Synthesis of 1,2-Benzoquinones by the Oxidation of 1,4-Benzodioxins by Peroxide Derivatives

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The oxidation reaction of 1,4-benzodioxin **1** by *m*-chloroperbenzoic acid (*m*-CPBA) and *t*-butyl hydroperoxide (*t*-BHP) are reported. 1,2-Benzoquinone **2** was given in moderate yields by the *m*-CPBA oxidation of 1,4-benzodioxin **1**, while 1,2-benzoquinone **2** was predominantly formed by *t*-BHP oxidation.

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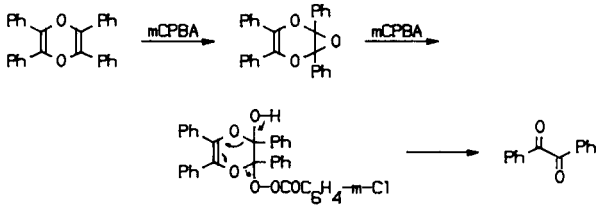
Many inorganic salts are widely used as oxidants for the synthesis of 1,2-benzoquinones [1]. However, since these oxidation with inorganic oxidants require severe reaction conditions, many 1,2-benzoquinones such as 2,3-naphthoquinone [2] have never been synthesized due to their great reactivity toward decomposition and polymerization. Therefore, a new methodology under mild conditions was required for the synthesis of such labile 1,2-benzoquinones. Recently, we indicated that 1,2-benzoquinones could be obtained by the ozonolysis of 1,4-benzodioxins followed by photolysis of the resulting ozonides under mild conditions [3]. As the extension of this work, we investigated the oxidation of 1,4-benzodioxins by peroxide derivatives.

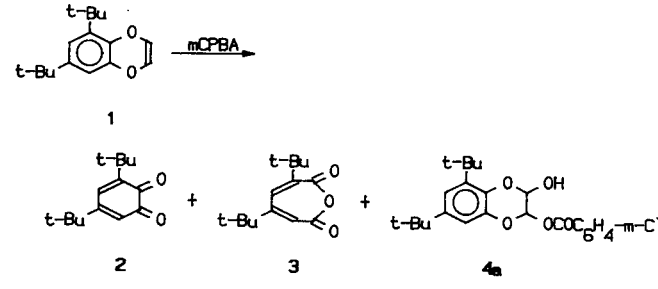
In 1970, Temple reported that excess amount of hydroperoxide caused the oxidative decomposition of epoxides to afford α-dicarbonyl compounds [4]. Further, according to the paper of Lopez, oxidation of 1,4-dioxins by *m*-chloroperbenzoic acid (*m*-CPBA) afforded α-dicarbonyl compounds through a similar oxidative decomposition of epoxides (Scheme 1) [5]. Since 1,2-benzoquinones are the α-dicarbonyl compounds fused to a benzene ring, the analogous peroxide oxidation of 1,4-benzodioxins were expected to afford 1,2-benzoquinones. We wish to report here the results of the oxidation reactions of 1,4-benzodioxins with *m*-chloroperbenzoic acid (*m*-CPBA) and *t*-butyl hydroperoxide (*t*-BHP).

Scheme 1



1,4-Benzodioxin **1** was prepared by the modified method of the reported procedures [6,7]. When 1,4-benzodioxin **1** was treated with two equivalents of *m*-chloroperbenzoic acid (*m*-CPBA) in dichloromethane, 1,2-benzoquinone **2** was obtained along with muconic anhydride **3** and 1,4-benzodioxan-2,3-diol *m*-chlorobenzoate **4a** in 11, 15, and 65% yield, respectively (Scheme 2). However, the formation of the desired 1,2-benzoquinones **2** was obtained in less satisfactory yield, and the main product was the undesired *m*-chlorobenzoate **4a**. In order to improve the yield of 1,2-benzoquinone **2**, the reaction mechanism of the formations of the products was further investigated.

