Electronic Supplementary Material (ESI) for Green Chemistry.


# Supporting Information

# Metal-Free Visible Light-Promoted Synthesis of Isothiazoles: a Catalytic Approach for N−S Bond Formation from Iminyl Radicals under Batch and Flow Conditions

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# Supporting Information

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# 1. General Information

Reaction temperatures are reported as the ones of the heat transfer medium surrounding the vessel unless otherwise stated.

The following solvents DCM, MeCN, PhMe and THF were purified by passing through a Pure SolvTM column drying system from Innovative Technology, Inc. Additional anhydrous solvents (≤50 ppm water) were purchased from Acros Organics, Sigma-Aldrich or Alfa Aesar and stored over molecular sieves under a nitrogen atmosphere. Commercially available chemicals were obtained from Acros Organics, Aldrich Chemical Co., Alfa Aesar, TCI Chemicals and Fluorochem, and used as received, unless otherwise stated.

Analytical thin layer chromatography (TLC) was performed on silica gel 60 F254 aluminum plates (Merck) and they were visualized by exposure to short wave ultraviolet light (254 nm, 366 nm) and/or by staining. For staining the TLC plates were dipped into a solution of $KMnO_4$ (1 g $KMnO_4$, 6 g $K_2CO_3$ and 0.1 g KOH in 100 mL $H_2O$) and developed with a heat gun if necessary. Flash chromatography was performed using Geduran® Silica Gel 60 (0.040 - 0.063 nm) or Iatrobeads 6RS - 8060 silica gel with appropriate mixtures of cyclohexane and ethyl acetate and compressed air.

NMR spectra were recorded at room temperature on a Bruker AV 300 or or 500 MHz spectrometer running at 300 or 500 MHz for $^{1}H$, 75 or 126 MHz for $^{13}C$, 282 or 471 MHz for $^{19}F$ in solvents as indicated. Chemical shifts (δ) for $^{1}H$- and $^{13}C$-NMR spectra are given in ppm relative to tetramethylsilane (TMS) using the residual solvent signals as references for $^{1}H$ and $^{13}C$ NMR spectra ($CDCl_3$: $\delta_H$ = 7.26 ppm, $\delta_C$ = 77.16 ppm, $(CD_3)_2CO$: $\delta_H$ = 2.05 ppm, $\delta_C$ = 29.84, 206.26 ppm, $C_6D_6$: $\delta_H$ = 7.16 ppm, $\delta_C$ = 134.19, 129.26, 128.25, 125.96 ppm, $CD_2Cl_2$: $\delta_H$ = 5.32 ppm, $\delta_C$ = 53.84 ppm).[1] $^{19}F$-NMR spectra are not externally calibrated and chemical shifts is given relative to $CCl_3F$ as received from the automatic data processing. $^{13}C$-NMR and $^{19}F$-NMR spectra were acquired on a broadband decoupled mode. Chemical shifts are generally reported with two ($^{1}H$) or one (all other nuclei) digits after the decimal point. NMR-data are reported as follows: chemical shift (multiplicity [s = singlet, d = doublet,

t = triplet, q = quartet, p = quintuplet, hept = heptuplet, m = multiplet, br = broad], coupling constants (*J*, Hz) and integration). All spectra were processed using the MestReNova program.

High-Resolution Mass Spectra (HRMS) were recorded on an Agilent Technologies 6120 Quadrupole LC/MS coupled with an SFC Agilent Technologies 1260 Infinity Series instrument for the ESI-MS (Electrospray Ionization) or on an Agilent Technologies 5977B MSD coupled with an Agilent Technologies 7820A GC System for the EI-MS (Electron Ionization mass spectroscopy). MassWorks software version 4.0.0.0 (Cerno Bioscience) was used for the formula identification. MassWorks is an MS calibration software which calibrates isotope profiles to achieve high mass accuracy and enables elemental composition determination on conventional mass spectrometers of unit mass resolution allowing highly accurate comparisons between calibrated and theoretical spectra.[2] Obtained data are expressed in mass/charge (m/z) units.

UV-Vis measurements were acquired on an Agilent 8453 UV-Vis Spectrophotometer controlled by UV-Visible ChemStation Software. Emission spectra were recorded on a JASCO Spectrofluorometer FP-8600 equipped with a TC-815 Peltier thermostated single cell holder (water-cooled) controlled by Spectra Manager Version 2.10.01. Time resolved emission spectra were carried out using an Edinburg Instruments FS5 Spectrofluorometer, and a 450 nm EPL laser.

Cyclic Voltammetry (CV) experiments were acquired on an IVIUM Technologies CompactStat controlled by IviumSoft version 2.124 offering a compliance voltage of up to ± 100 V (available at the counter electrode), ± 10 V scan range and ± 1 A current range. HPLC grade acetone solvent was used for all measurements. Tetra-*n*-butylammonium hexafluorophosphate was used as supporting electrolyte at 0.1 M concentration. All cyclic voltammetry experiments were performed using a conventional three-electrode system, containing a coiled Pt wire acting as counter electrode, an Ag/AgCl saturated solution as reference electrode and a glassy carbon working electrode (A = 0.071 $cm^2$) at 20 mV/s scan rate. All the electrodes were

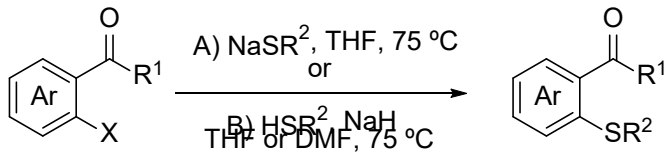
purchased from Metrohm. Redox-active species were dissolved at 1.0 nM concentration and these solutions were throughout the measurements.

A custom-made temperature-controlled photoreactor setup was used for the photocatalytic reactions (Figure S1). The irradiation takes place at the desired wavelengths (365, 385, 420, 450 or 540 nm) using 380 mW single LEDs, located 1 cm beneath the base of the vial. Reaction temperature is kept at 20-25 ºC using a recirculating chiller.

**Figure S1**. Experimental setup employed during photocatalytic reactions.

## 2. Synthesis and Characterization of Substrates

### 2.1. General Procedure and Characterization of Sulfides SI-1




X= Br, Cl, F **SI-1**

*General procedure A for the synthesis of sulfides **SI-1**:*

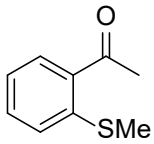
Compounds **SI-1a-c** were prepared following a slightly modified procedure reported in the literature.[3] 1-(2-bromophenyl)ethan-1-one (1 equiv) was added to a stirred solution of the corresponding sodium alkanethiolate (1.1. equiv) in THF (1.3M) and heated to 75 °C for 12 h. After this time, the reaction was cooled to room temperature, diluted with dichloromethane and washed with water (3x) and brine. The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced

pressure. Then, the solid residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure products **SI-1**.

*General procedure B for the synthesis of sulfides **SI-1**:*

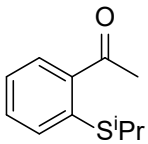
Compounds **SI-1d-s** were prepared following a slightly modified procedure reported in the literature.[3] The corresponding thiol (1.05 equiv) was added dropwise over 0.25 h to a stirred suspension of NaH (1.2 equiv) in THF or DMF (2 mL/mmol of thiol) at 0 °C (icebath). Afterwards, a solution of the bromide/chloride/fluoride compound (1 equiv) in THF or DMF (0.5 mL/mmol) was added and the reaction was heated to 75 °C for 12 h. After this time, the reaction was cooled to room temperature, diluted with dichloromethane and washed with water (3x) and brine. The organic phase was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Then, the solid residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure products **SI-1**.

**1-(2-(methylthio)phenyl)ethan-1-one (SI-1a)**



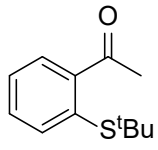

Following the general procedure A, the reaction of 1-(2-bromophenyl)ethan-1-one (2.1 mmol, 0.28 mL) and sodium methanethiolate (2.3 mmol, 160.1 mg) in THF (1.6 mL) at 75 ºC afforded the product **SI-1a** (88%, 305.3 mg) as a pale orange solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.71 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.37 – 7.29 (m, 1H), 7.17 (d, *J* = 7.9 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 2.46 (s, 3H), 2.27 (s, 3H). Spectral data is in accordance with the literature.[4]

**1-(2-(isopropylthio)phenyl)ethan-1-one (SI-1b)**



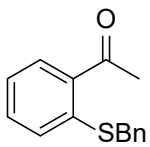

Following the general procedure A, the reaction of 1-(2-bromophenyl)ethan-1-one (2 mmol, 0.27 mL) and sodium 2-propanethiolate (2.2 mmol, 215.9 mg) in THF (1.5 mL) at 75 ºC afforded the product **SI-1b** (75%, 292.3 mg) as a yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.65 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.21 (ddd, *J* = 7.7, 6.7, 1.8 Hz, 1H), 3.46 (hept, *J* = 6.6 Hz, 1H), 2.60 (s, 3H), 1.33 (d, *J* = 6.6 Hz, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 200.5, 138.7, 137.8, 131.3, 129.6, 129.1, 124.7, 36.2, 29.3, 22.6.

**1-(2-(tert-butylthio)phenyl)ethan-1-one (SI-1c)**



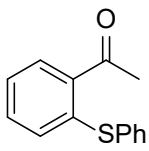

Following the general procedure A, the reaction of 1-(2-bromophenyl)ethan-1-one (2 mmol, 0.27 mL) and sodium 2-methyl-2-propanethiolate (2.2 mmol, 246.8 mg) in THF (1.5 mL) at 75 ºC afforded the product **SI-1c** (68%, 284.4 mg) as an yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** 7.58 (t, *J* = 8.3 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.32 – 7.25 (m, 1H), 2.29 (s, 3H), 1.22 (s, 9H). Spectral data is in accordance with the literature.[5]

**1-(2-(benzylthio)phenyl)ethan-1-one (SI-1d)**



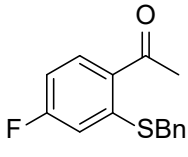

Following the general procedure B, the reaction of 1-(2-bromophenyl)ethan-1-one (2 mmol, 0.27 mL), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1d** (71%, 342.8 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 3.6 Hz, 2H), 7.39 (d, *J* = 6.5 Hz, 2H), 7.34 – 7.17 (m, 4H), 4.13 (s, 2H), 2.59 (s, 3H). Spectral data is in accordance with the literature.[6]

**1-(2-(phenylthio)phenyl)ethan-1-one (SI-1e)**




Following the general procedure B, the reaction of 1-(2-bromophenyl)ethan-1-one (2 mmol, 0.27 mL), NaH (60%, 2.4 mmol, 96 mg) and thiophenol (2.1 mmol, 0.21 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1e** (72%, 330.0 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.83 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.43 – 7.40 (m, 3H), 7.28 – 7.14 (m, 2H), 6.89 (dd, *J* = 8.0, 1.2 Hz, 1H), 2.67 (s, 3H). Spectral data is in accordance with the literature.[7]

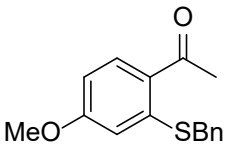
**1-(2-(benzylthio)-4-fluorophenyl)ethan-1-one (SI-1f)**




Following the general procedure B, the reaction of 1-(2-bromo-4-fluorophenyl)ethan-1-one (2.8 mmol, 600.0 mg), NaH (60%, 3.4 mmol, 134.4 mg) and benzyl mercaptan (3.0 mmol, 0.35 mL) in THF (7.7 mL) at 75 ºC afforded the product **SI-1f** (64%, 463.7 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.84 (dd, *J* = 8.7, 6.0 Hz, 1H), 7.43 – 7.37 (m, 2H),

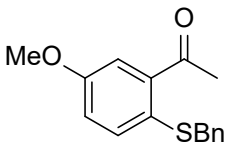
7.35 – 7.24 (m, 3H), 7.08 (dd, *J* = 10.5, 2.4 Hz, 1H), 6.84 (ddd, *J* = 8.7, 7.6, 2.4 Hz, 1H), 4.08 (s, 2H), 2.56 (s, 3H). **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.5, 164.8 (d, *J* = 255.0 Hz), 145.8 (d, *J* = 8.9 Hz), 135.5, 133.6 (d, *J* = 10.1 Hz), 130.7 (d, *J* = 2.6 Hz), 129.2, 128.8, 127.6, 113.0 (d = 25.1 Hz), 110.8 (d, *J* = 22.0 Hz), 37.7, 28.1; **$^{19}$F NMR (282 MHz, $CDCl_3$)** δ -105.6.

**1-(2-(benzylthio)-4-methoxyphenyl)ethan-1-one (SI-1g)**



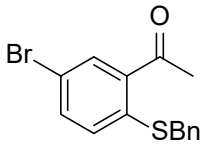

Following the general procedure B, the reaction of 1-(2-bromo-4-methoxyphenyl)ethan-1-one (2.4 mmol, 408.1 mg), NaH (60%, 2.9 mmol, 115.2 mg) and benzyl mercaptan (2.5 mmol, 0.3 mL) in DMF (6.6 mL) at 75 ºC afforded the product **SI-1g** (63%, 412.9 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.71 (d, *J* = 8.7 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.29 – 7.15 (m, 3H), 6.79 (d, *J* = 2.4 Hz, 1H), 6.57 (dd, *J* = 8.7, 2.4 Hz, 1H), 4.02 (s, 2H), 3.68 (s, 3H), 2.45 (s, 3H);**$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.1, 162.5, 144.8, 136.3, 133.7, 129.1, 128.6, 127.3, 127.1, 111.3, 108.8, 55.5, 37.3, 27.7.

**1-(2-(benzylthio)-5-methoxyphenyl)ethan-1-one (SI-1h)**




Following the general procedure B, the reaction of 1-(2-bromo-5-methoxyphenyl)ethan-1-one (2 mmol, 458.1 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1h** (60%, 327.5 mg) as a yellow solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.33 – 7.19 (m, 6H), 7.11 (d, *J* = 2.8 Hz, 1H), 6.91 (dd, *J* = 8.7, 2.8 Hz, 1H), 4.02 (s, 2H), 3.80 (s, 3H), 2.53 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 200.7, 157.6, 140.9, 136.9, 131.9, 128.9, 128.3, 127.2, 127.0, 117.0, 114.5, 55.3, 39.6, 29.4.

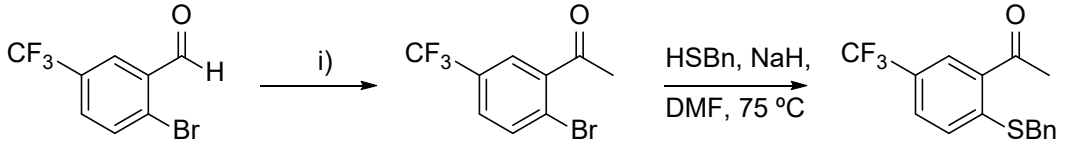
**1-(2-(benzylthio)-5-bromophenyl)ethan-1-one (SI-1i)**




Following the general procedure B, the reaction of 1-(2-fluoro-5-bromophenyl)ethan-1-one (2 mmol, 434.1 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1i** (57%, 367.3 mg) as a pale yellow solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.84 (d, *J* = 2.2 Hz, 1H), 7.48 (dd, *J* = 8.5, 2.2 Hz,

1H), 7.34 – 7.17 (m, 6H), 4.09 (s, 2H), 2.56 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 198.1, 139.5, 137.1, 135.7, 134.6, 133.1, 128.9, 128.5, 128.5, 127.4, 117.6, 37.8, 28.4.

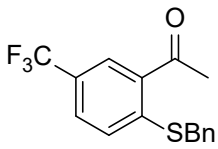
**1-(2-(benzylthio)-5-(trifluoromethyl)phenyl)ethan-1-one (SI-1j)**




**SI-2** **SI-1j**

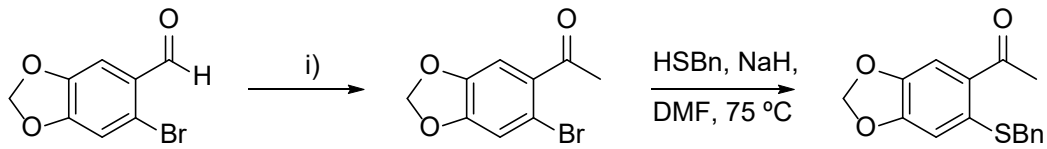
i) 1) MeMgBr, $Et_2O$, 0 ºC; 2) PCC, silica gel, DCM, rt.

Compound **SI-2** was prepared following a previously reported procedure[8] and spectral data is in accordance with the literature.[9]




Following the general procedure B, the reaction of 1-(2-bromo-5-(trifluoromethyl)ethan-1-one (**SI-2**) (1.7 mmol, 453.9 mg), NaH (60%, 2 mmol, 81.6 mg) and benzyl mercaptan (1.9 mmol, 0.22 mL) in DMF (4.7 mL) at 75 ºC afforded the product **SI-1j** (43%, 224.6 mg) as a pale yelow solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.98 (d, *J* = 0.8 Hz, 1H), 7.57 (dd, *J* = 8.5, 1.5 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H), 7.40 – 7.34 (m, 2H), 7.33 – 7.20 (m, 3H), 4.13 (s, 2H), 2.59 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.9, 146.4 (q, *J* = 1.0 Hz), 135.5, 134.6, 129.0, 128.7, 128.2 (q, *J* = 3.5 Hz), 127.6, 127.4 (q, *J* = 3.8 Hz), 126.4, 126.0 (q, *J* = 33.3 Hz), 123.8 (q, *J* = 271.8 Hz), 37.5, 28.1; **$^{19}$F NMR (282 MHz, $CDCl_3$)** δ -62.3.

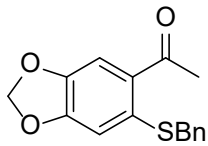
**1-(6-(benzylthio)benzo[*d*][1,3]dioxol-5-yl)ethan-1-one (SI-1k)**




**SI-3** **SI-1k**

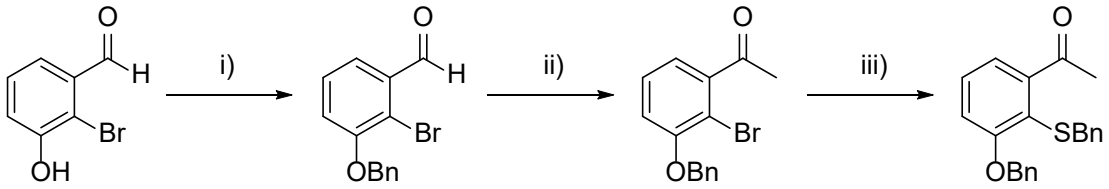
i) 1) MeMgBr, $Et_2O$, 0 ºC; 2) PCC, silica gel, DCM, rt.

Compound **SI-3** was prepared following a previously reported procedure[8] and spectral data is in accordance with the literature.[10]



Following the general procedure B, the reaction of 1-(6-bromobenzo[*d*][1,3]dioxol-5-yl)ethan-1-one (**SI-3**) (1.2 mmol, 291.7 mg), NaH (60%, 1.4 mmol, 57.6 mg) and benzyl mercaptan (1.3 mmol, 0.15 mL) in DMF (3.3 mL) at 75 ºC afforded the product **SI-1k** (57%, 195.8 mg) as a pale brown solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.40 – 7.24 (m, 5H), 7.22 (s, 1H), 6.88 (s, 1H), 6.01 (s, 2H), 4.06 (s, 2H), 2.50 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.6, 151.1, 145.1, 136.3, 129.2, 128.7, 127.4, 110.2, 107.4, 102.2, 38.6, 28.6.

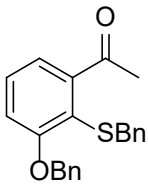
**1-(3-(benzyloxy)-2-(benzylthio)phenyl)ethan-1-one (SI-1l)**



**SI-4** **SI-5** **SI-1l**

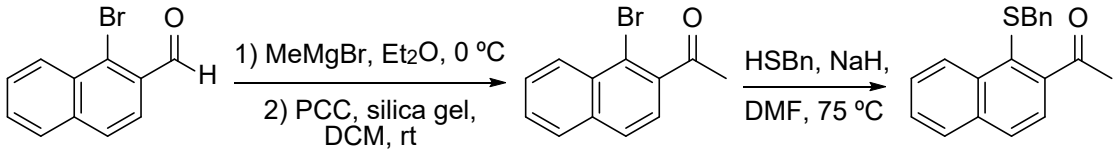
i) $K_2CO_3$, BnBr, DMF, rt; ii) 1) MeMgBr, $Et_2O$, 0 ºC; 2) PCC, silica gel, DCM, rt;
iii) HSBn, NaH, DMF, 75 ºC.

Compounds **SI-4** and **SI-5** were prepared following previously reported procedures[8,11] and spectral data is in accordance with the literature.[12]



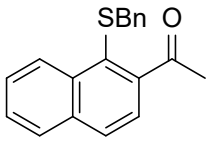
Following the general procedure B, the reaction of 1-(3-(benzyloxy)-2-bromophenyl)ethan-1-one (**SI-5**) (0.7 mmol, 213.6 mg), NaH (60%, 0.84 mmol, 33.6 mg) and benzyl mercaptan (0.74 mmol, 0.09 mL) in DMF (1.9 mL) at 75 ºC afforded the product **SI-1l** (61%, 150.0 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.45 – 7.39 (m, 2H), 7.37 – 7.25 (m, 3H), 7.22 – 7.15 (m, 1H), 7.12 – 7.03 (m, 3H), 7.00 – 6.94 (m, 2H), 6.91 (dd, *J* = 8.2, 0.7 Hz, 1H), 6.74 (dd, *J* = 7.6, 0.7 Hz, 1H), 5.08 (s, 2H), 3.95 (s, 2H), 2.20 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 203.9, 159.7, 149.1, 138.1, 136.6, 130.0, 129.0, 128.8, 128.4, 128.2, 127.4, 127.1, 118.8, 118.6, 113.8, 71.1, 39.3, 31.3.

**1-(1-(benzylthio)naphthalen-2-yl)ethan-1-one (SI-1m)**



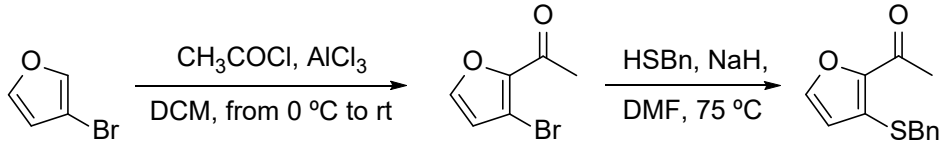

**SI-6** **SI-1m**

Compound **SI-6** was prepared following a previously reported procedure[8] and spectral data is in accordance with the literature.[13]



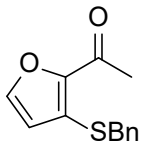

Following the general procedure B, the reaction of 1-(1-bromonaphthalen-2-yl)ethan-1-one (**SI-6**) (2 mmol, 498.2 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in DMF (5.5 mL) at 75 ºC afforded the product **SI-1m** (62%, 364.3 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.60 (d, *J* = 8.0 Hz, 1H), 8.07 – 7.77 (m, 2H), 7.56 (pd, *J* = 6.9, 1.1 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.22 – 7.03 (m, 3H), 7.09 – 6.88 (m, 2H), 3.96 (s, 2H), 2.49 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 204.6, 146.9, 137.4, 134.7, 134.1, 129.9, 128.8, 128.5, 128.3, 127.6, 127.4, 127.2, 127.0, 126.4, 122.7, 42.2, 31.6.

**1-(3-(benzylthio)furan-2-yl)ethan-1-one (SI-1n)**




**SI-7** **SI-1n**

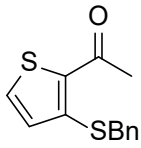
Compound **SI-7** was prepared following a previously reported procedure and spectral data is in accordance with the literature.[14]




Following the general procedure B, the reaction of 1-(3-bromofuran-2-yl)ethan-1-one (**SI-7**) (3.45 mmol, 652.1 mg), NaH (60%, 4.1 mmol, 166 mg) and benzyl mercaptan (3.6 mmol, 0.47 mL) in DMF (9.5 mL) at 75 ºC afforded the product **SI-1n** (87%, 696.9 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.33 (d, *J* = 1.9 Hz, 1H), 7.33 – 7.08 (m, 5H), 6.41 (d, *J* = 1.9 Hz, 1H), 4.06 (s, 2H), 2.35 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 186.7, 146.8,

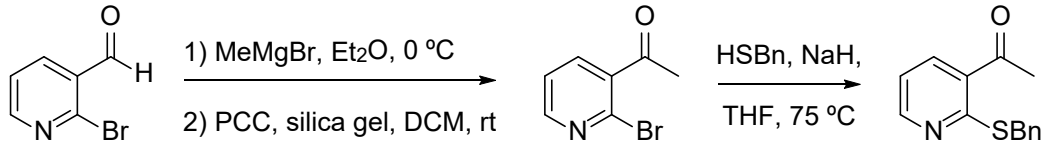
145.2, 136.1, 130.9, 128.7, 128.6, 127.4, 111.8, 37.1, 26.1.

**1-(3-(benzylthio)thiophen-2-yl)ethan-1-one (SI-1o)**



Following the general procedure B, the reaction of 1-(3-bromothiophen-2-yl)ethan-1-one (2 mmol, 408.1 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in DMF (5.5 mL) at 75 ºC afforded the product **SI-1o** (83%, 412.9 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.44 (d, *J* = 5.2 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.32 – 7.20 (m, 3H), 7.03 (d, *J* = 5.2 Hz, 1H), 4.19 (s, 2H), 2.47 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 189.8, 143.7, 136.2, 132.1, 131.4, 128.9, 128.7, 127.6, 127.3, 38.1, 28.8.

**1-(2-(benzylthio)pyridin-3-yl)ethan-1-one (SI-1p)**

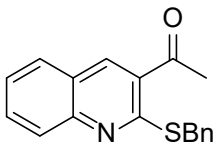



**SI-8** **SI-1p**

Compound **SI-8** was prepared following a previously reported procedure[8] and spectral data is in accordance with the literature.[15]

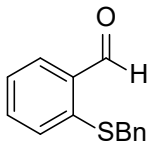
Following the general procedure B, the reaction of 1-(2-bromopyridin-3-yl)ethan-1-one (1 mmol, 110.4 mg), NaH (60%, 1.2 mmol, 48 mg) and benzyl mercaptan (1.05 mmol, 0.13 mL) in THF (2.8 mL) at 75 ºC afforded the product **SI-1p** (45%, 108.7 mg) as a pale yellow solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 8.58 (dd, *J* = 4.7, 1.8 Hz, 1H), 8.04 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.32 – 7.17 (m, 3H), 7.09 (dd, *J* = 7.8, 4.7 Hz, 1H), 4.44 (s, 2H), 2.57 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.6, 161.4, 151.7, 138.4, 138.0, 129.5, 129.0, 128.4, 126.9, 118.3, 34.9, 27.7.

**1-(2-(benzylthio)quinolin-3-yl)ethan-1-one (SI-1q)**



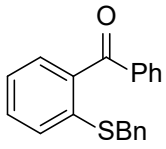
Following the general procedure B, the reaction of 1-(2-chloroquinolin-3-yl)ethan-1-one (0.8 mmol, 187.5 mg), NaH (60%, 1 mmol, 38.4 mg) and benzyl mercaptan (0.84 mmol, 0.10 mL) in DMF (2.2 mL) at 75 ºC afforded the product **SI-1q** (96%, 225.8 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.40 (s, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.79 – 7.70 (m, 2H), 7.53 (d, *J* = 7.1 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.25 – 7.17 (m, 1H), 4.56 (s, 2H), 2.64 (s, 3H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 197.5, 158.7, 148.4, 139.6, 138.4, 132.4, 129.5, 128.8, 128.3, 127.9, 127.7, 126.8, 125.9, 124.0, 35.0, 27.7.

**2-(benzylthio)benzaldehyde (SI-1r)**



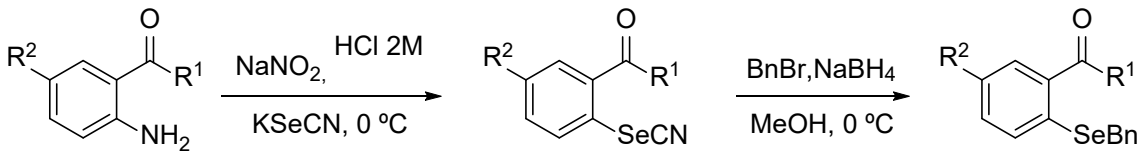
Following the general procedure B, the reaction of 2-bromobenzaldehyde (2 mmol, 370.0 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1r** (75%, 341.1 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.25 (s, 1H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.44 (dt, *J* = 7.4, 3.8 Hz, 2H), 7.33 – 7.17 (m, 6H), 4.11 (s, 2H). Spectral data is in accordance with the literature.[16]

**(2-(benzylthio)phenyl)(phenyl)methanone (SI-1s)**



Following the general procedure B, the reaction of (2-bromophenyl)(phenyl)methanone (2 mmol, 522.2 mg), NaH (60%, 2.4 mmol, 96 mg) and benzyl mercaptan (2.1 mmol, 0.25 mL) in THF (5.5 mL) at 75 ºC afforded the product **SI-1s** (63%, 385.4 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.62 (d, *J* = 8.3 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 3H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.15 – 7.06 (m, 6H), 3.91 (s, 2H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 196.6, 140.7, 137.3, 136.8, 135.3, 133.0, 131.1, 130.3, 130.0, 128.8, 128.7, 128.3, 127.0, 125.9, 39.6.

## 2.2. General Procedure and Characterization of Selenides SI-10




$R^1$= Me, $R^2$= H
$R^1$= H, $R^2$= Cl

**SI-9a**
**SI-9b**

**SI-10a**
**SI-10b**

*General procedure for the synthesis of selenides **SI-10**:*

Compounds **SI-10a** and **SI-10b** were prepared following a reported procedure in the literature.[17] The corresponding 2-aminoacetophenone or 2-amino-5-chlorobenzaldehyde (1.1 equiv) and an aqueous HCl solution (2M) were added to an Erlenmeyer flask. The solution was cooled to 0 ºC and a water solution of $NaNO_2$ (1 equiv, 2M) was added dropwise. At 0 ºC, sodium acetate (2.5 equiv) was added, followed by the addition of acetate buffer solution until pH 4.3. The KSeCN (1.5 equiv) was then added under vigorous agitation and the solution was kept 1 h at 0 ºC. Then, sodium acetate was added until pH 5.5. The resulting solution was extracted with dichloromethane (3x) and the combined organic phases were dried over anhydrous $MgSO_4$. The solvent was removed in vacuum and the residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure products **SI-9a** or **SI-9b**.

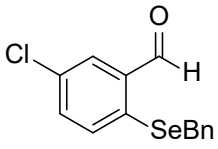
To a two necked round-bottomed flask under nitrogen, compound **SI-9a** or **SI-9b** (1 equiv) and methanol (5 mL/mmol) were added. The solution was cooled to 0 ºC and benzylbromide (4 equiv) was added, followed by the slow addition of $NaBH_4$ (1.1 equiv). The solution was stirred 2h at 0 ºC. The solvent was removed in vacuum and the residue was diluted in ethyl acetate followed by addition of saturated aqueous solution of $NH_4Cl$. After phase separation, the aqueous phase was extracted with ethyl acetate (2 x) and the combined organic phases were dried over $MgSO_4$. The solvent was removed in vacuum and the residue was subjected to flash

chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure products **SI-10a** or **SI-10b**.

**1-(2-(benzylselanyl)phenyl)ethan-1-one (SI-10a)**

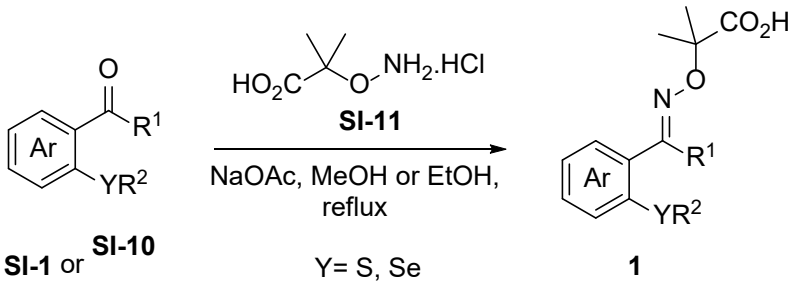
Following the general procedure, the reaction of 1-(2-selenocyanatophenyl)ethan-1-one (**SI-9a**) (2 mmol, 448.2 mg), $NaBH_4$ (2.2 mmol, 83.2 mg) and benzyl bromide (8.8 mmol, 1.05 mL) in MeOH (10 mL) at 0 ºC afforded the product **SI-10a** (71%, 411.7 mg) as a pale brown solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.93 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.42 (dd, *J* = 11.9, 7.2 Hz, 3H), 7.35 – 7.20 (m, 4H), 4.11 (s, 2H), 2.62 (s, 3H). Spectral data is in accordance with the literature.[17]

**2-(benzylselanyl)-5-chlorobenzaldehyde (SI-10b)**



Following the general procedure, the reaction of 5-chloro-2-selenocyanatobenzaldehyde (**SI-9b**) (2 mmol, 489.0 mg), $NaBH_4$ (2.2 mmol, 83.2 mg) and benzyl bromide (8.8 mmol, 1.05 mL) in MeOH (10 mL) at 0 ºC afforded the product **SI-10b** (76%, 469.3 mg) as an yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.05 (s, 1H), 7.79 (d, *J* = 2.4 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.43 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.26 – 7.20 (m, 5H), 4.10 (s, 2H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 191.5, 136.6, 134.5, 133.8, 133.7, 133.1, 132.3, 129.7, 129.0, 128.7, 127.3, 31.5.

## 2.3. General Procedure and Characterization of α-Imino-oxy Acids 1



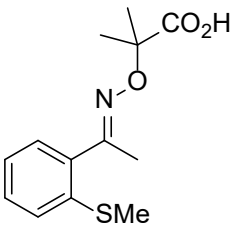

**SI-1** or **SI-10** **1**

Compound **SI-11** was prepared following a reported procedure in the literature and spectral data is in accordance with the literature.[18]

*General procedure for the synthesis of oximes **1**:*

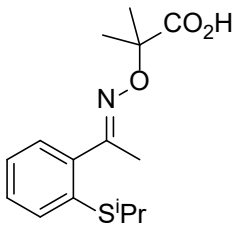
Compounds **1a-u** were prepared following a slightly modified procedure reported in the literature.[18] A solution of ketone (1.0 equiv) in MeOH or EtOH (0.2M) was treated with 2-(aminooxy)-2-methylpropanoic acid hydrochloride (**SI-11**) (1.2 equiv) and sodium acetate (2.4 equiv) and heated to reflux until completion by TLC analysis. The mixture was then allowed to cool to room temperature and water was added. The resulting aqueous solution was extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to provide the product. Then, the residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure products **1**.

**2-methyl-2-(((1-(2-(methylthio)phenyl)ethylidene)amino)oxy)propanoic acid (1a)**




Following the general procedure, the reaction of **SI-1a** (0.9 mmol, 149.6 mg), **SI-11** (1.08 mmol, 168.0 mg) and sodium acetate (2.2 mmol, 177.2 mg) in EtOH (4.5 mL) at reflux afforded the product **1a** (57%, 137.3 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.02 (bs, 1H), 7.35 – 7.22 (m, 3H), 7.18 – 7.11 (m, 1H), 2.38 (s, 3H), 2.28 (s, 3H), 1.62 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.5, 157.5, 137.7, 136.5, 129.1, 128.8, 126.8, 124.9, 81.3, 24.4, 16.8, 16.0; **HRMS** m/z (ESI): calcd. for $C_{13}H_{16}NO_3S$ $(M-H)^-$ 266.0856, found 266.0862.

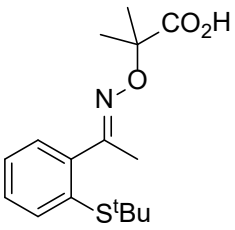
**2-(((1-(2-(isopropylthio)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1b)**




Following the general procedure, the reaction of **SI-1b** (1 mmol, 194.0 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1b** (75%, 22.7 mg) as a yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.20 (bs, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.25 (m, 1H), 7.22 (d, *J* = 4.1 Hz, 2H), 3.40 – 3.21 (m, 1H), 2.28 (s, 3H), 1.59 (s, 6H), 1.22 (d, *J* = 6.6 Hz, 6H); **$^{13}$C NMR (75 MHz, ($CDCl_3$)** δ 177.0, 160.0, 139.8, 134.5, 132.7, 129.2, 129.1, 126.8, 81.7, 38.7, 24.5, 23.0, 17.3.; **HRMS** m/z (ESI): calcd. for $C_{15}H_{20}NO_3S$

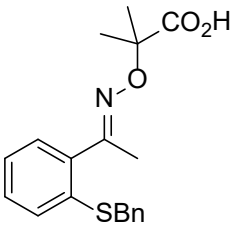
$(M-H)^-$ 294.1169, found 249.1165.

**2-(((1-(2-(tert-butylthio)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1c)**



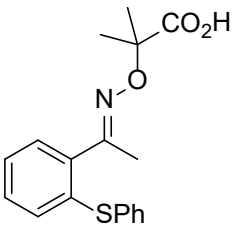

Following the general procedure, the reaction of **SI-1c** (0.3 mmol, 66.0 mg), **SI-11** (0.36 mmol, 56.0 mg) and sodium acetate (0.72 mmol, 59.1 mg) in EtOH (1.5 mL) at reflux afforded the product **1c** (60%, 55.9 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.63 – 7.54 (m, 1H), 7.38 – 7.32 (m, 2H), 7.31 – 7.25 (m, 1H), 2.29 (s, 3H), 1.58 (s, 6H), 1.22 (s, 9H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.0, 160.8, 144.3, 139.4, 131.4, 129.7, 129.2, 128.9, 81.5, 47.9, 31.3, 24.6, 18.8; **HRMS** m/z (ESI): calcd. for $C_{16}H_{22}NO_3S$ $(M-H)^-$ 308.1326, found 308.1336.

**2-(((1-(2-(benzylthio)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1d)**




Following the general procedure, the reaction of **SI-1d** (0.4 mmol, 100.2 mg), **SI-11** (0.48 mmol, 74.7 mg) and sodium acetate (0.96 mmol, 78.7 mg) in EtOH (2 mL) at reflux afforded the product **1d** (96%, 132.8 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.91 (bs, 1H), 7.38 – 7.34 (m, 1H), 7.31 – 7.24 (m, 8H), 4.09 (s, 2H), 2.29 (s, 3H), 1.65 (s, 6H);**$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.4, 158.3, 139.1, 137.4, 134.9, 131.1, 129.1, 129.0, 128.9, 128.4, 127.1, 126.5, 81.3, 39.5, 24.4, 16.7; **HRMS** m/z (ESI): calcd. for $C_{19}H_{20}NO_3S$ $(M-H)^-$ 342.1169, found 342.1162.

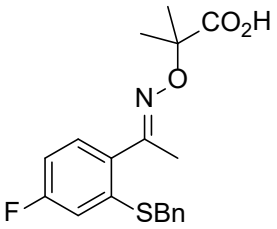
**2-methyl-2-(((1-(2-(phenylthio)phenyl)ethylidene)amino)oxy)propanoic acid (1e)**




Following the general procedure, the reaction of **SI-1e** (1 mmol, 228.3 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1e** (34%, 111.0 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.32 (bs, 1H), 7.39 – 7.24 (m, 9H), 2.36 (s, 3H), 1.61 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 177.3, 157.1, 137.3, 134.7, 134.1, 131.2, 130.5, 128.3, 128.2, 128.2, 126.2, 125.9, 80.5, 23.3, 15.4; **HRMS** m/z (ESI): calcd. for $C_{18}H_{18}NO_3S$ $(M-H)^-$ 328.1013,

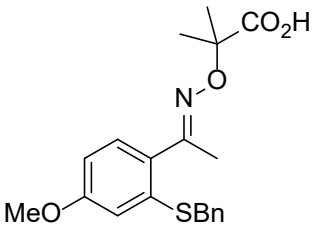
found 328.1017.

**2-(((1-(2-(benzylthio)-4-fluorophenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1f)**



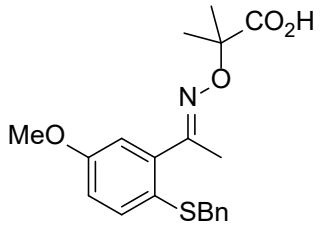

Following the general procedure, the reaction of **SI-1f** (0.4 mmol, 99.2 mg), **SI-11** (0.48 mmol, 74.7 mg) and sodium acetate (0.96 mmol, 78.7 mg) in EtOH (2 mL) at reflux afforded the product **1f** (88%, 126.9 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 9.99 (bs, 1H), 7.27 – 7.16 (m, 6H), 6.99 (dd, *J* = 9.5, 2.5 Hz, 1H), 6.83 (td, *J* = 8.3, 2.5 Hz, 1H), 4.03 (s, 2H), 2.20 (s, 3H), 1.57 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.0, 162.7 (d, *J* = 250.1 Hz), 157.3, 138.3 (d, *J* = 8.1 Hz), 136.6, 134.1 (d, *J* = 3.3 Hz), 130.7 (d, *J* = 8.8 Hz), 128.9, 128.7, 127.5, 116.5 (d, *J* = 23.7 Hz), 113.0 (d, *J* = 21.6 Hz), 81.5, 39.1, 24.4, 16.5; **$^{19}$F NMR (282 MHz, $CDCl_3$)** δ -111.98 (syn isomer), -112.59 (anti isomer); **HRMS** m/z (ESI): calcd. for $C_{19}H_{19}FNO_3S$ $(M-H)^-$ 360.1064, found 360.1050.

**2-(((1-(2-(benzylthio)-4-methoxyhenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1g)**



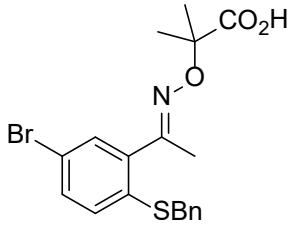

Following the general procedure, the reaction of **SI-1g** (0.5 mmol, 149.6 mg), **SI-11** (0.6 mmol, 93.3 mg) and sodium acetate (1.2 mmol, 98.4 mg) in EtOH (2.5 mL) at reflux afforded the product **1g** (70%, 143.0 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 9.89 (bs, 1H), 7.30 – 7.20 (m, 5H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.82 (d, *J* = 2.5 Hz, 1H), 6.71 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.04 (s, 2H), 3.71 (s, 3H), 2.23 (s, 3H), 1.59 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.6, 159.9, 158.3, 137.2, 136.8, 130.8, 130.2, 129.0, 128.6, 127.3, 115.8, 111.9, 81.4, 55.4, 39.3, 24.5, 16.8; **HRMS** m/z (ESI): calcd. for $C_{20}H_{22}NO_4S$ $(M-H)^-$ 372.1264, found 372.1264.

**2-(((1-(2-(benzylthio)-5-methoxyphenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1h)**



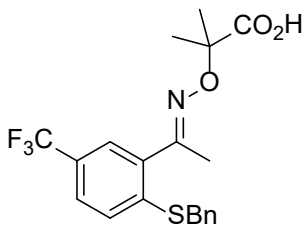
Following the general procedure, the reaction of **SI-1h** (1 mmol, 272.2 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1h** (71%, 266.5 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.33 – 7.05 (m, 6H), 6.88 – 6.59 (m, 2H), 3.91 (s, 2H), 3.78 (s, 3H), 2.20 (s, 3H), 1.58 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.1, 159.2, 159.1, 142.2, 137.8, 135.8, 128.9, 128.9, 128.3, 126.9, 124.2, 114.7, 81.4, 55.4, 41.2, 24.3, 17.1; **HRMS** m/z (ESI): calcd. for $C_{20}H_{22}NO_4S$ $(M-H)^-$ 372.1264, found 372.1259.

**2-(((1-(2-(benzylthio)-5-bromophenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1i)**



Following the general procedure, the reaction of **SI-1i** (1 mmol, 320.0 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1i** (74%, 313.8 mg) as a brown oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.35 – 7.30 (m, 2H), 7.26 – 7.17 (m, 5H), 7.12 (d, *J* = 9.0 Hz, 1H), 3.99 (s, 2H), 2.19 (s, 3H), 1.57 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.3, 157.1, 140.6, 136.9, 134.1, 132.5, 131.9, 131.8, 128.8, 128.5, 127.2, 120.2, 81.5, 39.4, 24.3, 16.4; **HRMS** m/z (ESI): calcd. for $C_{19}H_{19}BrNO_3S$ $(M-H)^-$ 420.0264, found 420.0277.

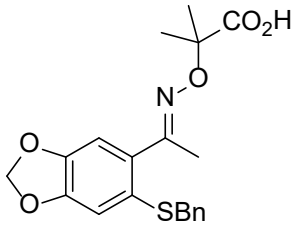
**2-(((1-(2-(benzylthio)-5-(trifluoromethyl)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1j)**



Following the general procedure, the reaction of **SI-1j** (0.6 mmol, 179.8 mg), **SI-11** (0.7 mmol, 112.0 mg) and sodium acetate (1.4 mmol, 118.1 mg) in EtOH (3 mL) at reflux afforded the product **1j** (89%, 211.8 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.12 (bs, 1H), 7.49 – 7.43

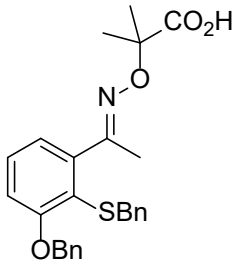
(m, 2H), 7.40 – 7.34 (m, 1H), 7.31 – 7.24 (m, 5H), 4.10 (s, 2H), 2.26 (s, 3H), 1.61 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.4, 156.3, 141.1 (q, *J* = 1.2 Hz), 137.8, 136.3, 128.8, 128.7, 128.6, 127.7 (q, *J* = 32.8 Hz), 127.4, 125.6 (q, *J* = 3.5 Hz), 125.4 (q, *J* = 3.6 Hz), 123.9 (q, *J* = 271.9 Hz), 81.6, 38.5, 24.3, 16.0; **$^{9}$F NMR (282 MHz, $CDCl_3$)** δ -62.43 (syn isomer), -62.48 (anti isomer); **HRMS** m/z (ESI): calcd. for $C_{20}H_{19}F_3NO_3S$ $(M-H)^-$ 410.1032, found 410.1026.

**2-(((1-(6-(benzylthio)benzo[d][1,3]dioxol-5-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1k)**



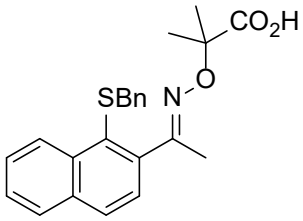

Following the general procedure, the reaction of **SI-1k** (0.1 mmol, 37.5 mg), **SI-11** (0.12 mmol, 18.7 mg) and sodium acetate (0.24 mmol, 19.7 mg) in EtOH (0.5 mL) at reflux afforded the product **1k** (81%, 41.0 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 7.26 – 7.13 (m, 5H), 6.79 (s, 1H), 6.68 (s, 1H), 5.94 (s, 2H), 3.93 (s, 2H), 2.15 (s, 3H), 1.56 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.0, 158.9, 148.1, 147.2, 137.5, 134.6, 128.8, 128.4, 127.1, 126.6, 113.4, 109.2, 101.7, 81.4, 41.1, 24.4, 17.2; **HRMS** m/z (ESI): calcd. for $C_{20}H_{20}NO_5S$ $(M-H)^-$ 386.1057, found 386.1096.

**2-(((1-(3-(benzyloxy)-2-(benzylthio)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1l)**



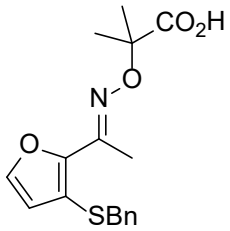

Following the general procedure, the reaction of **SI-1l** (0.3 mmol, 99.9 mg), **SI-11** (0.36 mmol, 56.0 mg) and sodium acetate (0.72 mmol, 59.1 mg) in EtOH (1.5 mL) at reflux afforded the product **1l** (59%, 75.6 mg) as a white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 8.63 (bs, 1H), 7.58 – 7.51 (m, 2H), 7.48 – 7.38 (m, 3H), 7.32 – 7.24 (m, 1H), 7.22 – 7.15 (m, 3H), 7.11 – 7.06 (m, 2H), 7.00 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.84 (dd, *J* = 7.6, 1.0 Hz, 1H), 5.18 (s, 2H), 4.06 (s, 2H), 2.07 (s, 3H), 1.60 (s, 6H);**$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 177.7, 160.2, 159.8, 143.9, 138.3, 136.7, 129.6, 129.0, 128.8, 128.4, 128.3, 128.2, 127.4, 127.0, 121.6, 113.2, 81.5, 71.1, 39.1, 24.5, 17.6; **HRMS** m/z (ESI): calcd. for $C_{26}H_{26}NO_4S$ $(M-H)^-$ 448.1577, found 448.1596.

**2-(((1-(1-(benzylthio)naphthalen-2-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1m)**



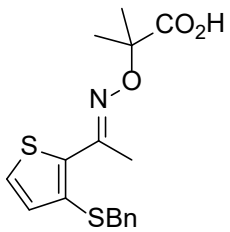
Following the general procedure, the reaction of **SI-1m** (1 mmol, 292.0 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1m** (78%, 305.3mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.60 (d, *J* = 7.8 Hz, 1H), 7.88 – 7.81 (m, 2H), 7.56 (pd, *J* = 6.8, 1.5 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.21 – 7.09 (m, 3H), 6.97 (dd, *J* = 6.8, 2.9 Hz, 2H), 3.93 (s, 2H), 2.19 (s, 3H), 1.61 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 177.3, 160.0, 141.5, 137.2, 134.5, 133.4, 129.8, 129.2, 128.4, 128.0, 127.8, 126.9, 126.6, 126.2, 126.0, 125.5, 81.0, 41.2, 24.0, 17.4; **HRMS** m/z (ESI): calcd. for $C_{23}H_{22}NO_3S$ $(M-H)^-$ 392.1326, found 392.1328.

**2-(((1-(3-(benzylthio)furan-2-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1n)**



Following the general procedure, the reaction of **SI-1n** (1.3 mmol, 302.0 mg), **SI-11** (1.56 mmol, 240.5 mg) and sodium acetate (3.1 mmol, 256.0 mg) in EtOH (6.5 mL) at reflux afforded the product **1n** (81%, 349.6 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.38 (d, *J* = 1.9 Hz, 1H), 7.35 – 7.20 (m, 5H), 6.40 (d, *J* = 1.9 Hz, 1H), 4.05 (s, 2H), 2.23 (s, 3H), 1.60 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.0, 150.0, 145.2, 142.7, 137.2, 128.6, 128.4, 127.1, 118.8, 113.2, 81.8, 38.1, 24.1, 11.7. **HRMS** m/z (ESI): calcd. for $C_{17}H_{18}NO_4S$ $(M-H)^-$ 332.0962, found 332.0960.

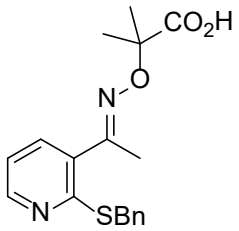
**2-(((1-(3-(benzylthio)thiophen-2-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1o)**



Following the general procedure, the reaction of **SI-1o** (0.6 mmol, 149.2 mg), **SI-11** (0.72 mmol, 112.1 mg) and sodium acetate (1.44 mmol, 118.1 mg) in EtOH (3 mL) at reflux afforded the product **1o** (84%, 176.3 mg) as a white solid. **$^1$H NMR (300**

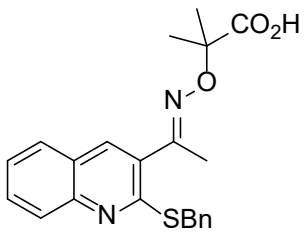
**MHz, $CDCl_3$)** δ 10.03 (bs, 1H), 7.32 – 7.19 (m, 6H), 6.95 (d, *J* = 5.3 Hz, 1H), 4.09 (s, 2H), 2.30 (s, 3H), 1.62 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.5, 152.4, 137.3, 133.1, 132.7, 129.5, 128.8, 128.6, 127.3, 125.7, 81.9, 39.5, 24.3, 15.4; **HRMS** m/z (ESI): calcd. for $C_{17}H_{18}NO_3S_2$ $(M-H)^-$ 348.0723, found 348.0746.

**2-(((1-(2-(benzylthio)pyridin-3-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1p)**



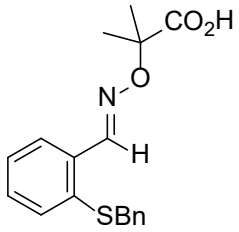

Following the general procedure, the reaction of **SI-1p** (0.2 mmol, 56.3 mg), **SI-11** (0.24 mmol, 37.4 mg) and sodium acetate (0.48 mmol, 39.4 mg) in EtOH (1 mL) at reflux afforded the product **1p** (77%, 61.7 mg) as a yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 9.92 (bs, 1H), 8.45 (dd, *J* = 4.8, 1.7 Hz, 1H), 7.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.31 – 7.18 (m, 3H), 7.00 (dd, *J* = 7.6, 4.8 Hz, 1H), 4.41 (s, 2H), 2.23 (s, 3H), 1.62 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.0, 157.3, 155.2, 148.7, 138.2, 135.9, 131.2, 129.2, 128.3, 126.9, 119.0, 81.7, 35.2, 24.4, 15.2; **HRMS** m/z (ESI): calcd. for $C_{18}H_{19}N_2O_3S$ $(M-H)^-$ 343.1111, found 343.1099.

**2-(((1-(2-(benzylthio)quinolin-3-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (1q)**



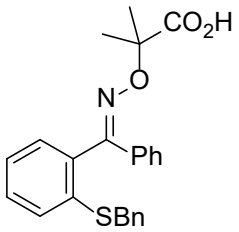

Following the general procedure, the reaction of **SI-1q** (0.7 mmol, 200.0 mg), **SI-11** (0.8 mmol, 130.7 mg) and sodium acetate (1.68 mmol, 137.8 mg) in EtOH (3.5 mL) at reflux afforded the product **1q** (80%, 215.1 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.87 (bs, 1H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.87 (s, 1H), 7.77 – 7.63 (m, 2H), 7.55 – 7.46 (m, 2H), 7.46 – 7.38 (m, 1H), 7.35 – 7.18 (m, 3H), 4.57 (s, 2H), 2.34 (s, 3H), 1.68 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.3, 157.4, 155.4, 147.4, 138.5, 135.2, 130.3, 129.8, 129.4, 128.4, 127.9, 127.8, 126.9, 125.7, 125.3, 81.8, 35.1, 24.5, 15.7; **HRMS** m/z (ESI): calcd. for $C_{22}H_{21}N_2O_3S$ $(M-H)^-$ 393.1278, found 393.1285.

**2-(((2-(benzylthio)benzylidene)amino)oxy)-2-methylpropanoic acid (1r)**



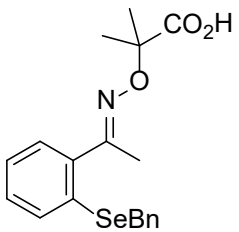
Following the general procedure, the reaction of **SI-1r** (1 mmol, 228.1 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1r** (88%, 290.9 mg) as a white solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 11.29 (bs, 1H), 8.63 (s, 1H), 7.73 (dd, J = 7.4, 1.8 Hz, 1H), 7.32 (dd, J = 7.7, 1.4 Hz, 1H), 7.28 – 7.05 (m, 7H), 3.98 (s, 2H), 1.60 (s, 6H);**$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 179.6, 148.3, 136.9, 135.6, 133.1, 132.7, 130.1, 128.8, 128.4, 127.3, 127.2, 127.2, 81.6, 40.3, 24.0; **HRMS** m/z (ESI): calcd. for $C_{18}H_{18}NO_3S$ $(M-H)^-$ 328.1013, found 328.1015.

**2-((((2-(benzylthio)phenyl)(phenyl)methylene)amino)oxy)-2-methylpropanoic acid (1s)**



Following the general procedure, the reaction of **SI-1s** (1 mmol, 304.1 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in MeOH (5 mL) at reflux afforded the product **1s** (67%, 272.8 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.45 – 7.25 (m, 9H), 7.24 – 7.10 (m, 5H), 4.00 (d, J = 9.8 Hz, 2H), 1.55 (d, J = 4.4 Hz, 6H);**$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 176.2, 157.6, 137.1, 135.6, 134.8, 133.7, 131.6, 129.9, 129.1, 129.0, 128.9, 128.4, 128.4, 127.3, 127.2, 127.0, 82.7, 39.1, 24.3; **HRMS** m/z (ESI): calcd. for $C_{24}H_{22}NO_3S$ $(M-H)^-$ 404.1326, found 404.1325.

