

## Supporting Information

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### Rapid Synthesis of CDP840 Using 2-Pyrimidyl Vinyl Sulfide as a Platform

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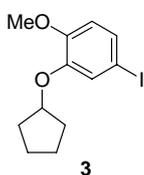
#### Contents

1. General methods.	S2
2. Experimental procedure and spectroscopic data.	S2
3. <sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>3</b> .	S4
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>4a</b> .	S6
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>4b</b> .	S8
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>4c</b> .	S10
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>4d</b> .	S12
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>5</b> .	S14
<sup>1</sup> H and <sup>13</sup> C NMR spectra for <b>1</b> .	S16

**General.**  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on Varian MERCURYplus-400 ( $^1\text{H}$  400 MHz,  $^{13}\text{C}$  100 MHz) spectrometers in  $\text{CDCl}_3$  using tetramethylsilane ( $^1\text{H}$ ,  $\delta = 0.00$ ) and  $\text{CDCl}_3$  ( $^{13}\text{C}$ ,  $\delta = 77.0$ ) as an internal standard. IR spectra were recorded on Shimadzu FTIR-8100 spectrophotometer. EI mass spectra were recorded on JMS-SX102A spectrometer. Unless otherwise noted, all reactions were carried out under an argon atmosphere. Column chromatography was performed with silica gel 60 A (SILICYCLE). Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification.

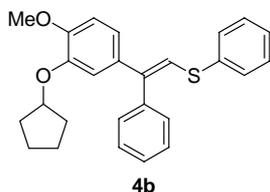
### Synthesis of 3.

To a solution of 5-iodo-2-methoxyphenol<sup>1</sup> (1.04 g, 4.14 mmol) in DMF (10 mL) were added cyclopentyl bromide (926 mg, 6.21 mmol) and  $\text{K}_2\text{CO}_3$  (859 mg, 6.21 mmol) at room temperature. The mixture was heated at 50 °C and vigorously stirred for 22 h. When the reaction completed, water was added to the mixture. The aqueous layer was extracted with  $\text{Et}_2\text{O}$ , and the combined organic layer was washed with water and brine, dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification of the residual solids by silica gel flash column chromatography (eluent: hexane/ $\text{EtOAc} = 20/1\sim 10/1$ ) afforded **3** (1.07 g, 81%) as colorless crystals.



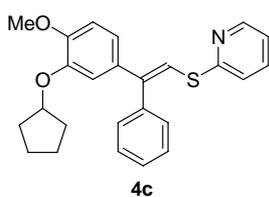
IR (KBr) 1250, 1225, 797  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.17 (dd,  $J = 5.0, 1.3$  Hz, 1H), 7.11 (d,  $J = 1.3$  Hz, 1H), 6.59 (d,  $J = 5.0$  Hz, 1H), 4.74–4.69 (m, 1H), 3.80 (s, 3H), 1.98–1.77 (m, 6H), 1.66–1.56 (m, 2H).  $^{13}\text{C}$  NMR (100 Hz,  $\text{CDCl}_3$ )  $\delta$  149.9, 148.5, 129.4, 123.6, 113.8, 82.3, 80.7, 56.1, 32.8, 24.1. LRMS (EI)  $m/z$  318 ( $\text{M}^+$ ). HRMS (EI) calcd. for  $\text{C}_{12}\text{H}_{15}\text{IO}_2$ : 318.0117, found: 317.0116.

### Spectroscopic data for 4b, c



**4b:** 78% yield. IR (KBr) 2959.2, 1259.7, 698.3  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42–7.38 (m, 4H), 7.36–7.29 (m, 4H), 7.23–7.20 (m, 1H), 6.83–6.77 (m, 2H), 6.75 (d,  $J = 1.3$  Hz, 1H), 6.73 (s, 1H), 4.66–4.62 (m, 1H), 3.83 (s, 3H), 1.84–1.77 (m, 6H), 1.56–1.53 (m, 2H).  $^{13}\text{C}$  NMR (100 Hz,  $\text{CDCl}_3$ )  $\delta$  149.6, 147.1, 141.5, 139.2, 136.7, 134.3, 129.6 ( $\times 2$ ), 129.0 ( $\times 2$ ), 128.9 ( $\times 2$ ), 128.2 ( $\times 2$ ), 127.6, 126.4, 121.4, 119.8, 114.4, 111.5, 80.5, 56.2, 32.9 ( $\times 2$ ), 24.2 ( $\times 2$ ). LRMS (EI)  $m/z$  402 ( $\text{M}^+$ ). HRMS (EI) calcd. for  $\text{C}_{26}\text{H}_{26}\text{O}_2\text{S}$ : 402.1657, found: 402.1652.

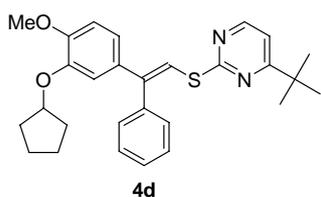
(1) Feldman, K. S. *J. Org. Chem.* **1997**, *62*, 4983-4990.



**4c:** 75% yield. IR (KBr) 2961, 1258, 804  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.47 (ddd,  $J = 3.0, 1.3, 0.5$  Hz, 1H), 7.59 (s, 1H), 7.46 (ddd,  $J = 5.4, 5.0, 1.3$  Hz, 1H), 7.42–7.38 (m, 2H), 7.36–7.33 (m, 3H), 7.15 (dt,  $J = 5.0, 0.5$  Hz, 1H), 7.00 (ddd,  $J = 5.0, 3.0, 0.5$  Hz, 1H), 6.88–6.86 (m, 2H), 6.77 (dd,  $J = 5.0, 0.8$  Hz, 1H), 4.70–4.66 (m, 1H), 3.82 (s, 3H), 1.87–1.81 (m, 6H), 1.58–1.54 (m, 2H).  $^{13}\text{C}$  NMR (100 Hz,  $\text{CDCl}_3$ )  $\delta$  157.4, 149.5, 149.5, 147.1, 140.5, 139.7, 136.1, 134.4, 129.5 ( $\times 2$ ), 128.2 ( $\times 2$ ), 127.6, 122.3, 120.0, 119.9, 117.2, 114.5, 111.5, 80.5, 56.1, 32.9 ( $\times 2$ ), 24.2 ( $\times 2$ ). LRMS (EI)  $m/z$  403 ( $\text{M}^+$ ). HRMS (EI) calcd. for  $\text{C}_{25}\text{H}_{25}\text{NO}_2\text{S}$ : 403.1606, found: 403.1606.

