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PHOTO-SENSITIZED OXYGENATION OF (1H)-1,2-DIAZEPINES

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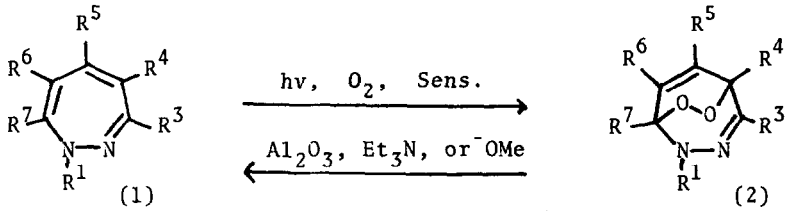
In connection with the interesting behavior of the dye-sensitized photo-oxygenation of various N-heterocycles[1] and seven-membered conjugated trienes such as cycloheptatrienes[2] and tropolones,[3] it seemed of general interest to examine such reaction of aza-cycloheptatrienes, e.g., azepines and diazepines. Therefore, we studied the photo-sensitized oxygenation of (1H)-1,2-diazepines (1), which were first prepared by Streith,[4] and the chemistry of diazepines has been widely investigated.[5-7]

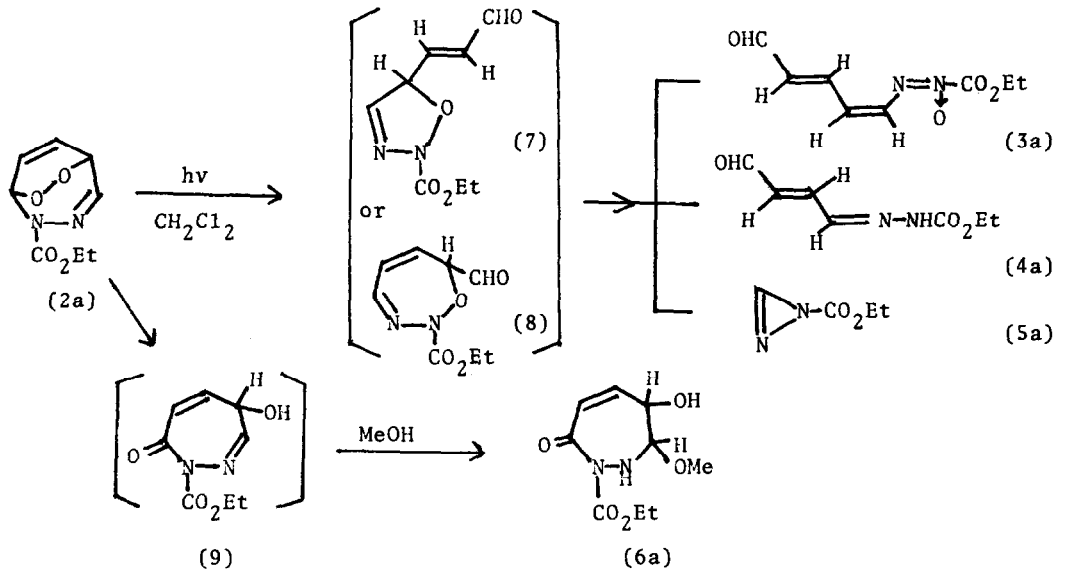
In a typical experiment, a solution of 1 g of the diazepine (1a) in 200 ml of dry methylene chloride containing 50 mg of Methylene Blue or Rose Bengal as a sensitizer was irradiated (100 W, high-pressure mercury lamp, Pyrex) for 10 hr, during which time a steady stream of oxygen was bubbled through the solution. After evaporation of the solvent in vacuo, the photolysate was chromatographed on silica gel to afford the relatively stable dioxide (2a), mp 100-101°, 40-50% as a main product, which was charactalized as 4,7-epidioxide of (1a) from the following spectral data: ν (KBr) 1720(C=O), 1640(C=C), and 1605(C=N) cm^{-1}; δ ($CDCl_3$) 4.70 (1H, m, 4-H), 6.32 (1H, m, 6-H), 6.71 (1H, m, 5-H), 6.80 (1H, m, 7-H), 7.01 (1H, d, 3-H), 1.36 and 4.34 (3H, t, and 2H, q, $CO_2\underline{Et}$), $J_{3,4}$ 5.4, $J_{4,5}$ 6.5, $J_{4,6}$ 1.5, $J_{4,7}$ 0.6, $J_{5,6}$ 6.6, $J_{5,7}$ 1.0, and $J_{6,7}$ 7.8 Hz.[8]

The dioxide (2a) was readily converted to the parent diazepine (1a) by passage through an alumina column or by treatment with sodium methoxide or triethylamine in methanol at room temperature.[9]



	R^1	R^3	R^4	R^5	R^6	R^7
a:	CO_2Et	H	H	H	H	H
b:	CO_2Et	Me	H	H	H	H
c:	CO_2Et	H	H	Me	H	H
d:	CO_2Et	H	Me	H	Me	H
e:	CO_2Et	Me	H	H	H	Me
f:	COMe	H	H	H	H	H

As minor products, aldehyde compounds, (3a) mp 99-100°, (4a) mp 158°, and N-ethoxycarbonyl diazirine (5a), bp 55-60°/10 mm Hg, were obtained in 1-5% yield respectively. When methanol was used as a solvent, an additional product, diazepinone (6a), mp 94-95°, was obtained besides the compounds (2a) to (5a). The structures of the minor products were elucidated from their spectral data.[10-13] The photooxygenation was negligible in the absence of a sensitizer.



