A New Caprylic Alcohol Glycoside from *Circaea lutetiana* ssp. *canadensis*

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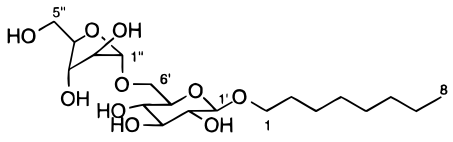
A new alcohol glycoside, 1-octyl α-D-arabinofuranosyl-(1→6)-β-D-glucopyranoside (**1**), four known compounds including three phenolics, isovitexin, astragalin, and methyl gallate 3-*O*-β-D-(6′-*O*-galloyl)-glucopyranoside (**2**), and the terpene glucoside icariside B_2 (**3**) have been isolated from the aerial parts of *Circaea lutetiana* ssp. *canadensis.*

Circaea lutetiana L. ssp. *canadensis* (L.) Asch. & Mag. (Onagraceae) is a perennial plant[2] that has been used in the treatment of colic, dysuria, and dysmenorrhea in Chinese folk medicine.[3] We report here the isolation and structure elucidation of the novel compound 1-octyl α-D-arabinofuranosyl-(1→6)-β-D-glucopyranoside (**1**), along with four known compounds, isovitexin, astragalin, methyl gallate 3-*O*-β-D-(6′-*O*-galloyl)-glucopyranoside (**2**), and icariside B_2 (**3**) from this plant.

A *n*-BuOH-soluble extract of *C. lutetiana* was purified as described in the Experimental Section to give five pure compounds. The flavonoid glycosides isovitexin and astragalin were identified by comparison of their spectral data with reported data.[4,5] Similarly, MS, ^{1}H- and ^{13}C-NMR, TOCSY, DEPT, HETCOR, and HMBC spectra in CD_3OD for compounds **2** and **3** indicated their structures to be methyl gallate 3-*O*-β-D-(6′-*O*-galloyl)-glucopyranoside (**2**) and icariside B_2 (**3**). These assignments were confirmed by re-recording their NMR spectra in the same solvents as in the literature and by direct comparison of the data with reported values.[6,7]



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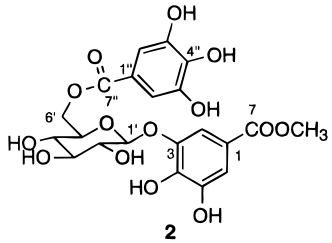

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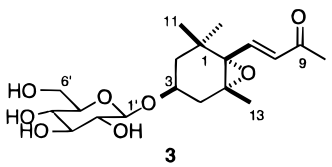

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Compound **1** was obtained as a colorless wax-like semisolid, $[\alpha]_D$ −75.0°. Its positive ion HRFABMS exhibited a peak at *m/z* 447.22091 $[M + Na]^+$, compatible with the molecular formula $C_{19}H_{36}O_{10}$. Its ^{1}H-NMR spectrum (Table 1) revealed the presence of two anomeric protons at δ_H 4.95 and 4.24. The disturbed triplet methyl signal at δ_H 0.89 (3H, J = 6.9 Hz) with the signals at δ_H 1.30 (8H, m), 1.36 (2H, m), and 1.63 (2H, m) indicated the presence of a saturated long-chain hydrocarbon. The cross peaks in a ^{1}H−^{1}H COSY spectrum for the oxygenated methylene protons at δ_H 3.85 and 3.52 (each 1 H, ddd, J = 10.2, 9.5, 2.7 Hz) correlated with the methylene protons at δ_H 1.63, and the molecular formula suggested the presence of 1-octanol as the aglycon. Acid hydrolysis yielded D-glucose and D-arabinose (identified by ^{1}H NMR, $[\alpha]_D$, and TLC) and 1-octanol (identified by TLC).

The sequence of the sugar part could be determined by the MS fragmentation peak at *m/z* 293 (M^+ − arabinose), which indicated that the D-arabinose moiety was the terminal sugar. The ^{13}C-NMR chemical shift of C-6′ in glucose at δ_C 68.06 ppm indicated glycosylation at this position, and the long-range correlation between δ_H 4.95 ppm (1H, d, J = 1.3 Hz, anomeric proton of D-arabinose) and δ_C 68.08 ppm ($C_{6'}$ of glucose) in the HMBC spectrum of **1** confirmed the interglycosidic linkage to be arabinose-(1→6)-glucose. The coupling constants of the anomeric protons in arabinose (J = 1.3 Hz) and glucose (J = 7.8 Hz) showed these sugars to have the α and β configurations, respectively, and the ^{13}C-NMR shifts of the arabinose carbons indicated that arabinose was in the furanose ring form. Based on these data, **1** is 1-octyl α-D-arabinofuranosyl-(1→6)-β-D-glucopyranoside. Interestingly, the related compound 1-octyl α-D-arabinopyranosyl-(1→6)-β-D-glucopyranoside has recently been reported from the Chinese plant *Rhodiola quadrifolia.*[8]

