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PHOTO-OXYGENATIONS OF 1H-AZEPINE DERIVATIVES
ISOLATION AND CHARACTERIZATION OF THE [6+2] CYCLOADDITION PRODUCT[1)]

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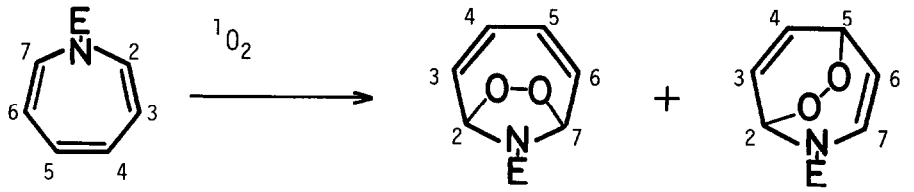
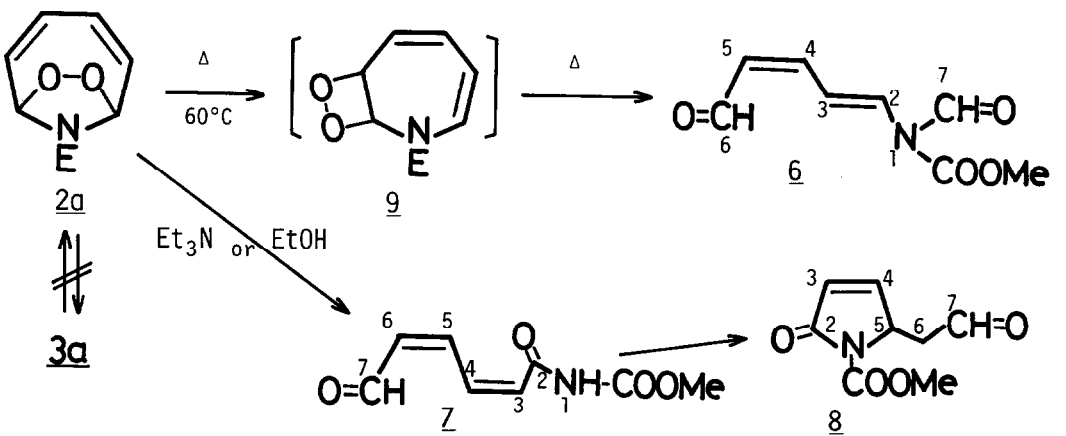
Summary : The reactions of 1H-azepine derivatives (1a-b and 4) with singlet oxygen gave the [6+2] cycloadducts (2a-b) and the [4+2] cycloadducts (3a-b and 5). The thermal and base-catalyzed rearrangements of the oxygen-adducts were investigated.

The manifold aspects related to the photo-oxygenation of carbocyclic and heterocyclic polyenes have been extensively investigated.[2)] Then, the reactions of singlet oxygen with cyclic polyenes might be expected to give the cycloaddition products in several manners because of the low activation barrier for cycloaddition process.[3)] For example, cycloheptatrienes produce the four types of adducts with singlet oxygen,[4)] whereas heteroepins such as azepine, 1,2-diazepine and 1,3-oxazepine are known to give the [4+2] cycloadducts as the sole product with singlet oxygen.[5,6)] Thus, we re-investigated the photo-oxygenation reaction of N-alkoxycarbonyl 1H-azepine (1) and found the formations of hither-to unknown [6+2] cycloadducts (2a and 2b) in addition to the [4+2] adducts (3a-b). Furthermore, the reaction of the 3,6-di-t-butyl derivative (4) with singlet oxygen was studied for the comparative purpose with that of tetracyanoethylene (TCNE), where the formation of the [6+2] adduct with TCNE has been reported by Photis.[7)]

The photo-oxygenation of N-methoxycarbonyl 1H-azepine (1a) was carried out by bubbling of oxygen in carbon tetrachloride under irradiation with Na-lamps (55W x6) in the presence of tetraphenylporphine as a sensitizer. After a low-temperature liquid chromatography (on silica gel at -50°C), the [6+2] cycloadduct (2a: mp 62-63°C)[8)] and the [4+2] adduct (3a: mp 90-91°C)[9)] were successfully isolated in 27 % and 65 % yields. The photo-oxygenation of N-ethoxycarbonyl derivative(1b) afforded also the [6+2] and the [4+2] cycloadduct (2b[8)] and 3b[9)]) in 31 % and 61 % yield, respectively, under the same condition. The structures of the oxygenated products were determined by the spectral properties and the chemical reactions.



