

A FACILE STEREOSELECTIVE SYNTHESIS OF \pm SESBANINE. 

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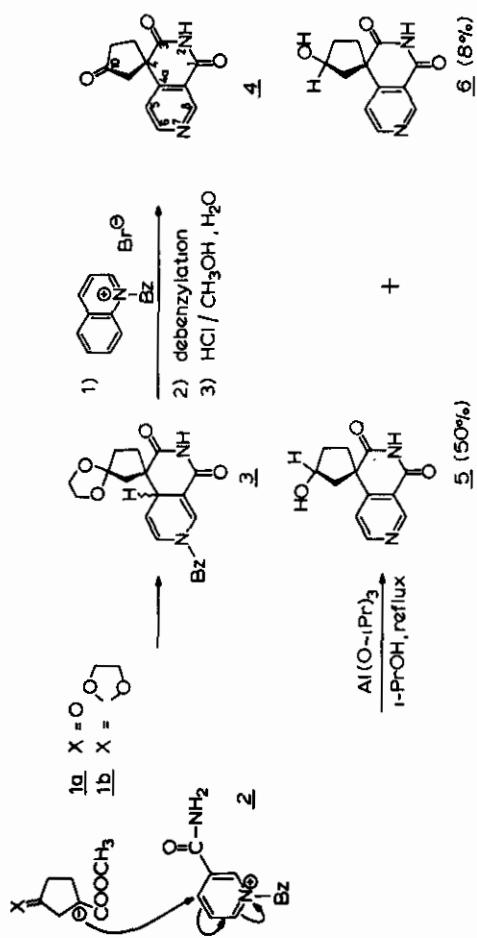
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Abstract. 10-Dehydrosesbanine (4), prepared via a sequence in which the tricyclic spiro cyclopentano-2,7-naphthyridine ring system is prepared by condensation of 3-(ethylenedioxy)cyclopentanecarboxylate ester anion with N-benzylnicotinamide, is stereoselectively reduced to a mixture of \pm Sesbanine and \pm 10-epi-Sesbanine (6:1).

The construction of the spiro cyclopentano-2,7-naphthyridine framework of Sesbanine (5)¹, in one practical step, by the reaction of cyclopentanyl ester anion with N-benzylnicotinamide, has been recently reported from this laboratory². In this communication we describe the stereoselective synthesis of \pm Sesbanine (5), utilizing the aforementioned synthetic approach. In terms of the number of steps, their practical convenience and the availability of the starting materials, this synthesis compares favourably with the ones reported thus far in the literature^{3a-c}.

Methyl 3-oxocyclopentanecarboxylate (1a) was prepared according to the procedure of Noyce and Fessenden⁴, involving a slight modification. 1a was converted into its acetal 1b (92%) and the anion of the latter (1 eq. LDA, THF, -30°) allowed to react with N-benzylnicotinamide (2), whereupon, following work-up, the tricyclic system 3⁵ was obtained in 50% yield. The dihydropyridine ring of 3 was oxidized by stirring with N-benzylquinolinium bromide in acetonitrile (2 days, room temp.), and the resulting pyridinium salt debenzylated by heating in vacuo (235°/0.01 mm) for 1 h. Subsequent deprotection of the carbonyl function gave dehydrosesbanine 4⁶. The overall yield of 4 from 3 was 44%.

 Dedicated to Professor T. Kametani.



The reduction of 4 by metal hydrides resulted in reaction mixtures in which the reduction of one of the imide carbonyls was distinctly observable, according to spectral data (IR, NMR, MS). The latter problem could be avoided by carrying out the reduction according to the Meerwein-Ponndorff-Verley procedure (aluminium isopropoxide, isopropanol). This method not only smoothly reduced the ketone function of 4, into the corresponding hydroxyl group, but the reduction proceeded stereoselectively and the reaction product (58%) was found to consist of a mixture of 5⁷ and 6⁸ in a ratio of 6:1. The spectral data of 5⁷ and 6⁸ attested to their structures and were in complete agreement with the data described by other workers^{1, 3a-c}.

References.

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5. 3: Oil. IR(CHCl₃): 3400, 1705, 1690, 1660, 1580 cm⁻¹, ¹H NMR (CDCl₃): δ 1.7 - 3.0 (m, 6H), 3.8 - 3.95 (m, 4H, -OCH₂CH₂O-), 4.33 (s, CH₂Ph), 4.75 (d x d, J=2, J=8, H₅), 5.90 (d x d x d, J=1.5, J=2, J=8, H₆), 7.25 (m, 6H, H₈ + Ph), 7.85 (s, broad, NH).
6. 4: M.p.: 278-280°C. IR(KBr): 2800-2400, 1740, 1710, 1700, 1600 cm⁻¹. ¹H NMR (DMSO-d₆): δ 2.3 - 2.6 (m, 4H, CH₂-CH₂), 2.7 - 2.9 (m, 2H, CH₂C=O), 7.71 (d, J=5.5, H₅), 4.83 (d, J=5.5, H₆), 9.10 (s, H₈), 11.6 (broad, NH).
7. 5: M.p.: 240-242°C. IR(KBr): 3510, 2850-2600, 1710, 1690, 1600 cm⁻¹. MS (70eV): M⁺=232, ¹H NMR (DMSO-d₆): δ 1.7-2.4 (m, 5H, cyclopentane CH) 2.65 (d x d J=5, J=14, cyclopentane CH), 4.50 (m, H₁₀), 5.10 (broad, OH), 7.87 (d, J=6, H₅), 8.80 (d, J=6, H₆), 9.04 (s, H₈), 10.7 (broad, N-H).
8. 6: M.p.: 235-237°C. IR(KBr): 3500, 2850-2500, 1710, 1690, 1600 cm⁻¹. NMR(DMSO-d₆): δ 4.50 (m, 1H), 5.0 (broad, OH), 7.45 (d, J=6, H₅), 8.74 (d, J=6, H₆), 9.05 (s, H₈).

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