Ozonolyses of 3-Benzoyloxy- and 3-Trimethylsiloxy-Substituted 2-Phenylindenes in Methanol: Substituent-Dependent Modes of Capture of the Carbonyl Oxide Intermediates by the Solvent

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Introduction

Carbonyl oxides, key intermediates in alkene ozonolysis, are efficiently captured by protic, nucleophilic solvents such as methanol.[2] Thus, the corresponding methoxyalkyl hydroperoxides and/or the hemiperacetals, derived from intramolecular cyclization, are usually obtained from the ozonolyses of cycloalkenes in methanol. In certain cases, however, intramolecular partial capture of the carbonyl oxide moiety by the adjacent carbonyl group occurs much faster than capture by the solvent, affording the corresponding α-hydroperoxy-α′-methoxy cyclic ethers instead.[3] We now report that, in the ozonolyses of 3-benzoyloxy- and 3-trimethylsiloxy-substituted 2-phenylindenes (**1** and **7**) in methanol, differences in the respective natures of the substituents at the 3-position appear to exert a significant influence on the mode of capture of the carbonyl oxide intermediates.

Results and Discussion

3-(Benzoyloxy)-2-phenylindene (**1**) was treated with ozone (1.5 equiv) in methanol−methylene chloride at −70 °C. After a conventional workup, ^{1}H and ^{13}C NMR spectral analysis of the crude product mixture suggested that 1-(benzoyloxy)-1-hydroxy-4-methoxy-4-phenyl-4,5-dihydro-1*H*-2,3-benzodioxepin (**5**) had been formed quantitatively (Scheme 1).[4] This product was, however, very labile and decomposed during column chromatography on silica gel into a complex mixture of products from which a solid material (47% yield) could be isolated by crystallization from diethyl ether−hexane. The structure of this new crystalline compound, as determined by X-ray crystallographic analysis (Figure 1),[5] was shown to be the novel 4-methoxy-4-phenyl-4,5-dihydro-1*H*-2,3-benzodioxepin-1-one (**6**), derived from elimination of benzoic acid from **5** (Scheme 1). A solution of **5** in $CDCl_3$ also decomposed to yield a mixture of **6** and benzoic acid with a half-life of ca. 1 day at room temperature.

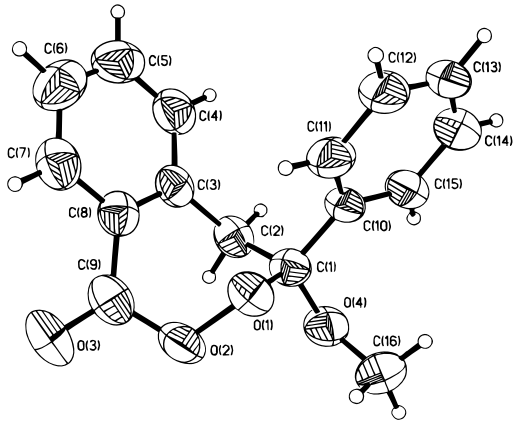
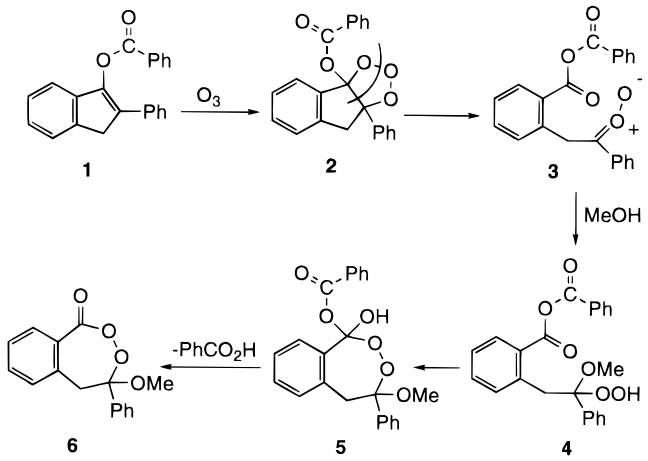
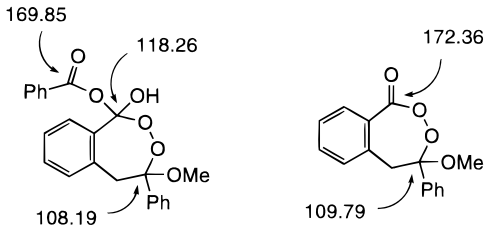


