Tetrahedron Letters, Vol.22, No.30, pp 2927 - 2928, 1981
Printed in Great Britain

0040-4039/81/302927-02$02.00/0

STEREOSPECIFIC TOTAL SYNTHESIS OF (±)-STREMPELIOPINE[1]

Josef HÁJÍČEK and Jan TROJÁNEK

Research Institute of Pharmacy and Biochemistry,
19404 Prague 9, Czechoslovakia

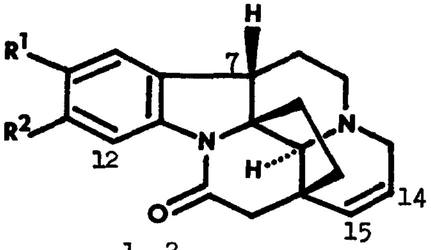
Summary: The 18-methylene-1,2-dehydroaspidospermidine (III) was stereospecifically transformed into the schizozygane alkaloid strempeliopine (II) in 16,6 % overall yield.

The schizozygane alkaloids (e.g. schizozygine I) represent a small group of hexacyclic acylindoline bases found in a single plant source, Schizozygia caffaeoides (Boj.) Baill.[2] Recently, (-)-strempeliopine (II), the parent base of this group was isolated[3] from Strempeliopsis strempelioides K. Schum. (Apocynaceae) endemic to Cuba.

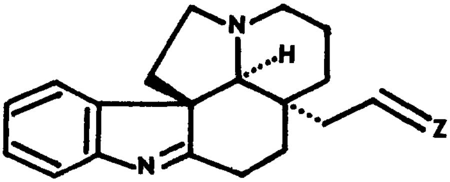
Very recently, we have reported[4] on the total synthesis of 18-methylene-1,2-dehydroaspidospermidine (III) and have postulated its versatility in the preparations of various aspidospermane alkaloids. Here, we describe the stereospecific transformation of this base into the racemic strempeliopine (II) which is based on the known[5] reductive rearrangement of indolenine IV to 1-demethylvallesamidine (V).

The indolenine III was heated with zinc[6] and $CuSO_4.5H_2O$ in acetic acid at 103 °C for 4 h. The mixture of bases VI [oil] and VII obtained by alumina column filtration was formylated by HCOOH - Ac_2O mixture (9 h at RT) to give the formylindoline VIII [33,6 %; mp 136-137,5 °C; ^{1}H-NMR ($CDCl_3$): δ 8.61 (1H, s; N-C$\underline{H}$O), 7.90 (1H, m; C(12)$\underline{H}$), 7.34-6.87 (3H, m; arom.$\underline{H}$), 5.72 (1H, m; C$\underline{H}$=CH_2), 5.02 (2H, m; CH=C$\underline{H_2}$), 3.17 (1H, t, J=7 Hz; C(7)$\underline{H}$). IR ($CHCl_3$): 1652 (C=O), 1596, 1475 cm^{-1}. UV (MeOH): nm (log ε) 286 (3,526), 279 (3,583), 252 (4,003). MASS: m/z(%) 322(M^+; 41), 294(36), 282(26), 281(100), 253(81), 160(21), 130 (50)], together with 18-methylenequebrachamine (VII) [1,5 %; oil].

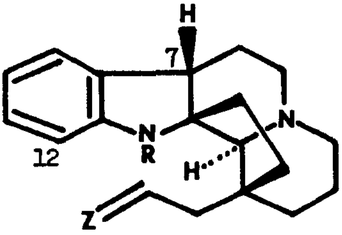
The olefin VIII afforded, upon ozonization in a mixture of 1 aq. HCl - MeOH (5:2) at RT for 0,5 h followed by oxidation with hydrogen peroxide (15 h at RT), the desired (±)-strempeliopine[7] (II) [49,3 %; mp 132-136 °C; ^{1}H-NMR ($CDCl_3$): δ 8.00 (1H, m; C(12)$\underline{H}$), 7.32-6.85 (3H, m; arom.$\underline{H}$), 3.20 (1H, t, J=7 Hz; C(7)$\underline{H}$). IR ($CHCl_3$): 1643 (C=O), 1597, 1475 cm^{-1}. UV (MeOH): nm (log ε) 291 (3,607), 281 (3,686), 255 (4,102). MASS: m/z(%) 294(M^+; 100), 293(93), 266(28), 265(20), 160(7), 143(9), 130(16)].



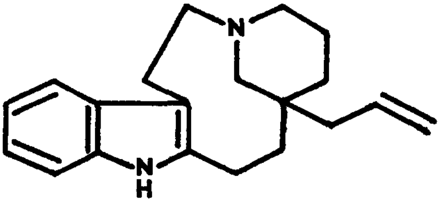
I: R^1+R^2 = OCH_2O
II: $R^1=R^2$ = H, 14,15-dihydro



III: Z = CH_2
IV: Z = H_2



V: R = H, Z = H_2
VI: R = H, Z = CH_2
VIII: R = CHO, Z = CH_2



VII

Experiments directed towards the determination of absolute configuration of natural (-)-strempeliopine (II) are under way.

REFERENCES and NOTES

1) On Alkaloids. XL. Part XXXIX: Hájíček J., Trojánek J.: Collect. Czech. Chem. Commun., in press
2) Renner U., Kernweisz P.: Experientia 19, 244 (1963); Renner U., Fritz H.: Helv. Chim. Acta 48, 308 (1965)
3) Laguna A.: PhD. thesis, Prague 1980
4) Hájíček J., Trojánek J.: Tetrahedron Lett., in press
5) Lévy J., Maupérin P., Döé de Maindreville M., Le Men J.: Tetrahedron Lett. 1971, 1003
6) It is to be noted that the ratio and/or the yields of reaction products vary considerably with the quality of zinc used. Moreover, our results obtained with indolenine IV differ in some instances from the original report^5. The details will be published elsewhere.
7) The synthetic base was shown by direct comparison to be identical with authentic (-)-strempeliopine in IR and mass spectra, and in TLC behavior in three solvent systems. We are greatly indebted to Dr. Buděšínský (Institute of Organic Chemistry and Biochemistry, Prague), who kindly supplied us with sample of natural (-)-strempeliopine.

(Received in UK 15 May 1981)