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Brownins D and E: New Limonoids from *Harrisonia brownii*

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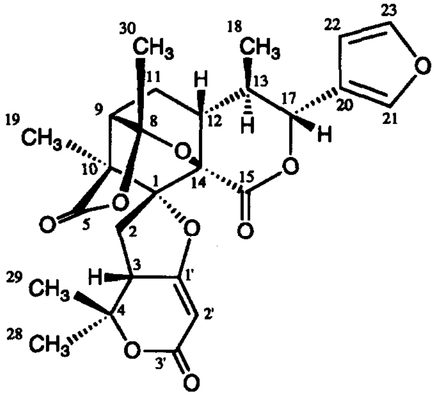
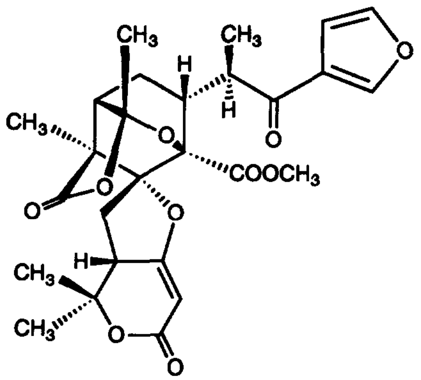
Abstract: Two new limonoids, brownin D (**1**) and E (**2**), were isolated from the bark of *Harrisonia brownii* (Simaroubaceae). Their relative stereostructures were established by spectroscopic methods and X-ray diffraction analysis of **1**.

Our previous paper[1] reported the isolation of two new limonoids from the $CHCl_3$ extract of the bark of *Harrisonia brownii* Juss. (Simaroubaceae).[2,3] In the present study, from remaining fractions of the same extract,[1] two new highly rearranged limonoids, brownin D (**1**) and brownin E (**2**) were isolated.

Brownin D (**1**)[4] was obtained as colorless prisms and its molecular formula was determined as $C_{26}H_{28}O_9$ by HREIMS (*m/z* 484.1717, M^+, Δ-0.8 mmu of calcd). All 26 carbons appeared in the ^{13}C-NMR spectrum, including typical signals for three lactones at δ 176.60 (C-5), 165.15 (C-15) and 168.08 (C-3'), trisubstituted double bond at δ 173.23 (C-1') and 89.64 (C-2'), and β-substituted furan at δ 108.85 (C-22), 122.92 (C-20), 142.36 (C-21) and 144.70 (C-23). The IR spectrum exhibited absorptions at 1782, 1710 and 1670 cm^{-1}, further supporting the presence of lactone functions. These functional groups accounted for 7 of 13 degrees of unsaturation introduced in the molecular formula. A ^1H-^{13}C COSY experiment demonstrated H-C connectivities, and two isolated spin systems were detected in a ^1H-^1H COSY experiment. These spin systems corresponded to H-9, H-11, H-12, H-13 (H-18), H-17 and H-2, H-3 identified in the ^1H-^1H COSY spectrum. H-3 showed *W*-type long-range coupling (J =2.4 Hz) with H-2'. Extensive ^2J and ^3J ^1H-^{13}C correlation indicated by a COLOC experiment clearly demonstrated C-C conectivities. In the COLOC spectrum of **1**, the spiro carbon at C-1 (δ 91.58) showed ^2J and ^3J cross-peaks with a nonequivalent methylene proton at H-2β (δ 2.32), bridge head methine H-12 (δ 2.45) and tertiary methyl H-19 (δ 1.35). The ketal carbon at C-8 (δ 108.11) showed ${}^2J$ and ${}^3J$ cross-peaks with a tertiary methyl at H-30 (δ 1.69) and H-11β (δ 1.85). The signal at C-21 (δ 142.36) of furan ring showed significant long-range correlation with H-17 (δ 5.12). 1 is thus shown to possess a novel heptacyclic skeleton containing a furan ring. In order to confirm unambiguously the structure and to establish the relative stereochemistry of all nine chiral C atoms, a single crystal X-ray diffraction analysis was subsequently carried out. A drawing of the final X-ray model of brownin D (1) is given in Figure 1.[5]



1



2

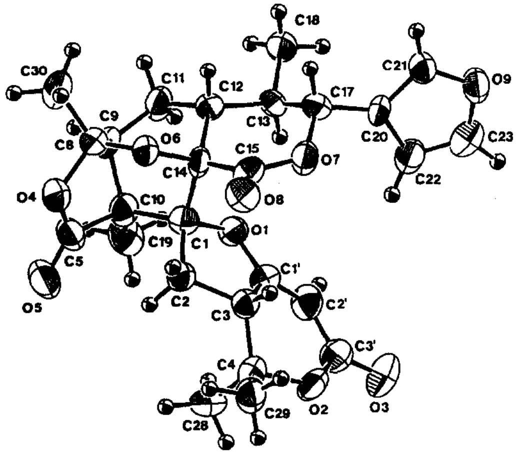


Figure 1. ORTEP Drawing of Brownin D (1)