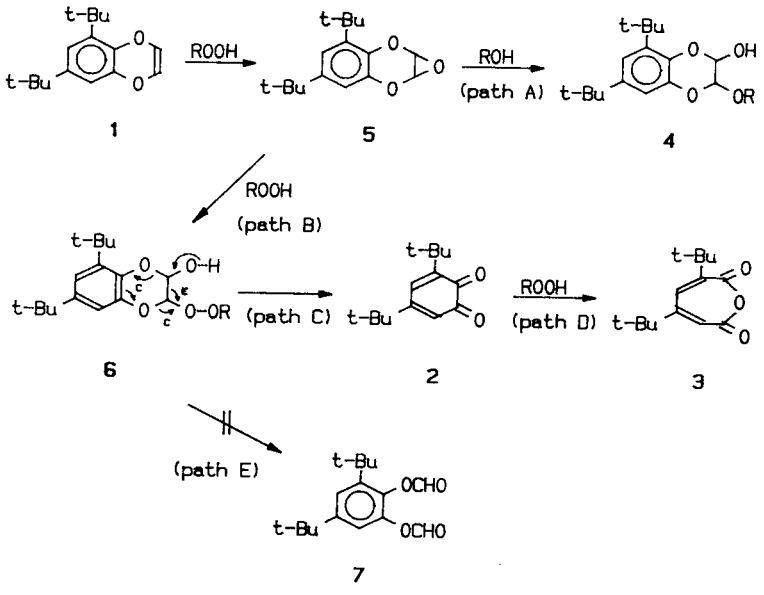
Scheme 2



The mechanism was speculated as shown in Scheme 3 (R = *m*-ClC_6H_4CO). One equivalent of *m*-CPBA reacted with 1,4-benzodioxin **1** to afford 1,4-benzodioxan-2,3-epoxide **5**. Then two pathways competed dependent on the reactivity of the epoxide **5** toward nucleophiles [8]. Since *m*-chlorobenzoic acid has larger nucleophilicity than *m*-CPBA, the epoxide **5** was attacked mainly by *m*-chlorobenzoic acid to give *m*-chlorobenzoate **4a** as a main product (path A). In contrast, a minor nucleophilic addition by *m*-CPBA (path B) affords the perester of 1,4-benzodioxan-2,3-diol **6a** (R = *m*-ClC_6H_4CO), which readily decomposed by the cleavage of the C-O bond on the dioxan ring to afford 1,2-benzoquinone **2** (path C). Unfortunately, since *m*-CPBA is reactive toward carbonyl moiety, muconic anhydride **3** was formed through Baeyer-Villiger oxidation of 1,2-benzoquinone **2** (path D) [9]. By the absence of diformylcatechol **7** in the reaction mixture, the cleavage of the C-C bond on the dioxan ring of the perester **6a** was excluded (path E).

From this speculation, it was indicated that the formation of 1,2-benzoquinone **2** was largely disturbed by the presence of an active nucleophile such as *m*-chlorobenzoic acid. Actually, when 1,4-benzodioxin **1** was treated with *m*-CPBA in the presence of methanol, 2-methoxy-1,4-

Scheme 3



benzodioxan-3-ol **8** was obtained along with 1,2-benzoquinone **2** and muconic anhydride **3** in 57, 20, and 2% yield, respectively. Therefore, the suppression of the nucleophilicity of *m*-chlorobenzoic acid should improve the yield of 1,2-benzoquinone **2**.

For this purpose, reactions were carried out under several conditions as summarized in Table 1. In dichloromethane-water mixture, the reactivity of *m*-chlorobenzoic acid was not suppressed and no change was observed in the ratio of the yields of the products (entry b, c). Under strongly basic conditions, the oxidation reaction was disturbed completely by the decomposition of *m*-CPBA (entry d). Also, under non-aqueous basic conditions, the formation of *m*-chlorobenzoate **4a** was still predominant, although further oxidation of 1,2-benzoquinone **2** to muconic anhydride **3** was suppressed (entry e).

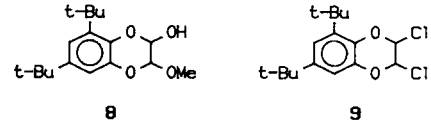
Table 1

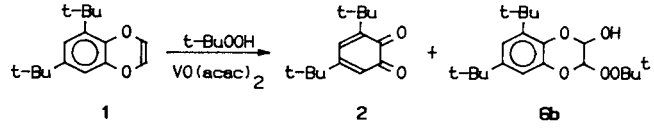
Oxidation of 1,4-benzodioxin **1** by *m*-CPBA

Entry	Conditions	Yields of the Products (%) [a]			
		2	**3**	**4a**	**1**
a	CH_2Cl_2	11	15	65	0
b	CH_2Cl_2/phosphate buffer (*p*H 6.8)	10	12	62	0
c	CH_2Cl_2/sat K_2CO_3	15	10	72	0
d	CH_2Cl_2/aq KOH (50%)	0	0	0	>95
e	CH_2Cl_2/K_2CO_3	24	0	71	0
f	CH_2Cl_2/K_2CO_3/TEBACl [b]	30	4	0	0

[a] The yields are those of isolated products. [b] Triethylbenzylammonium chloride.

