Chiral Aryl Iodide Catalysts for the Enantioselective Synthesis of $p$-Quinols

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Materials and Methods

Unless otherwise stated, reactions were performed in flame- or oven-dried glassware under an argon or nitrogen atmosphere using anhydrous solvents. Tetrahydrofuran (THF) was distilled from sodium/benzophenone. Methanol was dried over 3Å molecular sieves. 3-Chloroperoxybenzoic acid (≤ 77%) was purchased from Aldrich. Labeled $^{18}$O water was obtained from Isoflex USA (98.03% enrichment). Unless otherwise stated, reactions were monitored using thin-layer chromatography (TLC) using plates precoated with silica gel XHL w/ UV254 (250 mm) and visualized by UV light or KMnO$_4$, phosphomolybdic acid, or anisaldehyde stains, followed by heating. Silica gel (particle size 32–63 mm) was used for flash column chromatography.

$^1$H and $^{13}$C NMR spectra are reported relative to the residual solvent peak ($\delta$ 7.26 and $\delta$ 77.2 for $^1$H and $^{13}$C in CDCl$_3$, $\delta$ 3.31 and $\delta$ 49.0 for $^1$H and $^{13}$C in CD$_3$OD, respectively), or tetramethylsilane ($\delta$ 0.00 for $^1$H) when the residual solvent peak is obscured. Data for $^1$H NMR spectra are reported as follows: chemical shift (ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity is described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad singlet, app = apparent. IR samples were prepared on NaCl plates either neat or by evaporation from CHCl$_3$ or CH$_2$Cl$_2$.

Computational Methods

All geometries were fully optimized at the M06-2X level$^1$ of density functional theory. A mixed basis set comprised of 6–31G(d)$^2$ for C, H and O and the Stuttgart/Dresden basis set and pseudopotential (SDD)$^3$ for iodine. An ultrafine grid density was used for numerical integration.$^4$ Optimizations were performed with no frozen coordinates. The effects of CH$_2$Cl$_2$ (a lower polarity solvent that is commonly used in oxidative dearomatization reactions) and CH$_3$CN (a polar, non-nucleophilic solvent) solvation were included in the geometry optimizations using the SMD solvation model.$^5$ Energy minima and transition states were identified though frequency analysis. All calculations made use of the Gaussian 09 Rev A.02 suite$^6$ of electronic structure programs. The Gibbs energies are included below with the atomic coordinates.

Final structures, coordinates, and energies for the calculated structure of 7.

The final optimized geometry of each species is given below, along with the following:
(i) Number of imaginary frequencies (frequency if present)
(ii) Free energy (G) at 298.15 K and 1 atm. All energies are quoted in Hartrees.

**Compound 7 in CH\textsubscript{2}Cl\textsubscript{2}**

![Side view](image1)
![Top view](image2)

(side view) (top view, phenol is shaded darker)

I  -1.195000  -0.604700  -0.499300  
C  -0.343400  1.292300  -0.093900  
C  0.903300  3.701800  0.363800  
C  -0.416000  2.275400  -1.073600  
C  0.339000  1.471300  1.103900  
C  0.965400  2.696900  1.326800  
C  0.216400  3.493800  -0.831100  
H  -0.948300  2.099900  -2.002700  
H  0.391900  0.677700  1.842100  
H  1.506400  2.858300  2.253600  
H  0.169900  4.277300  -1.580700  
H  1.396800  4.651700  0.543200  
O  0.584300  -1.033700  -1.562500  
C  1.737300  -1.008900  -0.847700  
C  4.166500  -0.930700  0.590600  
C  2.030300  -1.990500  0.105000  
C  2.664700  0.017500  -1.071600  
C  3.861300  0.046400  -0.364600  
C  3.230000  -1.943900  0.812000  
H  1.310800  -2.785900  0.283700  
H  2.425500  0.786600  -1.800800
H     4.572300  0.848500  -0.550300
H     3.443800  -2.714900  1.548500
C     5.471600  -0.887800  1.344000
H     6.320500  -1.075300  0.676700
H     5.496200  -1.642400  2.135000
H     5.633500  0.092300  1.805100
O     -2.876400  0.245700  0.739000
C     -3.826000  -0.646600  0.738900
O     -3.736100  -1.782100  0.282700
C     -5.032700  -0.153300  1.499400
H     -5.430400  0.743000  1.016200
H     -4.735300  0.120800  2.515500
H     -5.796600  -0.930100  1.533400

*** 0 imaginary frequencies ***
G = -817.049054

**Compound 7 in CH₃CN**

(side view)

(top view, phenol is shaded darker)

I     -1.266200  -0.614100  -0.473400
C     -0.226600  1.198400  -0.133400
C     1.303200  3.453300  0.241800
C     -0.122500  2.110800  -1.175800
C     0.413600  1.371600  1.088600
C     1.184100  2.519300  1.269800
C     0.651900  3.253000  -0.974000
H     -0.625500  1.938600  -2.121900
H     0.325100  0.630000  1.875800
H     1.696200  2.674600  2.213900
H     0.745400  3.982000  -1.772600
H     1.908600  4.342000  0.388900
O     0.486800  -1.273500  -1.475900
C     1.648700  -1.161300  -0.786600
C  4.085600 -0.879200  0.616300
C  1.911200 -1.939700  0.345800
C  2.615000 -0.239600 -1.213700
C  3.813500 -0.109000 -0.521600
C  3.114800 -1.793500  1.033700
H  1.162100 -2.651300  0.685000
H  2.403500  0.371000 -2.087000
H  4.552000  0.611900 -0.866200
H  3.303400 -2.405300  1.912700
C  5.385600 -0.715300  1.361800
H  6.244300 -0.918300  0.712600
H  5.439800 -1.396300  2.215500
H  5.500500  0.307200  1.738200
O  -2.871100  0.449600  0.558300
C  -3.903000 -0.339100  0.727300
O  -3.922800 -1.500100  0.330900
C  -5.057400  0.307600  1.452500
H  -5.386100  1.192900  0.901400
H  -4.729200  0.634800  2.443000
H  -5.882100 -0.398600  1.549300

*** 0 imaginary frequencies ***
G = -817.049128
Potential energy scan of compound 7

A relaxed scan of the C2–I–O13–C14 dihedral in 7 was performed to confirm that the originally obtained structures were indeed minima. Scans were performed in the gas phase and with CH₃CN and CH₂Cl₂. The scan involved stepping the dihedral angle in 30º increments starting at 0º. The plot for each scan is shown in Figures S1 and S2. In both cases, the global minimum corresponds to the originally obtained structures, or their enantiomer.

Figure S1. Relaxed scan of C2–I–O13–C14 dihedral with CH₃CN solvation.

Figure S2. Relaxed scan of C2–I–O13–C14 dihedral with CH₂Cl₂ solvation.
**Aryl Iodide Catalyst Scope**

**Table S1: Full Results of Iodotetralone Catalysts**

<table>
<thead>
<tr>
<th>entry</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>temp</th>
<th>MeCN:H$_2$O</th>
<th>time (h)</th>
<th>yield (%)</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>OH</td>
<td>rt</td>
<td>2:1</td>
<td>1.5</td>
<td>36</td>
<td>60:40</td>
</tr>
<tr>
<td>2</td>
<td>Me</td>
<td>morpholine</td>
<td>8b</td>
<td>rt</td>
<td>3:1</td>
<td>1.5</td>
<td>33</td>
</tr>
<tr>
<td>3</td>
<td>Me</td>
<td>NHPH</td>
<td>rt</td>
<td>3:1</td>
<td>1.5</td>
<td>19</td>
<td>60:40</td>
</tr>
<tr>
<td>4</td>
<td>Me</td>
<td>NHBn</td>
<td>rt</td>
<td>3:1</td>
<td>1.5</td>
<td>34</td>
<td>61:39</td>
</tr>
<tr>
<td>5</td>
<td>Me</td>
<td>NHMes</td>
<td>rt</td>
<td>2:1</td>
<td>1.5</td>
<td>47</td>
<td>63:37</td>
</tr>
<tr>
<td>6</td>
<td>Br</td>
<td>NHPH</td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>48</td>
<td>40:60</td>
</tr>
<tr>
<td>7</td>
<td>Br</td>
<td>NHBn</td>
<td>rt</td>
<td>2:1</td>
<td>1.5</td>
<td>20</td>
<td>40:60</td>
</tr>
<tr>
<td>8</td>
<td>Br</td>
<td>NHMes</td>
<td>rt</td>
<td>2:1</td>
<td>0.3</td>
<td>45</td>
<td>35:65</td>
</tr>
<tr>
<td>9</td>
<td>Br</td>
<td>TMS</td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>80</td>
<td>37:63</td>
</tr>
<tr>
<td>10</td>
<td>TMS</td>
<td></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>94</td>
<td>28:72</td>
</tr>
<tr>
<td>11</td>
<td>Br</td>
<td></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>75</td>
<td>57:43</td>
</tr>
<tr>
<td>12</td>
<td>Br</td>
<td></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>70</td>
<td>37:63</td>
</tr>
<tr>
<td>13</td>
<td>Br</td>
<td></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>52</td>
<td>40:60</td>
</tr>
</tbody>
</table>
Table S2: Other Aryl Iodide Catalysts Results

