A New Derivative of Glucose and 2-*C*-Methyl-D-erythritol from *Ferula sinaica*

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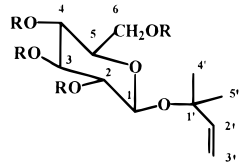
A new glucose derivative (**1**) and 2-*C*-methyl-D-erythritol (**2**) were isolated from the leaves of *Ferula sinaica.* The two structures were elucidated by highfield NMR spectroscopy, and that of **1** was confirmed by X-ray diffraction analysis.

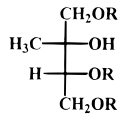
Ferula sinaica L. (Apiaceae) is widespread in the Sinai Desert, Egypt, and the resin from its roots is used in Egyptian folk medicine for the treatment of hysteria, and as a stomachic, and as a vermifuge.[1] Earlier investigations of the roots revealed the presence of daucanes, sesquiterpene coumarins, and monoterpenes.[2−4] We report here a new glucose derivative, isolated from the leaves of this species, namely, 1,1-dimethylprop-2-enyl 1-*O*-*β*-D-glucopyranoside (**1**) and 2-*C*-methyl-D-erythritol (**2**). This is the first report of the latter compound from the genus *Ferula*. We also detected in the leaves of *F. sinaica* lanceroldiol *p*-hydroxybenzoate,[3] jaeschkeanadiol *p*-hydroxybenzoate,[2] the *p*-hydroxybenzoyl ester of ferutiol,[2] and 4-*β*-hydroxy-6α-[(*p*-hydroxybenzoyl)oxy]-10α-(angeloxy)dauc-7-ene,[2] all of which were previously reported from the roots of this species.

The HRCIMS of **1** revealed a $[M + H]^+$ peak at *m/z* 249.1322 for $C_{11}H_{20}O_6$, and the ^{1}H-NMR spectrum gave signals in accord with the presence of a *β*-D-glucopyranoside substituent. The anomeric proton of the glucosyl moiety appeared as a doublet at *δ* 4.37, which was found to be coupled to a doublet of doublets at *δ* 3.08 for H-2 by ^{1}H−^{1}H COSY NMR. The other protons could be assigned by the same experiment (Table 1). The side-chain moiety was shown by ^{13}C-NMR and DEPT data analysis to contain five carbons, including a quatenary carbon, two methyls, and two olefinics. The ^{1}H-NMR spectrum exhibited two sharp methyl singlets at *δ* 1.24 and 1.27, a doublet of doublets at *δ* 5.85 for an olefinic proton, and two broad doublets at *δ* 5.18 and 5.12 for a methine group, in accord with the proposed structure of 1,1-dimethylprop-2-enyl 1-*O*-*β*-glucopyranoside. The ^{1}H-NMR spectral data of the tetracetate of **1** showed differences from those of the parent compound (Table 1); because signals for all ring protons shifted downfield except for the signal of H-1, it was concluded that the side chain must be located at C-1.

In order to confirm the structure of **1** as a new natural product, a crystal of the tetracetate (**1a**) (Figure 1) was analyzed by X-ray diffraction (see Experimental Section).

Compound **2** was isolated as its triacetyl derivative (**2a**) after acetylation of the isolated mixture. The ^{13}C-NMR spectrum of **2a** showed, in addition to the additional acetyl carbon atoms, only five carbons, in accord with a *C*-methyl-D-erythritol skeleton. The proton sequence was established by ^{1}H−^{1}H-COSY, and the carbons were assigned by hetero-COSY and DEPT experiments. The structure of **2a** was supported by the HRCIMS, which exhibited a molecular ion peak at *m/z* 263.1126 for $C_{11}H_8O_7$. The spectral data of **2a** were identical to those published for 2-*C*-methyl-1,3,4-triacetyl-D-erythritol.[5]





Experimental Section

Plant Material. Leaves of *F. sinaica* were collected from North Sinai, Egypt, in March 1987, by one of us (A.A.A.). A voucher specimen (AAA 110) is deposited in the Department of Botany, El-Minia University, Egypt.