Figure 1. Crystal structure of compound **6** (ORTEP,[10] 50% probability ellipsoids for non-hydrogen atoms).

Scheme 1





These results imply that under the directing effect of the benzoyloxy group,[6] the primary ozonide **2** undergoes

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(5) Crystal data for (**6**): $C_{16}H_{14}O_4$, M = 270.27, colorless needles, monoclinic, space group $P2_1/n$ (alt. setting No. 14), ***a*** 8.6664(11), ***b*** 13.791(2), ***c*** 11.7236(14) Å, β 101.142(9)°, U 1374.8(3) Å^3, Z = 4, D_c 1.306 g cm^{-3}, F(000) 568, μ (Mo Kα) 0.094 mm^{-1}, graphite monochromated Mo Kα, λ = 0.71073 Å, T = 293 K. Data were collected on a Siemens P4 diffractometer, and the structure was solved by direct methods.[10] Final discrepancy factors: R = 0.066 and R_w = 0.099.

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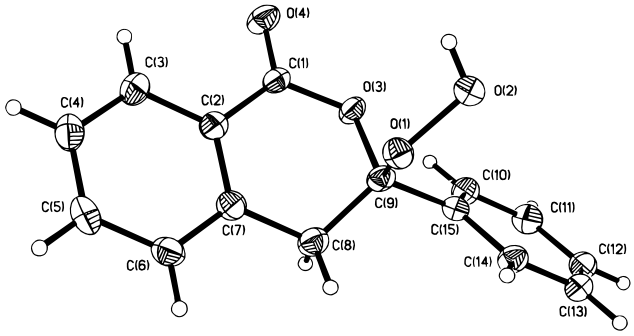
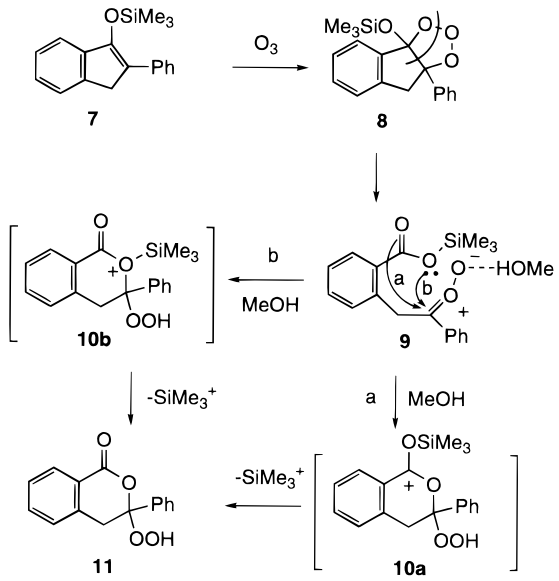


Figure 2. Crystal structure of compound **11** (ORTEP,[10] 50% probability ellipsoids for non-hydrogen atoms).

Scheme 2



cleavage to give exclusively the carbonyl oxide/carbonyl pair **3**, which readily undergoes solvent capture by methanol yielding the α-methoxyalkyl hydroperoxide **4**. Subsequent intramolecular cyclization of the hydroperoxy group on to the adjacent benzoyloxycarbonyl group produces the corresponding hemiperacetal **5** (Scheme 1).