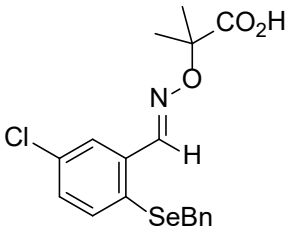
**2-(((1-(2-(benzylselanyl)phenyl)ethylidene)amino)oxy)-2-methylpropanoic acid (1t)**



Following the general procedure, the reaction of **SI-10a** (1 mmol, 289.2 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in MeOH (5 mL) at reflux afforded the product **1t** (76%, 295.5 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.57 – 7.47 (m, 1H), 7.37 – 7.20 (m, 8H), 4.08 (s, 2H), 2.26 (s, 3H), 1.63 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 177.7, 159.0, 139.0, 138.0,

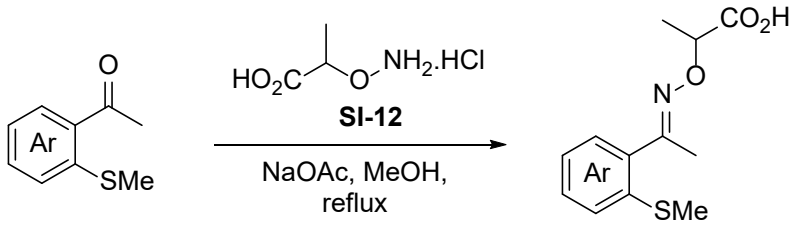
132.6, 131.1, 129.2, 128.9, 128.7, 128.4, 126.8, 126.5, 81.5, 32.3, 24.5, 16.1; **HRMS** m/z (ESI): calcd. for $C_{19}H_{20}NO_3Se$ $(M-H)^-$ 390.0614, found 390.0623.

**2-(((2-(benzylselanyl)-5-chlorobenzylidene)amino)oxy)-2-methylpropanoic acid (1u)**



Following the general procedure, the reaction of **SI-10b** (1 mmol, 309.7 mg), **SI-11** (1.2 mmol, 186.7 mg) and sodium acetate (2.4 mmol, 196.9 mg) in MeOH (5 mL) at reflux afforded the product **1u** (65%, 268.2 mg) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.53 (s, 1H), 7.75 (d, *J* = 2.4 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 1H), 7.33 – 7.16 (m, 6H), 4.04 (s, 2H), 1.68 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 178.6, 149.3, 137.6, 136.8, 135.6, 134.2, 130.0, 129.4, 128.8, 128.5, 127.3, 127.1, 82.0, 33.1, 24.1; **HRMS** m/z (ESI): calcd. for $C_{18}H_{17}ClNO_3Se$ $(M-H)^-$ 410.0068, found 410.0072.

*Procedure for the synthesis of oxime **1a´**:*

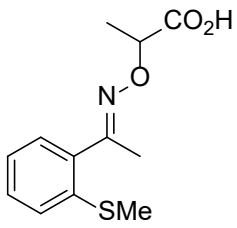



**SI-1a** **1a´**

Compound **SI-12** was prepared following a reported procedure in the literature.[18]

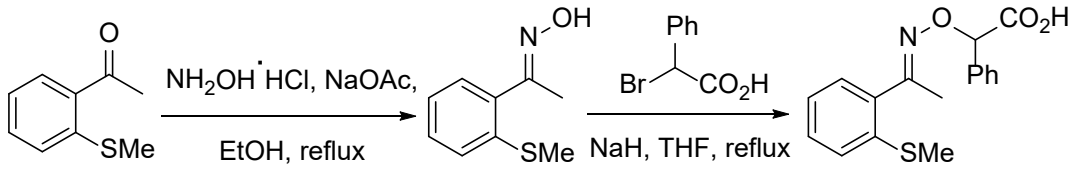
Compound **1a´** was prepared following a slightly modified procedure reported in the literature.[18] A solution of ketone (1.0 equiv) in EtOH (0.2M) was treated with 2-(aminooxy)propanoic acid hydrochloride (**SI-12**) (1.2 equiv), sodium acetate (2.4 equiv) and heated to reflux until completion by TLC analysis. The mixture was then allowed to cool to room temperature and water was added. The resulting aqueous solution was extracted with EtOAc (3x) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to provide the product. Then, the residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure product **1a´**.

**2-(((1-(2-(methylthio)phenyl)ethylidene)amino)oxy)propanoic acid (1a´)**



Following the procedure, the reaction of **SI-1a** (1 mmol, 166.2 mg), **SI-12** (1.2 mmol, 168.6 mg) and sodium acetate (2.4 mmol, 196.9 mg) in EtOH (5 mL) at reflux afforded the product **1a´** (78%, 198.0 mg) as a yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 10.19 (s, 1H), 7.27 – 7.00 (m, 4H), 4.77 (q, *J* = 7.0 Hz, 1H), 2.31 (s, 3H), 2.21 (s, 3H), 1.51 (d, *J* = 7.0 Hz, 3H); **$^{13}$C NMR (75 MHz, ($CDCl_3$)** δ 178.4, 158.4, 137.5, 136.6, 129.2, 128.8, 127.1, 125.1, 21.4, 16.9, 16.8, 16.3; **HRMS** m/z (ESI): calcd. for $C_{12}H_{14}NO_3S$ $(M-H)^-$ 252.0700, found 252.0704.

*Procedure for the synthesis of oxime **1a´´**:*

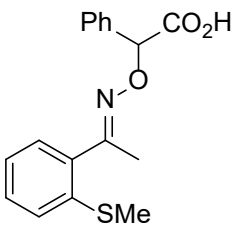



**SI-1a** **SI-13** **1a´´**

Compound **1a´´** was prepared following a slightly modified procedure reported in the literature.[19] A solution of **SI-1a** (0.8 mmol, 139.2 mg, 1.0 equiv) in EtOH (0.5 M) was treated with hydroxylamine hydrochloride (1.3 mmol, 93.1 mg, 1.6 equiv), sodium acetate (1.7 mmol, 137.4 mg, 2.0 equiv) and heated to reflux for 12 h. The mixture was then allowed to cool to room temperature and concentrated under vacuum to provide the product **SI-13** as a white solid, which was used for the next step without purification. Then, **SI-13** was added dropwise to a stirred suspension of NaH 60% in mineral oil (2.5 mmol, 60.3 mg, 3.0 equiv) in dry THF (1.5 M) at 0 °C (ice bath) under inert atmosphere and the mixture was stirred for 15 min. Afterwards, a solution of 2-bromo-2-phenylacetic acid (0.9 mmol, 198.1 mg, 1.1 equiv) in dry THF (0.5 M) was added and the reaction was heated to 75 °C for 12 h. After this time, the reaction was cooled to room temperature and concentrate hydrochloric acid was added until pH 2. The resulting solution was extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to provide the

product. Then, the residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure product **1a´´**.

**2-(((1-(2-(methylthio)phenyl)ethylidene)amino)oxy)-2-phenylacetic acid (1a´´)**



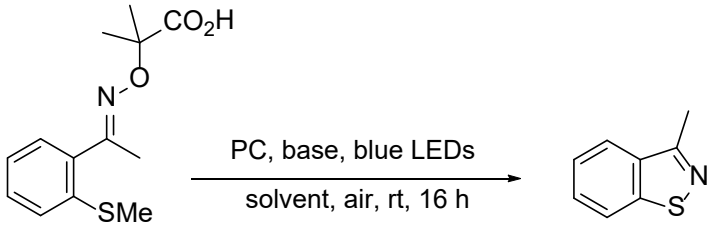

Following the procedure, the reaction of **SI-1a** (0.8 mmol, 139.2 mg) afforded the product **1a´´** (40% for two reaction steps, 106.5 mg) as white solid. **$^{1}$H NMR (300 MHz, $CDCl_3$)** δ 11.00 (bs, 1H), 7.66 – 7.58 (m, 2H), 7.47 – 7.40 (m, 3H), 7.37 – 7.26 (m, 3H), 7.23 – 7.16 (m, 1H), 5.81 (s, 1H), 2.41 (s, 3H), 2.37 (s, 3H);**$^{13}$C NMR (75 MHz, ($CDCl_3$)** δ 176.7, 159.1, 137.6, 136.5, 134.7, 129.3, 129.1, 128.9, 128.7, 127.7, 127.2, 125.1, 83.2, 16.9, 16.6; **HRMS** m/z (ESI): calcd. for $C_{17}H_{16}NO_3S$ $(M-H)^-$ 314.0856, found 314.0856.

## 3. Optimization of the Reaction Conditions

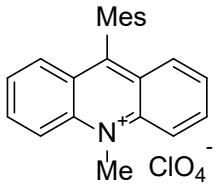
*General procedure for the optimization of the reaction conditions of the synthesis of isothiazoles **2**:*

In an oven-dried glass vial equipped with a stirring bar, 2-methyl-2-(((1-(2-(methylthio)phenyl)ethylidene)amino)oxy)propanoic acid (**1a**, 0.05 mmol, 13.4 mg, 1 equiv), the base (0.05 mmol, 1 equiv), the photocatalyst ($2.5 \cdot 10^{-3}$ mmol, 0.05 equiv) and the respective solvent (0.67 mL) were added under air. Then, the vial was closed with a PTFE/rubber septum perforated several times to enable the air enter into the reaction. Afterwards, the mixture was stirred and irradiated at 450 nm using 380 mW single LEDs in a custom-made temperature-controlled system (see Figure S1) for 16h at 20 ºC. Then, the volatiles were removed and yield was determined by $^{1}$H-NMR analysis using 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) as internal standard.

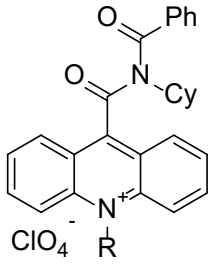
**Table S1.** Optimization of reaction conditions with **1a**.



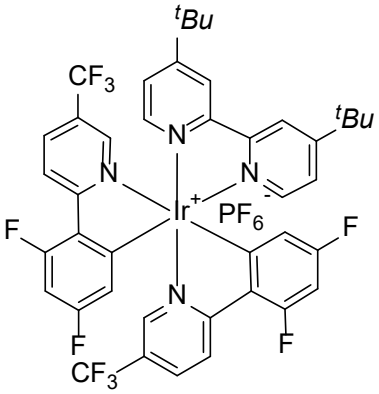

**1a** **2a**




**PC1**

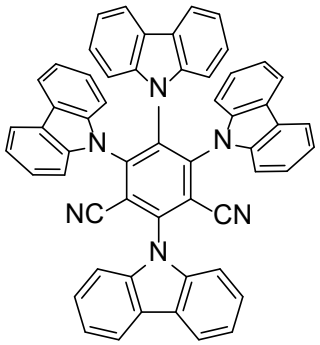



R =Ph **PC2** R = Me **PC3**




$Ir(dFCF_3ppy)_2(dtbbpy)PF_6$

**PC4**




4CzIPN

**PC5**

| entry | PC | base | solvent | yield (%)[a] |
|---|---|---|---|---|
| 1 | **PC1** | CsF | DCE | 17 |
| 2 | **PC1** | CsF | DCM | 20 |
| 3 | **PC1** | CsF | THF | 9 |
| 4 | **PC1** | CsF | DMF | 21 |
| 5 | **PC1** | CsF | MeCN | 10 |
| 6 | **PC1** | CsF | Acetone | 20 |
| 7 | **PC1** | $Cs_2CO_3$ | Acetone | 26 |
| 8 | **PC1** | $K_2CO_3$ | Acetone | 26 |
| 9 | **PC1** | $Na_2CO_3$ | Acetone | 53 |
| 10 | **PC1** | $Li_2CO_3$ | Acetone | 9 |
| 11 | **PC1** | NaF | Acetone | 17 |
| 12 | **PC1** | $Na_2HPO_4$ | Acetone | 41 |

| | | | | |
|---|---|---|---|---|
| 13 | **PC1** | $NaHCO_3$ | Acetone | 23 |
| **14** | **PC1** | **NaOAc** | **Acetone** | **56** |
| 15 | **PC2** | NaOAc | Acetone | 35 |
| 16 | **PC3** | NaOAc | Acetone | 31 |
| 17 | **PC4** | NaOAc | Acetone | 32 |
| 18 | **PC5** | NaOAc | Acetone | 44 |
| 19[b] | **PC1** | NaOAc | Acetone | 54 |
| 20[c] | **PC1** | NaOAc | Acetone | 4 |
| 21 | - | NaOAc | Acetone | 0 |
| 22 | **PC1** | - | Acetone | 0. |
| 23[d] | **PC1** | NaOAc | Acetone | 0. |

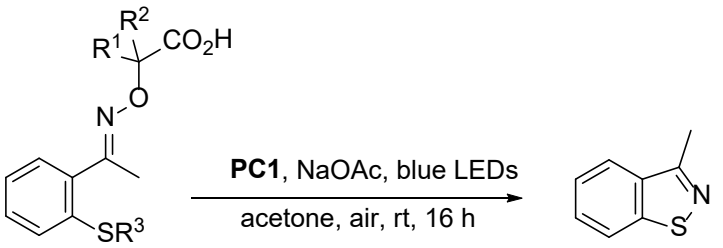
[a] The yield was determined from the crude $^1$H-NMR. [b] Oxygen was used instead air. [c] Argon was used instead air. [d] The reaction was performed in the dark. DCE = 1,2-Dichloroethane. DCM = Dichloromethane, THF = Tetrahydrofuran, DMF = *N,N*-Dimethylformamide.

## 4. Optimization of the α-Imino-oxy Acid Structure

*General procedure for the optimization of the α-imino-oxy acid structure in the synthesis of isothiazoles **2**:*

In an oven-dried glass vial equipped with a stirring bar, the corresponding α-imino-oxy acid **1** (0.05 mmol, 1 equiv), NaOAc (0.05 mmol, 4.1 mg, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate, ($2.5 \cdot 10^{-3}$ mmol, 1.05 mg, 0.05 equiv) and acetone (0.67 mL) were added under air. Then, the vial was closed with a PTFE/rubber septum perforated several times to enable the air enter into the reaction. Afterwards, the mixture was stirred and irradiated at 450 nm using 380 mW single LEDs in a custom-made temperature-controlled system (see Figure S1) for 16h at 20 ºC. Then, the volatiles were removed and yield was determined by $^1$H-NMR analysis using 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) as internal standard.

**Table S2.** Optimization of α-imino-oxy acid structure.

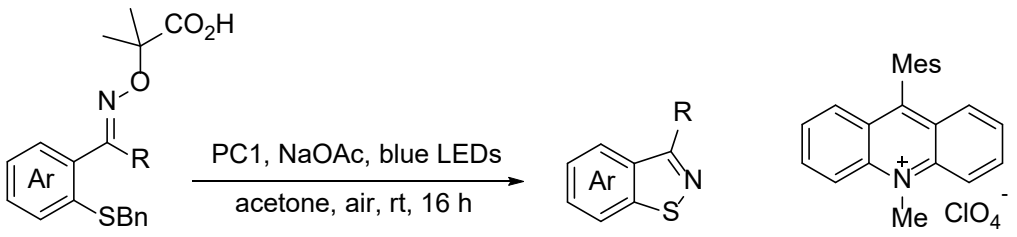



**1** **2a**

| entry | $R_1$ | $R_2$ | $R_3$ | yield (%)[a] |
|---|---|---|---|---|
| 1 | Me | H | Me | 33 |
| 2 | Me | Me | Me | 56 |
| 3 | Ph | H | Me | 58 |
| 4 | Me | Me | *i*-Pr | 44 |
| 5 | Me | Me | *t*-Bu | 68 |
| 6 | Me | Me | Ph | 4 |
| **7** | **Me** | **Me** | **Bn** | **85 (81)[b]** |
| 8[c] | Me | Me | Bn | 85 |

[a] The yield was determined from the crude $^1$H-NMR. [b] Isolated yield in 0.1 mmol scale in parentheses. [c] The reaction was performed with a blue LED spot of 40W instead of 380 mW single LEDs.

## 5. General Procedure and Characterization of Isothiazoles 2



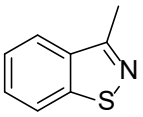

**1** **2** **PC1**

*General procedure for the synthesis of isothiazoles **2**:*

In an oven-dried glass vial equipped with a stirring bar, **1** (0.1 mmol, 1 equiv), NaOAc (0.1 mmol, 8.2 mg, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate, ($5\cdot10^{-3}$ mmol, 2.1 mg, 0.05 equiv) and acetone (1.33 mL) were

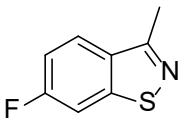
added under air. Then, the vial was closed with a PTFE/rubber septum perforated several times to enable the air enter into the reaction. Afterwards, the mixture was stirred and irradiated at 450 nm using 380 mW single LEDs in a custom-made temperature-controlled system (see Figure S1) for 16h at 20 ºC. Then, the volatiles were removed and the analytically pure product **2** was obtained by flash chromatography (Iatrobeads silica gel; cyclohexane/EtOAc).

**3-methylbenzo[*d*]isothiazole (2a)**



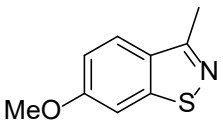
Following the general procedure, the reaction of **1d** (0.1 mmol, 34.0 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2a** (81%, 11.9 mg) as a yellow oil. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.97 – 7.90 (m, 2H), 7.56 – 7.49 (m, 1H), 7.48 – 7.40 (m, 1H), 2.76 (s, 3H). Spectral data is in accordance with the literature.[20]

**6-fluoro-3-methylbenzo[*d*]isothiazole (2b)**



Following the general procedure, the reaction of **1f** (0.1 mmol, 35.4 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2b** (82%, 13.4 mg) as a white solid. **$^1$H NMR (300 MHz, $C_6D_6$)** δ 7.05 (dd, *J* = 8.8, 4.9 Hz, 1H), 6.86 (dd, *J* = 8.5, 2.2 Hz, 1H), 6.70 (td, *J* = 8.7, 2.2 Hz, 1H), 2.26 (s, 3H); **$^{13}$C NMR (75 MHz, $C_6D_6$)** δ 162.6 (d, *J* = 249.6 Hz), 162.1, 154.2 (d, *J* = 10.4 Hz), 132.4, 124.9 (d, *J* = 10.2 Hz), 113.6 (d, *J* = 25.4 Hz), 105.9 (d, *J* = 25.6 Hz), 17.0; **$^{19}$F NMR (282 MHz, $C_6D_6$)** δ -113.77; **HRMS** m/z (ESI): calcd. for $C_8H_6FNS$ $(M)^+$ 167.0205, found 167.0200.

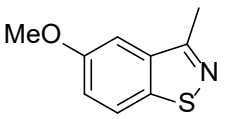
**6-methoxy-3-methylbenzo[*d*]isothiazole (2c)**



Following the general procedure, the reaction of **1g** (0.1 mmol, 37.1 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2c** (89%, 15.8 mg) as a white solid. **$^1$H NMR (300 MHz, $C_6D_6$)** δ 7.26 (d, *J* = 8.8 Hz, 1H), 6.87 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.74 (d, *J* = 2.2 Hz, 1H), 3.23 (s, 3H),

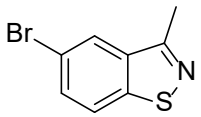
2.36 (s, 3H); **$^{13}$C NMR (75 MHz, $C_6D_6$)** δ 162.1, 160.0, 155.1, 130.3, 124.2, 115.9, 101.1, 55.1, 17.1; **HRMS** m/z (ESI): calcd. for $C_9H_{10}NOS$ $(M+H)^+$ 180.0478, found 180.0480.

**5-methoxy-3-methylbenzo[*d*]isothiazole (2d)**



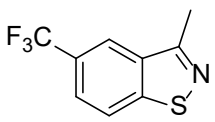

Following the general procedure, the reaction of **1h** (0.1 mmol, 37.3 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2d** (75%, 13.4 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 7.96 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 2.3 Hz, 1H), 7.23 (dd, J = 8.8, 2.3 Hz, 1H), 3.93 (s, 3H), 2.67 (s, 3H);**$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 163.1, 159.1, 146.0, 137.5, 121.7, 120.0, 105.4, 56.2, 17.6; **HRMS** m/z (ESI): calcd. for $C_9H_{10}NOS$ $(M+H)^+$ 180.0478, found 180.0482.

**5-bromo-3-methylbenzo[*d*]isothiazole (2e)**




Following the general procedure, the reaction of **1i** (0.1 mmol, 42.0 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2e** (68%, 15.6 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 8.28 (s, 1H), 8.09 (d, J = 8.6 Hz, 1H), 7.72 (d, J = 8.6 Hz, 1H), 2.73 (s, 3H);**$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 163.2, 152.1, 137.9, 131.2, 127.4, 122.9, 119.2, 17.5; **HRMS** m/z (ESI): calcd. for $C_8H_6BrNS$ $(M)^+$ 227.9477, found 226.9404.

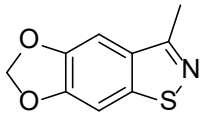
**3-methyl-5-(trifluoromethyl)benzo[*d*]isothiazole (2f)**




Following the general procedure, the reaction of **1j** (0.1 mmol, 40.6 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2f** (71%, 15.2 mg) as a white solid. **$^1$H NMR (300 MHz, $CD_2Cl_2$)** δ 8.28 – 8.22 (m, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.5, 1.4 Hz, 1H), 2.78 (s, 3H);**$^{13}$C NMR (75 MHz, $CD_2Cl_2$)** δ 163.9, 155.8, 135.4, 127.6 (q, *J* = 32.6 Hz), 125.0 (q, *J* = 272.0 Hz), 124.2 (q, *J* = 3.2 Hz), 121.5 (q, *J* = 4.3 Hz), 121.4, 17.8; **$^{19}$F NMR (282 MHz, $CD_2Cl_2$)** δ -61.17; **HRMS** m/z (ESI): calcd. for $C_9H_6F_3NS$ $(M)^+$ 217.0173, found

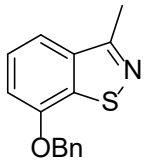
217.0166.

**3-methyl-[1,3]dioxolo[4',5':4,5]benzo[1,2-*d*]isothiazole (2g)**



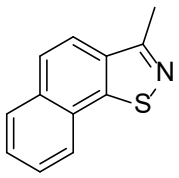
Following the general procedure, the reaction of **1k** (0.1 mmol, 36.0 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2g** (66%, 11.8 mg) as a white solid. **$^1$H NMR (300 MHz, $C_6D_6$)** δ 6.77 (s, 1H), 6.65 (s, 1H), 5.25 (s, 2H), 2.27 (s, 3H); **$^{13}$C NMR (75 MHz, $C_6D_6$)** δ 161.4, 149.8, 148.7, 147.4, 130.8, 102.0, 101.2, 98.6, 17.1; **HRMS** m/z (ESI): calcd. for $C_9H_8NO_2S$ $(M+H)^+$ 194.0270, found 194.0265.

**7-(benzyloxy)-3-methylbenzo[*d*]isothiazole (2h)**



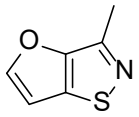
Following the general procedure, the reaction of **1l** (0.1 mmol, 44.8 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2h** (88%, 22.4 mg) as a white solid. **$^1$H NMR (300 MHz, $CD_2Cl_2$)** δ 7.55 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.46 – 7.33 (m, 4H), 6.98 (d, *J* = 7.6 Hz, 1H), 5.29 (s, 2H), 2.71 (s, 3H); **$^{13}$C NMR (75 MHz, $CD_2Cl_2$)** δ 163.7, 152.6, 143.0, 137.9, 137.0, 129.2, 128.7, 128.0, 127.0, 116.4, 108.8, 71.1, 17.9; **HRMS** m/z (ESI): calcd. for $C_{15}H_{14}NOS$ $(M+H)^+$ 256.0791, found 256.0800.

**3-methylnaphtho[2,1-*d*]isothiazole (2i)**



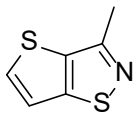
Following the general procedure, the reaction of **1m** (0.1 mmol, 39.3 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2i** (70%, 14.3 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 8.24 – 8.17 (m, 1H), 8.16 – 8.10 (m, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.76 – 7.68 (m, 2H), 2.79 (s, 3H); **$^{13}$C NMR (126 MHz, $(CD_3)_2CO$)** δ 164.7, 153.9, 133.9, 133.1, 130.0, 129.1, 128.4, 127.4, 127.3, 126.1, 121.6, 17.7; **HRMS** m/z (ESI): calcd. for $C_{12}H_9NS$ $(M)^+$ 199.0456, found 199.0465.

**3-methylfuro[2,3-*d*]isothiazole (2j)**



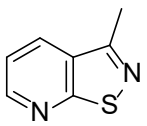
Following the general procedure, the reaction of **1n** (0.1 mmol, 33.3 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2j** (32%, 4.5 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 7.91 (dd, *J* = 3.7, 2.1 Hz, 1H), 7.01 (dd, *J* = 3.7, 2.1 Hz, 1H), 2.50 (d, *J* = 3.7 Hz, 3H); **$^{13}$C NMR (126 MHz, $(CD_3)_2CO$)** δ 152.0, 148.3, 146.4, 135.3, 107.4, 15.8; **HRMS** m/z (ESI): calcd. for $C_6H_6NOS$ $(M+H)^+$ 140.0165, found 140.0169.

**3-methylthieno[2,3-*d*]isothiazole (2k)**



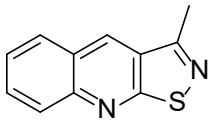
Following the general procedure, the reaction of **1o** (0.1 mmol, 35.0 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2k** (36%, 5.6 mg) as a brown oil. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 7.89 (d, *J* = 5.1 Hz, 1H), 7.48 (d, *J* = 5.1 Hz, 1H), 2.57 (s, 3H). Spectral data is in accordance with the literature.[21]

**3-methylisothiazolo[5,4-*b*]pyridine (2l)**



Following the general procedure, the reaction of **1p** (0.1 mmol, 34.2 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2l** (86%, 12.8 mg) as a white solid. **$^1$H NMR (300 MHz, $C_6D_6$)** δ 8.40 (dd, *J* = 4.5, 1.4 Hz, 1H), 7.19 (dd, *J* = 8.2, 1.4 Hz, 1H), 6.52 (dd, *J* = 8.2, 4.5 Hz, 1H), 2.19 (s, 3H). Spectral data is in accordance with the literature.[22]

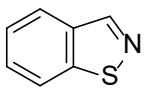
**3-methylisothiazolo[5,4-*b*]quinoline (2m)**



Following the general procedure, the reaction of **1q** (0.1 mmol, 39.2 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2m** (69%, 13.8 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 12 (s, 1H), 8.22 (d, *J* = 8.3 Hz, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 7.99 – 7.90 (m, 1H), 7.72 – 7.64 (m, 1H), 2.83 (s, 3H); **$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 171.3, 163.9, 149.2, 133.9, 132.8, 130.6, 129.3, 127.5, 126.9, 125.7, 18.3; **HRMS** m/z (ESI): calcd. for

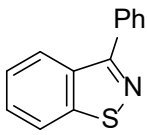
$C_{11}H_9N_2S$ $(M+H)^+$ 201.0481, found 201.0481.

**benzo[*d*]isothiazole (2n)**



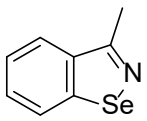
Following the general procedure, the reaction of **1r** (0.1 mmol, 32.9 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2n** (27%, 3.6 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 8.93 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.50 (m, 1H), 7.45 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H). Spectral data is in accordance with the literature.[23]

**3-phenylbenzo[*d*]isothiazole (2o)**



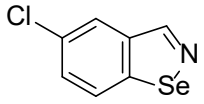
Following the general procedure, the reaction of **1s** (0.1 mmol, 28.3 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2o** (85%, 17.9 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 8.27 (d, *J* = 8.1 Hz, 1H), 8.24 (d, *J* = 8.1 Hz, 1H), 7.93 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.70 – 7.64 (m, 2H), 7.63 – 7.52 (m, 3H);**$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 165.1, 154.6, 136.3, 134.7, 130.4, 129.9, 129.7, 128.8, 126.4, 125.7, 121.4; **HRMS** m/z (ESI): calcd. for $C_{13}H_{10}NS$ $(M+H)^+$ 212.0528, found 212.0534.

**3-methylbenzo[*d*][1,2]selenazole (2p)**



Following the general procedure, the reaction of **1t** (0.1 mmol, 39.0 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2p** (82%, 16.1 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 8.19 (d, *J* = 8.0 Hz, 1H), 8.03 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.51 (ddd, *J* = 8.0, 7.1, 1.2 Hz, 1H), 2.65 (s, 3H);**$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 167.6, 153.0, 139.4, 128.8, 126.9, 125.9, 125.2, 20.1; **HRMS** m/z (ESI): calcd. for $C_8H_8NS$ $(M+H)^+$ 197.9816, found 197.9819.

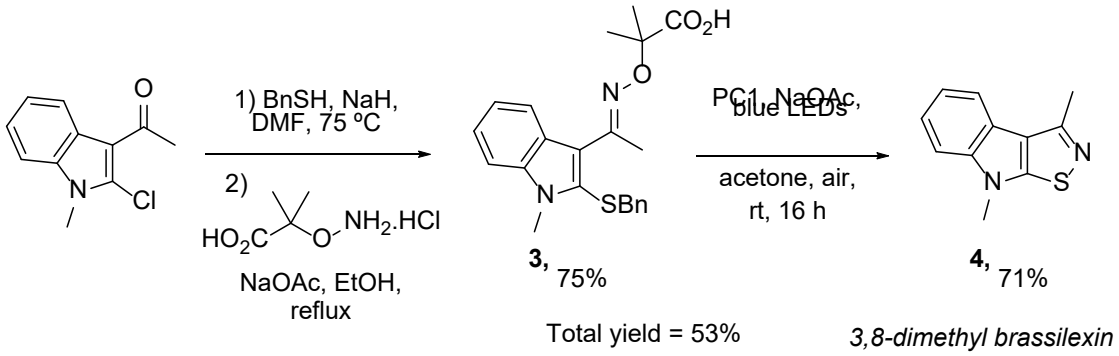
**5-chlorobenzo[d][1,2]selenazole (2q)**



Following the general procedure, the reaction of **1u** (0.1 mmol, 41.1 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **2q**

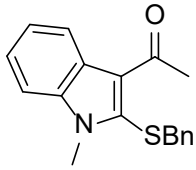
(60%, 13.0 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 9.47 (s, 1H), 8.27 (d, *J* = 8.6 Hz, 1H), 8.24 (d, *J* = 2.0 Hz, 1H), 7.57 (dd, *J* = 8.6, 2.0 Hz, 1H); **$^{13}$C NMR (75 MHz, $(CD_3)_2CO$)** δ 160.6, 151.7, 142.2, 132.0, 129.1, 126.7, 126.6; **HRMS** m/z (ESI): calcd. for $C_7H_4ClNSe$ $(M)^+$ 216.9197, found 216.9202.

## 6. Synthesis of Brassilexin Derivative 4




Following the general procedure for the synthesis of sulfides, benzyl mercaptan (0.53 mmol, 0.06 mL, 1.05 equiv) was added dropwise for 0.25 h to a stirred suspension of NaH (60%, 0.6 mmol, 24 mg, 1.2 equiv) in DMF (1.1 mL) at 0 °C (ice bath). Afterwards, a solution of the 3-acetyl-2-chloro-1-methyl-1*H*-indole (0.5 mmol, 103.8 mg, 1 equiv) in DMF (0.25 mL) was added and the reaction was heated to 75 °C for 12 h. After this time, the reaction was cooled to room temperature, diluted with dichloromethane and washed with water (3x) and brine. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Then, the solid residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure product 1-(2-(benzylthio)-1-methyl-1*H*-indol-3-yl)ethan-1-one.

**1-(2-(benzylthio)-1-methyl-1*H*-indol-3-yl)ethan-1-one (SI-1t)**

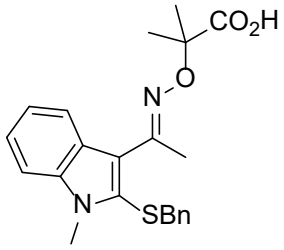


Following procedure, the reaction of 3-acetyl-2-chloro-1-methyl-1*H*-indole (0.5 mmol, 103.8 mg), NaH (60%, 0.6 mmol, 24 mg) and benzyl mercaptan (0.53 mmol, 0.06 mL) in DMF (1.35 mL) at 75 ºC afforded the product **SI-1t** (89%, 131.2 mg) as a pale yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 8.39 – 8.26 (m, 1H), 7.35 – 7.23 (m, 4H), 7.19 (d, *J* = 7.6 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 2H), 4.04 (s, 2H), 3.52 (s, 3H), 2.74 (s, 3H); **$^{13}$C**

**NMR (75 MHz, $CDCl_3$)** δ 194.8, 137.4, 137.1, 135.8, 128.7, 128.6, 127.6, 126.5, 123.9, 122.6, 122.5, 121.4, 109.9, 42.4, 30.6, 28.4.

Following the general procedure for the synthesis of oximes, a solution of 1-(2-(benzylthio)-1-methyl-1*H*-indol-3-yl)ethan-1-one (**SI-1t**, 0.44 mmol, 131.2 mg, 1 equiv) in EtOH (2.2 mL) was treated with 2-(aminooxy)-2-methylpropanoic acid hydrochloride (**SI-11**, 0.53 mmol, 82.2 mg, 1.2 equiv), sodium acetate (1.06 mmol, 86.6 mg, 2.4 equiv) and heated to reflux until completion by TLC analysis. The mixture was then allowed to cool to room temperature and water was added. The resulting aqueous solution was extracted with EtOAc (3x) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated under vacuum to provide the product. Then, the residue was subjected to flash chromatography (silica gel, cyclohexane/EtOAc) to give the analytically pure product **3**.

**2-(((1-(2-(benzylthio)-1-methyl-1H-indol-3-yl)ethylidene)amino)oxy)-2-methylpropanoic acid (3)**

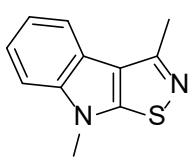



Following the procedure, the reaction of **SI-1t** (0.44 mmol, 131.2 mg), **SI-11** (0.53 mmol, 82.2 mg) and sodium acetate (1.06 mmol, 86.6 mg) in EtOH (2.2 mL) at reflux afforded the product **3** (84%, 145.7 mg) (75% for two steps) as a yellow solid. **$^1$H NMR (300 MHz, $CDCl_3$)** δ 7.75 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.11 (m, 6H), 6.95 (dd, *J* = 7.4, 1.8 Hz, 2H), 3.88 (s, 2H), 3.49 (s, 3H), 2.39 (s, 3H), 1.65 (s, 6H); **$^{13}$C NMR (75 MHz, $CDCl_3$)** δ 176.6, 155.8, 137.6, 137.3, 129.7, 128.7, 128.5, 127.4, 125.5, 123.5, 121.0, 120.5, 118.3, 110.0, 81.5, 42.6, 29.8, 24.6, 16.4; **HRMS** m/z (ESI): calcd. for $C_{22}H_{23}N_2O_3S$ $(M-H)^-$ 395.1435, found 395.1241.

Following the general procedure for the synthesis of isothiazoles, in an oven-dried glass vial equipped with a stirring bar, **3** (0.1 mmol, 39.6 mg, 1 equiv), NaOAc (0.1 mmol, 8.2 mg, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate, ($5\cdot10^{-3}$ mmol, 2.1 mg, 0.05 equiv) and acetone (1.33 mL) were added under air. Then, the vial was closed with a PTFE/rubber septum perforated several

times to enable the air enter into the reaction. Afterwards, the mixture was stirred and irradiated at 450 nm using 380 mW single LEDs in a custom-made temperature-controlled system (see Figure S1) for 16h at 20 ºC. Then, the volatiles were removed and the analytically pure product **4** was obtained by flash chromatography (Iatrobeads silica gel; cyclohexane/EtOAc).

**3,8-dimethyl-8H-isothiazolo[5,4-*b*]indole (4)**

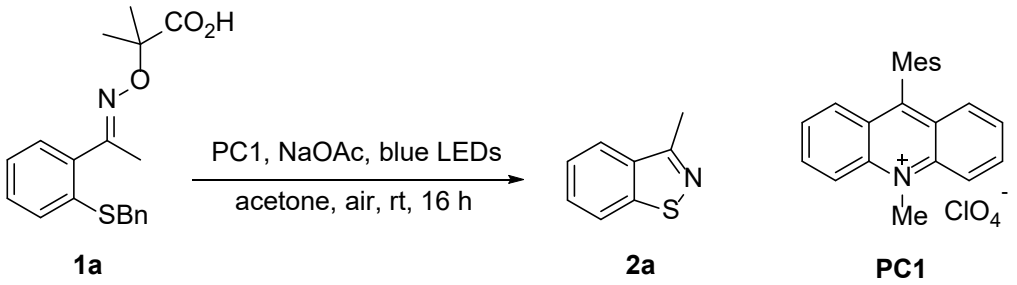


Following the procedure, the reaction of **3** (0.1 mmol, 39.6 mg), NaOAc (0.1 mmol, 8.2 mg) and photocatalyst **PC1** (5 mol%, 2.1 mg) in acetone (1.33 mL) irradiated at 450 nm afforded the product **4** (71%, 14.4 mg) as a white solid. **$^1$H NMR (300 MHz, $(CD_3)_2CO$)** δ 7.90 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 8.2 Hz, 1H), 7.36 (ddd, *J* = 8.2, 7.8, 1.3 Hz, 1H), 7.30 – 7.18 (m, 1H), 3.94 (s, 3H), 2.72 (d, *J* = 1.3 Hz, 3H); **$^{13}$C NMR (126 MHz, $(CD_3)_2CO$)** δ 161.4, 157.3, 144.7, 123.9, 123.0, 120.7, 120.2, 118.9, 109.8, 32.2, 17.9; **HRMS** m/z (ESI): calcd. for $C_{11}H_{10}N_2S$ $(M+H)^+$ 202.0565, found 202.0559.

## 7. Flow Setup for the Synthesis of Isothiazoles 2

*General procedure for the optimization of the reaction conditions for the flow setup:*

In a coil (V = 18 mL) made of perfluoroalkoxy (PFA) tubing (i.d. = 1.6 mm) irradiated with a blue LED spot (40 W), 2-(((1-(2-(benzylthio)phenyl)ethylidene) amino)oxy)-2-methylpropanoic acid (**1d**, 0.15 mmol, 36.3 mg, 1 equiv), NaOAc (0.15 mmol, 12.3 mg, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate and acetone (2 mL) were injected at 20 ºC. Then, the volatiles were removed and yield was determined by $^1$H-NMR analysis using nitromethane (8 µL, 0.15 mmol) as the internal standard. $O_2$ gas was employed in a segmented flow fashion and a BPR (1.6 bar) was added at the end of the coil to increase the pressure of the system.




**1a** **2a** **PC1**

**Table S3.** Optimization of reaction conditions for the flow setup.

| entry | conditions[a] | PC1 (mol%) | $t_R$ (min) | conv. (%)[b] | yield (%)[b] |
|---|---|---|---|---|---|
| 1 | No oxygen | 10 | 80 | 50 | 13 |
| 2 | Acetone sat. with $O_2$ BPR (1.6 bar) | 10 | 80 | 68 | 41 |
| 3 | $O_2$ | 10 | 80 | 84 | 47 |
| 4 | $O_2$ | 10 | 180 | 88 | 48 |
| 5 | $O_2$ BPR (1.6 bar) | 10 | 80 | 100 | 26 |
| **6** | **$O_2$** | **5** | **60** | **82** | **47** |

[a] Segmented flow (2 mm slugs) was made by passing oxygen gas and reaction solution through a T-union (1.25 mm thru-hole; 17.5 µl swept volume). [b] The yield was determined from the crude $^1$H-NMR. BPR = black pressure regulator

*General procedure for the synthesis of isothiazoles **2** in the flow setup:*

The corresponding oxime derivative **1** (0.33 mmol, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate (0.017 mmol, 6.8 mg, 0.05 equiv) and acetone (4.4 mL) were mixed at 20 ºC and passed through a packed bed reactor filled with NaOAc (Figure S2a). Afterwards, reaction solution and $O_2$ gas, used in a segmented flow fashion, were mixed through a T-union (Figure S2b), controlling the gas slugs (2 mm) with a micrometric valve. Compounds **1b**, **1c** and **1g** were injected consecutively (separated by 4 mL of acetone) in the coil (V = 18 mL) made of perfluoroalkoxy (PFA) tubing (i.d. = 1.6 mm) and irradiated with a blue LED spot (40 W) (Figure S3). After 2 h, isothiazoles **2** were collected in different vials. Then, the volatiles were removed and yield was determined by $^1$H-NMR analysis using

nitromethane (17.7 µL, 0.33 mmol) as the internal standard: **2b** (55%; 0.18 mmol), **2c** (58%; 0.19 mmol) and **2g** (44%; 0.14 mmol). In all the transformations the throughput of the reaction is ≈140 times higher than in conventional conditions and around 15% of starting material is recovered in all the cases.

a) b)

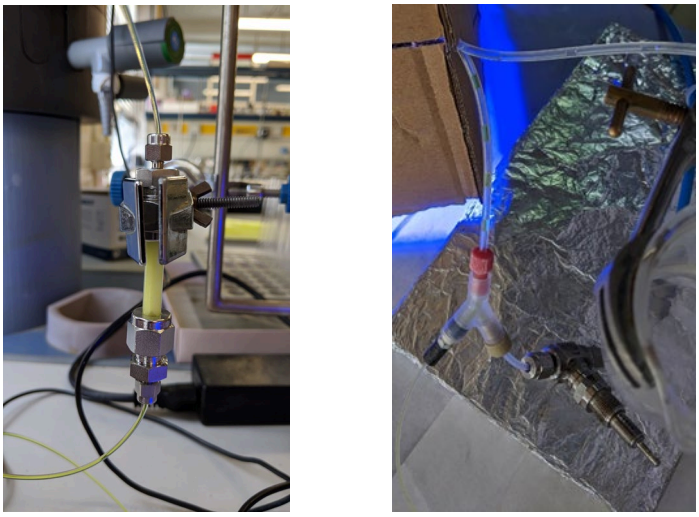


**Figure S2**. a) Packed bed reactor filled with NaOAc and b) T-union with a micrometric valve employed in flow setup.

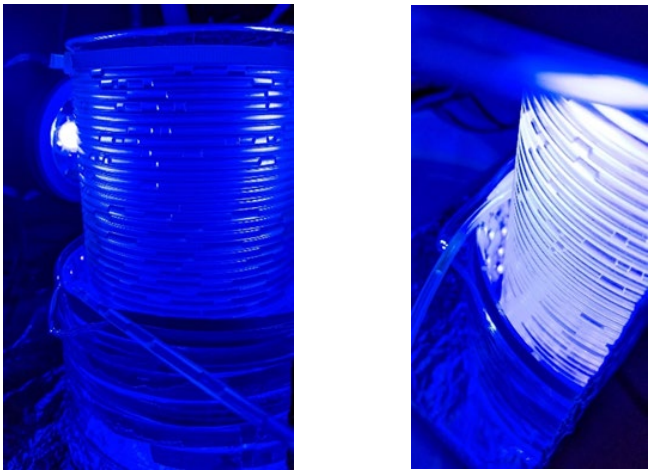


**Figure S3**. Coil of PFA with liquid and gas slugs employed in flow setup.

# 8. Mechanistic Studies

## 8.1. Cyclic Voltammetry of α-Imino-oxy Acids 1

Electrochemical studies of substrates **1a-d**, **1a´**and **1a´´** were performed employing

1 nM solution of the corresponding α-imino-oxy acid **1** freshly prepared in HPLC grade acetone along with 1 nM sodium acetate and 0.1 M supporting electrolyte (tetrabutylammonium hexafluorophosphate) solutions. Nitrogen was passed through each sample before measurements to avoid the influence of oxygen reduction.

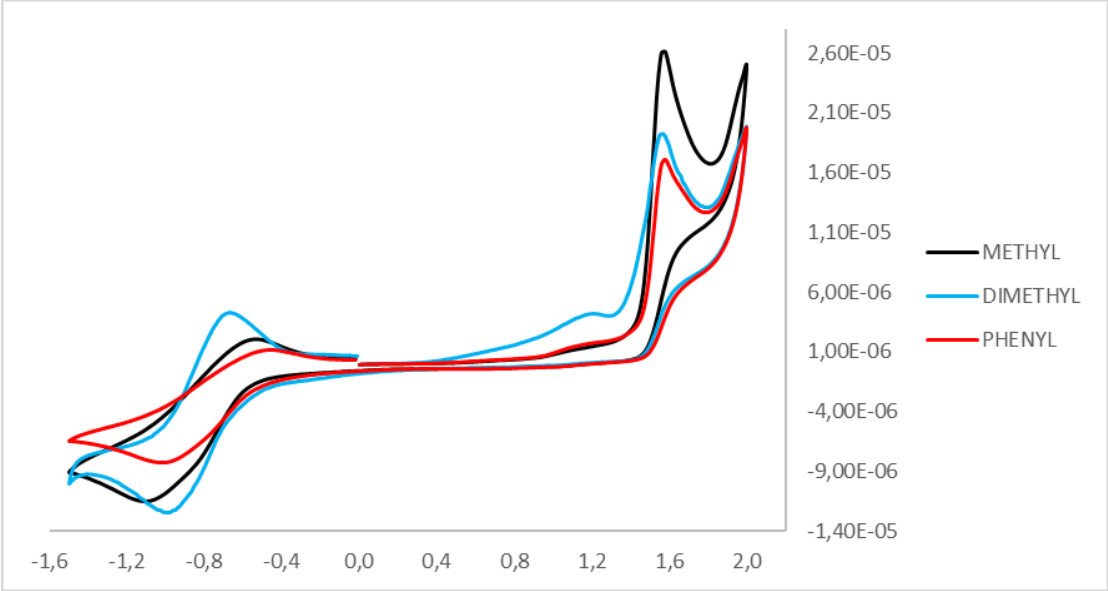
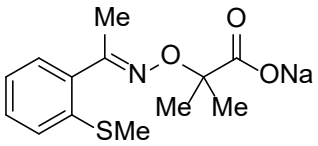
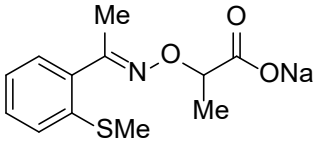
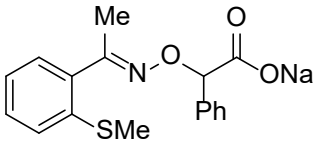



**Figure S4**. Cyclic voltammetry of α-imino-oxy acids **1a**, **1a´**and **1a´´**.

**Table S4.** Oxidation potentials of α-imino-oxy acids **1a**, **1a´**and **1a´´**.

| α-Imino-oxy acids | $E_{1/2}^{ox}$ (V) vs SCE |
|---|---|
|  **1a** | +1.58 |
|  **1a´** | +1.58 |
|  **1a´´** | +1.58 |

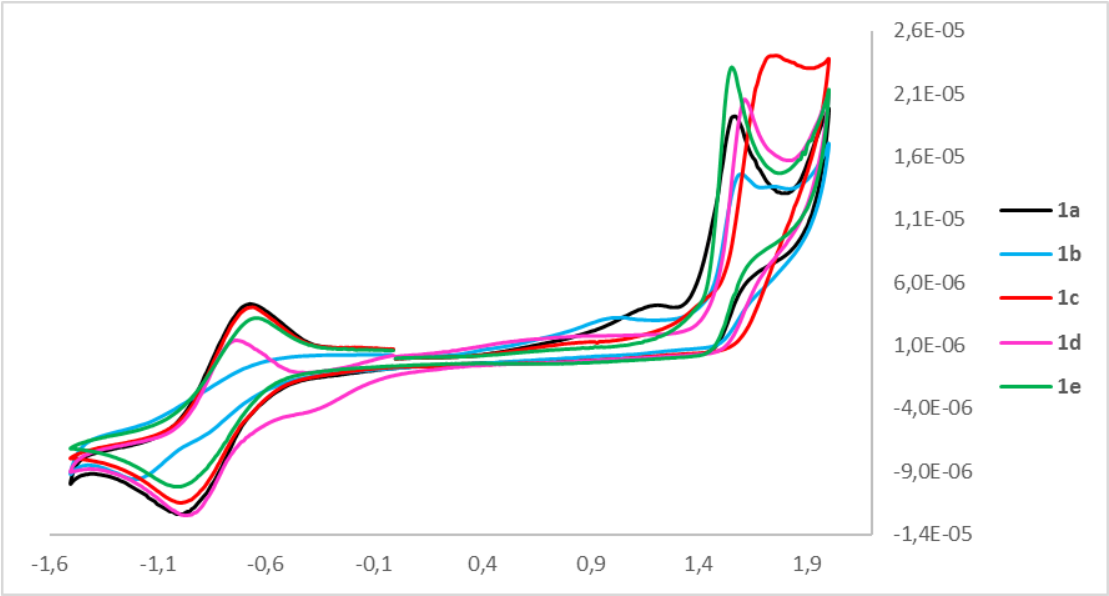
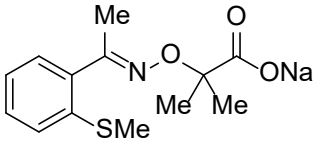
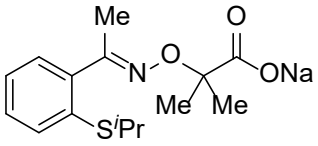
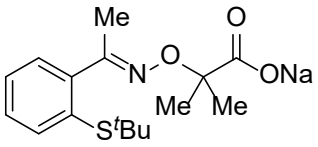
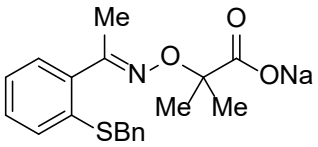
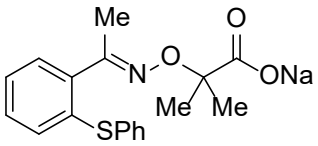



**Figure S5**. Cyclic voltammetry of α-imino-oxy acids **1a-d**.

**Table S5.** Oxidation potentials of α-imino-oxy acids **1a-d**.

| α-Imino-oxy acids | $E_{1/2}^{ox}$ (V) vs SCE |
|---|---|
|  **1a** | +1.56 |
|  **1b** | +1.58 |
|  **1c** | +1.72 |
|  **1d** | +1.62 |

| | |
|---|---|
|  **1e** | +1.56 |

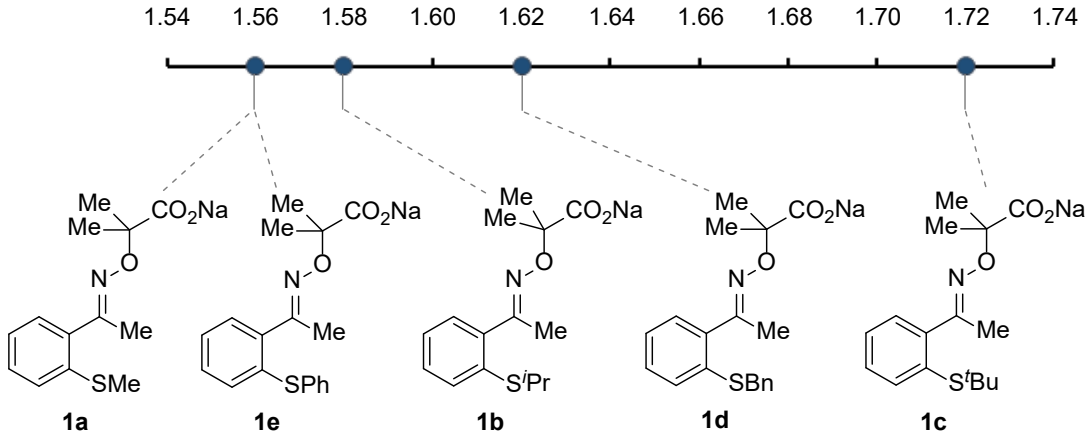


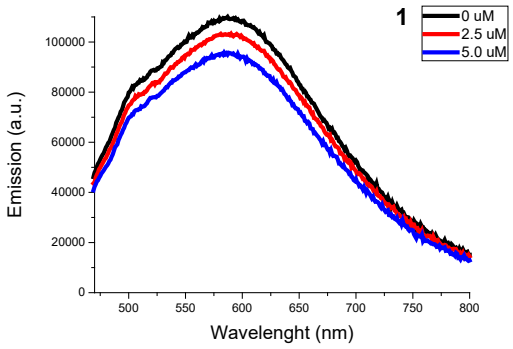

**Figure S6**. Electrochemical scale of α-imino-oxy acids **1a-d**.

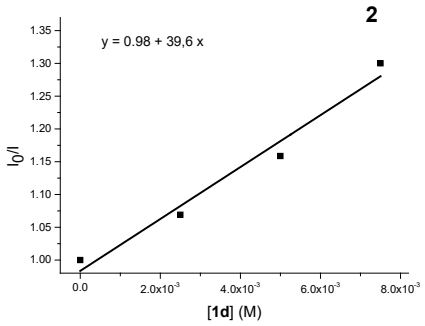
## 8.2. Fluorescence Quenching Studies

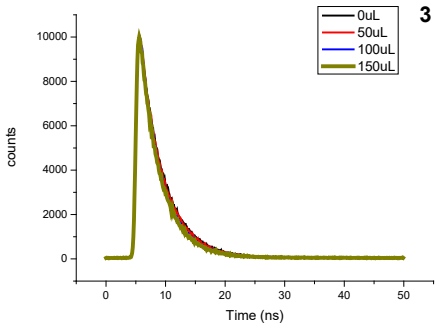
Emission intensities and time resolved emission spectra were recorded using an Edinburg Instruments FS5 Spectrofluorometer, and a 450 nm EPL laser.

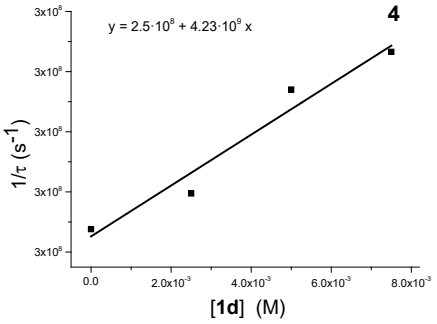
For the steady-state and time resolved fluorescence quenching studies, increasing concentrations of quencher were added to a solution 3,7 mM of **PC1** in acetone ($\lambda_{exc}$ = 450 nm).

a)



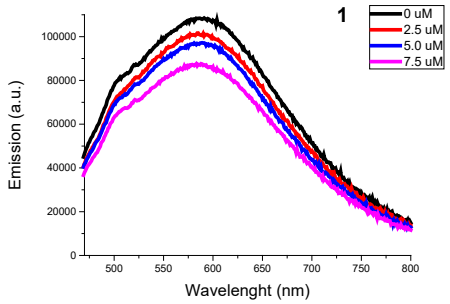



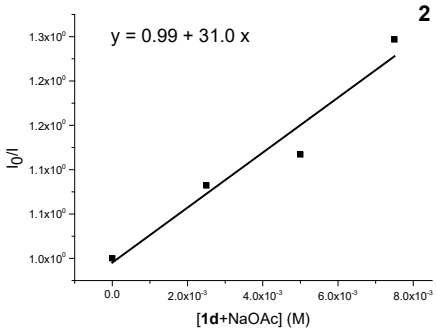



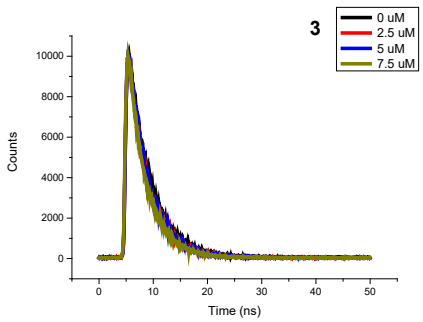

***Kq* = 4.2x10$^9$ M$^{-1}$ s$^{-1}$**

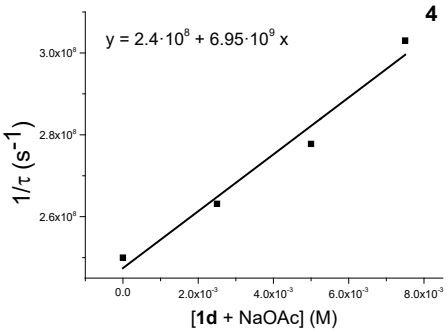
---

b)



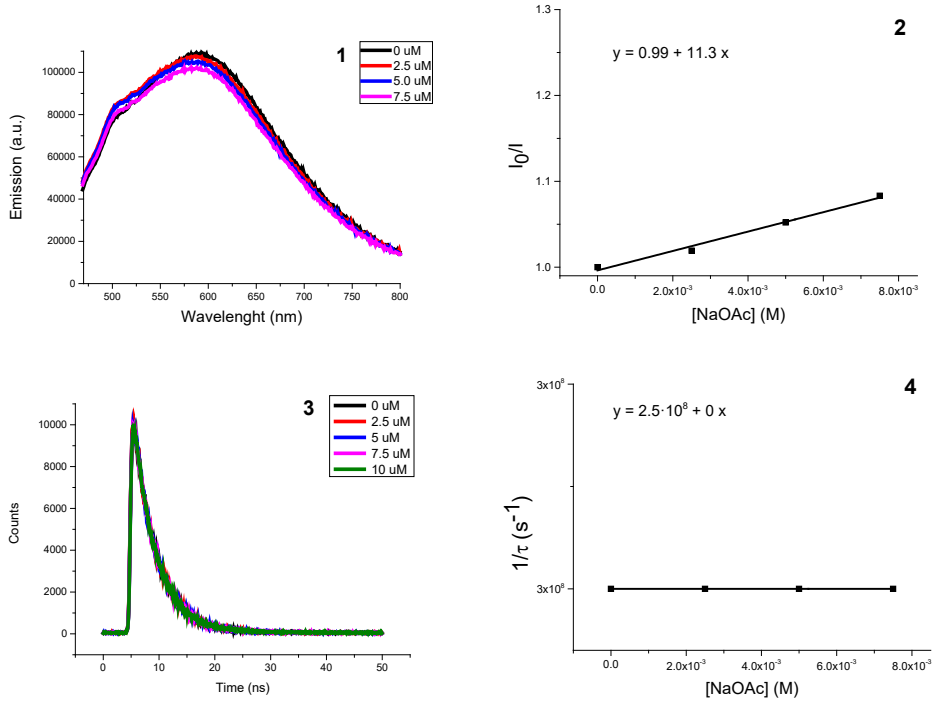




***Kq* = 6.95x10$^9$ M$^{-1}$ s$^{-1}$**

---

c)

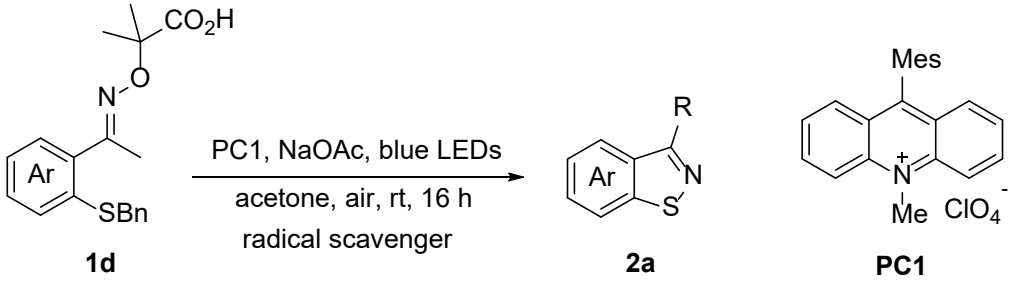



$Kq = 0\ M^{-1}\ s^{-1}$

**Figure S7**. Fluorescence quenching studies. a) Quenching studies of **PC1** with **1d**: (1) Steady state luminescence quenching spectrum and (2) Stern-Volmer plot of the steady state; (3) Time resolved luminescence quenching and (4) Stern-Volmer plot to obtain *Kq*; b) Quenching studies of **PC1** with **1d + NaOAc**: (1) Steady state luminescence quenching spectrum and (2) Stern-Volmer plot of the steady state; (3) Time resolved luminescence quenching and (4) Stern-Volmer plot to obtain *Kq*; c) Quenching studies of **PC1** with **NaOAc**: (1) Steady state luminescence quenching spectrum and (2) Stern-Volmer plot of the steady state; (3) Time resolved luminescence quenching and (4) Stern-Volmer plot to obtain *Kq*.

