O-METHYLCIMIACEROL, A NEW TRITERPENE FROM CIMICIFUGA ACERINA

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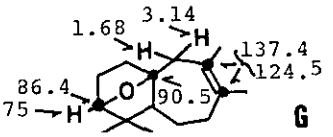
Abstract---The structure of O-methylcimiacerol, a new triterpene obtained from Cimicifuga acerina (Sieb. et Zucc.) C. Tanaka after hydrolysis of the glycosides, has been established by spectroscopic and X-ray crystallographic analysis.

In the course of the study of triterpenes obtained as aglycones on treatment of glycosides from Cimicifuga species with methanolic sulfuric acid, a new triterpene (1), named O-methylcimiacerol, was isolated along with acerinol, O-methylacerinol, acerionol and 24-O-acetylacerionol from C. acerina (Sieb. et Zucc.) C. Tanaka (Ranunculaceae, Japanese name : Ohobashôma).[1]
The physicochemical evidence indicates that this new compound belongs to a deformed triterpene skeleton, into which acerinol and its related compounds were grouped. The basic skeleton was deduced from physicochemical evidence of acerinol and its derivatives and by taking into consideration the general biosynthetic pathway of triterpenes, but the structure has not been clearly established until now.
O-Methylcimiacerol (1), colorless needles, mp 235 - 236°, $[\alpha]_D$ + 20.0° (c = 5.9, $CHCl_3$), was chosen for X-ray crystallographic analysis. Anal. Calcd. for $C_{31}H_{48}O_5$: C, 74.36; H, 9.66. Found : C, 74.36; H, 9.70. Mass spectrum showed ion peaks at m/e 500 (M^+), 485 (M^+-CH_3), 482 (M^+-H_2O). The presence of a hydroxy group was suggested by the IR absorption spectrum (3420, 1052 cm^{-1}).
The ^{1}H-NMR spectrum ($CDCl_3$, δ) of 1 displayed sharp singlets (0.91, 0.94, 0.95, 1.02 ppm, 3H × 4, four tertiary methyl groups, 1.30 and 1.32 ppm, 3H× 2, two tertiary methyl groups on carbon carrying an oxygen atom), a doublet (1.03 ppm, 3H, J = 6 Hz, a secondary methyl group), a pair of doublets (1.68 and 3.14 ppm, 1H each, J = 14 Hz, =C-CH_2-C-) and an unresolved doublet (3.75 ppm, 1H, J = 5 Hz, a hydrogen on carbon having an ethereal oxygen), along with additional signals of a methoxy group at 3.26 ppm, two hydrogens on carbon carrying ethereal oxygen at 3.37 ppm (d, J = 11 Hz) and 4.35 ppm (q, J = 8 Hz) and a carbinyl hydrogen at 3.81 ppm (d, J = 2 Hz, after the addition of D_2O, s). The ^{13}C-NMR spectrum($CDCl_3$-benzene-d_6) of 1 provided thirty-one signals, some of which could be assigned to the following partial structures.

137.4,124.5	109.5	55.6	90.5	86.4	83.9	85.5	76.8	73.2
>C=C<	>C(O)(OMe)		-C(O)-CH		>CH-O-C<		>CH-OH	>CH-O-
A	B		C		D		E	F

A pair of doublets at 1.68 and 3.14 ppm (1H each, J = 14 Hz) and a boublet at 3.75 (1H, J = 5 Hz) in the ^{1}H-NMR spectrum, and a pair of singlets at 137.4 and 124.5 ppm, a singlet at 90.5 ppm and a doublet at 86.4 ppm in the ^{13}C-NMR spectrum have been found similarly in those of acerinol and its related compounds, and attributed to the following partial structure G.[2]



G

The crystal for X-ray crystallographic analysis was obtained after recrystallization from a mixture of ethyl acetate - acetone and belongs to an orthorhombic space group $P2_12_12_1$. The cell parameters are a = 15.905(3), b = 18.235(3), c = 9.647 (3) Å, with V = 2797.9(1.3). The diffraction intensities were collected in the ω - scan mode using graphite monochromated MoKα radiation on a diffractometer and the data were corrected for Lorenz polarization and background effects.
The structure was resolved by direct methods using a Multan program and refined by full matrix least-squares calculations. The final R-factor was 0.0614 for 1898 reflections. The computer drawing of the molecule is shown in Fig. 1.
The final structure of 1 is depicted in Fig. 2.

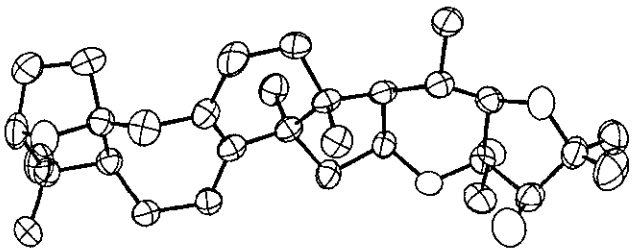


Fig. 1

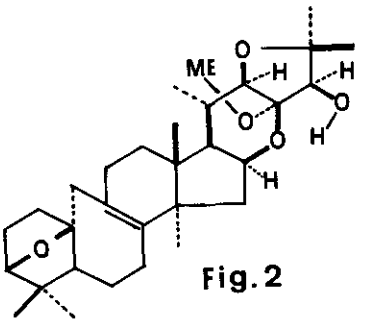


Fig. 2

Although O-methylcimiacerol (1) should be an artifact, this structural elucidation provides great contribution to clarify the structure of the genuine glycoside and strong support for the proposed structures of acerinol and its related compounds such as O-methylcimicifugenin A_2 obtained from the same plant and the several other species in the same genus. The last cimicifugenin A derivative showed strong inhibition of thymidine transport into phytohemagglutinin-stimutated lymphocytes.[3]

REFERENCES

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