New Phenylpropanoid Glycosides from Juniperus communis var. depressa

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Two new phenylpropanoid glycosides were isolated from the leaves and stems of Juniperus communis var. depressa (Cupressaceae) along with 14 known compounds. Their structures were determined by spectral analyses, in particular by 2D-NMR spectral evidence.

Key words Juniperus communis var. depressa; Cupressaceae; phenylpropanoid glycoside; lignan glycoside

In a survey of chemical components from useful plants grown in western North America, we have reported a number of chemical compounds (nine phenylpropanoids, six neolignans, fourteen flavonoids, seven catechins, and five terpenoids) from the leaves and stems of Juniperus communis var. depressa (Cupressaceae). In our continuing study on this plant, two new phenylpropanoid glycosides (1 and 4) were isolated together with six known phenylpropanoids (2, 3, 5–8), two known phenolic compounds (9, 10), and six known lignans (11–16). This paper describes the structural elucidation of these compounds as well as the characterization of the absolute structures of three lignans (11, 12, 14) based on NMR and circular dichroism (CD) spectral evidence.

The n-BuOH soluble part of the MeOH extract was separated by a combination of silica gel, octadecyl silica gel (ODS), and Sephadex LH-20 column chromatographies, followed by HPLC separation, to afford two new compounds (1 and 4) and 14 known compounds (2, 3, 5–16). The known compounds were identified as junipediol B 8-O-β-D-glucopyranoside (2), junipediol A 8-O-β-D-glucopyranoside (3), (73,85)-guaiaacylglycerol (5), (8,9) junipetrioloside A (6), trans-coniferyl aldehyde (7), 2-[4-(3-hydroxypropyl)-2-methoxyphenyl]-1,3-propanediol (8), vanillin (9), arbutin (10), (2S,3R)-2,3-dihydro-7-hydroxy-3-hydroxy-methyl-2-(4’-hydroxy-3’-methoxyphenyl)-5-benzofuranopropan 4’-O-β-D-glucopyranoside (13), (2R,3S)-2,3-di-hydro-3-hydroxy-methyl-7-methoxy-2-(4’-hydroxy-3’-methoxyphenyl)-5-benzofuranopropan 4’-O-β-D-glucopyranoside (15), and cupressoside A (16) by comparison of physical data with literature values and spectroscopic evidence. The structures of the isolates (1—16) are given in Chart 1.

Compound 1, a white amorphous powder, showed the [M–H]– ion peak at m/z 427.1615 in the negative ion HRFAB-MS, corresponding to the molecular formula of C31H36O15. The 1H- and 13C-NMR spectral data (Table 1) showed the presence of a β-D-glucopyranosyl and an α-L-arabinofuranosyl moieties in 1. Identification of monosaccharides, including its absolute configuration, was carried out by direct HPLC analysis of the acid hydrolysate. The 1H-NMR and 1H–1H correlation spectroscopy (COSY) spectra of 1 showed the presence of a 1,2,4-trisubstituted benzene ring [δ 6.83 (1H, s, H-2), 6.73 (1H, d, J = 8.1 Hz, H-5), and 6.75 (1H, br d, J = 8.1 Hz, H-6)], aliphatic CH2OH–CH(AR)–CH(O)moeity [δ 3.02 (1H, m, H-7), 4.07 (1H, dd, J = 10.6, 7.6 Hz, H-8a), 3.77 (1H, dd, J = 10.6, 4.0 Hz, H-8b), 3.84 (1H, dd, J = 11.6, 5.5 Hz, H-9a), and 3.73 (1H, overlapping signal, H-9b)], and a methylenedioxy group [δ 5.88 (2H, s, H-7)] (Table 1). In addition, long-range correlations between H-7/C-1 and H-10/C-3, C-4 were observed in the heteronuclear multiple bond correlation spectroscopy (HMBC) spectrum (Fig. 1). Based on this spectral evidence, the aglycone of 1 was determined to be junipediol B.7) The position of the glycosyl moiety in 1 was decided by the following HMBC and nuclear Overhauser enhancement spectroscopy (NOESY) experiments (Fig. 1), in which the HMBC correlations (H-1′/C-8 and H-1”/C-6′) as well as the NOESY correlations (H-1′/H-8 and H-1”/H-6′) were observed. Therefore the α-L-arabinofuranosyl-(1→6)-β-D-glucopyranosyl moiety was connected to 8-hydroxy group of junipediol B through a glycosidic bond. In the 1H- and 13C-NMR spectrum, anomic proton and anomic carbon signals of both glucose and arabinose in 1 appeared as sets of signals, respectively. This is attributed to the presence of the diastereomers as a result of the glycosidation at 8-hydroxy group of the achiral junipediol B.7) Attempts to separate both diastereomers were unsuccessful. In conclusion, the structure of 1 was determined to be junipediol B 8-O-(6’-O-α-L-arabinofuranosyl)-β-D-glucopyranoside.