## 8.3. Radical Trapping Experiments

**Table S6.** Radical Trapping Experiments.



| entry | Radical scavenger | yield (%)[a] |
|---|---|---|
| 1 | None | 85 |
| 2 | TEMPO | 33 |
| 3 | BHT | 39 |

[a] The yield was determined from the crude $^1$H-NMR.

Following the general procedure for the synthesis of isothiazoles **2**, in an oven-dried glass vial equipped with a stirring bar, 2-methyl-2-(((1-(2-(methylthio) phenyl)ethylidene)amino)oxy)propanoic acid (**1a**, 0.05 mmol, 13.4 mg, 1 equiv), the NaOAc (0.05 mmol, 4.1 mg, 1 equiv), photocatalyst **PC1**, 9-mesityl-10-methyl acridinium perchlorate, ($2.5 \cdot 10^{-3}$ mmol, 1 mg, 0.05 equiv), the corresponding radical scavenger (0.25 mmol, 5 equiv) and acetone (0.67 mL) were added under air. Then, the vial was closed with a PTFE/rubber septum perforated several times to enable the air enter into the reaction. Afterwards, the mixture was stirred and irradiated at 450 nm using 380 mW single LEDs in a custom-made temperature-controlled system (see Figure S1) for 16h at 20 ºC. Then, the volatiles were removed and yield was determined by $^1$H-NMR analysis using 1,3,5-trimethoxybenzene (8.4 mg, 0.05 mmol) as internal standard.

## 9. References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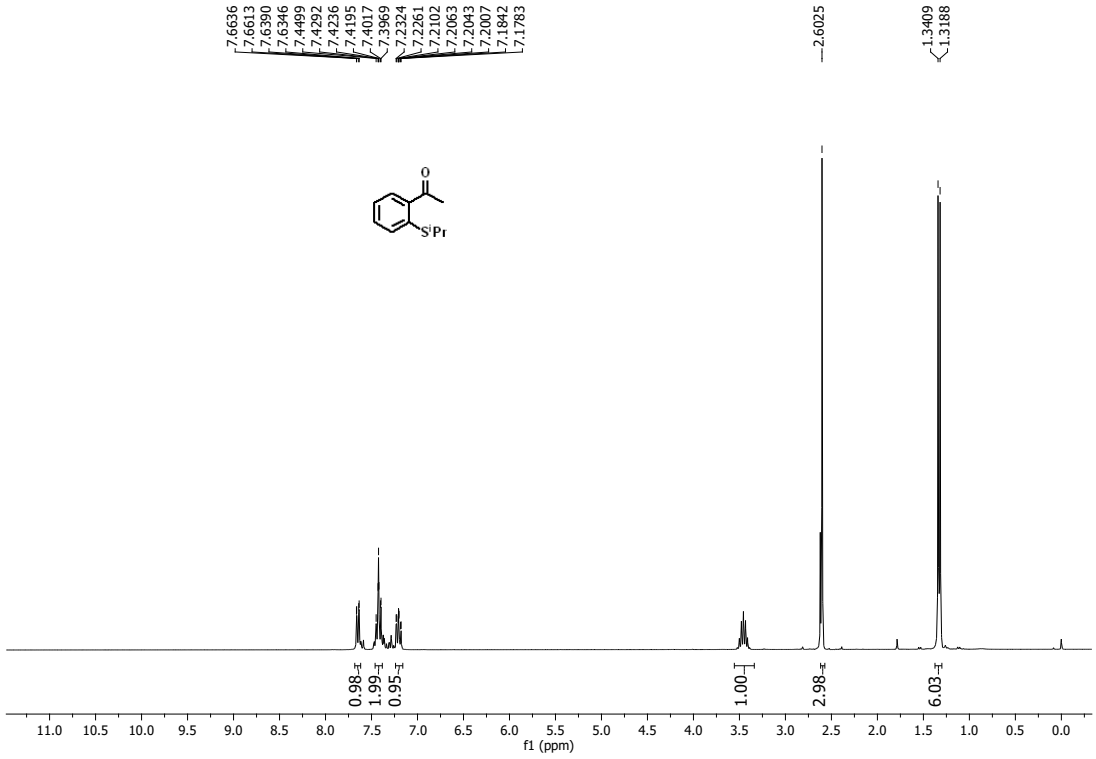
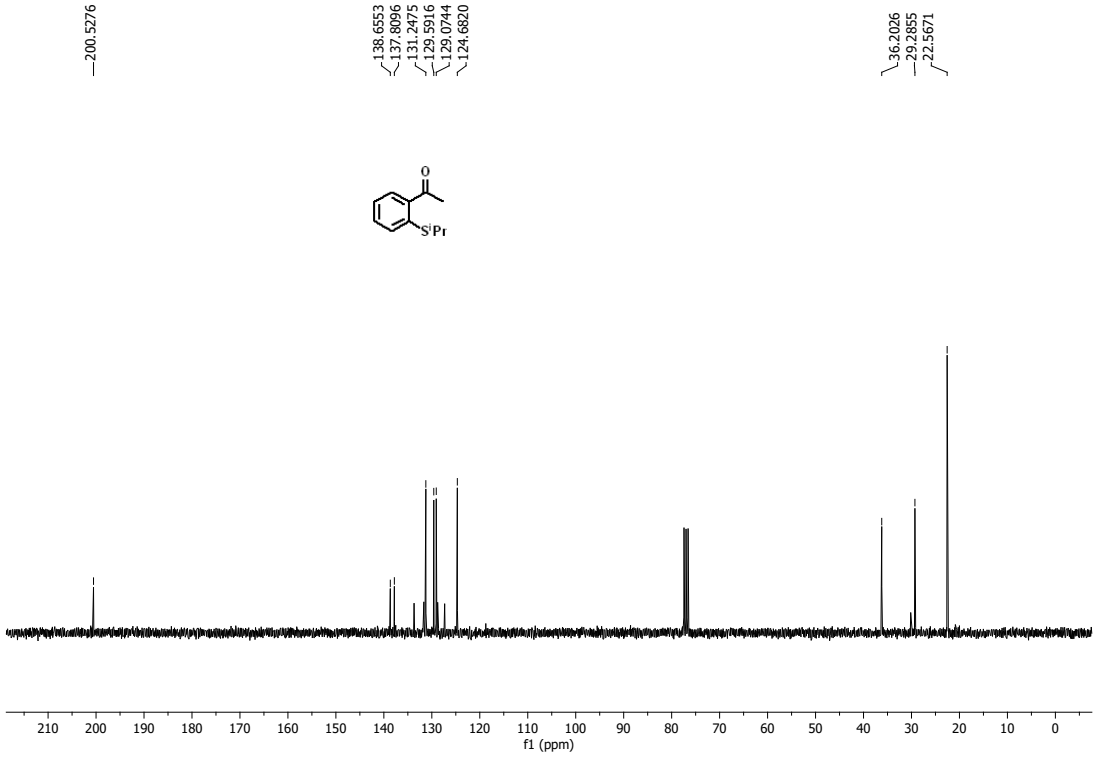
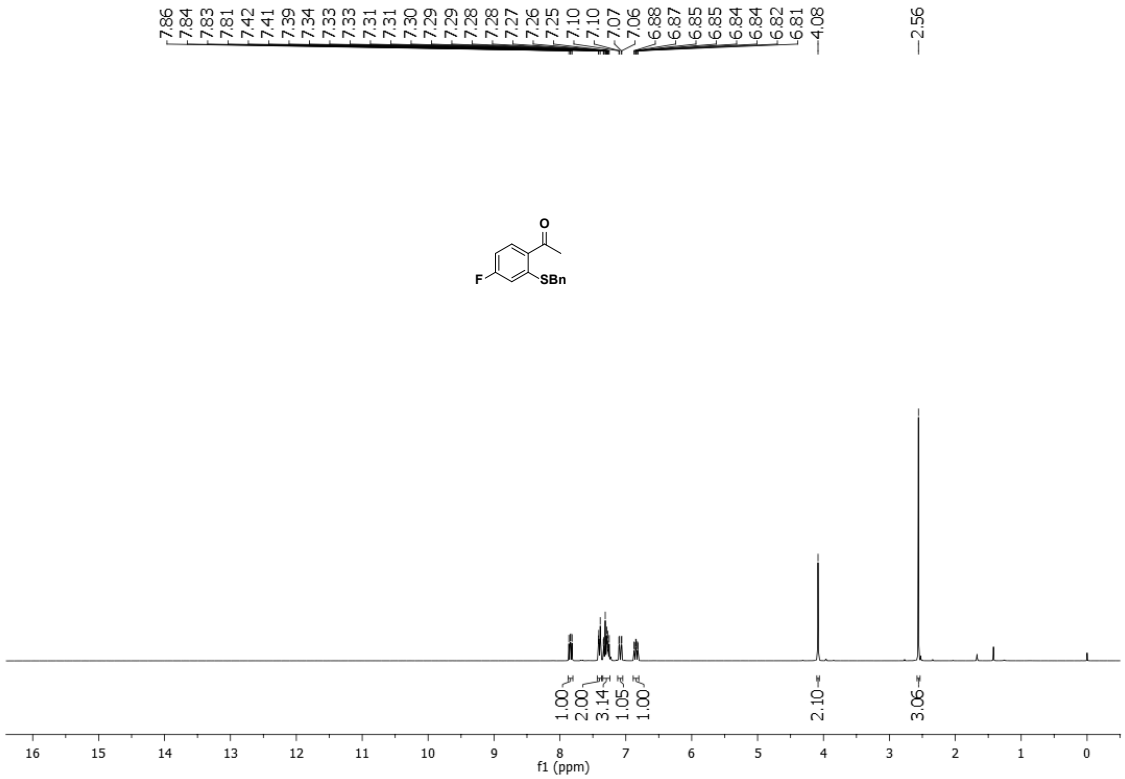
# 10. NMR Spectra

## 10.1. NMR Spectra of Sulfides SI-1

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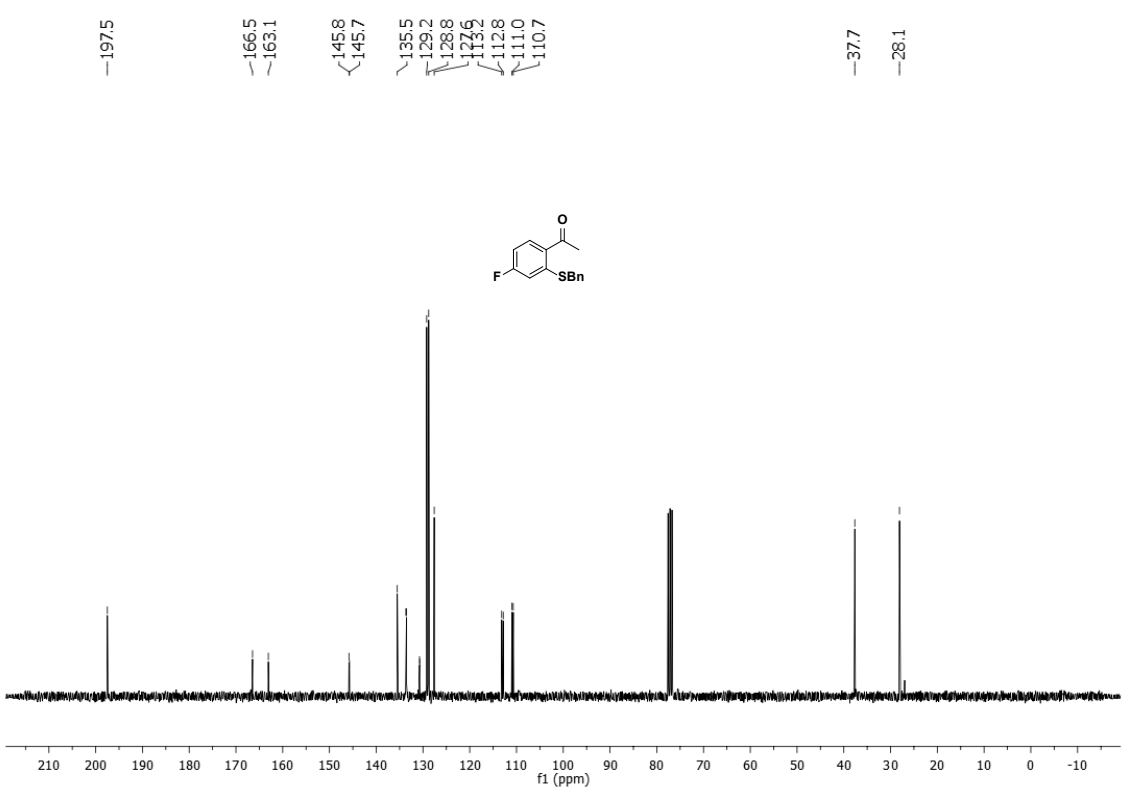
7.84
7.83
7.81
7.42
7.41
7.39
7.34
7.33
7.33
7.31
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.26
7.25
7.10
7.10
7.07
7.06
6.88
6.87
6.85
6.85
6.84
6.84
6.82
6.81
4.08
2.56
O
F
SBn
1.00
2.00
3.14
1.05
1.00
2.10
3.06
f1 (ppm)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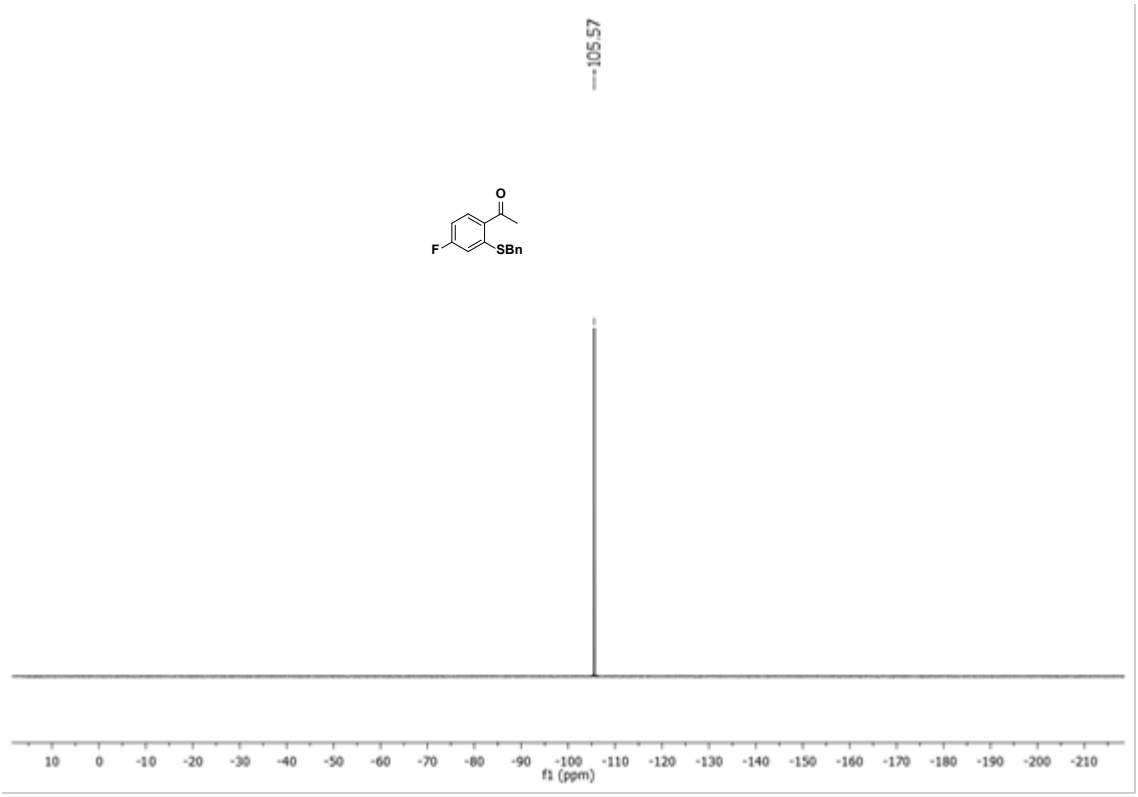
166.5
163.1
145.8
145.7
135.5
129.2
128.8
127.6
113.2
112.8
111.0
110.7
37.7
28.1
O
F
SBn
f1 (ppm)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O
F
SBn
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
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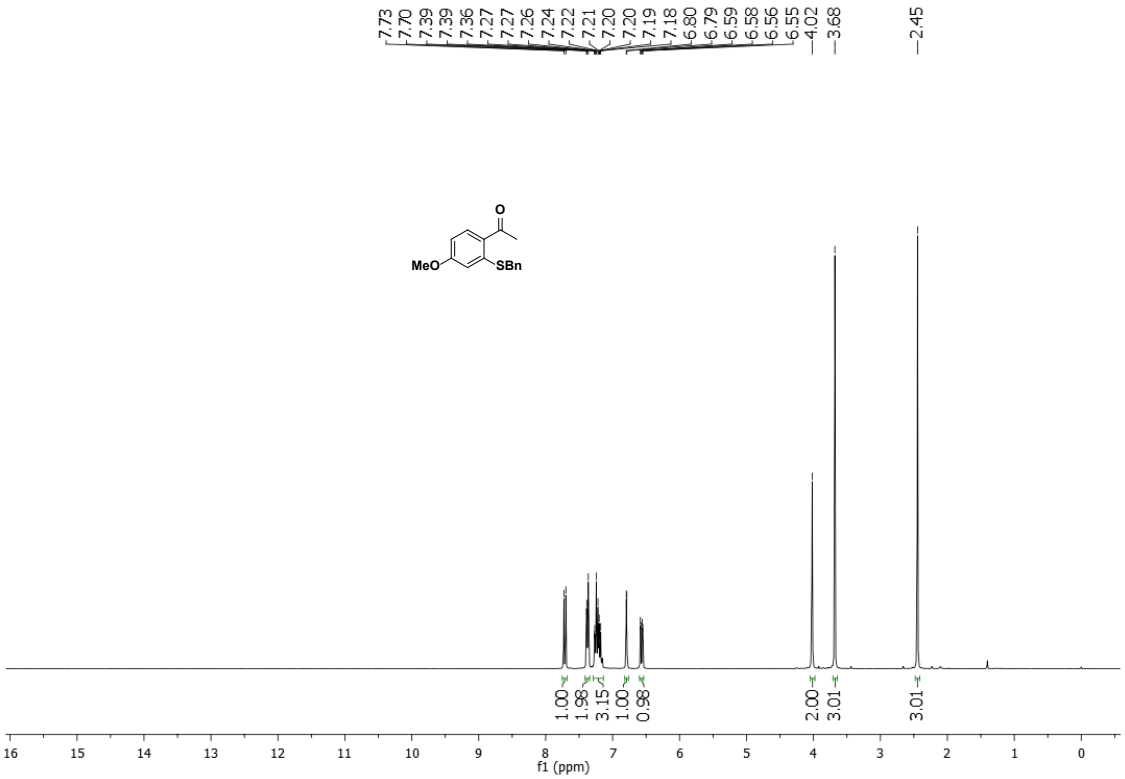
-160
-170
-180
-190
-200
-210
f1 (ppm)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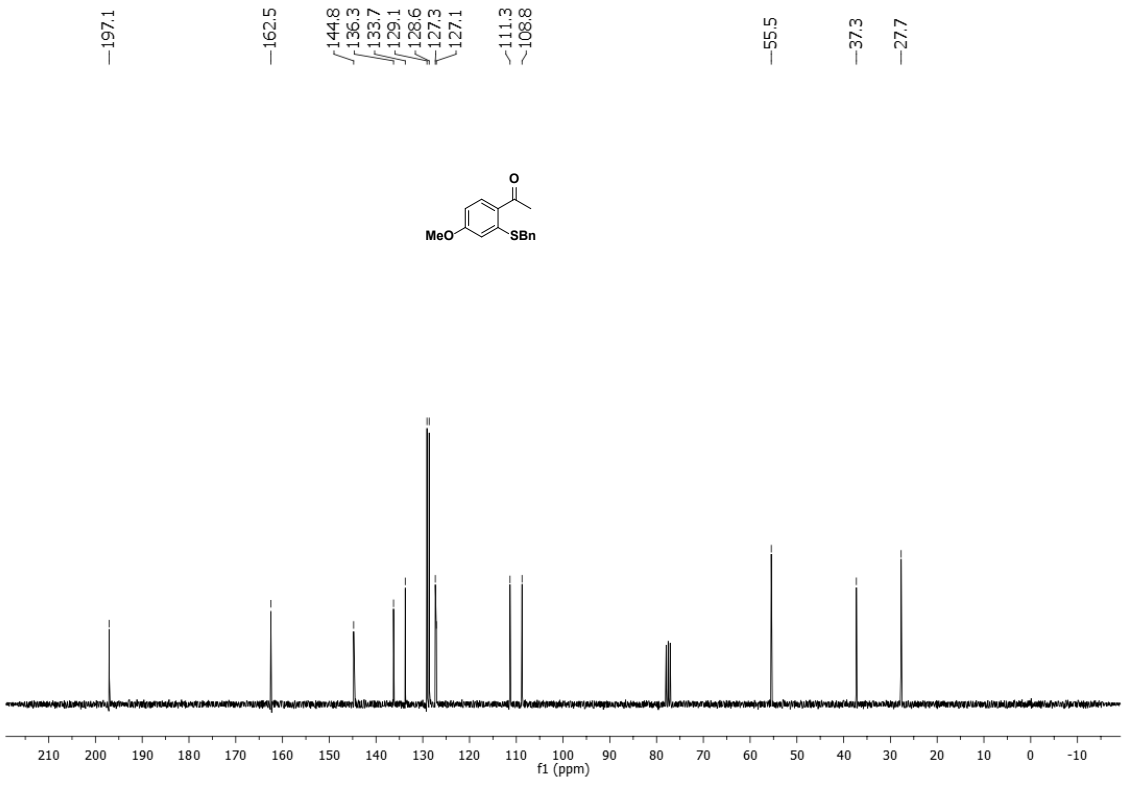
7.70
7.39
7.39
7.36
7.27
7.27
7.26
7.24
7.22
7.21
7.20
7.20
7.19
7.18
6.80
6.79
6.59
6.58
6.56
6.55
4.02
3.68
2.45
O
MeO
SBn
1.00
1.98
3.15
1.00
0.98
2.00
3.01
3.01
f1 (ppm)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129.1
128.6
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111.3
108.8
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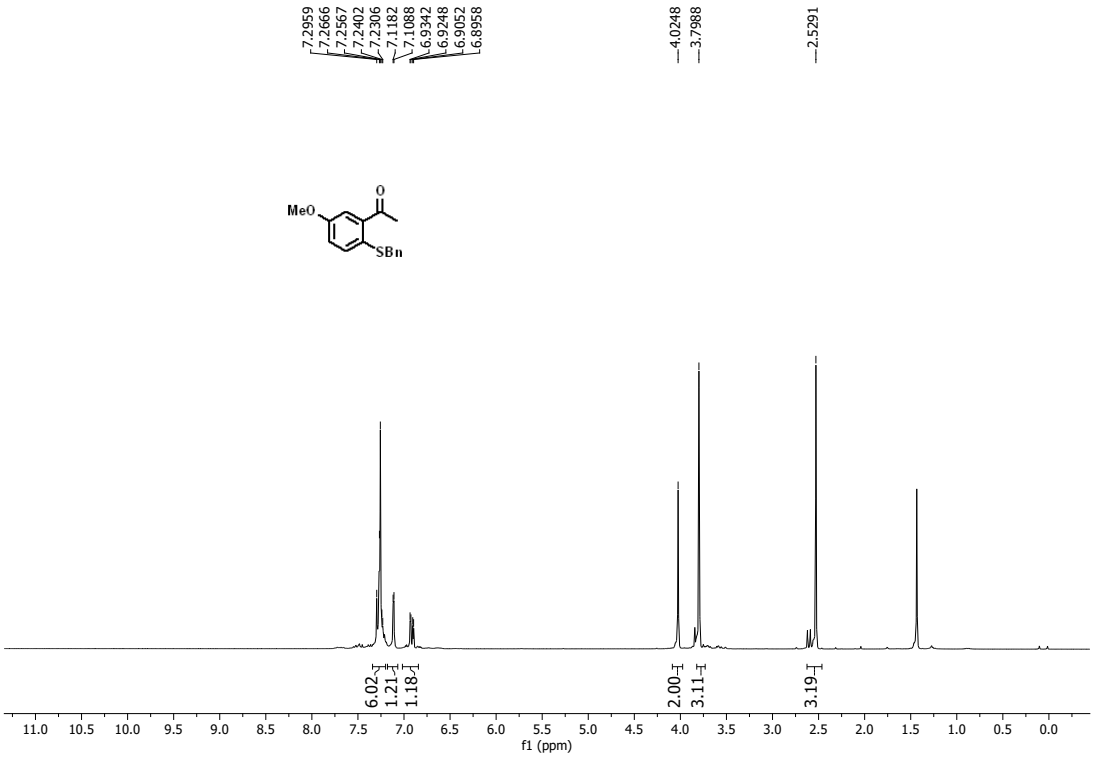
27.7
O
MeO
SBn
f1 (ppm)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7.2567
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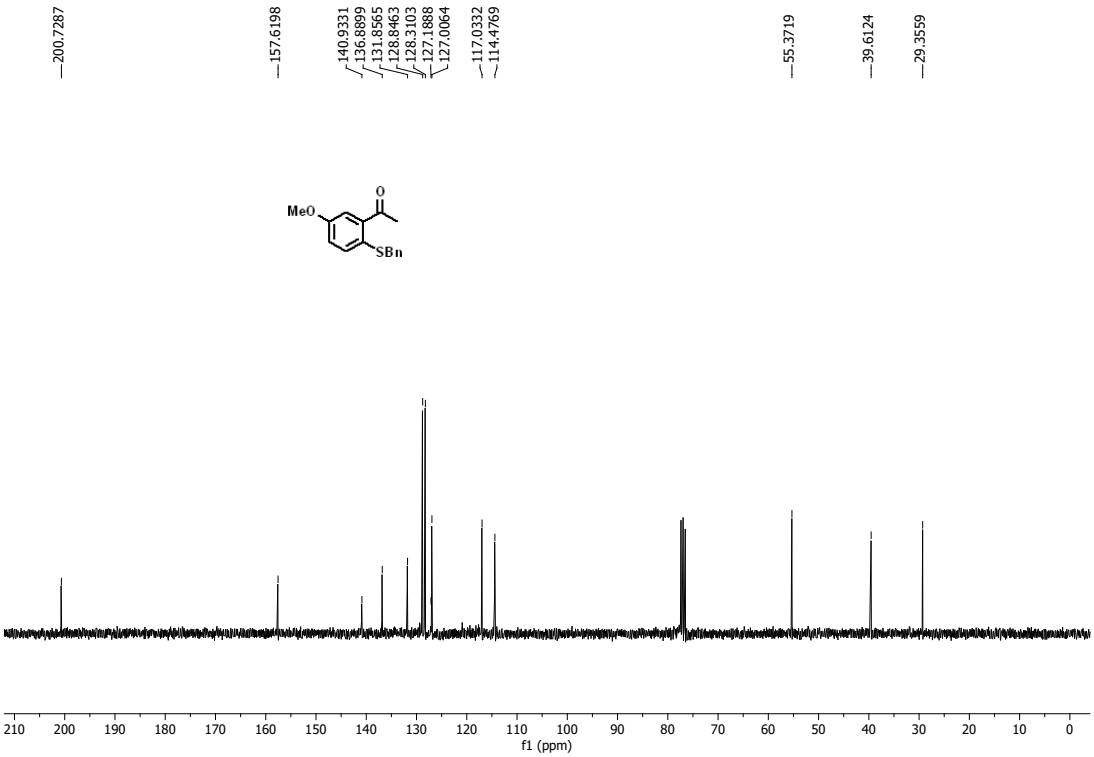
7.2306
7.1182
7.1088
6.9342
6.9248
6.9052
6.8958
4.0248
3.7988
2.5291
MeO
O
SBn
6.02
1.21
1.18
2.00
3.11
3.19
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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127.0064
117.0332
114.4769
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29.3559
MeO
O
SBn
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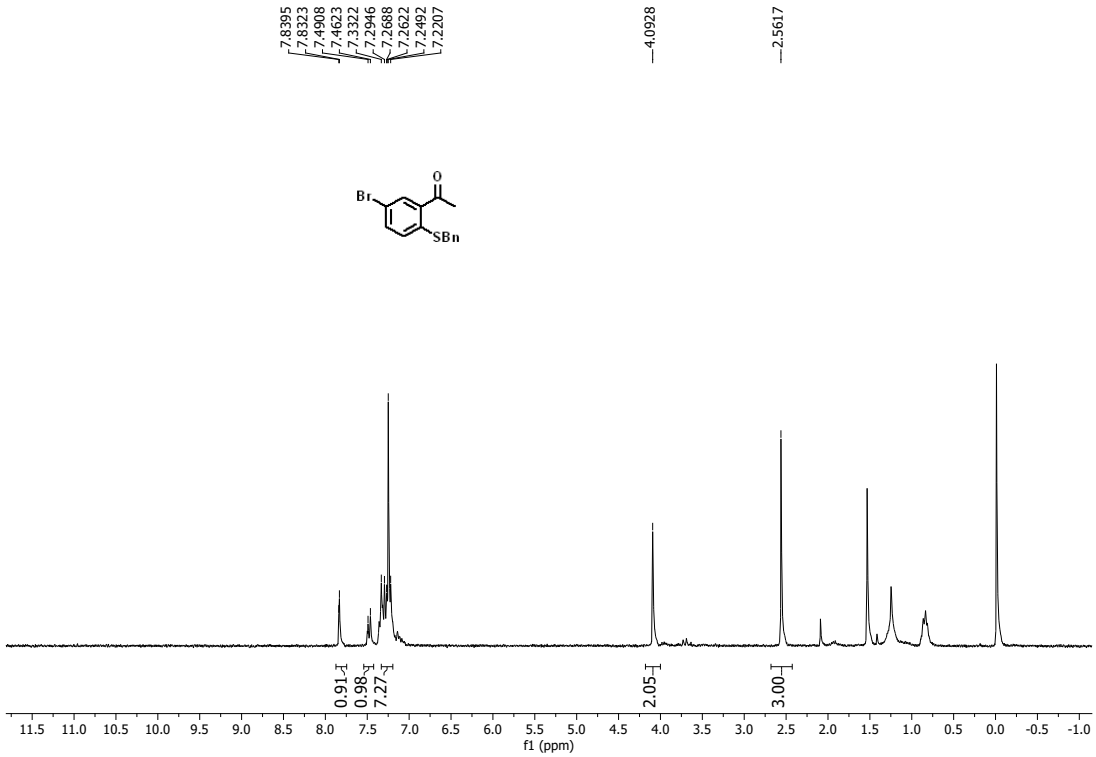
f1 (ppm)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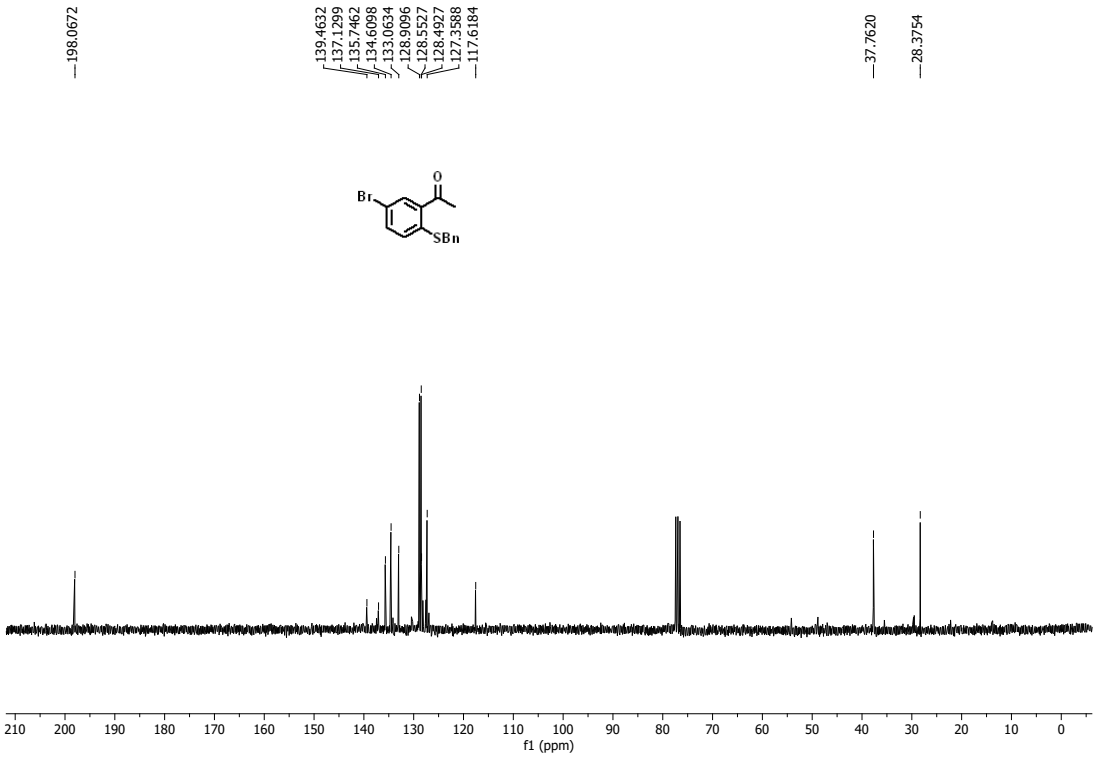
4.0928
2.5617
Br
O
SBn
0.91
0.98
7.27
2.05
3.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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134.6098
133.0634
128.9096
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128.4927
127.3588
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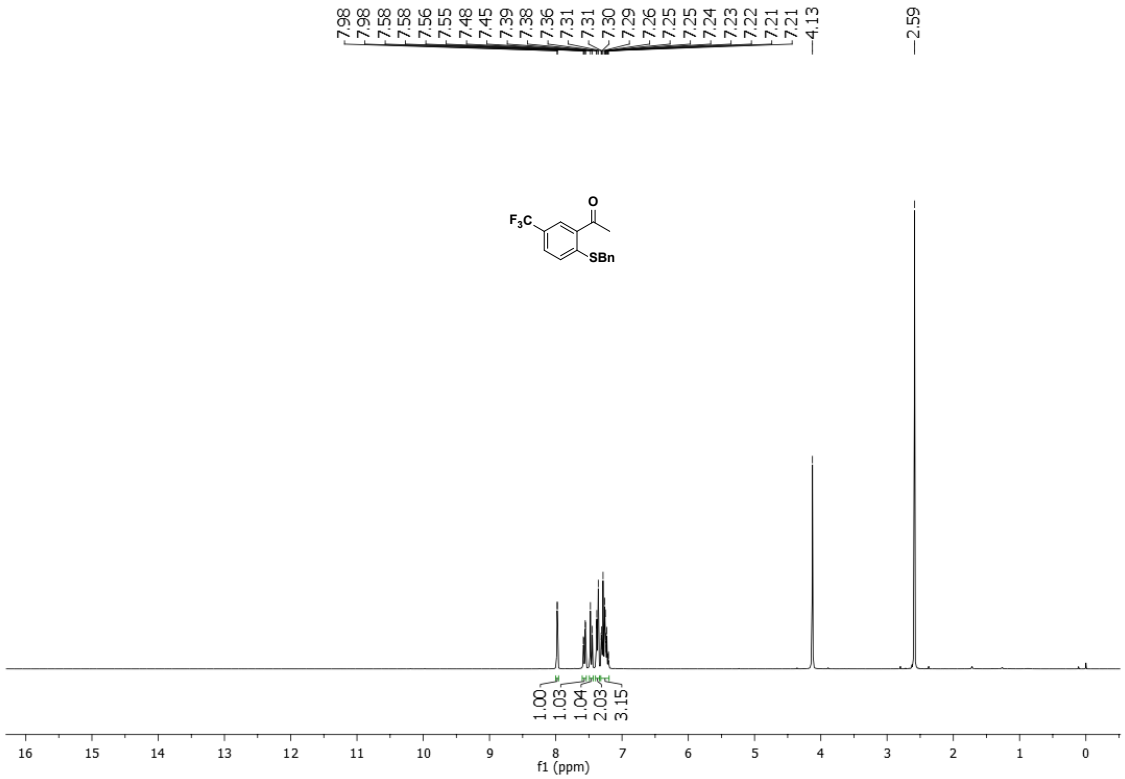
28.3754
Br
O
SBn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.30
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2.59
O
F3C
SBn
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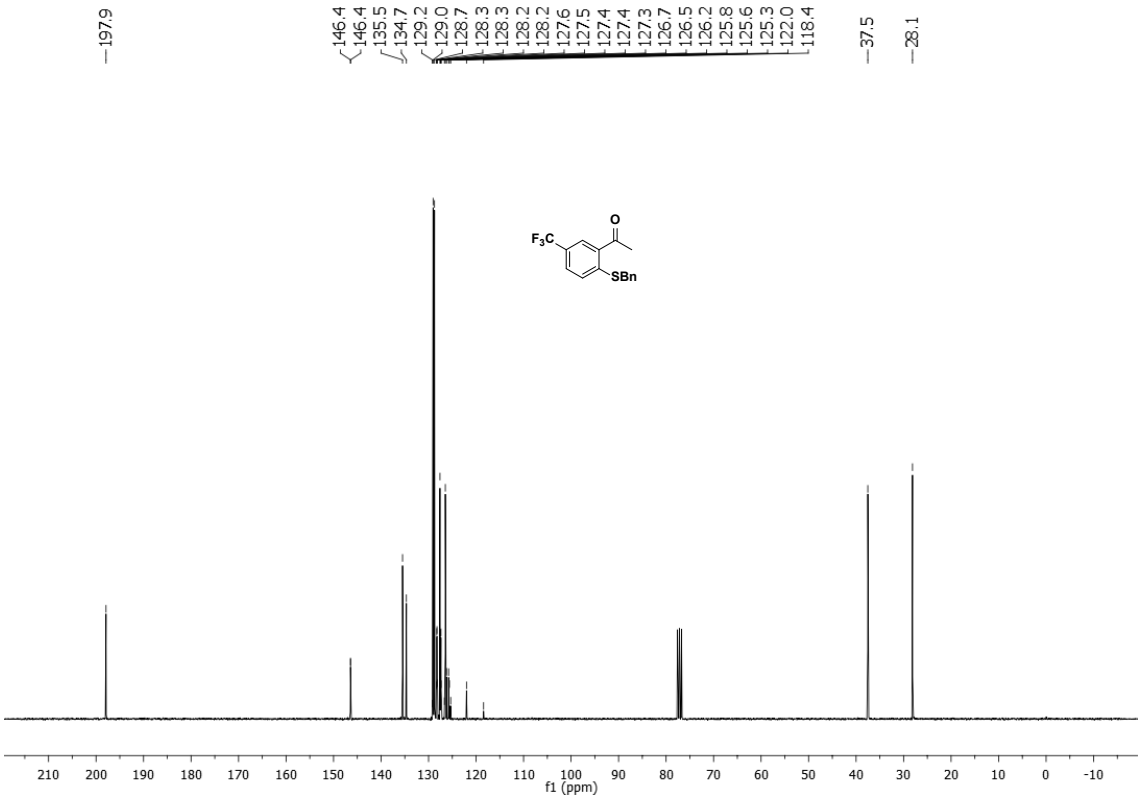
1.03
1.04
2.03
3.15
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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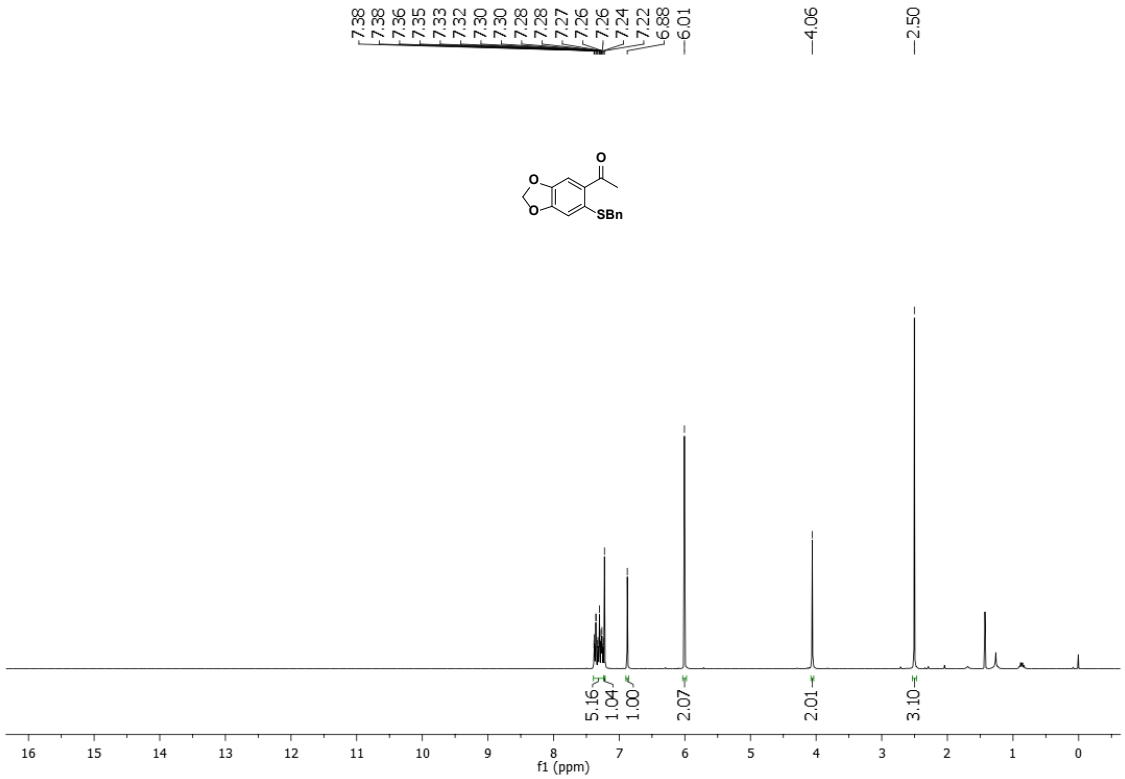
146.4
135.5
134.7
129.2
129.0
128.7
128.3
128.3
128.2
128.2
127.6
127.5
127.4
127.4
127.3
126.7
126.5
126.2
125.8
125.6
125.3
122.0
118.4
37.5
28.1
O
F3C
SBn
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


-62.32
O
F3C
SBn
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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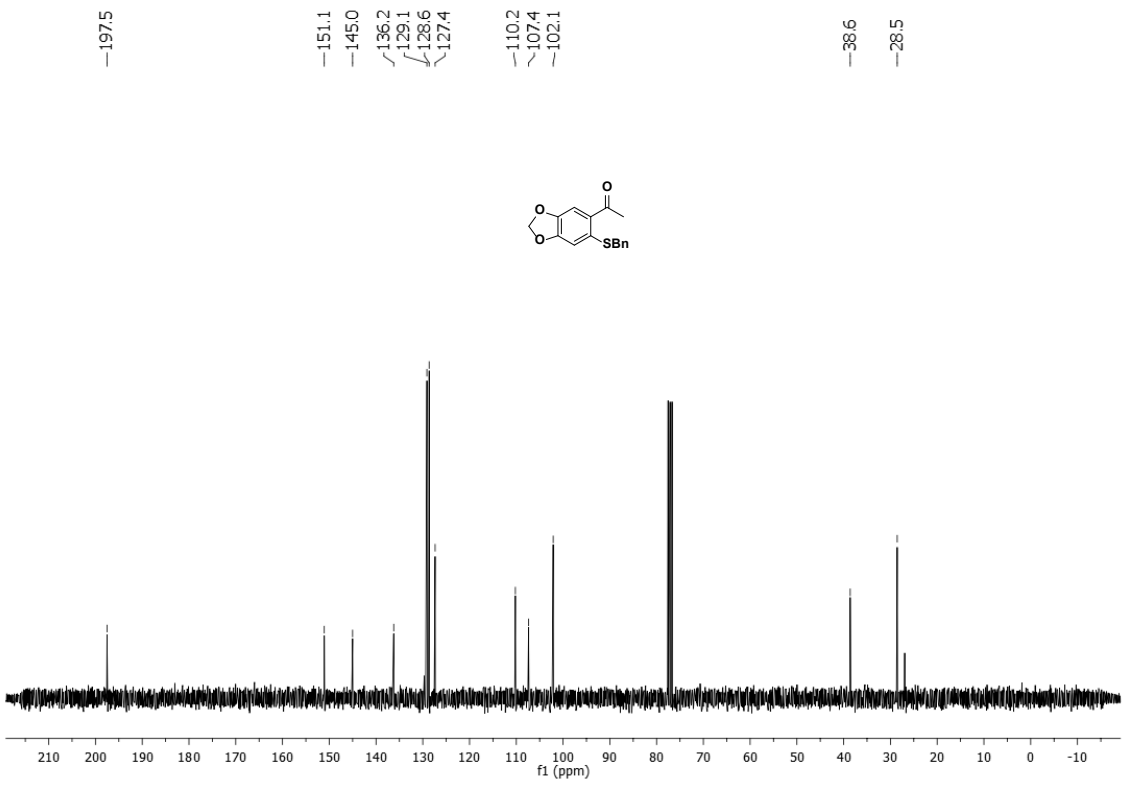
7.38
7.36
7.35
7.33
7.32
7.30
7.30
7.28
7.28
7.27
7.26
7.26
7.24
7.22
6.88
6.01
4.06
2.50
O
O
O
SBn
5.16
1.04
1.00
2.07
2.01
3.10
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)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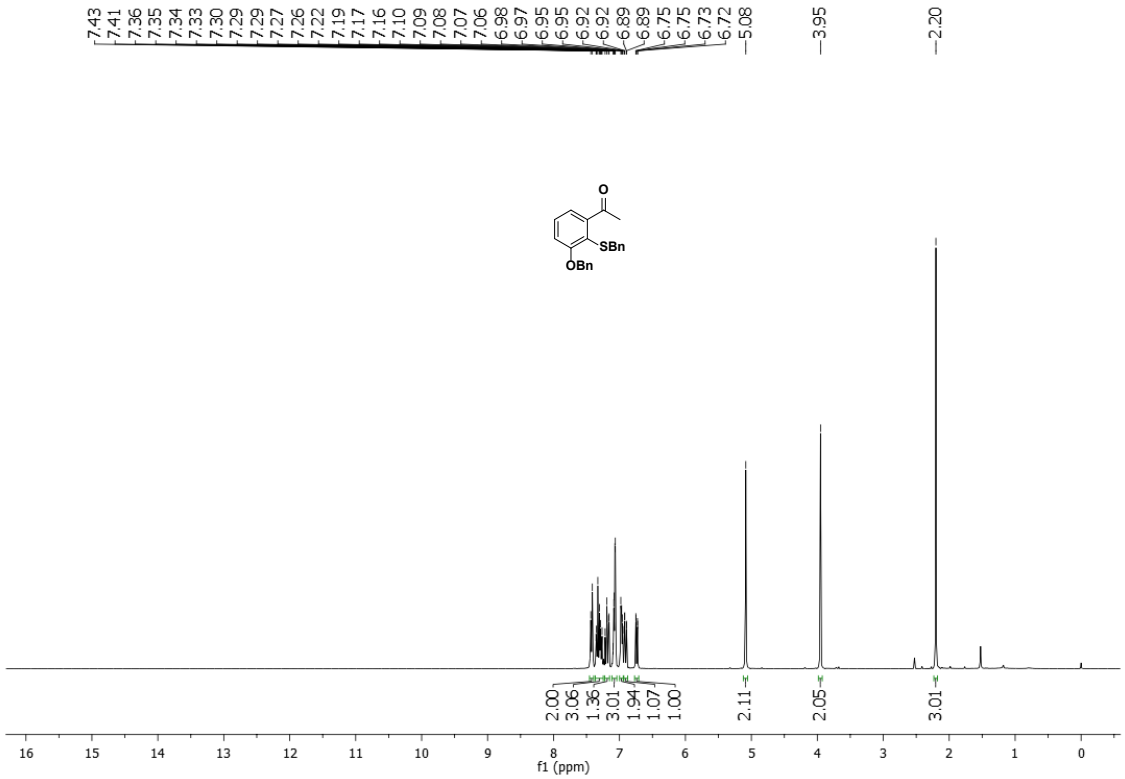
151.1
145.0
136.2
129.1
128.6
127.4
110.2
107.4
102.1
38.6
28.5
O
O
O
SBn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.41
7.36
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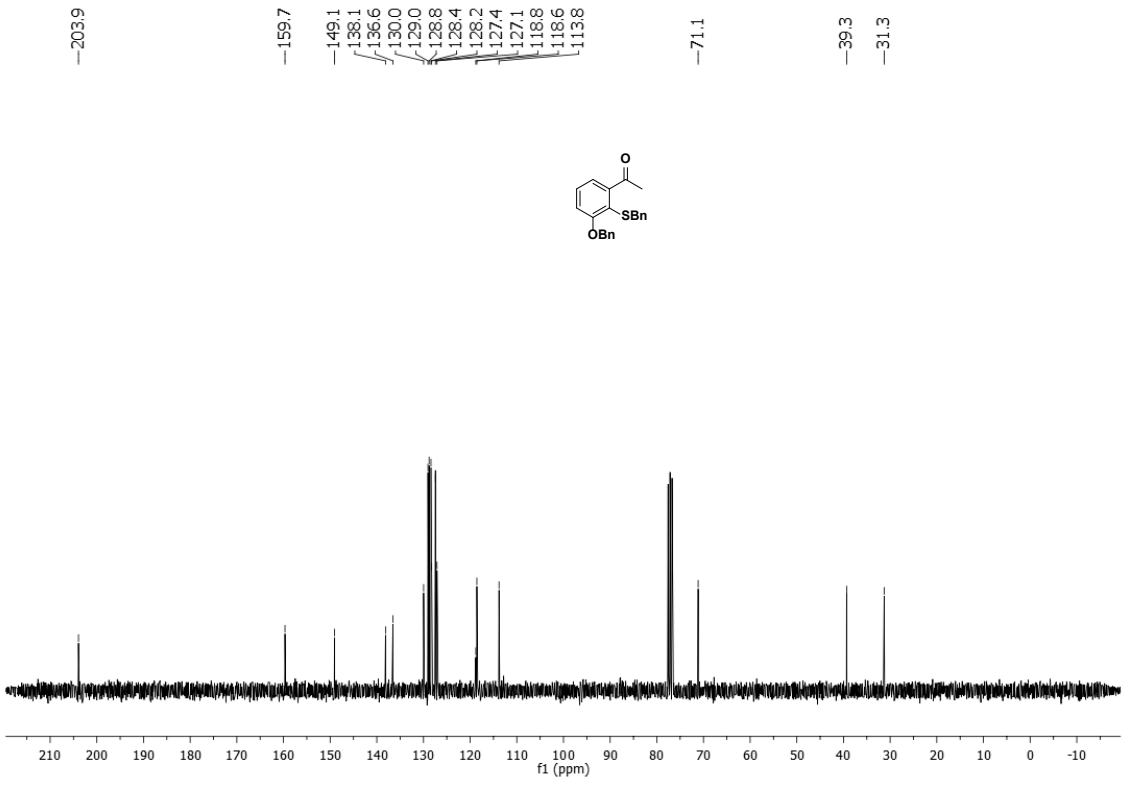
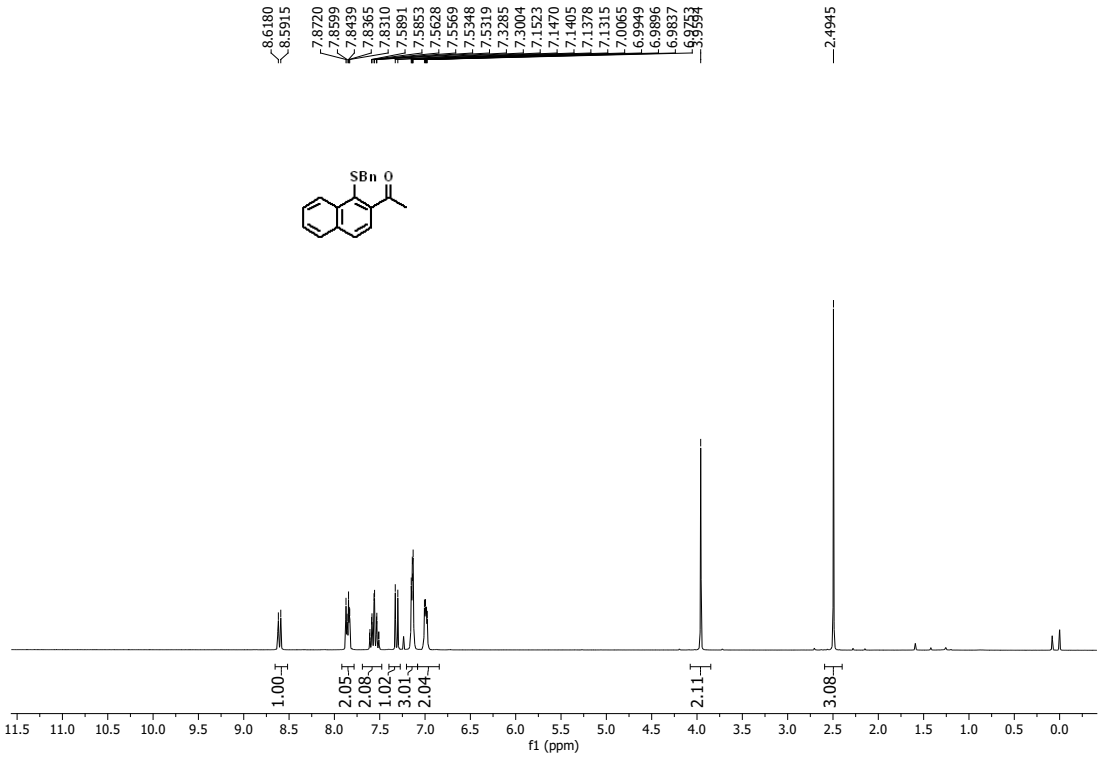
7.34
7.33
7.30
7.29
7.29
7.27
7.26
7.22
7.19
7.17
7.16
7.10
7.09
7.08
7.07
7.06
6.98
6.97
6.95
6.95
6.92
6.92
6.89
6.89
6.75
6.75
6.73
6.72
5.08
3.95
2.20
O
SBn
OBn
2.00
3.06
1.36
3.01
1.94
1.07
1.00
2.11
2.05
3.01
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


