New Neolignans that Inhibit DNA Polymerase β Lyase

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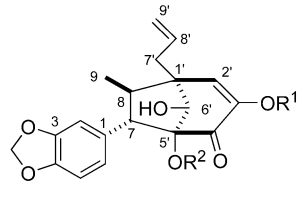
Bioassay-directed fractionation of a methyl ethyl ketone extract of the roots of *Endlicheria* aff. resulted in the isolation of four new neolignans (**1**−**4**) and eight known compounds, namely, canellin A (**5**), canellin C (**6**), 3′-methoxyguianin (**7**), (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,6′-dihydroxy-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan (**8**), armenin-B (**9**), dillapiole (**10**), 1-allyl-2,6-dimethoxy-3,4-methylenedioxybenzene (**11**), and ω-hydroxyisodillapiole (**12**). The structures of the new compounds (**1**−**4**) were established as (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-5′,6′-dihydroxy-3′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan, (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,5′,6′-trihydroxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan, 2,4-dimethoxy-5,6-methylenedioxy-1-(2-propenyl)benzene, and 2,6-dimethoxy-3,4-methylenedioxycinnamyl alcohol, respectively, on the basis of spectroscopic interpretation.

As described in a previous paper in this series,[1] the fact that the DNA repair enzyme DNA polymerase β (pol β) has an intrinsic deoxyribose phosphate (dRP) lyase activity,[2,3] in addition to its polymerase activity, was used to develop a new approach to the discovery of potential anticancer agents. Inhibitors of the lyase activity of pol β should be potentiators of the cytotoxicity of DNA-damaging agents, and it has already been shown at the University of Virginia that naturally occurring inhibitors of pol β can be found in nature.[4] We thus elected to begin a search for naturally occurring inhibitors of pol β lyase as a part of our continuing search for novel, naturally occurring anticancer agents.[5,6] The assay system used for this purpose has been described previously.[1]

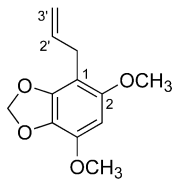
On the basis of its inhibitory activity toward pol β lyase, with strong activity at 16.2 μg/mL and moderate activity at 2.2 μg/mL, a methyl ethyl ketone extract of the roots of an *Endlicheria*-like species [*Endlicheria* aff. (Lauraceae)] was selected for bioassay-guided fractionation. The genus *Endlicheria* has previously been shown to be a rich source of a number of neolignans.[7]

Results and Discussion

Initial liquid−liquid partition of the crude extract resulted in equal distribution of the active principles between the hexane and $CHCl_3$ fractions of hexane/aqueous MeOH and $CHCl_3$/aqueous MeOH partitions, respectively. The hexane and $CHCl_3$ residues were then combined on the basis of their similar activity and their similar ^{1}H NMR and TLC patterns. The combined residue after separation by chromatography over MCI gel followed by reversed-phase preparative TLC and HPLC yielded the new neolignans **1**−**4** and the eight known compounds **5**−**11**. The structures of the eight known compounds were identified as canellin A (**5**),[8] canellin C (**6**),[9] 3′-methoxyguianin (**7**),[10] (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,6′-dihydroxy-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan (**8**),[9,11] armenin-B (**9**),[10,12] dillapiole (**10**),[13] 1-allyl-2,6-dimethoxy-3,4-methylenedioxybenzene (**11**),[14] and ω-hydroxyisodillapiole (**12**),[15] by comparison of their spectral data as reported in the literature. Since the ^{13}C NMR spectral data for the three known compounds canellin A (**5**), armenin-B (**9**), and ω-hydroxyisodillapiole (**12**) have not been reported in the literature, these spectra were assigned on the basis of HMQC and HMBC spectral data and are given in Table 1. Further, the ^{13}C NMR shift for the OCH_3-3 group in dillapiole (**10**) has been corrected to δ 59.9 from the value of δ 50.9 originally reported.[13]



