Synthesis of Simple Monocyclic 1,3-Diazepines from 1,2-Diazepines

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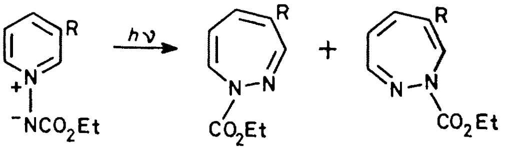
Summary Thermolysis of the 1*H*-1,2-diazepines having an electron-donating substituent in the 4- or 6-position affords the corresponding 1,3-diazepines, whereas 1,2-diazepines having electron-withdrawing substituents do not show this ring-conversion

WE have recently reported the first synthesis of fully unsaturated 1,3-diazepines condensed with aromatic rings such as benzene, thiophen, furan, or pyrrole[1] As part of our studies on diazepines, we wished to prepare some simple monocyclic 1,3-diazepines, as only two highly substituted examples have been reported[2,3] One of them, 5-acetoxy-1-benzoyl-6-methyl-7-phenyl-1*H*-1,3-diazepine, was prepared by thermal rearrangement of the 1,2-diazepine derivative[3] Prior to this work, the thermolysis of 1,2-diazepines had been investigated and did not give the corresponding 1,3-diazepines[4] These results prompted us to examine this thermolysis in more detail and we now report our results

Irradiation of the 3-substituted pyridine *N*-imides (**1**) resulted in the formation of the corresponding 4- and 6-substituted 1*H*-1,2-diazepines (**2**) and (**3**) in yields of 60—70% and 20—30%, respectively.†



(1) (2) (3)

SCHEME 1

The 1,2-diazepines (**4a**—**h**) thus obtained were heated at 90—140 °C in xylene to give the corresponding 1,3-diazepines (**5**) in 30—70% yields, as well as 2- or 6-ethoxycarbonylaminopyridines Heating of the diazabicyclo[3 2 0]-heptadienes (**6**), which are readily obtained in high yields by further irradiation of (**4**), also gave the 1,3-diazepines (**5**) Irradiation of (**5**) afforded the bicyclic compounds (**7**), which reverted back to (**5**) when heated at *ca* 150 °C ‡

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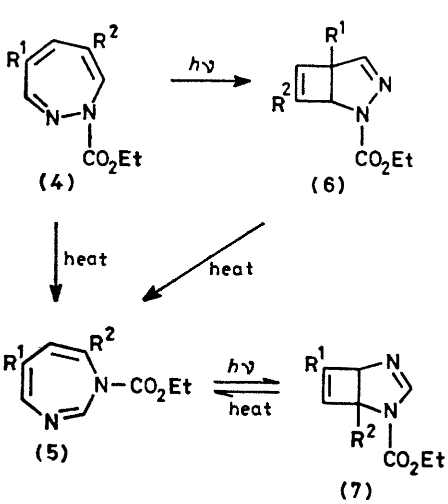
† Pyridine *N*-acylimides are known to undergo photo-induced rearrangement to give 1*H*-1,2-diazepines and the diazepines (**4a**—**c**) have already been reported, for a review, see M Nastasi, *Heterocycles*, 1976, **4**, 1509

‡ The new 1,3-diazepines (**5**) are extremely susceptible to decomposition by water, acids silica gel, and alumina, and thus can be isolated only by Sephadex chromatography Satisfactory elemental analyses and spectral data were obtained for all new compounds reported, *e g* , (**5a**) yellow oil, λ(ε) (EtOH) 245 (5800) and 310 nm (1500), δ ($CDCl_3$) 1 81 (3H, br, 5-Me), 5 41 (1H, dd, 6-H), 5 74 (1H, d, 7-H), 6 61 (1H, s, 2-H) 6 64 (1H, m, 4-H), and 1 32 and 4 25 (3H, t and 2H q CO_2Et), $J_{4,6}$ 1 5 $J_{6\ 7}$ 7 Hz (**5b**) yellow oil λ(ε) (EtOH) 243 (4500) and 293 nm (2200), δ ($CDCl_3$) 2 12 (3H, br, 7 Me) 5 89 (1H, m 6 H) 5 92 (1H m 5 H) 6 68 (1H s 2 H) 6 95 (1H d, 4-H), and 1 32 and 4 25 (3H, t, and 2H, q, CO_2Et), $J_{4\ 5}$ 8 $J_{5,6}$ 6 Hz, (**5c**) yellow oil λ(ε) (EtOH) 245 (5500) and 305 nm (1800), δ ($CDCl_3$) 3 61 (3H, s, OMe), 5 42 (1H, dd, 6-H) 5 91 (1H d, 7-H), 6 29 (1H, br d, 4-H), and 7 63 (1H s 2 H), $J_{4\ 6}$ 1 5 $J_{6\ 7}$ 7 Hz, (**7a**) colourless oil, δ ($CDCl_3$) 1 82 (3H, br, 5-Me), 4 57 (1H, m, 4-H), 4 90 (1H, m, 7-H), 5 96 (1H, m, 6-H), 7 48 (1H, s, 2-H), and 1 32 and 4 22 (3H, t, and 2H, q, OEt)

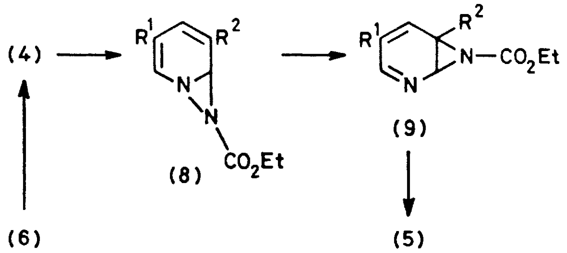


SCHEME 2

a: R¹ = Me, R² = H
b: R¹ = H, R² = Me
c: R¹ = OMe, R² = H
d: R¹ = H, R² = OMe
e: R¹ = Me, R² = Me
f: R¹ = NHAc, R² = H
g: R¹ = H, R² = NHAc
h: R¹ = NEt$_2$, R² = H

However, 1*H*-1,2-diazepines having an electron withdrawing substituent such as an acyl or halogen group in the 4- or 6-position, upon heating, gave the parent *N*-imides (**1**) and 2- or 6-aminopyridines, but no 1,3-diazepines. Similarly, 3-, 5-, or 7-substituted 1*H*-1,2-diazepines with either an electron-donating or -withdrawing substituent also gave no 1,3-diazepines. These results clearly indicate that the presence of an electron-donating substituent in the 4- and/or 6-position is essential for the thermal rearrangement of (**4**) into (**5**).

The formation of the 1,3-diazepines (**5**) from (**4**) may involve the diaziridine intermediate (**8**), which then rearranges to the aziridine (**9**) followed by ring-expansion to (**5**) which is analogous to the formation of condensed 1,3-diazepines[1,3] and 1,3-oxazepines[5] from the corresponding pyridine *N*-imides and *N*-oxides. The electron-donating groups may provide assistance for breaking the N–N bond in the diaziridine (**8**) and for cyclization of the resulting dipolar intermediate into aziridine (**9**) as suggested by Moore,[3] whereas electron-withdrawing groups would assist the C–N bond fission into (**1**).



SCHEME 3

The photochemical and thermal interconversion between the diazepines (**4**) and (**5**) and the bicyclic compounds (**6**) and (**7**) are analogous to those observed for various kinds of seven-membered ring heterocycles.[6]

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