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The Sensitized Photooxygenation of 2-Vinylbenzofurans

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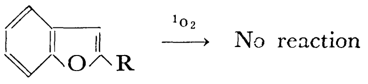
The sensitized photooxygenation of benzofuran, 2-methylbenzofuran, and six 2-vinylbenzofurans was investigated. Benzofuran and 2-methylbenzofuran were stable toward singlet oxygen. On the other hand, the vinylbenzofurans were easily photooxygenated to give the 1,4-endoperoxides. The 1,4-cycloaddition of singlet oxygen to the 2-benzofurans was confirmed to proceed with stereospecificity.

Recently, it has been found that, for some styrene derivatives$^{1)}$ and vinyl-substituted polynuclear aromatic hydrocarbons,$^{2)}$ an aromatic double bond in conjugation with extranuclear unsaturation produces an active diene system capable of undergoing the 1,4-cycloaddition of singlet oxygen. Vinyl-substituted heteroaromatics such as 2-vinylthiophene$^{3)}$ and 1-methyl-3-vinylindoles,$^{4)}$ have also been found to undergo the 1,4-cycloaddition of singlet oxygen. On the other hand, such aromatics as benzene, naphthalene, phenanthrene, and thiophene are themselves known to be stable to singlet oxygen.$^{5)}$ Of the heteroaromatics, furans have been most intensively studied in connection with their photooxygenation, though their benzo analogs, *i. e.*, benzofurans, have scarcely been known to undergo any sensitized photooxygenation.$^{5)}$ We have studied here the sensitized photooxygenation of **1** benzofurans and 2-vinylbenzofurans, **2**, in order to investigate the reactivities of the 2,3-double bond of the ring and a conjugated system composed of the 2-vinyl group and the 2,3-double bond of these aromatics.

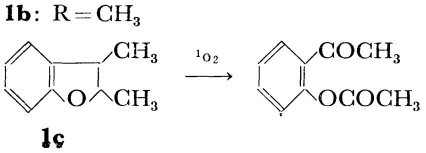
Results and Discussion

Preparation of 2-Vinylbenzofurans. Of six vinylbenzofurans, **2**, used in this work, 2-(2-methyl-1-propenyl)- (**2a**), *trans*-2-styryl- (**2c**), *cis*-2-styryl- (**2d**), and 2-isopropenylbenzofuran (**2f**) were prepared by the Witting reaction of 2-formylbenzofuran or 2-acetylbenzofuran and the corresponding methylenetriphenylphosphoranes. The other two, 2-vinyl- (**2b**) and 2-(1-phenylvinyl)benzofuran (**2e**) were obtained by the dehydration of the corresponding alcohols which themselves had been prepared from 2-acetylbenzofuran. The preparations of these vinylbenzofurans were described in detail in the Experimental Section.

Sensitized Photooxygenation of 2-Vinylbenzofurans
First, the sensitized photooxygenation of benzofuran (**1a**) and 2-methylbenzofuran (**1b**) as typical examples of 2- and 3-alkyl-substituted benzofurans were examined. When 2-methylbenzofuran (**1b**) was photooxygenated for 3 h as in the cases of the vinylbenzofurans **2** described below, scarcely no oxygen was consumed and the starting material was recovered. Benzofuran (**1a**) itself was also fairly stable under similar irradiation conditions. These results showed that, for benzofurans, the 2,3- double bond is more stable than for indoles,$^{6)}$ though 2,3-dimethylbenzofuran (**1c**) has been known to be the only substance to undergo the 1,2-addition of singlet oxygen to give *o*-acetoxyacetophenone.$^{7)}$

