

Electronic Supplementary Information

Trifluoroacetic Acid Catalyzed Highly Regioselective

Bromocyclization of Styrene-Type Carboxylic Acid

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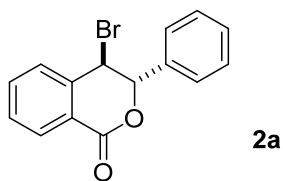
(A) General. All reactions were carried by standard procedures under atmosphere. Commercially available reagents from Alfa Aesar and Aldrich were used as received. Infrared spectra were recorded on a BIO-RAD FTS 165 FT-IR spectrophotometer and reported in wave numbers (cm⁻¹). Melting points were determined on a BÜCHI B-540b melting point apparatus. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AV500 (500 MHz). Chemical shifts (δ) are reported in ppm relative to TMS (δ 0.00) for the ¹H NMR and to chloroform (δ 77.0) for the ¹³C NMR measurements. High resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. Analytical thin layer chromatography (TLC) was performed with Merck pre-coated TLC plates, silica gel 60F-254, layer thickness 0.25 mm. Flash chromatography separations were performed on Merk 60 (0.040-0.063 mm) mesh silica gel. Substrates **1a–1n** were prepared using the literature procedure (*J. Org. Chem.* **2012**, *77*, 999–1009).

(B) General Procedure for the Trifluoroacetic Acid Catalyzed

Bromolactonization. To a mixture of styrene-type carboxylic acid **1** (0.15 mmol, 1.0 equiv) and trifluoroacetic acid (0.015 mmol, 0.1 equiv) in dry acetonitrile (1 mL) at 25 °C was added *N*-bromosuccinimide (0.165 mmol, 1.1 equiv) in the absence of light. The resulting mixture was stirred at 25 °C for 24 h. After the reaction was completed, acetonitrile was removed under vacuum at 25 °C. Then the reaction was quenched with saturated aqueous Na₂SO₃ (5 mL) and extracted with ethyl acetate (3 x 10 mL). The combined extracts were washed with brine (10 mL), dried with MgSO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography to yield the corresponding lactone **2**.

(C) General Procedure for One-pot Synthesis of Compound 6.

To a mixture of styrene-type carboxylic acid **1** (0.15 mmol, 1.0 equiv) and trifluoroacetic acid (0.015 mmol, 0.1 equiv) in dry acetonitrile (1 mL) at 25 °C was added *N*-bromosuccinimide (0.165 mmol, 1.1 equiv). The resulting mixture was stirred at 25 °C for 24 h in the absence of light. After the reaction was completed, acetonitrile and trifluoroacetic acid were removed under vacuum at 25 °C. Then freshly dry acetonitrile (2 mL) were added with thiophenol (0.225 mmol, 1.5 equiv) and K₂CO₃ (0.3 mmol, 2.0 equiv). The resulting mixture was stirred at 75 °C for 1 h. After the reaction was completed, the reaction mixture was concentrated *in vacuo*. The residue was purified by flash column chromatography to yield the corresponding lactone **6**.



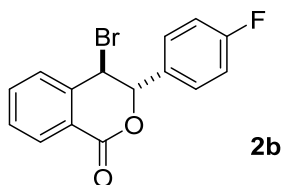
Colorless solid. mp= 89-90 °C

IR (KBr): 2996, 1716, 1601, 1111 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 8.18 (d, $J = 7.6$ Hz, 1H), 7.64-7.61 (m, 1H), 7.52-7.49 (m, 2H), 7.37-7.29 (m, 5H), 5.94 (d, $J = 4.5$ Hz, 1H), 5.59 (d, $J = 4.6$ Hz, 1H).

^{13}C NMR (125 MHz, CDCl_3): (δ , ppm) 163.09, 137.76, 136.34, 134.58, 130.42, 129.84, 128.97, 128.80, 128.35, 126.42, 124.16, 84.14, 46.10.

HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{12}\text{BrO}_2^+ [\text{M} + \text{H}]^+$: 303.0015; found: 303.0016.



