Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Divergent Synthesis of Hydropyridine Derivatives via Nitrogen-Containing Lewis Base Mediated Regioselective [4+2] Cyclizations

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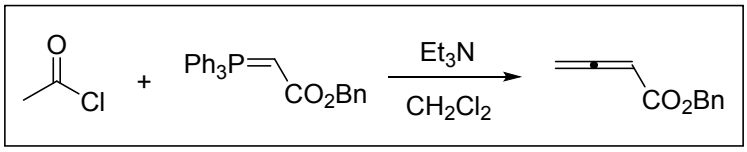
I. General information

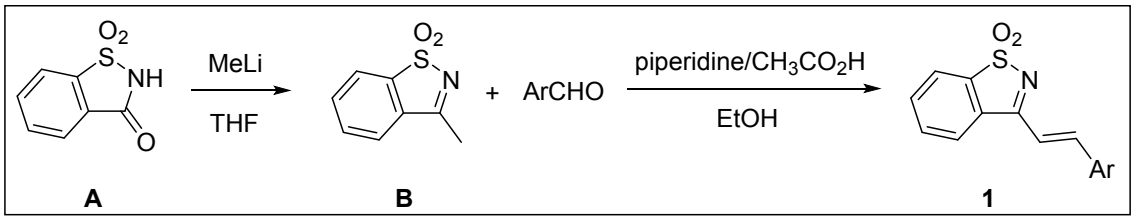
All the starting materials were obtained from commercial sources and used without further purification unless otherwise stated. Yields referred to isolated compounds through flash column chromatography performed using 300-400 mesh silica gel. NMR spectra were recorded on Varian Brucker ARX 400 spectrometer in $CDCl_3$ solution and the chemical shifts were reported in parts per million (ppm) relative to internal standard TMS (0 ppm) for ^1H NMR and chloroform-*d* (77.0 ppm) for ^{13}C NMR. Coupling constants were given in Hertz (Hz). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublet), brs (broad singlet) and m (multiplet). Infrared spectra (IR) spectra were recorded on a Perkin-Elmer 983G instrument. High resolution mass spectrometry (HRMS) were obtained on an IonSpec FT-ICR mass spectrometer with ESI or MALDI resource. Melting points were measured on a RY-I apparatus and are reported uncorrected.

II. Preparation of the allenic esters



Allenic esters is a known compound and synthesized according to a similar method developed by Hansen [1]. To a solution of benzyl (triphenylphosphoranylidene)acetate (0.1 mol) in CH_2Cl_2 (500 mL) was added 1.1 equivalent of Et_3N (0.11 mol). After stirred for about 15 minutes, 1.1 equivalent of acetyl chloride (0.11 mol) was added dropwise. Then the reaction mixture was stirred overnight at room temperature and was carefully evaporated to remove most of the solvent, and then the residue was extracted by petroleum ether (b.p. 30-60 ºC, 5 × 200 mL). The combined extracting was concentrated and the residue was subjected to column chromatography (eluant: 5 % EtOAc in petroleum ether) to provide the allenic esters as light yellow oil.

III. Preparation of the α,β-unsaturated cyclic ketimines



The Synthesis of B: To a flame dried 500 mL round bottle flask with a magnetic

stirring bar under Argon atmosphere was added saccharin **A** (0.030 mol, 5.49 g) and anhydrous THF (250 mL). The flask was cooled to -78 °C and 2 equiv (0.060 mol) of the appropriate lithium reagent were carefully added by syringe or cannula. The reaction was stirred at -78 °C for an additional 4 h, then 100 mL of H_2O was added, and the reaction mixture was warmed to room temperature. The solution was transferred to a separatory funnel where 200 mL of ether was added and the aqueous layer was separated. The organic layer was washed successively with 10% HCl (2×100 mL), 10% $NaHCO_3$ (2×125 mL), and 100 mL of H_2O and dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo gave a white solid, which was crystallized from absolute ethanol to give sulfonimine [2].

The Synthesis of 1: Piperidine (1 mmol) and acetic acid (1 mmol) were added to a solution of **B** (3-methyl-1,2-benzoisothiazole-1,1-dioxide) (10 mmol) and aldehyde (10 mmol) in EtOH and the mixture was refluxed for 3 hours. The mixture was cooled to 0 °C and the solid was collected by filtration, washed with cold EtOH, and dried to afford products **1** in 49-86% yield. They were generally used without further purification [3].

IV. References

[1] Lang, R. W.; Hansen, H.-J. *Organic Syntheses*. **1990**, *62*, 202-206.

[2] Davis, F. A.; Towson, J. C.; Vashi, D. B.; ThimmaReddy, R.; McCauley, J. P.; Jr.; Harakal, M. E.; Gosciniak, D. J. *J. Org. Chem.*, **1990**, *55*, 1254-1261.

[3] (a) Feng, X.; Zhou, Z.; Ma, C.; Yin, X.; Li, R.; Dong, L.; Chen, Y.-C. *Angew. Chem. Int. Ed*. **2013**, *52*, 14173-14176. (b) Li, E.; Jin, H.; Jia, P.; Dong, X.; Huang, Y. *Angew. Chem. Int. Ed*. **2016**, *55*, 11591-11594.

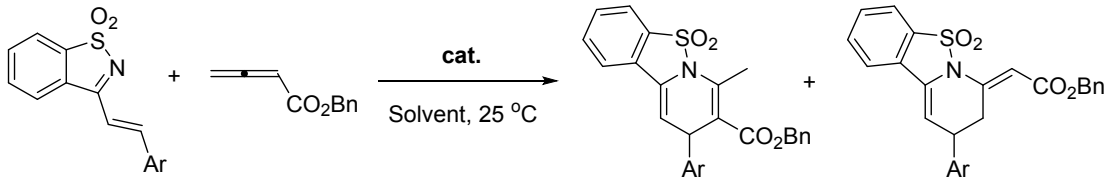
V. General procedure and spectroscopic data and HPLC chromatogram

Formal Synthesis processes for racemic systems:

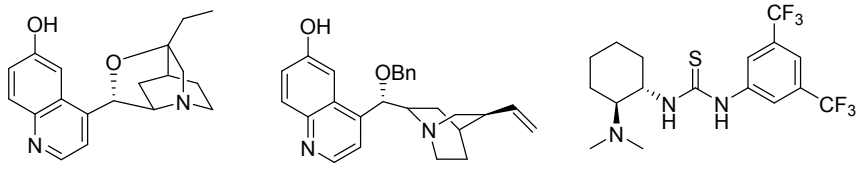
To a stirred solution of **1** (0.1 mmol) and **2** (0.12 mmol) in CH_2Cl_2 or CH_3CN (2.0 mL or 1 mL) at 40 °C or 60 °C, catalyst DMAP/DABCO was added in one portion. Then the reaction mixture was stirred at this temperature. After completion of the reaction (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give cycloadduct **3** and **4**.

Formal Synthesis processes for racemic systems:

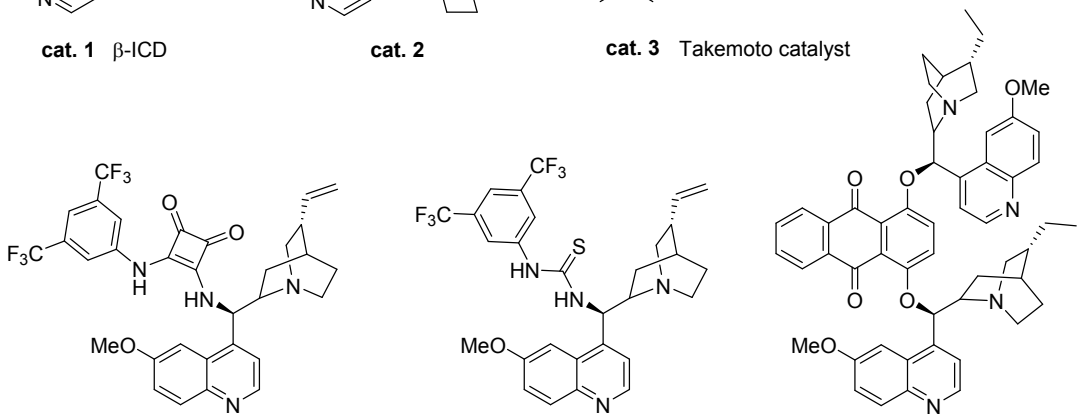
To a stirred solution of **1c** (0.1 mmol) and **2a** (0.12 mmol) in solvent (1 mL) at 25 °C, the chiral catalyst was added in one portion. Then the reaction mixture was stirred at this temperature. And the reaction was monitored by TLC, the reaction mixture was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give cycloadduct **3c** and **4c** (for details see below).



1c **2a** **3c** **4c**



cat. 1 β-ICD **cat. 2** **cat. 3** Takemoto catalyst



cat. 4 **cat. 5** **cat. 6** $(DHQD)_2AQN$

Entry	**Cat.**	Solvent	Time	Results	
				3c	**4c**
1	**Cat. 1**	CH_2Cl_2	36 h	12%, 25% ee	15%, 17% ee
2	**Cat. 1**	CH_3CN	120 h	no product	
3	**Cat. 1**	Toluene	36 h	16%, 1% ee	34%, (-) 23% ee
4	**Cat. 1**	THF	120 h	no product	
5	**Cat. 2**	CH_2Cl_2	120 h	no product	

6	**Cat. 2**	CH_3CN	120 h	no product	
7	**Cat. 2**	Toluene	120 h	no product	
8	**Cat. 2**	THF	120 h	trace, no detected	no product
9	**Cat. 3**	CH_2Cl_2	120 h	complex system, no detected	
10	**Cat. 3**	CH_3CN	120 h	no product	
11	**Cat. 3**	Toluene	120 h	no product	
12	**Cat. 3**	THF	120 h	no product	
13	**Cat. 4**	CH_2Cl_2	120 h	no product	trace, no detected
14	**Cat. 4**	CH_3CN	120 h	no product	
15	**Cat. 4**	Toluene	120 h	no product	
16	**Cat. 4**	THF	120 h	no product	
17	**Cat. 5**	CH_2Cl_2	120 h	no product	trace, no detected
18	**Cat. 5**	CH_3CN	120 h	no product	
19	**Cat. 5**	Toluene	120 h	no product	
20	**Cat. 5**	THF	120 h	no product	
21	**Cat. 6**	CH_2Cl_2	120 h	complex system, no detected	
22	**Cat. 6**	CH_3CN	120 h	complex system, no detected	
23	**Cat. 6**	Toluene	120 h	complex system, no detected	
24	**Cat. 6**	THF	120 h	no product	

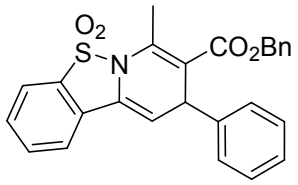
Further transformations reactions:

1) **Et_2O•BF_3 reduction**: To a stirred solution of **4c** (0.1 mmol) in CH_2Cl_2 (1.0 mL), reducing agent Et_3SiH (1.0 mmol) and Et_2O•BF_3 (1.0 mmol) was added in one portion. Then the reaction mixture was stirred at room temperature. After completion of the

reaction (monitored by TLC), the reaction mixture was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give **5** as white solid.

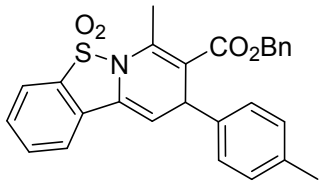
2) **LAH reduction**: To a stirred solution of **4c** (0.1 mmol) in THF (1.0 mL), reducing agent $LiAlH_4$ (0.15 mmol) was added in one portion. Then the reaction mixture was stirred at room temperature. After completion of the reaction (monitored by TLC, about 10 min), the reaction mixture was purified by flash chromatography on silica gel (EtOAc/petroleum ether) to give **6** as white solid.

Benzyl-7-methyl-9-phenyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3a)



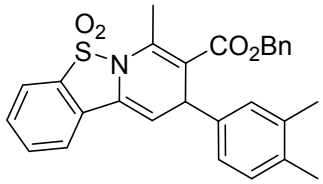
61% yield; white solid; mp 183-186°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.66 – 7.60 (m, 1H), 7.56 (d, J = 7.0 Hz, 2H), 7.32 – 7.23 (m, 6H), 7.20 (d, J = 7.3 Hz, 2H), 7.07 (s, 2H), 5.76 (d, J = 4.6 Hz, 1H), 5.00 (s, 2H), 4.73 (d, J = 4.2 Hz, 1H), 2.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.90, 144.77, 141.41, 135.76, 133.60, 131.89, 130.30, 128.82, 128.43, 128.13, 128.11, 128.03, 127.24, 127.11, 126.85, 121.05, 120.88, 107.63, 105.67, 66.28, 41.31, 14.96； IR (neat): ν 3117, 3013, 2352, 2318, 1703, 1599, 1325, 1225, 1174, 1160, 1012, 984, 851, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{21}NO_4S$ $[M+H]^+$ = 444.1270, found = 444.1275.

Benzyl-7-methyl-9-(p-tolyl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3c)



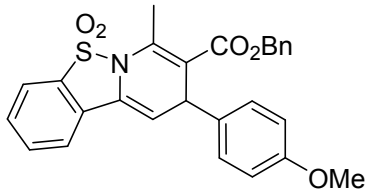
66% yield; white solid; mp 132-133°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.56 (t, J = 7.2 Hz, 2H), 7.28 (d, J = 4.8 Hz, 3H), 7.08 (s, 6H), 5.75 (d, J = 4.7 Hz, 1H), 5.01 (s, 2H), 4.70 (d, J = 4.6 Hz, 1H), 2.91 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.98, 141.84, 141.04, 136.80, 135.82, 133.58, 131.86, 130.25, 129.49, 128.39, 128.15, 128.03, 128.00, 127.30, 126.75, 121.03, 120.86, 107.88, 105.82, 66.24, 40.88, 21.12, 14.96; IR (neat): ν 2894, 2352, 2319, 1698, 1602, 1324, 1226, 1159, 1104, 1023, 983, 853, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{23}NO_4S$ $[M+H]^+$ = 458.1426, found = 458.1421.

Benzyl-9-(3,4-dimethylphenyl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3d)



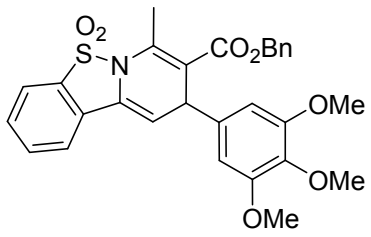
95% yield; white solid; mp 146-148°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.7 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.55 (t, J = 7.9 Hz, 2H), 7.27 (d, J = 7.9 Hz, 3H), 7.08 (d, J = 6.7 Hz, 2H), 7.04 (d, J = 8.1 Hz, 1H), 6.94 (s, 2H), 5.74 (d, J = 4.2 Hz, 1H), 5.08 – 4.94 (m, 2H), 4.67 (d, J = 4.2 Hz, 1H), 2.91 (s, 3H), 2.22 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.02, 142.26, 140.96, 136.98, 135.83, 135.45, 133.53, 131.87, 130.19, 130.08, 129.31, 128.35, 128.16, 127.97, 127.36, 126.64, 125.55, 121.01, 120.86, 107.89, 105.98, 66.24, 40.90, 19.81, 19.45, 14.95; IR (neat): ν 2873, 2352, 2313, 1699, 1599, 1323, 1225, 1159, 1104, 1023, 983, 785, 745 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{25}NO_4S$ $[M+H]^+$ = 472.1583, found = 472.1592.

Benzyl-9-(4-methoxyphenyl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3e)



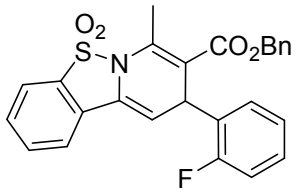
53% yield; white solid; mp 70-72°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.73 – 7.66 (m, 2H), 7.61 (t, J = 6.7 Hz, 1H), 7.43 – 7.29 (m, 5H), 7.16 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.33 (s, 1H), 5.99 (d, J = 3.7 Hz, 1H), 5.13 (q, J = 12.4 Hz, 2H), 3.79 (d, J = 6.7 Hz, 5H), 3.31 (dd, J = 16.6, 9.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.25, 158.79, 146.11, 136.16, 134.13, 133.79, 131.46, 130.45, 129.09, 128.53, 128.42, 128.25, 128.11, 127.97, 121.37, 121.13, 114.31, 106.54, 100.67, 65.90, 55.34, 36.44, 31.74; IR (neat): ν 2916, 2848, 2352, 2312, 1700, 1325, 1317, 1248, 1160, 1105, 1023, 982, 785, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{23}NO_5S$ $[M+H]^+$ = 474.1375, found = 474.1357.

Benzyl-7-methyl-9-(3,4,5-trimethoxyphenyl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3g)



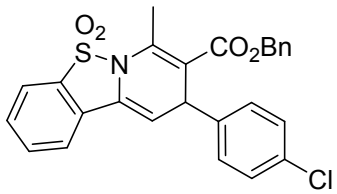
43% yield; white solid; mp 135-138°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.2 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.63 – 7.55 (m, 2H), 7.28 (dd, *J* = 8.7, 2.6 Hz, 3H), 7.09 (d, *J* = 2.1 Hz, 2H), 6.38 (d, *J* = 2.2 Hz, 2H), 5.81 – 5.71 (m, 1H), 5.03 (dd, *J* = 28.9, 12.4 Hz, 2H), 4.69 (s, 1H), 3.83 (d, *J* = 2.3 Hz, 3H), 3.71 (d, *J* = 2.2 Hz, 6H), 2.93 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.93, 153.47, 141.32, 140.57, 136.90, 135.68, 133.65, 131.91, 130.35, 128.42, 128.14, 128.08, 127.25, 126.78, 121.07, 120.91, 107.50, 105.69, 104.73, 66.37, 60.84, 56.04, 41.66, 14.94. IR (neat): 2907, 2850, 2352, 1700, 1324, 1315, 1249, 1158, 1105, 1023, 982, 794, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{29}H_{27}NO_7S$ [M+Na]+ = 556.1405, found = 556.1408.

Benzyl-9-(2-fluorophenyl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3h)



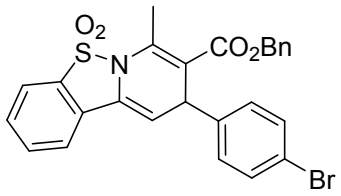
63% yield; white solid; mp 144-145°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1H), 7.66 – 7.53 (m, 3H), 7.29 – 7.16 (m, 5H), 7.12 – 6.91 (m, 4H), 5.78 (d, J = 4.6 Hz, 1H), 5.14 (d, J = 4.3 Hz, 1H), 5.01 (q, J = 12.4 Hz, 2H), 2.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.57, 143.35, 135.73, 133.65, 131.80, 131.72, 131.58, 130.39, 129.76, 129.72, 128.59, 128.51, 128.38, 127.95, 127.46, 127.10, 124.81, 121.04, 120.93, 115.54, 115.32, 105.55, 104.14, 66.24, 33.98, 14.97; IR (neat): ν 2895, 2352, 2318, 1698, 1324, 1252, 1158, 1105, 1022, 982, 893, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}FNO_4S$ $[M+H]^+$ = 462.1175, found = 462.1157.

Benzyl-9-(4-chlorophenyl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3i)



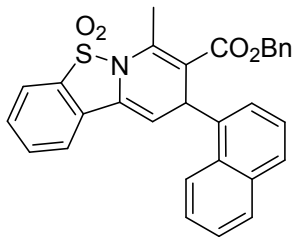
58% yield; white solid; mp 174-175°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.7 Hz, 1H), 7.68 – 7.61 (m, 1H), 7.58 (t, J = 7.6 Hz, 2H), 7.29 (d, J = 5.0 Hz, 3H), 7.20 (d, J = 7.3 Hz, 2H), 7.09 (dd, J = 11.3, 6.3 Hz, 4H), 5.70 (d, J = 4.0 Hz, 1H), 5.02 (dd, J = 28.8, 12.2 Hz, 2H), 4.70 (d, J = 4.3 Hz, 1H), 2.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.68, 143.32, 141.68, 135.60, 133.70, 132.88, 131.90, 130.48, 129.43, 128.90, 128.46, 128.26, 128.18, 127.10, 127.06, 121.10, 120.88, 107.25, 104.96, 66.35, 40.78, 14.97; IR (neat): ν 2895, 2352, 2318, 1700, 1324, 1252, 1159, 1104, 1022, 982, 893, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}ClNO_4S$ $[M+H]^+$ = 478.0880, found = 478.0874.

Benzyl-9-(4-bromophenyl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3k)



74% yield; white solid; mp 171-172°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.58 (t, J = 8.0 Hz, 2H), 7.35 (d, J = 7.5 Hz, 2H), 7.32 – 7.26 (m, 3H), 7.05 (t, J = 7.1 Hz, 4H), 5.70 (d, J = 4.4 Hz, 1H), 5.02 (dd, J = 32.7, 12.2 Hz, 2H), 4.69 (d, J = 4.1 Hz, 1H), 2.92 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.66, 143.84, 141.76, 135.59, 133.72, 131.86, 130.49, 129.80, 129.69, 128.48, 128.26, 128.19, 127.11, 127.04, 121.10, 121.01, 120.88, 107.14, 104.88, 66.36, 40.87, 14.97; IR (neat): ν 2895, 2352, 2318, 1699, 1324, 1252, 1159, 1104, 1023, 983, 893, 753 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}BrNO_4S$ $[M+H]^+$ = 522.0375, found = 522.0356.

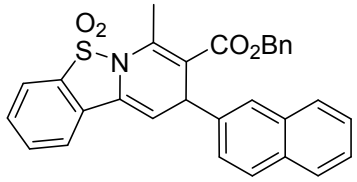
Benzyl-7-methyl-9-(naphthalen-1-yl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3n)



62% yield; white solid; mp 146-148°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.09 (m, 1H), 7.95 – 7.86 (m, 1H), 7.80 (d, J = 7.3 Hz, 1H), 7.74 (d, J = 6.4 Hz, 1H), 7.62 – 7.37 (m, 7H), 7.10 (t, J = 7.2 Hz, 1H), 6.97 (t, J = 7.3 Hz, 2H), 6.62 (d, J = 7.3 Hz, 2H), 5.86 (d, J = 4.4 Hz, 1H), 5.65 (s, 1H), 4.95 – 4.73 (m, 2H), 3.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.86, 135.34, 133.96, 133.54, 131.80, 130.23, 129.03,

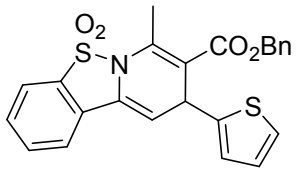
128.10, 127.70, 127.51, 127.28, 126.77, 126.60, 126.48, 126.20, 125.79, 122.50, 121.01, 120.87, 107.06, 105.15, 66.18, 14.85; IR (neat): ν 2895, 2352, 2313, 1703, 1324, 1249, 1160, 1105, 1022, 983, 893, 743 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{23}NO_4S$ $[M+H]^+$ = 494.1426, found = 494.1426.

Benzyl-7-methyl-9-(naphthalen-2-yl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3o)



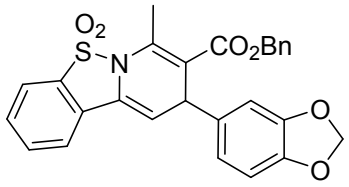
55% yield; white solid; mp 168-170°C; ^1H NMR (400 MHz, CDCl3) δ 7.80 (dd, J = 28.4, 8.7 Hz, 4H), 7.60 (t, J = 11.4 Hz, 4H), 7.47 (s, 2H), 7.36 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 6.6 Hz, 1H), 7.11 (t, J = 6.7 Hz, 2H), 6.96 (d, J = 6.8 Hz, 2H), 5.80 (s, 1H), 4.96 (s, 2H), 4.91 (s, 1H), 2.97 (s, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 166.90, 142.05, 141.50, 135.60, 133.62, 133.52, 132.62, 131.93, 130.34, 128.70, 128.29, 128.12, 127.98, 127.96, 127.65, 127.24, 126.93, 126.73, 126.27, 126.19, 125.86, 121.07, 120.87, 107.56, 105.46, 66.34, 41.54, 14.98. IR (neat): ν 2896, 2352, 2313, 1700, 1324, 1250, 1160, 1105, 1022, 987, 893, 745 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{23}NO_4S$ $[M+H]^+$ = 494.1426, found = 494.1415.

Benzyl-7-methyl-9-(thiophen-2-yl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3p)



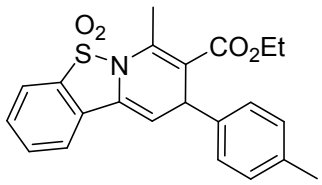
33% yield; white solid; mp 180-182°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1H), 7.70 – 7.54 (m, 3H), 7.31 (s, 3H), 7.23 – 7.08 (m, 3H), 6.90 (s, 1H), 6.82 (s, 1H), 5.84 (d, J = 4.8 Hz, 1H), 5.21 – 5.00 (m, 3H), 2.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.74, 148.80, 141.13, 135.81, 133.72, 131.94, 130.46, 128.50, 128.19, 128.12, 127.32, 127.12, 127.06, 124.82, 124.78, 121.10, 120.96, 107.43, 104.46, 66.40, 35.78, 14.94; IR (neat): ν 2914, 2873, 2380, 2312, 1699, 1325, 1247, 1159, 1103, 1022, 982, 893, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}NO_4S_2$ $[M+H]^+$ = 450.0834 , found = 450.0812.

Benzyl-9-(benzo[d][1,3]dioxol-5-yl)-7-methyl-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3r)



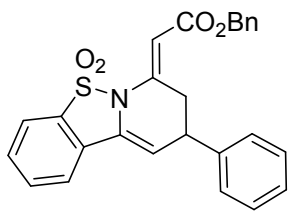
71% yield; white solid; mp 161-163°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.7 Hz, 1H), 7.69 – 7.50 (m, 3H), 7.30 (s, 3H), 7.14 (s, 2H), 6.66 (dd, J = 18.0, 9.3 Hz, 3H), 5.92 (s, 2H), 5.72 (d, J = 4.6 Hz, 1H), 5.04 (q, J = 12.3 Hz, 2H), 4.64 (d, J = 4.3 Hz, 1H), 2.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.92, 147.93, 146.64, 140.91, 138.86, 135.76, 133.62, 131.89, 130.31, 128.43, 128.28, 128.10, 127.25, 126.79, 121.31, 121.06, 120.85, 108.63, 108.40, 107.86, 105.54, 101.08, 66.31, 40.94, 14.92; IR (neat): ν 2917, 2849, 2352, 2318, 1698, 1323, 1247, 1159, 1104, 1023, 982, 893, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{21}NO_6S$ $[M+H]^+$ = 488.1168, found = 488.1155.

Ethyl-7-methyl-9-(p-tolyl)-9H-benzo[4,5]isothiazolo[2,3-a]pyridine-8-carboxylate 5,5-dioxide (3t)



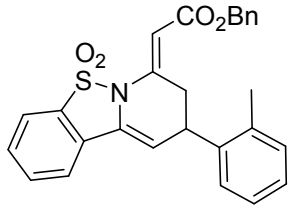
53% yield; white solid; mp 139-140°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.1 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.60 – 7.52 (m, 2H), 7.13 (dd, J = 17.5, 7.9 Hz, 4H), 5.76 (d, J = 4.7 Hz, 1H), 4.69 (d, J = 4.2 Hz, 1H), 4.03 (q, J = 7.1 Hz, 2H), 2.89 (s, 3H), 2.31 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.16, 141.92, 140.20, 136.80, 133.54, 131.95, 130.21, 129.41, 128.06, 127.38, 126.86, 121.03, 120.84, 108.42, 105.74, 60.33, 40.99, 21.09, 14.84, 14.00; IR (neat): ν 2946, 2912, 2352, 2319, 1698, 1350, 1267, 1158, 1105, 1023, 983, 893, 785, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{21}NO_4S$ $[M+H]^+$ = 396.1270, found = 396.1239.

Benzyl-(E)-2-(5,5-dioxido-9-phenyl-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4a)



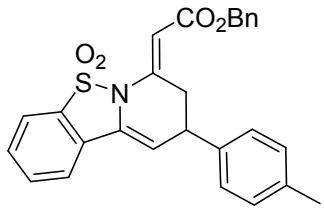
50% yield; white solid; mp 119-120°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.7 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.61 (t, J = 6.3 Hz, 1H), 7.35 (dd, J = 9.9, 5.8 Hz, 6H), 7.27 (dd, J = 14.7, 7.1 Hz, 4H), 6.34 (s, 1H), 6.01 (d, J = 3.7 Hz, 1H), 5.13 (q, J = 12.4 Hz, 2H), 3.87 (ddd, J = 12.6, 11.7, 4.9 Hz, 2H), 3.27 (dd, J = 14.7, 8.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.24, 146.01, 142.14, 136.13, 133.81, 131.47, 130.50, 129.28, 128.97, 128.53, 128.26, 128.12, 127.92, 127.42, 127.35, 121.39, 121.14, 106.18, 100.67, 65.93, 37.26, 31.59; IR (neat): ν 3029, 1708, 1672, 1620, 1494, 1471, 1453, 1394, 1327, 1248, 1183, 1162, 1130, 824, 754, 743 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{21}NO_4S$ $[M+H]^+$ = 444.1270, found = 444.1255.

Benzyl-(E)-2-(5,5-dioxido-9-(o-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4b)



82% yield; white solid; mp 70-73°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.69 (s, 2H), 7.60 (t, J = 6.5 Hz, 1H), 7.39 – 7.29 (m, 5H), 7.14 (s, 4H), 6.33 (s, 1H), 5.99 (d, J = 3.7 Hz, 1H), 5.13 (q, J = 12.4 Hz, 2H), 3.93 – 3.71 (m, 2H), 3.27 (dd, J = 14.6, 8.1 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.24, 146.13, 139.10, 136.99, 136.17, 133.78, 131.46, 130.43, 129.70, 129.62, 129.13, 128.52, 128.35, 128.25, 128.10, 127.97, 127.27, 121.36, 121.13, 106.48, 100.63, 65.89, 36.84, 31.62, 21.09; IR (neat): ν 3065, 3030, 2952, 1708, 1620, 1492, 1470, 1455, 1394, 1326, 1244, 1183, 1162, 1130, 833, 754, 743 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{23}NO_4S$ $[M+H]^+$ = 458.1426, found = 458.1409.

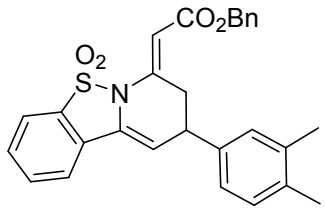
Benzyl-(E)-2-(5,5-dioxido-9-(p-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4c)



66% yield; white solid; mp 146-148°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.75 – 7.64 (m, 2H), 7.64 – 7.55 (m, 1H), 7.50 – 7.27 (m, 5H), 7.14 (s, 4H), 6.33 (s, 1H), 5.99 (d, J = 2.8 Hz, 1H), 5.13 (q, J = 12.5 Hz, 2H), 3.97 – 3.68 (m, 2H), 3.27 (dd, J = 14.6, 8.0 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.24,

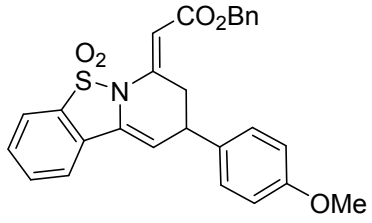
146.12, 139.09, 136.97, 136.15, 133.78, 131.45, 130.43, 129.61, 129.13, 128.52, 128.25, 128.10, 127.97, 127.26, 121.36, 121.12, 106.48, 100.62, 65.89, 36.84, 31.61, 21.09; IR (neat): ν 3063, 3030, 2321, 1708, 1620, 1513, 1471, 1454, 1394, 1327, 1249, 1183, 1162, 1129, 834, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{23}NO_4S$ $[M+H]^+$ =458.1426, found =458.1403.

Benzyl-(E)-2-(9-(3,4-dimethylphenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4d)



66% yield; white solid; mp 152-154°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 4.9 Hz, 2H), 7.60 (t, J = 6.8 Hz, 1H), 7.34 (dd, J = 15.6, 6.6 Hz, 5H), 7.10 (d, J = 7.6 Hz, 1H), 6.98 (t, 2H), 6.34 (s, 1H), 5.98 (d, J = 3.6 Hz, 1H), 5.21 – 5.06 (m, 2H), 3.93 (dd, J = 15.3, 5.7 Hz, 1H), 3.76 (dd, J = 8.8, 4.7 Hz, 1H), 3.18 (dd, J = 15.2, 9.2 Hz, 1H), 2.25 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.26, 146.30, 139.62, 137.16, 136.18, 135.64, 133.78, 131.43, 130.41, 130.16, 129.05, 128.69, 128.53, 128.27, 128.11, 128.00, 124.69, 121.35, 121.14, 106.76, 100.48, 65.89, 36.85, 31.67, 19.88, 19.44; IR (neat): ν 3064, 3032, 1708, 1673, 1620, 1501, 1471, 1453, 1394, 1327, 1291, 1255, 1183, 1163, 1130, 833, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{25}NO_4S$ $[M+H]^+$ =472.1583, found =472.1560.

