Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Materials to

Palladium-catalyzed haloallylation of aromatic ynol ethers with allyl chlorides: a highly regio- and stereoselective approach to (1*E*)-α-chloroenol ethers

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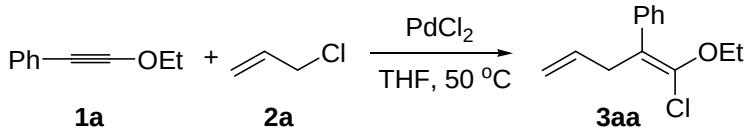
General: Unless otherwise noted, all reactions and manipulations were conducted under air atmosphere. Column chromatography was performed using silica gel (300-400 mesh) or neutral aluminum oxide (200-300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometers. Chemical shifts were reported in ppm downfield from tetramethylsilane with the solvent resonance as the internal standard. MS and microanalysis were performed in the state authorized analytical center of this university.

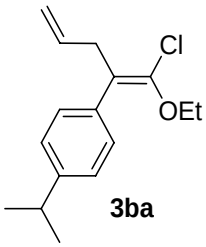
Materials: THF, toluene and dioxane was distilled from sodium prior to use. Unless otherwise noted, all the reagents were obtained commercially and used without further purification.

Representative Procedure for Palladium-Catalyzed Haloallylation of Ynol Ethers with Allyl Halides:



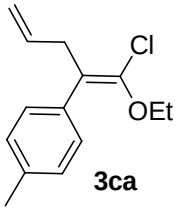
1a **2a** **3aa**

To a mixture of **2a** (114.0 mg, 1.5 mmol) and $PdCl_2$ (4.4 mg, 0.025 mmol) in 2 mL of THF was added **1a** (73 mg, 0.5 mmol). After stirring for 1 h at 50 °C, the reaction mixture was concentrated and purified by column chromatography on neutral aluminum oxide (petroleum ether) to give 103 mg (yield: 87%) of **3aa** as a colorless oil. The stereochemistry was assigned by NOE measurements. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, J = 7.2 Hz, 3 H), 3.26 (dt, J = 6.0, 1.6 Hz, 2 H), 3.93 (q, J = 7.2 Hz, 2 H), 5.00-5.15 (m, 2 H), 5.77-5.90 (m, 1 H), 7.18-7.41 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 38.2, 67.7, 115.8, 119.4, 126.8, 127.9 (2 C), 128.4 (2 C), 134.7, 138.3, 142.7; MS (EI, *m*/*z*): 224 (7), 222 (M^+, 21), 194 (2), 187 (3); Anal. Calcd. for $C_{13}H_{15}ClO$, HRMS: Cacl. 222.0811, Found: 222.0817.



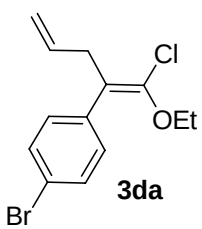
3ba

Compound **3ba**: yield: 78%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.17 (t, *J* = 7.2 Hz, 3 H), 1.27 (d, *J* = 7.2 Hz, 6 H), 2.84-2.97 (m, 1 H), 3.24 (d, *J* = 6.0 Hz, 2 H), 3.94 (q, *J* = 7.2 Hz, 2 H), 5.02-5.17 (m, 2 H), 5.78-5.90 (m, 1 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 23.9 (2 C), 33.8, 38.2, 67.7, 115.7, 119.1, 126.0 (2 C), 128.2 (2 C), 134.9, 135.5, 142.6, 147.3; MS (EI, *m*/*z*): 266 (10), 264 (M^+, 29), 209 (8), 207 (21), 185 (25); Anal. Calcd. for $C_{16}H_{21}ClO$, HRMS: Cacl. 264.1281, Found: 264.1277.



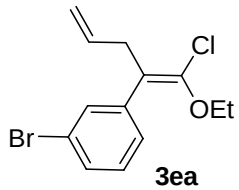
3ca

Compound **3ca**: yield: 85%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.13 (t, *J* = 7.2 Hz, 3 H), 2.32 (s, 3 H), 3.21 (dt, *J* = 6.0, 1.6 Hz, 2 H), 3.90 (q, *J* = 7.2 Hz, 2 H), 4.97-5.13 (m, 2 H), 5.73-5.86 (m, 1 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 21.2, 38.2, 67.7, 115.8, 119.2, 128.3 (2 C), 128.7 (2 C), 134.8, 135.2, 136.4, 142.5; MS (EI, *m*/*z*): 238 (6), 236 (M^+, 15), 181 (10), 179 (32); Anal. Calcd. for $C_{14}H_{17}ClO$, HRMS: Cacl. 236.0968, Found: 236.0965.



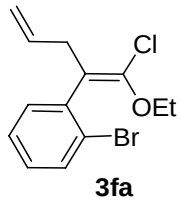
3da

Compound **3da**: yield: 81%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.33 (t, *J* = 7.2 Hz, 3 H), 3.20 (dt, *J* = 6.0, 1.6 Hz, 2 H), 3.91 (q, *J* = 7.2 Hz, 2 H), 4.94-5.11 (m, 2 H), 5.71-5.85 (m, 1 H), 7.18-7.24 (m, 2 H), 7.39-7.50 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 37.9, 67.7, 116.1, 118.0, 120.6, 130.1 (2 C), 131.0 (2 C), 134.4, 137.1, 143.0; MS (EI, *m*/*z*): 302 (24), 300 (M^+, 20), 274 (4), 272 (5); Anal. Calcd. for $C_{13}H_{14}BrClO$, HRMS: Cacl. 299.9917, Found: 299.9912.



3ea

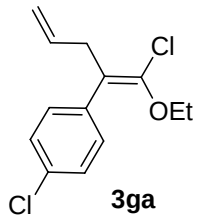
Compound **3ea**: yield: 76%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.17 (t, *J* = 7.2 Hz, 3 H), 3.21 (d, *J* = 6.0 Hz, 2 H), 3.94 (q, *J* = 7.2 Hz, 2 H), 5.02-5.14 (m, 2 H), 5.74-5.85 (m, 1 H), 7.18 (t, *J* = 8.0 Hz, 1 H), 7.27 (d, *J* = 8.0 Hz, 1 H), 7.36 (d, *J* = 8.0 Hz, 1 H), 7.51 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3, 37.9, 67.8, 116.2, 117.8, 121.9, 127.1, 129.4, 129.7, 131.5, 134.3, 140.3, 143.4; MS (EI, *m*/*z*): 302 (13), 300 (M^+, 11), 274 (2), 272 (2); Anal. Calcd. for $C_{13}H_{14}BrClO$, HRMS: Cacl. 299.9917, Found: 299.9923.



3fa

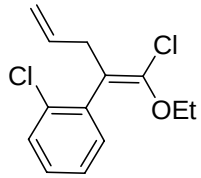
Compound **3fa**: yield: 68%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.06 (t, *J* = 7.2 Hz, 3 H), 3.05 (br, s, 1 H), 3.31 (br, s, 1 H), 3.90 (q, *J* = 7.2 Hz, 2 H), 4.94-5.06 (m, 2 H), 5.67-5.79 (m, 1 H), 7.05-7.20 (m, 2 H), 7.22-7.29 (m, 1 H), 7.58 (dd, *J* = 8.0, 0.8 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.5, 37.7, 67.3, 116.4, 119.6, 123.4, 126.9, 128.6, 131.4, 132.6, 133.8, 139.1, 142.4; MS (EI, *m*/*z*): 302 (17), 300 (M^+, 15), 267 (21), 265 (22); Anal.

Calcd. for $C_{13}H_{14}BrClO$, HRMS: Cacl. 299.9917, Found: 299.9914.



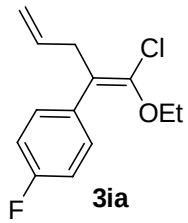
3ga

Compound **3ga**: yield: 83%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.14 (t, *J* = 7.2 Hz, 3 H), 3.21 (d, *J* = 6.0 Hz, 2 H), 3.92 (q, *J* = 7.2 Hz, 2 H), 4.99-5.12 (m, 2 H), 5.72-5.86 (m, 1 H), 7.25-7.33 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 38.0, 67.7, 116.1, 118.1, 128.1 (2 C), 129.8 (2 C), 132.4, 134.4, 136.6, 143.0; MS (EI, *m*/*z*): 258 (63), 256 (M^+, 100), 230 (8), 228 (14); Anal. Calcd. for $C_{13}H_{14}Cl_2O$, HRMS: Cacl. 256.0422, Found: 256.0430.



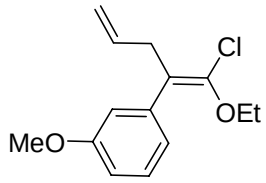
3ha

Compound **3ha**: yield: 79%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.05 (t, *J* = 7.2 Hz, 3 H), 3.18 (br, s, 2 H), 3.89 (q, *J* = 7.2 Hz, 2 H), 4.89-5.05 (m, 2 H), 5.66-5.78 (m, 1 H), 7.09-7.25 (m, 3 H), 7.33-7.42 (m, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 37.6, 67.3, 116.4, 117.9, 126.3, 128.4, 129.4, 131.3, 133.1, 133.9, 137.1, 142.3; MS (EI, *m*/*z*): 258 (58), 256 (M^+, 80), 230 (7), 228 (12); Anal. Calcd. for $C_{13}H_{14}Cl_2O$, HRMS: Cacl. 256.0422, Found: 256.0424.



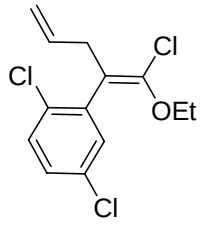
3ia

Compound **3ia**: yield: 82%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (t, *J* = 7.2 Hz, 3 H), 3.20 (dt, *J* = 6.0, 1.6 Hz, 2 H), 3.90 (q, *J* = 7.2 Hz, 2 H), 4.97-5.12 (m, 2 H), 5.72-5.85 (m, 1 H), 6.93-7.05 (m, 2 H), 7.22-7.34 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3, 38.2, 67.7, 114.8 (d, *J* = 21.1 Hz, 2 C), 116.0, 118.4, 130.1 (d, *J* = 7.9 Hz, 2 C), 134.1 (d, *J* = 3.4 Hz), 134.5, 142.7 (d, *J* = 1.3 Hz), 161.5 (d, *J* = 244.5 Hz); MS (EI, *m*/*z*): 242 (17), 240 (M^+, 50), 214 (2), 212 (9), 205 (8); Anal. Calcd. for $C_{13}H_{14}ClFO$, HRMS: Cacl. 240.0717, Found: 240.0722.



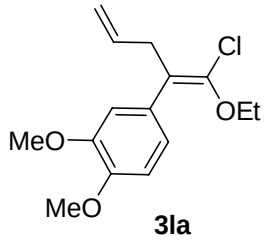
3ja

Compound **3ja**: yield: 74%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16 (t, *J* = 7.2 Hz, 3 H), 3.23 (d, *J* = 6.0 Hz, 2 H), 3.80 (s, 3 H), 3.93 (q, *J* = 7.2 Hz, 2 H), 5.00-5.16 (m, 2 H), 5.75-5.89 (m, 1 H), 6.79 (d, *J* = 7.6 Hz, 1 H), 6.90-6.96 (m, 2 H), 7.23 (t, *J* = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 38.2, 55.2, 67.8, 112.2, 114.2, 115.9, 119.2, 120.9, 128.9, 134.7, 139.6, 142.8, 159.1; MS (EI, *m*/*z*): 254 (11), 252 (M^+, 33), 197 (5), 195 (16); Anal. Calcd. for $C_{14}H_{17}ClO_2$, HRMS: Cacl. 252.0917, Found: 252.0915.



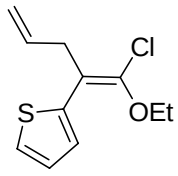
3ka

Compound **3ka**: yield: 76%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.08 (t, *J* = 7.2 Hz, 3 H), 3.16 (br, s, 2 H), 3.90 (q, *J* = 7.2 Hz, 2 H), 4.95-5.06 (m, 2 H), 5.63-5.76 (m, 1 H), 7.06 (d, *J* = 8.0 Hz, 1 H), 7.20 (dd, *J* = 8.0, 2.0 Hz, 1 H), 7.41 (d, *J* = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 37.4, 67.3, 116.6, 116.7, 126.7, 129.3, 132.1, 133.5, 133.6, 134.0, 135.7, 142.6; MS (EI, *m*/*z*): 292 (10), 290 (M^+, 6), 257 (3), 255 (1); Anal. Calcd. for $C_{13}H_{13}Cl_3O$, HRMS: Cacl. 290.0032, Found: 290.0036.



3la

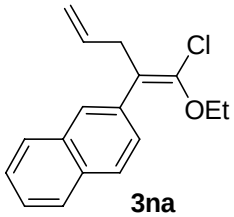
Compound **3la**: yield: 72%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.16 (t, *J* = 7.2 Hz, 3 H), 3.23 (d, *J* = 6.0 Hz, 2 H), 3.80-3.99 (m, 8 H), 5.00-5.16 (m, 2 H), 5.78-5.90 (m, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 6.91 (dd, *J* = 8.0, 2.0 Hz, 1 H), 6.98 (d, *J* = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.5, 38.3, 55.78, 55.80, 67.7, 110.5, 112.0, 115.8, 119.0, 120.7, 130.8, 134.9, 142.4, 147.7, 148.1; MS (EI, *m*/*z*): 284 (14), 282 (M^+, 48), 227 (27), 225 (100); Anal. Calcd. for $C_{15}H_{19}ClO_3$, HRMS: Cacl. 282.1023, Found: 282.1020.



3ma

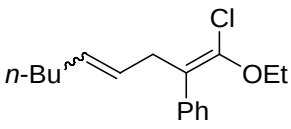
Compound **3ma**: yield: 77%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.44 (t, *J* = 7.2 Hz, 3 H), 3.37 (d, *J* = 6.0 Hz, 2 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 5.03-5.20 (m, 2 H), 5.83-5.97 (m, 1 H), 6.92-7.00 (m, 1 H), 7.11 (d, *J* = 3.6 Hz, 1 H), 7.23 (d, *J* = 5.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.5, 36.1, 67.5, 113.5, 115.9, 124.8, 125.0, 126.2, 134.6,

139.2, 141.7; MS (EI, *m*/*z*): 230 (22), 228 (M^+, 62), 199 (14), 173 (21), 171 (60); Anal. Calcd. for $C_{11}H_{13}ClOS$, HRMS: Cacl. 228.0376, Found: 228.0380.



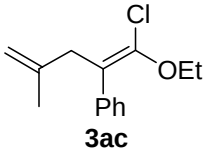
3na

Compound **3na**: yield: 75%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.13 (t, *J* = 7.2 Hz, 3 H), 3.35 (d, *J* = 6.0 Hz, 2 H), 3.95 (q, *J* = 7.2 Hz, 2 H), 5.00-5.19 (m, 2 H), 5.80-5.93 (m, 1 H), 7.40-7.56 (m, 3 H), 7.75-7.90 (m, 4 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 38.3, 67.8, 116.0, 119.4, 125.8, 125.9, 127.0, 127.1, 127.3, 127.5, 128.0, 132.3, 133.2, 134.7, 135.8, 143.1; Anal. Calcd. for $C_{17}H_{17}ClO$, HRMS (ESI): Cacl. 272.0968, Found: 272.0973.



3ab

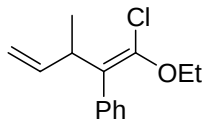
Compound **3ab**: yield: 82%, colorless oil; 4*E*/4*Z* = 64/36; MS (EI, *m*/*z*): 280 (17), 278 (M^+, 56), 244 (10), 243 (51), 215 (38); Anal. Calcd. for $C_{17}H_{23}ClO$, C: 73.23, H: 8.31, Cl: 12.72, O: 5.74, Found C: 73.01, H 8.57, Cl: 12.95.



3ac

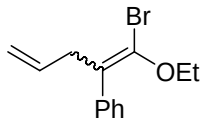
Compound **3ac**: yield: 73%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.15 (t, *J* = 7.2 Hz, 3 H), 1.75 (s, 3 H), 3.20 (s, 2 H), 3.93 (q, *J* = 7.2 Hz, 2 H), 4.71-4.77 (m, 2 H), 7.18-7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 22.6, 42.0, 67.7, 111.4, 119.4, 126.7,

127.8 (2 C), 128.4 (2 C), 138.2, 142.2, 143.3.; MS (EI, *m*/*z*): 238 (3), 236 (M^+, 10), 210 (1), 208 (2); Anal. Calcd. for $C_{14}H_{17}ClO$, HRMS: Cacl. 236.0968, Found: 236.0964.



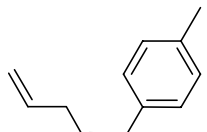
3ad

Compound **3ad**: yield: 71%, colorless oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.01-1.08 (m, 6 H), 3.65-3.74 (m, 1 H), 3.84 (t, *J* = 7.2 Hz, 2 H), 5.01-5.13 (m, 2 H), 5.78-5.88 (m, 1 H), 7.09-7.17 (m, 2 H), 7.21-7.35 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.3, 17.5, 39.9, 67.5, 113.8, 125.4, 126.8, 127.6 (2 C), 129.5 (2 C), 136.4, 140.6, 141.3; MS (EI, *m*/*z*): 238 (19), 236 (M^+, 60), 223 (22), 221 (22), 201 (33); Anal. Calcd. for $C_{14}H_{17}ClO$, HRMS: Cacl. 236.0968, Found: 236.0962.



