

Supporting Information

A Convenient Synthesis of Ethyl 4-Aryl-6-(trifluoromethyl)-2-oxo-2H-pyran-3-carboxylates and 4-Aryl-6-(trifluoromethyl)-2H-pyran-2-ones: Novel Highly Reactive CF₃-Containing Building Blocks

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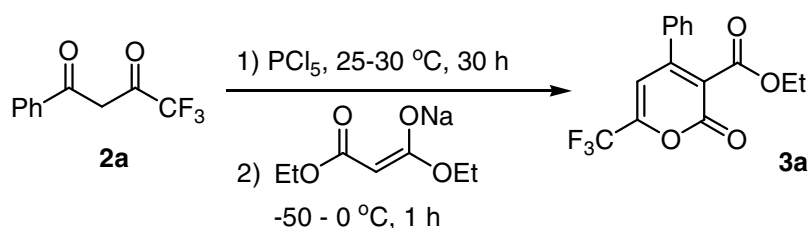
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General Considerations

¹H (400 MHz), ¹⁹F (376 MHz), and ¹³C (100 MHz) NMR spectra were recorded in CDCl₃. The chemical shifts (δ) are reported in ppm relative to the TMS (CFCl₃) as internal standard, *J* values are given in Hz. IR spectra were recorded as KBr discs. Melting points are uncorrected. All solvents used were dried and distilled per standard procedures. The starting 1-aryl-4,4,4-trifluorobutane-1,3-diones **2** were prepared according to described procedure.⁹

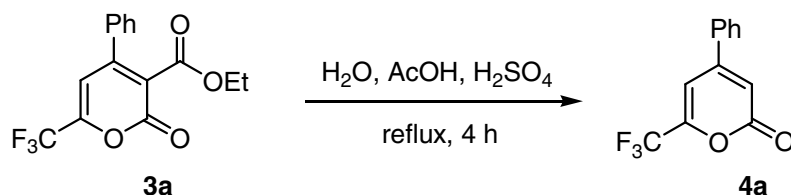
Ethyl 6-(trifluoromethyl)-2-oxo-4-phenyl-2H-pyran-3-carboxylate (**3a**).



A mixture of 4,4,4-trifluoro-1-phenylbutane-1,3-dione (**2a**) (34.6 g, 160 mmol), PCl₅ (37.1 g, 178 mmol), and CCl₄ (10 mL) was stirred at 25–30 °C for 30 h. After complete conversion as indicated by ¹⁹F NMR, volatile components were removed under reduced pressure. The residue was diluted with dry CH₂Cl₂ (100 mL), cooled to –50 °C and quenched with a cooled to –50 °C suspension of sodium diethyl malonate (720 mmol) in abs. ethanol (450 mL). After achieving 0 °C, the reaction was left under stirring for 1 h at this temperature. The dark red reaction mixture was quenched

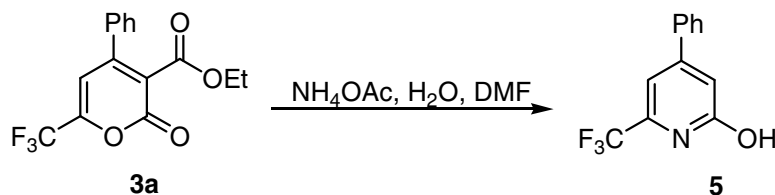
with 10% H₂SO₄ (1.5 L) and the organic layer was washed once with water. Distillation gave fraction over the range 120–180 °C (1 torr), which was then crystallized from ethanol (cooling to –30 °C) to afford pure **3a**. Yield 24%, mp 90 °C, light yellow solid; IR (KBr) 1758, 1714, 1667, 1581, 1559, 1494, 1471 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 1.11 (3H, t, *J* = 7.1 Hz, MeCH₂), 4.21 (2H, q, *J* = 7.1 Hz, OCH₂), 6.80 (1H, s, H-5), 7.42–7.55 (5H, m, Ph); ¹⁹F NMR (200 MHz, C₆D₆) δ –72.3 (CF₃, s); ¹³C NMR (100 MHz, CDCl₃) δ 13.61, 62.36, 107.09 (C-5, q, ⁴*J*_{C,F} = 3.6 Hz), 117.65 (CF₃, q, ¹*J*_{C,F} = 273.2 Hz), 121.85, 127.25, 129.17, 131.02, 134.37, 148.00 (C-6, q, ²*J*_{C,F} = 39.7 Hz), 152.11, 156.50, 163.40; EI-MS *m/z*: 312 (100, [M]⁺), 284 (72), 267 (75), 215 (69); HRMS *m/z*: found 312.05989, calcd for C₁₅H₁₁F₃O₄ [M]⁺ 312.06094. Anal. Calcd for C₁₅H₁₁F₃O₄: C, 57.70; H, 3.55. Found: C, 57.77; H, 3.53.

6-(Trifluoromethyl)-4-phenyl-2*H*-pyran-2-one (**4a**).