203.9
159.7
149.1
138.1
136.6
130.0
129.0
128.8
128.4
128.2
127.4
127.1
118.8
118.6
113.8
71.1
39.3
31.3
O
SBn
OBn
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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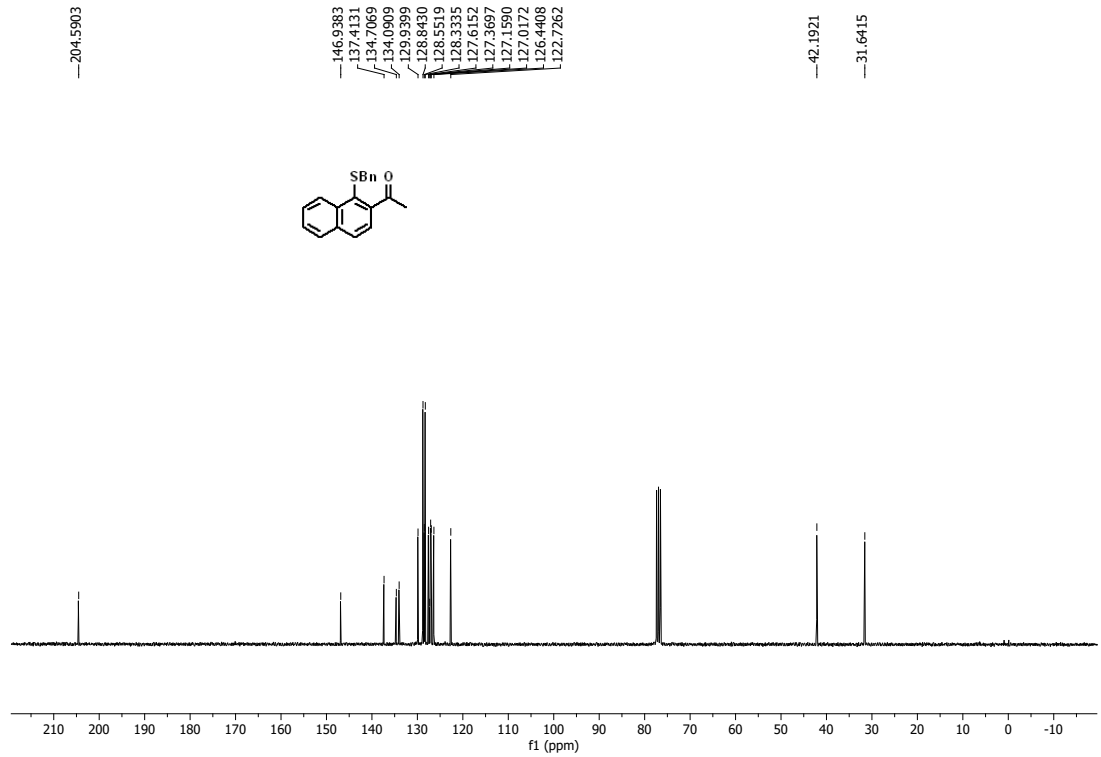
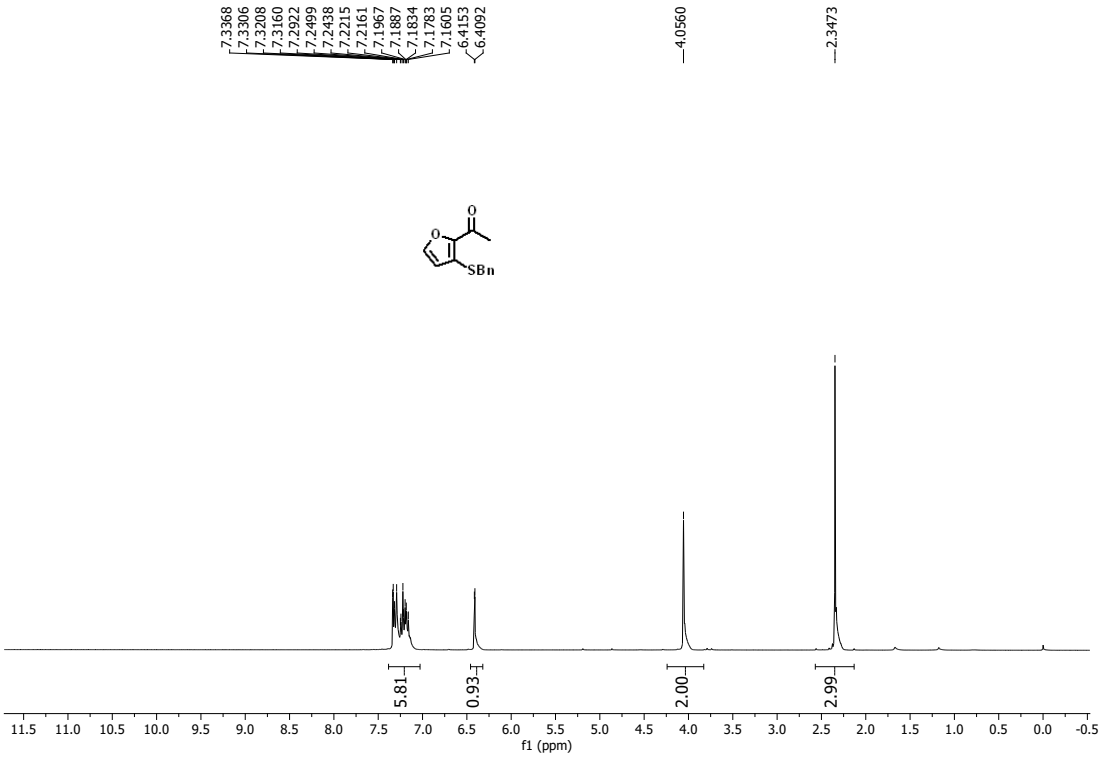
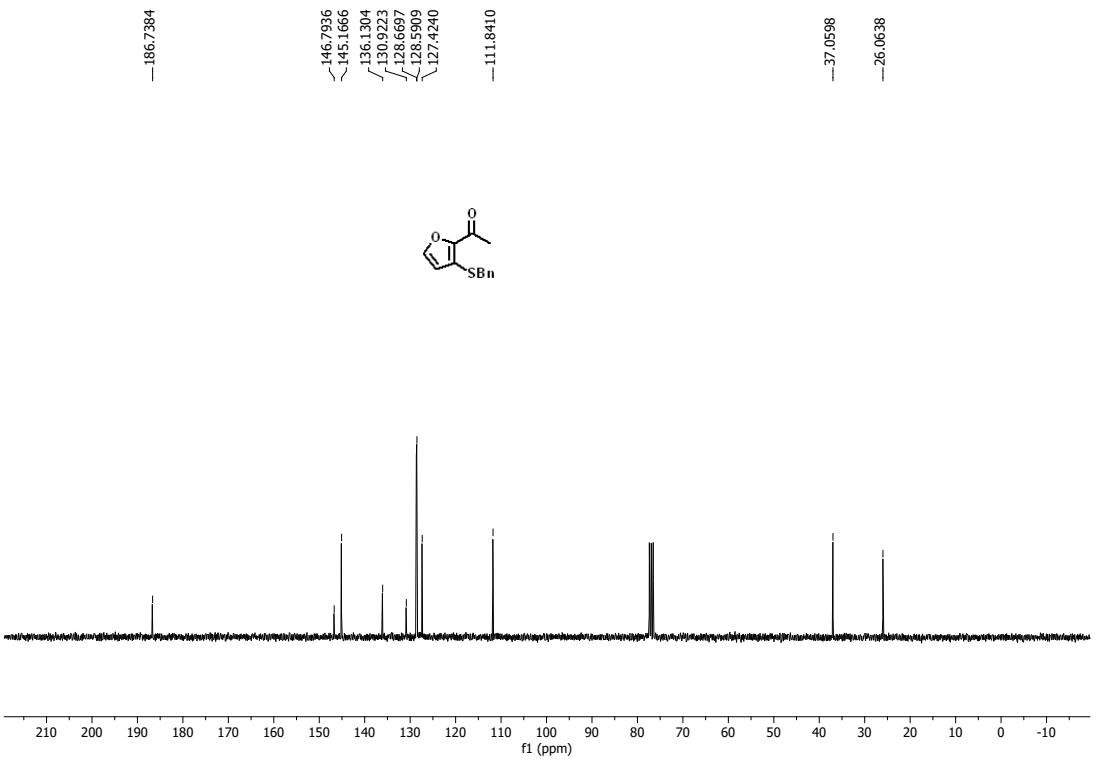
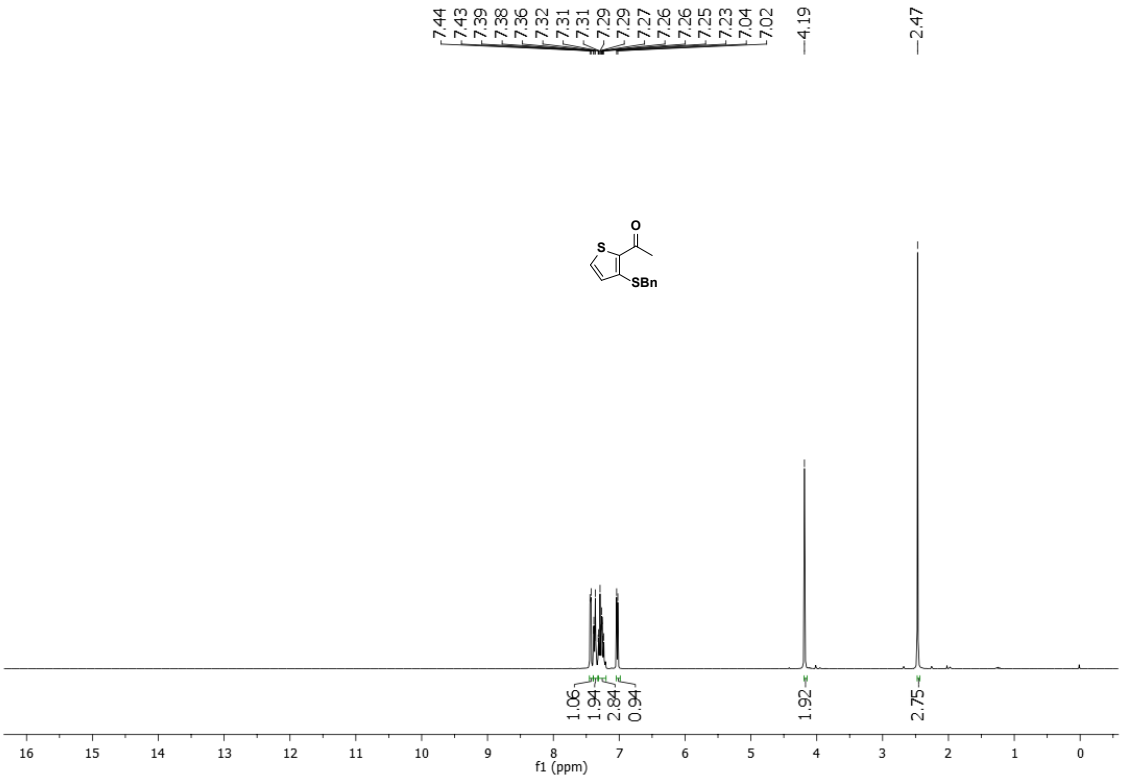
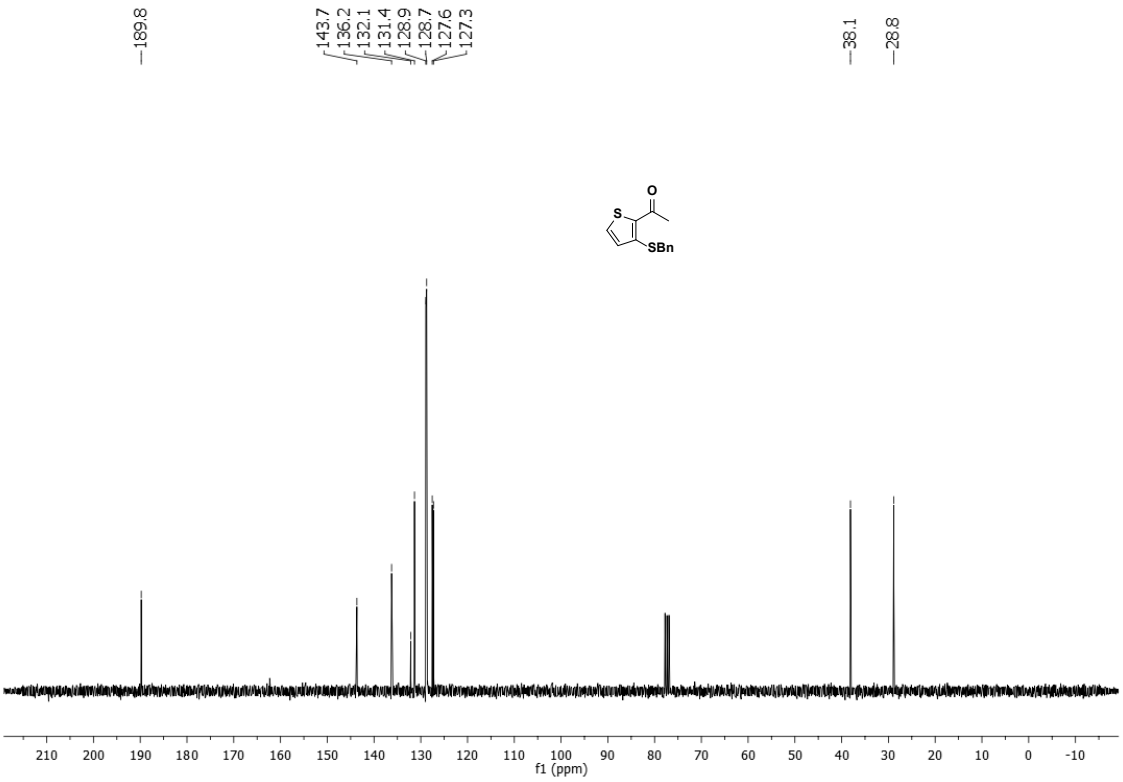
8.5915
7.8720
7.8599
7.8439
7.8365
7.8310
7.5891
7.5853
7.5628
7.5569
7.5348
7.5319
7.3285
7.3004
7.1523
7.1470
7.1405
7.1378
7.1315
7.0065
6.9949
6.9896
6.9837
3.9594
2.4945
SBn O
1.00
2.05
2.08
1.02
3.01
2.04
2.11
3.08
f1 (ppm)

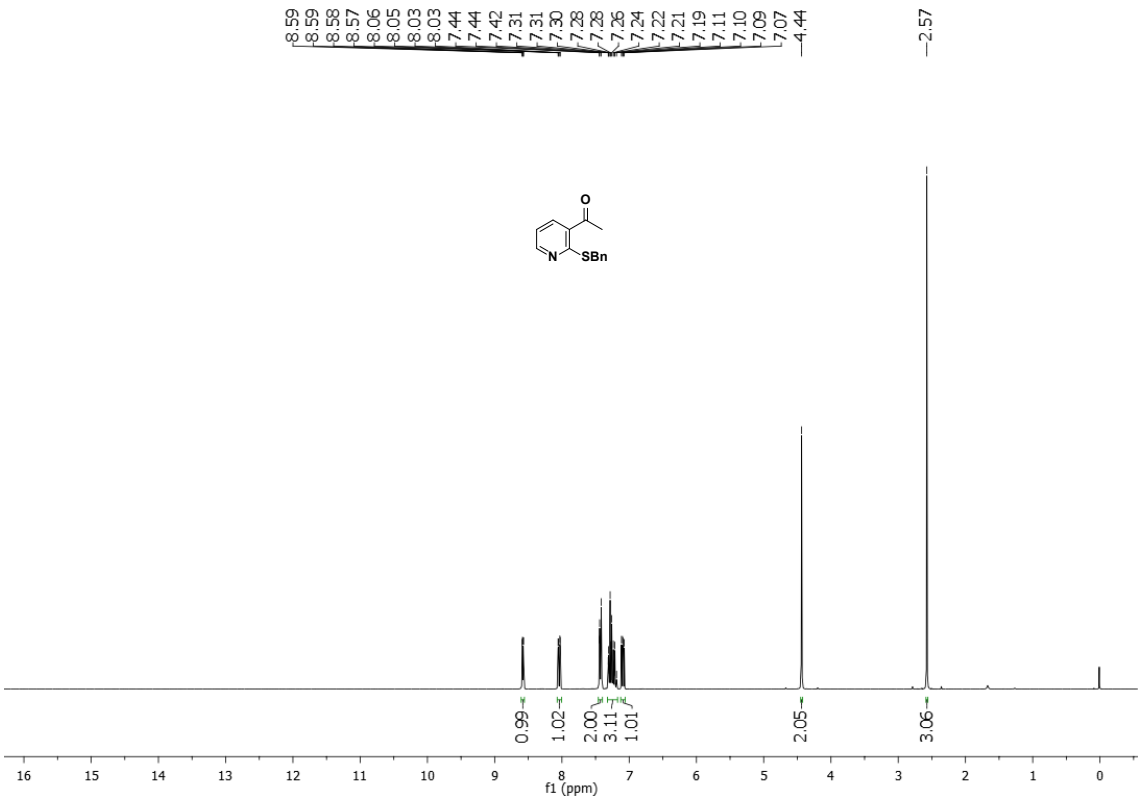

204.5903
146.9383
137.4131
134.7069
134.0909
129.9399
128.8430
128.5519
128.3335
127.6152
127.3697
127.1590
127.0172
126.4408
122.7262
42.1921
31.6415
SBn O
f1 (ppm)

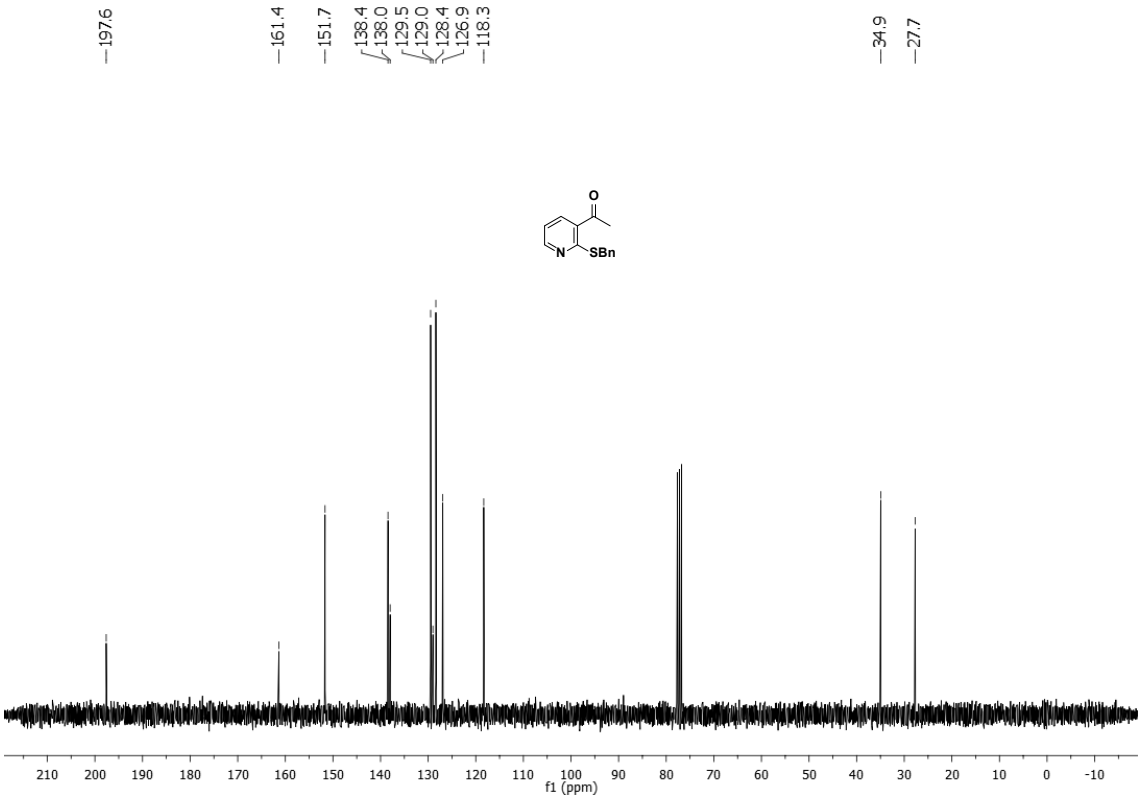

7.3368
7.3306
7.3208
7.3160
7.2922
7.2499
7.2438
7.2215
7.2161
7.1967
7.1887
7.1834
7.1783
7.1605
6.4153
6.4092
4.0560
2.3473
O
O
SBn
5.81
0.93
2.00
2.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

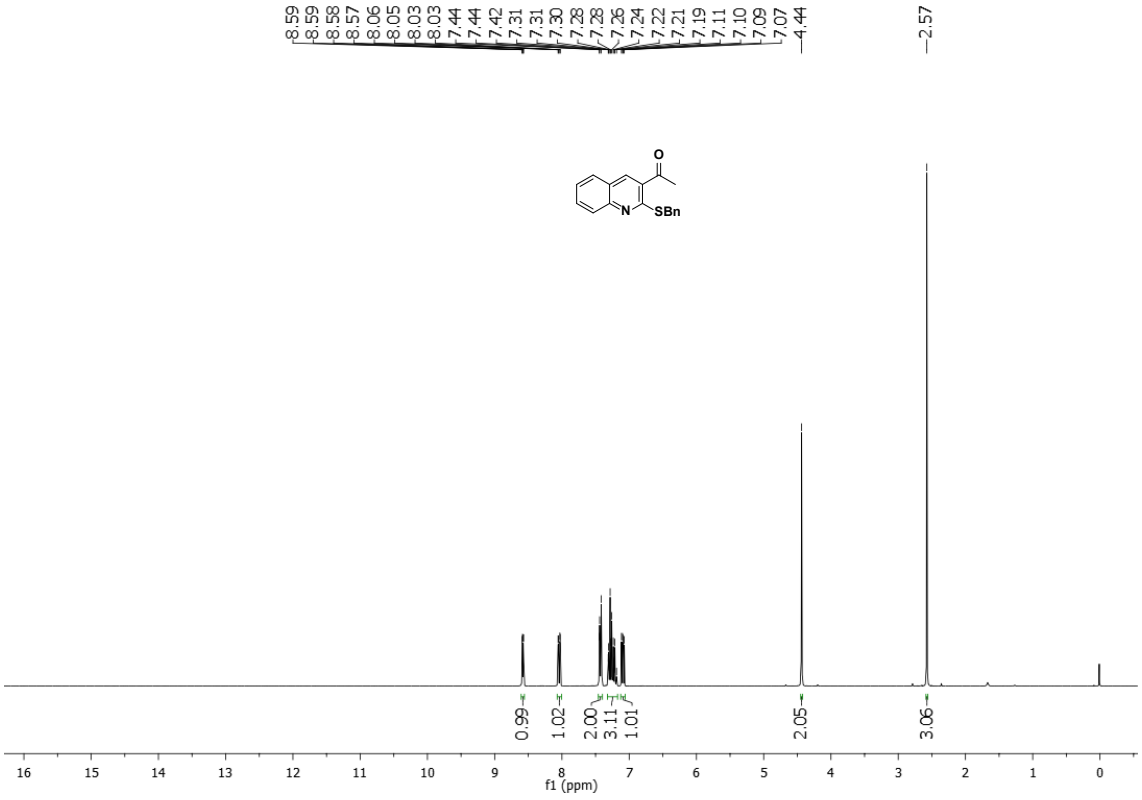

186.7384
146.7936
145.1666
136.1304
130.9223
128.6697
128.5909
127.4240
111.8410
37.0598
26.0638
O
O
SBn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

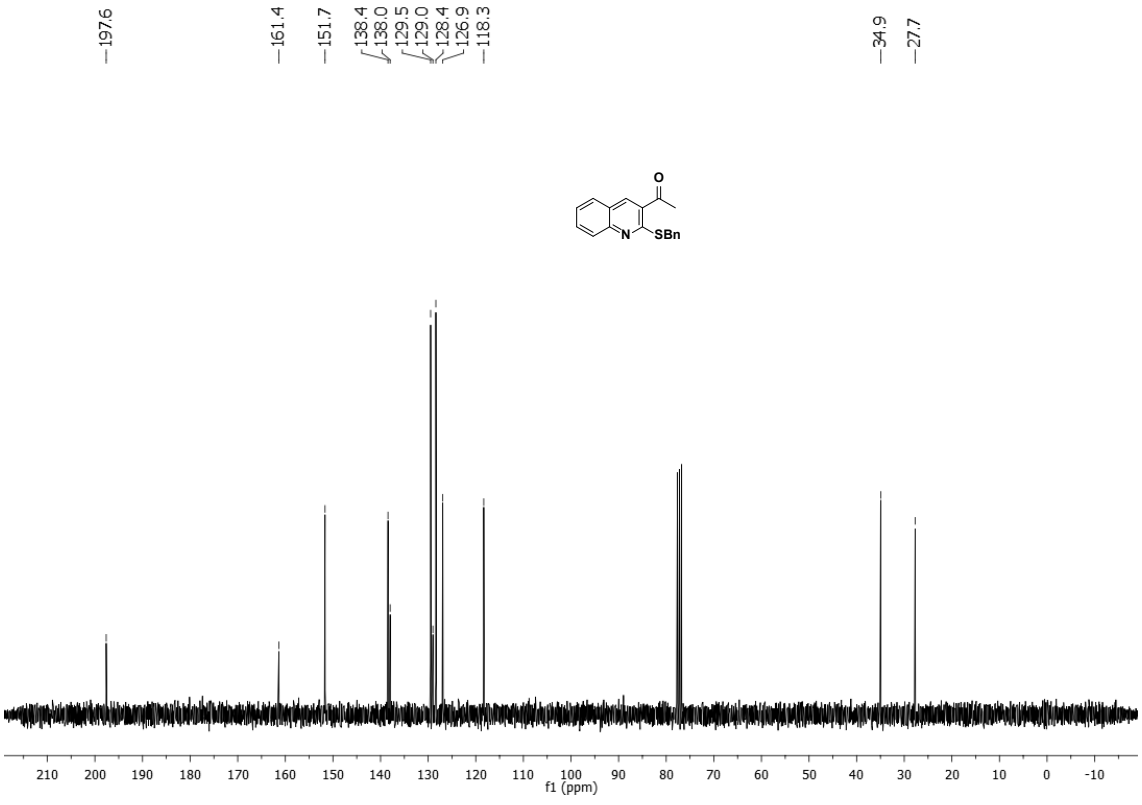

7.44
7.43
7.39
7.38
7.36
7.32
7.31
7.31
7.29
7.29
7.27
7.26
7.26
7.25
7.23
7.04
7.02
4.19
2.47
O
S
SBn
1.06
1.94
2.84
0.94
1.92
2.75
f1 (ppm)

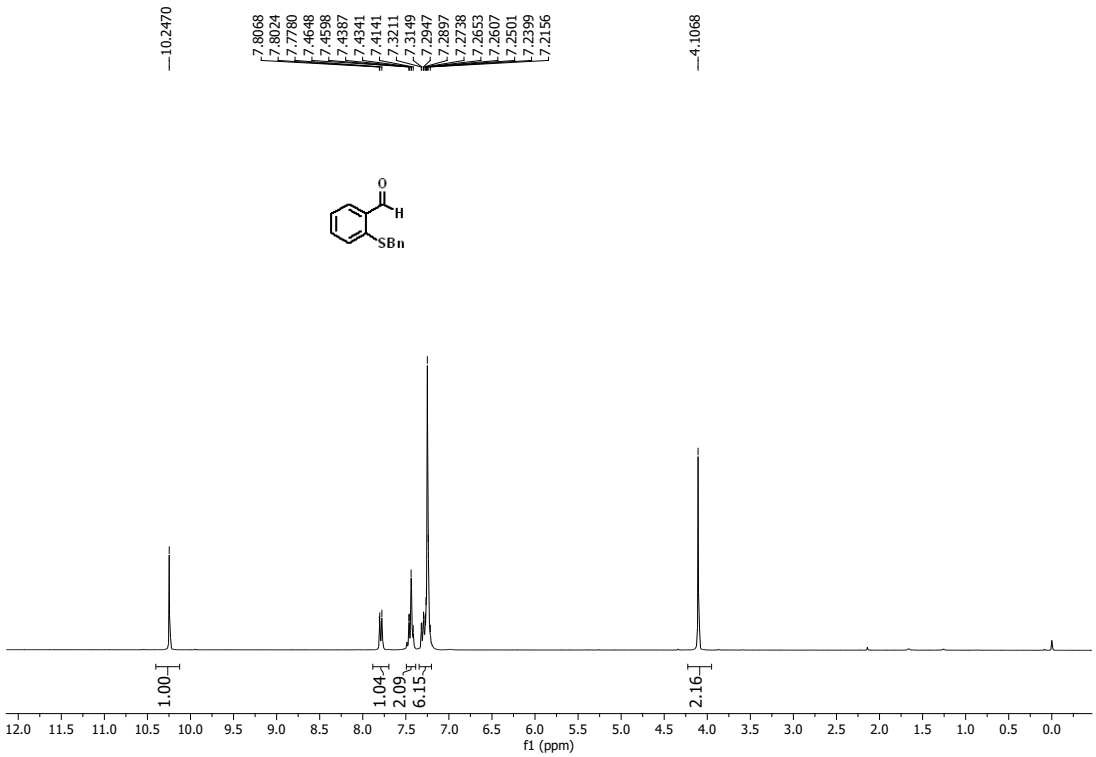

189.8
143.7
136.2
132.1
131.4
128.9
128.7
127.6
127.3
38.1
28.8
O
S
SBn
f1 (ppm)

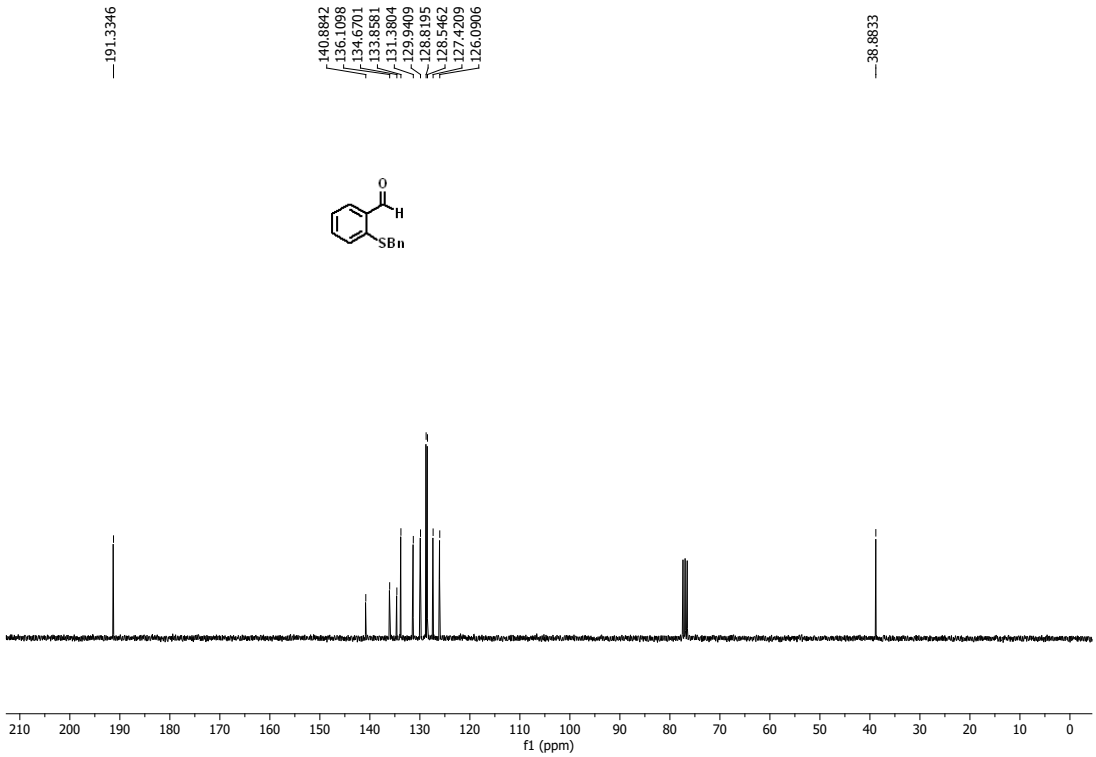

8.59
8.59
8.58
8.57
8.06
8.05
8.03
8.03
7.44
7.44
7.42
7.31
7.31
7.30
7.28
7.28
7.26
7.24
7.22
7.21
7.19
7.11
7.10
7.09
7.07
4.44
2.57
O
N
SBn
0.99
1.02
2.00
3.11
1.01
2.05
3.06
f1 (ppm)

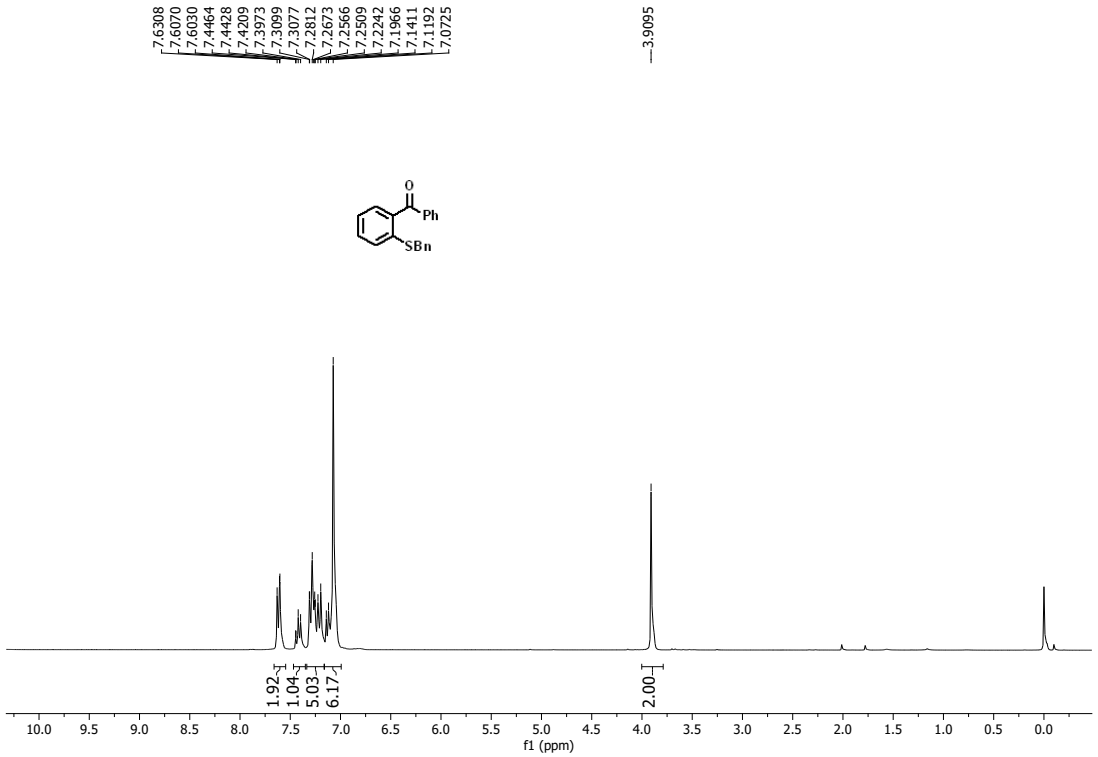

197.6
161.4
151.7
138.4
138.0
129.5
129.0
128.4
126.9
118.3
34.9
27.7
O
N
SBn
f1 (ppm)

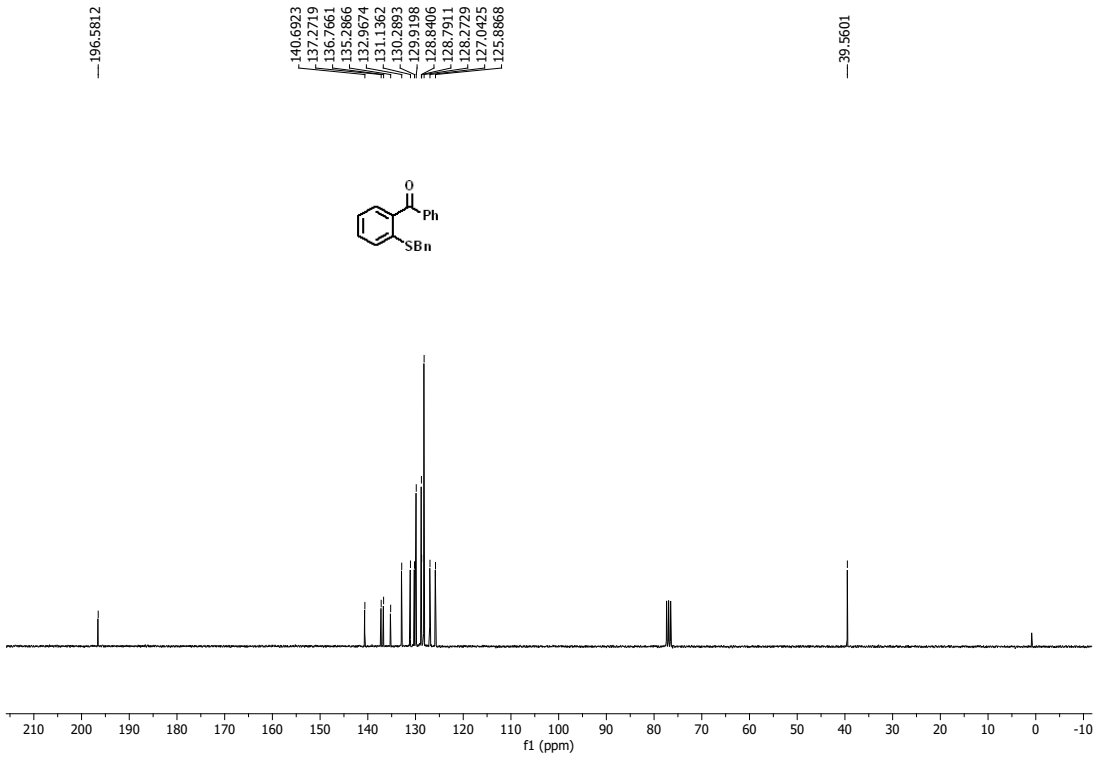

8.59
8.59
8.58
8.57
8.06
8.05
8.03
8.03
7.44
7.44
7.42
7.31
7.31
7.30
7.28
7.28
7.26
7.24
7.22
7.21
7.19
7.11
7.10
7.09
7.07
4.44
2.57
O
N
SBn
0.99
1.02
2.00
3.11
1.01
2.05
3.06
f1 (ppm)


197.6
161.4
151.7
138.4
138.0
129.5
129.0
128.4
126.9
118.3
34.9
27.7
O
N
SBn
f1 (ppm)

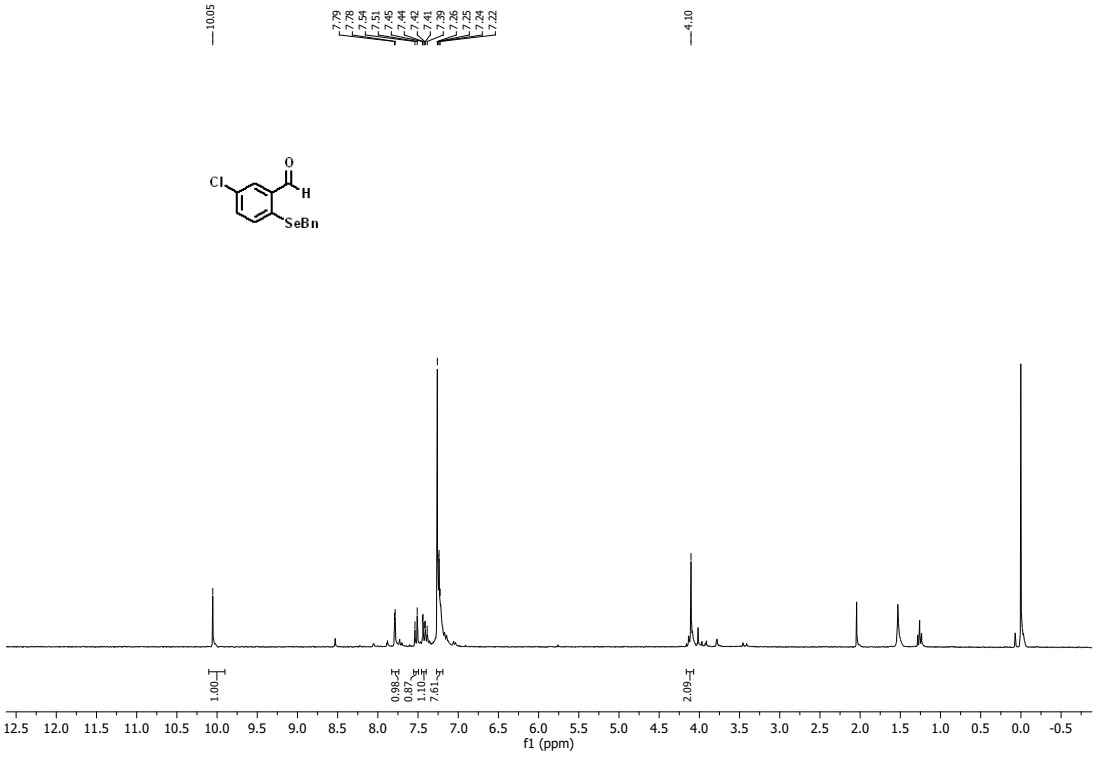

10.2470
7.8068
7.8024
7.7780
7.4648
7.4598
7.4387
7.4341
7.4141
7.3211
7.3149
7.2947
7.2897
7.2738
7.2653
7.2607
7.2501
7.2399
7.2156
4.1068
O
H
SBn
1.00
1.04
2.09
6.15
2.16
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

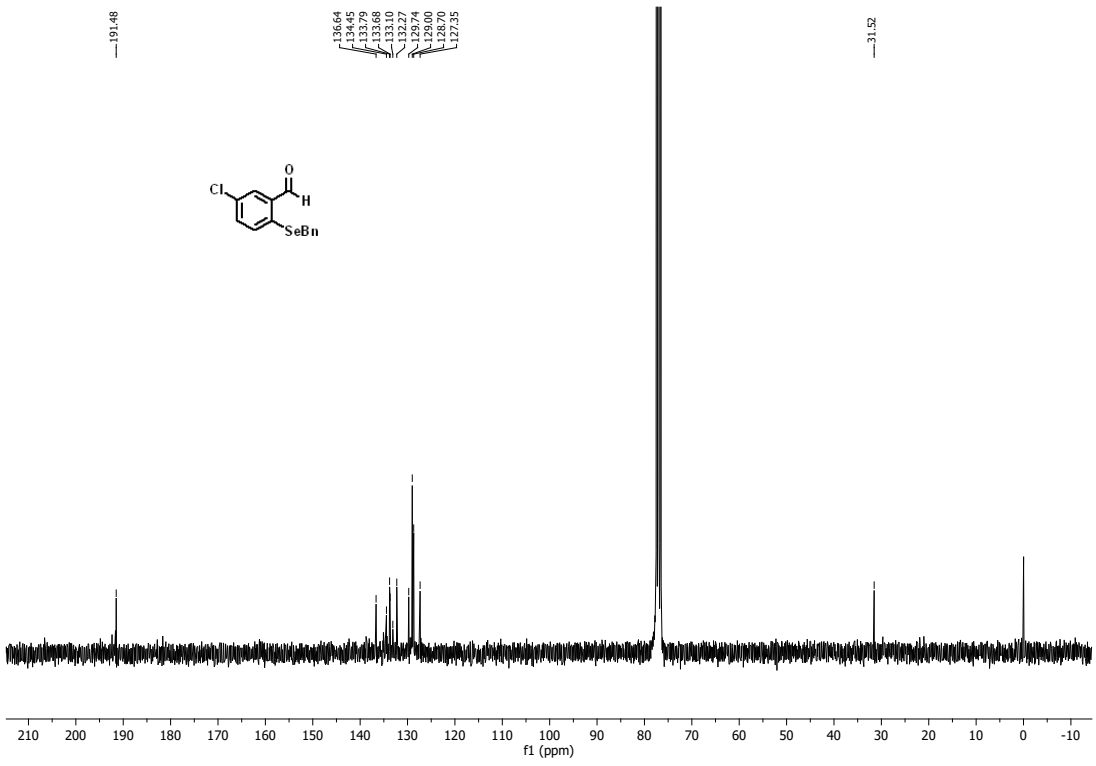

191.3346
140.8842
136.1098
134.6701
133.8581
131.3804
129.9409
128.8195
128.5462
127.4209
126.0906
38.8833
O
H
SBn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.6308
7.6070
7.6030
7.4464
7.4428
7.4209
7.3973
7.3099
7.3077
7.2812
7.2673
7.2566
7.2509
7.2242
7.1966
7.1411
7.1192
7.0725
3.9095
O
Ph
SBn
1.92
1.04
5.03
6.17
2.00
f1 (ppm)

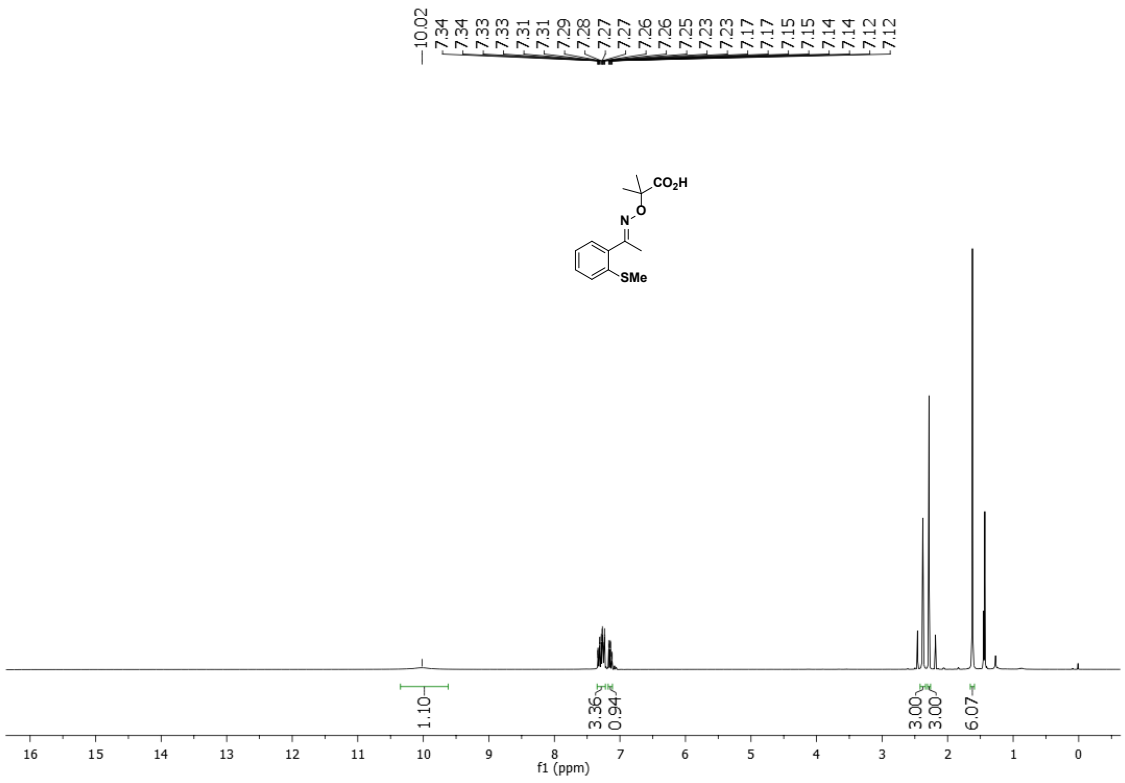

196.5812
140.6923
137.2719
136.7661
135.2866
132.9674
131.1362
130.2893
129.9198
128.8406
128.7911
128.2729
127.0425
125.8868
39.5601
O
Ph
SBn
f1 (ppm)

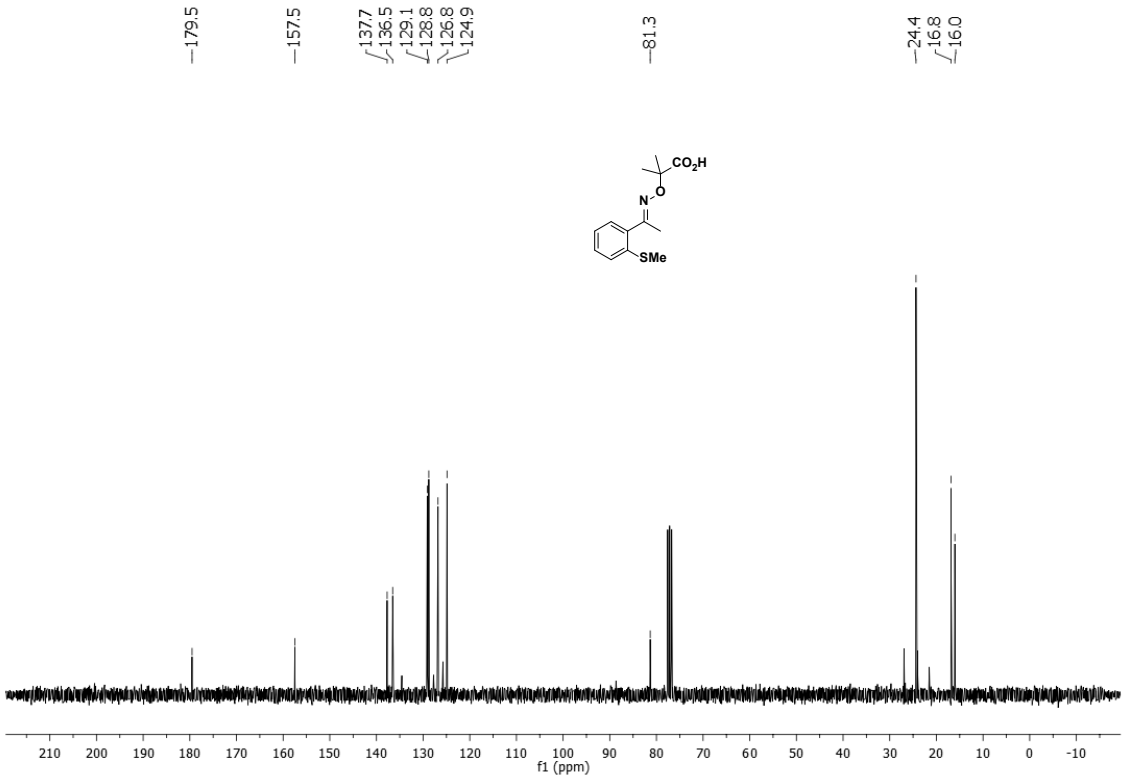
## 10.2. NMR Spectra of Selenides SI-10

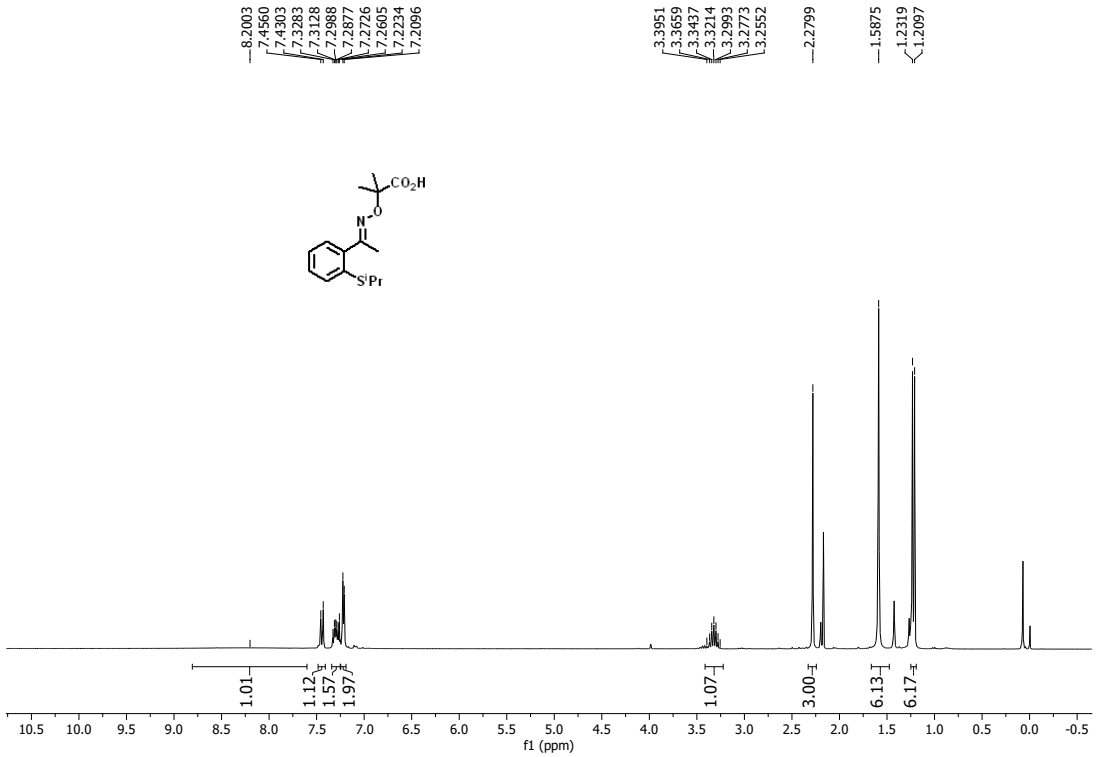


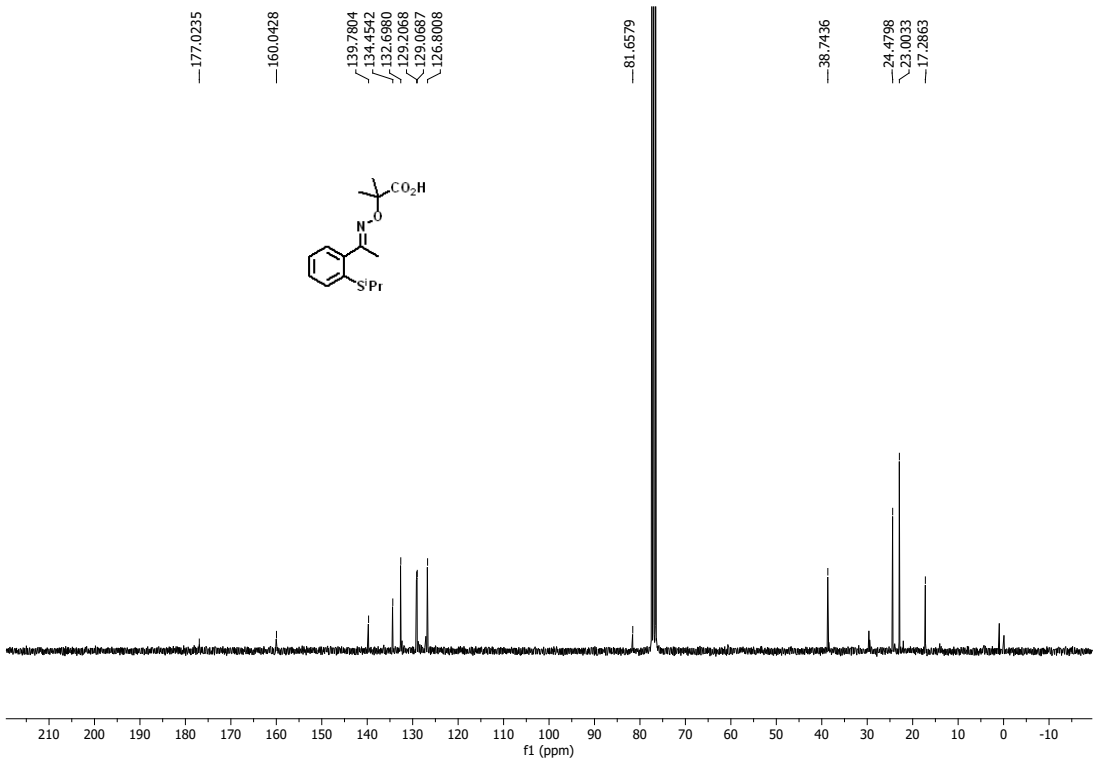



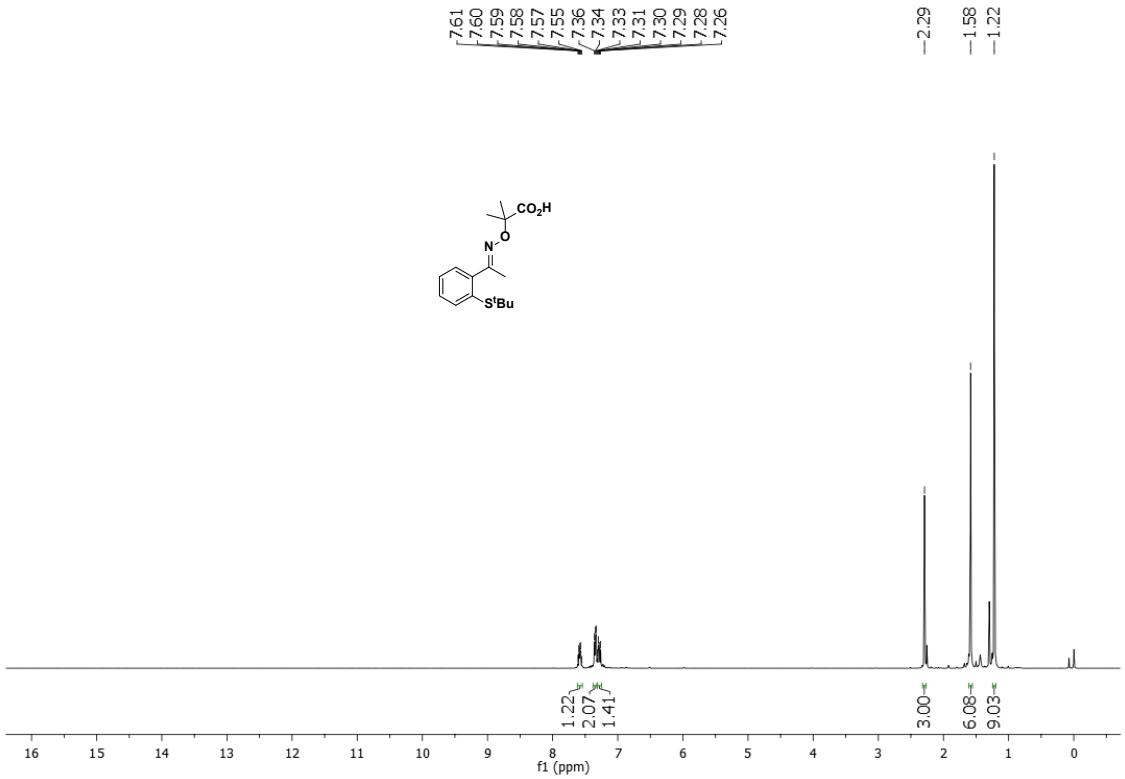
## 10.3. NMR Spectra of α-Imino-oxy Acids 1

