Stable 1*H*-Azepines

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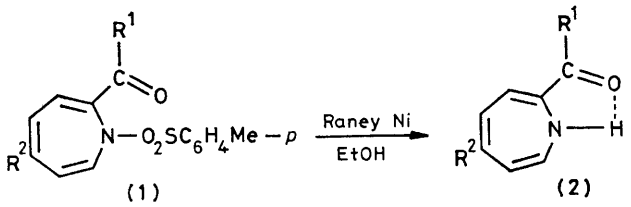
Summary The hitherto unknown 1*H*-azepines (**2**), stabilized by hydrogen bonding between the NH-hydrogen and the adjacent CO-oxygen, have been prepared by detosylation of their *N*-tosyl derivatives (**1**).

SEVERAL 2*H*-, 3*H*-, and 4*H*-azepine derivatives with substituents on one or more of the carbon atoms are known,[1] and a number of *N*-substituted 1*H*-azepines have also been reported.[2] We have reported the synthesis of *N*-tosyl deriva-

tives of 1*H*-azepines with electron-withdrawing substituents such as CO_2Me, Ac, and NO_2 α to the ring nitrogen,[3–5] but stable 1*H*-azepines have not been reported so far.[6] During the photolysis of phenyl azide in diethylamine, 2-diethylamino-1*H*-azepine was detected as an unstable intermediate on the basis of n.m.r. evidence,[7] but work-up gave only the 3*H*-azepine derivative.

We now report the synthesis of stable 1*H*-azepines, with CO_2Me or Ac subsituents α to the ring nitrogen atom. The *N*-tosylazepines (**1a**) and (**1b**)[3,5] were detosylated with Raney nickel to yield 2,5-bismethoxycarbonyl- (**2a**) and 2-acetyl-1*H*-azepine (**2b**).† Thus, a stirred mixture of (**1a**) and Raney nickel (1 ml) in ethanol (10 ml) was refluxed for 15 h. After removal of nickel and evaporation, column chromatography of a solution of the product on silica gel with benzene–ethyl acetate (4 : 1) as eluant gave (**2a**) as yellow needles, m.p. 112 °C (benzene) (70%) and unchanged (**1a**) (0·06 g). The 1*H*-azepine (**2a**) showed u.v.–visible absorptions at 234 and 396 nm, whereas (**1a**) showed absorption at 355 nm only; ν_{max} for (**2a**) 3340 (NH), and 1740 and 1700 cm^{-1} (free and hydrogen-bonded ester CO groups); ^1H n.m.r. δ 6·8—8 (m, NH and 4 azepine ring H), and 3·73 and 3·9 (CO_2Me); *m/e* 209 (M^+).

Similarly, (**2b**) was obtained from (**1b**) in 75% yield, platelets, m.p. 144 °C (from benzene); ν_{max} 3300 (NH) and



a; R^1 = OMe, R^2 = CO_2Me
b; R^1 = Me, R^2 = H

1640 cm^{-1} (hydrogen-bonded CO); *m/e* 135 (M^+); δ 6·7—7·9 (m, NH and 4 azepine ring H) and 2·7 (COMe). There was no indication of the presence of methylene or methine protons in the n.m.r. spectra of (**2a**) and (**2b**), thus ruling out the possibility of C*H*-azepine structures. In both compounds, the NH proton was strongly hydrogen-bonded to the adjacent CO group and was not exchangeable with D_2O; this hydrogen-bonding clearly stabilizes these compounds.

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† Satisfactory elemental analyses were obtained.

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