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Four novel lignans from *Rodgersia podophylla*

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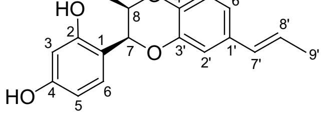
Abstract—Four novel lignans were isolated from the rhizomes of *Rodgersia podophylla*. It is interesting to note that an unusual 2,4-dihydroxyphenyl moiety was found in these compounds in addition to an acetylenic functionality in compounds **3** and **4**.

The rhizomes of *Rodgersia podophylla* A. Gray (Saxifragaceae) have been used as a treatment for enteritis and bacillary dysentery in China and are also known to have antipyretic and analgesic effects.[1] It has been reported that the rhizomes of this plant contain bergenin, β-peltoboykinolic acid, sterols, monoterpenes, and fatty acids.[1,2] Only a few chemical constituents were isolated from these rhizomes, partly due to the difficulties in isolating compounds present along with large amounts of tannins. Therefore, we attempted to remove tannins by the aid of polyvinylpolypyrrolidone (PVPP) resin, which was previously reported to be effective for this purpose.[3] Through this procedure, we were able to purify novel isomeric lignans from this plant. The MeOH extract (64 g) of *R. podophylla* rhizomes (600 g) was subjected to PVPP gel column chromatography (MeOH) and further separated by silica gel column chromatography (n-hexane/EtOAc = 3:1 → 1:1) and purified repeatedly by reversed-phase HPLC to afford four lignans.

Compound **1** (3.1 mg) possessed a molecular formula of $C_{18}H_{18}O_4$, which was determined by EI-HRMS. In the ^{1}H NMR spectrum of **1**, six aromatic peaks appeared. Three of the six signals were assigned to H-3 (δ_H 6.35, d, $J = 2.4$ Hz), H-5 (δ_H 6.40, dd, $J = 8.3$, 2.4 Hz), and H-6 (δ_H 7.02, d, $J = 8.3$ Hz), which suggested the existence of 1,2,4-trisubstituted benzene ring. The remaining three aromatic peaks were assigned to H-5′ (δ_H 6.81, d, $J = 8.4$ Hz), H-6′ (δ_H 6.88, dd, $J = 8.4$, 2.0 Hz), and H-7′ (δ_H 6.94, d, $J = 2.0$ Hz) in the 1,3,4-trisubstituted benzene ring.[4,5] It was found that compound **1** has a C_3 unit containing one methyl and two oxymethines at δ_H 1.20, 4.56, and 5.37, and a C_3 unit with one methyl and olefinic protons at δ_H 1.83, 6.10, and 6.28 in the ^{1}H NMR spectrum. These data suggested that **1** consisted of two phenylpropanoid moieties.

The connections between the C_3 units and benzene rings were established by HMBC technique. The correlation peaks between δ_H 5.37 (H-7) and δ_C 128.6 (C-6), 155.6 (C-2) exhibited the linkage of the C_3 unit containing oxymethines to the 1,2,4-trisubstituted benzene ring. The HMBC correlations between δ_H 6.28 (H-7′) and δ_C 114.2 (C-2′), 120.4 (C-6′) showed the connection of the C_3 unit containing olefinic protons with the 1,3,4-trisubstituted benzene ring. The linkage between the two phenylpropanoid units was determined by cross peaks between δ_H 4.56 (H-8) and δ_C 140.7 (C-4′) as well as δ_H 5.37 (H-7), and δ_C 142.1 (C-3′) in the HMBC spectrum.[6] Therefore, compound **1** was assumed to have a skeleton of 7,3′-dioxy-8,4′-neolignan.



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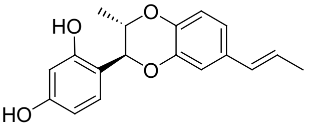

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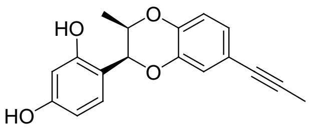

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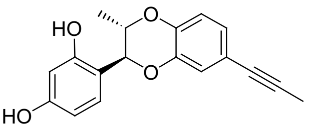

4

Keywords: *Rodgersia podophylla*; Benzodioxane type lignans; 2,4-Dihydroxy phenyl.