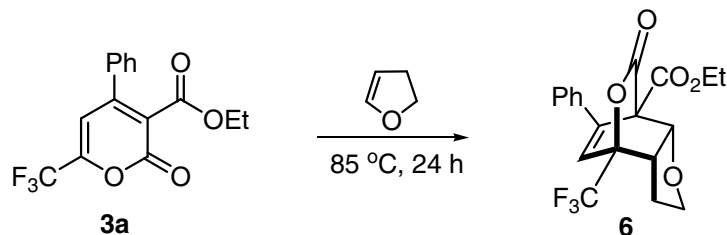
A solution of **3a** (10.0 g, 32 mmol) in AcOH-H₂O-H₂SO₄ (4:2:1, 100 mL) was refluxed for 4 h. When the reaction was complete, the reaction mixture was allowed to cool to room temperature and then diluted with water (100 mL). The solid (**4a**) was filtered and recrystallized from hexane. Yield 83%, mp 60 °C, colourless solid; IR (KBr) 1744, 1698, 1666, 1560 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.67 (1H, d, *J* = 0.9 Hz, H-3), 6.97 (1H, d, *J* = 0.9 Hz, H-5), 7.50–7.62 (5H, m, Ph); ¹⁹F NMR (200 MHz, C₆D₆) δ –72.4 (CF₃, s); ¹³C NMR (100 MHz, CDCl₃) δ 104.76, (C-5, q, ⁴*J*_{C,F} = 3.8 Hz), 113.76, 118.03 (CF₃, q, ¹*J*_{C,F} = 272.9 Hz), 126.64, 129.51, 131.52, 134.13, 148.47 (C-6, q, ²*J*_{C,F} = 39.2 Hz), 153.27, 159.31; EI-MS *m/z*: 240 (100, [M]⁺), 212 (92), 171 (58), 115 (80); HRMS *m/z*: found 240.03995, calcd for C₁₂H₇F₃O₂ [M]⁺ 240.03981. Anal. Calcd for C₁₂H₇F₃O₂: C, 60.01; H, 2.94. Found: C, 59.85; H, 3.00.

6-(Trifluoromethyl)-4-phenylpyridin-2-ol (**5**).



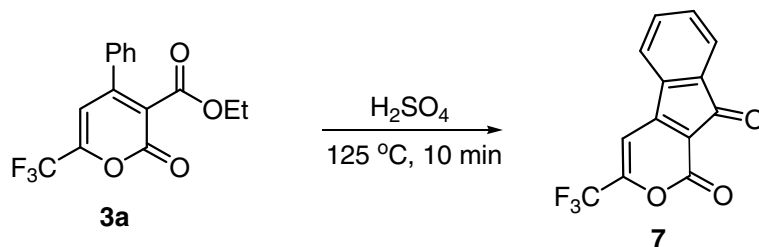
A solution of **3a** (0.40 g, 1.3 mmol) in 80% aqueous DMF (2.5 mL) was refluxed for 15 min. Then, the reaction mixture was allowed to cool to room temperature and diluted with water (5 mL). The solid (**5**) was filtered and recrystallized from toluene. Yield 0.21 g (69%), mp 213–214 °C, colourless solid; IR (KBr) 1658, 1632, 1567 cm^{-1} ; ^1H NMR (400 MHz, DMSO- d_6) δ 7.21 (s, 1H, H-3), 7.50–7.56 (m, 3H, arom.), 7.62 (s, 1H, H-5), 7.82–7.86 (m, 2H, arom.), 11.82 (bs, 1H, OH). Anal. Calcd for $\text{C}_{12}\text{H}_8\text{F}_3\text{NO}$: C, 60.26; H, 3.37; N, 5.86. Found: C, 60.45; H, 3.15; 5.97.

Bicyclic lactone (**6**).



A solution of **3a** (0.20 g, 0.64 mmol) in 2,3-dihydrofuran (0.5 mL) was heated in a sealed glass tube at 85 °C for 24 h. After evaporation of the solvent, crude product was recrystallized from heptane to give 0.15 g (61%) of lactone **6**, mp 160–162 °C, colourless solid; IR (KBr) 1770, 1741, 1633 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 0.81 (3H, t, $J = 7.2$ Hz, MeCH_2), 1.59–1.81 (1H, m, $\text{OCH}_2\text{-CHH}$), 2.11–2.27 (1H, m, $\text{OCH}_2\text{-CHH}$), 3.35 (1H, q, $J = 7.6$ Hz, OCHH-CH_2), 3.77–3.90 (1H, m, OCHH-CH_2), 3.94–4.12 (3H, m, CH_2Me , CH), 5.02 (1H, d, $J = 7.8$ Hz, CH), 5.02 (1H, s, CH), 7.26–7.39 (5H, m, Ph); ^{19}F NMR (376 MHz, CDCl_3) δ -78.76 (CF_3 , s). EI-MS m/z : 382 (5, $[\text{M}]^+$), 313 (47), 267 (42), 70 (100); HRMS m/z : found 382.10300, calcd for $\text{C}_{19}\text{H}_{17}\text{F}_3\text{O}_5$ $[\text{M}]^+$ 382.10281.

