Supporting Information

Stereoselective Synthesis of Highly Functionalized α-Diazo-β-ketoalkanoates via Catalytic One-pot Mukaiyama-Aldol Reactions

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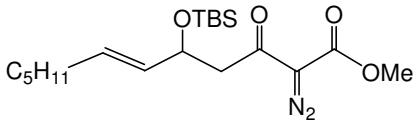
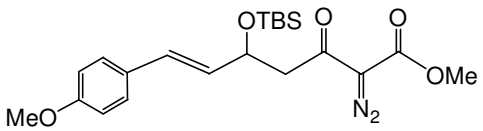
General. Reactions were performed in oven-dried (140 °C) or flame-dried glassware under an atmosphere of dry N_2. Dichloromethane (DCM) was passed through a solvent column prior to use and was not distilled. Methanol was not distilled. Thin layer chromatography (TLC) was carried out using EM Science silica gel 60 F_{254} plates. The developed chromatogram was analyzed by UV lamp (254 nm). Liquid chromatography was performed using flash chromatography of the indicated system on silica gel (230-400 mesh). Metal triflate salts were purchased from Aldrich and used as received. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance 400 MHz spectrometer. Chemical shifts were reported in ppm with the solvent signals as reference, and coupling constants (*J*) were given in Hertz. IR spectra were recorded on a Jasco FTIR 4100 spectrometer. Mass spectra were obtained with a JEOL AccuTOF-CS spectrometer.

General Procedure for Synthesis of 3 (Tables 1 and 2). To a flame-dried vial under a dry nitrogen atmosphere were added zinc triflate (11.0 mg, 3.0 mol%) and 5.0 mL of dry DCM. Methyl diazoacetoacetate **2** (142 mg, 1.00 mmol, 1.00 eq.), 2,6-lutidine (383 μL, 3.30 eq.), and aldehyde (1.10 mmol, 1.10 eq.) were added sequentially to the above mixture. The mixture was cooled to – 78 °C in a dry ice-acetone bath. *tert*-Butyldimethylsilyl trifluoromethanesulfonate (TBSOTf, 287 μL, 1.25 eq.) was then added dropwise. The mixture was stirred at – 78 °C then warmed to room temperature over 16 h after which the reaction was complete as monitored by TLC. After evaporation of the solvent under reduced pressure, the crude product was purified by flash column chromatography on silica gel using 5:1(v/v) hexanes:ethyl acetate as eluent to give pure compound **3** in high yield. Diazo carbon was not detected in ^{13}C NMR unless stated otherwise.

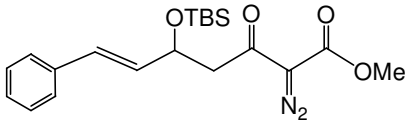


3a. Yellow oil, 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.55-5.61 (m, 1H), 5.39-5.45 (m, 1H), 4.56-4.61 (m, 1H), 3.80 (s, 3H), 3.21 (dd, 1H, *J* = 14.8, 8.0 Hz), 2.82 (dd, 1H, *J* = 14.8, 5.2 Hz), 1.94-2.02 (m, 2H), 1.19-1.36 (m, 9H), 0.82 (s, 9H), -0.01 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 161.9, 132.6, 131.7, 71.0, 52.4, 48.5, 32.2, 31.6, 29.0, 26.0, 22.7, 18.3, 14.2, -4.1, -4.8; HRMS (ESI) for $C_{19}H_{35}N_2O_4Si$ $[M+H]^+$ calcd: 383.2366; found: 383.2345; IR (neat): 2955, 2928, 2856, 2132, 1724, 1656 cm^{-1}.

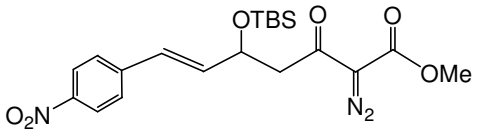


3b. Yellow oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, 2H, *J* = 8.8 Hz),

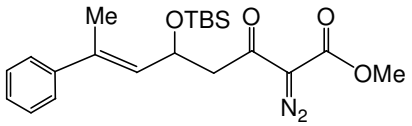
6.83 (d, 2H, *J* = 8.8 Hz), 6.46 (d, 1H, *J* = 15.6 Hz), 6.07 (dd, 1H, *J* = 15.6, 6.8 Hz), 4.81-4.86 (m, 1H, *J* = 7.6, 6.4 Hz), 3.82 (s, 3H), 3.78 (s, 3H), 3.32 (dd, 1H, *J* = 14.8, 8.0 Hz), 2.96 (dd, 1H, *J* = 14.8, 5.2 Hz), 0.84 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 161.9, 159.4, 130.1, 129.7, 129.4, 127.9, 114.2, 71.0, 55.5, 52.4, 48.5, 25.9, 18.3, -4.1, -4.8; HRMS (ESI) for $C_{21}H_{31}N_2O_5Si$ $[M+H]^+$ calcd: 419.2002; found: 419.2057; IR (neat): 2955, 2142, 1722, 1631 cm^{-1}.



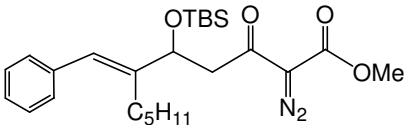
3c. Light yellow oil, 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.31 (m, 5H), 6.54 (d, 1H, *J* = 15.6 Hz), 6.21 (dd, 1H, *J* = 15.6, 6.8 Hz), 4.81-4.86 (m, 1H, *J* = 7.6, 6.4 Hz), 3.82 (s, 3H), 3.32 (dd, 1H, *J* = 14.8, 8.0 Hz), 2.96 (dd, 1H, *J* = 14.8, 5.2 Hz), 0.84 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.4, 161.8, 137.0, 132.3, 129.9, 128.8, 127.6, 126.7, 70.7, 52.4, 48.4, 25.9, 18.3, -4.1, -4.8; HRMS (ESI) for $C_{20}H_{28}N_2NaO_4Si$ $[M+Na]^+$ calcd: 411.1716; found: 411.1697; IR (neat): 2955, 2856, 2136, 1722, 1650 cm^{-1}.



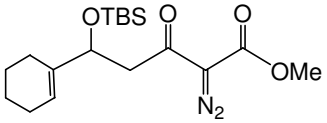
3d. Yellow oil, 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, 2H, *J* = 8.8 Hz), 7.46 (d, 2H, *J* = 8.8 Hz), 6.66 (d, 1H, *J* = 16.0 Hz), 6.45 (dd, 1H, *J* = 16.0, 6.0 Hz), 4.87-4.89 (m, 1H, *J* = 5.6, 6.0 Hz), 3.82 (s, 3H), 3.32 (dd, 1H, *J* = 15.6, 7.2 Hz), 3.01 (dd, 1H, *J* = 15.6, 5.6 Hz), 0.84 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.0, 161.8, 147.1, 143.5, 137.3, 127.7, 127.2, 124.2, 69.9, 52.5, 48.2, 25.9, 18.3, -4.3, -4.8; HRMS (ESI) for $C_{20}H_{28}N_3O_6Si$ $[M+H]^+$ calcd: 434.1747; found: 434.1784; IR (neat): 2954, 2930, 2856, 2133, 1720, 1651, 1517, 1340 cm^{-1}.



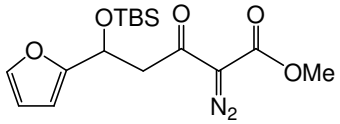
3e. Yellow oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17-7.33 (m, 5H), 6.48 (s, 1H), 4.70-4.73 (m, 1H, *J* = 8.8, 3.6 Hz), 3.82 (s, 3H), 3.46 (dd, 1H, *J* = 14.4, 9.2 Hz), 2.96 (dd, 1H, *J* = 14.4, 4.0 Hz), 1.87 (s, 1H), 0.84 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 161.9, 140.0, 137.8, 129.1, 128.3, 126.6, 126.0, 75.8, 52.4, 46.7, 25.9, 18.3, 13.4, -4.5, -5.1; HRMS (ESI) for $C_{21}H_{30}N_2NaO_4Si$ $[M+Na]^+$ calcd: 425.1873; found: 425.1839; IR (neat): 2954, 2929, 2132, 1722, 1655 cm^{-1}.



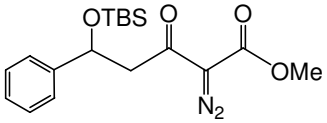
3f. Yellow oil, 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17-7.32 (m, 5H), 6.58 (s, 1H), 4.72-4.74 (dd, 1H, *J* = 9.2, 2.4 Hz), 3.81 (s, 3H), 3.39 (dd, 1H, *J* = 14.8, 9.2 Hz), 2.86 (dd, 1H, *J* = 14.8, 3.2 Hz), 2.32-2.40 (m, 1H), 2.02-2.12 (m, 1H), 1.22-1.56 (m, 9H), 0.84 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.9, 161.9, 144.8, 138.1, 129.9, 129.0, 128.7, 128.4, 126.5, 126.0, 73.6, 52.4, 47.9, 32.5, 28.9, 28.6, 26.0, 22.6, 18.3, 14.2, -4.2, -5.0; HRMS (ESI) for $C_{25}H_{38}N_2NaO_4Si$ $[M+Na]^+$ calcd: 481.2499; found: 481.2472; IR (neat): 2954, 2929, 2132, 1723, 1656 cm^{-1}.



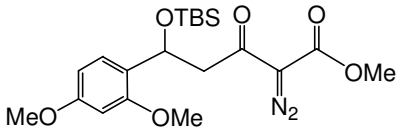
3g. Light yellow oil, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.61 (s, 1H), 4.51 (dd, 1H, *J* = 9.0, 4.0 Hz), 3.82 (s, 3H), 3.38 (dd, 1H, *J* = 14.0, 9.0 Hz), 2.68 (dd, 1H, *J* = 14.0, 4.0 Hz), 1.47-1.97 (m, 8H), 0.80 (s, 9H), -0.03 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 161.9, 140.0, 123.4, 74.6, 52.4, 46.6, 25.9, 25.2, 23.2, 22.8, 18.2, -4.5, -5.1; HRMS (ESI) for $C_{18}H_{30}N_2NaO_4Si$ $[M+Na]^+$ calcd: 389.1873; found: 389.1872; IR (neat): 2929, 2132, 1723, 1657 cm^{-1}.



