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Studies on Diazepines. VI.[1] Photolysis of 1H-1,2-Diazepine and Azepine Epidioxides

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The photolysis of 1H-1,2-diazepine 4,7-epidioxides (**1**) with a low pressure mercury lamp resulted in the formation of 5-ethoxy-1,3,4-oxadiazoles (**3**), azoxy compounds (**4**), and diene compounds (**5**). A reasonable mechanism for the formation of the products may involve initial isomerization to the 1,2,3-oxadiazoles (**8**), followed by decomposition and isomerization. However, the azepine 2,5-epidioxide (**2**) gave only the diene compound (**6**) in a low yield and did not give any other characterized products.

Keywords——photolysis; photo-induced isomerization; 1H-1,2-diazepine epidioxide; azepine epidioxide; 1,3,4-oxadiazoles; azoxy compounds

Previously we have reported the formation of the relatively stable epidioxides (**1** and **2**) from the corresponding 1H-1,2-diazepine and azepine derivatives by photo-sensitized oxygenation, and the base-catalysed isomerization and deoxygenation of the dioxides thus obtained.[3] In connection with the interesting photochemical and thermal studies of bridged cycloheptadienes[4] and of epidioxides of various seven-membered conjugated trienes such as cycloheptatrienes,[5] benzotropolones,[6] and oxazepines,[7] we examined the photochemical behaviour of the epidioxides of diazepine and azepine derivatives.

Irradiation of the 1H-1,2-diazepine 4,7-epidioxides (**1**)[3] with a low-pressure mercury lamp in methylene chloride for 6 hr resulted in the formation of the 5-ethoxy-1,3,4-oxadiazoles (**3**) as main products in 50—60% yields. As minor products, the azoxy compounds (**4**), ethoxycarbonylhydrazones (**5**), and the deoxygenated parent diazepines were also obtained in 15—20%, 2—5%, and 7—8% yields, respectively. Similarly, the azepine 2,5-epidioxide (**2**) was irradiated to give the diene compound (**6**) in *ca.* 5% yield and N-ethoxycarbonylaniline (**7**) in 18% yield, and any other characterized products could not be isolated in contrast with the case of **1**.

However, irradiation of the dioxides (**1** and **2**) with a high-pressure mercury lamp using a Pyrex filter resulted in recovery of almost all the starting dioxides unchanged. This result is consistent with the fact that the dioxides are obtained in good yields by the photo-oxygenation of the diazepines with a high-pressure mercury lamp using a Pyrex filter, but the yields decreased without the Pyrex filter.[8]

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1) Part V: T. Tsuchiya and J. Kurita, *Chem. Pharm. Bull.* (Tokyo), **26**, 1896 (1978).
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3) T. Tsuchiya, H. Arai, H. Hasegawa, and H. Igeta, *Tetrahedron Lett.*, **1974**, 4103; *idem*, *Chem. Pharm. Bull.* (Tokyo), **25**, 2749 (1977).
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7) O. Seshimoto, T. Tezuka, and T. Mukai, *Chem. Lett.*, **1976**, 793.
8) In the photo-oxygenation, the compounds (3) to (5) were also obtained in 1—5% yield respectively, besides the dioxides (1) and the parent diazepines.

