Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Efficient Synthesis of Tetrasubstituted 2,3-Allenoates and Preliminary Studies on Bioactivities

Yuan Yao,[a] Guirong Zhu,[a] Qin Chen,*[,a] Hui Qian,*[,a] and Shengming Ma*[,a,b]

[a] Research Center for Molecular Recognition and Synthesis，Department of Chemistry, Fudan University, 220 Handan Lu, Shanghai 200433, P. R. China

[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, P. R. China

E-mail: masm@sioc.ac.cn

qian_hui@fudan.edu.cn

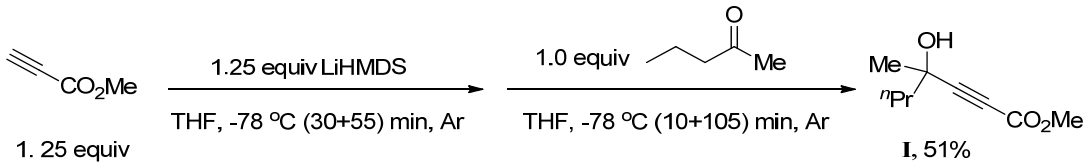
chenq@fudan.edu.cn

General Information. NMR spectra were taken with an Agilent-400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, and 376 MHz for ^{19}F NMR) in $CDCl_3$ or CD_3OD. ^{1}H NMR experiments were measured with tetramethylsilane (0 ppm) in $CDCl_3$ or the signal of residual CH_3OH (3.31 ppm) in CD_3OD as the internal reference; ^{13}C NMR experiments were measured in relative to the signal of $CDCl_3$ (77.0 ppm) or the signal of CD_3OD (49.0 ppm); ^{19}F NMR experiments were measured in relative to the signal of $CFCl_3$ (0 ppm) in $CDCl_3$. All reactions were carried out in oven-dried Schlenk tubes or vials. $Pd_2(dba)_3{\cdot}CHCl_3$ and tris(*o*-tolyl)phosphine were purchased from Energy Chemicals. Organoboronic acids were all commercially available: phenylboronic acid was purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) and recrystallized from ethyl acetate before use; other arylboronic acids (98% purity) were purchased from Shanghai Boka Chemical Technology Co., Ltd (Shanghai, China) and used as received. Petroleum ether (b.p. 60-90 ^{o}C) was purchased from Shanghai Titan Scientific Co., Ltd. THF was dried over sodium wire with benzophenone as the indicator and distilled freshly before use.

Experimental details and analytical data

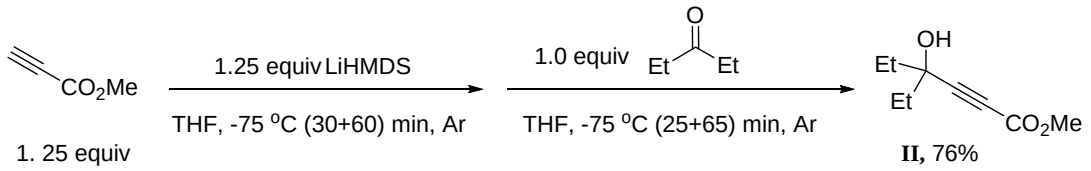
1. Preparation of 3-methoxycarbonyl propargylic alcohols[1]

(1) Preparation of methyl 4-hydroxy-4-methyl-2-heptynoate (I) (yy-01-017)



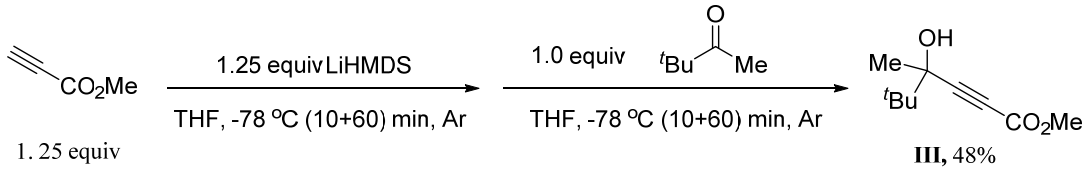
Typical Procedure I: To an oven oven-dried round-bottom flask were charged with anhydrous THF (50 mL) and methyl propiolate (5.3 mL, d = 0.945 g/mL, 5.009 g, 60.0 mmol). The solution was cooled to -78 °C under argon atmosphere, and LiHMDS (60 mL, 60.0 mmol, 1.0 M in THF) was added dropwise over 30 min. The resulting solution was stirred for 55 minutes before 2-pentanone (5.1 mL, d = 0.809 g/mL, 4.126 g, 48.0 mmol) was added dropwise to the solution over 10 min. After stirring for 105 minutes at this temperature, the resulting mixture was quenched with a saturated NH_4Cl (aq.) solution (30 mL) and diluted with H_2O (200 mL). The resulting mixture was extracted with ethyl acetate (3 x 150 mL), and the combined organic layer was washed with brine (100 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure, the residue was purified by column chromatography on silica gel to afford **I** (4.1777 g, 51%) [eluent: petroleum ether/ethyl acetate = 7/1 (~240 mL) to petroleum ether/ethyl acetate = 4/1 (~250 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 2.30 (s, 1 H, OH), 1.75-1.63 (m, 2 H, CH_2), 1.62-1.42 (m, 5 H, CH_2 and CH_3), 0.97 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 154.0, 91.1, 74.5, 67.9, 52.6, 44.9, 28.7, 17.6, 13.9; **IR** (neat): *ν* = 3411, 2961, 2875, 2233, 1715, 1699, 1434, 1371, 1239, 1159, 1135, 1086, 1032 cm^{-1}; **MS** (ESI) m/z: 188.0 ($M+NH_4^+$), 171.0 ($M+H^+$); **HRMS** calcd for $C_9H_{14}O_3$ [M^+]: 170.0943; found 170.0941.

(2) Preparation of methyl 4-hydroxy-4-ethyl-2-hexynoate (II) (yao-01-088)



Following **Typical Procedure I**, the reaction of methyl propiolate (4.4 mL, d = 0.945 g/mL, 4.158 g, 50.0 mmol), LiHMDS (50 mL, 1.0 M in THF, 50.0 mmol), and 3-pentanone (4.2 mL, d = 0.815 g/mL, 3.423 g, 40.0 mmol) in freshly distilled THF (40 mL) afforded **II** (5.1368 g, 76%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to petroleum ether/ethyl acetate = 40/7 (~230 mL)] to petroleum ether/ethyl acetate = 4/1 (~120 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 2.59 (s, 1 H, OH), 1.82-1.66 (m, 4 H, 2 x CH_2), 1.05 (t, *J* = 7.6 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.9, 90.1, 75.8, 72.0, 52.7, 33.7, 8.2; **IR** (neat): *v* = 3430, 2973, 2232, 1715, 1700, 1458, 1435, 1239, 1146, 1049, 1031 cm^{-1}; **MS** (ESI) m/z: 188 ($M+NH_4^+$), 171 ($M+H^+$); **HRMS** calcd for $C_9H_{18}O_3N$ [$M+NH_4^+$]: 188.1281; found 188.1279.

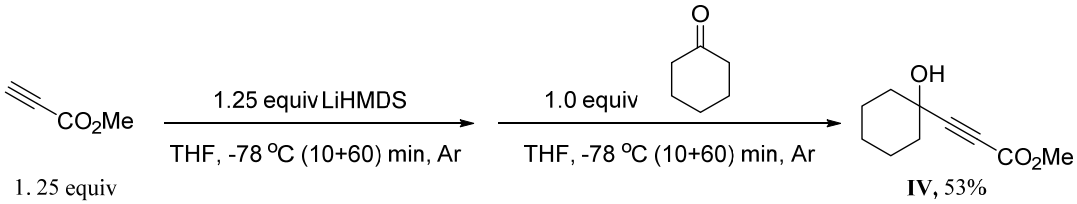
(3) Preparation of methyl 4-hydroxy-4,5,5-trimethyl-2-hexynoate (III) (yao-01-150)



Following **Typical Procedure I**, the reaction of methyl propiolate (2.2 mL, d = 0.945 g/mL, 2.079 g, 25.0 mmol), LiHMDS (25 mL, 25.0 mmol, 1.0 M in THF), and 3,3-dimethyl-2-butanone (2.5 mL, d = 0.809 g/mL, 2.023 g, 20.0 mmol) in freshly distilled THF (30 mL) afforded **III**[2] (1.7823 g, 48%) [eluent: petroleum ether/ethyl acetate = 10/1 (~220 mL) to petroleum ether/ethyl acetate = 8/1 (~90 mL)] to petroleum ether/ethyl acetate = 4/1 (~120 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 2.03 (s, 1 H, OH), 1.50 (s, 3 H, CH_3), 1.07 (s, 9 H, ^{t}Bu); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.9, 91.0, 75.7, 73.9, 52.7, 38.2, 24.9, 24.1; **IR**

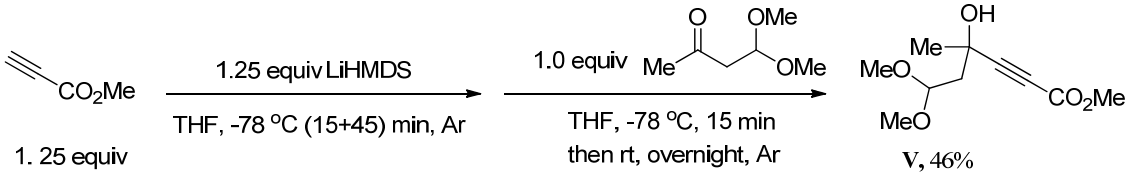
(neat): ν = 3490, 2965, 2232, 1706, 1439, 1367, 1242, 1107, 1146, 1049, 1031 cm^{-1}; **MS** (ESI) m/z: 202 ($M+NH_4^+$).

(4) Preparation of methyl 3-(1-hydroxycyclohexyl)propiolate (IV) (yao-01-151)



Following **Typical Procedure I**, the reaction of methyl propiolate (1.1 mL, d = 0.945 g/mL, 1.040 g, 12.5 mmol), LiHMDS (12.5 mL, 12.5 mmol, 1.0 M in THF), and cyclohexanone (1.03 mL, d = 0.95 g/mL, 0.979 g, 10.0 mmol) in freshly distilled THF (15 mL) afforded **IV**[3] (0.9610 g, 53%) [eluent: petroleum ether/ethyl acetate = 10/1 (~110 mL) to petroleum ether/ethyl acetate = 20/3 (~110 mL)] to petroleum ether/ethyl acetate = 5/1 (~120 mL) to petroleum ether/ethyl acetate = 4/1 (~120 mL)]: solid; **m.p.** 50.9-60.9 °C (petroleum ether/ethyl ether); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 2.08 (s, 1 H, OH), 2.02-1.90 (m, 2 H, CH_2), 1.80-1.49 (m, 7 H, 3 x CH_2 and one proton of CH_2), 1.34-1.21 (m, 1 H, one proton of CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 154.0, 90.8, 75.6, 68.4, 52.7, 39.0, 24.8, 22.8; **IR** (neat): ν = 3258, 2934, 2853, 2238, 1707, 1450, 1431, 1284, 1237, 1070, 1041 cm^{-1}; **MS** (ESI) 205 ($M+Na^+$), 200 ($M+NH_4^+$); Anal. Calcd. for $C_{10}H_{14}O_3$: C 65.92, H 7.74; found C 65.96, H 7.58.

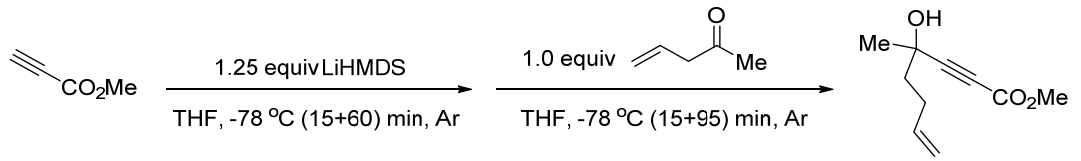
(5) Preparation of methyl 4-hydroxy-4-methyl-6,6-dimethoxy-2-hexynoate (V) (yy-01-027)



Following **Typical Procedure I**, the reaction of methyl propiolate (2.2 mL, d = 0.945 g/mL, 2.079 g, 25.0 mmol), LiHMDS (25 mL, 25.0 mmol, 1.0 M in THF), and

4,4-dimethoxy-2-butanone (2.7 mL, d = 0.996 g/mL, 2.689 g, 20.0 mmol) in freshly distilled THF (30 mL) afforded **V** (1.8775 g, 46%) [eluent: petroleum ether/ethyl acetate = 100/13 (~110 mL) to petroleum ether/ethyl acetate = 100/17 (~120 mL)] to petroleum ether/ethyl acetate = 5/1 (~120 mL) to petroleum ether/ethyl acetate = 10/3 (~130 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.85 (dd, J_1 = 8.4 Hz, J_2 = 3.6 Hz, 1 H, CH), 4.39 (s, 1 H, OH), 3.79 (s, 3 H, OCH_3), 3.48 (s, 3 H, OCH_3), 3.37 (s, 3 H, OCH_3), 2.08-1.95 (m, 2 H, CH_2), 1.53 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.7, 103.0, 89.7, 74.9, 65.2, 54.6, 52.64, 52.59, 43.6, 29.4; **IR** (neat): ν = 3459, 2939, 2234, 1714, 1435, 1369, 1243, 1118, 1041 cm^{-1}; **MS** (ESI) m/z: 234 ($M+NH_4^+$); **HRMS** calcd for $C_{10}H_{20}O_5N$ [$M+NH_4^+$]: 234.1336; found 234.1334.

(6) Preparation of methyl 4-hydroxy-4-methyloct-7-en-2-ynoate (VI) (yy-01-033)



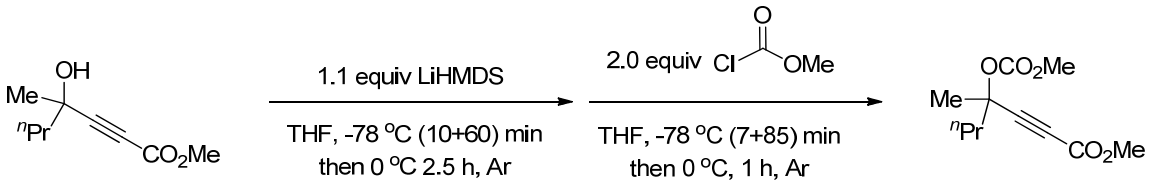
1. 25 equiv **VI**, 55%

Following **Typical Procedure I**, the reaction of methyl propiolate (2.2 mL, d = 0.945 g/mL, 2.079 g, 25 mmol), LiHMDS (25 mL, 1.0 M in THF, 25 mmol), and pent-4-en-2-one (2.3 mL, d = 0.847 g/mL, 1.948 g, 20.0 mmol) in freshly distilled THF (30 mL) afforded **VI** (2.0028 g, 55%) [eluent: petroleum ether/ethyl acetate = 100/13 (~110 mL) to petroleum ether/ethyl acetate = 10/1 (~220 mL)] to petroleum ether/ethyl acetate = 5/1 (~120 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.92-5.80 (m, 1 H, =CH), 5.10 (dq, J_1 = 17.2 Hz, J_2 = 1.8 Hz, 1 H, one proton of $=CH_2$), 5.01 (dq, J_1 = 10.2 Hz, J_2 = 1.5 Hz, 1 H, one proton of $=CH_2$), 3.79 (s, 3 H, CH_3), 2.40-2.20 (m, 3 H, CH_2 and OH), 1.90-1.74 (m, 2 H, CH_2), 1.55 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.9, 137.7, 115.4, 90.4, 75.2, 68.0, 52.8, 41.8, 29.1, 28.8; **IR** (neat): ν = 3420, 2953, 2234, 1715, 1699, 1642, 1435, 1371, 1248, 1018 cm^{-1}; **MS**

(ESI) m/z: 205 ($M+Na^+$), 200 ($M+NH_4^+$), 183 ($M+H^+$); **HRMS** calcd for $C_{10}H_{14}O_3$ [M^+]: 182.0943; found 182.0945.

2. Preparation of 3-methoxycarbonyl propargylic carbonates

(1) Preparation of methyl 4-((methoxycarbonyl)oxy)-4-methyl-2-heptynoate (1a) (yy-01-018)

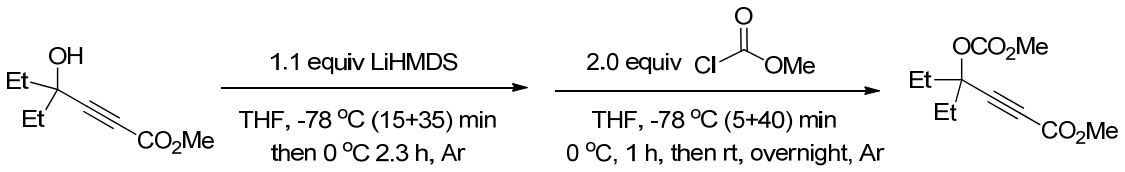


I **1a,** 66%

Typical Procedure II: To an oven-dried, round-bottom flask were charged with and **I** (4.1777 g, 24.6 mmol). The solution was cooled to -78 °C (dry ice-acetone bath) under argon atmosphere, and LiHMDS (27.1 mL, 27.1 mmol, 1.0 M in THF) was added dropwise over 10 min. The resulting solution was stirred for 1 hour at this temperature before stirring for 2.5 hours at 0 °C (ice-water bath). The reaction was cooled to -78 °C (dry ice-acetone bath) again, methyl chloroformate (3.8 mL, d = 1.223 g/mL, 4.647 g, 49.2 mmol) was added dropwise over 7 min. After being stirred for 1.5 hours at the same temperature, it was allowed to stir for 1 hour at 0 °C (ice-water bath). The reaction was quenched with a saturated NH_4Cl (aq.) solution (20 mL) and diluted with H_2O (100 mL). The resulting solution was extracted with ethyl acetate (3 x 150 mL), and the combined organic layer was washed with brine (100 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel to afford **1a** (3.6840 g, 66%) [eluent: petroleum ether/ethyl acetate = 20/1 (~200 mL) to petroleum ether/ethyl acetate = 5/1 (~120 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.784 (s, 3 H, OCH_3), 3.780 (s, 3 H, OCH_3), 2.12-1.94 (m, 1 H, one proton of CH_2), 1.91-1.80 (m, 1 H, one proton of CH_2), 1.73 (s, 3 H, CH_3), 1.65-1.41 (m, 2 H, CH_2), 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.5, 153.3, 86.3, 76.9, 76.0, 54.5, 52.7, 42.8, 25.5, 17.2, 13.7; **IR**

(neat): ν = 2961, 2238, 1754, 1716, 1437, 1378, 1236, 1028 cm^{-1}; **MS** (ESI) m/z: 251 ($M+Na^+$); **HRMS** calcd for $C_{11}H_{16}O_5$ [M^+]: 228.0998; found 228.1003.

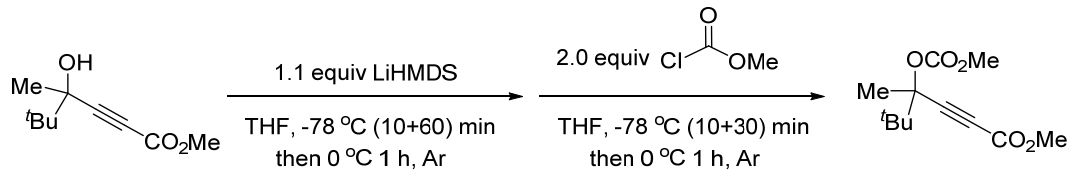
(2) Preparation of methyl 4-ethyl-4-((methoxycarbonyl)oxy)-2-hexynoate (1b) (yy-01-020)



II **1b,** 39%

Following **Typical Procedure II**, the reaction of **II** (2.0367 g, 12.0 mmol), LiHMDS (13.2 mL, 1.0 M in THF, 13.2 mmol), and methyl chloroformate (1.9 mL, d = 1.223 g/mL, 2.324 g, 24.0 mmol) in freshly distilled THF (15 mL) afforded **1b** (1.0822 g, 39%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 100/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 20/1 (~100 mL) to petroleum ether/ethyl acetate = 50/3 (~200 mL) to petroleum ether/ethyl acetate = 40/3 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 6 H, 2 x OCH_3), 2.12-1.92 (m, 4 H, 2 x CH_2), 1.02 (t, J =7.4 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.6, 153.3, 85.8, 80.3, 78.0, 54.6, 52.7, 30.2, 8.0; **IR** (neat): ν = 2979, 2235, 1753, 1716, 1437, 1234, 1149, 1124, 1050 cm^{-1}; **MS** (ESI) m/z: 251 ($M+Na^+$); **HRMS** calcd for $C_{11}H_{16}O_5$ [M^+]: 228.0998; found 228.0999.

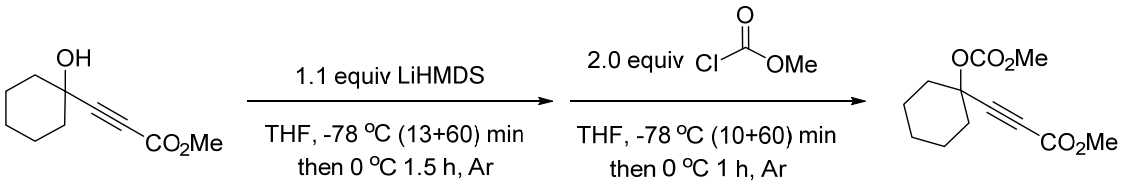
(3) Preparation of methyl 4-((methoxycarbonyl)oxy)-4,5,5-trimethyl-2-hexynoate (1c) (yy-01-026)



III **1c,** 56%

Following **Typical Procedure II**, the reaction of **III** (2.1820 g, 11.8 mmol), LiHMDS (13.0 mL, 13.0 mmol, 1.0 M in THF), and methyl chloroformate (1.8 mL, d = 1.223 g/mL, 2.201 g, 23.6 mmol) in freshly distilled THF (15 mL) afforded **1c** (1.6 g, 56%) [eluent: petroleum ether/ethyl acetate = 20/1 (~100 mL) to petroleum ether/ethyl acetate = 10/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 6 H, 2 x OCH_3), 1.74 (s, 3 H, CH_3), 1.11 (s, 9 H, ^{t}Bu); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.6, 153.5, 86.2, 81.8, 77.9, 54.5, 52.7, 39.3, 24.9, 20.0; **IR** (neat): ν = 2960, 2238, 1754, 1715, 1437, 1373, 1251, 1233, 1127, 1068, 1024, 1004 cm^{-1}; **MS** (ESI) m/z: 265 ($M+Na^+$), 260 ($M+NH_4^+$); **HRMS** calcd for $C_{12}H_{18}O_5$ [M^+]: 242.1154; found 242.1155.

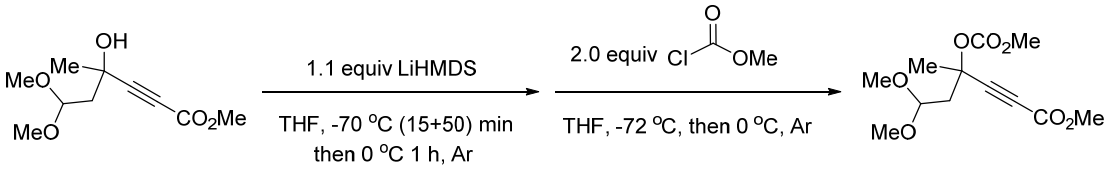
(4) Preparation of methyl 3-(1-((methoxycarbonyl)oxy)cyclohexyl)propiolate (1d) (yy-01-030)



IV **1d,** 66%

Following **Typical Procedure II**, the reaction of **IV** (2.5230 g, 13.8 mmol), LiHMDS (15.2 mL, 15.2 mmol, 1.0 M in THF), and methyl chloroformate (2.1 mL, d = 1.223 g/mL, 2.568 g, 27.6 mmol) in freshly distilled THF (15 mL) afforded **1d** (2.2068 g, 66%) [eluent: petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 20/1 (~100 mL)] to petroleum ether/ethyl acetate = 100/7 (~100 mL) to petroleum ether/ethyl acetate = 10/1 (~110 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.79 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 2.35-2.14 (m, 2 H, CH_2), 1.98-1.87 (m, 2 H, CH_2), 1.75-1.50 (m, 5 H, 2 x CH_2 and one proton of CH_2), 1.43-1.31 (m, 1 H, one proton of CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.5, 153.0, 86.0, 77.9, 76.2, 54.5, 52.6, 36.0, 24.6, 22.1; **IR** (neat): ν = 2940, 2863, 2234, 1752, 1715, 1437, 1275, 1230, 1118, 1017 cm^{-1}; **MS** (ESI) m/z: 263 ($M+Na^+$); **HRMS** calcd for $C_{12}H_{16}O_5$ [M^+]: 240.0998; found 240.0996.

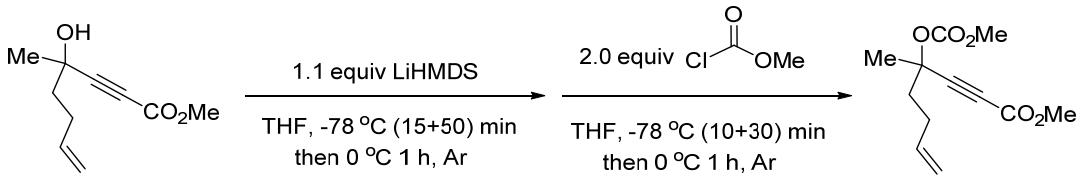
(5) Preparation of methyl 6,6-dimethoxy-4-((methoxycarbonyl)oxy)-4-methyl-2-hexynoate (1e) (yy-01-035)



V **1e,** 40%

Following **Typical Procedure II**, the reaction of **V** (1.8775 g, 8.7 mmol), LiHMDS (9.6 mL, 1.0 M in THF, 9.6 mmol), and methyl chloroformate (1.3 mL, d = 1.223 g/mL, 1.590 g, 17.4 mmol) in freshly distilled THF (15 mL) afforded **1e** (0.9467 g, 40%) [eluent: petroleum ether/ethyl acetate = 5/1 (~120 mL) to petroleum ether/ethyl acetate = 20/3 (~110 mL)] to petroleum ether/ethyl acetate = 10/1 (~220 mL) to petroleum ether/ethyl acetate = 5/1 (~240 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.65 (t, *J* = 5.0 Hz, 1 H, CH), 3.79 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 3.43-3.29 (m, 6 H, 2 x OMe), 2.38-2.24 (m, 2 H, CH_2), 1.78 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.4, 153.1, 101.0, 85.6, 77.27, 73.8, 54.6, 53.2, 52.8, 52.7, 42.7, 26.3; **IR** (neat): *ν* = 2957, 2835, 2241, 1754, 1716, 1437, 1376, 1239, 1111, 1085, 1059 cm^{-1}; **MS** (ESI) m/z: 297 ($M+Na^+$), 292 ($M+NH_4^+$). **HRMS** calcd for $C_{12}H_{18}O_7$ [M^+]: 274.1053; found 274.1056.

(6) Preparation of methyl 4-((methoxycarbonyl)oxy)-4-methyloct-7-en-2-ynoate (1f) (yy-01-036)



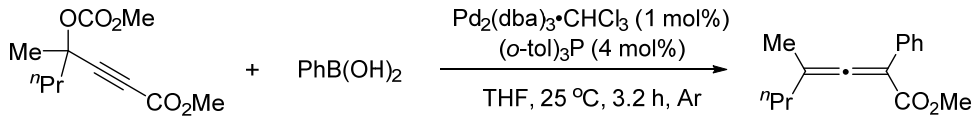
VI **1f,** 65%

Following **Typical Procedure II**, the reaction of **VI** (2.0028 g, 11.0 mmol), LiHMDS (12.1 mL, 1.0 M in THF, 12.1 mmol), and methyl chloroformate (1.7 mL, d = 1.223 g/mL, 2.079 g, 22.0 mmol) in freshly distilled THF (15 mL) afforded **1f**

(1.7256 g, 65%) [eluent: petroleum ether/ethyl acetate = 5/1 (~240 mL) to petroleum ether/ethyl acetate = 100/13 (~110 mL)] to petroleum ether/ethyl acetate = 10/1 (~220 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.88-5.74 (m, 1 H, =CH), 5.12-5.03 (m, 1 H, one proton of $=CH_2$), 5.03-4.96 (m, 1 H, one proton of $=CH_2$), 3.79 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 2.40-2.19 (m, 2 H, CH_2), 2.15-2.02 (m, 1 H, one proton of CH_2), 2.02-1.90 (m, 1 H, one proton of CH_2), 1.76 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 153.4, 153.2, 136.7, 115.3, 85.9, 77.2, 75.7, 54.6, 52.7, 40.0, 28.1, 25.6; **IR** (neat): ν = 2957, 2240, 1754, 1716, 1643, 1437, 1377, 1232, 1022 cm^{-1}; **MS** (ESI) m/z: 263 ($M+Na^+$), 258 ($M+NH_4^+$); **HRMS** calcd for $C_{12}H_{16}O_5$ [M^+]: 240.0998; found 240.0999.

3. Preparation of allenoates

(1) Preparation of methyl 4-methyl-2-phenyl-2,3-heptadienoate (3aa) (yao-01-060)

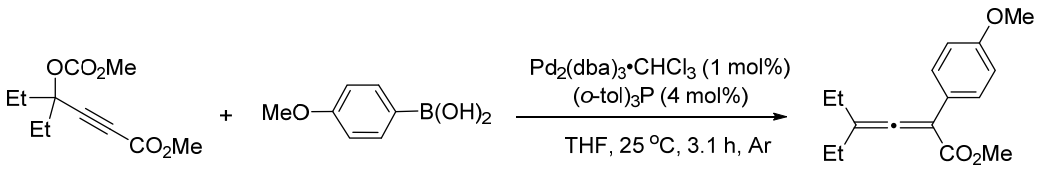


1a **2a** (1.1 equiv) **3aa,** 90%

Typical Procedure III: To an oven-dried Schlenk tube were added **2a** (135.9 mg, 1.1 mmol), $Pd_2(dba)_3$·$CHCl_3$ (11.1 mg, 0.01 mmol), and tris(*o*-tolyl)phosphine (12.8 mg, 0.04 mmol). After replacing air with argon for three times at rt by vaccum, **1a** (231.5 mg, 1.0 mmol) and freshly distilled THF (2.0 mL) were added. The resulting mixture was stirred for 3.2 h at 25 °C as monitored by TLC and then filtered through a short pad of silica gel eluted with ethyl acetate (15 mL x 3). After removal of the solvent under vacuum, the residue was purified by flash column chromatography on silica gel to afford **3aa** (209.4 mg, 90%) [eluent: petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~300 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.47 (d, J = 8.4 Hz, 2 H, Ar-H), 7.32 (t, J = 7.6 Hz, 2 H, Ar-H), 7.23 (t, J = 7.4 Hz, 1 H, Ar-H), 3.78 (s, 3 H, OCH_3), 2.20-2.07 (m, 2 H, CH_2), 1.87 (s,

3 H, CH_3), 1.60-1.46 (m, 2 H, CH_2), 0.93 (t, J = 7.2 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.4, 167.3, 134.0, 128.3, 128.0, 127.1, 105.0, 101.8, 52.0, 35.7, 20.5, 17.9, 13.6; **IR** (neat): ν = 2955, 1948, 1714, 1599, 1493, 1434, 1384, 1273, 1195, 1175, 1040, 1021 cm^{-1}; **MS** (70 eV, EI) m/z (%): 231 (M^++1, 5.71), 230 (M^+, 33.18), 128 (100); **HRMS** calcd for $C_{15}H_{18}O_2$ [M^+]: 230.1307; found 230.1303.

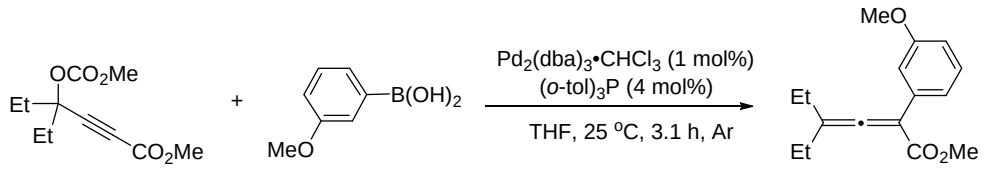
(2) Preparation of methyl 4-ethyl-2-(4-methoxyphenyl)-2,3-hexadienoate (3bb) (yy-01-045)



1b **2b** (1.1 equiv) **3bb,** 87%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.4 mg, 0.04 mmol), **2b** (170.6 mg, 1.1 mmol), and **1b** (226.8 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3bb** (225.9 mg, 87%) [eluent: petroleum ether/ethyl acetate = 40/1 (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~200 ml)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.43 (d, J = 8.8 Hz, 2 H, Ar-H), 6.87 (d, J = 8.8 Hz, Ar-H), 3.80 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 2.17 (q, J = 7.2 Hz, 4 H, 2 x CH_2), 1.09 (t, J = 7.4 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 208.2, 167.8, 158.8, 129.2, 126.4, 113.6, 113.5, 103.9, 55.2, 52.0, 25.7, 12.1; **IR** (neat): ν = 2966, 1942, 1713, 1607, 1510, 1434, 1375, 1245, 1196, 1169, 1025 cm^{-1}; **MS** (70 eV, EI) m/z (%): 261 (M^++1, 14.98), 260 (M^+, 84.66), 201 (100); **HRMS** calcd for $C_{16}H_{20}O_3$ [M^+]: 260.1412; found 260.1411.

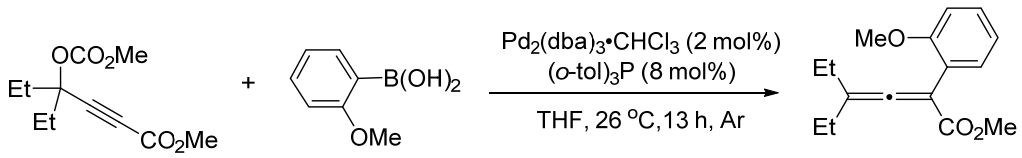
(3) Preparation of methyl 4-ethyl-2-(3-methoxyphenyl)-2,3-hexadienoate (3bc) (yao-01-050)



1b **2c** (1.1 equiv) **3bc,** 91%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.4 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.2 mg, 0.04 mmol), **2c** (171.5 mg, 1.1 mmol), and **1b** (227.6 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3bc** (235.4 mg, 91%) [eluent: petroleum ether (100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.27-7.18 (m, 1 H, Ar-H), 7.13-7.05 (m, 2 H, Ar-H), 6.82-6.77 (m, 1 H, Ar-H), 3.80 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 2.18 (q, *J* = 7.5 Hz, 4 H, 2 x CH_2), 1.09 (t, *J* = 7.4 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 208.6, 167.4, 159.3, 135.4, 129.0, 120.6, 113.8, 112.6, 104.3, 55.1, 52.0, 25.6, 12.0; **IR** (neat): *ν* = 2966, 1942, 1715, 1598, 1579, 1488, 1455, 1432, 1277, 1227, 1190, 1152, 1030 cm^{-1}; **MS** (70 eV, EI) m/z (%): 261 (M^++1, 17.66), 260 (M^+, 100); **HRMS** calcd for $C_{16}H_{20}O_3$ [M^+]: 260.1412; found 260.1408.

(4) Preparation of methyl 4-ethyl-2-(2-methoxyphenyl)-2,3-hexadienoate (3bd) (yao-01-122)

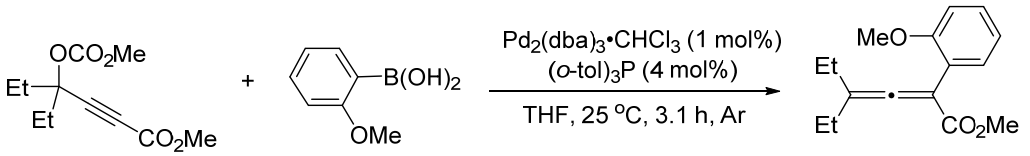


1b **2d** (1.5 equiv) **3bd,** 84%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (20.9 mg, 0.02 mmol), tris(*o*-tolyl)phosphine (24.5 mg, 0.08 mmol), **2d** (229.0 mg, 1.5 mmol), and **1b** (225.1 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3bd** (215.7 mg, 84%) [eluent: petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL) to petroleum ether/ethyl acetate = 50/3 (~200 mL) to petroleum ether/ethyl acetate = 25/2 (~100 mL)]: solid; **m.p.** 45.5-46.3 °C

(petroleum ether/ethyl ether); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.32-7.25 (m, 1 H, Ar-H), 7.21 (dd, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 1 H, Ar-H), 6.97-6.87 (m, 2 H, Ar-H), 3.80 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 2.21-2.04 (m, 4 H, 2 x CH_2), 1.10 (t, J = 7.4 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 207.7, 167.8, 157.0, 130.6, 129.0, 124.4, 120.4, 112.4, 111.1, 101.7, 55.6, 52.0, 25.5, 12.0; **IR** (neat): ν = 2967, 1956, 1718, 1597, 1492, 1451, 1433, 1259, 1194, 1170, 1112, 1080, 1048, 1030, 1019 cm^{-1}; **MS** (70 eV, EI) m/z (%): 261 (M^++1, 10.68), 260 (M^+, 62.34), 245 (100); Anal. Calcd. for $C_{16}H_{20}O_3$: C 73.82, H 7.74; found C 73.33, H 7.62.

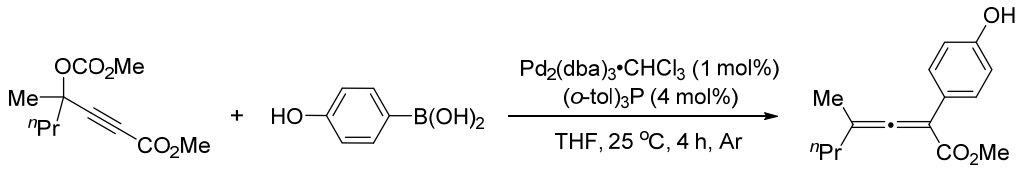
The reaction of 1b with 2d under the standard conditions （yao-01-051）



1b (1.0 mmol) **2d** (1.1 equiv) **3bd,** 75% NMR yield 23% recovery of **1b**

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.9 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (13.3 mg, 0.04 mmol), **2d** (168.0 mg, 1.1 mmol), and **1b** (229.5 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded a crude product. 75% NMR yield of **3bd** and 23% recovered of **1b** were determined by the NMR spectrum of the crude product with CH_2Br_2 (17.5 μL) as the internal standard.

(5) Preparation of methyl 2-(4-hydroxyphenyl)-4-methyl-2,3-heptadienoate (3ae) (yao-01-109)

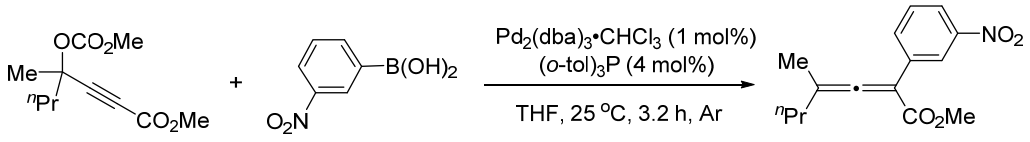


1a **2e** (1.1 equiv) **3ae,** 92%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.6 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (13.0 mg, 0.04 mmol), **2e** (155.1 mg, 1.1 mmol), and **1a** (223.4 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ae** (220.9 mg, 92%) [eluent: petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl

acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~100 mL) to petroleum ether/ethyl acetate = 50/3 (~100 mL) to petroleum ether/ethyl acetate = 10/1 (~100 mL) to petroleum ether/ethyl acetate = 5/1 (~200 mL)]: solid; **m.p.** 83.2-84.2 °C (petroleum ether/CH_2Cl_2); **^{1}H NMR** (400 MHz, CD_3OD): δ = 7.25 (d, *J* = 9.2 Hz, 2 H, Ar-H), 6.73 (d, *J* = 8.8 Hz, 2 H, Ar-H), 4.85 (s, 1 H, OH), 3.74 (s, 3 H, OCH_3), 2.20-2.05 (m, 2 H, CH_2), 1.84 (s, 3 H, CH_3), 1.52 (sextet, *J* = 7.4 Hz, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, CD_3OD): δ = 209.9, 169.4, 157.9, 130.5, 126.0, 115.9, 105.9, 102.8, 52.5, 36.7, 21.5, 18.2, 14.0; **IR** (neat): *v* = 3348, 2946, 1944, 1683, 1612, 1515, 1435, 1387, 1266, 1212, 1173, 1105, 1084, 1023 cm^{-1}; **MS** (EI) m/z (%): 247 (M^++1, 5.73), 246 (M^+, 32.20), 187 (100); Anal. Calcd. for $C_{15}H_{18}O_3$: C 73.15, H 7.37; found C 73.13, H 7.33.

(6) Preparation of methyl 4-methyl-2-(3-nitrophenyl)- 2,3-heptadienoate (3af) (yao-01-059)

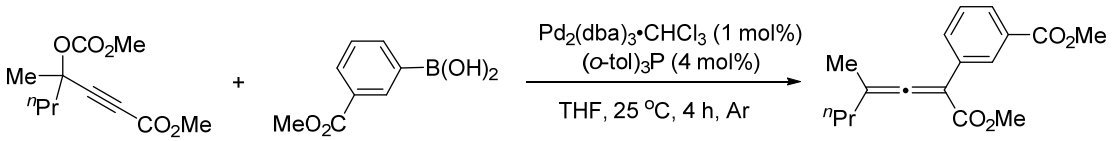


1a **2f** (1.1 equiv) **3af,** 85%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.8 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.7 mg, 0.04 mmol), **2f** (189.0 mg, 1.1 mmol), and **1a** (228.6 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3af** (235.0 mg, 85%) [eluent: petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 ml) to petroleum ether/ethyl acetate = 20/1 (~100 ml)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.37 (t, *J* = 2.0 Hz, 1 H, Ar-H), 8.12-8.06 (m, 1 H, Ar-H), 7.85 (dt J_1 = 8.0 Hz, J_2 = 1.4 Hz , 1 H, Ar-H), 7.49 (t, *J* = 8.0 Hz, 1 H, Ar-H), 3.82 (s, 3 H, OCH_3), 2.26-2.13 (m, 2 H, CH_2), 1.92 (s, 3 H, CH_3), 1.62-1.48 (m, 2 H, CH_2), 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 210.0, 166.6, 148.1, 136.0, 134.2, 128.9, 123.2, 121.9, 106.7, 100.1, 52.2, 35.6, 20.4, 17.8, 13.6; **IR** (neat): *v* = 2955, 1945, 1714, 1527, 1434, 1347, 1269, 1198, 1097, 1035 cm^{-1};

MS (70 eV, EI) m/z (%): 275 (M^+, 7.52), 246 (100); **HRMS** calcd for $C_{15}H_{17}NO_4$ [M^+]: 275.1158; found 275.1161.

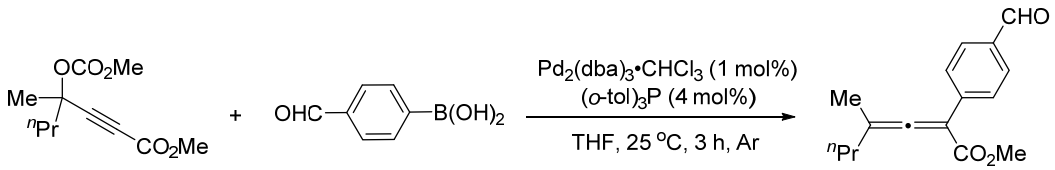
(7) Preparation of methyl 2-(3-methoxycarbonylphenyl)-4-methyl-2,3-heptadienoate (3ag) (yz-cfsy-186, yao-01-110)



1a **2g** (1.1 equiv) **3ag,** 83%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.5 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.4 mg, 0.04 mmol), **2g** (205.1 mg, 1.1 mmol), and **1a** (229.0 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ag** (239.4 mg, 83%) [eluent: petroleum ether (~200 mL) to petroleum ether/ethyl acetate = 20/1 (~300 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.14 (s, 1 H, Ar-H), 7.93 (d, 1 H, *J* = 8.0 Hz, Ar-H), 7.68 (d, J_1 = 8.0 Hz, 1 H, Ar-H), 7.40 (t, *J* = 7.8 Hz, 1 H, Ar-H), 3.91 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 2.23-2.10 (m, 2 H, CH_2), 1.89 (s, 3 H, CH_3), 1.61-1.47 (m, 2 H, CH_2), 0.94 (t, *J* = 7.6 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.7, 167.1, 167.0, 134.5, 132.8, 130.1, 129.5, 128.3, 128.1, 105.6, 101.1, 52.11, 52.05, 35.7, 20.4, 17.9, 13.6; **IR** (neat): *v* = 2953, 1945, 1714, 1602, 1583, 1435, 1288, 1257, 1194, 1170, 1108, 1037 cm^{-1}; **MS** (EI) m/z (%): 289 (M^++1, 5.41), 288 (M^+, 27.90), 169 (100); **HRMS** calcd for $C_{17}H_{20}O_4$ [M^+]: 288.1362; found 288.1367.

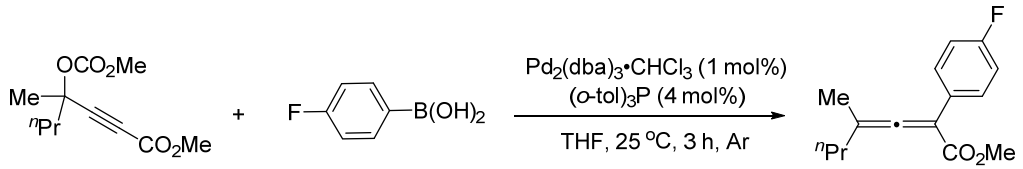
(8) Preparation of methyl 2-(4-formylphenyl)-4-methyl-2,3-heptadienoate (3ah) (yao-01-105)



1a **2h** (1.1 equiv) **3ah,** 87%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (11.0 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.6 mg, 0.04 mmol), **2h** (169.6 mg, 1.1 mmol), and **1a** (223.2 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ah** (220.7 mg, 87%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~200 mL) to petroleum ether/ethyl acetate = 100/3 (~200 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL) to petroleum ether/ethyl acetate = 50/3 (~100 mL) to petroleum ether/ethyl acetate = 25/2 (~100 mL) to petroleum ether/ethyl acetate = 8/1 (~90 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.99 (s, 1 H, CHO), 7.83 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.68 (d, *J* = 8.8 Hz, 2 H, Ar-H), 3.81 (s, 3 H, OCH_3), 2.24-2.11 (m, 2 H, CH_2), 1.91 (s, 3 H, CH_3), 1.62-1.46 (m, 2 H, CH_2), 0.94 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 210.4, 191.8, 166.7, 140,4, 134.9, 129.5, 128.7, 106.1, 101.2, 52.1, 35.6, 20.4, 17.7, 13.6; **IR** (neat): *ν* = 2956, 1943, 1714, 1699, 1602, 1569, 1434, 1381, 1277, 1196, 1180 cm^{-1}; **MS** (EI) m/z (%): 259 (M^++1, 3.97), 258 (M^+, 22.16), 128 (100); **HRMS** calcd for $C_{16}H_{18}O_3$ [M^+]: 258.1256; found 258.1253.

(9) Preparation of methyl 2-(4-fluorophenyl)-4-methyl-2,3-heptadienoate (3ai) (yao-01-104)

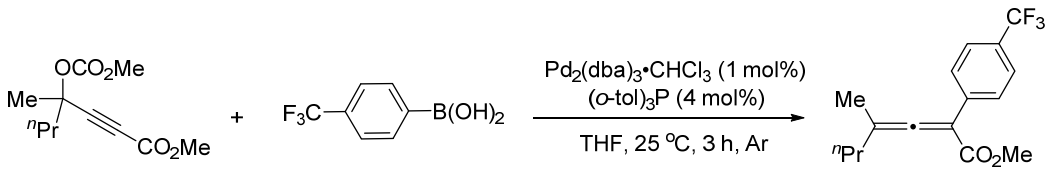


1a **2i** (1.1 equiv) **3ai,** 85%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (11.0 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.7 mg, 0.04 mmol), **2i** (154.9 mg, 1.1 mmol), and **1a**

(228.0 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ai** (210.6 mg, 85%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~100 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.48-7.42 (m, 2 H, Ar-H), 7.05-6.97 (m, 2 H, Ar-H), 3.78 (s, 3 H, OCH_3), 2.21-2.08 (m, 2 H, CH_2), 1.87 (s, 3 H, CH_3), 1.60-1.45 (m, 2 H, CH_2), 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.3, 167.3, 162.0 (d, *J* = 245.2 Hz), 130.0 (d, *J* = 8.4 Hz), 114.9 (d, *J* = 21.2 Hz), 105.2, 100.9, 52.0, 35.7, 20.5, 17.9, 13.6; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -115.7- (-115.9) (m); **IR** (neat): *v* = 2956, 1948, 1714, 1601, 1508, 1435, 1277, 1222, 1195, 1159 cm^{-1}; **MS** (70 eV, EI) m/z (%): 249 (M^++1, 5.92), 248 (M^+, 34.37), 146 (100); **HRMS** calcd for $C_{15}H_{17}O_2F$ [M^+]: 248.1213; found 248.1216.

