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MEBADONIN, A NEW ENT-KAURANE DITERPENOID FROM ISODON KAMEBA OKUYAMA

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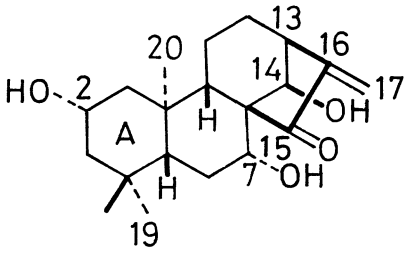
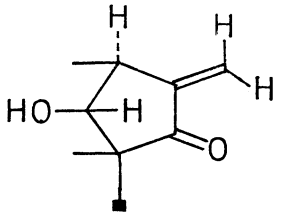
Mebadonin was isolated from Isodon Kameba Okuyama and the crystal and molecular structure were determined by means of X-ray analysis.

Mebadonin (1) was isolated from an ether extract of the dried leaves of Isodon Kameba Okuyama. After treatment of the ether extract with activated charcoal, the residue was chromatographed on silica gel. Elution with chloroform-methanol mixture yielded crystalline mebadonin (1), $C_{20}H_{30}O_4$, mp 271-273° (dec), $[\alpha]_D$ -158° (c 1.0, dioxane). It showed the following spectral data: λmax (EtOH) 232 nm (ε 8230); νmax 3240 (OH), 1730 (α,β-unsat. ketone), and 1640 cm^{-1} (double bond); δ ($CDCl_3$-C_5D_5N) 0.89, 1.06 and 1.46 (each 3H, s, tert-CMe), 3.08 (1H, m, H_{13}), 4.1 (1H, m, $W_{1/2}$ 16 Hz, H_2), 4.48 (1H, dd, J=10.5 and 5.5 Hz, H_7), 4.96 (1H, d, J=1 Hz, H_{14}), 5.29 and 5.87 ppm (each 1H, t, J=1 Hz, exocyclic methylene). Decoupling experiments demonstrated the presence of the partial structure (2). Furthermore, an ent-kaurane skeleton has been suggested for mebadonin from the analogy with congeners[1]. Because of the small amount of sample available it was decided to derive the structure by the X-ray diffraction method.



(1)



(2)

The crystals, $C_{20}H_{30}O_4$, are orthorhombic, space group $P2_12_12_1$; a=7.11 (1), b=13.66 (1), c=18.33 (1) Å; Dx=1.26 g/cm^3 (Z=4). Integrated Weissenberg intensity data were collected by means of Cu Kα radiation for seven layers on the a axis and three layers on the c axis. The independent 2100 reflections were observed but no corrections were made for absorption and extinction. Several sets of phases were obtained by the symbolic addition procedure followed by the tangent refinement[2]. An E-map was calculated by the use of 397 reflections with the phases in the most consistent set, and a suitable trial structure was derived. The positions of all the non-hydrogen atoms were easily located and refined by a least-squares method. When for the non-hydrogen atoms the anisotropic temperature factors were assigned, the conventional R factor was reduced to 0.098.

The structural and conformational features of the mebadonin molecule are illustrated in Fig. 1. The ring junction A/B is trans, while B/C is cis. The points of interest in the structure are the conformation of the ring A and the apparent crowding of C_{20} methyl group surrounded by C_{12}, C_{14} and C_{19} atoms. Because of strong 1,3 non-bonded interactions, intramolecular distances, C_{20}---C_{12}=3.47 Å, C_{20}---C_{14}=3.37 Å and C_{20}---C_{19}=3.38 Å, are all greater than 3.0 Å, so that the bond angles and torsional angles in rings A, B and C deviate from ideal values[3]. The ring A has a skew boat conformation with the ring torsional angles ranging from 24° to 65°, to avoid the strong steric strains which would be expected between C_{20} and C_{19}, and C_{20} and O_{21} in the case of chair conformation. The ring B is in a slightly distorted chair conformation with the ring torsional angles varying between 50° and 63°. The ring C has also a chair conformation, but distortion is more distinct, since C_8, C_{14} and C_{13} are also the members of a 5-membered ring. C_8, C_9, C_{12} and C_{13} are coplanar within 0.04 Å, and C_{11} and C_{14} deviate by 0.50 Å and 0.86 Å, respectively, towards the different direction from this plane. The ring D has the envelope conformation; C_8, C_{13}, C_{15}, C_{16}, C_{17} and O_{24} are coplanar within 0.03 Å and C_{14} is by 0.66 Å out of the plane.