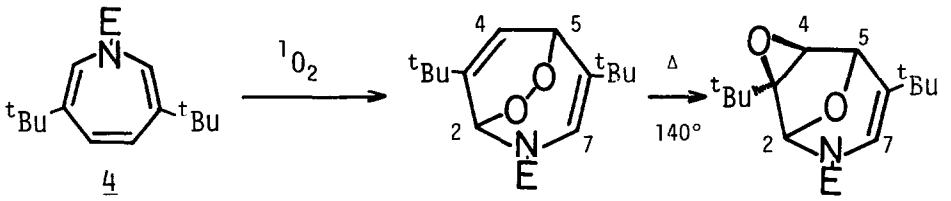
The [6+2] cycloadducts (2a-b) were less stable to acids, bases, and heat than the [4+2] adducts (3a-b), and gradually decomposed to tar on standing in the atmosphere. Nevertheless, the following reactions were successfully performed: When a benzene solution of 2a was warmed at 60°C in a degassed sealed-tube, the N-formylcarbamate (6)[10] was obtained in 54 % yield. Product 6 was air-sensitive and labile to moisture, where the structure was deduced from the spin-decoupled NMR spectra of the product. On the other hand, upon treating 2a with triethylamine at 0°C for a few minutes, it isomerized to give the unsaturated amide (7)[11] in 92 % yield, which in turn cyclized to the γ-lactam (8: mp 129-130°C)[12] upon standing. When an ethanol solution of 2a was allowed to stand overnight, the γ-lantam (8) was also obtained in 36 % yield.



The formation of 6 can be explained by the ring cleavage reaction of the dioxetane derivative (9) which originated from the [6+2] cycloadduct by 1,5-oxygen shift. The transformation of 2a leading to 7 is rationalized in terms of the base-catalyzed isomerization, which pattern was previously mentioned by Adam in the photo-oxygenations of cycloheptatrienes.[13]

In contrast to the [6+2] adducts, the thermal and base-catalyzed reactions of the [4+2] adducts (3a-b) gave only polymeric materials, although they were more stable at room temperature compared with 2a-b. The difference in the chemical behavior between 2a-b and 3a-b rules out the possiblity of the interconversions between the [6+2] and [4+2] adducts.

It was reported that the cycloaddition reaction of N-ethoxycarbonyl 1H-azepine (1b) with TCNE gave the Diels-Alder adduct, whereas that of the 3,6-di-t-butyl derivative (4) afforded the [6+2] cycloadduct.[7] For comparison, the photo-oxygenation of 4 was carried out under similar condition, where the [4+2] cycloaddition product (5: mp 111-112°C)[14] was obtained in 79 % yield as the sole oxygen-adduct. Although an attempted thermolysis of 3 afforded only a polymeric material, the di-t-butyl-substituted epidioxide (5) was heated at 140°C for 7 hr to result in an unusual rearrangement giving the epoxy-epioxide (10: mp 56-57°C)[15] in



95 % yield.

The introduction of t-butyl groups into the 1H-azepine ring interestingly affected the cycloaddition manner both with singlet oxygen and with TCNE. This phenomenone should be ascribed to the steric-effect induced by the t-butyl group, but the full elucidation of this strange steric-effect needs more detail experiments. Further studies are in progress to account for the cycloaddition reactions of 1H-azepines with active dienophiles such as TCNE and singlet oxygen.