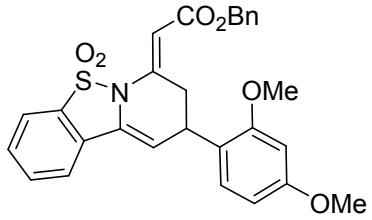
Benzyl-(E)-2-(9-(4-methoxyphenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4e)



57% yield; white solid; mp 122-123°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.8 Hz, 1H), 7.73 – 7.64 (m, 2H), 7.60 (t, J = 6.9 Hz, 1H), 7.45 – 7.27 (m, 5H), 7.15 (d, J = 7.6 Hz, 2H), 6.86 (d, J = 7.6 Hz, 2H), 6.34 (s, 1H), 5.98 (s, 1H), 5.20 – 5.02 (m, 2H), 3.79 (s, 5H), 3.31 (dd, J = 16.5, 10.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.24, 158.79, 146.12, 136.16, 134.13, 133.79, 131.46, 130.45, 129.09, 128.53, 128.41, 128.25, 128.11, 127.97, 121.36, 121.13, 114.31, 106.54, 100.66, 100.00, 65.89, 55.34, 36.43, 31.74; IR (neat): ν 3064, 3011, 1708, 1673, 1619, 1511, 1470, 1455, 1394,

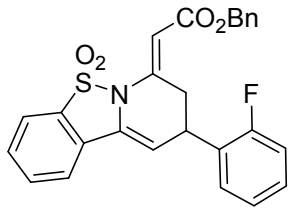
1327, 1249, 1183, 1162, 1140, 832, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{23}NO_5S$ $[M+H]^+$ =474.1375, found =474.1356.

Benzyl-(E)-2-(9-(2,4-dimethoxyphenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4f)



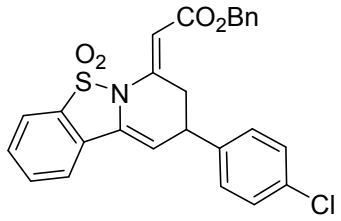
77% yield; white solid; mp 71-73°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 6.1 Hz, 1H), 7.69 (s, 2H), 7.59 (s, 1H), 7.36 (s, 5H), 7.03 (d, J = 7.2 Hz, 1H), 6.52 – 6.38 (m, 2H), 6.32 (s, 1H), 5.98 (s, 1H), 5.13 (s, 2H), 4.16 (s, 1H), 3.81 (d, J = 8.8 Hz, 6H), 3.65 – 3.41 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.32, 160.02, 157.78, 146.89, 136.27, 133.68, 131.29, 130.18, 128.93, 128.50, 128.26, 128.20, 128.16, 128.04, 122.28, 121.30, 121.05, 106.86, 104.17, 100.05, 98.85, 65.79, 55.45, 55.42, 30.26, 29.79; IR (neat): ν 2955, 2836, 2351, 2322, 1709, 1677, 1614, 1586, 1504, 1468, 1455, 1438, 1418, 1395, 1326, 1292, 1263, 1208, 1183, 1161, 1129, 833, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{25}NO_6S$ $[M+H]^+$ =504.1481, found =504.1462.

Benzyl-(E)-2-(9-(2-fluorophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4h)



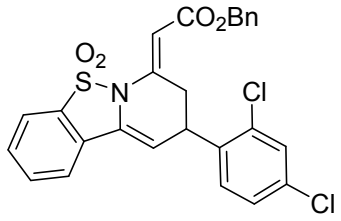
70% yield; white solid; mp 132-133°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.69 (q, J = 7.7 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.45 – 7.27 (m, 5H), 7.22 (dd, J = 17.2, 9.3 Hz, 2H), 7.08 (dd, J = 18.8, 8.6 Hz, 2H), 6.35 (s, 1H), 5.98 (d, J = 4.2 Hz, 1H), 5.22 – 5.04 (m, 2H), 4.18 (dd, J = 11.7, 6.2 Hz, 1H), 3.75 (dd, J = 15.4, 5.9 Hz, 1H), 3.48 (dd, J = 15.4, 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.20, 161.68, 159.24, 145.76, 136.10, 133.86, 131.39, 130.58, 129.60, 129.02, 128.94, 128.75, 128.55, 128.29, 128.15, 127.83, 124.64, 121.37, 121.20, 115.86, 115.64, 104.84, 100.79, 65.98, 30.26, 29.70; IR (neat): ν 3065, 3032, 2892, 2351, 1709, 1679, 1621, 1584, 1490, 1472, 1454, 1395, 1328, 1229, 1183, 1162, 1140, 834, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}FNO_4S$ $[M+H]^+$ =462.1175, found =462.1161.

Benzyl-(E)-2-(9-(4-chlorophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4i)



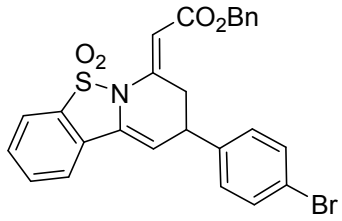
59% yield; white solid; mp 152-154°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.8 Hz, 1H), 7.76 – 7.67 (m, 2H), 7.63 (dd, J = 9.5, 3.8 Hz, 1H), 7.32 (dt, J = 21.8, 8.6 Hz, 7H), 7.17 (d, J = 8.2 Hz, 2H), 6.34 (s, 1H), 5.96 (d, J = 4.0 Hz, 1H), 5.23 – 5.02 (m, 2H), 3.79 (ddd, J = 20.8, 14.1, 5.8 Hz, 2H), 3.36 (dd, J = 15.0, 7.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.19, 145.49, 140.53, 136.05, 133.87, 133.12, 130.66, 129.57, 129.09, 128.78, 128.55, 128.26, 128.17, 127.75, 121.42, 121.18, 105.21, 101.06, 99.99, 65.99, 36.62, 31.40; IR (neat): ν 3080, 2892, 2351, 2322, 1709, 1679, 1621, 1553, 1492, 1471, 1454, 1434, 1395, 1327, 1229, 1183, 1162, 1141, 832, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}ClNO_4S$ $[M+H]^+$ =478.0880, found =478.0864.

Benzyl-(E)-2-(9-(2,4-dichlorophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4j)



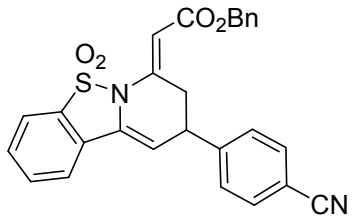
68% yield; white solid; mp 82-84°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.77 – 7.68 (m, 2H), 7.67 – 7.59 (m, 1H), 7.43 (s, 1H), 7.36 (s, 5H), 7.21 (d, J = 8.1 Hz, 1H), 7.14 (d, J = 8.3 Hz, 1H), 6.35 (s, 1H), 5.94 (d, J = 4.0 Hz, 1H), 5.22 – 5.04 (m, 2H), 4.31 (d, J = 5.0 Hz, 1H), 3.59 (ddd, J = 32.5, 15.4, 6.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.05, 145.06, 137.64, 135.99, 134.14, 133.92, 133.66, 131.44, 130.76, 130.13, 129.74, 129.22, 128.54, 128.31, 128.18, 127.72, 127.64, 121.43, 121.23, 103.82, 101.35, 66.04, 33.24, 29.42; IR (neat): ν 3080, 2892, 2352, 2321, 1710, 1679, 1621, 1554, 1471, 1380, 1329, 1264, 1184, 1162, 1141, 833, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{19}Cl_2NO_4S$ $[M+H]^+$ = 512.0466, found = 512.0476.

Benzyl-(E)-2-(9-(4-bromophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4k)



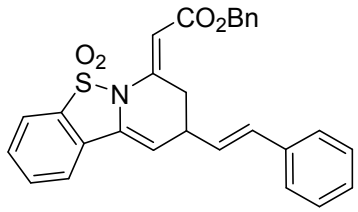
53% yield; white solid; mp 139-141°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.8 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.63 (dd, J = 9.5, 4.0 Hz, 1H), 7.45 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 39.2 Hz, 5H), 7.12 (d, J = 8.3 Hz, 2H), 6.34 (s, 1H), 5.95 (d, J = 3.7 Hz, 1H), 5.22 – 5.01 (m, 2H), 3.77 (dd, J = 23.7, 8.7 Hz, 2H), 3.36 (dd, J = 14.7, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.17, 145.45, 141.06, 136.05, 133.87, 132.04, 131.51, 130.67, 129.60, 129.14, 128.55, 128.26, 128.16, 127.73, 121.41, 121.18, 105.09, 101.08, 100.00, 65.99, 36.68, 31.32; IR (neat): ν 3080, 3031, 2890, 2321, 1708, 1674, 1621, 1487, 1472, 1454, 1398, 1264, 1184, 1162, 1140, 824, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{26}H_{20}BrNO_4S$ $[M+H]^+$ =522.0375, found =522.0365.

Benzyl-(E)-2-(9-(4-cyanophenyl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4l)



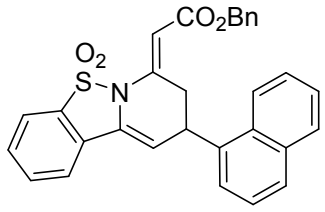
41% yield; white solid; mp 70-72°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.7 Hz, 1H), 7.73 (d, J = 2.7 Hz, 2H), 7.65 (dd, J = 14.5, 5.3 Hz, 3H), 7.36 (s, 7H), 6.35 (s, 1H), 5.95 (d, J = 4.0 Hz, 1H), 5.20 – 5.06 (m, 2H), 3.91 (d, J = 5.5 Hz, 1H), 3.72 (dd, J = 15.2, 5.6 Hz, 1H), 3.48 (dd, J = 15.3, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.11, 147.40, 144.84, 135.94, 133.96, 132.79, 131.58, 130.91, 130.11, 128.56, 128.28, 128.24, 127.52, 121.48, 121.24, 118.63, 111.34, 103.68, 101.47, 66.07, 37.18, 30.93; IR (neat): ν 2352, 2312, 2228, 1842, 1731, 1699, 1553, 1329, 1262, 1183, 1162, 1141, 821, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{20}N_2O_4S$ $[M+H]^+$ =469.1222, found =469.1205.

Benzyl-(E)-2-(5,5-dioxido-9-((E)-styryl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4m)



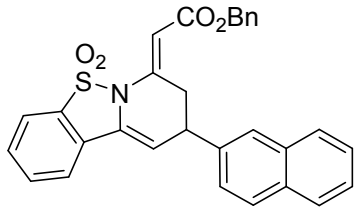
60% yield; white solid; mp 72-75°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.4 Hz, 1H), 7.77 – 7.67 (m, 2H), 7.64 – 7.58 (m, 1H), 7.49 – 7.27 (m, 10H), 6.53 (d, J = 15.9 Hz, 1H), 6.36 (s, 1H), 6.15 (dd, J = 15.9, 6.8 Hz, 1H), 5.92 (s, 1H), 5.34 – 5.06 (m, 2H), 3.60 – 3.51 (m, 1H), 3.51 – 3.38 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.37, 145.99, 136.66, 136.15, 133.77, 131.41, 130.46, 129.08, 129.02, 128.61, 128.53, 128.29, 128.12, 127.93, 127.71, 127.08, 126.39, 121.37, 121.10, 104.95, 100.97, 65.97, 34.44, 29.33; IR (neat): ν 3080, 3030, 2943, 2321, 1708, 1619, 1495, 1471, 1453, 1394, 1264, 1183, 1163, 1141, 842, 753 cm^{-1}; HRMS (ESI) m/z calcd for $C_{28}H_{23}NO_4S$ $[M+H]^+$ =470.1426, found =470.1428.

Benzyl-(E)-2-(9-(naphthalen-1-yl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4n)



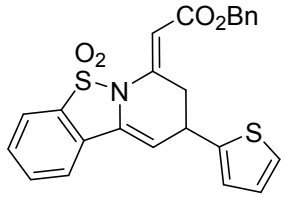
88% yield; white solid; mp 82-85°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.2 Hz, 1H), 7.90 (dd, J = 14.8, 7.9 Hz, 2H), 7.80 (d, J = 7.9 Hz, 1H), 7.70 (q, J = 8.0 Hz, 2H), 7.58 (ddd, J = 19.5, 14.6, 7.1 Hz, 3H), 7.48 – 7.37 (m, 2H), 7.29 (d, J = 27.9 Hz, 5H), 6.37 (s, 1H), 6.11 (d, J = 3.7 Hz, 1H), 5.09 (q, J = 12.4 Hz, 2H), 4.80 – 4.51 (m, 1H), 4.13 (dd, J = 15.2, 5.6 Hz, 1H), 3.42 (dd, J = 15.1, 9.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.14, 146.17, 137.50, 136.09, 134.12, 133.82, 131.46, 130.95, 130.49, 129.50, 129.26, 128.50, 128.27, 128.10, 128.06, 127.94, 126.66, 125.88, 125.63, 124.51, 122.77, 121.41, 121.19, 106.48, 100.73, 65.93, 33.05, 30.51; IR (neat): ν 3079, 2974, 2352, 2313, 1708, 1620, 1515, 1471, 1454, 1395, 1264, 1183, 1161, 1141, 833, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{23}ClNO_4S$ $[M+H]^+$ =494.1426, found =494.1420.

Benzyl-(E)-2-(9-(naphthalen-2-yl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4o)



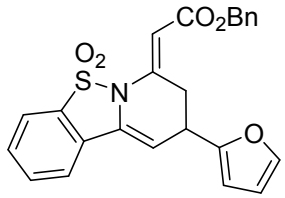
81% yield; white solid; mp 155-147°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.76 (m, 4H), 7.72 (dd, J = 14.0, 8.0 Hz, 3H), 7.61 (t, J = 7.4 Hz, 1H), 7.53 – 7.42 (m, 2H), 7.42 – 7.21 (m, 6H), 6.36 (s, 1H), 6.07 (d, J = 3.0 Hz, 1H), 5.11 (q, J = 12.4 Hz, 2H), 4.09 – 3.84 (m, 2H), 3.41 (dd, J = 14.8, 8.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.23, 145.95, 139.46, 136.11, 133.84, 133.51, 132.65, 131.52, 130.55, 129.45, 128.85, 128.51, 128.25, 128.11, 127.92, 127.81, 127.70, 126.37, 126.00, 125.96, 125.59, 121.40, 121.22, 105.94, 100.84, 65.93, 37.37, 31.51; IR (neat): ν 3079, 2352, 2320, 1708, 1620, 1537, 1471, 1454, 1395, 1265, 1183, 1162, 1141, 841, 752 cm^{-1}; HRMS (ESI) m/z calcd for $C_{30}H_{23}NO_4S$ $[M+H]^+$ =494.1426, found =494.1419.

Benzyl-(E)-2-(5,5-dioxido-9-(thiophen-2-yl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4p)



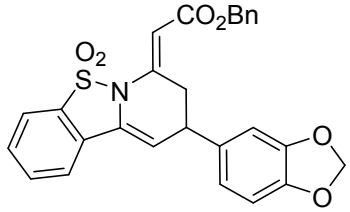
57% yield; white solid; mp 53-56°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.7 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.62 (t, J = 6.8 Hz, 1H), 7.36 (d, J = 12.3 Hz, 5H), 7.20 (d, J = 4.4 Hz, 1H), 6.95 (d, J = 8.1 Hz, 2H), 6.36 (s, 1H), 6.05 (d, J = 3.6 Hz, 1H), 5.16 (q, J = 12.4 Hz, 2H), 4.14 (d, J = 5.1 Hz, 1H), 3.74 (dd, J = 15.1, 5.3 Hz, 1H), 3.62 (dd, J = 15.0, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.21, 145.39, 145.03, 136.10, 133.86, 131.54, 130.66, 129.05, 128.55, 128.28, 128.14, 127.77, 127.08, 124.51, 124.38, 121.38, 121.26, 105.41, 101.30, 65.99, 32.43, 31.63; IR (neat): ν 2920, 2850, 2352, 2320, 1710, 1622, 1537, 1470, 1454, 1395, 1265, 1184, 1162, 1142, 745 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}NO_4S_2$ $[M+H]^+$ =450.0834, found =450.0832.

Benzyl-(E)-2-(9-(furan-2-yl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4q)



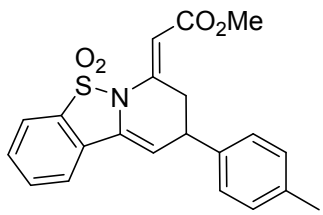
49% yield; white solid; mp 63-65°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.7 Hz, 1H), 7.71 (t, J = 8.3 Hz, 2H), 7.61 (t, J = 7.2 Hz, 1H), 7.43 – 7.32 (m, 6H), 6.40 – 6.27 (m, 2H), 6.15 (s, 1H), 6.03 (d, J = 4.0 Hz, 1H), 5.24 – 5.10 (m, 2H), 3.94 (dd, J = 11.4, 5.7 Hz, 1H), 3.76 (dd, J = 15.3, 5.5 Hz, 1H), 3.56 (dd, J = 15.3, 8.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.27, 154.05, 145.58, 142.07, 136.12, 133.81, 131.47, 130.60, 129.35, 128.55, 128.29, 128.15, 127.81, 121.35, 121.23, 110.41, 105.65, 102.93, 100.99, 66.00, 30.86, 28.09; IR (neat): ν 2962, 2894, 2352, 2320, 1711, 1622, 1537, 1471, 1454, 1395, 1263, 1184, 1162, 1141, 744 cm^{-1}; HRMS (ESI) m/z calcd for $C_{24}H_{19}NO_5S$ $[M+H]^+$ =434.1062, found =434.1068.

Benzyl-(E)-2-(9-(benzo[d][1,3]dioxol-5-yl)-5,5-dioxido-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4r)



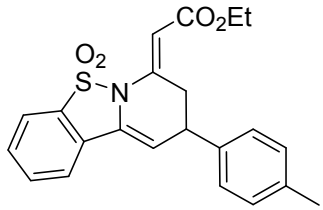
82% yield; white solid; mp 72-74°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 13.4 Hz, 2H), 7.61 (t, J = 6.3 Hz, 1H), 7.45 – 7.28 (m, 5H), 6.88 – 6.60 (m, 3H), 6.34 (s, 1H), 5.95 (s, 3H), 5.14 (q, J = 12.5 Hz, 2H), 3.79 (dd, J = 22.9, 8.4 Hz, 2H), 3.28 (dd, J = 13.9, 7.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.24, 148.04, 146.77, 145.92, 136.13, 135.94, 133.82, 131.47, 130.52, 129.23, 128.53, 128.27, 128.13, 127.88, 121.38, 121.14, 120.53, 108.56, 107.81, 106.12, 101.14, 100.75, 65.93, 36.95, 31.80; IR (neat): ν 2918, 2849, 2352, 2319, 1711, 1621, 1537, 1471, 1453, 1396, 1264, 1183, 1161, 1142, 745 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{21}NO_6S$ $[M+H]^+$ =488.1168, found =488.1171.

Methyl-(E)-2-(5,5-dioxido-9-(p-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4s)



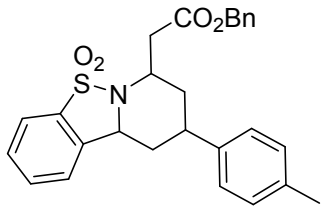
53% yield; white solid; mp 149-150°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.7 Hz, 1H), 7.68 (d, J = 12.9 Hz, 2H), 7.60 (t, J = 6.8 Hz, 1H), 7.14 (s, 4H), 6.30 (s, 1H), 5.98 (s, 1H), 3.85 – 3.75 (m, 2H), 3.68 (s, 3H), 3.28 (dd, J = 17.1, 10.2 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.85, 145.79, 139.11, 136.97, 133.79, 131.45, 130.45, 129.61, 129.12, 127.98, 127.26, 121.34, 121.14, 106.41, 100.61, 51.22, 36.84, 31.56, 21.09; IR (neat): ν 2948, 2352, 2314, 1710, 1622, 1533, 1471, 1454, 1385, 1266, 1187, 1162, 1145, 755 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{19}NO_4S$ $[M+H]^+$ = 382.1113, found = 382.1116.

Ethyl-(E)-2-(5,5-dioxido-9-(p-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-ylidene)acetate (4t)



59% yield; white solid; mp 108-110°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 6.5 Hz, 1H), 7.69 (s, 2H), 7.60 (s, 1H), 7.14 (s, 4H), 6.29 (s, 1H), 5.98 (s, 1H), 4.13 (s, 2H), 3.82 (d, J = 14.8 Hz, 2H), 3.27 (s, 1H), 2.33 (s, 3H), 1.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.44, 145.55, 139.17, 136.93, 133.78, 131.46, 130.43, 129.60, 129.14, 128.00, 127.27, 121.33, 121.15, 106.41, 101.12, 59.99, 36.86, 31.53, 21.09, 14.29; IR (neat): ν 2953, 2873, 2352, 2313, 1703, 1622, 1553, 1471, 1454, 1383, 1266, 1185, 1162, 1144, 754 cm^{-1}; HRMS (ESI) m/z calcd for $C_{22}H_{21}NO_4S$ $[M+H]^+$ = 396.1270, found = 396.1277.

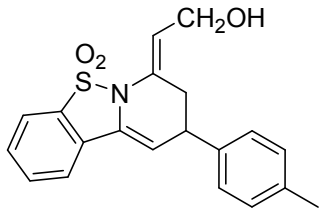
Benzyl-2-(5,5-dioxido-9-(p-tolyl)-8,9,10,10a-tetrahydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridin-7-yl)acetate (5)



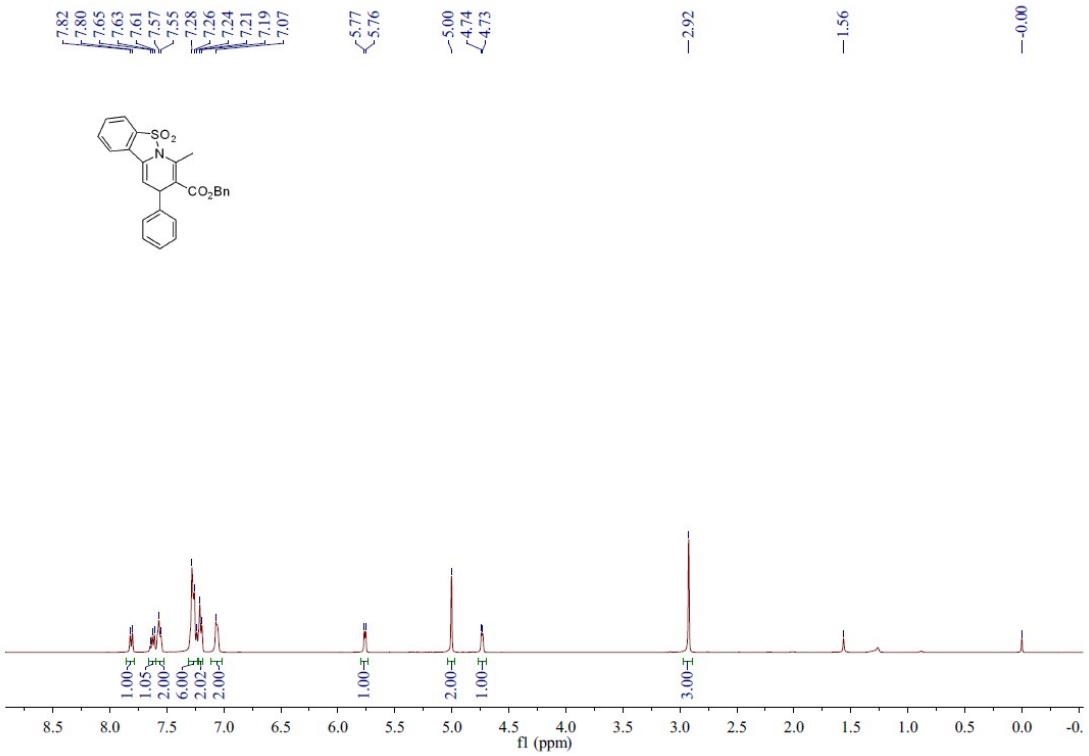
92% yield; white solid; mp 64-66°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.2 Hz, 1H), 7.54 (dt, J = 27.8, 7.1 Hz, 2H), 7.34 (s, 6H), 7.11 (d, J = 8.6 Hz, 4H), 5.14 (q, J = 12.1 Hz, 2H), 4.39 (d, J = 11.0 Hz, 1H), 3.96 (s, 1H), 3.67 (d, J = 15.8 Hz, 1H), 3.07 – 2.82 (m, 2H), 2.42 (d, J = 12.2 Hz, 1H), 2.32 (s, 3H), 2.09 (d, J = 12.3 Hz, 1H), 1.75 (dt, J = 23.3, 11.8 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 170.30, 140.85, 137.61, 136.59, 135.61, 132.87, 129.63, 129.43, 129.29, 128.60, 128.34, 127.29,

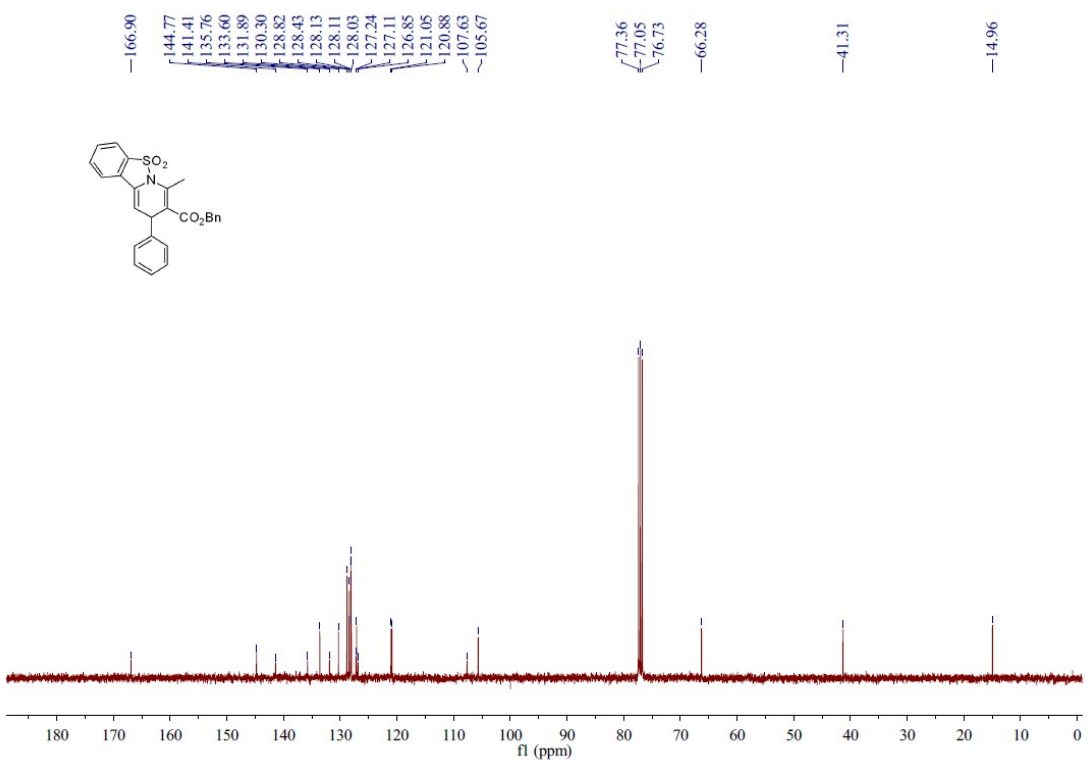
126.73, 122.75, 121.18, 66.69, 61.01, 53.73, 41.58, 38.28, 37.09, 36.94, 21.04; IR (neat): ν 3032, 2919, 2850, 2375, 2310, 1735, 1658, 1514, 1470, 1294, 1170, 1060, 967, 815, 748 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{27}NO_4S$ $[M+H]^+$ = 462.1739, found = 462.1735.

(E)-7-(2-hydroxyethylidene)-9-(p-tolyl)-8,9-dihydro-7H-benzo[4,5]isothiazolo[2,3-a]pyridine 5,5-dioxide (6)



53% yield; white solid; mp 125-128°C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.7 Hz, 1H), 7.66 (q, J = 7.8 Hz, 2H), 7.62 – 7.55 (m, 1H), 7.19 – 7.07 (m, 4H), 6.23 (t, J = 7.2 Hz, 1H), 5.83 (d, J = 3.4 Hz, 1H), 4.12 (dd, J = 17.6, 7.2 Hz, 2H), 3.79 (d, J = 4.8 Hz, 1H), 2.89 (dd, J = 13.8, 4.9 Hz, 1H), 2.64 (dd, J = 13.8, 7.1 Hz, 1H), 2.33 (s, 3H), 1.13 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.72, 137.01, 133.31, 132.01, 131.95, 130.25, 130.21, 129.54, 128.45, 127.37, 121.21, 121.06, 112.37, 103.68, 57.68, 38.06, 32.07, 21.06; IR (neat): ν 3059, 3021, 2922, 2860, 2378, 2319, 1711, 1672, 1513, 1470, 1316, 1275, 1175, 1158, 1132, 817, 751 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{19}NO_3S$ $[M+H]^+$ = 354.1164, found = 354.1153.


