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PRAXEROL, A NEW 9,10-DIHYDROPHENANTHRENE DERIVATIVE ISOLATED FROM *DIOSCOREA PRAINII*

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Abstract - Chemical investigation of the yam of *Dioscorea praineri* yielded a novel phenolic 9,10-dihydrophenanthrene derivative, designated as praxerol. The structure of this compound was settled as (1) from detailed chemical and spectroscopic investigations. The 2,3,4,5,6-penta oxygenation pattern of a 9,10-dihydrophenanthrene has not been reported previously.

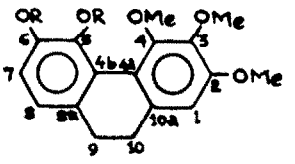
INTRODUCTION

Dioscorea praineri Prain and Burk (Dioscoreaceae) grows abundantly in the Darjeeling terai and other North Bengal regions in West Bengal[1] and is reported to contain Diosgenin ranging from 2 to 4.5%[2,3]. However the existing commercial methods for the isolation of diosgenin upto the desired limit of purity fail due to the presence of interfering oily and waxy substances. In the course of our investigation for an improved method for the commercial utilization of diosgenin from *D. praineri*, we have isolated a new 9,10-dihydrophenanthrene derivative, designated as praxerol, from the petroleum ether extract of the yams.

RESULTS AND DISCUSSION

Praxerol, $C_{17}H_{18}O_5$ (M^+ 302), m.p. 144-45°c, exhibited UV absorption maxima at 218 and 276 nm (log ε 4.64 & 4.32). Characteristic colour reaction with $FeCl_3$, coupled with alkali induced bathochromic shift of UV absorption maxima [$\lambda_{max}^{0.1(N)NaOH/EtOH}$ 230 and 300 nm; log ε 4.47 & 4.20] and appearance of IR absorption bands at 3100 and 3400 cm^{-1} indicated the presence of phenolic hydroxyl groups in the molecule. This was further confirmed by the appearance of two singlets at δ 6.05 and δ 8.98, exchangeable on deuteration in its 300 MHz ^1H NMR spectrum in $CDCl_3$. The low field value of one of the phenolic hydroxyl signals indicated its hydrogen bonding to a neighbouring oxygen. The ^1H NMR spectrum also exhibited signals for three aromatic protons (δ 6.69,1H, s, and an AB system at δ 6.71 and δ 6.78, J = 7.9 Hz) and three aromatic methoxyls (δ 3.71, δ 3.83 and δ 3.87). The 75.5 MHz ^{13}C-NMR spectrum of praxerol not only confirmed those features but also revealed that the benzylic proton signals at δ 2.59(4H,br,s) were associated with two methylene groupings of the 9,10-dihydrophenanthrene nucleus[4].

Formation of a diacetyl derivative (2), $C_{21}H_{22}O_7$, m.p. 128-32°c, with acetic anhydride/pyridine and dimethyl ether (3), $C_{19}H_{22}O_5$, with methyl iodide/KOH in DMSO confirmed the presence of two phenolic hydroxyl groups in praxerol.



1 : R = H
2 : R = Ac
3 : R = Me

The mass fragmentation pattern of praserol was not very informative showing only minor consecutive losses of methyl [m/z : 302 (M^+, base peak), 287, 272]. The diacetate exhibited consecutive losses of ketene from its molecular ion [m/z : 386 (M^+), 344 (M^+-42), 302(M^+-84, base peak)].

The absence of any aromatic proton signals beyond δ 8.00 in ^{1}H NMR spectrum of praserol suggested that both C_4 and C_5 positions were substituted[5,6] and this was further confirmed by the failure of its diacetate to undergo dehydrogenation with DDQ in boiling benzene[7].

