Photosensitized Oxygenation of Unconjugated Cyclic Dienes[1]

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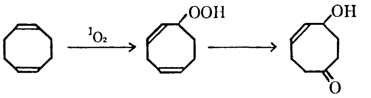
The present investigation was undertaken in order to see whether singlet oxygen-oxidation of unconjugated cyclic dienes having spatially close double bonds causes a particular transannular reaction as previously observed with 1,5-cyclooctadiene which gave 4-hydroxy-5-cyclooctenone. Most cyclic dienes tested underwent normal "ene" reaction to give allylic hydroperoxides. Thus, on dye-sensitized photooxygenation followed by reduction with sulfite, dicyclopentadiene, *cis,trans*-1,5-cyclodecadiene, *trans,trans,trans*-1,5,9-cyclododecatriene, 1,4-cyclooctadiene, 1,3-cyclooctadiene, and germacrone yielded a stereoisomeric mixture of tricyclo[5.2.1.$0^{2,6}$]decan-4,8-diene-3-ols, *cis,cis*-2,7-cyclodecadienol, a stereoisomeric mixture of two 2,5,9-cyclododecatrienols, 2,4-cyclooctadienol, *endo*-3,8-peroxide of cyclooctene, and germacra-3,7(11),10(14)-trien-9-ol-6-one(*E*), respectively. Under similar conditions, norbornadiene, and *cis,cis*-1,6-cyclodecadiene remained virtually unchanged.

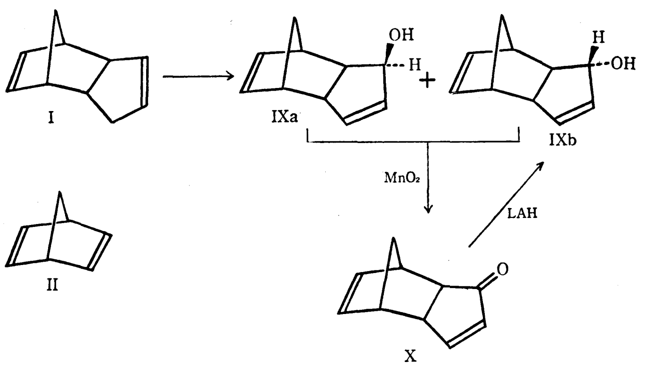
It was reported[2] that the rose bengal-sensitized photooxygenation of 1,5-cyclooctadiene gives 6-hydroperoxy-1,4-cyclooctadiene, a normal "ene" reaction product by singlet oxygen,[3] and 4-hydroxy-5-cyclooctenone which resulted from an unusual transannular reaction of the hydroperoxide, possibly due to the proximity of the reacting groups. As an extension of this type of transannular reaction, the photosensitized oxygenation of various unconjugated cyclic dienes and a triene, some of which are known to often undergo transannular reactions,[4] was investigated.



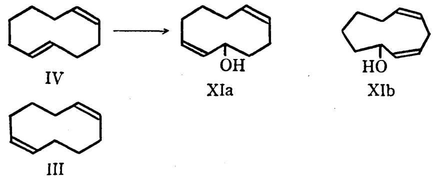
The photosensitized oxygenation of cyclic polyenes I—VIII was carried out in methanol or methylene chloride containing rose bengal or methylene blue as a sensitizer under irradiation with visible light. The reaction mixture was treated with aqueous sodium sulfite in order to reduce the initially formed peroxides. Contrary to our expectation, in most cases the main products were allylic alcohols resulting from a normal "ene" reaction, no particular transannular reaction product being obtained.

Photosensitized oxygenation of dicyclopentadiene (I) followed by reduction gave a 9: 1 mixture of *exo*- (IXa) and *endo*- (IXb) allylic alcohols in 72% yield, which was converted into a single α,β-unsaturated ketone X[5] by treating with active manganese dioxide. On reduction with lithium aluminum hydride X underwent a less-hindered side attack of hydride ion to give exclusively IXb. The structure of the *exo* isomer IXa was confirmed by its synthesis by the oxidation of I with selenium dioxide.[5] The results indicate that I undergoes "ene" reaction with predominant attack of singlet oxygen to the less hindered side of the molecule to give isomeric allylic hydroperoxides corresponding to IXa and IXb.

