Supporting Information for:

# *Serendipitous synthesis of cross-conjugated dienes by cascade deconstructive esterification of thiomorpholinone-tethered alkenoic acids*

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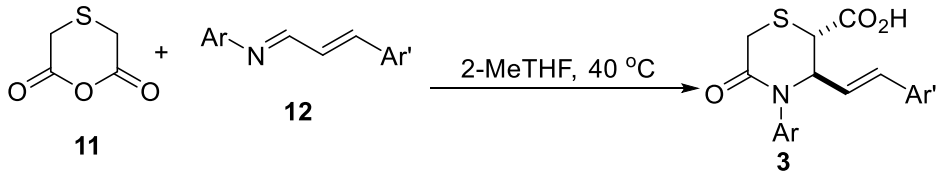
*Contents:*

## 2. Experimental Section

All experiments involving air and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Freshly purchased toluene and DMF were stored under 4 A° molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines and enals were newly purchased and used without further purification. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 µm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or CAM, *p*-anisaldehyde, or $KMnO_4$ stain. All reported temperatures were internal to a reaction vessel. Unless otherwise indicated, $^1H$, $^{13}C$, and DEPT-135 spectra were acquired using $CDCl_3$ as solvent, at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-$EI^+$ data were obtained using either electron spray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx). Brine solutions are saturated solutions of aqueous sodium chloride.

The 1,3-azadienes were prepared as previously reported by us.[1]

### General Procedure A: Synthesis of acid precursor 3




A 20 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of 1,3-azadiene **12** (5.0 mL, 0.10 M in freshly distilled 2-MeTHF, 5 mmol) was added to the vial at room temperature followed by anhydride **11** (660 mg, 5 mmol, 1 equiv) and sodium sulfate (0.50 g). The contents were placed in a pre-heated oil bath thermostatted at the desired temperature (usually 40 °C). After complete conversion (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature. It was then filtered to remove the sodium sulfate, then washed with THF. The solvents were removed *in vacuo* and the solid residue was washed several times with petroleum ether to afford acid **3**, which was then subjected to the esterification step (Procedure B or C) without further purification.

**General Procedure B: Deconstructive methyl esterification of 3**

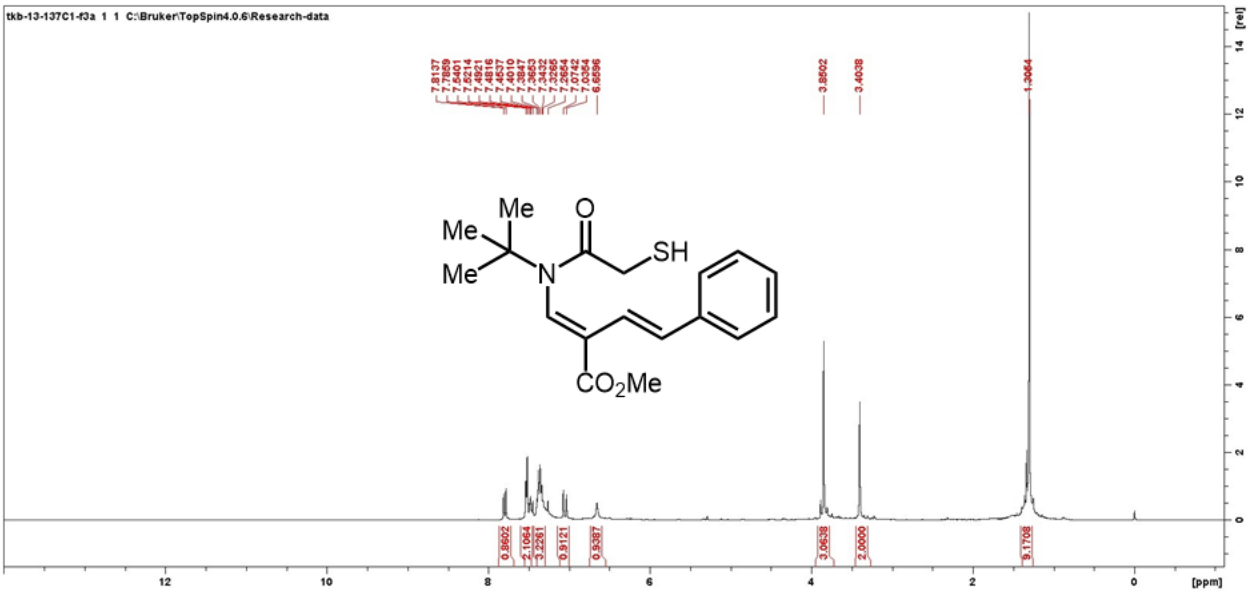
To a stirring suspension of acid **3** (1 mmol), dissolved in DMF (2 mL), and $K_2CO_3$ (3 equiv) was added methyl iodide (2 equiv) under nitrogen atmosphere. The reaction mixture was stirred for 12 – 22 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (2×20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the desired methyl ester, which was purified by flash chromatography on silica.

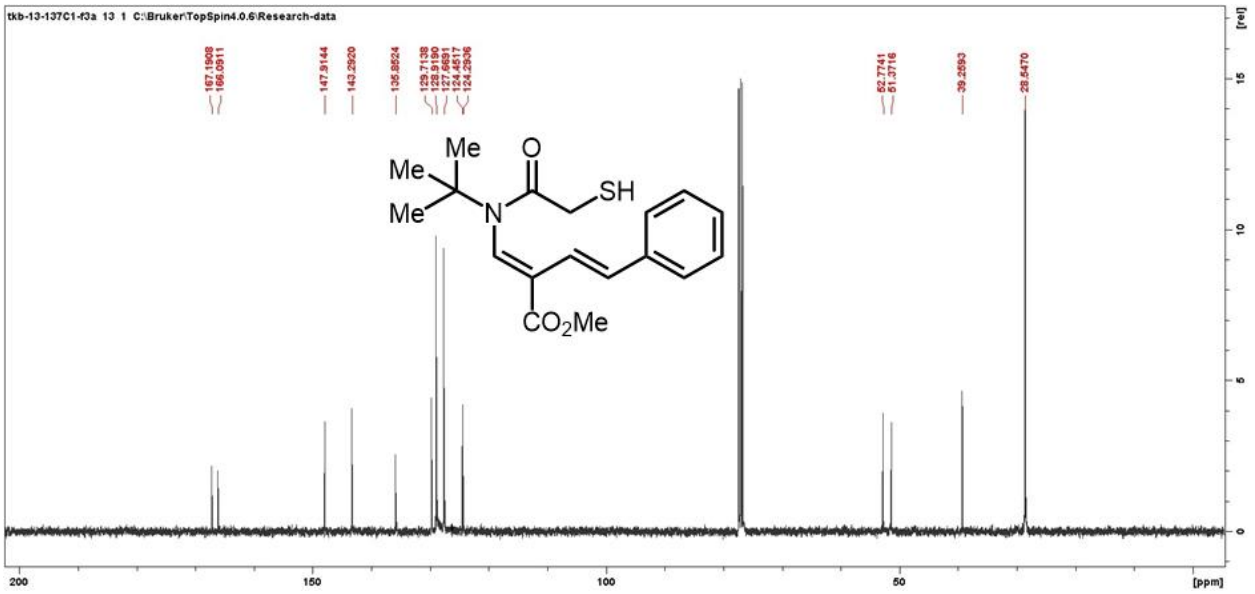
**General Procedure C: Deconstructive esterification of 3 with different organic bromides**

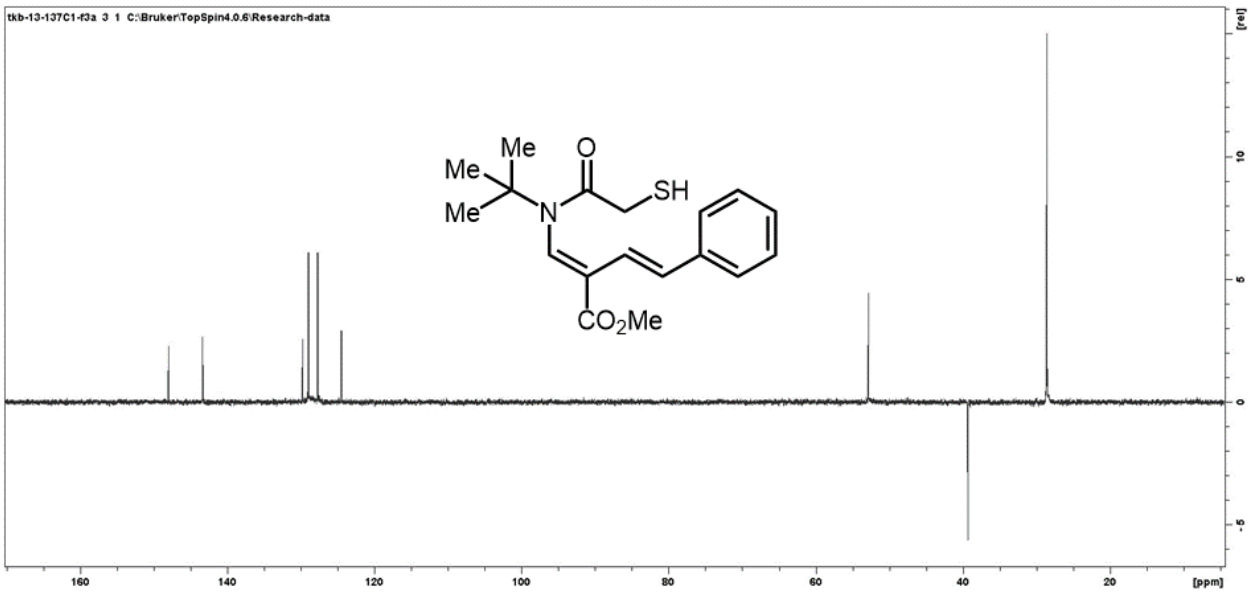
To a stirring suspension of acid **3** (1 mmol), dissolved in DMF (2 mL), and $K_2CO_3$ (3 equiv) was added the organic bromide (2 equiv) under nitrogen atmosphere. The reaction mixture was heated to 60 $^oC$ and stirred for 18 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (2×20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo* to give the desired ester, which was purified by flash chromatography on silica.

**Compound 4a**

Prepared in 3.00 mmol scale using **General Procedures A** and **B** but at 50 ºC for 18 h. Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 790.2 mg, 79%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 11.1 Hz, 1H), 7.54 – 7.45 (m, 2H), 7.40 – 7.26 (m, 3H), 7.06 (d, *J* = 11.1 Hz, 1H), 6.66 (s, 1H), 3.85 (s, 3H), 3.40 (s, 2H), 1.31 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.19, 166.09, 147.92, 143.30, 135.86, 129.72, 128.92, 127.67, 124.46, 124.30, 52.78, 51.38, 39.26, 28.55. FTIR (KBr): 2965.4, 1727.5, 1696.3, 1604.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 905.8, 839.0. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{18}H_{23}NO_3S$ $[M]^{+}$ 333.1399, found 333.1395.



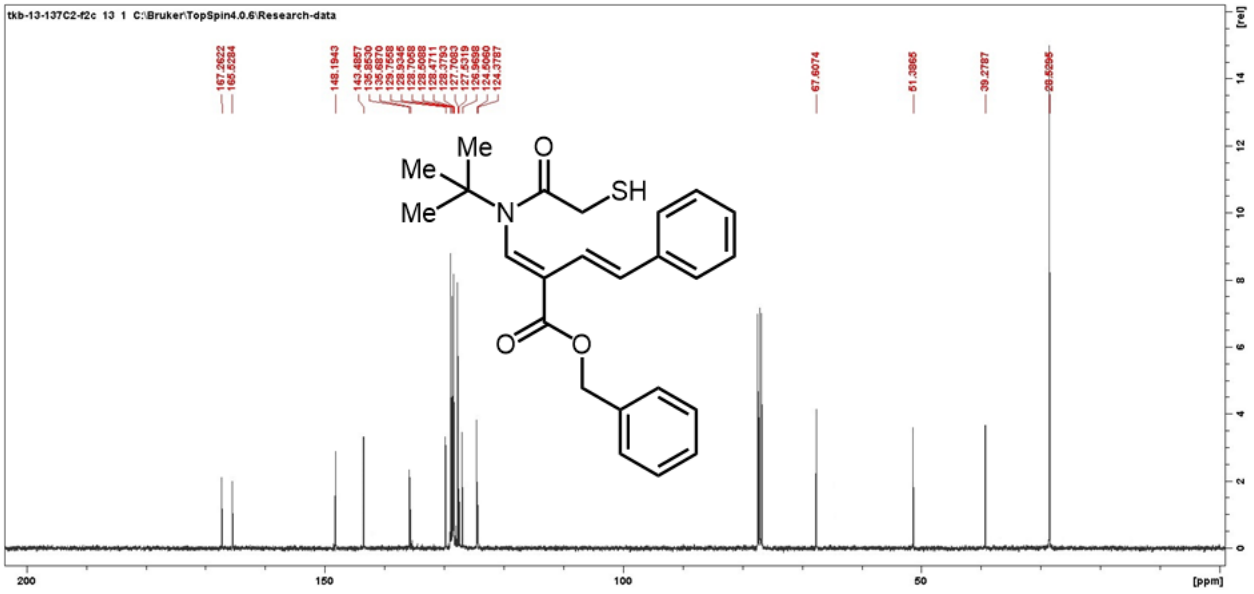


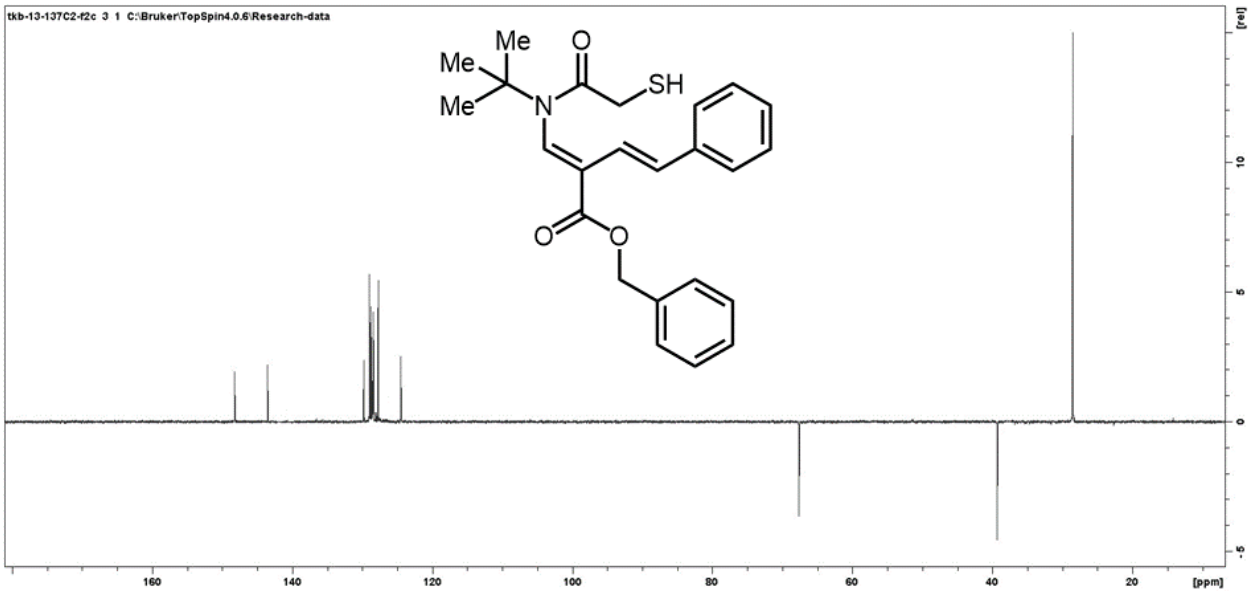




**Compound 4b**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using benzylbromide as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 344 mg, 84%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J$ = 11.1 Hz, 1H), 7.52 – 7.28 (m, 10H), 7.03 (d, $J$ = 11.1 Hz, 1H), 6.66 (s, 1H), 5.27 (s, 2H), 4.67 (s, 1H), 3.39 (s, 2H), 1.27 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.27, 165.53, 148.20, 143.49, 135.86, 135.69, 129.76, 128.94, 128.71, 128.51, 128.47, 128.38, 127.71, 126.97, 124.51, 67.61, 51.39, 39.28, 28.53.

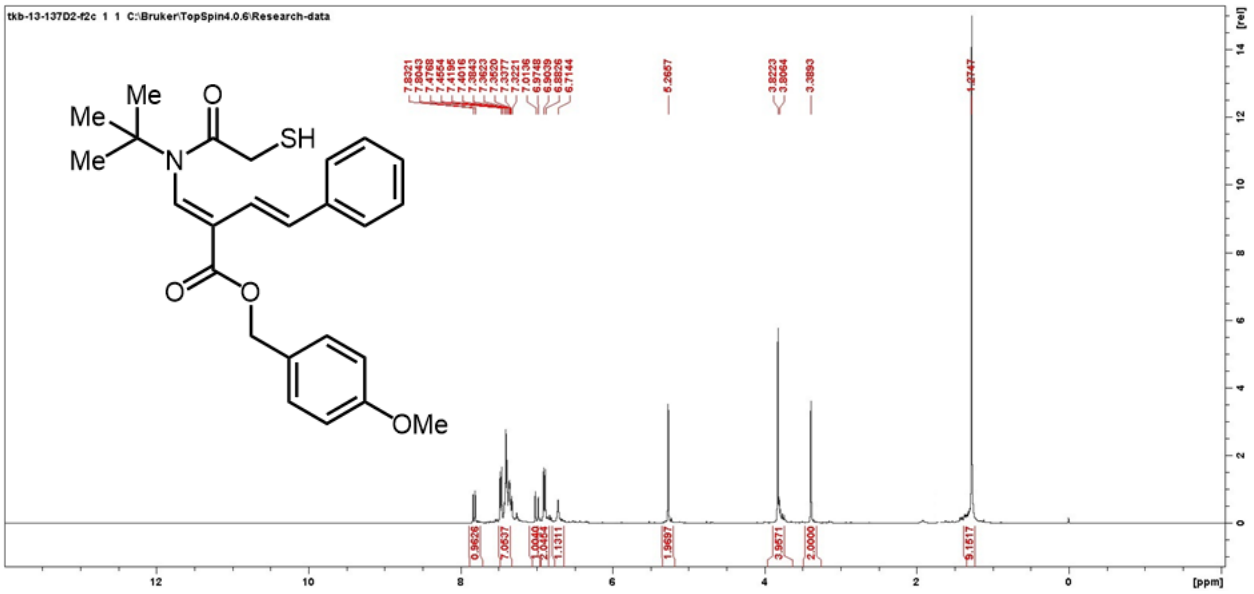
FTIR (KBr): 2984.1, 1733.5, 1654.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1299.7, 1242.5, 1179.3, 1031.8, 994.9, 823.7, 735.2. **HRMS-EI**$^+$ (*m/z*): calc for $C_{24}H_{27}NO_3S$ $[M]^+$ 409.1712, found 409.1717.




**Compound 4c**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 4-methoxybenzylbromide as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 382.4 mg, 87%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, $J$ = 11.1 Hz, 1H), 7.47 (d, $J$ = 8.4 Hz, 1H), 7.41 – 7.32 (m, 5H), 7.01 – 6.88 (m, 3H), 6.71 (s, 1H), 5.27 (s, 2H), 3.82 – 3.79 (m, 4H), 3.39 (s, 2H), 1.28 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.34, 165.72, 161.09, 148.92, 143.47, 135.81, 129.36, 128.69, 128.68, 128.40, 128.32, 122.42, 114.45, 67.47, 55.39, 51.33, 39.39, 28.53. FTIR (KBr): 2939.4, 1723.5, 1696.3, 1604.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 985.8, 833.0. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{25}H_{29}NO_4S$ $[M]^{+}$ 439.1817, found 439.1822.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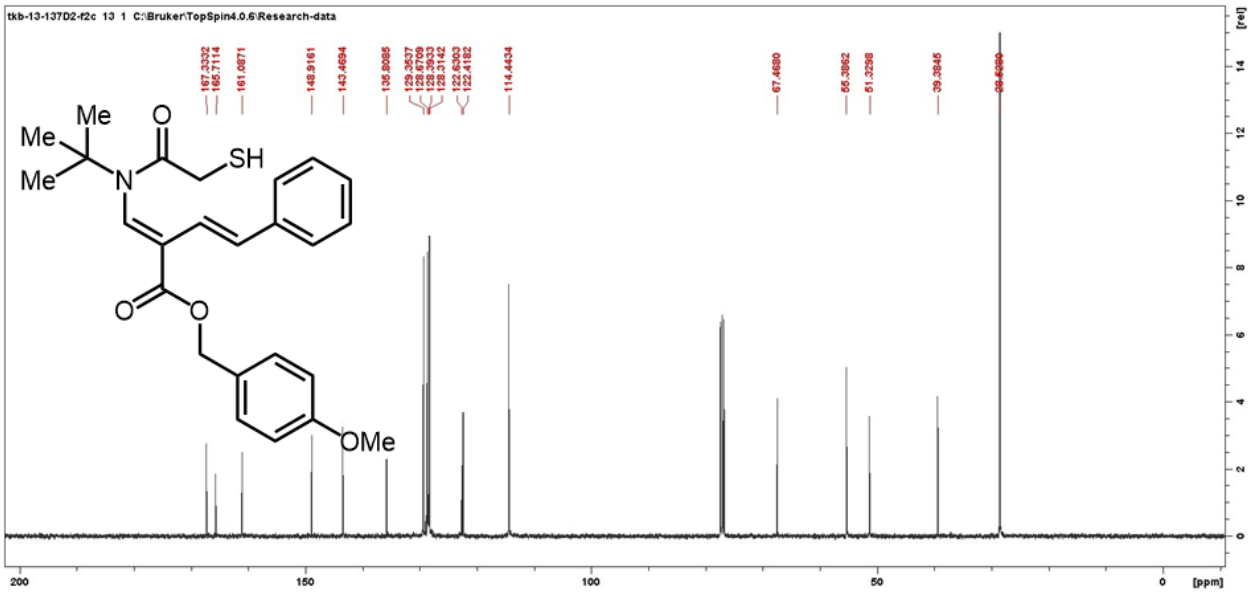
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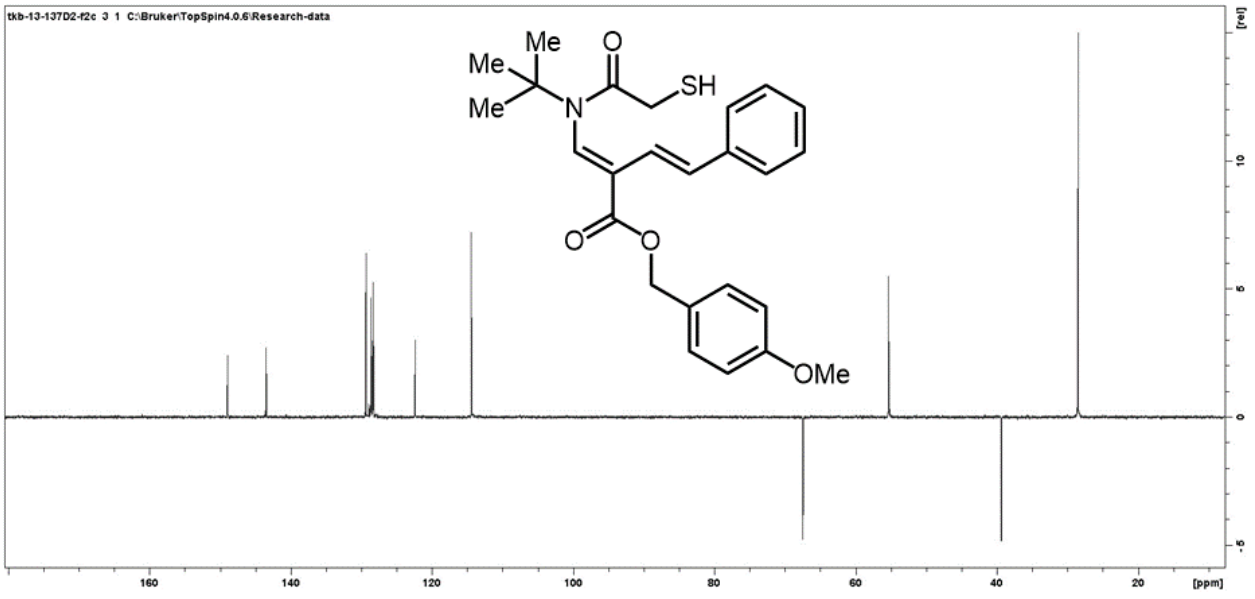
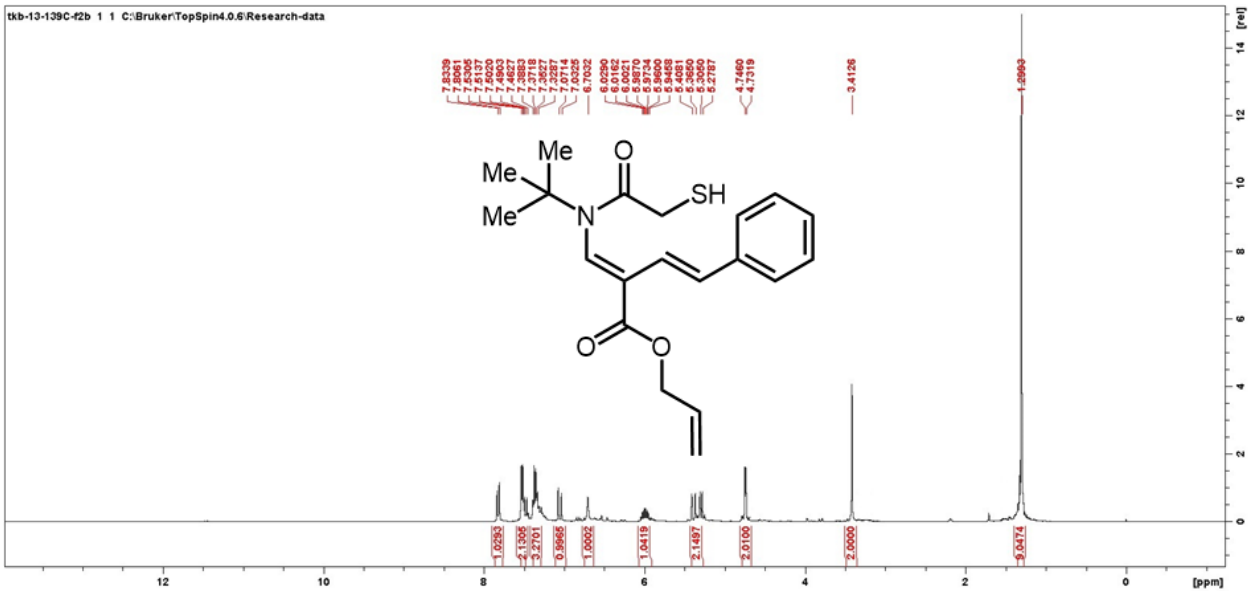



**Compound 4d**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using allylbromide as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 276.8 mg, 77%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 11.2 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.39 – 7.33 (m, 3H), 7.05 (d, *J* = 11.2 Hz, 1H), 6.70 (s, 1H), 5.97 (tdt, *J* = 16.5, 11.6, 5.9 Hz, 1H), 5.41 – 5.28 (m, 2H), 4.73 (d, 2H), 3.41 (s, 2H), 1.30 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.22, 165.23, 147.96, 143.34, 135.84, 131.92, 129.72, 128.92, 127.68, 124.49, 118.83, 66.38, 51.35, 39.21, 28.54. FTIR (KBr): 2985.4, 1737.5, 1691.2, 1644.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1002.8, 925.8, 791.0. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{20}H_{25}NO_3S$ $[M]^{+}$ 359.1555, found 359.1558.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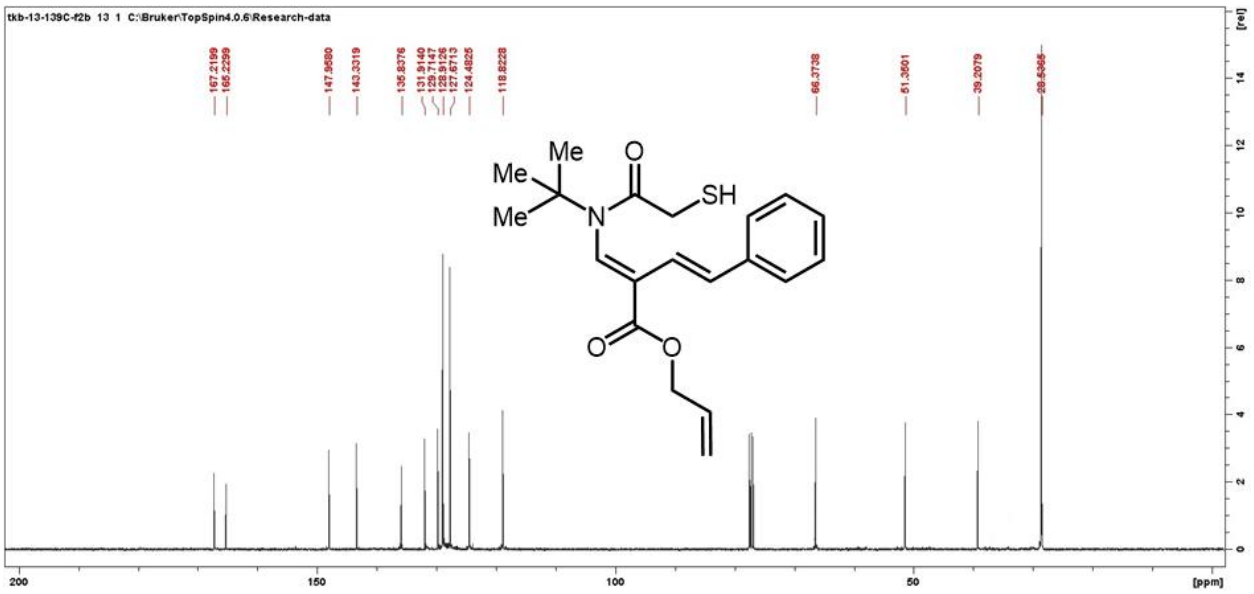
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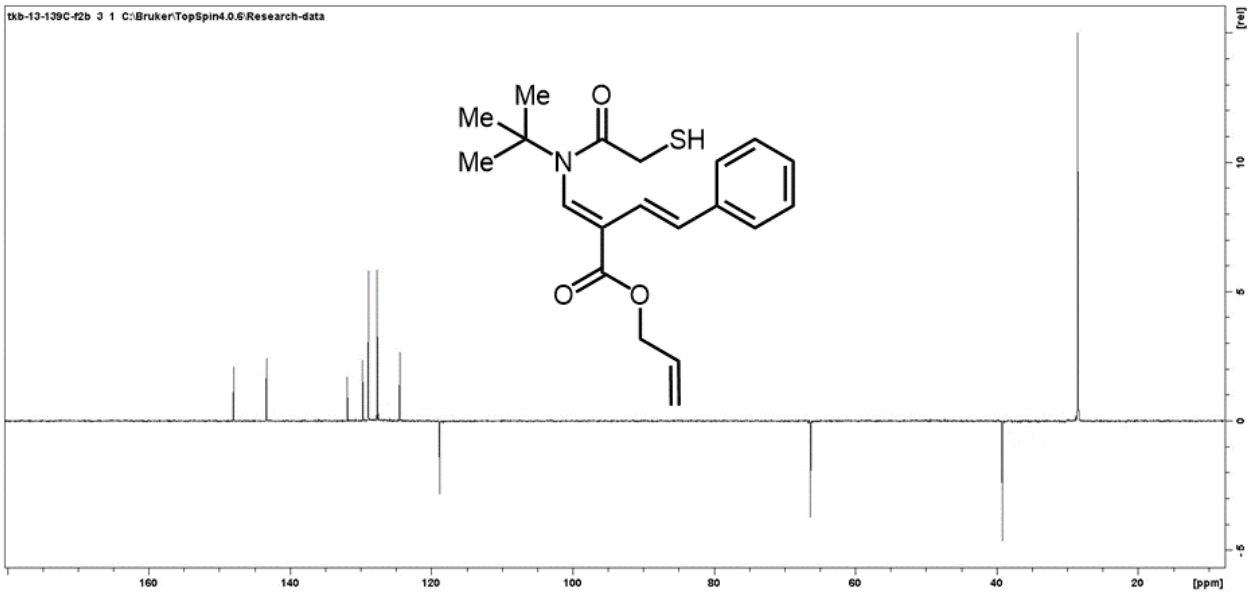
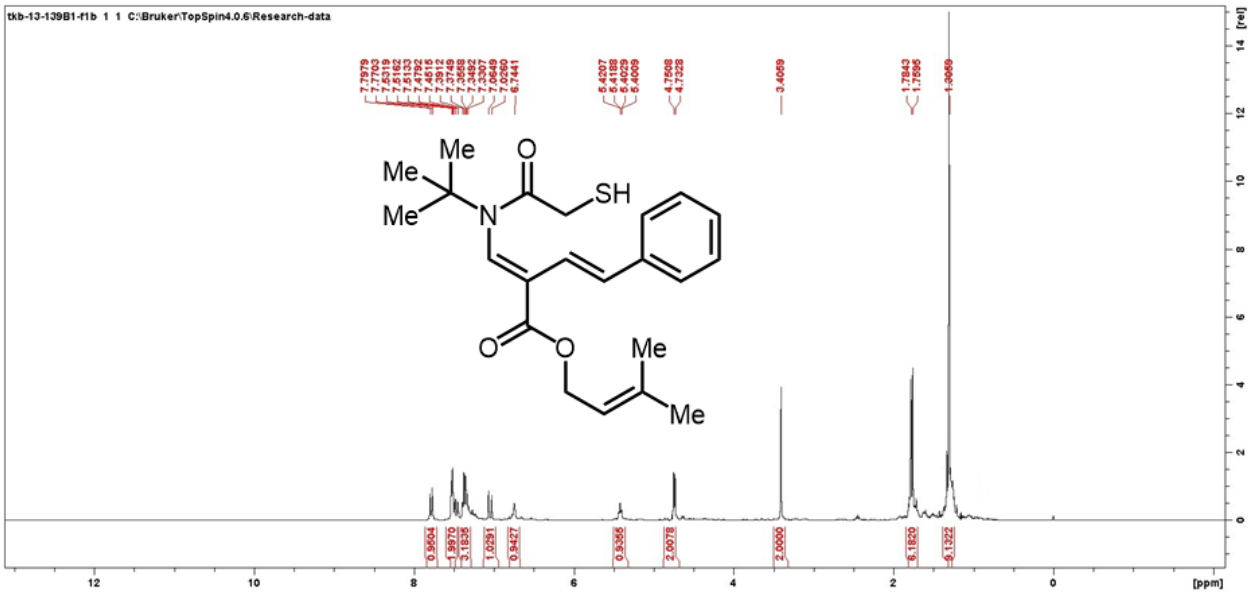



