EFFICIENT PHENOLIC OXIDATIONS TO CONSTRUCT ORTHO-SPIROLACTONE STRUCTURES USING OXO-BRIDGED HYPERVALENT IODINE(III) COMPOUND

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Abstract – The intramolecular ortho-spirocyclization of naphthols 1 bearing carboxylic acid moieties as internal nucleophiles using hypervalent iodine reagents is described. The use of the μ-oxo-bridged hypervalent iodine(III) compound is remarkably effective for this transformation, and spirolactones 2 were obtained in good to excellent yields using the μ-oxo-bis[trifluoroacetato-(phenyl)iodine] 4 [PhI(OCOCF₃)O(OCOCF₃)IPh].

This paper is dedicated to Professor Albert Eschenmoser on the occasion of his 85th birthday.

INTRODUCTION

Hypervalent iodine(III) reagents, such as PhI(OAc)₂ [phenyliodine diacetate, PIDA] and PhI(OCOCF₃)₂ [phenyliodine bis(trifluoroacetate), PIFA], are organo-oxidants having reactivities similar to those of the highly toxic heavy-metal oxidants, and are now recognized as useful tool for performing various environmentally benign oxidations.¹ Over the past 25 years, we have been engaged in the development of the hypervalent iodine(III)-mediated oxidation of phenol derivatives, and established its application for the synthesis of natural products.² In particular, for the efficient constructions of para-spirodieneone structures, we have previously demonstrated the PIDA- and PIFA-mediated intramolecular oxidative
cyclizations of phenols and their derivatives having pendent nucleophiles at the para-positions.²a In a continuation of our study on this theme,³ we now report the intramolecular ortho-spirocyclization of naphthols 1 bearing carboxylic acid moieties as the nucleophilic side-chains (Scheme 1).

![Scheme 1. ortho-Spirocyclization of naphthols 1 using hypervalent iodine(III) reagents.](image)

**RESULTS AND DISCUSSION**

A number of natural products having spirocyclic backbones exist, and most of them are attractive synthetic targets for organic chemists. In particular, ortho-spirolactone structures would be potentially useful subunits as precursors of bioactive compounds, such as lactonamycin and arnotin II.⁴ For the purpose of developing the efficient synthesis of these ortho-spirolactone structures, we surveyed a suitable reaction condition, selecting naphthol carboxylic acid 1a as the model case (Table 1). As shown in entries 1 and 2, all preliminary experiments based on our previous conditions for the para-spirocycliztions of phenols using PIDA and PIFA²a afforded the desired ortho-spirolactone product 2a in low yields only. Particularly, formation of the six-membered aryl lactone 3a, a dehydrative condensation product, occurred as an undesired background reaction when using PIFA in CH₂Cl₂ at room temperature (entry 2).

**Table 1. ortho-Spirocyclization of 1a using hypervalent iodine(III) reagents**

<table>
<thead>
<tr>
<th>entry</th>
<th>I(III)</th>
<th>solvent</th>
<th>time</th>
<th>2a</th>
<th>3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhI(OAc)₂ (PIDA)</td>
<td>CH₂Cl₂</td>
<td>1 h</td>
<td>11%</td>
<td>n.d.</td>
</tr>
<tr>
<td>2</td>
<td>PhI(OCOCF₃)₂ (PIFA)</td>
<td>CH₂Cl₂</td>
<td>2 h</td>
<td>17%</td>
<td>45%</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>CH₂Cl₂</td>
<td>1 h</td>
<td>47%</td>
<td>n.d.</td>
</tr>
<tr>
<td>4</td>
<td>//</td>
<td>MeCN</td>
<td>1 h</td>
<td>58%</td>
<td>n.d.</td>
</tr>
<tr>
<td>5ᵃ</td>
<td>//</td>
<td>MeCN</td>
<td>1 h</td>
<td>73%</td>
<td>n.d.</td>
</tr>
</tbody>
</table>