(10) Preparation of methyl 4-methyl-2-(4-trifluoromethylphenyl)-2,3-heptadienoate (3aj) (yao-01-106)

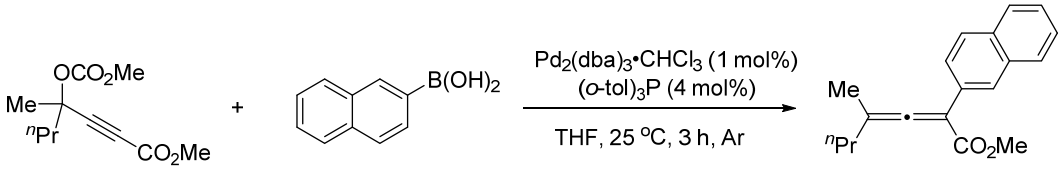


1a **2j** (1.1 equiv) **3aj,** 92%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (11.0 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.5 mg, 0.04 mmol), **2j** (214.8 mg, 1.1 mmol), and **1a** (224.3 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3aj** (269.8 mg, 92%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~100 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.57 (d, *J* = 8.4 Hz, 2 H, Ar-H), 3.80 (s, 3 H, OCH_3), 2.16 (t, *J* = 7.6 Hz, 2 H, CH_2), 1.89 (s, 3 H, CH_3), 1.61-1.47 (m, 2 H, CH_2), 0.94 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 210.1, 166.8, 137.9, 129.1 (q, *J* = 32.3 Hz), 128.5, 125.0 (q, *J* = 3.5 Hz), 124.2 (q, *J* = 270.5 Hz), 106.0, 100.9, 52.1, 35.6, 20.4, 17.8, 13.6; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -63.0; **IR** (neat): *v* = 2958, 1946, 1717,

1616, 1436, 1323, 1277, 1200, 1163, 1121, 1068, 1016 cm^{-1}; **MS** (EI) m/z (%): 299 (M^++1, 5.83), 298 (M^+, 30.37), 269 (100); **HRMS** calcd for $C_{16}H_{17}O_2F_3$ [M^+]: 298.1181; found 298.1188.

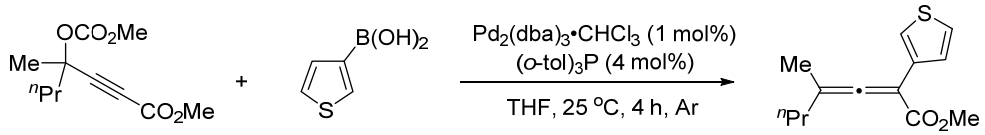
(11) Preparation of methyl 4-methyl-2-(2-naphthyl))-2,3-heptadienoate (3ak) (yao-01-103)



1a **2k** (1.1 equiv) **3ak,** 81%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (11.2 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.6 mg, 0.04 mmol), **2k** (195.6 mg, 1.1 mmol), and **1a** (222.7 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ak** (234.6 mg, 81%, purity = 94%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~100 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.05 (s, 1 H, Ar-H), 7.85-7.75 (m, 3 H, Ar-H), 7.52 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 1 H, Ar-H), 7.48-7.40 (m, 2 H, Ar-H), 3.83 (s, 3 H, OCH_3), 2.25-2.11 (m, 2 H, CH_2), 1.91 (s, 3 H, CH_3), 1.63-1.49 (m, 2 H, CH_2), 0.95 (t, J = 7.2 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.8, 167.4, 133.3, 132.5, 131.2, 128.2, 127.5, 127.4, 127.1, 126.4, 125.9, 125.8, 105.3, 101.9, 52.0, 35.7, 20.5, 18.0, 13.7; **IR** (neat): ν = 2953, 1943, 1713, 1598, 1504, 1434, 1367, 1240, 1164, 1124, 1031 cm^{-1}; **MS** (70 eV, EI) m/z (%): 281 (M^++1, 20.60), 280 (M^+, 95.38), 178 (100); **HRMS** calcd for $C_{19}H_{20}O_2$ [M^+]: 280.1463; found 280.1467.

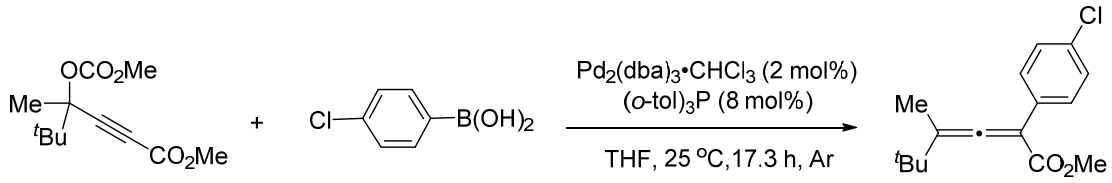
(12) Preparation of methyl 4-methyl-2-(2-thienyl)-2,3-heptadienoate (3al) (yao-01-107)



1a **2l** (1.1 equiv) **3al,** 84%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.9 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (13.0 mg, 0.04 mmol), **2l** (144.6 mg, 1.1 mmol), and **1a** (223.0 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3al** (193.5 mg, 84%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~100 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 (dd, J_1 = 3.2 Hz, J_2 = 1.2 Hz, 1 H, Ar-H), 7.22 (dd, J_1 = 5.0 Hz, J_2 = 3.0 Hz, 1 H, Ar-H), 7.11 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1 H, Ar-H), 3.78 (s, 3 H, OCH_3), 2.14 (t, J = 7.4 Hz, 2 H, CH_2), 1.86 (s, 3 H, CH_3), 1.60-1.47 (m, 2 H, CH_2), 0.94 (t, J = 7.2 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.0, 167.2, 133.6, 127.6, 124.5, 122.4, 105.3, 97.6, 52.0, 35.8, 20.5, 17.9, 13.7; **IR** (neat): ν = 2954, 1944, 1714, 1434, 1378, 1269, 1214, 1147, 1180, 1097, 1036 cm^{-1}; **MS** (70 eV, EI) m/z (%): 237 (M^++1, 8.16), 236 (M^+, 52.10), 149 (100); **HRMS** calcd for $C_{13}H_{16}O_2S$ [M^+]: 236.0871; found 236.0870.

(13) Preparation of methyl 2-(4-chlorophenyl)-4,5,5-trimethyl-2,3-hexadienoate (3cm) (yao-01-127)

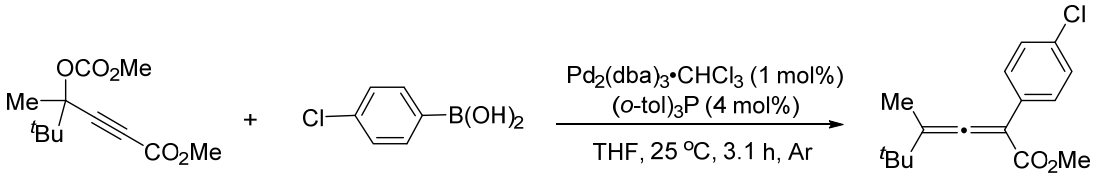


1c **2m** (1.5 equiv) **3cm,** 92%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (20.5 mg, 0.02 mmol), tris(*o*-tolyl)phosphine (24.6 mg, 0.08 mmol), **2m** (240.0 mg, 1.5 mmol), and **1c** (240.3 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3cm** (263.3 mg, 92%, purity = 97%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ

= 7.45 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.29 (d, *J* = 8.8 Hz, 2 H, Ar-H), 3.78 (s, 3 H, OCH_3), 1.87 (s, 3 H, CH_3), 1.15 (s, 9 H, ^{t}Bu); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 208.7, 167.3, 132.8, 132.5, 129.3, 128.3, 114.4, 101.0, 52.1, 34.8, 28.7, 14.0; **IR** (neat): *v* = 2963, 1940, 1716, 1491, 1434, 1361, 1275, 1194, 1170, 1091, 1037, 1012 cm^{-1}; **MS** (70 eV, EI) m/z (%): 281 (M^+ (^{37}Cl) +1, 1.67), 280 (M^+(^{37}Cl), 9.09), 279 (M^+ (^{35}Cl) +1, 4.62), 278 (M^+(^{35}Cl), 27.92), 222 (100); **HRMS** calcd for $C_{16}H_{19}{}^{35}ClO_2$ [M^+]: 278.1074; found 278.1069.

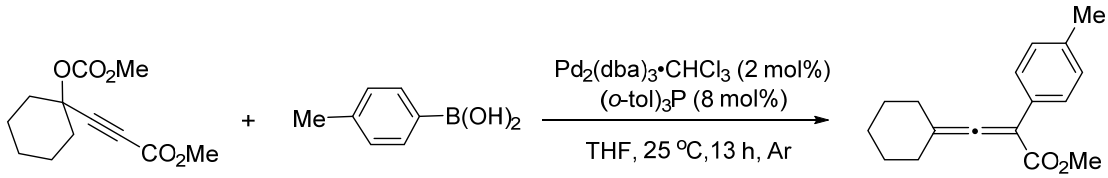
The reaction of 1c with 2m under the standard conditions (yy-01-048)



1c (1.0 mmol) **2m** (1.1 equiv) **3cm,** 52% NMR yield
52% recovery of **1c**

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.6 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.5 mg, 0.04 mmol), **2m** (178.5 mg, 1.1 mmol), and **1c** (246.7 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded a crude product. 52% NMR yield of **3cm** and 52% recovered of **1c** were determined by the NMR spectrum of the crude product with CH_2Br_2 (17.5 μL) as the internal standard.

(14) Preparation of methyl 4,4-pentamethylane-2-(4-methylphenyl)-2,3-butadienoate (3dn) (yao-01-123)

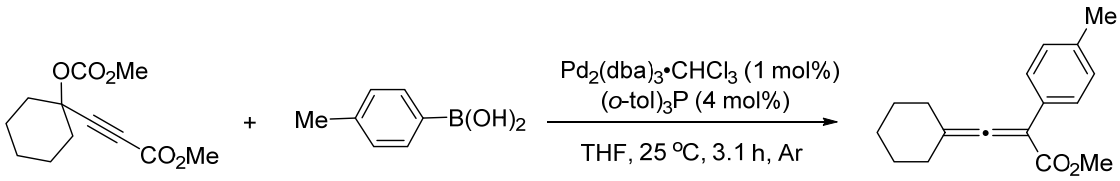


1d **2n** (1.5 equiv) **3dn,** 93%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (20.5 mg, 0.02 mmol), tris(*o*-tolyl)phosphine (24.8 mg, 0.08 mmol), **2n** (205.3 mg, 1.5 mmol), and **1d** (237.1 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3dn** (236.4 mg, 93%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1

(~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.14 (d, *J* = 7.6 Hz, 2 H, Ar-H), 3.78 (s, 3 H, OCH_3), 2.40-2.25 (m, 7 H, 2 x CH_2 and CH_3), 1.80-1.54 (m, 6 H, 3 x CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.3, 167.5, 136.8, 131.2, 128.8, 128.3, 107.2, 100.3, 52.0, 30.4, 27.1, 25.8, 21.1; **IR** (neat): *v* = 2926, 2852, 1947, 1714, 1511, 1433, 1274, 1222, 1162, 1089, 1032, 1017 cm^{-1}; **MS** (70 eV, EI) m/z (%): 257 (M^++1, 19.12), 256 (M^+, 100); **HRMS** calcd for $C_{17}H_{20}O_2$ [M^+]: 256.1463; found 256.1457.

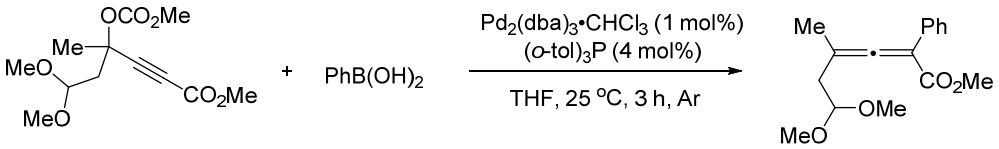
The reaction of 1d with 2n under the standard conditions (yy-01-049)



1d (1.0 mmol) **2n** (1.1 equiv) **3dn,** 89% NMR yield 16% recovery of **1d**

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (10.3 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.4 mg, 0.04 mmol), **2n** (150.3 mg, 1.1 mmol), and **1d** (238.0 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded a crude product. 89% NMR yield of **3dn** and 16% recovered of **1d** were determined by the NMR spectrum of the crude product with CH_2Br_2 (17.5 μL) as the internal standard.

(15) Preparation of methyl 6,6-dimethoxy-4-methyl-2-phenyl-2,3-hexadienoate (3ea) (yao-01-072)

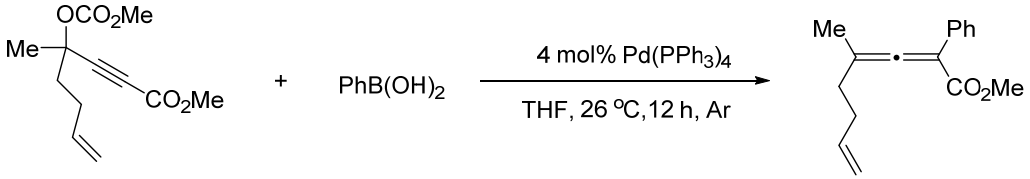


1e **2a** (1.1 equiv) **3ea,** 88%

Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (11.4 mg, 0.01 mmol), tris(*o*-tolyl)phosphine (12.4 mg, 0.04 mmol), **2a** (135.8 mg, 1.1 mmol), and **1e** (272.1 mg, 1.0 mmol) in freshly distilled THF (2.0 mL) afforded **3ea** (240.3 mg, 88%) [eluent: petroleum ether/ethyl acetate = 25/1 (~100 mL) to petroleum ether/ethyl

acetate = 20/1 (~100 mL) to petroleum ether/ethyl acetate = 25/2 (~100 mL) to petroleum ether/ethyl acetate = 25/3 (~100 mL) to petroleum ether/ethyl acetate = 10/1 (~200 mL) to petroleum ether/ethyl acetate = 5/1 (~100 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.56-7.48 (m, 2 H, Ar-H), 7.37-7.29 (m, 2 H, Ar-H), 7.28-7.21 (m, 1 H, Ar-H), 4.56 (t, *J* = 5.6 Hz, 1 H, CH), 3.80 (s, 3 H, OCH_3), 3.31 (s, 3 H, OCH_3), 3.27 (s, 3 H, OCH_3), 2.47 (d, *J* = 5.6 Hz, 2 H, CH_2), 1.92 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.9, 167.0, 133.4, 128.2, 128.1, 127.2, 102.7, 101.8, 100.8, 52.9, 52.8, 52.1, 36.9, 18.6; **IR** (neat): *v* = 2949, 2831, 1952, 1715, 1493, 1434, 1367, 1272, 1196, 1119, 1053, 1020 cm^{-1}; **MS** (ESI) m/z: 299 ($M+Na^+$), 277 ($M+H^+$), 245 $(M-OMe)^+$; **HRMS** calcd for $C_{16}H_{20}O_4$ [M^+]: 276.1362; found 276.1364.

(16) Preparation of methyl 4-methyl-2-phenyl-2,3,7-octatrienoate (3fa) (yao-01-117)

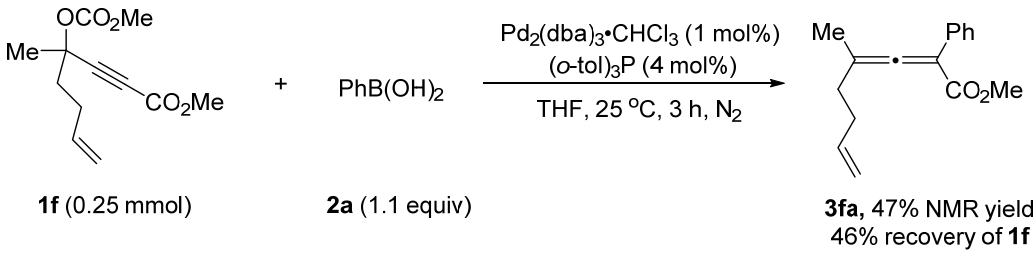


1f **2a** (1.1 equiv) **3fa,** 66%

To an oven-dried Schlenk tube were added **2a** (135.9 mg, 1.1 mmol), which was then transferred to a glovebox. After adding $Pd(PPh_3)_4$ (48.4 mg, 0.04 mmol) in glovebox, it was transferred out of the glovebox. After replacing nitrogen with argon for three times at rt by vaccum, **1f** (235.5 mg, 1.0 mmol) and freshly distilled THF (2.0 mL) were added. The resulting mixture was stirred for 12 h at 26 ^{o}C as monitored by TLC and filtered through a short pad of silica gel with ethyl acetate (15 mL x 3) as the eluent. After removal of the solvent under vacuum, the residue was purified by flash column chromatography on silica gel to afford **3fa** (156.0 mg, 66%) [eluent: petroleum ether (~100 mL) to petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 100/3 (~100 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.32 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.27-7.20 (m, 1 H, Ar-H), 5.90-5.75 (m, 1 H,

CH=), 5.02 (d, J = 17.2 Hz, 1 H, one proton of =CH_2), 4.95 (d, J = 10.8 Hz, 1 H, one proton of =CH_2), 3.78 (s, 3 H, OCH_3), 2.32-2.19 (m, 4 H, 2 x CH_2), 1.89 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.2, 167.2, 137.6, 133.8, 128.3, 128.1, 127.2, 115.1, 104.7, 102.3, 52.0, 33.0, 31.4, 18.1; **IR** (neat): ν = 2948, 1949, 1715, 1640, 1599, 1493, 1434, 1273, 1196, 1176, 1040 cm^{-1}; **MS** (70 eV, EI) m/z (%): 243 (M^++1, 1.73), 242 (M^+, 9.22), 141 (100); **HRMS** calcd for $C_{16}H_{18}O_2$ [M^+]: 242.1307; found 242.1310.

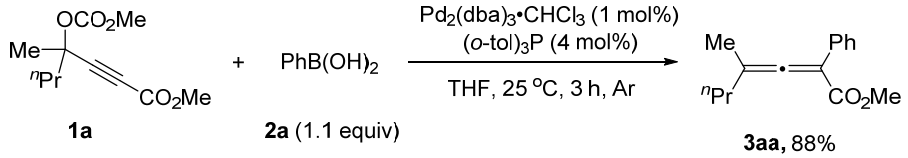
The reaction of 1f with 2a under the standard conditions (yao-01-112)



To an oven-dried vial were added **2a** (33.8 mg, 0.275 mmol), $Pd_2(dba)_3$·$CHCl_3$ (2.4 mg, 0.025 mmol), tris(*o*-tolyl)phosphine (2.9 mg, 0.01 mmol), which was then transferred to a glovebox. After adding **1f** (59.1 mg, 0.25 mmol) and freshly distilled THF (0.5 mL) in glovebox, it was transferred out of the glovebox. The resulting mixture was stirred for 3 h at 25 °C, then filtered through a short pad of silica gel with ethyl acetate (4 mL) as the eluent afforded a crude product. 47% NMR yield of **3fa** and 46% recovered of **1f** were determined by the NMR spectrum of the crude product with CH_2Br_2 (17.5 μL) as the internal standard.

4. Gram-scale reactions

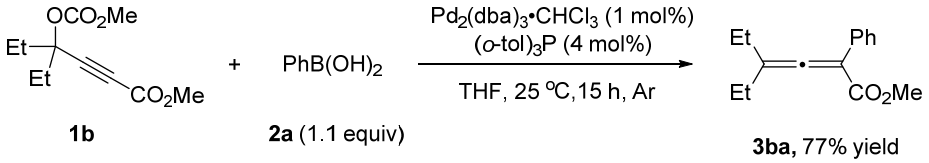
(1) Gram-scale preparation of methyl 2-phenyl-4-methyl-2,3-heptadienoate (3aa) (yao-01-132)



Following **Typical Procedure III**, the reaction of $Pd_2(dba)_3$·$CHCl_3$ (0.0625 g, 0.06 mmol), tris(*o*-tolyl)phosphine (0.0738 g, 0.24 mmol), **2a** (0.8062 g, 6.6 mmol),

and **1a** (1.3664 g, 6.0 mmol) in freshly distilled THF (12.0 mL) afforded **3aa** (1.2187 g, 88%) [eluent: petroleum ether (~200 mL) to petroleum ether/ethyl acetate = 50/1 (~200 mL) to petroleum ether/ethyl acetate = 100/3 (~200 mL) to petroleum ether/ethyl acetate = 25/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.52-7.43 (m, 2 H, Ar-H), 7.37-7.29 (m, 2 H, Ar-H), 7.29-7.22 (m, 1 H, Ar-H), 3.79 (s, 3 H, OCH_3,), 2.21-2.07 (m, 2 H, CH_2), 1.87 (s, 3 H, CH_3), 1.61-1.48 (m, 2 H, CH_2), 0.94 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 209.4, 167.3, 133.9, 128.3, 128.0, 127.1, 105.0, 101.7, 52.0, 35.6, 20.4, 17.9, 13.6.

(2) Gram-scale preparation of methyl 2-phenyl-4-methyl-2,3-heptadienoate (3ba) (yao-01-145)



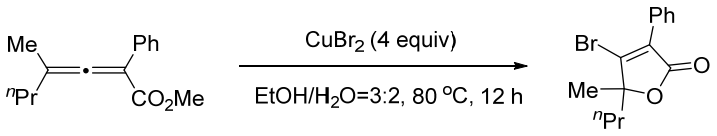
1b **2a** (1.1 equiv) **3ba,** 77% yield

Following **Typical Procedure III**, The reaction of $Pd_2(dba)_3$·$CHCl_3$ (0.0622 g, 0.06 mmol), tris(*o*-tolyl)phosphine (0.0737 g, 0.24 mmol), **2a** (0.8240 g, 6.6 mmol), and **1b** (1.3628 g, 6.0 mmol) in freshly distilled THF (12.0 mL) afforded **3ba** (1.0590 g, 77%) as an oil [eluent: petroleum ether (~200 mL) to petroleum ether/ethyl acetate = 60/1 (~240 mL) to petroleum ether/ethyl acetate = 50/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.54-7.47 (m, 2 H, Ar-H), 7.36-7.28 (m, 2 H, Ar-H), 7.27-7.21 (m, 1 H, Ar-H), 3.78 (s, 3 H, OCH_3), 2.18 (q, *J* = 7.3 Hz, 4 H, 2 x CH_2), 1.09 (t, *J* = 7.4 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 208.7, 167.5, 134.1, 128.10, 128.08, 127.1, 113.7, 104.4, 52.0, 25.6, 12.0; **IR** (neat): *ν* = 2967, 1945, 1714, 1599, 1493, 1434, 1273, 1194, 1174, 1084, 1040, 1022 cm^{-1}; **MS** (70 eV, EI) m/z (%): 231 (M^++1, 10.89), 230 (M^+, 66.27), 115 (100); **HRMS** calcd for $C_{15}H_{18}O_2$ [M^+]: 230.1307; found 230.1308.

5. Synthetic applications

(1) Preparation of 4-bromo-5-methyl-3-phenyl-5-propylfuran-2(*5H*)-one[4] (4)

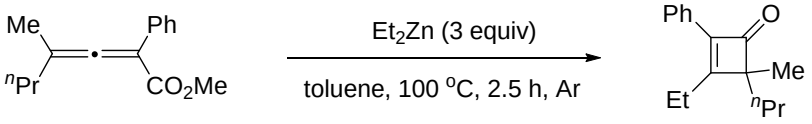
(yao-01-140)



3aa **4,** 76%

To a Schlenk tube were added $CuBr_2$ (451.2 mg, 2.0 mmol), **3aa** (114.0 mg, 0.5 mmol), EtOH (3.0 mL), and H_2O (2.0 mL) sequentially. Then the Schlenk tube was placed in an oil bath pre-heated at 80 °C with stirring for 12 h. To the mixture was added H_2O (5.0 mL). After extraction with ethyl acetate (5 mL x 3), the organic layer was then washed with brine (10 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by column chromatography on silica gel to afford **4** (113.8 mg, 76%, purity = 98%) [eluent: petroleum ether (~100 mL) to petroleum ether /dichloromethane/ethyl ether = 100/1/1 (~200 mL) to petroleum ether /dichloromethane/ethyl ether = 80/1/1 (~400 mL) to petroleum ether /dichloromethane/ethyl ether = 50/1/1 (~200 mL)]: solid; **m.p.** 79.6-80.6 °C (petroleum ether/CH_2Cl_2); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.75 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2 H, Ar-H), 7.50-7.39 (m, 3 H, Ar-H), 1.99-1.89 (m, 1 H, one proton of CH_2), 1.89-1.79 (m, 1 H, one proton of CH_2), 1.60 (s, 3 H, CH_3), 1.41-1.29 (m, 1 H, one proton of CH_2), 1.29-1.15 (m, 1 H, one proton of CH_2), 0.94 (t, 3 H, J = 7.4 Hz, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 169.1, 148.7, 129.4, 128.7, 128.5, 128.4, 88.5, 39.3, 24.3, 16.2, 13.8; **IR** (neat): ν = 3053, 2961, 2928, 2870, 1738, 1644, 1597, 1493, 1445, 1376, 1296, 1154, 1134, 1027, 1004 cm^{-1}; **MS** (70 eV, EI) m/z (%): 296 (M^+(^{81}Br), 10.20), 294 (M^+(^{79}Br), 9.93), 43 (100); Anal. Calcd. for $C_{14}H_{15}BrO_2$: C 56.97, H 5.12; found C 56.82, H 5.16.

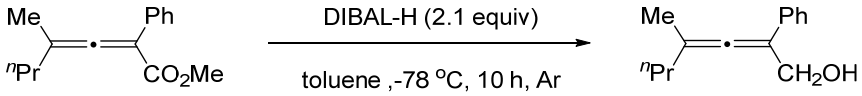
(2) Preparation of 3-ethyl-4-methyl-2-phenyl-4-propylcyclobut-2-enone[5] (5) (yao-01-142)



3aa **5,** 76%

To an oven-dried Schlenk tube were added **3aa** (114.0 mg, 0.5 mmol) and toluene (5.0 mL) under an argon atmosphere at room temperature. A solution of Et_2Zn in toluene (1.0 mL, 1.5 M, 1.5 mmol, 3 equiv) was added with a syringe dropwise within 2 min at rt and the tube was then submerged in an oil bath preheated to 100 °C. After being stirred for 2.5 h, the reaction mixture was quenched by dropwise addition of a saturated aqueous solution of NH_4Cl (10 mL) at 0 °C. After warming up to room temperature, H_2O (50 mL) was added and the resulting mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layer was washed sequentially with diluted HCl (5%, aq.), a saturated aqueous solution of $NaHCO_3$, and brine, and dried over anhydrous Na_2SO_4, After filtration and concentration under reduced pressure, the crude product was purified by column chromatography on silica gel to afford **5** (85.8 mg, 76%) [eluent: petroleum ether/ethyl ether = 100/1 (~100 mL) to petroleum ether/ethyl acetate = 60/1 (~200 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.68-7.61 (m, 2 H, Ar-H), 7.38 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.32-7.25 (m, 1 H, Ar-H), 2.92-2.71 (m, 2 H, CH_2), 1.75-1.65 (m, 1 H, one proton of CH_2), 1.62-1.51 (m, 1 H, one proton of CH_2), 1.40-1.25 (m, 8 H, 2 x CH_3 and CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 196.8, 180.8, 140.4, 130.2, 128.6, 128.1, 127.2, 67.0, 37.0, 21.8, 20.2, 19.3, 14.5, 11.4; **IR** (neat): *ν* = 2957, 2872, 1748, 1628, 1596, 1493, 1447, 1088, 1066 cm^{-1}; **MS** (70 eV, EI) m/z (%): 229 (M^++1, 2.62), 228 (M^+, 14.48), 199 (100); **HRMS** calcd for $C_{16}H_{20}O$ [M^+]: 228.1514; found 228.1517.

(3) Preparation of 4-methyl-2-phenyl-2,3-heptadien-1-ol (6) (yao-01-136)

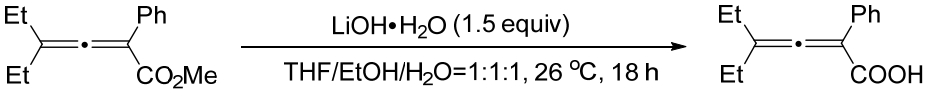


3aa **6,** 51%

To an oven-dried Schlenk tube were added **3aa** (115.3 mg, 0.5 mmol) and toluene (5.0 mL) under a argon atmosphere at room temperature, The solution was cooled to -78 ℃ and then DIBAL-H (1.0 M in hexane, 1.05 mL, 1.05 mmol) was added with a syringe dropwise at -78 °C. After stirring at -78 °C for 10 hours, the reaction was

quenched with MeOH (5 mL) and the resulting mixture was warmed up to room temperature. Then H_2O (10 mL) and 1 N HCl (10 mL) were added sequentially. After extraction with ethyl ether (10 mL x 3), the combined organic layer was washed with brine (10 mL) and dried over anhydrous Na_2SO_4. After filtration and concentration under reduced pressure, the crude product was purified by column chromatography on silica gel to afford **6** (55.3 mg, 51%, purity = 93%) [eluent: petroleum ether/ethyl acetate = 50/1 (~100 mL) to petroleum ether/ethyl acetate = 30/1 (~100 mL) to petroleum ether/ethyl acetate = 20/1 (~300 mL)]: oil; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.32 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.20 (t, *J* = 7.4 Hz, 1 H, Ar-H), 4.51 (s, 2 H, CH_2O), 2.17-2.01 (m, 2 H, CH_2), 1.84 (s, 3 H, CH_3), 1.66 (brs, 1 H, OH), 1.55-1.44 (m, 2 H, CH_2 of ^{n}Pr), 0.94 (t, *J* = 7.4 Hz, 3 H, CH_3 of ^{n}Pr); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 199.3, 135.6, 128.4, 126.7, 125.9, 106.6, 105.9, 61.6, 36.4, 20.9, 18.9, 13.9; **IR** (neat): *v* = 3357, 2957, 2930, 2871, 1948, 1598, 1494, 1456, 1397, 1368, 1057, 1025 cm^{-1}; **MS** (70 eV, EI) m/z (%): 203 (M^++1, 2.09), 202 (M^+, 13.02), 129 (100); **HRMS** calcd for $C_{14}H_{18}O$ [M^+]: 202.1358; found 202.1357.

(4) Preparation of 4-ethyl-2-phenyl-2,3-hexadienoic acid (7) [6] **(yao-01-149)**



3ba **7,** 70%

To a Schlenk tube were added **3ba** (114.0 mg, 0.5 mmol), THF (1.0 mL), LiOH•H_2O (32.4 mg, 0.75 mmol, 1.5 equiv.), EtOH (1.0 mL), and H_2O (1.0 mL) sequentially. The reaction mixture was stirred for 18 h at 26 ^{o}C. Then 2 M HCl solution (aqueous, 5 mL) and H_2O (10 mL) were added sequentially and the resulting mixture was extracted with ethyl acetate (10 mL x 3). Then the combined organic layer was washed with brine and dried over Na_2SO_4. After filtration and evaporation of the solvent, the crude product was purified by column chromatography on silica gel to afford **7** (75.0 mg, 70%) [eluent: petroleum ether/ ethyl acetate = 10/1 (~200 mL) to petroleum ether/ethyl acetate = 20/3 (~220 mL) to petroleum ether/ethyl acetate = 5/1 (~120 mL) to petroleum ether/ethyl acetate = 3/1 (~120 mL)]: solid; **m.p.** 86.7-87.9

^{o}C (petroleum ether/ethyl ether); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 11.6 (brs, 1 H, COOH), 7.52 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.33 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.30-7.25 (m, 1 H, Ar-H), 2.20 (q, *J* = 7.3 Hz, 4 H, 2 x CH_2), 1.12 (t, *J* = 7.2 Hz, 6 H, 2 x CH_3); **^{1}H NMR** (400 MHz, DMSO-d_6): δ = 12.5 (brs, 1 H, COOH), 7.43 (d, *J* = 6.8 Hz, 2 H, Ar-H), 7.33 (t, *J* = 6.6 Hz, 2 H, Ar-H), 7.20-7.28 (m, 1 H, Ar-H), 2.15 (d, *J* = 6.4 Hz, 4 H, 2 x CH_2), 1.01 (t, *J* = 6.6 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 210.4, 173.0, 133.6, 128.4, 128.1, 127.3, 114.1, 104.1, 25.6, 12.0; **IR** (neat): *ν* = 3400-2250, 1934, 1670, 1493, 1451, 1401, 1321, 1280, 1196, 1185 cm^{-1}; **MS** (70 eV, EI) m/z (%): 217 (M^++1, 14.22), 216 (M^+, 89.40), 201 (100); Anal. Calcd. for $C_{14}H_{16}O_2$: C 77.75, H 7.46; found C 77.45, H 7.36.

6. Evaluation of Biological Activity

(1) Cytotoxicity test

Human lung cancer A549 cells were purchased from ATCC (Manassas, VA) and cultured in RPMI 1640 containing 10% FBS, 100 U/mL penicillin, and 100 mg/mL streptomycin. Cells were seeded in 96-well plates at a density of 2000 cells/well. On the next day, the cells were treated with different concentrations of compounds for 72 h and the sulforhodamine B (SRB) assay was used to measure the cell mass as previously described.[7]

(2) Secretion of GLP-1 by STC-1 cells

STC-1 cells were kindly provided by Dr. Jia Li (Shanghai Institute of Materia Medica, Chinese Academy of Sciences) and cultured in DMEM containing 15% FBS, 100 U/mL penicillin, and 100 mg/mL streptomycin. STC-1 cells were seeded in 96-well plates at a density of 40000 cells/well and cultured overnight. After the cells were treated with 0.1% DPP-IV inhibitor PK44 in KRB buffer supplemented with 0.2% fatty acid-free BSA for 2 h, vehicle control (DMSO), positive control (1 μM PMA) or compounds at different concentrations were added and cells were further incubated for another 2 h. Then the level of GLP-1 in supernatant of the culture

medium was measured with active GLP-1 kits according to the manufacturer's instructions (Cisbio, Bedford, MA).