**Compound 4e**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 3,3-dimethylallyl bromide as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 310.0 mg, 80%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 11.1 Hz, 1H), 7.56 – 7.45 (m, 2H), 7.39 – 7.33 (m, 3H), 7.05 (d, *J* = 11.1 Hz, 1H), 6.74 (s, 1H), 5.42 (ddt, *J* = 8.7, 7.3, 1.5 Hz, 1H), 4.74 (d, *J* = 7.3 Hz, 2H), 3.41 (s, 2H), 1.78 – 1.75 (m, 6H), 1.31 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.27, 165.66, 147.62, 143.06, 139.55, 135.92, 129.63, 128.90, 127.63, 124.81, 124.55, 118.41, 62.73, 51.33, 39.29, 28.51, 25.79. FTIR (KBr): 2972.9, 2932.8, 1638.2, 1449.1, 1364.7, 1290.2, 1270.3, 1247.8, 1206.5, 1179.9, 1131.1, 1071.4, 994.4, 924.8, 881.7. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{29}NO_3S$ $[M]^+$ 387.1868, found 387.1873.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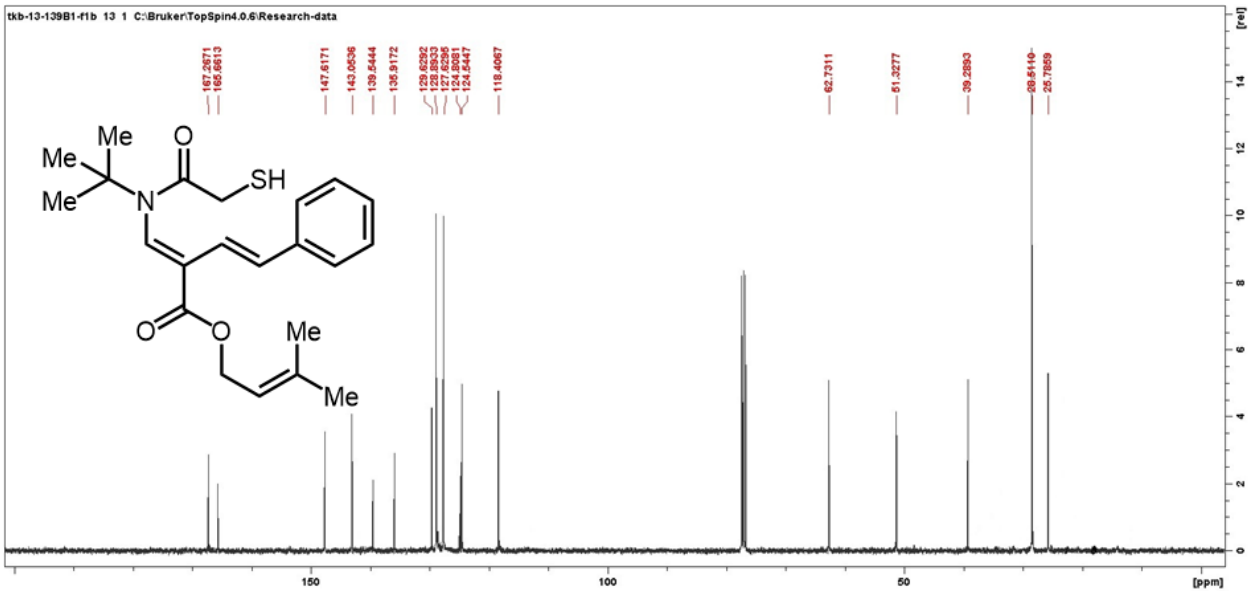
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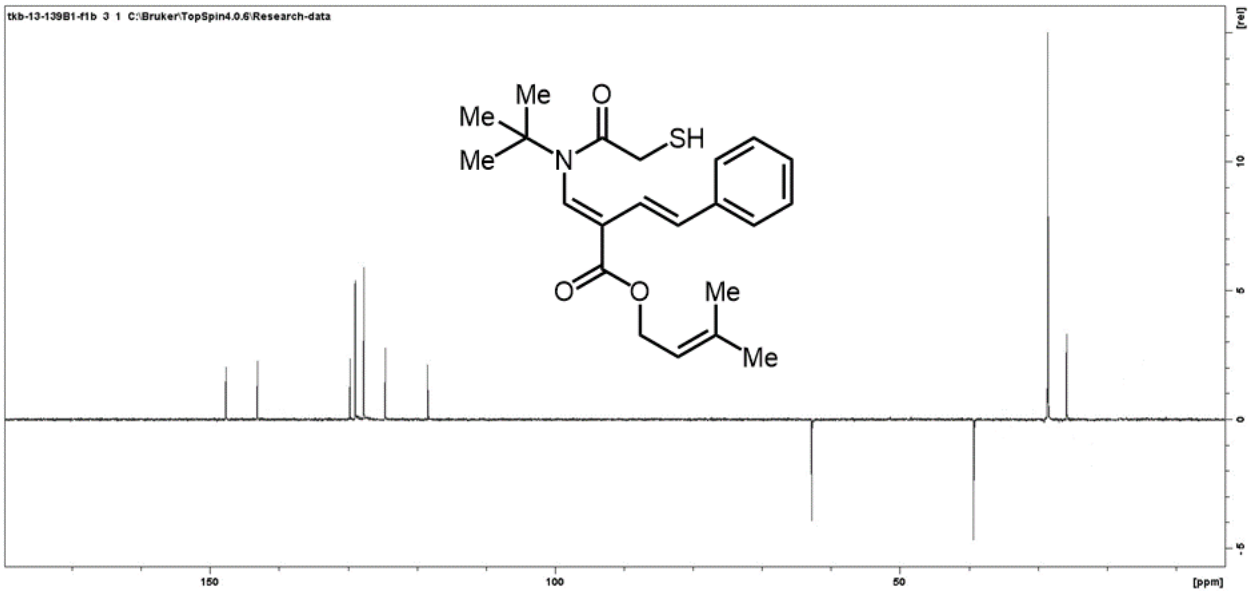
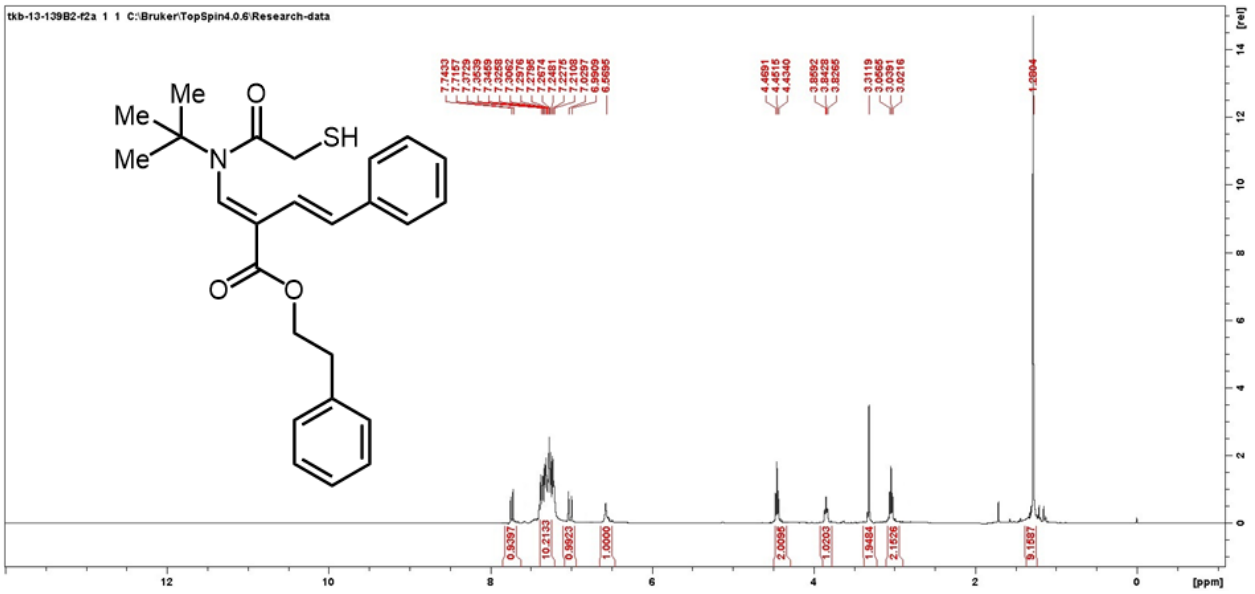



**Compound 4f**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using phenethyl bromide as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (85:15). Oily substance. Yield = 364.3 mg, 86%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 11.0 Hz, 1H), 7.37 – 7.21 (m, 10H), 7.01 (d, *J* = 11.0 Hz, 1H), 6.57 (s, 1H), 4.45 (t, *J* = 7.0 Hz, 2H), 3.84 (t, *J* = 6.7 Hz, 1H), 3.31 (s, 2H), 3.04 (t, *J* = 7.0 Hz, 2H), 1.28 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.28, 165.58, 147.89, 143.24, 137.65, 135.88, 129.72, 129.04, 128.97, 128.94, 128.64, 128.56, 127.70, 126.75, 126.43, 124.56, 66.29, 51.38, 39.15, 35.17, 28.56. FTIR (KBr): 2994.1, 1763.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 706.4. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{25}H_{29}NO_3S$ $[M]^{+}$ 423.1868, found 423.1876.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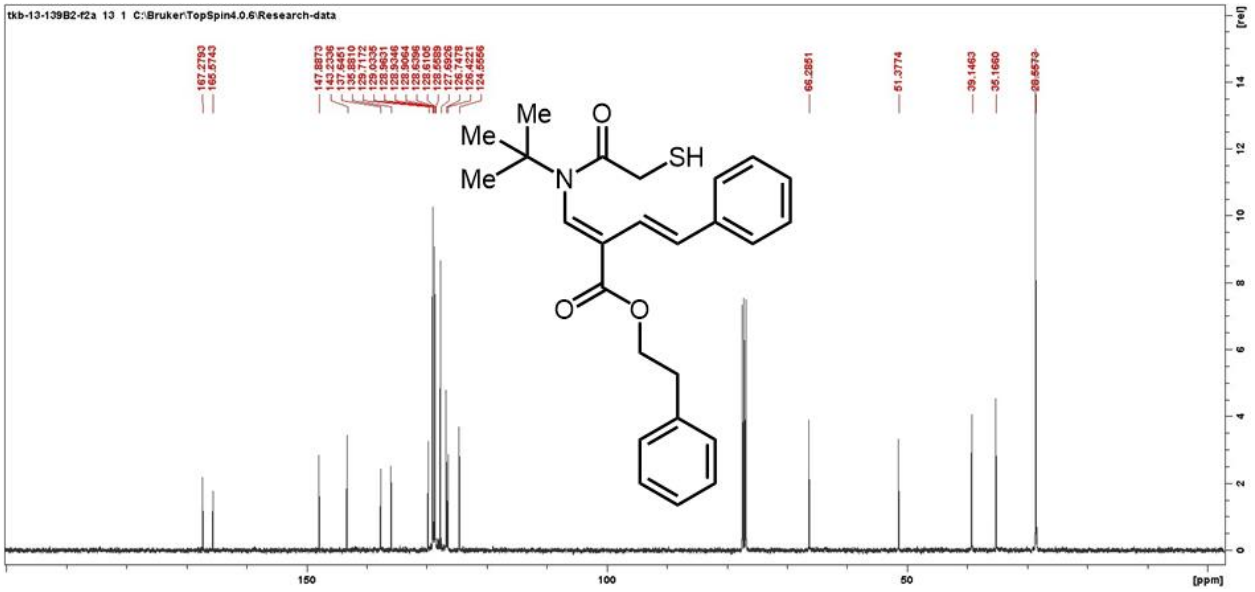
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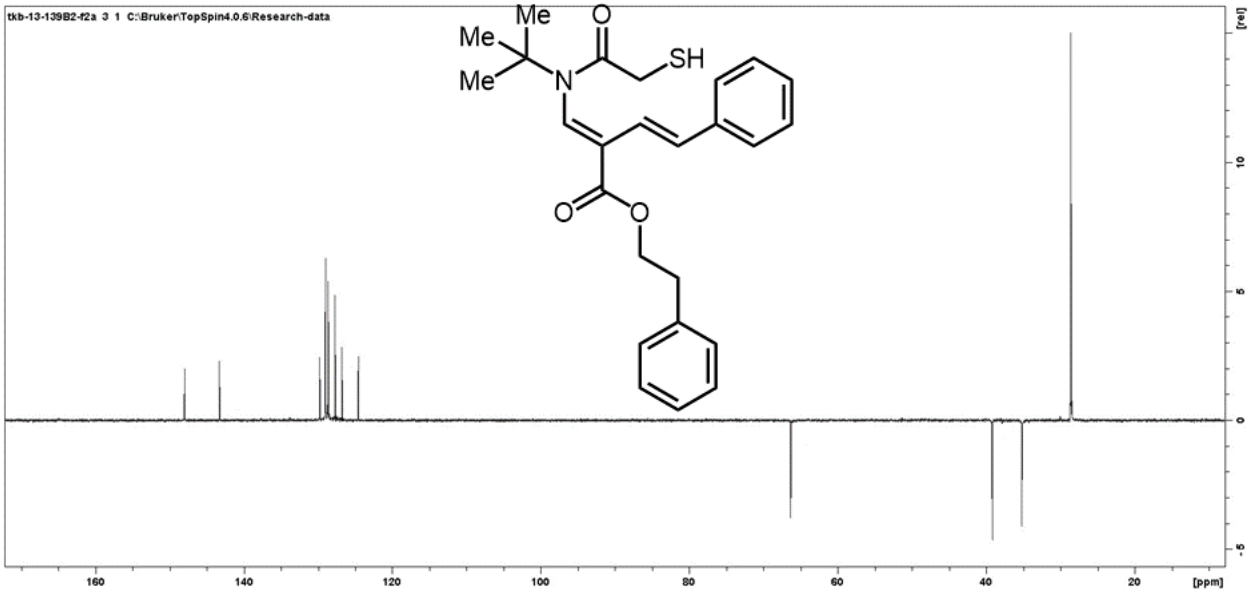
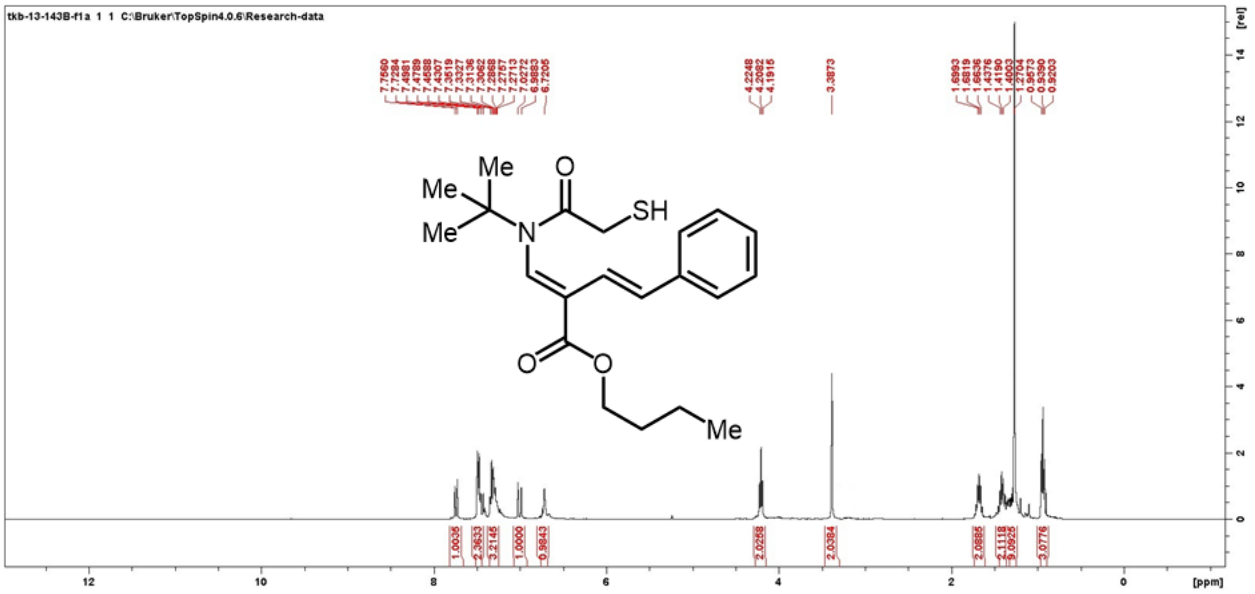



**Compound 4g**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 1-bromobutane as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (85:15). Oily substance. Yield = 338 mg, 90%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 11.1 Hz, 1H), 7.52 – 7.37 (m, 2H), 7.37 – 7.16 (m, 3H), 7.01 (d, *J* = 15.5 Hz, 1H), 6.72 (s, 1H), 4.20 (t, *J* = 7.0 Hz, 2H), 3.39 (s, 2H), 1.70 – 1.66 (m, 2H), 1.43 – 1.40 (m, 2H), 1.28 (s, 9H), 0.92 (t, *J* = 7.3 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.27, 165.58, 147.41, 142.96, 135.87, 129.60, 128.87, 127.60, 124.78, 124.52, 65.67, 51.28, 39.12, 30.72, 28.53, 28.51, 19.22, 13.73. FTIR (KBr): 3037.4, 2924.0, 1724.2, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1078.7, 1022.3, 996.4, 715.1. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{21}H_{29}NO_3S$ $[M]^{+}$ 375.1868, found 375.1873.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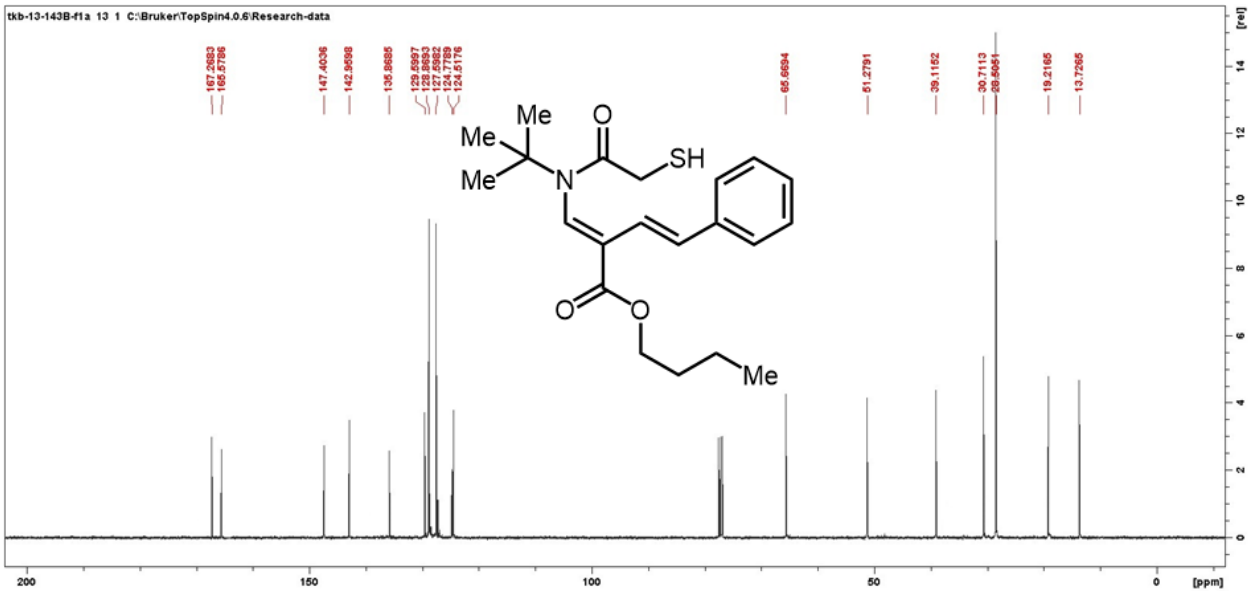
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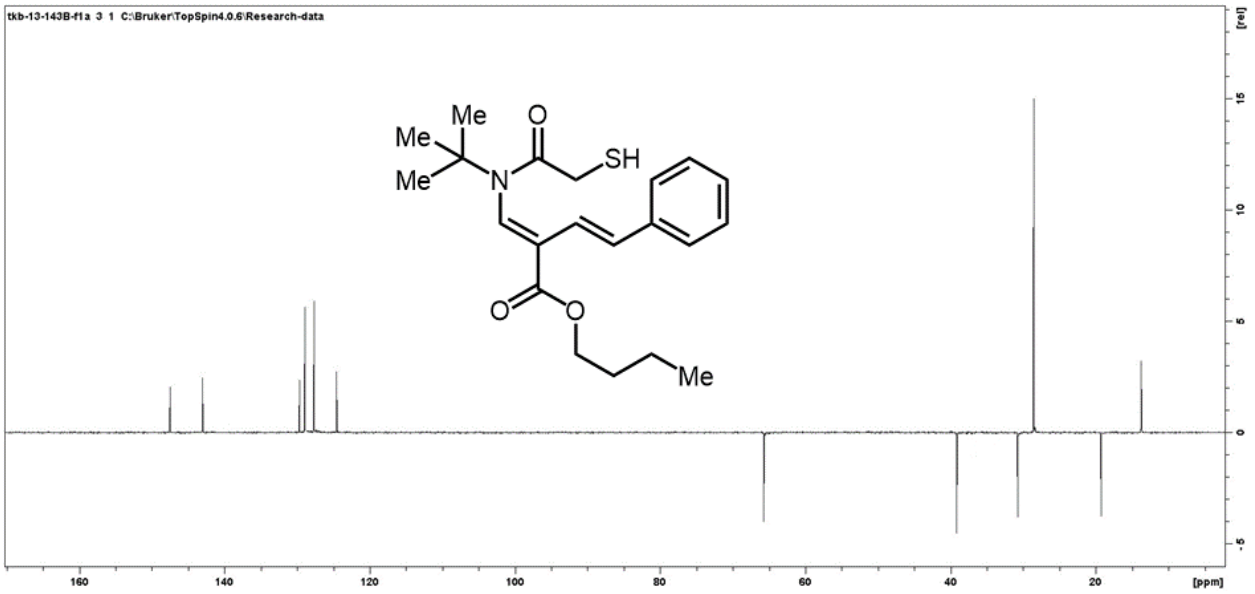
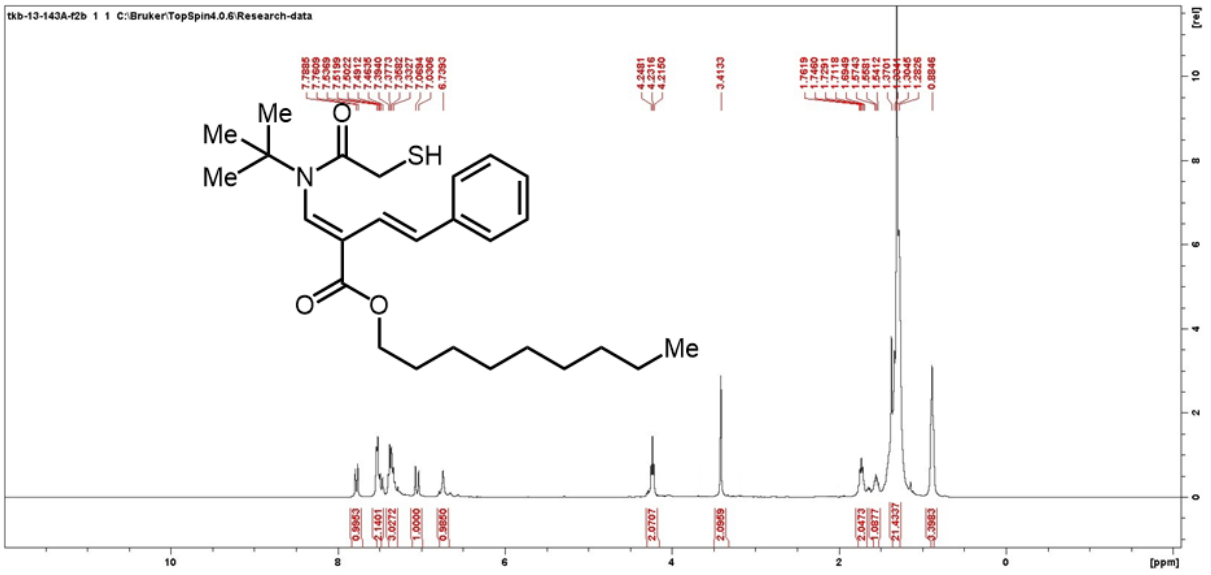



**Compound 4h**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 1-bromooctane as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (90:10). Oily substance. Yield = 374.4 mg, 84%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 11.1 Hz, 1H), 7.54 – 7.46 (m, 2H), 7.39 – 7.33 (m, 3H), 7.05 (d, *J* = 15.6 Hz, 1H), 6.74 (s, 1H), 4.23 (t, *J* = 6.8 Hz, 2H), 3.41 (s, 2H), 1.71 (tp, *J* = 13.7, 7.5, 6.9 Hz, 2H), 1.56 (p, *J* = 7.5, 6.5 Hz, 1H), 1.37 – 1.28 (m, 20H), 0.88 (d, *J* = 7.2 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.29, 165.66, 147.47, 143.03, 135.89, 129.63, 128.89, 127.62, 124.81, 124.54, 66.06, 51.35, 39.19, 31.84, 29.44, 29.24, 29.22, 28.67, 28.52, 25.98, 22.65, 14.08. FTIR (KBr): 3057.1, 2924.0, 1764.2, 1666.3, 1494.3, 1361.2, 1225.6, 1180.2, 1091.7, 1032.3, 996.4, 775.4. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{26}H_{39}NO_3S$ $[M]^{+}$ 445.2651, found 445.2655.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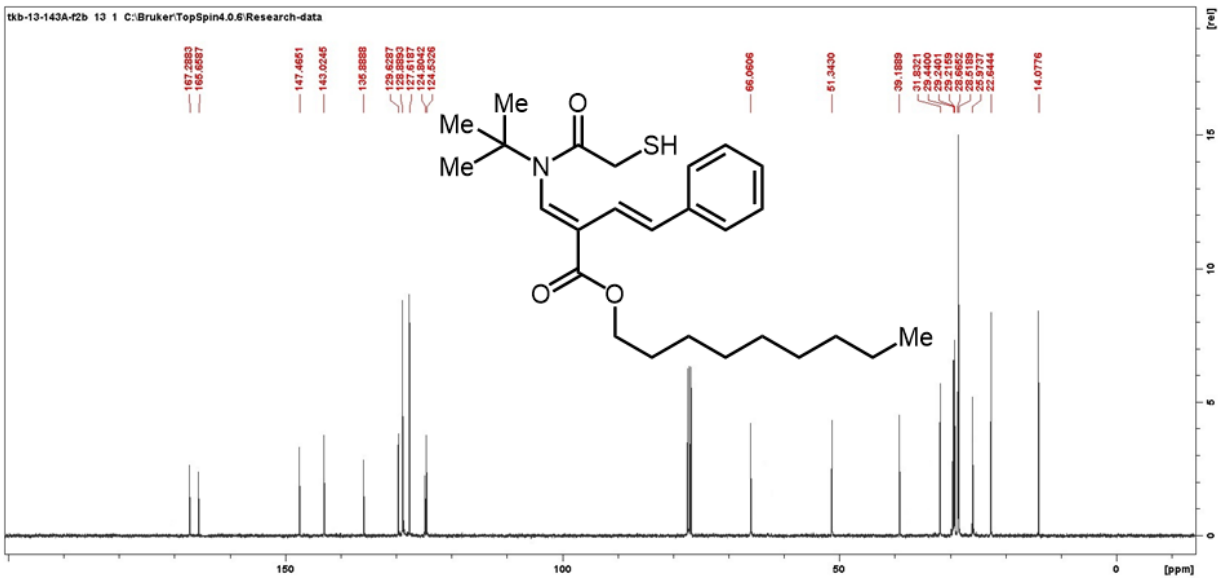
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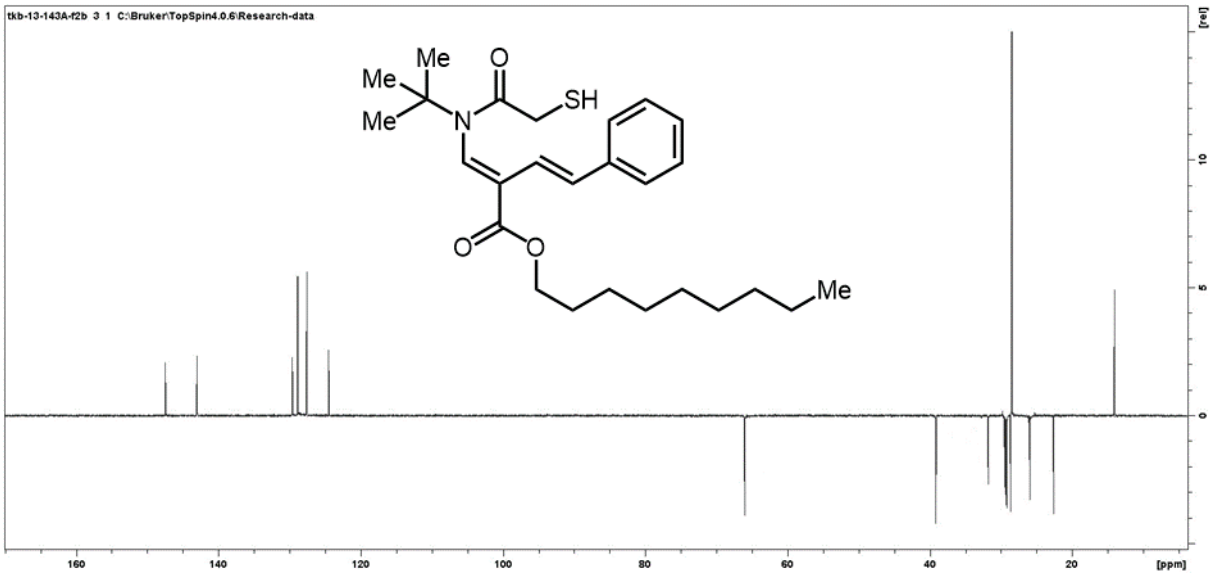
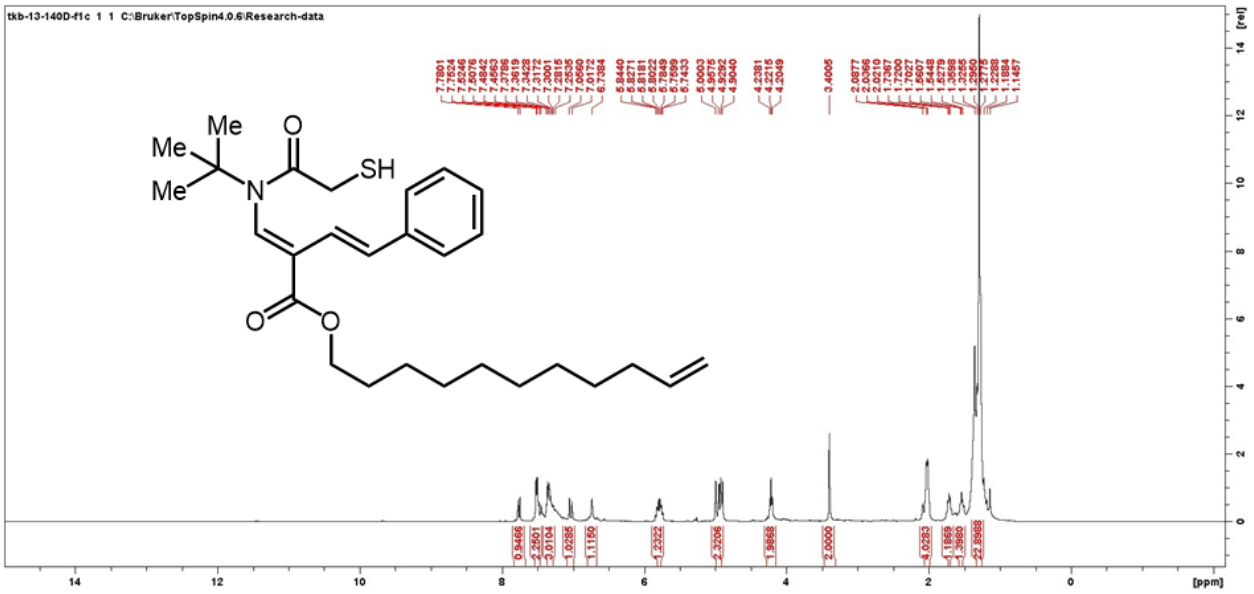



