Two Limonoids from the Root of *Dictamnus radicis* Cortex

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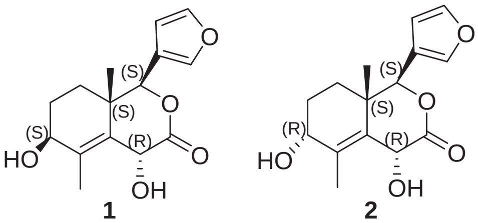
A new limonoid isodictamdiol (**1**) and a known dictamdiol (**2**), the first 5S/9S-type degraded limonoids, were isolated from the EtOAc extracts of *Dictamnus radicis* Cortex. The structures of compounds **1** and **2** were respectively elucidated by means of the modern spectroscopic methods, including IR, MS, NMR, a single-crystal X-ray diffraction, as well as CD. In addition, the absolute configuration of **2** was determined for the first time.

The root of *Dictamnus radicis* Cortex (Rutaceae), locally known as Bai-Xian-Pi (in Chinese), is a traditional Chinese medicine used for the treatment of jaundice, rheumatism, and various other diseases.[1] During our study on limonoid constituents from *D. radicis* Cortex, a pair of isomer named (2*S*,5*S*,7*R*,9*S*)-isodictamdiol (**1**) and (2*R*,5*S*,7*R*,9*S*)-dictamdiol (**2**), the first 5S/9S-type degraded limonoids, were isolated from the EtOAc extracts. Among them, **1** is a new compound. However, the spectroscopic data for **2** was inconsistent with its structure described,[2,3] so its spectral data have been slightly revised and the absolute configuration was determined for the first time. Herein, we mainly report the isolation and structure elucidation of **1** and **2** (Figure 1).

Isodictamdiol (**1**), $[\alpha]^{20}_{\mathrm{D}} - 22$ (*c* 0.57, MeOH) and colorless crystal, showed a molecular formula of $C_{15}H_{18}O_5$ as determined by HRESI-MS ($[M + NH_4]^+$ at m/z 296.1488, calcd. 296.1492) with seven degrees of unsaturation. IR absorptions exhibited the existence of two hydroxys (3362 and 3259 cm^{-1}), a δ-lactone (1724 cm^{-1}), a double bond (1600 cm^{-1}), and a furanyl ring (1506 and 873 cm^{-1}). In ^{1}H NMR spectrum, the characteristic signals at δ 7.65, 7.59, and 6.53 (each 1H, s) implied the β-substituted furyl ring, which was verified by four downfield carbon signals at δ_C 110.9 d, 121.4 s, 142.3 d, and 144.0 d in ^{13}C NMR spectrum.[2,4–7] In addition, the ^{1}H NMR spectrum (Table 1) exhibited signals due to a tertiary methyl (δ 1.02, 3H, s), a vinyl methyl (δ 1.86, 3H, s), two oxygen-bearing methines (δ 4.02, 1H, br s and δ 4.82, 1H, d, $J = 4.8$ Hz), and two secondary hydroxys (δ 4.02, 1H, br s and δ 5.33, 1H, d, $J = 4.8$ Hz). The ^{13}C NMR and DEPT spectra (Table 1) showed the presence of one ester carbonyl group, one β-furyl ring, one tetrasubstituted double bond, and eight sp^3 carbons [$2 \times CH_3$, $2 \times CH_2$, $3 \times CH$ (two oxygenated), $1 \times C$]. The planar structure of **1** was deduced by extensive 2D NMR experiments and single-crystal X-ray diffraction.



1 **2**

Figure 1. The structures of compounds **1** and **2**.

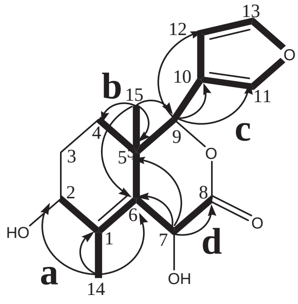


Figure 2. The planar structure of **1** based on 2D NMR experiments.

After assignments of all the direct ^{1}H–^{13}C bondings were made on the basis of the HMQC spectrum, four partial structures **a**–**d** were deduced from the ^{1}H–^{13}C NMR long-range correlations in the HMBC experiments (Figure 2). Furthermore, the HMBC cross-peaks: δ_H 4.02 (2-OH)/δ_C 70.2 (CH-2) and δ_H 5.33 (7-OH)/δc 67.9 (CH-7) as well as 135.1 (C-6) indicated that the two hydroxy groups were attached to C-2 and C-7, respectively. So the planar structure of **1** was established as shown in Figure 2.

The relative configurations at C-2, C-5, and C-9 were resolved using 2D NOESY experiments. The cross-peaks observed between the protons H-9/H-4β, H-4β/H-3β, H-3β/H-2, and H-2/H-4β indicated that H-2 and H-9 were on the same side and were arbitrarily assigned β-orientations. The NOESY correlation pairs of H-15/H-3α and H-15/H-4α suggested that H-15 had an α-orientation. Additionally, although the stereochemistry at C-7 could not be determined by the splitting pattern and relevant NOESY correlations, a single-crystal X-ray diffraction showed that 7-OH was in β-configuration. Consequently, the structure and relative stereochemistry of **1** were further confirmed by a single-crystal X-ray diffraction (Figure 3).

