Enantioselective Conjugate Addition of Nitroalkanes to Vinyl Sulfone: an Organocatalytic Access to Chiral Amines

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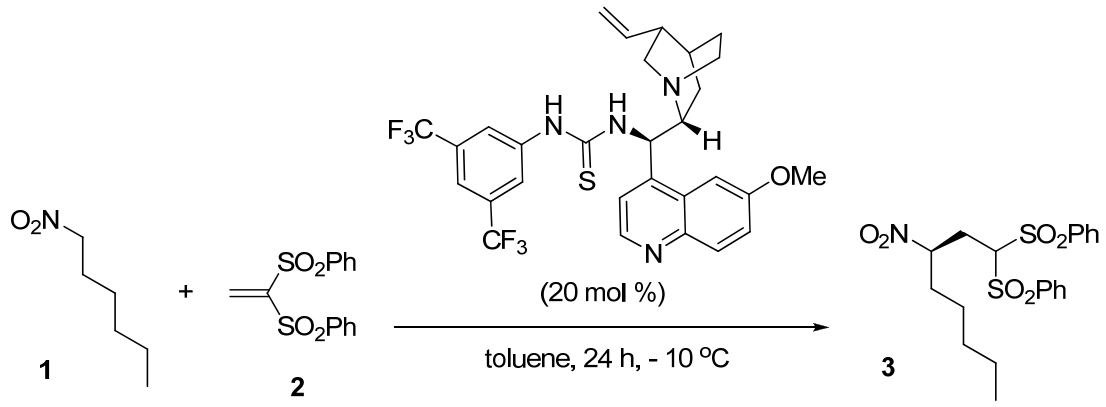
Supporting Information

A. General Information

Chemicals and solvents were purchased from commercial suppliers and used as received. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ACF300 or a DPX300 (300 MHz) or an AMX500 (500 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0). Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), br s (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode, and a Finnigan/MAT 95XL-T mass spectrometer in FAB mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. For thin-layer chromatography (TLC), Merck pre-coated TLC plates (Merck 60 F_{254}) were used, and compounds were visualized under a UV light at 254 nm. Further visualization was achieved by staining with iodine, or ceric ammonium molybdate followed by heating on a hot plate. Flash chromatographic separations were performed on Merck 60 (0.040 - 0.063 mm) mesh silica gel. The enantiomeric excesses of products were determined by chiral-phase HPLC analysis.

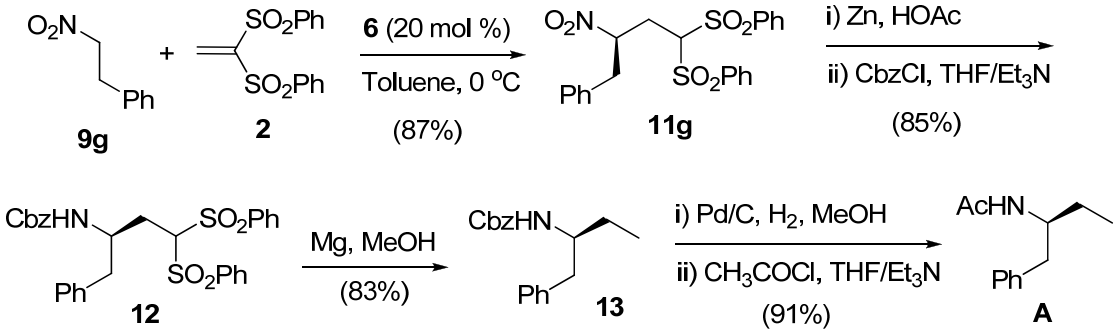
All the nitroalkanes and 1,2-bis(phenylsulfonyl)ethylene were purchased from Sigma-Aldrich or from commercial sources.

B. <u>Representative Procedure: addition of nitrohexane to 1,1-bis(benzenesulfonyl)ethylene catalyzed by quinidine-derived thiourea 6</u>



Nitrohexane (33 mg, 0.25 mmol) was added to a mixture of 1-(3,5-bis(trifluoromethyl)-phenyl)-3-((*S*)-(6-methoxyquinolin-4-yl)((2*S*)-8-vinylquinuclidin-2-yl)methyl)thiourea **6** (6.0 mg, 0.01 mmol), and 1,1-bis(benzenesulfonyl)ethylene (15.4 mg, 0.05 mmol) in anhydrous toluene (0.2 mL) in a sample vial at -10 ^{o}C. The vial was then sealed and the reaction mixture was stirred at -10 ^{o}C for 24 hours, and quenched with the addition of 1N HCl (2 mL). The organic layer was extracted with ethyl acetate several times (3 x 5 mL), and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by flash column chromatography (ethyl acetate/hexanes = 1:5 to 1:2) afforded the desired product as a white solid (19.1 mg, 87%). The enantiometric excess of product was determined by chiral HPLC analysis.

C. Determination of Absolute Configurations of the Michael Products



Following the representative procedure illustrated in section B, the Michael addition of 1-(2-nitroethyl)benzene to vinyl sulfone was performed to give the adduct **11g**, which was reduced to amine in situ, followed by protection with Cbz to afford **12**. Removal of the sulfone groups[1] gave **13**, which was deprotected and acylated to yield the known compound **A**, the configuration of which was determined by comparison with the literature data.[2] The configurations of other Michael adducts were assigned by analogy.

(*R*)-Benzyl 1-phenyl-4,4-bis(phenylsulfonyl)butan-2-ylcarbamate 12

To a solution of compound **11g** (112 mg, 0.20 mmol) in THF (2.0 mL) containing acetic acid (1.5 mL) was added zinc powder (406 mg, 7.0 mmol). After stirring at room temperature for 24 hours, the mixture was filtered, and the filtrate was concentrated and partitioned between aqueous $NaHCO_3$ and ethyl acetate. The organic layer was washed with brine and dried with Na_2SO_4. The solvent was removed to afford the crude product, which was directly used for the

next step. To a solution of crude amine in THF (5 mL) was added triethylamine (1.0 mmol, 0.14 mL) and CbzCl (41 mg, 0.24 mmol). The reaction mixture was stirred at room temperature for 3 hours and concentrated. The residue was taken up in ethyl acetate (10 mL), washed with water (2 x 5 mL), and dried over Na_2SO_4. After filtration, the filtrate was concentrated, and the residue was purified by column chromatography (ethyl acetate /hexanes = 1/5 to 2/5) to afford **12** as a yellow oil (96 mg, 85%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.07-2.28 (m, 1H), 2.37-2.39 (m, 1H), 2.72-2.76 (m, 1H), 2.89-2.93 (m, 1H), 3.85 (s, 3H), 4.08 (m, 1H), 4.71-4.74 (m, 2H), 5.07-5.13 (m, 2H), 7.11-7.13 (m, 2H), 7.31-7.38 (m, 8H), 7.45-7.49 (m, 4H), 7.65-7.66 (m, 2H), 7.79-7.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.10, 41.53, 51.40, 66.71, 77.38, 79.92, 126.86, 127.90, 128.15, 128.51, 128.69, 129.02, 129.31, 129.45, 134.30, 134.43, 136.35, 137.44, 137.54, 156.30; $[\alpha]_D$ = -19.5 (c = 0.40, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{30}H_{29}NO_6S_2$ $[M+Na]^+$ 586.1329, found 586.1326.

(*S*)-Benzyl 1-phenylbutan-2-ylcarbamate 13

The activated magnesium metal (108 mg, 4.5 mmol) was added into a solution of (*R*)-benzyl 1-phenyl-4,4-bis(phenylsulfonyl)butan-2-ylcarbamate **12** (85 mg, 0.15 mmol) in anhydrous methanol (10 mL) with stirring. After 30 minutes, the reaction mixture was brought to reflux for 2 hours. Upon cooling down to room temperature, the mixture was poured into 2 N HCl (aq.) (10 mL) and extracted with ether (3 x 10 mL). The organic extracts were combined, dried over Na_2SO_4 and filtered. Solvent was removed *in vacuo*, and the residue was purified by column chromatography (ethyl acetate /hexanes = 1/15 to 1/5) to afford the desired product as a white solid (35 mg, 83%).

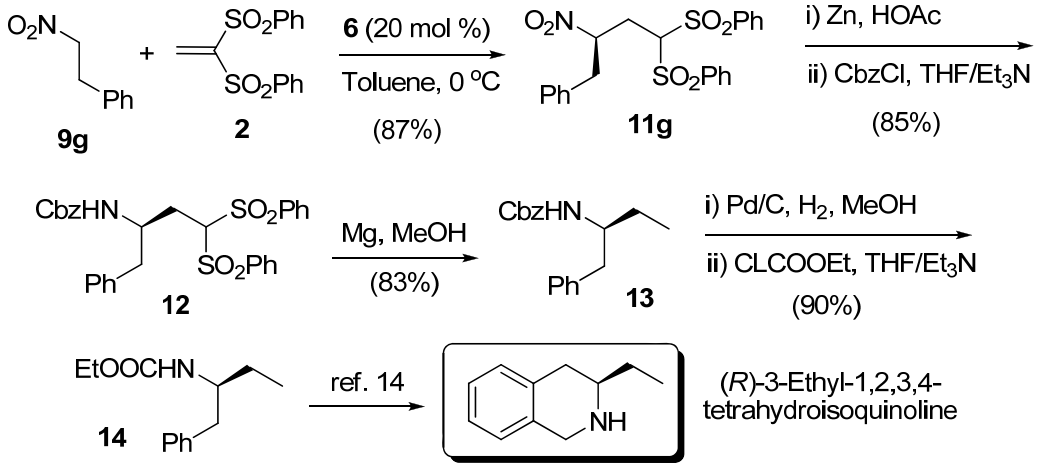
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89-0.94 (t, *J* = 7.4 Hz, 3H), 1.26-1.37 (m, 1H), 1.50-1.59 (m, 1H), 2.75-2.77 (d, *J* = 6.2 Hz, 2H), 3.80 (s, 1H), 4.48-4.51 (m, 1H), 5.05 (s, 2H), 7.14-7.32 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.27, 26.92, 40.74, 53.56, 66.42, 126.28, 127.90, 127.95, 128.28, 128.42, 129.39, 136.64, 137.95, 141.15; $[\alpha]_D$ = - 3.6 (c = 0.6, $CHCl_3$).

(*S*)-*N*-(1-Phenylbutan-2-yl)acetamide A

To a solution of carbamate **13** (15 mg, 0.053 mmol) in methanol (2 mL) was added 10% activated Pd/C (5 mg). The suspension was allowed to stir under a balloon of hydrogen gas. After 2 hours, the reaction mixture was filtered through Celite, and the filtrate was concentrated *in vacuo*. To the residue in THF (2 mL) at 0 ^{o}C was added triethylamine (42 μL, 0.3 mmol) and acetyl chloride (16 mg, 0.2 mmol). After stirring at room temperature for 30 minutes, the reaction mixture was concentrated and taken up in ethyl acetate (10 mL). The organic extracts were washed with 1N HCl (3 X 5 mL), 1N NaOH (3 X 5 mL) and brine, and dried over Na_2SO_4. After filtration, the filtrate was concentrated to afford the desired product as a colorless oil (9.2 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91-0.94 (t, *J* = 7.6 Hz, 3H), 1.31-1.37 (m, 1H), 1.53-1.58 (m, 1H), 1.92 (s, 3H), 2.77-2.79 (d, *J* = 6.3 Hz, 2H), 4.09-4.15 (m, 1H), 5.28-5.29 (m, 1H), 7.16-7.22 (m, 2H), 7.26-7.17 (m, 1H), 7.28-7.30 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.40, 23.44, 26.76, 40.38, 51.52, 126.38, 129.45, 138.05, 169.64; $[\alpha]_D$ = - 1.7 (c = 0.20, CH_3OH, *lit*[2] = - 1.9).

D. Synthesis of 4-Tetrahydroisoquinolin



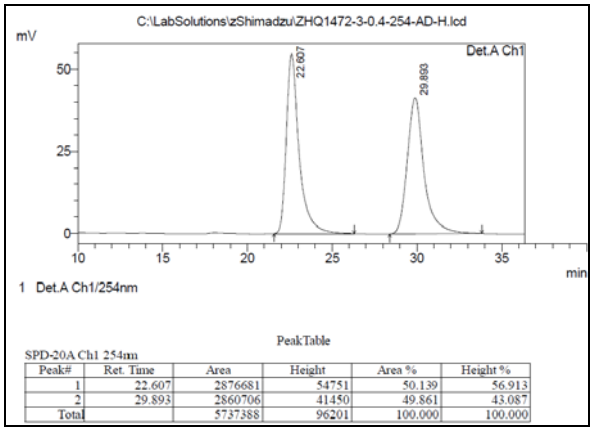
Compound **13** prepared in section C was converted to **14**, the conversion of which to 1,2,3,4-tetrahydroisoquinoline was described in the literature.[3]

(*S*)-Ethyl 1-phenylbutan-2-ylcarbamate 14

To a solution of carbamate **13** (15 mg, 0.053 mmol) in methanol (2 mL) was added 10% activated Pd/C (5 mg). The suspension was allowed to stir under a balloon of hydrogen gas. After 2 hours, the reaction mixture was filtered through Celite, and the filtrate was concentrated *in vacuo*. To the residue in THF (2 mL) at 0 °C was added triethylamine (42 μL, 0.3 mmol) and ethyl chloroformate (22 mg, 0.2 mmol). After stirring at room temperature for 30 minutes, the reaction mixture was concentrated and taken up in ethyl acetate (10 mL). The organic extracts were washed with brine, dried over Na_2SO_4 and filtered. The solvent was removed *in vacuo*, and

the residue was purified by column chromatography (ethyl acetate/hexanes = 1/20 to 1/6) to afford the desired **14** as a colorless oil (10.6 mg, 90%).

$[\alpha]_D$ = - 3.1 (c = 0.32, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.88-0.93 (t, *J* = 7.4 Hz, 3H), 1.16-1.20 (t, *J* = 7.1 Hz, 3H), 1.30-1.33 (m, 1H), 1.50-1.53 (m, 1H), 2.73-2.76 (d, *J* = 6.2 Hz, 3H), 3.76 (s, 1H), 4.01-4.08 (m, 2H), 4.39 (s, 1H), 7.14-7.26 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.25, 14.52, 26.88, 40.83, 53.35, 60.51, 126.24, 128.50, 129.38, 138.07; The ee value was 74%, t_R (major) = 22.61 min, t_R (minor) = 29.89 min (Chiralcel AD-H, λ = 254 nm, 3% *i*PrOH/hexanes, flow rate = 0.4 mL/min).

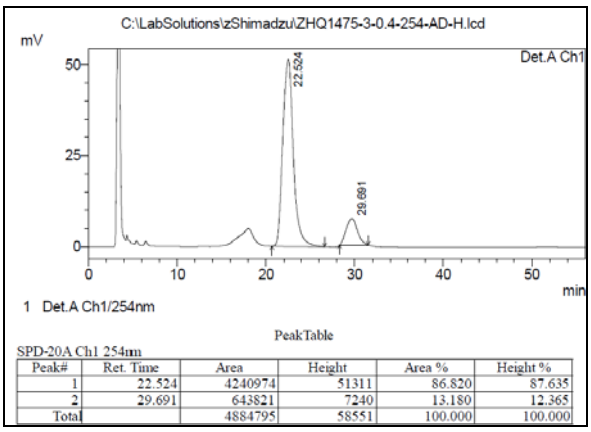


PeakTable

SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.607	2876681	54751	50.139	56.913
2	29.893	2860706	41450	49.861	43.087
Total		5737388	96201	100.000	100.000

(racemic **14**)



PeakTable

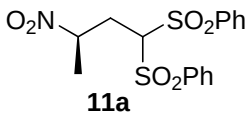
SPD-20A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.524	4240974	51311	86.820	87.635
2	29.691	643821	7240	13.180	12.365
Total		4884795	58551	100.000	100.000

(enatiometric enriched **14**)

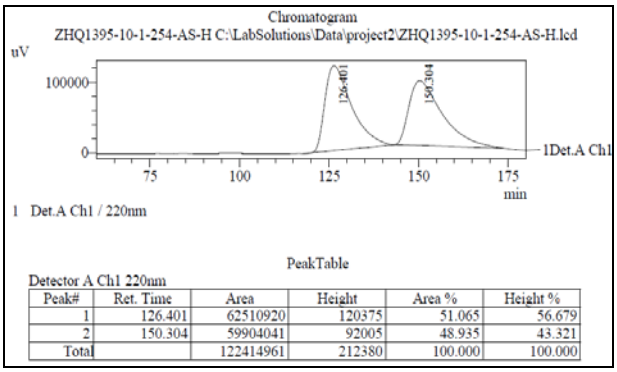
E. Analytical Data and HPLC Chromatogram of Michael Adducts

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)butylsulfonyl)benzene **11a**



11a

A pale yellow oil; The ee value was 84%, t_R (major) = 126.40 min, t_R (minor) = 150.30 min (Chiralcel AS-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.59-1.61 (d, *J* = 7.0 Hz, 3H), 2.55-2.61 (m, 1H), 2.75-2.81 (m, 1H), 4.59-4.61 (m, 1H), 4.71-4.74 (m, 1H), 5.12-5.16 (m, 1H), 7.55-7.62 (m, 4H), 7.71-7.74 (m, 2H), 7.82-7.84 (m, 2H), 7.96-7.97 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.53, 30.86, 79.57, 80.62, 129.34, 129.40, 129.44, 129.57, 135.01, 136.80, 137.83; $[\alpha]_D$ = +9.5 (c = 0.10, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{16}H_{17}NO_6S_2$ $[M+Na]^+$ 406.0414, found 482.0407.