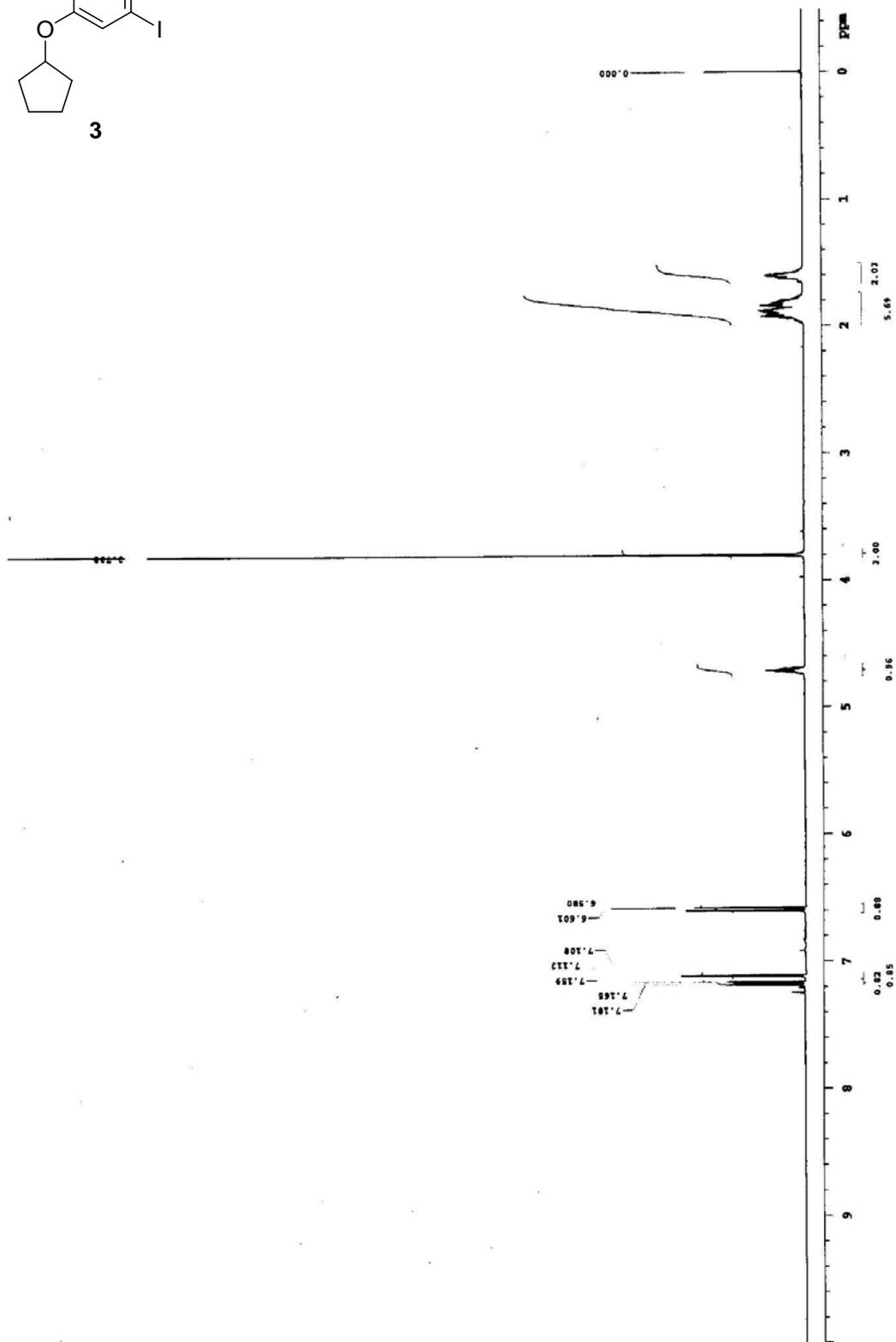
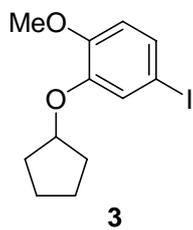
### Synthesis of 4d.

To a solution of **4a** (100 mg, 0.247 mmol) in THF (1.5 mL) was added dropwise a solution of *t*-BuLi (1.57 M in pentane, 0.17 mL, 0.272 mmol) at  $-78$   $^\circ\text{C}$ . The resultant solution was stirred for 30 min at the same temperature. Then the solution was gradually warmed to  $0$   $^\circ\text{C}$  and stirred for 2 h at  $0$   $^\circ\text{C}$ . The reaction mixture was quenched with acetic acid (16.3 mg, 0.272 mmol), and treated with a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ; 61.7 mg, 0.272 mmol) in THF (1.0 mL). The mixture was stirred for 30 min at room temperature and then treated with an aqueous solution of sodium hydroxide (0.25 M, 1.6 mL, 0.400 mmol). The layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layer was washed with water and brine, dried over  $\text{MgSO}_4$ , filtered, and concentrated. Purification of the residue by silica gel flash column chromatography (hexane/EtOAc = 5/2) afforded **4d** (109.1 mg, 96%) as colorless solids.

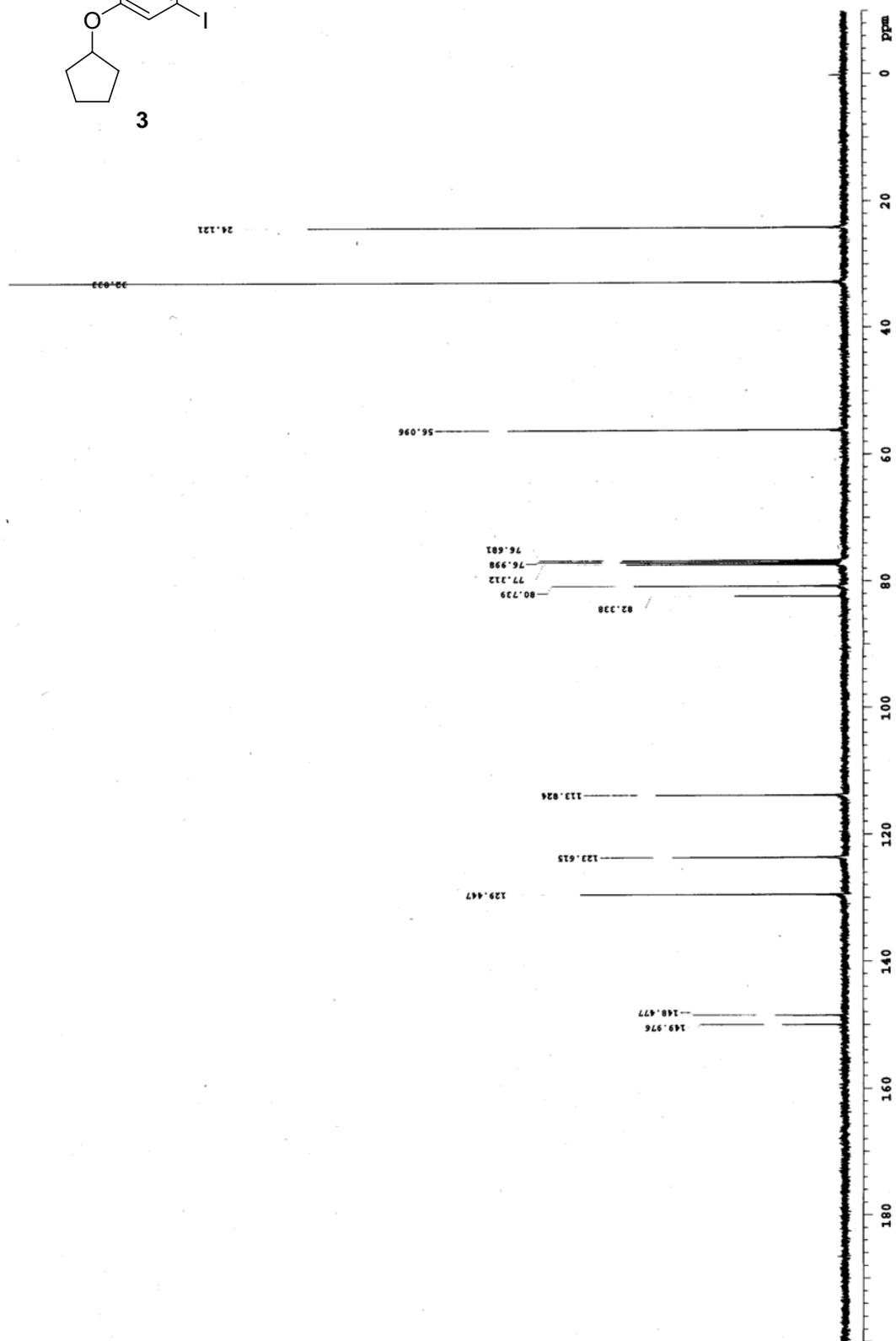
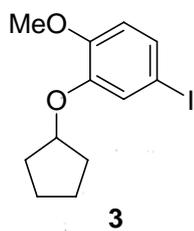


**4d:** IR (KBr) 2961, 1258, 758  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.42 (d,  $J = 3.3$  Hz, 1H), 7.78 (s, 1H), 7.42–7.38 (m, 2H), 7.36–7.31 (m, 3H), 6.99 (d,  $J = 3.3$  Hz, 1H), 6.94 (s, 1H), 6.78 (d,  $J = 0.8$  Hz, 2H), 4.75–4.70 (m, 1H), 3.84 (s, 3H), 1.90–1.79 (m, 6H), 1.60–1.57 (m, 2H), 1.36 (s, 9H).  $^{13}\text{C}$  NMR (100 Hz,  $\text{CDCl}_3$ )  $\delta$  177.9, 157.3, 139.7, 139.5, 134.3, 129.5 ( $\times 2$ ), 128.2 ( $\times 2$ ), 127.6 ( $\times 2$ ), 119.9, 117.8, 113.9, 112.5, 111.4, 80.3, 56.1, 37.9, 32.9 ( $\times 2$ ), 29.4 ( $\times 2$ ), 24.2 ( $\times 2$ ). LRMS (EI)  $m/z$  460 ( $\text{M}^+$ ). HRMS (EI) calcd. for  $\text{C}_{28}\text{H}_{32}\text{N}_2\text{O}_2\text{S}$ : 460.2184, found: 460.2188.

