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EVIDENCE OF SIMILARITY BETWEEN BIOOXYGENATION AND PHOTO-OXYGENATION: FORMATION OF QUINONE EPOXIDES

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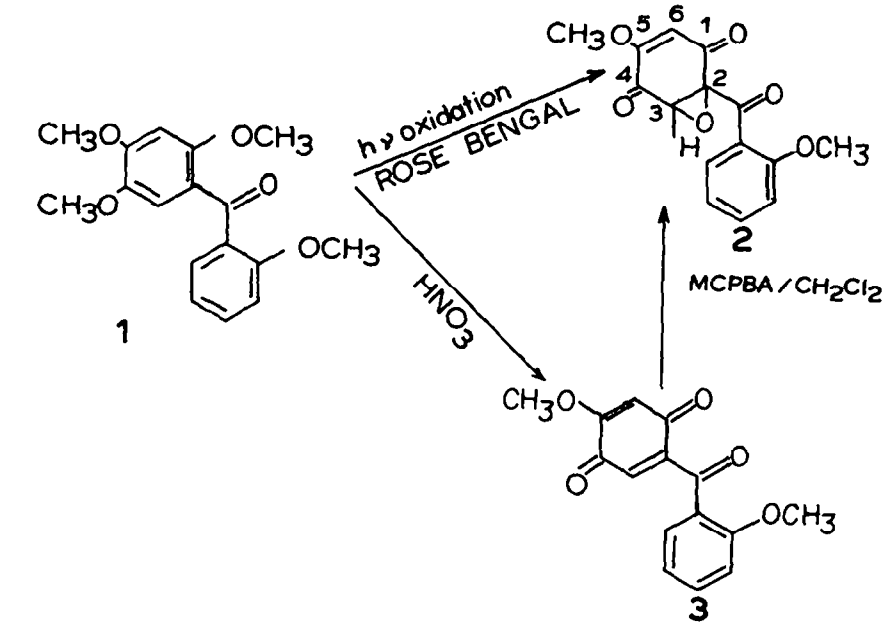
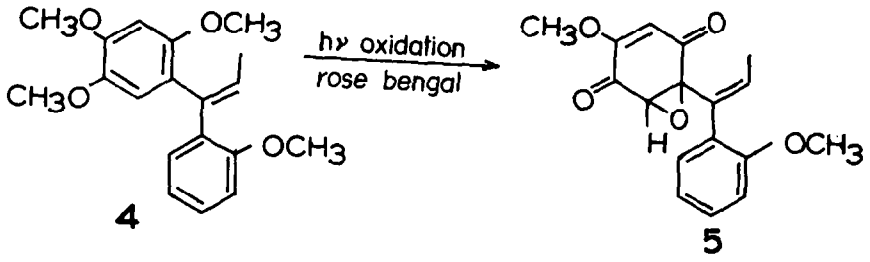
Abstract- Polymethoxybenzene derivatives form quinone epoxides by singlet oxygen oxidation. Thus 2',2,4,5-tetramethoxy benzophenone 1 furnished 2,3-epoxy-5-methoxy-2(2'-methoxy-benzoyl)- cyclohex-5-en-1,4-dione 2, identical with an authentic sample prepared by m-chloroperbenzoic acid oxidation of corresponding p-benzoquinone 3. Similarly isolatifolin dimethyl ether 4, 1-(2'-methoxyphenyl)-1(2,4,5-trimethoxyphenyl) ethylene 6 and asarone 8 gave the corresponding quinone epoxides.

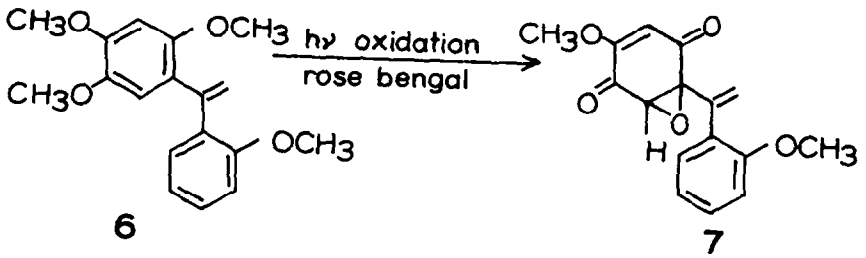
In recent years, there has been continuing wide spread interest in the field of dye sensitized photooxygenation involving singlet molecular oxygen $O_2[^1\Delta_g]$ While a large volume of work has been reported in the photooxygenation of olefins[1] and polynuclear aromatic compounds[2], the literature on photooxidation of methoxybenzenes is limited and incomplete[3]. In an earlier communication[4], we have reported the novel photooxidation of natural products like latifolin and related compounds. In continuation of this work, we report now formation of quinone epoxides by dye-sensitized photooxidation of some p-dimethoxy benzene derivatives.