The absolute configuration of **1** was determined by analysis of the CD spectrum. A single-crystal X-ray diffraction for **1** showed that the δ-lactone ring was in boat-conformation (H-9 and 7-OH is cis, and H-9 is axial), which corresponded to the

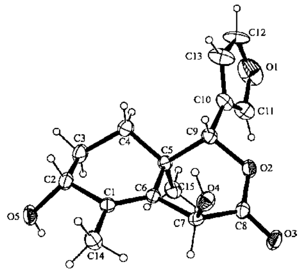


Figure 3. X-ray crystal structure of **1**.

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Table 1. NMR spectral data for **1** and **2** (CD_3COCD_3, δ in ppm, J in Hz)

Position	Compound **1**			Compound **2**		
	^{1}H		^{13}C	^{1}H		^{13}C
1	—	—	139.5 s	—	—	137.4 s
2	4.02	br s	70.2 d	3.90	t (4.8)	67.07 d
3α	1.76	m		1.78–1.71	m	
3β	2.05	m	28.9 t	1.96	tt (12.8, 3.2)	27.8 t
4α	1.14	dt (13.2, 3.2)		0.96	dt (12.8, 3.2)	
4β	1.54	ddd (14.0, 13.2, 3.2)	32.4 t	1.71–1.64	m	28.0 t
5	—	—	40.0 s	—	—	40.0 s
6	—	—	135.1 s	—	—	136.0 s
7	4.82	d (4.8)	67.9 d	4.81	d (5.2)	67.6 d
8	—	—	171.1 s	—	—	171.1 s
9	5.51	s	79.7 d	5.48	s	79.6 d
10	—	—	121.4 s	—	—	121.7 s
11	7.65	s	142.3 d	7.64	s	142.2 d
12	6.53	s	110.9 d	6.52	s	110.9 d
13	7.59	s	144.0 d	7.58	s	144.0 d
14	1.86	s	14.6 q	1.89	s	17.1 q
15	1.02	s	18.9 q	0.92	s	17.5 q
2-OH	4.02	br s	—	4.13	br s	—
7-OH	5.33	d (4.8)	—	5.36	m	—

peak centered at $\lambda_{\max}$ 222 nm in the CD spectrum.[8] According to the Klyne sector rule for the saturational lactone,[9] the positive Cotton effect, $[\theta]_{222} = +110000$, indicated that the absolute configuration at C-5 was assigned to S. And then, those at C-2, C-7, and C-9 were fixed to be S, R, and S, respectively. Thus, the structure of **1** was assigned as (2*S*,5*S*,7*R*,9*S*)-isodictamdiol.

Dictamdiol (**2**), $[\alpha]_D^{20} - 114$ (c 0.42, MeOH), was obtained as colorless crystal. Its molecular formula of $C_{15}H_{18}O_5$ was deduced from HRESI-MS ($[M + Na]^+$ at m/z 301.1048, calcd. 301.1046) with seven degrees of unsaturation. The IR spectrum displayed absorptions for two hydroxys (3422 and 3342 cm^{-1}), a δ-lactone (1732 cm^{-1}), a double bond (1592 cm^{-1}), and a furyl ring (1503 and 876 cm^{-1}). **2** gave the same $[M]^+$ and fragment peaks in the EI-MS and also had similar features in the ^{1}H and ^{13}C NMR spectra as **1** (Table 1). In comparison with the NMR data of **1**,[10] the H-2 and 2-OH proton signals of **2** exhibited a upfield shift from δ 4.02 to 3.90 and a downfield from δ 4.02 to 4.13, respectively, and the signal of C-2 was shifted upfield from δ 70.2 to 67.7, indicating that the stereochemistry at C-2 in **2** and **1** were firmly different, which was proposed from the ^{1}H NMR coupling constants: H-2 in **2** should be equatorial because of the small coupling constant observed between H-2 and H-3 ($J_{2,3} = 4.8$ Hz), whereas the large coupling constant between H-2 and H-3 [$J_{2,3} = 8.8$ Hz (after exchange by addition of D_2O)] in **1** implied that H-2 should be axial. Furthermore, its complete structure and relative configuration of **2** were established by an X-ray crystallographic study (Figure 4). As the case of **1**, the absolute configuration of **2** was determined as (2R,5S,7R,9S) using the CD spectral study and a single-crystal X-ray diffraction.[10] Therefore, the structure of **2** was named as (2*R*,5*S*,7*R*,9*S*)-dictamdiol.

To the best of our knowledge, the absolute configurations at C-5 and C-9 of limonoids reported were determined as S and S for the first time.

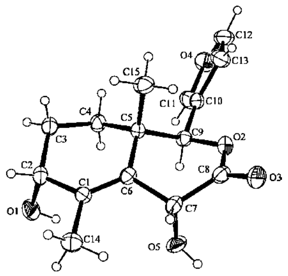

Figure 4. X-ray crystal structure of **2**.

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