Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Cyclization-Carbonylation-Cyclization Coupling Reaction of (*ortho*-Alkynyl Phenyl) (Methoxymethyl) Sulfides with Palladium(II)-Bisoxazoline Catalyst

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Supporting Information

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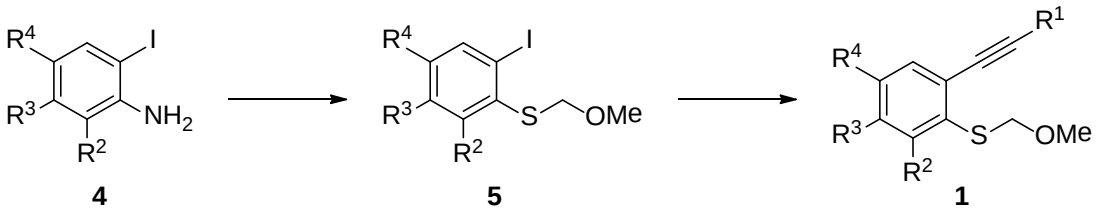
1. General Information

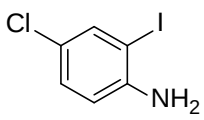
All melting points were measured on a Yanaco MP-3S micro melting point apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on JEOL ECS 400 and JEOL ECA 500 spectrometer spectrometers in $CDCl_3$ with Me_4Si as an internal reference. In the case of CD_2Cl_2 or DMSO-d_6, solvent peaks were used as a reference (5.32 or 2.50 ppm for ^{1}H, and 53.8 or 39.5 ppm for ^{13}C). ^{13}C NMR spectra were recorded at 100 MHz. High-resolution mass spectra (HR-MS) and fast atom bombardment mass spectra (FAB MS) were obtained with JEOL GC Mate II, JMS-SX102, LCMS-IT-TOF (Shimadzu, Tokyo, Japan) and JEOL JMS 600H spectrometer. ESI mass spectra were measured on JMS-T100LP (TOF). IR spectra were recorded with JASCO FT/IR-4100 spectrometer. All reagents were purchased from commercial sources and used without purification. All evaporations were performed under reduced pressure. For column chromatography, silica gel (Kieselgel 60) was employed.

2. Preparation of substrates **1a**, **b**, **e-l** and **n-u.**

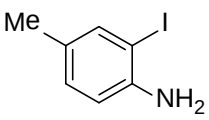
o-Alkynylphenyl methoxymethyl sulfides **1a**, **b**, **e-u** were synthesized by Sonogashira coupling reaction of *o*-iodophenyl methoxymethyl sulfides **5a**, **b**, **e-u** which were prepared from known *o*-iodoanilines[1a-d] by a modification of the published procedure.[2]



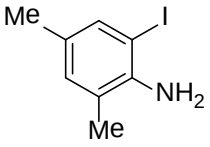
o-Iodoanilines **4** were prepared according to the literature. **4** were all known compounds. [1a-d]



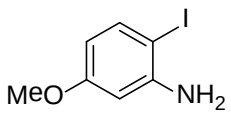
4n[1a]



4p[1b]



4q[1c]

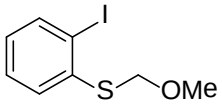


4r[1d]

2-1. Typical experimental procedure for the preparation of *o*-iodophenyl methoxymethyl sulfide 5a.

To a solution of 2-iodoaniline (2.19 g, 10 mmol) in ethanol (25 mL) at 0 °C was added tetrafluoroboric acid (42% in water, 4.2 mL), and the mixture was stirred for 15 min. Isoamyl nitrite (1.3 mL, 10 mmol) was added dropwise to the mixture at 0 °C, and stirred for 5 min. The resulting suspension was filtered, rinsed with ethanol (4 mL) to give the corresponding diazonium tetrafluoroborate as a cream-colored solid. The crude diazonium salt was added portionwise to a solution of potassium ethyl xanthate (1.60 g, 10 mmol) in acetone (25 mL) at -40 °C. The reaction mixture was stirred at 0 °C for 1h and at room temperature for 20 min. The resulting suspension was filtered off, and the filtrate was concentrated *in vacuo*. The residue was dissolved in ethyl acetate (100 mL) and washed with water (100 mL). The organic layer was dried over Mg_2SO_4 and concentrated *in vacuo*. The residue was passed through a short column of silica gel in hexane / ethyl acetate (200 / 1). Evaporation yielded crude dithiocarbonic acid *O*-ethyl ester. The crude product was dissolved in THF (25 mL). Separately, KOH (1.16g, 20.7 mmol) was dissolved in MeOH (30 mL). The two solutions were combined, heated to 40 °C for 2h, and concentrated *in vacuo*. The solid was washed with Et_2O (100 mL), and finely ground. Filtration and drying under vacuum at room temperature gave potassium salt as a crude brown powder. To a solution of the crude product in DMF (30 mL) at room temperature was added chloromethyl methyl ether (1.5 mL, 20 mmol) and stirred for 1h. The mixture was diluted with hexane / ethyl acetate (1 / 1, 100 mL), washed with water (100 mL). The organic layer was dried over Mg_2SO_4 and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane / ethyl acetate (200 / 1) afforded 2-iodophenyl methoxymethyl sulfide **5a**[3] (1.64g, 59%).

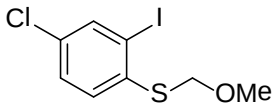
2-Iodophenyl methoxymethyl sulfide (5a)[3]



5a

44% yield, Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 (3H, s), 5.00 (2H, s), 6.89 (1H, dt, J = 1.2, 8.0 Hz), 7.31 (1H, dt, J = 1.2, 8.0 Hz), 7.58 (1H, dd, J = 1.2, 8.0 Hz), 7.80 (1H, dd, J = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.3, 77.3, 100.1, 127.5, 128.9, 128.9, 139.4, 141.2; IR (KBr): 2925, 1557, 1446, 1081, 746 cm^{-1}.

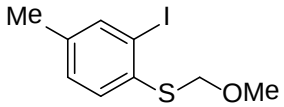
4-Chloro-2-Iodophenyl methoxymethyl sulfide (5n)



5n

36% yield, Yellow solid, mp 32 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 (3H, s), 4.97 (2H, s), 7.28 (1H, dd, J = 2.4, 8.4 Hz), 7.49 (1H, d, J = 8.4 Hz), 7.80 (1H, d, J = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.3, 77.5, 100.0, 129.0, 129.5, 132.3, 138.6, 139.9; IR (KBr) 2925, 1440, 1179, 1078, 889, 679 cm^{-1}; HRMS-EI: m/z: [M^{+}] calcd for C_8H_8ClIOS 313.9029, found 313.9023.

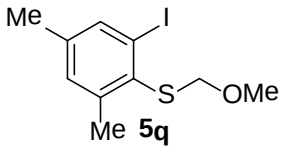
2-Iodo-4-methylphenyl methoxymethyl sulfide (5p)



5p

38% yield, White solid, mp: 55-56 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (3H, s), 3.44 (3H, s), 4.95 (2H, s), 7.10-7.13 (1H, m), 7.46 (1H, d, J = 8.0 Hz), 7.67 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 56.3, 77.9, 101.3, 129.7, 129.8, 137.2, 138.1, 140.0; IR (KBr) 2923, 1453, 1072, 678 cm^{-1}; HRMS-EI: m/z:[M^{+}] calcd for $C_9H_{11}IOS$ 293.9576, found 293.9575.

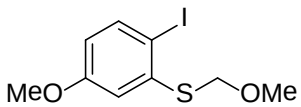
2-Iodo-4,6-dimethylphenyl methoxymethyl sulfide (5q)



5q

38% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (3H, s), 2.58 (3H, s), 3.46 (3H, s), 4.82 (2H, s), 7.04 (1H, m), 7.64 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 24.3, 57.3, 80.5, 111.0, 131.6, 134.5, 138.6, 140.6, 143.9; IR (KBr) 2919, 1531, 1085, 672 cm^{-1}; HRMS-EI: m/z: [M^{+}] calcd for $C_{10}H_{13}IOS$ 307.9732, found 307.9731.

5-Methoxy-2-Iodophenyl methoxymethyl sulfide (5r)



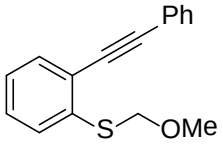
5r

31% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 3.78 (3H, s), 5.00 (2H, s), 6.50 (1H, dd, J = 2.8, 8.8 Hz), 7.19 (1H, d, J = 3.2 Hz), 7.64 (1H, d, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 56.2, 77.3, 88.2, 113.7, 114.9, 139.7, 142.2, 160.3; IR (KBr) 2925, 1576, 1458, 1284, 1080 cm^{-1}; HRMS-EI: m/z: [M^{+}] calcd for $C_9H_{11}IO_2S$ 309.9525, found 309.9524.

2-2. Typical experimental procedure for the preparation of substrate 1a.

To a mixture of 2-iodophenyl methoxymethyl sulfide (300 mg, 1.07 mmol), $(PPh_3)_2PdCl_2$ (14.3 mg, 0.02 mmol), and CuI (8.7 mg, 0.045 mmol) in triethylamine (7 ml) under argon was added ethynylbenzene (176 μL, 1.6 mmol). The reaction mixture was stirred for 2.5 at room temperature. The mixture was diluted with ether, washed with saturated aqueous ammonium chloride, water and brine and dried over Mg_2SO_4. The crude product was purified by silica gel column chromatography using hexane / ether (150 / 1) as eluent to obtain 2-(phenylethynyl)phenyl methoxymethyl sulfide **1a** in 92% yield.

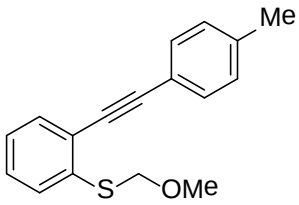
Methoxymethyl 2-(phenylethynyl)phenyl sulfide (1a)[3]



1a

90% yield, brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 (3H, s), 5.08 (2H, s), 7.17 (1H, dt, J = 1.6, 7.6 Hz), 7.28 (1H, dt, J = 1.6, 7.6 Hz), 7.34-7.36 (3H, m), 7.50 (1H, dd, J = 1.6, 7.6 Hz), 7.56-7.58 (2H, m), 7.61 (1H, dd, J = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.2, 76.4, 87.3, 95.1, 123.1, 123.4, 125.9, 128.3, 128.4（2C), 128.5, 128.9, 131.6（2C), 132.5, 139.0; IR (KBr): 2926, 2213, 1453, 1083, 755, 687 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{16}H_{14}OS$ 254.0765, found 254.0764.

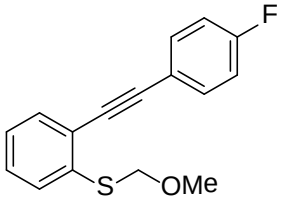
Methoxymethyl 2-[(4-methylphenyl)ethynyl]phenyl sulfide (1b)



1b

88% yield, Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (3H, s), 3.45 (3H, s), 5.08 (2H, s), 7.15-7.19 (3H, m), 7.24-7.29 (1H, m), 7.45-7.51 (3H, m), 7.59-7.61 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 56.1, 76.4, 86.7, 95.4, 120.1, 123.6, 125.9, 128.5, 128.7, 129.1 (2C), 131.4 (2C), 132.4, 138.6, 138.9; IR (KBr) 2212, 1514, 1083, 676 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{17}H_{16}OS$ 268.0922, found 268.0922.

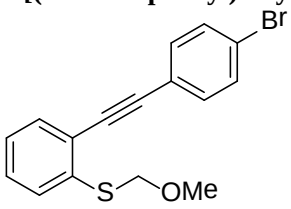
2-[(4-Fluorophenyl)ethynyl]phenyl methoxymethyl sulfide (1e)



1e

82% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 5.08 (2H, s), 7.02-7.08 (2H, m), 7.18 (1H, dt, J = 1.4, 8.0 Hz), 7.28 (1H, dt, J = 1.4, 8.0 Hz), 7.49 (1H, dd, J = 1.6, 8.0 Hz), 7.52-7.57 (2H, m), 7.60(1H, dd, J = 1.6, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.1, 76.3, 87.0, 94.0, 115.6 (2C, d, $^2J_{C\text{-}F}$ = 21.9 Hz), 119.2 (1C, d, $^4J_{C\text{-}F}$ = 2.9 Hz), 123.0, 125.9, 128.4, 129.0, 132.4, 133.5 (2C, d, $^3J_{C\text{-}F}$ = 8.5 Hz), 139.0, 162.5 (1C, d, $^1J_{C\text{-}F}$ = 247.9 Hz); IR (KBr) 2217, 1507, 1085, 836 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{16}H_{13}FOS$ 272.0671, found 272.0670.

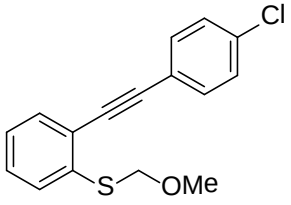
2-[(4-Bromophenyl)ethynyl]phenyl methoxymethyl sulfide (1f)



1f

89% yield, Light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 5.07 (2H, s), 7.18 (1H, dt, *J* = 1.2, 7.6 Hz), 7.29 (1H, dt, *J* = 1.6, 8.0 Hz), 7.40-7.44 (2H, m), 7.47-7.50 (3H, m), 7.60 (1H, dd, *J* = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 76.4, 88.4, 94.0, 122.1, 122.7, 122.9, 125.9, 128.5, 129.1, 131.6 (2C), 132.4, 133.0 (2C), 139.2; IR (KBr) 2920, 2290, 1490, 1086 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{16}H_{13}BrOS$ 331.9870, found 331.9870.

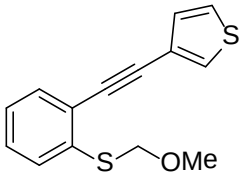
2-[(4-Chlorophenyl)ethynyl]phenyl methoxymethyl sulfide (1g)



1g

80% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 5.08 (2H, s), 7.18 (1H, dt, *J* = 1.4, 7.6 Hz), 7.28 (1H, dd, *J* = 1.6, 8.0 Hz), 7.31-7.34 (2H, m), 7.48-7.51 (3H, m), 7.61 (1H, dd, *J* = 1.2, 8.0 Hz) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 76.4, 88.3, 93.9, 121.7, 122.9, 125.9, 128.4, 128.7(2C), 129.1, 132.4, 132.7(2C), 134.4, 139.1; IR (KBr) 3741, 2255, 1086, 677 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{16}H_{13}ClOS$ 288.0376, found 288.0374.

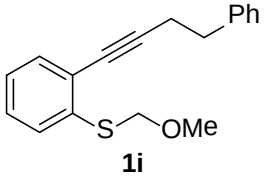
3-{2-[(methoxymethyl)thiophenyl]ethynyl}thiophene (1h)



1h

70% yield, Yellow solid, mp: 80-82 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 5.07 (2H, s), 7.17 (1H, dt, *J* = 1.2, 7.6 Hz), 7.22-7.32 (3H, m), 7.49 (1H, dd, *J* = 1.2, 7.6 Hz), 7.55 (1H, dd, *J* = 1.2, 2.8 Hz), 7.60 (1H, dd, *J* = 0.8, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2, 76.4, 86.7, 90.2, 122.1, 123.2, 125.4, 125.9, 128.5, 128.8, 128.9, 129.8, 132.4, 138.9; IR (KBr) 2194, 1579, 1460, 1085, 1063, 786 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{14}H_{12}OS_2$ 260.0330, found 260.0329.

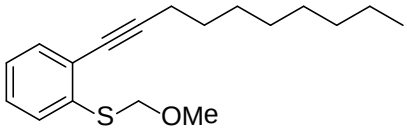
Methoxymethyl 2-(4-phenylbut-1-yn-1-yl)phenyl sulfide (1i)



1i

57% yield, Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77 (2H, t, *J* = 7.6 Hz), 2.96 (2H, t, *J* = 7.6 Hz), 3.42 (3H, s), 5.00 (2H, s), 7.09-7.13 (1H, m), 7.20-7.36 (7H, m), 7.52-7.54 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 35.1, 56.1, 76.3, 79.2, 95.6, 123.8, 125.8, 126.3, 128.2, 128.3, 128.4 (2C), 128.6 (2C), 132.6, 138.6, 140.6; IR (KBr) 3651, 2926, 2316, 1086, 698 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{18}H_{18}OS$ 282.1078, found 282.1077.

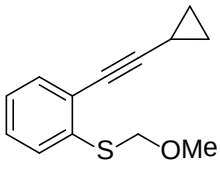
2-(Dec-1-yn-1-yl)phenyl methoxymethyl sulfide (1j)



1j

95% yield, Red oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, *J* = 7.2 Hz), 1.28-1.33 (8H, m), 1.46-1.52 (2H, m), 1.60-1.67 (2H, m), 2.47 (2H, t, *J* = 7.2 Hz), 3.43 (3H, s), 5.04 (2H, s), 7.11 (1H, t, *J* = 8.0 Hz), 7.19-7.23 (1H, m), 7.37 (1H, dd, *J* = 1.0, 7.5 Hz), 7.54 (1H, d, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 19.6, 22.6, 28.7, 28.9, 29.1, 29.2, 31.8, 56.1, 76.2, 78.5, 96.7, 125.7, 128.1, 128.2,130.2, 132.5, 138.5; IR (KBr) 2926, 2854, 2220, 1466, 1087 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{18}H_{26}OS$ 290.1704, found 290.1705.

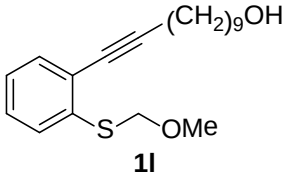
2-(Cyclopropylethynyl)phenyl methoxymethyl sulfide (1k)



1k

59% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83-0.92 (4H, m), 1.48-1.53 (1H, m), 3.43 (3H, s), 5.03 (2H, s), 7.09 (1H, dt, *J* = 1.2, 6.4 Hz), 7.20 (1H, dt, *J* = 1.2, 6.4 Hz), 7.35 (1H, dd, *J* = 1.2, 6.0 Hz), 7.52 (1H, d, *J* = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.4, 8.9 (2C), 56.1, 73.6, 76.2, 99.7, 123.9, 125.7, 128.0, 128.1, 132.4, 138.7; IR (KBr) 2224, 1467, 1085, 1063, 753 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{13}H_{14}OS$ 218.0765, found 218.0766.

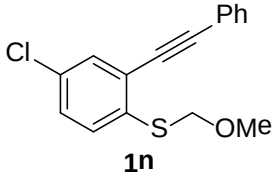
11-{2-[(methoxymethyl)thio]phenyl}undec-10-yn-1-ol (1l)



1l

59% yield, Colorless oil, ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.33-1.67 (15H, m), 2.46 (2H, t, *J* = 6.8 Hz), 3.41 (3H, s), 3.57 (2H, t, *J* = 6.8 Hz), 5.03 (2H, s), 7.12 (1H, dt, *J* = 1.2, 7.6 Hz), 7.23 (1H, dt, *J* = 1.6, 7.6 Hz), 7.36 (1H, dd, *J* = 1.6, 7.6 Hz), 7.52 (1H, dd, *J* = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 19.9, 26.2, 29.1, 29.3, 29.5, 29.8, 29.9, 33.3, 56.4, 63.2, 76.5, 78.8, 97.1, 124.4, 126.1, 128.5, 128.6, 132.8, 138.9; IR (KBr) 3855, 2927, 2138, 1542, 1087 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{19}H_{28}O_2S$ 320.1810, found 320.1810.

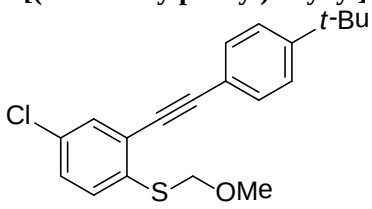
4-Chloro-2-(phenylethynyl)phenyl methoxymethyl sulfide (1n)



1n

83% yield, Yellow solid, mp 46-47 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.44 (3H, s), 5.05 (2H, s), 7.24 (1H, dd, *J* = 2.0, 8.4 Hz), 7.34-7.38 (3H, m), 7.49 (1H, d, *J* = 2.4 Hz), 7.54-7.57 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.2 , 76.4, 86.1, 96.2, 122.7, 124.9, 128.4 (2C), 129.0, 128.9, 129.8, 131.7 (2C), 131.8, 131.9, 137.5; IR (KBr) 2220, 1491, 1449, 1054, 758, 696, 687 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{16}H_{13}ClOS$ 288.0376, found 288.0375.

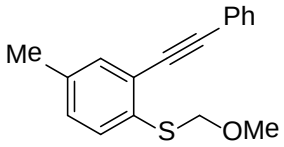
2-[(4-*tert*-Butylphenyl)ethynyl]-4-chlorophenyl methoxymethyl sulfide (1o)



1o

70% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (9H, s), 3.44 (3H, s), 5.04 (2H, s), 7.23 (1H, dd, *J* = 1.6, 8.4 Hz), 7.37-7.40 (2H, m), 7.48-7.53 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1 (3C), 34.8, 56.1 , 76.4, 85.5, 96.4, 119.6,125.1, 125.4 (2C), 128.8, 129.8, 131.8 (2C), 131.7, 131.9, 137.4, 152.1; IR (KBr) 2959, 2215, 1457, 1084, 677 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{20}H_{21}ClOS$ 344.1002, found 344.1003.

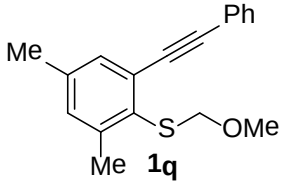
Methoxymethyl 4-methyl-2-(phenylethynyl)phenyl sulfide (1p)



1p

82% yield, Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (3H, s), 3.43 (3H, s), 5.04 (2H, s), 7.08-7.11 (1H, m), 7.33-7.36 (4H, m), 7.49 (1H, d, *J* = 8.0 Hz), 7.54-7.57 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 56.1, 77.0, 87.7, 94.5, 123.3, 123.9, 128.3 (2C), 128.4, 129.7, 129.9, 131.6 (2C), 133.1, 135.1, 136.2; IR (KBr) 2924, 2200, 1085, 756, 690 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{17}H_{16}OS$ 268.0922, found 268.0920.

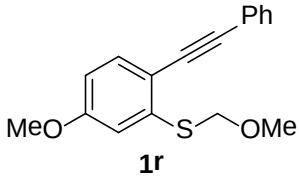
2,4-Dimethyl-6-(phenylethynyl)phenyl methoxymethyl sulfide (1q)



1q

89% yield, Yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (3H, s), 2.52 (3H, s), 3.43 (3H, s), 5.00 (2H, s), 7.04 (1H, m), 7.28-7.36 (4H, m), 7.51-7.54 (2H, m); ^{13}C NMR ($CDCl_3$) (100 MHz, $CDCl_3$) δ 20.8, 21.9, 56.7, 79.5, 89.3, 93.1, 123.5, 128.3, 128.4 (2C), 129.0, 131.5 (3C), 131.7, 131.8, 138.2, 142.7; IR (KBr) 2213, 1087, 756, 690 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{18}H_{18}OS$ 282.1078, found 282.1076.

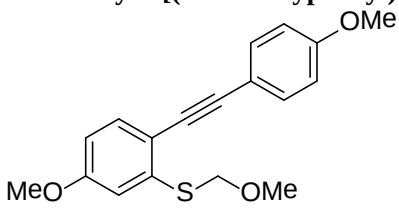
5-Methoxy-2-(phenylethynyl)phenyl methoxymethyl sulfide (1r)



1r

72% yield, Yellow oil, ^{1}H NMR ($CDCl_3$) (400 MHz, $CDCl_3$) δ 3.43 (3H, s), 3.79 (3H, s), 5.06 (2H, s), 6.71 (1H, dd, *J* = 2.4, 8.4 Hz), 7.17 (1H, d, *J* = 2.4 Hz), 7.29-7.35 (3H, m), 7.41 (1H, d, *J* = 8.4 Hz), 7.53-7.55 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 56.2, 76.4, 87.3, 93.7, 111.9, 114.1, 123.5, 128.1, 128.3 (2C), 131.4 (2C), 133.6, 140.7, 159.9; IR (KBr) 2213, 1590, 1494, 1231, 1084 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{17}H_{16}O_2S$ 284.0871, found 284.0873.

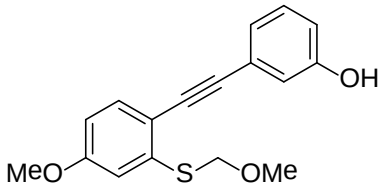
5-Methoxy-2-[(4-methoxyphenyl)ethynyl]phenyl methoxymethyl sulfide (1s)



1s

82% yield, Yellow solid, mp 66-69 °C, ^{1}H NMR ($CDCl_3$) (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 3.81 (3H, s), 3.82 (3H, s), 5.07 (2H, s), 6.71 (1H, dd, *J* = 2.4, 8.8 Hz), 6.85-6.88 (2H, m), 7.17 (1H, d, *J* = 2.4 Hz), 7.40 (1H, d, *J* = 8.8 Hz), 7.46-7.50 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.3, 55.4, 56.2, 76.4, 85.9, 93.6, 111.8, 113.9, 114.0 (2C), 115.6, 115.8, 132.9 (2C), 133.4, 140.5, 159.5, 159.6; IR (KBr) 2212, 1605, 1509, 1288, 1084, 1033 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{18}H_{18}O_3S$ 314.0977, found 314.0977.

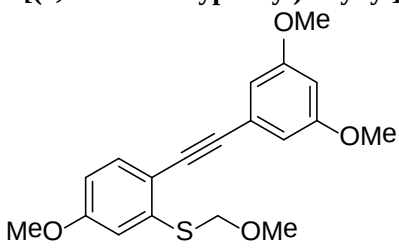
3-((4-Methoxy-2-((methoxymethyl)thio)phenyl)ethynyl)phenol (1t)



1t

50% yield, Yellow solid, mp 80-81 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.46 (3H, s), 3.82 (3H, s), 5.08 (2H, s), 6.72（1H, dd, *J* = 2.4, 8.4 Hz), 6.77-6.80 (1H, m), 7.00 (1H, m), 7.10-7.22 (3H, m), 7.42 (1H, d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 56.2, 76.4, 87.3, 93.3, 111.9, 114.1, 115.4, 115.6, 118.0, 124.0, 124.7, 129.6, 133.6, 140.7, 155.4, 160.0; IR (KBr) 3328, 2210, 1577, 1492, 1231, 1051 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{17}H_{16}O_3S$ 300.0820, found 300.0822.

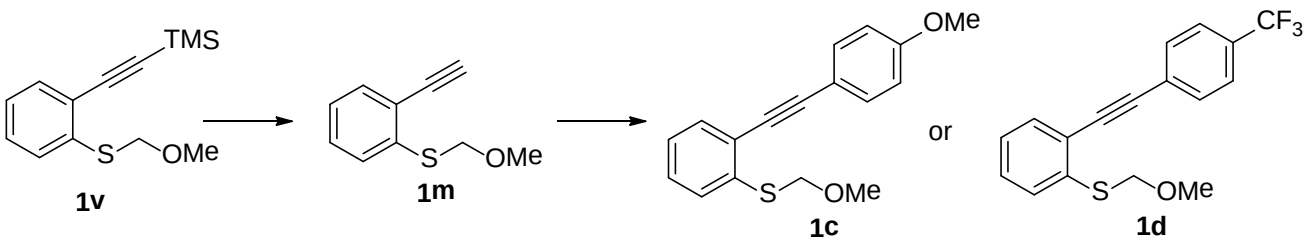
2-[(3,5-dimethoxyphenyl)ethynyl]-5-methoxyphenyl methoxymethyl sulfide (1u)



1u

42% yield, Colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (3H, s), 3.80 (6H, s), 3.82 (3H, s), 5.08 (2H, s), 6.45 (1H, t, *J* = 2.4 Hz), 6.70-6.74 (3H, m), 7.17 (1H, d, *J* = 2.4 Hz), 7.42 (1H, d, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 55.4 (2C), 56.2, 76.4, 86.9, 93.6, 101.6, 109.2 (2C), 111.8, 113.9, 115.2, 124.7, 133.6, 140.9, 160.0, 160.5 (2C); IR (KBr) 2200, 1589, 1156, 1085, 419 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{19}H_{20}O_4S$ 344.1082, found 344.1082.

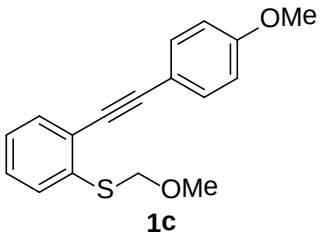
3. Preparation of substrates **1m**, **c** and **d.**



The crude methoxymethyl 2-(trimethysilylethynyl)phenyl sulfide **1v** was prepared by the Sonogashira coupling reaction of 2-iodophenyl methoxymethyl sulfide **1a** (300 mg, 1.07 mmol) with trimethylsilyl acetylene (315.2 mg, 3.21 mmol) (40 °C, 12h) according to the typical procedure. To a solution of the crude product **1v** in THF (8 mL) at room temperature was added tetrabutylammonium fluoride (1M in THF, 1.2 mL, 1.2 mmol), and stirred for 0.5h. The mixture was diluted with ethyl acetate (50 mL), washed with water (50 mL). The organic layer was dried over Mg_2SO_4 and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography using hexane / ethyl acetate (300 / 1) as eluent to obtain 2-ethynylphenyl methoxymethyl sulfide **1m** in 84% yield (149.4 mg). Brown oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.42 (1H, s), 3.44 (3H, s), 5.01 (2H, s), 7.16 (1H, dt, *J* = 1.2, 7.6 Hz), 7.30 (1H, dt, *J* = 1.6, 7.6 Hz), 7.48 (1H, dd, *J* = 1.6, 7.6 Hz), 7.58-7.60 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.1, 76.4, 81.4, 82.8, 122.3 ,125.9 , 128.7, 129.4, 133.3, 139.2; IR (KBr) 3285, 2104, 1464, 1086, 755 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{10}H_{10}OS$ 178.0452, found 178.0450.

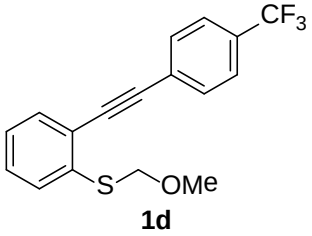
The substrates **1c** and **1d** were prepared by the Sonogashira coupling reaction of **1m** with the corresponding terminal alkynes according to the typical procedure.

Methoxymethyl 2-[(4-methoxylphenyl)ethynyl]phenyl sulfide (1c) [3]



63% yield. Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.45 (3H, s), 3.82 (3H, s), 5.08 (2H, s), 6.81-6.91 (2H, m), 7.16 (1H, dt, *J* = 1.2, 7.6 Hz), 7.25 (1H, dt, *J* = 1.6, 7.6 Hz), 7.47-7.53 (3H, m), 7.59 (1H, br-d, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 55.3, 56.2, 76.4, 86.1, 95.2, 114.0 (2C), 115.3, 123.7, 125.9, 128.5, 128.6, 132.3 , 133.1 (2C), 138.8, 159.8; IR (KBr): 2933, 2206, 1597, 1506, 1246, 1087, 828, 759 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{17}H_{16}O_2S$ 284.0871, found 284.0872.

Methoxymethyl 2-[(4-trifluoromethylphenyl)ethynyl]phenyl sulfide (1d) [3]



43% yield. Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 3.46 (3H, s), 5.08 (2H, s), 7.20 (1H, dt, *J* = 1.2, 7.6 Hz), 7.32 (1H, dt, *J* = 1.2, 7.6 Hz), 7.51 (1H, dd, *J* = 1.2, 7.6 Hz), 7.60-7.68 (5H, m); ^{13}C NMR (100 MHz, CD_2Cl_2): *δ* 56.4, 76.7, 90.0, 93.7, 122.9, 124.4(1C, q, $^1J_{C\text{-}F}$ = 270.8 Hz), 125.7(2C, q, $^3J_{C\text{-}F}$ = 3.9 Hz), 126.3, 127.4, 128.9, 129.8, 130.2 (1C, q, $^2J_{C\text{-}F}$ = 32.4 Hz), 132.1 (2C), 132.9, 140.0;IR (KBr): 2933, 2215, 1611, 1460, 1324, 1072, 836 cm^{-1}; HRMS-EI: m/z: [M$^+$] calcd for $C_{17}H_{13}F_3OS$ 322.0639, found 322.0640.

4. References

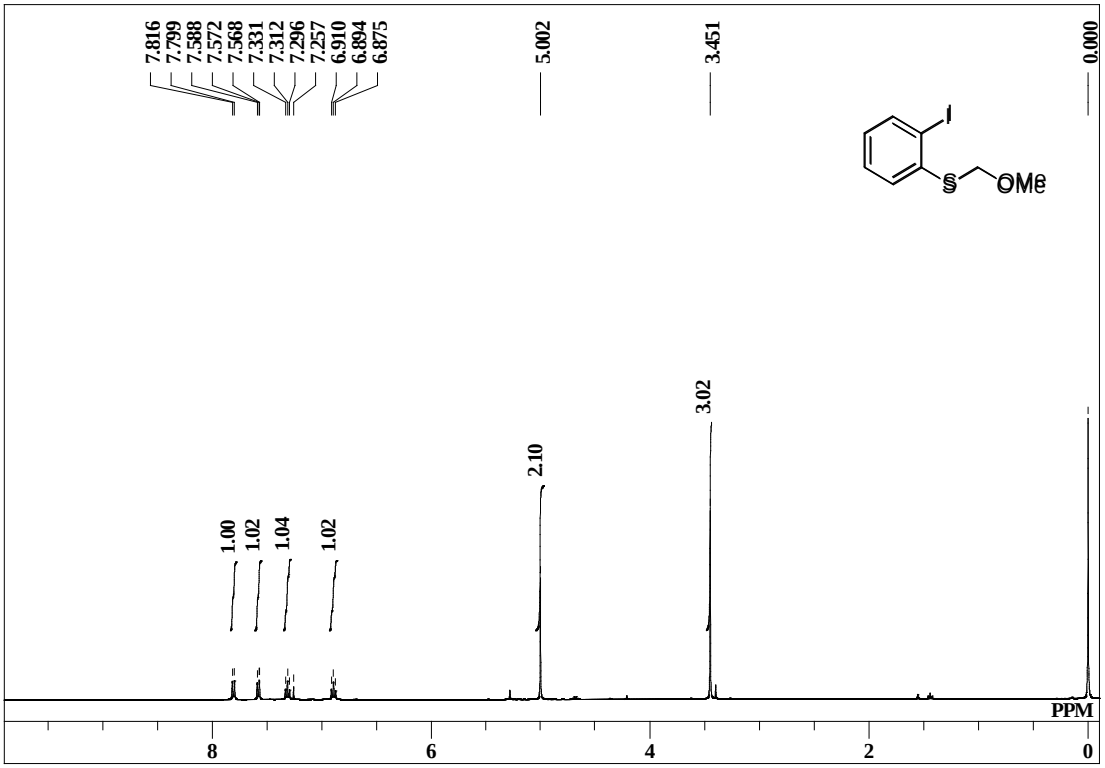
[1] (a) P. P. Sharp , M. G. Banwell, J. Renner, K. Lohmann, A. C. Willis , *Org. Lett.* **2013**, *15*, 2616; (b) D. S. Roman , Y. Takahashi, A. B. Charette, *Org. Lett.* **2011**, *13*, 3242; (c) David B. Guthrie and Dennis P. Curran, *Org. Lett.*, **2009**, *11*, 249. d) C. Ma , X. Liu , X. Li , J. Flippen-Anderson , S. Yu, J. M. Cook, *J. Org. Chem.* **2001**, *66*, 4525.

