8.04 (1H, *s*, OH ; ^{13}C NMR: δ23.16 (C-9'), 42.61 (C-7), 45.78 (C-7'), 55.94 (OMe) 69.16 (C-8'), 111.85, 115.21 (C-9), 115.77 (C-3, C-5), 130.02, 130.86 (C-2, C-6), 131.59, 132.08, 132.29, 150.14, 156.13, 156.41; MS *m/z* (rel. int.): 298 (100, M^+), 254 (34), 253 (43), 239 (17), 223 (6), 222 (5), 221 (8), 145 (10), 131 (11), 121 (4), 115 (9), 107 (12), 91 (5), 77 (6), 43 (13).

Zapotecone (**15**). Colourless oil (4 mg); R_f 0.2 (grey with anisaldehyde); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH), 1700 (C=O); UV λ_{max} nm (log ε): 280 (2.79); ^{1}H NMR: δ1.98 (3H, *s*, Me-9'), 3.56 (2H, *s*, H_2-7'), 3.69 (2H, *br s*, H_2-7), 3.84 (3H, *s*, OMe), 5.02 (2H, *m*, H_2-9), 6.68 (2H, AA'BB'-system, H-3, H-5), 6.8–7.3 (5H, *m*), 8.00 (1H, *s*, OH); (CD_3OD): δ1.98 (3H, *s*, Me-9'), 3.55 (2H, *r s*, H_2-7'), 3.66 (2H, *br s*, H_2-7), 3.81 (3H, *s*, OMe), 4.82 (*s*, OH + H_2O), 4.95 (2H, *m*, H_2-9), 6.57 (2H, AA'BB'-system, H-3, H-5), 6.78–7.15 (5H, *m*); ^{13}C NMR (100 MHz, Me_2CO-d_6): δ42.41 (C-7), 50.07 (C-7'), 55.85 (OMe), 111.91, 115.36, 115.71, 127.68, 130.18, 130.84, 131.37, 132.14, 132.51, 149.99, 156.42, 156.58; (100 MHz, CD_3OD): δ28.86 (C-9'), 42.99 (C-7), 50.62 (C-7'), 56.02 (OMe), 112.19, 115.32, 115.80 (C-3, C-5), 127.61, 130.35, 131.07 (C-2, C-4), 131.94, 132.54, 133.25, 150.47, 156.47, 157.15, 209.99 (C-8'); MS *m/z* (rel. int.): 296 (100, M^+), 254 (14), 253 (92), 221 (11), 131 (9), 115 (8), 107 (11), 77 (7), 43 (30).

4-[2-*Hydroxy*-2-(2-*methoxy*-5-(*E*)-*propenylphenyl*)*propyl*] *phenol* (**16**). Amorphous material (3 mg); R_f 0.25 (blue with anisaldehyde); $[\alpha]_D^{21} + 7°$ (MeOH; *c* 0.2); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580 (OH); UV λ_{max} nm (log ε): 260 (3.47); + NaOH: 247 (3.69), 289 (*sh*, 3.19); ^{1}H NMR (400 MHz, Me_2CO-d_6): δ1.51 (3H, *s*, Me-9), 1.78 (3H, *dd*, $J_1 = 7$, $J_2 = 2$ Hz, Me-9'), 3.05 (1H, *d*, $J = 13$ Hz, H_A-7), 3.18 (1H, *dd*, $J_1 = 13$, $J_2 = 2$ Hz, H_B-7), 3.93 (3H, *s*, OMe), 6.04 (1H, *dq*, $J_1 = 16$, $J_2 = 7$ Hz, H-8'), 6.28 (1H, *dm*, $J = 16$ Hz, H-7'), 6.59 (2H, AA'BB'-system, H-3, H-5), 6.87 (2H, AA'BB'-system, H-2, H-6), 6.94 (1H, *d*, $J = 8$ Hz, H-5'), 7.18 (1H, *dd*, $J_1 = 8$, $J_2 = 2$ Hz, H-6'), 7.42 (1H, *m*, H-2'), 7.96 (1H, *s*, OH); ^{13}C NMR (100 MHz, Me_2CO-d_6): δ18.40 (C-9'), 27.90 (C-9), 47.30 (C-7), 55.70 (OMe), 75.02 (C-8), 112.11, 115.12 (C-3, C-5), 123.34, 125.58, 125.94, 130.12, 130.52, 131.04, 131.93 (C-2, C-6), 136.62 (C-1), 156.43 (C-4 or C-4'), 156.46 (C-4' or C-4); MS *m/z* (rel. int.): 298 (1, M^+), 280 (1), 192 (11), 191 (100), 161 (8), 107 (9), 43 (42).

