HYPOESTOXIDE, A NEW DITERPENE FROM HYPOESTES ROSEA (ACANTHACEAE)

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Abstract - Hypoestoxide, a new diterpene from Hypoestes rosea (Acanthaceae) has been assigned the bicyclo[9,3,1]pentadecane structure 1.

Recent studies from our laboratories have led to the isolation of two new diterpenes from Hypoestes rosea (Acanthaceae)[1,2]. We now wish to report the isolation and structural determination of another new bicyclo[9,3,1]pentadecane diterpene, hypoestoxide (1) from the same plant.

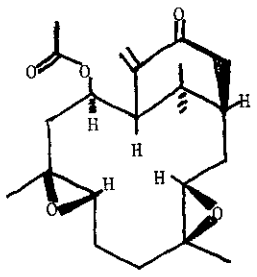
The gum (53.6g) obtained after removal of solvent from the hexane extract of the aerial parts of H. rosea (2.5 kg) was chromatographed on silica gel, eluting with increasing concentrations of diethyl ether in hexane. Elution with 30% diethyl ether in hexane gave hypoestoxide (1.02g). Hypoestoxide crystallized from hexane: ethyl acetate as small colorless needles, mp 257-259°C, $[\alpha]_D^{20}$ + 75.9° (c=0.55 $CHCl_3$). The high resolution mass spectrum of hypoestoxide indicated the molecular composition $C_{22}H_{32}O_5$, as evidenced by a molecular ion peak at m/e 376.2317. The mass spectrum (chemical ionization) showed significant ions at m/e 377 ($C_{22}H_{33}O_5$, M^+ +1, 15%), 317 ($C_{20}H_{29}O_3$, M^+ +1-CH_3COOH, 67), 299 ($C_{20}H_{27}O_2$, M^+ +1-CH_3COOH-H_2O, 61), 281 ($C_{20}H_{25}O$, M^+ +1-CH_3COOH-$2H_2O$, 21), 205 (55), 189 (57), 187 (78), 163 (88), 161 (80), 149 (61), 137 (83), 135 (96), 109 (73), 107 (71) and 93 (100). Elemental analysis[1] of hypoestoxide also indicated the molecular composition $C_{22}H_{32}O_5$ (Found C 69.96, H 8.79; $C_{22}H_{32}O_5$ required C 70.18, H 8.57). The uv spectrum of 1 (λ_{max}^{EtOH} 235, ϵ_{max} 8500) was indicative of the presence of an α,β-unsaturated carbonyl function. The ir specturm of 1 (KBr, cm^{-1}) had absorptions that were indicative of ester (1736, 1235) and α,β-unsaturated ketone (1689, 1613) groups. The ^1H nmr spectrum of hypoestoxide (δ, $CDCl_3$) contained signals for two tertiary methyl groups (1.07 and 1.18, each s, 3H), two methyl groups each attached to a fully substituted carbon bearing an oxygen function (1.27 and 1.44, each s, 3H), an acetoxy group (2.08, s. 3H), a methine proton of a secondary acetoxy group (5.50, br dd, J = 10 and 1Hz, 1H) and an exocyclic methylene group (5.69 and 6.06, each d, J = 1Hz, 1H). The ^{13}C nmr ($CDCl_3$, δ in ppm down field from Me_4Si) spectrum of hypoestoxide provided useful additional information on the structure of hypoestoxide. It confirmed the presence of the carbonyl groups of the enone and the acetoxy

functions (s at 202.4 and 169.8 ppm respectively), the exocyclic methylene group (t at 123.6 ppm) and the five methyl groups (including that of the acetoxy group) as quartets at 16.0, 16.7, 21.3, 24.6 and 27.3 ppm. The carbon attached to the exocyclic methylene group and the secondary carbon bearing the acetoxy group appeared respectively as a singlet at 143.2 ppm and a doublet at 69.0 ppm. There were also signals for two secondary and two tertiary oxygen-bearing carbon atoms at 59.5 (s), 61.8 (d), 61.9 (s), and 63.4 (d) ppm indicating the presence of two ether rings in hypoestoxide. In addition there were signals due to five methylene groups (t at 23.9, 31.4, 36.1, 42.2 and 42.8 ppm), two tertiary carbons (d at 44.9 and 46.5 ppm) and one quaternary carbon (s at 37.1 ppm).

The molecular formula of hypoestoxide and the preceeding spectral data indicated that the compound contained four rings. Hypoestoxide must therefore have two carbocyclic rings, since the ^{13}C nmr has indicated the presence of two ether rings.

The x-ray crystallographic analysis of hypoestoxide was undertaken for an unambiguous determination of its structure. The crystal had the space group $P2_1$ (monoclinic) with cell constants a = 9.189 (3) Å, b = 14.005 (6) Å, C = 9.165 (7) Å, β = 116.5 (3)°. The intensities of 2150 reflections were measured on Enraf-Nonius CAD_4 diffractometer using graphite-monochromated Mo-kα radiadiation of which 759 reflections had $I > 2.3\sigma(I)$. The structure was solved by MULTAN 79; preliminary refinement with isotropic temperature factors yielded R = 0.174. An ORTEP drawing of 1 (Figure 1) shows a puckering of the 12-membered ring in order to alleviate steric crowding among the three protons on the interior of the ring (H's on C1, C5, and C9).

