Supporting Information for:

Serendipitous synthesis of 2-alkenyl- and 2-aryl-4-thiazolidinones using dithiodiglycolic anhydride

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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 1,4-dioxane was stored under 4 Å molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines, alkenes and enals as well as 2-MeTHF 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, ^{1}H, ^{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 electronspray 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 azadienes were prepared as previously reported.[1,2]

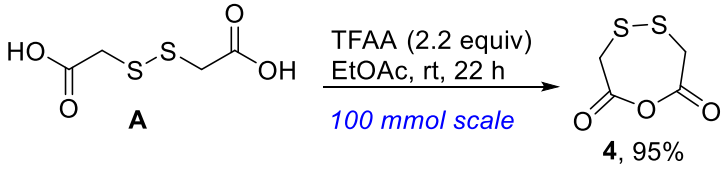
General Procedure A: Reaction of imines with anhydride 4: A 20 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the imine (5.0 mL, 0.10 M in freshly distilled 2-MeTHF) was added to the vial at room temperature followed by anhydride **4** (5 mmol, 1.0 equiv). The contents were stirred in a pre-heated oil bath thermostatted 40 ºC. After complete consumption of the imine (as judged by TLC and NMR), the mixture/suspension was cooled to room temperature and washed several times with ice-cold petroleum ether, then concentrated under reduced pressure to afford the crude product, which was directly subjected to flash column chromatography.

General procedure B: Synthesis of sulfoxides: A mixture of **5** or **6** (1.0 mmol, dissolved in minimum amount of 2-MeTHF (at most 0.5 mL)) and Selectfluor (1.0 mmol, 1.0 equiv) in H_2O (5.0 mL) was stirred for 12 h at room temperature (TLC and GC-MS monitoring). EtOAc (10 mL) was then added to the mixture. The resulting mixture was extracted with EtOAc (3×20 mL), and the combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired sulfoxide.

General procedure C: Synthesis of sulfones: A mixture of **5** or **6** (1.0 mmol, dissolved in minimum amount of 2-MeTHF (at most 0.5 mL)) and Selectfluor (2.2 mmol, 2.2 equiv) in H_2O (10.0 mL) was stirred for 22 h at room temperature (TLC and GC-MS monitoring). EtOAc (20 mL) was then added to the mixture. The resulting mixture was extracted with EtOAc (3×20 mL), and the combined organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired sulfone.

General procedure D: Oxidation of 6 to 11: To a 20 mL vial, in a 4 °C bath, equipped with a magnetic stir bar under a N_2 atmosphere, was added allylic lactam **6** (0.50 mmol) and CH_2Cl_2 (10 mL). *m*-CPBA (258 mg, 1.5 mmol, 3 equiv) was then added in one portion. After being stirred for 16 h, during which time the bath was allowed to expire (warm to rt), the reaction mixture was quenched by the addition of *sat.* $Na_2S_2O_3$(aq) solution (5 mL). The organic layer was washed 3 times with *sat.* $NaHCO_3$(aq) solution (0.5 mL). The organic layer was dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was then purified by flash column chromatography on silica gel.

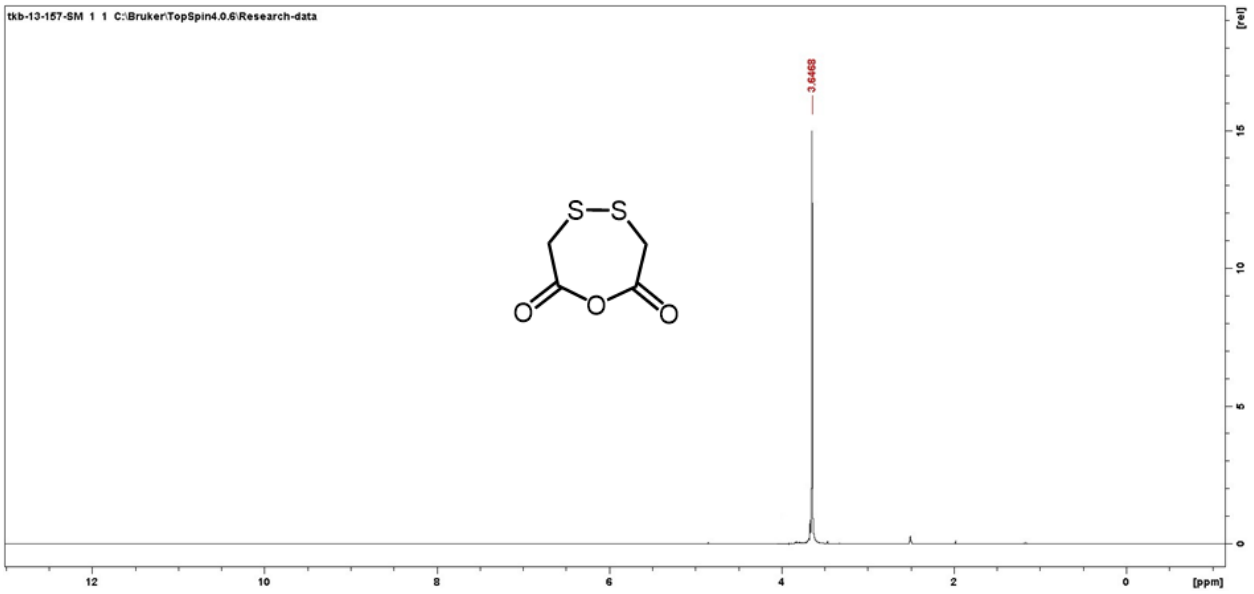
Synthesis of anhydride 4



To an oven-dried 500 mL round bottomed flask equipped with stir bar was added diacid **A** (18.20 g 100 mmol, 1 equiv) and dry ethyl acetate (250 mL). Trifluoroacetic anhydride (30.8 mL, 220 mmol, 2.2 equiv) was added slowly under nitrogen. The cloudy mixture was stirred at room temperature for 22 h (as judged by TLC and GC-MS). The mixture was concentrated under reduced pressure and washed three times with ice-cold petroleum ether to afford the anhydride, which was used without further purification.

Note: Any unused **4** should preferably be stored in the refrigerator.

^{1}H NMR (400 MHz, DMSO) δ 3.65 (s, 4H). ^{13}C NMR (101 MHz, DMSO) δ 170.89, 41.09.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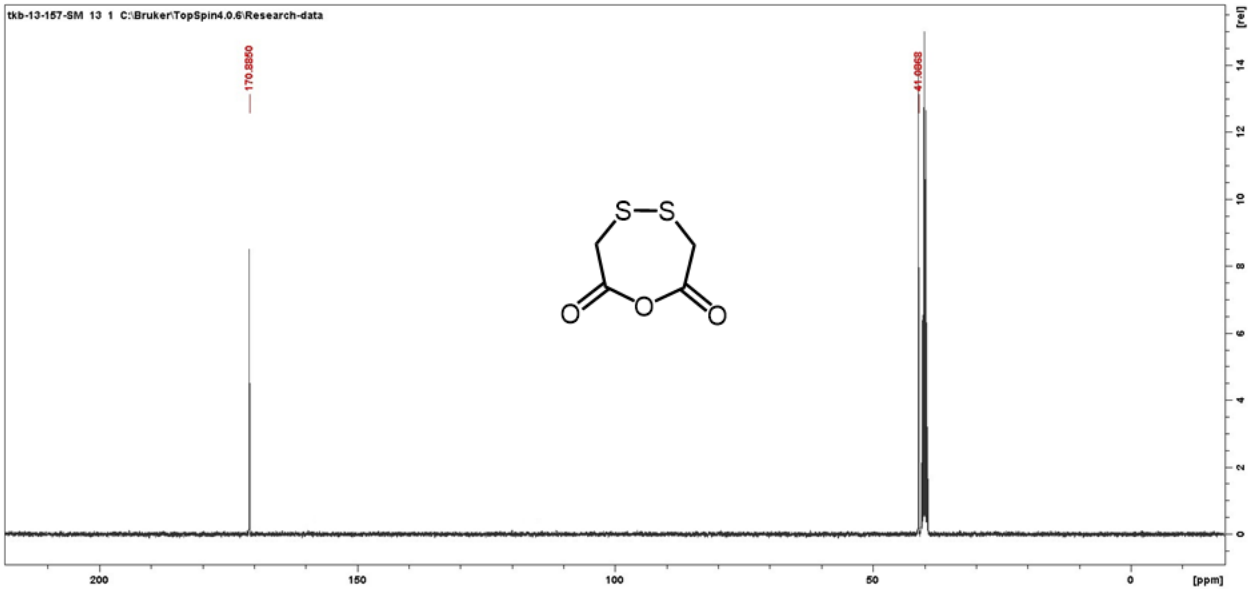
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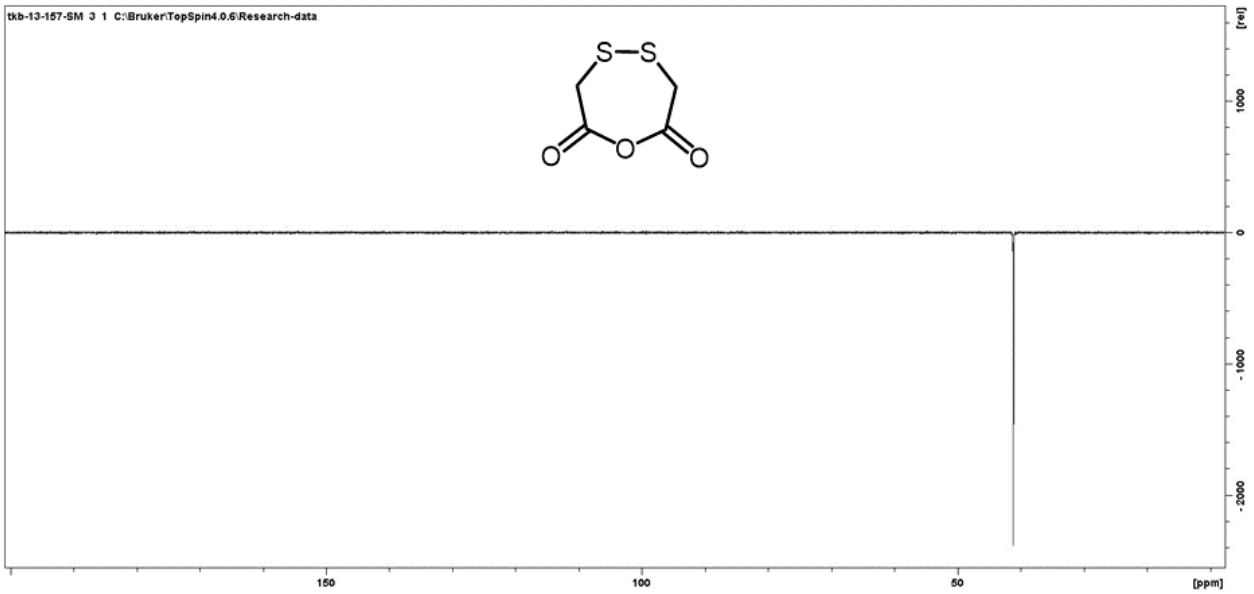
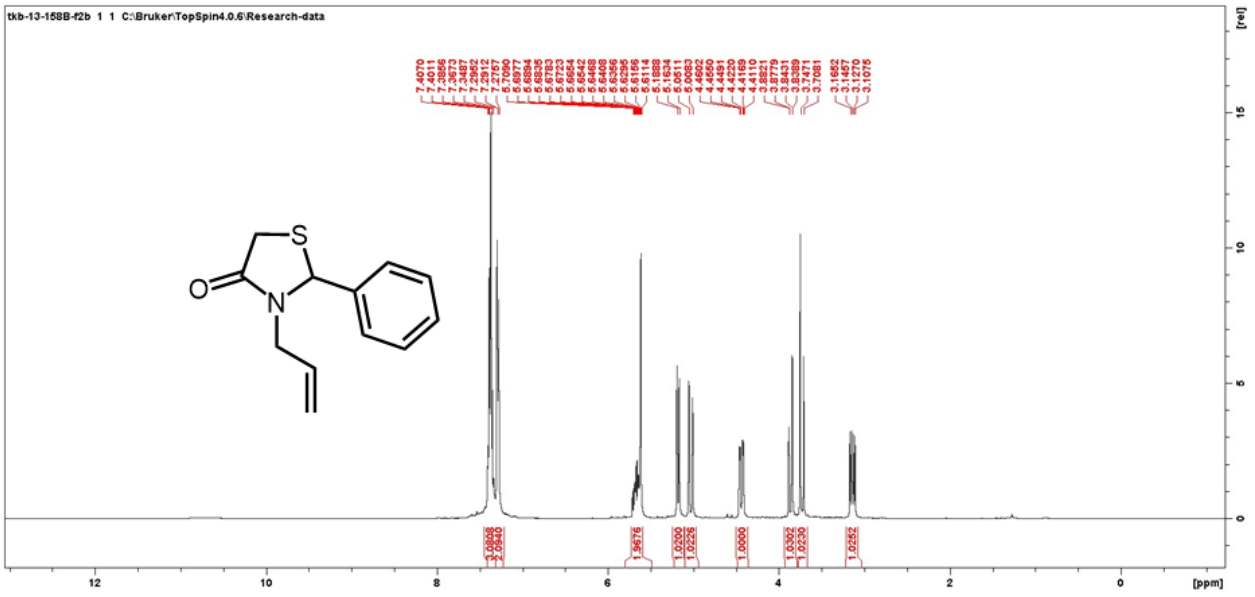


Compound 5a

Prepared in 5.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 975 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.28 (m, 5H), 5.73 – 5.59 (m, 2H), 5.17 (dd, *J* = 10.1, 1.6 Hz, 1H), 5.03 (dd, *J* = 17.2, 1.6 Hz, 1H), 4.44 (ddd, *J* = 15.3, 4.3, 2.0 Hz, 1H), 3.86 (dd, *J* = 15.7, 2.1 Hz, 1H), 3.73 (d, *J* = 15.7 Hz, 1H), 3.14 (dd, *J* = 15.3, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 139.2, 131.0, 129.2, 129.1, 127.1, 118.9, 63.1, 45.2, 32.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{12}H_{12}NOS$, 219.0718, found 219.0722. FTIR (KBr): 2976.0, 2927.2, 1721.7, 1650.1, 1492.0, 1438.4, 1362.2, 1320.5, 1290.1, 1206.3, 1180.3, 1146.7, 1132.3, 995.8, 918.8, 700.1.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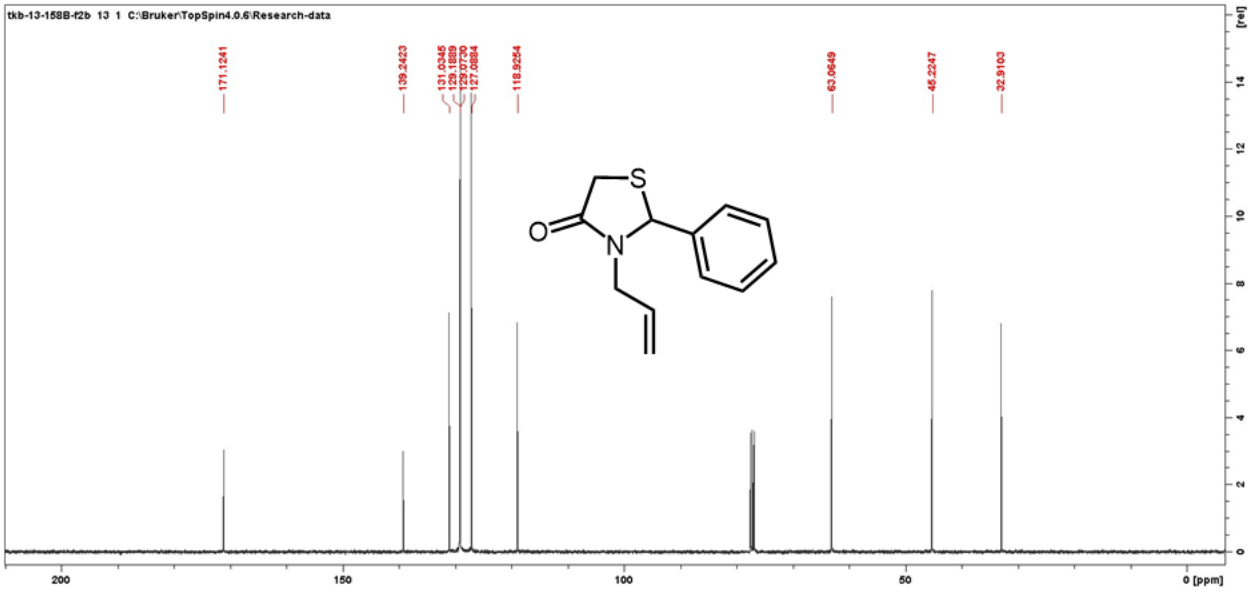
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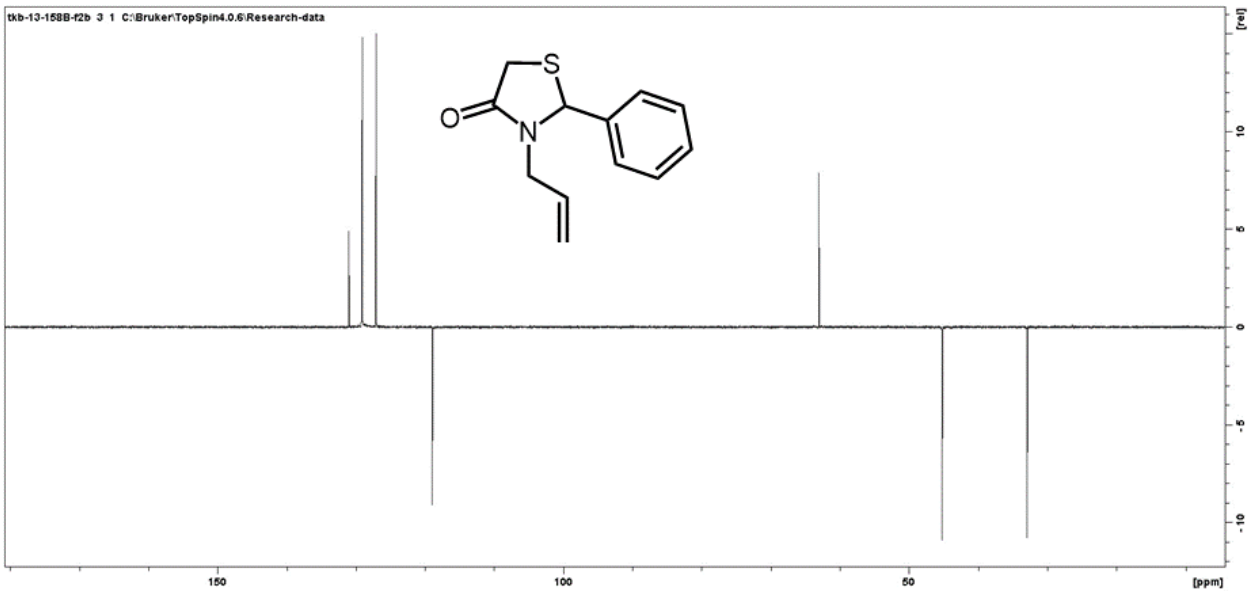
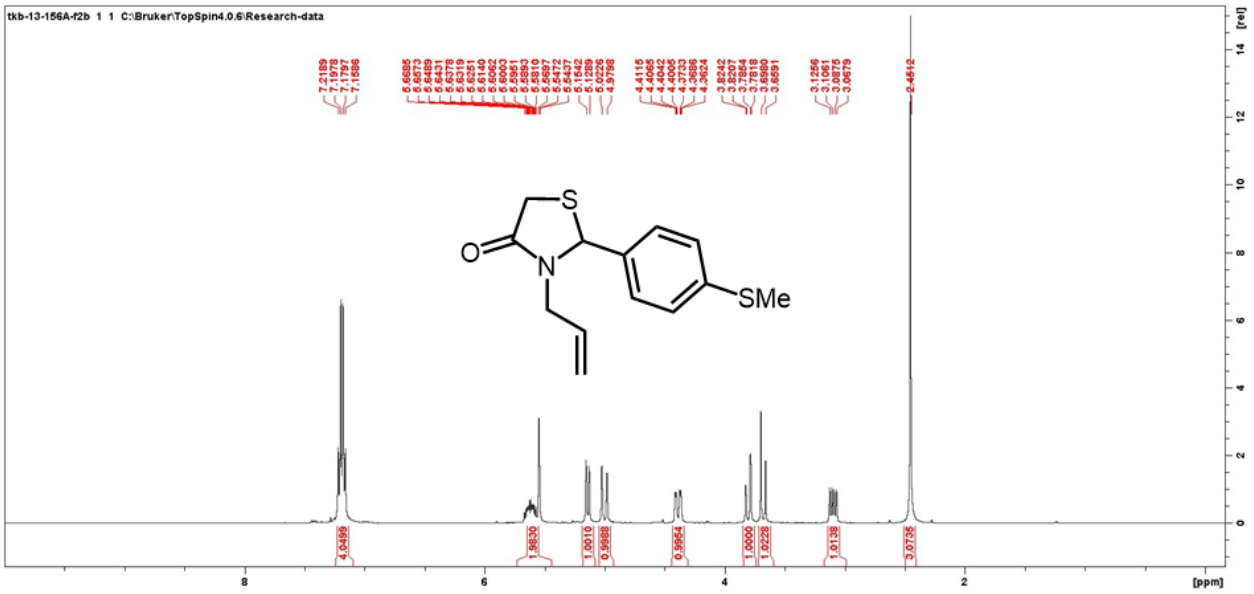


Compound 5b

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 246.5 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.14 (m, 4H), 5.62 (dddd, *J* = 17.6, 10.0, 7.8, 4.5 Hz, 1H), 5.55 (s, 1H), 5.14 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.00 (dq, *J* = 17.1, 1.4 Hz, 1H), 4.39 (ddt, *J* = 15.3, 4.2, 1.8 Hz, 1H), 3.80 (d, *J* = 15.6 Hz, 1H), 3.68 (d, *J* = 15.6 Hz, 1H), 3.10 (dd, *J* = 15.3, 7.8 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 140.1, 135.7, 131.1, 127.6, 126.6, 118.9, 62.6, 45.1, 32.9, 15.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{15}NOS_2$, 265.0595, found 265.0599.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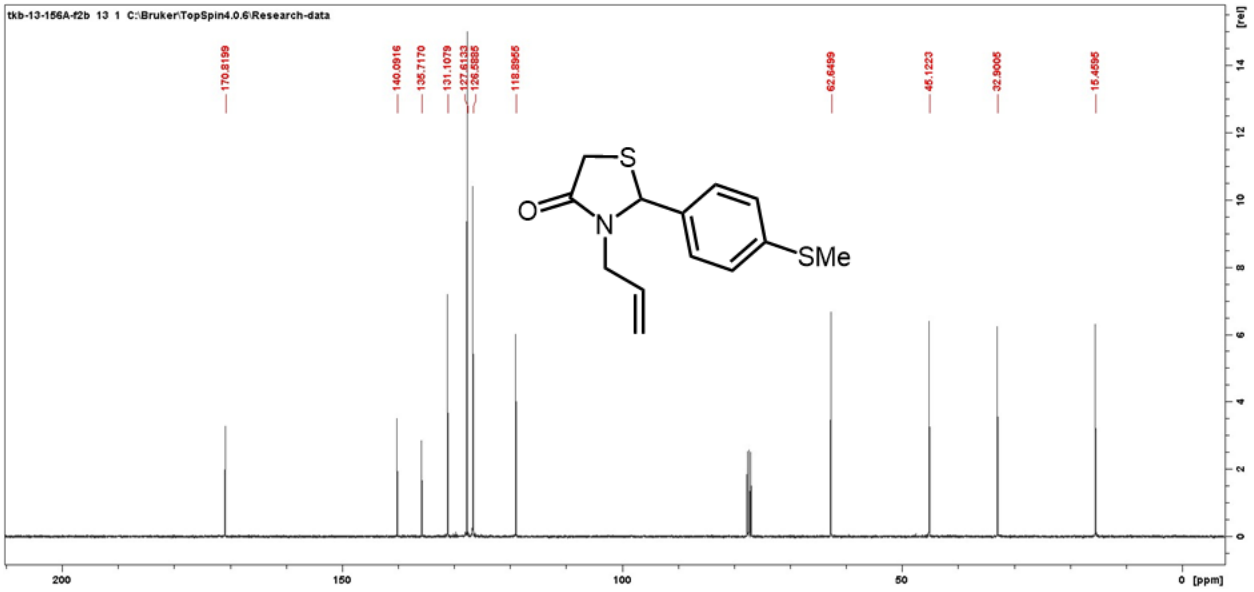
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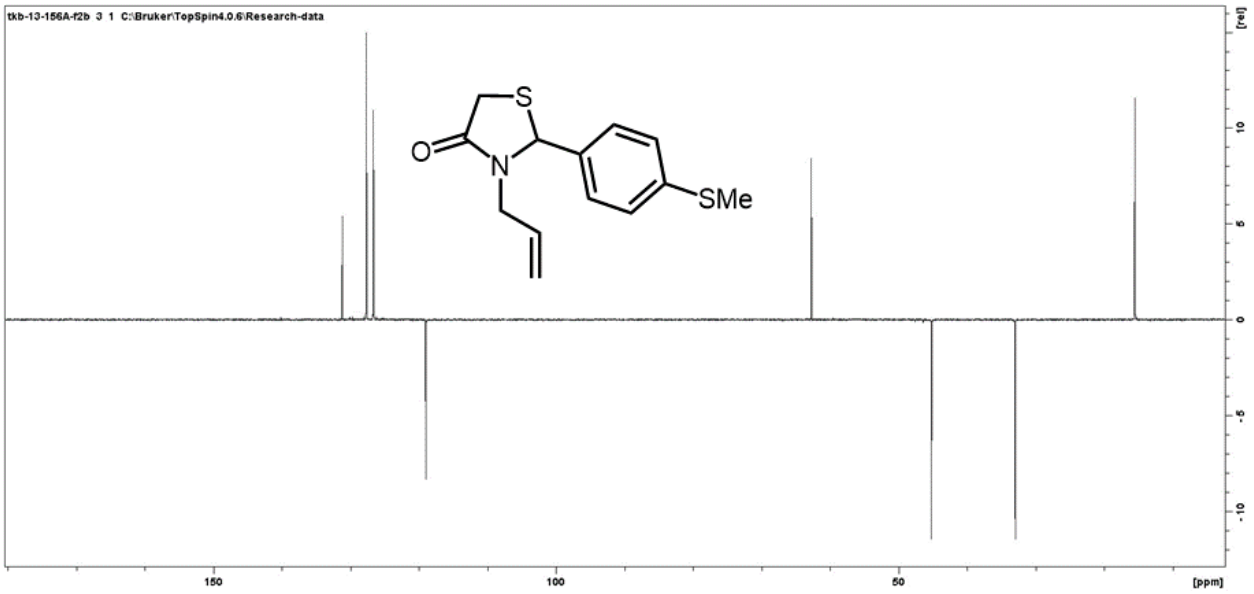
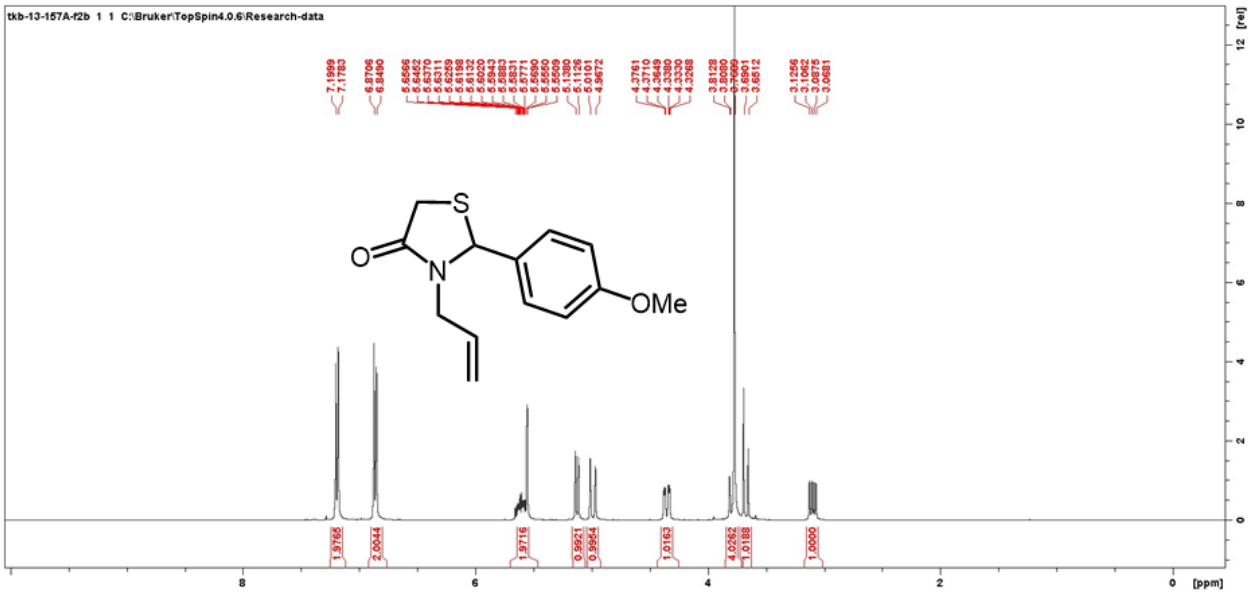
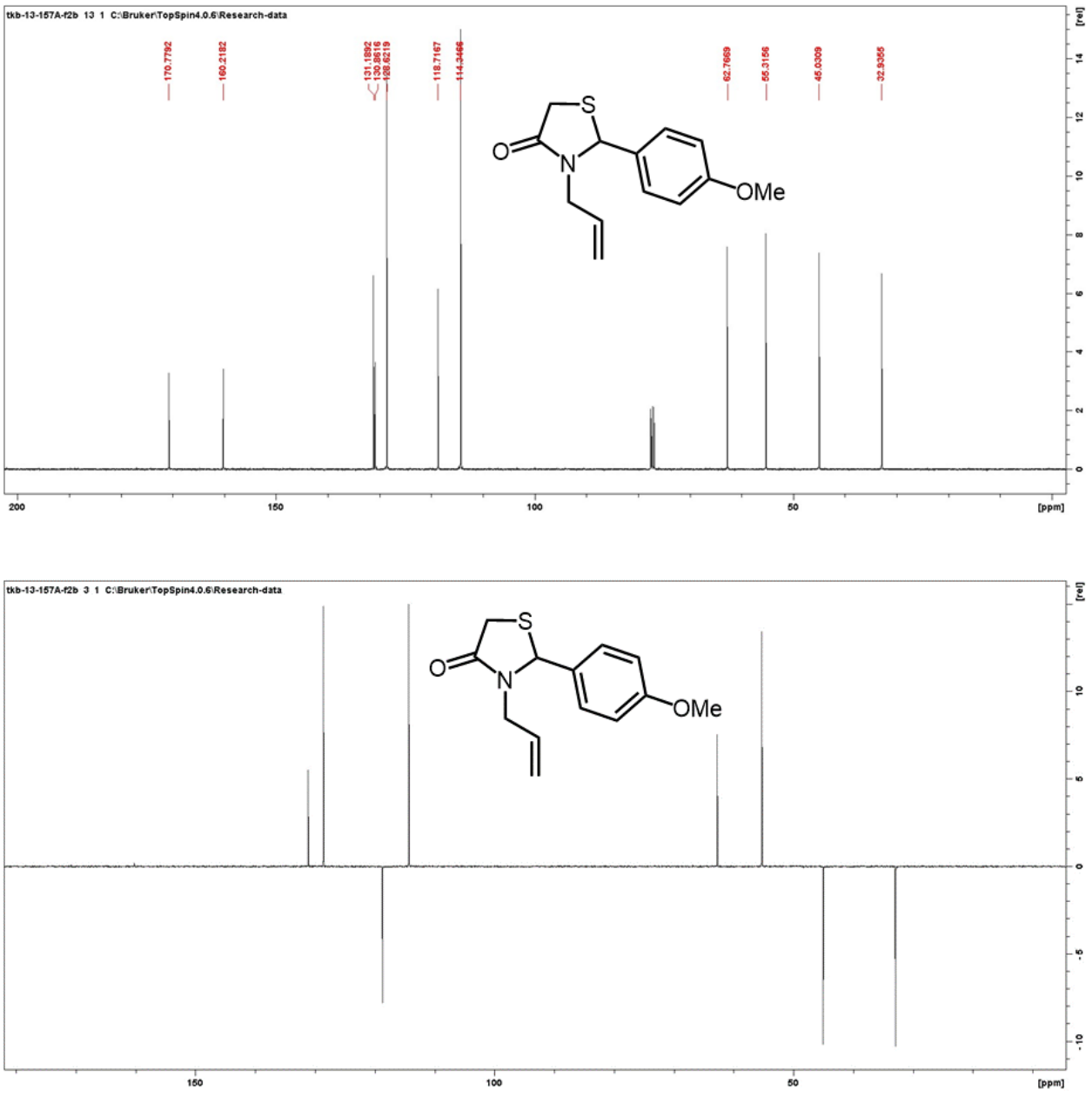


Compound 5c

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 224.2 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 2H), 5.68 – 5.55 (m, 1H), 5.55 (s, 1H), 5.12 (dq, *J* = 10.2, 1.2 Hz, 1H), 4.99 (dq, *J* = 17.0, 1.4 Hz, 1H), 4.35 (ddd, *J* = 15.3, 4.1, 2.0 Hz, 1H), 3.81 – 3.78 (m, 4H), 3.67 (d, *J* = 15.6 Hz, 1H), 3.15 – 3.04 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.78, 160.22, 131.19, 130.87, 128.62, 118.72, 114.35, 62.77, 55.32, 45.03, 32.94. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{15}NO_2S$, 249.0823, found 249.0828.

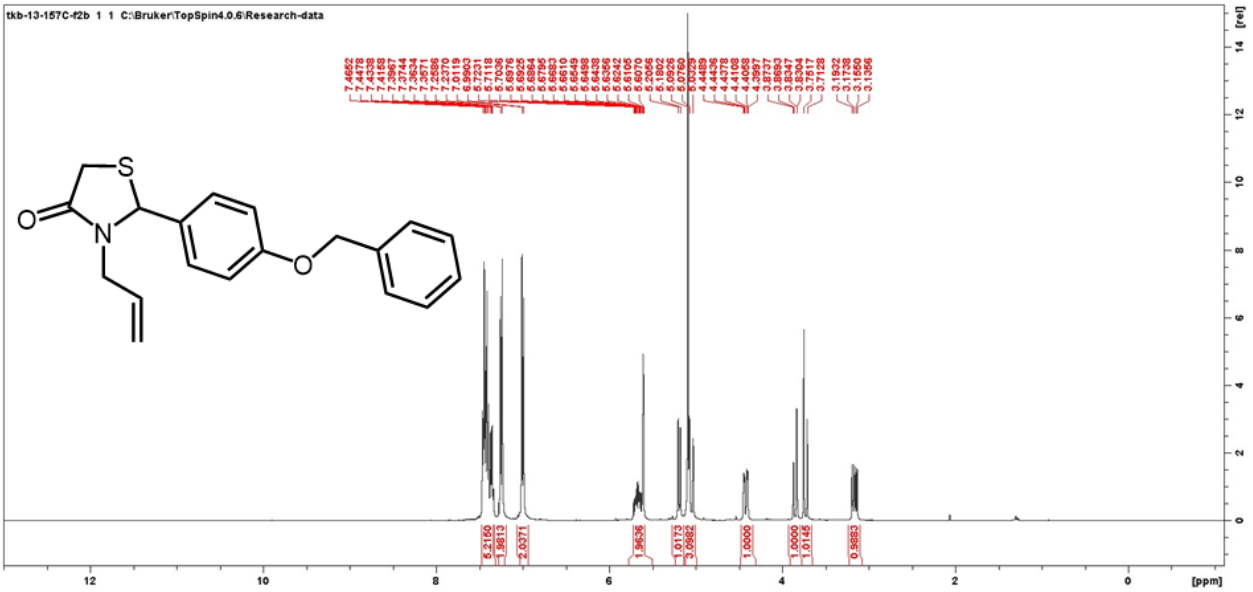


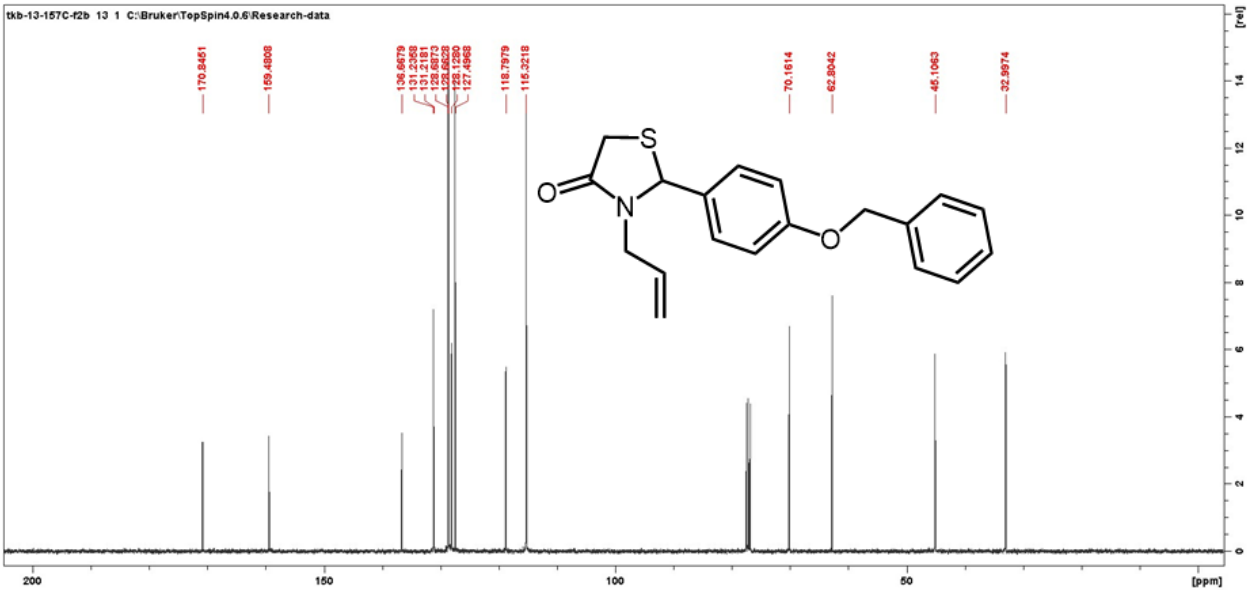


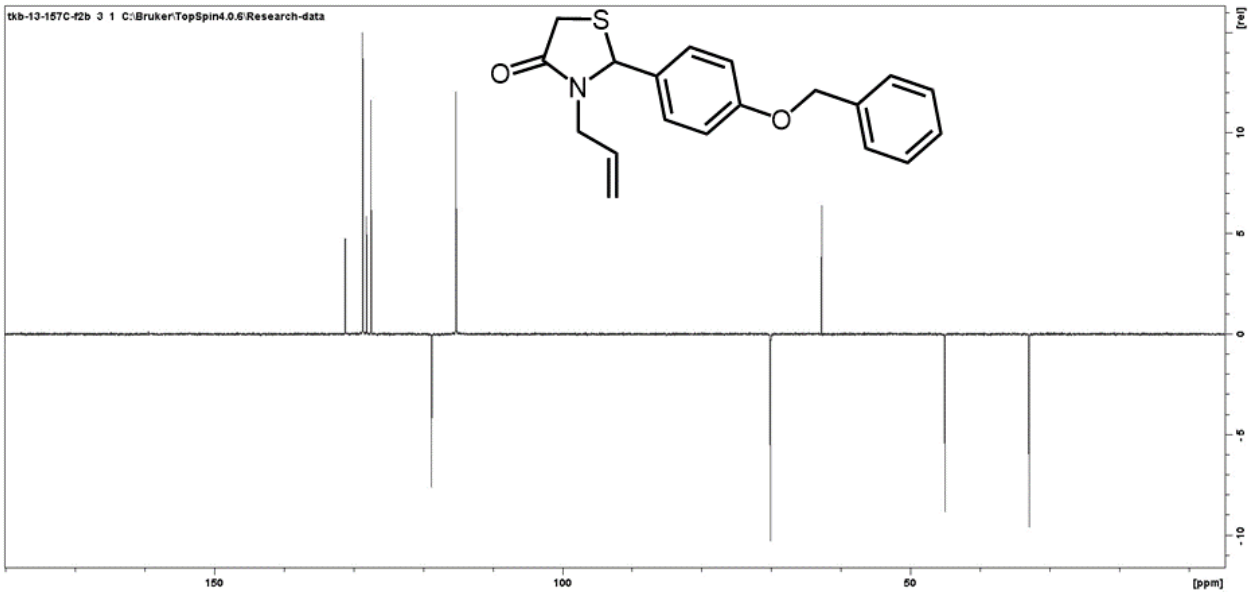
Compound 5d

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 282.8 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 5H), 7.26 – 7.23 (m, 2H), 7.00 (d, 2H), 5.67 (dddd, *J* = 17.6, 10.1, 7.7, 4.5 Hz, 1H), 5.61 (d, *J* = 2.0 Hz, 1H), 5.19 (dd, *J* = 10.2, 1.5 Hz, 1H), 5.09 (s, 2H), 5.05 (dd, *J* = 17.1, 1.6 Hz, 1H), 4.43 (ddd, *J* = 15.2, 4.1, 2.0 Hz, 1H), 3.85 (d, *J* = 15.5 Hz, 1H),

3.73 (d, J = 15.5 Hz, 1H), 3.16 (dd, J = 15.3, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 159.5, 136.7, 131.2, 129.1, 128.7, 128.6, 128.1, 127.5, 118.8, 115.3, 70.2, 62.8, 45.1, 33.0. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{19}NO_2S$, 325.1136, found 325.1141.

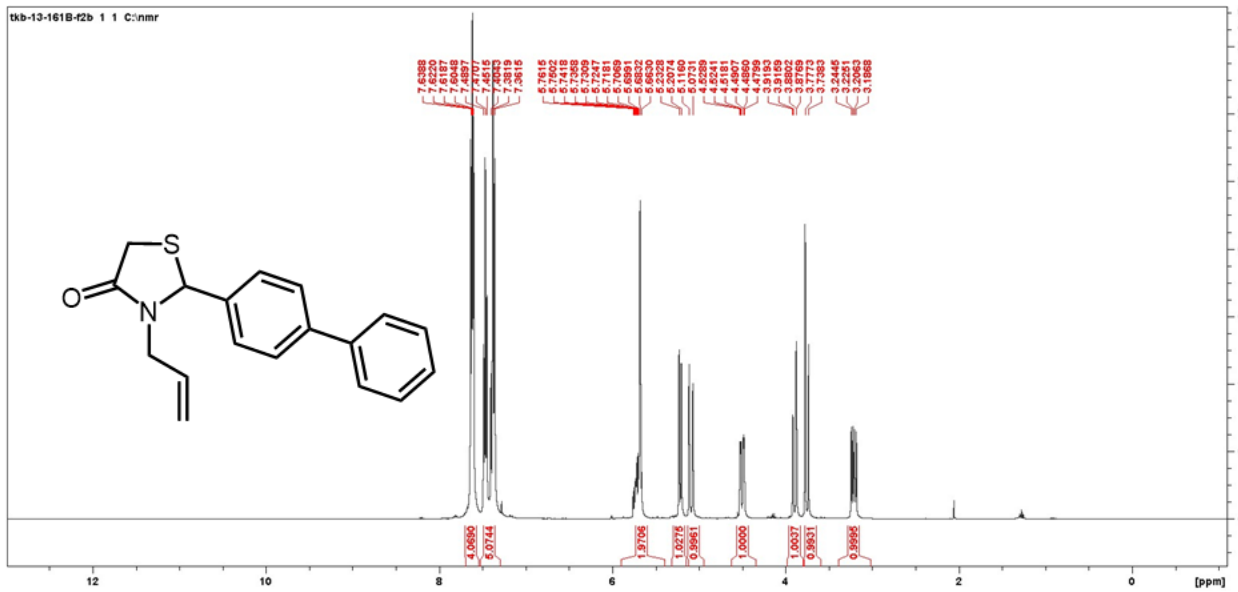






Compound 5e

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 250.8 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.58 (m, 4H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.38 (td, *J* = 8.3, 1.7 Hz, 3H), 5.78 – 5.64 (m, 2H), 5.22 (dd, *J* = 10.4, 1.6 Hz, 1H), 5.10 (dt, *J* = 17.2, 1.5 Hz, 1H), 4.50 (ddt, *J* = 15.3, 4.3, 1.7 Hz, 1H), 3.90 (d, *J* = 15.6 Hz, 1H), 3.76 (d, *J* = 15.6 Hz, 1H), 3.22 (dd, *J* = 15.3, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 142.1, 140.2, 138.3, 131.2, 128.9, 127.8, 127.7, 127.6, 127.1, 118.9, 62.8, 45.3, 32.9. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{17}NOS$, 295.1031, found 295.1034.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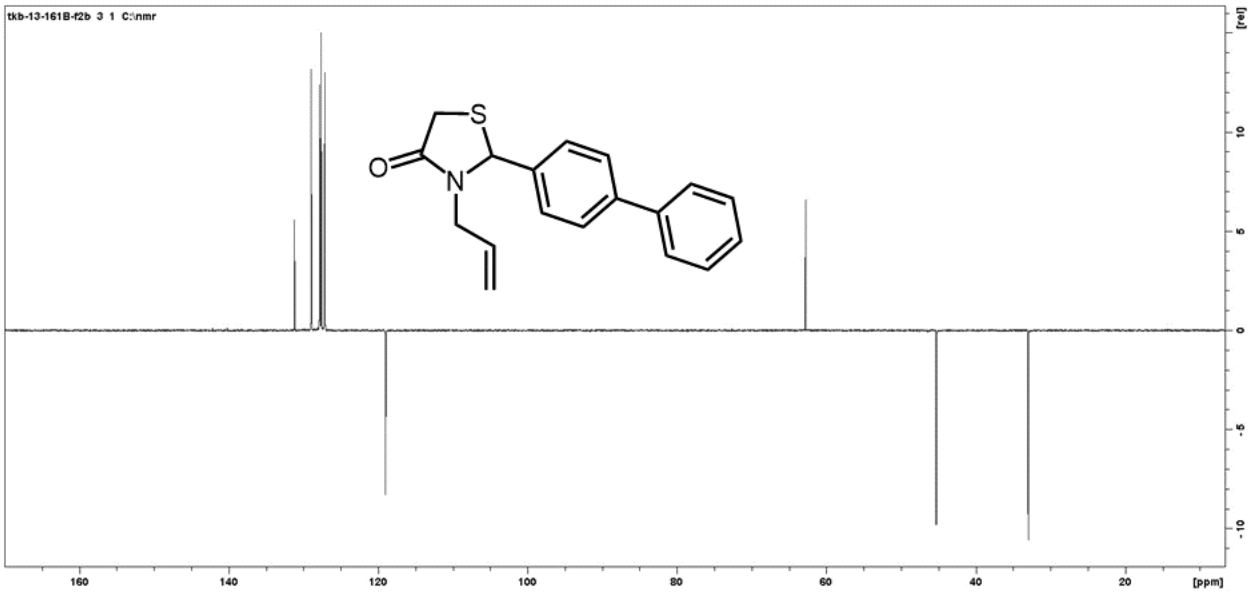
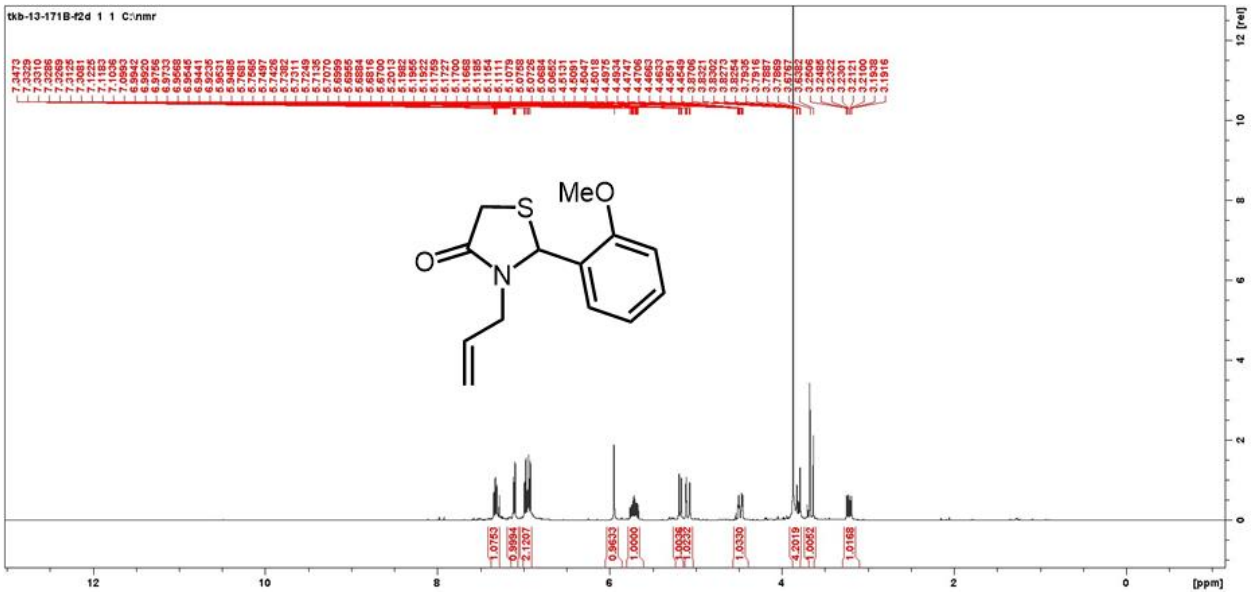


Compound 5f

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 196.7 mg, 79%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.21 (m, 1H), 7.11 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.06 – 6.86 (m, 2H), 5.95 (s, 1H), 5.72 (dddd, *J* = 17.4, 10.2, 7.4, 4.6 Hz, 1H), 5.18 (dq, *J* = 10.2, 1.3 Hz, 1H), 5.09 (dq, *J* = 17.1, 1.4 Hz, 1H), 4.48 (ddt, *J* = 15.4, 4.6, 1.7 Hz, 1H), 3.87 (s, 3H), 3.87 – 3.76 (m, 1H), 3.66 (d, *J* = 15.4 Hz, 1H), 3.22 (ddq, *J* = 15.4, 7.4, 1.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 157.0, 131.2, 129.9, 127.4, 126.6, 120.8, 118.4, 111.1, 57.9, 55.6, 55.5, 45.4, 32.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{15}NO_2S$, 249.0823, found 249.0828.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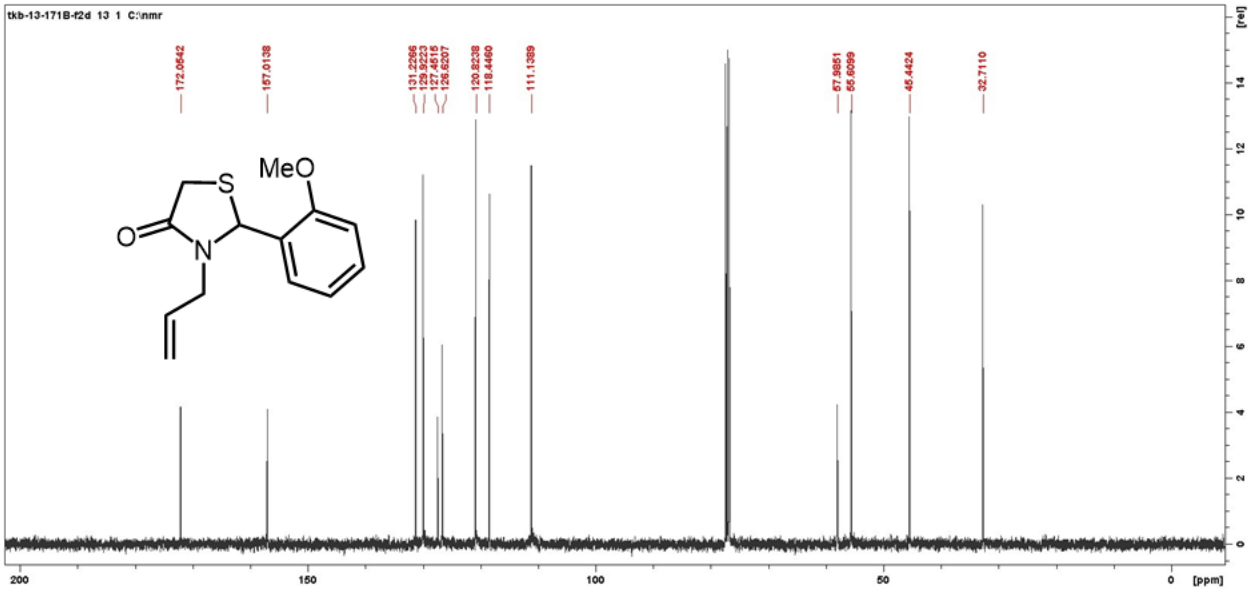
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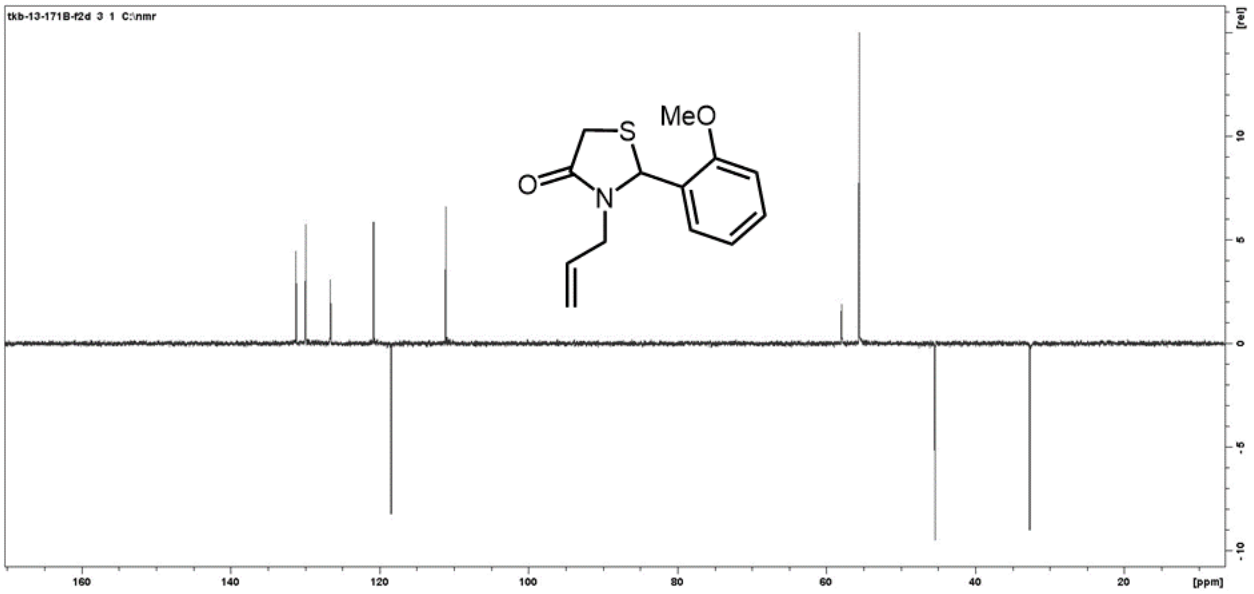
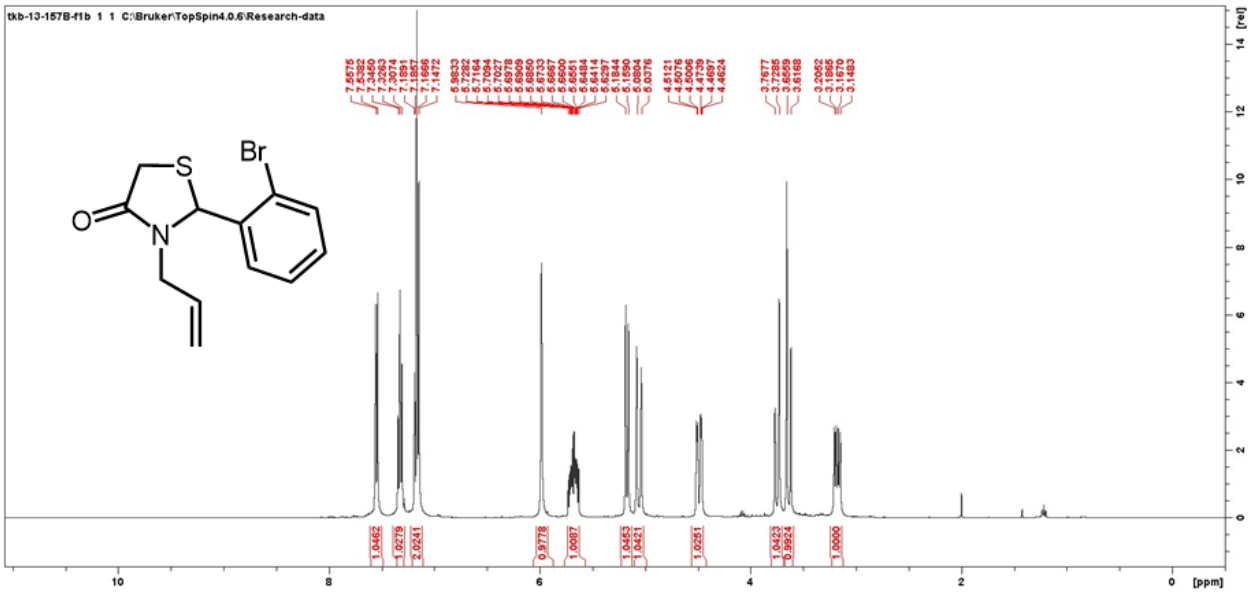