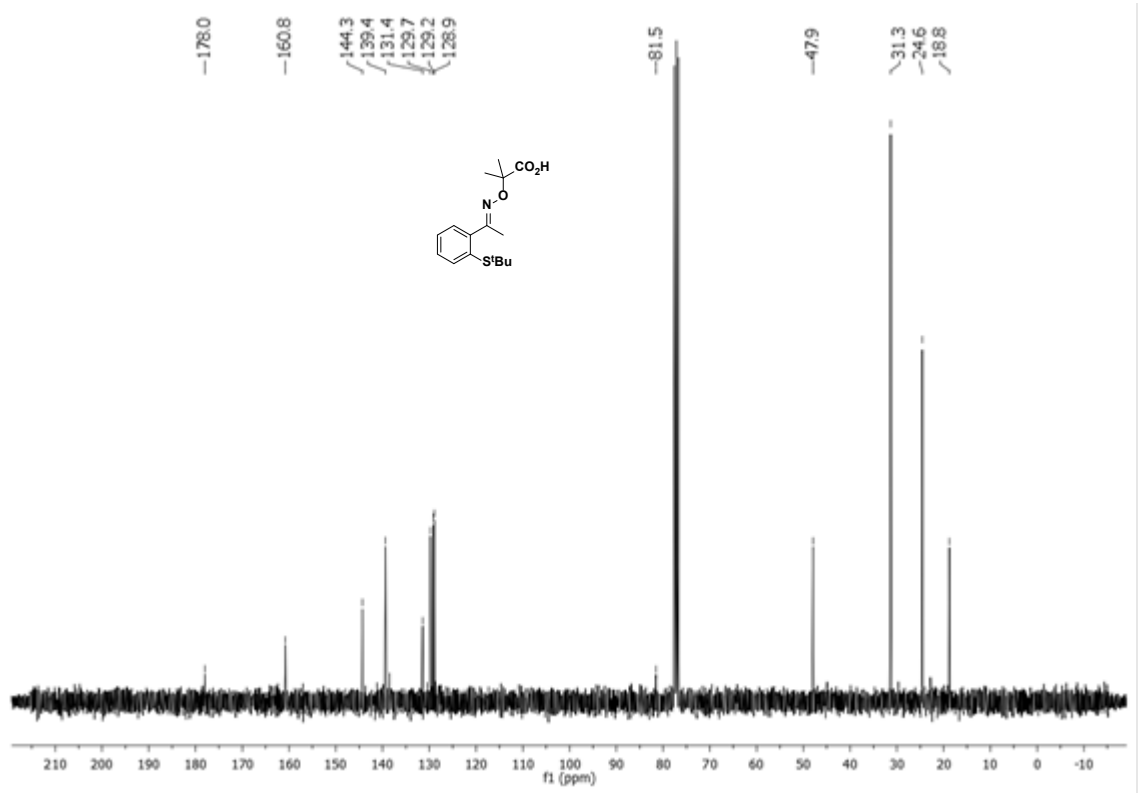


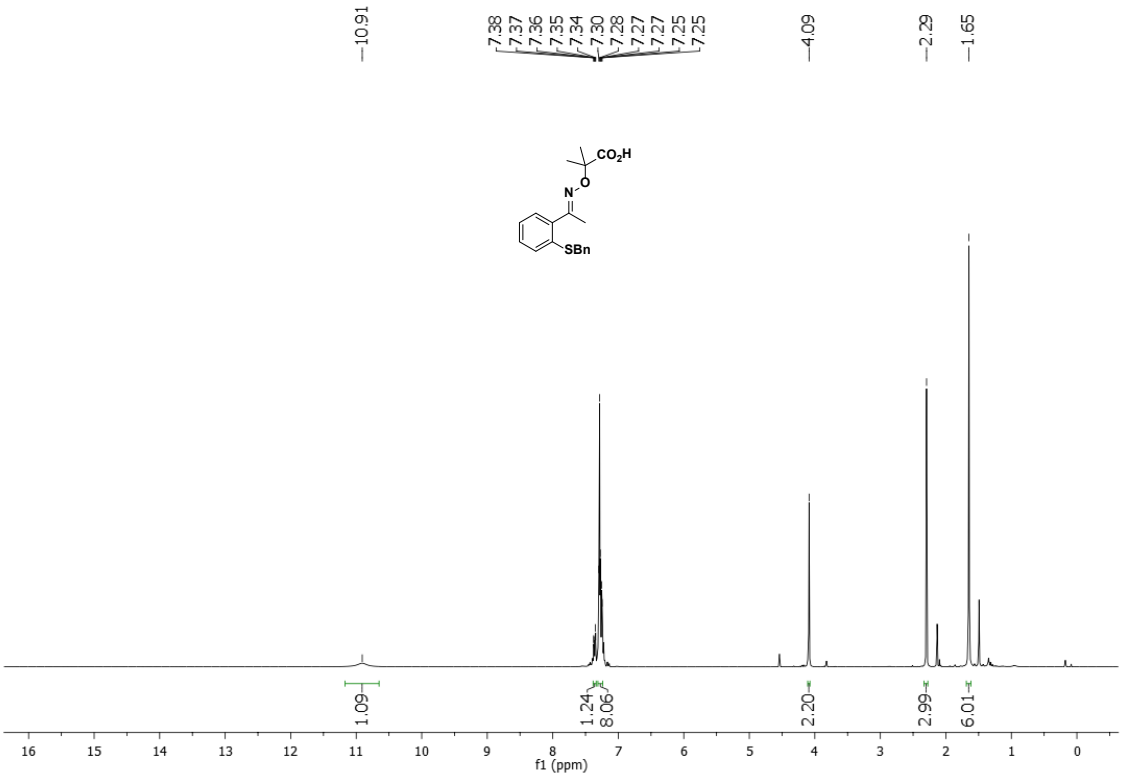



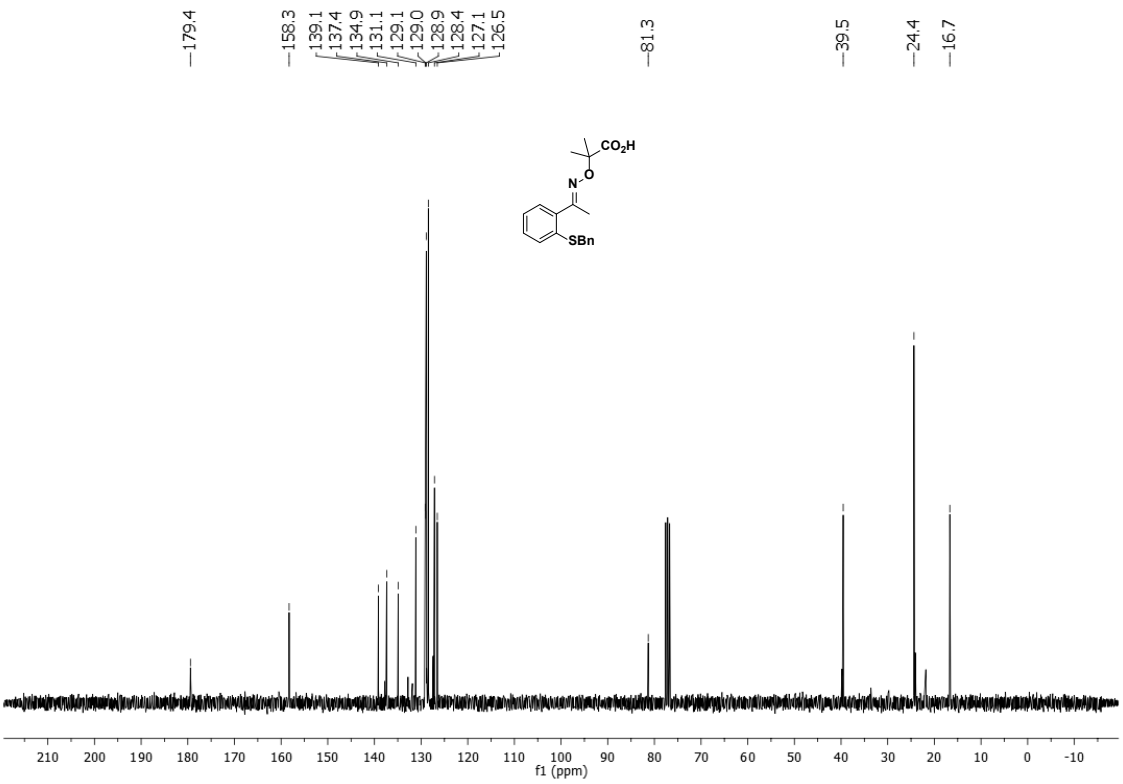

8.2003
7.4560
7.4303
7.3283
7.3128
7.2988
7.2877
7.2726
7.2605
7.2234
7.2096
3.3951
3.3659
3.3437
3.3214
3.2993
3.2773
3.2552
2.2799
1.5875
1.2319
1.2097
CO2H
N
O
SiPr
1.01
1.12
1.57
1.97
1.07
3.00
6.13
6.17
f1 (ppm)

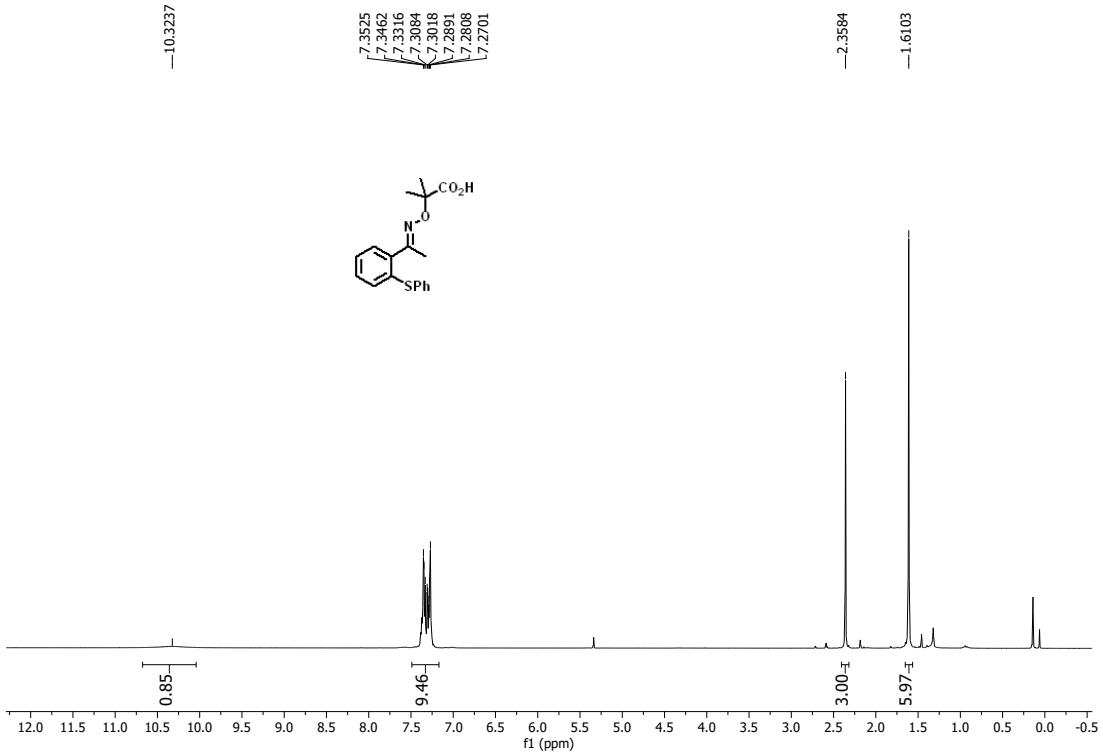

177.0235
160.0428
139.7804
134.4542
132.6980
129.2068
129.0687
126.8008
81.6579
38.7436
24.4798
23.0033
17.2863
CO2H
N
O
SiPr
f1 (ppm)

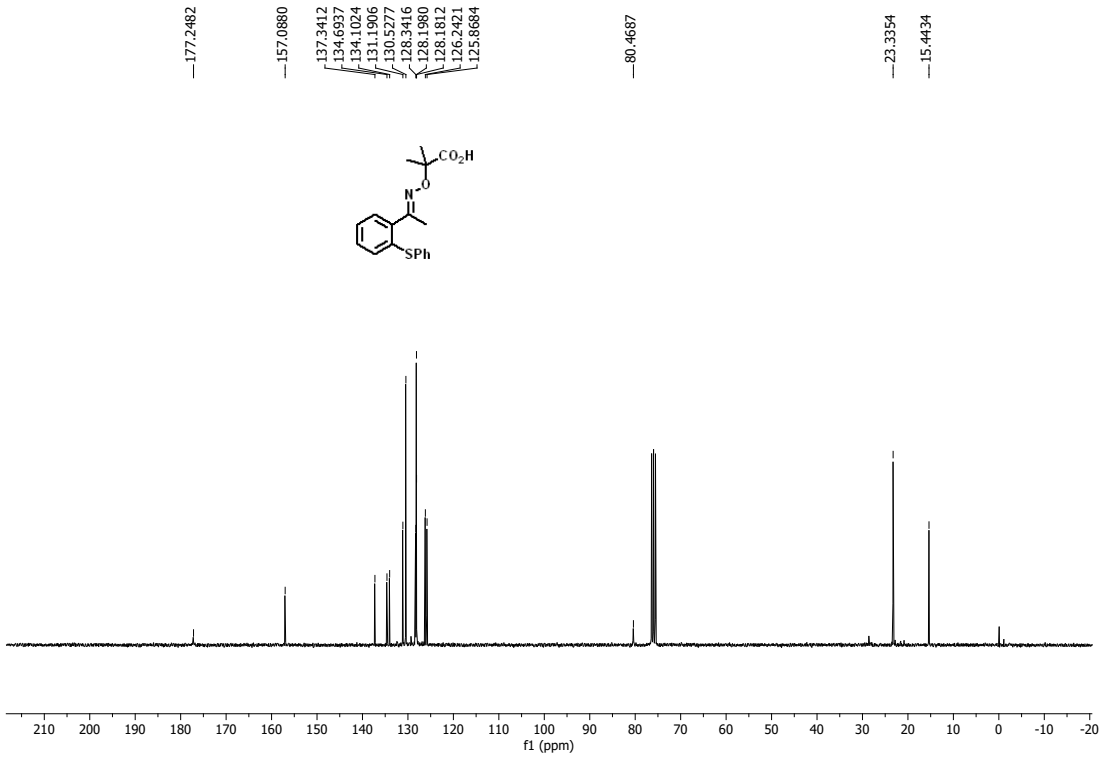

7.61
7.60
7.59
7.58
7.57
7.55
7.36
7.34
7.33
7.31
7.30
7.29
7.28
7.26
2.29
1.58
1.22
CO2H
N
O
StBu
1.22
2.07
1.41
3.00
6.08
9.03
f1 (ppm)

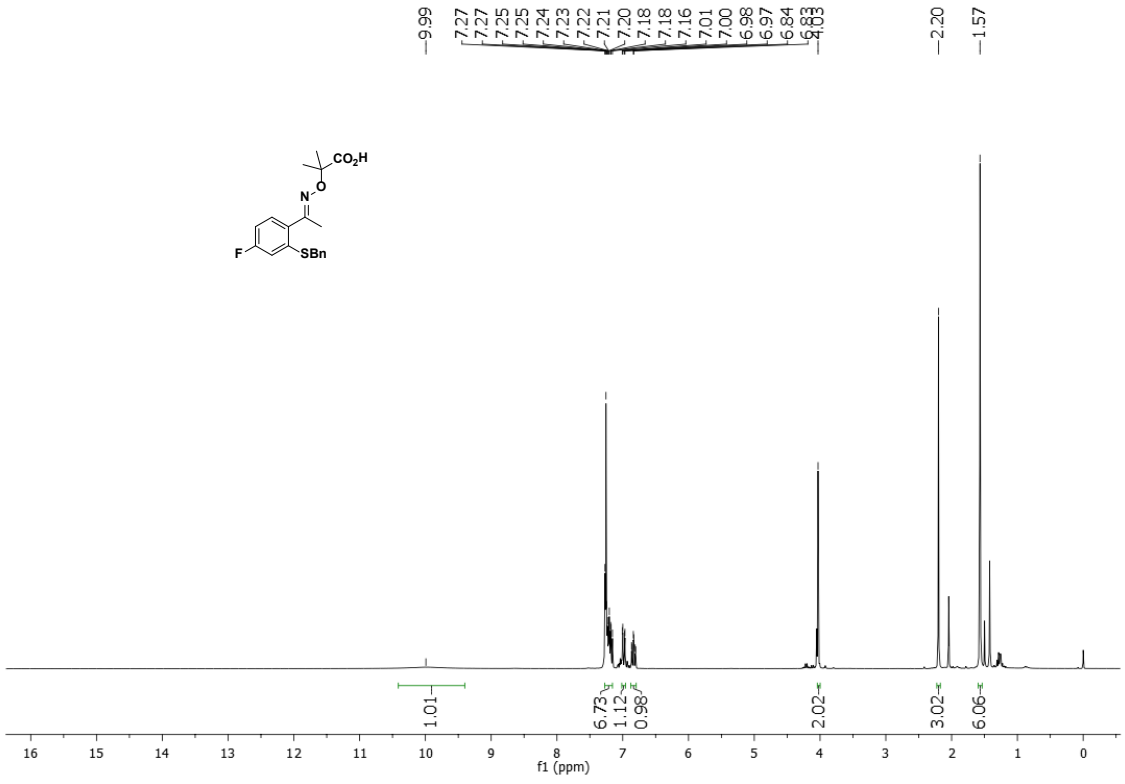

178.0
160.8
144.3
139.4
131.4
129.7
129.2
128.9
81.5
47.9
31.3
24.6
18.8
CO2H
N
O
StBu
f1 (ppm)

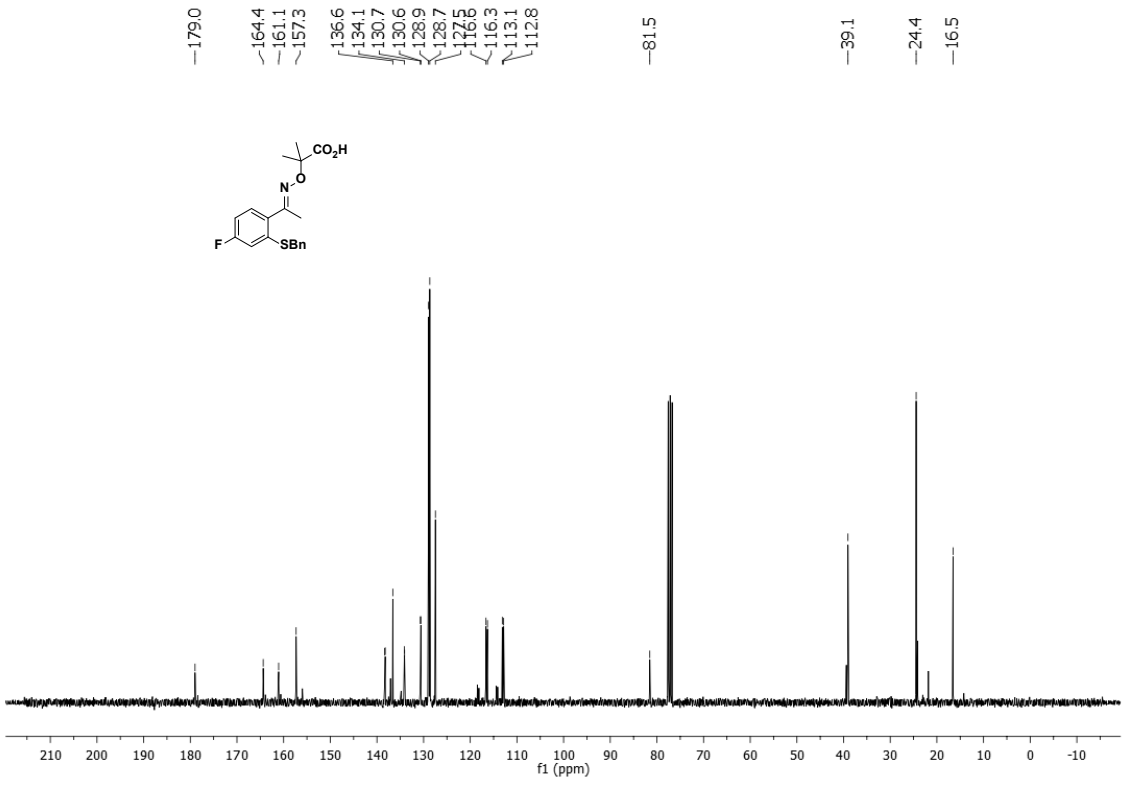

10.91
7.38
7.37
7.36
7.35
7.34
7.30
7.28
7.27
7.27
7.25
7.25
4.09
2.29
1.65
CO2H
N
O
SBn
1.09
1.24
8.06
2.20
2.99
6.01
f1 (ppm)


179.4
158.3
139.1
137.4
134.9
131.1
129.1
129.0
128.9
128.4
127.1
126.5
81.3
39.5
24.4
16.7
CO2H
N
O
SBn
f1 (ppm)


10.3237
7.3525
7.3462
7.3316
7.3084
7.3018
7.2891
7.2808
7.2701
2.3584
1.6103
CO2H
N
O
SPh
0.85
9.46
3.00
5.97
f1 (ppm)


177.2482
157.0880
137.3412
134.6937
134.1024
131.1906
130.5277
128.3416
128.1980
128.1812
126.2421
125.8684
80.4687
23.3354
15.4434
CO2H
N
O
SPh
f1 (ppm)


9.99
7.27
7.27
7.25
7.25
7.24
7.23
7.22
7.21
7.20
7.18
7.18
7.16
7.01
7.00
6.98
6.97
6.84
6.83
4.03
2.20
1.57
CO2H
N
O
F
SBn
1.01
6.73
1.12
0.98
2.02
3.02
6.06
f1 (ppm)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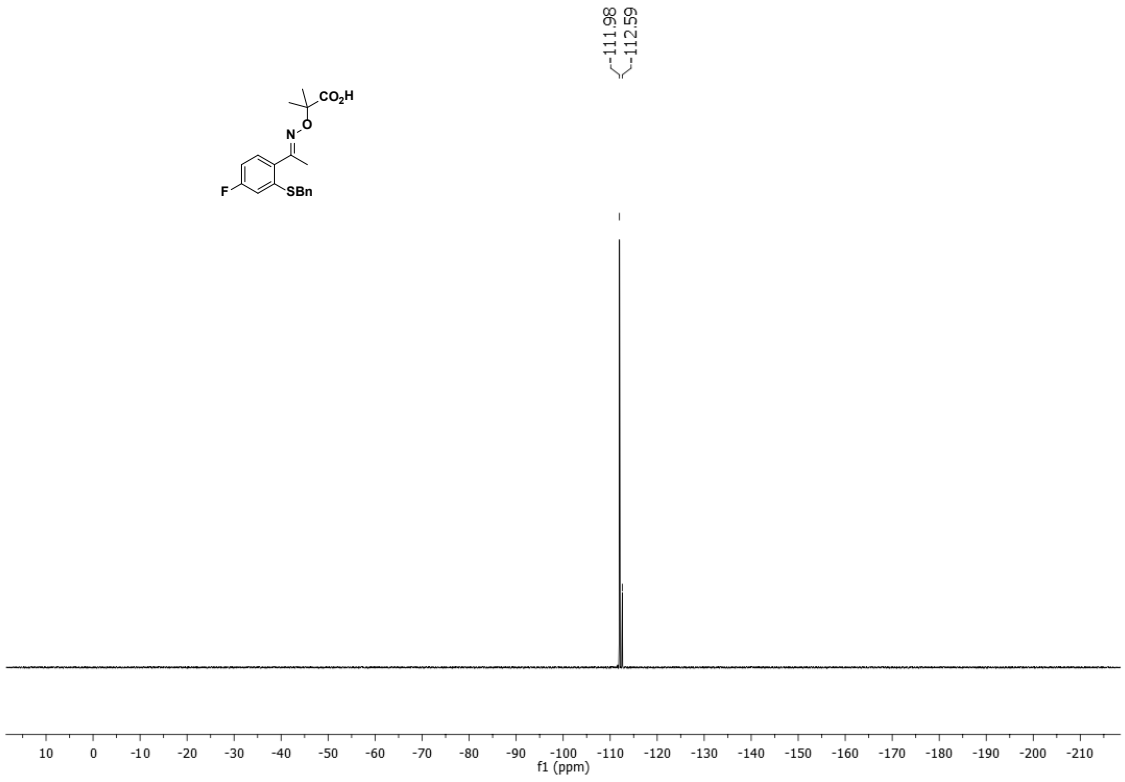
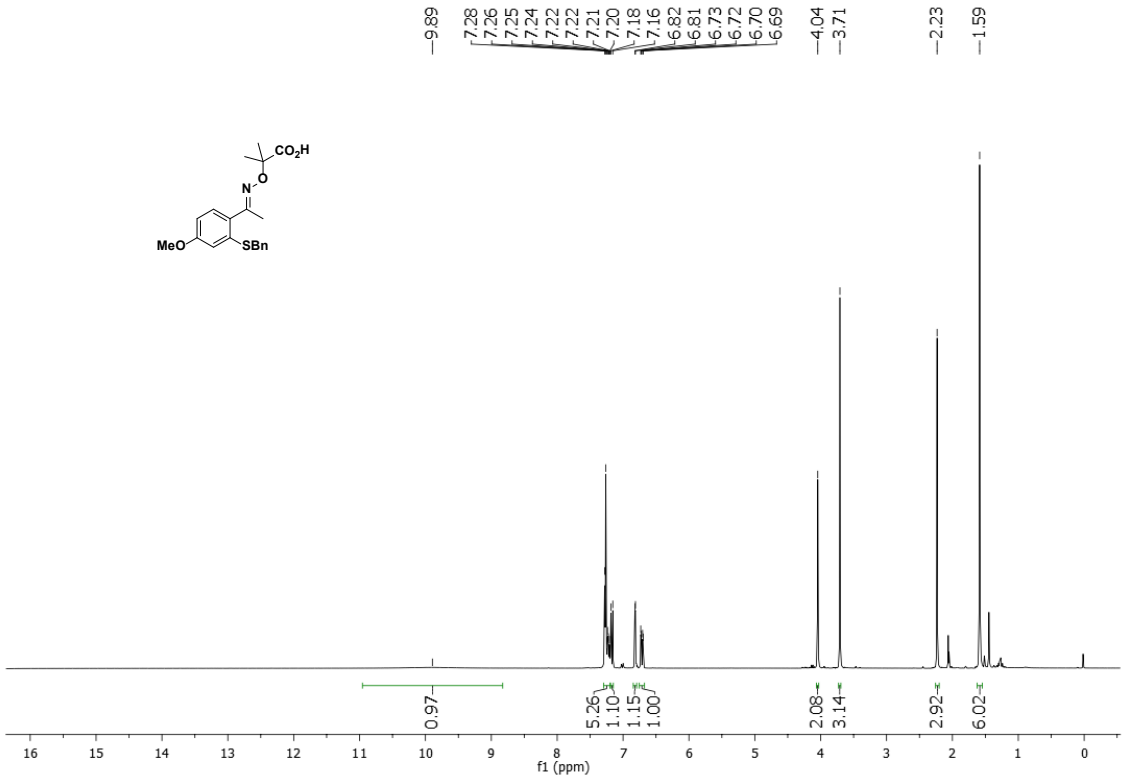
164.4
161.1
157.3
136.6
134.1
130.7
130.6
128.9
128.7
127.5
116.6
116.3
113.1
112.8
81.5
39.1
24.4
16.5
CO2H
N
O
F
SBn
f1 (ppm)


-111.98
-112.59
CO2H
N
O
F
SBn
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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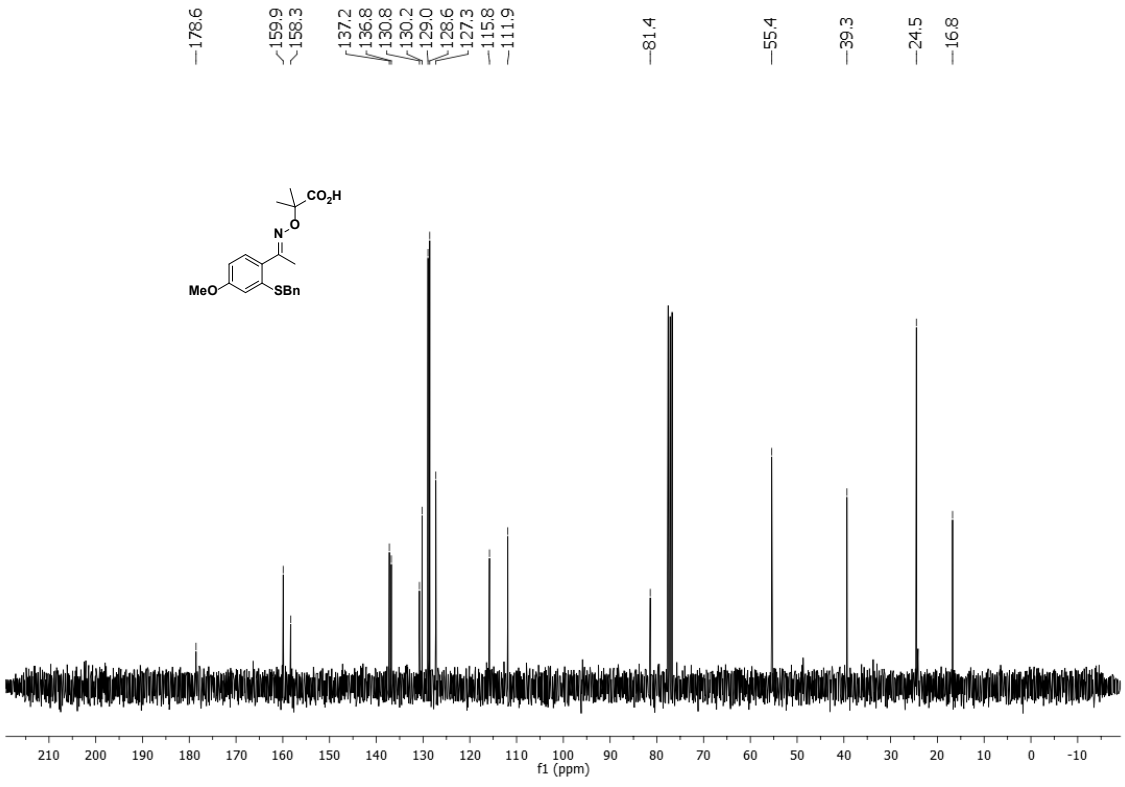
7.28
7.26
7.25
7.24
7.22
7.22
7.21
7.20
7.18
7.16
6.82
6.81
6.73
6.72
6.70
6.69
4.04
3.71
2.23
1.59
CO2H
N
O
MeO
SBn
0.97
5.26
1.10
1.15
1.00
2.08
3.14
2.92
6.02
f1 (ppm)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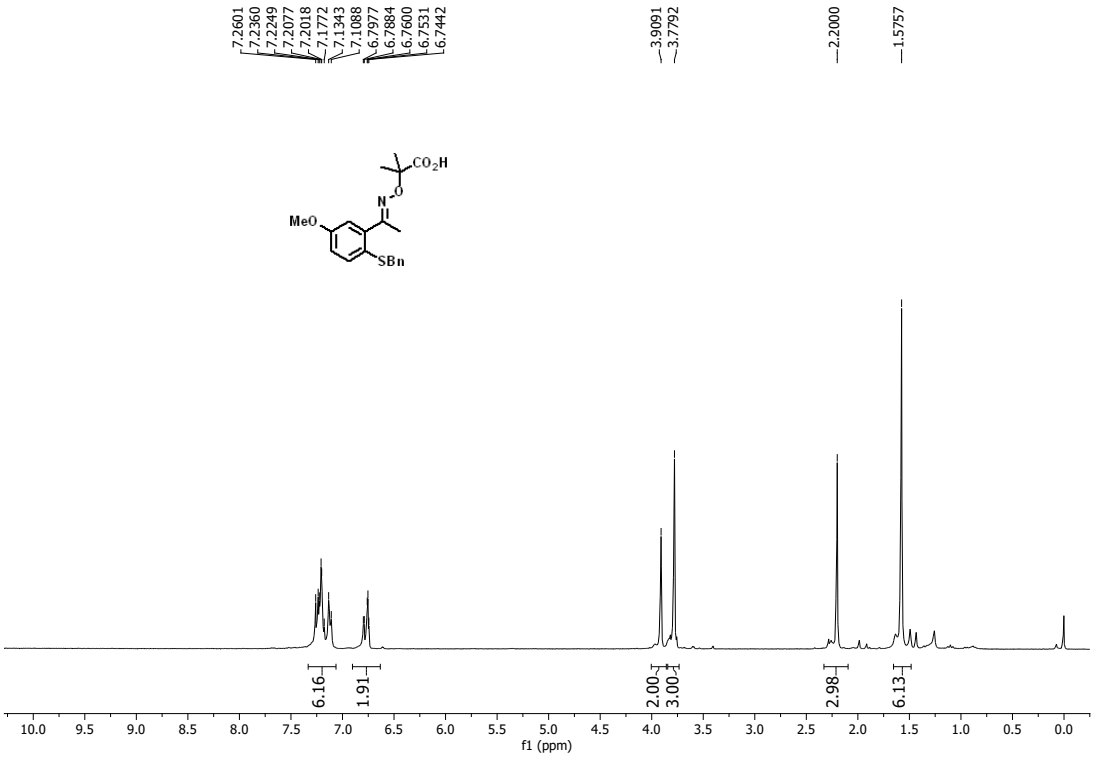
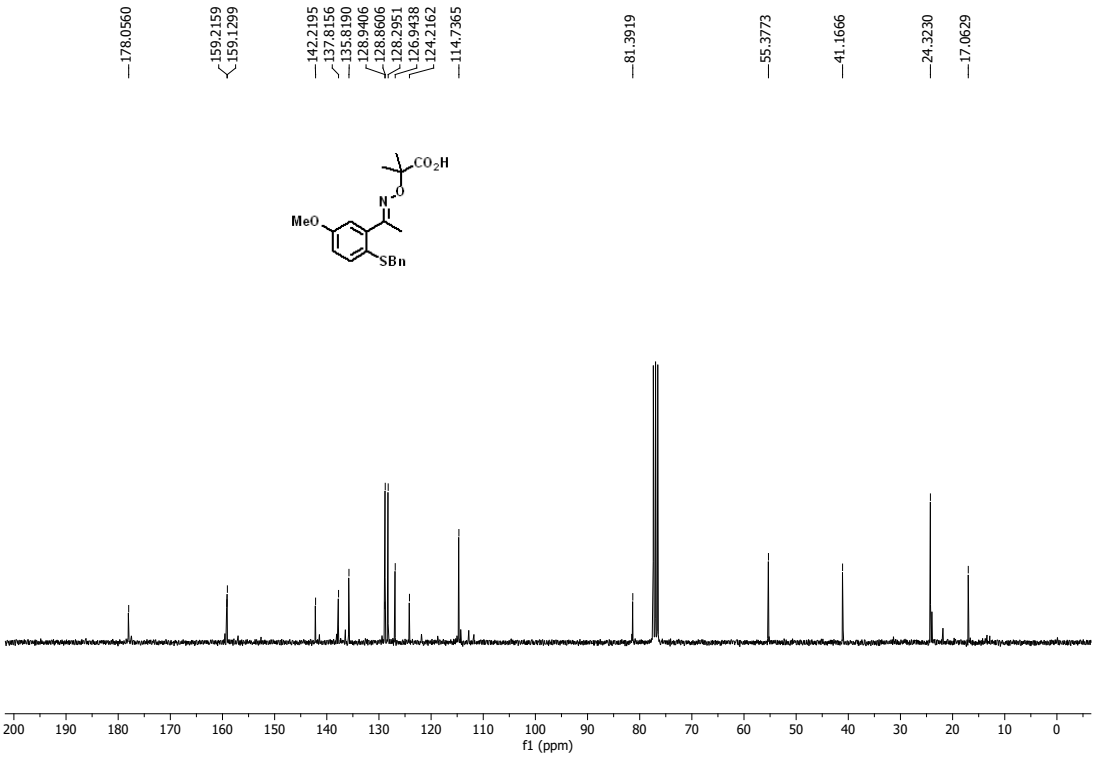
158.3
137.2
136.8
130.8
130.2
129.0
128.6
127.3
115.8
111.9
81.4
55.4
39.3
24.5
16.8
CO2H
N
O
MeO
SBn
f1 (ppm)


7.2601
7.2360
7.2249
7.2077
7.2018
7.1772
7.1343
7.1088
6.7977
6.7884
6.7600
6.7531
6.7442
3.9091
3.7792
2.2000
1.5757
CO2H
N
O
MeO
SBn
6.16
1.91
2.00
3.00
2.98
6.13
f1 (ppm)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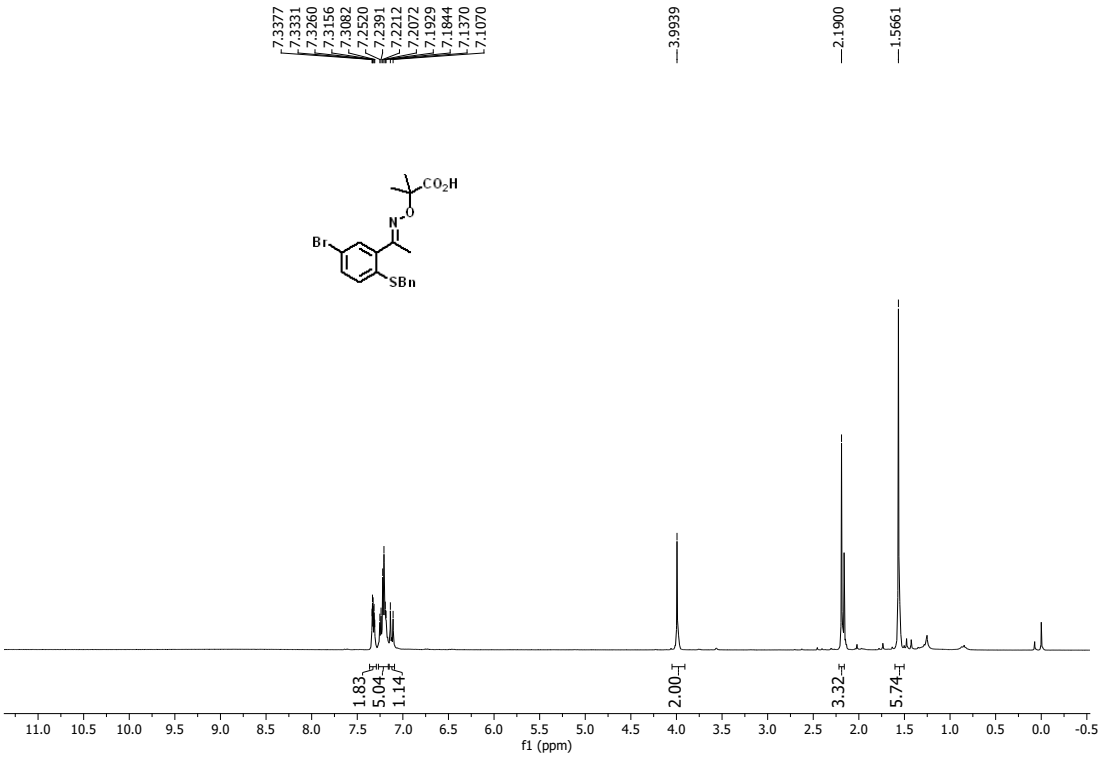
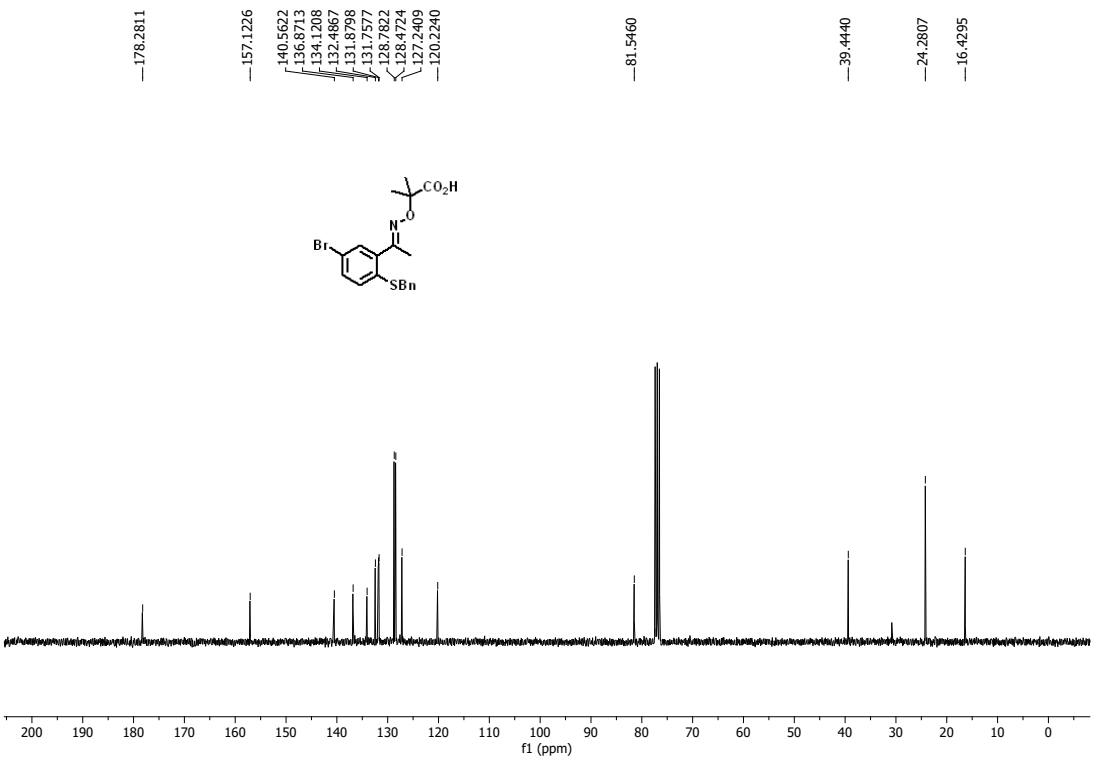
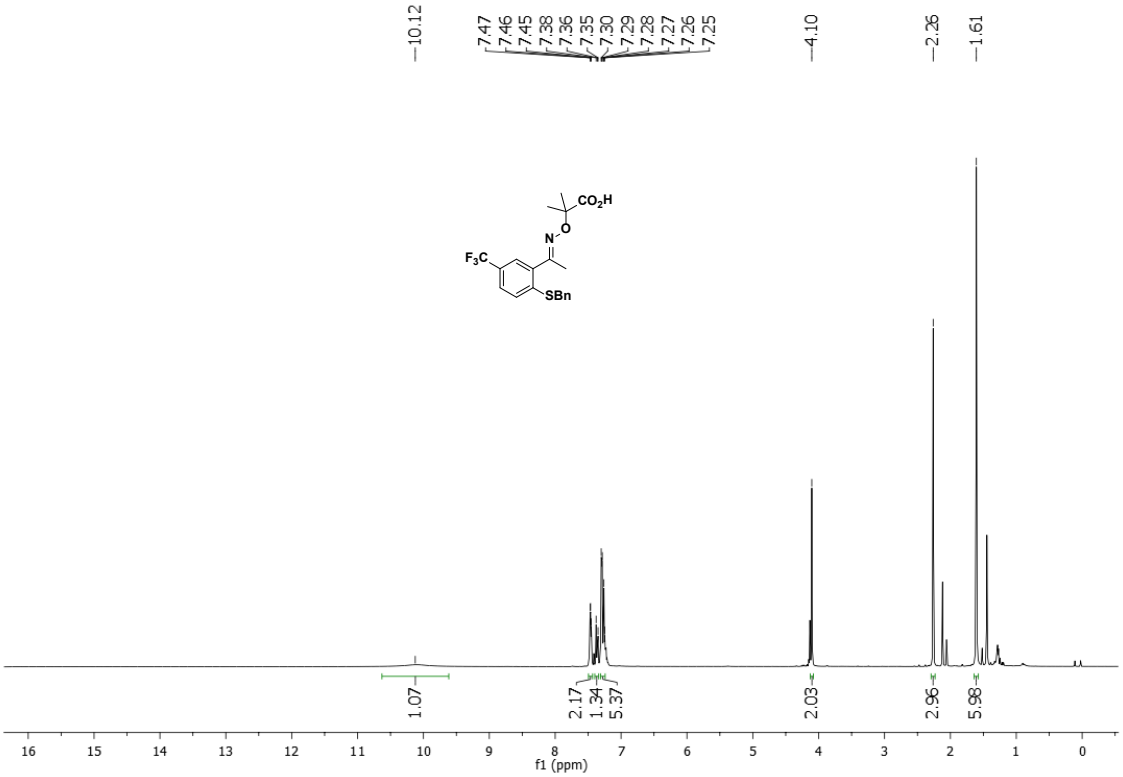
159.1299
142.2195
137.8156
135.8190
128.9406
128.8606
128.2951
126.9438
124.2162
114.7365
81.3919
55.3773
41.1666
24.3230
17.0629
CO2H
N
O
MeO
SBn
f1 (ppm)


7.3377
7.3331
7.3260
7.3156
7.3082
7.2520
7.2391
7.2211
7.2072
7.1929
7.1844
7.1370
7.1070
3.9939
2.1900
1.5661
CO2H
N
O
Br
SBn
1.83
5.04
1.14
2.00
3.32
5.74
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


178.2811
157.1226
140.5622
136.8713
134.1208
132.4867
131.8798
131.7577
128.7822
128.4724
127.2409
120.2240
81.5460
39.4440
24.2807
16.4295
CO2H
N
O
Br
SBn
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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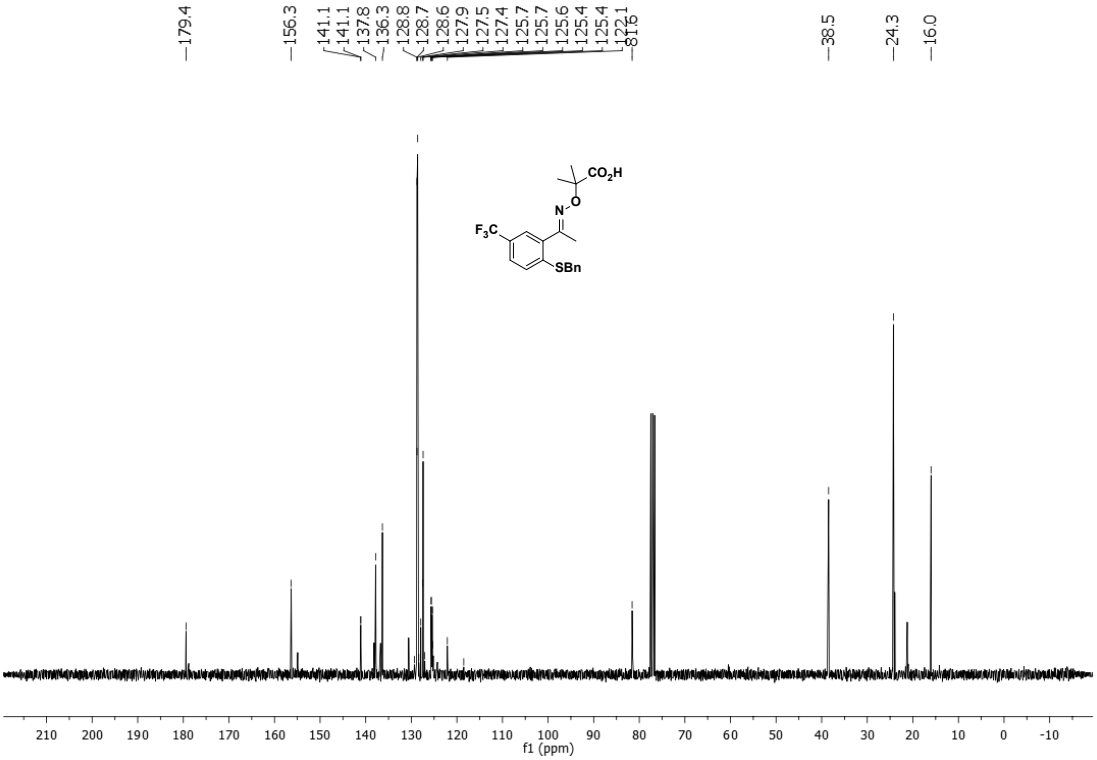
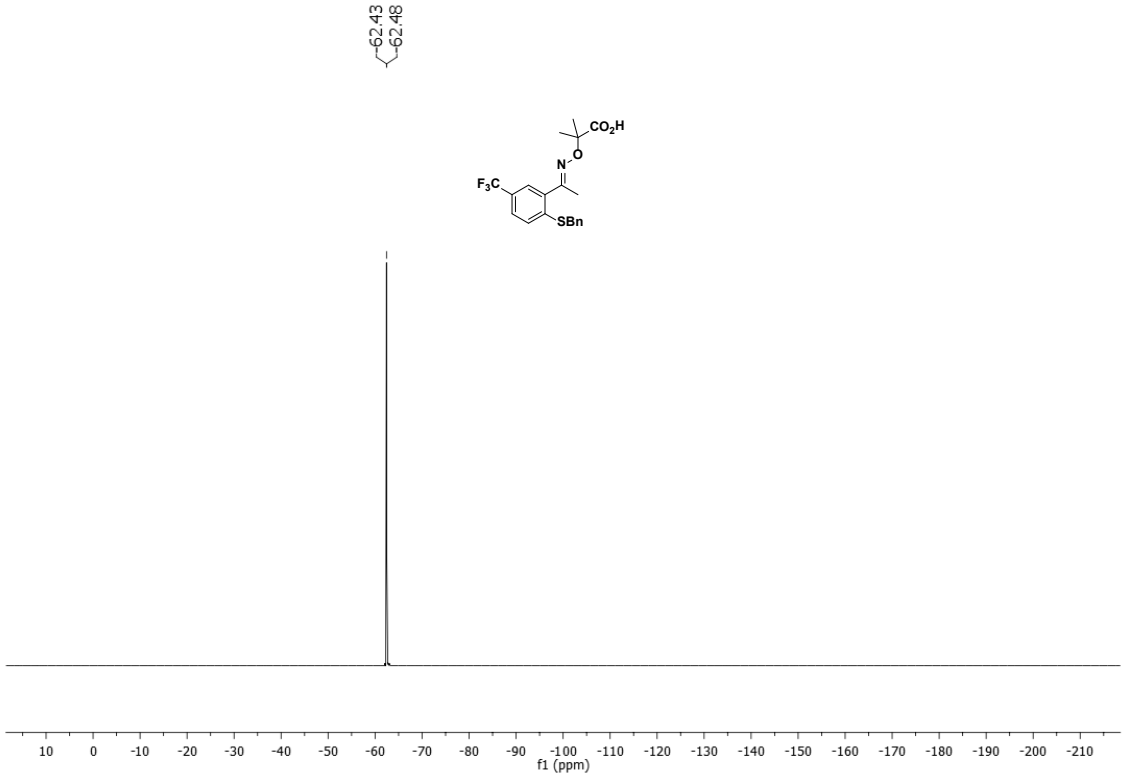
7.47
7.46
7.45
7.38
7.36
7.35
7.30
7.29
7.28
7.27
7.26
7.25
4.10
2.26
1.61
CO2H
N
O
F3C
SBn
1.07
2.17
1.34
5.37
2.03
2.96
5.98
f1 (ppm)


