THE CHEMICAL TRANSFORMATION OF GARDNERINE TO 2-ACYLINDOLE ALKALOID OCHROPINE

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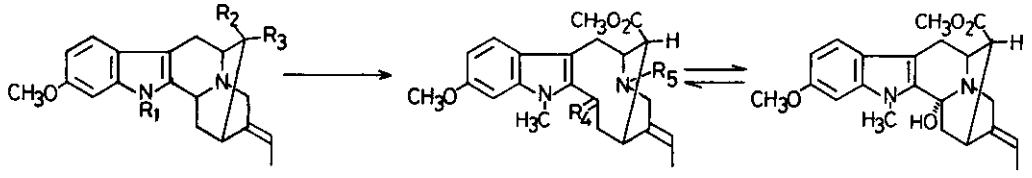
Sarpagine type indole alkaloid, Gardnerine (1), which is contained in Gardneria species of Loganiaceae family was chemically converted to a 2-acylindole alkaloid, Ochropine (2), which is contained in Ochrosia species of Apocynaceae family. Thus, the primary alcohol group of Na-methyl-gardnerine (3) was oxidized to the aldehyde compound (4) (mp 198°, in 76% yield) using NCS, Me_2S and Et_3N. Boiling of an oxime derivative (5) of (4) with acetic anhydride for 15 min. afforded a sole crystalline nitrile compound (6) of mp 285° (in 57% yield). Treatment of (6) with abs-MeOH : H_2SO_4 (3 : 1 v/v) at 110° for 30 min. gave a colorless crystalline ester derivative (7) (mp 204°, in 50% yield) which could be isomerized to 16-epi-ester derivative (8)(mp 166°) by use of sodium methoxide. The nmr spectra of the normal ester derivative (7) showed a methyl signal of carbomethoxy group shielded by indole nucleus at δ 3.07, while 16-epi-ester derivative (8) showed the corresponding signal at δ 3.66. The C/D ring opening reaction of ester (7) gave rise to N-cyano alcohol derivatives (9) constituted of two epimeric alcohols at C-3 using cyanogen bromide in the presence of Na_2CO_3 in aq-THF. Without further purification, the alcohol was oxidized to 3-keto derivative (10) by Cornforth method ($Py\text{-}CrO_3\text{-}H_2O$). Amorphous keto derivative (10) exhibited a characteristic absorption of 2-acylindole alkaloid at 340 nm in the uv spectrum.

Decyanation of (10) was achieved by refluxing with 5% aq-HOAc-NH_4OAc for 3hrs. Des-Nb-methyl-ochropine (11) was formed as colorless prisms mp186° in 57% yield. The base (11) was in an equilibrium state with a ring-opened ketone (12) in an ethanolic solution. Finally, the base (11) was methylated using formaldehyde and palladized charcoal with hydrogen. Synthesized ochropine showed the same ir spectrum with natural ochropine in a chloroform solution.



(11)

R_1= H, R_2= CH_2OH, R_3= H (1) R_1= CH_3, R_2= CH=NOH, R_3= H (5) R_4= $<^{H}_{OH}$, R_5= CN (9)
R_1= CH_3, R_2= CH_2OH, R_3= H (3) R_1= CH_3, R_2= CN , R_3= H (6) R_4= =O , R_5= CN (10)
R_1= CH_3, R_2= CHO , R_3= H (4) R_1= CH_3, R_2= $COOCH_3$, R_3= H (7) R_4= =O , R_5= H (12)
R_1= CH_3, R_2= H, R_3= $COOCH_3$ (8) R_4= =O , R_5= CH_3 (2)