PHOTO-SENSITIZED OXYGENATION OF 1H-1,2-BENZODIAZEPINES[1]

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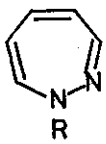
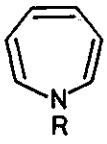
The dye-sensitized photooxygenation of 1H-1,2-benzodiazepines (6) and 1-methyl-1H-1,2-benzodiazepines (18) affords fragment products (7) to (11) and (20), respectively, which may be formed via 3- and 5-hydroperoxides. The other possible dioxides and their decomposition products are not obtained.

In connection with the interesting behaviour of the dye-sensitized photooxygenation of seven-membered conjugated trienes such as cycloheptatrienes[2] and tropolones,[3] we were interested in examining such reaction of aza-analogues, and already reported that the photooxygenation of 1,2-diazepines (1) and azepines (2) gave the relatively stable epidioxides (3) and (4) as the sole oxidized products.[4] On the other hand, 2-phenyl-1,3-oxazepine (5) is known to undergo initial 1,2- (or 1,6-) and 1,4-addition of singlet oxygen followed by decomposition to give several oxidized fragments.[5] In view of the above-mentioned studies, we report here the behaviour



(1)



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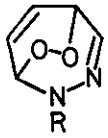

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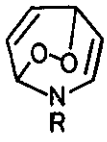

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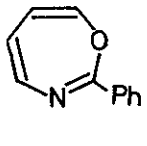


(5)

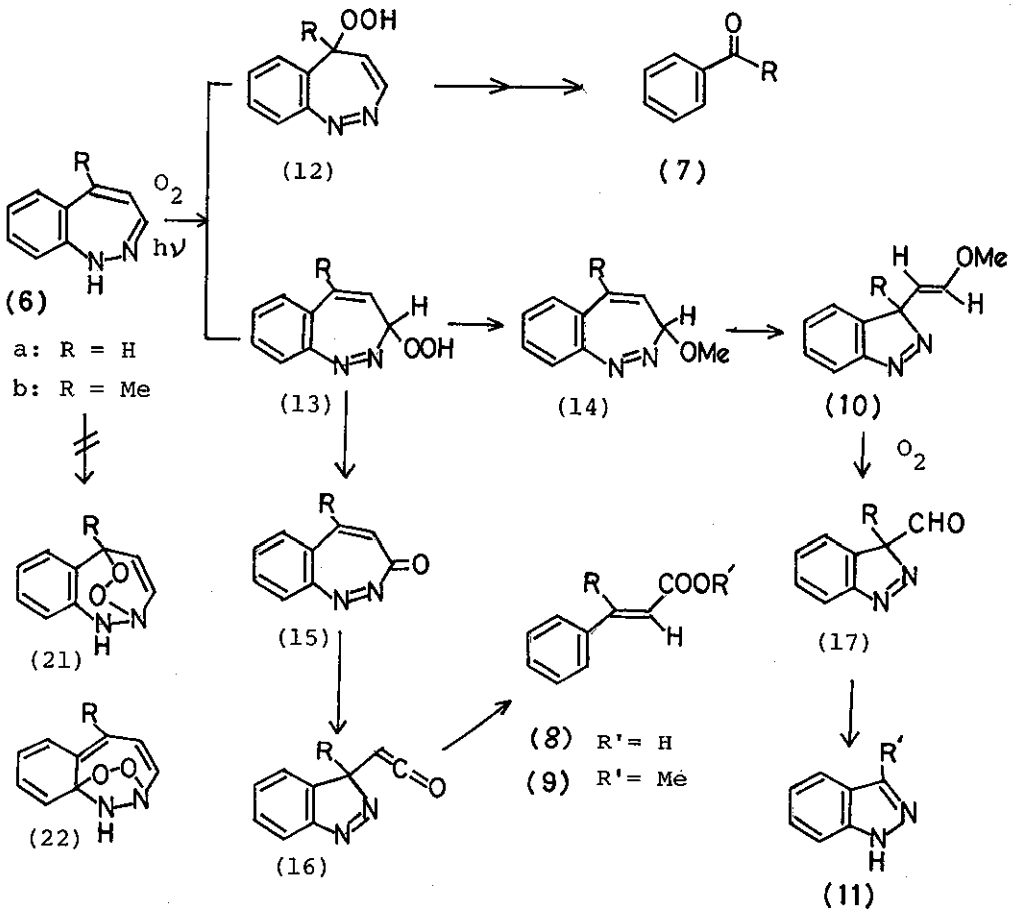
of photooxygenation of the 1H-1,2-benzodiazepines (6) and (18), which were expected to produce different types of dioxides because of the presence of the benzene ring.

