

Labdane Diterpenoids from *Leonurus sibiricus*

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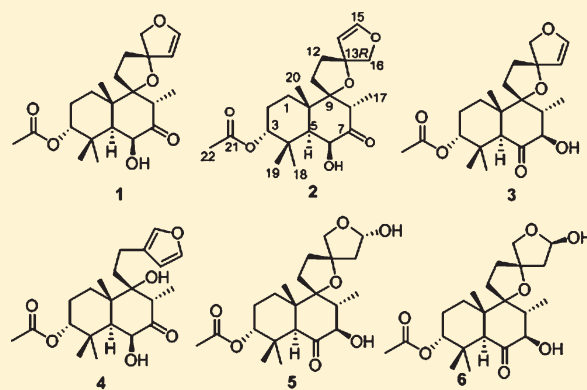
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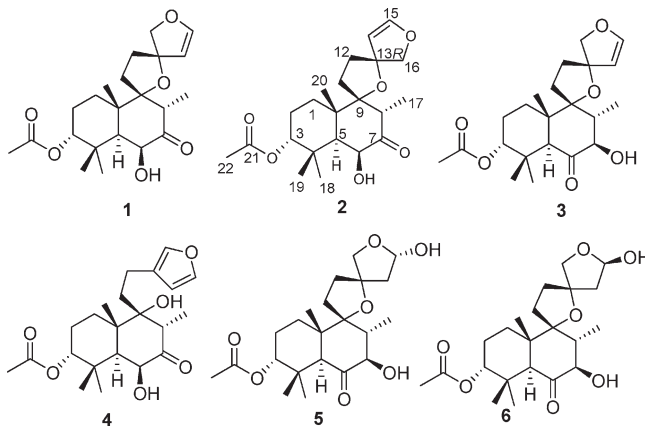
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S Supporting Information

ABSTRACT: Six new labdane diterpenoids, preleosibirone A (1), 13-*epi*-preleosibirone A (2), isopreleosibirone A (3), leosibirone A (4), leosibirone B (5), and 15-*epi*-leosibirone B (6), were isolated from the leaves of *Leonurus sibiricus*. The absolute configurations of 1, 2, 5, and 6 were established by X-ray crystallographic analyses, and leosibirone A (4) was shown to be an artifact of the isolation process.



Leonurus sibiricus L. (Lamiaceae) is a widely distributed medicinal plant in southern Siberia, China, Korea, Japan, Vietnam, and elsewhere in Southeast Asia. It is commonly known as “motherwort” in Asian countries. It has been introduced to Mexico and named “marihuaniilla” (Spanish “little marijuana”). The plant is used traditionally for various ailments, such as menstrual irregularities, high blood pressure, blood stasis, heart disorders, and dysentery.^{1–6} Leaves harvested from the flowering plant are dried and smoked as a marijuana substitute. The effects are described as mildly narcotic or cannabis-like.⁷ Previous phytochemical investigations resulted in the isolation of alkaloids, flavonoids, iridoids, and phenylpropanoid glycosides.^{8–12} In addition, there are several reports of labdane diterpenoids from *L. sibiricus*.^{8,13–16} Herein, we report the isolation and structure elucidation of six new labdane diterpenoids (1–6) from this species.



RESULTS AND DISCUSSION

The *n*-hexane extract of the aerial parts of *L. sibiricus* was passed through an MCI gel (DIAION HP20SS) column and eluted with MeOH to remove chlorophyll and then separated by semipreparative HPLC to give compounds 1–6.

Preleosibirone A (1) was obtained as a white powder, $[\alpha]_D^{25} -23.3$, and its molecular formula was determined as $C_{22}H_{32}O_6$ by HRESIMS (m/z 415.2086 $[M + Na]^+$). The 1H and ^{13}C NMR and HSQC spectroscopic data confirmed the presence of 22 carbons. Other features strongly suggested the presence of a spirobisdihydrofuran labdane, close to preleosibirin,¹⁷ precalyone,¹⁸ or isopreleoheterin.¹⁹ Thus, the characteristic signals of spiro carbons C-9 (δ_C 96.6) and C-13 (δ_C 93.7) and the diagnostic C-16 oxymethylene (δ_C 80.6; δ_H 4.27 and 4.00, d, $J = 10.0$ Hz) and the H₁₄–H₁₅ enol ether function (AB system, δ_H 6.40 and 5.02, d, $J = 2.4$ Hz) were observed. HMBC correlations of Me-18 and Me-19 established C-3, and those of H-3 and CH₃COO with CH₃COO pointed out the presence of an acetoxy group at C-3 and the A-ring structure as in precalyone.¹⁸ The correlation of Me-17 with a C=O fixed the carbonyl position at C-7, and other correlations permitted and confirmed the assignment of ring B hydroxy and carbonyl functionalities as in isopreleoheterin.¹⁹ The relative configuration of the stereogenic centers of 1 was deduced as follows. The H-5 and H-6 coupling constant ($J = 3.2$ Hz) placed the two protons *cis* to each other in

