Iridoids from the Rhizomes and Roots of *Valeriana jatamansi*

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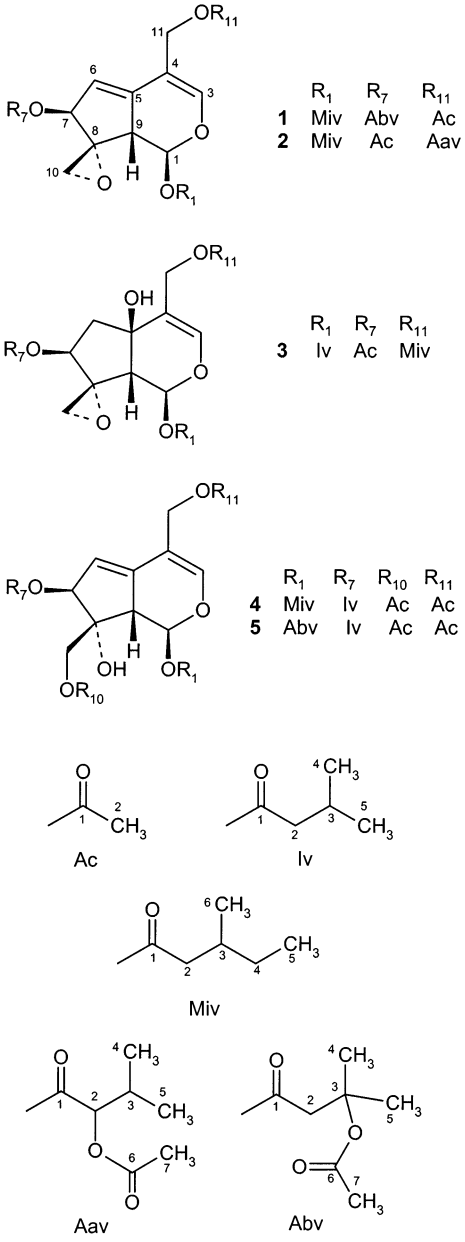
Five new iridoids, 1-homoacevaltrate (**1**), 1-homoisoacevaltrate (**2**), 11-homohydroxyldihydrovaltrate (**3**), 10-acetoxy-1-homovaltrate hydrin (**4**), and 10-acetoxy-1-acevaltrate hydrin (**5**), along with 10 known analogues, were isolated from the rhizomes and roots of *Valeriana jatamansi*. Structural elucidation was based on spectroscopic data interpretation.

The genus *Valeriana*, with about 200 species, belongs to the family Valerianaceae and has a distribution throughout the world. The roots and rhizomes of some *Valeriana* species have been used in traditional medicine as a sedative for centuries. A large number of species in the genus *Valeriana* have been studied so far,[1] with many iridoids associated with the sedative activity of *Valeriana* preparatives having been isolated from the roots and rhizomes of species in this genus.[2−6]

Valeriana jatamansi Jones, an annual herb distributed in the southwestern area of the People's Republic of China, is known in Chinese folk medicine to have tranquilizing hypnotic and antiviral activities.[7] Previous phytochemical studies on this plant revealed the presence of the sesquiterpenoids valerianananoids A−C and an essential oil.[7,8] However, no previous investigation has been reported on the iridoid constituents of this plant. The present study deals with the isolation and structural elucidation of five new iridoids (**1**−**5**), along with 10 known compounds, from the rhizomes and roots of this plant.

The dried roots and rhizomes of *V. jatamansi* were extracted with petroleum ether. The petroleum ether extract was separated by a combination of chromatographic procedures to afford five new iridoids (**1**−**5**) and 10 known compounds. The structures of the known compounds were identified as valtrate,[6,9,10] isovaltrate,[5,6,9] homovaltrate,[6,9] acevaltrate,[6,9,11] dihomovaltrate,[5,9] didrovaltrate,[6,9,11] 1-homodidrovaltrate,[9] acetylhydroxyldihydrovaltrate,[6,9] 10-isovaleroxyvaltrate hydrin,[11−14] and 10-isovaleroxydiavaltrate hydrin[12,13] by comparison of their spectral data with those reported in the literature.

