Communications to the Editor

[Chem. Pharm. Bull. 32(11)4694—4697(1984)]

PHOTOLYSIS OF PYRIDYL AZIDES IN THE PRESENCE OF METHOXIDE IONS: FORMATION OF FULLY UNSATURATED 1,3- AND 1,4-DIAZEPINES

Hiroyuki Sawanishi, Kayoko Tajima, Makoto Osada, and Takashi Tsuchiya*
School of Pharmacy, Hokuriku University,
Kanagawa-machi, Kanazawa 920-11, Japan

Photolysis of 4-azidopyridines (1) in the presence of methoxide ions resulted in ring-expansion to give the 6H-1,4-diazepines (4). Treatment of the diazepine (4a) with benzoyl chloride afforded the 1-benzoyl-1H-1,4-diazepine (5), whose structure was confirmed by some thermal reactions. Upon irradiation under similar conditions, 3-azidopyridines (10) gave the 5H-1,3-diazepines (13), but no 1,4-diazepines could be obtained. Treatment of the diazepines (13) with benzoyl chloride resulted in the formation of the 5-benzoylamino-2-methoxypyridines (16), presumably via the 1-benzoyl-1H-1,3-diazepines (14).

KEYWORDS ——— 3-azidopyridine; 4-azidopyridine; 6H-1,4-diazepine; 1H-1,4-diazepine; 5H-1,3-diazepine; photolysis; ring-expansion; nitrene

The singlet phenylnitrenes generated from azido-,[1] nitro-, and nitrosobenzenes[2] are known to undergo ring-expansion to give azepines via azirine intermediates upon photolysis or thermolysis in the presence of bases. However, such reaction of monocyclic pyridyl azides is little known, although the photolysis of benzopyridyl azides have been reported.[3] Therefore, we examined the photochemical behavior of 3- and 4-azidopyridines under a basic condition and report here the formation of monocyclic 1,3- and 1,4-diazepines. Recently, much attention has been given to the chemistry of new conjugated seven-membered heterocycles.[4] Of the diazepines, 1,2-,[5] 1,3-,[6] and 2,3-benzodiazepines[7] have been synthesized recently, as well as related fused diazepines condensed with aromatic heterocyclic rings.[8] Among the three possible monocyclic diazepines, the 1,2-diazepines have been most widely studied.[9] Of the 1,3- and 1,4-diazepines, only 1-acyl-1H-1,3-diazepines[10] and the highly substituted 6H-1,4-diazepines[11] had been reported prior to the present work.

The 4-azidopyridines (1a-d), prepared from the corresponding 4-chloropyridines by treatment with hydrazine followed by diazotization, were irradiated (400 W, high-pressure Hg lamp; Pyrex filter) in methanol-dioxane (1:1)[12] containing sodium methoxide (ca. 1.5 mol eq) to give the 6H-1,4-diazepines (4a-d)[13] in 50-70% yields as the sole ring-expansion products. The oily diazepines (4) are extremely susceptible to decomposition in passing through silica gel and alumina column and thus can be isolated only by Sephadex or kieselguhr chromatography. The NMR spectral data for the products (4), particularly for 4b,[13] are consistent with the proposed 6H-structure and eliminate other possible CH- and NH-tautomers.

The formation of the diazepines (4) may involve ring-expansion of the azirine intermediates (2) derived from the initially formed singlet nitrenes to the unstable antiaromatic NH-diazepines (3), which tautomerize to the more stable CH-form 4, by analogy with the formation of the 2-methoxy-3H-azepines from phenylnitrenes.[12]

Treatment of the 6H-diazepine (4a) with benzoyl chloride in pyridine resulted in tautomerization to give 1-benzoyl-5-methoxy-1H-1,4-diazepine (5: 65% yield),[14] which is the first example of 1H-1,4-diazepine derivatives. This behavior is analogous to those observed for the acylation of 4H-1,2-diazepines[15] and 5H-2,3-benzodiazepines.[7] The spectral data for the benzoylation product did not eliminate the other possible N-benzoyl structure 5', but the result of the following thermolysis is consistent with the proposed 5-methoxy structure 5.

Heating the diazepine (5) at 120-130 °C in xylene gave 5-benzoylamino-2-methoxypyridine (7: 95% yield),[16] presumably via the aziridine intermediate (6); this thermal behavior, including the mode of the azirine ring fission and the substituent effect, is similar to those observed for the thermolysis of 1,2-[4] and 1,3-diazepines.[10] If the structure of the benzoyl diazepine was 5', the thermolysis product would be 3-benzoylamino-4-methoxypyridine (7'). In addition, treatment of 4a with benzoyl chloride in the presence of potassium cyanide resulted in ring-opening to afford the compound (9),[17] presumably via the adduct (8).

