

## Supplementary material

### Synthesis, Antioxidant, and Anti-inflammatory Activity of 3-Arylphthalides

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#### 1. Characterization of compounds 2, 3, 4c-4f

**Table S1.** <sup>1</sup>H NMR and <sup>13</sup>C NMR data of compounds 2, 3, 4c-4f

#### 2. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra of compounds 5a-5g

**Figure S1.** <sup>1</sup>H NMR spectrum (400 MHz, CD<sub>3</sub>COCD<sub>3</sub>) of compound 5a

**Figure S2.** <sup>13</sup>C NMR spectrum (100 MHz, CD<sub>3</sub>COCD<sub>3</sub>) of compound 5a

**Figure S3.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound 5b

**Figure S4.** <sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound 5b

**Figure S5.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound 5c

**Figure S6.** <sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound 5c

**Figure S7.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound 5d

**Figure S8.** <sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound 5d

**Figure S9.** <sup>1</sup>H NMR spectrum (400 MHz, CD<sub>3</sub>OD) of compound 5e

**Figure S10.** <sup>13</sup>C NMR spectrum (100 MHz, CD<sub>3</sub>OD) of compound 5e

**Figure S11.** <sup>1</sup>H NMR spectrum (400 MHz, CD<sub>3</sub>OD) of compound 5f

**Figure S12.** <sup>13</sup>C NMR spectrum (100 MHz, CD<sub>3</sub>OD) of compound 5f

**Figure S13.** <sup>1</sup>H NMR spectrum (500 MHz, CDCl<sub>3</sub>) of compound 5g

**Figure S14.** <sup>13</sup>C NMR spectrum (125 MHz, CDCl<sub>3</sub>) of compound 5g

#### 3. Figure S15. Proposed mechanism of racemization process in 5a

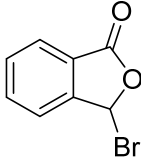
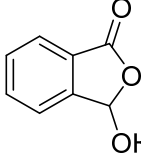
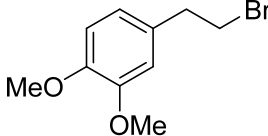
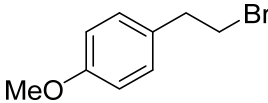
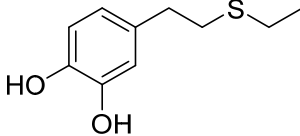
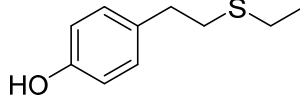
#### 4. Cell viability

**Figure S16.** Cell survival Bv.2 cells

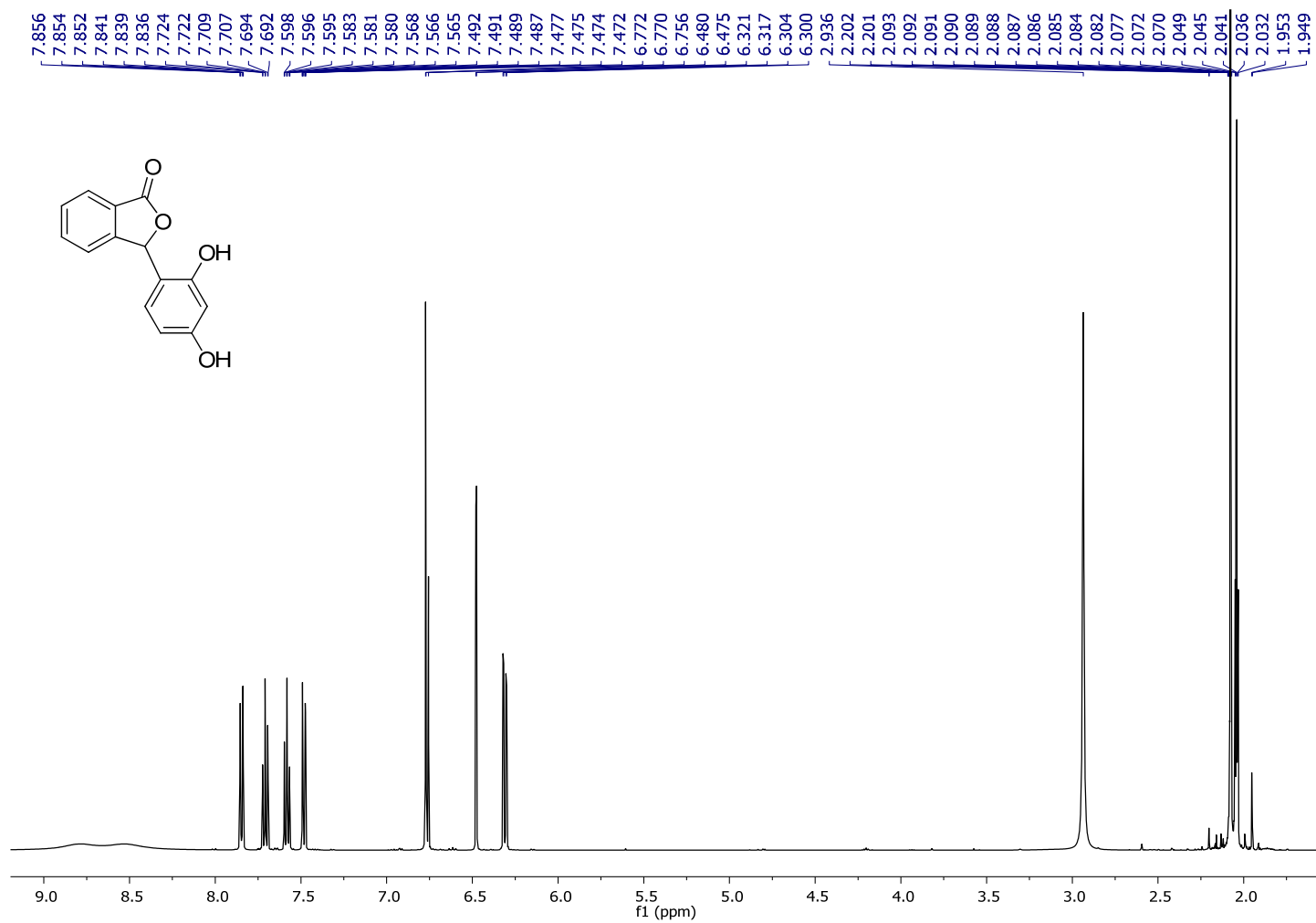
**Figure S17.** Cell survival RAW 264.7 cells