1 $R^1 = CH_3$; R^2 =H
2 $R^1 = R^2 = H$
7 $R^1 = R^2 = CH_3$
8 R^1 = H; R^2 = CH_3



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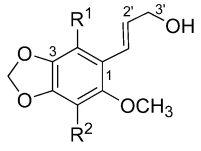
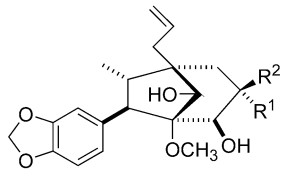
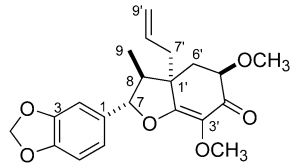


4 $R^1 = OCH_3$, R^2 = H
12 R^1 = H, $R^2 = OCH_3$



5 $R^1 = OCH_3$; R^2 = H
6 $R^1 = R^2$ = O



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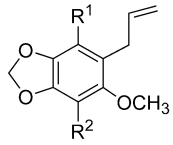

10 R^1 = H, $R^2 = OCH_3$
11 $R^1 = OCH_3$, R^2 = H

Compound **1** was isolated as an optically active viscous oil whose molecular formula was established as $C_{20}H_{22}O_6$ from HRFABMS, ^{13}C NMR, and APT (Attached Proton

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Table 1. NMR Data for Compounds **1**, **2**, **5**, and **9**[a,b]

	1		**2**		**5**	**9**
position	^{1}H	^{13}C	^{1}H	^{13}C	^{13}C	^{13}C
1		131.2		131.3	135.4	131.4
2	6.96 s	107.8	6.99 s	107.6	107.7	108.4
3		147.3		147.6	147.3	148.3
4		146.6		146.0	145.7	148.2
5	6.696 s	110.8	6.703 s	110.8	110.4	120.8
6	6.694 s	120.6	6.701 s	120.8	123.2	106.7
7	2.40 d 8.9	56.8	2.43 d 9.0	57.2	51.9	91.0
8	2.62 dq 8.9, 7.0	48.5	2.64 dq 9.0, 7.1	48.5	47.2	47.2
9	0.87 d 6.4	14.0	0.89 d 6.8	13.8	11.8	8.9
1′		51.2		51.8	47.5	53.4
2′	5.66 s	123.6	6.05 s	123.5	30.2	133.9
3′		152.0		146.9	76.9	169.8
4′		194.8		196.8	70.9	192.9
5′		82.6		82.8	85.3	77.3
6′	3.98 d 1.6	80.9	3.99 d 1.8	81.0	78.0	37.7
7′	2.42 m, 2.60 m	36.8	2.45 m, 2.62 m	36.9	38.9	38.7
8′	5.86 m	134.2	5.85 m	134.6	135.6	133.9
9′	5.24 dd 17.0, 0.9	118.4	5.22 dd 17.0, 1.0	118.5	117.5	119.5
	5.15 dd 10.5, 1.1		5.13 dd 10.5, 1.1			
$-OCH_2-$	5.92 d 1.6	101.2	5.93 d 1.4	100.9	100.8	101.5
	5.93 d 1.6		5.94 d 1.4			
OCH_3-3′	3.67 s	56.3			57.5	60.6
OCH_3-5′					52.2	59.2
OH-6′	2.37 d 1.9		2.36 d 2.1			

[a] Spectra obtained in $CDCl_3$; chemical shifts reported in ppm from TMS. [b] Assignments made on the basis of COSY, HMQC, and HMBC spectral data.

