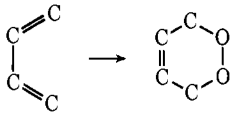
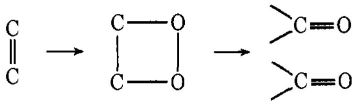
Chemistry of Singlet Oxygen. XVII. 1,4-Addition Products from Styrene Derivatives[1]

Sir:

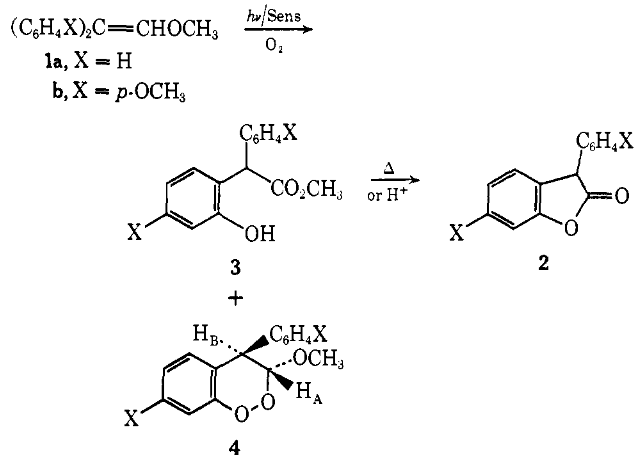
The photosensitized 1,4 cycloaddition of oxygen to dienes (reaction 1)[2] is believed to involve singlet ($^1\Delta_g$) oxygen as an intermediate.[3] More recently, 1,2 cycloadditions of singlet oxygen to electron-rich olefins (reaction 2) have been recognized.[4,5] 1,2-Dioxetane intermediates have been isolated from enamines[6] and vinyl ethers[5] and have been suggested as intermediates in other cases of oxidative double bond cleavage.[7,8]


(1)


(2)

We now report that photooxygenation of several styrene-type olefins proceeds *via* reaction 1 to give products of an unusual type; dioxetanes are not detected. 1,1-Diphenyl-2-methoxyethylene (**1a**)[9] was photooxygenated in benzene with dinaphthalenethiophene (sensitizer). One equivalent of O_2 was absorbed. Glc showed only 10% of benzophenone, the product of oxidative cleavage. The major product (85%) was γ-lactone **2a**.[10]

When the reaction mixture was chromatographed on silica gel, two new products were isolated. The first (mp 127.5–128.4°) was methyl ester **3a**. The other, colorless unstable crystals, mp 130.5–131.5° dec, gave an active O titer of 40% (competing rearrangement precludes quantitative titration). The mass spectral parent ion occurred at *m/e* 242. The ir spectrum ($CHCl_3$) had no carbonyl absorptions. The nmr spectrum (CCl_4) had peaks at δ 7.30 (m, 9 H), 5.52 (d, J = 13 Hz, 1 H), 4.80 (d, J = 13 Hz, 1 H), and 3.15 (s, 3 *H*). These data are consistent with structure **4a**; the 13-Hz AB coupling suggests H_A and H_B are trans quasiaxial in a six-membered ring. Reaction mixtures containing **3a** and **4a** were readily converted to **2a** by brief heating or treatment with acid.[11]

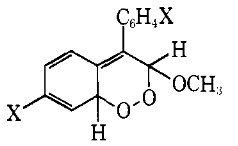

$(C_6H_4X)_2C{=}CHOCH_3 \xrightarrow[O_2]{h\nu/\text{Sens}}$

1a, X = H

b, X = *p*-OCH$_3$

3 + **4** + $(C_6H_4X)_2CO$; **3** $\xrightarrow[\text{or } H^+]{\Delta}$ **2**

Formation of these products suggests a 1,4 cycloaddition to give endoperoxide **5a**. The following experiments support this interpretation. The photooxygenation of **1a** was carried out at −78° in diethyl ether, and an unstable crystalline solid precipitated. The solvent was decanted and the product dried at low temperature. The nmr spectrum ($CDCl_3$, −30°) had peaks at δ 7.38 (m, 5 H), 5.55–6.60 (m, 6 H), and 3.55 (s, 3 H). The uv spectrum ($CHCl_3$, −30°) had intense absorption, λ_{max} 320 nm. Woodward's rules,[12] with data for phenyl-substituted olefins,[13] would predict λ_{max} 321 nm for **5a**, a structure which is in accord with the nmr spectrum.


