THERMOLYSIS OF 3,6-DIAZA- AND 6-AZA-3-OXABENZO[g]TRICYCLO[3.3.0.$0^{2,4}$]-OCTANES: FORMATION OF NOVEL 4,1-BENZOXAZOCINES

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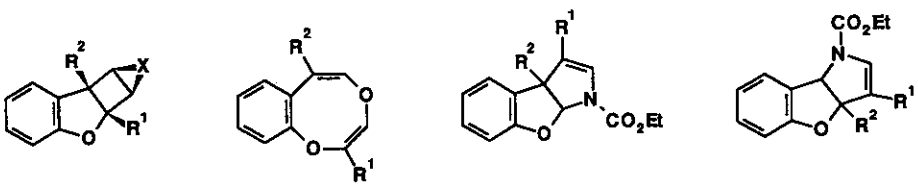
Abstract —— Thermolysis of the 3,6-diazabenzo[g]tricyclo[3.3.0.$0^{2,4}$]-octane (7) at 180 °C resulted in rearrangement to give the pyrroloindole (9), whereas flash vacuum pyrolysis of the 6-aza-3-oxabenzotricyclooctanes (8) at 530 °C resulted in both ring-expansion and rearrangement to afford the novel 4,1-benzoxazocines (10) and furoindoles (11).

A variety of monocyclic fully unsaturated 1,4-dihetero eight-membered ring compounds (1,4-diheterocines), isoelectronic with the cyclooctatetraene dianion, have been prepared and their molecular structures and properties have been studied.[1-3] However, 1,4-benzodiheterocines had not been prepared prior to our previous report,[4] although 1,6-benzodiheterocines are known.[5] We reported that the flash vacuum pyrolysis (f.v.p.) of the dioxabenzotricyclooctanes (1) resulted in ring-opening to give the novel 1,4-benzodioxocines (3),[4] whereas the pyrolysis of the oxaza derivatives (2) afforded only rearrangement products (4 and 5) and no ring-opening products.[6] These results prompted us to examine the thermal behavior of the title compounds and we report here that the f.v.p. of 6-aza-3-oxabenzo[g]tricyclo[3.3.0.$0^{2,4}$]octanes gave the novel 4,1-benzoxazocines along with rearrangement products, whereas the 3,6-diaza compound afforded only rearrangement product.

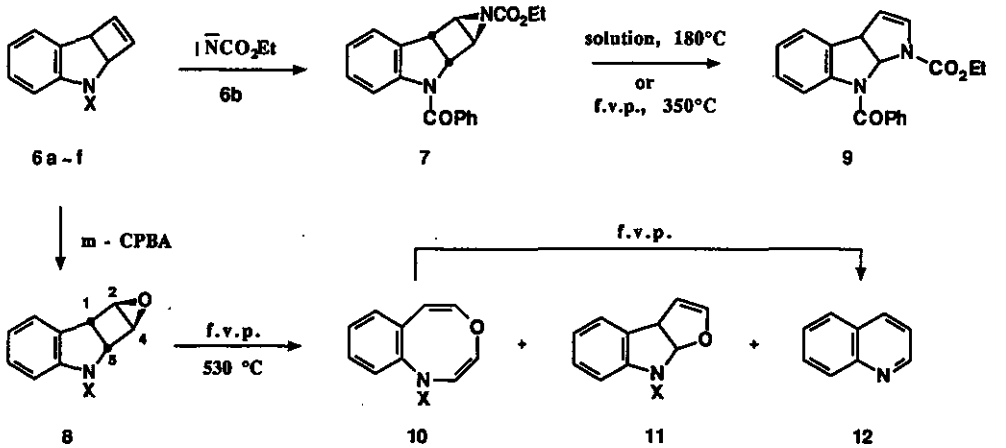


1: X = O
2: X = NCO_2Et

3 4 5

Scheme 1

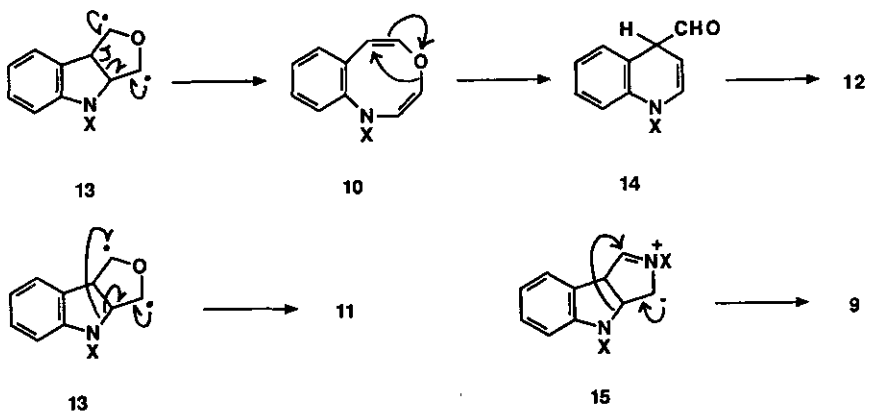
The starting 3,6-diaza- (7) and 6-aza-3-oxabenzotricyclooctanes (8) were prepared from the corresponding dihydro-3H-cyclobut[b]indoles (6)[7] by treatment with ethoxycarbonylnitrene[8] or m-chloroperbenzoic acid (m-CPBA) in 50-70% yields.[9] These tetracyclic compounds are considered to be the anti-structures shown in Scheme 2, by analogy with 1 and 2.[10] Heating the aziridine (7) in dichlorobenzene at 180 °C for 2 h resulted in rearrangement to give the pyrroloindole (9) in 90% yield.[11] F.v.p. of 7 at 350 °C also gave 9 in 72% yield and no ring-expansion product. On the other hand, even when the oxiranes (8) were heated in dichlorobenzene at 180 °C for 5 h, no reaction occurred. However, f.v.p. of 8a-d at 530 °C (3×10^{-5} mmHg) resulted in both ring-expansion and rearrangement to give the desired novel 4,1-benzoxazocines (10)[12] and furoindoles (11)[11] together with quinoline (12) in the yields shown in Scheme 2. Further f.v.p. of 10a-c afforded 12 (10-20% yields) and unchanged 10, but no rearrangement products (11), indicating that quinoline (12) is derived from the initially formed benzoxazocines (10). F.v.p. of the N-methyl (8e) and N-unsubstituted congeners (8f) gave complex mixtures and no characterizable products except for quinoline (12).