Test) spectral data. The IR spectrum showed the presence of hydroxyl (3025 cm^{-1}) and α,β-unsaturated carbonyl groups (1650 cm^{-1}) in its molecular structure. The presence of an α,β-unsaturated carbonyl group was supported by the presence of a signal at δ 194.8 in the ^{13}C NMR spectrum of **1**. The UV maxima observed at 235 and 267 nm suggested a neolignan skeleton.[9] The ^{1}H and ^{13}C NMR spectra (Table 1) of **1** revealed the presence of 2-propenyl and 3,4-methylenedioxyphenyl groups in its structure. This was supported by the mass fragments observed in the EIMS at *m/z* 317 ($M^+ - C_3H_5$) and 237 ($M^+ - C_7H_5O_2$), respectively. The ^{1}H NMR spectrum of **1** showed the presence of a methyl doublet at δ 0.87 (J = 6.4 Hz), an oxymethine as a doublet at δ 3.98 (J = 1.6 Hz), an olefinic proton singlet at δ 5.66, two methine protons at δ 2.40 (d, J = 8.9 Hz) and 2.62 (dq, J = 8.9, 7.0 Hz), and a methoxyl group singlet at δ 3.67. A literature search revealed that the above spectral data were very similar to those of 3′-methoxyguianin (**7**)[10] except for the absence of a signal for a methoxyl group. The presence of the basic skeleton of **7** in the new lignan **1** was supported by COSY (H-5/H-6; H-7/H-8; H-8/H-9; H-7′/H-8′; H-8′/H-9′) and HMBC (H-2/C-1, C-3, C-4, C-6, C-7; H-5/C-1, C-3, C-4, C-6; H-6/C-1, C-2, C-5, C-7; H-8/C-1, C-7, C-9, C-1′, C-5′; H-7′/C-8, C-1′, C-2′, C-6′, C-8′, C-9′; H-2′/C-8, C-1′, C-3′, C-4′, C-6′, C-7′) correlations (Figure 1). Both compound **1** and (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,6′-dihydroxy-5′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan (**8**)[11] are desmethyl derivatives of 3′-methoxyguianin, differing only in the location of the missing methyl group. Their NMR (^{1}H and ^{13}C) spectral data were not identical, and the placement of the remaining methoxyl group at the C-3′ position was suggested from the key HMBC correlations: OCH_3-3′/C-2′, C-3′, C-4′; H-6′/C-1′, C-2′, C-4′, C-5′ and H-2′/C-8, C-1′, C-3′, C-4′, C-6′, C-7′, OCH_3-3′. This was supported by the appearance of the C-6′ olefinic proton at δ 5.66, which was almost identical to that

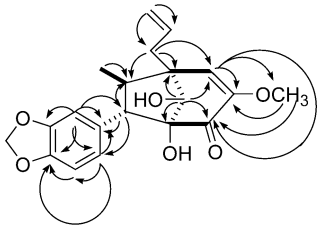

Figure 1. Selected HMBC correlations for **1**.

of **7**. The latter also has a methoxyl group at the C-3′ position.[10] The stereochemistry at each of the five chiral centers C-7, C-8, C-1′, C-5′, and C-6′ in **1** was assigned as that of **7** and **8** on the basis of the similar coupling constants of their respective protons, and their ^{13}C NMR values. This conclusion was supported by the CD spectrum of **1**, which gave molar ellipticity values almost identical to those of **8**.[11] On the basis of the above spectral data, compound **1** was assigned as (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-5′,6′-dihydroxy-3′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan.

Compound **2** was also obtained as a colorless viscous oil, and its molecular formula was assigned as $C_{19}H_{20}O_6$ on the basis of its HRFABMS. Its IR and UV spectra were almost identical to those of **1**, indicating their similar nature. The ^{1}H NMR spectrum of **2** was very similar to that of **1** (Table 1), except for the absence of the proton signals corresponding to the C-3′ methoxyl group at δ 3.67. The mass spectrum of **2**, which had a molecular ion peak 14 mass units less than that of **1**, suggested the replacement of the methoxyl group at the C-3′ position in **1** by a hydroxyl group. The presence of a hydroxyl group at the C-3′ position in **2** was further indicated by the appearance of the olefinic proton at the C-2′ position as a singlet at δ 6.05; this signal was very similar to the corresponding signal of **8**, which also has a hydroxyl group at C-3′.[11] The ^{13}C NMR values for all the carbons in **2** were assigned on the basis of HMQC and HMBC spectra and are given in Table 1. The relative stereochemistry at each of the chiral centers C-7, C-8, C-1′, C-5′, and C-6′ in **2** was assigned in a manner similar to **1**, on the basis of the very similar nature of the ^{1}H NMR signals at the respective chiral centers and its CD spectrum. Thus, compound **2** was established as (7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,5′,6′-trihydroxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan.

