Ring Expansion of α-Azidoazines: Formation of the First Examples of Fully Unsaturated Monocyclic 1,3,5-Triazepines

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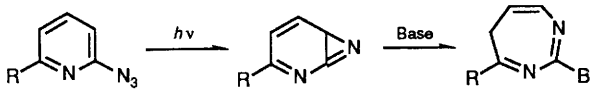
Photolysis of the 2-azidopyridines (**3**), 2-azidopyrazines (**6**), and 4-azidopyrimidines (**8**), having a strong electron-donating substituent, in the presence of methoxide ion or diethylamine results in ring expansion to give the corresponding fully unsaturated 1,3-diazepines (**5**) and 1,3,5-triazepines (**7**) and (**9**).

Thermal and photochemical ring contractions of α-azidopyridines[1] and α-azidodiazines[2] have been widely investigated,[3] as well as their azide (**1**)–tetrazole (**2**) isomerism, Scheme 1. However, the isolation of ring expansion products from α-azidoazines has not been reported, although in some cases, the key intermediates for the ring contractions have seemed to be unisolable ring expansion species.[1,2] On the other hand, aryl azides[4] including 3- and 4-azidopyridines[5] are known to undergo ring expansion *via* the singlet nitrenes either by thermolysis or by photolysis. However, 2-azidopyridines have not appeared to undergo such ring expansion because 2-azidopyridine and its methyl derivatives exist predominantly as the tetrazole form, and in fact, attempts to obtain ring expansion products from them have been unsuccessful. We report here the first examples of the isolation of ring expansion products from α-azidoazines and of a novel heterocyclic ring system, 1,3,5-triazepine.

(**1**) (**2**)

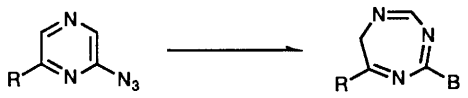
Scheme 1



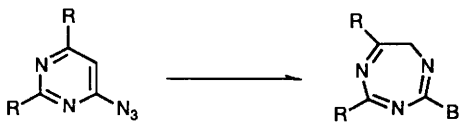
(**3**) (**4**) (**5**)

R = OMe, OPh, NEt_2 Base = $^-$OMe, Et_2NH
B = OMe, NEt_2

Scheme 2



(**6**) (**7**)



(**8**) (**9**)

R, B = OMe, NEt_2

Scheme 3

Irradiation (400 W, high-pressure Hg lamp; Pyrex) of the 2-azidopyridines (**3**) in methanol–dioxane (1 : 1) containing a large excess of sodium methoxide or diethylamine as a nucleophile until almost all of the starting azides had been consumed (20—45 min) resulted in ring expansion to give the corresponding 5*H*-1,3-diazepines (**5**) in 60—80% yields,† probably *via* the azirine intermediates (**4**) derived from nitrenes initially generated from (**3**), Scheme 2.

The 2-azidopyridines (**3**)‡ with a strong electron-donating group such as a methoxy or diethylamino group on the 6-position, showed azide absorption bands at around 2150 cm^{-1} in the IR spectra either in the solid state or in solution; indicating that the azide–tetrazole equilibrium lies on the side of the azide form. Thus the ring expansion reaction involving nitrene intermediates occurred. On the contrary, 2-azidopyridine and its methyl derivatives, which exist predominantly as the tetrazole form[1,3]§ and showed no IR azide band, were irradiated under similar conditions for 6—7 h, with almost complete recovery of the starting tetrazoles.

With regard to diazines, both 2-azidopyrazines (**6**) and 4-azidopyrimidines (**8**) having a methoxy or dimethylamino group, upon irradiation for 20—30 min, also underwent ring expansion to afford the 1,3,5-triazepines (**7**) and (**9**) in 40—50% and 50—70% yields, respectively. However, in the cases of 3-azidopyridazines (unsubstituted, 6-methyl-, and 6-methoxy-) known[2,3] to exist exclusively as the tetrazole form, even when irradiated for 10 h, no reaction occurred. In addition, the photolysis of 2-azidopyrazines and 4-azidopyr-

† Satisfactory elemental analyses and spectroscopic data were obtained for all new products reported. *Selected spectroscopic data* for (**5a**) (R = B = OMe) viscous oil, ^{1}H NMR ($CDCl_3$) δ 2.72 (2H, dt, 5-H_2), 3.76 (6H, s, 2- and 4-OMe), 4.82 (1H, dt, 6-H, $J_{5,6}$ 6, $J_{6,7}$ 8 Hz), 6.44 (1H, d, 7-H); ^{13}C NMR δ 31.9 (t, 6-C), 53.9 (q), 55.5 (q), 104.8 (d, 6-C), 137.8 (d, 7-C), 157.6 (s), and 163.2 (s). For (**7a**) (R = B = OMe) viscous oil, ^{1}H NMR δ 3.86 (6H, s, 2- and 7-OMe), 4.30 (2H, s, 6-H_2), and 7.67 (1H, s, 4-H); ^{13}C NMR δ 51.7 (t, 6-C), 54.8 (q), 55.8 (q), 157.5 (d, 4-C), 166.3 (s, 2- and 7-C). For (**7b**) (R = OMe, B = NEt_2) viscous oil, ^{1}H NMR δ 1.15 and 3.47 (6H, t, and 4H, q, *J* 8 Hz, NEt_2), 3.73 (3H, s, 7-OMe), 3.87 (2H, s, 6-H_2), 7.53 (1H, s, 4-H); ^{13}C NMR δ 13.6 (q), 41.8 (t), 51.2 (t, 6-C), 54.8 (q), 158.1 (s), 159.4 (d, 4-C), 163.4 (s). For (**9b**) (R = B = NEt_2) viscous oil, ^{1}H NMR δ 1.0—1.5 and 3.2—3.9 (18H, m, and 12H, m, 2-, 4-, and 7-NEt_2), 4.13 (2H, s, 6-H_2); ^{13}C NMR δ 12.5 (q), 13.2 (q), 13.5 (q), 15.4 (q), 40.2 (t), 43.0 (t), 43.2 (t), 43.7 (t), 44.9 (t, 6-C), 156.2 (s), 160.3 (s). The structures of these products were further confirmed by some chemical studies; details will be published in a full paper.

‡ The starting α-azidoazines used were prepared from the corresponding α-chloroazines by treatment with sodium azide or with hydrazine followed by sodium nitrite; *cf.* refs. 1 and 2.

§ It has been observed that the azide–tetrazole equilibria are usually shifted towards the side of azide forms in strong acids such as trifluoroacetic acid, trifluoromethanesulphonic acid, and conc. sulphuric acid. However, in the present basic conditions, the equilibria strongly lie on the side of tetrazole forms.

imidines with no strong electron-donating substituent resulted only in decomposition or recovery of the starting compounds, and no ring expansion products could be obtained, Scheme 3.

Much effort has recently been devoted to the synthesis of new fully unsaturated seven-membered heterocyclic rings with two or more hetero atoms.[6] With regard to monocyclic triazepines, 1,2,4-[7] and 1,2,5-triazepines[8] have been prepared, but other possible isomers, 1,2,3- and 1,3,5-triazepines, have remained unknown. The products (**7**) and (**9**) are the first examples of 1,3,5-triazepines.

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