7.82
7.80
7.65
7.63
7.61
7.57
7.55
7.28
7.26
7.24
7.21
7.19
7.07
5.77
5.76
5.00
4.74
4.73
2.92
1.56
0.00
SO2
N
CO2Bn
1.00
1.05
2.00
6.00
2.02
2.00
1.00
2.00
1.00
3.00
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.
f1 (ppm)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128.43
128.13
128.11
128.03
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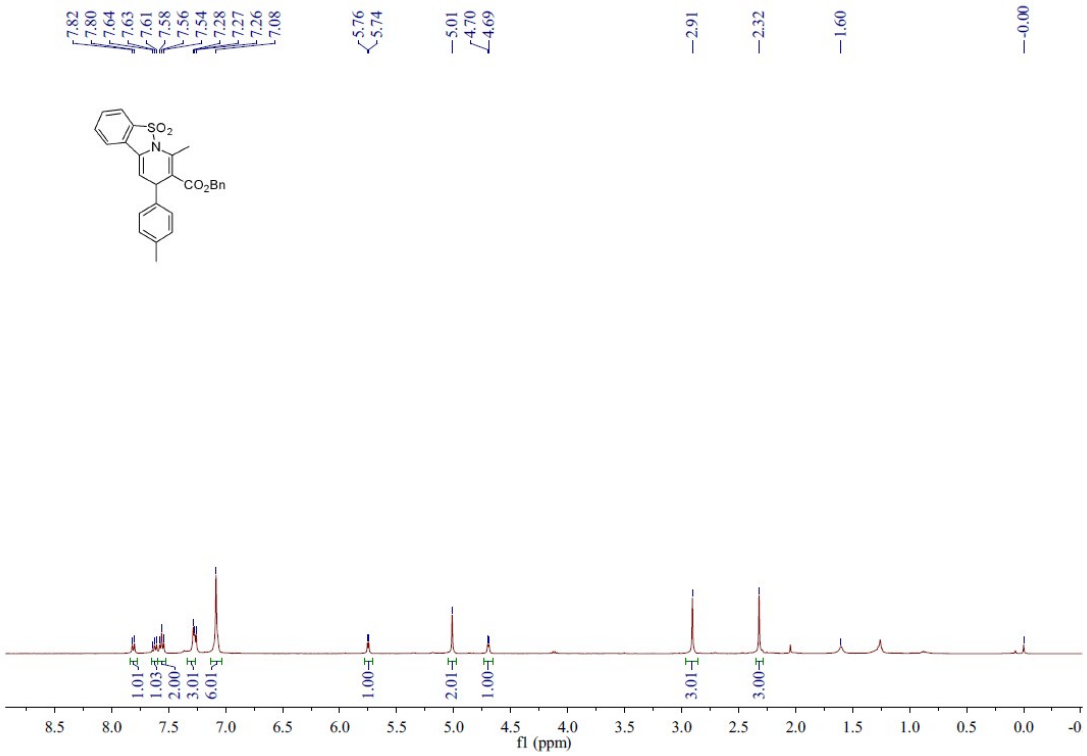
127.11
126.85
121.05
120.88
107.63
105.67
77.36
77.05
76.73
66.28
41.31
14.96
SO2
N
CO2Bn
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.56
7.54
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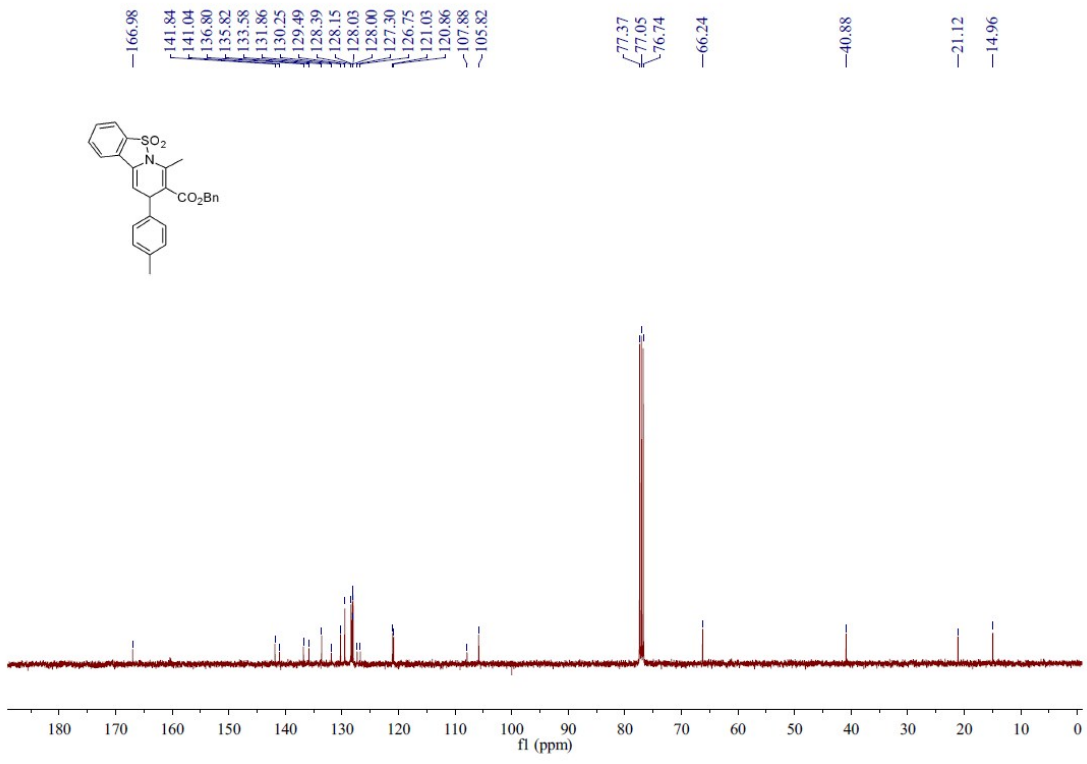
7.27
7.26
7.08
5.76
5.74
5.01
4.70
4.69
2.91
2.32
1.60
0.00
SO2
N
CO2Bn
1.01
1.03
2.00
3.01
6.01
1.00
2.01
1.00
3.01
3.00
fl (ppm)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127.30
126.75
121.03
120.86
107.88
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76.74
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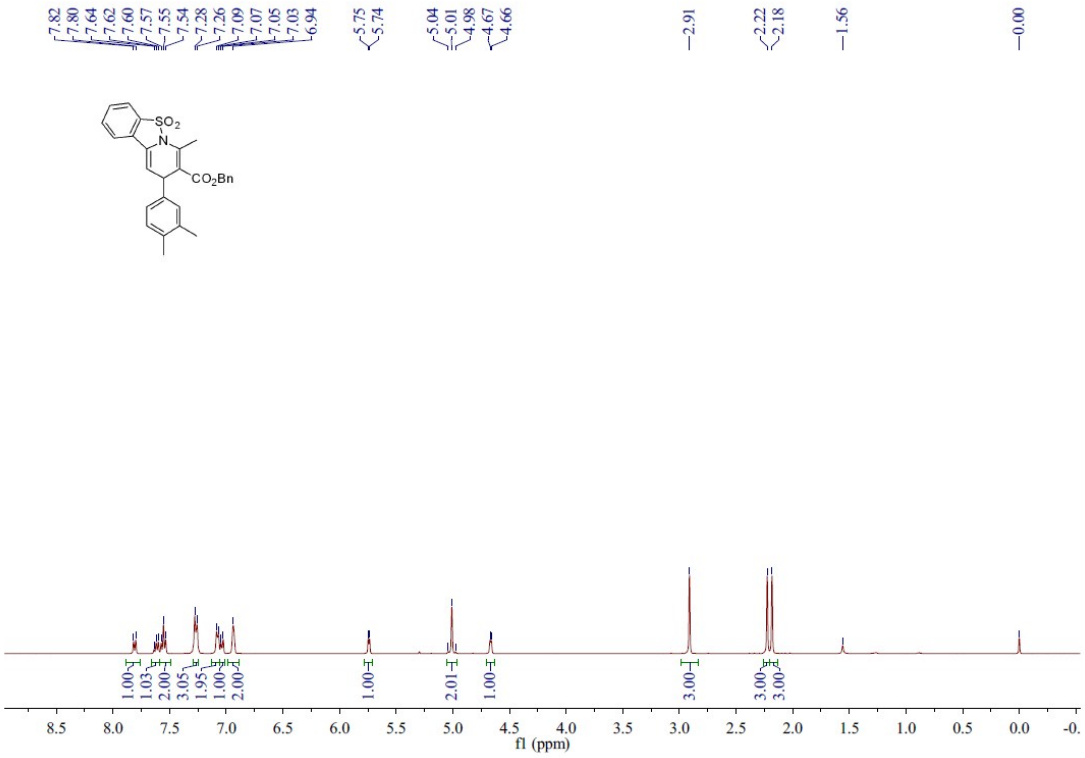
40.88
21.12
14.96
SO2
N
CO2Bn
fl (ppm)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7.09
7.07
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7.03
6.94
5.75
5.74
5.04
5.01
4.98
4.67
4.66
2.91
2.22
2.18
1.56
0.00
SO2
N
CO2Bn
1.00
1.03
2.00
3.05
1.95
1.00
2.00
1.00
2.01
1.00
3.00
3.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
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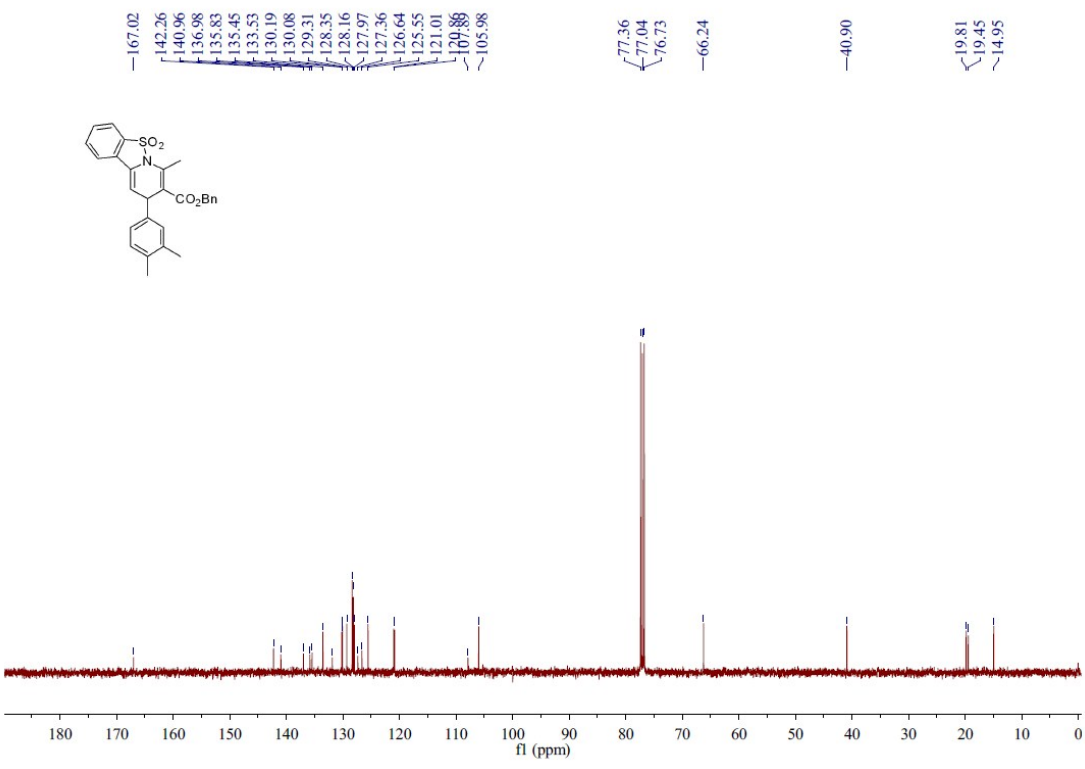
-0.
f1 (ppm)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126.64
125.55
121.01
105.98
77.36
77.04
76.73
66.24
40.90
19.81
19.45
14.95
SO2
N
CO2Bn
180
170
160
150
140
130
120
110
100
90
80
70
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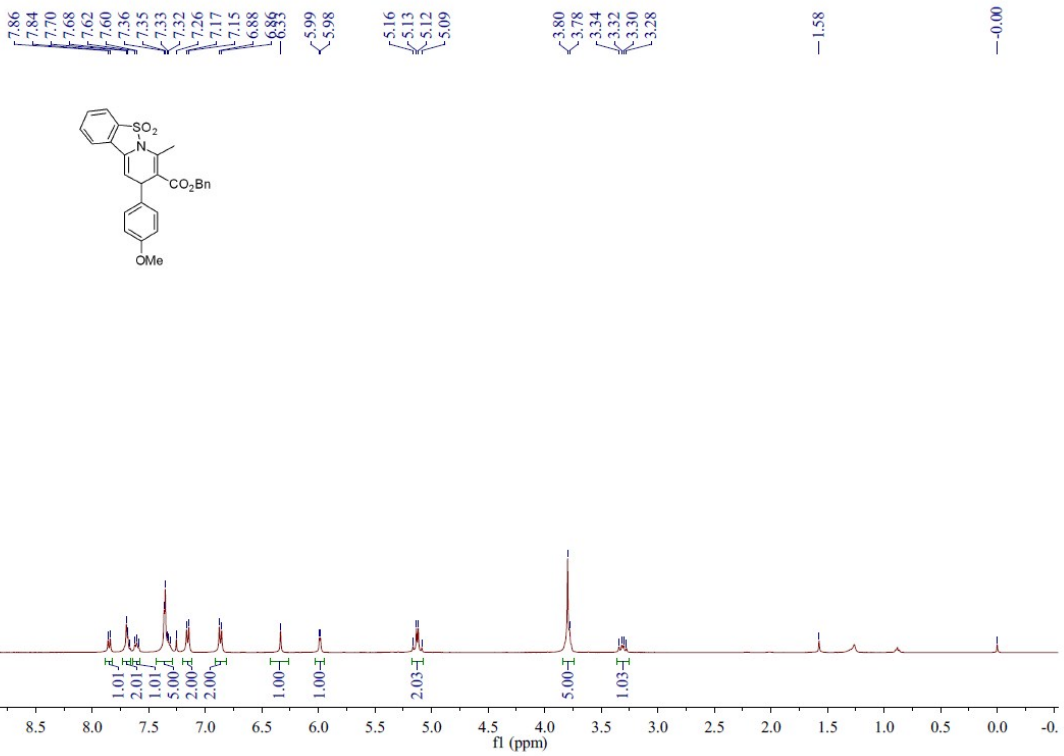
50
40
30
20
10
0
f1 (ppm)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7.35
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7.32
7.26
7.17
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6.88
6.85
6.83
5.99
5.98
5.16
5.13
5.12
5.09
3.80
3.78
3.34
3.32
3.30
3.28
1.58
0.00
SO2
N
CO2Bn
OMe
1.01
2.01
1.01
5.00
2.00
2.00
1.00
1.00
2.03
5.00
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.0
1.5
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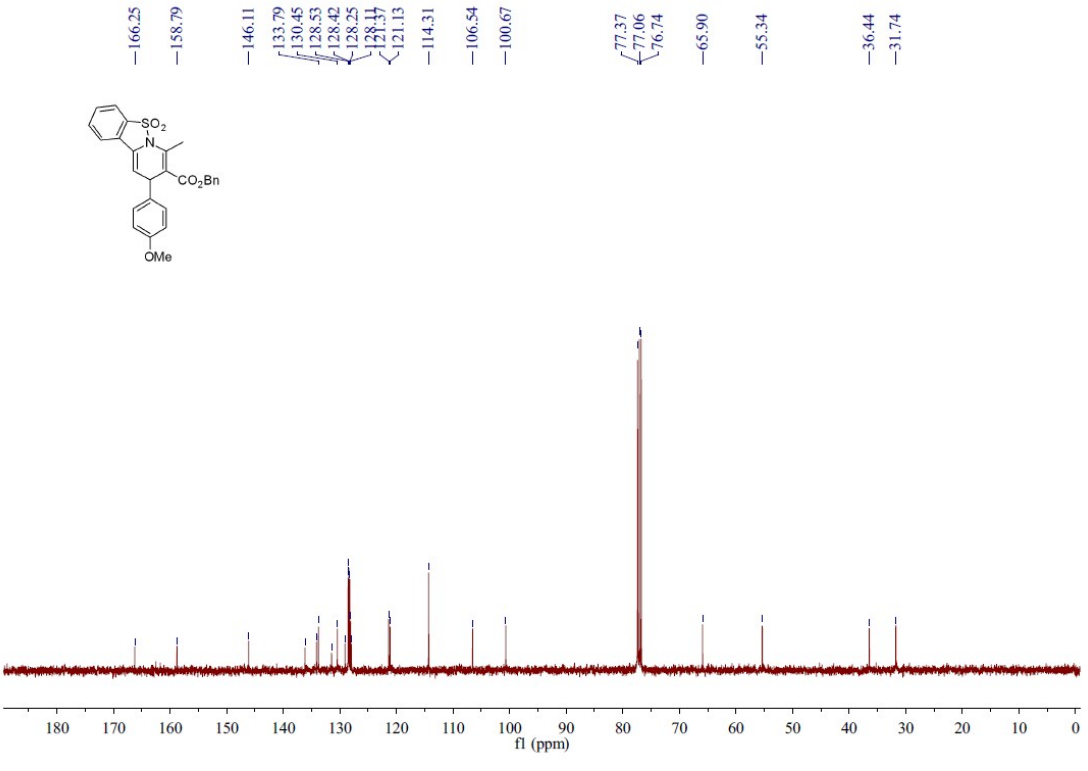
-0.
f1 (ppm)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146.11
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128.42
128.25
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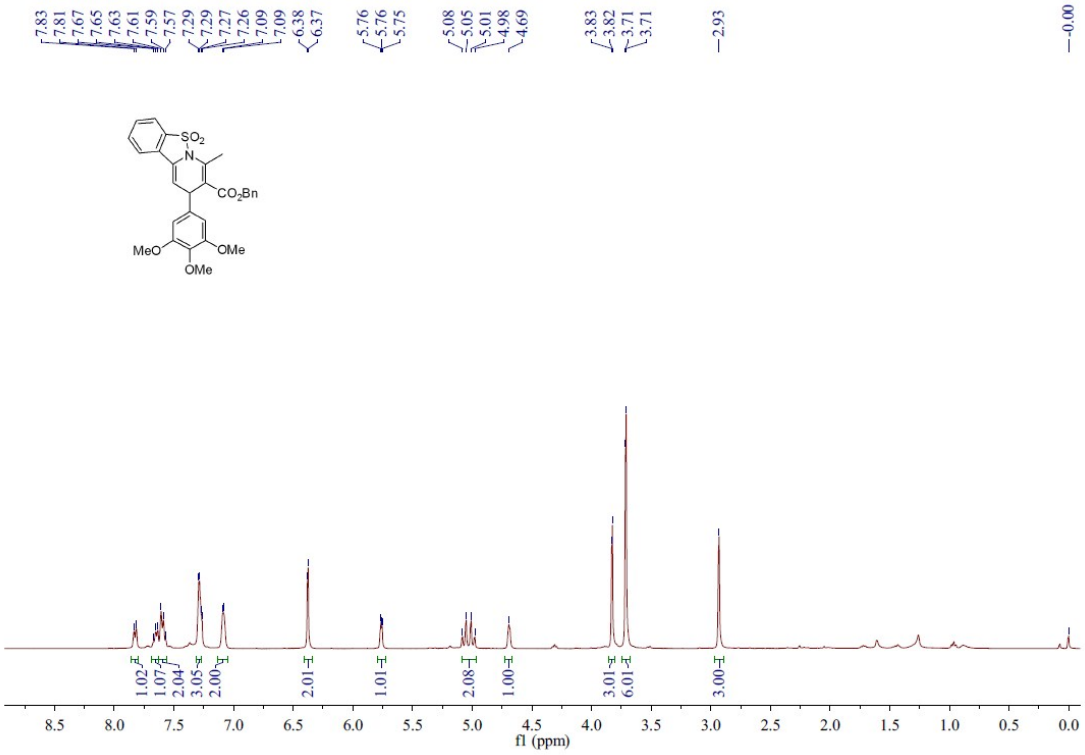
121.37
121.13
114.31
106.54
100.67
77.37
77.06
76.74
65.90
55.34
36.44
31.74
SO2
N
CO2Bn
OMe
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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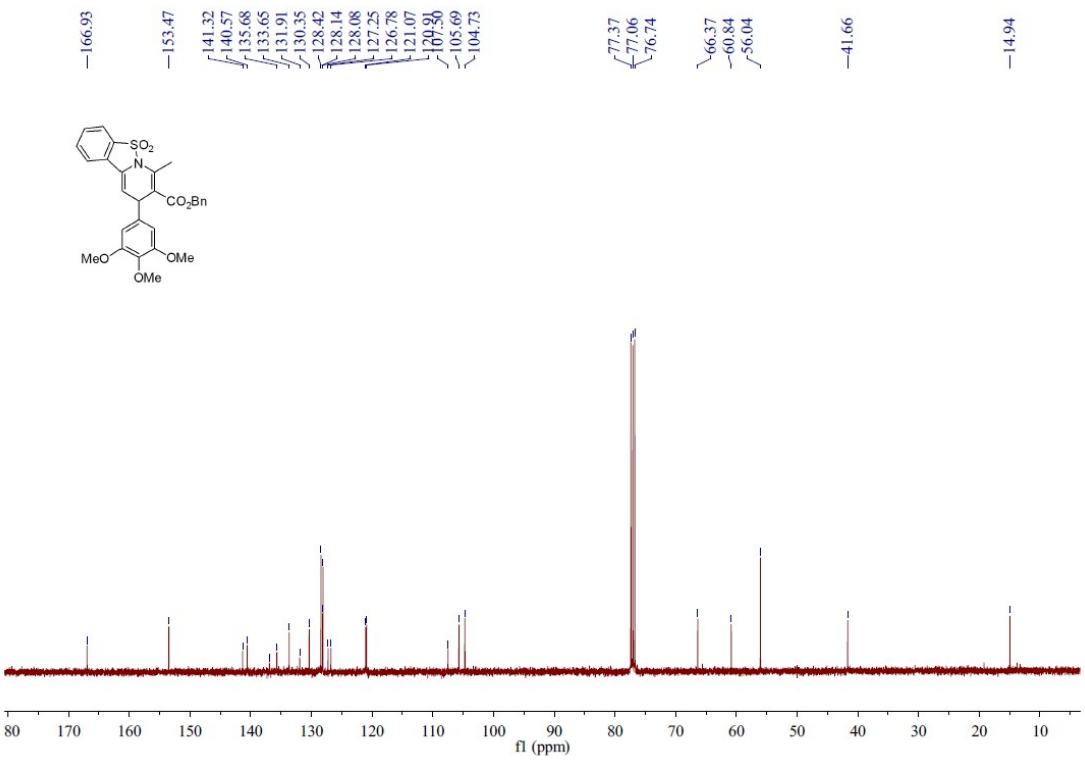
7.29
7.27
7.26
7.09
7.09
6.38
6.37
5.76
5.76
5.75
5.08
5.05
5.01
4.98
4.69
3.83
3.82
3.71
3.71
2.93
0.00
SO2
N
CO2Bn
MeO
OMe
OMe
1.02
1.07
2.04
3.05
2.00
2.01
1.01
2.08
1.00
3.01
6.01
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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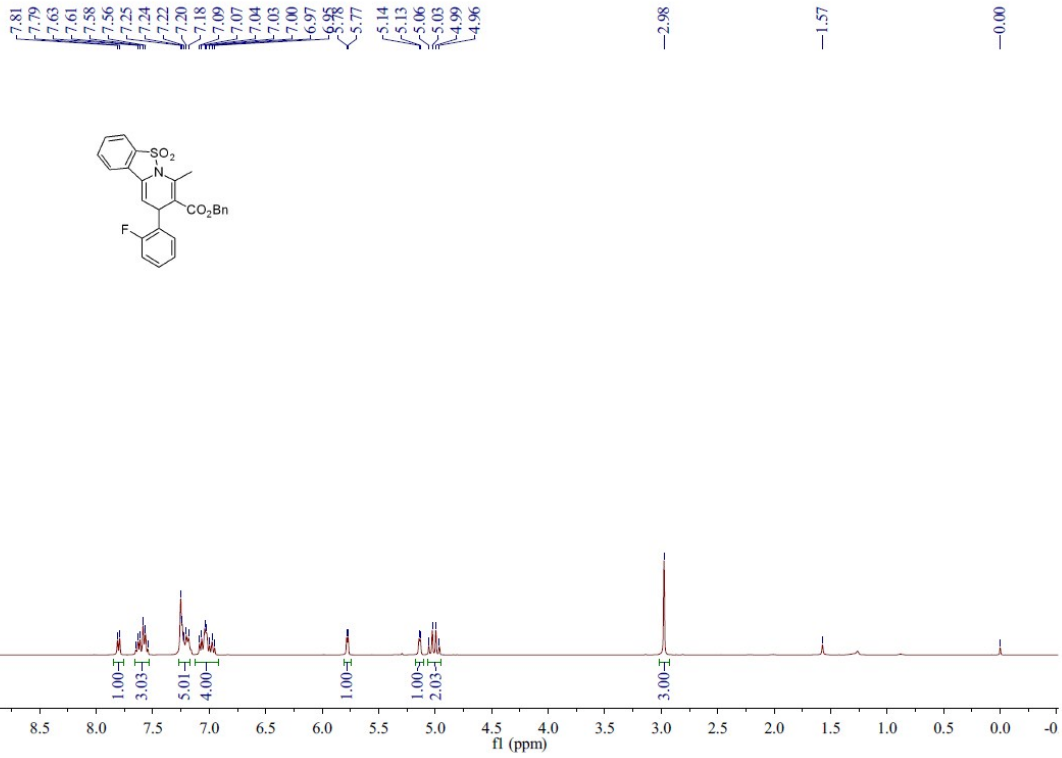
141.32
140.57
135.68
133.65
131.91
130.35
128.42
128.14
128.08
127.25
126.78
121.07
107.30
105.69
104.73
77.37
77.06
76.74
66.37
60.84
56.04
41.66
14.94
SO2
N
CO2Bn
MeO
OMe
OMe
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.22
7.20
7.18
7.09
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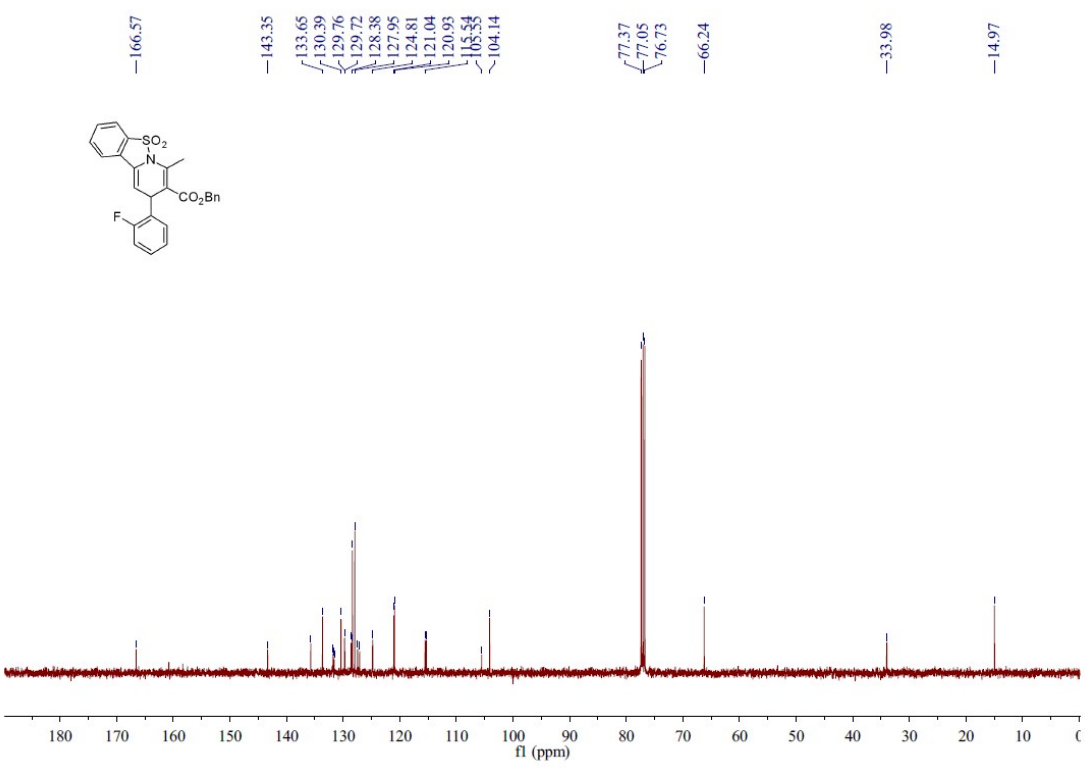
7.04
7.03
7.00
6.97
5.77
5.14
5.13
5.06
5.03
4.99
4.96
2.98
1.57
0.00
SO2
N
CO2Bn
F
1.00
3.03
5.01
4.00
1.00
1.00
2.03
3.00
f1 (ppm)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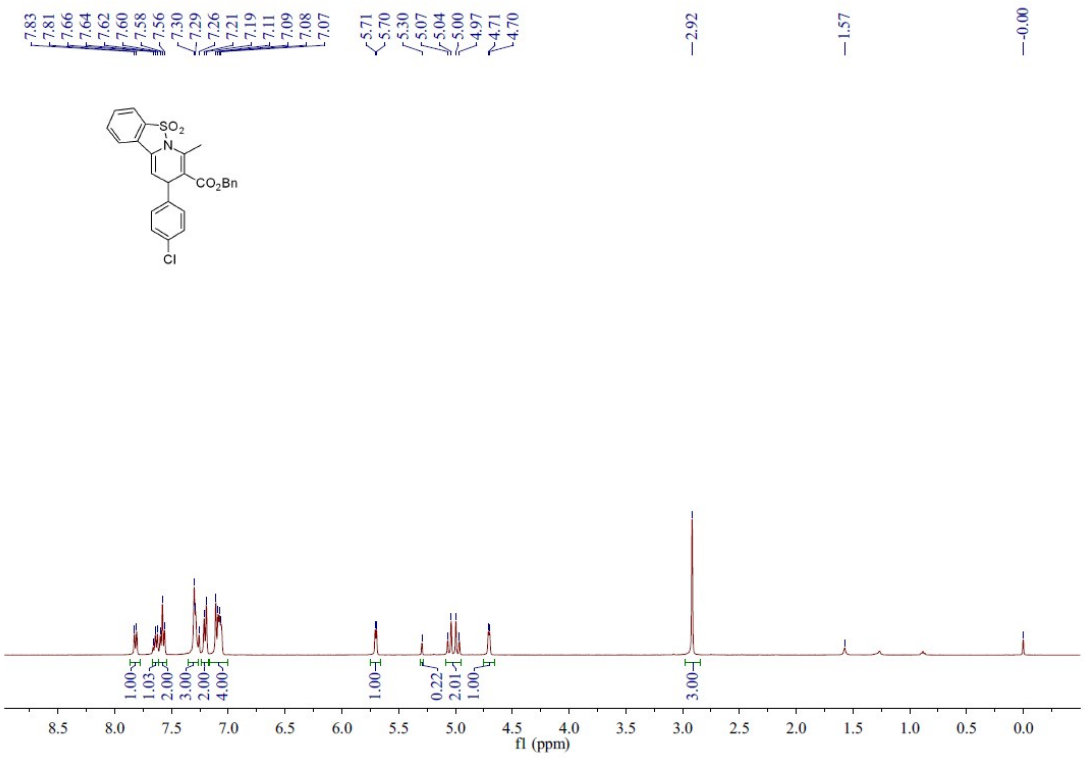
77.05
76.73
66.24
33.98
14.97
SO2
N
CO2Bn
F
f1 (ppm)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7.29
7.26
7.21
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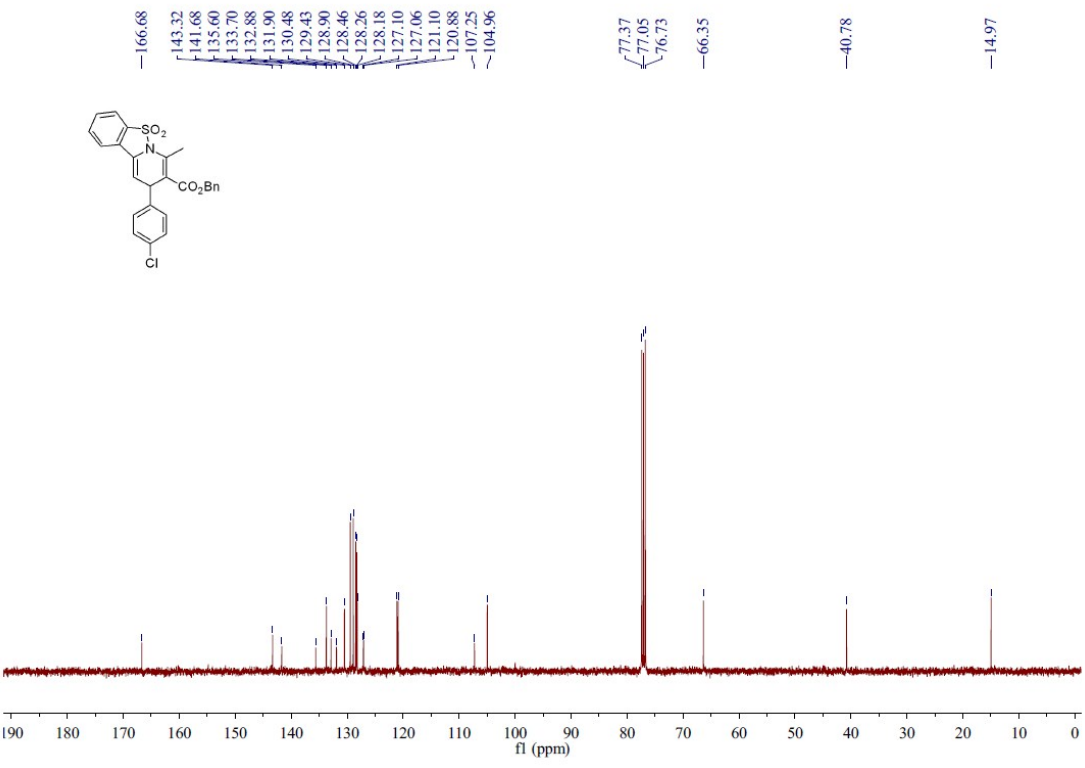
7.11
7.09
7.08
7.07
5.71
5.70
5.30
5.07
5.04
5.00
4.97
4.71
4.70
2.92
1.57
0.00
SO2
N
CO2Bn
Cl
1.00
1.03
2.00
3.00
2.00
4.00
1.00
0.22
2.01
1.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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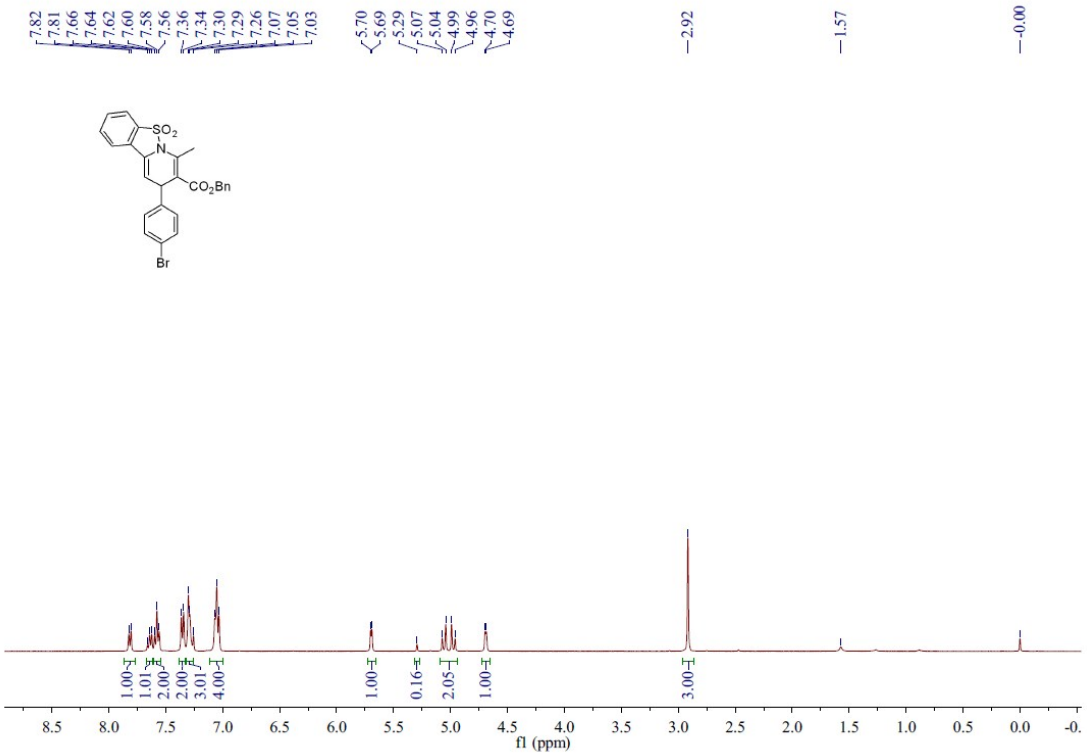
128.18
127.10
127.06
121.10
120.88
107.25
104.96
77.37
77.05
76.73
66.35
40.78
14.97
SO2
N
CO2Bn
Cl
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.56
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7.34
7.30
7.29
7.26
7.07
7.05
7.03
5.70
5.69
5.29
5.07
5.04
4.99
4.96
4.70
4.69
2.92
1.57
0.00
SO2
N
CO2Bn
Br
1.00
1.01
2.00
2.00
3.01
4.00
1.00
0.16
2.05
1.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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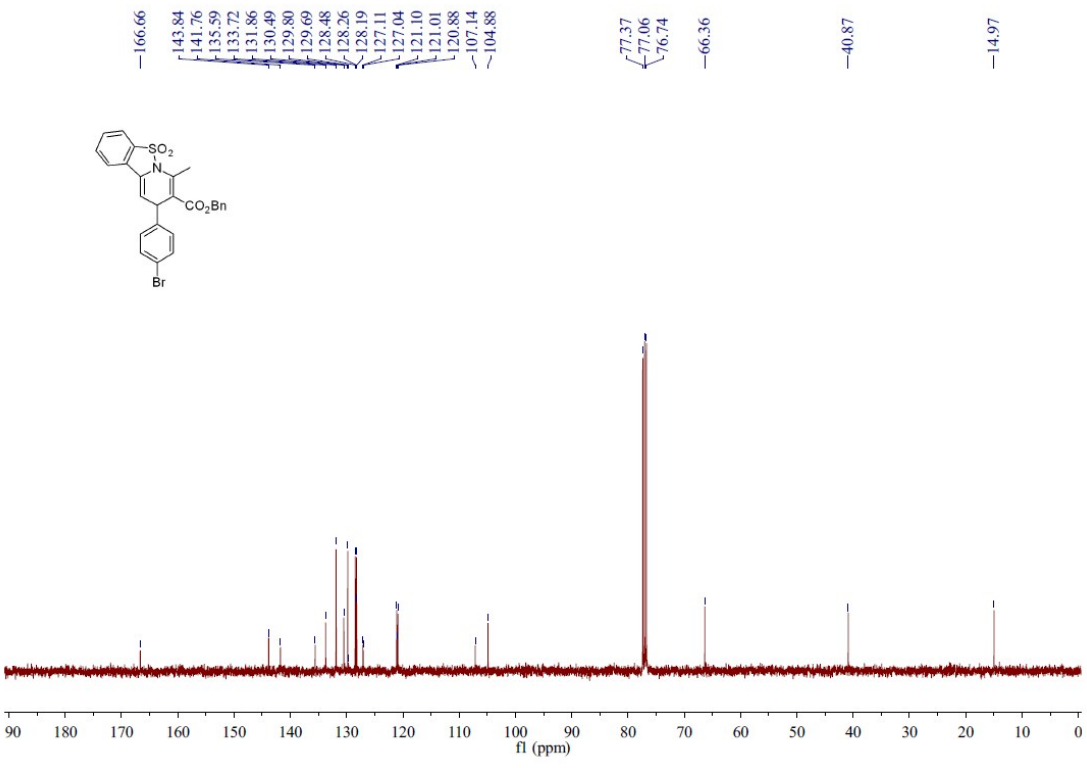
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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128.26
128.19
127.11
127.04
121.10
121.01
120.88
107.14
104.88
77.37
77.06
76.74
66.36
40.87
14.97
SO2
N
CO2Bn
Br
90
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
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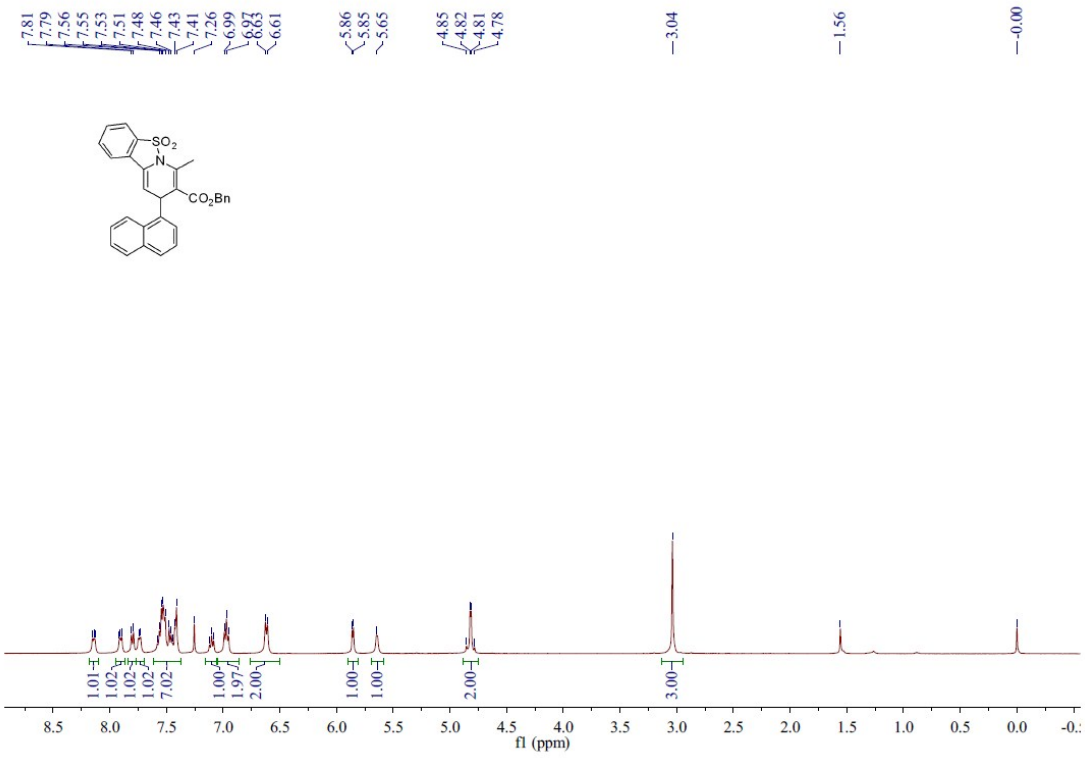
20
10
0
f1 (ppm)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7.41
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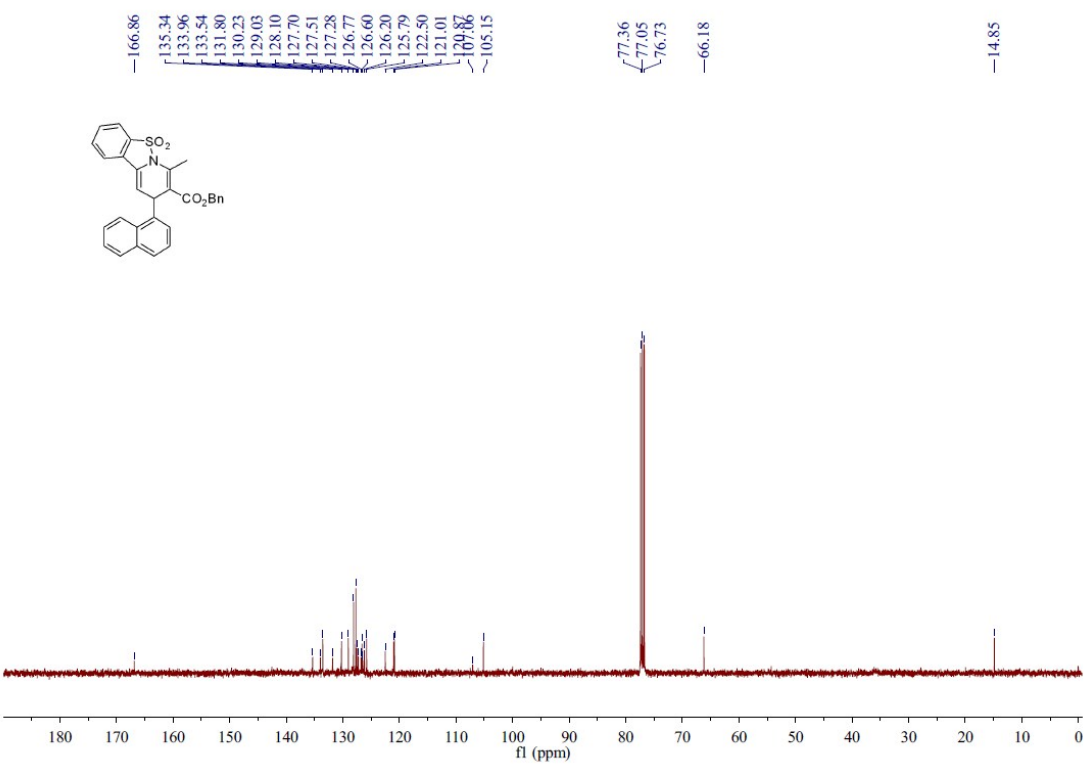
6.97
6.63
6.61
5.86
5.85
5.65
4.85
4.82
4.81
4.78
3.04
1.56
0.00
SO2
N
CO2Bn
1.01
1.02
1.02
1.02
7.02
1.00
1.97
2.00
1.00
1.00
2.00
3.00
f1 (ppm)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127.51
127.28
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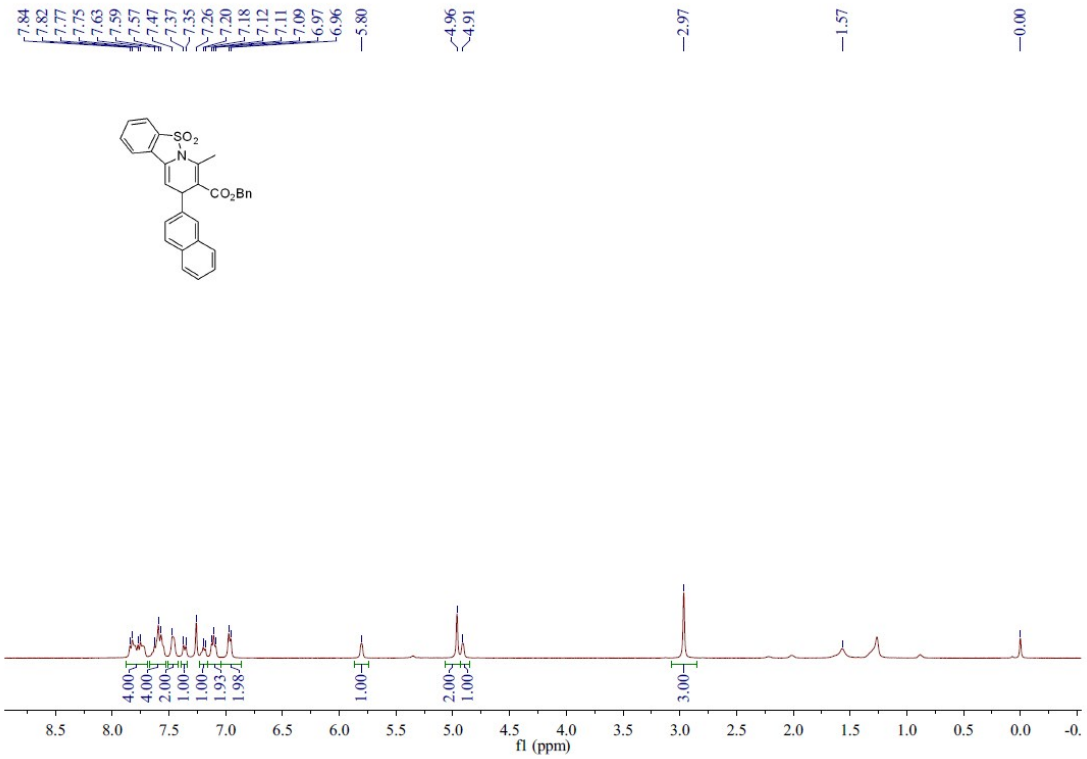
126.60
126.20
125.79
122.50
121.01
105.15
77.36
77.05
76.73
66.18
14.85
SO2
N
CO2Bn
f1 (ppm)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7.35
7.26
7.20
7.18
7.12
7.11
7.09
6.97
6.96
5.80
4.96
4.91
2.97
1.57
0.00
SO2
N
CO2Bn
4.00
4.00
2.00
1.00
1.00
1.93
1.98
1.00
2.00
1.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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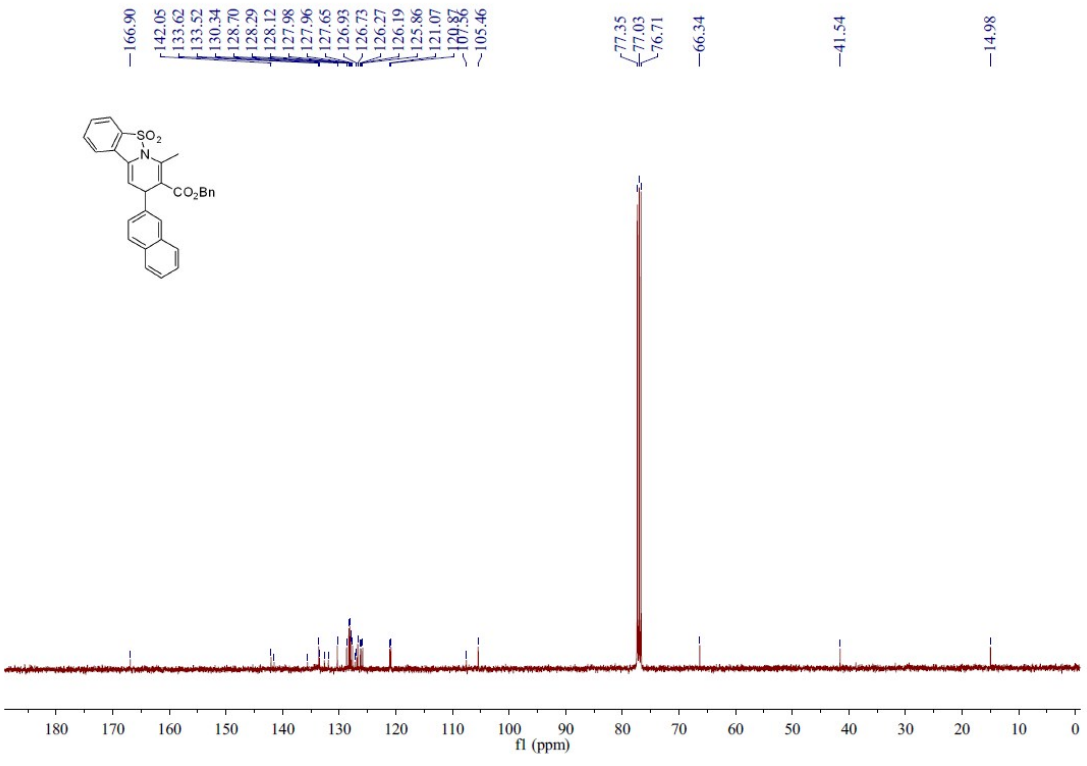
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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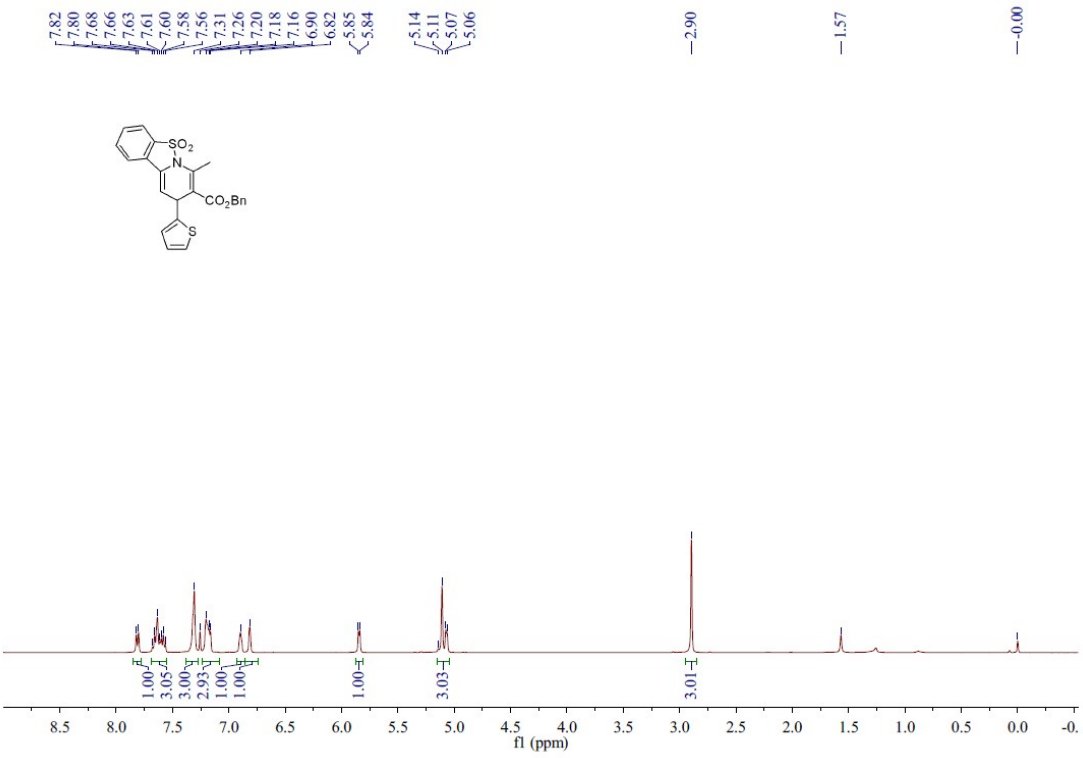
127.98
127.96
127.65
126.93
126.73
126.27
126.19
125.86
121.07
107.36
105.46
77.35
77.03
76.71
66.34
41.54
14.98
SO2
N
CO2Bn
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.31
7.26
7.20
7.18
7.16
6.90
6.82
5.85
5.84
5.14
5.11
5.07
5.06
2.90
1.57
0.00
SO2
N
CO2Bn
S
1.00
3.05
3.00
2.93
1.00
1.00
1.00
3.03
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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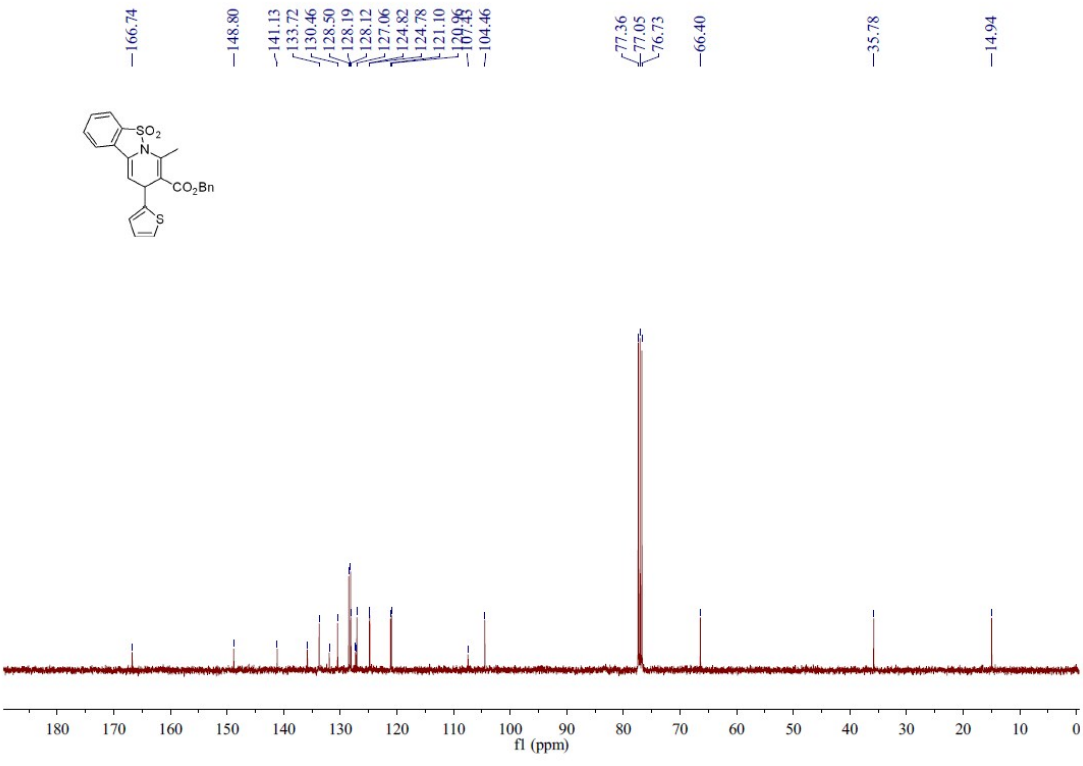
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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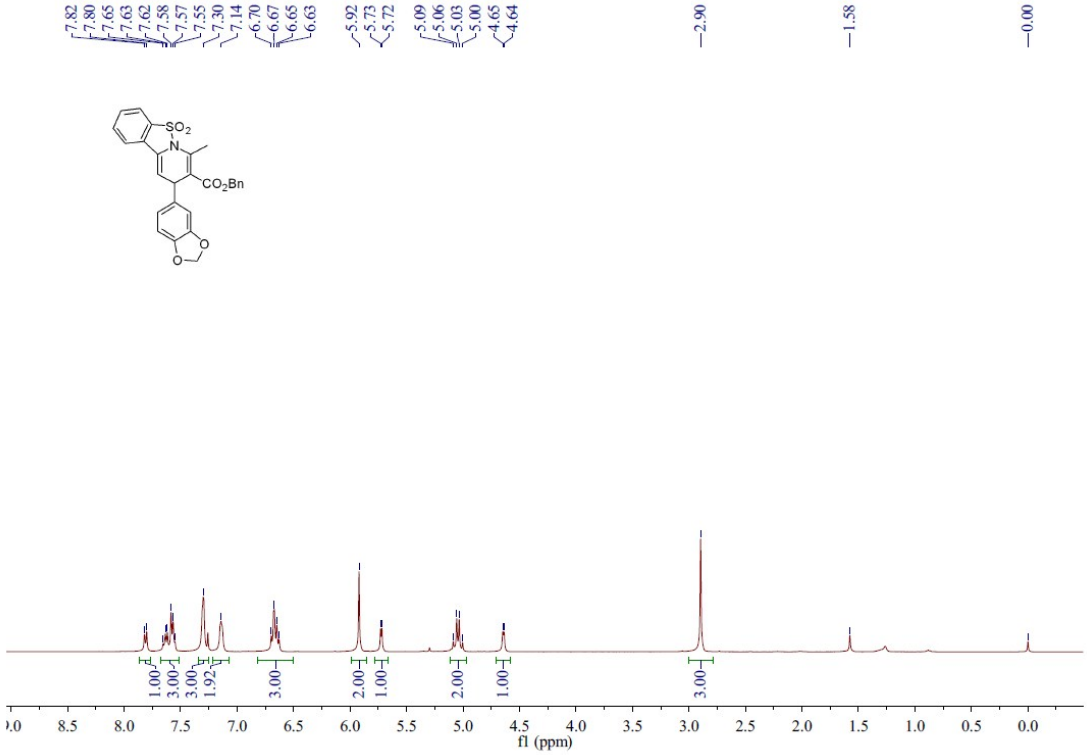
124.82
124.78
121.10
120.96
107.43
104.46
77.36
77.05
76.73
66.40
35.78
14.94
SO2
N
CO2Bn
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.80
7.65
7.63
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7.58
7.57
7.55
7.30
7.14
6.70
6.67
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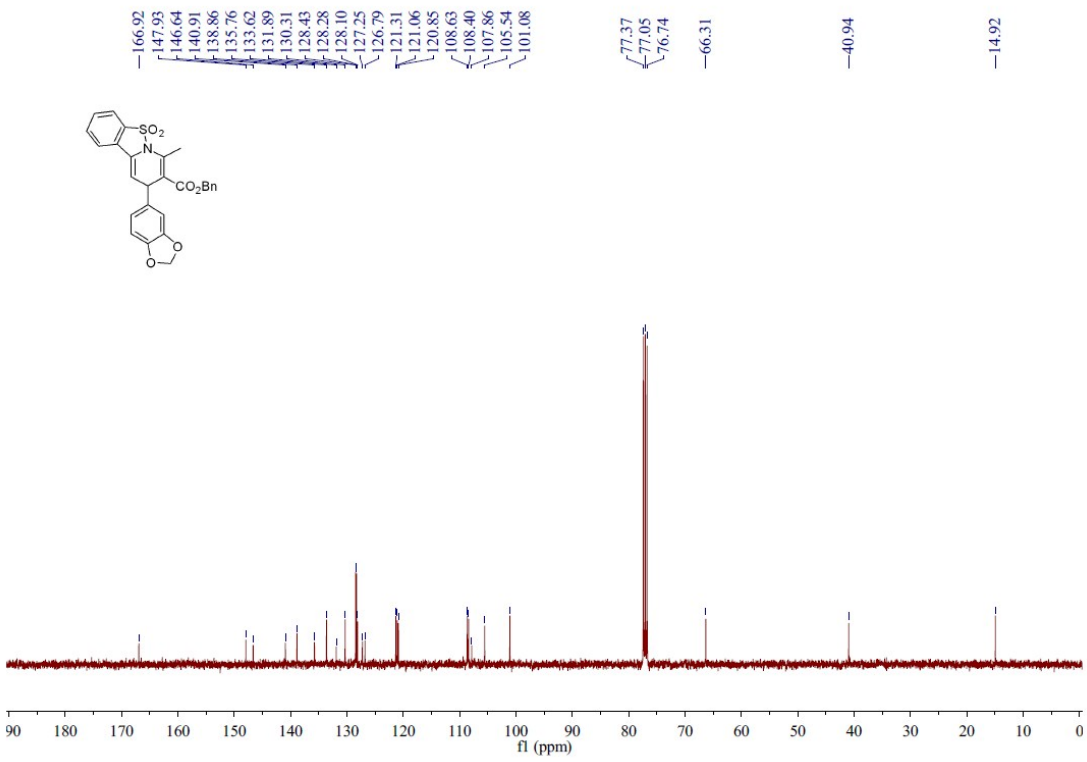
6.63
5.92
5.73
5.72
5.09
5.06
5.03
5.00
4.65
4.64
2.90
1.58
0.00
SO2
N
CO2Bn
O
O
1.00
3.00
3.00
1.92
3.00
2.00
1.00
2.00
1.00
3.00
f1 (ppm)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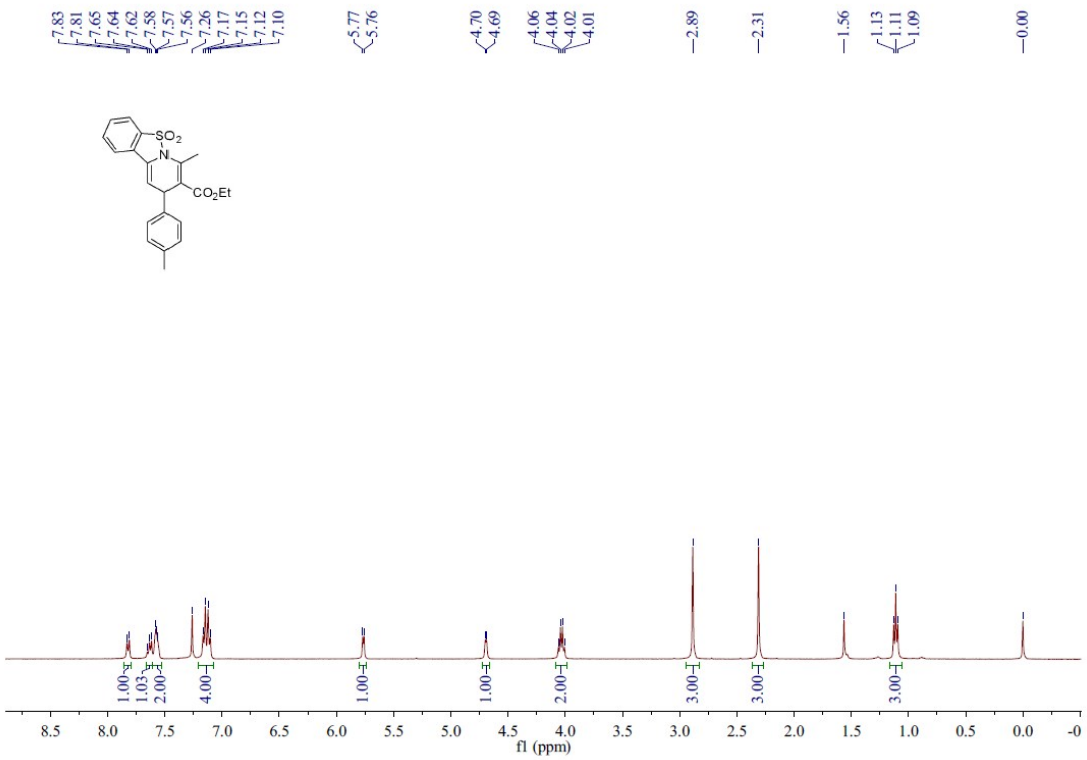
128.10
127.25
126.79
121.31
121.06
120.85
108.63
108.40
107.86
105.54
101.08
77.37
77.05
76.74
66.31
40.94
14.92
SO2
N
CO2Bn
O
O
f1 (ppm)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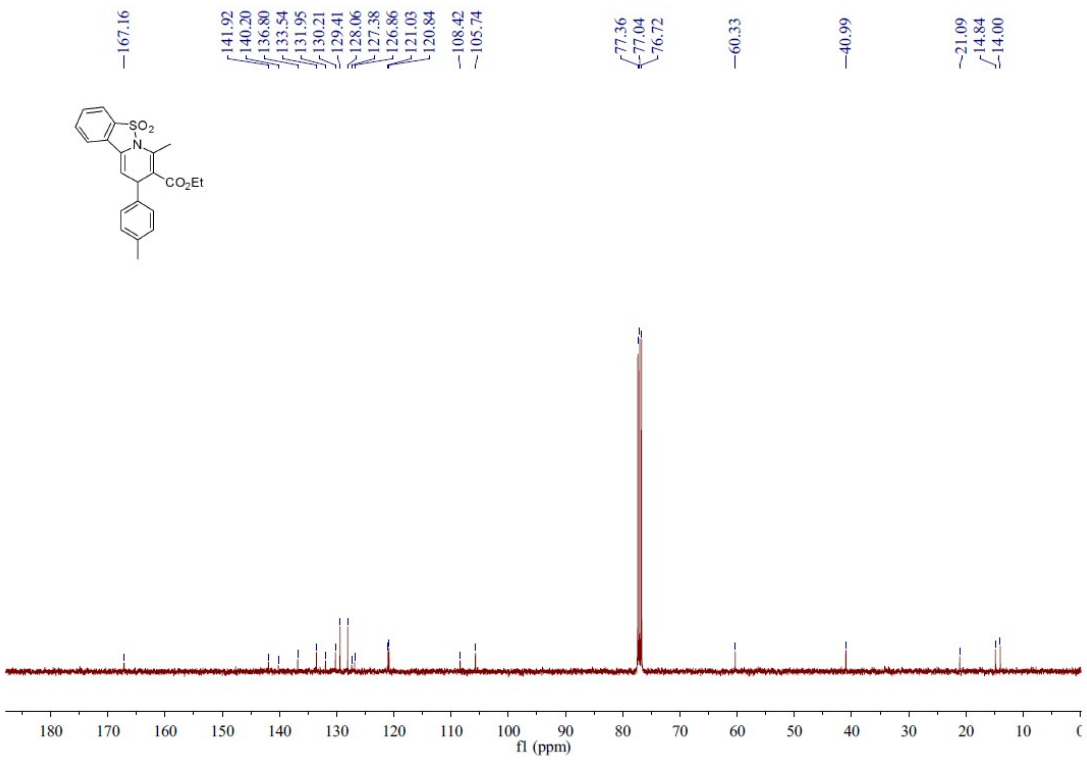
7.17
7.15
7.12
7.10
5.77
5.76
4.70
4.69
4.06
4.04
4.02
4.01
2.89
2.31
1.56
1.13
1.11
1.09
0.00
SO2
N
CO2Et
1.00
1.03
2.00
4.00
1.00
1.00
2.00
3.00
3.00
3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)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129.41
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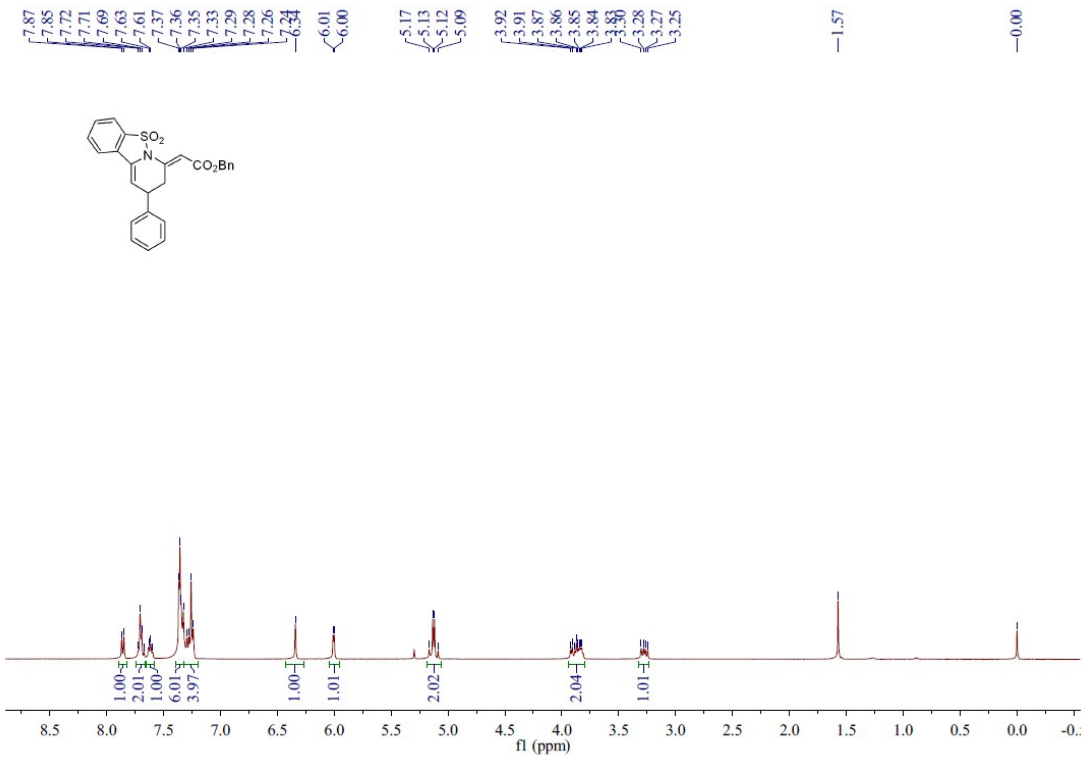
127.38
126.86
121.03
120.84
108.42
105.74
77.36
77.04
76.72
60.33
40.99
21.09
14.84
14.00
SO2
N
CO2Et
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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7.26
6.34
6.01
6.00
5.17
5.13
5.12
5.09
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3.87
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3.85
3.84
3.30
3.28
3.27
3.25
1.57
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SO2
N
CO2Bn
1.00
2.01
1.00
6.01
3.97
1.00
1.01
2.02
2.04
1.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
2.0
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1.0
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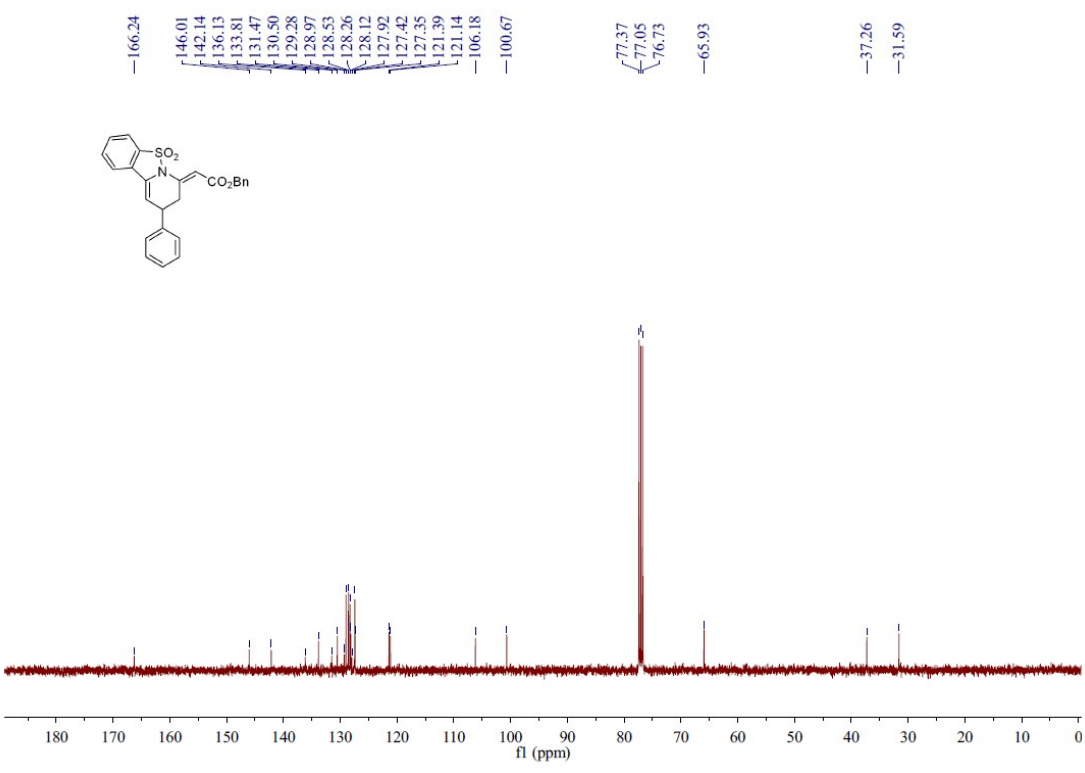
0.0
f1 (ppm)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127.92
127.42
127.35
121.39
121.14
106.18
100.67
77.37
77.05
76.73
65.93
37.26
31.59
SO2
N
CO2Bn
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.86
7.84
7.69
7.62
7.60
7.59
7.37
7.36
7.33
7.33
7.31
7.26
7.14
6.33
5.99
5.98
5.17
5.13
5.12
5.09
3.88
3.87
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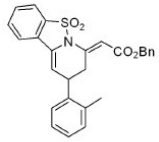
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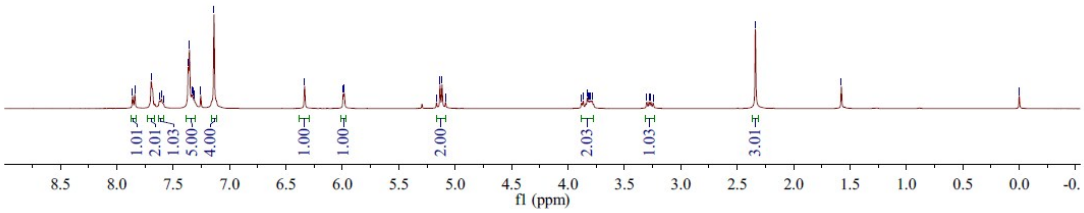
N
CO2Bn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2.00
2.03
1.03
3.01
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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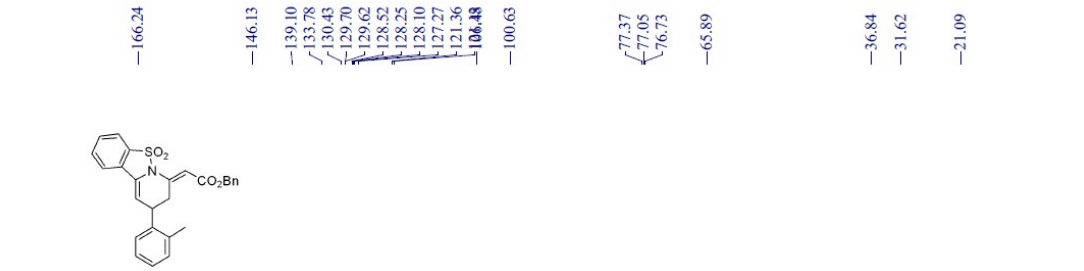
0.0
f1 (ppm)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129.62
128.52
128.25
128.10
127.27
121.36
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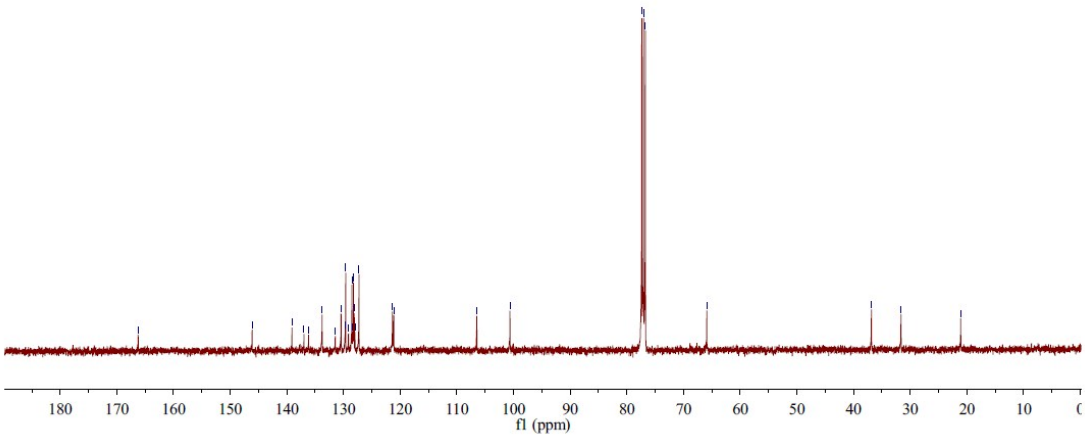
77.37
77.05
76.73
65.89
36.84
31.62
21.09