Compound **1** appeared as a colorless oil with $[\alpha]^{24}_D$ +175.9° (*c* 0.01, MeOH), whose molecular formula, $C_{25}H_{34}O_{10}$, was inferred by HRESIMS ($[M - H]^-$ *m*/*z* 493.2078). Its ^{13}C NMR and DEPT spectra showed 25 resonance lines, indicating six methyls, five methylenes, six methines, and eight quaternary carbons. The IR spectrum of **1** showed two dominant ester bands at 1765 and 1738 cm^{-1}. Analysis of the overall NMR spectral data revealed the presence of an iridoid skeleton with ester units.[5,6] The signals at δ 5.98 (1H, d, J = 10.0 Hz) and 92.6 (CH), respectively, were assignable to H-1 and C-1. The chemical shifts of two olefinic methine carbons at δ 148.6 and 118.6 and of olefinic quaternary carbons at δ 108.5 and 141.1, respectively, were assigned as C-3, C-6, C-4, and C-5. The quaternary carbon at δ 64.2 (C-8) and the methylene carbon at δ 48.0 (C-10) were characteristic for an epoxide ring at C-8 and C-10, corresponding to a valtrate-type iridoid.[5,6]



A methyl singlet, which appeared at δ 2.06 in the ^1H NMR spectrum of **1**, was assigned to the methyl protons

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Table 1. ^{1}H NMR Data of Compounds **1**−**5** [400 MHz, δ ppm, (J) Hz, $CDCl_3$][a]

position	1	2	3	4	5
1	5.98 (1H, d, 10.0)	5.99 (1H, d, 10.0)	6.08 (1H, d, 2.0)	6.18 (1H, d, 10.0)	6.20 (1H, d, 10.1)
3	6.70 (1H, s)	6.68 (1H, s)	6.68 (1H, s)	6.67 (1H, s)	6.68 (1H, s)
6	5.85 (1H, dd, 2.4, 2.6)	5.87 (1H, dd, 2.5, 2.6)	1.99 (1H, dd, 10.0, 13.0) 2.79 (1H, dd, 7.0, 13.0)	5.76 (1H, dd, 2.5, 3.2)	5.74 (1H, dd, 2.6, 3.1)
7	5.38 (1H, d, 2.6)	5.37 (1H, d, 2.6)	4.87 (1H, dd, 7.0, 10.0)	5.38 (1H, d, 2.5)	5.37 (1H, d, 2.6)
9	3.44 (1H, dd, 2.4, 10.0)	3.44 (1H, dd, 2.5, 10.0)	2.91 (1H, d, 2.0)	2.93 (1H, dd, 2.5, 10.0)	2.89 (1H, dd, 2.6, 10.1)
10	2.91, 3.02 (2H, [AB], 5.0)	2.90, 3.05 (2H, [AB], 5.0)	2.82, 3.12 (2H, [AB], 5.0)	4.27, 4.71 (2H, [AB], 11.4)	4.25, 4.68 (2H, [AB], 11.1)
11	4.66, 4.76 (2H, [AB], 12.4)	4.66, 4.77 (2H, [AB], 12.1)	4.72, 4.90 (2H, [AB], 12.6)	4.61, 4.71 (2H, [AB], 12.4)	4.60, 4.71 (2H, [AB], 12.5)
R_1 2	2.26 (2H, m)	2.26 (2H, m)	2.24 (2H, m)	2.24 (2H, m)	2.80, 3.04 (2H, [AB], 14.0)
3	2.11 (1H, m)	2.12 (1H, m)	2.11 (1H, m)	2.10 (1H, m)	
4	1.24 (2H, m)	1.24 (2H, m)	0.96 (3H, t, 6.6)	1.26 (2H, m)	1.52 (3H, s)[b]
5	0.94 (3H, t, 6.0)	0.93 (3H, t, 6.2)	0.96 (3H, t, 6.6)	0.93 (3H, t, 6.0)	1.53 (3H, s)[b]
6	1.08 (3H, d, 6.1)	1.09 (3H, d, 5.9)		1.07 (3H, d, 6.2)	
7					1.98 (3H, s)
R_7 2	2.81, 3.04 (2H, [AB], 14.2)	2.06 (3H, s)	2.06 (3H, s)	2.30 (2H, m)	2.31 (2H, m)
3				2.09 (1H, m)	2.09 (1H, m)
4	1.50 (3H, s)[b]			0.96 (3H, d, 6.4)[b]	0.97 (3H, d, 6.3)[c]
5	1.53 (3H, s)[b]			0.98 (3H, d, 6.4)[b]	0.98 (3H, d, 6.3)[c]
7	1.95 (3H, s)				
R_{10} 2				2.06 (3H, s)	2.06 (3H, s)
R_{11} 2	2.06 (3H, s)	4.80 (1H, d, 4.7)	2.25 (2H, m)	2.06 (3H, s)	2.06 (3H, s)
3		2.20 (1H, m)	2.10 (1H, m)		
4		0.98 (3H, d, 6.6)[b]	1.26 (2H, m)		
5		1.00 (3H, d, 6.6)[b]	0.93 (3H, t, 6.1)		
6			1.07 (3H, d, 6.0)		
7		2.10 (3H, s)			