[2] M. A. Biamonte, J. Shi, K. Hong, D. C. Hurst, L. Zhang, J. Fan, D. J. Busch, P. L. Karjian, A. A. Maldonado, J. L. Sensintaffar, Y-C Yang, A. Kamal, R. E. Lough, K. Lundgren, F. J. Burrows, G. A. Timony, M. F. Boehm, S. R. Kasibhatla, *J. Med. Chem.* **2006**, *49*, 817-828

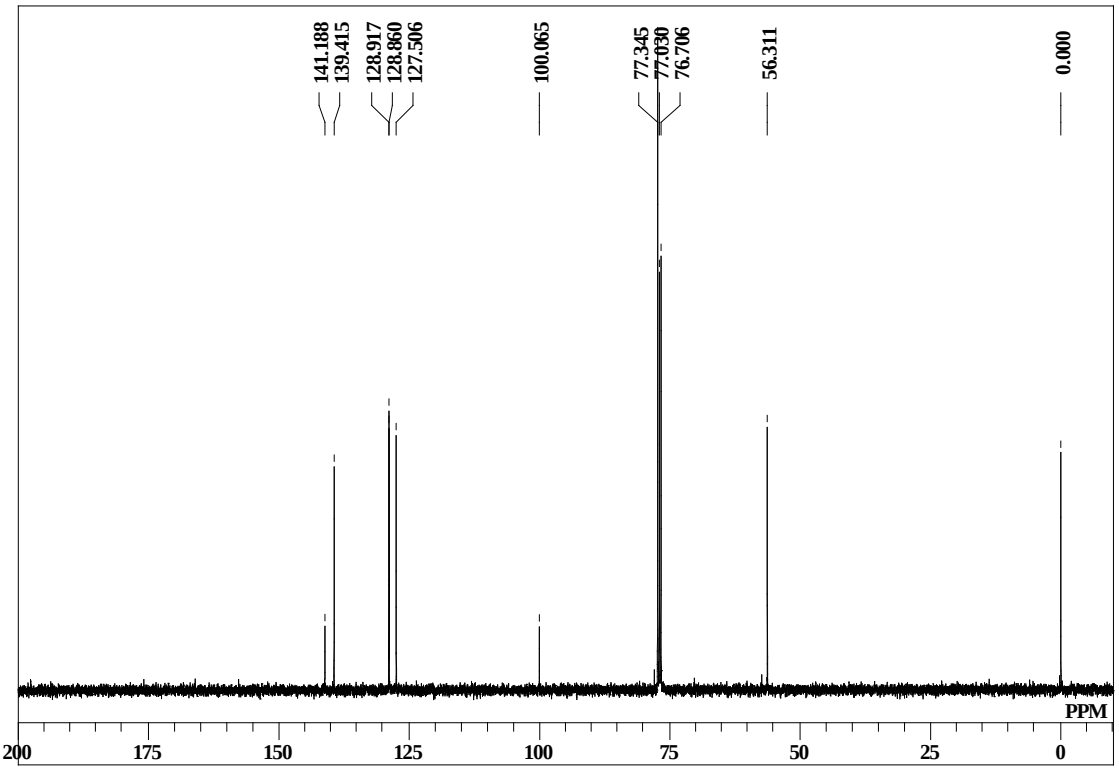
[3] I. Nakamura, T. Sato, Y. Yamamoto, *Angew. Chem. Int. Ed.* **2006**, *45*, 4473.

5. ^{1}H and ^{13}C NMR spectra

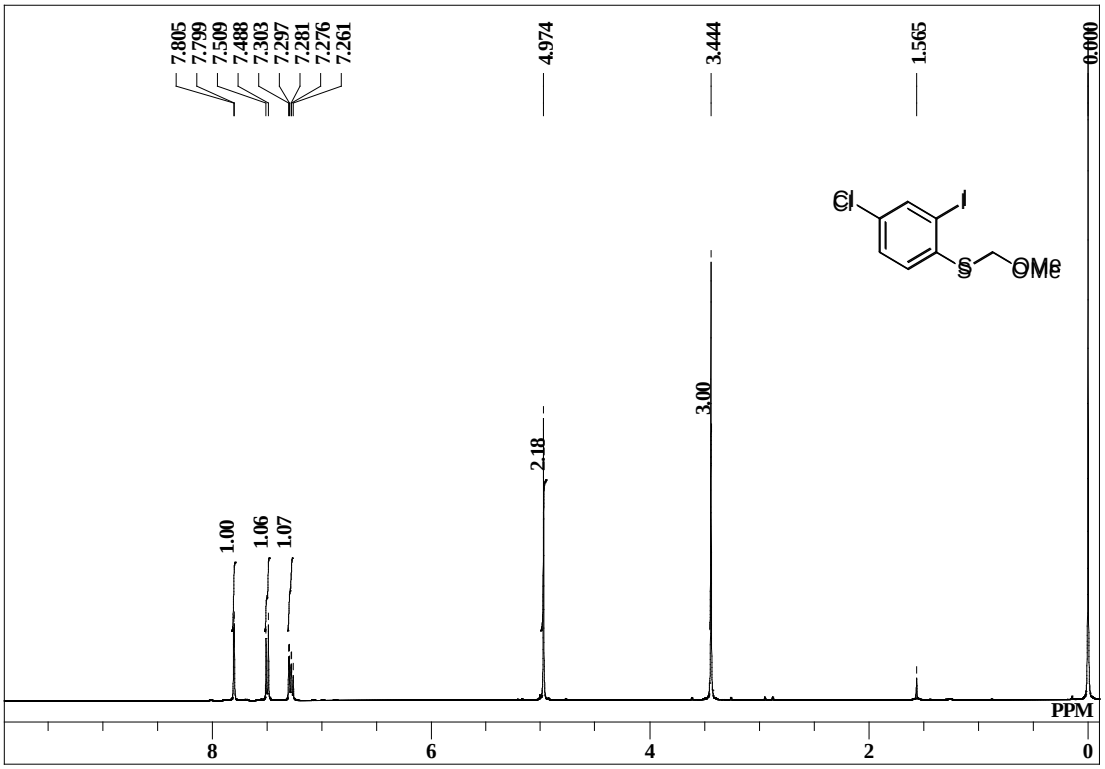
5a single_pulse



5a single pulse decoupled gated NOE



5n single_pulse



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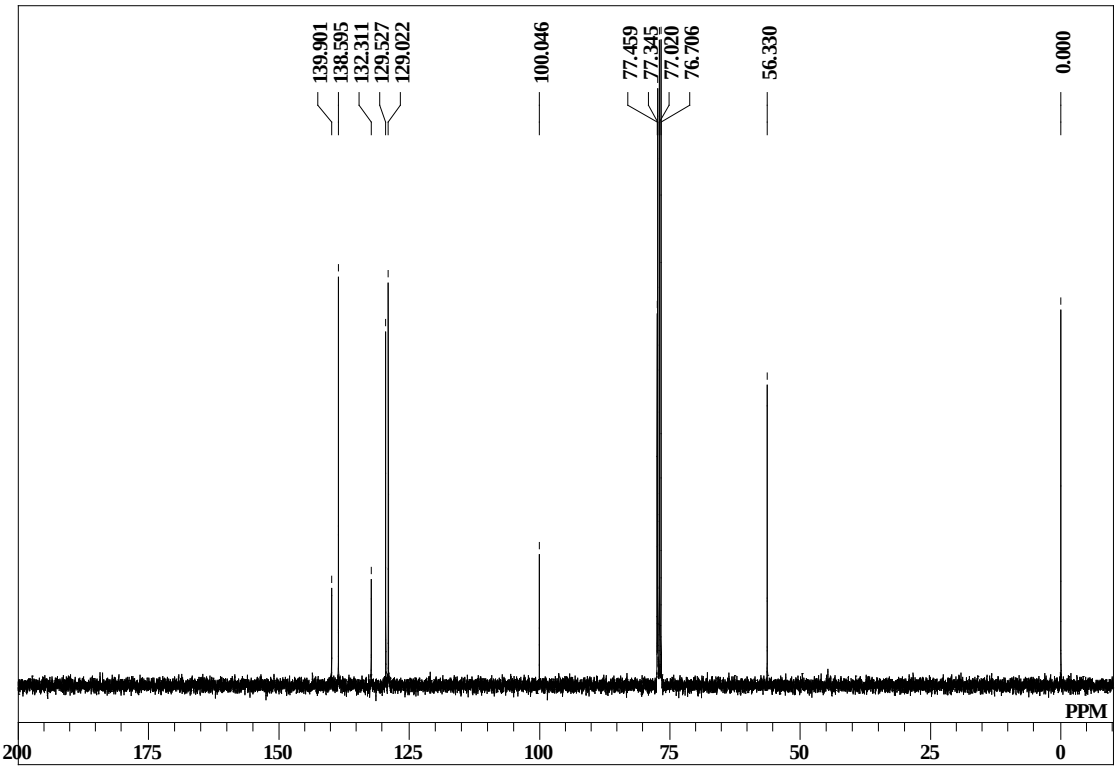

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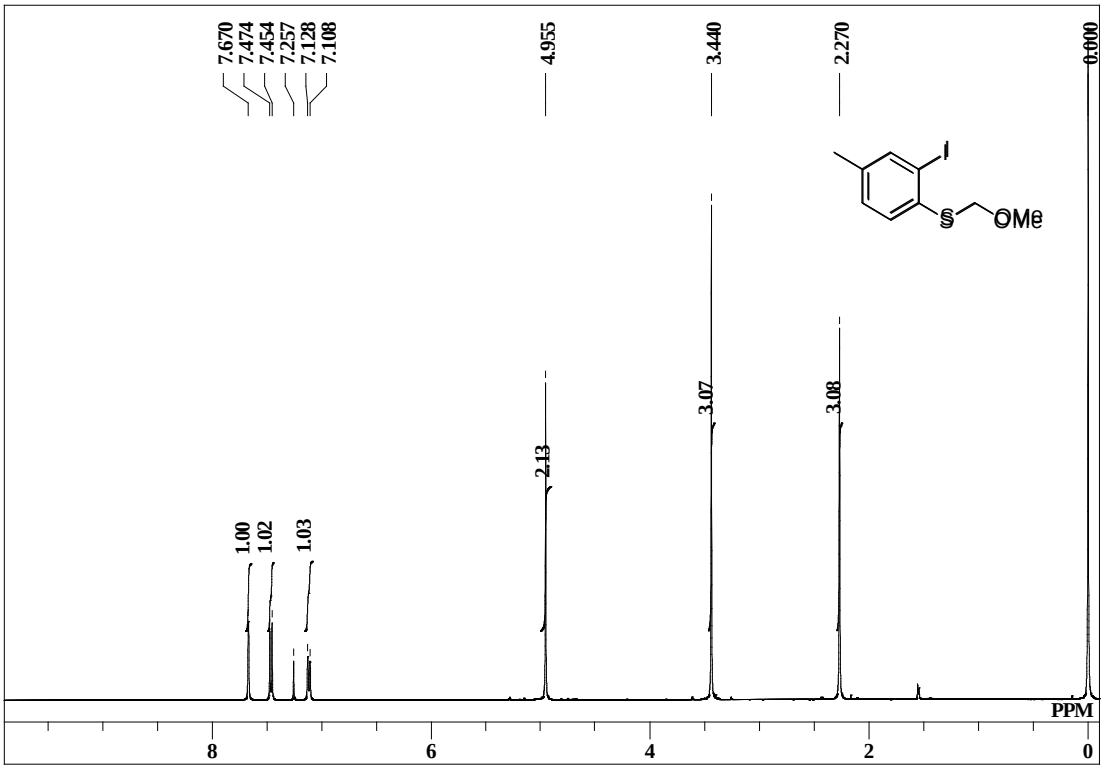

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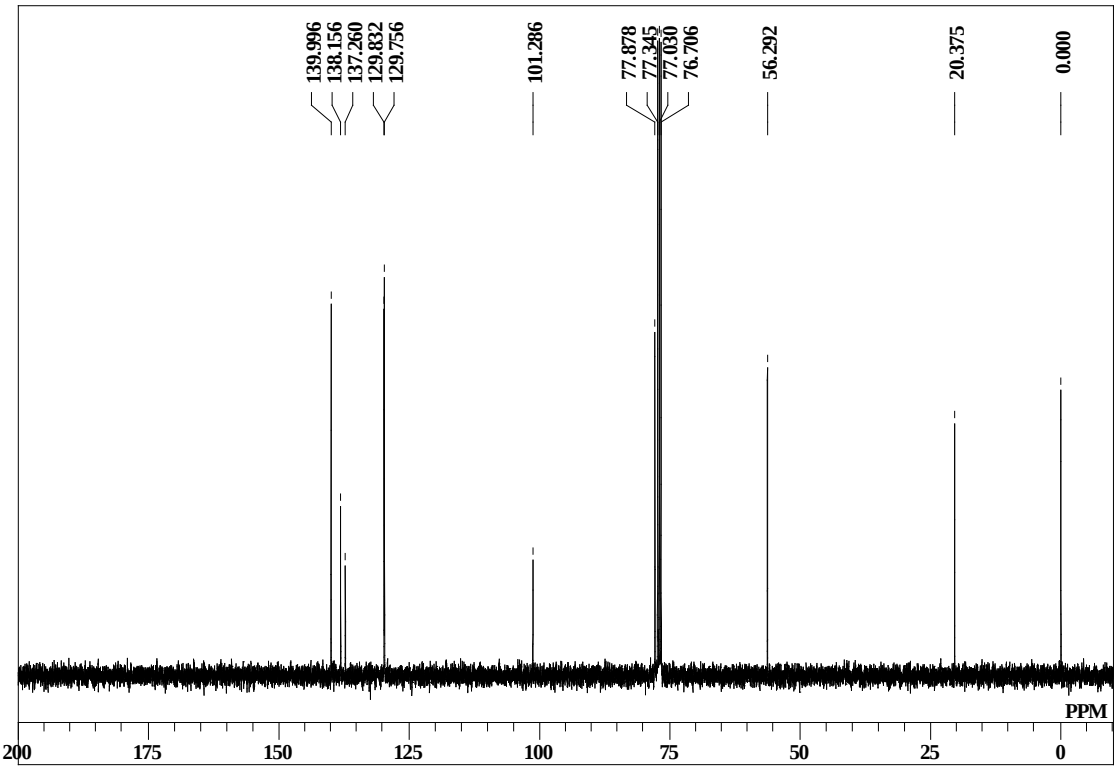
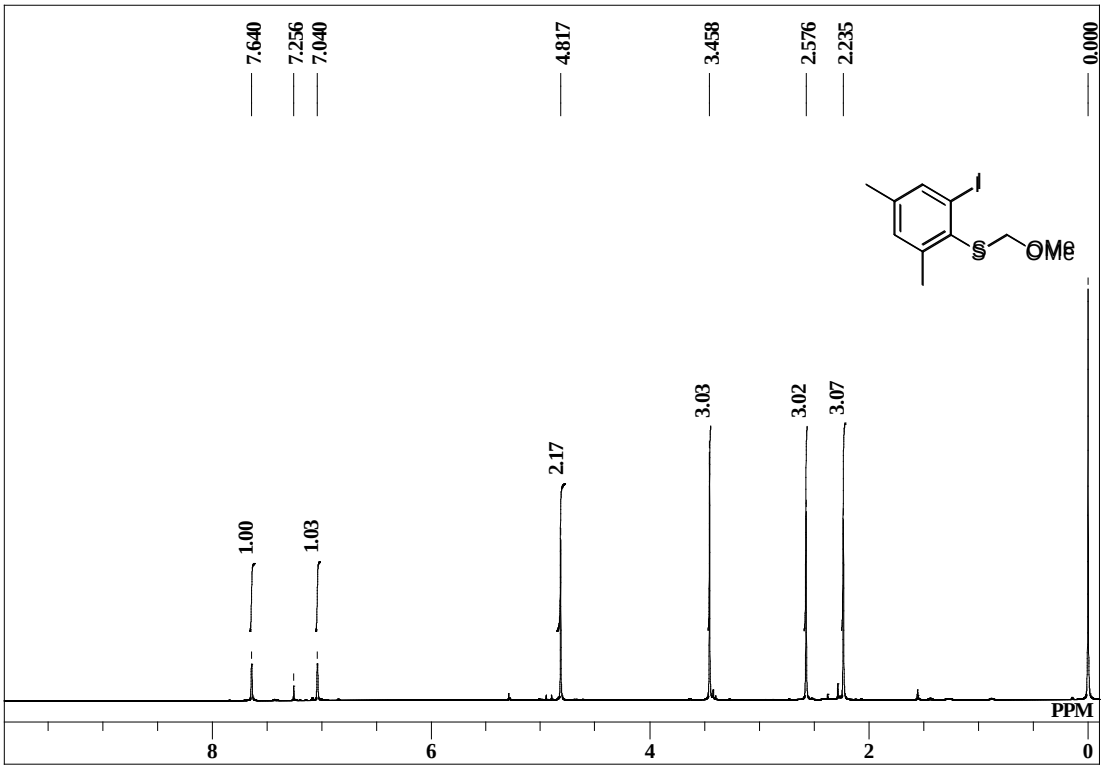
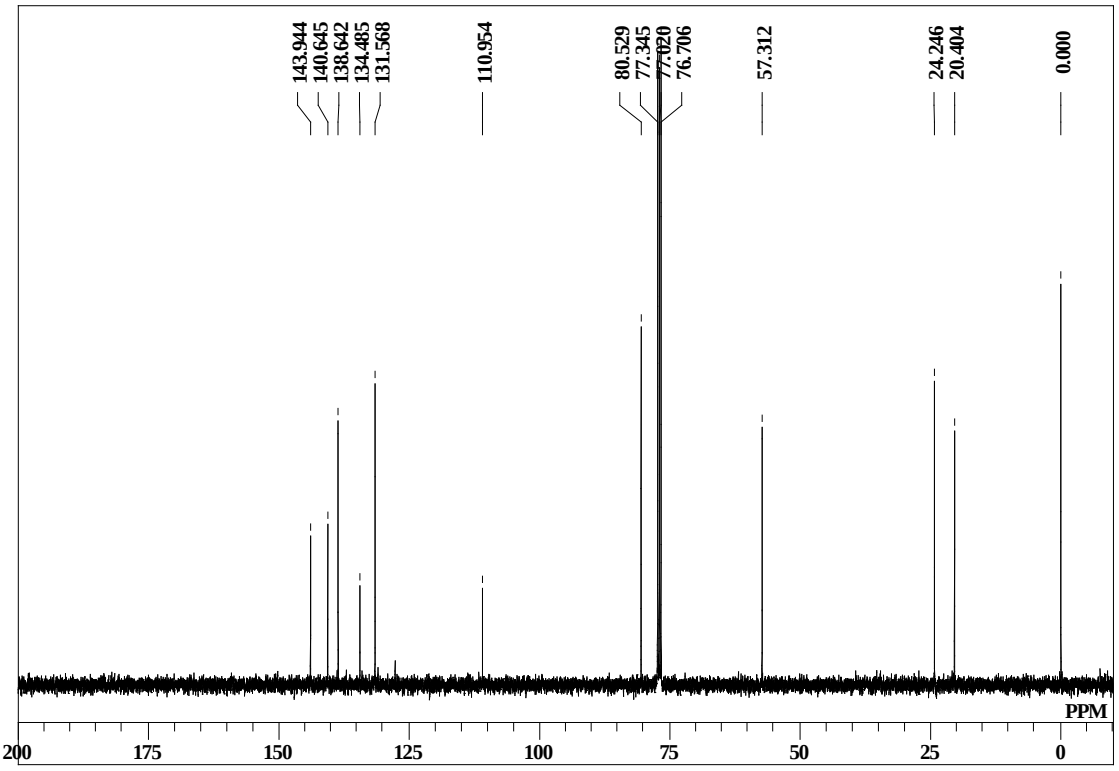


