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HEPTAZOLICINE, A CARBAZOLE ALKALOID FROM *CLAUSENA HEPTAPHYLLA*

P BHATTACHARYYA, A CHAKRABORTY and B K CHOWDHURY*

Department of Chemistry, Bose Institute, Calcutta 700009, India, *Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria, Nigeria

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Key Word Index—*Clausena heptaphylla*, Rutaceae, roots, heptazolicine, carbazole alkaloid

Abstract—A new carbazole alkaloid designated as heptazolicine has been isolated from the roots of *Clausena heptaphylla* On the basis of spectral and chemical evidence it has been identified as [2, 2-dimethyl-3, 4-dihydropyrano-(5, 6-a)]-3-formyl-8-hydroxy-carbazole

INTRODUCTION

From taxonomic considerations, we were interested to examine *Clausena heptaphylla* (Rutaceae, sub-family Aurantioideae) from which we reported carbazole alkaloids and a novel C_{25}-pentanortriterpenoid named clausenolide [1, 2] We now report the structure of another carbazole alkaloid from the phenolic fraction of the alcoholic extract of the roots of *C heptaphylla*

RESULTS AND DISCUSSION

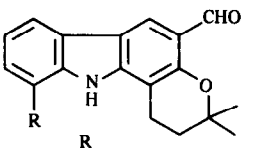
Heptazolicine **1**, $C_{18}H_{17}NO_3$ ($[M]^+$ *m/z* 295) mp 285° (d) was homogeneous by TLC and mass spectrometry The ready solubility of the compound in alkali and the formation of violet colour with ferric chloride indicated the presence of a phenolic hydroxyl group It gave a 2 4 DNPH derivative and reduced ammoniacal silver nitrate solution indicating the presence of an aldehyde function Isolation of carbazole, mp 235°, by zinc dust distillation of **1** confirmed its carbazole skeleton Its UV spectrum in EtOH with λ_{max} at 242 (log ε4 65), 275 (4 62) and 300 nm (4 40) indicated the presence of a 3-formyl carbazole chromophore [3] The IR spectrum showed absorption peaks at ν_{max}^{KBr} 3260 (OH, hydrogen bonded), 3000 (NH), 1700 (CHO), 1615 and 1517 cm^{-1} (aromatic) The ^1H NMR spectrum (60 MHz, DMSO-d_6) showed signals at δ11 2 (1H, *s*, OH proton, exchangeable with D_2O), δ10 4 (1H, *br s*, –NH proton, exchangeable with D_2O), 9 8 (1H, *s*, CHO proton), 8 3 (1H, *s*, aromatic proton at C-4), 7 5 (1H, *d*, $J = 8$ Hz, which is split further $J = 2$ Hz, aromatic proton at C-5), 6 7–7 2 (2H, *m*, aromatic proton, C-6, C-7) Two symmetrical triplets ($J = 7$ Hz) at δ3 03 and δ1 98 were due to the Ar–CH_2–CH_2 grouping and a singlet at δ1 45 integrating for six protons indicated a *gem* dimethyl group

Signals for C-4 and C-5 protons in the ^1H NMR spectrum of carbazole derivatives are usually observed at lower field than the other aromatic protons of the carbazole nucleus as these two protons are mutually deshielded and are therefore readily discernible Other aromatic protons appear at higher field as multiplets [1, 4] Thus the signal at δ7 5 [4] was assigned to the C-5 proton of heptazolicine The C-4 proton was deshielded due to the proximity of the aldehyde function at C-3 The C-4 proton was essentially a singlet indicating the absence of protons at the 2 and 3 positions The C-5 proton was *ortho* and *meta* coupled showing that the positions 6 and 7 were unsubstituted The signal for the hydroxyl proton in heptazolicine appeared downfield similar to that of 1-hydroxy carbazole [5] The hydrogen bonded hydroxyl should therefore occupy position 8 The two symmetrical triplets (δ3 03 and 1 98) and a sharp singlet for six protons at δ1 45 account for the 2 2 dimethyl dihydro pyran ring in **1** [1]

The mass spectrum of the compound showed an $[M]^+$ at *m/z* 295 The other significant peak at *m/z* 280 represented by the ionic species **2** also supported the presence of a 2 2 dimethyl pyran system in **1**

On acetylation **1** furnished an acetate **3**, mp 230° The IR spectrum of **3** showed a strong peak at 1745 cm^{-1} for the acetoxy function and the absence of a hydroxyl group The UV spectrum of **3** in ethanol with λ_{max} at 245 (log ε4 52), 255 (4 30), 280 (4 48) and 300 nm (4 58) was similar to [2,2-Dimethyl-3,4-dihydropyrano-(5,6-a)]-3-formyl carbazole **4** Since the angular fusion of the pyran ring in **4** has been established [6] it was clear that in heptazolicine acetate also a similar fusion was present Moreover heptazolicine is identical in all respects (mp, mmp, UV, IR) with the cyclized product of heptazoline **5** [5]

From all this evidence the structure of heptazolicine has been assigned as **1**



R
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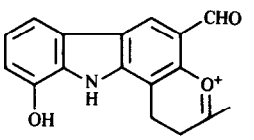
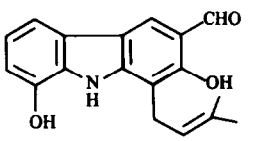
3 OAc
4 H



2



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EXPERIMENTAL

All mps are uncorr UV and IR spectra were recorded in EtOH and as KBr pellets, respectively

Isolation of heptazolicine Air dried finely powdered root (1 5 kg) of *C heptaphylla* Wt and Arn was first extracted with petrol After extraction the root powder was dried and re-extracted with EtOH for 36 hr The extract was freed from the solvent, the residue taken up in Et_2O and separated into acidic, basic and neutral fractions in the usual way The acidic fraction after removal of Et_2O was taken up in C_6H_6 and chromatographed over silica gel (450 g) eluting the column with petrol, C_6H_6 and $CHCl_3$ in succession From the $CHCl_3$ eluate a solid was obtained which on further crystallization from $CHCl_3$ furnished a homogeneous crystalline compound, mp 285° (d), yield 0 025% TLC on silica gel ($CHCl_3$–HOAc, 9 1, R_f 0 71) (Found C, 73 18, H, 5 75, N, 4 69 Calc for $C_{18}H_{17}NO_3$ C, 73 20, H, 5 80, N, 4 74%)

Zinc dust distillation of **1** Compound **1** (100 mg) was mixed with Zn dust (5 mg) and heated in a sealed tube for 3 hr The reaction product was taken up in Et_2O The Et_2O soluble portion of the reaction product on removal of Et_2O was taken up in C_6H_6 and chromatographed over silica gel (2 g) Elution with petrol furnished a colourless crystalline compound, mp 235°, which was identified as carbazole

Acetylation of **1** Heptazolicine (50 mg) was dissolved in pyridine and Ac_2O (5 ml) and refluxed for 3 hr The reaction mixture was poured into crushed ice and a colourless product was obtained On crystallization of the substance from C_6H_6, compound **3**, mp 230°, was obtained Yield 35 mg (Found C, 71 15, H, 5 60; N, 4 10 Calculated for $C_{20}H_{19}NO_4$ C, 71 20, H, 5 68, N, 4 15%)

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