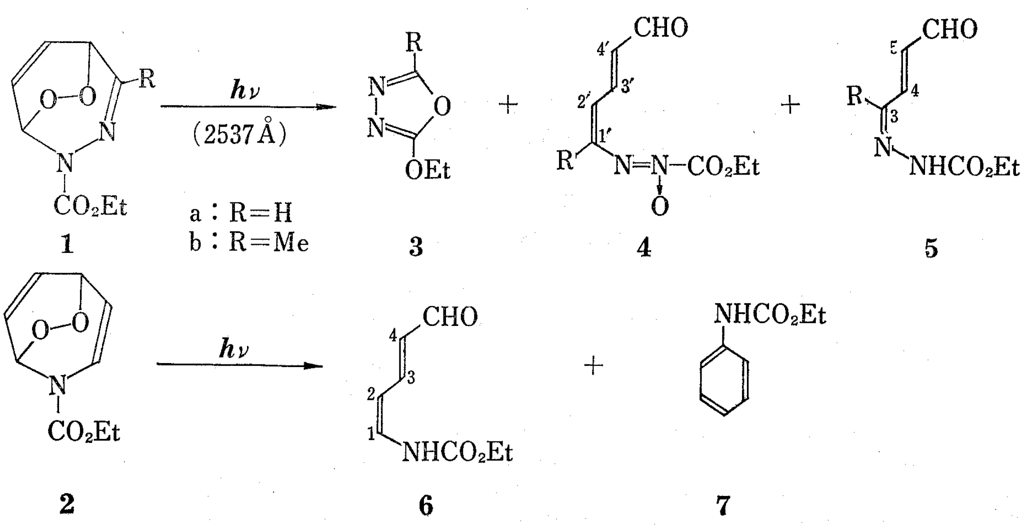

Chart 1

These products were characterized by microanalyses and infrared (IR), ultraviolet (UV), nuclear magnetic resonance (NMR), and mass (MS) spectrometry. The structure of **3a** was confirmed by comparison of spectral data with those of the known compound (**3b**).[9] The assignments of a *cis-trans* geometry to the diene function in **4** and **6**, and of a *trans* geometry to the olefin function in **5** are indicated by H–H coupling constants of 11.5 and 15.5 Hz in **4**, 12 and 15 Hz in **6**, and 15 Hz in **5**, respectively. The presence of the N-oxide group in **4** was confirmed by the following experiment. Namely, the irradiation of **4** in benzene yielded phenol analogous to that observed for amine N-oxides such as pyridine[10] and pyridazine[11] N-oxides, and azoxybenzene[12] which are known to undergo photo-induced oxygenation by oxygen transfer from the N-oxides to the aromatic ring. Although the oxygen atom of the

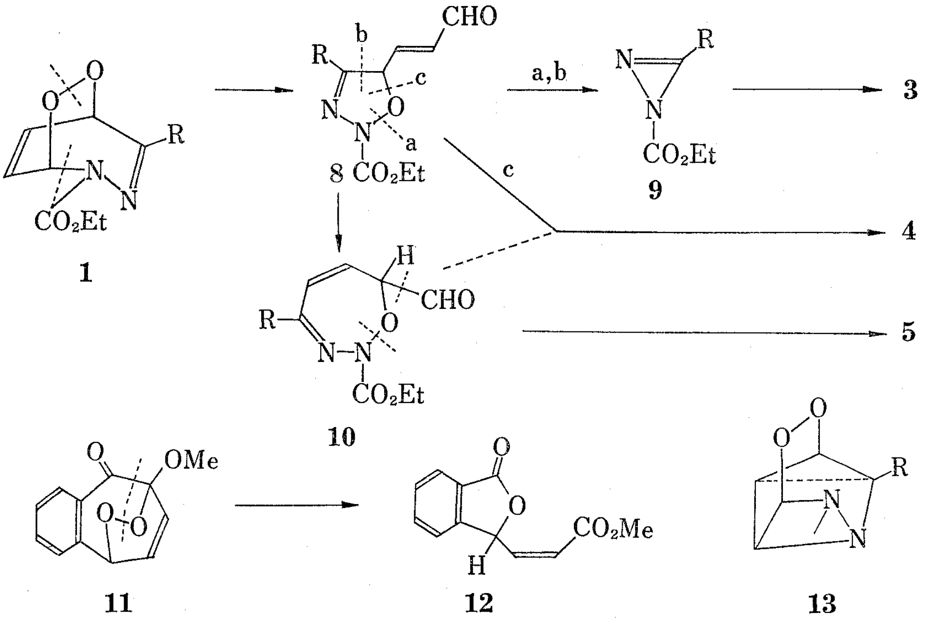

Chart 2

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[9] W. Lwowski, A. Hartenstein, C. deVita, and R.L. Smick, *Tetrahedron Lett.*, **1964**, 2497; R. Puttner and K. Hafner, *ibid.*, **1964**, 3119.

[10] J. Streith, B. Danner, and C. Sigwalt, *Chem. Commun.*, **1967**, 979.

[11] T. Tsuchiya, H. Arai, and H. Igeta, *Tetrahedron Lett.*, **1970**, 2213; and refs. cited therein.

[12] T. Tsuchiya and H. Arai, unpublished results.

N-oxides (**4**) is assumed to be in the 1-position from the following mechanistic consideration for the photolysis, the orientation has remained obscure.

These results are distinctly different from the behaviour of the epidioxides of cycloheptatrienes[5] and oxazepine,[7] but they rather resemble that of the benzotropolone dioxides (**11**).[6]

A plausible explanation for the formation of the products (**3**) to (**5**) is outlined in Chart 2. Although all attempts to isolate the intermediates (**8**) and (**9**) failed, the main path is believed to proceed through initial isomerization of **1** to the oxadiazole (**8**) by analogy with the case of the benzotolopolone derivative (**11**) into the lactone (**12**), followed rapidly by homolysis (a) and (b) to give the main products (**3**). The 1-ethoxycarbonyldiazirines (**9**) are known[13] to be unstable and to readily undergo isomerization to the oxadiazoles (**3**). The intermediacy of **9** can also be supported by the observation that the IR spectrum of a fraction containing **3** obtained by careful and rapidly chromatographic separation at a low temperature showed an absorption at 1720 cm^{-1} due to carbonyl group and the absorption gradually disappeared on standing.

