Two New 15,16-Seco-cycloartane Glycosides from Cimicifuga Rhizome

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Two new 15,16-seco-cycloartane glycosides (1, 2) were isolated from Cimicifuga Rhizome. Their structures were determined by spectroscopic analysis.

Key words Cimicifuga Rhizome; cycloartane glycoside; Cimicifuga sp.; Ranunculaceae

Our study of the chemical constituents in Ranunculaceous plants resulted in the isolation of two new 15,16-seco-cycloartane glycosides (1, 2) from Cimicifuga Rhizome. Cimicifuga Rhizome, originated from a rhizome of the genus Cimicifuga plants, has been used as anti-inflammatory, analgesic and antipyretic remedies in Chinese traditional medicine. This paper describes the structural elucidation of the new cycloartanes based on 2D NMR spectroscopic analysis and hydrolysis. The H2O fraction of the MeOH extract was separated by MCI gel CHP20P, Sephadex-LH20 and silica gel column chromatographies and finally HPLC to give two compounds 1 and 2.

Compound (1) was obtained as a white needle, [α]D 31.2° (MeOH). The molecular formula of 1 was determined as C37H56O12Na by high resolution (HR)-FAB-MS showing a [C37H56O12Na]+ ion at m/z 715.3678. One cyclopropane methylene at δ 0.57 (d, J = 3.7 Hz) and 1.18 (d, J = 3.7 Hz), six quaternary methyls at δ 1.06, 1.33, 1.61, 1.67, 1.96 and 1.98, a secondary methyl at δ 1.05 (J = 6.8 Hz), an acetyl methyl at δ 2.10, an olefinic proton at δ 5.86 (brd, J = 6.8 Hz) and an anomeric proton at δ 4.88 (d, J = 7.6 Hz) on the 1H-NMR spectrum suggested 1 to be a cycloartane glycoside. On acid hydrolysis, 1 afforded D-xylose, the structure of which was confirmed by the 1H-NMR coupling pattern and optical rotation using chiral detection in the HPLC analysis, together with several unidentified artificial sapogenols. Thirty carbon signals due to the aglycon part observed along with a xylose and an acetyl unit in the 13C-NMR spectrum. The structural assignment was achieved by 1H–13C COSY, 1H-detected heteronuclear multiple quantum coherence (HMOC) and heteronuclear multiple bond connection (HMBC) experiments. The 1H–13C COSY and HMBC led us to the plane structure of 1 as an 24-acetoxy-15,16-seco-cycloart-7-en-3-O-xyloside (Fig. 1). The long-range correlations between an acetyl methyl proton (δ 2.10) and an acetyl carbon (δ 170.9); H-24 (δ 5.38) and C-25 (δ 71.6) and an acetyl carbon (δ 170.9); two singlet methyl protons (δ 1.61, 1.67) and C-25 (δ 71.6) and C-24 (δ 79.7) indicated the terminal structure on the side chain. Furthermore, the long-range correlation cross-peaks between H-28 (δ 1.96) and C-13 (δ 43.9), C-14 (δ 57.1), C-8 (δ 144.3) and C-15 (δ 177.8); H-18 (δ 1.98) and C-12 (δ 33.2), C-13 (δ 43.9), C-17 (δ 56.7) and C-14 (δ 57.1); H-17 (δ 2.88) and C-18 (δ 23.0), C-20 (δ 27.6), C-13 (δ 43.9) and C-16 (δ 173.2); H-23 (δ 5.35) and C-16 (δ 173.2) resulted in the C–C bond cleavage between C-15 and C-16, and the six-membered lactone ring between C-16 and C-23. The nuclear Overhauser effect (NOE) correlations, H-29/H-3 and H-5, H-30/H-19, H-19/H-18, H-18/H-22β and H-23, H-21/H-22α and H-17, H-28/H-17, H-23/H-27 and H-24/H-26 in the NOESY and NOEDS spectrum, suggested 3S, 13R, 14R, 17R, 20R and 23R configurations. The anomeric center of the xylose moiety was determined to be β-configuration from the large δJH1,H2 value. The 4C1-conformation of xylose was shown by comparison of the carbon resonances for monosaccharide. From the above evidence, the structure of 1 was elucidated except for the stereo configuration at C-24.