179.4
156.3
141.1
141.1
137.8
136.3
128.8
128.7
128.6
127.9
127.5
127.4
125.7
125.7
125.6
125.4
125.4
122.1
81.6
38.5
24.3
16.0
CO2H
N
O
F3C
SBn
f1 (ppm)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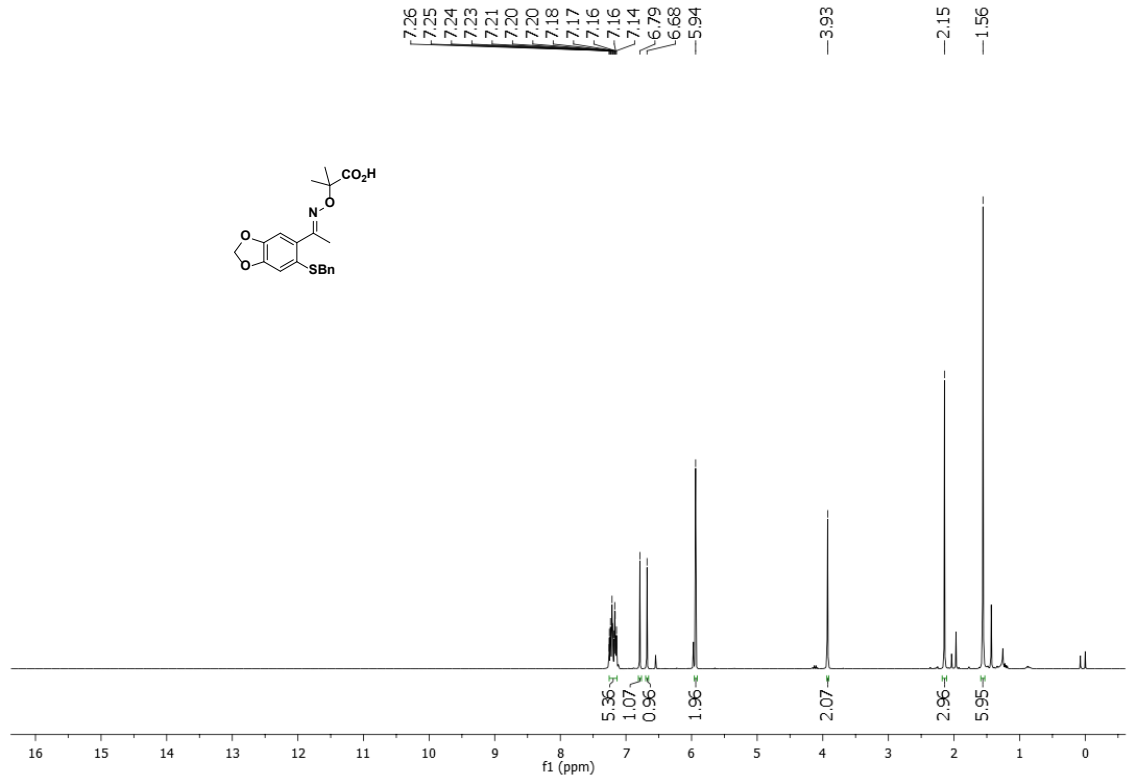
-62.48
CO2H
N
O
F3C
SBn
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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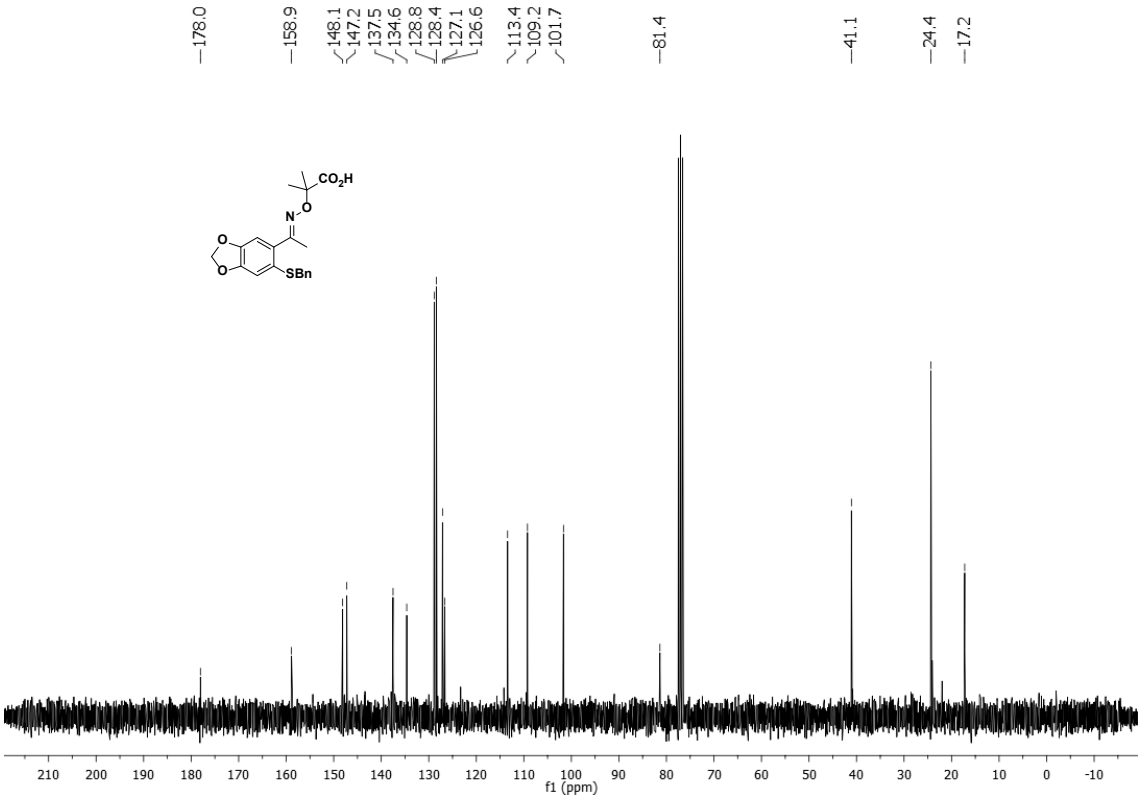
7.25
7.24
7.23
7.21
7.20
7.20
7.18
7.17
7.16
7.16
7.14
6.79
6.68
5.94
3.93
2.15
1.56
CO2H
N
O
O
O
SBn
5.36
1.07
0.96
1.96
2.07
2.96
5.95
f1 (ppm)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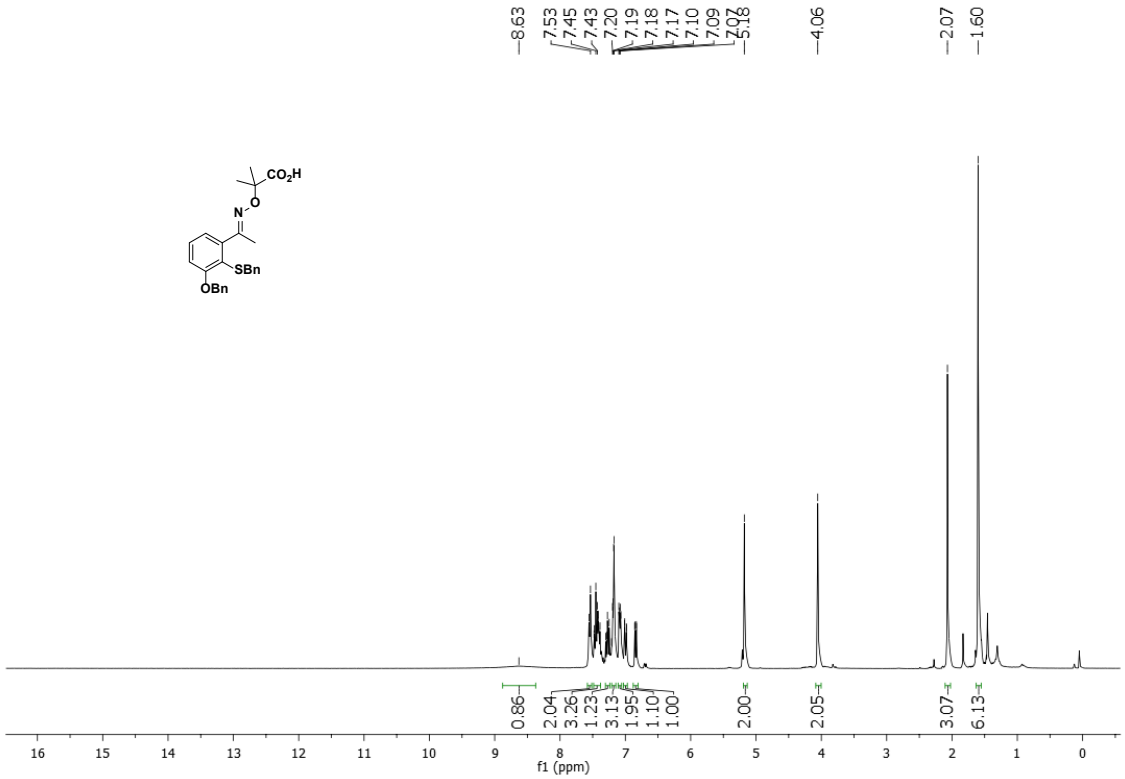
158.9
148.1
147.2
137.5
134.6
128.8
128.4
127.1
126.6
113.4
109.2
101.7
81.4
41.1
24.4
17.2
CO2H
N
O
O
O
SBn
f1 (ppm)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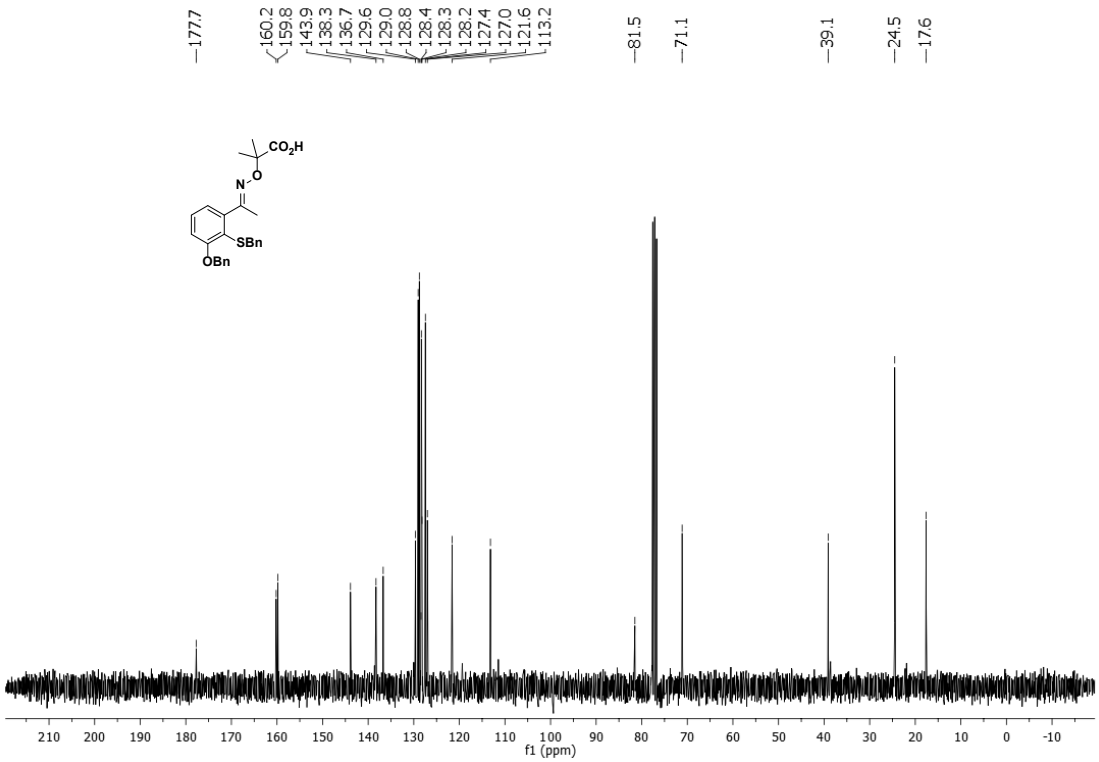
7.53
7.45
7.43
7.20
7.19
7.18
7.17
7.10
7.09
7.07
5.18
4.06
2.07
1.60
CO2H
N
O
SBn
OBn
0.86
2.04
3.26
1.23
3.13
1.95
1.10
1.00
2.00
2.05
3.07
6.13
f1 (ppm)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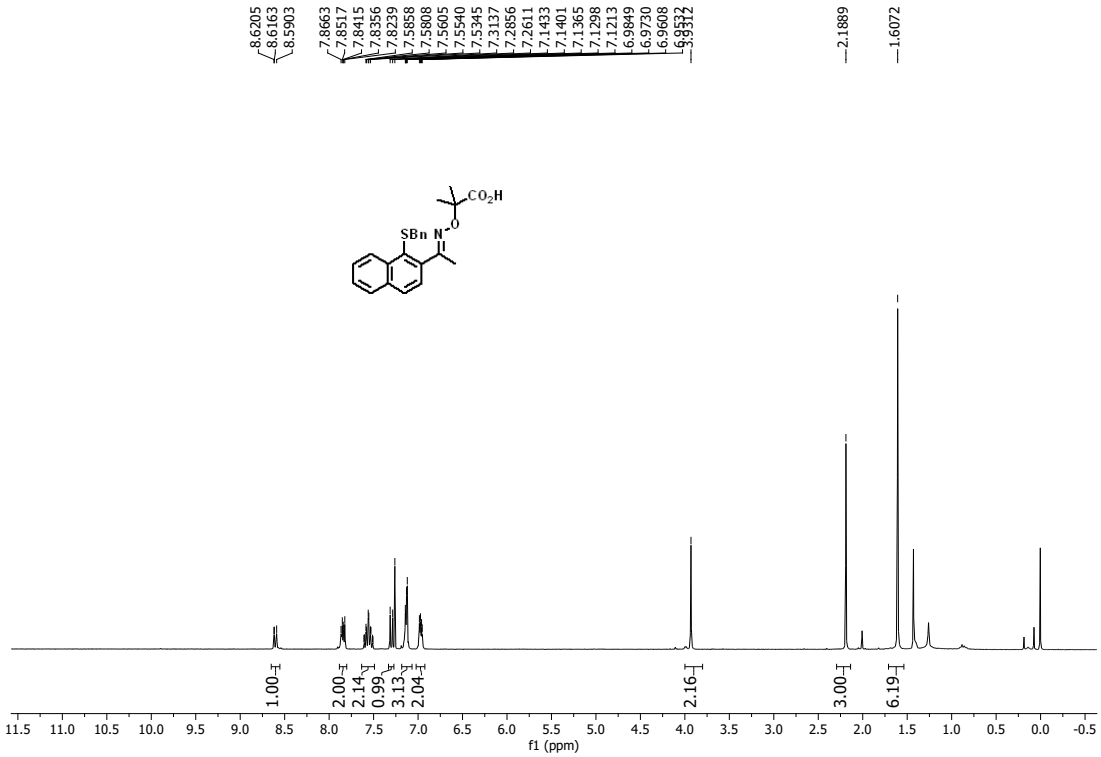
160.2
159.8
143.9
138.3
136.7
129.6
129.0
128.8
128.4
128.3
128.2
127.4
127.0
121.6
113.2
81.5
71.1
39.1
24.5
17.6
CO2H
N
O
SBn
OBn
f1 (ppm)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8.5903
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7.8517
7.8415
7.8356
7.8239
7.5858
7.5808
7.5605
7.5540
7.5345
7.3137
7.2856
7.2611
7.1433
7.1401
7.1365
7.1298
7.1213
6.9849
6.9730
6.9608
6.9532
3.9312
2.1889
1.6072
CO2H
SBn
N
O
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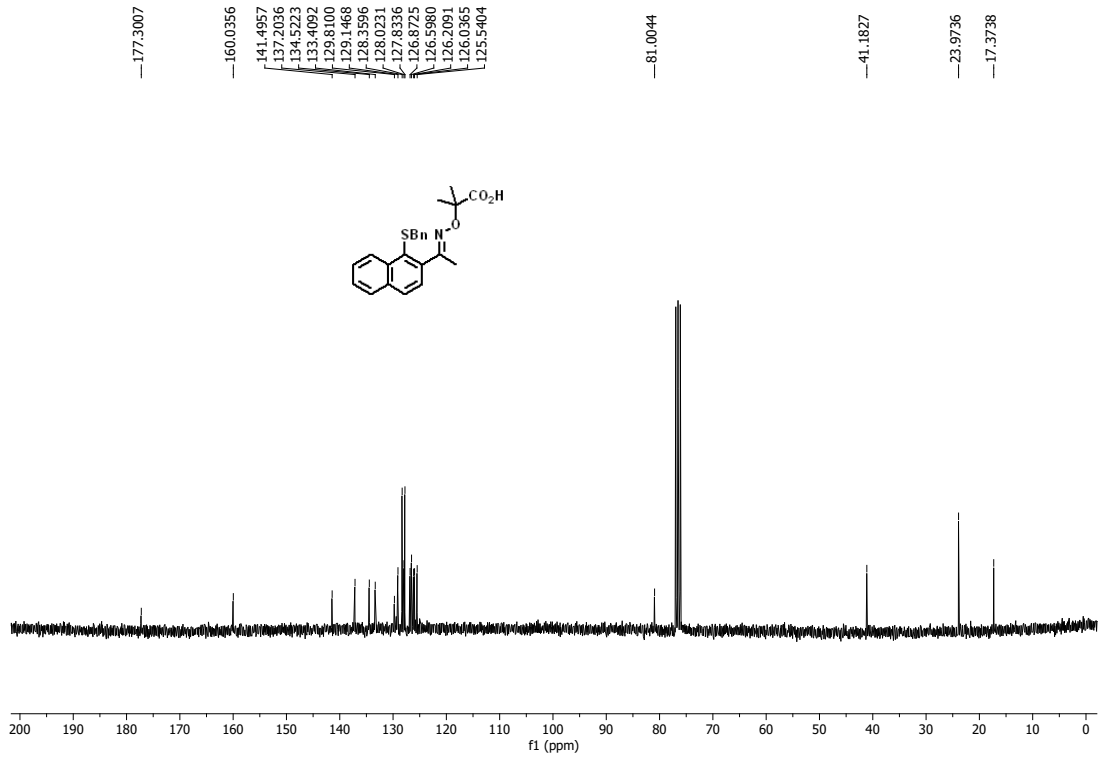
2.00
2.14
0.99
3.13
2.04
2.16
3.00
6.19
f1 (ppm)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134.5223
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129.8100
129.1468
128.3596
128.0231
127.8336
126.8725
126.5980
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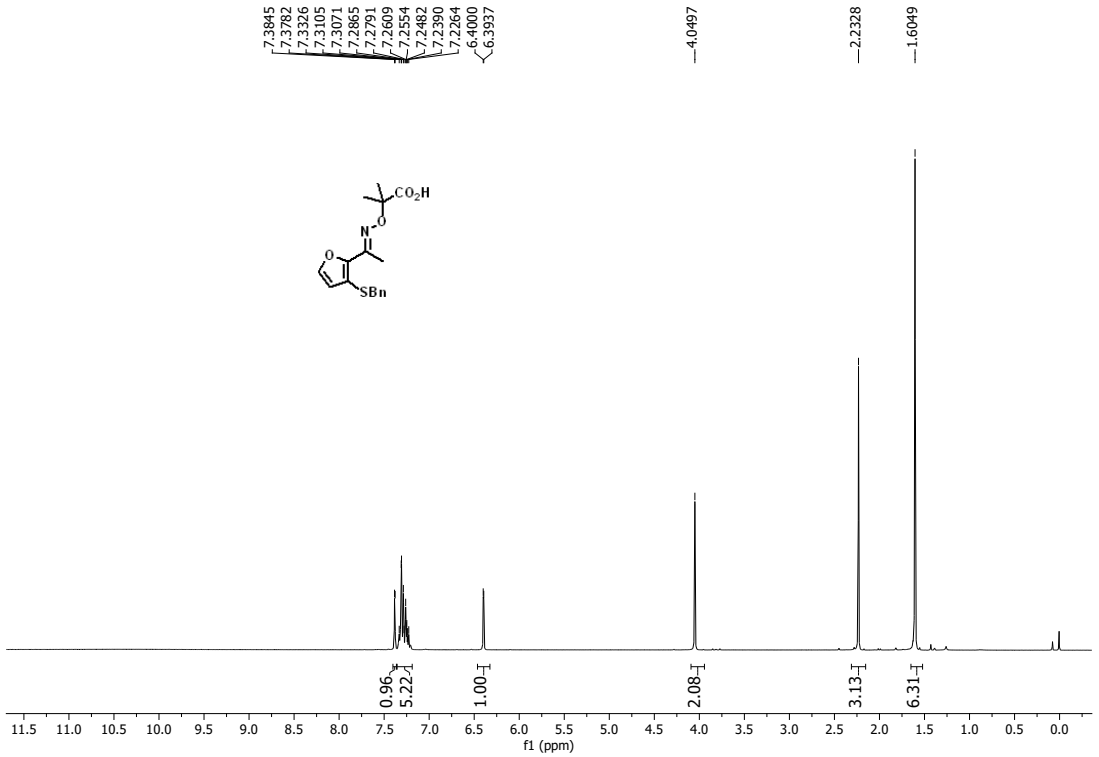
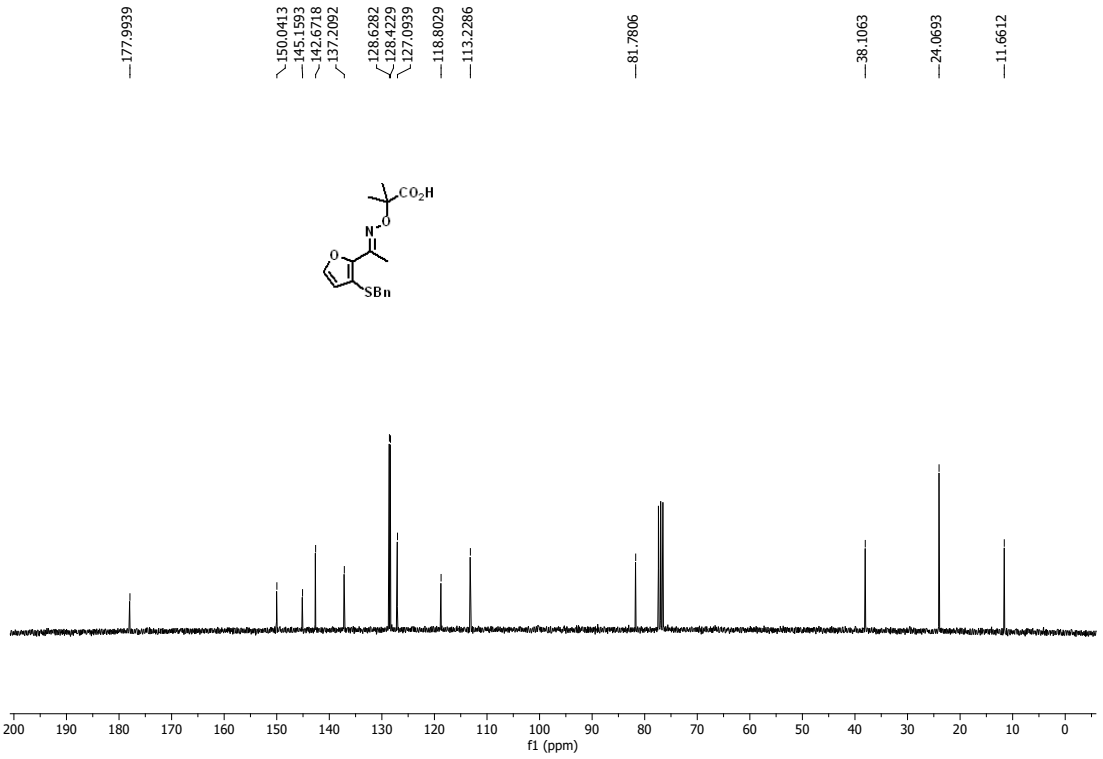
125.5404
81.0044
41.1827
23.9736
17.3738
CO2H
SBn
N
O
f1 (ppm)


7.3845
7.3782
7.3326
7.3105
7.3071
7.2865
7.2791
7.2609
7.2554
7.2482
7.2390
7.2264
6.4000
6.3937
4.0497
2.2328
1.6049
CO2H
N
O
O
SBn
0.96
5.22
1.00
2.08
3.13
6.31
f1 (ppm)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145.1593
142.6718
137.2092
128.6282
128.4229
127.0939
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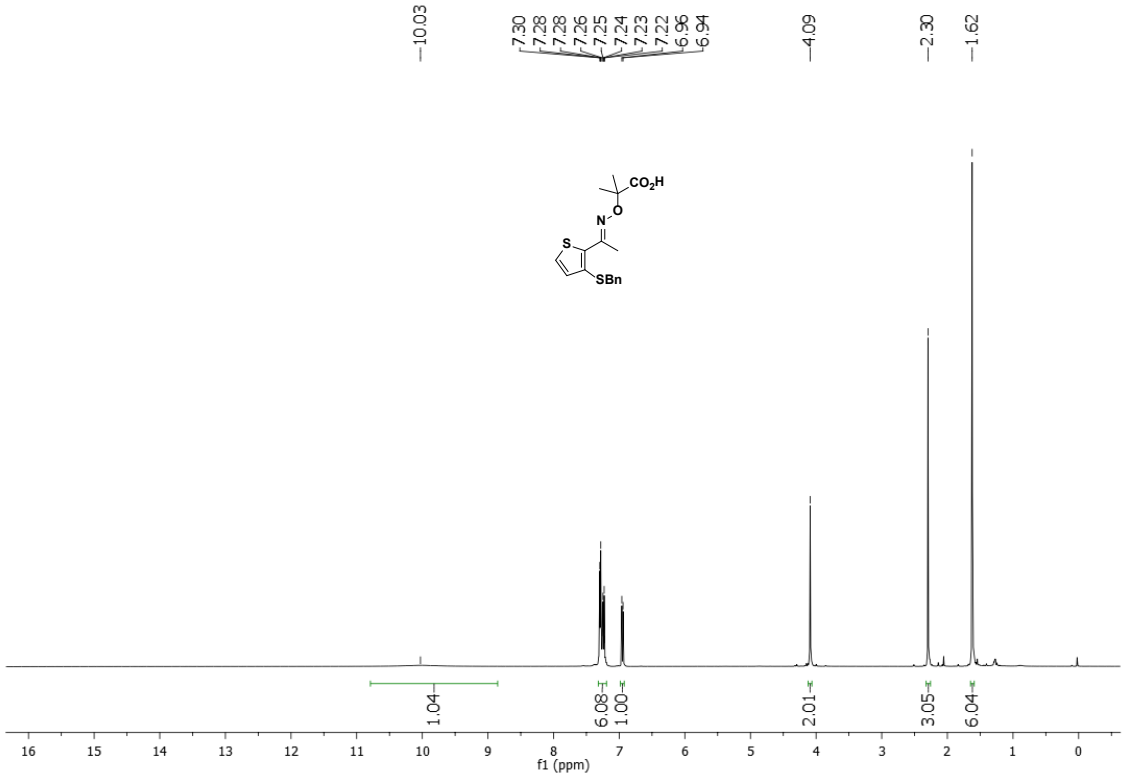
81.7806
38.1063
24.0693
11.6612
CO2H
N
O
O
SBn
f1 (ppm)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7.30
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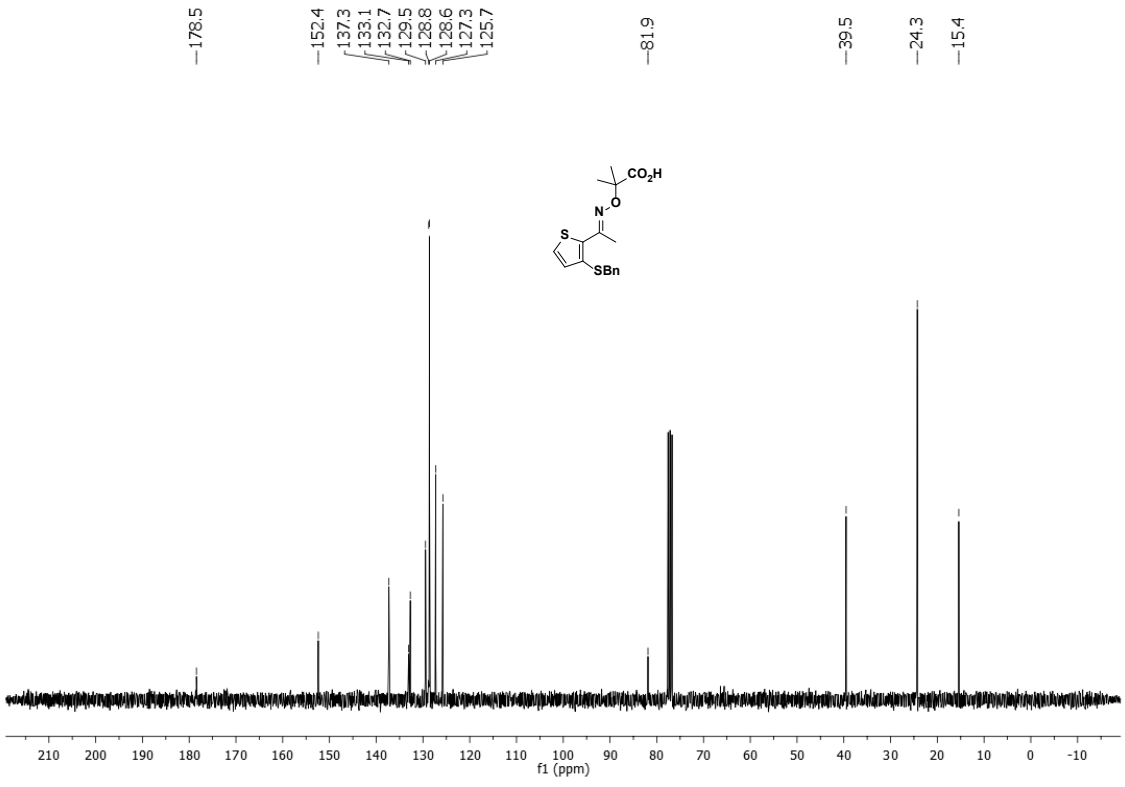
7.28
7.26
7.25
7.24
7.23
7.22
6.96
6.94
4.09
2.30
1.62
CO2H
N
O
S
SBn
1.04
6.08
1.00
2.01
3.05
6.04
f1 (ppm)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133.1
132.7
129.5
128.8
128.6
127.3
125.7
81.9
39.5
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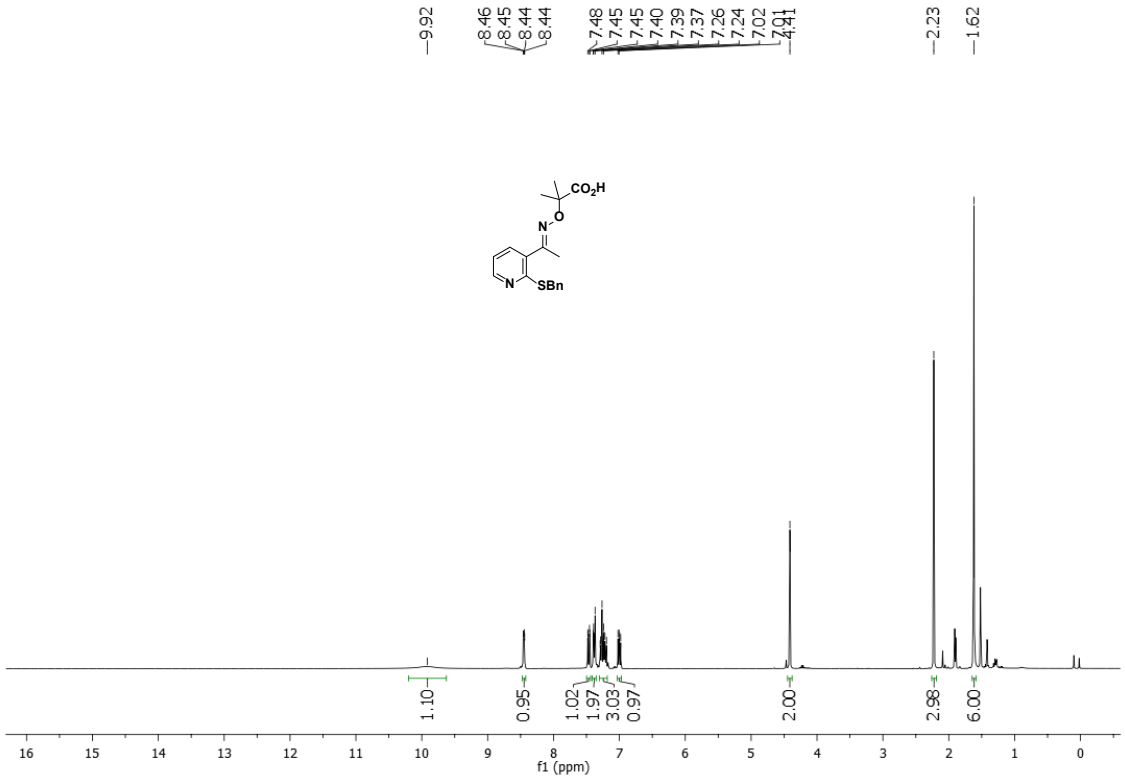
15.4
CO2H
N
O
S
SBn
f1 (ppm)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8.44
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7.45
7.45
7.40
7.39
7.37
7.26
7.24
7.02
7.01
4.41
2.23
1.62
CO2H
O
N
SBn
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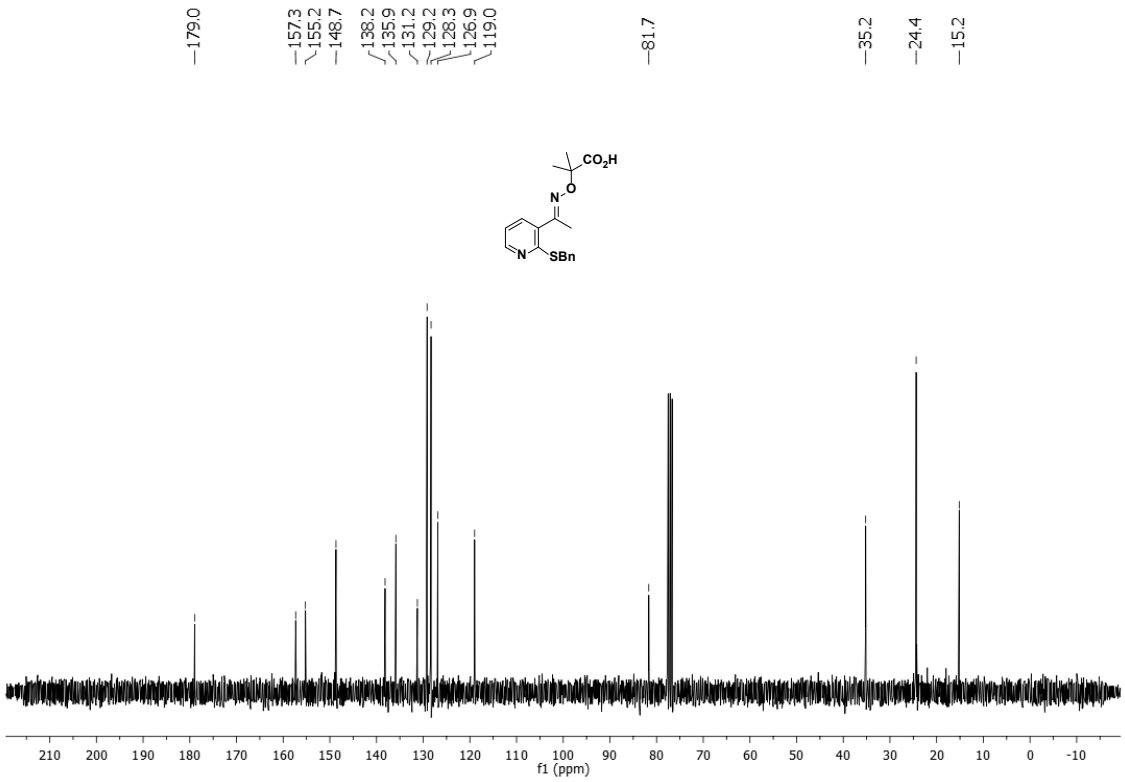
0.95
1.02
1.97
3.03
0.97
2.00
2.98
6.00
f1 (ppm)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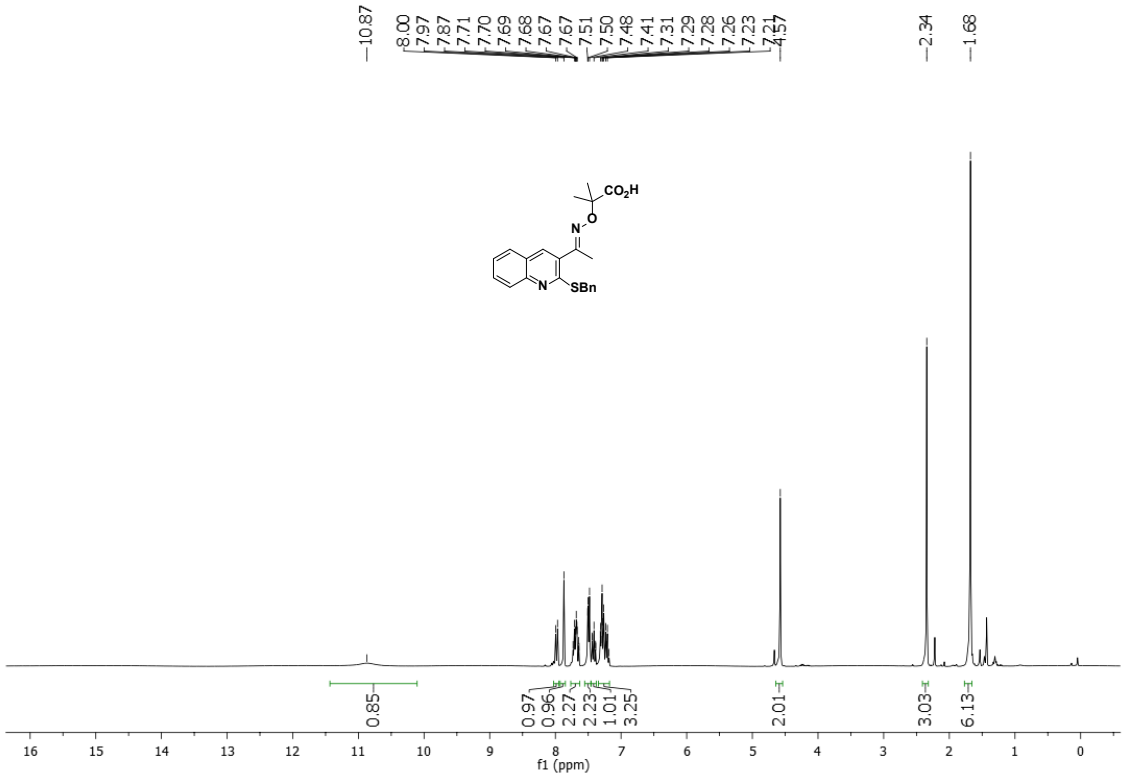
155.2
148.7
138.2
135.9
131.2
129.2
128.3
126.9
119.0
81.7
35.2
24.4
15.2
CO2H
O
N
SBn
f1 (ppm)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7.70
7.69
7.68
7.67
7.67
7.51
7.50
7.48
7.41
7.31
7.29
7.28
7.26
7.23
7.21
4.57
2.34
1.68
CO2H
N
O
N
SBn
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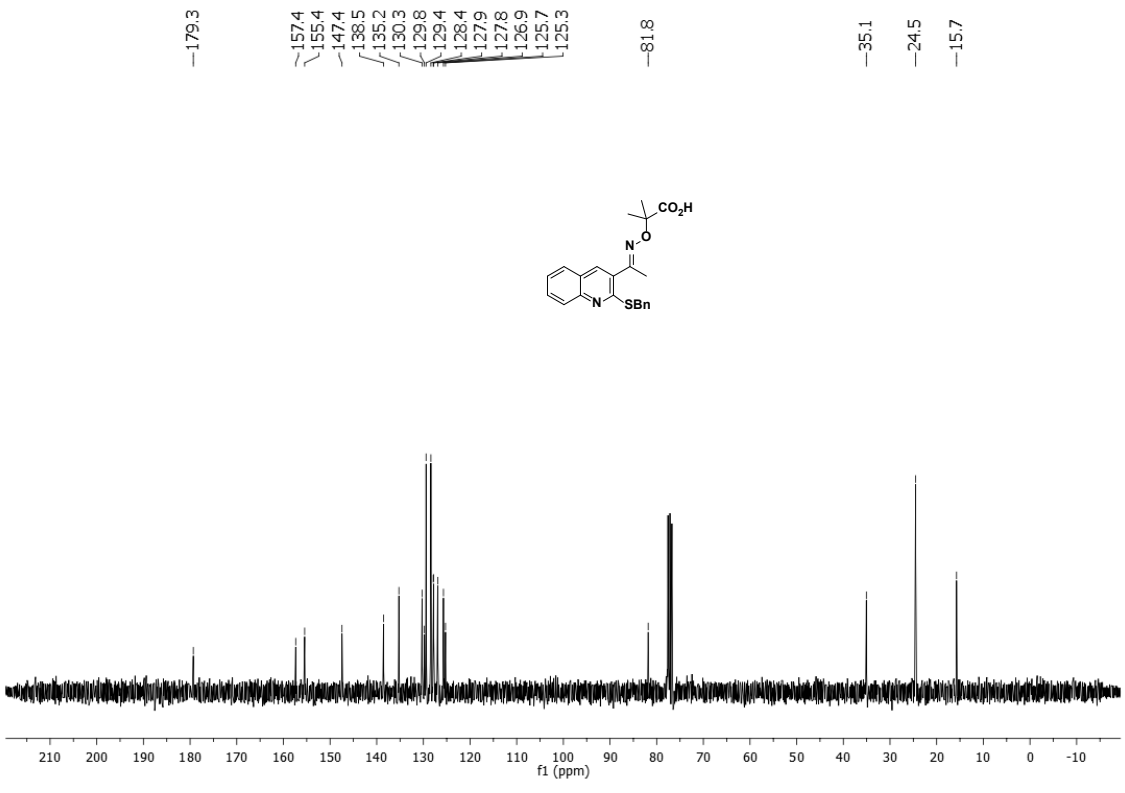
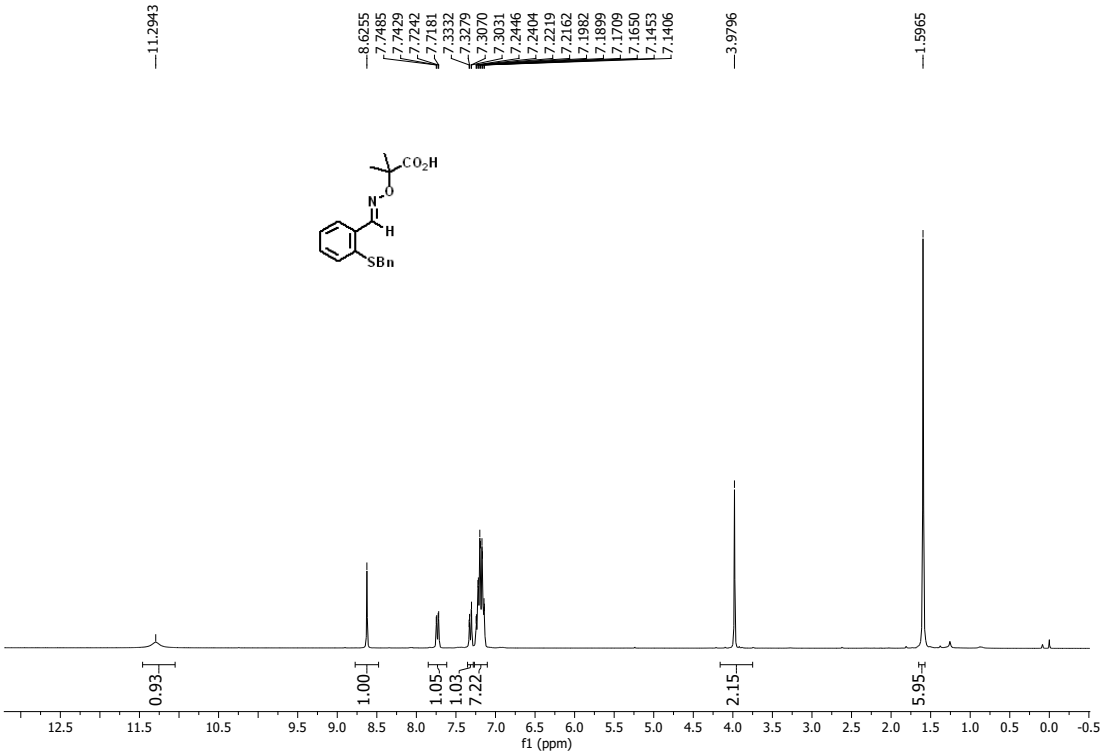
0.96
2.27
2.23
1.01
3.25
2.01
3.03
6.13
f1 (ppm)


179.3
157.4
155.4
147.4
138.5
135.2
130.3
129.8
129.4
128.4
127.9
127.8
126.9
125.7
125.3
81.8
35.1
24.5
15.7
CO2H
N
O
N
SBn
f1 (ppm)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7.7485
7.7429
7.7242
7.7181
7.3332
7.3279
7.3070
7.3031
7.2446
7.2404
7.2219
7.2162
7.1982
7.1899
7.1709
7.1650
7.1453
7.1406
3.9796
1.5965
CO2H
N
O
H
SBn
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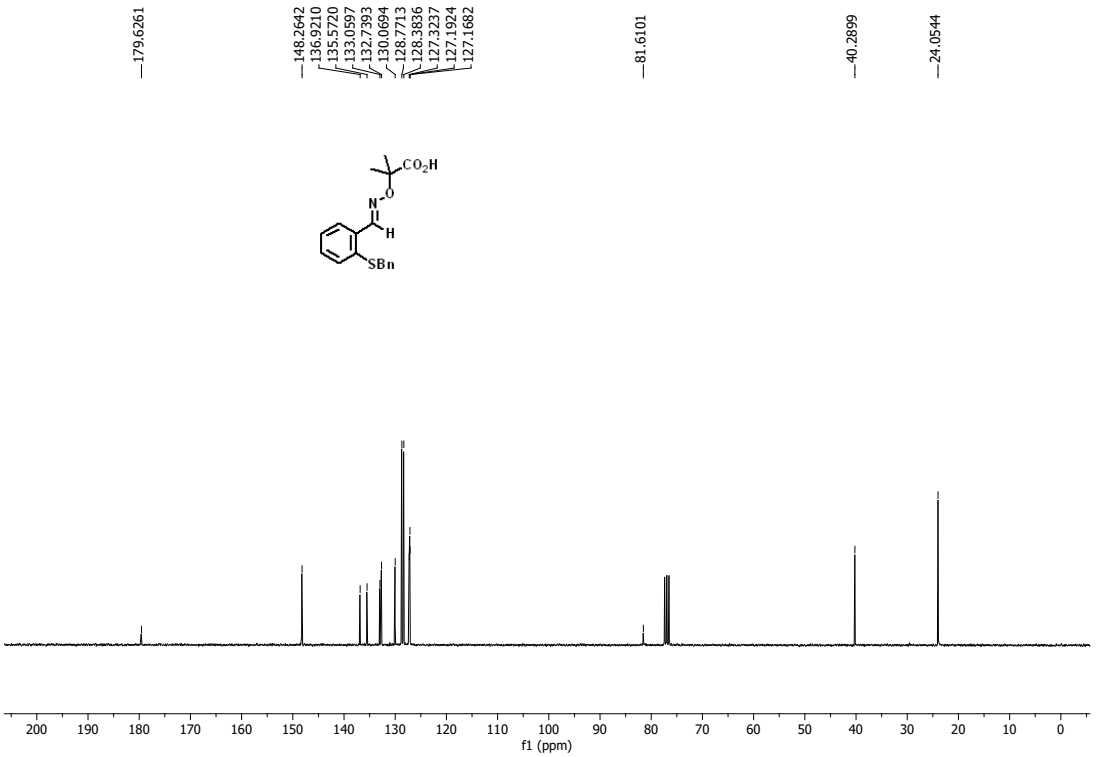
1.00
1.05
1.03
7.22
2.15
5.95
f1 (ppm)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132.7393
130.0694
128.7713
128.3836
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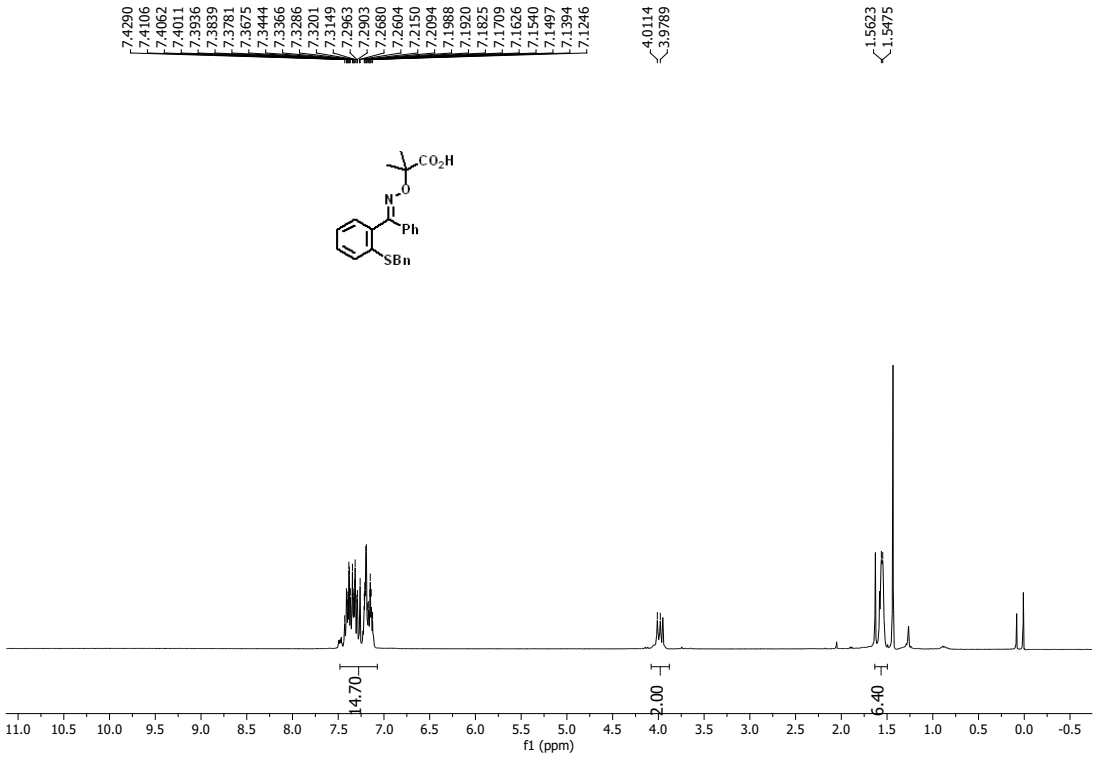
127.1924
127.1682
81.6101
40.2899
24.0544
CO2H
N
O
H
SBn
f1 (ppm)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7.3366
7.3286
7.3201
7.3149
7.2963
7.2903
7.2680
7.2604
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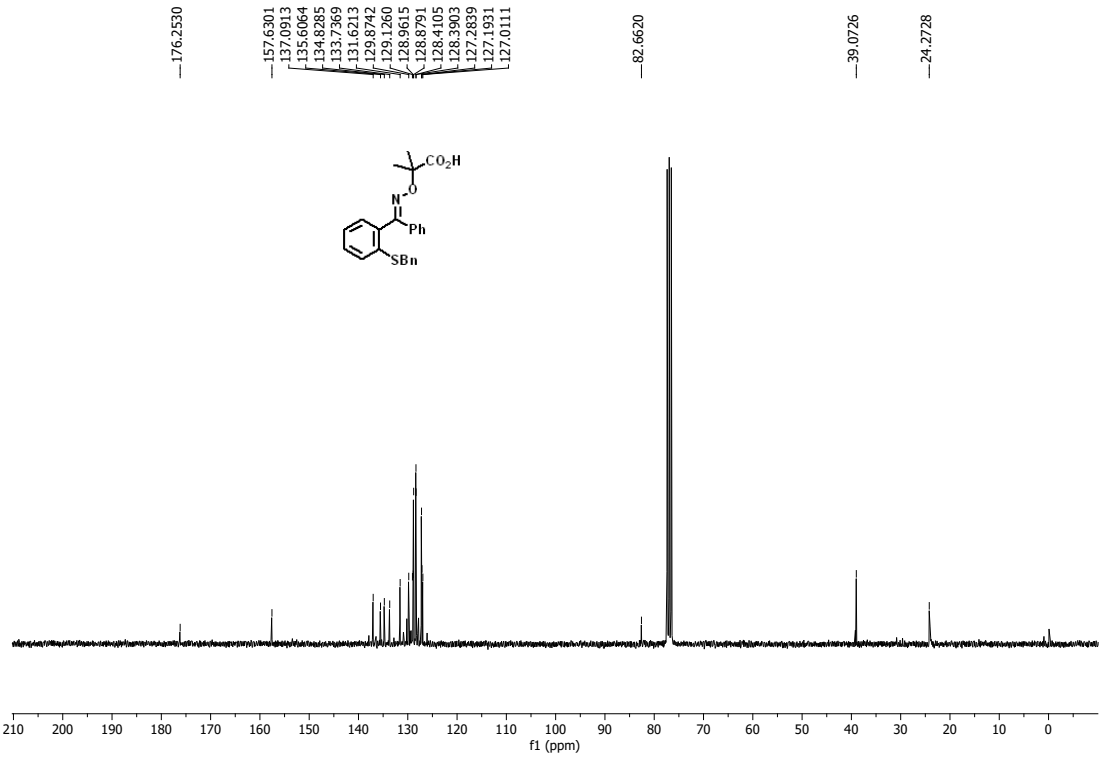
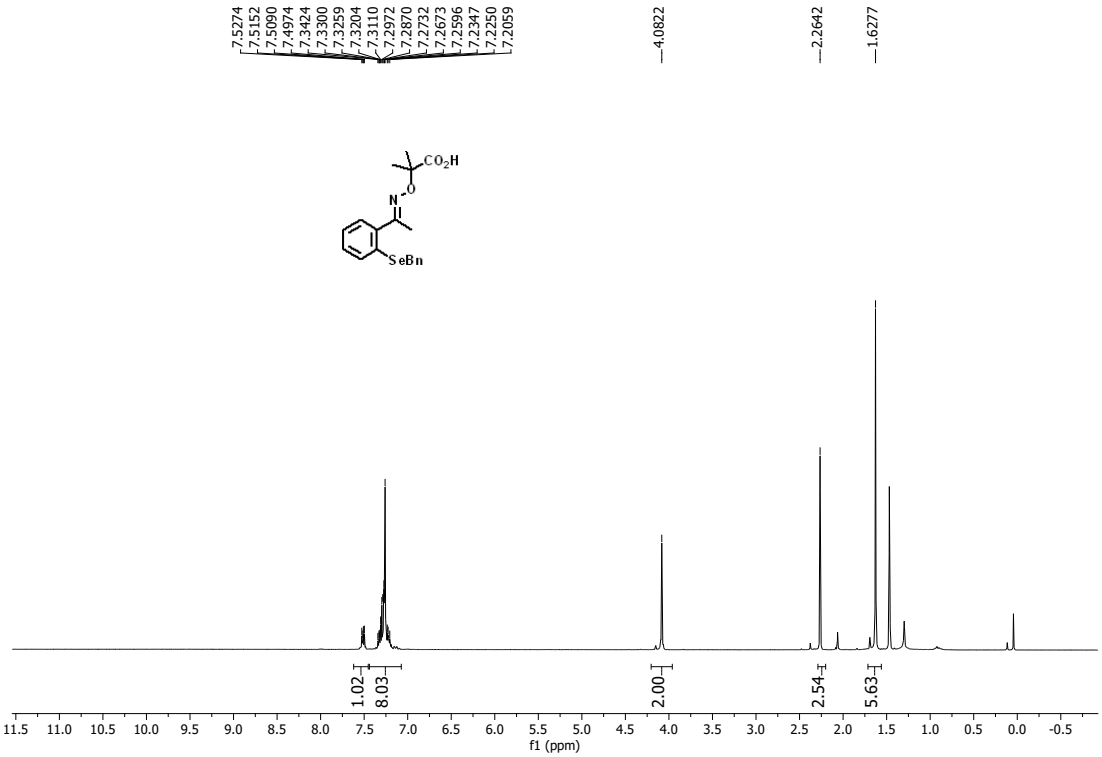
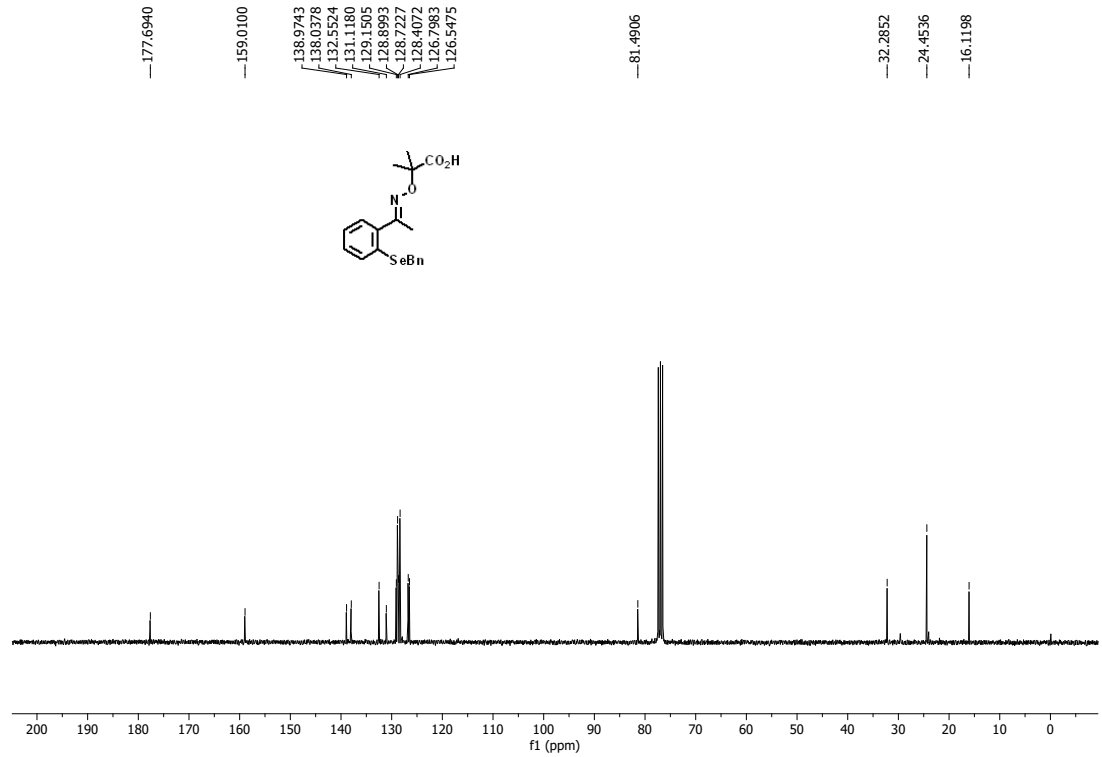
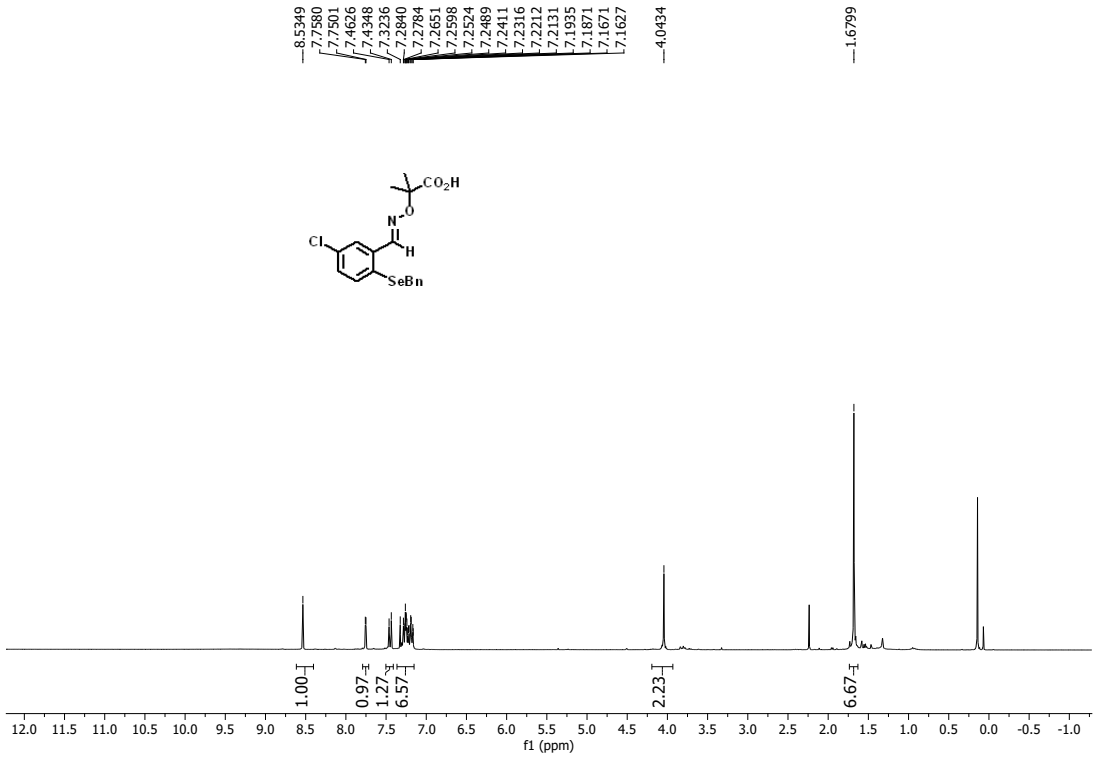
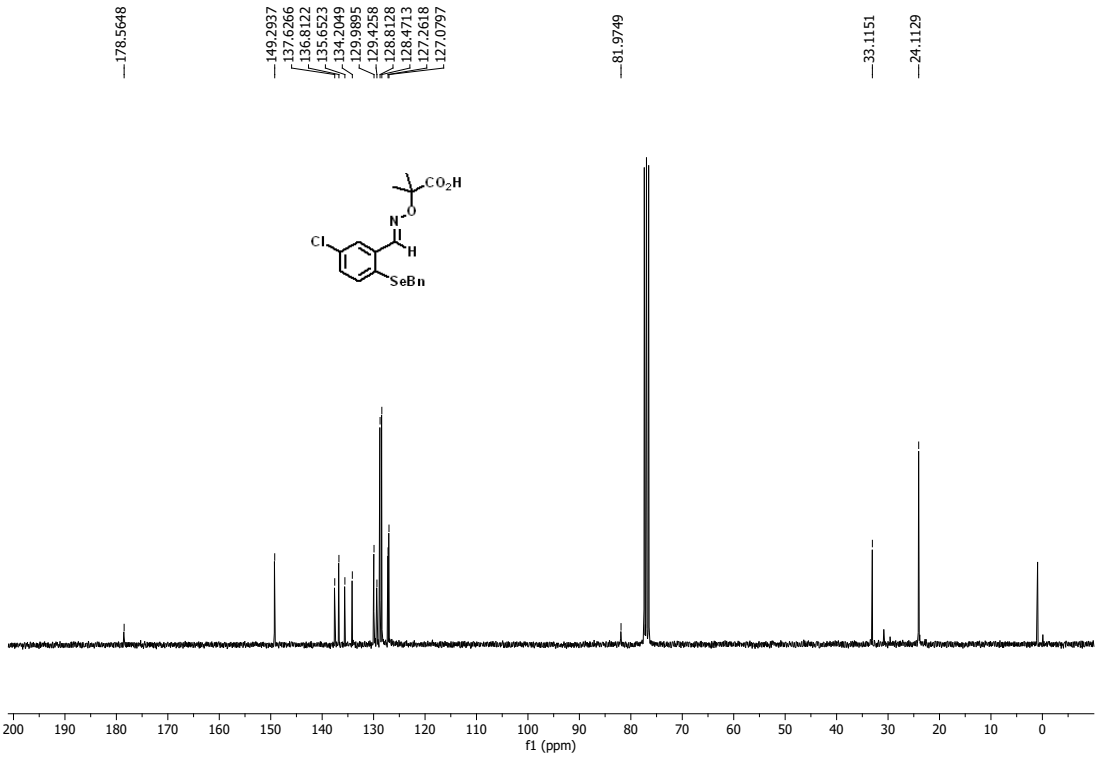
7.1988
7.1920
7.1825
7.1709
7.1626
7.1540
7.1497
7.1394
7.1246
4.0114
3.9789
1.5623
1.5475
CO2H
N
O
Ph
SBn
14.70
2.00
6.40
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