ᵃReaction was performed at 0 °C.
Extensive examinations using PIDA and PIFA under the standard conditions did not produce any good result. In marked contrast, we found that a $\mu$-oxo-bridged hypervalent iodine(III) reagent 4 (Figure 1) is exceptionally effective for allowing the oxidative ortho-spirocyclization of 1a leading to 2a as shown in entry 3. Among the employed iodine reagents, reagent 4 afforded a very promising result. We then screened several solvents and conditions using 4, and found that the use of MeCN at low temperature was remarkably effective for this transformation (entry 5). The use of fluoroalcohols such as (CF$_3$)$_2$CHOH or CF$_3$CH$_2$OH, was not effective in this case and treatment of PIDA, PIFA, and the compound 4 in (CF$_3$)$_2$CHOH did not show any distinct improvement of yield compared with the optimized reaction condition in entry 5.

![Figure 1. Hypervalent iodine(III) reagents for phenolic oxidations.](image)

The $\mu$-oxo-bridged hypervalent iodine(III) reagent 4 is a stable white powder and soluble in various organic solvents, such as CH$_2$Cl$_2$ and MeCN. The spirolactone 2a was obtained using the following experimental protocol; a solution of 1a (1.0 equiv) in MeCN was dropwise added to a stirred solution of 4 (0.55 equiv) in MeCN. The use of a half equivalent of 4 is enough to perform the reaction as the reagent has two reactive iodine(III) atoms in the molecule. The initially clear solution of the reaction mixture became slightly yellow as the reaction proceeded. After checking for the disappearance of the phenol 1a by TLC, the mixture was quenched with saturated NaHCO$_3$ aq. and extracted several times with CH$_2$Cl$_2$. The organic layers were combined and evaporated in vacuo. From the residue, the co-product iodobenzene, which was produced from reagent 4, was removed by column chromatography, giving the spirocyclized lactone 2a in 73% yield.

To confirm the high reactivity of the $\mu$-oxo-bridged hypervalent iodine(III) reagent 4, we further examined the scope of the substrates in the reactions. Selected examples are shown in Table 2. Electron-rich alkyl naphthols, such as 1b and 1c, afforded the corresponding spirolactones 2b and 2c in moderate yields (entries 2 and 3). On the other hand, naphthols bearing weak electron-withdrawing groups gave products 2d-g in good to excellent yields (entries 4-7). Oxygen-atom containing naphthol 1h was also applicable for the reaction (entry 8). Furthermore, the 2-naphthol derivatives also provided the expected spirolactones 2i and 2j (entries 9 and 10), respectively. These results clearly show the utility of
Table 2. *ortho*-Spirocyclization of various naphthols 1 using a hypervalent iodine(III) reagent 4<sup>a</sup>

<table>
<thead>
<tr>
<th>entry</th>
<th>Substrate</th>
<th>product</th>
<th>yield&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R = H (1a)</td>
<td>(2a)</td>
<td>73%</td>
</tr>
<tr>
<td>2</td>
<td>R = Et (1b)</td>
<td>(2b)</td>
<td>52%</td>
</tr>
<tr>
<td>3</td>
<td>R = Cy (1c)</td>
<td>(2c)</td>
<td>55%</td>
</tr>
<tr>
<td>4</td>
<td>R = Ph (1d)</td>
<td>(2d)</td>
<td>79%</td>
</tr>
<tr>
<td>5</td>
<td>R = Bn (1e)</td>
<td>(2e)</td>
<td>80%</td>
</tr>
<tr>
<td>6</td>
<td>R = Br (1f)</td>
<td>(2f)</td>
<td>93%</td>
</tr>
<tr>
<td>7</td>
<td>R = Bz (1g)</td>
<td>(2g)</td>
<td>99%</td>
</tr>
<tr>
<td>8</td>
<td>R = H (1h)</td>
<td>(2h)</td>
<td>87%</td>
</tr>
<tr>
<td>9</td>
<td>R = Br (1i)</td>
<td>(2i)</td>
<td>63%</td>
</tr>
<tr>
<td>10</td>
<td>R = Bz (1j)</td>
<td>(2j)</td>
<td>82%</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reactions were performed using 4 (0.55 equiv.) in MeCN (0.05 M) at 0 °C for 1 h unless otherwise noted.