3ag

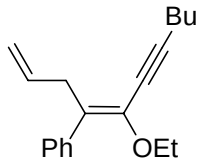
Compound **3ag**: yield: 83%, colorless oil; *E*/*Z* = 4/1; MS (EI, *m*/*z*): 268 (19), 266 (M^+, 17), 159 (22), 158 (20); Anal. Calcd. for $C_{13}H_{15}BrO$, C: 58.44, H: 5.66, Br: 29.91, O: 5.99, Found C: 58.62, H 5.88, Br: 29.75.



4a

Compound **4a**: To a mixture of 4-Me-$C_6H_4B(OH)_2$ (51 mg, 0.38 mmol), $Pd(OAc)_2$ (2.8 mg, 0.013 mmol), Cs_2CO_3 (163 mg, 0.5 mmol), Xphos (15 mg, 0.05 mol) in 2 mL of THF was added **3aa** (56 mg, 0.25 mmol). After stirring at 50 ^oC for 2 h, the reaction mixture was

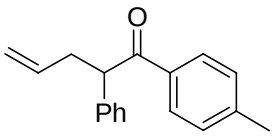
quenched with saturated $NaHCO_3$, extracted with EtOAc, washed with brine, and dried over anhydrous Na_2SO_4. Column chromatography on neutral aluminum oxide gave 54 mg (yield: 77%) of **4a** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.11 (t, *J* = 7.2 Hz, 3 H), 2.43 (s, 3 H), 3.12 (dt, *J* = 6.0, 1.6 Hz, 2 H), 3.54 (q, *J* = 7.2 Hz, 2 H), 4.95-5.07 (m, 2 H), 5.73-5.84 (m, 1 H), 7.22-7.30 (m, 3 H), 7.36-7.43 (m, 4 H), 7.44-7.48 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.1, 21.4, 37.2, 65.3, 115.4, 120.6, 126.2, 127.8 (2 C), 128.90 (2 C), 128.94 (2 C), 129.2 (2 C), 132.8, 137.1, 138.0, 140.0, 151.4; MS (EI, *m*/*z*): 279 (6), 278 (M^+, 41), 263 (6), 119 (100); Anal. Calcd. For $C_{20}H_{22}O$, HRMS: Cacl. 278.1671, Found: 278.1674.



4b

Compound **4b**: To a mixture of 1-hexyne (82 mg, 1.0 mmol), $Pd(OAc)_2$ (2.8 mg, 0.013 mmol), Cs_2CO_3 (163 mg, 0.5 mmol), Xphos (15 mg, 0.05 mol) in 2 mL of THF was added **3aa** (56 mg, 0.25 mmol). After stirring at 60 ^{o}C for 4 h, the reaction mixture was quenched with saturated $NaHCO_3$, extracted with EtOAc, washed with brine, and dried over anhydrous Na_2SO_4. Column chromatography on neutral aluminum oxide gave 43 mg (yield: 82%) of **4b** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.99 (t, *J* = 7.2 Hz, 3 H), 1.23 (t, *J* = 7.2 Hz, 3 H), 1.49-1.65 (m, 4 H), 2.48 (t, *J* = 6.8 Hz, 2 H), 3.39 (dt, *J* = 6.0, 1.6 Hz, 2 H), 4.01 (q, *J* = 7.2 Hz, 2 H), 4.99 (dd, *J* = 10.0, 1.6 Hz, 1 H), 5.09 (dd, *J* = 17.2, 1.6 Hz, 1 H), 5.78-5.94 (m, 1 H), 7.12-7.25 (m, 1 H), 7.31 (dt, *J* = 7.2, 1.6 Hz, 2 H) , 7.40-7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 13.6, 15.2, 19.2, 22.0, 30.7, 38.0, 65.0, 74.5, 97.5, 115.2, 124.2, 126.3, 127.7 (2 C), 128.7 (2 C), 135.5, 136.6, 138.5; MS (EI, *m*/*z*): 269 (5), 268 (M^+, 25), 240 (35), 225 (22), 211 (15); Anal. Calcd. for $C_{19}H_{24}O$, HRMS:

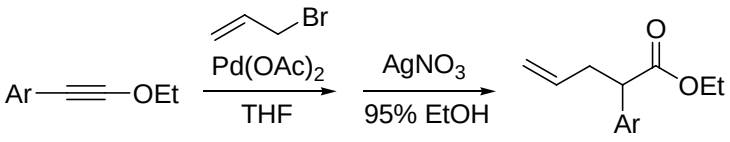
Cacl. 268.1827, Found: 268.1821.



5

To a solution of **4a** (50 mg, 0.18 mmol) in 1 mL of THF was added 1 mL of 6 N HCl at rt. After stirring at 50 ^{o}C for 1 h, the reaction mixture was quenched by saturated $NaHCO_3$, extracted with EtOAc, washed with brine, and dried over Na_2SO_4. Column chromatography on silica gel gave 43 mg (yield: 95%) of **5** as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.36 (s, 3 H), 2.54-2.64 (m, 1 H), 2.93-3.04 (m, 1 H), 4.64 (t, *J* = 7.2 Hz, 1 H), 4.95-5.11 (m, 2 H), 5.71-5.84 (m, 1 H), 7.16-7.24 (m, 3 H), 7.28-7.36 (m, 4 H), 7.89 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.6, 38.2, 53.4, 116.6, 127.1, 128.2 (2 C), 128.86 (2 C), 128.90 (2 C), 129.2 (2 C), 134.2, 136.1, 139.3, 143.7, 198.8; MS (EI, *m*/*z*): 250 (M^+, 2), 235 (1), 165 (3), 119 (100); Anal. Calcd. for $C_{18}H_{18}O$, HRMS: Cacl. 250.1358, Found: 250.1250.

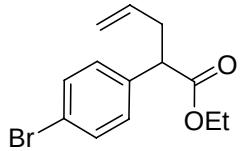
General Procedure of the Synthesis of α-Allylated Ester:



6a (Ar = Ph)

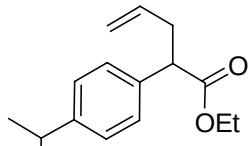
Compound 6a: To a mixture of allyl bromide (114.0 mg, 1.5 mmol) and $Pd(OAc)_2$ (5.6 mg, 0.025 mmol) in 2 mL of THF was added **1a** (73 mg, 0.5 mmol). After stirring for 1 h at 50 ^{o}C, the reaction mixture was concentrated and then dissolved in 2 mL of 95% EtOH, followed by adding of $AgNO_3$ (128 mg, 0.75 mmol). After stirring at 60 ^{o}C for 5 h, the reaction mixture was quenched by water, extracted with EtOAc, washed by brine, and concentrated. Column purification on silica gel gave compound 78 mg (yield: 76%) of **6a** as a colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (t, *J* = 7.2 Hz, 3 H), 2.47-2.58 (m, 1

H), 2.78-2.89 (m, 1 H), 3.60-3.68 (m, 1 H), 4.05-4.21 (m, 2 H), 4.98-5.13 (m, 2 H), 5.68-5.81 (m, 1 H), 7.23-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2, 37.7, 51.5, 60.8, 116.9, 127.3, 127.9 (2 C), 128.6 (2 C), 135.3, 138.7, 173.4; MS (EI, *m*/*z*): 204 (M^+, 1), 163 (8), 135 (13), 131 (100).



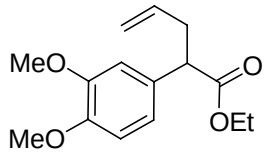
6b

Compound **6b**: yield: 67%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21 (t, *J* = 7.2 Hz, 3 H), 2.44-2.54 (m, 1 H), 2.75-2.86 (m, 1 H), 3.54-3.64 (m, 1 H), 4.04-4.21 (m, 2 H), 4.99-5.12 (m, 2 H), 5.64-5.76 (m, 1 H), 7.21 (dd, *J* = 8.4, 2.0 Hz, 2 H), 7.45 (dd, *J* = 8.4, 2.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 37.5, 50.9, 61.0, 117.3, 121.3, 129.7 (2 C), 131.7 (2 C), 134.8, 137.6, 173.0; MS (EI, *m*/*z*): 285 (3), 283 (M^++H, 3), 243 (30), 241 (29), 211 (100), 209 (87); Anal. Calcd. for $C_{13}H_{15}BrO_2$, HRMS: Cacl. 283.0334 (M^++H), Found: 283.0337.



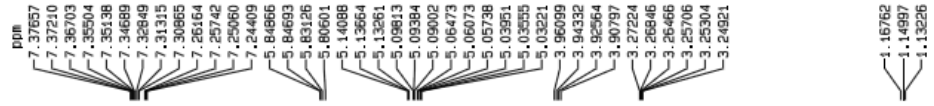
6c

Compound **6c**: yield: 62%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.18-1.33 (m, 9 H), 2.46-2.57 (m, 1 H), 2.78-2.97 (m, 2 H), 3.62 (dd, *J* = 8.8, 6.4 Hz, 1 H), 4.04-4.23 (m, 2 H), 4.99-5.15 (m, 2 H), 5.69-5.83 (m, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.25 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2, 24.0 (2 C), 33.7, 37.8, 51.2, 60.7, 116.8, 126.6 (2 C), 127.8 (2 C), 135.5, 136.0, 147.8, 173.6; MS (EI, *m*/*z*): 246 (M^+, 3), 231 (3), 206 (7), 205 (54), 173 (100); Anal. Calcd. for $C_{16}H_{22}O_2$, HRMS: Cacl. 246.1620, Found: 246.1627.



6d

Compound **6d**: yield: 71%, colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21 (t, J = 7.2 Hz, 3 H), 2.43-2.54 (m, 1 H), 2.73-2.84 (m, 1 H), 3.50-3.59 (m, 1 H), 3.86 (s, 3 H), 3.88 (s, 3 H), 4.03-4.21 (m, 2 H), 4.97-5.13 (m, 2 H), 5.66-5.78 (m, 1 H), 6.78-6.90 (m, 3 H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2, 37.8, 51.0, 55.8, 55.9, 60.7, 110.8, 111.1, 116.9, 120.1, 131.2, 135.4, 148.2, 148.9, 173.6; MS (EI, m/z): 265 (4), 264 (M^+, 25), 224 (13), 223 (100), 191 (34).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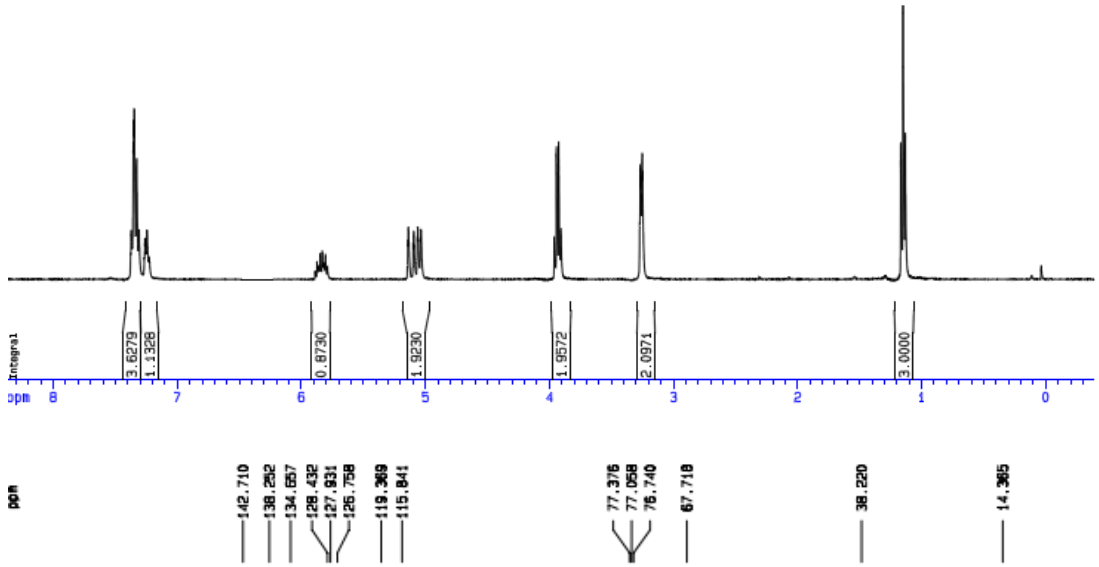
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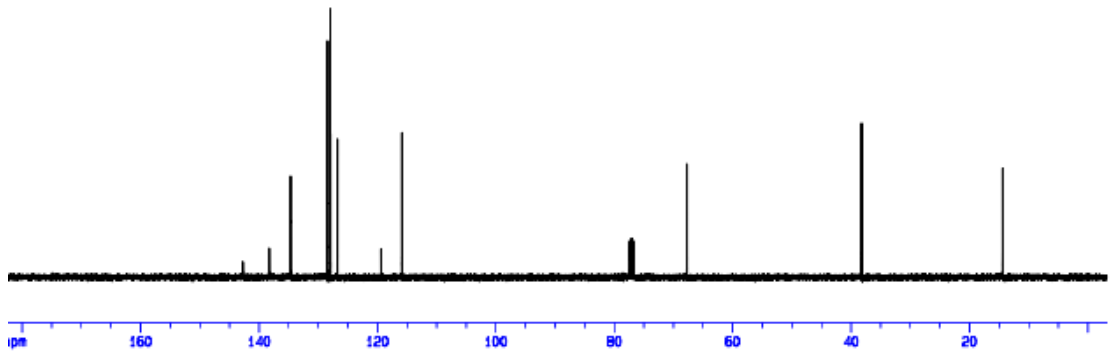
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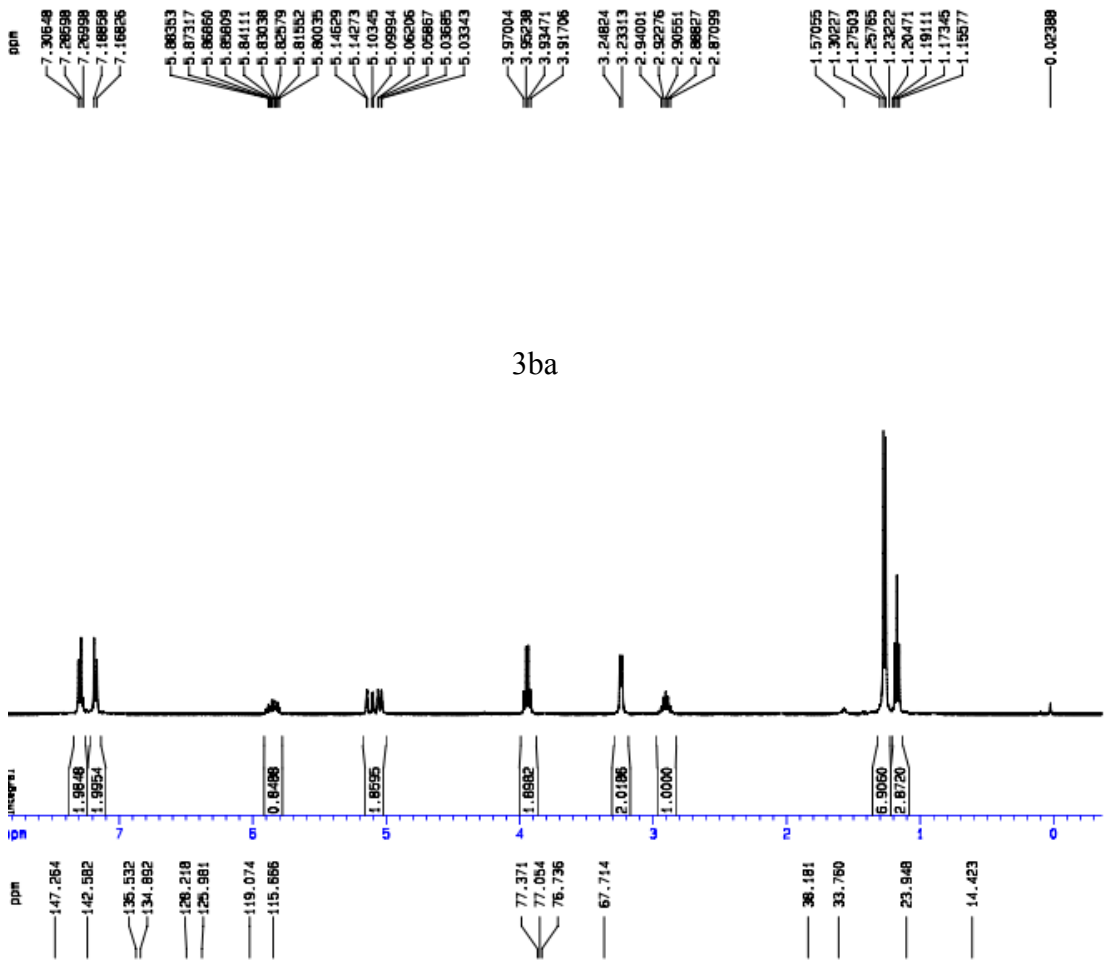