# 1. Characterization of compounds 2, 3, 4c-4f

Table S1

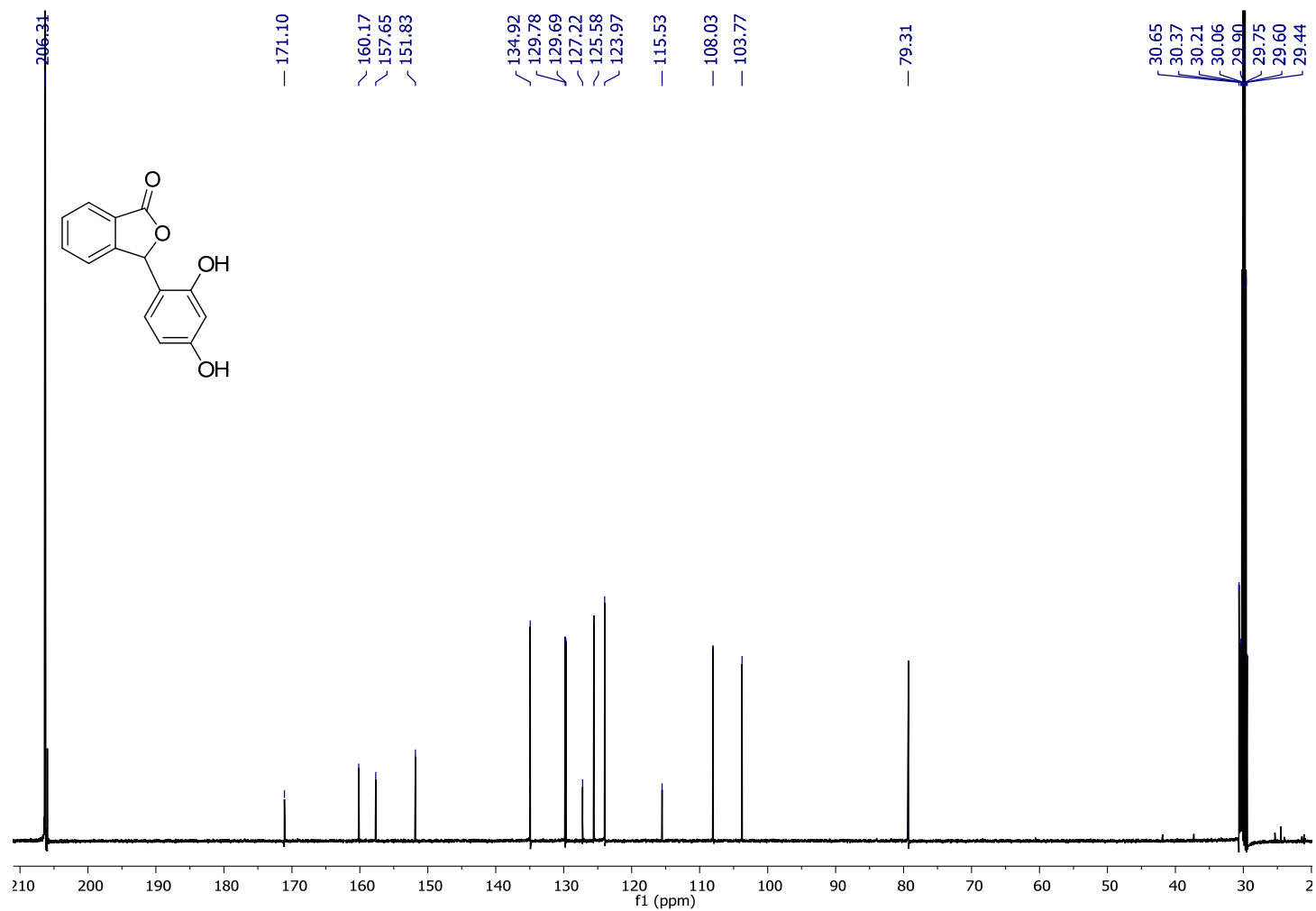
Compound	<sup>1</sup> H NMR and <sup>13</sup> C NMR data
3-bromophthalide ( <b>2</b> ): 	<sup>1</sup> H-NMR (CDCl <sub>3</sub> , 399.945 MHz): δ 7.94 (1H, brd, 7.5 Hz, H-7), δ 7.78 (1H, ddd, 7.3, 7.3, 1.1 Hz, H-6), δ 7.64 (1H, brd, 7.5 Hz, H-4), δ 7.62 (1H, dd, 7.6, 7.6 Hz, H-5), δ 7.40 (1H, s, H-3). <sup>13</sup> C-NMR (CDCl <sub>3</sub> , 100.576 MHz): δ 167.3 (s, C-1), δ 148.8 (s, C-3a), δ 135.2 (d, C-5), δ 130.9 (d, C-6), δ 125.9 (d, C-7), δ 124.1 (s, C-7a), δ 123.5 (d, C-4), δ 74.6 (d, C-3).
3-hydroxyphthalide ( <b>3</b> ): 	<sup>1</sup> H-NMR (CD <sub>3</sub> COCD <sub>3</sub> , 399.945 MHz): δ 7.84 (1H, brd, 8.0 Hz, H-7), δ 7.80 (1H, ddd, 7.5, 7.4, 1.0 Hz, H-5), δ 7.72 (1H, brd, 7.7 Hz, H-4), δ 7.66 (1H, brdd, 7.4, 7.4 Hz, H-6), δ 6.75 (1H, s, H-3). <sup>13</sup> C-NMR (CD <sub>3</sub> COCD <sub>3</sub> , 100.576 MHz): δ 169.1 (s, C-1), δ 147.9 (s, C-3a), δ 135.0 (d, C-5), δ 131.3 (d, C-6), δ 127.7 (s, C-7a), δ 125.3 (d, C-7), δ 124.3 (d, C-4), δ 98.7 (d, C-3).
1,2-dimethoxy-4-(2-bromoethyl)benzene ( <b>4c</b> ): 	<sup>1</sup> H-NMR (CDCl <sub>3</sub> , 399.945 MHz): δ 6.82 (1H, brd, 8.2 Hz, H-6), δ 6.76 (1H, dd, 8.2, 1.9 Hz, H-5), δ 6.72 (1H, brd, 1.9 Hz, H-3), δ 3.88 (3H, s, -OMe), δ 3.86 (3H, s, -OMe), δ 3.54 (2H, t, 7.6 Hz, H-2'), δ 3.10 (2H, t, 7.6 Hz, H-1'). <sup>13</sup> C-NMR (CDCl <sub>3</sub> , 100.576 MHz): δ 148.9 (s, C-2), δ 148.0 (s, C-1), δ 131.5 (s, C-4), δ 120.6 (d, C-5), δ 111.9 (d, C-3), δ 111.3 (d, C-6), δ 55.9 (2 x q, -OMe), δ 39.1 (t, C-1'), δ 33.2 (t, C-2').
1-(2-bromoethyl)-4-methoxybenzene ( <b>4d</b> ): 	<sup>1</sup> H-NMR (CD <sub>3</sub> OD, 399.945 MHz): δ 7.14 (2H, d, 8.6 Hz, H-3, H-5), δ 6.86 (2H, d, 8.6 Hz, H-2, H-6), δ 3.80 (3H, s, -OMe), δ 3.54 (2H, t, 7.6 Hz, H-2'), δ 3.12 (2H, t, 7.6 Hz, H-1'). <sup>13</sup> C-NMR (CD <sub>3</sub> OD, 100.576 MHz): δ 158.5 (s, C-4), δ 131.0 (s, C-1), δ 129.6 (s, C-3, C-5), δ 114.0 (d, C-2, C-6), δ 55.2 (q, -OMe), δ 38.6 (t, C-1'), δ 33.4 (t, C-2').
4-(2-(ethylthio)ethyl)benzene-1,2-diol ( <b>4e</b> ): 	<sup>1</sup> H-NMR (CDCl <sub>3</sub> , 399.945 MHz): δ 6.79 (1H, d, 8.4 Hz, H-6), δ 6.73 (1H, d, 1.7 Hz, H-3), δ 6.63 (1H, dd, 8.0, 1.9 Hz, H-5), δ 2.76-2.72 (4H, m, H-1' y H-2'), δ 2.57 (2H, q, 7.2 Hz, -CH <sub>2</sub> CH <sub>3</sub> ), δ 1.25 (3H, t, 7.6 Hz, -CH <sub>2</sub> CH <sub>3</sub> ). <sup>13</sup> C-NMR (CDCl <sub>3</sub> , 100.576 MHz): δ 143.6 (s, C-2), δ 142.0 (s, C-1), δ 133.7 (s, C-4), δ 120.8 (d, C-5), δ 115.6 (d, C-6), δ 115.4 (d, C-3), δ 35.5 (t, C-2'), δ 33.3 (t, C-1'), δ 26.0 (t, -CH <sub>2</sub> CH <sub>3</sub> ), δ 14.7 (q, -CH <sub>2</sub> CH <sub>3</sub> ).
4-(2-(ethylthio)ethyl)phenol ( <b>4f</b> ): 	<sup>1</sup> H-NMR (CDCl <sub>3</sub> , 399.945 MHz): δ 7.07 (2H, d, 8.8 Hz, H-3, H-5), δ 6.76 (2H, d, 8.8 Hz, H-2, H-6), δ 2.82 (2H, m, H-1'), δ 2.74 (2H, m, H-2'), δ 2.55 (2H, q, 7.6 Hz, -CH <sub>2</sub> CH <sub>3</sub> ), δ 1.26 (3H, t, 7.6 Hz, -CH <sub>2</sub> CH <sub>3</sub> ). <sup>13</sup> C-NMR (CDCl <sub>3</sub> , 100.576 MHz): δ 154.0 (s, C-1), δ 132.9 (s, C-4), δ 129.6 (d, C-3, C5), δ 115.3 (d, C-2, C-6), δ 35.4 (t, C-1'), δ 33.4 (t, C-2'), δ 26.1 (t, -CH <sub>2</sub> CH <sub>3</sub> ), δ 14.7 (q, -CH <sub>2</sub> CH <sub>3</sub> ).