The generality of the reaction was observed in the case of the diazepine (1b) to (1f).

We assumed that the products (3) to (6) were derived from the epidioxide (2) and examine the following reactions in order to clarify this assumption. Irradiation of the isolated dioxide (2a) with a low-pressure mercury lamp in methylene chloride afforded (3a) in 15%, (4a) in 2-3%, (5a) in ca.30%, and the parent diazepine (1a) in 20-30% yield. However, irradiation of (2a) with a medium-pressure mercury lamp resulted in recovery of almost all the starting dioxide unchanged. These results are consistent with the fact that the yield of (2) decreased on irradiation using a high-pressure mercury lamp without the Pyrex filter. The diazepinone (6a) was also obtained from (2a) by treatment with methanol or irradiation in methanol.

These results show that the dioxide (2) is the sole adduct and other possible adducts, e.g., 2,5- and 3,7-dioxide, and oxetanes, are not formed by the photooxygenation. A possible route for the formation of the products (3) to (5) might be isomerization of (2) to the oxadiazole (7) or oxadiazepine (8) by analogy with the case of tropolones,[3] followed by decomposition. The product (6) might be formed from the keto-hydroxy compound (9) by the addition of the solvent methanol, which has not yet been isolated probably because of its instability.

The above-mentioned results indicate that the photooxygenation of the diazepines proceeds through ($4\pi + 2\pi$) cycloaddition of singlet oxygen as a high energy dienophile[14] to the diene rather than to the azadiene system, and does not involve ($6\pi + 2\pi$) or ($2\pi + 2\pi$) cycloaddition to the triene unit analogous to that observed in cycloheptatrienes.[2]

References and Footnotes

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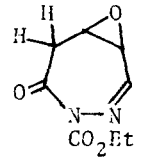
8. Satisfactory elemental analyses and mass spectral data were obtained for all new compounds. N.m.r. spectral assignment were confirmed by spin decoupling experiments.

9. At low temperatures (0-5°), the epoxide (10a) was obtained mainly besides deoxygenated parent diazepine (1a). (10a), mp 175°; ν (KBr) cm^{-1}: 1780(C=O), 1710(C=O), 1595 (C=N); δ ($CDCl_3$): 2.95 (1H, br, 6-H), 3.01 (1H, d, 6-H), 4.71 (1H, m, 5-H), 5.61 (1H, d, 4-H), 7.08 (1H, br, 3-H), 1.34 and 4.30 (3H, t, and 2H, q, CO_2Et).


(10a)

10. Compound (3a); ν (KBr) cm^{-1}: 1755(C=O), 1690(C=O), 1650(C=C) and 1609(C=N); λ_{max} nm (ε): 281 (19,500) and 286 (20,300); ^{1}H-δ ($CDCl_3$): 7.48 (1H, d, 3-H), 7.68 (1H, dd, 4-H), 7.22 (1H, dd, 5-H), 6.52 (1H, dd, 6-H), 9.70 (1H, d, 8-H), $J_{3,4}$= 11.2, $J_{4,5}$= 11.0, $J_{5,6}$= 14.5, and $J_{6,7}$= 7.2 Hz; ^{13}C-δ ($CDCl_3$): 142.7 (3-C), 139.3 and 142.1 (4- and 5-C), 132.1 (6-C), 192.2 (7-C), 157.0 (CO), 13.9 and 64.3 (OEt).

These spectral data are consistent with the proposed structure and eliminate isomeric structures (7) and (8).

11. Compound (4a); ν (KBr) cm^{-1}: 1740(C=O), 1680(C=O), 1610(C=N), 3200 and 3400 (NH); δ (acetone-d_6): 1.28 (3H, t), 3.80 (1H, br), 6.38 (1H, dd, J= 7.5 and 15.0), 7.34 (1H, dd, J= 9.0 and 15.0), 8.00 (1H, d, J=9.0) and 9.69 (1H, d, J= 7.5 Hz).

12. Compound (5a); ν (liq.) cm^{-1}: 1720(C=O) and 1605(C=N); δ ($CDCl_3$): 1.49 (3H, t), 4.56 (2H, q),and 7.99 (1H,s).

13. Compound (6a); ν (KBr) cm^{-1}: 3370(OH), 3305(NH), 1750(C=O), and 1670(C=O); δ ($CDCl_3$): 4.09 (1H, dd, 3-H), 4.35-4.62 (1H, m, 4-H), 6.51 (1H, dd, 5-H), 5.93 (1H, dd, 6-H), 5.34 (1H, b, NH), 3.50 (3H, s, OCH_3), 1.33 and 4.31 (3H, t, and 2H, q, CO_2Et).

14. It was found that the diazepines (1) were converted into the (4 + 2) cycloaddition prducts with tetracyanoethylene[6] or 4-phenyl-1,2,4-triazolone-3,5-dione. (T. Tsuchiya, unpublished results).