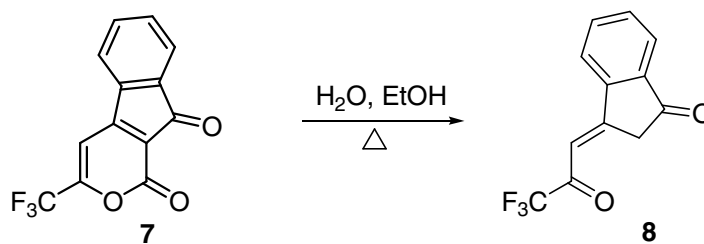
3-(Trifluoromethyl)indeno[2,1-c]pyran-1,9-dione (**7**).



A solution of **3a** (0.20 g, 0.64 mmol) in H_2SO_4 (2 mL) was heated at 125 °C for 10 min. The reaction mixture was allowed to cool to room temperature and then diluted with water (100 mL). The solid was filtered and recrystallized from toluene to give 0.07 g (41%) of pyranoindanone **7**, mp 244–245 °C, yellow solid; IR (KBr) 1776, 1698, 1633, 1599, 1550 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.15 (1H, s, =CH), 7.57–7.66 (3H, m, arom.), 7.75–7.79 (1H, m, arom.); ^{19}F NMR (376

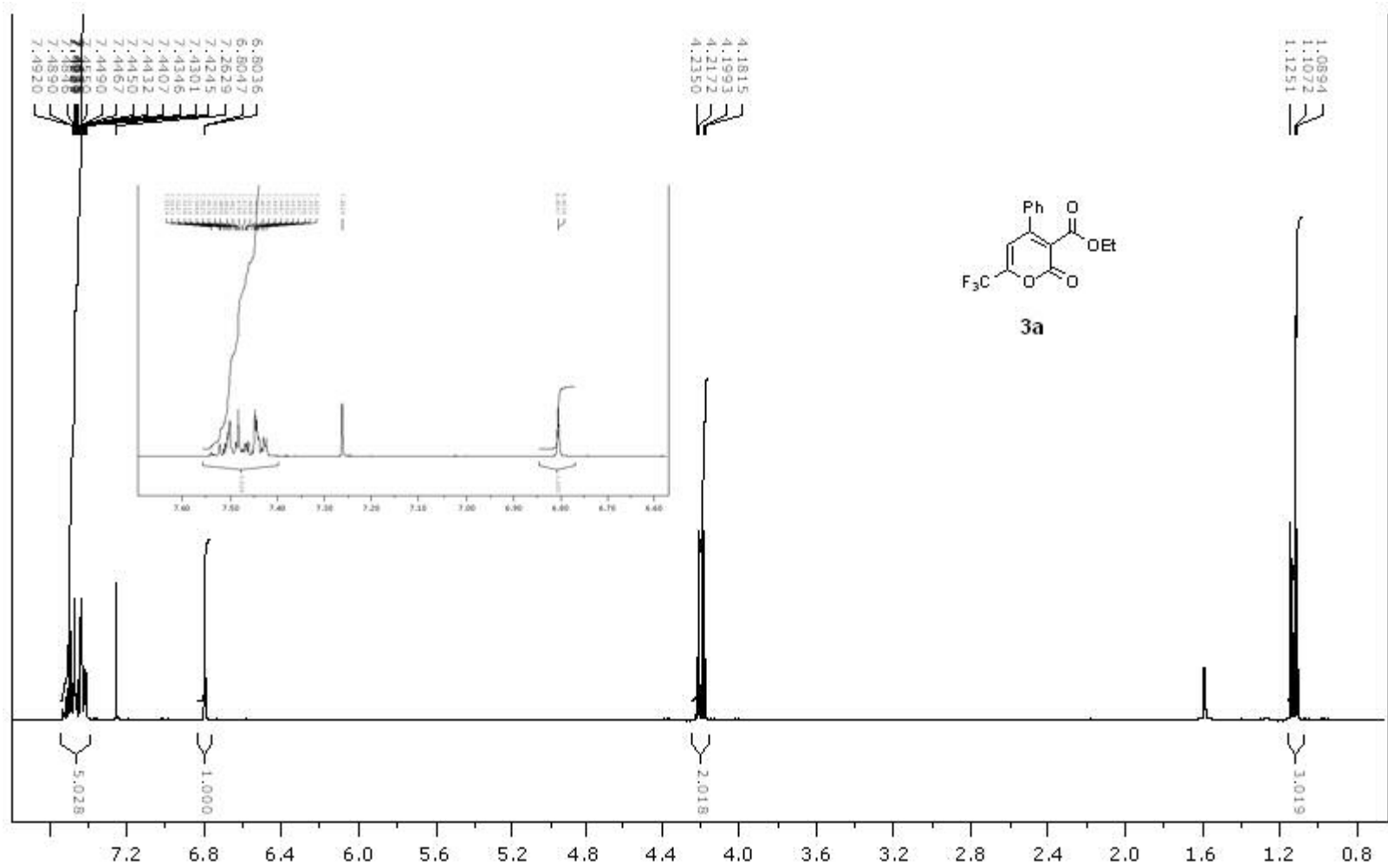
MHz, CDCl₃) δ -72.54 (CF₃, s). Anal. Calcd for C₁₃H₅F₃O₃: C, 58.66; H, 1.89. Found: C, 58.31; H, 1.76.