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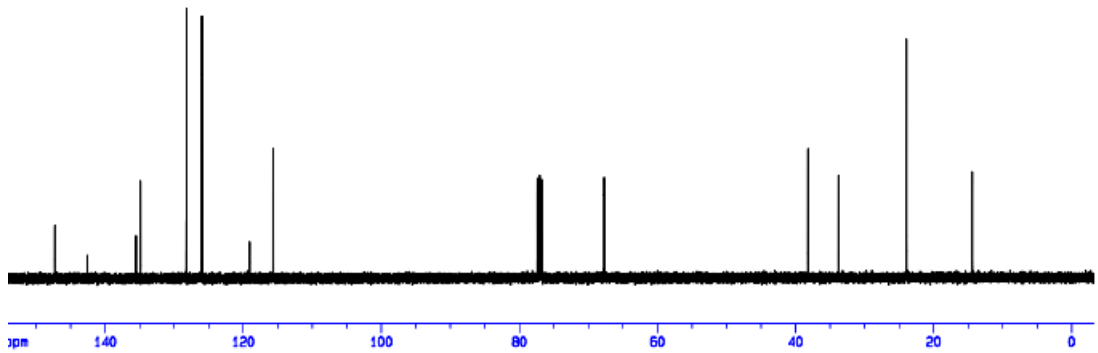

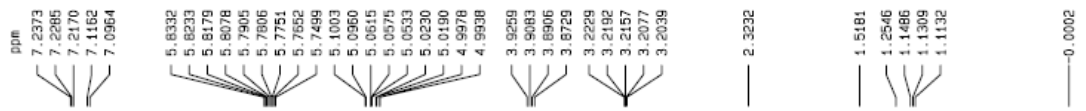
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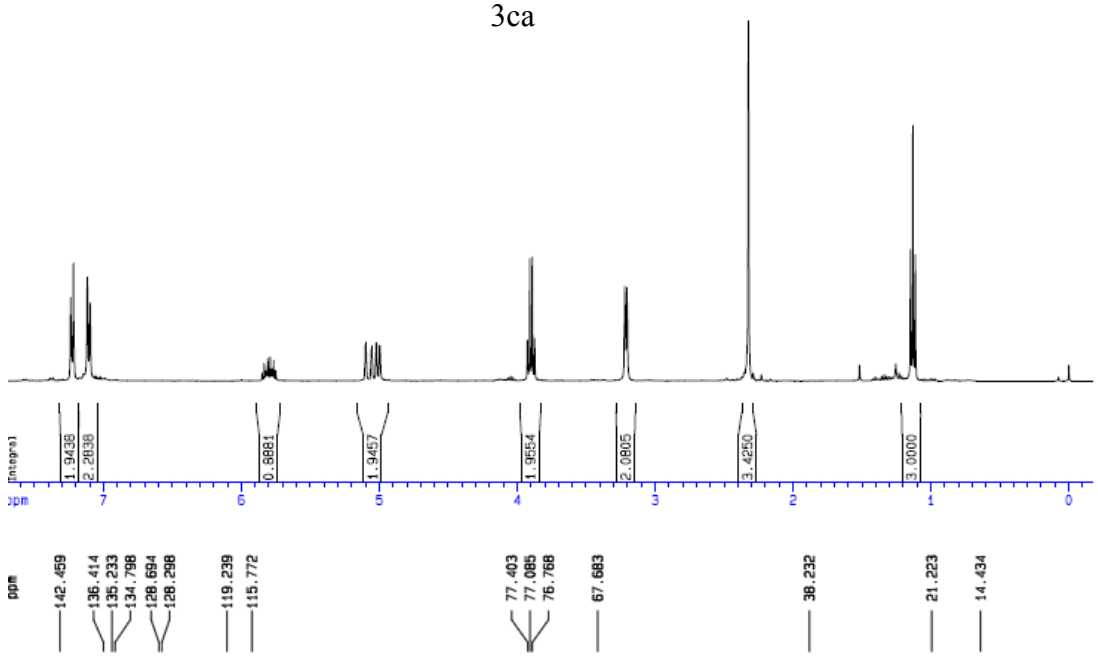
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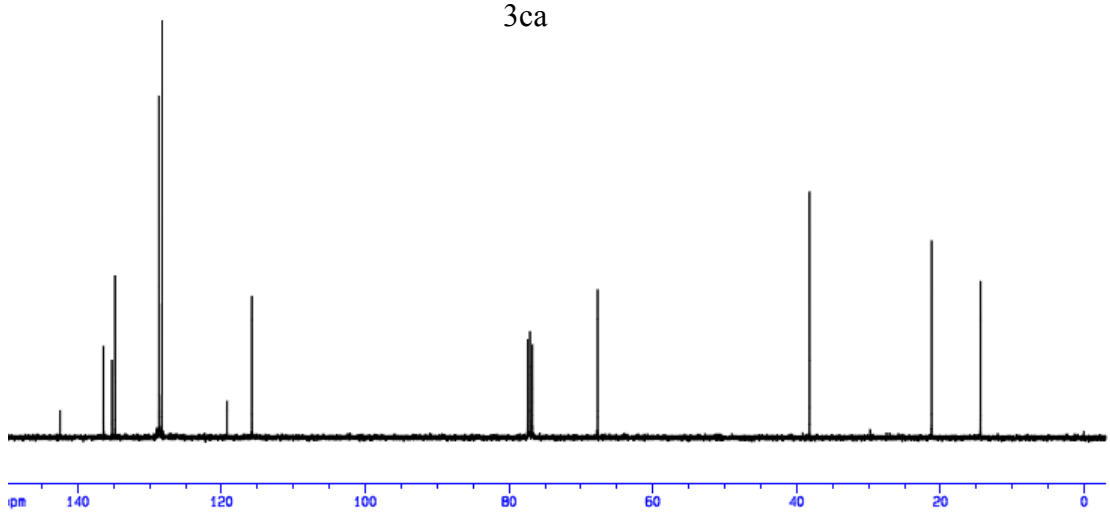
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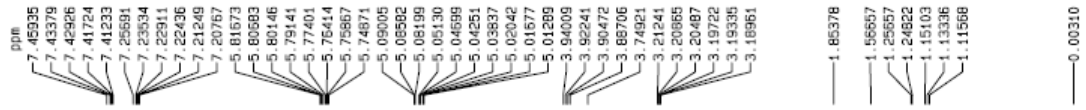
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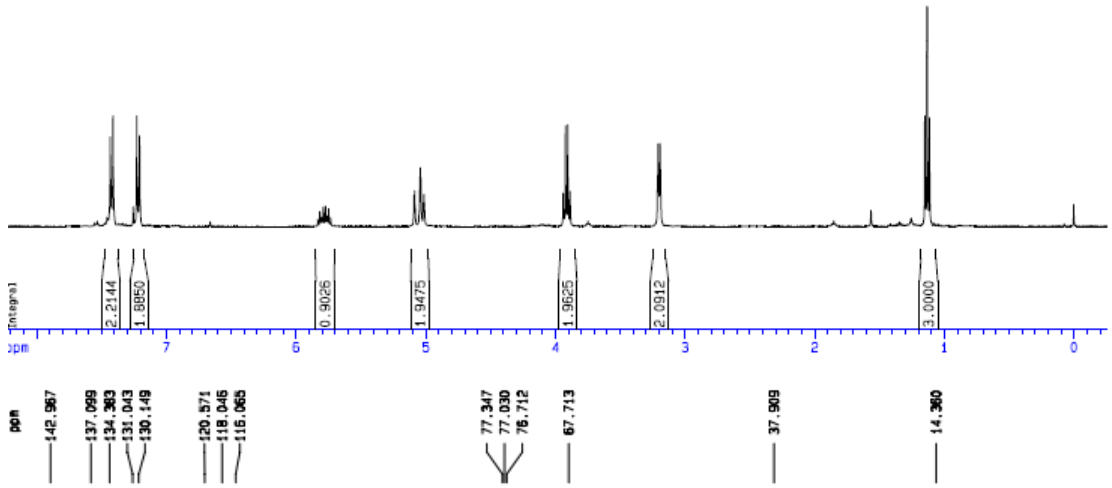
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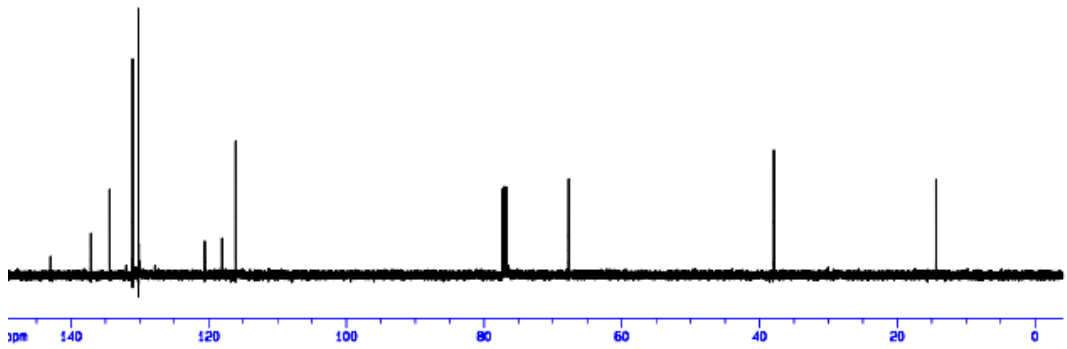
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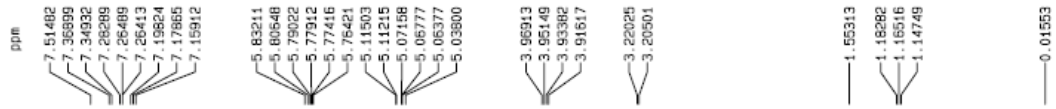
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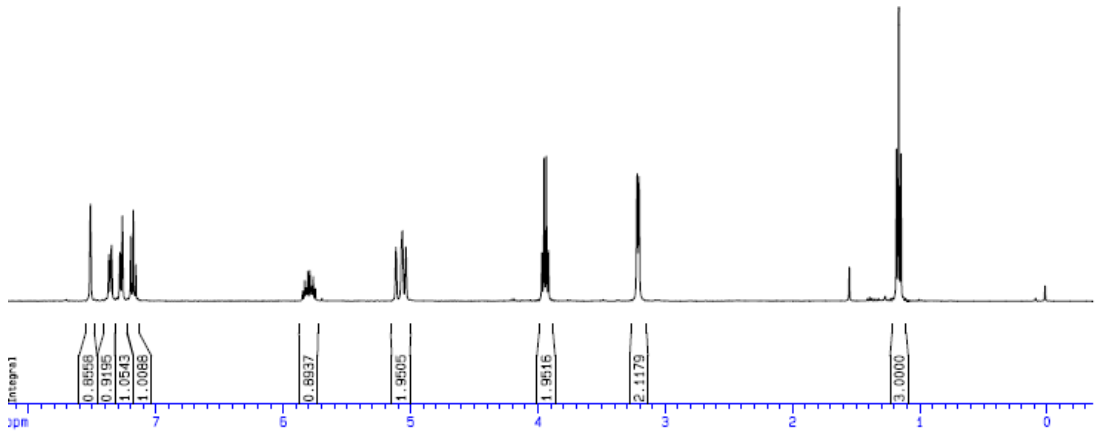
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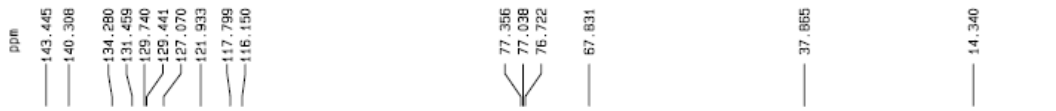
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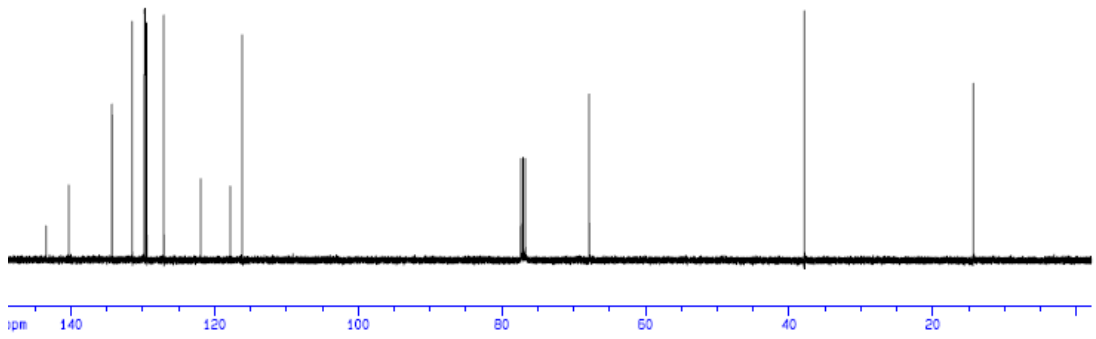
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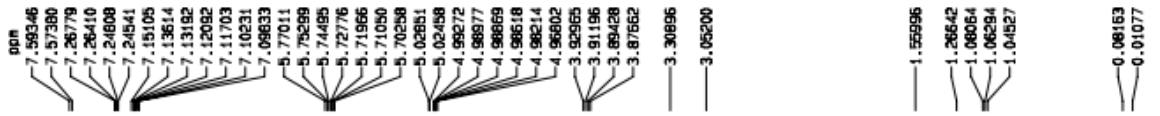
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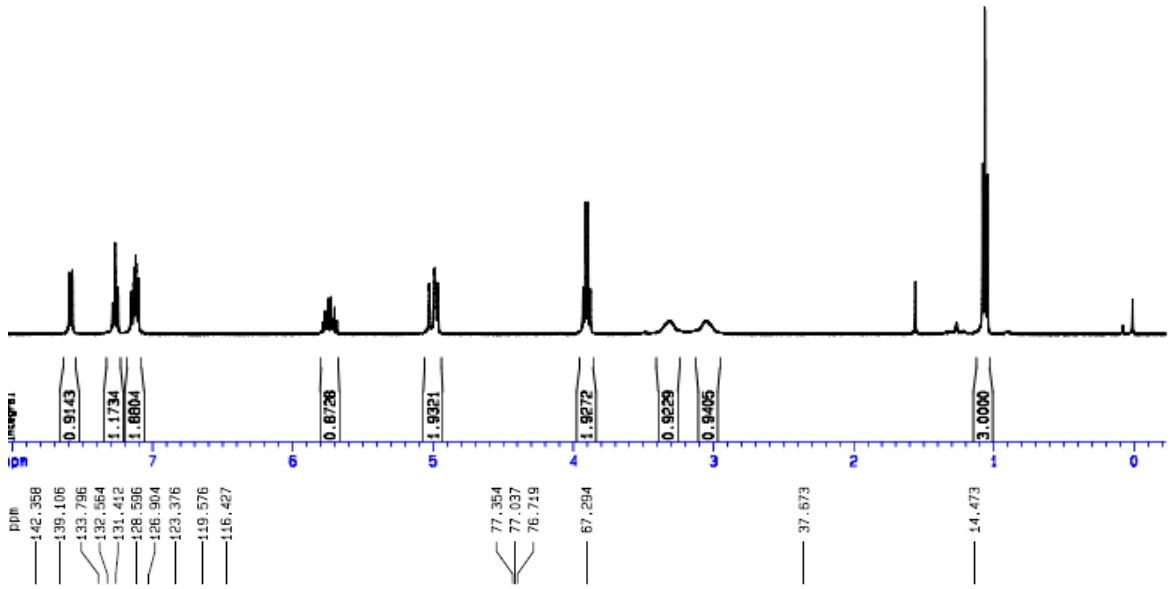
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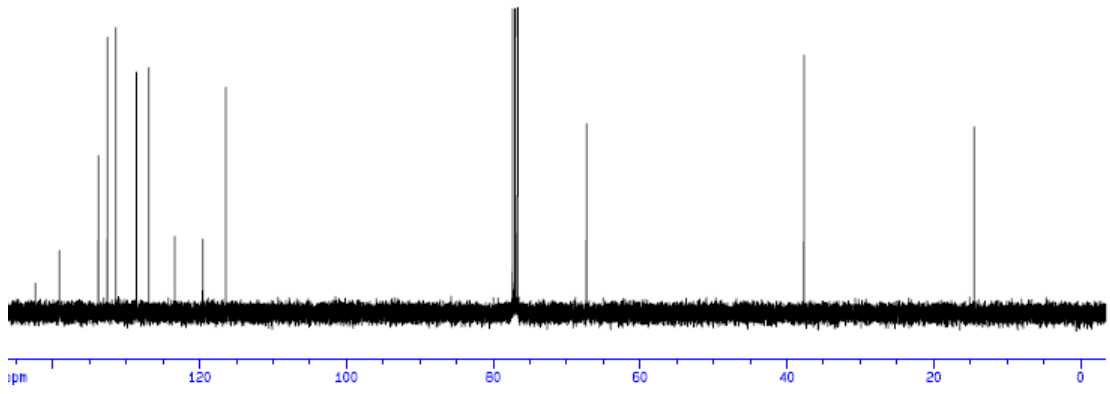
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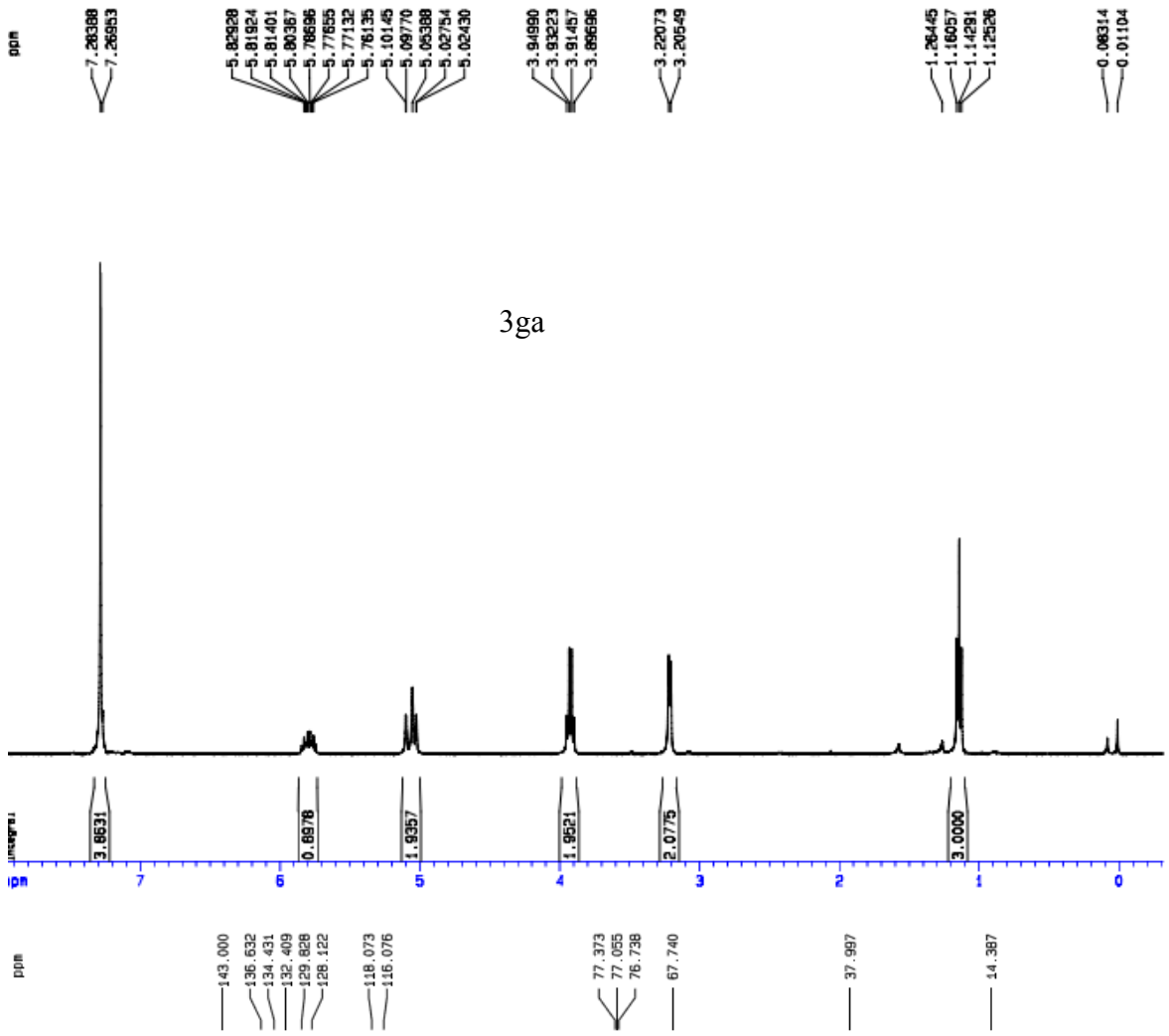
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5.09770
5.05388
5.02754
5.02430
3.94990
3.93223
3.91457
3.89696
3.22073
3.20549
1.26445
1.16057
1.14291
1.12526
0.08314
0.01104
3.8631
0.8978
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1.9521
2.0775
3.0000
ppm
7
6
5
4
3
2
1
0
ppm
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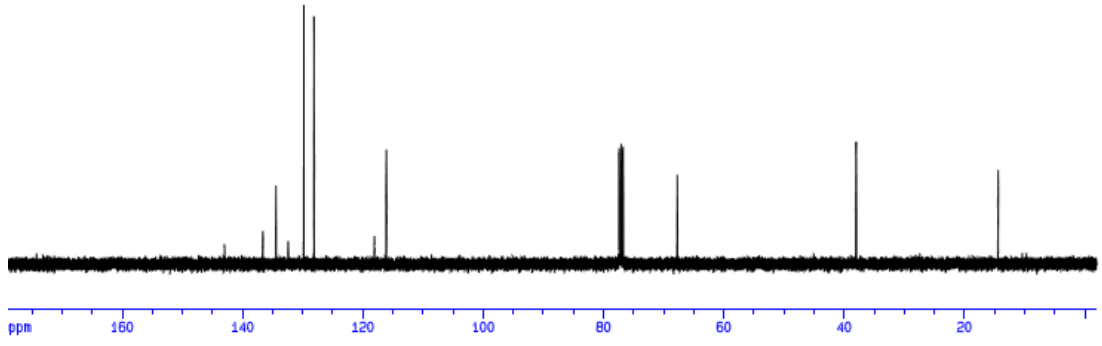
3ga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60
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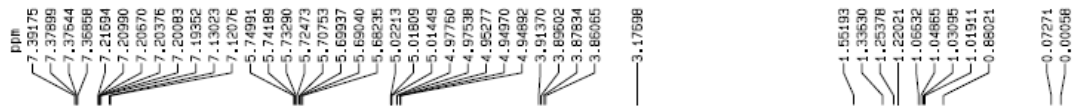
3ga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7.12076
5.74991
5.74189
5.73290
5.72473
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5.69937
5.69040
5.68235
5.02213
5.01809
5.01449
4.97760
4.97538
4.95277
4.94970
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3.86065
3.17698
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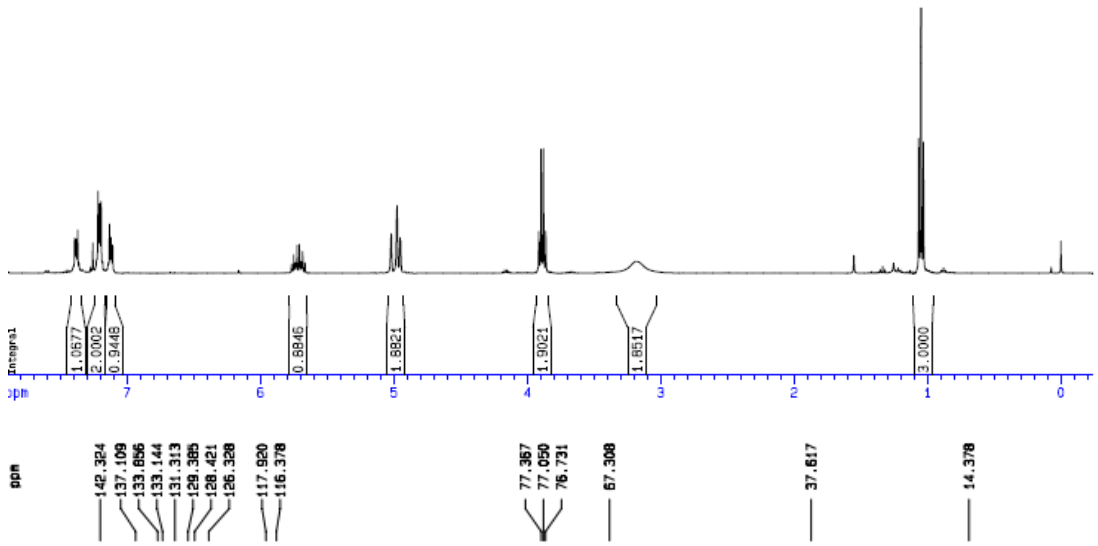
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3.0000
ppm
7
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5
4
3
2
1
0

