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STRUCTURAL DETERMINATION OF CAPAURIMINE AND CAPAURINE

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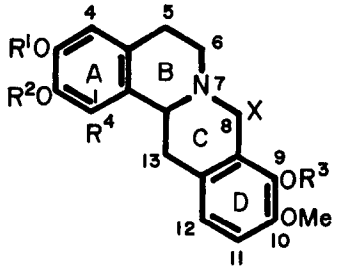
Capaurimine and capaurine, alkaloids isolated from a number of Corydalis species,[1] were assigned to (I)[2] and (II)[3], respectively, through chemical degradations by Manske. Present authors[4] synthesised the compound (I), which had trans-quinolizidine skeleton, and spectral data of (I) were not identical with those of capaurimine. Therefore, reinvestigations of the structures of capaurimine (I) and capaurine (II) were attempted by physical methods[5].



(I) $R^1 = R^2 = Me$, $R^3 = X = H$, $R^4 = OH$

(II) $R^1 = R^2 = R^3 = Me$, $R^4 = OH$, $X = H$

(III) $R^1 + R^2 = -CH_2-$, $R^3 = Me$, $R^4 = H$, $X = CH_2CHOHCH_3$

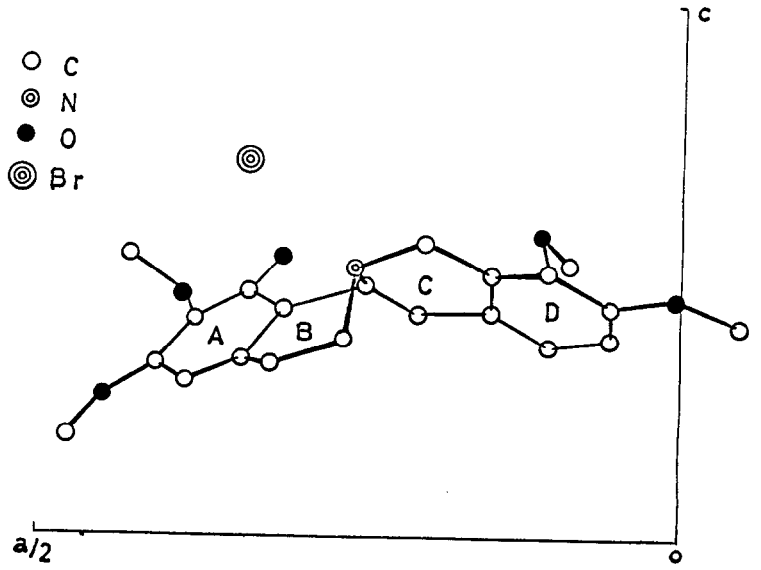
At first, X-ray analysis of capaurine (II) hydrobromide was carried out as follow. Crystals of capaurine hydrobromide were grown from methanol solution as pale yellow plates. Crystallographic and physical data are: $C_{21}H_{26}O_5NBr$, M.W. = 452.4, m.p. 198 - 199°, $[\alpha]_D = -423°$, orthorhombic, a = 24.79, b = 8.08, c = 10.32 Å, U = 2067 Å^3, space group $P2_12_12_1$, Dm = 1.458 g. cm^{-3}, Dc = 1.543 g. cm^{-3}, Z = 4.

Multiple-film equi-inclination Weisenberg photographs were taken about the

b and c axes, using Cu-Kα radiation. Relative intensities were estimated visually. The structure was solved by the heavy-atom method. In the first heavy-atom Fourier synthesis, all the atoms of the main skeleton, which is the dibenzo[a,g]quinolizidine, were recognised as resolved peaks, but peaks for some methoxy carbon were low and a few ghost peaks were found near the methoxy carbon. The only contributions from the skeleton atoms were included in the phase calculation. The second Fourier synthesis showed clearly the whole molecule. Fourier and least squares refinements were made and the discrepancy factor was reduced to 0.113 at the present stage. Further refinements are in progress.[6]

The following figure shows the molecular structure of capaurine hydrobromide as projected along the b axis. As seen from the figure, BC ring junction is cis-fused and both rings are in the half chair conformation.