**Compound 4i**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 11-bromoundecene as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (90:10). Oily substance. Yield = 405.7 mg, 86%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 11.1 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.38 – 7.25 (m, 3H), 7.04 (d, *J* = 15.6 Hz, 1H), 6.74 (s, 1H), 5.84 – 5.74 (m, 1H), 5.00 – 4.90 (m, 2H), 4.22 (t, *J* = 6.8 Hz, 1H), 3.40 (s, 2H), 2.03 (q, *J* = 7.3 Hz, 4H), 1.73 (q, *J* = 7.1 Hz, 1H), 1.54 (p, *J* = 7.0 Hz, 1H), 1.36 – 1.11 (m, 21H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.29, 165.64, 147.45, 143.01, 139.11, 139.07, 135.88, 129.62, 128.88, 127.62, 124.54, 114.16, 66.03, 51.32, 39.17, 33.77, 29.43, 29.41, 29.39, 29.10, 29.07, 28.90, 28.52, 25.78. FTIR (KBr): 2998.4, 2924.0, 1734.2, 1668.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1144.2, 1081.7, 1038.3, 986.4, 705.2. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{28}H_{41}NO_3S$ $[M]^{+}$ 471.2807, found 471.2811.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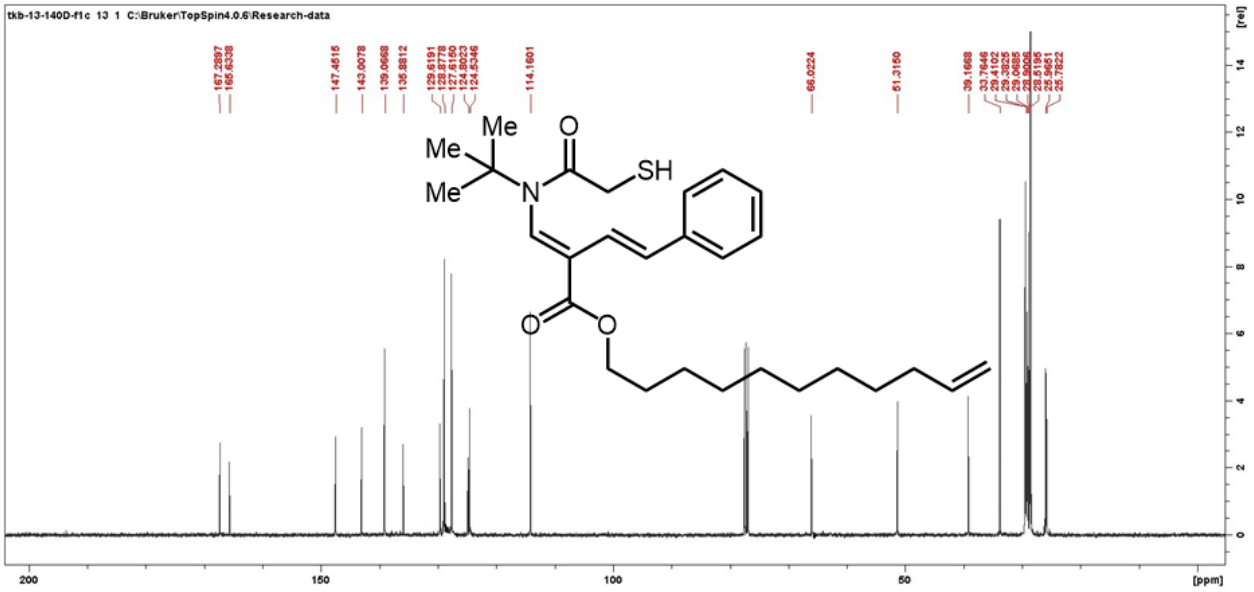
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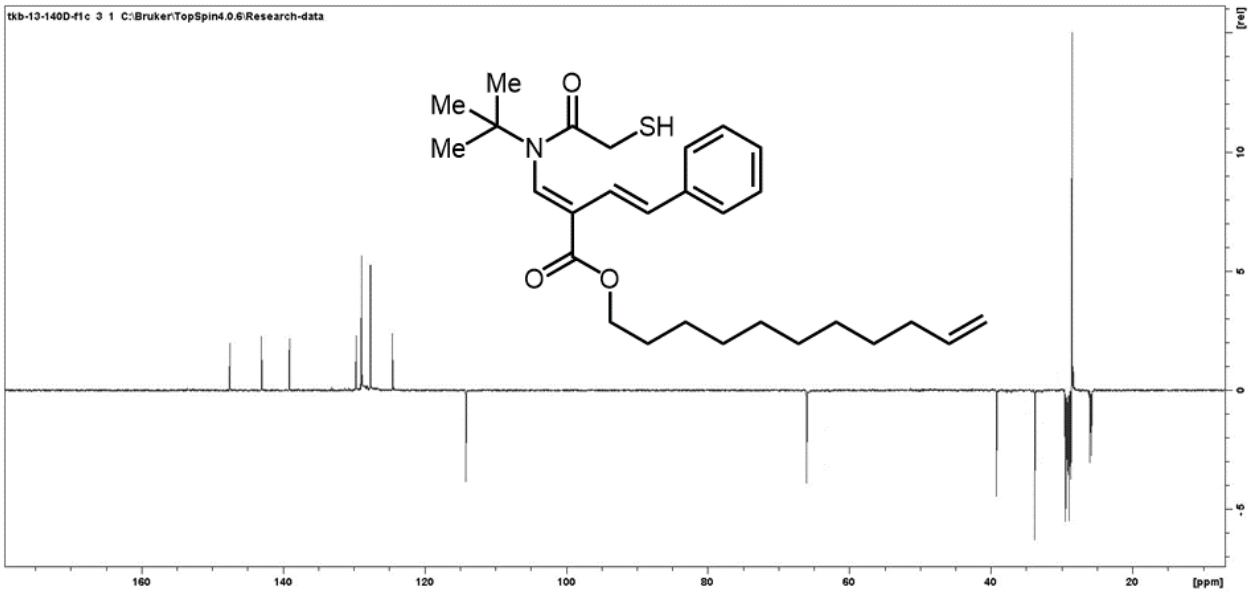
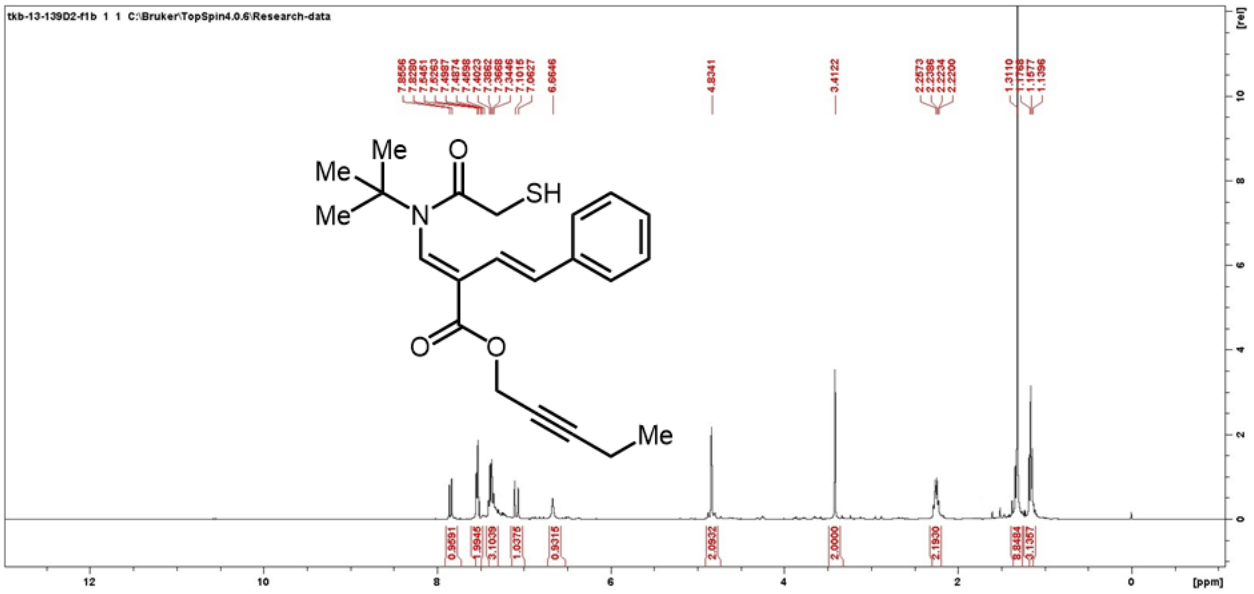



**Compound 4j**

Prepared in 1.00 mmol scale using **General Procedures A** and **C**, using 1-bromo-2-pentyne as the organic bromide. Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 339.3 mg, 88%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 11.1 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.42 – 7.34 (m, 3H), 7.08 (d, *J* = 15.5 Hz, 1H), 6.66 (s, 1H), 4.84 (s, 2H), 3.41 (s, 2H), 2.31 – 2.15 (q, 2H), 1.31 (s, 9H), 1.18 – 1.15 (t, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.1, 165.1, 148.5, 143.6, 135.8, 129.8, 128.9, 127.7, 124.5, 123.9, 89.4, 73.1, 54.0, 51.4, 39.3, 28.5, 13.5, 12.5. FTIR (KBr): 2994.1, 1763.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 706.4. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{22}H_{27}NO_3S$ $[M]^{+}$ 385.1712, found 385.1717.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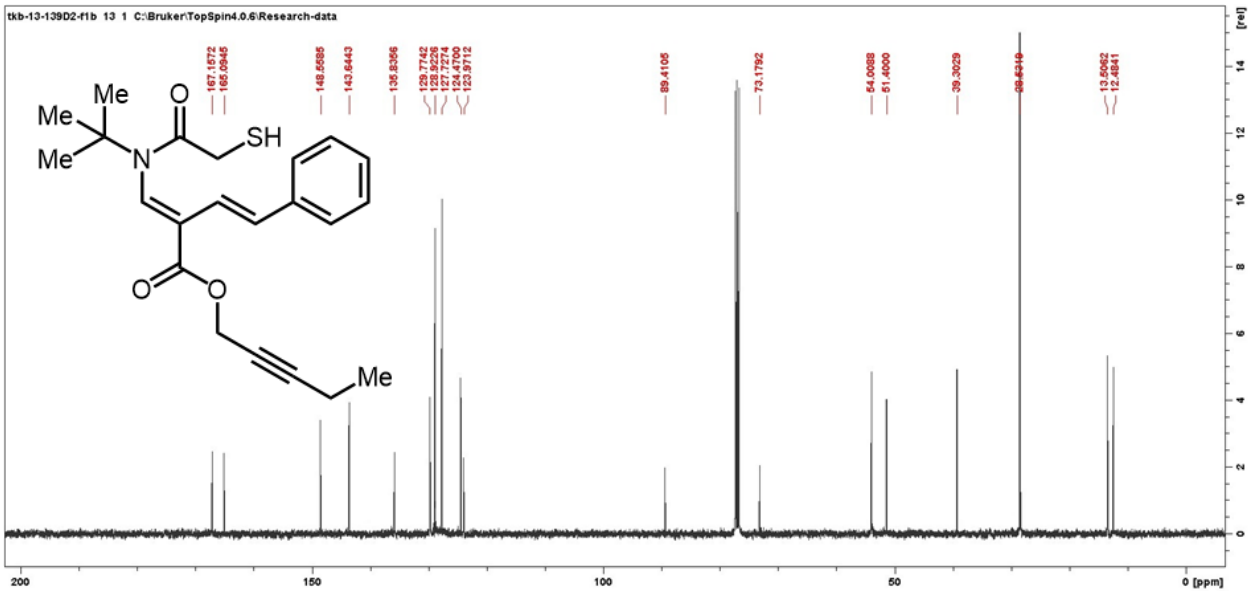
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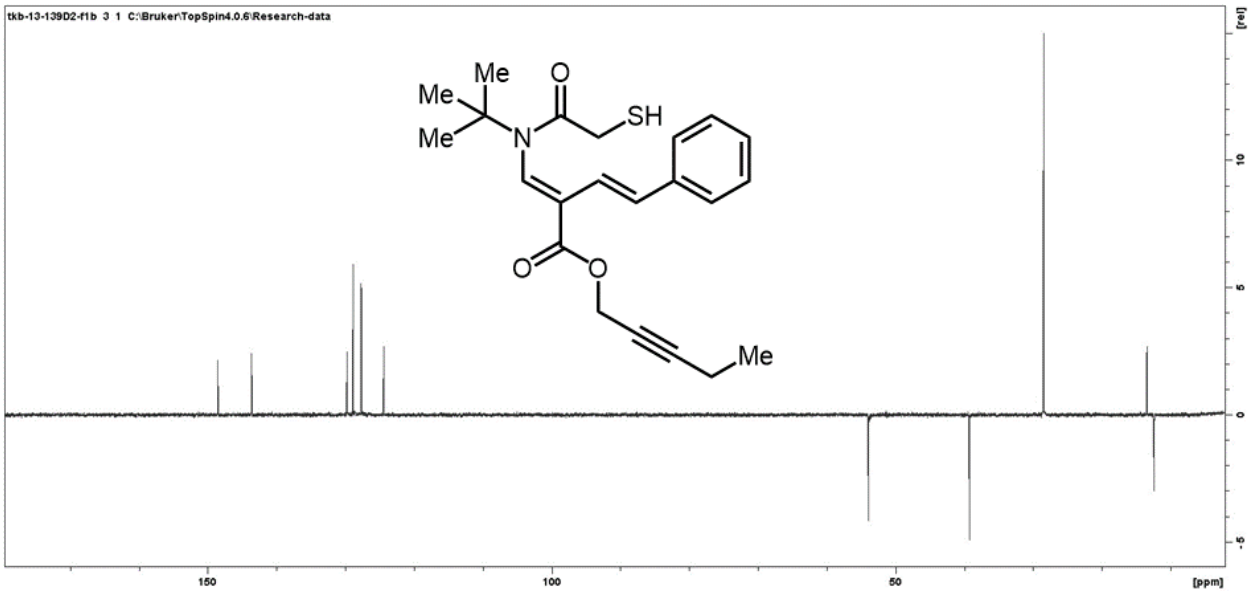
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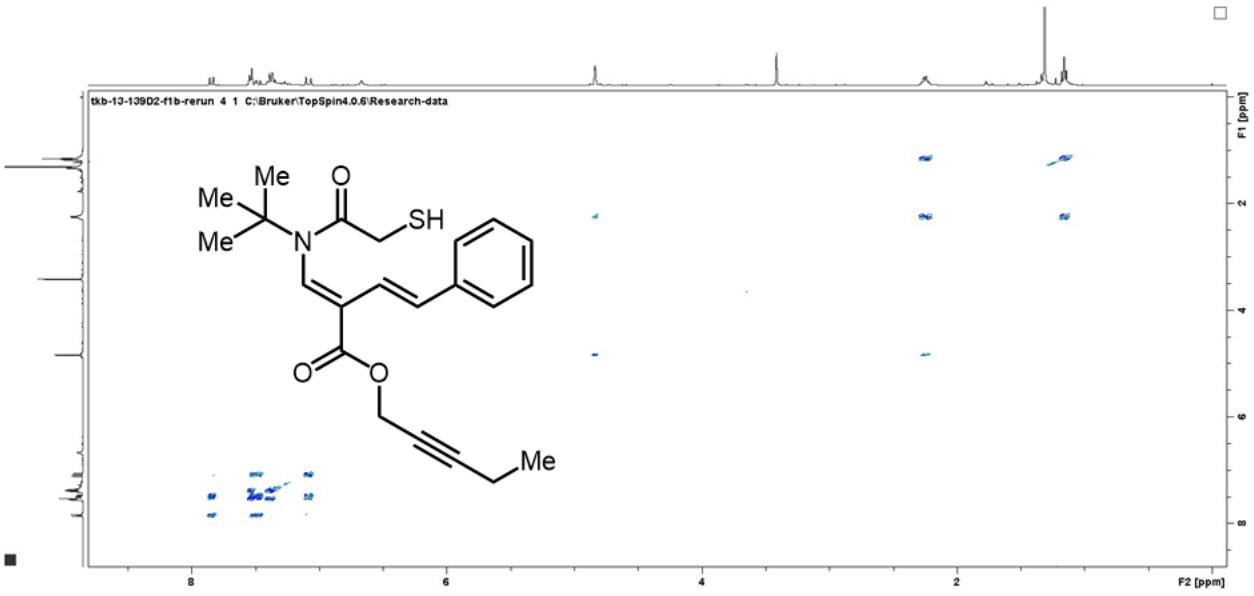
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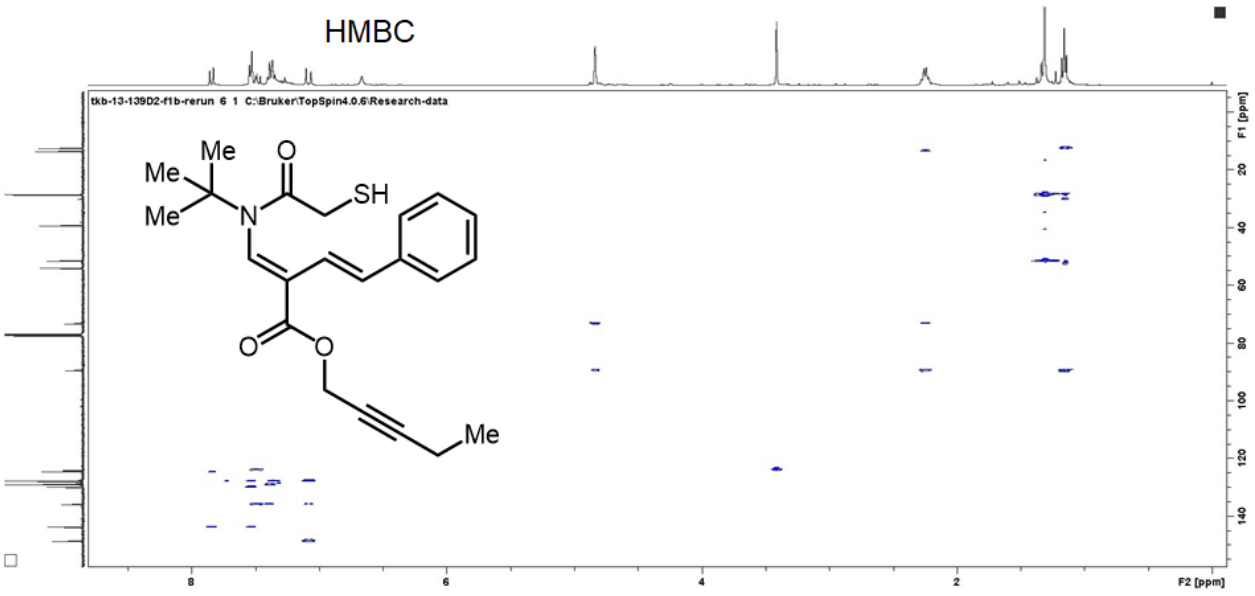
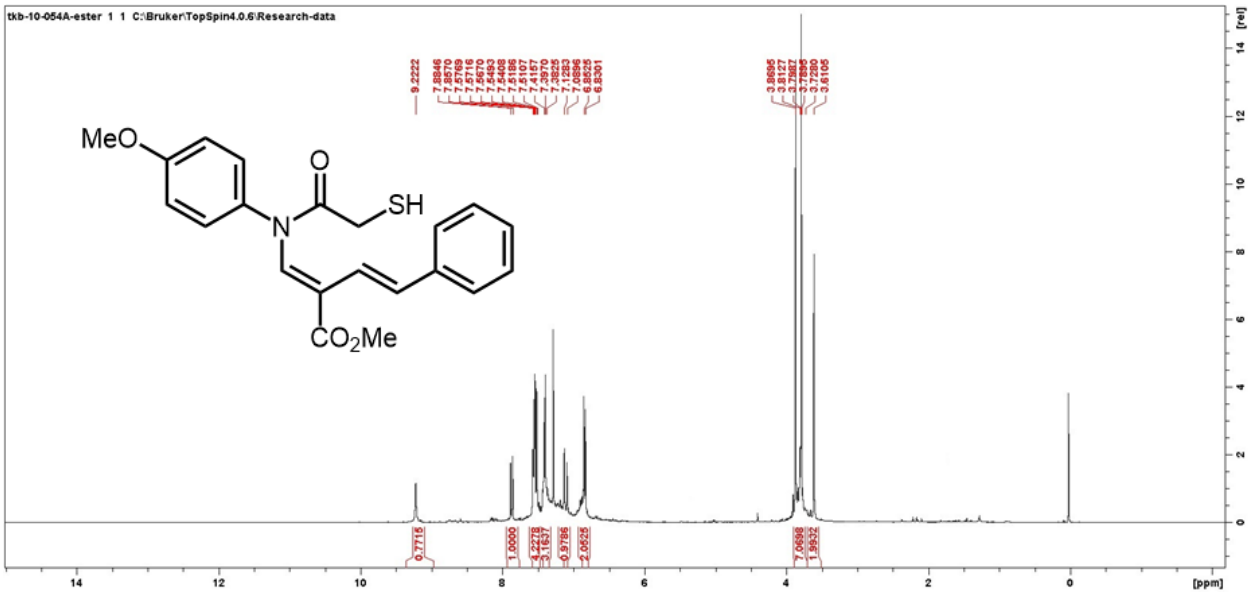



**Scheme 2 results**

**Compound 4k**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 314.4 mg, 82%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.28 (s, 1H), 7.84 (d, *J* = 11.0 Hz, 1H), 7.56 – 7.45 (m, 5H), 7.41 – 7.30 (m, 2H), 7.05 (d, *J* = 15.6 Hz, 1H), 6.91 – 6.72 (d, 2H), 3.83 (s, 3H), 3.74 (s, 3H), 3.62 (s, 1H), 3.60 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.7, 166.5, 156.3, 149.0, 144.0, 135.8, 131.3, 129.9, 128.9, 127.8, 124.5, 121.5, 114.1, 114.0, 55.4, 53.0, 39.9. FTIR (KBr): 3020.0, 2834.3, 1724.9, 1646.3, 1474.3, 1452.8, 1361.9, 1342.0, 1205.6, 1140.2, 1077.7, 996.4, 766.2. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{21}H_{21}NO_4S$ $[M]^{+}$ 383.1191, found 383.1194.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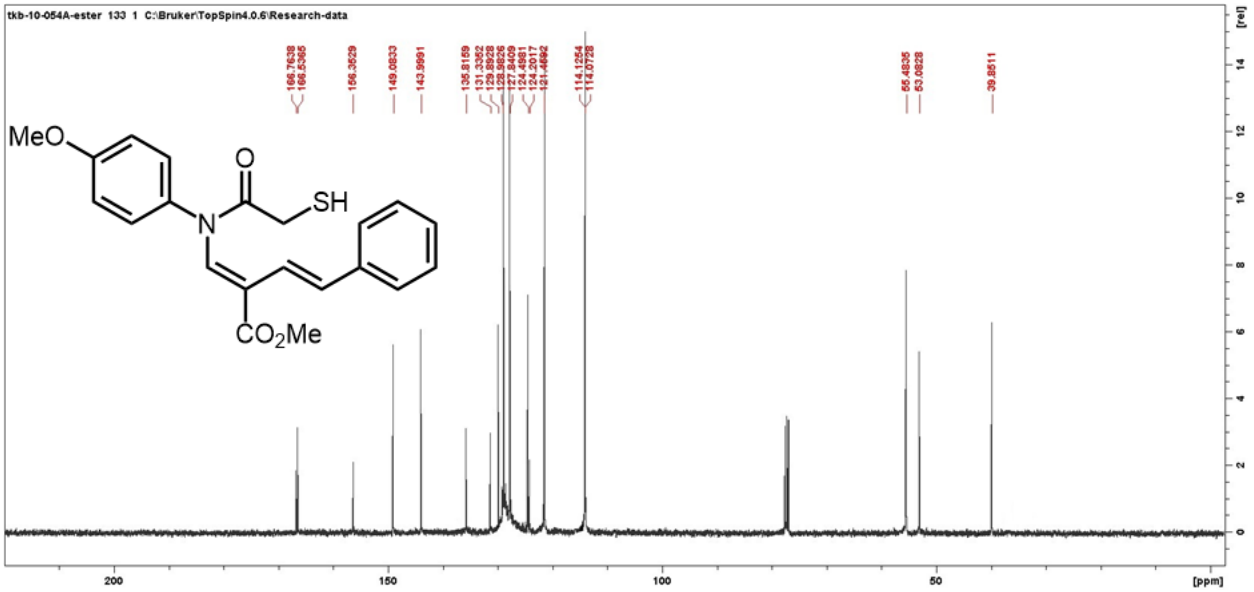
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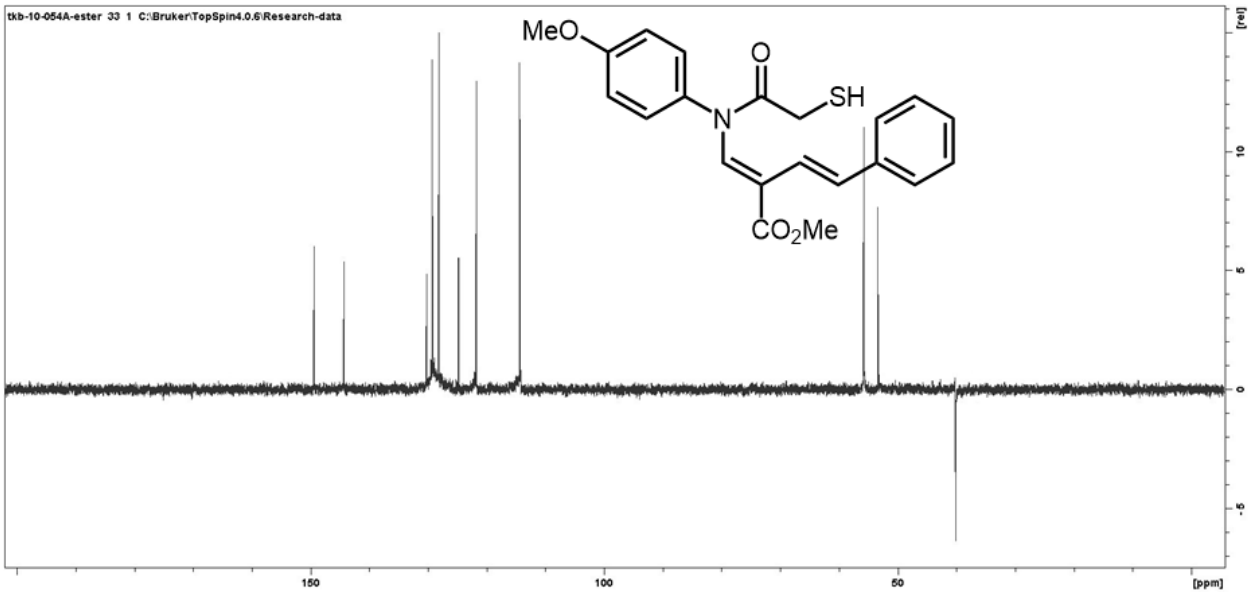
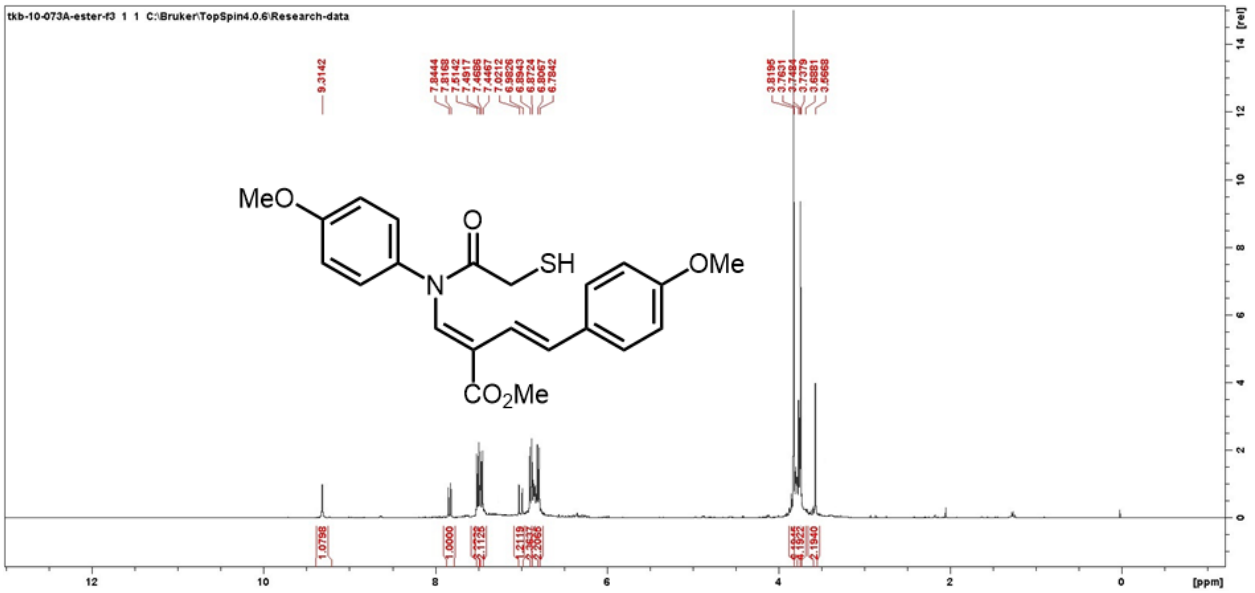



**Compound 4l**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 314.3 mg, 76%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 7.83 (d, *J* = 11.1 Hz, 1H), 7.51 – 7.44 (m, 4H), 6.99 (d, *J* = 11.1 Hz, 1H), 6.89 – 6.72 (m, 4H), 3.81 – 3.68 (m, 10H), 3.57 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.73, 161.19, 156.37, 149.97, 144.13, 131.32, 129.55, 128.62, 122.35, 122.33, 121.63, 121.51, 114.48, 114.21, 114.16, 114.15, 114.12, 114.08, 114.03, 55.50, 55.46, 53.00, 40.01. **HRMS-EI$^{+}$** (*m/z*): calc for $C_{22}H_{23}NO_5S$ $[M]^{+}$ 413.1297, found 413.1293.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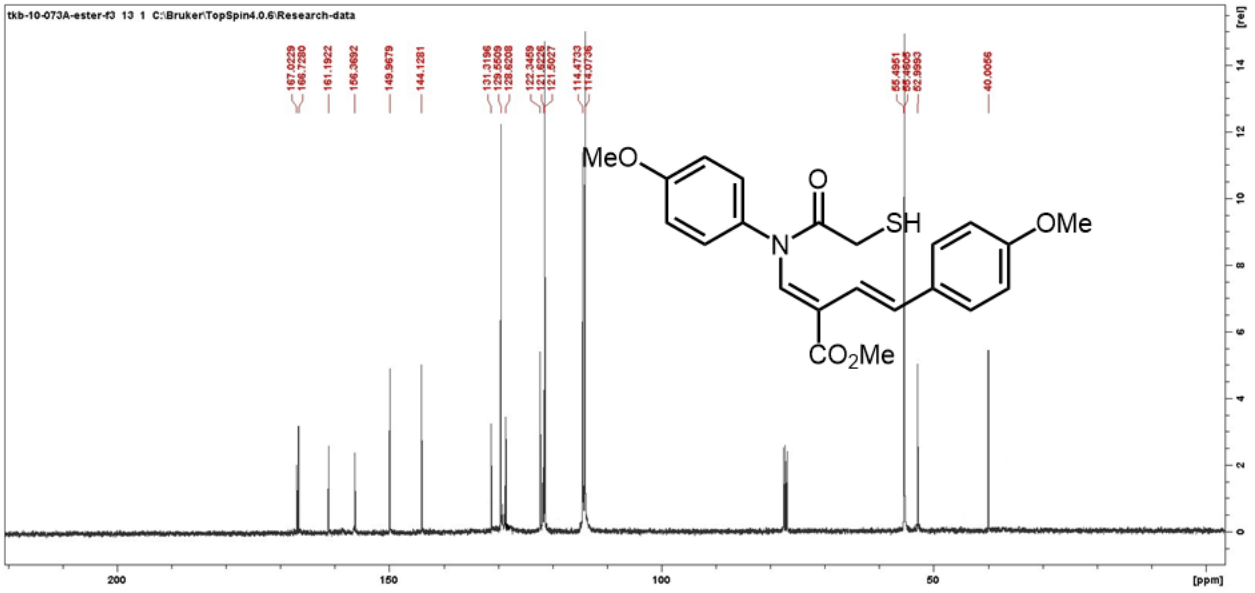
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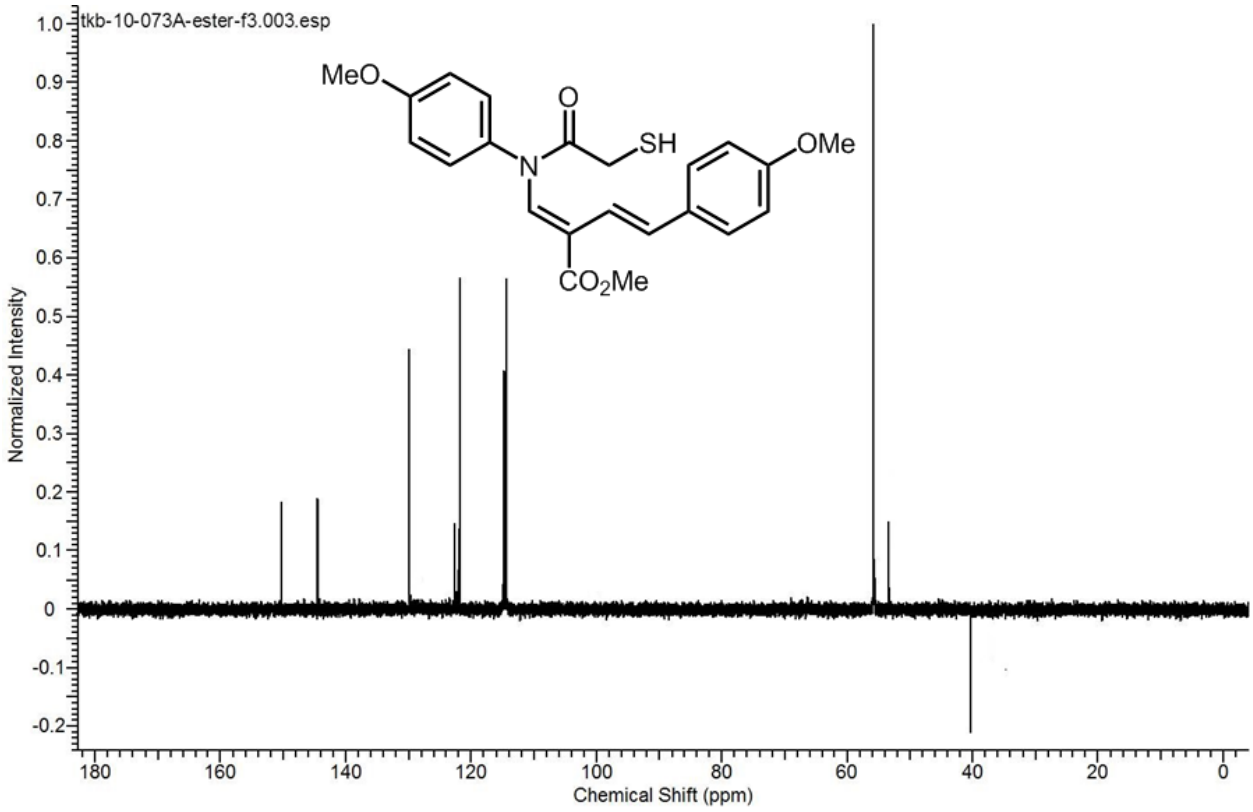
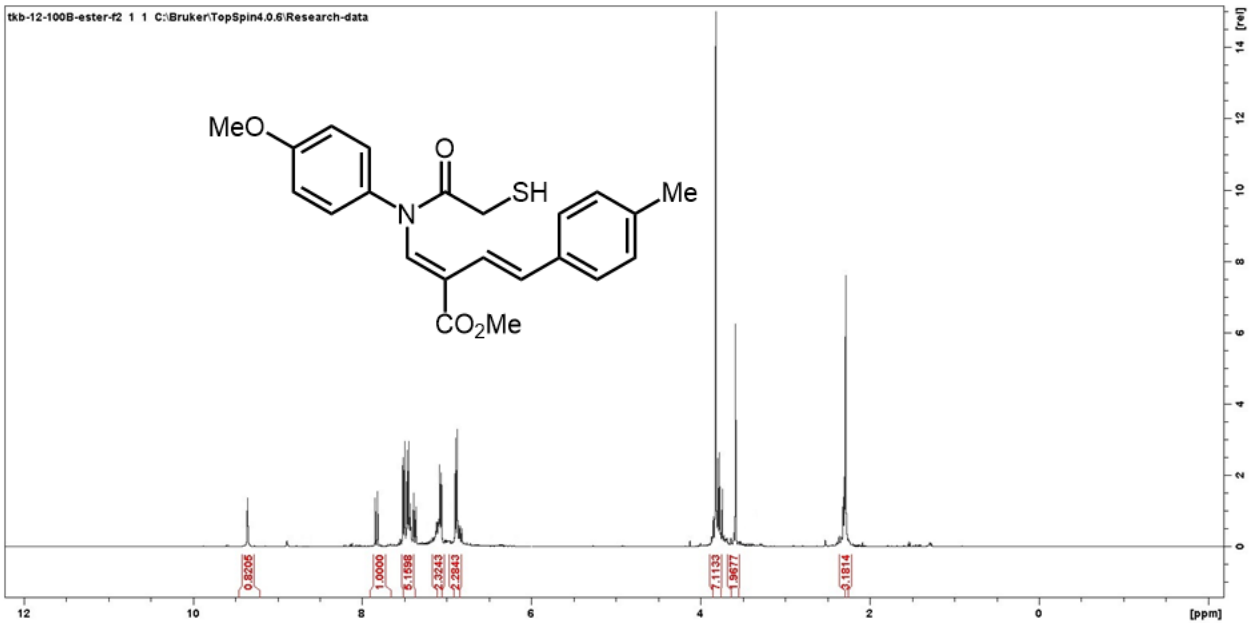