ppm
142.324
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133.144
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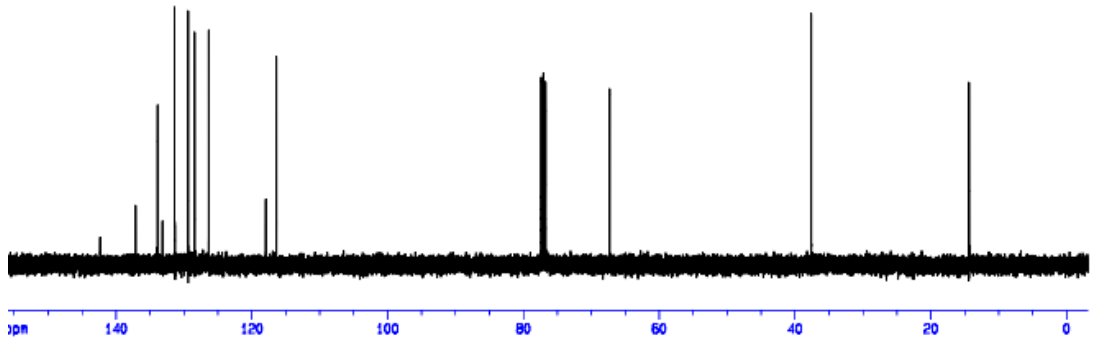
3ha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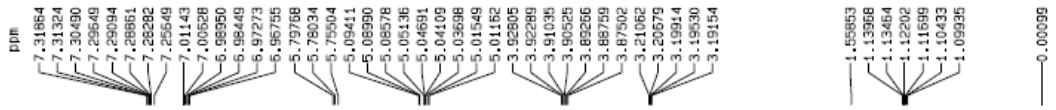

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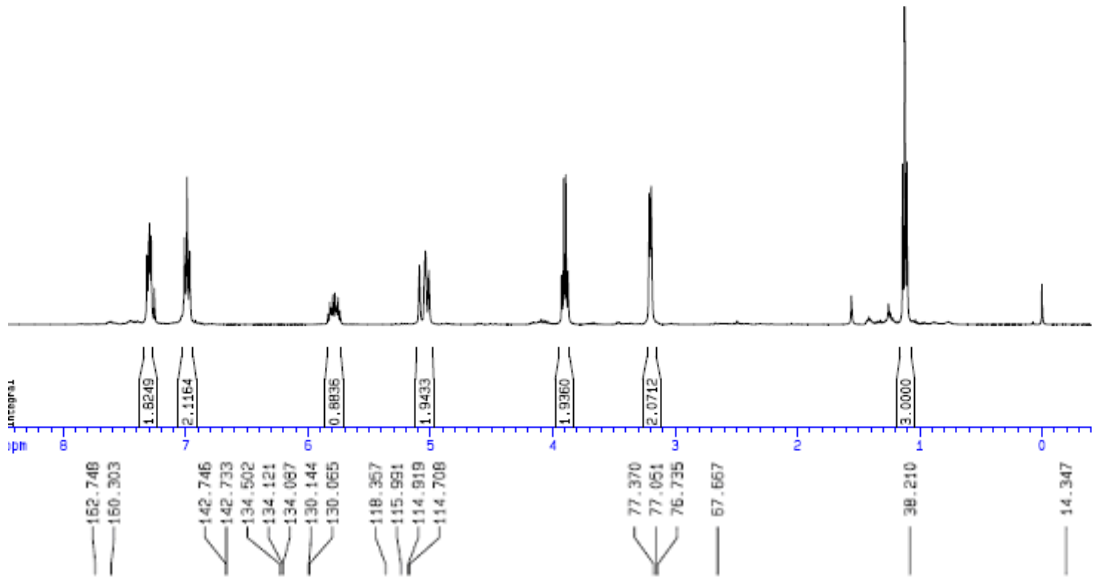

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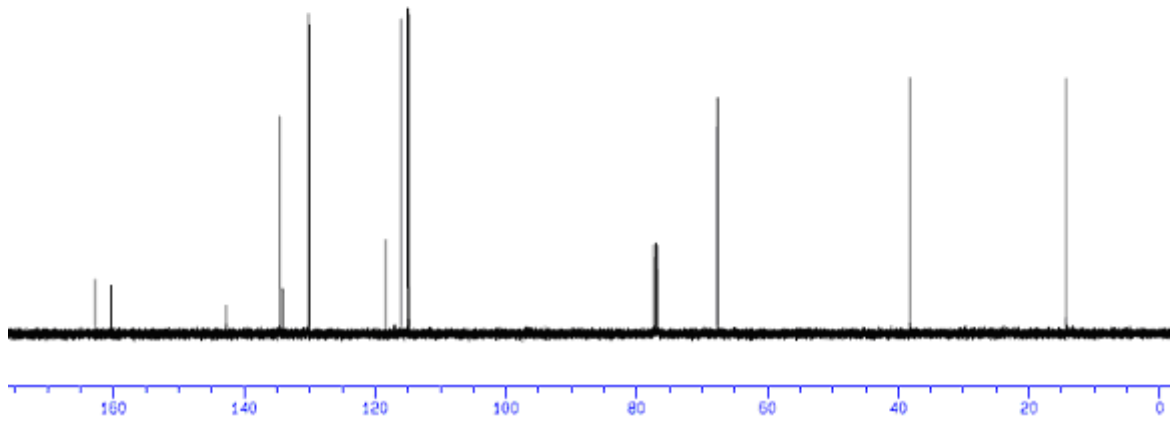

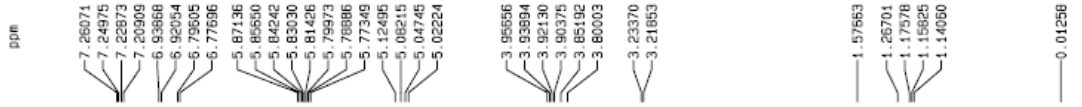
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5.83030
5.81426
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5.77349
5.12495
5.08215
5.04745
5.02224
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3.92130
3.90375
3.85192
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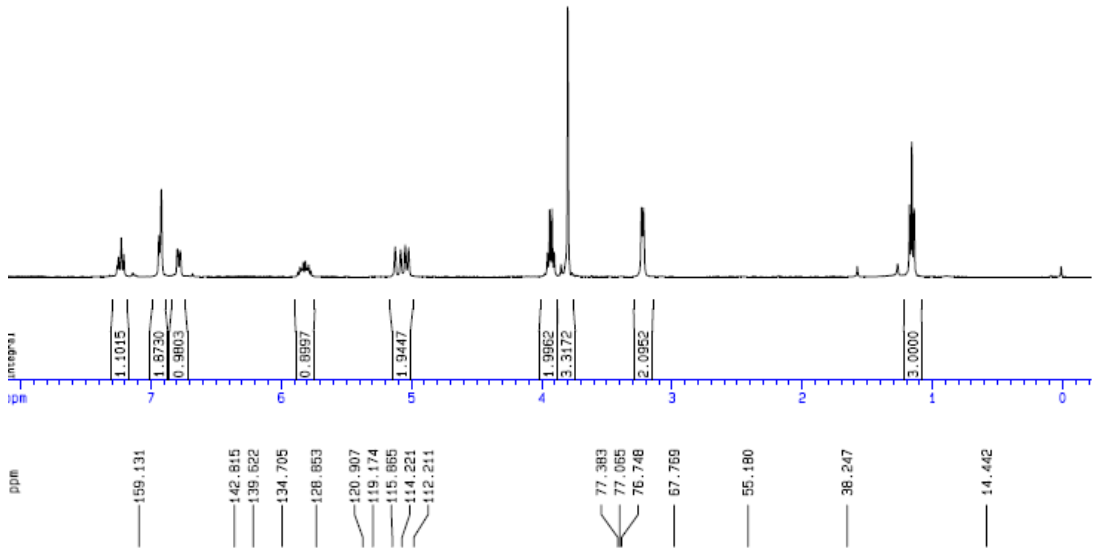
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1.9962
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3.0000
ppm
7
6
5
4
3
2
1
0