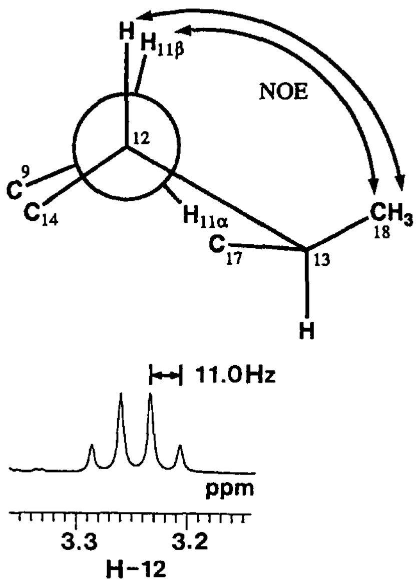


Figure 2.

Brownin E (2)[6] was obtained as colorless prisms. Its molecular formula, $C_{27}H_{30}O_{10}$, was determined by HREIMS (*m/z* 514.1827, M^+, Δ-0.3 mmu of calcd). The IR spectrum showed the presence of ketone, lactone and olefinic functions. The ^{1}H and ^{13}C-NMR spectra of **2** were similar to those of brownin D (**1**), though there was no doublet signal at δ 5.12 due to the methine proton at H-17. A new methoxycarbonyl group [δ_H 3.57 (3H, s), δ_C 52.72 and 165.96] and ketone (δ_C 197.69) due to cleavage of δ-lactone with loss of H-17 was observed. The remaining NMR assignments for **2**, shown in Table 1, were based on ^{1}H-^{1}H COSY, HMQC, HMBC and phase-sensitive NOESY spectra. The stereochemistry of brownin E (**2**) could be established by the interpretation of the phase-sensitive NOESY experiment. Analysis of the coupling constants between H-11 and H-12 ($J_{11\alpha,12}=J_{11\beta,12}=11.0$ Hz) and between H-12 and H-13 ($J_{12,13}=11.0$ Hz) revealed that C-11-C-12-C-13 bonds of **2** are expected to have eclipsed-anticonformation.[7] (Figure 2) Furthermore, as can be seen in Figure 2, the NOESY correlation between H-18 and H-11β, and between H-18 and H-12 were observed. From these facts, the configuration at C-13 can be *R*. The structure of brownin E is thus **2**.

To our knowledge, this paper reports for the first time the isolation of a new class of highly rearranged limonoids.

Table 1. ^{13}C and ^{1}H -NMR Spectral Data for Brownins D (**1**) and E (**2**) [a]

	1				**2**			
Assignment	δ_C	δ_H	mult.	(*J*, Hz)	δ_C	δ_H	mult.	(*J*, Hz)
1	91.58				92.15			
2	29.50	3.00 α	ddd	(13.7, 9.0, 1.0)	29.88	2.46 α	dd	(14.7, 10.3)
		2.32 β	dd	(13.7, 10.3)		2.23 β	m	
3	46.08	3.31	m		47.29	3.49	m	
4	81.57				83.09			
5	176.60				177.32			
8	108.11				107.61			
9	45.54	2.59	dd	(5.3, 1.1)	45.68	2.63	br d	(4.4)
10	52.62				53.39			
11	18.78	2.27 α	m		18.95	2.23 α	m	
		1.85 β	ddd	(14.1, 10.0, 1.1)		2.03 β	ddd	(14.3, 11.0, 1.0)
12	43.03	2.45	q	(10.0)	41.58	3.25	q	(11.0)
13	38.24	2.73	m		45.64	3.83	m	
14	78.10				81.91			
15	165.15				165.96			
17	82.70	5.12	d	(10.8)	197.69			
18	14.49	0.84	d	(6.4)	17.12	1.17	d	(7.3)
19	12.64	1.35	s		13.25	1.35	s	
20	122.92				127.43			
21	142.36	7.70	br s		148.04	8.52	br s	
22	108.85	6.59	d	(1.4)	109.20	6.96	d	(1.4)
23	144.70	7.49	t	(1.4)	145.11	7.61	t	(1.4)
28	20.21	1.28	s		20.11	1.35	s	
29	28.24	1.23	s		28.27	1.20	s	
30	21.83	1.69	s		21.98	1.75	s	
1'	173.23				175.25			
2'	89.64	5.71	d	(2.4)	88.40	5.87	d	(2.6)
	(${}^1J_{CH}$=171 Hz)							
3'	168.08				170.11			
OMe					52.72	3.57	s	

[a] pyridine-d_5, ^{13}C, 100 MHz, ^{1}H, 400 MHz.