Experimental Section

General Experimental Procedures. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were taken with a Perkin-Elmer Model 241 polarimeter. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Unity 400 spectrometer at 400 and 100.57 MHz, respectively, with TMS as internal standard. ^{1}H−^{1}H COSY, DEPT, HETCOR, and HMBC NMR experiments were performed on the same spectrometer, using standard Varian pulse sequences. Flash chromatography was performed using Si gel Merck G60 (230−400 mesh) and Sorbsil RP-18 (Phase Separations Ltd). Sephadex LH-20 (Sigma) was employed for gel permeation chromatography.

Plant Material. Aerial parts of *C. lutetiana* ssp. *canadensis* were collected from a shaded location late

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Table 1. NMR Data for **1** (CD_3OD)

position	δ_C[a]	δ_H	HMBC
1	71.1 (CH_2)	3.85 (1 H, ddd, 10.2, 9.5, 2.7)	C-2, C-3, C-1′
		3.52 (1 H, ddd, 10.2, 9.5, 2.7)	C-2, C-3, C-1′
2	30.8 (CH_2)	1.63 (2 H, m)	C-1, C-3, C-4
3	27.1 (CH_2)	1.36 (2 H, m)	C-2, C-4, C-5
4	30.6 (CH_2)	1.26−1.34 (8 H, m)	C-3, C-4, C-5, C-6
5	30.4 (CH_2)		
6	33.0 (CH_2)		
7	23.7 (CH_2)		
8	14.4 (CH_3)	0.89 (3 H, t, 6.9)	C-6, C-7
1′	104.4 (CH)	4.24 (1 H, d, 7.8)	C-1, C-2′, C-3′
2′	75.1 (CH)	3.15 (1 H, dd, 8.9, 7.8)	C-1′. C-3′
3′	78.0 (CH)	3.32 (1 H, m)	C-2′, C-4′
4′	72.0 (CH)	3.28 (1 H, m)	C-3′, C-5′, c-6′
5′	76.7 (CH)	3.42 (1 H, ddd, 9.5, 6.0, 2.4)	C-4′, C-6′
6′	68.1 (CH_2)	4.00 (1 H, dd, 11.1, 2.4)	C-4′, C-5′, C-1″
		3.60 (1 H, dd, 11.0, 5.9)	
1″	109.9 (CH)	4.95 (1 H, d, 1.3)	C-6′, C-2″, C-3″
2″	85.9 (CH)	3.98 (1 H, dd, 3.3, 1.5)	C-3″
3″	78.9 (CH)	3.81 (1 H, dd, 5.8, 3.3)	C-5″
4″	83.2 (CH)	3.96 (1 H, ddd, 5.8, 5.8, 3.4)	C-5″
5″	63.1 (CH_2)	3.73 (1 H, dd, 11.7, 3.3)	C-3″
		3.63 (1 H, dd, 11.7, 5.5)	

[a] Carbon type deduced from a DEPT experiment ; assignments based on $^1H-^{13}C$ HETCOR and HMBC data.

in the day during their flowering period (July 1995) in Virginia, as populations observed in this area were homogeneous. The plant was authenticated by Mr. T. F. Wieboldt of the Massey Herbarium, Virginia Polytechnic Institute and State University. The collected plant material was immediately chopped and extracted as described below.[9]