ppm
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134.705
128.853
120.907
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77.065
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67.769
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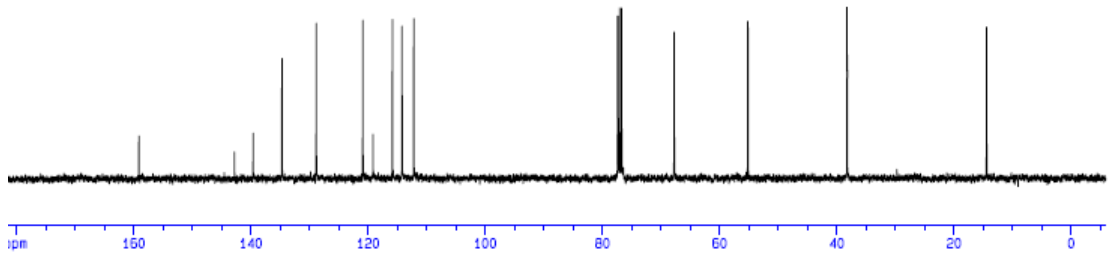
3ja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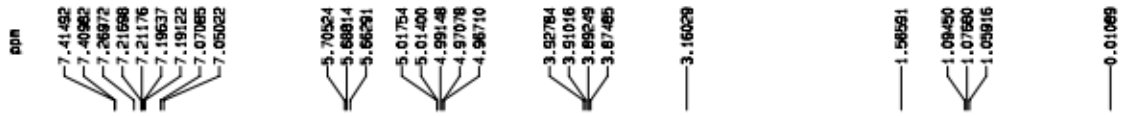
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5.68814
5.66291
5.01754
5.01400
4.99148
4.97078
4.96710
3.92784
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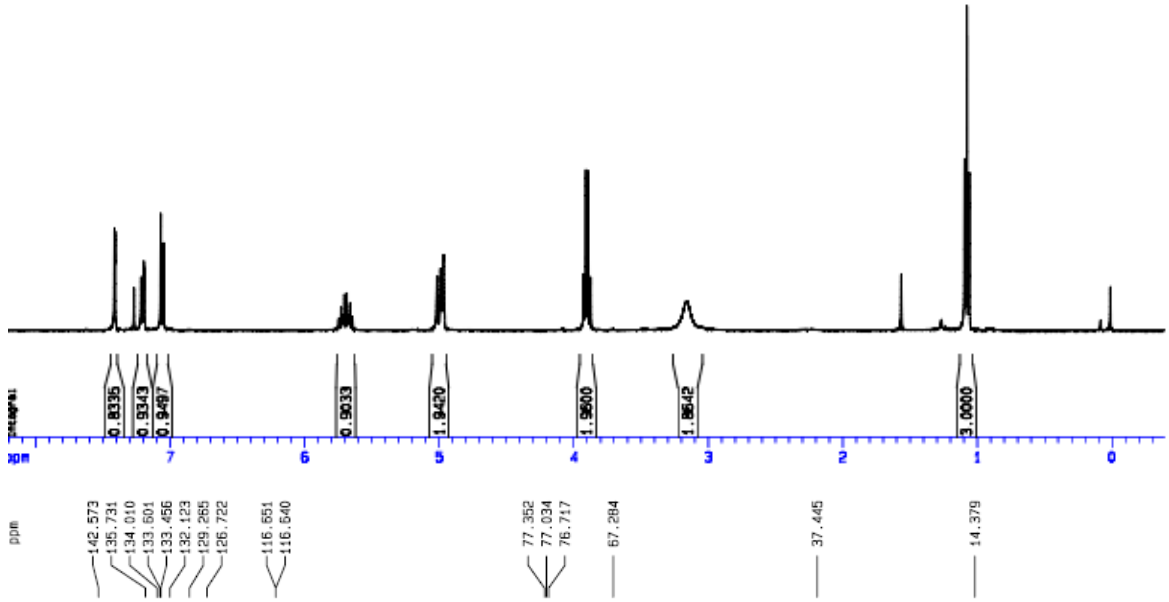
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ppm
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4
3
2
1
0

ppm
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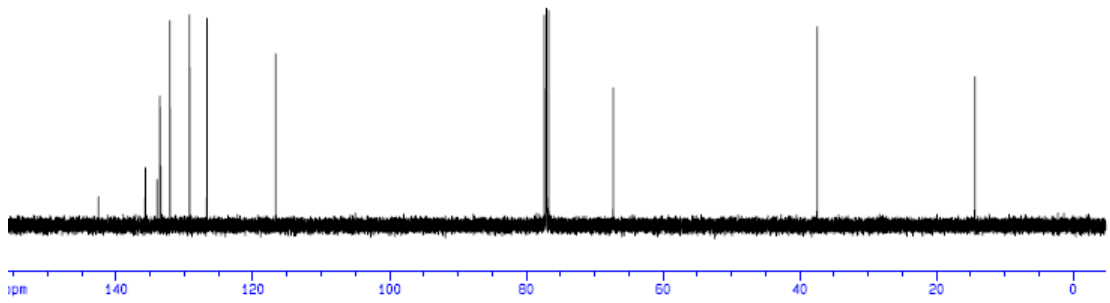
3ka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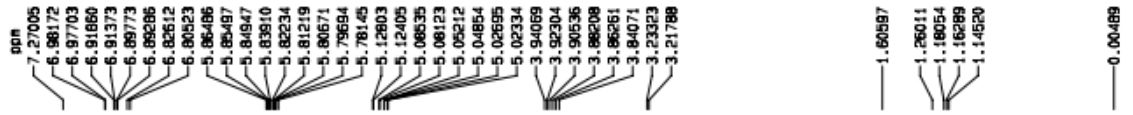

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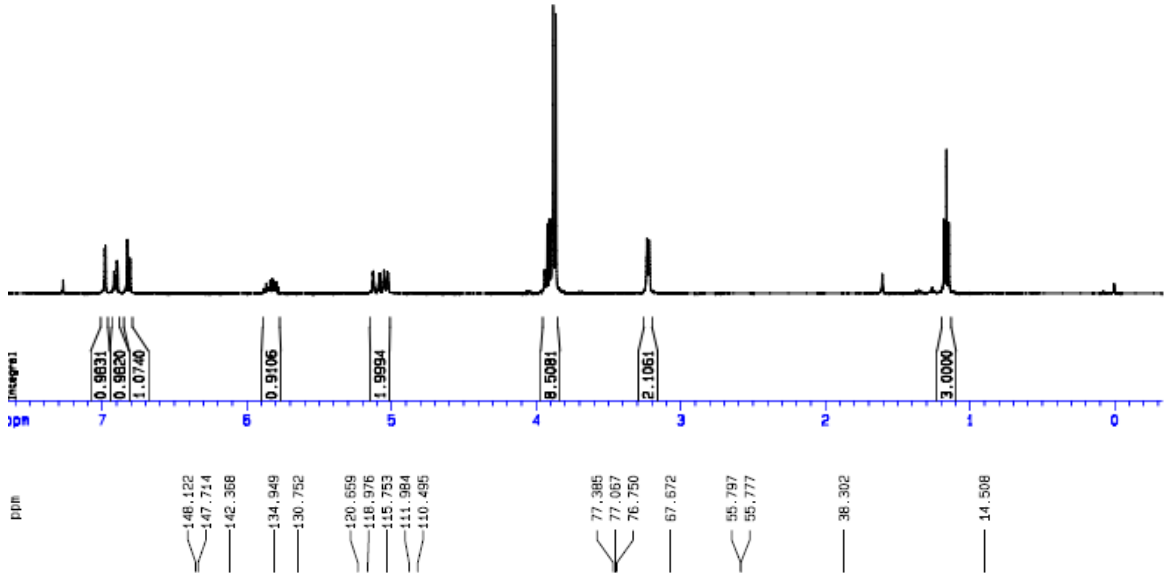

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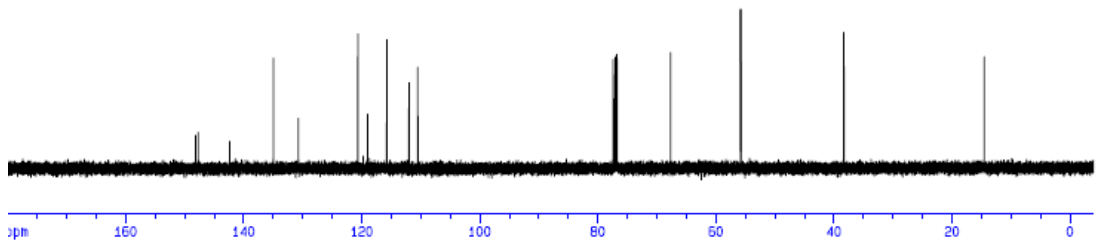


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5.92343
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5.89409
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5.85282
5.18568
5.14385
5.09393
5.06859
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4.16842
4.15072
4.13313
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3.36249
3.36009
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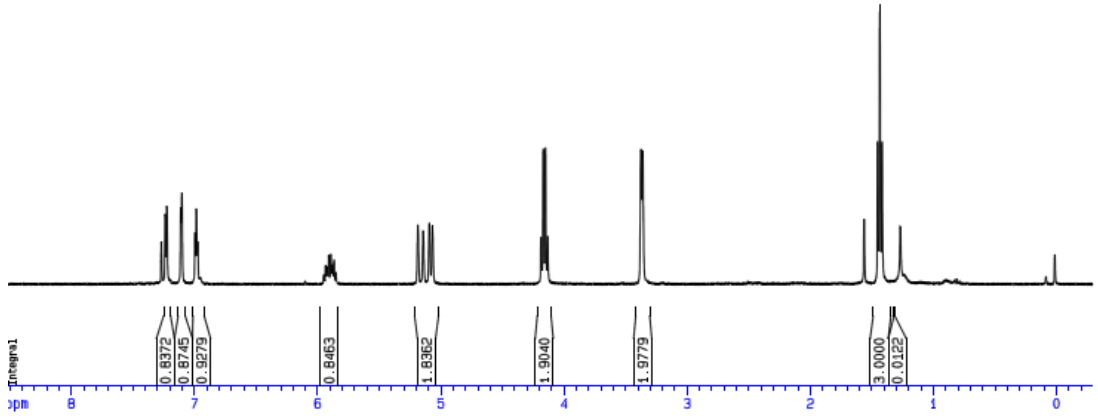
3ma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3
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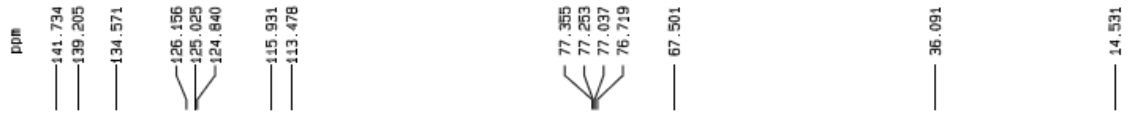
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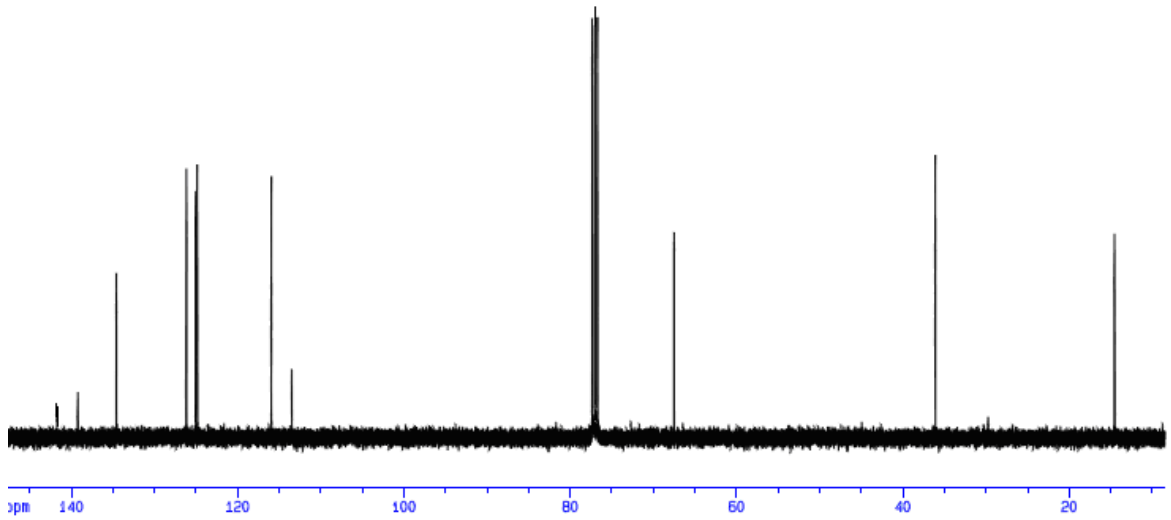
3ma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80
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40
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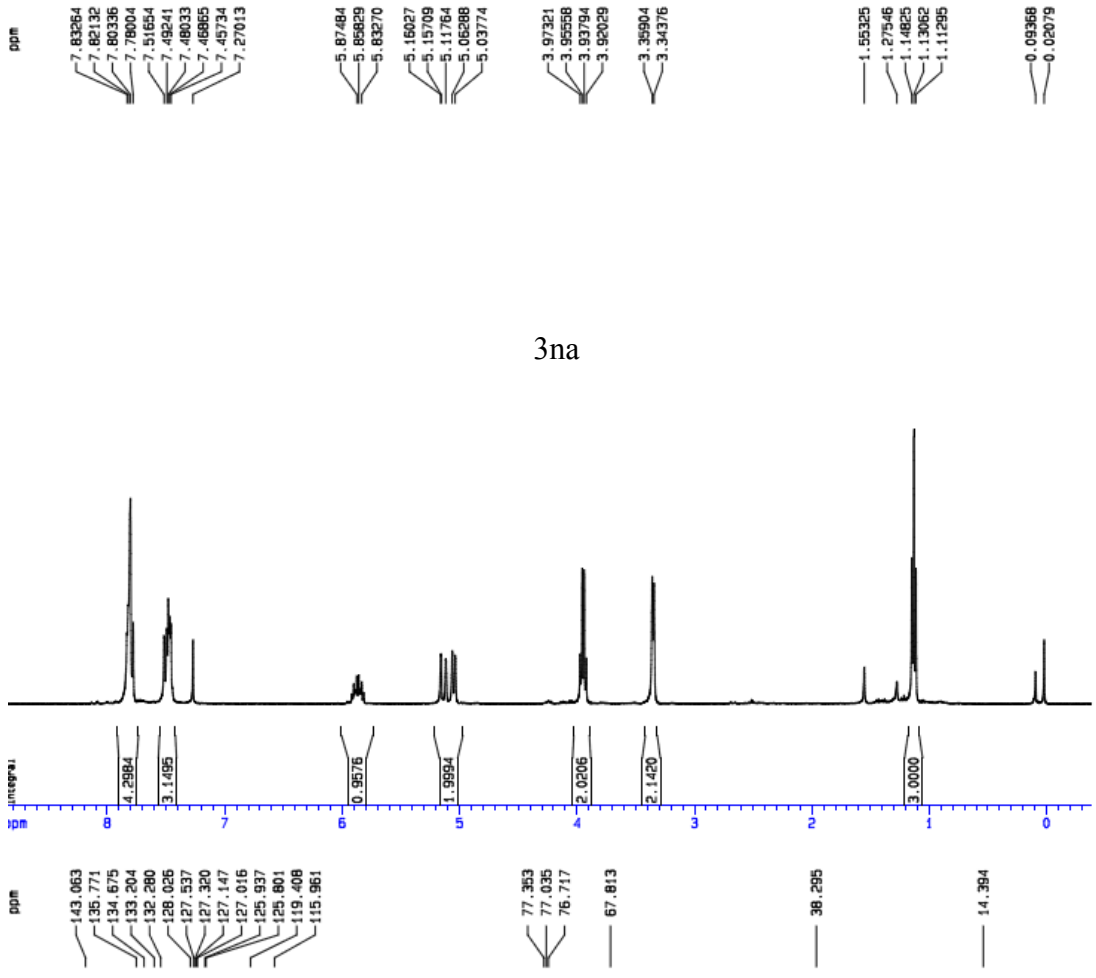
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3.93794
3.92029
3.35904
3.34376
1.55325
1.27546
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Integral
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127.016
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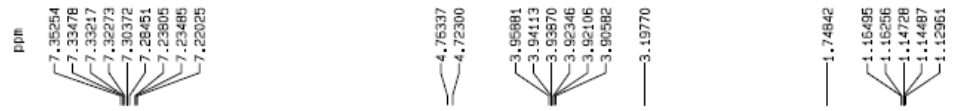
3na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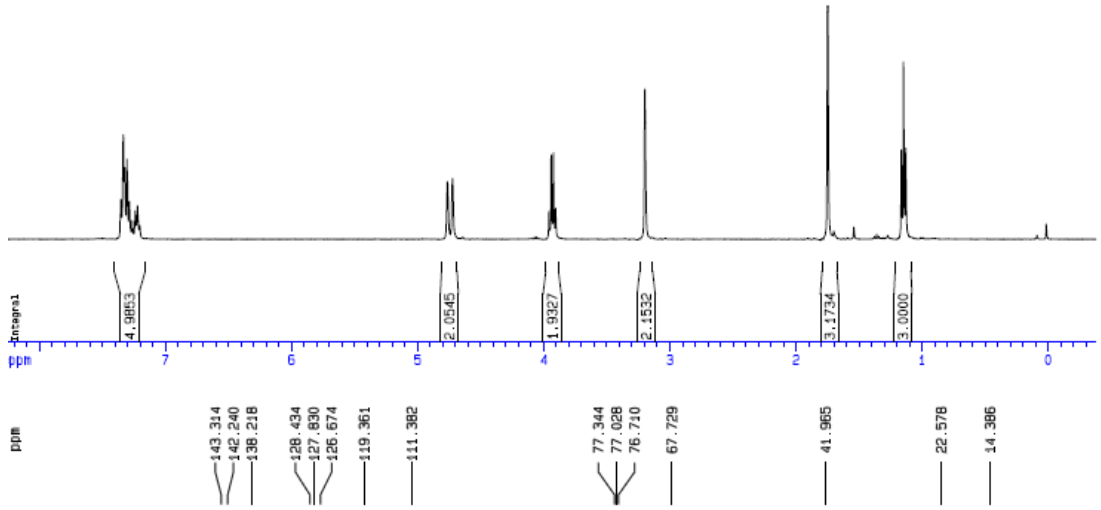
3ac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ppm
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6
5
4
3
2
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ppm
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128.434
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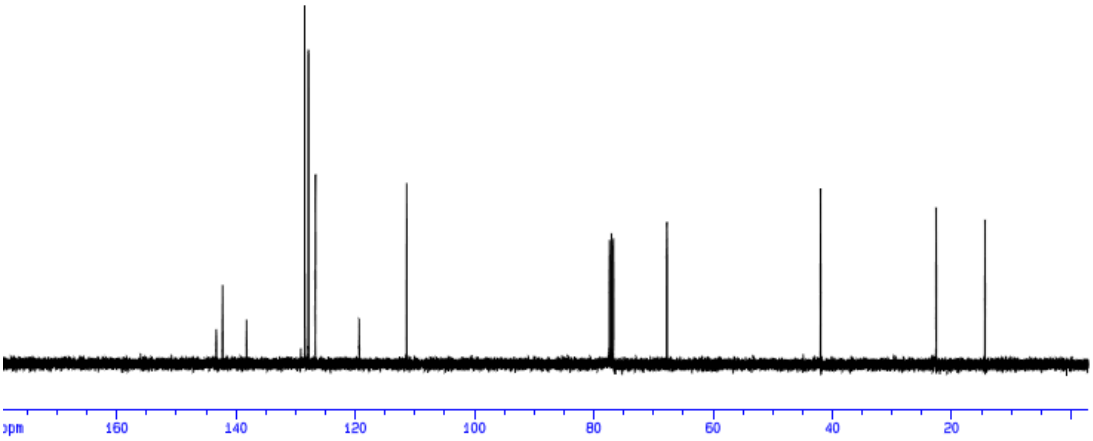
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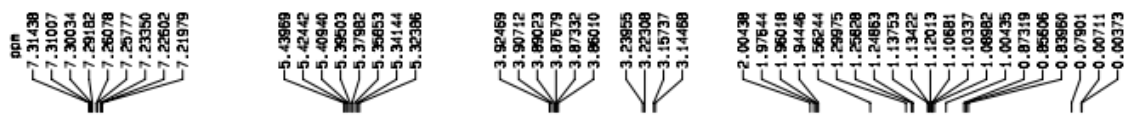