[a] All assignments based on extensive 1D and 2D NMR measurements (DEPT, DQF-COSY, TOCSY, NOESY, HMQC, and HMBC). [b,c] Assignments may be interchangeable in each column.

of an acetate residue. A ^{13}C NMR signal at δ 170.8 was assigned to the carbonyl carbon of the acetate residue, on the basis of its long-range ^{13}C−^{1}H correlation to the methyl signal (δ 2.06), whereas the carbonyl carbon showed a three-bond correlation with H-11 at δ 4.66 and 4.76 [2H, (AB), J = 12.4 Hz] in the HMBC spectrum. These data revealed the presence of an acetate group at C-11. A TOCSY experiment showed correlations among the C-2−C-6 protons of a β-Me-isovalerate function, at δ 2.26 (2H, m), 2.11 (1H, m), 1.24 (2H, m), 0.94 (3H, t, J = 6.0 Hz), and 1.08 (3H, d, J = 6.1 Hz),[15] demonstrating that they belong to the same spin system. The C-2 protons of the β-Me-isovalerate group showed a long-range ^{13}C−^{1}H correlation with a carbonyl carbon at δ 170.4, whereas the carbonyl carbon showed a three-bond correlation with H-1 (δ 5.98) in the HMBC spectrum. These data suggested the presence of a β-Me-isovalerate group at C-1. In addition to the signals for the valtrate-type skeleton, an acetate group, and a β-Me-isovalerate group, the ^{1}H NMR spectrum revealed signals for three methyl groups at δ 1.50, 1.53, and 1.95 (each 3H, s) and one methylene at δ 2.81 and 3.04 [2H, (AB), J = 14.2 Hz] linked to a carbonyl residue. Furthermore, the ^{13}C NMR and DEPT spectra showed seven carbon signals due to three methyl carbons (δ 22.2, 26.6, and 26.7), a methylene carbon (δ 44.2) linked to a carbonyl residue, one quaternary carbon (δ 79.3) having an oxygen function, and two ester carbonyl carbons (δ 168.9 and 170.5). These spectral data suggested an β-OAc-isovalerate group[9,16] in the molecule of **1**. The HMBC experiment showed a long-range correlation between H-7 (δ 5.38) and one of the ester carbonyl carbons of the β-OAc-isovalerate group (δ 168.9), revealing the site of attachment of the β-OAc-isovalerate function to be at C-7. All of these data were used to assign compound **1** as 1-homoacevaltrate.

Compound **2** was obtained as a colorless oil with $[\alpha]^{24}_D$ +198.5° (*c* 0.01, MeOH). The IR spectrum of **2** was very similar to that of **1**. The molecular formula, $C_{25}H_{34}O_{10}$, was inferred by HRESIMS ([M − H]$^-$ *m*/*z* 493.2072) and was supported by ^{13}C NMR and DEPT spectra. The 1D and 2D NMR spectra of **2** also showed the presence of a valtrate-type skeleton with an acetate residue at C-7 and a β-Me-isovalerate group at C-1. Additionally, the ^{1}H NMR spectrum revealed signals for three methyl groups at δ 0.98 and 1.00 (6H, 2d, J = 6.6 Hz) and 2.10 (3H, s), one methine proton at δ 4.80 (1H, d, J = 4.7 Hz) adjacent to an oxygen function, and one methine proton at δ 2.20 (1H, m). Furthermore, the ^{13}C NMR and DEPT spectra showed seven carbon signals due to three methyl carbons (δ 17.2, 18.6, and 20.7), a methine carbon (δ 76.9) having an oxygen function, one methine carbon (δ 29.8), and two ester carbonyl carbons (δ 169.8 and 173.1). These spectral data suggested the presence of an α-OAc-isovalerate group[5,16,17] in the molecule of **2**. The HMBC experiment showed a long-range correlation between H-11 at δ 4.66 and 4.77 [2H, (AB), J = 12.5 Hz] and one ester carbonyl carbon of a α-OAc-isovalerate group (δ 169.8), revealing the site of attachment of the α-OAc-isovalerate function to be at C-11. The structure of compound **2** was therefore characterized as 1-homoisoacevaltrate.