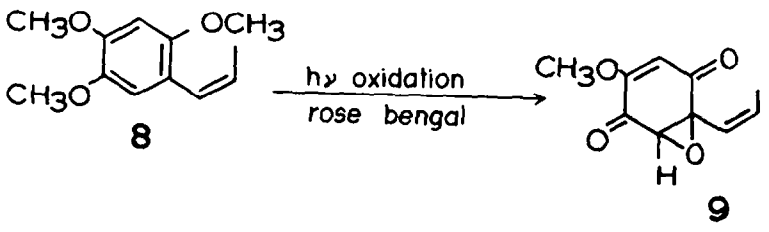
2,2',4,5-tetramethoxybenzophenone 1 on dye sensitized (rose bengal) photooxidation in methanol gave a new photoproduct whose structure has been deduced as 2 for the following reasons. Its mass spectrum (M^+ at m/z 288) and elemental analysis agreed with the molecular formula of 2. ^1H NMR spectrum of 2 showed the presence of only two methoxy groups (δ 3.8 and δ3.7) implying the loss of two methoxy peaks at δ 3.85 and 3.75 originally present in 1. In the aromatic region, its NMR spectrum showed only four proton multiplets and signals due to two para protons, present in 1 were absent in 2. However, the spectrum contained two new singlets of one proton each at δ5.9 and δ3.9, which could be respectively assigned protons at C-3 and C-6 position by a comparison of the NMR spectrum of benzoquinone 3 in which these protons appeared at δ5.9 and δ6.8 respectively. The upfield chemical shift of the proton at δ6.8 of 3 to δ3.9 in 2 clearly suggests epoxidation of 2$\triangle$bond rather than 5$\triangle$bond. Further the presence of quinonoid system in 2 was also supported by strong IR absorptions due to carbonyl groups at 1650 and 1690 cm^{-1}. The UV spectrum of 2 showed λmax at 259 and 316 nm. The presence of epoxide ring in the molecule was also indicated by a positive colour test with 4- (p-nitrobenzyl) pyridine[5].

Communication No. 342


hν oxidation
ROSE BENGAL
HNO3
MCPBA / CH2Cl2
1
2
3


hν oxidation
rose bengal
4
5


hν oxidation
rose bengal
6
7


hν oxidation
rose bengal
8
9

Chemical proof for the above structure 2 was obtained by two step conversion of 1 to 2. Thus HNO_3 oxidation of 1 gave the known benzoquinone[6] 3 which on treatment with m-chloroperbenzoic acid (MCPBA) exclusively furnished 2.

Extension of the above reaction to 4 (isolatifolin dimethyl ether), 6(2,2', 4,5-tetramethoxy-1,1-diphenyl ethylene) and 8 (β-cis asarone) similarly gave 5,7 and 9 respectively. In all these photoproducts the NMR signal due to proton at C-6 resonated at δ 5.9 and that due to proton at C-3 appeared at δ 3.9 in addition to other spectral data.

The literature abounds examples of oxidative demethylation of ortho and para dimethoxybenzene systems to corresponding quinones by chemical oxidants like HNO_3, periodic acid and chromic acid, but as far as we are aware there is no report of oxidative demethylation to quinone epoxides by singlet oxygen which is known to work only in the case of quinol partial ether[3,4]. The formation of quinone epoxides in the present case is therefore both surprising and novel. The novelities in this reaction are (a) although apparently it involves the intermediate formation of quinones, yet when a quinone is used deliberately as an intermediate, formation of 2 is extremely slow. This may be due to an intermediate complex which stabilises only at the epoxide stage by as yet an unknown mechanism and (b) the regioselectivity of the epoxide formation. In all the examples so far examined it involves double bond between C_2 and C_3 of the quinones. It is never formed on the alternative double bond between C_5 and C_6 of the quinone. There is striking similarity of regioselectivity of this photooxidation with similar selectivity observed in the co-occurrence of fungal metabolites like fumigatin oxide, terric acid and terrimutin alongwith the corresponding quinones[7].

Specific formationof p-quinone system rather than o-quinone is understandable due to the lower redox potential of the former. However, the reason for regioselectivity noticed in this epoxidation process is not very clear.