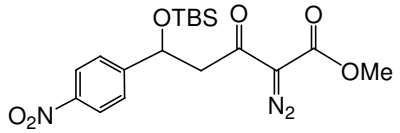
3h. Yellow oil, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, 1H, *J* = 1.6Hz), 6.27 (dd, 1H, *J* = 3.0, 1.6 Hz), 6.20 (d, 1H, *J* = 3.0 Hz), 5.27 (dd, 1H, *J* = 8.8, 4.8 Hz), 3.82 (s, 3H), 3.60 (dd, 1H, *J* = 16.0, 8.8 Hz), 3.12 (dd, 1H, *J* = 16.0, 4.8 Hz), 0.80 (s, 9H), 0.01 (s, 3H), -0.11 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9, 161.8, 156.2, 110.3, 106.4, 65.1, 52.5, 46.9, 25.8, 18.2, -4.8, -5.1; HRMS (ESI) for $C_{16}H_{24}N_2NaO_5Si$ $[M+Na]^+$ calcd: 375.1352; found: 375.1331; IR (neat): 2955, 2133, 1719, 1656 cm^{-1}.



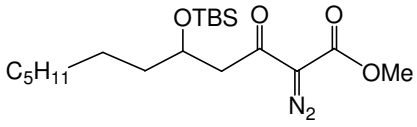
3i. Pale yellow oil, 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.29 (m, 5H), 5.20 (dd, 1H, *J* = 9.0, 4.0 Hz), 3.81 (s, 3H), 3.49 (dd, 1H, *J* = 14.6, 9.0 Hz), 2.92 (dd, 1H, *J* = 14.6, 4.0 Hz), 0.80 (s, 9H), -0.04 (s, 3H), -0.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 161.8, 144.6, 128.4, 127.6, 126.2, 72.2, 52.4, 50.7, 25.8, 18.2, -4.6, -5.1; HRMS (ESI) for $C_{18}H_{27}N_2O_4Si$ $[M+H]^+$ calcd: 363.1740; found: 363.1730; IR (neat): 2954, 2131, 1721, 1656 cm^{-1}.



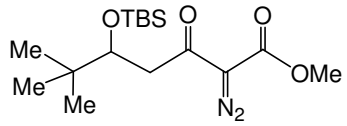
3j. Light yellow oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, 1H, *J* = 8.4 Hz), 6.50 (dd, 1H, *J* = 8.4, 2.4 Hz), 6.41 (d, 1H, *J* = 2.4 Hz), 5.20 (dd, 1H, *J* = 8.8, 3.2 Hz), 3.84 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H), 3.58 (dd, 1H, *J* = 14.8, 9.2 Hz), 2.84 (dd, 1H, *J* = 14.8, 4.0 Hz), 0.85 (s, 9H), 0.02 (s, 3H), -0.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 161.7, 159.9, 156.3, 127.8, 125.1, 104.1, 97.8, 65.5, 55.2, 52.1, 48.6, 25.7, 18.0, -4.9, -5.4; HRMS (ESI) for $C_{20}H_{30}N_2NaO_6Si$ $[M+Na]^+$ calcd: 445.1771; found: 445.1724; IR (neat): 2955, 2131, 1722 cm^{-1}.



3k. Yellow solid, 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, 1H, *J* = 8.8 Hz), 7.58 (d, 1H, *J* = 8.8 Hz), 5.34 (dd, 1H, *J* = 8.4, 4.4 Hz), 3.82 (s, 3H), 3.45 (dd, 1H, *J* = 15.2, 8.4 Hz), 3.03 (dd, 1H, *J* = 15.2, 4.4 Hz), 0.84 (s, 9H), 0.00 (s, 3H), -0.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3, 161.5, 151.8, 147.2, 126.8, 123.6, 70.8, 52.2, 50.1, 25.6, 17.9, -4.9, -5.3; HRMS (ESI) for $C_{18}H_{26}N_3O_6Si$ $[M+H]^+$ calcd: 408.1591; found: 408.1589; IR (neat): 2954, 2134, 1713, 1646, 1514, 1344 cm^{-1}.



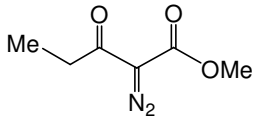
3l. Pale yellow oil, 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.22-4.25 (m, 1H), 3.85 (s, 3H), 3.18 (dd, 1H, *J* = 15.2, 7.2 Hz), 2.87 (dd, 1H, *J* = 15.2, 5.2 Hz), 1.48-1.51 (m, 2H), 1.29-1.35 (m, 10H), 0.90 (t, 3H, *J* = 6.8 Hz), 0.89 (s, 9H), 0.06 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.2, 161.6, 69.2, 52.1, 47.1, 37.9, 31.8, 29.6, 29.2, 25.7, 24.9, 22.6, 17.9, 14.1, -4.6, -4.9; HRMS (ESI) for $C_{19}H_{37}N_2O_4Si$ $[M+H]^+$ calcd: 385.2523; found: 385.2494; IR (neat): 2925, 2135, 1722, 1648 cm^{-1}.



3m. Pale yellow oil, 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08 (t, 1H, *J* = 5.2 Hz), 3.86 (s, 3H), 3.05 (d, 1H, *J* = 5.2 Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.08 (s, 3H), -0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.6, 161.7, 75.3, 52.1, 44.1, 35.8, 25.9, 25.7, 18.2, -4.3, -4.8; HRMS (ESI) for $C_{16}H_{31}N_2O_4Si$ $[M+H]^+$ calcd: 343.2053; found: 343.2040; IR (neat): 2955, 2132, 1723, 1659 cm^{-1}.

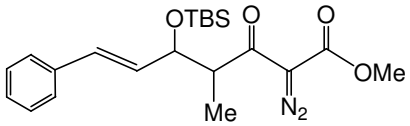
Low Temperature ^{1}H NMR Study. To a flame-dried vial under nitrogen atmosphere were added methyl diazoacetoacetate **2** (20.0 mg, 1.00 mmol, 1.00 eq.), 2,6-lutidine (45.0 μL, 3.00 eq.), and 1.5 mL of dry $CDCl_3$ at room temperature. The mixture was cooled to – 78 °C. TBSOTf (40.0 μL, 1.25 eq.) was then added dropwise to the above mixture to give a bright yellow solution. The resulting mixture was then submitted to low temperature ^{1}H NMR (– 74 °C) after 15 min. ^{1}H NMR showed the formation of methyl 3-*tert*-butyldimethylsilanyloxy-2-diazobu-3-enoate (> 95%).

Procedure for Synthesis of 4. Methyl 3-oxo-pentanoate (2.00 g, 1.00 eq.), methanesulfonyl azide (2.23 g, 1.20 eq.) and triethylamine (3.20 mL, 1.50 eq.) were dissolved in 50.0 mL of dry THF at room temperature under nitrogen atmosphere. The resulting colorless mixture was stirred for 16 h, during which time the mixture turned pale green. After evaporation of solvent a light yellow liquid was obtained. The yellow liquid was purified by flash column chromatography on silica gel using 5:1(v/v) hexanes:ethyl acetate as eluent to give pure compound **4** as bright yellow oil in 90% yield. The diazo carbon was not detected in ^{13}C NMR.

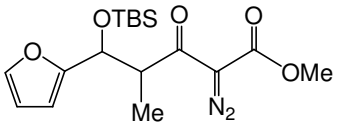


4. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 2.80 (q, 2H, *J* = 7.2Hz), 1.08 (t, 3H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.5, 162.0, 52.3, 33.9, 8.37; HRMS (ESI) for $C_6H_9N_2O_3$ $[M+H]^+$ calcd: 157.0613; found: 157.0646; IR (neat): 2982, 2127, 1716, 1653 cm^{-1}.

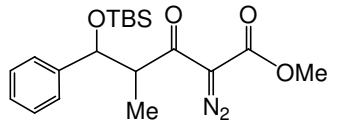
General Procedure for Synthesis of 5 (Table 3). To a flame-dried vial under nitrogen atmosphere were added zinc triflate (11.0 mg, 3.0 mol%) and 5 mL of dry DCM. Methyl 2-diazo-3-oxo-pentanoate **4** (156 mg, 1.00 mmol, 1.00 eq.), 2,6-lutidine (383 μL, 3.30 eq.), and aldehyde (1.10 mmol, 1.10 eq.) were added to the above mixture sequentially. The mixture was cooled to – 78 °C. TBSOTf (287 μL, 1.25 eq.) was then added dropwise. The mixture was stirred at – 78 °C and warmed to room temperature over 18 h, during which timethe reaction was complete monitored by TLC. After evaporation of solvent, crude product was purified by flash column chromatography on silica gel using 5:1(v/v) hexanes:ethyl acetate as eluent to give pure compound **5** in high yield. Diazo carbon was not detected in ^{13}C NMR unless stated otherwise.



5c. Yellow oil, 95% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.31 (m, 5H), 6.50 (d, 1H, *J* = 16.0 Hz), 6.10 (dd, 1H, *J* = 16.0, 8.0 Hz), 4.48 (ap t, 0.28H, *J* = 6.8 Hz), 4.40 (ap t, 0.72H, *J* = 8.8 Hz), 3.90-3.93 (m, 1H), 3.79 (s, 3H), 1.16 (d, 0.84H, *J* = 7.2 Hz), 1.00 (d, 2.16H, *J* = 7.2 Hz), 0.81 (s, 9H), 0.01 (s, 3H), -0.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7, 161.8, 136.8, 132.1, 130.7, 128.7, 127.6, 126.7, 74.9, 52.2, 47.8, 25.8, 18.1, 13.6, -4.0, -5.1; HRMS (ESI) for $C_{21}H_{30}N_2NaO_4Si$ $[M+Na]^+$ calcd: 425.1873; found: 425.1824; IR (neat): 2954, 2140, 1723, 1655 cm^{-1}.