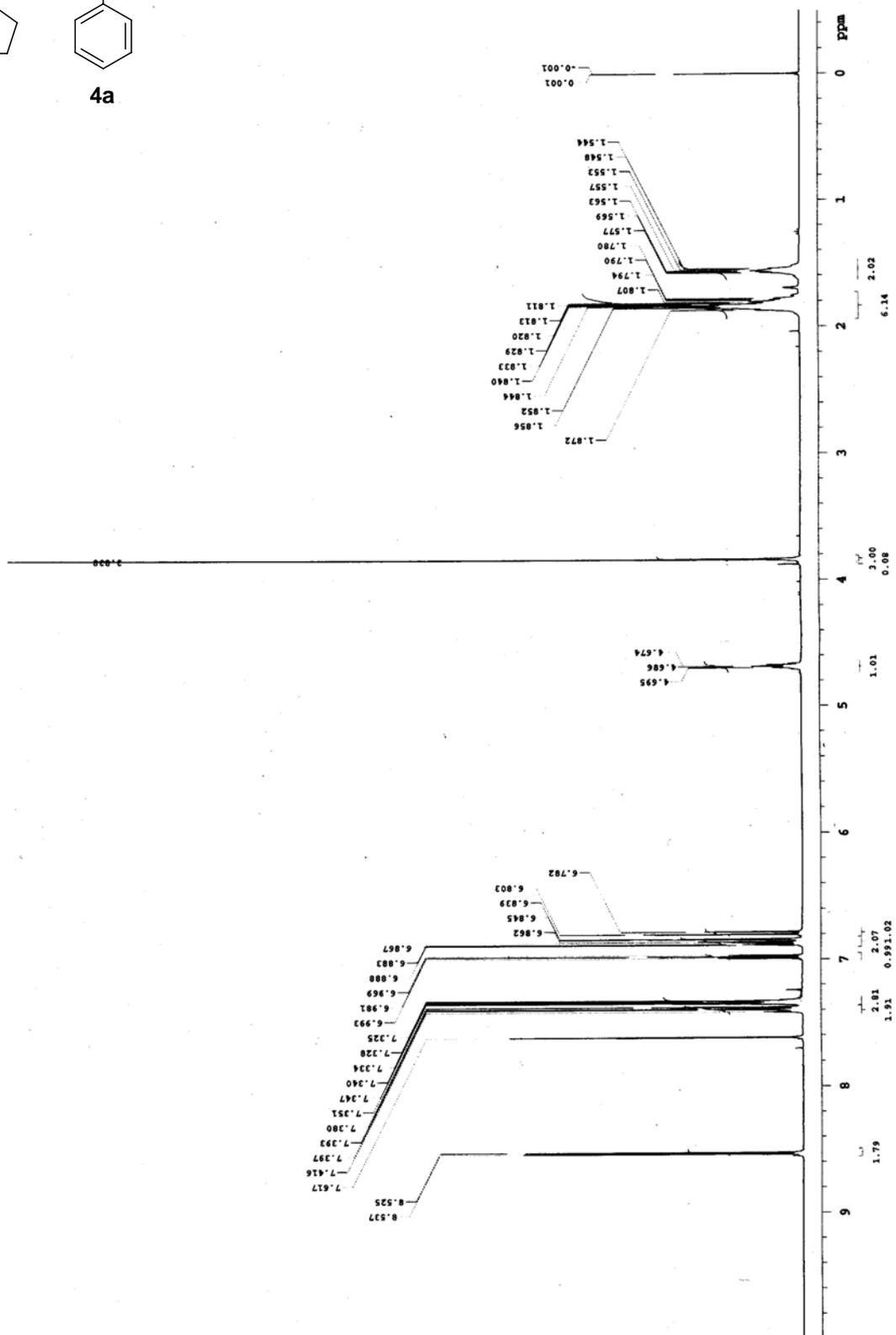
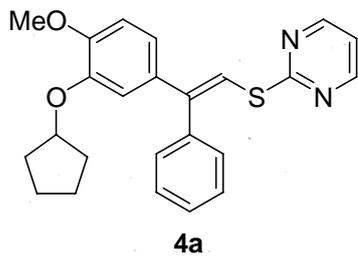
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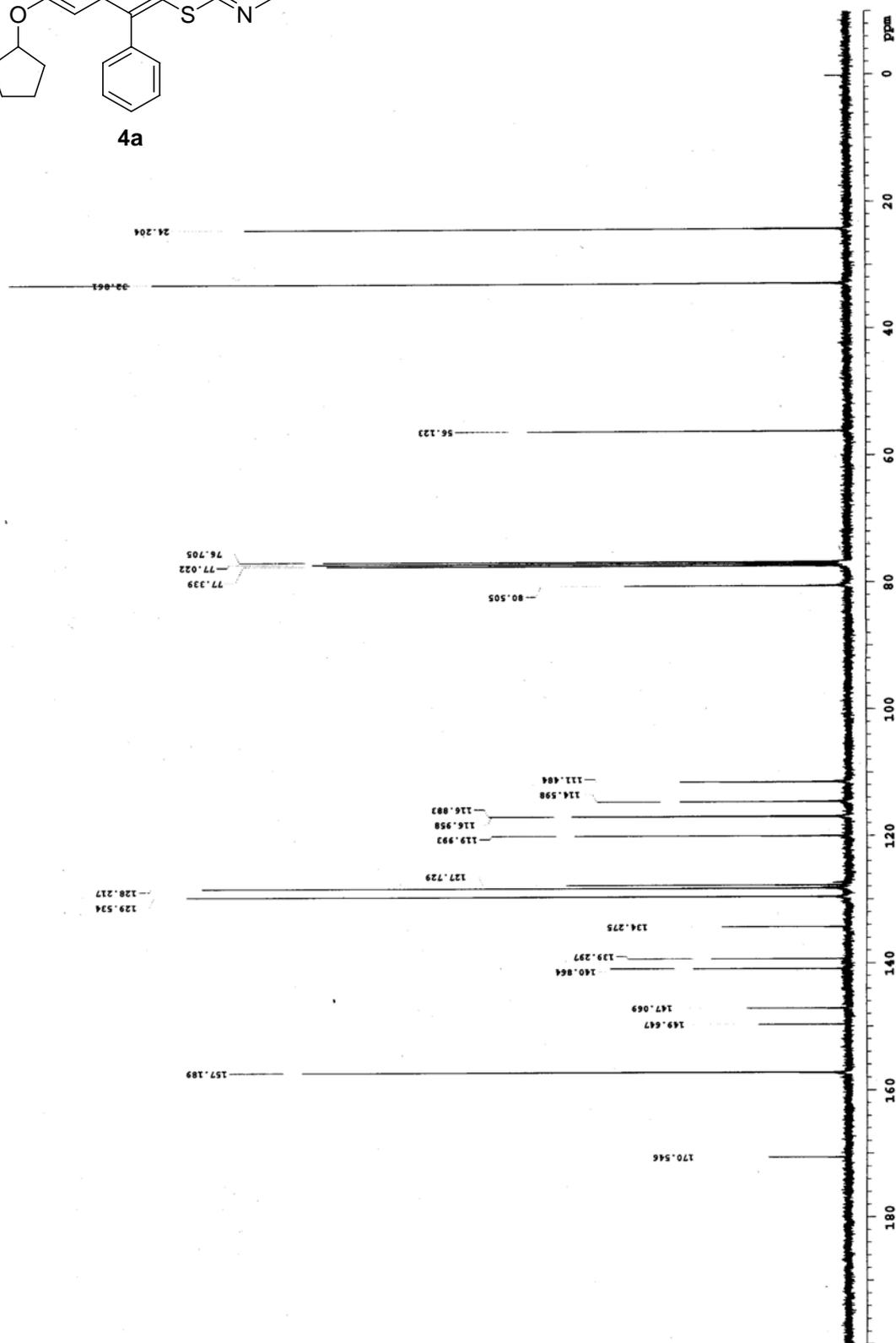
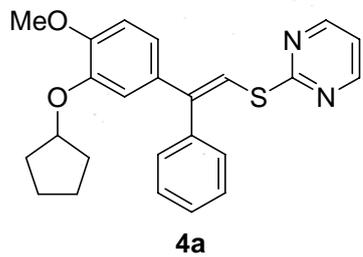
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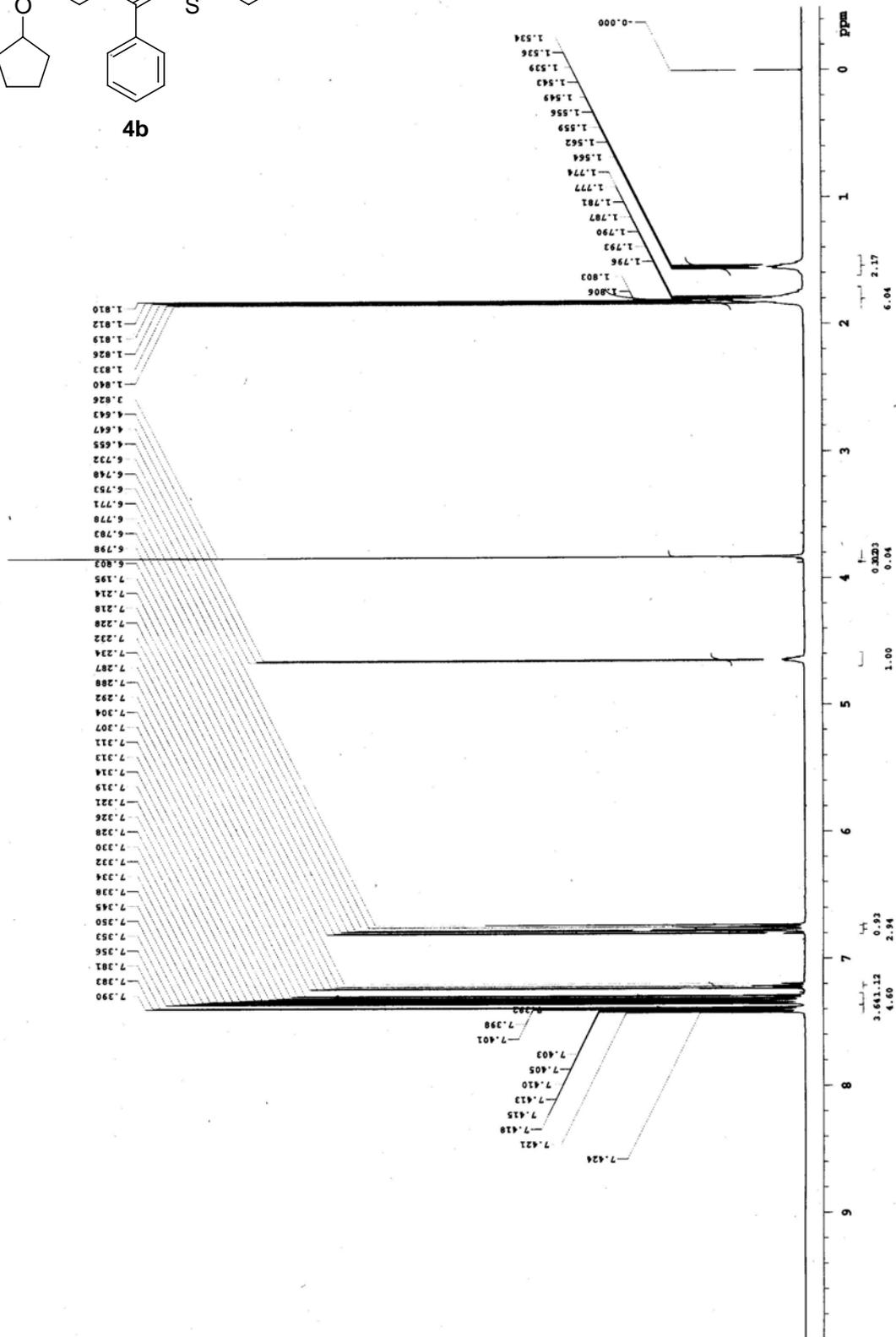