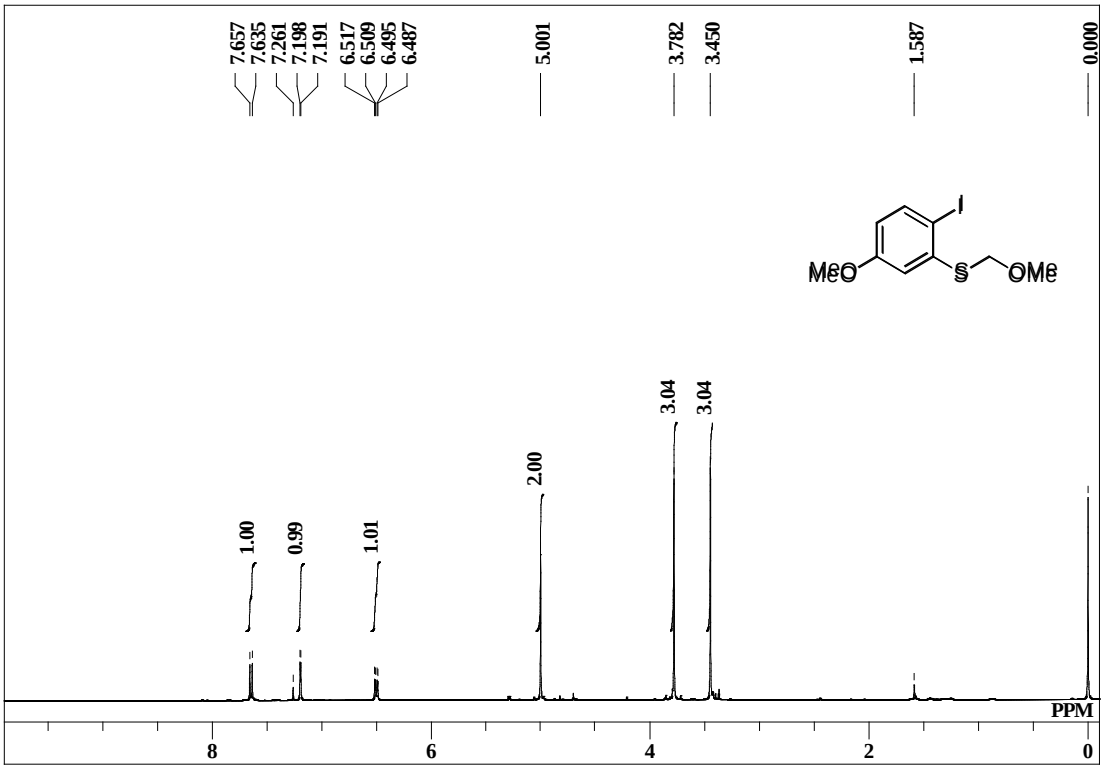
5q single_pulse



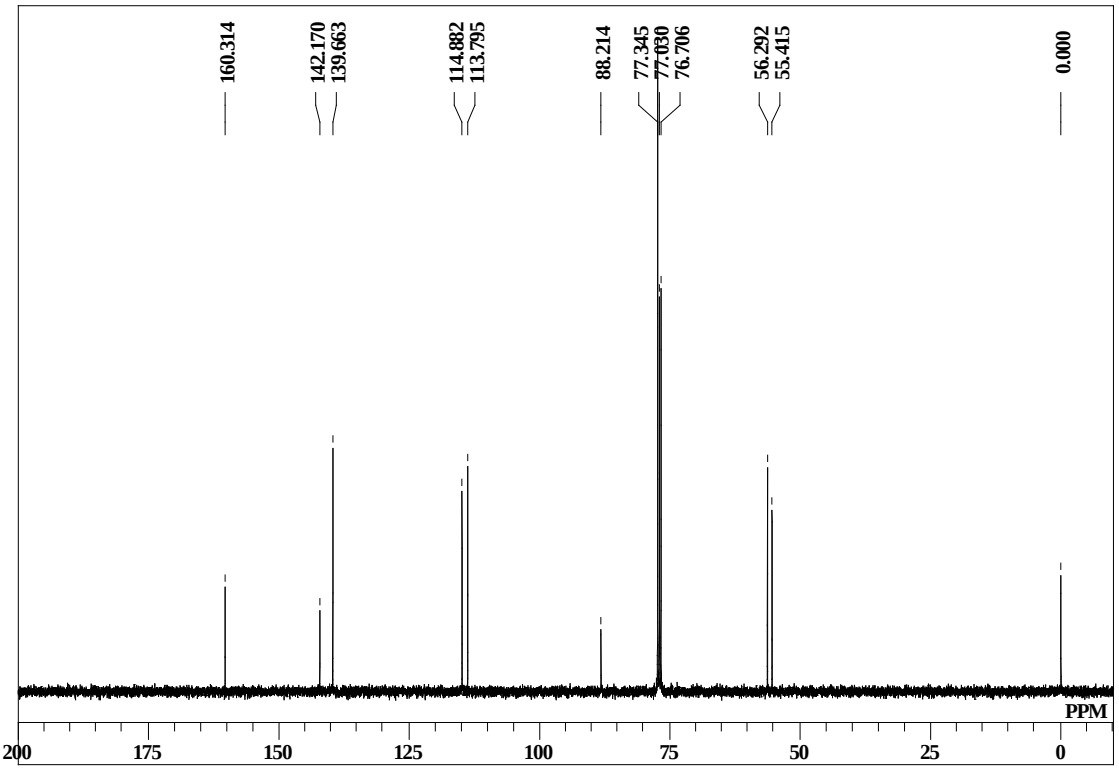
5q single pulse decoupled gated NOE



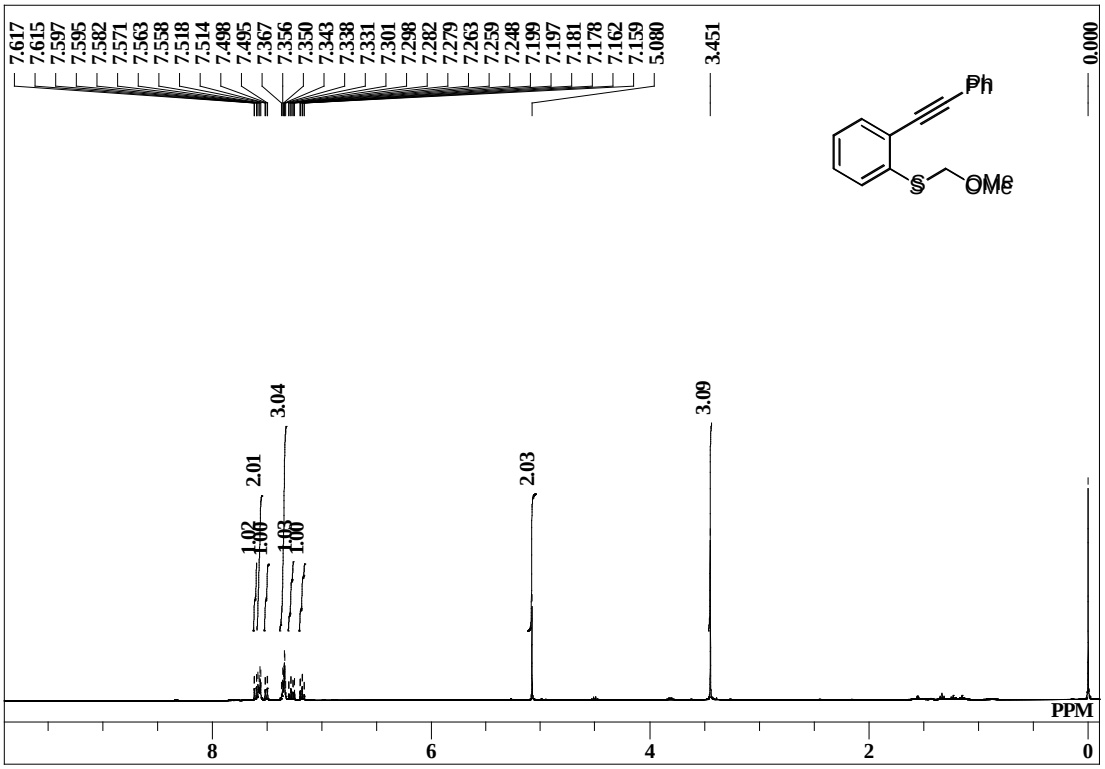
5r single_pulse



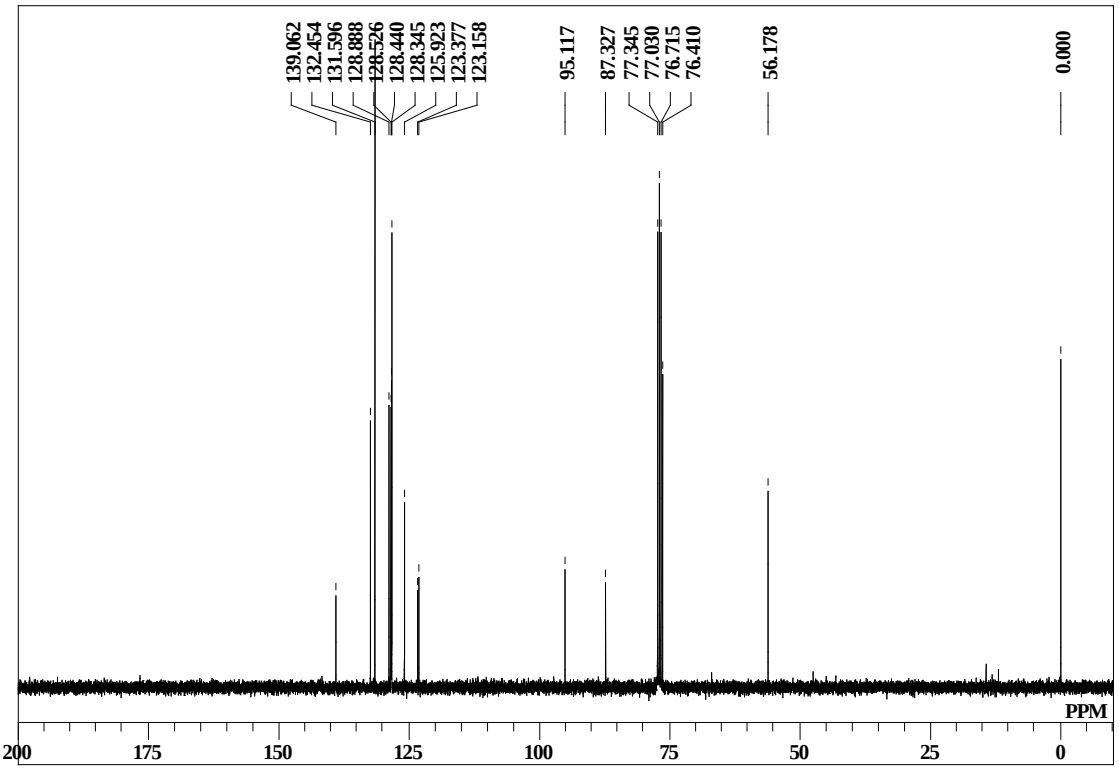
5r single pulse decoupled gated NOE



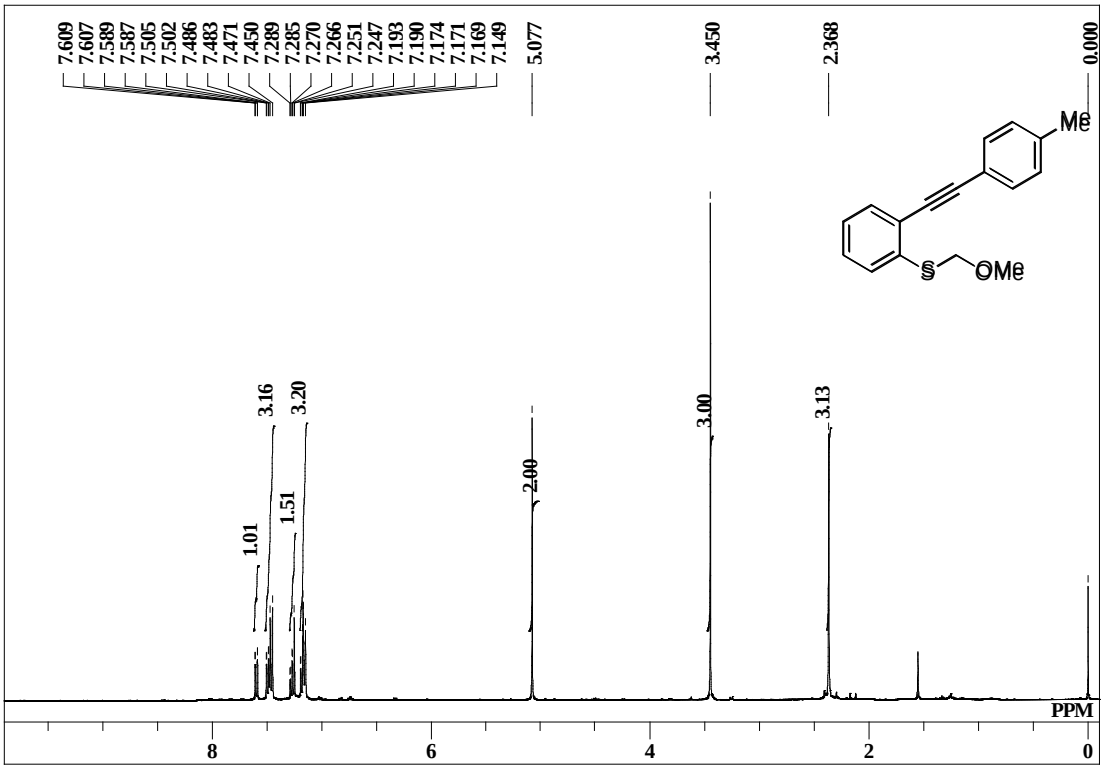
1a single_pulse



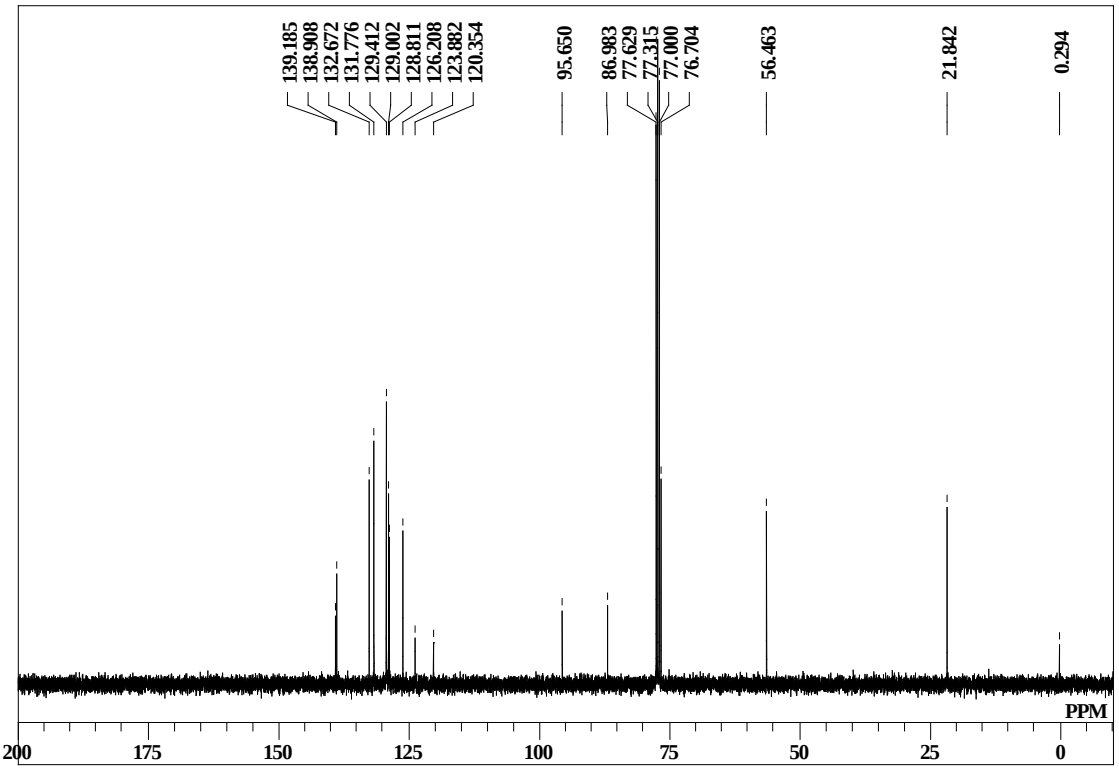
1a single pulse decoupled gated NOE



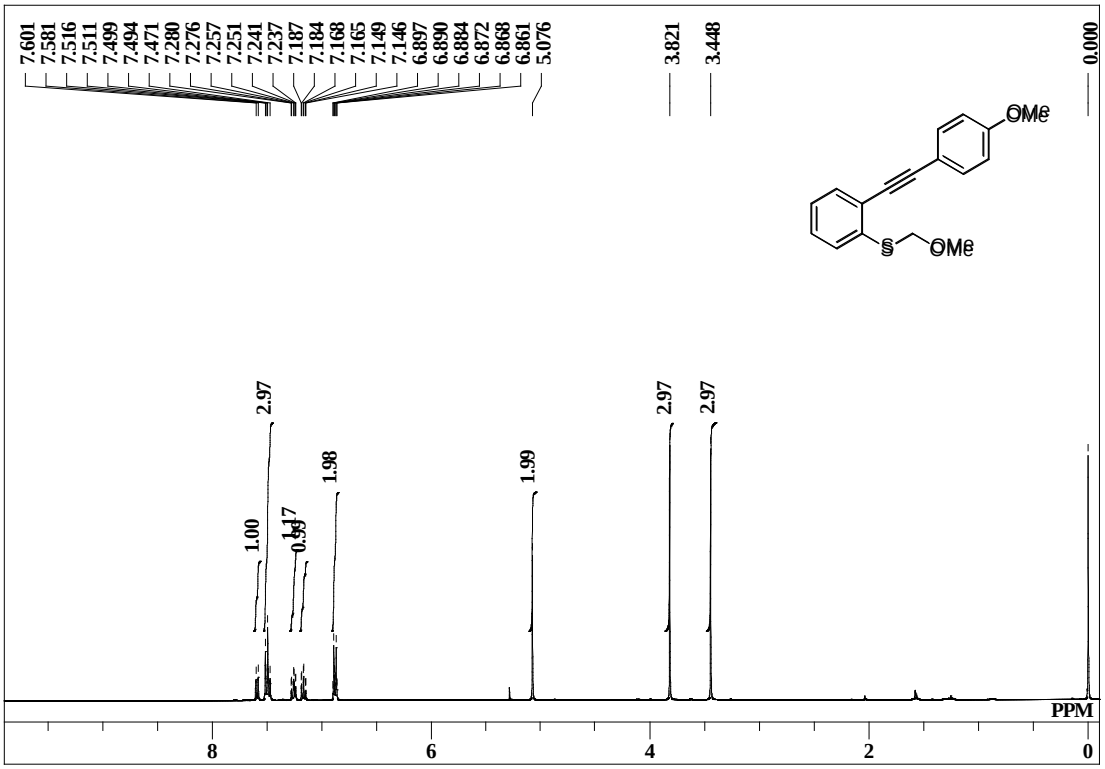
1b single_pulse



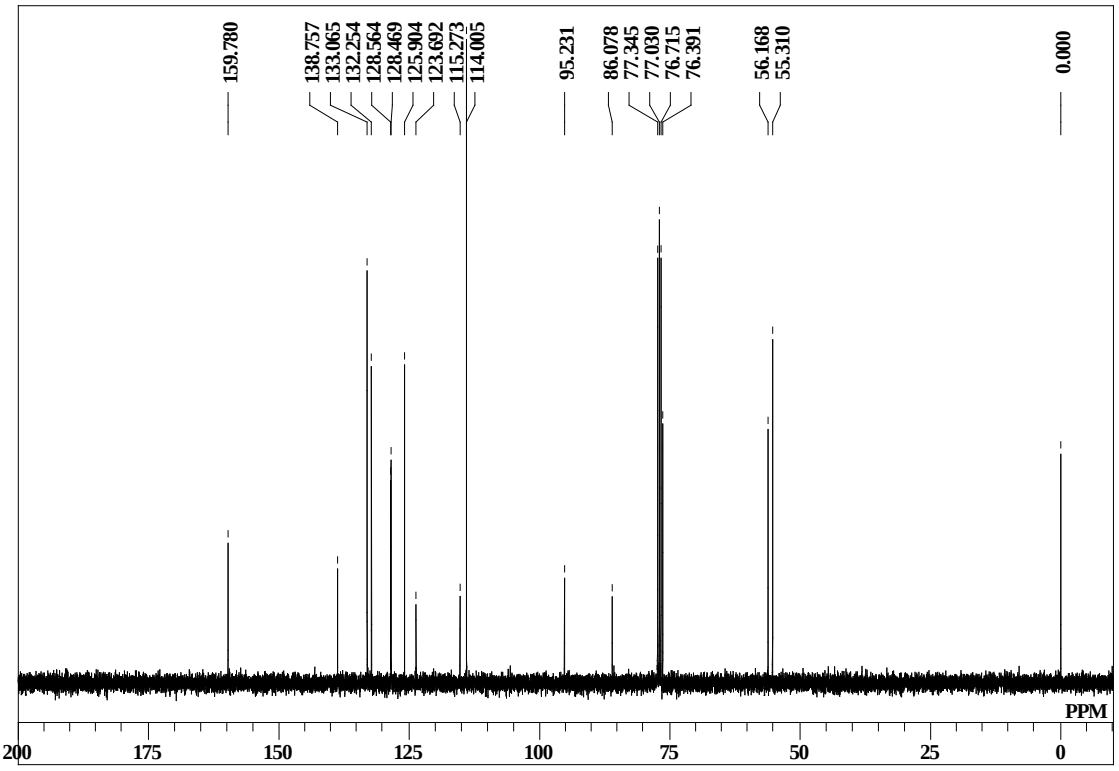
1b single pulse decoupled gated NOE



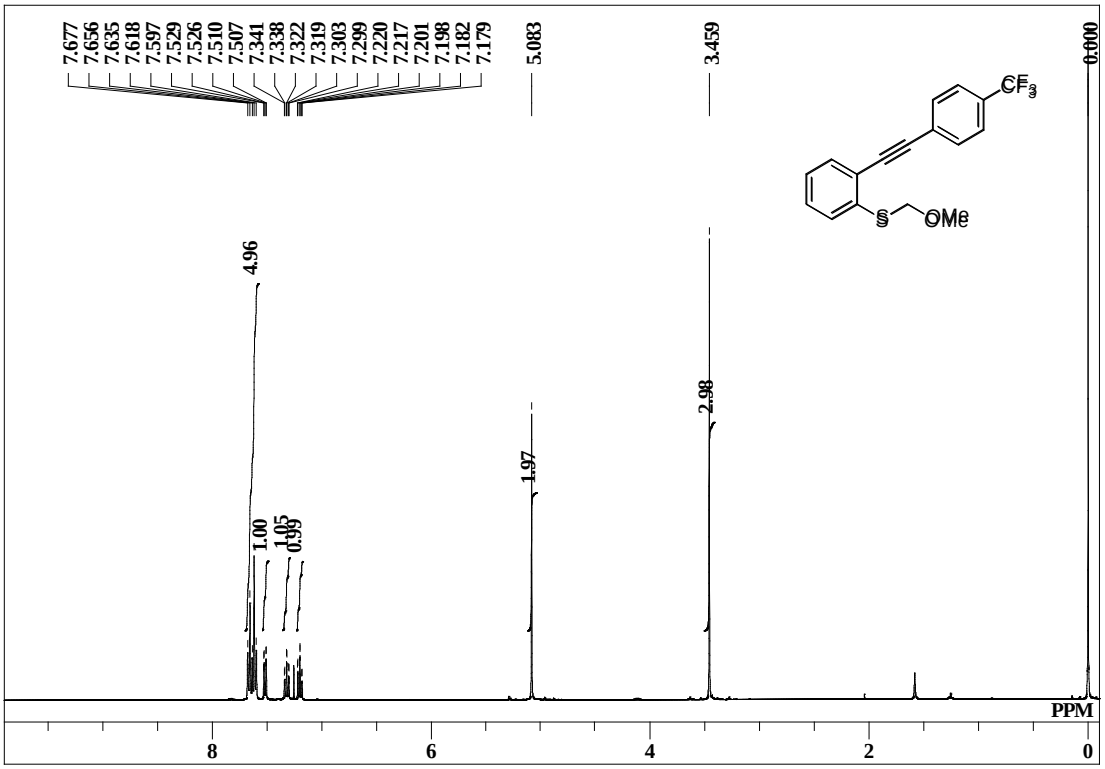
1c single_pulse



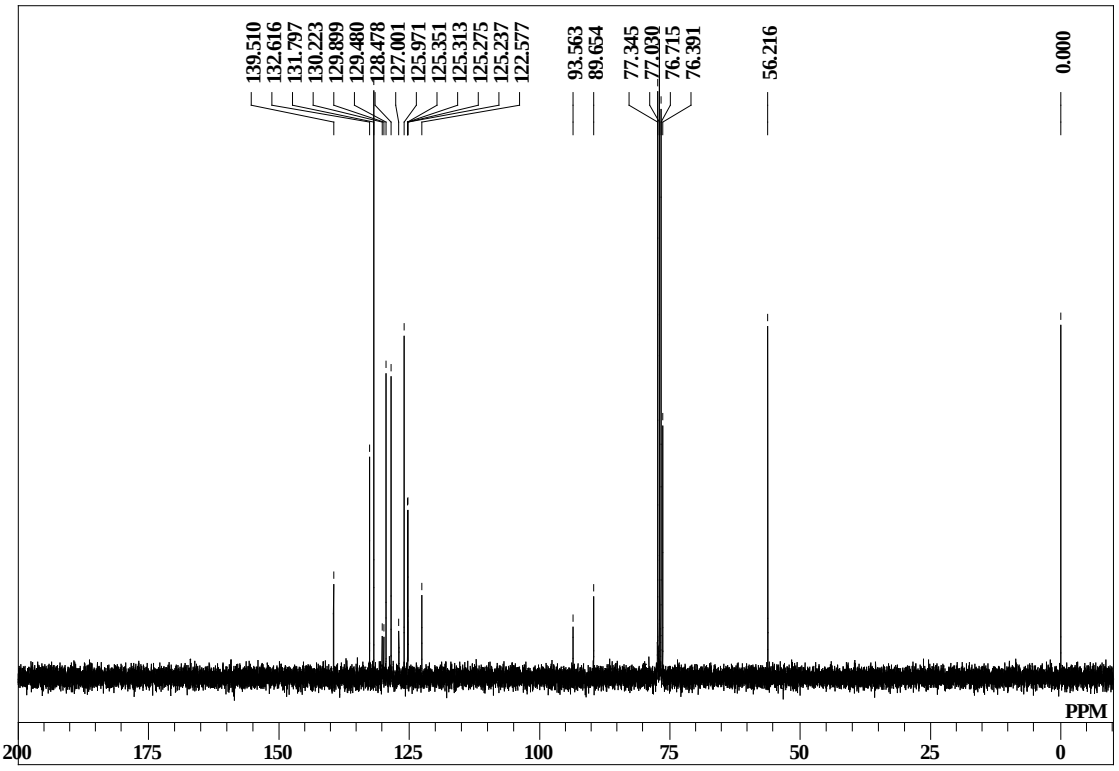
1c single pulse decoupled gated NOE



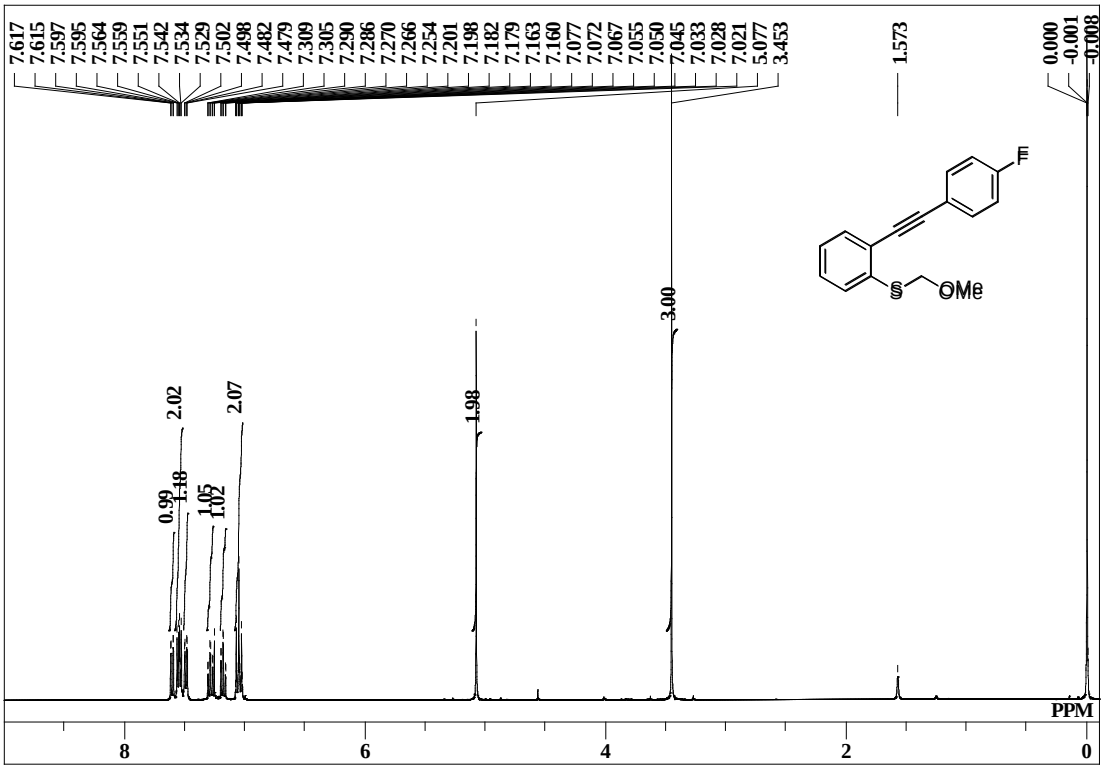
1d single_pulse



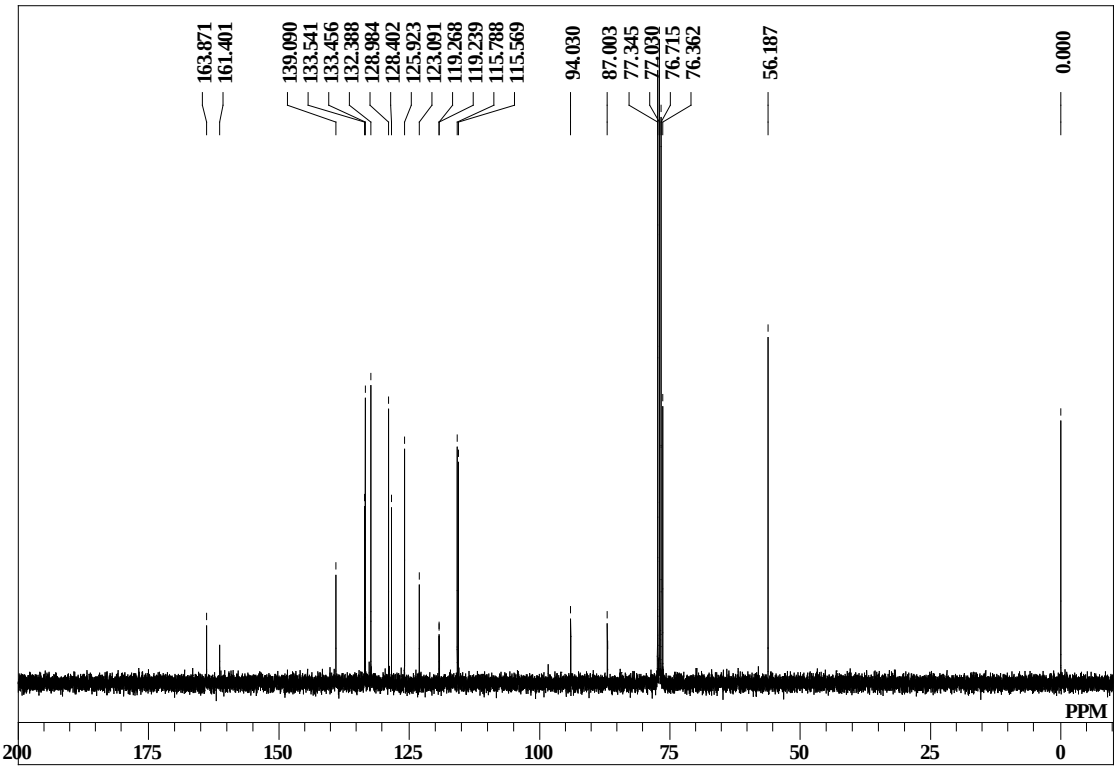
1d single pulse decoupled gated NOE



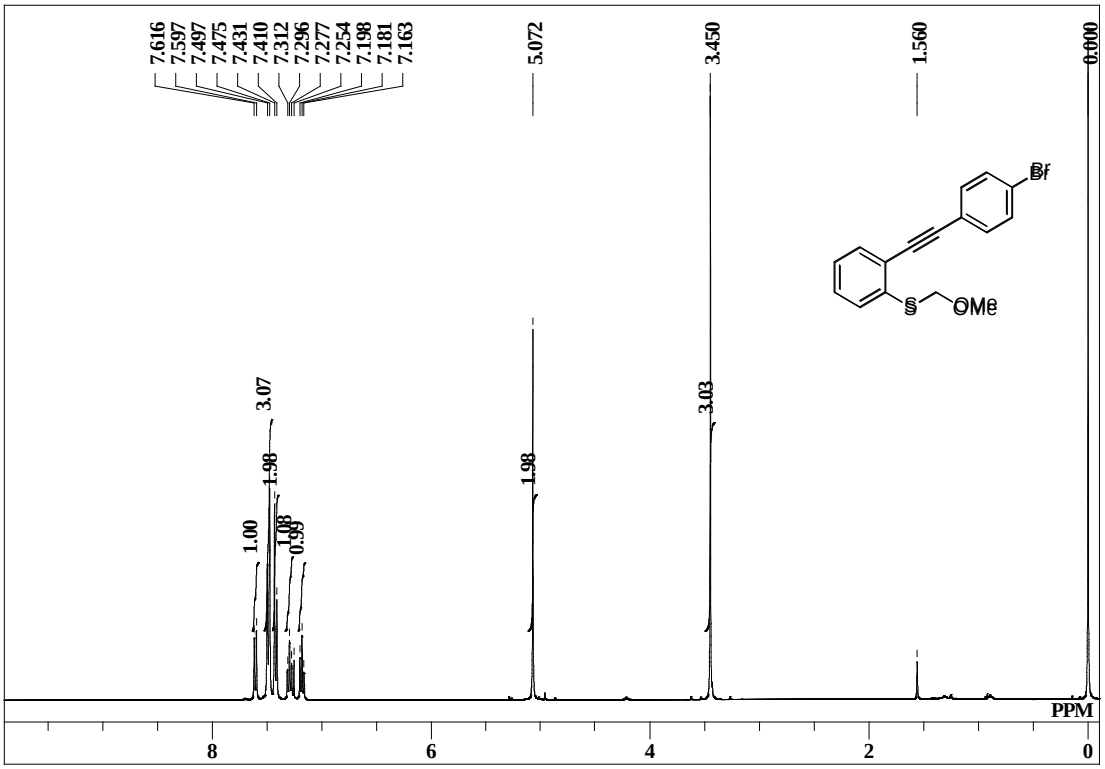
1e single_pulse



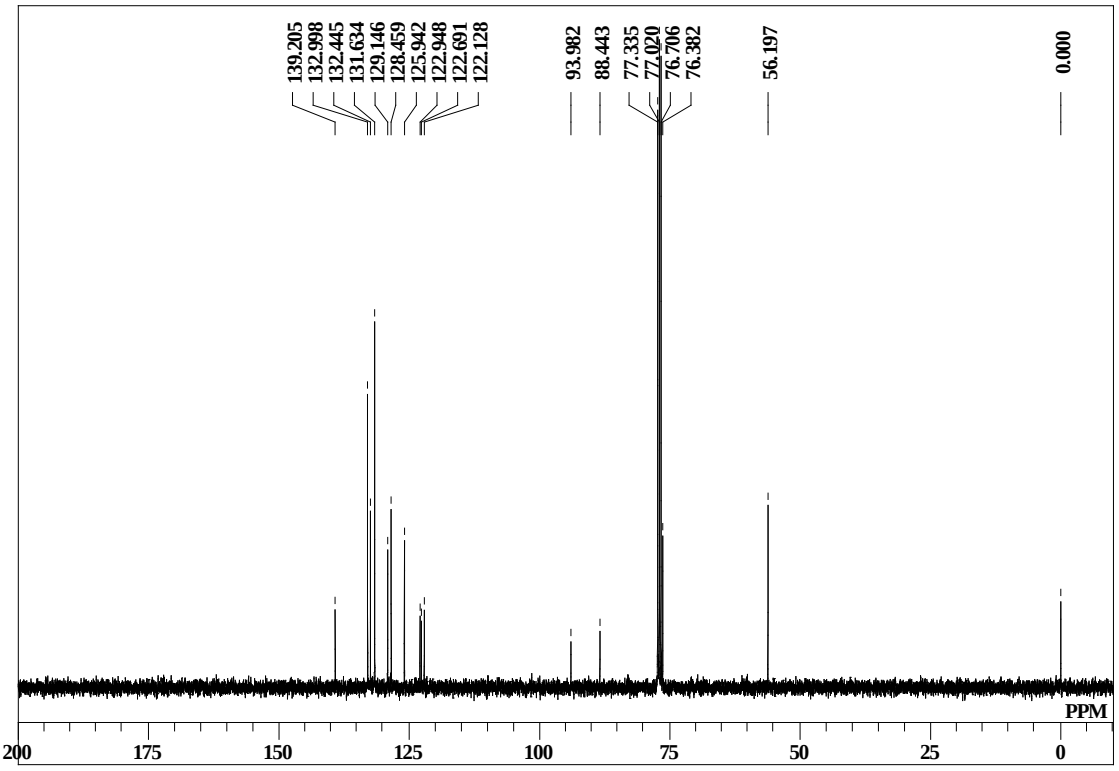