## 2. $^1\text{H}$ NMR and $^{13}\text{C}$ NMR spectra of compounds 5a-5g



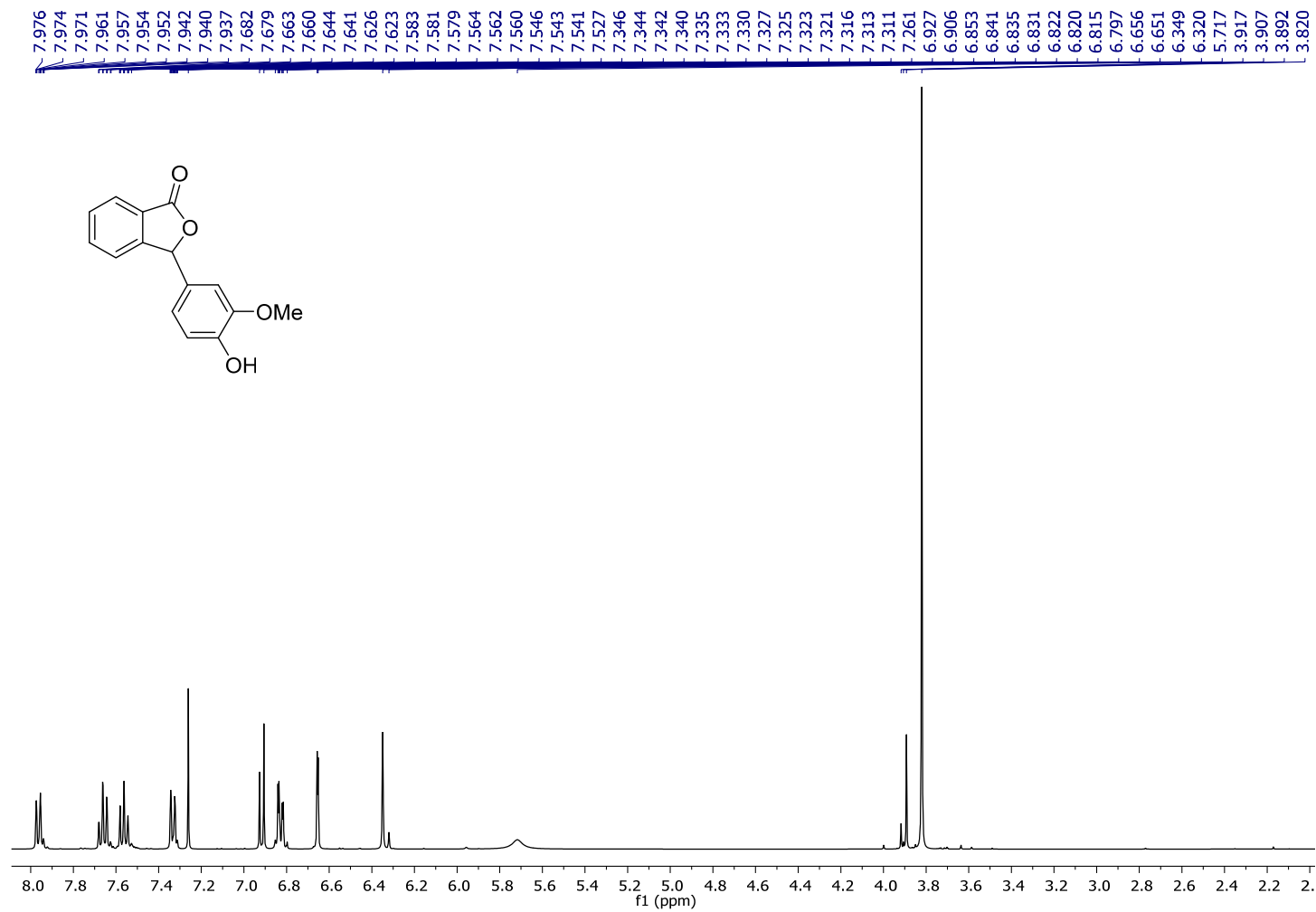
S1

Figure S1.  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CD}_3\text{COCD}_3$ ) of compound 5a

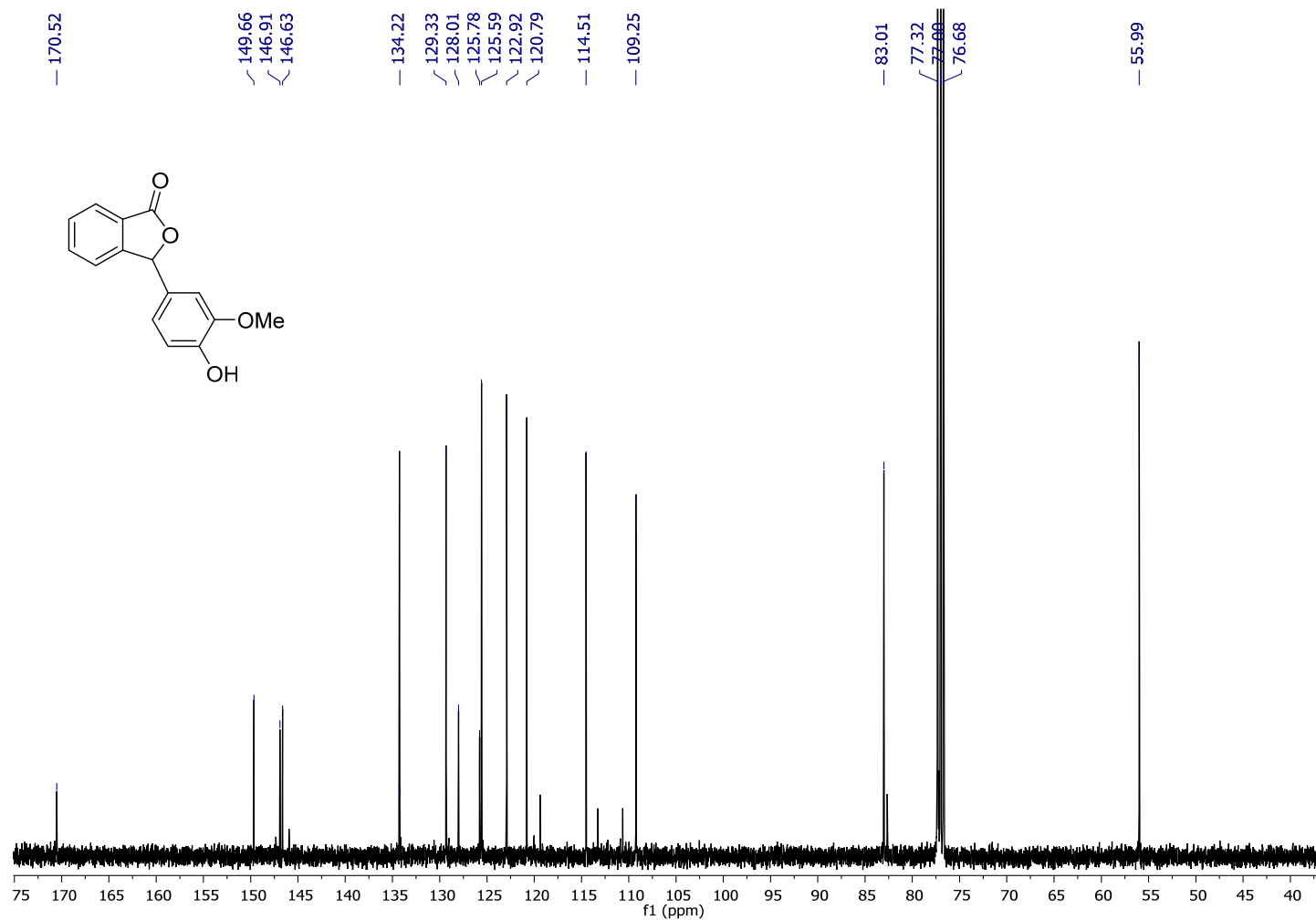


S2

Figure S2. <sup>13</sup>C NMR spectrum (100 MHz, CD<sub>3</sub>COCD<sub>3</sub>) of compound 5a