(E)-3-(3,3,3-Trifluoro-2-oxopropylidene)indan-1-one (8).

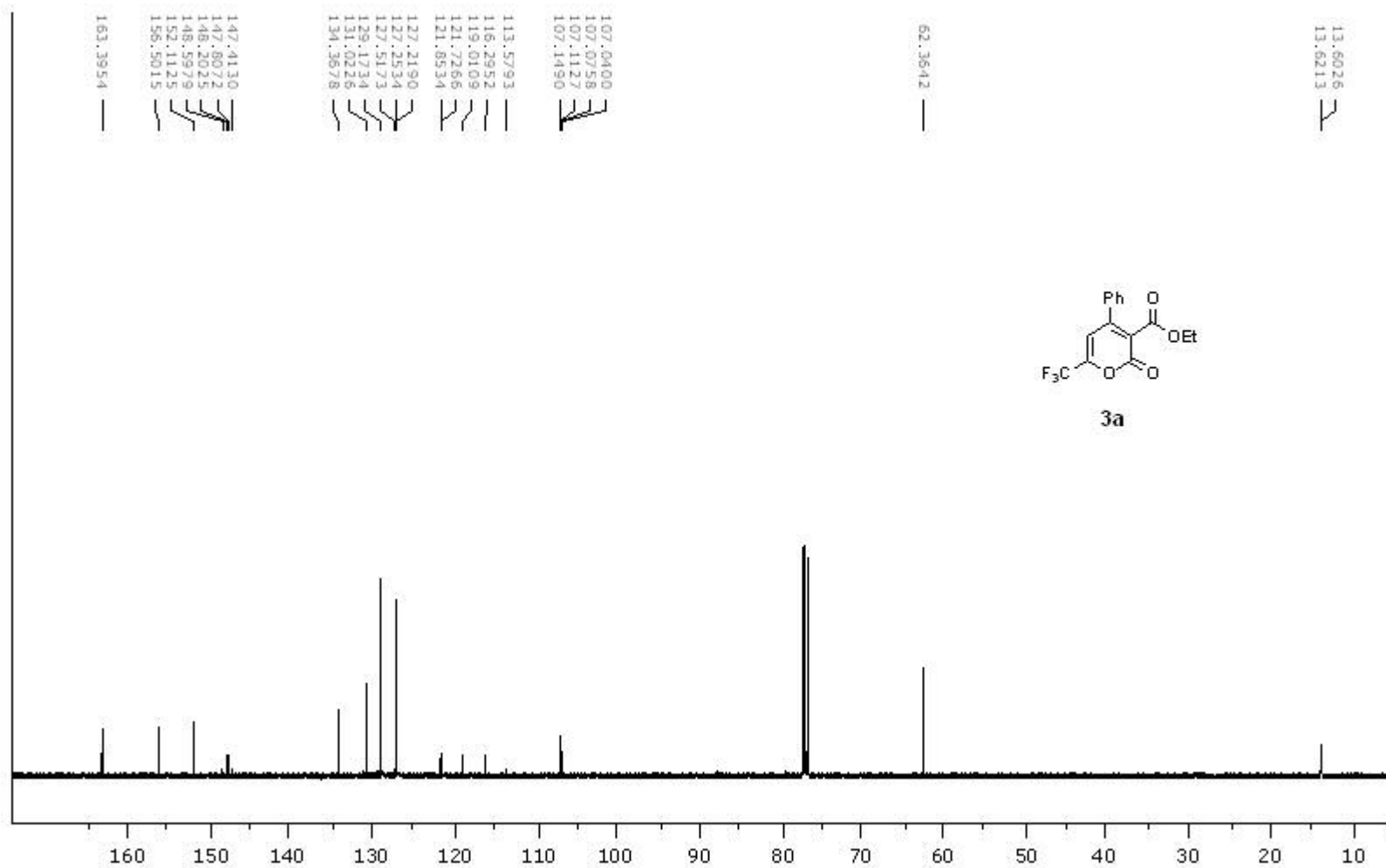


Pyranoindanone **7** (0.10 g, 0.38 mmol) was refluxed in 70% aqueous ethanol for 1 min. After cooling in ice, the solid was collected by filtration to give 0.030 g (33%) of indanone **8**. Light green solid; IR (KBr) 1717, 1707, 1615, 1589, 1467 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.82 (2H, d, J = 2.0 Hz, CH₂), 7.13 (1H, bs, CH), 7.71 (1H, td, J = 7.5, 0.8 Hz, H-6), 7.78 (1H, td, J = 7.5, 1.3 Hz, H-5), 7.91 (1H, d, J = 7.6 Hz, H-7), 7.99 (1H, d, J = 7.8 Hz, H-4); ¹⁹F NMR (376 MHz, CDCl₃) δ -79.90 (CF₃, s). Anal. Calcd for C₁₂H₇F₃O₂: C, 60.01; H, 2.94. Found: C, 60.00; H, 2.91.