1e single pulse decoupled gated NOE



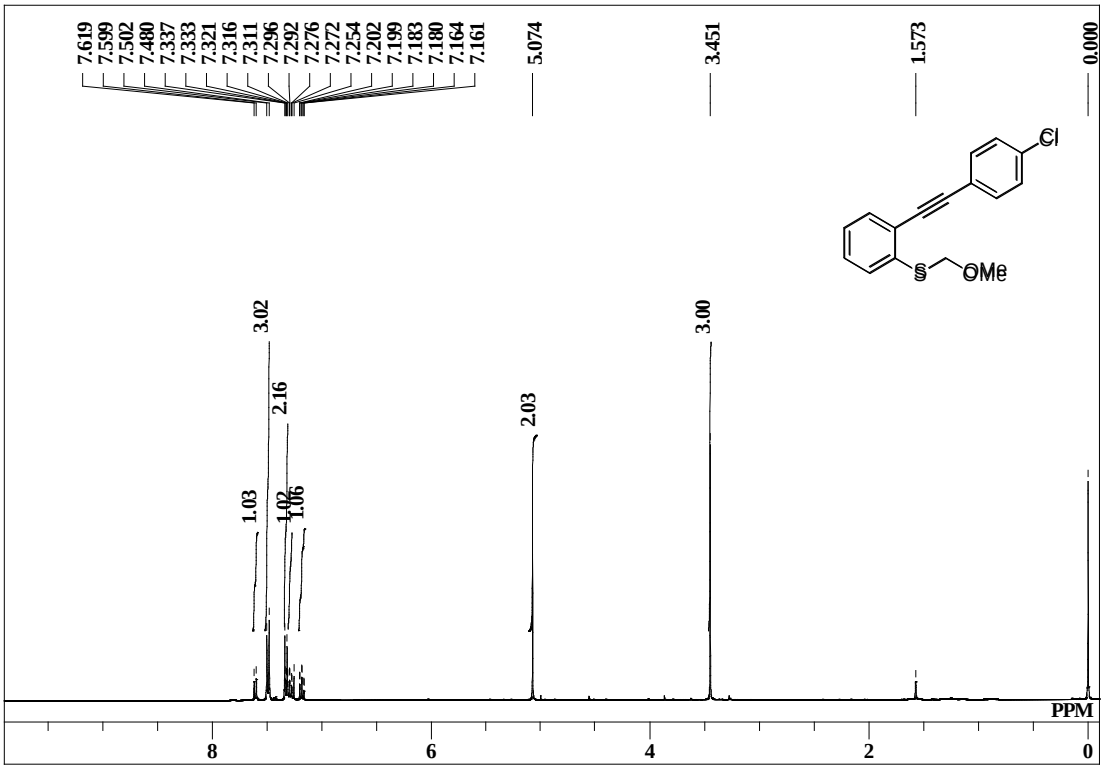
1f single_pulse



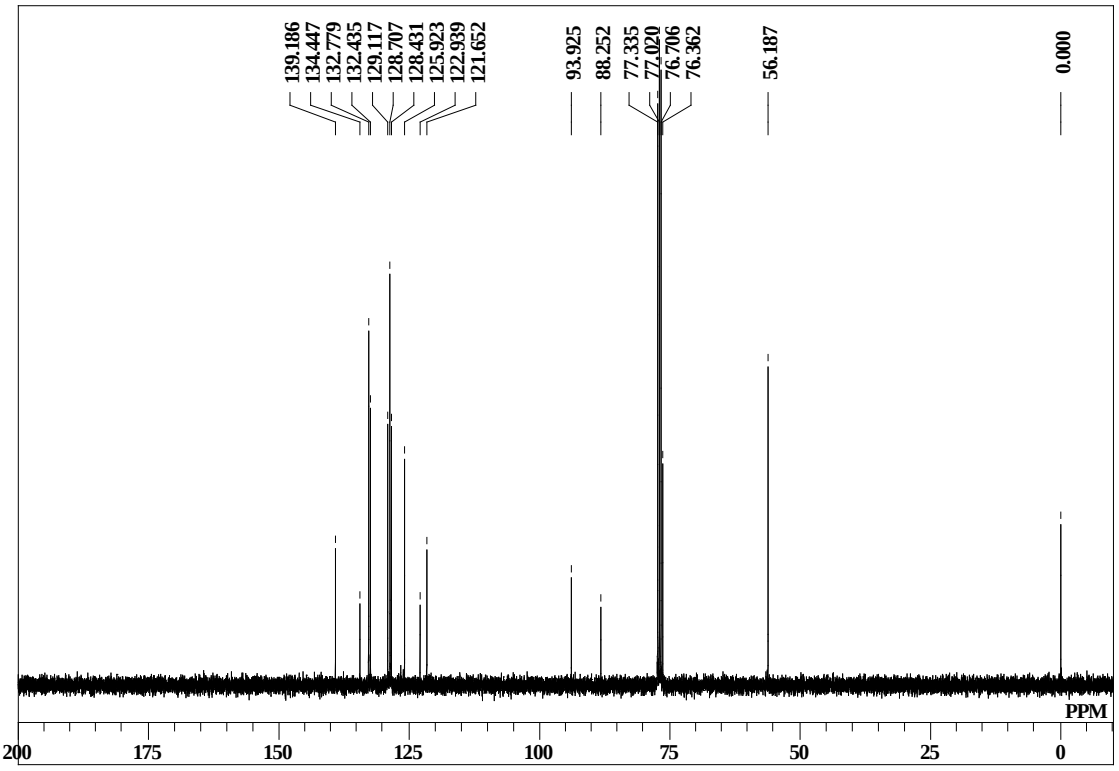
1f single pulse decoupled gated NOE



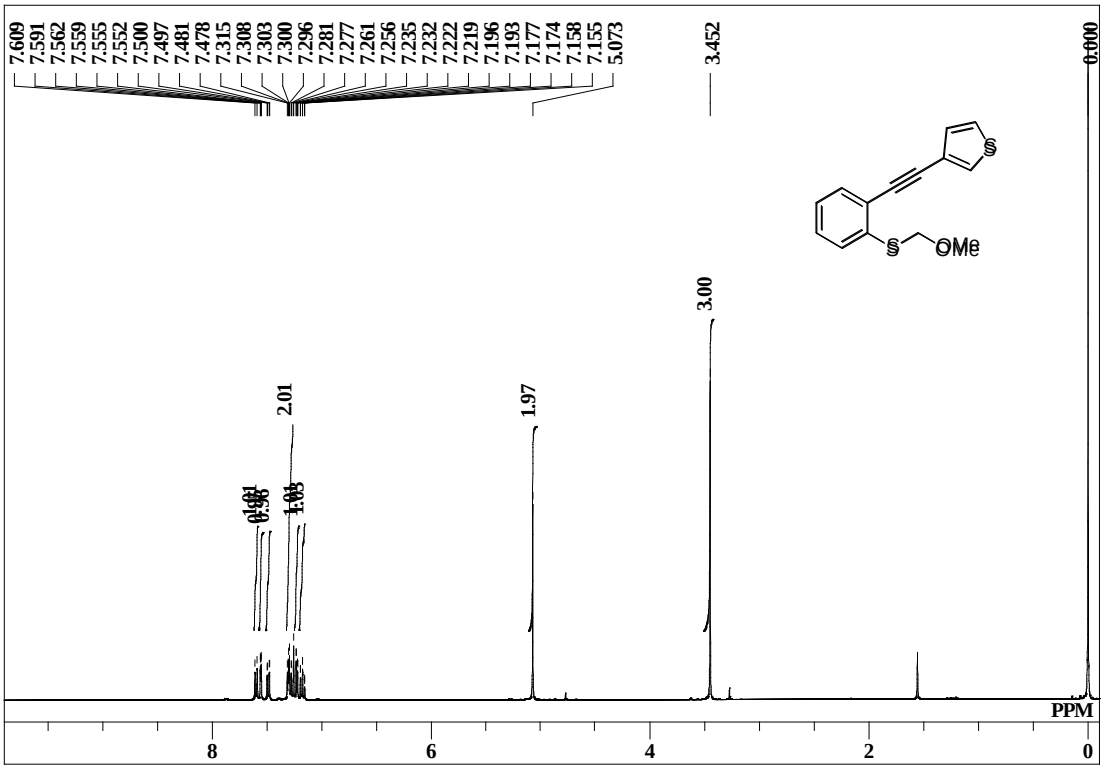
1g single_pulse



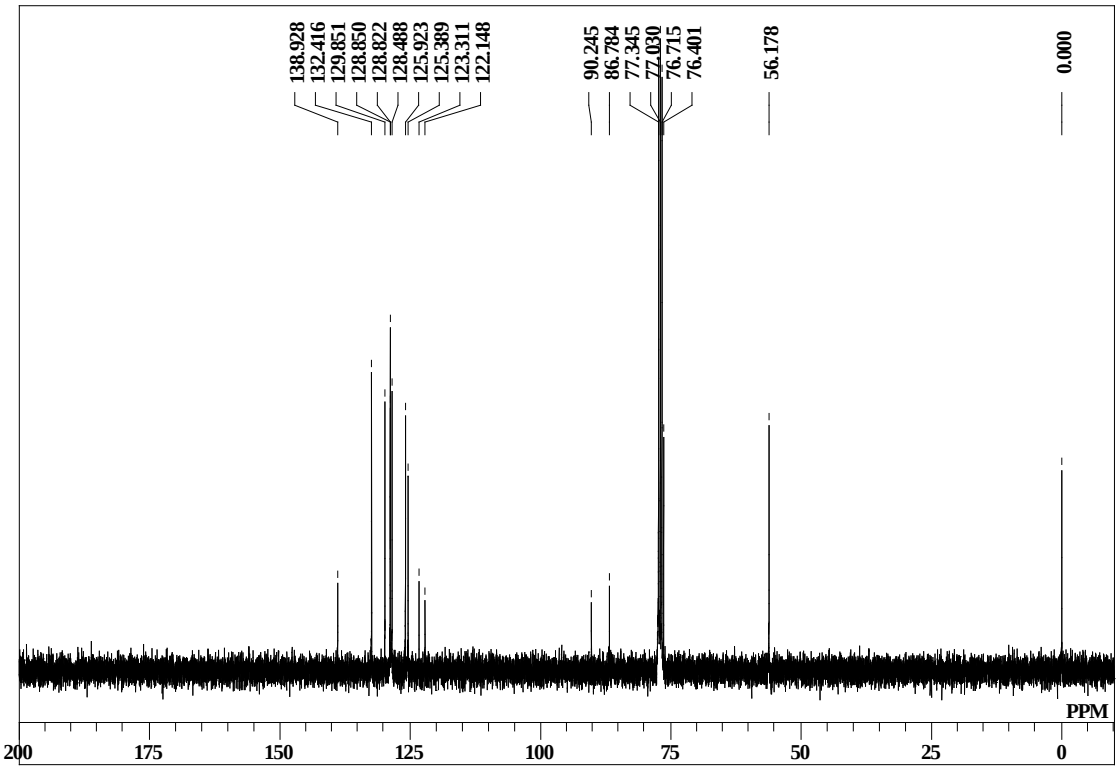
1g single pulse decoupled gated NOE



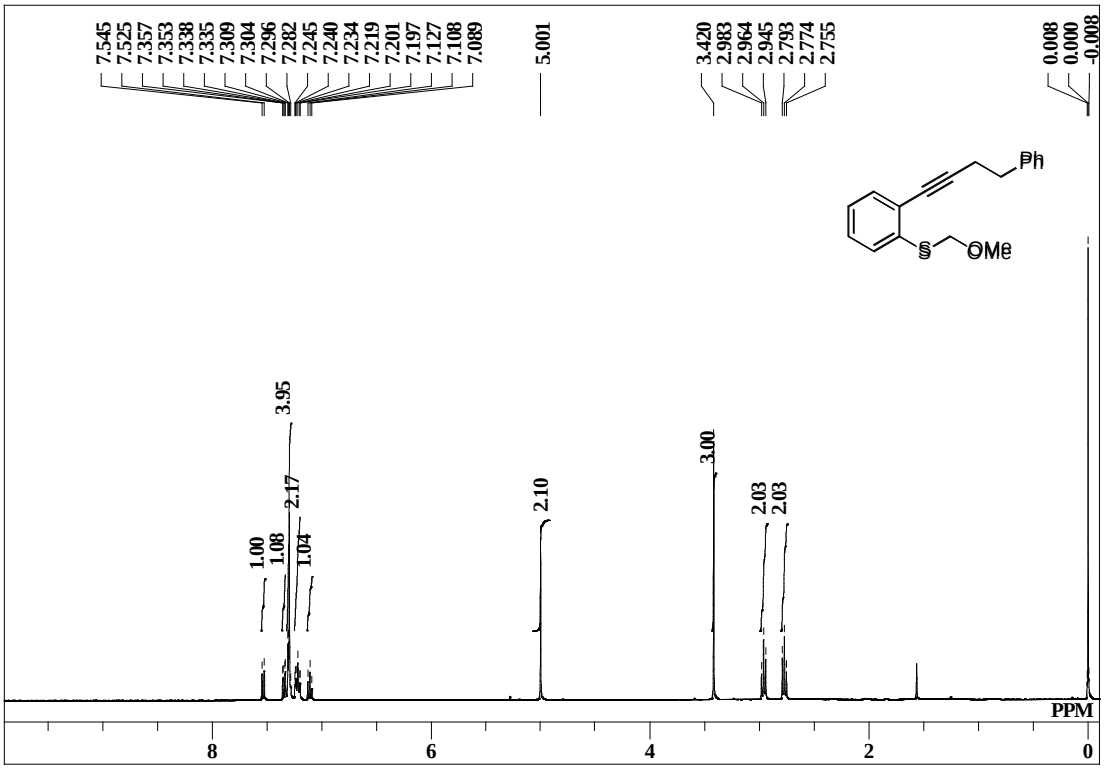
1h single_pulse



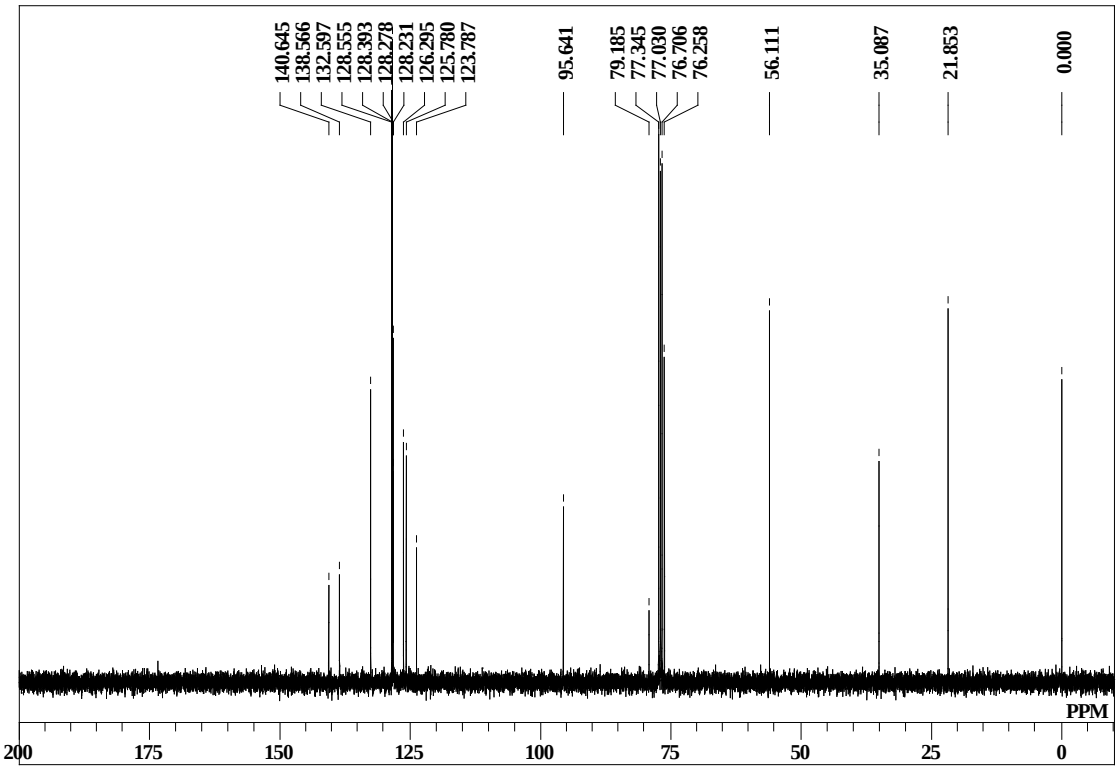
1h single pulse decoupled gated NOE



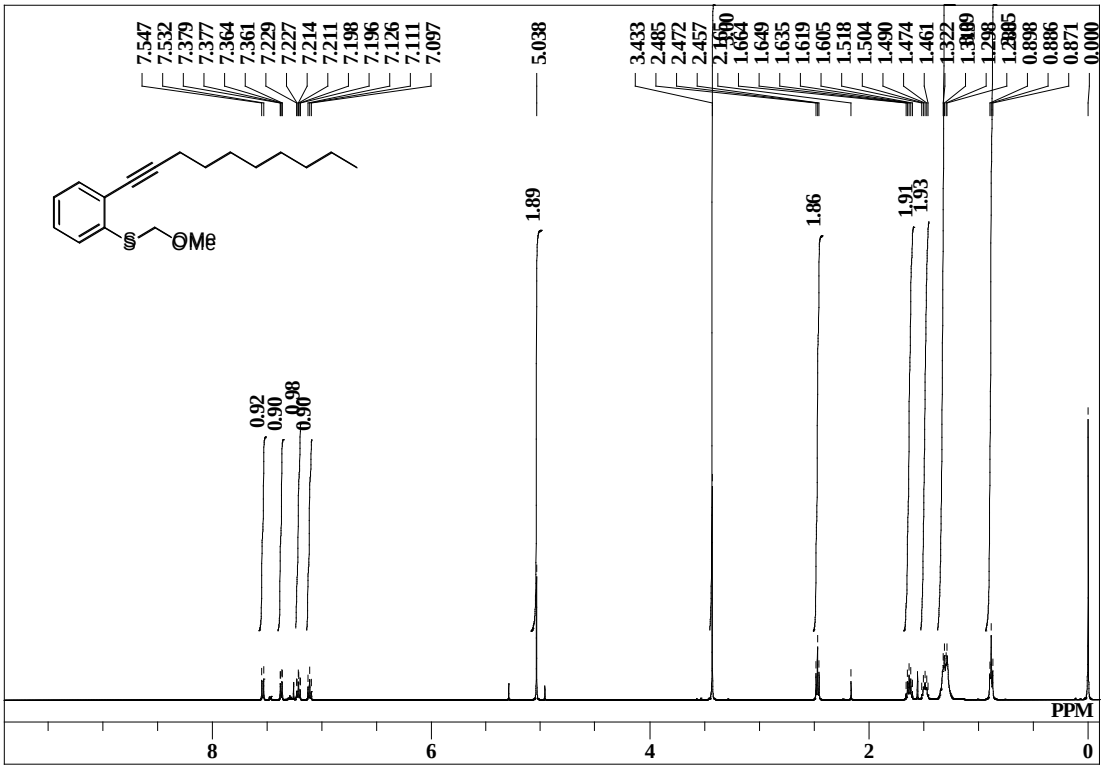
1i single_pulse



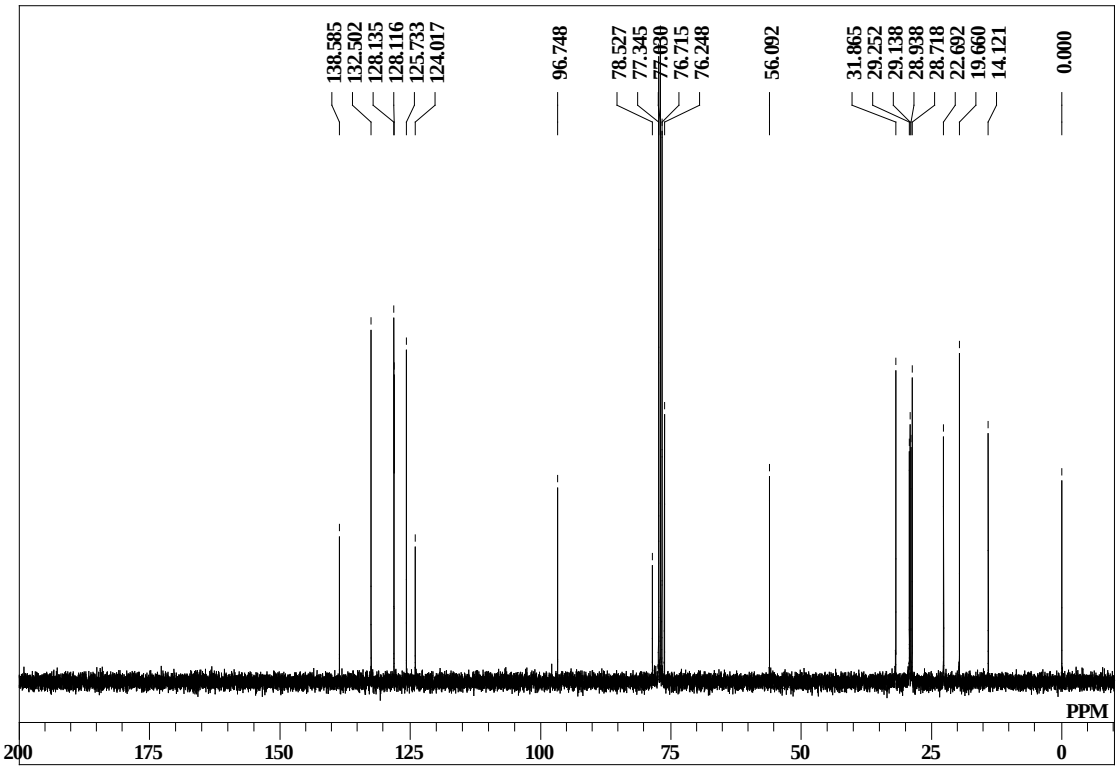
1i single pulse decoupled gated NOE



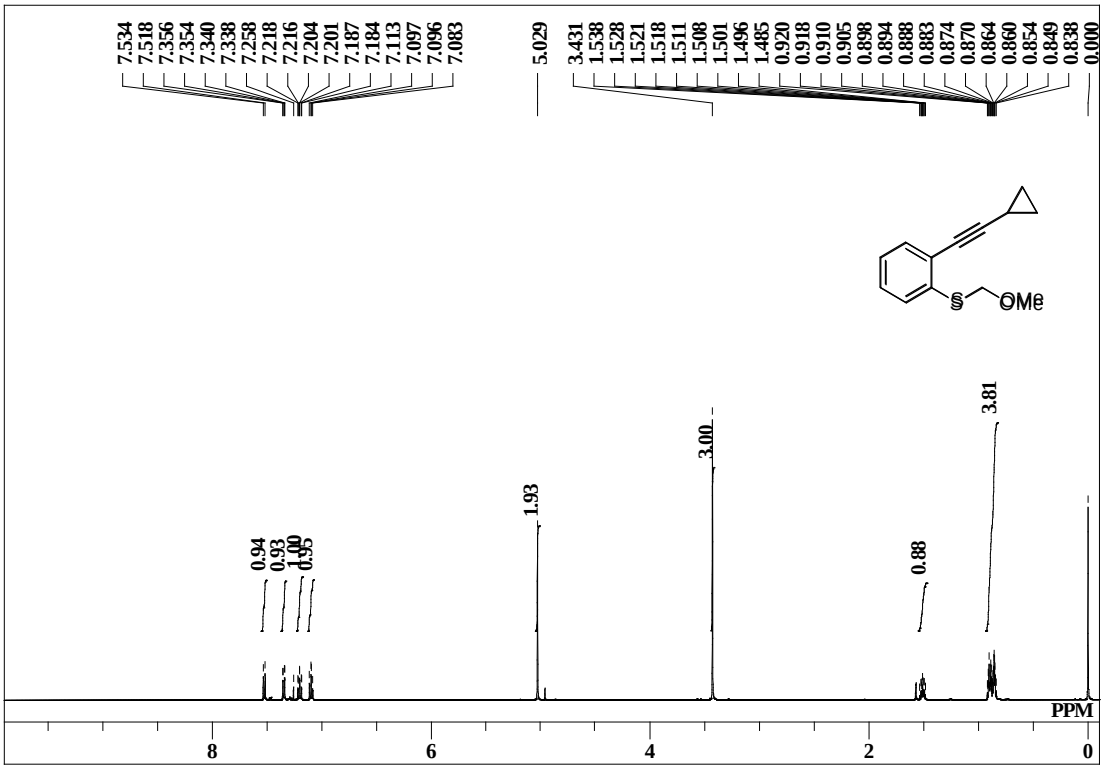
1j Single Pulse Experiment



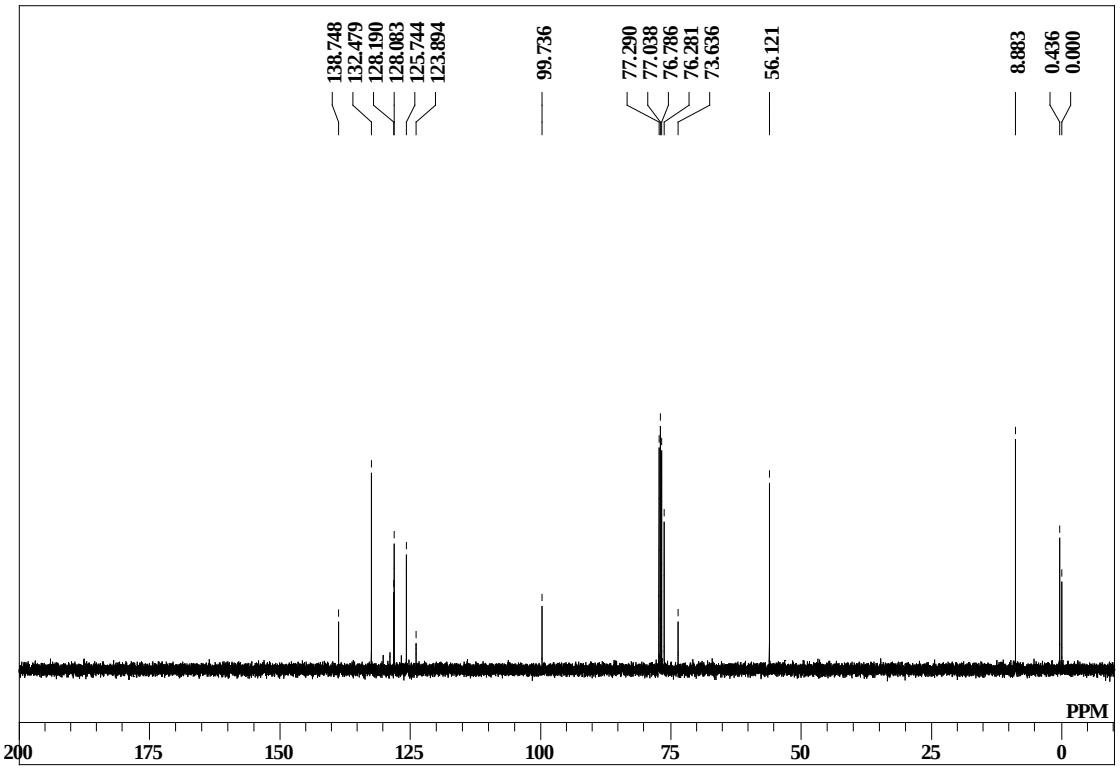
1j single pulse decoupled gated NOE



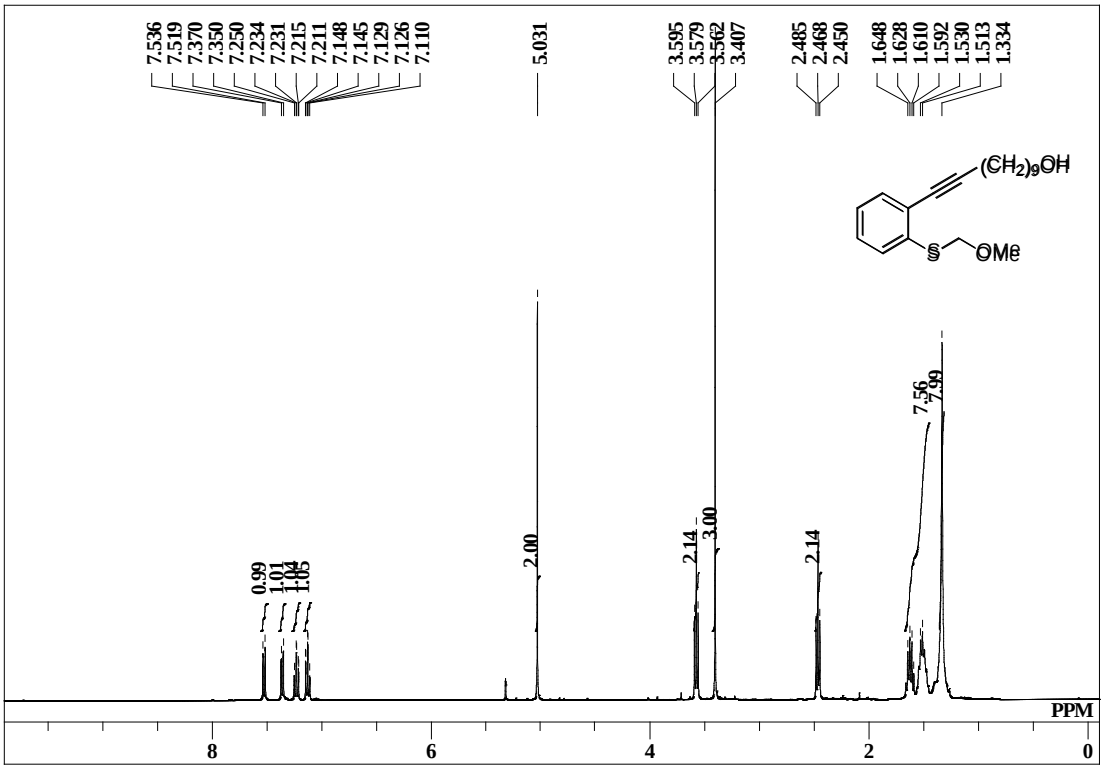
1k Single Pulse Experiment



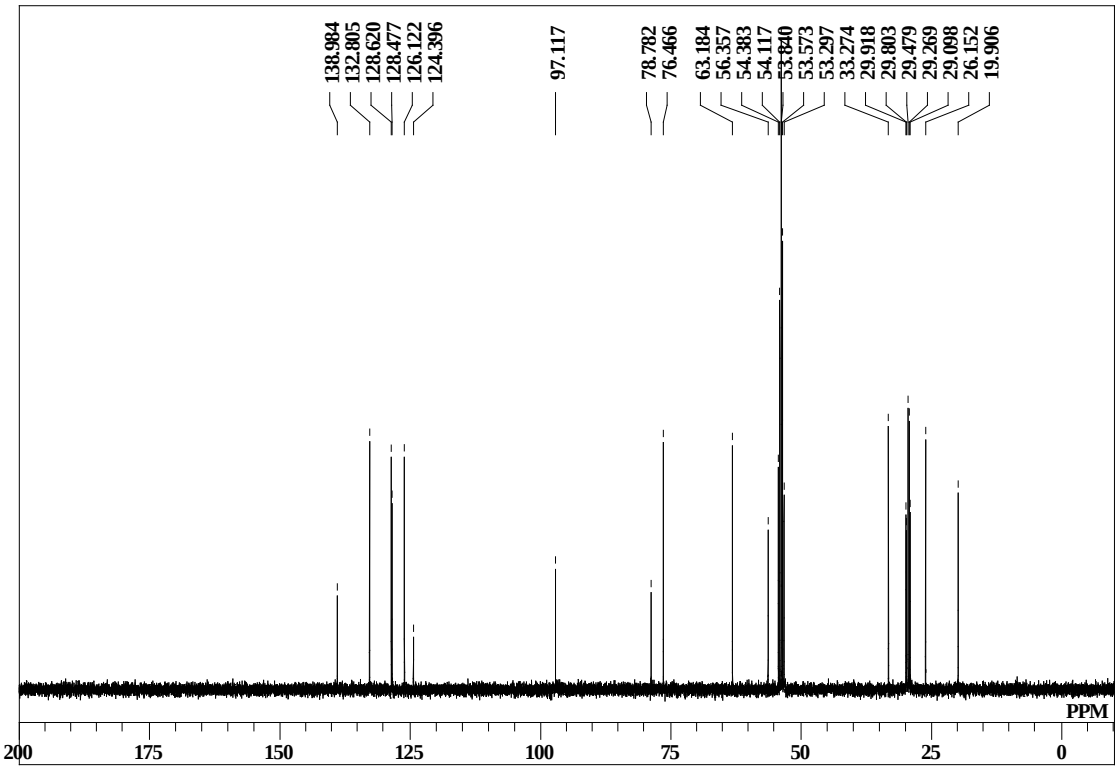
1k Single Pulse with Broadband Decoupling