Compound 4, a white amorphous powder, showed the [M–H]– ion peak at m/z 427.1615 in the negative ion HRFAB-MS, corresponding to the molecular formula of C32H38O16. The 1H- and 13C-NMR spectra of 4 closely resembled those of rosarin [=trans-cinnamyl alcohol 9-O-(6’-O-α-L-arabinofuranosyl)-β-D-glucopyranoside] isolated from the same plant.7) However, in the 1H-NMR spectrum, the coupling constant between H-7 and H-8 (J = 11.6 Hz) in 4 was smaller than that of rosarin (J = 15.9 Hz), indicating the H-7/H-8 cis configuration of the aglycone. Thus the structure of 4 was concluded to be cis-cinnamyl alcohol 9-O-(6’-O-α-L-arabinofuranosyl)-β-D-glucopyranoside.

Compound 11, a white amorphous powder, gave the [M–H]– ion peak at m/z 545.1667 in the negative ion HRFAB-MS, indicating the molecular formula to be C32H36O12.

In addition, the negative ion FAB-MS gave a fragment peak
at m/z 383 due to the loss of a hexosyl unit from the [M−H]⁻ ion. The ¹H- and ¹³C-NMR spectral data exhibited the presence of a β-D-glucopyranosyl moiety as the sugar part (Table 2). The ¹H-NMR and ¹H–¹H COSY spectra indicated the presence of a 1,2,3,5-tetrasubstituted benzene ring [δ 6.33 (2H, br s, H-2 and H-6)], a 1,2,4,5-tetrasubstituted benzene ring [δ 6.62 (1H, s, H-2) and 6.34 (1H, s, H-5)], two methoxy groups [δ 3.63 (6H, s)], a methylenedioxy group [δ 5.80 (1H, d, J = 1.2 Hz) and 5.79 (1H, d, J = 1.2 Hz)], and aliphatic [−CH₂−CH(CH₂)−CH(CO)−(C)CH(C)−] proton signals as the aglycone moiety of 11 (Table 2). The ¹H–¹H COSY and HMBC correlations (Fig. 2) indicated that the plane structure of the aglycone of 11 was the same as that of 4-demethyldeoxypodophyllotoxin. The HMBC and NOESY correlations (Fig. 2) indicated that the β-D-glucosyl moiety was linked to the 4-OH of the aglycone through a glycosidic bond. The absolute configurations of the three chiral centers of the aglycone were determined as follows. Klyne et al. reported that 7α-aryl (=7R) derivatives in 7-aryltetralin type