Compound **3** appeared as a colorless oil with $[\alpha]^{24}_D$ −67.3° (*c* 0.01, MeOH), whose molecular formula, $C_{23}H_{34}O_9$, was inferred by HRESIMS ([M − H]$^-$ *m*/*z* 453.2129). ^{13}C NMR and DEPT spectra showed 23 resonance lines, indicating five methyls, six methylenes, six methines, and six quaternary carbons. The IR spectrum of **3** showed two dominant ester bands at 1764 and 1738 cm^{-1}. The signals at δ 6.08 (1H, d, J = 2.0 Hz) and 88.5 (CH), respectively, were assignable to H-1 and C-1. The chemical shifts of one olefinic methine carbon at δ 145.4 and of an olefinic quaternary carbon at δ 111.3, respectively, were assigned to C-3 and C-4. The chemical shifts of one quaternary carbon having an oxygen function at δ 69.7 and one

methylene carbon at δ 40.4, respectively, were assigned to C-5 and C-6. The quaternary carbon at δ 62.4 (C-8) and the methylene carbon at δ 48.9 (C-10) were characteristic for an epoxide ring at C-8 and C-10, corresponding to a hydroxyldihydrovaltrate-type iridoid.[6,9] The 1D and 2D NMR spectra of **3** also showed the presence of an acetate residue at C-7 and a β-Me-isovalerate group at C-11. Furthermore, the ^{13}C NMR and DEPT spectra (Table 1) showed five carbon signals due to two methyl carbons (δ 22.2 and 22.3), one methylene carbon (δ 42.9) linked to a carbonyl, one methine carbon (δ 25.5), and one ester carbonyl carbon (δ 170.7). These spectral data suggested an isovalerate group[9,18] in the molecule of **3**. The HMBC experiment showed a long-range correlation between H-1 at δ 6.08 and the ester carbonyl carbon of the isovalerate group (δ 170.7), revealing the site of attachment of the isovalerate function to be at C-1. Therefore, compound **3** was determined as 11-homohydroxyldihydrovaltrate.

Compound **4** appeared as a colorless oil with $[\alpha]^{24}_D$ +197.5° (*c* 0.01, MeOH), whose molecular formula, $C_{25}H_{36}O_{10}$, was inferred by HRESIMS ($[M - H]^-$ *m/z* 495.2238). The ^{13}C NMR and DEPT spectra showed 25 resonance lines, indicating six methyls, five methylenes, seven methines, and seven quaternary carbons. The IR spectrum of **4** showed two dominant ester bands at 1754 and 1723 cm^{-1}. The signals at δ 6.18 (1H, d, J = 10.0 Hz) and 92.5 (CH), respectively, were assignable to H-1 and C-1. The chemical shifts of two olefinic methine carbons at δ 148.1 and 117.5 and olefinic quaternary carbons at δ 108.8 and 139.1, respectively, were assigned to C-3, C-6, C-4, and C-5. The chemical shifts of one methine carbon having an oxygen function at δ 83.1, one quaternary carbon at δ 80.1, and two methylene carbons having an oxygen function at δ 65.8 and 61.0 respectively, were assigned to C-7, C-8, C-10, and C-11. These spectral data suggested a valtrate hydrin-type skeleton for **4**.[6,12,13] Additionally, the 1D and 2D NMR spectra of **4** also showed the presence of two acetate residues at C-10 and C-11, a β-Me-isovalerate group at C-1, and an isovalerate unit at C-7. Therefore, compound **4** was identified as 10-acetoxy-1-homovaltrate hydrin.

