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DYE-SENSITIZED PHOTOOXIDATION OF SPIROCYCLIC VINYLCYCLOPROPANES IN THE PRESENCE OF SODIUM AZIDE

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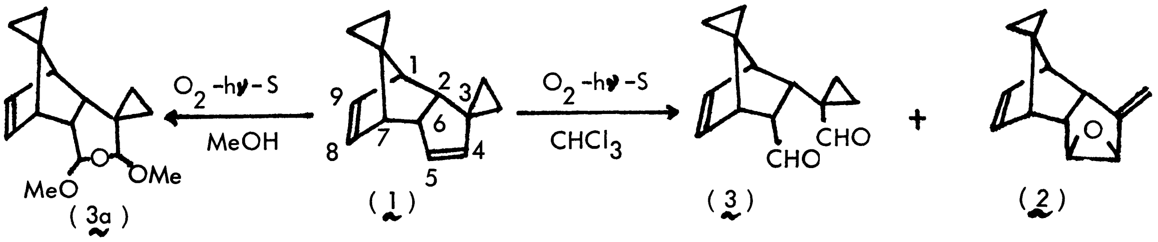
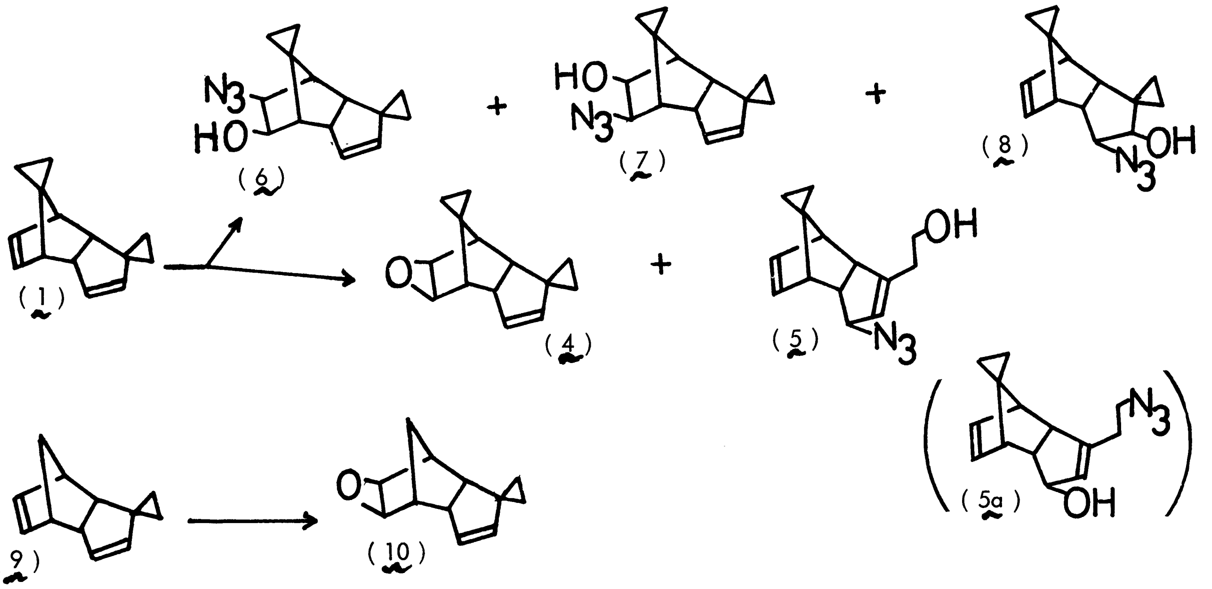
The effects of azide ion in the sensitized photooxygenation of spirocyclic vinylcyclopropanes, suitable substrates for stereochemical analysis of the mechanism, were investigated. Two types of products, azidoalcohols and an epoxide, obtained were different from the genuin products of singlet oxygen oxidation : The formers were shown to be formed by an initial attack of azide radical non-selectively to the both double bonds, and the latter, being formed by no skeletal rearrangement, was shown to be oxygenated at the norbornene moiety.

As previously reported,[1)] a spirocyclic vinylcyclopropane, 1, afforded a novel fragmentation product, 2, together with a dioxetane-related dialdehyde, 3, upon the singlet oxygen oxidation. As a part of studies to clarify the mechanism of formation of 2, we have extended the oxygenation to those with added azide ion, a potent nucleophile, which is currently suspected to cause an independent oxidation under the conditions of photosensitized oxygeanation.[2-4)] This paper will describe the findings which provided a strong support for an initial attack of azide radical into the substrates to give azidoalcohols.