Table 1. ¹H- (600 MHz) and ¹³C-NMR (150 MHz) Spectral Data of 1 and 4 in MeOH-d₄

<table>
<thead>
<tr>
<th>No.</th>
<th>δ H</th>
<th>δ C</th>
<th>δ H</th>
<th>δ C</th>
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</thead>
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<td>7.23-7.26 (m)</td>
<td>137.9</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>6.83 (s)</td>
<td>109.7</td>
<td>7.35 (br dd, 7.6, 7.6)</td>
<td>129.4</td>
</tr>
<tr>
<td>3</td>
<td>149.0</td>
<td>147.7</td>
<td>7.35 (br dd, 7.6, 7.6)</td>
<td>129.4</td>
</tr>
<tr>
<td>4</td>
<td>147.7</td>
<td>6.73 (d, 8.1)</td>
<td>122.6</td>
<td>7.23-7.26 (m)</td>
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<tr>
<td>5</td>
<td>6.75 (br d, 8.1)</td>
<td>109.0</td>
<td>7.35 (br dd, 7.6, 7.6)</td>
<td>129.4</td>
</tr>
<tr>
<td>6</td>
<td>7.02 (m)</td>
<td>49.2</td>
<td>6.61 (br d, 11.6)</td>
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</tr>
<tr>
<td>7</td>
<td>4.07 (dd, 10.6, 7.6)</td>
<td>72.2</td>
<td>5.90 (dd, 11.6, 6.9, 6.0)</td>
<td>129.4</td>
</tr>
<tr>
<td>8</td>
<td>3.77 (dd, 10.6, 4.0)</td>
<td>64.8</td>
<td>4.63 (dd, 12.8, 6.0, 1.8)</td>
<td>67.4</td>
</tr>
<tr>
<td>9</td>
<td>3.84 (dd, 11.6, 5.5)</td>
<td>3.73</td>
<td>4.44 (dd, 12.8, 6.9, 1.8)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>5.88 (s)</td>
<td>102.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Glc 1° | 4.29 (d, 7.8) | 4.32 (d, 7.8) |
| 2° | 3.17 (dd, 9.0, 7.8) | 71.5 |
| 3° | 3.32 (dd, 9.0, 9.0) | 78.0 |
| 4° | 3.26 (dd, 9.0, 9.0) | 72.0 |
| 5° | 3.44 (dd, 9.0, 5.5, 2.5) | 76.8 |
| 6° | 4.02 (dd, 11.6, 2.5) | 68.2 |
| 7° | 3.58 (dd, 11.6, 5.5) | 3.60 (dd, 11.2, 5.7) |

Ara (f) 1° | 4.95 (br s) | 4.96 (br s) |
| 2° | 3.99 (dd, 3.6, 1.0) | 83.2 |
| 3° | 3.82 (dd, 5.6, 3.6) | 78.9 |
| 4° | 3.96 (dd, 5.6, 5.4, 4.0) | 85.9 |
| 5° | 3.77 (dd, 11.6, 4.0) | 63.1 |
| 6° | 3.61 (dd, 11.6, 5.6) | 3.62 (dd, 11.8, 5.5) |

a) Overlapping with other signals.  b) Appeared as sets of signals.

Fig. 1. Selected 2D NMR Spectral Data of 1.
lignans afforded the positive Cotton effect around 280—290 nm, while 7β-aryl (＝7S) derivatives showed the negative Cotton curve in the CD spectrum. Consequently, 11 showed a positive Cotton effect at 288 nm and hence, the absolute configurations of C-8 and C-8′ were assigned as both R. Based on the evidence, the structure of 11 was determined to be (7R,8R,8′R)-4-demethyleoxy-

podophyllotoxin 4-O-β-D-glucopyranoside. Up to now, 4-
demethyleoxypodophyllotoxin 4-O-glucopyranoside, having the same planar structure as the aglycone part in 11, have already been isolated from Podophyllum emodi,19) P. peeltatum,19) and P. versipelle.20) However, in these papers, unambiguous structural determination procedures were not discussed and hence the absolute structure of 11 is represented here for the first time.