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an α -axial, α -equatorial orientation, leaving the hydroxy group as β -axial. The unusually low-field signal (δ_{H} 3.39) of H-8 for an α -carbonyl proton could only be explained if this hydrogen is perpendicular to the vicinal carbonyl group above the molecular plane, leaving the C-17 methyl as α -equatorial, which agreed with the coupling constant of $J = 6.8$ Hz, as axial methyl groups exhibit a larger coupling constant (8.0 Hz). An X-ray crystallography study of disordered cocrystals of **1** and **2** (Figure 1) revealed the acetoxy group to be connected to C-3, and H-5, H-6, and Me-17 as α -oriented, with Me-20 and H-5 in β -axial and α -axial orientations, respectively. The NOESY correlation between H-14 and Me-17 confirmed the 13*S*-configuration.

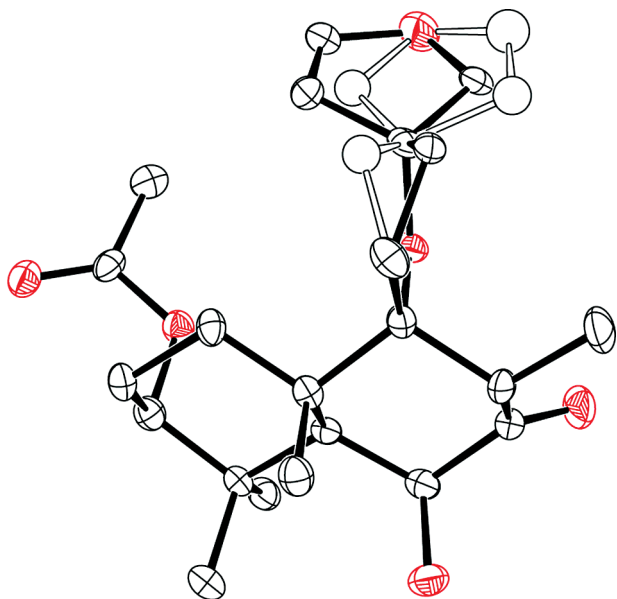


Figure 1. ORTEP drawing of cocrystals of **1** and **2**. The atoms represented as outlines are the minor (23.9%) component **1**. H atoms are not shown.

These data conclusively proved the new structure of **1** as 3 α -acetoxy-9 α ,13*S*;15,16-diepoxy-6 β -hydroxylabd-14-en-7-one, which has been named preleosibirone A.

13-*epi*-Preleosibirone A (**2**) was obtained as a white solid, $[\alpha]_{\text{D}}^{25} - 19.0$, and its molecular formula determined as $\text{C}_{22}\text{H}_{32}\text{O}_6$ by HRESIMS (m/z 415.2086 $[\text{M} + \text{Na}]^+$). The ^1H and ^{13}C NMR data of **2** were similar to those of **1** (Tables 1 and 2). Similar to the arguments advanced for compound **1**, the NOESY correlation between H-16 and Me-17 confirmed the 13*R*-configuration. An X-ray crystallographic analysis of cocrystals of **1** and **2** (Figure 1) similarly revealed the C-3 acetoxy group as α -oriented, with H-5, H-6, and Me-17 also α -oriented. Thus, the structure of **2** was determined as 3 α -acetoxy-9 α ,13*R*;15,16-diepoxy-6 β -hydroxylabd-14-en-7-one and, as an epimer of **1**, thus named 13-*epi*-preleosibirone A.