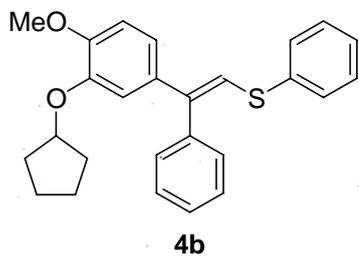
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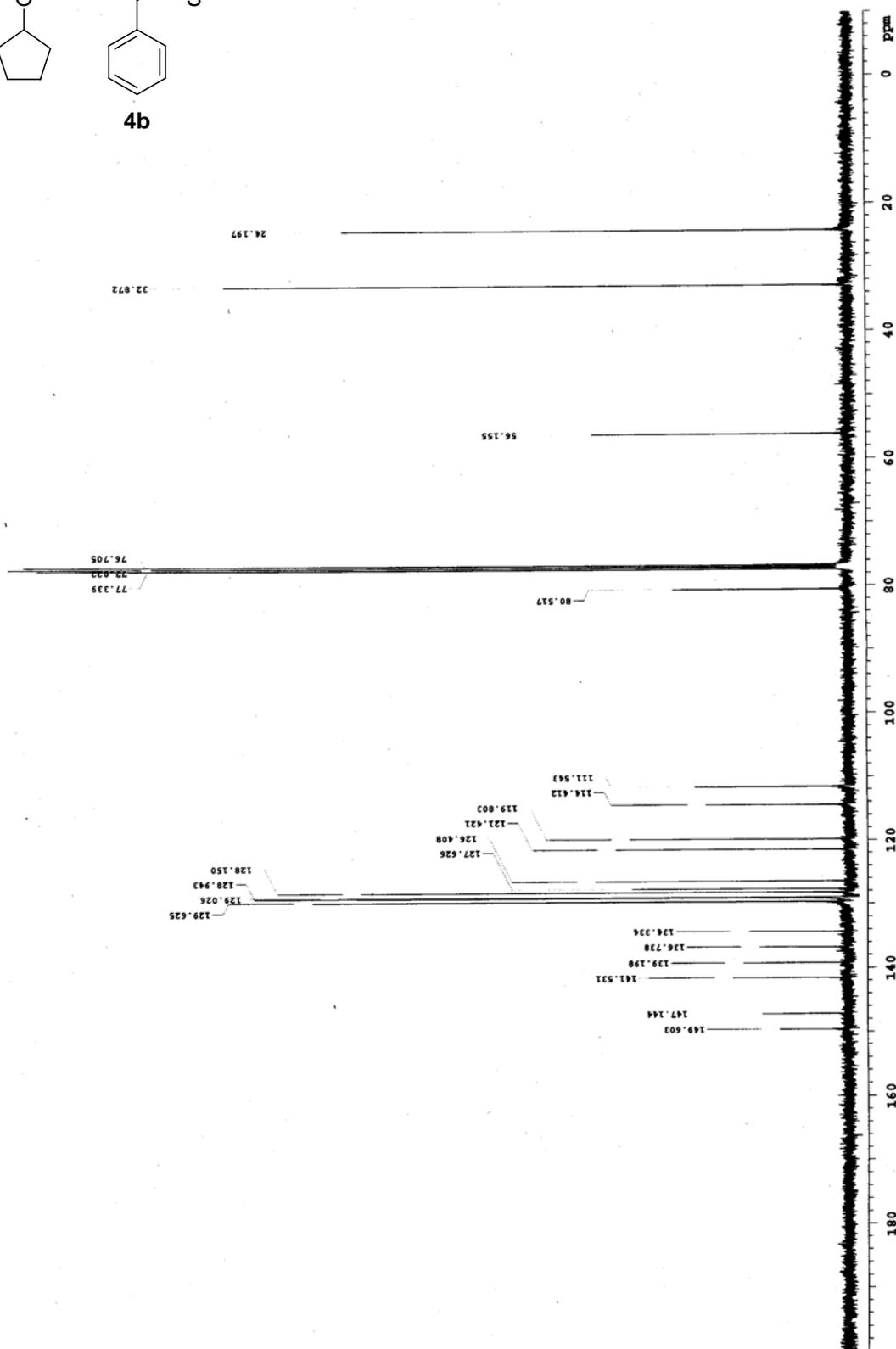
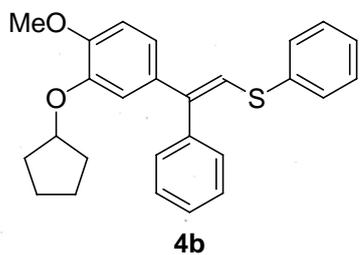
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