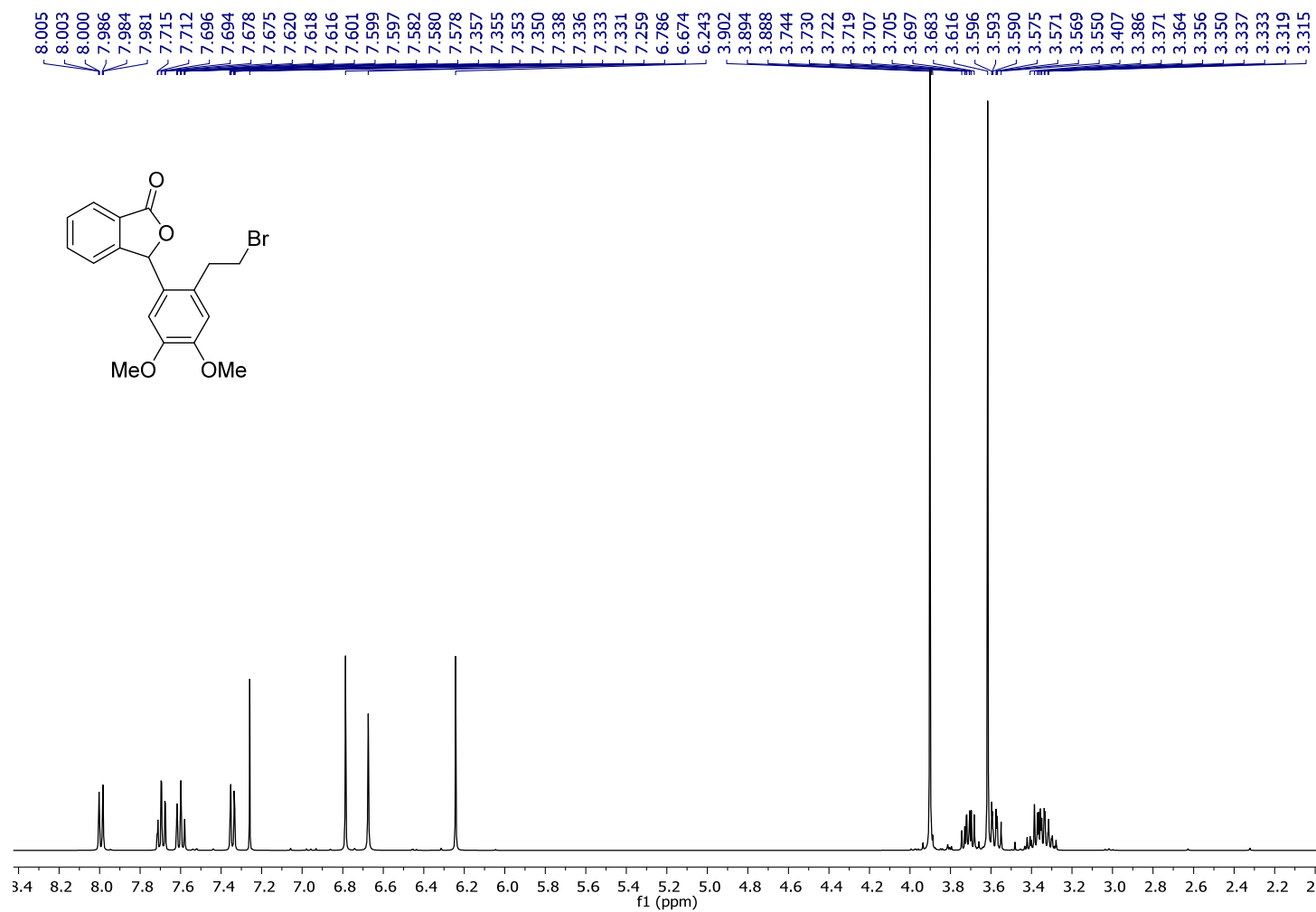


**Figure S3.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound **5b**



**S4**

**Figure S4.**  $^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound **5b**



S5

Figure S5. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of compound 5c

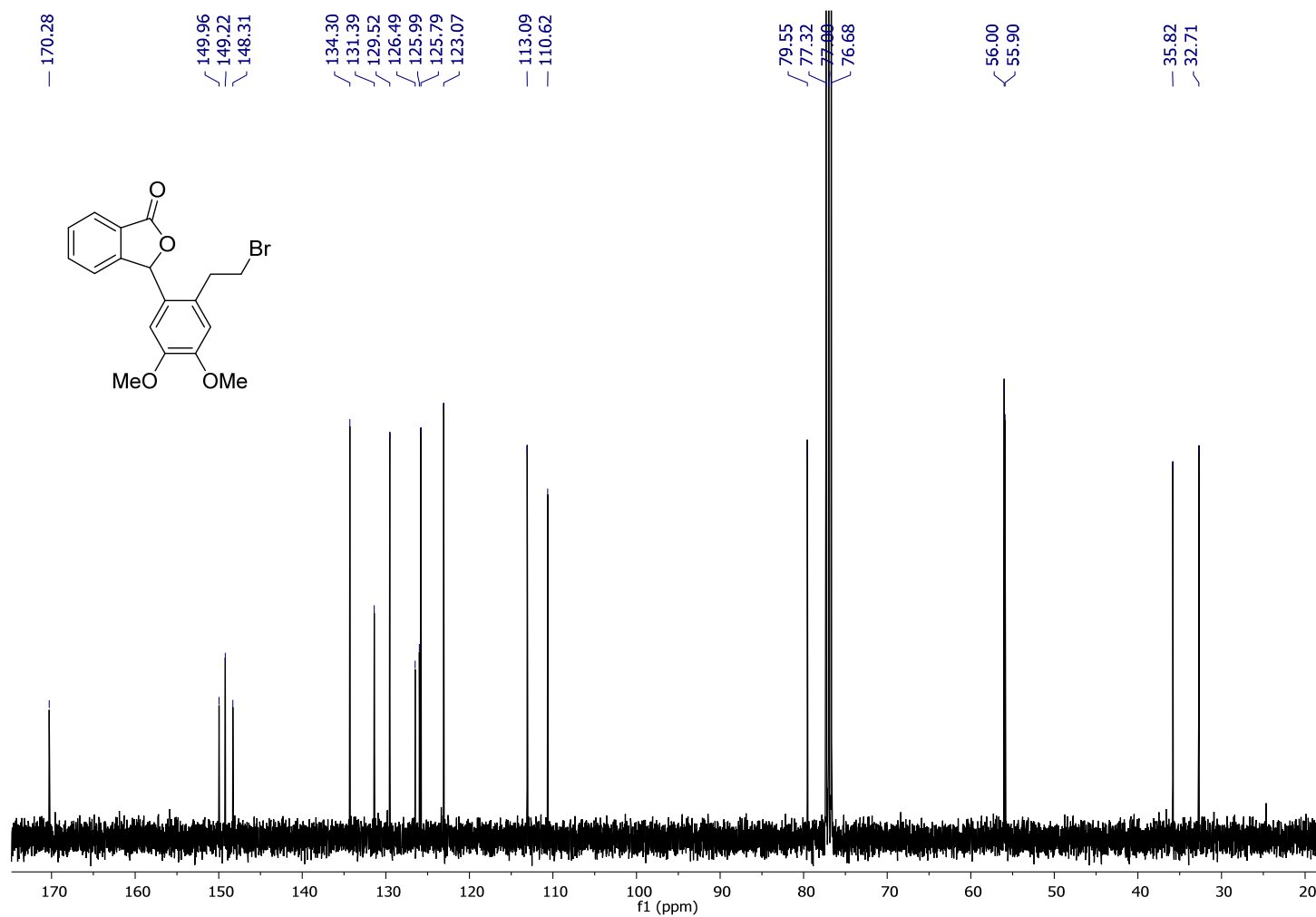
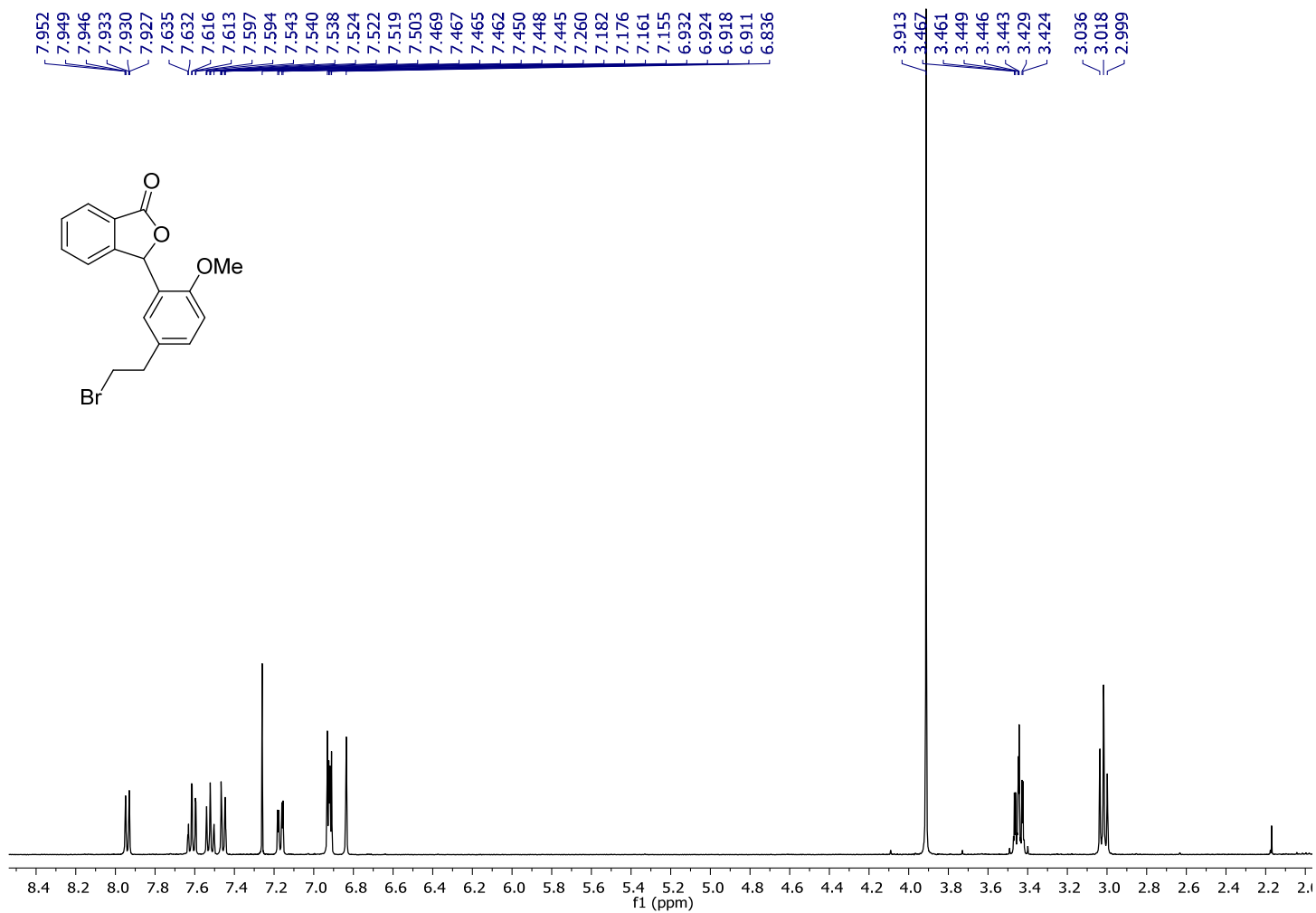