A different type of product was obtained from the ozonolysis of 2-phenyl-3-(trimethylsiloxy)indene (**7**) under similar conditions (Scheme 2). The ^{1}H NMR spectrum of the crude product mixture was not consistent with the formation of a methanol-derived product. On subsequent purification by column chromatography on silica gel, a crystalline compound was isolated in 65% yield and shown by X-ray analysis to be 3-hydroperoxy-3-phenyl-3,4-dihydro-1*H*-2-benzopyran-1-one (**11**) (Figure 2).[7]

From the structure of the product **11**, the direction of cleavage of the primary ozonide **8** must also be highly selective, yielding exclusively the carbonyl oxide/carbonyl pair **9** (Scheme 2).[8] In addition to any solvent effects, the sterically crowded nature of intermediate **9** should favor the participation of either of the neighboring ester group oxygen atoms in an intramolecular nucleophilic attack on the electrophilic carbon of the solvated carbonyl oxide, thereby yielding the pivotal intermediates **10a,b**. Subsequent loss of the trimethylsilyl group from **10a,b** would provide the hydroperoxy lactone **11**. Although methanol was not incorporated into the observed product, its presence appears to be essential for the formation of **11** because ozonolysis of **7** in an aprotic solvent such as diethyl ether provided a complex mixture of unidentified products.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ with $SiMe_4$ as standard. 3-(Benzoyloxy)-2-phenylindene (**1**)[4] was prepared by the reported method: white powder; mp 119−120 °C (from CH_2Cl_2−hexane); ^{1}H NMR δ 3.92 (s, 2 H), 7.0−8.3 (m, 14 H); IR 1740, 1255, 1245 cm^{-1}. The ozonolysis procedures have been previously described.[9]

Caution. Because organic peroxides are potentially hazardous compounds, they must be handled with due care. Avoid exposure to strong heat or light, mechanical shock, oxidizable organic materials, or transition-metal ions. No particular difficulties were experienced in handling any of the new organic peroxides synthesized in this work using the reaction scales and procedures described below, together with the safeguard mentioned above.

Preparation of 2-Phenyl-3-(trimethylsiloxy)indene (7). 2-Phenylindanone (5 g, 24 mmol) in dry THF (100 mL) was stirred with LDA (from 26 mmol of diisopropylamine and 26 mmol of *n*-BuLi) in THF (100 mL) at −78 °C for 15 min, and then a solution of chlorotrimethylsilane (2.87 g, 26 mmol) was added dropwise. The solution was allowed to warm to room temperature and stirred for 2.5 h. After evaporation of THF under reduced pressure, hexane was added to precipitate the lithium salt. After concentration of the filtrate, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (3:97) gave indene **7** (4.2 g, 83%): white powder; mp 91−92 °C (from ethyl acetate−hexane); ^{1}H NMR δ 0.22 (s, 9 H), 3.69 (s, 2 H), 7.2−7.8 (m, 9 H); ^{13}C NMR δ 0.83, 35.96, 118.37, 121.82, 123.27, 126.09, 126.33, 126.90, 128.23, 136.06, 140.78, 142.86, 149.33. Anal. Calcd for $C_{18}H_{20}OSi$: C, 77.09; H, 7.19. Found: C, 76.91; H, 7.21.

Ozonolysis of 3-(Benzoyloxy)-2-phenylindene (1) in MeOH−CH_2Cl_2. To a solution of indene **1** (320 mg, 1.00 mmol) in MeOH−CH_2Cl_2 (15 mL, 1:2, v/v) was passed a slow stream of ozone (1.5 equiv) at −70 °C. The solvent of the reaction mixture was remove by evaporation under reduced pressure to yield an oily residue that gave ^{1}H and ^{13}C NMR spectral data consistent with 1-(benzoyloxy)-1-hydroxy-4-methoxy-4-phenyl-4,5-dihydro-1*H*-2,3-benzodioxepin (**5**): ^{1}H NMR δ 3.30 (s, 1 H), 3.35 (s, 1 H), 3.42 (s, 3 H), 4.40 (br s, 1 H, H−D exchange in D_2O), 6.7−8.2 (m, 14 H); ^{13}C NMR δ 36.66, 49.97, 108.19, 118.26, 125.66, 125.91, 126.36, 126.73, 127.28, 127.49, 127.84, 129.43, 133.68, 134.75, 135.49, 139.73, 169.85.