Compound **3** was obtained as colorless viscous oil and was determined to have the molecular formula $C_{12}H_{14}O_4$ by HRFABMS and ^{13}C NMR spectral data. The IR spectrum did not show any absorption bands corresponding to common functional groups. The ^{1}H NMR spectrum of **3** showed the presence of two multiplets centered at δ 5.90 (1H) and 5.02 (2H) and a methylene group at δ 3.30 (dt, J = 6.4, 1.4 Hz) corresponding to a 2-propenyl group similar to that observed in **1** and **2**. The mass fragment observed at *m/z* 181 ($M^+ - C_3H_5$) in the EIMS supported the presence of a 2-propenyl substituent in **3**. The ^{1}H NMR spectrum also showed the presence of an aromatic singlet at δ 6.35 (1H), a singlet corresponding to methylenedioxy group at δ 5.87, and two methoxyl groups at δ 3.75 and 4.00. The ^{13}C NMR values for all the carbons in **3** were assigned on the basis of HMQC and HMBC spectra and are given in Table 2. These data indicate the presence of five sp^2 quaternary carbons, one sp^2 methylene, two sp^2 methines, two sp^3 methylenes, and two sp^3 methyls in the structure. From the above spectral data, the structure of **3** was determined to have a pentasubstituted phenyl ring having two methoxyls, a methylenedioxy, and a 2-propenyl group.

Table 2. NMR Data for Compounds **3**, **4**, and **12** ($CDCl_3$)[a,b]

	3		**4**		**12**
position	^{1}H	^{13}C	^{1}H	^{13}C	^{13}C
1		126.2		121.4	123.6
2		152.1		149.6	98.6
3	6.35 s	91.4		127.6	137.4
4		146.5		142.4	137.6
5		130.6	6.30 s	90.8	137.9
6		149.6		146.8	145.2
1′	3.30 dt 6.4, 1.4	29.6	6.47 d 16.0	131.4	128.0
2′	5.90 m	137.5	6.21 dt 16.0, 6.1	125.6	125.6
3′	5.02 m	115.7	4.16 d 5.5	64.6	64.2
$-OCH_2O-$	5.87 s	101.2	5.91 s	102.1	101.4
OCH_3-2	3.75 s	56.3	3.76 s	60.8	
OCH_3-4	4.00 s	59.6			61.7
OCH_3-5					60.2
OCH_3-6			4.00 s	56.8	

[a] Spectra obtained in $CDCl_3$; chemical shifts reported in ppm from TMS. [b] Assignments made on the basis of COSY, HMQC, and HMBC spectral data.

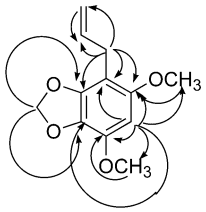

Figure 2. Selected HMBC correlations for **3**.