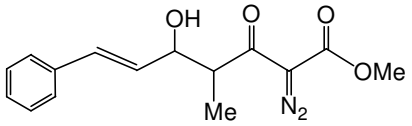
5h. Yellow oil, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, 0.69H, *J* = 1.2 Hz), 7.30 (d, 0.31H, *J* = 0.8 Hz), 6.28 (dd, 0.69H, *J* = 3.2, 2.0 Hz), 6.25 (dd, 0.31H, *J* = 3.2, 2.0 Hz), 6.22 (d, 0.69H, *J* = 2.8 Hz), 6.20 (d, 0.31H, *J* = 2.8 Hz), 4.95 (d, 0.31H, *J* = 7.6 Hz), 4.84 (d, 0.69H, *J* = 9.6 Hz), 4.21-4.28 (m, 0.69H), 4.03-4.10 (m, 0.31H), 3.82 (s, 2.07H), 3.80 (s, 0.93H), 1.19 (d, 0.93H, *J* = 6.8 Hz), 0.81 (d, 2.07H, *J* = 6.8 Hz), 0.73 (s, 9H), -0.06 (s, 3H), -0.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 161.9, 142.0, 109.9, 108.1, 71.0, 52.2, 47.0, 25.6, 18.1, 13.4, -5.4, -5.7; HRMS (ESI) for $C_{17}H_{26}N_2NaO_5Si$ $[M+Na]^+$ calcd: 389.1509; found: 389.1491; IR (neat): 2955, 2139, 1724, 1655 cm^{-1}.



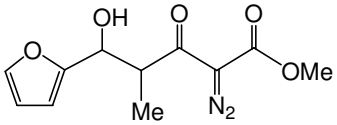
5i. Yellow oil, 97% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.34 (m, 5H), 4.92 (d, 0.31H, *J* = 6.4 Hz), 4.68 (d, 0.69H, *J* = 9.6 Hz), 4.07-4.11 (m, 1H), 3.84 (s, 2.07H), 3.78 (s, 0.97H), 1.12 (d, 0.97H, *J* = 6.8 Hz), 0.76 (d, 2.07H, *J* = 6.8 Hz), 0.73 (s, 9H), -0.10 (s, 3H), -0.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 161.9, 142.9, 128.3, 127.9, 127.5, 126.9, 79.0, 52.3, 49.4, 25.6, 18.0, 13.8, -4.6, -5.3; HRMS (ESI) for $C_{19}H_{28}N_2NaO_4Si$ $[M+Na]^+$ calcd: 399.1716; found: 399.1685; IR (neat): 2954, 2138, 1722, 1655 cm^{-1}.

General Procedure for Synthesis of 6 (Table 4). To a flame-dried vial under nitrogen atmosphere at were added methyl 2-diazo-3-oxo-pentanoate **4** (312 mg, 2.00 mmol, 1.00 eq.), DIPEA (*N,N*-diisopropylethylamine, 0.70 mL, 2.00 eq.) and 5.0 mL of dry DCM. Di-*n*-butylboron tirfluoromethanesulfonate (Bu_2BOTf, 1.0 M in DCM, 2.20 mL, 1.10 eq.) was added dropwise to the above mixture over 5 min, during which the pale yellow solution turned orange and reddish brown. The resulting mixture was stirred at 0 °C for 15 min, and then aldehyde (2.00 mmol, 1.00 eq.) was added. The resulting reddish brown mixture was stirred at 0 °C for 2-3 h, during which the reaction was complete as monitored by TLC. After evaporation of solvent, crude product was purified by flash column chromatography on silica gel using 2:1(v/v) hexanes:ethyl acetate as eluent to give pure compound **6** in good yield. Diazo

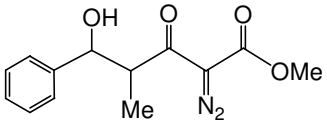
carbon was not detected in ^{13}C NMR unless stated otherwise.



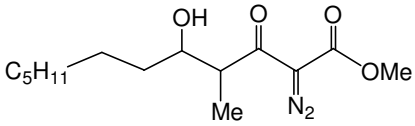
6c. Light yellow oil, 73% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.42 (m, 2H), 7.31-7.35 (m, 2H), 7.24-7.28 (m, 1H), 6.69 (d, 1H, *J* = 16.0 Hz), 6.21 (dd, 1H, *J* = 16.0, 5.6 Hz), 4.69-4.72 (m, 1H), 3.87 (s, 3H), 3.79-3.85 (m, 1H), 3.11 (d, 1H, *J* = 2.8 Hz), 1.22 (d, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.6, 161.5, 136.7, 131.1, 128.8, 128.5, 127.6, 126.5, 72.4, 52.3, 46.6, 10.7; HRMS (ESI) for $C_{15}H_{16}N_2NaO_4$ $[M+Na]^+$ calcd: 311.1008; found: 311.1000; IR (neat): 3514, 2142, 1715, 1641 cm^{-1}.



6h. Light yellow oil, 71% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, 1H, *J* = 1.6 Hz), 6.34 (dd, 1H, *J* = 3.2, 1.6 Hz), 6.31 (d, 1H, *J* = 1.6 Hz), 5.13 (t, 1H, *J* = 4.0 Hz), 4.00-4.06 (m, 1H), 3.87 (s, 3H), 3.15 (d, 1H, *J* = 4.0 Hz), 1.22 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.2, 161.2, 154.2, 141.8, 110.2, 106.6, 68.4, 52.4, 46.0, 11.3; HRMS (ESI) for $C_{11}H_{13}N_2O_5$ $[M+H]^+$ calcd: 253.0824; found: 253.0859; IR (neat): 3492, 2143, 1716, 1641 cm^{-1}.

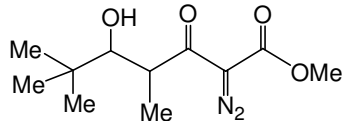


6i. Light yellow solid, 75% yield. Diazo carbon was detected in ^{13}C NMR at 75.9 ppm. ^1H NMR (400 MHz, $CDCl_3$): δ 7.22-7.40 (m, 5H), 5.11 (ap s, 1H), 3.89-3.92 (m, 1H), 3.82 (s, 3H), 3.37 (d, 1H, *J* = 2.0 Hz), 1.08 (d, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 161.2, 141.6, 128.1, 127.2, 126.0, 75.9, 73.0, 52.3, 48.2, 9.9; HRMS (ESI) for $C_{13}H_{15}N_2O_4$ $[M+H]^+$ calcd: 263.1032; found: 263.1022; IR (neat): 3485, 2952, 2130, 1709, 1631 cm^{-1}.



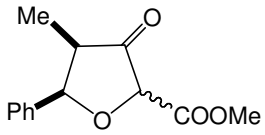
6l. Light yellow oil, 69% yield. Diazo carbon was detected in ^{13}C NMR at 75.8 ppm. ^1H NMR (400 MHz, $CDCl_3$): δ 3.91-3.95 (m, 1H), 3.85 (s, 3H), 3.58-3.64 (m, 1H), 2.91 (d, 1H, *J* = 2.8 Hz), 1.27-1.55 (m, 12H), 1.16 (d, 3H, *J* = 7.2 Hz), 0.88 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 161.4, 75.8, 71.4, 52.3, 45.8, 33.9,

31.8, 29.5, 29.2, 25.6, 22.6, 14.0, 9.9; HRMS (ESI) for $C_{14}H_{25}N_2O_4$ $[M+H]^+$ calcd: 285.1814; found: 285.1812; IR (neat): 3517, 2927, 2141, 1719, 1638 cm^{-1}.



6m. Light yellow oil, 69% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 3.92-3.98 (m, 1H), 3.86 (s, 3H), 3.65 (t, 1H, *J* = 4.0 Hz), 2.54 (d, 1H, *J* = 2.8 Hz), 1.20 (d, 3H, *J* = 7.2 Hz), 0.97 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 161.2, 77.3, 52.2, 42.6, 35.5, 26.8, 12.3; HRMS (ESI) for $C_{11}H_{19}N_2O_4$ $[M+H]^+$ calcd: 243.1345; found: 243.1334; IR (neat): 3529, 2956, 2140, 1717, 1634 cm^{-1}.

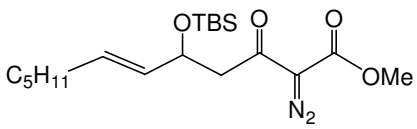
Procedure for Synthesis of 7. To a refluxing green dry DCM (5.0 mL) solution of $Rh_2(OAc)_4$ (5.0 mg, 1.0 mol%) was added a solution of compound **6i** (300 mg, 1.15 mmol) in 5.0 mL of dry DCM over 15 min under nitrogen atmosphere. After completion of the addition, the mixture was refluxed for 2 h, and then cooled to room temperature to give a greenish solution. The reaction mixture was passed through a Celite plug to remove the catalyst, which was rinsed with dry DCM. The solvent was then removed under reduced pressure and the crude product **7** was obtained as yellow oil in 96% yield.