SO2
N
CO2Bn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120
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100
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80
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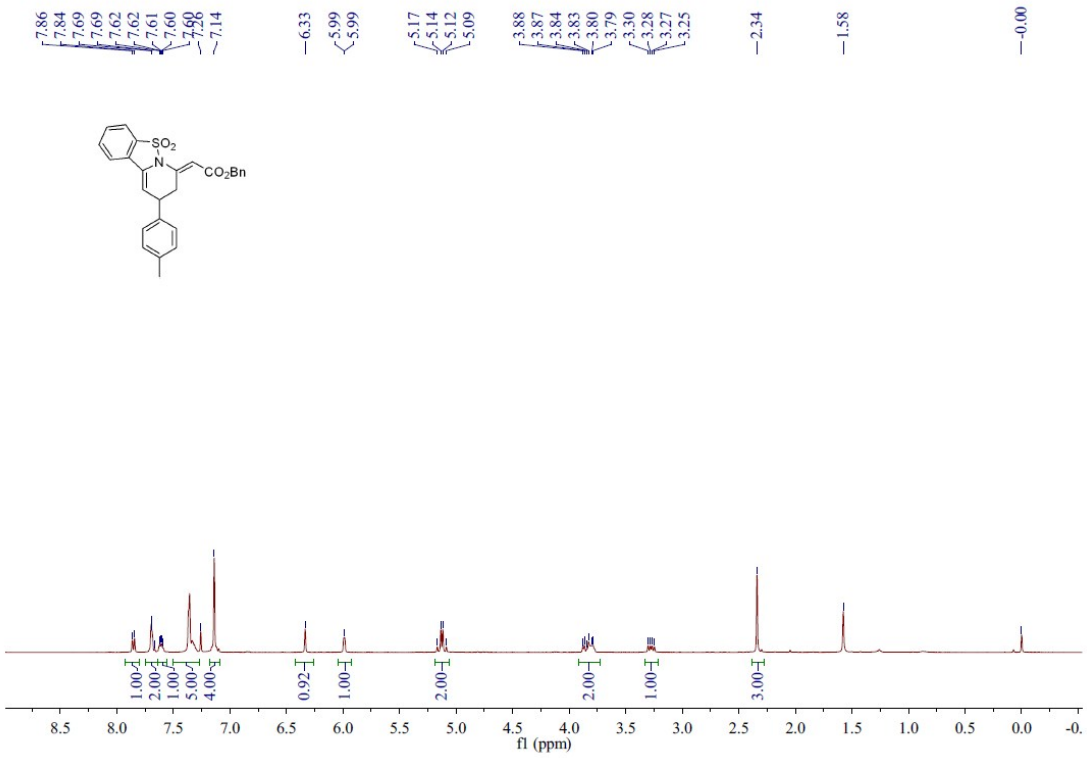
60
50
40
30
20
10
f1 (ppm)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5.17
5.14
5.12
5.09
3.88
3.87
3.84
3.83
3.80
3.79
3.30
3.28
3.27
3.25
2.34
1.58
0.00
SO2
N
CO2Bn
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2.00
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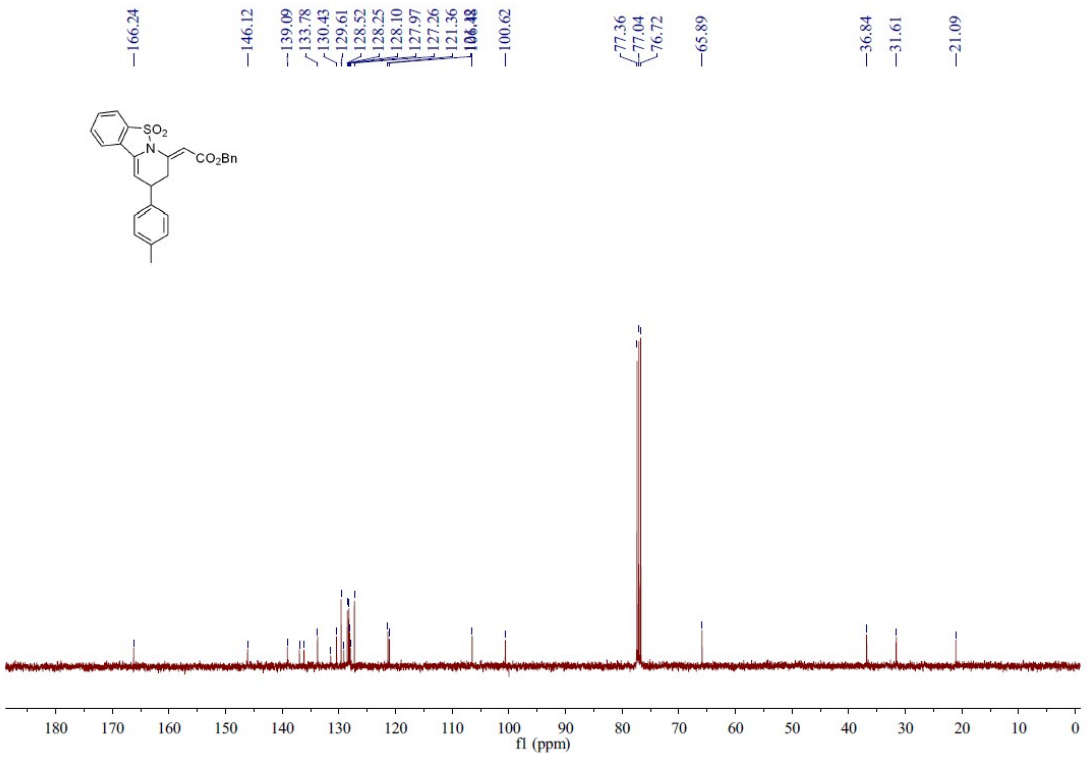
5.00
4.00
0.92
1.00
2.00
2.00
1.00
3.00
f1 (ppm)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128.25
128.10
127.97
127.26
121.36
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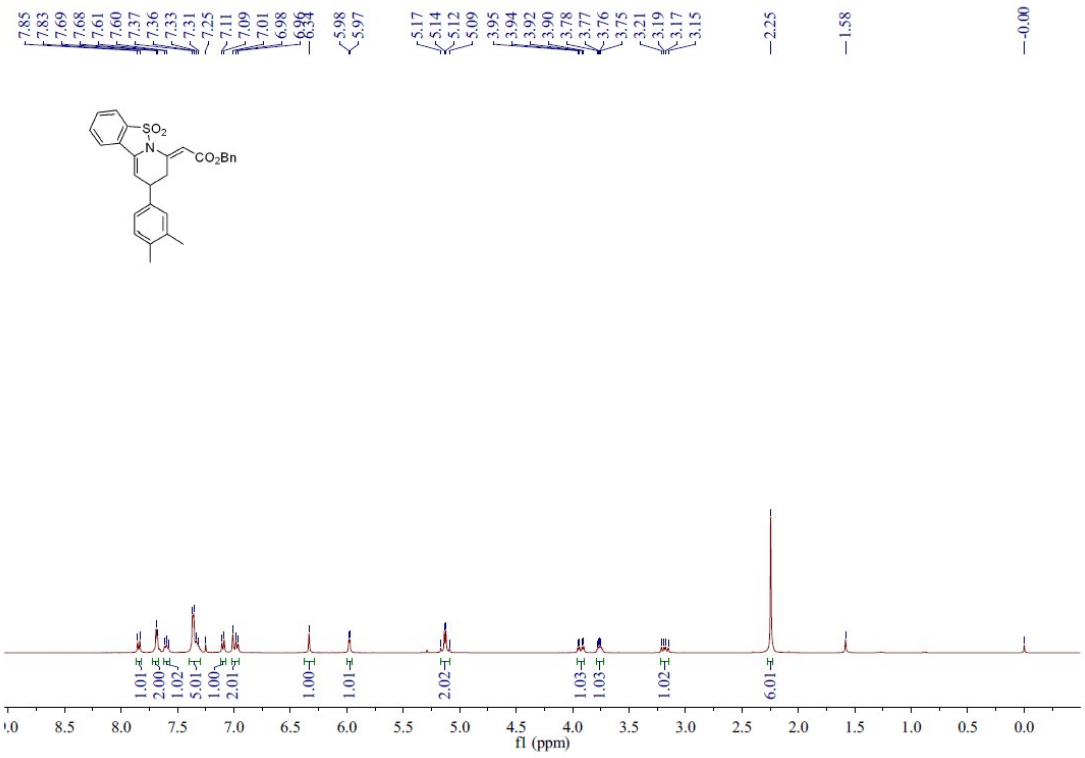
77.04
76.72
65.89
36.84
31.61
21.09
SO2
N
CO2Bn
f1 (ppm)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7.31
7.25
7.11
7.09
7.01
6.98
5.98
5.97
5.17
5.14
5.12
5.09
3.95
3.94
3.92
3.90
3.78
3.77
3.76
3.75
3.21
3.19
3.17
3.15
2.25
1.58
0.00
SO2
N
CO2Bn
1.01
2.00
1.02
5.01
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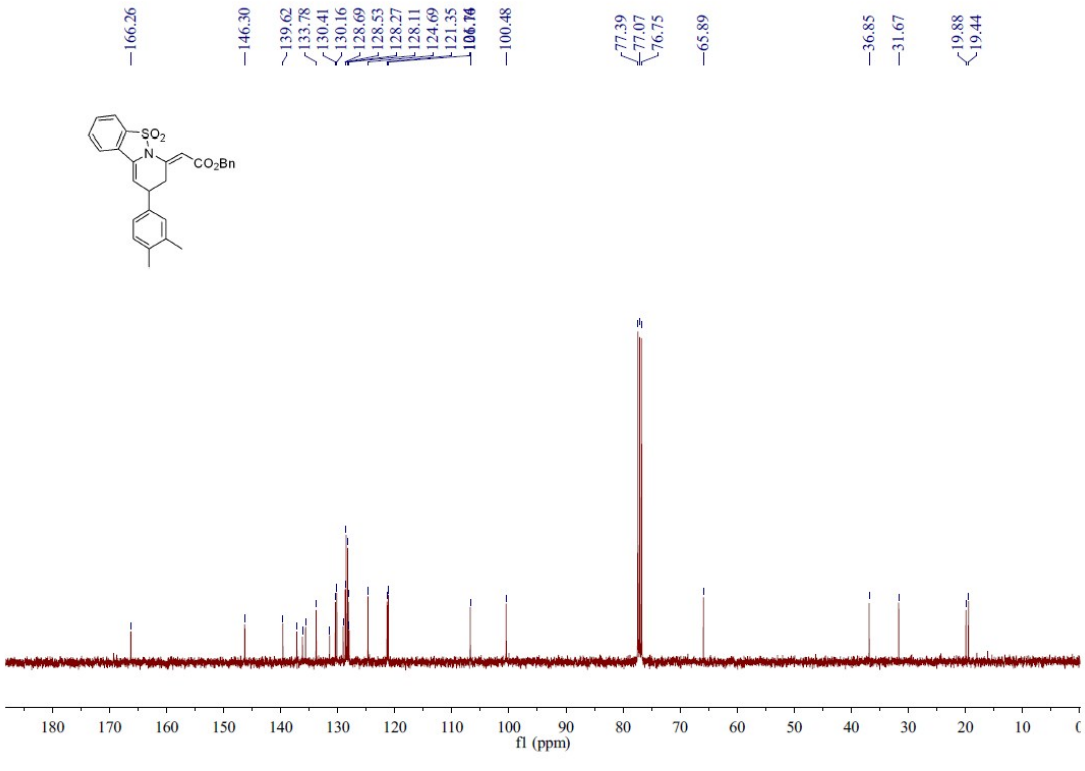
2.01
1.00
1.01
2.02
1.03
1.03
1.02
6.01
fl (ppm)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128.11
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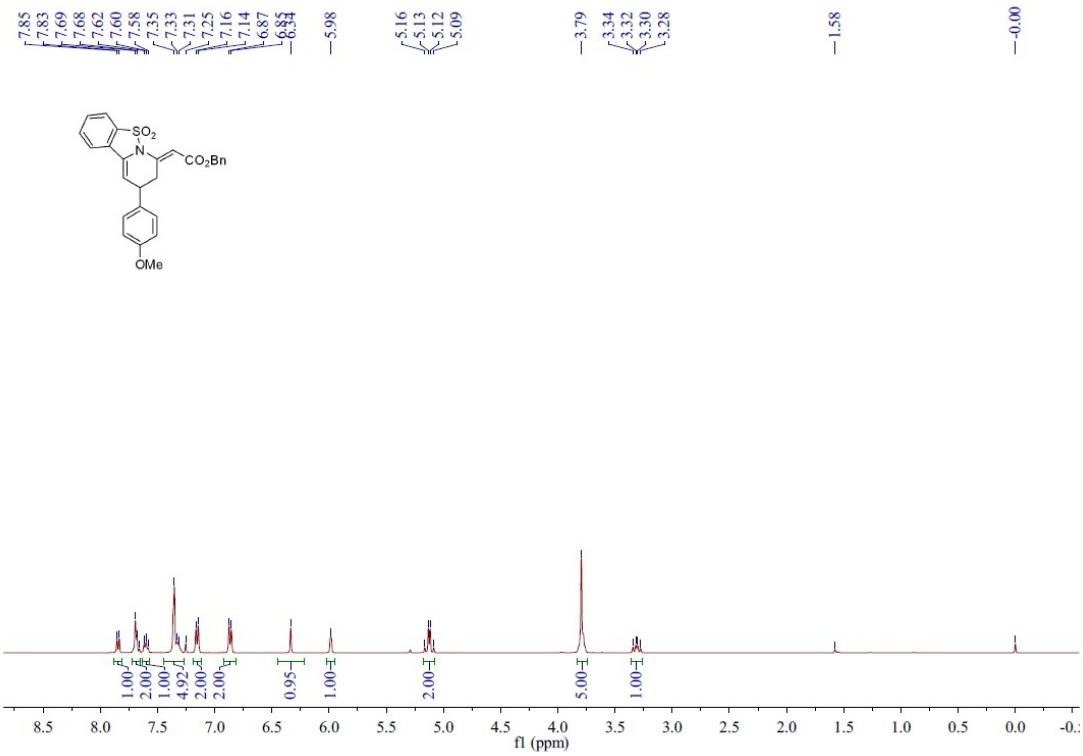
19.88
19.44
SO2
N
CO2Bn
fl (ppm)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7.68
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7.58
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7.33
7.31
7.25
7.16
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6.85
6.84
5.98
5.16
5.13
5.12
5.09
3.79
3.34
3.32
3.30
3.28
1.58
-0.00
SO2
N
CO2Bn
OMe
1.00
2.00
1.00
4.92
2.00
2.00
0.95
1.00
2.00
5.00
1.00
8.5
8.0
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7.0
6.5
6.0
5.5
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3.0
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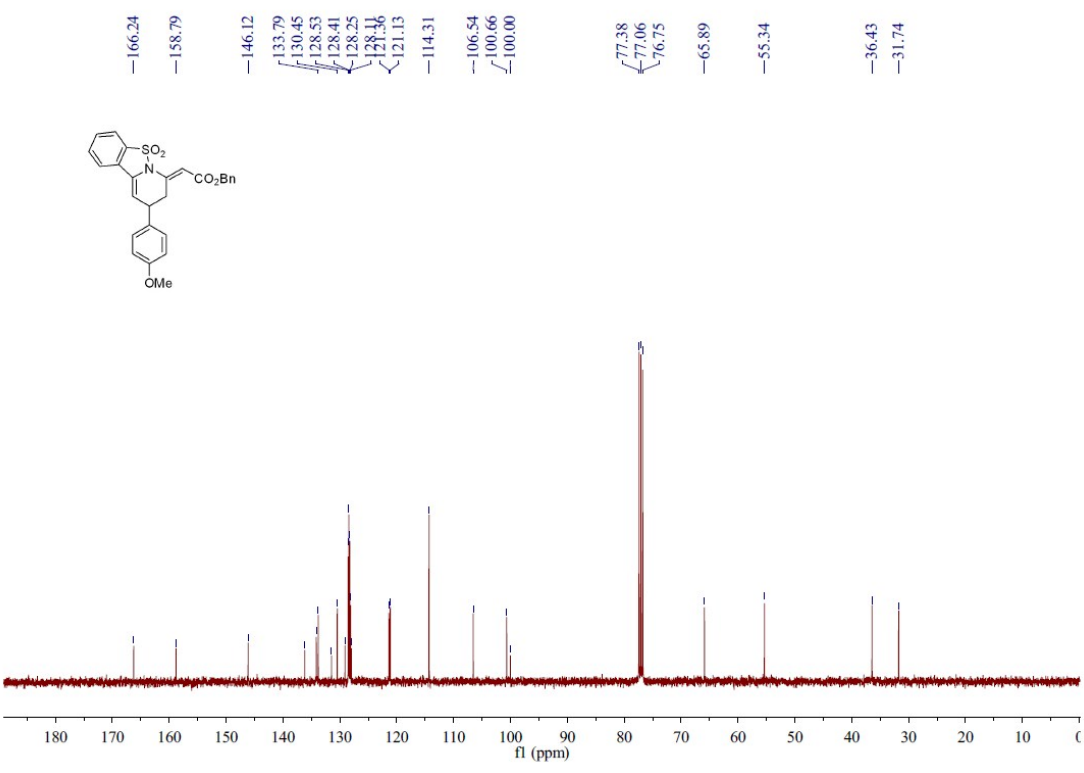
0.0
f1 (ppm)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128.11
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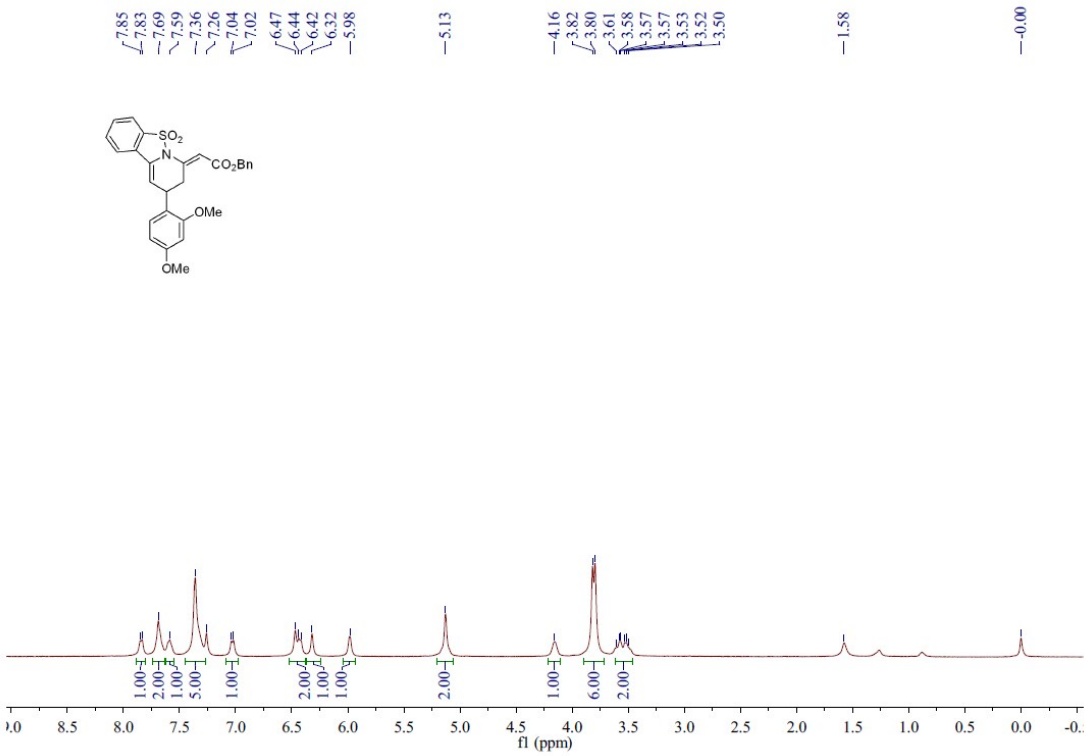
121.13
114.31
106.54
100.66
100.00
77.38
77.06
76.75
65.89
55.34
36.43
31.74
SO2
N
CO2Bn
OMe
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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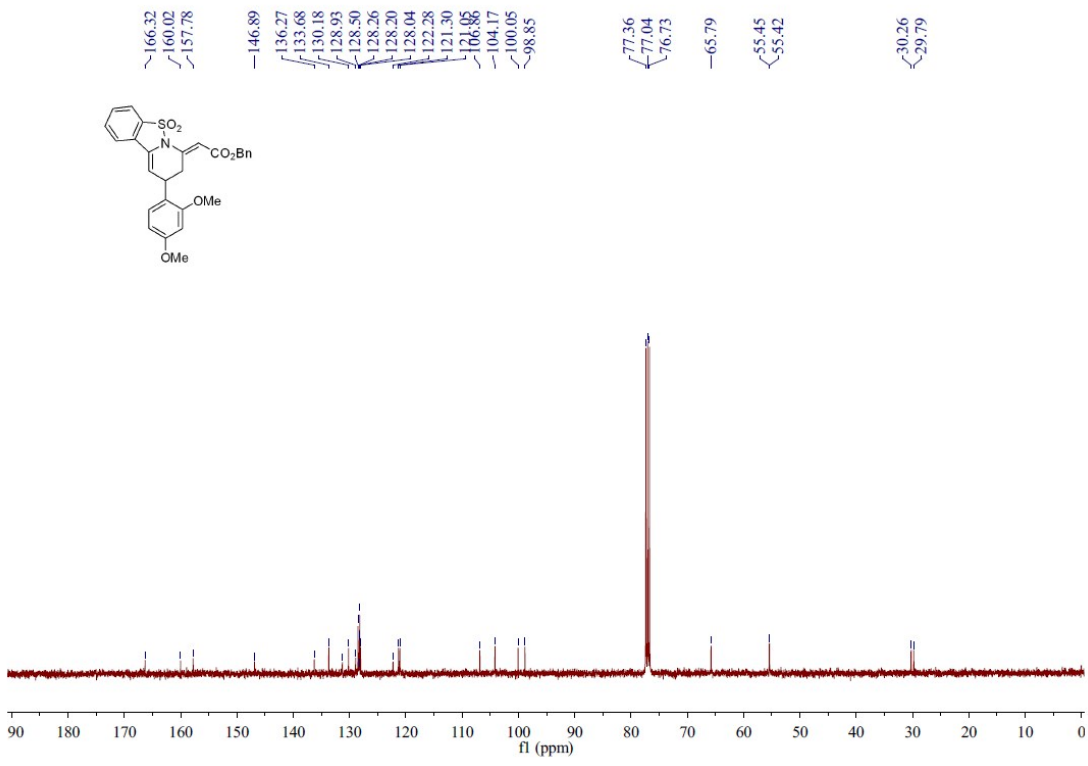
5.98
5.13
4.16
3.82
3.80
3.61
3.58
3.57
3.57
3.53
3.52
3.50
1.58
0.00
SO2
N
CO2Bn
OMe
OMe
1.00
2.00
1.00
5.00
1.00
2.00
1.00
1.00
2.00
1.00
6.00
2.00
f1 (ppm)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122.28
121.30
104.17
100.05
98.85
77.36
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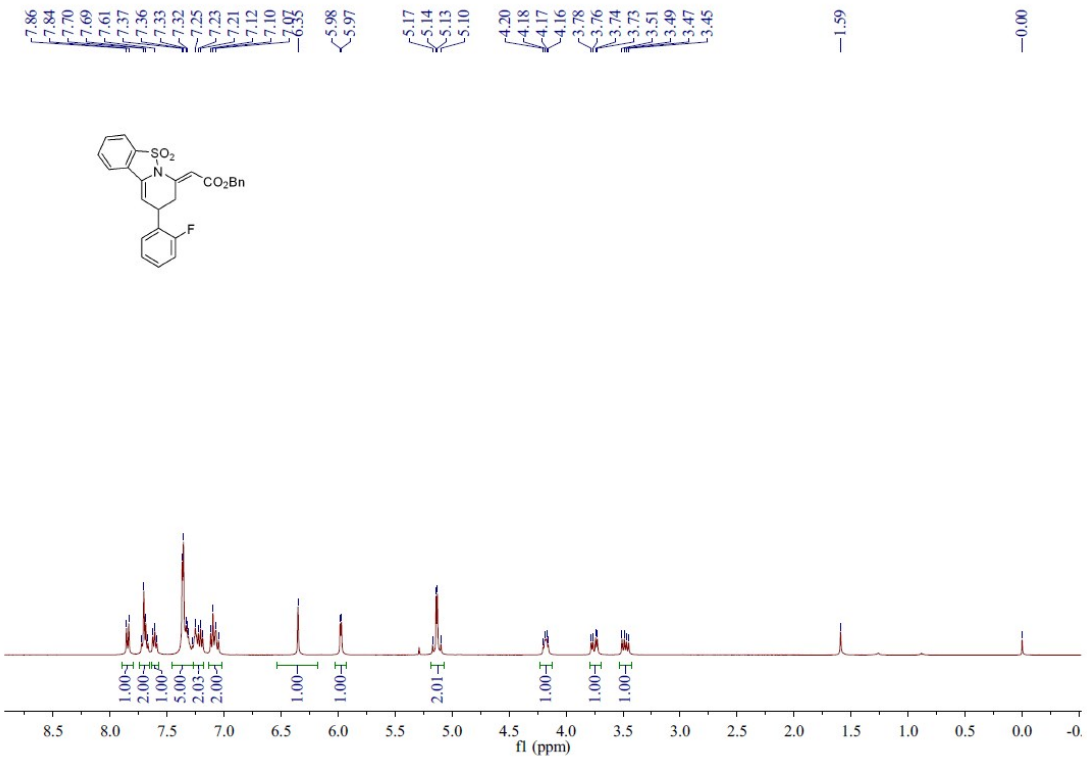
55.45
55.42
30.26
29.79
SO2
N
CO2Bn
OMe
OMe
f1 (ppm)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7.12
7.10
6.35
5.98
5.97
5.17
5.14
5.13
5.10
4.20
4.18
4.17
4.16
3.78
3.76
3.74
3.73
3.51
3.49
3.47
3.45
1.59
0.00
SO2
N
CO2Bn
F
1.00
2.00
1.00
5.00
2.03
2.00
1.00
1.00
2.01
1.00
1.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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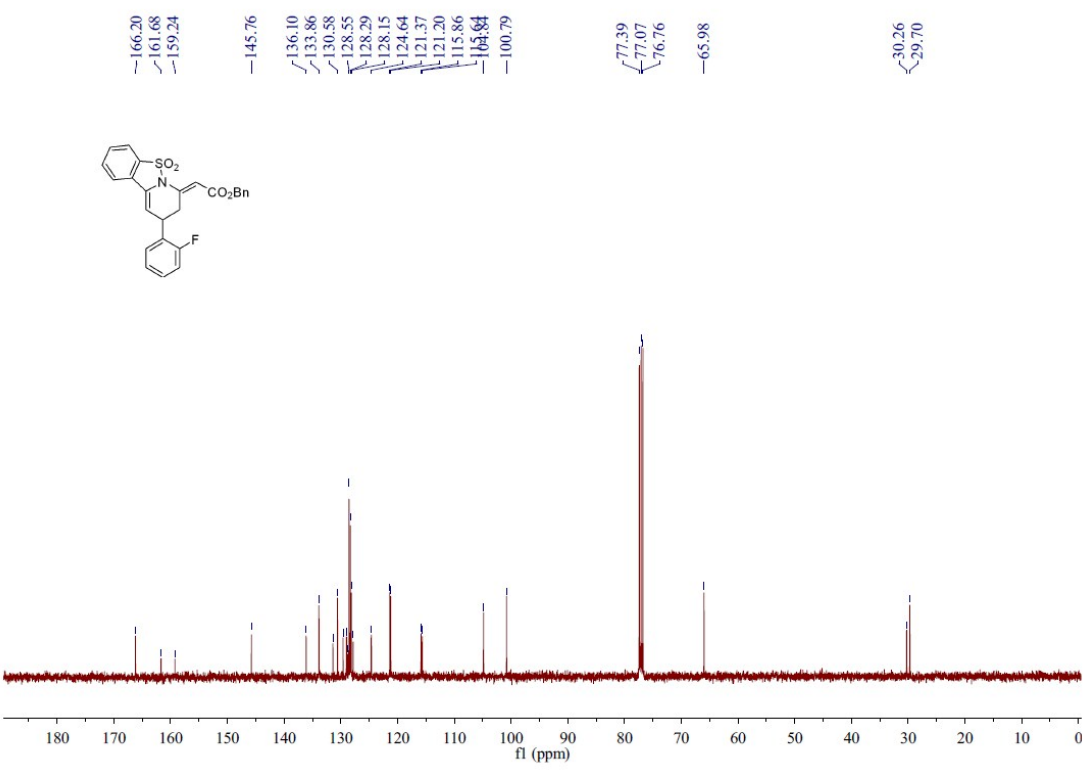
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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121.37
121.20
115.86
100.79
77.39
77.07
76.76
65.98
30.26
29.70
SO2
N
CO2Bn
F
180
170
160
150
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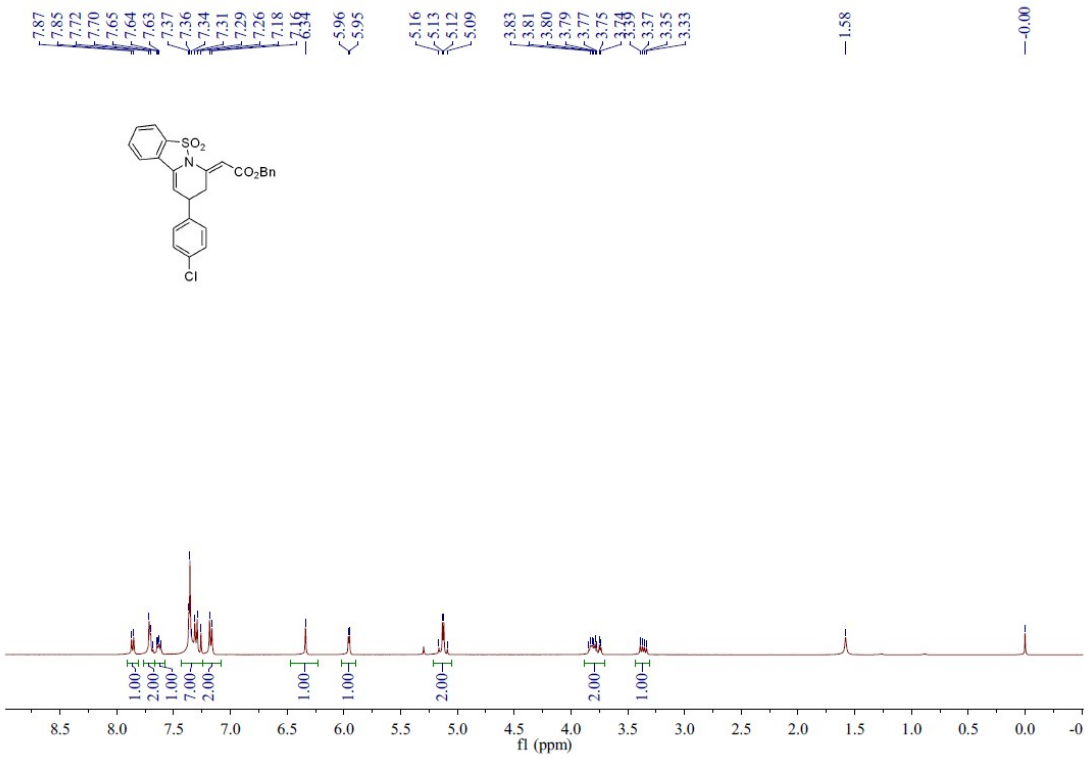
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.36
7.34
7.31
7.29
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5.12
5.09
3.83
3.81
3.80
3.79
3.77
3.75
3.37
3.35
3.33
1.58
0.00
SO2
N
CO2Bn
Cl
1.00
2.00
1.00
7.00
2.00
1.00
1.00
2.00
2.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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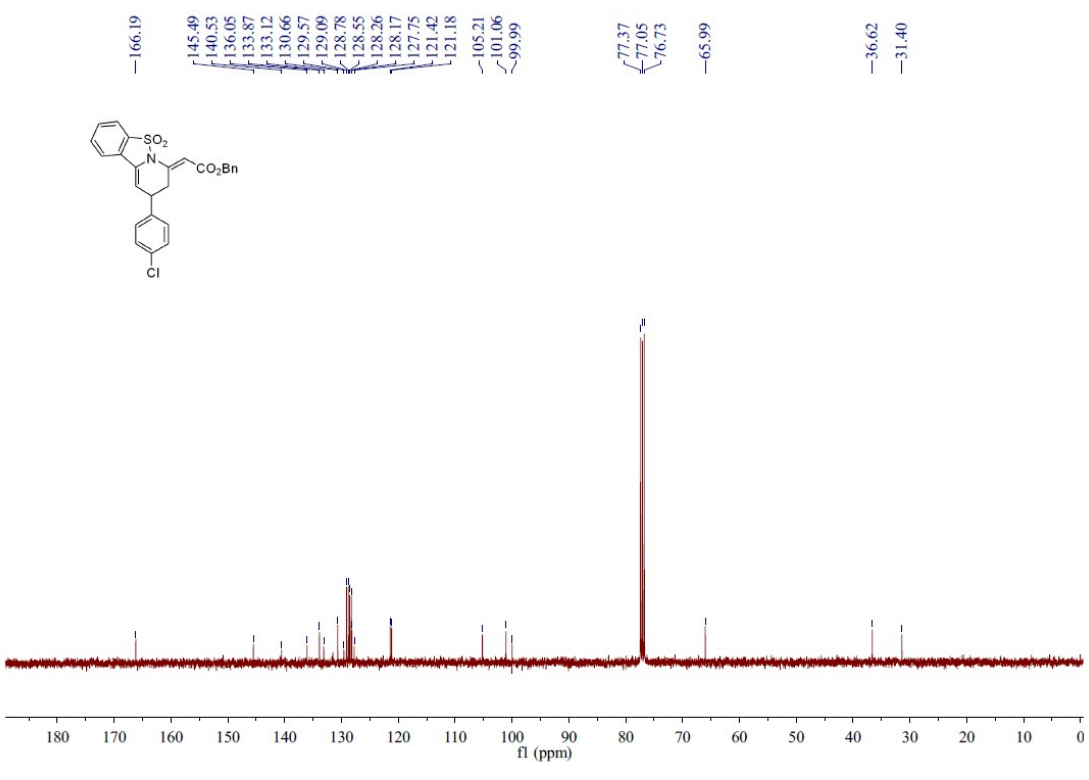
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)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128.26
128.17
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121.42
121.18
105.21
101.06
99.99
77.37
77.05
76.73
65.99
36.62
31.40
SO2
N
CO2Bn
Cl
180
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110
100
90
80
70
60
50
40
30
20
10
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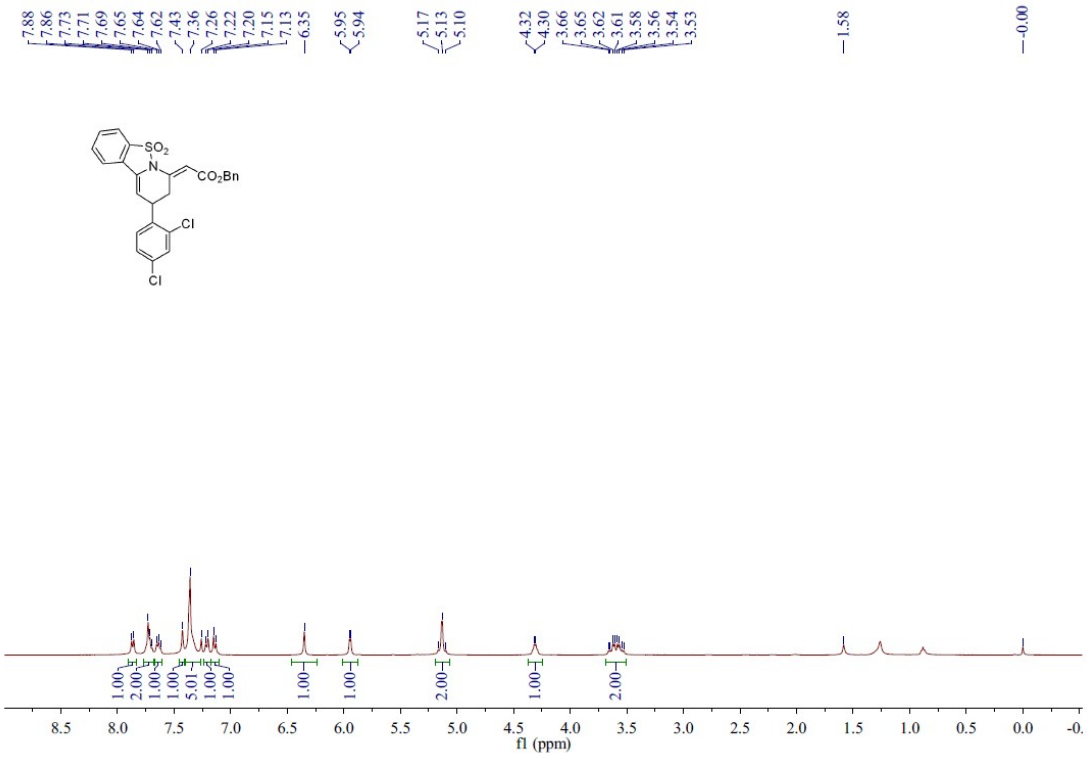
f1 (ppm)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7.13
6.35
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5.94
5.17
5.13
5.10
4.32
4.30
3.66
3.65
3.62
3.61
3.58
3.56
3.54
3.53
1.58
0.00
SO2
N
CO2Bn
Cl
Cl
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2.00
1.00
1.00
5.01
1.00
1.00
1.00
1.00
2.00
1.00
2.00
8.5
8.0
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7.0
6.5
6.0
5.5
5.0
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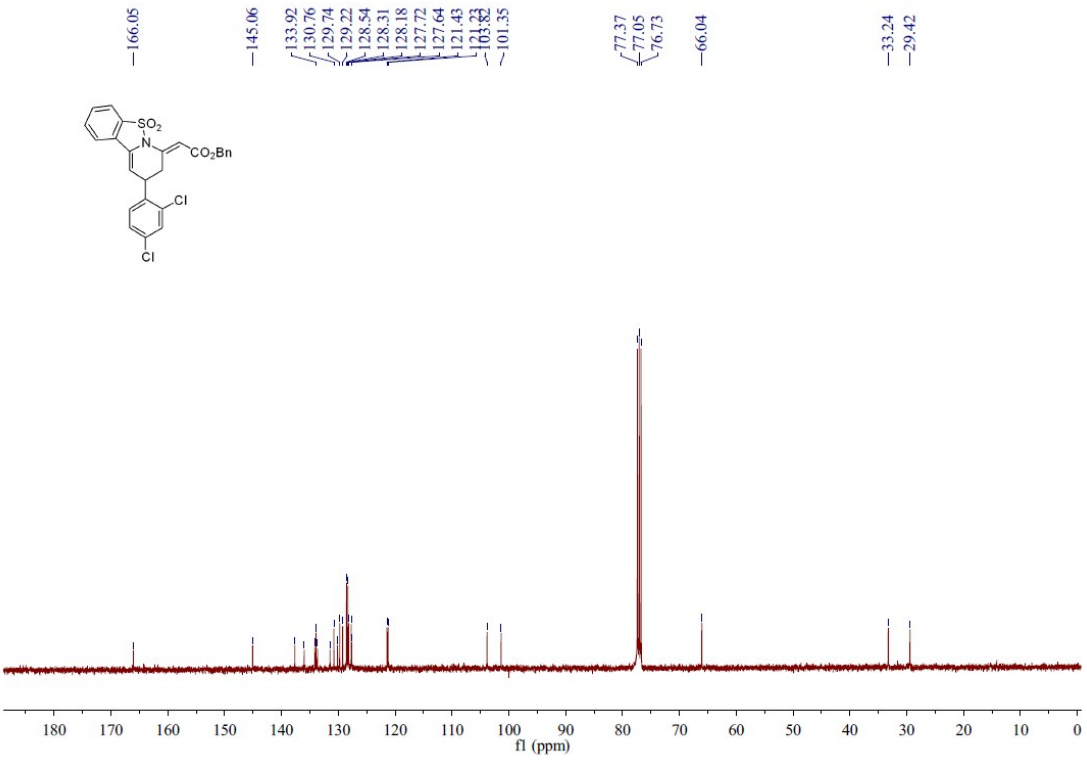
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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127.72
127.64
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121.22
103.82
101.35
77.37
77.05
76.73
66.04
33.24
29.42
SO2
N
CO2Bn
Cl
Cl
180
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110
100
90
80
70
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50
40
30
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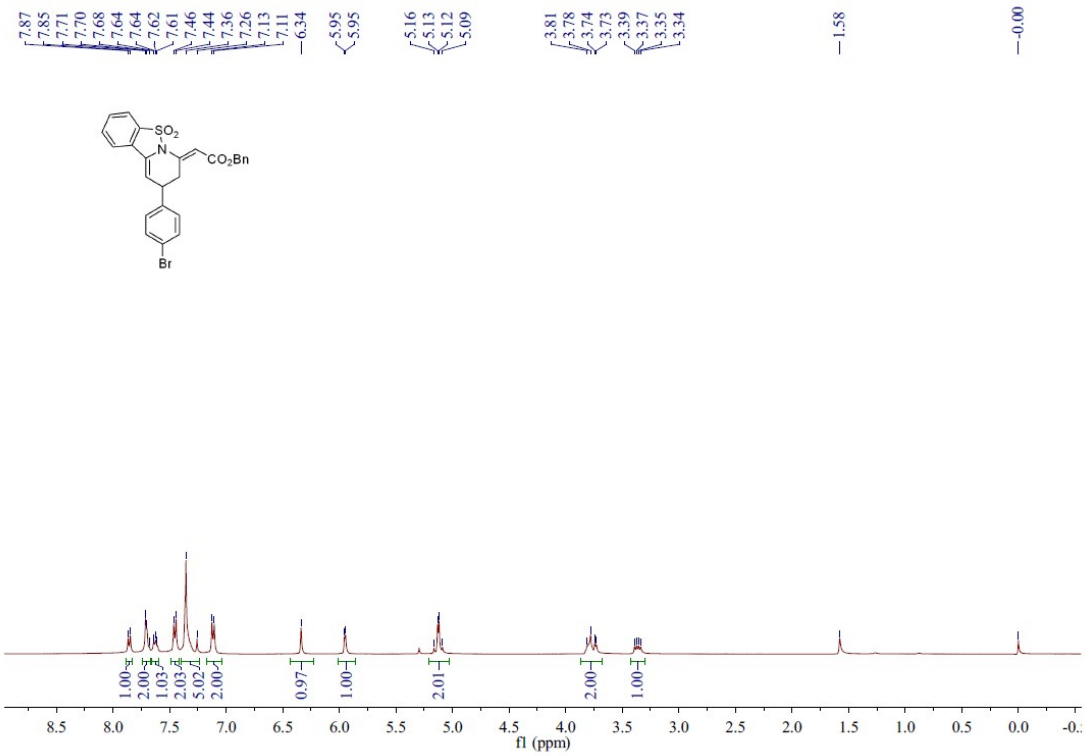
10
0
f1 (ppm)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7.13
7.11
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5.13
5.12
5.09
3.81
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3.74
3.73
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3.37
3.35
3.34
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CO2Bn
Br
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2.00
1.03
2.03
5.02
2.00
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1.00
2.01
2.00
1.00
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7.0
6.5
6.0
5.5
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2.5
2.0
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1.0
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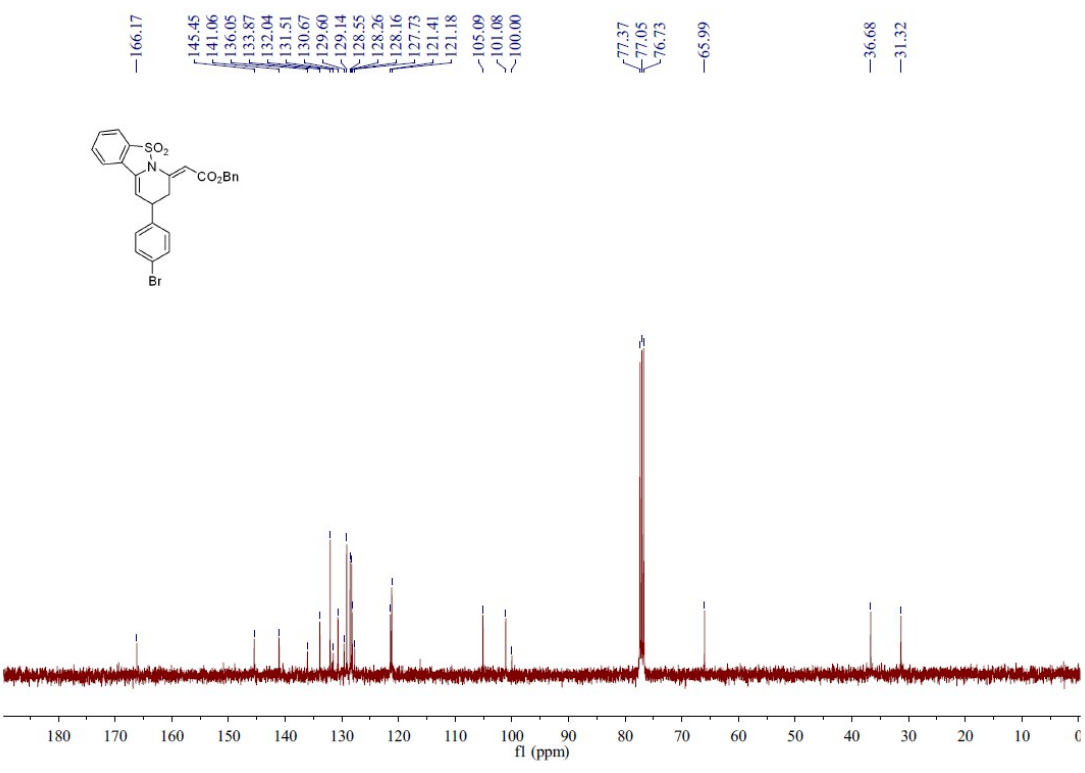
f1 (ppm)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145.45
141.06
136.05
133.87
132.04
131.51
130.67
129.60
129.14
128.55
128.26
128.16
127.73
121.41
121.18
105.09
101.08
100.00
77.37
77.05
76.73
65.99
36.68
31.32
SO2
N
CO2Bn
Br
180
170
160
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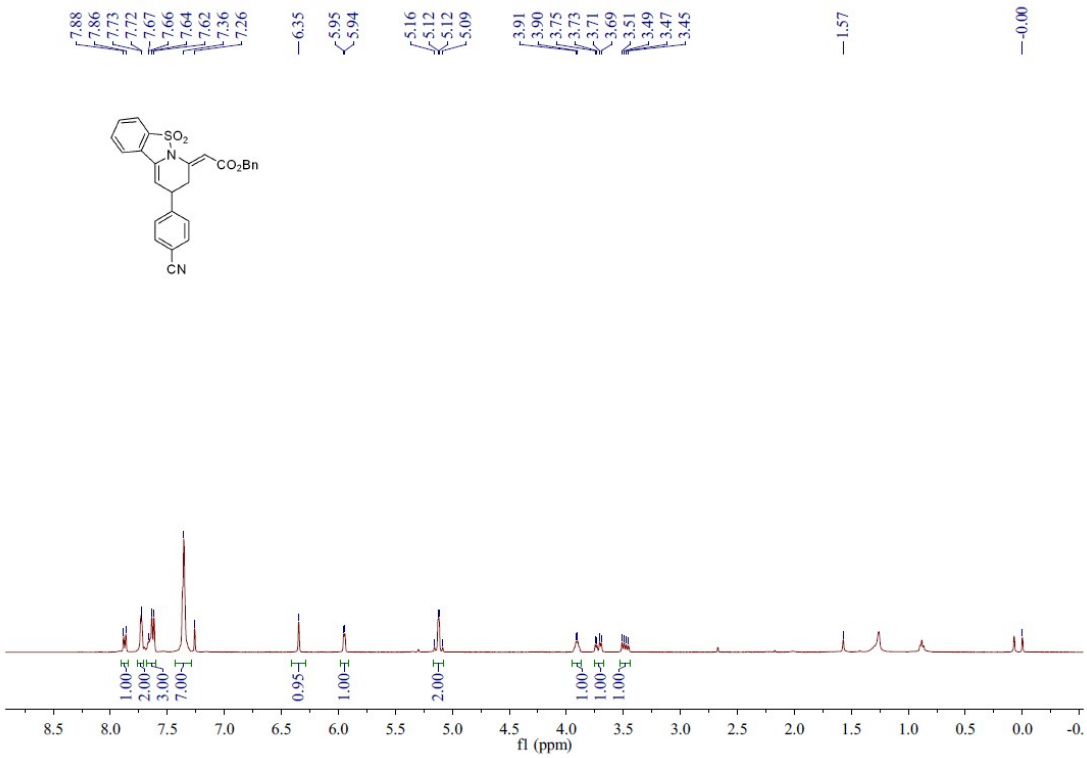
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.62
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7.26
6.35
5.95
5.94
5.16
5.12
5.12
5.09
3.91
3.90
3.75
3.73
3.71
3.69
3.51
3.49
3.47
3.45
1.57
0.00
SO2
N
CO2Bn
CN
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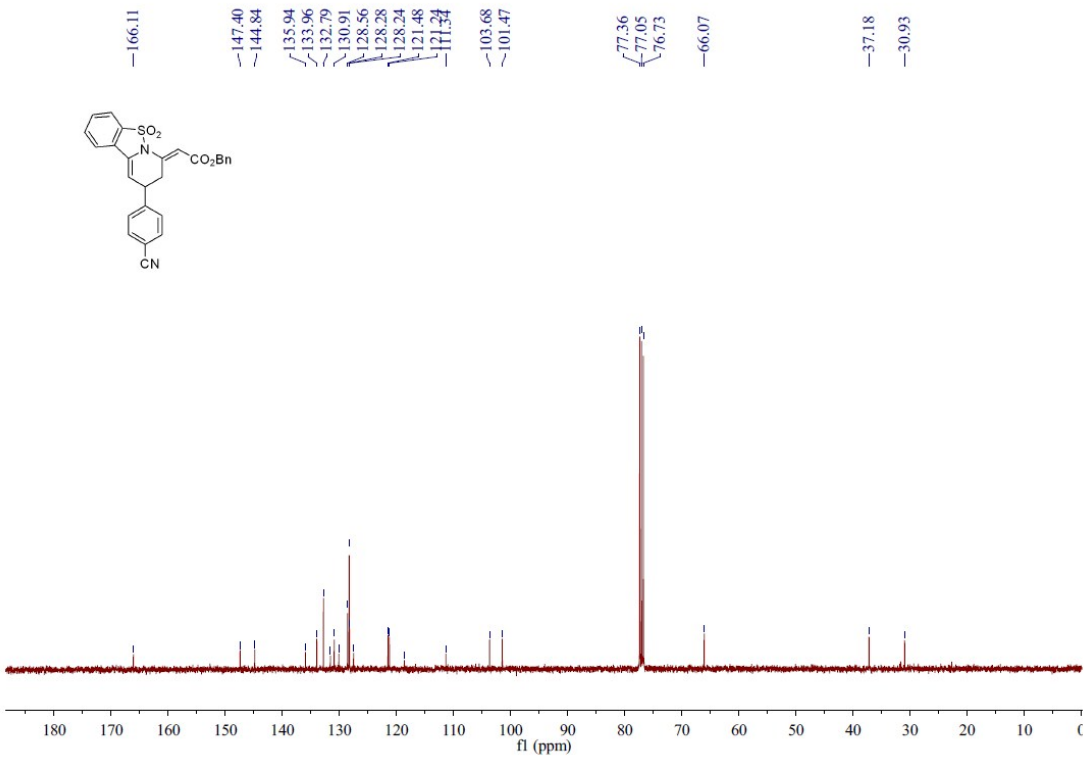
3.00
7.00
0.95
1.00
2.00
1.00
1.00
1.00