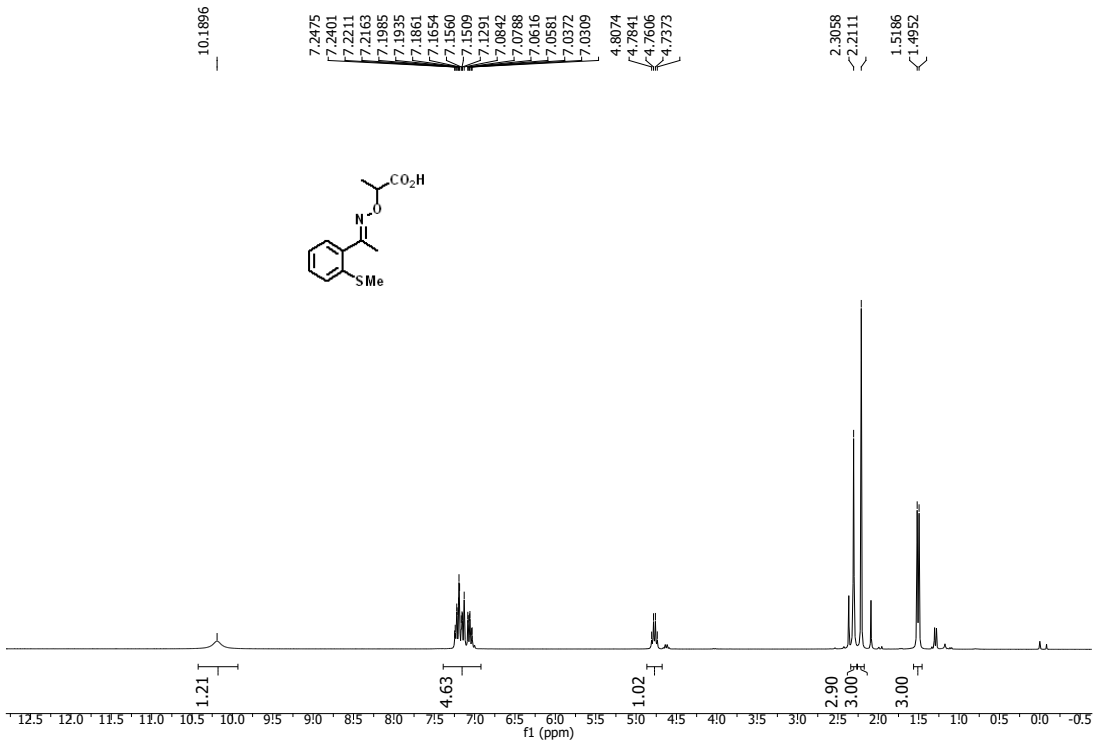

176.2530
157.6301
137.0913
135.6064
134.8285
133.7369
131.6213
129.8742
129.1260
128.9615
128.8791
128.4105
128.3903
127.2839
127.1931
127.0111
82.6620
39.0726
24.2728
CO2H
N
O
Ph
SBn
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

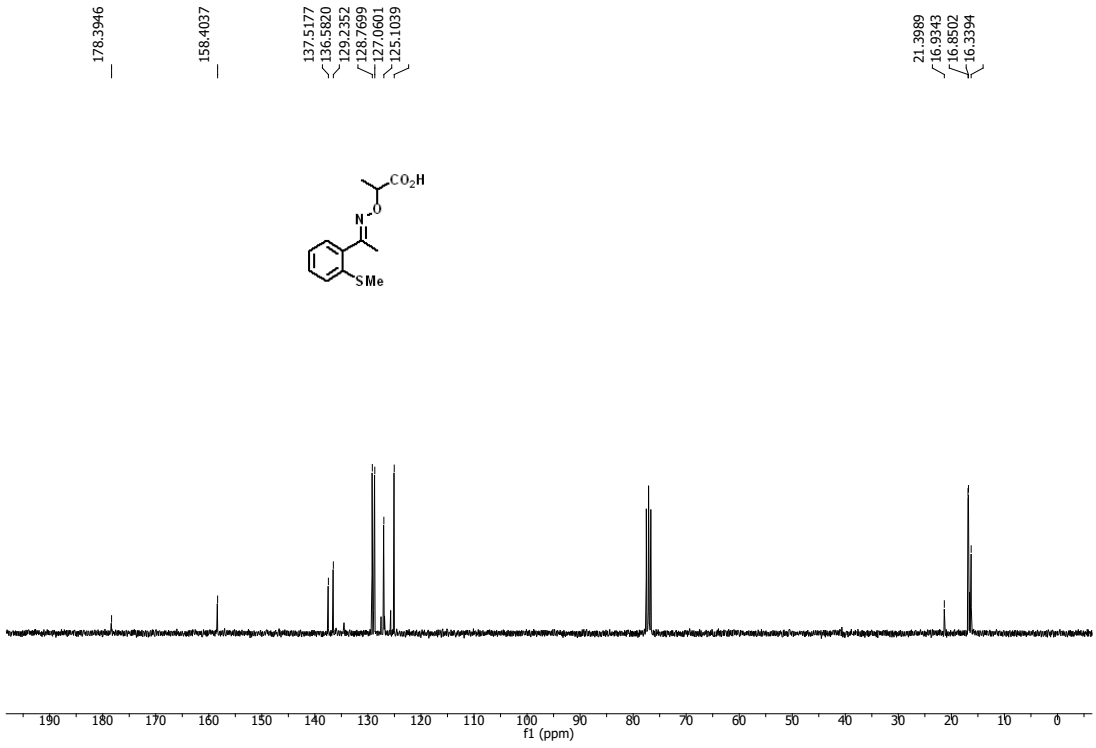

7.5274
7.5152
7.5090
7.4974
7.3424
7.3300
7.3259
7.3204
7.3110
7.2972
7.2870
7.2732
7.2673
7.2596
7.2347
7.2250
7.2059
4.0822
2.2642
1.6277
CO2H
N
O
SeBn
1.02
8.03
2.00
2.54
5.63
f1 (ppm)

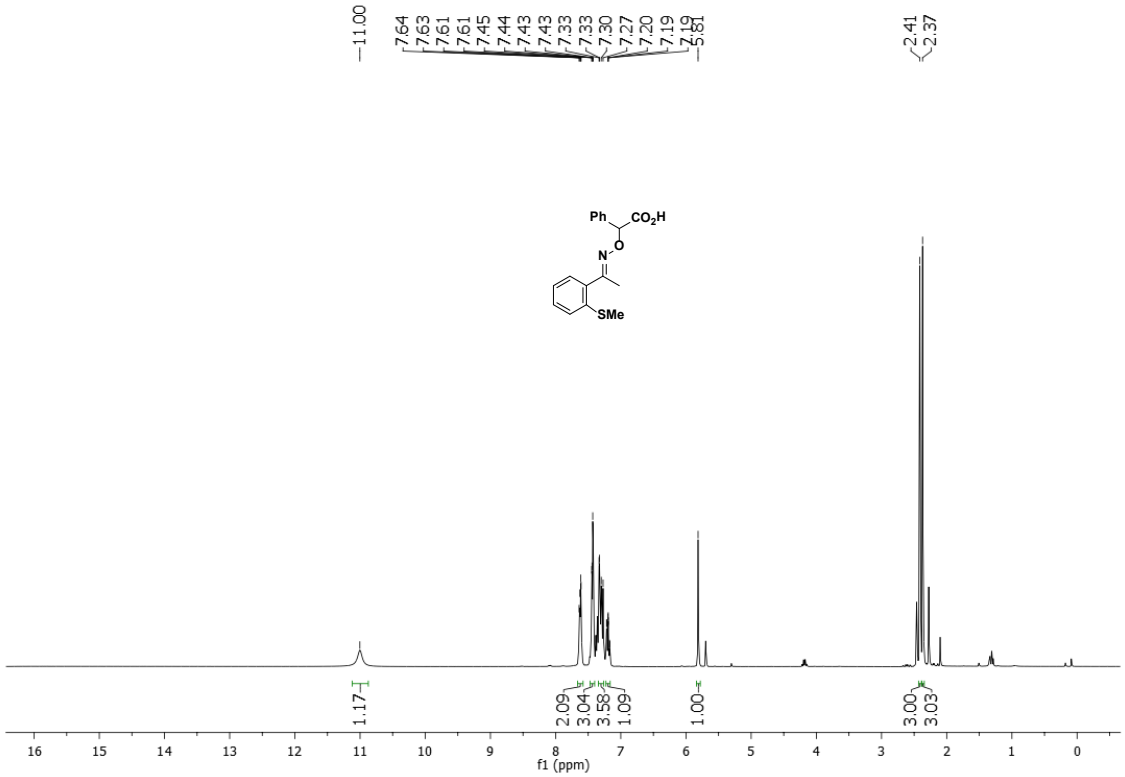

177.6940
159.0100
138.9743
138.0378
132.5524
131.1180
129.1505
128.8993
128.7227
128.4072
126.7983
126.5475
81.4906
32.2852
24.4536
16.1198
CO2H
N
O
SeBn
f1 (ppm)

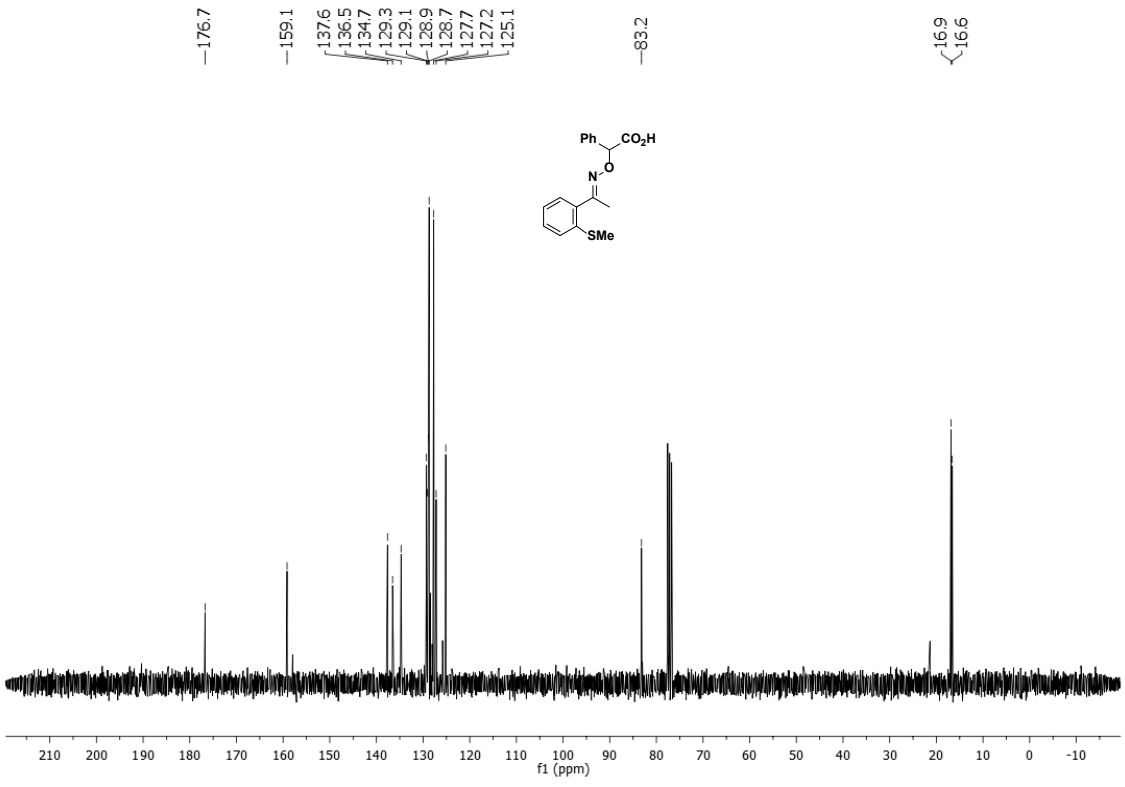

8.5349
7.7580
7.7501
7.4626
7.4348
7.3236
7.2840
7.2784
7.2651
7.2598
7.2524
7.2489
7.2411
7.2316
7.2212
7.2131
7.1935
7.1871
7.1671
7.1627
4.0434
1.6799
CO2H
N
O
H
Cl
SeBn
1.00
0.97
1.27
6.57
2.23
6.67
f1 (ppm)


178.5648
149.2937
137.6266
136.8122
135.6523
134.2049
129.9895
129.4258
128.8128
128.4713
127.2618
127.0797
81.9749
33.1151
24.1129
CO2H
N
O
H
Cl
SeBn
f1 (ppm)

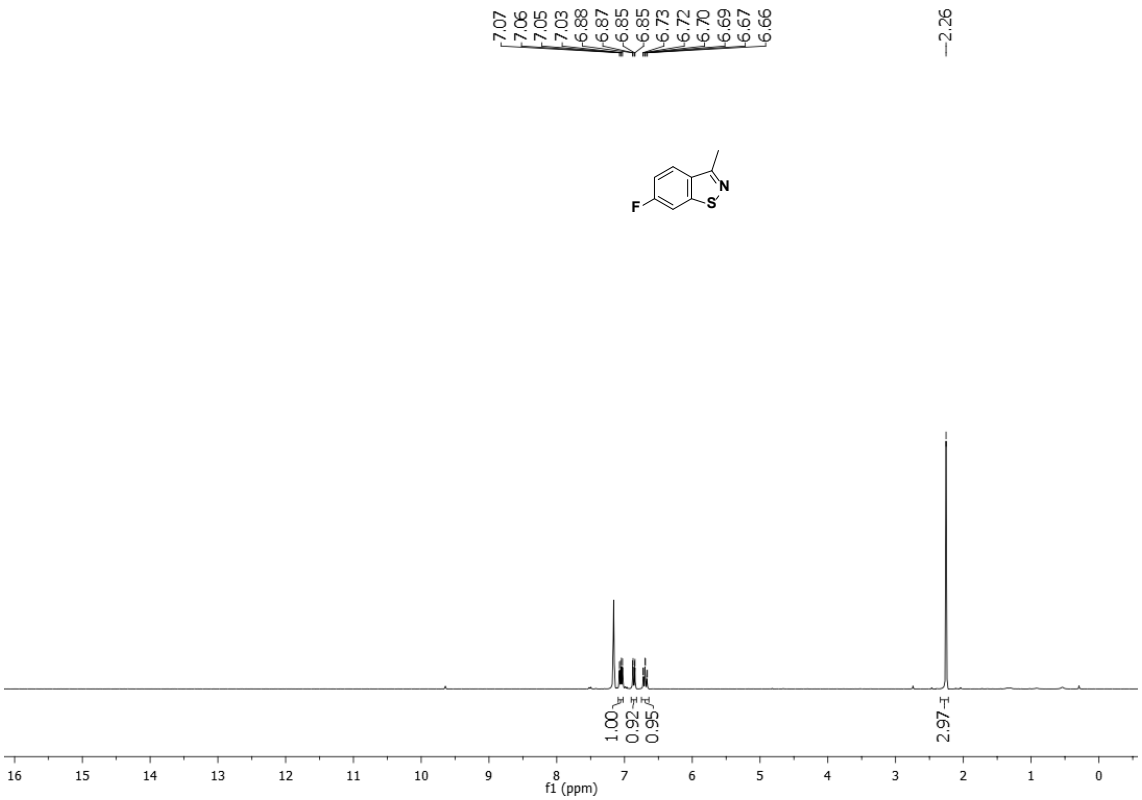

10.1896
7.2475
7.2401
7.2211
7.2163
7.1985
7.1935
7.1861
7.1654
7.1560
7.1509
7.1291
7.0842
7.0788
7.0616
7.0581
7.0372
7.0309
4.8074
4.7841
4.7606
4.7373
2.3058
2.2111
1.5186
1.4952
CO2H
N
O
SMe
1.21
4.63
1.02
2.90
3.00
3.00
f1 (ppm)

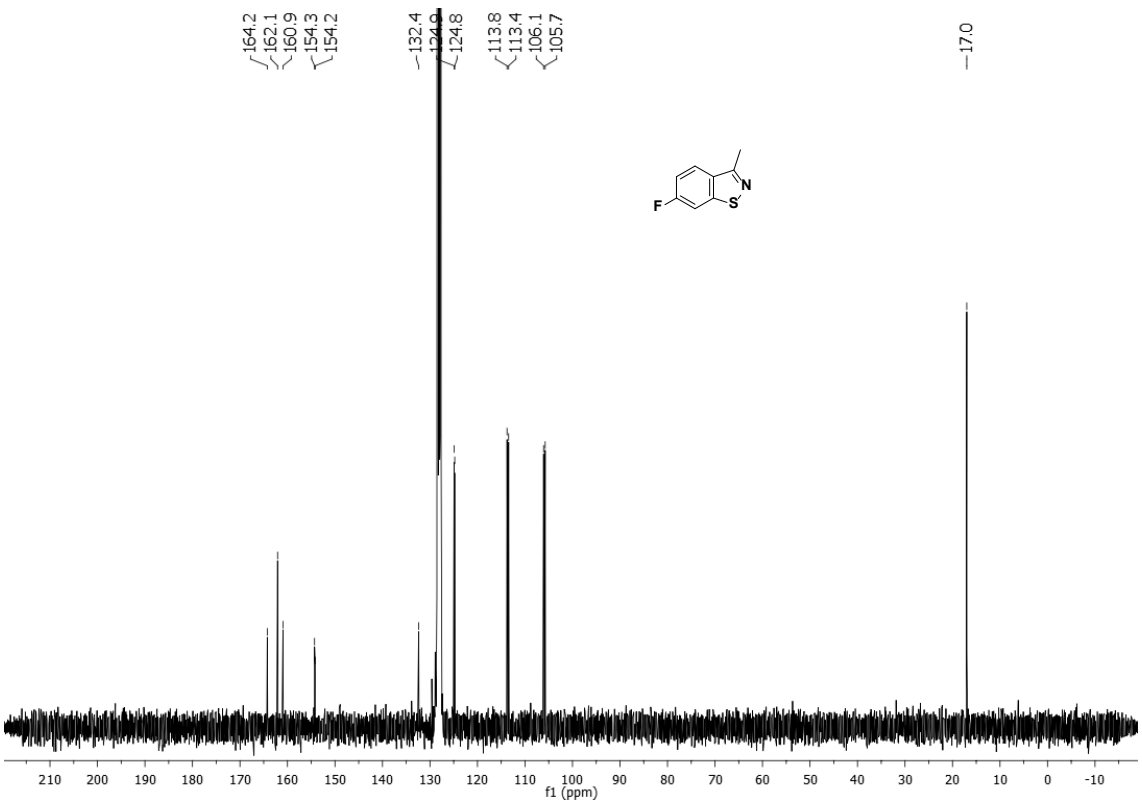

178.3946
158.4037
137.5177
136.5820
129.2352
128.7699
127.0601
125.1039
21.3989
16.9343
16.8502
16.3394
CO2H
N
O
SMe
f1 (ppm)

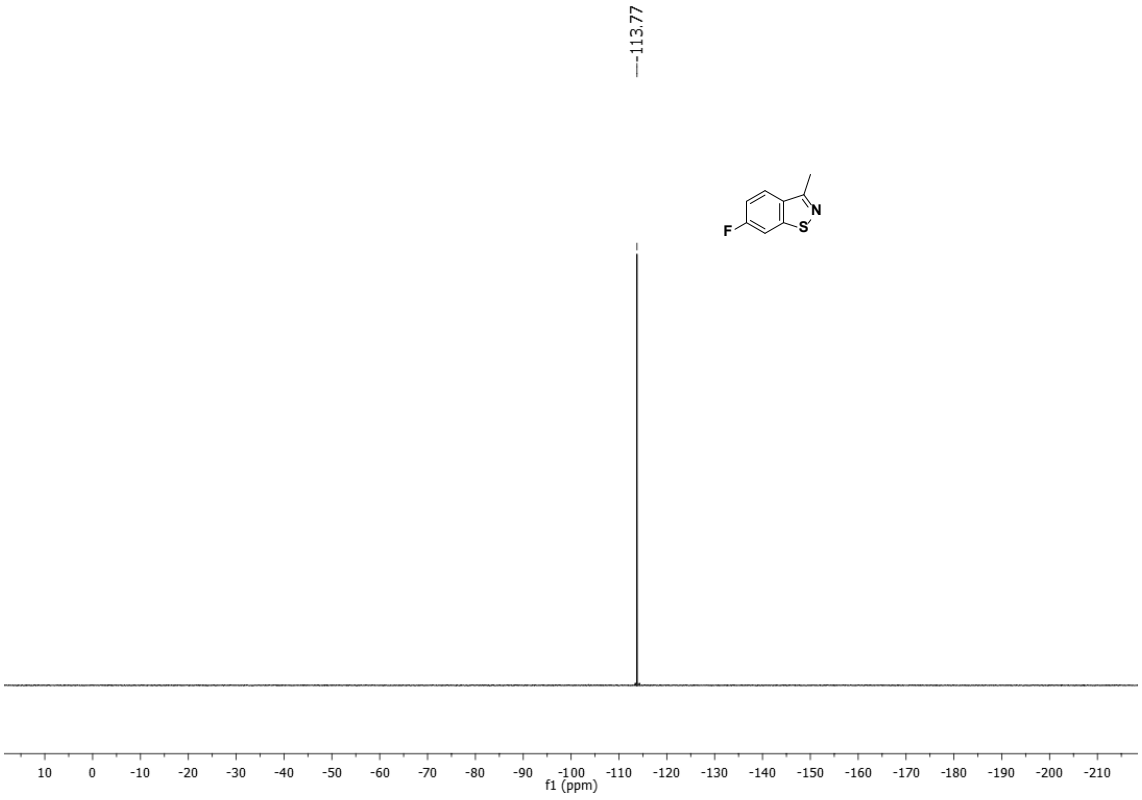

11.00
7.64
7.63
7.61
7.61
7.45
7.44
7.43
7.43
7.33
7.33
7.30
7.27
7.20
7.19
7.19
5.81
2.41
2.37
Ph
CO2H
N
O
SMe
1.17
2.09
3.04
3.58
1.09
1.00
3.00
3.03
f1 (ppm)

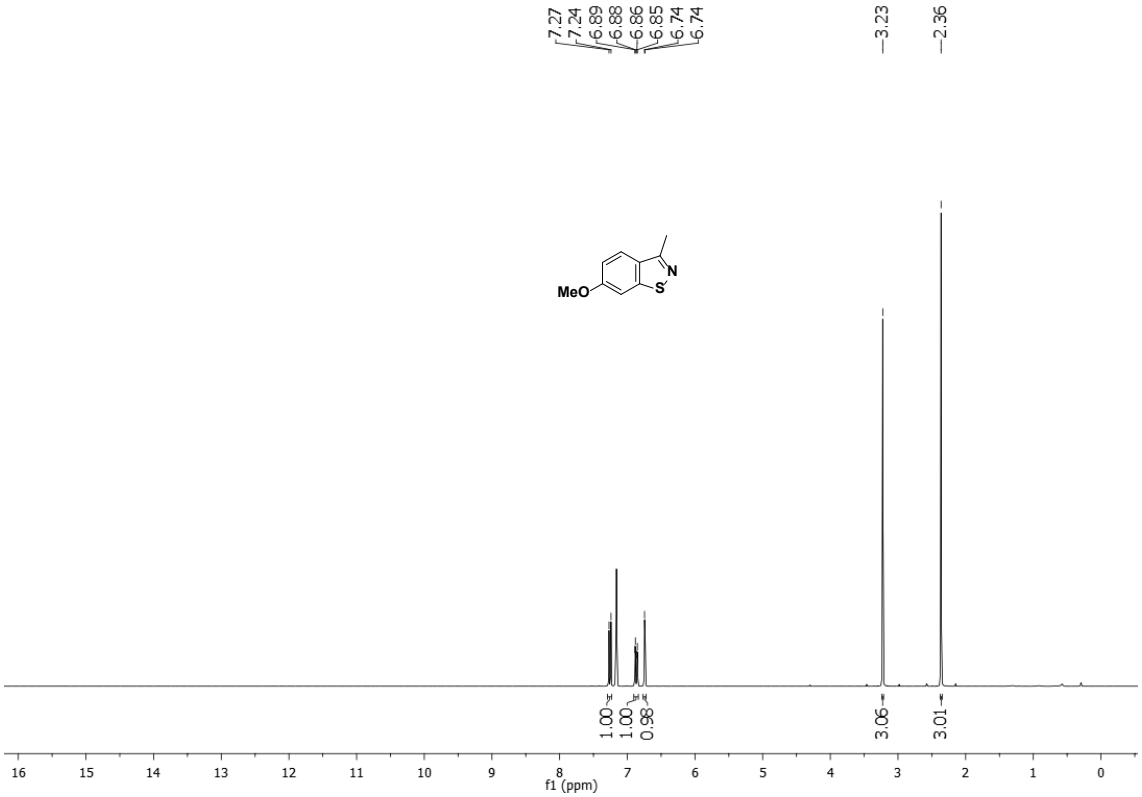

176.7
159.1
137.6
136.5
134.7
129.3
129.1
128.9
128.7
127.7
127.2
125.1
83.2
16.9
16.6
Ph
CO2H
N
O
SMe
f1 (ppm)

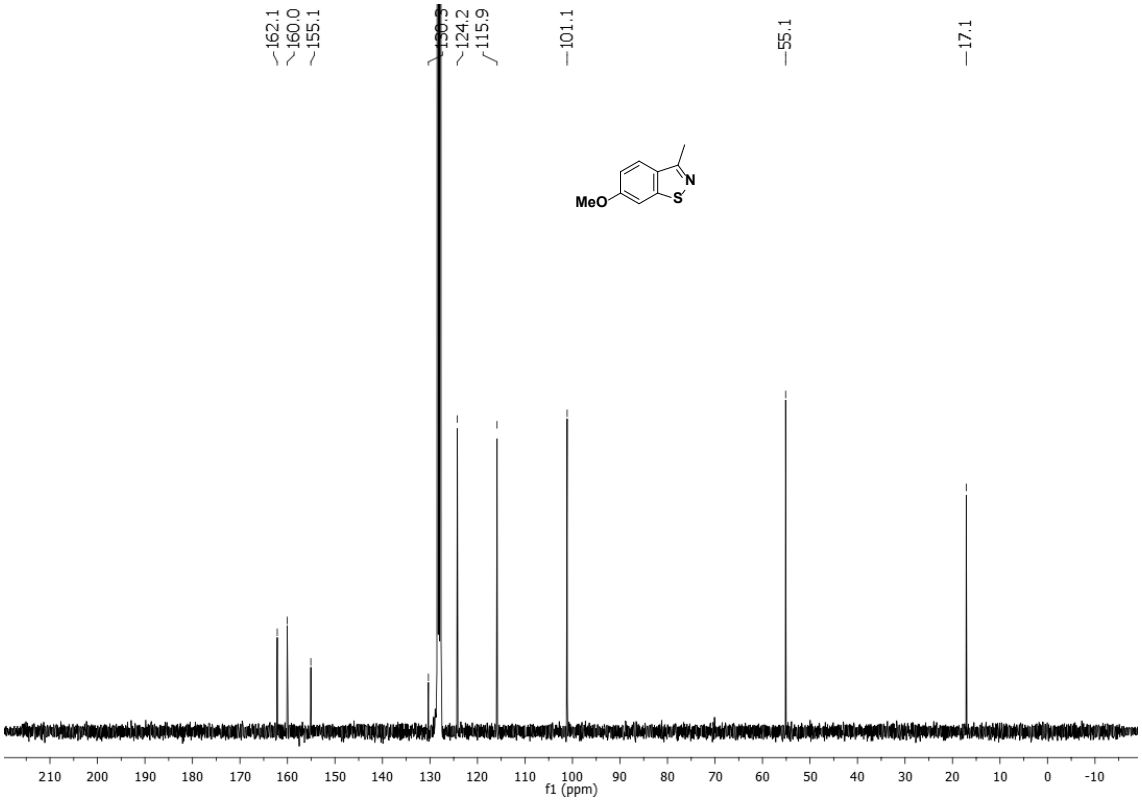
## 10.4. NMR Spectra of Isothiazoles 2

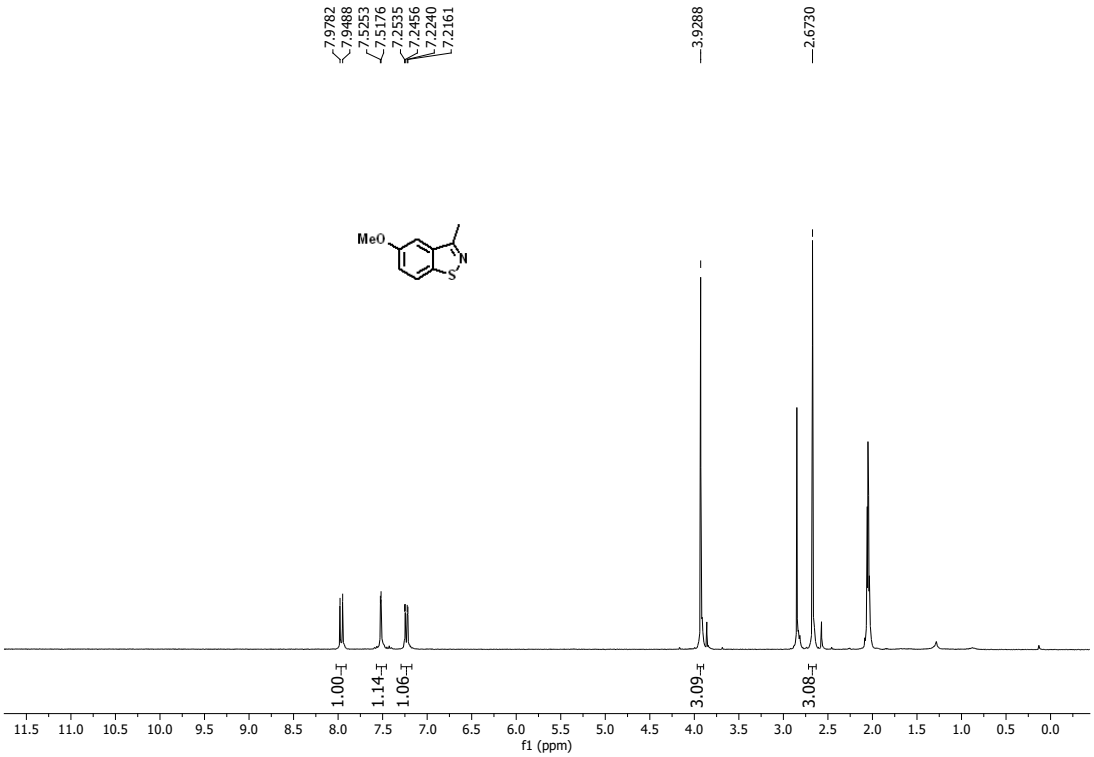


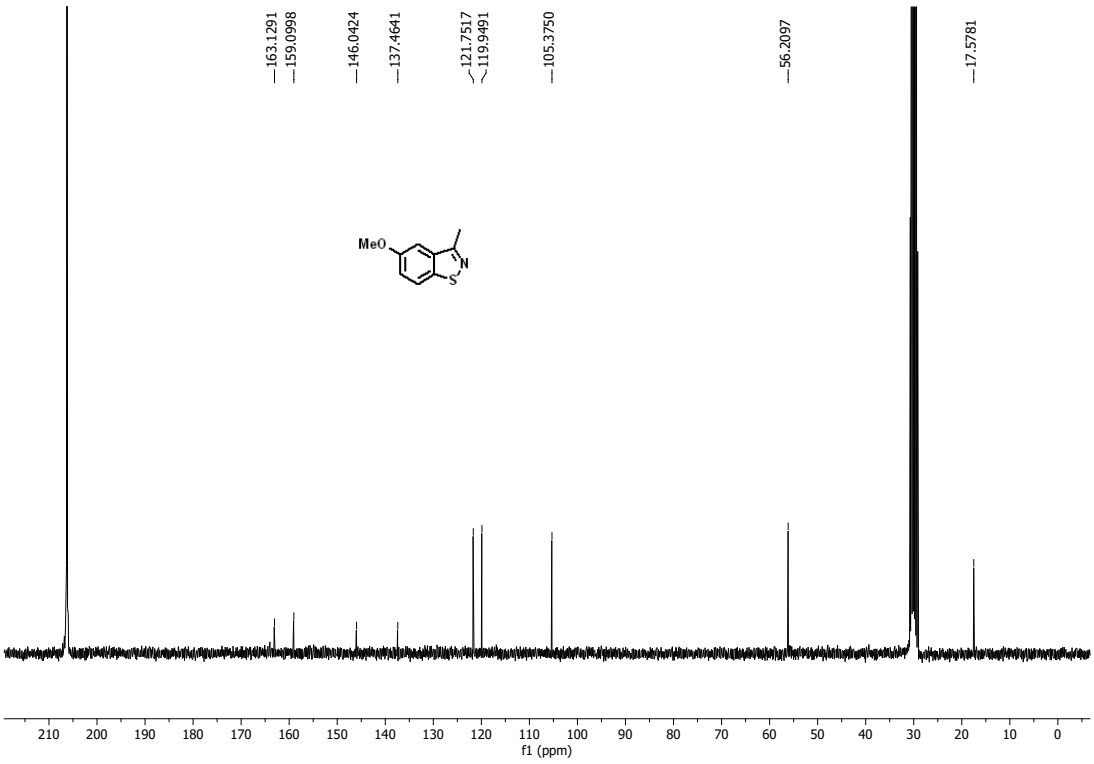



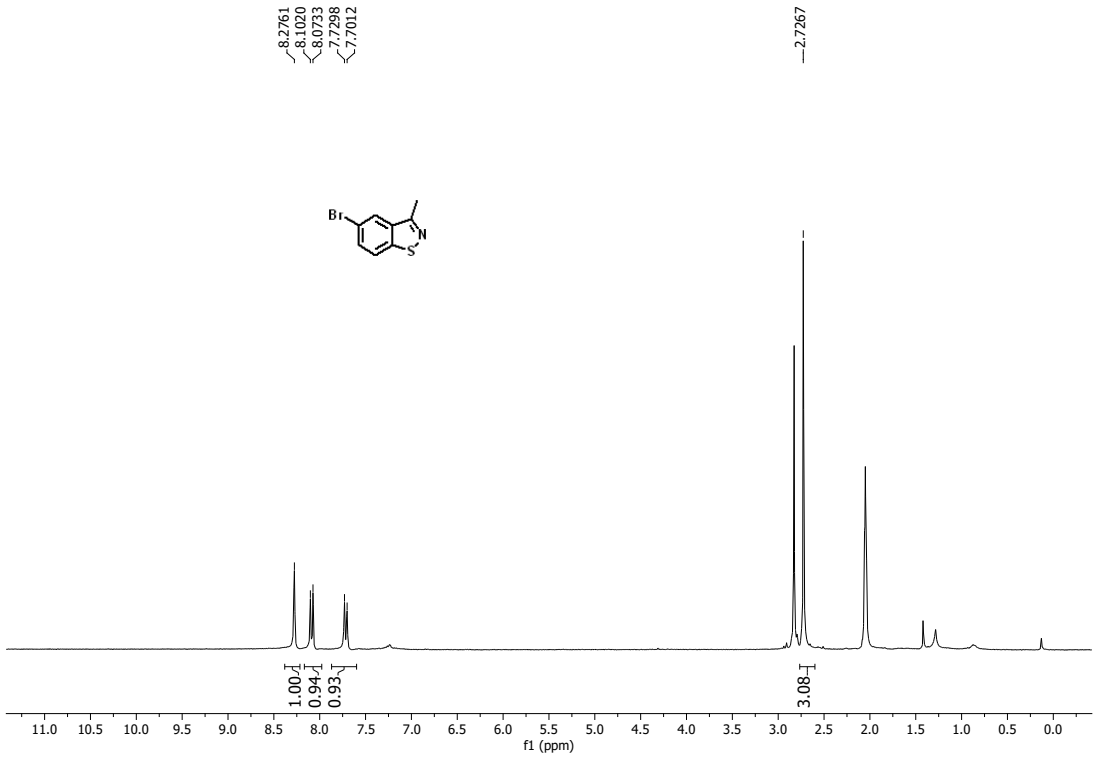

-113.77
F
N
S
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

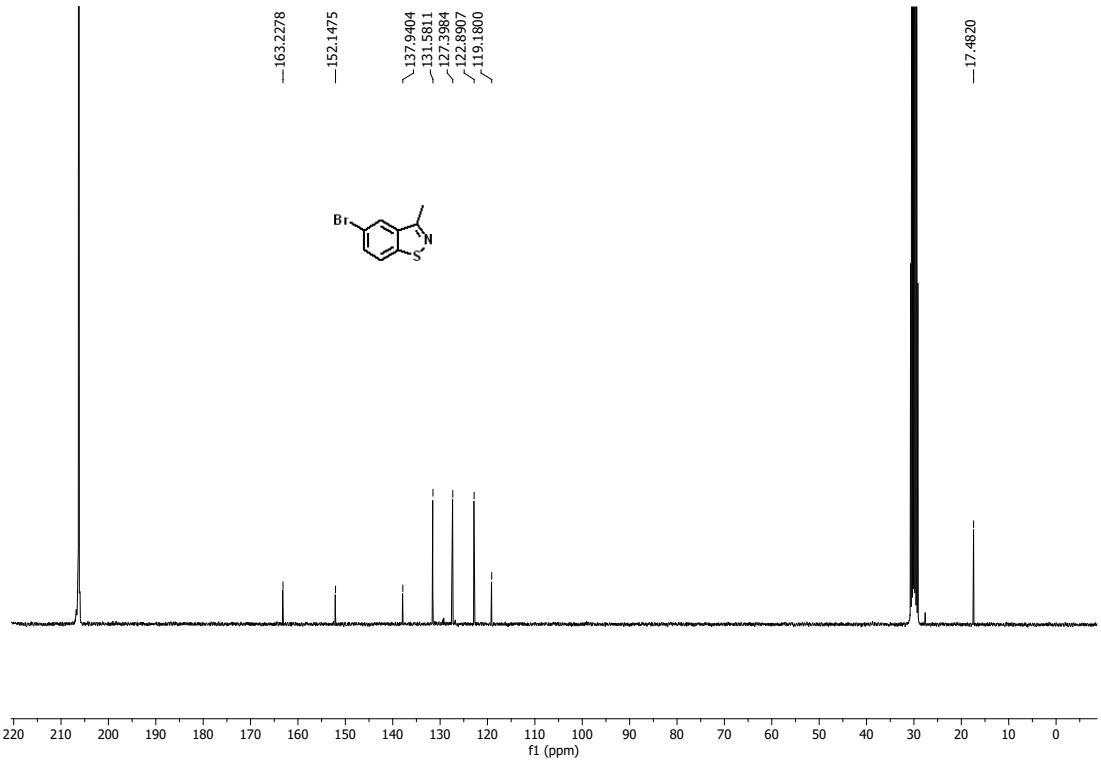

7.27
7.24
6.89
6.88
6.86
6.85
6.74
6.74
3.23
2.36
MeO
N
S
1.00
1.00
0.98
3.06
3.01
f1 (ppm)

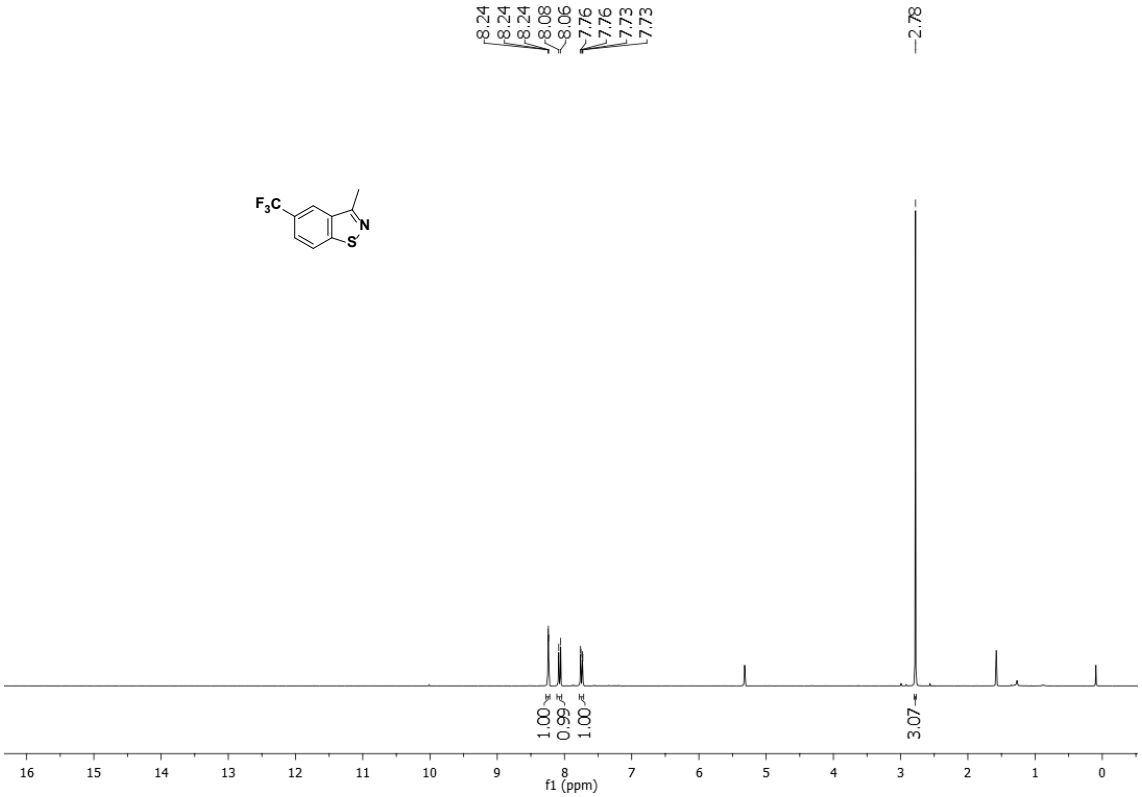

162.1
160.0
155.1
130.3
124.2
115.9
101.1
55.1
17.1
MeO
N
S
f1 (ppm)

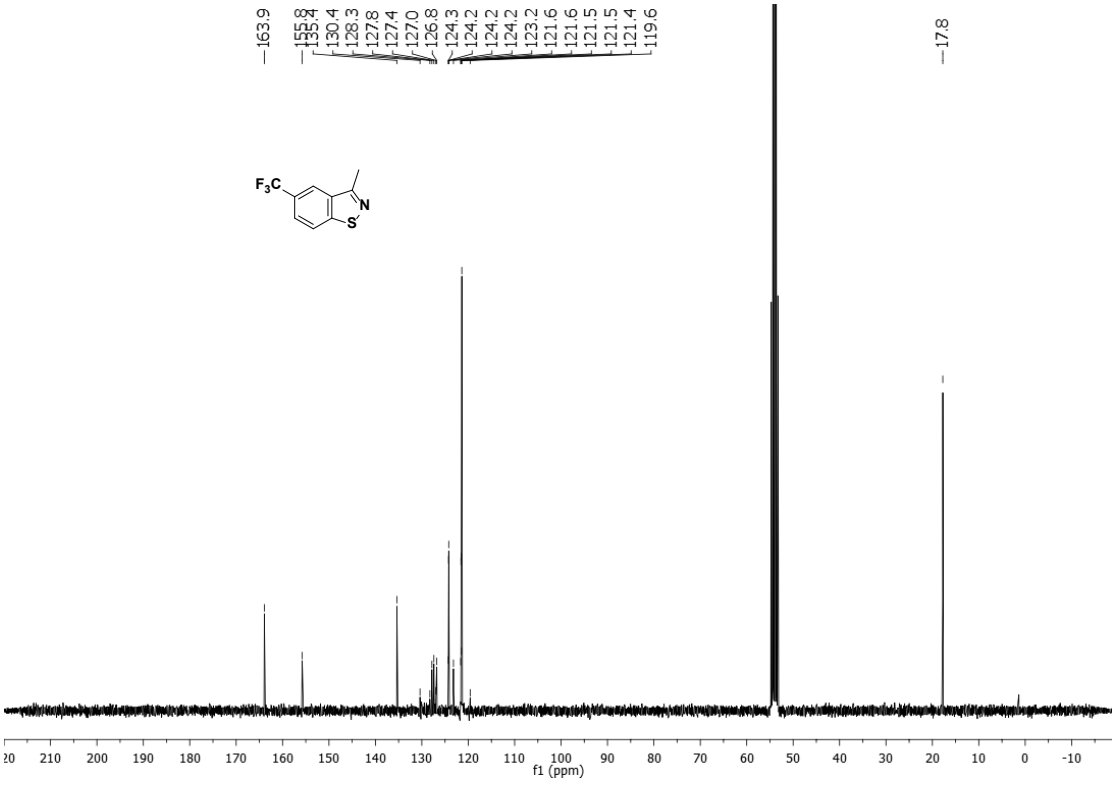

7.9782
7.9488
7.5253
7.5176
7.2535
7.2456
7.2240
7.2161
3.9288
2.6730
MeO
N
S
1.00
1.14
1.06
3.09
3.08
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

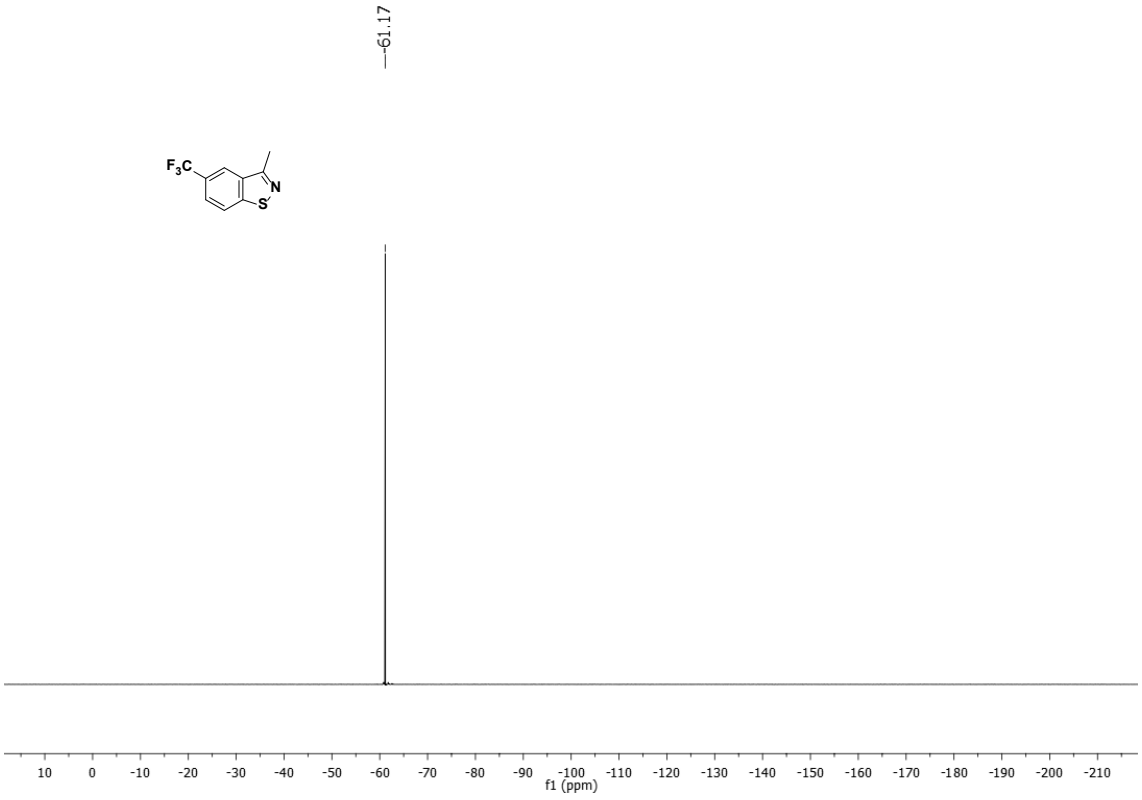

163.1291
159.0998
146.0424
137.4641
121.7517
119.9491
105.3750
56.2097
17.5781
MeO
N
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

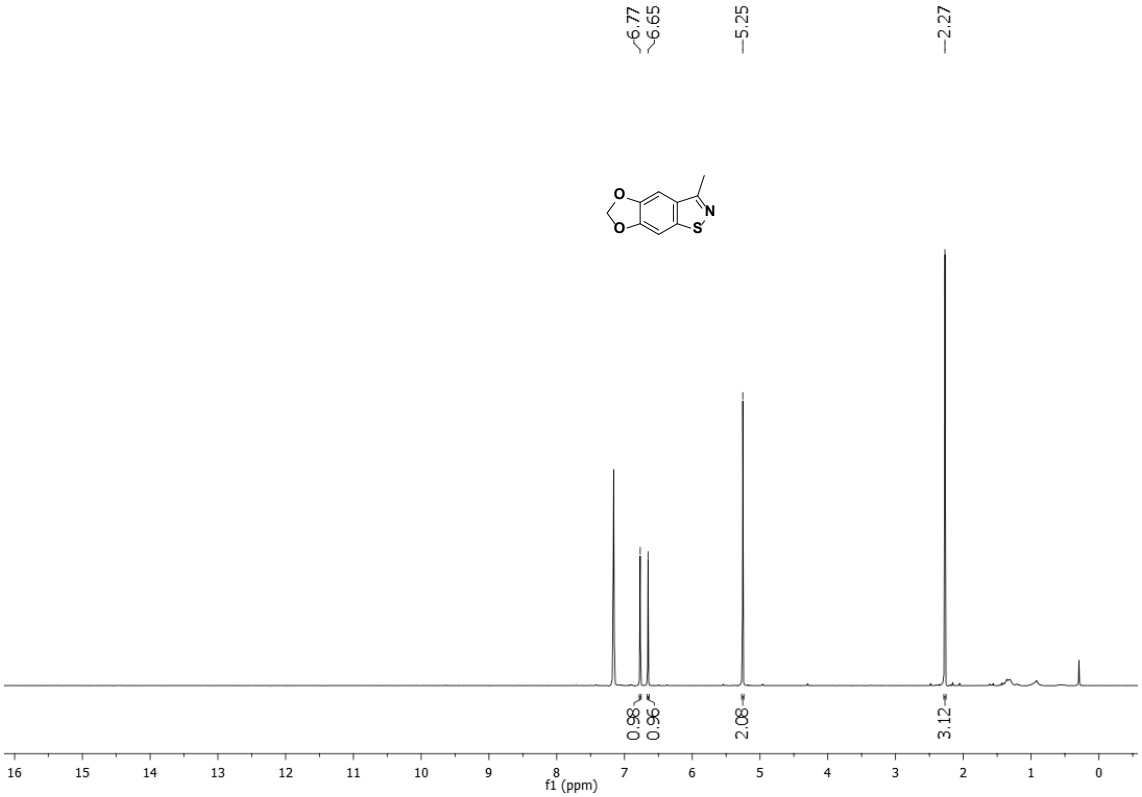

8.2761
8.1020
8.0733
7.7298
7.7012
2.7267
Br
N
S
1.00
0.94
0.93
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

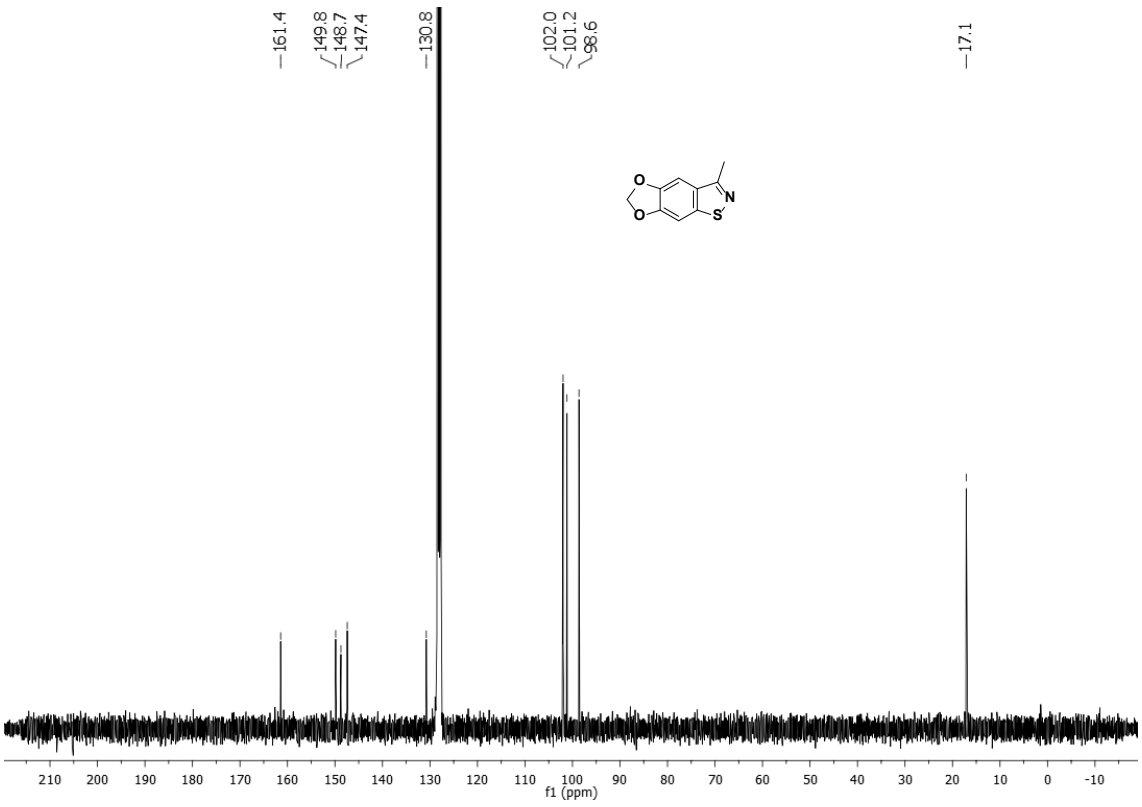

163.2278
152.1475
137.9404
131.5811
127.3984
122.8907
119.1800
17.4820
Br
N
S
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

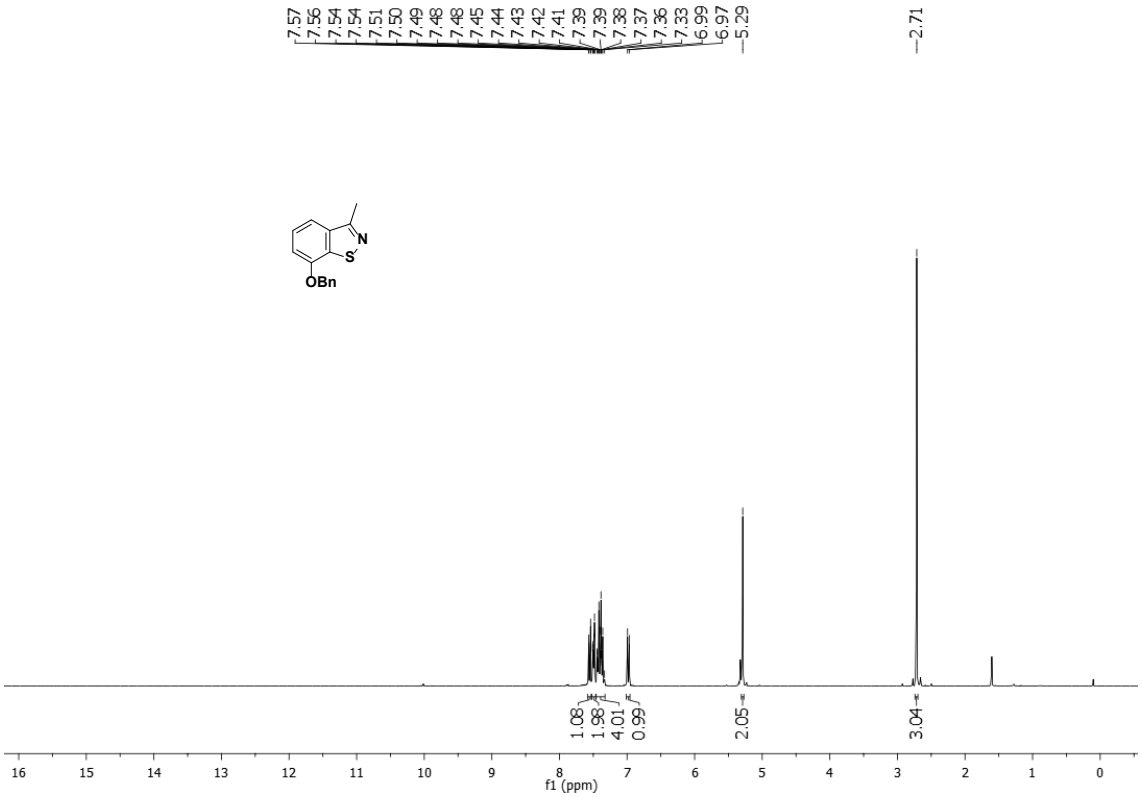

8.24
8.24
8.24
8.08
8.06
7.76
7.76
7.73
7.73
2.78
F3C
N
S
1.00
0.99
1.00
3.07
f1 (ppm)