Only one of rigid cis and trans forms of the tetrahydroprotoberberine system is isolable, when the nitrogen is quaternary or protonated, in stereochemically homogeneous state, especially in crystalline state. The result of X-ray analysis on capaurine hydrobromide might not show the true structure of capaurine itself,



as interconversion between cis and trans forms might be possible in a more mobile system of the free base. However, in some cases, the interconversion between them is fully restricted and one or both are obtainable even in liquid state. Therefore, detailed investigations of natural capaurimine, capaurine and synthetic base were done by means of n.m.r. spectroscopy.

Brossi and coworkers[7] reported that cis-and trans-2-(4-chlorophenyl)-1,2,3,4, 6,7-hexahydro-11bH-benzo[a]quinolizidine could be materialised in liquid system and characterised in terms of chemical shift at C_{11b}-proton. They elucidated that the angular proton of trans-quinolizidine resonances at a higher field than τ 6.2 whereas that of cis-conformer is characterised by a downfield signal below τ 6.2. In the 60 MC spectra [in $CDCl_3$ and/or $(CD_3)_2SO$] of capaurimine and capaurine, there appeared a quartet centered at τ 6.0 and 5.95, respectively, with splitting of J_{ae} = 3 c./sec. and J_{aa} = 11 c./sec., attributable to the angular C_{13a}-equatorial proton. In the region of our synthetic base[4], no one-proton signal below τ 6.2 attributable to the angular C_{13a}-proton was observed. Moreover, aromatic protons on ring D in protoberberines (III) showed a AB type quartet (J = 8 c./sec.) centered at τ 3.37 in case of trans-conformer, but a singlet at τ 3.48 in cis-conformer.[8] The protons at the same position in our synthetic base showed a AB type quartet at τ 3.37 (J = 8 c./sec.), and those of capaurimine and capaurine were observed at τ 3.27 and 3.26 as singlets, respectively. Therefore, the above results revealed that capaurimine and capaurine should be assigned exclusively to cis-conformer and the synthetic base to trans-conformer and the interconversion between cis- and trans-conformers does not occur even partially in solution.

Mass spectra of capaurimine and our synthetic sample were closely similar each other except relative intensity; thus, both compounds showed m/e 357 (M^+) (72.6 %; 39.5 %), 356 ($M^+ - 1$) (40.7; 21.5), 208 ($M^+ - 149$) (100; 100), 206 ($M^+ - 151$) (32.4; 51.5), 150 ($M^+ - 207$) (25.7; 62.0), and 135 ($M^+ - 222$) (27.3; 47.4). On the other hand, the mass spectrum of capaurine hydrochloride also showed m/e 371 ($M^+ - HCl = M_1^+$), 370 ($M_1^+ - 1$), 208 ($M_1^+ + 1 - 164$), 206 ($M_1^+ + 1 - 166$), 164 ($M_1^+ - 207$) and 149 ($M_1^+ - 222$). These data indicated that capaurimine and capaurine should have three substituents on ring A and two substituents on

ring D.[9]

Therefore, the skeleton of capaurimine and capaurine would be cis-quinolizidine, on the base of the spectral data described above together with chemical degradations by Manske. Regarding the capauridine, racemate of II, which could not be available, its stereochemistry is remained unclear.

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5. N.m.r. spectra were determined on a Hitachi H-60 and Varian A-60 spectrometer with deuteriochloroform (capaurine) and deuteriodimethyl sulphoxide (capaurimine and our synthetic base) as solvents and tetramethylsilane as internal reference. Mass spectra were measured on a Hitachi RMU-6D and Japan Erectron Optics Lab. JMS-OISG mass spectrometer equipped with a direct inlet system; chamber voltage 70eV; total emission 70μA; evaporation temp., 100 - 180°; ion chamber temp., 250° in all samples.
6. Precise paper will be published elswhere.
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