Scheme 4





In contrast, in the presence of a phase transfer catalyst, *m*-chlorobenzoic acid was less nucleophilic and the formation of *m*-chlorobenzoate **4a** was completely suppressed (entry f). However, the main product was found to be 2,3-dichloro-1,4-benzodioxan **9**. This anomalous product **9** was speculated to be formed through the reaction of 1,4-benzodioxin **1** with chlorine, which was generated in the reaction of *m*-CPBA with chloride anion.

After all, it was found that the formation of 1,2-benzoquinone **2** was largely suppressed due to the high nucleophilicity of *m*-chlorobenzoic acid, which is a by-product in the epoxidation with *m*-CPBA. Therefore, oxidants which are converted to less reactive compounds are required in order to synthesize 1,2-benzoquinones by the oxidation of 1,4-benzodioxins. Meanwhile, *t*-butyl hydroperoxide (*t*-BHP) generates less nucleophilic *t*-butyl alcohol as the by-product in the oxidation of olefins. Furthermore, *t*-BHP

was reported to epoxidize olefins with vanadium complexes, which enhance the electrophilicity of *t*-BHP [10]. Therefore, *t*-BHP-vanadium catalyst system was expected to be a good oxidant for the preparation of 1,2-benzoquinones. When 1,4-benzodioxin **1** was treated with *t*-BHP in the presence of a catalytic amount of vanadium(IV) oxyacetylacetonate ($VO(acac)_2$) in benzene for 30 minutes, the desired 1,2-benzoquinone **2** was obtained in 23% yield along with 2-*t*-butylperoxy-1,4-benzodioxan-3-ol *6b* (R = *t*-Bu) in 66% yield (Scheme 4). In this case, the addition of *t*-BHP to the epoxide **5** occurred exclusively, and the addition product of *t*-butyl alcohol on the epoxide **5** could not be detected.

Since the peroxide **6b** was a precursor of 1,2-benzoquinone **2**, the peroxide **6b** was treated with potassium carbonate in benzene to give 1,2-benzoquinone **2** in 78% yield. Furthermore, when 1,4-benzodioxin **1** was oxidized by *t*-BHP-vanadium catalyst system followed by the treatment with potassium carbonate without isolation, 1,2-benzoquinone **2** was obtained in 68% yield. On the contrary, oxidation of 1,4-benzodioxin **1** by *t*-BHP did not proceed in the presence of potassium carbonate and 1,4-benzodioxin **1** was recovered completely, because the formation of the active species for oxidation was presumably disturbed under basic conditions.

It was concluded that the oxidation of 1,4-benzodioxin **1** by *m*-CPBA afforded 1,2-benzoquinone **2** in moderate yields. On the contrary, *t*-BHP was found to be an effective oxidant for the formation of 1,2-benzoquinone **2** from 1,4-benzodioxin **1**, because of the suppression of the formation of nucleophilic by-product.

EXPERIMENTAL

Melting points were measured on Yanagimoto Micro Melting Point Apparatus, and are uncorrected. The ir spectra were measured on JASCO IRA-1 Infrared Spectrophotometer. The ^{1}H- and ^{13}C-nmr spectra were measured on JEOL FX-100 (100 MHz) and FX-90Q (90 MHz) Spectrometer, respectively, using tetramethylsilane as an internal standard.

5,7-Di-*t*-butyl-1,4-benzodioxan.

To a solution of 3,5-di-*t*-butylcatechol (30 mmoles) and 1,2-dibromoethane (60 mmoles) in 50 ml of ethylene glycol, anhydrous potassium carbonate (63 mmoles) was added and the mixture was heated at 120° for 4 hours under an argon atmosphere. After heating, the organic material was extracted with dichloromethane, washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the resulting residue was purified by chromatography on silica gel with *n*-hexane-benzene (5:1) as an eluent to give the product in 86% yield, bp 120-125°/4 mm Hg; ir (potassium bromide): ν max 1595, 1495 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.27 (s, 9H), 1.37 (s, 9H), 4.21 (s, 4H), 6.77 (ABq, 1H, J = 2.4 Hz), 6.88 (ABq, 1H, J = 2.4 Hz) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.8 (q), 31.5 (q), 34.4 (s), 35.1 (s), 63.5 (t), 64.1 (t), 112.4 (d), 115.7 (d), 137.9 (s), 140.0 (s), 143.0 (s) ppm.

Anal. Calcd. for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.54; H, 9.82.

2,3-Dibromo-5,7-di-*t*-butyl-1,4-benzodioxan.