Compound 5g

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 219.0 mg, 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.33 (td, *J* = 7.5, 1.3 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 2H), 5.98 (s, 1H), 5.68 (dddd, *J* = 17.4, 10.0, 7.5, 4.7 Hz, 1H), 5.17 (dt, *J* = 10.2, 1.2 Hz, 1H), 5.06 (dd, *J* = 17.2, 1.8 Hz, 1H), 4.49 (ddt, *J* = 15.4, 4.7, 1.7 Hz, 1H), 3.75 (dd, *J* = 15.7, 1.9 Hz, 1H), 3.64 (d, *J* = 15.7 Hz, 1H), 3.18 (dd, *J* = 15.3, 7.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 138.3, 133.6, 130.7, 130.1, 128.2, 126.9, 122.7, 119.2, 61.8, 45.7, 32.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{12}H_{12}BrNOS$, 296.9823, found 296.9828.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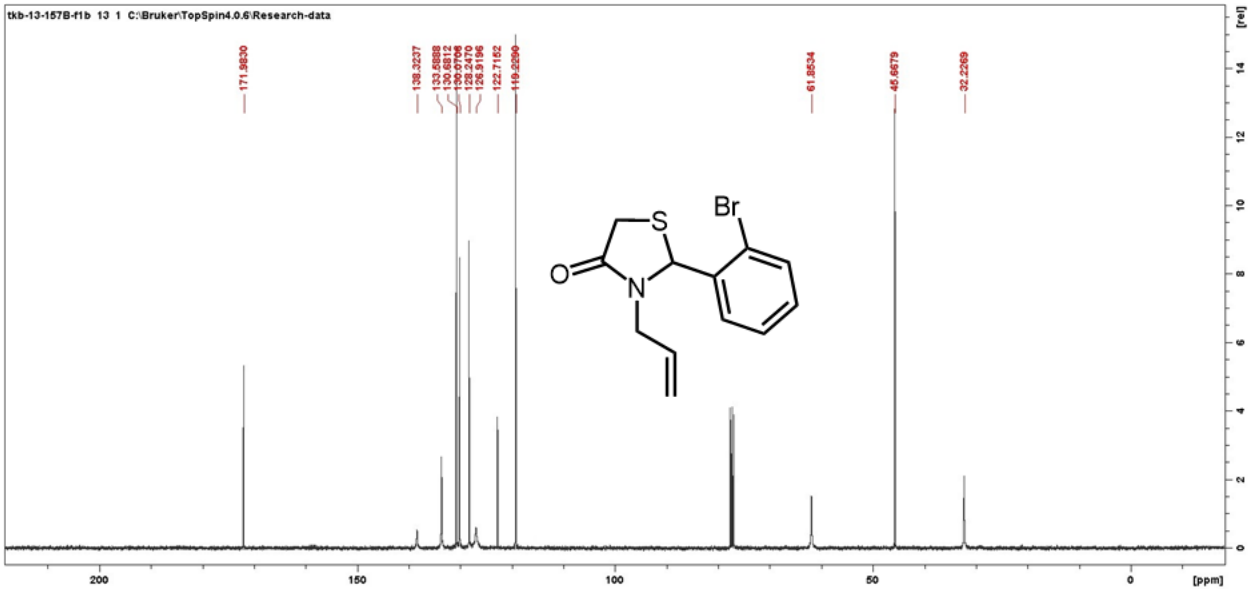
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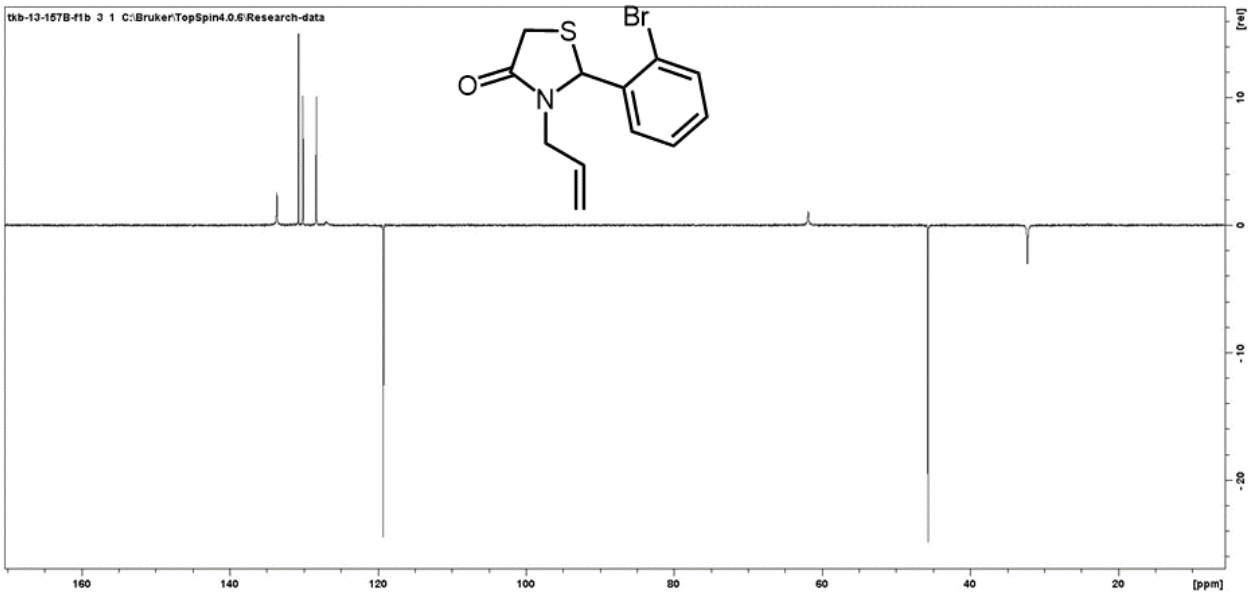
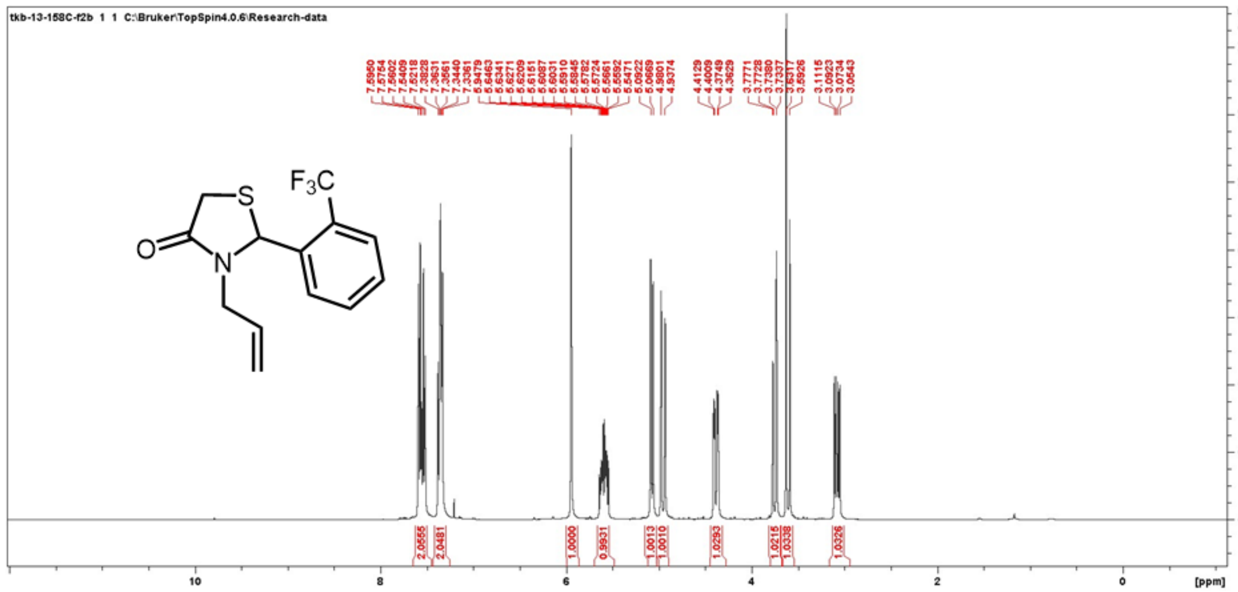


Compound 5h

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 203.8 mg, 71%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 2H), 7.38 – 7.34 (m, 2H), 5.95 (s, 1H), 5.60 (dddd, *J* = 17.5, 10.0, 7.6, 4.8 Hz, 1H), 5.08 (dt, *J* = 10.1, 1.1 Hz, 1H), 4.96 (dd, *J* = 17.2, 1.7 Hz, 1H), 4.39 (ddt, *J* = 15.3, 4.8, 1.7 Hz, 1H), 3.76 (d, *J* = 15.7 Hz, 1H), 3.61 (d, *J* = 15.7 Hz, 1H), 3.08 (dd, *J* = 15.2, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 139.3, 133.0, 130.5, 128.6, 128.0, 127.9, 127.6, 127.3, 127.0, 126.9, 126.3, 126.20, 126.1, 125.3, 122.6, 119.8, 119.3, 57.8, 45.7, 32.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{12}F_3NOS$, 287.0592, found 287.0599.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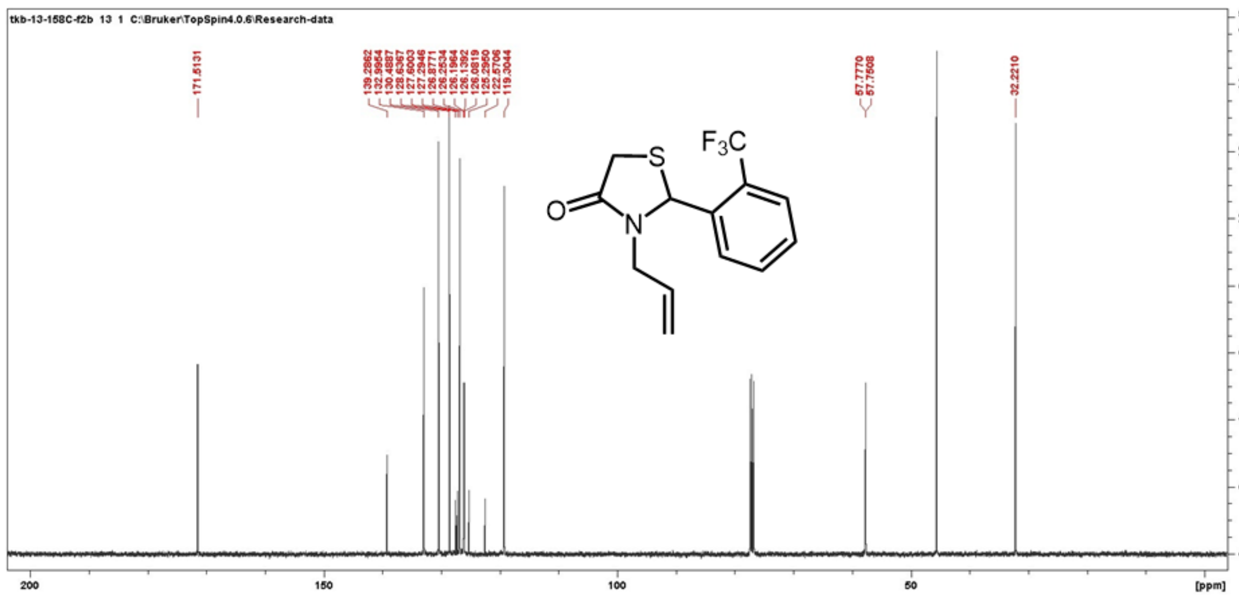
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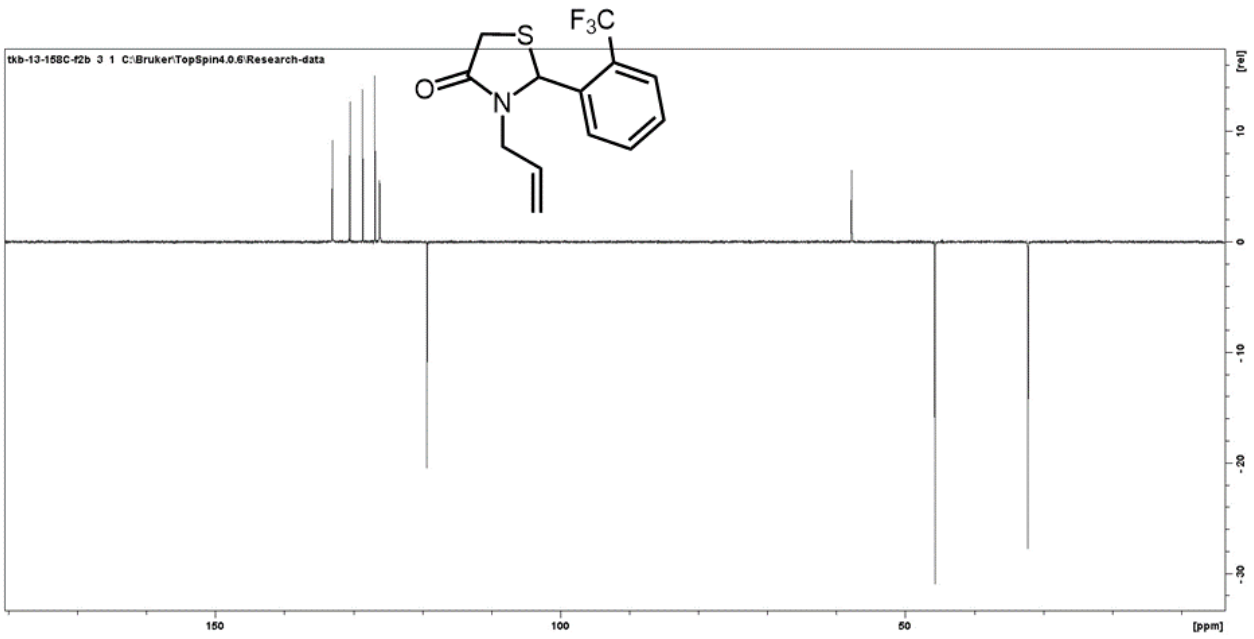
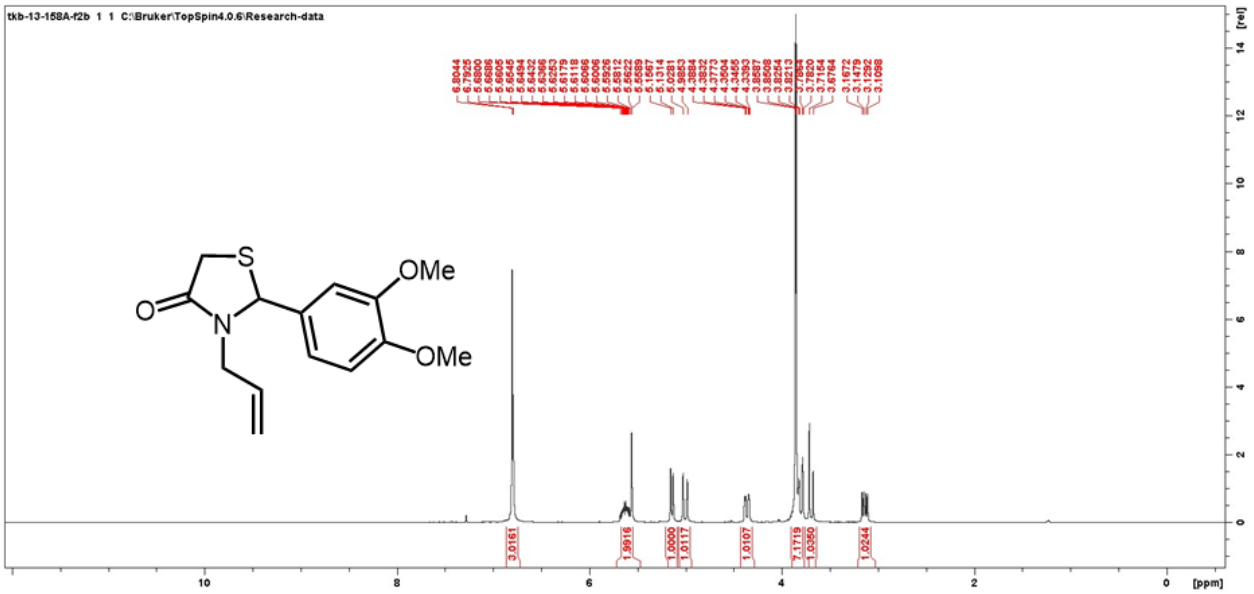


Compound 5i

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 251.1 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 – 6.78 (m, 3H), 5.63 (dddd, *J* = 17.6, 10.0, 7.7, 4.5 Hz, 1H), 5.56 (s, 1H), 5.18 – 5.11 (m, 1H), 5.01 (dq, *J* = 17.0, 1.4 Hz, 1H), 4.37 (ddd, *J* = 15.3, 4.2, 2.1 Hz, 1H), 3.93 – 3.74 (m, 7H), 3.70 (d, *J* = 15.6 Hz, 1H), 3.14 (dd, *J* = 15.2, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 149.8, 149.7, 131.2, 131.1, 120.0, 118.7, 110.9, 109.8, 63.2, 56.0, 55.9, 45.1, 33.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{14}H_{17}NO_3S$, 279.0929, found 279.0933.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OMe
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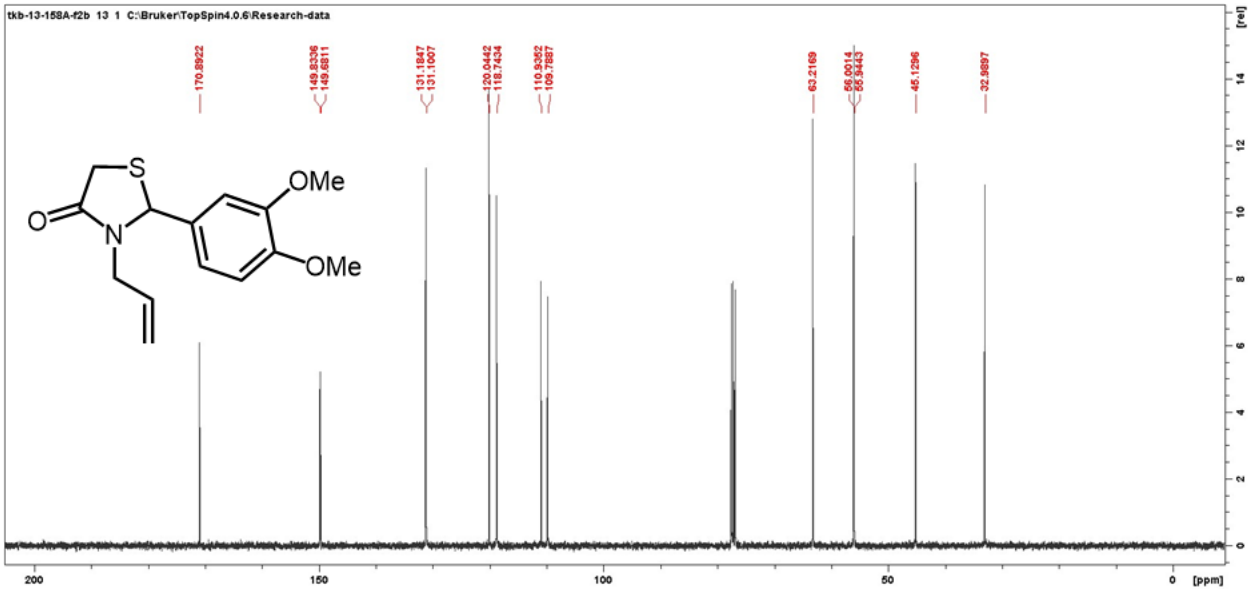
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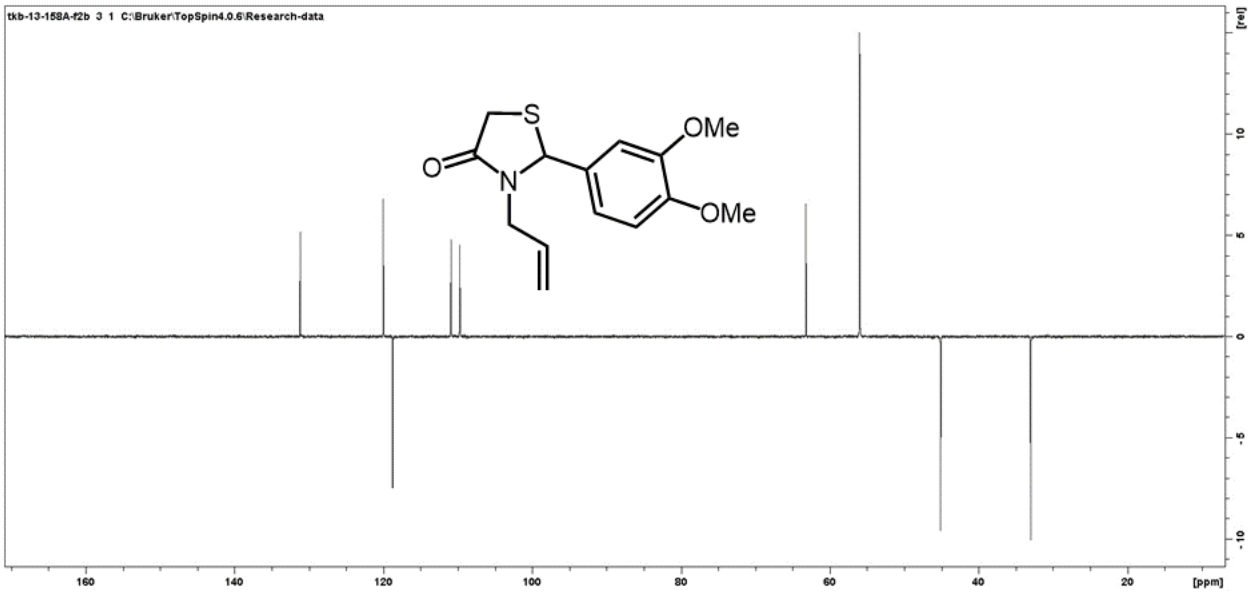
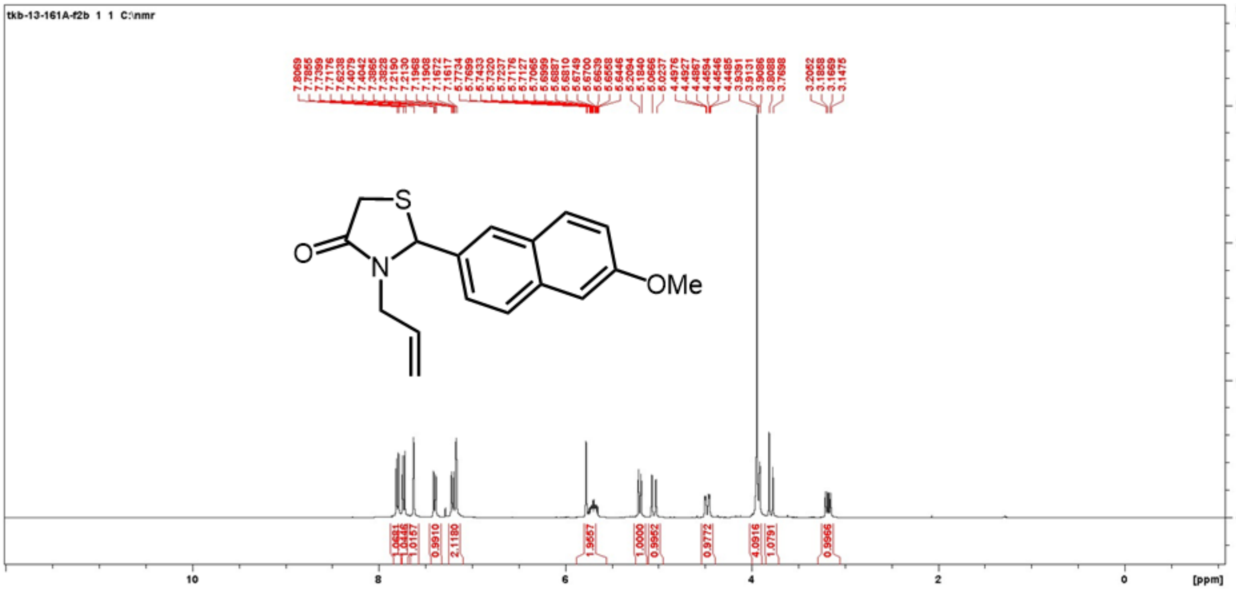


Compound 5j

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 260.1 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.6 Hz, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.62 (d, *J* = 1.9 Hz, 1H), 7.40 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.24 – 7.14 (m, 2H), 5.77 (d, *J* = 2.1 Hz, 1H), 5.69 (dddd, *J* = 17.6, 9.9, 7.7, 4.5 Hz, 1H), 5.20 (dt, *J* = 10.2, 1.3 Hz, 1H), 5.05 (dt, *J* = 17.1, 1.5 Hz, 1H), 4.48 (ddd, *J* = 15.3, 4.0, 2.0 Hz, 1H), 3.94 (s, 3H), 3.93 (dd, *J* = 15.4, 2.4 Hz, 1H), 3.79 (d, *J* = 15.6 Hz, 1H), 3.18 (dd, *J* = 15.3, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 158.5, 135.0, 134.0, 131.1, 129.5, 128.3, 128.3, 126.5, 124.6, 119.5, 118.9, 105.9, 63.4, 55.4, 45.2, 33.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{17}NO_2S$, 299.0980, found 299.0986.



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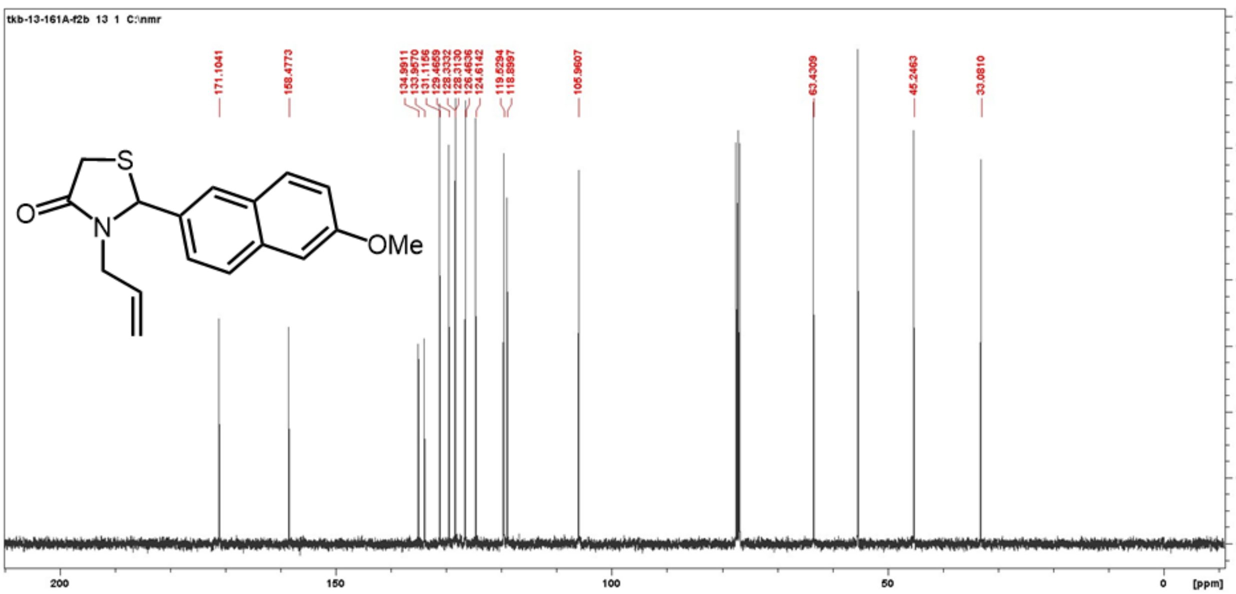

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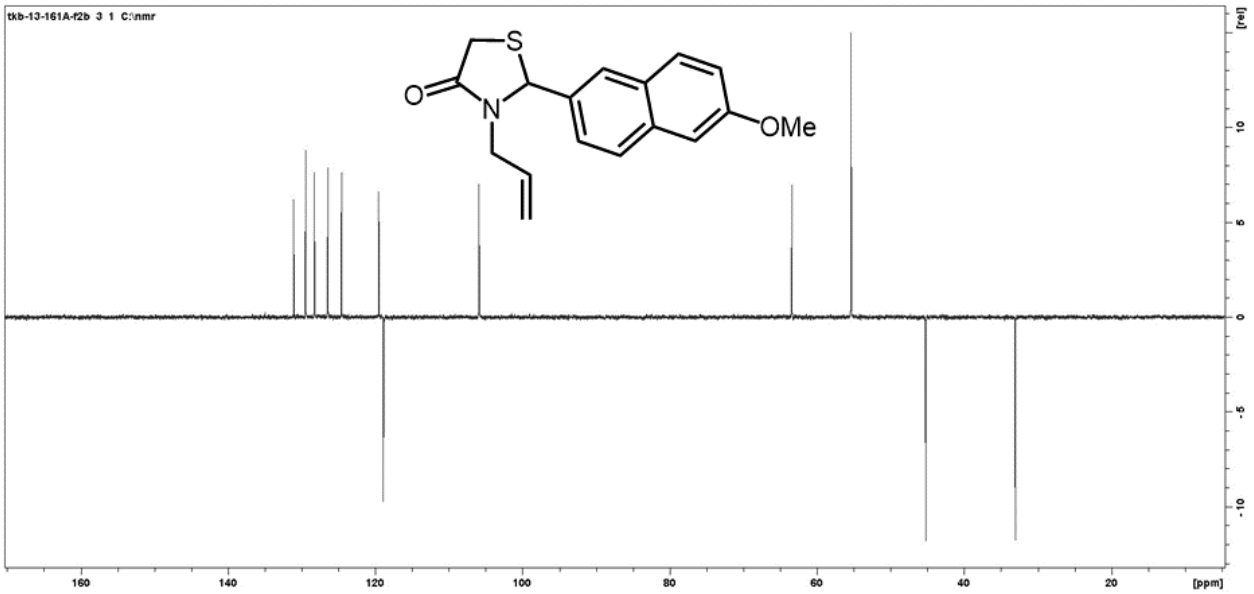
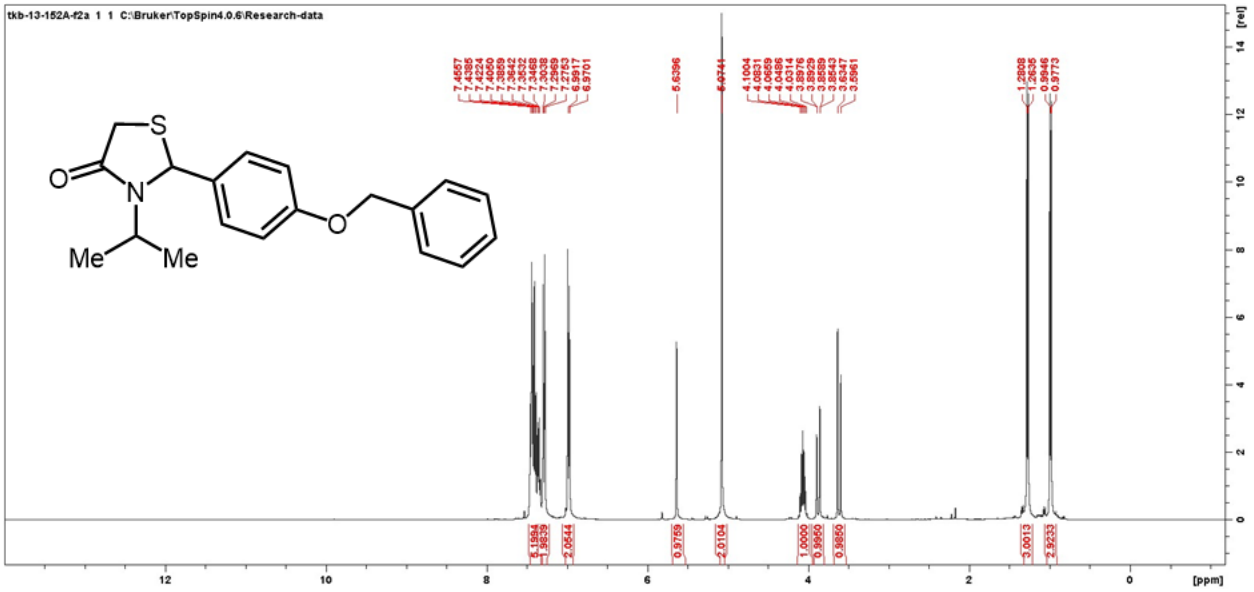
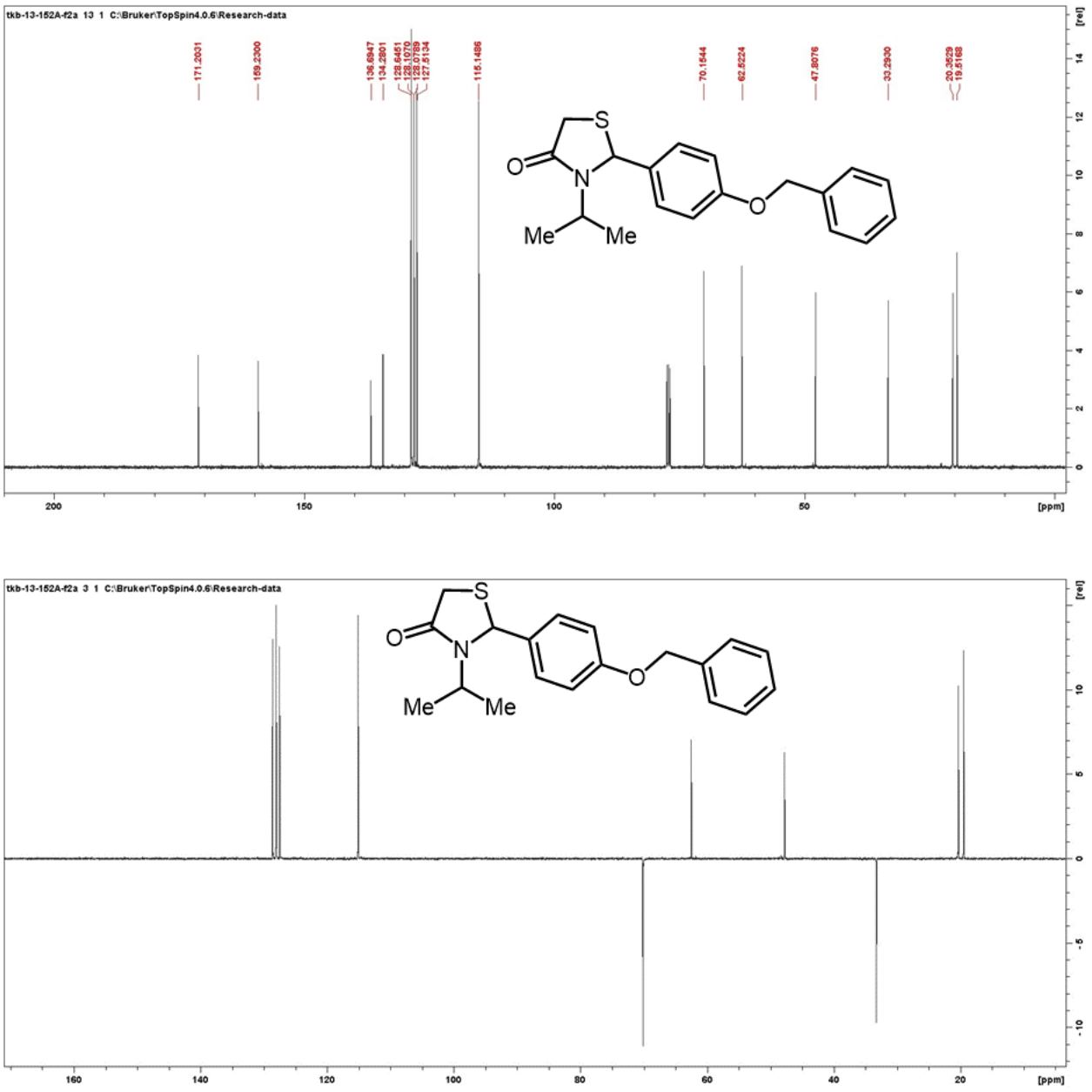


Compound 5k

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 297.6 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.28 (m, 7H), 6.98 (d, *J* = 7.9 Hz, 2H), 5.64 (s, 1H), 5.07 (s, 2H), 4.07 (hept, *J* = 6.9 Hz, 1H), 3.88 (d, *J* = 15.5 Hz, 1H), 3.62 (d, *J* = 15.5 Hz, 1H), 1.27 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 159.2, 136.7, 134.3, 128.7, 128.1, 127.5, 115.1, 70.2, 62.5, 47.8, 33.3, 20.4, 19.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{21}NO_2S$, 321.1293, found 321.1298.

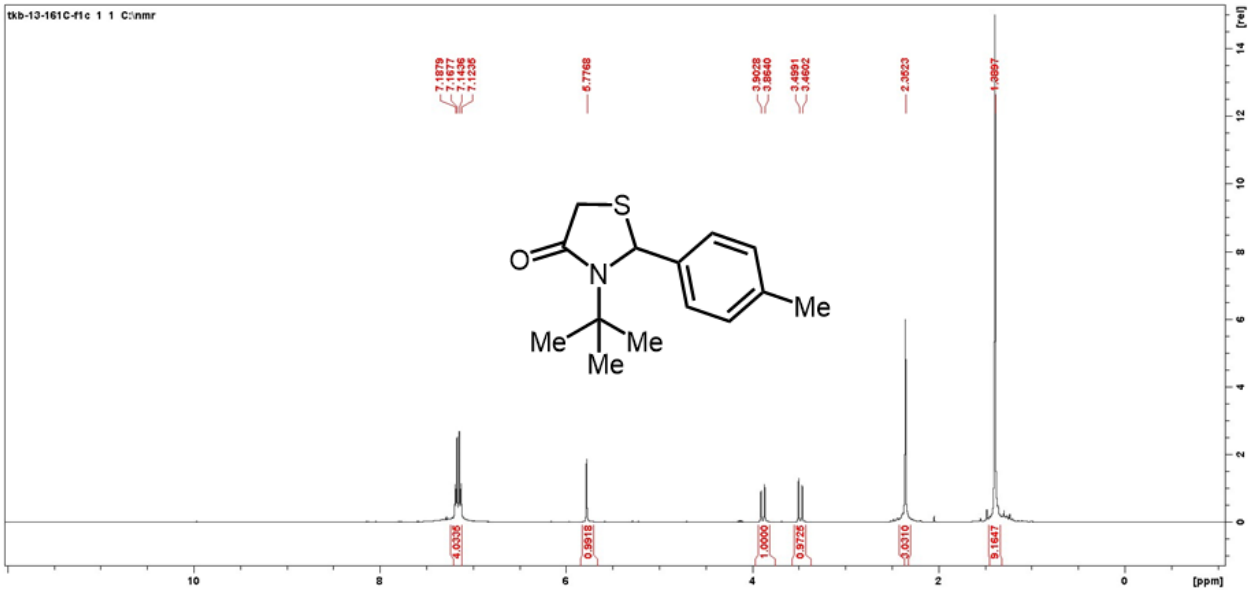


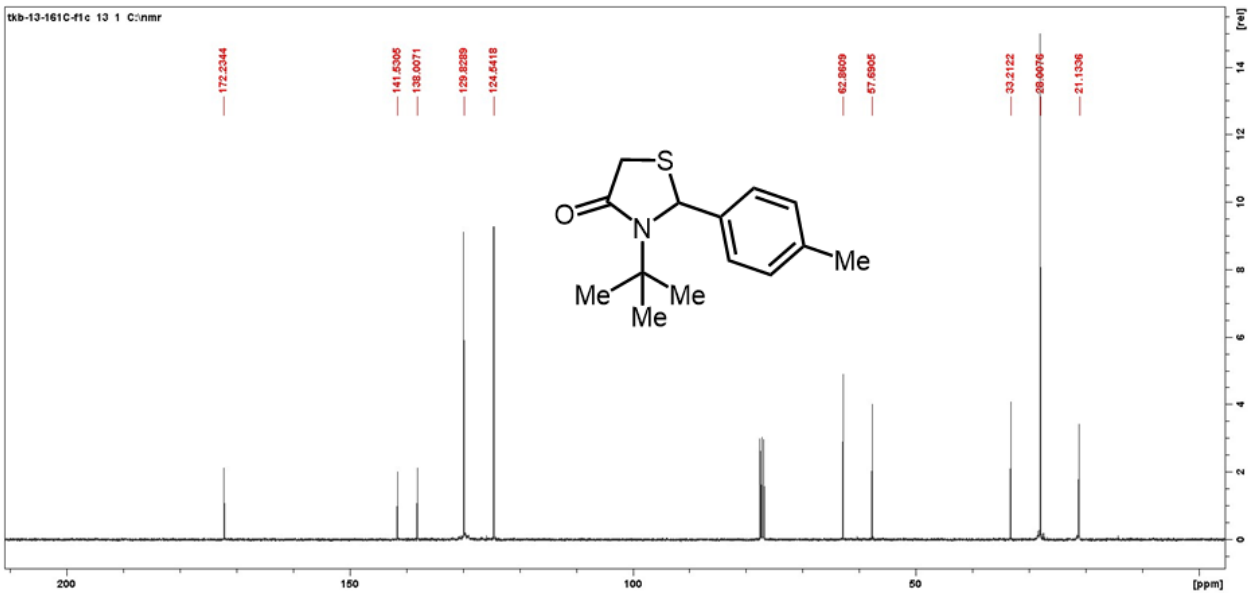


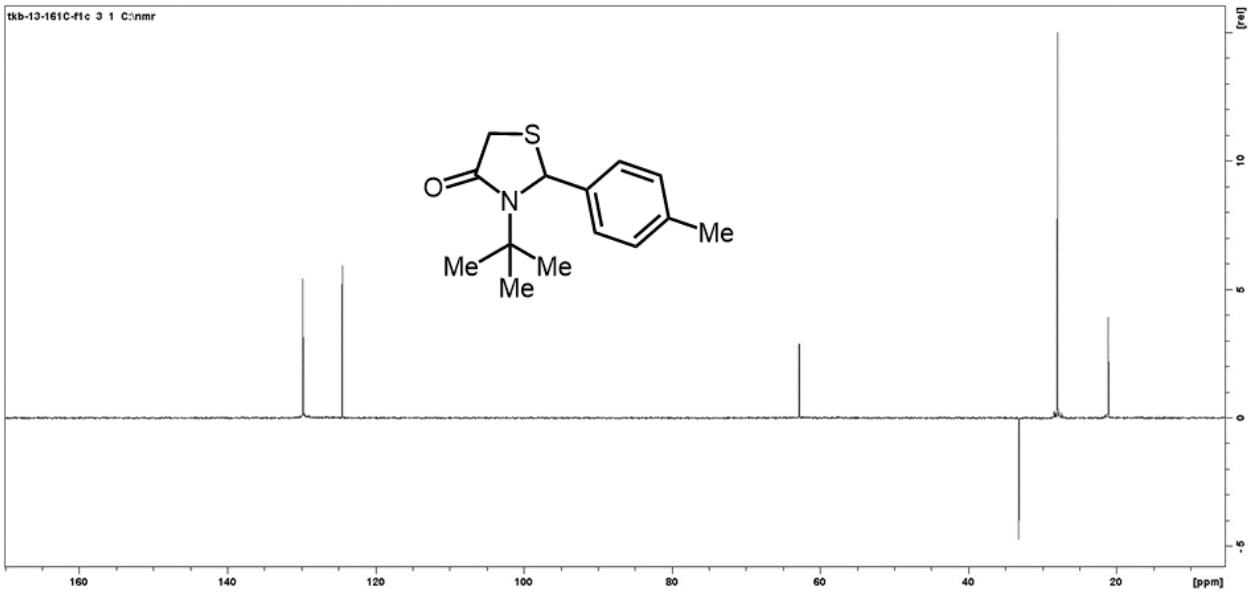
Compound 5l

Prepared in 3.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 642.4 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.12 (m, 4H), 5.78 (d, J = 1.4 Hz, 1H), 3.88 (d, J = 15.6 Hz, 1H), 3.48 (d, J = 15.6 Hz, 1H), 2.35 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 141.5, 138.0,

129.8, 124.5, 62.9, 57.7, 33.2, 28.0, 21.1. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{14}H_{19}NOS$, 249.1187, found 249.1192.

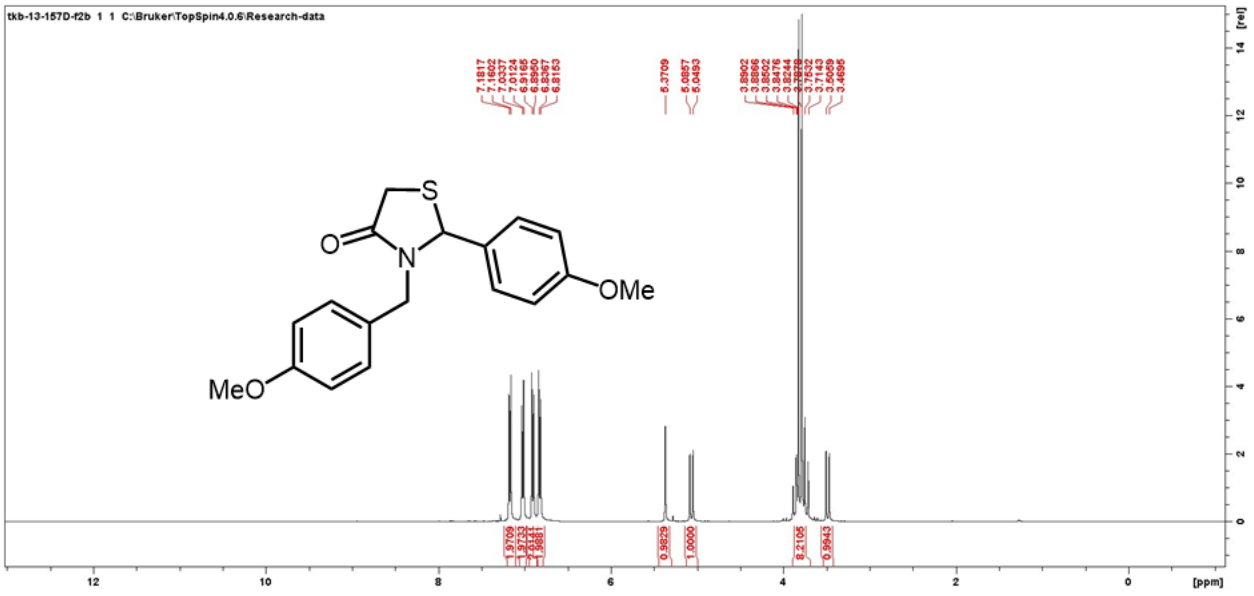


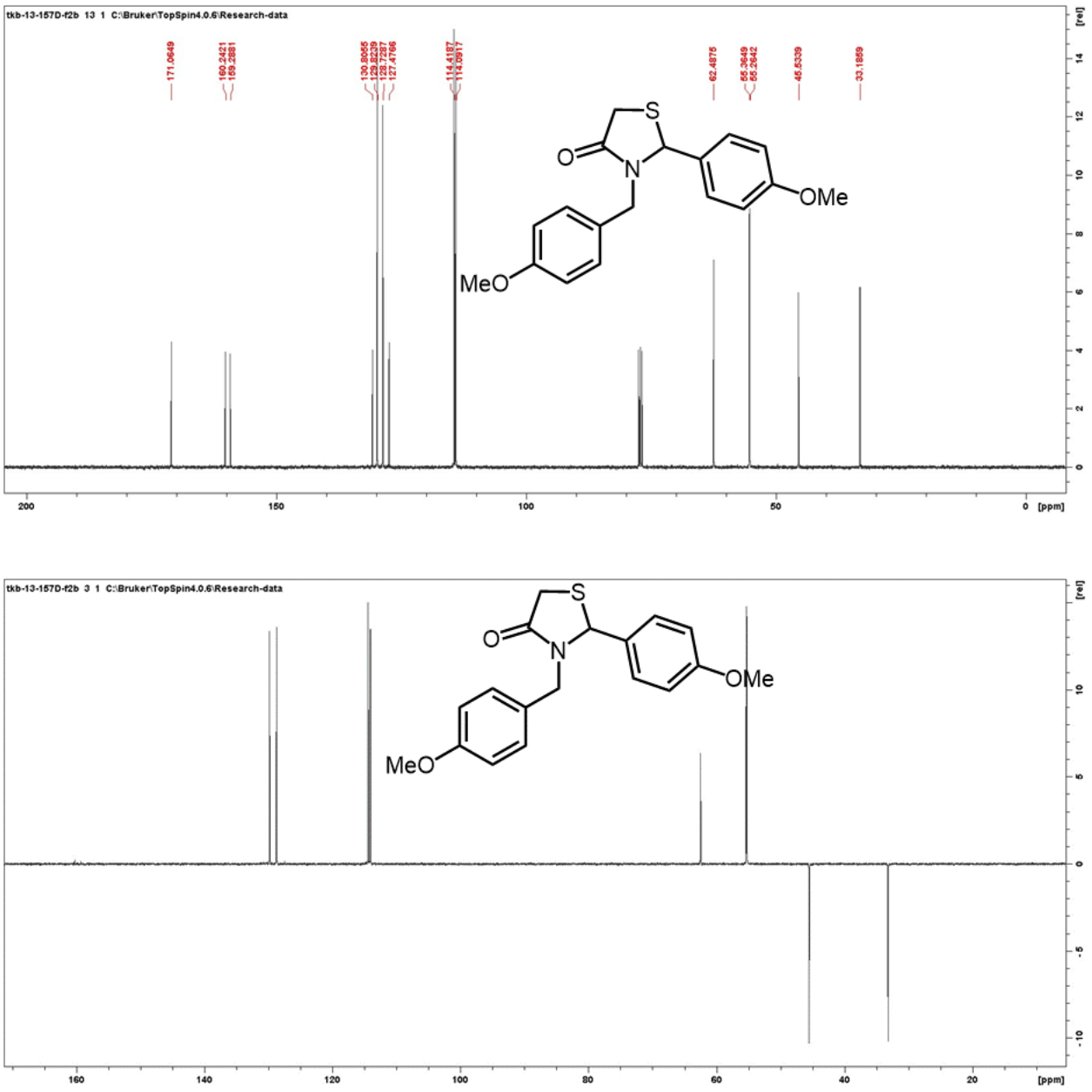




Compound 5m

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 282.1 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 6.90 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 7.8 Hz, 2H), 5.37 (s, 1H), 5.07 (d, *J* = 14.6 Hz, 1H), 3.89 – 3.71 (m, 8H) 3.49 (d, *J* = 14.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 160.2, 159.3, 130.8, 129.8, 128.7, 127.5, 114.4, 114.1, 62.5, 55.4, 55.3, 45.5, 33.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{19}NO_3S$, 329.1086, found 329.1092.

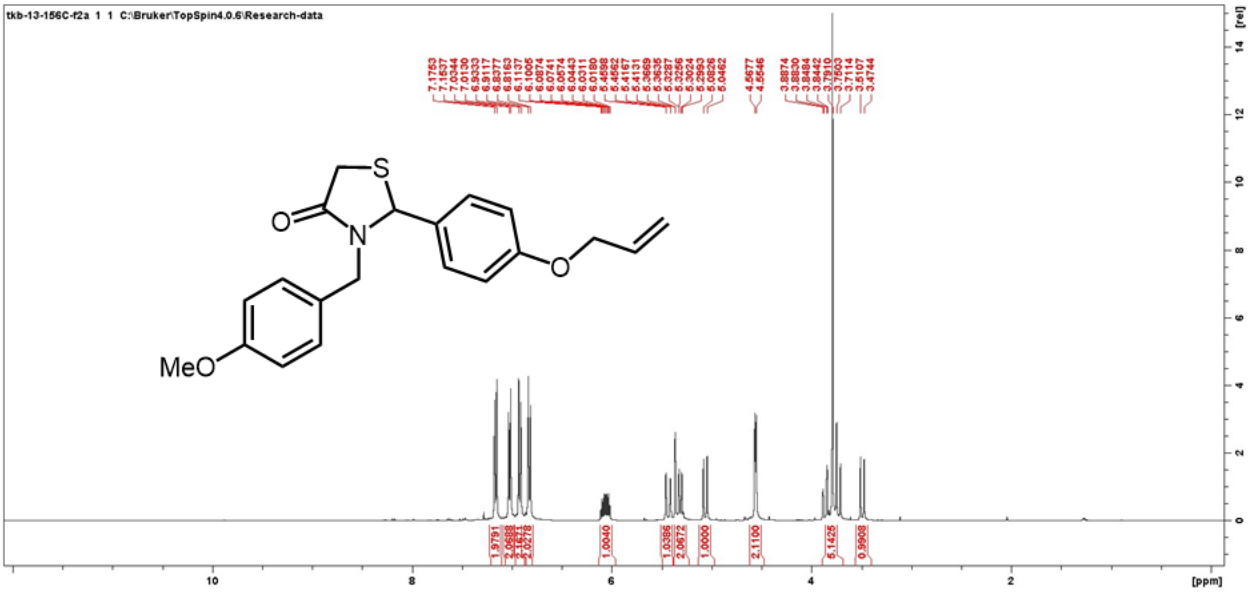


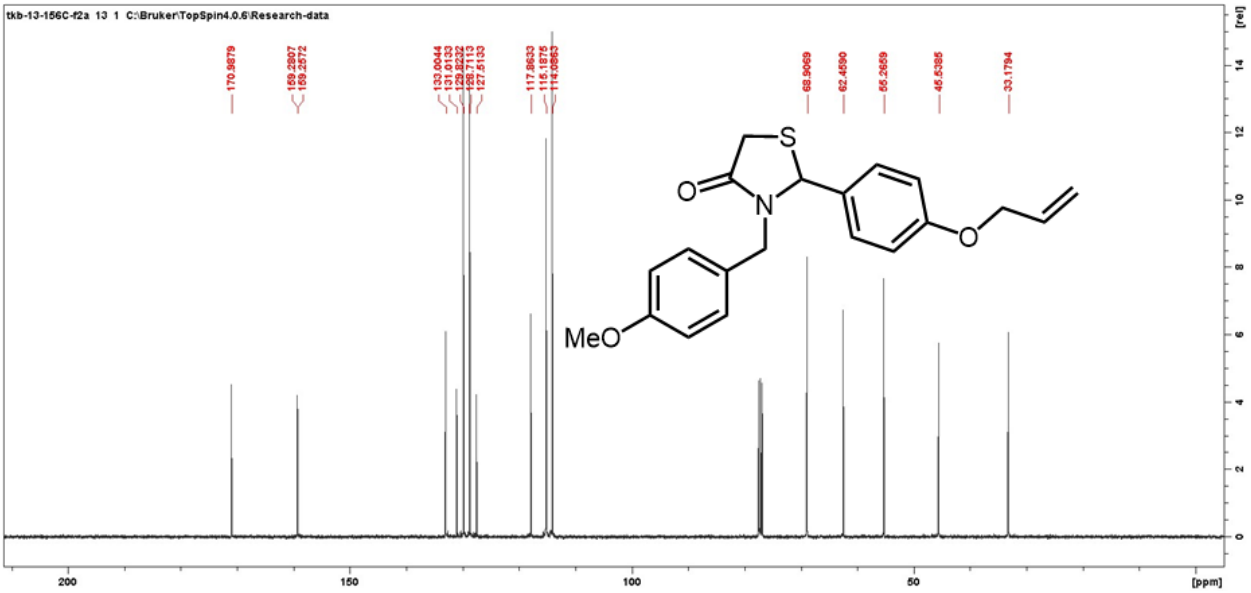


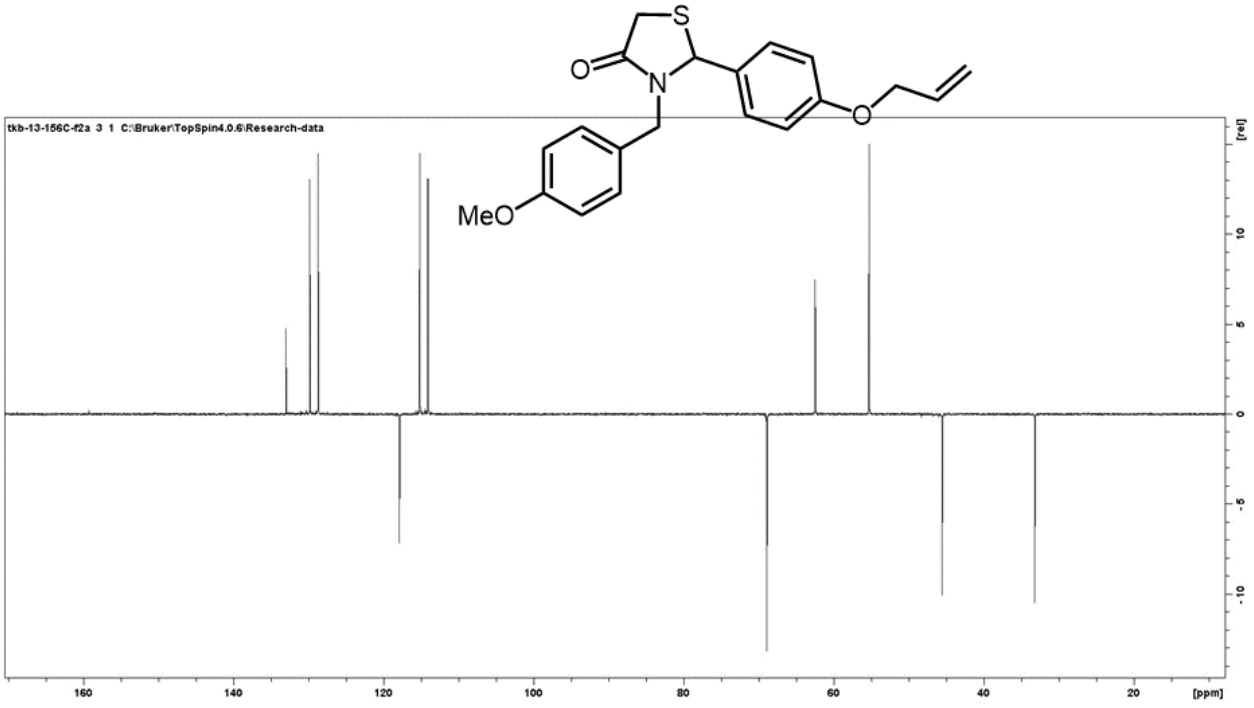
Compound 5n

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 316 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 7.6 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 7.6 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 6.07 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 5.44 (dq, *J* = 17.3, 1.7 Hz, 1H), 5.37 (d, *J* = 1.9 Hz, 1H), 5.36 – 5.25 (m, 1H), 5.06 (d, *J* = 14.6 Hz, 1H), 4.56 (dt, *J* = 5.3, 1.6 Hz, 2H),

3.87 (dd, J = 15.6, 2.0 Hz, 1H), 3.79 (s, 3H), 3.73 (d, J = 15.6 Hz, 1H), 3.49 (d, J = 14.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 159.3, 159.3, 133.0, 131.0, 129.8, 128.7, 127.5, 117.9, 115.2, 114.1, 68.9, 62.5, 55.3, 45.5, 33.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{21}NO_3S$, 355.1242, found 355.1245.