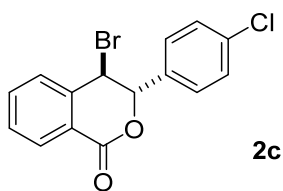
Colorless solid. mp= 127-129 °C

IR (KBr): 2934, 1733, 1459, 1223 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 8.16 (d, $J = 7.8$ Hz, 1H), 7.63 (t, $J = 7.6$ Hz, 1H), 7.53-7.49 (m, 2H), 7.31-7.27 (m, 2H), 7.03 (t, $J = 8.6$ Hz, 2H), 5.84 (d, $J = 5.5$ Hz, 1H), 5.51 (d, $J = 5.5$ Hz, 1H).

^{13}C NMR (125 MHz, CDCl_3): (δ , ppm) 162.98, 162.90 (d, $J = 247.5$ Hz), 137.78, 134.72, 132.27 (d, $J = 3.3$ Hz), 130.53, 129.89, 128.62, 128.55, 124.04, 115.87 (d, $J = 21.7$ Hz), 83.56, 46.29.

HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{11}\text{BrFO}_2^+ [\text{M} + \text{H}]^+$: 320.9921; found: 320.9917.



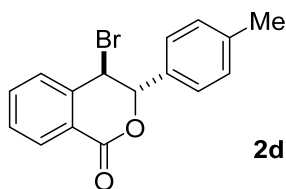
Colorless solid. mp= 131-133 °C

IR (KBr): 2956, 1725, 1455, 1260 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.15 (d, $J = 7.4$ Hz, 1H), 7.64-7.60 (m, 1H), 7.51-7.48 (m, 2H), 7.32-7.30 (m, 2H), 7.26-7.23 (m, 2H), 5.84 (d, $J = 5.2$ Hz, 1H), 5.50 (d, $J = 5.2$ Hz, 1H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): (δ , ppm) 162.89, 137.63, 135.08, 134.87, 134.74, 130.52, 129.94, 129.05, 128.46, 127.97, 123.98, 83.44, 45.98.

HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{11}\text{BrClO}_2^+$ [$\text{M} + \text{H}$] $^+$: 336.9625; found: 336.9624.



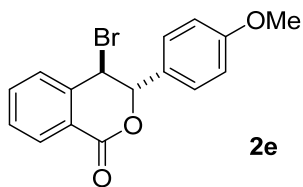
Colorless solid. mp= 94-96 °C

IR (KBr): 2920, 1718, 1457, 1264 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.15 (d, $J = 7.7$ Hz, 1H), 7.61-7.57 (m, 1H), 7.49-7.45 (m, 2H), 7.16-7.11 (m, 4H), 5.88 (d, $J = 4.4$ Hz, 1H), 5.54 (d, $J = 4.5$ Hz, 1H), 2.30 (s, 3H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): (δ , ppm) 163.17, 138.91, 137.88, 134.52, 133.43, 130.40, 129.79, 129.47, 128.36, 126.33, 124.25, 84.12, 46.22, 21.08.

HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{14}\text{BrO}_2^+$ [$\text{M} + \text{H}$] $^+$: 317.0172; found: 317.0174.



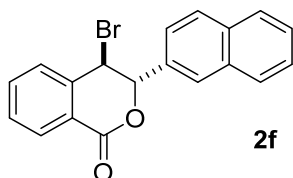
Colorless solid. mp= 101-102 °C

IR (KBr): 2954, 1724, 1460, 1237 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.14 (d, $J = 7.0$ Hz, 1H), 7.62-7.59 (m, 1H), 7.50-7.47 (m, 2H), 7.18 (d, $J = 8.7$ Hz, 2H), 6.83 (d, $J = 8.7$ Hz, 2H), 5.84 (d, $J = 4.9$ Hz, 1H), 5.53 (d, $J = 4.9$ Hz, 1H), 3.76 (s, 3H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): (δ , ppm) 163.20, 159.95, 137.99, 134.53, 130.40, 129.76, 128.43, 127.89, 124.21, 114.15, 104.95, 83.98, 55.24, 46.42.

HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{14}\text{BrO}_3^+$ [$\text{M} + \text{H}$] $^+$: 333.0121; found: 333.0122.