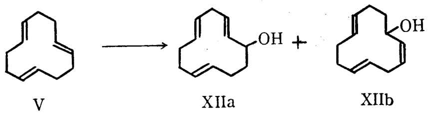
Under similar conditions, norbornadiene (II), and *cis,cis*-1,6-cyclodecadiene (III) remained virtually unchanged, although the former gave a complex mixture of products in a small yield on prolonged photooxygenation. However, *cis,trans*-1,5-cyclodecadiene (IV) suffered photosensitized oxygenation to give, after reduction, a single crystalline cyclodecadienol in 44%



yield, for which one of two structures XIa and XIb is possible because of the absence of IR band around 970 cm^{-1} characteristic of a *trans* double bond.[6] Structure XIb was excluded by the fact that the MNR spectrum showed no signal of diallylic methylene protons (C=C–CH$_2$–C=C) usually appearing at δ 2.78.[7] Predominant formation of XIa from IV indicates that the *trans* double bond of IV is more susceptible to the attack of singlet oxygen than the *cis* double bond, probably due to the more strained nature of the *trans* double bond or to the more axial-like conformation of hydrogens allylic to the *trans* double bond.[8]

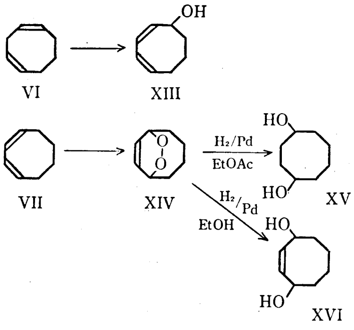


Litt and Nickon reported the photosensitized oxygenation of *trans,trans,trans*-1,5,9-cyclododecatriene (V).[9] They pointed out that no *cis-trans* isomerization occurred during photooxygenation but did not describe the reaction products. Photooxygenation of V under the usual conditions gave an about 1: 1.3 mixture of two 2,5,9-cyclododecatrienols in 41% yield and crystalline products in 3% yield. The structures of these two cyclododecatrienols were tentatively assigned as XIIa and XIIb on the basis of the following facts. The NMR spectrum of the mixture was in accord with these structures (see Experimental), and on catalytic hydrogenation the mixture gave cyclodecanol as the sole single product. The crystalline product appeared to be a mixture of cyclododecatrienediols but was not further examined.

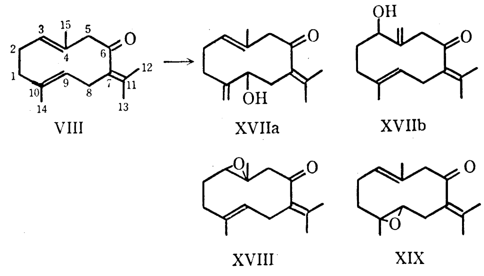


Similar sensitized photooxygenation of 1,4-cyclooctadiene (VI) gave a single product for which structure XIII was deduced from its spectral data (see Experimental).

The photosensitized oxygenation of a conjugated cyclic diene, 1,3-cyclooctadiene (VII) was also examined. Both sensitized[10] and unsensitized[11] photooxygenations of VII have been reported. By sensitized photooxygenation, VII is known to give an *endo*-peroxide XIV formed by the 1,4-addition of singlet oxygens to a conjugated diene system.[10] We observed also that methylene blue-sensitized photooxygenation of VII in methylene chloride gave XIV in 53% yield, and that rose bengal-sensitized photooxygenation in methanol gave a complex mixture of products, probably due to participation of the solvent methanol. Peroxide XIV was converted into *cis*-cyclooctane-1,4-diol (XV)[11] and *cis*-2-cyclooctene-1,4-diol (XVI) by controlled hydrogenation.