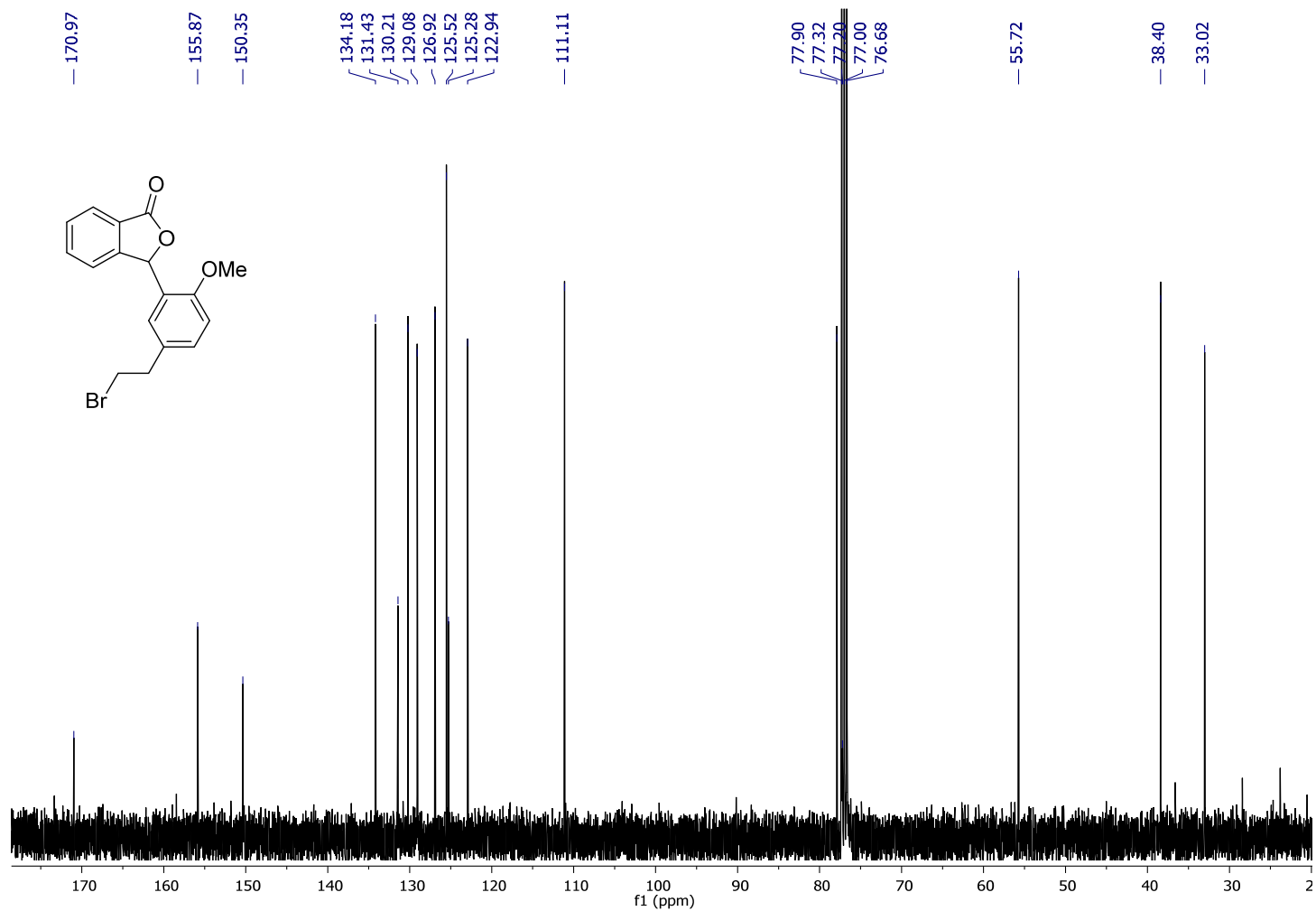
Figure S6.  $^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CDCl}_3$ ) of compound 5c