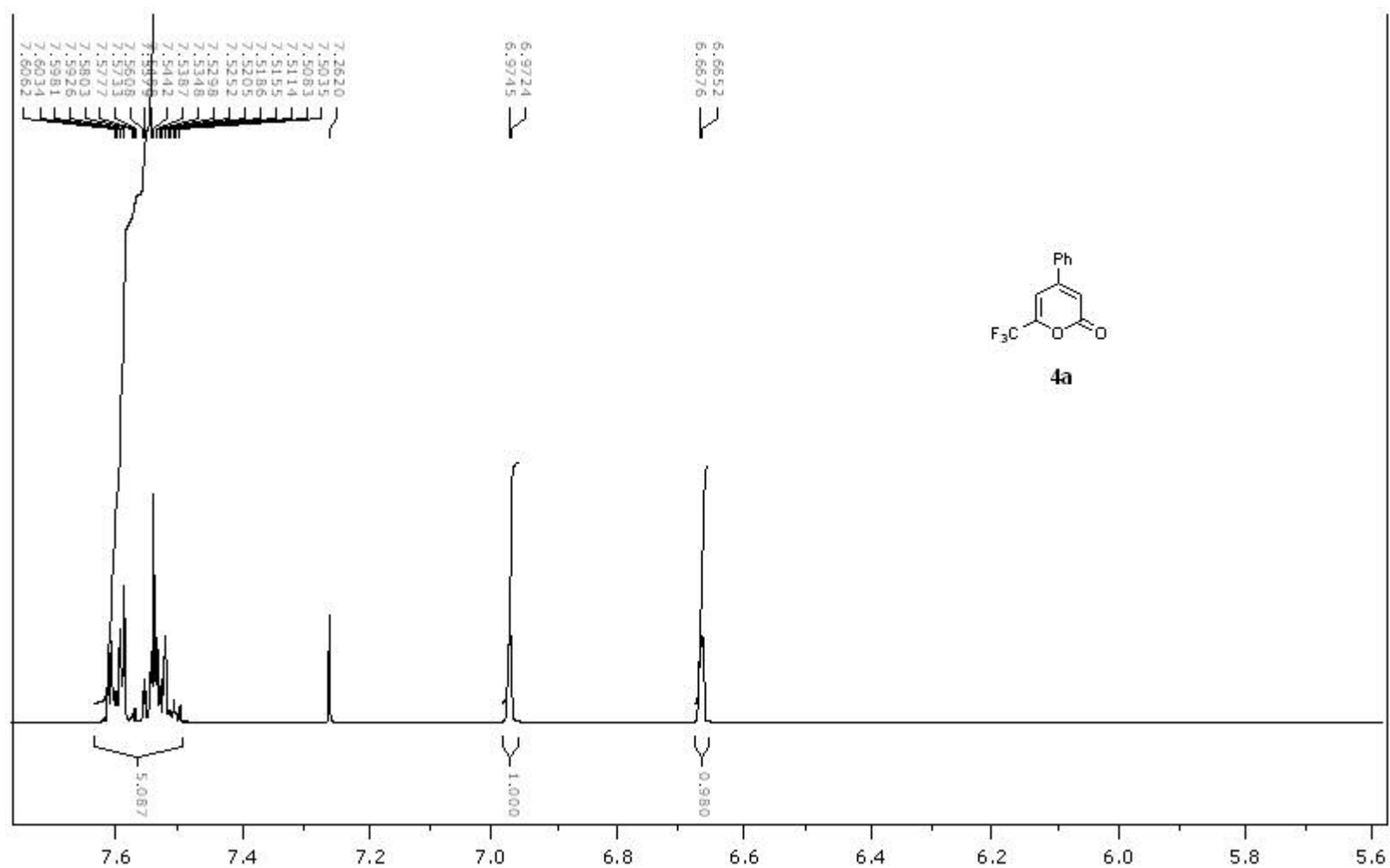
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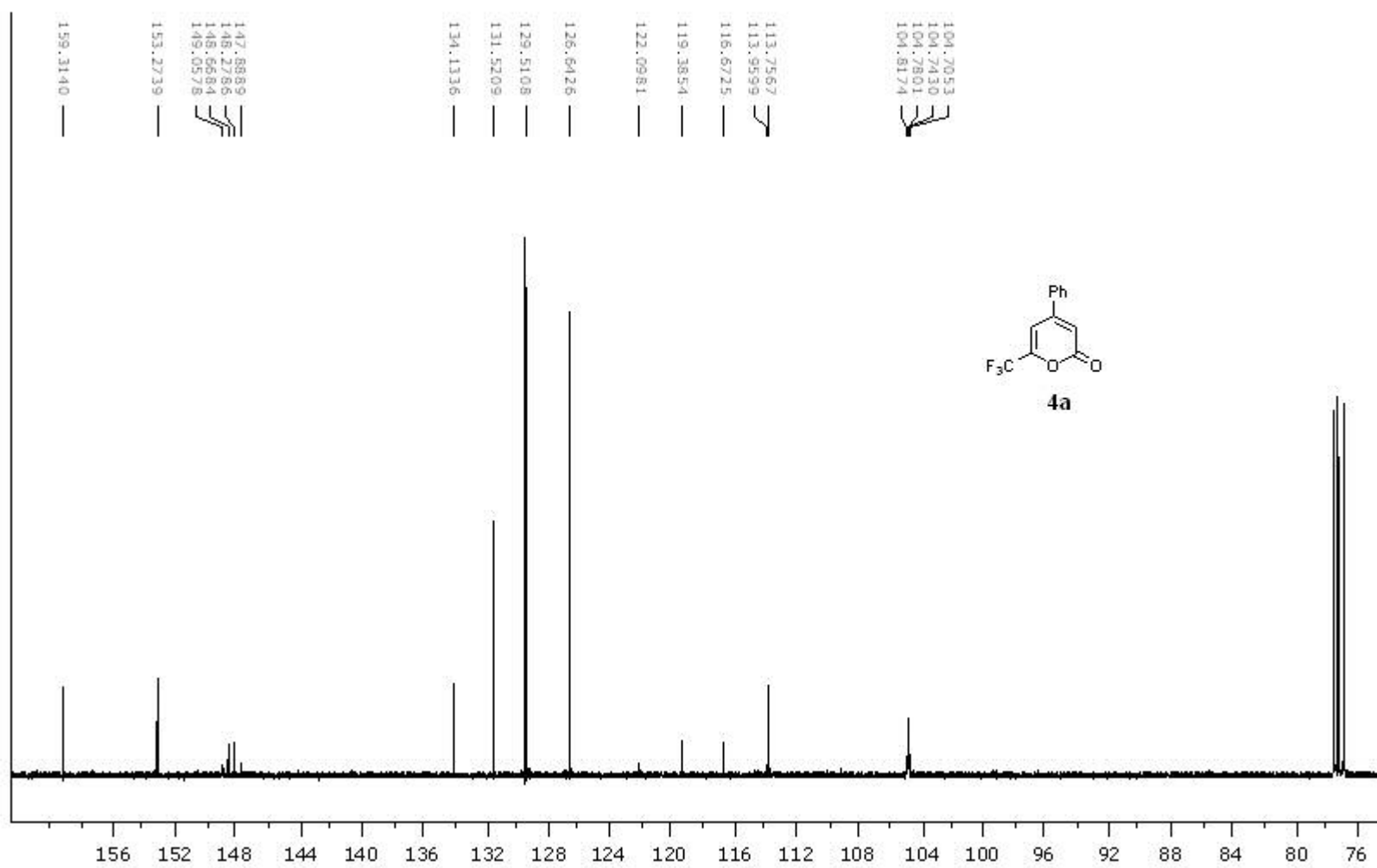
