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Minor diarylheptanoid glycosides of *Alnus rubra* bark

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Abstract

The diarylheptanoid (*S*)-1,7-bis-(4-hydroxyphenyl)-heptan-3-one-5-*O*-β-D-xylopyranoside, and two known compounds, 1,7-bis-(3,4-dihydroxyphenyl)-heptan-3-one-5-*O*-β-D-glucopyranoside and platyphylloside were isolated from *Alnus rubra* bark. Structures were established by application of spectrometric techniques. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: *Alnus rubra*; Betulaceae; Diarylheptanoids; Bark

1. Introduction

Alnus rubra Bong is a fast-growing deciduous tree commonly found throughout the coastal river valleys and shore flats of the Pacific Northwest. This plant serves an important ecological role as a nitrogen fixer and seasonal food source for cervids (Leslie, Starkey & Vavra, 1984). Contemporary indigenous healers also use the bark for various medicinal teas (Turner & Hebda, 1990; Forlines, Tavenner, Malan & Karchesy, 1992). Previous research has shown the bark to have antibiotic properties which were attributed to the diarylheptanoid xyloside, oregonin (Saxena, Farmer, Hancok & Towers, 1995). Other acylated diarylheptanoids and diarylheptenones also have been found in the bark (Chen, Karchesy & Gonzalez-Laredo, 1998; Gonzalez-Laredo, Helm, Chen & Karchesy, 1998). In continuing research, into the more minor phenolic components of the bark, a new diarylheptanoid xyloside and two known glycosides were isolated.

2. Results and discussion

Compounds (**1**–**3**) were isolated from fractions adjacent to those containing oregonin on chromatography of a crude bark extract over Sephadex LH-20 (Gonzalez-Laredo et al., 1998). Final purifications were accomplished using alternating separations on silica gel, Sephadex LH-20 and Toyopearl HW-40. Compounds **1** and **2** were identified by ^{1}H- and ^{13}C-NMR, FABMS, and $[\alpha]_D$. Data was consistent with that published for **1** and **2** (Smite et al., 1993; Ohta et al., 1984; Ohta, Koyama, Aoki & Suga, 1985). Compound **1**, called platyphylloside, has been previously isolated from *Betula platyphylla* and *B. pendula* (Smite, Lundgren & Andersson, 1993; Ohta, Koyama, Aoki & Suga, 1985; Terazawa, Koga, Okuyama & Miyake, 1973; Sunnerheim, Palo, Theander & Knutsson, 1988). Compound **2** has been previously reported in *Alnus serrulatoides* flowers (Ohta et al., 1984). In both **1** and **2**, the absolute configuration of C-5 was shown to be *S* (Ohta et al., 1984; Ohta et al., 1985).

NMR data for **3** was virtually identical to that of platyphylloside (**1**) (Smite et al., 1993; Ohta et al., 1985) with the exception of the sugar signals (Table 1). This indicated a common aglycone for the two compounds. The *para* hydroxy substituted aromatic rings were indicated by three sets of characteristic *ortho* coupled doublets with $J = 8.4$ Hz in each case, at δ 6.99 (2H, H-2′, 6′), 6.97 (2H, H-2″, 6″) and 6.67 (4H, H-3′, 5′, 3″ 5″). Correspondingly, in the ^{13}C-NMR spectrum, the hydroxy bearing aromatic carbons (C-4′,

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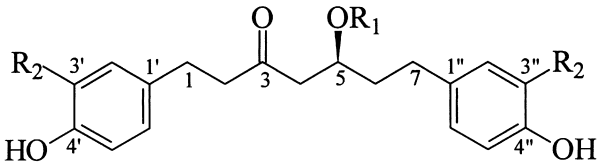
Table 1
NMR spectroscopic data for **3** (in CD_3OD)

Position	13C (ppm)	1H, δ (J Hz)
1	29.7	2.74, *s* (4H)
2	46.4	2.74, *s* (4H)
3	211.7	
4a/b	48.7	2.81, *dd*, *J* = 6.8, 16.8 2.57, *dd*, *J* = 5.3, 16.8
5	76.2	4.10, *m*
6	38.5	1.74, *m* (2H)
7	31.4	2.52, *m* (2H)
1′, 1″	133.1, 134.2	
2′, 6′, 2″, 6″	130.3 (4×)	6.99, *d*, *J* = 8.4 (2H) 6.97, *d*, *J* = 8.4 (2H)
3′, 5′, 3″, 5″	116.1 (2×), 116.0 (2×)	6.67, *d*, *J* = 8.4 (4H)
4′, 4″	156.4, 156.2	
xylose		
1	104.2	4.21, *d*, *J* = 7.6
2	75.0	3.13, *m*
3	77.8	3.33, *m*
4	71.1	3.52, *m*
5	66.8	3.84, *dd*, *J* = 5.4, 11.4 3.17, *dd*, *J* = 9, 11.4