Compound 12, a white amorphous powder, gave a molecular formula of C_{52}H_{43}O_{10} based on the [M−H]− ion peak at m/z 505.2073 in the negative ion HR-FAB-MS. The 1H- and 13C-NMR spectra suggested that 12 was a dihydrobenzofuran-type neolignan glycoside carrying an α-L-rhamnopyranosyl moiety as a sugar part (Table 3). The structure of the aglycone in 12 was elucidated from 1H−1H COSY and HMBC experiments (Fig. 3). The relative configurations of H-2 and H-3 were determined to be trans based on the NOESY correlations (H-2/H-3, H-5′/H-6′) (Fig. 3). The positive Cotton effect at 241 nm in the CD spectrum assigned the absolute stereochemistries of C-2 and C-3 to be S and R, respectively.15) In conclusion, the structure of 12 is determined to be (2S,3R)-2,3-dihydro-3-hydroxymethyl-7-methoxy-2-(4′-hydroxy-3′-methoxyphenyl)-5-benzoferanopropan-3α-O-α-L-rhamnopyranoside. Dihydrobenzofuran-type neolignan rhamnoses, having the same plane structure as the aglycone part in 12, have already been isolated from Pinus massoniana,21) Baseonema acuminatum,22) and Junipe-

![Fig. 2. Selected 2D NMR Spectral Data of 11](image_url)
rus polycarpus. However, in these papers, the absolute configurations on the dihydrobenzofuran ring were not discussed and hence the absolute structure of 12 based on CD analyses is represented here for the first time.

Compound 14, a white amorphous powder, had the molecular formula C_{26}H_{34}O_{11}, which was determined based on the [M—H]~ ion at m/z 521.2038 in negative ion HR-FAB-MS. The 1H- and 13C-NMR spectral data exhibited the presence of two dihydrobenzofuran-type neolignan glucosides having the same structure as 14 from Phlomis viscose. However, no chemical and spectral data of this compound were provided in the report. Thus the 1H- and 13C-NMR assignments in Table 3 and other physical properties in the experimental are reported here for the first time.

**Experimental**

1H- and 13C-NMR spectra were measured on a JEOL JNM-ECA 600 (1H at 600 MHz and 13C at 150 MHz) or JEOL JNM-GX 400 (1H at 400 MHz and 13C at 100 MHz) spectrometer. Chemical shifts are given in δ values (ppm) relative to tetramethylsilane (TMS) as an internal standard. FAB- and HR-FAB-MS spectra in negative mode (matrix, triethanolamine) were obtained on a JEOL JMS-700T spectrometer. FTIR (film) cm⁻¹: 3350, 2924, 1069, 1038. UV λ max (MeOH) nm (log ε): 294 (4.30), 228 (sh, 3.73), 284 (3.50). 1H- and 13C-NMR data are reported in Table 1. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 18.9° (c=0.40, MeOH). HR-FAB-MS (negative mode) m/z: 489.1604 [M—H]~ (Calcd for C_{21}H_{29}O_{13}, 489.1608). IR (film) cm⁻¹: 3350, 2924, 1069, 1038. UV λ max (MeOH) nm (log ε): 294 (4.30), 228 (sh, 3.73), 284 (3.50). 1H- and 13C-NMR data are reported in Table 1. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 70.1° (c=0.89, MeOH). FAB- and HR-FAB-MS (negative mode) m/z: 427.1615 [M—H]~ (Calcd for C_{26}H_{33}O_{10}, 427.1628). IR (film) cm⁻¹: 3358, 2924, 1509, 1274, 1213, 1139, 1048. UV λ max (MeOH) nm (log ε): 207 (4.21), 244 (3.98). 1H- and 13C-NMR data are reported in Table 1. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 45.7° (c=0.47, MeOH). FAB- and HR-FAB-MS (negative mode) m/z: 545.1667 [M—H]~ (Calcd for C_{25}H_{38}O_{12}, 545.1659). IR (film) cm⁻¹: 3375, 2923, 1767, 1559, 1485, 1227, 1122, 1037. UV λ max (MeOH) nm (log ε): 214 (3.36), 230 (sh, 4.13), 290 (3.62). CD (c=9.90; 10 molal, MeOH) Δε (λ nm): 14.12 (277), 0.23 (288). 1H- and 13C-NMR data are reported in Table 2. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 45.0° (c=0.31, MeOH). FAB- and HR-FAB-MS (negative mode) m/z: 505.2073 [M—H]~ (Calcd for C_{25}H_{38}O_{12}, 505.2074). IR (film) cm⁻¹: 3363, 2923, 1604, 1517, 1456, 1274, 1213, 1139, 1048. UV λ max (MeOH) nm (log ε): 207 (4.21), 244 (3.98). 1H- and 13C-NMR data are reported in Table 1. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 45.7° (c=0.47, MeOH). FAB- and HR-FAB-MS (negative mode) m/z: 545.1667 [M—H]~ (Calcd for C_{25}H_{38}O_{12}, 545.1659). IR (film) cm⁻¹: 3375, 2923, 1767, 1559, 1485, 1227, 1122, 1037. UV λ max (MeOH) nm (log ε): 214 (3.36), 230 (sh, 4.13), 290 (3.62). CD (c=9.90; 10 molal, MeOH) Δε (λ nm): 14.12 (277), 0.23 (288). 1H- and 13C-NMR data are reported in Table 2. cis-Cinnamyl Alcohol 9-O-(6′-α-cis-arabinofuranosyl)-β-D-glucopyranoside (1): A white amorphous powder, [α]D~ 45.0° (c=0.31, MeOH). FAB- and HR-FAB-MS (negative mode) m/z: 505.2073 [M—H]~ (Calcd for C_{25}H_{38}O_{12}, 505.2074). IR (film) cm⁻¹: 3363, 2923, 1604, 1517, 1456, 1274, 1213, 1139, 1048. UV λ max (MeOH) nm (log ε): 207 (4.21), 244 (3.98). 1H- and 13C-NMR data are reported in Table 1.
\(\lambda_{\text{max}}\) (MeOH) nm (log e): 210 (4.48), 225 (sh, 4.20), 282 (3.85). CD (c=7.95\times10^{-3}\text{mol/l, MeOH}) \Delta\varepsilon (\lambda\text{ nm}): +5.25 (210), +0.36 (225), +1.88 (241), +1.05 (291). \(^1^H\) and \(^1^C\)-NMR data are given in Table 3.