Acetylation caused the AB system of the aromatic protons to move downfield, while the chemical shift of the singlet at δ 6.57 moved only slightly upfield. This indicated that the two hydroxyl groups were on the same aromatic ring and hence either ortho or para oriented. Further, acetylation caused the deshielding of one of the methoxyl signals by about 0.3 ppm. This is only possible if praserol is a 4-methoxy-5-hydroxy-9,10-dihydro-phenanthrene derivative. The substitution pattern in ring-C should, therefore, be either 5,6- or 5,8-dihydroxy. The 5,6-dihydroxy pattern was confirmed from XHCORR spectrum optimised for a long range coupling (J = 7 Hz)[8,9], enhancing particularly the 3-bond couplings in aromatic systems.

All these data along with the analysis of 300 MHz ^{1}H NMR, 75.5 MHz ^{13}C-NMR (both broadband decoupled and fully coupled and two dimensional heteronuclear shift correlation) spectra[8,9] of praserol, its diacetate and dimethyl ether finally established the substitution pattern in praserol as (1). The XHCORR pulse sequence with parameters optimised for one bond coupling as well as long range couplings in separate experiments was used to obtain 2D-spectra[9]. The position of the third aromatic proton appearing as singlet at δ 6.53 of the dimethyl ether was also established from the XHCORR (long-range)2D-spectrum (Fig I). This proton exhibited long range coupling with the quaternary carbons at δ 152.41 (C_2), δ 140.79 (C_5) and δ 118.64 (C_{4a}) and the methylene carbon at δ 31.32. The corresponding carbon at δ 105.99 showed 3-bond coupling with the benzylic protons at δ 2.49-2.58. This would be possible only if the third aromatic proton was attached to C_1. The 2D-XHCORR spectra for long range couplings of praserol dimethyl ether (3) is shown in Fig 1. In the dimethyl ether, one of the protonated aromatic carbons (δ 121.06) in ring-C showed a 3-bond coupling with benzylic protons indicating its ortho-position to the benzylic group and hence confirming the 5,6-substitution pattern of this ring. Further in the coupled spectra of all these compounds each of the benzylic carbons showed a quartet, fine splitting of each triplet signal, indicating 2-bond coupling with the adjacent methylene as well as a 3-bond coupling with an ortho proton. These NMR data confirmed the substitution pattern in praserol and its derivatives. The complete ^{13}C-NMR assignments and various C-H correlations both 1-bond and long-range as expressed by coupling data are shown in Table 1.

Table 1. Chemical Shifts[a](δ) and coupling constants[b] of prazerol (1), its diacetate (2) and dimethyl ether[c] (3)