The formation of the azoxy compounds (**4**) may involve the C–O bond fission (c) of **8** or the isomerization of **8** to the oxadiazepines (**10**) followed by the rupture of the C–O bond, and by photo-induced *cis-trans* isomerization. The minor products (**5**) might be formed from the intermediates (**10**) by successive N–O bond cleavage and extrusion of the formyl group.

Another route *via* the polycyclic intermediate (**13**) analogous to that observed in the photolysis of bridged cycloheptadienes[4] seems less likely for the present photolysis. Although the photolysis of the azepine dioxide (**2**) seems to proceed through a similar manner considered for **1**, it is not clear because **6** is the only isolated photo-product and the yield is very low. The dioxide (**2**) is known[3] to undergo deoxygenation to the parent azepine followed by isomerization to give the aniline derivative (**7**) by base treatment or heating.

Experimental

Melting points were measured on a Yamato MP-1 apparatus and are uncorrected. IR spectra were determined with a JASCO IRA-1 spectrometer and MS spectra were obtained on a JEOL JMS-D100 instrument. NMR spectra were recorded on Hitachi R-20 and JEOL JNM-MH100 spectrometers in $CDCl_3$ solution using tetramethylsilane as internal standard unless otherwise stated and spectral assignments were confirmed by spin-decoupling experiments and, in the case of NH protons, by exchange with D_2O. UV spectra were recorded on a Hitachi 323 spectrophotometer in EtOH solution. Microanalyses were performed in the Microanalytical laboratory, Showa University, by Miss T. Kihara and Mrs. K. Shiobara. Photolyses were carried out in an immersion apparatus equipped with a 30 W low-pressure Hg lamp or a 100 W high-pressure Hg lamp.

Photolysis of 1-Ethoxycarbonyl-1H-1,2-diazepine 4,7-Epidioxide (1a)——A solution of **1a** (1 g) in CH_2Cl_2 (200 ml) was irradiated with a low-pressure Hg lamp (2537 Å) for 6 hr and the reaction solution was evaporated *in vacuo*. The resulting residue was chromatographed over silica gel. From the eluate with benzene, 1-ethoxycarbonyl-2-[1′-(4′-formyl-1′,3′-butadienyl)]diimide 1-oxide (**4a**) was obtained. Then from the eluate with benzene-AcOEt mixture, 5-ethoxy-1,3,4-oxadiazole (**3a**) and fumaraldehyde ethoxycarbonylhydrazone (**5a**) were obtained successively.

3a: 58% yield, bp_{10} 65° (bath temp.). MS *m/e*: 114 (M^+). IR ν_{max}^{film} cm^{-1}: 1620 (C=N). NMR δ: 1.15 and 4.55 (3H, t, and 2H, q, OEt), 8.0 (1H, s). *Anal.* Calcd. for $C_4H_6N_2O_2$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.20; H, 5.26; N, 24.61.

4a: *ca.* 20% yield, mp 99—101° (from isopropyl ether). MS *m/e*: 198 (M^+). UV λ_{max}^{EtOH} nm (ε): 283 (27000). IR ν_{max}^{KBr} cm^{-1}: 1740 (CHO), 1690 (CO_2Et). NMR δ: 1.37 and 4.37 (3H, t, and 2H, q, CO_2Et), 6.52 (1H, dd, 4′-H), 7.22 (1H, dd, 3′-H), 7.43 (1H, d, 1′-H), 7.68 (1H, dd, 2′-H), 9.70 (1H, d, CHO), $J_{1',2'}=11.4$, $J_{2',3'}=12$, $J_{3',4'}=15.4$, $J_{4',CHO}=7$ Hz. *Anal.* Calcd for $C_8H_{10}N_2O_3$: C, 48.48; H, 5.09; N, 14.14. Found: C, 48.51; H, 5.39; N, 14.37.