EXPERIMENT

Melting points are uncorrected. UV spectra were recorded in methanol solution on a Varian-634 spectrometer. IR spectra were recorded on a Perkin Elmer-457 spectrometer. PMR spectra were recorded at 60 MHz with Varian EM-360 L spectrometer in $CDCl_3$ and TMS as internal reference. Mass spectra were recorded on Jeol JMS D-300 spectrometer in the EI-mode.

Photooxidation of 2,2',4,5-tetramethoxybenzophenone (1)

Compound 1 (1 g) in methanol (200 ml) containing rose bengal (5 mg) was irradiated with a light from a tungsten lamp (600 W), while a gentle stream of air was bubbled through the solution. After 8 hrs. of irradiation, methanol was removed under vaccum and the residue was chromatographed over a column of silica gel eluting with (i) benzene and (ii) ethyl acetatebenzene (5-95) respectively.

The benzene eluate gave unchanged 1 (300 mg). The ethylacetatebenzene eluate gave 2 as a pale yellow solid (600 mg). It crystallised from methanol as pale yellow needles, m.p. 120-121° (Found: C,62.8: H,4.31, $C_{15}H_{12}O_6$ requires, C,62.5; H, 4.2%). λ_{max}^{MeOH} 258 and 316 nm. ν_{max}^{nujol}:1690 and 1650 cm^{-1}. MS:288(M^+). NMR ($CDCl_3$): δ 3.7 (3H, s, OCH_3), 3.8 (3H, s, OCH_3), 3.9 (1 H,H_3), 5.9 (1H,s,H_6), 8.0-7.0 (4H, m, Aromatic).

Chemical oxidation of 2-(2-methoxybenzoyl)-5-methoxy-1,4-benzoquinone to 2.

Quinone[6] 3 (500mg)was dissolved in dichloromethane (25 ml) and treated with m-chloro-perbenzoic acid (50mg) for half an hour. The solution was washed with brine, the solvent evaporated and the product purified by column chromatography to give 2(300mg) identical in all respects with sample of 2 obtained above.

Photooxidation of isolatifolin dimethyl ether 4:

Isolatifolin dimethyl ether 4 (100 mg) on irradiation as above gave a pale yellow product 5 (60 mg) which crystallised from benzene as pale yellow plates m.p. 82-83°. (Found: C,68.2; H, 5.5: $C_{17}H_{16}O_5$ requires C,68.0; H,5.3%). λ_{max}^{MeOH} 250 nm, ν_{max}^{nujol} 1710 and 1650 cm^{-1}. MS: 300 (M^+). NMR ($CDCl_3$) δ: 1.5 (3H,d, J=15Hz, CH_3), 3.7 (3H,s, OCH_3), 3.8 (3H,s, OCH_3) 3.9 (1H,s, H_3), 5.8 (1H, s, H_6), 6.4 (1H, q, CH), 7.5-7.0 (4H, s, aromatic).

Photooxidation of 2,2',4,5-tetramethoxy-1,2 diphenylethylene 6:

Compound 6 (1 g) in methanol (500 ml) was photolysed and worked up as above when it gave besides unchanged 6 (100 mg) a new product 7 as a pale yellow solid which on crystallisation from methanol gave pale yellow needles, m.p. 140-142°C. (Found:C,66.9; H,4.9, $C_{16}H_{14}O_5$ requires C, 67.13; H,4.9%). λ_{max}^{MeOH} 247 nm. ν_{max}^{nujol}: 1690 and 1650 cm^{-1} MS: 286 (M^+), NMR ($CDCl_3$) δ : 3.7 (3H,s,OCH_3), 3.8 (3H, s, OCH_3), 3.9 (1H, s, H_3), 5.6 (2H, s,CH_2), 5.9 (1H,s, H_6), 7.5-7.0 (4H,m, aromatic).

Photooxidation of β-cis-asarone 8 :

β-cis asarone 8 (500 mg) in methanol was irradiated and worked up as above, when it gave besides unchanged asarone 8, a pale yellow new product 9, which was crystallised from methanol as yellow needles, m.p. 130-132° (Found C,62.0; H,5.2. $C_{10}H_{10}O_4$ requires C 61.9; H, 5.2%). λ_{max}^{MeOH} 259 nm; ν_{max}^{nujol} :1700 and 1640cm^{-1} MS: 194 (M^+). NMR ($CDCl_3$) δ :1.9 (3H, d, CH_3), 3.8 (3H, s, OCH_3), 3.95 (1H,s,H_3) 5.9 (1H, s, H_6), 6.2 (1H, m, CH).

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