<table>
<thead>
<tr>
<th>entry</th>
<th>Ar*I</th>
<th>temp (°C)</th>
<th>time (h)</th>
<th>yield (%)</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(S1)</td>
<td>rt</td>
<td>1</td>
<td>27</td>
<td>44:56</td>
</tr>
<tr>
<td>2</td>
<td>(S2)</td>
<td>rt</td>
<td>1.5</td>
<td>29</td>
<td>46:54</td>
</tr>
<tr>
<td>3</td>
<td>(S3)</td>
<td>rt</td>
<td>1</td>
<td>28</td>
<td>47:53</td>
</tr>
<tr>
<td>4</td>
<td>(S4)</td>
<td>rt</td>
<td>1</td>
<td>35</td>
<td>46:54</td>
</tr>
<tr>
<td>5</td>
<td>(S5)</td>
<td>rt</td>
<td>1</td>
<td>39</td>
<td>45:55</td>
</tr>
</tbody>
</table>
Table S3: Full Results of Substrate Scope

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>temp</th>
<th>solvent</th>
<th>time (h)</th>
<th>yield (%)</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td>rt</td>
<td>MeCN:HO</td>
<td>1.5</td>
<td>47</td>
<td>38:62</td>
</tr>
<tr>
<td>1</td>
<td><img src="image3.png" alt="Image" /></td>
<td><img src="image4.png" alt="Image" /></td>
<td>rt</td>
<td>MeCN:HO</td>
<td>16</td>
<td>52</td>
<td>38:62</td>
</tr>
<tr>
<td>2</td>
<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
<td>0 °C</td>
<td>2:1</td>
<td>3</td>
<td>21</td>
<td>32:68</td>
</tr>
<tr>
<td>2</td>
<td><img src="image7.png" alt="Image" /></td>
<td><img src="image8.png" alt="Image" /></td>
<td>rt</td>
<td>2:1</td>
<td>0.3</td>
<td>45</td>
<td>35:65</td>
</tr>
<tr>
<td>3</td>
<td><img src="image9.png" alt="Image" /></td>
<td><img src="image10.png" alt="Image" /></td>
<td>0 °C</td>
<td>2:1</td>
<td>1</td>
<td>76</td>
<td>35:65</td>
</tr>
<tr>
<td>3</td>
<td><img src="image11.png" alt="Image" /></td>
<td><img src="image12.png" alt="Image" /></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>65</td>
<td>35:65</td>
</tr>
<tr>
<td>4</td>
<td><img src="image13.png" alt="Image" /></td>
<td><img src="image14.png" alt="Image" /></td>
<td>0 °C</td>
<td>2:1</td>
<td>0.5</td>
<td>21</td>
<td>24:76b</td>
</tr>
<tr>
<td>4</td>
<td><img src="image15.png" alt="Image" /></td>
<td><img src="image16.png" alt="Image" /></td>
<td>0 °C</td>
<td>9:1</td>
<td>7</td>
<td>58</td>
<td>21:79</td>
</tr>
<tr>
<td>5</td>
<td><img src="image17.png" alt="Image" /></td>
<td><img src="image18.png" alt="Image" /></td>
<td>0 °C</td>
<td>2:1</td>
<td>0.5</td>
<td>23</td>
<td>47:53b</td>
</tr>
<tr>
<td>5</td>
<td><img src="image19.png" alt="Image" /></td>
<td><img src="image20.png" alt="Image" /></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>43</td>
<td>50:50</td>
</tr>
<tr>
<td>6</td>
<td><img src="image21.png" alt="Image" /></td>
<td><img src="image22.png" alt="Image" /></td>
<td>0 °C</td>
<td>2:1</td>
<td>1</td>
<td>20</td>
<td>33:67</td>
</tr>
<tr>
<td>7</td>
<td><img src="image23.png" alt="Image" /></td>
<td><img src="image24.png" alt="Image" /></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>53</td>
<td>67:33</td>
</tr>
<tr>
<td>8</td>
<td><img src="image25.png" alt="Image" /></td>
<td><img src="image26.png" alt="Image" /></td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>41</td>
<td>38:62</td>
</tr>
<tr>
<td>9</td>
<td><img src="image27.png" alt="Image" /></td>
<td><img src="image28.png" alt="Image" /></td>
<td>0 °C</td>
<td>1:0</td>
<td>1</td>
<td>27</td>
<td>40:60c</td>
</tr>
<tr>
<td>10</td>
<td><img src="image29.png" alt="Image" /></td>
<td><img src="image30.png" alt="Image" /></td>
<td>0 °C</td>
<td>MeOH</td>
<td>3</td>
<td>60</td>
<td>35:65</td>
</tr>
</tbody>
</table>

*a* all reactions carried out on a 0.17 mmol scale with 2.2 equiv of m-CPBA, 10 mol % catalyst.

*b* quinol product was converted to the t-butyl malonate derivative in order for separation on the HPLC.

*c* spirolactone product was transesterified with aqueous MeOH–NaHCO₃ in order for separation on the HPLC.
Table S4: Solvent Screen Results

<table>
<thead>
<tr>
<th>entry</th>
<th>solvent (9:1)</th>
<th>yield (%)</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeCN-H₂O</td>
<td>53</td>
<td>67:33</td>
</tr>
<tr>
<td>2</td>
<td>THF-H₂O</td>
<td>33</td>
<td>62:38</td>
</tr>
<tr>
<td>3</td>
<td>CF₃CH₂OH-H₂O</td>
<td>&lt;10</td>
<td>nd</td>
</tr>
<tr>
<td>4</td>
<td>MeNO₂-H₂O</td>
<td>62</td>
<td>53:47</td>
</tr>
<tr>
<td>5</td>
<td>acetone-H₂O</td>
<td>66</td>
<td>68:32</td>
</tr>
</tbody>
</table>

Table S5: Ishihara Catalysts with Phenol 4c

<table>
<thead>
<tr>
<th>entry</th>
<th>R</th>
<th>temp</th>
<th>MeCN:H₂O</th>
<th>time [h]</th>
<th>yield [%]</th>
<th>er</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3,5-dimethyl</td>
<td>0 °C</td>
<td>2:1</td>
<td>2</td>
<td>36</td>
<td>61:39</td>
</tr>
<tr>
<td>2</td>
<td>mesityl</td>
<td>rt</td>
<td>9:1</td>
<td>16</td>
<td>57</td>
<td>67:33</td>
</tr>
</tbody>
</table>
**Experimental Procedures**

**Synthesis of Aryl Iodide Catalysts**

**General Procedure A: Ketalization with (+)-Dimethyl L-tartrate**

The aryl iodo ketone (1 equiv) was dissolved in methanol (0.65 M) and treated with trimethyl orthoformate (5 equiv) followed by p-toluenesulfonic acid monohydrate (10 mol %). The mixture was refluxed overnight and then concentrated in vacuo. In the same flask, the residue was dissolved in toluene (0.2 M) and (+)-dimethyl L-tartrate (2.1 equiv) was added, followed by BF$_3$·OEt$_2$ (5 mol %). The mixture was heated and the methanol removed by azeotrope. After 3 h, the reaction was cooled to r.t., quenched with saturated aq. NaHCO$_3$, and extracted with EtOAc (3×). The combined organic layers were washed with brine and then concentrated under reduced pressure to give a viscous oil. The oil was treated with a 1:1 mixture of MeOH and 2 N NaOH for 1 hr, and then transferred to a separatory funnel. The aqueous layer was washed with ether, acidified with 10% aq. HCl, and then extracted with EtOAc. The combined organic layers were washed with brine, dried over Na$_2$SO$_4$, and concentrated under reduced pressure.

**General Procedure B: Amide Synthesis**

The aryl iodotartrate was dissolved in DCM (0.1 M) and treated with oxalyl chloride (3.5 equiv) and DMF (10 µL) at room temperature for 3 h. The resulting dark solution was concentrated in vacuo and re-dissolved in DCM (0.2 M). Into the same flask was added the respective aniline or amine (4 equiv) and pyridine (4 equiv). The mixture was stirred at r.t. overnight, then quenched with 10% aq. HCl and extracted with DCM. The organic layer was washed with brine, dried (Na$_2$SO$_4$), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (hexanes/EtOAc).