Isopreleosibirone A (**3**) was obtained as a white solid, $[\alpha]_{\text{D}}^{25} - 9.0$, and its molecular formula determined as $\text{C}_{22}\text{H}_{32}\text{O}_6$ by HRESIMS (m/z 415.2089 $[\text{M} + \text{Na}]^+$). Most of the ^1H and ^{13}C NMR signals indicated a spirobisdihydrofuran and ring A moieties identical to **1**. The different arrangement of ring B substituents was based on correlations of H-5 (singlet) and H-7 with the C-6 carbonyl, and Me-17 with C-7 and C-9, as well as H-5 with C-9, allowed the assignment of substituents in ring B. The relative configurations of C-5 and C-7 were determined from their NOESY data. Correlation of H-7 with H-5 indicated their α -orientation. As for compounds **1** and **2**, the 13*S*-configuration of **3** was deduced from the NOESY correlation between H-14 and Me-17. Compared with preleoheterin²⁰ and 13-*epi*-preleoheterin,¹⁹ compound **3** shared most of the spectroscopic observations. Thus, the structure of **3** was assigned as 3 α -acetoxy-9 α ,13*S*;15,16-diepoxy-7 β -hydroxylabd-14-en-6-one, an isomer of **1**, and named isopreleosibirone A. It is possible that **3** is an artifact arising from preleosibirone A (**1**) by an α -ketol rearrangement leading to interchange of the hydroxy and carbonyl groups.

Leosibirone A (**4**) was obtained as a white solid, $[\alpha]_{\text{D}}^{25} - 20.0$, and its molecular formula determined as $\text{C}_{22}\text{H}_{32}\text{O}_6$ by

Table 1. ^1H NMR Data of Compounds **1**–**6** (δ in ppm, J in Hz, 400 MHz)

position	1 ^a	2 ^a	3 ^a	4 ^a	5/6 ^b
1	1.63, m	1.49, m	1.80, m	1.98, m	1.82, m
2	1.90, m	1.88, m	1.70, m	2.05, m	1.70, m
3	4.46, m	4.12, m	4.51, br s	4.52, br s	4.35, br s
5	2.10, overlap	2.10, m	3.30, s	2.20, br s	3.03, s
6	4.07, d (3.2)	4.05, br s		4.17, br s	
7			3.80, d (4.0)		3.84, br s
8	3.39, q (6.8)	3.54, q (6.8)	1.90, m	3.55, q (6.8)	1.85, m
11	2.02, m	2.10, m	2.10, m	2.10, m	2.09, m
12	2.22, m	2.20, m	2.20, m	2.56, m	2.10, m
14	5.02, d (2.4)	5.22, d (2.4)	5.31, d (2.4)	6.38, s	1.70, m 2.37, m
15	6.40, d (2.4)	6.48, d (2.4)	6.59, d (2.4)	7.44, s	5.40, d (4.4) / 5.27, s
16	4.00, d (10.0)	4.04, d (10.4)	4.23, d (10.0)	7.37, s	3.56, d (7.6)
	4.27, d (10.0)	4.28, d (10.4)	4.58, d (10.0)		3.80, d (7.6)
17	0.98, d (6.8)	0.98, d (6.8)	1.22, d (6.8)	1.11, d (6.8)	1.05, d, (6.8)
18	0.89, s	0.93, s	0.95, s	0.96, s	0.84, s
19	1.31, s	1.37, s	1.35, s	1.42, s	1.25, s
20	1.45, s	1.49, s	0.91, s	1.55, s	0.78, s
22	2.00, s	1.95, s	2.16, s	2.05, s	2.00, s/2.01, s

^a Measured in acetone- d_6 . ^b Measured in DMSO- d_6 .

Table 2. ^{13}C NMR Data of Compounds 1–6 (δ in ppm, 100 MHz)