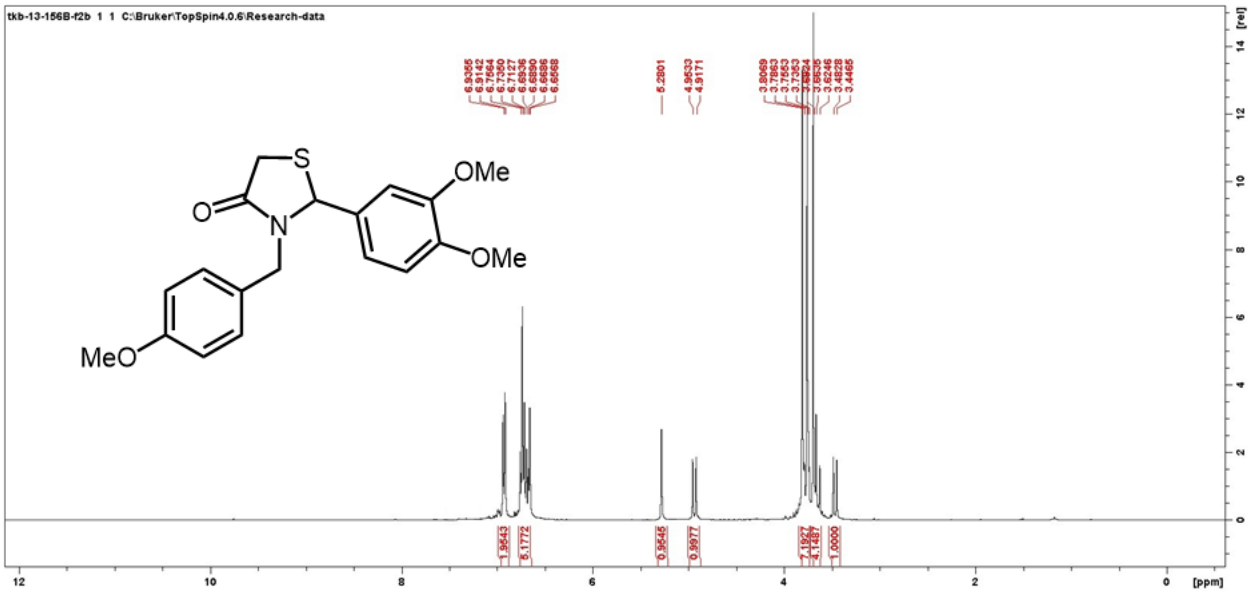






Compound 5o

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 301.6 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (d, *J* = 7.5 Hz, 2H), 6.76 – 6.66 (m, 5H), 5.28 (s, 1H), 4.94 (d, *J* = 14.5 Hz, 1H), 3.81 – 3.62 (m, 11H), 3.46 (d, *J* = 14.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 159.3, 149.8, 149.7, 131.0, 129.8, 127.6, 120.2, 114.0, 110.9, 109.9, 63.0, 56.0, 55.3, 45.7, 33.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{21}NO_4S$, 359.1191, found 359.1196.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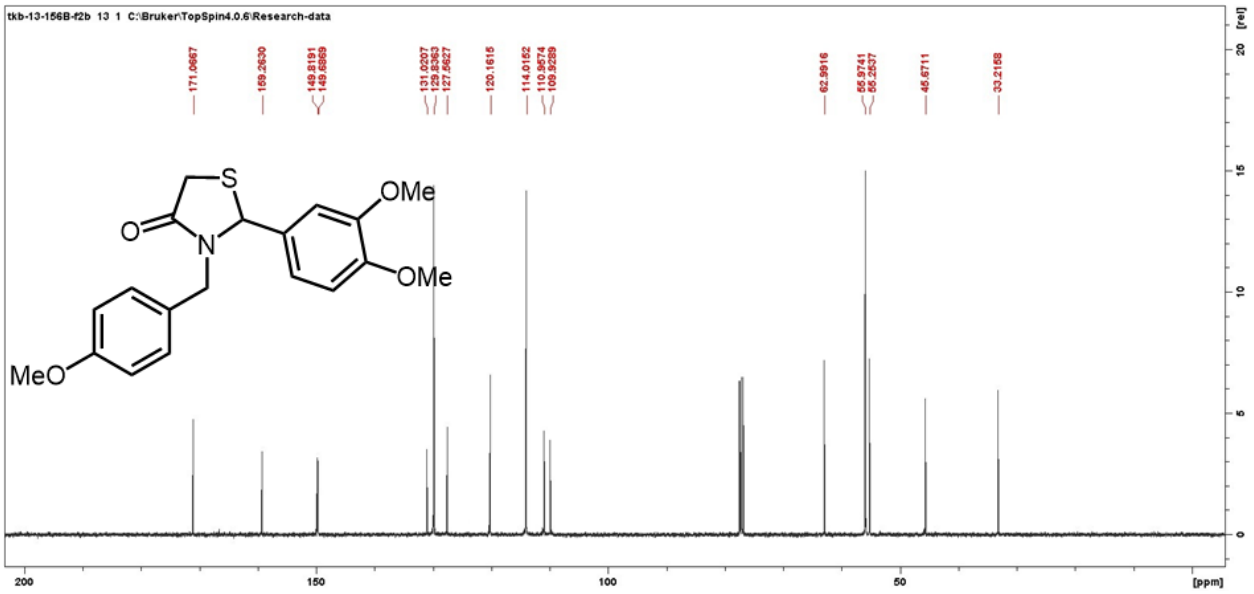
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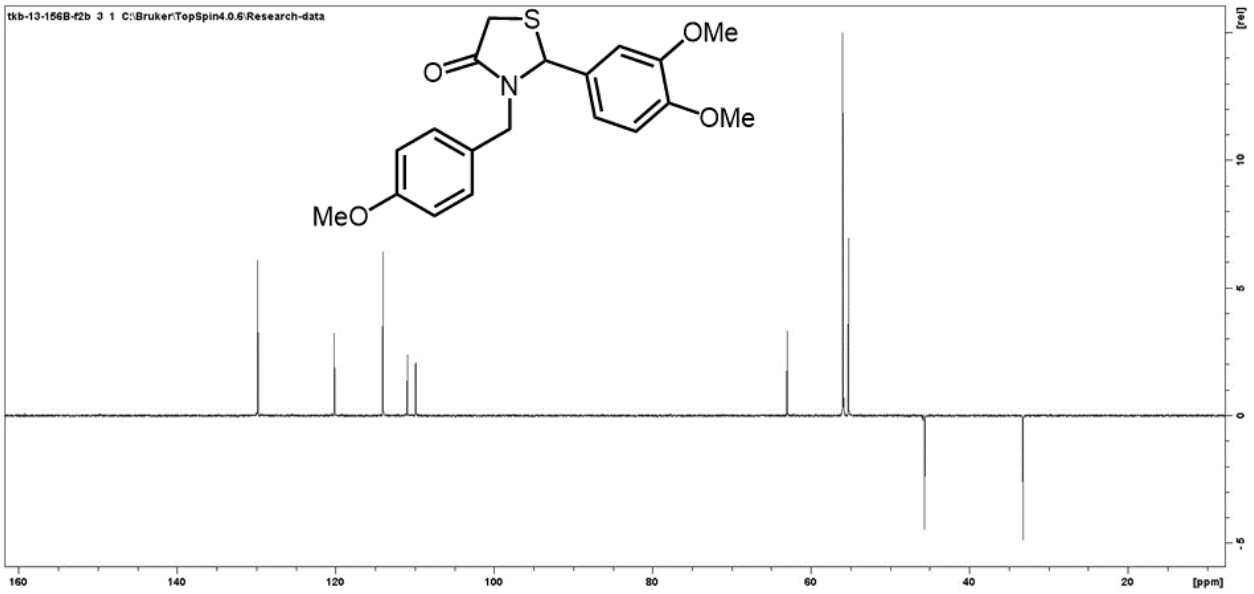
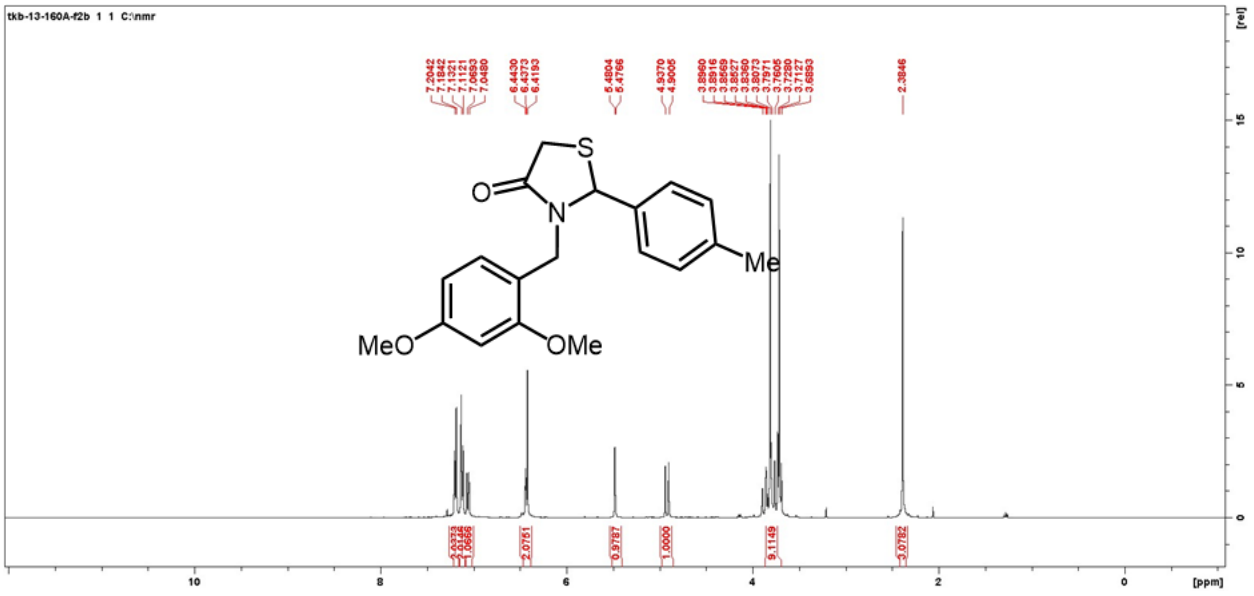
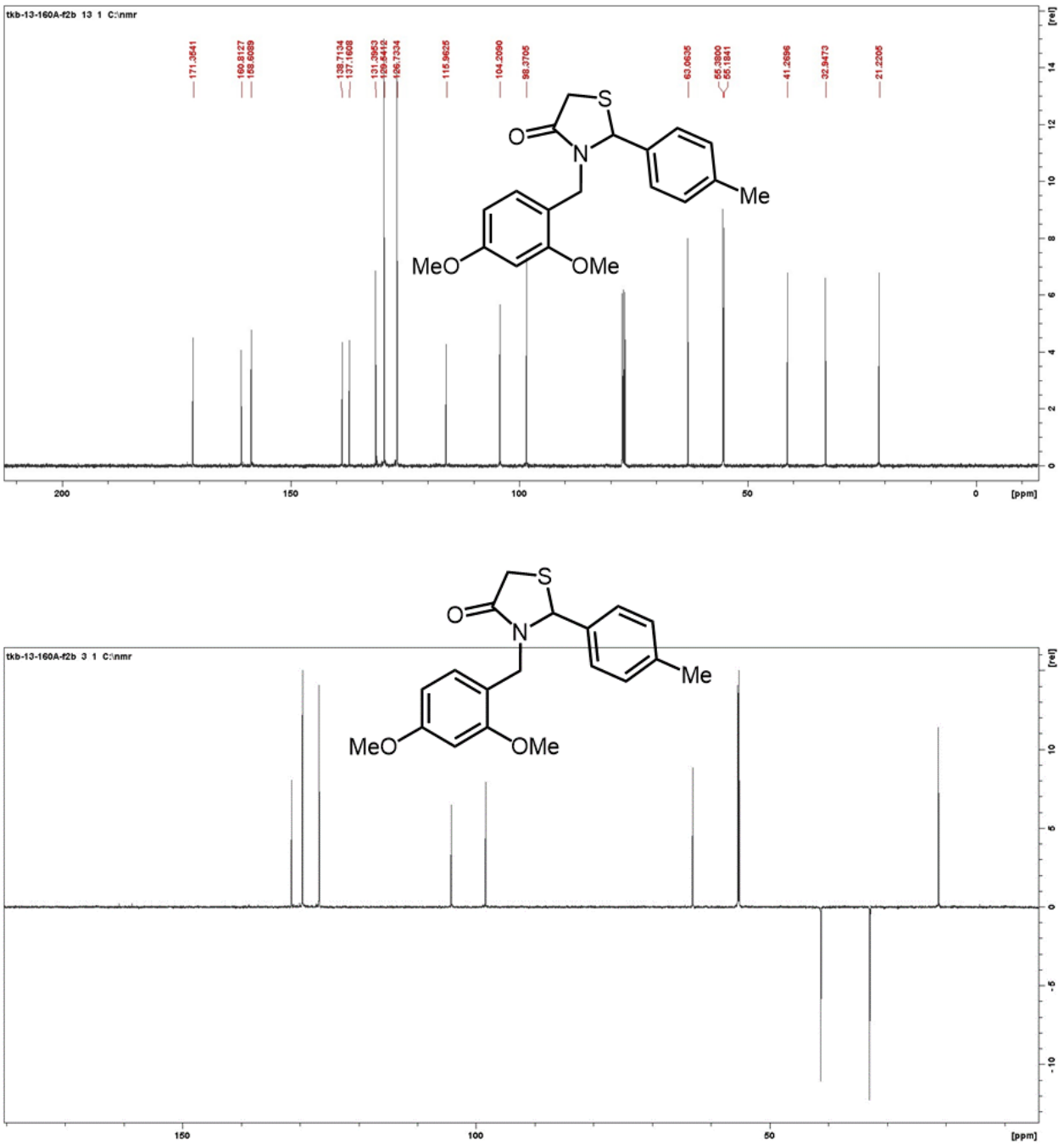


Compound 5p

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 301.8 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.09 – 7.02 (m, 1H), 6.44 – 6.41 (m, 2H), 5.48 (d, *J* = 2.0 Hz, 1H), 4.92 (d, *J* = 14.6 Hz, 1H), 3.90 – 3.69 (m, 9H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 160.8, 158.6, 138.7, 137.2, 131.4, 129.5, 126.7, 116.0, 104.2, 98.4, 63.1, 55.4, 55.2, 41.3, 32.9, 21.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{21}NO_3S$, 343.1242, found 343.1248.

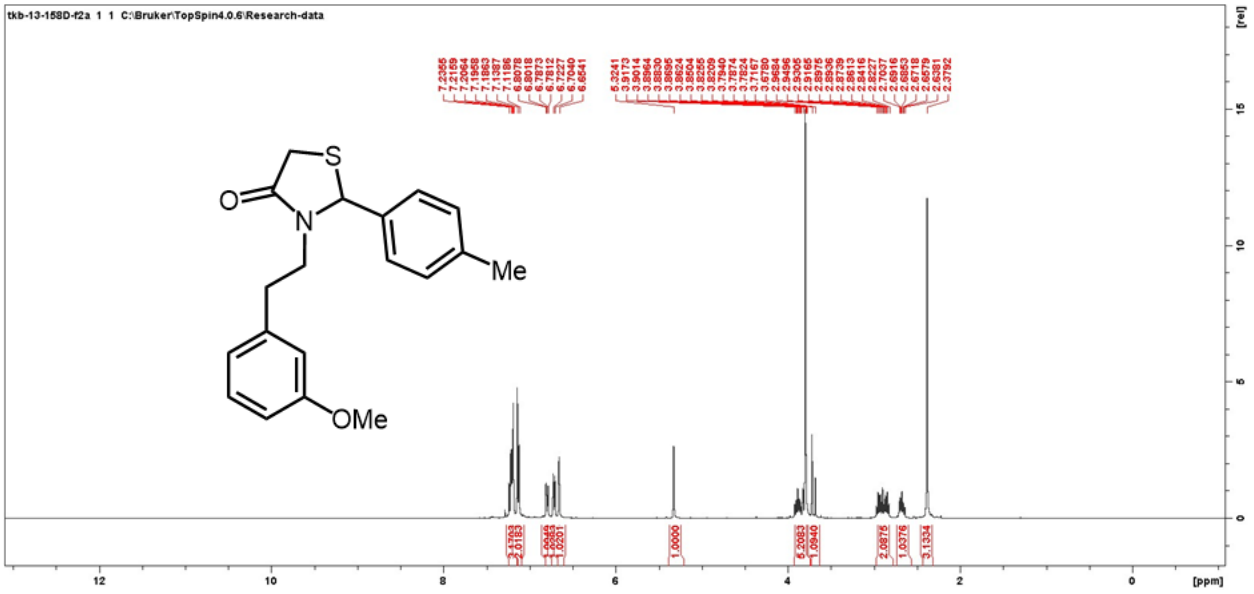


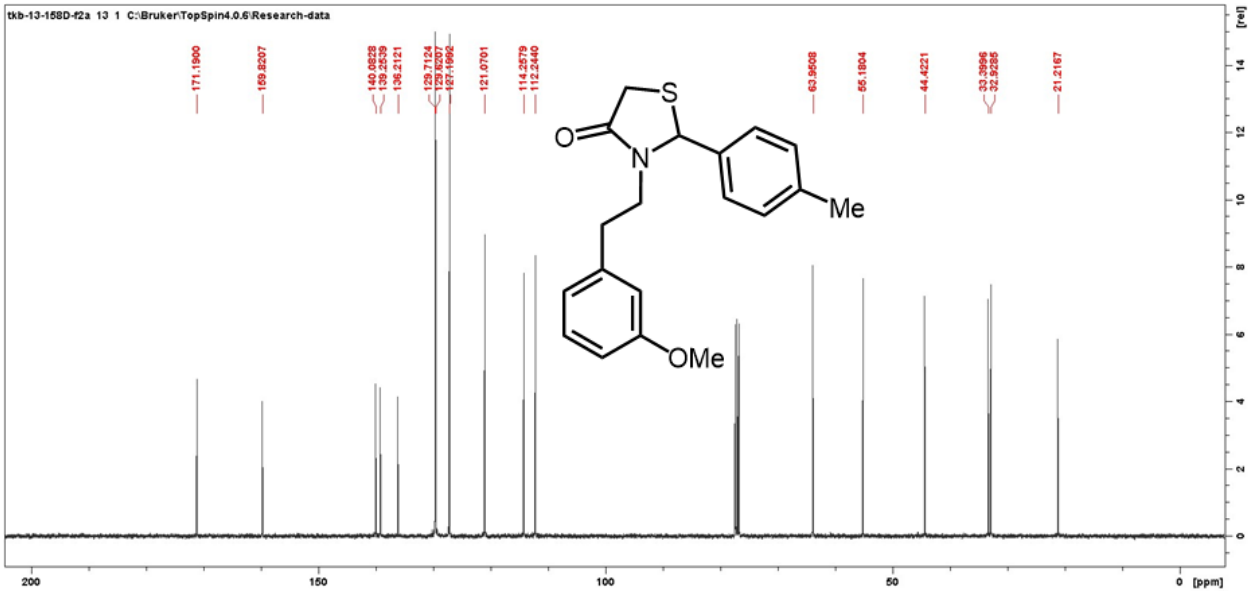


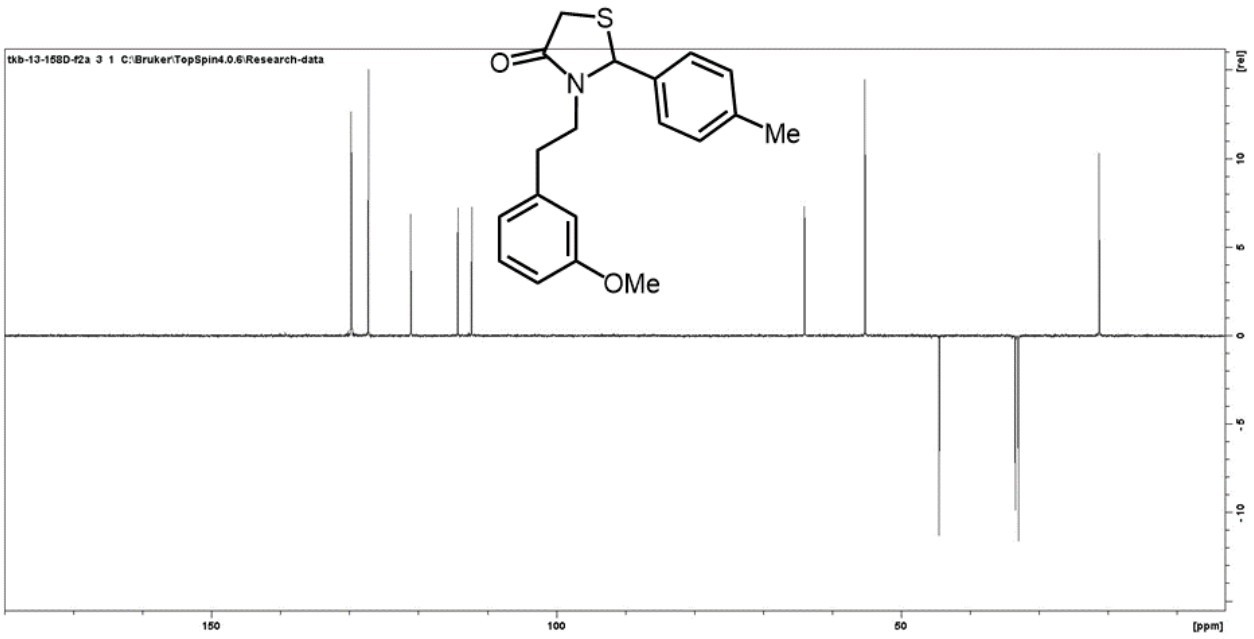
Compound 5q

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 278 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 3H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.79 (dd, *J* = 8.3, 2.6 Hz, 1H),

6.71 (dd, J = 7.5, 1.5 Hz, 1H), 6.65 (t, J = 2.0 Hz, 1H), 5.32 (d, J = 2.0 Hz, 1H), 3.94 – 3.74 (m, 2H), 3.79 (s, 3H), 3.70 (d, J = 15.5 Hz, 1H), 2.90 (ddt, J = 30.1, 13.1, 7.6 Hz, 2H), 2.67 (ddd, J = 13.5, 7.8, 5.4 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 159.8, 140.1, 139.3, 136.2, 130.2, 129.7, 129.6, 127.4, 127.2, 121.1, 114.3, 112.2, 63.9, 55.2, 44.4, 33.4, 32.9, 21.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{21}NO_2S$, 327.1293, found 327.1298.

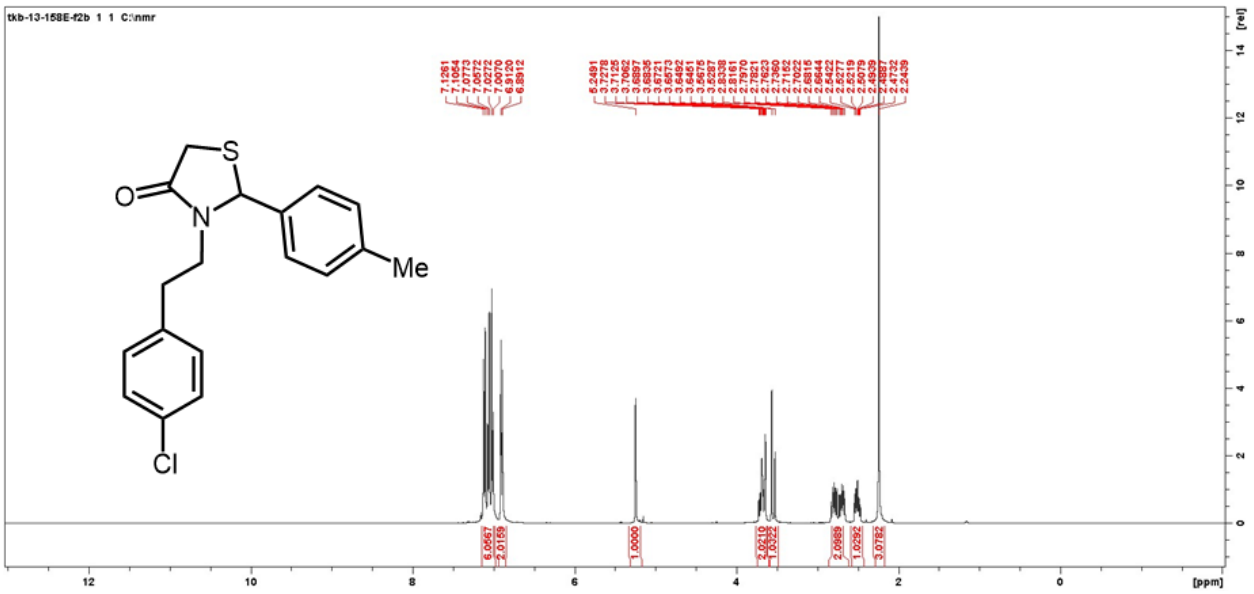






Compound 5r

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 268.1 mg, 81%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 – 7.00 (m, 6H), 6.90 (d, *J* = 8.3 Hz, 2H), 5.25 (s, 1H), 3.73 – 3.65 (m, 2H), 3.55 (d, *J* = 15.5 Hz, 1H), 2.86 – 2.64 (m, 2H), 2.51 (ddd, *J* = 13.9, 8.3, 5.8 Hz, 1H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.3, 139.4, 136.9, 136.1, 132.4, 130.1, 129.8, 129.0, 128.7, 128.6, 127.2, 126.7, 63.9, 44.3, 32.9, 32.7, 21.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{18}ClNOS$, 331.0798, found 331.0795.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N
Me
Cl
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[ppm]


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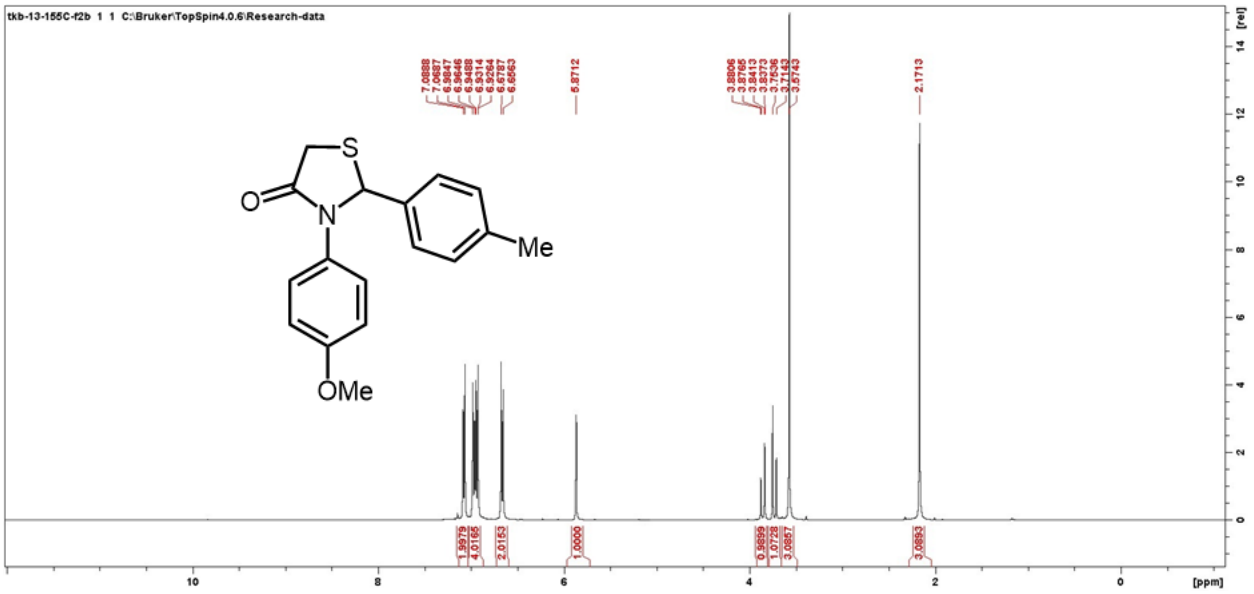
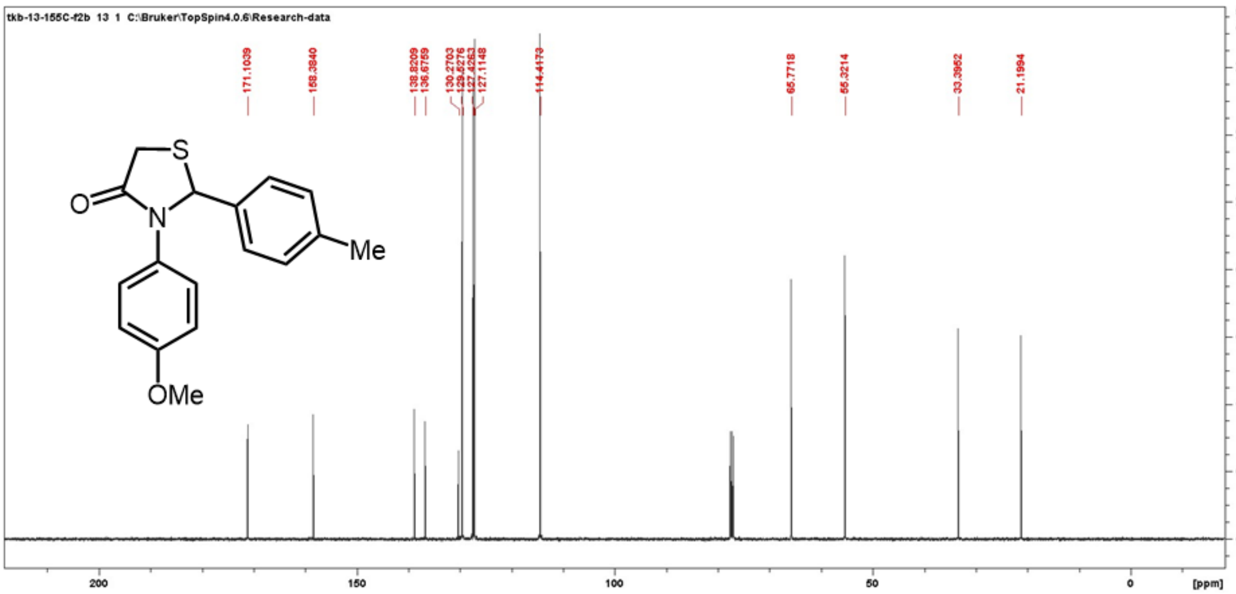
32.6577
21.2480
S
O
N
Me
Cl
[rel]
[ppm]

Compound 5s

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 224.3 mg, 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.1 Hz, 2H), 7.01 – 6.90 (m, 4H), 6.68 (d, *J* = 8.1 Hz, 2H), 5.87 (d, *J* = 1.7 Hz, 1H), 3.86 (d, *J* = 15.8 Hz, 1H), 3.73 (d, *J* = 15.8 Hz, 1H), 3.57 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 158.4, 138.8, 136.7, 130.3, 129.5, 127.4, 127.1, 114.4, 65.8, 55.3, 33.4, 21.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{17}NO_2S$, 299.0980, found 299.0984.

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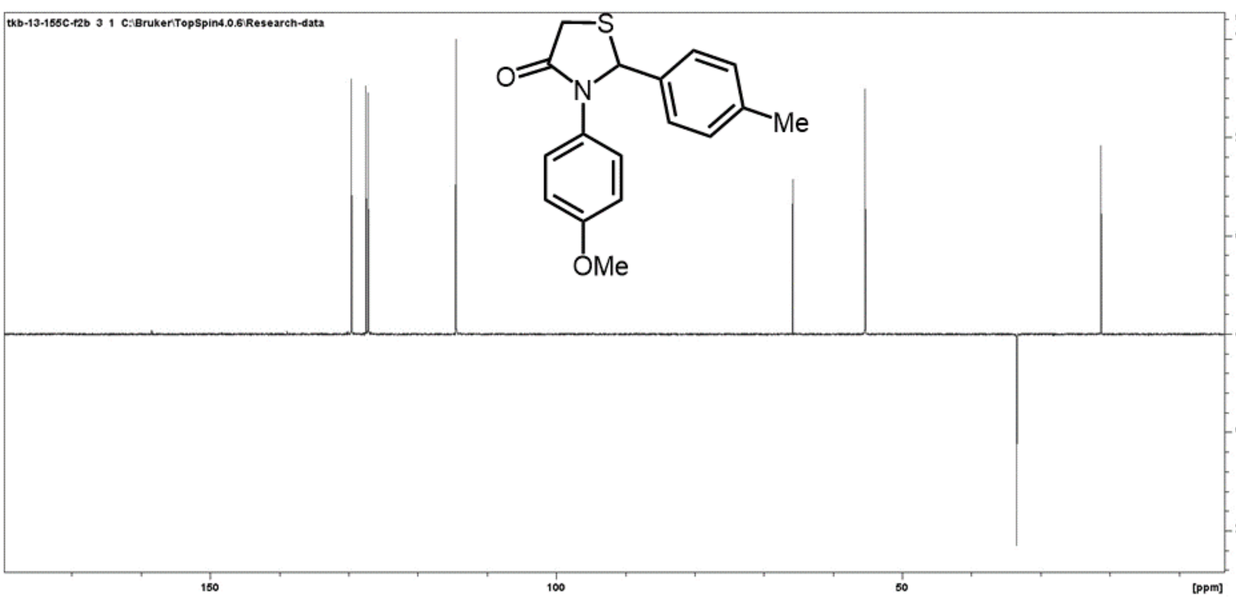
[ppm]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S
O
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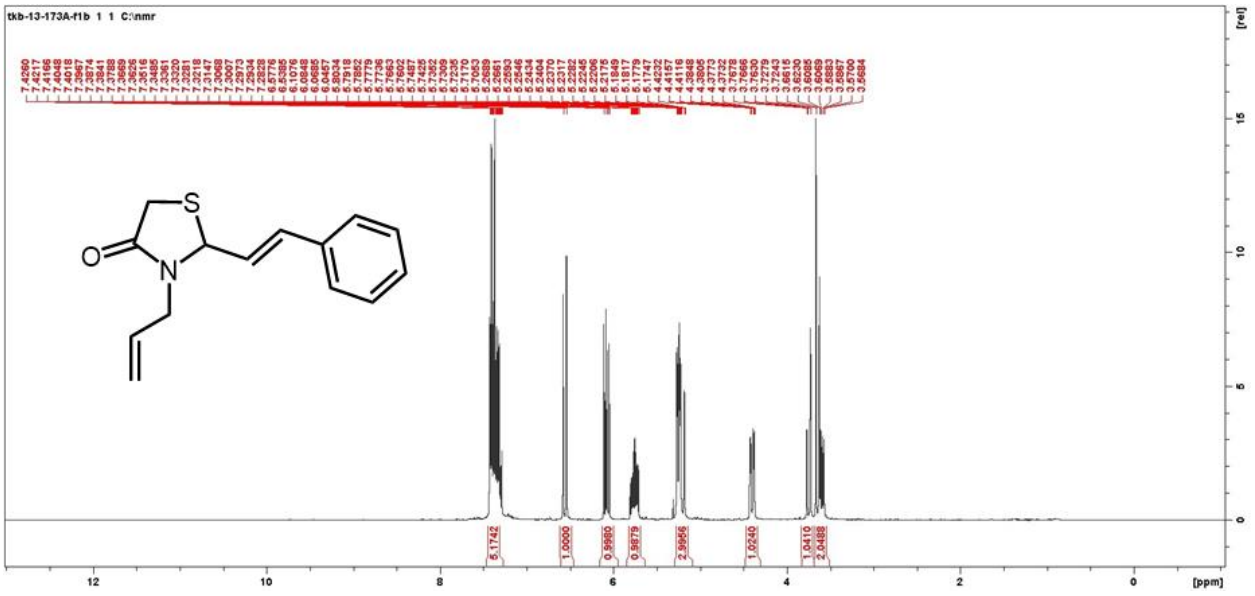
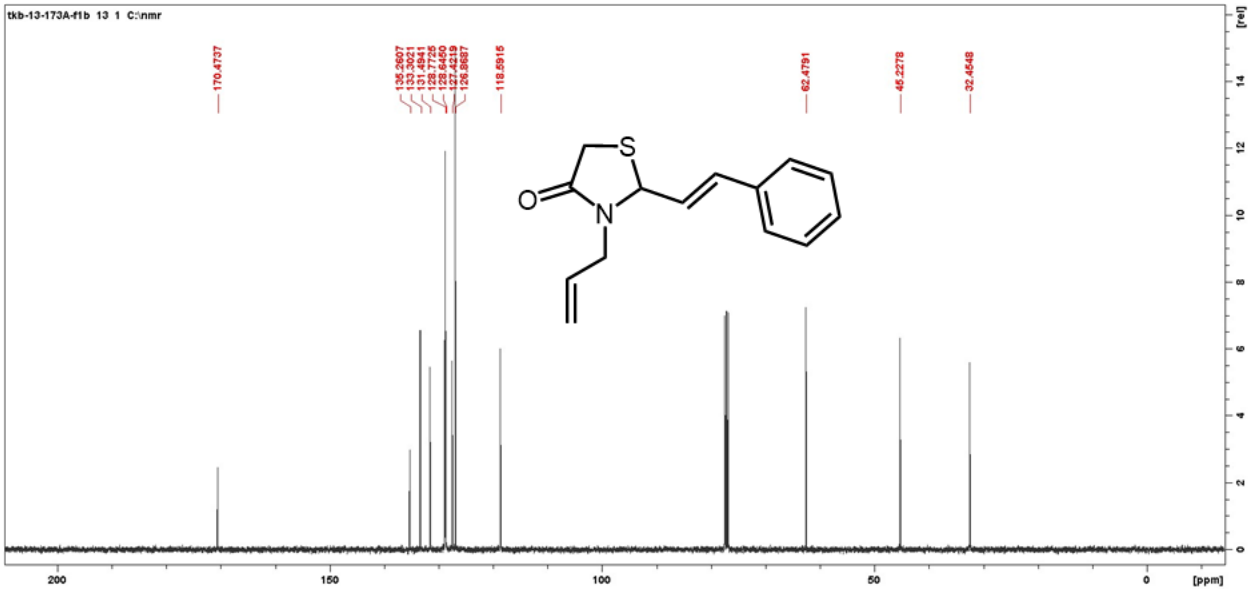
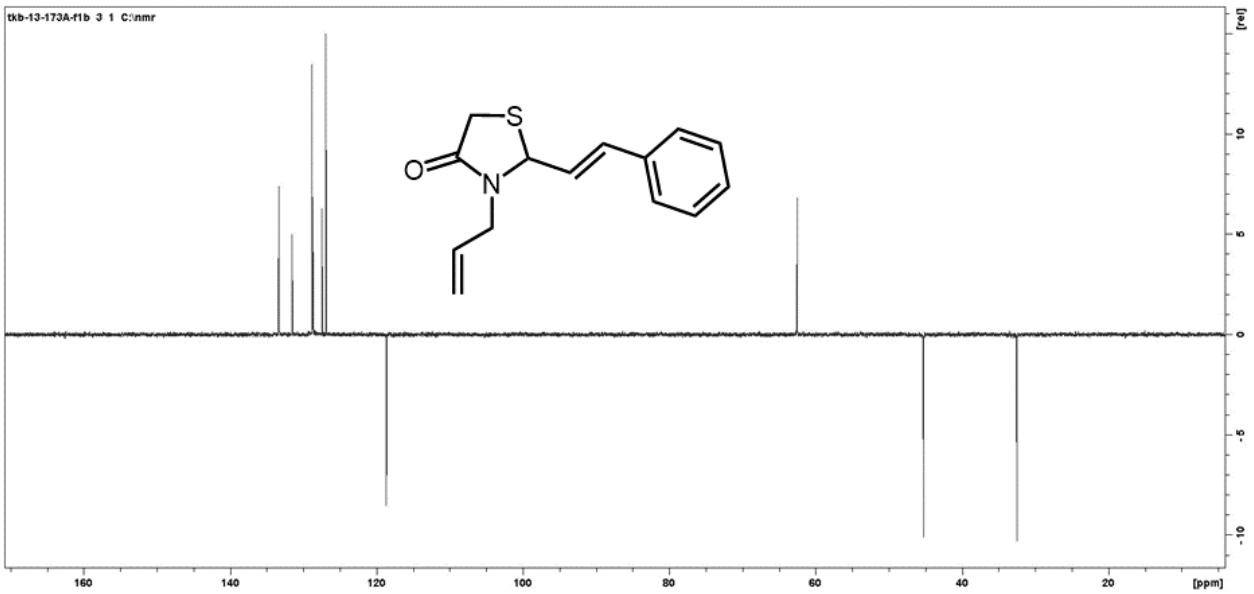
[rel]
[ppm]

Compound 6a

Prepared in 2.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 446 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.08 (dd, *J* = 15.6, 9.1 Hz, 1H), 5.75 (dddd, *J* = 17.4, 10.2, 7.3, 4.7 Hz, 1H), 5.27 – 5.15 (m, 3H), 4.40 (ddt, *J* = 15.4, 4.7, 1.7 Hz, 1H), 3.75 (d, *J* = 15.5 Hz, 1H), 3.68 – 3.52 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 135.3, 133.3, 131.5, 128.8, 128.6, 127.4, 126.9, 118.6, 62.5, 45.2, 32.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{14}H_{15}NOS$, 245.0874, found 245.0879.

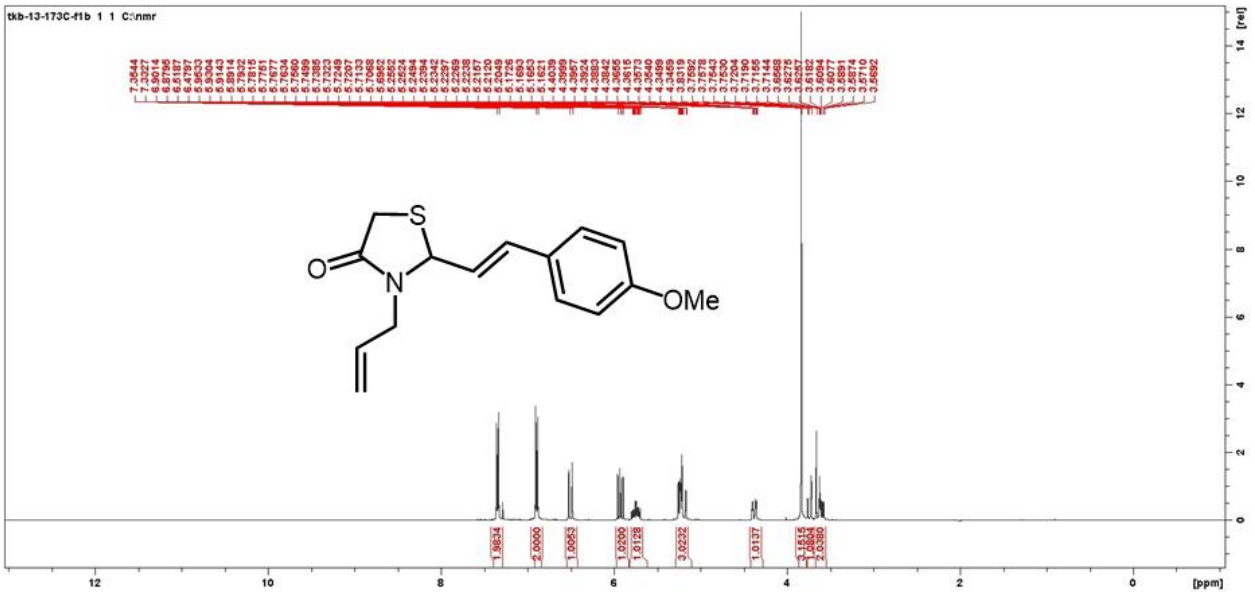






Compound 6b

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 264 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.6 Hz, 2H), 6.89 (d, *J* = 7.6 Hz, 2H), 6.50 (d, *J* = 15.6 Hz, 1H), 5.92 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.74 (dddd, *J* = 17.3, 10.2, 7.2, 4.7 Hz, 1H), 5.28 – 5.19 (m, 2H), 5.23 – 5.14 (m, 1H), 4.38 (ddt, *J* = 15.4, 4.7, 1.7 Hz, 1H), 3.83 (s, 3H), 3.74 (d, *J* = 15.5 Hz, 1H), 3.64 (d, *J* = 15.5 Hz, 1H), 3.64 – 3.54 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 160.0, 133.0, 131.5, 128.2, 127.9, 125.0, 118.5, 114.2, 62.8, 55.3, 45.2, 32.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{15}H_{17}NO_2S$, 275.0980, found 275.0984.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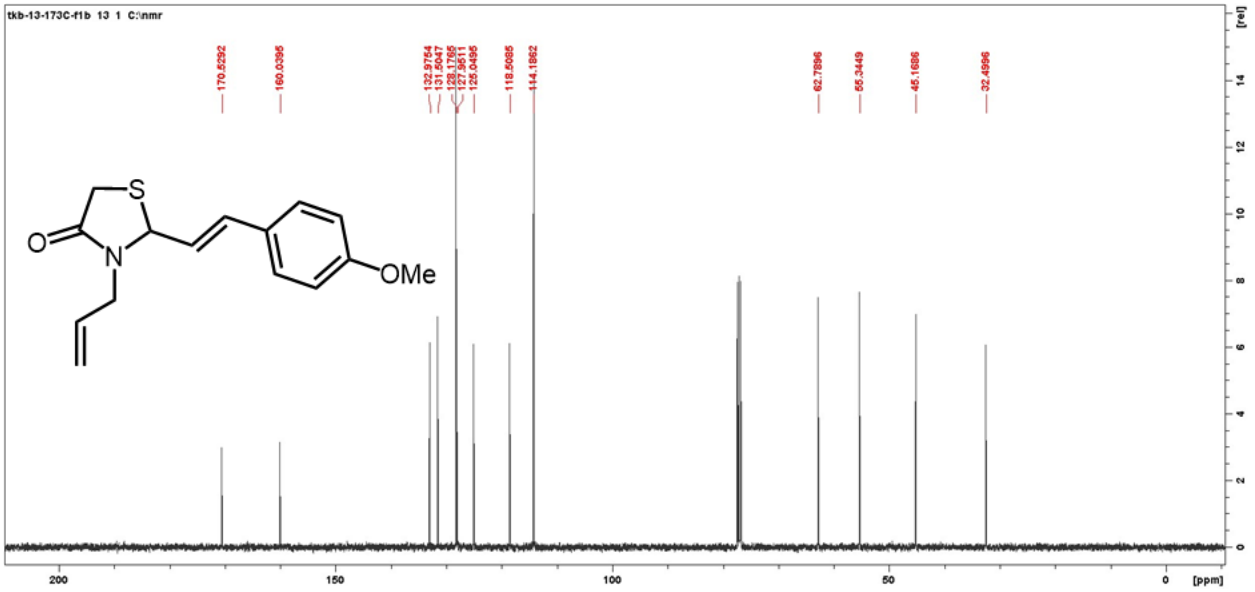
O
N
OMe
[ppm]
[rel]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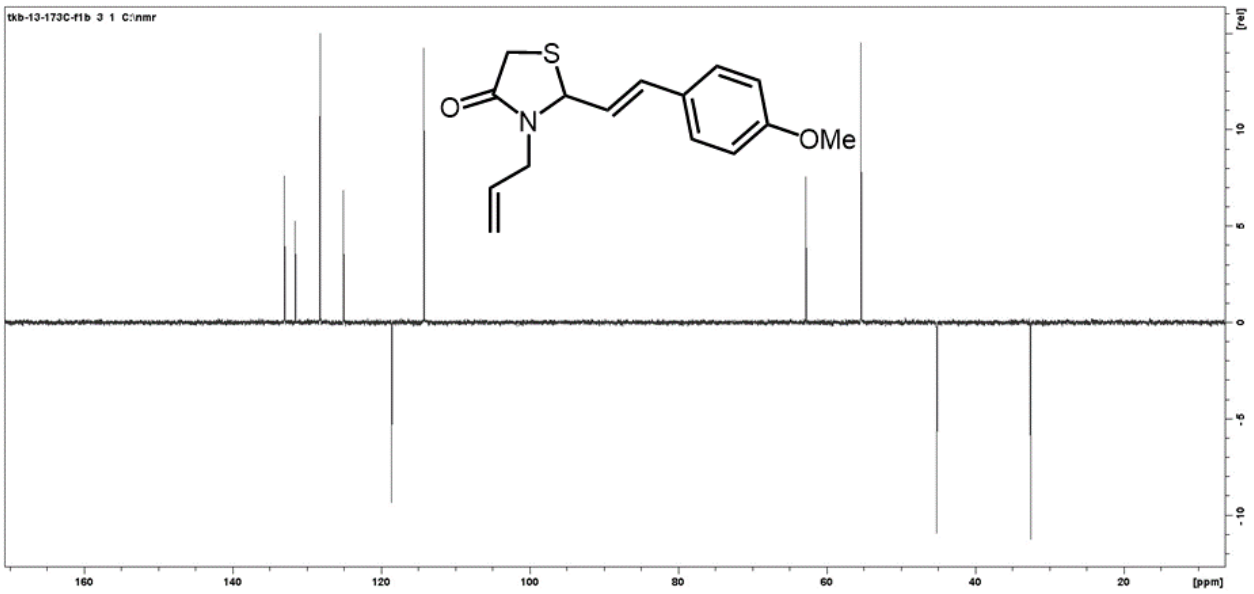
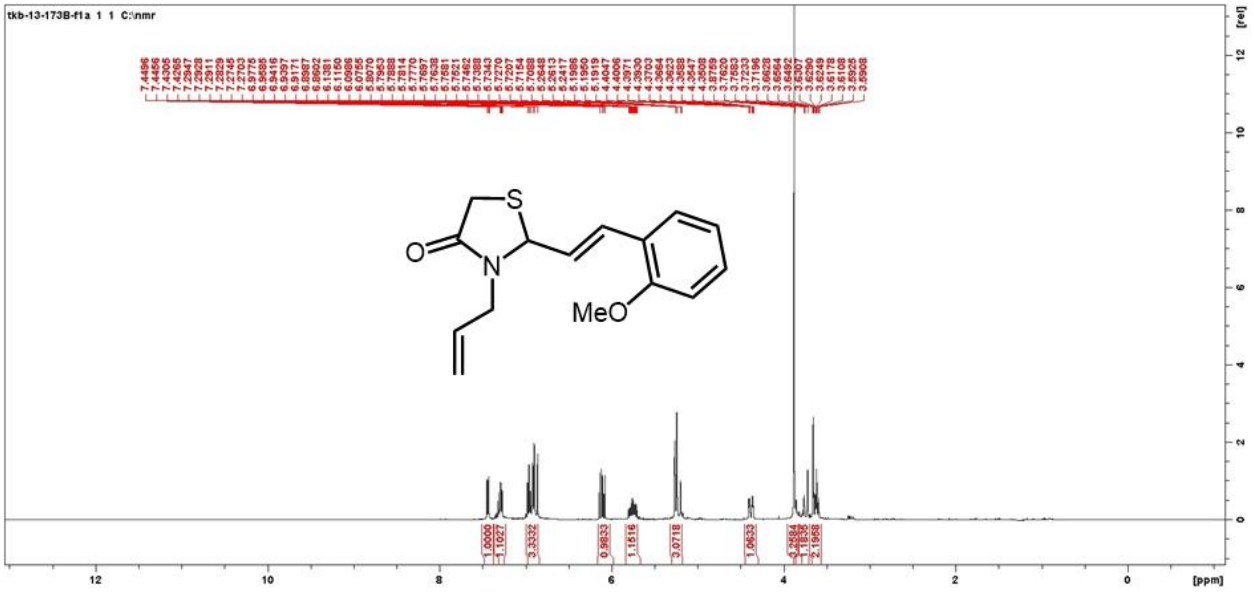
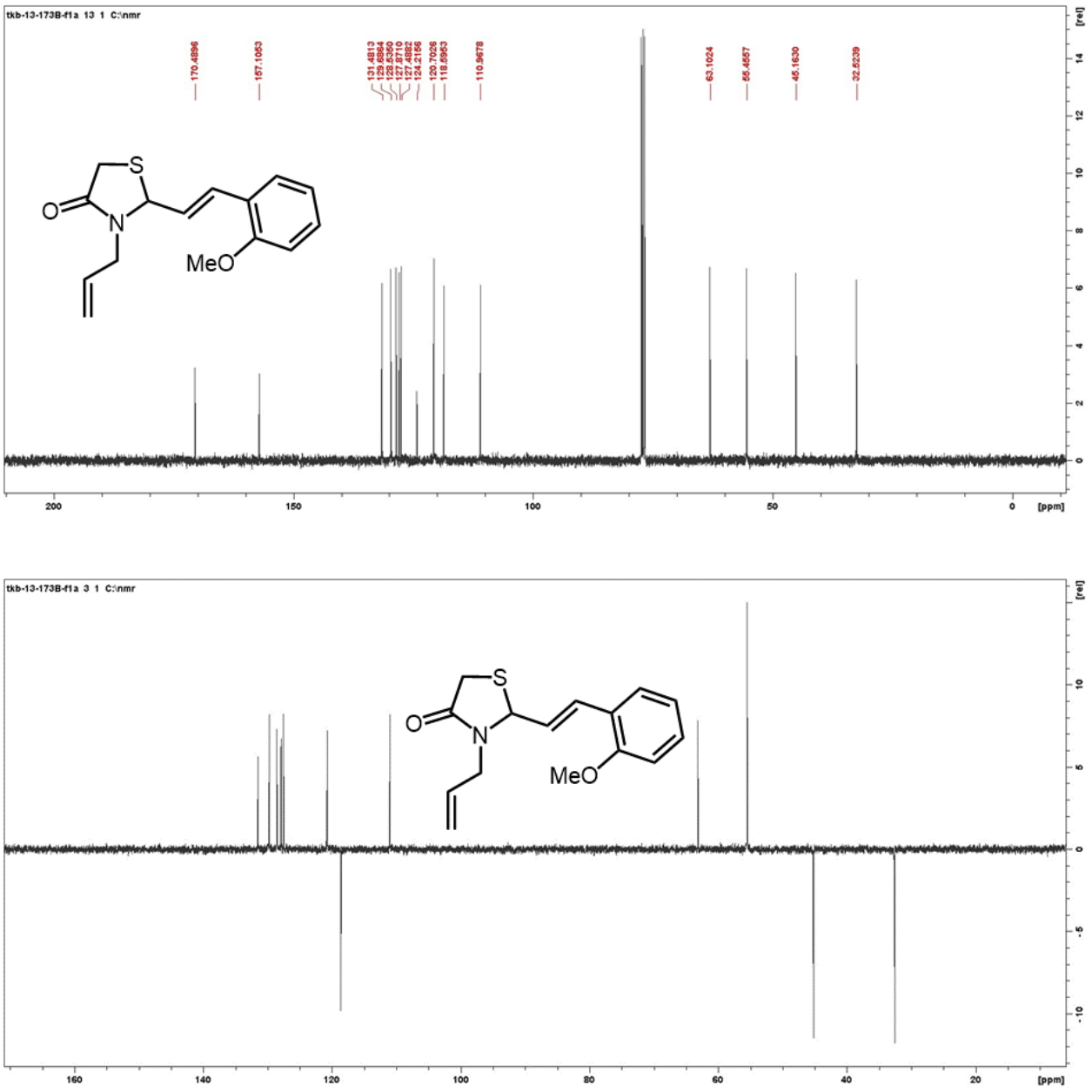


Compound 6c

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 240 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.6 Hz, 1H), 7.29 – 7.27 (m, 1H), 7.02 – 6.84 (m, 3H), 6.11 (dd, *J* = 15.8, 9.2 Hz, 1H), 5.83 – 5.66 (m, 1H), 5.26 (t, *J* = 1.5 Hz, 1H), 5.27 – 5.15 (m, 2H), 4.38 (ddt, *J* = 15.3, 4.7, 1.7 Hz, 1H), 3.88 (s, 3H), 3.65 (dd, *J* = 6.4, 5.3 Hz, 1H), 3.64 – 3.55 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 157.1, 131.5, 129.8, 128.5, 127.9, 127.5, 124.2, 120.7, 118.6, 111.0, 63.1, 55.5, 45.2, 32.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{15}H_{17}NO_2S$, 275.0980, found 275.0984.



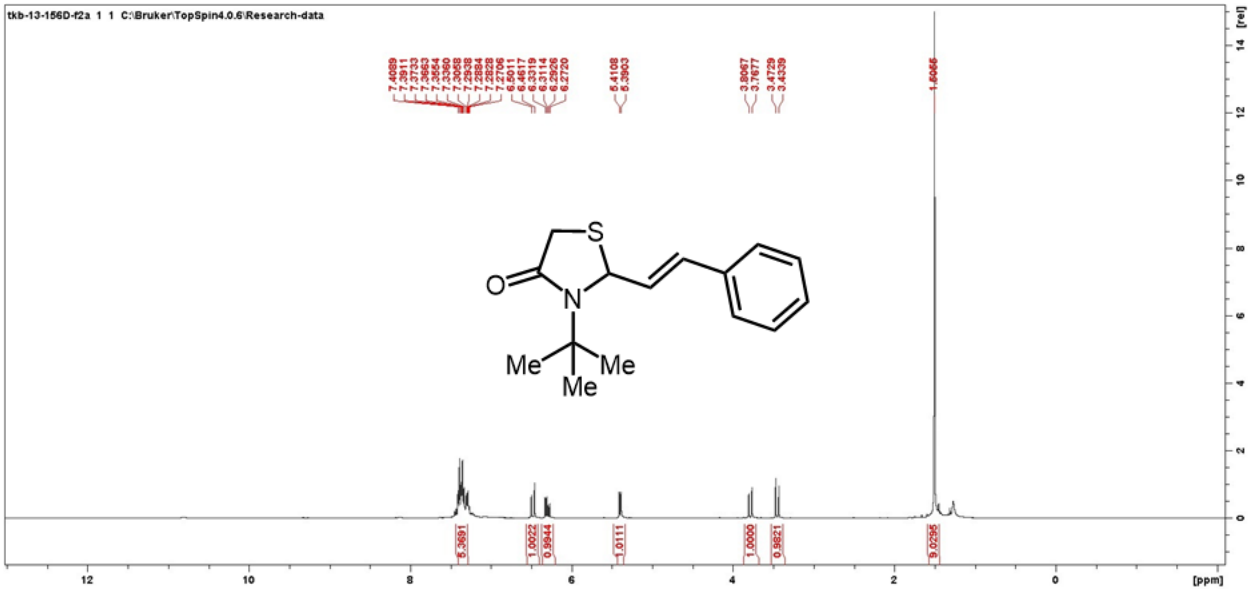


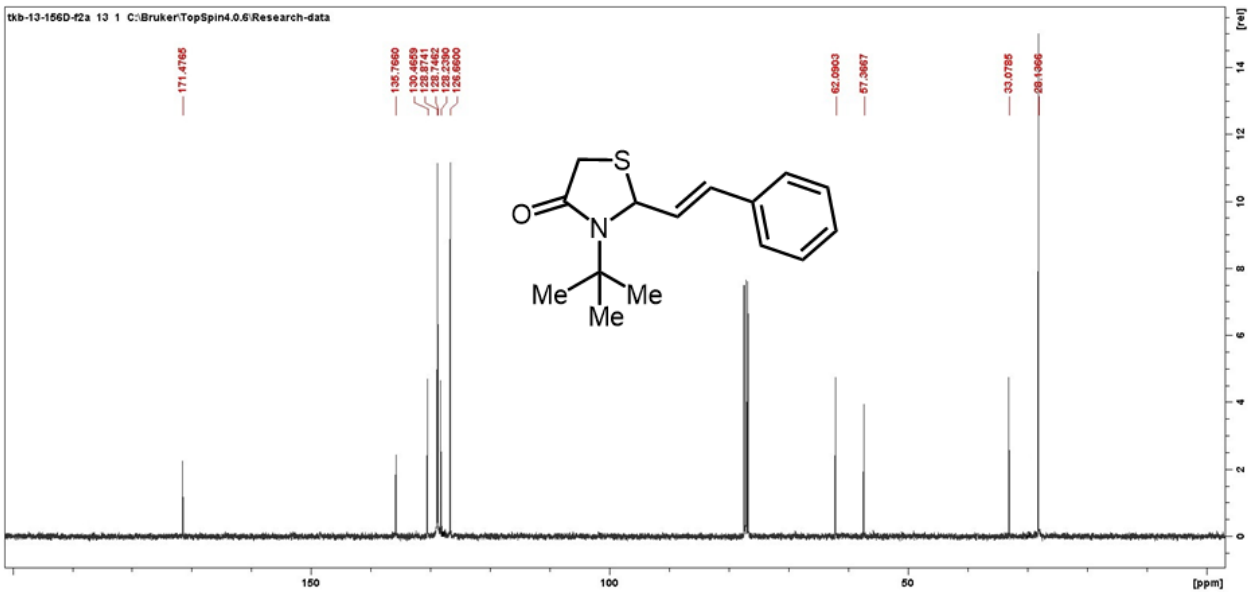
Compound 6d

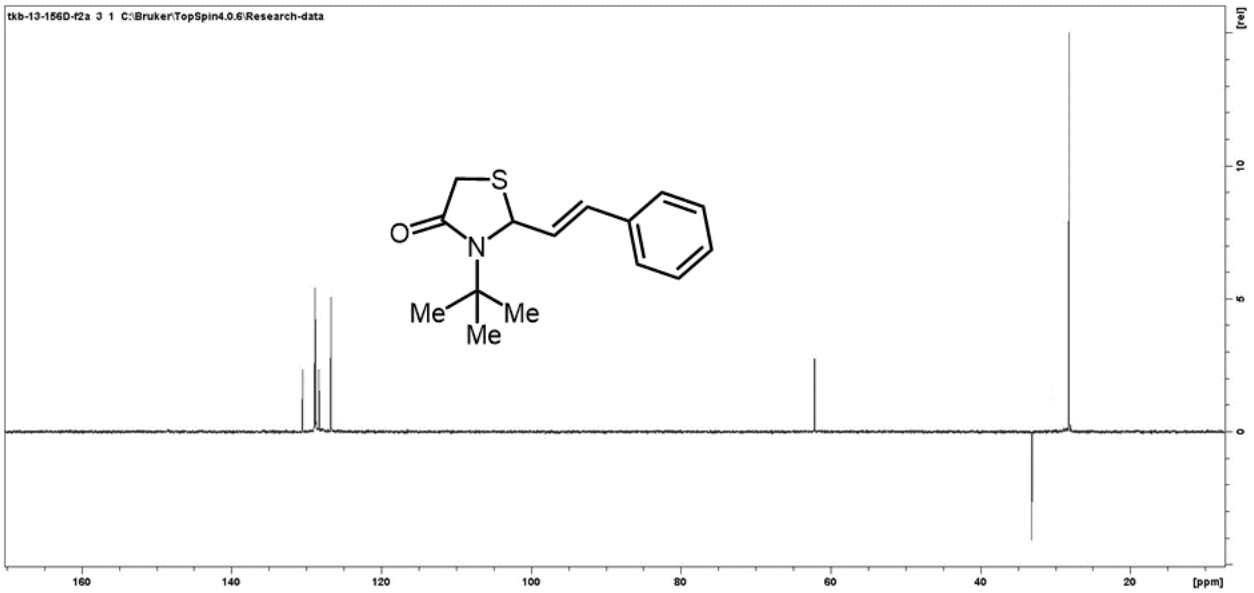
Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25). Oily substance. Yield = 219.2 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 5H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.30 (dd, *J* = 15.7, 8.2 Hz, 1H), 5.40 (d, *J* = 8.3 Hz, 1H), 3.79 (d, *J* = 15.7 Hz, 1H), 3.45 (d, *J* = 15.6 Hz, 1H), 1.51 (s, 9H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 171.5, 135.8, 130.5, 128.9, 128.7, 128.2, 126.7, 62.1, 57.4, 33.1, 28.1.

HRMS-EI$^+$ (*m/z*): calc for $C_{15}H_{19}NOS$, 261.1187, found 261.1194.