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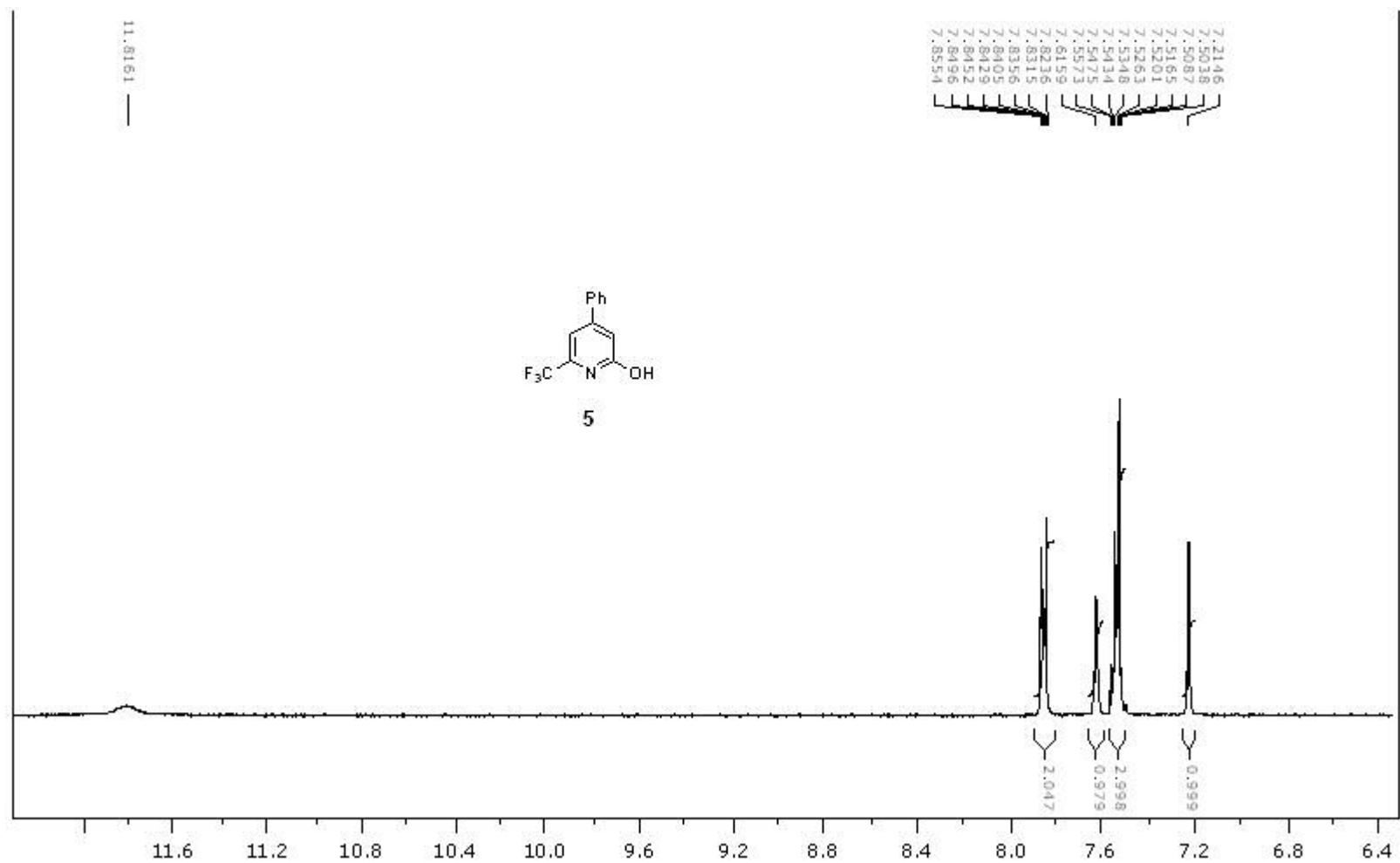
S3