<sup>b</sup> Isolated yield after purification.
the present system using the μ-oxo-bridged hypervalent iodine(III) reagent 4 for the ortho-spirocyclization of the phenol derivatives. Finally, we demonstrated an example aiming at application of the method to natural product synthesis although this project is still currently underway. That is, the reaction system is applied to substrate 1k to provide a tetracyclic compound 2k containing the model ABCD rings of lactonamycin (Eq. 1).

Although the excellent role of reagent 4 over other iodine(III) reagents in the reactions remains unclear, we tentatively presume that its high reactivity would be derived from the unique μ-oxo-bridged structure. Previous report on the crystal structure of 4 revealed that the two types of I-O bond distances of the μ-oxo-bridged I-O and another I-OCOCF₃ are quite different. Indeed, the I-O distance of the latter bond is remarkably longer than that of the former, which seems to facilitate the dissociation of the trifluoroacetoxo anion to produce the highly electrophilic iodine(III) center by the trans effect of the μ-oxo-bridged oxygen atom, resulting in the enhancement of the reactivity of 4 toward nucleophiles during the ligand exchange step. We have confirmed the high reactivities of μ-oxo-bridged iodine(III) reagent 4 in many other reactions over the classical iodine(III) reagents, such as PIDA and PIFA.

In summary, we have developed an efficient oxidative ortho-spirocyclizing reaction by the appropriate choice of the highly reactive reagent, μ-oxo-bridged hypervalent iodine(III) compound 4. The intriguing feature of the present transformation is the easy availability of the various ortho-spirolactones 2 from the readily prepared naphthol carboxylic acids 1. The resulting five-membered spirolactones 2 would be promising intermediates for the syntheses of biologically active natural products. We are currently studying its synthetic application for the construction of some natural products as well as the design of new iodine reagents having the unique μ-oxo-bridged structures suitable for these types of transformations.

EXPERIMENTAL

Melting points (mp) are uncorrected. All ¹H and ¹³C-NMR spectra of the products were measured in CDCl₃ using tetramethylsilane (δ 0.00 for ¹H and ¹³C) as an internal standard. Data are reported as
follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a Hitachi 270-50 spectrometer; absorptions are reported in reciprocal centimeters. The high resolution mass spectra and elemental analysis were performed by the Elemental Analysis Section of Osaka University. Flash column chromatography was performed with SiO$_2$ (Merck Silica Gel 60 (230-400 mesh)).

**Preparation of μ-oxo-bridged hypervalent iodine(III) reagent 4**

μ-Oxo-bridged hypervalent iodine(III) reagent 4 was prepared according to the literature procedure.$^5$

**Synthesis of naphthol carboxylic acids 1**

1a was prepared by hydrolysis of 3,4-dihydro-2H-naphtho[1,2-b]pyran-2-one$^8$ under basic conditions. Other naphthol carboxylic acids (1b-1j) were obtained from the corresponding naphthols by similar procedures.$^9$ Tricyclic 1k was synthesized according to the reported method.$^{4a}$

**General procedure for the experiments in Table 2** (**ortho-spirolactonization**)

To a stirred solution of μ-oxo-bridged hypervalent iodine(III) reagent 4 (35.8 mg, 0.11 x 1/2 mmol) in MeCN (1.0 mL) a solution of 3-(1-hydroxy-2-naphthyl)propionic acid 1a (21.6 mg, 0.10 mmol) in MeCN (1.0 mL) was added dropwise at 0 °C. The reaction mixture was stirred for 1 h at the same temperature. After the reaction completion, saturated NaHCO$_3$ aq. was added to the mixture, and it was then extracted with CH$_2$Cl$_2$. The combined organic layers were washed with brine and dried over anhydrous Na$_2$SO$_4$. After removal of the solvents, the residue was subjected to column chromatography on silica-gel (eluents: n-hexane/AcOEt = 2/1) to give 2a (15.6 mg, 0.073 mmol) in 73% yield.