Hypoestoxide is thus the third example of a naturally occurring diterpene having a bicyclo [9,3,1] pentadecane skeleton. This uncommon diterpene skeleton consisting of a cyclohexane ring fused to a 12-membered carboxycylic ring had previously been encountered only in verticillol[3] and cleomeolide[4,5].



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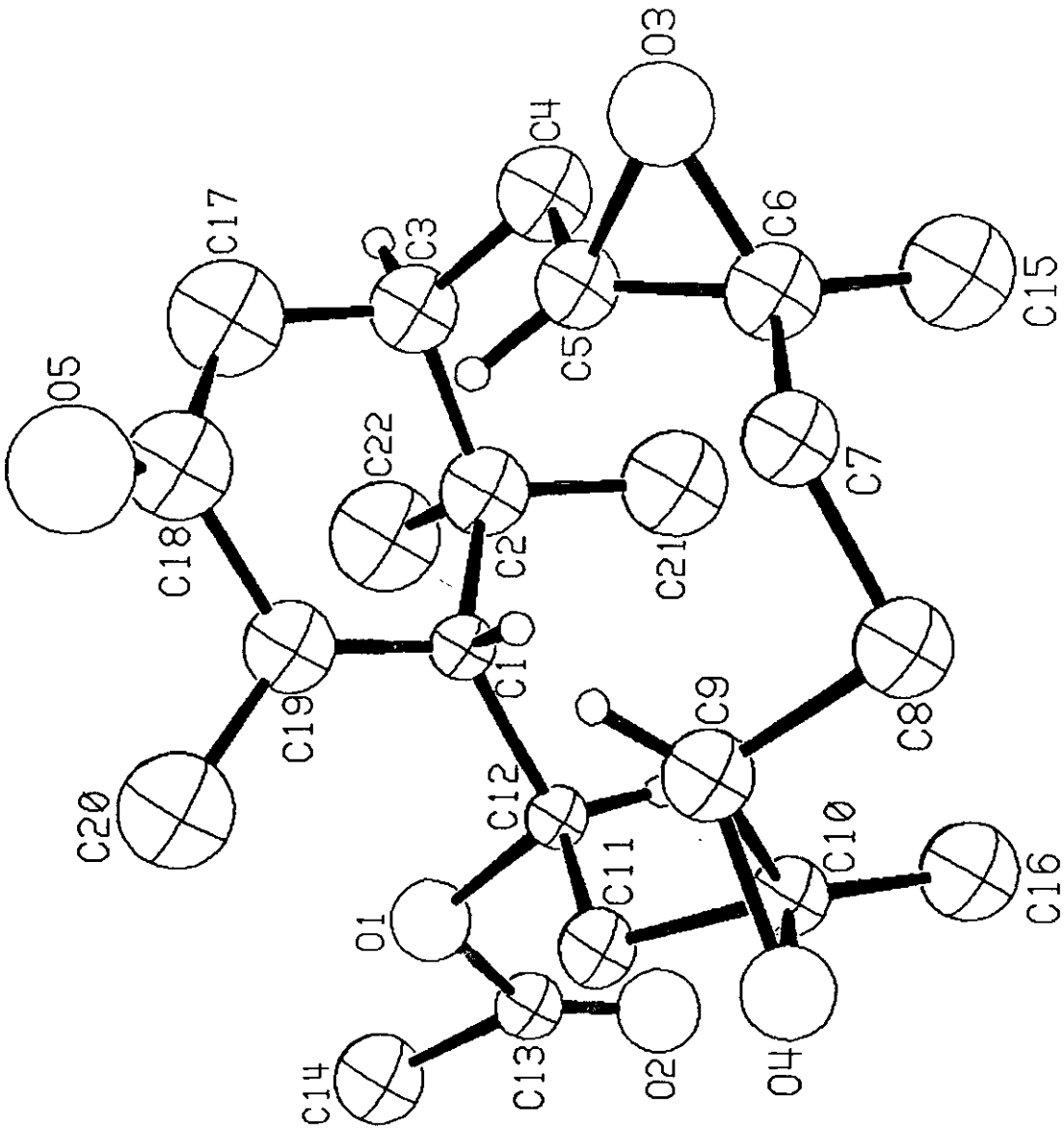
O3
C4
C17
C3
C6
C15
O5
C5
C22
C7
C18
C2
C21
C10
C19
C9
C8
C20
C12
C11
C10
C16
O1
O2
O4
C14
C13

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REFERENCES

1. J. I. Okogun, A. A. Adesomoju, G. A. Adesida, H. J. Lindner, and G. Habermehl, Z. Naturforsh., 1982, 37c, 558.

2. A. A. Adesomoju, J. I. Okogun, M. P. Cava, and P. J. Carroll, Phytochemistry, in press.

3. B. Karlsson, A. Pilotti, A. Soderholm, T. Norin, S. Sundin and M. Sumimoto, Tetrahedron, 1978, 34, 2349.

4. S. B. Mahato, B. C. Pal, T. Kawasaki, K. Miyahana, O. Tanaka and K. Yamasaki, J. Am. Chem. Soc., 1979, 101, 4720.

5. B. A. Burke, W. R. Chan, V. A. Honkan, J. F. Blount and P. S. Manchand, Tetrahedron, 1980, 36, 3489.

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