Germacra-3,9-diene derivatives have been considered to be important precursors of various types of bicyclic sesquiterpenes, which may be formed by transannular cyclisation *in vivo*.[12] Such types of biogenetic-type syntheses have drawn considerable attention.[13] In an attempt to obtain such a germacradiene precursor having an alcoholic oxygen function, the photosensitized oxygenation of germacrone (VIII) was carried out. Rose bengal-sensitized oxygenation of VIII in methanol yielded a complex mixture of products, from which a crystalline substance was obtained in a low yield. Its IR spectrum showed bands at 3400 (hydroxyl), 1660 (α,β-enone), and 895 cm^{-1} (end methylene). In the NMR spectrum new signals due to vinyl protons at δ 4.86 (singlet) and 5.05 (singlet) and a triplet signal due to a -$\overset{|}{C}\underline{H}$-OH proton at δ 3.78 (J=6 Hz) appeared, instead of one of the two methyl signals, δ 1.45 and 1.62, and one of the two di-π-methylene signals at δ 3.16 in VIII. These data suggest two possible structures XVIIa and XVIIb for the product. However, assignment of the NMR spectrum of the photooxygenation product in comparison with those of germacrone (VIII)[14] and of germacrone epoxides XVIII and XIX[15] reveals that the correct structure must be XVIIa, since a doublet signal at δ 2.6 (J=6 Hz), which couples with the -$\overset{|}{C}\underline{H}$-OH proton, is not assignable to structure XVIIb. It should be noted that in the photosensitized oxygenation of germacrene (1(10),4,7(11)-germacratriene(E,E)) singlet oxygen attacks predominantly the exocyclic double bond at 7 position but the triphenylphosphite-ozone adduct attacks the most strained double bond at 5 position.[16]



Experimental

Materials. Commercial olefins, dicyclopentadiene (I), norbornadiene (II), *trans, trans, trans*-1,5,9-cyclododecatriene (V), and 1,3-cyclooctadiene (VII) were used. The preparation of 1,4-cyclooctadiene (VI) was carried out according to the method of Moon and Gang.[7] *cis, cis*-1,6-Cyclodecadiene (III) and *cis,trans*-1,5-cyclodecadiene (IV) were supplied by Dr. P. Heinbach, Max-Planck-Institut für Kohlenforschung, Mülheim/Ruhr, and germacrone (VIII) by Dr. Y. Hirose, Institute of Food Chemistry, Osaka, and Dr. Y. Tomita, Shionogi Research Laboratories, Osaka.*

Photosensitized Oxygenation of Dicyclopentadiene (I). A solution of I (10 g) and rose bengal (200 mg) in methanol (230 ml) was irradiated with a tungsten-bromine lamp under bubbling oxygen until 0.45 mol equivalent of oxygen (810 ml) was consumed. The reaction mixture was diluted with methanol to 250 ml. In order to determine the peroxide content, an aliquot was analyzed by iodometry which showed that the mixture contained 91 mol % of peroxide based on the consumed oxygen. The reaction mixture was treated with sodium sulfite (7 g) in water (300 ml) under ice-cooling and vigorously stirring for 1 hr. The mixture was concentrated and the aqueous residue was extracted with light petroleum and then with ether. Evaporation of the extracts followed by vacuum distillation gave a mixture of tricyclo[5.2.1.$0^{2,6}$]deca-4,8-diene-3-ols (IXa and IXb) as an oil (3.17 g; 72% yield based on the consumed oxygen); bp 95 °C (bath temperature)/2 mmHg; Mass: m/e 148 (M$^+$); IR (neat): 3300 (OH), 2940, and 1035 cm^{-1}; NMR (CCl_4): δ 5.4—6.0 (m, 4H), 4.0 (br. s, 1H), 3.8 (br. s, 1H, OH), 3.4 (m, 1H), 3.02 (br. s, 1H), 2.8 (m, 1H), 2.6 (m, 1H), and 1.2—1.7 (m, 2H). Vpc analysis (Silicon DC 550; 180 °C; carrier gas, hydrogen; 1 kg/cm^2) of the oil revealed that it consisted of a 9: 1 mixture of IXa (retention time, 5.0 min) and IXb (4.2 min). The identity of IXa and IXb was confirmed by comparison of their vpc retention times with those of authentic samples, and also by their conversion into X (see below). The authentic samples of IXa and IXb were prepared by selenium dioxide oxidation of I[5] and lithium aluminum hydride reduction of X.[17] The IR spectrum of the oil was almost identical with that of IXa prepared as above.