(4R,5R)-8'-iodo-3',4'-dihydro-2'H-spiro[[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxylic acid (8a).

The iodo tetralone (7) (902 mg, 3.31 mmol) was dissolved in dry methanol (5 mL, 0.65 M) and to this was added trimethyl orthoformate (2.5 mL, 23 mmol), which was followed by p-toluenesulfonic acid monohydrate (2 mg). The reaction was refluxed overnight, concentrated in vacuo, and carried on immediately without isolation. Into the same flask was added dry benzene (4 mL), 3 Å molecular sieves, (+)-dimethyl L-tartrate (890 mg, 4.97 mmol), and scandium triflate (2 mg). The resulting mixture was stirred, heated to 90 °C, and left open to the atmosphere for 3 h. After such time, the reaction mixture was concentrated in vacuo and the resulting residue was dissolved in EtOAc, transferred to a separatory funnel and washed with saturated aq. NaHCO$_3$, H$_2$O, and brine. It was then dried (Na$_2$SO$_4$), filtered, and concentrated under reduced pressure, affording a viscous, colorless oil. This was treated with MeOH (2 mL) and 2 N NaOH (2 mL) for 1.5 h. After such time, the mixture was washed with EtOAc and the aqueous layer acidified with 10% aq. HCl. The product was extracted with EtOAc, dried (Na$_2$SO$_4$), filtered, and concentrated under reduced pressure to give a reddish orange solid (844 mg, 63% yield). No further purification was performed.

IR (thin film) 3052, 2942, 2624, 1728, 1437, 1165, 1096 cm⁻¹

¹H NMR (300 MHz, CD₃OD): 6 7.85 (dd, J = 7.7, 1.1 Hz, 1H), 7.16 (dd, J = 7.6, 1.1 Hz, 1H), 6.92 (t, J = 7.7 Hz, 1H), 5.19 (d, J = 7.0 Hz, 1H), 5.08 (d, J = 7.0 Hz, 1H), 5.00 (bs, exchangeable OHs), 2.85 (t, J = 6.1 Hz, 2H), 2.24–2.16 (m, 1H), 2.07 (dd, J = 7.9, 5.9 Hz, 1H), 1.85 (dt, J = 11.2, 5.6 Hz, 2H).

¹³C NMR (75 MHz, CDCl₃, DEPT) 6 174.1 (C), 171.5 (C), 143.7, (C) 141.9 (CH), 134.8 (C), 131.4 (CH), 130.6 (CH), 111.9 (C), 94.7 (C), 78.0 (CH), 35.7 (CH₂), 32.1 (CH₂), 20.8 (CH₂).

HRMS (ESI–) 402.9684 calculated for C₁₄H₁₂IO₆ found 402.9672

[α]D –10.2 (c 0.02, MeOH)

(4R,5R)-8'-iodo-3',4'-dihydro-2'H-spiro[[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxylic acid (8b).

Using general procedure B, 8b was synthesized from 8a in 81% yield after flash column chromatography (4:1 hexanes/EtOAc).

IR (thin film) 2958, 2924, 2857, 1644, 1441, 1274, 1114, 978 cm⁻¹

¹H NMR (300 MHz, CDCl₃): 6 7.87 (dd, J = 7.7, 1.3 Hz, 1H), 7.12 (dd, J = 7.6, 1.2 Hz, 1H), 6.90 (t, J = 7.7 Hz, 1H), 5.77 (d, J = 6.8 Hz, 1H), 5.66 (d, J = 6.8 Hz, 1H), 3.92–3.59 (m, 1H), 2.84 (t, J = 6.2 Hz, 2H), 2.11–2.07 (m, 2H), 1.85–1.77 (m, 2H).

HRMS (ESI+) 565.0806 calculated for C₂₂H₂₇IN₂NaO₆ found 565.0799

(4R,5R)-8'-iodo-N⁴,N⁵-diphenyl-3',4'-dihydro-2'H-spiro[[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxamide (8c).

Using general procedure B, 8c was obtained from 8a and isolated as an orange solid in 74% yield after purification by flash column chromatography (4:1 hexanes/EtOAc).

IR (thin film) 3383, 3288, 3055, 2933, 1699, 1599, 1538, 1445, 1095 cm⁻¹

¹H NMR (300 MHz, CDCl₃) 6 9.03 (s, 1H), 8.63 (s, 1H), 7.92 (dd, J = 7.8, 0.7 Hz, 1H), 7.67–7.63 (m, 4H), 7.41–7.33 (m, 4H), 6.97 (t, J = 7.7 Hz, 1H), 5.25 (d, J = 7.6 Hz, 1H), 5.05 (d, J = 7.6 Hz, 1H), 2.91 (dq, J = 9.7, 5.1 Hz, 2H), 2.30–2.14 (m, 2H), 1.92 (qd, J = 9.1, 4.3 Hz, 2H).

¹³C NMR (75 MHz, CDCl₃, DEPT) 6 168.3 (C), 167.1 (C), 142.8 (C), 141.2 (CH), 137.6 (C), 136.6 (C), 133.0 (C), 130.8 (CH), 129.9 (CH), 129.3 (CH × 2), 129.2 (CH × 2), 125.3 (CH), 124.7 (CH), 120.5 (CH × 2), 119.8 (CH × 2), 111.5 (C), 94.0 (C), 78.4 (CH), 77.3 (CH), 34.9 (CH₂), 31.3 (CH₂), 19.9 (CH₂).
HRMS (ESI+) 577.0595 calculated for C\textsubscript{26}H\textsubscript{23}IN\textsubscript{2}NaO\textsubscript{4} found 577.0641
\([\alpha]\)\textsubscript{D}\textsuperscript{25} – 37.2 (c 0.01, EtOAc)

(4\textit{R},5\textit{R})-N\textsuperscript{4},N\textsuperscript{5}-dibenzyl-8’-iodo-3’,4’-dihydro-2’H-spiro[[1,3]dioxolane-2,1’-naphthalene]-4,5-dicarboxamide (8d).

Using general procedure B, 8d was obtained from 8a and isolated as a brown solid in 86% yield after purification by flash column chromatography (3:1 hexanes/EtOAc).

(4\textit{R},5\textit{R})-8’-iodo-N\textsuperscript{4},N\textsuperscript{5}-dimesityl-3’,4’-dihydro-2’H-spiro[[1,3]dioxolane-2,1’-naphthalene]-4,5-dicarboxamide (8e).

Using general procedure B, 8e was obtained from 8a and isolated as a brown solid in 86% yield after purification by flash column chromatography (3:1 hexanes/EtOAc).

IR (thin film) 3368, 3267, 3006, 2947, 2920, 2863, 1704, 1510, 1093 cm\textsuperscript{-1}

\(^1\text{H}\) NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.44 (s, 2H), 7.91 (d, \(J = 7.5\) 1H), 7.15 (d, \(J = 7.6\) Hz, 1H), 6.95–6.90 (m, 5H), 5.44 (d, \(J = 8.2\) Hz, 1H), 5.13 (d, \(J = 8.2\) Hz, 1H), 2.93–2.87 (m, 2H), 2.40–2.35 (m, 1H), 2.27 (s, 12H), 2.25 (s, 6H), 2.00–1.93 (m, 2H).

\(^{13}\text{C}\) NMR (75 MHz, CDCl\textsubscript{3}, DEPT) \(\delta\) 169.3 (C), 166.4 (C), 142.6 (C), 141.2 (CH), 137.3 (C), 135.0 (C \(\times 2\)), 134.9 (C \(\times 2\)), 133.2 (C), 130.7 (CH), 130.3 (C), 130.2 (C), 129.8 (CH), 129.2 (CH \(\times 4\)), 111.1 (C), 94.1 (C), 78.0 (CH), 77.7 (CH), 34.8 (CH\textsubscript{2}), 31.4 (CH\textsubscript{2}), 21.0 (CH\textsubscript{3} \(\times 2\)), 20.0 (CH\textsubscript{2}), 19.1 (CH\textsubscript{3} \(\times 2\)), 18.7 (CH\textsubscript{3} \(\times 2\)).

HRMS (ESI+) 661.1534 calculated for C\textsubscript{32}H\textsubscript{35}IN\textsubscript{2}NaO\textsubscript{4} found 661.1531
[\alpha]\textsubscript{D}\textsuperscript{24} + 4.4 (c 0.01, MeOH)
(4R,5R)-\(N^4, N^6\)-bis(2,6-dibromo-4-isopropylphenyl)-8'-iodo-3',4'-dihydro-2'H-spiro[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxamide (8f).

Using general procedure B, 8f was obtained from 8a and isolated as a brown solid in 76% yield after purification by flash column chromatography (9:1 hexanes/EtOAc).