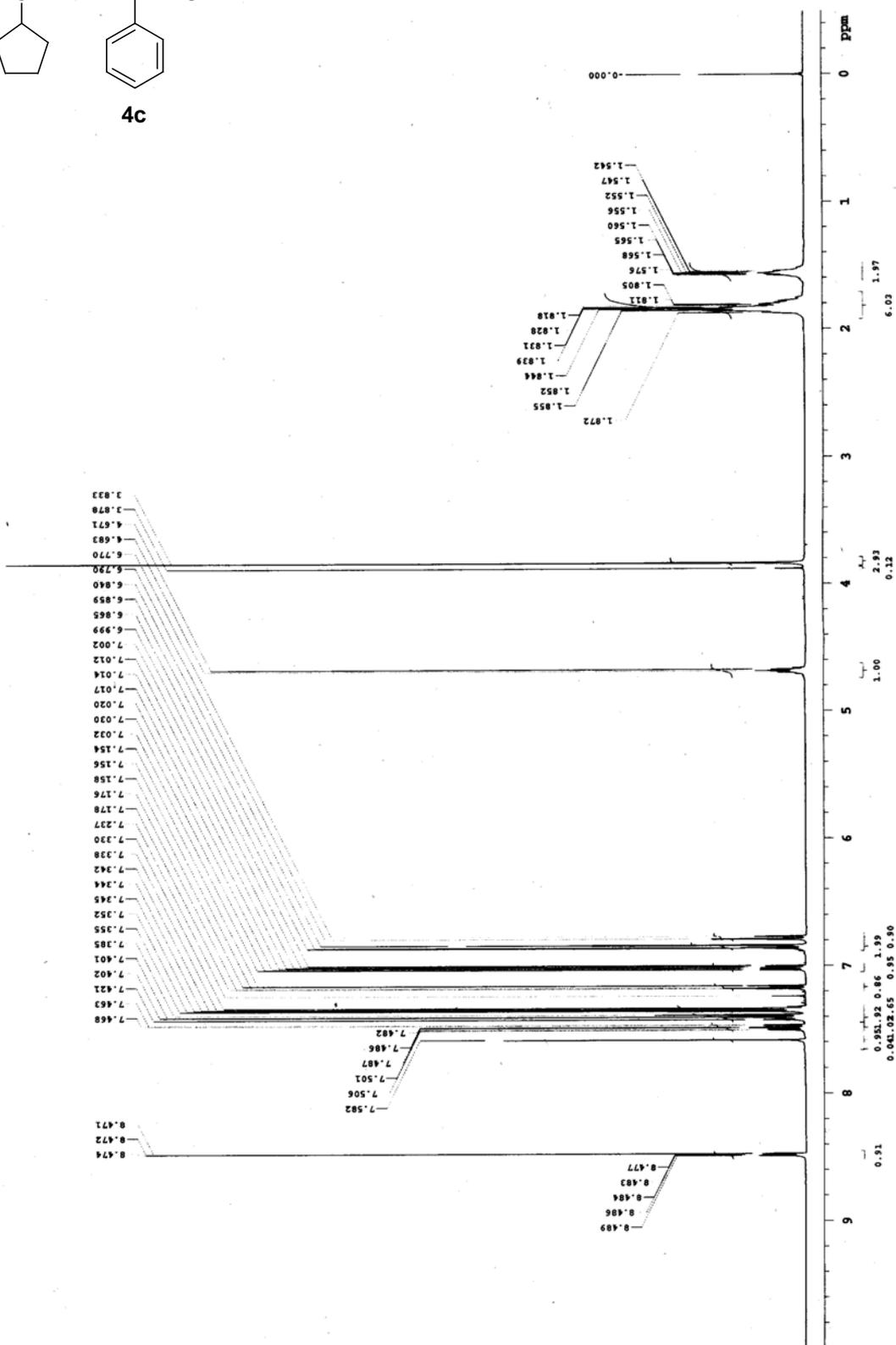
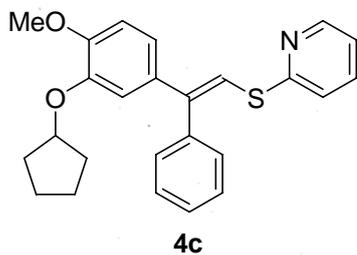
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



