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Studies on Diazepines. XXIV.[1] Reactions of Monocyclic 1*H*-1,3-Diazepines. (2).[1] Photo-Sensitized Oxygenation

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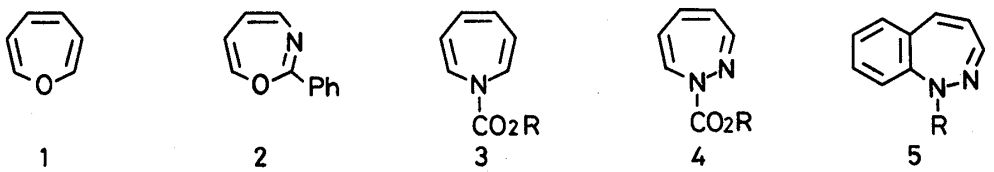
The photo-sensitized oxygenation of monocyclic 1*H*-1,3-diazepines (**6**) gave several fragment products (**7**—**12**). 3-Pyrrolin-2-one derivatives (**7** and **8**) and ethyl aminoformates (**9** and **10**) are assumed to originate from the initially formed 4,7-endoperoxides (**13**), and vinylaminoformates (**11** and **12**) from the 4,5-dioxetanes (**14**).

Keywords——sensitized photooxygenation; 1*H*-1,3-diazepine; endoperoxide; dioxetane; 3-pyrrolin-2-one; aminoformate

The reaction of photochemically generated singlet oxygen with a variety of five- and six-membered heterocycles[2] and seven-membered conjugated trienes such as cycloheptatrienes[3] and tropolones[4] has been well studied. However, only a few reports have appeared on seven-membered heterocyclic compounds. The photooxygenation of oxepin (**1**) gives only phenol,[5] while that of 1-benzoxepin affords the relatively stable 2,5-endoperoxide.[6] The 1,3-oxazepine (**2**) has been shown to undergo initial 1,2- (or 1,6-) and 1,4-cycloaddition of singlet oxygen, followed by decomposition to give rise to several products.[7] Therefore, we were interested in examining such a reaction of fully unsaturated seven-membered N-heterocyclic systems. We have already reported that the photo-sensitized oxygenation of monocyclic azepines (**3**)[8] and 1*H*-1,2-diazepines (**4**)[8,9] gave the relatively stable 2,5- and 4,7-endoperoxides, respectively, as the sole oxidized products, while the 1*H*-1,2-benzodiazepines (**5**) afforded several fragment products derived from the initially formed 3- or 5-hydroperoxides.[10] These results prompted us to examine the photooxygenation behavior of the monocyclic 1*H*-1,3-diazepines (**6**), which are new N-heterocycles prepared recently by us,[11] and we present the results here.



1 2 3 4 5

Chart 1

A solution of a 1*H*-1,3-diazepine (**6**) in carbon tetrachloride was irradiated with a halogen lamp in the presence of *meso*-tetraphenylporphine as a sensitizer for 0.5—2 h while oxygen was slowly passed through the solution. The photolysate, which gave a positive test[12] for peroxide with potassium iodide, was treated with water in tetrahydrofuran and then chromatographed on silica gel to give the products **7** to **12** shown in Chart 2. The yields of these products from the diazepines (**6a**—**c**) are summarized in Table I. These products were characterized by elemental analyses and infrared (IR), mass (MS), and proton nuclear magnetic resonance (^{1}H-NMR) spectral analyses. The structure of **7** and **8** were confirmed by spectral comparison with various 3-pyrrolin-2-ones already reported.[13] Although the geo-

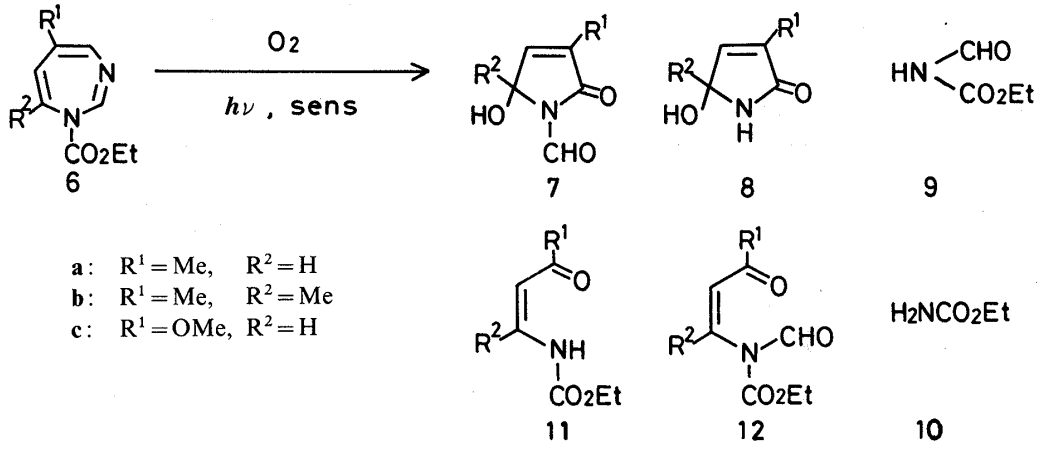


Chart 2

metry of **11** and **12** was not examined in detail, their double bonds are tentatively assigned as *Z*-forms based on the mechanism shown in Chart 3.