Extraction and Isolation. Air-dried leaves of *F. sinaica* (500 g) were extracted with MeOH−CH_2Cl_2 (1:1). The extract was defatted and chromatographed on a Si gel column packed into petroleum ether (bp 40−60 °C) and eluted with a petroleum ether−Et_2O step

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Table 1. ^{1}H-NMR Spectral Data (500 MHz) for Compound **1**

proton(s)	**1**[a]	**1a**[b]	**1a**[c]
H-1	4.37 d (8)	4.48 d (8)	4.39 d (8)
H-2	3.08 dd (9.5, 8.0)	4.91 dd (9.5, 8.0)	5.18 dd (9.5, 8.0)
H-3	3.34 dd (9.5, 8.5)	4.93 dd (9.5, 8.5)	5.20 dd (9.5, 8.5)
H-4	3.22 t (8.5, 8.5)	5.15 t (8.5, 8.5)	5.31 t (8.5, 8.5)
H-5	3.26 ddd (8.5, 6, 2.5)	3.56 ddd (8.5, 6, 2.5)	3.15 ddd (8.5, 6, 2.5)
H-6_a	3.45 dd (12.5, 2.5)	4.05 dd (12.5, 2.5)	3.98 dd (12.5, 2.5)
H-6_b	3.74 dd (12.5, 2.5)	4.14 dd (12.5, 2.5)	4.16 dd (12.5, 2.5)
H-2′	5.85 dd (17.5,11.0)	5.80 dd (17.5,11.0)	5.82 dd (17.5,11.0)
H-3′-trans	5.18 d (17.5)	5.15 d (17.5)	5.10 d (17.5)
H-3′-cis	5.12 d (11.0)	5.16 d (11.0)	4.99 d (11.0)
H-4′	1.24 s	1.23 s	1.19 s
H-5′	1.27 s	1.26 s	1.21 s
AcO		1.98, 1.99	1.69, 1.71
		2.00, 2.02	1.76

[a] In D_2O. [b] In $CDCl_3$. [c] In C_6D_6.

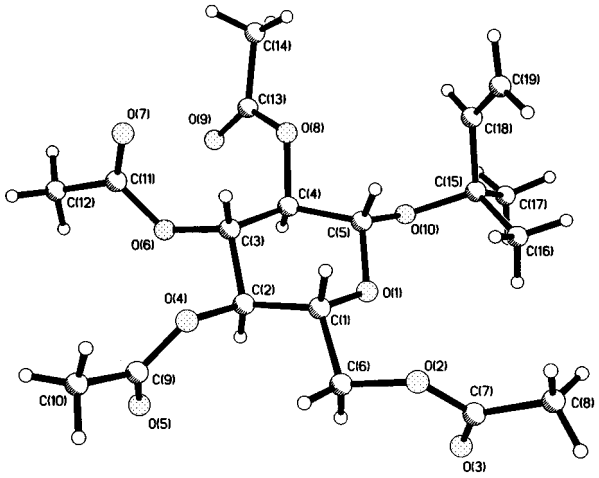

Figure 1. Stereoviews of compound **1a**.

gradient. The fractions eluted with petroleum ether−Et_2O (1:1 and 75:25) were combined and further chromatographed on a Sephadex LH-20 column with an initial solvent of Et_2O−CH_2Cl_2−MeOH (7:4:0.5) to give 22 mg of lanceroldiol *p*-hydroxybenzoate, 7 mg of jaeschkeanadiol *p*-hydroxybenzoate, 13 mg of *p*-hydroxybenzoyl ester of ferutiol, and 4 mg of 4-*β*-hydroxy-6α-[(*p*-hydroxybenzoyl)oxy]-10α-(angeloxy)dauc-7-ene. The fraction eluted with Et_2O yielded 35 mg of impure **2** and was acetylated (Ac_2O, 2 h, 70 °C) to give 25 mg of **2a**. The fraction eluted with Et_2O−MeOH (90:10) gave 60 mg of a crude extract and was purified over a Sephadex LH-20 column using Et_2O−CH_2Cl_2−MeOH (7:4:1) to give 50 mg of **1**.

1,1-Dimethylprop-2-enyl 1-*O*-*β*-D-glucopyranoside (1): obtained as a colorless oil; $[\alpha]_D$ −0.33° (*c* 0.0265, EtOH); HRCIMS (70 eV) *m/z* $[M + H]^+$ 249.13225 (40) ($C_{11}H_{21}O_6$, calcd 249.13381), $[M - H_2O]^+$ 231.12322 (100), 163.06158 $[M - H_2O - C_5H_9]^+$ (90); NMR data are given in Tables 1 and 2.