The molecular packing and hydrogen bonding in mebadonin are shown in Fig. 2. An intramolecular hydrogen bond was formed between O_{22} and O_{23} (2.613 Å). Two intermolecular separations, O_{21}---O_{22} of 2.719 Å and O_{21}---O_{23} of 2.734 Å correspond to hydrogen bonds which link the molecules in layers parallel to (0 1 0) plane.

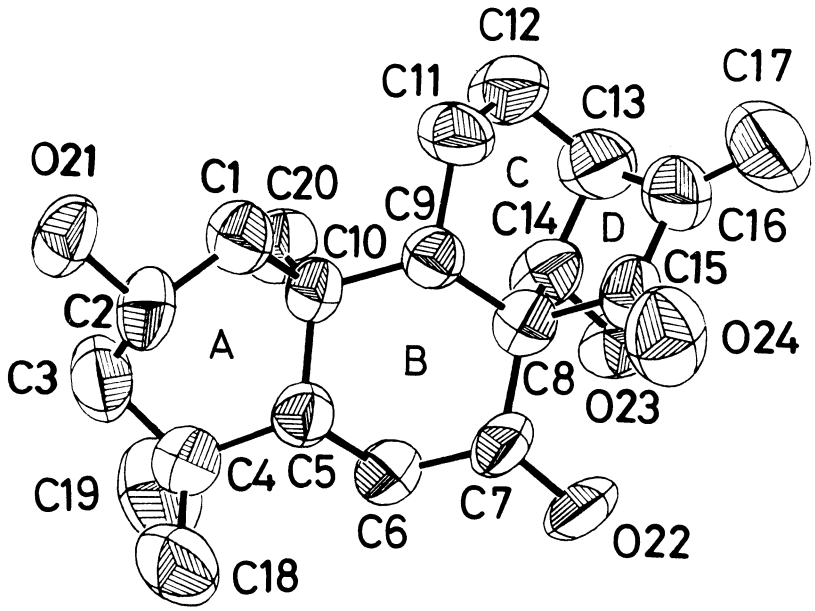


Figure 1. The molecular structure of mebadonin.

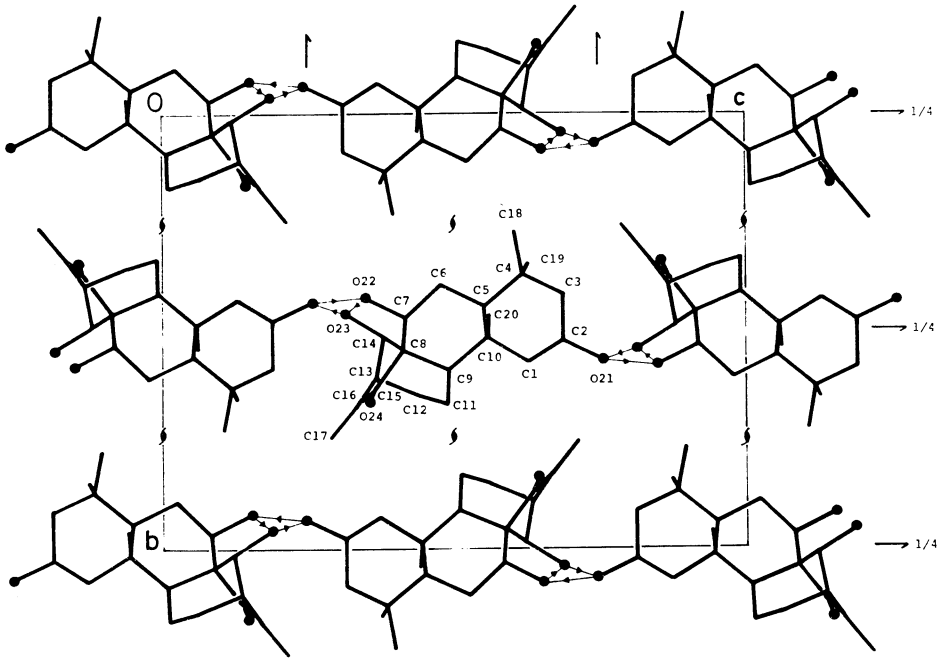


Figure 2. Molecular packing and hydrogen bonding as viewed down the a axis.

Mebadonin is of interest in that it is the first instance of an ent-kaurane type diterpenoid having the intact C_{20} methyl group, while all the other known kaurane type diterpenoids (about 25) isolated from Isodon species are oxygenated at C_{20}[1]. Also a C_2 oxygenated ent-kaurane diterpenoid has not been found previously in Isodon species.

References

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