References

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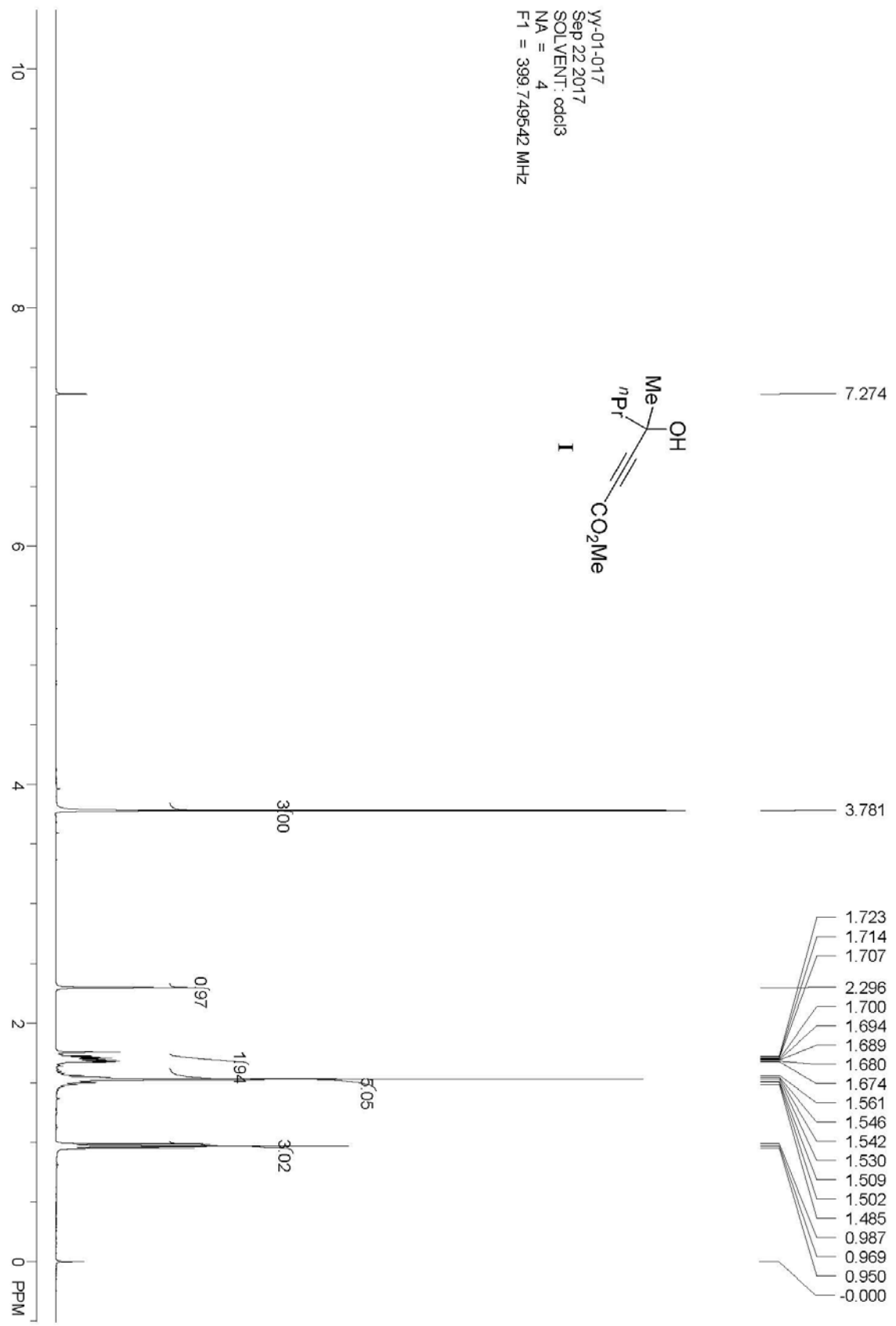
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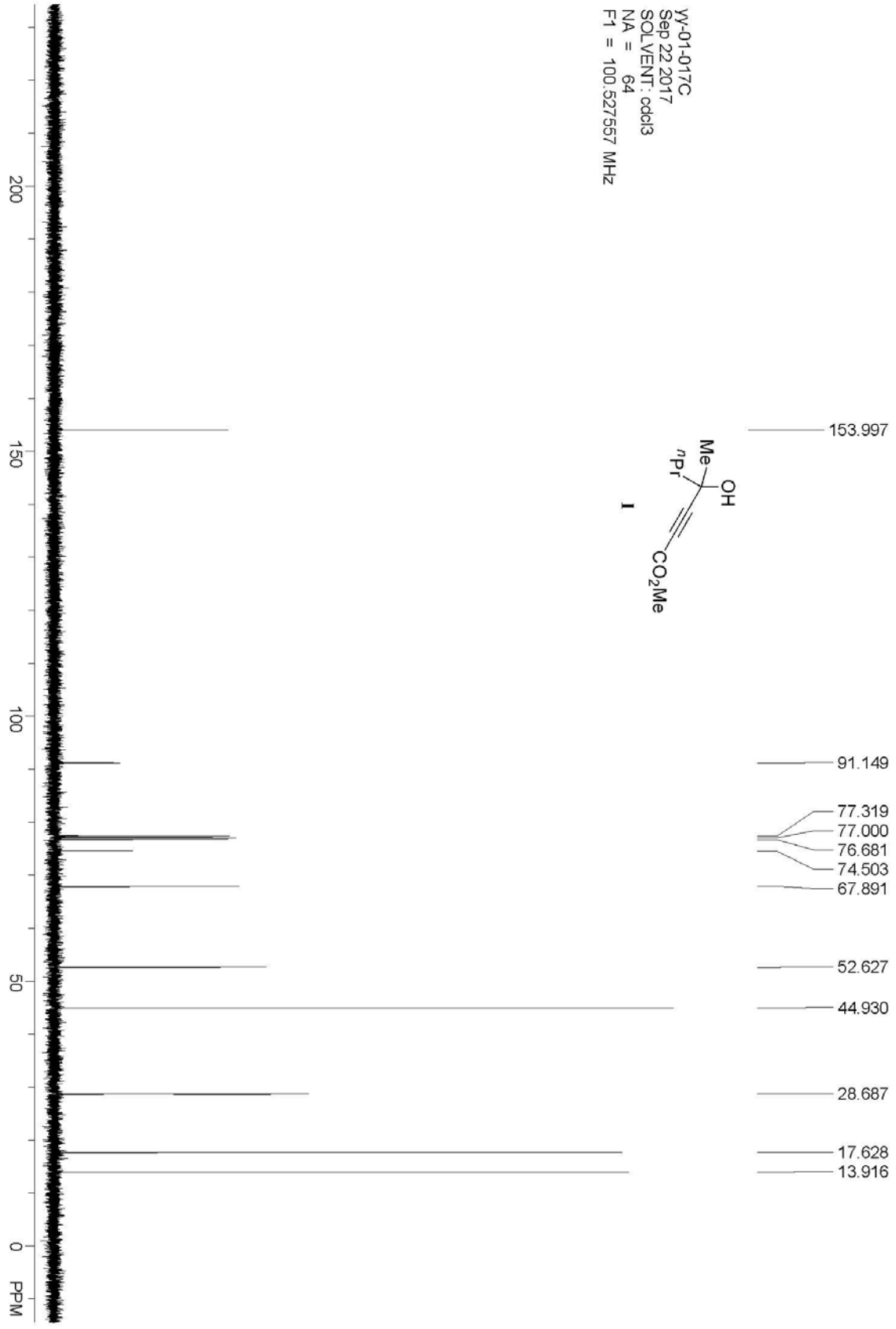
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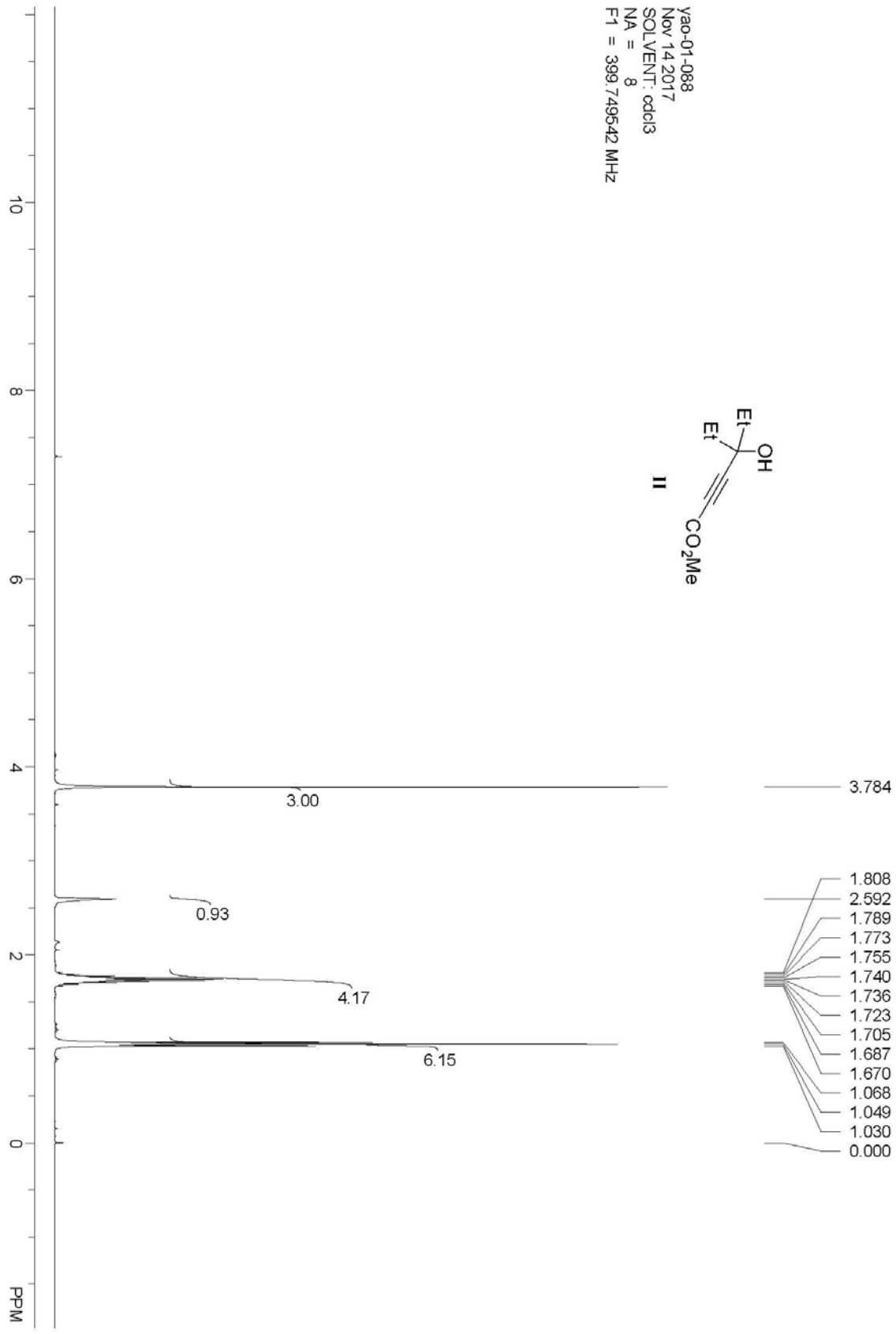
PPM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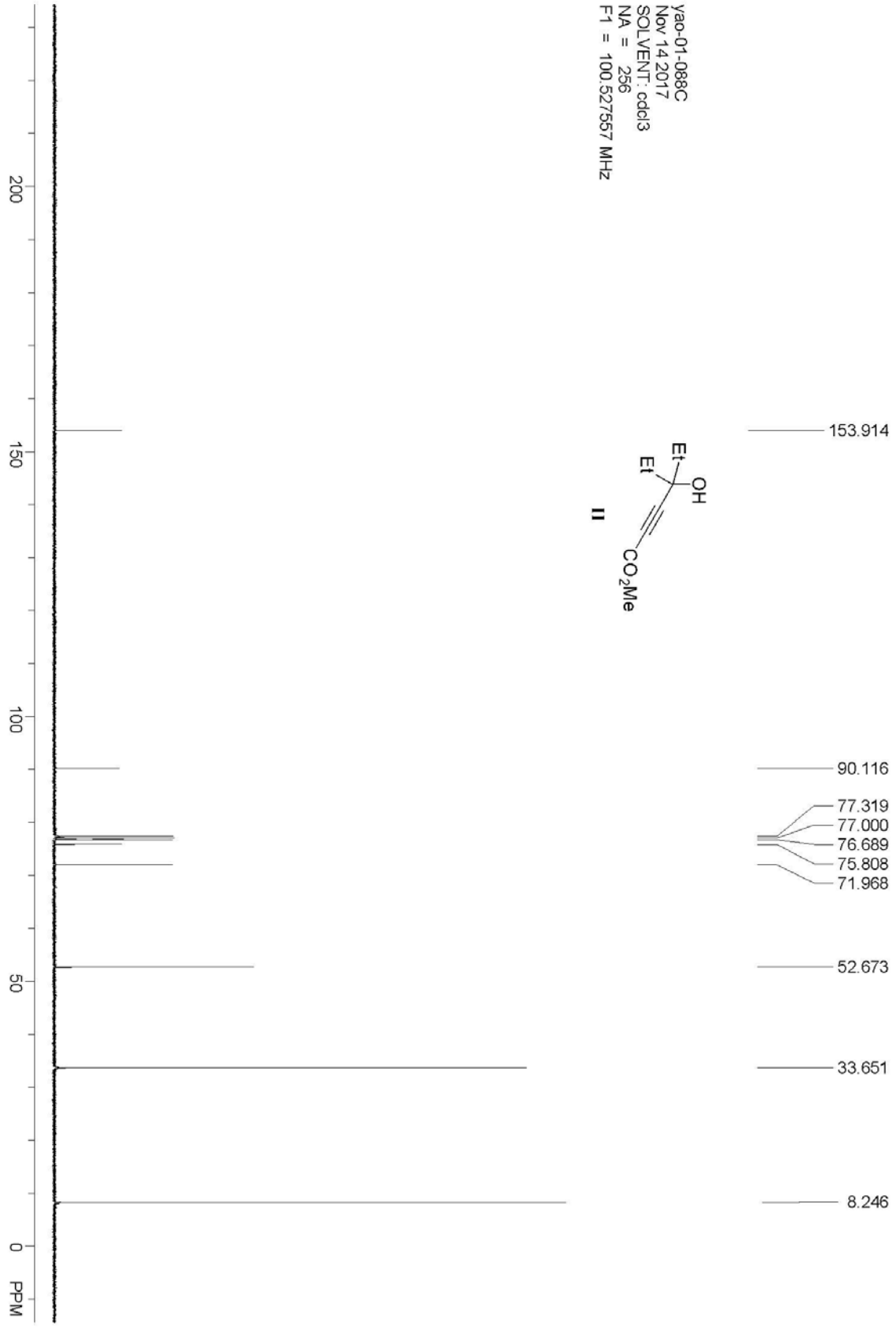
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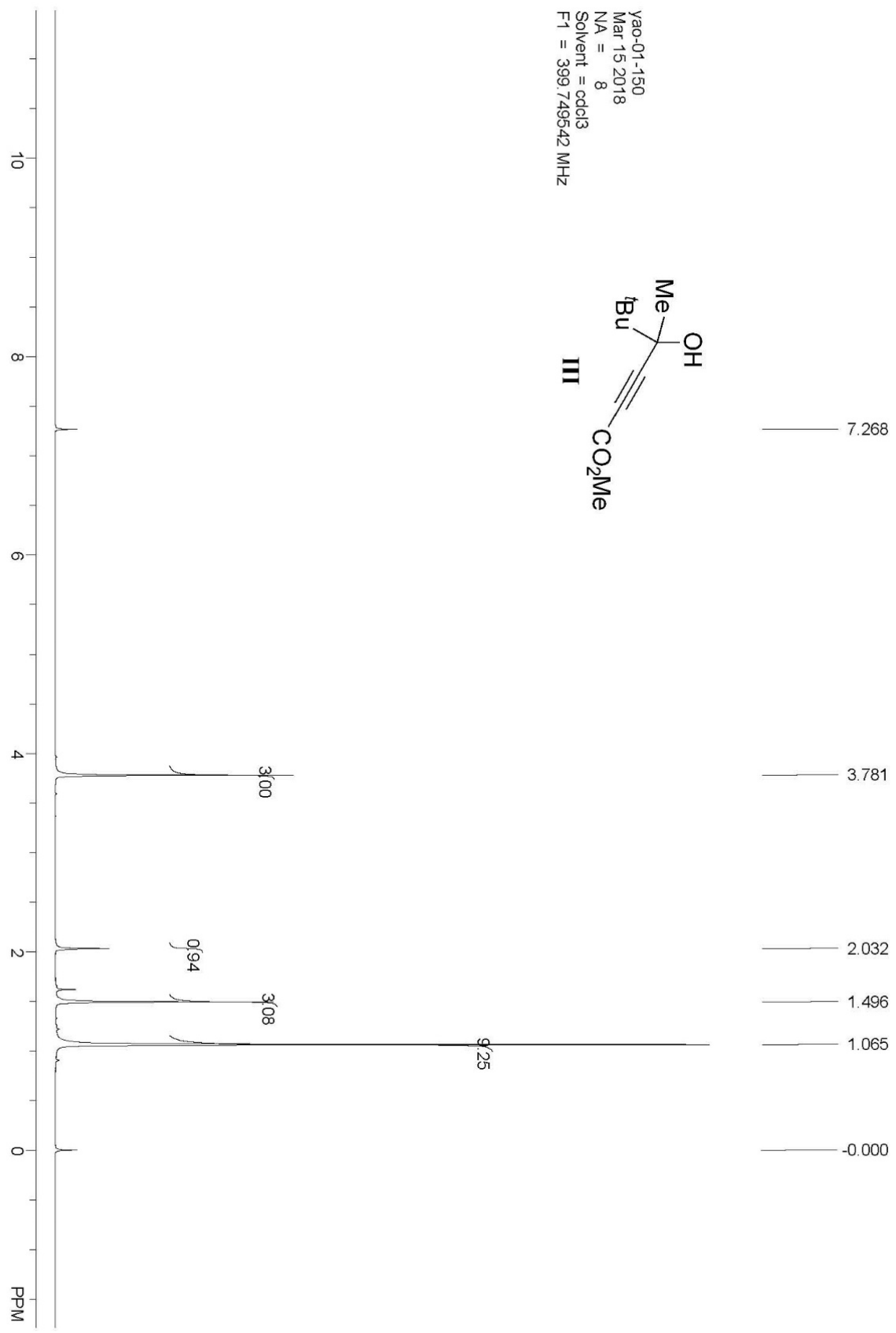
PPM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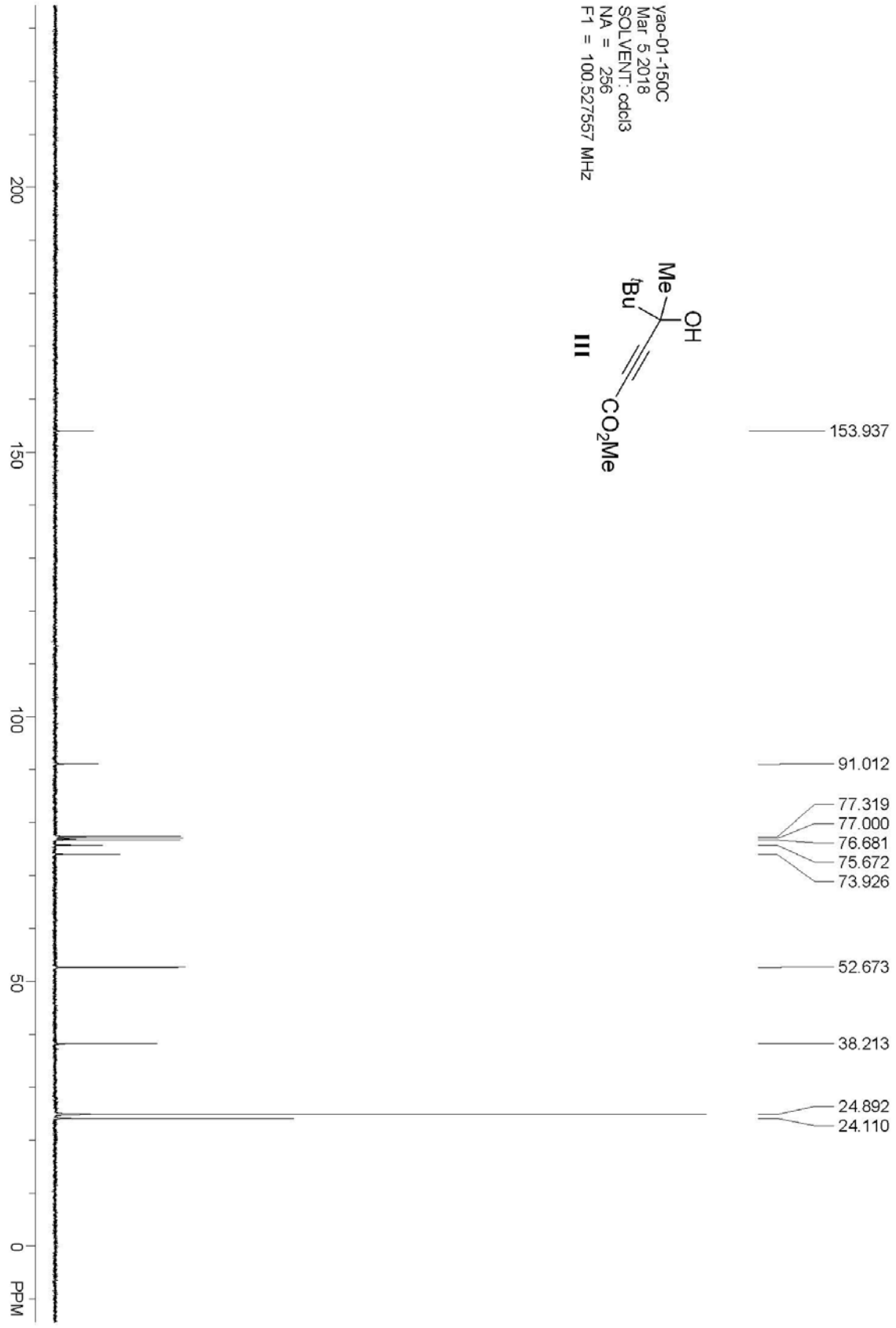
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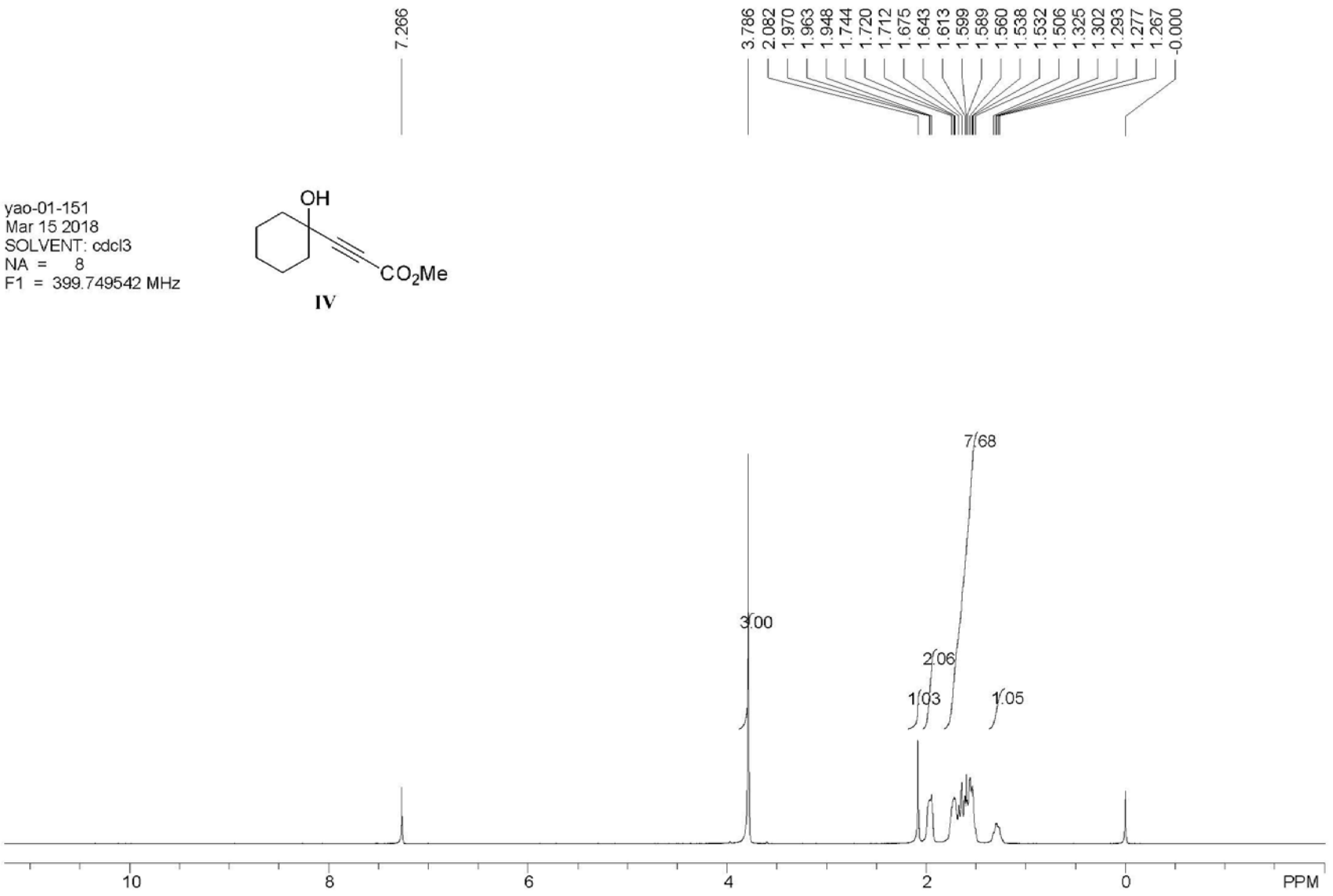
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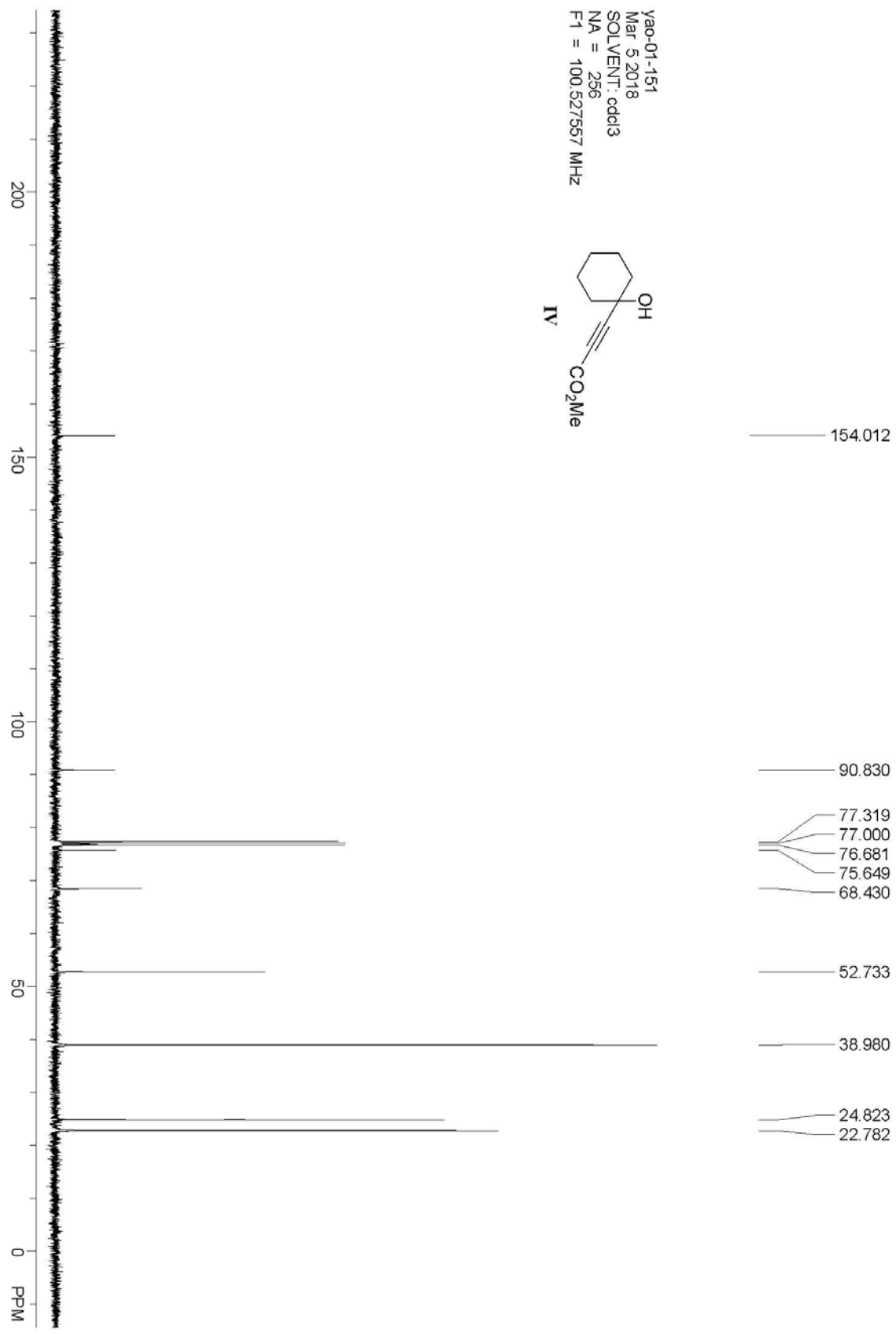
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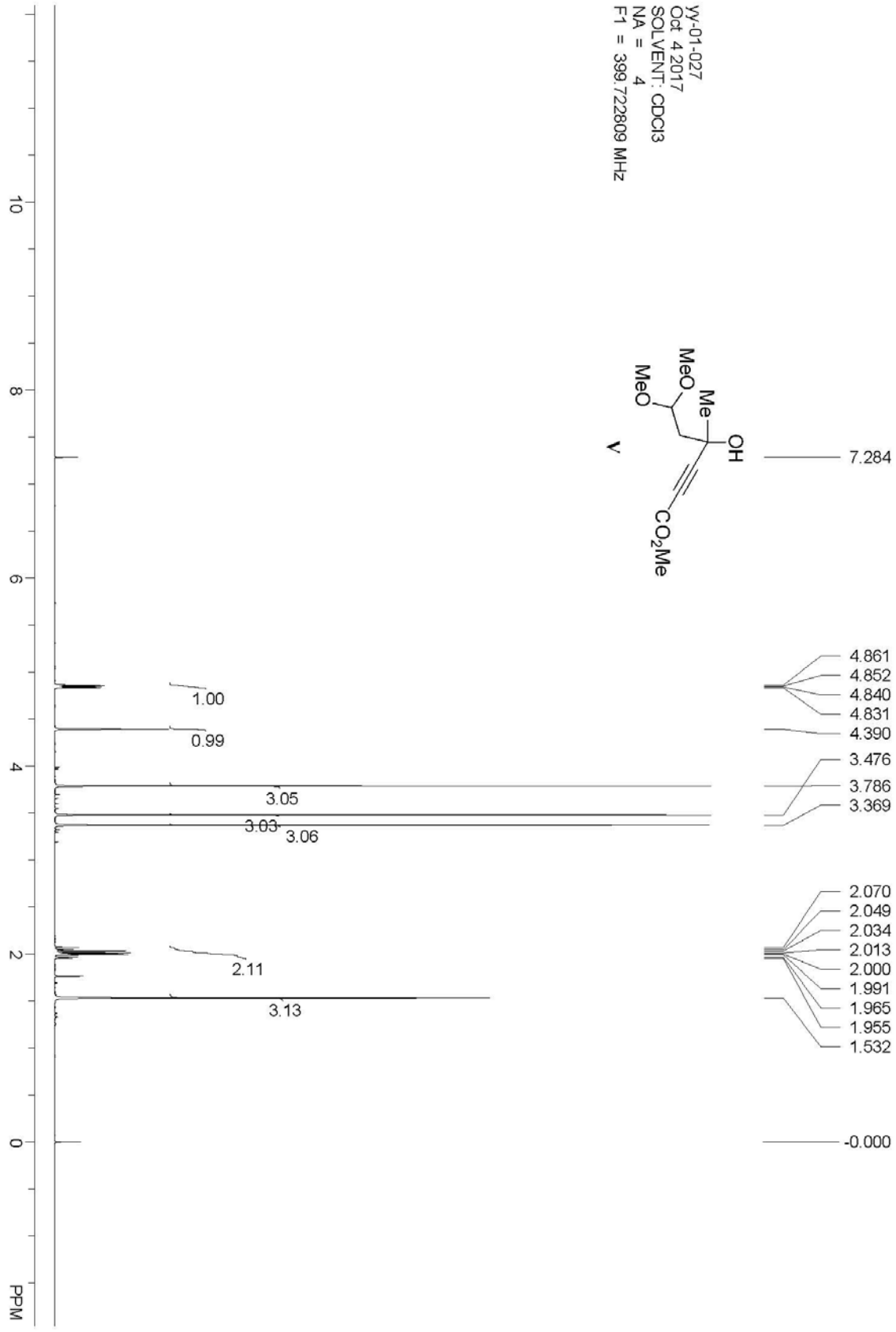
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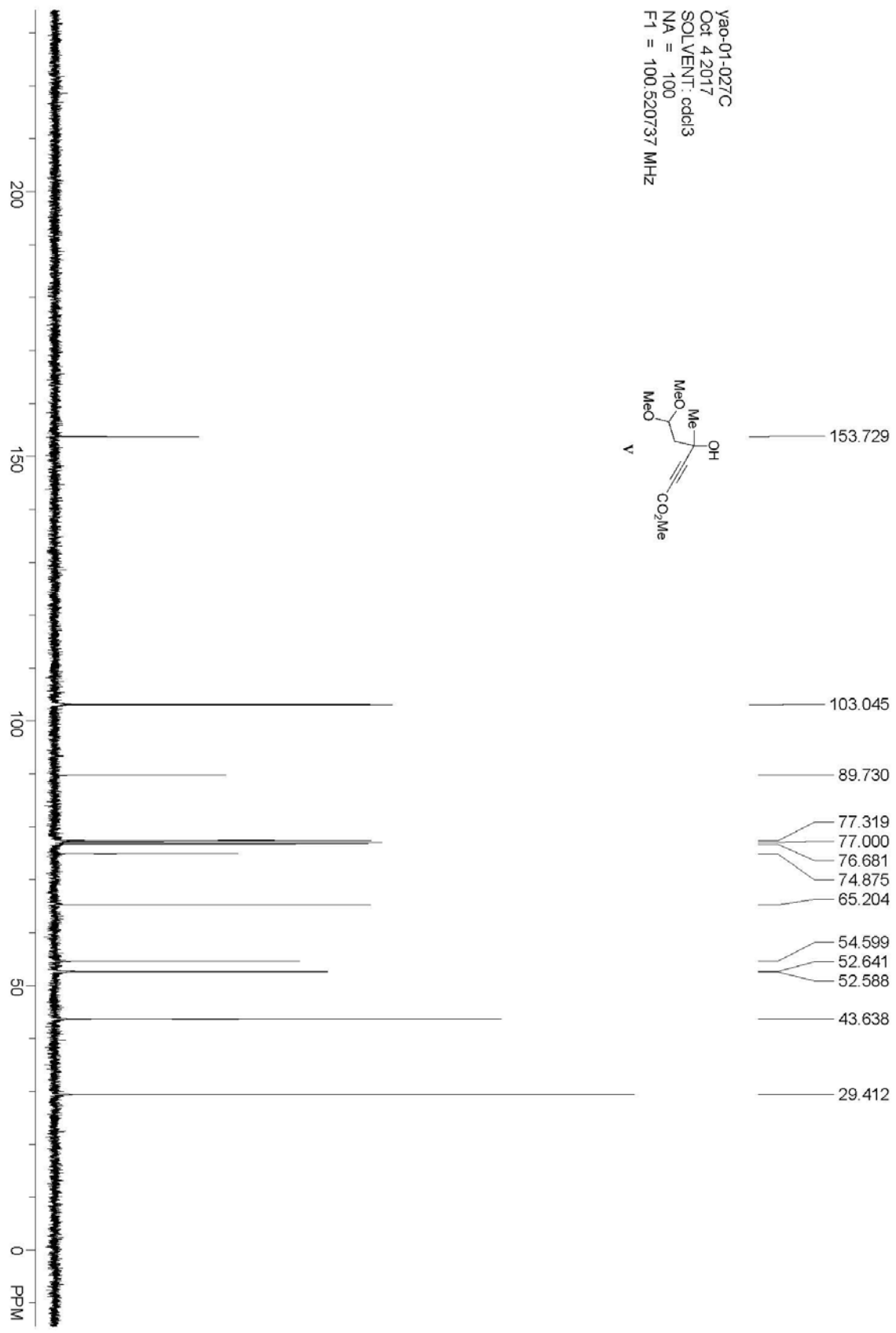
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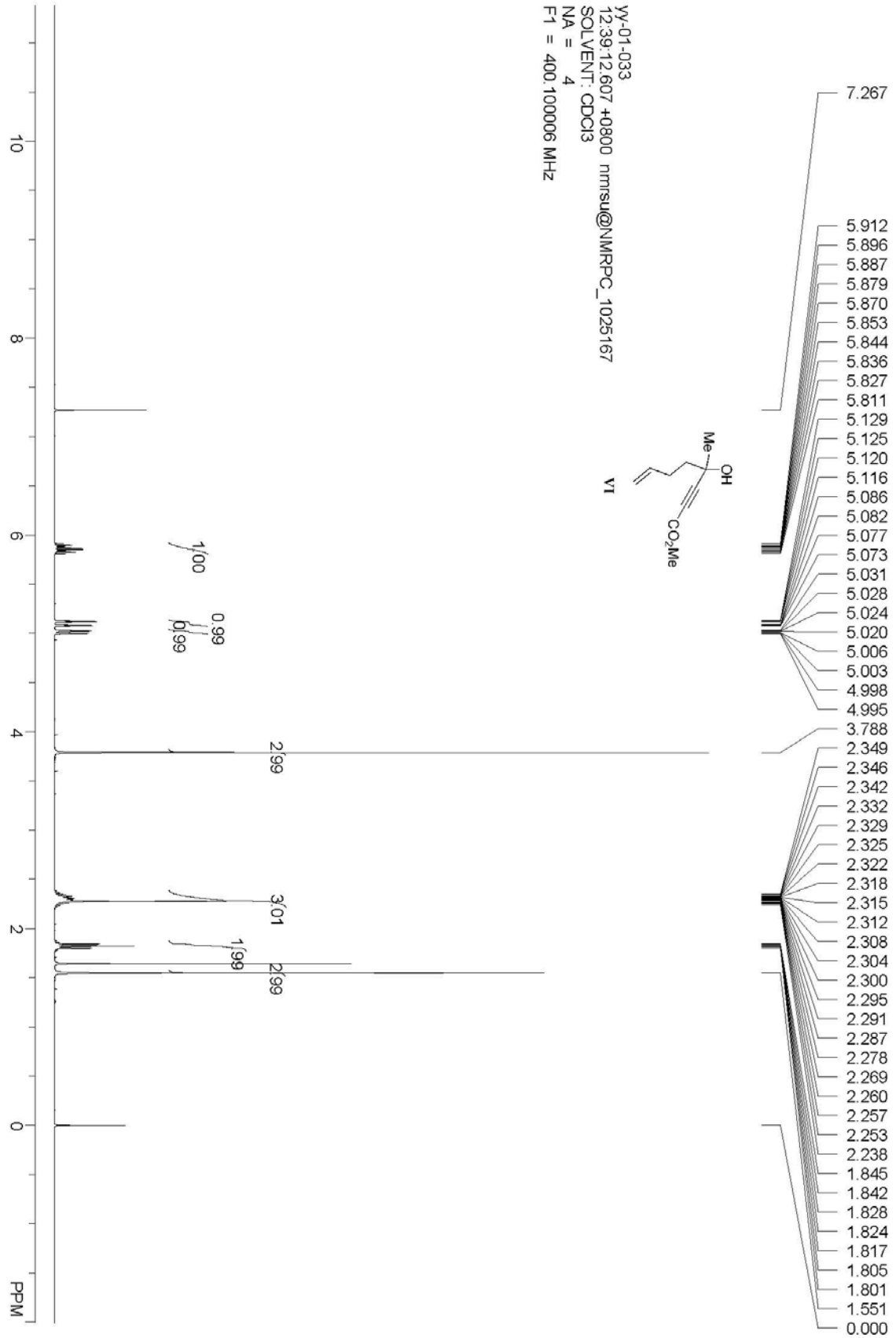
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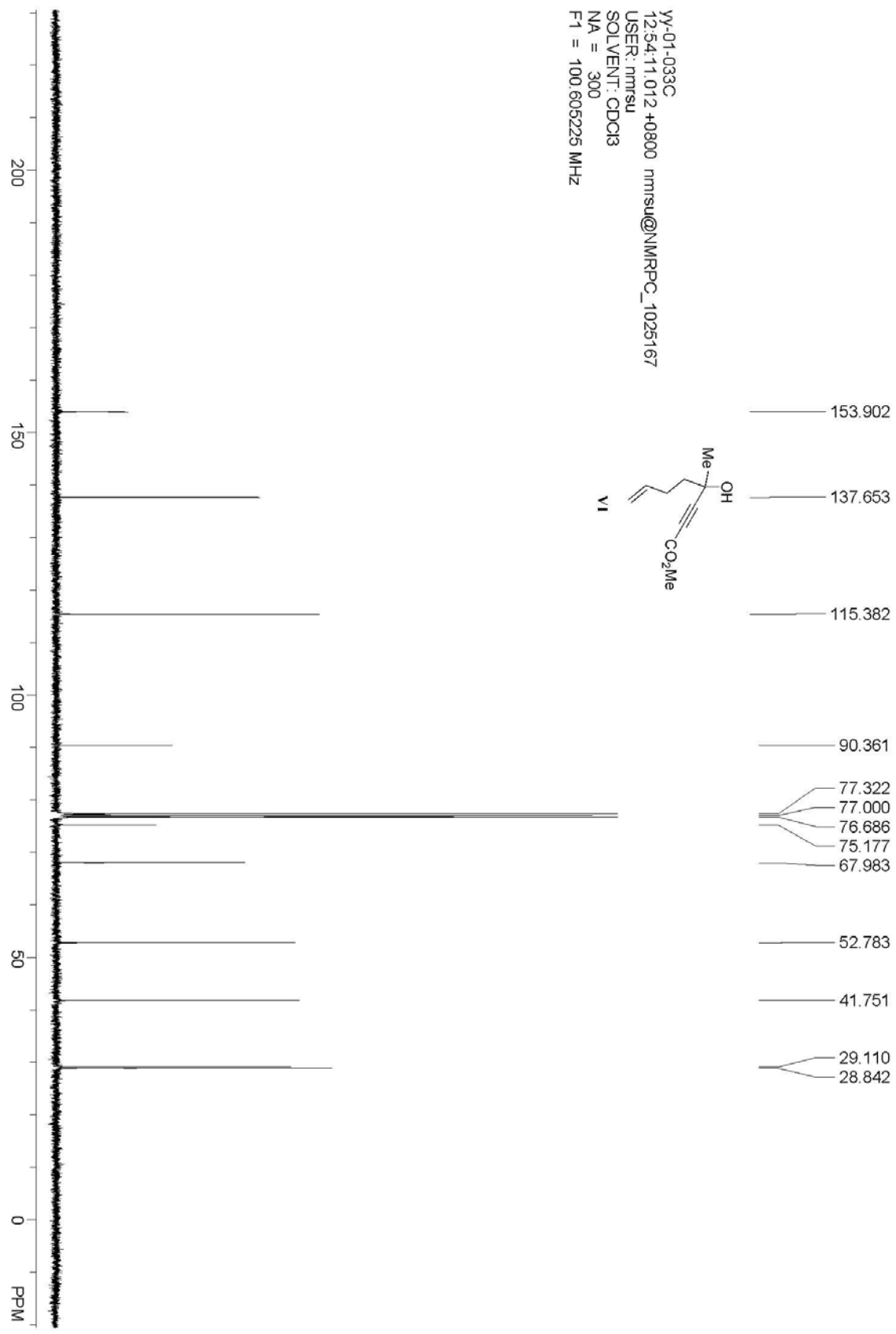
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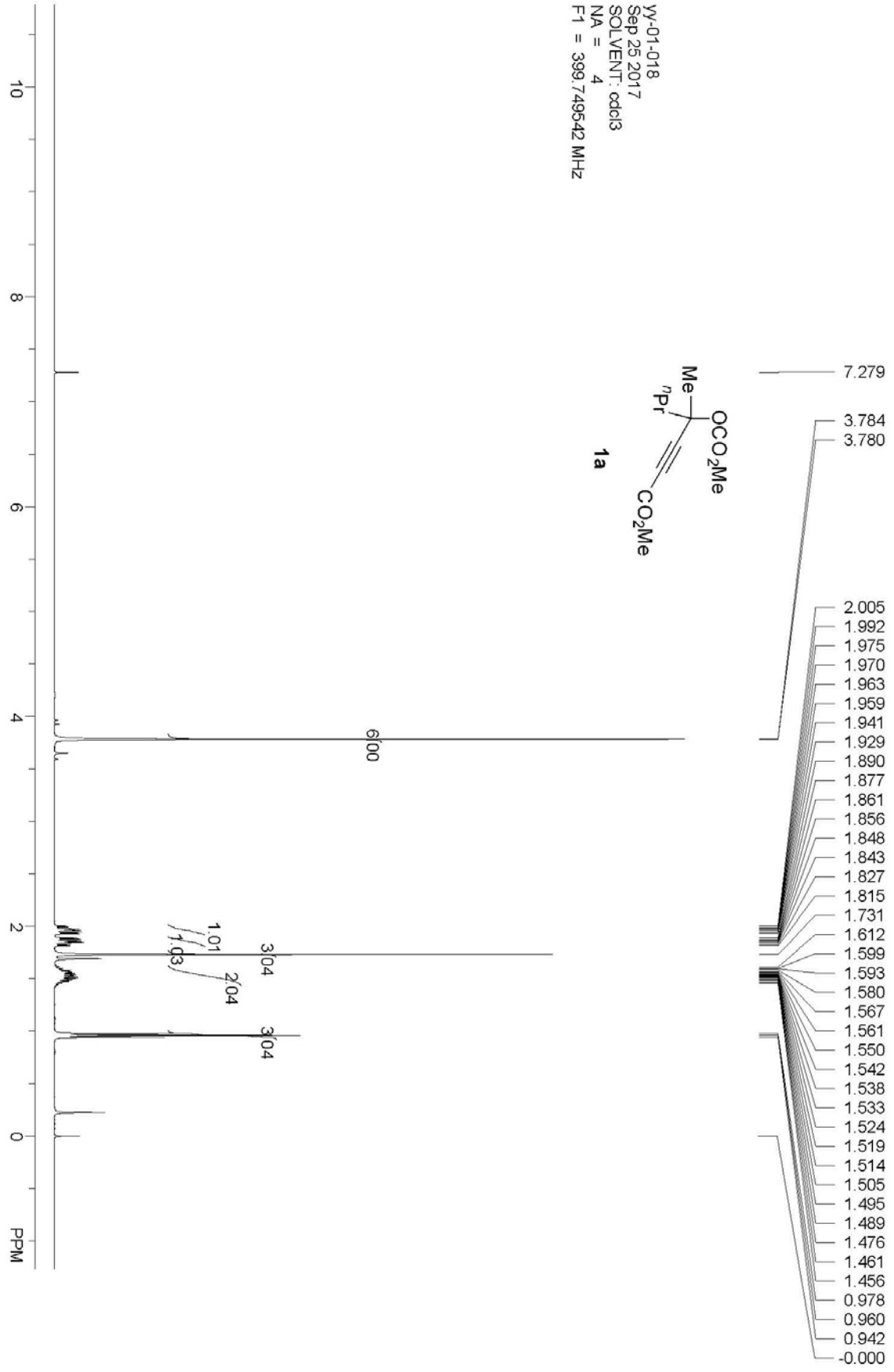
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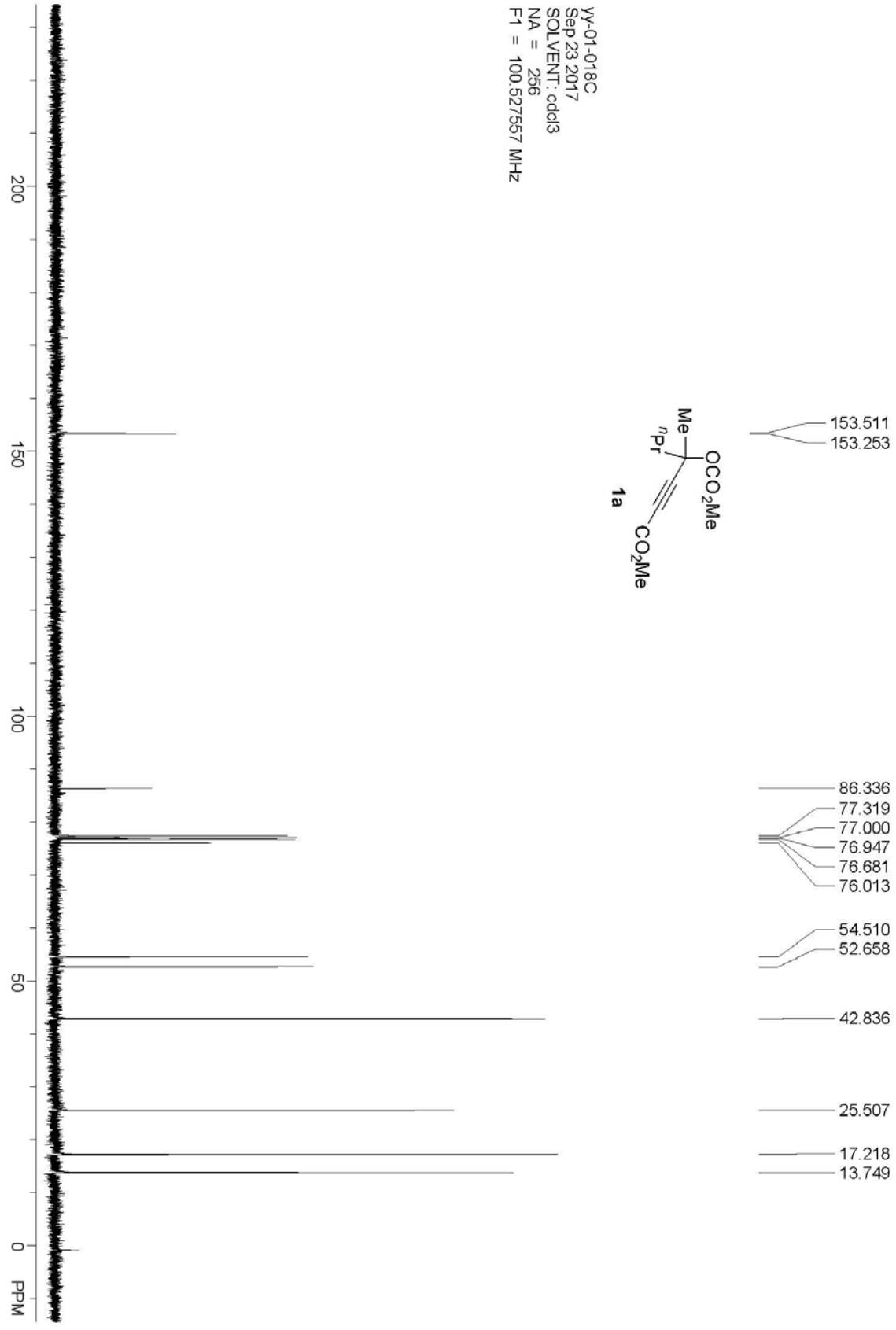
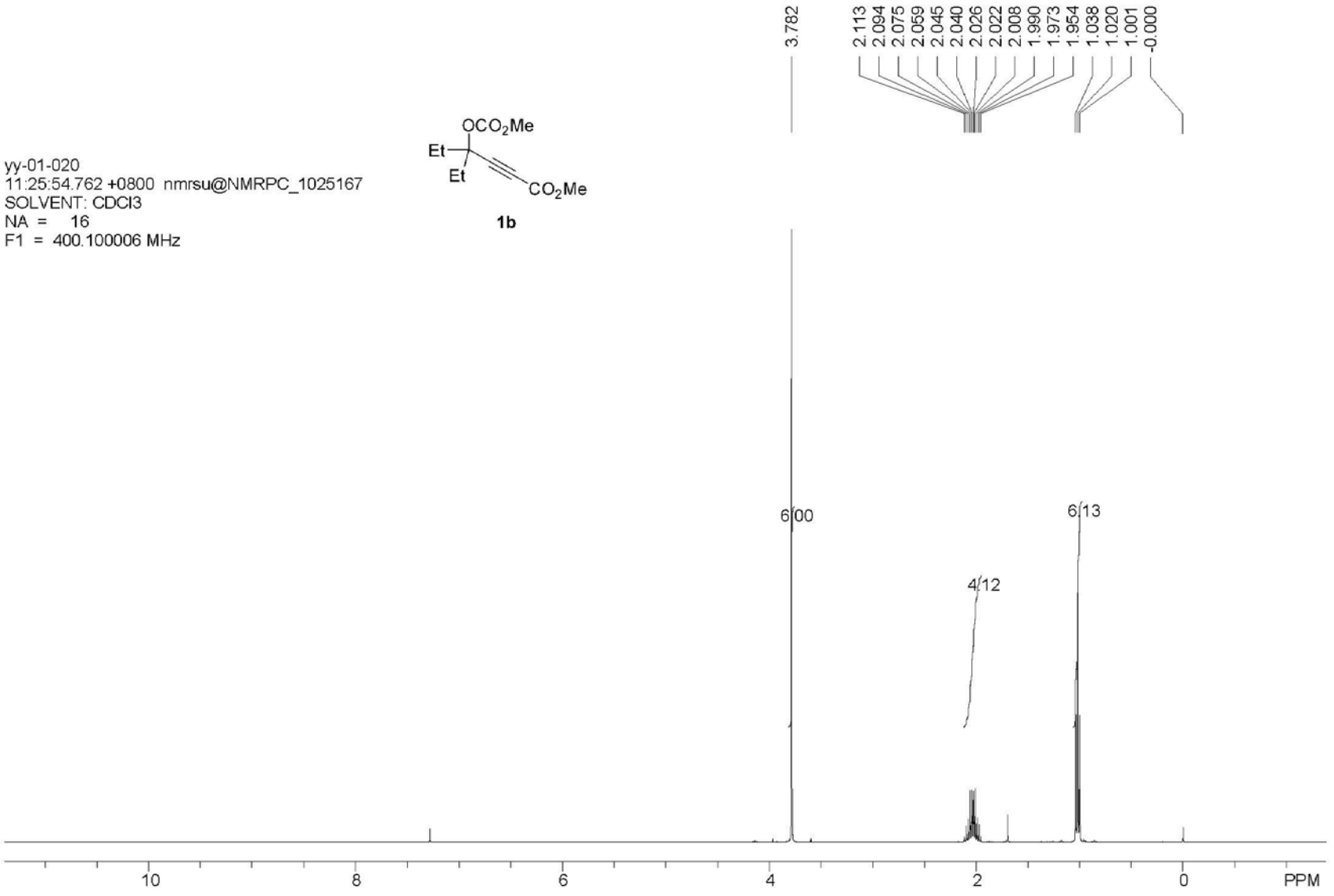
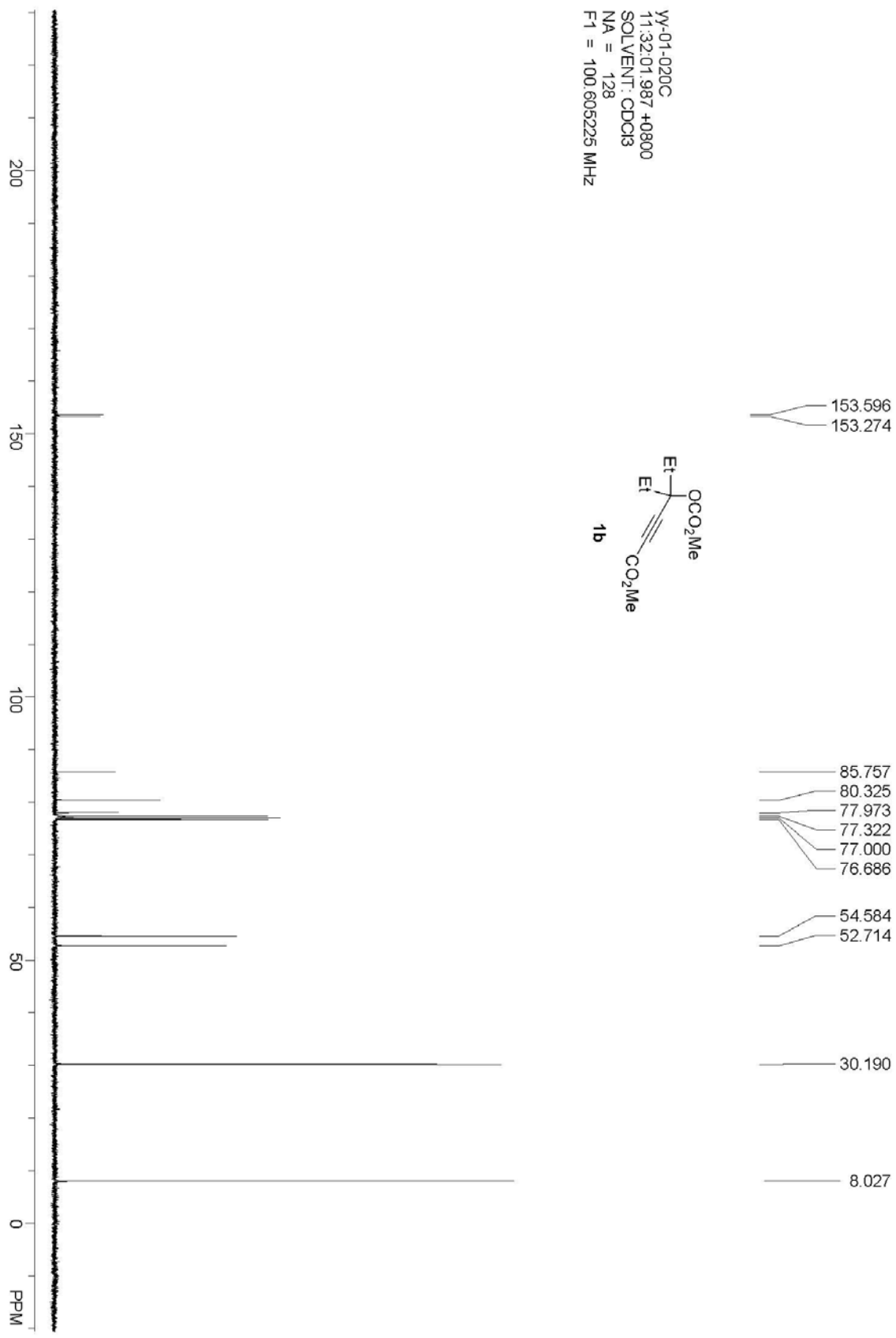
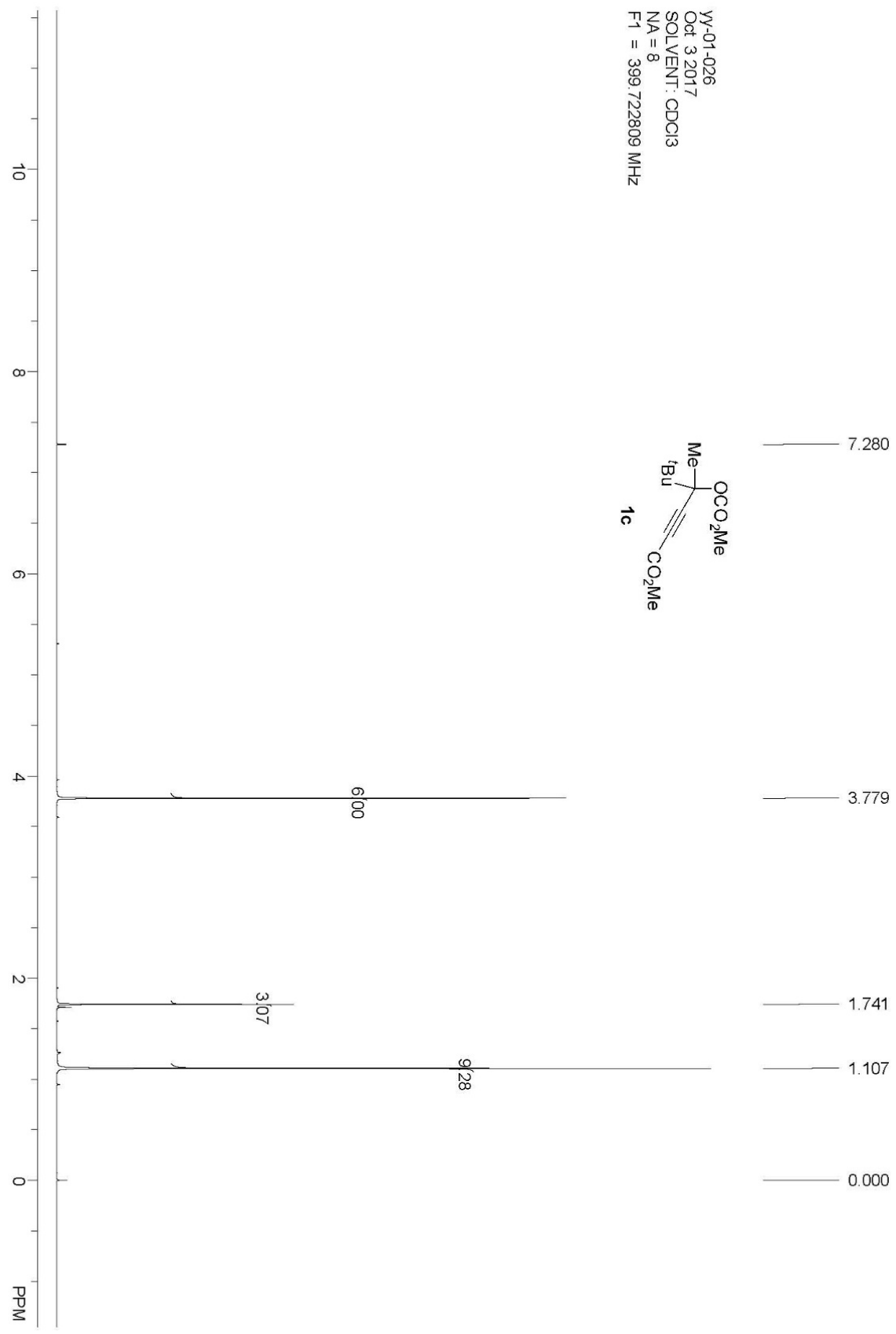
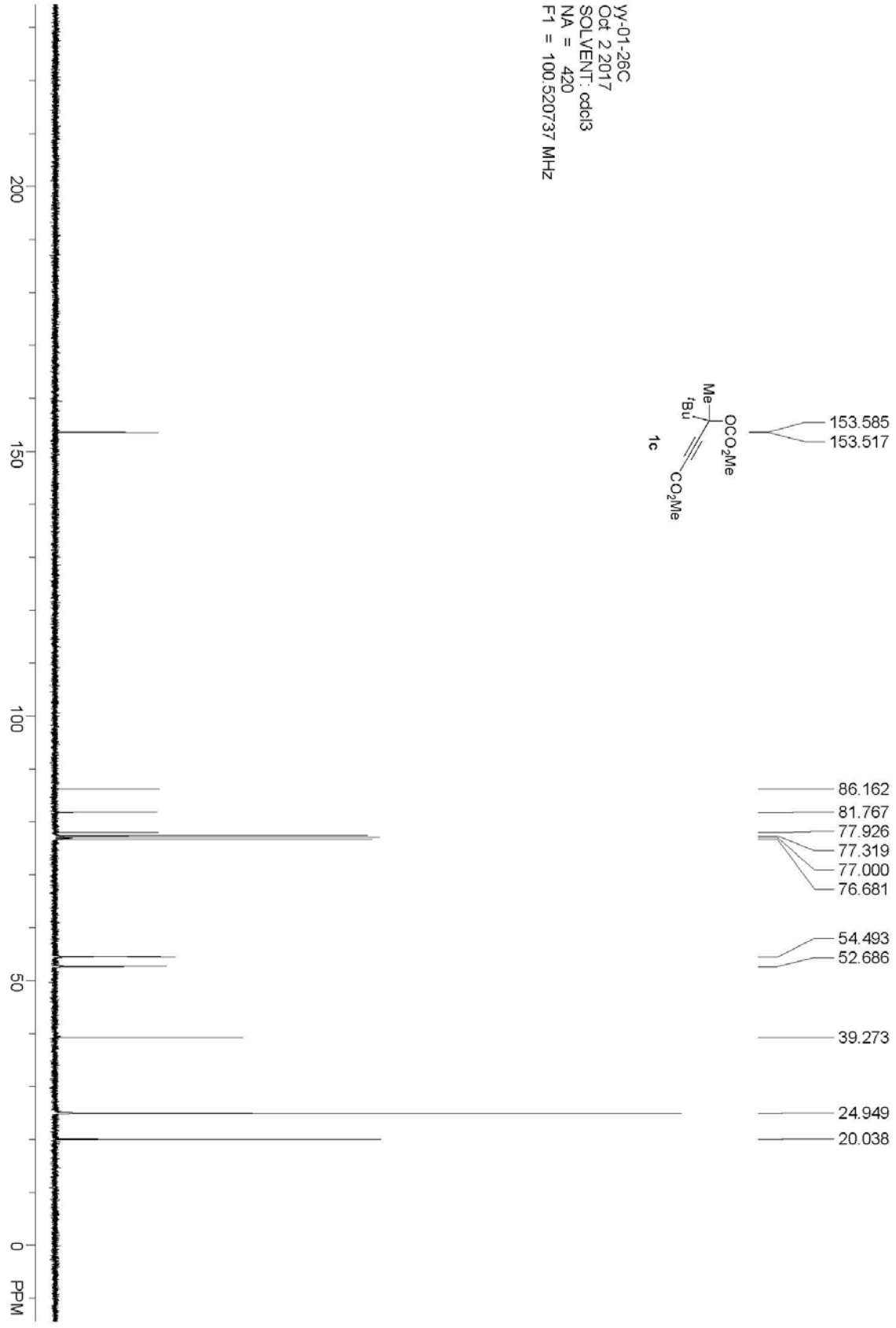
-0.000
6.00
3.04
1.01
1.03
2.04
3.04
10
8
6
4
2
0
PPM