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Table 1. ^1H and ^{13}C NMR data for compounds **1**–**4** in $CDCl_3$ (*J* values in parentheses)[a]

	1		**2**		**3**		**4**	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1		113.7		113.9		113.7		113.9
2		155.6		156.1		155.3		156.0
3	6.35 d (2.4)	103.9	6.39 br s	104.4	6.34 br s	103.8	6.38 br s	104.4
4		156.6		157.4		156.7		157.4
5	6.40 dd (8.3, 2.4)	107.8	6.40 d (7.9)	107.9	6.39 d (8.3)	107.9	6.40 d (8.4)	108.0
6	7.02 d (8.3)	128.6	6.98 d (7.9)	130.0	7.03 d (8.3)	126.1	6.99 d (8.4)	126.0
7	5.37 d (2.4)	77.0	4.80 d (8.0)	80.5	5.36 d (2.2)	77.0	4.81 d (8.0)	80.1
8	4.56 qd (6.5, 2.4)	72.9	4.33 dq (8.0, 6.4)	72.6	4.58 qd (6.6, 2.2)	72.9	4.32 qd (8.0, 6.4)	72.8
9	1.20 d (6.5)	12.5	1.19 d (6.6)	17.4	1.18 d (6.6)	12.6	1.12 d (6.4)	17.3
1′		131.7		131.8		128.5		130.3
2′	6.94 d (2.0)	114.2	6.93 d (1.7)	114.2	6.99 d (1.7)	116.7	6.97 br s	116.9
3′		142.1		142.5		141.7		143.5
4′		140.7		142.4		141.8		142.2
5′	6.81 d (8.4)	117.8	6.82 d (8.3)	117.0	6.80 d (8.3)	117.7	6.80 d (8.3)	117.0
6′	6.88 dd (8.4, 2.0)	120.4	6.88 dd (8.3, 1.7)	120.2	6.91 dd (8.3, 1.7)	120.2	6.94 d (8.3)	120.3
7′	6.28 d (14.0)	130.1	6.27 d (15.3)	130.3		79.0		79.1
8′	6.10 qd (14.0, 6.5)	124.4	6.06 dq (15.3, 6.6)	124.4		84.3		84.3
9′	1.83 d (6.5)	18.4	1.83 d (6.6)	18.4	2.00 s	4.3	2.00 s	4.3

[a] The ^1H and ^{13}C NMR spectra were measured at 400 and 100 MHz, respectively.

The relative stereochemistry of **1** was determined based on the *J* values measured in the ^1H NMR spectrum. The coupling constants observed between H-7′ and H-8′ ($J = 15.0$ Hz) suggested a *trans* configuration. The configuration of H-7 and H-8 was found to be *cis* by observing their *J* values ($J = 2.2$ Hz). Comparison of CD curve of **1** with that of the known eusiderin C suggested the plausible configurations of C-7 and C-8 as *S* and *R*, respectively.[7–9]

Molecular formula of **2** (1.4 mg), $C_{18}H_{18}O_4$, was supported by the $[M]^+$ ion peak at m/z 298.1197 (calcd 298.1205) of EI-HRMS. The ^1H NMR and ^{13}C NMR data as well as 2D correlation spectra suggested that both the functional groups and the general substitution patterns present in **2** were similar to those of **1**. The significant difference between **2** and **1** was found in the chemical shifts and coupling constants of H-7 and H-8. The signals of H-7 and H-8 in **2** in the ^1H NMR spectrum were appeared at slightly lower fields (δ_H 4.80 and 4.33, respectively) with a larger coupling constant ($J = 8.0$ Hz) indicating a *trans* orientation of H-7 and H-8 in **2**. The configuration of C-7 and C-8 in **2** was presumed to be *S* and *S*, respectively, by CD value ($[\theta]_{254.5} - 6301$), which was similar to that of the reference moiety reported previously.[7,10]