Carbons	Prazerol	Prazerol diacetate	Prazerol dimethyl ether
C-1	109.07 dt ^1J = 158.2 $^3J_{(10)}$ = 2.2	106.76 dt ^1J = 158.6 $^3J_{(10)}$ = 3.8	105.99 dt ^1J = 158.2 $^3J_{(10)}$ = 2.2
C-2	152.23 qd $^3J_{(OMe)}$ = 4.5 $^2J_{(1)}$ = 2.5	152.85 qd $^3J_{(OMe)}$ = 4.0 $^2J_{(1)}$ = 3.0	152.41 qd $^3J_{(OMe)}$ = 3.9 $^2J_{(1)}$ = 2.2
C-3	140.87 qd $^3J_{(OMe)}$ = 4.0 $^3J_{(1)}$ = 8.0	140.95 qd $^3J_{(OMe)}$ = 3.5 $^3J_{(1)}$ = 7.5	140.79 qd $^3J_{(OMe)}$ = 3.5 $^3J_{(1)}$ = 7.7
C-4	148.66 qd $^3J_{(OMe)}$ = 3.5 $^4J_{(1)}$ = 1.5	152.14 qd $^3J_{(OMe)}$ = 4.5 $^4J_{(1)}$ = 2.0	152.41 qd $^3J_{(OMe)}$ = 3.9 $^4J_{(1)}$ = 2.2
C-4a	119.21 d with f.s. $^3J_{(1)}$ = 7.4	117.87 d with f.s. $^3J_{(1)}$ = 8.0	118.64 dt $^3J_{(1)}$ = 7.6 $^3J_{(10)}$ = 1.2
C-4b	119.76 d with f.s. $^3J_{(8)}$ = 7.6	126.88 d with f.s. $^3J_{(8)}$ = 7.3	126.06 dt $^3J_{(8)}$ = 8.3 $^3J_{(9)}$ = 1.1
C-5	140.22 m	136.51 t $^3J_{(7)}$ = 8.0	147.52 m
C-6	145.77 m	141.86 dd $^3J_{(8)}$ = 11.0 $^2J_{(7)}$ = 4.0	151.63 dqd $^3J_{(OMe)}$ = 4.0 $^3J_{(8)}$ = 9.4 $^2J_{(7)}$=2.5
C-7	112.34 dd ^1J = 160.0 $^3J_{(6-OH)}$ = 7.2	121.09 d ^1J = 164.7	111.03 d ^1J = 158.6
C-8	119.41 dm(br) ^1J = 159.2	124.25 dt ^1J = 161.6 $^3J_{(9)}$ = 3.8	121.06 dm(br) ^1J = 159.9
C-8a	130.46 d $^3J_{(7)}$ = 8.0	137.96 m	132.99 d $^3J_{(7)}$ = 8.0
C-9	30.16 tq ^1J = 129.8 $^2J_{(10)}$ & $^3J_{(1)}$ = 4.9	30.55 tq ^1J = 130.5 $^3J_{(8)}$ = 4.3	30.22 tq ^1J = 130.0 $^3J_{(8)}$ and $^2J_{(9)}$ = 5.0
C-10	31.22 tq ^1J = 129.8 $^2J_{(9)}$ & $^3J_{(8)}$ = 4.9	30.25 tq ^1J = 130.5 $^3J_{(1)}$ = 4.8	31.32 tq ^1J = 129.8 $^3J_{(8)}$ & $^2J_{(9)}$ = 4.8
C-10a	136.55 d $^2J_{(1)}$ = 2.0	139.13 td with f.s. $^2J_{(10)}$ = 7.6	136.23 br, s

Contd... (ii)

Contd...(ii)

Carbons	Praserol	Praserol diacetate	Praserol dimethyl ether
C_2-O$\underline{C}H_3$	55.99 q $^1J_{CH}$ = 143.4	55.83 q $^1J_{CH}$ = 144.1	60.69 q $^1J_{CH}$ = 144.2
C_3-O$\underline{C}H_3$	61.21 q $^1J_{CH}$ = 144.4	60.98 q $^1J_{CH}$ = 144.3	55.91 q $^1J_{CH}$ = 144.1
C_4-O$\underline{C}H_3$	62.36 q $^1J_{CH}$ = 146.7	61.34 q $^1J_{CH}$ = 144.9	60.69 q $^1J_{CH}$ = 144.2
C_5-O$\underline{C}H_3$	-	-	60.35 q $^1J_{CH}$ = 144.0
C_6-O$\underline{C}H_3$	-	-	56.19 q $^1J_{CH}$ = 143.8
C_5-OCO-$\underline{C}H_3$	-	20.84 * q $^1J_{CH}$ = 129.7	-
C_6-OCO-$\underline{C}H_3$	-	20.87 * q $^1J_{CH}$ = 129.6	-
C_5-O$\underline{C}$O-	-	168.36 * q $^2J_{(CH_3)}$ = 7.0	-
C_6-O$\underline{C}$O-	-	167.71 * q $^2J_{(CH_3)}$ = 7.0	-

[a] Chemical shifts in ppm downfield from TMS;

[b] The multiplicity in the coupled spectrum is given with the coupling constant values (in Hz)

[c] Abbreviations : f.s. = fine splitting;
s = singlet; d = doublet; t = triplet;
m = multiplet; br = broad; q = quartet;