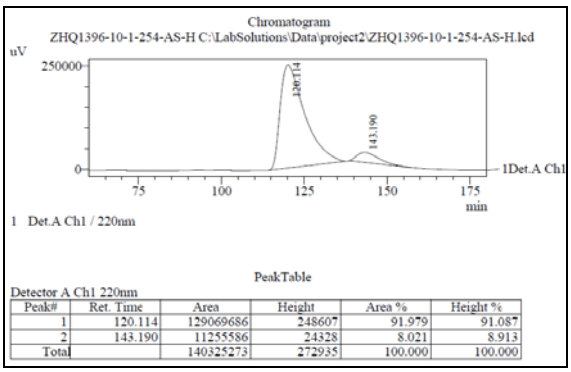


PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	126.401	62510920	120375	51.065	56.679
2	150.304	59904041	92005	48.935	43.321
Total		122414961	212380	100.000	100.000

(racemic **11a**)



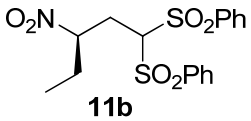
PeakTable

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	120.114	129069686	248607	91.979	91.087
2	143.190	11255586	24328	8.021	8.913
Total		140325273	272935	100.000	100.000

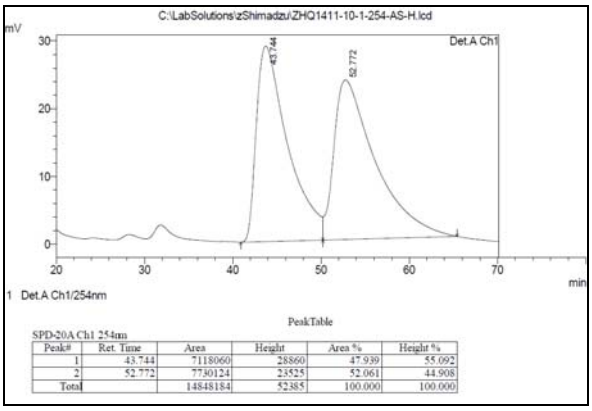
(enatiometric enriched **11a**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)pentylsulfonyl)benzene **11b**

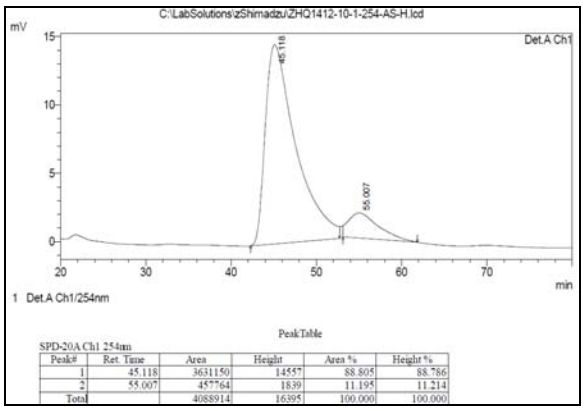


11b

A pale yellow oil; The ee value was 78%, t_R (major) = 43.74 min, t_R (minor) = 52.77 min (Chiralcel AS-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 1.0 mL/min); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98-1.01 (d, *J* = 7.6 Hz, 3H), 1.87-1.89 (m, 1H), 1.94-1.99 (m, 1H), 2.63-2.66 (m, 1H), 2.72-2.75 (m, 1H), 4.44-4.47 (m, 1H), 4.98-5.00 (m, 1H), 7.57-7.62 (m, 4H), 7.71-7.74 (m, 2H), 7.81-7.83 (m, 2H), 7.96-7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.82, 27.26, 29.24, 79.57, 87.12, 128.49, 129.33, 129.38, 129.45, 129.57, 135.00, 136.77, 137.94, 140.39; $[\alpha]_D$ = -6.1 (c = 0.21, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{17}H_{19}NO_6S_2$ $[M+Na]^+$ 420.0570, found 420.0562.

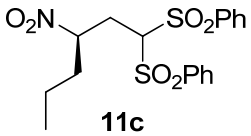


(racemic **11b**)



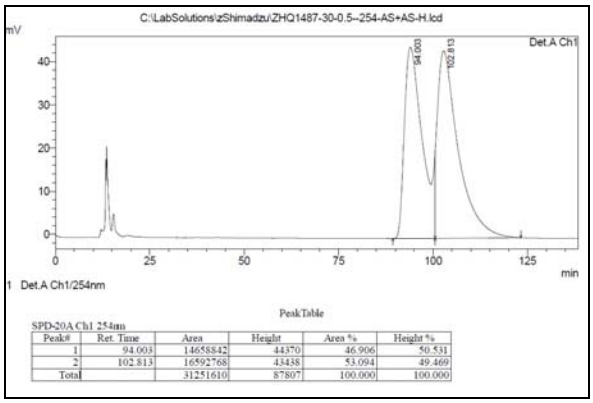
(enatiometric enriched **11b**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)hexylsulfonyl)benzene **11c**

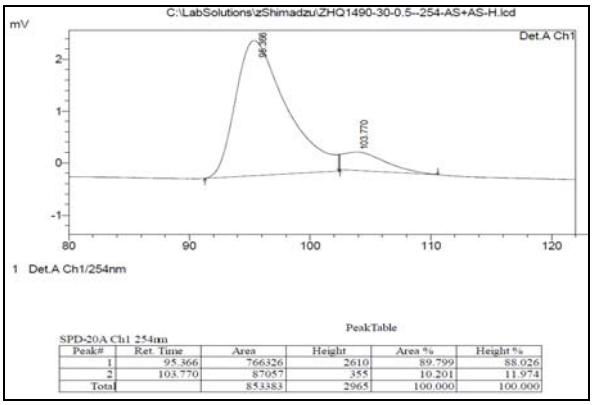


11c

A pale yellow oil; The ee value was 80%, t_R (major) = 94.00 min, t_R (minor) = 102.81 min (Chiralcel (AS+AS)-H, λ = 254 nm, 30% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92-0.97 (t, *J* = 7.4 Hz, 3H), 1.26-1.39 (m, 2H), 1.67-1.77 (m, 1H), 1.90-1.97 (m, 1H), 2.57-2.79 (m, 2H), 4.42-4.46 (m, 1H), 5.00-5.09 (m, 1H), 7.54-7.67 (m, 4H), 7.68-7.74 (m, 2H), 7.76-7.83 (m, 2H), 7.95-7.97 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.24, 18.70, 29.49, 35.75, 79.40, 85.64, 129.26, 129.29, 129.38, 129.45, 134.93, 136.62, 137.87; $[\alpha]_D$ = +2.5 (c = 1.30, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{18}H_{21}NO_6S_2$ $[M+Na]^+$ 434.0703, found 434.0711.

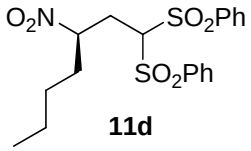


(racemic **11c**)



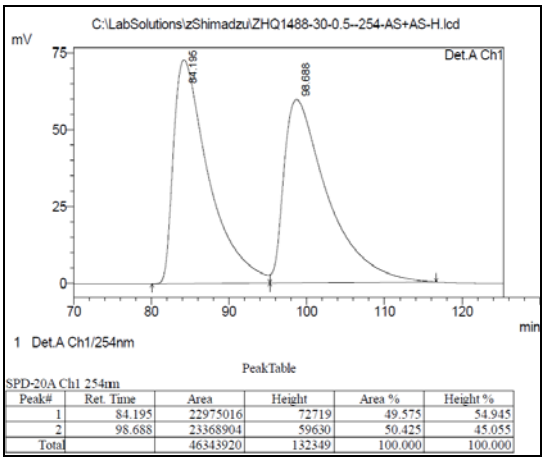
(enatiometric enriched **11c**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)heptylsulfonyl)benzene **11d**



11d

A white solid; The ee value was 83%, t_R (major) = 84.20 min, t_R (minor) = 98.69 min (Chiralcel (AS+AS)-H, λ = 254 nm, 30% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87-0.92 (t, *J* = 6.7 Hz, 3H), 1.26-1.35 (m, 4H), 1.70-1.74 (m, 1H), 1.82-1.98 (m, 1H), 2.57-2.79 (m, 2H), 4.42-4.46 (m, 1H), 4.99-5.08 (m, 1H), 7.54-7.69 (m, 4H), 7.68-7.74 (m, 2H), 7.80-7.83 (m, 2H), 7.95-7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.58, 21.89, 27.34, 29.49, 33.52, 79.41, 85.87, 129.25, 129.29, 129.37, 129.44, 134.92, 136.63, 137.87; $[\alpha]_D$ = +2.2 (c = 0.30, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{19}H_{23}NO_6S_2$ $[M+Na]^+$ 434.0703, found 434.0711.



PeakTable

SPD-20A Ch1 254nm

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1	84.195	22975016	72719	49.575	54.945
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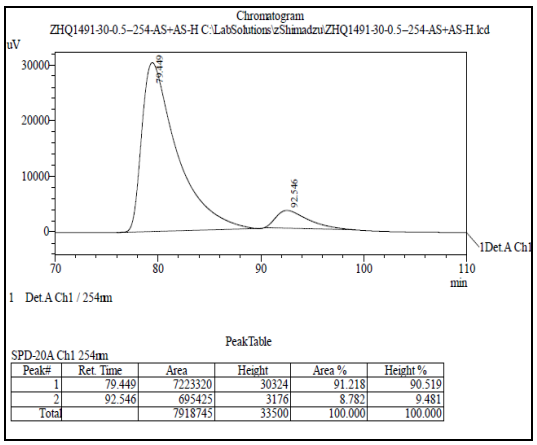
Total		46343920	132349	100.000	100.000

(racemic **11d**)



PeakTable

SPD-20A Ch1 254nm

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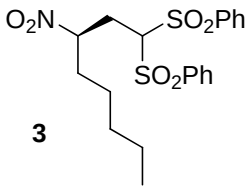
2	92.546	695425	3176	8.782	9.481
Total		7918745	33500	100.000	100.000

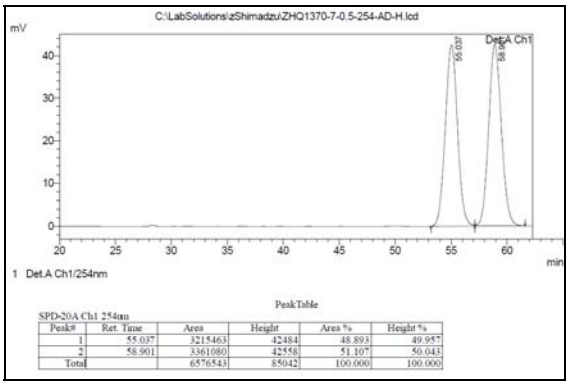
(enatiometric enriched **11d**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)octylsulfonyl)benzene **3**

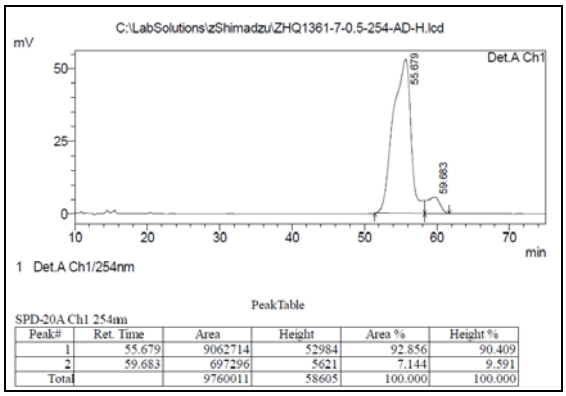


3

A white solid; The ee value was 87%, t_R (major) = 55.04 min, t_R (minor) = 58.90 min (Chiralcel AD-H, λ = 254 nm, 7% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86-0.89 (t, *J* = 6.6 Hz, 3H), 1.26-1.29 (m, 6H), 1.74-1.78 (m, 1H), 1.90-1.97 (m, 1H), 2.62-2.80 (m, 2H), 4.43-4.47 (m, 1H), 5.01-5.04 (m, 1H), 7.55-7.60 (m, 4H), 7.68-7.73 (m, 2H), 7.80-7.83 (m, 2H), 7.96-7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.74, 22.13, 24.94, 29.50, 30.85, 33.78, 79.45, 85.88, 129.24, 129.29, 129.36, 129.44, 134.90, 136.68, 137.89; $[\alpha]_D$ = +7.2 (c = 0.30, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{20}H_{25}NO_6S_2$ $[M+Na]^+$ 462.1040, found 462.1035.

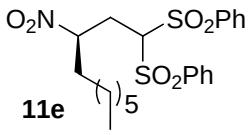


(racemic **3**)



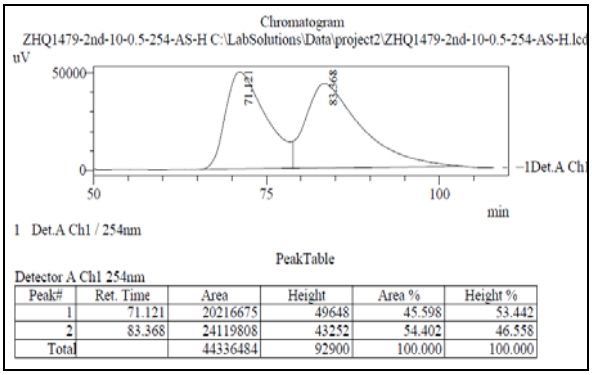
(enatiometric enriched **3**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)hexylsulfonyl)benzene **11e**

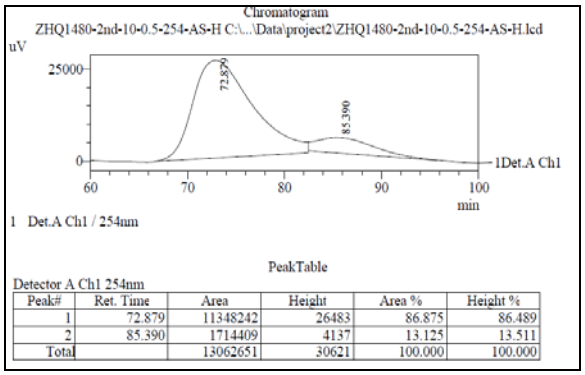


11e

A white solid; The ee value was 74%, t_R (major) = 71.12 min, t_R (minor) = 83.37 min (Chiralcel AS-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.86-0.89 (t, *J* = 7.6 Hz, 3H), 1.25-1.29 (m, 10H), 1.73-1.77 (m, 1H), 1.90-1.97 (m, 1H), 2.62-2.80 (m, 2H), 4.42-4.45 (m, 1H), 5.02-5.05 (m, 1H), 7.55-7.62 (m, 4H), 7.70-7.75 (m, 2H), 7.81-7.82 (m, 2H), 7.96-7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.96, 22.47, 25.28, 28.70, 28.75, 29.49, 31.49, 33.83, 79.41, 85.89, 129.25, 129.29, 129.36, 129.45, 134.91, 136.63, 137.87; $[\alpha]_D$ = +3.2 (c = 1.20, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{22}H_{29}NO_6S_2$ $[M+Na]^+$ 490.1319, found 490.1321.

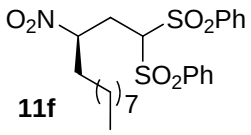


(racemic **11e**)



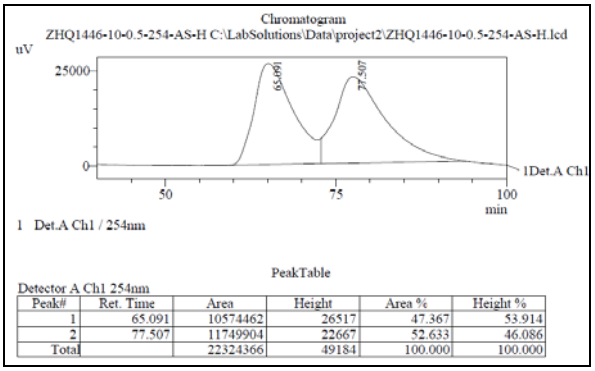
(enatiometric enriched **11e**)

(*R*)-1-(3-Nitro-1-(phenylsulfonyl)hexylsulfonyl)benzene **11f**



11f

A white solid; The ee value was 80%, t_R (major) = 65.09 min, t_R (minor) = 77.51 min (Chiralcel AS-H, λ = 254 nm, 10% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86-0.90 (t, *J* = 7.1 Hz, 3H), 1.25-1.27 (m, 15H), 1.74-1.76 (m, 1H), 1.90-1.95 (m, 1H), 2.62-2.80 (m, 2H), 4.41-4.45 (m, 1H), 5.01-5.02 (m, 1H), 7.55-7.60 (m, 4H), 7.68-7.73 (m, 2H), 7.80-7.83 (m, 2H), 7.96-7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.00, 22.56, 25.28, 28.74, 29.08, 29.11, 29.25, 29.50, 31.72, 33.83, 79.45, 85.89, 129.23, 129.29, 129.36, 129.45, 134.90, 136.67, 137.90; $[\alpha]_D$ = +3.1 (c = 0.32, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{24}H_{33}NO_6S_2$ $[M+Na]^+$ 518.1642, found 518.1645.