**Compound 4m**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 318 mg, 80%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.48 (d, *J* = 6.8 Hz, 1H), 7.70 – 7.42 (m, 5H), 7.14 – 7.02 (m, 2H), 6.91 (d, *J* = 7.8 Hz, 2H), 3.72 – 3.66 (m, 7H), 3.42 (s, 2H), 2.25 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.01, 166.88, 161.22, 149.97, 144.18, 135.63, 133.89, 129.59, 129.56, 129.49, 128.66, 127.68, 122.35, 122.32, 120.23, 119.88, 114.50, 114.21, 55.48, 53.02, 40.12, 20.99. **HRMS-EI**$^{+}$ calc for $C_{22}H_{23}NO_4S$ $[M]^{+}$ 397.1348, found 397.1352.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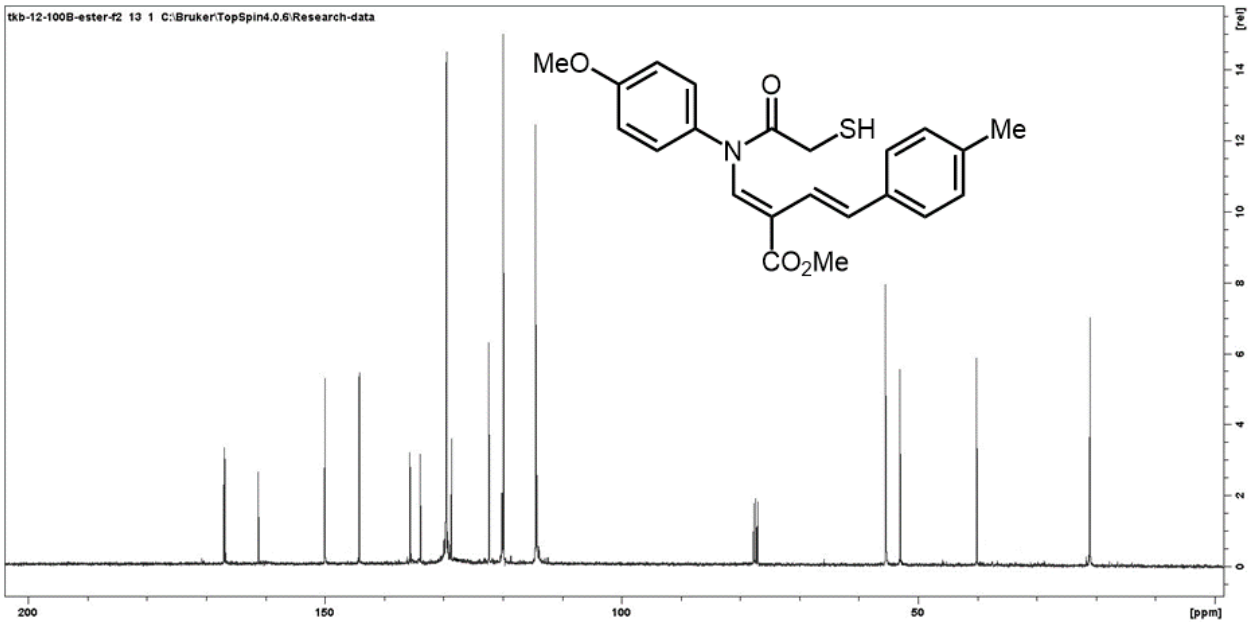
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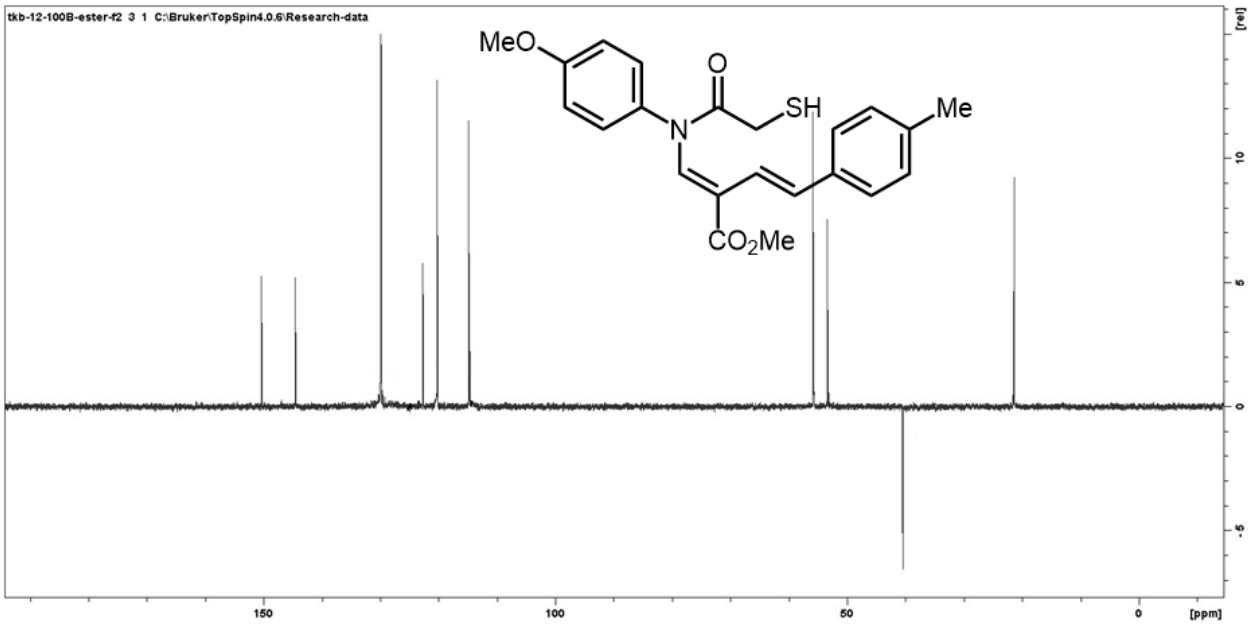
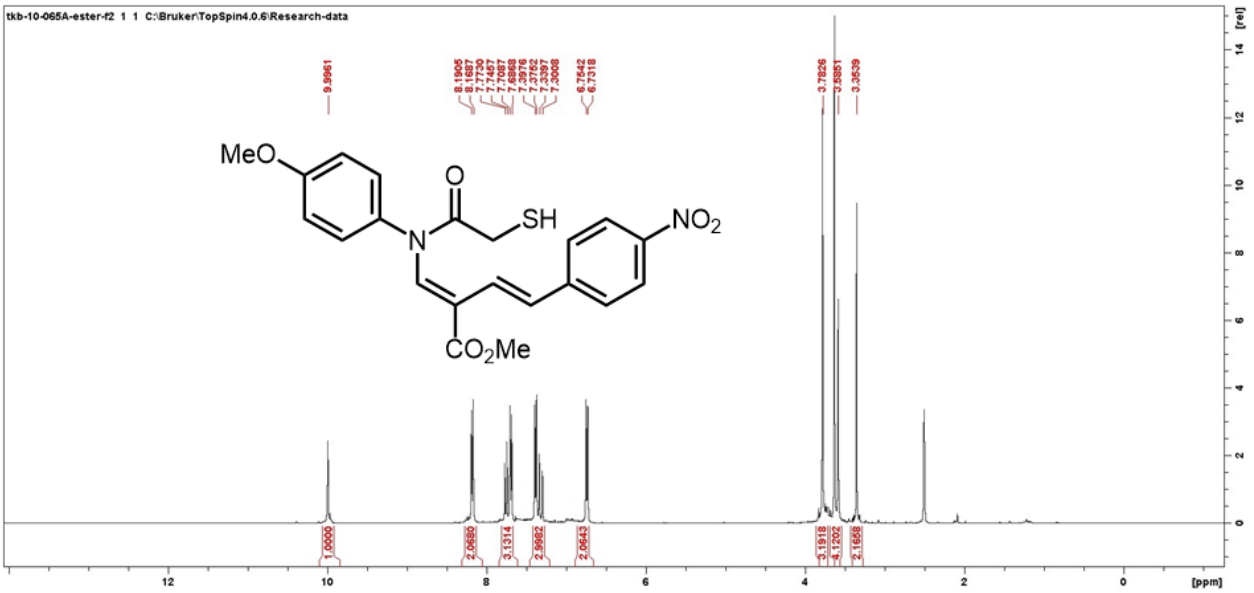



**Compound 4n**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 381.4 mg, 89%. $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 10.00 (s, 1H), 8.26 – 8.14 (d, 2H), 7.76 (d, $J$ = 10.9 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.58 – 7.32 (m, 3H), 6.79 – 6.70 (d, 10.9 Hz, 2H), 3.63 (s, 3H), 3.59 (s, 3H), 3.52 (s, 1H), 3.35 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.55, 165.54, 155.74, 147.59, 146.58, 142.86, 139.85, 132.49, 129.21, 128.71, 127.89, 124.53, 121.10, 114.21, 55.54, 53.20, 38.55. FTIR: 3305.8, 2950.6, 1710.3, 1660.5, 1595.7, 1510.7, 1462.8, 1434.7, 1412.6, 1340.5, 1301.1, 1270.8, 1234.9, 1179.9, 1109.4, 1034.1, 976.2, 915.2, 865.5. **HRMS-EI$^{+}$** calc for $C_{21}H_{20}N_2O_6S$ $[M]^{+}$ 428.1042, found 428.1049.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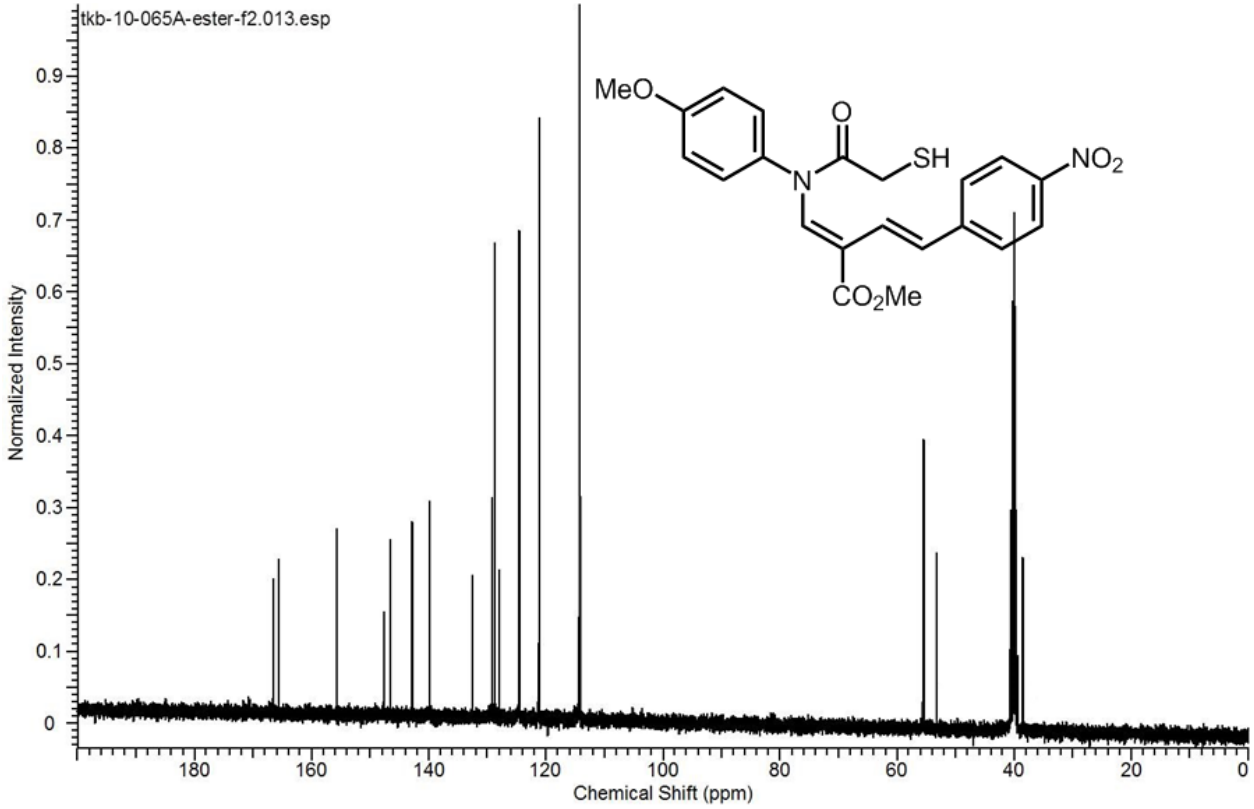
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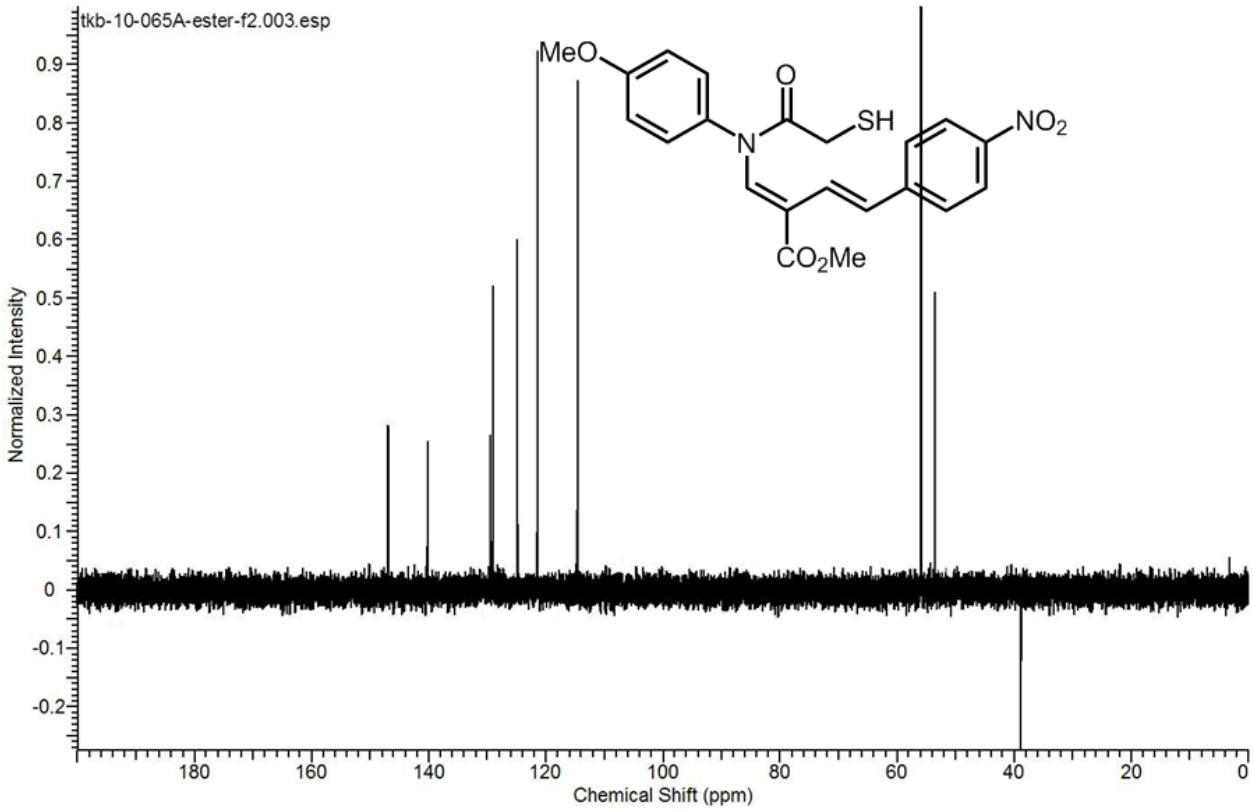
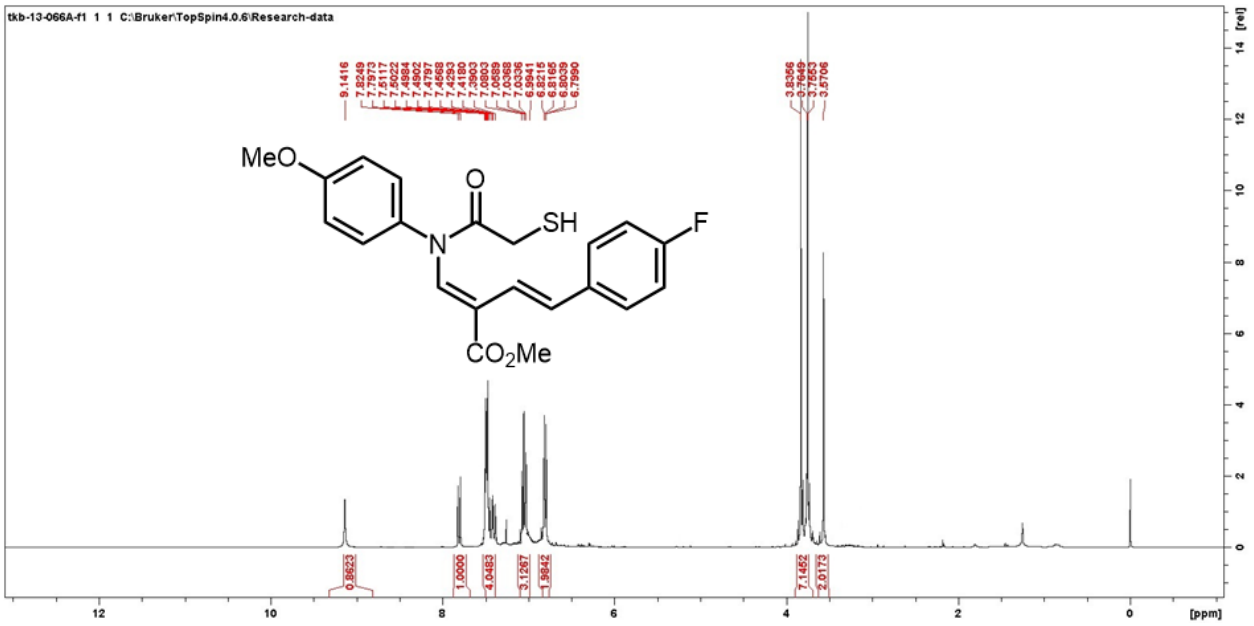
Normalized Intensity
Chemical Shift (ppm)




**Compound 4o**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 345.2 mg, 86%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.81 (d, *J* = 11.0 Hz, 1H), 7.51 – 7.39 (m, 4H), 7.08 – 6.99 (m, 3H), 6.81 (d, *J* = 6.8 Hz, 2H), 3.84 – 3.76 (m, 7H), 3.57 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.69, 166.29, 164.85, 162.35, 156.42, 148.86, 142.59, 132.07, 132.04, 131.18, 129.61, 129.53, 124.22, 124.18, 124.16, 121.37, 116.18, 115.97, 114.08, 55.44, 53.03, 39.90. **HRMS-EI**$^{+}$ calc for $C_{21}H_{20}FNO_4S$ $[M]^{+}$ 401.1097, found 401.1093.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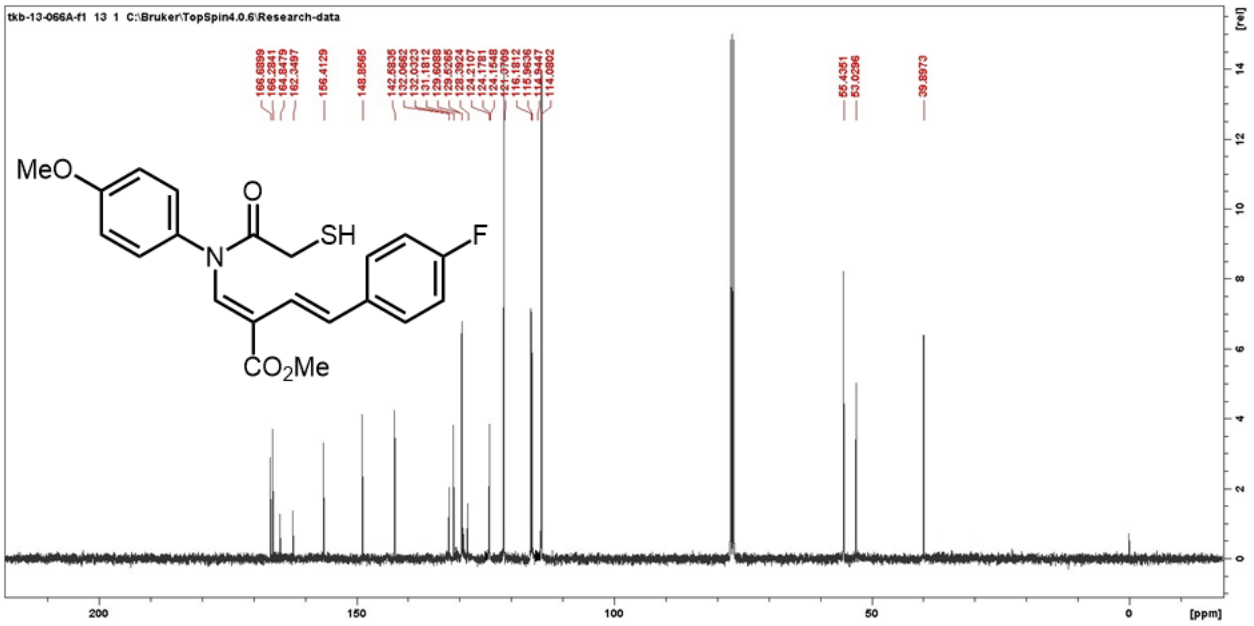
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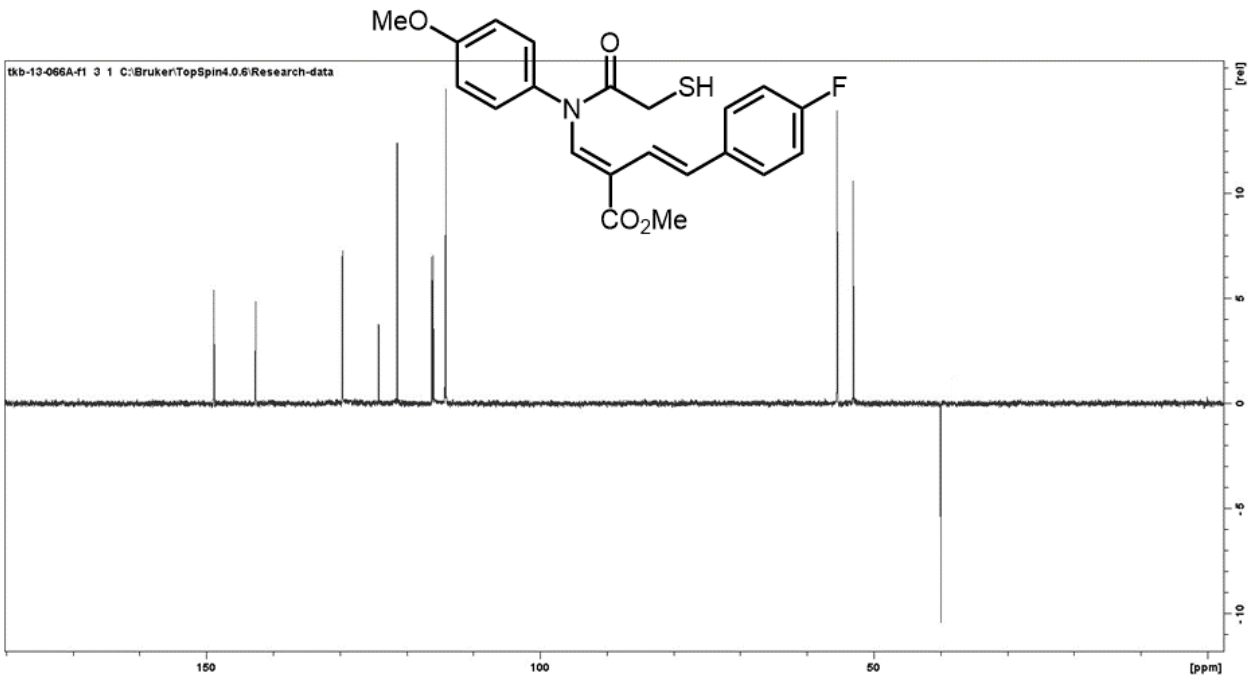
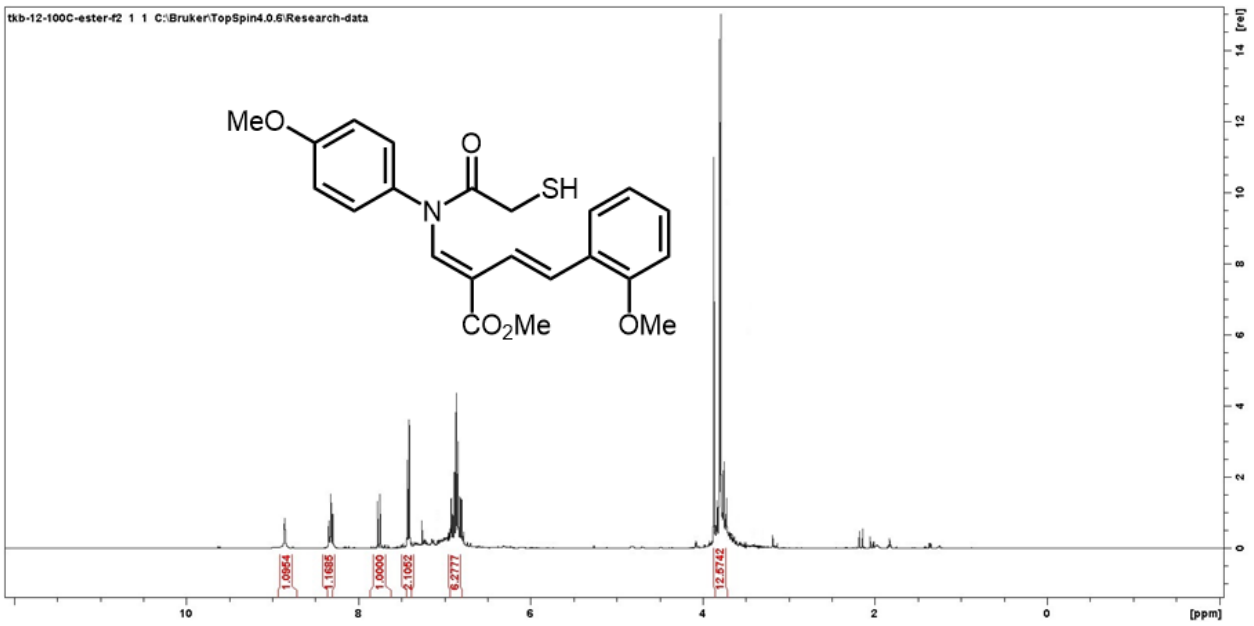



**Compound 4p**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 301.8 mg, 73%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.36 (dd, *J* = 9.8, 8.0 Hz, 2H), 7.81 (d, *J* = 11.1 Hz, 1H), 7.30 (m, 2H), 6.95 – 6.72 (m, 6H), 3.80 – 3.66 (m, 12H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.55, 166.03, 160.97, 148.49, 143.05, 129.37, 128.87, 124.35, 124.06, 122.50, 121.10, 121.06, 119.94, 119.83, 114.40, 110.20, 110.13, 55.88, 55.47, 52.74, 39.38. **HRMS-EI**$^{+}$ calc for $C_{22}H_{23}NO_5S$ $[M]^+$ 413.1297, found 413.1293.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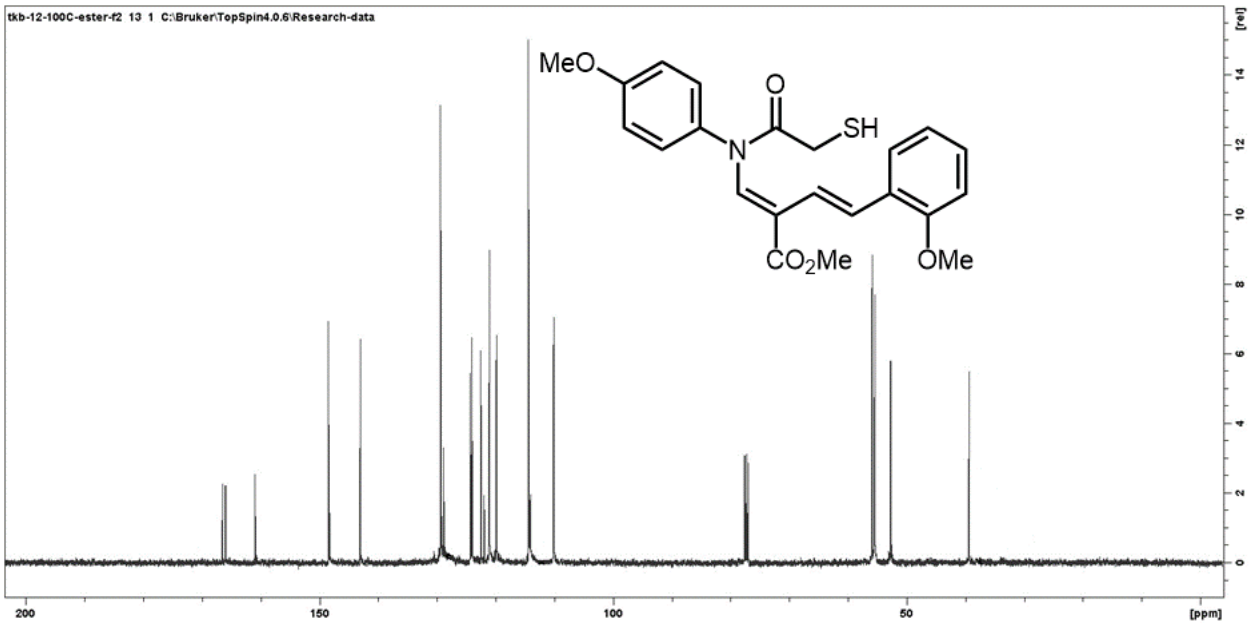
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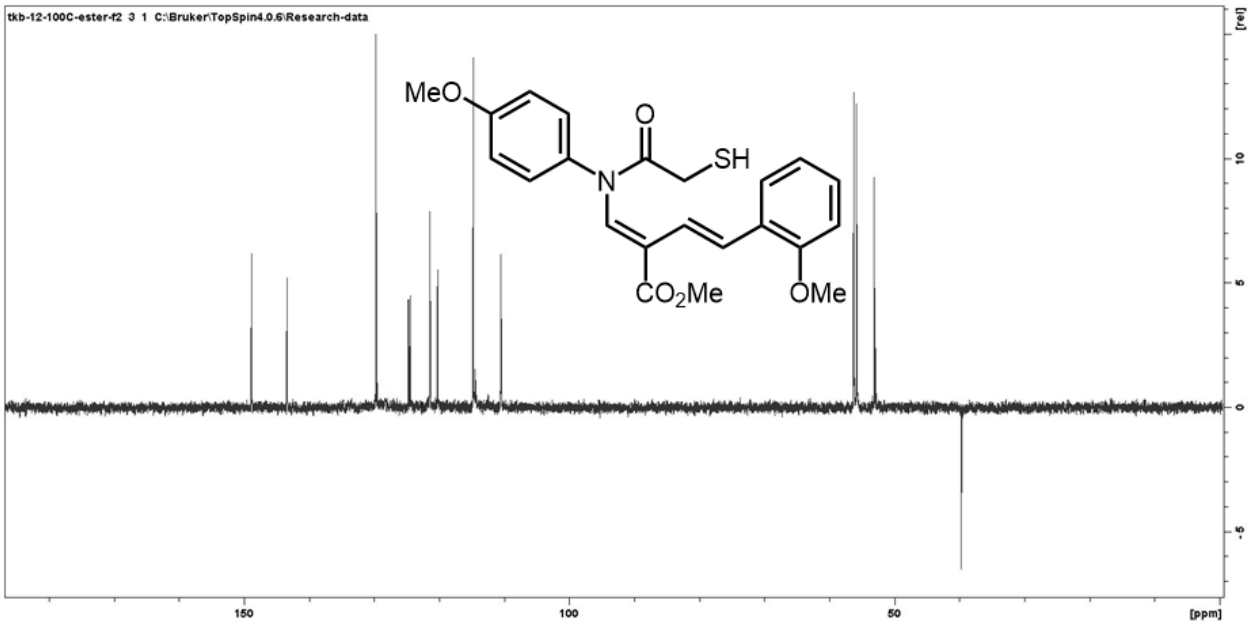
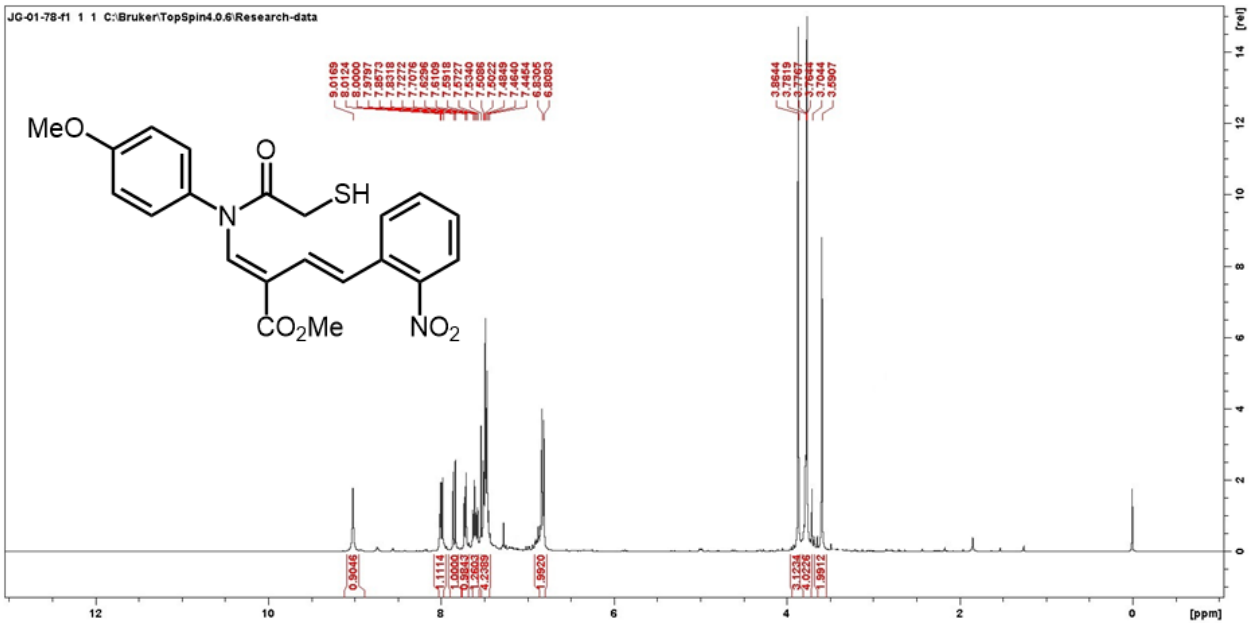