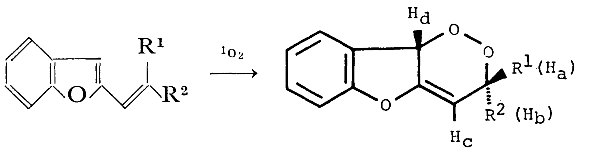


1a: R=H
1b: R=CH$_3$



1c

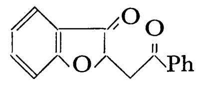
Second, the sensitized photooxygenation of 2-vinylbenzofurans **2** was carried out. A solution of 2-(2-methyl-1-propenyl)benzofuran (**2a**) and tetraphenylporphine (TPP) (used as a sensitizer) in carbon tetrachloride was irradiated externally with low-pressure sodium vapor lamps under an oxygen atmosphere at 5 °C. After the irradiation, the photolysate was condensed and purified by chromatography on silica gel to give a 1,4-endoperoxide **3a** as colorless plates in a 90% yield. The structure of **3a** was assigned on the basis of spectral evidence and combustion analyses. In this examination, scarcely no 1,2-cycloaddition of singlet oxygen to the 2,3-double bond of the side chain or the "ene" reaction was observed. The similar photooxygenation of 2-vinylbenzofuran (**2b**) afforded the corresponding 1,4-endoperoxide **3b** as an oil in a 41% yield. Then, in order to investigate the stereochemical features of the 1,4-cycloaddition of singlet oxygen to 2-vinylbenzofurans **2**, *trans*-2-styrylbenzofuran (**2c**) and its *cis*-isomer **2d** were individually photooxygenated under similar conditions. The *trans*-isomer **2c** gave the corresponding 1,4-endoperoxide **3c** in a 70% yield. On the other hand, the peroxide **3d** was obtained from the *cis*-isomer in a 75% yield. The olefin **2c** gave no **3d**, whereas the isomer **2d** gave no **3c**. Consequently the results obtained here confirm that the 1,4-cycloaddition of singlet oxygen to 2-vinylbenzofurans **2** proceeds with stereospecificity.



2a: R^1, R^2=CH$_3$
2b: R^2, R^2=H
2c: R^1=H, R^2=C$_6$H$_5$
2d: R^1=C$_6$H$_5$, R^2=H

3a: R^1, R^2=CH$_3$
3b: R^1, R^2=H
3c: R^1=H, R^2=C$_6$H$_5$
3d: R^1=C$_6$H$_5$, R$_2$=H

The endoperoxides **2a**—**d** were thermally stable, but were easily changed under basic conditions. When the peroxide **3c** was treated with a catalytic amount of triethylamine in ether at an ambient temperature, 2-benzoylmethyl-3(2*H*)-benzofuranone (**4**) was obtained in a 58% yield,



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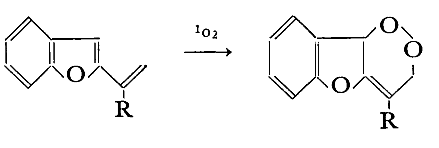
The 1,4-cycloaddition of singlet oxygen has been found to take place with 1-vinylnaphthalenes,[2a] 9-vinylphenanthrenes,[2b] and 2-vinylthiophenes[3] bearing no substituent and a β-substituent on the side chain. An α-substituent of these aromatics has been known to cause significantly different results; for the naphthalene or the phenanthrene derivatives, no 1,4-cycloaddition but "ene" reaction of singlet oxygen occurs,[2] hereas, for the vinylthiophenes, both the 1,4-cycloaddition and the "ene" reaction occur competitively.[3] The 2-vinylbenzofurans **2** seemed to behave much like the 2-vinylthiophenes in the reaction with singlet oxygen. When 2-(1-phenylvinyl)benzofuran **2e** was photooxygenated as in the cases described above, the corresponding peroxide **3e** was formed. A similar irradiation of 2-isopropenylbenzofuran (**2f**) also gave the expected peroxide **3f**. Neither peroxide **3e** or **3f** could be isolated in a pure form because of their instabilities. In particular, the former, **3e**, was highly explosive. These differences between a pair of 2-vinylthiophenes and 2-vinylbenzofurans **2**, and a pair of 1-vinylnaphthalenes and 9-vinylphenanthrenes may be due to steric and electronic factors. For the vinylnaphthalenes and vinylphenanthrenes with an α-substituent on the side chain, a steric repulsion between the 8-hydrogen and the α-substituent may hinder the favorable conformation of the side chain for 1,4-cycloaddition, though this hindrance seems to be overcome at higher temperatures.[8] On the other hand, in the cases of 2-vinylthiophenes and 2-vinylbenzofurans **2** such steric repulsion need not be considered and carbons in both the β-position of the side chain and the 3-position of the aromatic nucleus may be activated toward electrophiles, such as singlet oxygen, more than the corresponding carbons in the naphthalene or phenanthrene analogs, by the sulfur or the oxygen atom. These suggestion may be supported by the fact that maleic anhydride reacts more easily with **2e** and **2f** (in refluxing benzene)[9b] than with naphthalene and phenanthrene analogs (in refluxing xylene).[8]