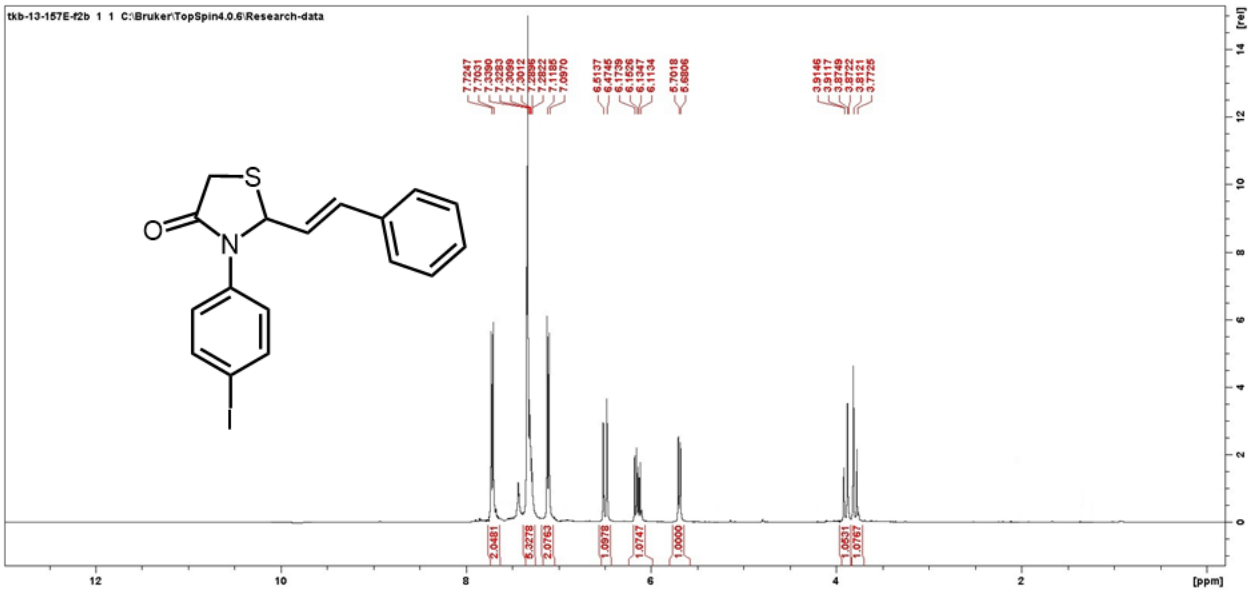


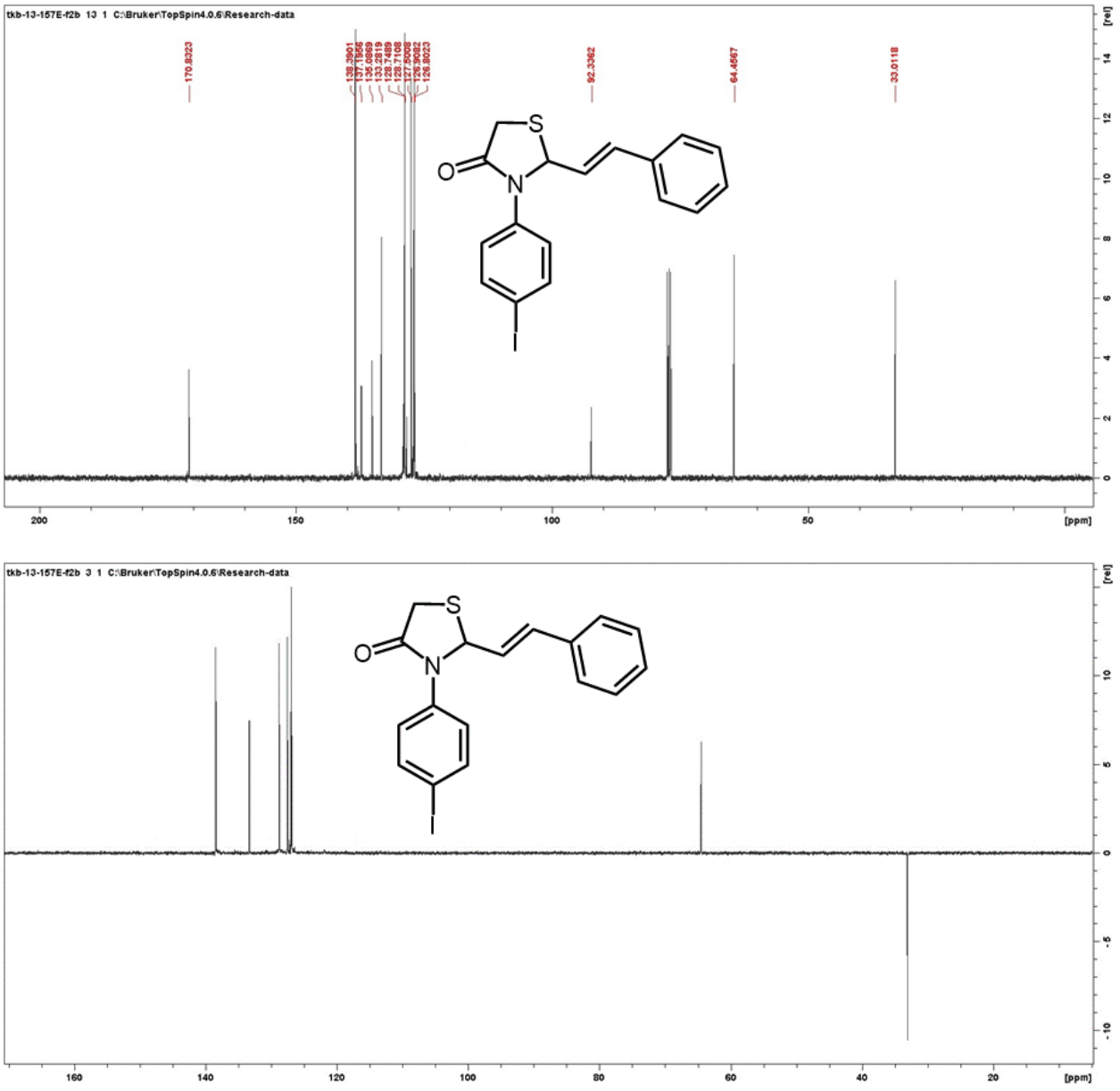




Compound 6e

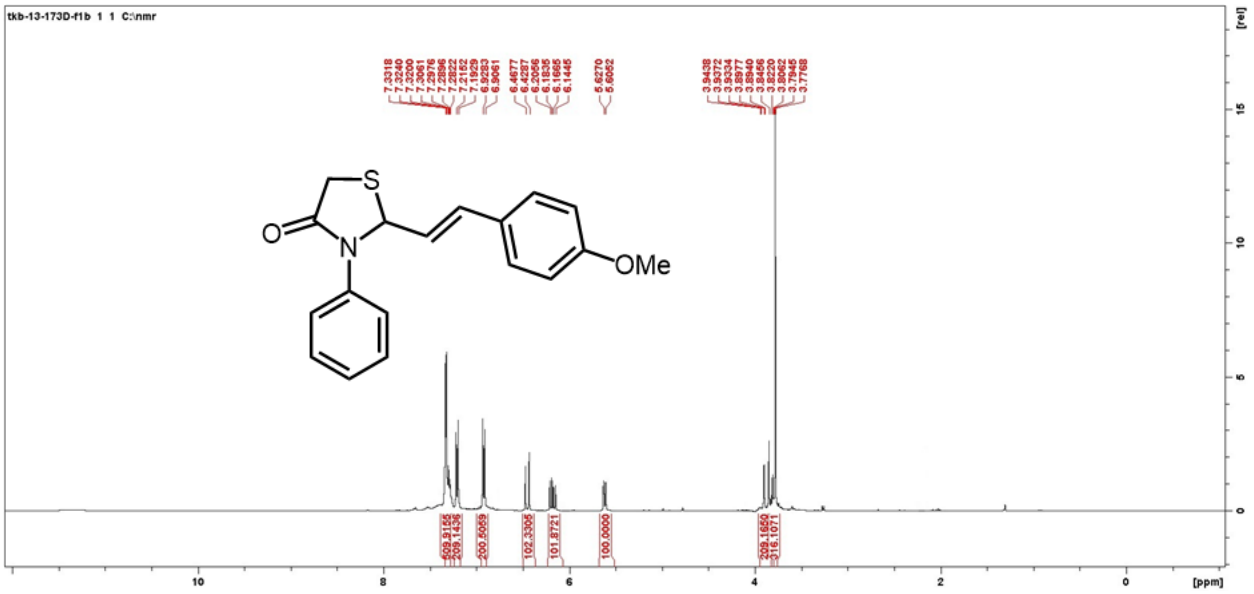
Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 358.1 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.1 Hz, 2H), 7.36 – 7.28 (m, 5H), 7.10 (d, *J* = 7.1 Hz, 2H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.14 (dd, *J* = 15.7, 8.5 Hz, 1H), 5.69 (d, *J* = 8.5 Hz, 1H), 3.89 (d, *J* = 15.9 Hz, 1H), 3.79 (d, *J* = 15.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 138.4, 137.2, 135.1, 133.3, 128.7, 128.7, 127.5, 126.9, 126.8, 92.3, 64.5, 33.0. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{14}INOS$, 406.9841, found 406.9844.





Compound 6f

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (35:65). Oily substance. Yield = 286.1 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 5H), 7.20 (d, *J* = 7.2 Hz, 2H), 6.91 (d, d, *J* = 7.2 Hz, 2H), 6.45 (d, *J* = 15.6 Hz, 1H), 6.18 (dd, *J* = 15.6, 8.8 Hz, 1H), 5.62 (d, *J* = 8.8 Hz, 1H), 3.92 (d, *J* = 15.8 Hz, 1H), 3.83 (d, *J* = 15.8 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.37, 158.91, 133.25, 128.70, 128.56, 127.90, 127.55, 127.33, 126.88, 114.73, 65.33, 55.43, 32.98. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{17}NO_2S$, 311.0980, found 311.0984.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O
N
OMe
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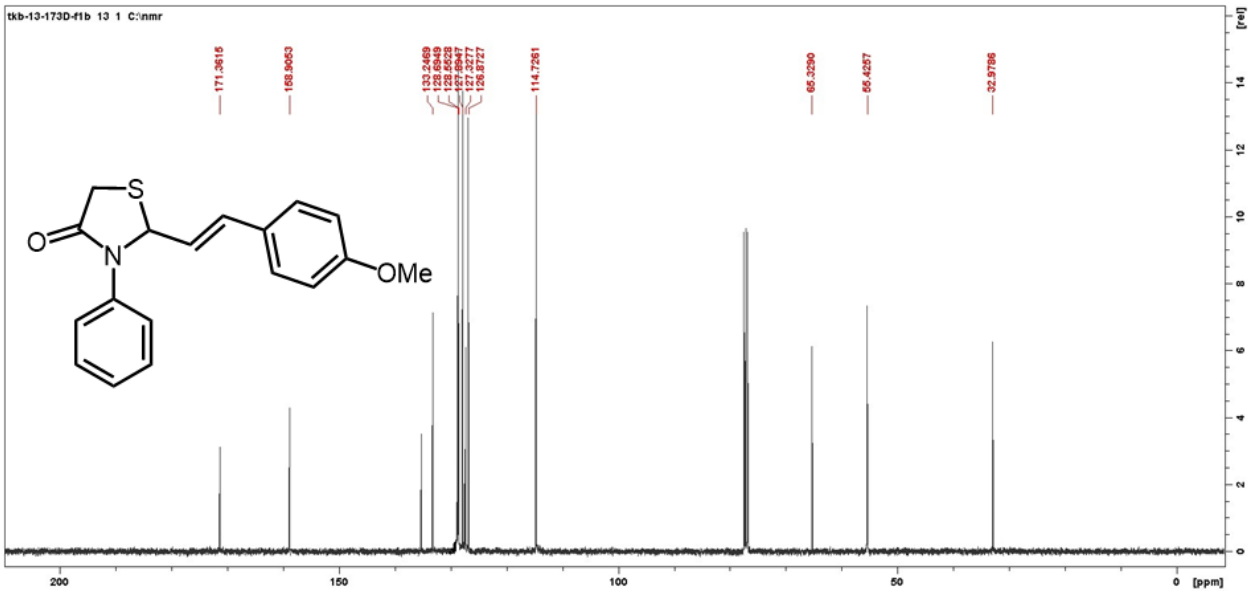
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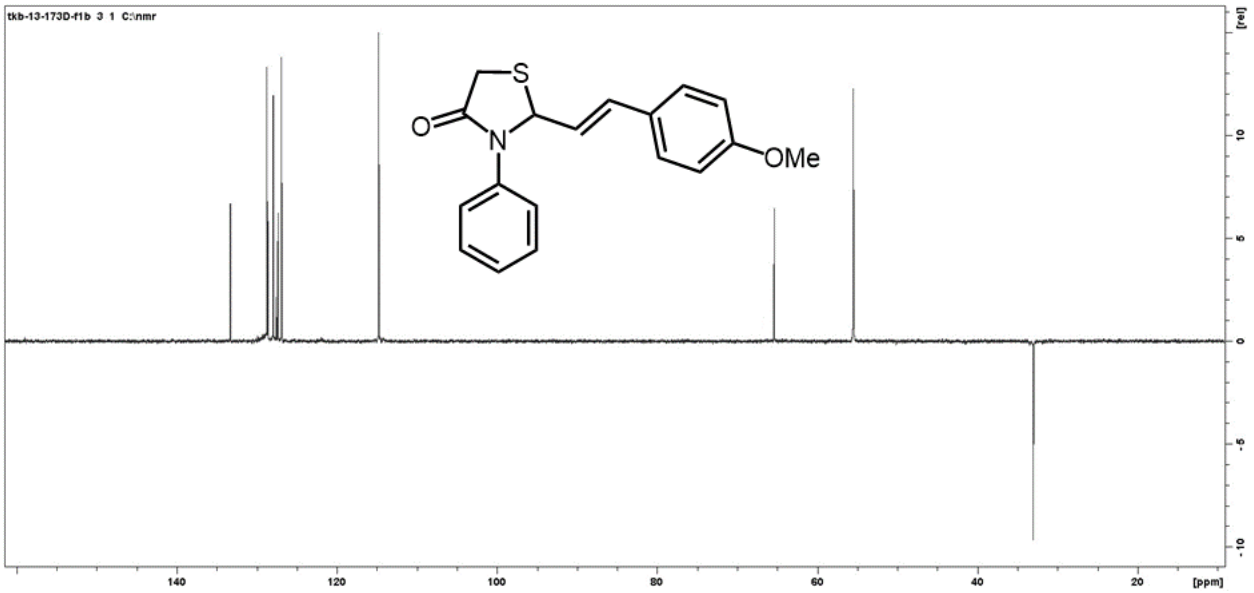
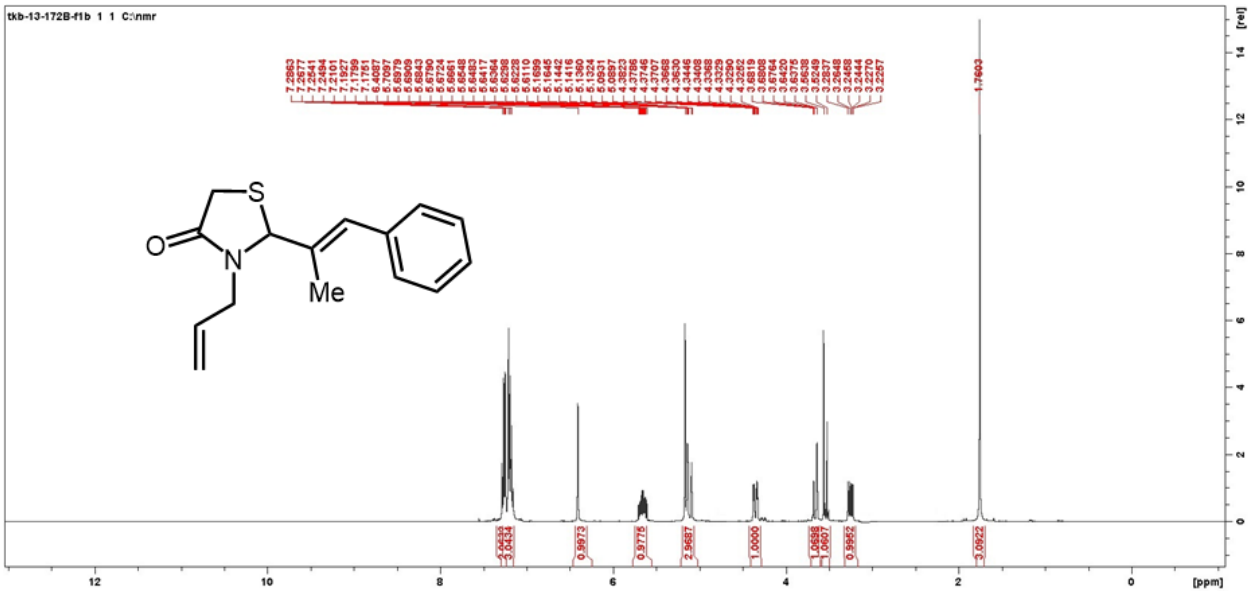
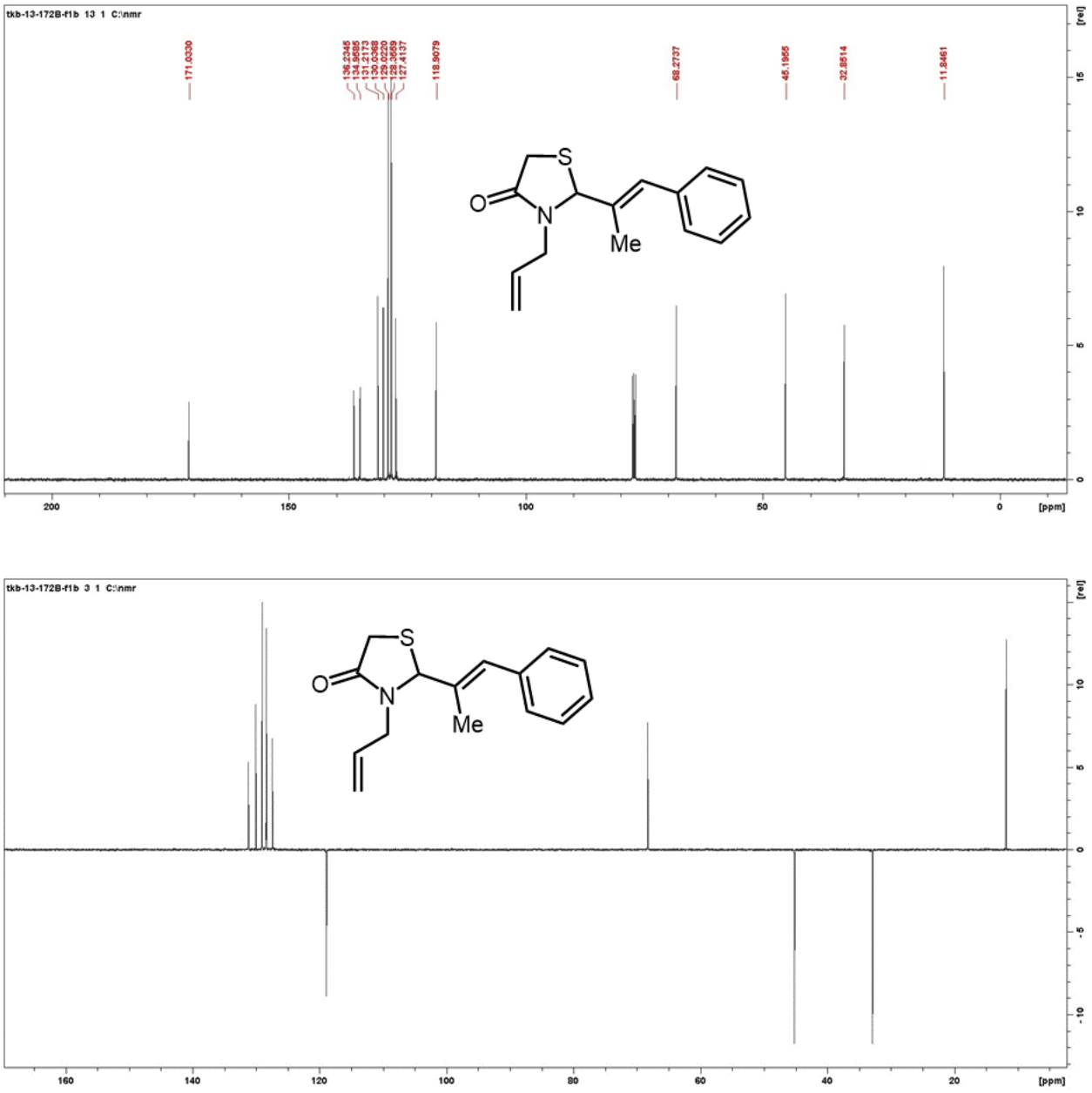


Compound 6g

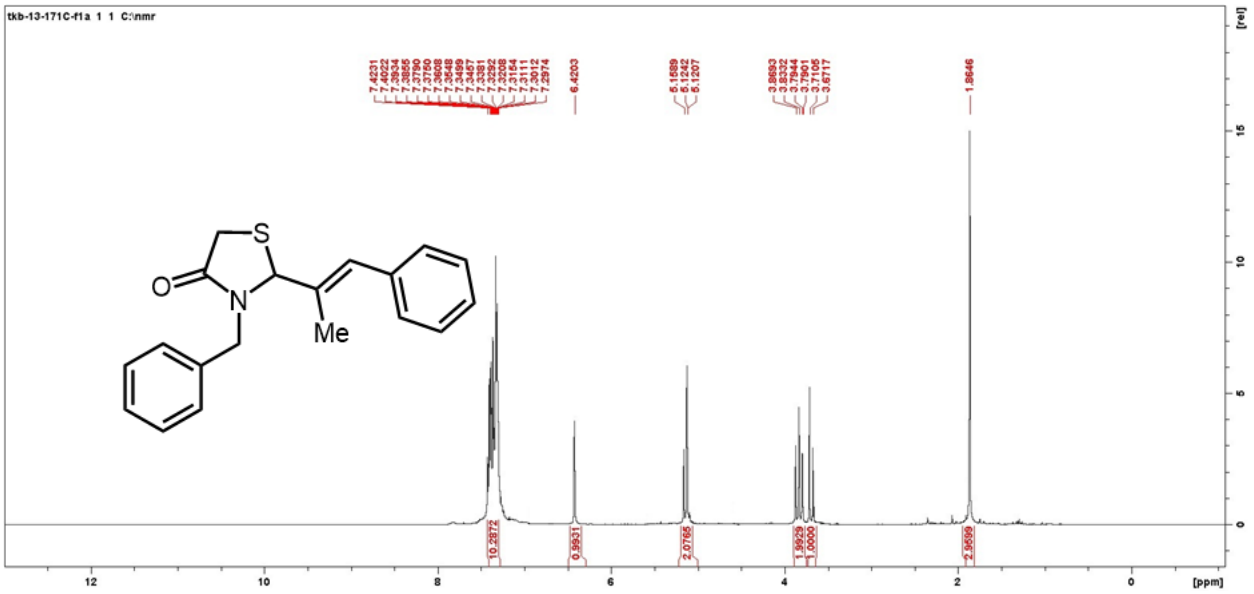
Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 240.9 mg, 93%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.18 (m, 5H), 6.41 (s, 1H), 5.66 (dddd, *J* = 17.0, 10.2, 7.6, 4.7 Hz, 1H), 5.19 – 5.12 (m, 3H), 4.35 (ddt, *J* = 15.1, 4.8, 1.6 Hz, 1H), 3.67 (d, *J* = 15.5 Hz, 1H), 3.54 (d, *J* = 15.5 Hz, 1H), 3.25 (ddq, *J* = 15.1, 7.6, 1.1 Hz, 1H), 1.76 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.04, 136.24, 134.96, 131.22, 130.04, 129.03, 128.36, 127.42, 118.91, 68.28, 45.20, 32.86, 11.85. **HRMS-EI^{+}** (*m/z*): calc for $C_{15}H_{17}NOS$, 259.1031, found 259.1033.





Compound 6h

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 275.1 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 10H), 6.42 (s, 1H), 5.16 – 5.12 (m, 2H), 3.87 – 3.79 (m, 2H), 3.69 (d, *J* = 15.5 Hz, 1H), 1.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 136.2, 135.6, 134.9, 130.3, 129.1, 128.9, 128.6, 128.4, 128.4, 128.1, 128.0, 127.5, 68.2, 46.4, 32.9, 11.8. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{19}NOS$, 309.1187, found 309.1191.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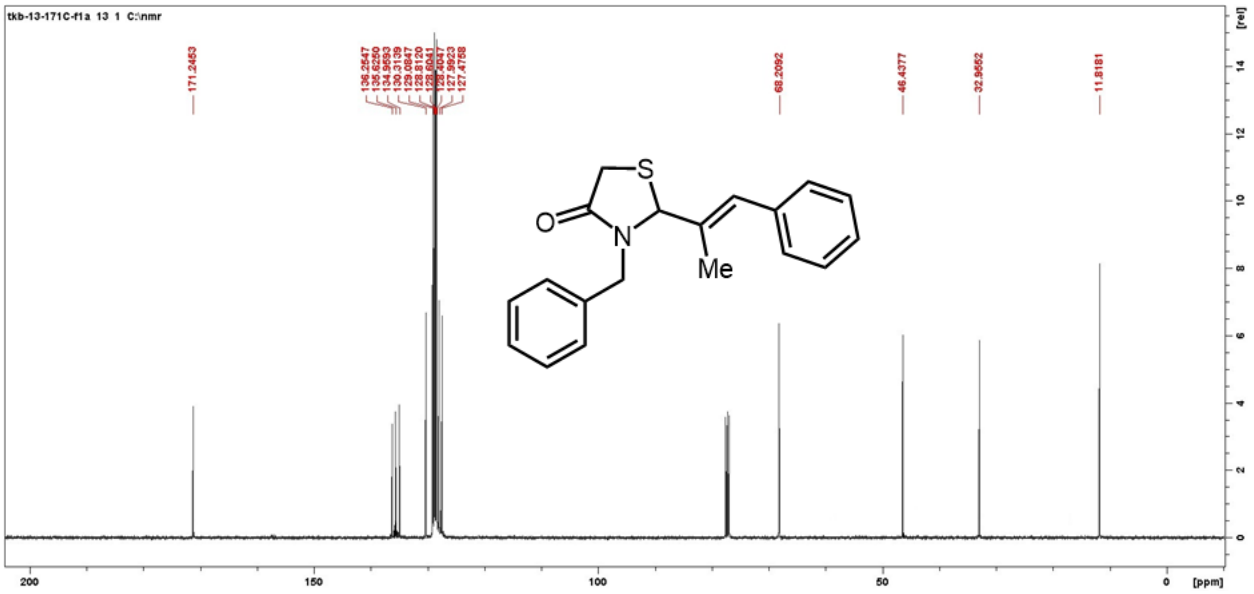
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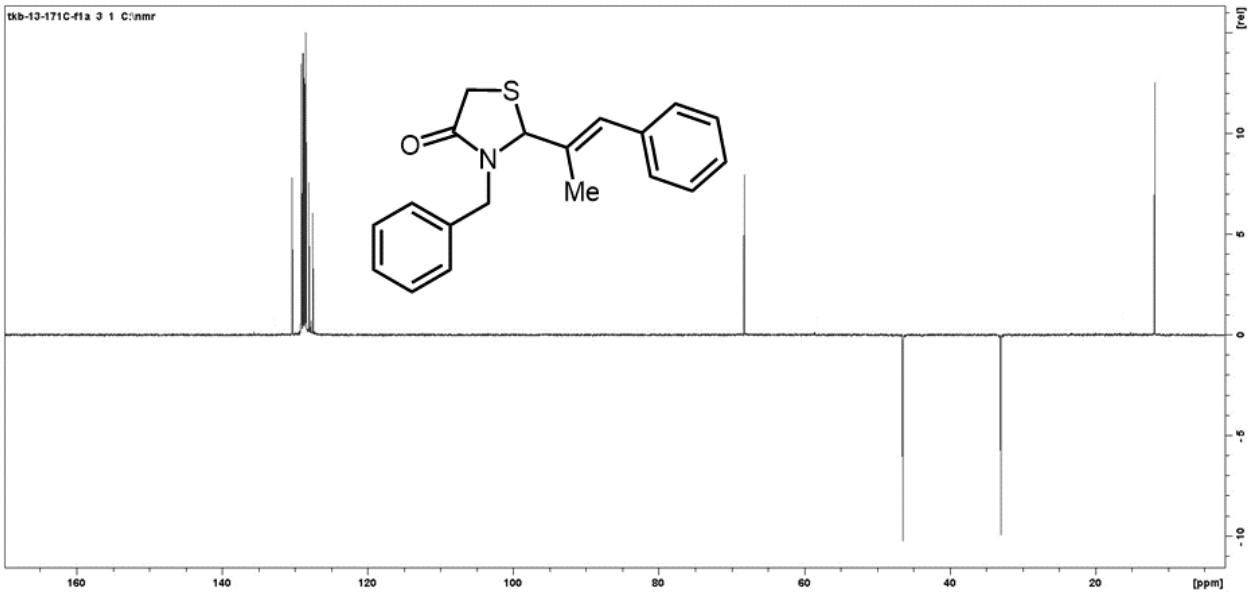
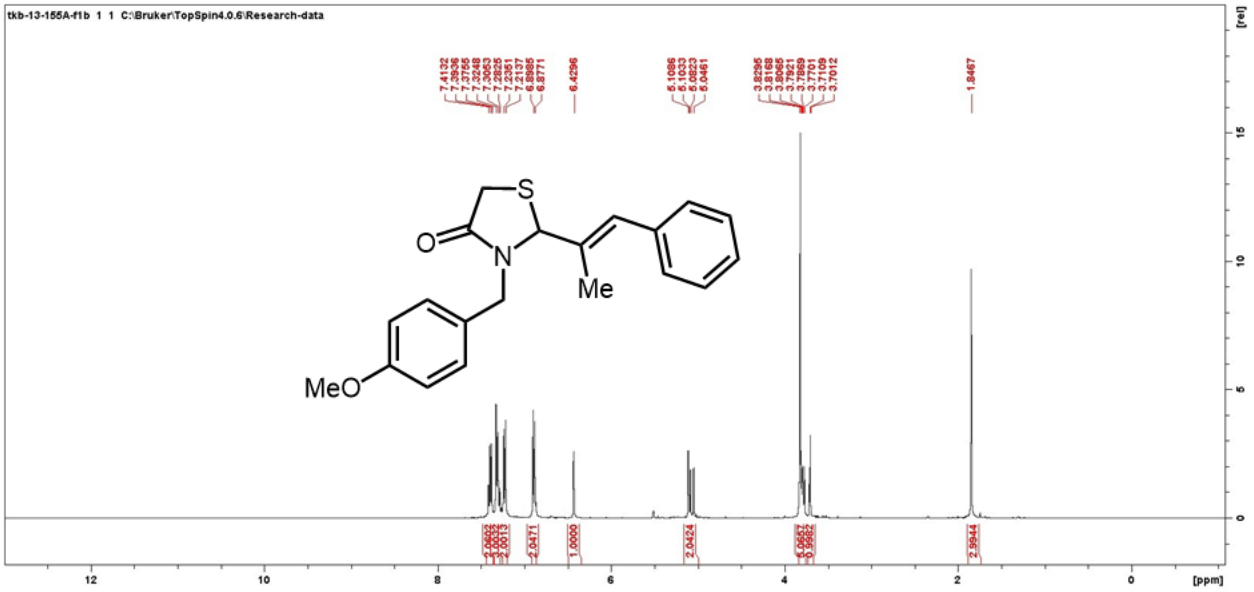
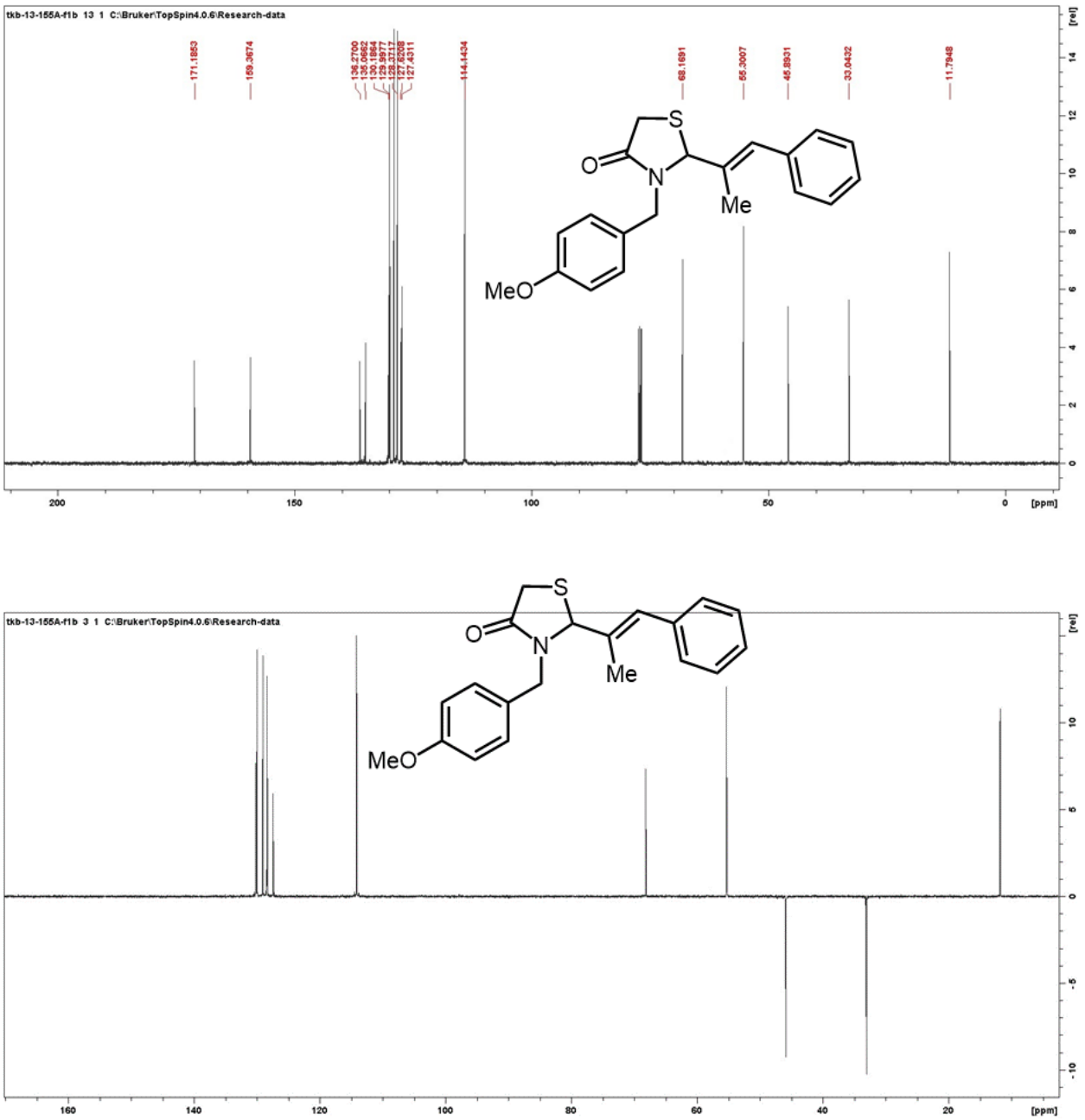


Compound 6i

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 318.7 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 2H), 7.32 – 7.28 (m, 3H), 7.23 – 7.21 (m, 2H), 6.88 (d, *J* = 7.2 Hz, 2H), 6.43 (s, 1H), 5.11 (s, 1H), 5.05 (t, *J* = 13.9 Hz, 1H), 3.82 (s, 3H), 3.85 – 3.75 (m, 2H), 1.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.19, 159.37, 136.27, 135.07, 130.19, 130.00, 129.06, 128.38, 127.62, 127.43, 114.15, 68.17, 55.30, 45.90, 33.05, 11.80. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{21}NO_2S$, 339.1293, found 339.1297.

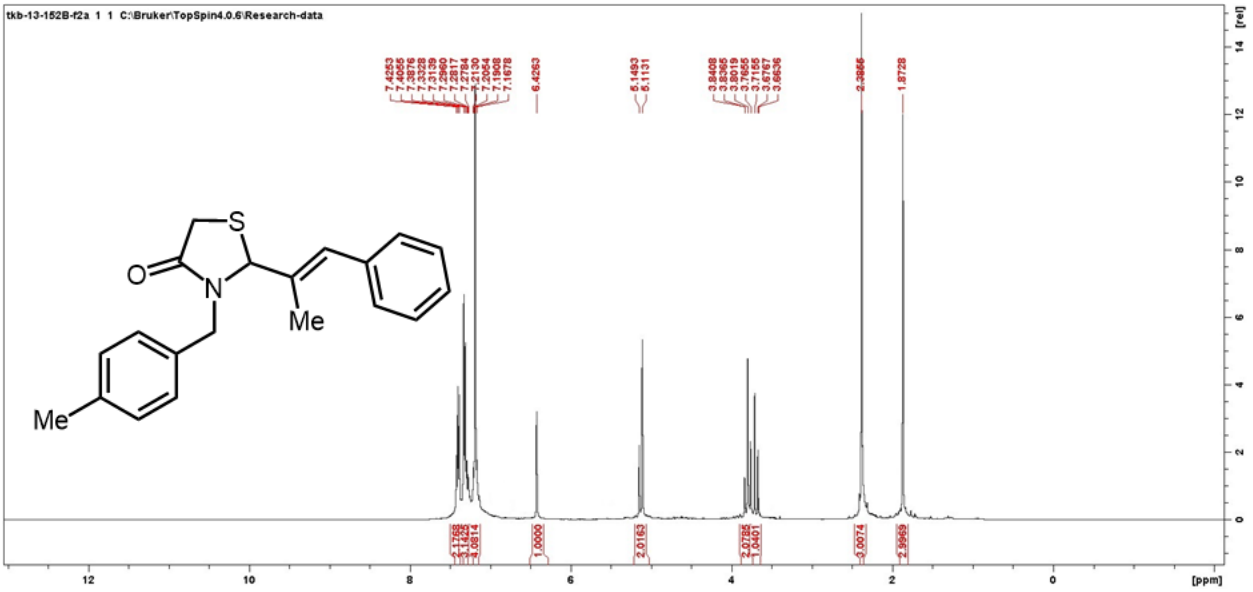


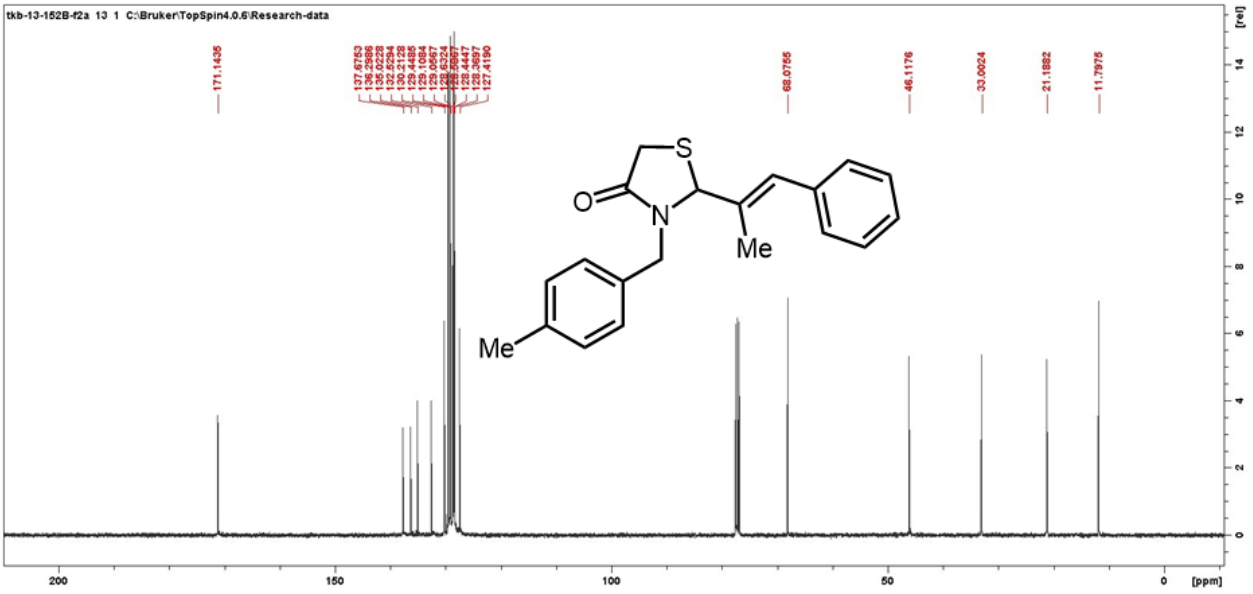


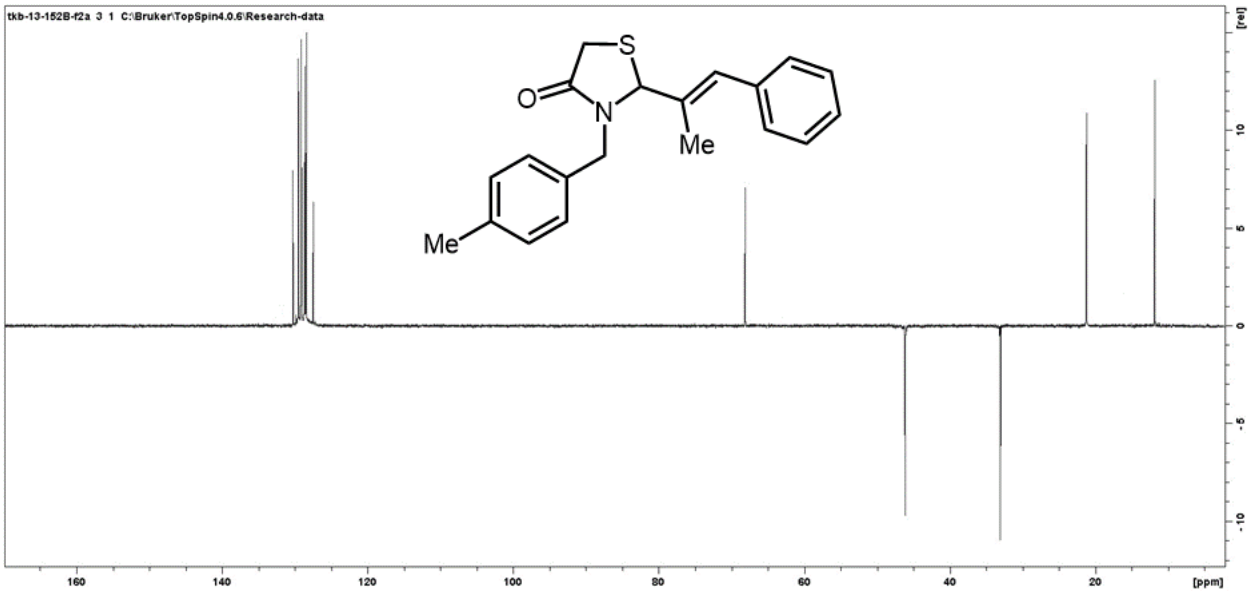
Compound 6j

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (60:40). Oily substance. Yield = 293.9 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), 7.21 – 7.17 (m, 4H), 6.43 (s, 1H), 5.17 – 5.09 (m, 2H), 3.84 – 3.66 (m, 3H), 2.39 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 137.7, 136.3,

135.0, 132.5, 130.2, 129.4, 129.1, 128.6, 128.4, 127.4, 68.1, 46.1, 33.0, 21.2, 11.8. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{20}H_{21}NOS$, 323.1344, found 323.1347.

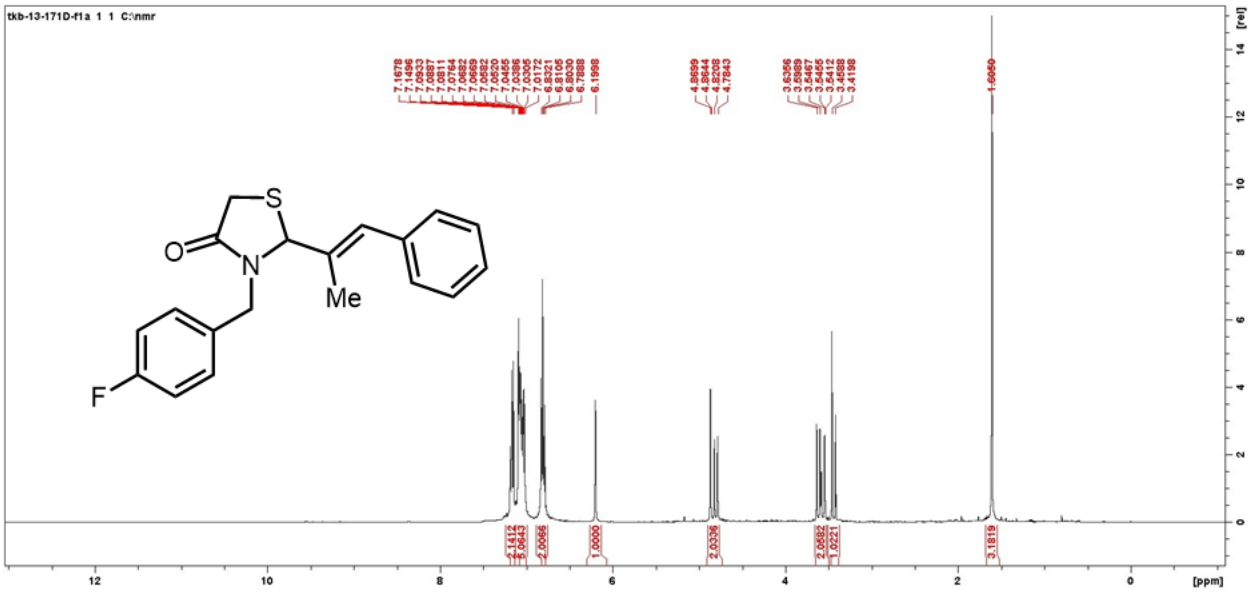


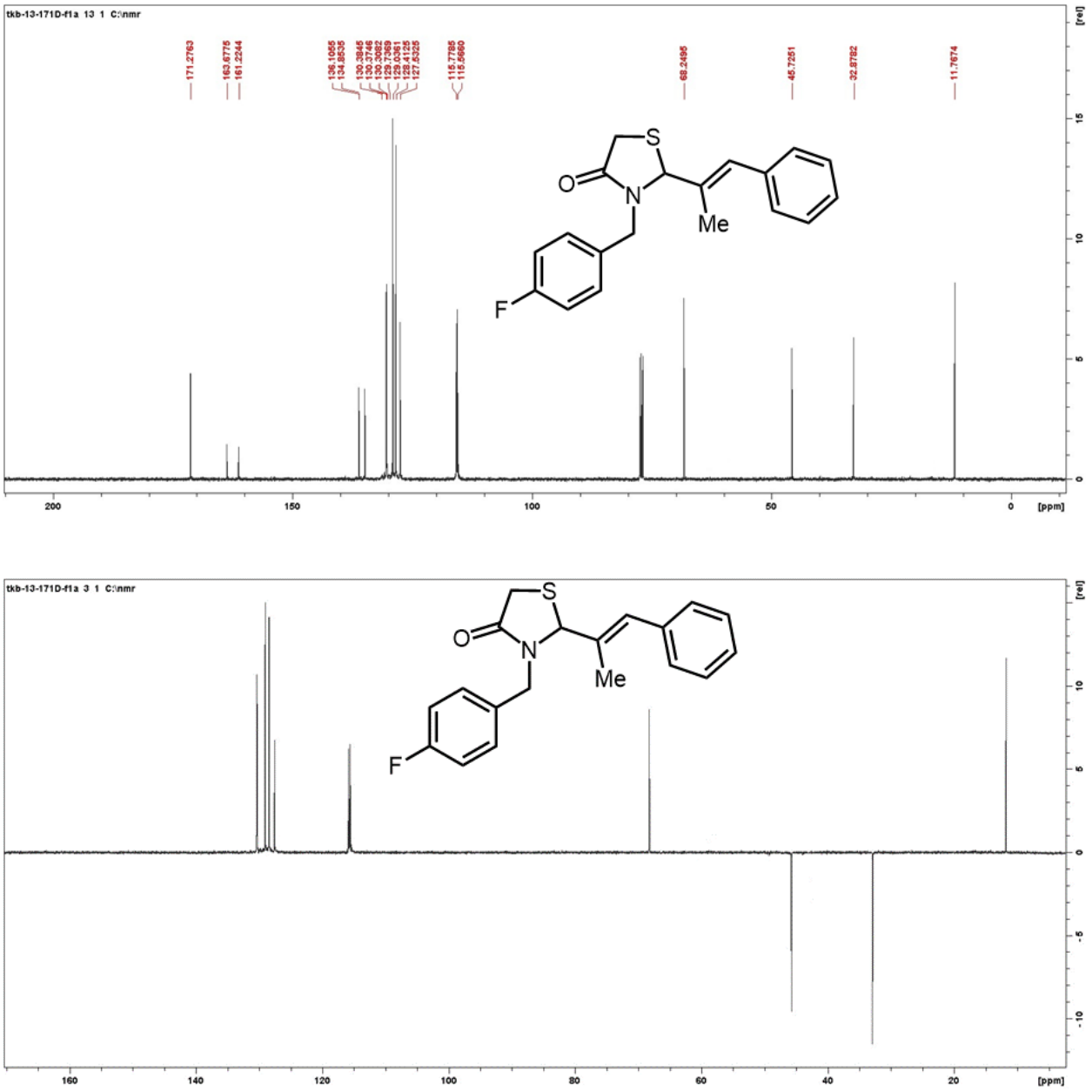




Compound 6k

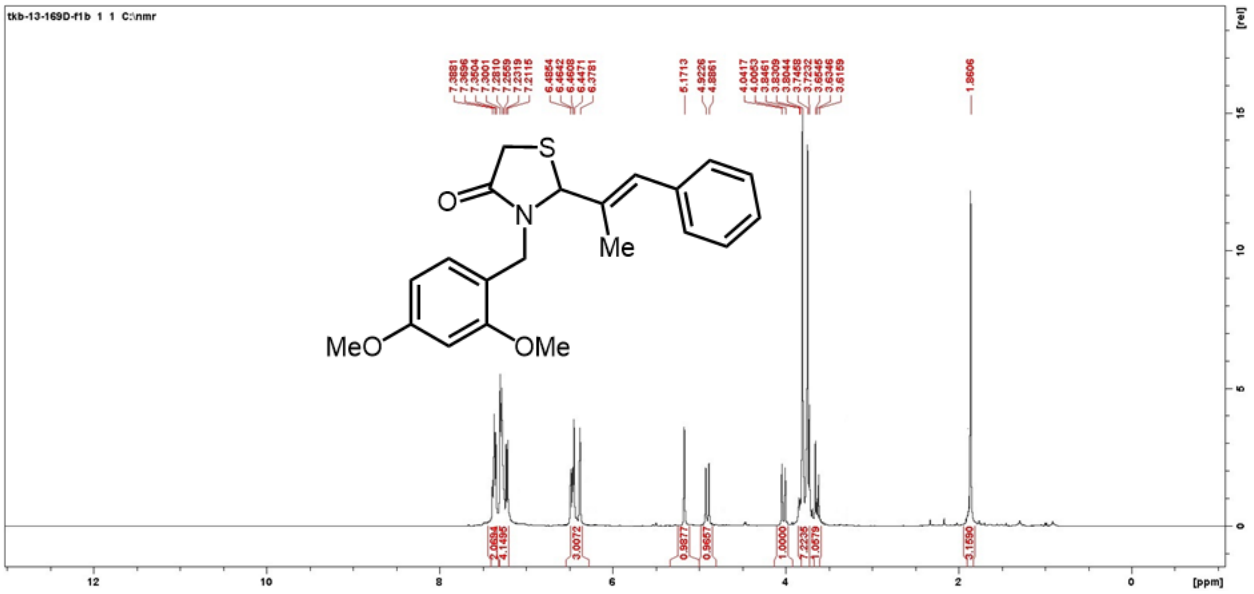
Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 278 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 – 7.14 (m, 2H), 7.14 – 6.96 (m, 5H), 6.89 – 6.72 (m, 2H), 6.20 (s, 1H), 4.87 (s, 1H), 4.78 (d, *J* = 18.1 Hz, 1H), 3.63 – 3.41 (m, 3H), 1.61 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 163.68, 161.2, 136.1, 134.9, 130.4, 130.3, 130.2, 129.7, 129.0, 128.4, 127.5, 115.8, 115.6, 68.2, 45.7, 32.9, 11.8. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{18}FNOS$, 327.1093, found 327.1096.





Compound 6l

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75). Oily substance. Yield = 354.2 mg, 96%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.21 (m, 6H), 6.52 – 6.42 (m, 2H), 6.38 (s, 1H), 5.17 (s, 1H), 4.91 (d, *J* = 14.6 Hz, 1H), 4.02 (d, *J* = 14.6 Hz, 1H), 3.85 – 3.72 (m, 7H), 3.64 (d, *J* = 15.2 Hz, 1H), 1.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.17, 160.77, 158.59, 136.56, 135.50, 131.23, 129.40, 129.03, 128.66, 128.29, 127.21, 116.57, 104.30, 98.43, 68.35, 55.36, 55.30, 40.96, 32.94, 11.86. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{23}NO_3S$, 369.1399, found 369.1395.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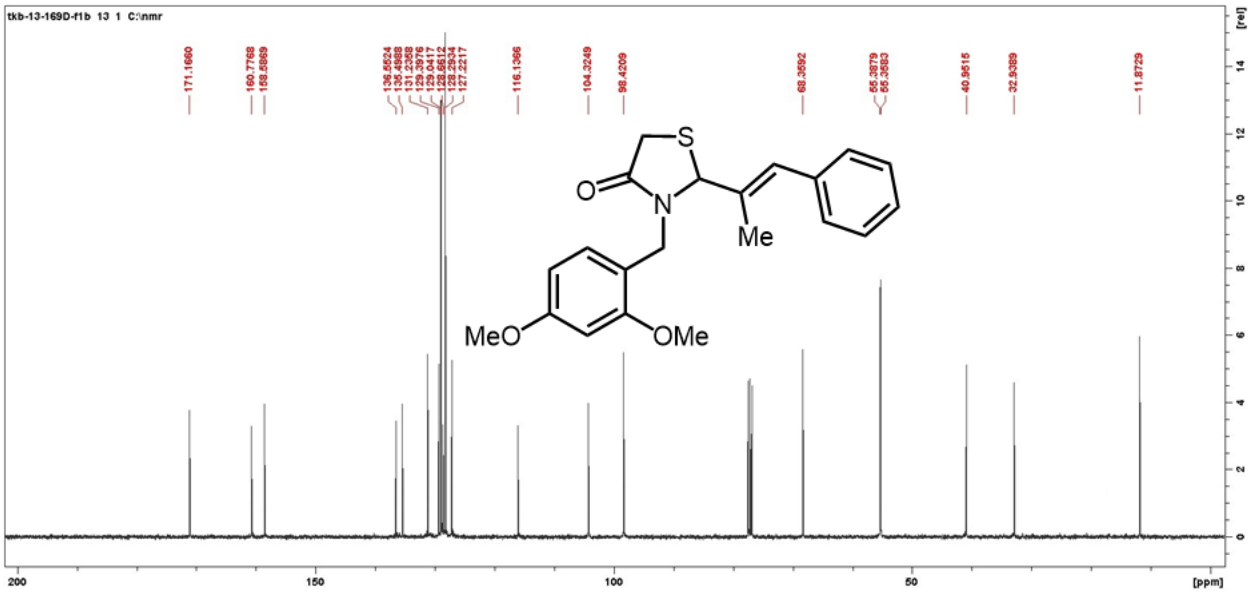
S
O
N
Me
MeO
OMe
[rel]
[ppm]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55.3879
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11.8729
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N
Me
MeO
OMe
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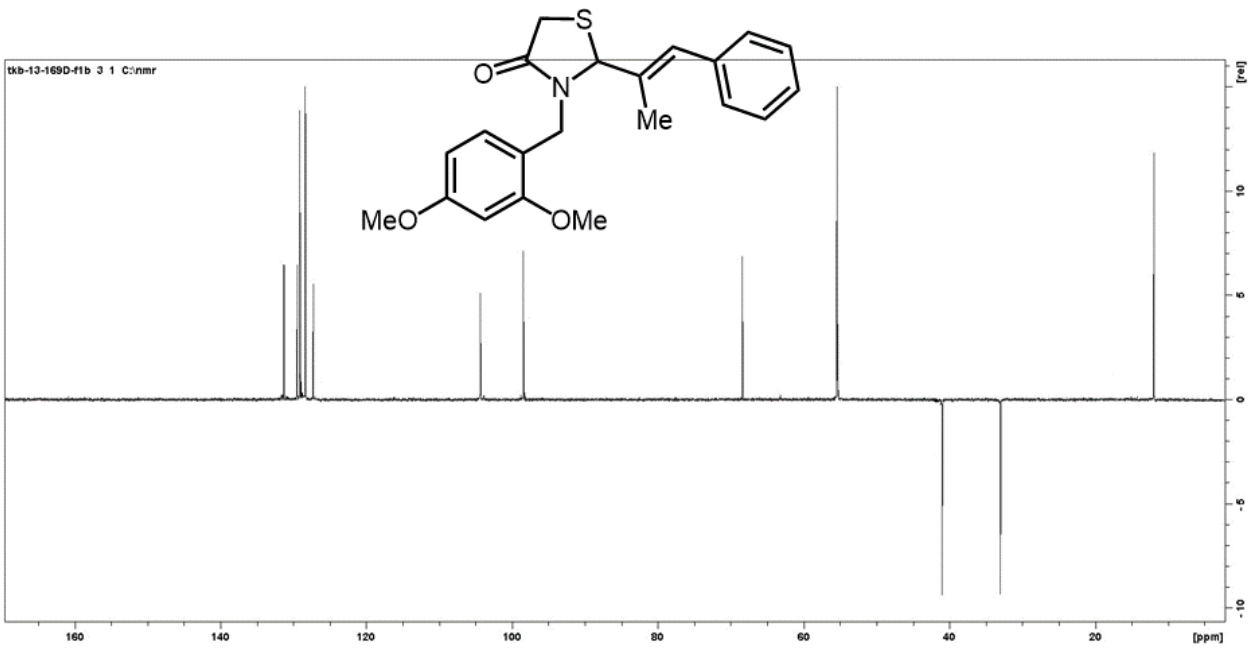
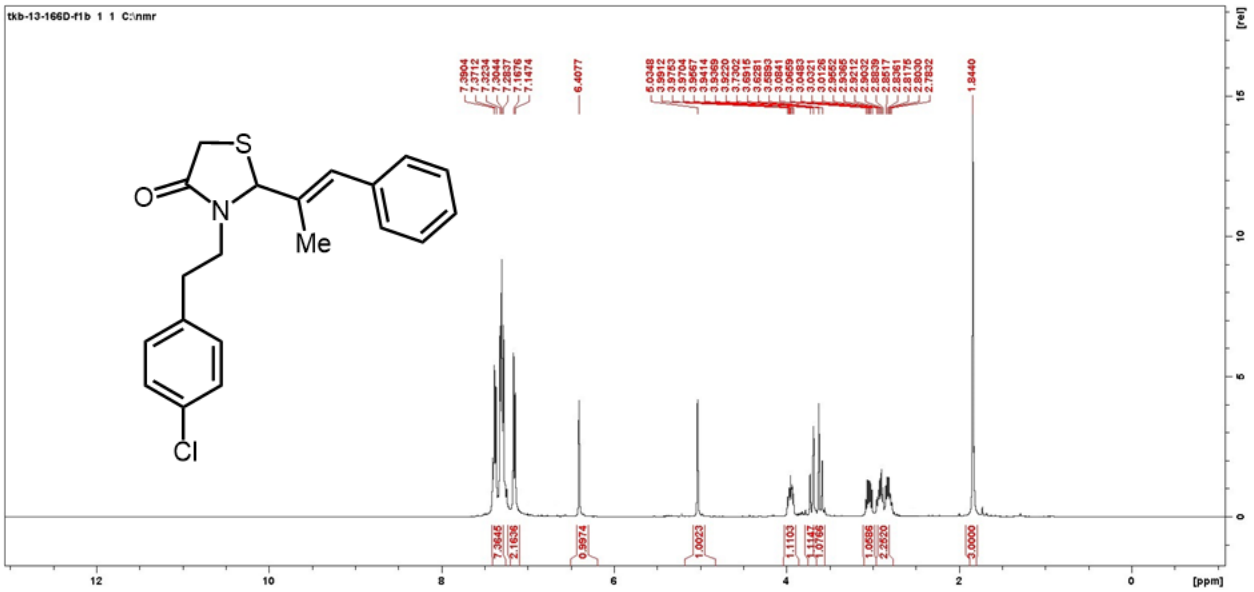
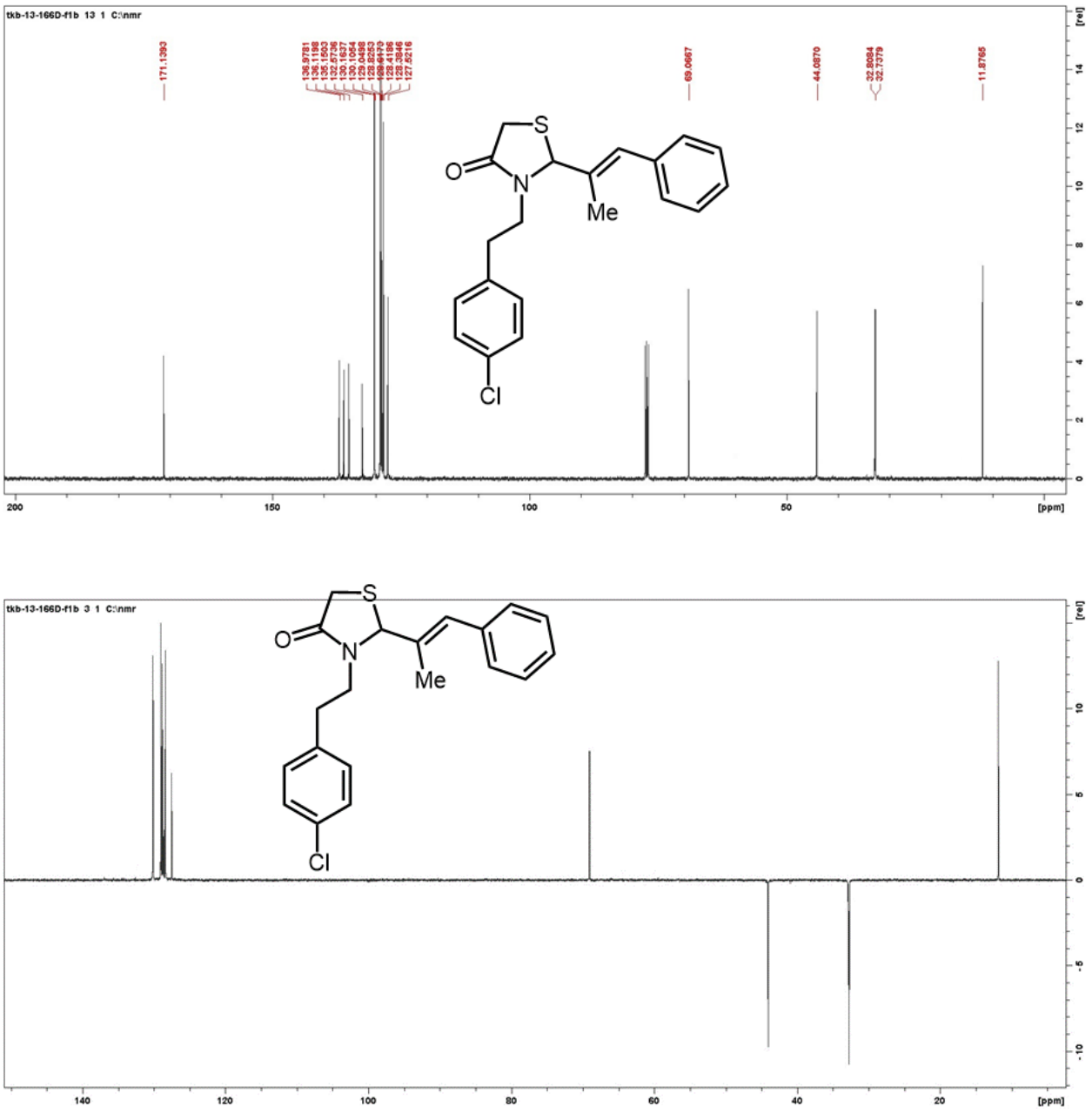
[ppm]



Compound 6m

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 307.1 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 7H), 7.15 (d, *J* = 9.1 Hz, 2H), 6.41 (s, 1H), 5.03 (s, 1H), 3.99 – 3.92 (m, 1H), 3.71 (d, *J* = 15.5 Hz, 1H), 3.60 (d, *J* = 15.5 Hz, 1H), 3.05 (dt, *J* = 13.2, 7.5 Hz, 1H), 2.98 – 2.78 (m, 2H), 1.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 136.9, 136.1, 135.1, 132.6, 130.1, 130.1, 129.0, 128.8, 128.6, 128.4, 128.4, 127.5, 69.1, 44.1, 32.8, 32.7, 11.9. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{20}ClNOS$, 357.0954, found 357.0958.