A comparison of the ^{1}H and ^{13}C NMR values of **3** with those of compounds having similar substitution patterns such as dillapiole (**10**),[13] 1-allyl-2,6-dimethoxy-3,4-methylenedioxybenzene (**11**),[14] apiole,[16] and pseudodillapiole[17] indicated that its NMR values did not match any of them, suggesting the possible placement of the 2-propenyl, the two methoxyls, and the methylenedioxy groups at either the C-1, C-2, C-4, and C-5/C-6 or the C-1, C-4, C-5, and C-2/C-3 positions. The NOESY spectrum of **3**, in which the aromatic proton at δ 6.35 showed correlations to the two methoxyl groups at δ 3.75 and 4.00, suggested the placement of the 2-propenyl, the two methoxyls, and the methylenedioxy groups at the C-1, C-2, C-4, and C-5/C-6 positions, respectively, as shown in **3**. This was supported by the key HMBC correlations: H-3/C-1, C-2, C-4, C-5, OCH_3-2, OCH_3-4; OCH_3-2/C-1, C-2, C-3; OCH_3-4/C-3, C-4, C-5; $-OCH_2O-$/C-5, C-6; and H-1′/C-1, C-2, C-6, C-2′, C-3′ (Figure 2). This compound has previously been reported as a synthetic product,[18] but this is the first report of its occurrence as a natural product. Its NMR data have not previously been reported. On the basis of the above spectral data, **3** was assigned as 2,4-dimethoxy-5,6-methylenedioxy-1-(2-propenyl)benzene.

Compound **4** was isolated as a colorless viscous oil, with a molecular formula of $C_{12}H_{14}O_5$ (HRFABMS). The UV spectrum of **4** was almost identical to that of **12**,[15] suggesting the presence of a substituted cinnamyl alcohol skeleton in its structure. The absence of a fragment ion at *m*/*z* 197 $(M - C_3H_5)^+$ and the appearance of an ion at *m*/*z* 181 $(M - C_3H_5O)^+$ in the EIMS of **4** suggested the replacement of the 2-propenyl group in **3** by a 3-hydroxy-1-propenyl group. The ^{1}H NMR spectrum of **4**, which showed the presence of two olefinic protons at δ 6.47 (d, J = 16.0 Hz) and 6.21 (dt, J = 16.0, 6.1 Hz) and a hydroxymethylene group at δ 4.16 (d, J = 5.5 Hz), further supported the presence of a 3-hydroxy-1-propenyl group. The ^{1}H NMR spectrum also showed the presence of an aromatic proton at δ 6.30 (1H), a singlet corresponding to a methylenedioxy group at δ 5.91, and two methoxyl singlets at δ 3.76 and 4.00. The ^{13}C NMR values for all of the carbons in **4** were assigned on the basis of HMQC and HMBC spectra and are given in Table 2. These data indicated the presence of five sp^2 quaternary carbons, three sp^2 methines, two sp^3 methylenes, and two sp^3 methyls in **4**. From the above spectral data, the structure of **4** was determined to have a pentasubstituted phenyl ring having two methoxyls, a methylenedioxy, and a 3-hydroxy-1-propenyl group. Since the ^{1}H NMR values of **4** did not match those of similar compounds reported in the literature, namely, ω-hydroxyisodillapiole (**12**)[15] and 2,5-dimethoxy-3,4-methylenedioxycinnamyl alcohol,[19] the two methoxyl groups and the methylenedioxy group could only be placed at one of the several possible locations: either the C-4, C-5, and C-2/C-3; or C-2, C-4, C-5/C-6; or C-2, C-5, C-3/C-4; or C-2, C-6, C-3/C-4; or C-2, C-3, C-5/C-6; or C-3, C-4, C-5/C-6 positions. The positions of these groups were assigned as C-2, C-6, and C-3/C-4 on the basis of the key HMBC correlations: H-5/C-1, C-3, C-4, C-6, OCH_3-6; OCH_3-2/C-1, C-2, C-3; OCH_3-6/C-1, C-5, C-6; $-OCH_2O-$/C-3, C-4; and H-1′/C-1, C-2, C-6, C-2′, C-3′. The NOESY spectrum of **4**, in which the aromatic proton at δ 6.30 showed a correlation to the methoxyl group at the C-6 position, also confirmed that the two methoxyl groups and the methylenedioxy group were at the C-2, C-6, and C-3/C-4 positions, respectively. The *E* stereochemistry of the double bond between the C-1′ and C-2′ carbons was supported by the large coupling constants of their respective protons.[15,19] The structure of **4** was thus assigned as 2,6-dimethoxy-3,4-methylenedioxycinnamyl alcohol.