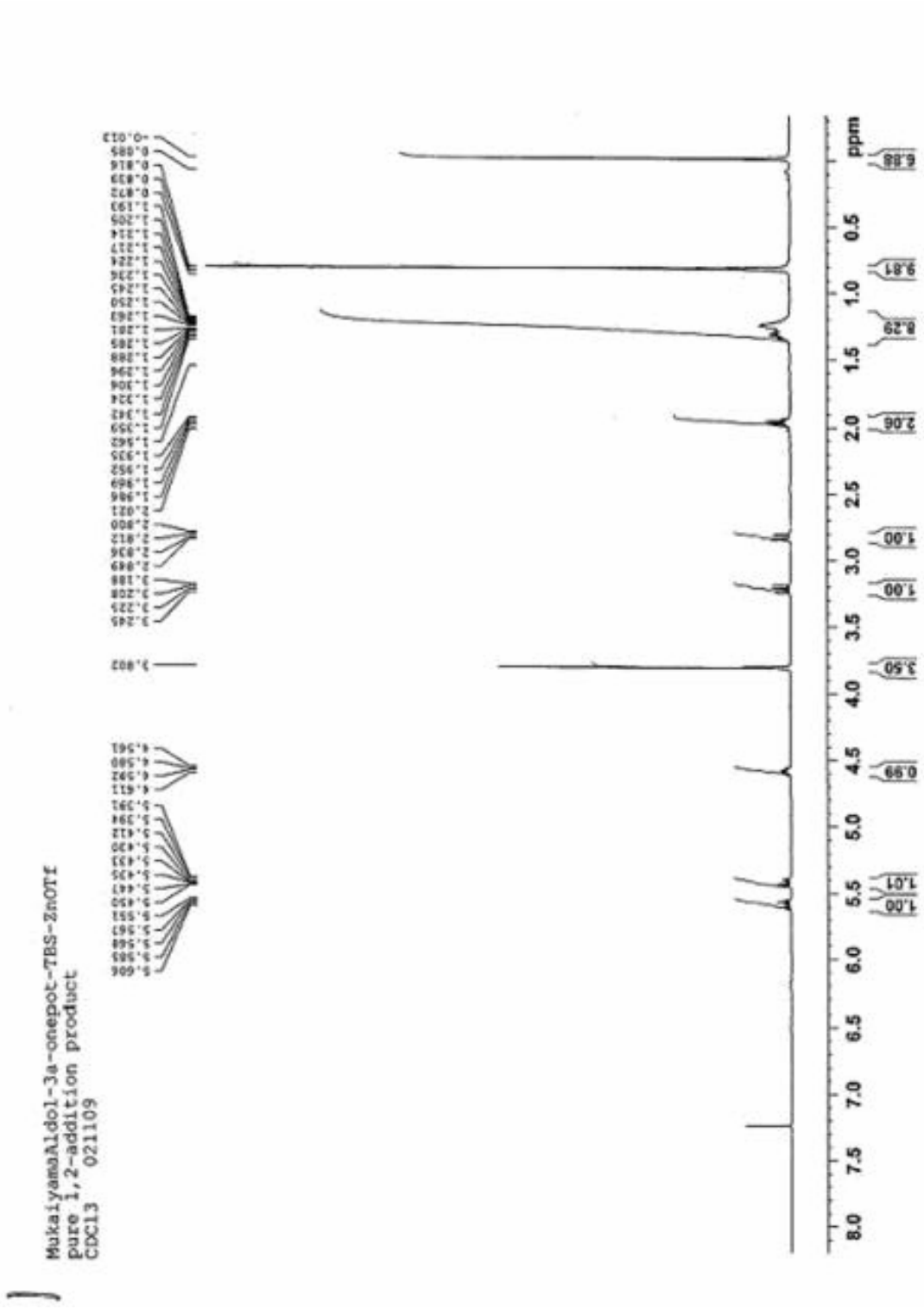


7. Data for the major diastereomer: ^1H NMR (400 MHz, $CDCl_3$): δ 7.28-7.43 (m, 5H), 5.80 (d, 0.62H, *J* = 7.2 Hz), 5.46 (d, 0.38H, *J* = 6.0 Hz), 4.89 (s, 0.62H), 4.68 (s, 0.38H), 3.89 (s, 1.14H), 3.86 (s, 1.86H), 2.83-2.92 (m, 0.62H), 2.77-2.82 (m, 0.38H), 0.85 (d, 1.86H, *J* = 7.2Hz), 0.83 (d, 1.14H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 166.9, 137.0, 128.4, 128.0, 126.3, 82.3, 79.2, 53.0, 45.6, 11.6; HRMS (ESI) for $C_{13}H_{14}NaO_4$ $[M+Na]^+$ calcd: 257.0790; found: 257.0787; IR (neat): 2954, 1769, 1742 cm^{-1}.

NMR spectra of New Compounds.

3a

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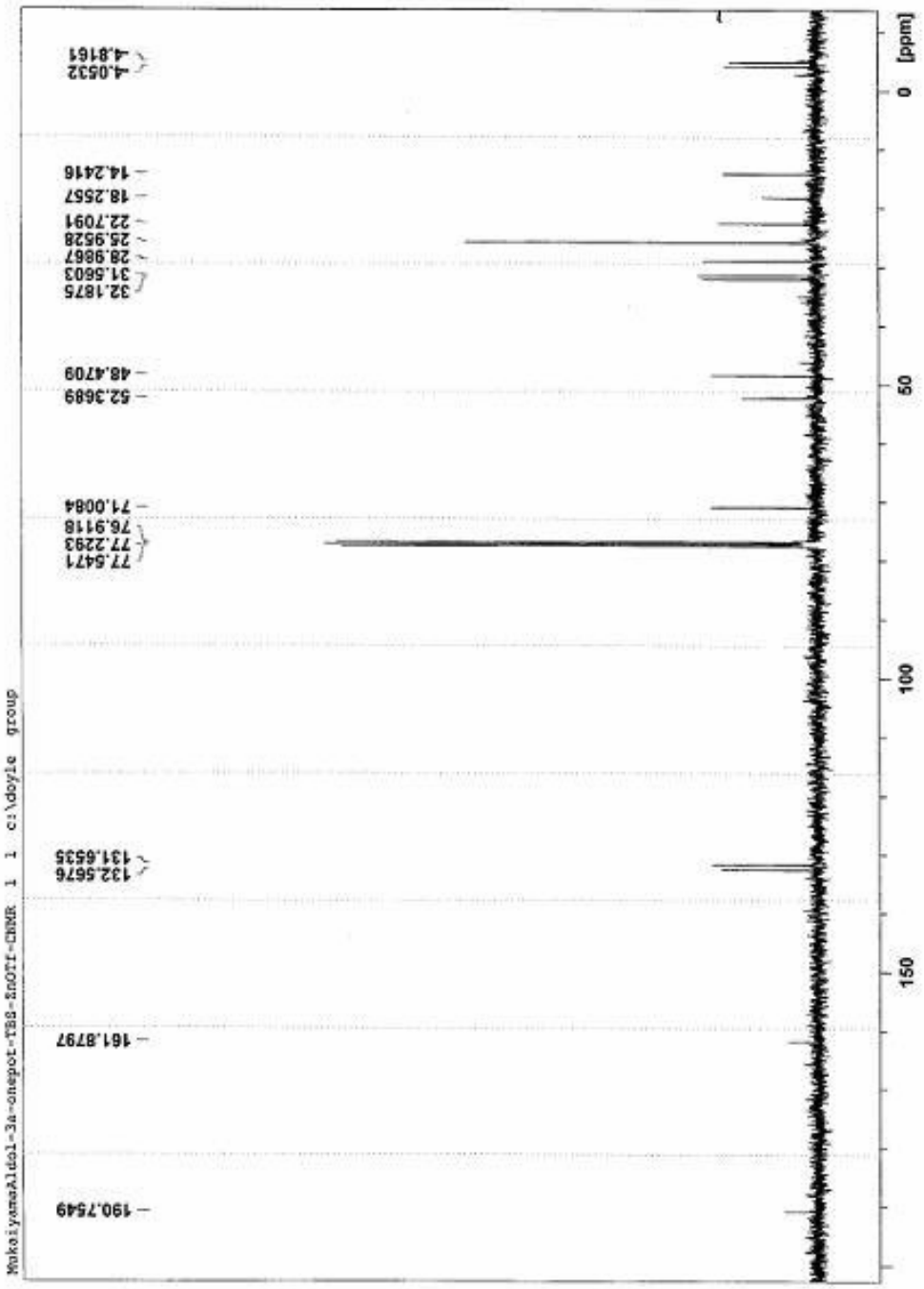
2.06
1.00
1.00
3.50
0.99
1.00
1.01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71.0084
52.3689
48.4709
32.1875
31.5603
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25.9528
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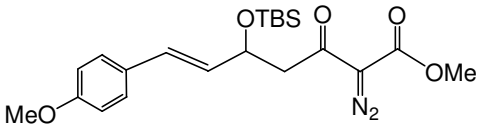
4.8161
[ppm]
0
50
100
150