5a, X = H

b, X = OCH$_3$

Very similar results were obtained with 1,1-di-*p*-anisyl-2 methoxyethylene (**1b**). Photooxygenation at room temperature followed by silica gel chromatography led to isolation of peroxide **4b**, mp 112–116° dec. This compound had chemical and spectral properties analogous to those of **4a**; on treatment with acid, it was smoothly converted to **2b**, mp 153.6–154.6°. The spectral data for **2b** were analogous to those of **2a**. Peroxide **5b** seems to be more reactive than **5a** at low temperatures, as 1.6 mol of oxygen was taken up at −78°. The product was not completely characterized. It seems likely that the rearrangement **5b** → **4b** at room temperature prevents addition of the second oxygen.

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[1] Paper XVI: C. S. Foote, E. H. Peterson, and K.-W. Lee, *J. Amer. Chem. Soc.*, **94**, 1032 (1972). This work was supported by Public Health Service Grant No. AP00681 and National Science Foundation Grant No. GP-25, 790. All new isolated compounds gave satisfactory microanalytical data.

[2] K. Gollnick and G. O. Schenck in "1,4-Cycloaddition Reactions," J. Hamer, Ed., Academic Press, New York, N. Y., 1967, 255.

[3] C. S. Foote, *Accounts Chem. Res.*, **1**, 104 (1968); K. Gollnick, *Advan. Photochem.*, **6**, 1 (1968).

[4] (a) C. S. Foote and J. W.-P. Lin, *Tetrahedron Lett.*, 3267 (1968); (b) J. E. Huber, *ibid.*, 3271 (1968).

[5] (a) P. D. Bartlett and A. P. Schaap, *J. Amer. Chem. Soc.*, **92**, 3223 (1970); (b) S. Mazur and C. S. Foote, *ibid.*, **92**, 3225 (1970).

[6] Monomeric dioxetanes have now been isolated from several enamines: C. S. Foote and A. A. Dzakpasu, unpublished results.

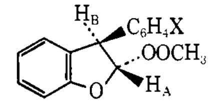
[7] L. J. Bollyky, *J. Amer. Chem. Soc.*, **92**, 3231 (1970).

[8] (a) G. Rio and J. Bertholet, *Bull. Soc. Chim. Fr.*, 3609 (1969); (b) W. H. Richardson and V. Hodge, *J. Org. Chem.*, **35**, 1216 (1970); (c) W. Fenical, D. R. Kearns, and P. Radlick *J. Amer. Chem. Soc.*, **91**, 3396 (1969); (d) D. R. Kearns, *Ann. N. Y. Acad. Sci.*, **171**, 34 (1970); (e) W. Adam and J.-C. Liu, *J. Chem. Soc., Chem. Commun.*, 73 (1972); *J. Amer. Chem. Soc.*, **94**, 1206 (1972).

[9] Prepared by the method of G. Wittig and M. Schlosser, *Chem. Ber.*, **94**, 1373 (1961).

[10] R. D. Kimbrough, Jr., K. W. Kraus, and J. J. Partridge, Jr., *J. Org. Chem.*, 30, 4333 (1965).

[11] The alternate structure **4a′** suggested by a referee is unlikely because **3a** retains the methoxyl group; in addition, no reasonable mode of formation for **4a′** is apparent, and the AB coupling is too large for a five-membered ring.

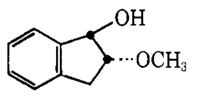

4a′

[12] R. B. Woodward, *J. Amer. Chem. Soc.*, **63**, 1123 (1941).

[13] J. H. Pinkard, B. Willard, and L. Zechmeister, *ibid.*, **70**, 1938 (1948); A. Smakula and A. Wasserman, *Z. Phys. Chem., Abt. A*, **155**, 353 (1931).