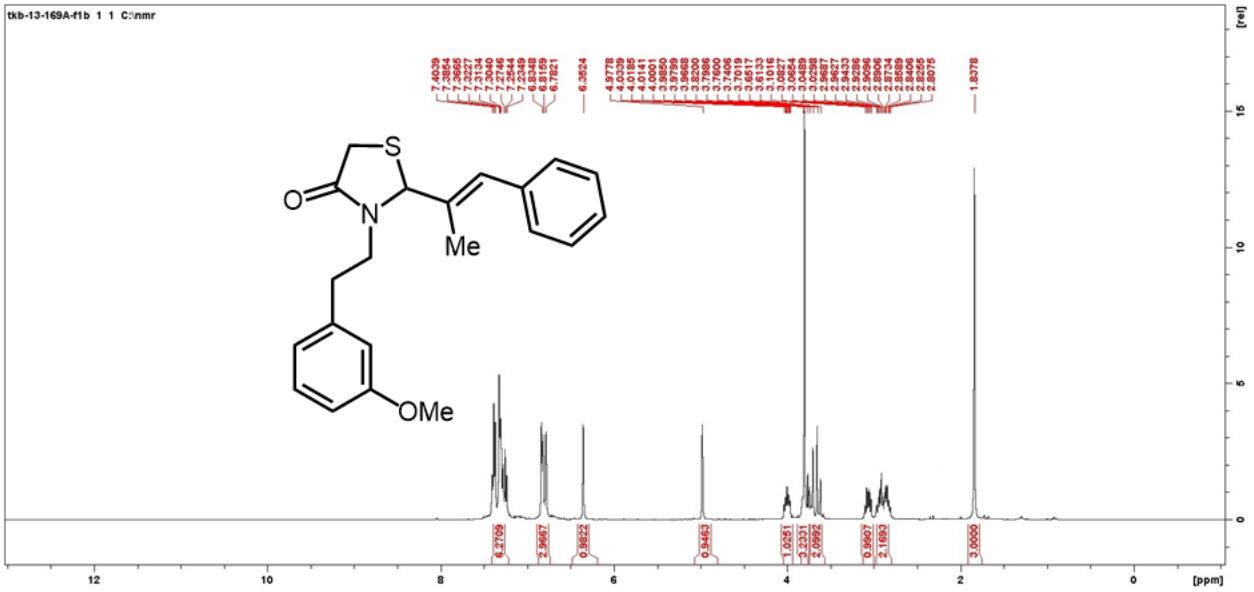


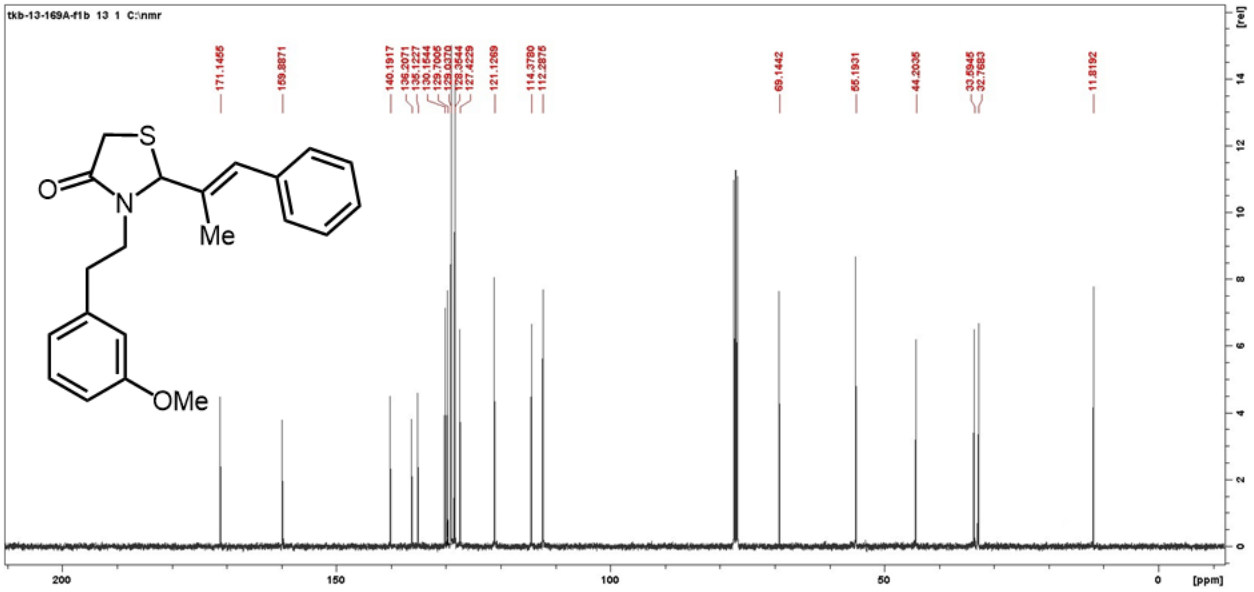


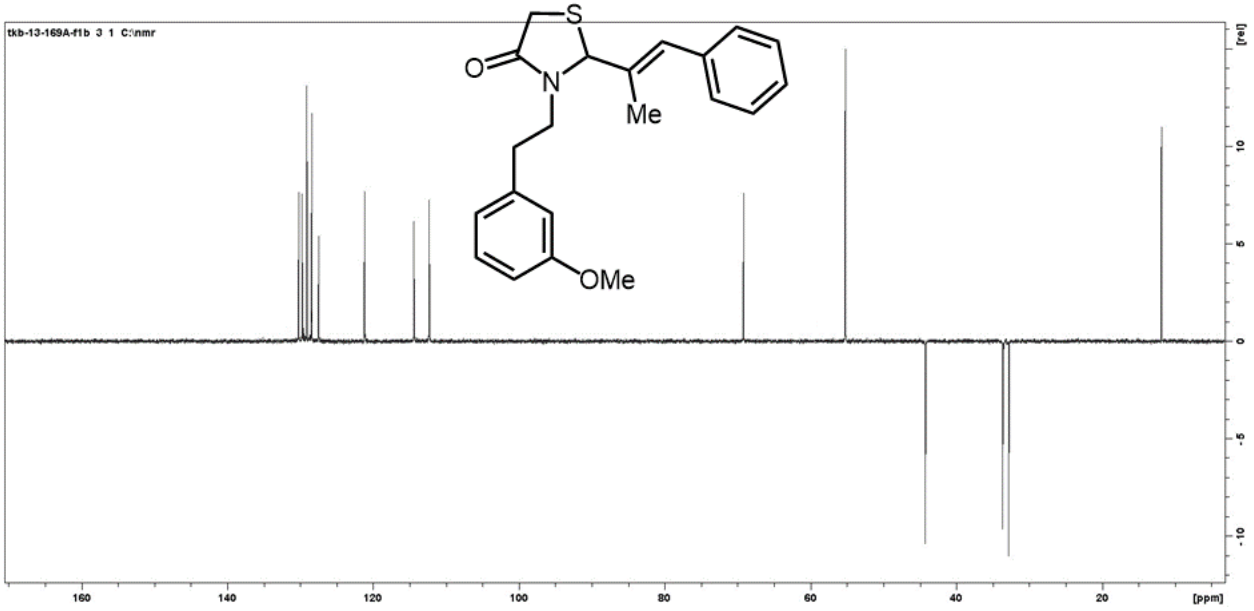
Compound 6n

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 314 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.18 (m, 6H), 6.86 – 6.73 (m, 3H), 6.35 (s, 1H), 4.98 (d, *J* = 2.2 Hz, 1H), 4.00 (ddd, *J* = 13.5, 8.1, 5.5 Hz, 1H), 3.80 (d, *J* = 1.5 Hz, 3H), 3.78 – 3.59 (m, 2H), 3.07 (dt, *J* = 12.9, 7.6 Hz, 1H), 2.99 – 2.77 (m, 2H), 1.84 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 159.9,

140.2, 136.2, 135.1, 130.2, 129.7, 129.0, 128.4, 127.4, 121.1, 114.4, 112.3, 69.2, 55.2, 44.2, 33.6, 32.8, 11.8. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{21}H_{23}NO_2S$, 353.1449, found 353.1444.

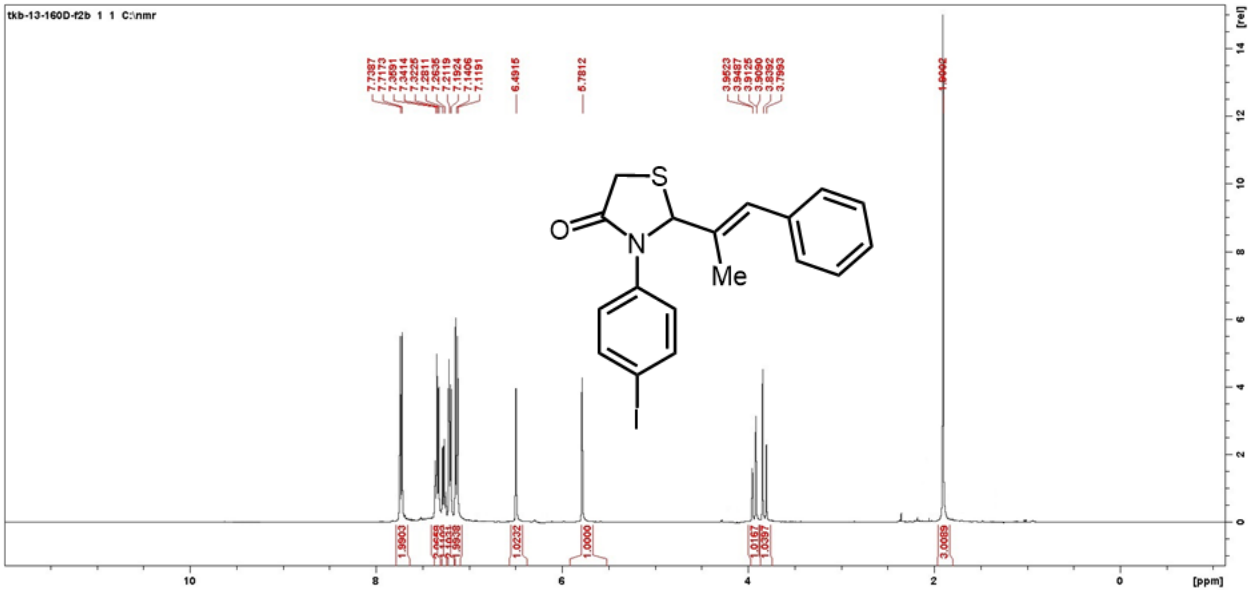


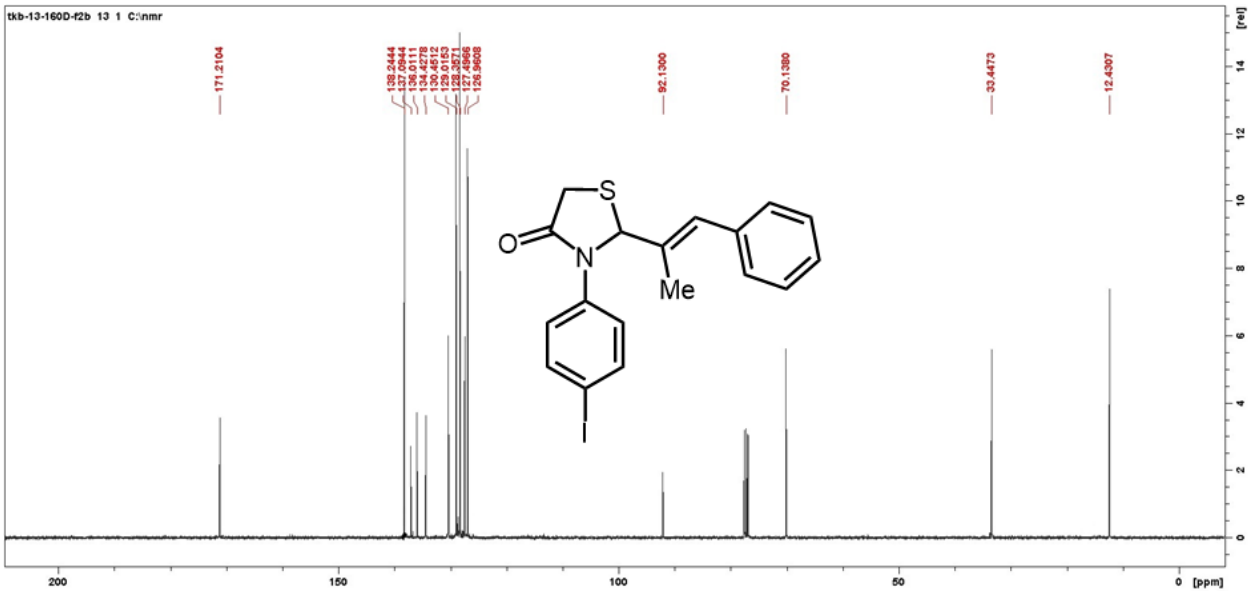




Compound 6o

Prepared in 1.0 mmol scale using **General Procedure A.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Oily substance. Yield = 357.94 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.36 – 7.11 (m, 7H), 6.49 (s, 1H), 5.78 (s, 1H), 3.93 (d, *J* = 15.9 Hz, 1H), 3.82 (d, *J* = 15.9 Hz, 1H), 1.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 138.2, 137.1, 136.0, 134.4, 130.4, 129.0, 128.4, 127.5, 126.9, 92.1, 70.1, 33.4, 12.4. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{16}INOS$, 420.9997, found 420.9992.

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136.6111
134.4278
130.4512
129.0153
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Me
I
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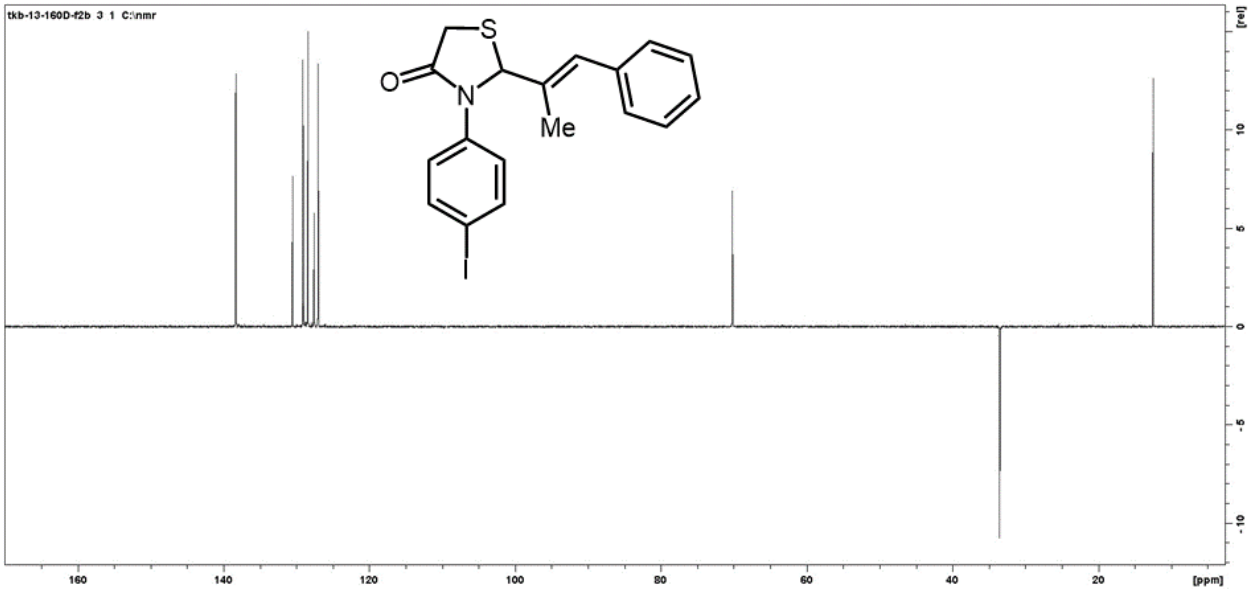
100
50
0 [ppm]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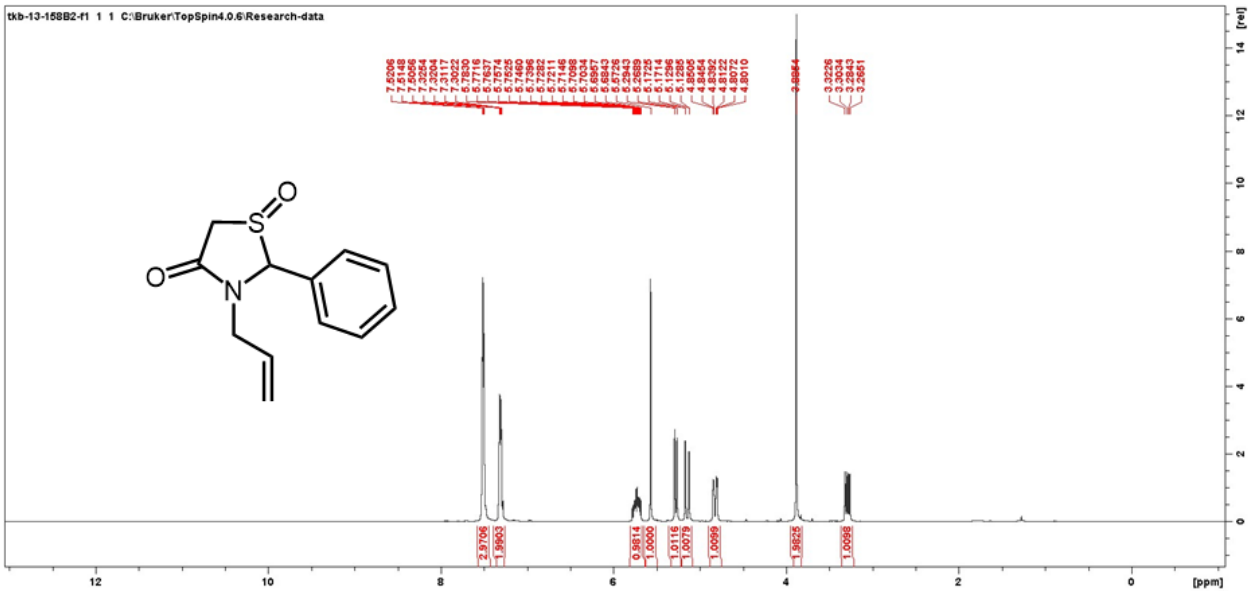
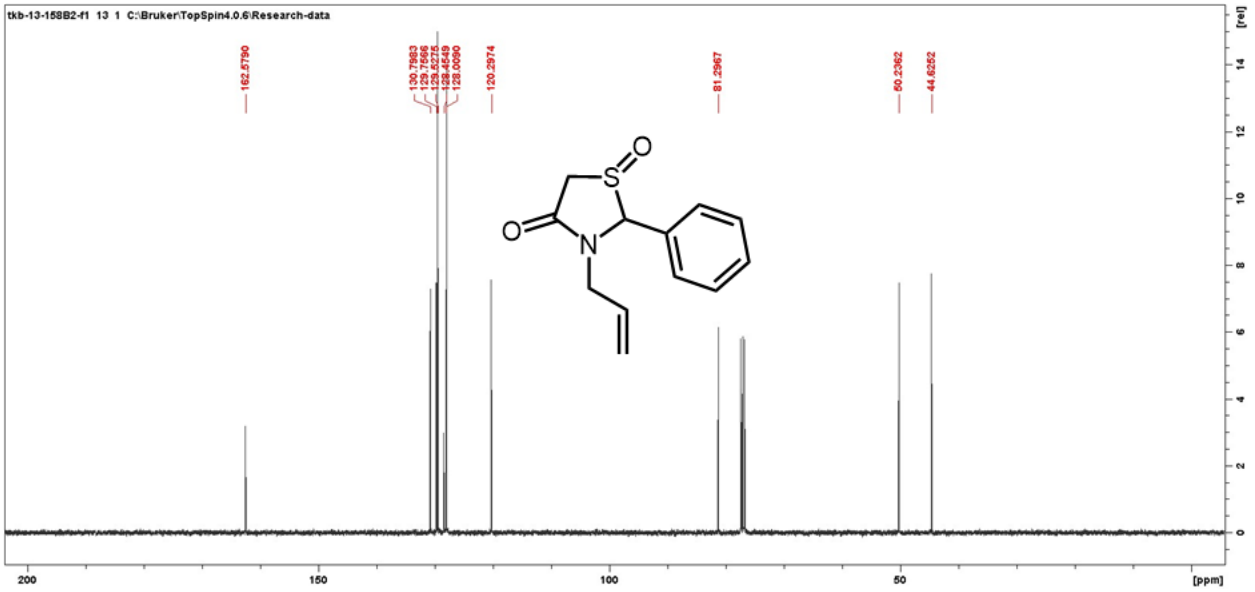
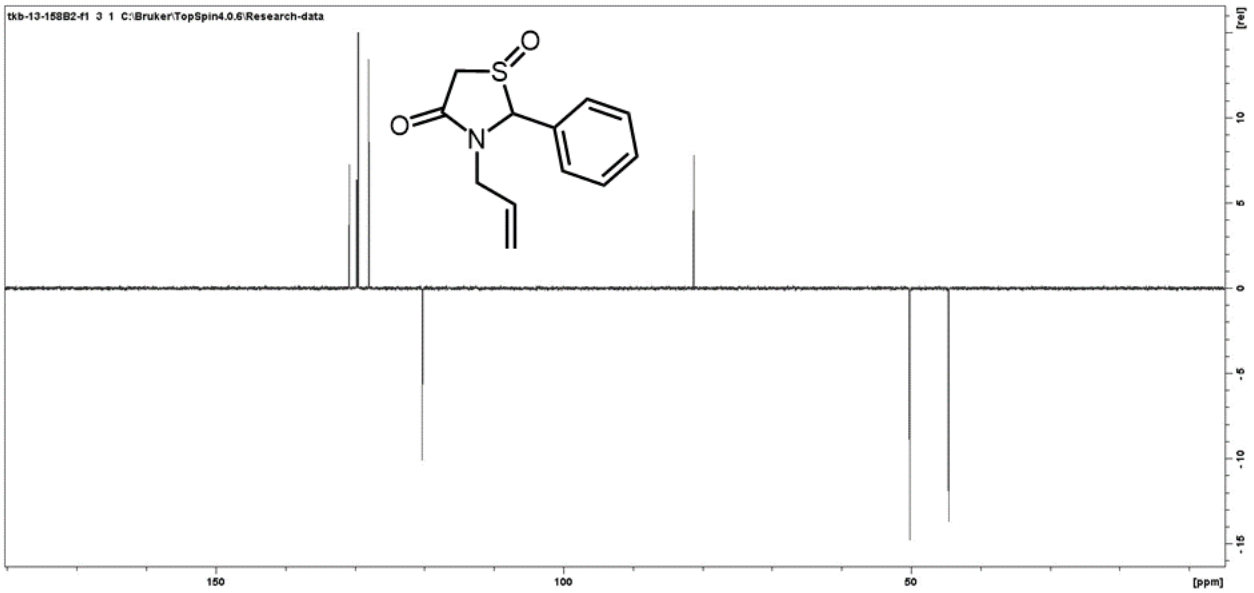
O
N
Me
I
[rel]
160
140
120
100
80
60
40
20
[ppm]

Compound 7a

Prepared in 2.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 10:90). Oily substance. Yield = 427.7 mg, 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.50 (m, 3H), 7.33 – 7.30 (m, 2H), 5.73 (dddd, *J* = 17.5, 10.1, 7.7, 4.6 Hz, 1H), 5.57 (s, 1H), 5.28 (dd, *J* = 10.1, 1.3 Hz, 1H), 5.15 (ddt, *J* = 17.1, 2.0, 1.1 Hz, 1H), 4.83 (ddd, *J* = 15.4, 4.2, 2.0 Hz, 1H), 3.89 (s, 2H), 3.29 (dd, *J* = 15.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 130.8, 129.7, 129.5, 128.5, 128.0, 120.3, 81.3, 50.2, 44.6. **HRMS-EI$^+$** (*m/z*): calc for $C_{12}H_{13}NO_2S$, 235.0667, found 235.0669.

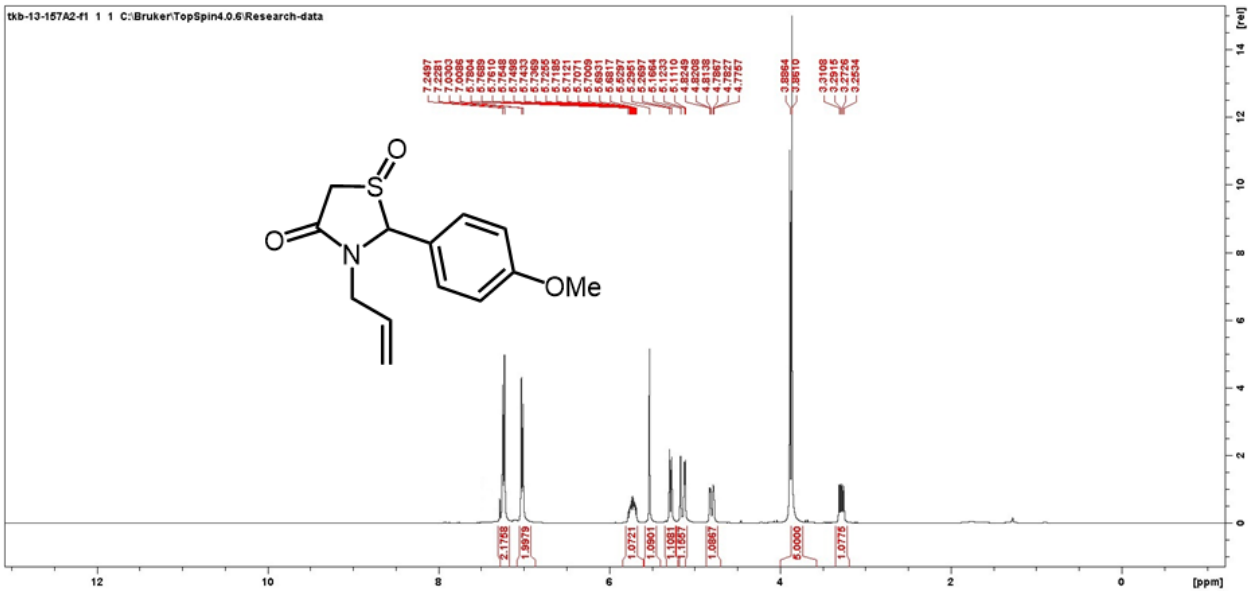


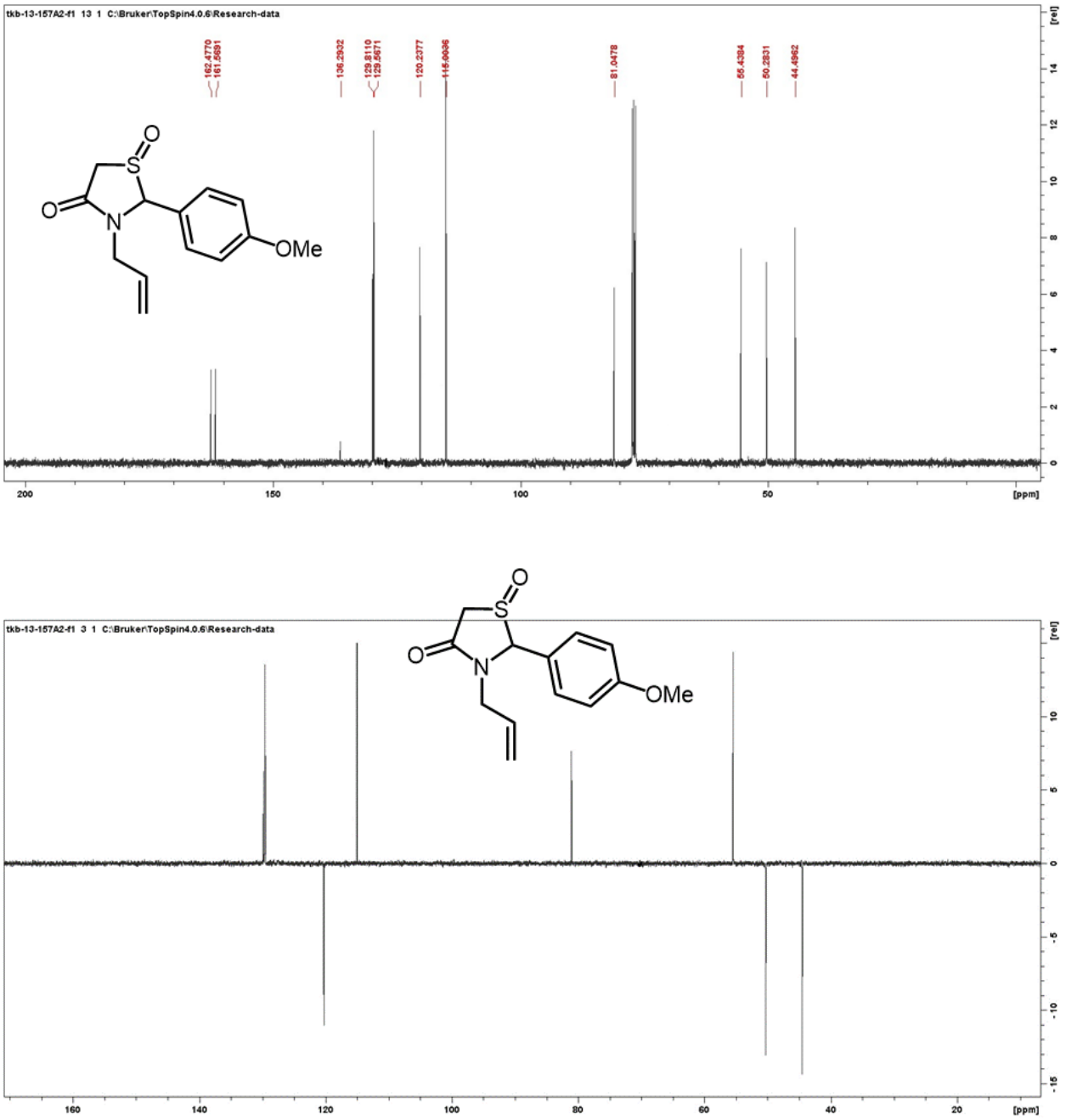




Compound 7b

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (25:75 to 0:100). Oily substance. Yield = 249.1 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.3 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 5.73 (dddd, *J* = 17.5, 10.1, 7.7, 4.6 Hz, 1H), 5.53 (s, 1H), 5.28 (d, *J* = 9.9 Hz, 1H), 5.19 – 5.09 (m, 2H), 4.80 (ddt, *J* = 15.2, 4.6, 1.7 Hz, 1H), 3.89 – 3.86 (m, 5H), 3.28 (dd, *J* = 15.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 161.6, 136.3, 129.8, 129.6, 120.2, 115.0, 81.0, 55.4, 50.3, 44.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{15}NO_3S$, 265.0773, found 265.0778.

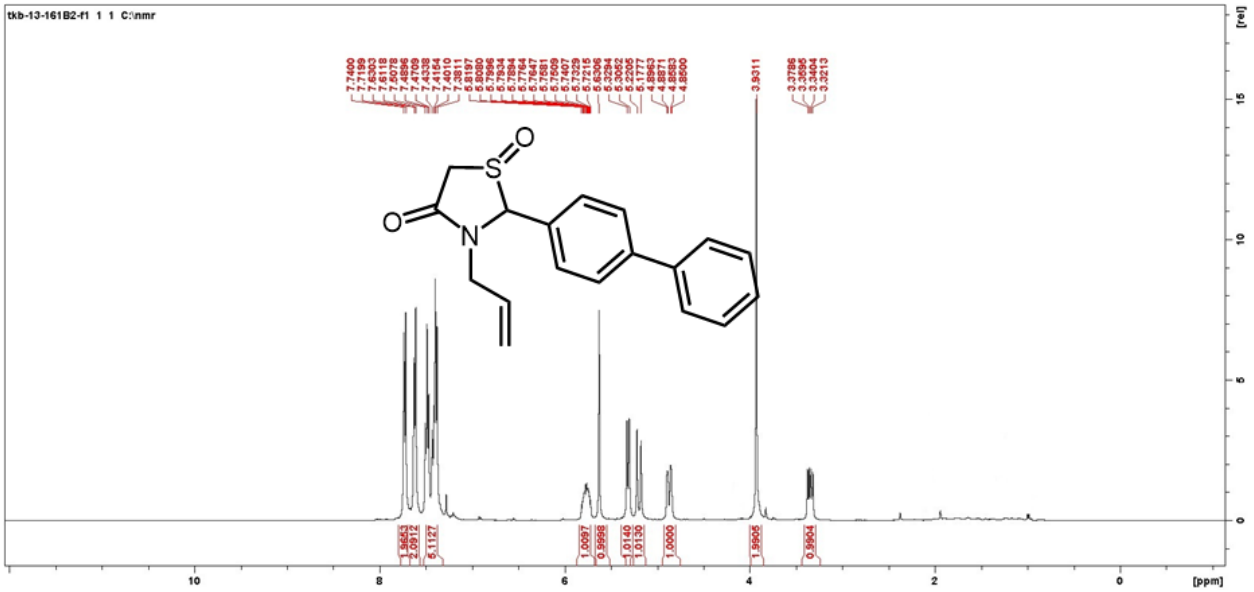


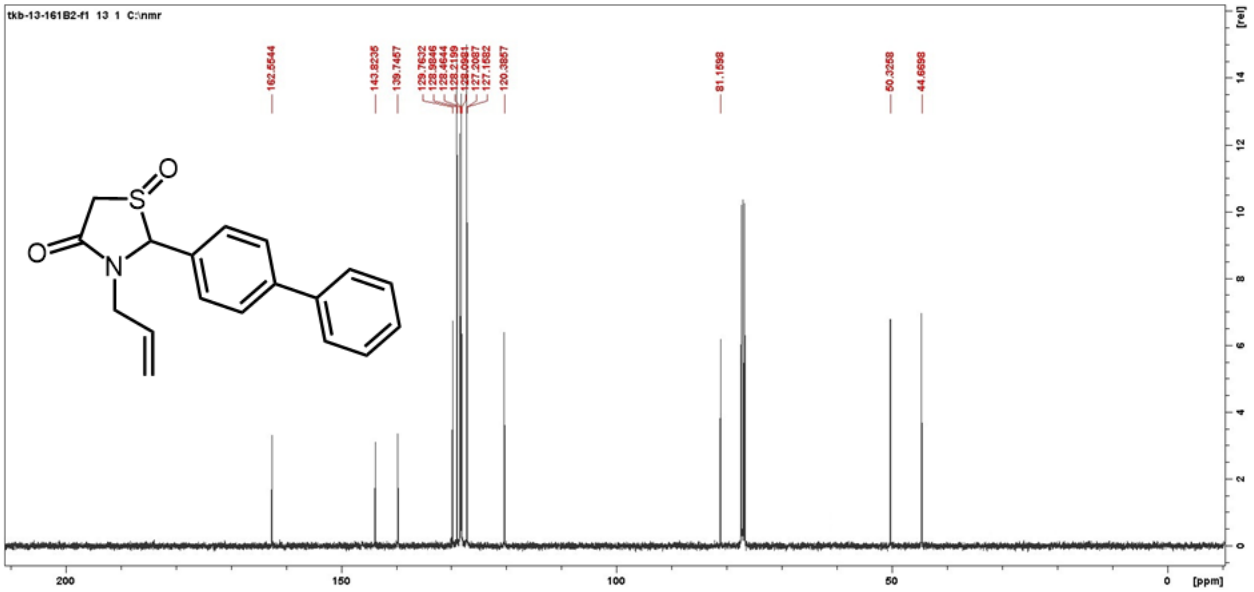


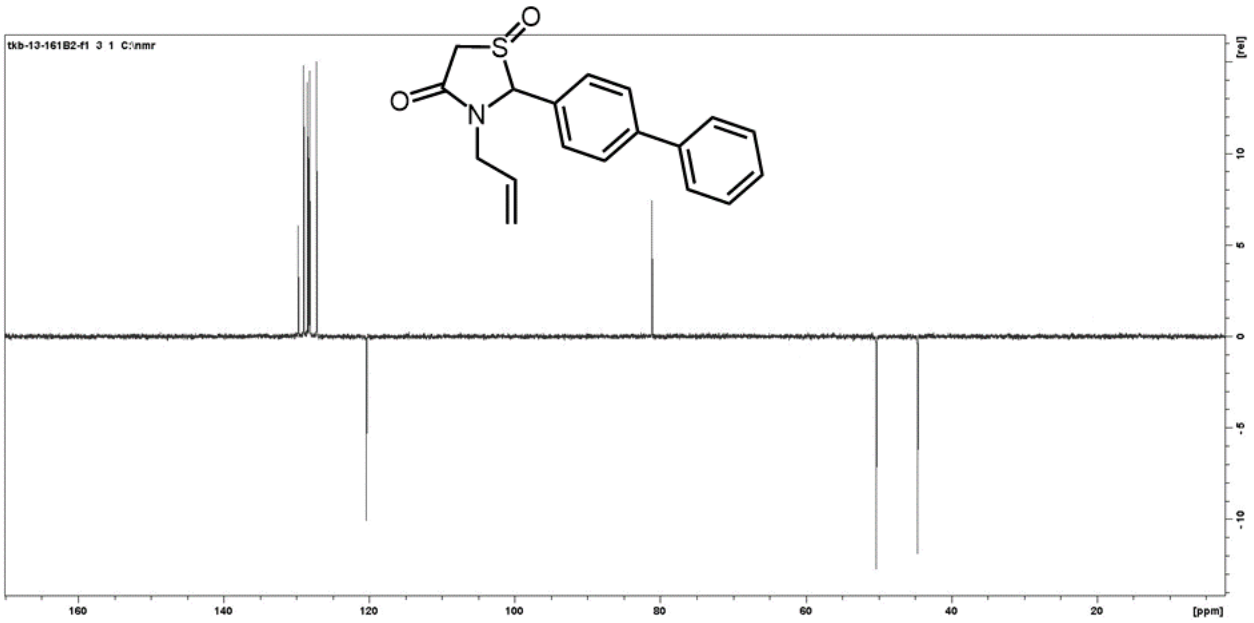
Compound 7c

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Oily substance. Yield = 280 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 2H), 7.62 (d, J = 6.8 Hz, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.41 (dd, J = 13.6, 7.5 Hz, 3H), 5.77 (dddd, J = 17.5, 10.1, 7.8, 4.5 Hz, 1H), 5.63 (s, 1H), 5.35 – 5.28 (m, 1H), 5.20 (d, J = 17.1 Hz, 1H), 4.87 (dd, J = 15.5, 4.5 Hz, 1H), 3.93 (s, 2H), 3.35 (dd, J = 15.4, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 143.8, 139.8, 129.8, 129.0,

128.5, 128.2, 128.1, 127.2, 120.4, 81.2, 50.3, 44.7. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{18}H_{17}NO_2S$, 311.0980, found 311.0987.

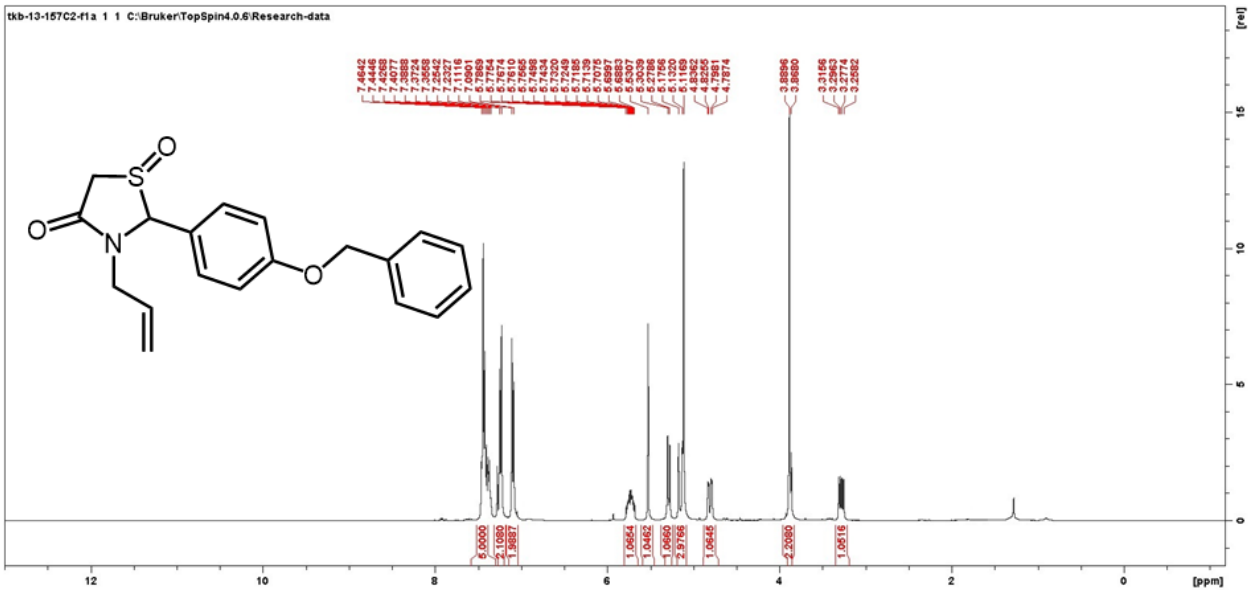


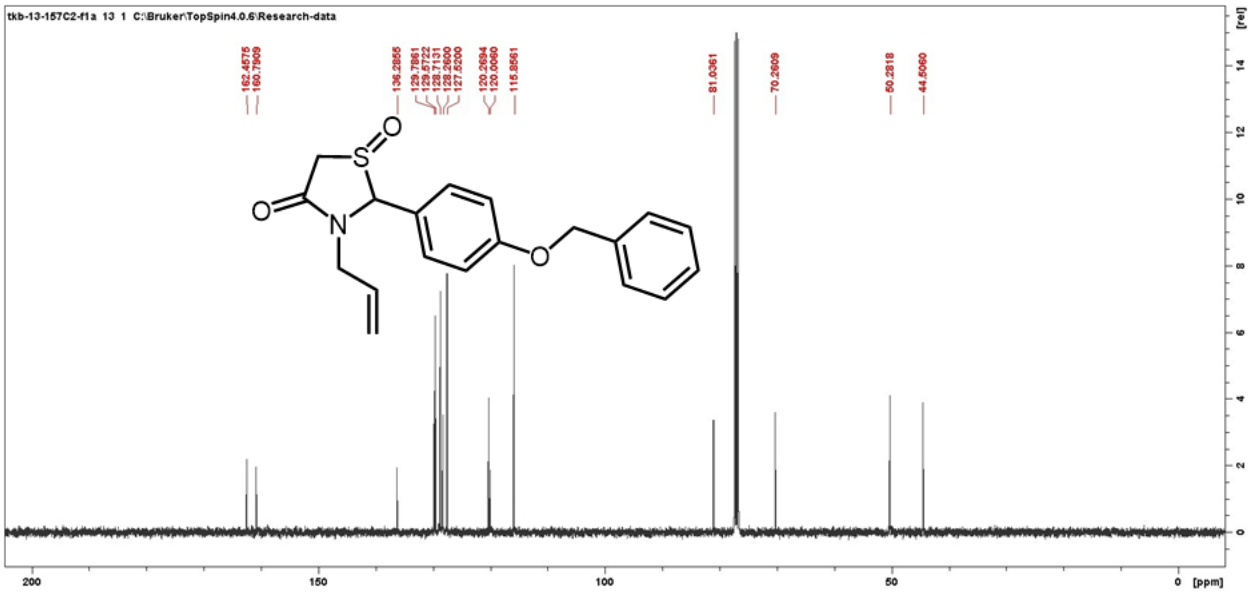


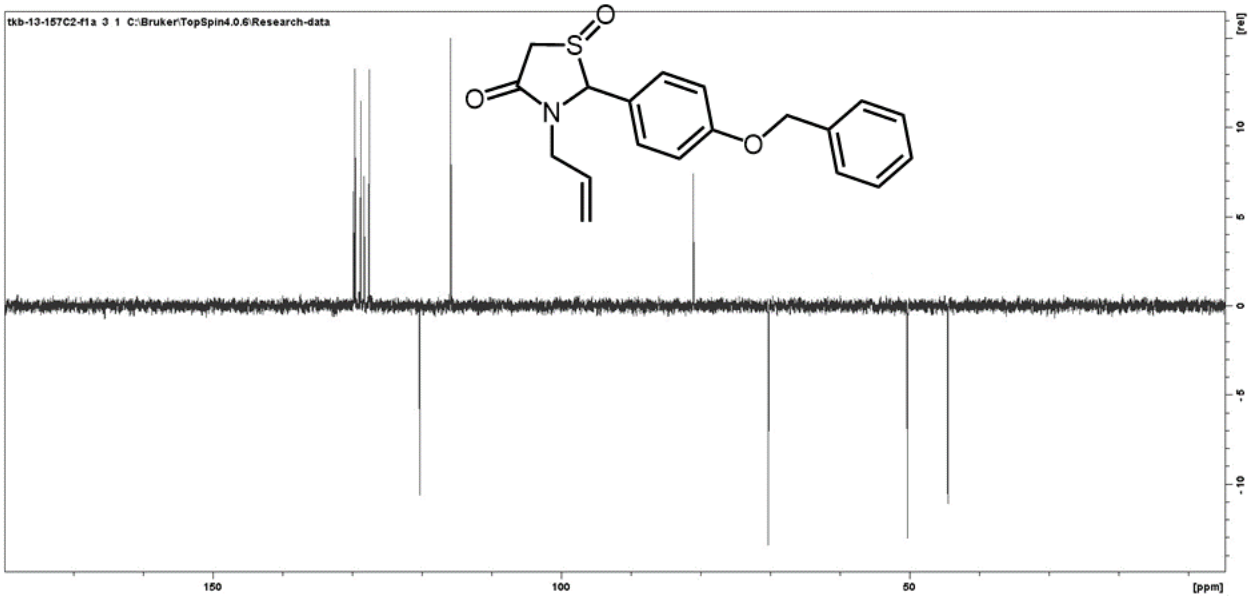


Compound 7d

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 324 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.36 (m, 5H), 7.24 (d, *J* = 7.0 Hz, 2H), 7.10 (d, *J* = 7.0 Hz, 2H), 5.74 (dddd, *J* = 17.6, 10.1, 7.6, 4.5 Hz, 1H), 5.53 (s, 1H), 5.29 (d, *J* = 10.1 Hz, 1H), 5.15 (d, *J* = 17.0 Hz, 1H), 5.12 (s, 2H), 4.86 – 4.76 (m, 1H), 3.89 (s, 2H), 3.29 (dd, *J* = 15.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 160.8, 136.3, 129.8, 129.6, 128.7, 128.3, 127.5, 120.3, 120.0, 115.9, 81.0, 70.3, 50.3, 44.5. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{19}NO_3S$, 341.1086, found 341.1092.



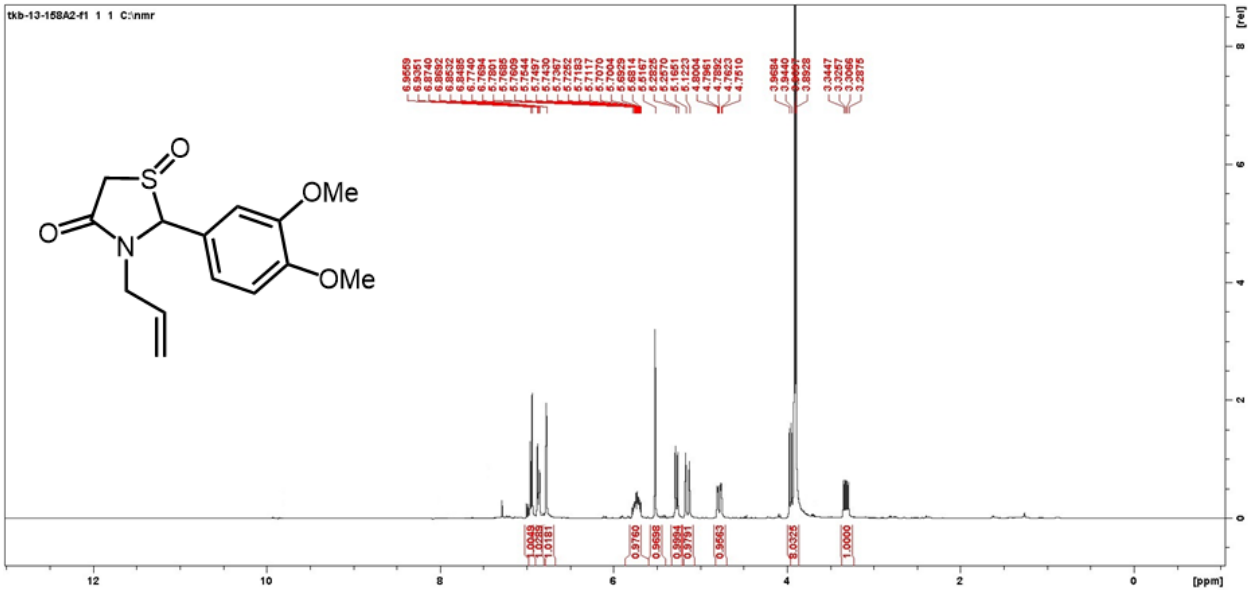


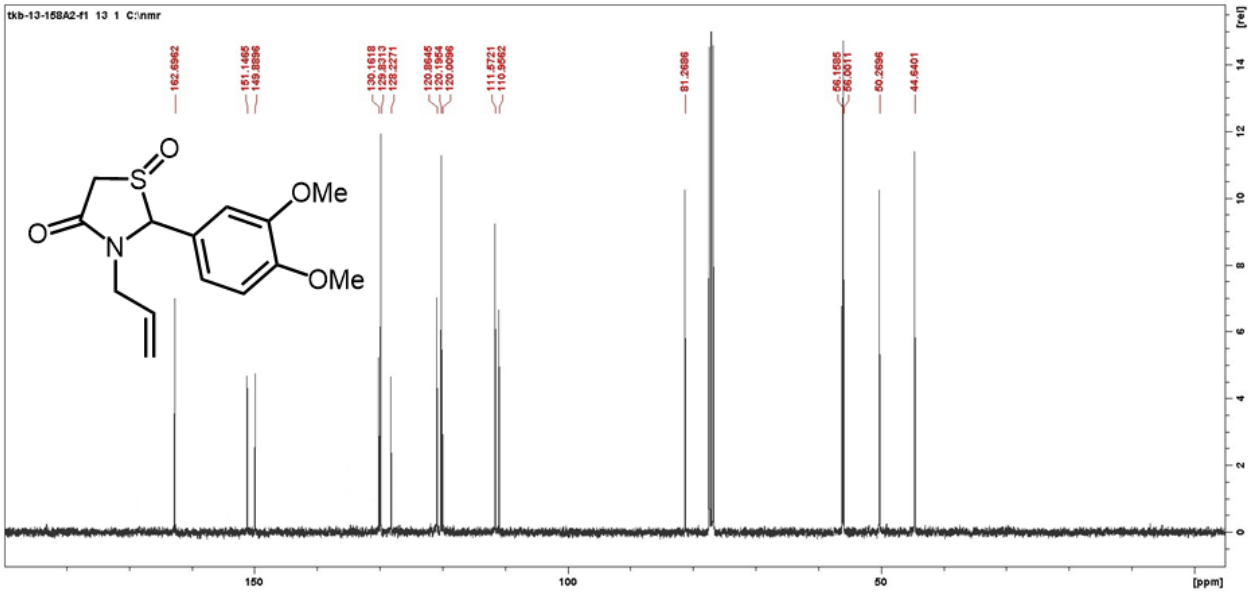


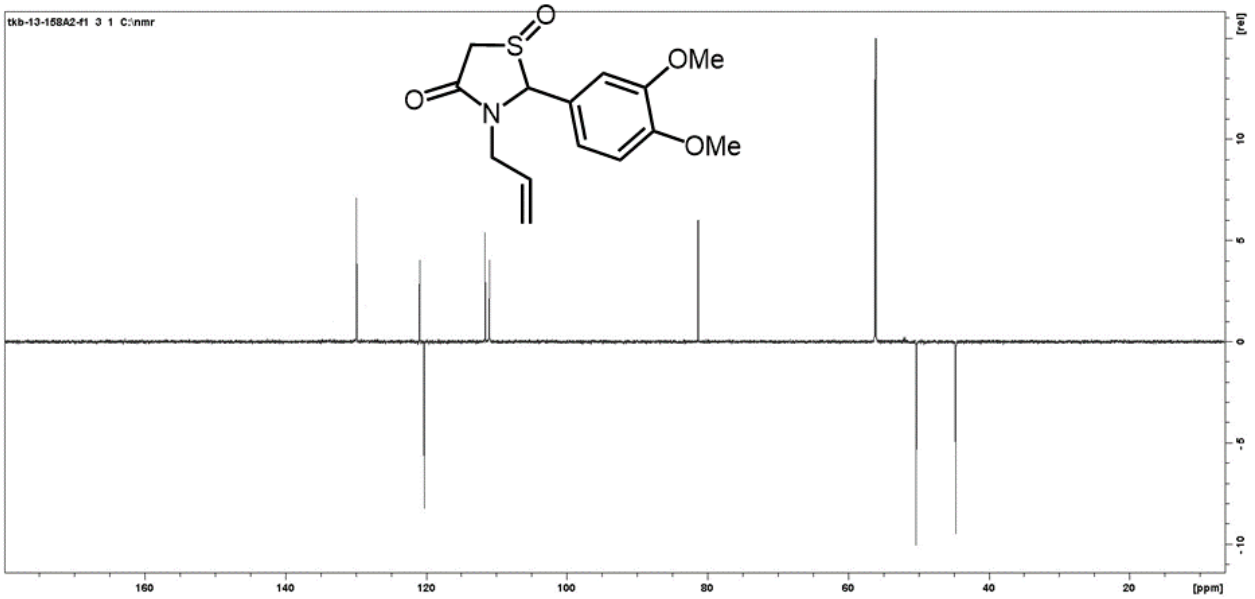
Compound 7e

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 129.8 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.86 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.77 (d, *J* = 2.2 Hz, 1H), 5.73 (dddd, *J* = 17.5, 10.1, 7.6, 4.6 Hz, 1H), 5.52 (s, 1H), 5.30 – 5.23 (m, 1H), 5.19 – 5.10 (m, 1H), 4.78 (ddd, *J* = 15.3, 4.2, 2.2 Hz, 1H), 3.99 – 3.79 (m, 8H), 3.32 (dd, *J* = 15.3, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 151.1, 149.9, 130.2, 129.8, 128.2, 120.9, 120.2, 120.0,

111.6, 110.9, 81.3, 56.2, 56.0, 50.3, 44.6. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{14}H_{17}NO_4S$, 295.0878, found 295.0882.

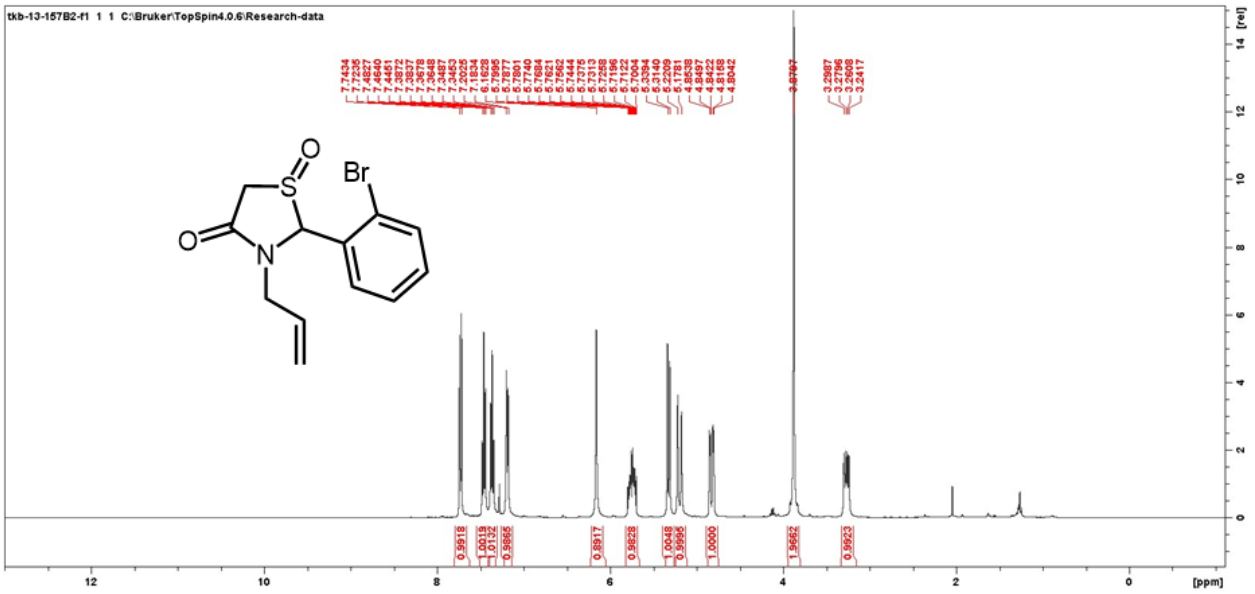


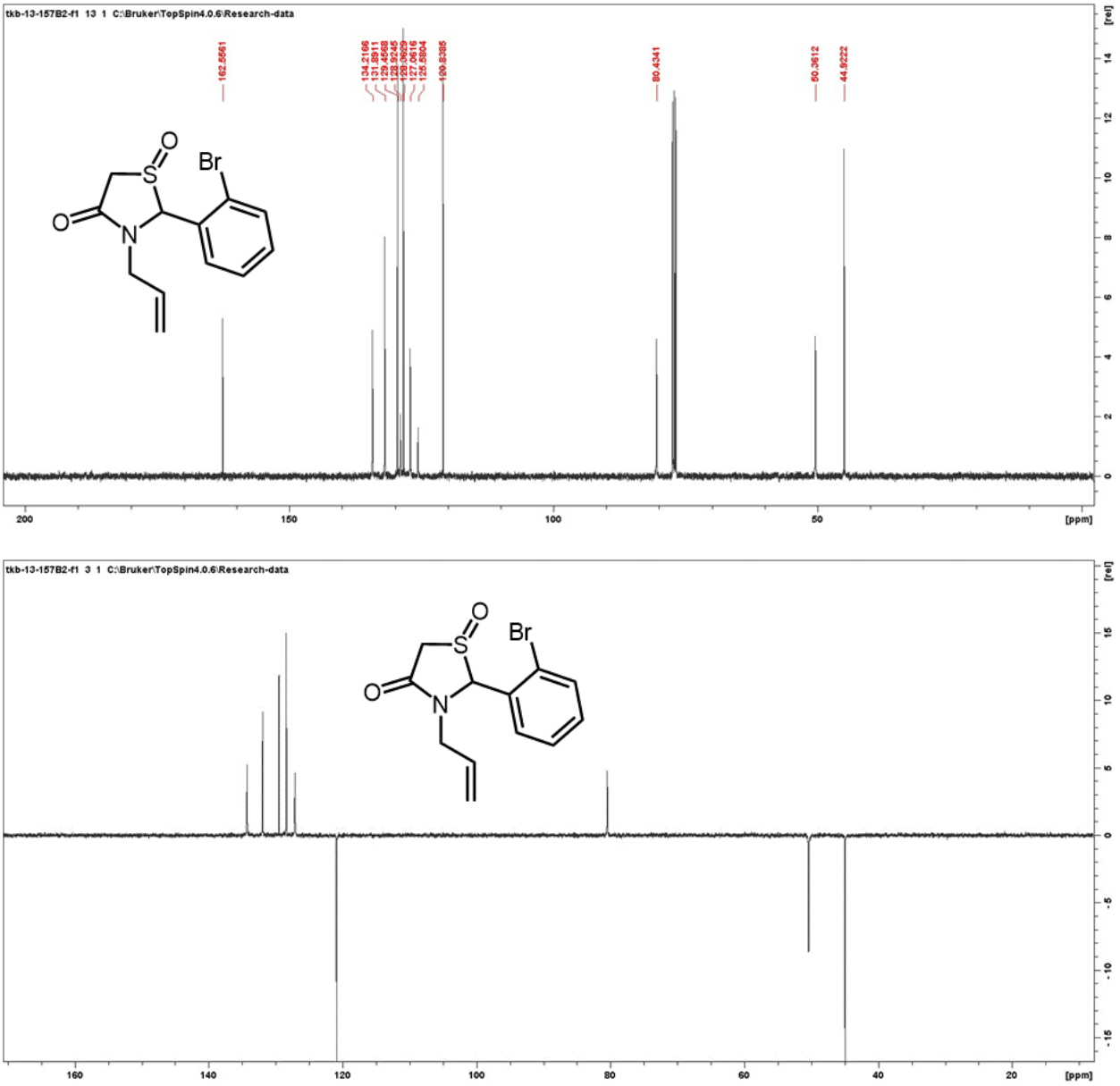




Compound 7f

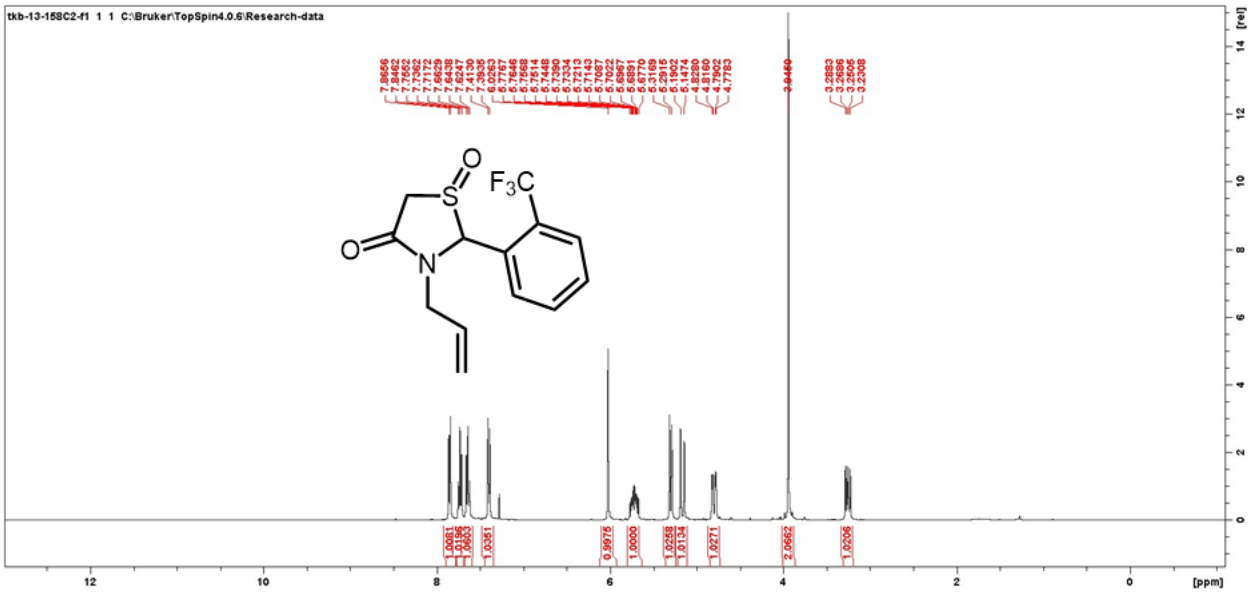
Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 278.6 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H), 7.37 (td, *J* = 7.7, 1.7 Hz, 1H), 7.19 (dd, *J* = 7.8, 1.7 Hz, 1H), 6.16 (s, 1H), 5.75 (dddd, *J* = 17.5, 10.0, 7.7, 4.7 Hz, 1H), 5.33 (d, *J* = 10.2 Hz, 1H), 5.20 (d, *J* = 17.1 Hz, 1H), 4.83 (ddt, *J* = 15.2, 4.6, 1.6 Hz, 1H), 3.88 (s, 2H), 3.27 (dd, *J* = 15.3, 7.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 134.2, 131.9, 129.5, 128.9, 128.4, 127.1, 125.6, 120.8, 80.4, 50.4, 44.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{12}H_{12}BrNO_2S$, 312.9772, found 312.9777.