A solution of the 1H-1,2-benzodiazepines[6] (6a,b: 1 g) in methanol containing Rose Bengal was irradiated with a halogen lamp for 0.5-1 hr while a steady stream of oxygen was bubbled through the solution. After evaporation of the solvent, the photolysate was chromatographed over silica gel to give phenyl ketones (7a,b: 25-30%), cinnamic acids (8a,b: ca. 10%), methyl cinnamates (9a,b: 15-20%), 3H-3-vinylindazole (10b: 6%), 3-formylindazole (11a: 2-3%), and 3-methylindazole (11b: 3%).

The products (7), (8), (9), and (11) are known and were confirmed by comparison with authentic samples, respectively. The new compound (10b) was characterized by comparison of its spectral data[7] with that of the 3-vinylindazoles already reported.[8]

Although all attempts to isolate the key intermediates (12) and (13) failed, we believe that a reasonable mechanism for the reaction involves initial formation of 5- and 3-hydroperoxides (12) and (13), followed by isomerization and decomposition to give the fragment products reported as shown in

Scheme 1. Benzaldehyde (7a) and acetophenone (7b) were not obtained by further photooxygenation of cinnamates (9) and the other products. Thus, 7a,b may be formed from the 5-hydro-



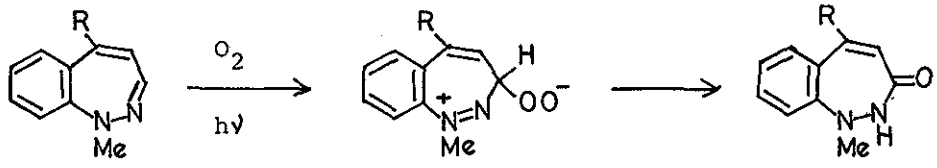
Scheme 1

peroxides (12) by C_4- C_5 bond cleavage and extrusion of nitrogen. The 3H-1,2-benzodiazepines are known to readily undergo photo-

chemical rearrangement to the corresponding 3-vinylindazoles.[8] Therefore, the 3-vinylindazoles (10) may be formed from the 3-hydroperoxides (13) via the 3-methoxy-3H-diazepines (14). Cinnamic acids (8) and cinnamates (9) may also form from the 3-hydroperoxides (13) via the 3-oxo-diazepines (15) and the ketene intermediates (16). The 3H-3-vinylindazole (10b) isolated was further photooxygenated to yield the indazole (11b). Thus, the formation of (11) may involve oxidation of the olefinic double bond to the formylindazoles (17) followed by 1,3-proton migration or deformylation.

Next, methanol solution of 1-methyl-1H-1,2-benzodiazepines (18a,b)[9] were photooxygenated under similar conditions to give 3-oxobenzodiazepines (20a,b)[10] in 60-65% yields as the sole products. In the case, other possible dioxides and decomposition products could not be isolated. This reaction may involve initial formation of the zwitterionic 3-peroxides (19) and of no 5-peroxides.

In conclusion, it should be noted that no products from 2,5- (21) and 2,7- (22) dioxides have been detected. There-



(18) a: R = H
b: R = Me

(19)

(20)

Scheme 2

fore, in both cases, the formation of hydroperoxides occurs predominantly and 1,4-cycloaddition of singlet oxygen does not occur in the aza-diene system and the diene involving benzene ring.

REFERENCES AND NOTES

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7 10b: colorless oil, δ ($CDCl_3$) 1.58 (3H, s, 3-Me), 3.25 (3H, s, OMe), 5.21 (1H, d, J = 13 Hz), 6.37 (1H, d, J = 13 Hz), and 7.4-8.2 (4H, m, Ar-H).

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9 The compounds (18) were prepared from (6) by treatment with methyl iodide in the presence of n-butyl lithium at -60° in 80-90% yields; (18a): mp 61-62 °C, (18b): oil.

10 (20a): mp 170-172 °C; ν (KBr) 2850 (NH), 1660 (C=O); δ ($CDCl_3$) 3.12 (3H, s, NMe), 6.23 (1H, d, 4-H), 6.99 (1H, d, 5-H), 6.9-7.4 (4H, m, Ar-H), 8.4 (1H, br, NH), $J_{4,5}$= 11 Hz. (20b): mp 201-203 °C; ν (KBr) 2900 (NH), 1670 (C=O); δ ($CDCl_3$) 2.25 (3H, s, 5-Me), 3.09 (3H, s, NMe), 6.25 (1H, s, 4-H), 7.0-7.5 (4H, m, Ar-H), 9.0 (1H, br, NH). These compounds are the first examples of 3-oxo-1,2-diazepines.

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