SYNTHESES OF 1,4-OXAZEPINES, 1,4-DIAZEPINES, AND THEIR 5-OXO DERIVATIVES FROM 2-PYRIDONES

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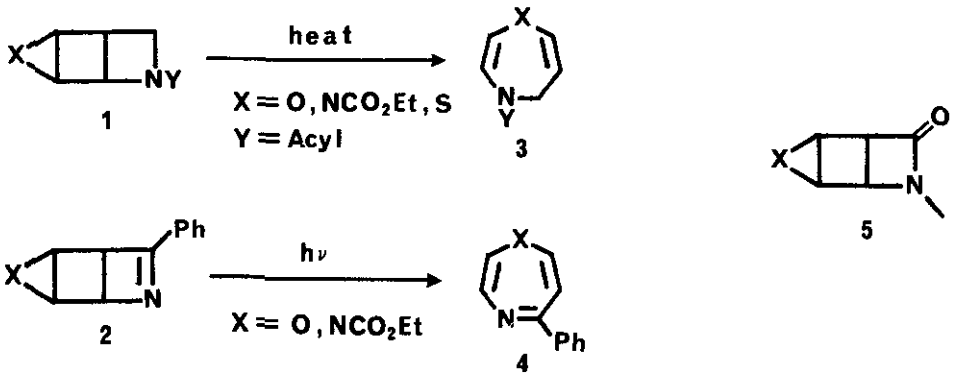
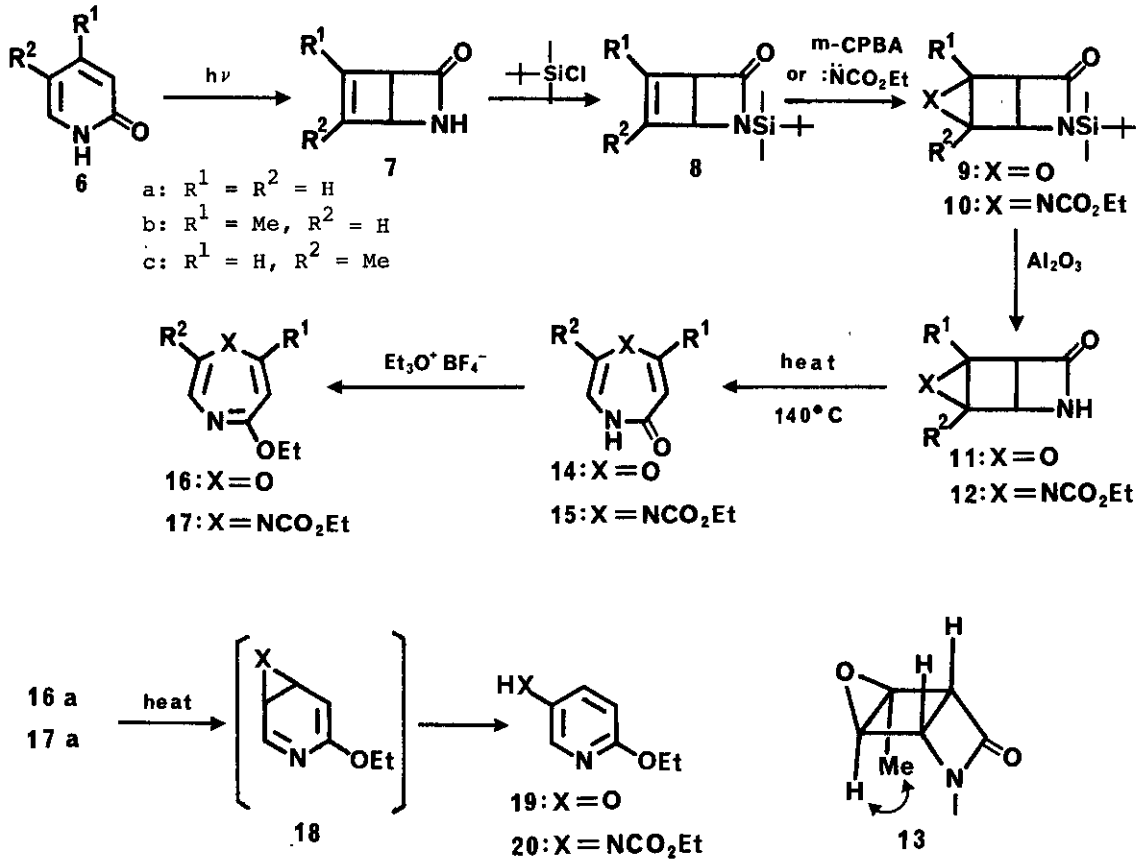
Abstract —— Thermolysis of the 3-aza-7-oxa- (11) and 3,7-diaza-4-oxotricyclo[4.1.0.$0^{2,5}$]heptanes (12), prepared from 2-pyridones via four steps, resulted in valence isomerization with ring opening to give the novel 1,4-oxazepin-5-ones (14) and 1,4-diazepin-5-ones (15), respectively, which were treated with triethyloxonium tetrafluoroborate to afford the fully unsaturated 1,4-oxazepines (16) and 1,4-diazepines (17), respectively.