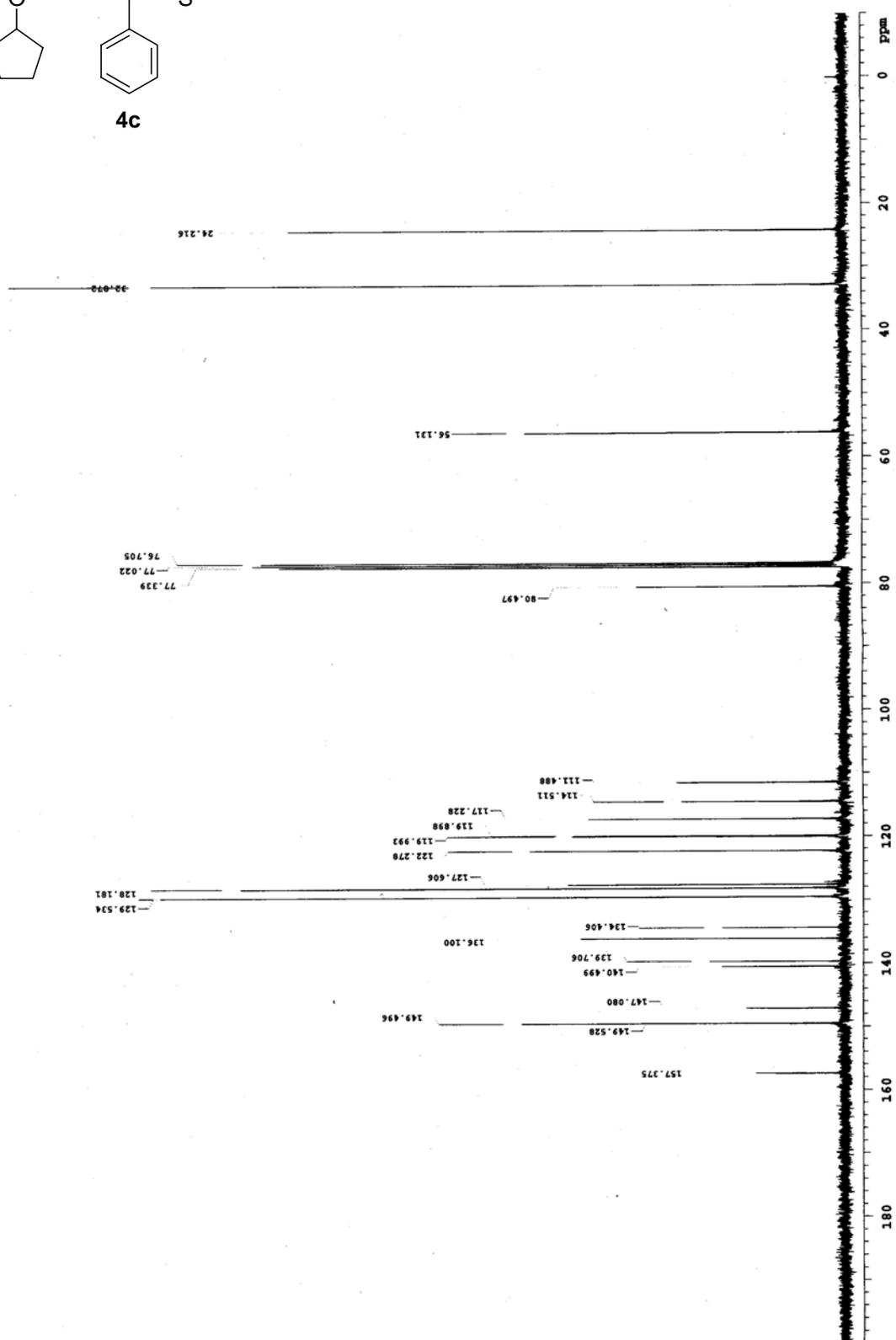
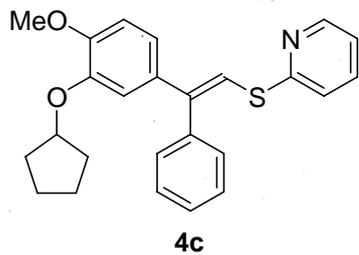
<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)