* Values are interchangeable

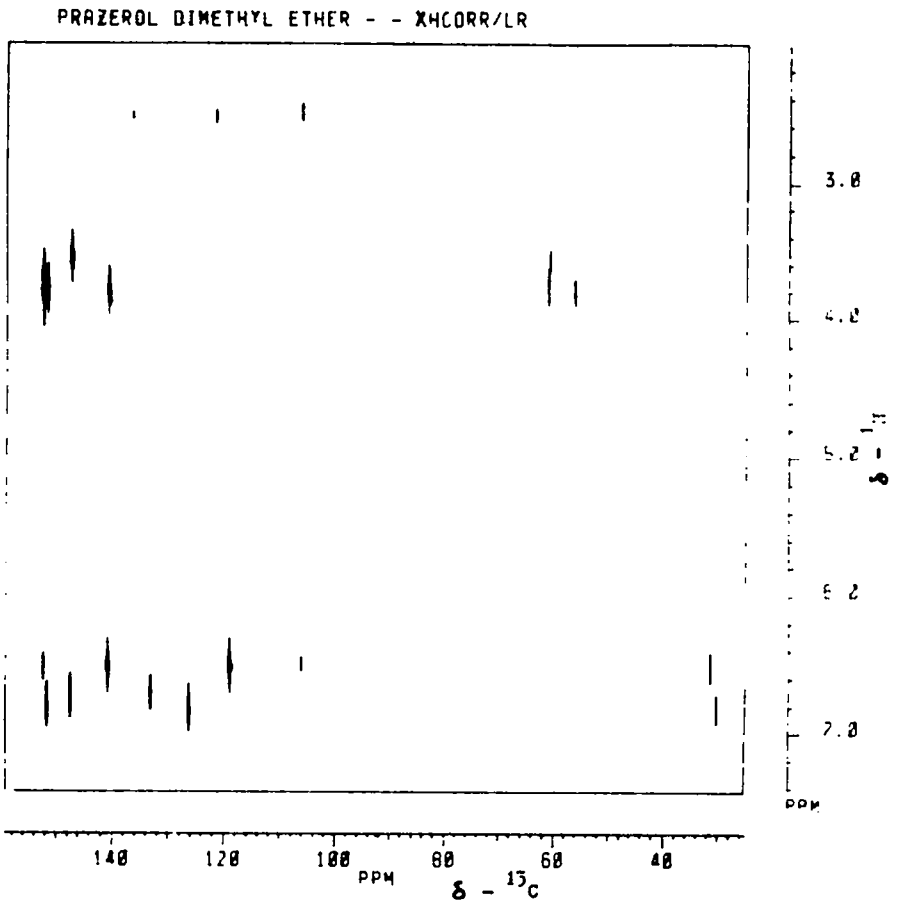


Fig - 1

EXPERIMENTAL

Mps are uncorrected. UV spectra were recorded in 95% EtOH, IR spectra in KBr discs. ^{1}H NMR spectra were recorded in $CDCl_3$ using TMS as internal standard at 300 MHz. ^{13}C NMR spectra were recorded on Bruker AM-300 L instrument with an ASPECT-3000 computer at 75.5 MHz in $CDCl_3$ (referencing was done with $CDCl_3$ = 77.0). MS were recorded with a direct inlet system at 70 eV. XHCORR spectra were recorded using the following pulse sequence suggested by Bax and Morris[8],

^{1}H = Dec.off - 90° - Dϕ - - Dϕ - D5 - 90° - - CPD Dec.
^{13}C = D1 - 180° - 90° -D4 - FID

with D1=2.0-2.5 sec., D3,D4=0.0037 sec., 0.002 sec for 1-bond CH couplings; 0.07 sec., 0.04 sec. for long range couplings optimised for J = 7 Hz.