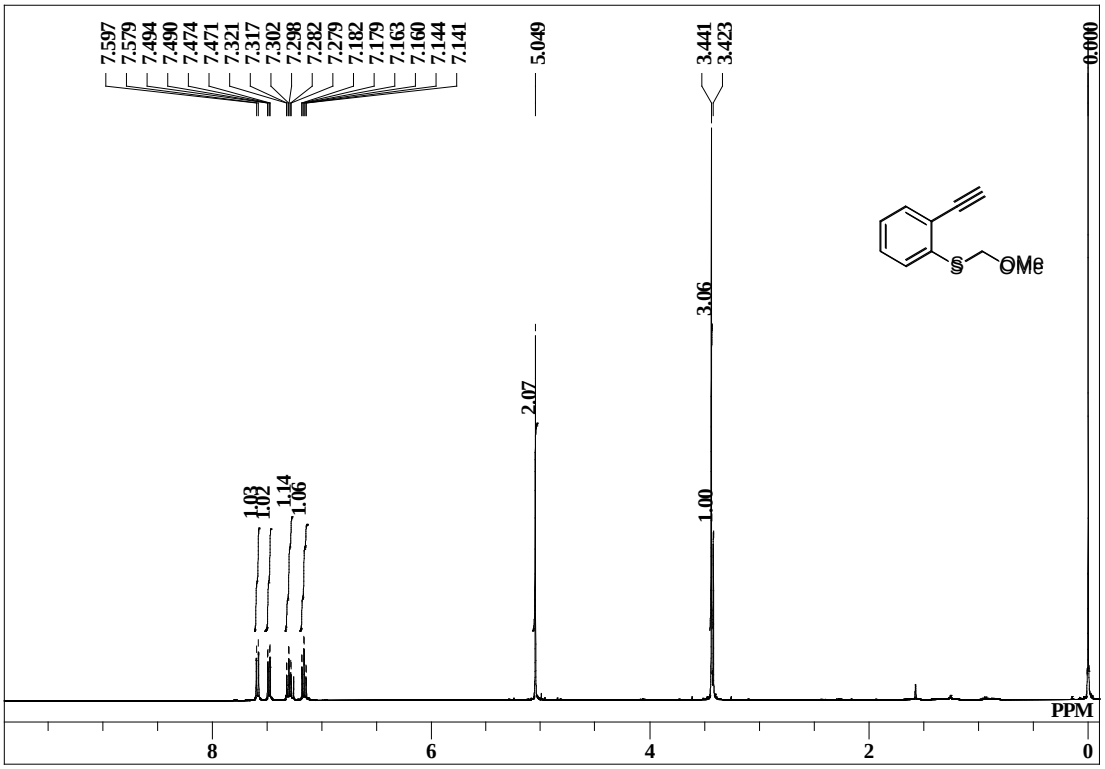
1l single_pulse



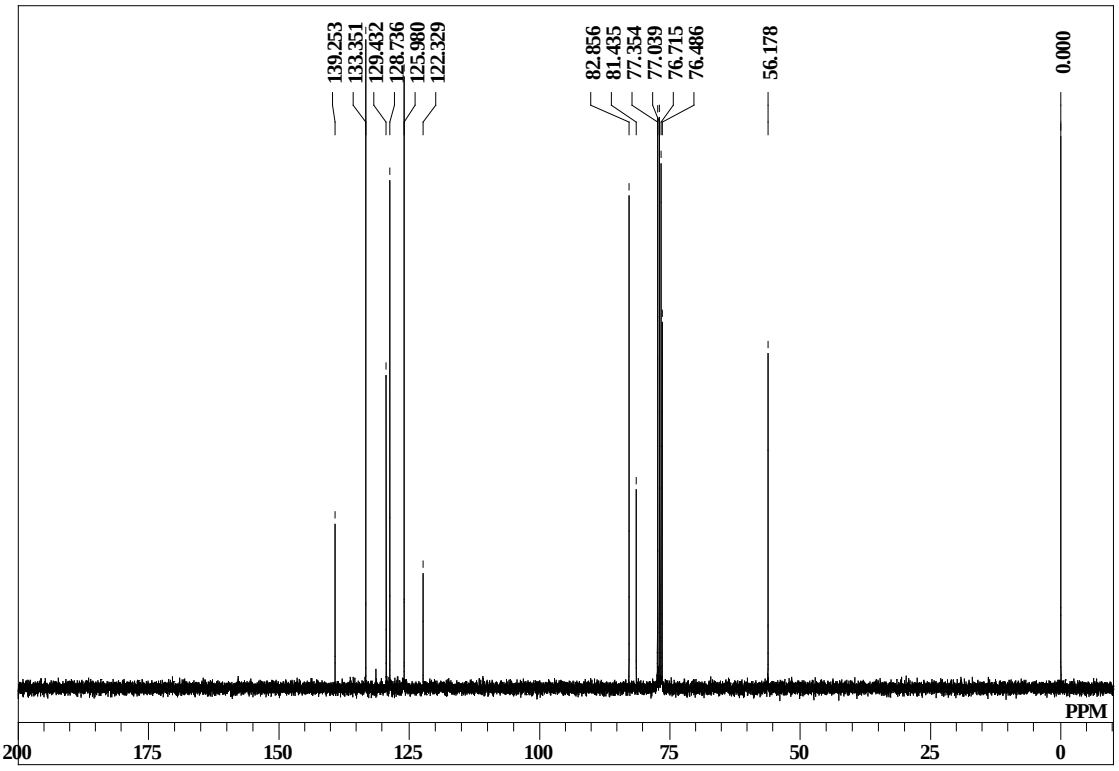
1l single pulse decoupled gated NOE



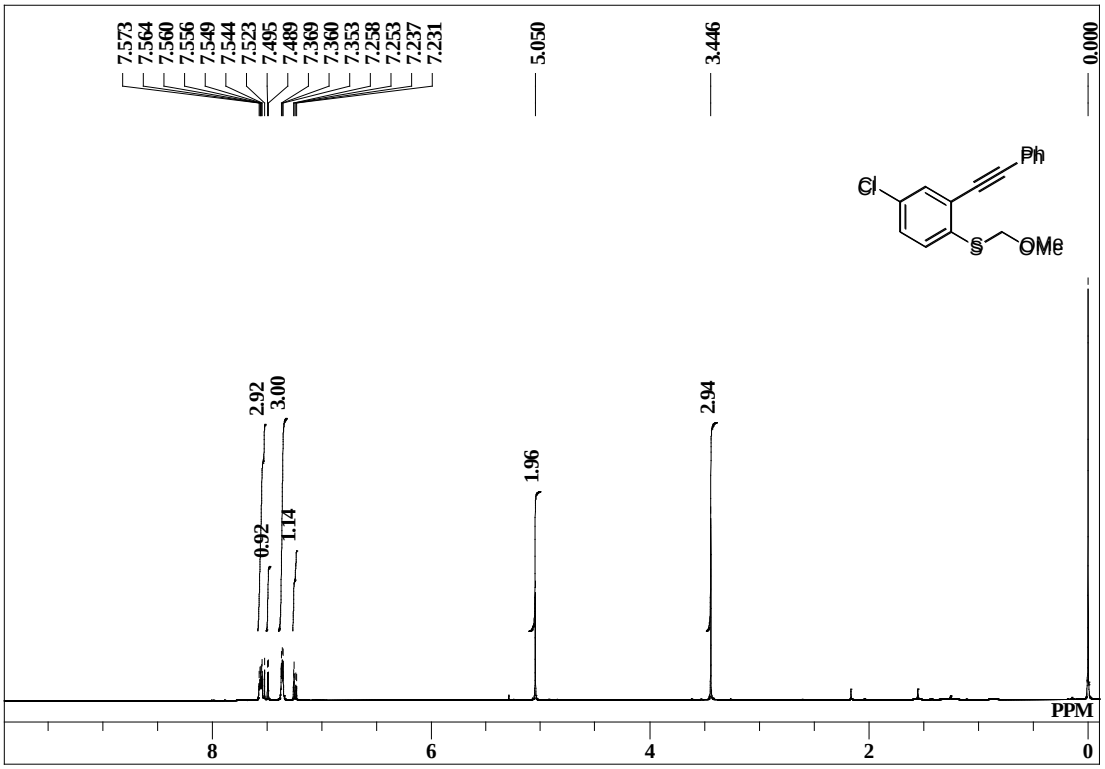
1m single_pulse



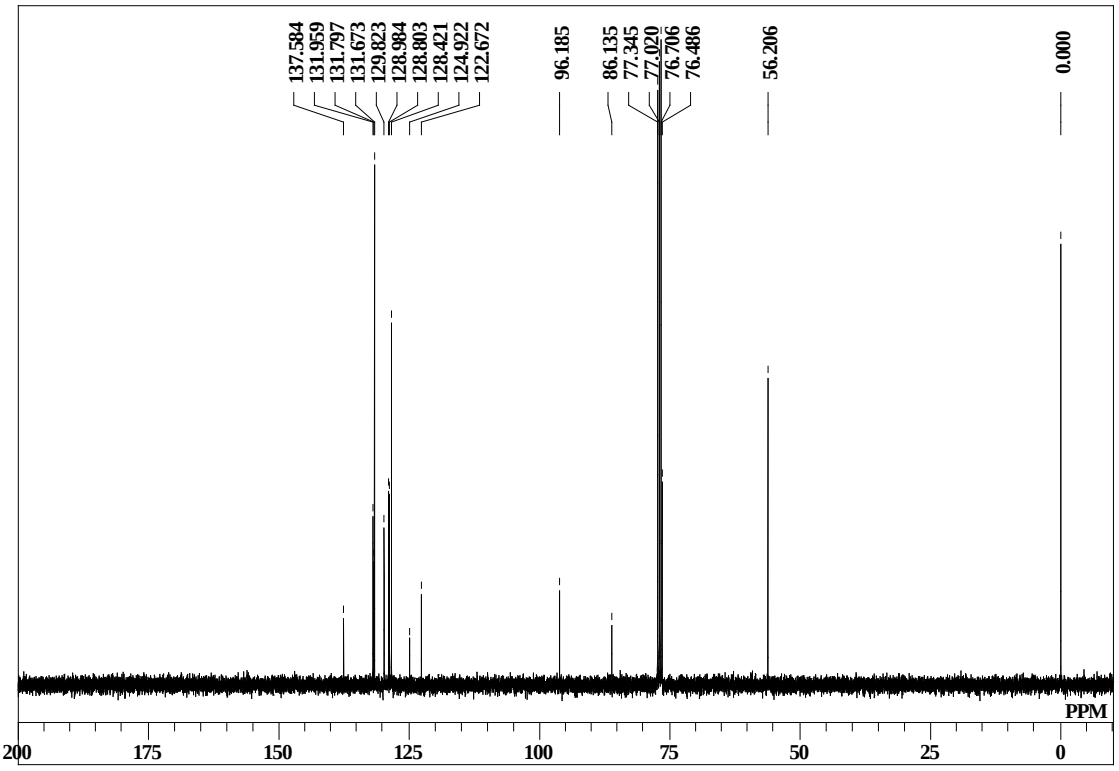
1m single pulse decoupled gated NOE



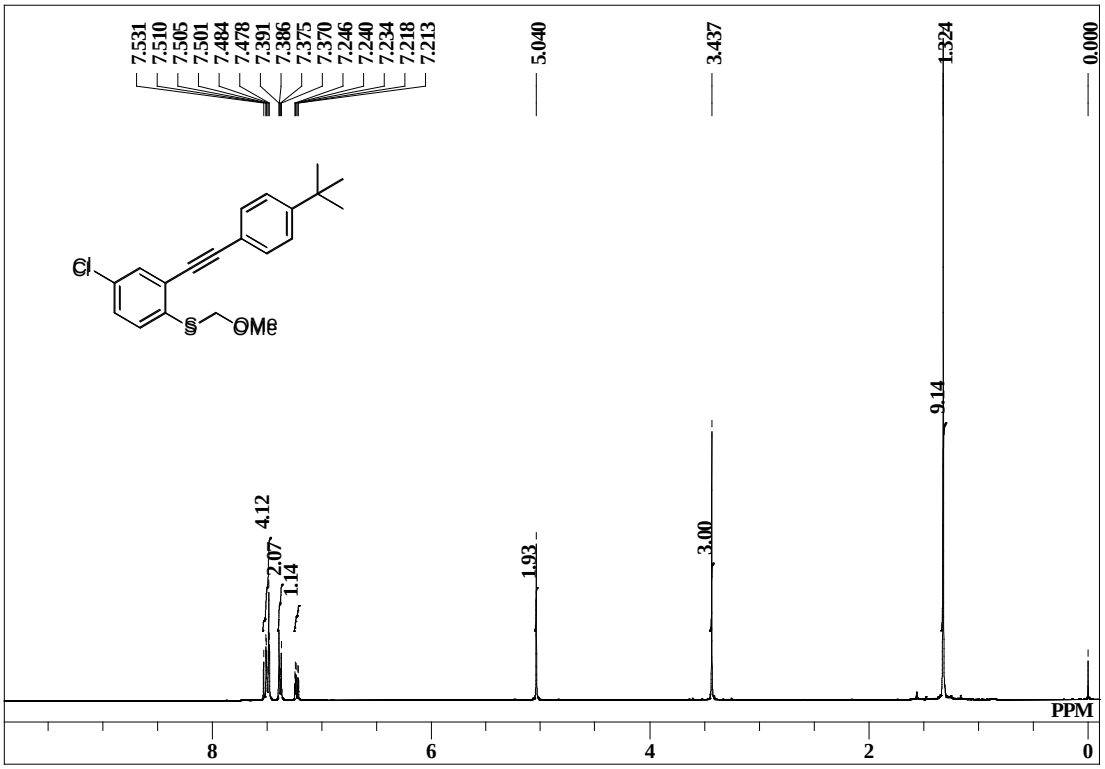
1n single_pulse



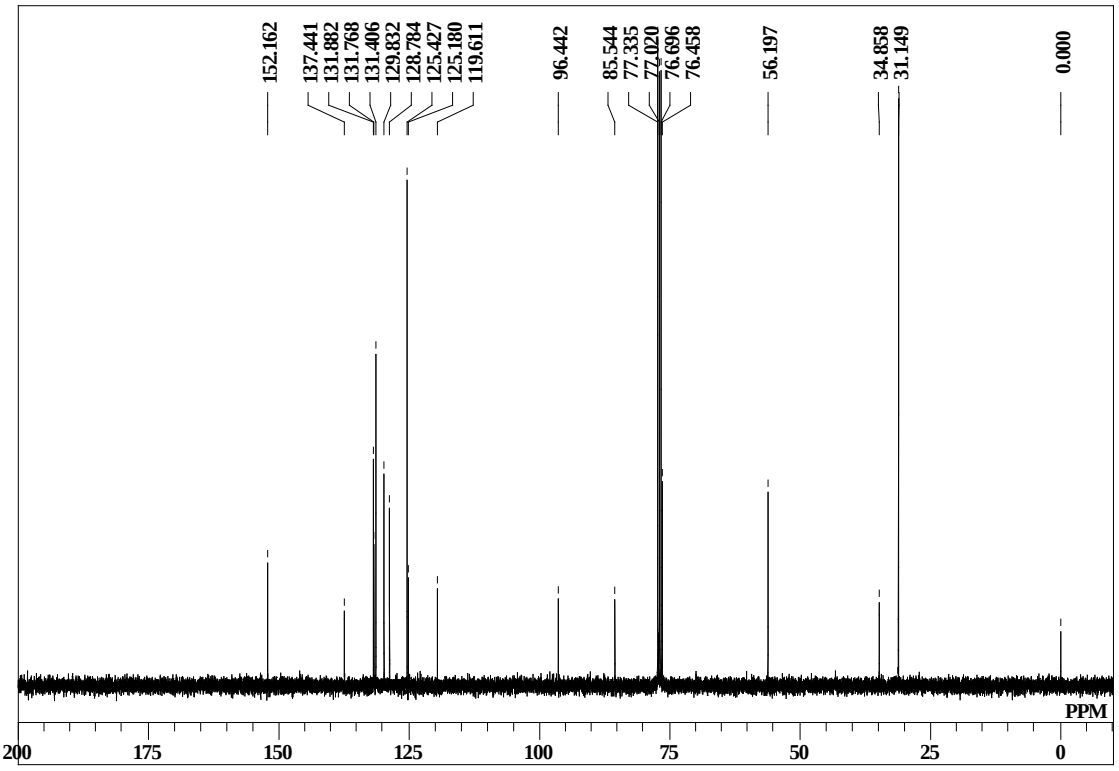
1n single pulse decoupled gated NOE



1o single_pulse

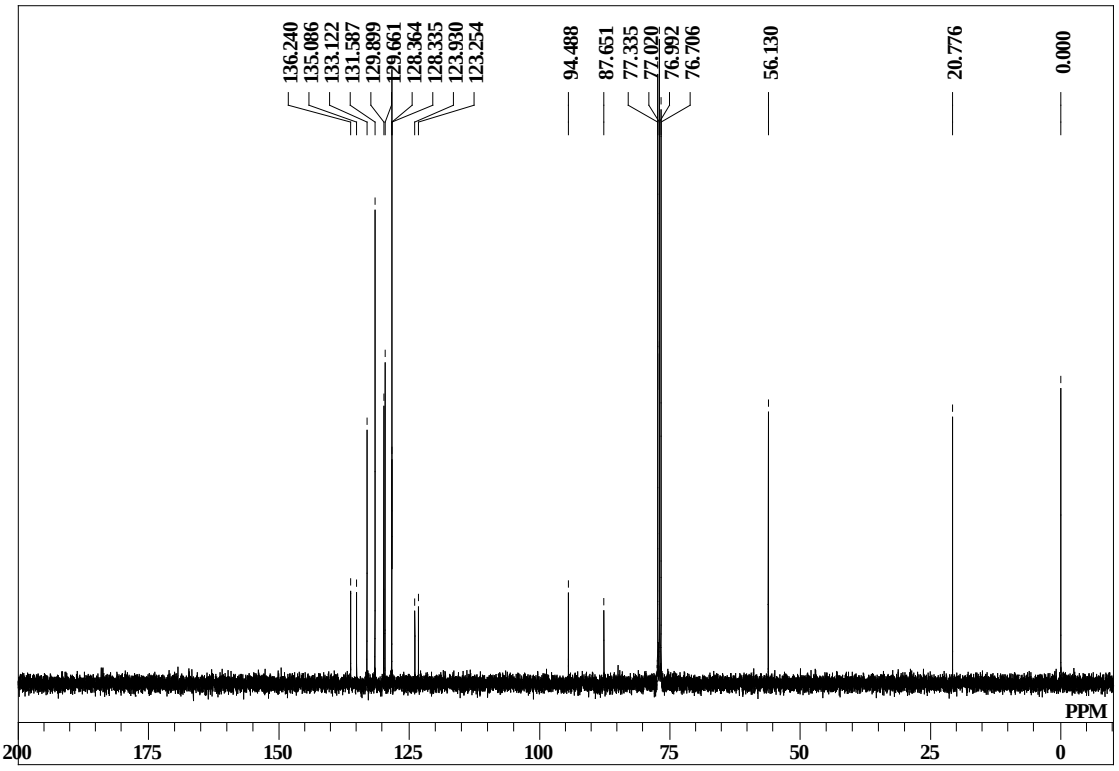


1o single pulse decoupled gated NOE

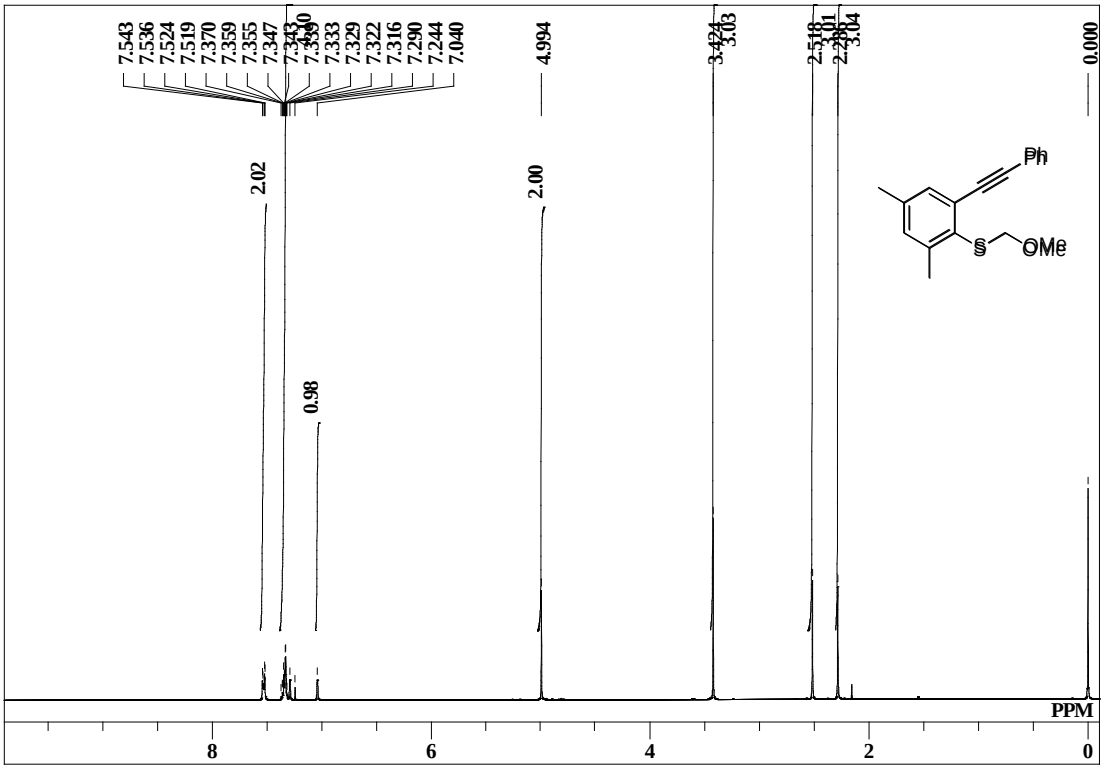


1p single_pulse

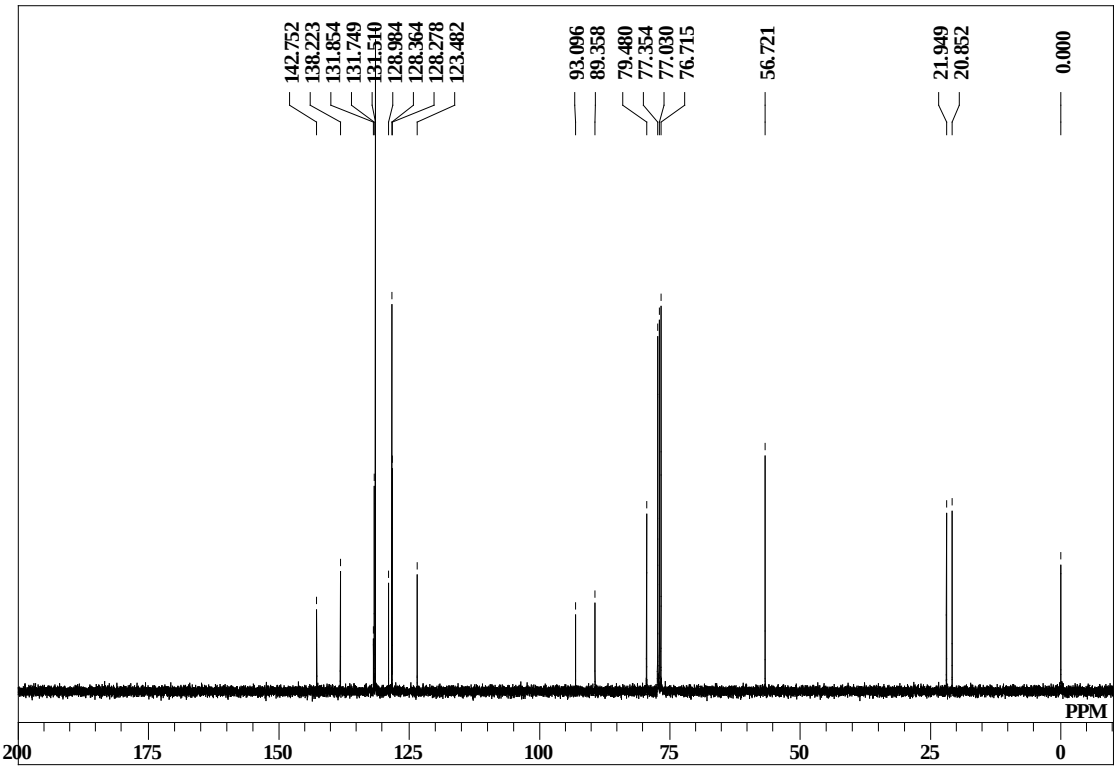
1p single pulse decoupled gated NOE



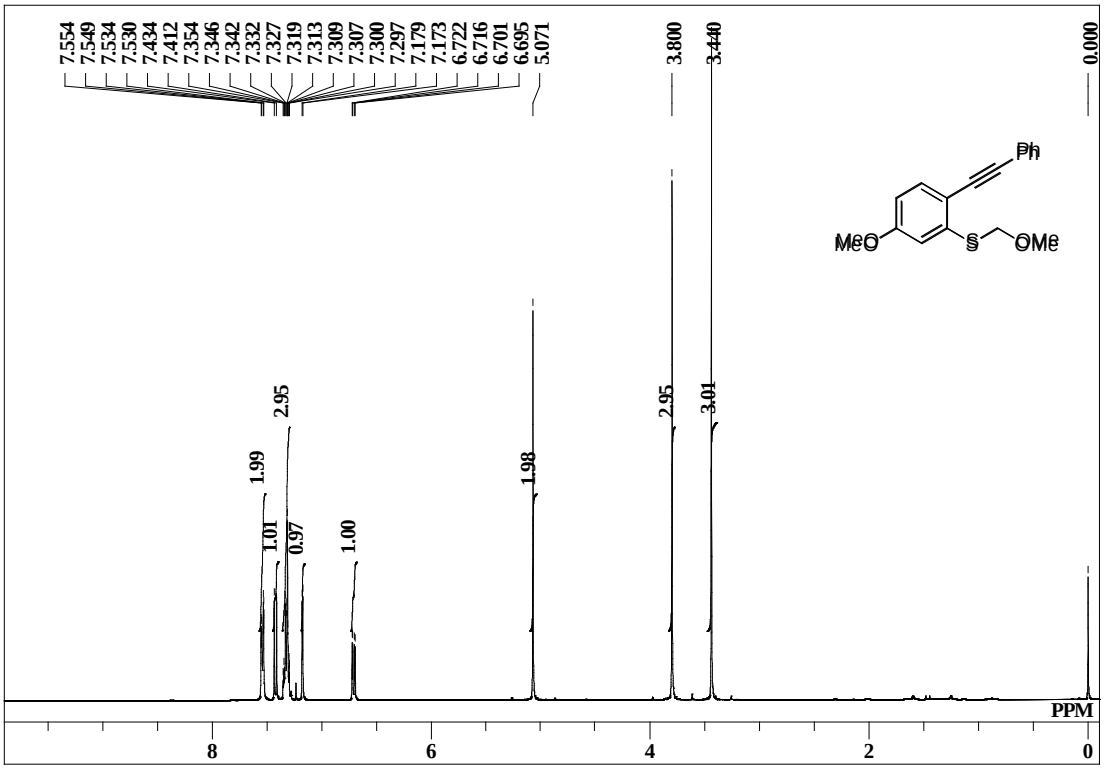
1q single_pulse



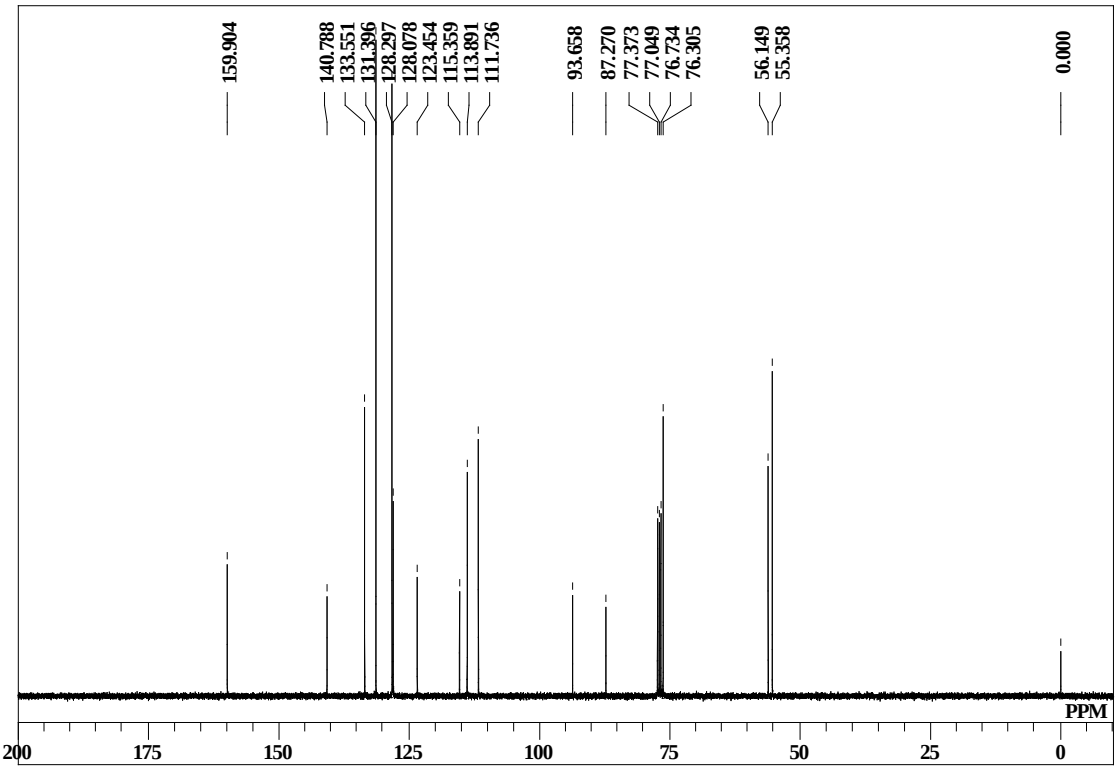
1q single pulse decoupled gated NOE



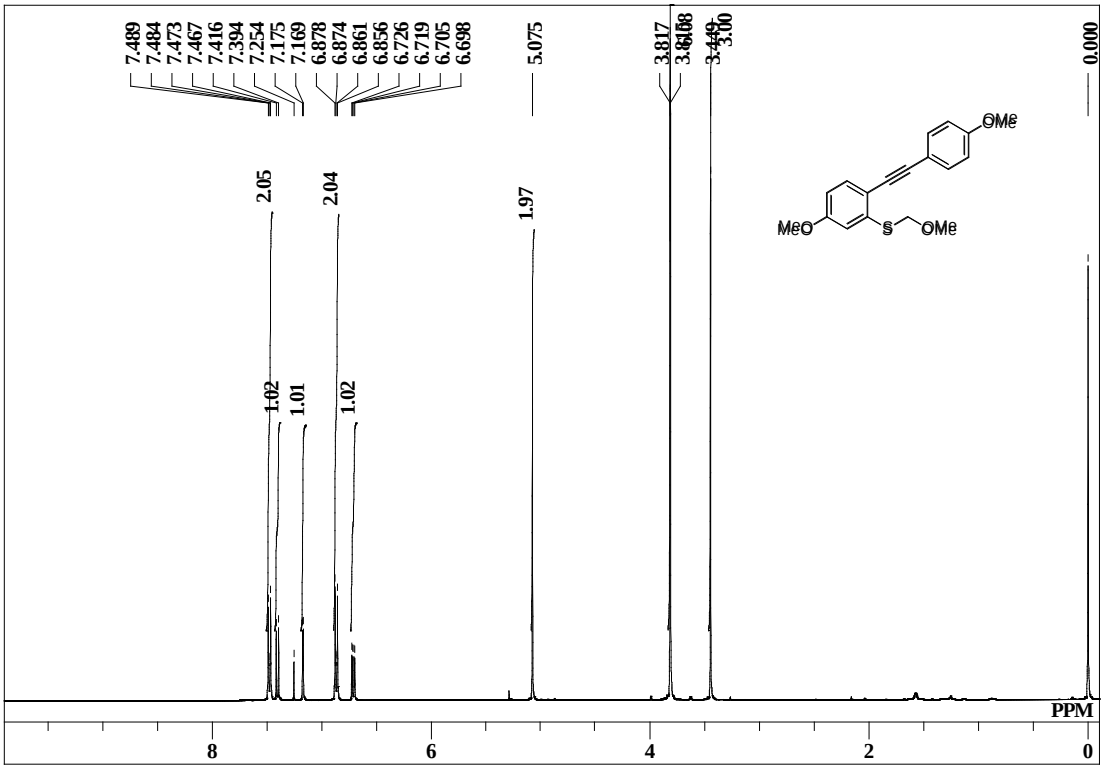
1r single_pulse



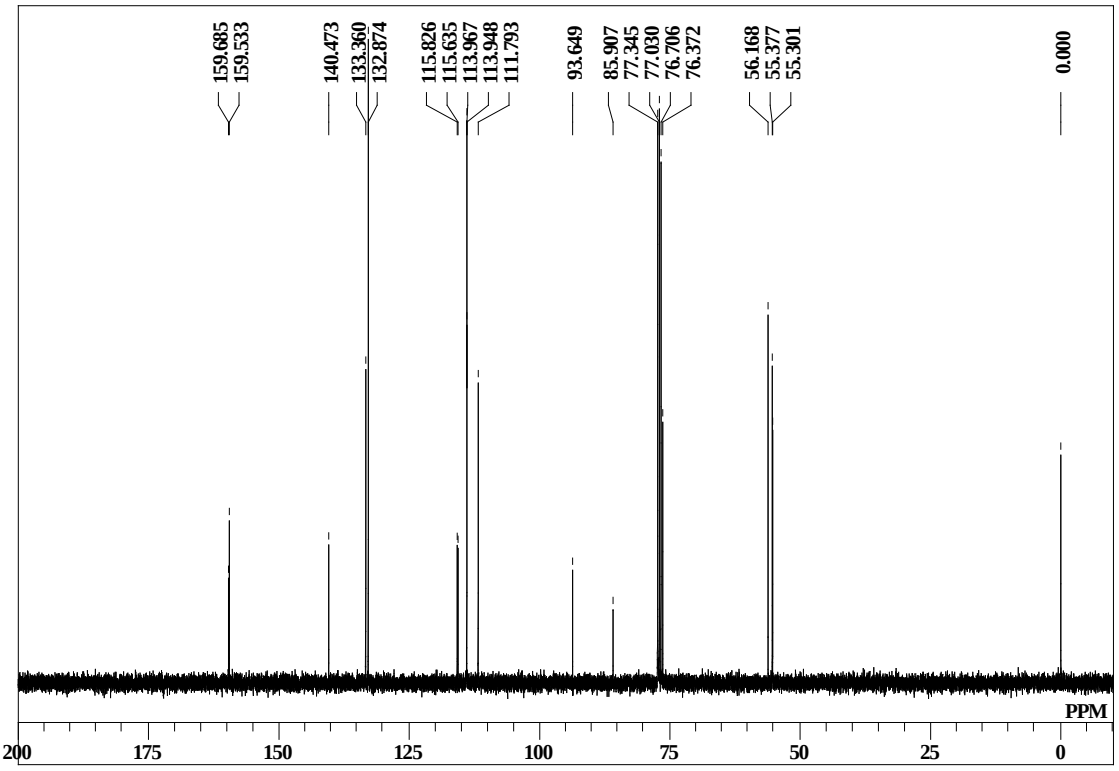
1r single pulse decoupled gated NOE