Compound **5** was obtained as a colorless oil with $[\alpha]^{24}_D$ +194.6° (*c* 0.01, MeOH). The IR spectrum of **5** was very similar to those of **4**. The molecular formula, $C_{26}H_{36}O_{12}$, was inferred by HRESIMS ($[M - H]^-$ *m/z* 539.2120), and it was supported by the ^{13}C NMR and DEPT spectra. Its ^{1}H and ^{13}C NMR spectra also showed the presence of a valtrate hydrin-type skeleton. Additionally, the 1D and 2D NMR spectra of **5** also showed the presence of two acetate residues at C-10 and C-11, a β-OAc-isovalerate group at C-1, and an isovalerate unit at C-7. The structure of compound **5** was therefore characterized as 10-acetoxy-1-acevaltrate hydrin.

Table 2. ^{13}C NMR Data of Compounds **1**−**5** (100 MHz, δ ppm, $CDCl_3$)[a]

position	1	2	3	4	5
1	92.6	92.7	88.5	92.5	92.7
3	148.6	148.9	145.4	148.1	148.4
4	108.5	108.0	111.3	108.8	108.5
5	141.1	140.9	69.7	139.1	139.2
6	118.6	118.7	40.4	117.5	117.3
7	83.6	83.3	73.3	83.1	83.2
8	64.2	64.1	62.4	80.1	80.3
9	43.3	43.1	48.2	48.5	48.5
10	48.0	48.0	48.9	65.8	65.8
11	61.0	61.3	61.9	61.0	60.9
R_1 1	170.4	170.5	170.7	171.1	167.9
2	41.2	41.4	42.9	41.3	44.0
3	31.7	31.4	25.5	31.9	79.2
4	29.4	29.6	22.2[b]	29.1	26.5
5	11.4	11.5	22.3[b]	11.3	27.0
6	19.2	19.5		19.1	170.7[b]
7					22.3[c]
R_7 1	168.9	170.3	170.4	171.9	171.8
2	44.2	21.0	20.9	43.4	41.4
3	79.3			25.7	25.7
4	26.6[b]			22.3[b]	22.3[c]
5	26.7[b]			22.4[b]	22.4[c]
6	170.5				
7	22.2				
R_{10} 1				170.8[c]	170.8[b]
2				20.7[d]	20.8[d]
R_{11} 1	170.8	169.8	170.9	170.9[c]	170.9[b]
2	20.8	76.9	41.4	20.9[d]	20.9[d]
3		29.8	32.0		
4		17.2[b]	29.4		
5		18.6[b]	11.3		
6		173.1	19.2		
7		20.7			

[a] All assignments based on extensive 1D and 2D NMR measurements (DEPT, DQF-COSY, TOCSY, NOESY, HMQC, and HMBC). [b−d] Assignments may be interchangeable in each column.

Experimental Section

General Experimental Procedures. Optical rotations were recorded with a Perkin-Elmer model 241 polarimeter. IR spectra were measured on a Shimadzu UV-1601 instrument and on a Perkin-Elmer 983 spectrometer, respectively. All NMR spectra were run on a Bruker DRX-400 instrument operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C, using standard pulse sequences. Chemical shifts are reported on the δ scale in parts per million, downfield from TMS. Carbon multiplicities were determined from DEPT-135 and DEPT-90 experiments. All 2D NMR spectra were recorded using pulsed field gradients. ^{1}H−^{1}H correlations were observed in double quantum filtered (DQF) COSY and TOCSY experiments. One-bond ^{13}C−^{1}H correlations were observed in a HMQC experiment. Long-range ^{13}C−^{1}H correlations were observed in HMBC experiments. ESIMS were obtained on a PE Biosystems Mariner System 5140 LC/MS spectrometer. Column chromatography was performed on Si gel (Marine Chemical Factory, Qingdao, People's Republic of China) and RP-18 (Shimadzu). Other conditions were as previously described.[19]

Plant Material. The roots and rhizomes of *Valeriana jatamansi* Jones were collected in November 2001 from Luosan, Sichuan Province, People's Republic of China, and the plant was identified by Dr. Chunfeng Qiao, Department of Pharmacognosy, School of Pharmacy, Fudan University, Shanghai, People's Republic of China. After collection, the rhizomes and roots were allowed to dry at ambient temperature for about one week and were then crushed and immediately extracted. A voucher specimen (No. SIOC-Bio-200103801) has been deposited in the State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, People's Republic of China.