2e: R=C_6H_5 **3e**: R=C_6H_5
2f: R=CH_3 **3f**: R=CH_3

In summary, we have found that, for 2-vinylbenzofurans **2**, the 2,3-double bond, which is scarcely active itself in response to singlet oxygen, in conjugation with 2-ethylenic double bond produces an active diene system capable of undergoing the 1,4-cycloaddition of singlet oxygen.

Experimental

All the melting points and boiling points are uncorrected. The NMR spectra were recorded with a Varian HA-100 spectrometer, with TMS as the internal standard. The

TABLE 1. NMR SPECTRAL DATA OF THE PEROXIDES **3**[a]

Chemical shifts (ppm).

	H_a	H_b	H_c	H_d	R^1	R^2
3a	—	—	6.10	5.06	1.28[b]	1.38[b]
3b	4.50	4.91	6.15	5.17	—	—
3c	5.48	—	6.24	5.30	—	7.1—7.4[c]
3d	—	5.90	6.37	5.36	7.1—7.5[c]	—

Coupling Constants (Hz).

	J_{ab}	J_{ac}	J_{ad}	J_{bc}	J_{bd}	J_{cd}
3a	—	—	—	—	—	2.5
3b	15.0	2.5	2.5	3.0	2.5	2.5
3c	—	3.0	2.0	—	—	3.0
3d	—	—	—	2.5	2.0	2.5

a) Measured in CCl_4. b) Methyl group. c) Phenyl group.

NMR spectral data of the peroxide **3** are summarized in Table 1. The mass spectra were obtained with a Hitachi RMU-6E spectrometer. The light source was consisted of eight 60-W low pressure sodium-vapor lamps (National SOI-60).

*Preparation of 2-Methylbenzofuran (**1b**).* To a solution of coumarone (1.18 g, 10 mmol) in tetrahydrofuran (THF) (30 ml) was added 10 mmol of *n*-butyllithium (6.4 ml of a 10% hexane solution) under an argon atmosphere at room temperature. After 30 min, methyl iodide (1.42 g, 10 mmol) in THF (5 ml) was added to the solution of the carbanion of coumarone, and the mixture was stirred for 1 h. After the usual work-up, the crude product was purified by chromatography on silica gel. The furan **1b** was obtained as a colorless oil [bp 195 °C (lit,[10] bp 192 °C/744 mmHg)] in an 81% yield (1.07 g)

*Preparation of 2-(2-Methyl-1-propenyl)benzofuran (**2a**).* Under an argon atmosphere, to a solution of isopropylidenetriphenylphosphorane (prepared from 10 mmol of isopropyltriphenylphosphonium bromide and an equimolar amount of *n*-butyllithium) in THF (20 ml) was added 2-formylbenzofuran (1.46 g, 10 mmol) at an ambient temperature. After 1 h, the reaction mixture was poured into brine and extracted with hexane. The hexane solution was dried over $MgSO_4$ and condensed. The residue was chromatographed on silica gel and eluted with hexane to yield 1.35 g of the furan **2a** (78%) (colorless needles; mp 48—49.5 °C, from hexane); IR (KBr): 3027, 1660, 1455, 1258, 1194, 940, 750 cm^{-1}; NMR (CCl_4): δ 1.92 (s, 3H), 2.08 (s, 3H), 6.07 (m, 1H), 6.34 (s, 1H), 6.9—7.5 (m, 4H) ppm.