**3,4-Dihydrospiro[2H-furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2a)**

White powder; mp 104-105 °C; IR (KBr, cm$^{-1}$): 1788, 1693, 1597, 1481, 1454, 1323, 1296, 1178, 1123, 1032, 930, 787, 696; $^1$H-NMR (300 MHz, CDCl$_3$): 2.13-2.25 (m, 1H), 2.39-2.47 (m, 1H), 2.55-2.65 (m, 1H), 2.85-2.98 (m, 1H), 6.21 (d, $J$ = 9.9 Hz, 1H), 6.66 (d, $J$ = 9.9 Hz, 1H), 7.26 (d, $J$ = 7.2 Hz, 1H), 7.41 (t, $J$ = 7.5 Hz, 1H), 7.64 (t, $J$ = 7.5 Hz, 1H), 8.02 (d, $J$ = 7.8 Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.4, 31.0, 83.4, 127.1, 127.5, 127.8, 127.9, 128.8, 132.1, 135.6, 136.7, 176.5, 196.5; HRMS (FAB) calcd for C$_{13}$H$_{11}$O$_3$ (M$^+$ + H): 215.0708, found: 215.0694.

**4’-Ethyl-3,4-dihydrospiro[2H-furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2b)**
White powder; mp 96-97 °C; IR (KBr, cm⁻¹): 2968, 2937, 2878, 1787, 1597, 1452, 1294, 1211, 1175, 1032, 931, 849, 750, 707; ¹H-NMR (300 MHz, CDCl₃): 1.26 (t, J = 7.2 Hz, 3H), 2.13-2.22 (m, 1H), 2.36-2.45 (m, 1H), 2.54-2.64 (m, 3H), 2.82-2.96 (m, 1H), 6.00 (s, 1H), 7.42 (t, J = 7.5 Hz, 1H), 7.46 (d, J = 8.1 Hz, 1H), 7.68 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 8.05 (dd, J = 7.8 Hz, 1.5 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): 12.2, 24.8, 26.7, 31.4, 83.7, 124.2, 127.0, 127.3, 127.8, 128.4, 135.4, 137.3, 138.1, 176.5, 196.8; HRMS (EI) calcd for C₁₂H₁₄O₃ (M⁺): 242.0943, found: 242.0941.

4’-Cyclohexyl-3,4-dihydrospiro[furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2c)
White powder; mp 151-152 °C; IR (KBr, cm⁻¹): 2928, 2853, 1789, 1693, 1593, 1450, 1294, 1175, 1034, 853, 712; ¹H-NMR (300 MHz, CDCl₃): 1.21-1.51 (m, 5H), 1.75-2.13 (m, 5H), 2.16-2.20 (m, 1H), 2.36-2.44 (m, 1H), 2.53-2.65 (m, 2H), 2.80-2.92 (m, 1H), 5.97 (s, 1H), 7.40 (t, J = 7.2 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.67 (dd, J = 7.8 Hz, 1.5 Hz, 1H), 8.04 (dd, J = 7.5 Hz, 1.5 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): 26.2, 26.7, 31.5, 32.5, 32.8, 38.5, 83.9, 124.0, 125.9, 127.7, 128.1, 128.2, 135.3, 137.0, 141.8, 176.5, 196.9; HRMS (FAB) calcd for C₁₉H₂₁O₃ (M⁺+ H): 297.1412, found: 297.1505.

3,4-Dihydro-4’-phenylspiro[furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2d)
White powder; mp 172-174 °C; IR (KBr, cm⁻¹): 3554, 3059, 3032, 2982, 2930, 2253, 1965, 1944, 1788, 1769, 1745, 1682, 1643, 1593, 1566, 1493, 1479, 1454, 1443; ¹H-NMR (300 MHz, CDCl₃): 2.21-2.33 (m, 1H), 2.48-2.67 (m, 2H), 2.85-2.96 (m, 1H), 6.12 (s, 1H), 7.15 (d, J = 7.7 Hz, 1H), 7.34-7.35 (m, 2H), 7.40-7.44 (m, 4H) 7.55 (t, J = 7.4 Hz, 1H), 8.05 (d, J = 7.4 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): 26.8, 31.5, 83.7, 127.2, 127.4, 128.0, 128.3, 128.5, 128.8, 130.4, 135.2, 137.2, 137.4, 139.7, 187.2, 196.2; HRMS (EI) calcd for C₁₉H₁₄O₃ (M⁺): 290.0943, found: 290.0960.