**IR (thin film)** 3379, 3258, 2961, 2869, 1724, 1681, 1501, 1096 cm\(^{-1}\)

**\(^1\)H NMR** (500 MHz, CDCl\(_3\)) \(\delta\) 8.73 (s, 1H), 8.63 (s, 1H), 7.91 (d, \(J = 8.0\) Hz, 1H), 7.46 (s, 2H), 7.44 (s, 2H), 7.14 (d, \(J = 7.6\) Hz, 1H), 6.92 (t, \(J = 7.7\) Hz, 1H), 5.56 (d, \(J = 8.1\) Hz, 1H), 5.28 (d, \(J = 8.1\) Hz, 1H), 2.95–2.83 (m, 4H), 2.40–2.27 (m, 2H), 1.98–1.95 (m, 2H), 1.232 (d, \(J = 6.9\), 6H), 1.227 (d, \(J = 6.9\)).

**\(^{13}\)C NMR** (125 MHz, CDCl\(_3\), DEPT) \(\delta\) 169.3 (C), 166.1 (C), 151.7 (C), 151.6 (C), 142.6 (C), 141.1 (CH), 133.1 (C), 131.1 (C), 131.05 (C), 130.74 (CH), 130.69 (CH), 129.6 (CH), 123.7 (C), 123.6 (C), 111.5 (C), 94.6 (C), 77.6 (CH), 77.2 (CH), 35.0 (CH\(_2\)), 33.75 (CH), 33.73 (CH), 31.4 (CH\(_2\)), 23.7 (CH\(_3\) \(\times 4\)), 20.1 (CH\(_2\)).

**HRMS** (ESI+) 976.7917 calculated for C\(_{32}\)H\(_{31}\)Br\(_4\)IN\(_2\)NaO\(_4\) found 976.7964

(4R,5R)-\(N^4, N^6\)-bis(3,5-bis(trifluoromethyl)phenyl)-8'-iodo-3',4'-dihydro-2'H-spiro[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxamide (8g).

Using general procedure B, 8g was obtained from 8a and isolated as a yellow solid in 51% yield after purification by flash column chromatography (5:1 hexanes/EtOAc).

**IR (thin film)** 3267, 2924, 1708, 1381, 1278, 1137 cm\(^{-1}\)

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) 9.11 (s, 1H), 8.77 (s, 1H), 8.15 (s, 4H), 7.92 (d, \(J = 7.8\) Hz, 1H), 7.70 (s, 1H), 7.66 (s, 1H), 7.16 (d, \(J = 7.7\) Hz, 1H), 6.98 (t, \(J = 7.7\) Hz, 1H), 5.30 (d, \(J = 7.3\) Hz, 1H), 5.11 (d, \(J = 7.3\) Hz, 1H), 2.88 (t, \(J = 6.0\) Hz, 2H), 2.27–2.06 (m, 2H), 1.93 (t, \(J = 4.6\) Hz, 2H).

**\(^{13}\)C NMR** (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 168.8 (C), 167.7 (C), 142.8 (C), 141.2 (CH), 138.8 (C), 137.9 (C), 132.9 d, \(J = 18.8\) Hz, C–CF\(_3\)), 132.6 (d, \(J = 18.8\) Hz, C–CF\(_3\)), 131.2 (CH), 130.1 (CH),
123.15 (d, J = 271.3 Hz, CF$_3$), 123.08 (d, J = 272.5 Hz, CF$_3$), 120.0 (CH), 119.6 (CH), 118.8 (m, CH), 118.2 (m, CH), 112.19 (C), 78.3 (CH), 77.0 (CH), 34.9 (CH$_2$), 31.2 (CH$_2$), 19.8 (CH$_2$).

**HRMS** (ESI+) 849.0090 calculated for C$_{36}$H$_{19}$F$_{12}$IN$_2$NaO$_4$ found 849.0080

$[\alpha]_{D}^{25}$ – 4.0 (c 0.01, EtOAc)

(4R,5R)-N$_4$N$_5$-di(anthracen-9-yl)-8'-iodo-3',4'-dihydro-2'H-spiro[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxamide (8h).

Using general procedure B, 8h was obtained from 8a and isolated as a yellow solid in 45% yield after purification by flash column chromatography (9:1 hexanes/EtOAc).

**IR** (thin film) 3358, 3053, 2924, 2853, 1670, 1496, 1354 cm$^{-1}$

$^1$H NMR (500 MHz, CDCl$_3$) δ 9.23 (s, 1H), 9.05 (s, 1H), 8.49 (s, 1H), 8.43 (s, 1H), 8.30 (d, J = 8.7 Hz, 2H), 8.13 (d, J = 8.7 Hz, 2H), 8.04 (d, J = 8.4 Hz, 1H), 8.00 (app d, J = 8.1 Hz, 2H, 1H), 7.58 (app t, J = 7.3 Hz, 2H), 7.52–7.44 (m, 6H), 7.22 (d, J = 7.6 Hz, 1H), 6.99 (t, J = 7.7 Hz, 1H), 5.98 (d, J = 8.0 Hz, 1H), 5.68 (d, J = 8.0 Hz, 1H), 3.02–2.92 (m, 2H), 2.60 (dt, J = 9.3, 4.4 Hz, 1H), 2.45 (td, J = 12.4, 3.3 Hz, 1H), 2.11–2.01 (m, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$, DEPT) δ 169.9 (C), 168.5 (C), 142.9 (C), 141.2 (CH), 133.2 (C), 131.71 (C), 131.66 (C), 130.8 (CH), 130.0 (CH), 128.9 (CH × 2), 128.8 (CH × 2), 128.2 (C), 128.0 (C), 127.7 (CH), 127.2 (CH), 126.8 (C), 126.7 (CH × 2), 126.6 (CH × 2), 126.1 (C), 125.5 (CH × 2), 125.4 (CH × 2), 123.4 (CH × 2), 123.2 (CH × 2), 111.9 (C), 94.2 (C), 78.6 (CH), 78.4 (CH), 35.0 (CH$_2$), 31.4 (CH$_2$), 20.1 (CH$_2$).

**HRMS** (ESI+) 777.1221 calculated for C$_{42}$H$_{31}$IN$_2$NaO$_4$ + found 777.1296

$[\alpha]_{D}^{25}$ + 30.6 (c 0.004, EtOAc)

(4R,5R)-8'-iodo-N$_4$N$_5$-di(naphthalen-1-yl)-3',4'-dihydro-2'H-spiro[1,3]dioxolane-2,1'-naphthalene]-4,5-dicarboxamide (8i).

Using general procedure B, 8i was obtained from 8a and isolated as a brown solid in 71% yield after purification by flash column chromatography (8:1 hexanes/EtOAc).

**IR** (thin film) 3296, 3054, 2925, 2854, 1711, 1670, 1598, 1503, 1260, 1095 cm$^{-1}$

(8) Complex splitting due to multiple C–F coupling interactions.
$^1$H NMR (500 MHz, CDCl$_3$) δ 9.52 (s, 1H), 9.17 (s, 1H), 8.26 (d, $J = 7.5$ Hz, 1H), 8.19 (d, $J = 7.5$ Hz, 1H), 8.13 (d, $J = 8.4$ Hz, 1H), 8.05–8.03 (m, 1H), 7.94 (d, $J = 7.7$ Hz, 1H), 7.90–7.88 (m, 6H), 7.77 (d, $J = 8.2$ Hz, 1H), 7.71 (d, $J = 8.2$ Hz, 1H), 6.97 (t, $J = 7.7$ Hz, 1H), 5.59 (d, $J = 7.7$ Hz, 1H), 5.31 (d, $J = 7.7$ Hz, 1H), 3.00–2.90 (m, 2H), 2.35 (qt, $J = 13.1$, 6.3 Hz, 2H), 2.00 (dt, $J = 11.3$, 5.9 Hz, 2H).

$^{13}$C NMR (125 MHz, CDCl$_3$, DEPT) δ 169.1 (C), 167.8 (C), 142.8 (C), 141.2 (CH), 134.3 (C), 134.2 (C), 133.2 (C), 132.2 (C), 131.4 (C), 130.8 (CH), 129.9 (CH), 129.9 (CH), 128.9 (CH), 126.9 (C), 126.7 (CH), 126.6 (CH), 126.49 (C), 126.46 (CH), 126.3 (CH), 125.9 (CH), 125.8 (CH), 125.6 (CH), 121.3 (CH), 120.8 (CH), 120.4 (CH), 119.5 (CH), 111.8 (C), 94.1 (C), 78.8 (CH), 78.0 (CH), 35.1 (CH$_2$), 31.4 (CH$_2$), 20.01 (CH$_2$).

HRMS (ESI+) 677.0908 calculated for C$_{34}$H$_{27}$IN$_2$NaO$_4$ found 677.0914

$[\alpha]_{D}^{26} = 51.6$ (c 0.01, EtOAc)

(4$R$,5$R$)-2-(2-iodophenyl)-2-methyl-1,3-dioxolane-4,5-dicarboxylic acid (S1).