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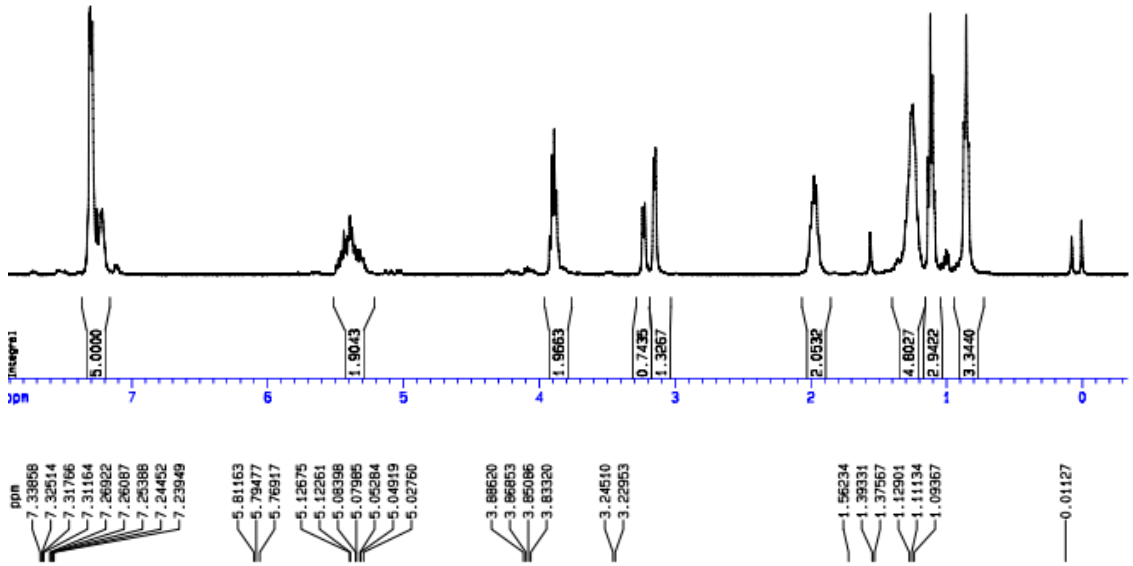

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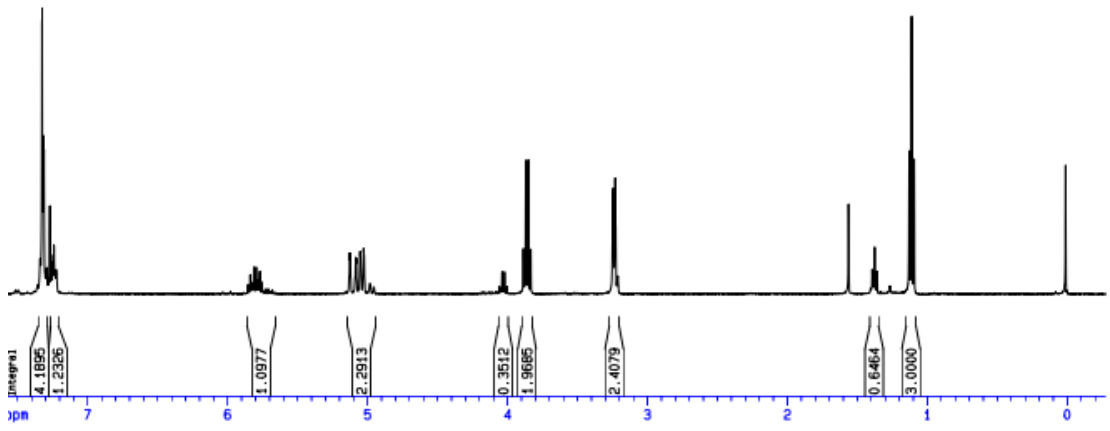

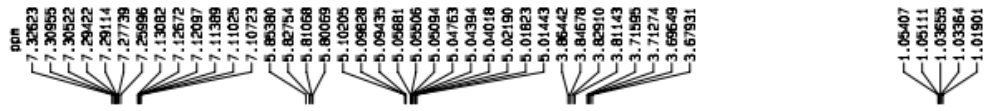
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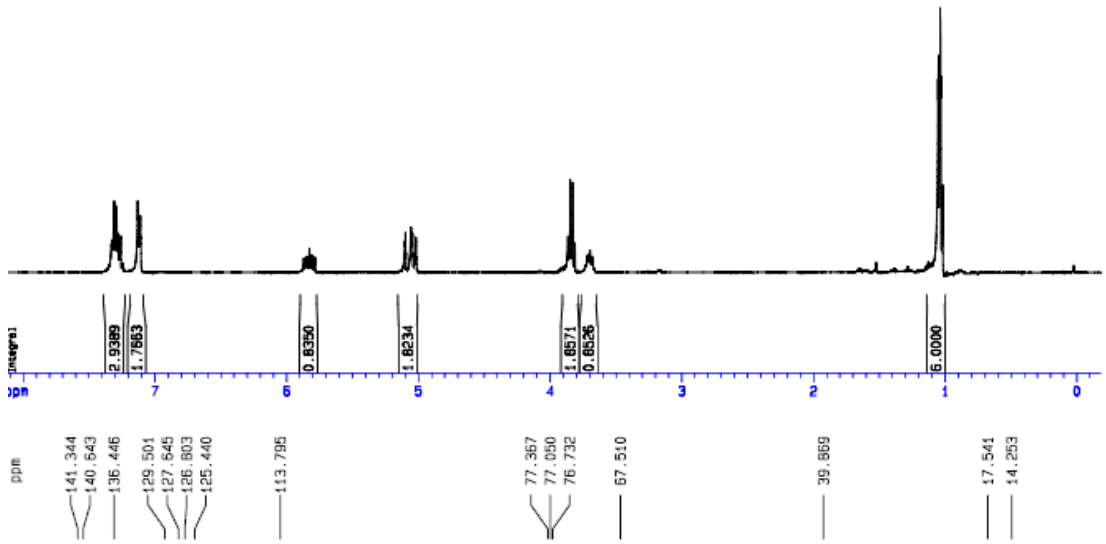
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ppm
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5
4
3
2
1
0

ppm
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129.501
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76.732
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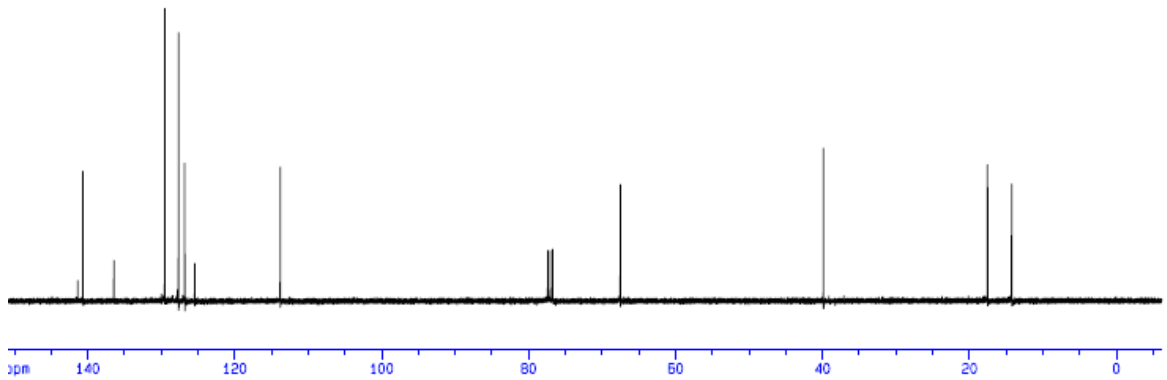
3ad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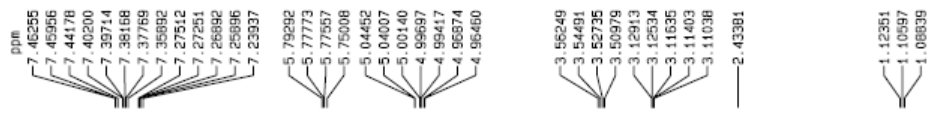
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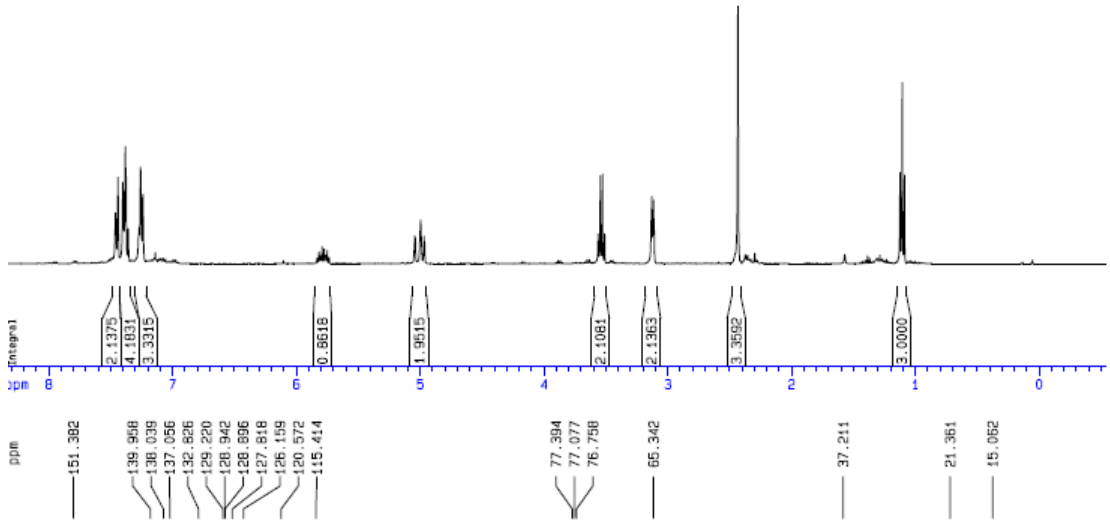
4a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7
6
5
4
3
2
1
0

ppm
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138.039
137.056
132.826
129.220
128.942
128.896
127.818
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120.572
115.414
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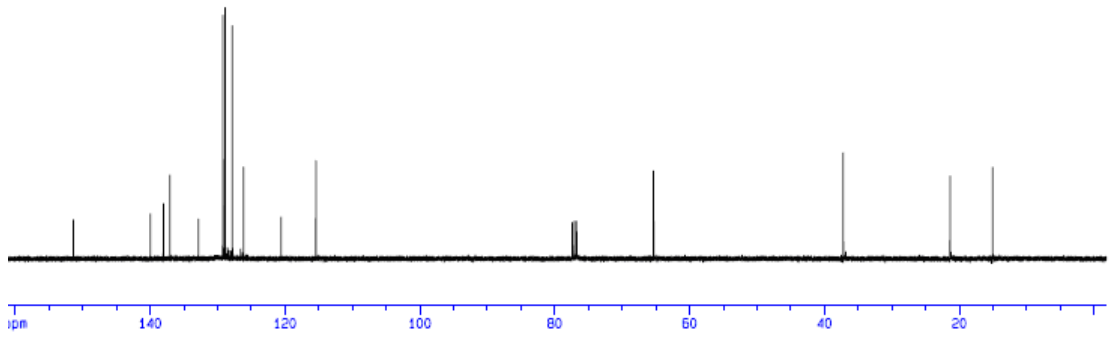
4a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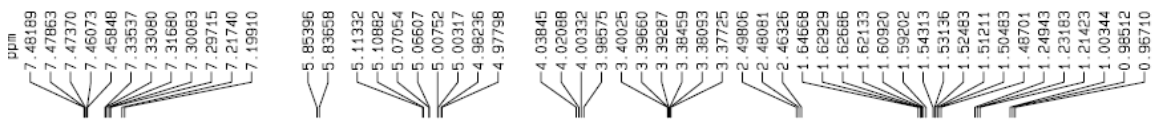
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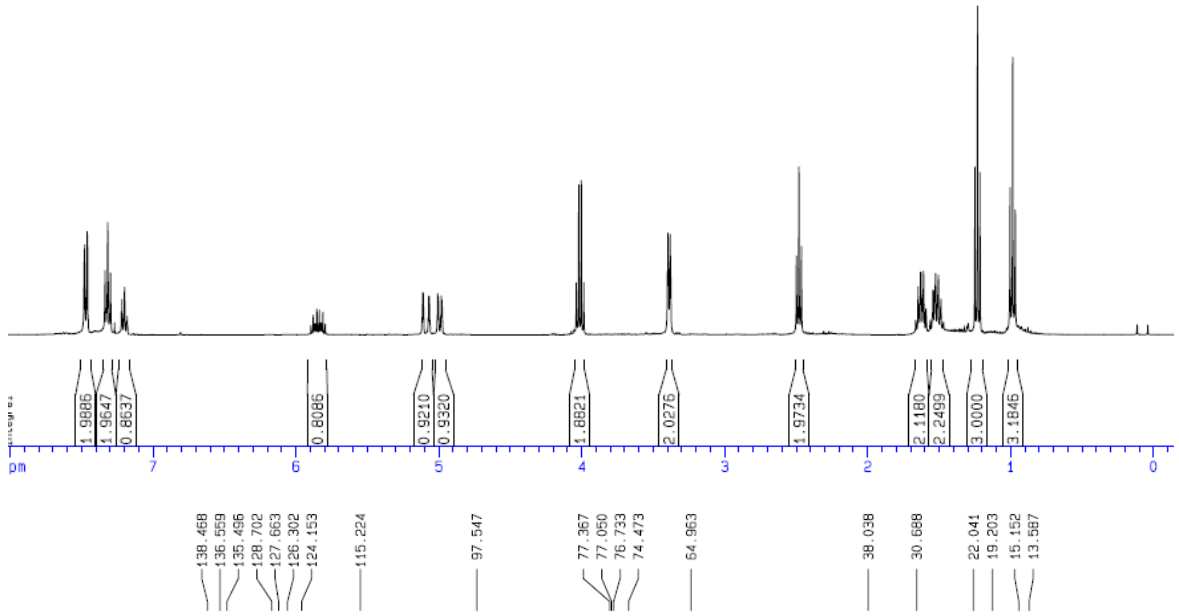
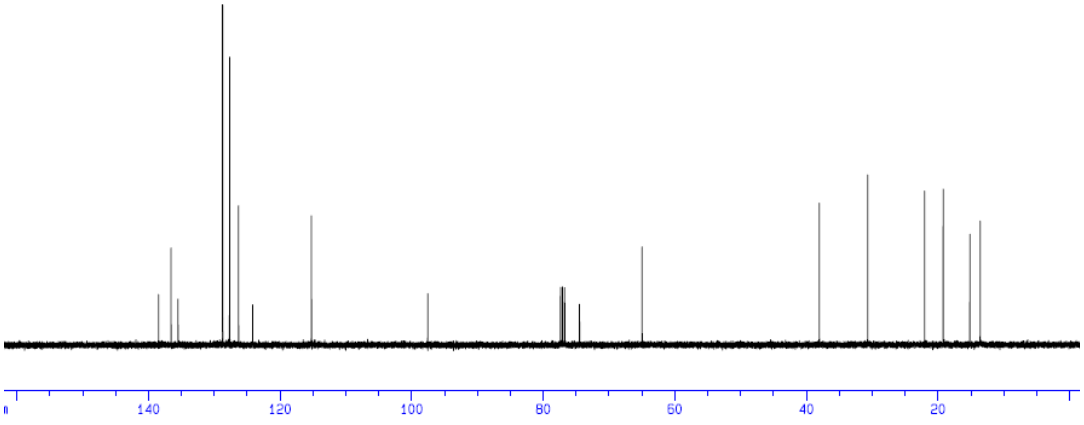
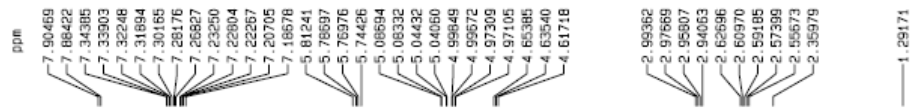
7.47863
7.47370
7.46073
7.45848
7.33537
7.33080
7.31680
7.30083
7.29715
7.21740
7.19910
5.85396
5.83658
5.11332
5.10882
5.07054
5.06607
5.00752
5.00317
4.98236
4.97798
4.03845
4.02088
4.00332
3.98575
3.40025
3.39660
3.39287
3.38459
3.38093
3.37725
2.49806
2.48081
2.46326
1.64668
1.62929
1.62686
1.62133
1.60920
1.59202
1.54313
1.53136
1.52483
1.51211
1.50483
1.48701
1.24943
1.23183
1.21423
1.00344
0.98512
0.96710