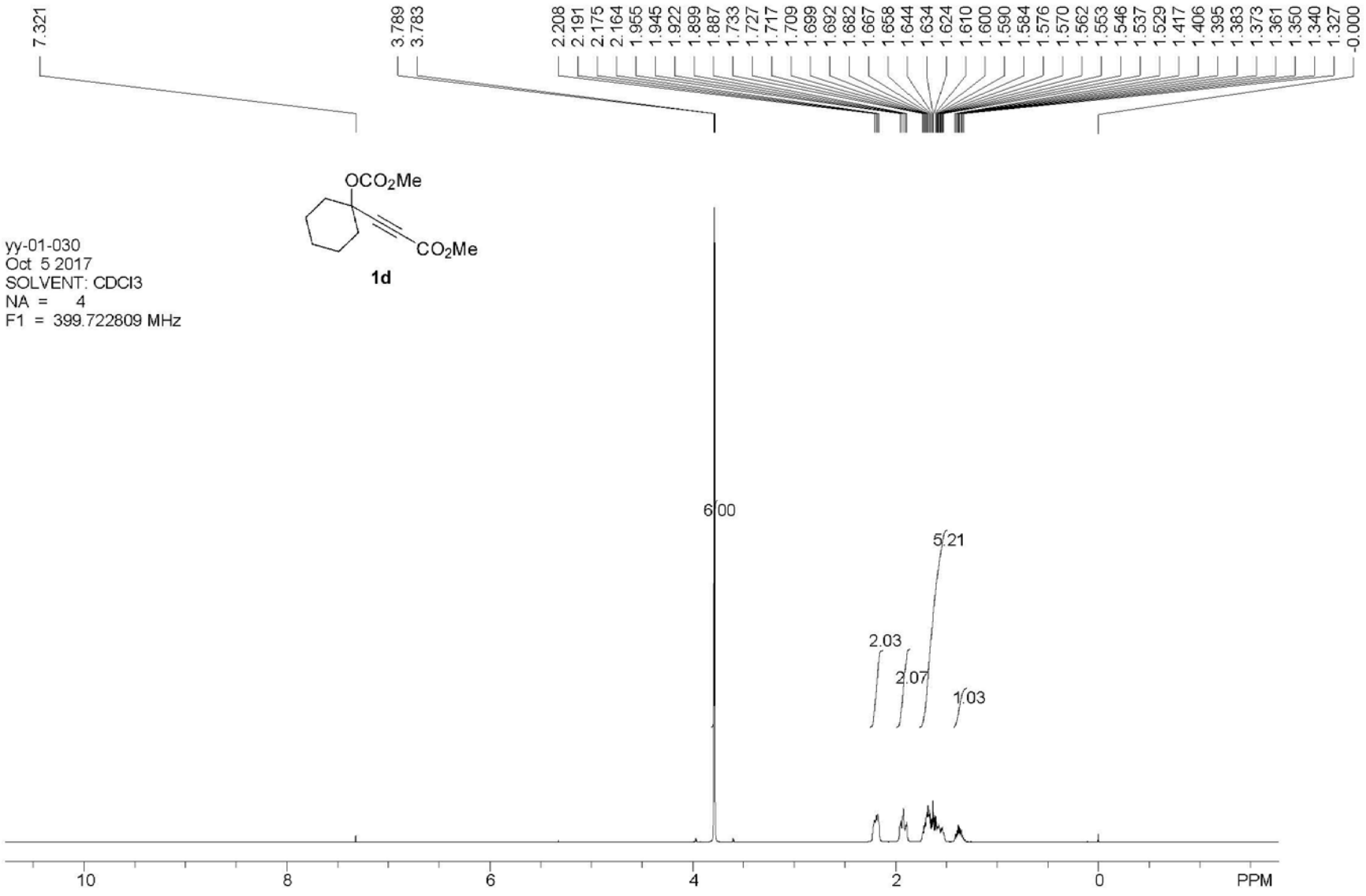

yy-01-018C
Sep 23 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
Me
nPr
OCO2Me
CO2Me
1a
153.511
153.253
86.336
77.319
77.000
76.947
76.681
76.013
54.510
52.658
42.836
25.507
17.218
13.749
200
150
100
50
0
PPM

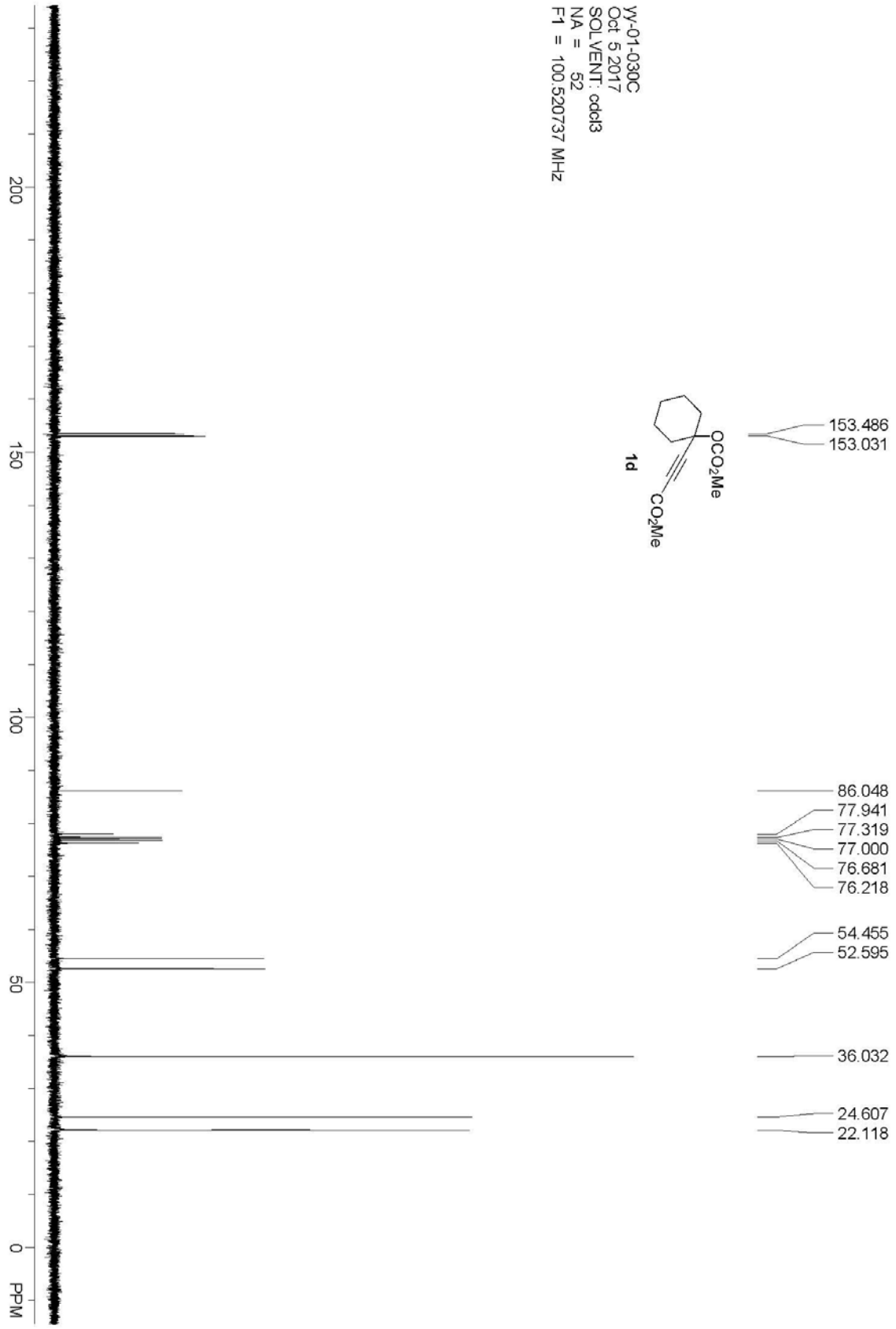

yy-01-020
11:25:54.762 +0800 nmrsu@NMRPC_1025167
SOLVENT: CDCl3
NA = 16
F1 = 400.100006 MHz
OCO2Me
Et
Et
CO2Me
1b
3.782
2.113
2.094
2.075
2.059
2.045
2.040
2.026
2.022
2.008
1.990
1.973
1.954
1.038
1.020
1.001
-0.000
6.00
4.12
6.13
10
8
6
4
2
0
PPM

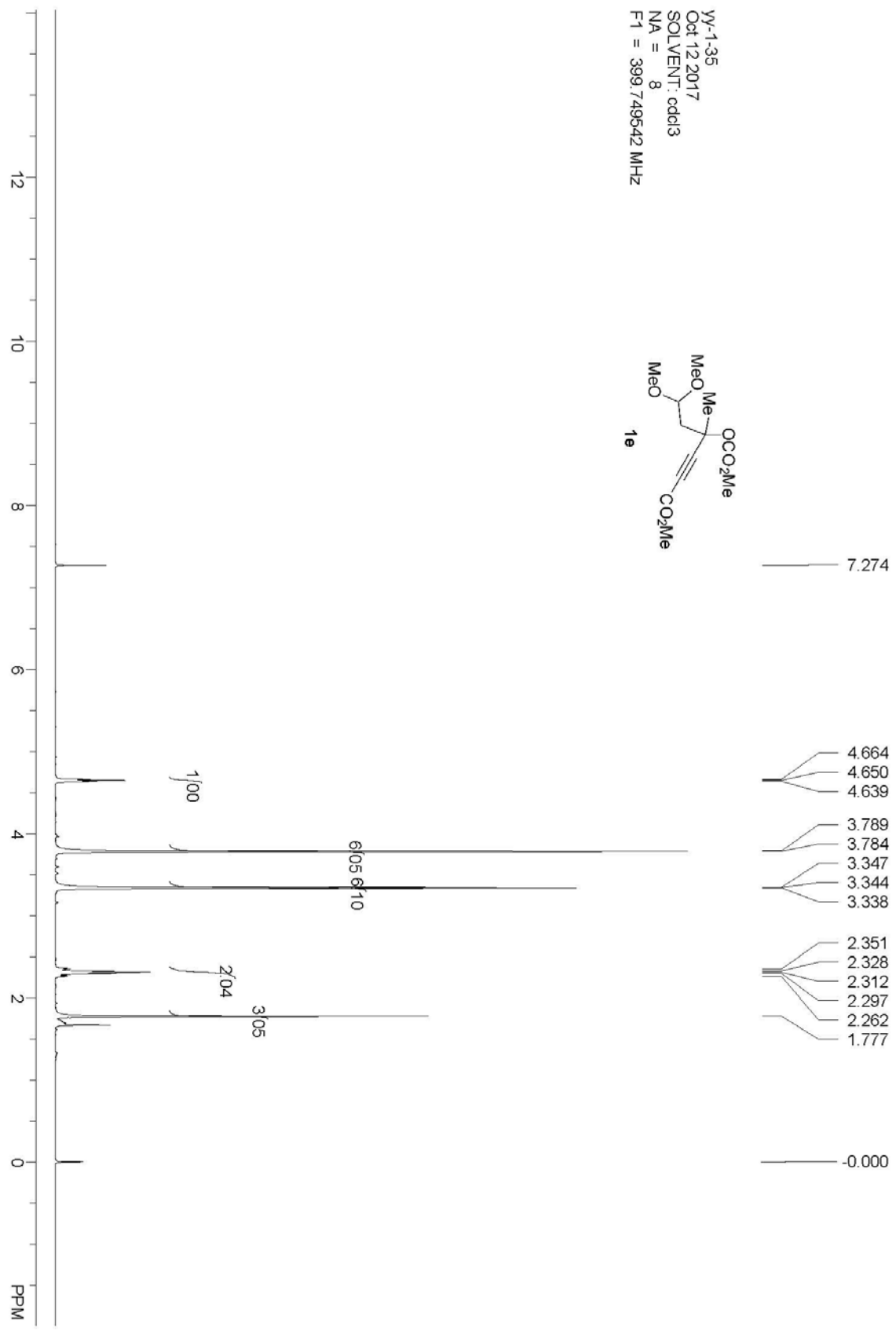

yy-01-020C
11:32:01.987 +0800
SOLVENT: CDCl3
NA = 128
F1 = 100.605225 MHz
1b
Et
Et
OCO2Me
CO2Me
153.596
153.274
85.757
80.325
77.973
77.322
77.000
76.686
54.584
52.714
30.190
8.027
200
150
100
50
0
PPM

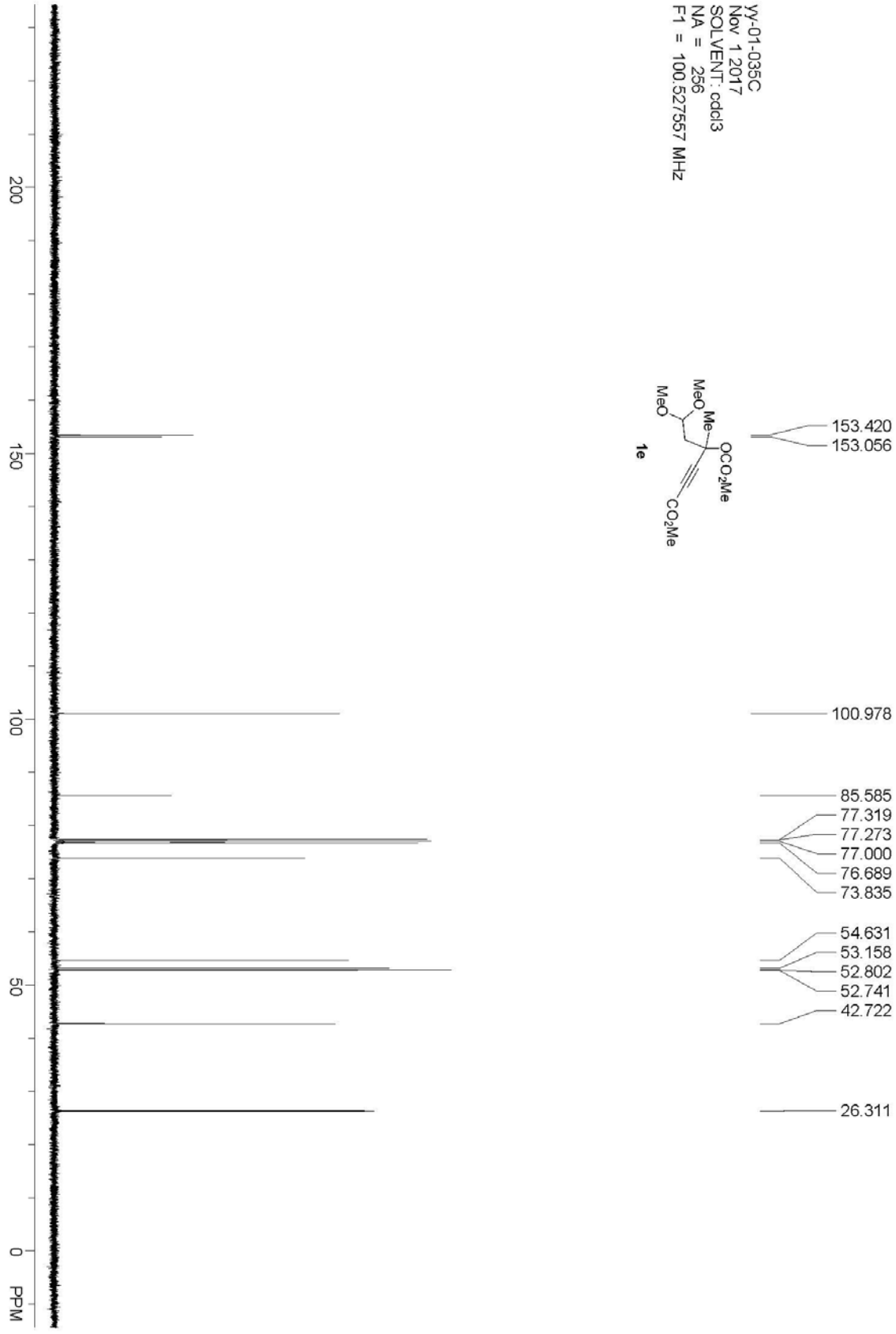

yy-01-026
Oct 3 2017
SOLVENT: CDCl3
NA = 8
F1 = 399.722809 MHz
Me
tBu
OCO2Me
CO2Me
1c
7.280
3.779
1.741
1.107
0.000
6.00
3.07
9.28
PPM

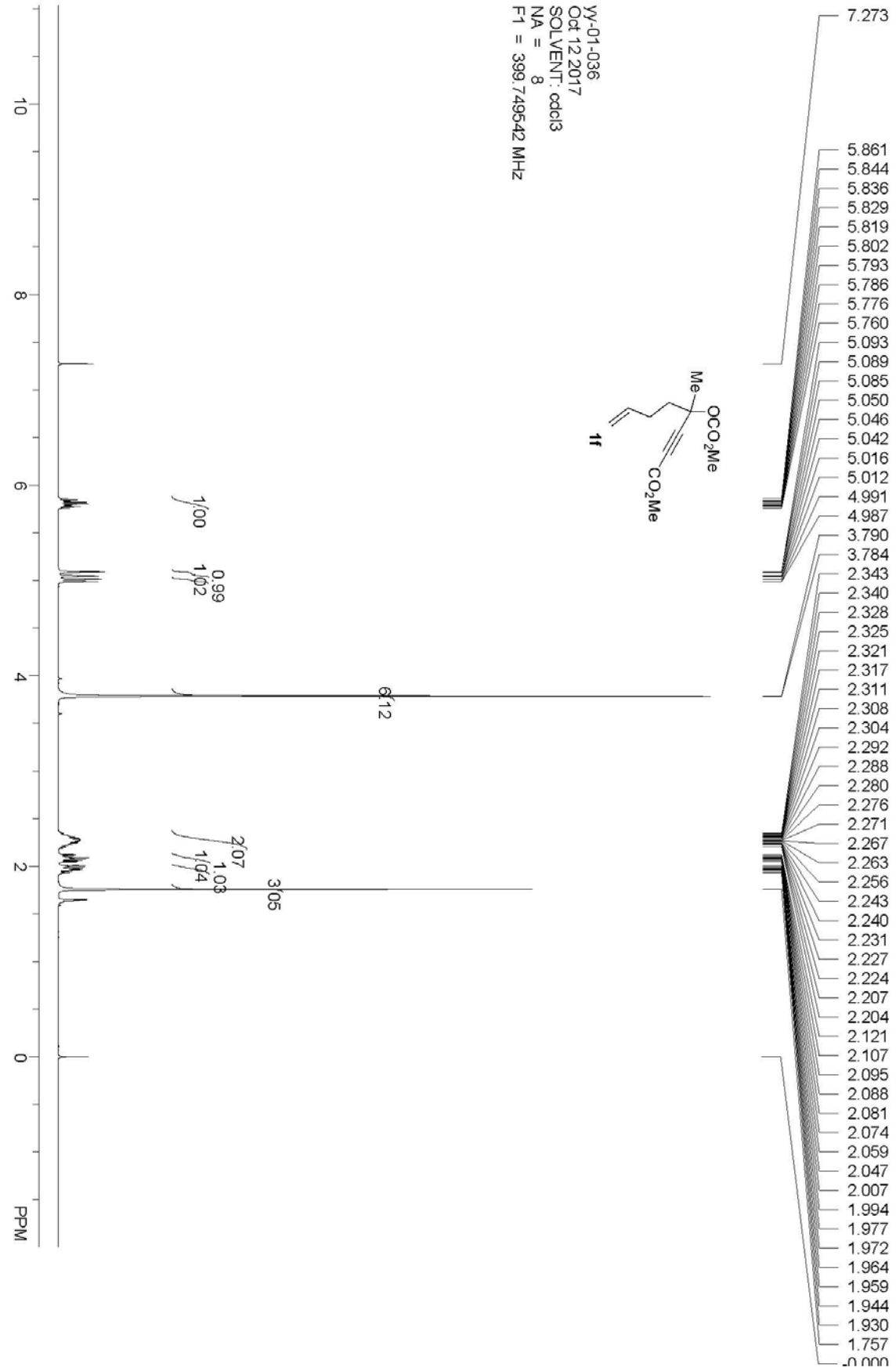

yy-01-26C
Oct 2 2017
SOLVENT: cdcl3
NA = 420
F1 = 100.520737 MHz
Me
tBu
OCO2Me
CO2Me
1c
153.585
153.517
86.162
81.767
77.926
77.319
77.000
76.681
54.493
52.686
39.273
24.949
20.038
200
150
100
50
0
PPM

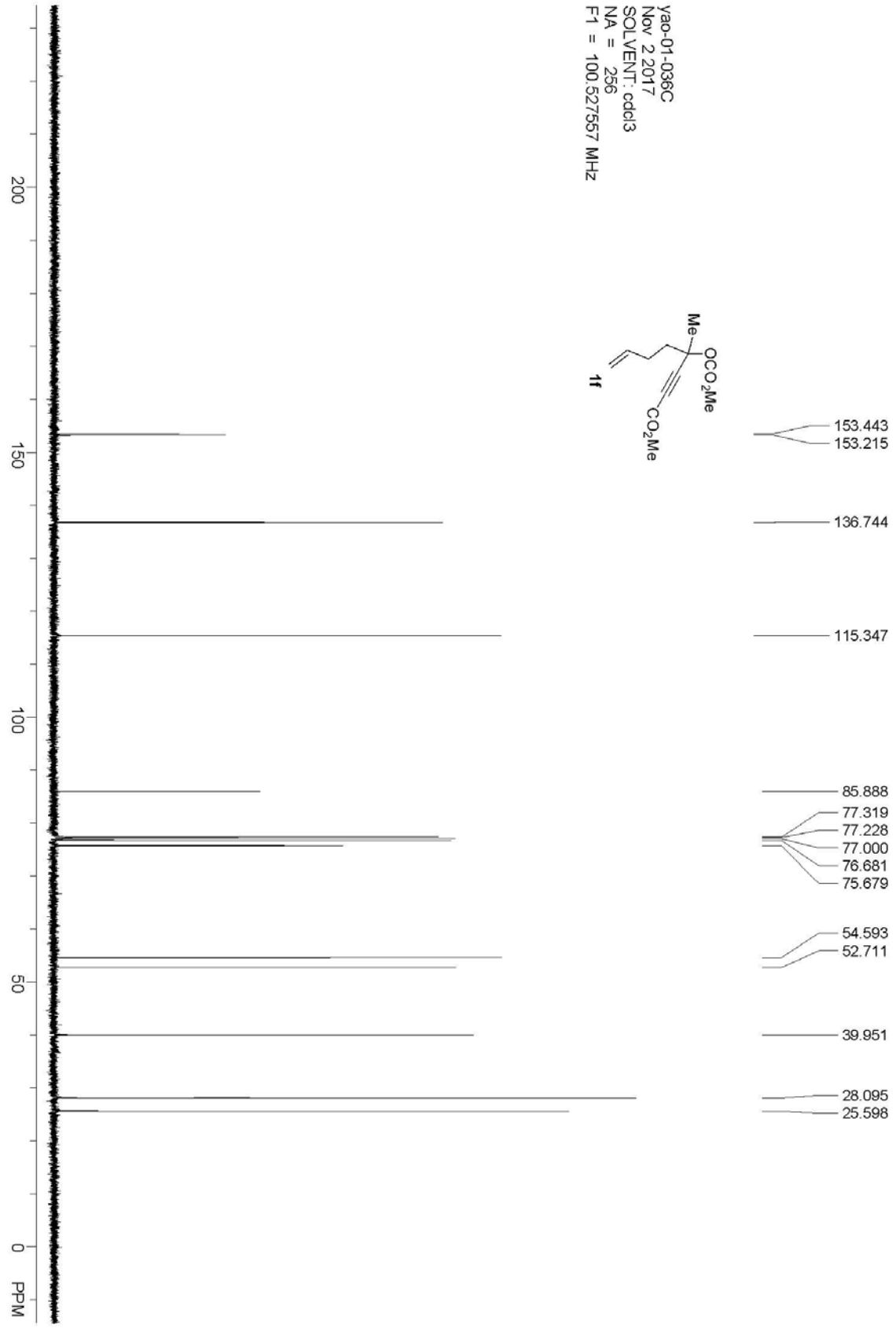

7.321
3.789
3.783
2.208
2.191
2.175
2.164
1.955
1.945
1.922
1.899
1.887
1.733
1.727
1.717
1.709
1.699
1.692
1.682
1.667
1.658
1.644
1.634
1.624
1.610
1.600
1.590
1.584
1.576
1.570
1.562
1.553
1.546
1.537
1.529
1.417
1.406
1.395
1.383
1.373
1.361
1.350
1.340
1.327
-0.000
OCO2Me
CO2Me
1d
yy-01-030
Oct 5 2017
SOLVENT: CDCl3
NA = 4
F1 = 399.722809 MHz
6.00
5.21
2.03
2.07
1.03
10
8
6
4
2
0
PPM

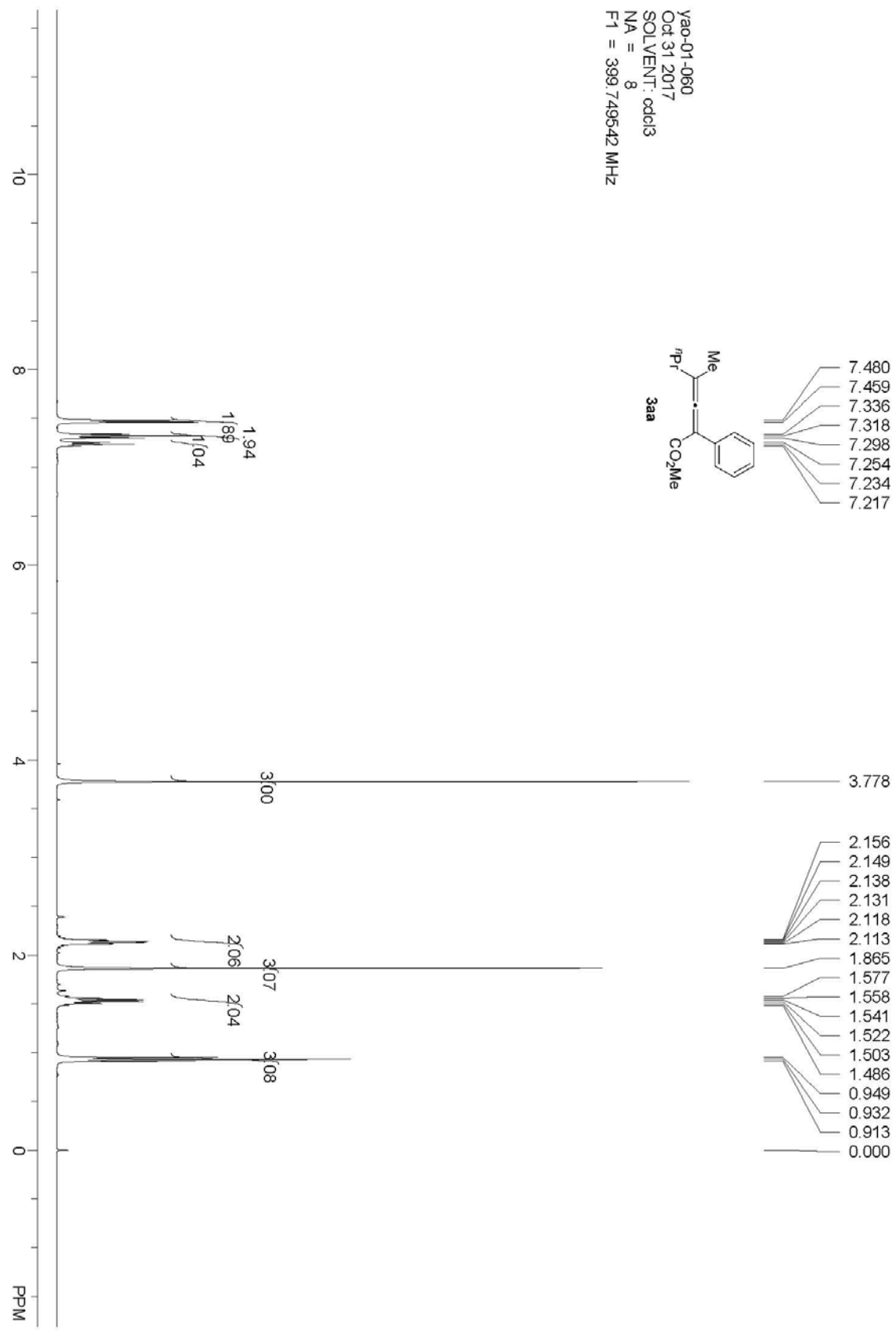

yy-01-030C
Oct 5 2017
SOLVENT: cdcl3
NA = 52
F1 = 100.520737 MHz
1d
OCO2Me
CO2Me
153.486
153.031
86.048
77.941
77.319
77.000
76.681
76.218
54.455
52.595
36.032
24.607
22.118
200
150
100
50
0
PPM

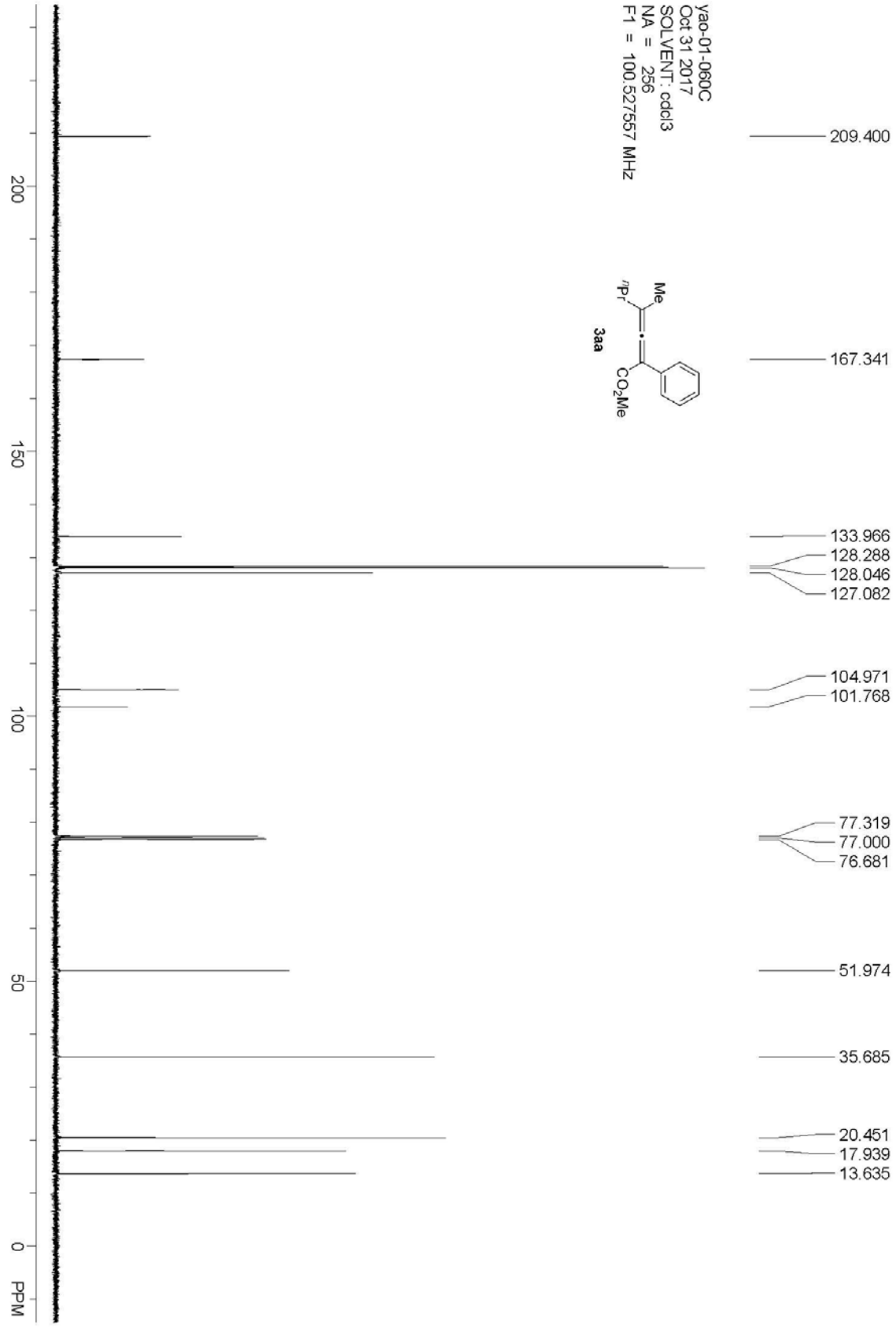

yy-1-35
Oct 12 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
MeO
MeO
Me
OCO2Me
CO2Me
1e
7.274
4.664
4.650
4.639
3.789
3.784
3.347
3.344
3.338
2.351
2.328
2.312
2.297
2.262
1.777
-0.000
1.00
6.05
6.10
2.04
3.05
PPM

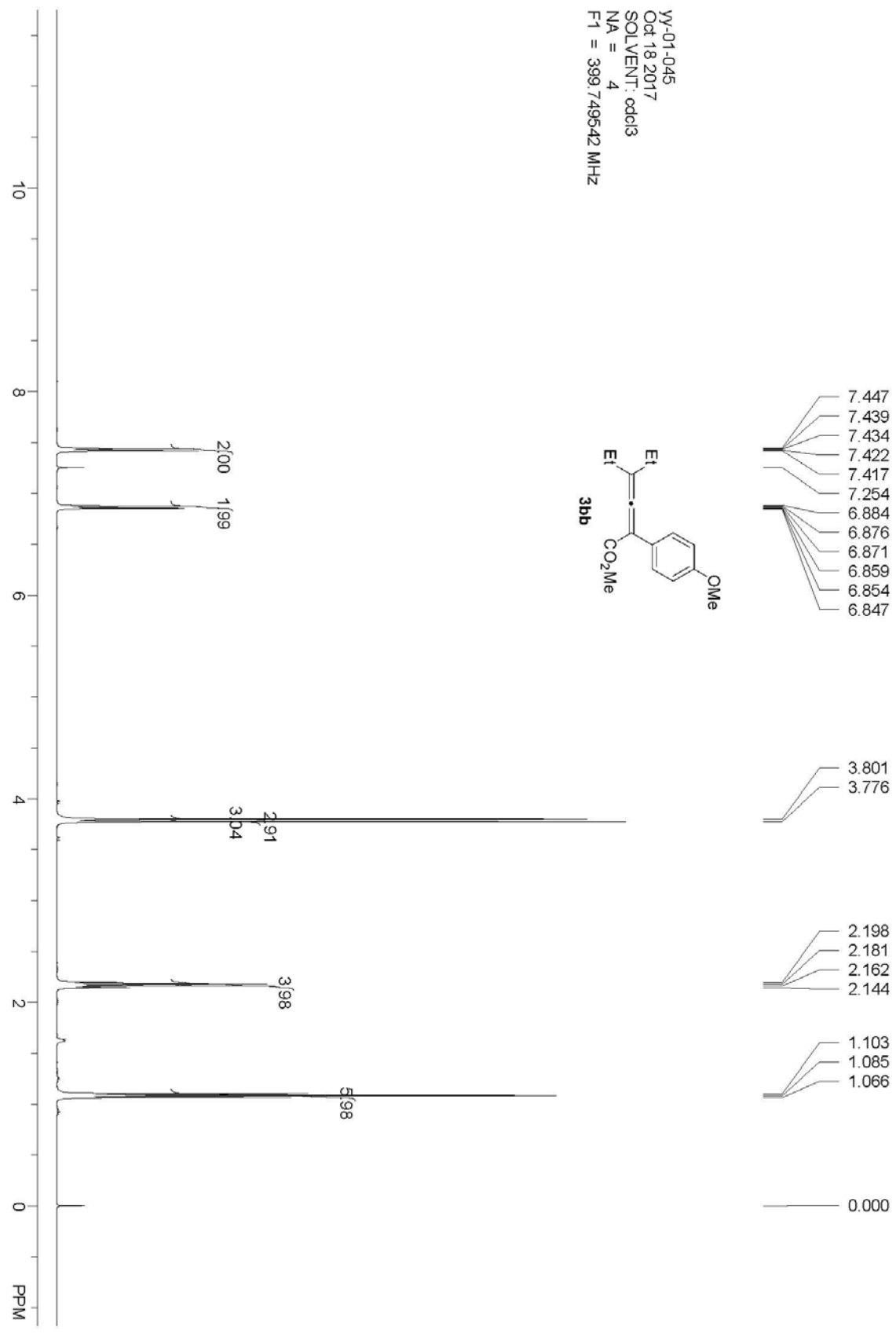

yy-01-035C
Nov 1 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
MeO
MeO
Me
OCO2Me
CO2Me
1e
153.420
153.056
100.978
85.585
77.319
77.273
77.000
76.689
73.835
54.631
53.158
52.802
52.741
42.722
26.311
200
150
100
50
0
PPM

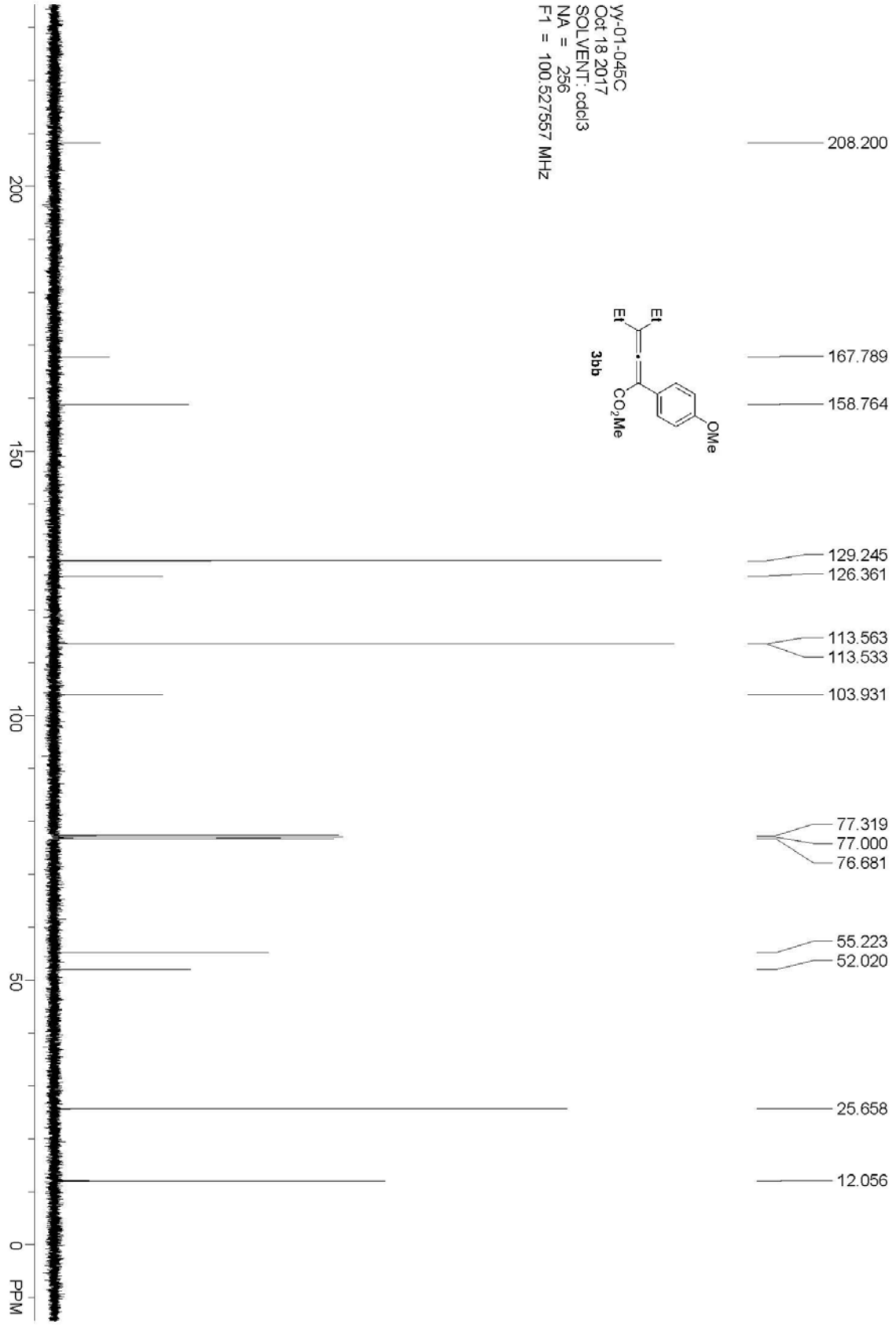

yy-01-036
Oct 12 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
1f
Me
OCO2Me
CO2Me
7.273
5.861
5.844
5.836
5.829
5.819
5.802
5.793
5.786
5.776
5.760
5.093
5.089
5.085
5.050
5.046
5.042
5.016
5.012
4.991
4.987
3.790
3.784
2.343
2.340
2.328
2.325
2.321
2.317
2.311
2.308
2.304
2.292
2.288
2.280
2.276
2.271
2.267
2.263
2.256
2.243
2.240
2.231
2.227
2.224
2.207
2.204
2.121
2.107
2.095
2.088
2.081
2.074
2.059
2.047
2.007
1.994
1.977
1.972
1.964
1.959
1.944
1.930
1.757
1.00
0.99
1.02
6.12
2.07
1.03
1.04
3.05
10
8
6
4
2
0
PPM

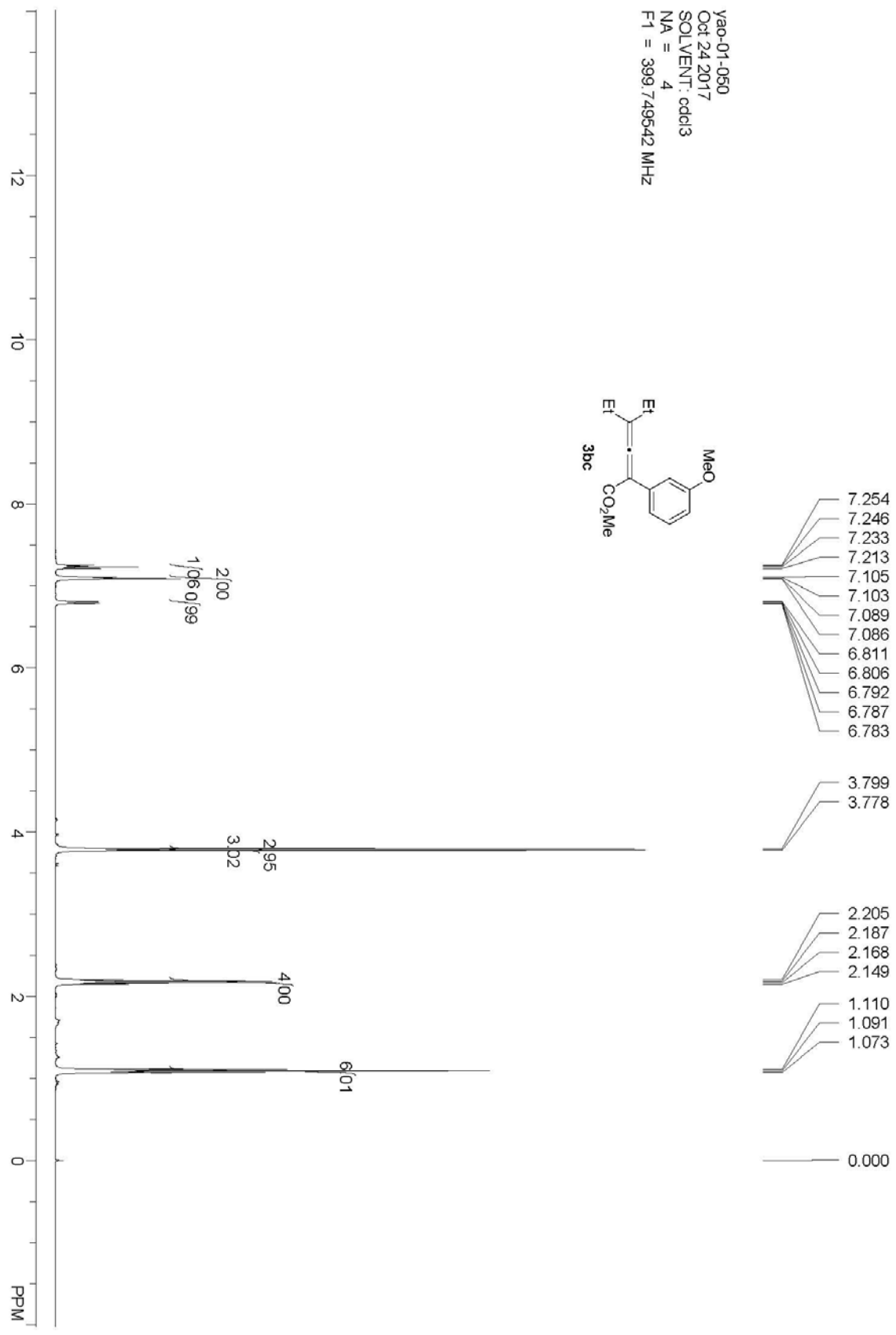

yao-01-036C
Nov 2 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
1f
Me
OCO2Me
CO2Me
153.443
153.215
136.744
115.347
85.888
77.319
77.228
77.000
76.681
75.679
54.593
52.711
39.951
28.095
25.598
200
150
100
50
0
PPM

