THE PARTIAL SYNTHESIS OF BURNAMICINE

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The indole alkaloid burnamicine and its 19,20-dihydro derivative were partially synthesized from geissoschizine methyl ether and hirsutine respectively, using a C/D ring opening reaction with ethyl chlorocarbonate.

Burnamicine[1] was found as the first cryptopine-type indole alkaloid from Hunteria eburnea Pichon (Apocynaceae) in 1963 by Taylor et al.. Subsequently, we prepared dihydroburnamicine (6b) from dihydrocorynantheine with a new C/D ring opening reaction.[2]

We now report on the partial synthesis of burnamicine (6a) from geissoschizine methyl ether (1a) (isolated from Uncaria rhynchophylla Miq. by us[3]) and of (6b) from hirsutine (1b) with another C/D ring opening reaction. It has recently been reported that chlorocarbonates are good reagents for the C/D ring cleavage of indole alkaloids and for the formation of vobasine type alkaloid from sarpagine type alkaloid.[4]

Hirsutinol (2b) mp 168-169° and geissoschizol (2a) were formed from (1b) and (1a) respectively, by hydrolysis, decarboxylation and the subsequent $NaBH_4$ reduction. Reaction of ethyl chlorocarbonate with both alcohols (2a,b) in the presence of Na_2CO_3 and an excess EtOH in $CHCl_3$ at room temperature gave rise to neutral 3,4-seco derivatives (3a,b) as epimeric mixtures (in ca. 70% yield respectively). The chlorination of (3a,b) with one equivalent

of t-BuOCl in CH_2Cl_2, followed by treatment with aq-N HCl gave the 2-acylindole derivatives (4a, in 50% yield, amorphous, λ_{max}^{EtOH} 238, 316 nm, M^+ m/e 384) and (4b, in 67% yield, amorphous, λ_{max}^{EtOH} 238, 314 nm, M^+ m/e 386). The reduction of (4a,b) with $LiAlH_4$ in THF for 5hrs at room temperature yielded corresponding alcohols (5a, in 83% yield, amorphous, uv: indolic, M^+ m/e 328) and (5b, in 97% yield, amorphous, uv: indolic, M^+ m/e 330). The both alcohols (5a,b) were oxidized with active MnO_2[5] in CH_2Cl_2 to give burnamicine [6a, in 40% yield, mp 193-195°, $|\alpha|_D^{24°}$: -240° in $CHCl_3$, CD (in dioxane) $\Delta\varepsilon_{max}$(nm): -4.6 (333), +1.3 (310), -1.6(290), +8.1(260)] , which was identical spectroscopically with the authentic burnamicine[1], and dihydroburnamicine[2] [6b in 38% yield, mp 98-100°, $|\alpha|_D^{29°}$: +207° in dioxane, +125° in $CHCl_3$, CD (in dioxane) $\Delta\varepsilon_{max}$(nm): -0.3(365), +2.0(335), -0.4(311), +1.8 (290), -5.8(261), +3.3(233)].

Both bases (6a,b) exhibited nearly opposite circular dichroism spectra and this was presumably due to approximately antipodal ten membered ring construction with regard to the plane of 2-acylindole. Though the both bases (6a,b) showed the opposite optical activities, the absolute configuration of C_{15} of (6a,b) are the same as evident from the Scheme. The absolute configuration of natural burnamicine has now been determined unambiguously through the present chemical conversion from geissoschizine methyl ether (1a), which has been correlated[3] with dihydrocorynantheine and corynantheidine with known absolute configurations.

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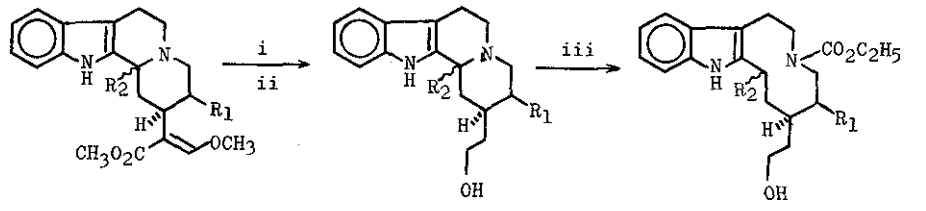
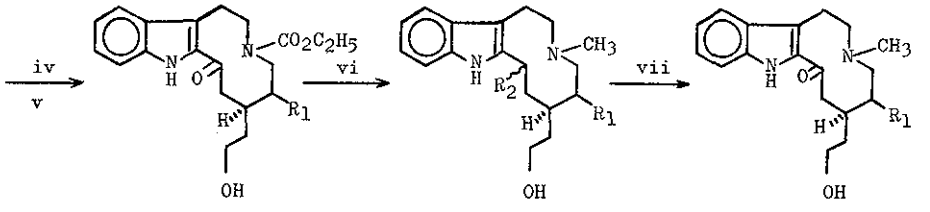


(1a) R_2= α H (2a) R_2= α H (3a,b) R_2= mixture α,β OC_2H_5

(1b) R_2= β H (2b) R_2= β H



(4a,b) (5a,b) R_2= mixture α,β OH (6a,b)

series a, R_1= =CH-CH_3 (E). series b, R_1= α C_2H_5

i, H_2O (H^+); ii, $NaBH_4$; iii, $ClCO_2C_2H_5$/ C_2H_5OH,$CHCl_3$,Na_2CO_3;

iv, t-BuOCl; v, H_2O (H^+); vi, $LiAlH_4$; vii, MnO_2.

Scheme

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