carbon	1 ^a	2 ^a	3 ^a	4 ^a	5/6 ^b
	δ_{C} , mult.	δ_{C} , mult.	δ_{C} , mult.	δ_{C} , mult.	δ_{C} , mult.
1	28.7, CH ₂	27.5, CH ₂	28.4, CH ₂	35.2, CH ₂	29.0/29.1, CH ₂
2	22.5, CH ₂	22.5, CH ₂	21.8, CH ₂	22.6, CH ₂	25.1/25.5, CH ₂
3	78.5, CH	78.7, CH	78.0, CH	78.4, CH	77.8/78.0, CH
4	37.6, C	37.8, C CH ₂	35.4, C	37.7, C	35.6/35.7, C
5	43.4, CH	44.3, CH	51.2, CH	43.4, CH	51.5/51.9, CH
6	75.0, CH	75.4, CH	211.06, C	75.3, CH	211.5/211.5, C
7	207.6, C	208.0, C	77.5, CH	208.9, C	77.7/77.8, CH
8	44.7, CH	45.2, CH	46.1, CH	45.2, CH	46.0/46.5, CH
9	96.6, C	96.6, C	94.2, C	81.5, C	91.8/92.2, C
10	42.8, C	42.5, C	47.7, C	43.5, C	47.4/47.5, C
11	27.6, CH ₂	27.5, CH ₂	28.4, CH ₂	27.2, CH ₂	29.0/29.1, CH ₂
12	37.9, CH ₂	36.9, CH ₂	37.5, CH ₂	22.6, CH ₂	38.4/39.1, CH ₂
13	93.7, C	93.3, C	92.2, C	125.5, C	90.6/91.1, C
14	107.2, CH	107.2, CH	107.5, CH	110.8, CH	46.0/46.5, CH ₂
15	148.1, CH	147.7, CH	148.2, CH	142.8, CH	97.5/98.0, CH
16	80.6, CH ₂	80.3, CH	80.6, CH	138.6, CH	74.5/76.8, CH
17	8.6, CH ₃	8.7, CH ₃	12.9, CH ₃	7.8, CH ₃	13.4/13.6, CH ₃
18	28.7, CH ₃	28.1, CH ₃	26.1, CH ₃	27.4, CH ₃	26.9/26.9, CH ₃
19	23.7, CH ₃	23.7, CH ₃	21.4, CH ₃	23.9, CH ₃	22.1/22.2, CH ₃
20	19.5, CH ₃	19.0, CH ₃	19.3, CH ₃	18.6, CH ₃	19.7/19.9, CH ₃
21	169.4, C	171.8, C	169.3, C	169.6, C	170.0/170.0, C
22	20.2, CH ₃	20.2, CH ₃	20.3, CH ₃	20.2, CH ₃	21.3/21.4, CH ₃

^a Measured in acetone-*d*₆. ^b Measured in DMSO-*d*₆.

HRESIMS (m/z 415.2072 [$\text{M} + \text{Na}$]⁺). The ^1H NMR spectrum (Table 1) indicated the presence of a furanolabdane system. Thus, it exhibited the typical proton resonances of a β -substituted furan moiety at δ_{H} 7.44, 7.37, and 6.38, three methyl singlets at δ_{H} 1.55, 1.42, and 0.96, and one methyl doublet at δ_{H} 1.11 ($J = 6.8$ Hz), coupled with a vicinal proton (3.55, q, $J = 6.8$ Hz). The HMBC correlations of Me-18 and Me-19 with C-3, and H-3 with the acetoxy carbonyl group, indicated the location of the acetoxy group at C-3 rather than at C-6. Correlations of H-5, H-6, H-8, and Me-17 with the C-7 carbonyl confirmed the structure of ring B. Compound 1 was not stable in solution and was readily converted into 4 under very mild acidic conditions, even in 90% MeOH/water overnight at room temperature. The mechanism of this conversion is presented in Scheme 1. This type of conversion has been reported before, as exemplified by precalyone being converted to calyone,¹⁸ preleosibirin being converted to leosibirin with Amberlite IR-120(H⁺),¹³ preleoheterin being converted to leoheterin with aqueous 0.5% HCl,²⁰ and pregaleopsin being quantitatively converted to galeopsin during storage at +4 °C for 2–3 months.²¹ Thus, the structure of 4 was established as 3 α -acetoxy-15,16-epoxy-6 β ,9 α -dihydroxyabd-13(16), 14-dien-7-one and named leosibirone A.

Leosibirone B (5) and 15-*epi*-leosibirone B (6) were isolated as a mixture of two isomers with the molecular formula C₂₂H₃₄O₇, as determined by HRESIMS ([$\text{M} + \text{Na}$]⁺ 433.2197, [$\text{M} + \text{NH}_4$]⁺ 428.2629). Their ^{13}C NMR data showed the presence of a ketone carbonyl and an acetoxy group but no further sp²-hybridized carbon atoms that indicated a tetracyclic structure of 5/6. Closer scrutiny of the ^1H and ^{13}C NMR data revealed the structure of 5/6 to be quite similar to

those of leopersin C and 15-*epi*-leopersin C,²² except for the presence of an acetoxy group (δ_{H} 2.00/2.01, s, 3H each; δ_{C} 21.3/21.4 and 170.0 \times 2) in 5/6. In the HMBC spectrum, correlations between H-3 (δ_{H} 4.35)/-OCOCH₃ (δ_{H} 2.01) and -OCOCH₃ (δ_{C} 170.0) and between H-3 and C-5/Me-18/Me-19 suggested that the acetoxy group resides at C-3. The relative configurations of C-5, C-7, C-8, C-9, C-10, and C-13 in 5/6 were assigned on the basis of NOESY correlations. The observation of cross-peaks in the NOESY spectrum between H-5/H-7, H-5/Me-18, H-7/Me-17, and Me-17/H-5 indicated that they are all α -cofacial, while the interactions between H-8/Me-20, H₂-11/Me-20, and Me-19/Me-20 revealed these to be on the β -face. Additional NOE interactions between Me-17 and H-16 indicated the 13S-configuration.

