Synthesis of Azetidin-3-ol

By S. S. CHATTERJEE and D. J. TRIGGLE*

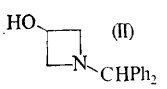
(*Department of Biochemical Pharmacology, School of Pharmacy and The Center For Theoretical Biology, State University of New York at Buffalo, Buffalo, New York,* 14214)

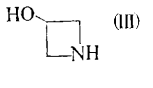
DESPITE current interest in the synthesis and chemistry of substituted azetidin-3-ols,[1-4] there has been no report of the synthesis of the title compound. We now report a convenient synthesis of azetidin-3-ol hydrochloride (III).

3-Chloro-1-diphenylmethylamino-2-hydroxypropane† (I), obtained from benzhydrylamine and 1-chloro-2,3-epoxypropane, had m.p. 201° (HCl salt) and was cyclised[3] to 1-diphenylmethylazetidin-3-ol (II), m.p. 115°. Hydrogenolysis of (II) (as the HCl salt) in ethanol at 60 lb./in.^{2} with 5% Pd–C catalyst gave azetidin-3-ol hydrochloride (III), m.p. 91—92°; ν_{max} (Nujol) 3300 (OH,NH); 2600, 2350, 1530 cm.$^{-1}$ (NH_2^+); n.m.r. (in D_2O) shows a multiplet at δ 4·2.

Assignment of structure (II) was supported by elemental analysis and further confirmed by mass spectrometry which gave a molecular formula $C_{16}H_{17}NO$ [M^+, 239; *m/e* $M-18$ ($C_{16}H_5N$), $M-72$ ($C_{13}H_{11}$), $M-167$ (C_3H_6NO)]. The infrared spectrum showed ν_{max} (Nujol) 3180 (bonded OH) and 1580 cm.$^{-1}$ (aromatic) and the n.m.r. spectrum (in $CDCl_3$, Me_4Si reference) showed two two-proton triplets centred at δ 2·9 and 3·5 ($J \sim 7$ c./sec.), assignable to the ring methylene groups of (II), and a one-proton multiplet at δ 4·4 assignable to the C-3 proton, in addition to the signals expected for the aromatic (δ 7·3), hydroxyl (δ 3·4), and benzylic (δ 4·3) protons.

$Ph_2CH\cdot NH\cdot CH_2\cdot CH(OH)\cdot CH_2Cl$ (I)





The satisfactory elemental analysis of the product of hydrogenolysis (III) and its non-identity (m.p., mixed m.p., and infrared spectrum) with 2-hydroxypropylamine hydrochloride eliminated the possibility that ring opening had occurred during the hydrogenolysis of (II). Attempts to synthesise (III) from benzylamine and 1-chloro-2,3-epoxypropane failed because 3-chloro-1-benzylamino-2-hydroxypropane could not be cyclised: this accords well with a previous conclusion[5] that a bulky nitrogen substituent is necessary to promote cyclisation over competing intermolecular reactions.

This work was supported by the U.S. Public Health Service, National Institutes of Health.

(*Received, December 11th,* 1967; *Com.* 1326.)

† Satisfactory elemental analyses were obtained for all new compounds.

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