Cycloaddition of 1-Azirines to 1,2,4,5-Tetrazines. Synthesis and Rearrangement of 1,2,4-Triazepines

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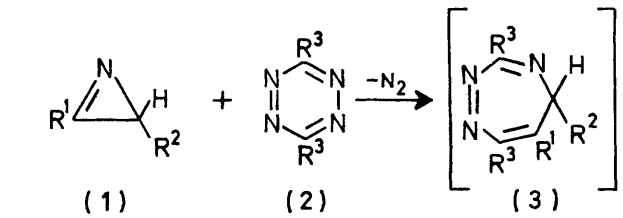
Summary Thermal 1:1 cycloaddition of 1-azirines to *sym*-tetrazines provides a synthesis of the as yet unknown class of 1,2,4-triazepines and also leads *via* these intermediates to pyrimidines, pyrazoles, and 2:1 adducts.

As part of our work on the development[1] of the 1-azirines (**1**) as dienophilic components in Diels–Alder reactions we have demonstrated[1a–d] that 2*H*- and 3*H*-azepines may be conveniently prepared from (**1**) and cyclopentadienones (*via* loss of CO). The *sym*-tetrazines (**2**) react with olefins and acetylenes, with extrusion of N_2, to yield the corresponding heterocyclic systems.[2] We have now examined the reaction of the 1-azirines (**1**) with the *sym*-tetrazines (**2**) as a possible route to the as yet unknown 1,2,4-triazepine system.

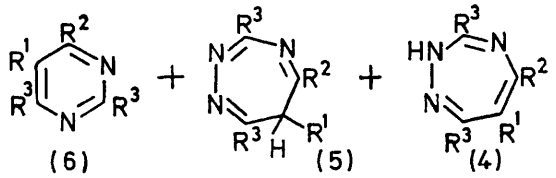
When an excess of the azirines (**1a**—**c**) was treated with



(1) (2) (3)

(a) R^1 = Ph, R^2 = H
(b) R^1 = Ph, R^2 = Me
(c) R^1 = H, R^2 = Bu^t

(a) R^3 = Ph
(b) R^3 = *p*-Tol
(c) R^3 = 2-Py

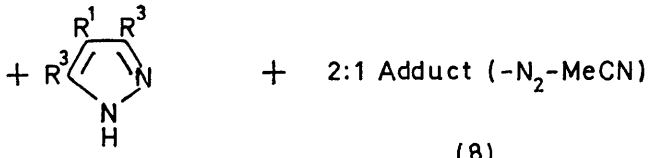


(6) (5) (4)

(a) R^1 = R^3 = Ph, R^2 = H
(b) R^1 = R^3 = Ph, R^2 = Me
(c) R^1 = H, R^2 = Bu^t, R^3 = Ph
(d) R^1 = Ph, R^2 = Me, R^3 = *p*-Tol

(a) R^1 = R^3 = Ph, R^2 = Me
(b) R^1 = Ph, R^2 = Me, R^3 = *p*-Tol
(c) R^1 = H, R^2 = Bu^t, R^3 = 2-Py

(a) R^1 = R^3 = Ph, R^2 = H
(b) R^1 = Ph, R^2 = Me, R^3 = 2-Py
(c) R^1 = H, R^2 = Bu^t, R^3 = 2-Py



(7) (8)

(a) R^1 = R^3 = Ph
(b) R^1 = Ph, R^3 = *p*-Tol
(c) R^1 = Ph, R^3 = 2-Py

(a) R^1 = R^3 = Ph, R^2 = Me
(b) R^1 = Ph, R^2 = Me, R^3 = *p*-Tol
(c) R^1 = Ph, R^2 = Me, R^3 = 2-Py

the tetrazines (**2a**—**c**) in toluene under reflux, until t.l.c. showed the disappearance of the brilliant red or purple tetrazines, several products were isolated: the isomeric triazepines (**4**) and (**5**),† the pyrimidines (**6**)‡ the pyrazoles (**7**),§ and an adduct (**8**) analysing for 2 molecules of the azirine (**1b**) and 1 molecule of the tetrazine (**2a**—**c**) minus the units of N_2 and MeCN. This adduct of uncertain structure was the major product (40%) from the azirine (**1b**) and the tetrazines (**2a**) and (**2b**), although adducts possessing structures (**4**)—(**7**) were also isolated.

When the more reactive compound (**2c**) was heated with (**1b**), the reaction required only 1 h for completion [as opposed to 40—70 h for (**2a**) or (**2b**)]. This enabled the isolation of the triazepine (**4b**) in 95% yield. Similarly, cycloaddition of (**1c**)[1c] to (**2c**) gave the triazepine (**4c**) in 82% yield, whereas interaction of (**1c**) with (**2a**) afforded solely (92%) the pyrimidine (**6c**).

Although the 5*H*-1,2,4-triazepine (**3**) was never isolated, the formation of the 2*H*-1,2,4-triazepines (**4**) may be rationalised in terms of a thermally allowed [1,5]-hydrogen shift involving (**3**). This is completely analogous to the 2*H*- → 3*H*-azepine isomerisations reported.[1b,c] A subsequent [1,5]-hydrogen shift of (**4**) would afford the 6*H*-isomer (**5**). Thermal decompositions of the triazepines may lead to the pyrimidines (**6**) (*via* equilibrations to triazanorcaradienes followed by loss of NH) or to the pyrazoles (**7**) (*via* loss of MeCN). Indeed when the triazepine (**4b**) was heated in toluene under reflux for 4 days, the pyrazole (**7c**) was the sole product (89%) isolated. Similarly, the pyrimidine (**6a**) was isolated (together with other products) from the thermolysis of the triazepine (**4a**) in diglyme under reflux. Analogy for these observations is found[3] in the formation of pyridines and pyrazoles from 1*H*-1,2-diazepines.

Since reaction of the triazepine (**4b**) with excess of the azirine (**2b**) afforded the 2:1 adduct (**8c**), it is possible that the adducts (**8**) possess a triazocine structure, formed *via* cycloaddition of a further molecule of azirine to either the triazepine (**4**) or a bicyclic isomer,[5] followed by extrusion of MeCN.

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† Structure elucidation of the triazepines (**4**) and (**5**) is based on i.r., n.m.r., elemental analysis, and mass spectra, their pyrolytic behaviour, and consistency with analogous mechanistic pathways[1,2] elucidated for azepine formation. For instance, the orange (**4a**) showed NH absorption at 3310 cm^{-1}, a molecular ion at *m/e* 323 (57%), and metastable peaks corresponding to loss of HCN and PhCN. The triazepine (**5b**) (yellow) showed no NH bands, the 6-proton appeared as a singlet at τ 2·05 and the C-5 methyl absorption at 7·67.

‡ Structure proof for the pyrimidines (**6**) rests largely on spectral data and elemental analysis. For example, the methyl absorption of (**6b**) was at τ7·52 compared to 7·45 for the reported [4a] 4,6-dimethylpyrimidine. The 6-proton in (**6a**) is found at τ1·22 compared to 1·23 in pyrimidine while the 5-proton in (**6c**) appeared at τ2·40 compared to 2·64 in pyrimidine. In addition the *o*-protons of the aromatic substituent at position 2 of (**6a**) or (**6d**) were considerably deshielded (τ1·5—1·25), in agreement with observed[4b] downfield shifts in 2-phenylpyrimidine.

§ Characterization of the pyrazole (**7a**) was achieved by comparison with an authentic sample,[4c] The other pyrazoles (**7**) were determined by spectral comparison with (**7a**) and elemental analysis.

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