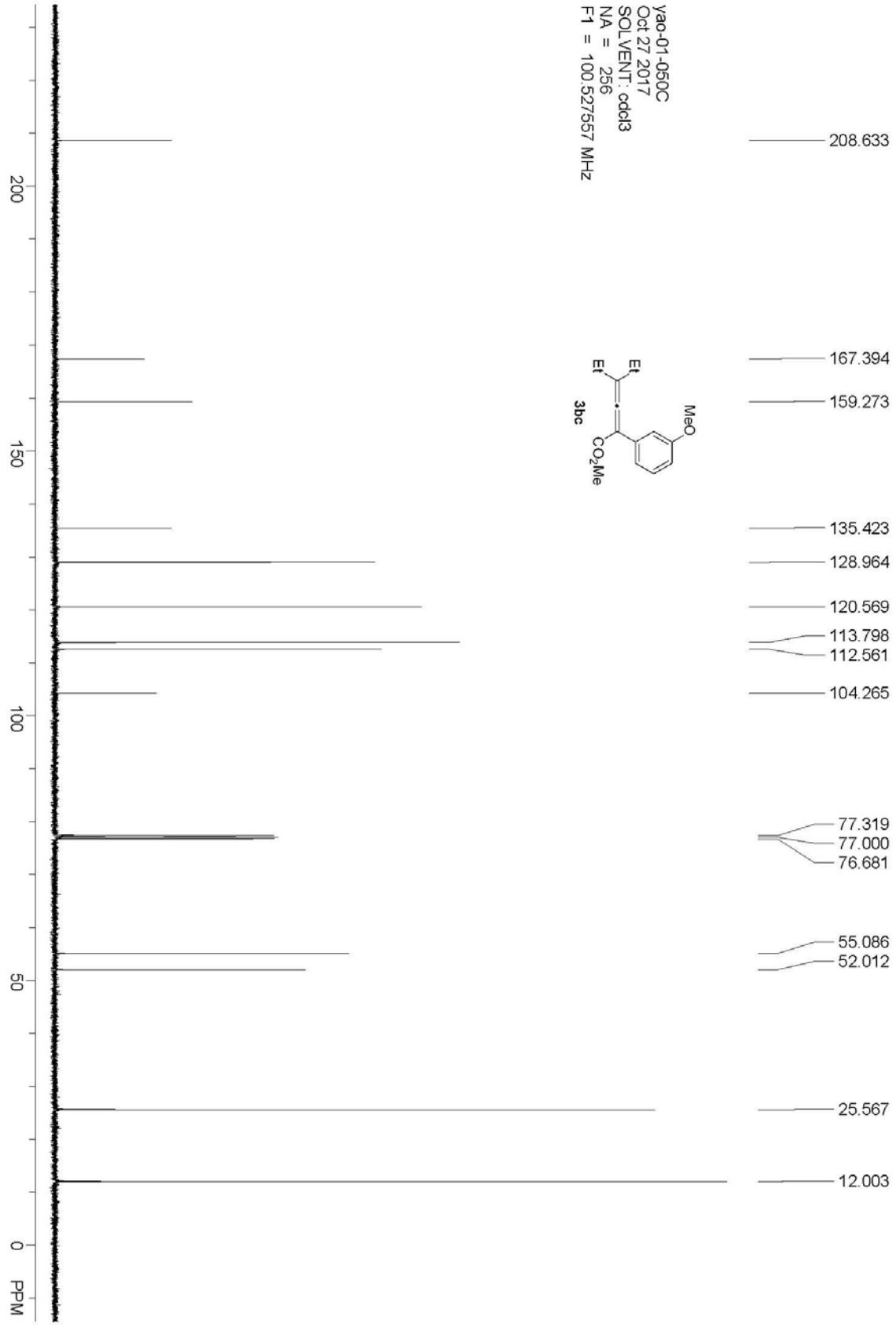

yao-01-060
Oct 31 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3aa
Me
iPr
CO2Me
7.480
7.459
7.336
7.318
7.298
7.254
7.234
7.217
3.778
2.156
2.149
2.138
2.131
2.118
2.113
1.865
1.577
1.558
1.541
1.522
1.503
1.486
0.949
0.932
0.913
0.000
1.94
1.89
1.04
3.00
2.06
3.07
2.04
3.08
10
8
6
4
2
0
PPM

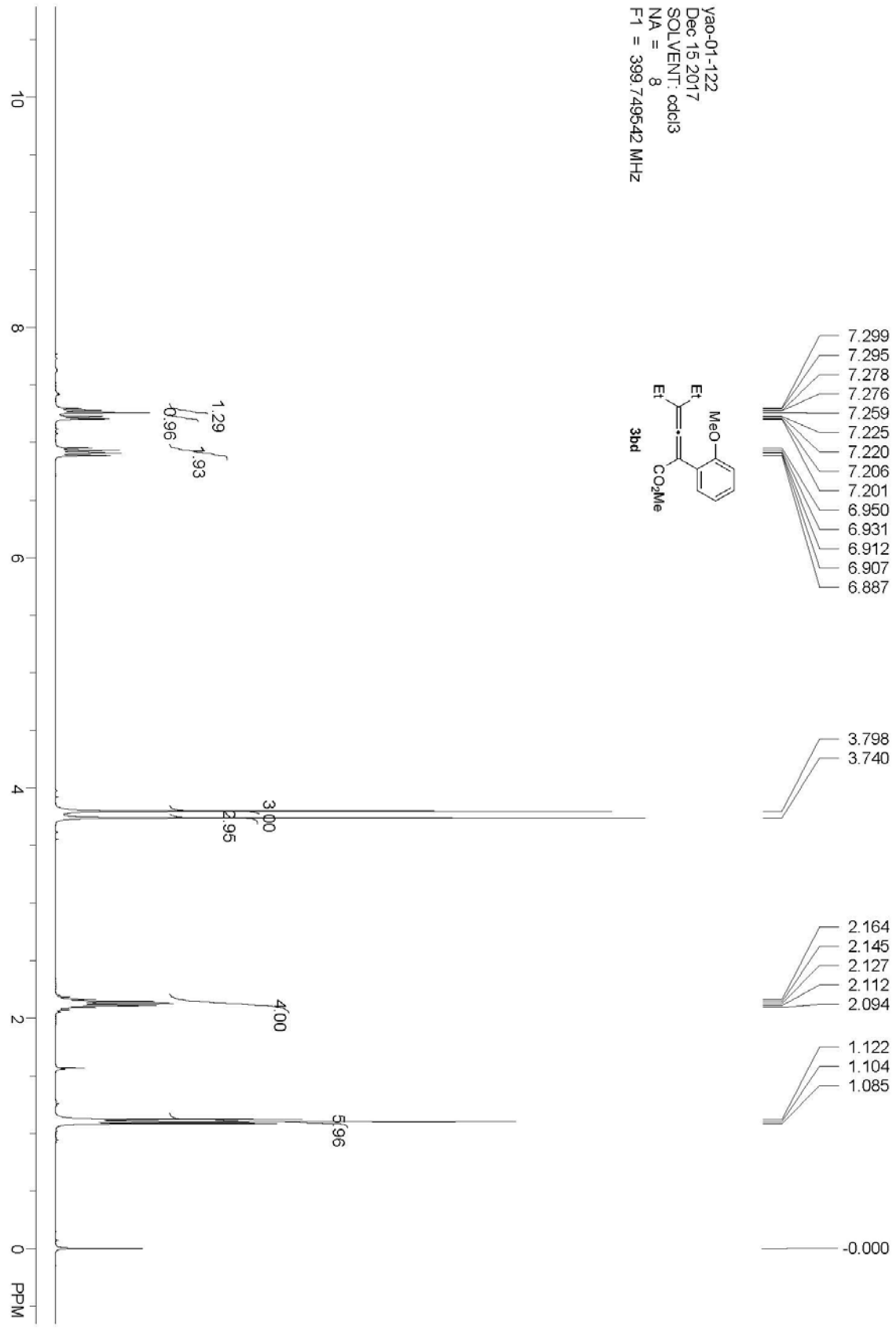

yao-01-060C
Oct 31 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
Me
iPr
CO2Me
3aa
209.400
167.341
133.966
128.288
128.046
127.082
104.971
101.768
77.319
77.000
76.681
51.974
35.685
20.451
17.939
13.635
200
150
100
50
0
PPM

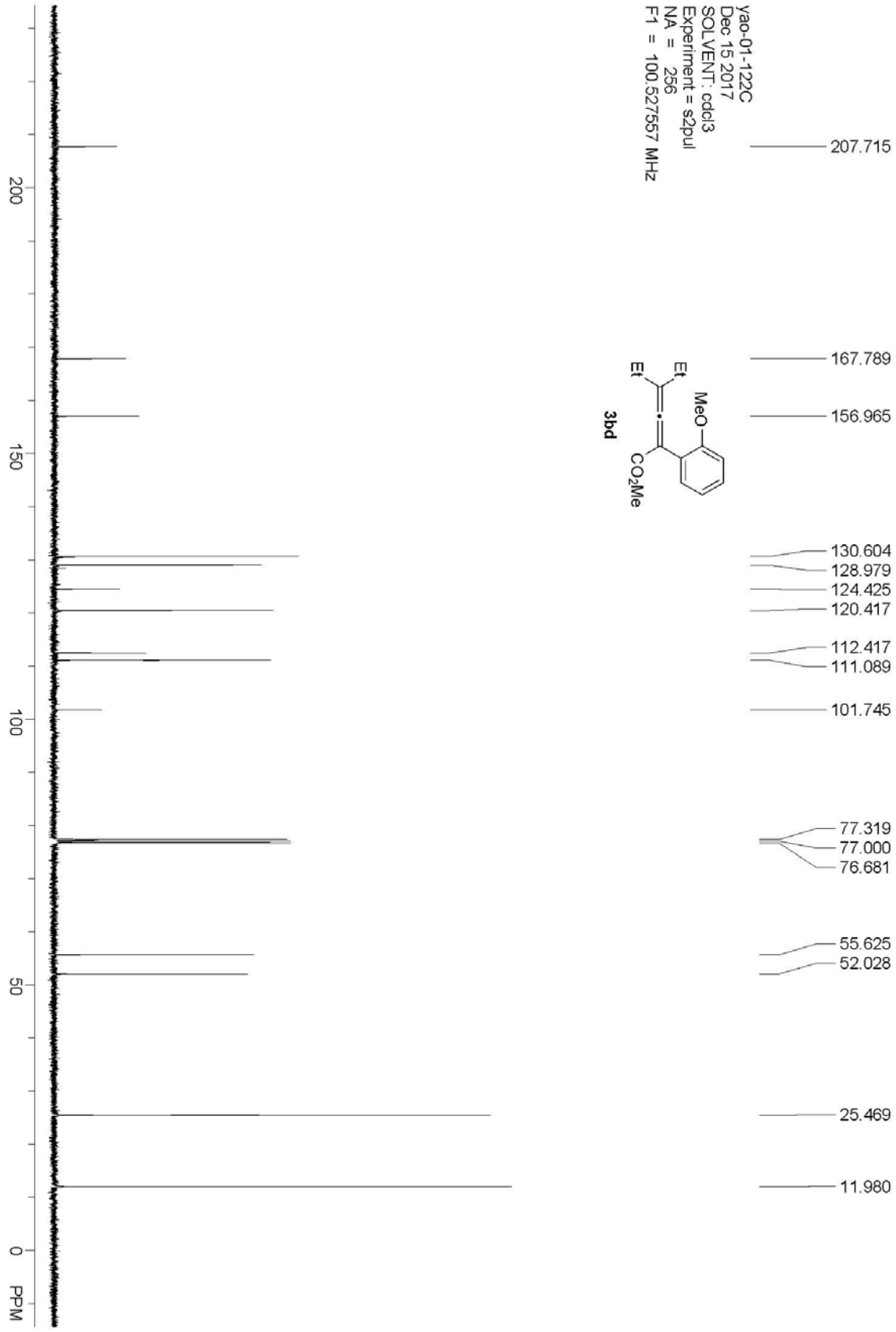

yy-01-045
Oct 18 2017
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz
Et
Et
CO2Me
OMe
3bb
7.447
7.439
7.434
7.422
7.417
7.254
6.884
6.876
6.871
6.859
6.854
6.847
3.801
3.776
2.198
2.181
2.162
2.144
1.103
1.085
1.066
0.000
2.00
1.99
3.04
2.91
3.98
5.98
10
8
6
4
2
0
PPM

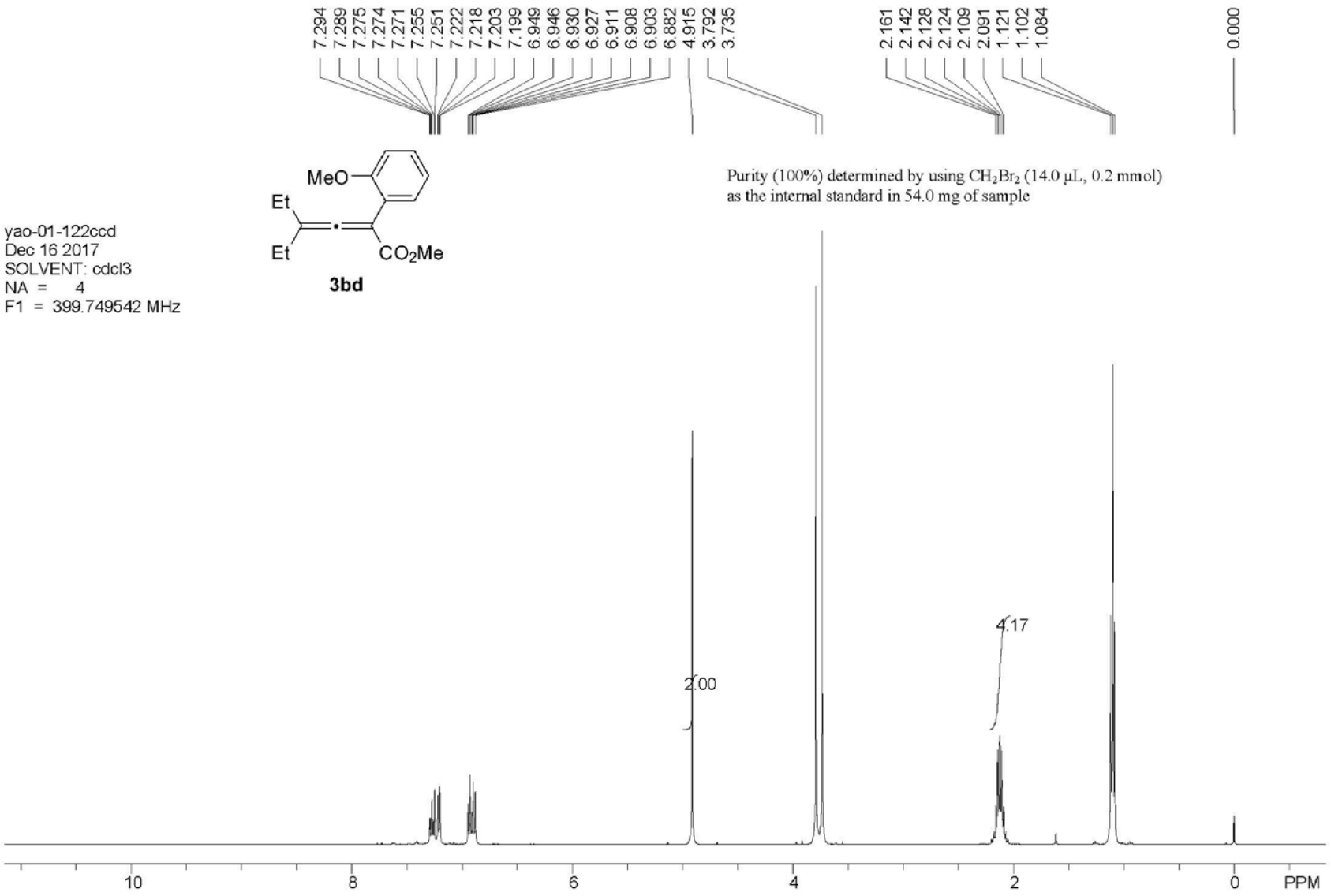

yy-01-045C
Oct 18 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3bb
Et
Et
CO2Me
OMe
208.200
167.789
158.764
129.245
126.361
113.563
113.533
103.931
77.319
77.000
76.681
55.223
52.020
25.658
12.056
200
150
100
50
0
PPM

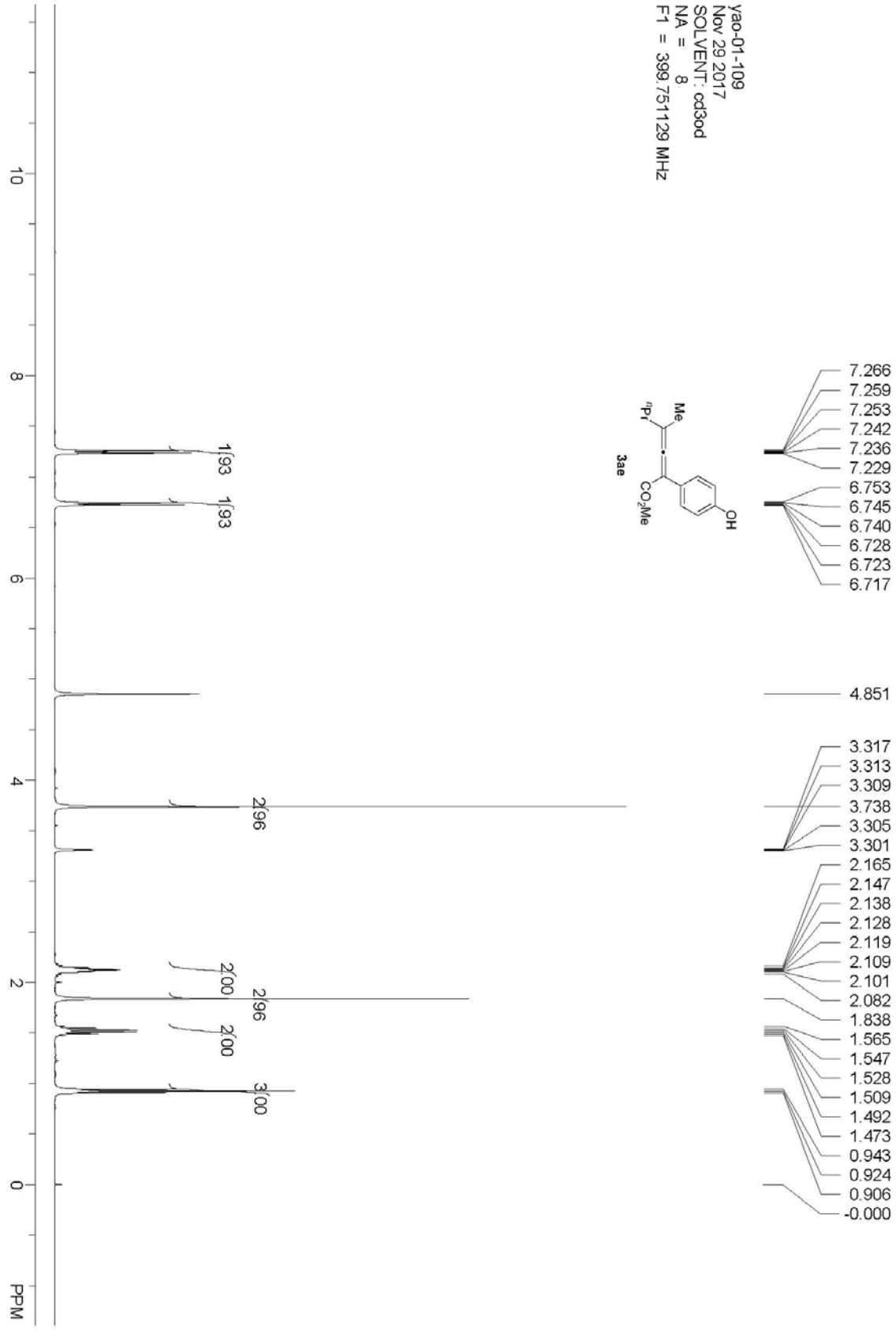

yao-01-050
Oct 24 2017
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz
Et
Et
MeO
CO2Me
3bc
7.254
7.246
7.233
7.213
7.105
7.103
7.089
7.086
6.811
6.806
6.792
6.787
6.783
3.799
3.778
2.205
2.187
2.168
2.149
1.110
1.091
1.073
0.000
2.00
1.06
0.99
3.02
2.95
4.00
6.01
12
10
8
6
4
2
0
PPM

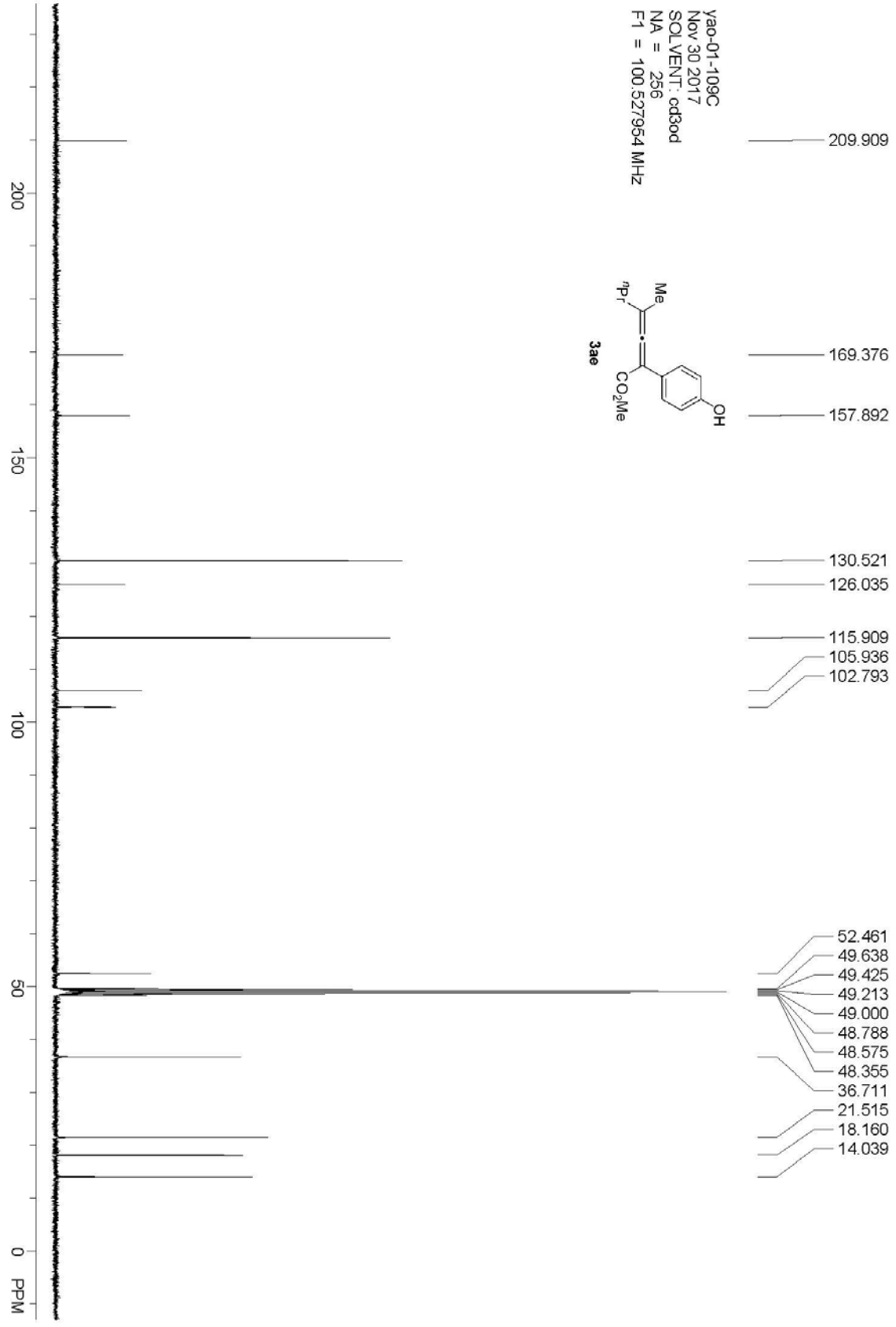

yao-01-050C
Oct 27 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3bc
Et
Et
MeO
CO2Me
208.633
167.394
159.273
135.423
128.964
120.569
113.798
112.561
104.265
77.319
77.000
76.681
55.086
52.012
25.567
12.003
200
150
100
50
0
PPM

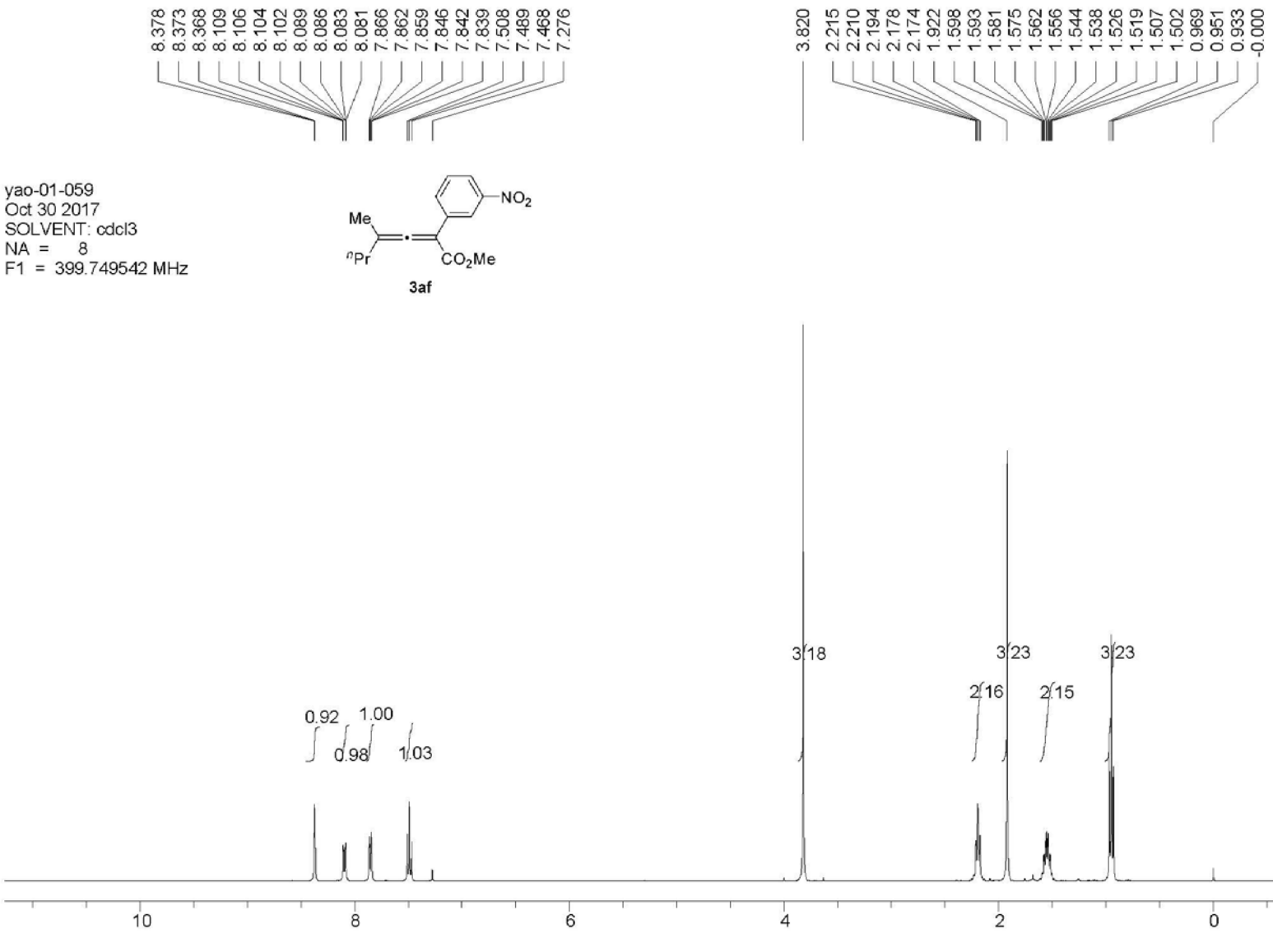

yao-01-122
Dec 15 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3bd
Et
Et
MeO
CO2Me
7.299
7.295
7.278
7.276
7.259
7.225
7.220
7.206
7.201
6.950
6.931
6.912
6.907
6.887
3.798
3.740
2.164
2.145
2.127
2.112
2.094
1.122
1.104
1.085
-0.000
1.29
0.96
1.93
3.00
2.95
4.00
5.96
10
8
6
4
2
0
PPM

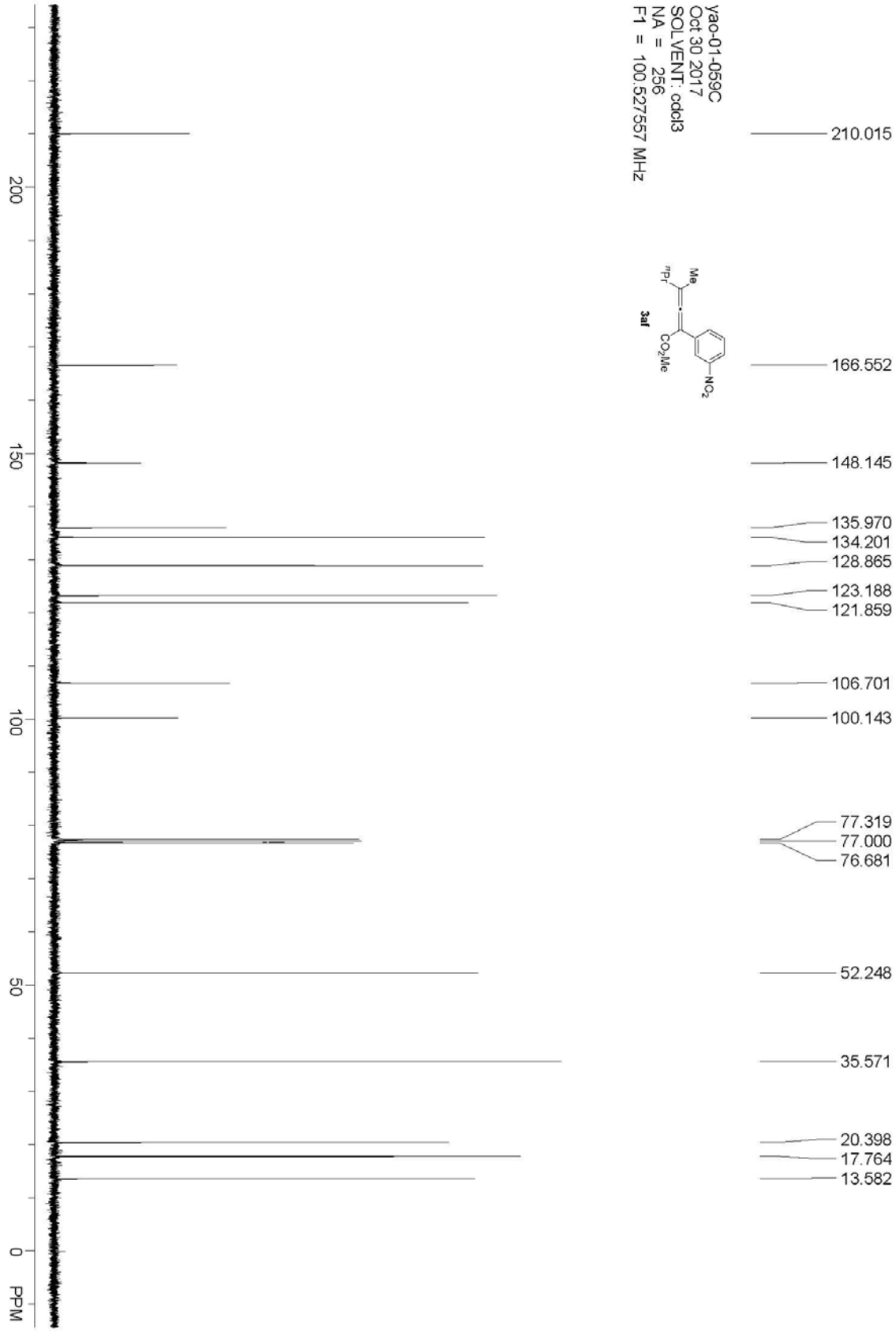

yao-01-122C
Dec 15 2017
SOLVENT: cdcl3
Experiment = s2pul
NA = 256
F1 = 100.527557 MHz
207.715
167.789
156.965
130.604
128.979
124.425
120.417
112.417
111.089
101.745
77.319
77.000
76.681
55.625
52.028
25.469
11.980
Et
Et
MeO
CO2Me
3bd
200
150
100
50
0
PPM

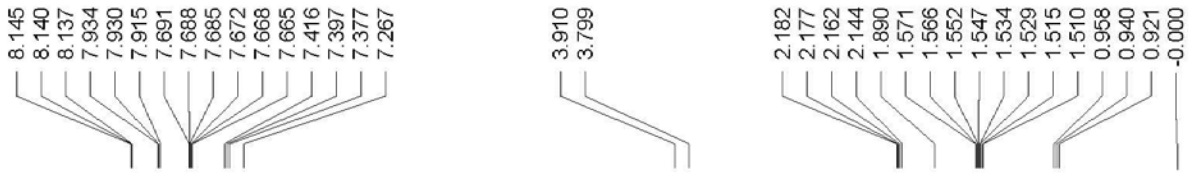

7.294
7.289
7.275
7.274
7.271
7.255
7.251
7.222
7.218
7.203
7.199
6.949
6.946
6.930
6.927
6.911
6.908
6.903
6.882
4.915
3.792
3.735
2.161
2.142
2.128
2.124
2.109
2.091
1.121
1.102
1.084
0.000
MeO
Et
Et
CO2Me
3bd
Purity (100%) determined by using CH2Br2 (14.0 µL, 0.2 mmol)
as the internal standard in 54.0 mg of sample
yao-01-122ccd
Dec 16 2017
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz
2.00
4.17
10
8
6
4
2
0
PPM


yao-01-109
Nov 29 2017
SOLVENT: cd3od
NA = 8
F1 = 399.751129 MHz
3ae
Me
iPr
CO2Me
OH
7.266
7.259
7.253
7.242
7.236
7.229
6.753
6.745
6.740
6.728
6.723
6.717
4.851
3.317
3.313
3.309
3.738
3.305
3.301
2.165
2.147
2.138
2.128
2.119
2.109
2.101
2.082
1.838
1.565
1.547
1.528
1.509
1.492
1.473
0.943
0.924
0.906
-0.000
1.93
1.93
2.96
2.00
2.96
2.00
3.00
PPM

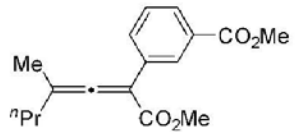

yao-01-109C
Nov 30 2017
SOLVENT: cd3od
NA = 256
F1 = 100.527954 MHz
3ae
209.909
169.376
157.892
130.521
126.035
115.909
105.936
102.793
52.461
49.638
49.425
49.213
49.000
48.788
48.575
48.355
36.711
21.515
18.160
14.039
200
150
100
50
0
PPM


8.378
8.373
8.368
8.109
8.106
8.104
8.102
8.089
8.086
8.083
8.081
7.866
7.862
7.859
7.846
7.842
7.839
7.508
7.489
7.468
7.276
3.820
2.215
2.210
2.194
2.178
2.174
1.922
1.598
1.593
1.581
1.575
1.562
1.556
1.544
1.538
1.526
1.519
1.507
1.502
0.969
0.951
0.933
-0.000
yao-01-059
Oct 30 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
Me
nPr
NO2
CO2Me
3af
0.92
0.98
1.00
1.03
3.18
2.16
3.23
2.15
3.23
10
8
6
4
2
0
PPM

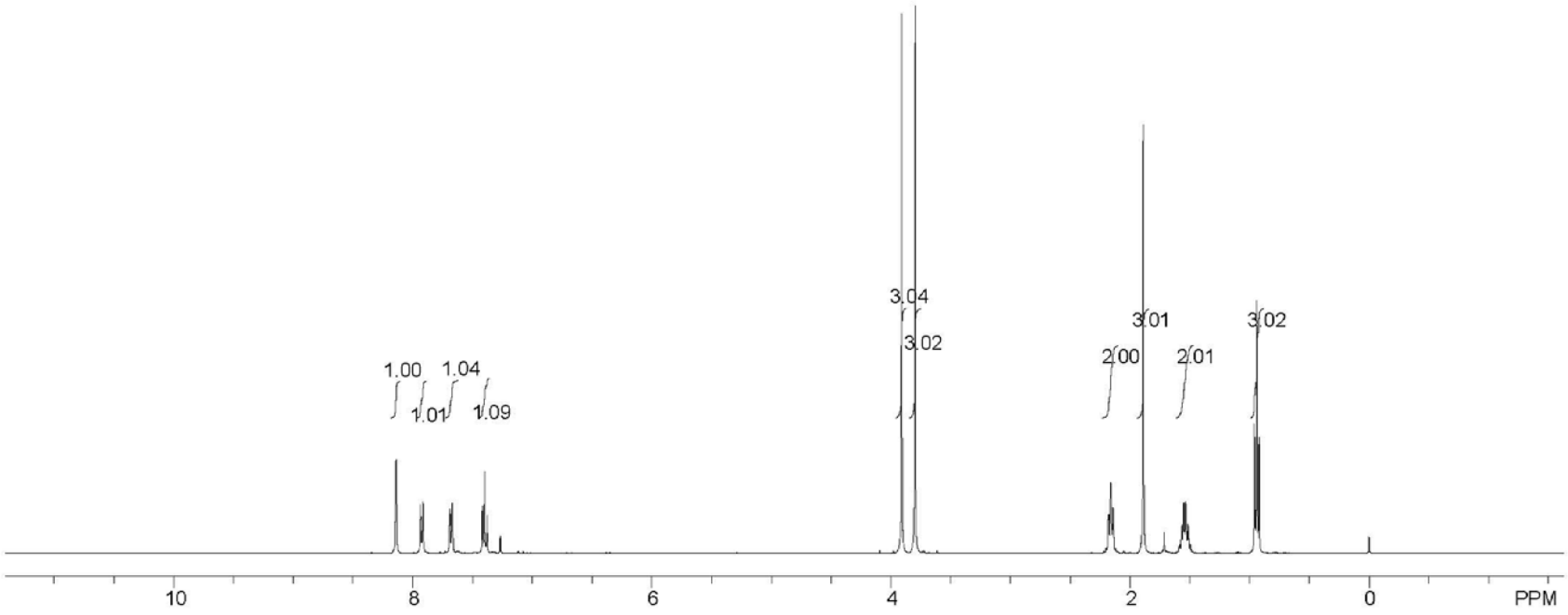

yao-01-059C
Oct 30 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3af
210.015
166.552
148.145
135.970
134.201
128.865
123.188
121.859
106.701
100.143
77.319
77.000
76.681
52.248
35.571
20.398
17.764
13.582
200
150
100
50
0
PPM

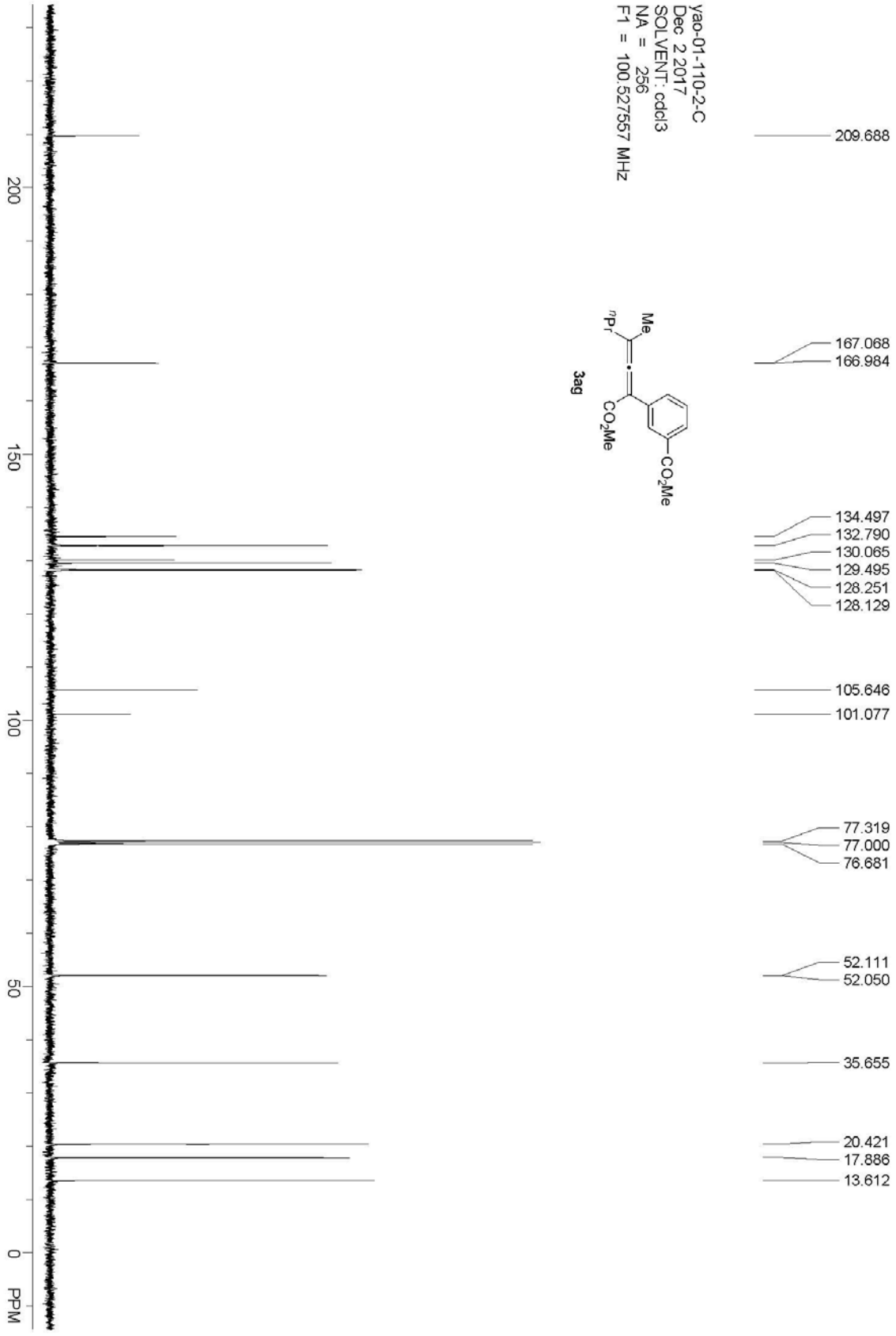


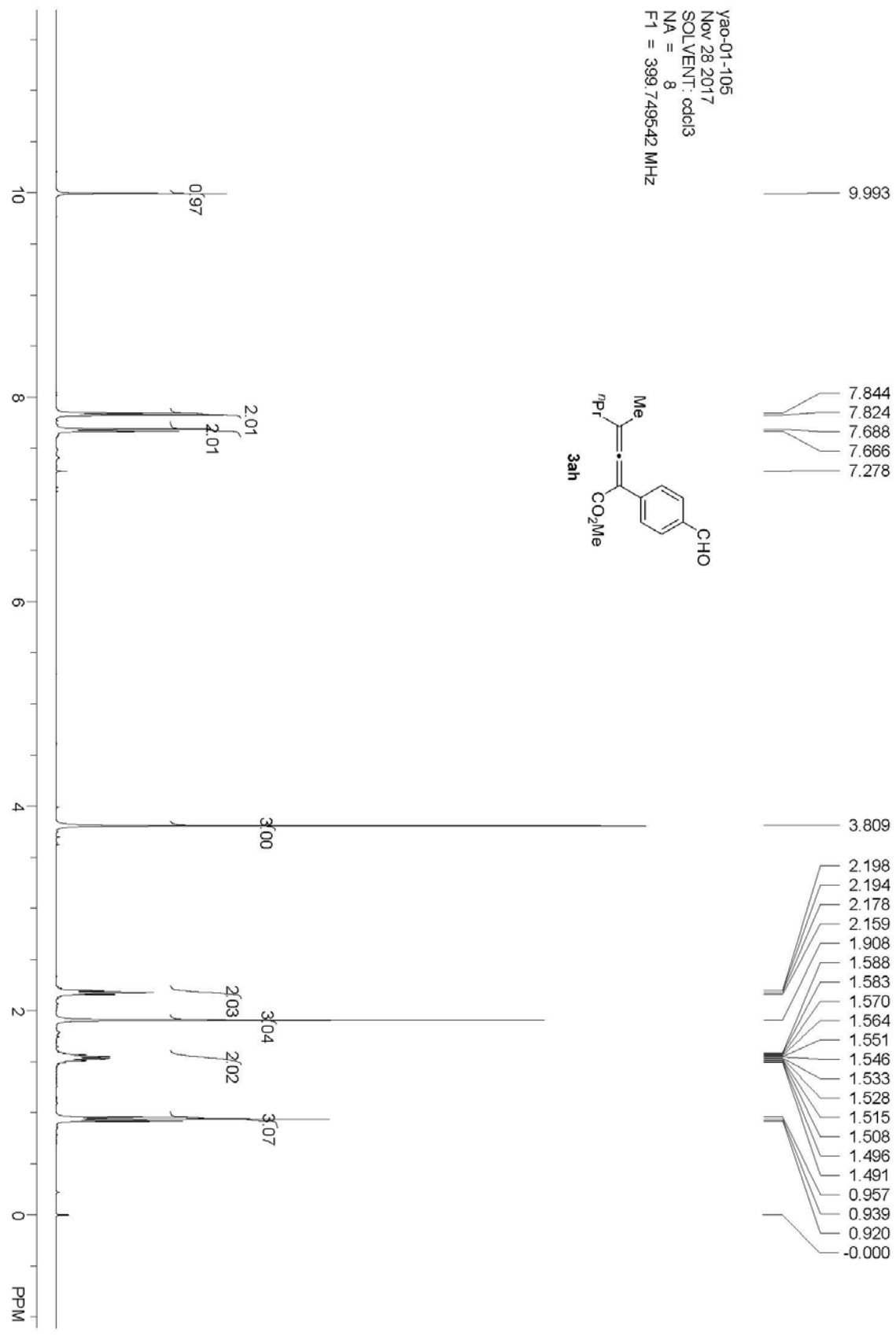
yao-01-110-2
Dec 2 2017
SOLVENT: cdcl3
NA = 1
F1 = 399.749542 MHz