The absolute configuration of 5 was established by a low-temperature single-crystal X-ray analysis (Figure 2). Interestingly, compound 5 was selected manually from the mixture of 5 and 6 as transparent crystals. However, 6, a white solid, was not suitable for X-ray analysis. A crystallization of the 5/6 mixture from MeCN yielded excellent cocrystals isomorphous with the structure of 5. The structure of the minor (ca. 23.9%) component 6 is shown in Figure 3. In solution, compounds 5 and 6 were inseparable and underwent spontaneous α,β -anomerization similar to the process of mutarotation of the hemiacetal functionality in carbohydrates. Thus, compounds 5/6 were identified as 3 α -acetoxy-7 β ,15 α -dihydroxy-9 α ,13 α ;15,16-diepoxyabd-6-one and 3 α -acetoxy-7 β ,15 β -dihydroxy-9 α ,13 α ;15,16-diepoxyabd-6-one and named leosibirone B and 15-*epi*-leosibirone B, respectively. It is possible that compounds 5 and 6 are produced from water addition to the enol ether functionality of compound 3 (Scheme 1).

Genkwanin (apigenin 7-*O*-methyl ether) was obtained as a light yellow precipitate by addition of MeOH to the *n*-hexane extract and

Scheme 1. Possible Transformation of 1 to 2–6

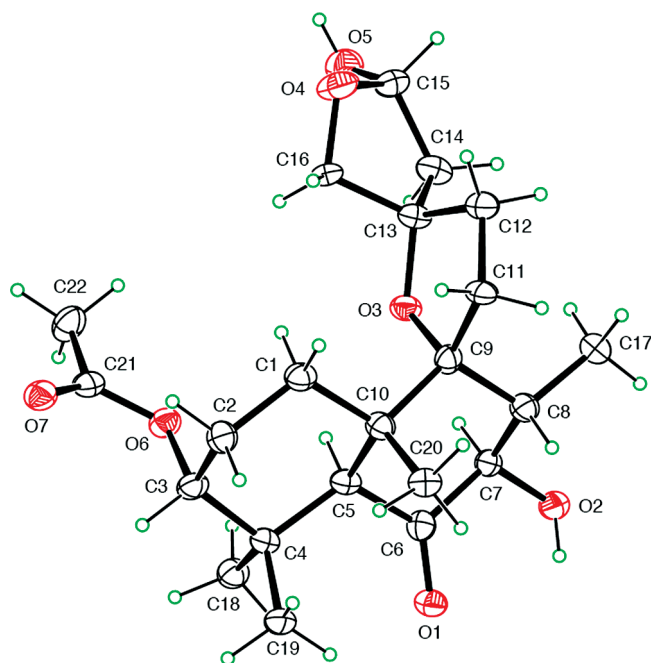
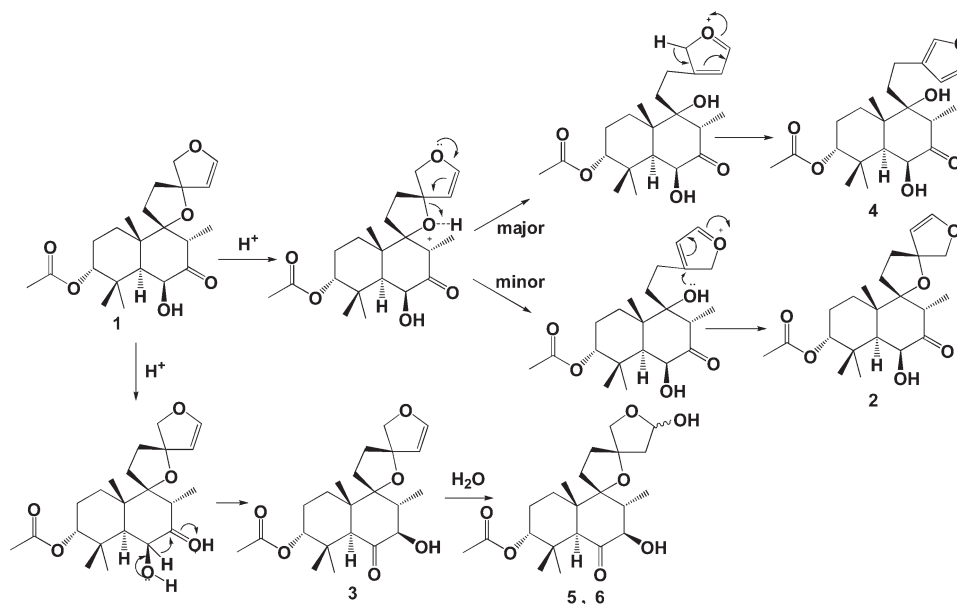


