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THE 1,4-ADDITION OF SINGLET OXYGEN TO 2,6-DIMETHOXY-1-(2-METHOXYETHENYL)-BENZENE AND 2-METHOXY-1-(2-METHOXYETHENYL)NAPHTHALENE. THE 1,4-ENDO-PEROXIDES AS EQUIVALENTS OF 6-OXO-2,4-CYCLOHEXADIENYLIDENACETATES.

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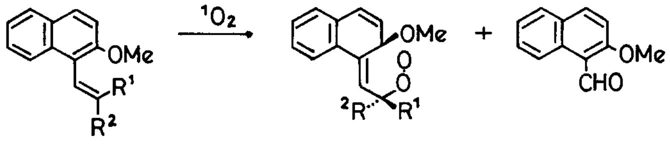
Summary: The sensitized photooxygenation of vinylarenes 1 and 2 gave the corresponding 1,4-endoperoxides which were decomposed under mild conditions into quinone methides bearing ester function at the exocyclic carbon.

Recent investigation in the reaction of singlet oxygen ($^1O_2$) with vinylarenes[1] and its synthetic application[2] stimulate us to study sensitized photooxygenation of crowded vinylarenes with substituents at both ortho positions. To know a scope of the reaction, we have investigated the reaction of $^1O_2$ with 2-methoxy-1-(2-methoxyethenyl)naphthalene (1) and 2,6-dimethoxy-1-(2-methoxyethenyl)benzene (2) as a representative.

Sensitized photooxygenation of trans-isomer of 1 occurred smoothly at 5°C[3] to give a 1,4-endoperoxide, trans-3[4], in a 98% yield with a trace amount of 2-methoxy-1-naphthaldehyde (4). On the other hand, cis-isomer of 1 was slowly oxygenated under the similar condition to afford the corresponding peroxide, cis-3[5], and the aldehyde 4 in 46 and 40% yield, respectively. In both reactions, no scramble of the isomeric products was observed. A competition experiment of the two isomers of 1 showed that trans-1 was consumed six-fold faster than cis-1 in CH_2Cl_2 and CCl_4. These results disclose some important facts as follows. (i) As with o,o'-unsubstituted systems,[1] 1 gives 1,4-addition of $^1O_2$ to the β-position of the side chain and the 2-position of the ring. (ii) The 1,4-addition proceeds in complete retention of stereochemistry. (iii) cis-Directing effect of a methoxy group of the side chain is not observed in the system of 1 at all.

Such a effect is recognized in both the experimental[2a] and the theoretical studies[6] on the reaction of $^1O_2$ with methoxystyrenes. Contrary to the known cases, the cis-isomer is less susceptible to the 1,4-addition than the trans-one in the case of 1. The absence of the cis-directing effect suggests that, in 1, cis-methoxy group suffers from larger steric repulsion of 2-methoxy group and the peri hydrogen of the ring than the trans-one. Hence cis-methoxy group may be in sterically and electronically unfavorable conformation for the 1,4-addition. This is consistent with the fact that the 1,4-addition of $^1O_2$ to cis-1 competed with the 1,2-addition affording 4.[7]

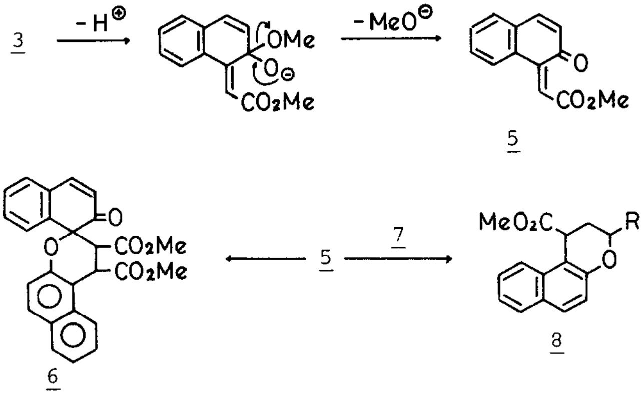


1 3 4

trans: R^1=H, R^2=OMe trans: R^1=H, R^2=OMe
cis : R^1=OMe, R^2=H cis : R^1=OMe, R^2=H