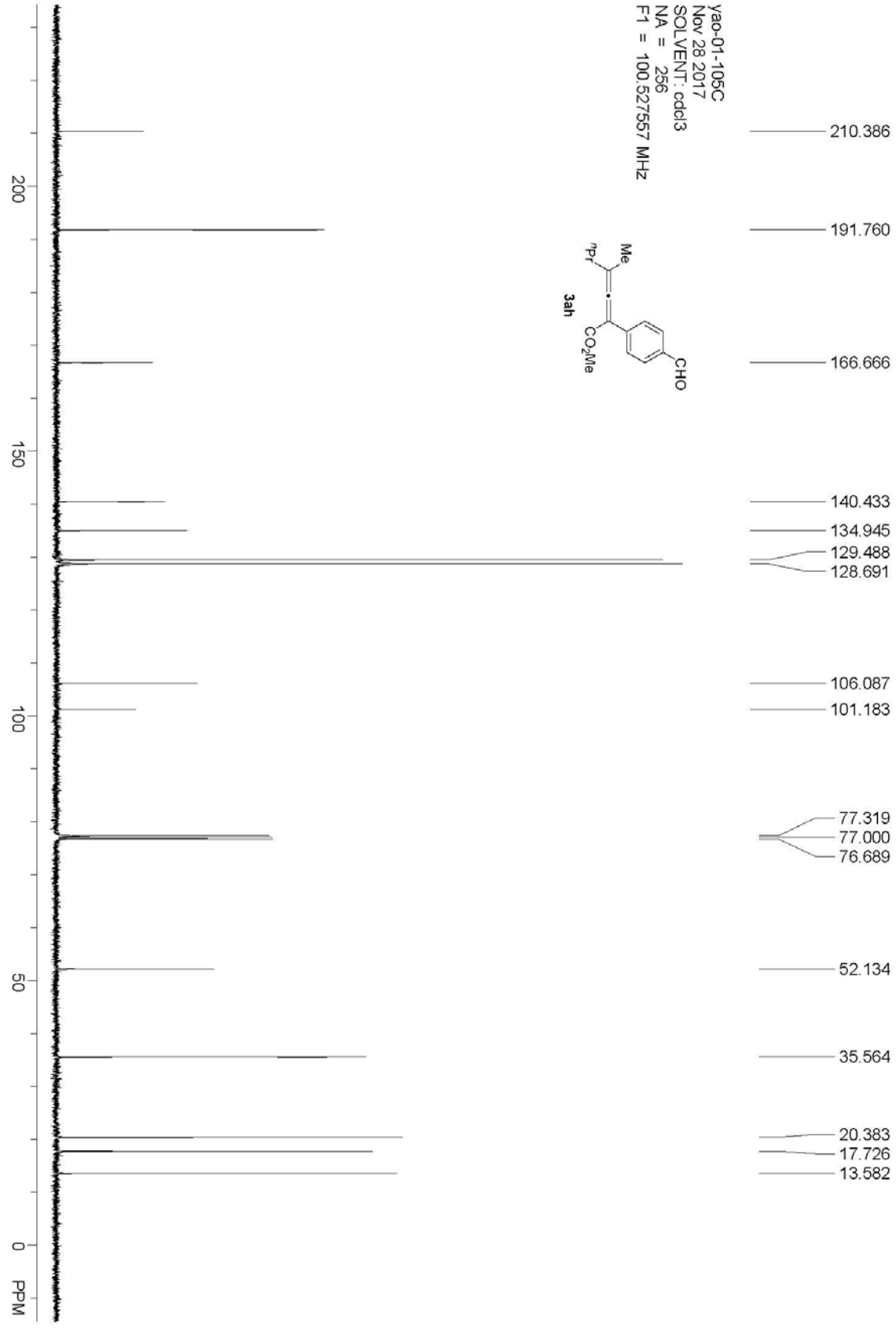


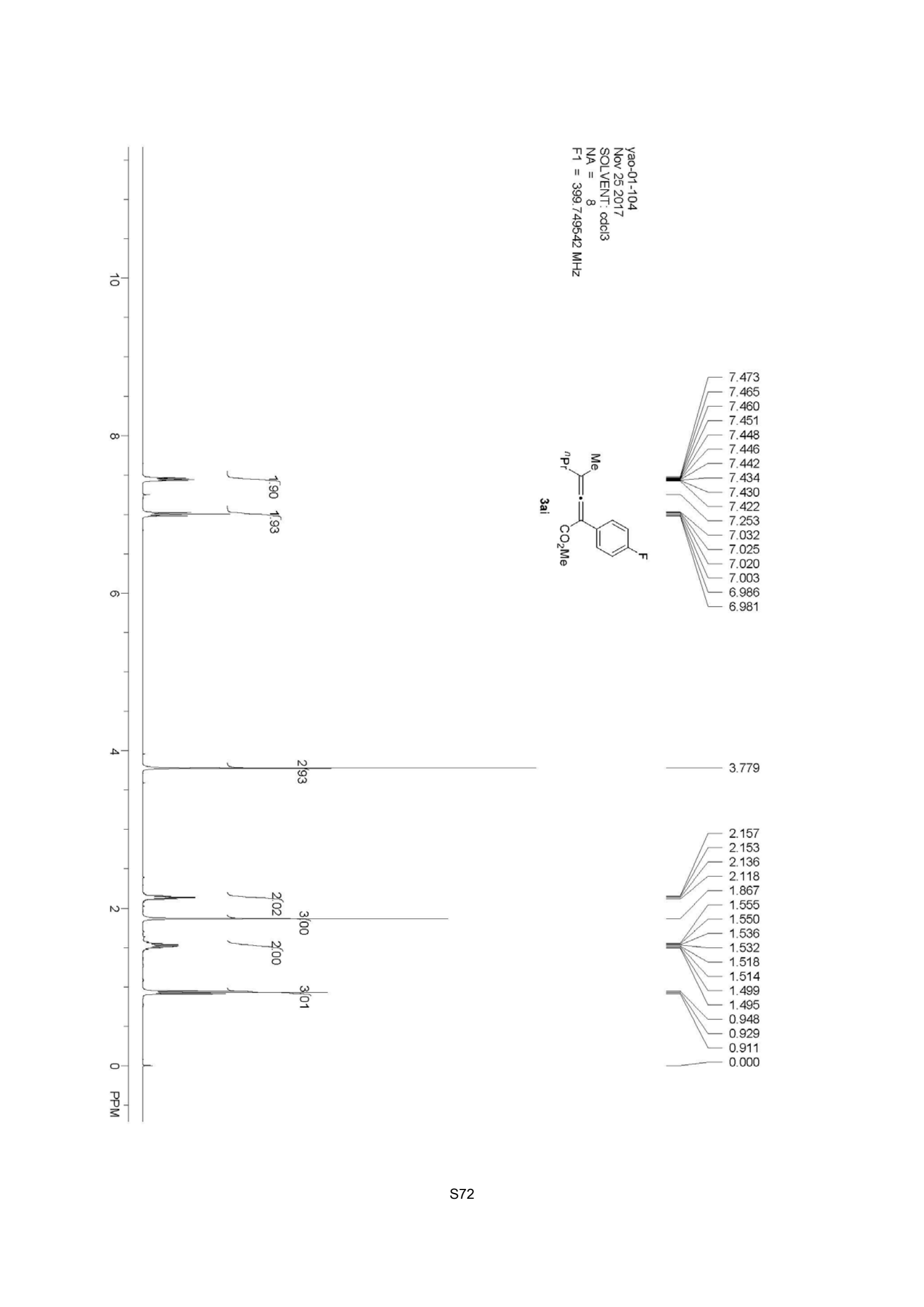
3ag

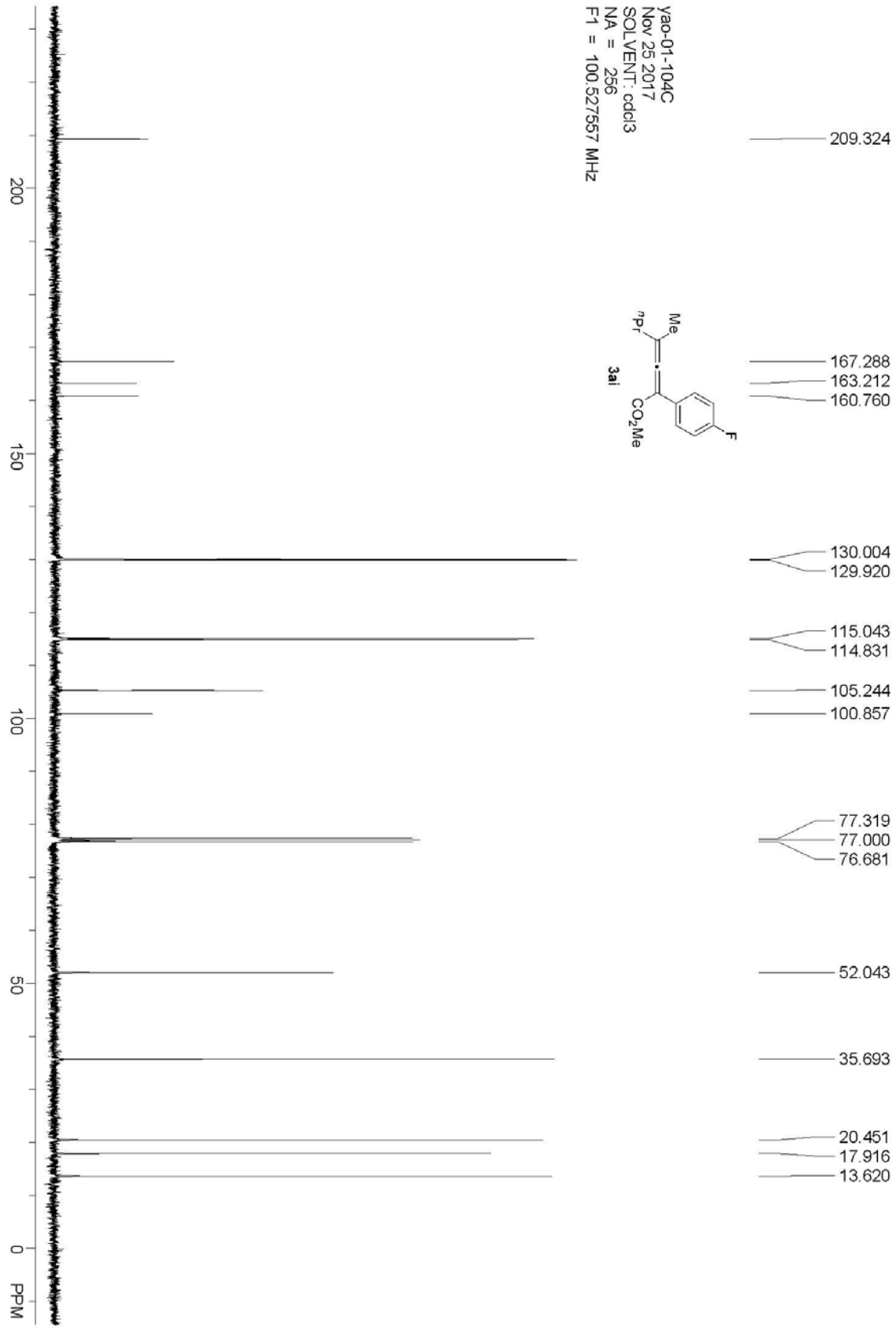


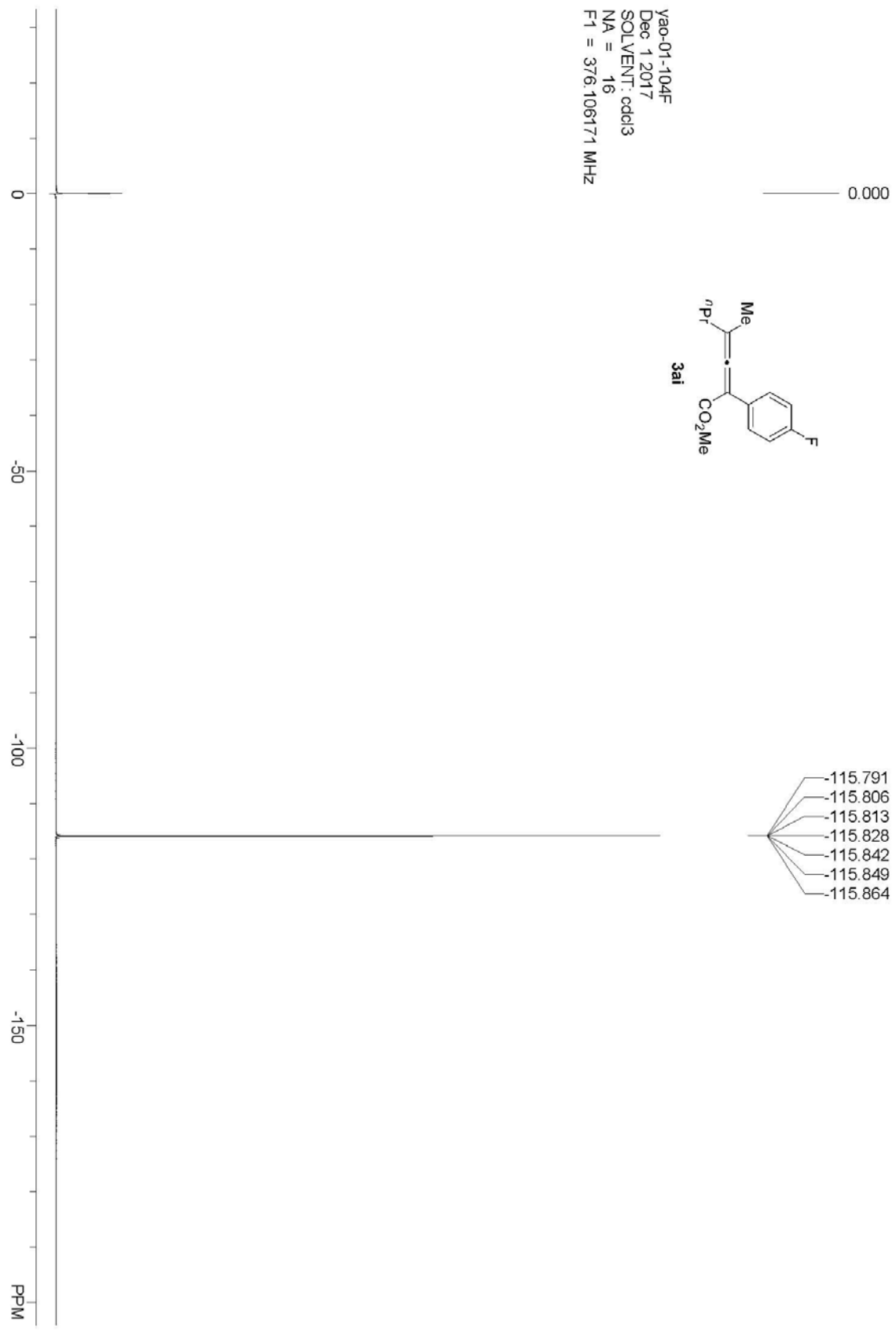

yao-01-110-2-C
Dec 2 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ag
Me
nPr
CO2Me
CO2Me
209.688
167.068
166.984
134.497
132.790
130.065
129.495
128.251
128.129
105.646
101.077
77.319
77.000
76.681
52.111
52.050
35.655
20.421
17.886
13.612
200
150
100
50
0
PPM

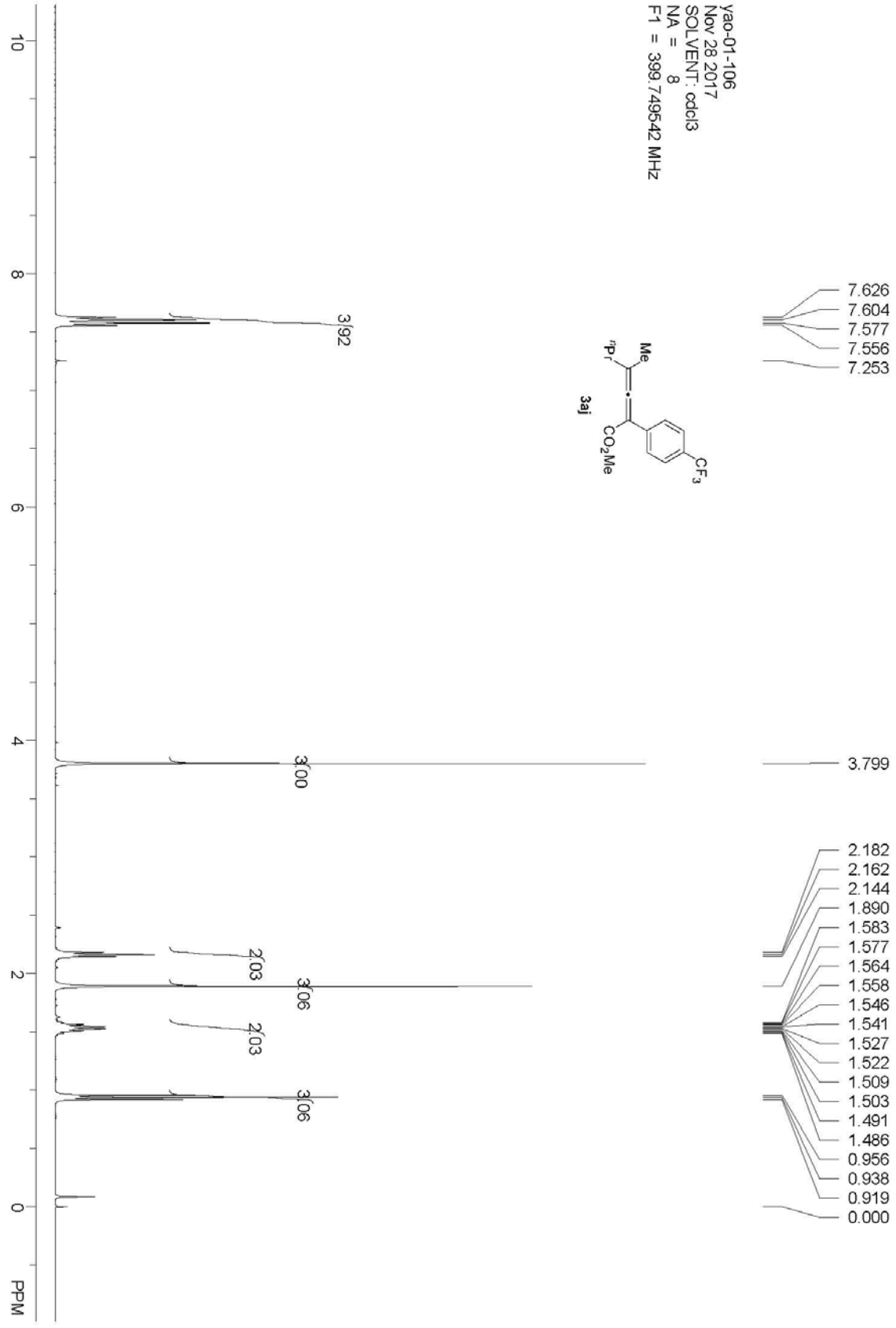

yao-01-105
Nov 28 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
9.993
7.844
7.824
7.688
7.666
7.278
3.809
2.198
2.194
2.178
2.159
1.908
1.588
1.583
1.570
1.564
1.551
1.546
1.533
1.528
1.515
1.508
1.496
1.491
0.957
0.939
0.920
-0.000
0.97
2.01
2.01
3.00
2.03
3.04
2.02
3.07
3ah
Me
nPr
CO2Me
CHO
10
8
6
4
2
0
PPM

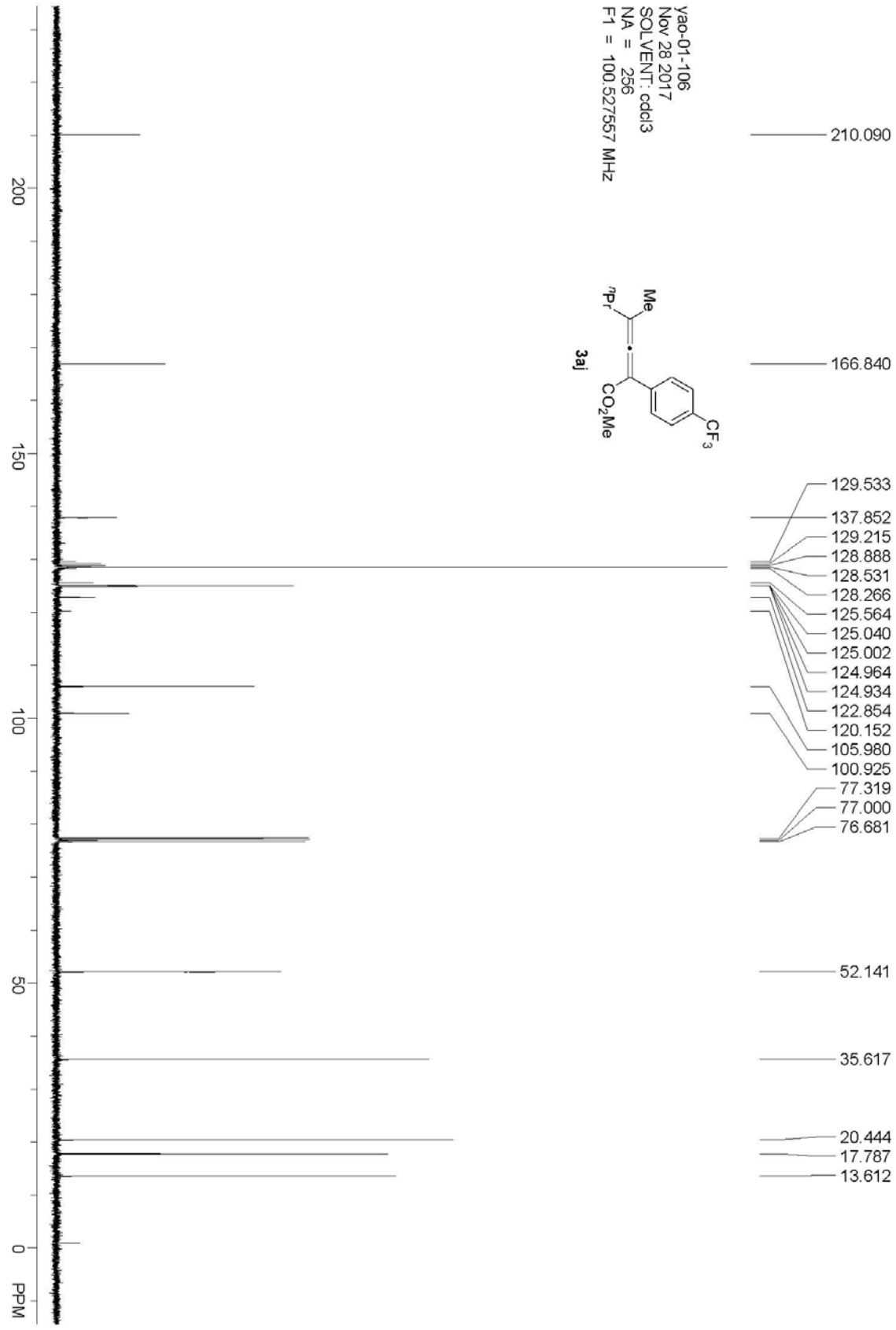

yao-01-105C
Nov 28 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ah
Me
nPr
CO2Me
CHO
210.386
191.760
166.666
140.433
134.945
129.488
128.691
106.087
101.183
77.319
77.000
76.689
52.134
35.564
20.383
17.726
13.582
200
150
100
50
0
PPM

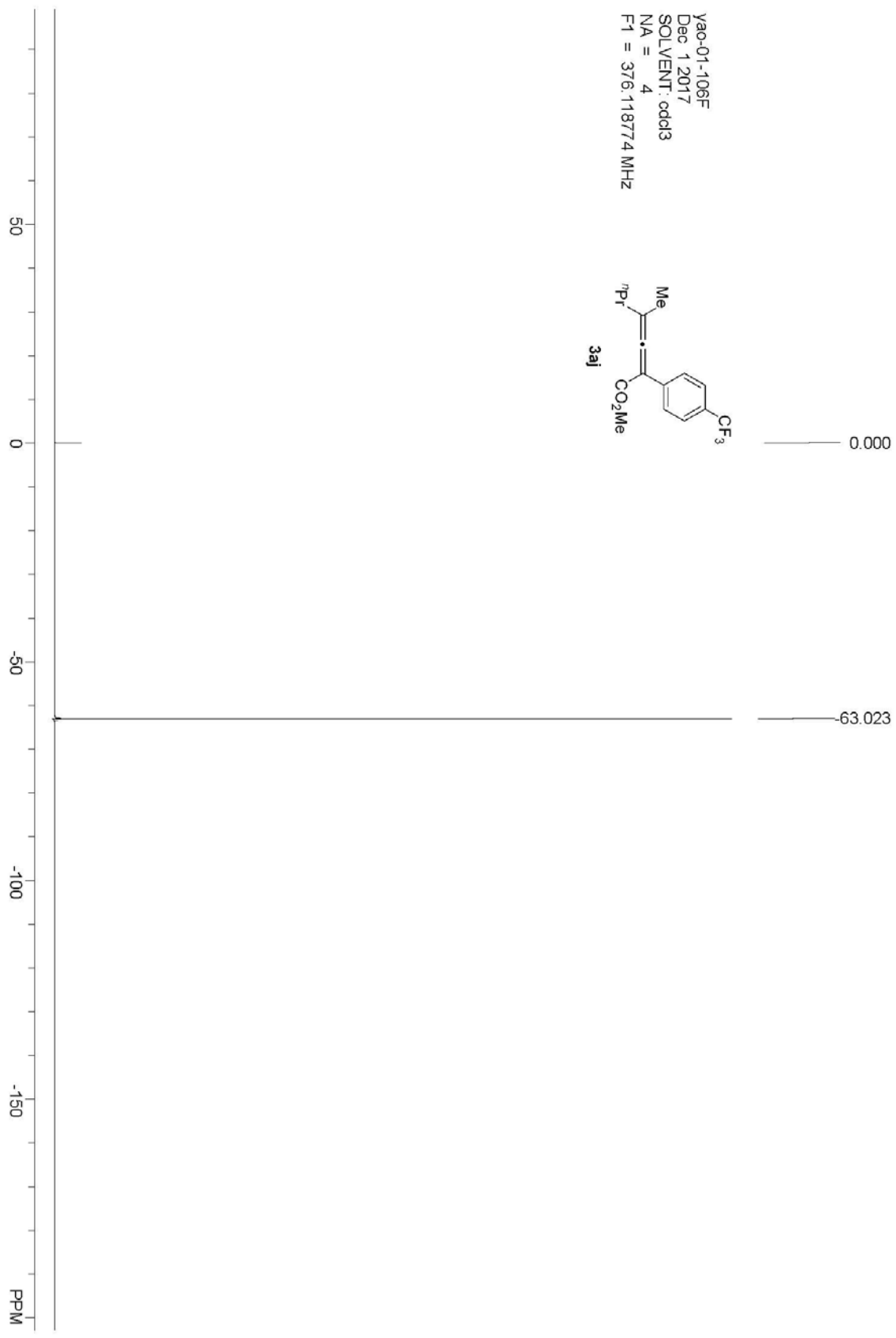

yao-01-104
Nov 25 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3ai
Me
nPr
CO2Me
F
7.473
7.465
7.460
7.451
7.448
7.446
7.442
7.434
7.430
7.422
7.253
7.032
7.025
7.020
7.003
6.986
6.981
3.779
2.157
2.153
2.136
2.118
1.867
1.555
1.550
1.536
1.532
1.518
1.514
1.499
1.495
0.948
0.929
0.911
0.000
1.90
1.93
2.93
2.02
3.00
2.00
3.01
10
8
6
4
2
0
PPM

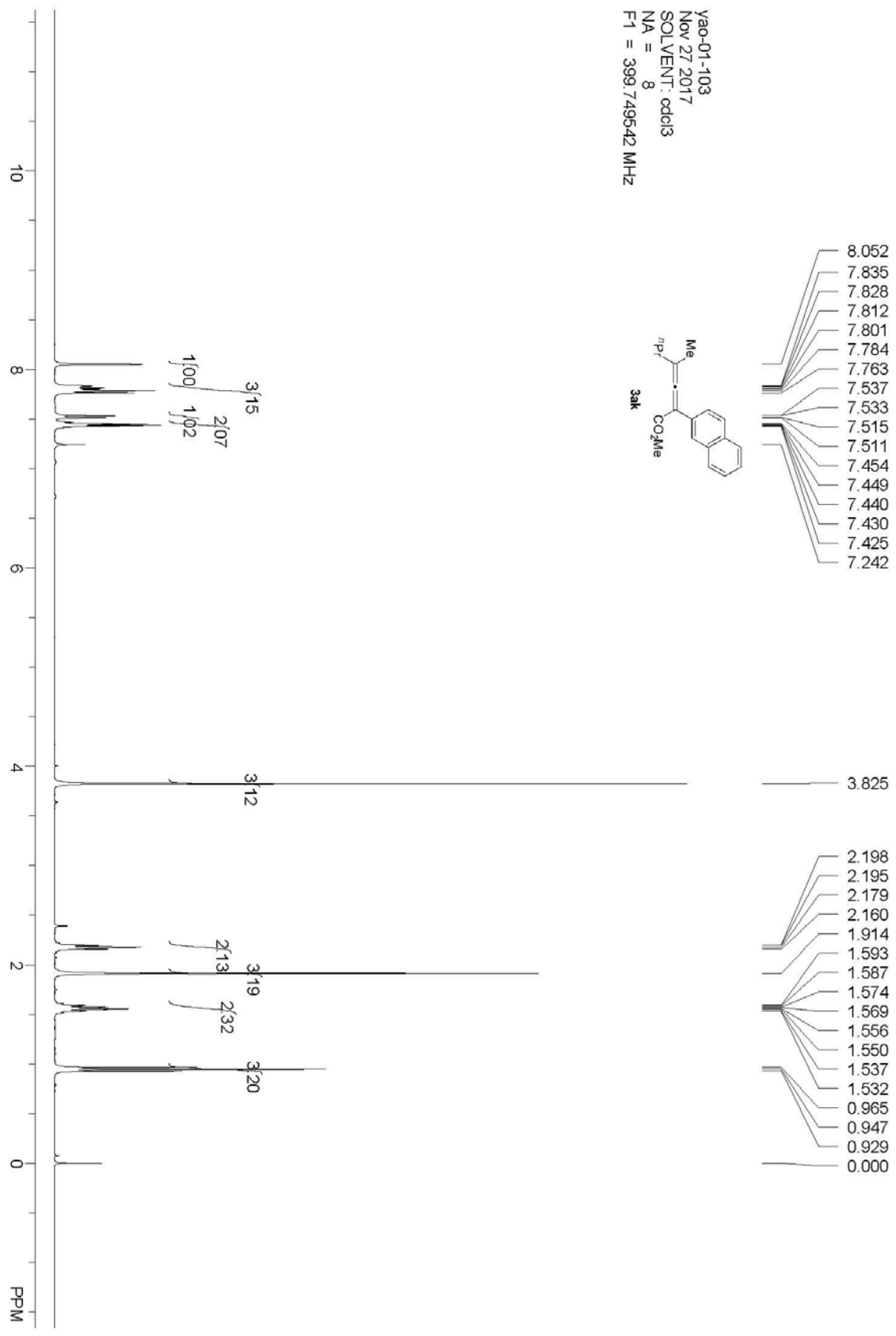

yao-01-104C
Nov 25 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ai
209.324
167.288
163.212
160.760
130.004
129.920
115.043
114.831
105.244
100.857
77.319
77.000
76.681
52.043
35.693
20.451
17.916
13.620
200
150
100
50
0
PPM

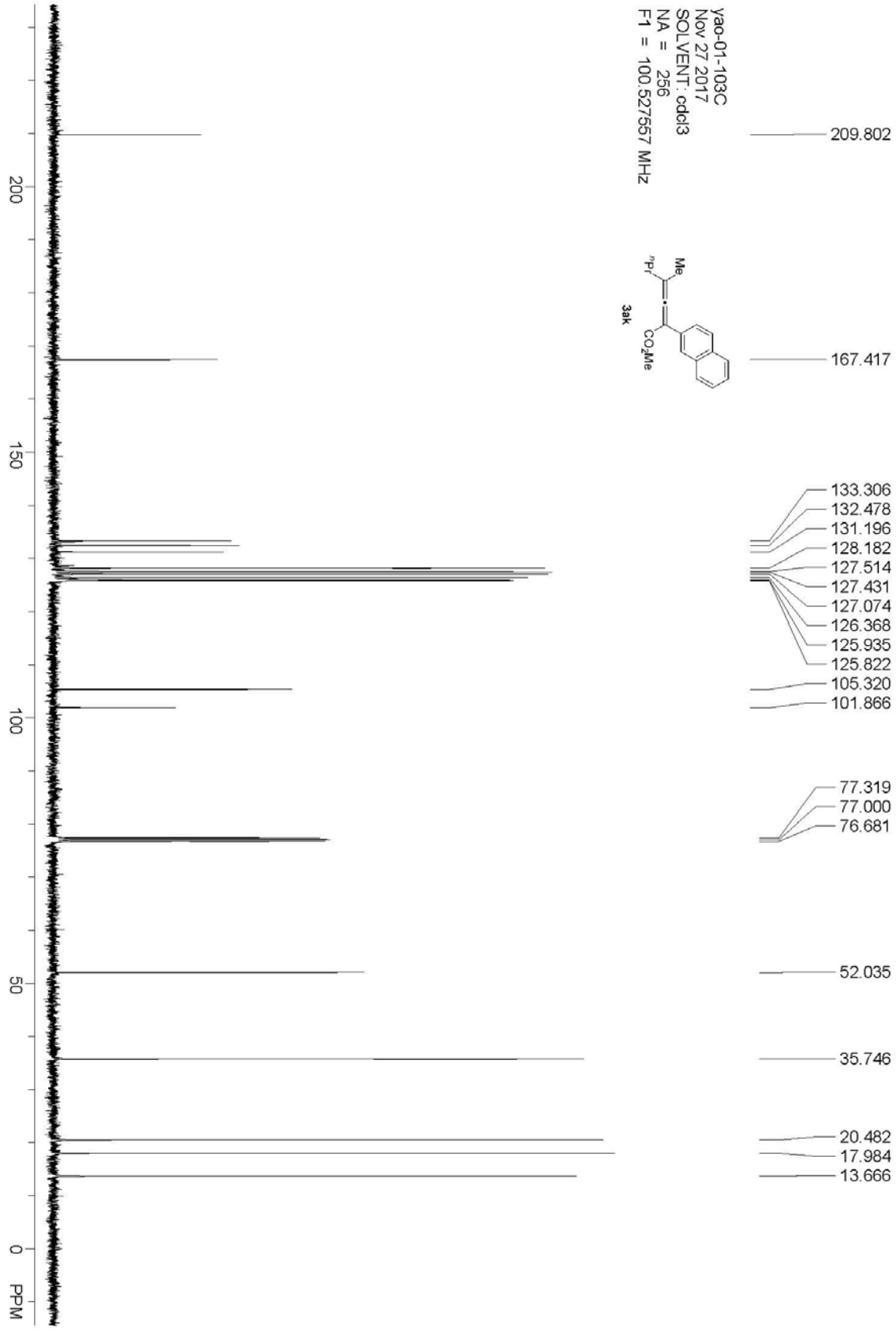

yao-01-104F
Dec 1 2017
SOLVENT: cdcl3
NA = 16
F1 = 376.106171 MHz
0.000
3ai
Me
nPr
CO2Me
F
-115.791
-115.806
-115.813
-115.828
-115.842
-115.849
-115.864
0
-50
-100
-150
PPM

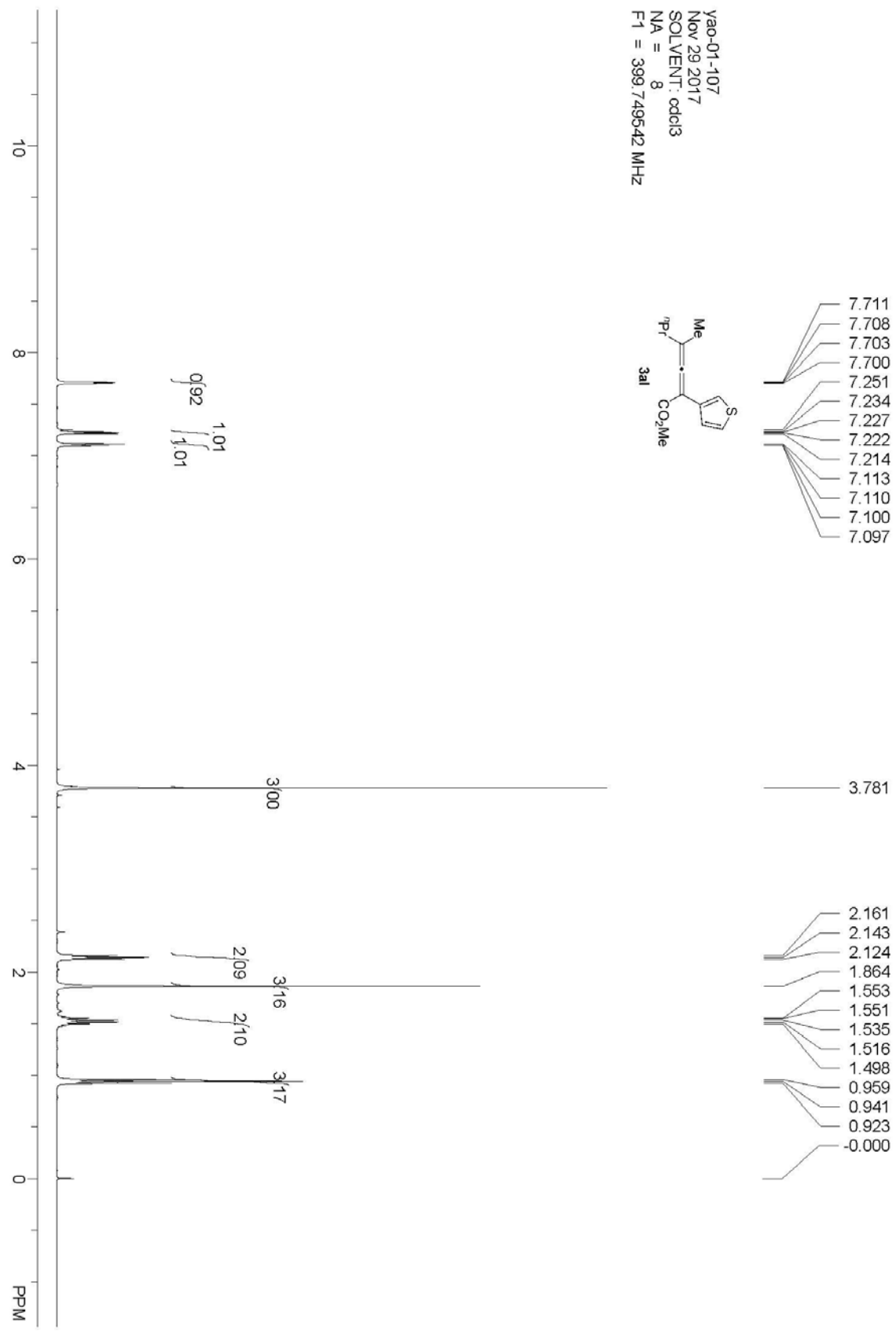

yao-01-106
Nov 28 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3aj
Me
iPr
CO2Me
CF3
7.626
7.604
7.577
7.556
7.253
3.799
2.182
2.162
2.144
1.890
1.583
1.577
1.564
1.558
1.546
1.541
1.527
1.522
1.509
1.503
1.491
1.486
0.956
0.938
0.919
0.000
3.92
3.00
2.03
3.06
2.03
3.06
10
8
6
4
2
0
PPM

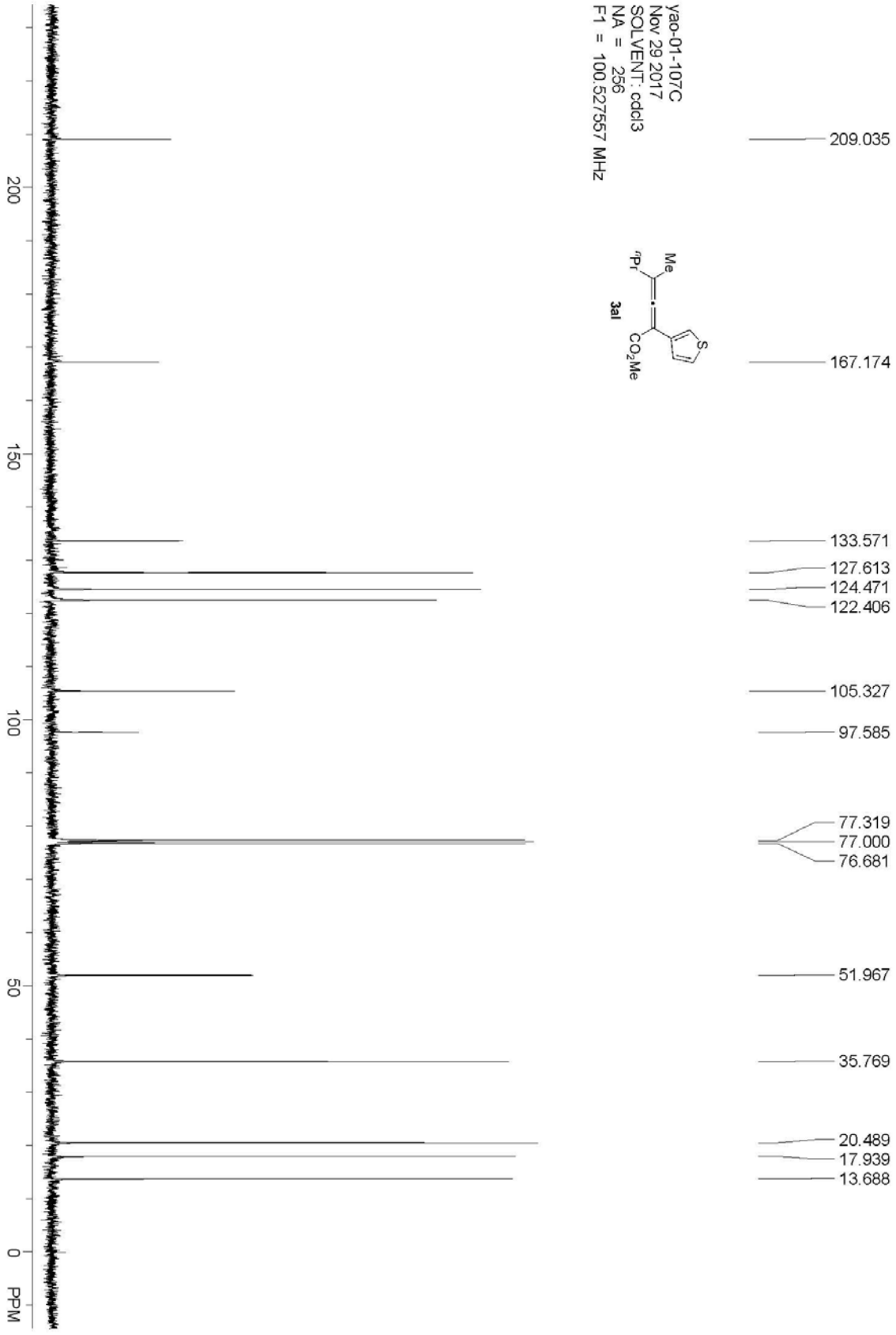

yao-01-106
Nov 28 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3aj
Me
nPr
CO2Me
CF3
210.090
166.840
129.533
137.852
129.215
128.888
128.531
128.266
125.564
125.040
125.002
124.964
124.934
122.854
120.152
105.980
100.925
77.319
77.000
76.681
52.141
35.617
20.444
17.787
13.612
200
150
100
50
0
PPM

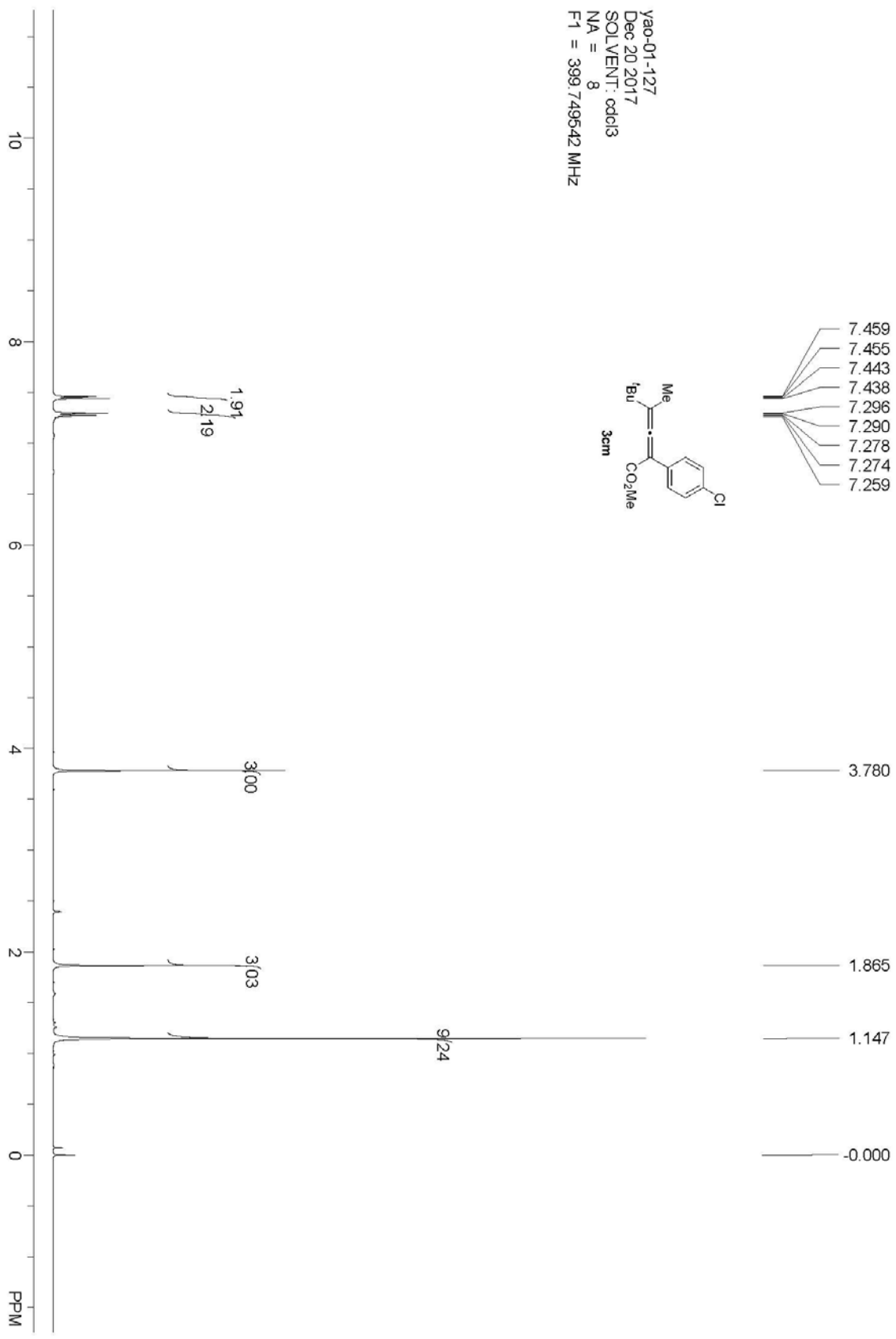

yao-01-106F
Dec 1 2017
SOLVENT: cdcl3
NA = 4
F1 = 376.118774 MHz
3aj
Me
nPr
CO2Me
CF3
0.000
-63.023
50
0
-50
-100
-150
PPM

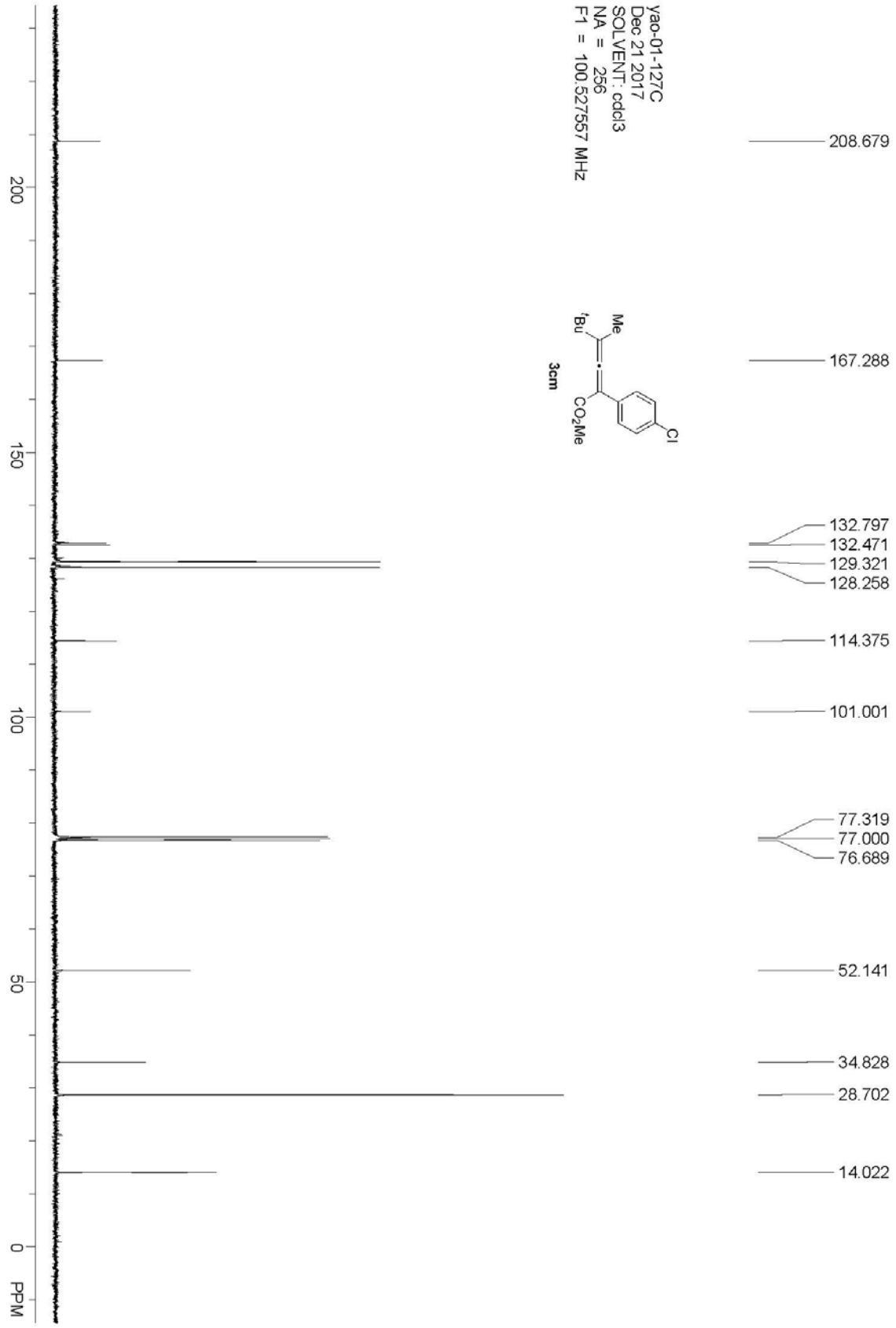

yao-01-103
Nov 27 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3ak
Me
nPr
CO2Me
8.052
7.835
7.828
7.812
7.801
7.784
7.763
7.537
7.533
7.515
7.511
7.454
7.449
7.440
7.430
7.425
7.242
3.825
2.198
2.195
2.179
2.160
1.914
1.593
1.587
1.574
1.569
1.556
1.550
1.537
1.532
0.965
0.947
0.929
0.000
3.15
2.07
1.00
1.02
3.12
2.13
3.19
2.32
3.20
10
8
6
4
2
0
PPM