**Compound 4q**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 359.9 mg, 84%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.04 –7.96 (m, 1H), 7.84 (d, *J* = 10.2 Hz, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.65 – 7.44 (m, 5H), 6.81 (d, *J* = 8.2 Hz, 2H), 3.86 (s, 3H), 3.78 (d, *J* = 2.3 Hz, 1H), 3.76 (s, 3H), 3.59 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.28, 166.21, 156.46, 148.09, 147.44, 137.49, 133.39, 131.41, 131.10, 129.71, 128.97, 128.75, 127.24, 124.95, 121.44, 114.10, 55.46, 53.18, 39.59. **HRMS-EI$^+$** calc for $C_{21}H_{20}N_2O_6S$ $[M]^+$ 428.1042, found 428.1049.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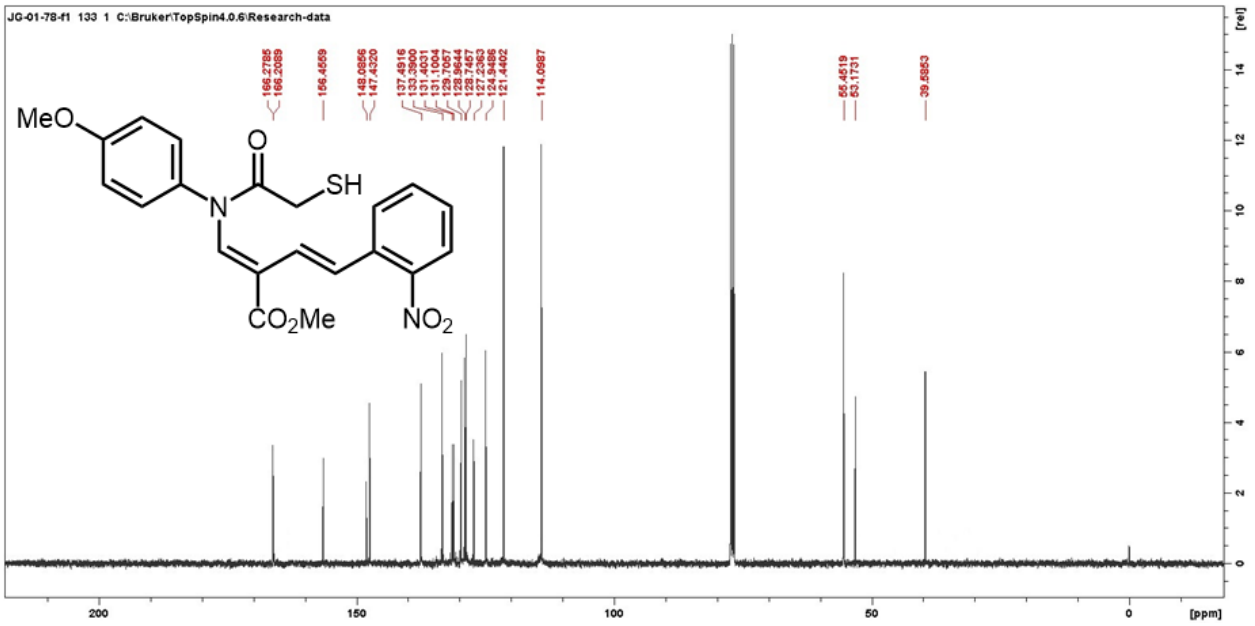
N
SH
CO2Me
NO2
[ppm]
[rel]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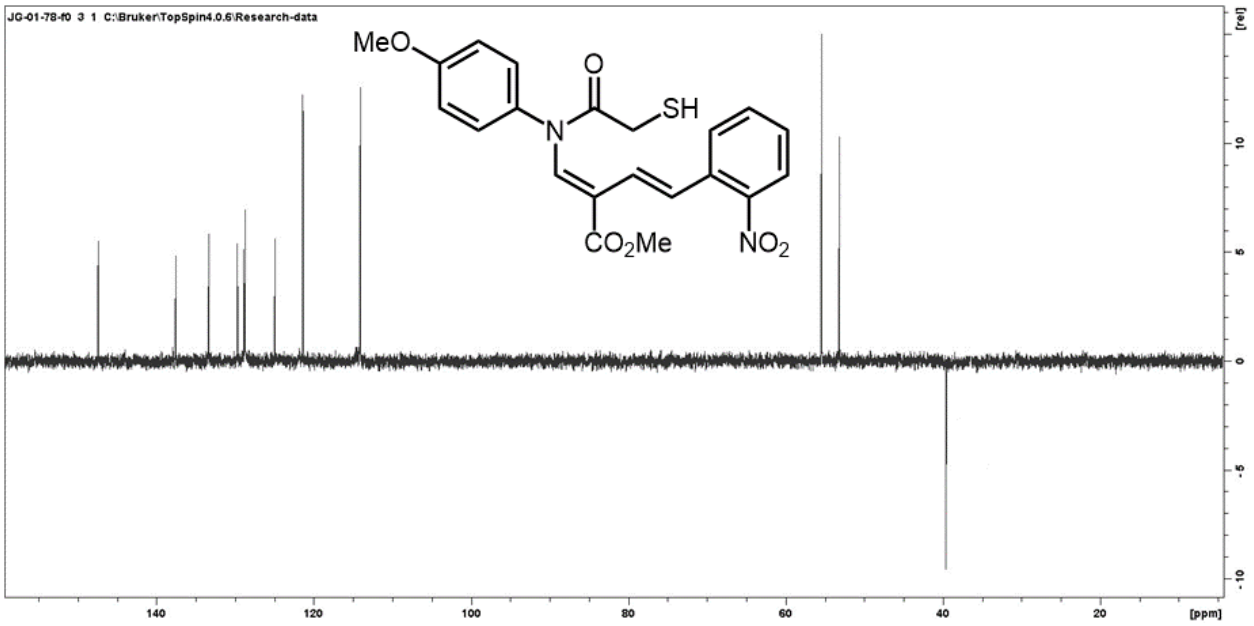
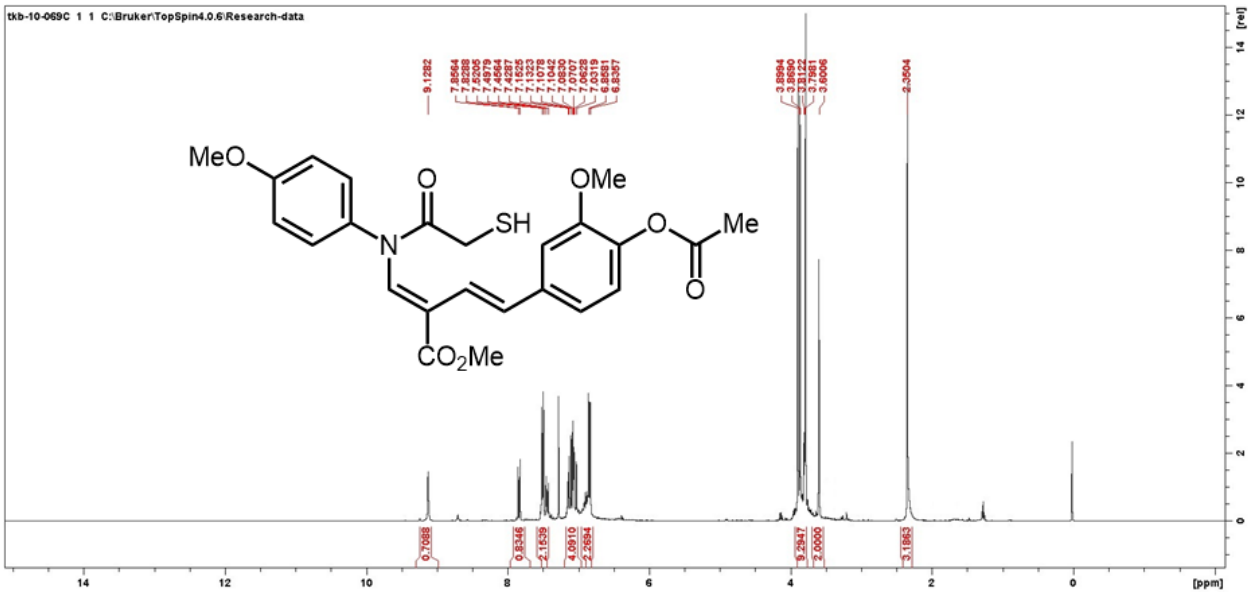



**Compound 4r**

Prepared in 0.5 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (20:80). Oily substance. Yield = 186.3 mg, 79%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.13 (s, 1H), 7.84 (dd, *J* = 11.1, 0.8 Hz, 1H), 7.56 – 7.39 (m, 2H), 7.20 – 6.97 (m, 4H), 6.96 – 6.82 (m, 2H), 3.90 (s, 3H), 3.87 (m, 4H), 3.79 (s, 3H), 3.60 (s, 2H), 2.35 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.89, 166.75, 166.31, 156.47, 151.53, 148.83, 143.35, 141.21, 134.79, 131.17, 124.60, 123.37, 121.41, 120.92, 114.15, 111.05, 53.16, 39.96, 20.75. FTIR (KBr): 3307.5, 2951.9, 1764.3, 1707.5, 1678.7, 1601.0, 1539.9, 1511.3, 1464.4, 1435.3, 1414.9, 1369.5, 1286.5, 1268.5, 1246.0, 1197.2, 1154.7, 1121.6, 1033.6, 978.8, 907.1, 829.2. **HRMS-EI$^{+}$** calc for $C_{24}H_{25}NO_7S$ $[M]^{+}$ 471.1352, found 471.1359.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O
Me
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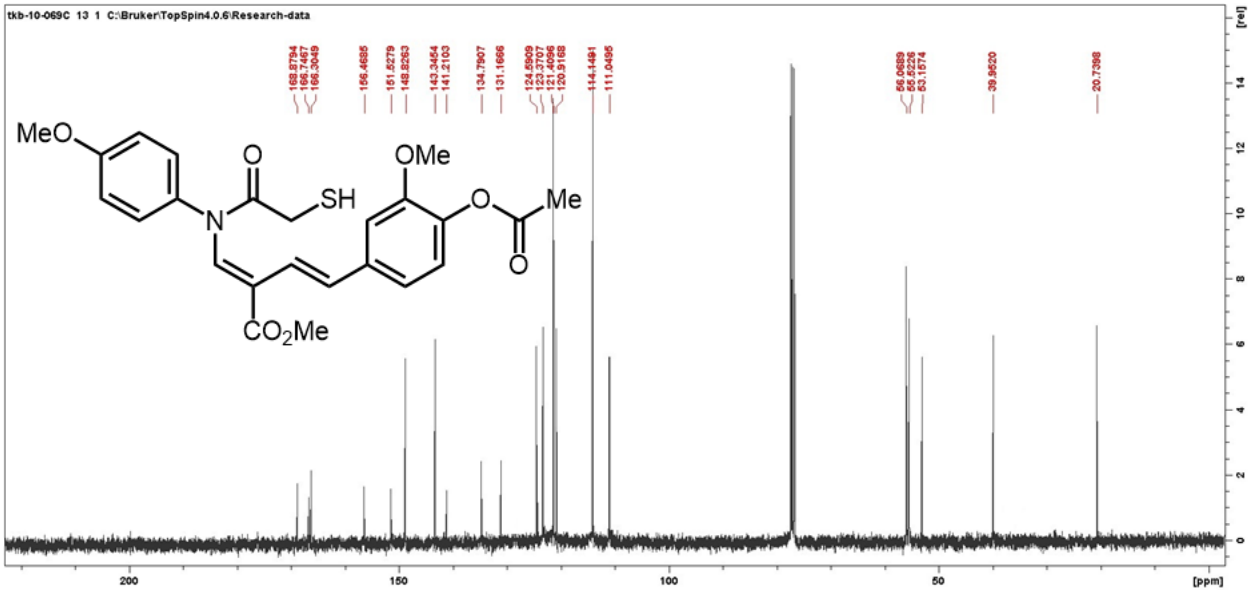
[rel]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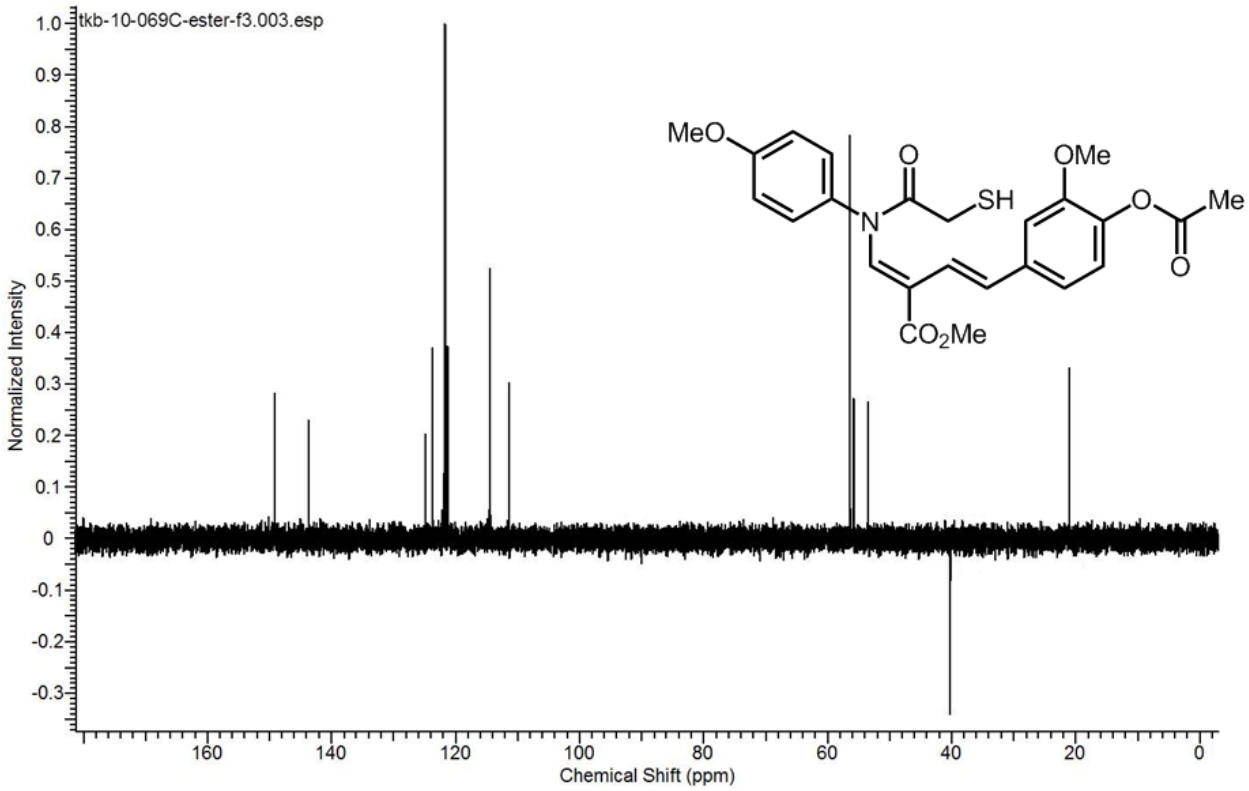
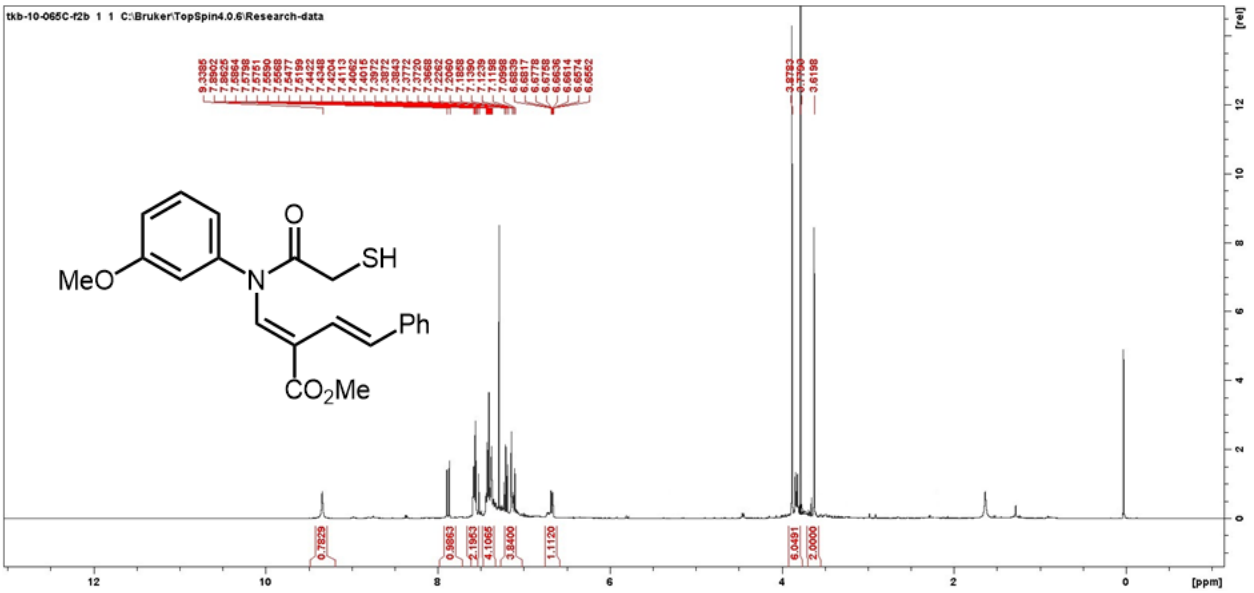



**Compound 4s**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 306.8 mg, 80%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.34 (s, 1H), 7.87 (d, *J* = 11.1 Hz, 2H), 7.59 – 7.45 (m, 2H), 7.37 – 7.23 (m, 4H), 7.27 – 7.16 (m, 3H), 6.65 – 6.63 (m, 1H), 3.55 – 3.71 (m, 7H), 3.62 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.83, 166.65, 160.17, 149.18, 144.32, 139.23, 135.76, 130.03, 129.68, 129.04, 127.88, 124.35, 111.95, 110.40, 105.24, 55.31, 53.17, 40.17. FTIR (KBr): 3318.3, 2949.3, 1708.1, 1685.5, 1608.4, 1577.4, 1546.8, 1492.8, 1453.3, 1432.6, 1266.3, 1226.4, 1158.0, 1044.6, 976.2, 854.1, 774.9, 749.5, 690.3. **HRMS-EI$^{+}$** calc for $C_{21}H_{21}NO_4S$ $[M]^{+}$ 383.1191, found 383.1191.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Ph
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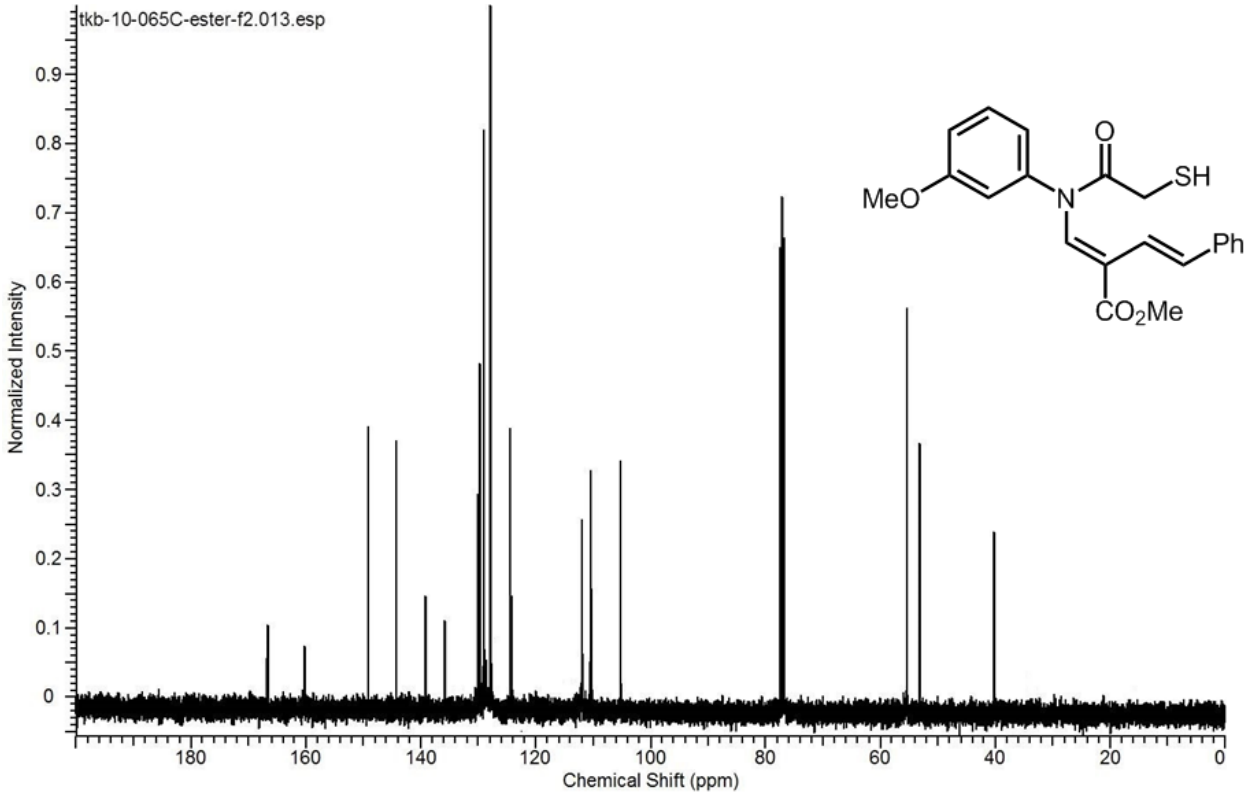
[ppm]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Chemical Shift (ppm)
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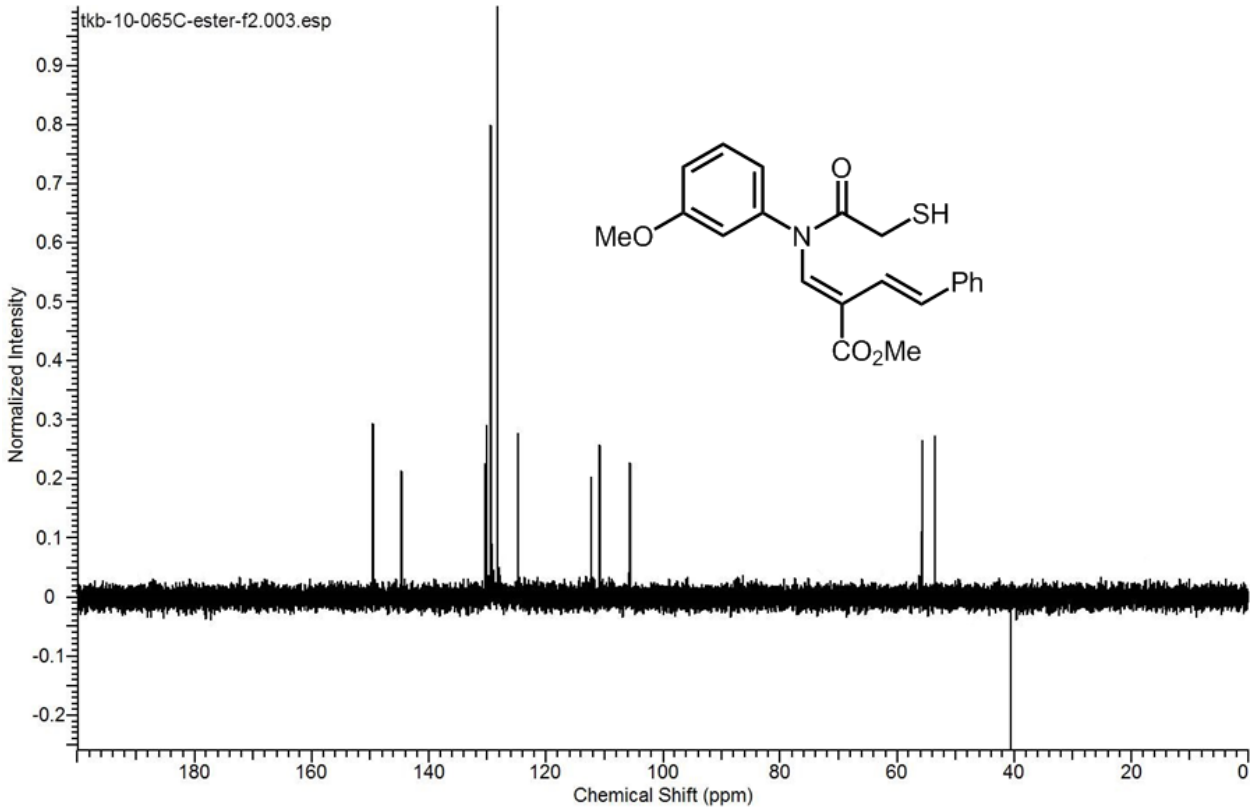
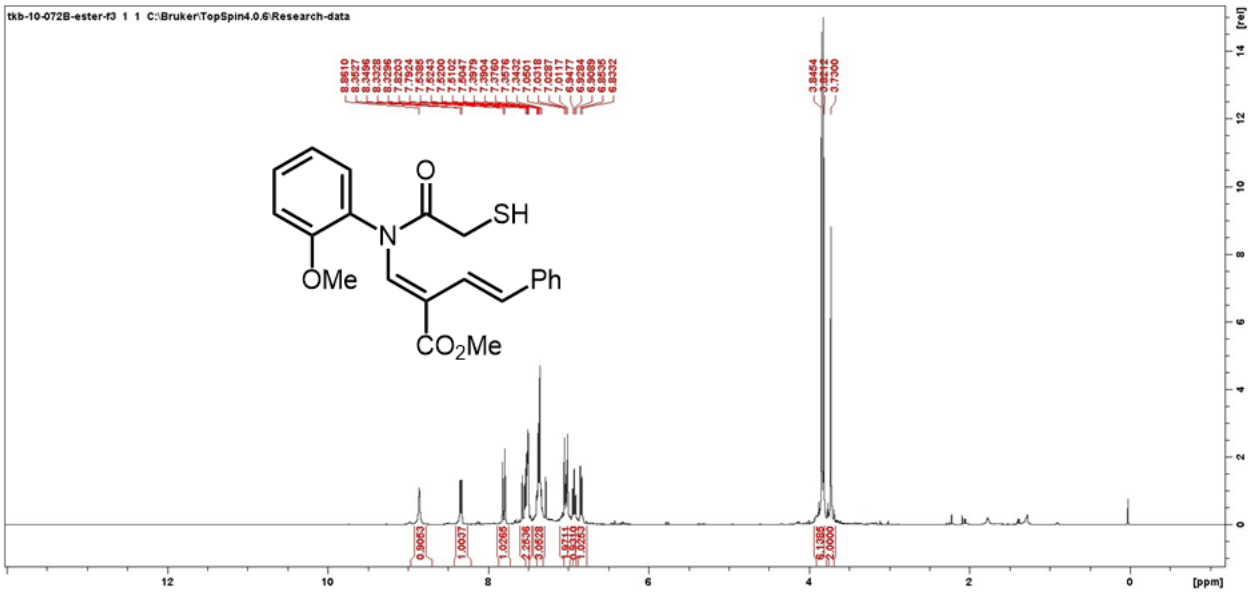
N
O
SH
Ph
CO2Me




**Compound 4t**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 295.3 mg, 77%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 8.34 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.81 (d, *J* = 11.2 Hz, 1H), 7.60 – 7.49 (m, 2H), 7.50 (d, *J* = 1.6 Hz, 1H), 7.46 – 7.29 (m, 2H), 7.12 – 6.98 (m, 2H), 6.93 (td, *J* = 7.8, 1.4 Hz, 1H), 6.84 (dd, *J* = 8.1, 1.4 Hz, 1H), 3.95 – 3.80 (m, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.36, 165.82, 147.74, 143.06, 136.05, 129.64, 128.92, 127.72, 124.57, 124.06, 121.10, 119.82, 110.08, 55.83, 52.83, 39.25. **HRMS-EI$^+$** calc for $C_{21}H_{21}NO_4S$ $[M]^+$ 383.1191, found 383.1191.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Ph
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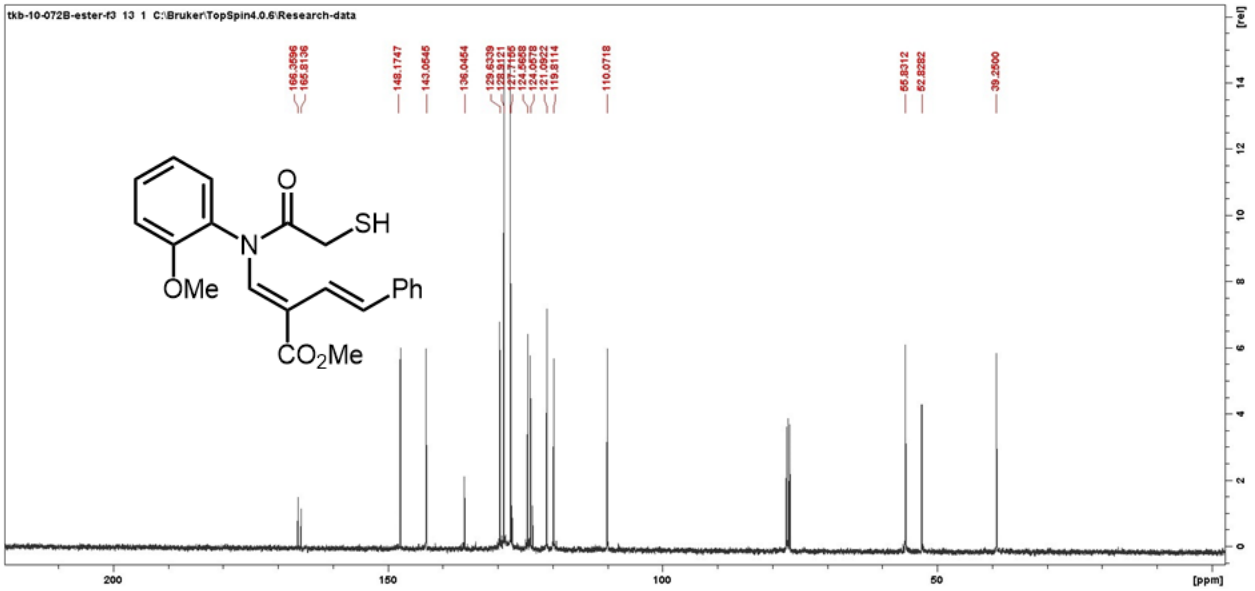
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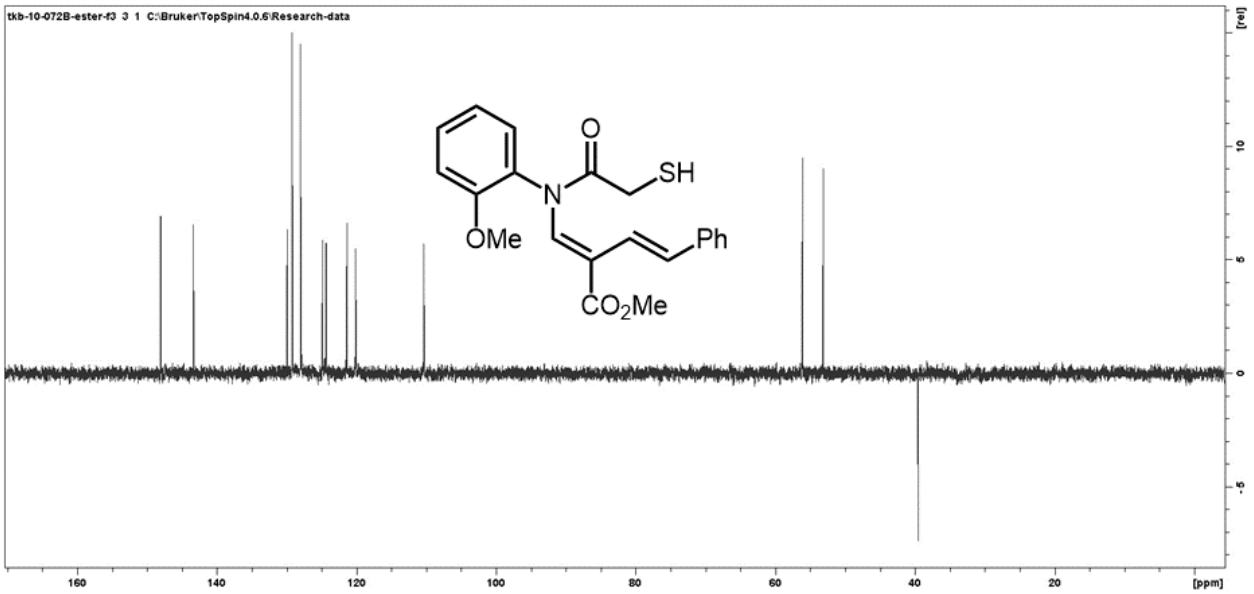
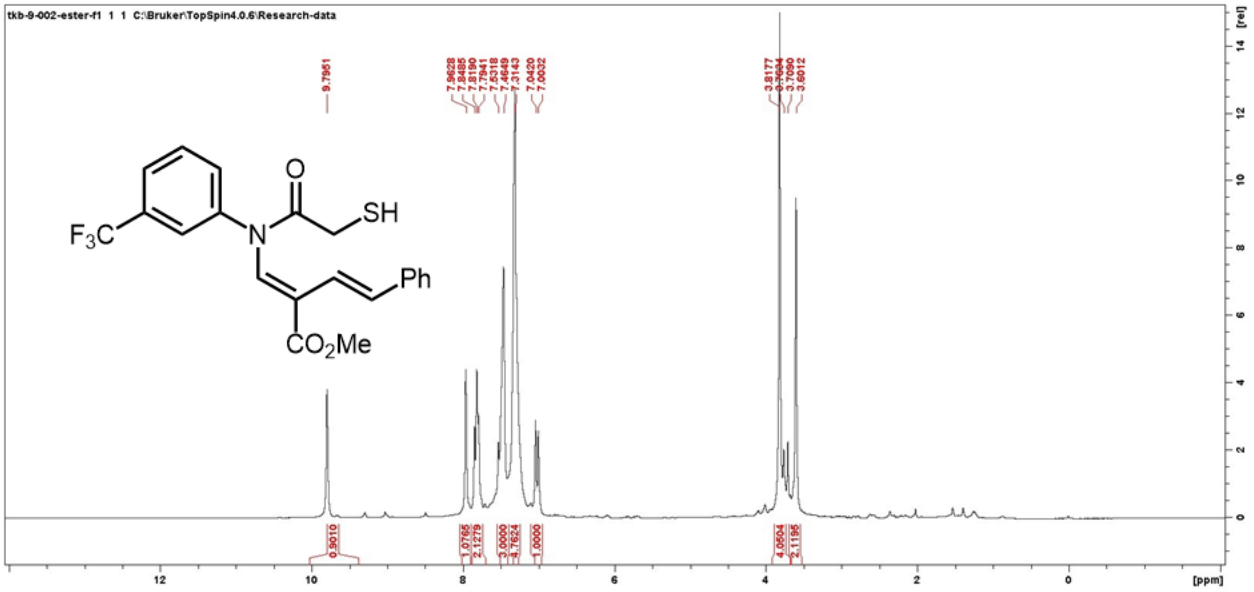
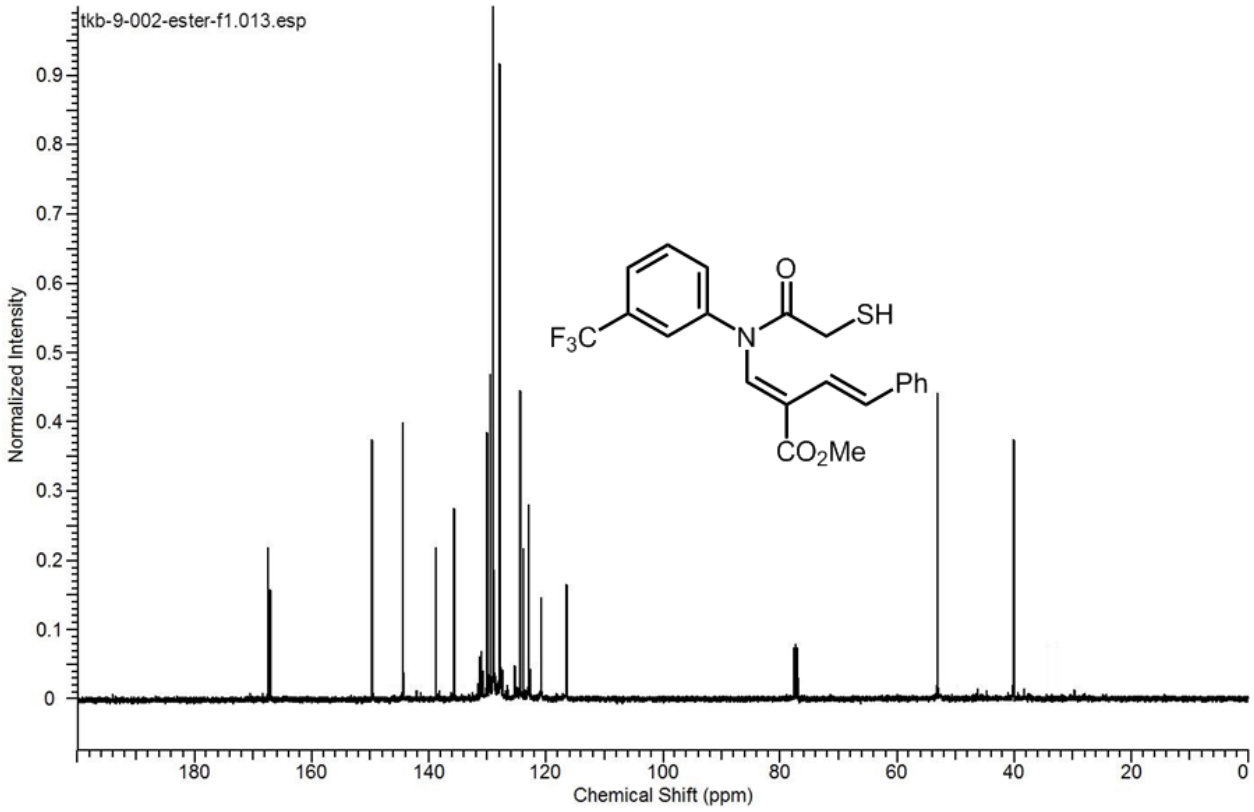