The mixture of 5,7-di-*t*-butyl-1,4-benzodioxan (5 mmoles), *N*-bromosuccinimide (12 mmoles), and AIBN (20 mg) in 60 ml of carbon tetrachloride was refluxed for 12 hours under argon atmosphere. After heating, the yellow precipitate was filtered off and the organic solution was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the resulting residue was purified by chromatography on silica gel with *n*-hexane-benzene (3:1) as an eluent to give the product in 86% yield, mp 125-126° (from ethanol); ir (potassium bromide): ν max 1595, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.29 (s, 9H), 1.38 (s, 9H), 6.72 (s, 1H), 6.78 (s, 1H), 6.86 (d, 1H, J = 2.4 Hz), 7.10 (1H, d, J = 2.4 Hz) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.8 (q), 31.3 (q), 34.6 (s), 34.9 (s), 77.4 (d), 78.1 (d), 113.2 (d), 119.1 (d), 133.2 (s), 136.7 (s), 139.0 (s), 146.7 (s) ppm.

Anal. Calcd. for $C_{16}H_{22}Br_2O_2$: C, 47.31; H, 5.45. Found: C, 47.59; H, 5.58.

5,7-Di-*t*-butyl-1,4-benzodioxin (**1**).

The mixture of 2,3-dibromo-5,7-di-*t*-butyl-1,4-benzodioxan (5 mmoles) and sodium iodide (25 mmoles) in 50 ml of acetone was refluxed for 2 hours under argon atmosphere. After heating, the organic material was extracted with dichloromethane, washed with aqueous sodium thiosulfate solution and dried over anhydrous magnesium sulfate. After removal of the solvent, the resulting residue was purified by chromatography on silica gel with *n*-hexane as an eluent to give **1** in 92% yield, mp 38-40° (from ethanol); ir (film): ν max 1700, 1670, 1595, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.24 (s, 9H), 1.31 (s, 9H), 5.86 (d, 1H, J = 4.9 Hz), 5.90, (d, 1H, J = 4.9 Hz), 6.53 (d, 1H, J = 2.4 Hz), 6.84 (d, 1H, J = 2.4 Hz) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.7 (q), 31.3 (q), 34.4 (s), 34.8 (s), 111.7 (d), 118.2 (d), 126.4 (d), 126.9 (d), 136.7 (s), 139.0 (s), 142.5 (s), 145.8 (s) ppm.

Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.00; H, 9.00. Found: C, 77.81; H, 9.10.

General Procedure for the Oxidation of 5,7-Di-*t*-butyl-1,4-benzodioxin **1** by *m*-CPBA.

To the solution of 1,4-benzodioxin **1** (2 mmoles) in 20 ml of distilled dichloromethane, the solution of *m*-CPBA (4.5 mmoles) in 20 ml of distilled dichloromethane was added dropwise at 0°. After stirring for 3 hours at room temperature, the organic solution was washed with aqueous sodium hydrogen carbonate solution and dried over anhydrous magnesium sulfate. After removal of the solvent, the products were purified by chromatography on silica gel with *n*-hexane-ethyl acetate-chloroform (6:1:1) as an eluent. 3,5-Di-*t*-butyl-1,2-benzoquinone (**2**) was identified by the comparison with an authentic sample [11].

2,4-Di-*t*-butyl-muconic Anhydride (**3**).

This compound showed mp 108-109° (from *n*-hexane); ir (chloroform): ν max 1780, 1730, 1615, 1600, 1490, 1485 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.17 (s, 9H), 1.28 (s, 9H), 6.15 (d, 1H, J = 1.5 Hz), 6.46 (d, 1H, J = 1.5 Hz) ppm; ^{13}C-nmr (deuteriochloroform): δ 28.7 (q), 29.2 (q), 36.6 (s), 36.8 (s), 115.8 (d), 124.2 (d), 148.4 (s), 159.3 (s), 160.6 (s), 162.1 (s) ppm.

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.15; H, 8.53. Found: C, 71.11; H, 8.58.

2-(3-Chlorobenzoyloxy)-5,7-di-*t*-butyl-1,4-dioxan-3-ol (**4a**).

This compound showed mp 165-166° (from chloroform-*n*-hexane); ir (chloroform): ν max 3550, 3450, 1730, 1595, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.26 and 1.28 (2 singlets, 9H), 1.36 and 1.46 (2 singlets, 9H), 4.7 (broad, 1H), 5.6 (broad, 1H), 6.5-6.6 (m, 1H), 6.9-7.1 (m, 2H), 7.2-7.6 (m, 2H), 7.8-8.0 (m, 2H) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.8 (q), 31.4 (q), 34.5 (s), 35.1 (s), 87.1 (d), 87.3 (d), 87.6 (d), 88.0 (d), 112.7 (d), 113.0 (d), 117.0 (d), 117.5 (d), 128.1 (d), 129.8 (d), 129.9 (d), 130.7 (d), 133.7 (d), 134.6 (s), 138.2 (s), 138.4 (s), 139.2 (s), 144.3 (s), 145.0 (s), 163.8 (s), 163.9 (s) ppm.