When the photolysate was chromatographed without treatment with water, the yields of products were greatly decreased; this fact clearly indicates that the initially formed peroxides are susceptible to decomposition, and water is required for the formation of the products obtained. Although no adducts of the 1,3-diazepines (**6**) with singlet oxygen could be isolated, the formation of the products (**7**—**12**) in the present photooxygenation can be understood in terms of the initial formation of the 4,7-endoperoxides (**13**) and 4,5-dioxetanes (**14**), which are then transformed to the products presumably *via* the pathways shown in Chart 3.

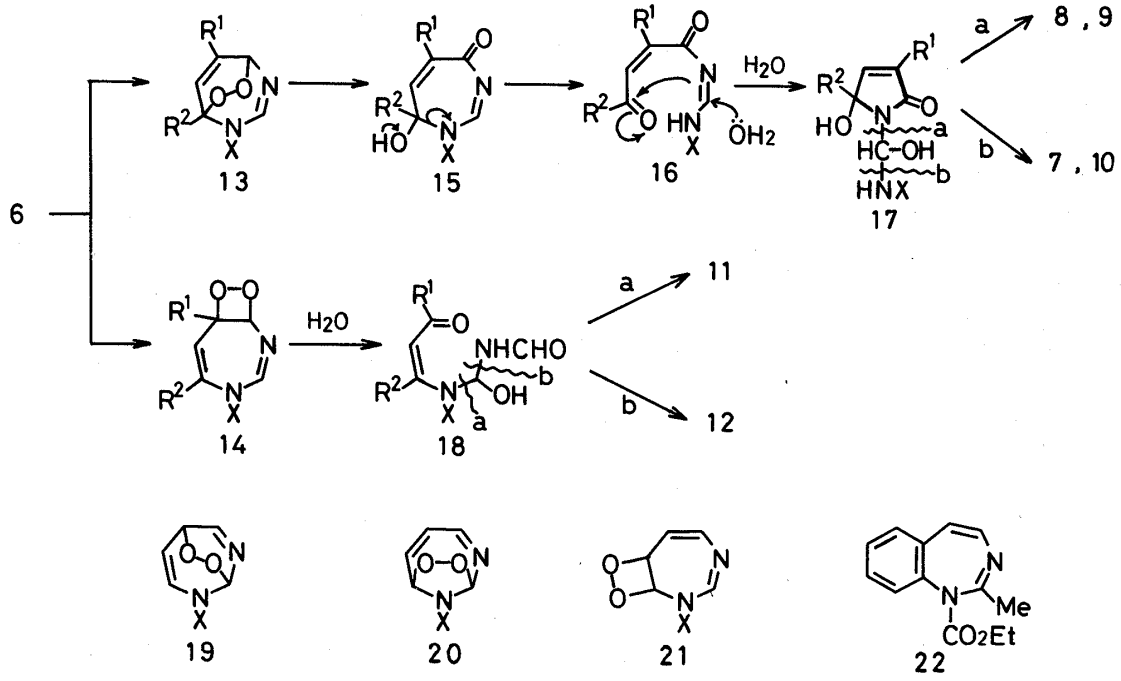


Chart 3

The ring-opened intermediates (**16**) formed from the 4,7-endoperoxides (**13**) *via* **15** undergo cyclization with addition of water to give the 3-pyrrolin-2-one intermediates (**17**). The cleavage of the N–C bond (pathway a) of **17** gives the N-unsubstituted pyrrolinones (**8**) and ethyl formylaminoformate (**9**), and the N–C bond fission (pathway b) affords the *N*-formylpyrrolinones (**7**) and ethyl aminoformate (**10**). On the other hand, the dioxetanes (**14**) give the ring-opened products **11** and **12** *via* the intermediates (**18**) by bond fission similar to

TABLE I. The Yields of Products (**7**—**12**) Obtained by Photooxygenation of **6**

6	Yield (%)					
	7	**8**	**9**	**10**	**11**	**12**
6a	19	53	32	18	—	—
6b	8	40	28	11	2	2
6c	—	47	40	—	11	8

those in the case of **17**. The result for the 5-methoxydiazepine (**6c**), in which the yields of **11** and **12** are higher than those for **6a**, **b**, may show that the electron-donating methoxy group increases the formation of the dioxetane (**14**). The photo-sensitized 1,2-cycloaddition of singlet oxygen to electron-rich olefins is well known.[14]