Figure 2. ORTEP drawing of compound 5.

identified on the basis of NMR data. It is very common in *Leonurus* and is considered as a chemotaxonomic marker of this genus.¹⁴

Pre-furanoid and furanoid diterpenes are abundant in many species of the family Lamiaceae. However, it is inevitable that the rupture of the C-9 α and C-13 epoxy bridge or solvent addition to the C-14–C-15 double bond during the isolation process would produce furanoid diterpenes or tetrahydrofurans. To establish whether the isolated compounds are true natural products or artifacts, HPLC was used to analyze the stability of the compounds in the extract. A series of chromatograms indicated that compound 1 was dominant among the three compounds in the initial fraction. Compound 4 was absent in the original fraction. After 12 h in 90% MeOH/H₂O, 4 was present in a significant

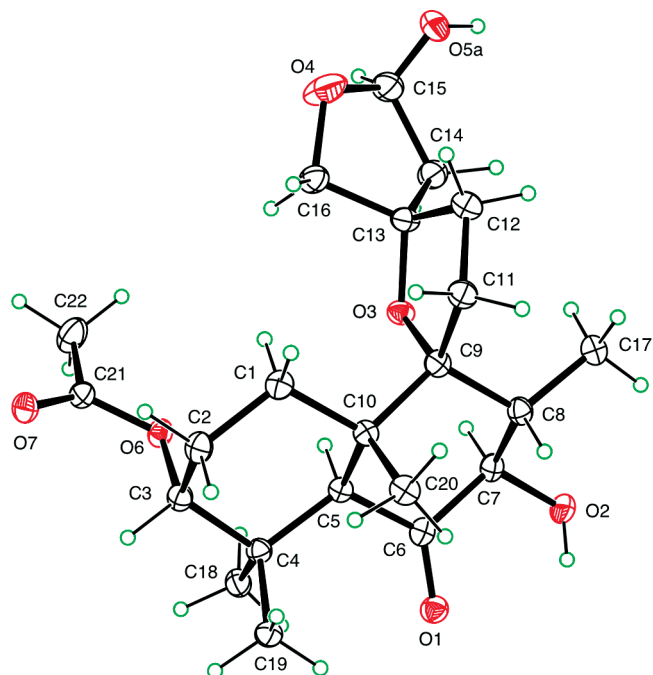


Figure 3. ORTEP drawing of the minor component 6, in the disordered cocrystal of 5 and 6.

concentration, with the increase in concentration continuing until the seventh day, when it represented the main component in the mixture (Figure 4). These results indicate that compound 2 is more stable under the prevailing conditions than 1. This may be explained by the fact that the conversion of 1 into 4 requires a *trans*-elimination of H and OR, which is not permitted in 2, and, during the process of conversion, 2 (a minor product) was formed (Scheme 1). Thus, this experiment and the observations made have demonstrated that some of the furanoid-diterpenoids may have been produced during extraction and isolation.