4b


1.9886
1.9647
0.8637
0.8086
0.9210
0.9320
1.8821
2.0276
1.9734
2.1180
2.2499
3.0000
3.1846
pm
7
6
5
4
3
2
1
0
138.468
136.559
135.496
128.702
127.663
126.302
124.153
115.224
97.547
77.367
77.050
76.733
74.473
64.963
38.038
30.688
22.041
19.203
15.152
13.587

4b


140
120
100
80
60
40
20


ppm
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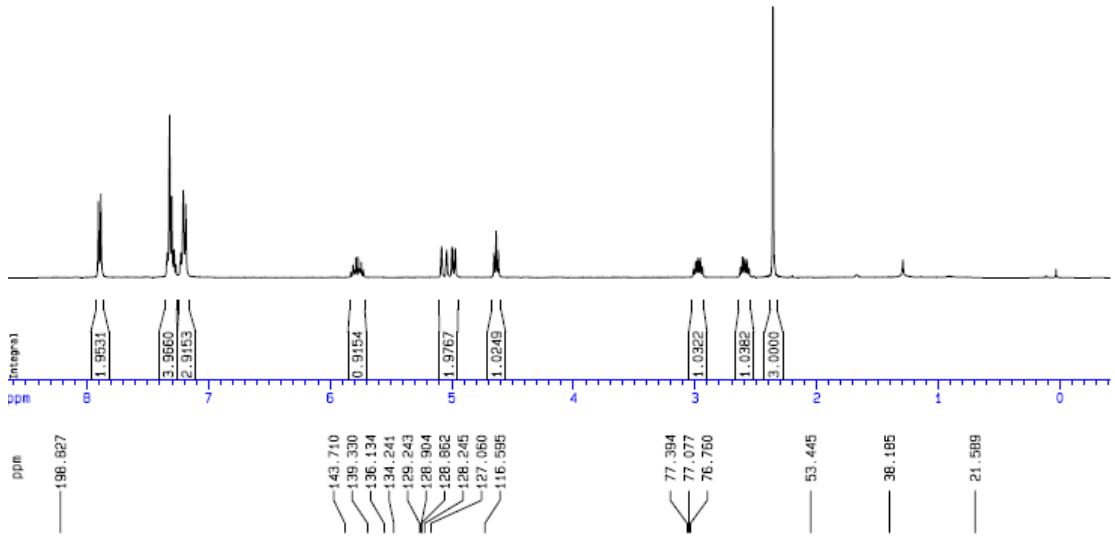
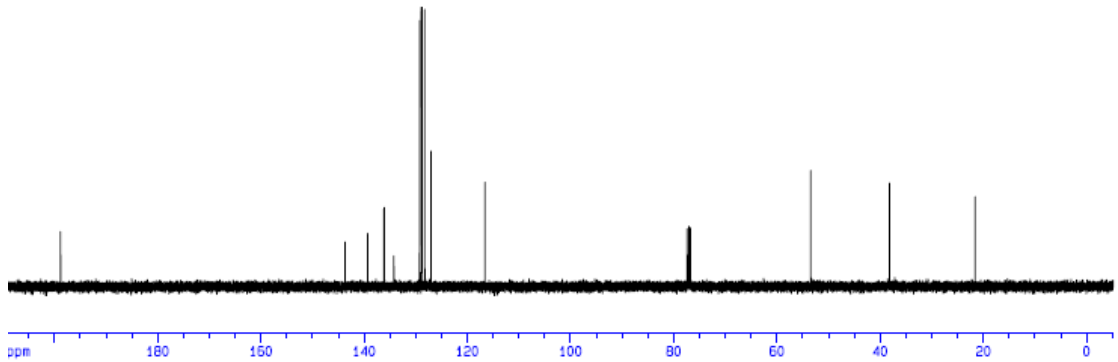
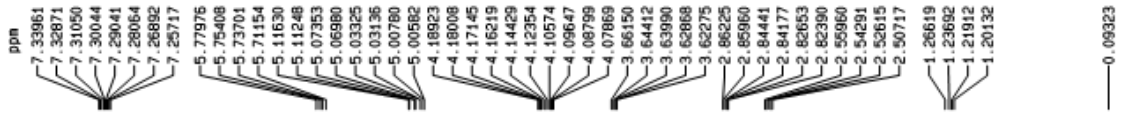
7.88422
7.34385
7.33903
7.32248
7.31894
7.30165
7.28176
7.26827
7.23250
7.22804
7.22267
7.20705
7.18678
5.81241
5.78697
5.76976
5.74426
5.08694
5.08332
5.04432
5.04060
4.99849
4.99572
4.97309
4.97105
4.65385
4.63540
4.61718
2.99362
2.97669
2.95807
2.94063
2.62696
2.60970
2.59185
2.57399
2.55673
2.35979
1.29171

5

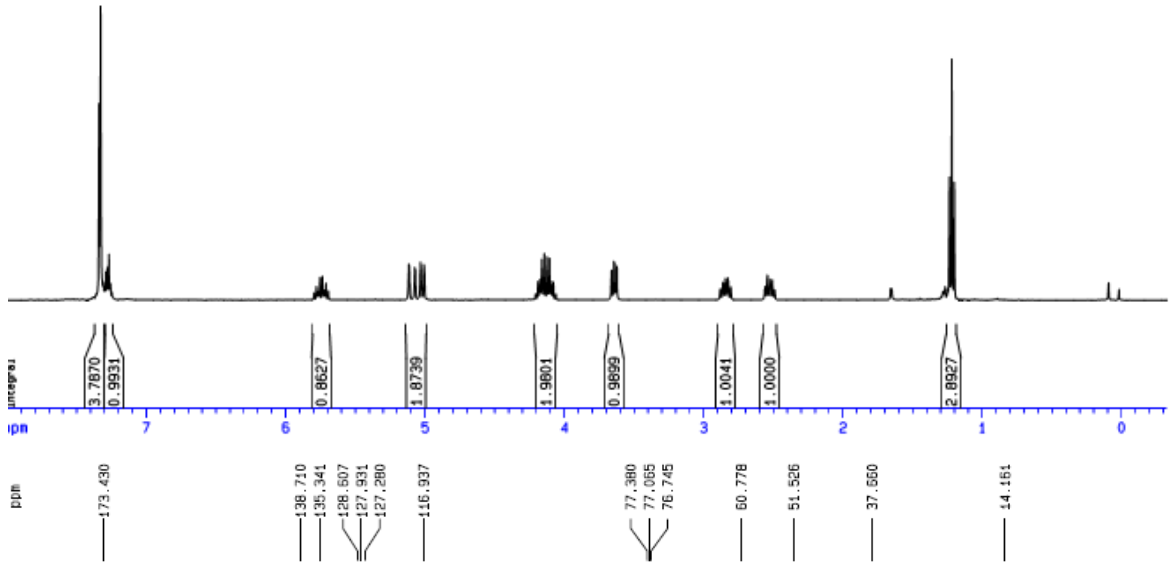

Integral
1.9531
3.9660
2.9153
0.9154
1.9767
1.0249
1.0322
1.0382
3.0000
ppm
8
7
6
5
4
3
2
1
0
ppm
198.827
143.710
139.330
136.134
134.241
129.243
128.904
128.862
128.245
127.060
116.595
77.394
77.077
76.760
53.445
38.185
21.589

5

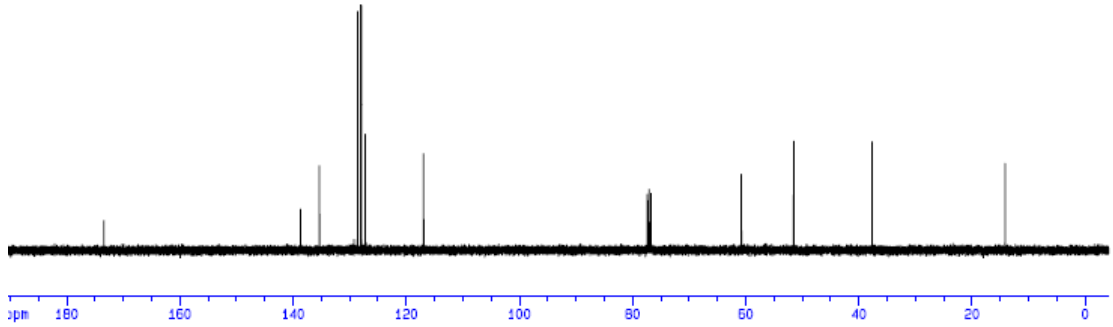

ppm
180
160
140
120
100
80
60
40
20
0

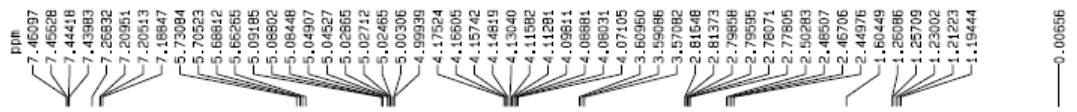

ppm
7.33961
7.32871
7.31050
7.30044
7.29041
7.28064
7.26892
7.25717
5.77976
5.75408
5.73701
5.71154
5.11630
5.11248
5.07353
5.06980
5.03325
5.03136
5.00780
5.00582
4.18923
4.18006
4.17145
4.16219
4.14429
4.12354
4.10574
4.09647
4.08799
4.07869
3.66150
3.64412
3.63990
3.62868
3.62275
2.86225
2.85960
2.84441
2.84177
2.82653
2.82390
2.55960
2.54291
2.52615
2.50717
1.26619
1.23692
1.21912
1.20132
0.09323

6a


3.7870
0.9931
0.8627
1.8739
1.9801
0.9899
1.0041
1.0000
2.8927
ppm
7
6
5
4
3
2
1
0
ppm
173.430
138.710
135.341
128.607
127.931
127.280
116.937
77.380
77.065
76.745
60.778
51.526
37.660
14.161

6a


ppm
180
160
140
120
100
80
60
40
20
0


ppm
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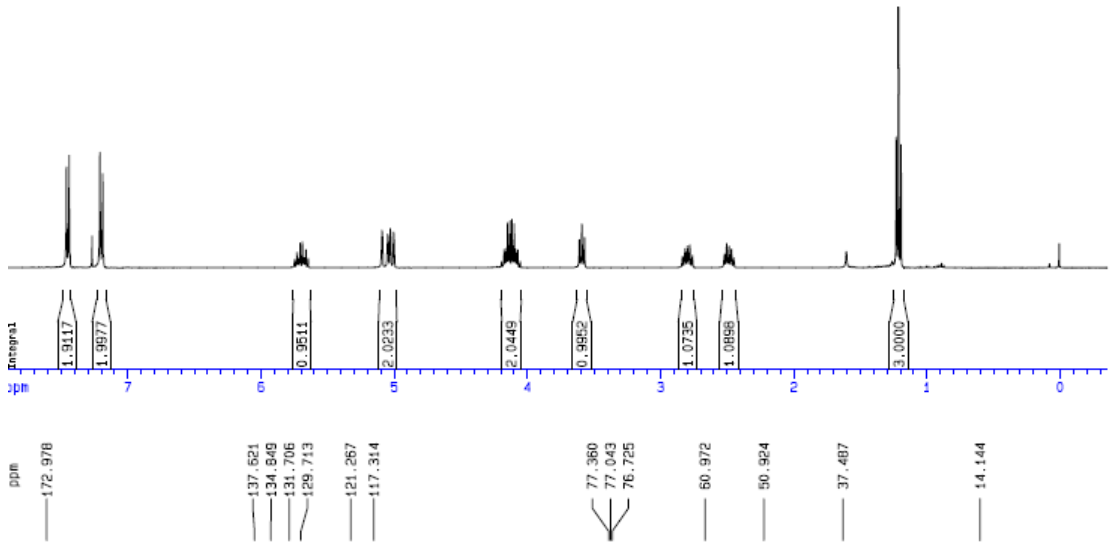
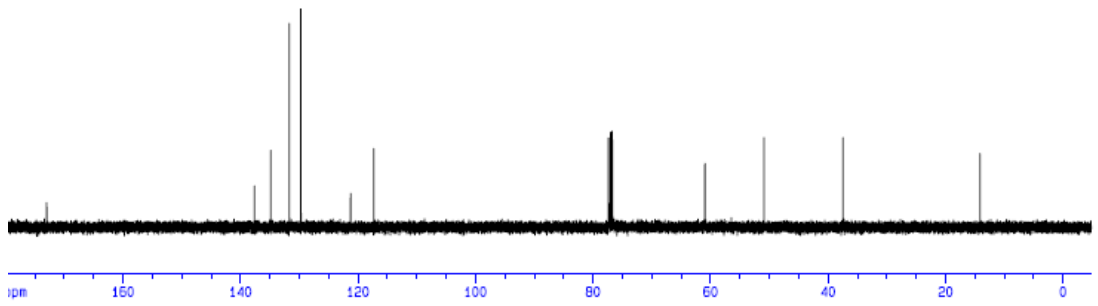
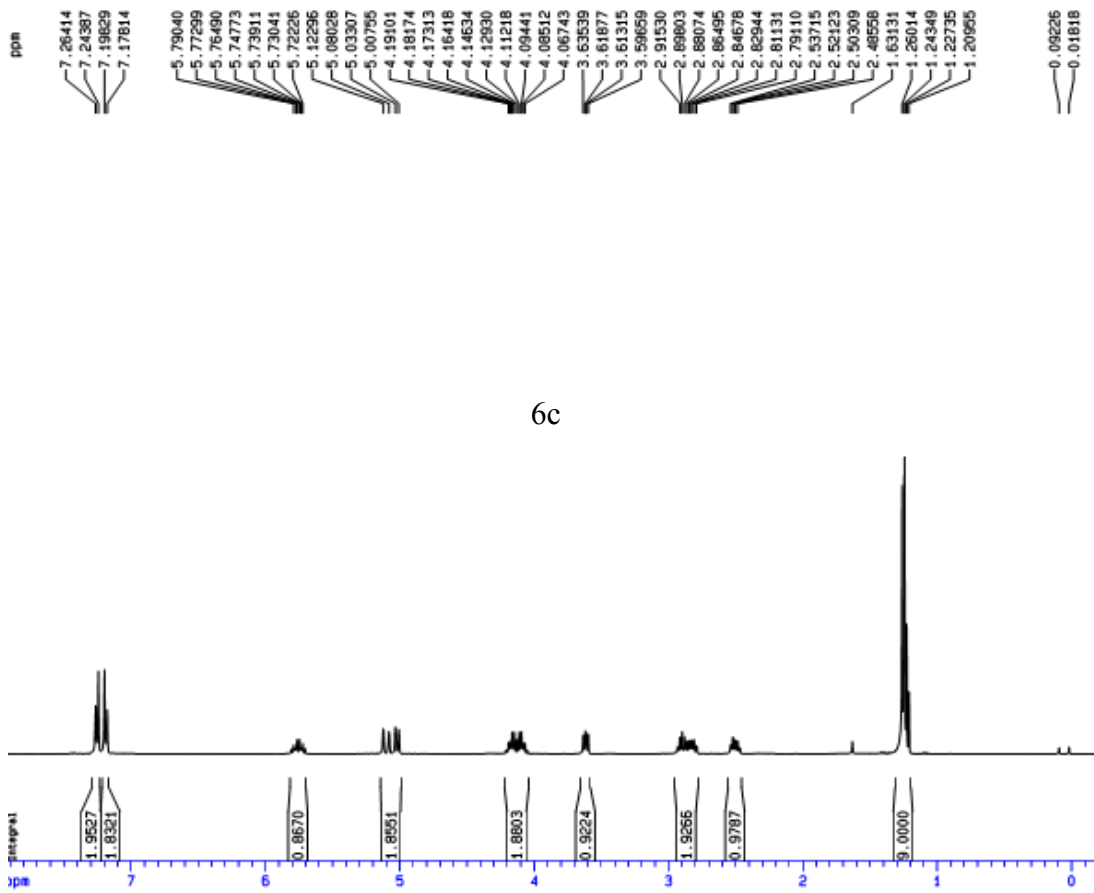
7.45628
7.44418
7.43983
7.26832
7.20951
7.20513
7.18847
5.73084
5.70523
5.68812
5.66265
5.09185
5.08802
5.08448
5.04907
5.04527
5.02865
5.02712
5.02465
5.00306
4.99939
4.17524
4.16605
4.15742
4.14819
4.13040
4.11582
4.11281
4.09811
4.08881
4.08031
4.07105
3.60960
3.59086
3.57082
2.81648
2.81373
2.79858
2.79595
2.78071
2.77805
2.50283
2.48507
2.46706
2.44976
1.60449
1.26086
1.25709
1.23002
1.21223
1.19444
0.00656