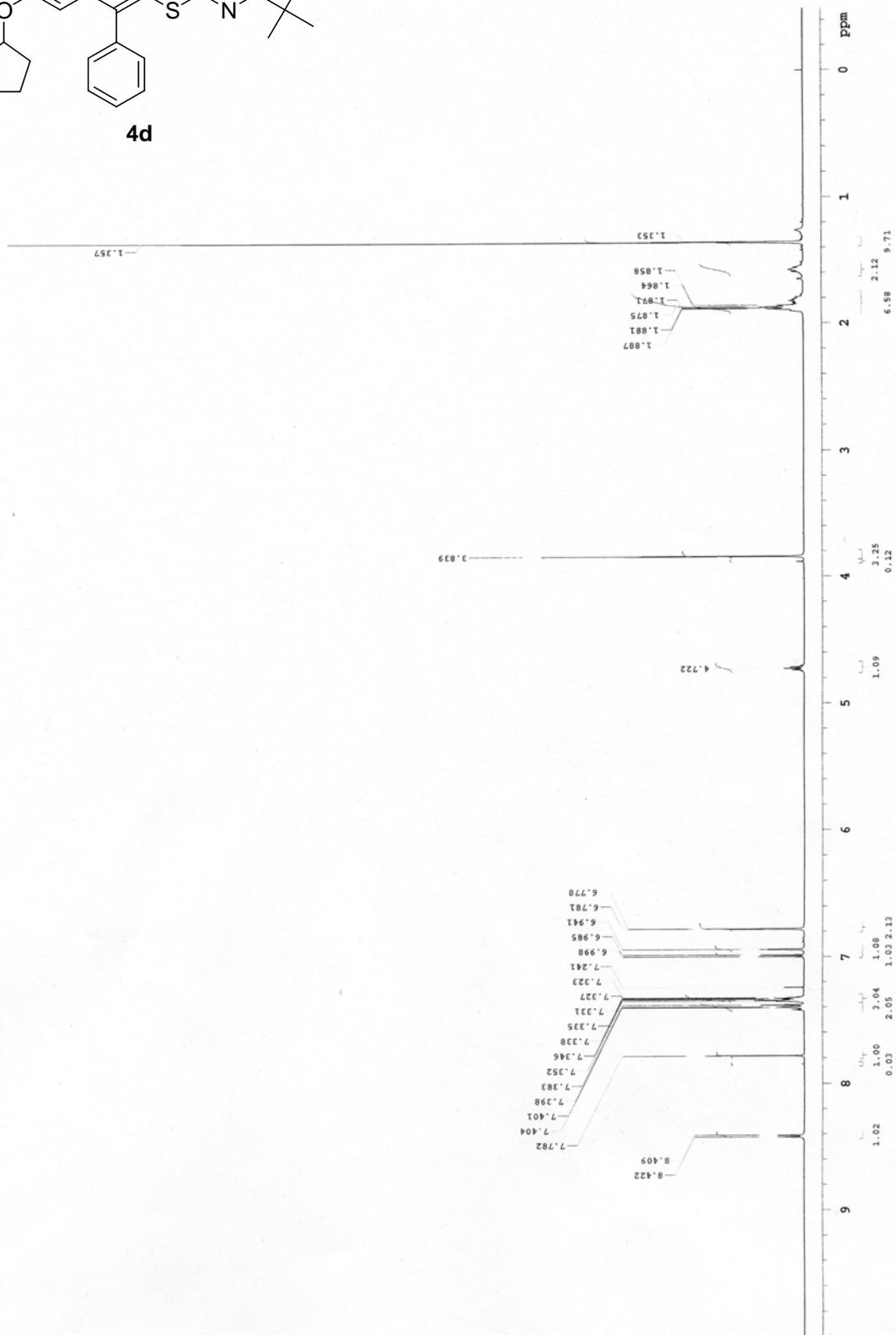
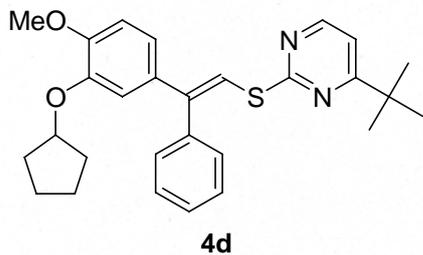
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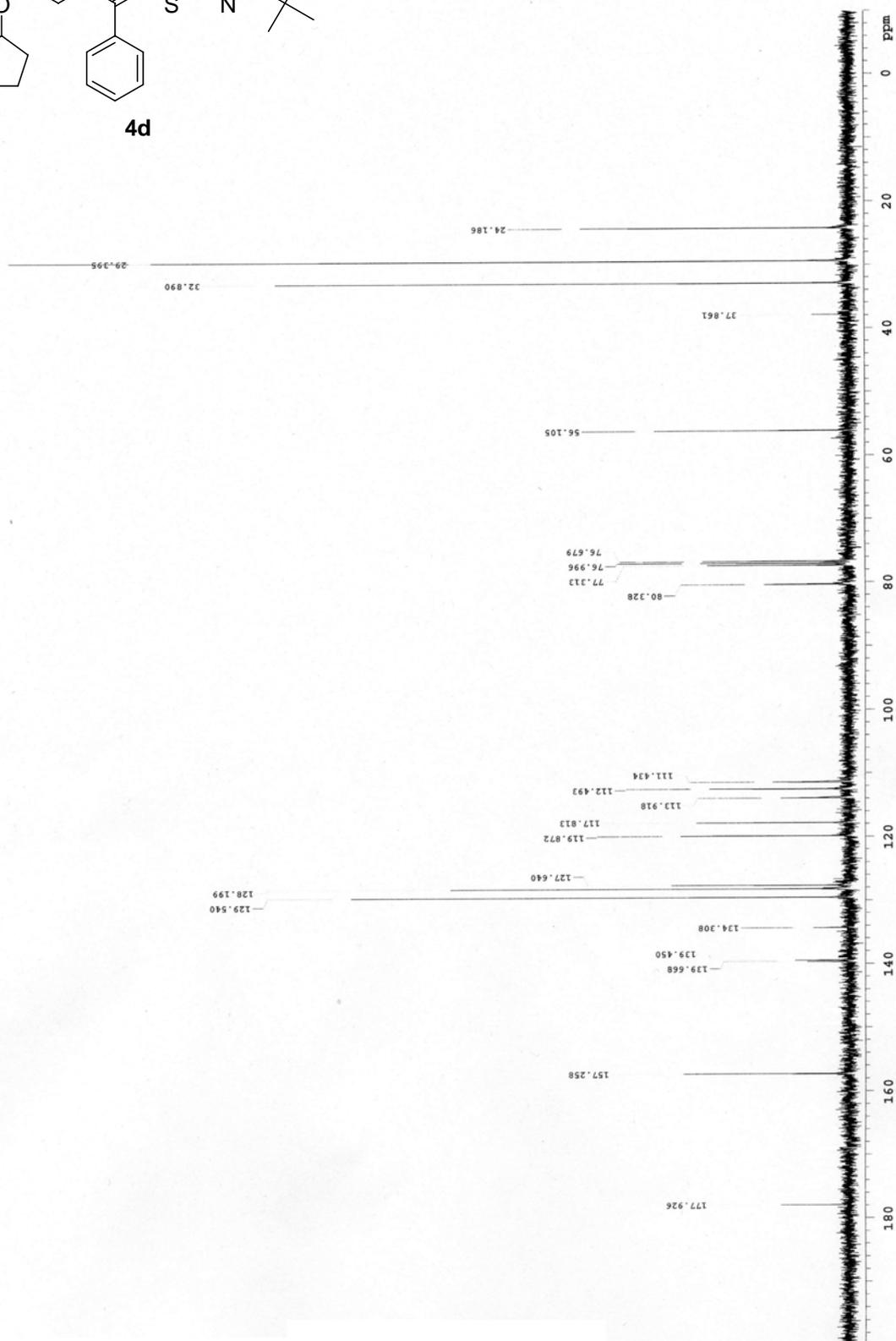
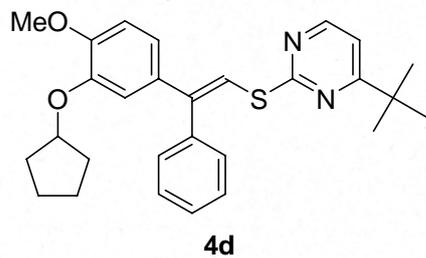
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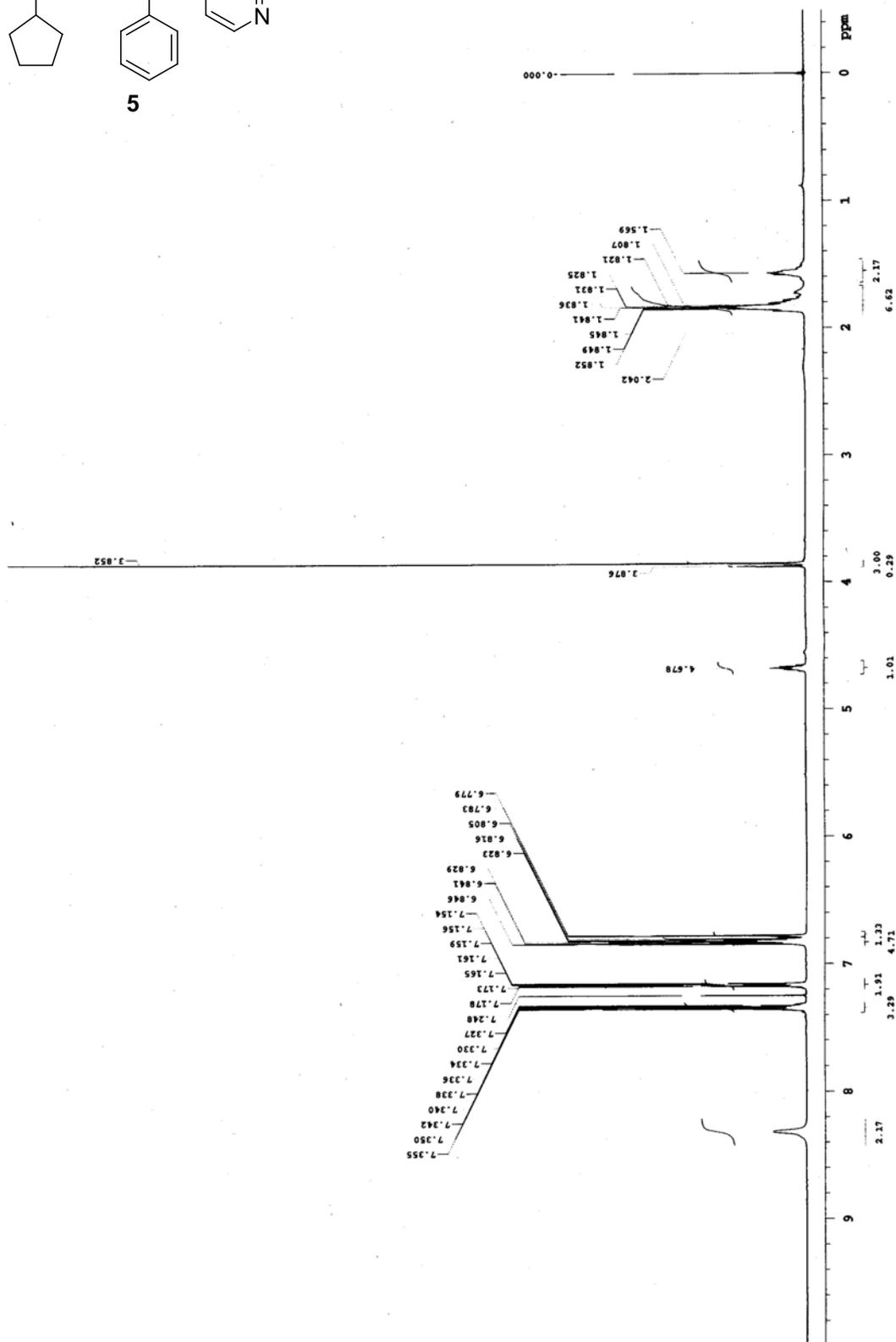
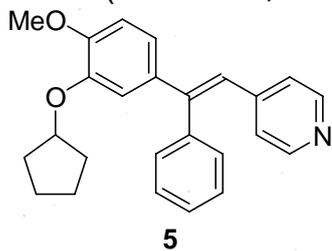
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



