A New Caffeoyl Conjugate from Erigeron Breviscapus

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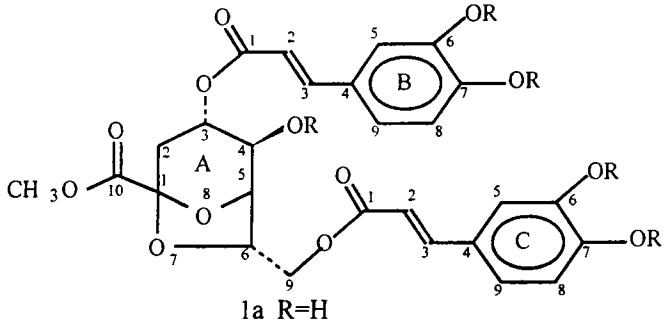
Abstract: Erigoster A (**1a**), a new compound with a novel basic skeleton, was isolated from *Erigeron breviscapus*. The structure elucidation and complete proton and carbon NMR assignments were achieved by the utilization of a combination of two-dimensional NMR techniques.



1a R=H
2a R=Ac

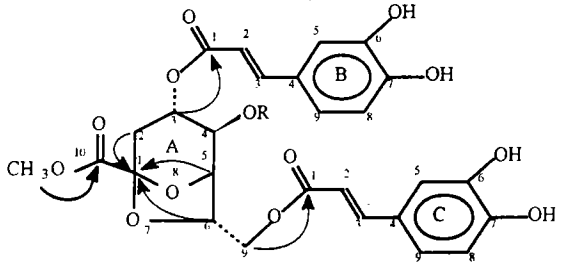


Fig.1 The COLOC spectrum of erigoster A

Erigeron breviscapus (Van.) Hand-Mazz (Compositae) is a well known drug in traditional Chinese medicine. The whole herb is used to treat a variety of paralysis and its sequelae originated from apoplexy and atherothrombosis of brain[1]. Previous research works [1,2] indicated that scutellarin in this plant was the bioactive constituent.

We thus examined the chemical constituents of this plant and reported the chemical constituents from the butanol soluble fraction of this plant [3]. This paper describes the isolation and structure elucidation of a new compound erigoster A (**1a**) from its ethyl acetate soluble fraction.

Erigoster A(**1a**) was isolated as a yellow amorphous powder (0.01% yield) with chemical composition $C_{27}H_{26}O_{13}$ deduced from ^{13}CNMR and MS(FAB^+, FAB^- and EI).The spectral data indicated the presence of hydroxyl groups (IR 3000-3600cm^{-1}), a methoxy group (^{1}HNMR 3.8ppm, s, 3H), three ester groups (IR 1750 and 1690cm^{-1}; ^{13}CNMR 169.30, 169.14 and 168.71 ppm). The ^{1}HNMR and ^{13}CNMR spectra indicated the presence of two caffeoyls. The spectra data mentioned above suggested that **1a** is most likely composed of one nucleus subunit A bearing two caffeoyl groups B and C. The determination of subunit A is the key step for the structural elucidation.

The structural elucidation and complete proton and carbon assignments were achieved by DEPT, ^{1}H-^{13}C correlation spectrum, ^{1}H-^{1}H COSY and COLOC techniques. The ^{1}H-^{13}C NMR correlation was performed to reveal the direct attachment between protons and carbons, and thus afforded an initial assignment of the protons in the subunits A, B and C. According to the chemical shifts of carbons and protons, the oxygen-bearing and non-oxygen-bearing carbons could be distinguished. The ^{1}H-^{1}H COSY was used to reveal the coupling correlation of the geminal and vicinal protons, and to determine the connectivity of carbons in subunit A. In the ^{1}H-^{1}H COSY, the H-4α proton signal correlating with the H-3ß and H-5ß proton signals indicated that C-4 methine is connected with the C-3 and C-5 methine groups. The H-3ß assuming geminal with a oxygen group has a very strong contour with the H-2ß, suggesting that it is connected with the C-2 methylene. The connectivity of the C-5 and C-6 was determined by the cross-peak between the H-5ß and H-6ß in the ^{1}H-^{1}H COSY. Both the C-5 and C-6 have respectively borne an oxygen group judging from their carbons and protons chemical shifts. The ^{1}H-^{1}H COSY contours between the H-6ß, H-9a and H-9b signals served to distinguish the connectivity of C-6 and C-9. The carbon and proton chemical shifts also indicated the C-9 bearing a oxygen group. It thus permitted the presence of a

six carbons connected partial structure -CH_2-CH-CH-CH-CH-CH_2- in the subunit A. The COLOC experiment was principally recorded to reveal the long-range correlations of three or/ and two bonds between the carbons and the correlated protons. and offered the opportunity to assign the quaternary carbons (Fig.1). The quaternary carbon at 169.30 ppm and the exclusive methoxy group at 57.37 ppm were assigned to a methoxycarbonyl (CH_3OOC-) which was attached to the C-1. The H-5ß and H-6ß correlating with the C-1 (104.55ppm) indicated the presence of ketal group. This was supported by the quaternary carbon at 104.55ppm and two tertiary carbons at 81.04 ppm and 78.34 ppm in the ^{13}CNMR spectrum [4,5]. The COLOC experiment also indicated that the two caffoeyl groups were located at the C-3 and C-9 respectively. This was supported by the downfield shifted signals of H-3ß, H-9a and H-9b due to the acylation shift effects. The planar structure of erigoster A (**1a**) was thus elucidated.