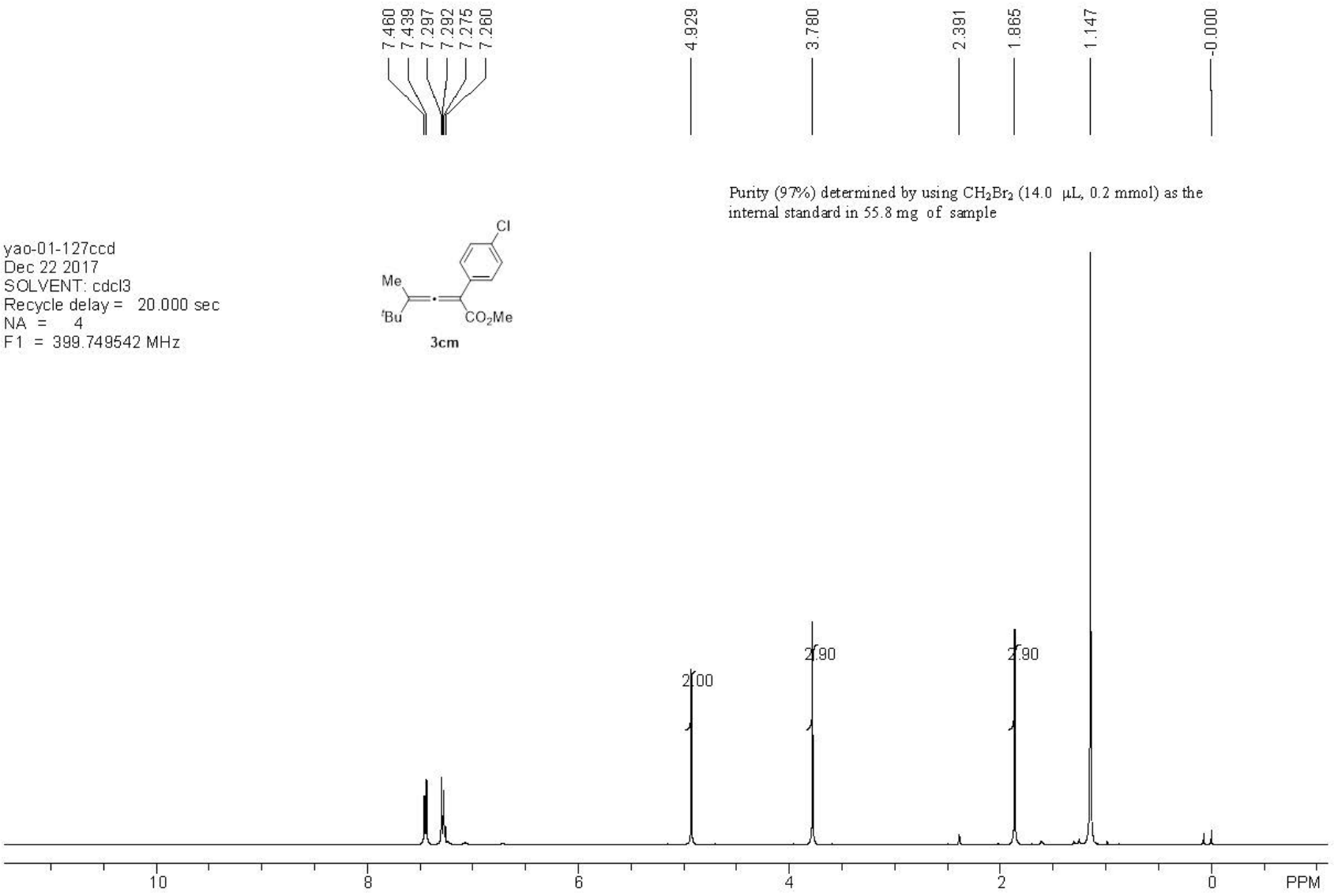

yao-01-103C
Nov 27 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ak
Me
nPr
CO2Me
209.802
167.417
133.306
132.478
131.196
128.182
127.514
127.431
127.074
126.368
125.935
125.822
105.320
101.866
77.319
77.000
76.681
52.035
35.746
20.482
17.984
13.666
200
150
100
50
0
PPM

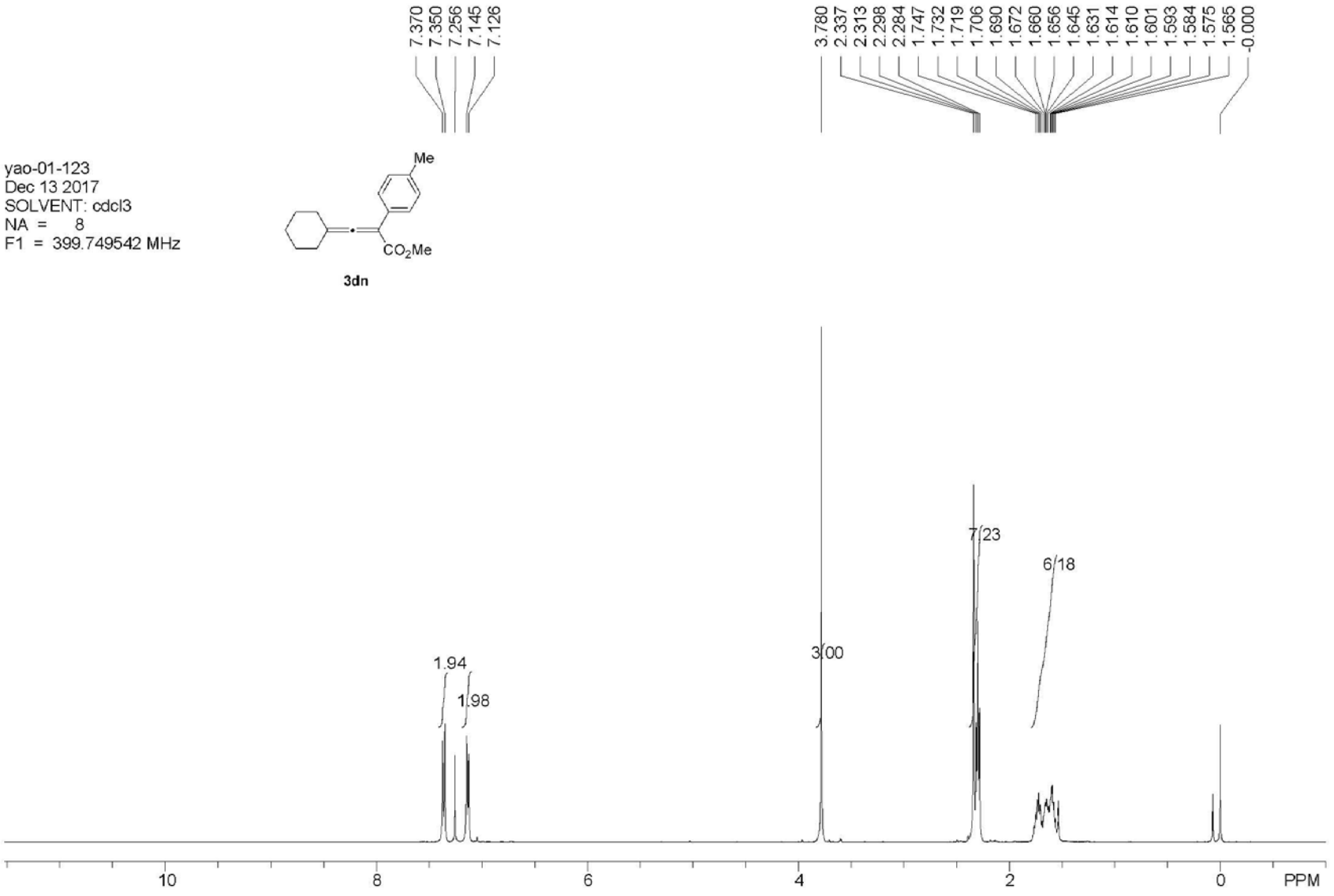

yao-01-107
Nov 29 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3al
Me
nPr
CO2Me
S
7.711
7.708
7.703
7.700
7.251
7.234
7.227
7.222
7.214
7.113
7.110
7.100
7.097
3.781
2.161
2.143
2.124
1.864
1.553
1.551
1.535
1.516
1.498
0.959
0.941
0.923
-0.000
0.92
1.01
1.01
3.00
2.09
3.16
2.10
3.17
10
8
6
4
2
0
PPM

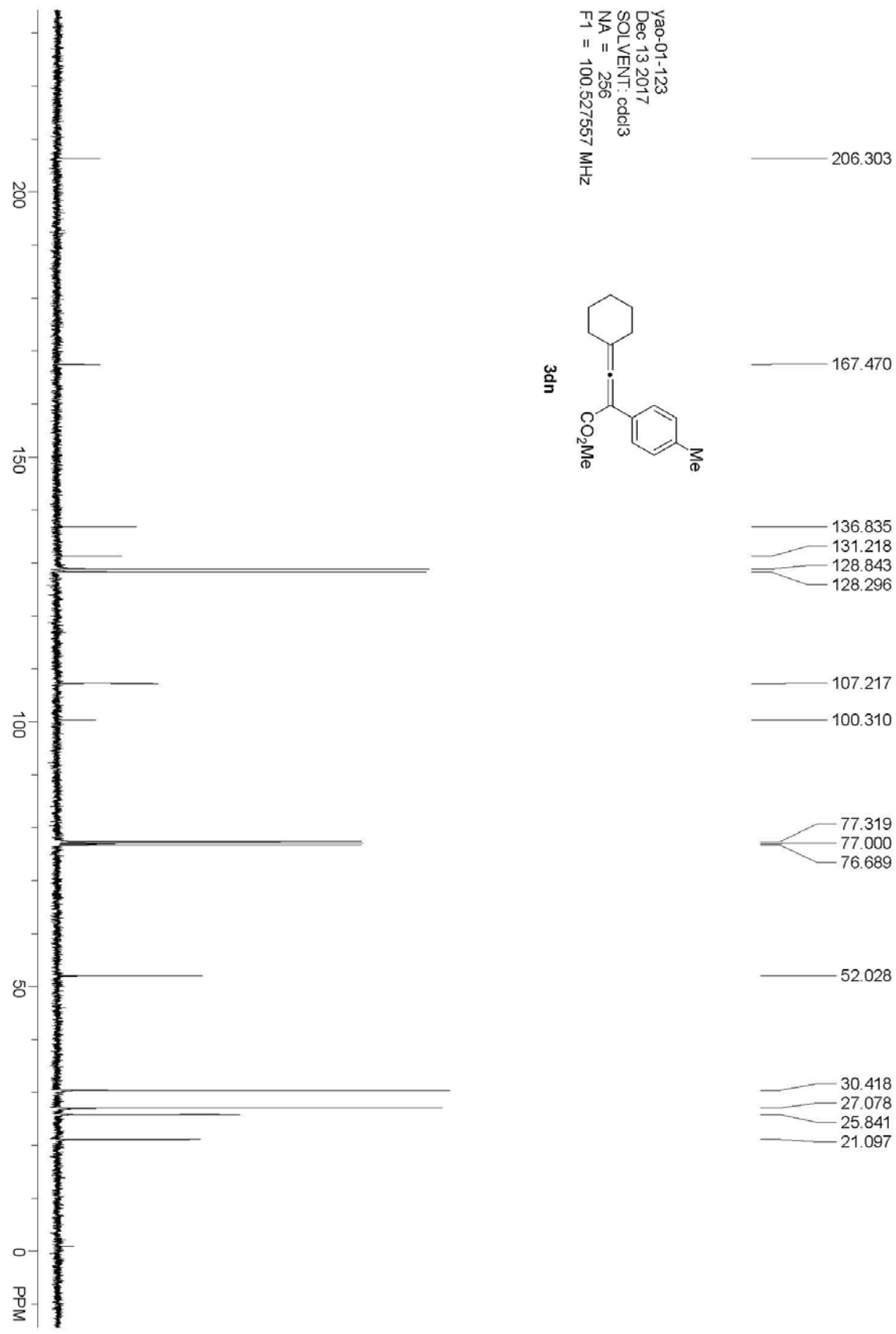

yao-01-107C
Nov 29 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3al
Me
iPr
CO2Me
S
209.035
167.174
133.571
127.613
124.471
122.406
105.327
97.585
77.319
77.000
76.681
51.967
35.769
20.489
17.939
13.688
200
150
100
50
0
PPM

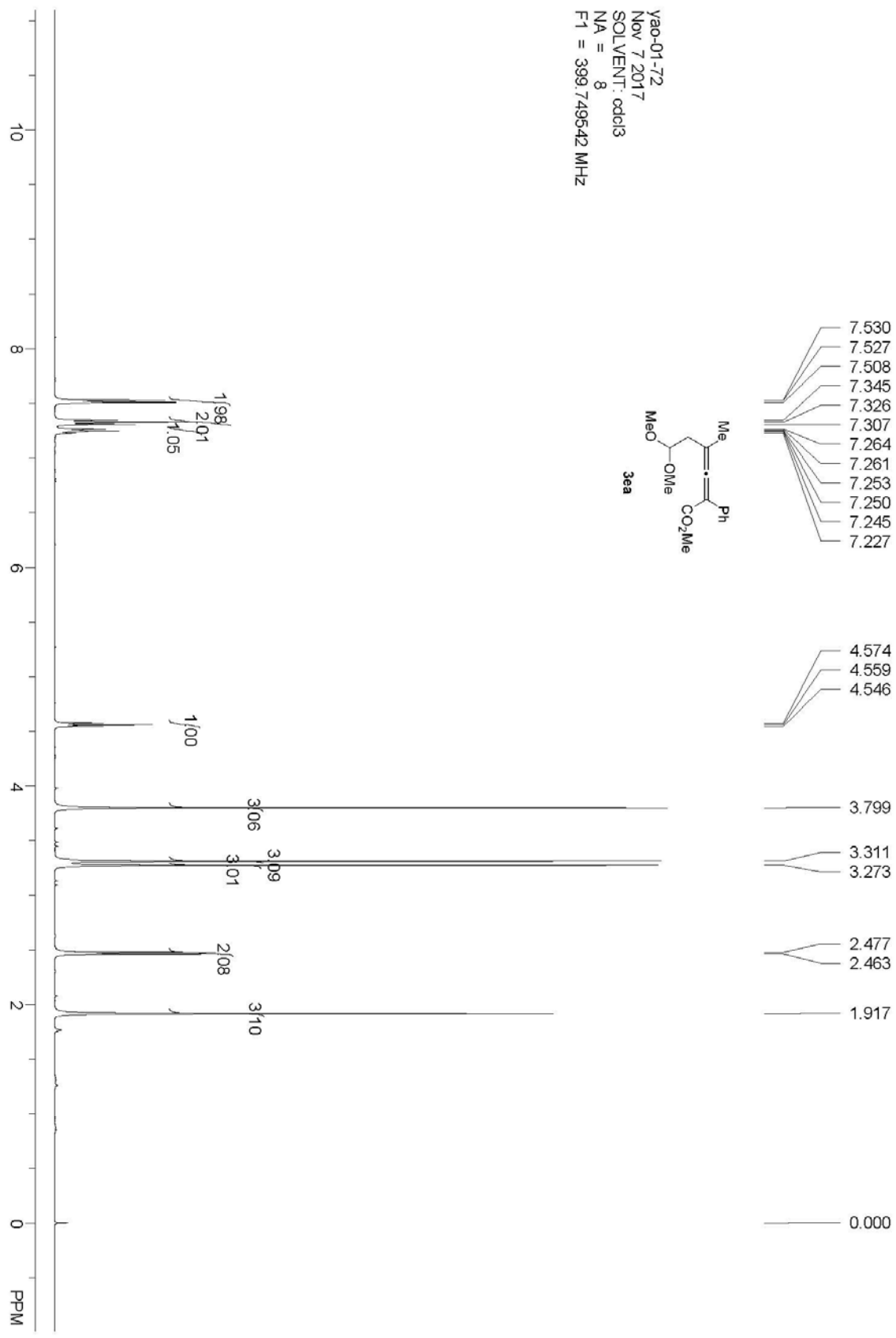

yao-01-127
Dec 20 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3cm
Me
tBu
CO2Me
Cl
7.459
7.455
7.443
7.438
7.296
7.290
7.278
7.274
7.259
3.780
1.865
1.147
-0.000
1.91
2.19
3.00
3.03
9.24
10
8
6
4
2
0
PPM

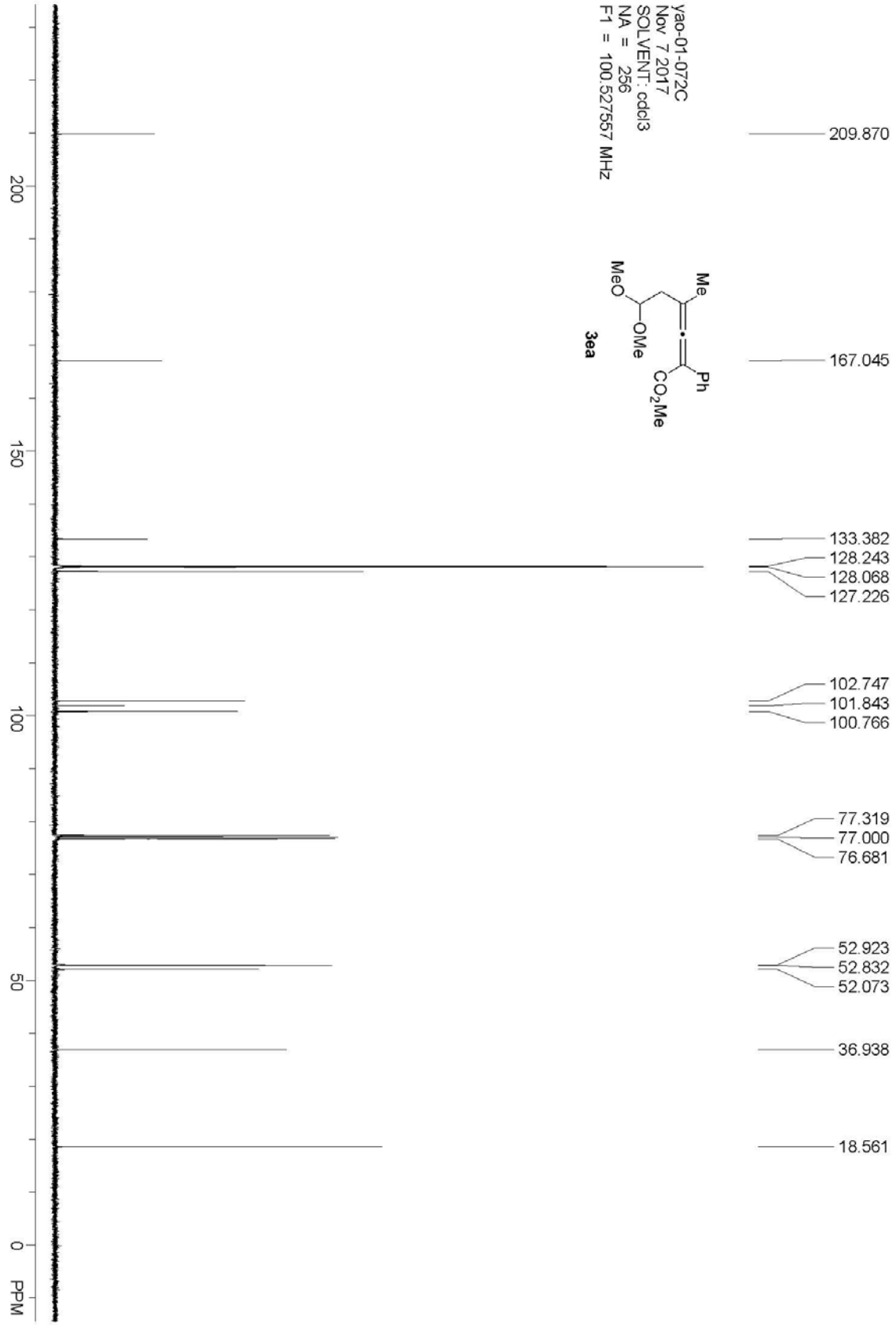

yao-01-127C
Dec 21 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3cm
Me
tBu
CO2Me
Cl
208.679
167.288
132.797
132.471
129.321
128.258
114.375
101.001
77.319
77.000
76.689
52.141
34.828
28.702
14.022
200
150
100
50
0
PPM

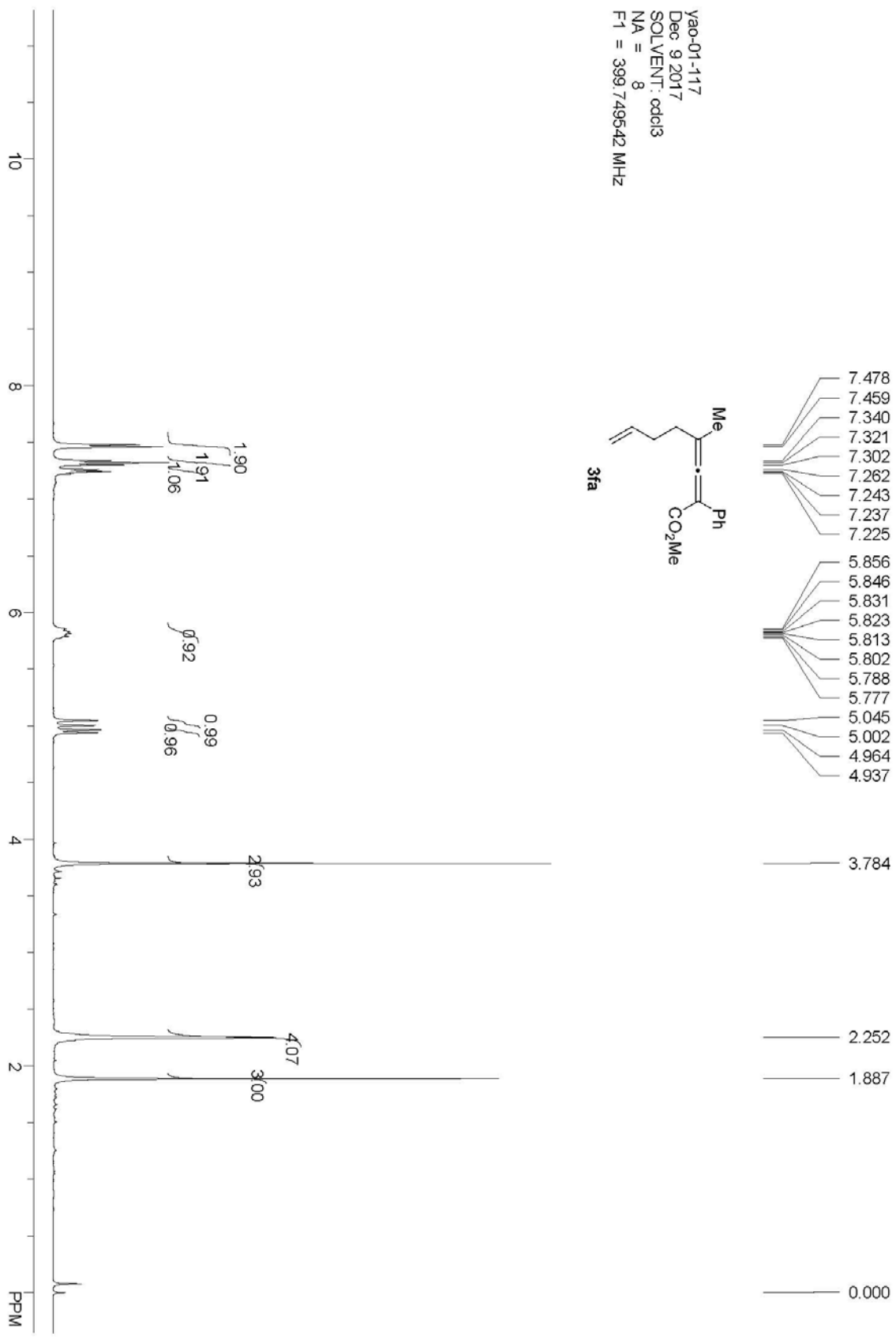

7.460
7.439
7.297
7.292
7.275
7.260
4.929
3.780
2.391
1.865
1.147
-0.000
Purity (97%) determined by using CH_2Br_2 (14.0 µL, 0.2 mmol) as the internal standard in 55.8 mg of sample
yao-01-127ccd
Dec 22 2017
SOLVENT: cdcl3
Recycle delay = 20.000 sec
NA = 4
F1 = 399.749542 MHz
Cl
Me
tBu
CO2Me
3cm
2.00
2.90
2.90
10
8
6
4
2
0
PPM

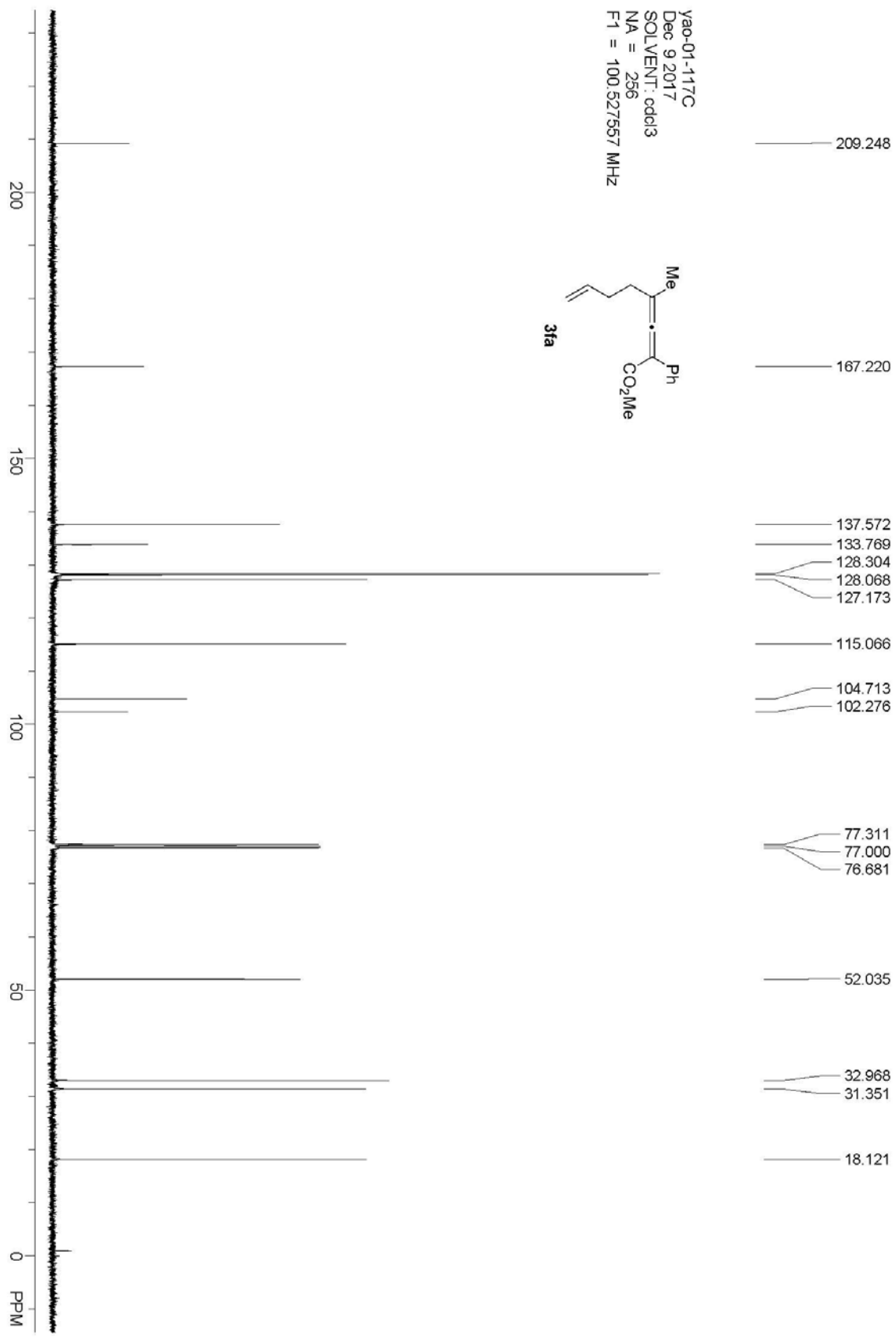

7.370
7.350
7.256
7.145
7.126
3.780
2.337
2.313
2.298
2.284
1.747
1.732
1.719
1.706
1.690
1.672
1.660
1.656
1.645
1.631
1.614
1.610
1.601
1.593
1.584
1.575
1.565
-0.000
yao-01-123
Dec 13 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
Me
CO2Me
3dn
1.94
1.98
3.00
7.23
6.18
10
8
6
4
2
0
PPM

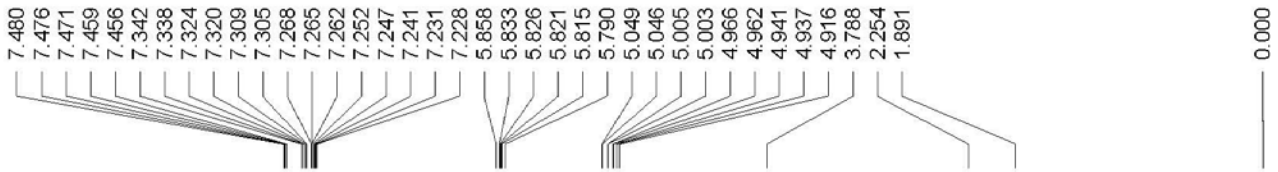

yao-01-123
Dec 13 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3dn
CO2Me
Me
206.303
167.470
136.835
131.218
128.843
128.296
107.217
100.310
77.319
77.000
76.689
52.028
30.418
27.078
25.841
21.097
200
150
100
50
0
PPM


yao-01-72
Nov 7 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3ea
7.530
7.527
7.508
7.345
7.326
7.307
7.264
7.261
7.253
7.250
7.245
7.227
4.574
4.559
4.546
3.799
3.311
3.273
2.477
2.463
1.917
0.000
1.98
2.01
1.05
1.00
3.06
3.09
3.01
2.08
3.10
PPM

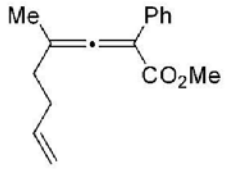

yao-01-072C
Nov 7 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ea
Me
MeO
OMe
Ph
CO2Me
209.870
167.045
133.382
128.243
128.068
127.226
102.747
101.843
100.766
77.319
77.000
76.681
52.923
52.832
52.073
36.938
18.561
200
150
100
50
0
PPM


yao-01-117
Dec 9 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
3fa
Me
Ph
CO2Me
7.478
7.459
7.340
7.321
7.302
7.262
7.243
7.237
7.225
5.856
5.846
5.831
5.823
5.813
5.802
5.788
5.777
5.045
5.002
4.964
4.937
3.784
2.252
1.887
0.000
1.90
1.91
1.06
0.92
0.99
0.96
2.93
4.07
3.00
10
8
6
4
2
PPM


yao-01-117C
Dec 9 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3fa
Me
Ph
CO2Me
209.248
167.220
137.572
133.769
128.304
128.068
127.173
115.066
104.713
102.276
77.311
77.000
76.681
52.035
32.968
31.351
18.121
200
150
100
50
0
PPM

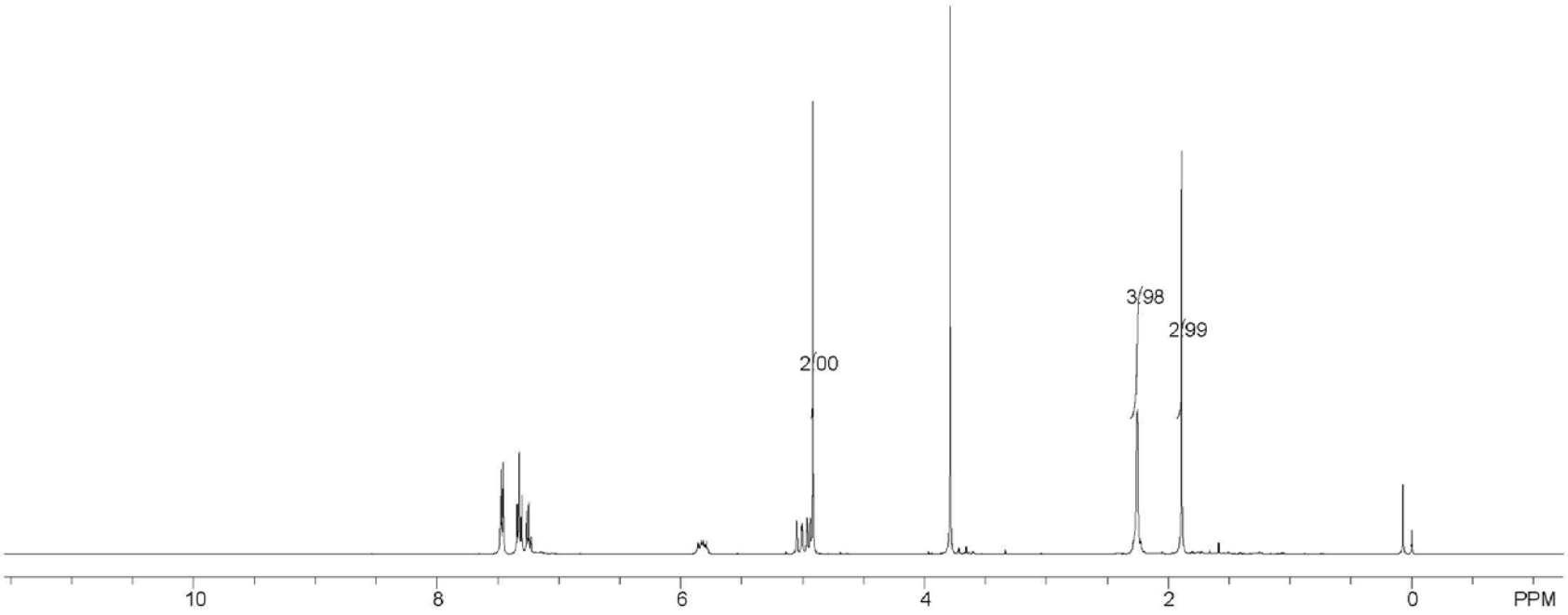


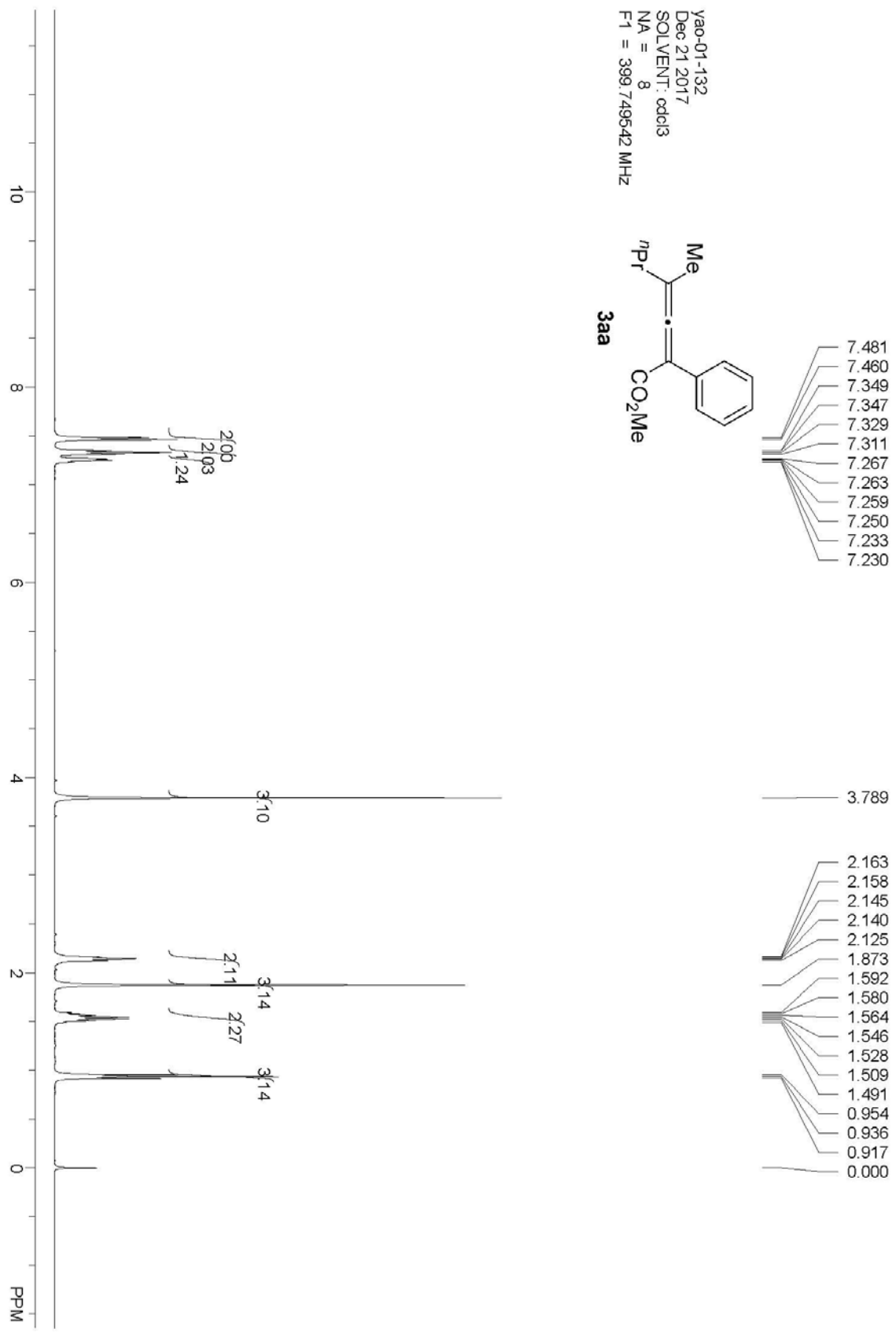
yao-01-117ccd
Dec 9 2017
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz

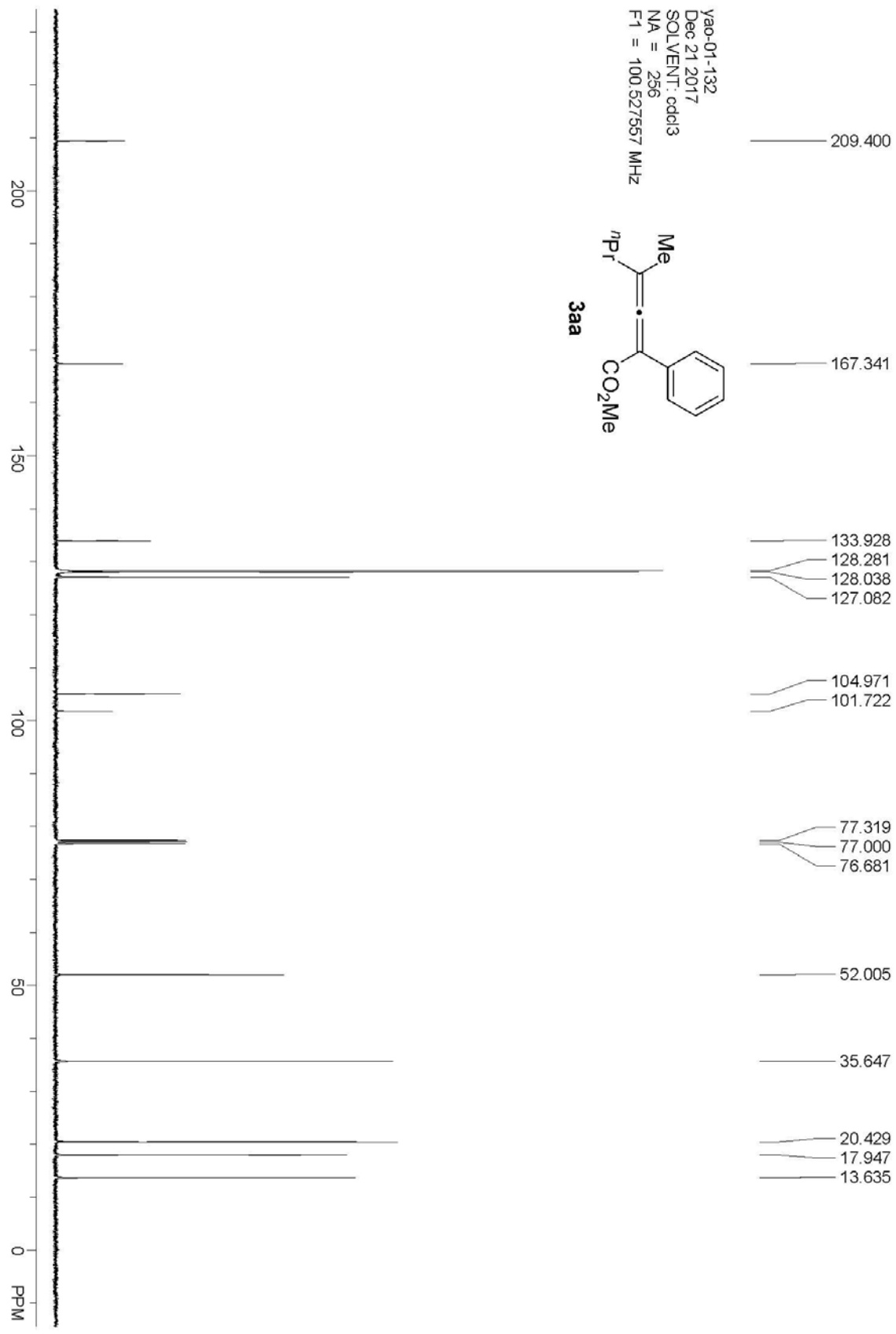


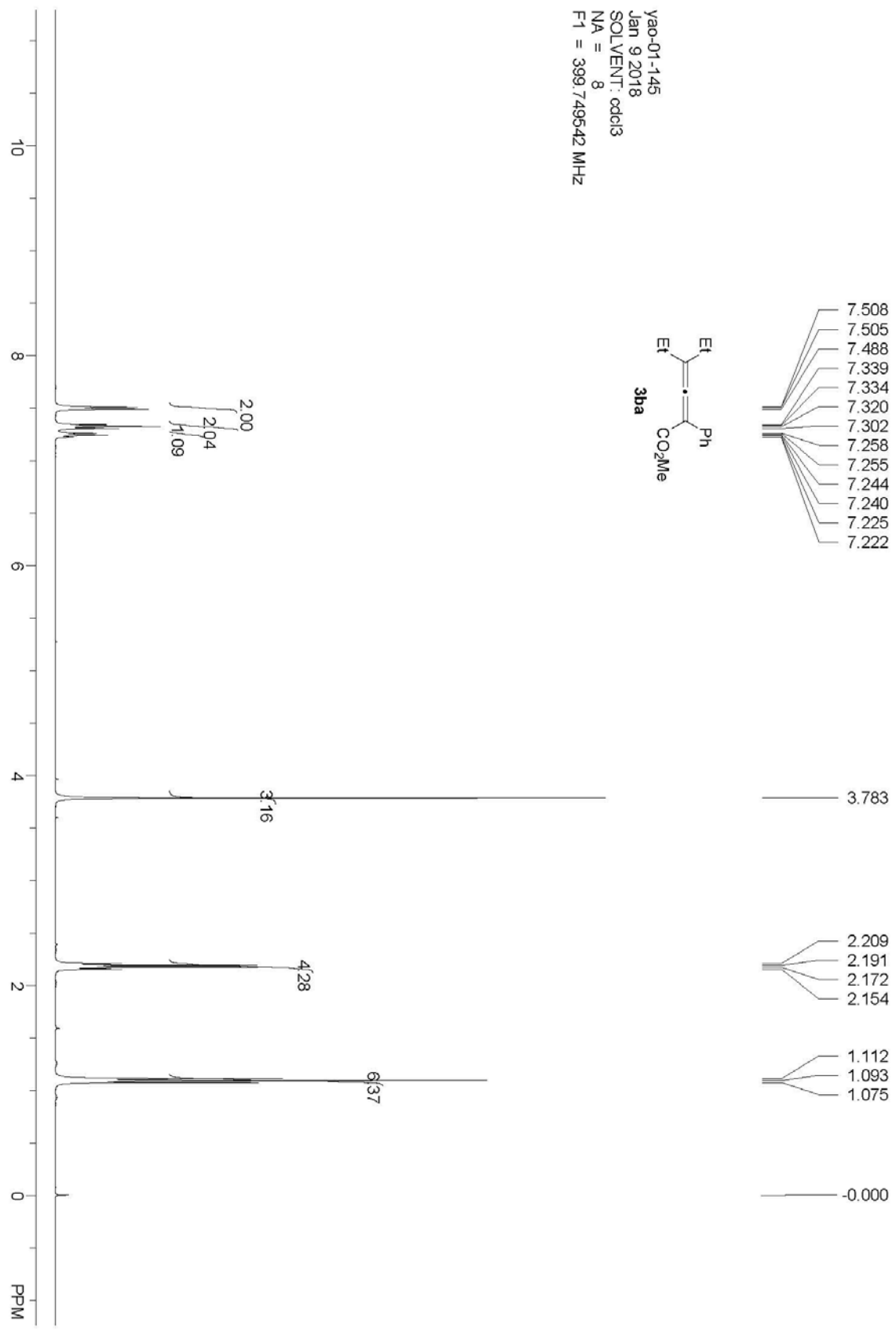
3fa

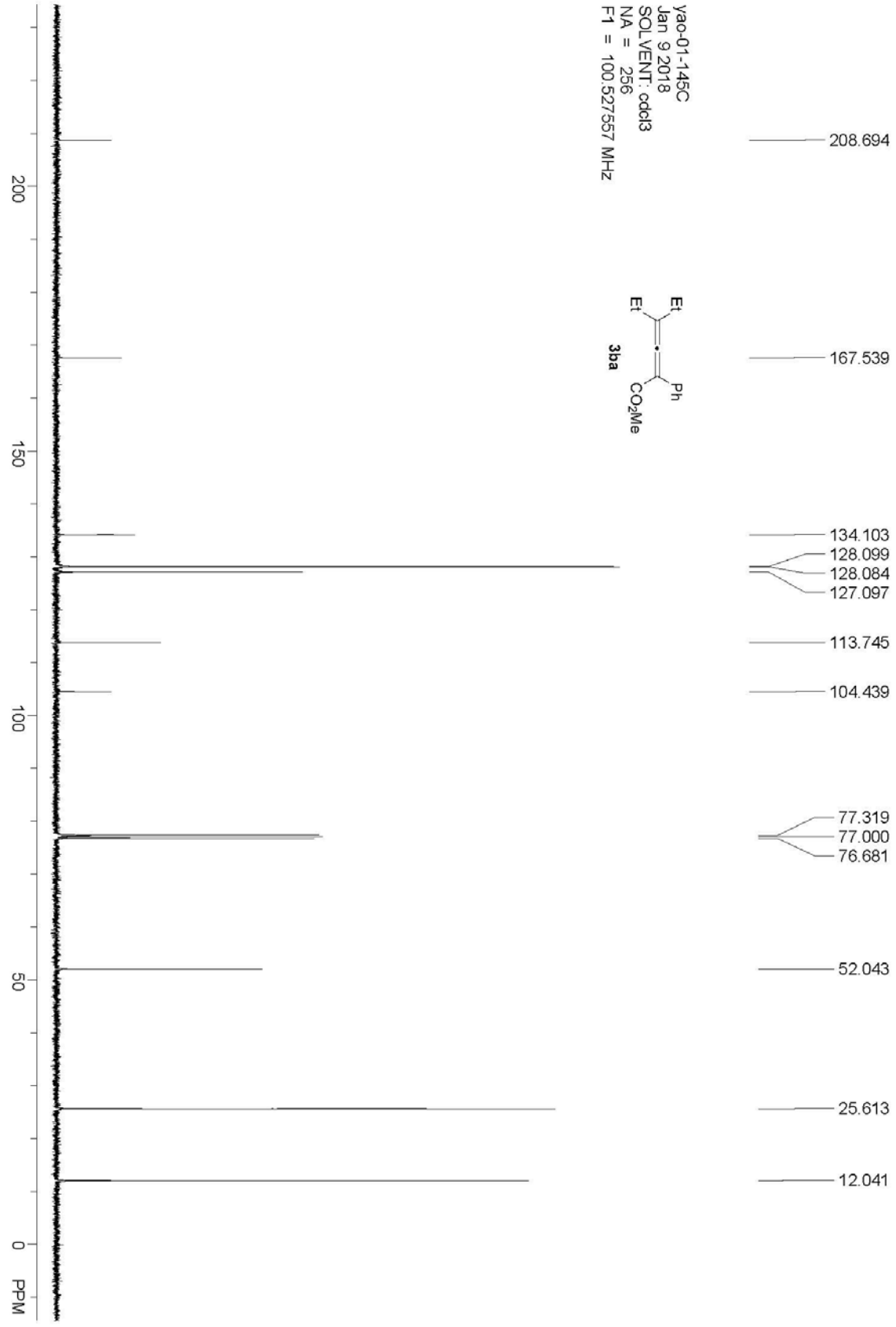
Purity (100%) determined by using CH_2Br_2 (14.0 μL, 0.2 mmol) as the internal standard in 48.0 mg of sample.