5a: 3% yield, mp 156—158° (from acetone–ether). MS *m/e*: 170 (M^+). UV λ_{max}^{EtOH} nm (ε): 297 (25000). IR ν_{max}^{KBr} cm^{-1}: 3200 (NH), 1740 (CHO), 1660 (CO_2Et). NMR (acetone-d^6) δ: 1.28 and 3.22 (3H, t, and 2H, q, CO_2Et), 6.39 (1H, dd, 5-H), 7.85 (1H, dd, 4-H), 8.01 (1H, d, 3-H), 9.69 (1H, d, CHO), $J_{3,4}=9$, $J_{4,5}=15$, $J_{5,CHO}=7.5$ Hz. *Anal.* Calcd. for $C_7H_{10}N_2O_3$: C, 49.40; H, 5.92; N, 16.46. Found: C, 49.65; H, 5.86; N, 16.73.

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13) R. Huisgen and H. Blaschke, *Ann. Chem.*, **686**, 145 (1965); and refs. cited therein.

Photolysis of 3-Methyl-1-ethoxycarbonyl-1H-1,2-diazepine 3,7-Epidioxide (1b)——A solution of **1b** (1 g) in CH_2Cl_2 (200 ml) was irradiated and then worked up similarly to the procedure described for **1a** to give 1-ethoxycarbonyl-2-[1′-(4′-formyl-1′-methyl-1′,3′-butadienyl)]diimide 1-oxide (**4b**), 2-methyl-5-ethoxy-1,3,4-oxadiazole (**3b**), and β-formylvinyl methyl ketone ethoxycarbonylhydrazone (**5b**).

3b: 55% yield, bp_{10} 75° (bath temp.). This conpound was identical with an authentic sample prepared by the method of literatures$^{9)}$.

4b: 15% yield, mp 84—85° (from isopropyl ether). MS *m/e*: 212 (M^+). UV λ_{max}^{EtOH} nm (ε): 286 (29000). IR ν_{max}^{KBr} cm^{-1}: 1750 (CHO), 1695 (CO_2Et). NMR δ: 1.35 and 4.36 (3H, t, and 2H, q, CO_2Et), 2.40 (3H, br s, Me), 6.50 (1H, dd, 4′-H), 7.29 (1H, dd, 3′-H), 7.65 (1H, br. d, 2′-H), 9.73 (1H, d, CHO), $J_{2',3'}=11.6$, $J_{3',4'}=15.4$, $J_{4',CHO}=7$ Hz. *Anal.* Calcd. for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found; C, 51.03; H, 5.81; N, 13.49.

5b: 2% yield, mp 140—142° (from acetone–ether). MS *m/e*: 184 (M^+). UV λ_{max}^{EtOH} nm (ε): 294 (24000). IR ν_{max}^{KBr} cm^{-1}: 3200 (NH), 1740 (CHO), 1660 (CO_2Et). NMR (acetone-d_6) δ: 1.27 and 3.22 (3H, t, and 2H, q, CO_2Et), 2.20 (3H, s, Me), 6.38 (1H, dd, 5-H), 7.48 (1H, d, 4-H), 9.71 (1H, d, CHO), $J_{4,5}=15$, $J_{5,CHO}=7.5$ Hz. *Anal.* Calcd. for $C_8H_{12}N_2O_3$: C, 52.16; H, 6.57; N, 15.21. Found: C, 52.41; H, 6.73; N, 15.08.

Photolysis of 1-Ethoxycarbonylazepine 2,5-Epidioxide (2)——A solution of **2** (1 g) in CH_2Cl_2 (200 ml) was irradiated and worked up similarly to the procedure described for **1a**. From the eluate with benzene–AcOEt mixture, 1-ethoxy-carbonylamino-4-formyl-1,3-butadiene (**6**) was obtained. 5% yield, viscous oil. MS *m/e*: 169 (M^+). UV λ_{max}^{EtOH} nm (ε): 318 (45000). IR ν_{max}^{film} cm^{-1}: 3190 (NH), 1730 (CHO), 1660 (CO_2Et). NMR δ: 1.29 and 4.22 (3H, t, and 2H, q. CO_2Et), 5.90 (1H, dd, 2-H), 6.00 (1H, dd, 4-H), 7.08 (1H, dd, 3-H), 7.24 (1H, br. d, 1-H), 7.30 (1H, br., NH), 9.48 (1H, d, CHO), $J_{1,2}=12$, $J_{2,3}=10$, $J_{3,4}=15$, $J_{4,CHO}=7.2$ Hz. *Anal.* Calcd. for $C_8H_{11}NO_3$: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.91; H, 6.84; N, 8.45.

Besides **2**, N-ethoxycarbonylaniline (**7**), 18% yield, mp 50—51° (lit.$^{3)}$ 50—51°), was obtained from the eluate with benzene–AcOEt mixture.