References and Notes

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8. Product 2a : IR (KBr) 1724 cm^{-1}; ^{1}H-NMR(in C_6D_6, 90 MHz) δ 3.27(COOMe,s), 5.53-5.73(4H, m), 5.96-6.03(2H,m); ^{13}C-NMR(in CCl_4, 200 MHz) δ 52.8(OMe), 83.3($C_{2,7}$), 129.1 and 129.2 ($C_{3,6}$ and $C_{4,5}$), 152.5(CO); UV (in cyclohexane) λ_{max}= 245.5 nm (ε 4,470).
Product 2b : IR (oil) 1725 cm^{-1}; ^{1}H-NMR(in C_6D_6, 90 MHz) δ 0.95(COOEt,t), 3.95(COOEt,q), 5.67-5.83(4H,m), 5.98-6.13(2H,m); UV (in cyclohexane) λ_{max}= 247 nm (ε 4,270).
9. Product 3a : IR (KBr) 1710, 1630, 1433 cm^{-1}; NMR(in $CDCl_3$, 100 MHz) δ 3.82(COOMe,s), 4.62 (H_5,d.d.d), 5.28(H_6,d.d),6.14(H_3,d.d.d),6.60(H_2,d.d), 6.74(H_4,d.d.d), 6.82(H_7,d), $J_{2,3}$= 7.0, $J_{2,4}$= 1.0, $J_{3,4}$= 9.0, $J_{3,5}$= 1.5, $J_{4,5}$= 6.5, $J_{5,6}$= 7.3, $J_{6,7}$= 9.0 Hz. ; UV (in cyclohexane) λ_{max}= 248.5 nm (ε 7,700).
Product 3b : IR (oil) 1715, 1635 cm^{-1}; The isolation of 3b was reported by Tsuchiya et al.[5]
10. Product 6 : NMR(in C_6D_6, 90 MHz) δ 3.28(COOMe,s), 5.65(H_5,d.d.d), 6.23(H_4,d.d), 6.78(H_2,d.d), 7.83(H_3,d.d.d), 8.84(H_7,d), 10.00(H_6,d), $J_{2,3}$= 14.3, $J_{2,7}$= 0.7, $J_{3,4}$= 12.0, $J_{3,5}$= 1.0, $J_{4,5}$= 11.4, $J_{5,6}$= 7.5 Hz.
11. Product 7 : NMR(in CD_3COCD_3, 90 MHz) δ 3.72(COOMe,s), 6.07(H_6,d.d), 6.77(H_3,d), 7.69(H_4,d.d), 8.06(H_5,d.d), 9.6(NH,broad s), 10.31(H_7,d), $J_{3,4}$= 10.5, $J_{4,5}$= 12.0, $J_{5,6}$= 11.0, $J_{6,7}$= 7.5 Hz.
12. Product 8 : IR (KBr) 1755, 1670 cm^{-1}; NMR(in CD_3SOCD_3, 100MHz) δ 2.84(H_{6a},d.d.d), 3.10(H_{6b}, d.d.d), 3.90(COOMe,s), 5.06(H_5,d.d.t), 6.18(H_3,d.d), 7.48(H_4,d.d), 9.68(H_7,d.d), $J_{3,4}$= 6.0, $J_{3,5}$= $J_{4,5}$= 2.0, $J_{5,6a}$= 7.0, $J_{5,6b}$= 5.2, $J_{6a,6b}$= 17.3, $J_{6b,7}$= 1.4, $J_{6b,7}$= 1.8 Hz.
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14. Product 5 : IR (KBr) 1705, 1650 cm^{-1}; NMR(in CCl_4, 100MHz) δ 1.12(t-Bu,9H), 1.14(t-Bu,9H), 1.36(COOEt,t), 4.26(COOEt,q), 4.64(H_5,d.t), 6.24(H_4,d.d), 6.54(H_2,m), 6.68(H_7,m), $J_{2,4}$= 2.0, $J_{2,5}$= 1.6, $J_{4,5}$= 7.0, $J_{5,7}$= 1.6 Hz.; UV (in cyclohexane) λ_{max}= 202 nm (ε 11,700), 219 nm (sh.ε 7,300), 250 nm (ε 5,970).
15. Product 10 : IR (KBr) 1710, 1630 cm^{-1}; NMR(in CCl_4, at -20°C, 100MHz) δ 1.08(t-Bu,18H), 1.29 and 1.32 (COOEt,t), 3.42 and 3.45 (H_5,s), 4.14 and 4.16 (COOEt,q), 4.36 and 4.44 (H_4,s), 5.67 and 5.72 (H_2,s), 5.88 and 5.92 (H_7,s); NMR(in CCl_4, at 30°C, 100MHz) δ 1.07(t-Bu,18H), 1.28 (COOEt,t), 3.40(H_5,s), 4.12(COOEt,q), 4.45(H_4,s), 5.78(H_2,s), 5.97(H_7,s); UV (in cyclohexane) λ_{max}= 209 nm (ε 5,460); The NMR spectrum of 10 at -20°C shows that it is a mixture of two isomers (rotamers). The steric repulsion between 3-t-butyl group and N-COOEt group seems to suppress the free rotation of the ethyl ester at low temperature.

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