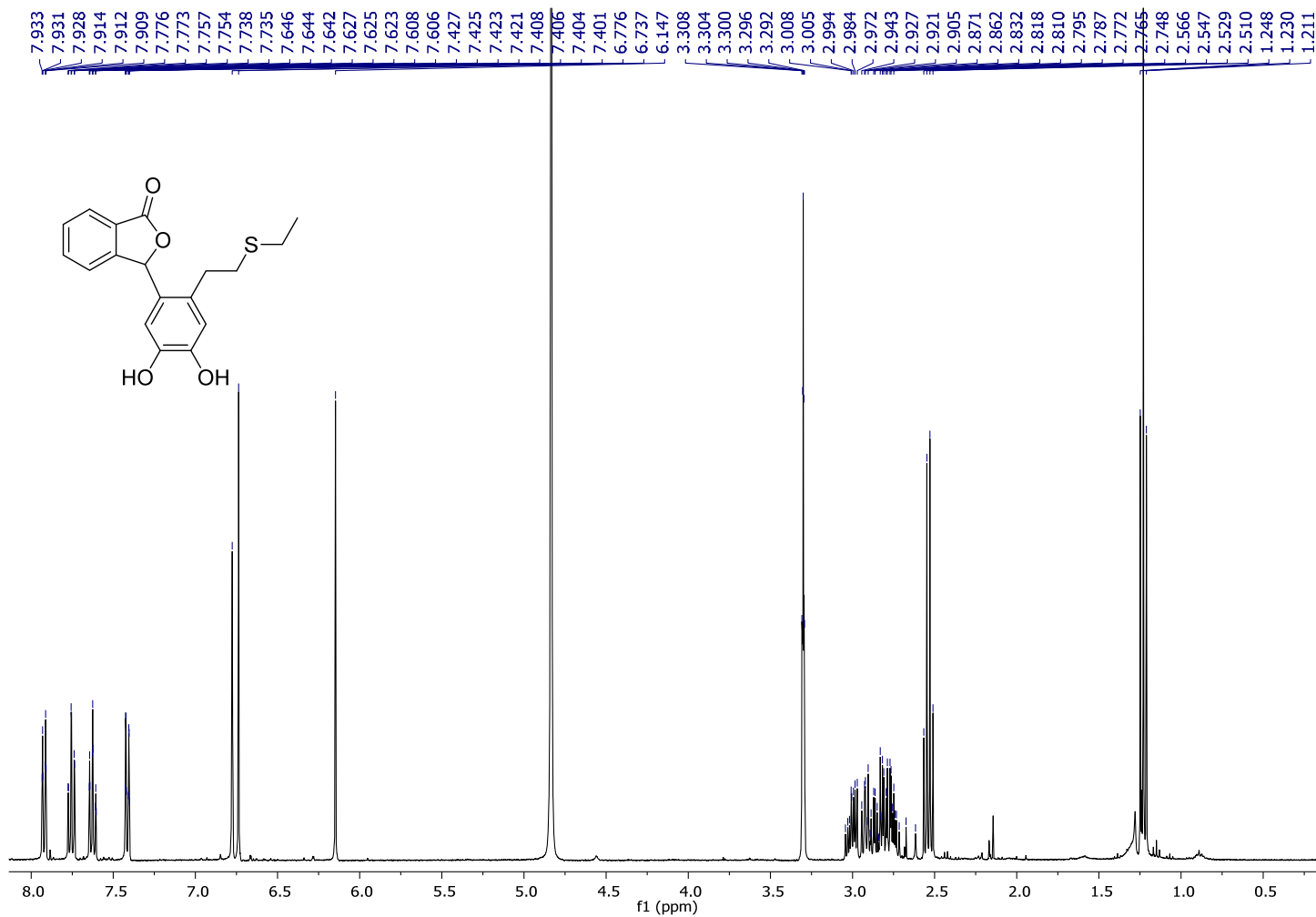
**S7**

**Figure S7.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of compound **5d**



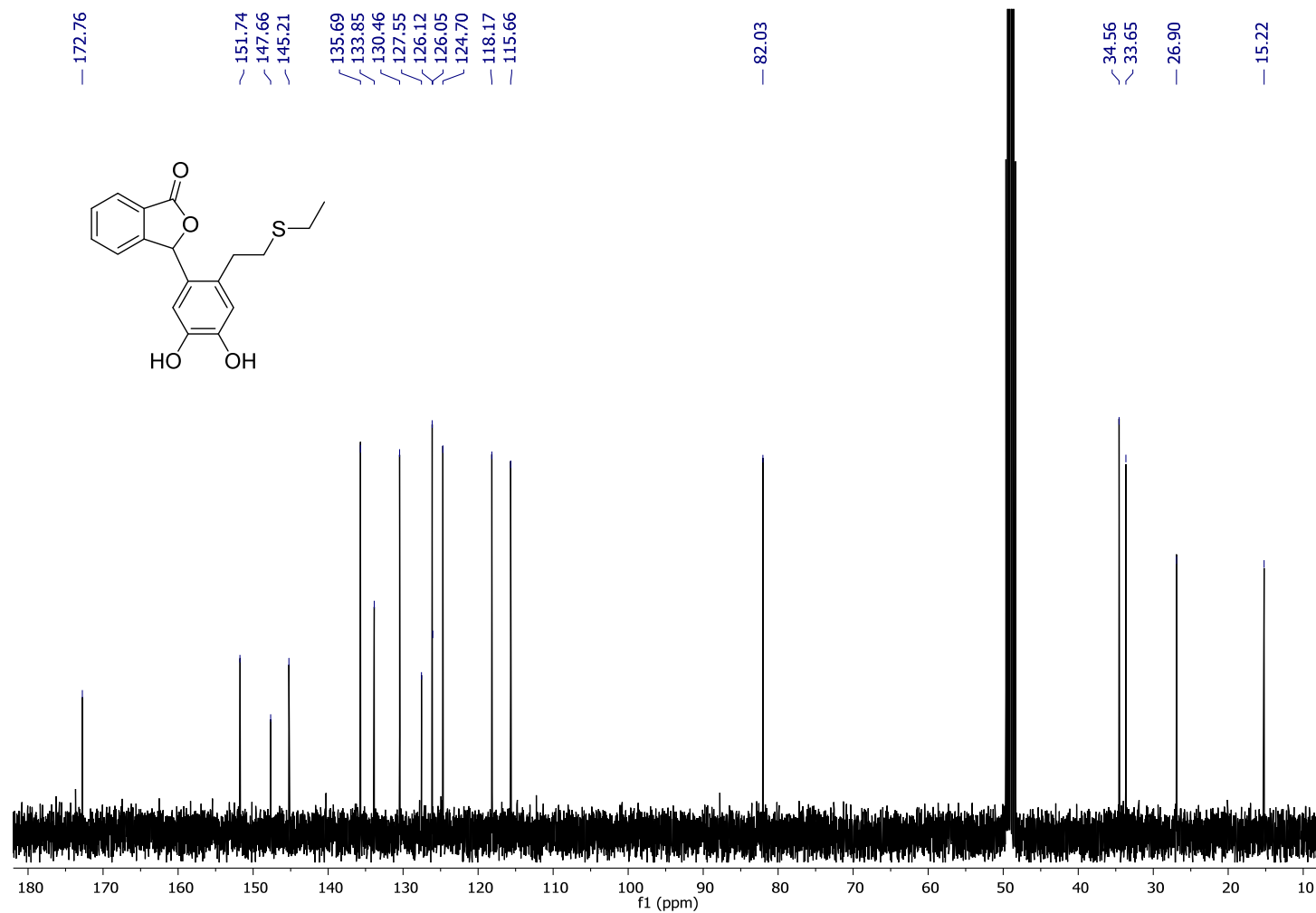
S8

Figure S8. <sup>13</sup>C NMR spectrum (100 MHz, CDCl<sub>3</sub>) of compound **5d**



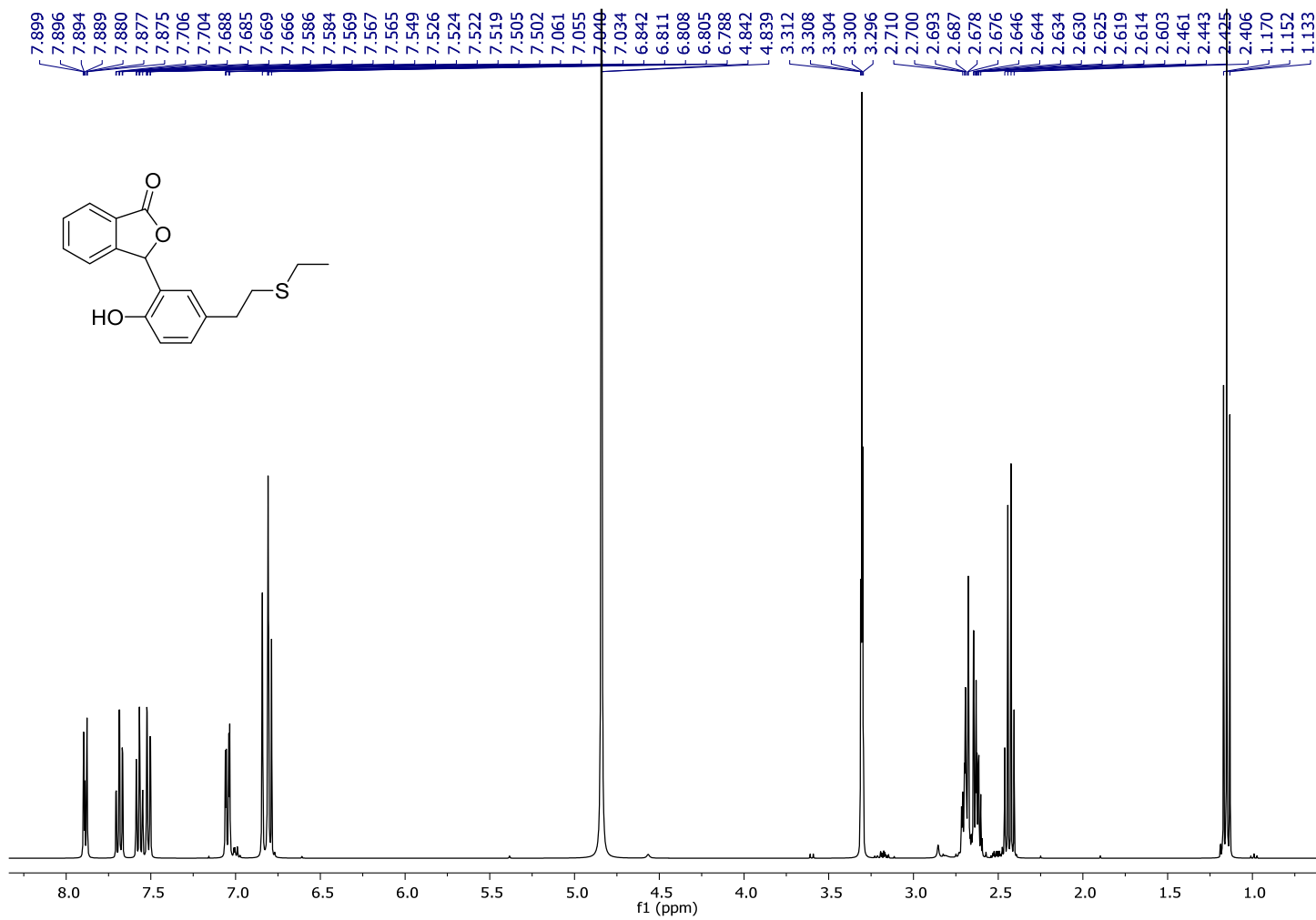
S9

Figure S9. <sup>1</sup>H NMR spectrum (400 MHz, CD<sub>3</sub>OD) of compound **5e**