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4. **Brownin D (1)**. Colorless prisms (MeOH), mp >300°, $[\alpha]^{20}_D$ +40.5° (*c*, 1.2, pyridine). UV (MeOH) nm (log ε): 239 (3.77). IR (KBr) cm^{-1}: 1782, 1710, 1670, 1285, 1200, 1180, 1025, 980, 895. EIMS, *m/z* (relative intensity) 484 (M^+, 12), 440 (9), 396 (5), 376 (3), 358 (10), 343 (2),318 (7), 275 (6), 245 (13), 221 (20), 203 (10), 175 (8), 161 (12), 145 (8), 135 (14), 121 (6), 108 (67), 91(17), 79 (22), 69 (14), 55 (11), 43 (100). HREIMS, *m/z* 484.1717$[M]^+$($C_{26}H_{28}O_9$, Δ-0.8 mmu of calcd). COLOC: C-1→ H-2β, H-3, H-12, H-19; C-3→H-28, H-29; C-4→H-2β, H-3, H-28, H-29; C-5→ H-19, C-8→H-11β, H-30; C-10→H-2β, H-11α, H-19; C-12→H-18; C-14→H-2β, C-11α, H-12; C-17→H-18; C-20→H-21, H-23; C-21→H-17, H-22, H-23; C-23→H-21, H-22; C-28→H-29; C-29→H-28; C-1' →H-2α, H-3.
5. Crystals of 1, crystallization from methanol, belong to a monoclinic space group $P2_1$. Lattice constants and intensity data were measured on a Rigaku AFC-5R diffractometer equipped with a device for graphite-monochromated CuKα radiation. Crystal data: $C_{26}H_{28}O_9 \cdot CH_3OH$, *a* =8.478 (1), *b* =11.934 (2), *c* =12.464 (3) Å, β =91.66 (1)°, Z =4, Dc =1.361g/cm^3, μ(CuKα) =8.81 cm^{-1}. A total of 1633 independent reflections with $|F_o| > 3\sigma(|F_o|)$ was used for structure analysis. Structure was determined by a direct method (MITHRIL system)[8] and refined by full-matrix least squares (SHELX76).[9] Final refinement cycle gave R =0.071 (Rw =0.088). The final Fourier difference synthesis showed a maximum and minimum of + 0.30 and -0.30 e^- /$Å^3$, respectively. Atomic coordinates, bond lengths, bond angles, thermal parameters and structure factors have been entered into the Cambridge Crystallographic Data Centre.
6. **Brownin E (2)**. Colorless prisms (MeOH), mp >300°, $[\alpha]^{20}_D$ +40.6° (*c*, 1.0, pyridine). UV (MeOH) nm (log ε): 242 (3.97). IR (KBr) cm^{-1}: 1782, 1725, 1705, 1680, 1565, 1505, 1395, 1205, 1180, 1050, 1025, 980, 900, 840. EIMS, *m/z* (relative intensity) 514 (M^+, 56), 496 (13), 470 (20), 425 (6), 391 (9), 373 (21), 346 (5), 319 (12), 301 (9), 237 (10), 221 (17), 203 (8), 124 (18), 95 (100), 79 (7), 69 (10), 55 (6), 42 (66). HREIMS, *m/z* 514.1827 $[M]^+$ ($C_{27}H_{30}O_{10}$, Δ -0.3 mmu of calcd). Phase-sensitive NOESY : H-2α→H-19, H-28; H-2β→H-3; H-3→H-29; H-9→H-11α, H-13, H-19, H-30; H-11β→H-12, H-18; H-12→H-18; H-13→H-21. HMBC:H-2β→C-3, C-10; H-3→C-14; H-9→ C-1, C-8, C-10, C-11, C-12, C-19; H-11α→C-14; H-11β→C-8, C-10, C-12, C-13, C-30; H-12→ C-1, C-11, C-13, C-14; H-13→ C-18; H-18→C-12, C-13; H-19→C-1, C-9, C-10; H-21→C-20, C-22, C-23; H-22→ C-20, C-21, C-23; H-23→C-20, C-21; H-28→C-3, C-4 , C-29; H-29→C-3, C-4, C-28; H-30→C-8, C-9; H-2' →C-1', C-3.
7. Selected torsion angles of **1**: H11α-C11-C12-H12=138°, H11β-C11-C12-H12=18° and H12-C12-C13-H13=177°.
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