Extraction and Isolation. Chopped aerial parts (4.0 kg) of freshly collected *C. lutetiana* ssp. *canadensis* were extracted with MeOH. The MeOH extract (30 g) was partitioned between $CHCl_3$ and H_2O, and then between *n*-BuOH and H_2O, to yield $CHCl_3$, *n*-BuOH, and aqueous extracts. The *n*-BuOH extract (5.7 g) was subjected to gel permeation chromatography on Sephadex LH-20 with elution by MeOH to yield a total of six fractions designated LH1−LH6. Fraction LH2 (740 mg) was chromatographed on a column of Si gel ($CHCl_3$−MeOH−H_2O, 4:1:0.1 → $CHCl_3$−MeOH, 1:1) to obtain five fractions SA1−SA5. Fraction SA2 (21 mg) was further subjected to Si gel column chromatography (EtOAc−MeOH, 9:1), followed by a Si gel column chromatography ($CHCl_3$−*i*PrOH, 7:3) to yield icariside B_2 (**3**, 4.0 mg). Fraction SA3 (139 mg) was subjected to Si gel column chromatography (EtOAc−MeOH, 9:1 → 4:1) to yield three fractions SB1−SB3. Fraction SB1 was subjected to Si gel column chromatography (EtOAc−MeOH, 9:1), followed by a second Si gel column chromatography ($CHCl_3$−*i*PrOH, 7:3), followed by reversed-phase C-18 column chromatography (MeOH−H_2O, 1:1) to yield 1-octyl α-D-arabinofuranosyl-(1→6)-*β*-D-glucopyranoside (**1**, 20.0 mg); the remaining components of the fraction were not identified. Fraction LH3 (3.0 g) was subjected to flash chromatography on Si gel ($CHCl_3$−MeOH, 7:3 → 1:1) to give the four fractions SC1−SC4. Fraction SC1 (700 mg) was purified by Si gel column chromatography ($CHCl_3$−MeOH−H_2O, 4:1:0.1 → 7:3:0.3) to yield the six fractions SD1−SD6. Fraction SD3 (61 mg) was further purified by reversed-phase C-18 column chromatography (MeOH−H_2O, 1:1) to yield astragalin (34 mg). Fraction SD6 (72 mg) was purified by reversed-phase C-18 preparative TLC (MeOH−H_2O, 1:1) to yield methyl gallate 3-*O*-*β*-D-(6′-*O*-galloyl)-glucopyranoside (**2**, 20.6 mg). Fraction SC2 (1.18 g) was also purified by Si gel column chromatography (EtOAc−MeOH, 9:1 → 7:3) to give fractions SE1−SE4. Fraction SE2 (655 mg) was purified by reversed-phase C-18 column chromatography (MeOH−H_2O, 1:1) and a final Si gel column chromatography (EtOAc−MeOH, 4:1) to afford isovitexin (360 mg).

1-Octyl α-D-arabinofuranosyl-(1→6)-*β*-D-glucopyranoside (1): colorless wax-like semisolid: $[\alpha]^{26}_D$ −75.0° (*c* 0.60, MeOH) ; FABMS (positive mode) *m*/*z* $[M + H]^+$ 425 (25), 325 (12), 295 (100), 293 (100), 163 (18), 133 (73); HRFABMS (positive mode) *m*/*z* $[M + Na]^+$ 447.2209 (calcd for $C_{19}H_{38}O_{10}$ 477.2206); ^1H and ^{13}C NMR (CD_3OD), Table 1.

Acid Hydrolysis of 1. Compound **1** (8 mg) was refluxed with 3% H_2SO_4 for 3 h. The reaction mixture was diluted with H_2O and neutralized with $BaCO_3$, then filtered. The filtrate showed the presence of 1-octanol (identified by TLC comparison using hexane−Me_2CO, 9:1, detection with vanillin−H_2SO_4) and arabinose and glucose (identified by TLC comparison using $CHCl_3$−MeOH−H_2O, 7:3:0.3, detection with anisaldehyde−H_2SO_4). The filtrate was evaporated and subjected to flash chromatography on Si gel and eluted with $CHCl_3$−MeOH−H_2O (7:3:0.3) to yield two sugars. One sugar (2.9 mg) showed identical $[\alpha]_D$ −117.2° (*c* 0.14, H_2O), R_f value (0.19) on TLC (SiO_2, $CHCl_3$−MeOH−H_2O), and ^1H-NMR spectrum with D-arabinose, and the other (3.7 mg) showed identical $[\alpha]_D$ 40.5° (*c* 0.18, H_2O), R_f value (0.10), and ^1H-NMR spectrum with D-glucose. Finally, the identities of the sugars were confirmed by comparing their ^1H-NMR spectra with those of standard samples of D-arabinose and D-glucose.

Methyl gallate 3-*O*-*β*-D-(6′-*O*-galloyl)-glucopyranoside (2): pale yellow amorphous powder; mp 177−178 °C [lit.[6] 178−180 °C]; $[\alpha]^{26}_D$ −61.8° (*c* 0.94, MeOH); identified by comparison of FABMS, ^1H-, and ^{13}C-NMR data with those reported (Me_2CO-d_6 + D_2O).[6]

Icariside B_2 (3): colorless amorphous powder; mp 168−170 °C [lit.[7] 172.5−174 °C] ; $[\alpha]^{26}_D$ −95.5° (*c* 0.20, MeOH) [lit.[7] −102.1° (MeOH)].[10] Identified by comparison of FABMS, ^1H- and ^{13}C-NMR data with those reported (C_5D_5N).[7]

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References and Notes

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(9) A referee has raised the concern that the compounds reported in this paper could have been produced by microbes on storage of the plant material. This does not appear to be likely, however, since the plant material was extracted within an hour or two of its collection, and there was thus not enough time for a significant post-harvest growth of epiphytes or endophytes.
(10) The slight differences between the literature data and our mp and rotation data for icariside B_2 are most probably due to the fact that our sample was a small one and could not be recrystallized to constant mp.

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