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STRUCTURE ELUCIDATION OF A MIXTURE OF TWO NOVEL ISOMERIC SESQUITERPENOIDS

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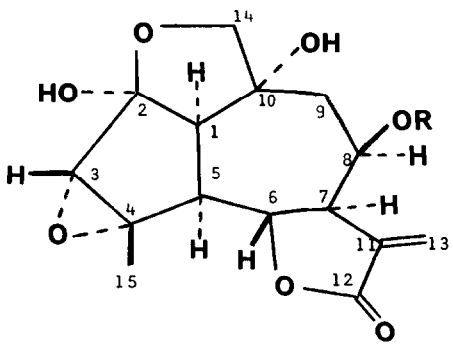
In a search for biologically active natural products, several new metabolites have been isolated from Eupatorium anomalum Nash. X-ray diffraction and spectroscopic investigations of a crystalline material of composition $C_{20}H_{26}O_8$ (mp 152-3°) have established that it is a mixture of two novel sesquiterpenoid lactones with isomeric ester side chains 2-methylbutanoate (major component, 1) and isovalerate (minor component, 2).



1 R = $COCHMeCH_2Me$

2 R = $COCH_2CHMe_2$

The esters co-crystallize, in ca. 2:1 ratio, in the orthorhombic space group $P2_12_12_1$ with cell dimensions a = 6.849(3), b = 28.479(7), c = 21.659(5) Å. The X-ray intensities were

measured with Mo-Kα radiation on a computer-controlled four-circle diffractometer. The crystal structure was elucidated by direct phasing methods and the atomic parameters were adjusted by least-squares calculations. Currently, R is 0.078 for 2630 reflections. The asymmetric crystal unit comprises two $C_{20}H_{26}O_8$ molecules linked by a water molecule.

The electron-density distribution obtained in the X-ray analysis was interpreted in terms of structure (1). However, the unusual spread of electron density, and concomitant high thermal parameters, associated with the terminal atoms of the ester side chain in both molecules of the asymmetric crystal unit, together with the difficulty in assigning some ^{13}C and ^{1}H NMR signals, indicated the possible co-existence of isomers or homologues.[1] The high-resolution mass spectrum showed only one molecular ion $C_{20}H_{26}O_8$, with no evidence of a lower homologue, and a peak C_5H_9O corresponding to the methylbutanoyl ion is very strong. Both the ^{1}H and ^{13}C NMR spectra showed signals characteristic of $COCHMeCH_2CH_3$ and $COCH_2CHMe_2$.

Spectroscopic data

IR (KBr pellet)

3500(OH), 1780 and 1670 (α,β-unsatd. γ-lactone), 1735 cm^{-1} (ester).

^{1}H NMR

2.63d (10, H-1), 3.50 (H13), 2.90dd (10, H-5), 4.49dd (12, 9, H-6), 3.06m (9, 3.5, 3, 3, H-7), 5.69m (H-8), 2.33m (H-9), 6.32d (3.5, H-13a), 5.55d (3, H-13b), 4.32d (12, H-14a), 4.10d (12, H-14b), 1.64 (3p, H-15)

α-methylbutyrate side chain: 2.4m (H-2'), 1.46m, 1.6m (H-3'), 0.89t (7, H-4'), 1.10d (7, H-5)

isovalerate side chain: 2.1m (H-2"), 2m (H-3"), 0.94d, 0.91d (H-4", H-5").

^{13}C NMR

58.02d (C-1), 114.23 (C-2), 64.63d (C-3), 65.97 (C-4), 51.26d* (C-5), 75.36d (C-6), 49.81d* (C-7), 65.78d (C-8), 38.62t (C-9), 81.88 (C-10), 134.03 (C-11), 168.16 (C-12), 122.21t (C-13), 60.49t (C-14), 19.01q (C-15)

α-methylbutyrate side chain: 175.35 (C-1'), 41.37d (C-2'), 26.61t (C-3'), 11.60q (C-4'), 16.83q (C-5')

isovalerate side chain: 171.65 (C-1"), 43.44t (C-2"), 25.66d (C-3"), 22.31q (C-4", C-5")

* Assignments may be interchanged

The pure 2-methylbutanoate ester (anomalide, mp 152-3°) has subsequently been isolated in Florida from Eupatorium mohrii Greene.

References

[1]S.F. Watkins, J.D. Krop, I. Bernal, D.L. Perry, N.S. Bhacca and N.K. Fischer, J.C.S. Perkin II, 599, 1978

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