All the isolated compounds were tested for inhibition of DNA polymerase β lyase activity,[1] and the results are given in Table 3.

Table 3. IC_{50} of Polymerase β Lyase Inhibition of Compounds Isolated from *Endlicheria* Species[a]

compound	IC_{50} (μM)
oleanolic acid[1]	8.8
1	15.3
2	>50
3	18.6
4	43.5
5	26.5
6	32.4
7	>50
8	21.6
9	12.3
10	>50
11	34.2
12	>50

[a] Data are the mean of three determinations.

Experimental Section

General Experimental Procedures. Melting points were recorded with an Electrothermal digital apparatus and are uncorrected. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter. IR (KBr) and UV (MeOH) spectra were measured on MIDAC M-series FTIR and Shimadzu UV-1201 spectrophotometers, respectively. NMR spectra were obtained on a JEOL Eclipse 500 spectrometer. The HRFABMS were obtained on a JEOL HX-110 instrument. The chemical shifts are given in ppm (δ) with TMS (tetramethylsilane) as an internal reference, and coupling constants (J) are in Hz. MCI gel CHP20P was used for column chromatography. Reversed-phase HPLC was performed on a Shimadzu LC-10AT instrument with an ODS C-18 column (250 × 10 mm).

Plant Material. The roots of a plant identified as *Endlicheria* aff. (Lauraceae) were collected under a contract from the National Cancer Institute in Peru in February 1980. Herbarium voucher specimens are deposited in the Smithso-

nian Institution National Herbarium, Washington, DC, and at The New York Botanical Garden, Bronx, NY. The plant material was assigned the number B855213.

Extraction and Isolation. A methyl ethyl ketone extract of *E.* aff. was prepared by the National Cancer Institute and supplied as B855213. The crude extract (0.45 g) was suspended in aqueous MeOH (MeOH−H_2O, 9:1, 100 mL) and extracted with hexane (three100 mL portions). The aqueous layer was then diluted to 70% MeOH (v/v) with H_2O and extracted with three 100 mL portions of $CHCl_3$. The aqueous layer was concentrated, and the residue obtained was suspended in H_2O (25 mL) and extracted with two 25 mL portions of *n*-BuOH. The $CHCl_3$ extract was fractionated further based on its activity and ^{1}H NMR patterns. The residue from the $CHCl_3$ extract (0.40 g) was fractionated by chromatography over MCI gel using MeOH−H_2O (1:1 to 100:0) to yield 10 fractions (A−J), of which fractions C−I were found to be active. Fraction C, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (60:40), yielded the new neolignan **3** (2.2 mg, t_R 12.4 min). Fraction D, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (70:30), yielded the two known neolignans **10** (1.8 mg, t_R 10.6 min) and **12** (2.1 mg, t_R 12.6 min). Fraction E, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (70:30), furnished the new neolignan **1** (1.8 mg, t_R 11.1 min) and the known neolignan **11** (1.5 mg, t_R 13.2 min). Fraction F, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (85:15), yielded the two known compounds **10** (1.4 mg, t_R 9.7 min) and **5** (2.1 mg, t_R 16.2 min). Fraction G, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (85:15), yielded the five known compounds **5** (16.2 mg, t_R 11.2 min), **6** (2.4 mg, t_R 12.3 min), **7** (2.2 mg, t_R 14.6 min), **8** (1.8 mg, t_R 16.7 min), and **9** (2.3 mg, t_R 18.6 min). Fraction H, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (90:10), yielded the new neolignan **2** (1.4 mg, t_R 7.4 min) and the two known compounds **5** (2.2 mg, t_R 9.4 min) and **7** (1.3 mg, t_R 11.6 min). Fraction I, upon reversed-phase HPLC with the mobile phase CH_3CN−H_2O (95:5), yielded the new neolignan **4** (1.8 mg, t_R 8.2 min) and the two known compounds **5** (1.6 mg, t_R 6.4 min) and **6** (1.4 mg, t_R 10.1 min). The structures of the known compounds **5**−**12** were identified by comparison of their spectral data with literature values.[8−15]