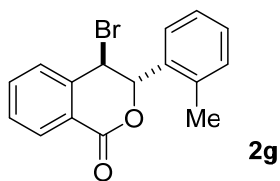
Colorless solid. mp= 132-134 °C

IR (KBr): 2910, 1729, 1458, 1254 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.18 (d, $J = 8.0$ Hz, 1H), 7.83-7.77 (m, 3H), 7.73 (s, 1H), 7.58 (t, $J = 7.7$ Hz, 1H), 7.50-7.46 (m, 4H), 7.39 (d, $J = 8.6$ Hz, 1H), 6.08 (d, $J = 4.5$ Hz, 1H), 5.68 (d, $J = 4.5$ Hz, 1H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): (δ , ppm) 163.14, 137.77, 134.60, 133.64, 133.19, 132.86, 130.44, 129.86, 128.84, 128.34, 128.20, 127.64, 126.84, 126.71, 126.16, 124.19, 123.35, 84.23, 46.03.

HRMS (APCI) calcd for $\text{C}_{19}\text{H}_{14}\text{BrO}_2^+$ [$\text{M} + \text{H}$] $^+$: 353.0172; found: 353.0168.



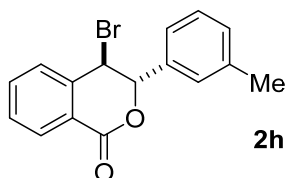
Colorless solid. mp= 104-106 °C

IR (KBr): 2959, 1732, 1457, 1258 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 8.19 (d, $J = 8.2$ Hz, 1H), 7.64 (t, $J = 7.6$ Hz, 1H), 7.53-7.50 (m, 2H), 7.25-7.21 (m, 2H), 7.12-7.05 (m, 2H), 1H), 6.09 (d, $J = 5.3$ Hz, 1H), 5.54 (d, $J = 5.3$ Hz, 1H), 2.48 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3): (δ , ppm) 163.35, 138.03, 136.03, 134.59, 134.39, 131.08, 130.43, 129.80, 129.00, 128.60, 126.31, 125.95, 124.16, 81.51, 45.68, 19.52.

HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{14}\text{BrO}_2^+$ [$\text{M} + \text{H}$] $^+$: 317.0172; found: 317.0173.



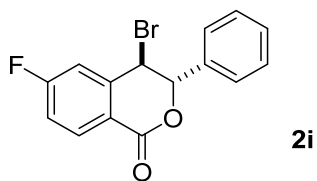
Colorless solid. mp= 124-126 °C

IR (KBr): 2922, 1716, 1373, 1244 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 8.15 (d, $J = 7.2$ Hz, 1H), 7.61-7.58 (m, 1H), 7.50-7.46 (m, 2H), 7.20 (t, $J = 7.6$ Hz, 1H), 7.12-7.03 (m, 3H), 5.88 (d, $J = 4.5$ Hz, 1H), 5.56 (d, $J = 4.6$ Hz, 1H), 2.31 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3): (δ , ppm) 163.12, 138.67, 137.86, 136.33, 134.53, 130.41, 129.81, 129.74, 128.66, 128.37, 127.09, 124.22, 123.45, 84.21, 46.18, 21.41.

HRMS (APCI) calcd for $\text{C}_{16}\text{H}_{14}\text{BrO}_2^+$ [$\text{M} + \text{H}$] $^+$: 317.0172; found: 317.0162.



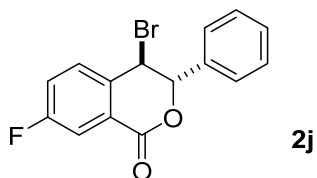
Colorless solid. mp= 137-139 °C

IR (KBr): 2951, 1711, 1456, 1266 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 8.19 (dd, $J_1 = 8.6$ Hz, $J_2 = 5.6$ Hz, 1H), 7.36-7.29 (m, 5H), 7.21-7.14 (m, 2H), 5.86 (d, $J = 5.3$ Hz, 1H), 5.50 (d, $J = 5.3$ Hz, 1H).