3b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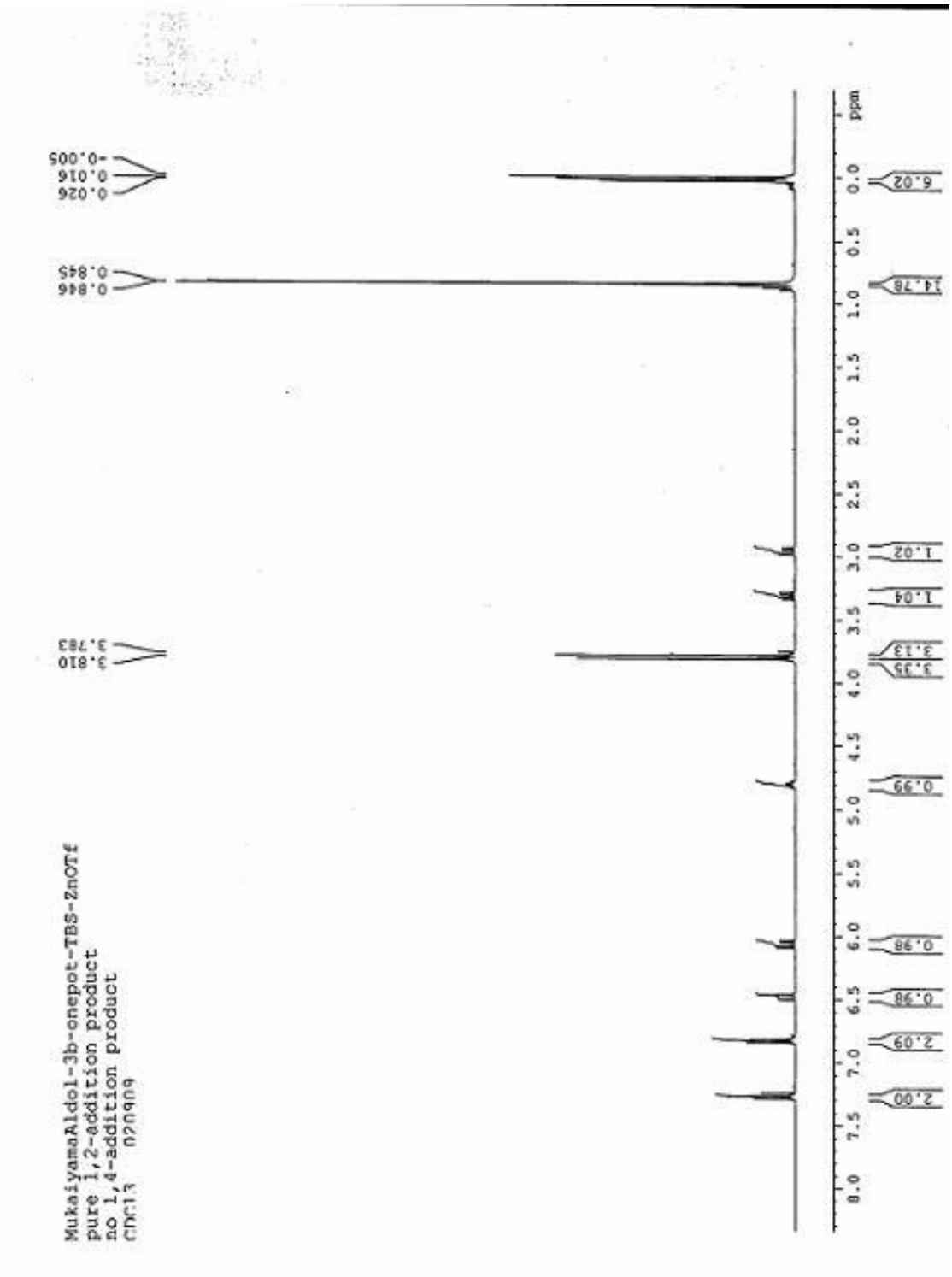
O
OMe
MeO
N2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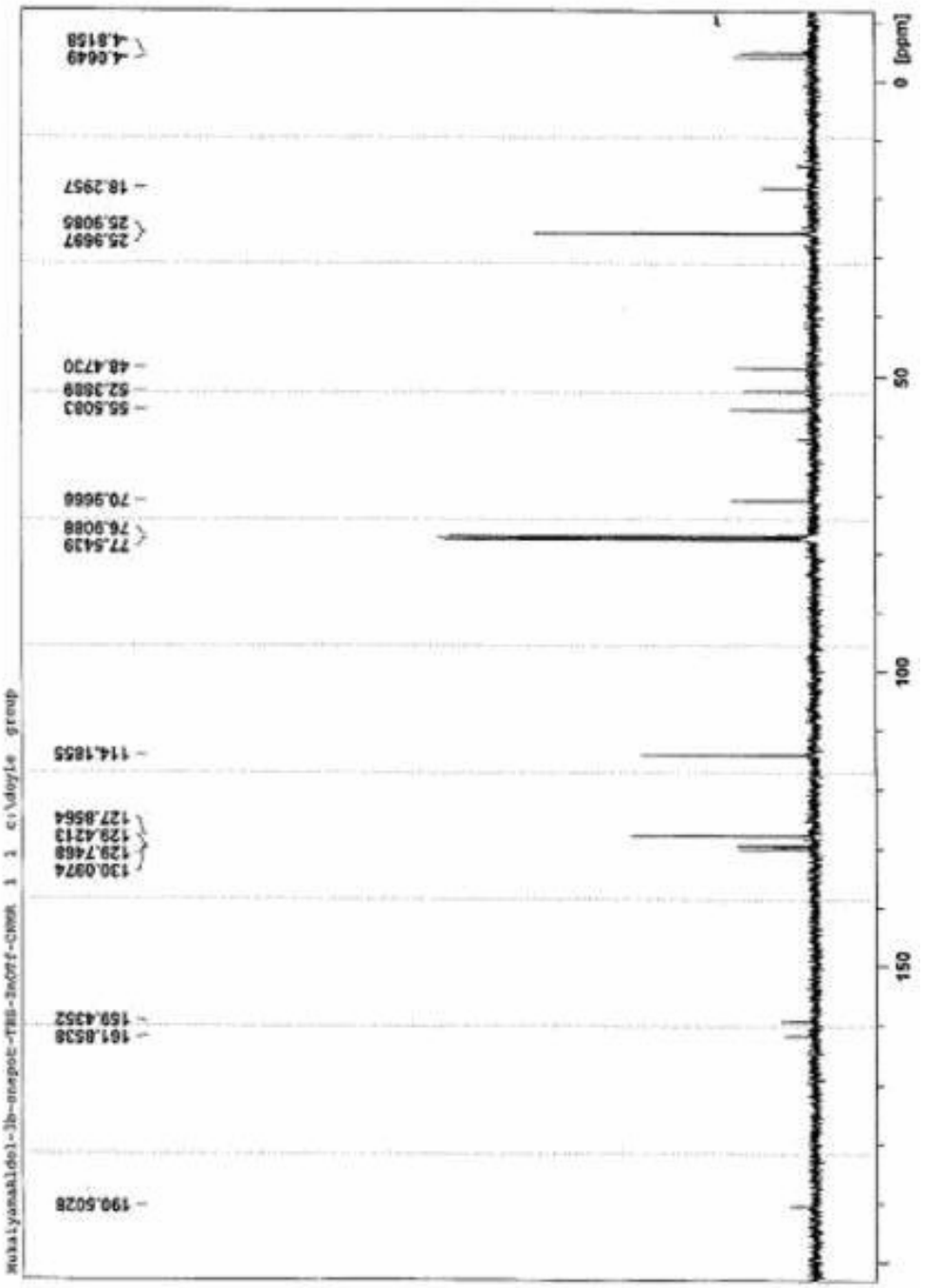
no 1,4-addition product
ppm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18.2957
25.9697
25.9086
48.4730
52.3089
55.5083
70.9666
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77.5439
114.1855
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161.8538
190.5028
[ppm]
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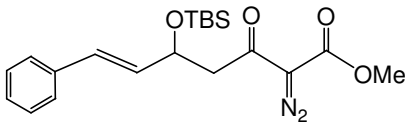
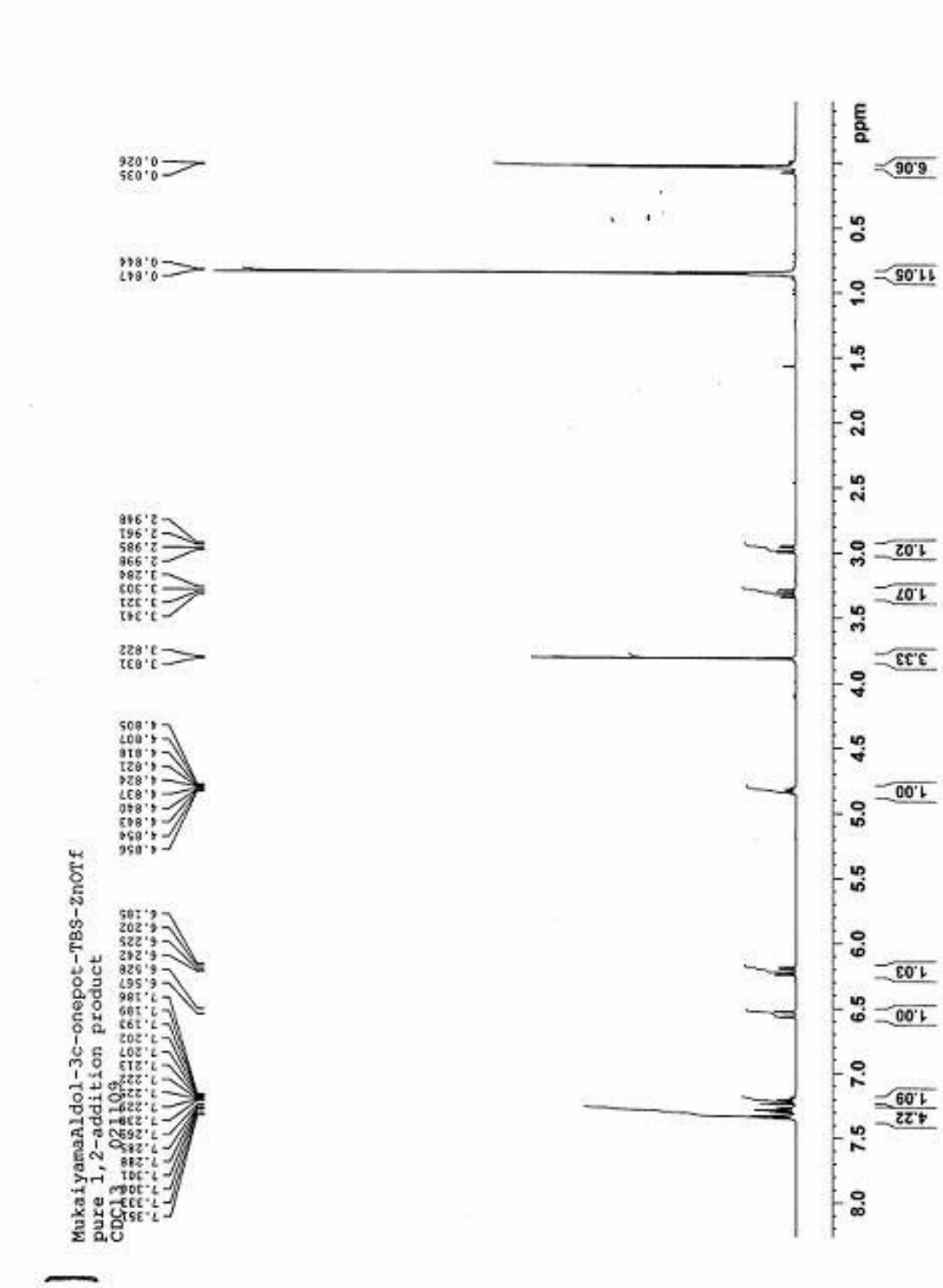
50
100
150