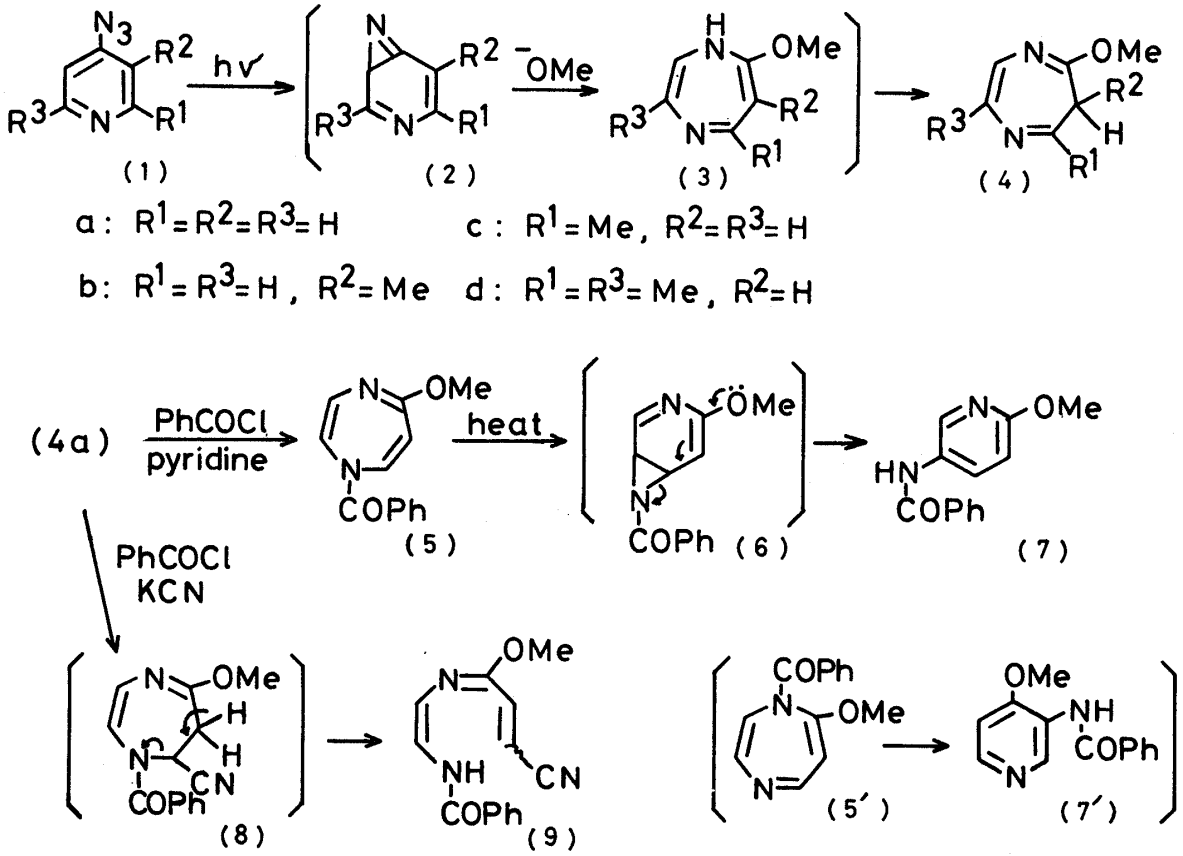

Chart 1

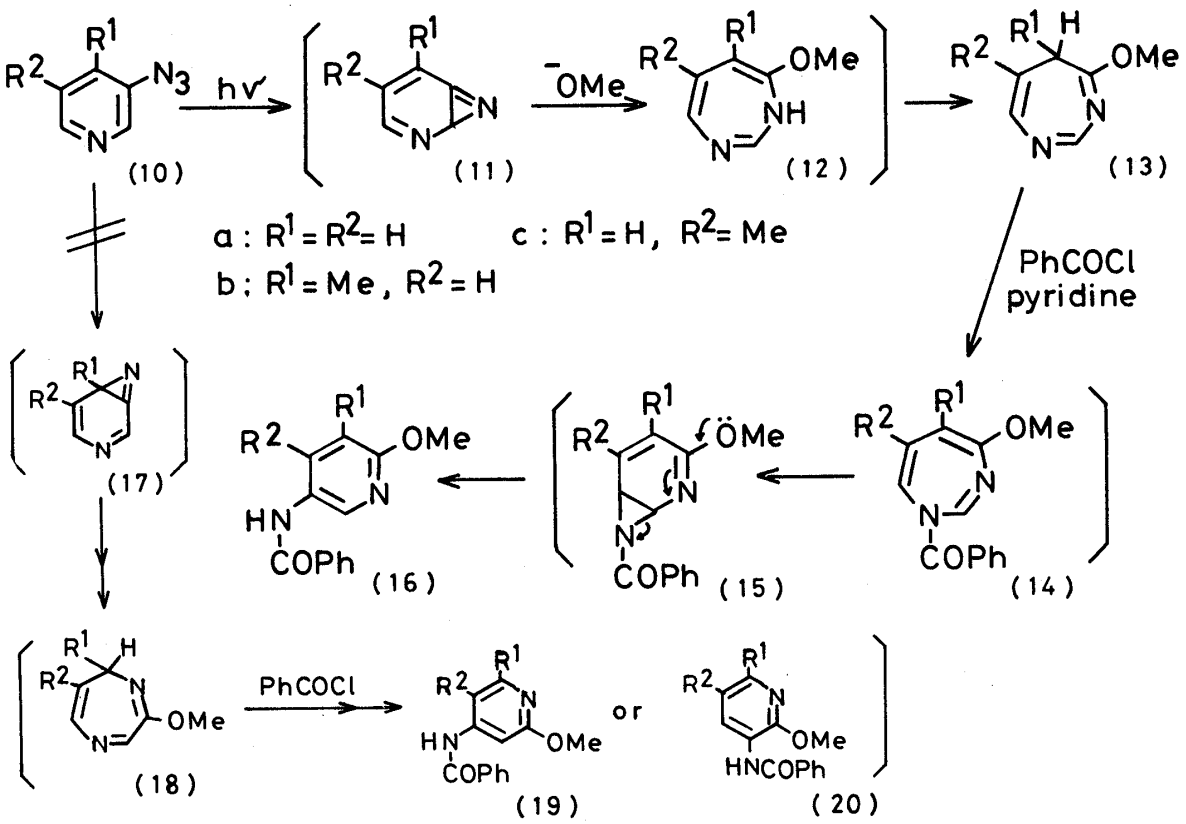

Chart 2

Next, the 3-azidopyridines (10a-c) were irradiated under similar conditions to give the 4-methoxy-5H-1,3-diazepines (13)[18] in 35-55% yields, as the sole characterizable products. In contrast to the 1,4-diazepine (4a), treatment of the 5H-1,3-diazepines (13) with benzoyl chloride in pyridine gave the 5-benzoylamino-2-methoxypyridines (16) directly. This reaction may proceed by initial formation of the 1-benzoyl-4-methoxy-1H-1,3-diazepines (14), which rearrange to the pyridine derivatives (16) via the aziridine intermediates (15), although the key 1H-diazepines (14) could not be isolated. The NMR spectral data and the results of the benzoylation of the diazepines (13) are compatible with the assigned 5H-1,3-diazepine structure.

In the photolysis of the 3-azidopyridines (10), the formation of the 1,4-diazepines such as 18 via the other possible azirine intermediate (17) was not observed. Even though the reaction product without separation was treated with benzoyl chloride, neither 19 nor 20 could be obtained and only 16 was isolated. This direction of the azirine formation of the 3-pyridylnitrenes generated from 10 is analogous to that of the phenylnitrenes having an electron-withdrawing group in the 3-position; the cyclization of the phenylnitrenes to azirines occurs at the 2-position predominantly over at the 4-position.[1,2]

In conclusion, the diazepines (5) and (13) thus obtained are the first examples of NH-type 1,4-diazepines and CH-type 1,3-diazepines, respectively. The present results provide a useful synthetic method for preparing monocyclic 1,3- and 1,4-diazepines. Further investigations are in progress.