Among the three possible fully unsaturated monocyclic dihetero seven-membered ring isomers (diheteroepines) due to the isomeric positions of the two hetero atoms, 1,2- and 1,3-diheteroepines such as 1,2-[1] and 1,3-diazepines[2] and 1,3-oxazepines[3] are known, but as for 1,4-isomers, only highly substituted 6H-1,4-diazepines[4] had been reported prior to our works.[5-7] We have recently shown that the tricyclic compounds (1 and 2) having a highly strained bicyclopentane ring system undergo



Scheme 1



Scheme 2

thermal or photochemical valence isomerization with ring opening to give the dihydro (3)[6] and fully unsaturated (4)[7] 1,4-dihetroepines, respectively. On the other hand, with regards to monocyclic diheteroepinones, only 1,2-diazepinones are known.[8] Therefore, we were interested in the ring opening of the oxo derivatives (5) of 1 and report here the formation of 1,4-diheteroepin-5-ones and fully unsaturated 1,4-diheteroepines.

The 2-aza-3-oxobicyclo[2.2.0]hex-5-enes (7a-c), prepared from the corresponding 2-pyridones (6) by irradiation,[9] were treated with t-butyldimethylsilyl chloride in dimethylformamide to give the N-t-butyldimethylsilyl derivatives (8) in ca. 90% yields. Treatment of 8a-c with m-chloroperbenzoic acid (m-CPBA) afforded the oxirane compounds (9), 3-aza-7-oxa-4-oxotricyclo[4.1.0.$0^{2,5}$]heptanes, in 90-95% yields. The reaction of 8a-c with ethoxycarbonylnitrene generated from N-ethoxycarbonyl-p-nitrobenzenesulfonylhydroxylamine by treatment with benzyltriethyl-

ammonium bromide and sodium hydrogencarbonate[10] resulted in the formation of the aziridine compounds (10), 3,7-diaza-4-oxotricyclo[4.1.0.$0^{2,5}$]heptanes, in 40-60% yields. The protecting silyl group of 9 and 10 could be removed by passing through a short alumina column using ether-methanol (50:1) as an eluent, giving rise to the desired N-free lactam compounds (11 and 12) quantitatively. The compounds (11 and 12) were also obtained directly from the N-free bicyclic compounds (7) by treatment with m-CPBA or ethoxycarbonylnitrene, but in very low yields (10-20%). The structures of 11 and 12 were confirmed by their spectral data,[11] particularly by ^{1}H-nmr spectral comparison with 1[6] and 2.[7] In the ^{1}H-nmr spectrum of 9b, a nuclear Overhauser effect (NOE) enhancement (15%) was observed only between the 1-H (δ 4.08) and the 6-Me (δ 1.64) signals; indicating that the compound (9b) is the anti-endo stereostructure (13), and consequently, all of the tricyclic compounds (9-12) are considered to be similar stereostructure.