The relative configuration of 1a was assigned on the basis of the proton coupling constants and the NOESY spectrum of its penta-acetylated derivative. The coupling constant between H-2ß and H-3ß may indicated a preferred α-orientation for the caffeoyloxyl group at C-3 position. The C-4 hydroxyl likely take a ß-orientation judging from the correlating contour between the H-2ß and C-4-OAc in the NOESY spectrum of its penta-acetylated derivative (**1b**). The geometric stereoisomer of **1a** has been assigned as an endo-isomer by the coupling constant between the H-5ß and H-6ß ($J_{5,6}$=4.2Hz). If it were an exo-isomer. the H-5ß and H-6ß would be effectively decoupled since they form approximately a 90° dihedral angle [6].

The conformation of **1a** was also tentatively assigned on the basis of proton coupling constants. This assignment indicated that the six-membered ring of the subunit A take the chair conformation, and supported by the correlating between the H-2ß and C-4-OAc in the NOESY spctrum of its penta-acetylated derivative. The five-membered ring of subunit A definitely has a envelope conformation since it is combining with an six-membered ring which take a preferred chair conformation. A molecular model can be easily constructed according to the this conformation.

Erigoster A (**1a**). $C_{27}H_{26}O_{13}$ yellow amorphous powder, mp 126 °C. UV (nm): 203, 218, 234, 245,296 and 318. IR (cm^{-1}): 3000-3600 (-OH), 1750 (-$COOCH_3$), 1690 (caffeoyl), 1630 (double bond), 1600 and 1520 (aromatics). ^{1}HNMR (CD_3OD) δH (ppm), subunit A: 2.42 (1H,dd,J=15.3, 5.3Hz, H-2ß), 2.32 (1H, d, J=15.3Hz, H-2α), 5.46(1H,dd, J=5.3, 5.2Hz,H-3ß), 4.26 (1H,dd, J=5.2,4.8Hz, H-4α), 4.56 (1H,dd, J=4.8, 4.2Hz, H-5ß), 4.56 (1H,ddd, J=8.1,4.2,2.4Hz,H-6ß), 4.59 (1H,dd,J=11.0, 2.4Hz, H-9b) and 5.31 (1H, dd, J=11.0, 8.1Hz, H-9a) and 3.78 (3H, s,-OCH3); Subunit B:6.46 (d,J=15.8Hz, H-2), 7.65(d, J=15.8Hz, H-3), 7.10 (d, J=1.9Hz, H-5),6.76(d, J=8.1Hz, H-8) and 6.99 (dd, J=8.1, 1.9Hz, H-9). Subunit C: 6.35 (d, J=15.8Hz, H-2), 7.55 (d,J=15.8Hz, H-3), 7.18(d, J=1.9Hz, H-5), 6.81(d, J=8.1Hz, H-8) and 6.99 (dd, J=8.1, 1.9Hz, H-9). ^{13}CNMR (see table 1). FAB$^+$MS, 559 $[M+1]^+$. FAB$^-$MS 557$[M-1]^-$. EIMS,$[M]^+$(1%) 396$[M-162]^+$(5%), 378$[M-180]^+$(15%), 180, 163, 44 (100%).

Penta-acetate of erigoster A (**1b**), yellow gum. ^{1}HNMR (CD_3OD) δ (ppm), subunit A: 5.60 (1H,dd, J=5.2, 4.8 Hz, H-α), 5.38 (1H, dd, J=5.3, 5.2Hz, H-3α), 5.21 (1H, dd, J=11.1, 8.1Hz, H-9a), 4.71 (1H, dd, J=4.8, 4.2Hz, H-5ß), 4.60 (1H, ddd, J=8.1, 4.2, 2.4Hz, H-6ß), 4.53 (1H, dd, J=11.1, 2.4Hz, H-9b), 2.55(1H, dd, J=15.3, 5.3Hz, H-2ß), 2.33 (1H, d, J=15.3Hz, H-2α), 2.03 (3H, s, Ac); subunit B and C: 7.71, 7.65 (each 1H, d, J=15.8Hz, H-3), 7.55 (2H, s, H-5), 7.54, 7.51 (each 1H, d, J=8.1Hz, H-8), 7.25(each 1H, d, J=8.1Hz, H-9), 2.28, 2.27,2.26, 2.20 (each 3H, s, 4 x -Ac).

Table 1 ^{13}CNMR data of erigoster A

Carbons	A	B	C
1	104.50	169.14	168.70
2	38.80	115.63	114.79
3	67.92	147.32	147.16
4	67.77	127.86	127.86
5	81.04	115.31	115.31
6	78.34	146.70	146.70
7		149.47	149.47
8		116.39	116.52
9	64.10	123.07	123.37
10	169.30		
CH_3O-	53.37		

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