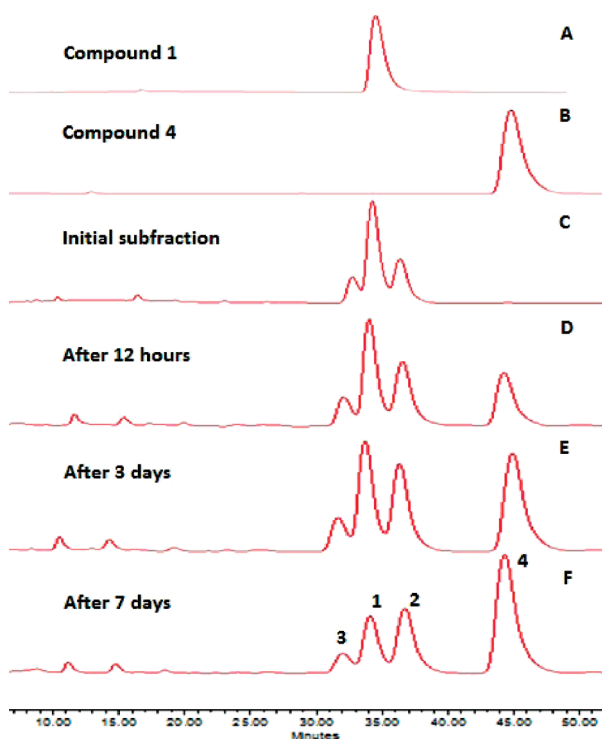


Figure 4. HPLC profiles of the extract and stability (condition 65% MeOH/water).

EXPERIMENTAL SECTION

General Experimental Procedures. Optical rotations were acquired with a Rudolph Research Analytical Autopol V automatic polarimeter. IR spectra were recorded on a Bruker Tensor 27 spectrophotometer. IR spectra were recorded on a Bruker DRX NMR spectrometer operating at 400 MHz for ^1H and 100 MHz for ^{13}C with a 3 mm direct carbon probe. The mass detector was time-of-flight (model G1969A) equipped with an electrospray ionization interface and was controlled by Aligent software (Aligent Mass Hunter workstation, A.02.01). HPLC was carried out using a Delta Prep 4000 (Waters Corporation, Milford, MA) instrument equipped with a dual-wavelength detector model 2487 adjusted at 210 and 254 nm. The HPLC column was a Phenomenex Luna C₈ (250 × 10.00 mm, 5 μm).

Plant Material. The leaves of *L. sibiricus* were purchased from IAmShaman Shop (P.O. Box 12618, Chicago, IL 60612) in June 2010 and authenticated by C. L. Burandt, Jr. A voucher specimen (code: hkwu-LS-20100806) was deposited at the Department of Pharmacognosy, School of Pharmacy, University of Mississippi.

Extraction and Isolation. The dried and powdered leaves of *L. sibiricus* (20 g) were extracted with *n*-hexane (2 × 300 mL) by sonication at room temperature. The solvent was evaporated under reduced pressure at 40 °C to yield 0.5 g (2.5%) of a viscous syrup. Addition of MeOH (10 mL) gave a yellowish precipitate identified as genkwanin. After filtering, the filtrate was passed through a short column packed with DIAION HP20SS resin. This was eluted with MeOH to give 163.5 mg of a light yellow semisolid after concentration. The semisolid was purified further by semipreparative HPLC (65% aqueous MeOH, flow rate: 2 mL/min) to afford compounds 1–6: 1 (t_{R} = 38.1 min, 1.3 mg), 2 (t_{R} = 39.6 min, 1.4 mg), 3 (t_{R} = 35.7 min, 0.8 mg), 4 (t_{R} = 47.5 min, 1.5 mg), 5/6 (t_{R} = 18.3 min, 1.0 mg).

Preleosibirone A (1): white powder; $[\alpha]_{\text{D}}^{25}$ –23.3 (c 0.09, MeOH); IR (KBr) ν_{max} 3434, 2929, 2877, 1713, 1640, 1616, 1457, 1367, 1250 cm^{-1} ; ^1H and ^{13}C NMR data, Tables 1 and 2; HRESIMS m/z 415.2086 $[\text{M} + \text{Na}]^+$ (calcd for C₂₂H₃₂O₆Na 415.2096).

13-*epi*-Preleosibirone A (2): white powder; $[\alpha]_{\text{D}}^{25}$ –19.0 (c 0.11, MeOH); IR (KBr) ν_{max} 2942, 2881, 1717, 1612, 1461, 1376, 1258, 1140, 1079 cm^{-1} ; ^1H and ^{13}C NMR data, Tables 1 and 2; HRESIMS m/z 415.2086 $[\text{M} + \text{Na}]^+$ (calcd for C₂₂H₃₂O₆Na 415.2096).

Isopreleosibirone A (3): white powder; $[\alpha]_{\text{D}}^{25}$ –9.0 (c 0.20, MeOH); IR (KBr) ν_{max} 3454, 2978, 2942, 2893, 1730, 1607, 1469, 1372, 1245, 1144 cm^{-1} ; ^1H and ^{13}C NMR data, Tables 1 and 2; HRESIMS m/z 415.2089 $[\text{M} + \text{Na}]^+$ (calcd for C₂₂H₃₂O₆Na 415.2096).