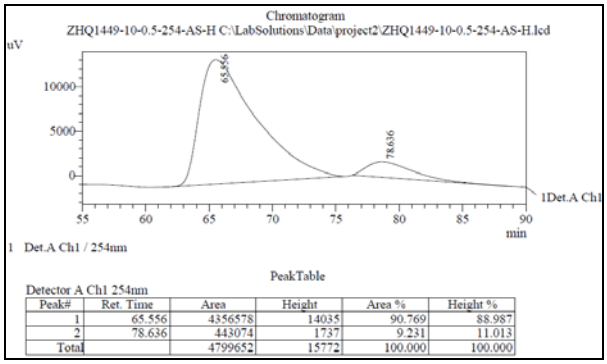


PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	65.091	10574462	26517	47.367	53.914
2	77.507	11749904	22667	52.633	46.086
Total		22324366	49184	100.000	100.000

(racemic **11f**)



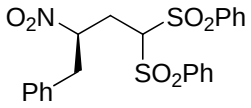
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	65.556	4356578	14035	90.769	88.987
2	78.636	443074	1737	9.231	11.013
Total		4799652	15772	100.000	100.000

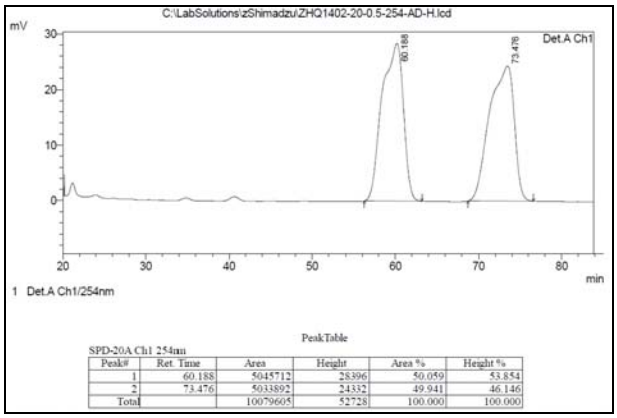
(enatiometric enriched **11f**)

(*R*)-1-(2-Nitro-4,4-bis(phenylsulfonyl)butyl)benzene **11g**

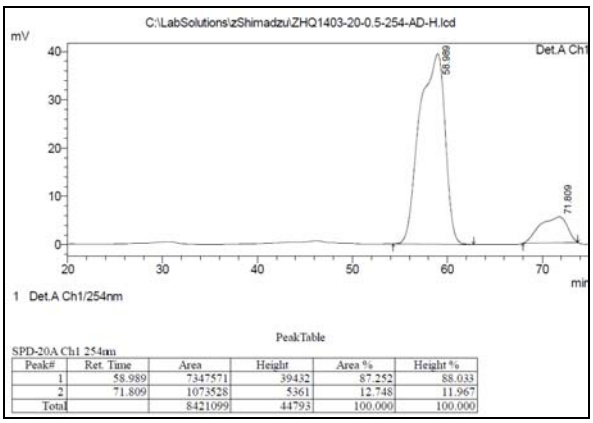


11g

A colorless oil; The ee value was 75%, t_R (major) = 60.19 min, t_R (minor) = 73.48 min (Chiralcel AD-H, λ = 254 nm, 20% *i*PrOH/hexanes, flow rate = 0.5 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55-2.59 (m, 1H), 2.74-2.78 (m, 1H), 3.03-3.10 (m, 1H), 3.34-3.39 (m, 1H), 4.47-4.50 (m, 1H), 5.29-5.37 (m, 1H), 7.19 (m, 2H), 7.34-7.37 (m, 3H), 7.50-7.69 (m, 4H), 7.71-7.74 (m, 4H), 7.80-7.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.81, 39.97, 79.40, 86.21, 127.84, 129.11, 129.24, 129.40, 129.78, 134.04, 134.93, 136.94; $[\alpha]_D$ = +12.8 (c = 0.91, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{22}H_{21}NO_6S_2$ $[M+Na]^+$ 482.0703, found 482.0705.

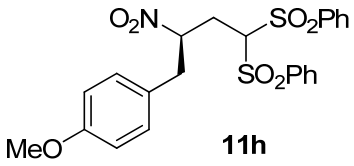


(racemic **11g**)



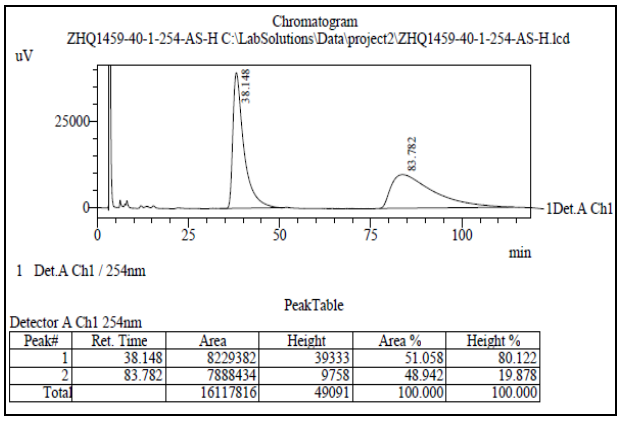
(enatiometric enriched **11g**)

(*R*)-1-Methoxy-4-(2-nitro-4,4-bis(phenylsulfonyl)butyl)benzene 11h



11h

A colorless oil; The ee value was 72%, t_R (minor) = 37.69 min, t_R (major) = 80.32 min (Chiralcel AS-H, λ = 254 nm, 40% *i*PrOH/hexanes, flow rate = 1.0 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57-2.60 (m, 1H), 2.76-2.79 (m, 1H), 3.02-3.06 (m, 1H), 3.29-3.34 (m, 1H), 3.85 (s, 3H), 4.49-4.50 (m, 1H), 5.29-5.32 (m, 1H), 6.90-6.91 (d, *J* = 8.9 Hz, 2H), 7.10-7.12 (d, *J* = 8.9 Hz, 2H), 7.54-7.61 (m, 4H), 7.72-7.78 (m, 4H), 7.83-7.84 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.72, 39.28, 55.34, 79.50, 86.40, 114.52, 125.97,128.49, 129.17, 129.30, 129.42, 129.85, 129.87,130.03, 134.94, 137.00; $[\alpha]_D$ = -3.4 (c = 0.31, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{23}H_{23}NO_6S_2$ $[M+Na]^+$ 512.0808, found 512.0811.



Peak#	Ret. Time	Area	Height	Area %	Height %
1	38.148	8229382	39333	51.058	80.122
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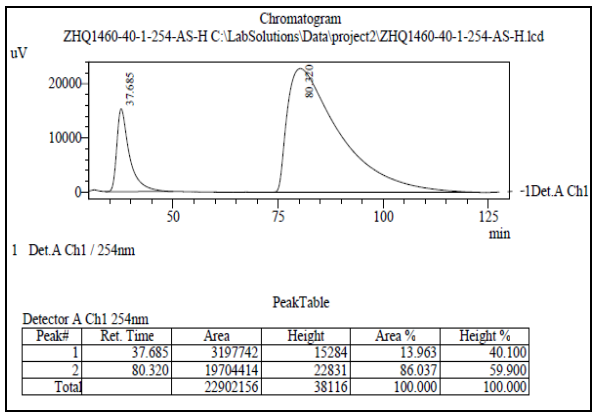
Total		16117816	49091	100.000	100.000

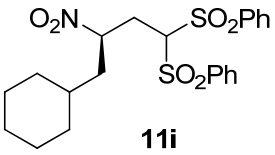
(racemic **11h**)



Peak#	Ret. Time	Area	Height	Area %	Height %
1	37.685	3197742	15284	13.963	40.100
2	80.320	19704414	22831	86.037	59.900
Total		22902156	38116	100.000	100.000

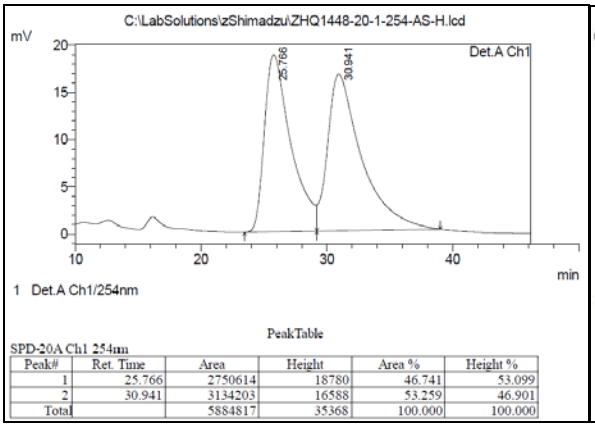
(enatiometric enriched **11h**)

(*R*)-1-(4-Cyclohexyl-3-nitro-1-(phenylsulfonyl)butylsulfonyl)benzene **11i**

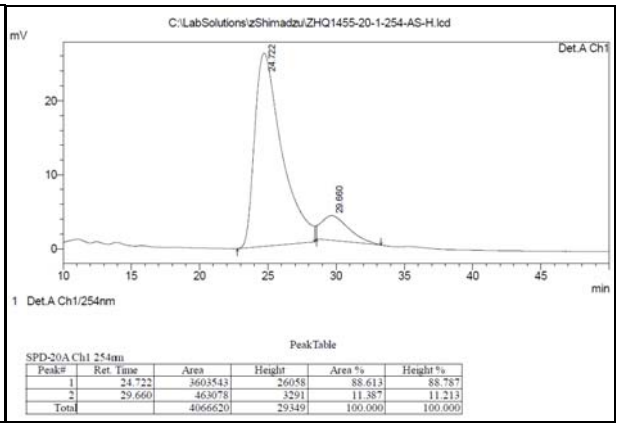


11i

A colorless oil; The ee value was 78%, t_R (major) = 25.77 min, t_R (minor) = 30.94 min (Chiralcel AS-H, λ = 254 nm, 20% *i*PrOH/hexanes, flow rate = 1.0 mL/min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90-0.92 (m, 2H), 1.17-1.20 (m, 4H), 1.65-1.70 (m, 6H), 2.64-2.71 (m, 2H), 4.40-4.43 (m, 1H), 5.12-5.13 (m, 1H), 7.57-7.81 (m, 8H), 7.95-7.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.71, 26.05, 30.00, 32.39, 32.97, 34.28, 41.40, 79.36, 83.88, 129.24, 129.31, 129.36, 129.43, 134.88, 136.65, 137.93; $[\alpha]_D$ = +9.5 (c = 0.40, $CHCl_3$); HRMS (ESI) m/z calcd for $C_{22}H_{27}NO_6S_2$ $[M+Na]^+$ 418.1172, found 418.1179.



(racemic **11i**)



(enatiometric enriched **11i**)

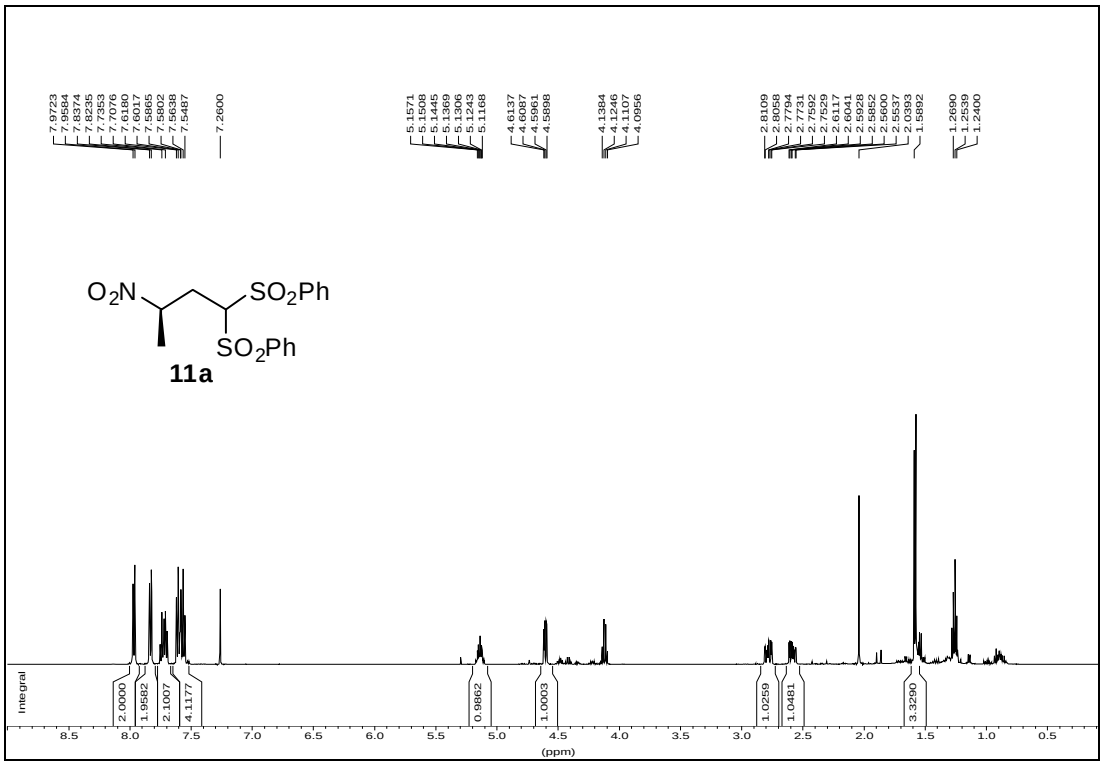
References:

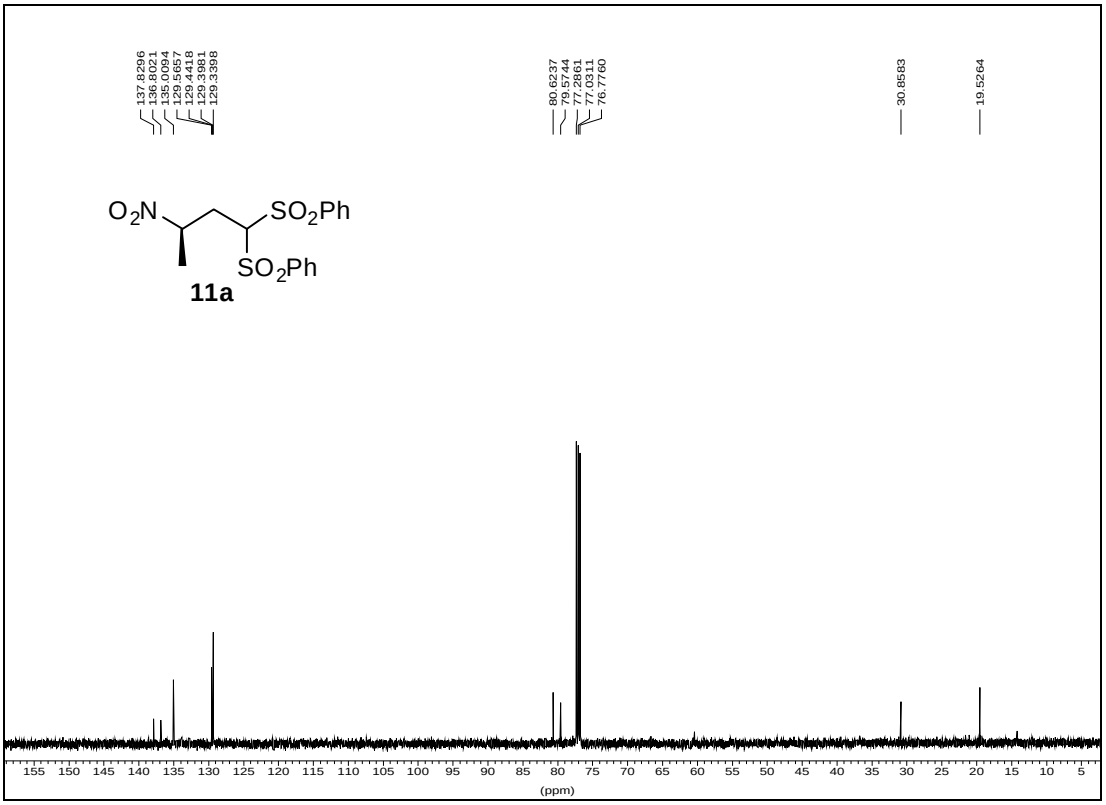
(1) Kundig, E. P.; Cunningham, A. F., Jr. *Tetrahedron* **1988**, *44*, 6855.