fl (ppm)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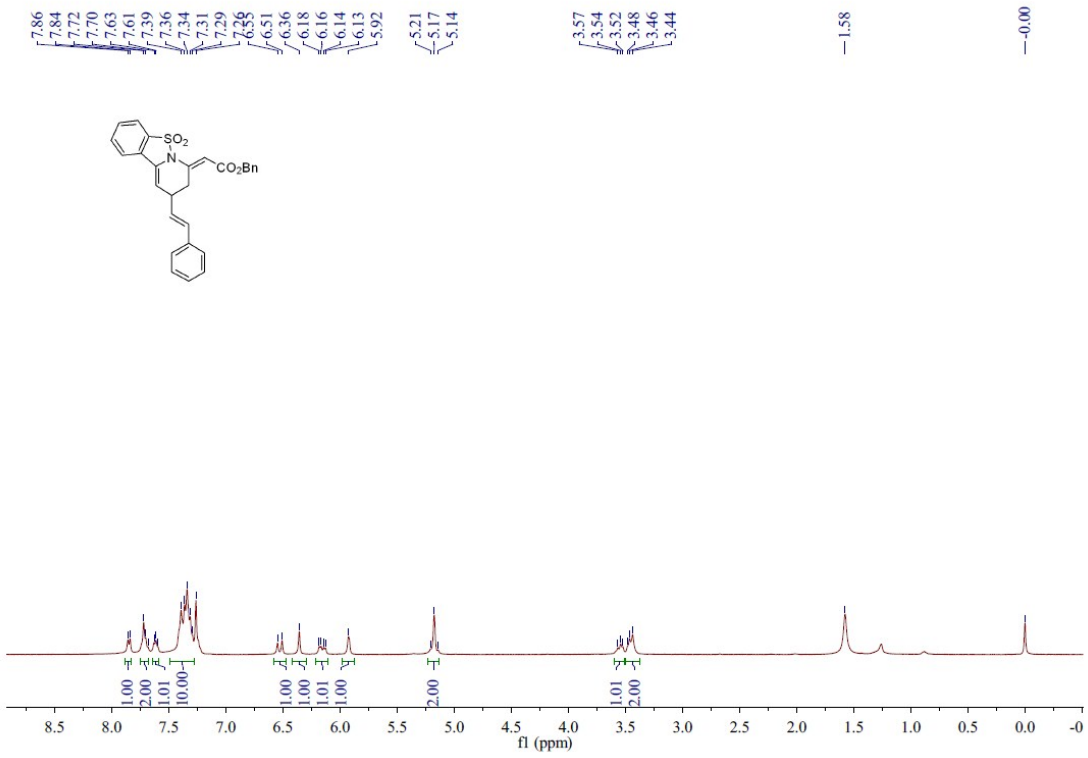
121.24
121.14
103.68
101.47
77.36
77.05
76.73
66.07
37.18
30.93
SO2
N
CO2Bn
CN
fl (ppm)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7.84
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7.36
7.34
7.31
7.29
7.26
6.55
6.51
6.36
6.18
6.16
6.14
6.13
5.92
5.21
5.17
5.14
3.57
3.54
3.52
3.48
3.46
3.44
1.58
0.00
SO2
N
CO2Bn
1.00
2.00
1.01
10.00
1.00
1.00
1.01
1.00
2.00
1.01
2.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
1.5
1.0
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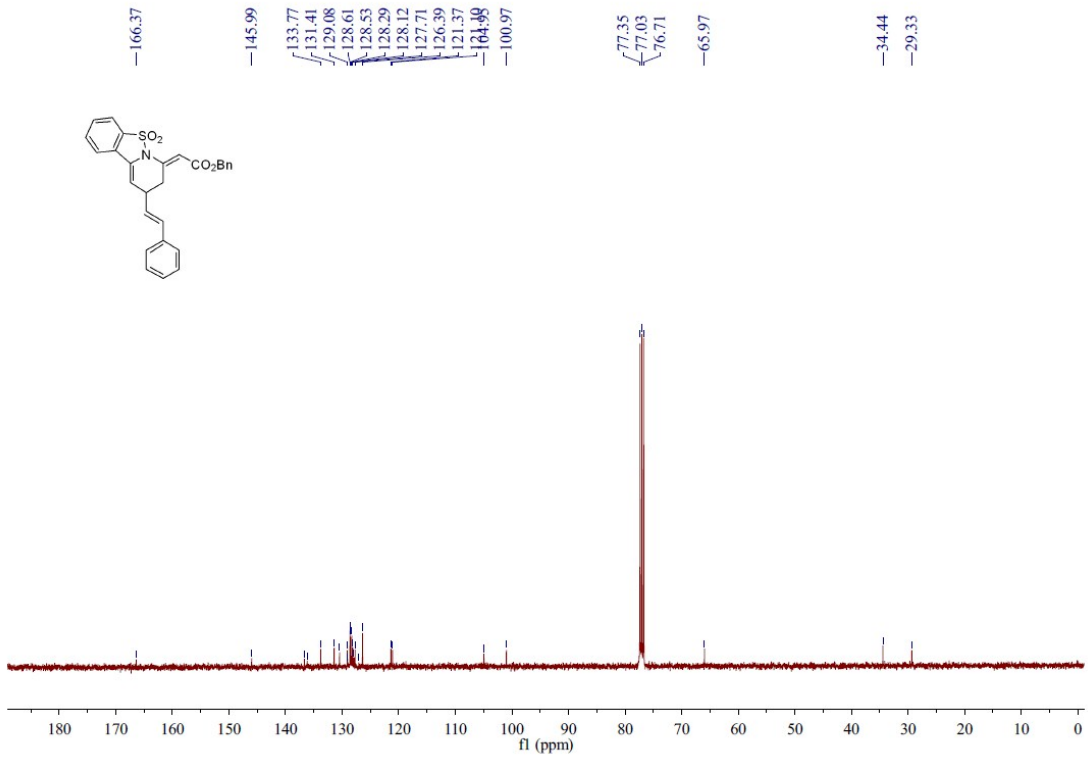
f1 (ppm)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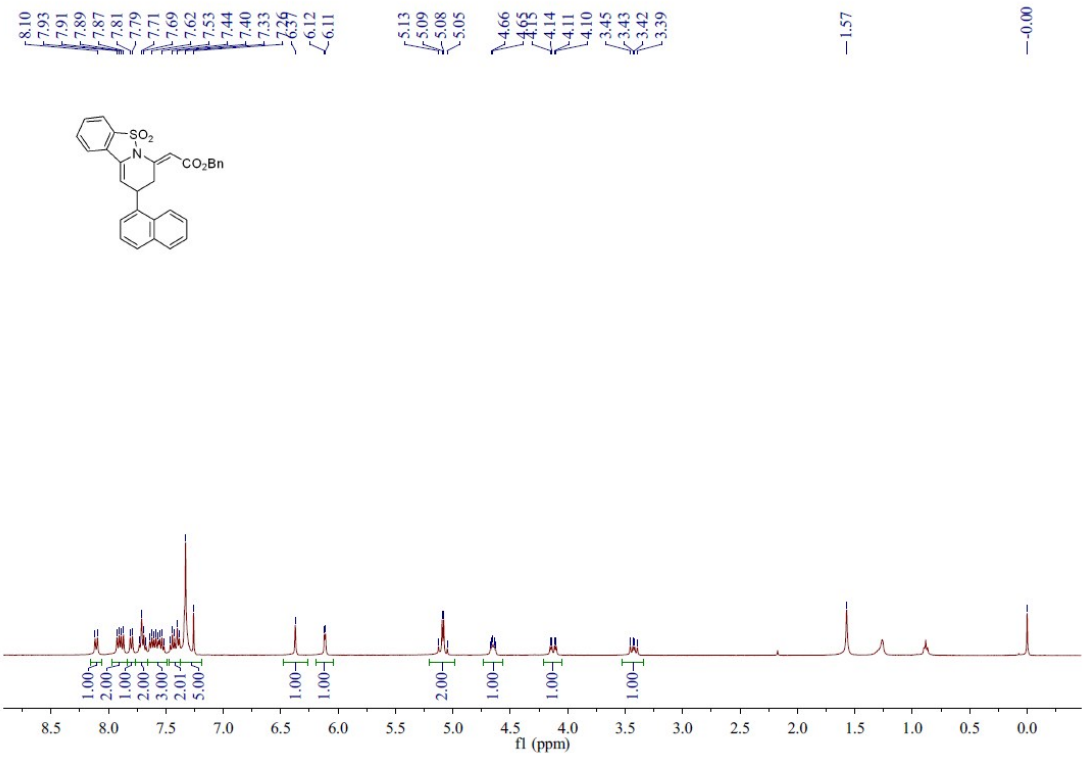
127.71
126.39
121.37
100.97
77.35
77.03
76.71
65.97
34.44
29.33
SO2
N
CO2Bn
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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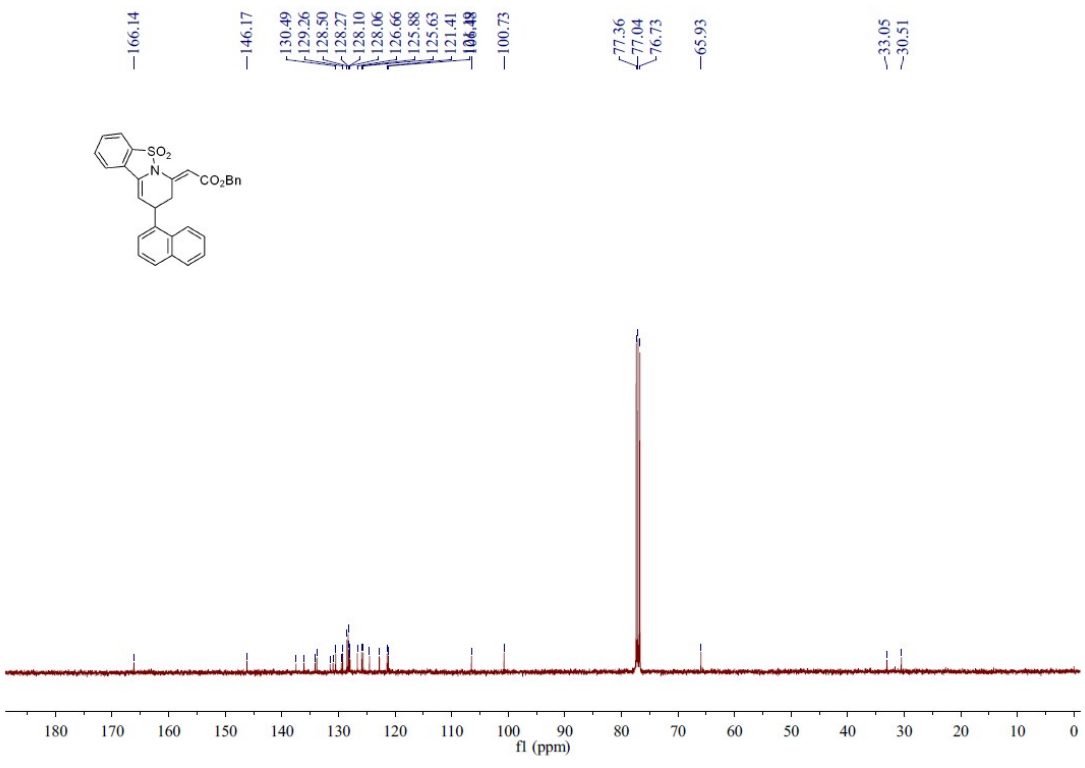
7.93
7.91
7.89
7.87
7.81
7.79
7.71
7.69
7.62
7.53
7.44
7.40
7.33
6.12
6.11
5.13
5.09
5.08
5.05
4.66
4.65
4.15
4.14
4.11
4.10
3.45
3.43
3.42
3.39
1.57
0.00
SO2
N
CO2Bn
1.00
2.00
1.00
2.00
3.00
2.01
5.00
1.00
1.00
2.00
1.00
1.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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125.63
121.41
100.73
77.36
77.04
76.73
65.93
33.05
30.51
SO2
N
CO2Bn
180
170
160
150
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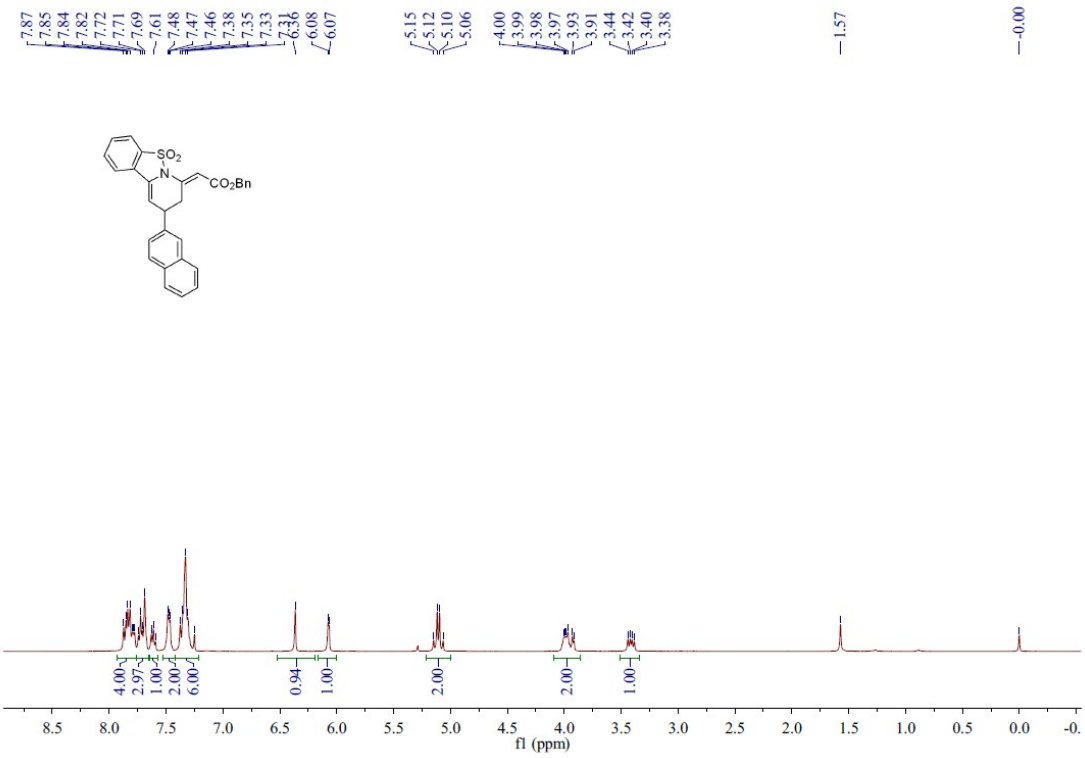
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.85
7.84
7.82
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7.71
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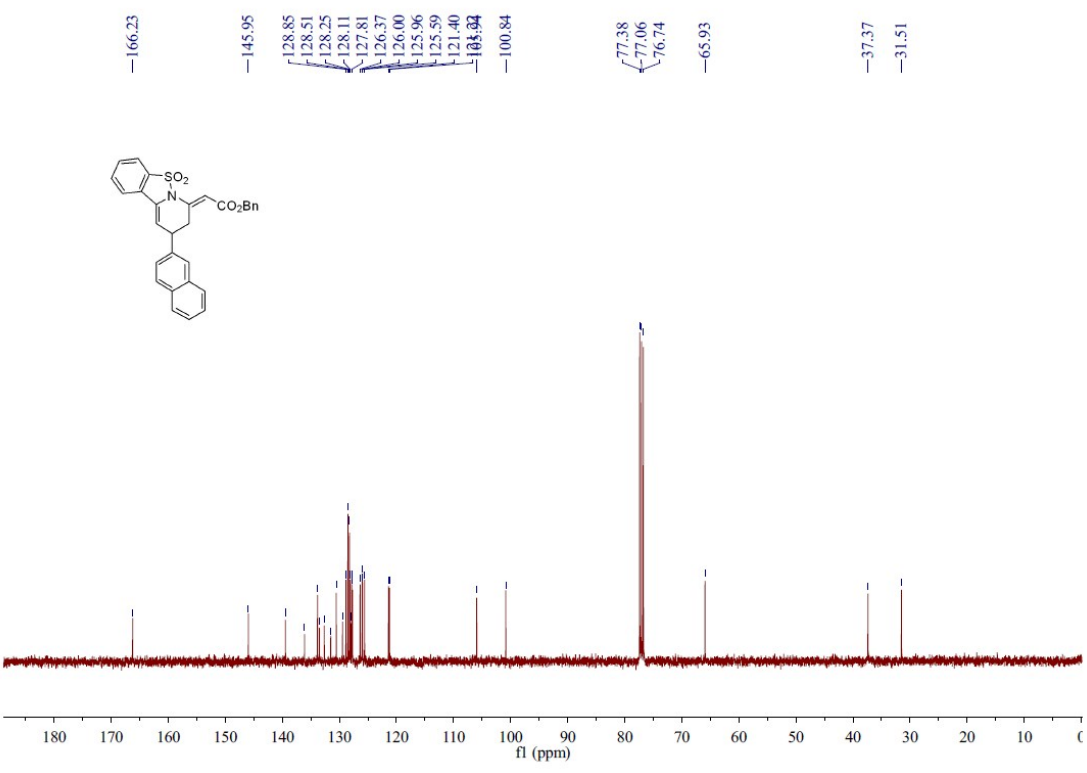
7.61
7.48
7.47
7.46
7.38
7.35
7.33
7.31
6.36
6.08
6.07
5.15
5.12
5.10
5.06
4.00
3.99
3.98
3.97
3.93
3.91
3.44
3.42
3.40
3.38
1.57
0.00
SO2
N
CO2Bn
4.00
2.97
1.00
2.00
6.00
0.94
1.00
2.00
2.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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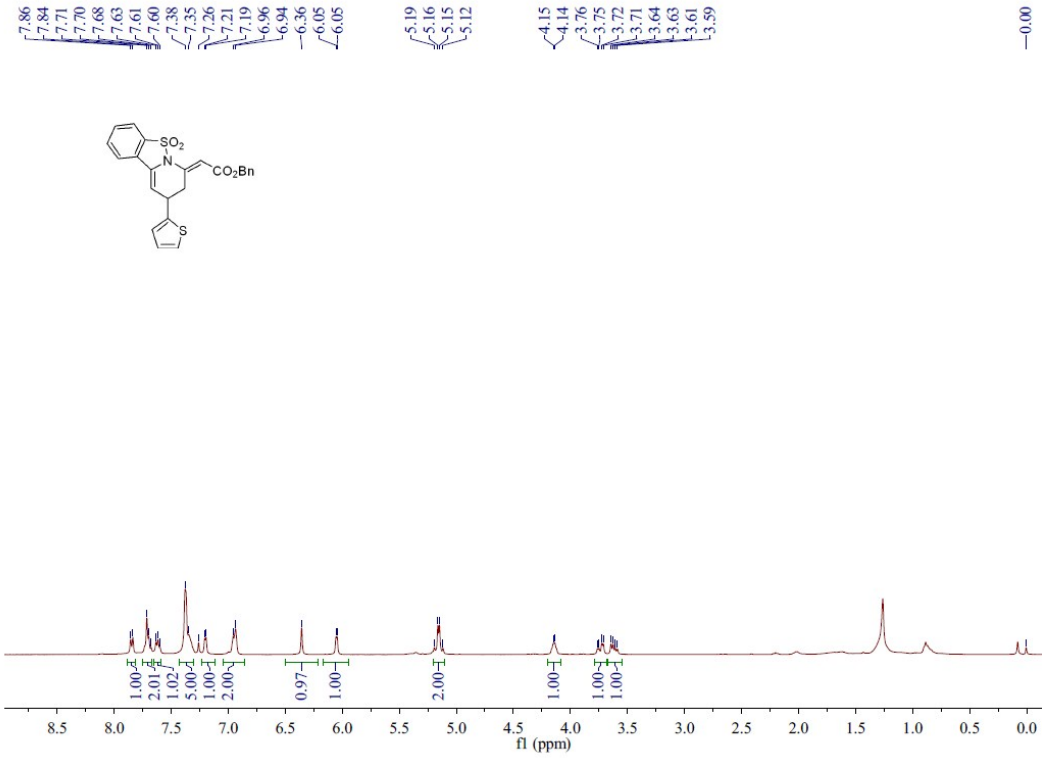
128.11
127.81
126.37
126.00
125.96
125.59
121.40
100.84
77.38
77.06
76.74
65.93
37.37
31.51
SO2
N
CO2Bn
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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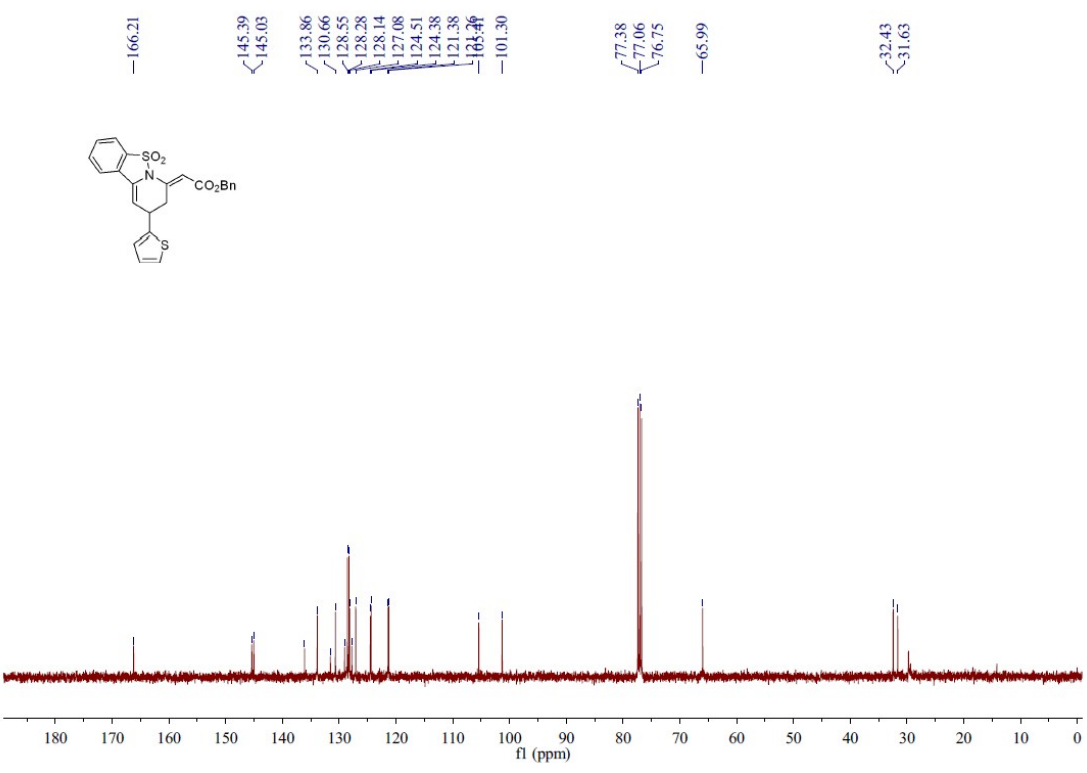
7.84
7.71
7.70
7.68
7.63
7.61
7.60
7.38
7.35
7.26
7.21
7.19
6.96
6.94
6.36
6.05
6.05
5.19
5.16
5.15
5.12
4.15
4.14
3.76
3.75
3.72
3.71
3.64
3.63
3.61
3.59
0.00
SO2
N
CO2Bn
S
1.00
2.01
1.02
5.00
1.00
2.00
0.97
1.00
2.00
1.00
1.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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145.03
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130.66
128.55
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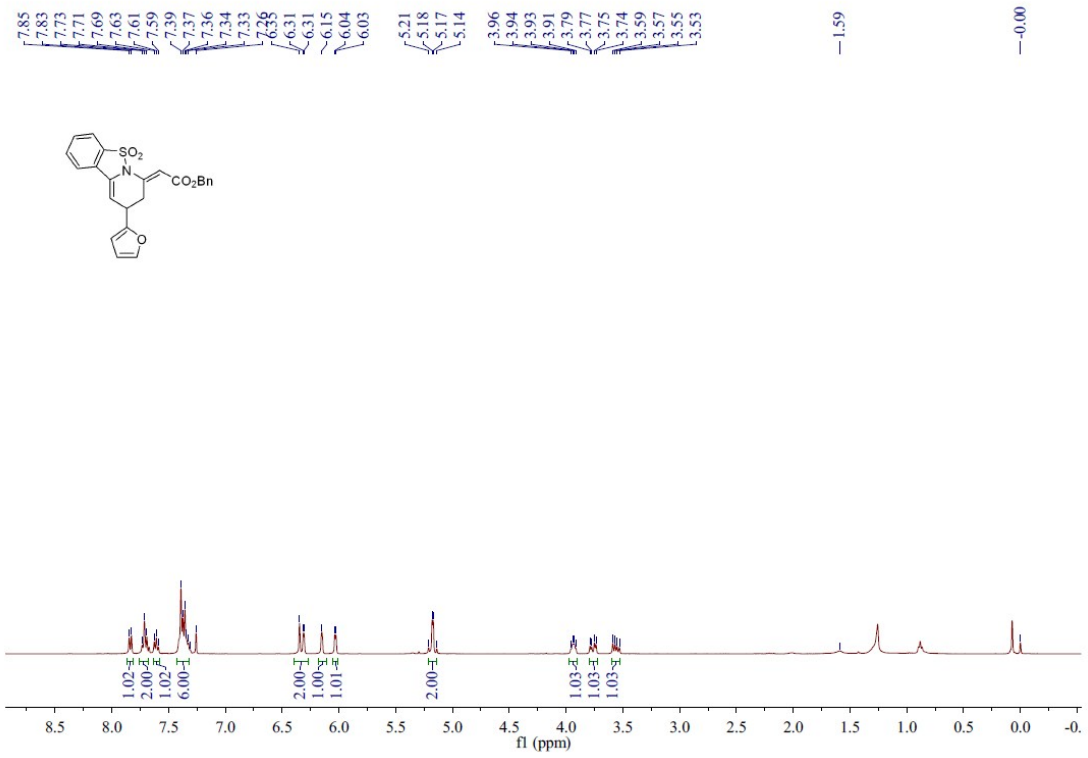
124.51
124.38
121.38
101.30
77.38
77.06
76.75
65.99
32.43
31.63
SO2
N
CO2Bn
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.73
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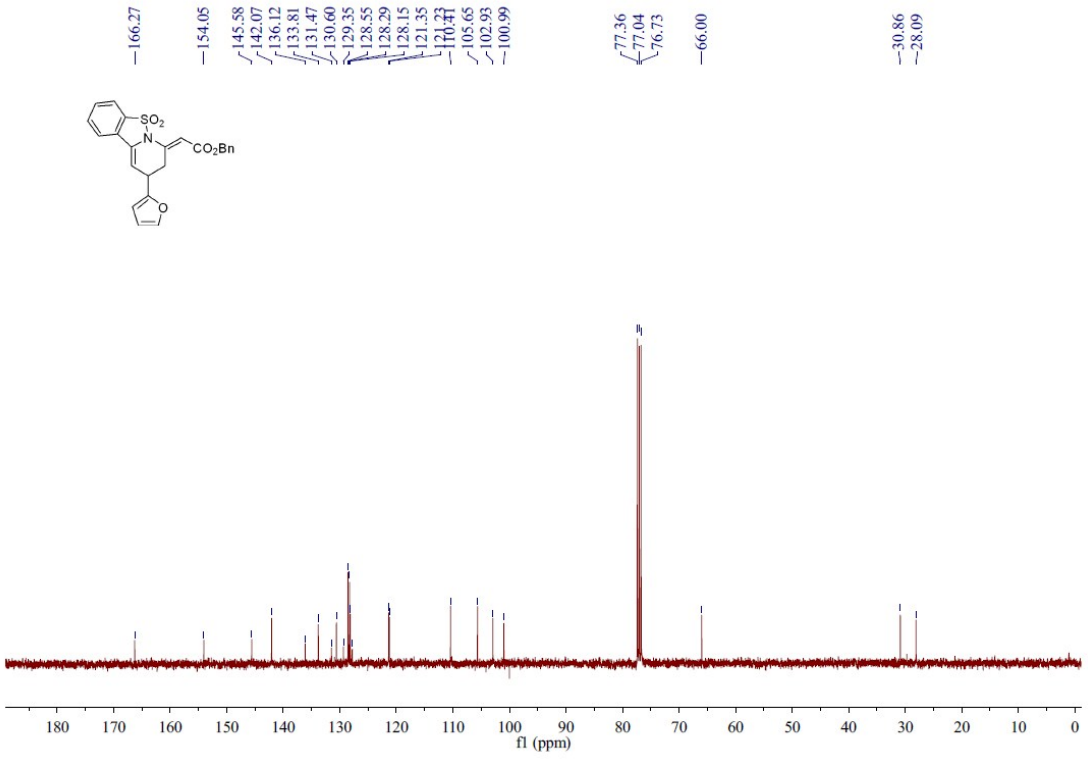
7.63
7.61
7.59
7.39
7.37
7.36
7.34
7.33
7.26
6.35
6.31
6.31
6.15
6.04
6.03
5.21
5.18
5.17
5.14
3.96
3.94
3.93
3.91
3.79
3.77
3.75
3.74
3.59
3.57
3.55
3.53
1.59
0.00
SO2
N
CO2Bn
O
1.02
2.00
1.02
6.00
2.00
1.00
1.01
2.00
1.03
1.03
1.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)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154.05
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142.07
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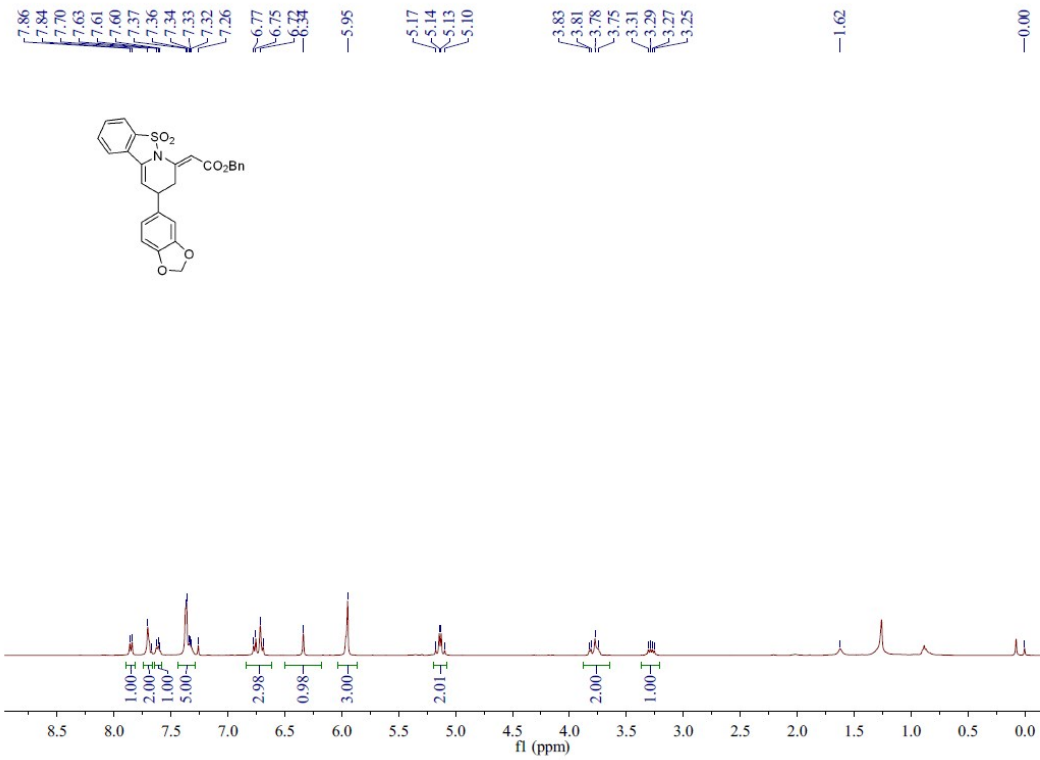
130.60
129.35
128.55
128.29
128.15
121.35
121.23
110.41
105.65
102.93
100.99
77.36
77.04
76.73
66.00
30.86
28.09
SO2
N
CO2Bn
O
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.63
7.61
7.60
7.37
7.36
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7.33
7.32
7.26
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6.34
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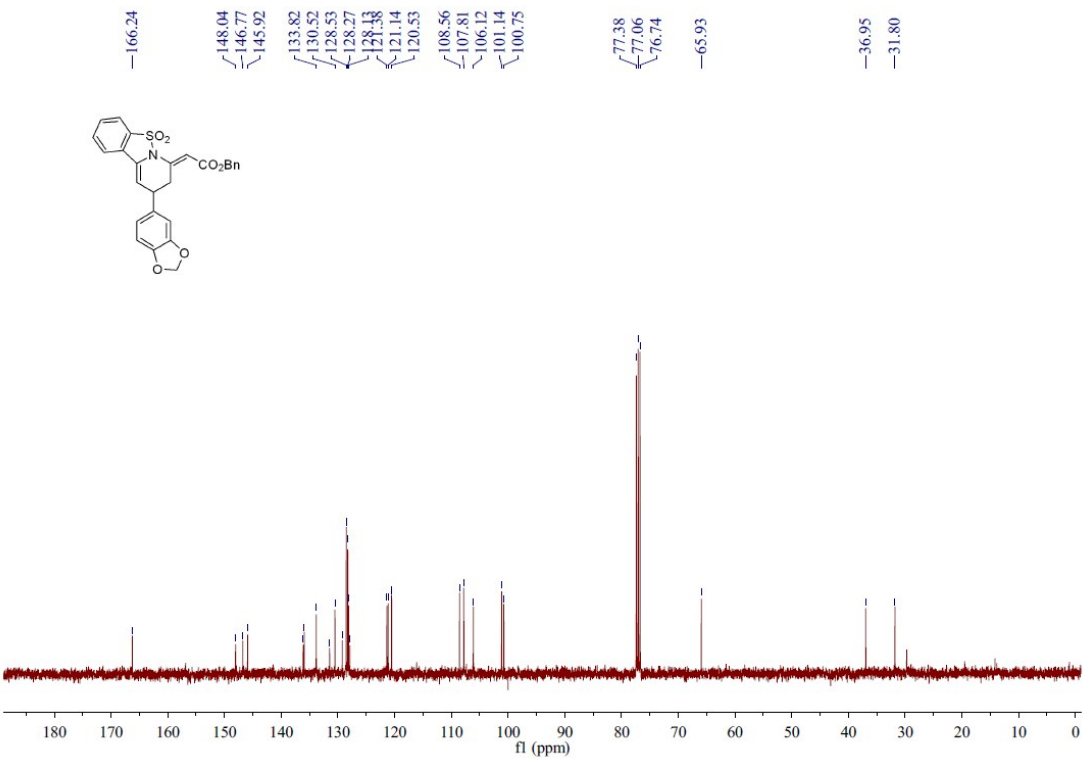
5.14
5.13
5.10
3.83
3.81
3.78
3.75
3.31
3.29
3.27
3.25
1.62
0.00
SO2
N
CO2Bn
O
O
1.00
2.00
1.00
5.00
2.98
0.98
3.00
2.01
2.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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120.53
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107.81
106.12
101.14
100.75
77.38
77.06
76.74
65.93
36.95
31.80
SO2
N
CO2Bn
O
O
180
170
160
150
140
130
120
110
100
90
80
70
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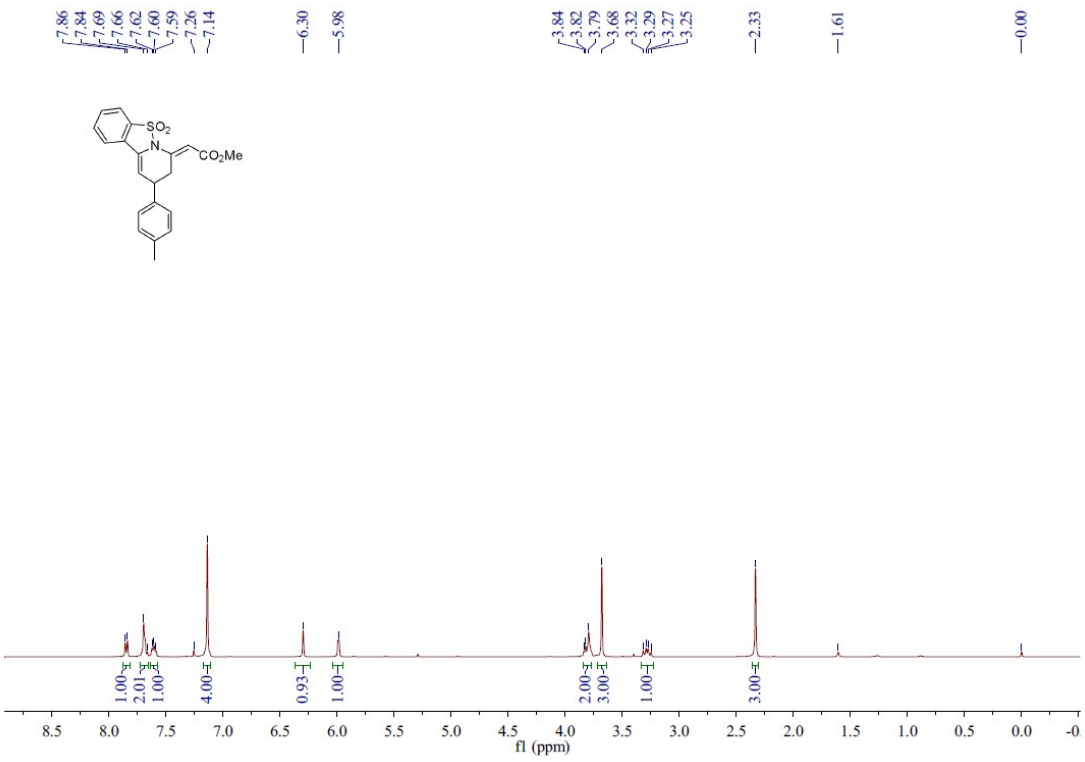
50
40
30
20
10
0
f1 (ppm)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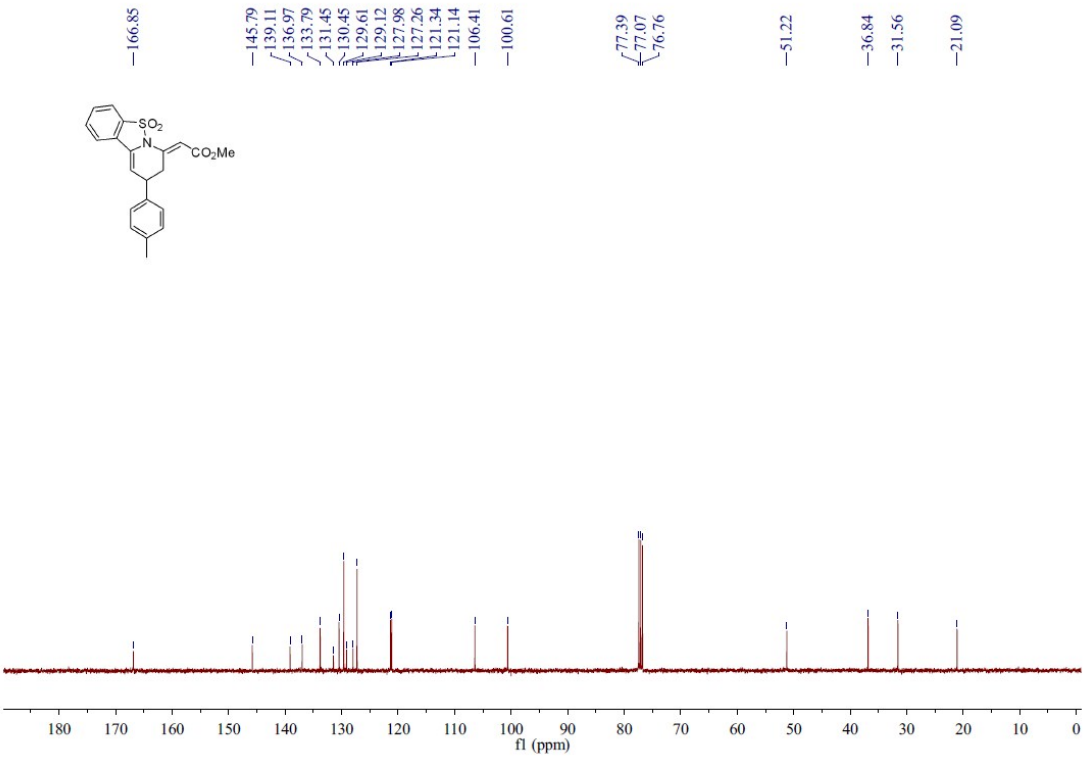
7.26
7.14
6.30
5.98
3.84
3.82
3.79
3.68
3.32
3.29
3.27
3.25
2.33
1.61
0.00
SO2
N
CO2Me
1.00
2.01
1.00
4.00
0.93
1.00
2.00
3.00
1.00
3.00
f1 (ppm)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127.98
127.26
121.34
121.14
106.41
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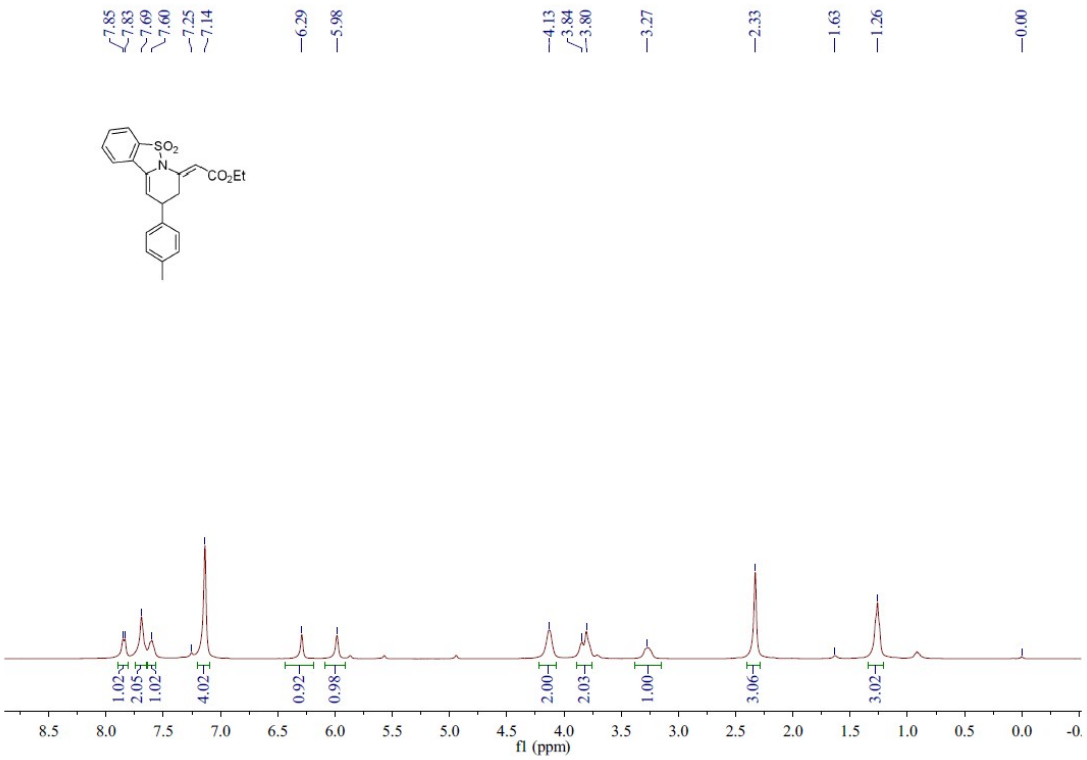
77.07
76.76
51.22
36.84
31.56
21.09
SO2
N
CO2Me
f1 (ppm)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7.60
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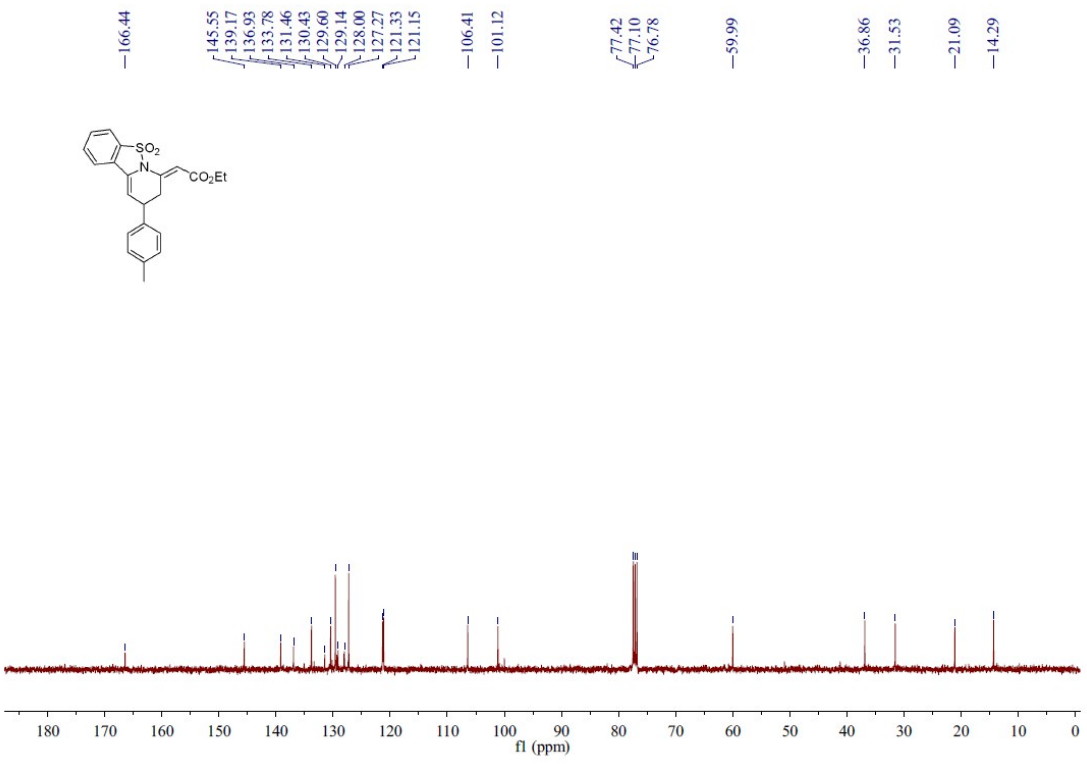
7.14
6.29
5.98
4.13
3.84
3.80
3.27
2.33
1.63
1.26
0.00
SO2
N
CO2Et
1.02
2.05
1.02
4.02
0.92
0.98
2.00
2.03
1.00
3.06
3.02
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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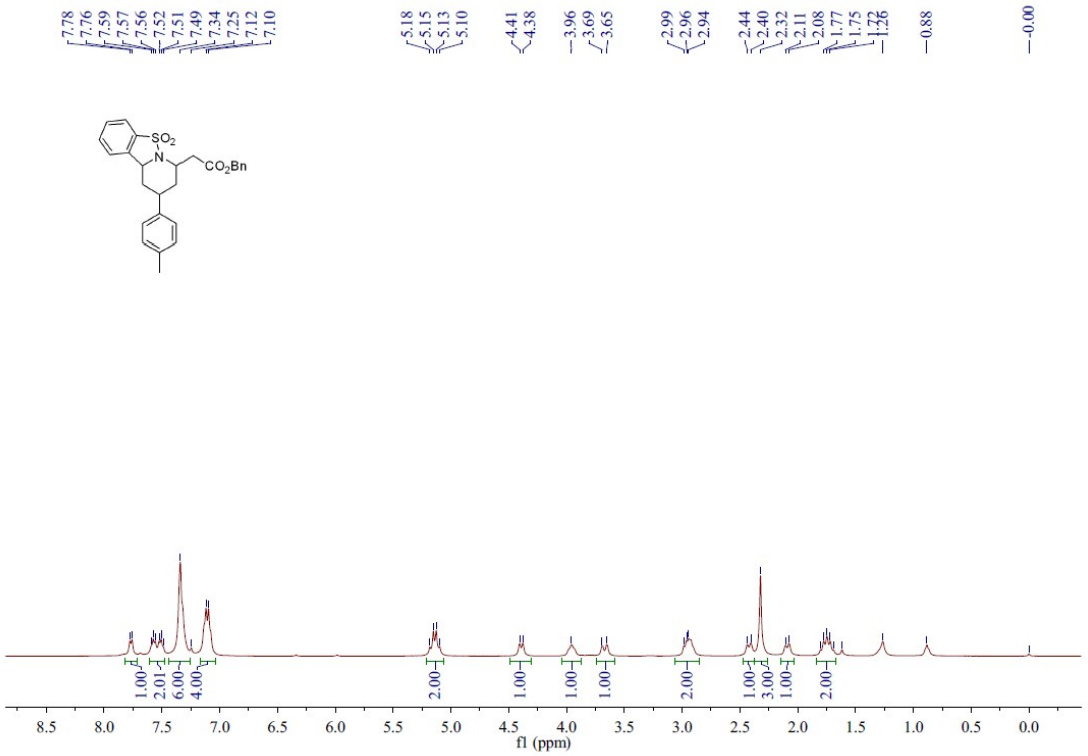
127.27
121.33
121.15
106.41
101.12
77.42
77.10
76.78
59.99
36.86
31.53
21.09
14.29
SO2
N
CO2Et
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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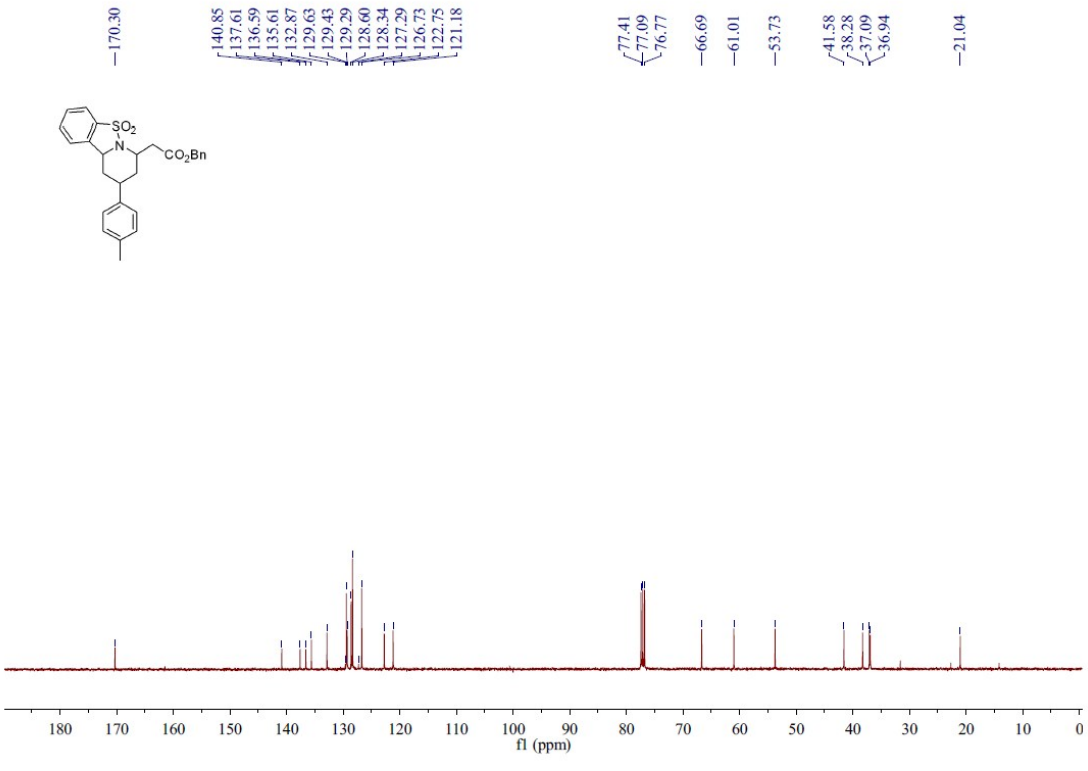
7.25
7.12
7.10
5.18
5.15
5.13
5.10
4.41
4.38
3.96
3.69
3.65
2.99
2.96
2.94
2.44
2.40
2.32
2.11
2.08
1.77
1.75
1.72
1.26
0.88
0.00
SO2
N
CO2Bn
1.00
2.01
6.00
4.00
2.00
1.00
1.00
1.00
2.00
1.00
3.00
1.00
2.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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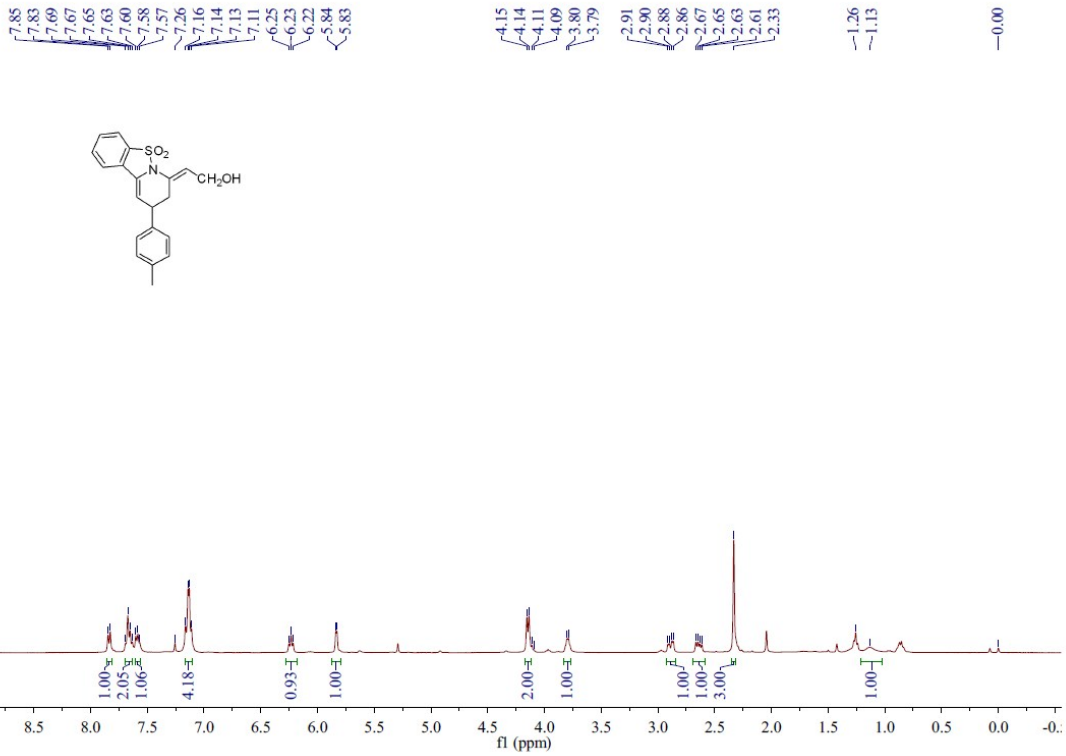
129.43
129.29
128.60
128.34
127.29
126.73
122.75
121.18
77.41
77.09
76.77
66.69
61.01
53.73
41.58
38.28
37.09
36.94
21.04
SO2
N
CO2Bn
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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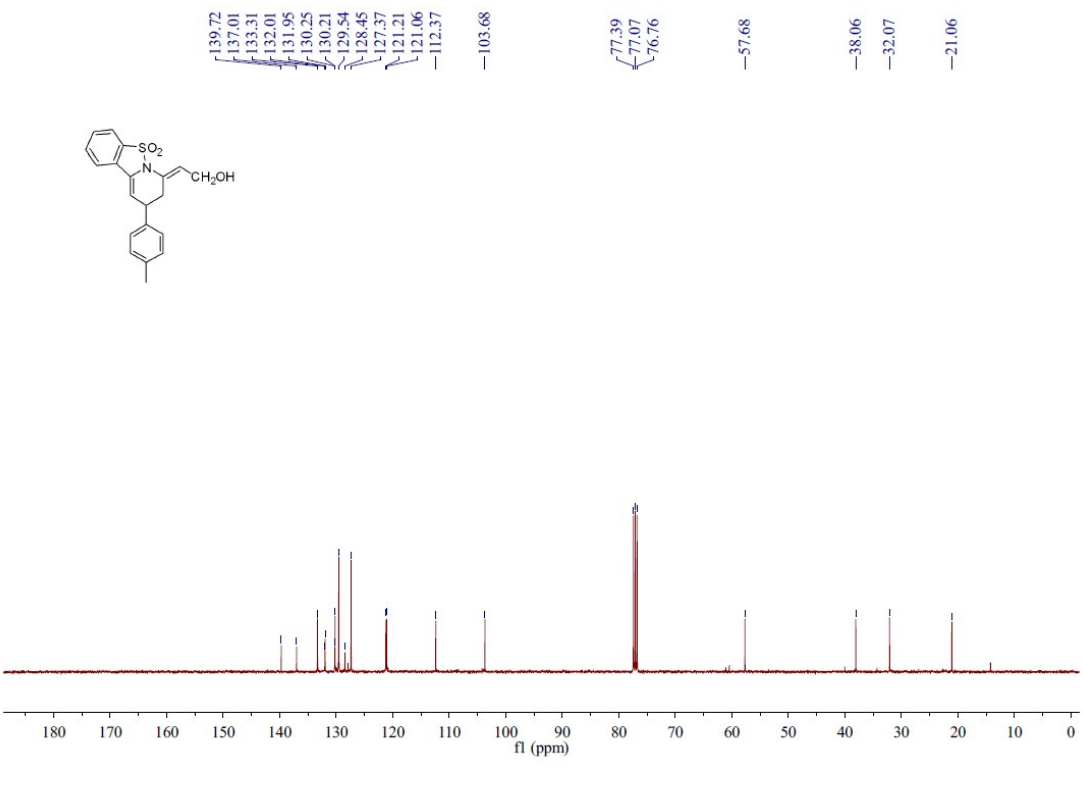
7.83
7.69
7.67
7.65
7.63
7.60
7.58
7.57
7.26
7.16
7.14
7.13
7.11
6.25
6.23
6.22
5.84
5.83
4.15
4.14
4.11
4.09
3.80
3.79
2.91
2.90
2.88
2.86
2.67
2.65
2.63
2.61
2.33
1.26
1.13
0.00
SO2
N
CH2OH
1.00
2.05
1.06
4.18
0.93
1.00
2.00
1.00
1.00
1.00
3.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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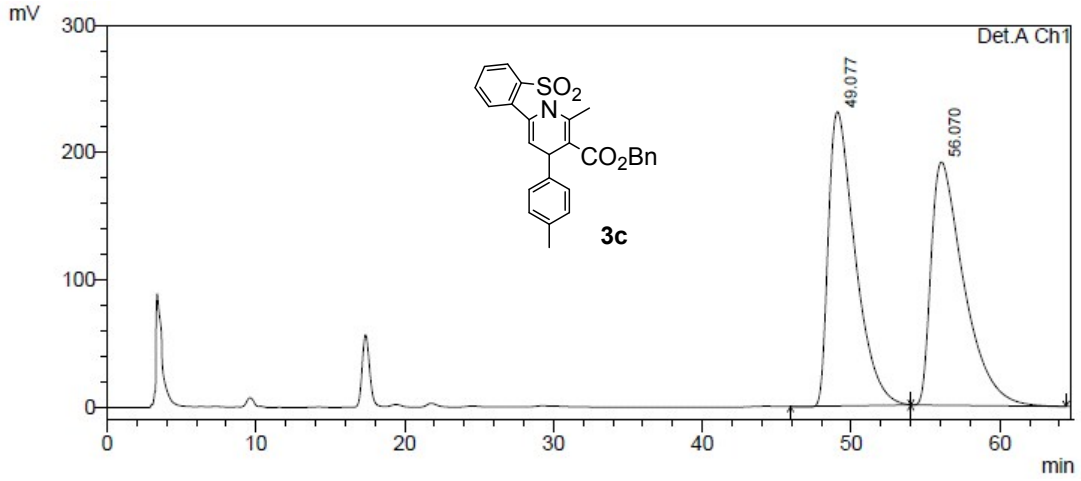
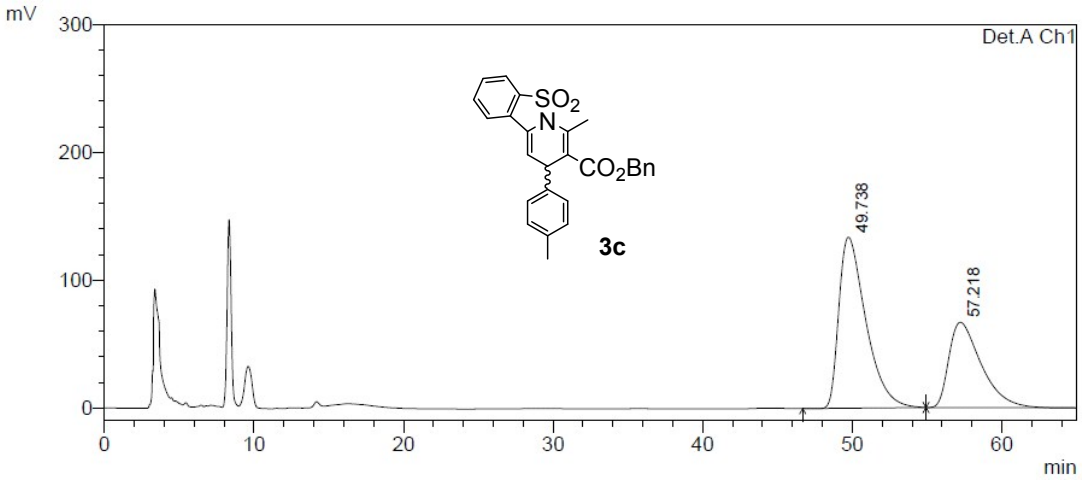
127.37
121.21
121.06
112.37
103.68
77.39
77.07
76.76
57.68
38.06
32.07
21.06
SO2
N
CH2OH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.077	28915204	230905	49.658	54.742
2	56.070	29313431	190905	50.342	45.258
Total		58228635	421810	100.000	100.000