^{13}C NMR (125 MHz, CDCl_3): 166.11 (d, $J = 255.5$ Hz), 162.25, 140.89 (d, $J = 10.1$ Hz), 136.03, 133.61 (d, $J = 9.2$ Hz, 1H), 129.20, 128.89, 126.52, 120.52, 117.41 (d, $J = 22.1$ Hz), 115.62 (d, $J = 23.8$ Hz), 84.05, 45.42.

HRMS (APCI) calcd for $\text{C}_{15}\text{H}_{11}\text{BrFO}_2^+ [\text{M} + \text{H}]^+$: 320.9921; found: 320.9914.



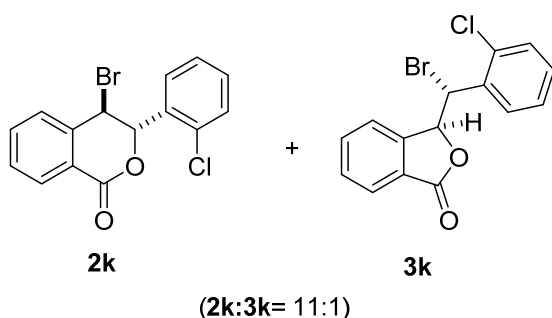
Colorless solid. mp= 123-125 °C

IR (KBr): 3083, 1723, 1480, 1278 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3): (δ , ppm) 7.83 (dd, $J_1 = 8.3$ Hz, $J_2 = 2.6$ Hz, 1H), 7.47 (dd, $J_1 = 8.5$ Hz, $J_2 = 4.9$ Hz, 1H), 7.36-7.25 (m, 6H), 5.93 (d, $J = 4.3$ Hz, 1H), 5.55 (d, $J = 4.4$ Hz, 1H).

^{13}C NMR (125 MHz, CDCl_3): 163.0 (d, $J = 229.9$ Hz), 161.91, 136.06, 133.81, 130.66 (d, $J = 7.6$ Hz), 129.12, 128.92, 126.31, 126.24, 122.03 (d, $J = 22.3$ Hz), 117.04 (d, $J = 23.4$ Hz), 84.37, 45.15.

HRMS (APCI) calcd for $C_{15}H_{11}BrFO_2^+$ $[M + H]^+$: 320.9921; found: 320.9908.



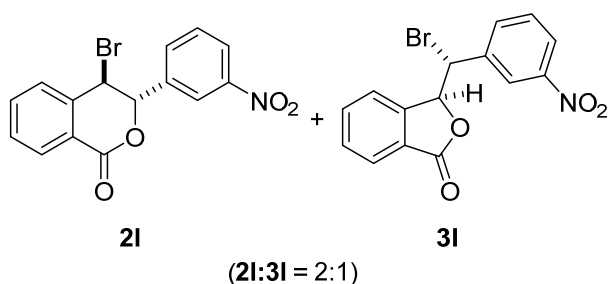
The physical data of compound **2k** are shown below:

IR (KBr): 2922, 1731, 1457, 1236 cm^{-1} ;

1H NMR (500 MHz, $CDCl_3$): (δ , ppm) 8.23 (d, J = 7.8 Hz, 1H), 7.63-7.60 (m, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.45-7.40 (m, 2H), 7.29-7.27 (m, 1H), 7.20-7.17 (m, 1H), 7.13-7.11 (m, 1H), 6.33 (d, J = 3.5 Hz, 1H), 5.66 (d, J = 3.6 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$): (δ , ppm) 163.10, 137.34, 134.70, 133.79, 132.51, 130.35, 130.21, 130.12, 130.03, 128.35, 127.46, 127.23, 123.94, 81.62, 43.93.

HRMS (APCI) calcd for $C_{15}H_{11}BrClO_2^+$ $[M + H]^+$: 336.9625; found: 336.9619.