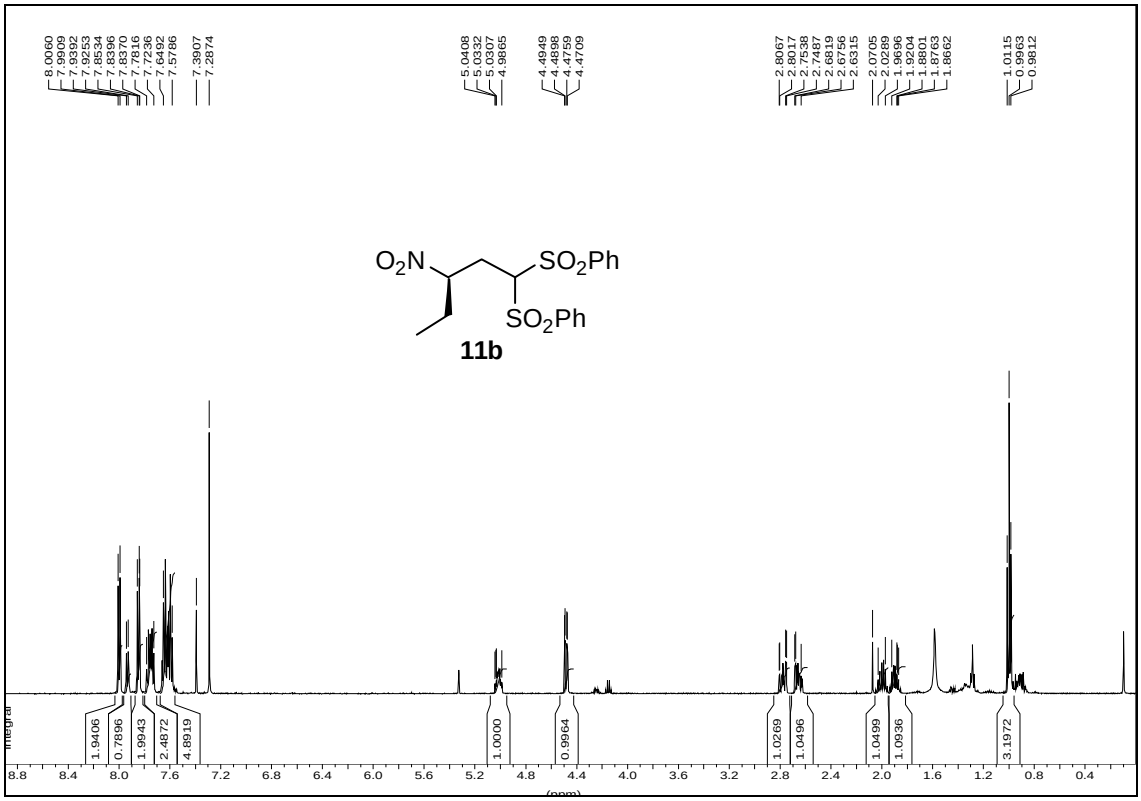
(2) Campbell, M. J.; Johnson, J. S. *Org. Lett.* **2007**, *9*, 1521.

(3) Grunewald, G. L.; Sall, D. J.; Monn, J. A. *J. Med. Chem.* **1988**, *31*, 824.