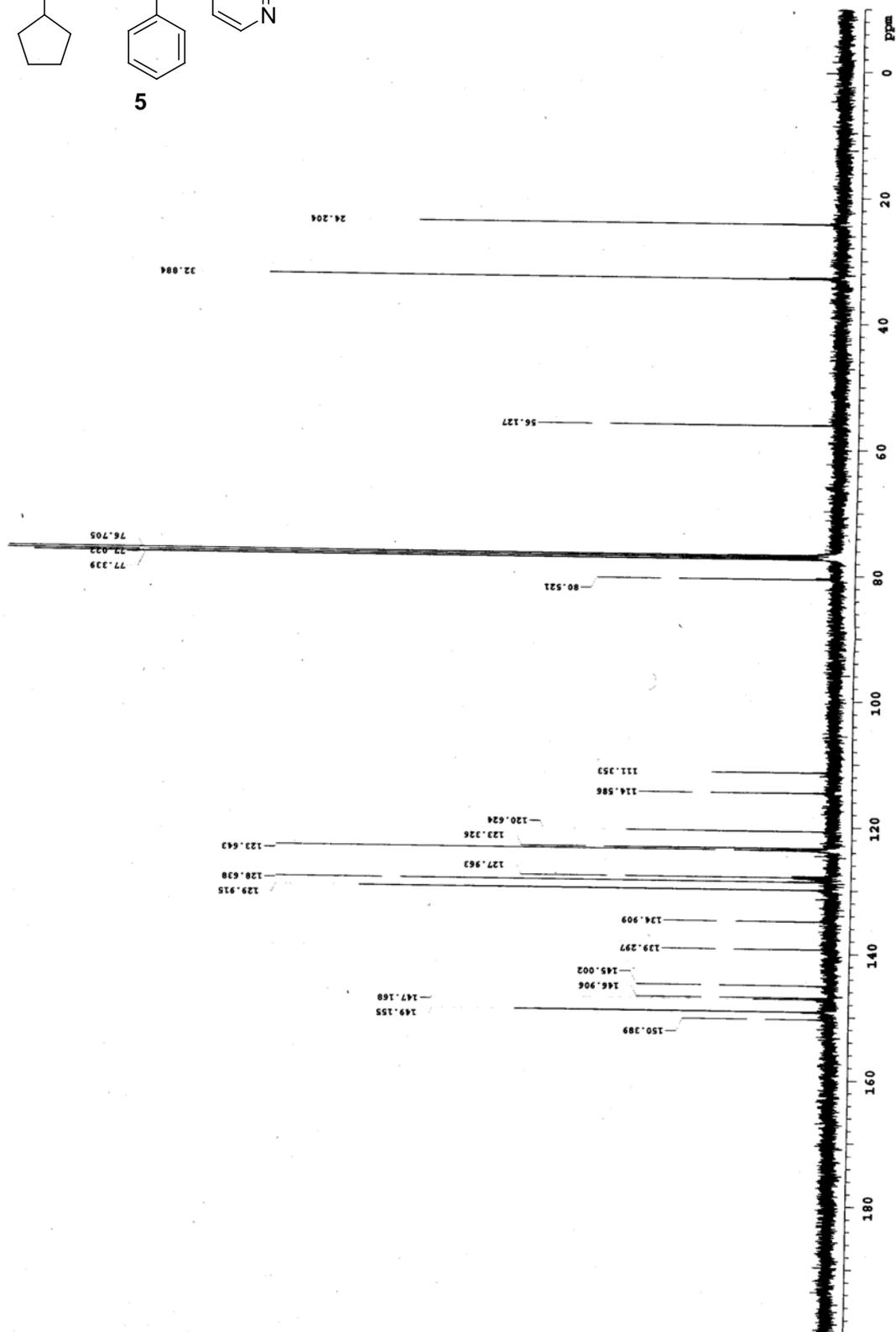
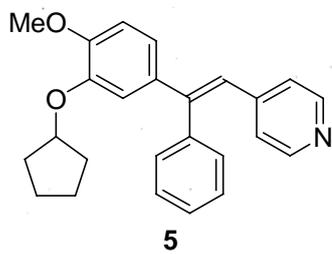
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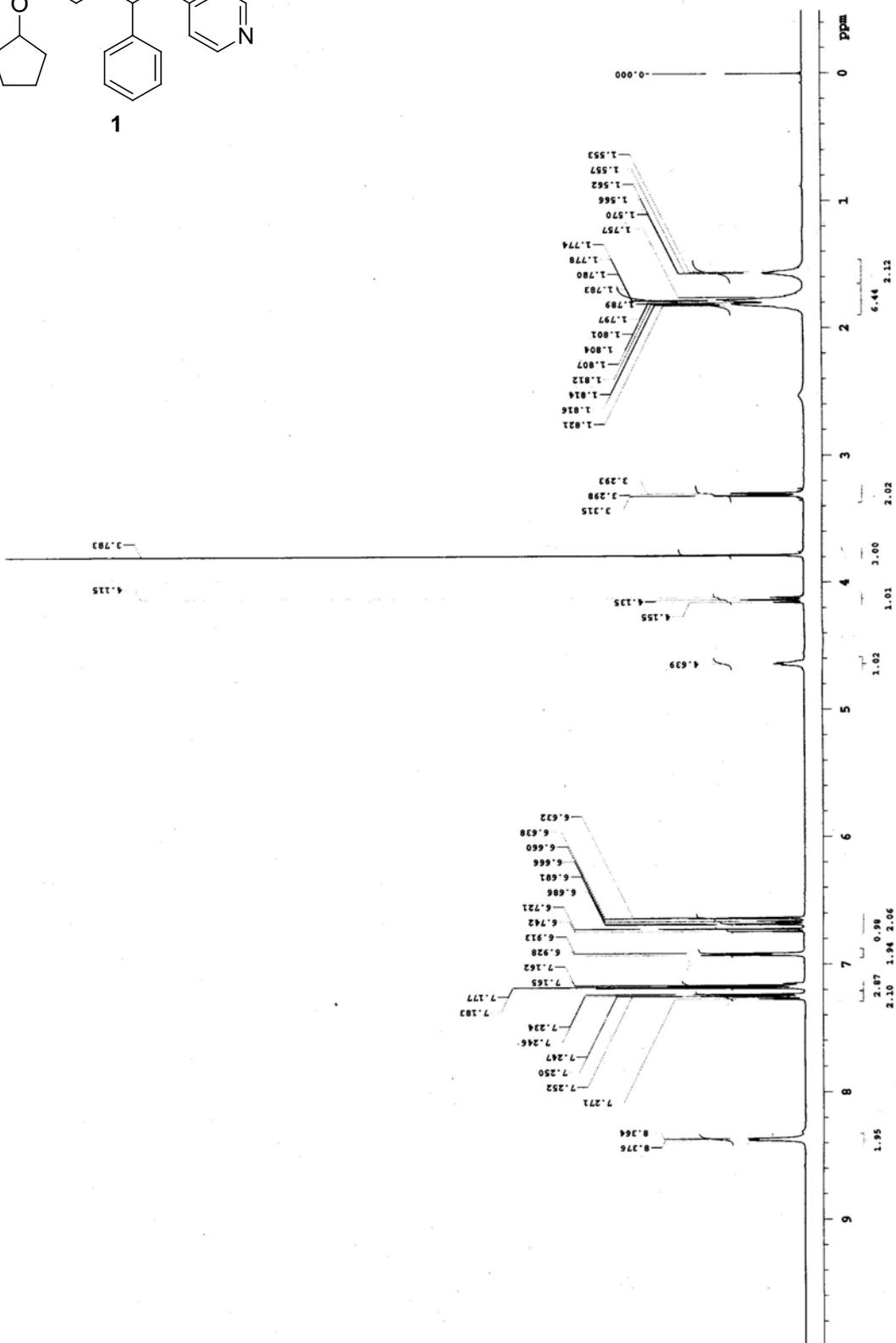
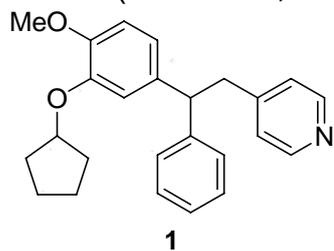
$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )



<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)