**Compound 4u**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 366.6 mg, 87%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.80 (s, 1H), 7.96 (s, 1H), 7.82 (dd, *J* = 13.1, 9.4 Hz, 2H), 7.55 – 7.31 (m, 7H), 7.02 (d, *J* = 15.7 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 1H), 3.60 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.53, 167.05, 149.66, 144.43, 138.78, 135.70, 130.01, 129.49, 128.98, 127.86, 124.35, 123.86, 122.90, 120.78, 120.74, 116.46, 116.42, 53.11, 40.09. **HRMS-EI**$^{+}$ calc for $C_{21}H_{18}F_3NO_3S$ $[M]^{+}$ 421.0959, found 421.0963.

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Chemical Shift (ppm)
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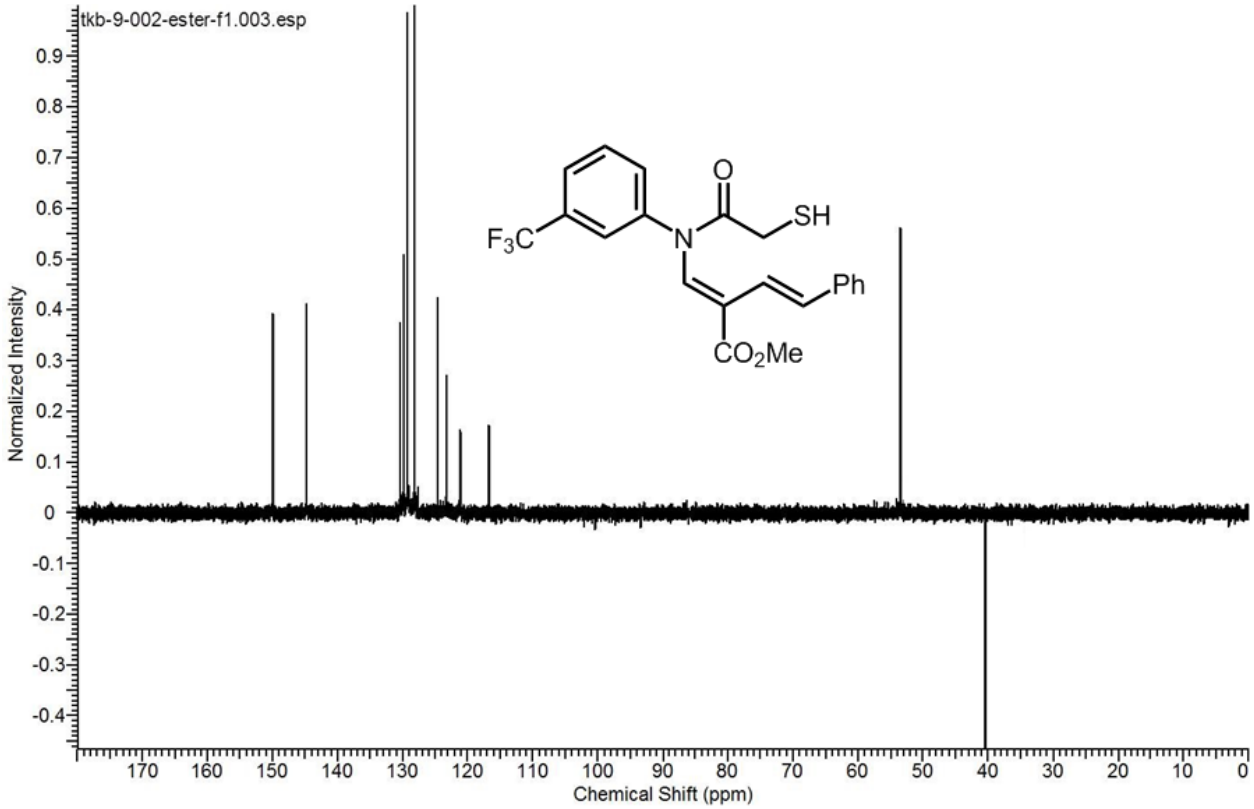
O
SH
N
Ph
CO2Me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Normalized Intensity
Chemical Shift (ppm)
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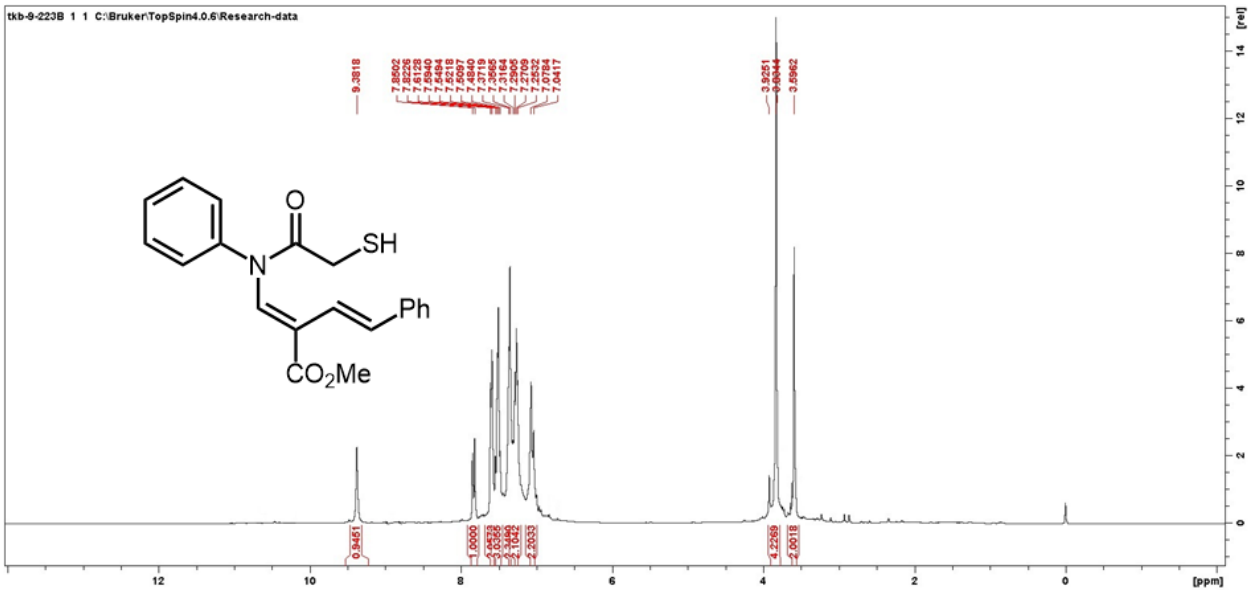
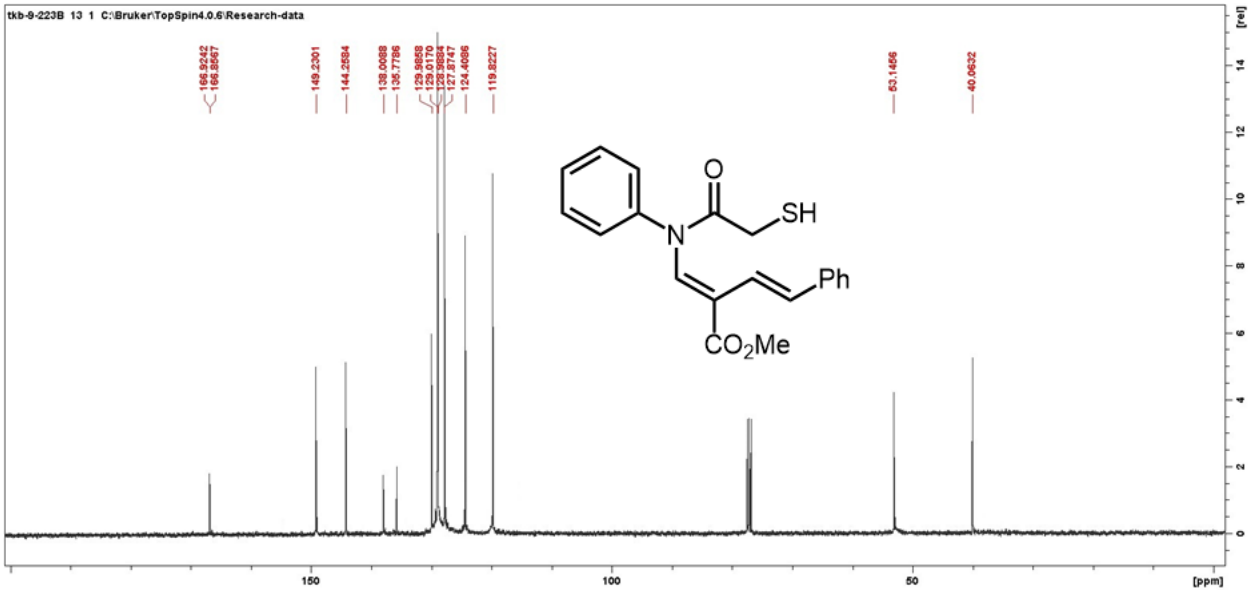
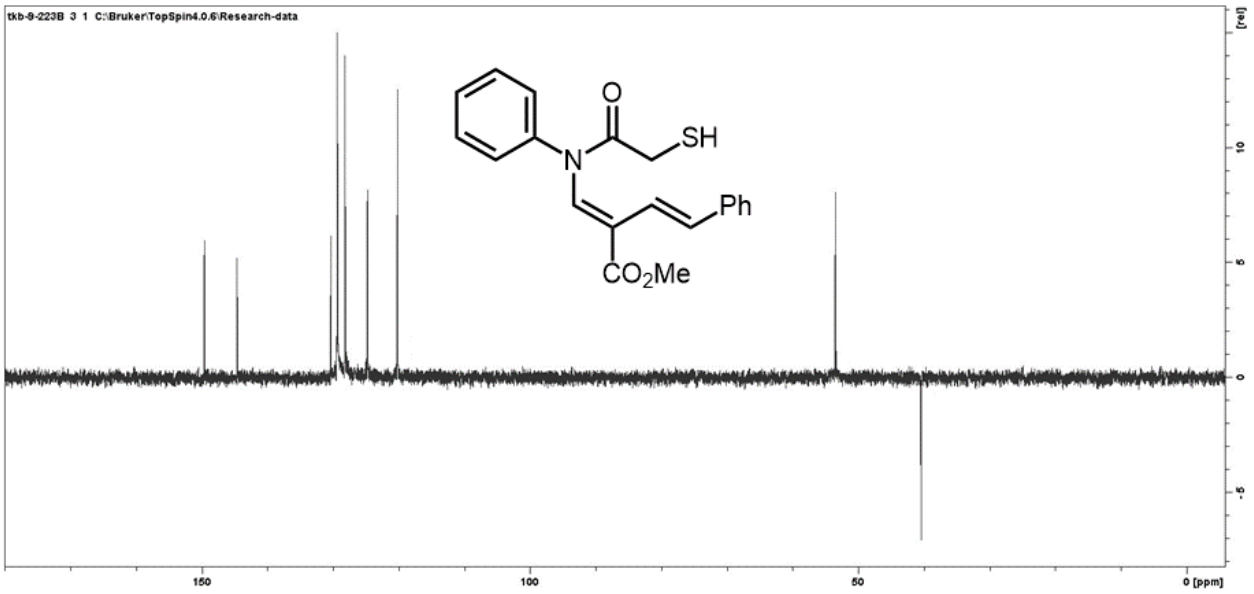
O
SH
N
Ph
CO2Me

**Compound 4v**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 296.9 mg, 84%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.38 (s, 1H), 7.84 (d, *J* = 11.1 Hz, 1H), 7.64 – 7.28 (m, 9H), 7.15 – 6.95 (m, 2H), 3.83 (s, 3H), 3.76 – 3.62 (m, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.93, 166.86, 149.23, 144.26, 129.99, 129.02, 128.99, 127.88, 124.43, 124.41, 119.83, 53.15, 40.07. **HRMS-EI**$^{+}$ calc for $C_{20}H_{19}NO_3S$ $[M]^{+}$ 353.1086, found 353.1092.

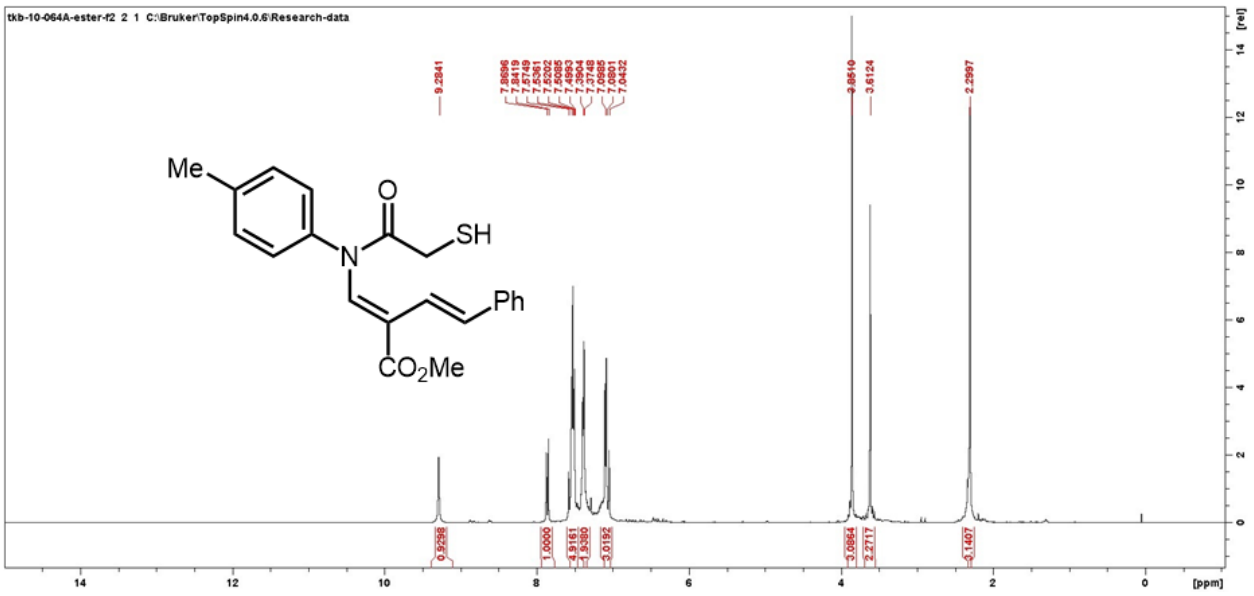


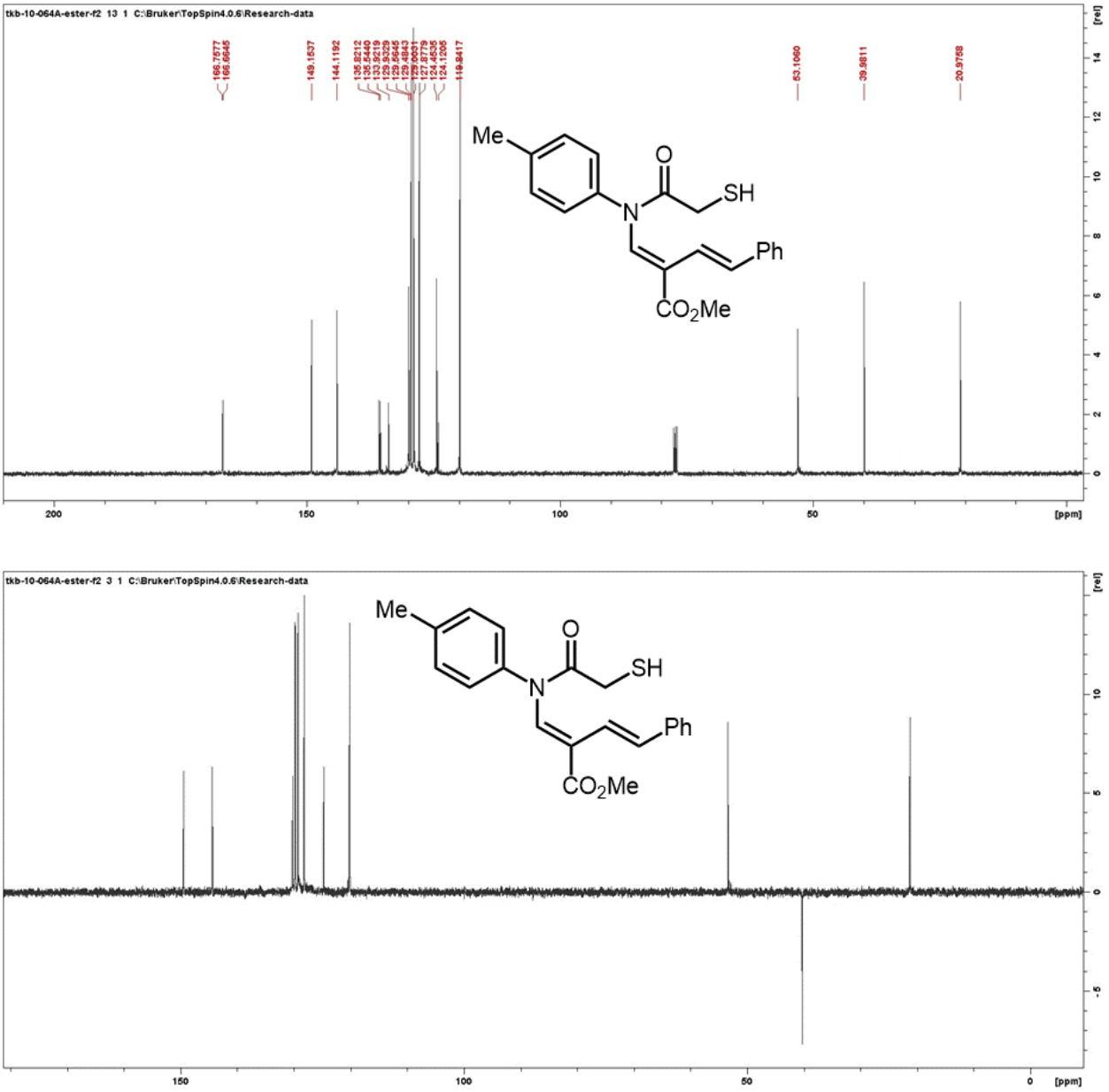






**Compound 4w**

Prepared in 1.0 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 286.6 mg, 78%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.28 (s, 1H), 7.86 (d, *J* = 11.1 Hz, 1H), 7.60 – 7.42 (m, 5H), 7.45 – 7.29 (m, 2H), 7.17 – 7.02 (m, 3H), 3.85 – 3.79 (m, 4H), 3.61 (s, 2H), 2.30 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.67, 149.16, 144.12, 135.82, 135.55, 133.93, 129.94, 129.49, 129.01, 127.88, 124.46, 119.85, 53.11, 39.98, 20.98. FTIR (KBr): 3305.6, 1708.2, 1684.3, 1659.5, 1607.6, 1577.1, 1533.7, 1513.7, 1447.6, 1433.8, 1405.1, 1320.1, 1301.8, 1266.6, 1228.5, 1179.8, 1161.7, 1043.5, 976.6. **HRMS-EI**$^{+}$ calc for $C_{21}H_{21}NO_3S$ $[M]^{+}$ 367.1242, found 367.1247.

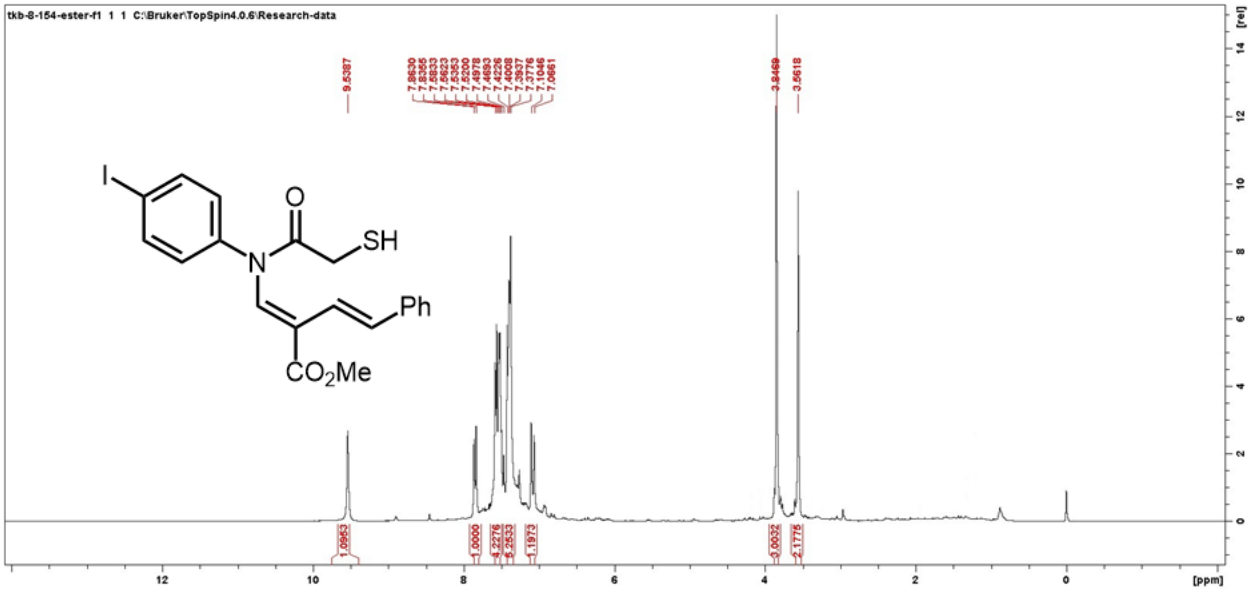


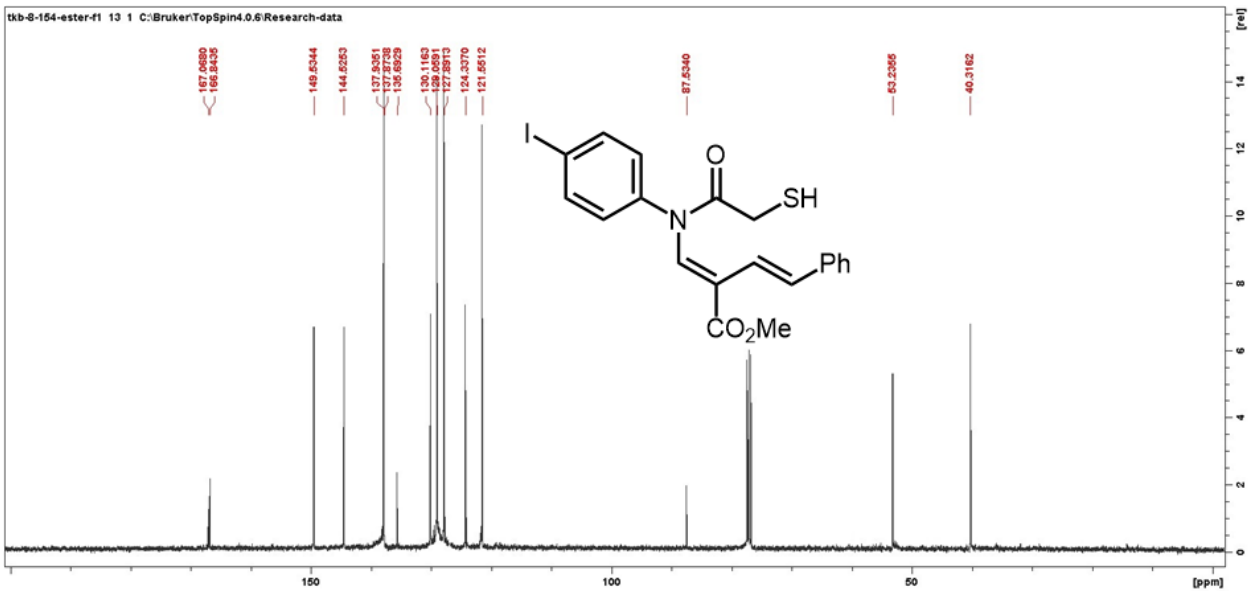


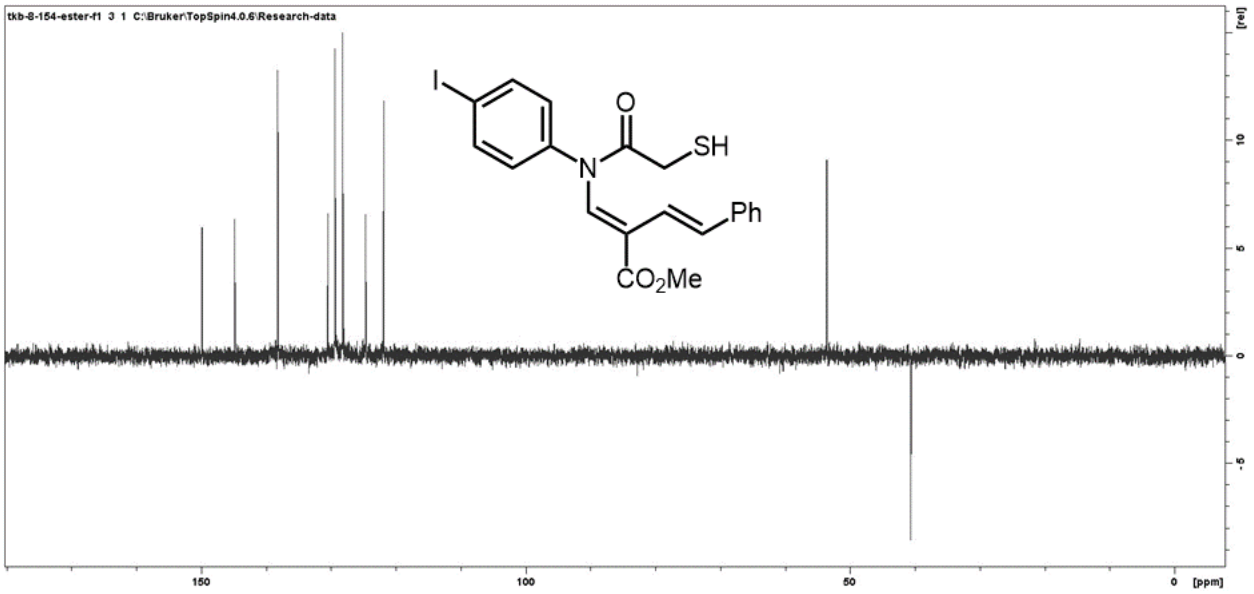

**Compound 4x**

Prepared in 0.50 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 194.2 mg, 81%. $^{1}$H NMR (400 MHz, Chloroform-*d*) δ 9.54 (s, 1H), 7.85 (d, *J* = 11.1 Hz, 1H), 7.76 – 7.35 (m, 9H), 7.09 (d, *J* = 15.4 Hz, 1H), 3.85 (s, 3H), 3.56 (s, 3H), 3.34 (dd, *J* = 24.2, 14.1 Hz, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.07, 166.85, 149.54, 144.53, 137.94, 137.88, 135.70, 130.12,

129.06, 127.90, 124.34, 121.56, 87.54, 53.24, 40.32. **HRMS-EI**$^{+}$ calc for $C_{20}H_{18}INO_3S$ $[M]^{+}$ 479.0052, found 479.0059.