Oxidation of IXa and IXb into Tricyclo[5.2.1.$0^{2,6}$]decan-4,8-

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* The authors are grateful for the generous supply of these samples.

diene-3-one (X). A 9: 1 mixture of IXa and IXb (865 mg) in light petroleum (100 ml) was stirred vigorously with active manganese dioxide (9 g) for 5 hr. After filtration the mixture was concentrated and the residue was purified by sublimation followed by recrystallization from *n*-hexane to give X (582 mg) as colorless prisms; mp 61—63 °C (lit, mp 65.3—65.6 °C[5]; 59—59.5 °C[17]; $\lambda_{\max}^{\mathrm{EtOH}}$ 225 nm (ε 8600); NMR (CCl_4) δ 7.3 (dd, 1H, J=2.2 and 6 Hz) and 5.6—6.1 (m, 3H). (Found: C, 81.97; H, 7.14%. Calcd for $C_{10}H_{10}O$: C, 82.11; H, 6.90%).

Photosensitized Oxygenation of cis,trans-*1,5-Cyclodecadiene (IV).* A solution of IV (1.5 g) and rose bengal (200 mg) in methanol (230 ml) was photooxygenated. After being treated with sodium sulfite, the mixture was worked up in a similar manner to the case of I to give XIa (660 mg, 44%) as crystals; mp 96—96.5 °C (from light petroleum); Mass: *m/e* 152 (M^+); NMR (CCl_4): δ 5.3 (m, 4H), 4.32 (m, 1H), 2.34 (s, 1H, OH), 2.22 (m, 2H), 1.85 (m, 4H), and 1.62 (m, 4H).

Found: C, 78.61; H, 10.82%. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59%.

Photosensitized Oxygenation of trans,trans,trans-*1,5,9-Cyclododecatriene.* A solution of V (16.2 g) and rose bengal (300 mg) in methanol (310 ml) was photooxygenated for 25 hr, consuming 0.22 mole equivalent of oxygen (490 ml). After treatment with sodium sulfite, the mixture was worked up as above. Evaporation of the light petroleum extract followed by vacuum distillation gave an oil (1.49 g; 41% based on the consumed oxygen); bp 103 °C/2 mmHg; Mass: *m/e* 178 (M^+); IR (neat): 3300, 2900, 1650, 1440, and 970 cm^{-1}. Vpc analysis revealed that it consisted of 1: 1.3 mixture of XIIa and XIIb. A solution of the oil (0.21 g) in ethyl acetate (10 ml) was hydrogenated in the presence of platinum black (25 mg). After filtration, the mixture was evaporated. Recrystallization of the residue from *n*-hexane gave cyclododecanol as crystals, mp 79—80 °C, which were identified by comparison of IR, glc and tlc with those of a commercial sample.

Ether extraction of the original aqueous layer followed by evaporation gave a solid, which on recrystallization from ethyl acetate yielded crystals (110 mg; 3% yield); mp 131—139 °C; IR (Nujol) 3150, 2850, 1660, 1440, 1025, 1010, and 970 cm^{-1}. (Found: C, 74.19; H, 9.44%. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%). These crystals appear to be a mixture of cyclododecatrienediols but were not further examined.

*Photosensitized Oxygenation of 1,4-Cycclooctadiene (VI).*** A solution of VI (1.64 g) and rose bengal (100 mg) in methanol (130 ml) was photooxygenated for 13 hr, consuming 0.81 mol equivalent of oxygen (275 ml). After treatment with sodium sulfite, the mixture was worked up as above to give an oil (806 mg) which on vacuum distillation afforded 2,4-cyclooctadienol (XIII) as an oil (530 mg; 39% based on the consumed oxygen); bp 105 °C (bath temperature)/3 mmHg; Mass: *m/e* 124 (M^+); IR (neat) 3330, 3005, 2925, 2850, 1690, 1445, and 1040 cm^{-1}; NMR (CCl_4): δ 5.9—5.4 (m, 4H), 4.6—4.2 (m, 1H), 2.32 (s, 1H, OH), and 2.7—1.2 (m, 6H); $\lambda_{\max}^{\mathrm{EtOH}}$ 210 nm (ε 5600).