Compound (2) was obtained as a white needle, [α]D −39.8° (MeOH). The molecular formula of 2 was determined as C35H54O10Na by HR-FAB-MS showing a [C35H54O10Na]+ ion at m/z 657.3622. The 1H-NMR spectrum of 2 and 1 were almost identical, with the remarkable difference being the H-24 (δ 3.76) signal which was 1.62 ppm upfield, the appearance of the aldehyde (δ 9.85) signal and the disappearance of the acetyl signal. Meanwhile, in the 13C-NMR spectrum of 2, the signals due to the A-ring of the aglycon moiety and the sugar moiety were in good agreement with those of 1. On acid hydrolysis, 2 afforded D-xylose together with several unidentified artificial sapogenols. Furthermore, the HMBC showed long-range correlations between H-24 (δ 3.76) and C-25 (δ 72.5); two singlet methyl protons (δ 1.69, 1.74) and C-25 (δ 72.5) and C-24 (δ 80.0); H-28 (δ 1.62) and C-13 (δ 43.2), C-14 (δ 59.6), C-8 (δ 140.4) and C-15 (δ 200.4); H-18 (δ 1.56) and C-12 (δ 31.3), C-13 (δ 43.2), C-17 (δ 55.6) and C-14 (δ 59.6); H-17 (δ 2.74) and C-18 (δ 22.2), C-20 (δ 28.2), C-13 (δ 43.2) and C-16 (δ 173.8); H-23 (δ 5.15) and C-16 (δ 173.8). The above data suggested that 2 was accompanied with the disappearance of an acetyl group at C-24 and the presence of an alde-
hydride group at C-15 of 1. The NOE correlations, H-29/H-3 and H-5, H-30/H-19, H-19/H-18, H-18/H-15 and H-22β, H-20/H-22β and H-23, H-21/H-22α and H-17, H-28/H-17, H-23/H-27 and H-24/H-26, indicated that C-3, C-13, C-14, C-17, C-20 and C-23 of 2 had the same configurations as 1 had, respectively.

The 14R configuration of 1 was supported by the following 1H-NMR data. The H-18 and H-20 signals, which were observed at δ 1.56 and 2.21 in 2, were shifted to lower field to appear at δ 1.98 and 2.43, respectively, in 1 (Fig. 2). Meanwhile, the 24R configuration of 1 determined that the signal due to H-22α (δ 1.56) was shifted upfield by 0.37 ppm and the signal due to H-23 (δ 5.35) shifted downfield by 0.15 ppm in the latter compound, in a comparative study of the 1H-NMR spectrum of 1 with that of 2. These shifts were caused by the carbonyl group of an acetyl group at C-24 in 1 (Fig. 2). A similar shift pattern was observed in the 24R- and 24S-α-acetylhydroshengmanol analogous having a six-membered hemiketal between C-16 and C-23, a hydroxyl group at C-15 and an acetyl group at C-241) might biosynthetically cause C–C bond cleavage between C-15 and C-16.