G. NMR Spectra of Products



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7.6492
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5.0077
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4.4949
4.4898
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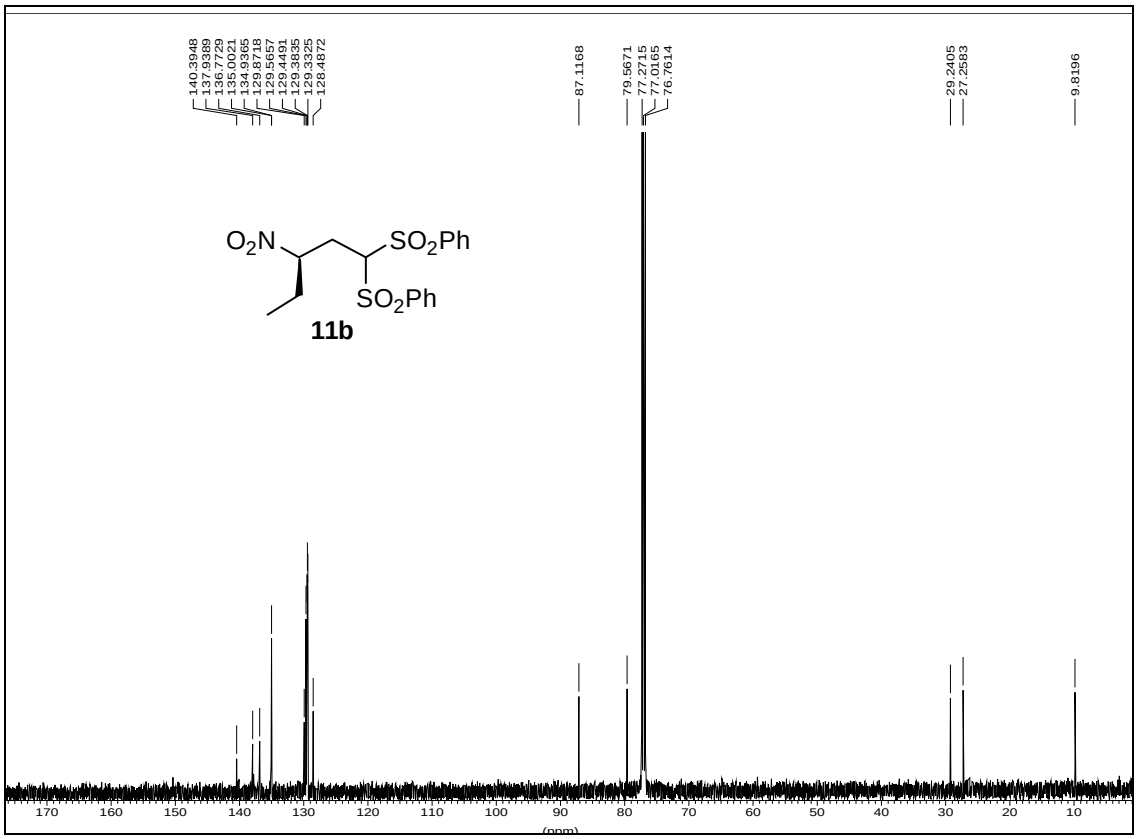
2.7487
2.6819
2.6756
2.6315
2.0705
2.0289
1.9896
1.9704
1.8801
1.8763
1.8662
1.0115
0.9963
0.9812
O2N
SO2Ph
SO2Ph
11b
Integral
1.9406
0.7896
1.9943
2.4872
4.8919
1.0000
0.9964
1.0269
1.0496
1.0499
1.0936
3.1972
8.8 8.4 8.0 7.6 7.2 6.8 6.4 6.0 5.6 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4 2.0 1.6 1.2 0.8 0.4
(ppm)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79.5671
77.2715
77.0165
76.7614
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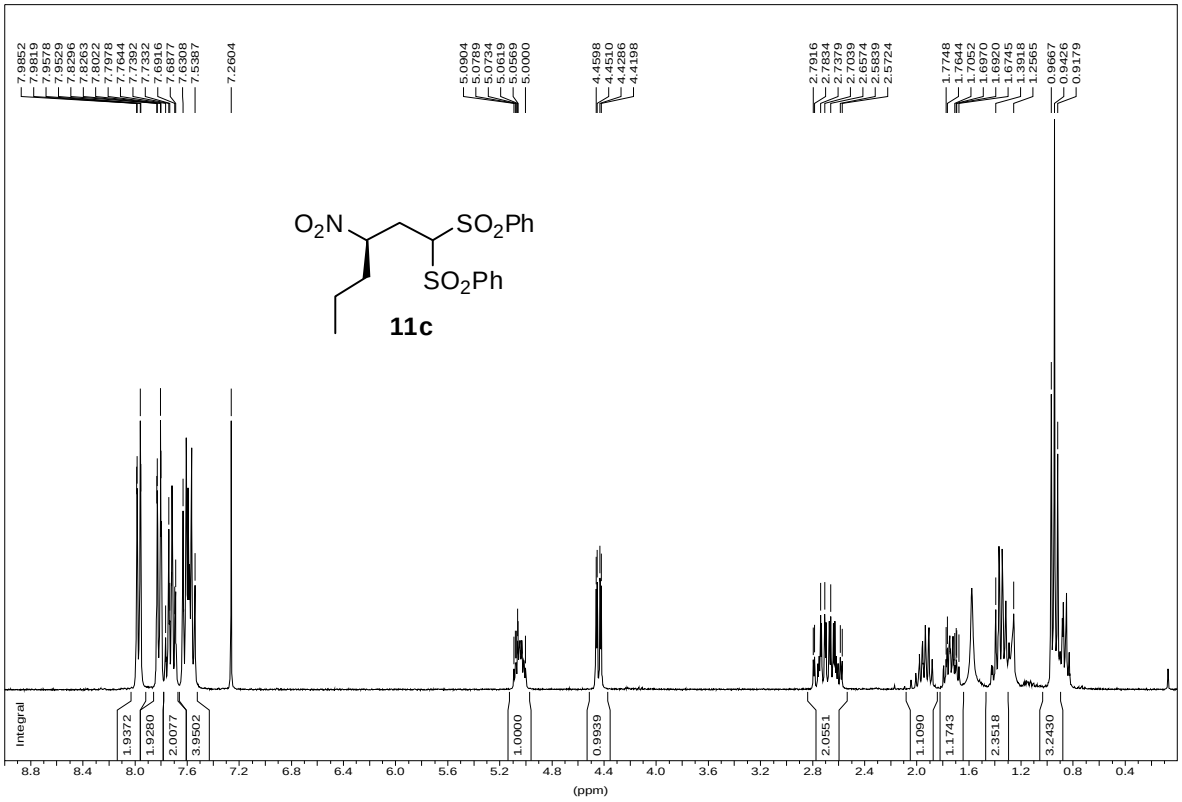
9.8196
O2N
SO2Ph
SO2Ph
11b
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
(ppm)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5.0734
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5.0569
5.0000
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4.4510
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4.4198
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2.7834
2.7379
2.7039
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1.6920
1.6745
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SO2Ph
SO2Ph
11c
Integral
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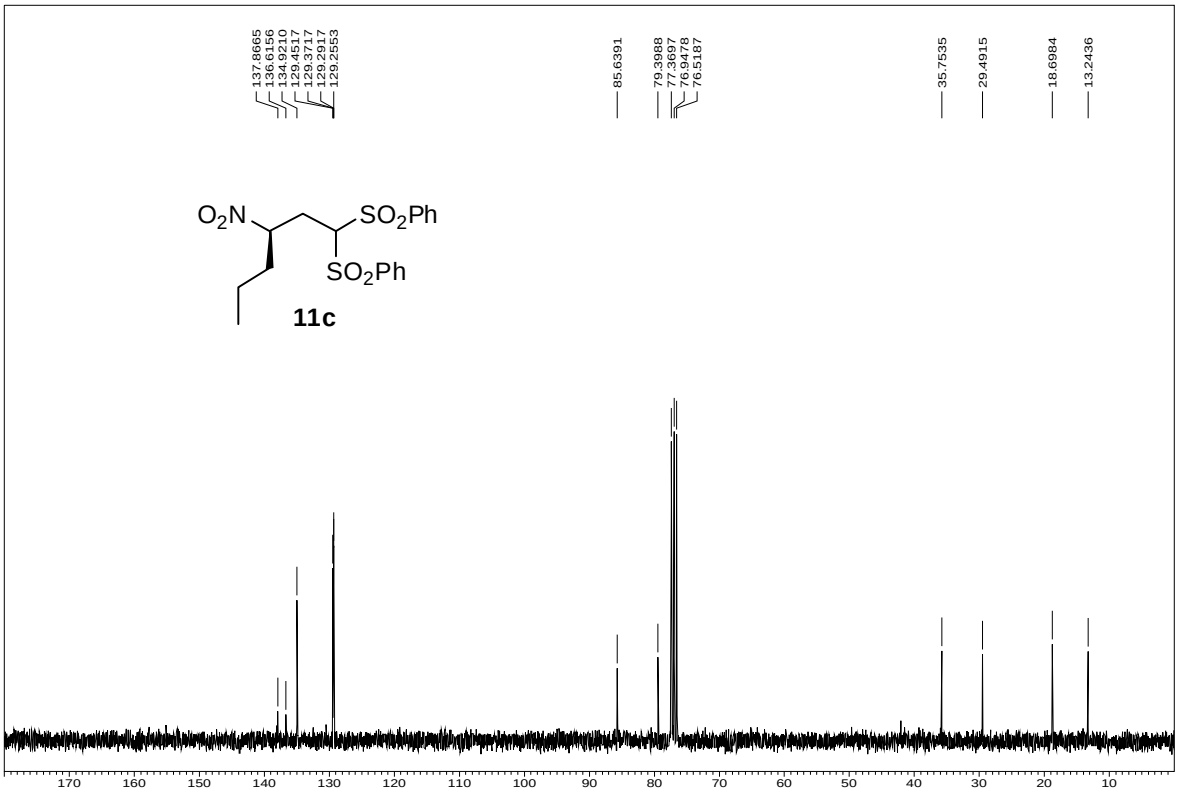
3.2430
(ppm)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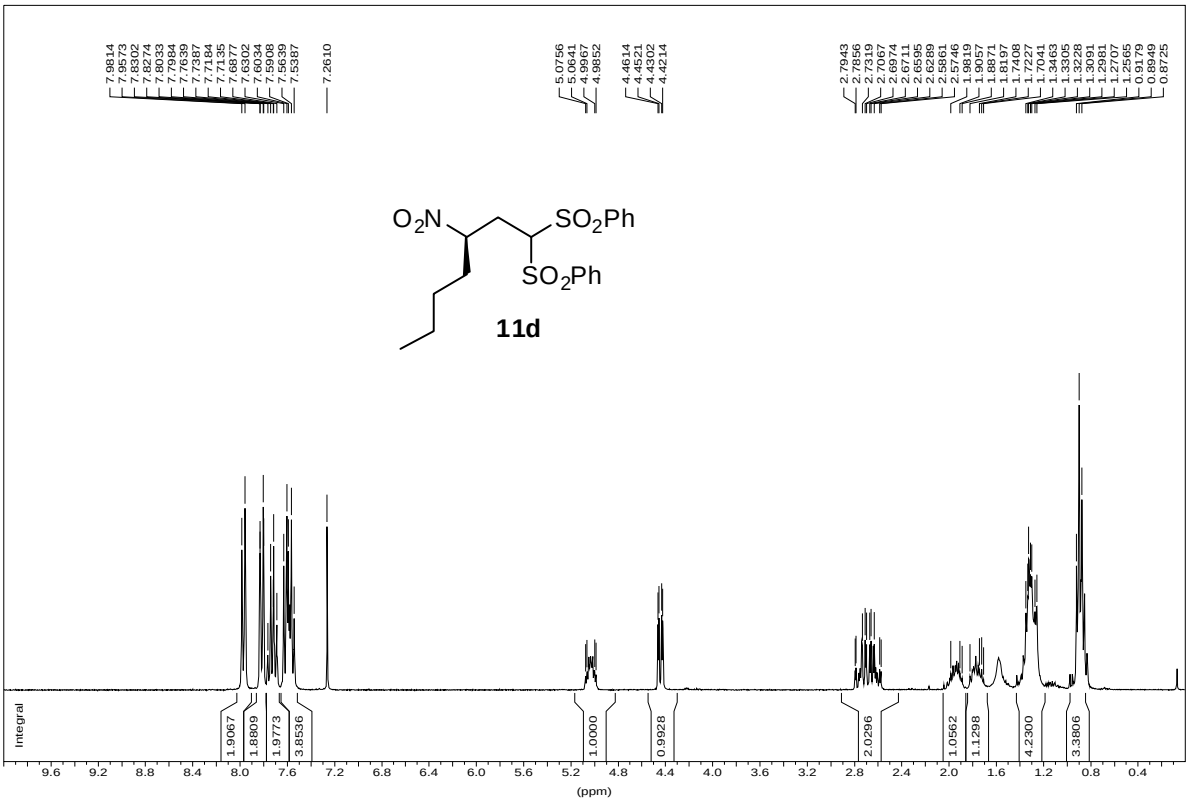
O2N
SO2Ph
SO2Ph
11c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1.7227
1.7041
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1.3091
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O2N
SO2Ph
SO2Ph
11d
Integral
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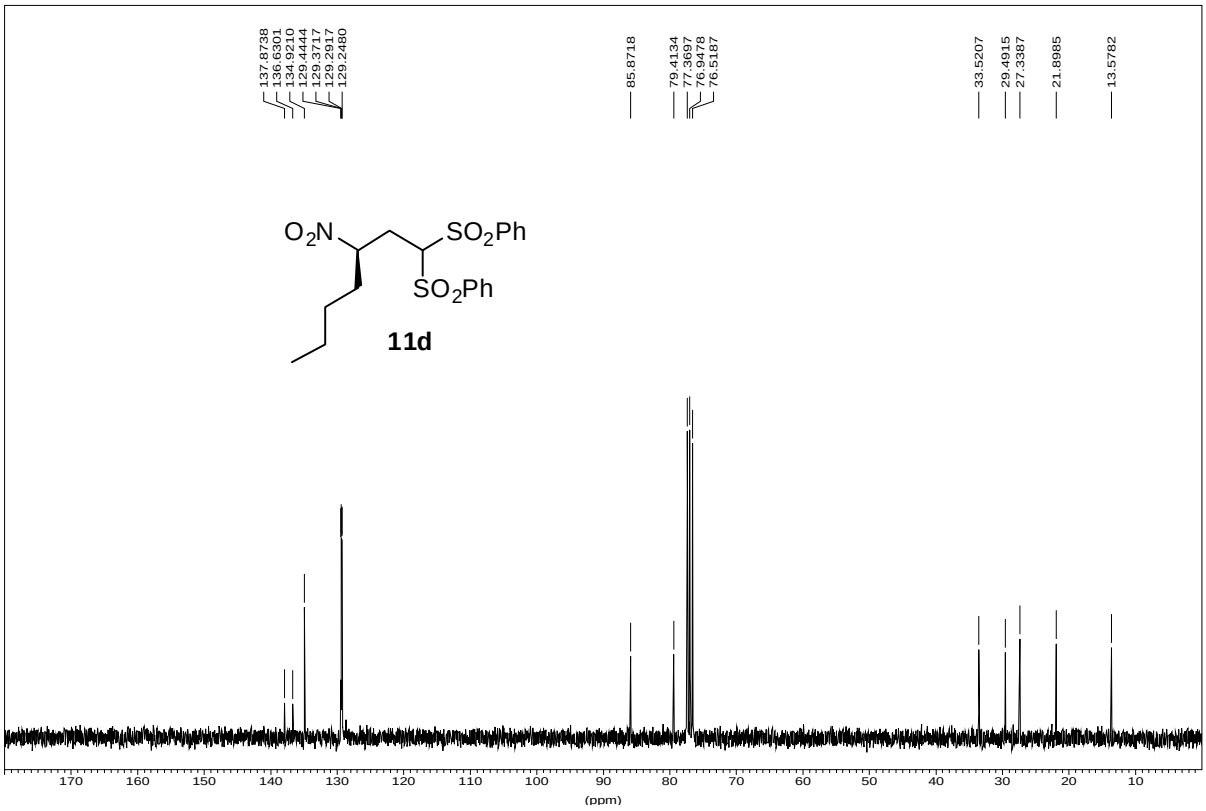
(ppm)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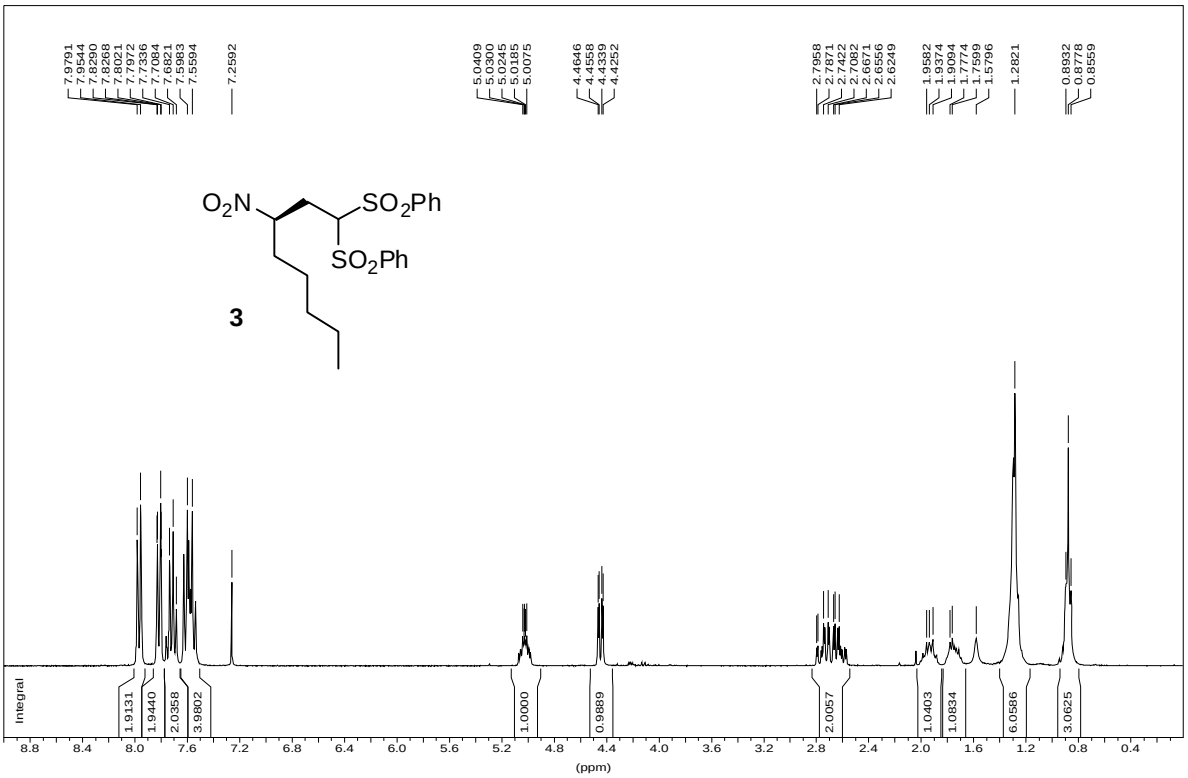
O2N
SO2Ph
SO2Ph
11d
(ppm)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7.5594
7.2592
5.0409
5.0300
5.0245
5.0185
5.0075
4.4646
4.4558
4.4339
4.4252
2.7958
2.7871
2.7422
2.7082
2.6671
2.6556
2.6249
1.9582
1.9374
1.9094
1.7774