(7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-5′,6′-Dihydroxy-3′-methoxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan (1): viscous oil; $[\alpha]_D^{25}$ −42.2° (*c* 0.62, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 235 (3.24), 267 (4.28) nm; CD (*c* 0.36 mg/10 mL, EtOH) $[\theta]_{223}$ −12 800, $[\theta]_{259}$ +8460, $[\theta]_{291}$ +2450, $[\theta]_{318}$ −4800; IR ($CHCl_3$) ν_{max} 3025, 2945, 1650, 1245, 1145, 1100, 1050, 850 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 358 $[M]^+$ (42), 340 (21), 326 (8), 317 (16), 294 (11), 285 (21), 253 (18), 237 (18), 227 (8), 220 (15), 218 (14), 204 (23), 190 (14), 172 (14), 158 (32), 135 (100), 105 (21), 93 (23), 43 (140, 41 (26); HRFABMS *m*/*z* 358.1431 $[M]^+$ (calcd for $C_{20}H_{22}O_6$ 358.1416).

(7*S*,8*R*,1′*S*,5′*S*,6′*R*)-Δ$^{2',8'}$-3′,5′,6′-Trihydroxy-3,4-methylenedioxy-4′-oxo-8.1′,7.5′-neolignan (2): viscous oil; $[\alpha]_D^{25}$ −18.8° (*c* 0.46, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 232 (3.24), 273 (3.45) nm; CD (*c* 0.35 mg/10 mL, EtOH) $[\theta]_{223}$ −11 900, $[\theta]_{259}$ +8860, $[\theta]_{291}$ +2900, $[\theta]_{318}$ −5200; IR ($CHCl_3$) ν_{max} 3045, 2955, 1640, 1130, 1080, 1040, 840 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 1; EIMS *m*/*z* 344 $[M]^+$ (28), 326 (8), 312 (14), 303 (25), 294 (11), 285 (18), 280 (21), 253 (18), 237 (18), 227 (8), 220 (15), 218 (14), 204 (23), 190 (21), 183 (160, 171 (14), 135 (62), 124 9100), 115 (17), 106 (16), 93 (132), 91 (150), 41 (64); HRFABMS *m*/*z* 344.1272 $[M]^+$ (calcd for $C_{19}H_{20}O_6$ 344.1260).

2,4-Dimethoxy-5,6-methylenedioxy-1-(2-propenyl)benzene (3): viscous oil; $[\alpha]_D^{25}$ +24.5° (*c* 0.53, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 216 (4.21), 278 (3.48) nm; IR ($CHCl_3$) ν_{max} 3245, 3050, 2945, 1620, 1210, 1120, 1085, 1035, 940, 860, 760 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 2; EIMS *m*/*z* 222 $[M]^+$ (100), 191 (25), 181 (18), 160 (18), 115 (17), 93 (23); HRFABMS *m*/*z* 222.0894 $[M]^+$ (calcd for $C_{12}H_{14}O_4$ 222.0892).

2,6-Dimethoxy-3,4-methylenedioxycinnamyl alcohol (4): viscous oil; $[\alpha]_D^{25}$ −12.5° (*c* 0.42, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 215 (3.46), 272 (3.64), 303 (3.89) nm; IR ($CHCl_3$) ν_{max} 3550, 2925, 1610, 1230, 1135, 1105, 1065, 1050, 1020, 935, 750 cm^{-1}; ^{1}H and ^{13}C NMR, see Table 2; EIMS *m*/*z* 238 $[M]^+$ (100), 220 (14), 207 (17), 181 (25), 176 (23), 160 (18), 115 (17), 93 (16), 68 (23), 41 (34); HRFABMS *m*/*z* 238.0864 $[M]^+$ (calcd for $C_{12}H_{14}O_5$ 238.0865).

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Supporting Information Available: ^{1}H NMR spectral data for compounds **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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