This reaction is a novel example of the Diels–Alder reaction with singlet oxygen. Many examples of 1,4 addition of various dienophiles to styrene derivatives are known,[14] although this is the first involving singlet oxygen.[15] The benzophenone may or may not be derived from a small amount of dioxetane. The interesting question of why these olefins add oxygen 1,4 while the 1,2-dimethoxystilbenes[16] and the enamine analogous to **1**[4,6] add it 1,2 is under investigation. We believe a very delicate electron density requirement exists for dioxetane formation. Peroxides **4a** and **b** are the first with peroxide directly bonded to an aromatic ring.

These results suggested that a reinvestigation of the photooxygenation of indene was warranted; the original observations were that, in $CHCl_3$, the product was homophthalaldehyde, while in methanol, products **6–8** were obtained.[8c] Repetition has confirmed these observations, but the reaction is extremely slow in aprotic solvents and is accompanied by dye bleaching; several other products (including indene oxide) are formed. In methanol, the reaction is much faster, and product proportions vary.[17] To clarify the mechanism, photooxygenation of several indenes was carried out at −78°: under these conditions the reaction is much faster and unexpected products are formed in excellent yield.



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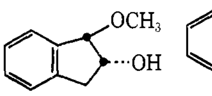

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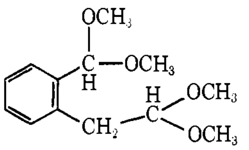

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Indene (0.96 *M*) in acetone containing Rose Bengal was photooxygenated in a Dry Ice–acetone bath; oxygen uptake was 1.5 mol/mol of indene. Both the nmr and the tlc of the crude residue showed mainly starting material and a single new product (isolated in 58% yield), colorless crystals, mp 105.0–105.5° dec, which freed I_2 from acidified KI.

Similar photooxidation at −78° of 2,3-diphenyl-, 3-isopropyl-, and 3-methyl-2-phenylindene gave more rapid O_2 uptake (2.0 equiv of O_2 in each case) and gave products in 93, 74, and 78% yield; the first two had mp 107–108° dec and 95.3–96.5° dec; the third melted near 135°, then resolidified and melted again at 183–189°.

All four compounds gave analyses and mass spectra consistent with starting material + $2O_2$; the mass spectra had major peaks at P − 32 (loss of O_2). The ir spectra had no C=O or OH peaks but many bands between 820 and 1100 cm^{-1}; all had several strong bands near 840–870 cm^{-1} (epoxide). The chemical shifts are summarized in Table I; the analyses (checked by double resonance) are in Table II. Structures **10a–d** are the only ones consistent with the spectra.[18]

Table I. Chemical Shifts (δ, TMS, 60 MHz) of Ring Protons[a]

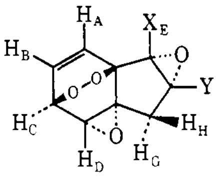
Proton	**10a**	**10b**	**10c**	**10d**	**14**
H_A	6.50	6.45	6.63	6.55	3.63
H_B	6.27	6.22	6.23	6.35	3.43
H_C	5.15	5.06	5.03	5.07	3.29
H_D	3.7	3.81	3.65	3.73	3.77
H_E	3.7				
H_F	3.62		3.60		
H_G[b]	2.10	2.55	2.20	2.45	2.05
H_H[b]	2.73	3.43	2.75	3.20	3.05

[a] Substituent absorptions omitted for clarity. Shifts are approximate multiplet centers. [b] Lower field of G,H assigned as H because phenyl substituent has larger effect on this resonance.

Table II. Couplings (Hz) Derived from Peaks of Table I

J	**10a**	**10b**	**10c**	**10d**	**14**
AB	8.4	8.6	8.8	8.4	2.0
AC	1.8	2.0	1.6	1.8	1.5
BC	5.7	5.6	5.7	5.6	3
CD	4.0	4.0	4.0	4.2	3
BD	~0.8[b]	~0.6	~0.8	~0.6	
GH	16	16	16	16	14
F(H)[a]	~1				

[a] Proton F to lower field of G or H; assignment as H consistent with observed coupling as shown by models. [b] Obscured in D by overlap of E resonance.