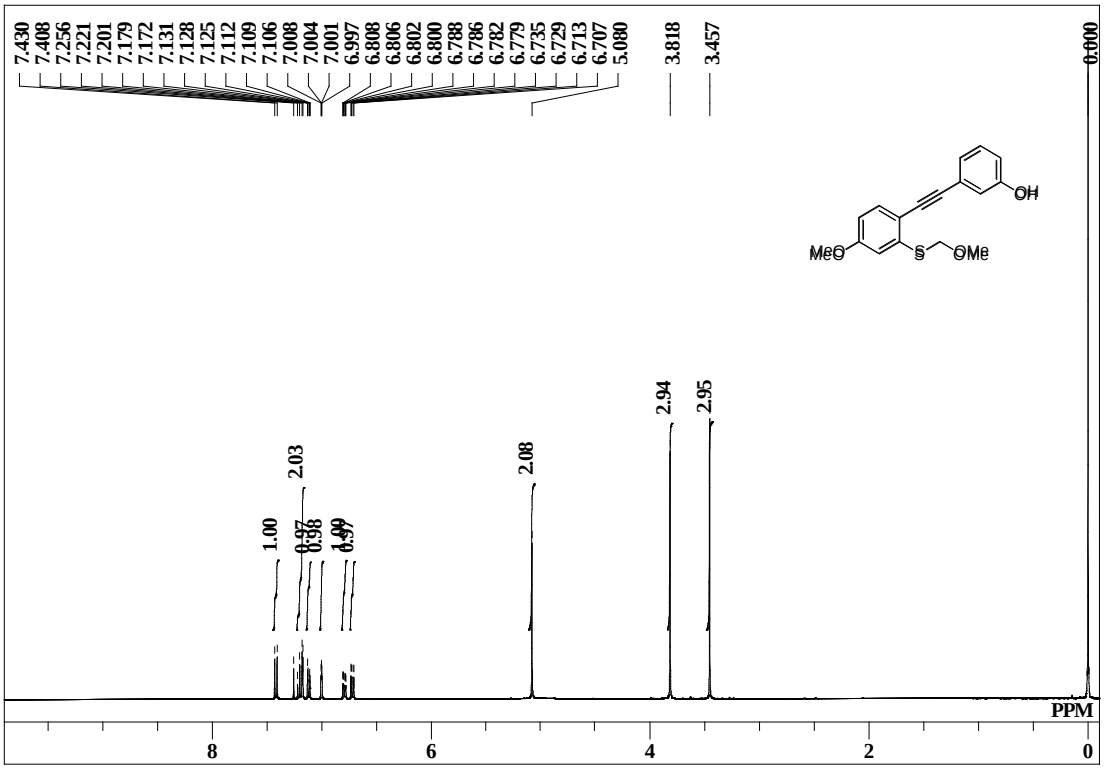
1s single_pulse



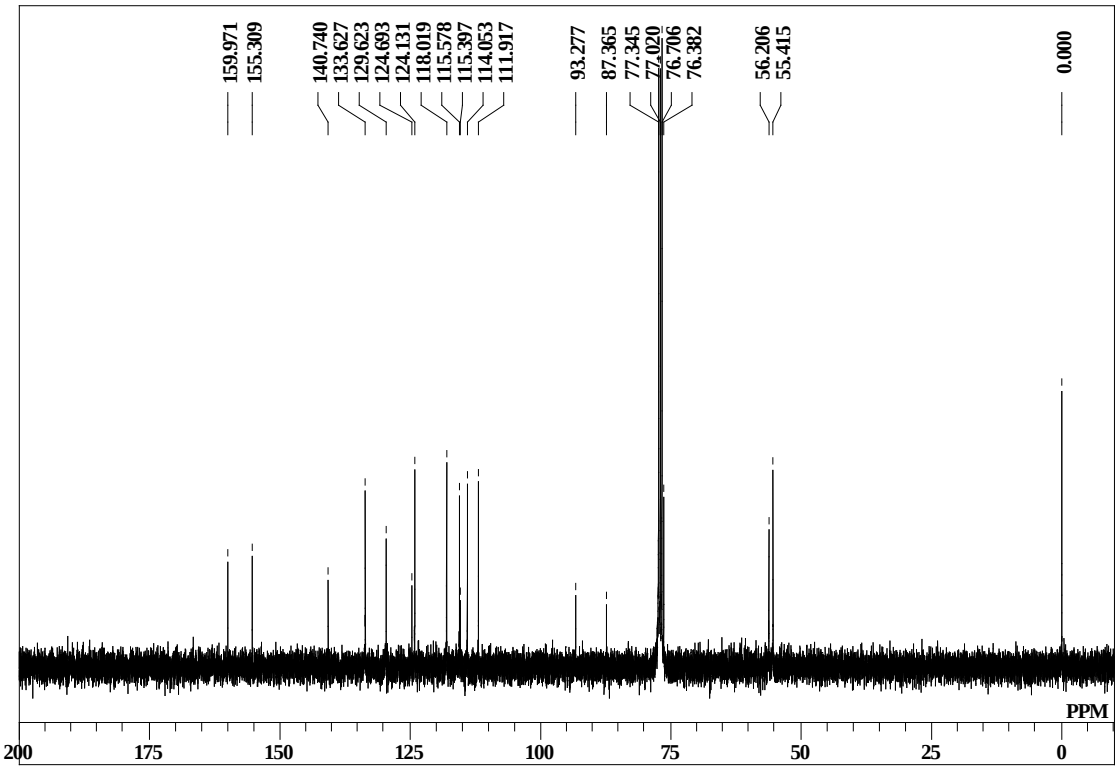
1s single pulse decoupled gated NOE



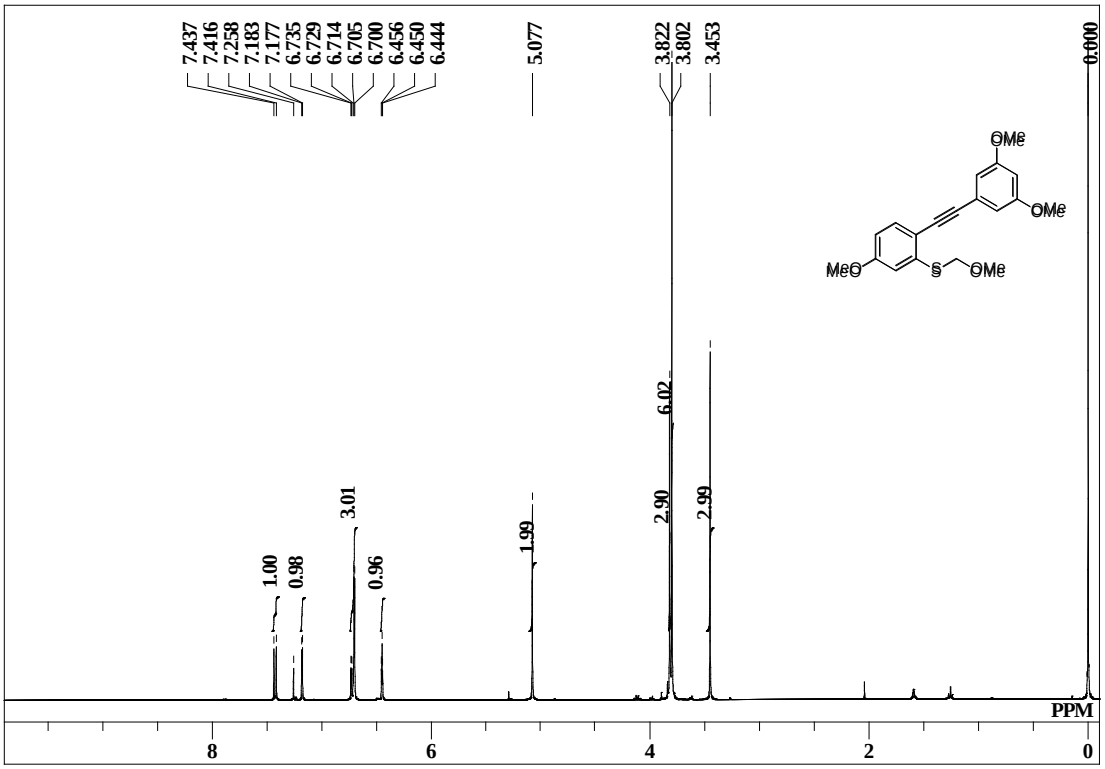
1t single_pulse



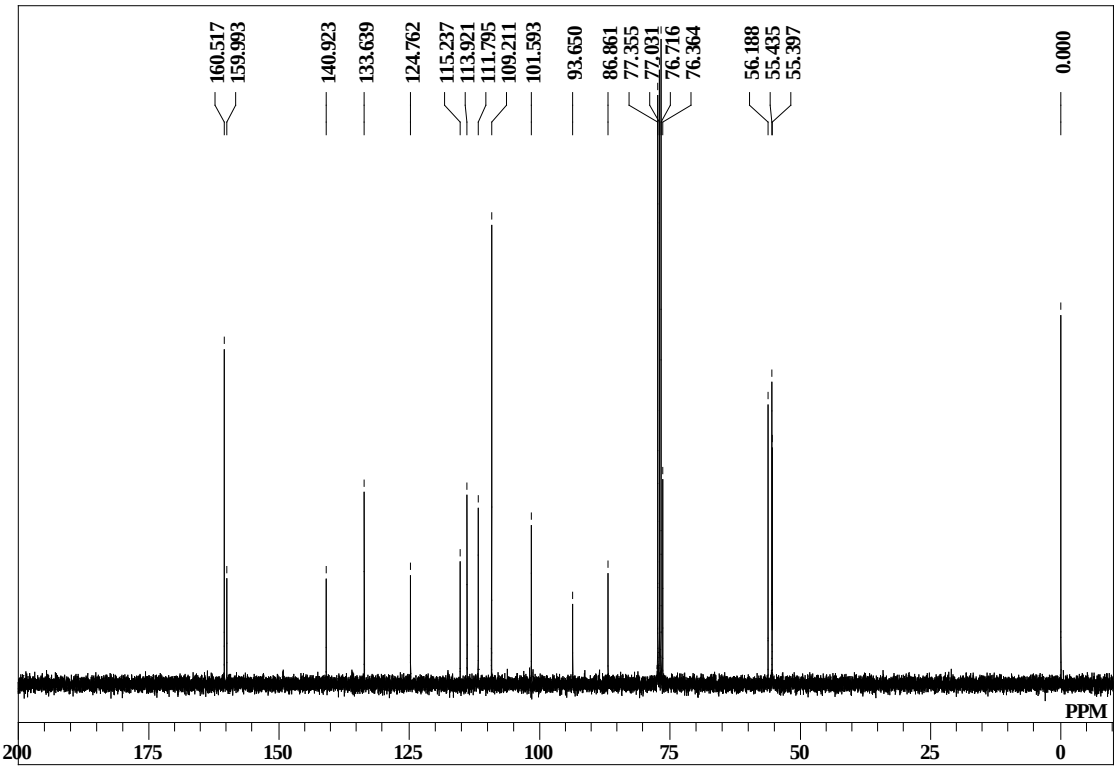
1t single pulse decoupled gated NOE



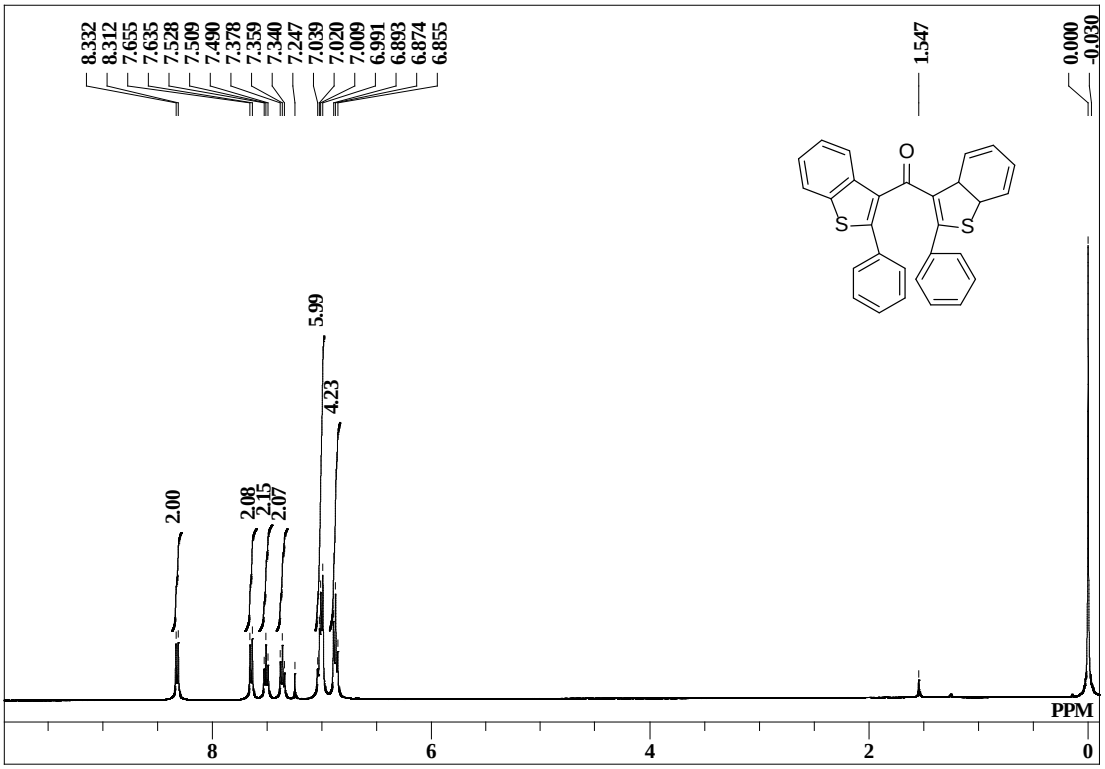
1u single_pulse



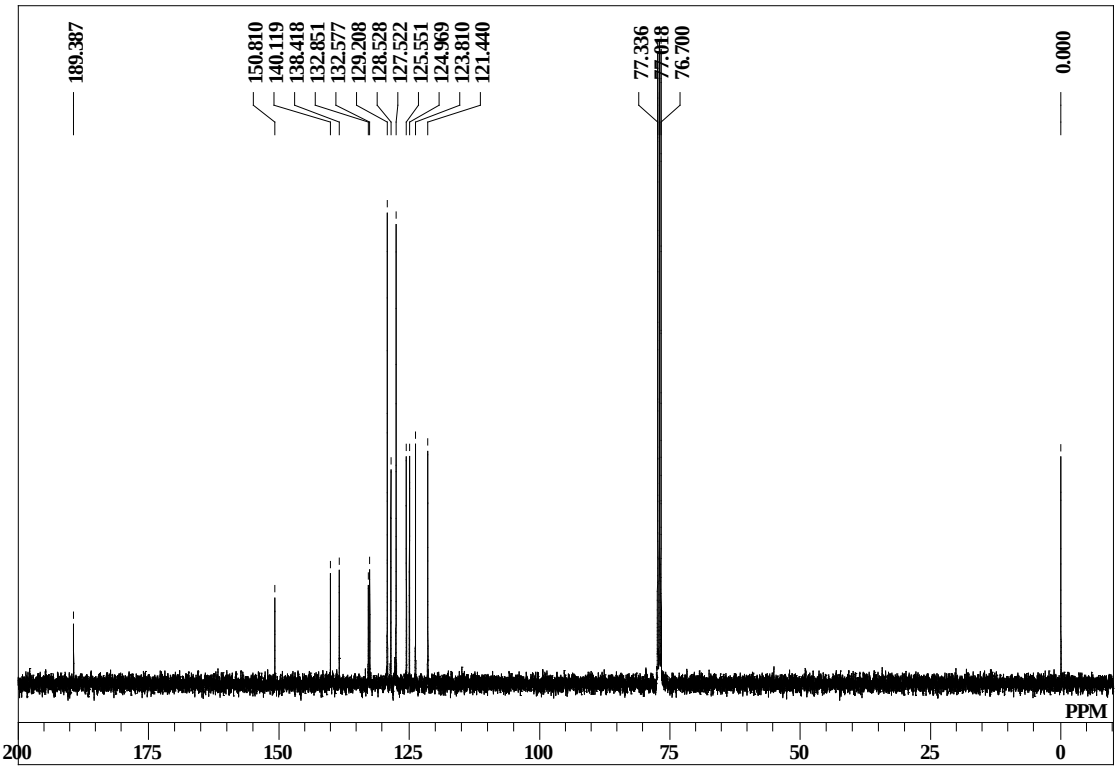
1u single pulse decoupled gated NOE



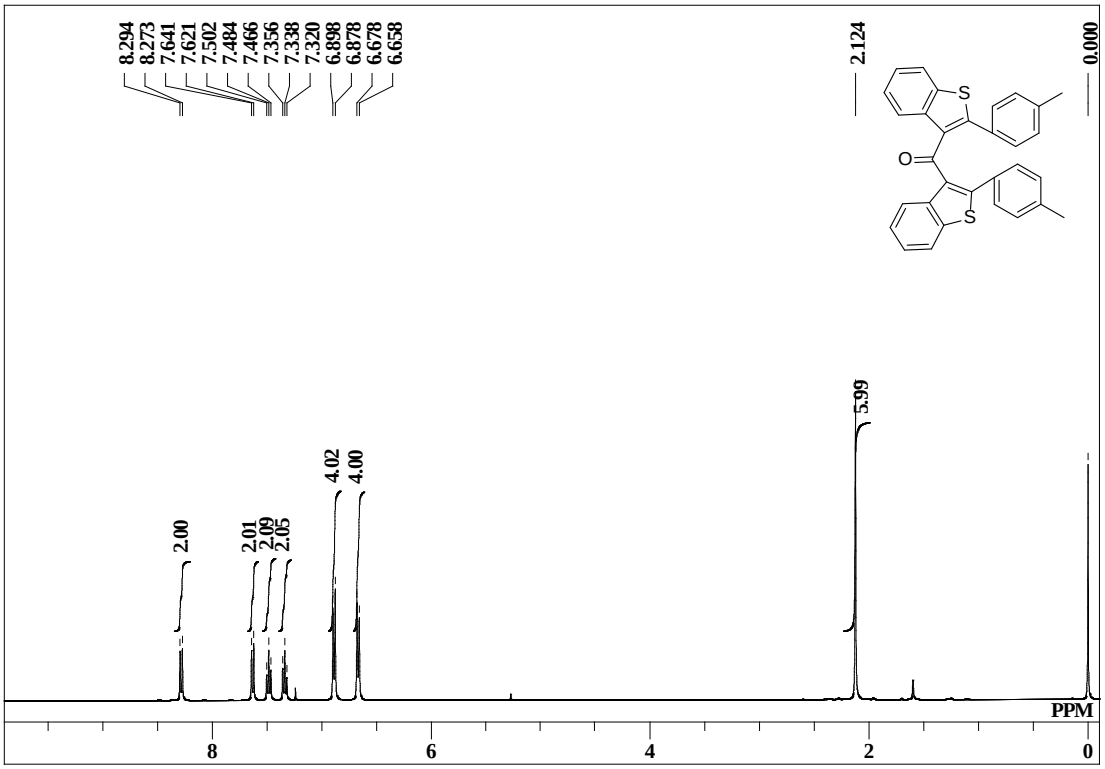
2a single_pulse



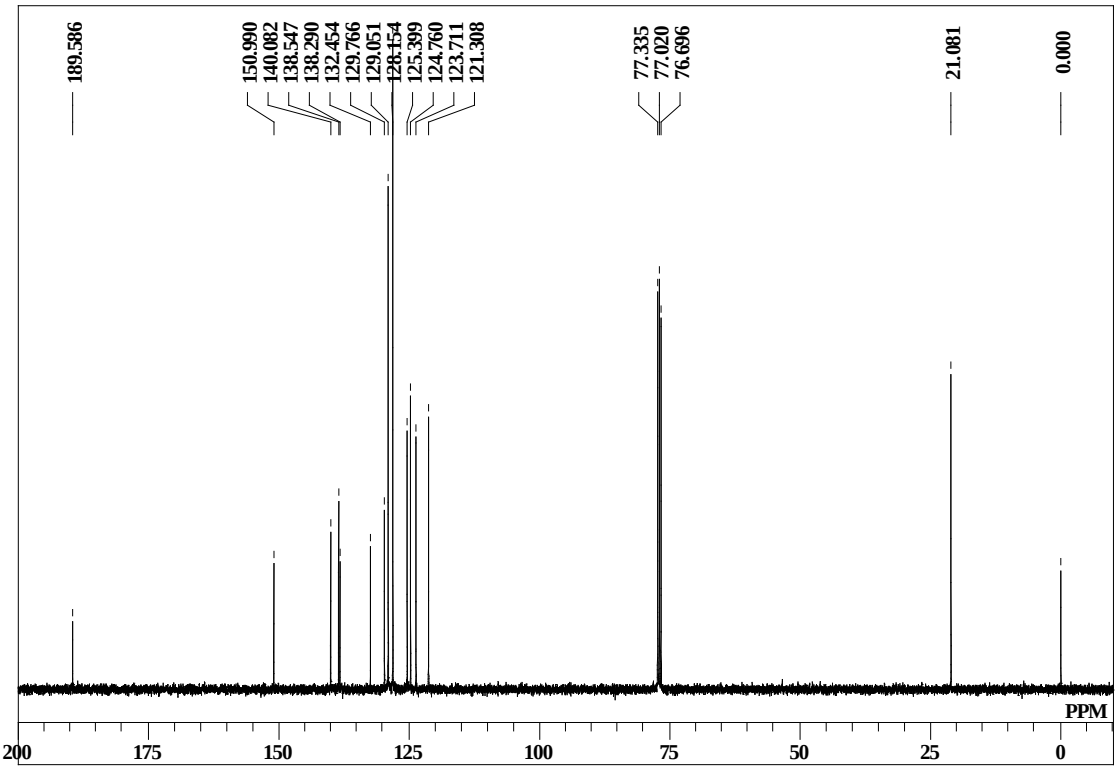
2a single pulse decloupled gated NOE



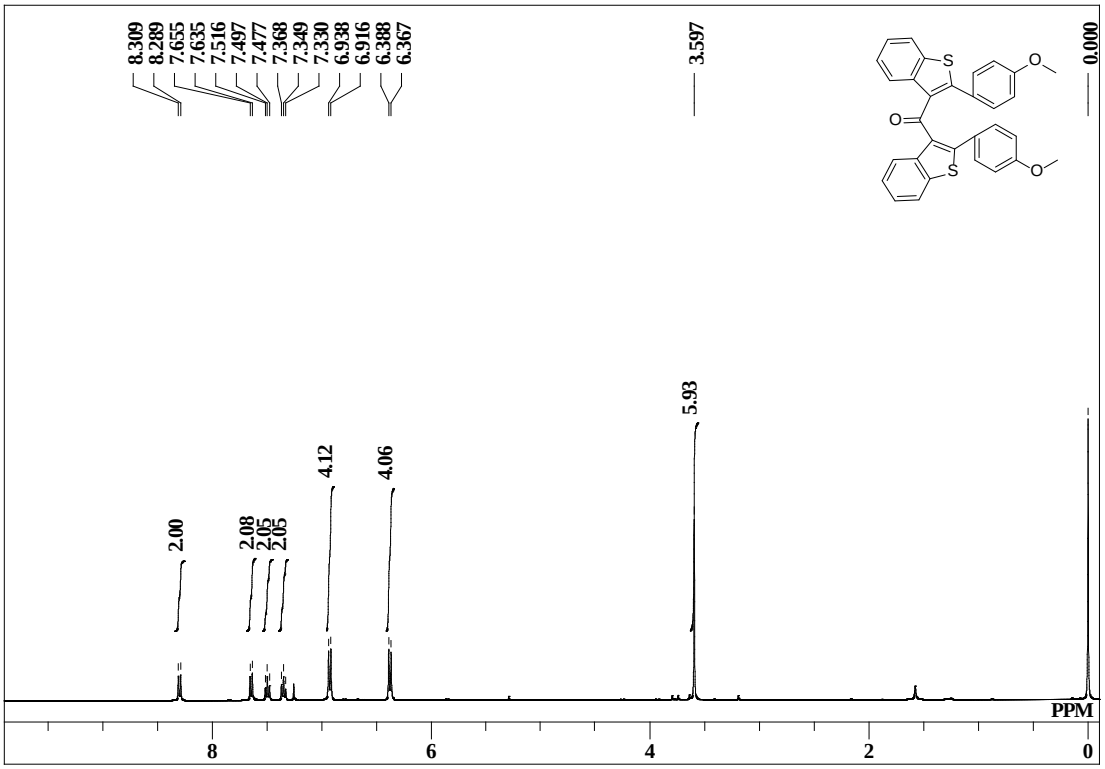
2b single_pulse



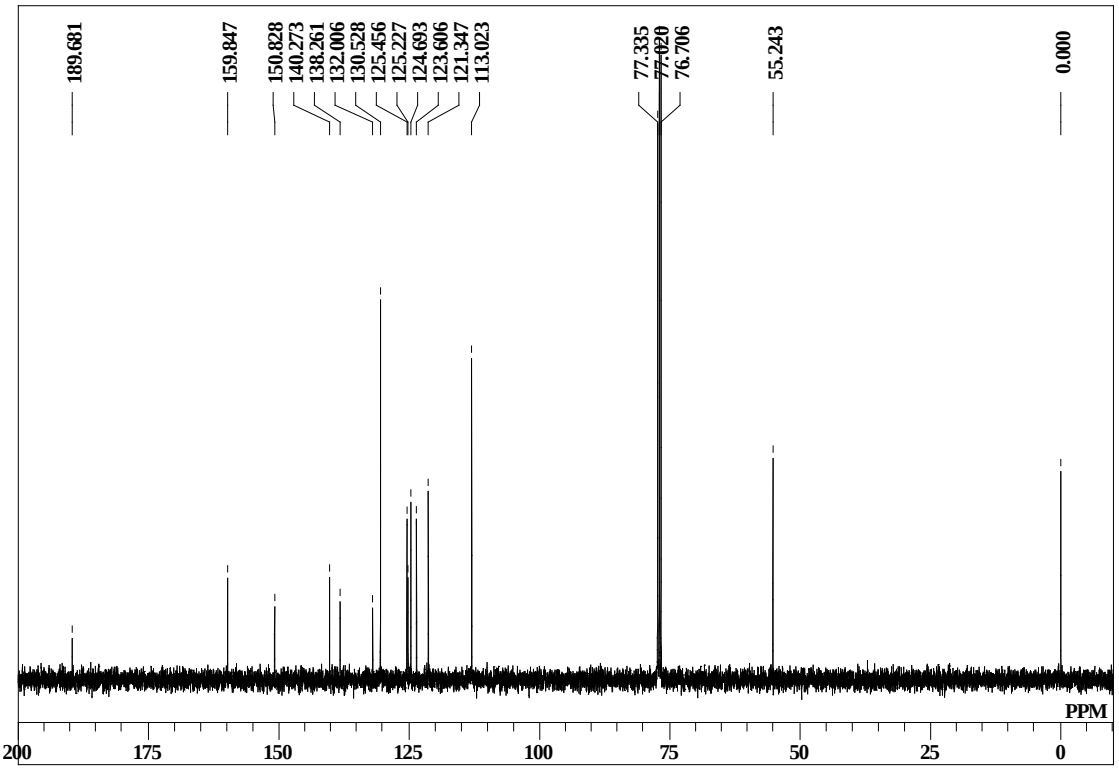
2b single pulse decoupled gated NOE



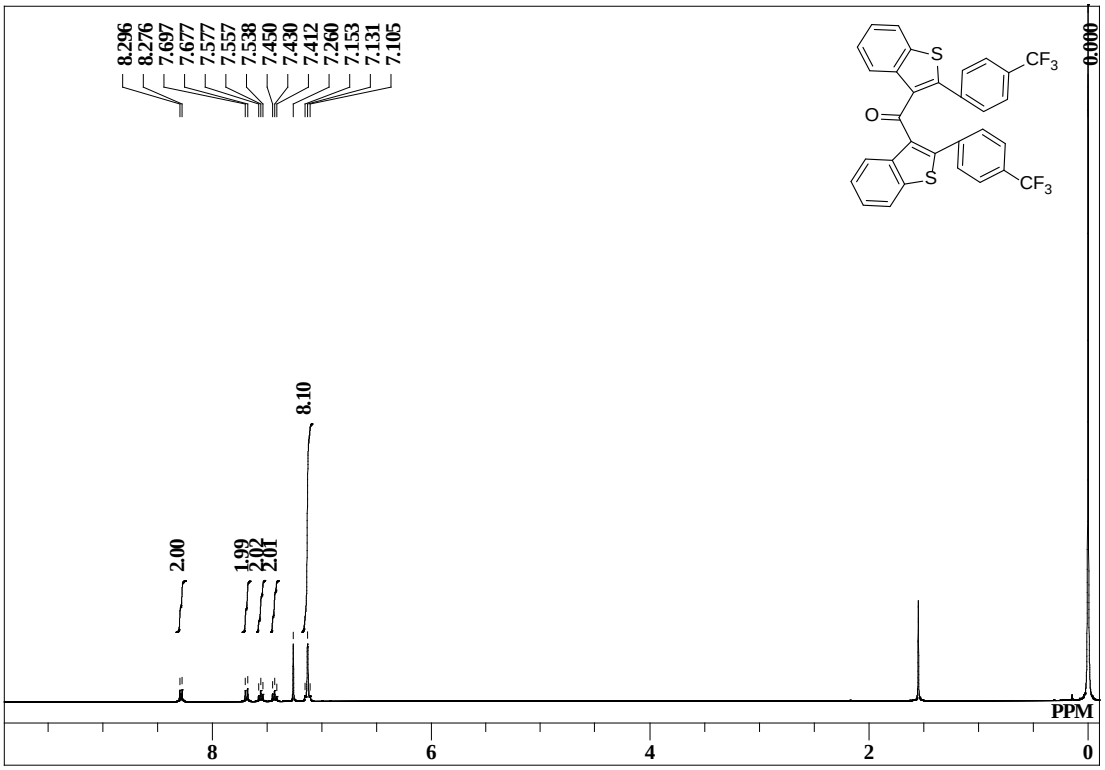
2c single_pulse



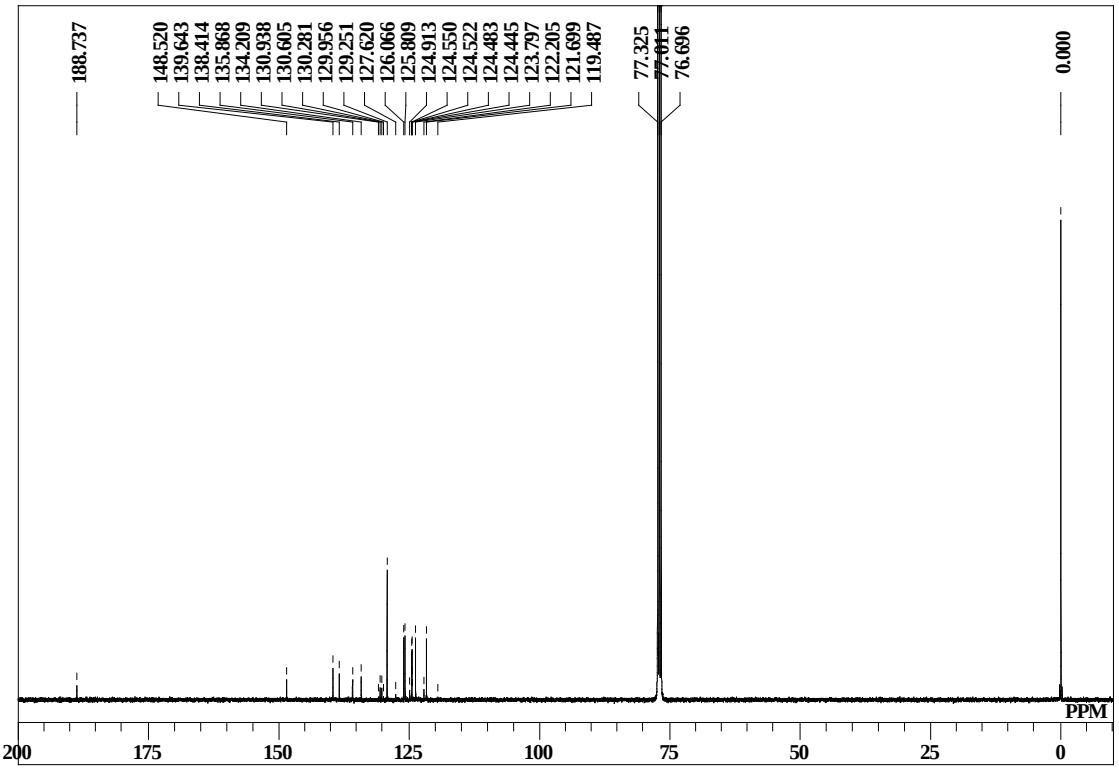
2c single pulse decoupled gated NOE



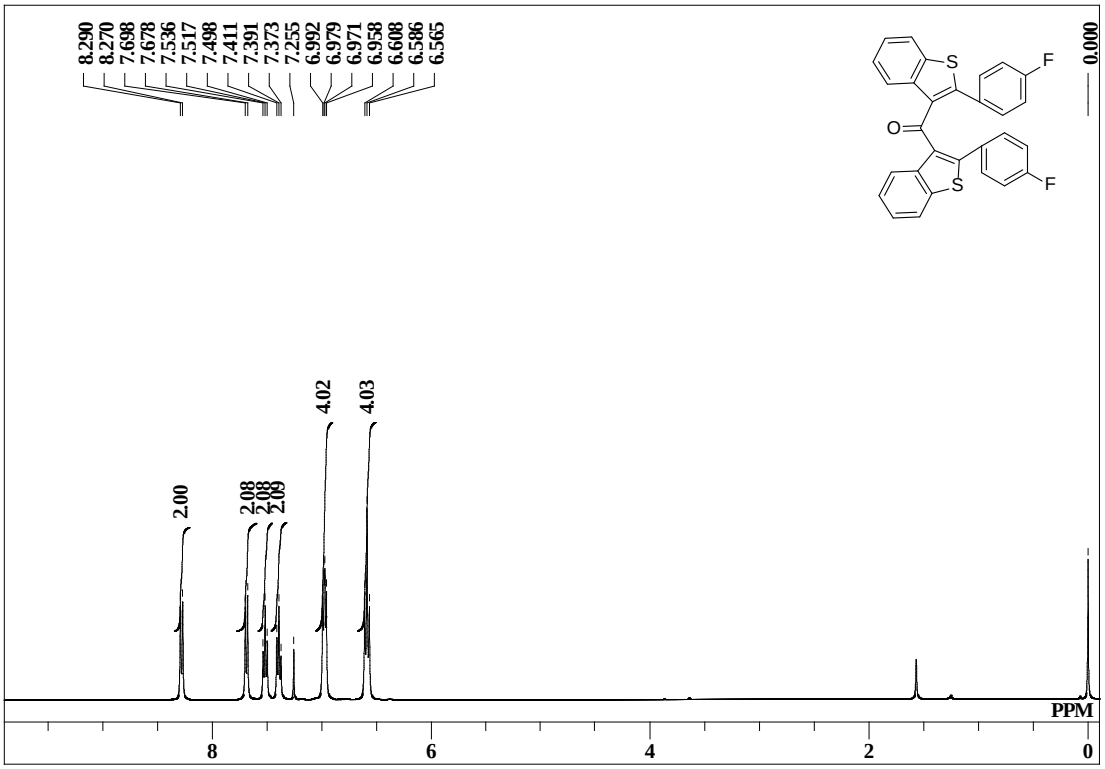
2d single_pulse