1.7599
1.5796
1.2821
0.8932
0.8778
0.8559
O2N
SO2Ph
SO2Ph
3
Integral
1.9131
1.9440
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1.0834
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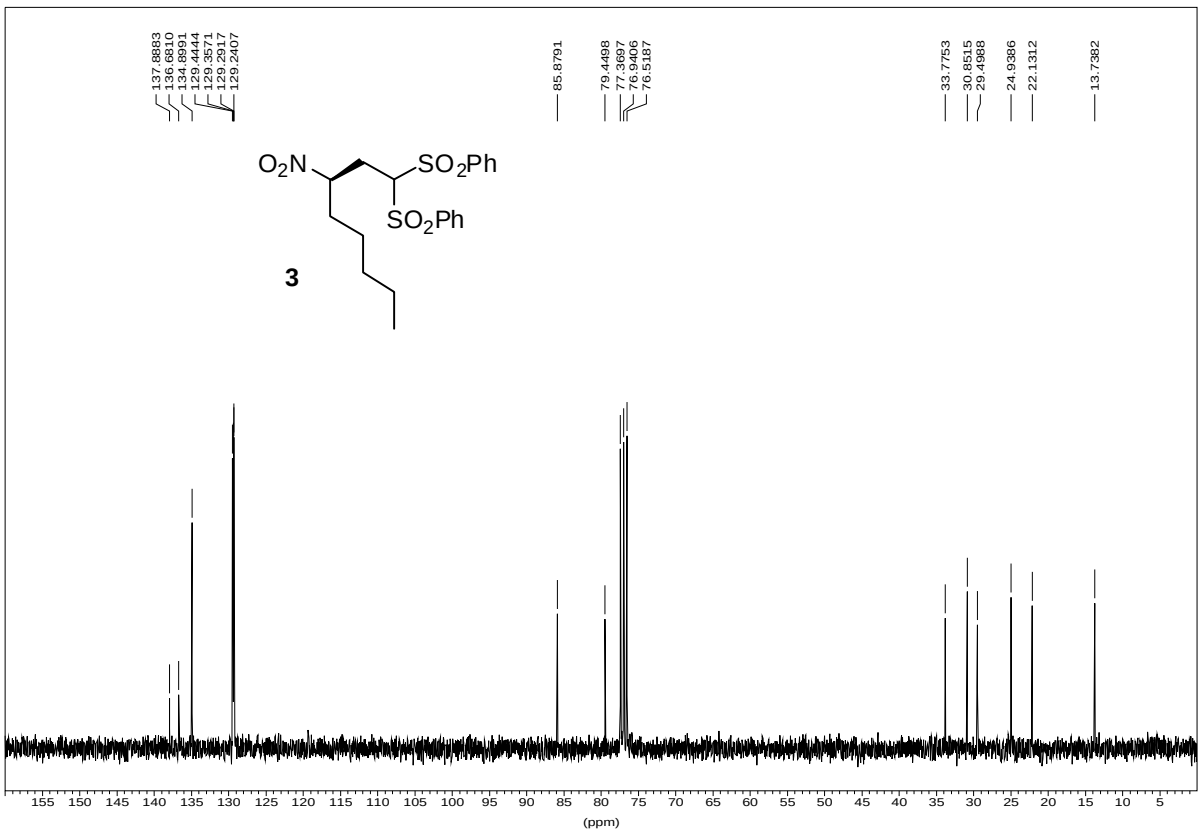
(ppm)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76.5187
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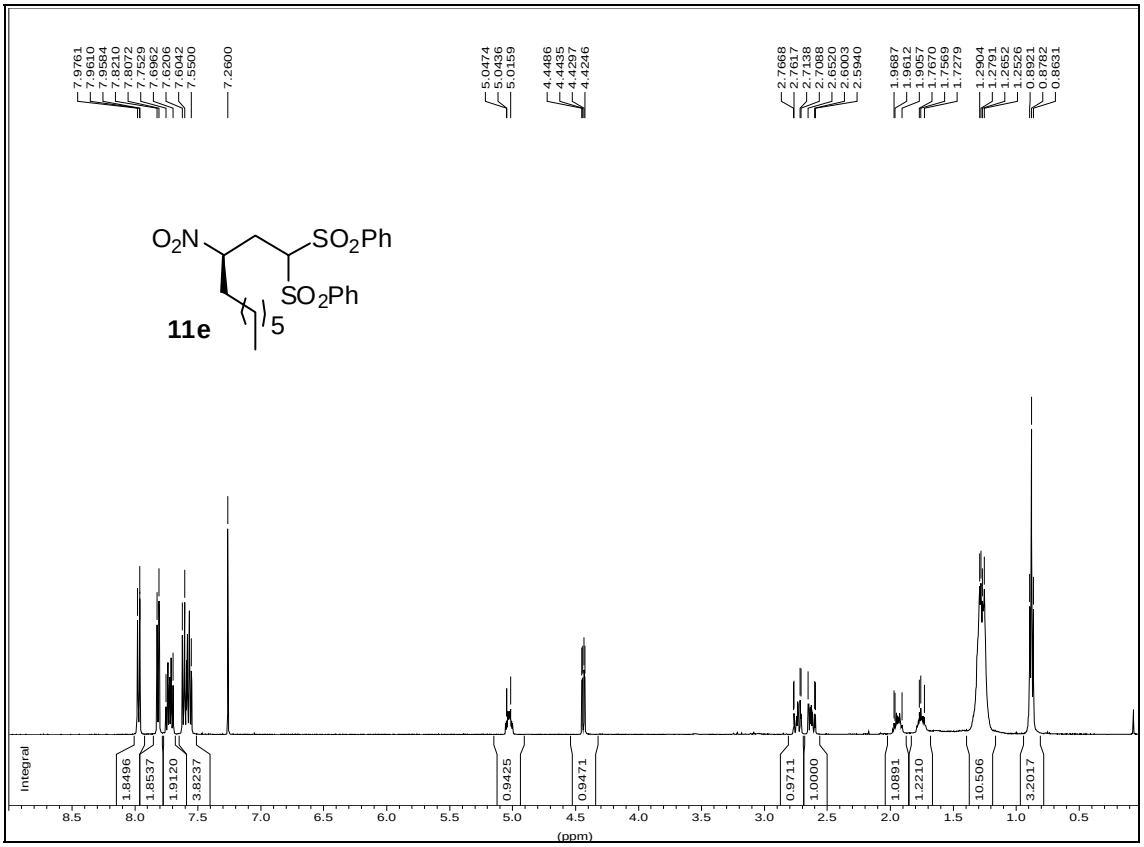
29.4988
24.9386
22.1312
13.7382
O2N
SO2Ph
SO2Ph
3
(ppm)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7.2600
5.0474
5.0436
5.0159
4.4486
4.4435
4.4297
4.4246
2.7668
2.7617
2.7138
2.7088
2.6520
2.6003
2.5940
1.9687
1.9612
1.9057
1.7670
1.7569
1.7279
1.2904
1.2791
1.2652
1.2526
0.8921
0.8782
0.8631
O2N
SO2Ph
SO2Ph
5
11e
Integral
1.8496
1.8537
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0.9471
0.9711
1.0000
1.0891
1.2210
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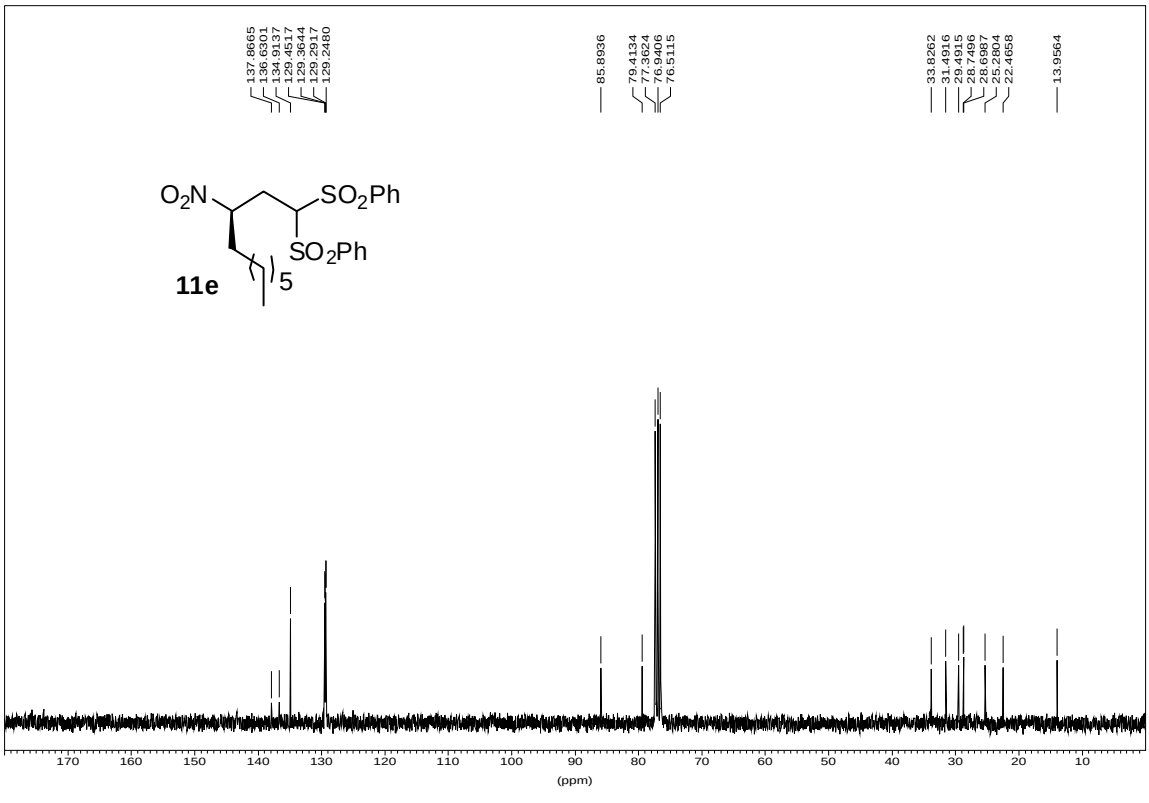
3.2017
(ppm)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76.5115
33.8262
31.4916
29.4915
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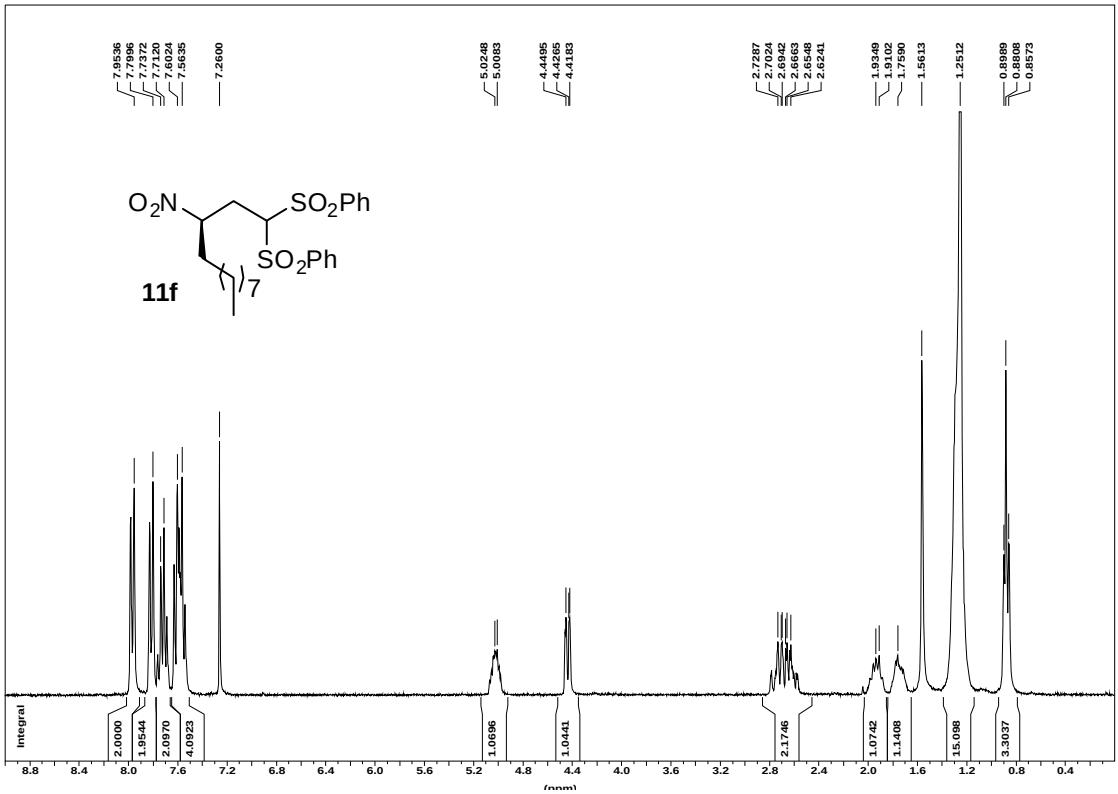
25.2804
22.4658
13.9564
O2N
SO2Ph
SO2Ph
5
11e
(ppm)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4.4183
2.7287
2.7024
2.6942
2.6663
2.6548
2.6241
1.9349
1.9102
1.7950
1.5613
1.2512
0.8989
0.8808
0.8573
O2N
SO2Ph
SO2Ph
7
11f
Integral
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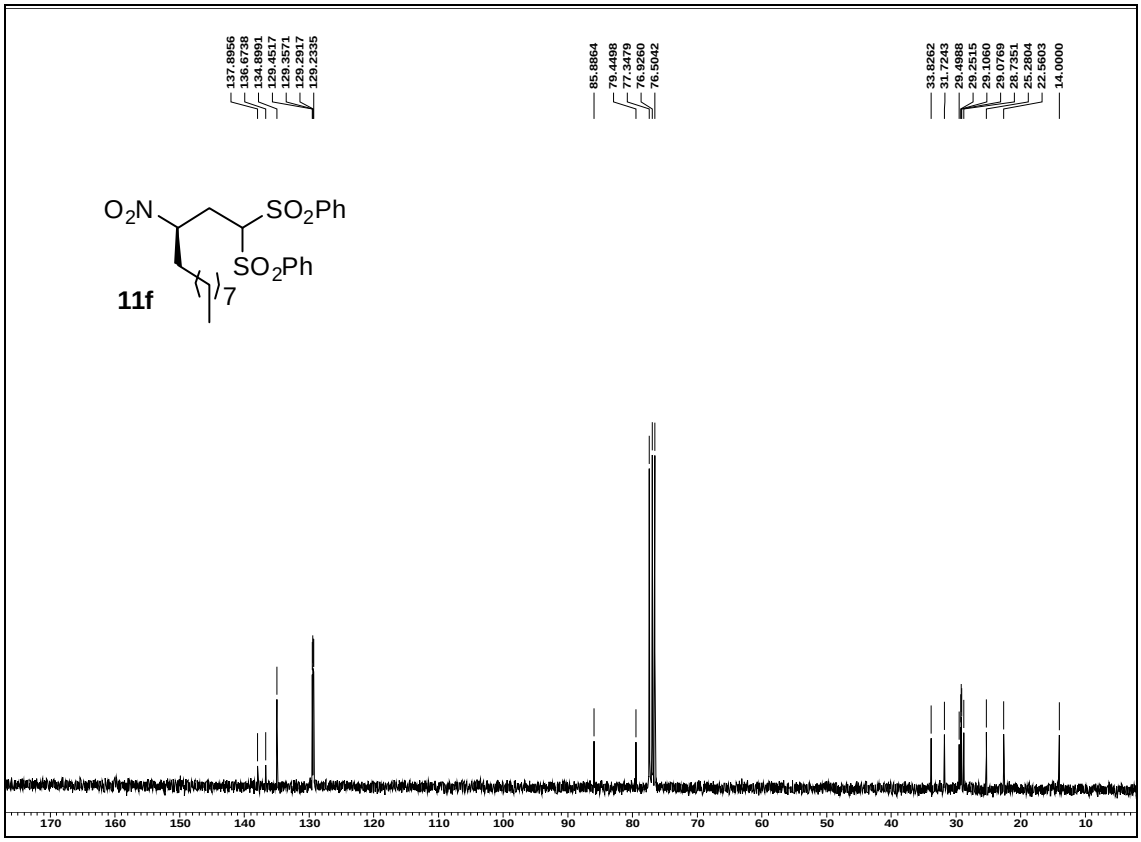
1.9544
2.0970
4.0923
1.0696
1.0441
2.1746
1.0742
1.1408
15.098
3.3037
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
(ppm)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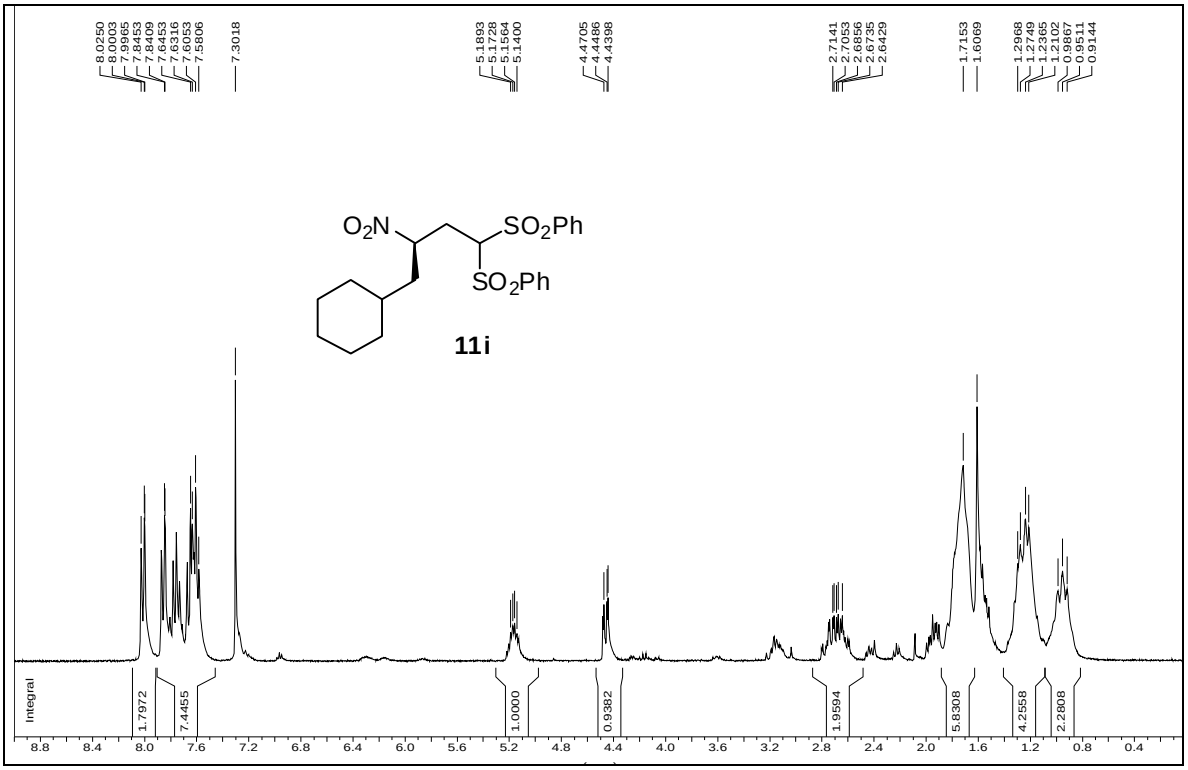
76.9260
76.5042
33.8262
31.7243
29.4988
29.2515
29.1060
29.0769
28.7351
25.2804
22.5603
14.0000
O2N
SO2Ph
SO2Ph
7
11f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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5.1893
5.1728
5.1564
5.1400
4.4705
4.4486
4.4398
2.7141
2.7053
2.6856
2.6735
2.6429
1.7153
1.6069
1.2968
1.2749
1.2365
1.2102
0.9867
0.9511
0.9144
O2N
SO2Ph
SO2Ph
11i
Integral
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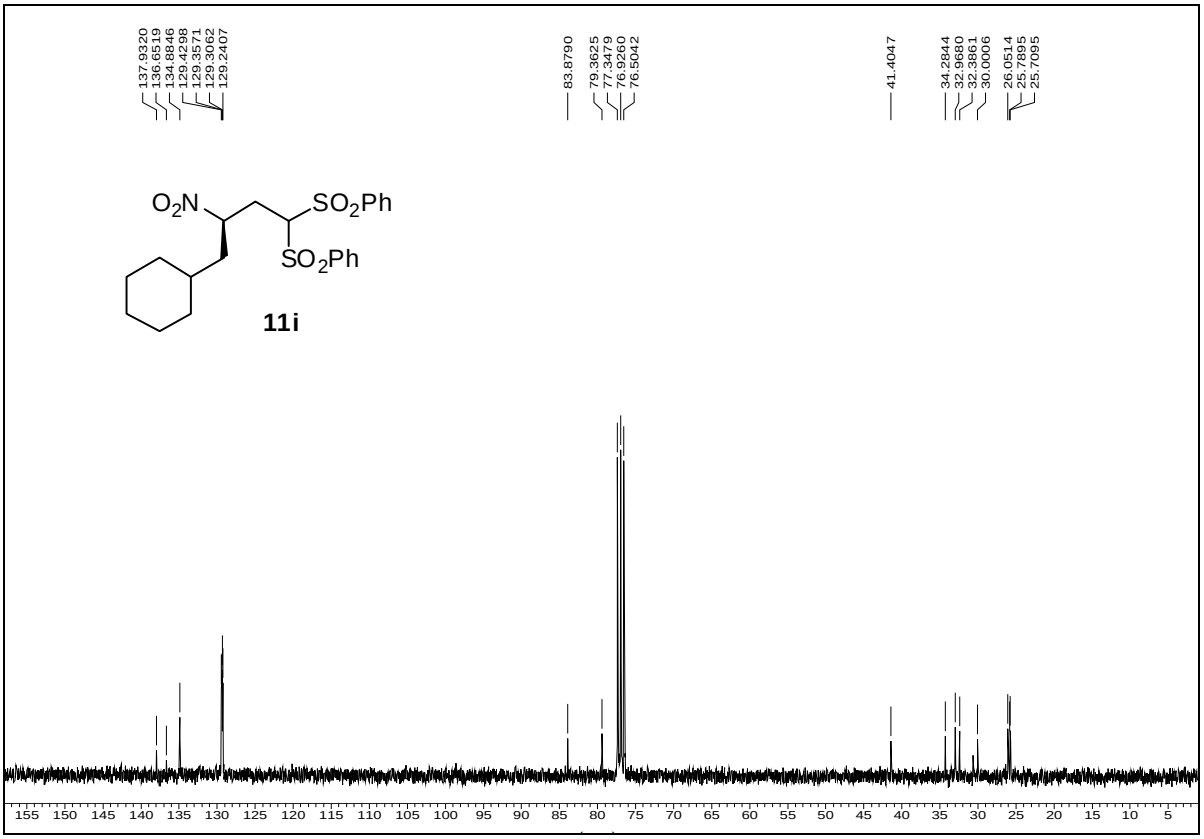
1.0000
0.9382
1.9594
5.8308
4.2558