Using general procedure A, S1 was synthesized from commercially available 2-iodoacetophenone. A yellow solid was obtained (38% yield).

IR (thin film) 3405, 3059, 2991, 2933, 1727, 1605, 1426, 1191, 1085 cm$^{-1}$

$^1$H NMR (300 MHz, CD$_3$OD): δ 7.92 (dd, $J = 7.8$, 1.2 Hz, 1H), 7.87 (dd, $J = 7.9$, 1.7 Hz, 1H), 7.33 (td, $J = 7.6$, 1.1 Hz, 1H), 6.96 (td, $J = 7.6$, 1.7 Hz, 1H), 5.04 (bs, exchangeable OHs), 4.61 (d, $J = 8.0$ Hz, 1H), 4.39 (d, $J = 8.0$ Hz, 1H), 1.84 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$, DEPT) δ 173.4 (C), 173.1 (C), 144.8 (CH), 143.2 (C), 130.8 (CH), 129.4 (CH), 128.8 (CH), 112.5 (C), 93.5 (C), 78.4 (CH), 77.5 (CH), 26.6 (CH$_3$).

HRMS (ESI–) 376.9528 calculated for C$_{12}$H$_{10}$IO$_6$ found 376.9483

$[\alpha]_{D}^{26} + 28.6$ (c 0.03, MeOH)

(4$R$,5$R$)-2-(2-iodophenyl)-$N^4$, $N^6$-dimesityl-2-methyl-1,3-dioxolane-4,5-dicarboxamide (S2).

Compound S2 was synthesized from S1 using general procedure B and purified by flash column chromatography (1:0 hexanes → 4:1 hexanes/EtOAc) to obtain a brown solid (81% yield).

IR (thin film) 3358, 3269, 2919, 1695, 1506, 1189 cm$^{-1}$

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.96 (s, 1H), 8.48 (s, 1H), 7.94 (dd, $J = 7.9$, 1.2 Hz, 1H), 7.89 (dd, $J = 7.9$, 1.7 Hz, 1H), 7.43 (td, $J = 7.6$, 1.2 Hz, 1H), 7.02 (td, $J = 7.6$, 1.8 Hz, 1H), 6.88 (s, 2H),
6.84 (s, 2H), 4.94 (d, J = 8.3 Hz, 1H), 4.77 (d, J = 8.3 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 2.22 (s, 6H), 2.07 (s, 3H), 1.87 (bs, 6H).

13C NMR (75 MHz, CDCl3, DEPT) δ 169.1 (C), 165.5 (C), 142.9 (C), 142.6 (CH), 137.6 (C), 136.9 (C), 135.0 (C), 134.8 (C), 130.5 (CH), 129.5 (C), 129.1 (CH), 129.0 (CH), 127.4 (CH), 112.5 (C), 93.7 (C), 78.4 (CH), 77.3 (CH), 26.6 (CH3), 21.1 (CH3), 18.6 (CH3), 18.0 (CH3).

HRMS (ESI+) 635.1277 calculated for C30H33IN2NaO4 found 635.1418

[α]D25 + 12.3 (c 0.01, EtOAc)

(4R,5R)-2-(2-iodophenyl)-2-phenyl-1,3-dioxolane-4,5-dicarboxylic acid (S3).

Using general procedure A, S3 was synthesized from known compound 2-iodoacetophenone.9 A beige solid was obtained (37% yield).

IR (thin film) 3061, 2627, 1733, 1450, 1248, 1202, 1105 cm⁻¹

1H NMR (300 MHz, CD3OD) δ 7.93 (dd, J = 7.8, 1.2 Hz, 1H), 7.86 (dd, J = 7.8, 1.7 Hz, 1H), 7.45–7.37 (m, 3H), 7.32–7.30 (m, 3H), 7.03 (td, J = 7.6, 1.7 Hz, 1H), 5.06 (bs, exchangeable OHs), 4.88 (d, J = 6.9 Hz, 1H), 4.82 (d, J = 6.9 Hz, 1H).

13C NMR (75 MHz, CDCl3, DEPT) δ 171.8 (C), 171.6 (C), 143.3 (CH), 143.0 (C), 140.5 (C), 131.28 (CH), 130.3 (CH), 129.9 (CH), 129.8 (CH), 128.8 (CH), 128.4 (CH), 114.1 (C), 96.2 (C), 78.8 (CH), 78.1 (CH).

HRMS (ESI–) 438.9684 calculated for C17H12IO6 found 438.9621

[α]D25 + 22.0 (c 0.01, EtOH)

(4R,5R)-2-(2-iodophenyl)-N4,N5-dimesityl-2-phenyl-1,3-dioxolane-4,5-dicarboxamide (S4).

Using general procedure B, S4 was synthesized from S3 and purified by flash column chromatography (1:0 → 4:1 hexanes/EtOAc) to afford a beige solid (55% yield).

IR (thin film) 3370, 3267, 3059, 2919, 2857, 1699, 1506, 1201, 1100 cm⁻¹

1H NMR (300 MHz, CDCl3) δ 8.53 (s, 1H), 8.39 (s, 1H), 8.03 (dd, J = 7.8, 1.7 Hz, 1H), 7.94 (dd, J = 7.8, 1.2 Hz, 1H), 7.53–7.45 (m, 3H), 7.39–7.34 (m, 3H), 7.08 (td, J = 7.6, 1.7 Hz, 1H), 6.87 (s, 2H), 6.84 (s, 2H), 5.18 (d, J = 7.6 Hz, 1H), 5.07 (d, J = 7.6 Hz, 1H), 2.25 (d, J = 3.9 Hz, 6H), 2.16 (s, 6H), 1.92 (s, 6H).

\[ ^{13}\text{C}\text{ NMR} (75 \text{ MHz, CDCl}_3, \text{ DEPT}) \delta 168.0 (\text{C}), 166.1 (\text{C}), 142.6 (\text{CH}), 141.4 (\text{C}), 138.4 (\text{C}), 137.4 (\text{C}), 137.1 (\text{C}), 135.0 (\text{C}), 134.9 (\text{C}), 130.9 (\text{CH}), 130.3 (\text{C}), 129.8 (\text{C}), 129.5 (\text{CH}), 129.1 (\text{CH}), 128.6 (\text{CH}), 128.3 (\text{CH}), 127.8 (\text{CH}), 113.5 (\text{C}), 95.8 (\text{C}), 79.1 (\text{CH}), 78.3 (\text{CH}), 21.0 (\text{CH}_3), 18.6 (\text{CH}_3), 18.2 (\text{CH}_3).\]

\[ \text{HRMS (ESI+)} 697.1534 \text{ calculated for C}_{35}\text{H}_{35}\text{IN}_2\text{NaO}_4 \text{ found 697.1580}\]

\[ [\alpha]^{25}_D + 44.0 (c 0.004, \text{EtOAc})\]

(4R,5R)-2-(1-iodonaphthalen-2-yl)-2-methyl-1,3-dioxolane-4,5-dicarboxylic acid (S5).

**Synthesis of Phenol Substrates**

Substrates 4a–f were synthesized as previously described.\(^{11}\)

2-(\text{tert}-\text{butyldimethylsilyl})-4-methylphenol (4g).\(^{12}\)

Into a round bottom flask was placed commercially available 2-bromo-4-methyl phenol (1.96 g, 10.5 mmol), imidazole (0.93 g, 13.6 mmol) and DCM (12 mL) and cooled to 0 °C. The TBS-Cl (1.9 g, 12.6 mmol) was then added and the reaction stirred overnight, allowing to slowly warm to r.t. The DCM was removed in vacuo, giving a colorless oil. Into the same flask

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was added THF (30 mL) and the solution was cooled to –78 °C under N₂. To this, n-BuLi (2.5 M, 4.2 mL) was slowly added. The reaction was allowed to slowly warm to r.t. and after 2 h was quenched with saturated aq. NH₄Cl. The mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (1:0 hexanes → 9:1 hexanes/EtOAc) to give a pale yellow oil (1.99 g, 86% yield).

IR (thin film) 3537, 2953, 2927, 2855, 1493, 1388, 1254, 822 cm⁻¹

¹H NMR (300 MHz, CDCl₃) δ 7.15 (d, J = 2.2 Hz, 1H), 7.05 (dd, J = 8.1, 2.3 Hz, 1H), 6.62 (d, J = 8.1 Hz, 1H), 4.68 (s, 1H), 2.30 (s, 3H), 0.94 (s, 9H), 0.34 (s, 6H).