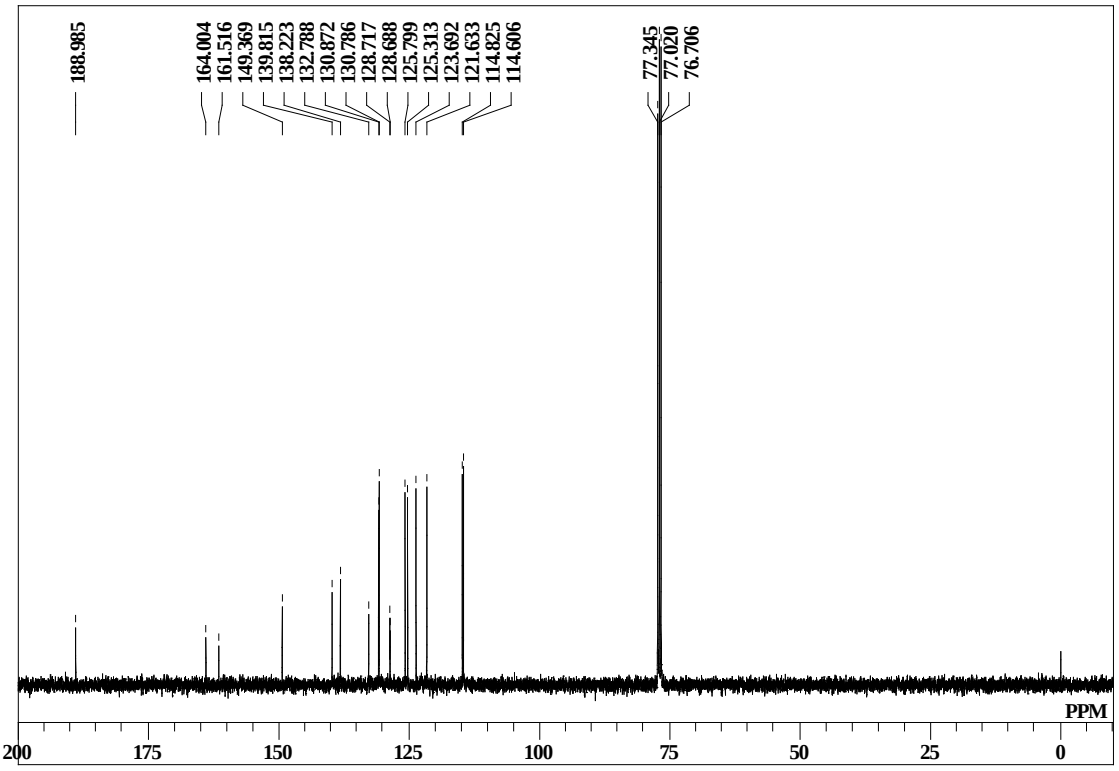
2d single pulse decoupled gated NOE



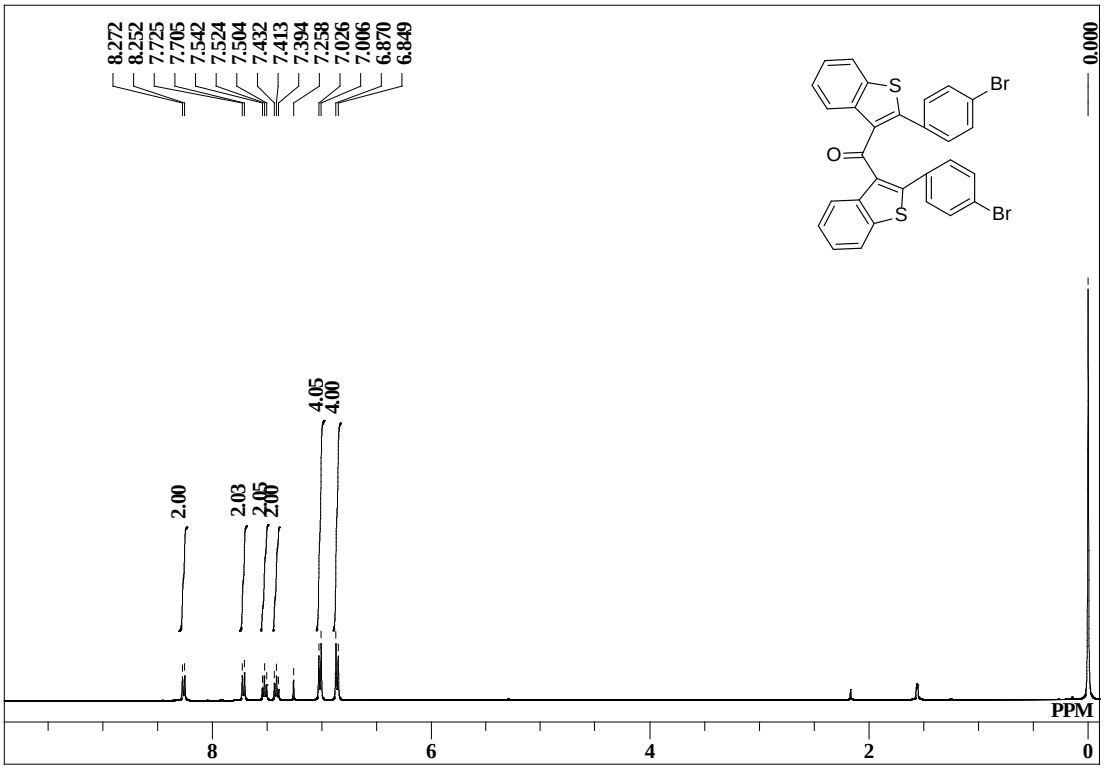
2e single_pulse



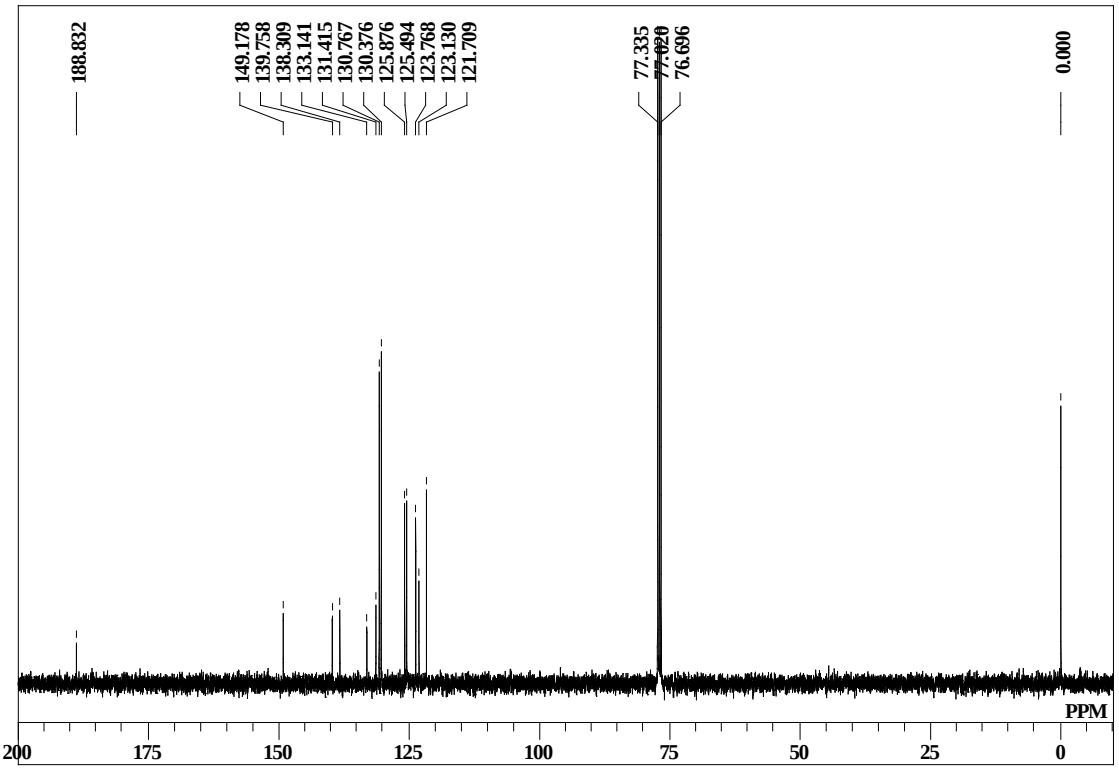
2e single pulse decoupled gated NOE



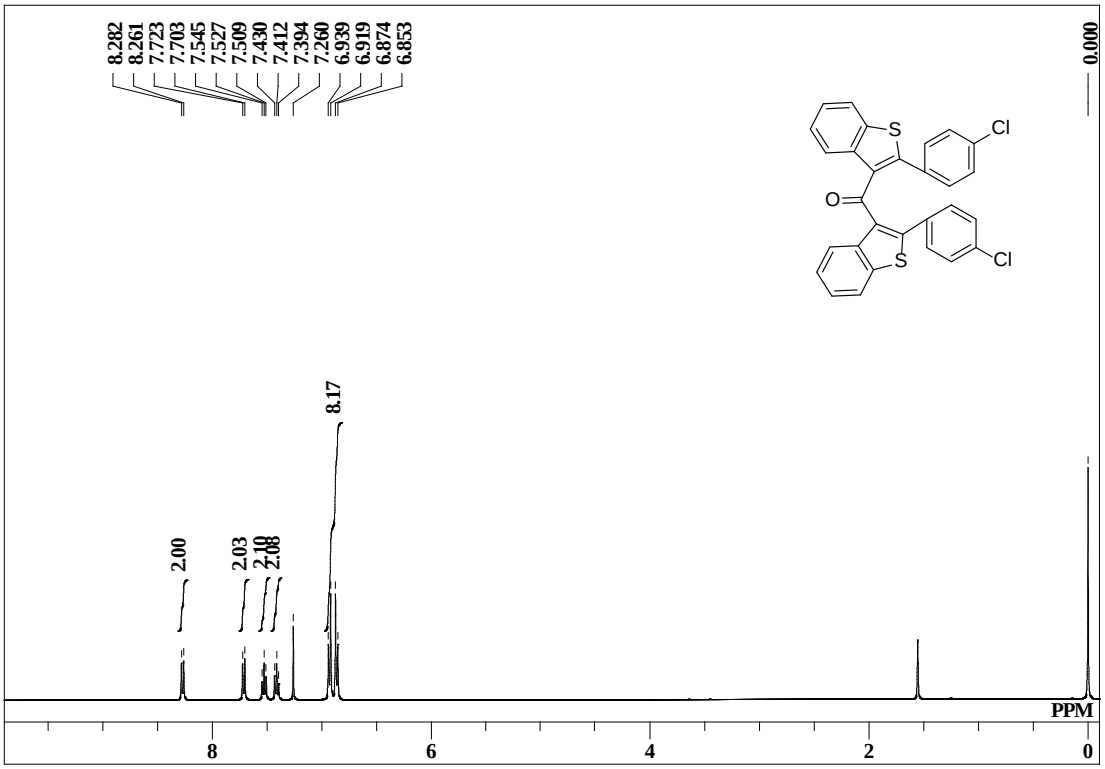
2f single_pulse



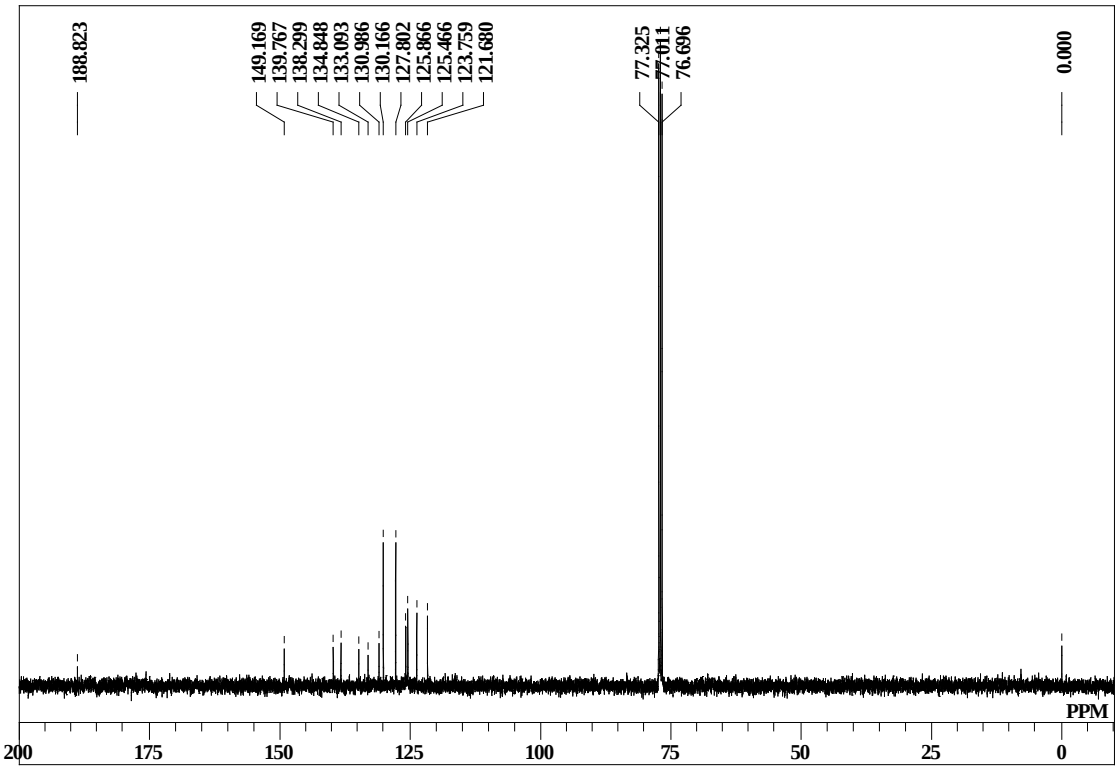
2f single pulse decoupled gated NOE



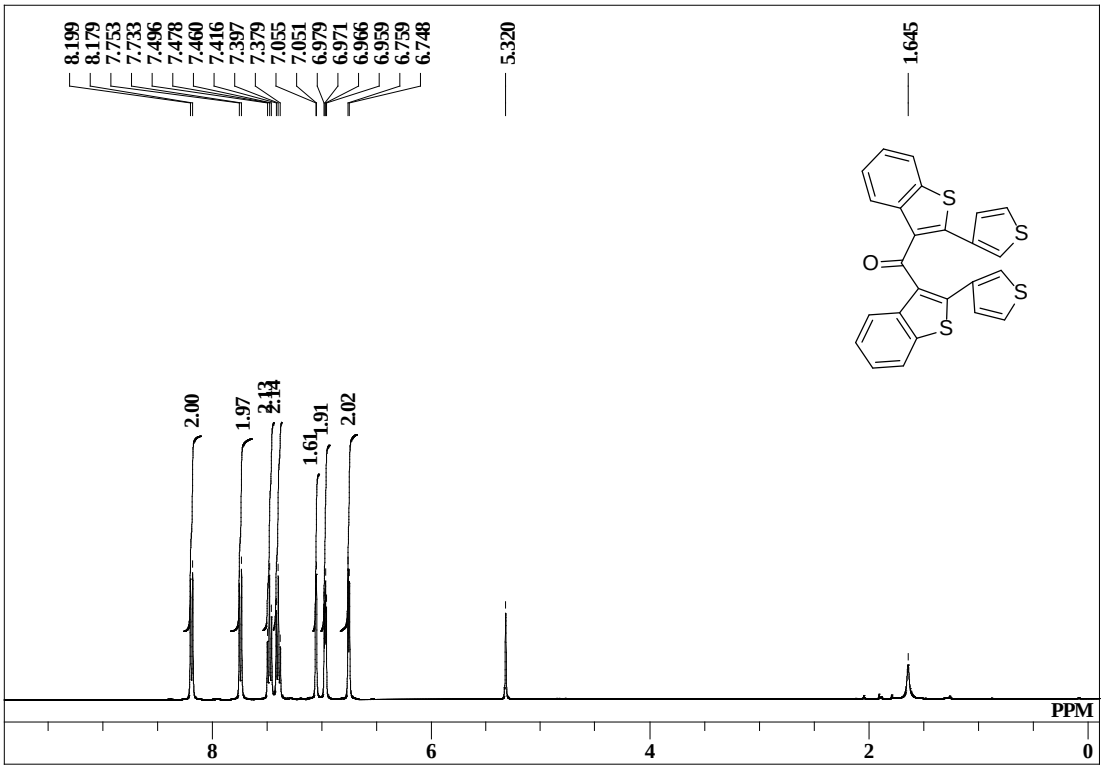
2g single_pulse



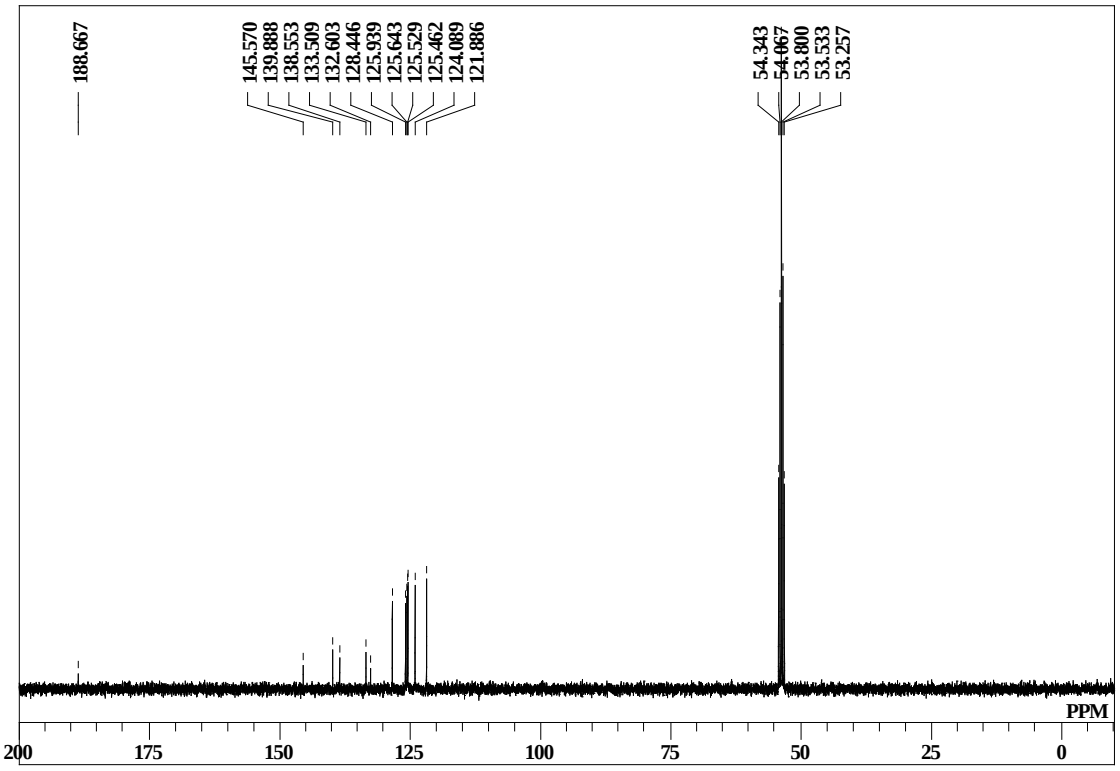
2g single pulse decoupled gated NOE



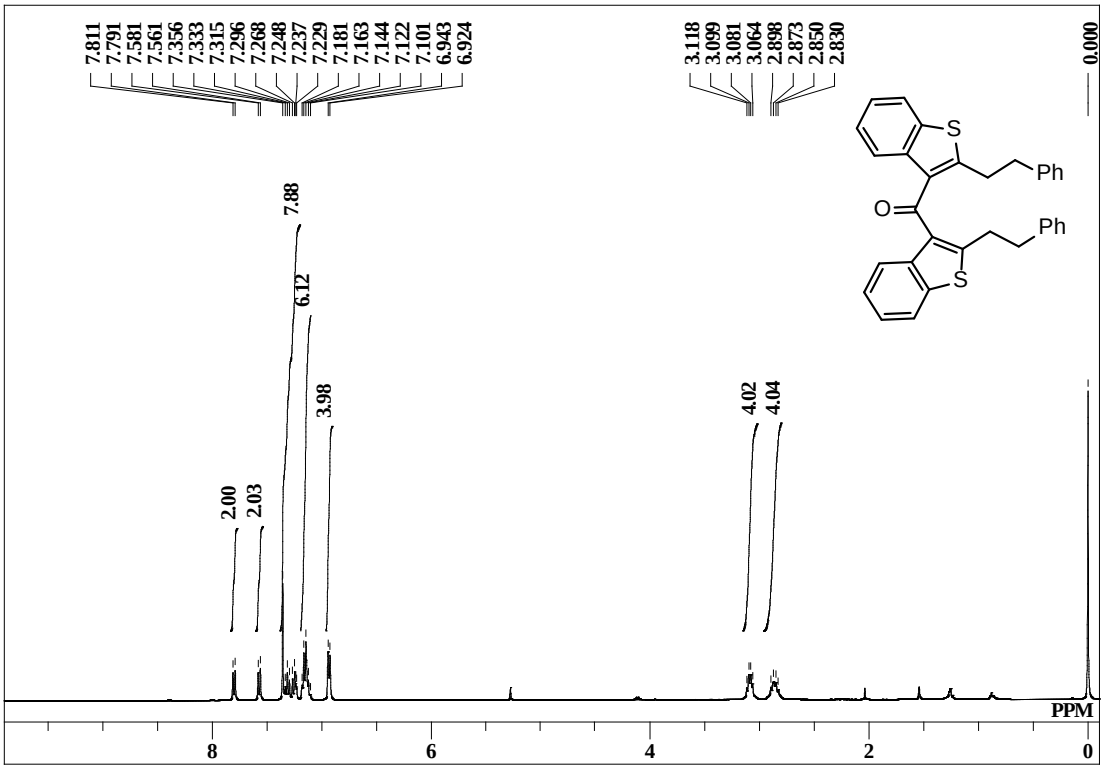
2h single_pulse



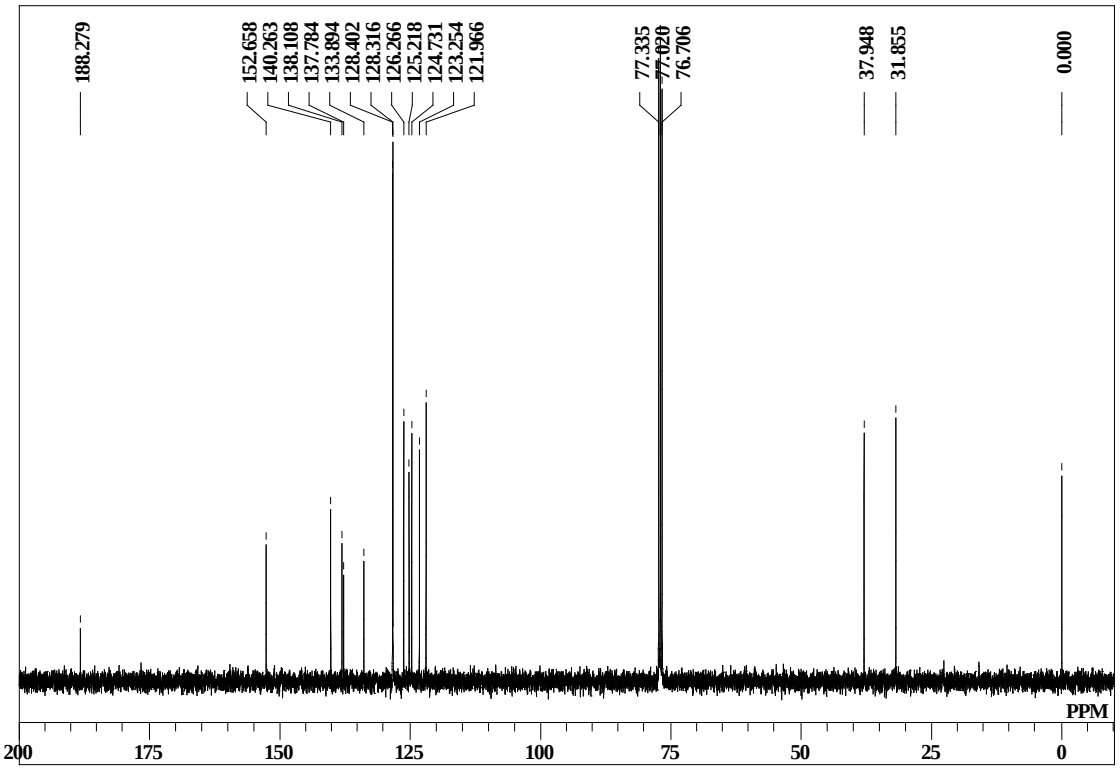
2h single pulse decoupled gated NOE



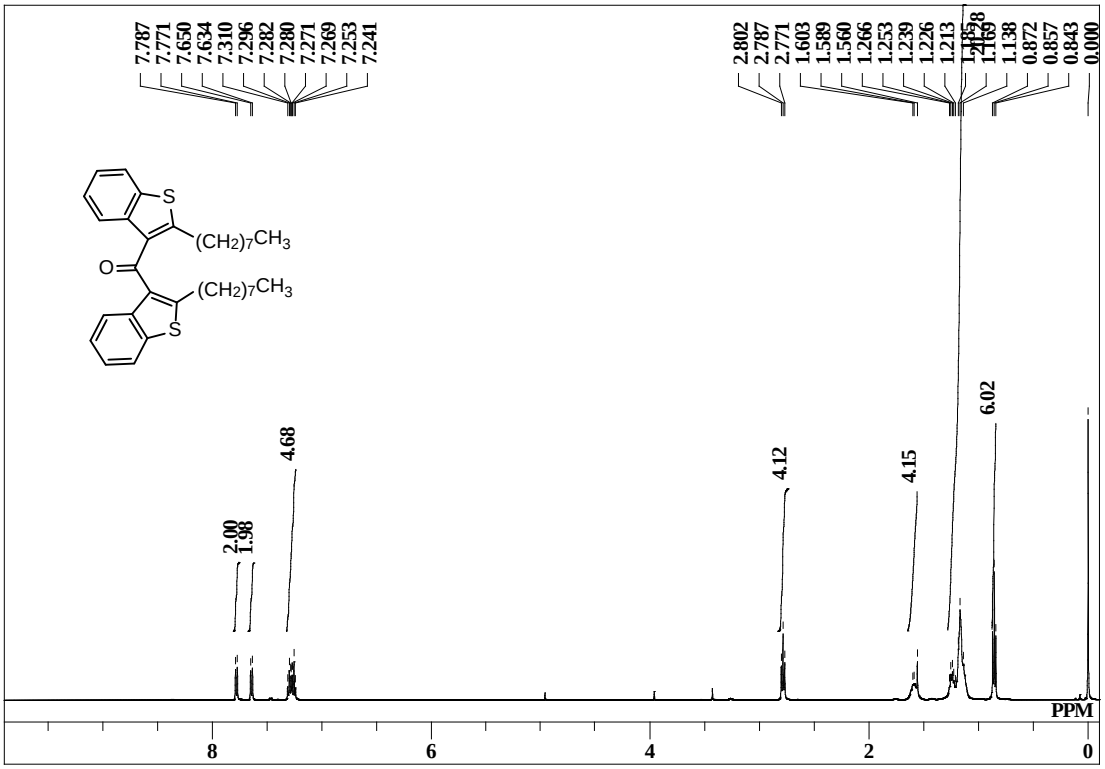
2i single_pulse



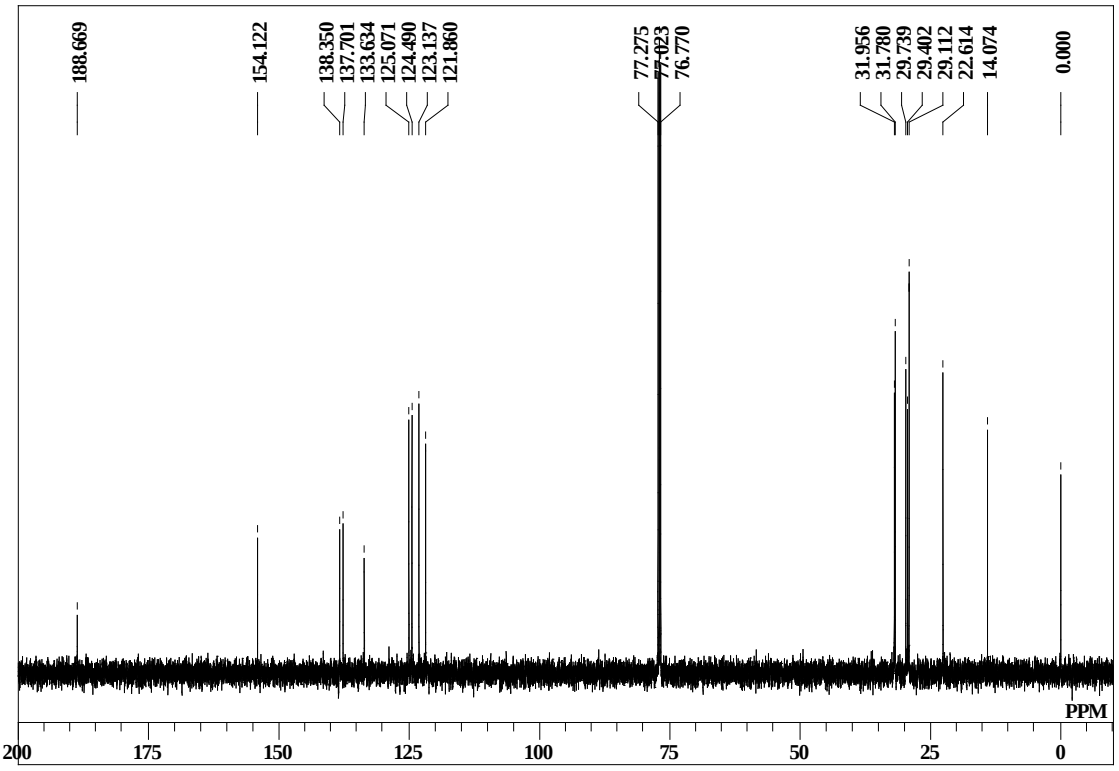
2i single pulse decoupled gated NOE



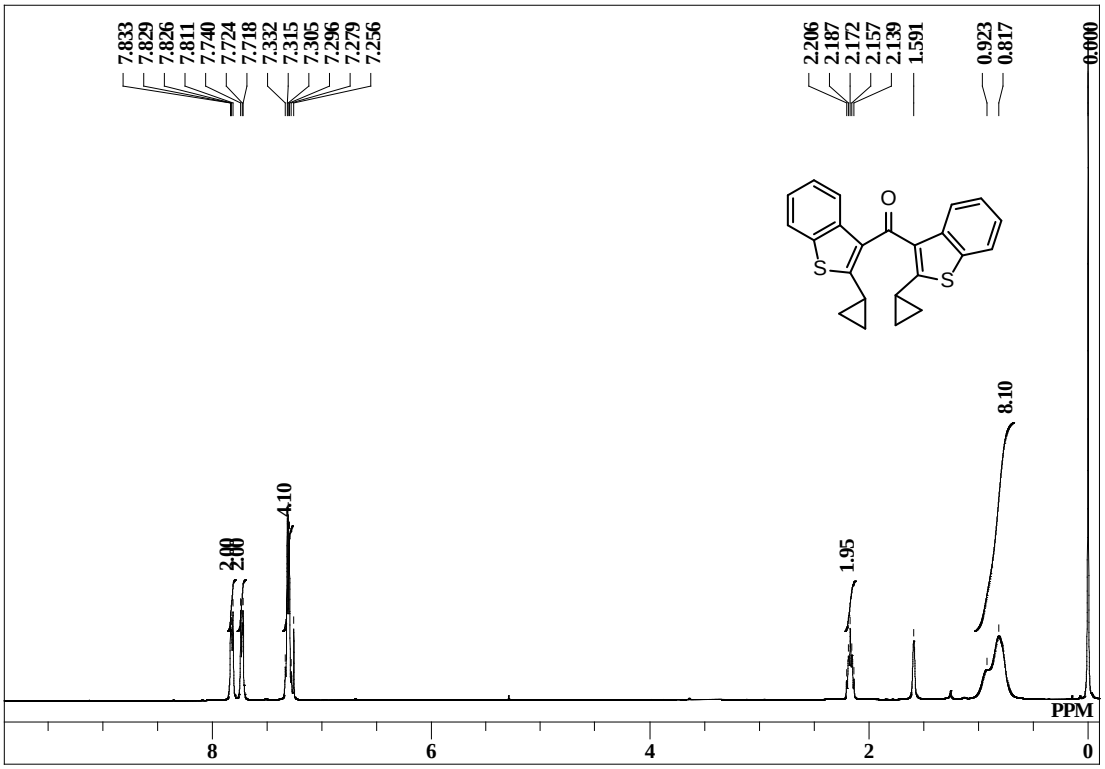
2j Single Pulse Experiment



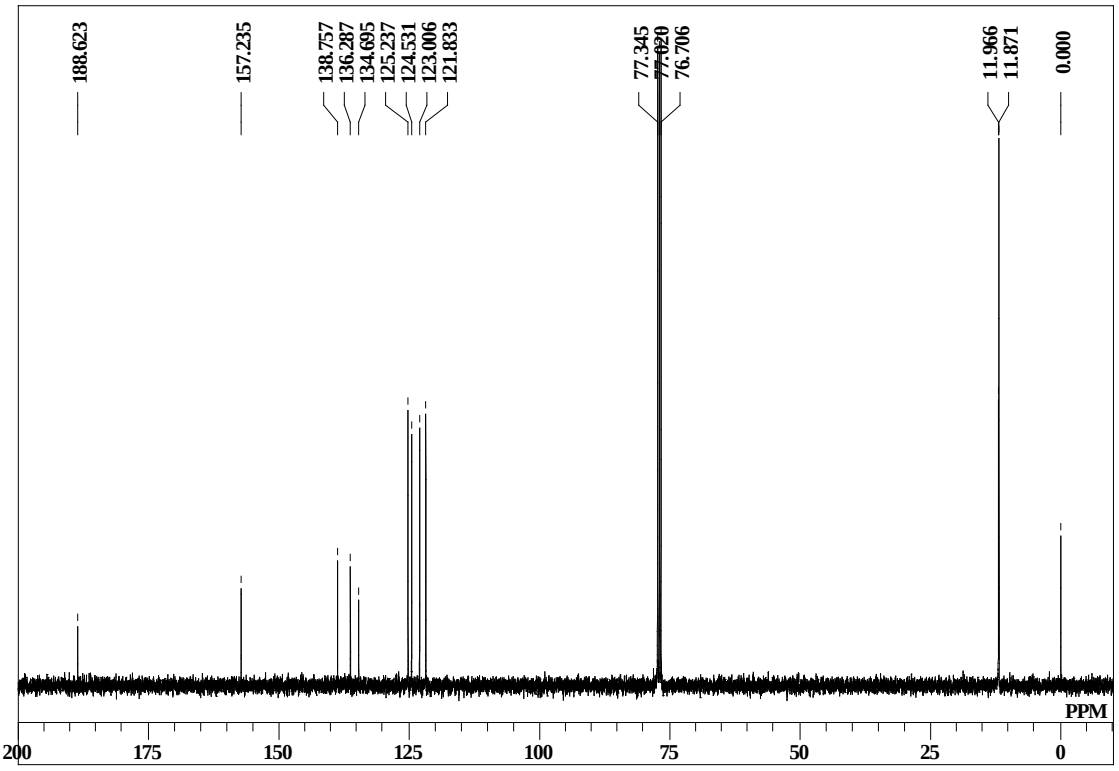
2j Single Pulse with Broadband Decoupling