Alternatively, the reaction mixture was poured into ice-cold aqueous $NaHCO_3$ and extracted with ether. After the combined organic extratcs were dried (anhydrous $MgSO_4$) and concentrated under reduced pressure, the residue was crystallized from ether−hexane to give 4-Methoxy-4-phenyl-4,5-dihydro-1*H*-2,3-benzodioxepin-1-one (**6**) (130 mg, 47%): white powder; mp 91−93 °C (from ether−hexane); ^{1}H NMR δ 3.08 (d, J = 14 Hz, 1 H), 3.38 (s, 3 H), 3.68 (d, J = 14 Hz, 1 H), 6.7−8.2 (m, 9 H); ^{13}C NMR δ 45.73, 51.18, 109.79, 126.17, 128.00, 128.34, 128.43,

(7) Crystal data for (**11**): $C_{15}H_{12}O_4$, M = 256.25, colorless needles, monoclinic, space group $P2_1/n$ (alt. setting No. 14), ***a*** 7.4180(10), ***b*** 10.9760(10), ***c*** 14.844(3) Å, β 95.930(10)°, U 1202.1(3) Å^3, Z = 4, D_c 1.416 g cm^{-3}, F(000) 536, μ (Mo Kα) 0.103 mm^{-1}, graphite monochromated Mo Kα λ = 0.71073 Å, T = 160 K. Data were collected on a Siemens P4 diffractometer, and the structure was solved by direct methods.[10] Final discrepancy factors: R = 0.050 and R_w = 0.106. The authors have deposited the atomic coordinates for the crystal structures of **6** and **11** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained on request from the Director, the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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(10) SHELXTL/PC (Vers 5.03); Sheldrick, G. M.; Siemens Analytical X-ray Instruments Inc., Madison, WI.

128.86, 129.88, 130.15, 130,50, 132.78, 133.78, 172.36; IR 1750, 3400 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_4$: C, 70.40; H, 5.14. Found: C, 70.49; H, 5.16.

Ozonolysis of 2-Phenyl-3-(trimethylsiloxy)indene (7) in MeOH−Ether. To a solution of **7** (280 mg, 2.0 mmol) in methanol−ether (15 mL, 1:2 v/v) was passed a slow stream of ozone (1.5 equiv) at −70 °C. Then, the reaction mixture was poured into ice-cold aqueous $NaHCO_3$ and extracted with ether. After the combined organic extracts were dried (anhydrous $MgSO_4$) and concentrated under reduce pressure, the residue was separated by column chromatography on silica gel. Elution with ether−hexane (1:3, v/v) gave 3-Hydroperoxy-3-phenyl-3,4-dihydro-1*H*-2-benzopyran-1-one (**11**) (165 mg, 65%): white powder; mp 133−135 °C (from ethyl acetate−hexane); ^{1}H NMR δ 3.50 (d, J = 17 Hz, 1 H), 3.64 (d, J = 17 Hz, 1 H), 7.1−8.1 (m, 9 H), 9.20 (br s, 1 H); ^{13}C NMR δ 37.23, 108.99, 123.90, 125.89, 127.55, 127.78, 128.61, 129.31, 130.26, 134.50, 136.24, 137.59, 164.20; IR 1720, 3300 cm^{-1}. Anal. Calcd for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72. Found: C, 70.09; H, 4.74.

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Supporting Information Available: Tables of data derived from the X-ray crystallographic analyses of compounds **6** and **11**.

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