¹³C NMR (75 MHz, CDCl₃, DEPT) δ 158.5 (C), 137.2 (CH), 131.3 (CH), 129.1 (C), 122.5 (C), 114.9 (CH), 27.0 (CH₃ × 3), 20.7 (CH₃), 17.7 (C), -4.6 (CH₃ × 2).

LRMS (ESI+) 221.14 calculated for C₁₃H₂₁NaOSi found 221.19

4-methyl-2-(triisopropylsilyl)phenol (4h).

Phenol 4h was synthesized from 2-bromo-4-methyl phenol in the same fashion as 4g, except that TIPS-Cl was used instead of TBS-Cl. A white solid (30% yield) was obtained after purification by flash column chromatography (50:1 hexanes/EtOAc).

IR (thin film) 3522, 2942, 2861, 1492, 1386, 1175 cm⁻¹

¹H NMR (300 MHz, CDCl₃) δ 7.17 (d, J = 2.1 Hz, 1H), 7.03 (dd, J = 8.1, 2.2 Hz, 1H), 6.59 (d, J = 8.1 Hz, 1H), 4.53 (s, 1H), 2.28 (s, 3H), 1.48 (sept, J = 7.5 Hz, 3H), 1.10 (d, J = 7.4 Hz, 18H).

¹³C NMR (75 MHz, CDCl₃, DEPT) δ 158.6 (C), 137.2 (CH), 130.9 (CH), 129.1 (C), 120.3 (C), 114.8 (CH), 19.03 (CH₃ × 7), 11.8 (CH × 3).

HRMS (ESI+) 263.1837 calculated for C₁₆H₂₇NaOSi found 263.1211

4-isopropyl-2-(trimethylsilyl)phenol (4i).

Phenol 4g was synthesized from commercially available 2-bromo-4-isopropyl phenol. A colorless oil (61% yield) was obtained after purification by flash column chromatography (95:5 hexanes/EtOAc).

IR (thin film) 3535, 2958, 2898, 2870, 11596, 1403, 1314, 1245, 1074, 862, 838 cm⁻¹

¹H NMR (300 MHz, CDCl₃) 7.29 (d, J = 2.0 Hz, 1H), 7.17 (dd, J = 8.2, 2.3 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 4.84 (d, J = 3.3 Hz, 1H), 2.93 (hept, J = 6.9 Hz, 1H), 1.31 (d, J = 6.9 Hz, 6H), 0.41 (s, 9H).

¹³C NMR (75 MHz, CDCl₃, DEPT) δ 158.5 (C), 140.7 (C), 133.5 (CH), 128.4 (CH), 125.2 (C), 114.5 (CH), 33.5 (CH), 24.5 (CH₃ × 2), -0.72 (CH₃ × 3).
2-(tert-butylidimethylsilyl)-4-isopropylphenol (4j).\textsuperscript{12}

\[
\text{TBS} \quad \text{OH} \quad \text{OH}
\]

Into a round bottom flask was placed commercially available 2-bromo-4-isopropylphenol (763 mg, 3.55 mmol), imidazole (314 mg, 4.61 mmol) and DCM (3.5 mL) and cooled to 0 °C. The TBS-Cl (64 mg, 4.3 mmol) was then added and the reaction stirred overnight, allowing to slowly warm to r.t. The DCM was removed in vacuo, giving a colorless oil. Into the same flask was added THF (20 mL) and the solution was cooled to –78 °C under N\textsubscript{2}. To this, n-BuLi (2.5 M, 1.4 mL) was slowly added. The reaction was allowed to slowly warm to r.t. and after 2 h was quenched with saturated aq. NH\textsubscript{4}Cl. The mixture was extracted with EtOAc and the combined organic layers were washed with brine, dried over Na\textsubscript{2}SO\textsubscript{4}, filtered, and concentrated under reduced pressure. The crude oil was purified by flash column chromatography (1:0 hexanes → 9:1 hexanes/EtOAc) to give a pale yellow oil (696 mg, 78% yield).

IR (thin film) 3610, 3011, 2957, 2927, 2856, 1595, 1487, 1402, 1314, 1176, 1073 cm\textsuperscript{-1}

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) δ 7.20 (d, J = 2.3 Hz, 1H), 7.11 (dd, J = 8.2, 2.3 Hz, 1H), 6.64 (d, J = 8.2 Hz, 1H), 4.67 (s, 1H), 2.87 (hept, J = 6.9 Hz, 1H), 1.24 (d, J = 6.9 Hz, 6H), 0.93 (s, 9H), 0.35 (s, 6H).

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}, DEPT) δ 158.7 (C), 140.3 (C), 134.8 (CH), 128.4 (CH), 122.3 (C), 114.8 (CH), 33.5 (CH), 26.9 (CH\textsubscript{3} × 3), 24.4 (CH\textsubscript{3} × 2), 17.8 (C), -4.6 (CH\textsubscript{3} × 2).

LRMS (CI) 251 calculated for C\textsubscript{15}H\textsubscript{27}OSi\textsuperscript{+} found 251

2-(tert-butylidimethylsilyl)-4-(3-hydroxypropyl)phenol (9).

\[
\text{TBS} \quad \text{OH} \quad \text{OH}
\]

Into a vial was placed 3-(3-bromo-4-hydroxyphenyl)propanoic acid (206 mg, 0.841 mmol) and dissolved in THF (4 mL). At 0 °C, BH\textsubscript{3}•S(CH\textsubscript{3})\textsubscript{2} (110 µL) was added dropwise. The mixture was stirred for 2 h and MeOH was then added slowly until bubbling ceased. The mixture was diluted with EtOAc and washed with brine (3 × 2 mL), dried with Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. The crude oil was dissolved in DCM (1 mL), cooled to 0 °C and treated with imidazole (143 mg, 2.10 mmol) followed by TBS-Cl (317 mg, 2.10 mmol). The mixture stirred overnight, slowly warming to rt. After such time, the mixture was diluted with EtOAc and filtered over a plug of celite. The solvent was removed and the crude oil was stirred in THF (5 mL) and cooled to –98 °C under N\textsubscript{2}. n-BuLi (400 µL) was added slowly dropwise. The mixture was allowed to warm to rt slowly and stir for 1 h. After such time, a saturated solution of NH\textsubscript{4}Cl was added and the product extracted with EtOAc (3 × 3 mL). The combined organic layers were washed with brine, dried with Na\textsubscript{2}SO\textsubscript{4}, filtered and concentrated. The crude product was dissolved in ethanol (8 mL) and pyridinium p-toluenesulfonate (21 mg, 0.084 mmol) was added and the mixture stirred rt overnight. After such time, the ethanol was removed in vacuo and the product was purified by flash column chromatography (4:1 hexanes/EtOAc). A white solid was obtained (66.0 mg) in 29% yield over four steps.

IR (thin film) 3335, 2951, 2928, 2855, 1509, 1471, 1401, 1254, 836 cm\textsuperscript{-1}

20
\[^1\text{H}\text{ NMR}\ (500\text{ MHz}, \text{CDCl}_3)\ \delta\ 7.14\ (s,\ 1\text{H}),\ 7.05\ (d,\ J = 8.1\text{ Hz},\ 1\text{H}),\ 6.62\ (dd,\ J = 8.1,\ 1.9\text{ Hz},\ 1\text{H}),\ 4.82\ (s,\ 1\text{H}),\ 3.69\text{-}3.68\ (m,\ 2\text{H}),\ 2.63\ (t,\ J = 6.8\text{ Hz},\ 2\text{H}),\ 1.86\ (\text{quintet},\ J = 6.6\text{ Hz},\ 2\text{H}),\ 0.90\ (s,\ 9\text{H}),\ 0.32\ (s,\ 6\text{H}).\]

\[^{13}\text{C}\text{ NMR}\ (125\text{ MHz}, \text{CDCl}_3, \text{DEPT})\ \delta\ 159.0\ (\text{C}),\ 136.6\ (\text{CH}),\ 133.1\ (\text{C}),\ 130.6\ (\text{CH}),\ 122.7\ (\text{C}),\ 115.0\ (\text{CH}),\ 62.6\ (\text{CH}_2),\ 34.8\ (\text{CH}_2),\ 31.5\ (\text{CH}_2),\ 27.0\ (\text{CH}_3 \times 3),\ 17.8\ (\text{C}),\ -4.6\ (\text{CH}_3 \times 2).\]

HRMS (ESI+) 289.1594 calculated for C_{15}H_{26}NaO_{2}Si found 289.1595

**Synthesis of Racemic Quinols**

Quinols 5a, 5b, 5c, 5e, and 5f were prepared as previously described.\(^{11}\)

**2-chloro-4-hydroxy-4-methylcyclohexa-2,5-dienone (5d).**

Commercially available 2-chloro-4-methyl phenol (20 µL, 0.16 mmol) was dissolved in a mixture of MeCN/H_2O (0.17 M, 2:1). (Diacetoxyiodo)benzene (56 mg, 0.17 mmol) was added and the mixture was stirred r.t. overnight. The mixture was then quenched with saturated aq. NaHCO_3 and extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (4:1 hexanes/EtOAc) and a yellow crystalline solid (18 mg, 67% yield) was isolated.