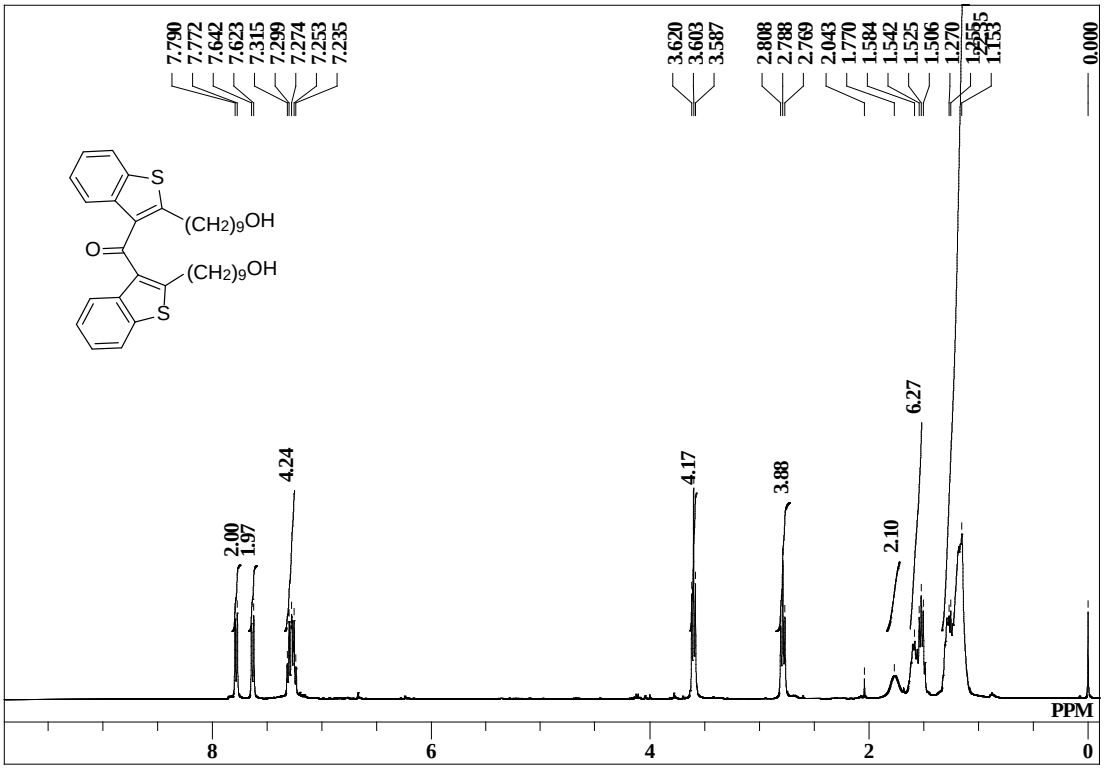
2k single_pulse



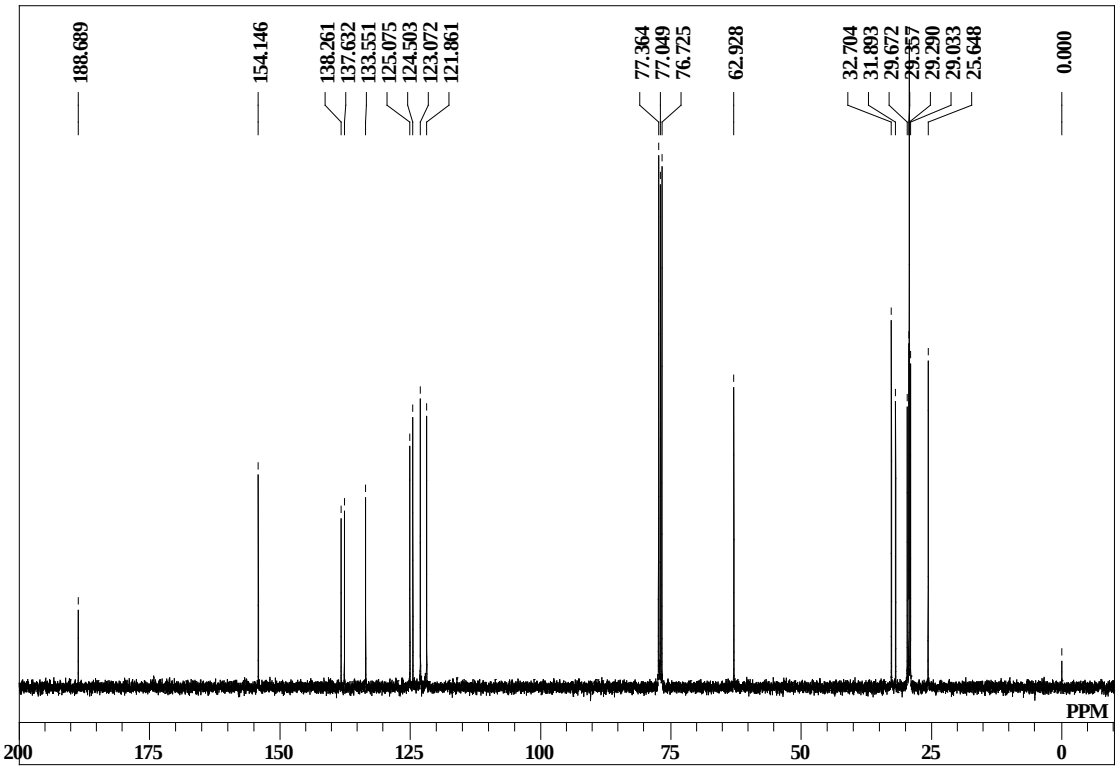
2k single pulse decoupled gated NOE



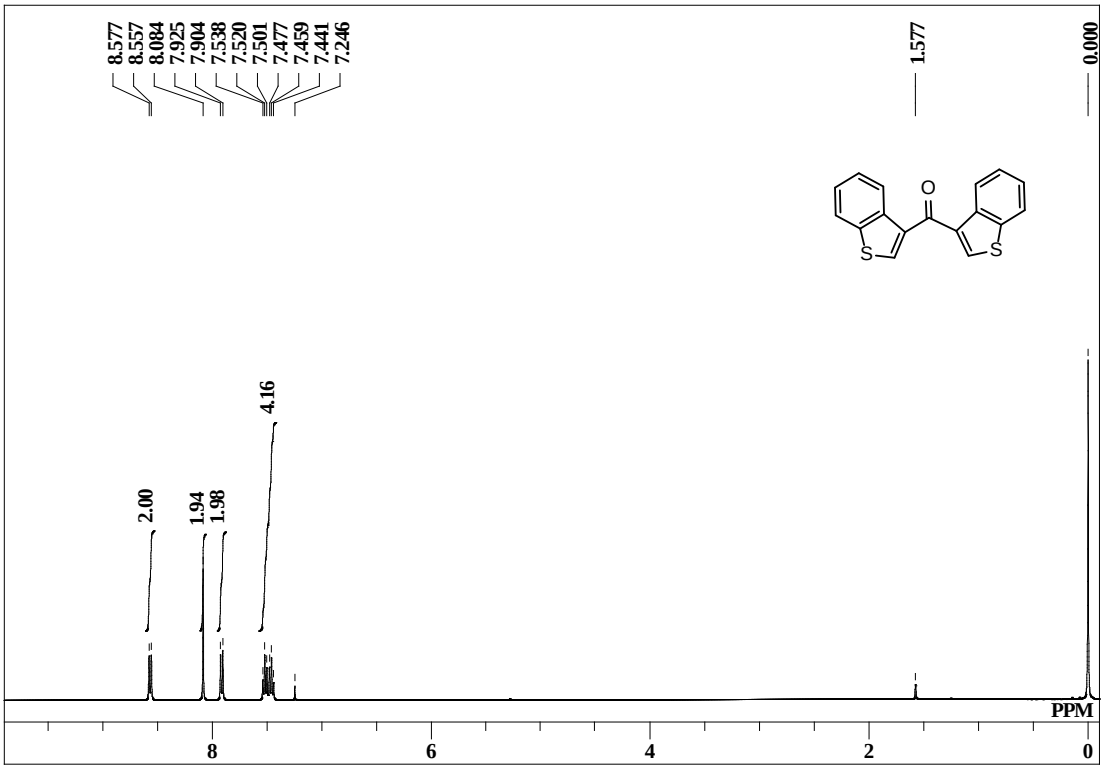
2l single_pulse



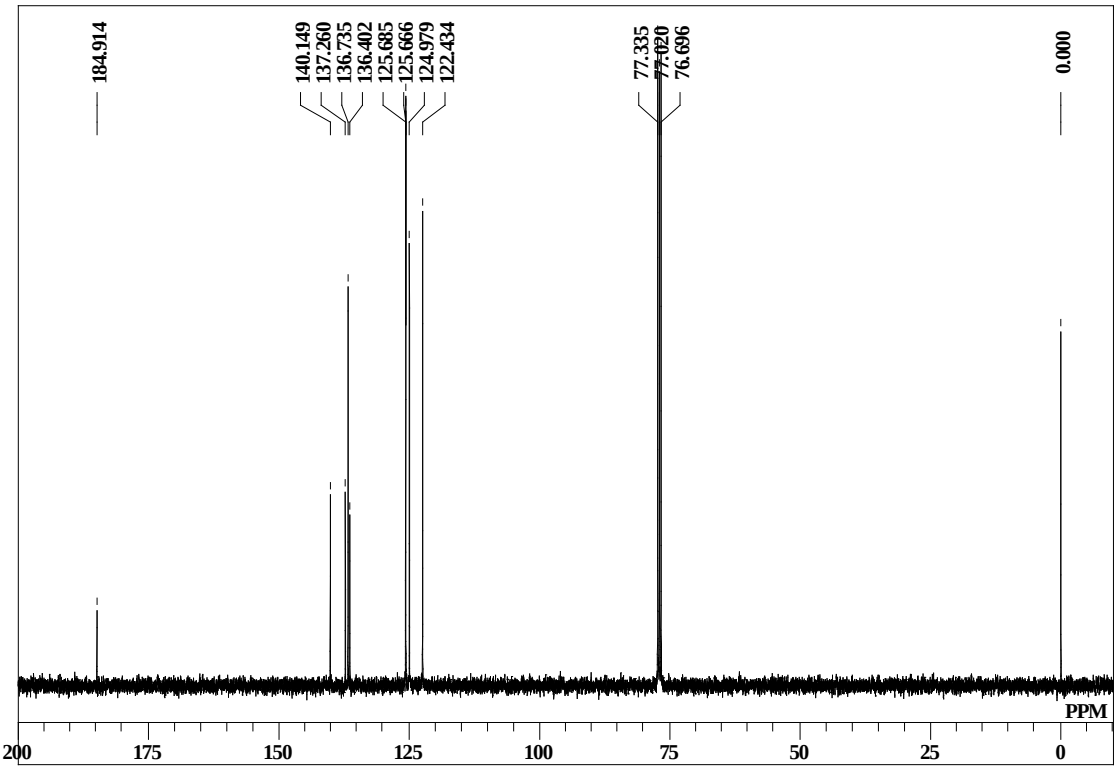
2l single pulse decoupled gated NOE



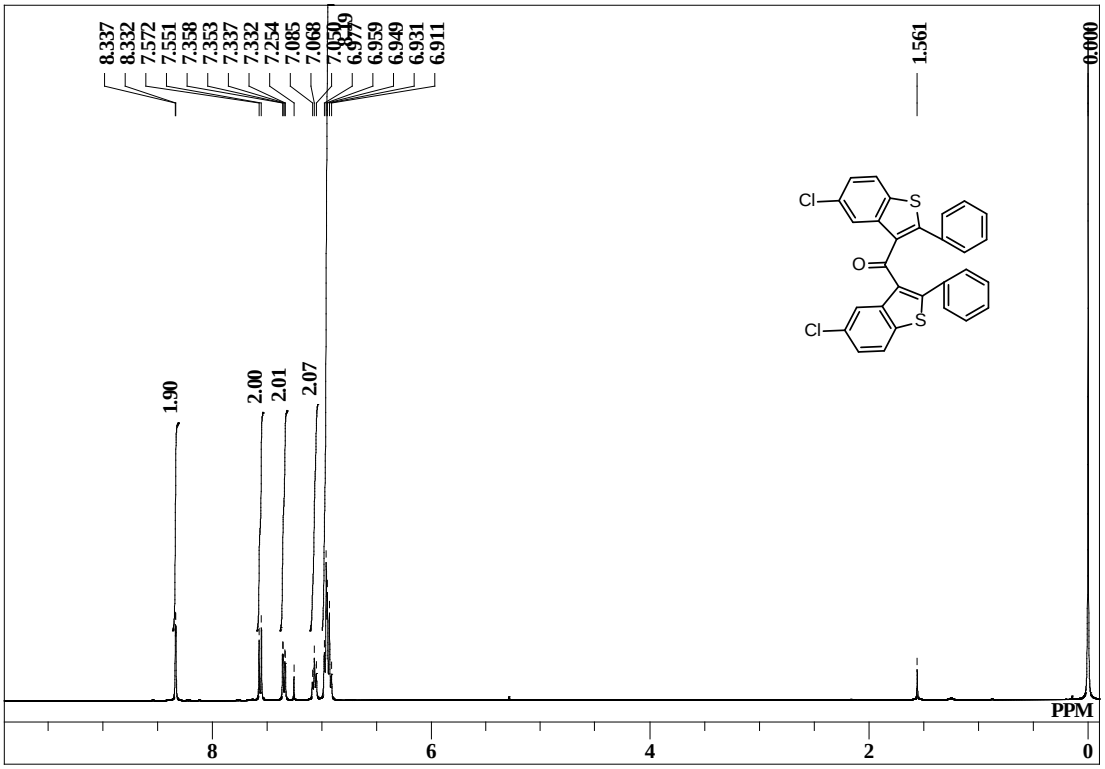
2m single_pulse



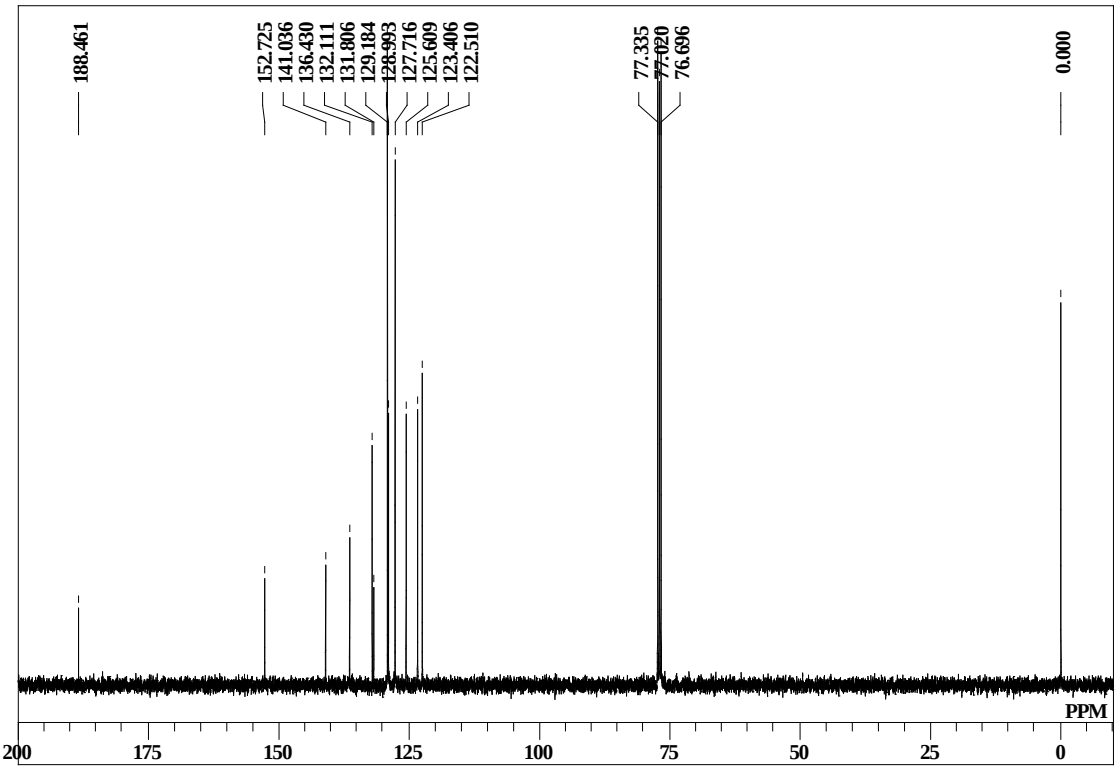
2m single pulse decoupled gated NOE



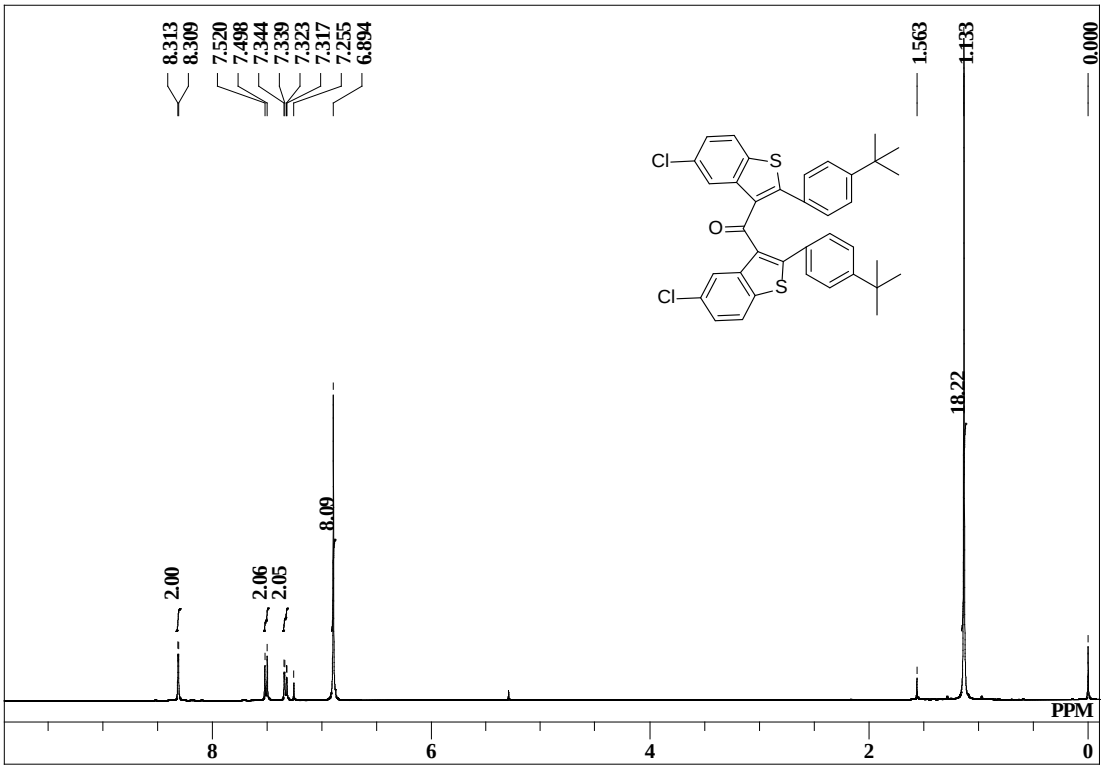
2n single_pulse



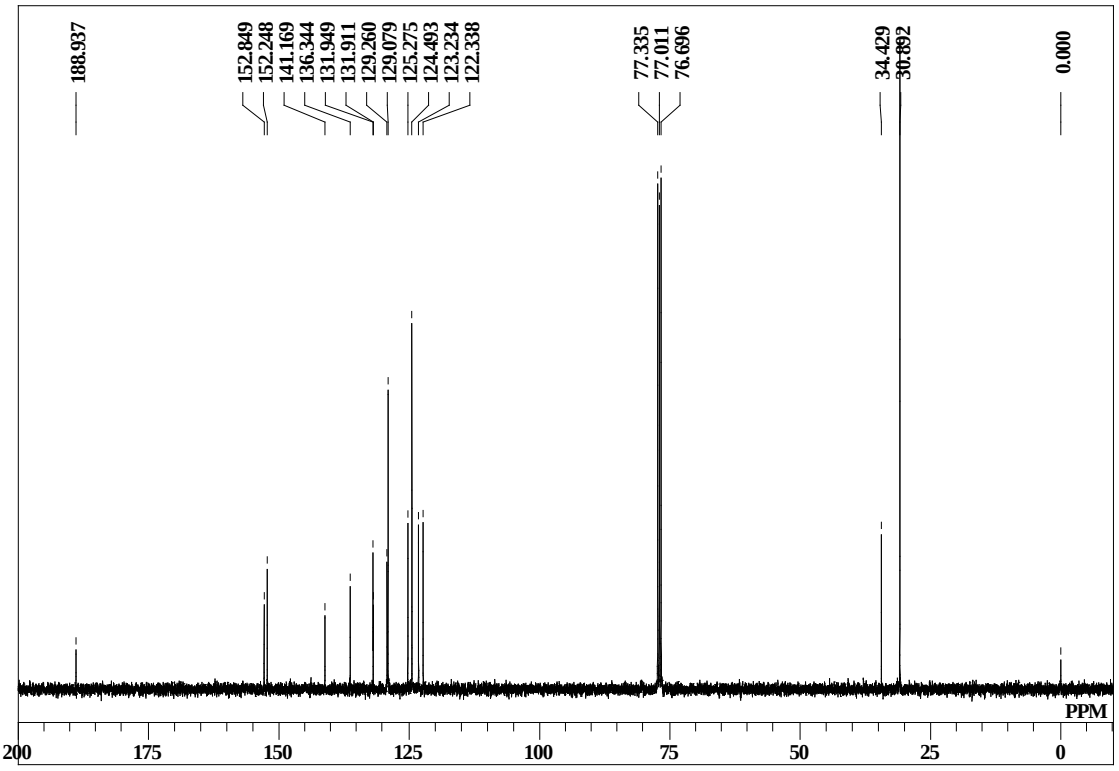
2n single pulse decoupled gated NOE



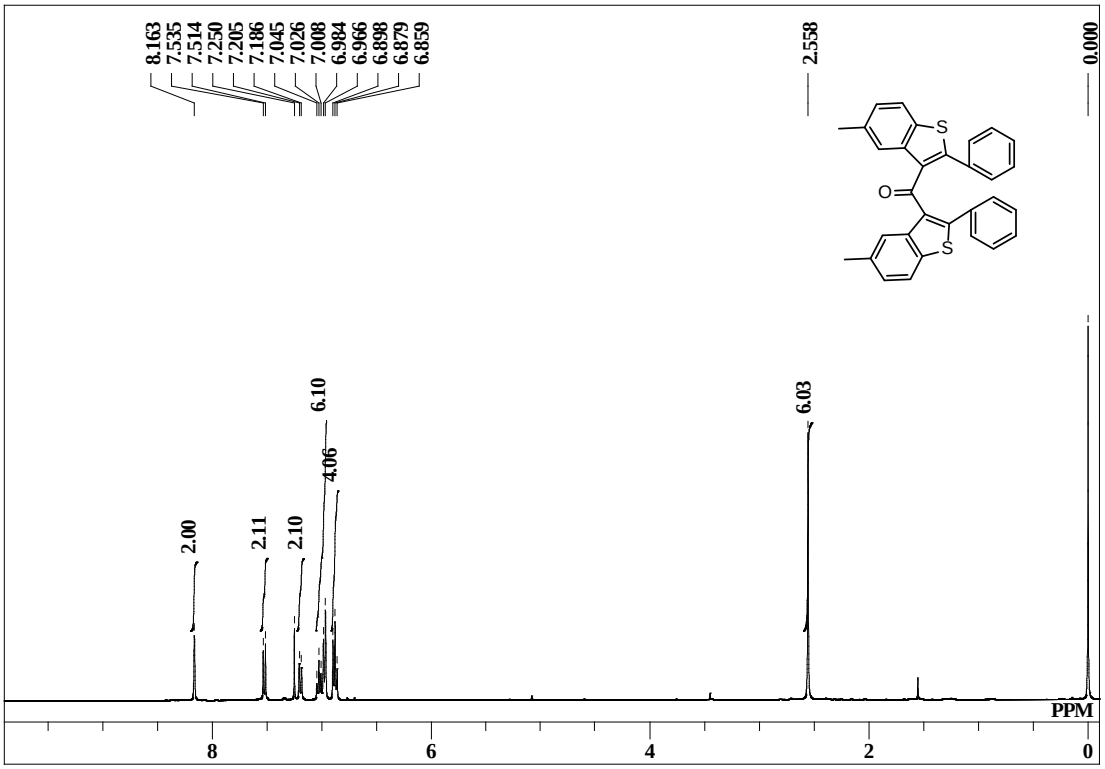
2o single_pulse



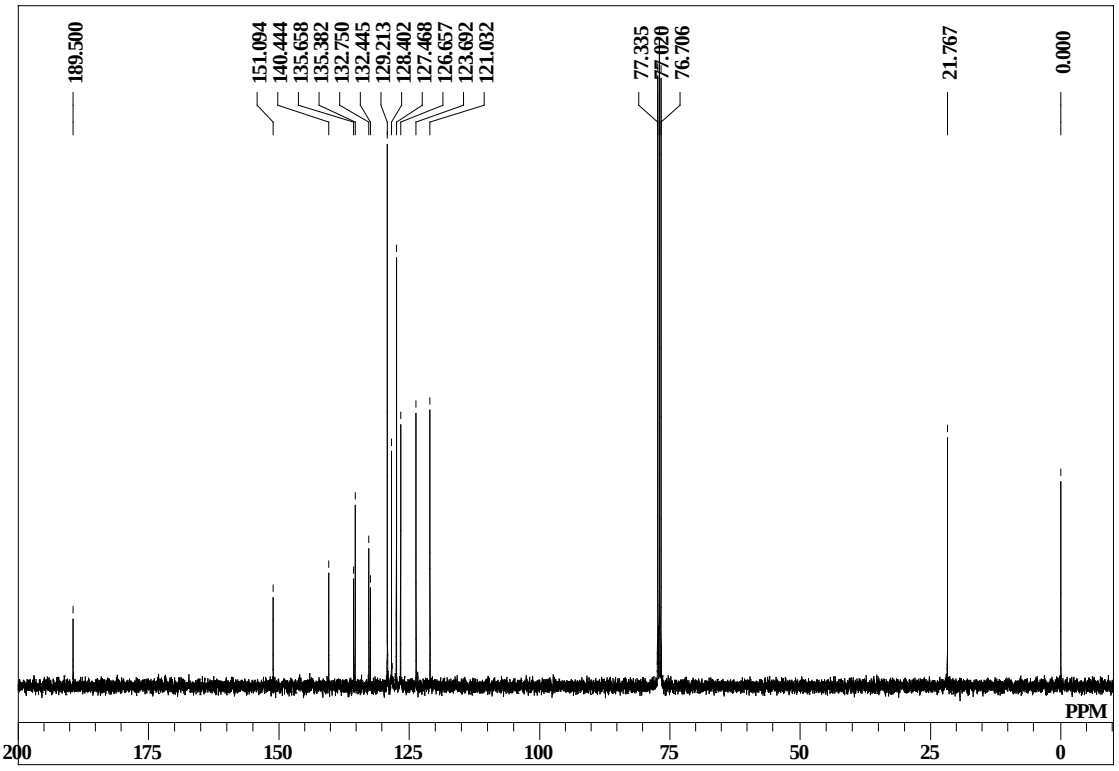
2o single pulse decoupled gated NOE



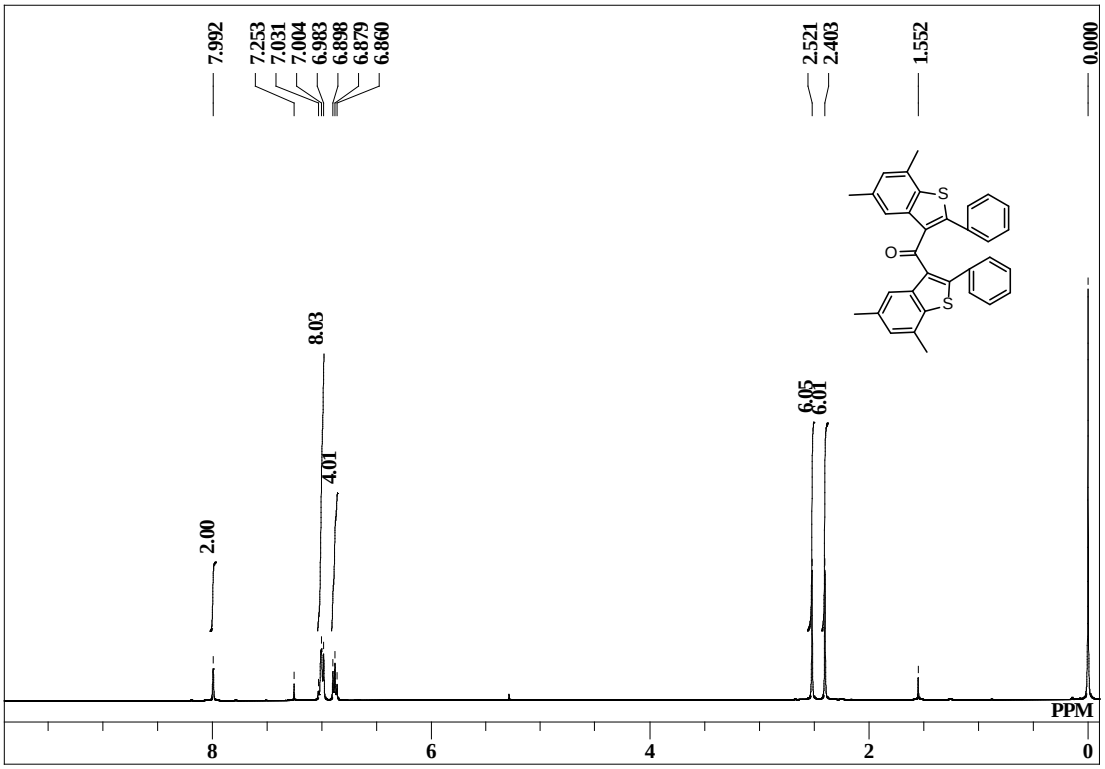
2p single_pulse



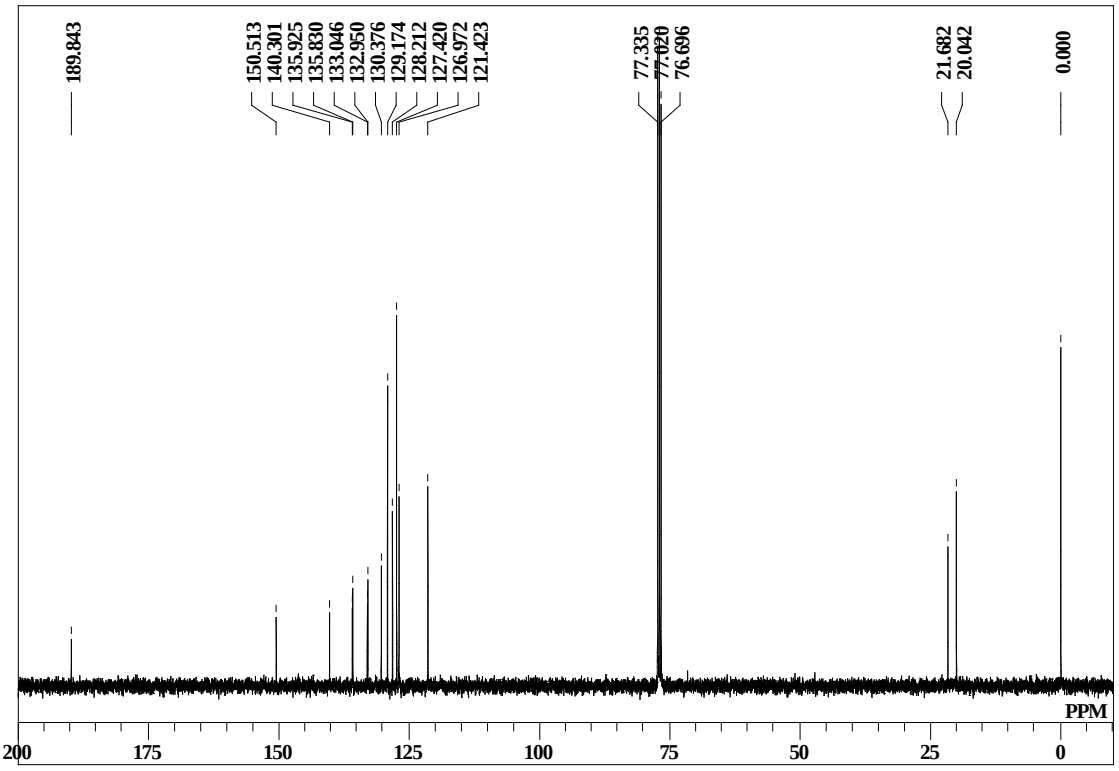
2p single pulse decoupled gated NOE



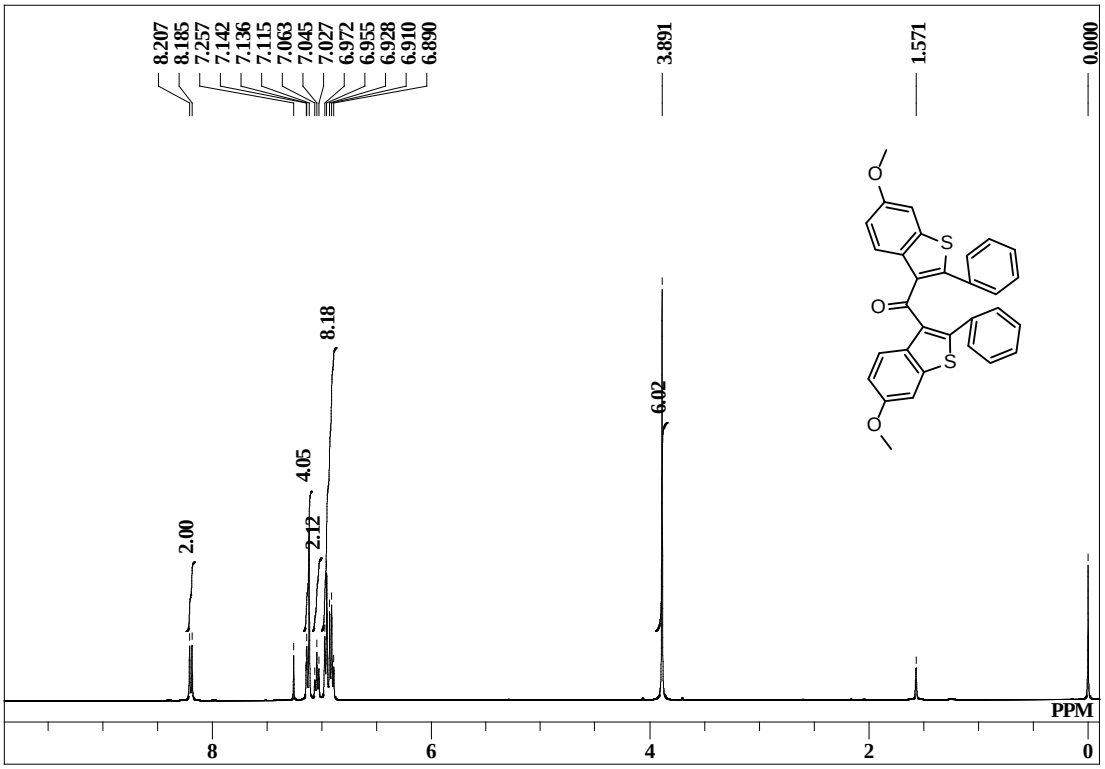
2q single_pulse



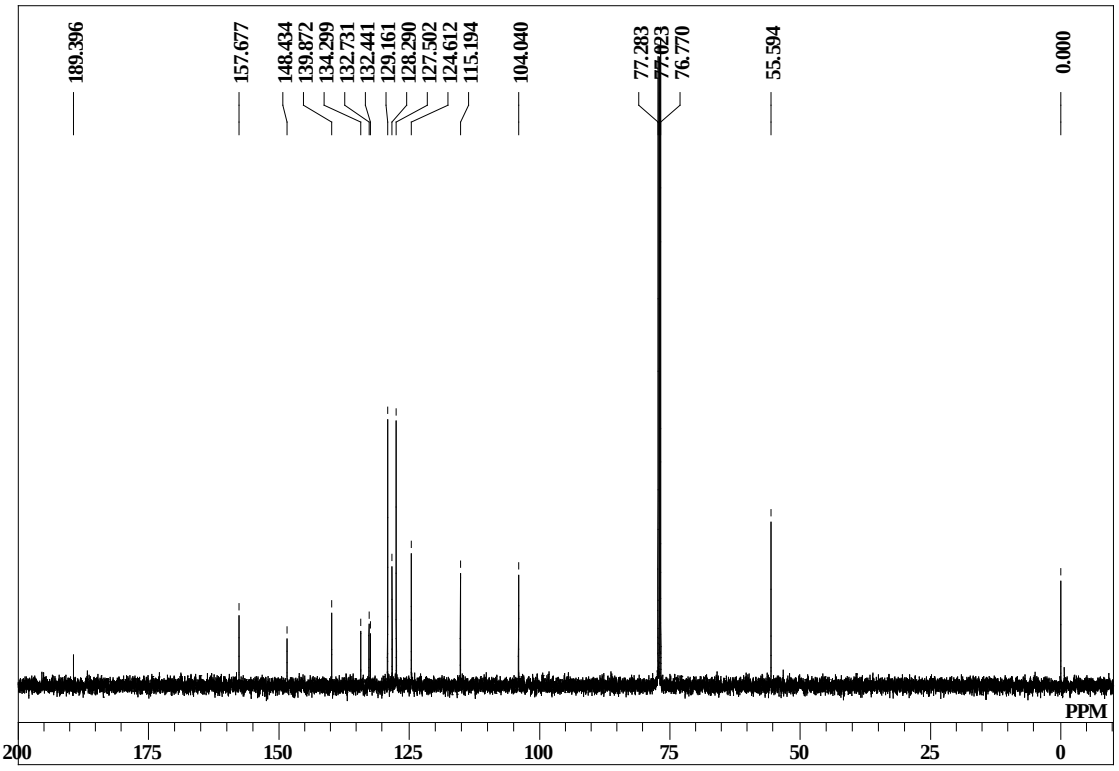
2q single pulse decoupled gated NOE



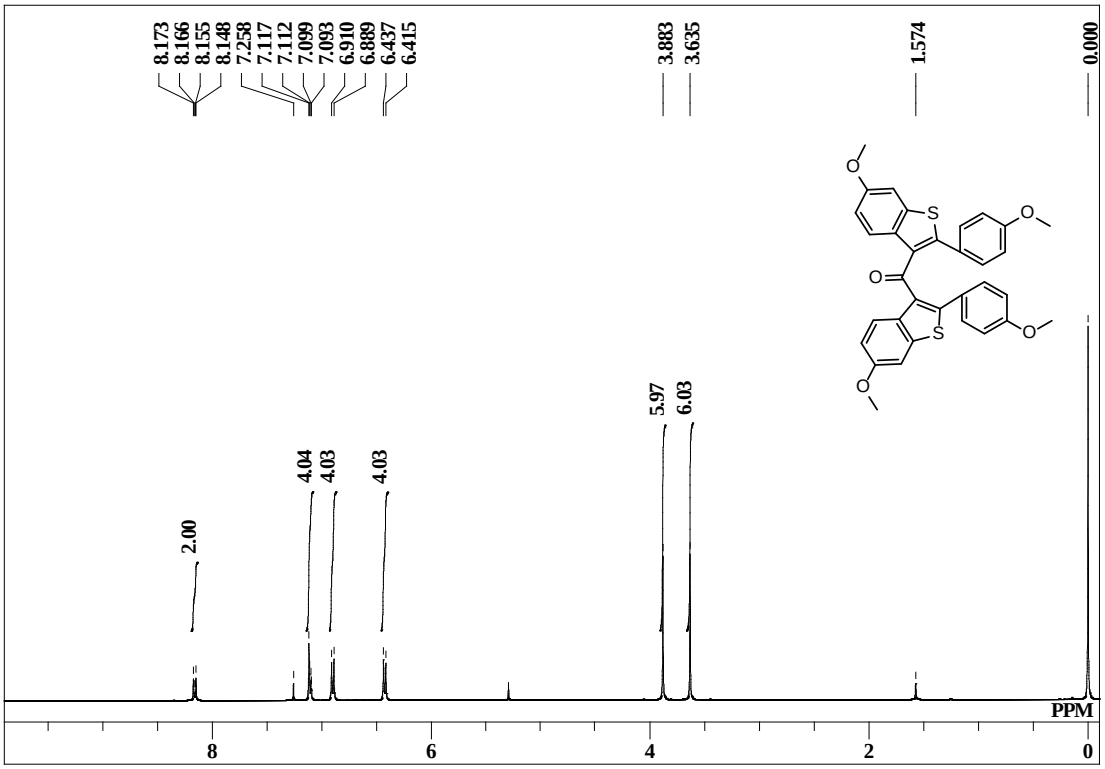
2r single_pulse



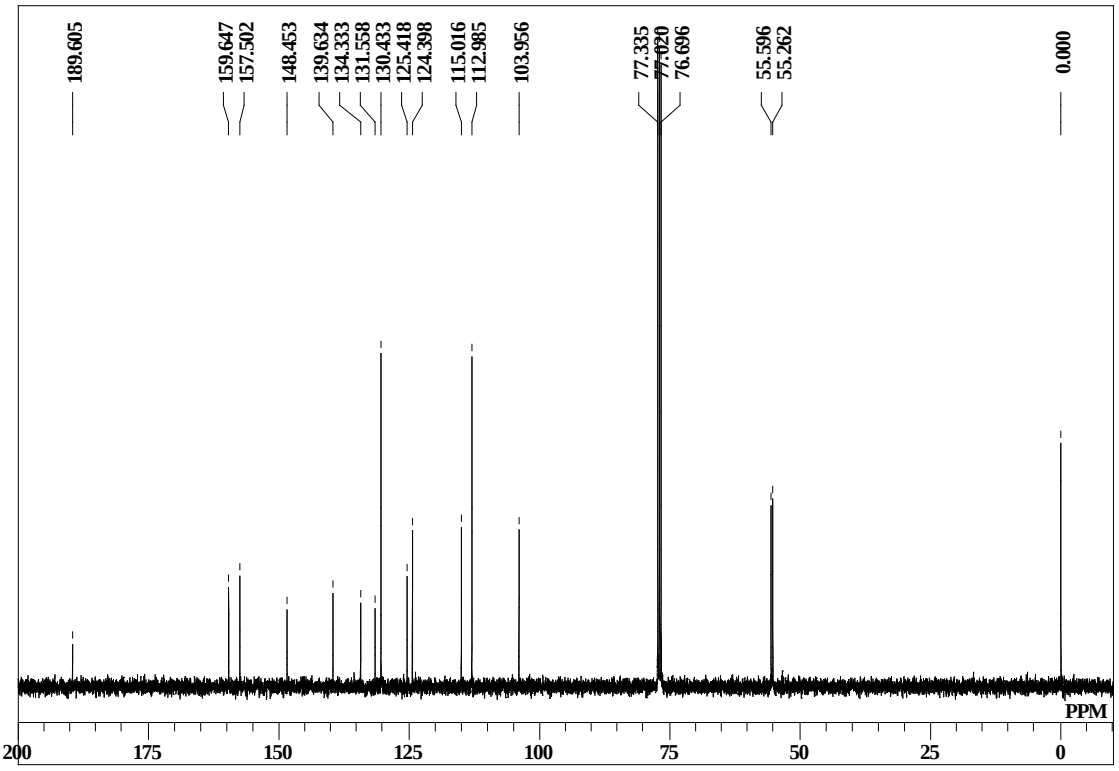
2r Single Pulse with Broadband Decoupling



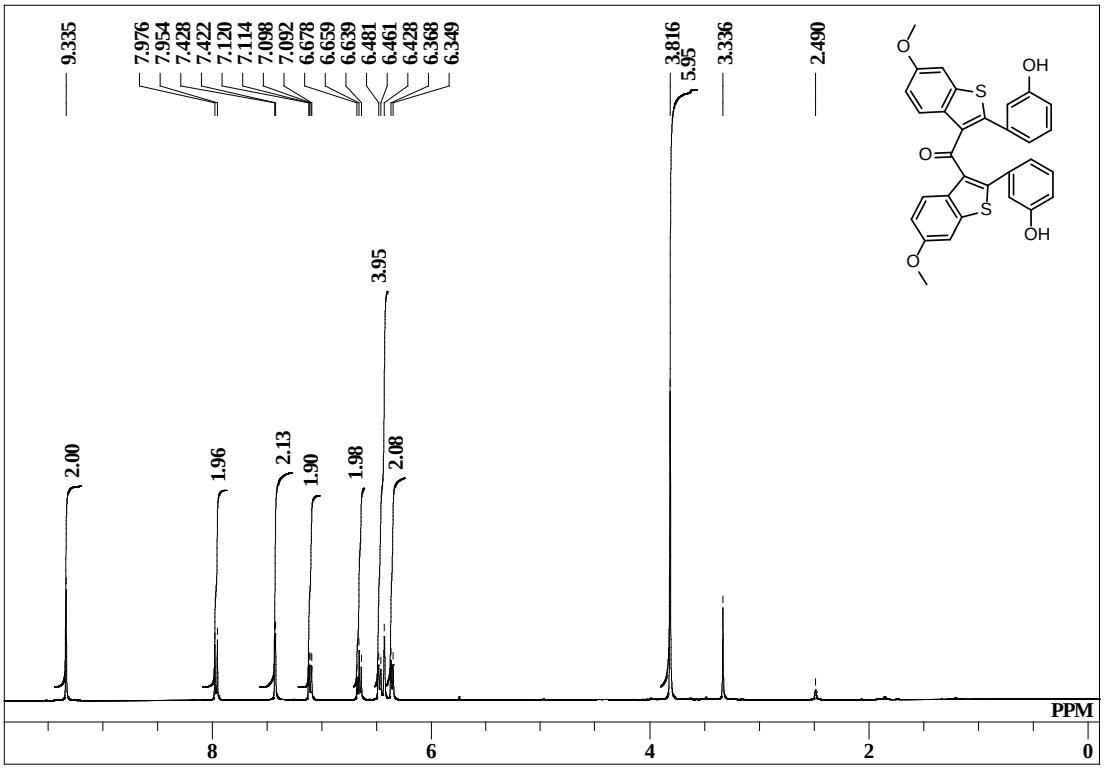
2s single_pulse



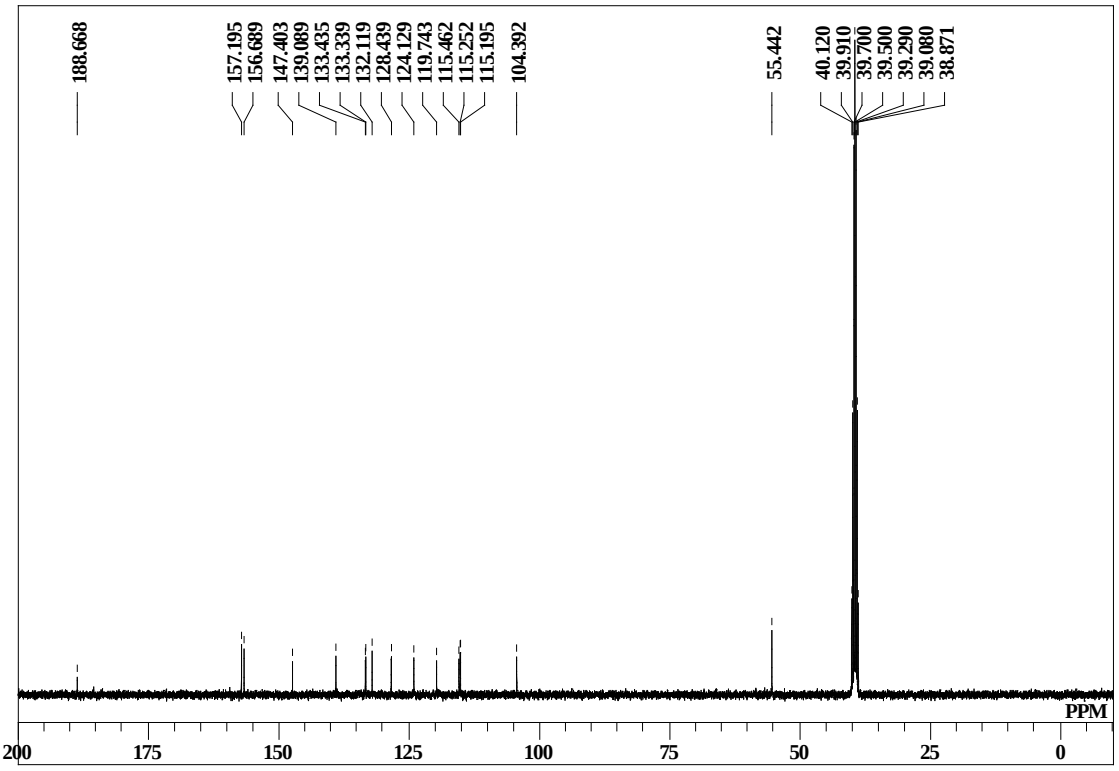
2s single pulse decoupled gated NOE



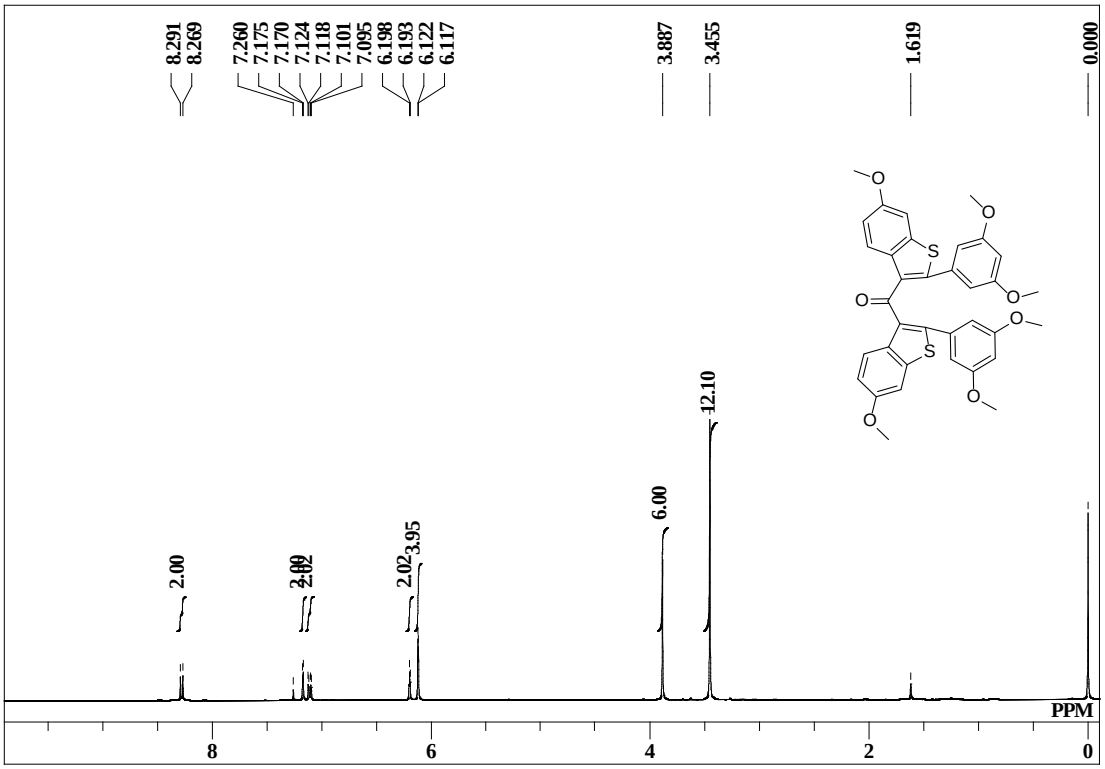
2t single_pulse



2t single pulse decoupled gated NOE



2u single_pulse



2u single pulse decoupled gated NOE