(2R,3S)-2,3-Dihydro-3-hydroxymethyl-7-(4'-hydroxy-3'-methylphenyl)-5-benzofuranpropanol 5c: A white amorphous powder, \([\alpha]_D^{24}=-12.4^0\) (c=0.18, MeOH). HR-FAB-MS (negative mode) \(m/z\): 521.2038 [M–H]\(^-\) (Calcd for \(C_{26}H_{31}O_7\), 521.2023). IR (film) cm\(^{-1}\): 3365, 2936, 1605, 1518, 1455, 1276, 1212, 1030. UV \(\lambda_{\text{max}}\) (MeOH) nm (log e): 210 (4.54), 226 (sh, 4.21), 282 (3.80). CD (c=6.90\times10^{-3}\text{mol/l, MeOH}) \Delta\varepsilon (\lambda\text{ nm}): -3.69 (211), +0.23 (225), -1.19 (243), -0.54 (294). \(^1^H\) and \(^1^C\)-NMR data are given in Table 3.

Acid Hydrolysis of Compounds 1, 4, 11, 12, and 14 Each glycoside (ca. 1 mg) in 1 m HCl (1.0 ml) was heated at 95 °C for 3 h. After cooling, the reaction mixture was neutralized with Amberlite IRA-93ZU (Organo Co., Ltd., Tokyo, Japan) and passed through an Oasis HLB cartridge column. The solution was concentrated to give a sugar fraction, which was analyzed by HPLC under the following conditions: column, COSMOSIL Sugar-D Ltd., Tokyo, Japan) and passed through an Oasis HLB cartridge column. H2O (4 : 1); flow rate, 1.0 ml/min; detection, optical rotation, JASCO OR-2090 Plus. Identification of D-glucose (from (4.6 mm i.d. (MeOH) nm (log e) 746 V ol. 58, No. 5

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References and Notes
1) Present address: San-Ei Gen FEF, Inc.; Toyonaka, Osaka 561–8588, Japan.
11) Vanillin and arbutin were identified by comparison of their physical and spectral data with those of commercially available samples (Tokyo Kasei Kogyo).