3c


OTBS
O
O
OMe
N2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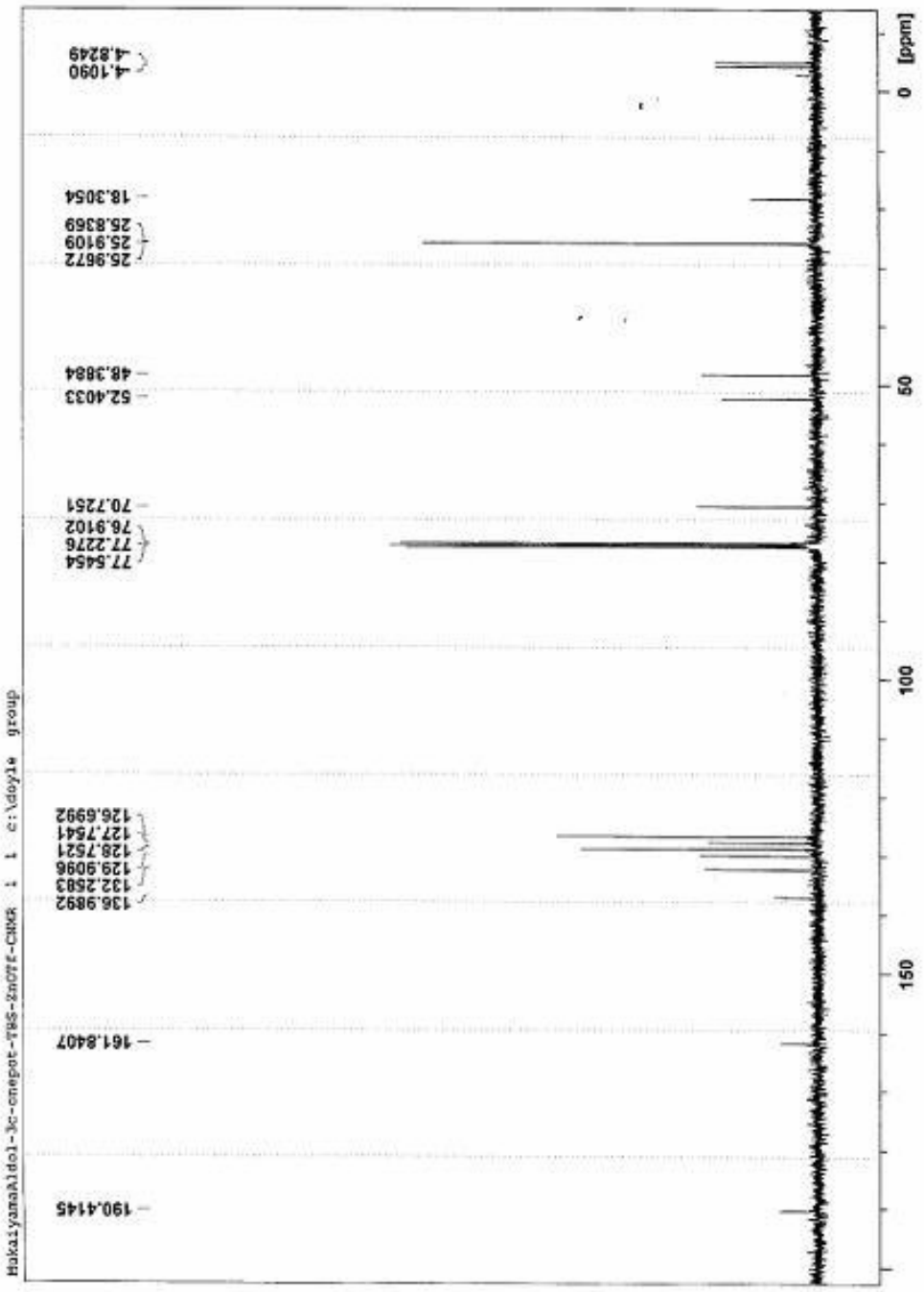
pure 1,2-addition product
CDCl3
ppm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128.7521
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77.2276
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4.8249
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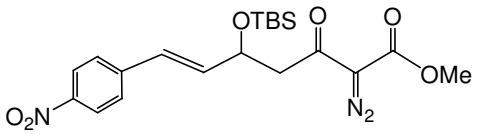
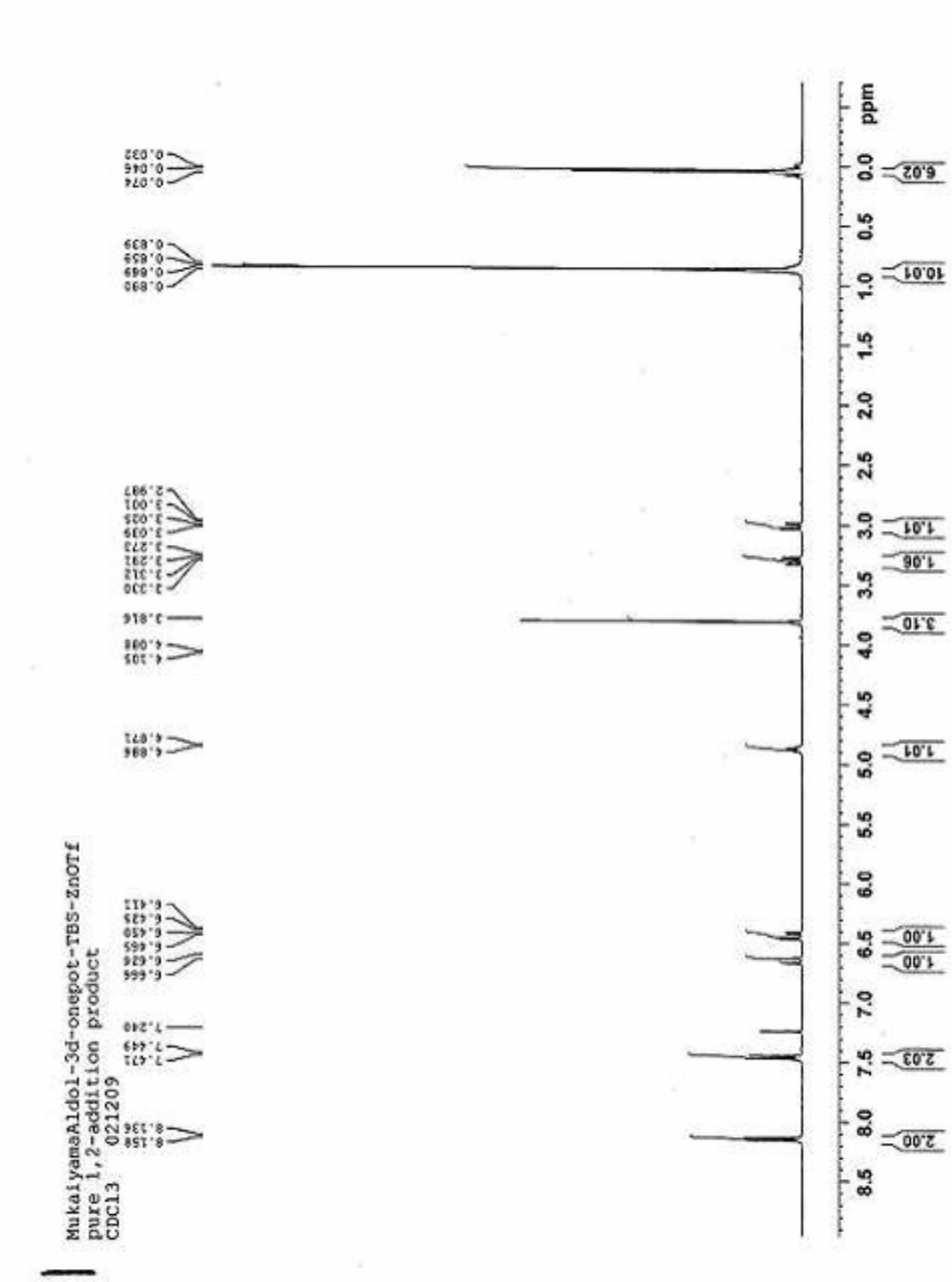
100
150

