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PARTIAL SYNTHESIS OF TCHIBANGENSINE AND DERIVATIVES

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Abstract - The alkaloid tchibangensine 1 and two of its derivatives 6a and 6b were synthesised. Catalytic hydrogenation of 6a,b and acetylation of 1 were described.

Recently the structure 1 for tchibangensine has been established by a combination of spectral evidences and chemical correlations with usambarensine and ochrolifuanines-C and -D[1].

Preparation of optically active tchibangensine was now achieved along the lines of the synthesis of (±)-3',4'-dihydrousambarensine as described by Yamada and colleague[2]. Thus tryptamide 3, obtained by condensation of tryptamine with geissoschizoic acid 2 (DCC, DME/DMF, 20°C, 6 days, quantitative yield), was refluxed in $CHCl_3$, with $POCl_3$ for 4 h. to give a compound identical in every respect with tchibangensine 1 (30 % yield).

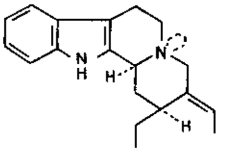
On reduction with potassium borohydride, tchibangensine 1 yielded two derivatives epimeric at C(17) which were separated by column chromatography on alumina : 6a - the less polar -$(\alpha)_D$ - 11.3° (EtOH)-(46 % yield), 6b - the more polar - $(\alpha)_D$ + 41° (EtOH)-(34 % yield). Both derivatives were acetylated (Ac_2O : 6a,b → 7a,b) or methylated (CH_2O, AcOH, $NaBH_3CN$: 6a,b → 8a,b) in good yields.

Pictet-Spengler reaction between tryptamine and geissoschizal 4 (phosphate buffer ; pH 4-5 ; 20°C) led to two derivatives (1 : 1 mixture ; 23 % yield) identical with the aforementioned reduction products.

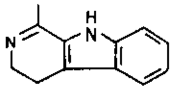
As expected, catalytic hydrogenation (PtO_2/MeOH) transformed 6a into ochrolifuanine -C 9a (23 %) and 6b into ochrolifuanine-D 9b (33 %). This reaction was accompanied by inversion of the nitrogen lone pair as already observed in the hydrogenation of tchibangensine[1].

Along with 9a and 9b, two Emde fragmentation products were obtained : 10a - $(\alpha)_D$ - 66° (EtOH) - $UV_{EtOH}^{\lambda max}$ (log ε) 227 (4.75) 283 (4.12) 291 (4.04) - MS : $M^{+\cdot}$440, characteristic peaks at m/e 440, 438, 423, 410, 396, 383 ($M^{+\cdot}-C_4H_9$), 366, 354, 310, 281, 267, 253, 237, 225, 223, 221, 197, 184, 171 (100 %), 156, 144, 130 - $NMR_{CDCl_3}^{\delta}$ 0.84 (d, 3H, J6), 1.24 (t, 3H, J8) - (14 % yield) and 10b $(\alpha)_D$ + 5° (EtOH) - U.V. and mass spectra identical with those of 10a - $NMR_{CDCl_3}^{\delta}$ 0.84 (d, 3H, J6), 1.24 (t,3H, J8) - (30 % yield).

When treated with acetic anhydride in pyridine, tchibangensine 1 afforded the secoderivative 5 in

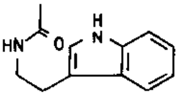


1 tchibangensine : R =



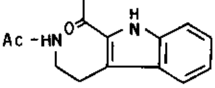
2 R = -COOH

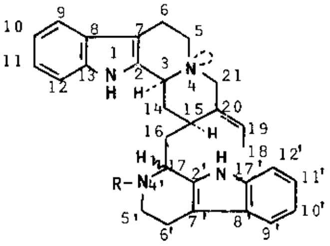
3 R =



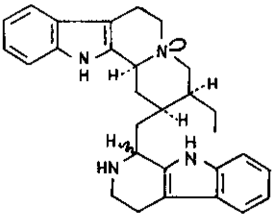
4 R = -CHO

5 R =

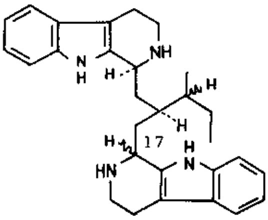




6a R=H, 17αH
6b R=H, 17βH
7a R=Ac,17αH
7b R=Ac,17βH
8a R=Me,17αH
8b R=Me,17βH



9a Ochrolifuanine C : 17αH
9b Ochrolifuanine D : 17βH



10a 17αH
10b 17βH

70 % yield : $(\alpha]_D$ + 20° (EtOH) - $UV^{\lambda max}_{EtOH}$ (log ε) 226 (4.65) 286 (4.05) 293 (4.10) 315 (4.22) - I.R.$^{\nu}_{CHCl_3}$ 3460, 3330, 1660 - MS : $M^{+\cdot}$494, characteristic peaks at m/e 494, 476 ($M^{+\cdot}$ $-H_2O$), 465, 422 ($M^{+\cdot}$ - Ac-NH=CH_2), 408, 265, 250, 249, 247, 235, 232, 221, 219, 185, 172, 158, 156, 154, 144, 143, 130 - NMR$^{\delta}_{CDCl_3}$ 5.88 (t, 1H, J6), 5.5 (q, 1H, J6.5), 4.4 (m, 1H), 1.52 (d, 3H, J6.5). Such a ring cleavage is precedented in the harmaline series[3].

References

1 . C.Richard, C.Delaude, L.Le Men-Olivier and J.Le Men, Phytochemistry, 1978, *17*, 539.

2 . K.Yamada, K.Aoki and D.Uemura, J.Org.Chem., 1975, *40*, 2572.

3 . A.u.Rahman, J.Chem.Soc.Perkin Trans.I, 1972, 731.

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