S-2-(4-*Hydroxyphenyl*)-5-(2-*hydroxypropyl*)-3-*methylbenzofuran* (**17**). Colourless oil (3 mg); R_f 0.12 (red with anisaldehyde); $[\alpha]_D^{21} + 9°$ (MeOH; *c* 0.3); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH); UV λ_{max} nm (log ε): 308 (3.56); + NaOH: 322 (3.61); ^{1}H NMR: δ1.15 (3H, *d*, $J = 6$ Hz, Me-10), 2.43 (3H, *s*, Me-3), 2.8–2.9 (*m*, Ar–CH_2–CHOH–, H_2O), 3.50 (1H, H/D exchangeable, *d*, $J = 5$ Hz, –CHOH–), 3.8–4.2 (1H, *m* –CH_2–CHOH–), 6.97 (2H, AA'BB'-system, H-3', H-5'), 7.11 (1H, *dd*, $J_1 = 9$, $J_2 = 2$ Hz, H-6), 7.35 (1H, *br d*, $J = 9$ Hz,, H-7), 7.42 (1H, *br s*, H-4), 7.68 (2H, AA'BB'-system, H-2', H-6'), 8.66 (1H, H/D exchangeable, OH); ($CDCl_3$): δ1.30 (3H, *d*, $J = 6$Hz, Me-10), 2.41 (3H, *s*, Me-3), 2.7–3.0 (2H, *m*, Ar–CH_2–), 3.8–4.3 (1H, *m*, –CHOH–), 5.2 (1H, *br s*, OH), 6.90 (2H, AA'BB'-system, H-3', H-5'), 7.09 (1H, *dd*, $J_1 = 9$, $J_2 = 2$ Hz, H-6), 7.34 (1H, *br s*, H-4), 7.39 (1H, *br d*, $J = 9$ Hz, H-7), 7.69 (2H, AA'BB'-system, H-2', H-6'); ^{13}C NMR (100 MHz, Me_2CO-d_6): δ9.42 (Me-3), 23.39 (C-10), 46.69 (C-8), 69.35 (C-9), 109.86 (C-3 or C-7), 110.76 (C-7 or C-3), 116.51 (C-3', C-5'), 120.44 (C-4), 123.48 (C-1'), 126.41 (C-6), 129.01 (C-2', C-6'), 132.18 (C-3a), 134.69 (C-5), 152.04 (C-2 or C-7a), 153.21 (C-7a or C-2), 158.41 (C-4'); MS *m/z* (rel. int.): 282 (100, M^+), 238 (61), 237 (90).

2-(4-*Hydroxyphenyl*)-5-(2-*oxopropyl*)-3-*methylbenzofuran* (**18**). Amorphous material (6 mg); R_f 0.22 (grey with anisaldehyde); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590 (OH), 1705 (C=O); UV λ_{max} nm (log ε): 309 (4.19); + NaOH: 326 (4.24); ^{1}H NMR (90 MHz, $CDCl_3$): δ2.19 (3H, *s*, –CO–Me), 2.39 (3H, *s*, Me-3), 3.81 (2H, *s*, –CH_2–CO–), 5.30 (1H, *br s*, OH), 6.90 (2H, AA'BB'-system, H-3', H-5'), 7.05 (1H, *dd*, $J_1 = 8$, $J_2 = 2$ Hz, H-6), 7.30 (1H, *br d*, $J = 2$ Hz, H-4), 7.42 (1H, *br d*, $J = 8$ Hz, H-7), 7.65 (2H, AA'BB'-system, H-2', H-6'); (90 MHz, CD_3OD): δ2.16 (3H, *s*, –CO–Me), 2.40 (3H, *s*, Me-3), 3.83 (2H, *s*, –CH_2–CO–), 4.82 (OH + H_2O), 6.90 (2H, AA'BB'-system, H-3', H-5'), 7.08 (1H, *dd*, $J_1 = 8$, $J_2 = 2$ Hz, H-6), 7.34 (1H, *dd*, $J_1 = 2$, $J_2 = 1$ Hz, H-4), 7.38 (1H, *dd*, $J_1 = 8$, $J_2 = 1$ Hz, H-7), 7.62 (2H, AA'BB'-system, H-2', H-6'); ^{13}C NMR (CD_3OD): δ9.32 (Me-3), 29.12 (C-10), 51.41 (C-8), 110.05 (C-3), 111.49 (C-7),

116.61 (C-3', C-5'), 120.78 (C-5), 124.12 (C-1'), 126.33 (C-6), 129.29 (C-2', C-6'), 130.02 (C-5), 133.08 (C-3a), 153.13 (C-2 or C-7a), 154.18 (C-7a or C-2), 158.84 (C-4'), 209.87 (C-9); MS *m/z* (rel. int.): 280 (66, M^+), 238 (22), 237 (100), 165 (4), 43 (13).

Determination of the absolute configuration of **14** and **17**. The enantiomeric yield in the phenyl butyric acid anhydride (6.2 mg) after reaction with **14** (3 mg) and **17** (3 mg), respectively—was determined by reaction with (*R*)-1-phenylethylamine (5.5 mg) followed by GC analysis (capillary column, SE 54, 25 m) of the resulting diastereoisomeric amides [9]. Compound **14** as well as **17** produced a significant excess of the amide of (*R*)-1-phenylbutyric acid, thus indicating *S*-configuration [9].

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