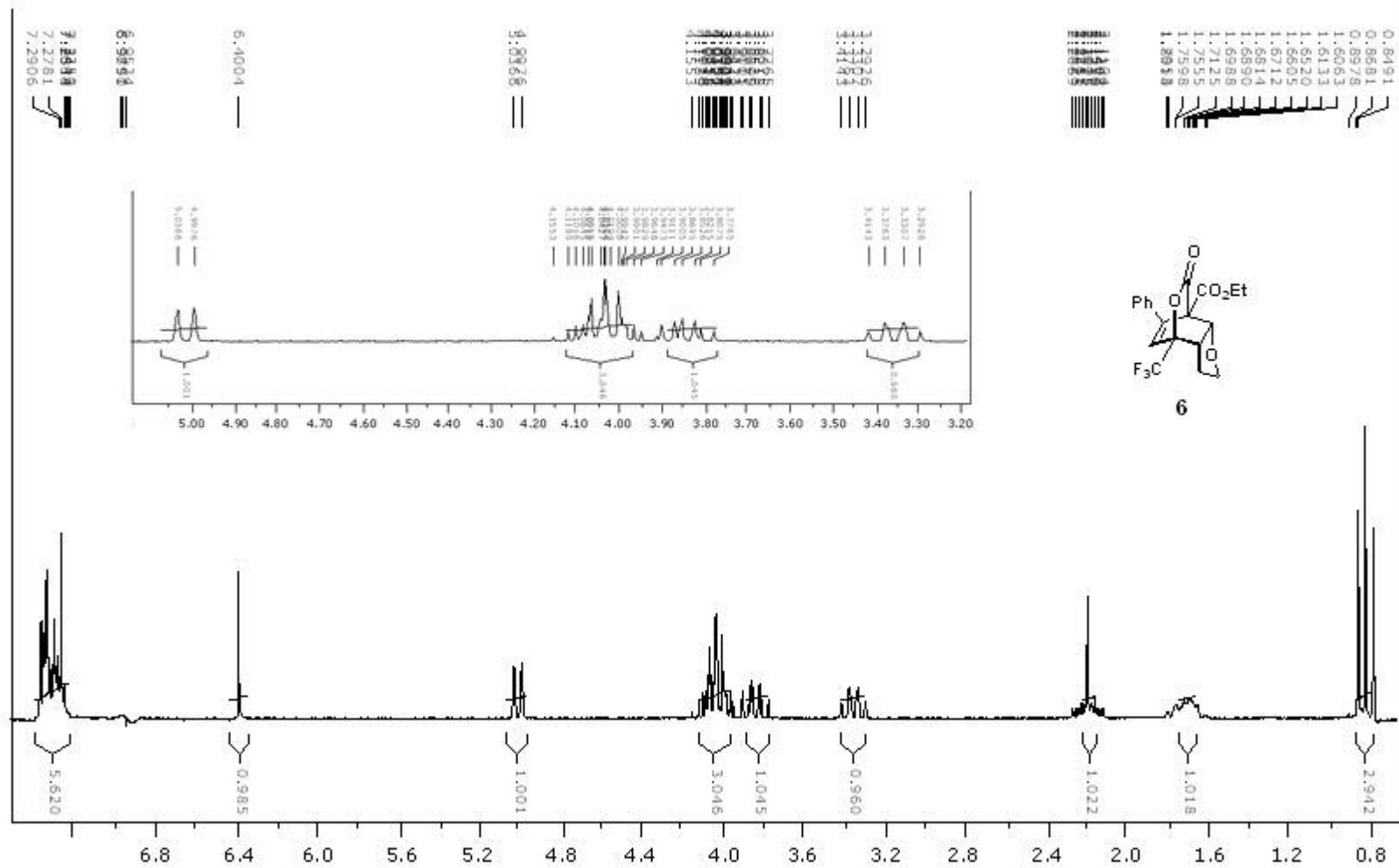


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