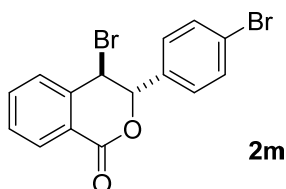


IR (KBr): 3102, 1776, 1736, 1523 cm^{-1} ;

1H NMR (500 MHz, $CDCl_3$): (δ , ppm) 8.25-8.15 (m, 8H), 7.84-7.79 (m, 3H), 7.73-7.64 (m, 5H), 7.60-7.51 (m, 8H), 6.00 (d, J = 6.8 Hz, 1H), 5.89 (d, J = 6.5 Hz, 2H), 5.57 (d, J = 6.6 Hz, 2H), 5.17 (d, J = 6.8 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 168.66, 162.55, 148.32, 148.05, 145.85, 138.53, 138.37, 137.38, 134.99, 134.69, 134.29, 132.90, 130.64, 130.37, 130.03, 129.93, 129.82, 128.68, 126.31, 126.05, 124.12, 123.91, 123.75, 123.66, 123.43, 122.00, 82.87, 81.85, 50.90, 45.90.

HRMS (APCI) calcd for C₁₅H₁₁BrNO₄⁺ [M + H]⁺: 347.9866; found: 347.9850.



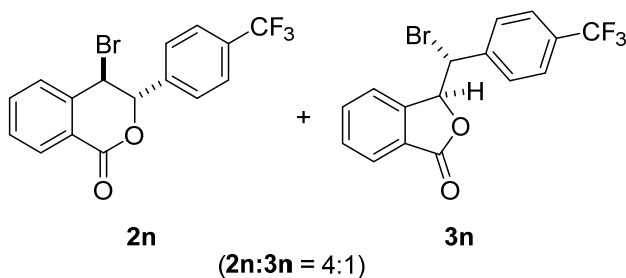
Colorless solid. mp= 121-122 °C

IR (KBr): 2910, 1729, 1490, 1260 cm⁻¹;

¹H NMR (500 MHz, CDCl₃): (δ, ppm) 8.15-8.14 (m, 1H), 7.63-7.60 (m, 1H), 7.51-7.45 (m, 4H), 7.18 (d, *J* = 8.6 Hz, 2H), 5.83 (d, *J* = 5.2 Hz, 1H), 5.50 (d, *J* = 5.2 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 162.85, 137.59, 135.38, 134.74, 132.00, 130.51, 129.94, 128.44, 128.22, 123.96, 123.22, 83.46, 45.87.

HRMS (APCI) calcd for C₁₅H₁₁Br₂O₂ [M + H]⁺: 380.9120; found: 380.9113.

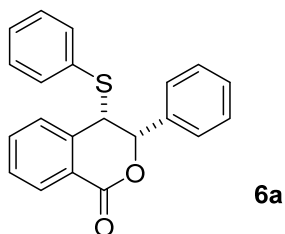


IR (KBr): 2957, 1761, 1727, 1456, 1427 cm⁻¹;

¹H NMR (500 MHz, CDCl₃): (δ, ppm) 8.17-8.15 (m, 4H), 7.85-7.45 (m, 40H), 5.96 (d, *J* = 6.5 Hz, 1H), 5.92 (d, *J* = 5.2 Hz, 4H), 5.55 (d, *J* = 5.3 Hz, 4H), 5.17 (d, *J* = 6.5 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 168.84, 162.72, 146.00, 140.16, 140.10, 137.45, 134.84, 134.08, 131.41, 131.15, 130.88, 130.56, 130.23, 130.03, 129.06, 128.45, 127.05, 126.89, 126.52, 126.00, 125.82 (q, *J* = 3.6 Hz), 125.64 (q, *J* = 3.8 Hz), 124.72, 123.89, 123.68, 122.56, 83.36, 82.06, 51.77, 45.68.

HRMS (APCI) calcd for C₁₆H₁₁BrF₃O₂⁺ [M + H]⁺: 370.9889; found: 370.9887.



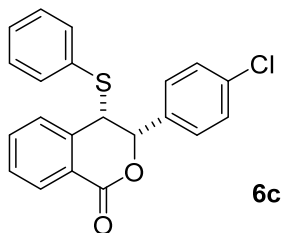
Colorless solid. mp= 158-159 °C

IR (KBr): 3054, 1721, 1453, 1263 cm⁻¹;

¹H NMR (500 MHz, CDCl₃): (δ, ppm) 8.10-8.08 (m, 1H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.47-7.37 (m, 5H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 2H), 6.99 (t, *J* = 7.9 Hz, 2H), 6.93 (d, *J* = 7.6 Hz, 1H), 5.92 (d, *J* = 2.3 Hz, 1H), 4.51 (d, *J* = 2.5 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 164.39, 140.91, 136.28, 135.45, 133.43, 131.81, 130.53, 128.71, 128.58, 128.49, 128.47, 128.42, 127.30, 126.26, 124.24, 80.69, 52.80.