	X	Yields (%) 10	11	12
8a	COMe	21	39	12
8b	COPh	18	28	13
8c	CHO	36	30	15
8d	CO_2Me	10	43	19
8e	Me	—	—	30
8f	H	—	—	trace

Scheme 2

The structures of the 4,1-benzoxazocines (10) were characterized mainly by spectroscopic analyses. For example, in the ^{1}H-nmr spectra of 10, signals due to the four heterocyclic ring protons lie in the olefinic range (δ 6.0-6.8) as two pairs of doublets and the vicinal coupling constants are relatively small (e.g., $J_{2,3}$= 5.5 and $J_{5,6}$= 4.8 Hz for 10a). These spectral properties are similar to those of the non-aromatic 1,4-dioxocines[1] and 1,4-[4] and 1,6-benzodioxocines,[5] and are different from those of the aromatic monocyclic 1,4-diazocines[3] and 1,4-oxazocines,[2] which are known to have a planer structure. Moreover, the ^{1}H-nmr spectra of 10 showed a temperature dependence and in the case of 10a, the acetyl methyl signal split to appear at δ 1.63, 1.68, and 2.23 (5:1:1) at 25 °C. These observations may indicate that the oxazocines exist in mixtures of rotational isomers and undergo temperature-dependent inversion of the oxazocine ring.[13]



Scheme 3

The pyrolysis of the oxiranes (8) may proceed via homolytic C—C bond fission in the oxirane ring only at a high temperature to the biradical intermediates (13), which might undergo ring-opening of the indole ring to give the oxazocines (10) and C—N bond cleavage followed by migration of the anilino group to form the furoindoles (11) as shown in Scheme 3. Although detailed mechanism for the formation of 12 is not clear, we assume that it arises via [1,3]-sigmatropic rearrangement of 10 to the formyl intermediates (14) followed by aromatization. In contrast, the ring conversion of the aziridine (7) into 9 may involve the ionic intermediate (15), which might undergo migration of the anilino group to form 9. Such difference in thermolysis between oxirane and aziridine rings has been widely observed.[4,6,14]

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9. 7: mp 142-144 °C, ir (KBr) 1740 (C=O) and 1680 (C=O) cm^{-1}; ^{1}H-nmr ($CDCl_3$) δ 1.16 and 4.16 (3H, q, and 2H, t, J=7 Hz, CO_2Et), 3.32 (1H, dd, J=2 and 2 Hz, 2-H), 3.48 (1H, dd, J=3 and 2 Hz, 4-H), 4.02 (1H, dd, J=4 and 2 Hz, 1-H), 4.50 (1H, dd, J=4 and 3 Hz, 5-H), 7.10-7.62 (9H, m, Ph-H); 8a: mp 150-151 °C; 8b: mp 187-189 °C; 8c: mp 122-124 °C; 8d: mp 110-113 °C.
10. In the ^{1}H-nmr spectrum of 8q (X = Ac, 5-Me), a nuclear Overhauser effect enhancement (ca. 20%) was observed only between the methyl signal and a proton signal due to 1-H; indicating that this compound is the anti-stereostructure, and consequently, all of 7 and 8 are considered to be similar stereostructures.
11. The structures of the pyrroloindole (9) and furoindoles (11) were confirmed by their spectral data and the results of some reactions, e.g., further thermolysis of 9 gave o-(3-N-ethoxycarbonylpyrrolyl)-N-benzoylaniline; details will be reported in a full paper.
12. 10a: mp 99-100 °C; ir (KBr) 1672 (C=O) cm^{-1}; ^{1}H-nmr ($CDCl_3$) at 25 °C δ 1.63, 1.68, and 2.23 (3H, 5:1:1, each s, COMe), 5.98 nad 6.04 (1H, 1:6, each d, J=4.8 Hz, 6-H), 6.03 and 6.42 (1H, 1:6, each d, J=4.8 Hz, 5-H), 6.13 and 6.21 (1H, 1:6, each d, J=5.5 Hz, 2-H), 6.23 and 6.28 (1H, 1:6, each d, J=5.5 Hz, 3-H), 7.0-7.5 (4H, m, Ph-H); at 65 °C δ 1.52, 1.63, and 2.23 (3H, 1:5:1, each s, COMe), 6.03 (1H, br d, J=4.8 Hz, 6-H), 6.23 (2H, br s, 2- and 3-H), 6.44 (1H, br d, J=4.8 Hz, 5-H), 7.1-7.5 (4H, m, Ph-H); 10b: 98-99 °C; 10c: viscous oil; 10d: viscous oil.
13. Details of these conformational problems will be published in a full paper.
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Received, 20th January, 1992