REFERENCES AND NOTES

1) R. Purvis, R.K. Smalley, H. Suschitzky, and M.A. Alkhader, J. Chem. Soc., Perkin Trans. 1, 1984, 248; Y. Ohba, S. Kubo, T. Nishiwaki, and N. Aratani, Heterocycles, 22, 457 (1984); and refs. cited therein.
2) F.R. Atherson and R.W. Lambert, J. Chem. Soc., Perkin Trans. 1, 1973, 1079; T. Boer, J.I.G. Cadgan, H.M. McWilliam, and A.G. Rowley, J. Chem. Soc., Perkin Trans. 2, 1975, 554.
3) F. Hollywood, B. Nay, E.F.V. Scriven, H. Suschitzky, Z.U. Khan, and R. Hull, J. Chem. Soc., Perkin Trans. 1, 1982, 421.
4) For a review, see T. Mukai, T. Kumagai, and Y. Yamashita, Heterocycles, 15, 1569 (1981).
5) T. Tsuchiya, J. Kurita, and V. Snieckus, J. Org. Chem., 42, 1856 (1977); T. Tsuchiya and J. Kurita, Chem. Pharm. Bull., 26, 1890 (1978); L. Garanti and G. Zecchi, J. Chem. Soc., Perkin Trans. 1, 1980, 116.
6) T. Tsuchiya, M. Enkaku, and S. Okajima, Chem. Pharm. Bull., 28, 2602 (1980); idem, ibid., 29, 3173 (1981).
7) A.A. Reid, J.T. Sharp, H.R. Sood, and P.B. Thorogood, J. Chem. Soc., Perkin Trans. 1, 1973, 2543; J. Kurita, M. Enkaku, and T. Tsuchiya, Chem. Pharm. Bull., 30, 3764 (1982).
8) For reviews, see T. Tsuchiya, Yuki Gosei Kagaku Kyokai Shi, 39, 99 (1981); 41, 641 (1983).
9) For reviews, see M. Nastasi, Heterocycles, 4, 1509 (1976); V. Snieckus and J. Streith, Acc. Chem. Res., 14, 348 (1981).
10) J. Kurita, H. Kojima, and T. Tsuchiya, Chem. Pharm. Bull., 29, 3688 (1981); J. Kurita, H. Kojima, M. Enkaku, and T. Tsuchiya, ibid., 29, 3696 (1981).
11) R.W. Begland, D.R. Hartter, F.N. Jones, D.J. Sam, W.A. Sheppard, O.W. Webster, and F.J. Weigert, J. Org. Chem., 39, 2341 (1974); G. Reisenweber and J. Sauer, Tetrahedron Lett., 1977, 4389.
12) It is known that 1,4-dioxane stabilizes the singlet nitrene and thus promotes the present azirine formation [cf., H. Takeuchi, K. Kinoshita, S.M. Abdul-Hai, M. Mitani, T. Tsuchida, and K. Koyama, J. Chem. Soc., Perkin Trans. 2, 1976, 1201 and ref. 3].
13) Satisfactory elemental analyses and spectral data were obtained for 4; e.g., (4a): ^{1}H-NMR ($CDCl_3$) δ : 2.92 (2H, br d, J=6 Hz), 3.68 (3H, s), 6.60-6.70 (2H, m), and 6.94 (1H, d, J=6 Hz); ^{13}C-NMR δ : 38.65 (t), 55.00 (q), 127.66 (d), 128.36 (d), 139.36 (d), and 146.30 (s); (4b): ^{1}H-NMR δ : 1.66 (3H, d, J=7 Hz), 1.84-2.04 (1H, m), 3.74 (3H, s), 6.40 (1H, d, J=4 Hz), 6.70 (1H, d, J=5 Hz), and 6.97 (1H, d, J=5 Hz); ^{13}C-NMR δ : 11.23 (q), 43.12 (d), 55.13 (q), 127.19 (d), 128.02 (d), 144.23 (d), and 147.30 (s).
14) (5): oil; ^{1}H-NMR ($CDCl_3$) δ : 3.72 (3H, s), 5.34 (1H, d, J=8 Hz), 5.70 (1H, d J=5 Hz), 6.00 (1H, d, J=5 Hz), 6.82 (1H, d, J=8 Hz), and 7.30-7.80 (5H, m); IR ($CHCl_3$) cm^{-1}: 1650 (C=O).
15) D.J. Harris, G. Kan, V. Snieckus, and O. Buchardt, Synthesis, 1975, 603.
16) The pyridine (7=16a) was identical with an authentic sample prepared by benzoylation of 5-amino-2-methoxypyridine, which was synthesized according to the reported method [O. Magidson and G. Menschkoff, Ber., 58, 117 (1900)]. The other pyridines (16b,c) were characterized by comparison with 7.
17) (9): 30% yield, mp 147-149 °C; IR (KBr) cm^{-1}: 3400, 2240, 1665, and 1640; ^{1}H-NMR ($CDCl_3$) δ : 3.84 (3H, s), 6.16 (1H, d, J=16 Hz), 6.40 (1H, d, J=8 Hz), 6.92 (1H, q, J=8 and 9 Hz), 7.12 (1H, d, J=16 Hz), 7.5-7.8 (5H, m), and 8.80 (1H, br d, J=9 Hz, NH).
18) Satisfactory elemental analyses and spectral data were obtained for 13; e.g., (13a): oil; ^{1}H-NMR ($CDCl_3$) δ : 2.70 (2H, d, J=7 Hz), 3.72 (3H, s), 5.04 (1H, dd, J=7 and 7 Hz), 6.74 (1H, d, J=7 Hz),and 7.92 (1H, s); ^{13}C-NMR δ : 33.29 (t), 55.65 (q), 109.35 (d), 138.95 (d), 151.89 (d), and 159.00 (s); (13b): oil; ^{1}H-NMR δ : 1.34 (3H, d, J=6 Hz), 2.10-2.40 (1H, m), 3.72 (3H, s), 4.76 (1H, dd, J=6 and 6 Hz), 6.70 (1H, d, J=6 Hz), and 7.91 (1H, s).

(Received September 27, 1984)