HRMS (APCI) calcd for C₂₁H₁₇O₂S⁺ [M + H]⁺: 333.0944; found: 333.0936.



Colorless solid. mp= 131-133 °C

IR (KBr): 3067, 1733, 1460, 1263 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.08 (d, $J = 7.5$ Hz, 1H), 7.50-7.39 (m, 6H),

7.23-7.20 (m, 1H), 7.12-7.09 (m, 2H), 7.00-6.96 (m, 3H), 5.89 (d, $J = 2.5$ Hz, 1H),

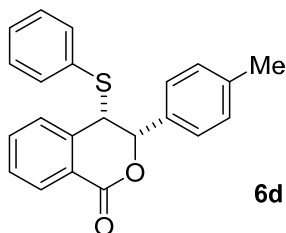
4.49 (d, $J = 2.6$ Hz, 1H).

$^{13}\text{C NMR}$ (125 MHz, CDCl_3): (δ , ppm) 164.10, 140.52, 135.28, 134.79, 134.33,

133.59, 131.60, 130.56, 128.79, 128.72, 128.60, 128.55, 127.66, 127.38, 124.11,

80.03, 52.61.

HRMS (APCI) calcd for $\text{C}_{21}\text{H}_{14}\text{ClO}_2\text{S}$ $[\text{M} - \text{H}]^-$: 365.0398; found: 365.0394.



Colorless solid. mp= 112-114 °C

IR (KBr): 2920, 1729, 1437, 1117 cm^{-1} ;

$^1\text{H NMR}$ (500 MHz, CDCl_3): (δ , ppm) 8.12-8.10 (m, 1H), 7.50-7.41 (m, 4H),

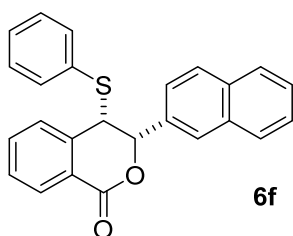
7.29-7.27 (m, 2H), 7.23 (t, $J = 7.5$ Hz, 1H), 7.12 (t, $J = 7.5$ Hz, 2H), 7.03 (d, $J = 7.7$

Hz, 2H), 6.94-6.91 (m, 1H), 5.92 (d, $J = 2.4$ Hz, 1H), 4.52 (d, $J = 2.6$ Hz, 1H), 2.43(s,

3H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 164.50, 140.89, 138.22, 135.52, 133.33, 131.79, 130.51, 129.11, 128.67, 128.53, 128.43, 127.55, 127.29, 126.13, 124.30, 80.68, 52.82, 21.22.

HRMS (APCI) calcd for C₂₂H₁₉O₂S⁺ [M + H]⁺: 347.1100; found: 347.1093.



Colorless solid. mp= 181-182 °C

IR (KBr): 2921, 1727, 1264, 1086 cm⁻¹;

¹H NMR (500 MHz, CDCl₃): (δ, ppm) 8.18-8.15 (m, 2H), 7.97-7.89 (m, 3H), 7.60-7.54 (m, 3H), 7.50-7.44 (m, 2H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.06-6.97 (m, 5H), 6.12 (d, *J* = 2.4 Hz, 1H), 4.66 (d, *J* = 2.6 Hz, 1H).

¹³C NMR (125 MHz, CDCl₃): (δ, ppm) 164.43, 140.88, 135.53, 133.55, 133.47, 133.23, 133.13, 131.66, 130.61, 128.66, 128.64, 128.46, 128.34, 128.24, 127.72, 127.40, 126.43, 126.39, 125.79, 124.33, 123.42, 80.74, 52.70.

HRMS (APCI) calcd for C₂₅H₁₇O₂S⁻ [M - H]⁻: 381.0944; found: 381.0932.