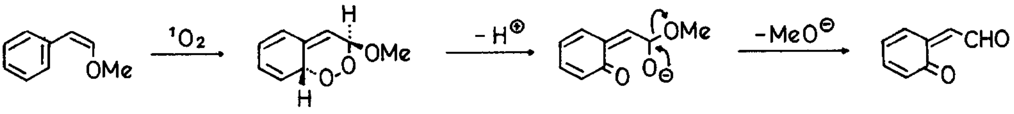
The peroxide trans-3 was stable in hot hexane but decomposed in hot toluene into a quinone methide, a methyl 6-oxo-2,4-cyclohexadienylidenacetate (5), which was isolated as a dimer 6[8] in an 86% yield. The base catalyst such as potassium carbonate and triethylamine accelerated the decomposition of trans-3 into 5. The reactive intermediate 5 was capable of undergoing the Diels-Alder addition with electron-rich olefins. When trans-3 was reacted with excess isobuthyl vinyl ether (7a) in the presence of triethylamine catalyst, a chromane 8a[9] was formed in a quantitative yield. Styrene (7b) was also used as a dienophile to afford the corresponding chromane 8b in a 31% yield, while electron-deficient olefin such as methyl vinyl ketone was scarcely active toward 5. The stereoisomer cis-3 also decomposed and formed the adduct 8a with 7a, though it was more stable than trans-3 under the basic condition. The reaction may proceed through a proton abstraction as shown in the scheme 1. The decomposition of 3 was in a striking contrast to that of the 1,4-endoperoxides of cis-β-methoxystyrenes which yielded formylmethide quinones (see scheme 2).

scheme 1



a: R=OBu^i
b: R=Ph

scheme 2

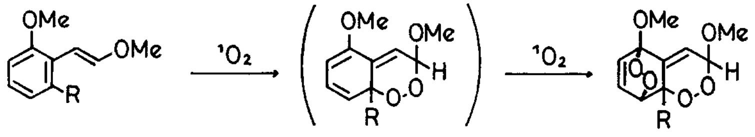


The *trans*-methoxystyrene (2) was then photooxygenated; the irradiation at 5°C gave a complex mixture containing 2,6-dimethoxybenzaldehyde (9), while that at -78°C afforded an explosive mixture, which seemed to contain a peroxide 10 as a main product by low temperature NMR analysis. The existence of 10 was confirmed as follows; when the photolysate obtained by low temperature irradiation was treated, without purification, with 7a in the presence of triethylamine at 5°C in CH_2Cl_2 overnight, a chromane 11[10] was obtained as an oil in a yield of 42%. The chromane 11 may be formed through a peroxide 12 as shown in the scheme 3. Unlike β-methoxystyrene,[1] the olefin 2 gave scarcely a 1:1 endoperoxide 15. The tendency of addition of two oxygen molecules onto 2 is accounted for by considering that a cyclohexadiene moiety is activated by a methoxy group of the ring in the intermediary 1:1 adduct 15.

The steric and electronic effects of *ortho* methoxy group in the reaction of $^1O_2$ with methoxyvinylarenes was further cleared by the reaction of *trans*-2-methoxy-1-(2-methoxyethenyl)benzene (13). Similar irradiation of 13 gave a mixture of two stereoisomers of 1:2 peroxide 14 in a quantitative yield.[10] In this reaction, the regiospecificity of attack of $^1O_2$ was completely controlled by *ortho* methoxy group, which enhanced the secondary attack of $^1O_2$ to the system.

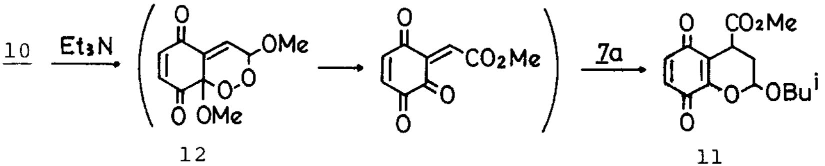
In conclusion, $^1O_2$ can effectively add to a diene system comprised of the side chain and an aromatic double bond even in sterically crowded methoxyvinylarenes such as 1 and 2. The resulting 1,4-endoperoxides are used as precursors of the quinone methide bearing an ester function at the exocyclic carbon.