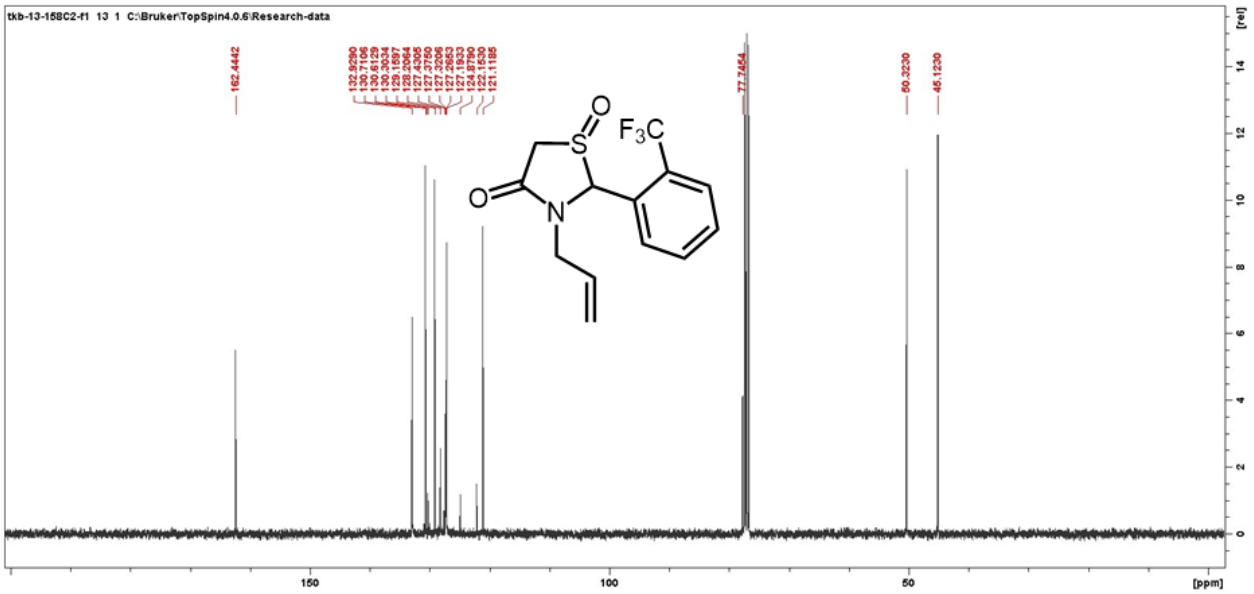


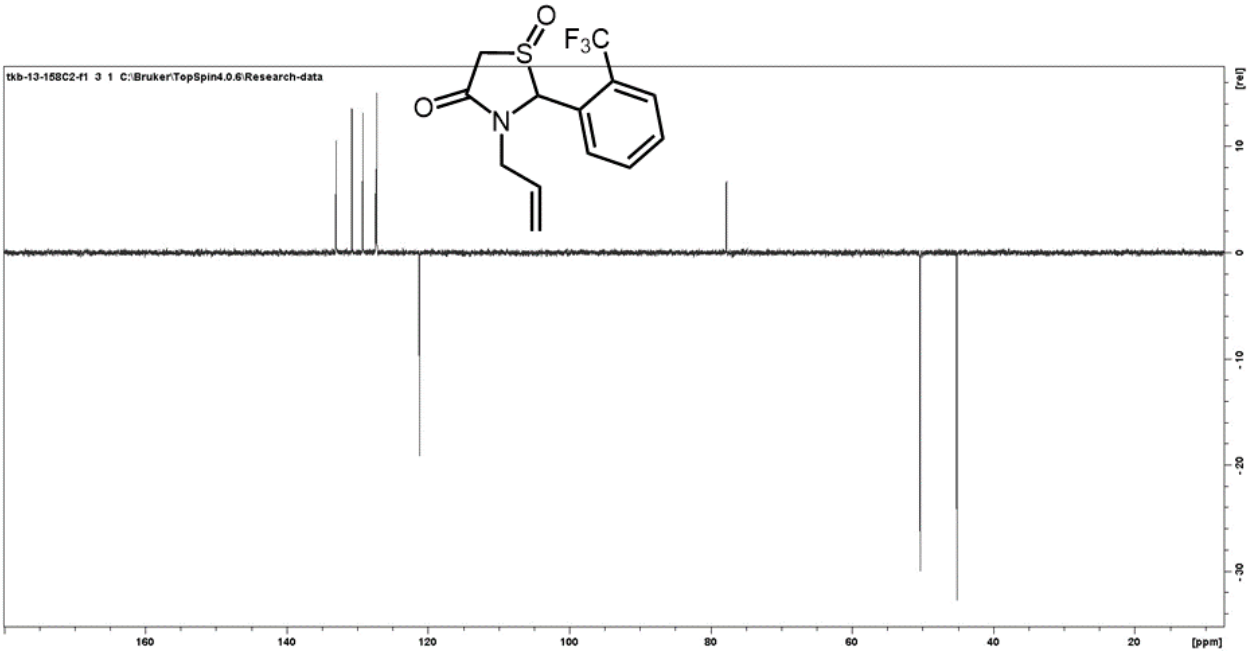


Compound 7g

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 287.9 mg, 95%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 7.7 Hz, 1H), 7.64 (t, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 6.03 (s, 1H), 5.73 (dddd, *J* = 17.6, 10.0, 7.9, 4.8 Hz, 1H), 5.30 (d, *J* = 10.1 Hz, 1H), 5.17 (d, *J* = 17.1 Hz, 1H), 4.80 (ddt, *J* = 15.1, 4.8, 1.6 Hz, 1H), 3.95 (s, 2H), 3.26 (dd, *J* = 15.1, 7.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 132.9, 130.7, 130.6, 130.3, 129.2, 128.2, 127.6, 127.4, 127.3, 127.2, 124.9, 122.2, 121.1, 77.8, 50.3, 45.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{12}F_3NO_2S$, 303.0541, found 303.0541.

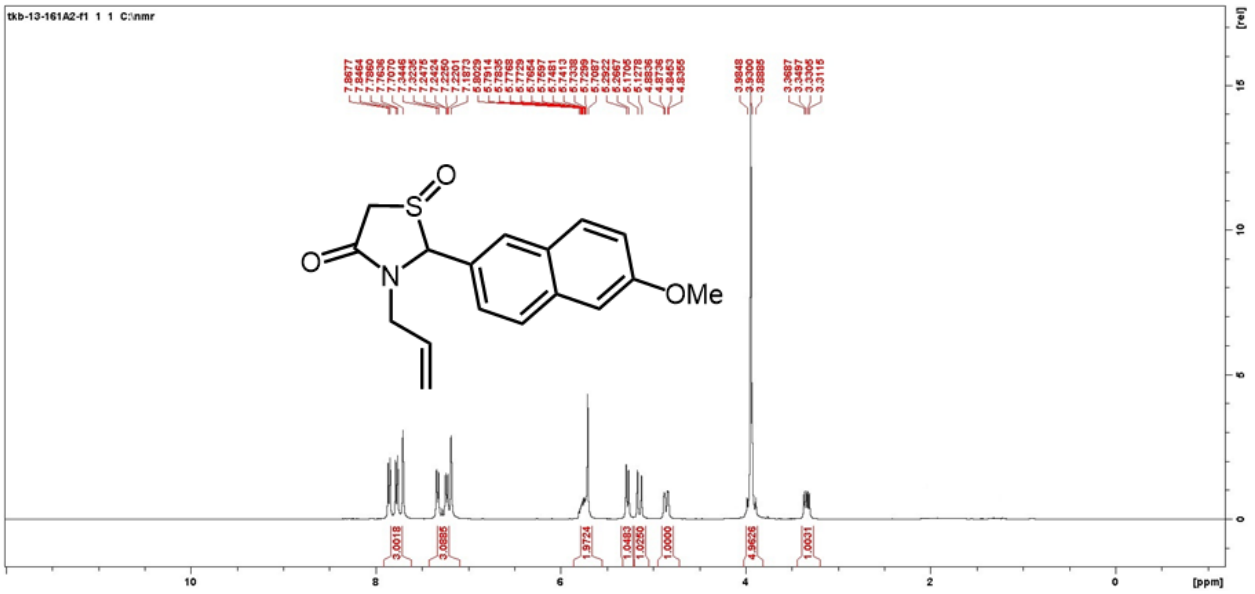

tkb-13-158C2-f1 1 1 C:\Bruker\TopSpin4.0.6\Research-data
F3C
[ppm]


tkb-13-158C2-f1 13 1 C:\Bruker\TopSpin4.0.6\Research-data
F3C
[ppm]



Compound 7h

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 296.1 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.33 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.23 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.18 (d, *J* = 2.6 Hz, 1H), 5.83 – 5.70 (m, 1H), 5.71 (s, 1H), 5.28 (d, *J* = 10.1 Hz, 1H), 5.15 (d, *J* = 17.1 Hz, 1H), 4.91 – 4.81 (m, 1H), 3.96 – 3.89 (m, 4H), 3.34 (dd, *J* = 15.4, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.7, 159.0, 135.7, 129.8, 129.8, 128.6, 128.4, 128.0, 124.9, 123.2, 120.2, 120.1, 105.9, 81.6, 55.4, 50.3, 44.7. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{17}NO_3S$, 315.0929, found 315.0922.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S
N
OMe
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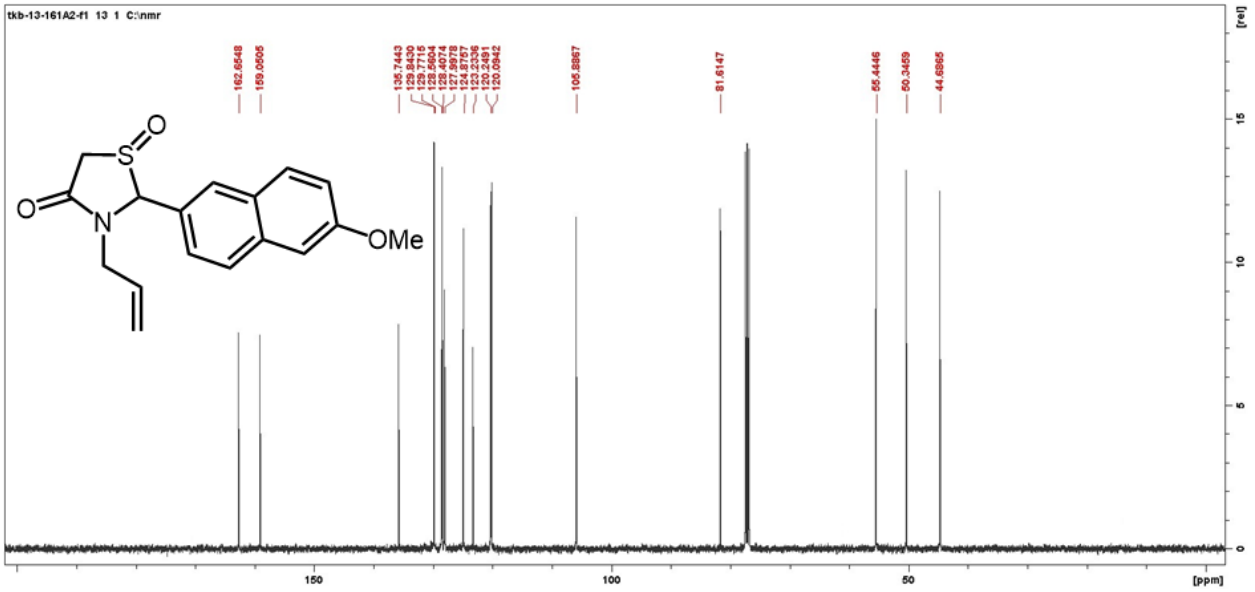
[ppm]


tkb-13-161A2-f1 13 1 C!nmr
O
S
N
OMe
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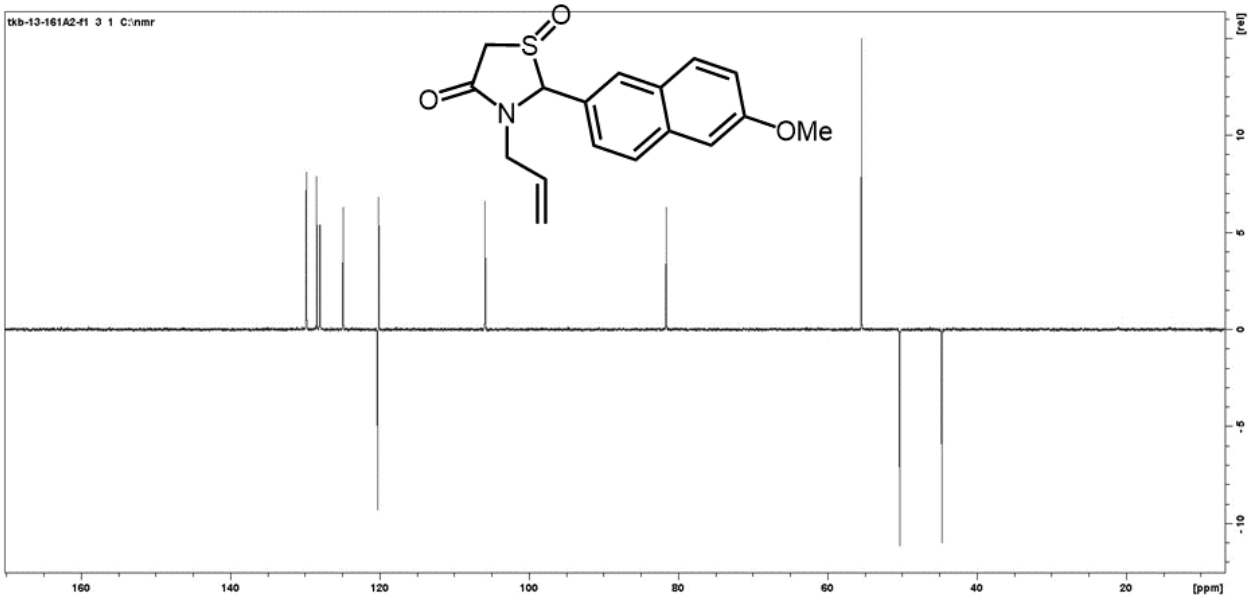
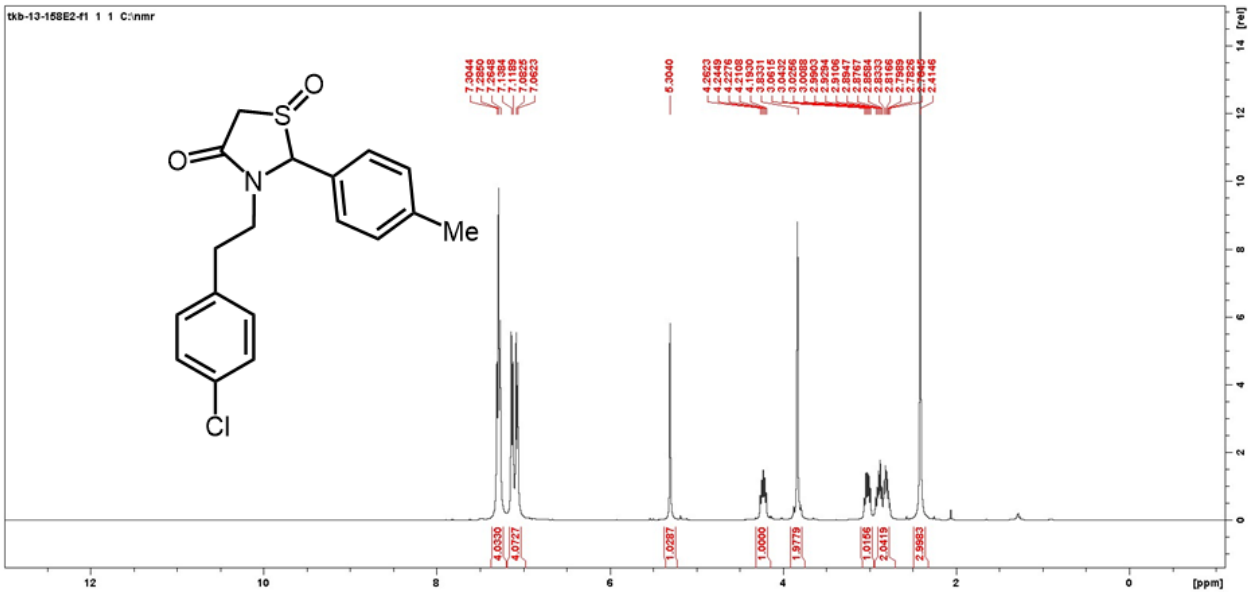
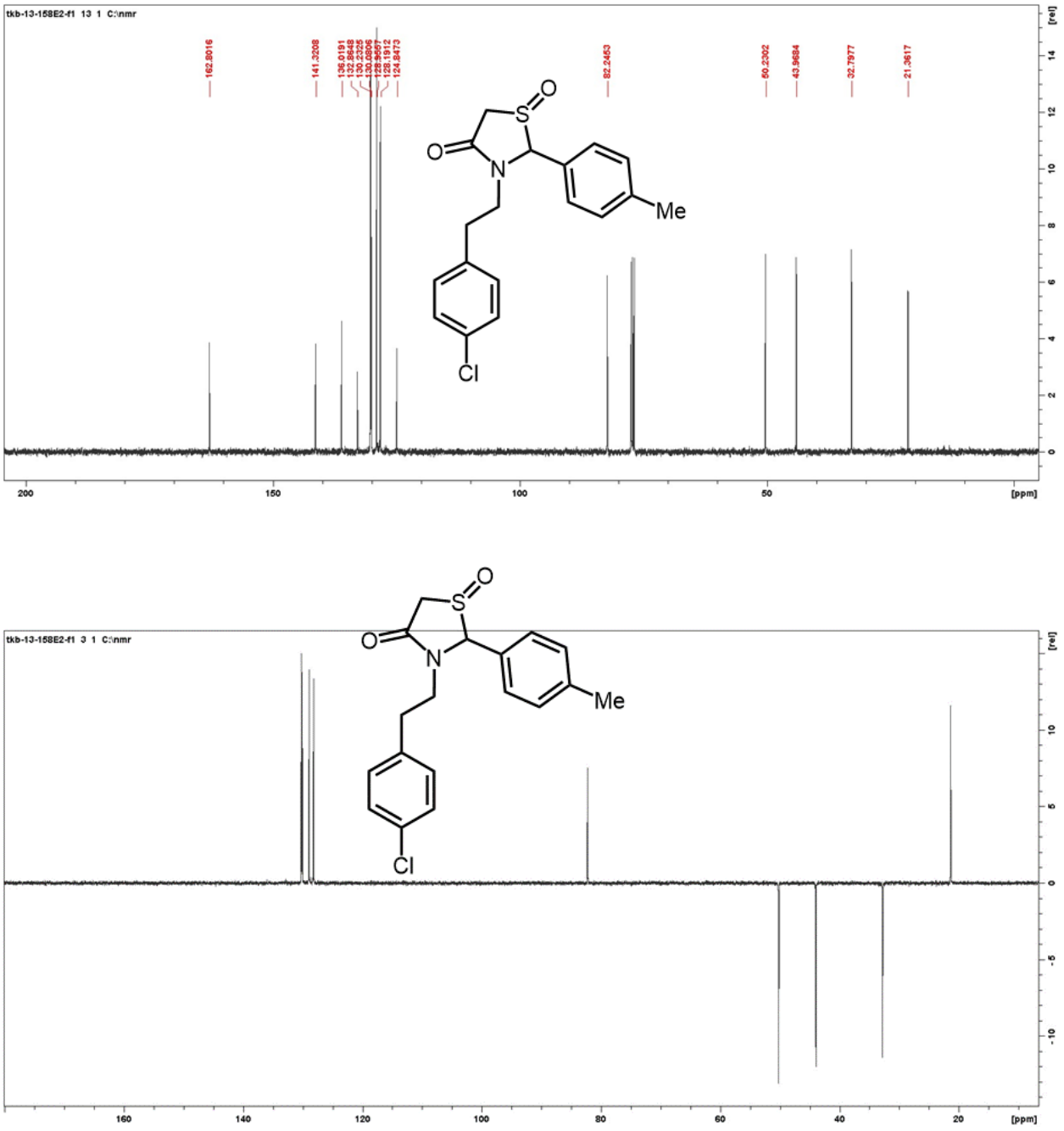
[ppm]



Compound 7i

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 308.8 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 4H), 7.14 – 7.06 (m, 4H), 5.30 (s, 1H), 4.29 – 4.17 (m, 1H), 3.83 (s, 2H), 3.83 – 2.76 (m, 3H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 141.3, 136.0, 132.9, 130.2, 130.1, 129.0, 128.2, 124.8, 82.2, 50.2, 44.0, 32.8, 21.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{18}ClNO_2S$, 347.0747, found 347.0753.

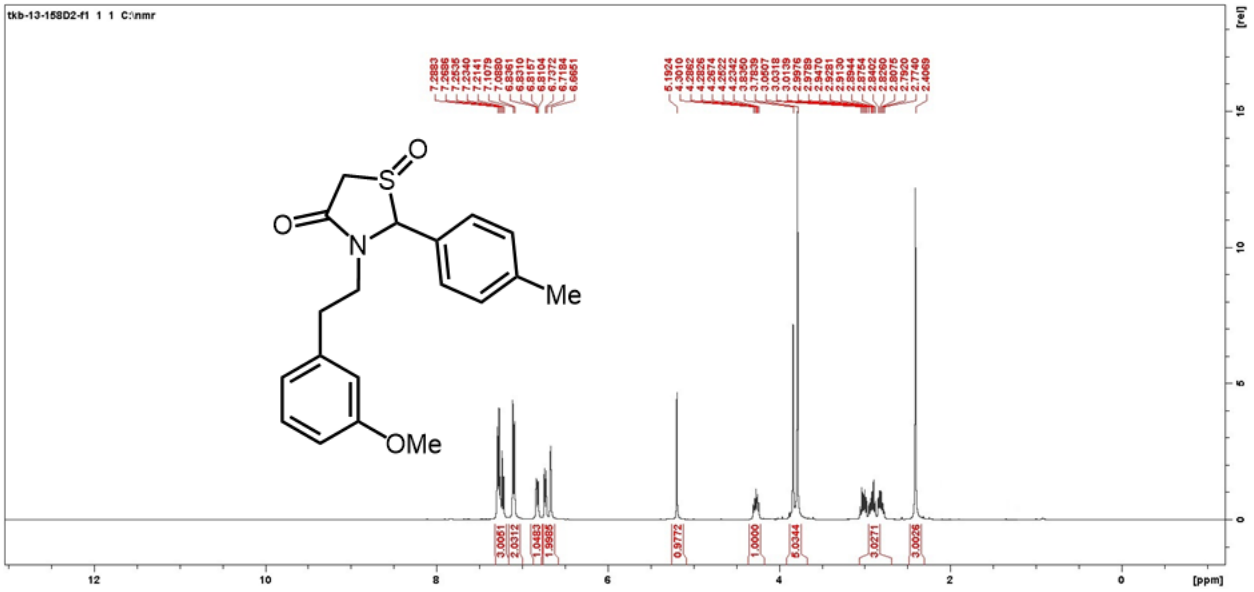


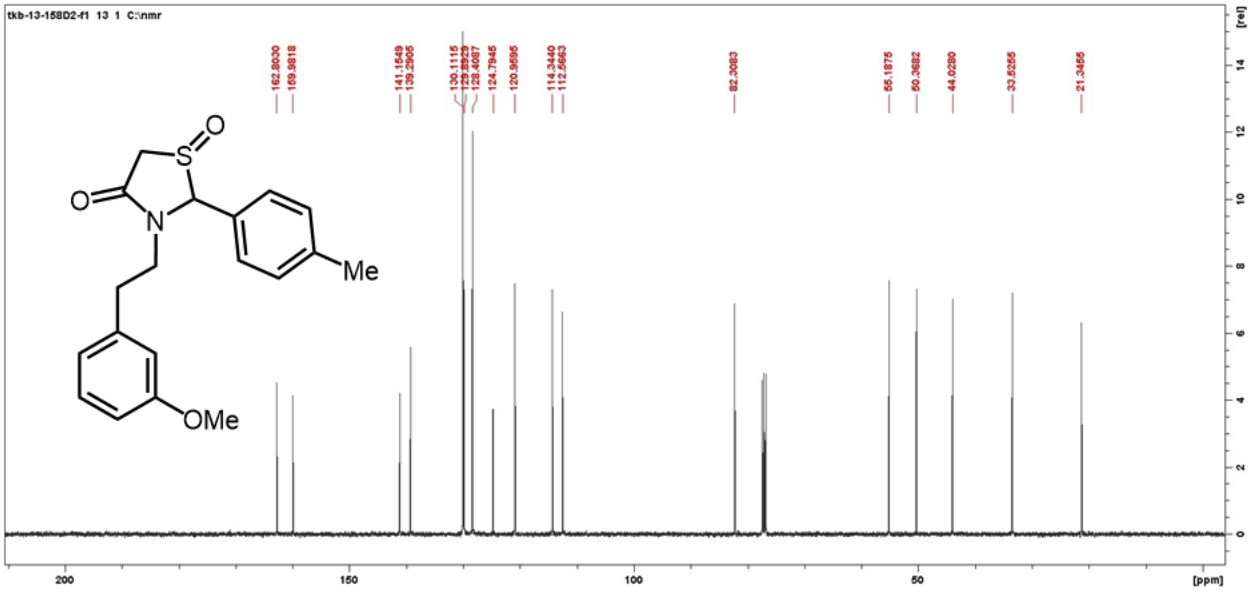


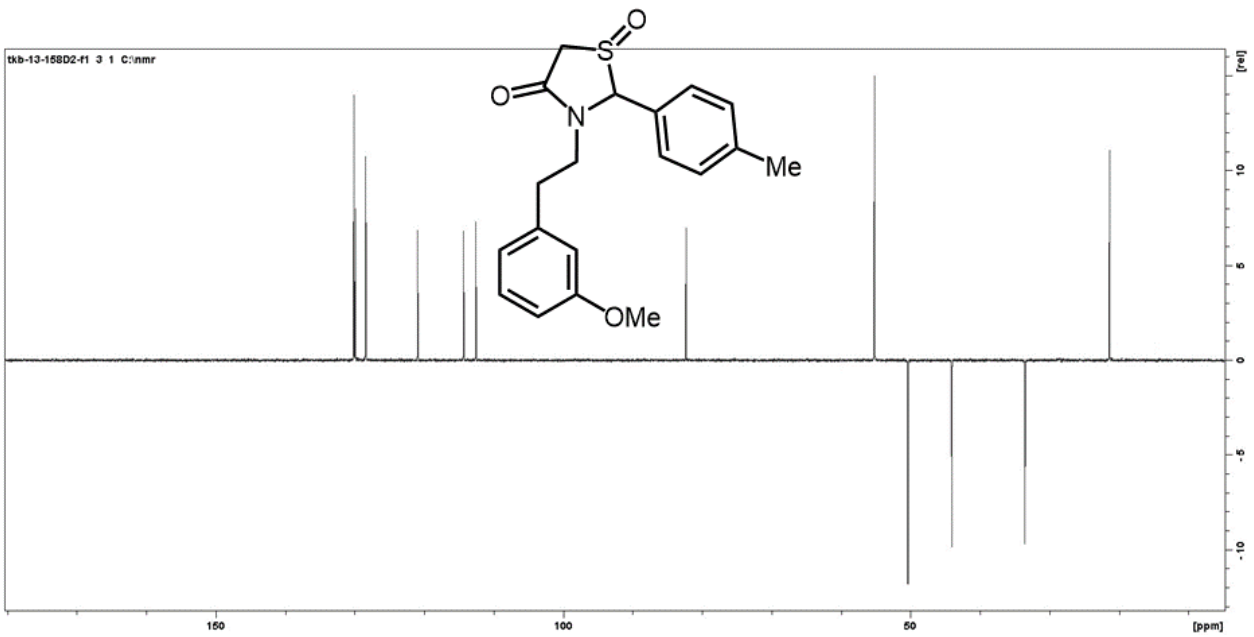
Compound 7j

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 157.8 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 3H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.82 (dd, *J* = 8.4, 2.6 Hz, 1H), 6.73 (d, *J* = 7.5 Hz, 1H), 6.66 (t, *J* = 2.0 Hz, 1H), 5.19 (s, 1H), 4.27 (ddd, *J* = 13.4, 7.6, 5.5 Hz, 1H), 3.83-3.78 (m, 5H), 3.01 (dt, *J* = 14.0, 7.5 Hz, 1H), 2.91 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.81 (ddd, *J* = 13.5, 7.6, 5.5 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 156.0, 141.2, 139.3, 130.1,

129.9, 128.4, 124.8, 120.9, 114.3, 112.6, 82.3, 55.2, 50.4, 44.0, 33.5, 21.3. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{19}H_{21}NO_3S$, 343.1242, found 343.1247.

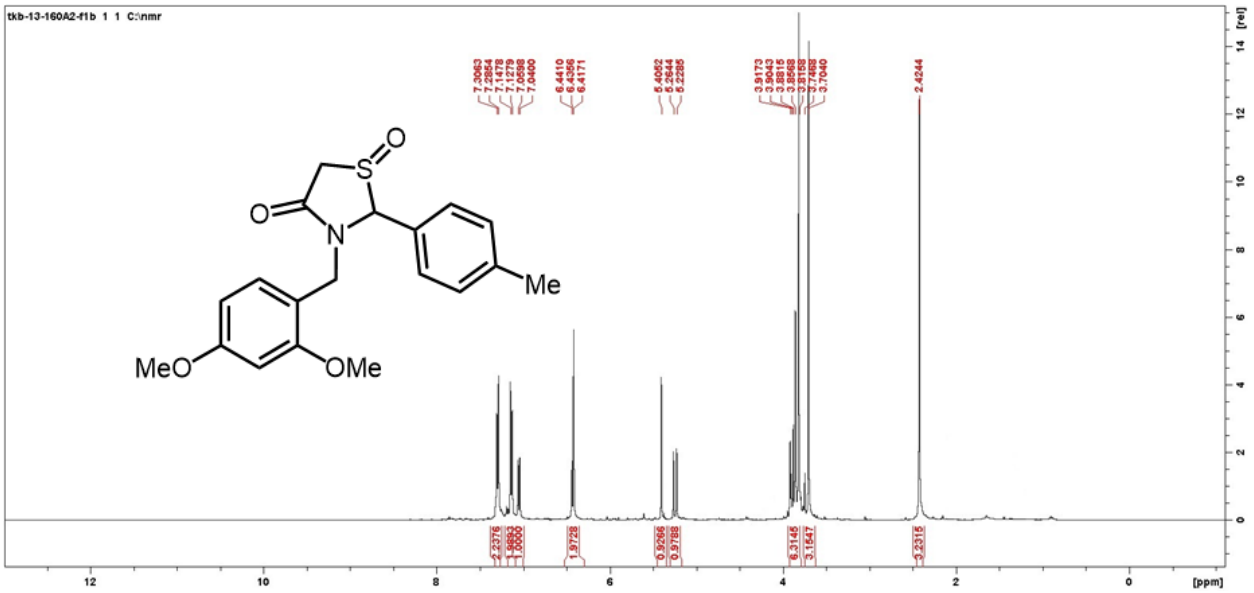


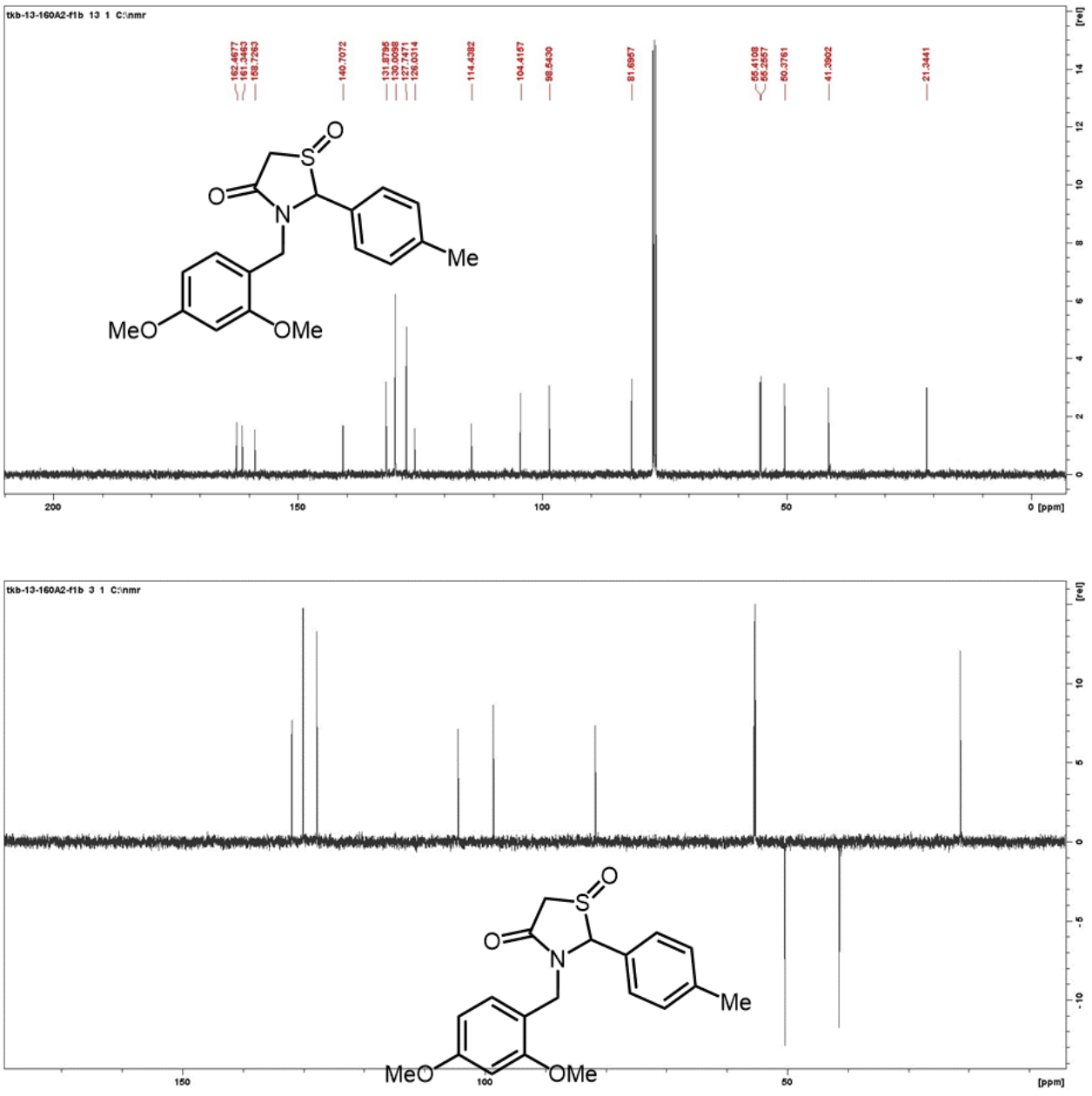




Compound 7k

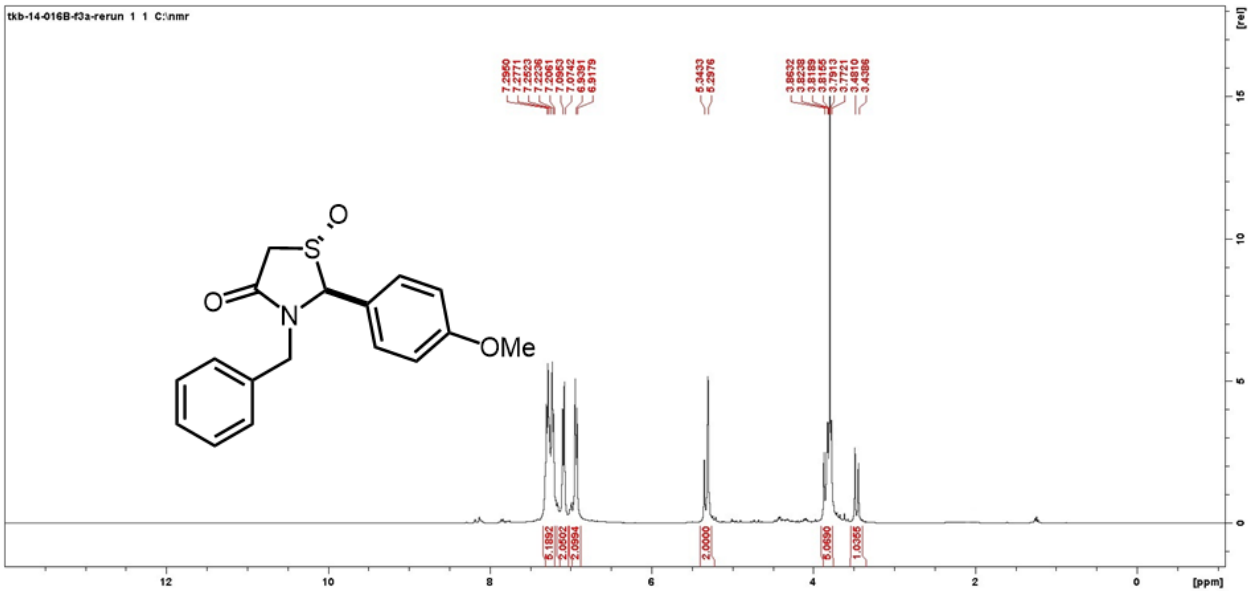
Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 156.2 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 1H), 6.44 (d, *J* = 2.3 Hz, 1H), 6.42 (s, 1H), 5.41 (s, 1H), 5.25 (d, *J* = 14.4 Hz, 1H), 3.92 – 3.81 (m, 6H), 3.70 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 161.3, 158.7, 140.7, 131.9, 130.0, 127.8, 126.0, 114.4, 104.4, 98.5, 81.7, 55.4, 55.3, 50.4, 41.4, 21.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{21}NO_4S$, 359.1191, found 359.1196.





Compound 7l

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 156.2 mg, 87%. Spectroscopic data as previously reported.[3]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7.2523
7.2336
7.2061
7.0953
7.0742
6.8981
6.8179
5.3433
5.2976
3.8632
3.8238
3.8189
3.8156
3.7913
3.7721
3.4810
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5.1892
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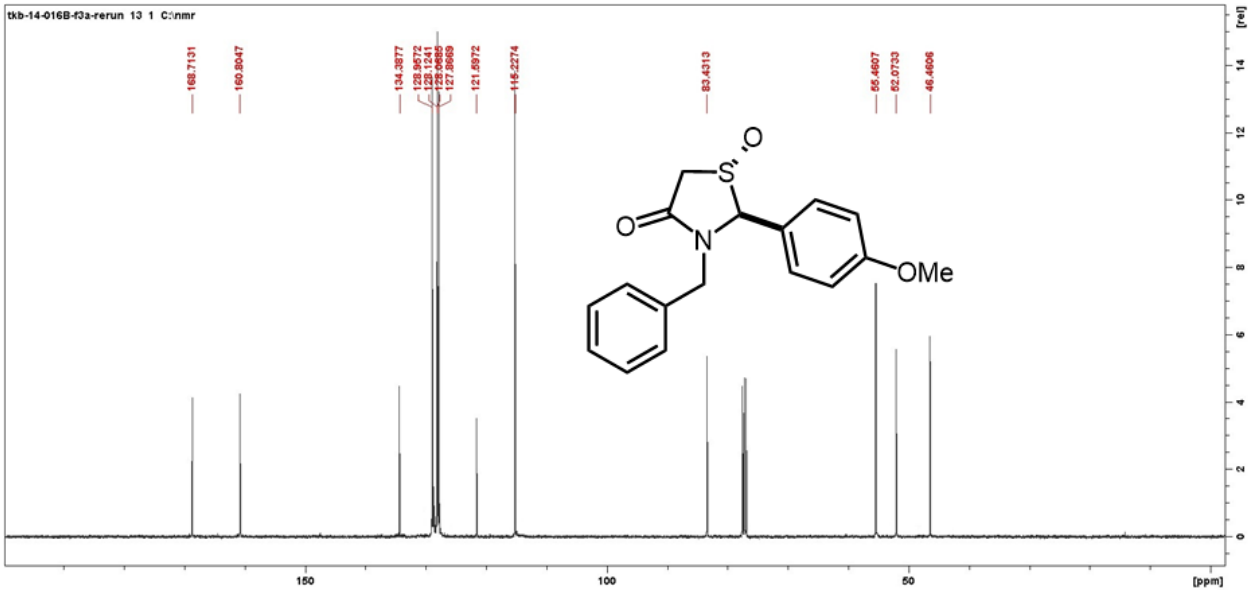
2.0994
2.0000
6.0690
1.0355
OMe
[rel]
[ppm]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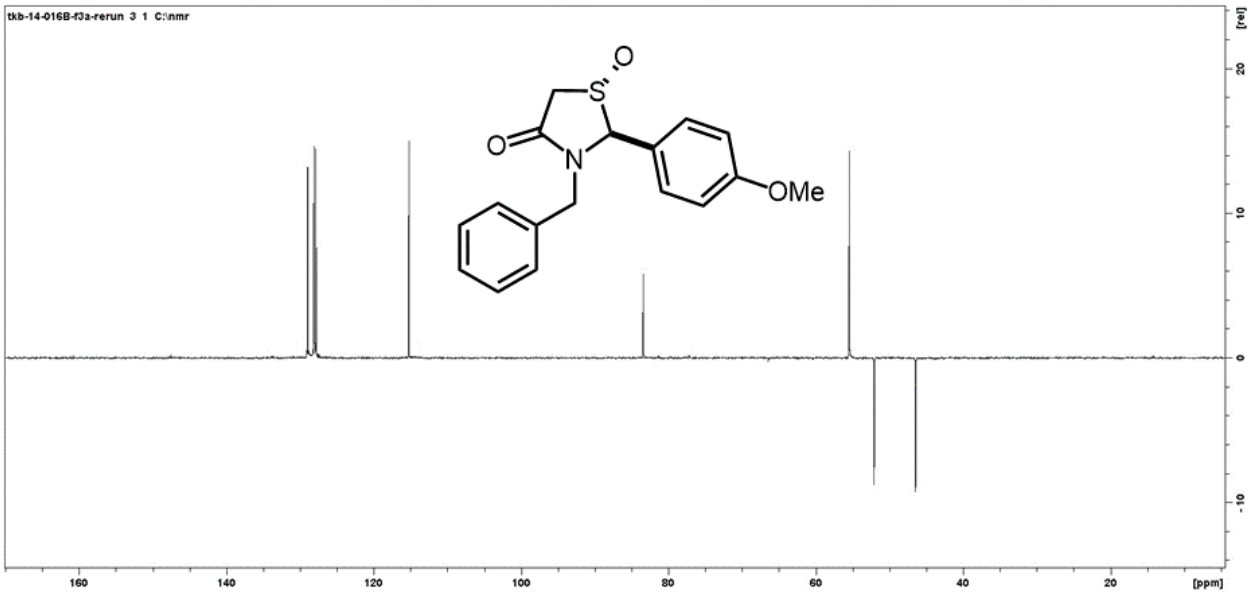
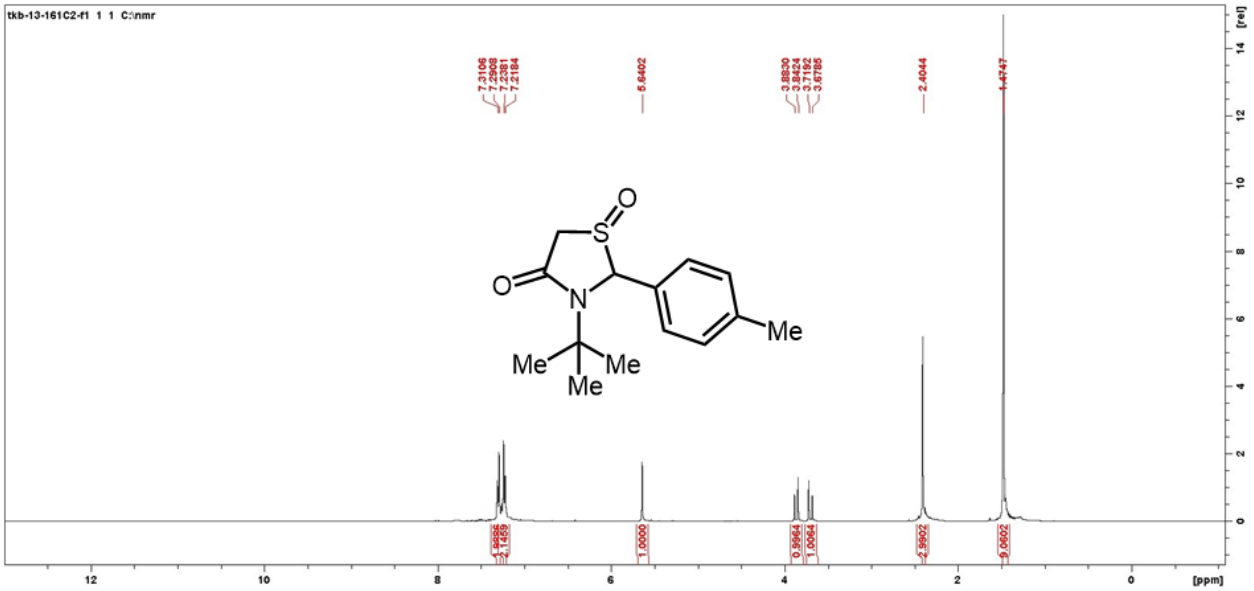
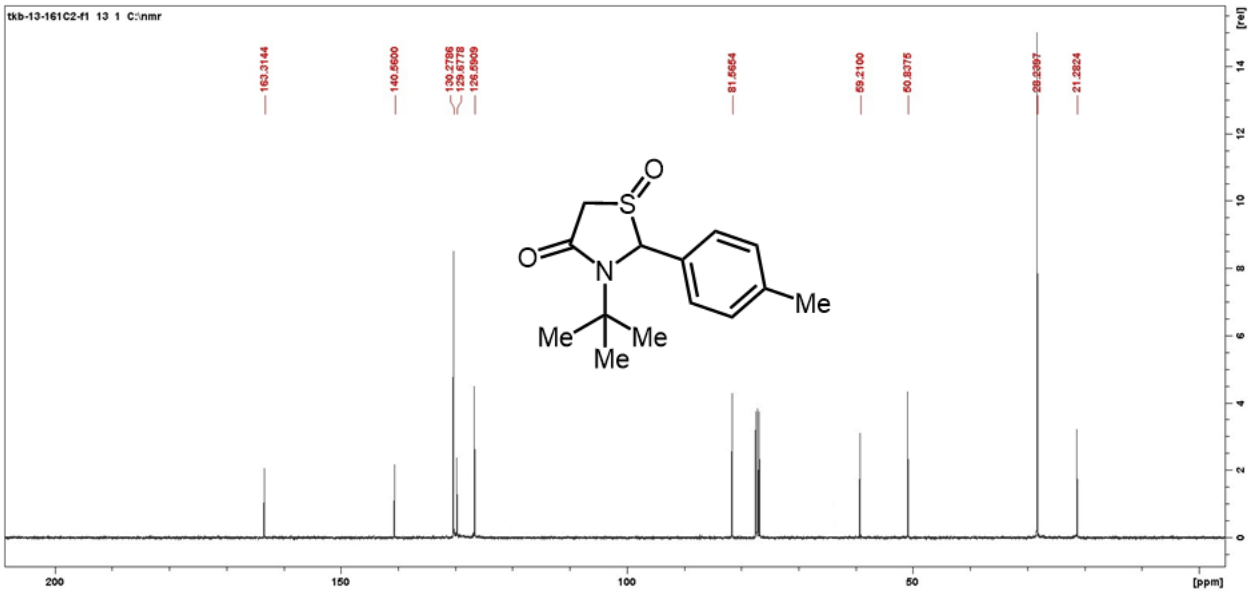
160.8047
134.3877
128.9572
128.1241
127.8969
121.5972
116.2274
83.4313
55.4607
52.0733
46.4606
OMe
[rel]
[ppm]

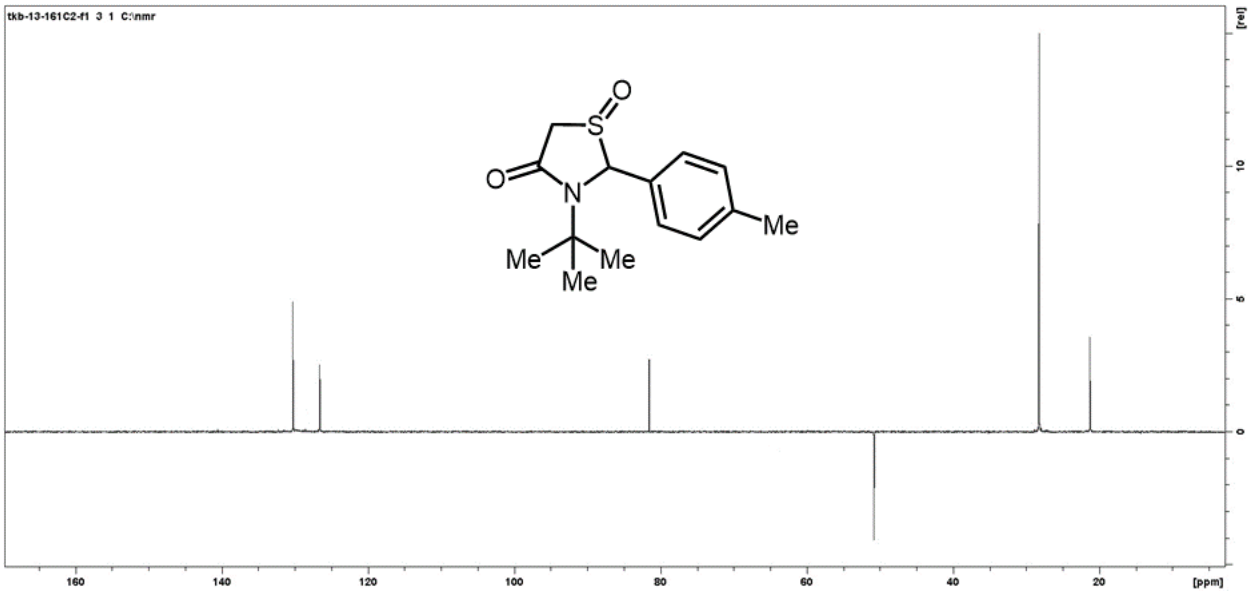


Compound 7m

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (75:25 to 0:100). Yield = 238.5 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.22 (m, 4H), 5.64 (s, 1H), 3.86 (d, *J* = 16.3 Hz, 1H), 3.70 (d, *J* = 16.3 Hz, 1H), 2.40 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3, 140.7, 131.5, 130.3, 129.7, 128.6, 126.6, 81.6, 59.2, 50.8, 28.2, 21.3. **HRMS-EI$^+$** (*m/z*): calc for $C_{14}H_{19}NO_2S$, 265.1136, found 265.1141.

