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ISOBHARANGIN, A NEW BIOGENETICALLY SIGNIFICANT DITERPENOID QUINONEMETHIDE FROM PYGMACOPREMNA HERBACEA (ROXB.) MOLDENKE

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Abstract - Isobharangin isolated from the hexane extract of the root nodules of the Ayurvedic drug, Pygmacopremna herbacea (Roxb) Moldenke has been shown to be 3β(R),11-dihydroxy-5,7,9,13-abietatetraene-2,12-dione (1) unequivocally from a consideration of its mass spectrum, UV, IR, ^{1}H NMR and CD spectra, long range couplings in its ^{13}C NMR spectrum and its 2D NOESY spectrum. It represents the first naturally occurring diterpenoid quinonemethide derived from an abietane skeleton with an unusual substitution pattern.

The isolation of three pigments designated bharangin, isobharangin and bharanginin from the hexane extract of the root nodules of the Ayurvedic drug, Pygmacopremna herbacea (Roxb) Moldenke syn. Premna herbacea (Roxb)(Verbenaceae, Telugu: Gantubharangi) and structure elucidation of bharangin[1] and bharanginin[2] have been reported earlier. Isobharangin, brown solid, m.p.74-76°C (petroleum ether,40-60°), $[\alpha]_D^{26}$=-465° (c,0.115,$CHCl_3$) and molecular formula,$C_{20}H_{24}O_4$(M^+,328.1674) is isomeric with bharangin[1]. Its UV absorption λ_{max}(Methanol):418 nm (log ε 3.64);IR absorptions (KBr ν_{max} :1598 cm^{-1}(>C=O,quinonemethide), 3308 cm^{-1}(-OH attached to quinonemethide, ^{1}H NMR absorption: δ7.82, exchangeable with D_2O) and ^{13}C NMR absorption 22.5 MHz:178.63(dd,>C=O,quinonemethide) compare closely with the corresponding data of 15-deoxyfuerstion[3], fuerstion and 3 β -acetoxyfuerstion[4]. The signals at 6.98(s,1H); 6.78(d,J=6.8Hz,1H);6.58(d,J=6.45Hz,1H);3.15 (septet,J=6.6Hz,1H);1.18(d,J=6.1Hz,3H);1.19(d,J=6.1Hz,3H);1.55(s,3H);1.49(s,3H);1.12(s,3H) in the ^{1}H NMR spectrum ($CDCl_3$, chemical shifts in δ values with TMS as internal standard) of isobharangin compare closely with those of the protons at carbon atoms 14,7,6,15,16,17,18,19 and 20 respectively of 15-deoxyfuerstion[3]. Thus, the structural features of rings B and C and the gem-dimethyl group of ring A of 15-deoxyfuerstion are preserved in the structure of isobharangin and this is confirmed by the proximity of corresponding chemical shifts and multiplicities of its ^{13}C NMR signals with those of bharangin[1] and 3 β-acetoxyfuerstion[4].

The molecular formula of isobharangin results by the addition of two oxygen atoms to and subtraction of two hydrogen atoms from that of 15-deoxyfuerstion ($C_{20}H_{26}O_2$)[3]. The presence of a second hydroxy absorption at 3480 cm^{-1} and another carbonyl absorption at 1715 cm^{-1} in the IR spectrum of isobharangin is confirmed by the signal at 3.76 (exchangeable with D_2O) in the ^{1}H NMR spectrum and carbonyl signal at 209.19 (s,br)[5] in its ^{13}C NMR spectrum suggesting that two methylene groups of ring A of 15-deoxyfuerstion are modified to a six membered ketone and a secondary hydroxy group in its structure. The contiguity of the carbonyl and hydroxyl functional groups and the location of the carbonyl group at C-2 in ring A of isobharangin is inferred from the presence of a signal at 4.14(s) assignable to the methine proton of a carbon atom carrying a secondary hydroxyl group and an AB quartet for the methylene protons adjacent to a carbonyl group (4.09,d and 2.70,d,J=14Hz) in its ^{1}H NMR spectrum[5]. The hydroxyl group has been placed

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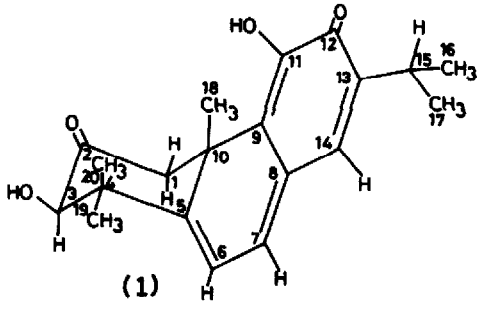
unambiguously at C-3 in preference to C-1 in the structure of isobharangin (1) since, the methylene carbon atom adjacent to the carbonyl group exhibited long range ^{3}J coupling with the protons of the methyl group at C-10 (18-CH_3) in addition to the ^{1}J couplings in its ^{13}C NMR spectrum (46.16,ddq,^{1}J=ca. 126 and ca. 141Hz and ^{3}J-3.7Hz). The chemical shift and multiplicity



(1)

of the carbon atom carrying the secondary hydroxyl group (80.24,d,J=150.1Hz) and those of the remaining carbon atoms[1,4] at C-4 (47.62,septet,^{3}J=5Hz); C-5 (158.86,s,br); C-6 (120.93,d,^{1}J=159.9Hz); C-7 (136.70,dd,^{1}J=162.4Hz and $^{3}J_{H-14}$=5Hz); C-8 (125.21,s,br); C-9 (128.30,dd,^{3}J=2.4 and 6.1Hz); C-10 (46.11,s,br); C-11 (146.34,s); C-12 (178.63,dd,$^{3}J_{H-14}$=6.7Hz,$^{3}J_{H-15}$=2.7Hz); C-13 (142.49,m); C-14 (133.29,dt,^{1}J=158.7Hz and $^{3}J_{H7}$=$^{3}J_{H-15}$=6.1Hz); C-15 (27.04,doublet of septets, ^{1}J=125.6Hz,^{3}J=6.1Hz); C-16 and C-17 (21.89,qq,^{1}J=125.6Hz,^{3}J=5Hz); 6-18 (24.06,qt,^{1}J=129.0Hz, ^{3}J=5Hz); C-19 (27.52,qq,^{1}J=130.5Hz,^{3}J=5Hz); C-20 (28.01,qq,^{1}J=125.6Hz,^{3}J=5Hz) in the ^{13}C NMR spectrum of isobharangin confirm structure (1) assigned to it. The absolute configurations of the methyl group at C-10 position (S) and the hydroxy group at C-3 position (R) in the structure of isobharangin are the same as those of 3β-acetoxyfuerstion[4] in view of the similarity of their CD spectra [1,4]. Chair conformation for the ring A of isobharangin (1) has been inferred from a consideration of the cross signals noticed between 18β-CH_3 (1.55,axial) and 20β-CH_3 (1.12,a); 19α-CH_3 (1.49,equitorial) and 3α-H (4,14,a); 3α-H and 1α-H (2.70,a); 1β-H (4.09,e) and 18β-CH_3 and 19α-CH_3 and 6-H (6.58) in its 2D NOESY spectrum (H....H)[6]. The mass spectrum of isobharangin showed intense ions (EIMS,70eV) at m/z(%), 328(M^+,16), 257(25), 256(93), 229(30), 228(100), 213(26) and 185(10). Isobharangin is the first of the abietane group of diterpenoid quinonemethides with the ring A modified to a vicinal-hydroxy-keto system. Examples of similar pattern of ring A substitution system in the other class of diterpenoids have been, however, encountered earlier[5,7,8,9].

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