Found: C, 77.13; H, 9.70%. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74%.

Photooxygenation of 1,3-Cyclooctadiene (VII). A solution of VII (5.40 g) and methylene blue (100 mg) in methylene chloride (240 ml) was photooxygenated for 23 hr, consuming 0.6 mol equivalent of oxygen (875 ml). The mixture was washed with water and dried over anhydrous sodium sulfate. Evaporation of the solvent followed by vacuum distillation gave *endo*-3,8-peroxide of cyclooctene (XIV) as crystals (2.58 g; 53% based on the consumed oxygen); bp 80—97 °C/2 mmHg; mp 60—65 °C (lit, mp 50.5—55.5 °C[10]); IR (Nujol,): 1000, 975, 920, and 760 cm^{-1}; NMR (CCl_4): δ 6.23—6.07 (q) 2H), 4.76 (m, 2H), and 2.3—1.3 (m, 8H).

Catalytic Hydrogenation of XIV. Palladium Black: A solution of XIV (100 mg) in ethyl acetate (10 ml) was hydrogenated in the presence of palladium black (30 mg). After removal of the catalyst, the mixture was evaporated to give an oil which was chromatographed on a neutral alumina column (30 g). Elution with 1: 1 benzene-acetone yielded 1,4-cyclooctanediol (XV) (54 mg; 55%). Recrystallization from ethyl acetate gave crystals, mp 84—87 °C (lit, mp for *cis*-diol 85—86.5 °C[11]). (Found: C, 66.06; H, 11.42%. Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18%).

Palladium Charcoal: A solution of crude XIV prepared by the methylene blue-sensitized photooxygenation of VII (2.7 g) in ethanol (20 ml) was hydrogenated in the presence of palladium charcoal (200 mg) and treated in the same manner as above to give *cis*-2-cyclooctene-1,4-diol (XVI) (105 mg; 38% based on the consumed oxygen in the photooxygenation). Recrystallization from ethyl acetate gave crystals; mp 143—151 °C; IR (Nujol) 3200, 1050, 1030, 960, and 750 cm^{-1}; Mass: *m/e* 142 (M^+).

Found: C, 67.57; H, 9.93%. Calcd for $C_8H_{14}O_2$: C, 68.00; H, 9.95%.

Photosensitized Oxygenation of Germacrone (VIII). A solution of VIII (6 g) and rose bengal (200 mg) in methanol (350 ml) was photooxygenated for 4 hr until VIII was completely consumed. The mixture was found by iodometry to contain 0.75 mol equivalent of peroxide on the basis of the consumed oxygen (1.1 l). The mixture was treated with sodium sulfite (4.8 g) in water (200 ml) under ice cooling, concentrated under reduced pressure and then extracted with light petroleum and ether successively. The organic layers were dried over anhydrous sodium sulfate and evaporated. The residue from the light petroleum extract was recrystallized from carbon terachloride to give germacra-3,7(11),10(14)-trien-9-ol-6-one(*E*) (XVIIa) as crystals (153 mg; 2.5%); mp 91.5—92.5 °C; IR (KBr): 3400, 1660, 1015, and 895 cm^{-1}; NMR (CCl_4): δ 1.60 (d, 3H, J=1 Hz), 1.78 (s, 3H), 1.81 (s, 3H), 2.2 (m, 4H), 2.3 (s, 1H, OH), 2.60 (d, 2H, J=6 Hz, $-CH(OH)-\mathbf{CH_2}-$), 3.15 (s, 2H, $=C-CH_2-CO-$), 3.78 (t, 1H, J=6 Hz), 4.86 (s, 1H), 5.05 (s, 1H), and 5.35 (m, 1H).

Found: C, 76.79; H, 9.69%. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46%.

The mother liquor from XVIIa and the ether extract (1.91 g) were found to be complex mixtures, from which isolation of pure products was unsuccessful.

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