scheme 3



2: R=OMe 15: R=OMe 10: R=OMe

13: R=H 14: R=H



12 11

References and Notes

1. a)D. Lerdal and C. S. Foote, *Tetrahedron Lett.*, **1978**, 3227;b)M. Matsumoto and K. Kuroda, *ibid.*, **1979**, 1607;c)D. S. Steichen and C. S. Foote, *ibid.*, **1979**, 4363.
2. M. Matsumoto and K. Kuroda, *Angew. Chem.*, submitted. For a review, see M. Matsumoto and K. Kondo, *J. Syn. Org. Chem.*, **35**, 188 (1977).
3. A solution of trans-1 (1.30g) and tetraphenylporphine (5mg) in CCl$_4$ (70ml) was irradiated externally with sodium vapor lamps (National SOI-60, 60Wx8) under an oxygen atmosphere at 5°C for 1h.
4. Colorless plates from ether, mp 117-118°C. NMR(in CDCl$_3$)δ3.36(s,3H), 3.52 (s,3H), 5.15(d,J=3Hz,1H), 5.90(d,J=10Hz,1H), 5.97(d,J=3Hz,1H), and 7.00-7.46(m,4H)ppm. IR(KBr)1085, 1060, and 1030cm^{-1}. MS(m/z) 246(M$^+$,1.2), 214(100), 183(38), 171(33), 155(39), and 127(80). Anal. Calcd for $C_{14}H_{14}O_4$: C68.28, H5.73; Found C68.28, H5.70.
5. Colorless granules from ether, mp85-86°C. NMR(in CCl$_4$)δ3.25(s, 3H), 3.45 (s,3H), 5.55(d,J=1.5Hz,1H), 5.70-5.88(m,2H), 6.45(d,J=10Hz,1H), and 6.85-7.46(m,4H)ppm. IR(KBr) 1075 and 1030cm^{-1}. MS(m/z) 246(M$^+$,4.5), 214(74), 186(30), 184(50), 171(72), 156(50), 128(100), and 115(46).
6. a)S. Inagaki, H. Fujimoto, and K. Fukui, *Chem. Lett.*, **1976**, 749;b)L. B. Harding and W. A. Goddard, III, *Tetrahedron Lett.*, **1978**, 747.
7. A control experiment excluded the possibility of degradation of cis-3 into 4 under the oxygenation condition.
8. Pale yellow plates from CCl$_4$, mp227-229°C. NMR(in CDCl$_3$)δ3.46(s,3H), 3.59 (s,3H), 3.90(d,J=9Hz,1H), 4.70(d,J=9Hz,1H), 6.08(d,J=10Hz,1H), 7.10-7.87 (m,11H)ppm. IR(KBr) 1735, 1665, and 1220cm^{-1}. MS(m/z) 428(M$^+$, 12), 364 (27), 337(100), and 183(33).
9. Colorless oil: NMR(in CCl$_4$) δ0.86 and 0.88(two s, J=6.5Hz, 6H), 1.60-2.45 (m,3H), 3.20-3.82(m,2H), 3.54(s,3H), 4.18(m,1H), 5.30(d of d, J=6.5 and 3.0Hz,1H), and 6.88-7.70(m,6H)ppm. IR(liquid film) 2940 and 1745cm^{-1}. MS(m/z) 314(M$^+$,31), 199(43), 181(100), and 152(20).
10. Pale yellow oil: NMR(in CCl$_4$) δ0.85 and 0.86(two d, J=6.5Hz,6H), 1.60-2.10 (m,1H), 1.94-2.40(m,2H), 3.26-3.80(m,3H), 3.70(s,3H), 5.37(m,1H), and 6.68 (s,2H)ppm. IR(liquid film) 1750, 1685, and 1650cm^{-1}. MS(m/z) 294(M$^+$, trace), 222(21), 194(100), and 178(43).
11. One of the isomers was obtained as colorless granules (from ether) melted at 93°C: NMR(in CCl$_4$) δ3.50(s,3H), 3.60(s,3H), 4.44-4.52(m,1H), 4.86-4.98 (m,1H), 5.04-5.14(m,1H), 6.18-6.26(m,1H), and 6.60-6.90(m,2H)ppm. IR(KBr) 1062 and 1015cm^{-1}.

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