Communications to the Editor

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REGIO-SELECTIVE DIAZEPINE FORMATION FROM 3-AZIDOPYRIDINES: THE FIRST EXAMPLES OF MONOCYCLIC 2H-1,4-DIAZEPINES

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Photolysis of the 2-substituted 3-azidopyridines (5) having no substituent in the 4-position in the presence of sodium methoxide gave the novel 2H-1,4-diazepines (8), whereas 2-unsubstituted (1) and 2,4-disubstituted 3-azidopyridines (10), upon irradiation under similar conditions, afforded the 5H-1,3-diazepines.

KEYWORDS ——— 3-azidopyridine; pyridylnitrene; ring-expansion; photolysis; 5H-1,3-diazepine; 2H-1,4-diazepine; azirine intermediate

Thermal and photochemical ring-expansion of aryl azides such as phenyl,[1] pyridyl,[2,3] and benzopyridyl azides[4,5] to seven-membered N-heterocyclic rings *via* singlet nitrene intermediates under basic conditions have been widely studied. We have recently reported that the photolysis of the 2-unsubstituted 3-azidopyridines (1) in the presence of methoxide ions resulted in the formation of the 5H-1,3-diazepines (4), presumably *via* the azirines (2) and the unstable anti-aromatic NH-diazepines (3).[2] We report here that the photolysis of 2-substituted 3-azidopyridines under similar conditions gave a different novel diazepine ring system from that obtained from the 2-unsubstituted derivatives (1).

The 2-substituted 3-azidopyridines (5a-c), having no substituent in the 4-position, were prepared from the corresponding 3-aminopyridines by diazotization followed by treatment with sodium azide. Then they were irradiated (400 W, high-pressure Hg lamp; Pyrex filter) in methanol-dioxane (1:1) containing a large excess of sodium methoxide for *ca.* 1 h under ice cooling to give the 3-methoxy-2H-1,4-diazepines (8)[6] in 30-40% yields. In contrast, photolysis of the 2,4-dimethyl-3-azidopyridines (10a,b) under similar conditions afforded the 4-methoxy-5H-1,3-diazepines (12);[7] this result is analogous to that of the 2-unsubstituted 3-azidopyridines (1).[2]

The above results may indicate that in unsubstituted (1) and 2,4-disubstituted compounds (10), the initial intramolecular cyclization of the 3-pyridylnitrenes generated from the starting azides takes place predominantly at the 2-position of the pyridine ring rather than the 4-position to form tha azirine intermediates (2,11). And these undergo ring-expansion to give the 1,3-diazepines (4,12) *via* the NH-diazepines such as 3. This route of azirine formation is analogous to that of monosubstituted phenylnitrenes[1,8] in which electron-withdrawing groups favor the cyclization at the 2-position. In contrast, in 2-substituted 3-azidopyridines (5), the cyclization occurs at the vacant 4-position to

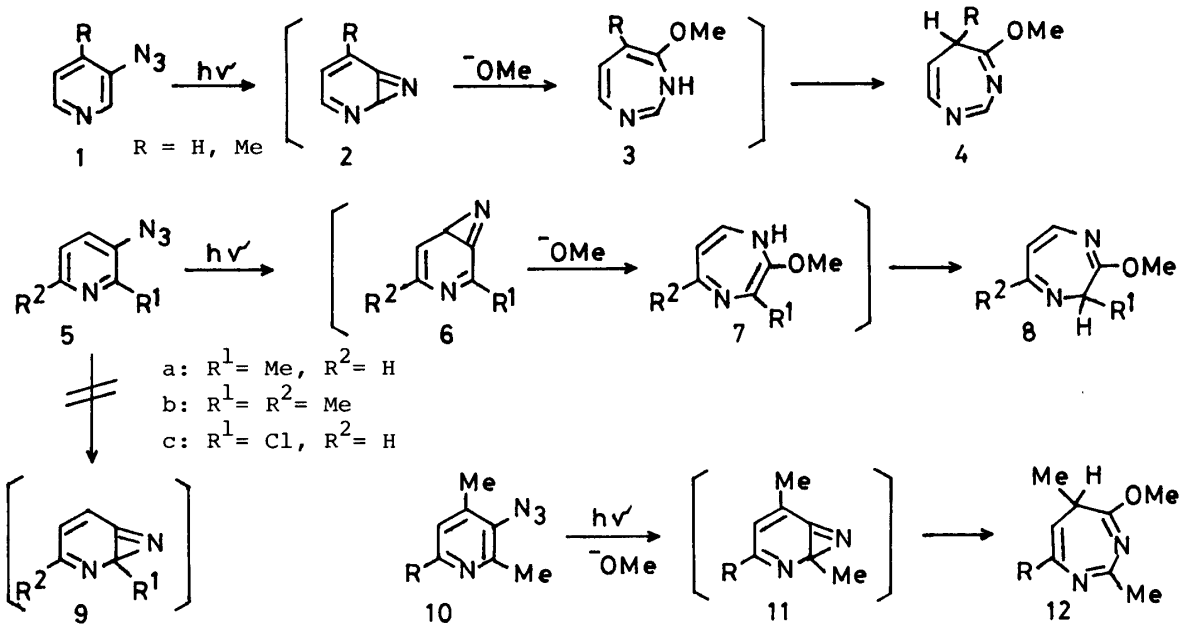

Chart 1

give the 1,4-diazepines (8) via the azirines (6) and the NH-diazepines (7). The formation of 1,3-diazepines derived from the isomeric azirines (9) was not observed. This behavior is analogous to that of 2-substituted phenylnitrenes, which are known to cyclize preferentially at the vacant 3-position.[1,8]