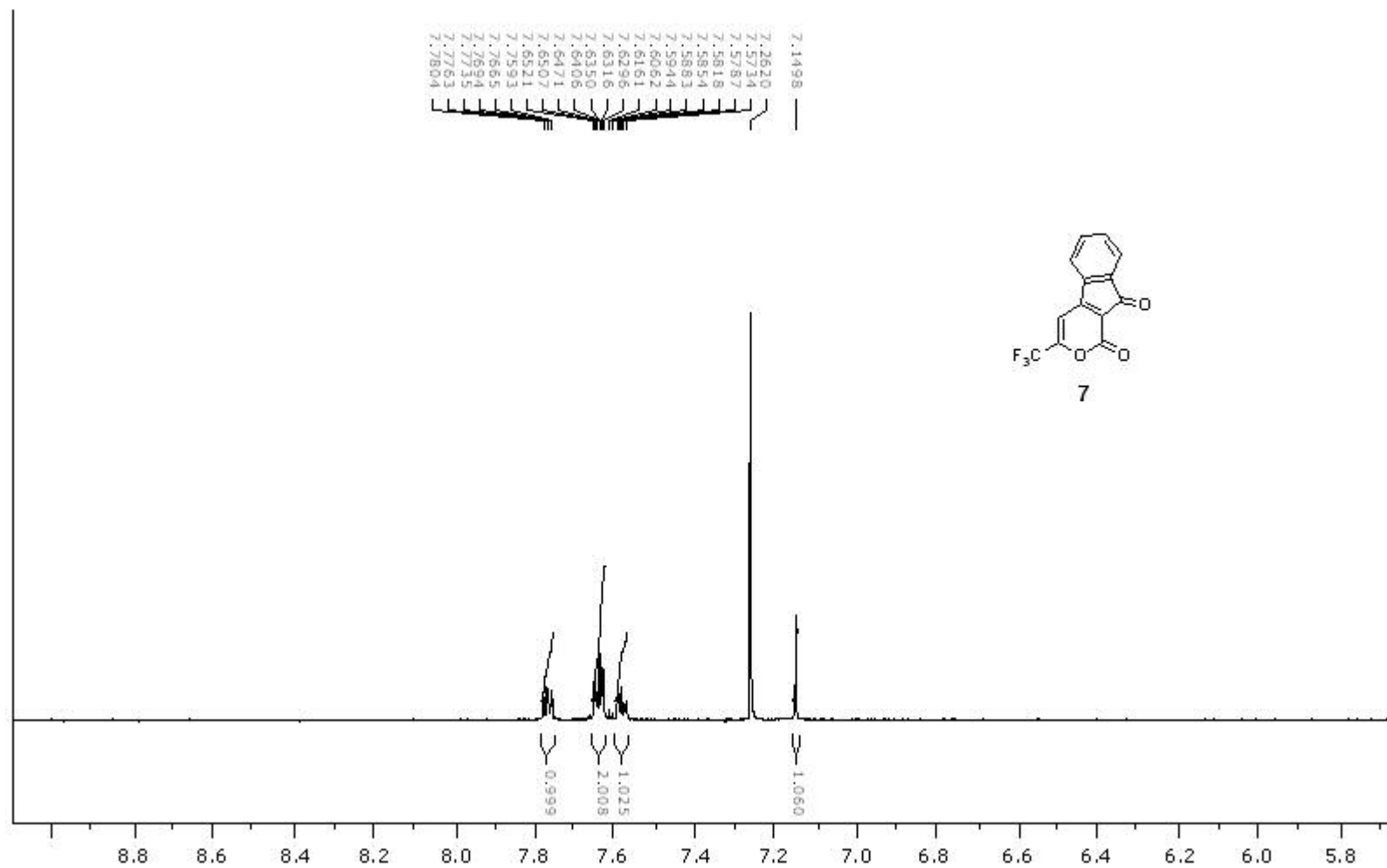


S5





S7



S8