*Preparation of 2-Vinylbenzofuran (**2b**).* 2-Acetylbenzofuran[11] (3.6 g, 23 mmol) was reduced as usual with lithium aluminium hydride (0.4 g, 10 mmol) in dried ether (15 ml) overnight at room temperature to give 2-(1-hydroxyethyl)-benzofuran. The crude alcohol was dehydrated with alumina (Woelm neutral, for column chromatography) at 140 °C (bath temperature). Thus, **2b** was obtained as a colorless oil [bp 52 °C/2 mmHg (lit,[9b] 50 °C/0.1 mmHg)] in a 62% yield; IR (liquid film): 3050, 1548, 1452, 1255, 980, 910 cm^{-1}; NMR (CCl_4): δ 5.22 (d of d, J=11.0 and 2.0 Hz, 1H) 5.84 (d of d, J=18.0 and 2.0 Hz, 1H), 6.38 (s, 1H), 6.47 (d of d, J=18.0 and 11.0 Hz, 1H), 6.9—7.5 (m, 4H) ppm

Preparation of trans-*2-Styrylbenzofuran (**2c**) and* cis-*2-Styrylbenzofuran (**2d**).* To a solution of benzylidenetriphenylphosphorane (prepared from 10 mmol of benzyltriphenylphosphonium bromide and an equimolar amount of *n*-butyllithium in THF was added 2-formylbenzofuran (1.46 g, 10 mmol) under an argon atmosphere at room temperature. The reaction mixture was then treated as in the case of **2a** to give a mixture of **2c** and **2d** (**2c**/**2d**=71/29, 1.30 g). The separation of the mixture was performed by chromatography on silica gel in hexane.

2c: Colorless crystals (mp 123 °C) from ethanol; IR (KBr): 3050, 1444, 1255, 960, 945, 805 cm^{-1}, NMR (CCl_4): δ 6.49 (s, 1H), 6.82 (d, J=16.0 Hz, 1H), 6.9—7.5 (m, 10H) ppm.

2d: A colorless viscous oil; IR (liquid film): 3050, 1452, 1260, 945, 810 cm^{-1}; NMR (CCl_4): δ 6.42 (s, 1H), 6.46 (q_{AB}, J_{AB}=13.0 Hz, 2H), 6.9—7.5 (m, 9H) ppm.

Preparation of 2-(1-Phenylvinyl)benzofuran (2e). To a solution of phenylmagnesium bromide (prepared from 25 mmol of bromobenzene and an equimolar amount of magnesium) in ether was added 2-acetylbenzofuran 3.0 g, 19 mmol) under an argon atmosphere. The usual work-up afforded the crude 2-(α-hydroxy-α-methylbenzyl)benzofuran, which was subsequently dehydrated with phosphorus pentaoxide in ether at room temperature for 2 h. The ether solution was then washed with water and dried over $MgSO_4$. After the evaporation of ether, the crude product was chromatographed on silica gel in hexane to give **2e** as a pale yellow oil in a 43% yield: the spectral data were identical with those in the literature.[9b)]

2-Isopropenylbenzofuran (2f) was prepared by a Witting reaction of 2-acetylbenzofuran and methyltriphenylphosphonium bromide in accord with the method described in the literature,[9a)]

Irradiation of Benzofuran (1a) and 2-Methylbenzofuran (1b). A solution of 1.00 g of **1a** and 5 mg of TPP in CCl_4 (60 ml) was irradiated under an oxygen atmosphere at 5 °C for 3h. Scarcely no oxygen was consumed, and no products were observed by TLC. The furan (**1b**) was also stable under similar irradiation conditions.

Photooxygenation of 2-(2-Methyl-1-propenyl)benzofuran (2a). A solution of 1.35 g (8 mmol) of **2a** was photooxygenated in 60 ml of CCl_4 until 158 ml of oxygen has been consumed (30 min). After the removal of the solvent, the photolysate was chromatographed on silica gel and eluted with a hexane $-CH_2Cl_2$ (1 : 1) mixture to give 1.42 g of the endoperoxide **3a** (colorless plates (mp 107.5—109.0 °C) from ether) (90% yield); IR (KBr): 3070, 2973, 1610, 1460, 1088, 1043, 760 cm^{-1}; MS m/e: 204 (M$^+$, 15), 172 (100), 161 (55), 157 (33), 131 (24), 77 (25), 43 (61).

Found: C, 70.53; H, 5.93%. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92%.