3d


OTBS
O
O
OMe
O_2N
N_2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pure 1,2-addition product
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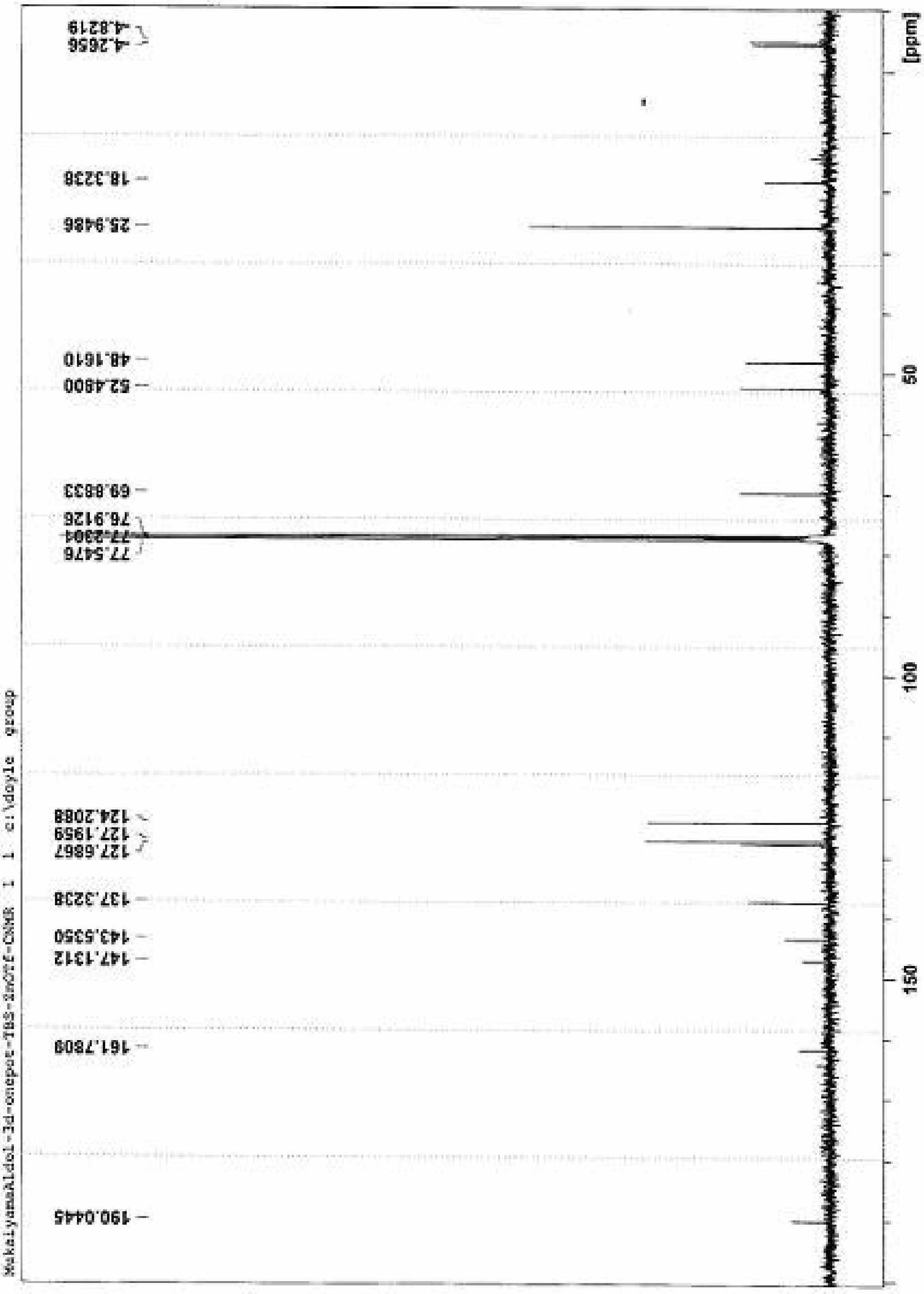
1.01
1.00
1.00
2.03
2.00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77.5476
124.2088
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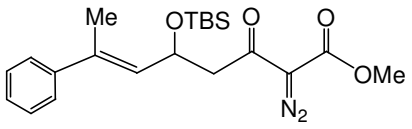
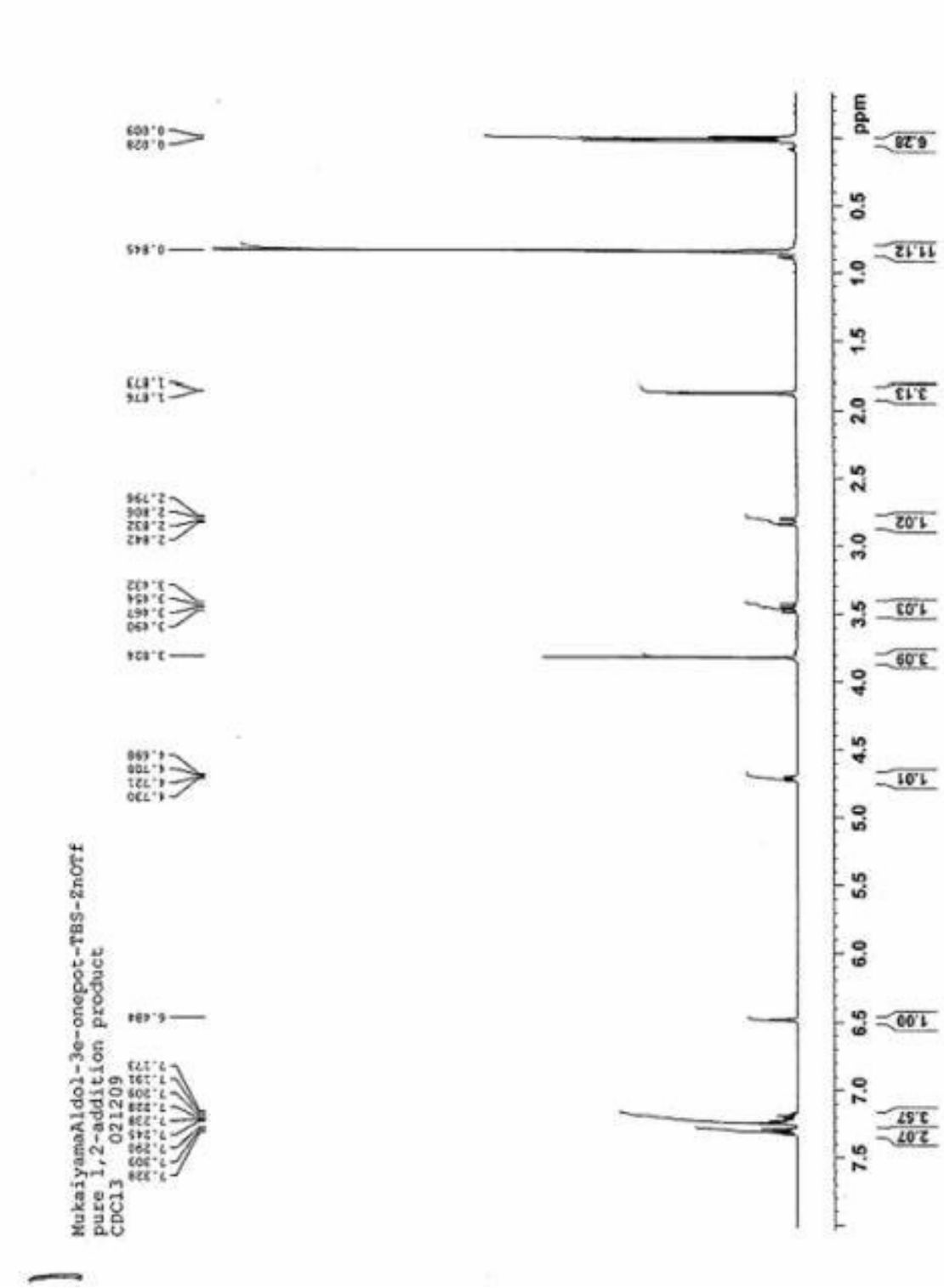
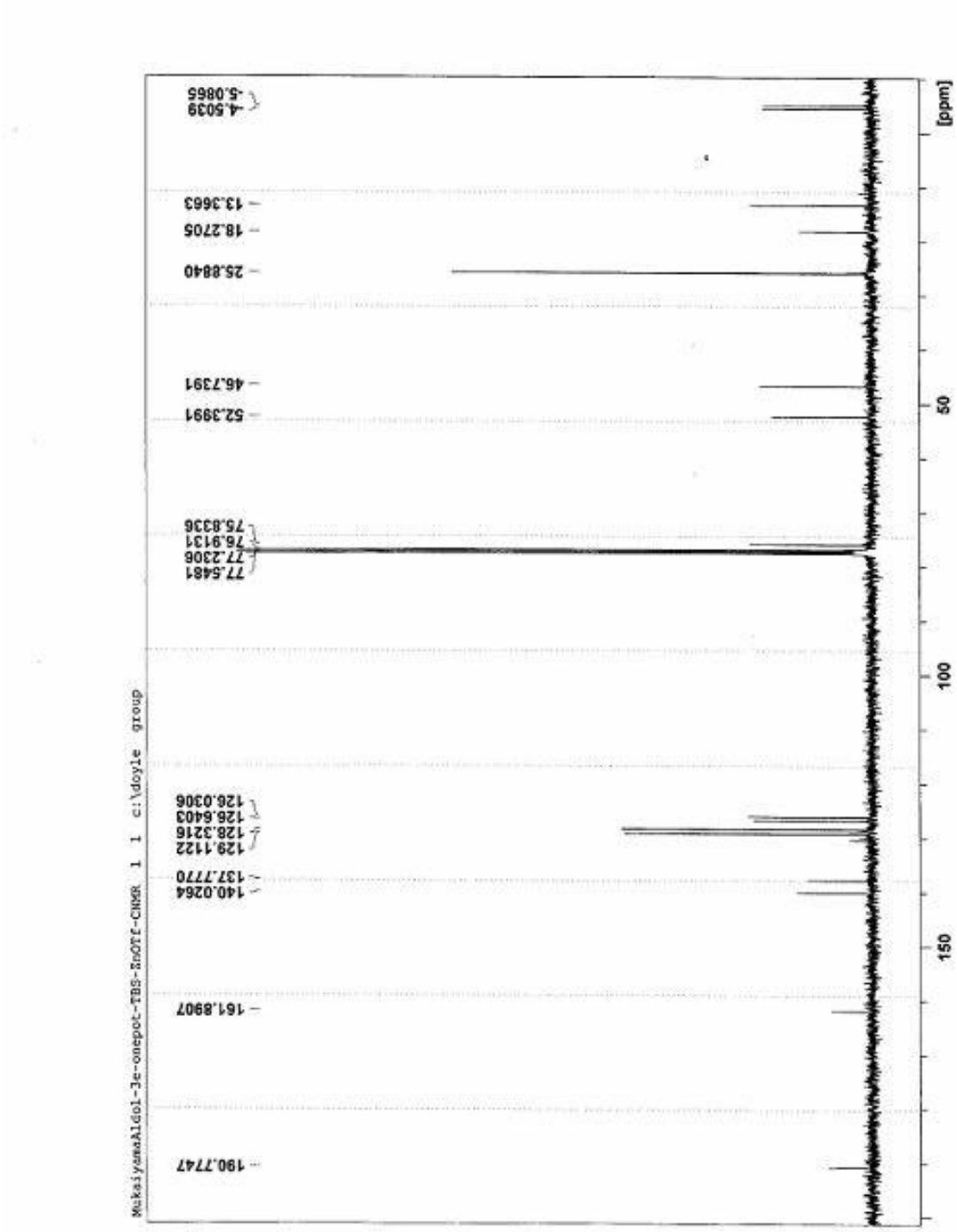
100
150