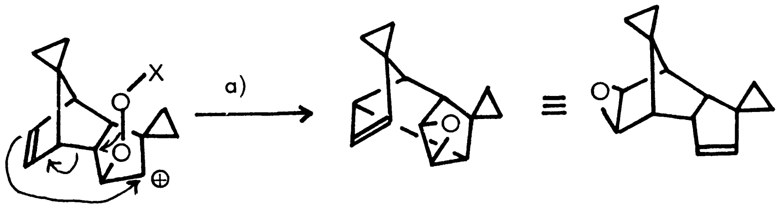


When a methanolic solution of 1 and methylene blue was irradiated by means of a 500 W tungsten lamp under oxygen stream for 14 hr, a neat reaction occurred to solely give the known dialdehyde (3) as a solvated form, 3a, a colorless oil. However no reaction occurred when this mixture was kept in the dark for a prolonged period.

Then, a methanol solution of 1 (2.0 g, 10.9 m mol), containing small amounts of Rose Bengal and sodium azide (0.3 M), was exposed to the light under the oxygen stream for 230 hr. After reduction of the mixture with sodium borohydride, the products were fractionated by silica-gel column or by high-pressure liquid chromatography to obtain colorless needles, 4, and colorless oils (5, 6, 7 and 8). Chromatographic detection of 2 and 3 in the mixture has failed. Structural determination of these products was accomplished on the spectroscopic grounds.



Crystalline product (4), mp 54-54.5°C (1 %), was shown to be an epoxide on the basis of IR[ν: 920 cm^{-1}] and NMR[δ5): 0.0-0.9(8H, m), 1.74(1H, dm, J=4.5 Hz), 1.94(1H, dm, J=4.5 Hz), 2.63(1H, dd, J=9, 4.5 Hz), 3.18(1H, dd, J=4, 1.5 Hz), 3.52(1H, m), 3.54(1H, dd, J=4, 1.5 Hz), 5.19(1H, dd, J=5.5, 2 Hz), and 5.57(1H, dd, J=5.5, 2 Hz)] spectral evidences. Since the intactness of the spiroheptene moiety was obvious, the oxidation should take place on the norbornene C=C, which was known to be quite unreactive under the usual singlet oxygen oxidation conditions.6) The formation of 4 might be explained by either a) a Woodward-Katz type rearrangement7) as depicted or b) an oxidation with different species in the manner of skeletal retention.



These two possibilities can be discriminated by use of a mixed Diels-Alder adduct. In this regard, 9, obtained from spiroheptadiene (A) and cyclopentadiene (B)8) should be appropriate as shown in the NMR[δ: 0.3-0.7 (4H, m), 1.22(1H, dm, J=8 Hz), 1.44(1H, dt, J=8, 2 Hz), 2.47(1H, dd, J=8, 4 Hz), 2.68(1H, m), 2.86 (1H, m), 3.42(1H, ddt, J=8, 4, 2 Hz), 4.88(1H, dd, J=5.5, 2 Hz), 5.34(1H, dd, J=5.5, 2 Hz), 5.78(1H, dd, J=6, 3 Hz), and 5.96(1H, dd, J=6, 3 Hz)] spectrum. The photooxygenation of 9 under the conditions as above with sodium azide afforded a colorless oil, 10, with some unidentified products. 10 was identical with the product prepared independently by m-chloroperbenzoic acid oxidation of 9, and the NMR[δ: 0.5-0.95(5H, m), 1.39(1H, dm, J=10 Hz), 2.40(2H, m), 2.58(1H, dm, J=4 Hz), 3.01(1H, dd, J=4, 1 Hz), 3.30(1H, m), 3.36(1H, d, J=4 Hz), 5.15(1H, dd, J=6, 2 Hz), and 5.55(1H, dd, J=6, 2 Hz)] spectrum proved the retention of the framework. Therefore, 4 and 10 should be formed by the route b).