It should be noted that no product assumed to originate from the other possible dioxides such as 2,5- (**19**) and 2,7-endoperoxides (**20**) and 6,7-dioxetanes (**21**) has been detected. Therefore, in the present photooxygenation of 1*H*-1,3-diazepines, neither 1,4- nor 1,6-cycloaddition of singlet oxygen occurs in the aza-diene and aza-triene moieties. This behavior is analogous to that of monocyclic 1*H*,1,2-diazepines,[8,9] and 1*H*-1,2-benzodiazepines,[10] but is in contrast to that of 1,3-oxazepines,[7] imidazoles,[15] and pyrazines.[16]

When 1*H*-1,3-benzodiazepine (**22**)[17] was photooxygenated under similar conditions, it decomposed, giving no characterizable products.

Experimental

The general experimental procedures were the same as in Part XXIII.[1] Photolyses were carried out using an immersion apparatus equipped with a halogen lamp (Ushio JCV100-200 GC), which was cooled internally with running water.

Starting Materials——The 1*H*-1,3-diazepines (**6a**—**c**) were prepared by the reported method.[11]

Photooxygenation of 1-Ethoxycarbonyl-5-methyl-1*H*-1,3-diazepine (6a)——A solution of **6a** (900 mg) in carbon tetrachloride (300 ml) containing *meso*-tetraphenylporphine (60 mg) was irradiated with a halogen lamp for 30 min while a steady stream of oxygen was bubbled through the solution, and then concentrated *in vacuo* below 30 °C. The resulting residue gave a positive test for peroxide with acidified starch-iodide paper. The residue was dissolved in tetrahydrofuran (50 ml) and water was added to the solution. The mixture was stirred for 6 h at room temperature, and then diluted with CH_2Cl_2 (100 ml), dried over $MgSO_4$ and evaporated to dryness *in vacuo*. The residue was chromatographed on silica gel using CH_2Cl_2–MeOH as an eluent to give **9**, **7a**, **10**, and **8a**, successively.

1-Formyl-5-hydroxy-3-methyl-3-pyrrolin-2-one (**7a**): 144 mg, 19% yield, mp 89—90 °C (dec.), colorless plates (from *n*-hexane–ether). MS *m/z*: 141 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1735 and 1705 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.96 (3H, br d, J=*ca.* 1 Hz, 3-Me), 4.6 (1H, br, OH), 6.07 (1H, br s, 5-H), 6.86 (1H, m, 4-H), 9.01 (1H, s, CHO). *Anal.* Calcd for $C_6H_7NO_3$: C, 51.07; H, 5.00; N, 9.93. Found: C, 51.01; H, 5.00; N, 10.02.

5-Hydroxy-3-methyl-3-pyrrolin-2-one (**8a**): 300 mg, 53% yield, mp 119—121 °C, colorless prisms (from AcOEt). MS *m/z*: 113 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 3200 (NH), 1680 (C=O). ^{1}H-NMR (acetone-d_6) δ: 1.78 (3H, br d, J= 1 Hz, 3-Me), 4.9 (1H, br, OH), 5.48 (1H, br s, 5-H), 6.60 (1H, m, 4-H), 7.5 (1H, br, NH). *Anal.* Calcd for $C_5H_7NO_2$: C, 53.09; H, 6.24; N, 12.38. Found: C, 52.90; H, 6.23; N, 12.34.

Ethyl *N*-Formylaminoformate (**9**): 185 mg, 32% yield, mp 47.5—48.5 °C, colorlss needles (from *n*-hexane–isopropyl ether). MS *m/z*: 89 (M−CO). IR ν_{max}^{KBr} cm^{-1}: 3250 (NH), 1740 and 1690 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.35 and 4.31 (3H, t, and 2H, q, CO_2Et), 8.5 (1H, br, NH), 8.97 (1H, d, J=9 Hz, CHO). *Anal.* Calcd for $C_4H_7NO_3$: C, 41.02; H, 6.03; N, 11.96. Found: C, 40.93; H, 5.98; N, 11.92.

Ethyl Aminoformate (**10**): 81 mg, 18% yield, mp 48—50 °C; this compound was identical with an authentic sample obtained from Tokyo Kasei Kogyo Co., Ltd., Tokyo.

Photooxygenation of 1-Ethoxycarbonyl-5,7-dimethyl-1*H*-1,3-diazepine (6b)——A solution of **6b** (570 mg) in CCl_4 (400 ml) containing *meso*-tetraphenylporphine (50 mg) was photooxygenated for 2 h and worked up as described for **6a** to give **12b**, **11b**, **9**, **7b**, **10**, and **8b**, successively.

