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MUPAMINE FROM *GLYCOSMIS PENTAPHYLLA*

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Key Word Index—*Glycosmis pentaphylla*; Rutaceae; C_{18} carbazole alkaloids; mupamine; partial synthesis.

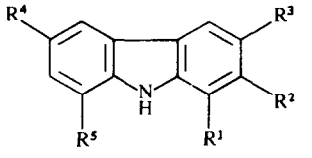
Abstract—A carbazole alkaloid with a C-18 carbon skeleton from *Glycosmis pentaphylla* has been characterized as mupamine by new partial synthesis.

INTRODUCTION

From taxonomic and biogenetic considerations [1] we were interested to isolate some carbazole alkaloids [2] built on a C_{18} carbon skeleton from *Glycosmis pentaphyll.* Glycozoline (**1**), glycozolidine (**2**) and some of their biologically related alkaloids [3, 4] based on a C_{13} skeleton have been reported. The isolation of the first C_{18} alkaloid from the genus *Glycosmis*, identified as mupamine [5] (**3**) by comparison with a partially synthetic specimen is reported in the present communication.

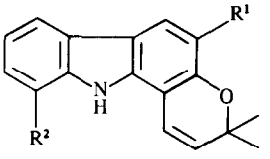
RESULTS AND DISCUSSION

From the leaves of *G. pentaphylla*, a homogenous, neutral compound $C_{19}H_{19}NO_2$ $[M]^+$ *m/z* 293 mp 152°, was isolated which showed IR, UV and mass spectral (*m/z* 263, 248) characteristics for a pyranocarbazole system like those of girinimbine [2] (**4**). The mass and ^1H NMR spectrum of the compound showed the presence of a NH function (δ8.0), a singlet for a C-4 proton (δ7.05), an *ortho* and *meta* coupled C-5 proton (δ7.09, *dd*, $J=10$ and 2 Hz) and two other aromatic protons (δ6.80 *m*). The signal for a six proton singlet together with the two vinylic proton doublets (δ6.65 and 5.68, each $J=10$ Hz) confirmed the presence of a 2′:2′ dimethyl-$\Delta^{3'}$-pyran system in the compound. It also showed signals for an aromatic methyl (δ2.3, *s*, 3H) and an aromatic methoxy group (δ4.0, *s*, 3H). All these data together with biogenetic considerations, are suggestive of the identity of the compound as mupamine (**3**), previously isolated from *Clausena anisata* [5] (Willd) Oliv. This has now been confirmed by its identification with a partially synthesized specimen of mupamine starting from heptazoline (**5**). Heptazoline (**5**) on acid

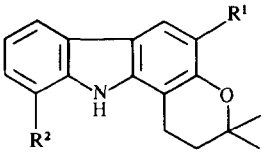


1 $R^1 = R^2 = R^5 = H$; $R^3 = Me$; $R^4 = OMe$
2 $R^1 = R^5 = H$; $R^2 = R^4 = OMe$; $R^3 = Me$

5 $R^1 =$; $R^2 = R^5 = OH$; $R^3 = CHO$; $R^4 = H$



3 $R^1 = Me$; $R^2 = OMe$
4 $R^1 = Me$; $R^2 = H$



6 $R^1 = CHO$; $R^2 = OH$
7 $R^1 = CHO$; $R^2 = OMe$
8 $R^1 = Me$; $R^2 = OMe$

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catalysed cyclisation with phosphoric acid [2] furnished cycloheptazoline (**6**). This on methylation with diazomethane afforded the *O*-methyl derivative (**7**) which on prolonged reduction with lithium aluminium hydride afforded dihydromupamine (**8**). This on dehydrogenation (10% Pd/C) for 8 hr afforded mupamine (**3**), mp 150°C (lit. mp 152°) identical with the natural compound.

EXPERIMENTAL

Isolation of mupamine (**3**). Air-dried powdered leaves of *G. pentaphylla* (Retz.) DC (1 kg) was extracted in a Soxhlet for 12 hr with petrol (60–80°). The residue left after the removal of solvent was dissolved in C_6H_6 and chromatographed over silica gel G. A solid obtained from the C_6H_6–$CHCl_3$ eluents on crystallization from C_6H_6–$CHCl_3$ gave a crystalline, homogeneous [TLC in C_6H_6–$CHCl_3$ (1:1), $R_f = 0.3$] compound, mp 145°, yield 30 mg [λ_{max} 238, 272, 282, 320 nm with log ε 4.89, 4.09, 4.49, 3.43; ν_{max} 3360, 1645, 1570, 1380, 1255, 885 cm^{-1}]. The compound was identical to a synthetic specimen of mupamine (mmp IR, UV).

Synthesis of mupamine (**3**) *from heptazoline* (**5**). (i) *O-Methyl cycloheptazoline* (**7**). Cycloheptazoline [6] (450 mg) obtained by H_3PO_4 cyclization of heptazoline [2] in MeOH soln (20 ml) on methylation with CH_2N_2 gave a solid, mp 175° after recrystallization from C_6H_6–petrol, yield 80%. UV λ_{max} 238, 273, 283, 315, 330 nm with log ε 4.80, 4.38, 4.43, 3.75, 3.89; IR: ν_{max} 3280 (NH) 1691 (CHO), 1590 (Ar-H), 1380, 1250 (Ar. substitution) cm^{-1}. (ii) *Dihydromupamine* (**8**). *O*-Methylcycloheptazoline (110 mg) in THF (100 ml) was stirred with $LiAlH_4$ (1 g) for 6 hr. The reaction mixt on usual work-up and purification by CC over Al_2O_3 yielded a compound which after crystallization from C_6H_6–petrol gave mp 205° (yield 40%). UV: λ_{max} 221, 229, 236, 295, 333 nm with log ε 4.70, 4.85, 4.80, 4.50, 3.80 nm; IR ν_{max} 3440 (NH), 1590 (Ar-H), 1385, 1215 cm^{-1}. (iii) *Mupamine* (**3**). Dihydromupamine (50 mg) in *p*-cymene (5 ml) was dehydrogenated (Pd/C; 20 mg) in a sealed tube for 8 hr at 210–220°. The reaction product after usual work-up and chromatography over Al_2O_3 furnished after recrystallization from C_6H_6–petrol, a compound mp 150° (lit mp 152°). Its IR, UV and NMR were identical to those reported for mupamine.

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