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References and Notes
3) 1H-NMR spectrum of 1 (in pyridine-d$_5$) δ 1.36, 1.71 (each 1H, H-1), 2.00, 2.38 (each 1H, H-2), 3.53 (1H, dd, J = 3.8, 11.3 Hz, 3-H), 1.36 (1H, H-5), 1.64, 1.95 (each 1H, H-6), 5.86 (1H, brd, J = 6.8 Hz, H-7), 1.40, 2.10 (each 1H, H-11), 1.92 (2H, H-12), 2.88 (1H, d, J = 3.0 Hz, H-17), 1.98 (3H, s, H-18), 0.57, 1.18 (each 1H, d, J = 3.7 Hz, H-19), 2.43 (1H, m, H-20), 1.05 (3H, d, J = 6.8 Hz, H-21), 1.56 (1H, dd, J = 11.6, 13.8 Hz, H-22), 2.18 (1H, dd, J = 6.7, 13.8 Hz, H-22), 5.33 (1H, brd, J = 11.6 Hz, H-23), 5.38 (1H, brs, H-24), 1.67 (3H, s, H-26), 1.61 (3H, s), 1.96 (3H, s, H-28), 1.33 (3H, s, H-29), 1.06 (3H, s, H-30), 2.10 (3H, s, Ac), 4.88 (1H, d, J = 7.6 Hz, xyl H-1), 4.05 (1H, dd, J = 7.6, 8.7 Hz, xyl H-2), 4.18 (1H, dd, J = 8.7, 8.7 Hz, xyl H-3), 4.26 (1H, m, xyl H-4), 3.77 (1H, dd, J = 10.3, 11.4 Hz, xyl H-5), 4.40 (1H, dd, J = 5.0, 11.4 Hz, xyl H-5). 13C-NMR spectrum of 1 (in pyridine-d$_5$) δ: 31.0 (C-1), 29.7 (C-2), 88.1 (C-3), 40.5 (C-4), 41.4 (C-5), 22.4 (C-6), 118.0 (C-7), 144.3 (C-8), 20.2 (C-9), 28.8 (C-10), 25.0 (C-11), 33.2 (C-12), 43.9 (C-13), 57.1 (C-14), 177.8 (C-15), 173.2 (C-16), 56.7 (C-17), 23.0 (C-18), 28.6 (C-19), 27.6 (C-20), 25.3 (C-21), 36.1 (C-22), 75.7 (C-23), 79.7 (C-24), 71.6 (C-25), 26.6 (C-26), 28.2 (C-27), 24.8 (C-28), 25.7 (C-29), 14.1 (C-30), 21.0 (Ac), 179.9 (Ac), 107.5 (xyl C-1), 75.6 (xyl C-2), 78.7 (xyl C-3), 71.3 (xyl C-4), 67.2 (xyl C-5).
4) 1H-NMR spectrum of 2 (in pyridine-d$_5$) δ: 1.27, 1.69 (each 1H, H-1), 1.97, 2.33 (each 1H, H-2), 5.49 (1H, dd, J = 3.9, 11.2 Hz, 3-H), 1.29 (1H, H-5), 1.54, 1.93 (each 1H, H-6), 5.28 (1H, brd, J = 6.4 Hz, H-7), 1.29, 2.09 (each 1H, H-11), 1.84 (2H, H-12), 9.85 (1H, s, H-15), 2.74 (1H, d, J = 4.4 Hz, H-17), 1.56 (3H, s, H-18), 0.51, 0.92 (each 1H, d, J = 3.6 Hz, H-19), 2.18 (1H, m, H-20), 1.02 (3H, d, J = 6.8 Hz, H-21), 1.93 (1H, dd, J = 11.6, 13.0 Hz, H-22), 2.13 (1H, dd, J = 6.2, 13.0 Hz, H-22), 5.15 (1H, brd, J = 11.6 Hz, H-23), 3.76 (1H, brs, H-24), 1.69 (3H, s, H-26), 1.74 (3H, s, H-27), 1.62 (3H, s, H-28), 1.31 (3H, s, H-29), 1.05 (3H, s, H-30), 4.87 (1H, d, J = 7.3 Hz, xyl H-1), 4.06 (1H, dd, J = 7.3, 8.7 Hz, xyl H-2), 4.18 (1H, dd, J = 8.7, 8.7 Hz, xyl H-3), 4.26 (1H, m, xyl H-4), 3.77 (1H, dd, J = 10.2, 11.0 Hz, xyl H-5), 4.40 (1H, dd, J = 5.1, 11.0 Hz, xyl H-5). 13C-NMR spectrum of 2 (in pyridine-d$_5$) δ: 31.1 (C-1), 29.6 (C-2), 88.0 (C-3), 40.5 (C-4), 40.7 (C-5), 22.6 (C-6), 122.2 (C-7), 140.4 (C-8), 19.1 (C-9), 28.7 (C-10), 25.0 (C-11), 31.3 (C-12), 43.2 (C-13), 59.6 (C-14), 200.4 (C-15), 173.8 (C-16), 55.6 (C-17), 22.2 (C-18), 28.8 (C-19), 28.2 (C-20), 25.0 (C-21), 36.5 (C-22), 78.3 (C-23), 80.0 (C-24), 72.5 (C-25), 26.1 (C-26), 29.4 (C-27), 18.9 (C-28), 25.6 (C-29), 14.0 (C-30), 107.6 (xyl C-1), 75.6 (xyl C-2), 78.7 (xyl C-3), 71.3 (xyl C-4), 67.2 (xyl C-5).

Fig. 2. NOE Correlations of 1 in Pyridine-d$_5$.