1-Formyl-3,5-dimethyl-5-hydroxy-3-pyrrolin-2-one (**7b**): 37 mg, 8% yield, colorless viscous oil. MS *m/z*: 155 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1730 and 1700 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.83 (3H, s, 5-Me), 1.94 (3H, br s, 3-Me), 4.3 (1H, br, OH), 6.83 (1H, m, 4-H), 9.01 (1H, s, CHO). *Anal.* Calcd for $C_7H_9NO_3$: C, 54.19; H, 5.85; N, 9.03.

Found: C, 53.92; H, 5.91; N, 8.87.

3,5-Dimethyl-5-hydroxy-3-pyrrolin-2-one (**8b**): 139 mg, 40% yield, mp 152—154 °C (dec), colorless needles (from CH_2Cl_2). MS *m/z*: 127 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3350 (OH), 3200 (NH), 1685 (C=O). ^{1}H-NMR (methanol-d_4) δ: 1.52 (3H, s, 5-Me), 1.83 (3H, d, J=1 Hz, 3-Me), 6.58 (1H, m, 4-H). *Anal.* Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.59; H, 7.30; N, 11.05.

Ethyl *N*-Formylaminoformate (**9**): 96 mg, 28% yield.

Ethyl Aminoformate (**10**): 29 mg, 11% yield.

Ethyl (1-Methoxy-2-acetylvinyl)aminoformate (**11b**): 12 mg, 2% yield, colorless solid (mp <40 °C), MS *m/z*: 171 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3350 (NH), 1740 and 1640 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.30 and 4.17 (3H, t, and 2H, q, CO_2Et), 2.12 (3H, s, COMe), 2.33 (3H, br s, 1-Me), 5.32 (1H, br s, 2-H), 9.2 (1H, br, NH). *Anal.* Calcd for $C_8H_{13}NO_3$: C, 56.12; H, 7.65; N, 8.18. Found: C, 56.09; H, 7.78; N, 8.01.

Ethyl (1-Methyl-2-acetylvinyl)formylaminoformate (**12b**): 11 mg, 2% yield, colorless viscous oil. MS *m/z*: 199 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 and 1700 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.35 and 4.40 (3H, t, and 2H, q, CO_2Et), 2.09 (3H, d, 1-Me), 2.19 (3H, s, COMe), 6.41 (1H, m, 2-H), 9.21 (1H, s, CHO). *Anal.* Calcd for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 53.89; H, 6.53; N, 6.83.

Photooxygenation of 1-Ethoxycarbonyl-5-methoxy-1*H*-1,3-diazepine (6c)——A solution of **6c** (1.17 g) in CCl_4 (400 ml) containing *meso*-tetraphenylporphine (50 mg) was photooxygenated for 1 h and worked up as described for **6a** to give **12c**, **11c**, **9**, and **8c**, successively.

5-Hydroxy-3-methoxy-3-pyrrolin-2-one (**8c**): 353 mg, 47% yield, mp 143.5—145.5 °C, colorless prisms (from methanol–isopropyl ether). MS *m/z*: 129 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 3200 (NH), 1690 and 1710 (C=O). ^{1}H-NMR (methanol-d_6) δ: 3.76 (3H, s, OMe), 5.47 (1H, d, J=1.5 Hz, 5-H), 5.72 (1H, d, J=1.5 Hz, 4-H). *Anal.* Calcd for $C_5H_7NO_3$: C, 46.51; H, 5.47; N, 10.85. Found: C, 46.61; H, 5.40; N, 10.54.

Ethyl Formylaminoformate (**9**): 279 mg, 40% yield.

Ethyl (2-Methoxycarbonylvinyl)aminoformate (**11c**): 110 mg, 11% yield, colorlss solid (mp <30 °C). MS *m/z*: 173 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3300 (NH), 1740 and 1685 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.31 and 4.26 (3H, t, and 2H, q, CO_2Et), 3.71 (3H, s, OMe), 5.06 (1H, d, J=9 Hz, 2-H), 7.27 (1H, dd, J=11 and 9 Hz, 3-H), 9.7 (1H, br, NH). *Anal.* Calcd for $C_7H_{11}NO_4$: C, 48.55; H, 6.40; N, 8.09. Found: C, 48.51; H, 6.22; N, 7.86.

Ethyl (2-Methoxycarbonylvinyl)formylaminoformate (**12c**): 97 mg, 6% yield, colorless viscous oil. MS *m/z*: 201 (M^+). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1750 and 1720 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 1.33 and 4.29 (3H, t, and 2H, q, CO_2Et), 3.66 (3H, s, OMe), 5.83 (1H, d, J=9 Hz, 2-H), 6.53 (1H, d, J=9 Hz, 1-H), 8.98 (1H, s, CHO). *Anal.* Calcd for $C_8H_{11}NO_5$: C, 47.76; H, 5.51; N, 6.96. Found: C, 47.68; H, 5.61; N, 6.72.

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