The major product (5), obtained in 23 %, was analyzed to be $C_{14}H_{17}ON_3$ and the presence of hydroxy group[ν: 3500-3200 cm^{-1}] and azido group[ν: 2090 cm^{-1}] was ascertained. The NMR[δ: 0.46(4H, m), 1.80

(1H, O<u>H</u>), 2.28(1H, m), 2.33(2H, tm, J=6.5 Hz), 2.45(1H, dm, J=4.5 Hz), 2.91(1H, ddd, J=7.5, 4.5, 2.5 Hz), 3.50(1H, dm, J=7.5 Hz), 3.70(1H, dm, J=2.5 Hz), 3.79(2H, t, J=6.5 Hz), 5.35(1H, br. s), and 6.06(2H, m)] disclosed an intactness of the norbornene moiety and a cleavage of one of the cyclopropane rings. These data could not distinguish the possible two structures, **5** and **5a**, but the mass spectral fragmentation patterns indicated a favor for **5**, as the loss of oxygen atom was always accompanied by loss of CH_2 unit, <u>i.e.</u>,

$$(C_{14}H_{16}ON)[214,\ M\text{-}N_2H] \longrightarrow (C_{13}H_{14}N)[184,\ 214\text{-}CH_2O]$$

$$(C_{13}H_{14}ON)[200,\ M\text{-}CN_2H_3] \longrightarrow (C_{12}H_{12}N)[170,\ 200\text{-}CH_2O]$$

In addition, the NMR spectrum measured in dimethyl sulfoxide-d_6[δ:2.18(2H, t, J=7 Hz), 3.55(2H, td, J=7, 5 Hz), and 4.52(1H, O<u>H</u>, t, J=5 Hz)] finally excluded **5a**.

The remaining products, **6**(4%), **7**(4%) and **8**(4%), were separated by an intensive use of a high-pressure liquid chromatography apparatus. The structures of these products were also deducible by the NMR and IR spectral analyses. Thus, **6**[δ:0.15-0.50(2H, m), 0.57-0.95(6H, m), 1.40(1H, dd, J=5, 1.5 Hz), 1.75(1H, dd, J=5.5, 1.5 Hz), 2.38(1H, O<u>H</u>, d, J=7.5 Hz), 2.53(1H, dd, J=10, 5 Hz), 3.46(1H, ddt, J=10, 5.5, 2 Hz), 4.06 (1H, dd, J=7.5, 6 Hz, changed to d, J=6 Hz by addition of D_2O), 4.14(1H, d, J=6 Hz), 5.14(1H, dd, J=6, 2 Hz), and 5.53(1H, dd, J=6, 2 Hz). ν:3580, 2110, 1260 cm^{-1}] and **7**[δ:0.15-0.50(2H, m), 0.50-0.95(6H, m), 1.35(1H, dd, J=5, 1.5 Hz), 1.77(1H, dd, J=5.5, 1.5 Hz), 2.44(1H, O<u>H</u>, d, J=9 Hz), 2.50(1H, dd, J=10, 5 Hz), 3.49(1H, ddt, J=10, 5.5, 2 Hz), 3.98(1H, d, J=6.5 Hz), 4.29(1H, dd, J=9, 6.5 Hz, changed to d, J=6.5 Hz by addition of D_2O), 5.19(1H, dd, J=6, 2 Hz), and 5.49(1H, dd, J=6, 2 Hz). ν:3570, 2100, 1260 cm^{-1}] showed closely resembled spectral features. Both **6** and **7** have the spiroheptene group intact, the azidoalcohol function should therefore be introduced to the norbornene part. The <u>cis-exo-vic</u>-relationship seemed to be certain, for a formation of strong intramolecular hydrogen bonding with the azido nitrogen (disclosure of doublet hydroxyl signal in $CDCl_3$) and an observed spin-spin slpitting pattern of the methine protons ($J_{8,9}$=6-6.5 Hz as an AB-type with D_2O added). Considerations based on the anisotropic effects, a high-field shift for C_8-<u>endo</u>-H by the confronted C=C group and a low-field shift for C_9-<u>endo</u>-H by the cyclopropane ring bearing C_3,9) deduced **6** to be 9-azido-8-hydroxy derivative and **7** to be 8-azido-9-hydroxy isomer. **8** was also a <u>cis-exo-vic</u>-azidoalcohol of the other type. The NMR[δ:0.08-0.88(8H, m), 1.64(1H, O<u>H</u>, d, J=8 Hz), 1.98(1H, m), 2.32 (1H, m), 2.82(2H, m), 3.16(1H, t, J=8 Hz), 3.95(1H, t, J=8 Hz, changed to d, J=8 Hz by addition of D_2O), and 6.29(2H, m)] and the IR[ν:3630, 2090, 1260 cm^{-1}] spectra were compatible with the structure depicted. The low yields for **6**, **7** and **8** should be at least partly due to their instability under the reaction conditions.