The high-resolution EI-MS of **3** (0.8 mg) gave the molecular formula of $C_{18}H_{16}O_4$ ($[M]^+$ m/z 296.1042, calcd 296.1049). By careful inspection of the NMR data, it was found that the aromatic units were almost identical to those of **1**. Significant differences in the ^1H NMR spectrum between **3** and **1** were the absence of the signals for olefinic protons in **3**. Instead, an acetylenic moiety was observed in **3**, and this fact was confirmed by observing acetylenic carbons at δ_C 77.0 and 84.3 (C-7′ and 8′, respectively) in the ^{13}C NMR spectrum. H-7 and H-8 were oriented *cis*, since the coupling constant ($J = 2.2$ Hz) between H-7 and H-8 was identical to those of **1**. The configurations of C-7 and C-8 were determined as *S* and *R*, respectively, by the CD value ($[\theta]_{258.0}$ +14,834) of **3**.[7,11]

Compound **4** (4.3 mg), obtained as an amorphous powder, had the molecular formula of $C_{18}H_{16}O_4$ as shown by EI-HRMS ($[M]^+$ m/z 296.1042, calcd 296.1049). The NMR data of **4** were almost identical to those of **3** except for the signal of the H-7 and H-8 protons that were appearing at the lower field with larger coupling constants indicating a *trans* orientation of H-7 and H-8. It was possible to determine the configuration of C-7 and C-8 of **4** as *S* and *S*, respectively, by CD value ($[\theta]_{256.5}$ −10,017).[7,12]

All of the above compounds **1**–**4**, newly isolated from natural resource, belong to the benzodioxane type lignans with an unusal 2,4-dihydroxy phenyl ring. Compounds **3** and **4** are particularly notable in possessing an acetylenic bond that is not found in naturally occurring lignans to date.

Acknowledgements

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9. Compound **1**: white amorphous powder; EI-HRMS $[M]^+$ *m/z* 298.1201 (calcd for $C_{18}H_{18}O_4$, 298.1205); $[\alpha]_D^{20}$ +79.9 (*c* 0.18, MeOH); UV (MeOH) λ_{max} nm ($\log\varepsilon$): 266 (3.88); CD (MeOH, *c* 0.021 mg/mL) $[\theta]_{220.0}$ −6778, $[\theta]_{247.0}$ 0, $[\theta]_{260.0}$ +6353; ^{1}H and ^{13}C NMR, see Table 1.
10. Compound **2**: white amorphous powder; $[M]^+$ *m/z* 298.1197 (calcd for $C_{18}H_{18}O_4$, 298.1205); $[\alpha]_D^{20}$ +24.8 (*c* 0.075, MeOH); UV (MeOH) λ_{max} nm ($\log\varepsilon$): 267 (3.97); CD (MeOH, *c* 0.034 mg/mL) $[\theta]_{220.5}$ +23,841, $[\theta]_{237.5}$ 0, $[\theta]_{254.5}$ −6301; ^{1}H and ^{13}C NMR, see Table 1.
11. Compound **3**: white amorphous powder; EI-HRMS $[M]^+$ *m/z* 296.1042 (calcd for $C_{18}H_{16}O_4$, 296.1049); $[\alpha]_D^{20}$ +62.0 (*c* 0.030, MeOH); UV (MeOH) λ_{max} nm ($\log\varepsilon$): 256 (4.24), 285 (3.84), 301 (3.76); CD (MeOH, *c* 0.0156 mg/mL) $[\theta]_{222.0}$ −12,739, $[\theta]_{229.5}$ 0, $[\theta]_{258}$ +14,834; ^{1}H and ^{13}C NMR, see Table 1.
12. Compound **4**: white amorphous powder; EI-HRMS $[M]^+$ *m/z* 296.1042 (calcd for $C_{18}H_{16}O_{40}$, 296.1049); $[\alpha]_D^{20}$ +18.7 (*c* 0.270, MeOH); UV (MeOH) λ_{max} nm ($\log\varepsilon$): 256 (4.11), 286 (3.69), 301 (3.60); CD (MeOH, *c* 0.0235 mg/mL) $[\theta]_{216.5}$ +56,285, $[\theta]_{233.5}$ 0, $[\theta]_{256.5}$ −10,017; ^{1}H and ^{13}C NMR, see Table 1.