Photooxygenation of 2-Vinylbenzofuran (2b). A solution of 1.0 g (7 mmol) of **2b** and 5 mg of TPP in 60 ml of CCl_4 was irradiated for 3.5 h (O_2 uptake=129 ml). The photolysate was then condensed and chromatographed on alumina (Woelm neutral) previously treated with 20% water. Elution with hexane gave 0.50 g (41%) of the peroxide **3b** as an oil: IR (liquid film): 3050, 1610, 1460, 1095, 1050, 750, 740 cm^{-1}; MS m/e: 176 (M$^+$, 18), 147 (100), 146 (51), 134(85).

Photooxygenation of trans-*2-Styrylbenzofuran (2c).* A solution of 0.93 g (4 mmol) of **2c** and TPP in 60 ml of CCl_4 was irradiated for 3 h (O_2 uptake=91 ml). The chromatographic purification of the photolysate on silica gel in a hexane $-CH_2Cl_2$ (1 : 1) mixture afforded 0.74 g (70%) of the peroxide **3c** (colorless needles (mp 75.5—76.5 °C) from ether); IR (KBr): 3050, 1610, 1460, 1092, 1050, 755, 739, 695 cm^{-1}; MS m/e: 252 (M$^+$, 15), 220 (100), 147 (24), 105 (45), 77 (54), 51 (26).

Found: C, 76.58; H, 4.63%. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%.

Photooxygenation of cis-*2-Styrylbenzofuran (2d).* A solution of 0.24 g (1 mmol) of **2d** and TPP in 60 ml of CCl_4 was photooxygenated for 2.5 h. After the irradiation, the photolysate was treated as in the case of **2c** to give 0.19 g (75%) of the peroxide **3d** (colorless granules, mp 115.0—116.5 °C) from ether; IR (KBr): 3040, 1622, 1465, 1095, 1045, 750, 700 cm^{-1}; MS m/e: 252 (M$^+$, 9), 220 (100), 105 (27), 77 (49), 51 (26).

Found: C, 75.83; H, 4.96%. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%.

Photooxygenation of 2-(1-Phenylvinyl)benzofuran (2e). A solution of 1.10 g (5 mmol) and TPP in CCl_4 (70 ml) was oxygenated for 1 h. After the removal of CCl_4, the reaction mixture was chromatographed on silica gel and eluted with CH_2Cl_2 to give a viscous oil of the peroxide **3e** (10% yield), which crystallized on standing and exploded when subjected to weak friction; NMR (CCl_4): δ 4.29 (q_{AB}, J=15.0 Hz, 2H), 6.22 (s, 1H), 6.7—7.6 (m, 9H) ppm.

Photooxygenation of 2-Isopropenylbenzofuran (2f). A solution of 1.0 g (6 mmol) of **2f** and TPP in CCl_4 (60 ml) was irradiated for 3.5 h. The NMR spectrum (CCl_4) of the crude photolysate revealed the formation of the corresponding endoperoxide **3f**; δ 1.70 (s with fine coupling, 3H, CH_3), 4.56 (q_{AB} with fine coupling, J=15 Hz, 2H, $-CH_2O-$), and 6.20 (m, 1H, -CHO-)ppm. All the efforts to purify **3f** by chromatography on silica or alumina were unsuccessful; when the photolysate was adsorbed on the absorbent, immediately an exothermic reaction was occurred to give complex products.

Isomerization of the Peroxide 3c. Triethylamine (100 mg) was added to a solution of 350 mg of the peroxide **3c** in 10 ml of ether and the mixture was stirred for 20 min at an ambient temperature. Then, the mixture was condensed and chromatographed on silica gel. Elution with CH_2Cl_2 gave 200 mg of 2-benzoylmethyl-3(2*H*)-benzofuranone (**4**) as pale yellow granules (mp 113 °C, from ether); IR (KBr): 3070, 2930, 2900, 1725, 1710, 1687, 1615 cm^{-1}; MS m/e: 252 (M$^+$, 25), 147 (38), 105 (100), 77 (45); NMR ($CDCl_3$): δ 3.55 (m, 2H), 5.08 (m, 1H), 6.9—8.0 (m, 9H) ppm.

Found: C, 76.07; H, 4.96%. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79%.

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