10a, X = Y = H
10b, X = Y = C_6H_5
10c, X = *i*-C_3H_7; Y = H
10d, X = CH_3; Y = C_6H_5

The ^{13}C spectrum of **10d** (63.1 MHz) shows the quaternary carbon atoms appearing at 54.7, 68.7, 71.8, and 90.0 ppm (TMS), consistent with attachment to oxygen (and, in the last case, peroxide); the shifts and multiplicities of all carbon atoms in **10a–d** are consistent with the assigned structures; assignments were checked by off-resonance decoupling and by proton on-resonance decoupling in the ^{13}C spectra of most compounds.[19]

The formation of these compounds is readily understood if Diels–Alder addition to the indenes is the

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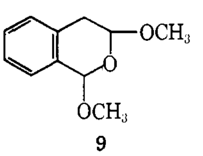
(14) A. S. Onishchenko, "Diene Synthesis," translated by L. Mandel, Israel Program for Scientific Translations, Jerusalem, 1964.

(15) Since the submission of the original manuscript, another example has been reported: G. Rio, D. Bricout, and L. Lacombe, *Tetrahedron Lett.*, 3583 (1972).

(16) G. Rio and D. Bricout, *Bull. Soc. Chim. Fr.*, 3555 (1971).

(17) Instead of **8**, compound **9** was isolated.



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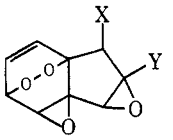
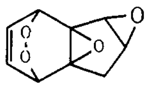
(18) Alternative formulations such as **11a** are not consistent with the spectra of **10b–d**. Structure **11b** does not have the correct number of protons α to epoxide or the correct coupling pattern.



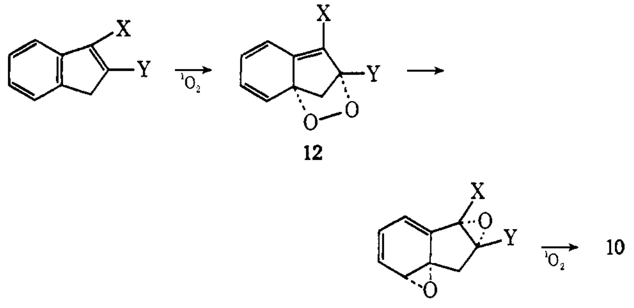
11a



11b

(19) We thank N. Roy Easton, Jr., and Professor F. A. L. Anet for measurement of these spectra and their interpretation.

first step, giving **12**. Rearrangement of this highly strained peroxide to **13** is a reaction similar to one which proceeds readily at higher temperatures in less-strained systems.[20] Addition of a second singlet oxygen molecule to the resulting product would be rapid, to give **10**. Because of the mode of formation, the epoxide groups are assigned to be cis; models show the top face is the less hindered, so that the peroxide bridge is suggested to be trans to the epoxides.

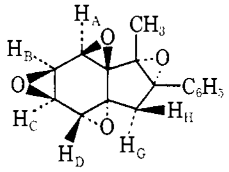


12

13

The intermediacy of **12** provides a rationale for the formation of compounds **6–8** as well. Rearrangement of **12** to the 2,3-dioxetane followed by cleavage has analogy,[20b] and would account for the formation of homophthalaldehyde and **8**; **6** and **7** could derive either from the dioxetane or from **12** directly by nucleophilic attack followed by allylic shift.

The behavior of compound **10d** on heating provides further evidence for the assigned structure. Warming gives rapid rearrangement to a mixture of two compounds, of which the major (>70% by nmr) product, an isomer by analysis and mass spectrum, had mp 184.5–186°; the compound has neither C=O nor OH bands in the ir; nmr shows no peaks (except phenyl) below 3.8 ppm. The spectrum and its analysis are summarized in Tables I and II. On the basis of its spectra and analogy, the compound was assigned the tetraepoxide (*benzene trioxide!*) structure **14**. The ^{13}C spectra agree with the assignment.[19] An exactly analogous rearrangement in a simpler system has been found by Foster and Berchtold.[21] Nmr chemical shifts of **14** agree well with the values of these authors.