Heating the tricyclic compounds (11a-c and 12a-c) in dichlorobenzene at 140 °C for 1.5-2 h resulted in ring opening to give the expected novel 1,4-oxazepin-5-ones (14) and 1,4-diazepin-5-ones (15), respectively, in 70-90% yields.[12] The structures of the new diheteroepinones were elucidated from their spectral data and the results of the following chemical studies. Treatment of the heteroepinones (14 and 15) with triethyloxonium tetrafluoroborate in dichloromethane resulted in O-alkylation predominantly to give the fully unsaturated 5-ethoxy-1,4-oxazepines (16) and 5-ethoxy-1,4-diazepines (17) in 75-90% yields, respectively.[13]

Heating the oxazepine (16a) in benzene at 45 °C for 1 h gave 2-ethoxy-5-hydroxypyridine (19) in 60% yield, presumably via the norcaradiene intermediate (18). Similarly, the thermolysis of the diazepine (17a) at 170 °C for 15 h afforded 2-ethoxy-5-ethoxycarbonylaminopyridine (20) in 80% yield. These thermal behaviors of 16a and 17a are similar to those observed in the thermolysis of 1,4-oxazepines and 1,4-diazepines already reported by us.[5,7]

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11. Satisfactory elemental analyses and spectral data were obtained for all new compounds reported; 11a: mp 105-106 °C; ir (KBr): 3284 (NH), 1734 (C=O) cm^{-1}; ^{1}H-nmr ($CDCl_3$) δ : 3.79 (1H, m, 5-H), 4.06 (1H, dd, J=3.5 and 1.5 Hz, 2-H), 4.25 (2H, m, 1- and 6-H), 7.0 (1H, br, NH); 11b: mp 112-113 °C; 11c: mp 86-87 °C; 12a: mp 110-112 °C; 12b: mp 89-90 °C; 12c: mp 90-91 °C.

12. Compound 14a: mp ca. 20 °C; ir ($CHCl_3$): 3420 (NH), 1670 (C=O) cm^{-1}; ^{1}H-nmr δ : 4.79 (1H, dd, 6-H), 4.99 (1H, dd, 3-H), 5.50 (1H, d, 2-H), 6.26 (1H, d, 7-H), 7.1 (1H, br, 4-NH), $J_{2,3}$= 6, $J_{3,4}$= 6, $J_{4,6}$= 2, $J_{6,7}$= 8 Hz; 14b: mp 94-95 °C; 14c: mp ca. 25 °C; 15a: mp 65-66 °C; ir (KBr): 3432 (NH), 1734 and 1678 (C=O) cm^{-1}; ^{1}H-nmr δ : 1.32 and 4.27 (3H, t, and 2H, q, CO_2Et), 4.92 (1H, dd, 6-H), 5.18 (1H, dd, 3-H), 5.85 (1H, d, 2-H), 6.98 (1H, d, 7-H), 7.4 (1H, br, 4-NH), $J_{2,3}$= 8, $J_{3,4}$= 6, $J_{4,6}$= 2, $J_{6,7}$= 10 Hz; 15b: mp 139-140 °C; 15c: mp 138-139 °C.

13. Compound 16a: oil; ir (neat): 1650 (C=N) cm^{-1}; ^{1}H-nmr δ : 1.23 and 4.20 (3H, t, and 2H, q, OEt), 5.09 (1H, d, 6-H), 5.45 (1H, d, 3-H), 5.89 (1H, d, 2-H), 5.93 (1H, d, 7-H), $J_{2,3}$= 5, $J_{6,7}$= 6 Hz; 16b: oil; 16c: oil; 17a: mp 36.5-37 °C; ir (KBr): 1728 (C=O), 1660 (C=N) cm^{-1}; ^{1}H-nmr δ : [1.27 and 1.30 (each 3H, t), 4.12 and 4.19 (each 2H, q), CO_2Et and OEt], 5.12 (1H, d, 6-H), 5.55 (1H, d, 3-H), 5.87 (1H, d, 2-H), 6.57 (1H, d, 7-H), $J_{2,3}$= 6, $J_{6,7}$= 9 Hz; 17b: oil; 17c: oil.

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