Isolation of prazerol : Petroleum ether extract of yams of Dioscorea prazeri yielded a red gummy residue which upon chromatographic purification over silica gel gave prazerol (1). Prazerol crystallised as colourless needles, m.p. 144-45°c, $[\alpha]_D$ 0.0° ($CHCl_3$); UV (λ_{max} in nm) : 276 (log ϵ 4.32); IR (ϕ_{max} in cm^{-1}) : 3400, 3100, 1590, 850, 820; ^{1}H NMR (δ) : 2.59 (4H,br,s, CH_2 of C_9 & C_{10}); 3.71, 3.83 & 3.87 (each 3H, s, OMe at C_4, C_2 & C_5); 6.69 (1H, s, C_1-H); 6.71 & 6.78 (each 1H, d,J = 7.9 Hz, C_8-H and C_7-H respectively); 6.05 (1H, s, D_2O exch, C_6-OH) & 8.98 (1H, s, D_2O exch, Hydrogen-bonded C_5-OH).

Acetylation of Prasorol (1) : Prasorol was acetylated with Ac_2O/Pyridine in the usual manner to give 2 (98% yield), which crystallised from $CHCl_3$-MeOH, m.p. 128-32°c. UV (λ_{max} nm) : 278 (log ε 4.39). IR (ν_{max} cm^{-1}) : 1760 & 1220 (OAc), 1585, 850 & 830. ^1H NMR (δ) : 2.18 & 2.20 (each 3H, s, OCOC$\underline{H}_3$); 2.59 (4H, br-s, CH_2 of C_9 and C_{10}); 3.42, 3.82 and 3.85 (each 3H, s, -OC$\underline{H}_3$); 6.57 (1H,s,C_1-H); 7.00 & 7.09 (each 1H, d, J = 8.1 Hz, C_7-H and C_8-H).

Methylation of Prasorol (1) : Compound 1 (40 mg) in DMSO (2 ml) was treated with 1 ml MeI and 0.5 ml of 1(N) KOH for 4 days at room temperature. The mixture was then poured into ice-water and extracted with ether and washed with dil. HCl and finally with cold water. The ether layer was dried and the solvent removed to give residue 3 (30 mg, 75% yield). The IR spectrum of 3 showed complete disappearance of hydroxylic band. IR (ν_{max} in cm^{-1}) : 1595, 850, 830. ^1H NMR (δ) : 2.49-2.58 (4H,br,s,CH_2 of C_9 and C_{10}); 3.56, 3.72 & 3.80 (each 3H, s, -OC$\underline{H}_3$); 3.82 (6H,s, two-OC$\underline{H}_3$); 6.53 (1H, s, C_1-H); 6.71 & 6.85 (each 1H, d, J = 8.1 Hz, C_7-H & C_8-H).

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References :

1. Prain, D and Burkhill, I H, Ann. R. Bot. Gard., (Calcutta) 14 (Part I) (1956), 25.
2. Asolkar (Miss) L V & Chadha Y R
"Diosgenin and other steroid drug Percursors" (P & I Directorate, C S I R, New Delhi) (1979), 36.
3. Chakravarti, R.N. Das, S.N. and Chakraverti, Debi, J. Inst. Chemists(India)42(1970), 165.
4. P.L. Majumdar and (Miss) M. Joardar, Ind. J. Chem., 24B, 1192 (1985) and ref. cited therein.
5. Letcher, R.M. and Weng. K.M., J.C.S., Perkin Trans. I, 739 (1978).
6. P.L. Majumder, A. Kar and J.N. Schoolery, Phytochemistry, 24, 2085 (1985).
7. Letcher, R.M. and Nhamo, L.R.M., J.C.S. Perkin I, 1973, 1265.
8. A. Bax and G. Morris, Jour. Magnetic Resonance, 42, 501 (1981).
9. A.C. Derome, Modern NMR Techniques in Chemistry Research, Pergamon Press, London, 1987.