Extraction and Isolation. The dried and crushed roots and rhizomes (7.5 kg) were extracted five times with petroleum ether at room temperature for 24 h each time, and solvent was removed under reduced pressure. The extract (370.8 g) was concentrated and subjected to silica gel column chromatography eluting with *n*-hexane−EtOAc (100:1) followed by stepwise addition of EtOAc to yield 15 fractions. Fraction 5 (29.9 g) was eluted with *n*-hexane−EtOAc (10:1) and was purified by HPLC (RP_{18}, 4 μm, 208 nm, MeCN−H_2O, 60:40) to give **1** (5 mg), **2** (6 mg), valtrate (30 mg), isovaltrate (14 mg), homovaltrate (11 mg), acevaltrate (14 mg), dihomovaltrate (16 mg), didrovaltrate (10 mg), and 1-homodidrovaltrate (12 mg), respectively. Using the same system, fraction 6 afforded **3** (7 mg) and acetylhydroxyldihydrovaltrate (16 mg); fraction 7 gave **4** (4 mg), **5** (5 mg), 10-isovaleroxyvaltrate hydrin (14 mg), and 10-isovaleroxydiavaltrate hydrin (16 mg).

1-Homoacevaltrate (1): oil, $[\alpha]_D^{24}$ +175.9° (*c* 0.01, MeOH); IR (KBr) ν_{max} 1765, 1738, 1648, 1611, 1380 cm^{-1}; ^1H NMR ($CDCl_3$), see Table 1; ^{13}C NMR ($CDCl_3$), see Table 2; HRESIMS (negative mode, MeOH) *m*/*z* 493.2078 $[M - H]^-$ (calcd for $C_{25}H_{33}O_{10}$, 493.2074).

1-Homoisoacevaltrate (2): oil, $[\alpha]_D^{24}$ +198.5° (*c* 0.01, MeOH); IR (KBr) ν_{max} 1764, 1738, 1659, 1474, 1440, 1385 cm^{-1}; ^1H NMR ($CDCl_3$), see Table 1; ^{13}C NMR ($CDCl_3$), see Table 2; HRESIMS (negative mode, MeOH) *m*/*z* 493.2072 $[M - H]^-$ (calcd for $C_{25}H_{33}O_{10}$, 493.2074).

11-Homohydroxyldidrovaltrate (3): oil, $[\alpha]_D^{24}$ −67.3° (*c* 0.01, MeOH); IR (KBr) ν_{max} 1764, 1738, 1655, 1607, 1378 cm^{-1}; ^1H NMR ($CDCl_3$), see Table 1; ^{13}C NMR ($CDCl_3$), see Table 2; HRESIMS (negative mode, MeOH) *m*/*z* 453.2129 $[M - H]^-$ (calcd for $C_{23}H_{33}O_9$, 453.2125).

10-Acetoxy-1-homovaltrate hydrin (4): oil, $[\alpha]_D^{24}$ +197.5° (*c* 0.01, MeOH); IR (KBr) ν_{max} 1754, 1723, 1701, 1625, 1610, 1474, 1387, 1382 cm^{-1}; ^1H NMR ($CDCl_3$), see Table 1; ^{13}C NMR ($CDCl_3$), see Table 2; HRESIMS (negative mode, MeOH) *m*/*z* 495.2238 $[M - H]^-$ (calcd for $C_{25}H_{35}O_{10}$, 495.2231).

10-Acetoxy-1-acevaltrate hydrin (5): oil, $[\alpha]_D^{24}$ +194.6° (*c* 0.01, MeOH); IR (KBr) ν_{max} 1753, 1722, 1701, 1622, 1610, 1475, 1387, 1380 cm^{-1}; ^1H NMR ($CDCl_3$), see Table 1; ^{13}C NMR ($CDCl_3$), see Table 2; HRESIMS (negative mode, MeOH) *m*/*z* 539.2120 $[M - H]^-$ (calcd for $C_{26}H_{35}O_{12}$, 539.2129).

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