SYNTHESIS OF SOME PYRIDO-, THIENO-, AND FURO-1,2-DIAZEPINES: NOVEL HETEROCYCLIC RING SYSTEMS

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The novel heterocyclic ring systems, pyrido-, thieno-, and furo-1H-1,2-diazepines (4a-f), are prepared from the corresponding parent fused pyridines (1) via the N-iminopyridinium ylides (2), and are converted to their 3H-isomers (5).

Simple 1,2-diazepines represent a recently discovered class of hetrocycles whose chemistry has been widely investigated.[1-3] However, little is known about condensed 1,2-diazepines. To date only one member of this family, the 1,2-benzodiazepines, has been described[4,5] and we are interested in the preparation of 1,2-diazepines condensed with various heterocyclic rings. We report here the synthesis of the title condensed diazepines which are all previously unknown bicyclic ring systems.

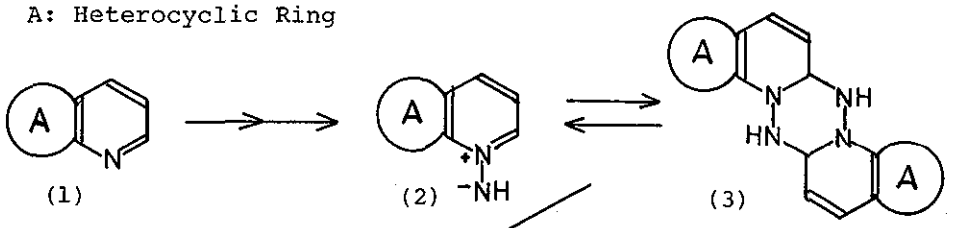
The fused pyridines, 1,5- and 1,8-naphthyridine (1a and 1b), thieno[2,3-b]- and thieno[3,2-b]-pyridine (1c and 1e), and furo[2,3-b]- and furo[3,2-b]-pyridine (1d and 1f), were aminated[6] with O-mesitylenesulfonylhydroxylamine to give the

N-aminopyridinium mesitylenesulfonates. Treatment of the salts with an alkali such as K_2CO_3 or KOH gave the N-iminopyridinium ylides (2). The ylides (2a,b) are isolated as the dimers (3) by analogy with cases of quinolines.[4] However, the other ylides (2c-f) do not form their dimers and are unstable, so they were used in the following photolysis without isolation. Irradiation of 2 or 3 in CH_2Cl_2 solution containing AcOH or in MeOH solution resulted in the formation of the corresponding condensed 1H-1,2-diazepines (4).[7] The ^{1}H-NMR spectral data[8] are consistent with the proposed structures and eliminate from further consideration the tautomeric 2H-, 3H-, and 5H-1,2-diazepine structures.

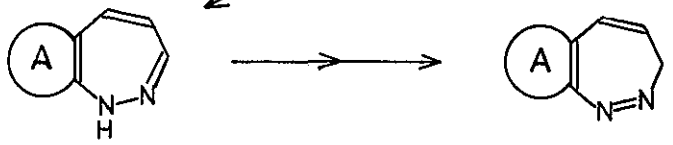
The 1H-diazepines (4) were converted to the 3H-isomers (5)[9] in good yields by $LiAlH_4$ reduction followed by dehydrogenation with 4-phenyl-1,2,4-triazoline-3,5-dione. The 3H-isomers (5) were readily tautomerized to the parent 1H-diazepines (4) by treatment with NaOMe in MeOH analogous to the case of 1,2-benzodiazepines.[5]

The monocyclic 1H-1,2-diazepines are 8 π electron aza-analogues of the unstable cycloheptatrienyl anion and can be isolated only as their iron tricarbonyl complexes[3] or N-substituted derivatives[1] whose substituents are electron withdrawing groups such as acyl groups. The N-unsubstituted diazepines (4a,b) condensed with pyridine ring are isolated as stable crystals similarly with the case of benzene ring.[4] However, the thienodiazepines are less stable than 4a,b but

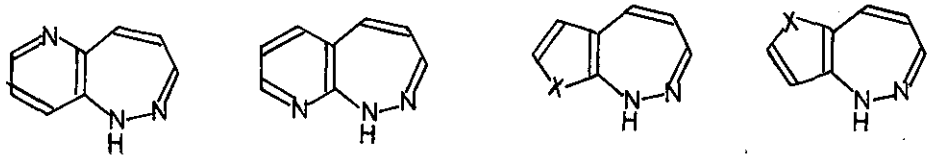
A: Heterocyclic Ring



(1) (2) (3)



(4) (5)



(4a) (4b) (4c) X = S (4e) X = S

(4d) X = O (4f) X = O

more stable than the furodiazepines (4d,f) which are gradually decomposed on standing. The results may indicate that the stability of the diazepines depends on the aromaticity of the heterocyclic ring condensed with diazepines.

An analogous route for pyrrolodiazepines has not been successful because the corresponding ylides (2) tautomerize rapidly to their isomers such as 7-amino-7H-7-azaindole.

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7 4a: mp 119-120° (25%), 4b: mp 113-114° (20%), 4c: mp 81-83° (70%), 4d: oil (20%), 4e: mp 94-95° (65%), 4f: oil (25%). Satisfactory elemental analyses and mass spectral data were obtained for all new diazepines.

8 For an example, 4a: δ ($CDCl_3$) 6.18 (1H, dd, 4-H), 7.02(1H, 5-H), 7.16 (1H, d, 3-H), 6.8-7.3 (2H, m, 8- and 9-H), 8.26 (1H, d, 7-H), 6.6 (1H, br, NH), $J_{3,4}$= 4, $J_{4,5}$= 11 Hz.

9 For an example, 6a: mp 35-37°, δ ($CDCl_3$) 4.21 (2H, br d, 3-H_2), 6.05 (1H, m, 4-H), 8.64 (1H, d, 5-H), 7.33 (1H, dd, 8-H), 8.11 (1H, d, 9-H), 8.64 (1H, d, 7-H), $J_{3,4}$= 7, $J_{4,5}$= 9 Hz.

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