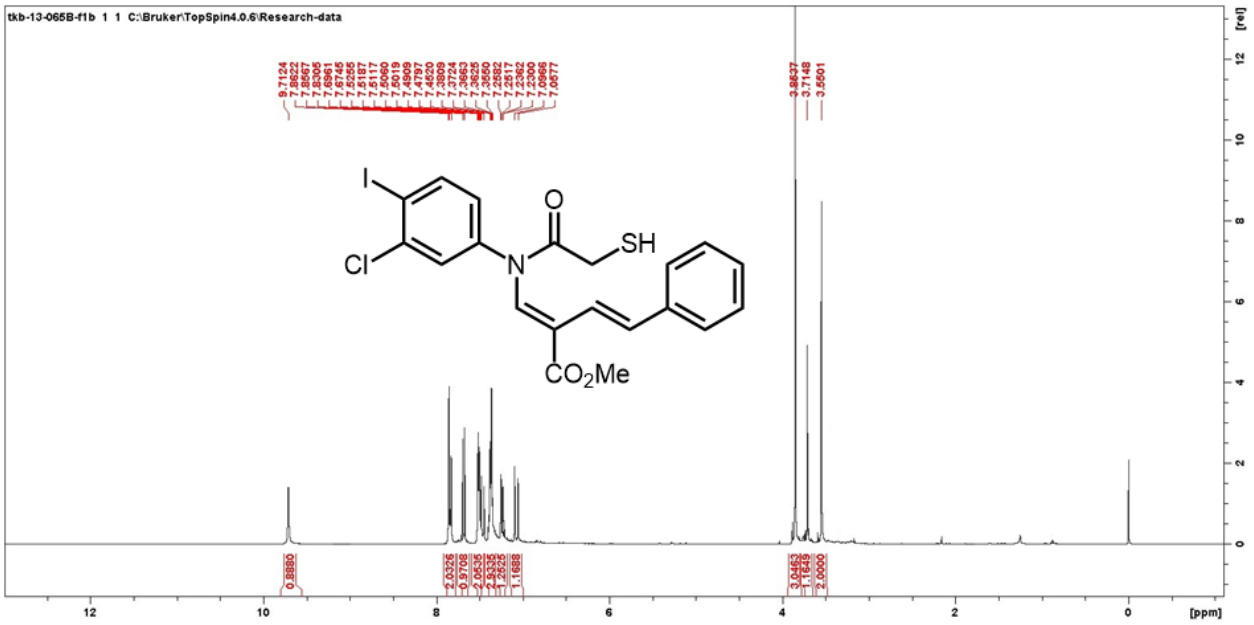


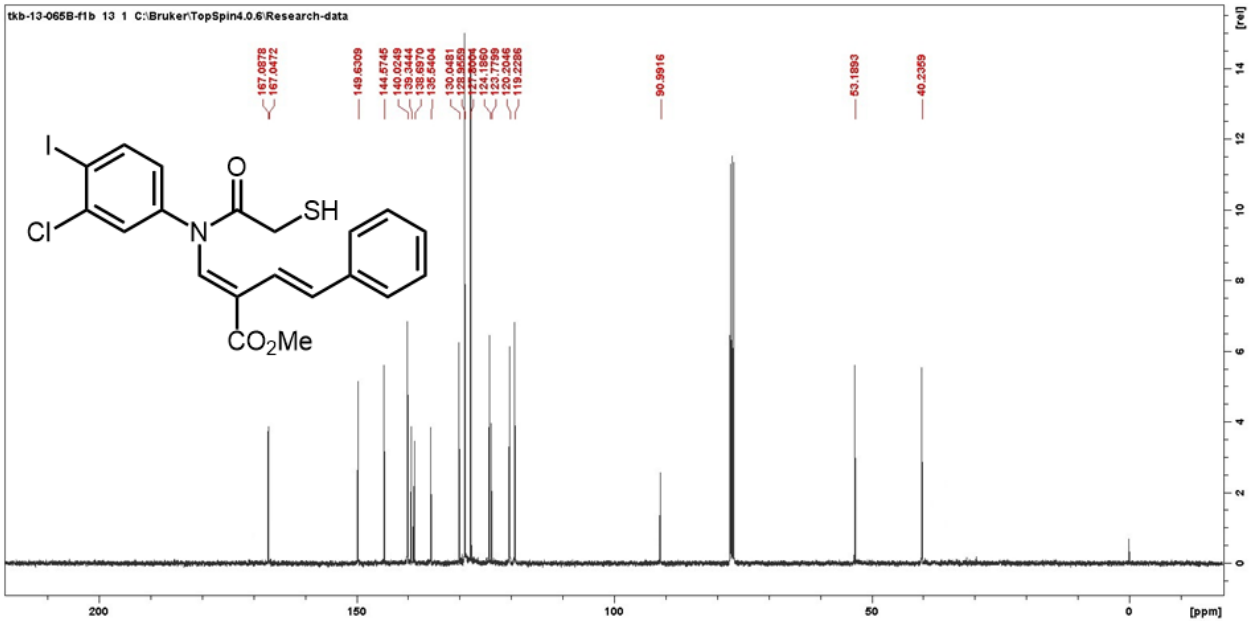



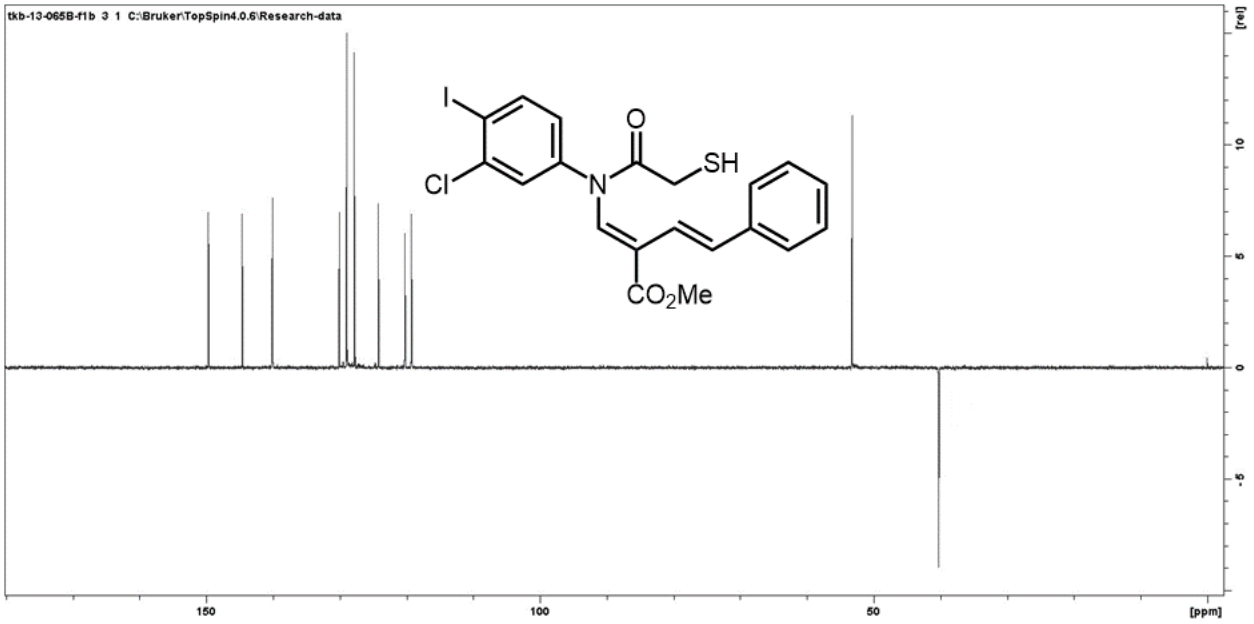



**Compound 4y**

Prepared in 0.50 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 218.4 mg, 85%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.89 – 7.81 (m, 2H), 7.77 – 7.64 (m, 1H), 7.45 – 7.31 (m, 2H), 7.25 – 7.15 (m, 3H), 7.09 (d, *J* = 15.6 Hz, 1H), 3.86 (s, 3H), 3.72 (s, 1H), 3.55 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 167.13, 167.02, 149.64, 144.61, 140.05, 139.38, 138.73, 135.57, 130.08, 128.98, 127.82, 124.21, 123.84, 120.22, 119.23, 90.98, 53.21, 40.28. **HRMS-EI$^{+}$** calc for $C_{20}H_{17}ClINO_3S$ $[M]^{+}$ 512.9662, found 512.9668.



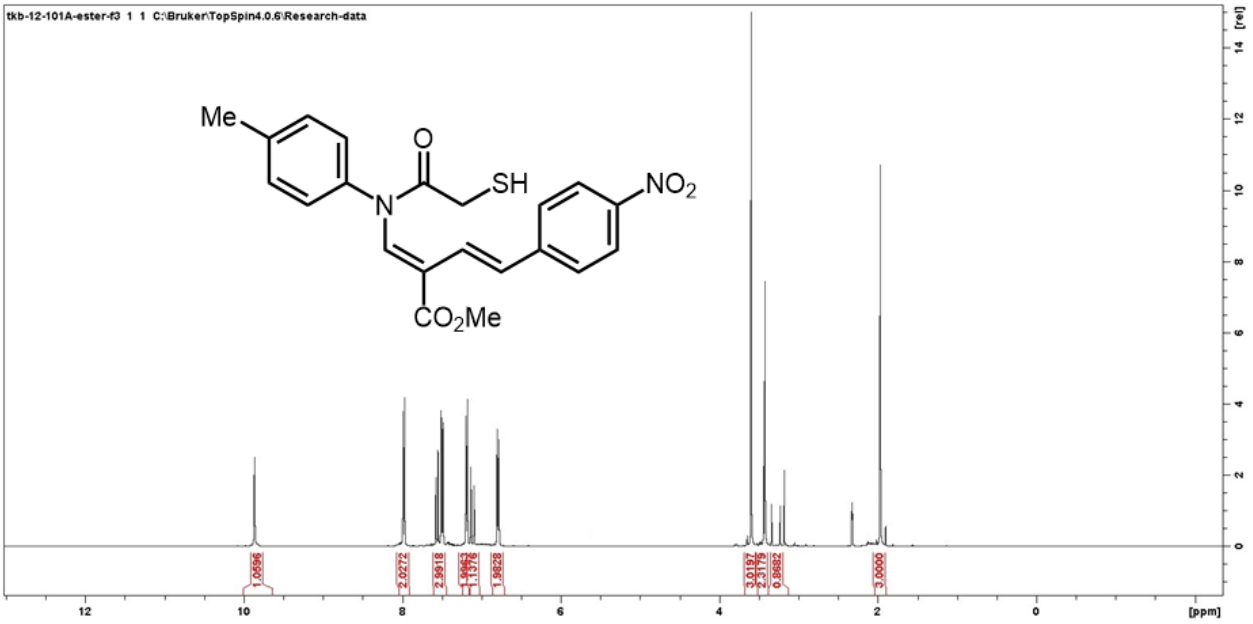


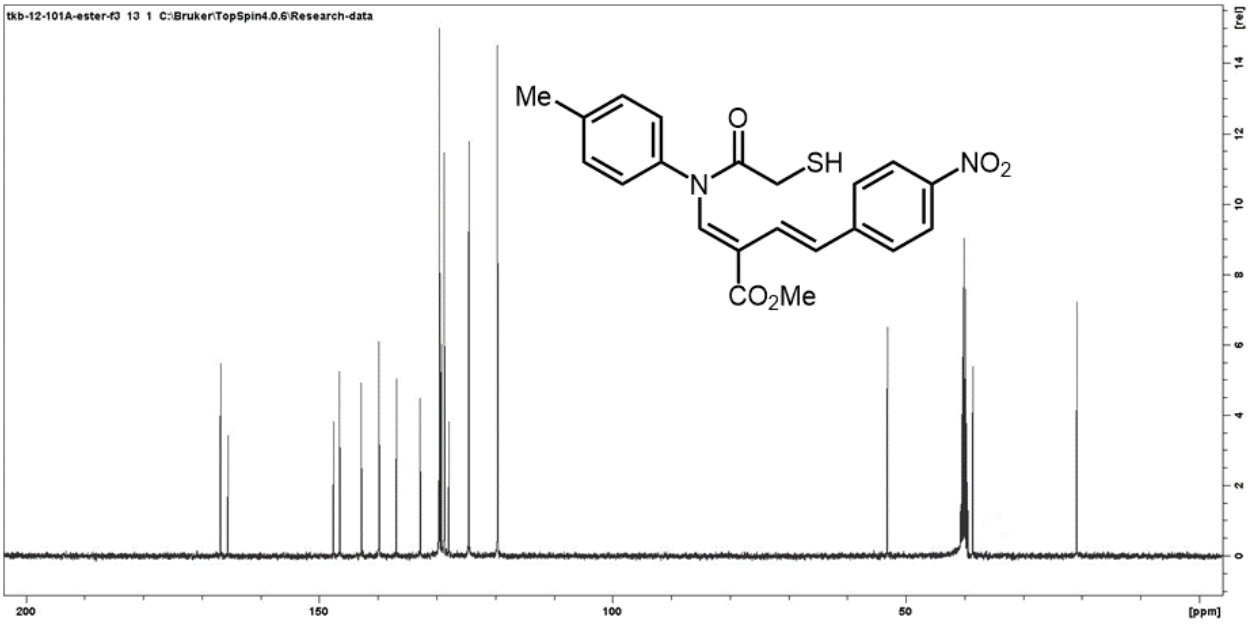



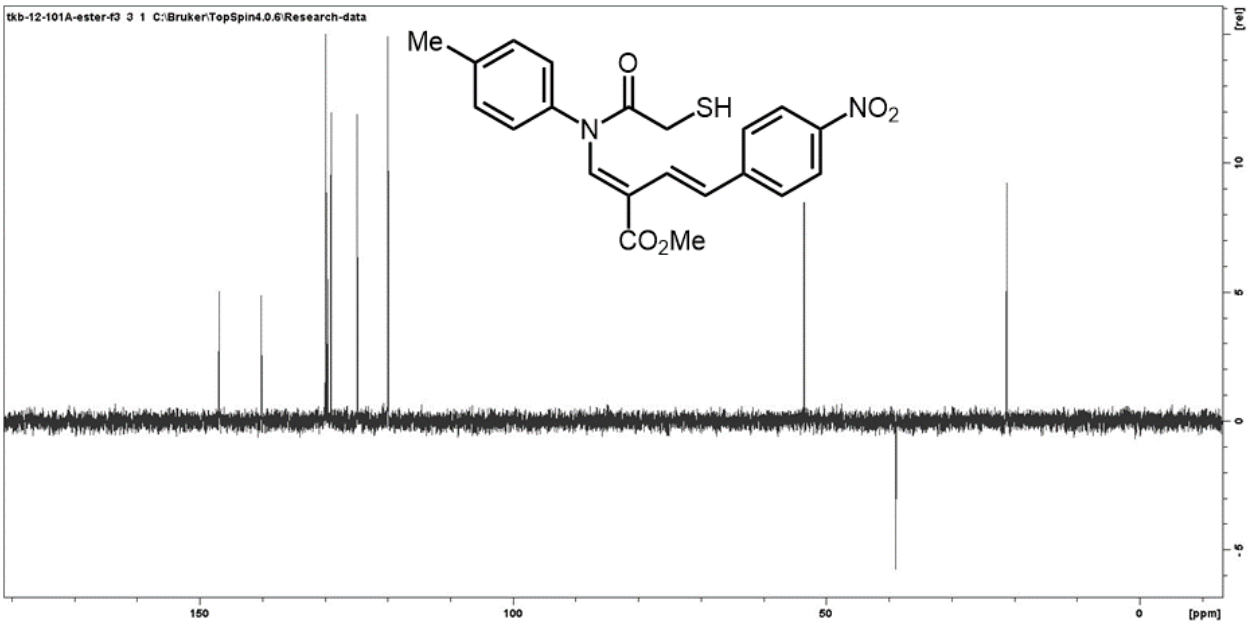

**Compound 4z**

Prepared in 0.50 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 171.2 mg, 83%. $^{1}$H NMR (400 MHz, DMSO) δ 9.86 (s, 1H), 8.02 (d, *J* = 8.2 Hz, 2H), 7.53 – 7.45 (m, 3H), 7.32 – 7.22 (m, 3H), 6.79 (d, *J* = 8.2 Hz, 2H), 3.59 (s, 3H), 3.44 (s, 2H), 3.18 (s, 1H), 1.96 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO) δ 166.84, 165.53, 147.58, 146.53, 142.85, 139.84, 136.86, 132.80, 129.51, 129.18, 128.71, 127.88, 124.51, 119.60, 53.19, 38.61, 20.85. **HRMS-EI$^+$** calc for $C_{21}H_{20}N_2O_5S$ $[M]^+$ 412.1093, found 412.1088.

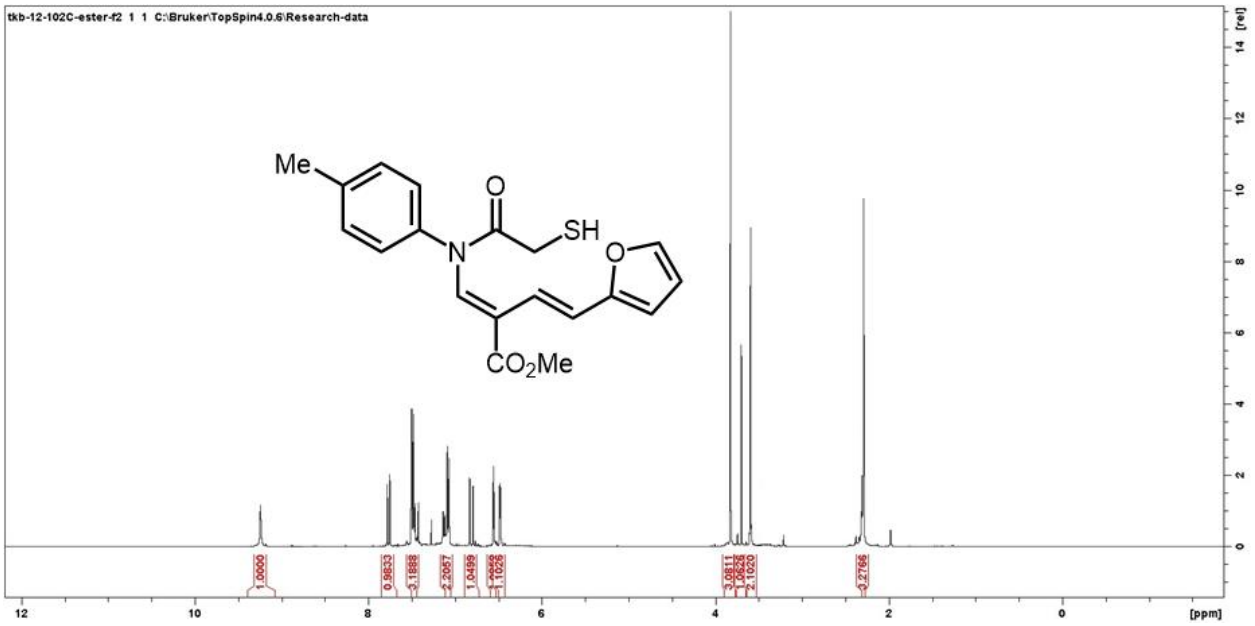





**Compound 4z1**

Prepared in 1.00 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 314.5 mg, 88%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.80 (d, *J* = 11.5 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.14 – 7.10 (m, 2H), 6.80 (d, *J* = 15.3 Hz, 1H), 6.55 (d, *J* = 3.4 Hz, 1H), 6.47 (d, *J* = 3.4 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 1H), 3.59 (s, 2H), 2.31 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.73, 166.56, 152.16, 148.60, 144.79, 135.50, 133.93, 129.98, 129.58, 129.46, 123.76, 122.53, 119.91, 119.80, 114.03, 112.65, 53.09, 39.99, 20.98. **HRMS-EI**$^{+}$ calc for $C_{19}H_{19}NO_4S$ $[M]^{+}$ 357.1035, found 357.1039.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SH
O
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2.2057
1.0499
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1.0628
2.1020
3.2766
12
10
8
6
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0
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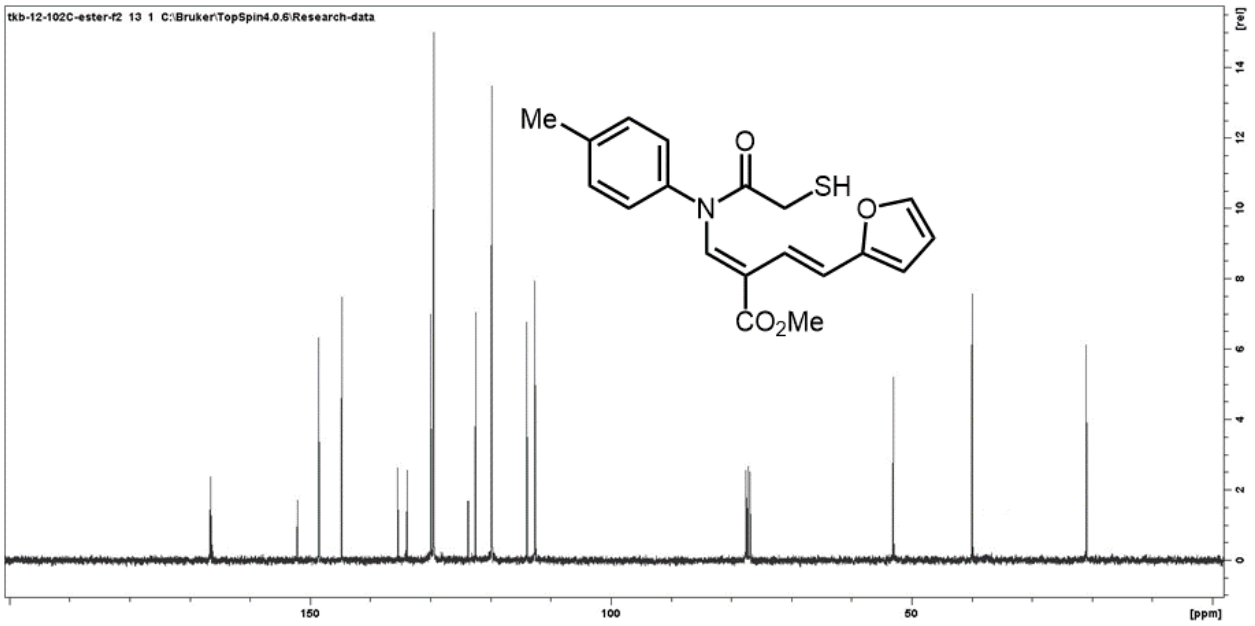
[rel]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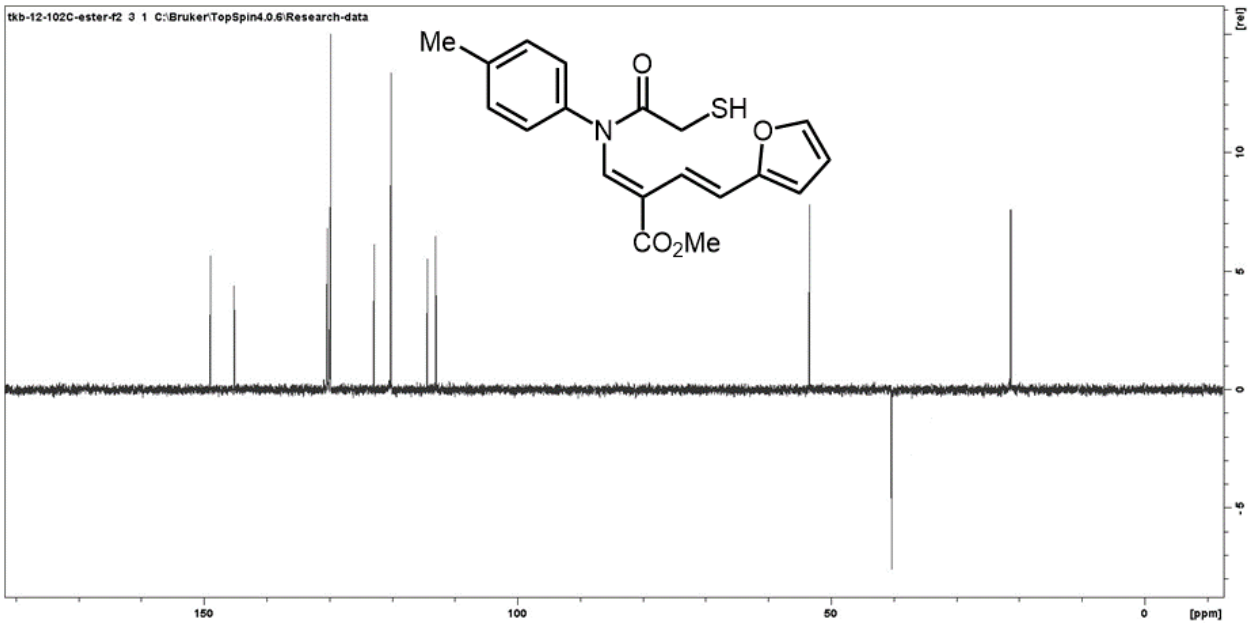
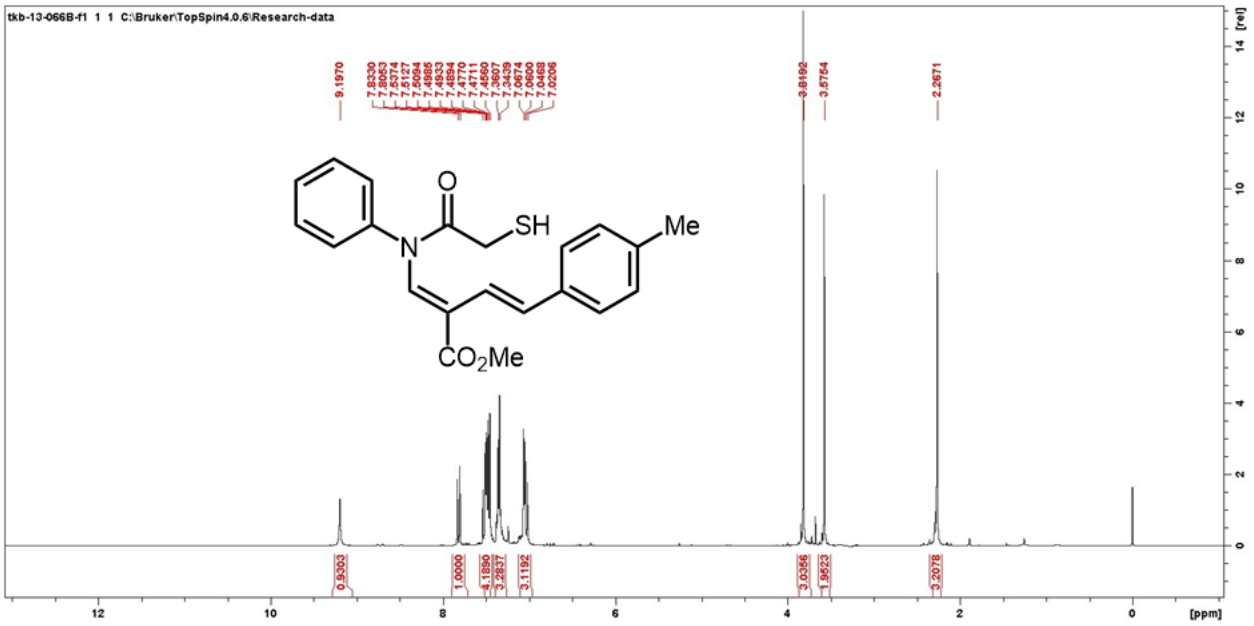



**Compound 4z2**

Prepared in 1.00 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (80:20). Oily substance. Yield = 305 mg, 83%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 7.82 (d, *J* = 11.1 Hz, 1H), 7.56 – 7.40 (m, 4H), 7.40 – 7.29 (m, 3H), 7.16 – 6.98 (m, 3H), 3.82 (s, 3H), 3.58 (s, 2H), 2.27 (s, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.46, 149.00, 144.07, 135.78, 135.47, 133.87, 129.88, 129.42, 128.95, 127.80, 124.38, 124.12, 119.76, 53.02, 39.96, 20.88. **HRMS-EI**$^{+}$ calc for $C_{21}H_{21}NO_3S$ $[M]^{+}$ 367.1242, found 367.1248.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7.0674
7.0600
7.0468
7.0206
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3.5764
2.2671
O
SH
N
Me
CO2Me
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8
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4
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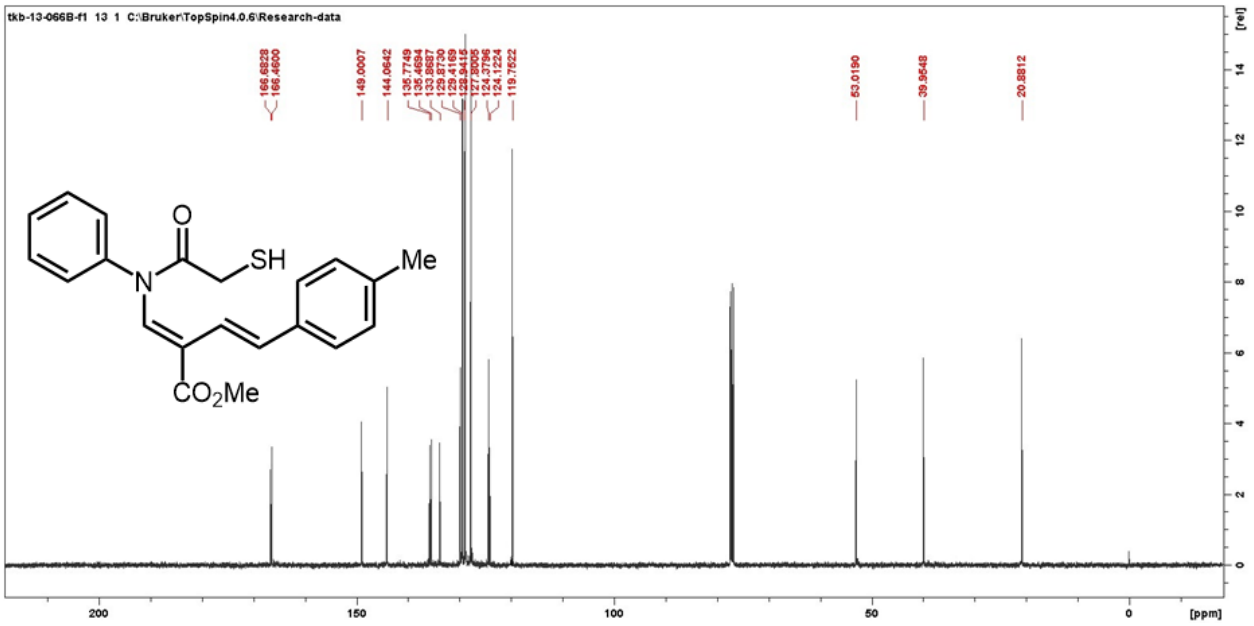
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200
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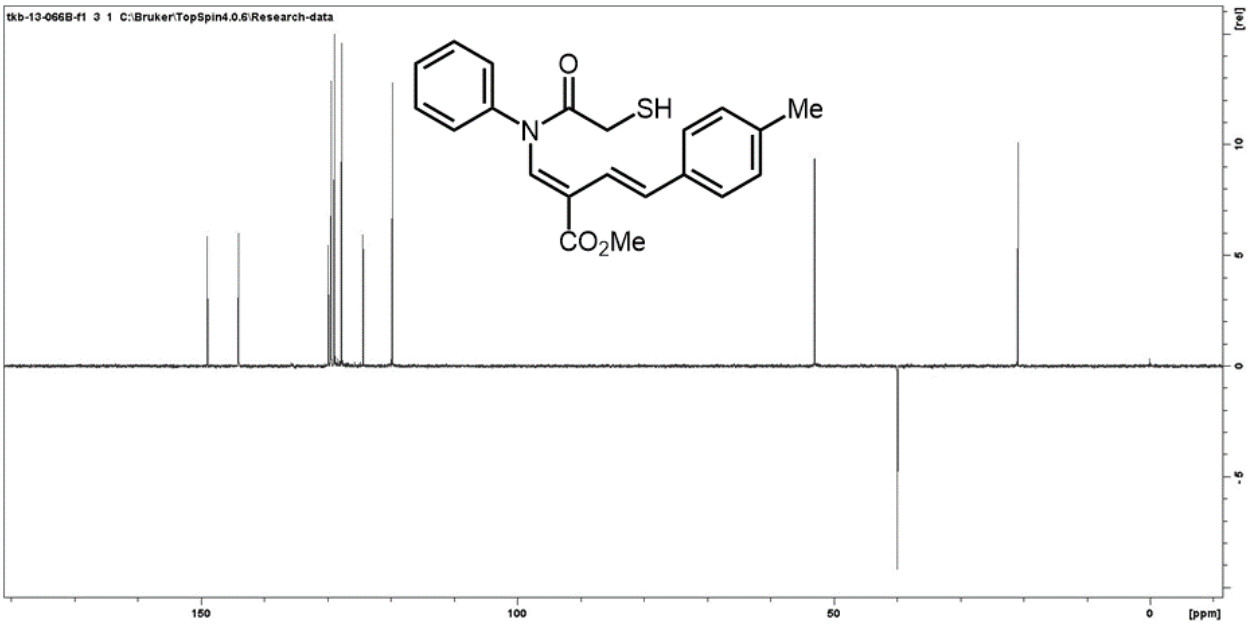
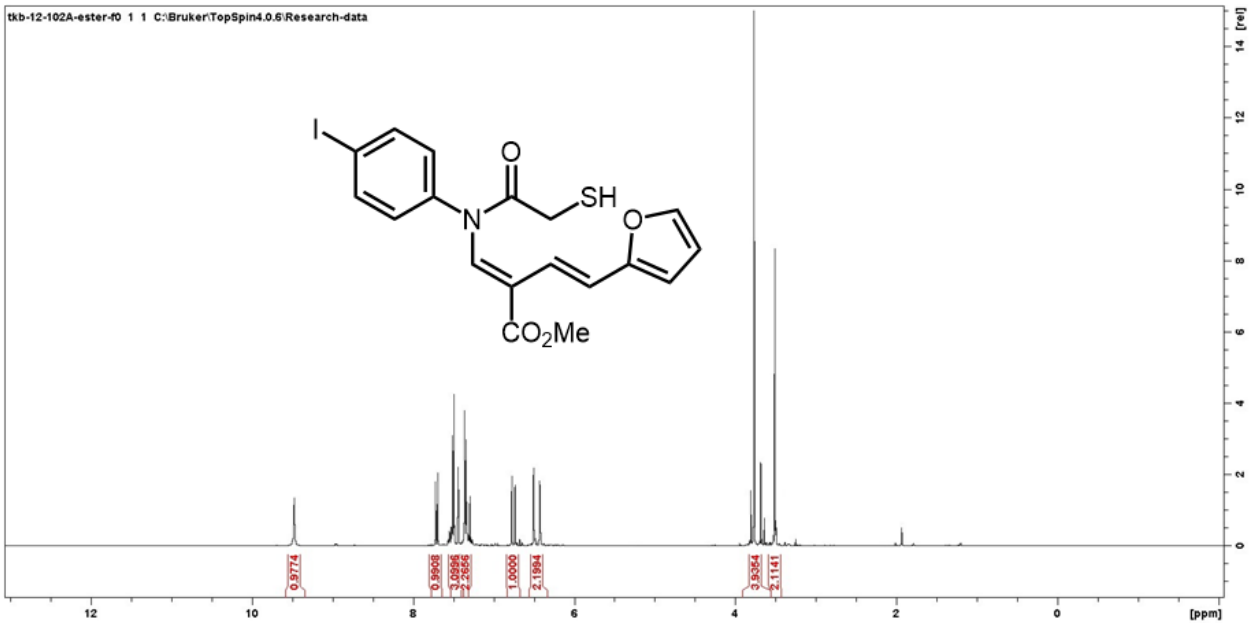