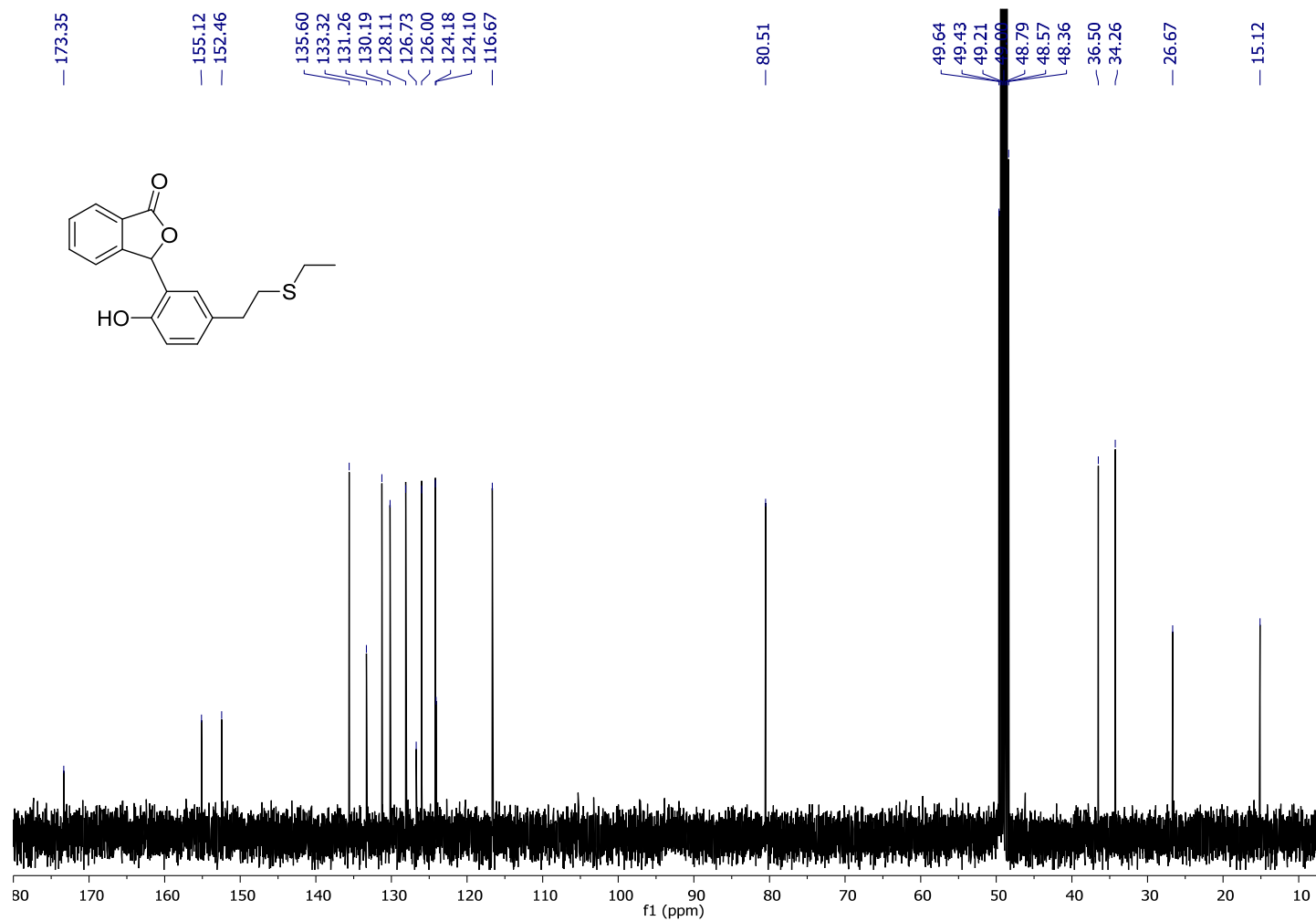
S10

Figure S10.  $^{13}\text{C}$  NMR spectrum (100 MHz,  $\text{CD}_3\text{OD}$ ) of compound 5e