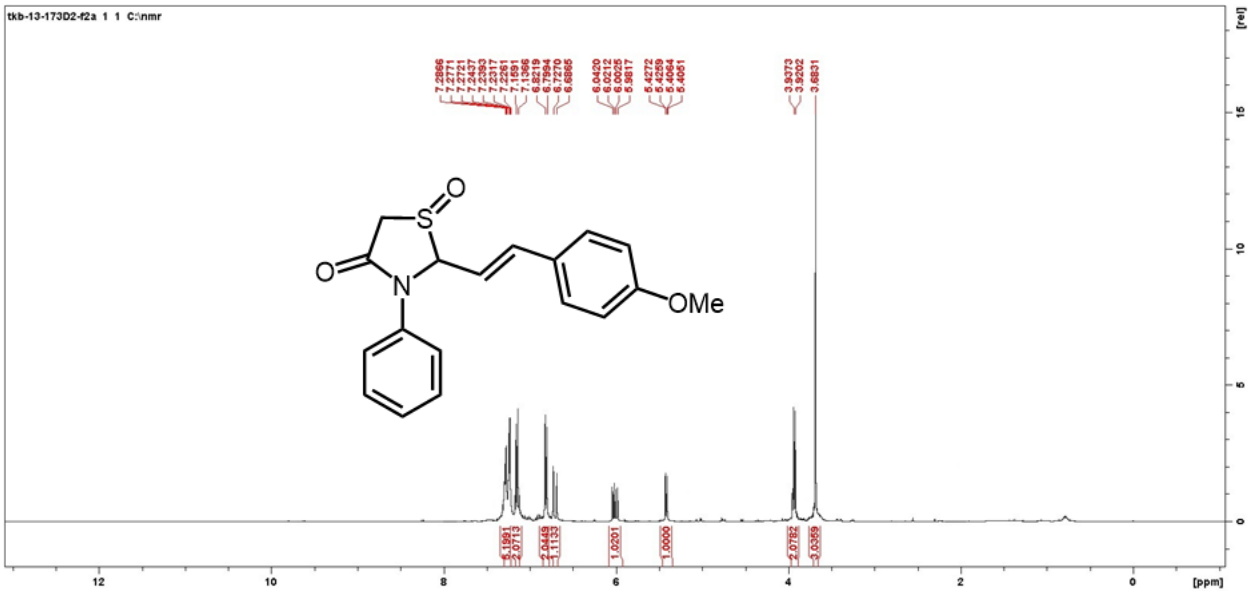






Compound 7n

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 294.3 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 5H), 7.14 (d, *J* = 6.8 Hz, 2H), 6.81 (d, *J* = 6.8 Hz, 2H), 6.74 (d, *J* = 15.8 Hz, 1H), 6.01 (dd, *J* = 15.8, 8.3 Hz, 2H), 5.42 (d, *J* = 8.3 Hz, 1H), 3.94 – 3.92 (m, 2H), 3.68 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 159.2, 140.1, 134.5, 129.5, 128.8, 127.6, 127.3, 114.8, 82.4, 55.5, 51.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{17}NO_3S$, 327.0929, found 327.0932.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7.2317
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6.6865
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6.0272
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5.4051
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2.0713
2.0449
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12
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8
6
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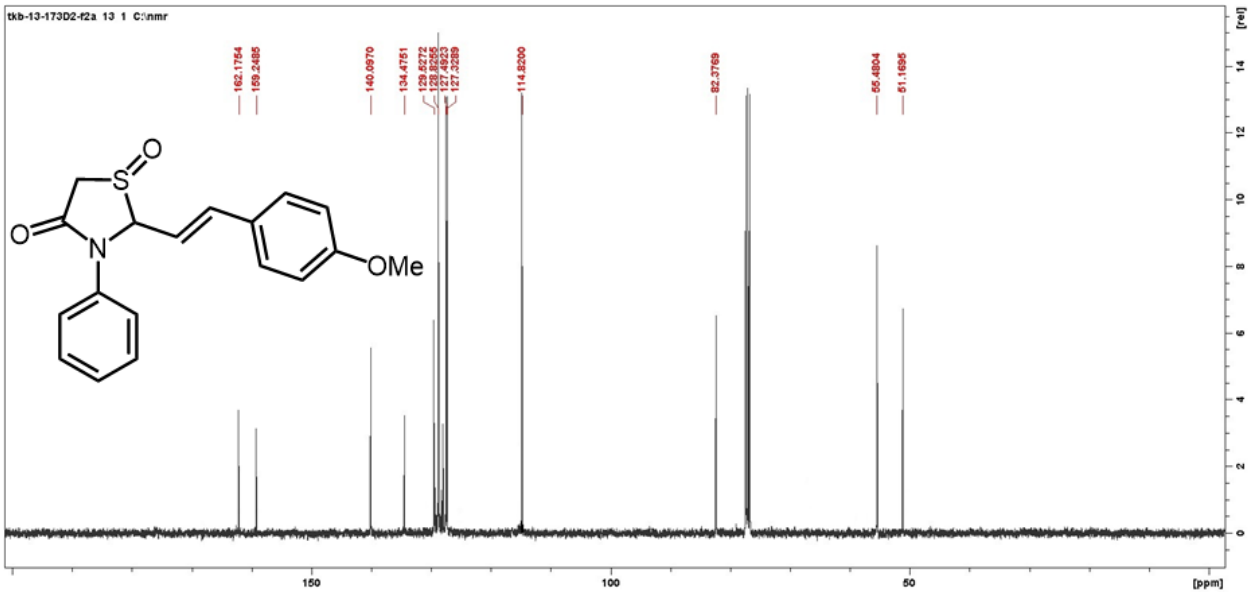
0
[ppm]
[rel]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128.8255
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S
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N
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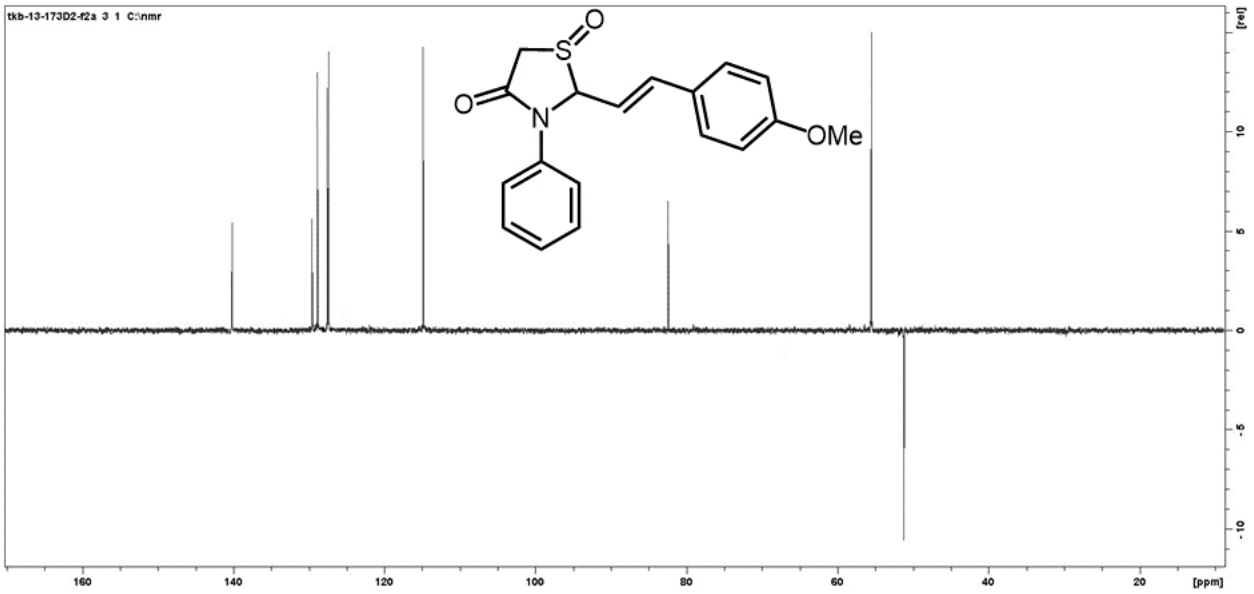
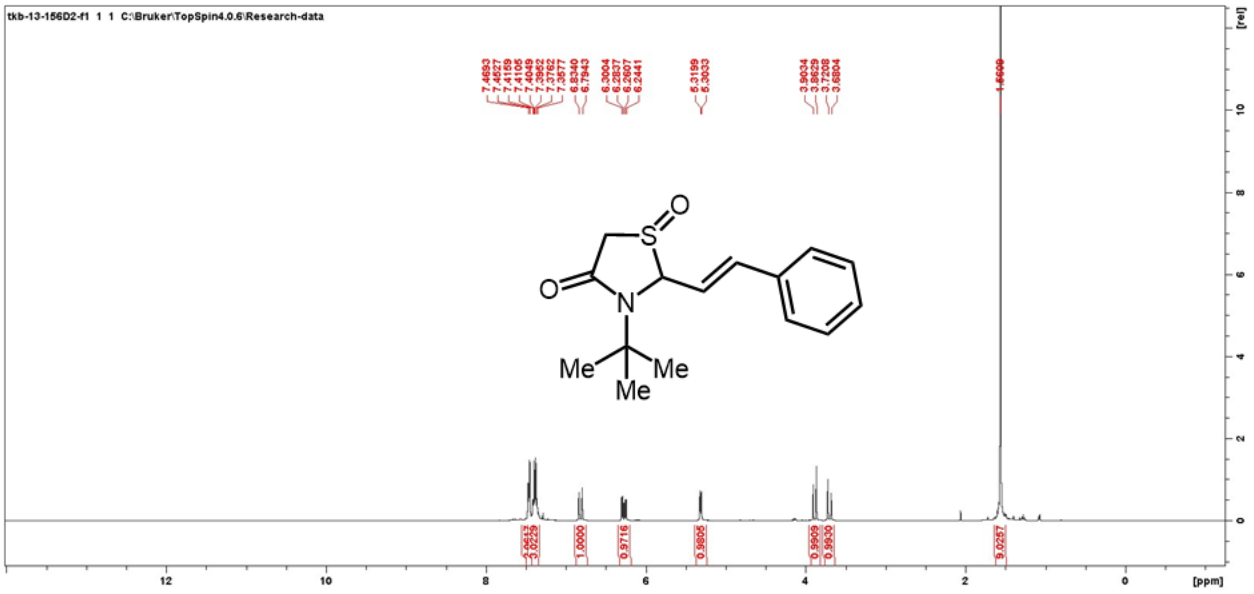
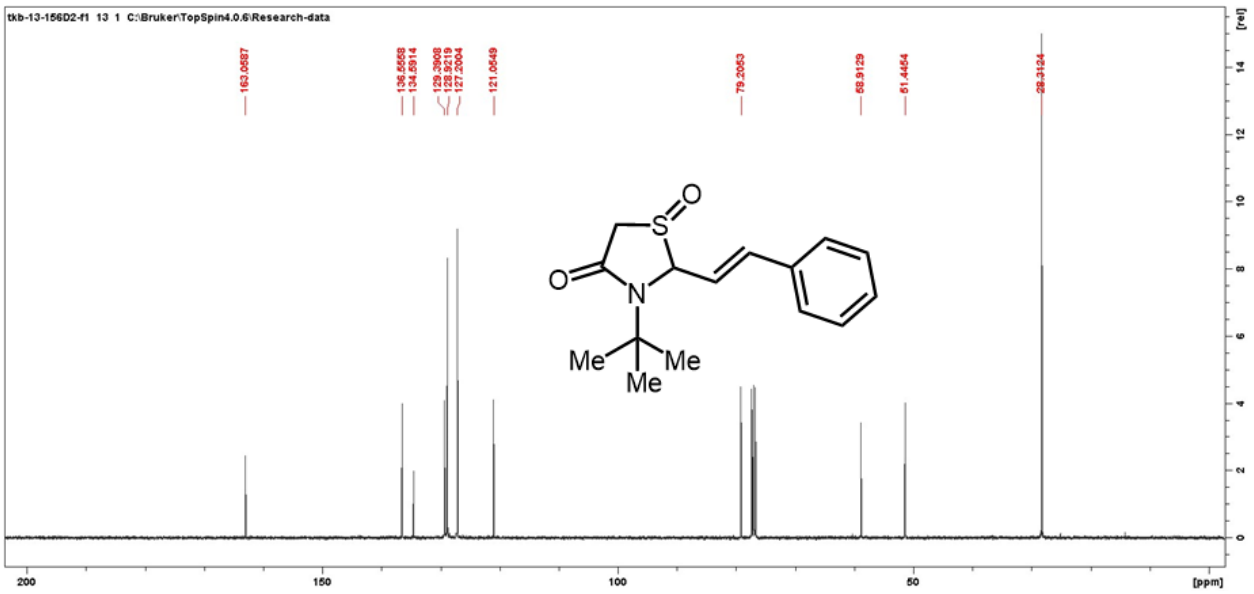
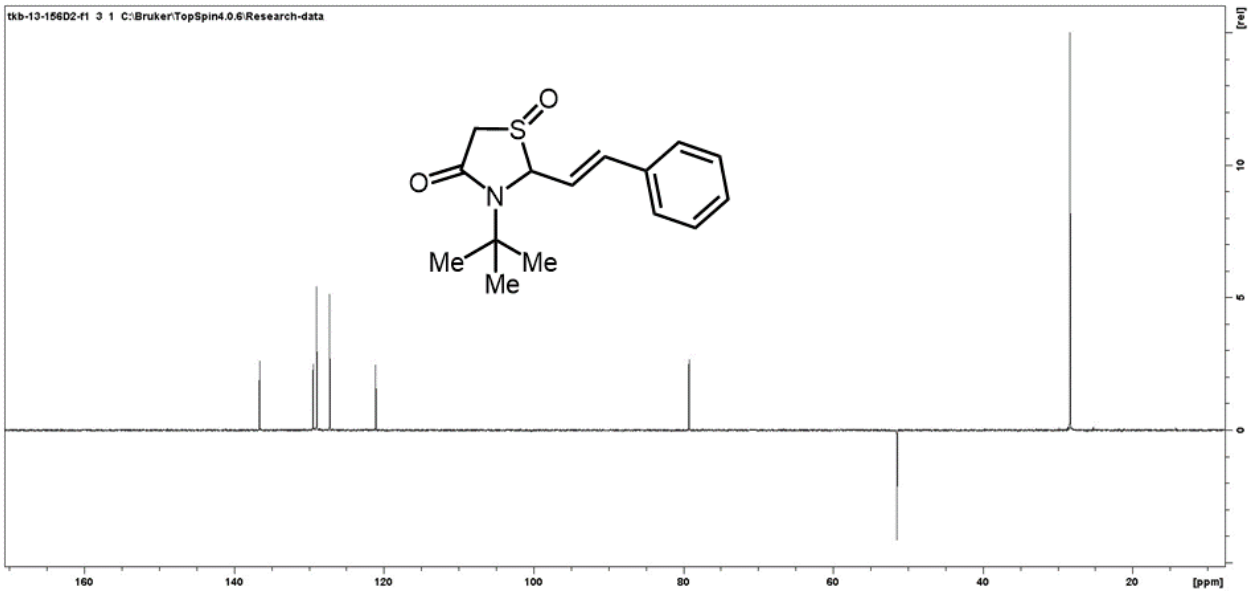


Compound 7o

Prepared in 1.0 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 260.4 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 5H), 6.81 (d, *J* = 15.9 Hz, 1H), 6.27 (dd, *J* = 15.9, 6.6 Hz, 1H), 5.31 (d, *J* = 6.6 Hz, 1H), 3.88 (d, *J* = 16.2 Hz, 1H), 3.70 (d, *J* = 16.1 Hz, 1H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 136.6, 134.6, 129.4, 128.9, 127.2, 121.1, 79.2, 58.9, 51.4, 28.3. **HRMS-EI$^+$** (*m/z*): calc for $C_{15}H_{19}NO_2S$, 277.1136, found 277.1131.

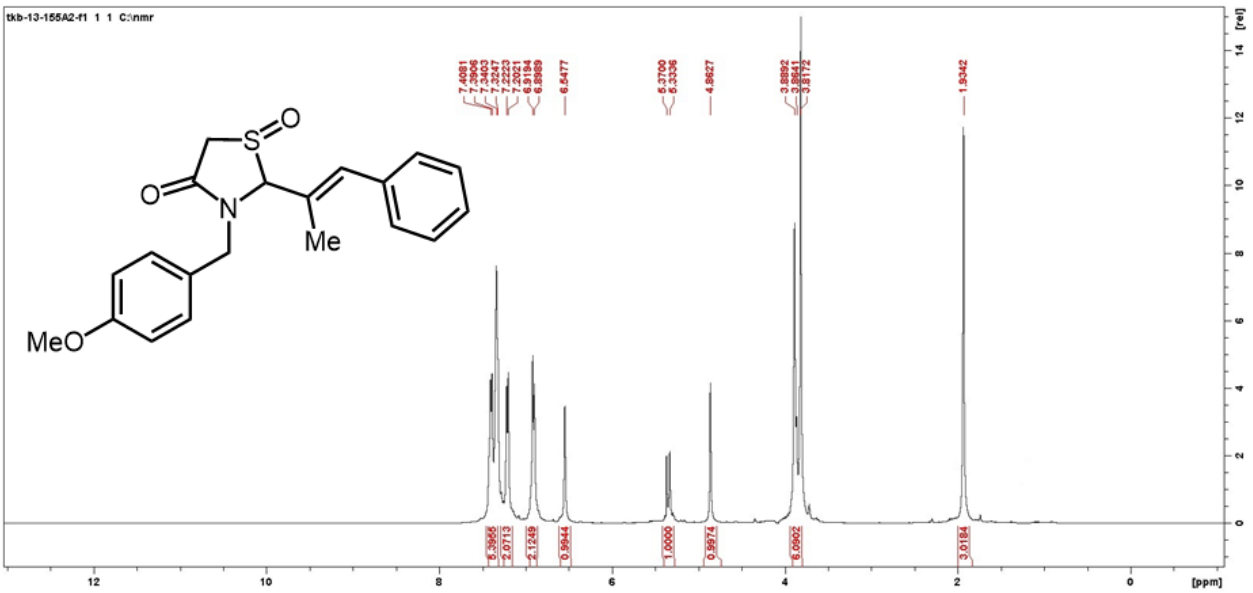






Compound 7p

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 163.3 mg, 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.32 (m, *5*), 7.21 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.3 Hz, 2H), 6.55 (s, 1H), 5.35 (d, 1H), 4.86 (s, 1H), 3.88 – 3.81 (m, 6H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.4, 159.8, 135.3, 134.5, 130.3, 130.1, 129.3, 128.5, 128.4, 128.1, 126.9, 126.5, 125.7, 114.5, 85.1, 55.3, 51.1, 45.5, 14.7. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{21}NO_3S$, 355.1242, found 355.1248.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4.8827
3.8892
3.8841
3.8172
1.5342
6.3955
2.0713
2.1249
0.9644
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6.0902
3.0184
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Me
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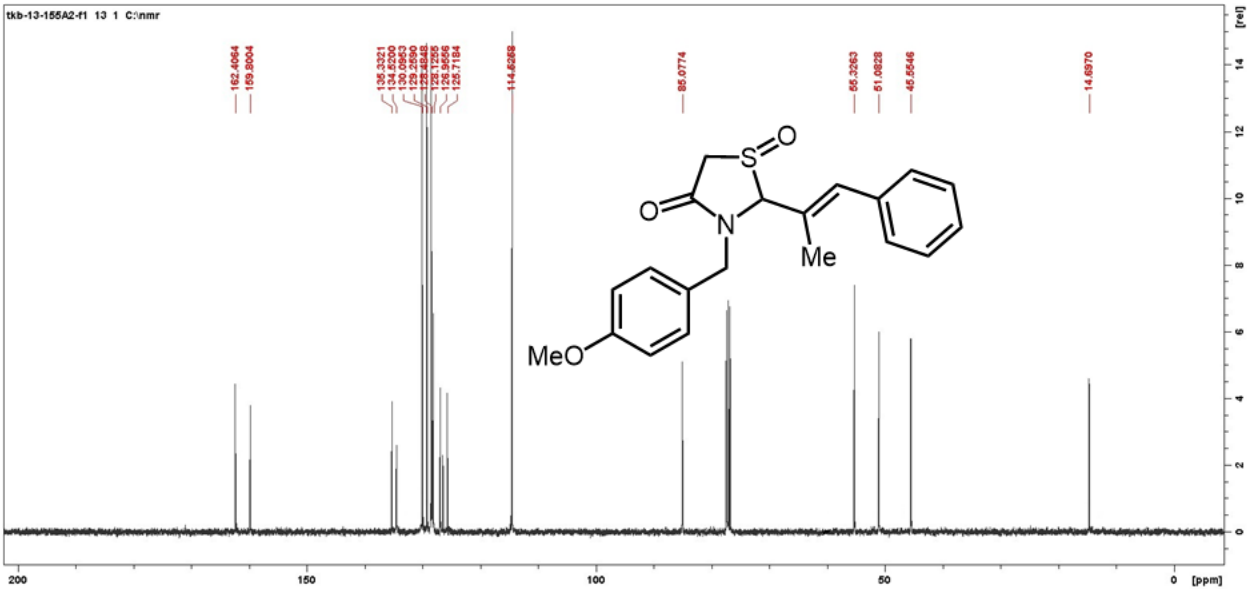
[rel]
[ppm]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14.6970
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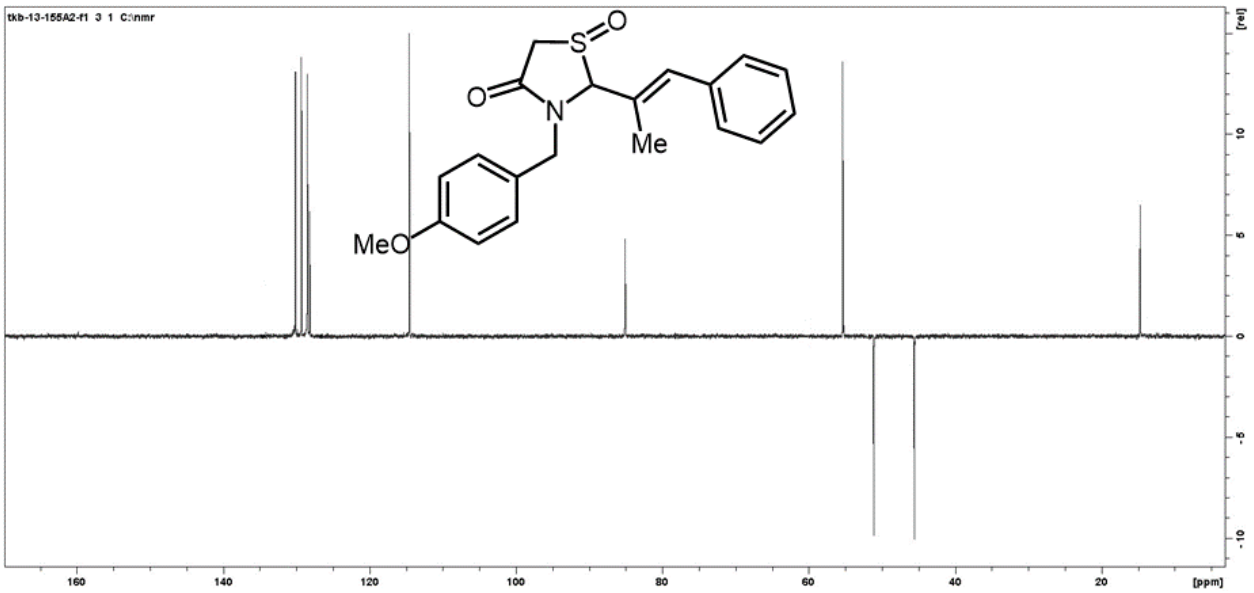
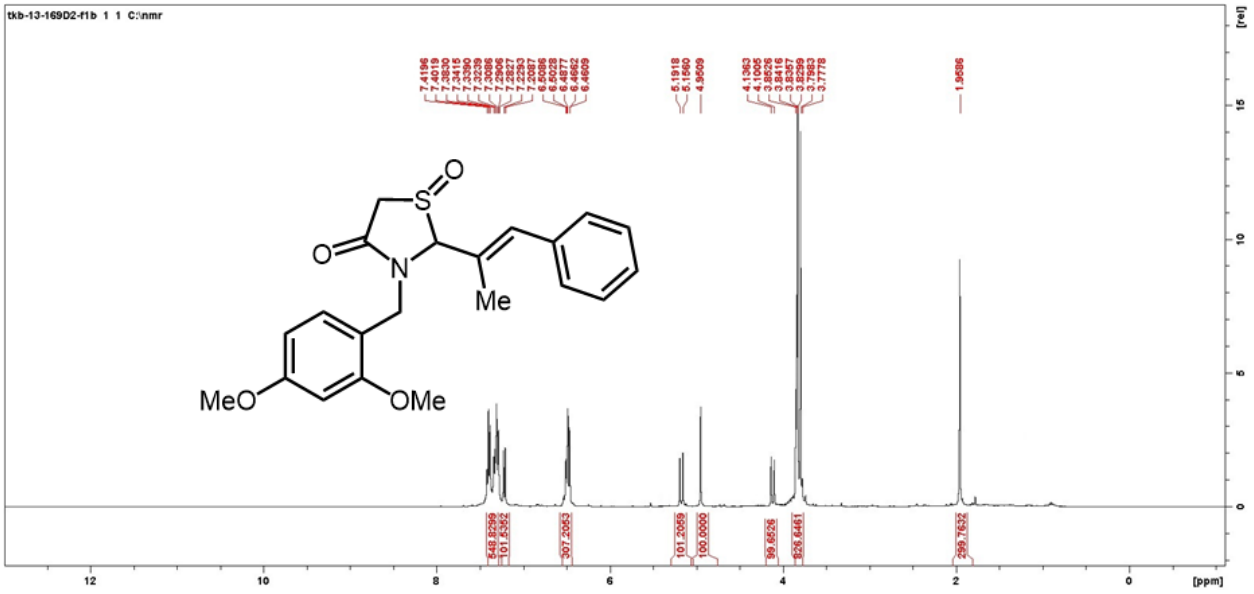
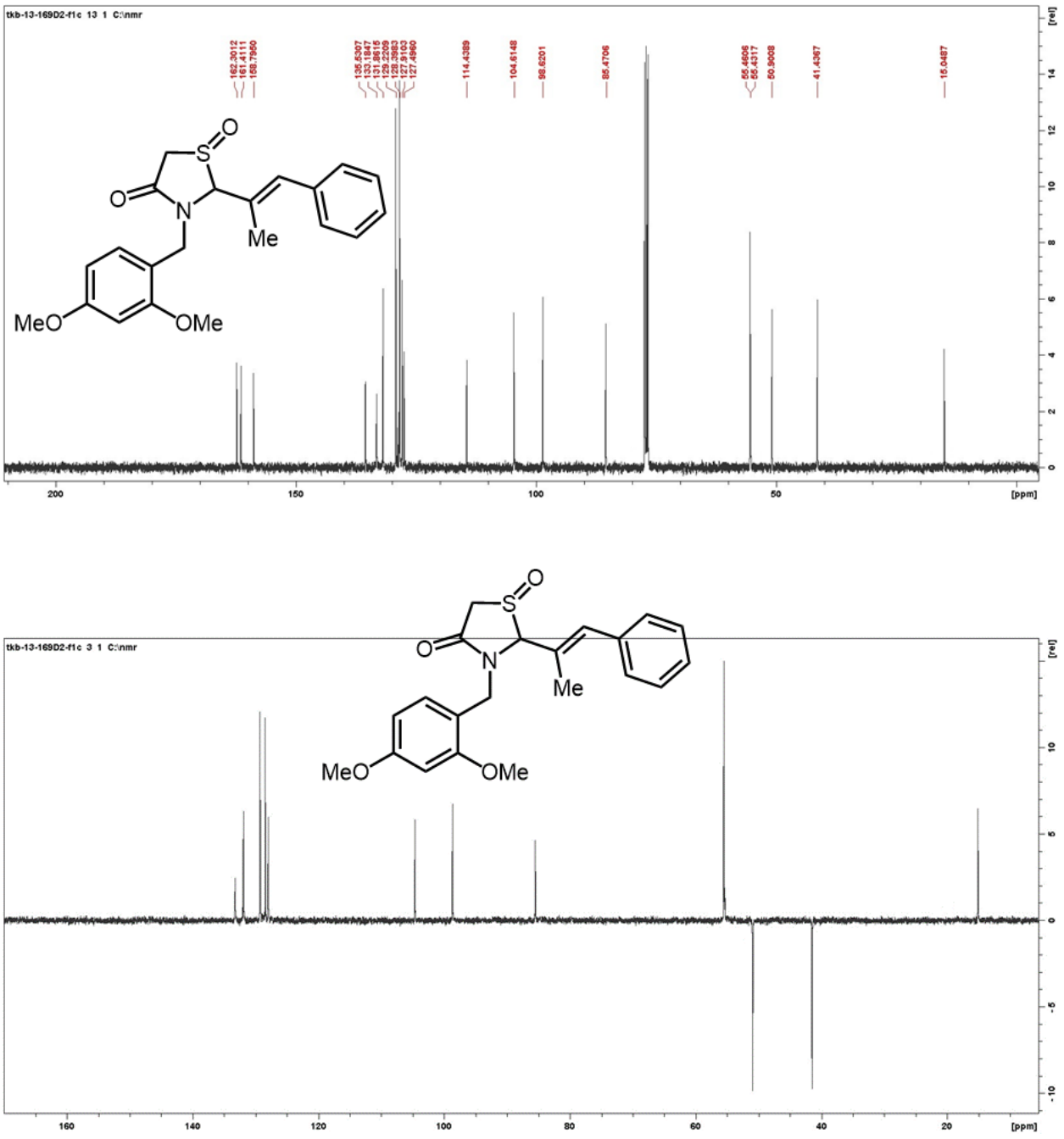
O
N
Me
MeO
[rel]
[ppm]



Compound 7q

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 173.2 mg, 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 -7.28 (m, 5H), 7.21 (d, 1H), 6.50 – 6.46 (m, 3H), 5.17 (d, *J* = 14.3 Hz, 1H), 4.95 (s, 1H), 4.12 (d, *J* = 14.3 Hz, 1H), 3.85 – 3.78 (m, 8H), 1.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.3, 161.4, 158.8, 135.5, 133.2, 131.9, 129.2, 128.4, 127.9, 127.5, 114.4, 104.6, 98.6, 85.5, 55.5, 55.4, 50.9, 41.4, 15.0. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{23}NO_4S$, 385.1348, found 385.1352.

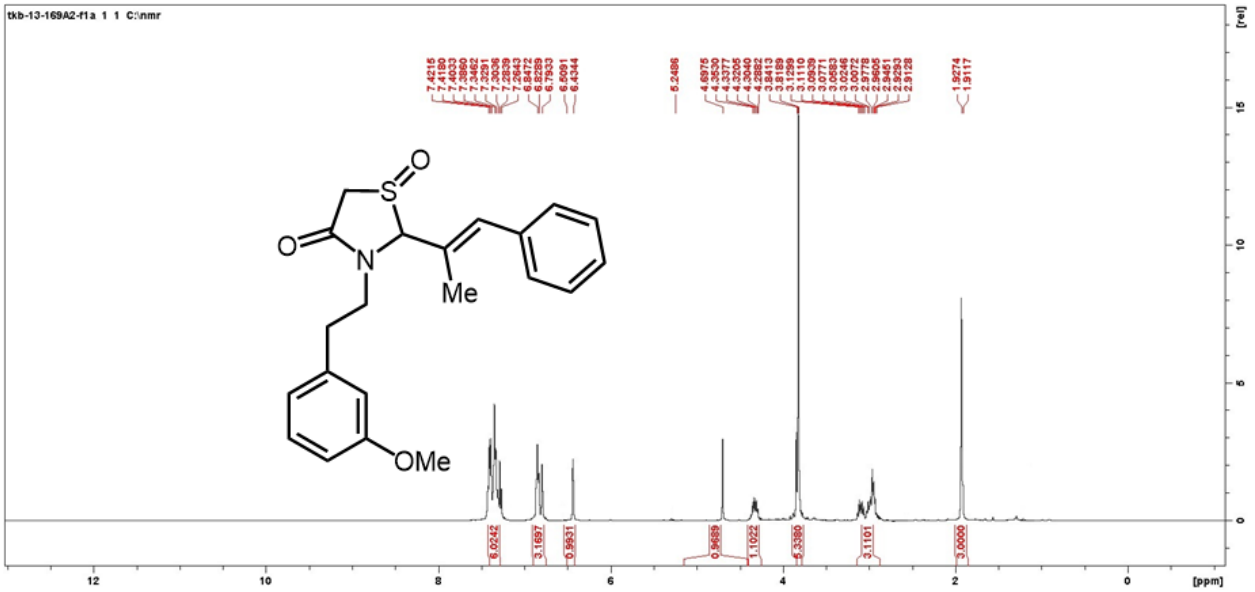


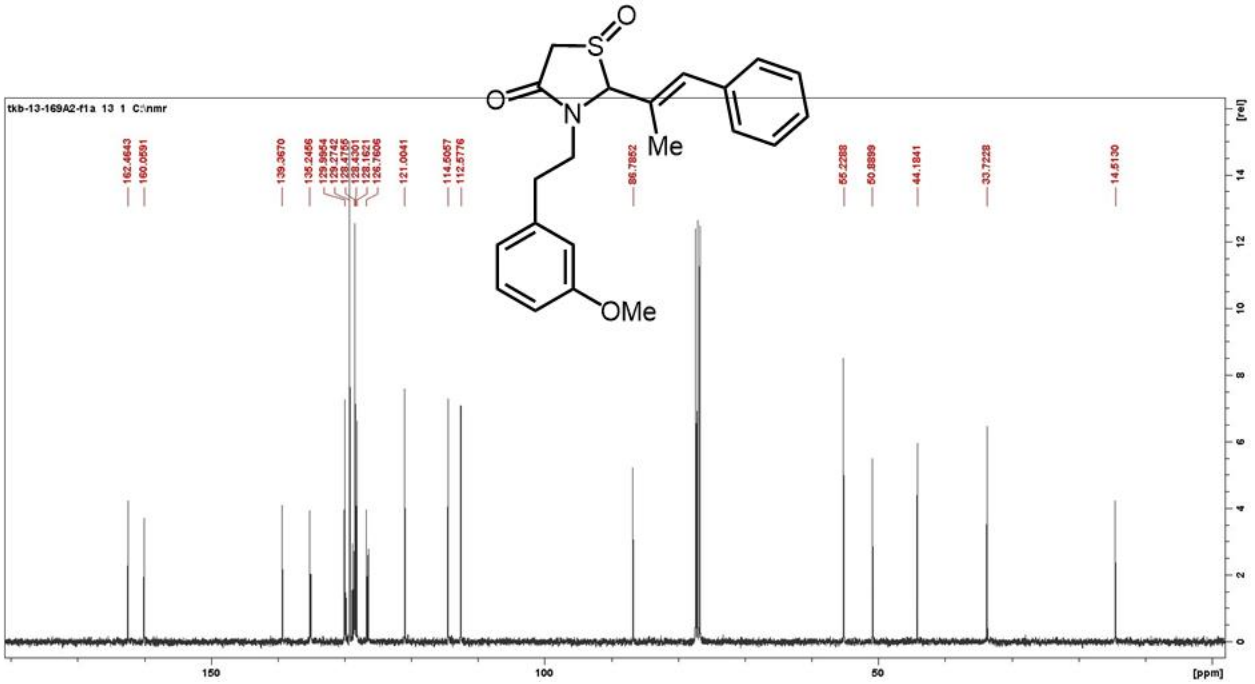


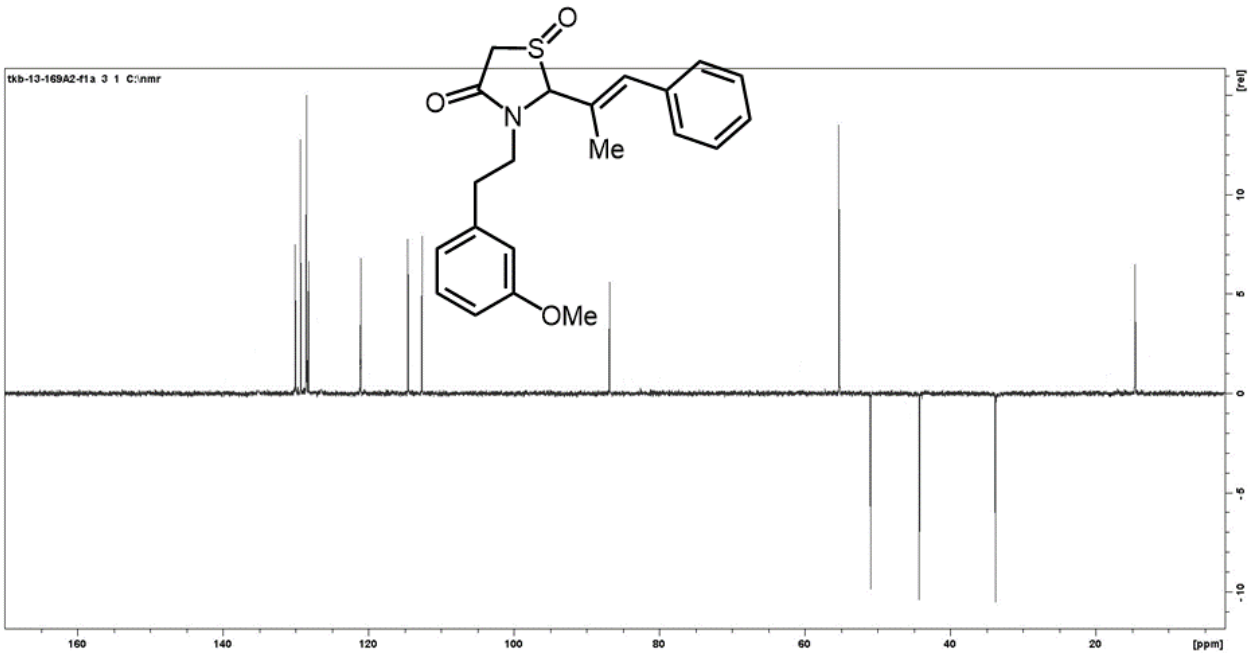
Compound 7r

Prepared in 0.5 mmol scale using **General Procedure B.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 173.4 mg, 94%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 6H), 6.85 – 6.79 (m, 3H), 6.50 (s, 1H), 4.70 (s, 1H), 4.34 (tt, *J* = 13.2, 6.9 Hz, 1H), 3.84 – 3.81 (m, 5H), 3.13 – 2.91 (m, 3H), 1.93 (s, 3H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 162.5, 160.1, 139.4, 135.2, 129.9, 129.3, 128.5, 128.2, 126.8, 121.0, 114.5, 112.6, 86.8, 55.2, 50.9, 44.2, 33.7, 14.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{23}NO_3S$, 369.1399, found 369.1395.






tkb-13-169A2-f1a 3 1 C:\nmr
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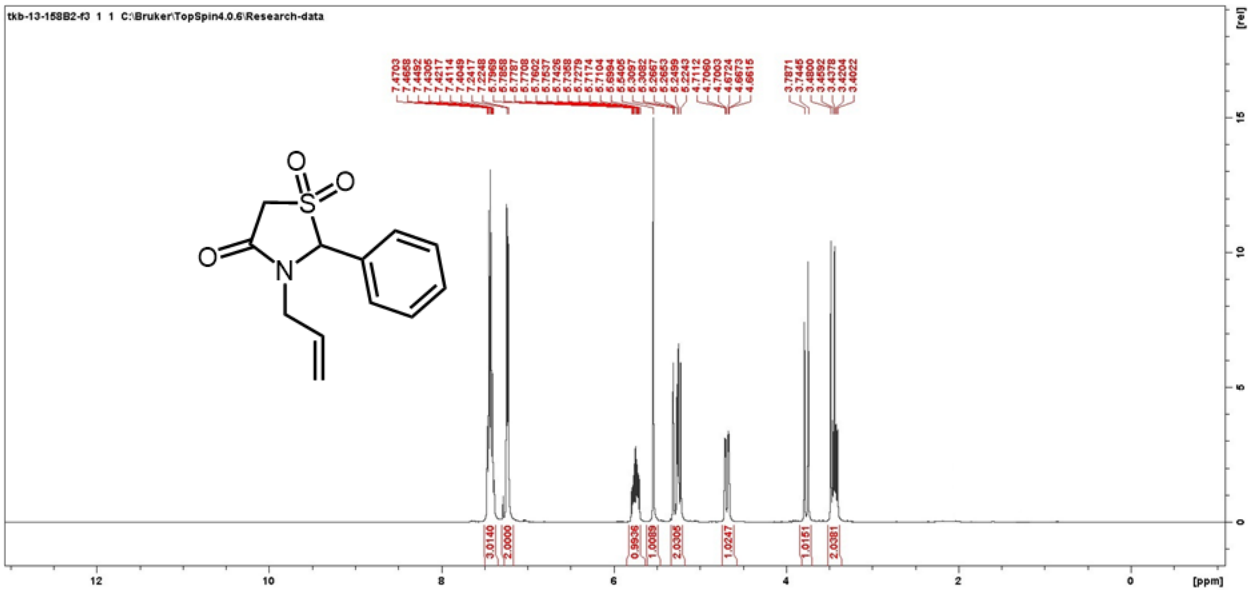
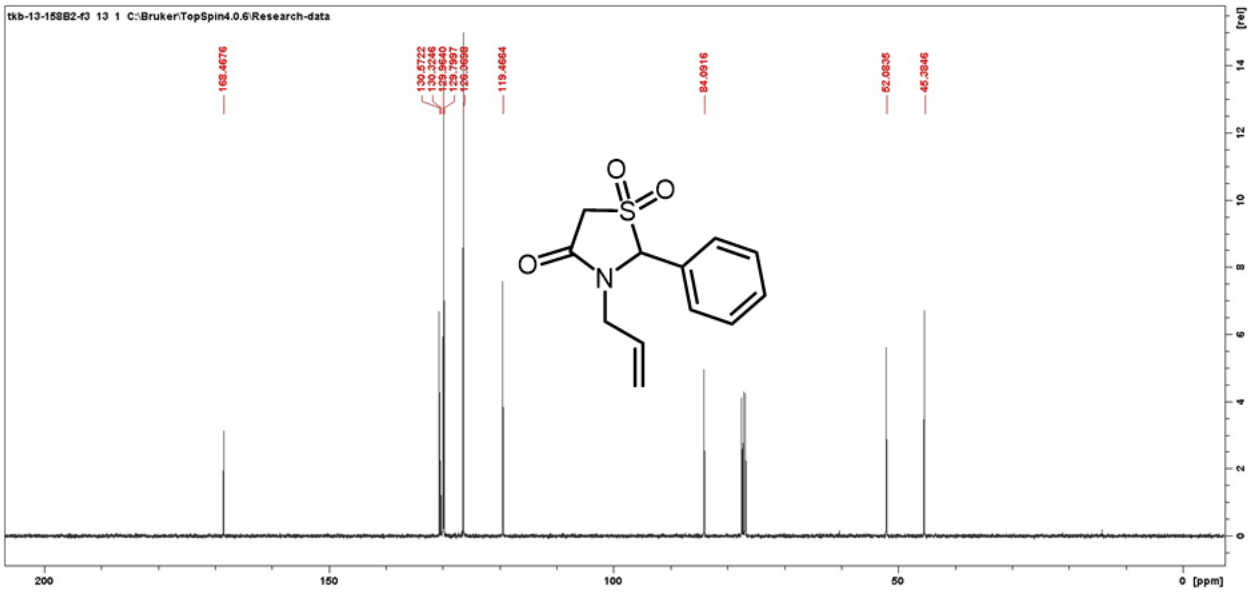
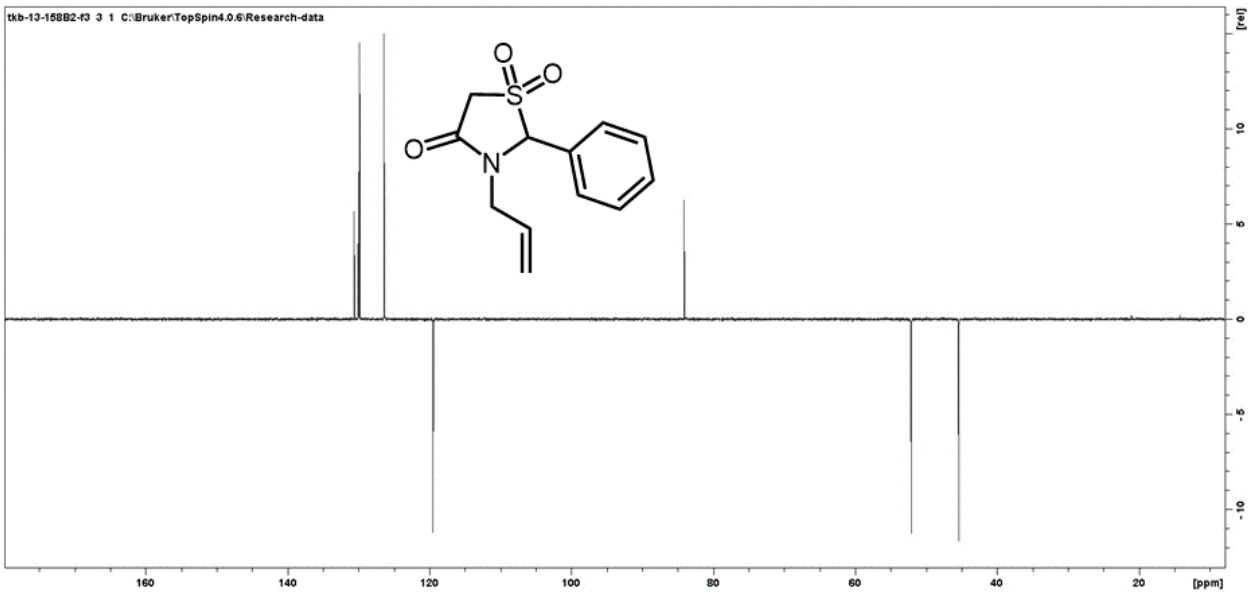
S
O
N
Me
OMe
[rel]
10
5
0
-5
-10
160
140
120
100
80
60
40
20
[ppm]

Compound 8a

Prepared in 1.0 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 215.9 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.36 (m, 3H), 7.27 – 7.20 (m, 2H), 5.75 (dddd, *J* = 17.3, 10.0, 7.2, 4.4 Hz, 1H), 5.54 (s, 1H), 5.29 (ddd, *J* = 17.1, 2.1, 1.0 Hz, 1H), 5.24 (dt, *J* = 10.2, 1.2 Hz, 1H), 4.69 (ddd, *J* = 15.5, 4.2, 2.0 Hz, 1H), 3.77 (d, *J* = 17.0 Hz, 1H), 3.50 – 3.38 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 130.6, 130.3, 130.0, 129.8, 126.6, 126.4, 119.5, 84.1, 52.1, 45.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{12}H_{13}NO_3S$, 251.0616, found 251.0622.

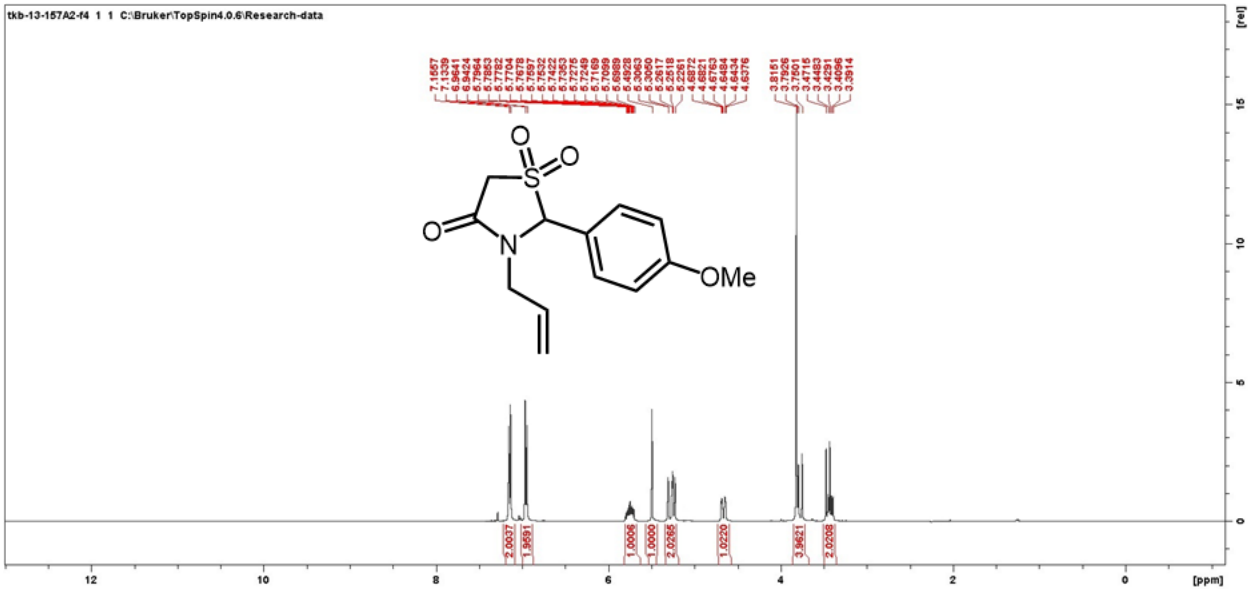


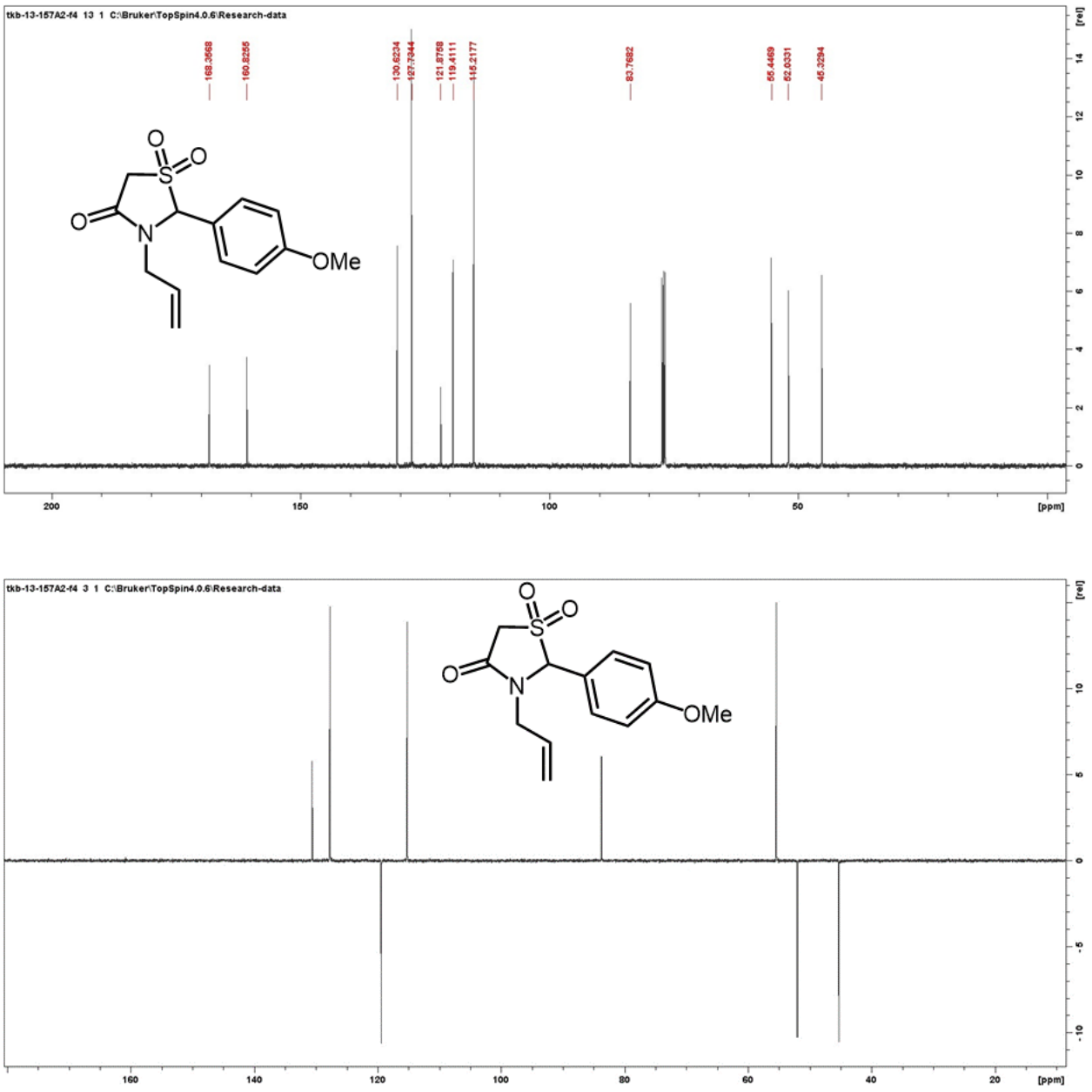




Compound 8b

Prepared in 1.0 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 250.1 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.2 Hz, 2H), 6.95 (d, *J* = 8.2 Hz, 2H), 5.75 (dddd, *J* = 17.3, 10.0, 7.3, 4.4 Hz, 1H), 5.49 (s, 1H), 5.28 (ddd, *J* = 17.1, 2.1, 1.1 Hz, 1H), 5.28 – 5.20 (m, 1H), 4.66 (ddt, *J* = 15.5, 4.1, 1.8 Hz, 1H), 3.81 – 3.74 (m, 4H), 3.47 – 3.39 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 160.8, 130.6, 127.8, 121.9, 119.4, 115.2, 83.8, 55.4, 52.0, 45.3. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{15}NO_4S$, 281.0722, found 281.0726.

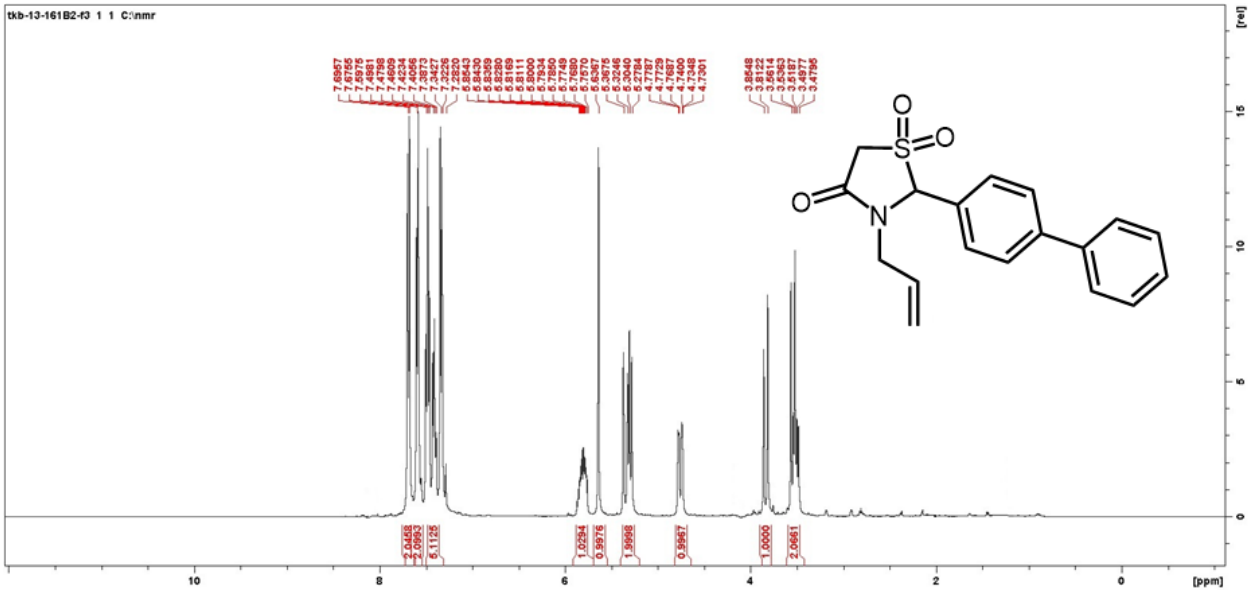


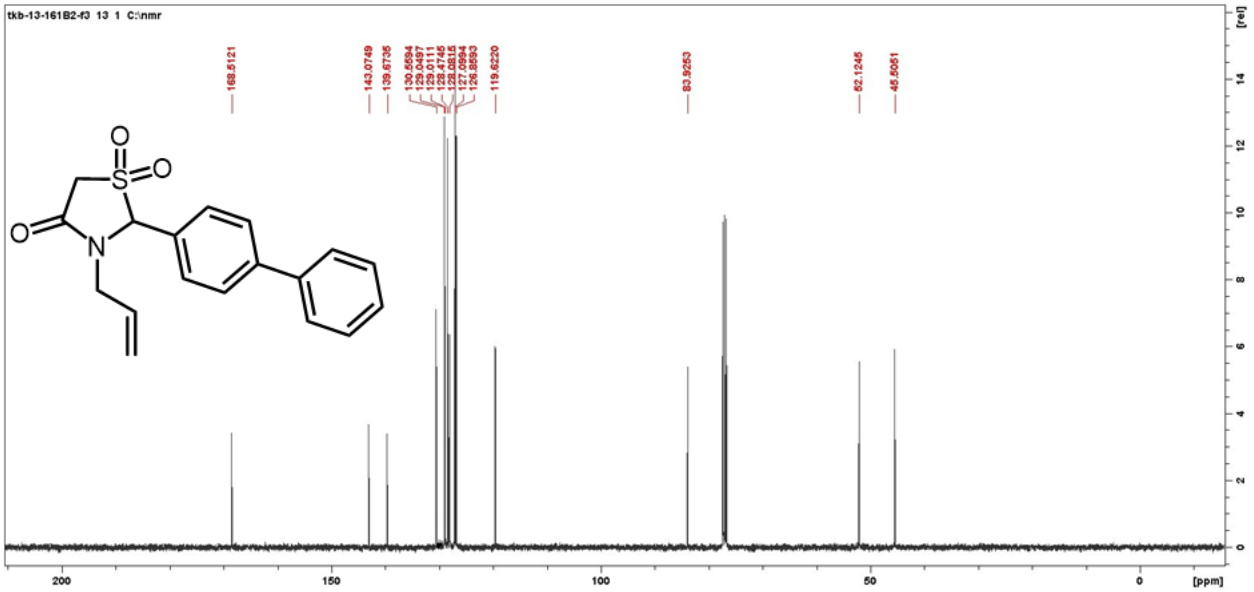


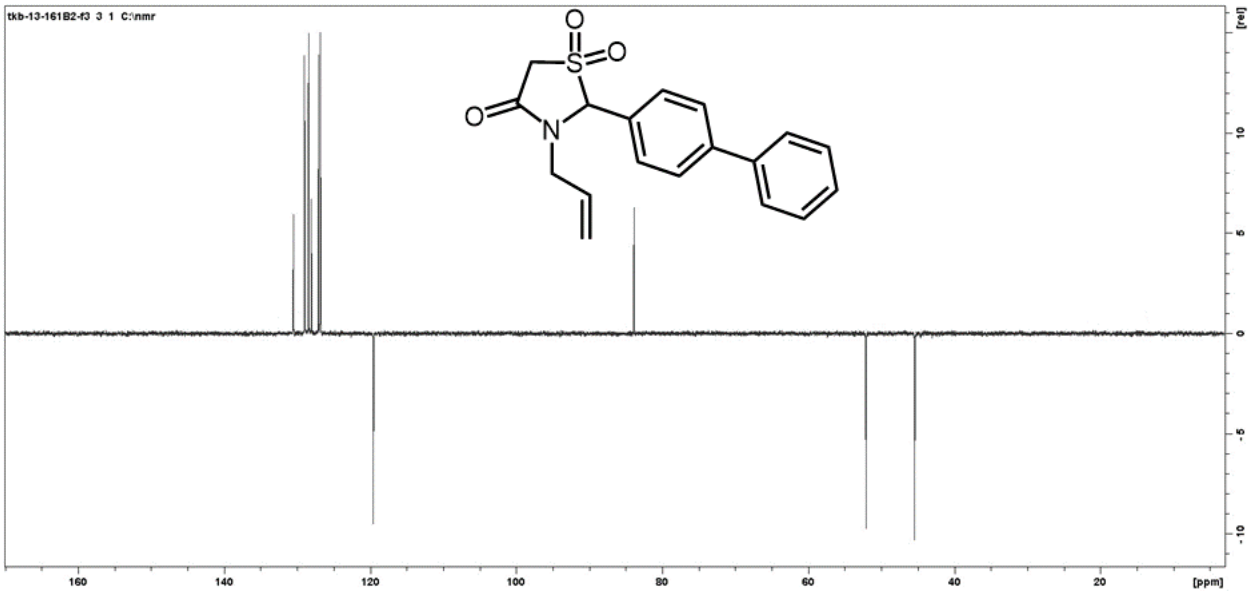
Compound 8c

Prepared in 1.0 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 278 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.0 Hz, 2H), 7.62 – 7.52 (m, 2H), 7.52 – 7.30 (m, 5H), 5.81 (dddd, J = 17.3, 10.0, 7.2, 4.4 Hz, 1H), 5.64 (s, 1H), 5.35 (d, J = 17.1 Hz, 1H), 5.29 (d, J = 10.3 Hz, 1H), 4.75 (ddt, J = 15.6, 4.1, 1.8 Hz, 1H), 3.83 (d, J = 17.1 Hz, 1H), 3.58 – 3.44 (m, 2H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 168.5, 143.1, 139.7, 130.6, 129.0, 128.5, 128.1, 127.1, 126.9, 119.6, 83.9, 52.1, 45.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{17}NO_3S$, 327.0929, found 327.0933.

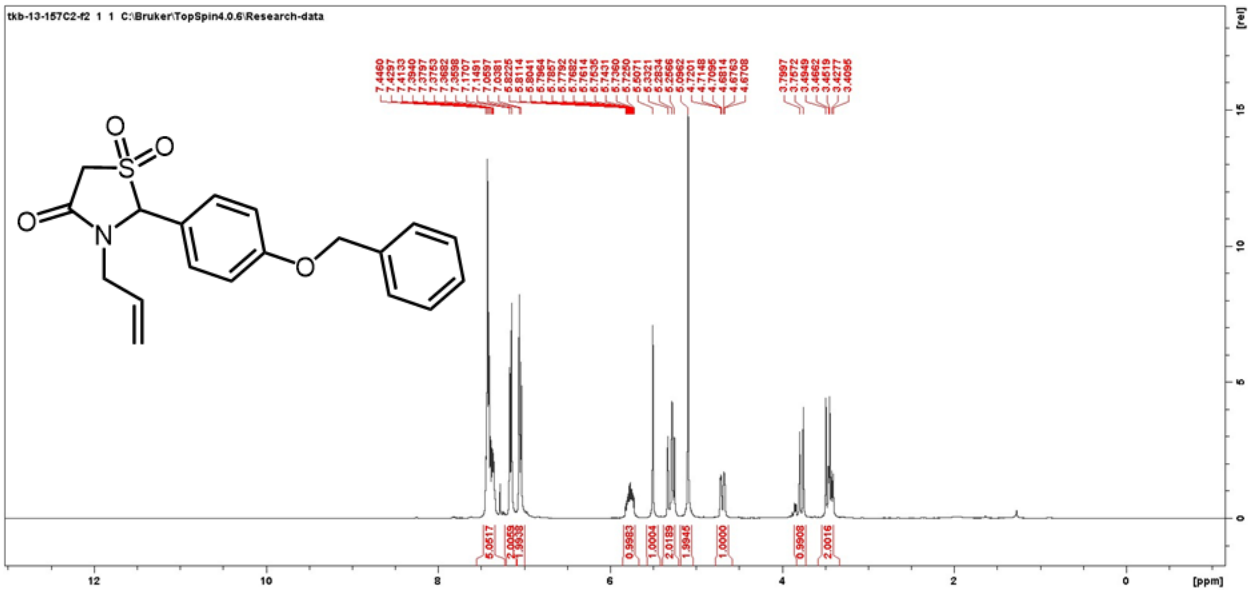


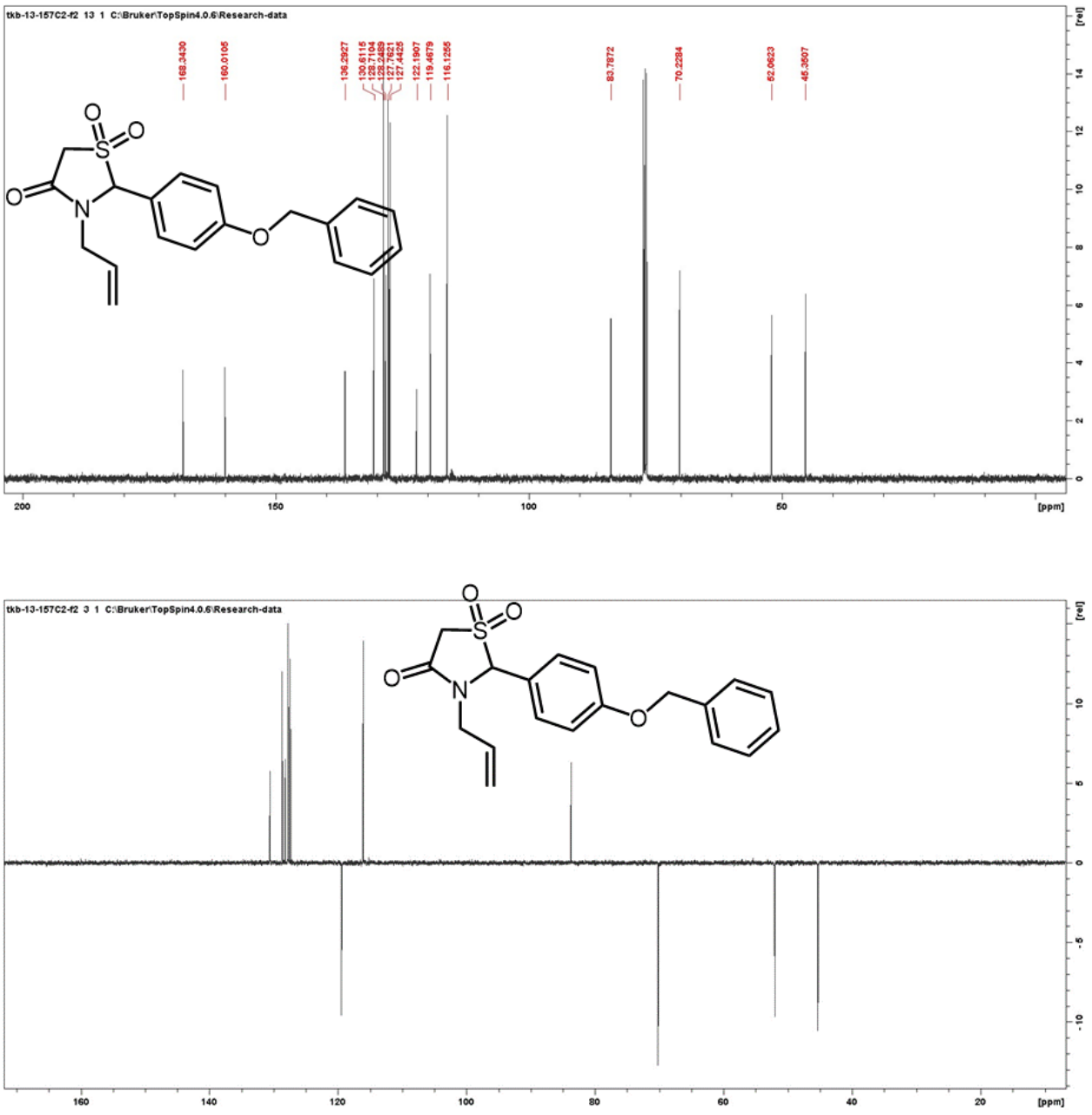




Compound 8d

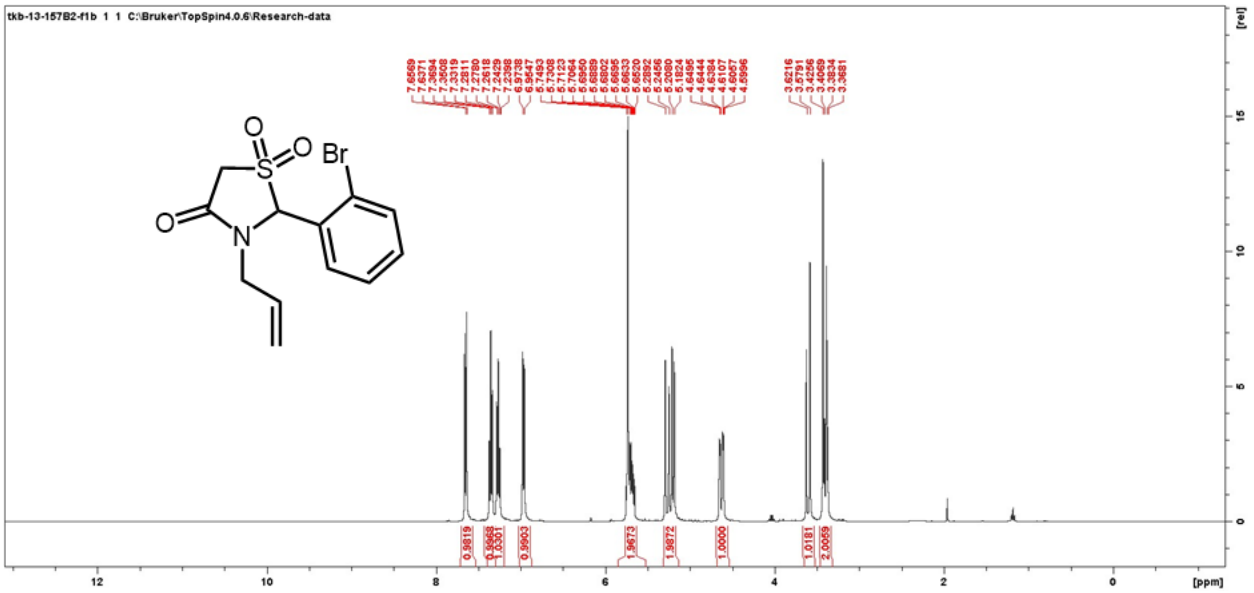
Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 157.1 mg, 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.37 (m, 5H), 7.36 (d, *J* = 7.3 Hz, 2H), 7.03 (d, *J* = 7.3 Hz, 2H), 5.77 (dddd, *J* = 17.3, 10.0, 7.3, 4.4 Hz, 1H), 5.51 (s, 1H), 5.36 – 5.23 (m, 2H), 5.10 (s, 2H), 4.70 (ddt, *J* = 15.5, 4.1, 1.8 Hz, 1H), 3.89 – 3.73 (m, 1H), 3.49 – 3.41 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 160.0, 136.3, 130.6, 128.7, 128.2, 127.8, 127.4, 122.2, 119.5, 116.1, 83.8, 70.2, 52.1, 45.3. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{19}NO_4S$, 357.1035, found 357.1038.