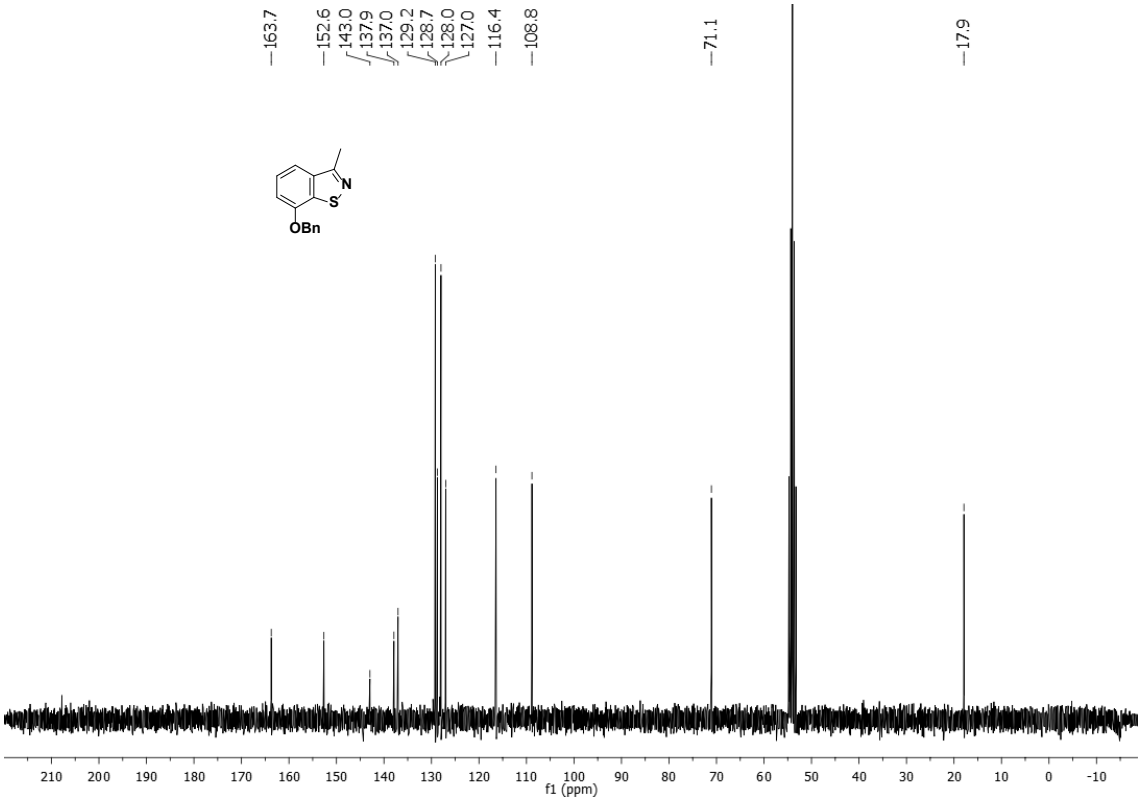

163.9
155.8
135.4
130.4
128.3
127.8
127.4
127.0
126.8
124.3
124.2
124.2
124.2
123.2
121.6
121.6
121.5
121.5
121.4
119.6
17.8
F3C
N
S
f1 (ppm)

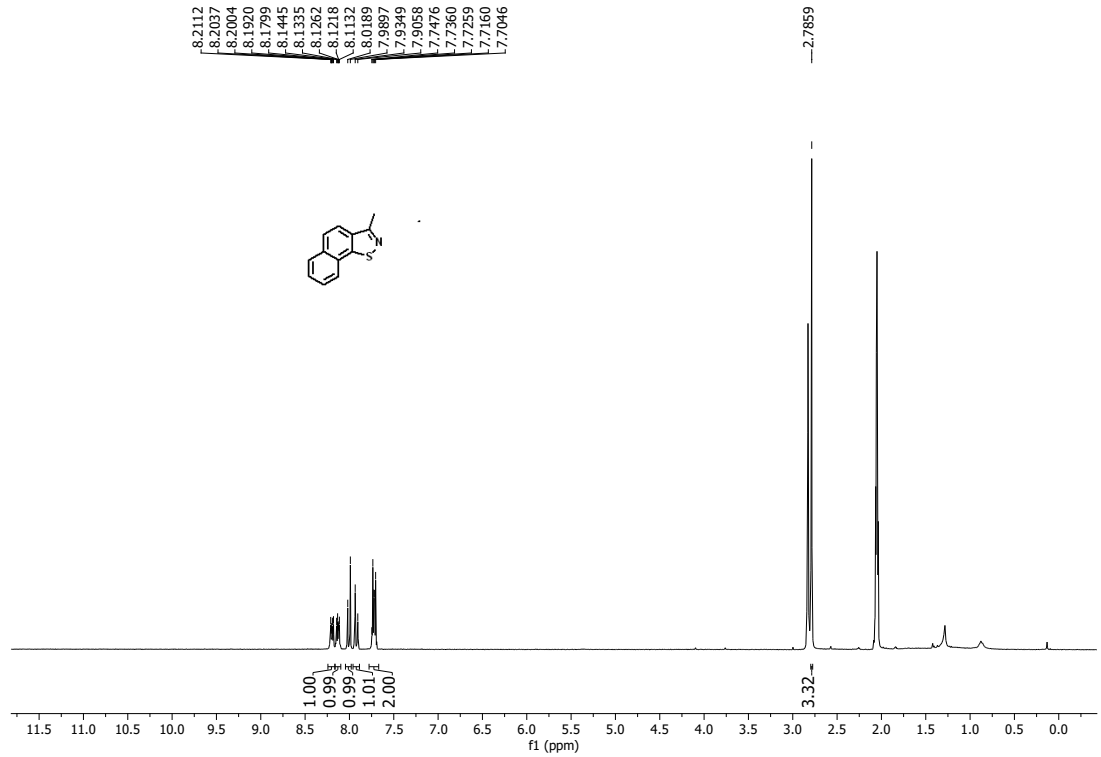

-61.17
F3C
N
S
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

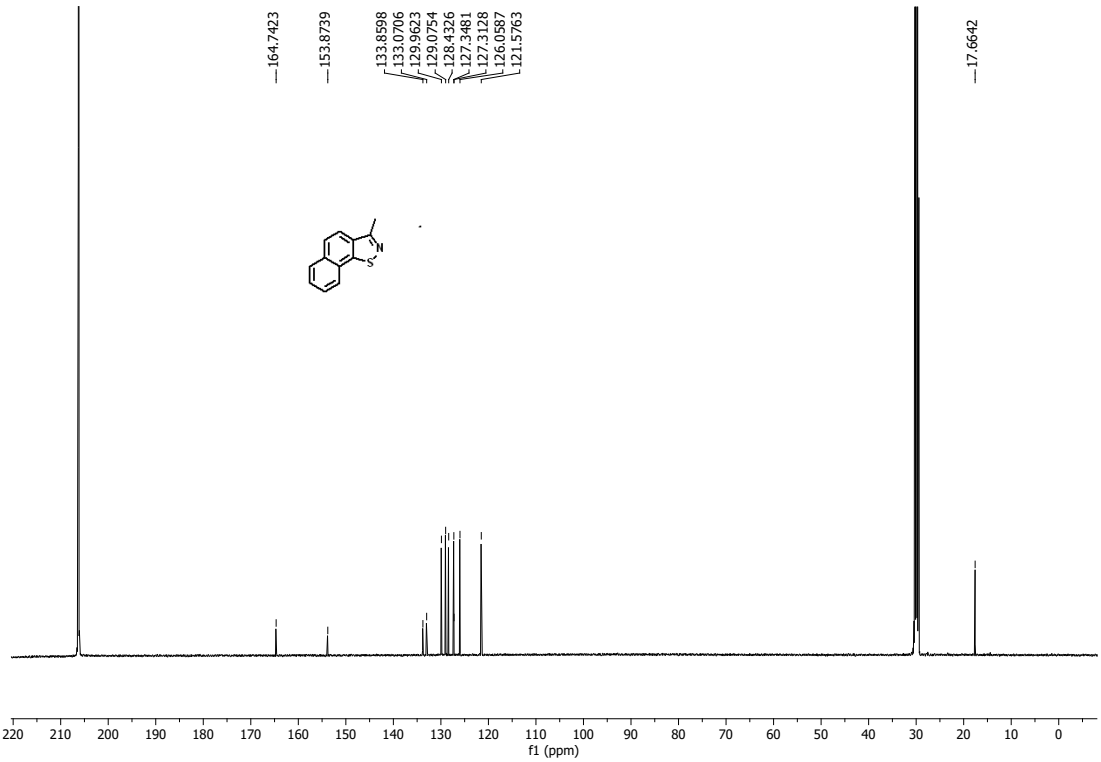

6.77
6.65
5.25
2.27
O
O
N
S
0.98
0.96
2.08
3.12
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

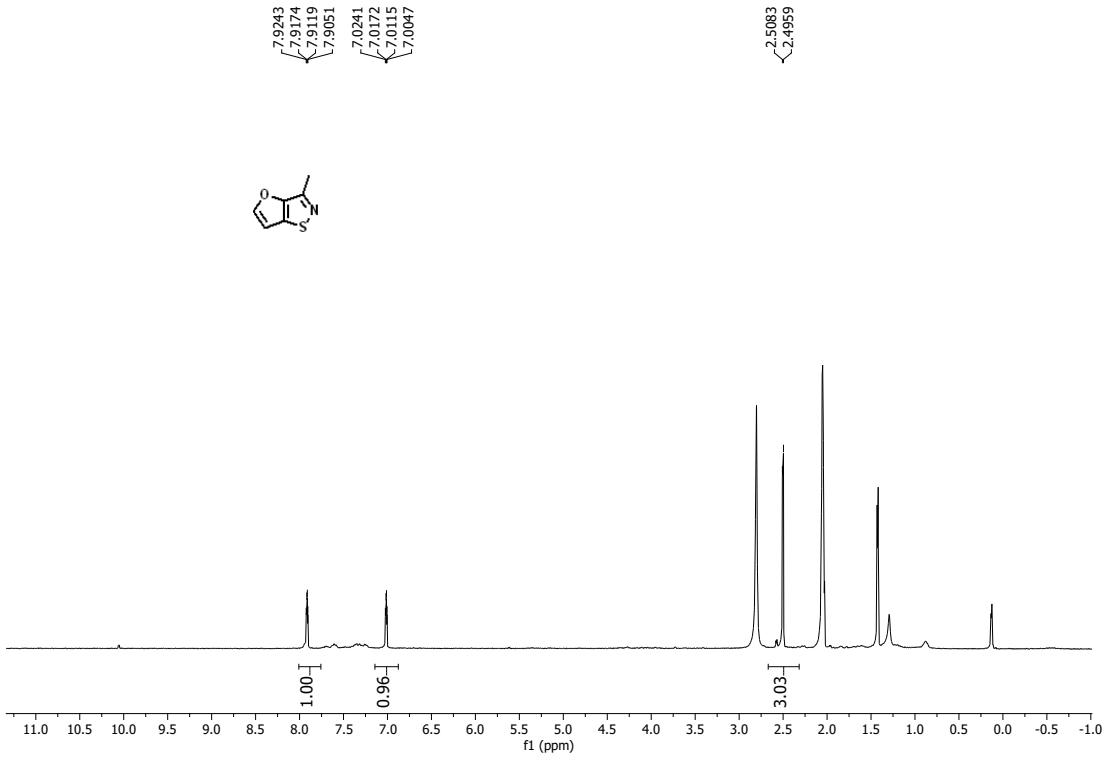

161.4
149.8
148.7
147.4
130.8
102.0
101.2
98.6
17.1
O
O
N
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

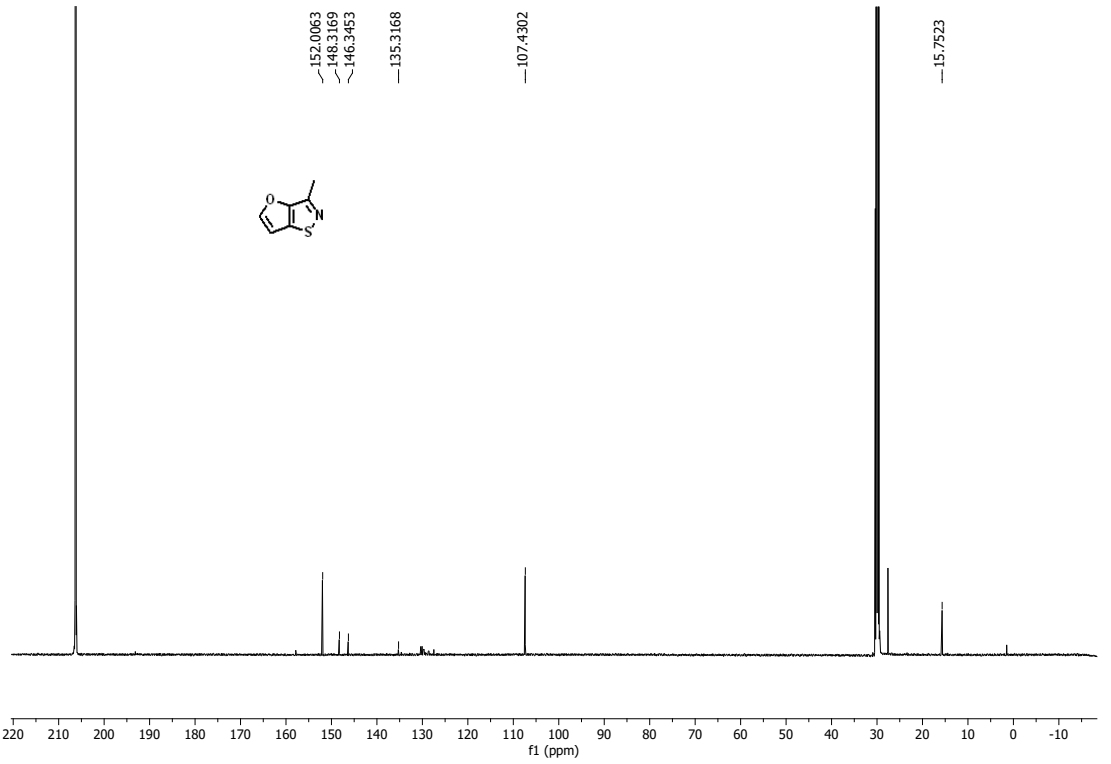

7.57
7.56
7.54
7.54
7.51
7.50
7.49
7.48
7.48
7.45
7.44
7.43
7.42
7.41
7.39
7.39
7.38
7.37
7.36
7.33
6.99
6.97
5.29
2.71
N
S
OBn
1.08
1.98
4.01
0.99
2.05
3.04
f1 (ppm)

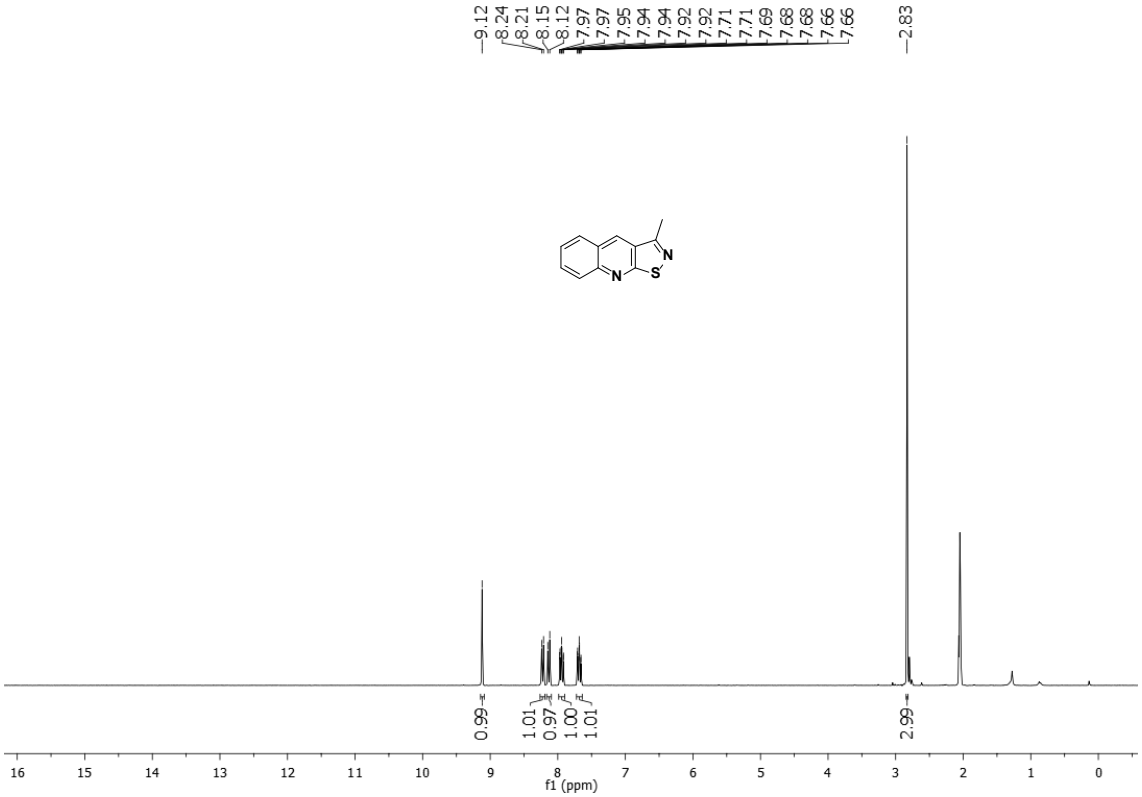

163.7
152.6
143.0
137.9
137.0
129.2
128.7
128.0
127.0
116.4
108.8
71.1
17.9
N
S
OBn
f1 (ppm)

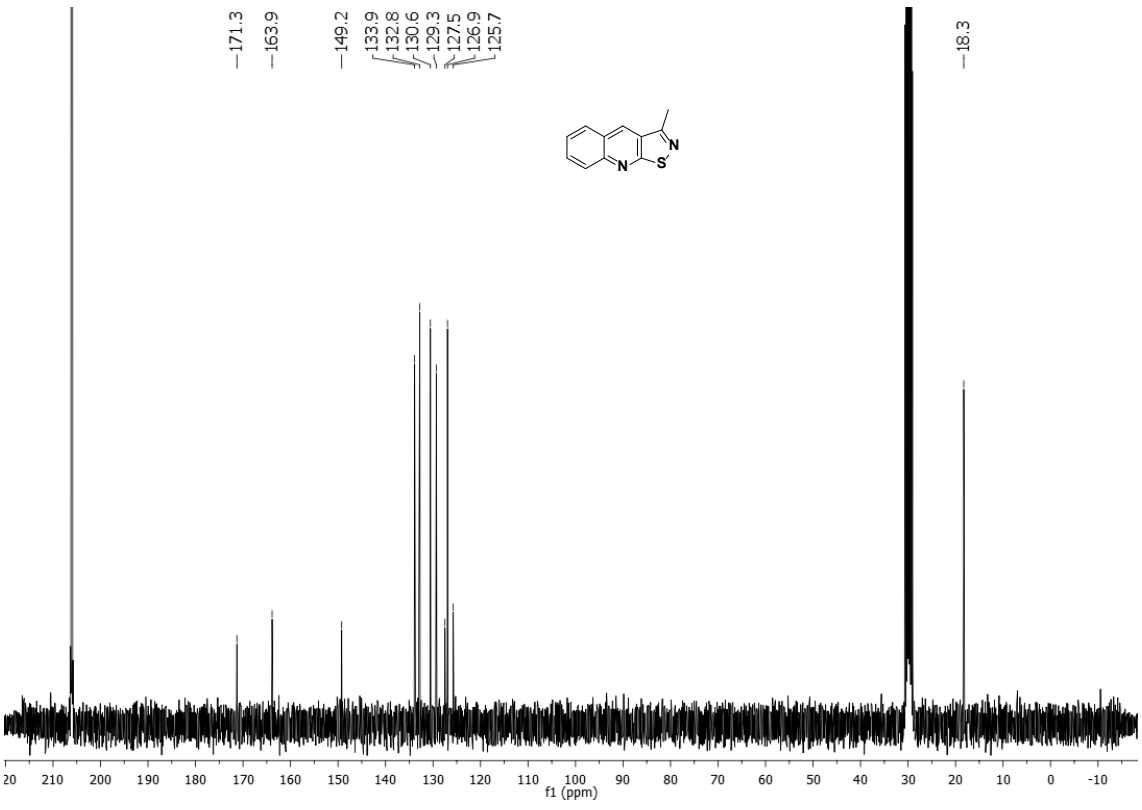

8.2112
8.2037
8.2004
8.1920
8.1799
8.1445
8.1335
8.1262
8.1218
8.1132
8.0189
7.9897
7.9349
7.9058
7.7476
7.7360
7.7259
7.7160
7.7046
2.7859
1.00
0.99
0.99
1.01
2.00
3.32
f1 (ppm)

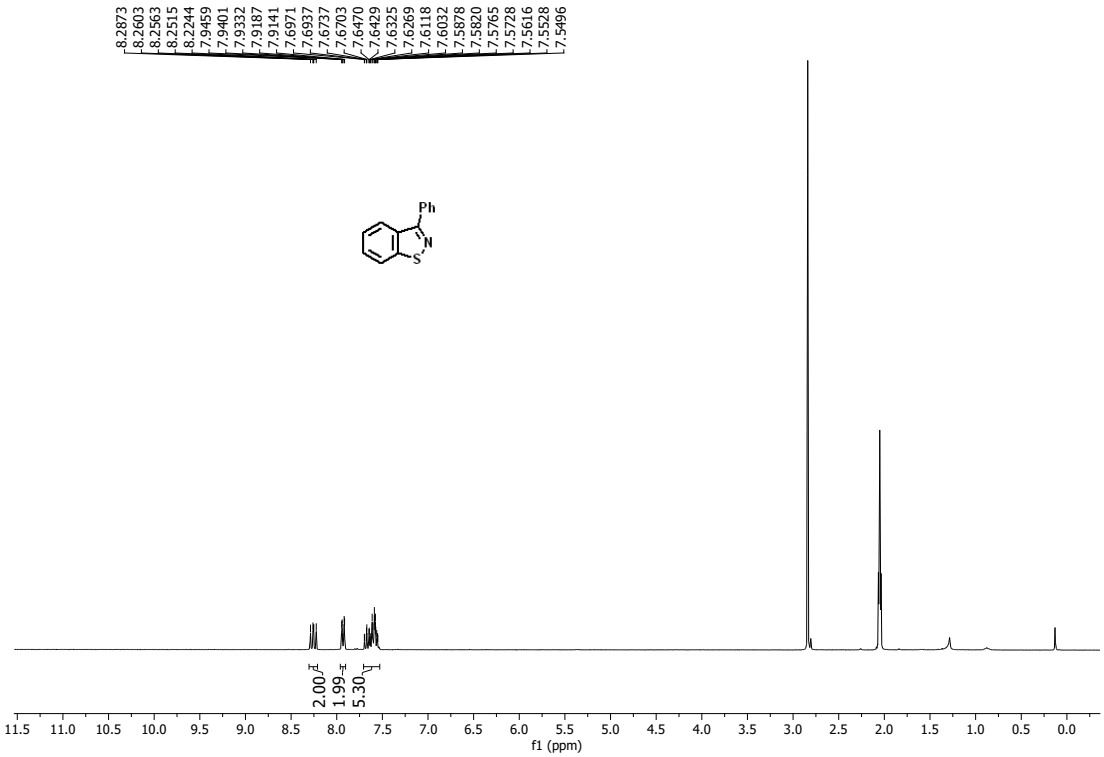

164.7423
153.8739
133.8598
133.0706
129.9623
129.0754
128.4326
127.3481
127.3128
126.0587
121.5763
17.6642
f1 (ppm)

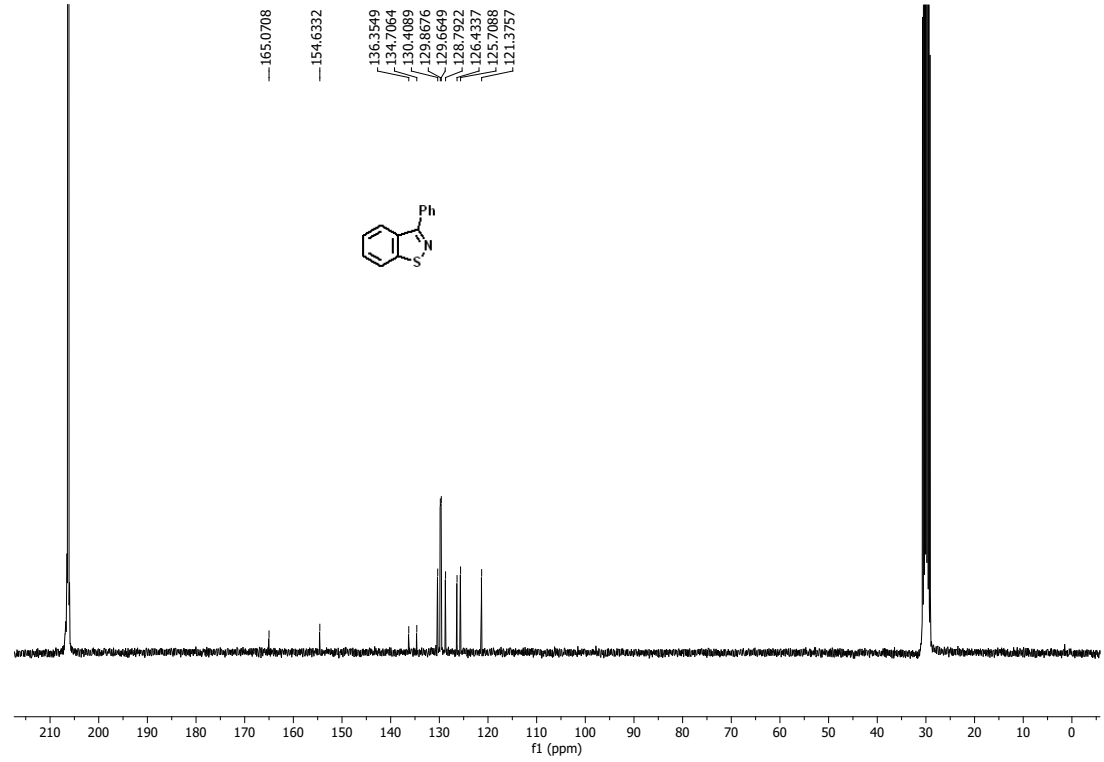

7.9243
7.9174
7.9119
7.9051
7.0241
7.0172
7.0115
7.0047
2.5083
2.4959
1.00
0.96
3.03
f1 (ppm)

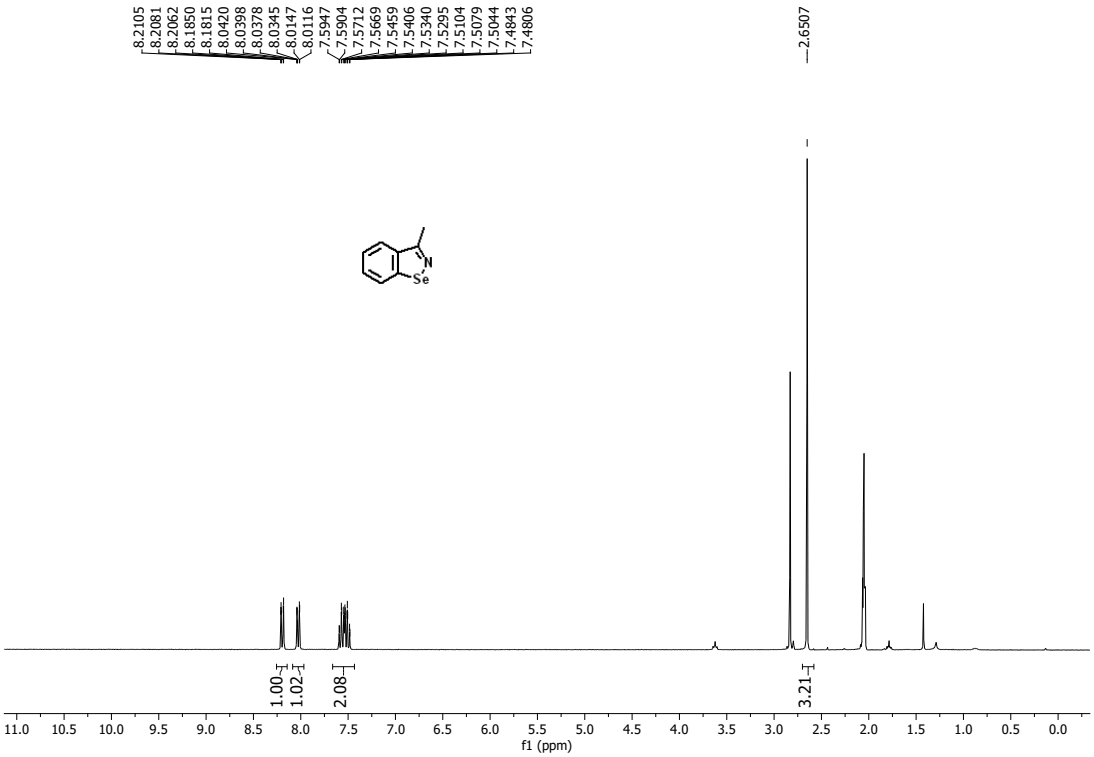

152.0063
148.3169
146.3453
135.3168
107.4302
15.7523
f1 (ppm)

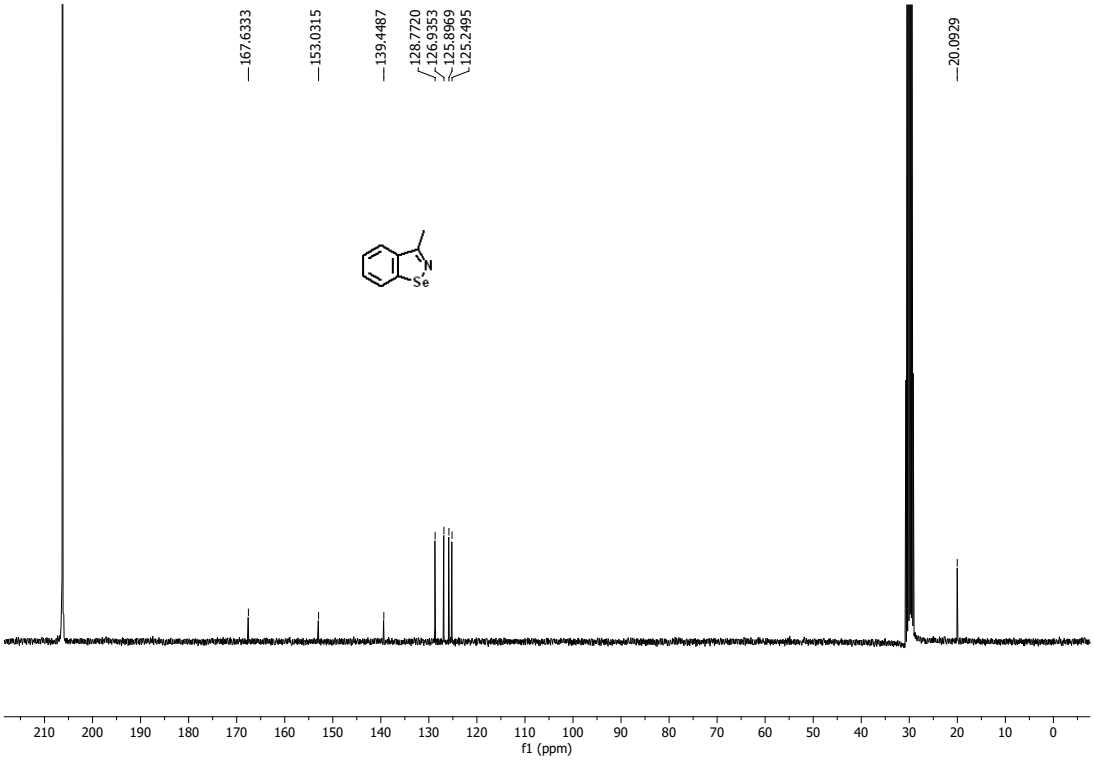

9.12
8.24
8.21
8.15
8.12
7.97
7.97
7.95
7.94
7.94
7.92
7.92
7.71
7.71
7.69
7.68
7.68
7.66
7.66
2.83
N
N
S
0.99
1.01
0.97
1.00
1.01
2.99
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

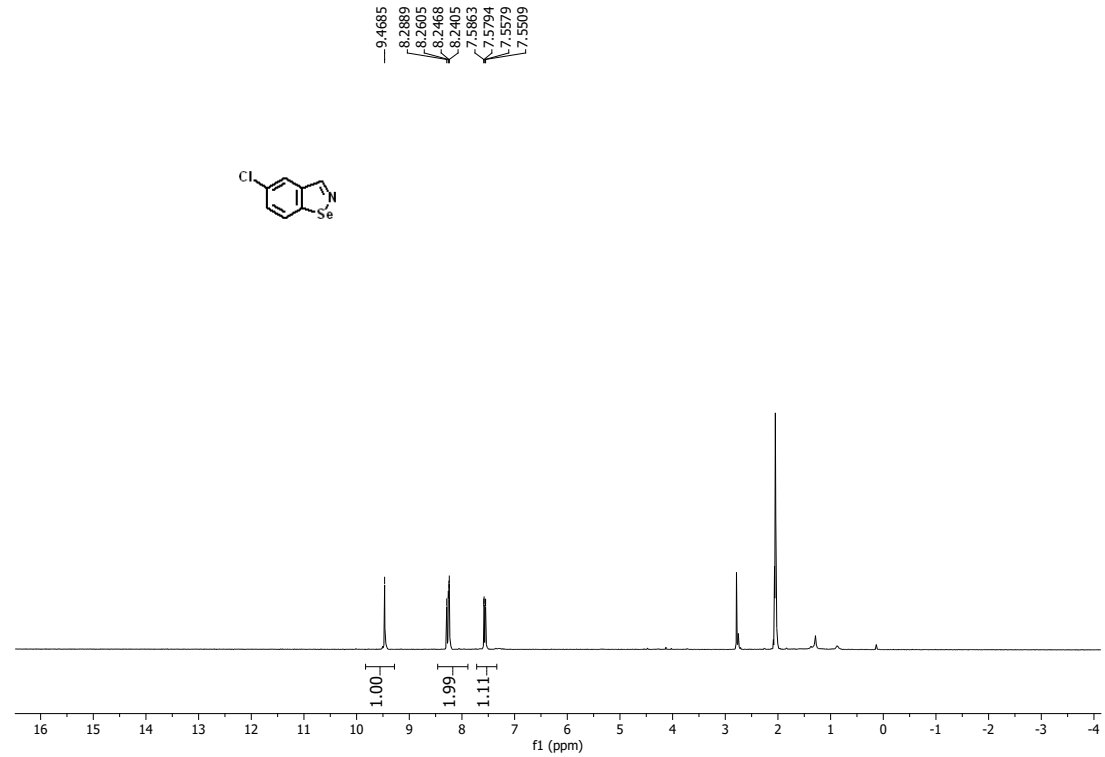

171.3
163.9
149.2
133.9
132.8
130.6
129.3
127.5
126.9
125.7
18.3
N
N
S
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

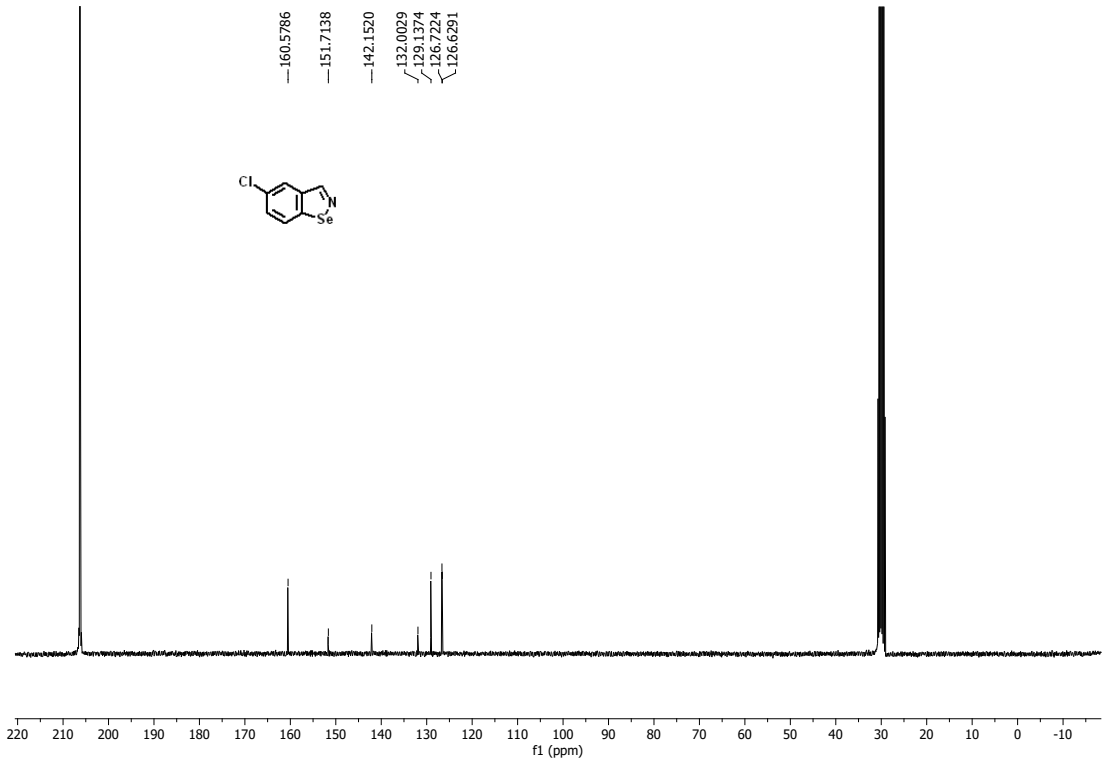

8.2873
8.2603
8.2563
8.2515
8.2244
7.9459
7.9401
7.9332
7.9187
7.9141
7.6971
7.6937
7.6737
7.6703
7.6470
7.6429
7.6325
7.6269
7.6118
7.6032
7.5878
7.5820
7.5765
7.5728
7.5616
7.5528
7.5496
Ph
N
S
2.00
1.99
5.30
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


165.0708
154.6332
136.3549
134.7064
130.4089
129.8676
129.6649
128.7922
126.4337
125.7088
121.3757
Ph
N
S
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

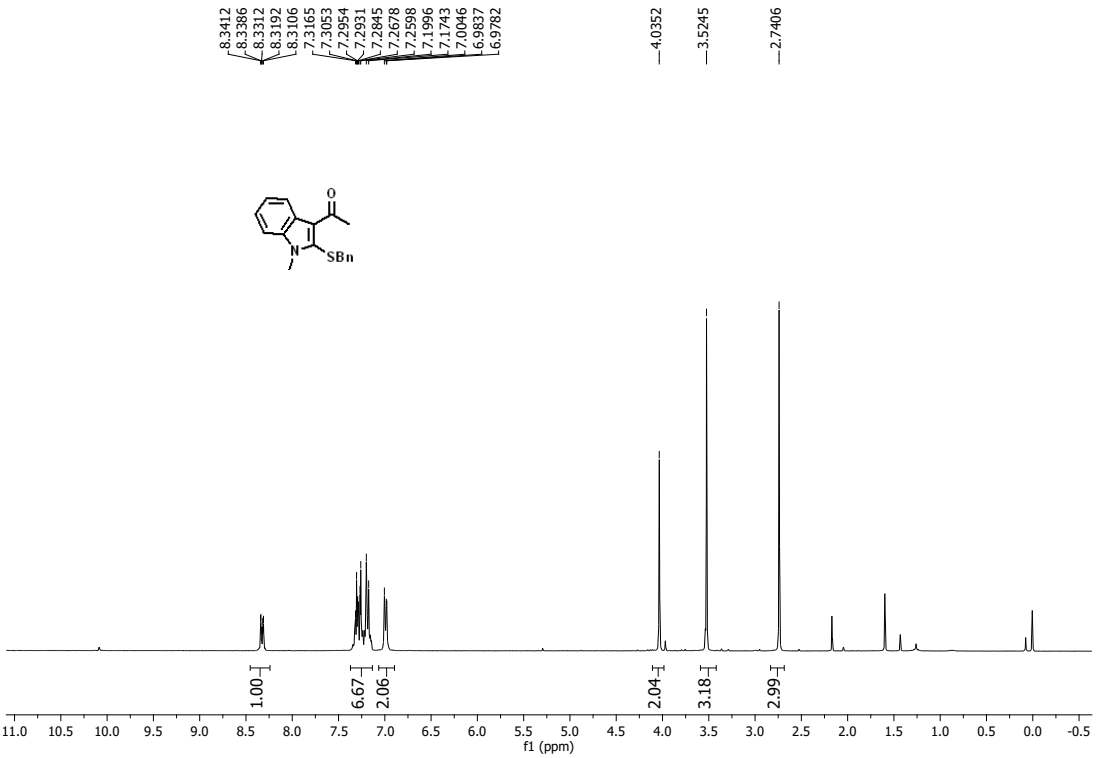

8.2105
8.2081
8.2062
8.1850
8.1815
8.0420
8.0398
8.0378
8.0345
8.0147
8.0116
7.5947
7.5904
7.5712
7.5669
7.5459
7.5406
7.5340
7.5295
7.5104
7.5079
7.5044
7.4843
7.4806
2.6507
Se
N
1.00
1.02
2.08
3.21
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

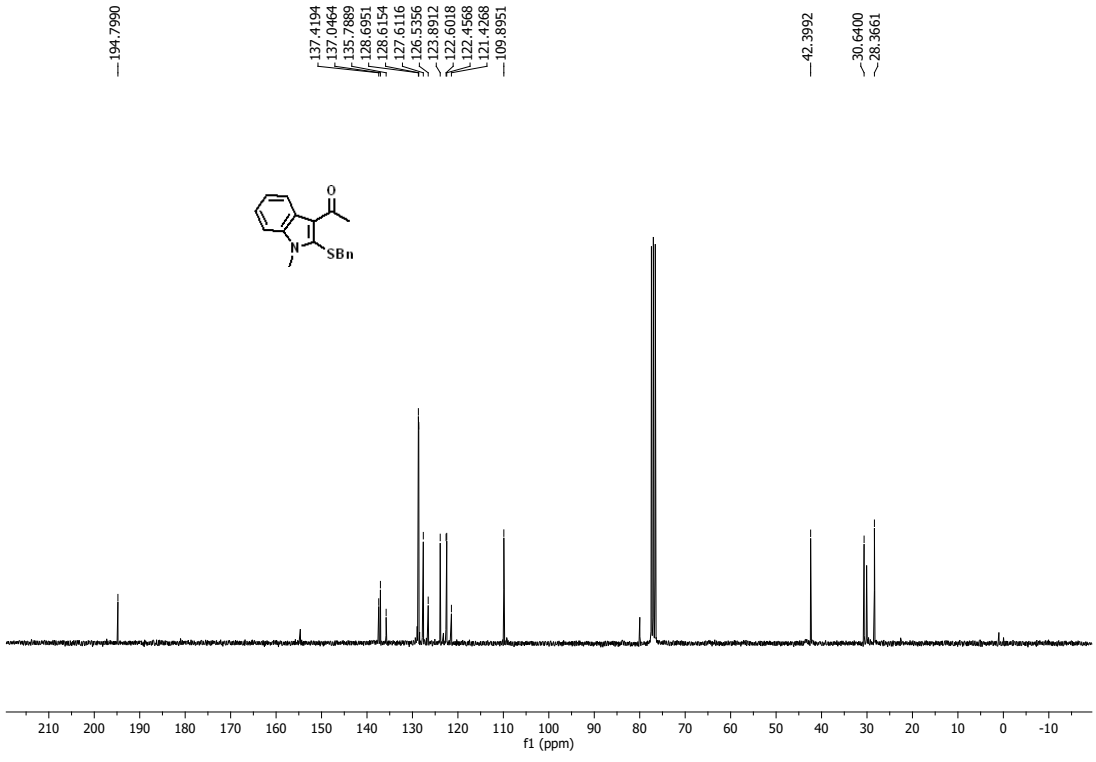

167.6333
153.0315
139.4487
128.7720
126.9353
125.8969
125.2495
20.0929
Se
N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

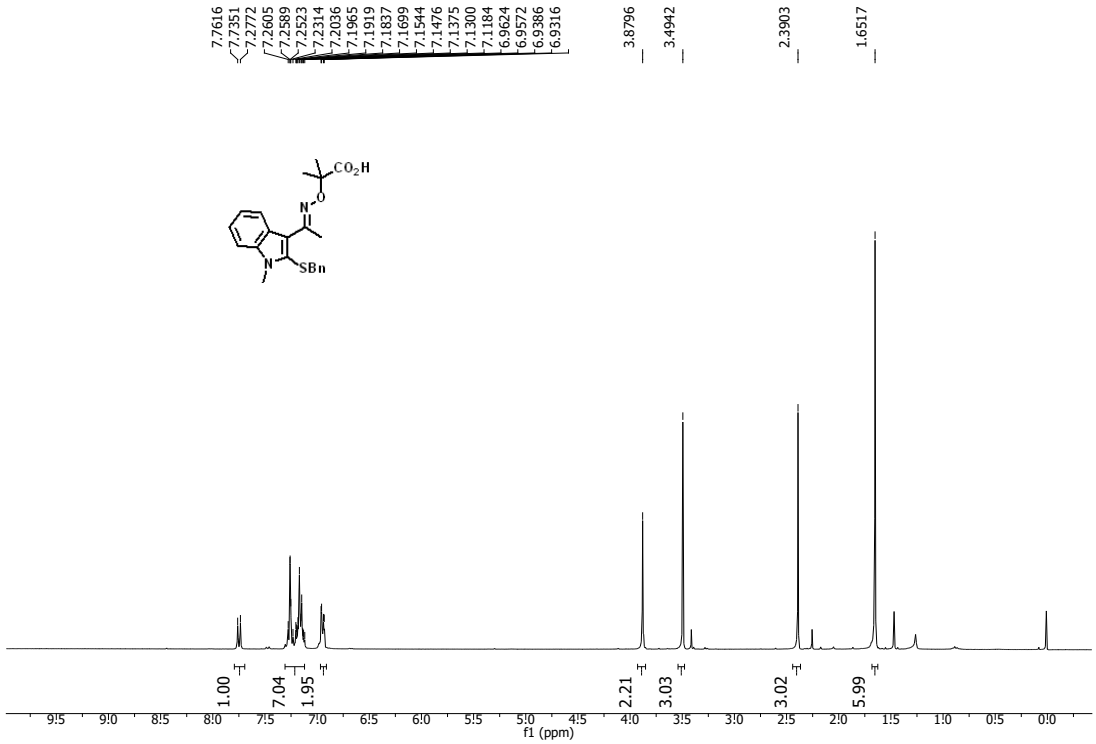

9.4685
8.2889
8.2605
8.2468
8.2405
7.5863
7.5794
7.5579
7.5509
Cl
N
Se
1.00
1.99
1.11
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

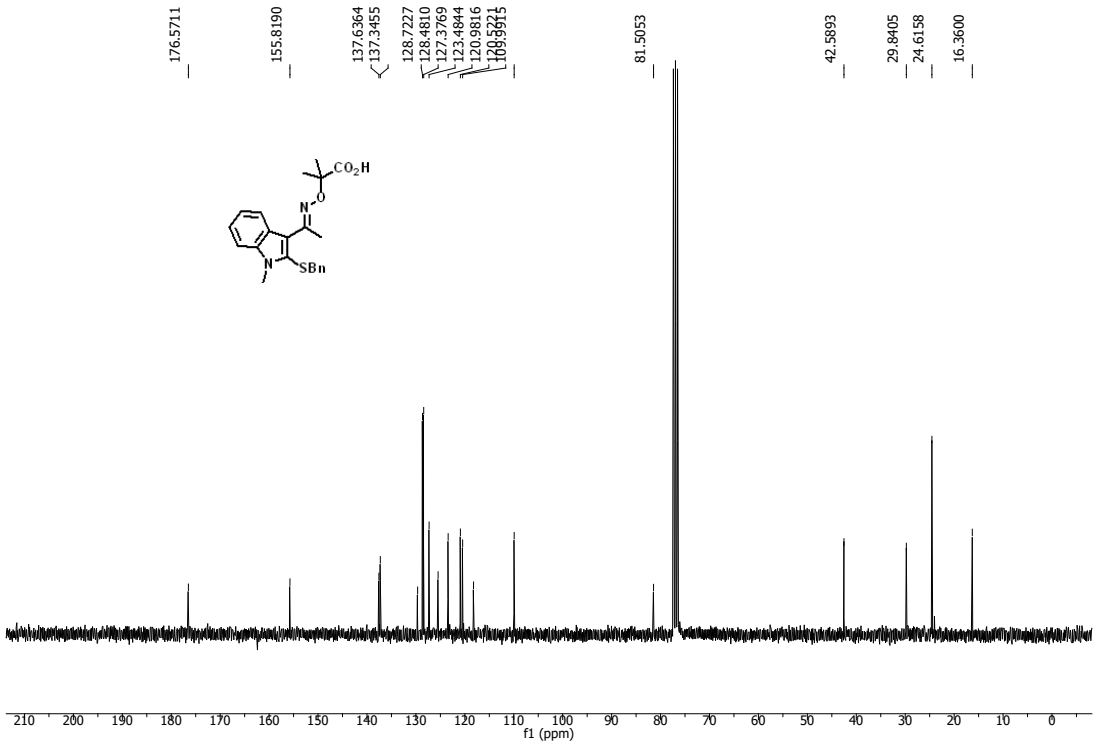

160.5786
151.7138
142.1520
132.0029
129.1374
126.7224
126.6291
Cl
N
Se
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

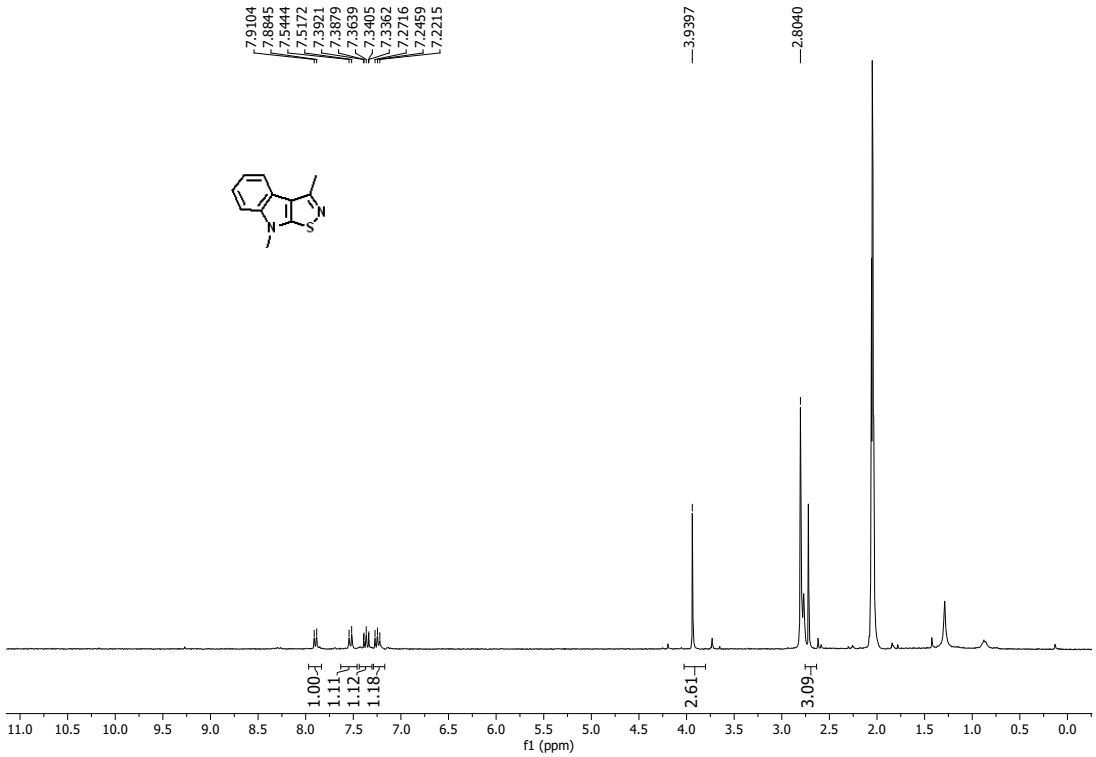
## 10.5. NMR Spectra of Brassilexin Derivative 4

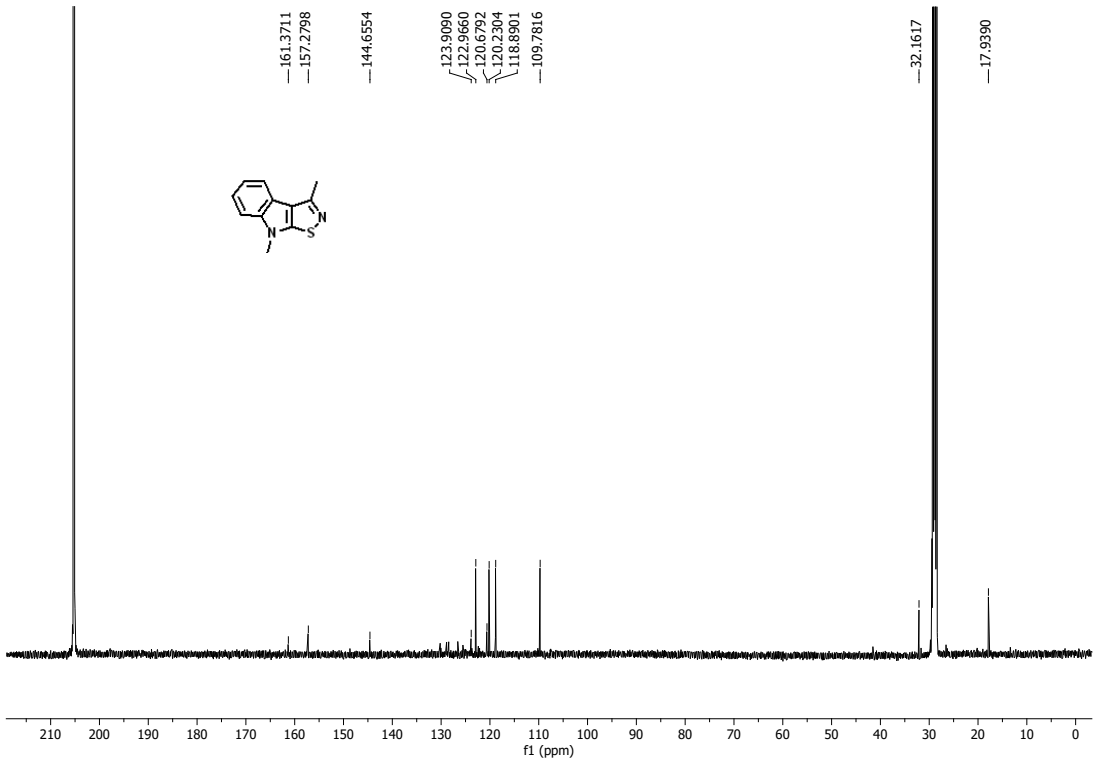



7.7616
7.7351
7.2772
7.2605
7.2589
7.2523
7.2314
7.2036
7.1965
7.1919
7.1837
7.1699
7.1544
7.1476
7.1375
7.1300
7.1184
6.9624
6.9572
6.9386
6.9316
3.8796
3.4942
2.3903
1.6517
CO2H
N
O
SBn
1.00
7.04
1.95
2.21
3.03
3.02
5.99
f1 (ppm)


176.5711
155.8190
137.6364
137.3455
128.7227
128.4810
127.3769
123.4844
120.9816
120.5221
109.9915
81.5053
42.5893
29.8405
24.6158
16.3600
CO2H
N
O
SBn
f1 (ppm)


7.9104
7.8845
7.5444
7.5172
7.3921
7.3879
7.3639
7.3405
7.3362
7.2716
7.2459
7.2215
3.9397
2.8040
1.00
1.11
1.12
1.18
2.61
3.09
f1 (ppm)


161.3711
157.2798
144.6554
123.9090
122.9660
120.6792
120.2304
118.8901
109.7816
32.1617
17.9390
f1 (ppm)