Transannular Route to the Pyrrolizidine Skeleton. *X*-Ray Crystal Structure of 1-Bromopyrrolizidine

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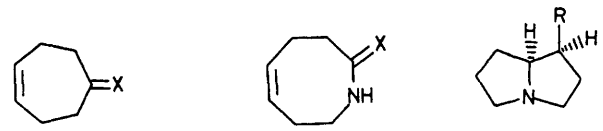
Summary The synthesis of pyrrolizidine was achieved by transannular bromination of 1-azacyclo-oct-4-ene followed by reduction with $LiAlH_4$.

PYRROLIZIDINE alkaloids were first isolated from a species of *Senecio* by Watt in 1909.[1] Since their discovery there has been widespread interest in the synthesis and pharmacology of these heptatotoxins.[2] In connection with our interest in a general, transannular approach to the synthesis of 1-substituted alkaloids of this class, we report such a cyclization which forms the pyrrolizidine ring system and the C-1 substitution in a single, stereospecific step.



(1) (2) (3)

a; X = NOH a; X = O a; R = Br

b; X = $NOSO_2C_6H_4Me$-*p* b; X = H_2 b; R = H

The oxime of cyclohept-4-enone[3]† (**1a**) (m.p. 57—58 °C) was allowed to react with toluene-*p*-sulphonyl chloride in pyridine to give (**1b**) (73%, m.p. 83—84 °C), which underwent a Beckmann rearrangement in aqueous tetrahydrofuran to yield the lactam (**2a**) [89%, m.p. 82—83 °C, i.r. 3400 and 1645 cm^{-1}, n.m.r. ($CDCl_3$); δ 7·00 (1H, br s), 5·65 (2H, m), 3·47 (2H, q), and 2·2—2·8 (6H, m)]. The lactam (**2a**) was reduced to the amine (**2b**) with $LiAlH_4$ [54%, b.p. 90—100 °C (20 mmHg), i.r. 3300 cm^{-1}, n.m.r. ($CDCl_3$): δ 5·75 (2H, m), 2·80 (4H, m), 2·10 (6H, m), and 1·60 (1H, m), picrate m.p. 148—149 °C]. The reaction of the amine (**2b**) with bromine in dichloromethane yielded (**3a**)[4] [HBr salt, 95%, m.p. 120—130 °C; picrate salt m.p. 224—226 °C, n.m.r. [$(CD_3)_2CO$], δ 8·61 (2H, s), 4·93 (1H, m), 4·64 (1H, m), 3·86 (2H, m), 3·41 (2H, m), 2·95 (4H, s), 2·82 (1H, m), 2·55 (1H, m), and 2·27 (1H, m)]. The structure of (**3a**) was determined by a single crystal *X*-ray diffraction experiment

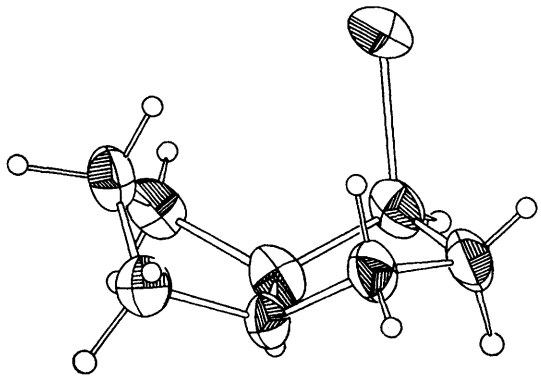


FIGURE. ORTEP drawing of $[C_7H_{13}NBr]^+$ Br^- (**3a**).

(Figure).‡ Treatment of (**3a**) with NaOH gave the free base which was reduced with $LiAlH_4$ to yield the pyrrolizidine (**3b**) (47%, picrate m.p. 234—235 °C, lit.[5] m.p. 245 °C).

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† All compounds have n.m.r., i.r., and mass spectra in complete accordance with the assigned structure. All new compounds gave correct microanalyses.

‡ Compound (**3a**) HBr crystallizes in the space group $P2_1/n$ with four molecules in the unit cell. Cell constants at −160 °C are a = 10·068(12), b = 13·469(9), c = 7·135(3) Å, and β = 97·30(2)°. Crystallographic data for this paper may be obtained in microfiche form for $2.50 from the Chemistry Library, Indiana University, Bloomington, Indiana, 47401. Refer to J. C. Huffman, Indiana University Molecular Structure Reports No. 7603, 1976. This transannular cyclization product has stereochemistry consistent with a disfavoured *exo* (J. E. Baldwin, *J.C.S. Chem. Comm.*, 1976, 734) mode of cyclization and is that expected from opening of the bromonium ion by the nitrogen. An alternative mechanism has not been ruled out, however.

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