3,4-Dihydro-4’-(phenylmethyl)spiro[furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2e)
White powder; mp 159-160 °C; IR (KBr, cm⁻¹): 3061, 3028, 2970, 1963, 1597, 1495, 1452, 1294, 1211, 1172, 1032, 930, 735, 700, 654; ¹H-NMR (300 MHz, CDCl₃): 2.11-2.31 (m, 1H), 2.45 (t, J = 11.0 Hz, 1H), 2.52-2.62 (m, 1H), 2.82-2.95 (m, 1H), 3.89 (s, 2H), 5.90 (s, 1H), 7.23-7.42 (m, 7H), 7.59 (t, J = 7.8 Hz, 1H), 8.05 (d, J = 7.8 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): 26.6, 31.4, 38.5, 83.6, 125.0, 126.7, 127.4, 127.9, 128.57, 128.64, 130.7, 135.4, 135.7, 137.0, 137.3, 176.4, 196.5; HRMS (FAB) calcd for C₂₀H₁₇O₃ (M⁺+ H): 305.1099, found: 305.1168.

4’-Bromo-3,4-dihydrospiro[furan-2(5H),2’(1’H)-naphthalene]-1’,5-dione (2f)
Pale yellow powder; mp 156 °C (decomposed); IR (KBr, cm⁻¹): 3684, 3622, 3018, 2945, 2895, 2399, 1788, 1697, 1628, 1591; ¹H-NMR (300 MHz, CDCl₃): 2.16-2.31 (m, 1H), 2.45 (t, J = 11.0 Hz, 1H), 2.61
(dd, J = 17.2, 9.3 Hz, 1H), 2.81-2.95 (m, 1H), 6.66 (s, 1H), 7.46-7.52 (m, 1H), 7.74 (d, J = 3.8 Hz, 2H), 8.02 (d, J = 7.6 Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.4, 31.1, 84.2, 122.4, 127.3, 127.9, 128.8, 130.1, 133.4, 135.1, 135.9, 175.7, 194.7; Anal. Calcd for C$_{13}$H$_9$BrO$_3$: C, 53.27; H, 3.09; Br, 27.26. Found: C, 53.03; H, 3.02; Br, 27.09.

4'-Benzoyl-3,4-dihydrospiro[furan-2(5H),2'(1'H)-naphthalene]-1',5-dione (2g)
White powder; mp 97-98°C; IR (KBr, cm$^{-1}$): 2925, 1791, 1665, 1595, 1450, 1276, 1244, 1172, 1033, 990, 937, 913, 775, 735, 662; $^1$H-NMR (400 MHz, CDCl$_3$): 2.22-2.30 (m, 1H), 2.47-2.63 (m, 2H), 2.85-2.94 (m, 1H), 6.37 (s, 1H), 7.39 (d, $J$ = 7.8 Hz, 1H), 7.44-7.50 (m, 3H), 7.57-7.65 (m, 2H), 7.95 (dd, $J$ = 8.3, 1.2 Hz, 2H), 8.11 (dd, $J$ = 7.8, 1.2 Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.3, 31.2, 82.7, 126.9, 127.4, 128.5, 128.9, 129.8, 130.1, 134.0, 134.2, 134.3, 135.8, 135.9, 137.5, 175.9, 194.5, 195.2; HRMS (EI) calcd for C$_{20}$H$_{14}$O$_4$ (M$^+$): 318.0892, found: 318.0888.

5'-Benzyloxy-3,4-dihydrospiro[furan-2(5H),2'(1'H)-naphthalene]-1',5-dione (2h)
Pale yellow powder; mp 173-174°C; IR (KBr, cm$^{-1}$): 2918, 1789, 1689, 1590, 1455, 1266, 1178, 1033, 939, 749; $^1$H-NMR (400 MHz, CDCl$_3$): 2.08-2.20 (m, 1H), 2.37-2.42 (m, 1H), 2.53-2.59 (m, 1H), 2.81-2.91 (m, 1H), 5.12 (s, 2H), 6.14 (d, $J$ = 10.0 Hz, 1H), 7.14 (d, $J$ = 10.0 Hz, 1H), 7.19 (d, $J$ = 8.3 Hz, 1H), 7.29-7.43 (m, 6H), 7.61 (d, $J$ = 7.8 Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.5, 31.2, 82.7, 126.9, 127.4, 128.5, 128.9, 129.8, 130.1, 134.0, 134.2, 134.3, 135.8, 135.9, 137.5, 175.9, 194.5, 195.2; HRMS (EI) calcd for C$_{20}$H$_{16}$O$_4$ (M$^+$): 320.1049, found: 320.1051.