**Compound 4z3**

Prepared in 1.00 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 394.2 mg, 84%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H), 7.74 (d, *J* = 11.4 Hz, 1H), 7.60 – 7.51 (m, 3H), 7.36 – 7.27 (m, 2H), 6.76 (d, *J* = 15.3 Hz, 1H), 6.52 (d, *J* = 3.4 Hz, 1H), 6.48 (d, *J* = 3.4 Hz, 1H), 3.78 – 3.74 (m, 4H), 3.50 (s, 2H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.98, 166.96, 152.07, 149.05, 144.90, 137.94, 137.84, 130.22, 123.56, 122.44, 121.61, 114.30, 112.74, 87.59, 53.20, 40.24. **HRMS-EI**$^{+}$ calc for $C_{18}H_{16}INO_4S$ $[M]^{+}$ 468.9845, found 468.9849.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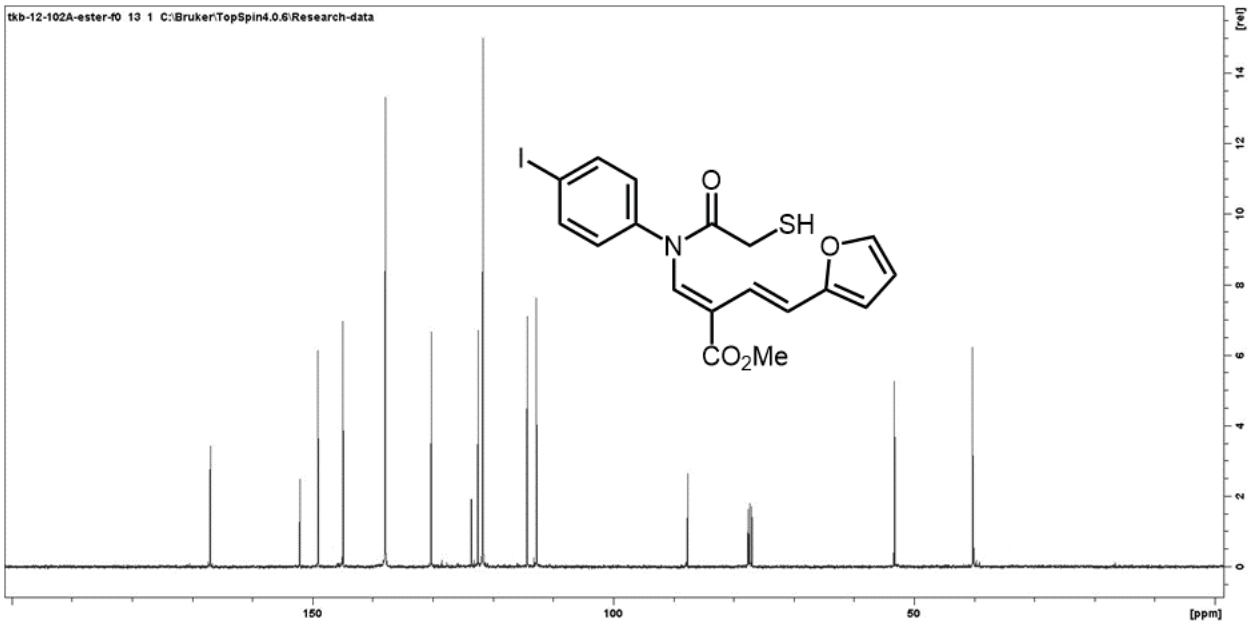
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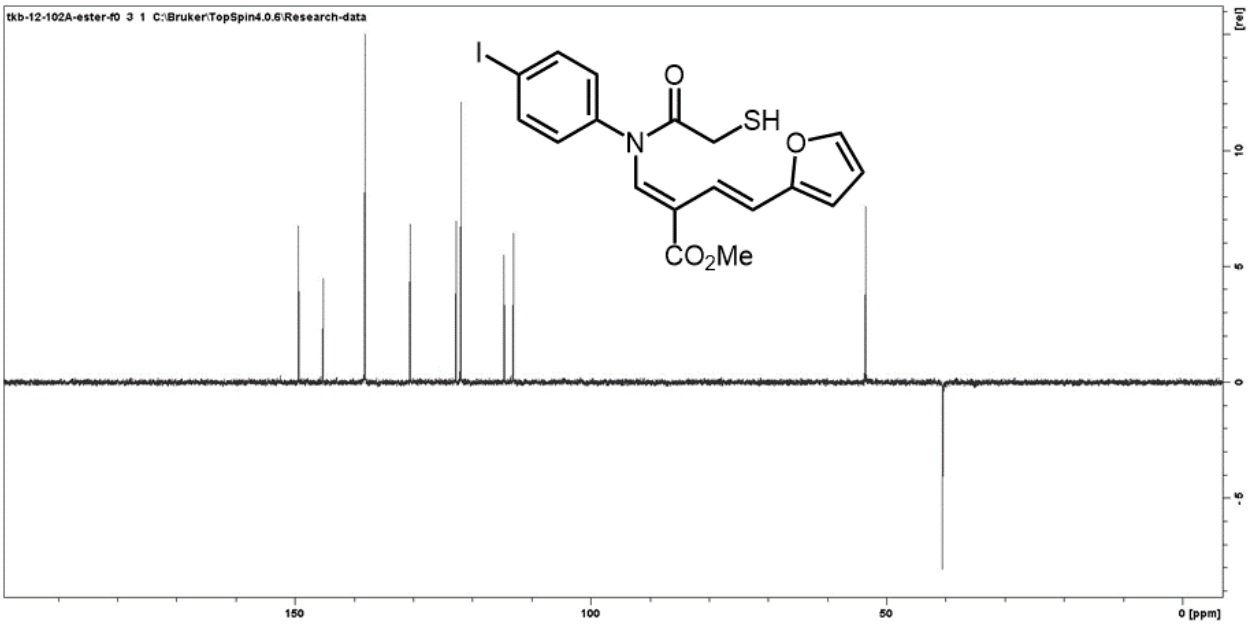
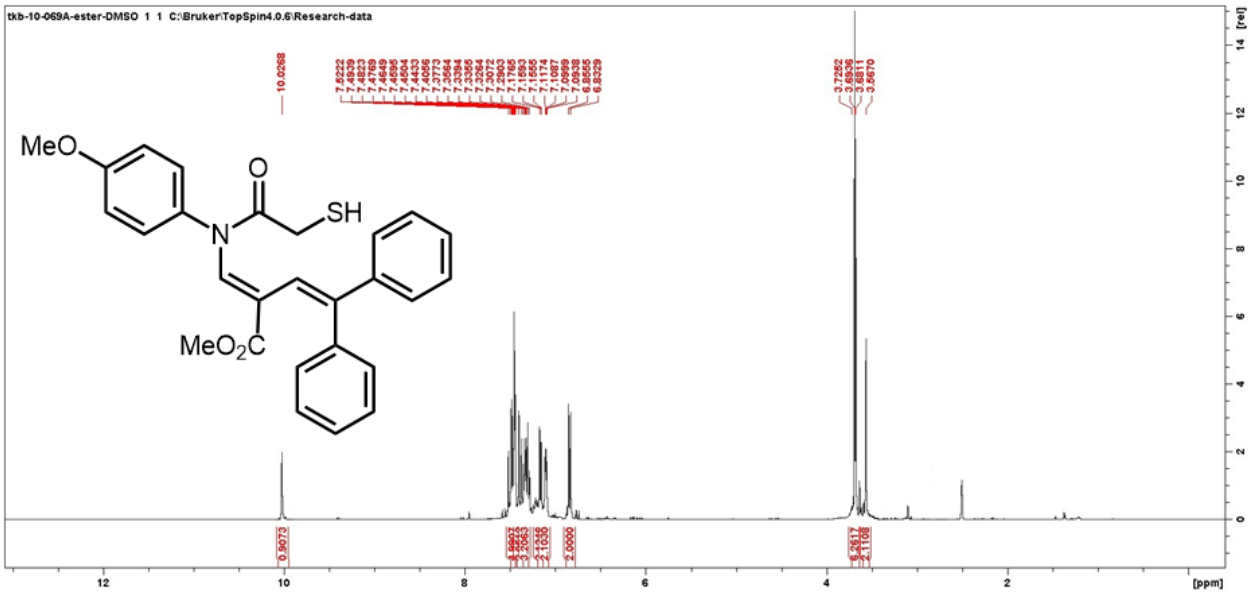



**Scheme 3 Results**

**Compound 4z4**

Prepared in 1.00 mmol scale using **General Procedures A** and **B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (70:30). Oily substance. Yield = 362.6 mg, 79%. $^{1}$H NMR (400 MHz, DMSO-$d_6$) δ 10.03 (s, 1H), 7.63 – 7.21 (m, 9H), 7.24 – 7.10 (m, 4H), 6.84 (d, 2H), 3.72 – 3.68 (m, 6H), 3.57 (s, 2H). $^{13}$C NMR (101 MHz, DMSO) δ 166.79, 165.77, 155.83, 152.32, 145.15, 141.19, 138.72, 132.66, 130.57, 129.20, 129.04, 129.01, 128.44, 126.22, 124.38, 121.20, 114.34, 55.66, 53.04, 38.66. FTIR (KBr): 3306.7, 2949.6, 1708.6, 1659.3, 1599.7, 1572.3, 1542.7, 1510.1, 1442.5, 1412.5, 1386.9, 1246.6, 1232.4, 1178.1, 1135.8, 1036.1, 830.1, 767.1, 700.7. **HRMS-EI**$^{+}$ calc for $C_{27}H_{25}NO_4S$ $[M]^{+}$ 459.1504, found 459.1508.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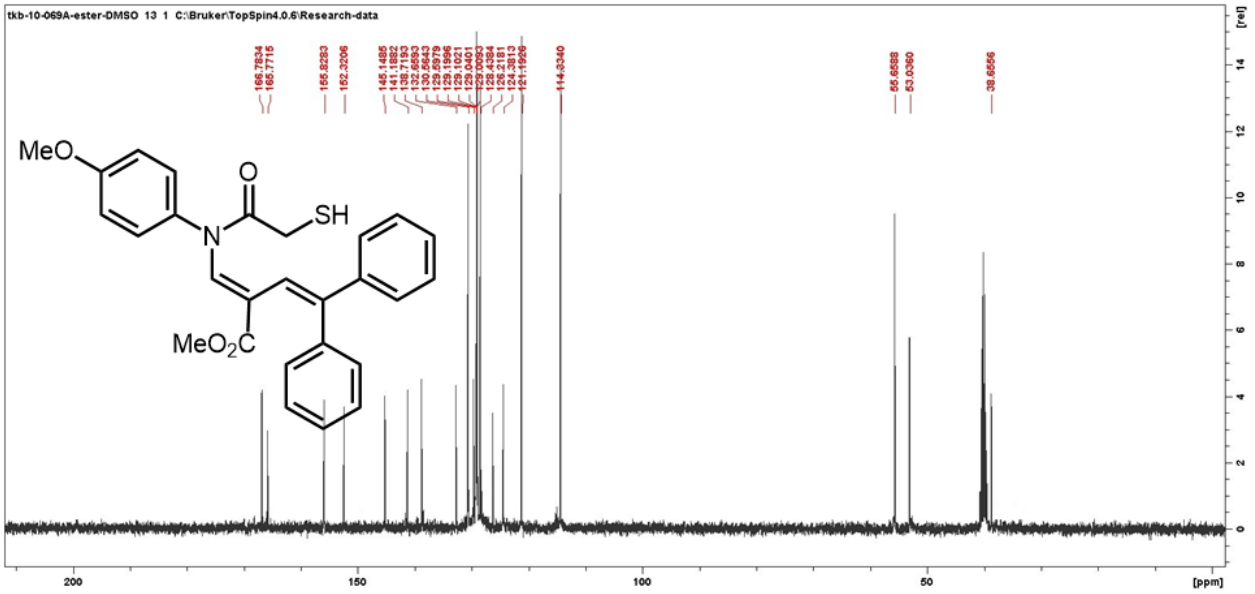
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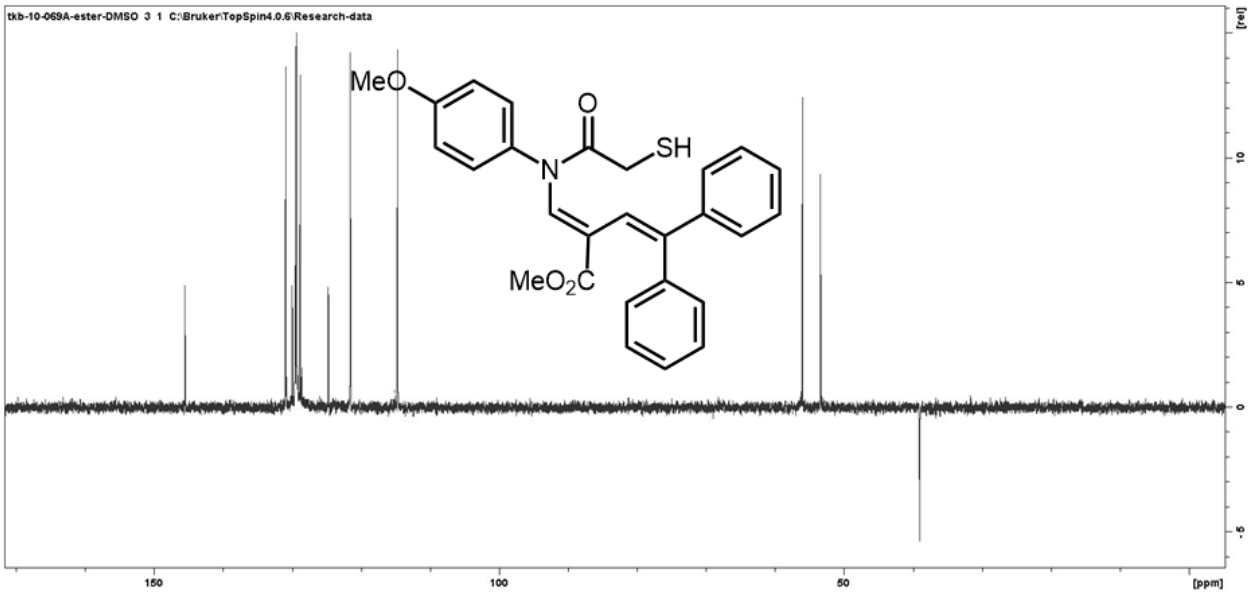
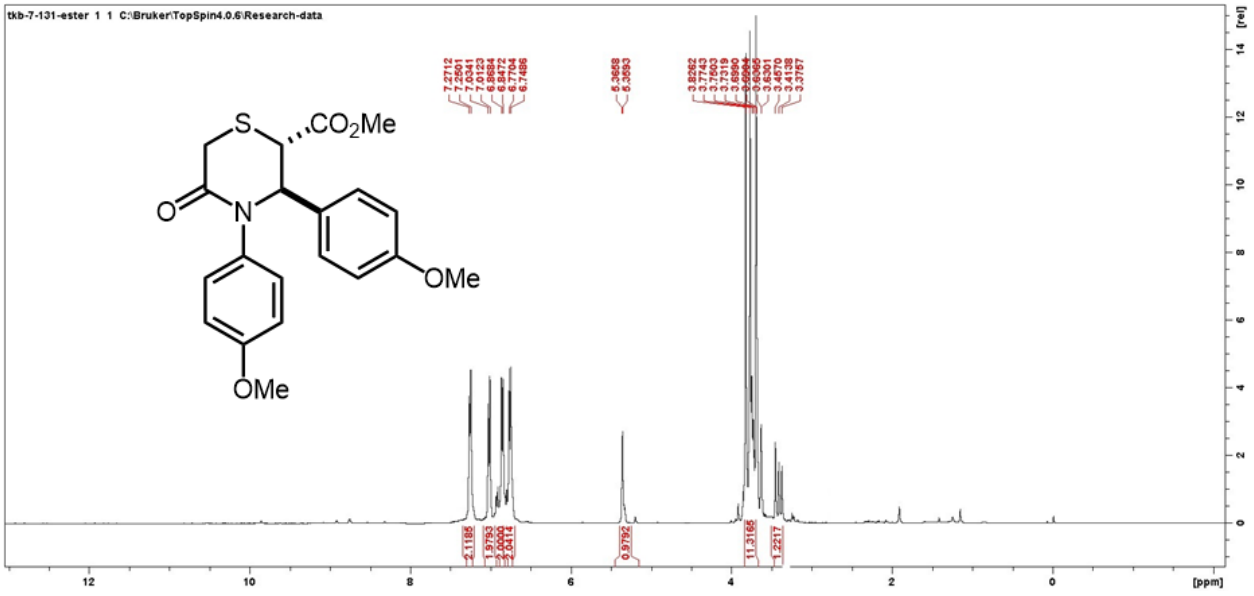
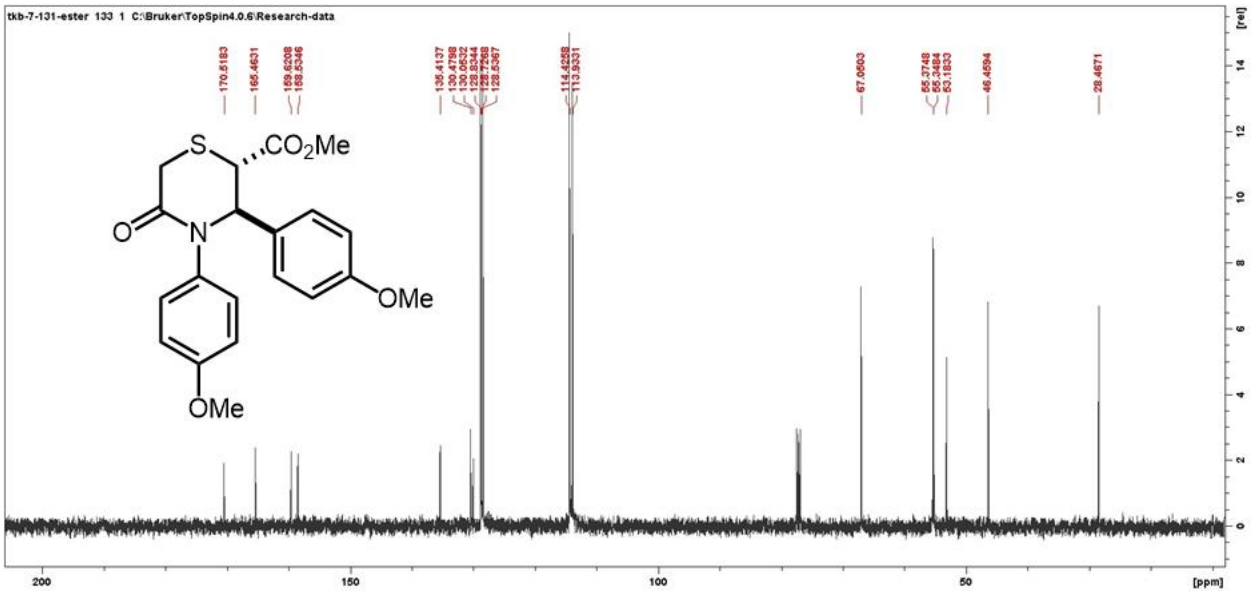
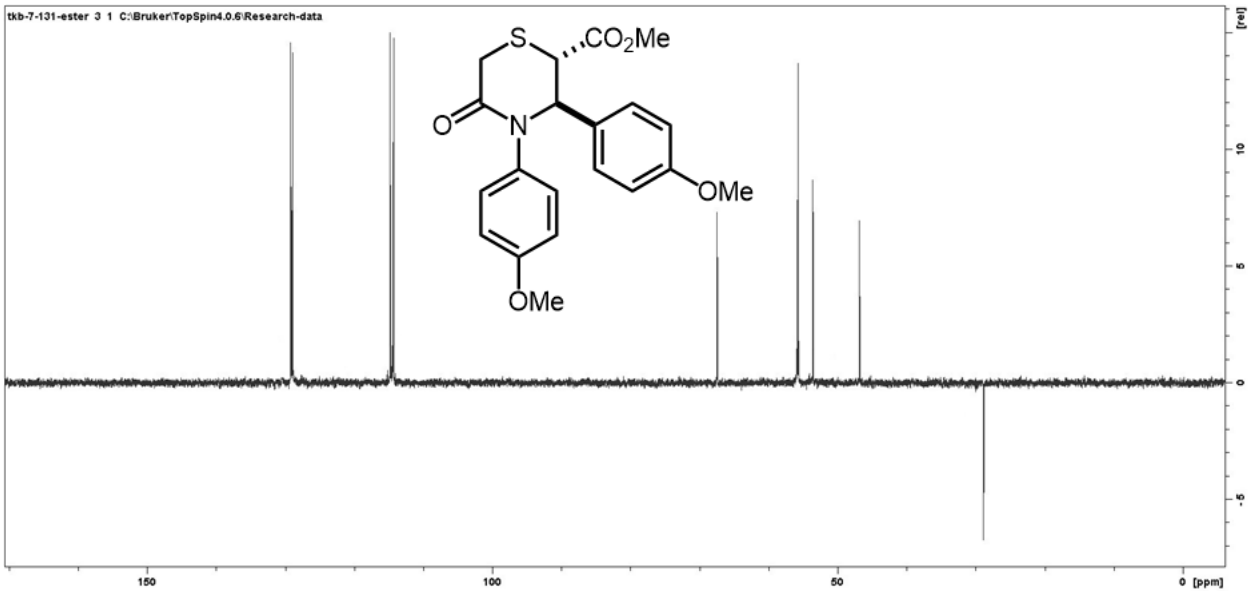



**Compound 10a**

Prepared from the corresponding acid,[2] in 0.50 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 176.3 mg, 91%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.76 (d, *J* = 8.6 Hz, 2H), 5.35 (d, *J* = 3.8 Hz, 1H), 3.83 – 3.63 (m, 11H), 3.47 – 3.38 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 170.52, 165.47, 159.62, 158.54, 135.42, 130.48, 128.84, 128.54, 114.43, 113.94, 67.05, 55.38, 55.35, 53.19, 46.46, 28.47. HRMS calc for $C_{20}H_{21}NO_5S$ 387.1140, found 387.1145.



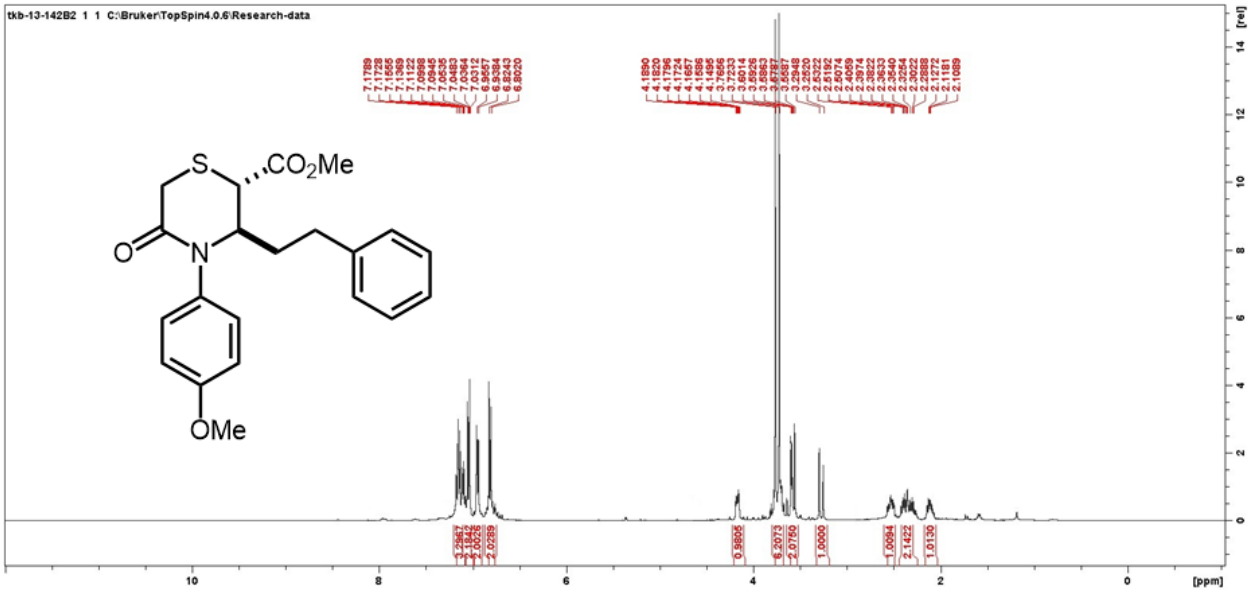


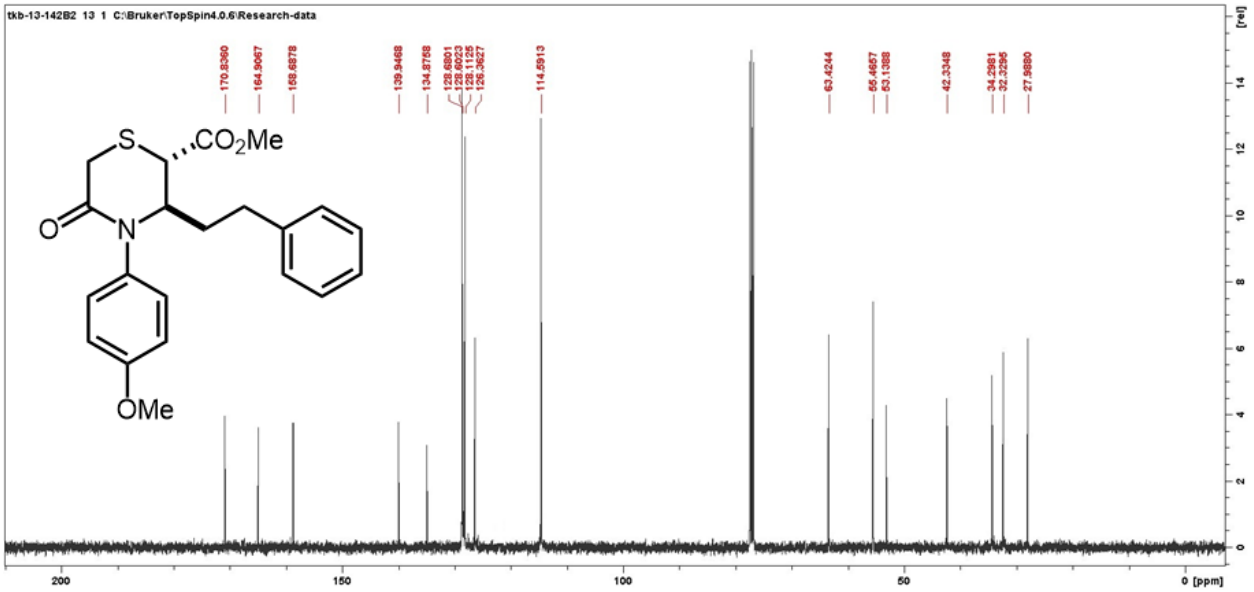



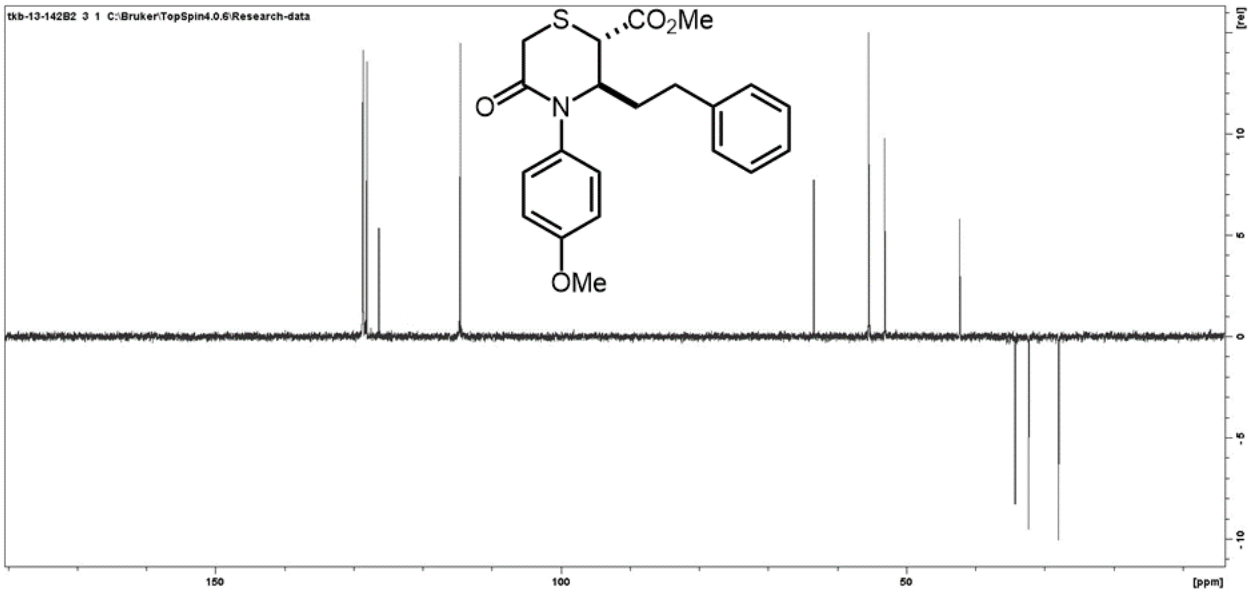

**Compound 10b**

Prepared in 0.50 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 181.2 mg, 94%. $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.03 (m, 5H), 6.96 – 6.94 (m, 2H), 6.81 (d, 2H), 4.21 – 4.13 (m, 1H), 3.77 – 3.72 (m, 6H), 3.62 – 3.56 (m, 2H), 3.27 (d, 1H), 2.53 (ddd, *J* = 12.4, 9.5, 4.8 Hz, 1H), 2.45 – 2.22 (m, 2H), 2.17 – 2.05 (m, 1H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 170.84, 164.91, 158.69, 139.95,

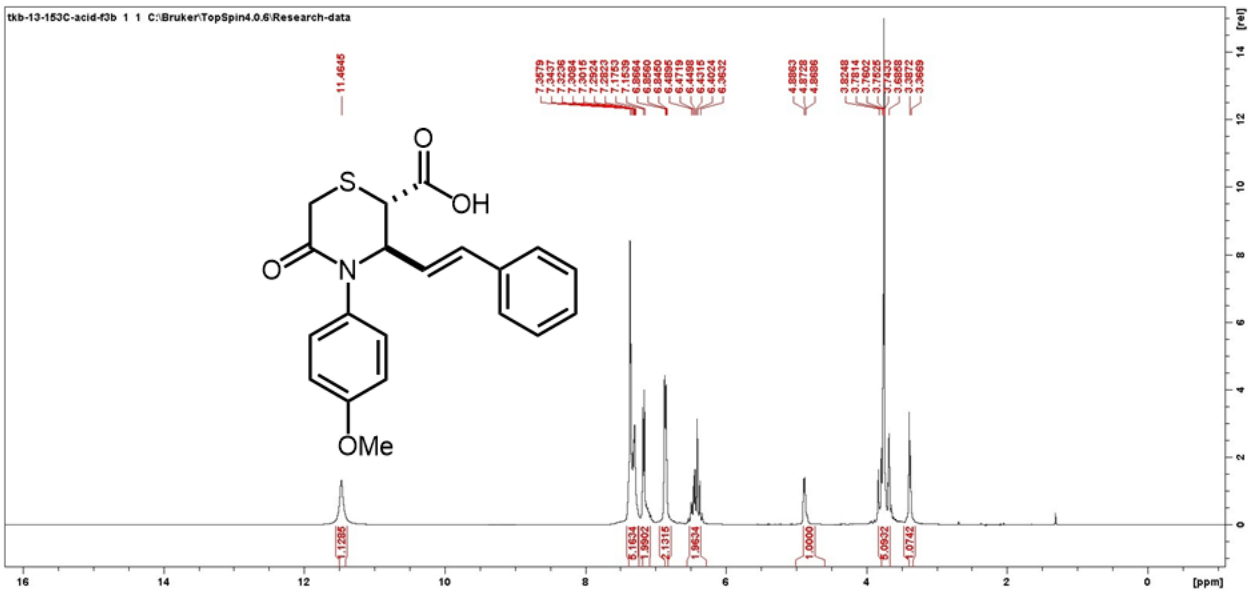
134.88, 128.68, 128.61, 128.12, 126.37, 114.60, 63.43, 55.47, 53.14, 42.34, 34.30, 32.33, 27.99. HRMS calc for $C_{21}H_{23}NO_4S$ 385.1348, found 385.1348.

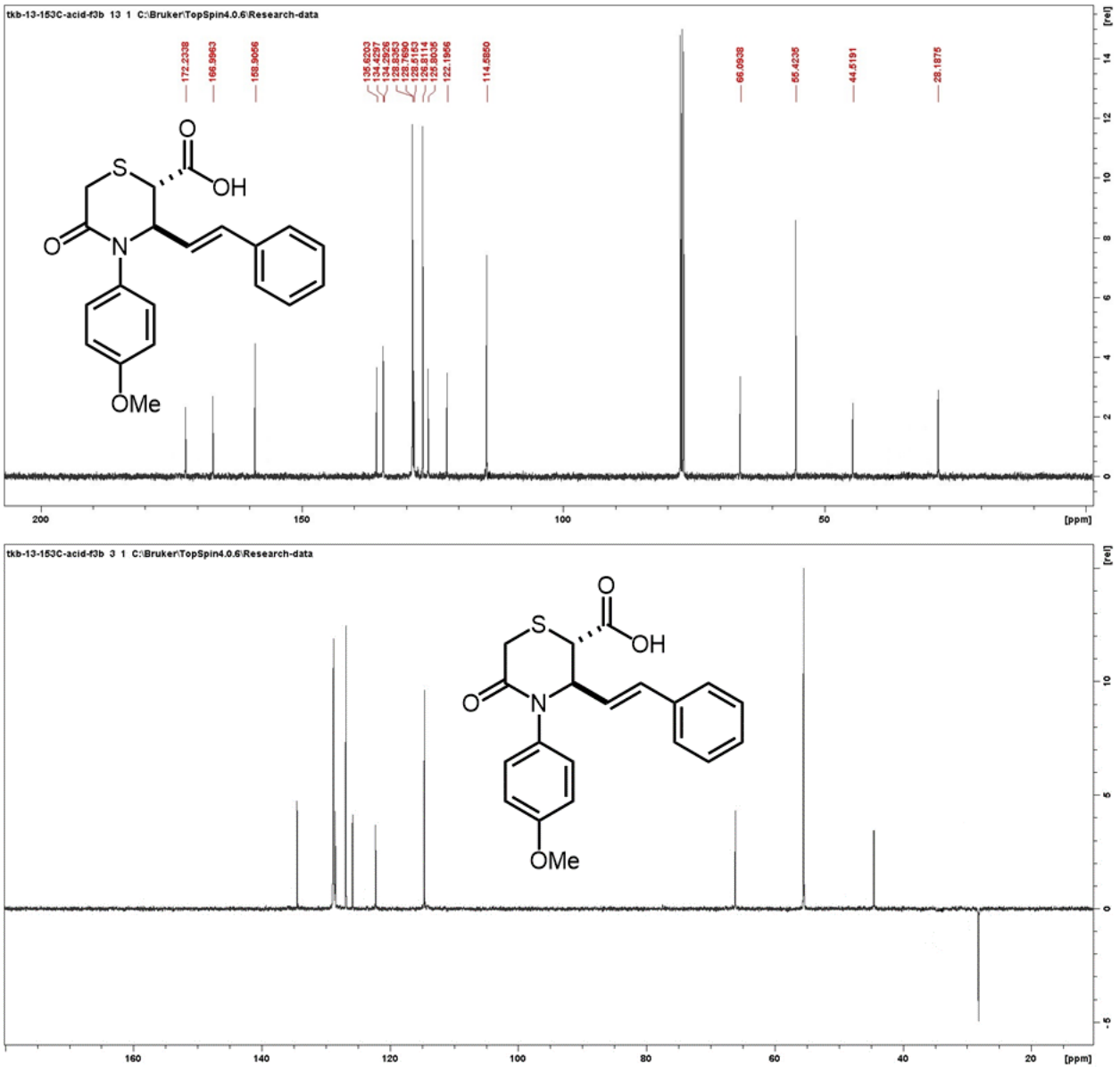





NMR data for acid **3b**






**References**

(1) Braunstein, H.; Langevin, S.; Khim, M.; Adamson, J.; Hovenkotter, K.; Kotlarz, L.; Mansker, B.; Beng, T. K. *Org. Biomol. Chem.* **2016**, *14*, 8864.

(2) Dar'in, D.; Bakulina, O.; Chizhova, M.; Krasavin, M. *Org. Lett.* **2015**, *17*, 3930.