Synthesis of Azetidin-3-ols

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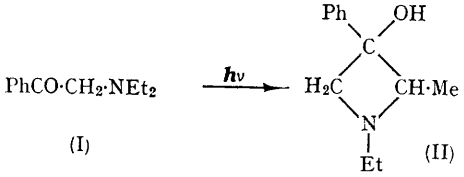
No direct synthetic routes to azetidines bearing a functional group on a ring carbon atom have been reported, other than β-lactams and azetidine-2-carboxylic acid, and in fact the synthetic approaches to azetidines are in general limited, as shown by Moore in his recent Review.[1] We report that azetidin-3-ols may be obtained readily by ultraviolet irradiation of β-dialkylamino-ketones.

For example, 1-ethyl-2-methyl-3-phenylazetidin-3-ol (II), b.p. 72—73° (0·05 mm.), was isolated in 26% yield, following the irradiation of a dilute ether solution of *NN*-diethylphenacylamine (I) with a 200 w, water-cooled, high-pressure mercury lamp.

Assignment of structure (II) was supported by the elemental analysis, which was in excellent agreement with theory, and by the infrared and n.m.r. spectra. The infrared spectrum showed the absorptions at 2·99, 7·65, and 8·65μ expected of a tertiary alcohol, and no carbonyl absorptions. The n.m.r. spectrum (of a carbon tetrachloride solution) showed two one-proton doublets, centred at τ 6·87 and 7·26 (coupling constant 8 c./sec.) for the ring methylene group, a three-proton doublet at τ 8·63 for the 2-methyl group, and a one-proton, solvent-sensitive singlet at τ 7·17 for the hydroxyl proton, in addition to the absorptions expected for the phenyl, *N*-ethyl, and C-2 methine protons.



(I) (II)

Further confirmation of the structure was afforded by isolation of the acetate ester of (II), b.p. 65—67° (2 mm.) from the reaction of the azetidinol (II) with acetic anhydride. The elemental analysis of this ester and its infrared and n.m.r. spectra were in agreement with the structure assigned.

Analogous photocyclization of *NN*-dimethylphenacylamine and of *NN*-di-isopropylphenacylamine to give 1-methyl-3-phenylazetidin-3-ol, b.p. 56—57° (0·05 mm.), and 2,2-dimethyl-1-isopropyl-3-phenylazetidin-3-ol, b.p. 88—89° (0·05 mm.), was also observed. These products were isolated in yields of 9% and 22%, respectively, and their structures were confirmed by analytical and spectral data.

The chief limitation to the yields of azetidin-3-ols by this method appeared to be a tendency for cleavage of the phenacylamines by a Norrish type II process. Acetophenone and the trimer of the imine expected from this process were isolated in yields of 30—55% in each case.

This reaction appears to represent the first C–C ring closure of an azetidine, other than a β-lactam, and thus introduces a new type of azetidine synthesis. It is analogous to the photosynthesis of cyclobutanols from appropriate ketones[2–4] and to the recently reported photosynthesis of oxetan-3-ols from alkyl phenacyl ethers.[5] The corresponding photosynthesis of a thietan-3-ol from a phenacyl sulphide, however, has not been achieved.[6]

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