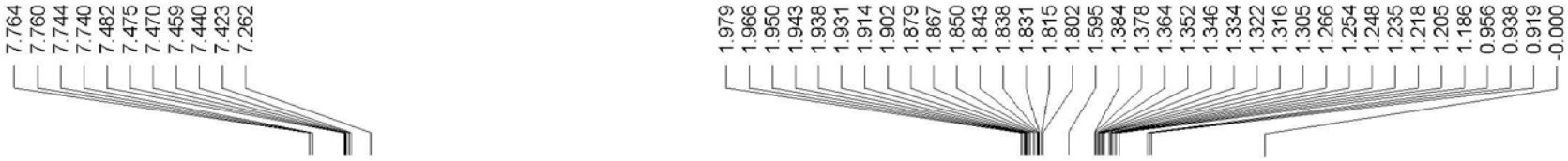


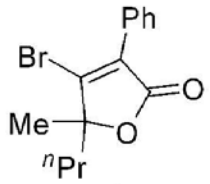

yao-01-132
Dec 21 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
Me
nPr
CO2Me
3aa
7.481
7.460
7.349
7.347
7.329
7.311
7.267
7.263
7.259
7.250
7.233
7.230
3.789
2.163
2.158
2.145
2.140
2.125
1.873
1.592
1.580
1.564
1.546
1.528
1.509
1.491
0.954
0.936
0.917
0.000
2.00
2.03
1.24
3.10
2.11
3.14
2.27
3.14
10
8
6
4
2
0
PPM


yao-01-132
Dec 21 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3aa
Me
nPr
CO2Me
209.400
167.341
133.928
128.281
128.038
127.082
104.971
101.722
77.319
77.000
76.681
52.005
35.647
20.429
17.947
13.635
200
150
100
50
0
PPM


yao-01-145
Jan 9 2018
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
Et
Et
Ph
CO2Me
3ba
7.508
7.505
7.488
7.339
7.334
7.320
7.302
7.258
7.255
7.244
7.240
7.225
7.222
3.783
2.209
2.191
2.172
2.154
1.112
1.093
1.075
-0.000
2.00
2.04
1.09
3.16
4.28
6.37
PPM

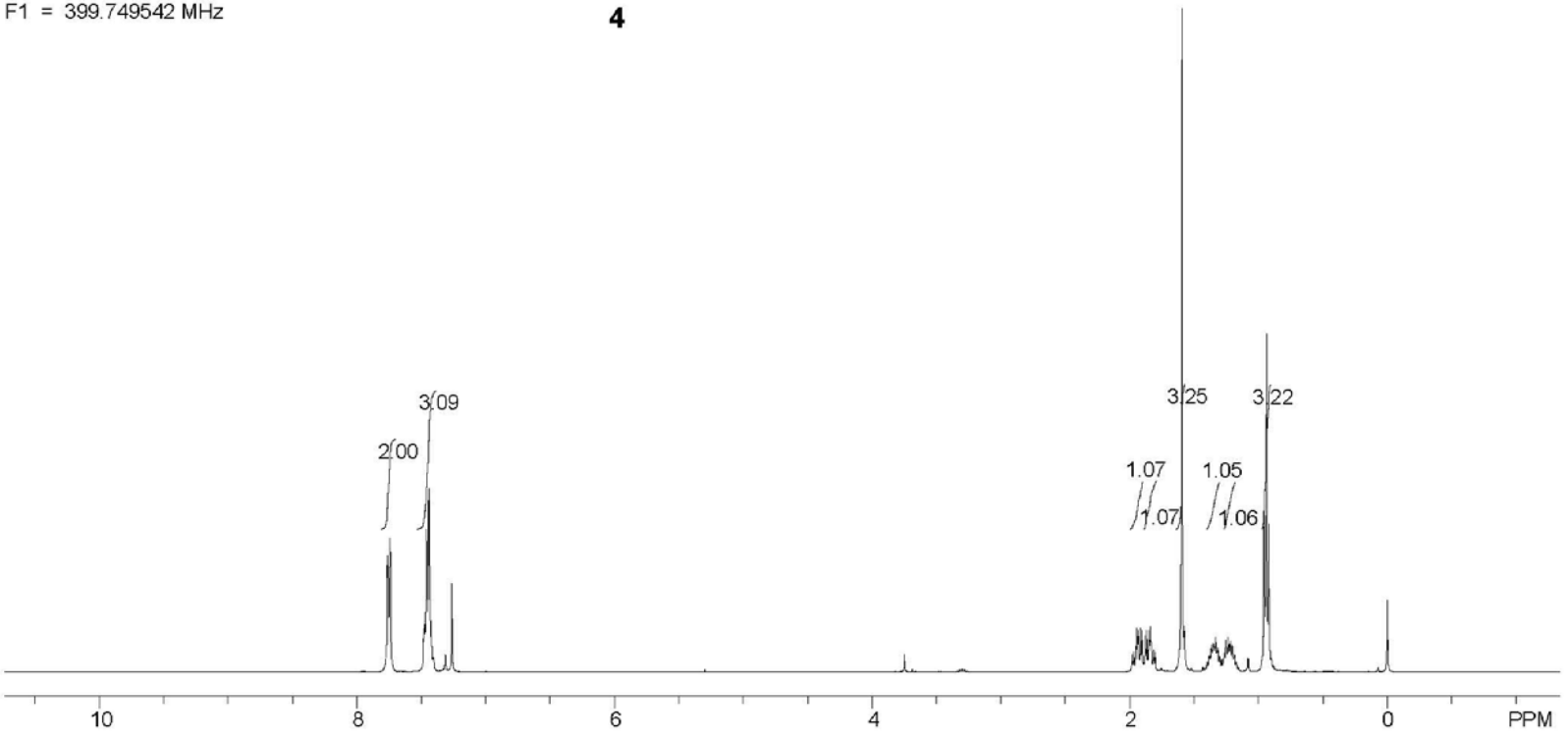

yao-01-145C
Jan 9 2018
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
3ba
Et
Et
Ph
CO2Me
208.694
167.539
134.103
128.099
128.084
127.097
113.745
104.439
77.319
77.000
76.681
52.043
25.613
12.041
200
150
100
50
0
PPM

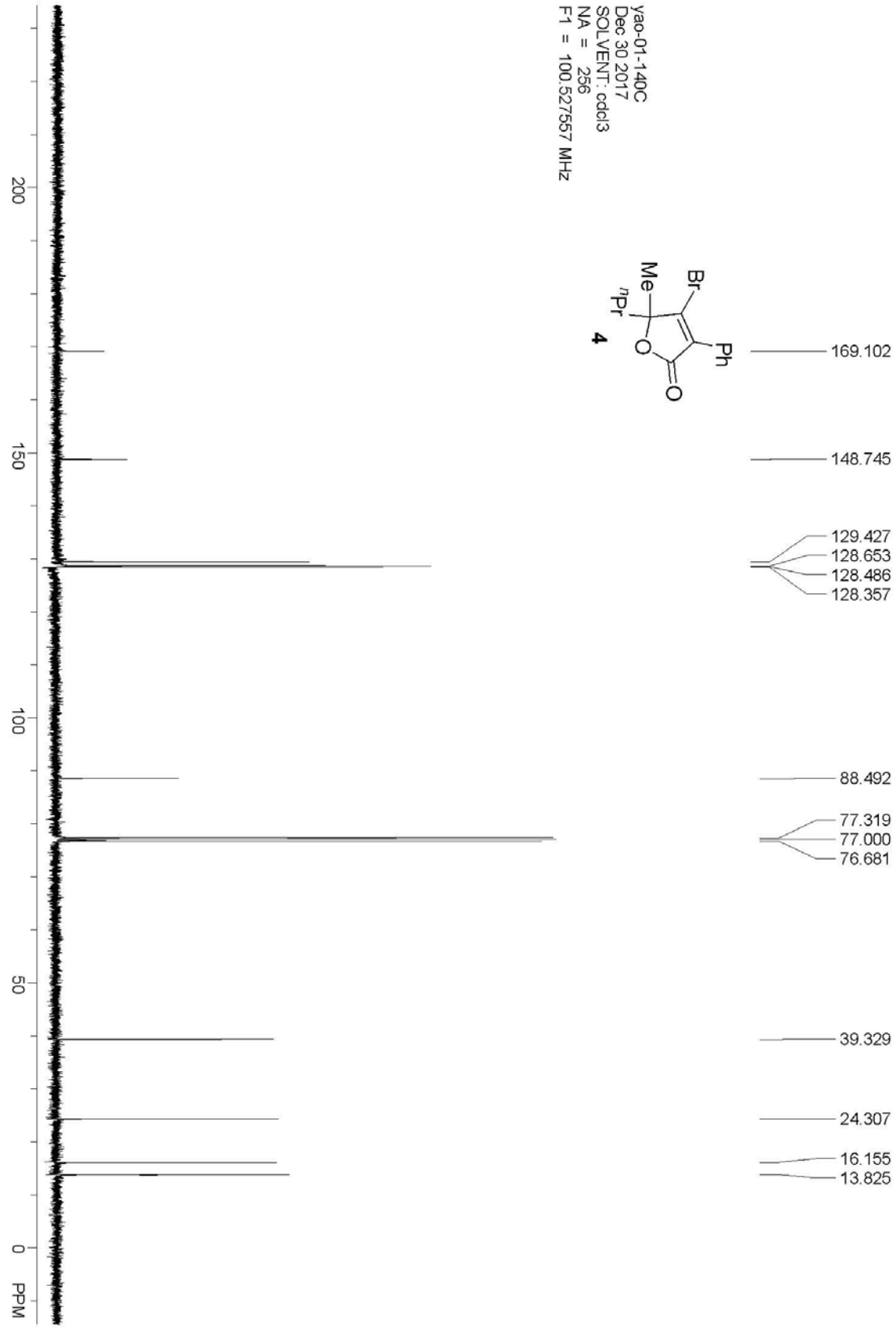




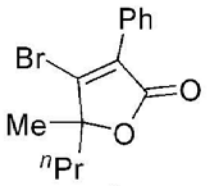
4

yao-01-140
Dec 30 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz



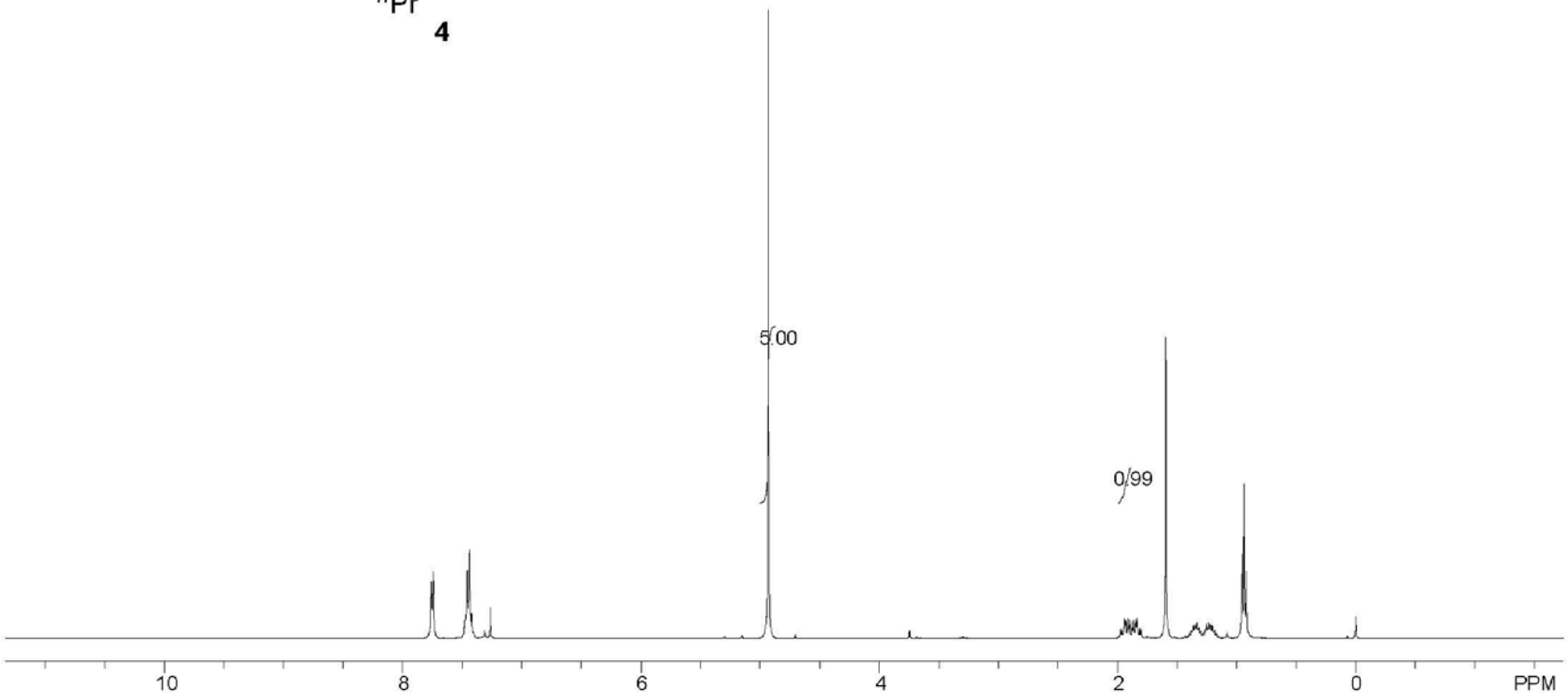

yao-01-140C
Dec 30 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
Br
Me
nPr
Ph
O
O
4
169.102
148.745
129.427
128.653
128.486
128.357
88.492
77.319
77.000
76.681
39.329
24.307
16.155
13.825
200
150
100
50
0
PPM

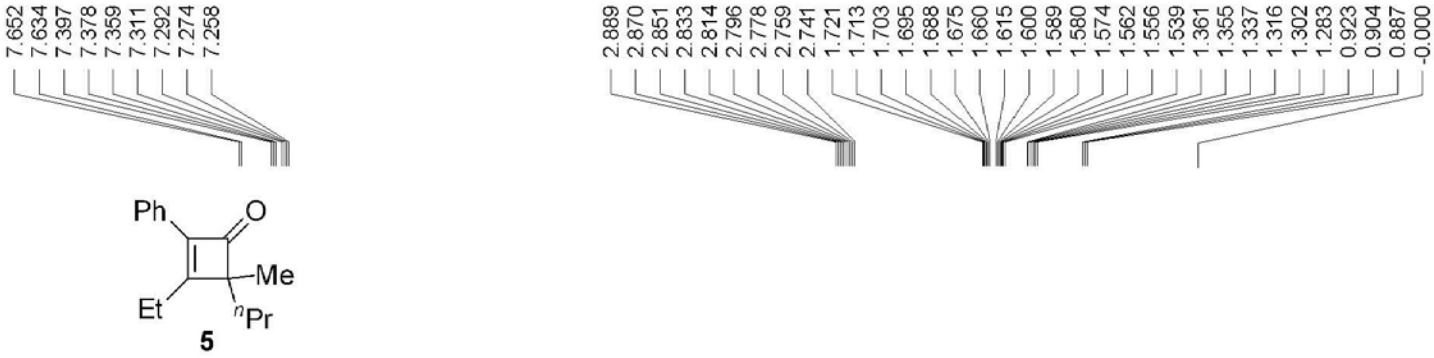
yao-01-140ccd
Jan 6 2018
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz

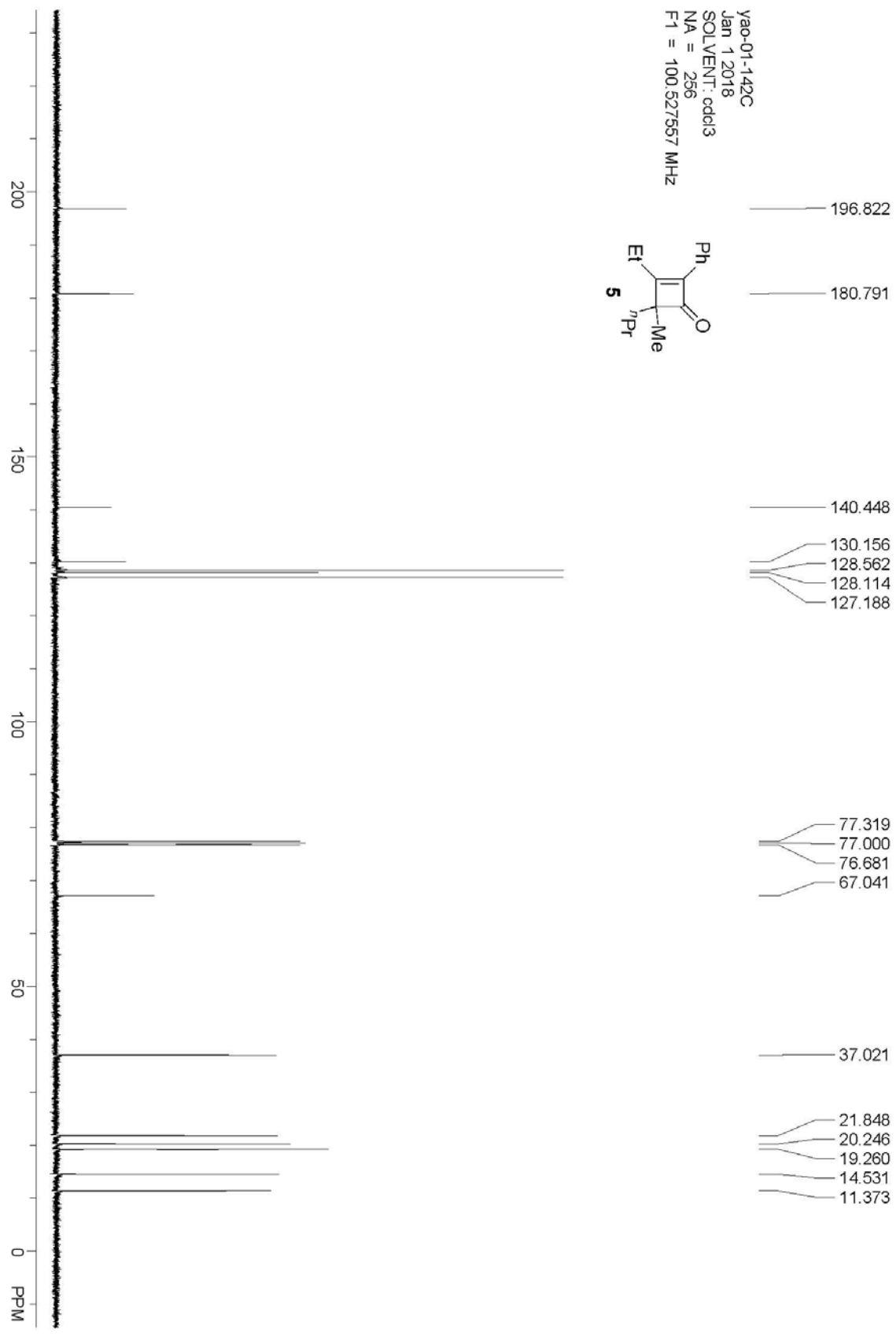


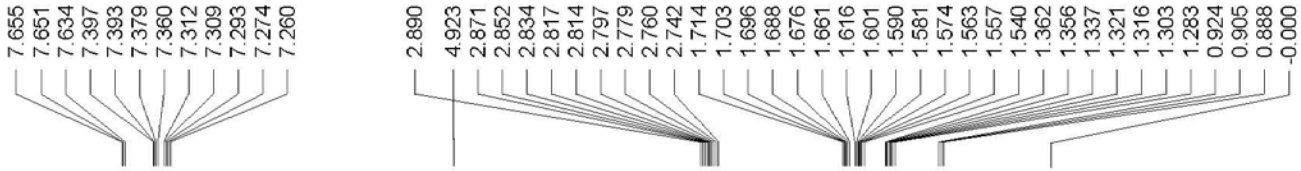
4

Purity (98%) determined by using CH_2Br_2 (17.5 μL, 0.25 mmol) as the standard in 29.7 mg of sample

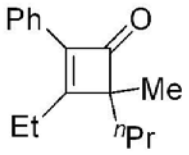



7.652
7.634
7.397
7.378
7.359
7.311
7.292
7.274
7.258
2.889
2.870
2.851
2.833
2.814
2.796
2.778
2.759
2.741
1.721
1.713
1.703
1.695
1.688
1.675
1.660
1.615
1.600
1.589
1.580
1.574
1.562
1.556
1.539
1.361
1.355
1.337
1.316
1.302
1.283
0.923
0.904
0.887
-0.000
Ph
O
Me
Et
nPr
5
yao-01-142
Jan 1 2018
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
1.92
1.92
1.10
2.00
1.09
1.03
8.08
3.11
10
8
6
4
2
0
PPM

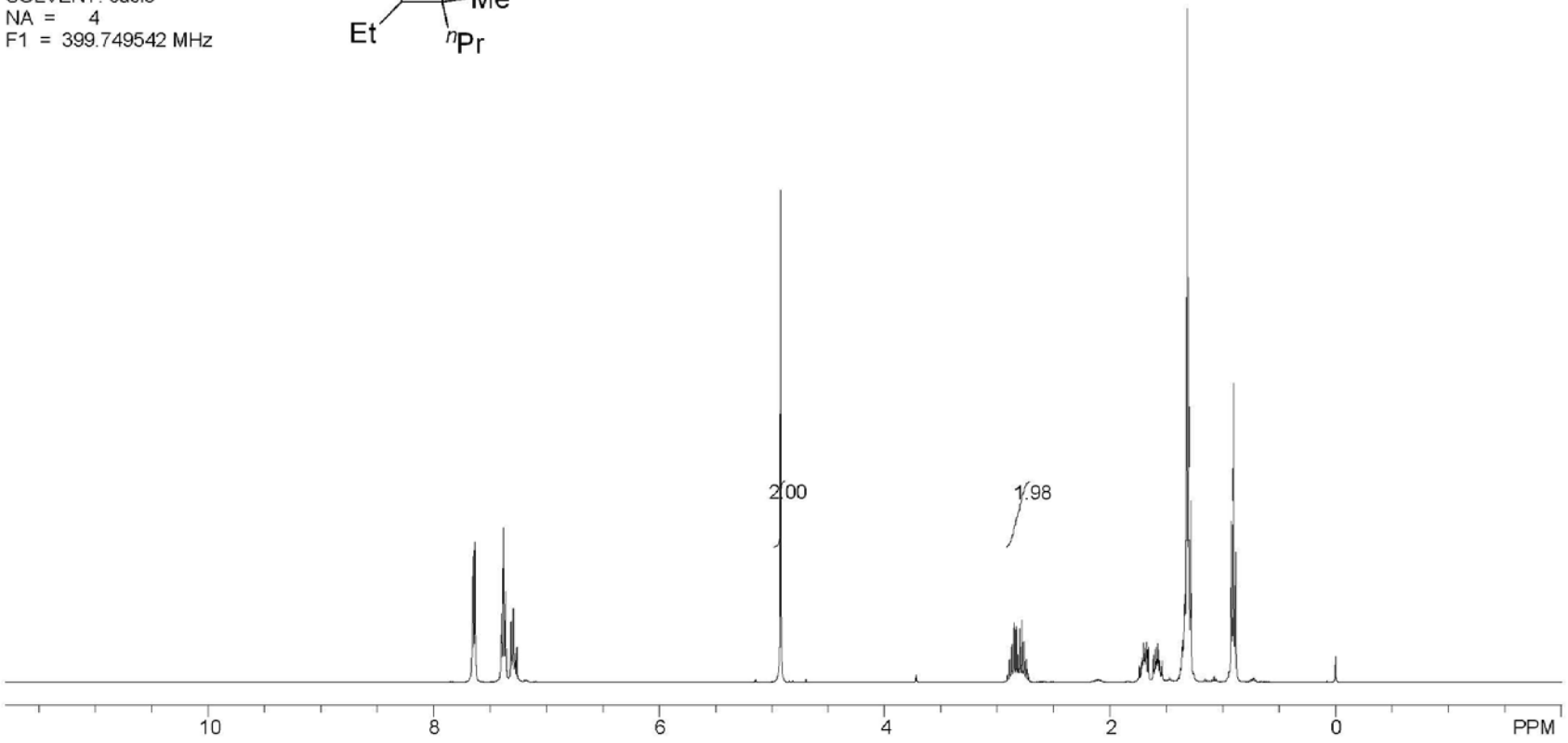

yao-01-142C
Jan 1 2018
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
Et
Ph
O
Me
nPr
5
196.822
180.791
140.448
130.156
128.562
128.114
127.188
77.319
77.000
76.681
67.041
37.021
21.848
20.246
19.260
14.531
11.373
200
150
100
50
0
PPM

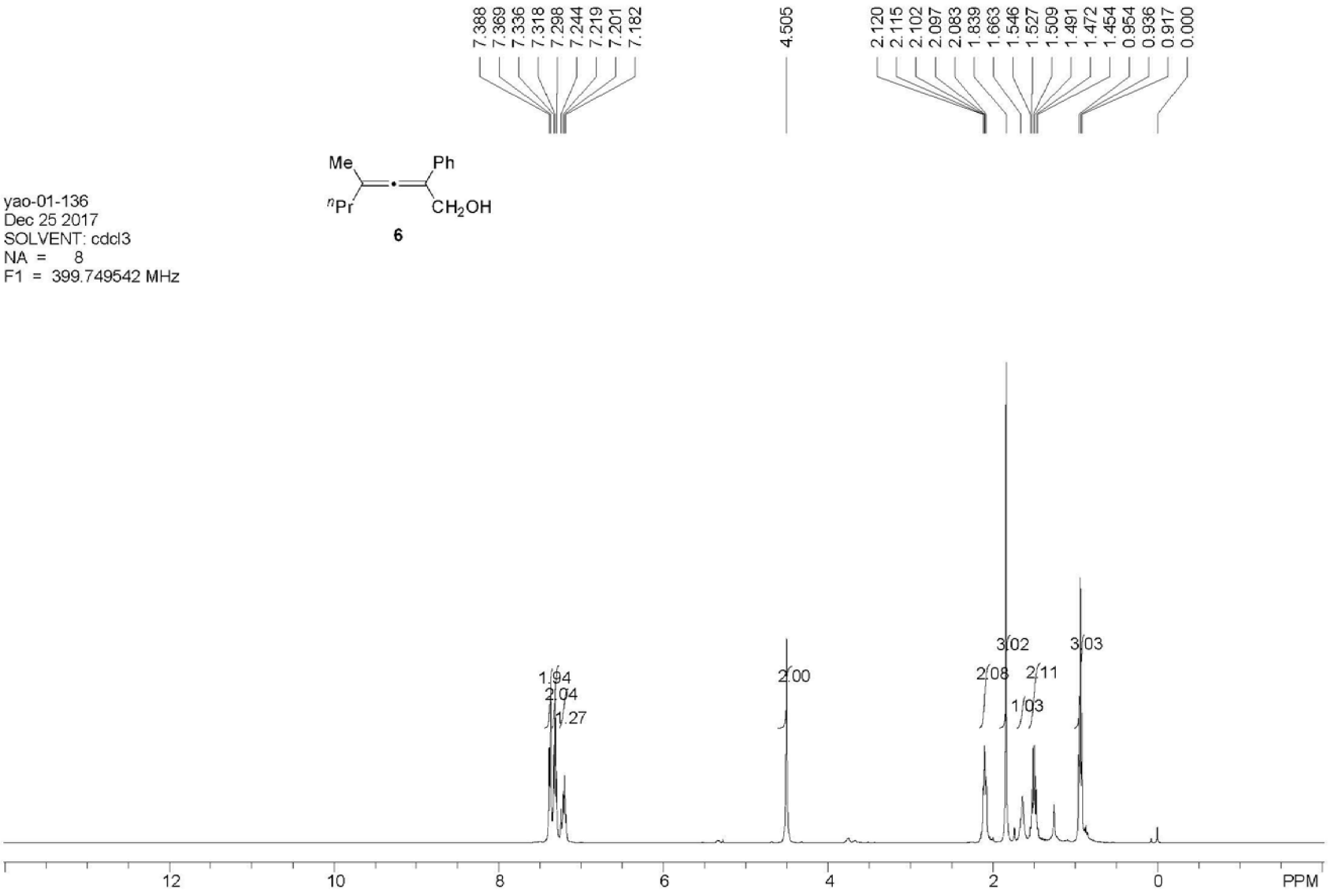


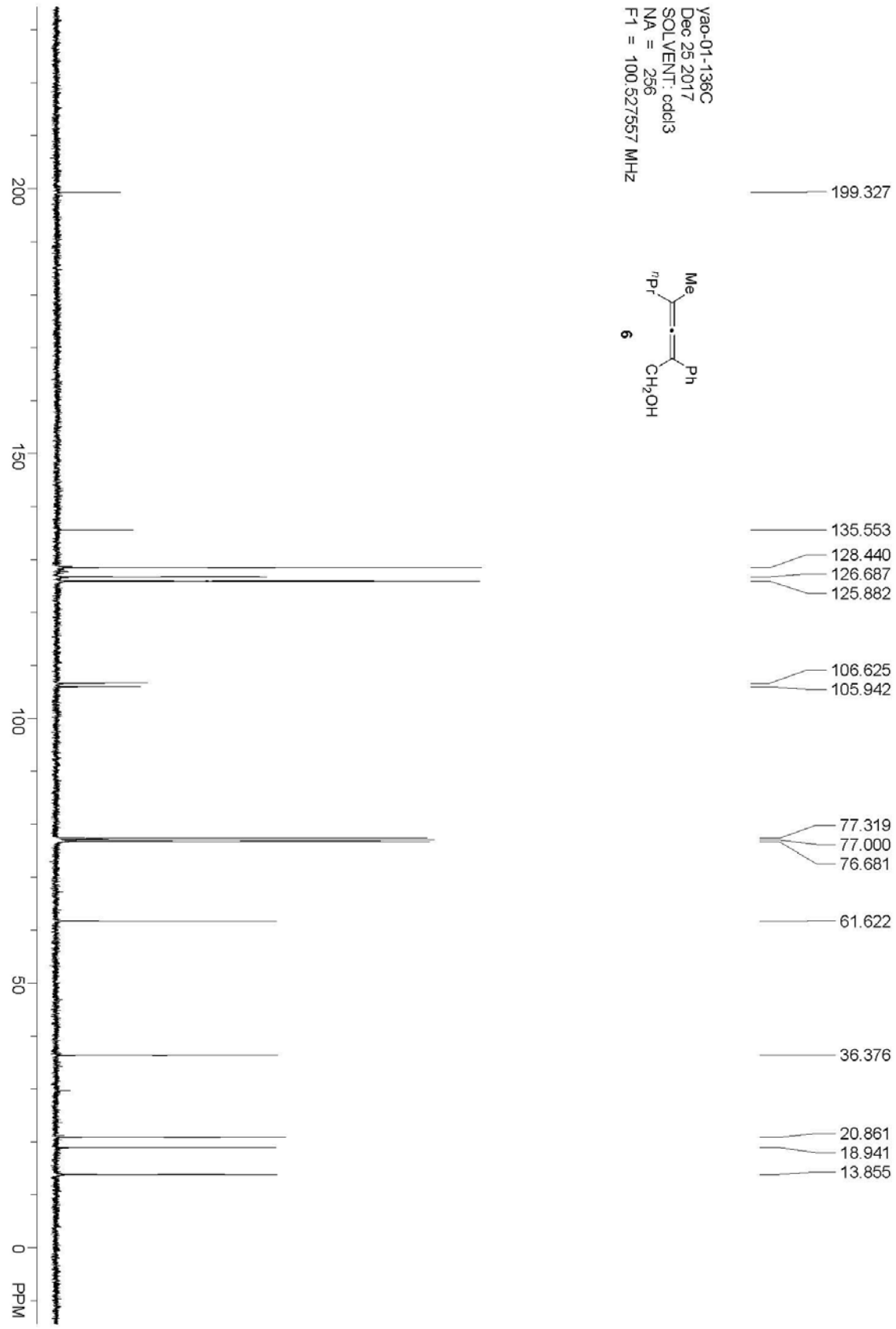
yao-01-142ccd
Jan 6 2018
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz

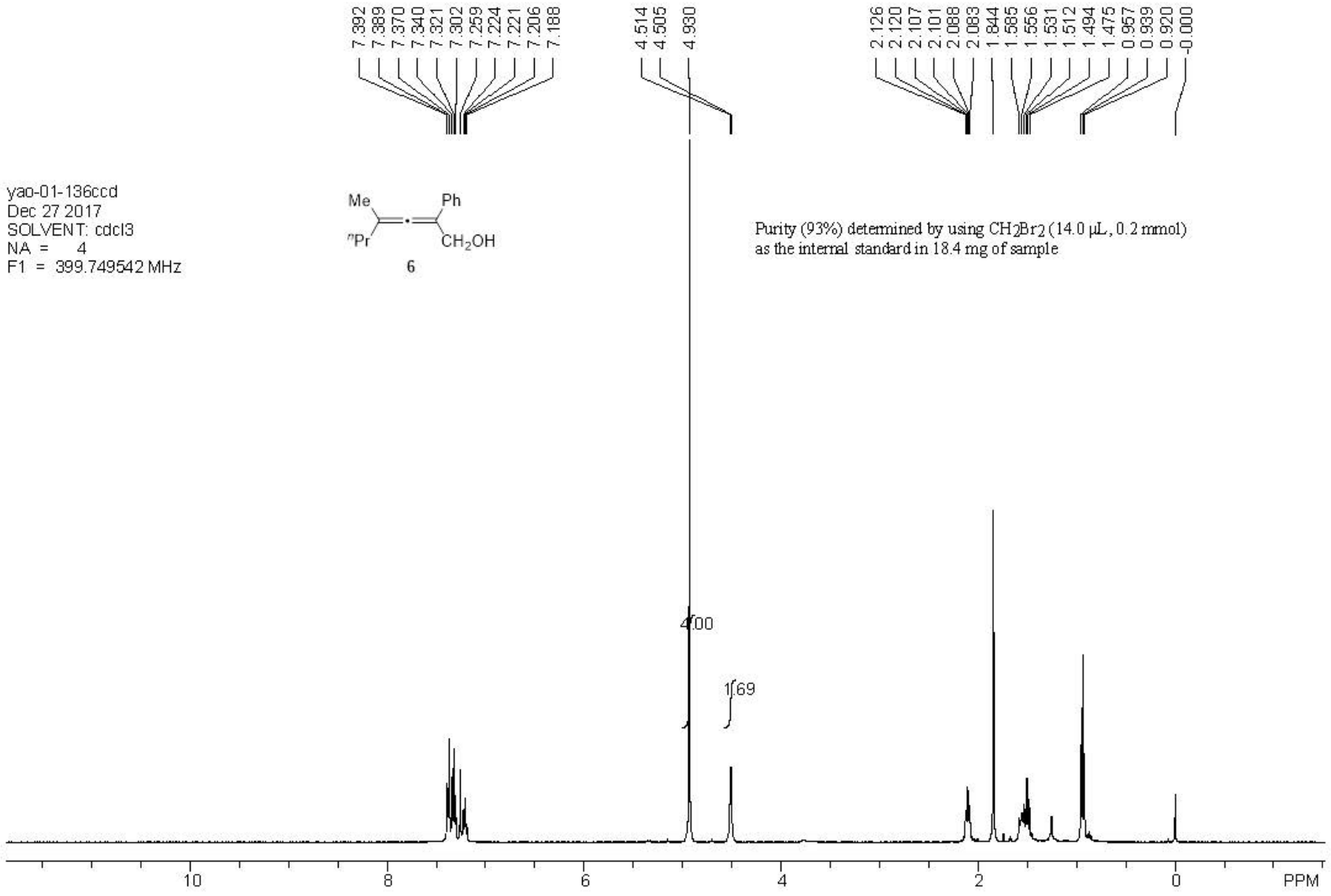


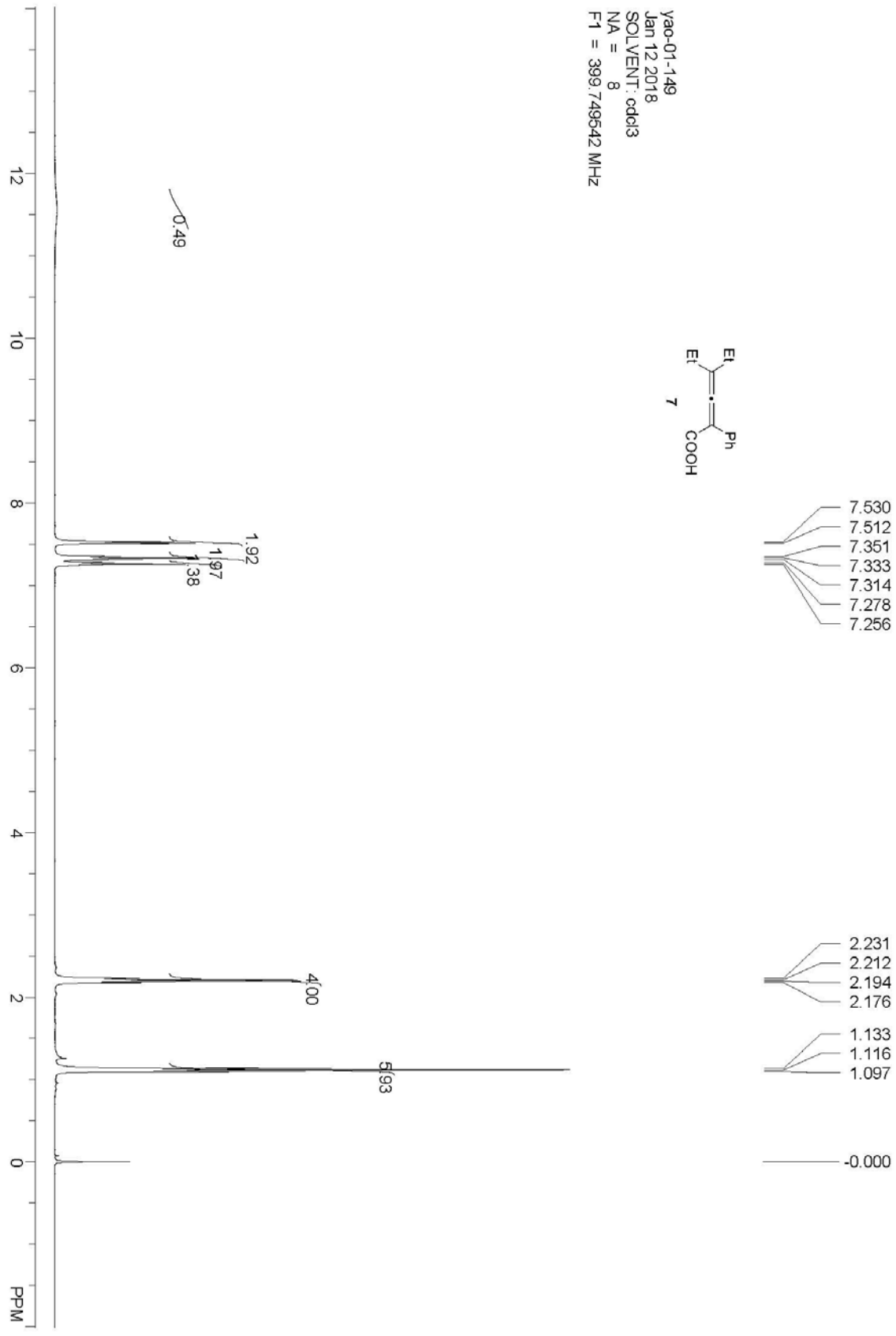
Purity (99%) determined by using CH_2Br_2 (14.0 μL, 0.2 mmol) as the internal standard in 45.5 mg of sample

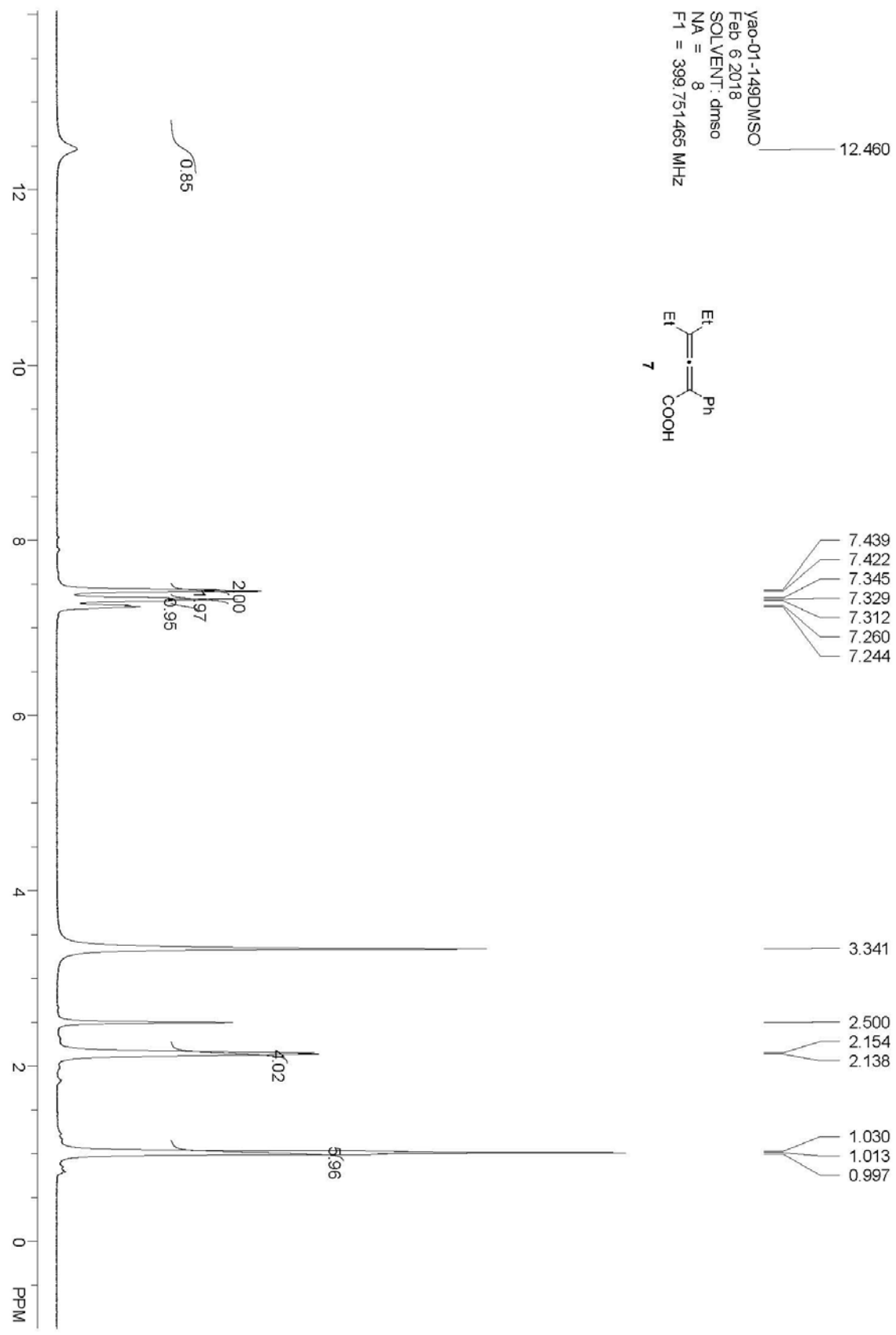


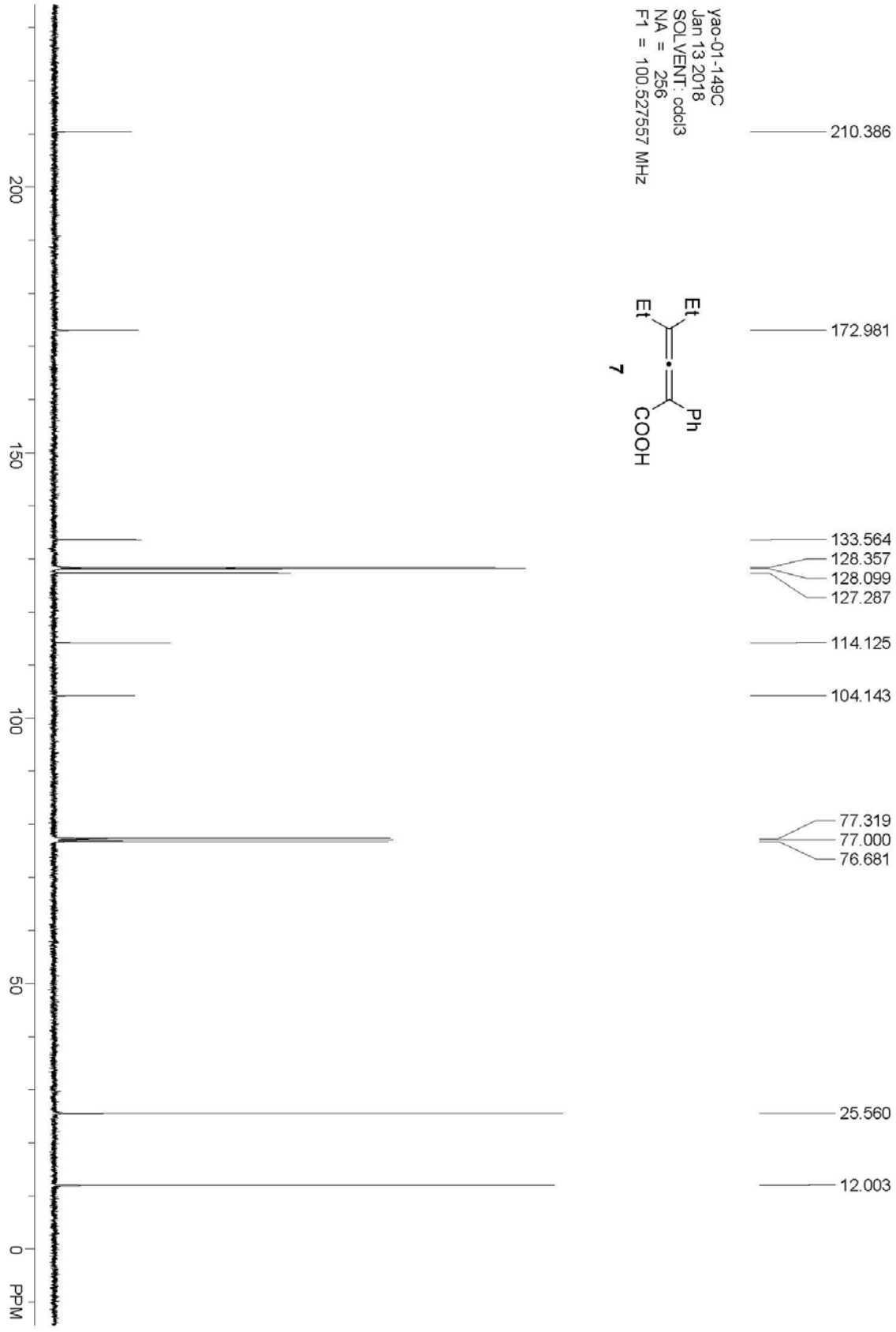

7.388
7.369
7.336
7.318
7.298
7.244
7.219
7.201
7.182
4.505
2.120
2.115
2.102
2.097
2.083
1.839
1.663
1.546
1.527
1.509
1.491
1.472
1.454
0.954
0.936
0.917
0.000
Me
Ph
nPr
CH2OH
6
yao-01-136
Dec 25 2017
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
1.94
2.04
1.27
2.00
2.08
3.02
2.11
1.03
3.03
12
10
8
6
4
2
0
PPM


yao-01-136C
Dec 25 2017
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
6
Me
nPr
Ph
CH2OH
199.327
135.553
128.440
126.687
125.882
106.625
105.942
77.319
77.000
76.681
61.622
36.376
20.861
18.941
13.855
200
150
100
50
0
PPM


7.392
7.389
7.370
7.340
7.321
7.302
7.259
7.224
7.221
7.206
7.188
4.514
4.505
4.930
2.126
2.120
2.107
2.101
2.088
2.083
1.844
1.585
1.556
1.531
1.512
1.494
1.475
0.957
0.939
0.920
-0.000
yao-01-136ccd
Dec 27 2017
SOLVENT: cdcl3
NA = 4
F1 = 399.749542 MHz
Me
Ph
nPr
CH2OH
6
Purity (93%) determined by using CH2Br2 (14.0 µL, 0.2 mmol)
as the internal standard in 18.4 mg of sample
4.00
1.69
10
8
6
4
2
0
PPM


yao-01-149
Jan 12 2018
SOLVENT: cdcl3
NA = 8
F1 = 399.749542 MHz
Et
Et
Ph
COOH
7
7.530
7.512
7.351
7.333
7.314
7.278
7.256
2.231
2.212
2.194
2.176
1.133
1.116
1.097
-0.000
0.49
1.92
1.97
1.38
4.00
5.93
PPM


yao-01-149DMSO
Feb 6 2018
SOLVENT: dmso
NA = 8
F1 = 399.751465 MHz
12.460
7.439
7.422
7.345
7.329
7.312
7.260
7.244
3.341
2.500
2.154
2.138
1.030
1.013
0.997
0.85
2.00
1.97
0.95
4.02
5.96
Et
Et
Ph
COOH
7
PPM


yao-01-149C
Jan 13 2018
SOLVENT: cdcl3
NA = 256
F1 = 100.527557 MHz
Et
Et
Ph
COOH
7
210.386
172.981
133.564
128.357
128.099
127.287
114.125
104.143
77.319
77.000
76.681
25.560
12.003
200
150
100
50
0
PPM