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Compounds **10a–c** undergo similar rearrangements in good yield. The stereochemistry is assigned as shown consistent with that of **10d**; only in this stereochemistry do protons A and C but not B and D have the W arrangement required for long-range coupling.[22] These novel compounds are all produced in synthetically useful yields. The above experiments make it less likely that **6** and **7** are derived from any intermediate related to the ene reaction.[8c] The greater rate of photooxidation of indene at low temperature suggests that the formation of **12** may be reversible at higher temperatures; attempts to trap **12** are in progress.

(20) (a) J. Boche and O. A. Rundquist, *J. Org. Chem.*, **33**, 4285 (1968); (b) J.-P. LeRoux and J.-J. Basselier, *C. R. Acad. Sci. Paris*, **271**, 461 (1970).

(21) C. H. Foster and G. A. Berchtold, *J. Amer. Chem. Soc.*, **94**, 7939 (1972). We thank Professor Berchtold for a prepublication copy of his manuscript.

(22) Other formulations in which some of the oxygen bridges are not epoxides are less likely because they would be expected to have nmr absorption at lower field for the α protons.

(23) Eastman Kodak Fellow, 1970–1971.

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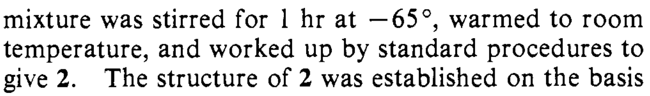
Specific Ortho Alkylation of Aromatic Amines

Sir:

Of the various methods available for the formation of C–C bonds to aromatic rings, the classical Friedel–Crafts reaction is undoubtedly the best known and the most widely used.[1] We now wish to describe a simple experimental procedure which permits the specific ortho alkylation of aromatic amines. The application of this process provides a superior method for the synthesis of certain isomerically pure polysubstituted aromatic compounds.

In a typical procedure, 1 equiv (*ca.* 0.1 mol) of *tert*-butyl hypochlorite[2] in 10 ml of methylene chloride[3] was added to a vigorously stirred solution of 1 equiv (*ca.* 0.1 mol) of aniline (**1**) in 400 ml of methylene chloride[3] at −65°.[4] The reaction mixture was stirred for 25 min and 3 equiv of dimethyl sulfide was added dropwise at −65°.[4] The reaction mixture was stirred for 40 min and a solution of 1.2 equiv of sodium methoxide in 50 ml of methanol was added at −65°. The reaction mixture was stirred for 1 hr at −65°, warmed to room temperature, and worked up by standard procedures to give **2**. The structure of **2** was established on the basis of its spectroscopic properties and its facile conversion to **3** on reduction with Raney nickel at room temperature. Table I lists a series of aniline derivatives which have been converted to the corresponding 2-thiomethoxymethylanilines according to this procedure. As can be seen from Table I addition of the thiomethoxymethyl group occurs only in the position ortho to the amino function. Hence, ortho- and para-sub-



1 **2** **3**

(1) C. Friedel and J. M. Crafts, *C. R. Acad. Sci.*, **84**, 1392, 1450 (1877). For a recent detailed account of the Friedel–Crafts reaction see G. A. Olah, "Friedel–Crafts and Related Reactions," Interscience, New York, N. Y., 1963–1965.

(2) In addition to *tert*-butyl hypochlorite, *N*-chlorosuccinimide and calcium hypochlorite (HTH) have been used as sources of chlorine in this reaction.

(3) The reaction can be run in a wide variety of solvents. Solvents as extreme in polarity as toluene and methanol have been used. Methylene chloride has been the most commonly used solvent.

(4) The reaction can be run over a broad temperature range. In part, the preferred temperature is dictated by the substituents on the aromatic ring, since these determine the stability of the intermediate *N*-chloroanilines[5] (*vide post*). The reaction can be run in the vicinity of 0°, but improved yields are obtained at lower temperatures.

(5) P. G. Gassman and G. Campbell, *J. Amer. Chem. Soc.*, **94**, 3891 (1972).