Compound 8e

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 131.6 mg, 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.35 (td, *J* = 7.6, 1.3 Hz, 1H), 7.30 – 7.18 (m, 1H), 6.96 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.77 – 5.62 (m, 2H), 5.32 – 5.23 (m, 1H), 5.20 (dt, *J* = 10.3, 1.3 Hz, 1H), 4.63 (ddd, *J* = 15.7, 4.2, 2.0 Hz, 1H), 3.60 (d, *J* = 17.0 Hz, 1H), 3.40 (dd, *J* = 16.1, 6.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 134.2, 131.4, 130.4, 129.3, 128.5, 126.5, 124.1, 119.6, 83.7, 52.1, 45.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{12}H_{12}BrNO_3S$, 328.9721, found 328.9727.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N
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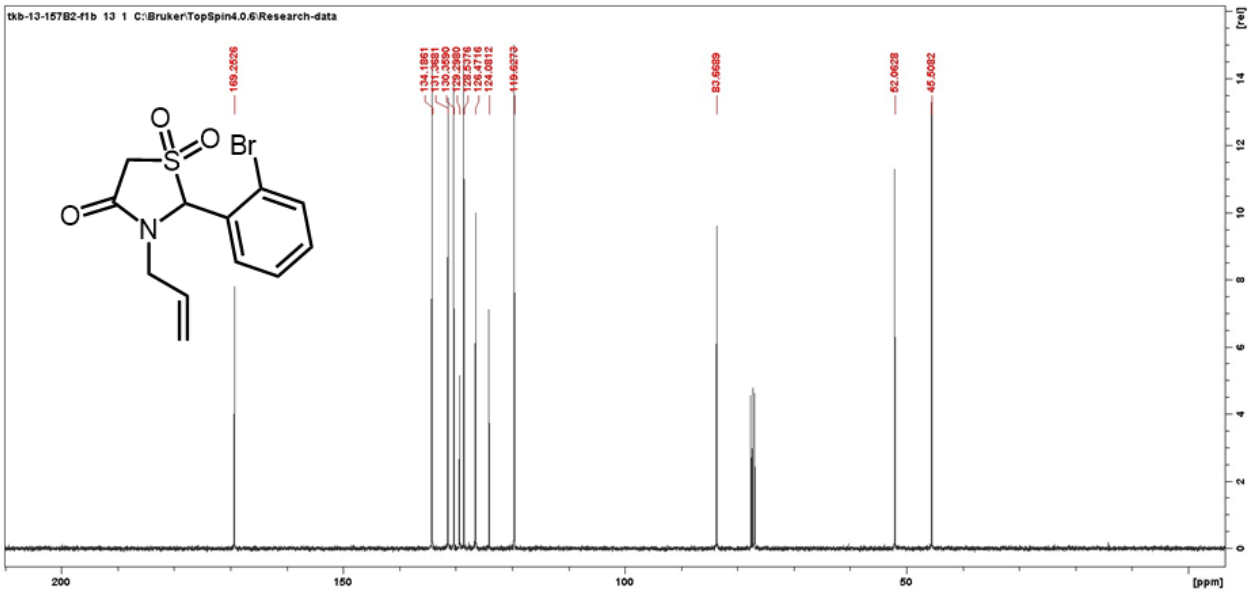
[ppm]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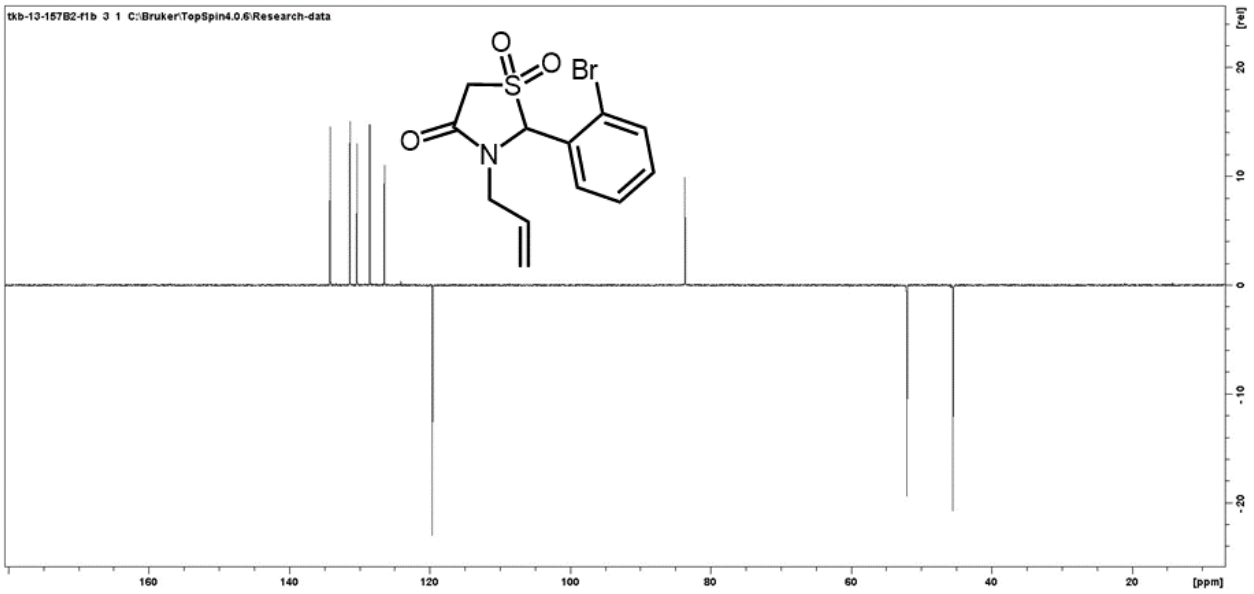
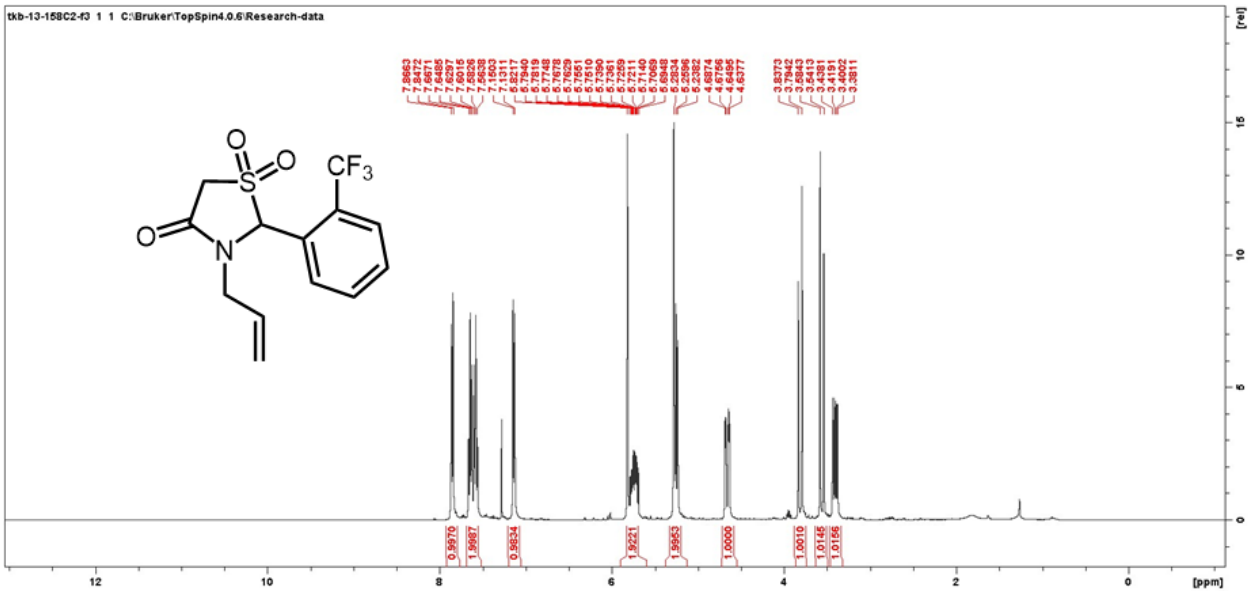
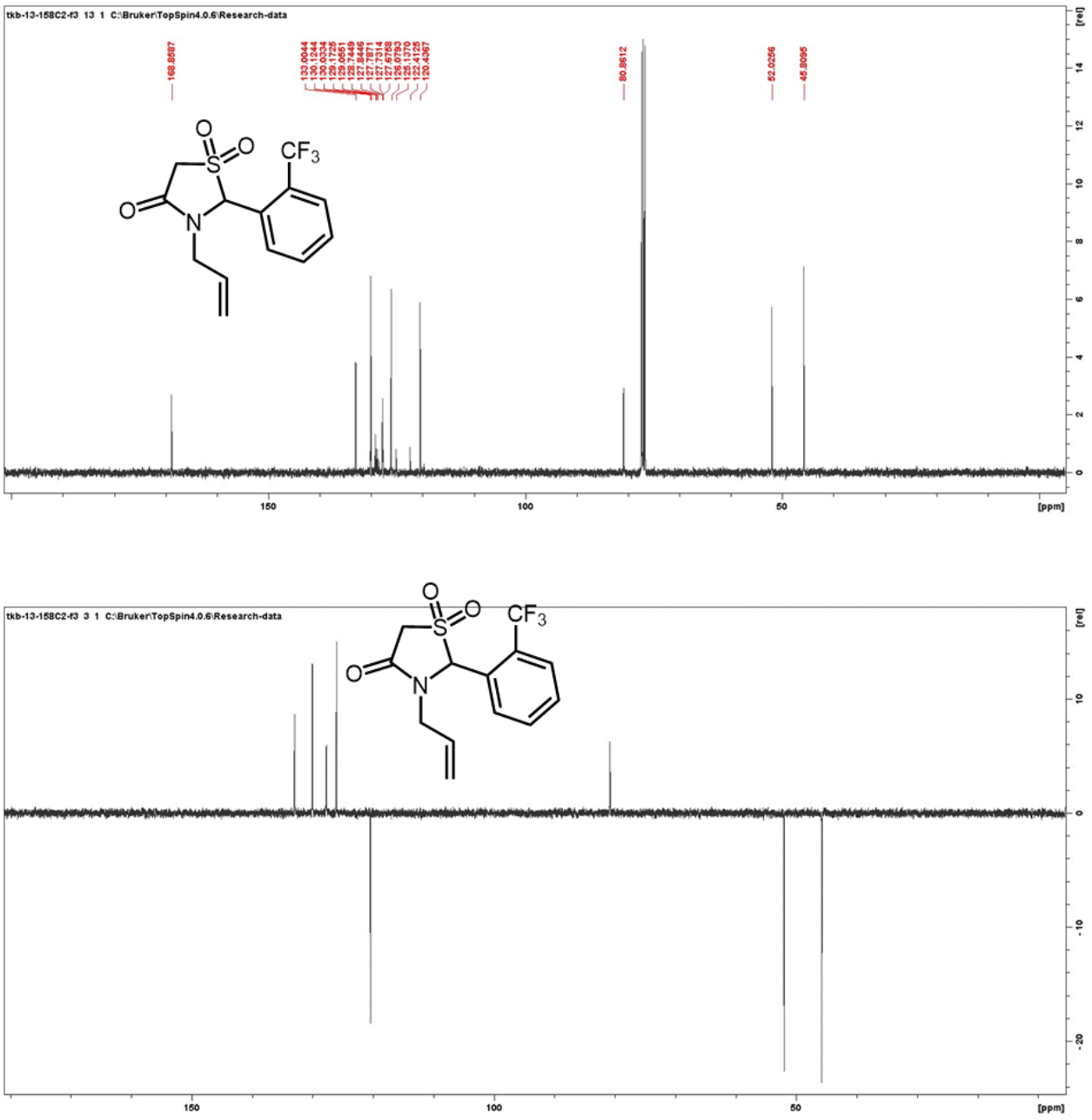


Compound 8f

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 134 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 7.7 Hz, 1H), 5.82 (s, 1H), 5.74 (dddd, *J* = 16.2, 10.3, 7.7, 4.8 Hz, 1H), 5.31 – 5.21 (m, 1H), 4.67 (ddd, *J* = 15.3, 4.3, 2.2 Hz, 1H), 3.82 (d, *J* = 17.2 Hz, 1H), 3.56 (d, *J* = 17.2 Hz, 1H), 3.41 (dd, *J* = 15.2, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 133.0, 130.1, 130.0, 129.2, 129.1, 127.8, 127.7, 126.1, 125.1, 122.4, 120.4, 80.9, 52.0, 45.8. **HRMS-EI^{+}** (*m/z*): calc for $C_{13}H_{12}F_3NO_3S$, 319.0490, found 319.0498.

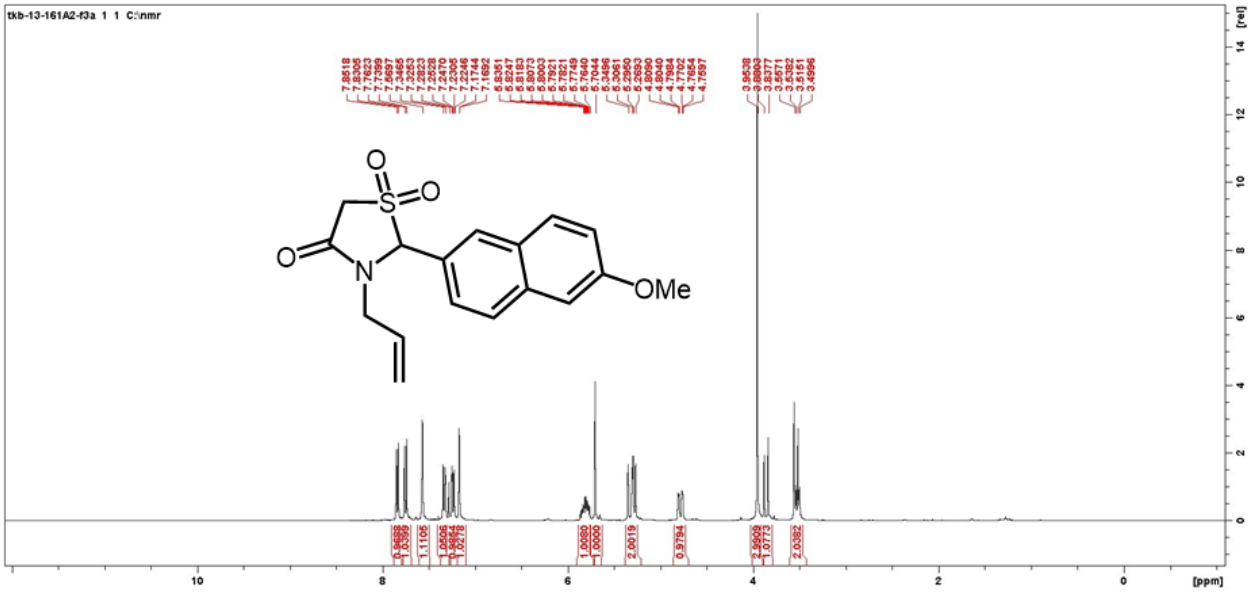


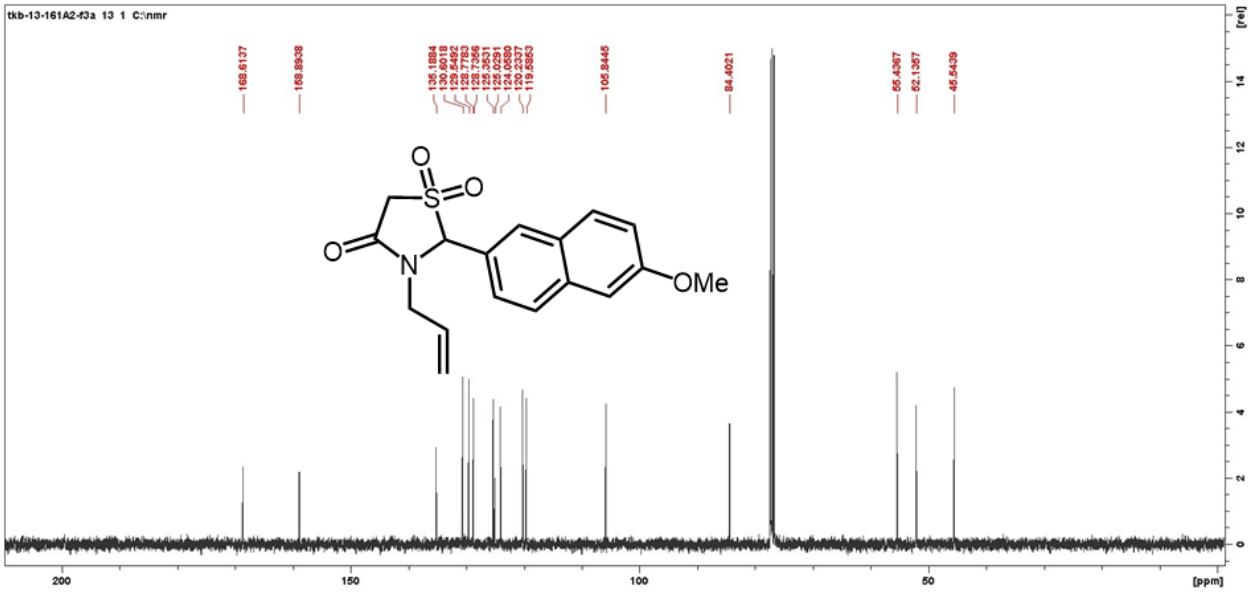


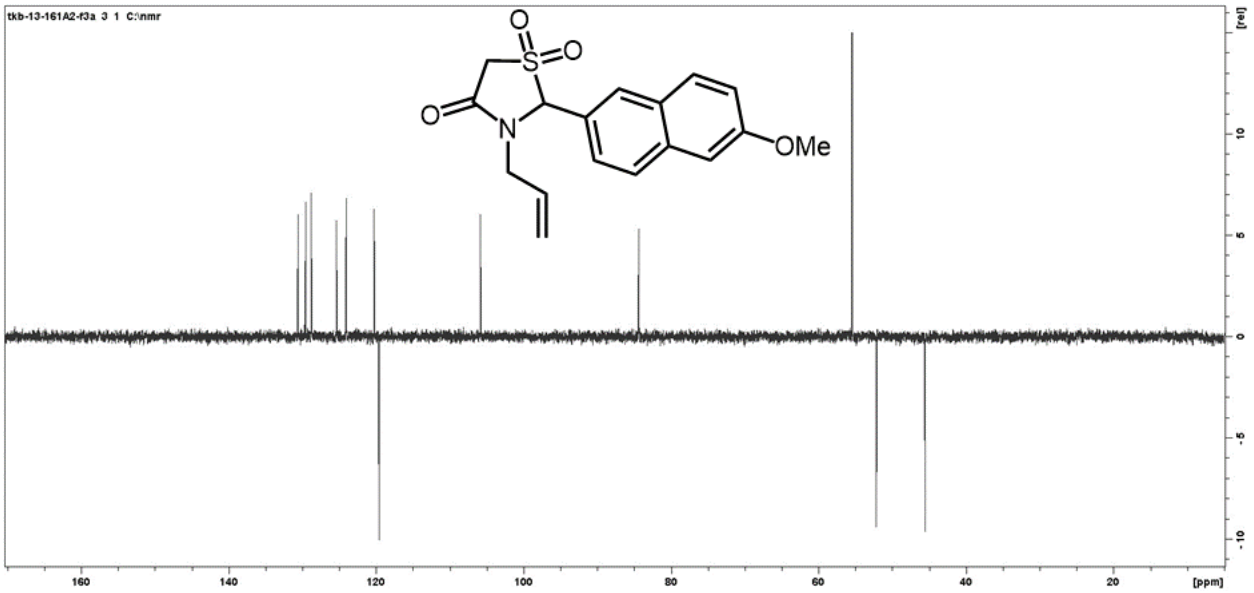
Compound 8g

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 144 mg, 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.57 (d, *J* = 1.9 Hz, 1H), 7.33 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.17 (d, *J* = 2.5 Hz, 1H), 5.81 (dddd, *J* = 17.3, 9.9, 7.3, 4.4 Hz, 1H), 5.70 (s, 1H), 5.38 – 5.28 (m, 1H), 5.32 – 5.22 (m, 1H), 4.78 (ddt, *J* = 15.5, 4.2, 1.7 Hz, 1H), 3.95 (s, 3H), 3.86 (d, *J* = 17.0 Hz, 1H), 3.53 (dd, *J* = 16.1, 7.0 Hz, 2H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 168.6, 158.9, 135.2, 130.6, 129.5, 128.8, 128.7, 125.4, 125.0, 124.1, 120.2, 119.6, 105.8, 84.4, 55.4, 52.1, 45.5. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{17}NO_4S$, 331.0878, found 331.0883.

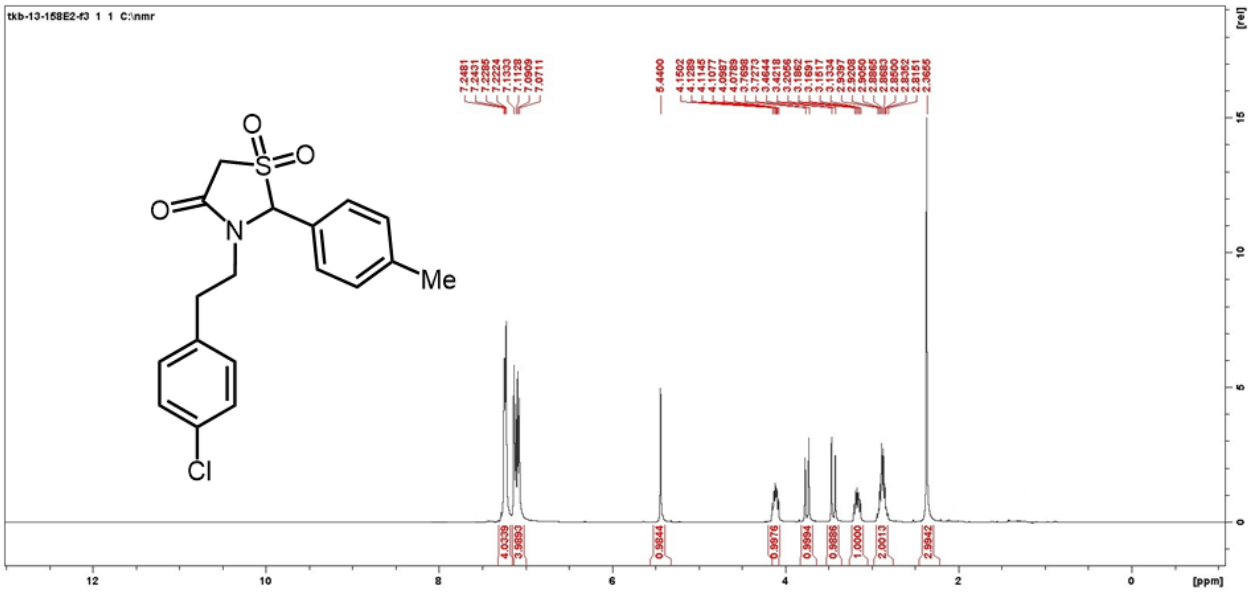


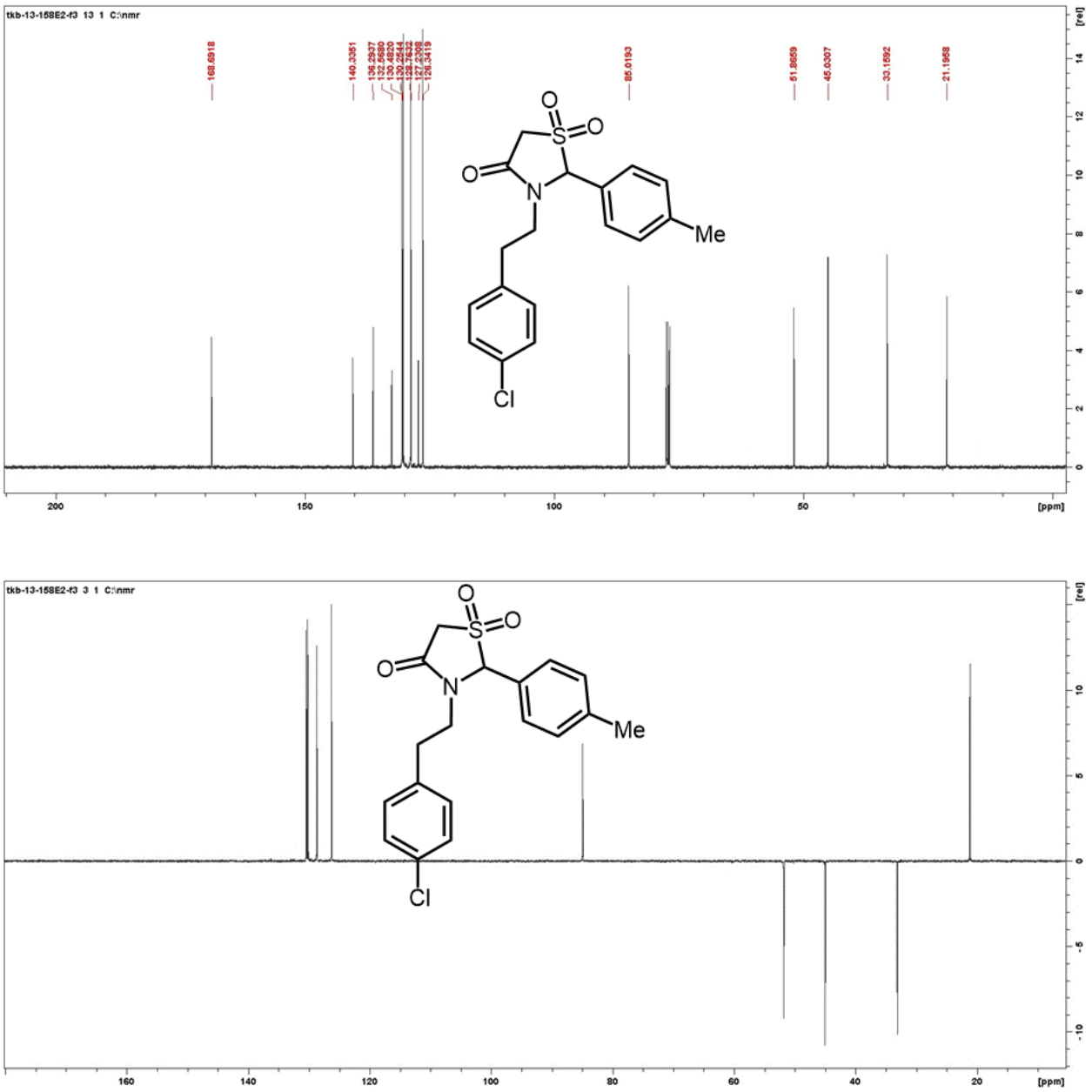




Compound 8h

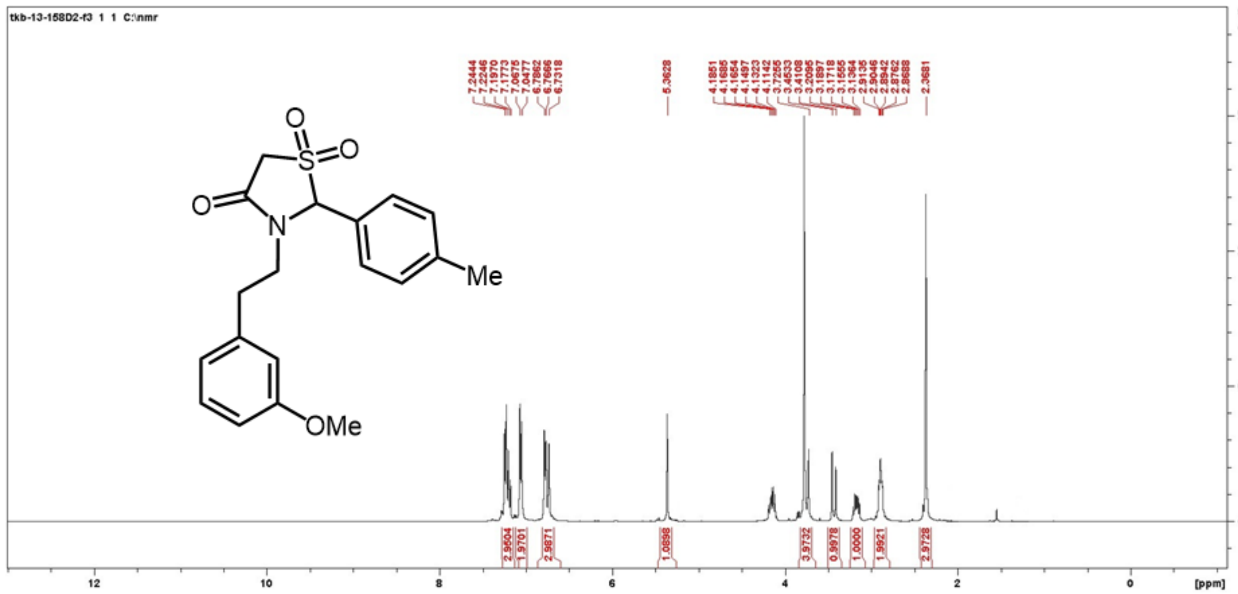
Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 148.8 mg, 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.22 (m, 4H), 7.13 – 7.07 (m, 4H), 5.44 (s, 1H), 4.11 (tt, *J* = 8.3, 6.4 Hz, 1H), 3.75 (d, *J* = 17.0 Hz, 1H), 3.44 (d, *J* = 17.1 Hz, 1H), 3.17 (ddd, *J* = 14.3, 8.5, 6.7 Hz, 1H), 2.88 (h, *J* = 6.5 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 140.3, 136.3, 132.6, 130.5, 129.7, 128.9, 127.2, 126.3, 85.0, 60.4, 51.9, 45.0, 33.2, 21.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{18}ClNO_3S$, 363.0696, found 363.0691.





Compound 8i

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 154.4 mg, 86%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.17 (m, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 6.79 – 6.73 (m, 3H), 5.36 (s, 1H), 4.15 (ddd, *J* = 14.2, 8.2, 6.5 Hz, 1H), 3.75 –3.71 (m, 4H), 3.43 (d, *J* = 17.0 Hz, 1H), 3.23 – 3.10 (m, 1H), 2.97 – 2.79 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 159.8, 140.2, 139.5, 130.4, 129.7, 127.4, 126.5, 121.1, 114.3, 112.5, 85.2, 55.7, 52.0, 45.1, 33.9, 21.2. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{21}NO_4S$, 359.1191, found 359.1195.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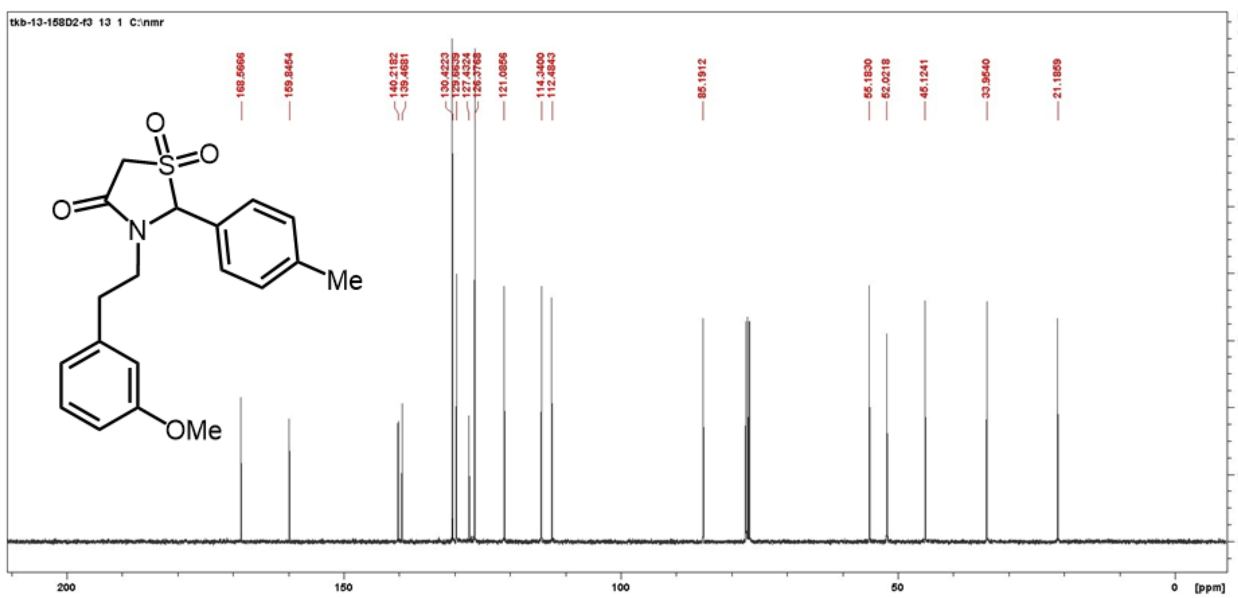
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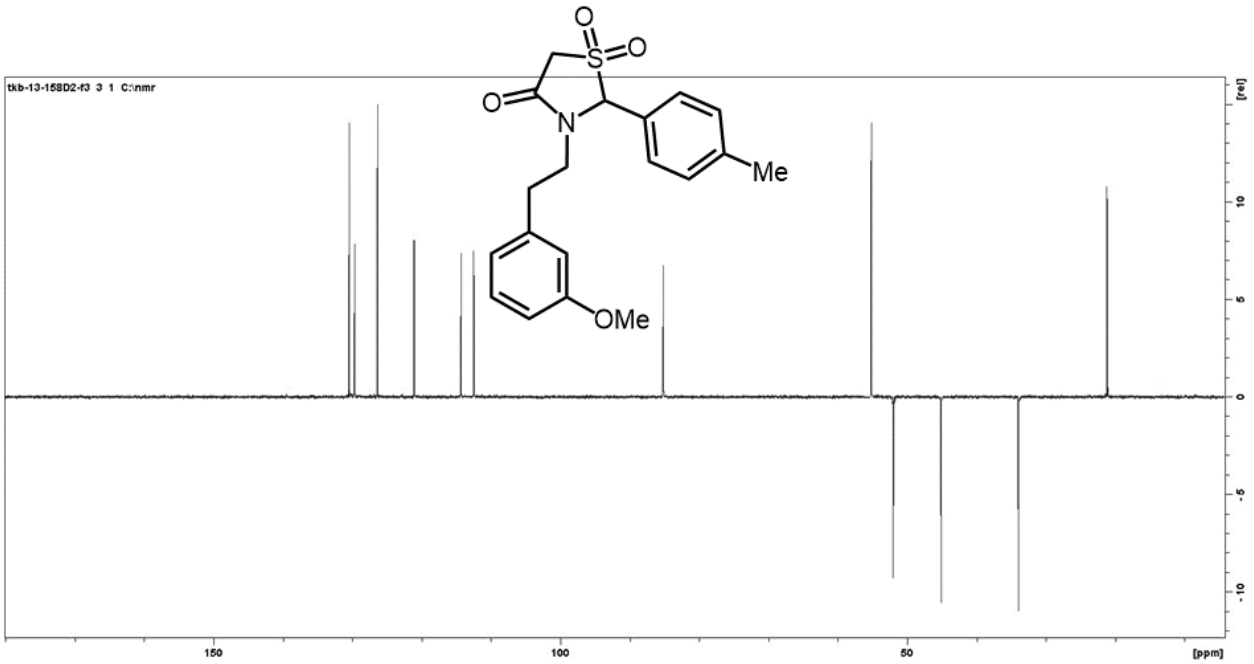
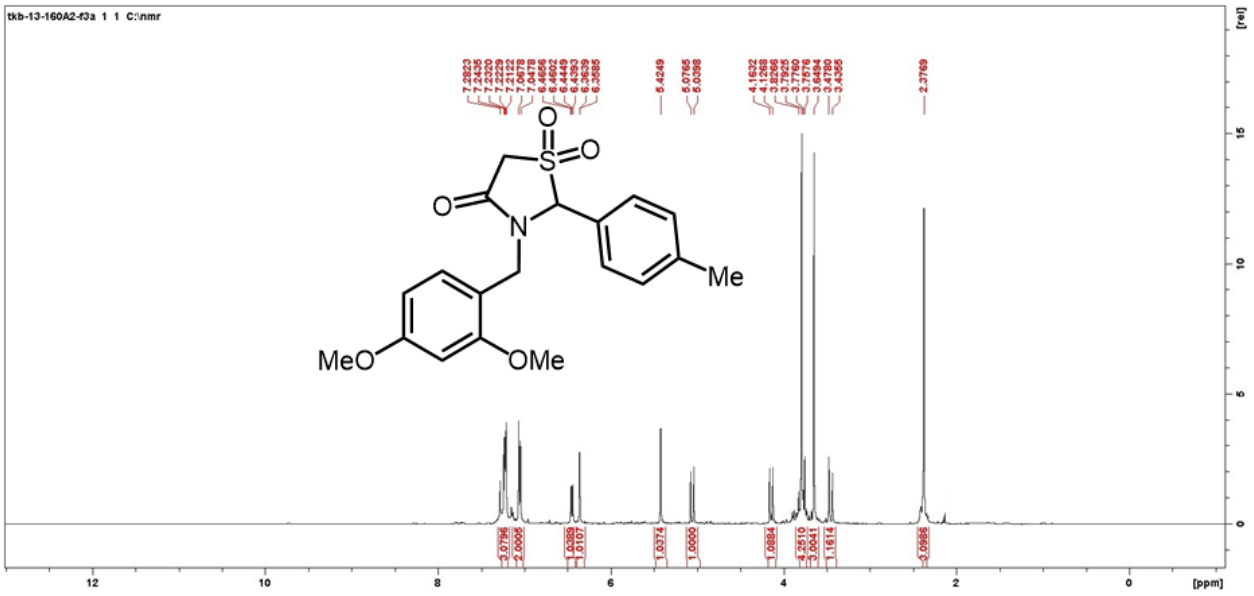
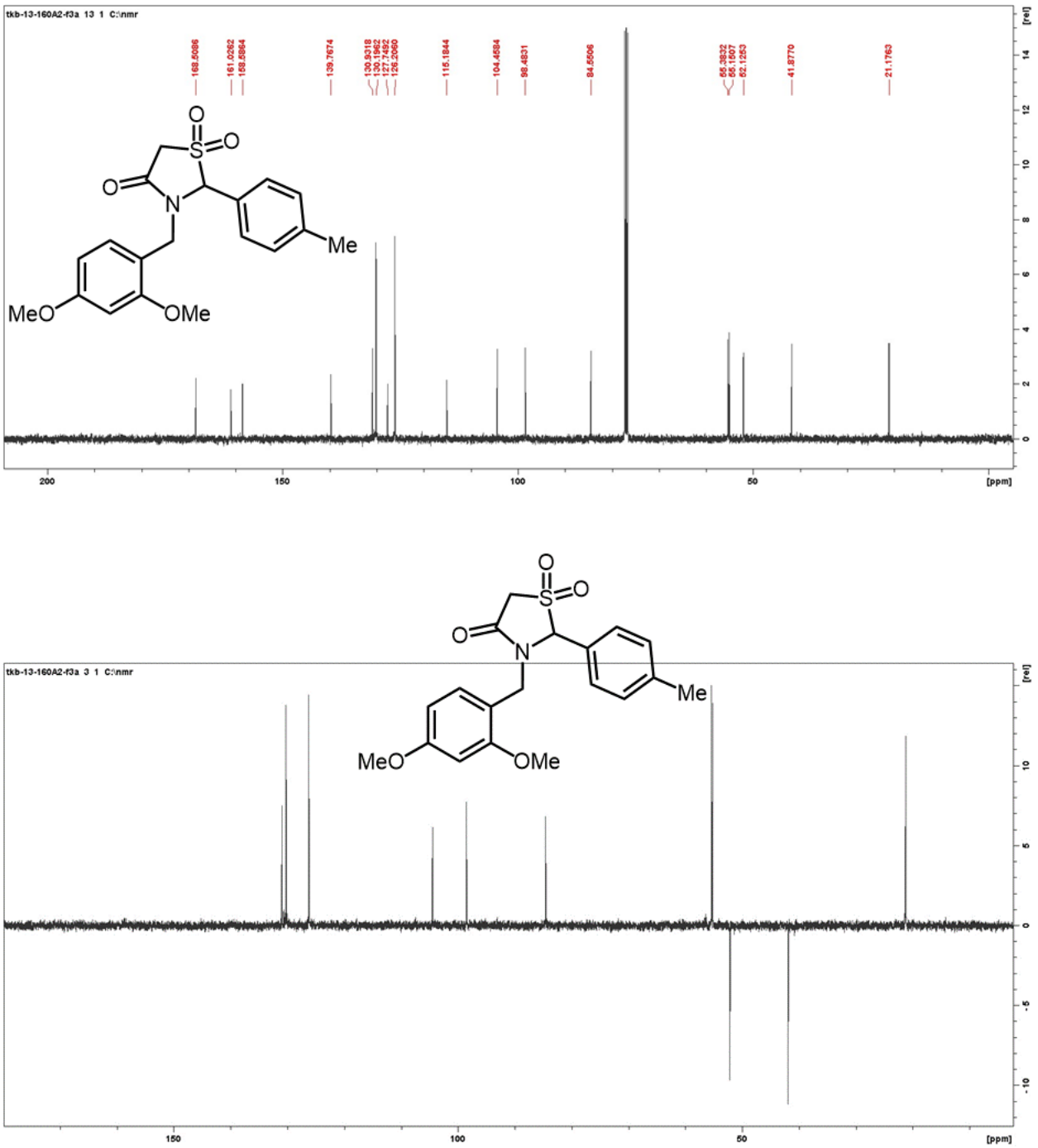


Compound 8j

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 166.9 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.09 (m, 3H), 7.06 (d, *J* = 7.9 Hz, 2H), 6.45 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.36 (d, *J* = 2.4 Hz, 1H), 5.43 (s, 1H), 5.06 (d, *J* = 14.7 Hz, 1H), 4.15 (d, *J* = 14.6 Hz, 1H), 3.95 – 3.74 (m, 4H), 3.65 (s, 3H), 3.46 (d, *J* = 17.0 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 161.0, 158.6, 139.8, 130.9, 130.2, 127.7, 126.2, 115.2, 104.5, 98.5, 84.6, 55.4, 55.2, 52.1, 41.9, 21.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{19}H_{21}NO_5S$, 375.1140, found 375.1146.

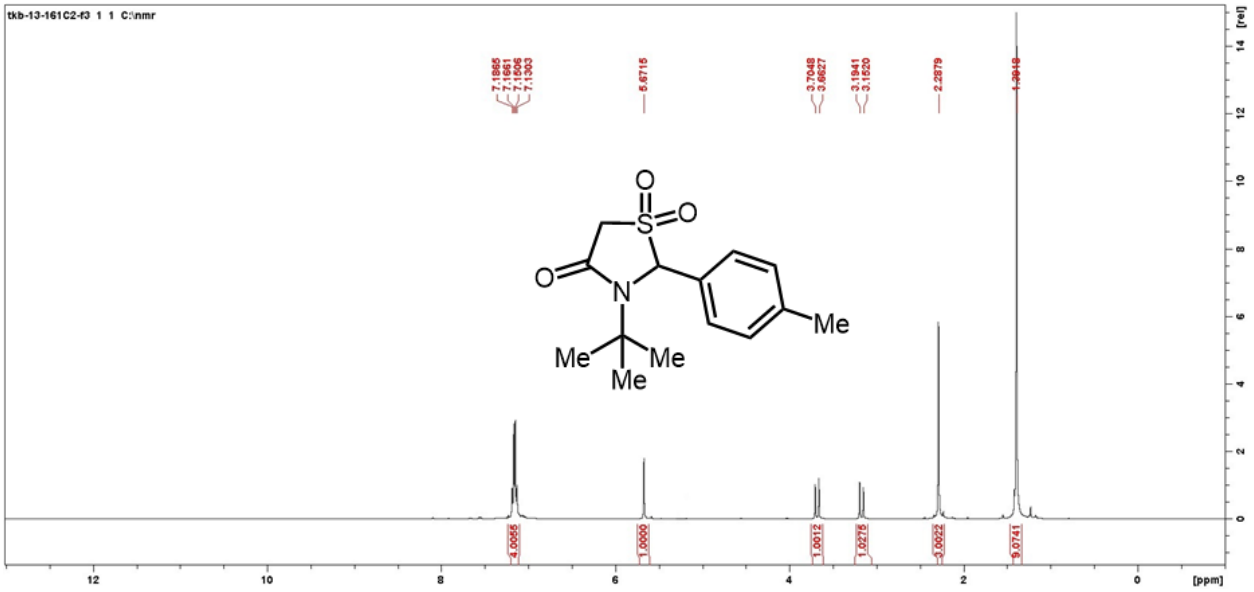


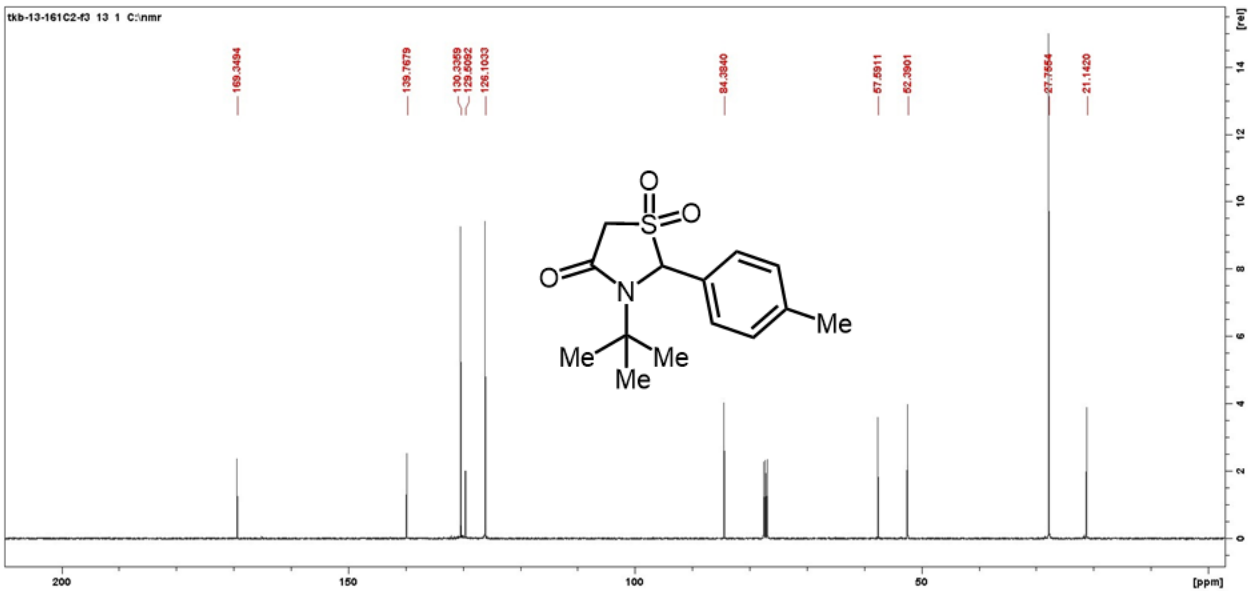


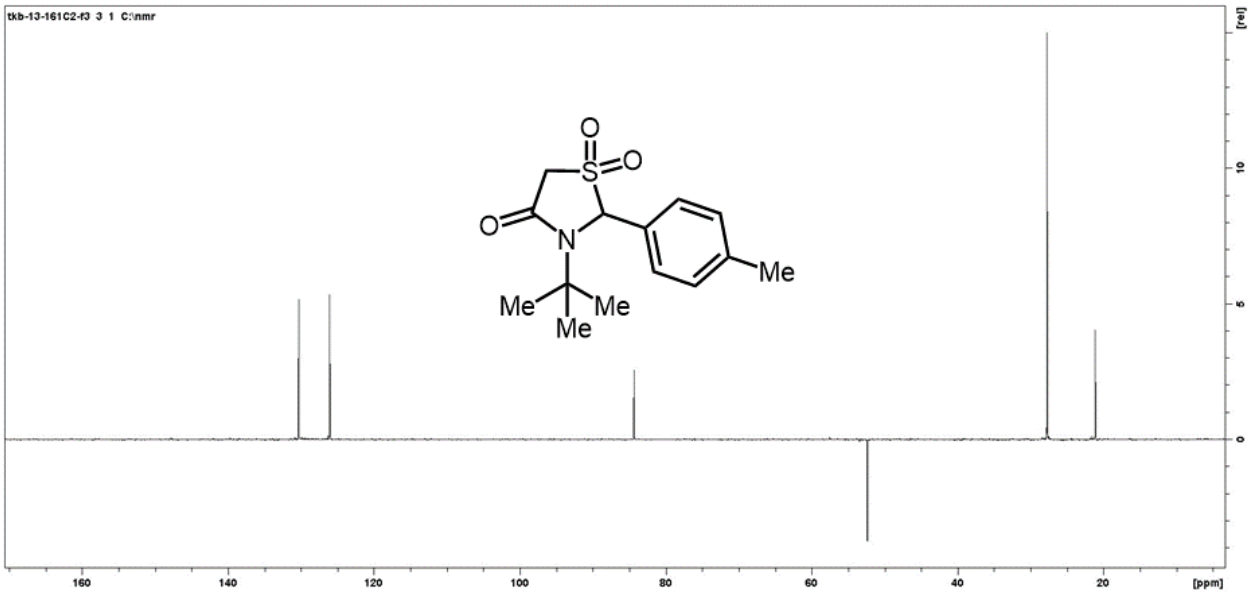
Compound 8k

Prepared in 0.5 mmol scale using **General Procedure C.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50 to 0:100). Yield = 119.4 mg, 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.13 (m, 4H), 5.67 (s, 1H), 3.68 (d, J = 16.8 Hz, 1H), 3.17 (d, J = 16.9 Hz, 1H), 2.29 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.35, 139.77, 130.34, 129.51,

126.11, 84.39, 57.60, 52.39, 27.76, 21.15. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{14}H_{19}NO_3S$, 281.1086, found 281.1092.






tkb-13-161C2-f3 3 1 C:\nmr
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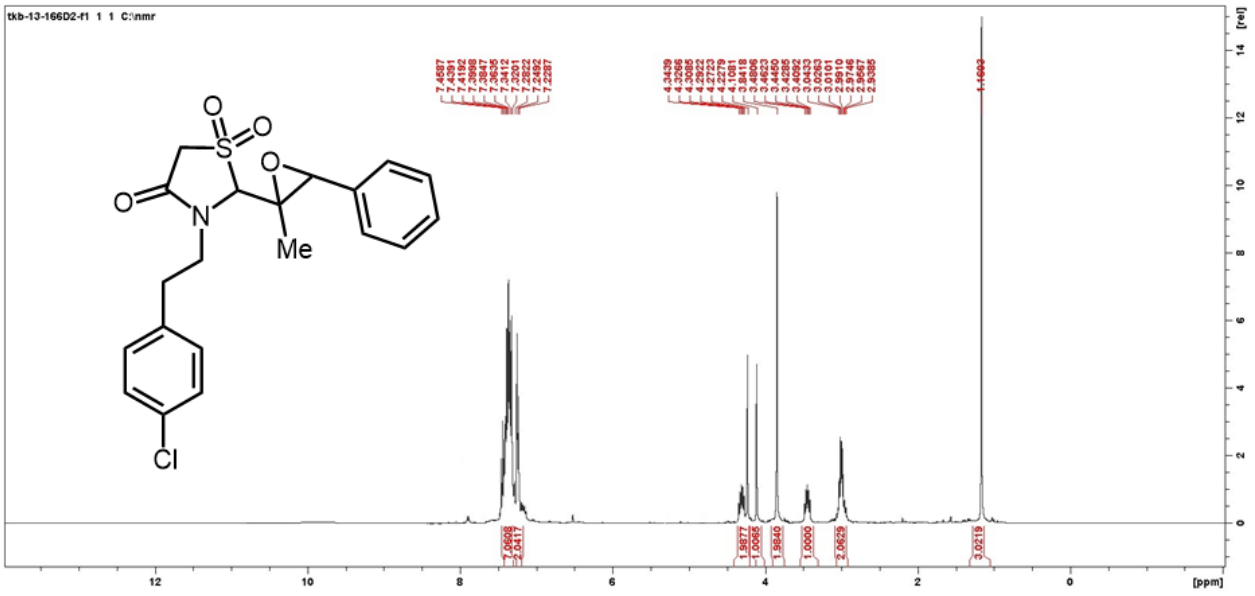
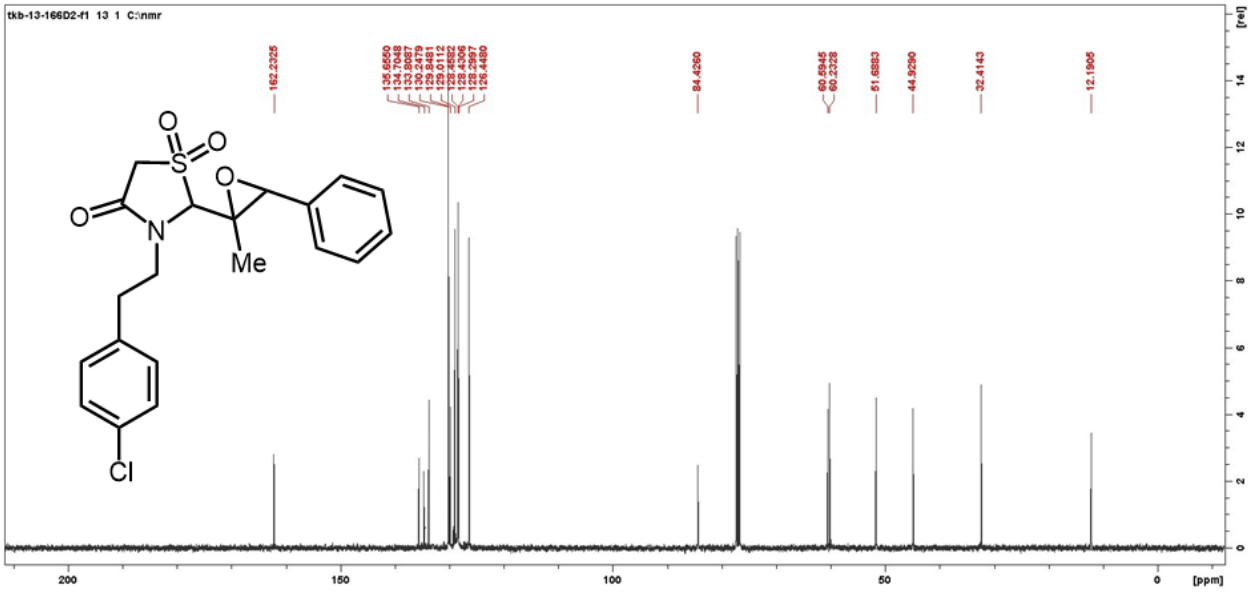
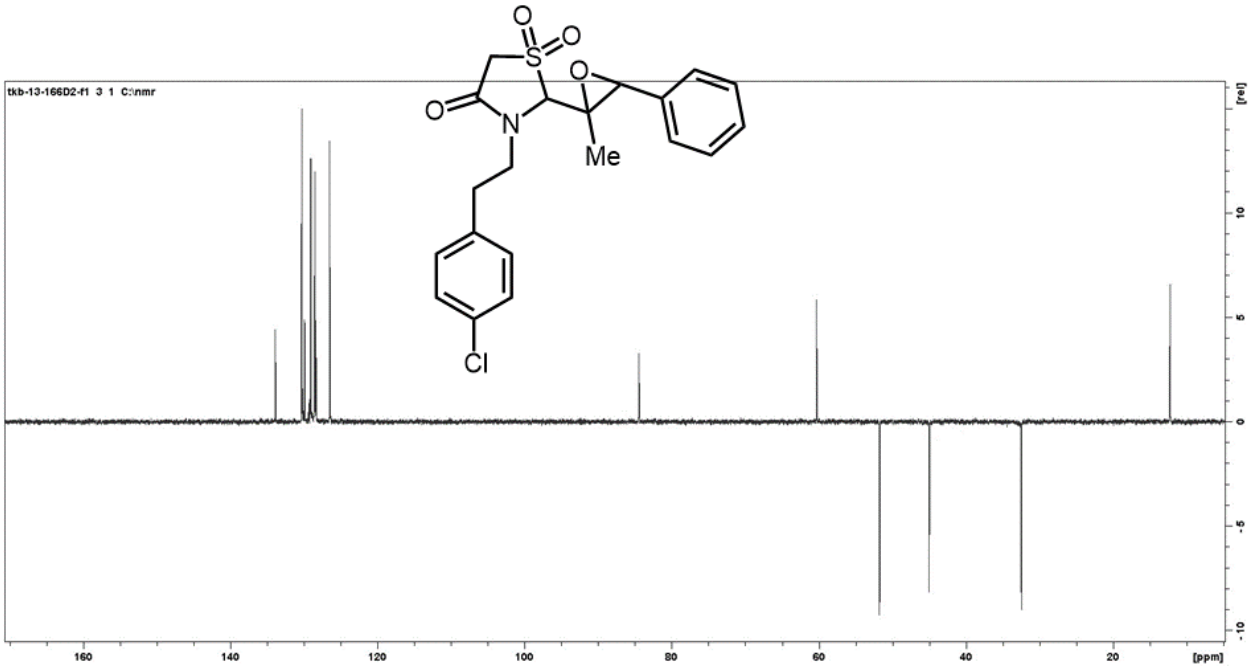
Compound 12

Prepared in 0.5 mmol scale using **General Procedure D.** Purification: Flash chromatography on silica eluting with hexane/EtOAc (50:50). Yield = 180.6 mg, 89%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.23 (m, 9H), 4.31 (ddd, *J* = 14.5, 8.5, 6.5 Hz, 1H), 4.23 (s, 1H), 4.11 (s, 1H), 3.84 (s, 2H), 3.44 (ddd, *J* = 14.3, 8.4, 6.5 Hz, 1H), 3.09 – 2.82 (m, 2H), 1.16 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.23, 135.66, 134.71, 133.81, 130.25, 129.85, 129.01, 128.46, 128.43, 128.30, 126.45, 84.43, 60.60, 60.24, 51.69, 44.93, 32.42, 12.19. **HRMS-EI^{+}** (*m/z*): calc for $C_{20}H_{20}ClNO_4S$, 405.0802, found 405.0808.







References

(1) H. Braunstein, S. Langevin, M. Khim, J. Adamson, K. Hovenkotter, L. Kotlarz, B. Mansker and T. K. Beng, *Org. Biomol. Chem.*, 2016, **14**, 8864-8872;

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

(3) A. Colombo , J. C. Fernandez, D. Fernandez-Forner, N. de la Figuera, F. Albericio, P. Forns, *Tetrahedron Lett*, 2008, **49**, 1569–1572.