IR (thin film) 3406, 3047, 2981, 2930, 1673, 1644, 1603, 1130, 1057 cm\(^{-1}\)

\[^1\text{H}\text{ NMR}\ (300\text{ MHz}, \text{CDCl}_3)\ \delta\ 7.05\ (d,\ J = 2.9\text{ Hz},\ 1\text{H}),\ 6.90\ (dd,\ J = 10.0,\ 2.9\text{ Hz},\ 1\text{H}),\ 6.21\ (d,\ J = 10.0\text{ Hz},\ 1\text{H}),\ 2.44\ (s,\ 1\text{H}),\ 1.53\ (s,\ 4\text{H}).\]

\[^{13}\text{C}\text{ NMR}\ (75\text{ MHz}, \text{CDCl}_3, \text{DEPT})\ \delta\ 178.5\ (\text{C}),\ 152.4\ (\text{CH}),\ 148.0\ (\text{CH}),\ 131.7\ (\text{C}),\ 126.2\ (\text{CH}),\ 69.4\ (\text{C}),\ 26.8\ (\text{CH}_3).\]

HRMS (ESI+) 181.0027 calculated for C_7H_7ClNaO_2^+ found 181.0021

**2-(tert-butyldimethylsilyl)-4-hydroxy-4-methylcyclohexa-2,5-dienone (5g).**

Into a 1 dram vial was placed 4g (48.1 mg, 0.22 mmol) and 4-iodotoluene (10 mol %, 7 mg) in a mixture of acetonitrile/H_2O (1.3 mL, 9:1). Last was added m-CPBA (107 mg, 0.41 mmol) and the mixture was capped and stirred overnight at r.t. After such time, the reaction was quenched with 10% aq Na_2S_2O_3 (1 mL) and stirred 5 min before saturated aq. NaHCO_3 (1 mL) was added. The mixture was extracted with EtOAc (3 × 1 mL) and the combined organic layers were washed with brine, dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (5:1 hexanes/EtOAc). A white solid was obtained (23.5 mg, 46% yield).
IR (thin film) 3384, 2954, 2928, 2856, 1655, 1618, 1363, 1249, 1058, 838 cm⁻¹

¹H NMR (500 MHz, CDCl₃) δ 7.04 (d, J = 2.9 Hz, 1H), 6.82 (dd, J = 10.0, 2.9 Hz, 1H), 6.08 (d, J = 10.0 Hz, 1H), 2.11 (s, 1H), 1.45 (s, 3H), 0.87 (s, 9H), 0.17 (app d, 6H).

¹³C NMR (125 MHz, CDCl₃, DEPT) δ 188.0 (C), 161.6 (CH), 150.6 (CH), 137.6 (C), 128.4 (CH), 67.1 (C), 27.3 (CH₃), 27.2 (CH₃ × 3), 17.0 (C), -5.2 (CH₃), -5.3 (CH₃).

HRMS (ESI+) 261.1281 calculated for C₁₃H₂₂NaO₂Si found 261.1297

4-hydroxy-4-methyl-2-(triisopropylsilyl)cyclohexa-2,5-dienone (5h).

Dienone 5h was synthesized from 4h in the same fashion as 5g. A white solid (59% yield) was obtained after purification by flash column chromatography (5:1 hexanes/EtOAc).

IR (thin film) 3383, 2944, 2889, 2866, 1654, 1617, 1464, 1228, 883 cm⁻¹

¹H NMR (500 MHz, CDCl₃) δ 7.08 (d, J = 2.2 Hz, 1H), 6.83 (dd, J = 10.0, 2.2 Hz, 1H), 6.09 (d, J = 10.0 Hz, 1H), 2.24 (bs, 1H), 1.45 (s, 3H), 1.36 (dt, J = 7.5 Hz, 3H), 1.03 (dd, J = 7.3, 2.5 Hz, 18H).

¹³C NMR (75 MHz, CDCl₃, DEPT) δ 188.6 (C), 162.6 (CH), 150.6 (CH), 135.0 (C), 128.4 (CH), 67.2 (C), 27.5 (CH₃), 18.9 (CH₃ × 6), 11.2 (CH × 3).

HRMS (ESI+) 303.1751 calculated for C₁₆H₂₈NaO₂Si found 303.1749

4-hydroxy-4-isopropyl-2-(trimethylsilyl)cyclohexa-2,5-dienone (5i).

Dienone 5i was synthesized from 4i in the same fashion as 5d, except that a mixture of 3:1 acetonitrile-H₂O was used. A white crystalline solid (55% yield) was obtained after purification by flash column chromatography (9:1 hexanes/EtOAc).

IR (thin film) 3373, 2961, 2549, 1694, 1650, 1304, 1263, 844 cm⁻¹

¹H NMR (300 MHz, CDCl₃) δ 6.93 (d, J = 3.2 Hz, 1H), 6.76 (dd, J = 10.1, 3.2 Hz, 1H), 6.19 (d, J = 10.1 Hz, 1H), 2.13 (bs, 1H), 1.97 (hept, 6.9 Hz, 1H), 0.95 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H), 0.18 (s, 9H).

¹³C NMR (75 MHz, CDCl₃, DEPT) δ 188.7 (C), 158.0 (CH), 149.0 (CH), 141.7 (C), 130.1 (CH), 72.1 (C), 36.9 (CH), 17.2 (CH₃ × 3), 17.3 (CH₃), 17.1 (CH₃), -1.38 (CH₃ × 3).

HRMS (ESI+) 247.1125 calculated for C₁₂H₂₀NaO₂Si¹ found 247.1141
2-(tert-butyldimethylsilyl)-4-hydroxy-4-isopropylcyclohexa-2,5-dienone (5j).

Dienone 5j was synthesized from 4j in the same fashion as 5g. A white crystalline solid (61% yield) was obtained after purification by flash column chromatography (1:0 → 9:1 hexanes/EtOAc).

**IR** (thin film) 3385, 2958, 2928, 2881, 2856, 1653, 1617, 1470, 1363, 1249, 1004, 838 cm\(^{-1}\)

**\(^1\)H NMR** (300 MHz, CDCl\(_3\)) \(\delta\) 6.97 (d, \(J = 3.2\) Hz, 1H), 6.74 (dd, \(J = 10.1, 3.2\) Hz, 1H), 6.18 (d, \(J = 10.1\) Hz, 1H), 2.05 (bs, 1H), 1.97 (hept, \(J = 6.9\) Hz, 1H), 0.94 (app t, \(J = 6.9\) Hz, 3H), 0.89 (s, 9H), 0.17 (s, 3H), 0.15 (s, 3H).

**\(^{13}\)C NMR** (75 MHz, CDCl\(_3\), DEPT) \(\delta\) 188.4 (C), 159.9 (CH), 148.4 (CH), 139.9 (C), 130.3 (CH), 72.3 (C), 36.9 (CH), 27.3 (CH\(_3\) \times 3), 17.3 (CH\(_3\)), 17.1 (CH\(_3\)), 17.0 (C), -5.1 (CH\(_3\)), -5.2 (CH\(_3\)).

**HRMS** (ESI+) 289.1594 calculated for C\(_{15}\)H\(_{26}\)NaO\(_2\)Si\(^+\) found 289.1593

7-(tert-butyldimethylsilyl)-1-oxaspiro[4.5]deca-6,9-dien-8-one (10).

Spirocycle 10 was obtained from 9 in the same fashion as 5g except that MeCN was used as the solvent. A white solid was obtained in 34% yield after purification by flash column chromatography (6:1 hexanes/EtOAc).

**IR** (thin film) 2953, 2927, 2856, 1656, 1628, 1248, 1229, 1035, 835 cm\(^{-1}\)

**\(^1\)H NMR** (500 MHz, CDCl\(_3\)) \(\delta\) 6.95 (d, \(J = 3.1\) Hz, 1H), 6.76 (dd, \(J = 10.0, 3.1\) Hz, 1H), 6.08 (dd, \(J = 10.0, 0.6\) Hz, 1H), 4.08 (t, \(J = 6.9\) Hz, 2H), 2.15 (quintet, \(J = 6.9\) Hz, 2H), 2.02 (t, \(J = 7.2\) Hz, 2H), 0.87 (s, 9H), 0.16 (s, 6H).