6b

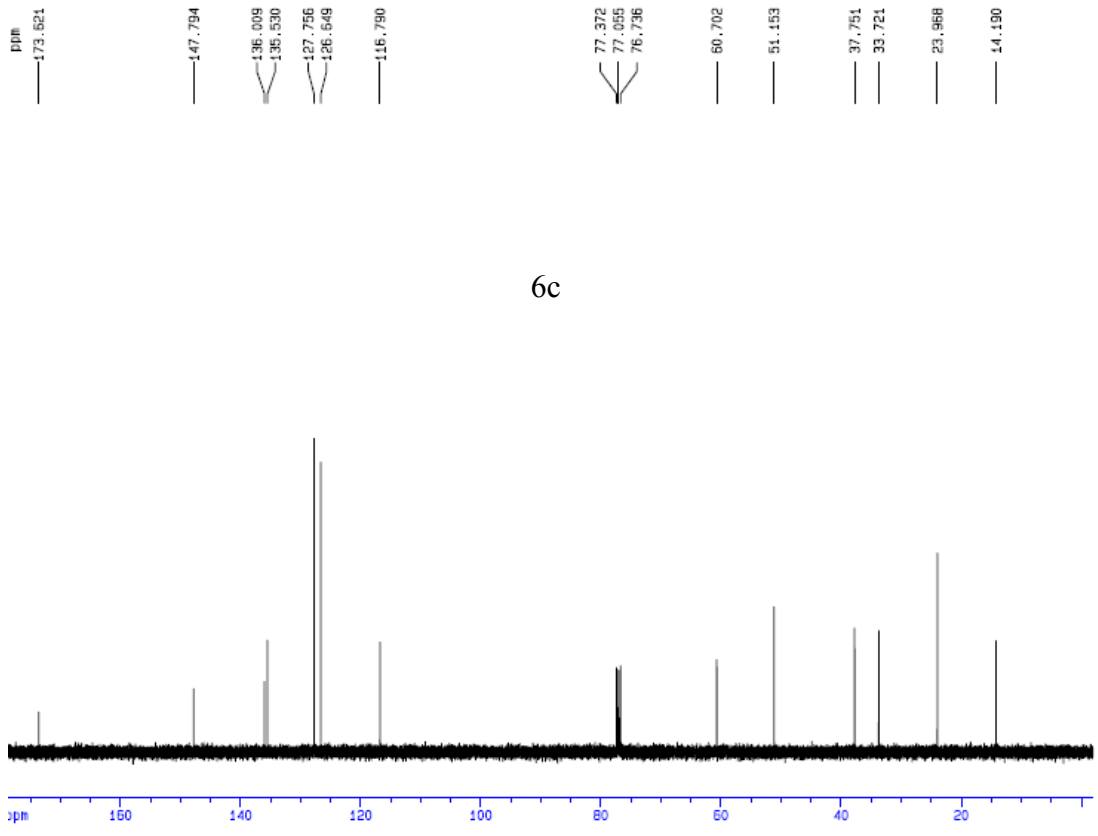

Integral
1.9117
1.9977
0.9511
2.0233
2.0449
0.9852
1.0735
1.0896
3.0000
ppm
7
6
5
4
3
2
1
0
ppm
172.978
137.621
134.849
131.706
129.713
121.267
117.314
77.360
77.043
76.725
60.972
50.924
37.487
14.144

6b

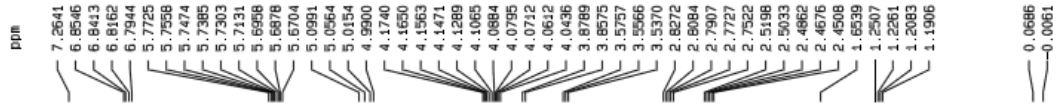

ppm
160
140
120
100
80
60
40
20
0


ppm
7.26414
7.24387
7.19829
7.17814
5.79040
5.77299
5.76490
5.74773
5.73911
5.73041
5.72226
5.12296
5.08028
5.03307
5.00755
4.19101
4.18174
4.17313
4.16418
4.14634
4.12930
4.11218
4.09441
4.08512
4.06743
3.63539
3.61877
3.61315
3.59659
2.91530
2.89803
2.88074
2.86495
2.84678
2.82944
2.81131
2.79110
2.53715
2.52123
2.50309
2.48558
1.63131
1.26014
1.24349
1.22735
1.20965
0.09226
0.01818
Integral
1.9527
1.8321
0.8670
1.8551
1.8803
0.9224
1.9266
0.9787
9.0000
ppm
7
6
5
4
3
2
1
0

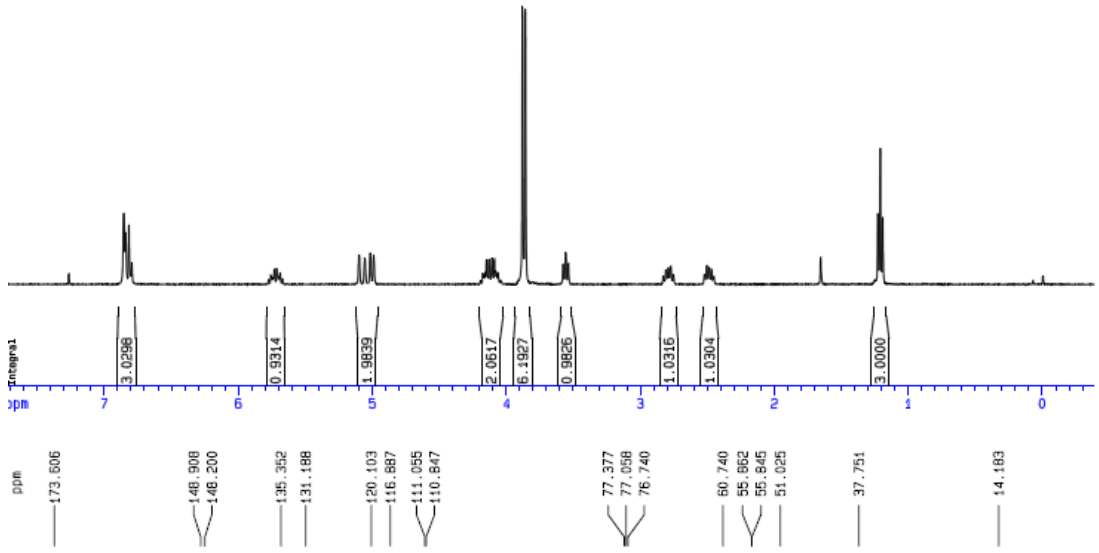
6c


ppm
173.621
147.794
136.009
135.530
127.756
126.649
116.790
77.372
77.055
76.736
60.702
51.153
37.751
33.721
23.968
14.190
ppm
160
140
120
100
80
60
40
20

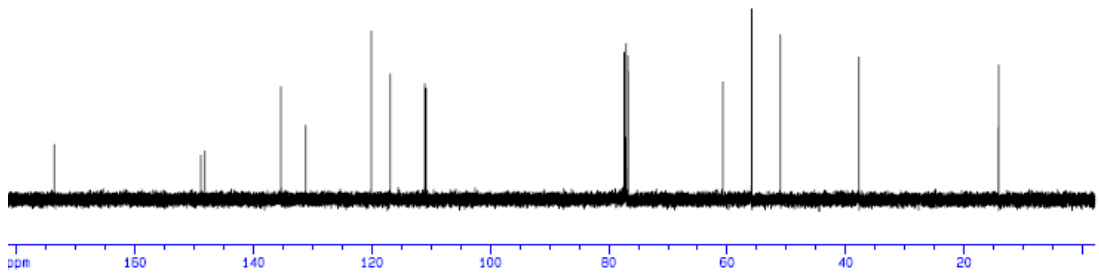
6c


ppm
7.2641
6.8546
6.8413
6.8162
6.7944
5.7725
5.7558
5.7474
5.7385
5.7303
5.7131
5.6958
5.6878
5.6704
5.0991
5.0564
5.0154
4.9900
4.1740
4.1650
4.1563
4.1471
4.1289
4.1065
4.0884
4.0795
4.0712
4.0612
4.0436
3.8789
3.8575
3.5757
3.5566
3.5370
2.8272
2.8084
2.7907
2.7727
2.7522
2.5198
2.5033
2.4862
2.4676
2.4508
1.6539
1.2507
1.2261
1.2083
1.1906
0.0686
-0.0061

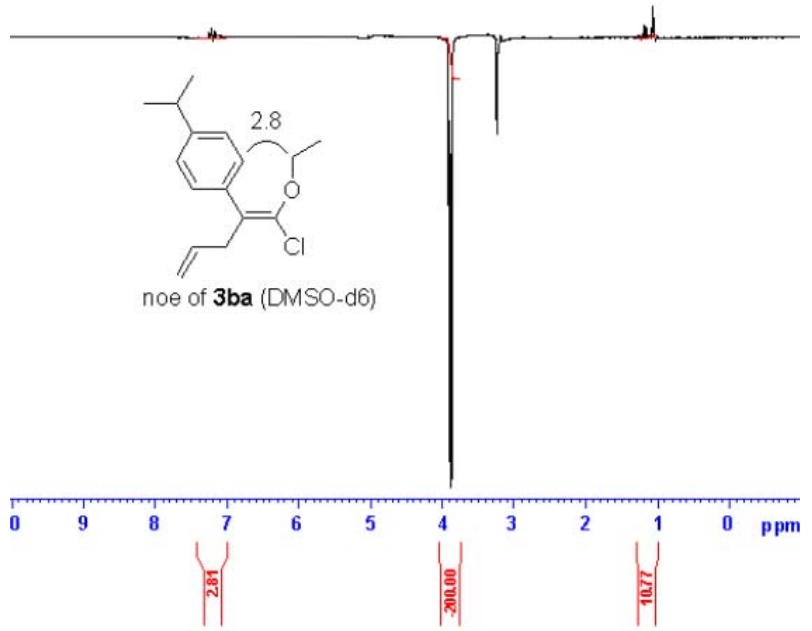
6d

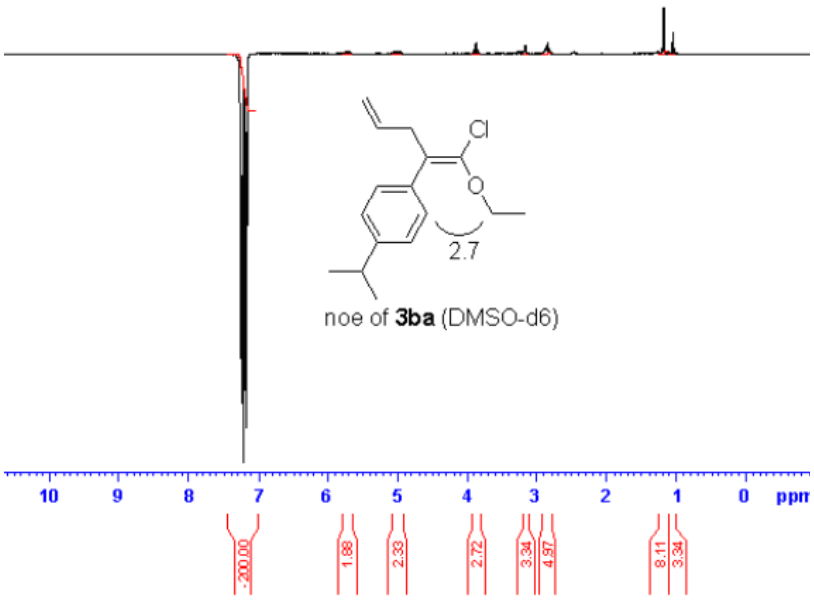

Integral
3.0298
0.9314
1.9839
2.0617
6.1927
0.9826
1.0316
1.0304
3.0000
ppm
7
6
5
4
3
2
1
0
ppm
173.606
148.908
148.200
135.352
131.188
120.103
116.887
111.055
110.847
77.377
77.058
76.740
60.740
55.862
55.845
51.025
37.751
14.183

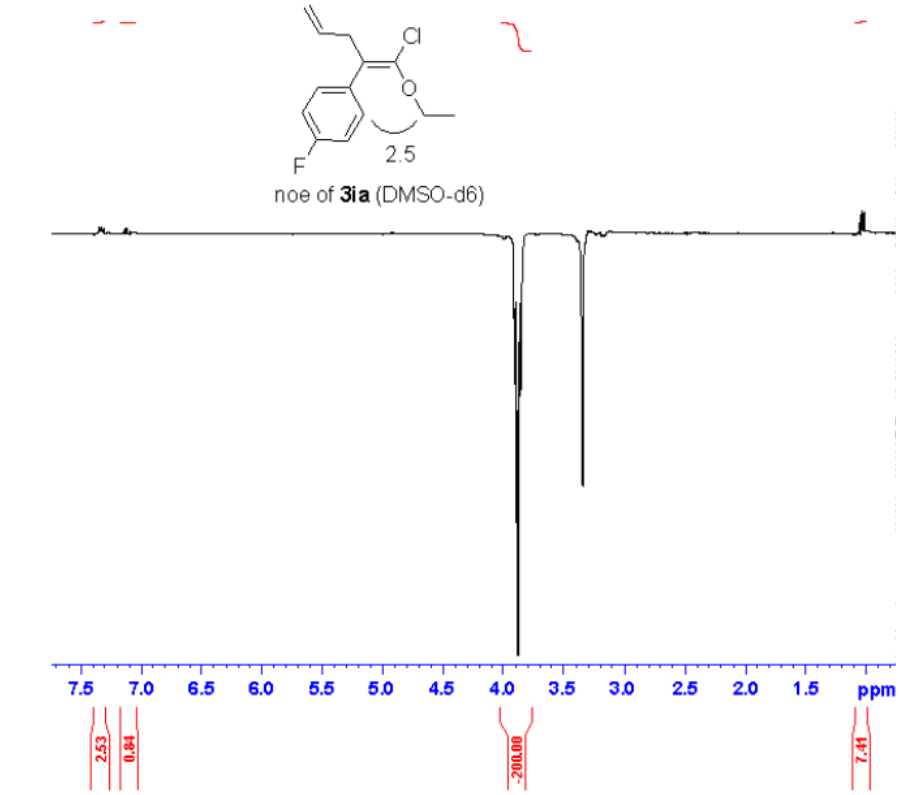
6d

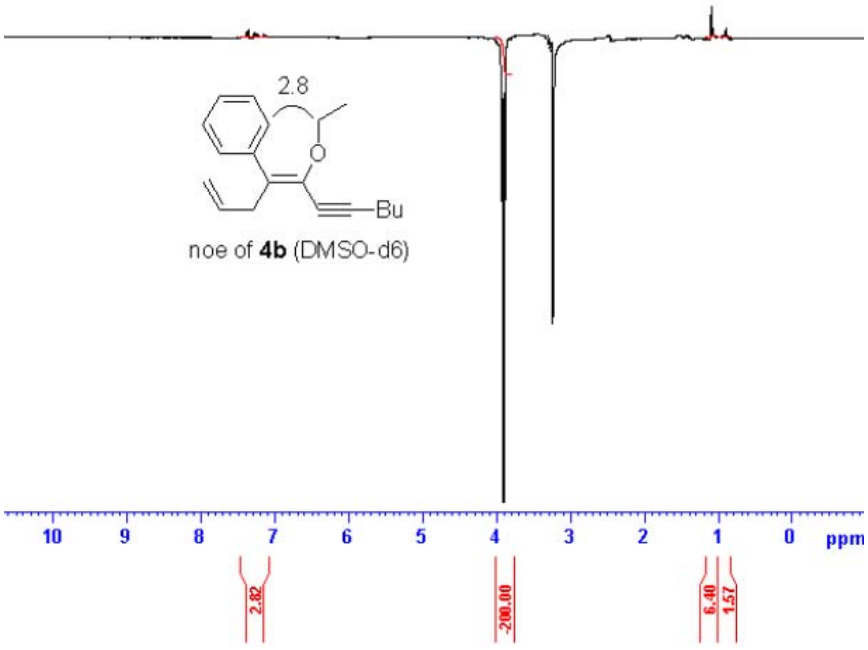

ppm
160
140
120
100
80
60
40
20

Selected NOE data






Cl
O
F
2.5
noe of 3ia (DMSO-d6)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
2.53
0.84
-200.00
7.41


2.8
O
Bu
noe of 4b (DMSO-d6)
10
9
8
7
6
5
4
3
2
1
0
ppm
2.82
-200.00
6.40
1.57