Anal. Calcd. for $C_{23}H_{27}ClO_5$: C, 65.94; H, 6.49. Found: C, 65.67; H, 6.58.

5,7-Di-*t*-butyl-2-methoxy-1,4-benzodioxan-3-ol (**8**).

This compound showed bp 160-165°/10^{-4} mm Hg; ir (chloroform): ν max 1595, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.27 and 1.28 (2 singlets, 9H), 1.39 and 1.43 (2 singlets, 9H), 3.5 (broad, 1H), 3.48 and 3.53 (2 singlets, 3H), 4.90 (d, 1/2H, J = 1.0 Hz), 4.99 (d, 1/2H, J = 1.5 Hz),

5.33 (1H, broad t, J = 7.3 Hz), 6.7-6.8 (m, 1H), 6.9-7.0 (1H, m) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.9 (q), 30.0 (q), 31.5 (q), 34.4 (s), 35.0 (s), 35.2 (s), 55.8 (q), 56.7 (q), 87.8 (d), 87.9 (d), 95.1 (d), 95.5 (d), 112.8 (d), 113.1 (d), 117.0 (d), 117.2 (d), 137.9 (s), 138.1 (s), 138.9 (s), 139.3 (s), 144.0 (s), 144.3 (s) ppm.

Anal. Calcd. for $C_{17}H_{26}O_4$: C, 69.35; H, 8.90. Found: C, 69.52; H, 9.01.

5,7-Di-*t*-Butyl-2,3-dichloro-1,4-benzodioxan (**9**).

This compound showed mp 116-117° (from chloroform-*n*-hexane); ir (chloroform): ν max 1590, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.27 and 1.29 (2 singlets, 9H), 1.38 and 1.39 (2 singlets, 9H), 6.08 (d, 1H, J = 7.3 Hz), 6.27 (d, 1H, J = 7.3 Hz), 6.88 (d, 1H, J = 2.4 Hz), 7.04 (dd, 1H, J = 2.4 and 5.4 Hz) ppm; ^{13}C-nmr (deuteriochloroform): δ 29.89 (q), 31.4 (q), 34.6 (s), 35.1 (s), 84.2 (d), 84.4 (d), 85.6 (d), 84.8 (d), 112.7 (d), 113.2 (d), 118.2 (d), 118.8 (d), 135.4 (s), 138.8 (s), 139.1 (s), 139.8 (s), 146.1 (s), 146.4 (s) ppm.

Anal. Calcd. for $C_{16}H_{22}Cl_2O_2$: C, 60.57; H, 6.99. Found: C, 60.31; H, 6.84.

General Procedure for the Oxidation of 5,7-Di-*t*-butyl-1,4-benzodioxin **1** by *t*-BHP.

To the mixture of 1,4-benzodioxin **1** (2 mmoles) and vanadium(IV) oxyacetylacetonate (50 mg) in 20 ml of distilled benzene, the solution of *t*-butyl hydroperoxide (20 mmoles) in 20 ml of distilled benzene was added dropwise at room temperature. After stirring for 30 minutes, the organic solution was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent, the products were purified by chromatography on silica gel with *n*-hexane-ethyl acetate-chloroform (10:1:1) as an eluent.

2-*t*-Butylperoxy-5,7-di-*t*-butyl-1,4-benzodioxan-3-ol (**6b**).

This compound showed bp >160°/10^{-4} mm Hg dec; ir (chloroform): ν max 1600, 1495 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 1.16 and 1.19 (2 singlets, 9H), 1.27 (s, 9H), 1.38 and 1.44 (2 singlets, 9H), 3.3 (broad, 1H), 5.5 (m, 2H), 6.8-7.0 (m, 2H) ppm; ^{13}C-nmr (deuteriochloroform): δ 26.2 (q), 26.3 (q), 29.9 (q), 30.0 (q), 31.5 (q), 34.4 (s), 35.0 (s), 35.2 (s), 86.4 (d), 86.5 (d), 95.8 (d), 96.2 (d), 112.8 (d), 113.2 (d), 117.0 (d), 135.6 (s), 135.9 (s), 138.2 (s), 138.3 (s), 139.2 (s), 139.4 (s), 144.2 (s), 144.5 (s) ppm.

Anal. Calcd. for $C_{20}H_{32}O_5$: C, 68.15; H, 9.15. Found: C, 68.02; H, 9.23.

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