**\(^{13}\)C NMR** (125 MHz, CDCl\(_3\), DEPT) \(\delta\) 188.4 (C), 159.5 (CH), 148.4 (CH), 137.6 (C), 128.2 (CH), 77.35 (C), 69.4 (CH\(_2\)), 37.6 (CH\(_2\)), 27.3 (CH\(_3\) \times 3), 27.1 (CH\(_2\)), 17.0 (C), -5.3 (CH\(_3\) \times 2).

**HRMS** (ESI+) 287.1438 calculated for C\(_{15}\)H\(_{26}\)NaO\(_2\)Si found 287.1429
General Procedure for the Synthesis of Enantioenriched Quinols 5a–h

Into a 1 dram vial was placed phenol 4 (0.165 mmol) and iodine catalyst 8 (10 mol %) in a mixture of acetonitrile/H\textsubscript{2}O (0.16 M, 9:1). Last was added \textit{m}-CPBA (2.2 equiv) and the mixture was stirred overnight at r.t. After such time, the reaction was quenched with 10% aq Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (1 mL) and stirred 5 min before saturated aq. NaHCO\textsubscript{3} (1 mL) was added. The mixture was extracted with EtOAc (3 × 1 mL) and the combined organic layers were washed with brine, dried (Na\textsubscript{2}SO\textsubscript{4}), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:0 → 9:1 hexanes/EtOAc) to afford quinol 5.

Procedure for the synthesis of O\textsuperscript{18} labeled quinol 5a

Into a 1 dram vial was placed phenol 4a (0.165 mmol, 19 \(\mu\)L) and iodine catalyst 8e (10 mol %, 11.0 mg) in a mixture of acetonitrile (0.9 mL) and \textsuperscript{18}O labeled water (0.1 mL). Last was added \textit{m}-CPBA (0.364 mmol, 81.6 mg) and the mixture was stirred overnight at r.t. After such time, the reaction was quenched with 10% aq Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3} (1 mL) and stirred 5 min before saturated aq. NaHCO\textsubscript{3} (1 mL) was added. The mixture was extracted with EtOAc (3 × 1 mL) and the combined organic layers were washed with brine, dried (Na\textsubscript{2}SO\textsubscript{4}), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:0 → 6:1 hexanes/EtOAc) to afford quinol 5a\textsuperscript{*} (9.5 mg, 41% yield) as a beige solid.
**Stoichiometric Iodine Experiment**

![Reaction Scheme](image)

A literature procedure was adapted.\(^{13}\) Aryl iodide 8a (103 mg, 0.255 mmol) was stirred in acetic acid (0.25 mL) at rt. To this was added \(m\)-CPBA (63 mg, 0.280 mmol) and the homogenous mixture stirred for 2 h. After such time, the mixture became heterogeneous and was filtered. The filtrate was dried under vacuum to obtain a yellow solid, which was subsequently dissolved in a mixture of acetonitrile (440 \(\mu\)L) and water (50 \(\mu\)L). The mixture was treated with an excess of 2-bromo-4-methylphenol and stirred rt for 4 h. After such time, the reaction was quenched with 10% aq \(\text{Na}_2\text{S}_2\text{O}_3\) (1 mL) and stirred 5 min before saturated aq. \(\text{NaHCO}_3\) (1 mL) was added. The mixture was extracted with EtOAc (3 \(\times\) 1 mL) and the combined organic layers were washed with brine, dried (\(\text{Na}_2\text{SO}_4\)), filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography (1:0 \(\rightarrow\) 9:1 hexanes/EtOAc) to afford quinol 5.

\(^{13}\) M. Iinuma, K. Moriyama, and H. Togo, *Synlett* 2012, **23**, 2663.
Labelled Water Experiment Results – Mass Spectrum (Cl with MeOH)

Electronic Supplementary Material (ESI) for Chemical Communications
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<table>
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HPLC Traces

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5d with catalyst 8e:

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<td>49.8</td>
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5f with catalyst 8e:

<table>
<thead>
<tr>
<th>Retention Time (min)</th>
<th>Area Percent</th>
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</thead>
<tbody>
<tr>
<td>9.8</td>
<td>69.2</td>
</tr>
<tr>
<td>11.3</td>
<td>30.8</td>
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</tbody>
</table>
5g – racemic:

<table>
<thead>
<tr>
<th>Retention Time (min)</th>
<th>Area Percent</th>
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<tbody>
<tr>
<td>12.0</td>
<td>50.4</td>
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<tr>
<td>13.3</td>
<td>49.6</td>
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5g with catalyst 8e:

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<th>Area Percent</th>
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5h – racemic:

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<td>21.7</td>
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<tr>
<td>23.0</td>
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</table>

5h with catalyst 8e:

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<tbody>
<tr>
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<tr>
<td>22.9</td>
<td>64.3</td>
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</table>
5i – racemic:

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<th>Area Percent</th>
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<tbody>
<tr>
<td>11.8</td>
<td>49.3</td>
</tr>
<tr>
<td>12.7</td>
<td>50.7</td>
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</tbody>
</table>

5i with catalyst 8e:

<table>
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<tr>
<th>Retention Time (min)</th>
<th>Area Percent</th>
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<tbody>
<tr>
<td>11.5</td>
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<tr>
<td>12.2</td>
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5j – racemic:

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<th>Retention Time (min)</th>
<th>Area Percent</th>
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<tbody>
<tr>
<td>11.5</td>
<td>49.3</td>
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<tr>
<td>12.5</td>
<td>50.7</td>
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5j with catalyst 8e:

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<th>Retention Time (min)</th>
<th>Area Percent</th>
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<tr>
<td>11.3</td>
<td>37.0</td>
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<tr>
<td>12.0</td>
<td>63.0</td>
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10 – racemic:

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<th>Area Percent</th>
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<td>8.8</td>
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<td>49.9</td>
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10 with catalyst 8e:

<table>
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<tr>
<th>Retention Time (min)</th>
<th>Area Percent</th>
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</thead>
<tbody>
<tr>
<td>8.9</td>
<td>69.8</td>
</tr>
<tr>
<td>9.8</td>
<td>30.2</td>
</tr>
</tbody>
</table>
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8a
(CD$_3$OD, 300 MHz)
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Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013

8e
(CDCl₃, 75 MHz)
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The image contains a chemical structure labeled as 8f, along with a 1H NMR spectrum and a 13C NMR spectrum. The spectra are labeled with chemical shifts in ppm.

The chemical structure shows a molecule with multiple functional groups and substituents, including iodine (I), oxygen (O), and bromine (Br). The spectra provide detailed information about the chemical environment of the atoms in the molecule.

The spectra are obtained in CDCl₃ at 125 MHz, indicating high-resolution NMR analysis.
(CDCl₃, 125 MHz)
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8h (CDCl₃, 75 MHz)
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(CDC\textsubscript{3}, 500 MHz)
$^{13}$C NMR Spectra of Compound 8i (CDCl$_3$, 125 MHz)

- 20.01 ppm
- 31.41 ppm
- 35.11 ppm
- 76.91 ppm
- 77.16 ppm
- 77.41 ppm
- 78.04 ppm
- 78.78 ppm
- 94.13 ppm
- 111.81 ppm
- 119.50 ppm
- 120.37 ppm
- 120.80 ppm
- 121.28 ppm
- 125.64 ppm
- 125.84 ppm
- 125.88 ppm
- 126.15 ppm
- 126.33 ppm
- 126.46 ppm
- 126.49 ppm
- 126.61 ppm
- 126.67 ppm
- 126.93 ppm
- 128.87 ppm
- 129.91 ppm
- 130.83 ppm
- 131.40 ppm
- 132.16 ppm
- 133.23 ppm
- 134.21 ppm
- 134.29 ppm
- 141.22 ppm
- 142.79 ppm
- 167.76 ppm
- 169.09 ppm

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\[ \text{HO-} \]
\[ \text{O} \]  
\[ \text{O} \]
\[ \text{O} \]
\[ \text{HO} \]
\[ \text{Me} \]
\[ \text{S}1 \]
\[ (\text{CD}_3\text{OD, 75 MHZ}) \]
Electronic Supplementary Material (ESI) for Chemical Communications
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H\(^{+}\)

\(\text{O}^{2-}\)

\(\text{O}^{2-}\)

\(\text{OH}^{-}\)

\(\text{HO}^{-}\)

\(\text{S}^3\)

(CD$_3$OD, 75 MHz)
<table>
<thead>
<tr>
<th>ppm</th>
<th>200</th>
<th>160</th>
<th>120</th>
<th>80</th>
<th>40</th>
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<tbody>
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</tr>
</tbody>
</table>

![Chemical structure](image)

4g

(CDCl$_3$, 75 MHz)
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TIPS

(CDCl₃, 75 MHz)
(CDCl$_3$, 500 MHz)

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TIPS
O
Me
OH

5h
(CDCl₃, 500 MHz)
TIPS
Me
OH

(CDC\textsubscript{3}, 125 MHz)
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