2.2808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76.9260
76.5042
41.4047
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32.3861
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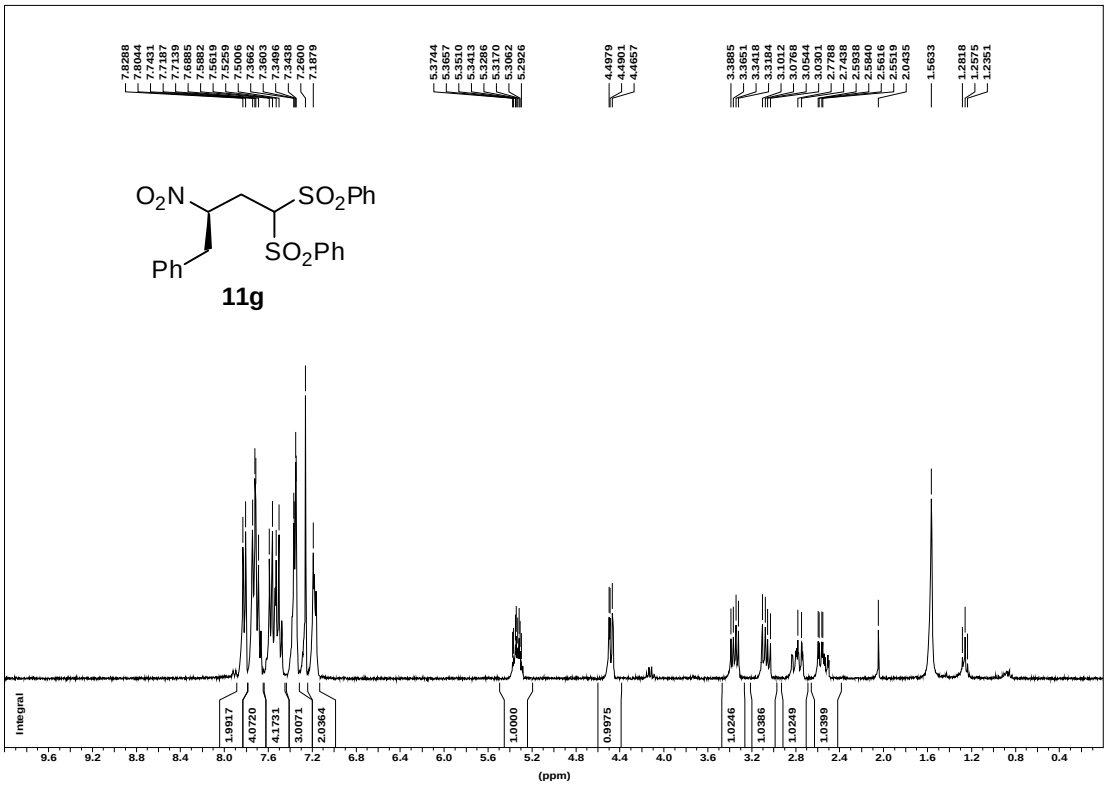
26.0514
25.7895
25.7095
O2N
SO2Ph
SO2Ph
11i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7.3662
7.3603
7.3486
7.3438
7.2600
7.1879
5.3744
5.3657
5.3510
5.3413
5.3286
5.3170
5.3062
5.2926
4.4979
4.4901
4.4657
3.3885
3.3651
3.3418
3.3184
3.1012
3.0768
3.0544
3.0301
2.7788
2.7438
2.5938
2.5840
2.5616
2.5519
2.0435
1.5633
1.2818
1.2575
1.2351
O2N
SO2Ph
SO2Ph
Ph
11g
Integral
1.9917
4.0720
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2.0364
1.0000
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1.0386
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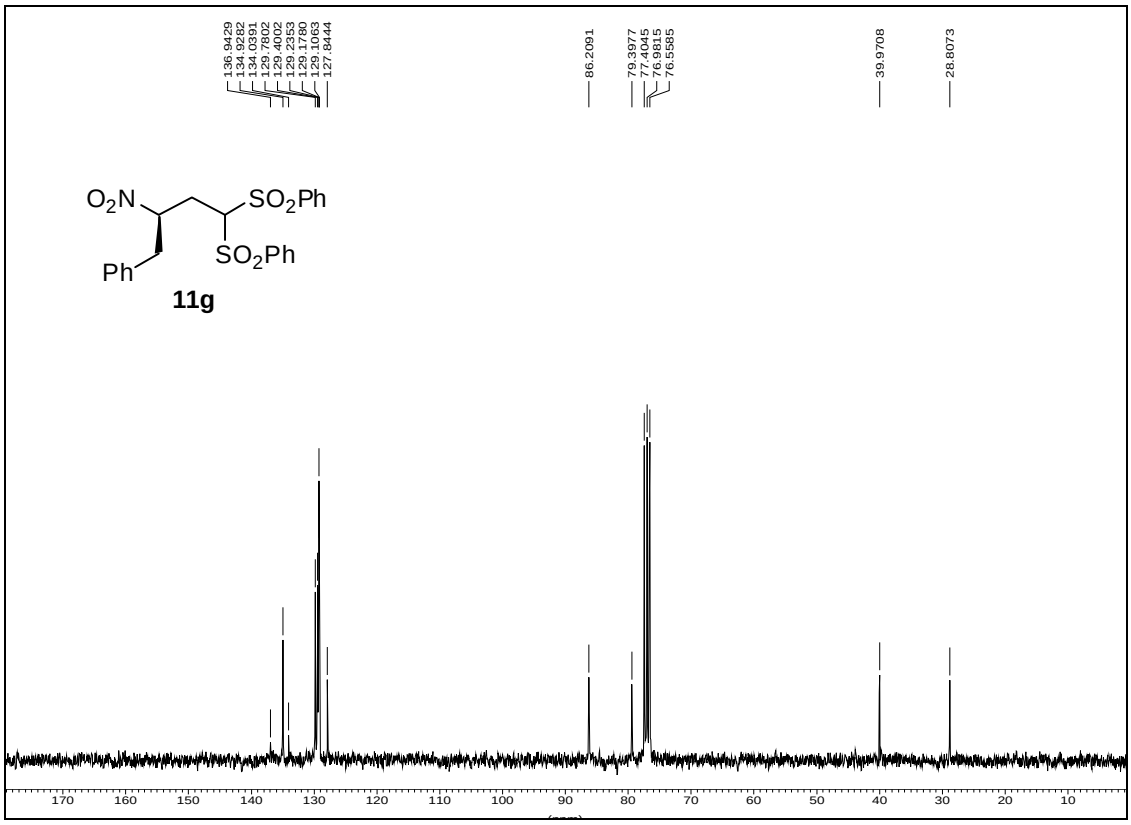
1.0399
(ppm)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86.2091
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39.9708
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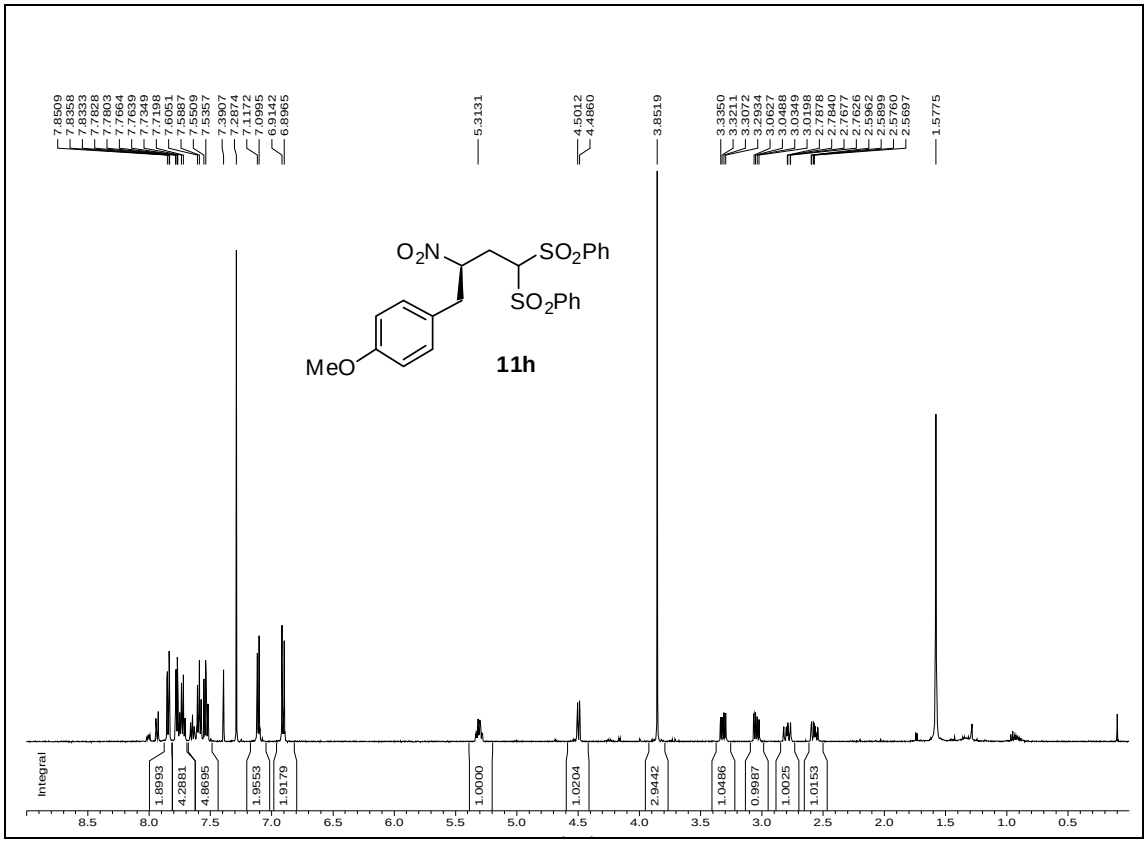
O2N
SO2Ph
SO2Ph
Ph
11g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7.5509
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7.3907
7.2874
7.1172
7.0995
6.9142
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5.3131
4.5012
4.4860
3.8519
3.3350
3.3211
3.3072
3.2934
3.0627
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3.0349
3.0198
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2.7840
2.7677
2.7626
2.5962
2.5899
2.5760
2.5697
1.5775
O2N
SO2Ph
SO2Ph
MeO
11h
Integral
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4.2881
4.8695
1.9553
1.9179
1.0000
1.0204
2.9442
1.0486
0.9987
1.0025
1.0153
8.5
8.0
7.5
7.0
6.5
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4.5
4.0
3.5
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2.5
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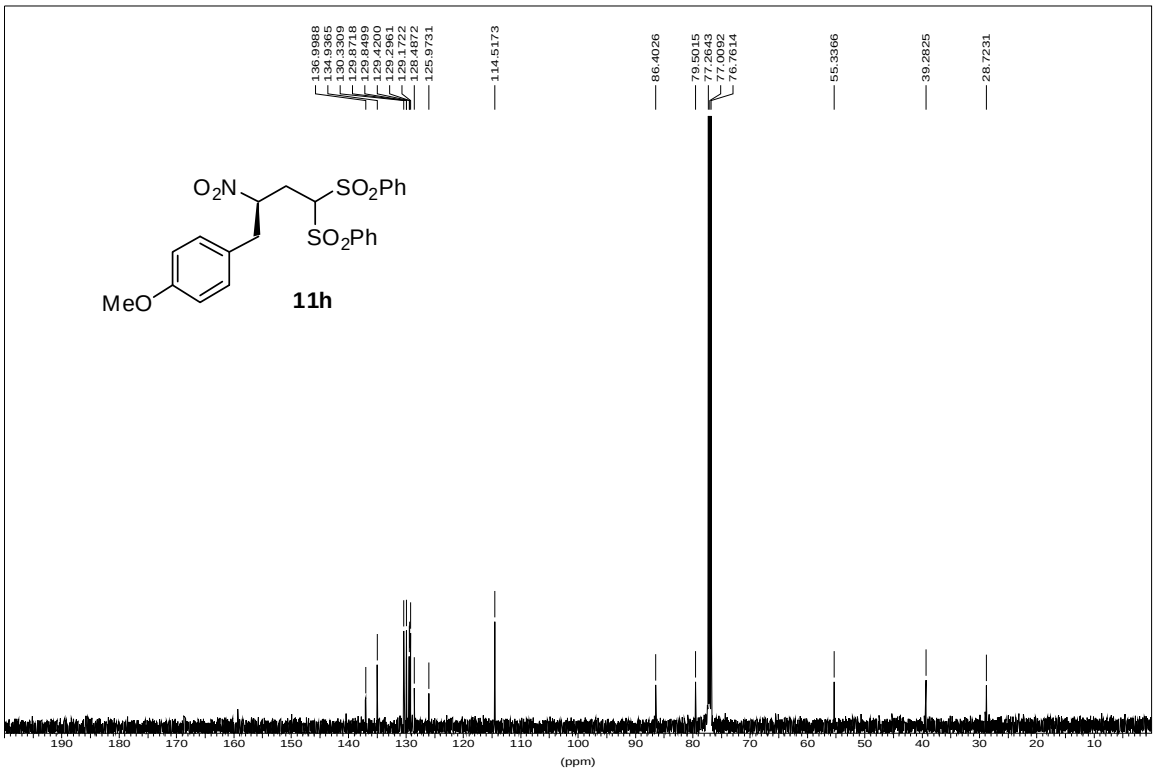
1.5
1.0
0.5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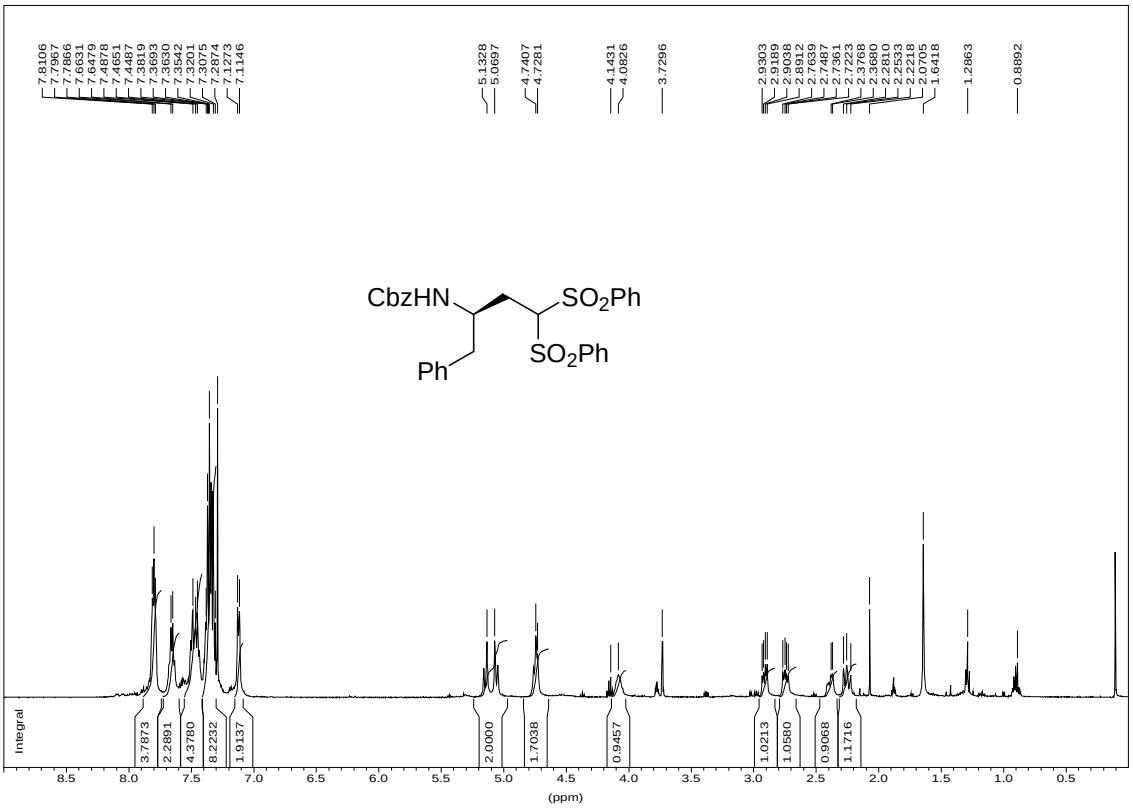
79.5015
77.2643
77.0092
76.7614
55.3366
39.2825
28.7231
O2N
SO2Ph
SO2Ph
MeO
11h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)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7.3542
