Synthesis of the First Examples of Fully Unsaturated Monocyclic 1,4-Oxazepines

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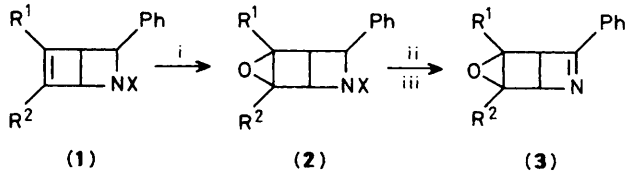
Photolysis of the 3-aza-7-oxatricyclo[4.1.0.0^{2,5}]hept-3-enes (**3**), prepared from pyridines *via* five steps, results in ring expansion to give the novel 1,4-oxazepines (**4**).

There is considerable current interest in the synthesis of new seven-membered rings with two heteroatoms.[1] With regard to fully unsaturated monocyclic compounds, all three possible diazepines, 1,2-,[2] 1,3-,[3] and 1,4-,[4] have been reported. 1,3-Oxazepines have also been synthesized mainly from pyridine *N*-oxides,[5] pyrylium salts,[6] or bicycloheptadienes.[7] However, 1,4-oxazepines have not been reported, although dihydro[8] and perhydro[1b] derivatives are known. Here we report the first synthesis of fully unsaturated 1,4-oxazepines and some results of their reactions.

The starting 2-azabicyclo[2.2.0]hex-5-enes (**1a—c**) were prepared from the corresponding pyridines by treatment with phenylmagnesium bromide in the presence of benzyl chloroformate followed by irradiation.[9] The 3-aza-7-oxatricyclo[4.1.0.0^{2,5}]hept-3-enes (**3**) were synthesized from (**1**) *via* the oxiranes (**2**) as shown in Scheme 1.†



(**1**) (**2**) (**3**)

X = CO_2CH_2Ph

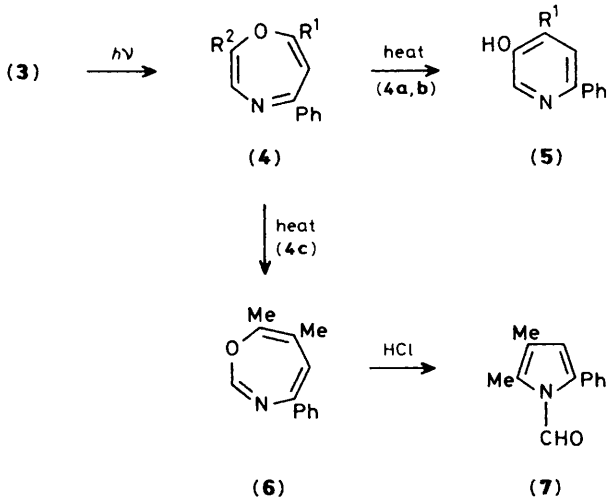
a; $R^1 = R^2 = H$
b; $R^1 = Me$, $R^2 = H$
c; $R^1 = R^2 = Me$

Scheme 1. *Reagents:* i, *m*-chloroperbenzoic acid, 85—95%; ii, H_2, Pd–C, 75—80%; iii, Bu^{t}OCl–1,8-diazabicyclo[5.4.0]undec-7-ene, 70—80%.

† Satisfactory elemental analyses and spectral data were obtained for all new compounds reported; *e.g.*, (**3a**): m.p. 32—35 °C; i.r. $\nu_{max.}$ (KBr) 1560 (C=N) cm^{-1}; u.v. λ (ε) (EtOH) 253 (15 000) nm; n.m.r. δ ($CDCl_3$) 3.95 (1H, dd, 5-H), 4.22 (1H, dd, 6-H), 4.29 (1H, dd, 1-H), 4.52 (1H, dd, 2-H), and 7.2—7.8 (5H, m, Ph-H), $J_{1,5}$ 3.5, $J_{1,6}$ 2, $J_{2,5}$ 1, and $J_{2,6}$ 4 Hz; (**3b**): m.p. 110—113 °C; (**3c**): m.p. 78—80 °C. The stereochemistry of (**2**) and (**3**) is not known at present.