The present results, obtained with **1**, having two sites of reaction, should have constituted the most clear-cut evidences for the free radical incorporation of azide group during the photosensitized oxygenation: The formation of **5** and **8** determined the species initially attacked on the substrate to be not oxygen but azide group, and the <u>exo-cis</u>-stereochemistry for the substituents of **6**, **7** and **8** excluded the concerted ionic addition process.10) A lack of the selectivity on the reaction sites also supported the radical mechanism. An absence of the <u>endo-cis</u>-adduct would be explained simply in terms of a steric hindrance.

Furthermore, when **1** was oxidized by hydrogen peroxide and ferrous sulfate in presence of sodium azide, that was known to generate azide radical,11) a rather complicated reaction occurred. Nevertheless, the main product was again **5**(14%) accompanied by **4**(1-2%). A failure to detect **6**, **7** and **8** in this case should be again attributable to their instability under the conditions.

These observations were also parallel to a kinetic analysis of the reaction over an extended range of the initial concentrations of 1 ($[1]_o$). The reciprocals of the concentrations of 1 reacted, $\{[1]_o - [1]\}^{-1}$, measured by glc-determination, were linear to $[1]_o^{-1}$ when no azide ion was added. But the addition of azide ion resulted in a marked deviation from the linearity. Should azide ion simply behave as a quencher, the plots must retain the relationship. Furthermore, it should be noted that a certain range of $[1]_o$ caused no depression of the reaction rates but acceleration, in accord with a view of generation of new active species[3] (Figure 1).

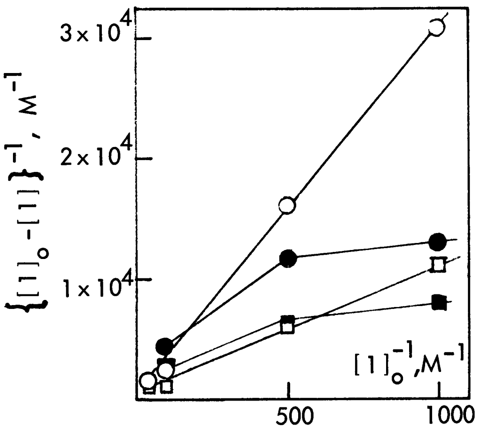


Figure 1: The oxidationof 1 with [RB]=200 mg·l^{-1} after 60 min = ○, ●; after 140 min = □, ■. ○,□ ; [NaN_3]=0; ●,■; [NaN_3]=0.05 M.

At the present stage, we can not specify the direct precursor of azide radical, and any of the following steps should be considered for that. A quenching of the singlet state of dyes by azide ion has been confirmed,[12] and this might produce azide radical (at the early step of the sequence, seemed combenient to explain our rate enhancement phenomena), or previously suggested formation of a new active species from singlet oxygen and azide ion[3] would generate the radical (at the later step). We are interested in the latter concept which might be connected with the epoxide formation.

$$\begin{tikzcd}
S \arrow[r, "h\nu"] & {}^1S^* \arrow[r] \arrow[d, "N_3^{\ominus}"] & {}^3S^* \arrow[r, "O_2"] & {}^1O_2 \arrow[r, "N_3^{\ominus}"] & \{N_3 \cdots O_2\}^{\ominus} \arrow[r] \arrow[d] & \dot{O}-O^{\ominus} \arrow[r, "R'OH"'] & H_2O_2 + O_2 \\
 & \bullet N_3 & & & \bullet N_3 & &
\end{tikzcd}$$

References and Notes

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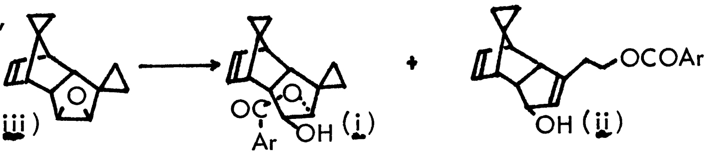
8) Diels-Alder reaction of A and B produced, together with two homo-adducts, only one mixed-adduct (9).
9) This was also applicable to 4. The NMDR assignment deduced that δ: 3.18 for C_8-H, and 3.54 for C_9-H.
10) Together with 4, two hydroxyesters, i and ii, assumed to be formed from the other epoxide (iii) were obtained by m-chloroperbenzoic acid oxidation of 1.



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