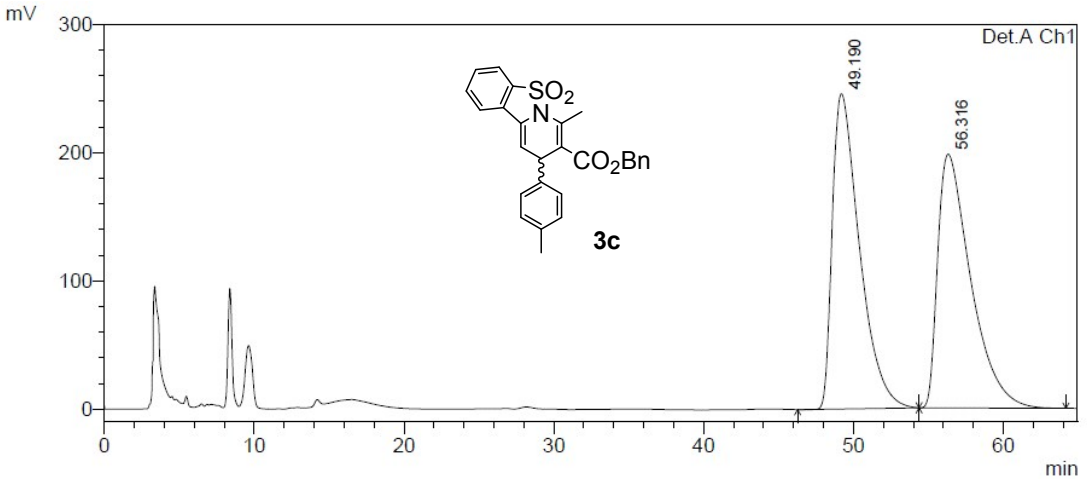
The racemic system of **3c**, determined by HPLC (Chiralpak OD-H, hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25°C; λ = 210 nm)



Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.738	16782464	133841	62.606	66.730
2	57.218	10024163	66729	37.394	33.270
Total		26806627	200570	100.000	100.000

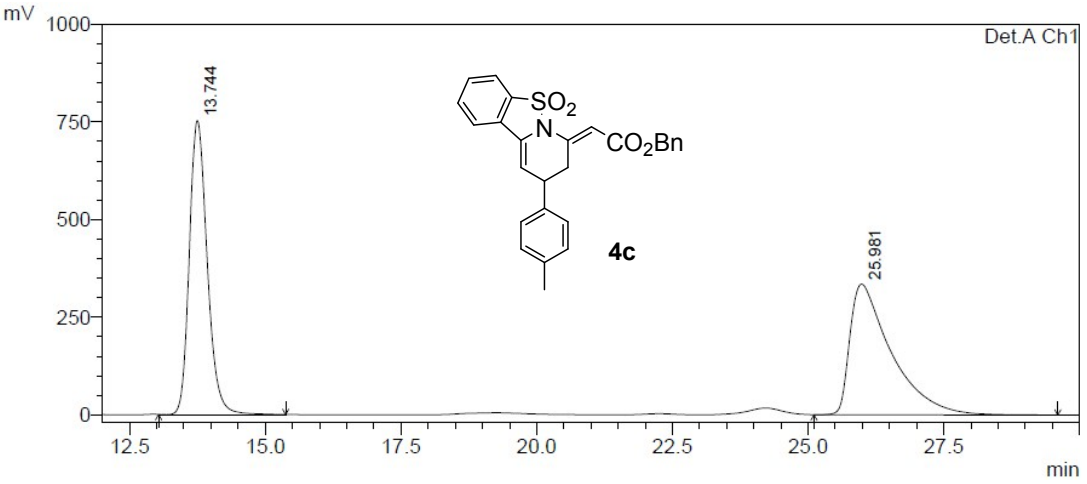
The asymmetric system of **3c** with the chiral **cat.1** (β-ICD) in CH_2Cl_2, enantiomeric excess: 25%, determined by HPLC (Chiralpak OD-H, hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25°C; λ = 210 nm)



Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	49.190	30999490	245876	50.567	55.396
2	56.316	30303842	197978	49.433	44.604
Total		61303332	443854	100.000	100.000

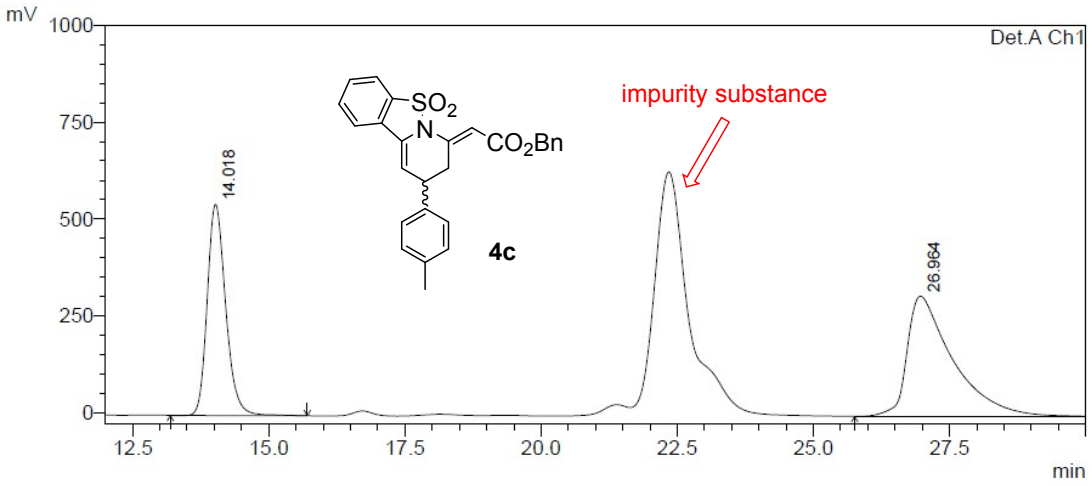
The asymmetric system of **3c** with the chiral **cat.1** (β-ICD) in toluene, enantiomeric excess: 1%, determined by HPLC (Chiralpak OD-H, hexane/2-propanol = 99/1; flow rate 1.0 mL/min; 25°C; λ = 210 nm)



Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.744	17242480	752692	49.226	69.234
2	25.981	17784567	334478	50.774	30.766
Total		35027046	1087170	100.000	100.000

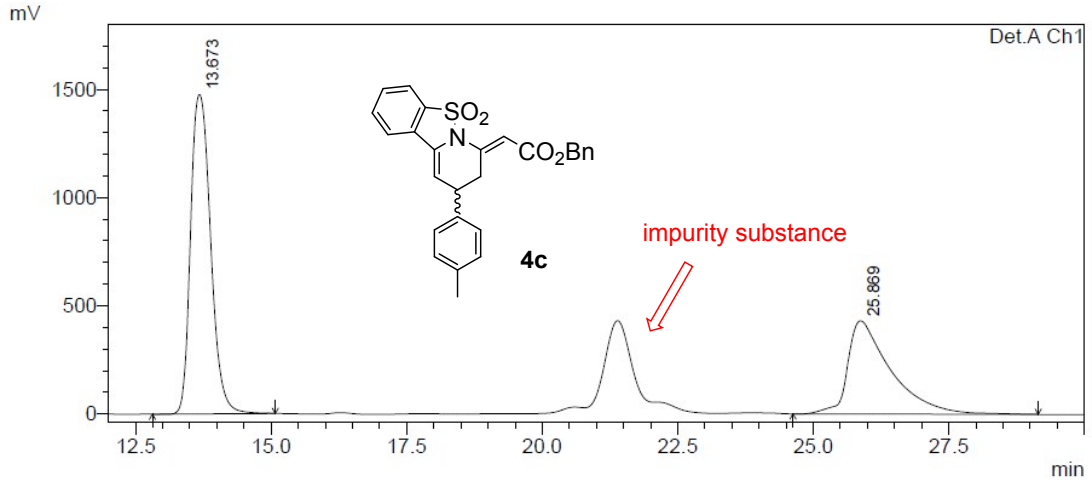
The racemic system of **4c**, determined by HPLC (Chiralpak IA, hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25°C; λ = 210 nm)



Detector A Ch1 210nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.018	12863863	545348	41.540	63.732
2	26.964	18103563	310347	58.460	36.268
Total		30967426	855696	100.000	100.000

The asymmetric system of **4c** with the chiral **cat.1** (β-ICD) in CH_2Cl_2, enantiomeric excess: 17%, determined by HPLC (Chiralpak IA, hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25°C; λ = 210 nm) (The impurity substance peak in HPLC chromatogram could be detected in the ^{1}H NMR, but we could not know the structure of the impurity substance).

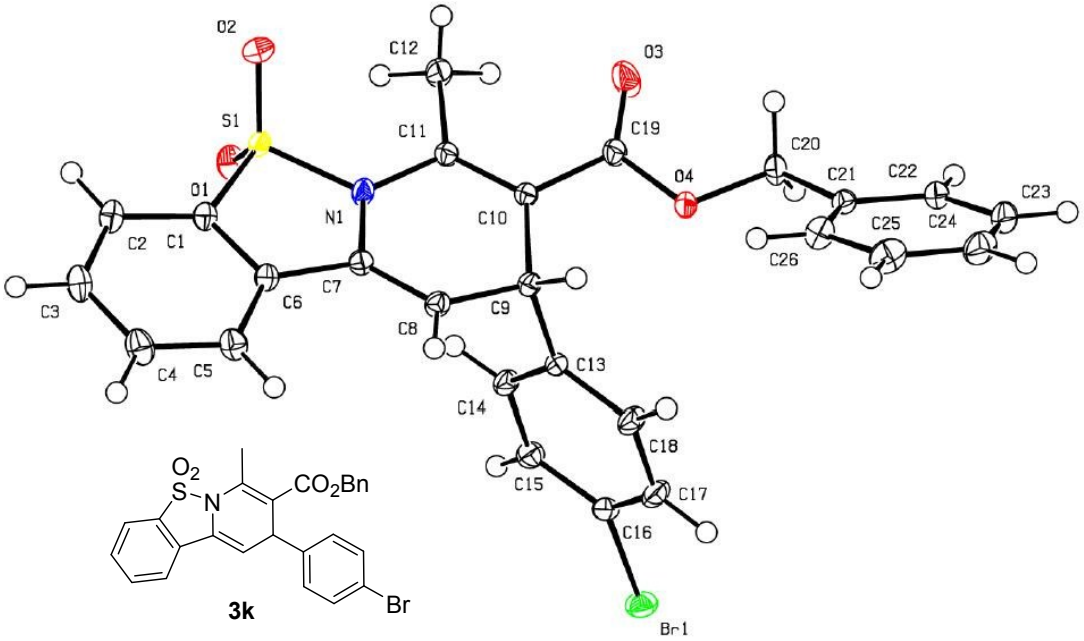


Detector A Ch1 210nm

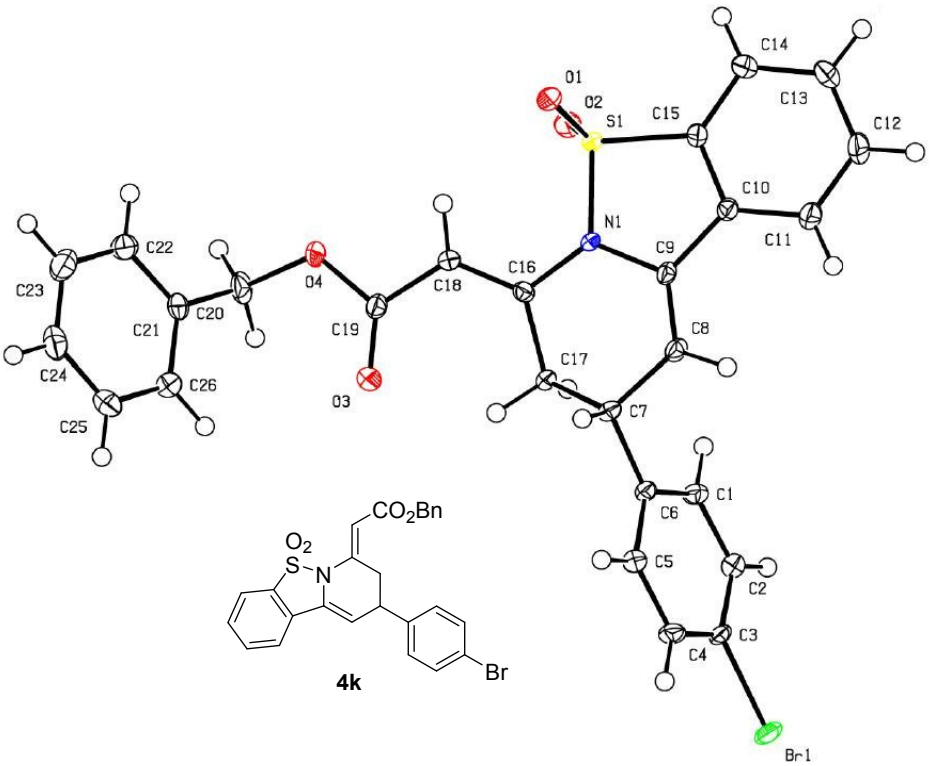
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.673	37891202	1475713	61.338	77.393
2	25.869	23883160	431055	38.662	22.607
Total		61774361	1906768	100.000	100.000

The asymmetric system of **4c** with the chiral **cat.1** (β-ICD) in toluene, enantiomeric excess: (-)23%, determined by HPLC (Chiralpak IA, hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25°C; λ = 210 nm) (The impurity substance peak in HPLC chromatogram could be detected in the ^{1}H NMR, but we could not know the structure of the impurity substance).

VI. X-Ray crystal structure of 3k and 4k



X-ray structure of **3k** (The H-atoms are omitted for clarity) CCDC NO.1438835



X-ray structure of **4k** (The H-atoms are omitted for clarity) CCDC NO. 1438830