3,4-Dihydrospiro[furan-2(5H),1'(2'H)-naphthalene]-2',5-dione (2i)
White powder; mp 137-138°C; IR (KBr, cm$^{-1}$): 2957, 1786, 1680, 1568, 1244, 1173, 1038, 902, 832, 757, 462; $^1$H-NMR (400 MHz, CDCl$_3$): 2.08 (m, 1H), 2.59-2.67 (m, 2H), 2.78-2.87 (m, 1H), 6.15 (d, $J$ = 9.8 Hz, 1H), 7.32-7.40 (m, 2H), 7.43-7.47 (m, 2H), 7.53 (d, $J$ = 7.7 Hz, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.6, 35.8, 53.4, 85.8, 122.6, 125.8, 129.1, 129.7, 131.0, 140.6, 146.0, 176.4, 197.5; HRMS (EI) calcd for C$_{13}$H$_{10}$O$_3$ (M$^+$): 214.0630, found: 214.0646.

3'-Bromo-3,4-dihydrospiro[furan-2(5H),1'(2'H)-naphthalene]-2',5-dione (2j)
White powder; mp 135-136°C; IR (KBr, cm$^{-1}$): 2925, 1790, 1692, 1345, 1160, 1038, 912, 797, 744, 670, 582, 468; $^1$H-NMR (300 MHz, CDCl$_3$): 2.11-2.20 (m, 1H), 2.62-2.68 (m, 2H), 2.80-2.90 (m, 1H), 7.27 (d, $J$ = 7.2 Hz, 1H), 7.40 (dd, $J$ = 7.4, 1.2 Hz, 1H), 7.48-7.54 (m, 2H), 7.89 (s, 1H); $^{13}$C-NMR (75 MHz, CDCl$_3$): 26.4, 36.1, 86.4, 118.3, 126.0, 128.9, 129.4, 129.6, 131.4, 139.9, 147.3, 175.8, 191.2; HRMS (EI) calcd for C$_{13}$H$_{16}$BrO$_3$ (M$^+$): 291.9735, found: 291.9725.
Danishefsky’s lactone 2k

White powder; mp 142.5 °C (decomposed); IR (KBr, cm⁻¹): 3153, 2939, 2851, 2359, 2340, 1790, 1693, 1666, 1595; ¹H-NMR (300 MHz, CDCl₃): 2.83 (d, J = 18.0 Hz, 1H), 3.18 (dd, J = 18.0 Hz, 4.8 Hz, 1H), 3.98 (s, 3H), 4.75 (d, J = 4.8 Hz, 1H), 4.92, 5.08 (ABq, J = 12.8 Hz, 2H), 7.45 (td, J = 7.1 Hz, 2.0 Hz, 1H), 7.64-7.71 (m, 2H), 7.90 (d, J = 7.1 Hz, 1H); ¹³C-NMR (75 MHz, CDCl₃): 37.9, 59.3, 69.0, 79.4, 88.4, 110.6, 124.1, 127.4, 128.3, 129.5, 135.47, 135.52, 149.9, 174.7, 192.1. HRMS (FAB) calcd for C₁₅H₁₃O₅ (M⁺+H) 273.0763, found: 273.0762.

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REFERENCES


6. In contrast, the cyclohexa-2,4-dienones obtained from the oxidations of simple phenol carboxylic acids are generally quite reactive and have high propensity toward self-dimerization through the Diels-Alder process. For selected example, see: I. Drutu, J. T. Njardarson, and J. L. Wood, *Org. Lett.*, 2002, **4**, 493.