7.3201
7.3075
7.2874
7.1273
7.1146
5.1328
5.0697
4.7407
4.7281
4.1431
4.0826
3.7296
2.9303
2.9189
2.9038
2.8912
2.7639
2.7487
2.7361
2.7223
2.3768
2.3680
2.2810
2.2553
2.2218
2.0705
1.6418
1.2863
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CbzHN
SO2Ph
SO2Ph
Ph
Integral
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4.3780
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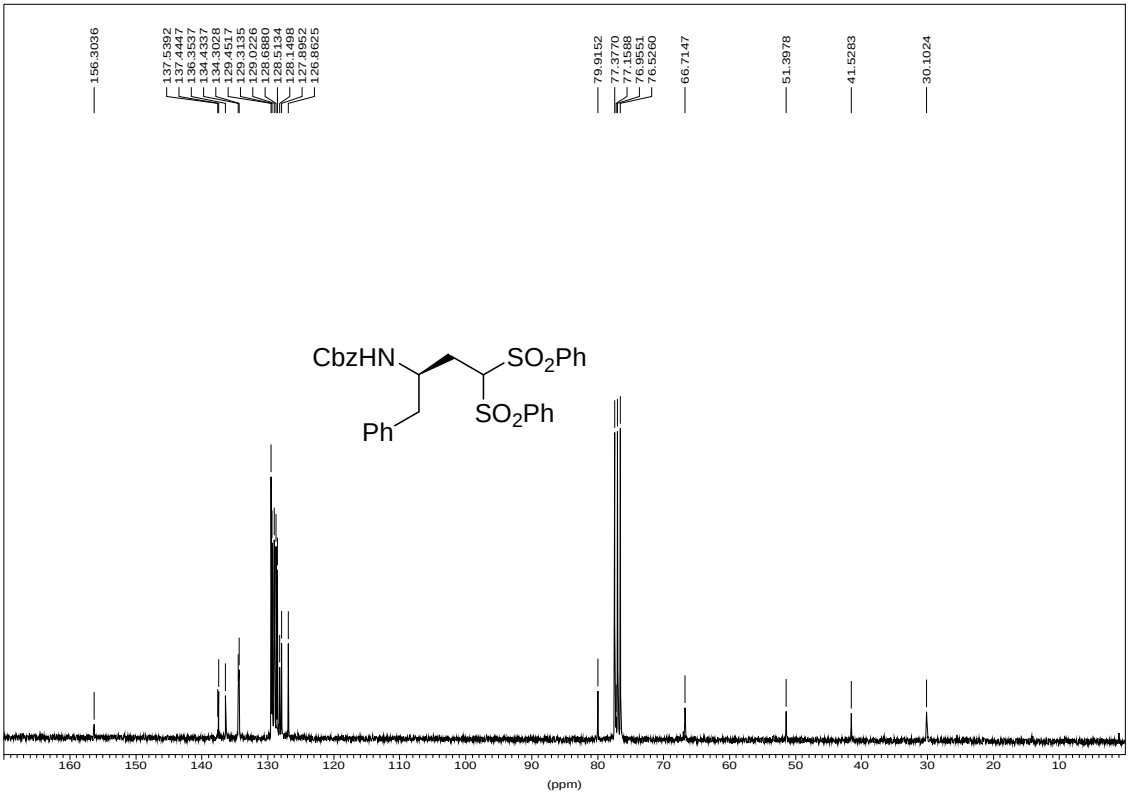
(ppm)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127.8952
126.8625
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77.3770
77.1588
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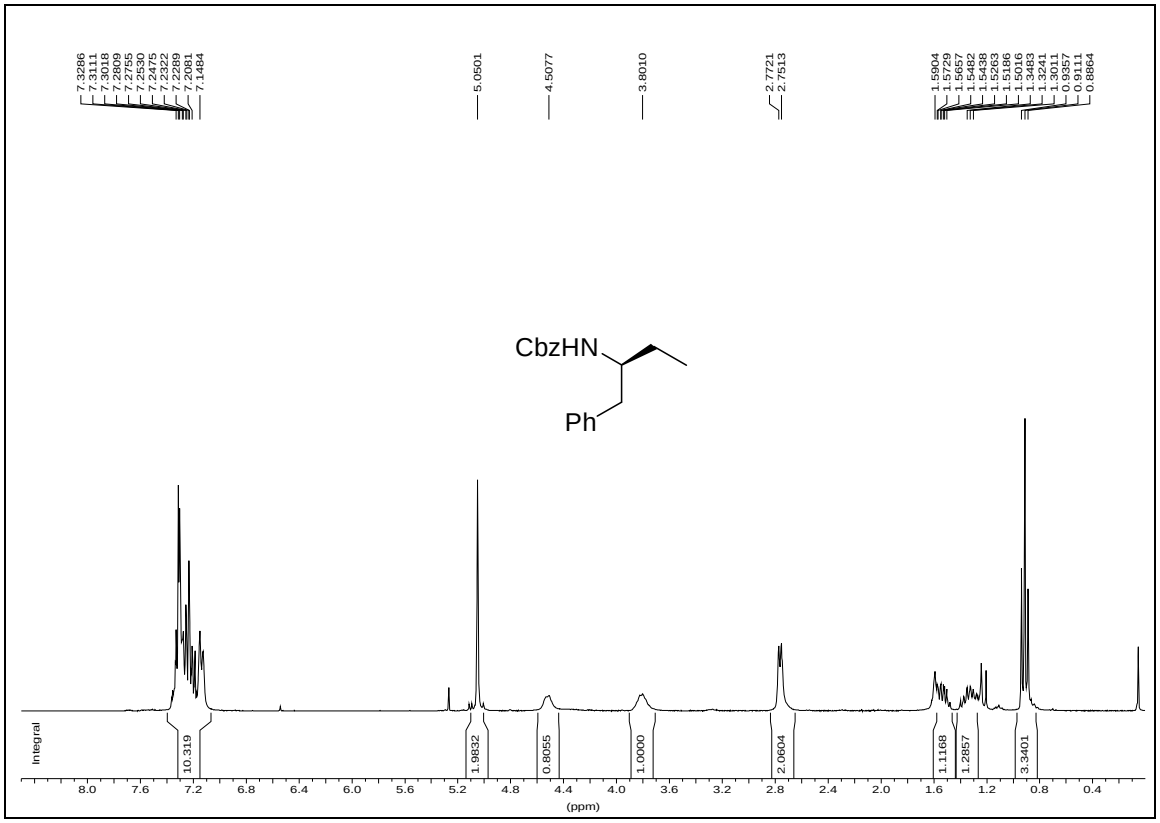
CbzHN
SO2Ph
SO2Ph
Ph
(ppm)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7.2530
7.2475
7.2332
7.2269
7.2081
7.1484
5.0501
4.5077
3.8010
2.7721
2.7513
1.5904
1.5729
1.5657
1.5482
1.5438
1.5263
1.5186
1.5016
1.3486
1.3241
1.3011
0.9357
0.9111
0.8864
CbzHN
Ph
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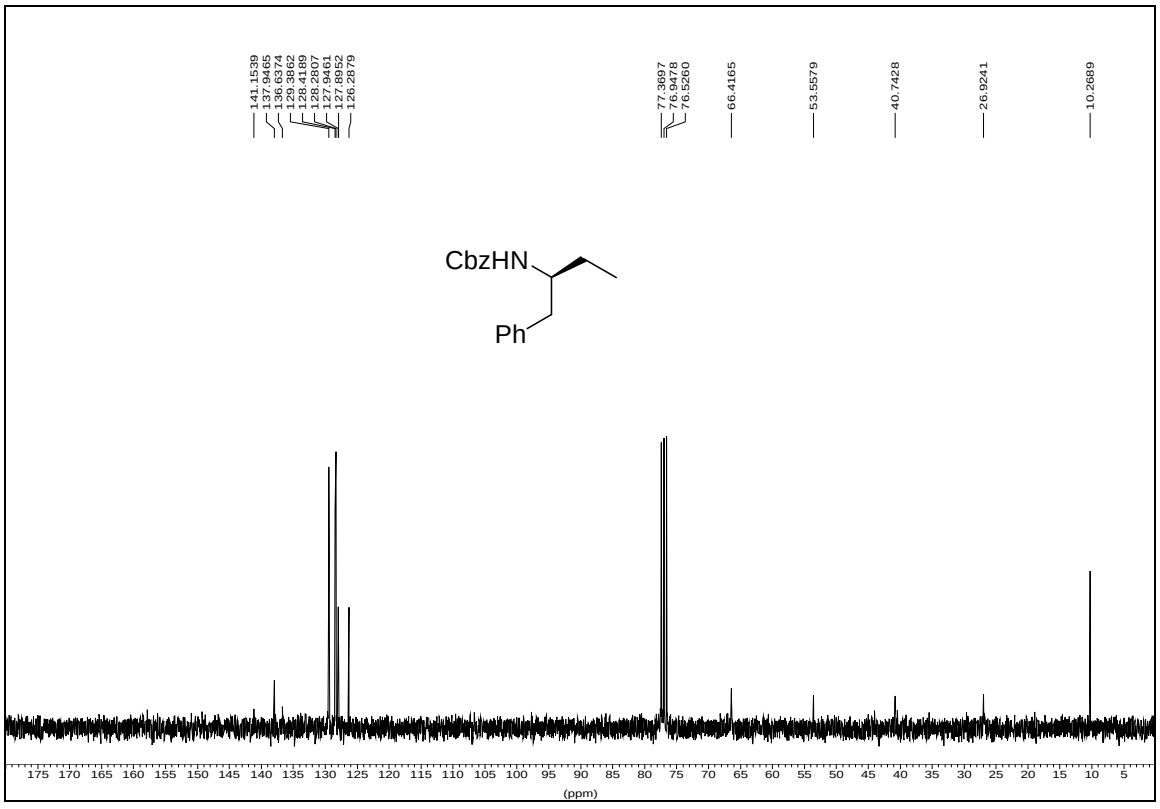
(ppm)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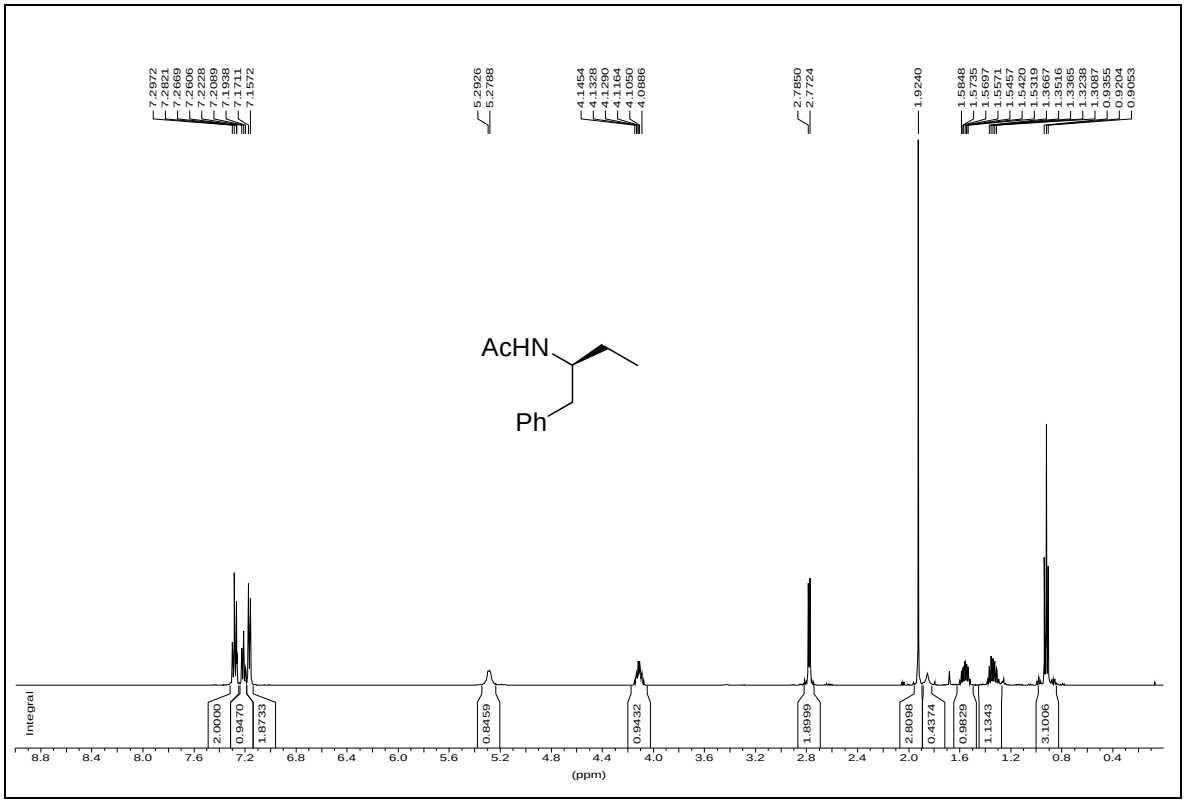
CbzHN
Ph
(ppm)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5.2788
4.1454
4.1328
4.1290
4.1164
4.1050
4.0886
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2.7724
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1.5848
1.5735
1.5697
1.5571
1.5457
1.5420
1.5319
1.3667
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1.3238
1.3087
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0.9204
0.9053
AcHN
Ph
Integral
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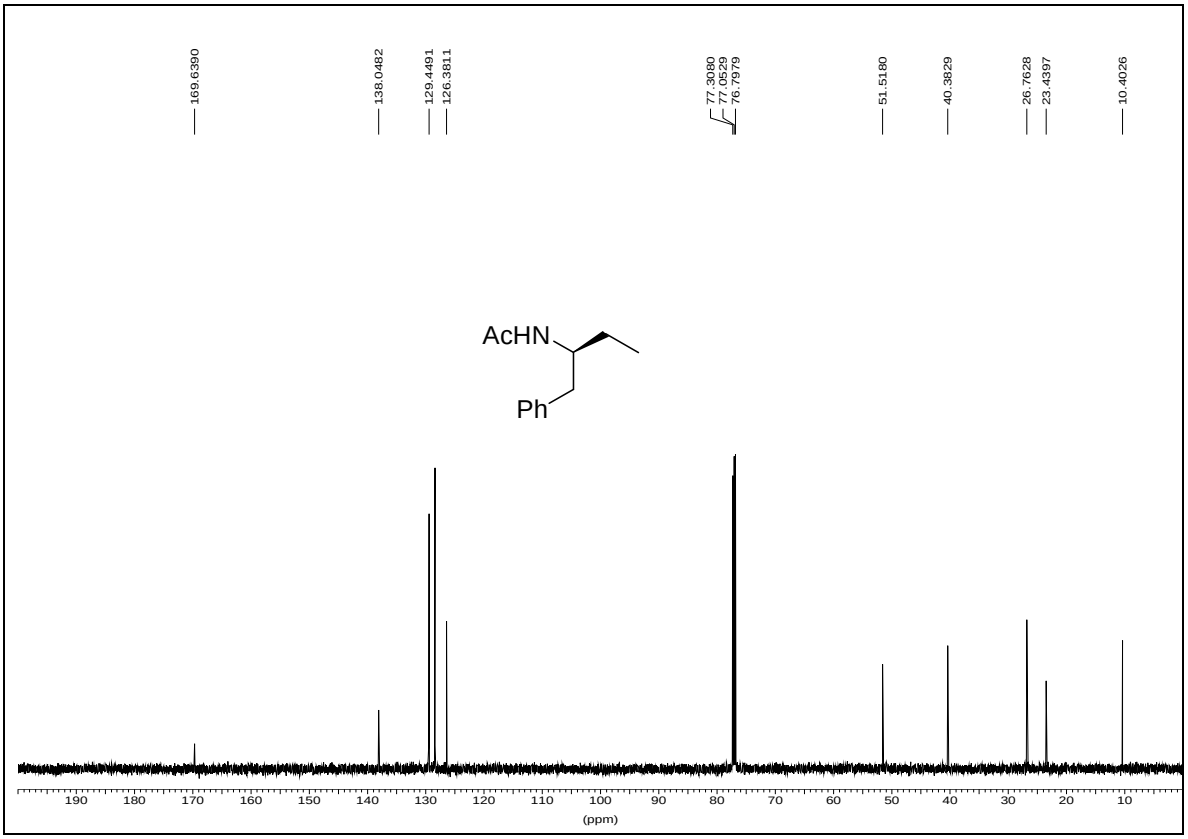
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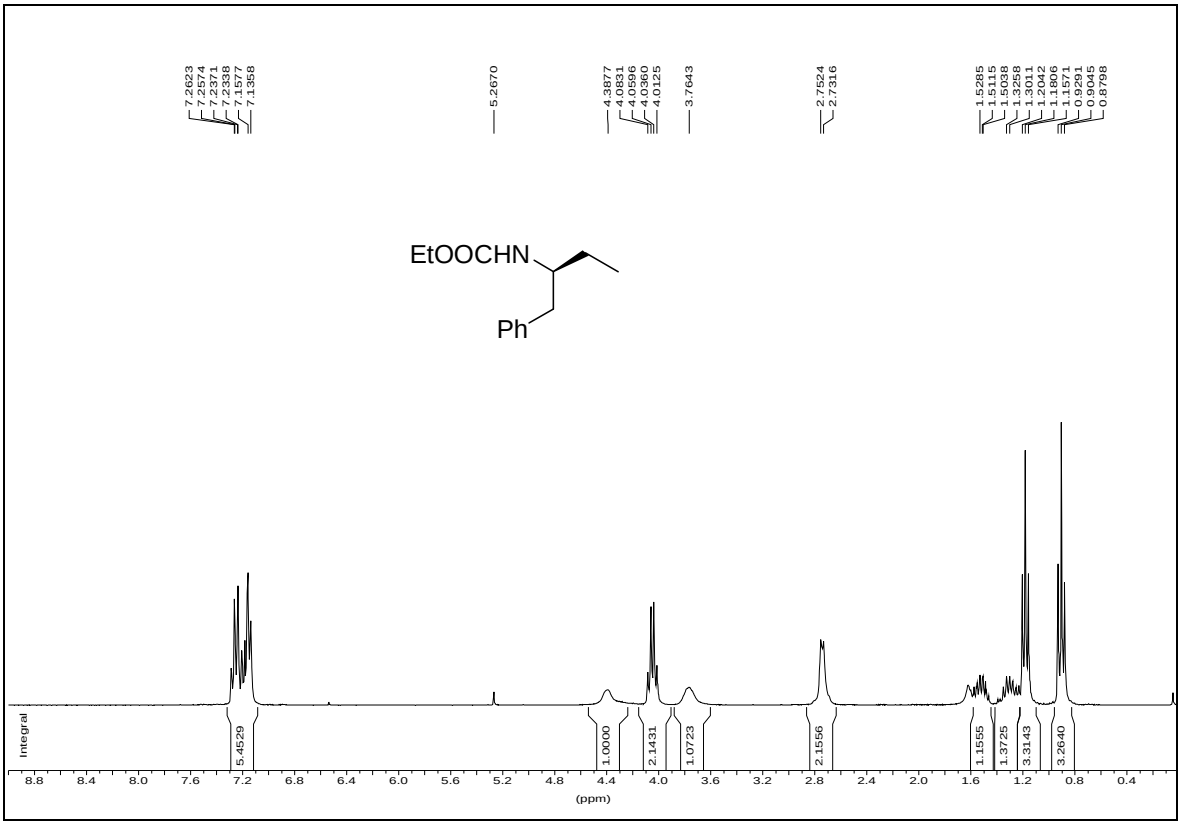
AcHN
Ph
(ppm)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4.0125
3.7643
2.7524
2.7316
1.5285
1.5115
1.5038
1.3258
1.2011
1.2042
1.1806
1.1571
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0.9045
0.8798
EtOOCHN
Ph
Integral
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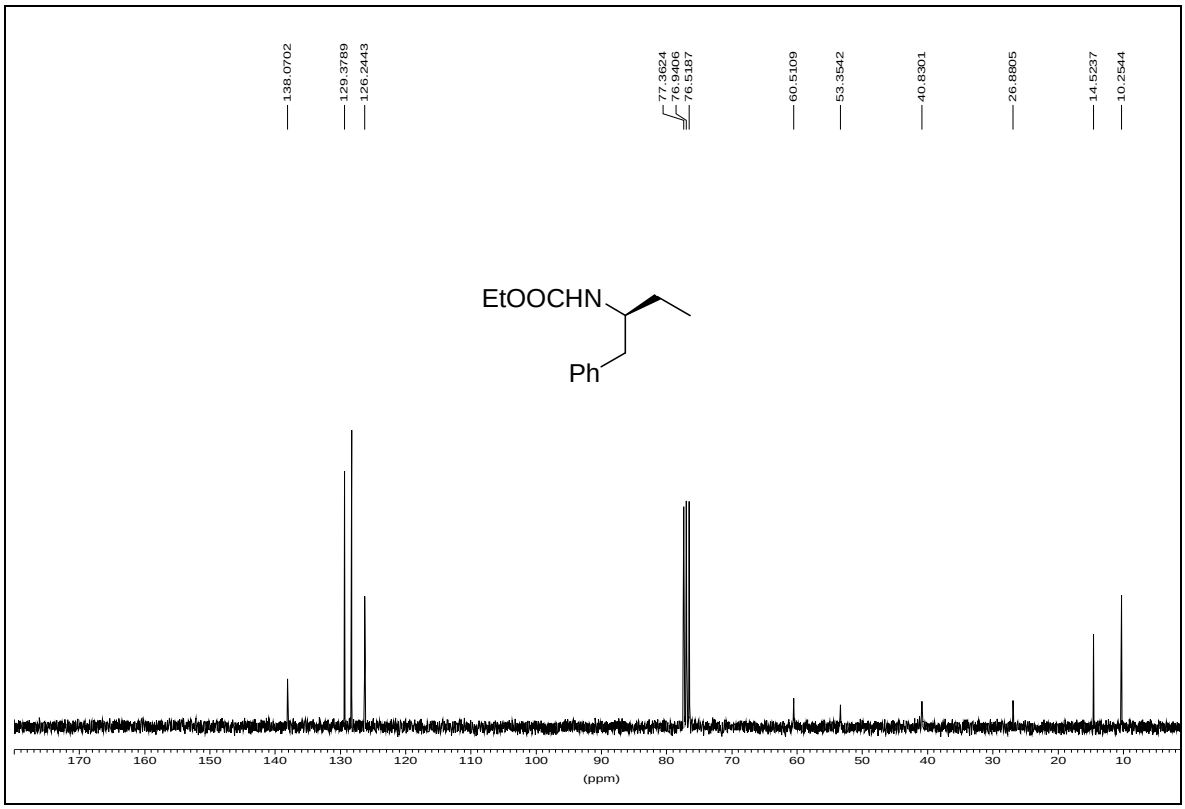
(ppm)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26.8805
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10.2544
EtOOCHN
Ph
(ppm)