1,1-Dimethylprop-2-enyl 2,3,4-triacetyl-1-*O*-*β*-D-glucopyranoside) (1a): obtained as white crystals by acetylation of **1**; $[\alpha]_D$ −0.14° (*c* 0.0135, EtOH); HRCI MS *m/z* $[M + H]^+$ 417.17493 (10) ($C_{19}H_{29}O_{10}$, calcd 417.17607), $[M - C_5H_{10}]^+$ 331.10237 (100).

X-ray Analysis of 1a. A colorless needle was mounted on a glass fiber at room temperature. Preliminary examination and data collection were performed on a Rigaku AFC5 (oriented graphite monochromator; Mo Kα radiation) at 193(2) K. Cell parameters were calculated from the least-squares fitting for 25 high-angle reflections ($2\theta \geq 15$ deg). Omega scans for several intense reflections indicated acceptable crystal quality.

Data were collected from 2.96° to 47.10° 2θ at 193(2) K. The scan width for data collections was 1.5 + 0.3 tan(θ)° in omega with a variable scan rate between 8 and 16 deg/min. Weak reflections were rescanned (maximum of two rescans), and the counts for each scan were accumulated. The three standards, collected every 150 reflections, showed no significant trends. Background measurements were acquired by stationary crystal and stationary counter techniques at the begining and the end of each scan for 1/2 the total scan time.

Lorentz and polarization corrections were applied to 1944 reflections. A total of 1944 reflections was used in further calculations. Systemic absences in the data indicated the choice of the space groups $P2_12_12_1$ with cell dimensions a = 5.802(3) Å, b = 1.8156(6) Å, c = 21.028(4) Å. The structure was solved by direct methods.[6] Full-matrix least-squares anisotropic refinement for all non-hydrogen atoms yielded $R(F)$ = 0.059 and $wR(F^2)$ = 0.119 at convergence.[7] An extinction correction was applied.[8] Hydrogen atoms were placed in idealized positions with isotropic thermal parameters fixed at 0.08 Å^3. Neutral atom scattering factors and anomalous scattering factors were taken from the *International Tables for X-ray Crystallography*, *Vol. C*.

Table 2. ^{13}C -NMR Spectral Data (125 MHz) for Compound **1a**

carbon	**1**[a]	**1a**[b]
C-1	97.1	95.9
C-2	73.0	72.0
C-3	75.6	71.3
C-4	69.7	68.6
C-5	75.4	71.2
C-6	60.7	62.2
C-1′	79.0	78.4
C-2′	142.4	142.6
C-3′	114.4	114.6
C-4′	24.9	25.8
C5″	26.1	26.8
AcO		20.5, 20.4
		20.4, 20.3
		169.0, 169.3
		170.2, 170.5

[a] In D_2O and assigned by ^{1}H−^{13}C COSY. [b] In $CDCl_3$.

2-*C*-Methyl-1,3,4-triacetyl-D-erythritol (2a): $[\alpha]_D$ +0.25° (*c* 0.0166, EtOH); HRCIMS *m/z* $[M + H]^+$ 263.11265 (85) ($C_{11}H_8O_7$, calcd 263.11307), $[M - H_2O]^+$ 245.10157 (73), $[M - CH_3COOH]^+$ 203.09145 (100): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.15 (1H, dd, J = 8.5, 2.5 Hz, H-3), 4.51 (1H, dd, J = 12.0, 2.5 Hz, H-4), 4.16 (1H, dd,

J = 12.0, 8.5 Hz, H-4′), 4.15 (1H, d, J = 11.5 Hz, H-1), 3.85 (1H, d, J = 11.5 Hz, H-1′), 1.22 (3H, s, H-5); ^{1}H NMR (C_6D_6) δ 5.26 (1H, dd, J = 8.5, 2.5 Hz, H-3), 4.51 (1H, dd, J = 12.0, 2.5 Hz, H-4), 4.12 (1H, dd, J = 12.0, 8.5 Hz, H-4′), 4.11 (1H, d, J = 11.5 Hz, H-1), 3.81 (1H, d, J = 11.5 Hz, H-1′), 1.10 (3H, s, H-5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 170.3, 169.6 (C═O, acyl groups), 72.0 (C-3), 71.1 (C-2), 67.4 (C-1), 62.1 (C-4), 20.0, 19.9, 19.2 (Me of 3 acyl groups), 18.9 (C-5).

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