The aza-cycloheptatrienes such as azepines and diazepines can in theory display annular tautomerism between one or more unstable antiaromatic NH forms and relatively stable CH forms.[9] As for 1,4-diazepines, the NH form is also unstable and can be isolated only as its N-substituted derivatives whose substituents are electron-withdrawing groups such as acyl groups.[2,10] Among the three possible CH-tautomers of 1,4-diazepines, only 6H-tautomers have been reported.[2,11] The products (8) are the first examples of fully unsaturated 2H-1,4-diazepines. The NMR spectral data and the results of the following reactions of 8 are compatible

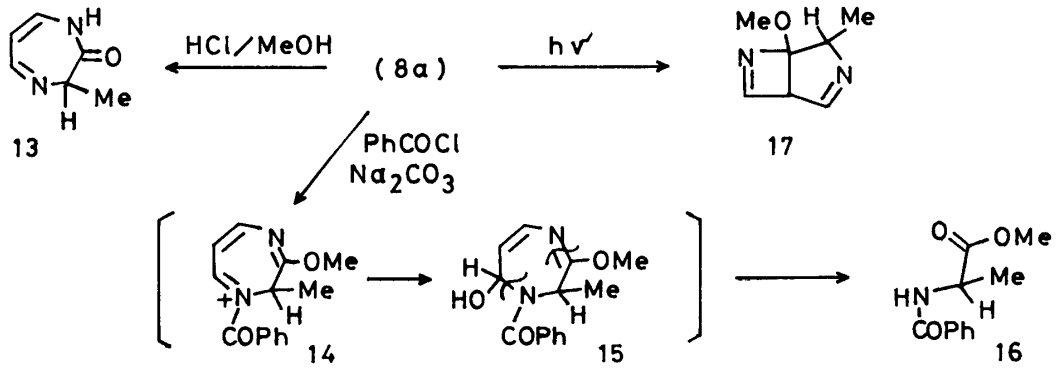

Chart 2

with the assigned novel 2H-1,4-diazepine structure.

Hydrolysis of the diazepine (8a) with hydrochloric acid in methanol gave the diazepinone (13)[12] in 60% yield. Treatment of 8a with benzoyl chloride in the presence of sodium carbonate resulted in decomposition to give the alanine derivative (16) in ca. 20% yield as a fragment product, presumably via 14 and 15 successively. Irradiation of 8a in benzene for 2 h afforded the unstable bicyclic compound (17);[13] similar cyclization is widely observed in the photolysis of aza-cycloheptatrienes.[9]

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6) Satisfactory spectral data were obtained for the new diazepines (8); e.g., (8a): viscous oil; MS m/z: 138 (M^+); ^{1}H-NMR δ ($CDCl_3$): 1.72 (3H, d, J=7 Hz, 2-Me), 3.04 (1H, qd, J=7 and 2 Hz, 2-H), 3.70 (3H, s, OMe), 6.08 (1H, dd, J=8 and 4 Hz, 6-H), 7.12 (1H, dd, J=8 and 2 Hz, 5-H), 7.88 (1H, ddd, J-4, 2, and 2 Hz, 7-H); ^{13}C-NMR δ : 16.62 (q, 2-Me), 55.15 (q, OMe), 59.39 (d, 2-C), 114.33 (d, 6-C), 144.51 (d, 5-C), 153.98 (s, 3-C), 159.51 (d, 7-C). In the case of the 2-chloro compound (5c), the chloro group was replaced by a methoxy group during the reaction to give 2,3-dimethoxy-2H-1,4-diazepine (8c).

7) The structures of the 5H-1,3-diazepines (12) were confirmed by their ^{1}H-NMR spectral data [e.g., 12a: δ ($CDCl_3$) 1.30 (3H, d, J=8 Hz, 5-Me), 2.1-2.3 (1H, m, 5-H), 2.24 (3H, s, 2-Me), 3.70 (3H, s, OMe), 4.70 (1H, dd, J=7 and 6 Hz, 6-H), 6.64 (1H, d, J=7 Hz, 7-H). These spectral data are similar to that of the 5H-1,3-diazepine (4: R=Me) (ref. 2) and eliminate the 2H-1,4-diazepine structure.

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12) (13): mp 128-129 °C; IR (KBr) cm^{-1}: 1670 (C=O); ^{1}H-NMR δ ($CDCl_3$): 1.64 (3H, d, J=7 Hz, 2-Me), 3.44 (1H, qd, J=7 and 2 Hz, 2-H), 5.72 (1H, dd, J=8 and 2 Hz, 6-H), 6.26 (1H, d, J=8 Hz, 5-H), 7.70 (1H, m, 7-H).

13) 5-Methoxy-4-methyl-3,6-diazabicyclohepta-2,6-diene (17) readily decomposed at room temperature, so its structure was determined by only NMR spectral analysis: 1.26 (3H, d, J=8 Hz, 4-Me), 3.50 (3H, s, 5-OMe), 3.98 (1H, q, J=8 Hz, 4-H), 4.30 (1H, d, J=3 Hz, 1-H), 7.62 (1H, d, J=3 Hz, 2-H), 8.52 (1H, s, 7-H). Treatment of 17 with methanol at room temperature resulted in the formation of an unstable methanol-adduct assumed to be 5,7-dimethoxy-4-methyl-3,6-diazabicyclohept-2-ene. This formation was also observed in the photolysis of the 3-azidopyridine (5a) in methanol and thus may cause the decrease in yields of the 1,4-diazepines (8).

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