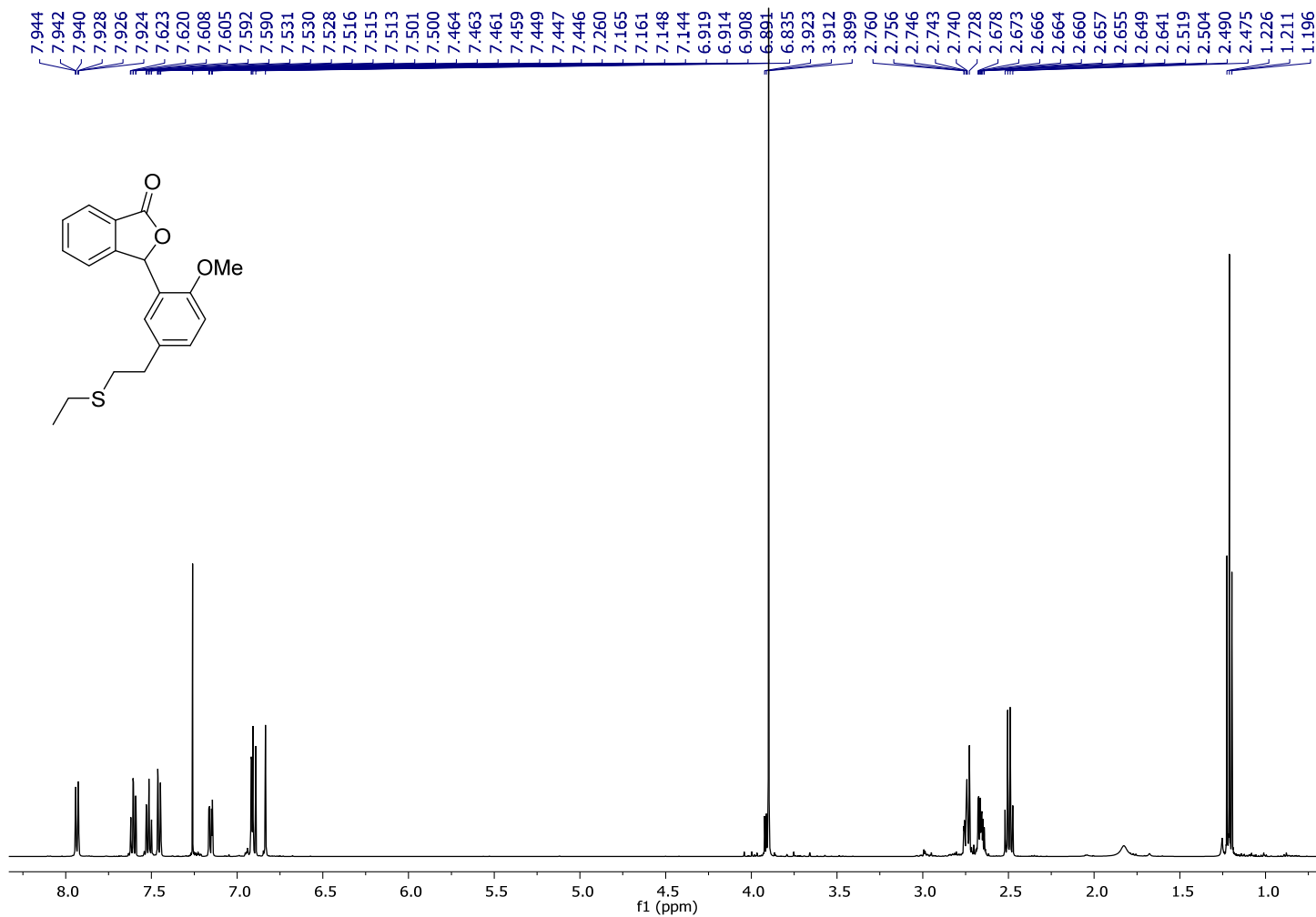


**S11**

**Figure S11.** <sup>13</sup>C NMR spectrum (400 MHz, CD<sub>3</sub>OD) of compound **5f**

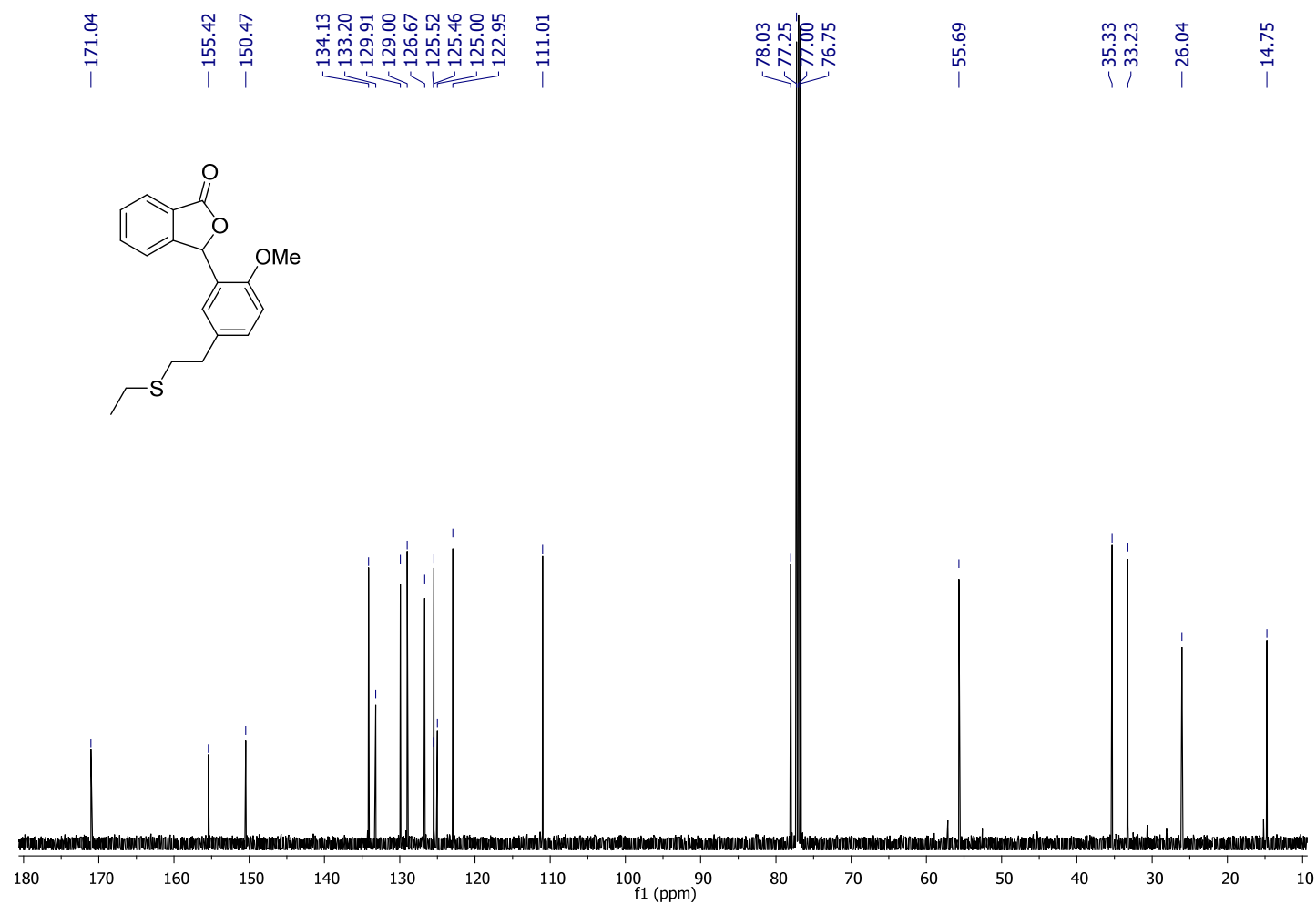


S12



**S13**

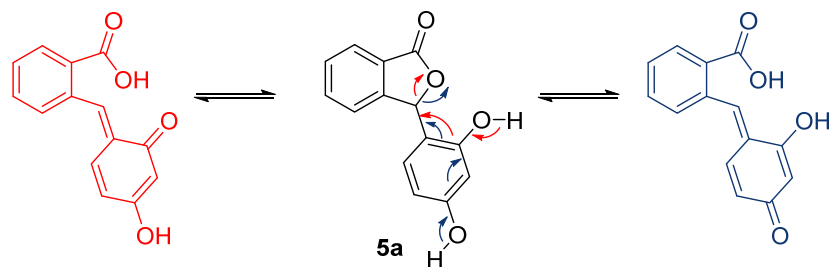
**Figure S13.** <sup>1</sup>H NMR spectrum (500 MHz, CDCl<sub>3</sub>) of compound 5g



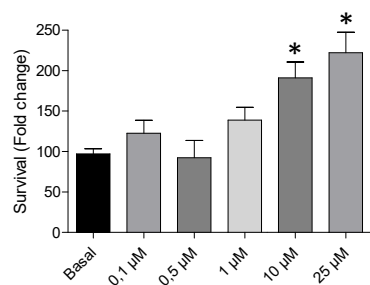
**S14**

**Figure S14.** <sup>13</sup>C NMR spectrum (125 MHz, CDCl<sub>3</sub>) of compound **5g**

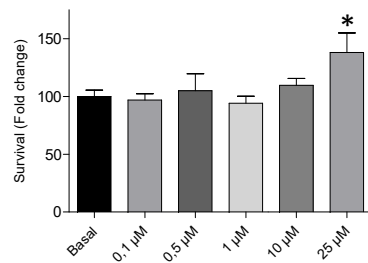




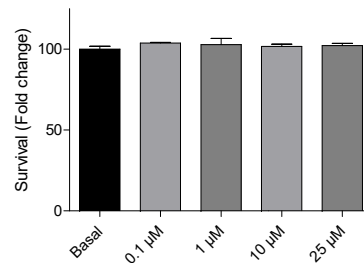
**Figure S15.** Proposed mechanism of racemization process in 5a.



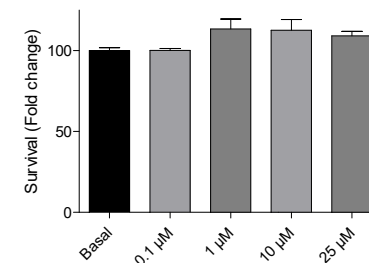
Compound **5a**



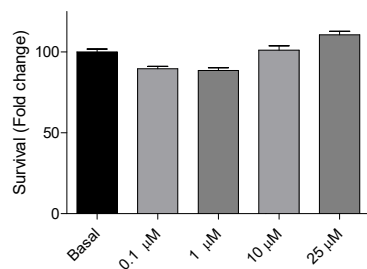
Compound **5b**



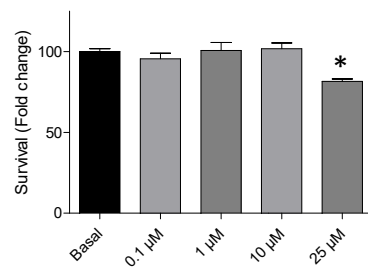
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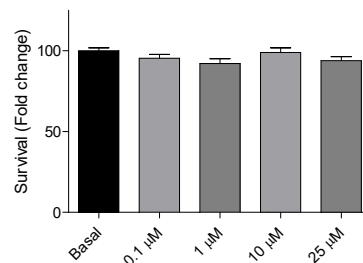
Compound **5d**



Compound **5e**



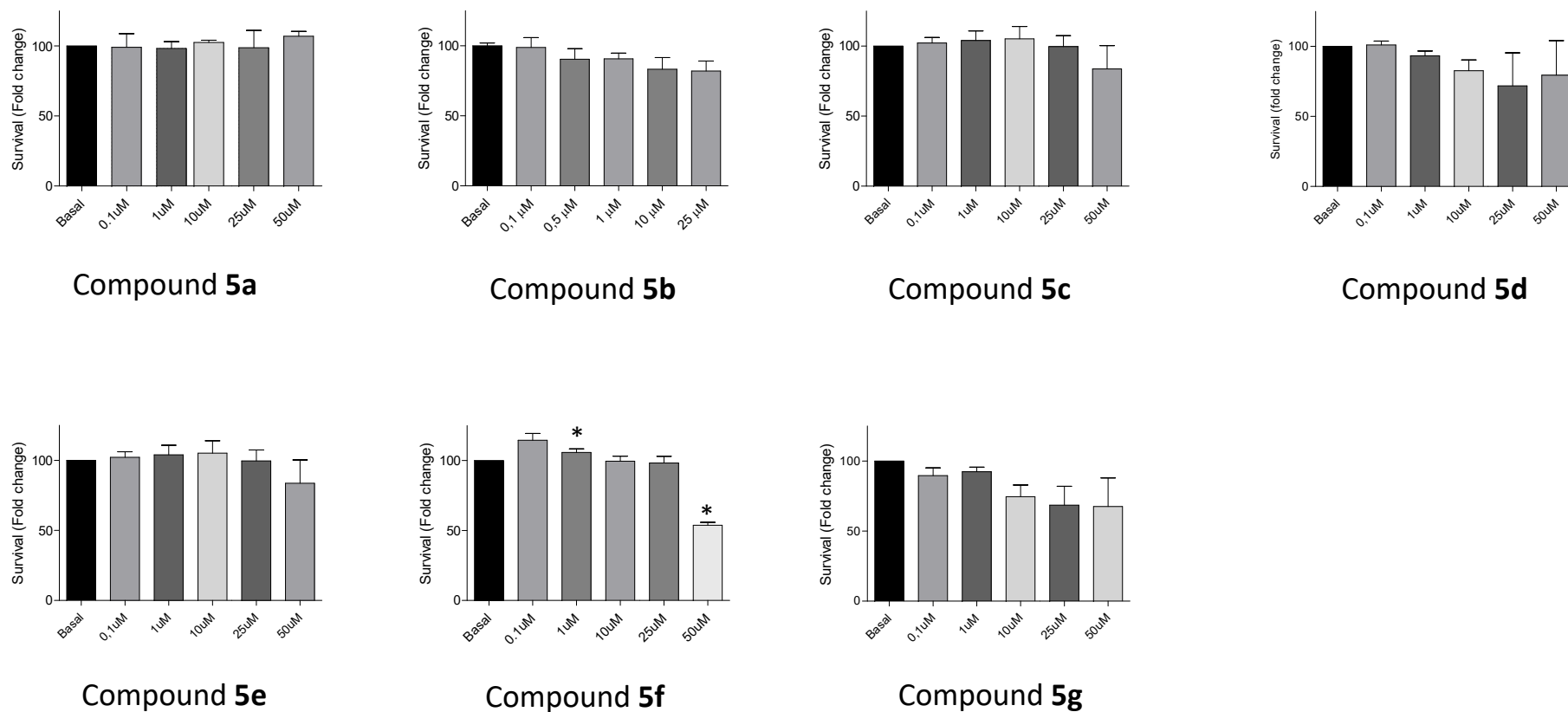
Compound **5f**



Compound **5g**

**S16**

**Figure S16.** Dose-response cell viability of Bv.2 cells was determined by cristal violet assay. Colorimetric quantification was performed, and the results are mean  $\pm$  SD ( $n \geq 3$  independent experiments performed in duplicate). Significant differences were determined by one way ANOVA followed by Bonferroni t-test \* $p \leq 0.05$  vs Basal.



**Figure S17.** Dose-response cell viability of RAW 264.7 cells was determined by crystal violet assay. Colorimetric quantification was performed, and the results are mean  $\pm$  SD ( $n \geq 3$  independent experiments performed in duplicate). Significant differences were determined by one way ANOVA followed by Bonferroni t-test  $*p \leq 0.05$  vs Basal.