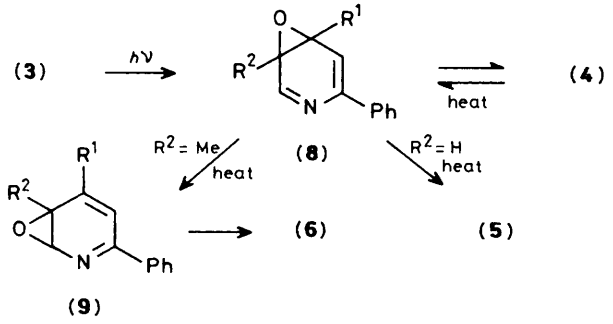
Irradiation (30 W, low-pressure Hg lamp) of the tricycloheptenes (**3a—c**) in acetonitrile for 10—15 min resulted in valence isomerization to give the corresponding novel 1,4-oxazepines (**4a—c**) in 90—95% yields as orange oils. The structures of the new oxazepines (**4**) were elucidated from their spectral data [*e.g.*, (**4a**): *m/z* 171 (M^+); i.r. $\nu_{max.}$ (film) 1650 (C=N) cm^{-1}; u.v. λ (ε) (EtOH) 253 (12 000) nm; n.m.r. δ ($CDCl_3$) 5.20 (1H, d, *J* 4 Hz, 2-H), 5.71 (1H, d, *J* 5 Hz, 6-H), 5.81 (1H, d, *J* 5 Hz, 7-H), 6.62 (1H, d, *J* 4 Hz, 3-H), and 7.0—7.6 (5H, m, Ph-H)] and by the results of the following thermal study.

Thermolysis of the 2-unsubstituted 1,4-oxazepines (**4a,b**) in toluene at 100—120 °C gave the 2-phenyl-5-hydroxypyridines (**5**) in 65—75% yields (Scheme 2),‡ whereas the 2,7-



Scheme 2

‡ Compound (**5a**): m.p. 190—191.5 °C; (**5b**): m.p. 177—178 °C.



Scheme 3

dimethyloxazepine (**4c**), upon heating at 80 °C, underwent ring conversion to afford the 1,3-oxazepine (**6**) in *ca.* 90% yield.§ Treatment of (**6**) with hydrochloric acid in tetrahydrofuran gave the *N*-formylpyrrole derivative (**7**) quantitatively;¶ this result is analogous to those for 2-phenyl-1,3-oxazepines[10] and 3,1-benzoxazepines.[1b]

The formation of the 1,4-oxazepines (**4**) from (**3**) may involve the oxanorcaradiene intermediates (**8**), which isomerize to give (**4**) (Scheme 3). Norcaradienes are well known to undergo ring expansion to seven-membered rings.[1] The thermolysis of (**4**) may proceed by initial thermal reversion to the intermediates (**8**). In the case of R^2 = H, the intermediates (**8a**,**b**) would be converted into the 5-hydroxypyridines (**5**) by C–O bond fission followed by hydrogen atom transfer, analogous to the thermolysis of various diazepines.[1–4] In contrast, in the case of R^2 = Me, the intermediate (**8c**) might undergo a walk rearrangement to give (**9**), which would then give the 1,3-oxazepine (**6**) by ring-opening. Similar walk processes have been widely observed in reactions involving norcaradiene intermediates having an oxirane or aziridine ring.[1a,3] Other possible mechanisms *via* initial homolytic or ionic oxirane ring fission seem unlikely, because fully saturated tricycloheptanes with an oxirane ring such as (**2**) are known not to undergo photochemical ring-opening.[8]

In addition, the formation of the 1,4-oxazepines (**4**) was also observed in the thermolysis of the tricycloheptenes (**3**), but complex mixtures were obtained and thus the yields of (**4**) were very low.

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§ Compound (**6**): pale yellow oil; i.r. $\nu_{max.}$ (film) 1640 (C=N) cm^{-1}; u.v. λ (ε) (EtOH) 223 (15 000), 262 (14 000), and 312 (10 000) nm; n.m.r. δ ($CDCl_3$) 1.83 (3H, s, 7-Me), 2.01 (3H, d, *J* 1 Hz, 6-Me), 6.16 (1H, q, *J* 1 Hz, 5-H), 6.35 (1H, s, 2-H), and 7.1—7.6 (5H, m, Ph-H).

¶ Compound (**7**): m.p. 40—41.5 °C; i.r. $\nu_{max.}$ (KBr) 1715 (C=O) cm^{-1}; n.m.r. δ ($CDCl_3$) 2.04 (3H, s, 3-Me), 2.52 (3H, s, 2-Me), 6.12 (1H, s, 4-H), 7.3—7.5 (5H, m, Ph-H), and 9.08 (1H, s, CHO).

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