Leosibirone A (4): white powder; $[\alpha]_{\text{D}}^{25}$ –20.0 (c 0.10, MeOH); IR (KBr) ν_{max} 3454, 2967, 2932, 2882, 1716, 1466, 1381, 1264, 1159 cm^{-1} ; ^1H and ^{13}C NMR data, Tables 1 and 2; HRESIMS m/z 415.2072 $[\text{M} + \text{Na}]^+$ (calcd for C₂₂H₃₂O₆Na 415.2096).

Leosibirone B (5) and 15-*epi*-Leosibirone B (6): white solid; $[\alpha]_{\text{D}}^{20}$ –10.0 (c 0.18, MeOH); IR (KBr) ν_{max} 2944, 2877, 1731, 1710, 1448, 1375, 1244, 1022 cm^{-1} ; ^1H and ^{13}C NMR data, Tables 1 and 2; HRESIMS m/z 433.2197 $[\text{M} + \text{Na}]^+$ (calcd for C₂₂H₃₄O₇Na 433.2202).

X-ray Crystallography. The crystal structures of a disordered cocrystal of 1 and 2, of 5, and of a disordered cocrystal of 5 and 6 were determined, using data collected at $T = 90$ K with Cu K α radiation ($\lambda = 1.54178$ Å) on a Bruker APEX-II CCD diffractometer, equipped with an Oxford Cryostream cooler. Structures were solved using the program SHELXS-97²³ and refined anisotropically by full-matrix least-squares on F^2 using SHELXL-97.²³ For each disordered cocrystal, the populations of the two components were refined and constrained to sum to unity. The absolute configurations were determined by refinement of the Flack²⁴ parameter based on resonant scattering of the light atoms and computation of the Hooft parameter,²⁵ in all cases yielding a probability of 1.000 that the reported configuration is correct. Crystal data: 1/2 cocrystal, C₂₂H₃₂O₆, $M_r = 392.48$, monoclinic space group $P2_1$, $a = 12.1972(10)$ Å, $b = 8.9304(5)$ Å, $c = 18.0154(14)$ Å, $\beta = 90.176(5)^\circ$, $V = 1962.3(2)$ Å³, $Z = 4$, $D_x = 1.328$ Mg m⁻³, $\theta_{\text{max}} = 68.1^\circ$, $R = 0.028$ for 6870 data and 553 refined parameters. There are two independent molecules in the asymmetric unit, both of which exhibit disorder, with partial occupancy of the two epimers. Refinement of populations led to 11.1(7)% 1; 88.9(7)% 2 for one molecule and 0.368(6)% 1; 63.2(6)% 2 for the other. Thus, the overall population of the two epimers in the crystal is 23.9(5)% 1 and 76.1(5)% 2. The Flack parameter is 0.02(10) and the Hooft parameter is 0.04(4) for 3106 Bijvoet pairs. 5: C₂₂H₃₄O₇, $M_r = 410.49$, orthorhombic space group $P2_12_12_1$, $a = 11.373(3)$ Å, $b = 11.703(2)$ Å, $c = 15.508(3)$ Å, $V = 2064.1(8)$ Å³, $Z = 4$, $D_x = 1.321$ Mg m⁻³, $\theta_{\text{max}} = 58.3^\circ$, $R = 0.052$ for 2873 data and 270 refined parameters, Hooft parameter 0.0(2) for 1210 Bijvoet pairs. 5/6: cocrystal, C₂₂H₃₄O₇, $M_r = 410.49$, orthorhombic space group $P2_12_12_1$, $a = 11.3687(9)$ Å, $b = 11.7108(9)$ Å, $c = 15.5053(11)$ Å, $V = 2064.3(3)$ Å³, $Z = 4$, $D_x = 1.321$ Mg m⁻³, $\theta_{\text{max}} = 68.3^\circ$, $R = 0.031$ for 3706 data and 281 refined parameters. Populations refined to 78.1(4)% 5 and 21.9(4)% 6. The Flack parameter is 0.09(15) and the Hooft parameter is 0.08(4) for 1543 Bijvoet pairs. Crystallographic data for the compounds 1/2 (CCDC 795187), 5 (CCDC 795188), and 5/6 (CCDC 796447) have been deposited with the Cambridge Crystallographic Data Centre. They are available free of charge upon request via the Internet at <http://www.ccdc.cam.ac.uk/>.

ASSOCIATED CONTENT

Supporting Information. 1D and 2D NMR spectra of compounds 1–6. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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