4″) gave signals at 156.4 and 156.2 ppm. In the ^{13}C-NMR spectrum of **3**, the series of signals at 104.2, 75.0, 77.8, 71.1, and 66.8 were indicative of a β-D-xylopyranoside moiety (Agrawal, 1992). The xylose anomeric proton ^{1}H signal at δ 4.21, which was a doublet with J = 7.6 Hz, confirmed the β-configuration. Confirmation that the xylopyranoside moiety was linked to heptane C-5 position was seen in the HMBC spectrum which showed connectivity of the anomeric xylopyranoside proton signal (δ 4.21) to the C-5 carbon signal (76.2 ppm). Hydrolysis of **3** gave D-xylose and its aglycone platyphyllonol (**4**). Identity of **4** was confirmed by NMR, FABMS and $[\alpha]_D$ data (Ohta et al., 1985; Terazawa, Koga, Okuyama & Miyake, 1984). Absolute configuration of C-5 in **4** has been established previously as *S*. Absolute configuration of the xylose as D was determined by derivatization with (-)-2-butanol to give the (-)-2-butoxy xyloside which was analyzed by GC as its TMSi ether against D and L xylose reference compounds (Gerwig, Kamerling & Vliegenthart, 1978). An intense $[M-H]^-$ ion peak in the negative ion HR-FABMS at m/z 445.18586 ($C_{24}H_{29}O_8$ needs 445.18629) confirmed the molecular weight of **3** and identity as (*S*)-1,7-bis-(4-hydroxyphenyl)-heptan-3-one-5-*O*-β-D-xylopyranoside.

3. Experimental

NMR spectra were recorded at 300 MHz for ^{1}H and 75 MHz for ^{13}C on a Bruker AM300. Negative ion FABMS was done in a matrix of dithiothreitol and dithioerythritol using a Kratos model MS-5OTC



1 R_1 = β-D-glucopyranoside, R_2 = H
2 R_1 = β-D-glucopyranoside, R_2 = OH
3 R_1 = β-D-xylopyranoside, R_2 = H
4 R_1 = H, R_2 = H

instrument and optical rotations were done on a JASCO DIP-370 polarimeter. TLC on silica gel 60 using hexane–EtOAc–MeOH 2 : 2 : 1 (solvent A) was used to monitor isolations.

Red alder bark (voucher specimen deposited at Oregon State University Herbarium) was extracted with an acetone–water (7 : 3) and chromatographed over Sephadex LH-20 as previously described (Chen et al., 1998). The fraction eluted with methanol–water (1 : 4) was rechromatographed over Sephadex LH-20 with 50% aq. MeOH and then over silica gel 60 with solvent A to give 10 mg of **1** and 168 mg of **2**. The fraction eluted from the first chromatography of the bark extract over Sephadex LH-20 with MeOH–H_2O (2 : 3) was rechromatographed over silica gel 60 with solvent A and then over Sephadex LH-20 with 50% aq. MeOH. Final purification was done over Toyopearl HW-40 with 50% aq. EtOH to give 18 mg of **3**. Hydrolysis of **3** (12 mg) was carried out at 80°C for 2 h in 10% HCl. After neutralization, xylose was purified over a C-18 Sep Pak with H_2O, dried and derivatized with (-)-2-butanol (Aldrich) and analyzed as its TMSi ether on a DB-5 capillary column by GC (Gerwig et al., 1978). Authentic D- and L-xylose derivatives (Sigma) were used for standards. The aglycone **4** (4 mg) was extracted from the hydrolysate with EtOAc.

Compound **1**. R_f 0.41; $[\alpha]^{27}$ − 8.6° (*c* 0.44, MeOH); $[M-H]^-$ m/z 475; NMR spectral data (Smite et al., 1993; Ohta et al., 1984).

Compound **2**. R_f 0.23; $[\alpha]^{28}$ − 10° (*c* 1.14, MeOH); $[M-H]^-$ m/z 507; NMR spectral data (Ohta et al., 1985).

Compound **3**. R_f 0.52; $[\alpha]^{28}$ − 19.3° (*c* 0.20, MeOH); $[M-H]^-$ m/z 445; NMR spectral data, see Table 1.

Compound **4**. R_f 0.88; $[\alpha]^{26}$ − 3.3° (*c* 0.4, MeOH); $[M-H]^-$ m/z 313; NMR spectral data (Ohta et al., 1985; Terazawa et al., 1984).

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