3e


Me
OTBS
O
O
OMe
N2


Mukaiyama Aldol-3e-onepot-TBS-ZnOTf
pure 1,2-addition product
CDCl3
021209
ppm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140.0264
137.7770
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128.3216
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76.8336
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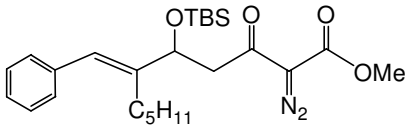
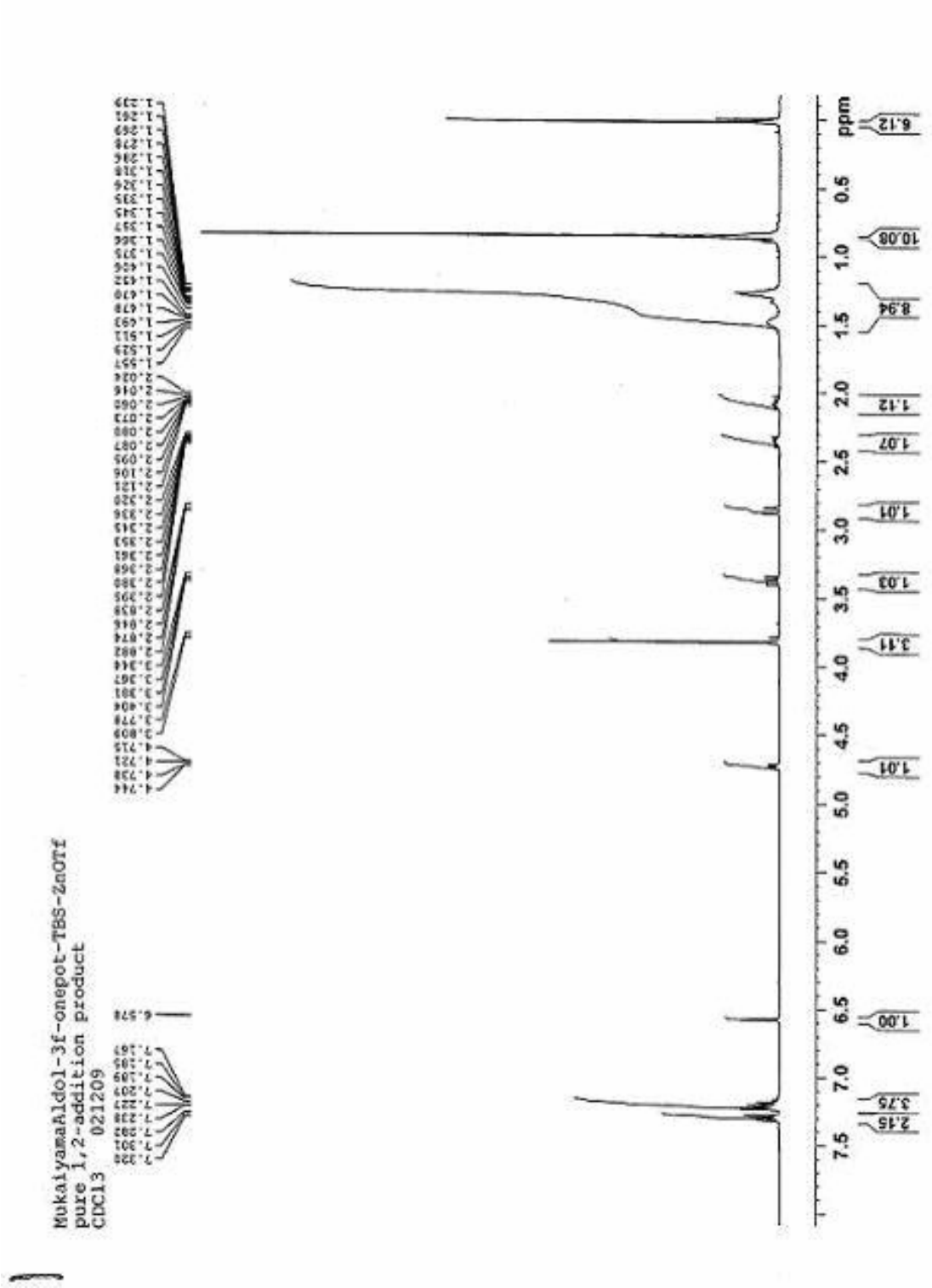
50

3f


OTBS
O
O
OMe
C_5H_{11}
N_2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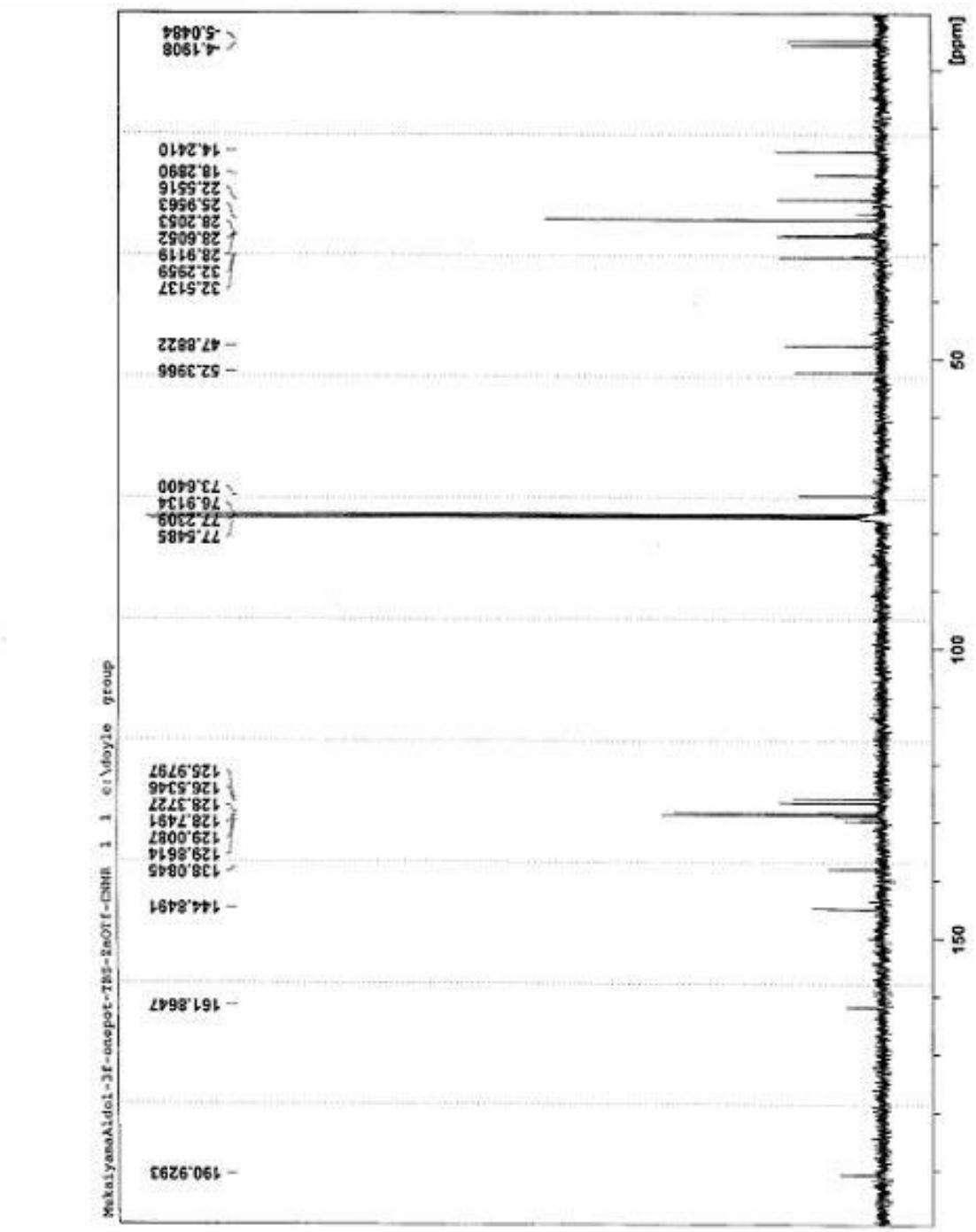
1.03
3.11
1.01
1.00
3.75
2.15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25.9563
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28.9119
32.2959
32.5137
47.8822
52.3966
73.6400
76.9134
77.2309
77.6485
125.9797
126.5346
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128.7491
129.0087
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144.8491
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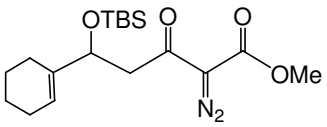
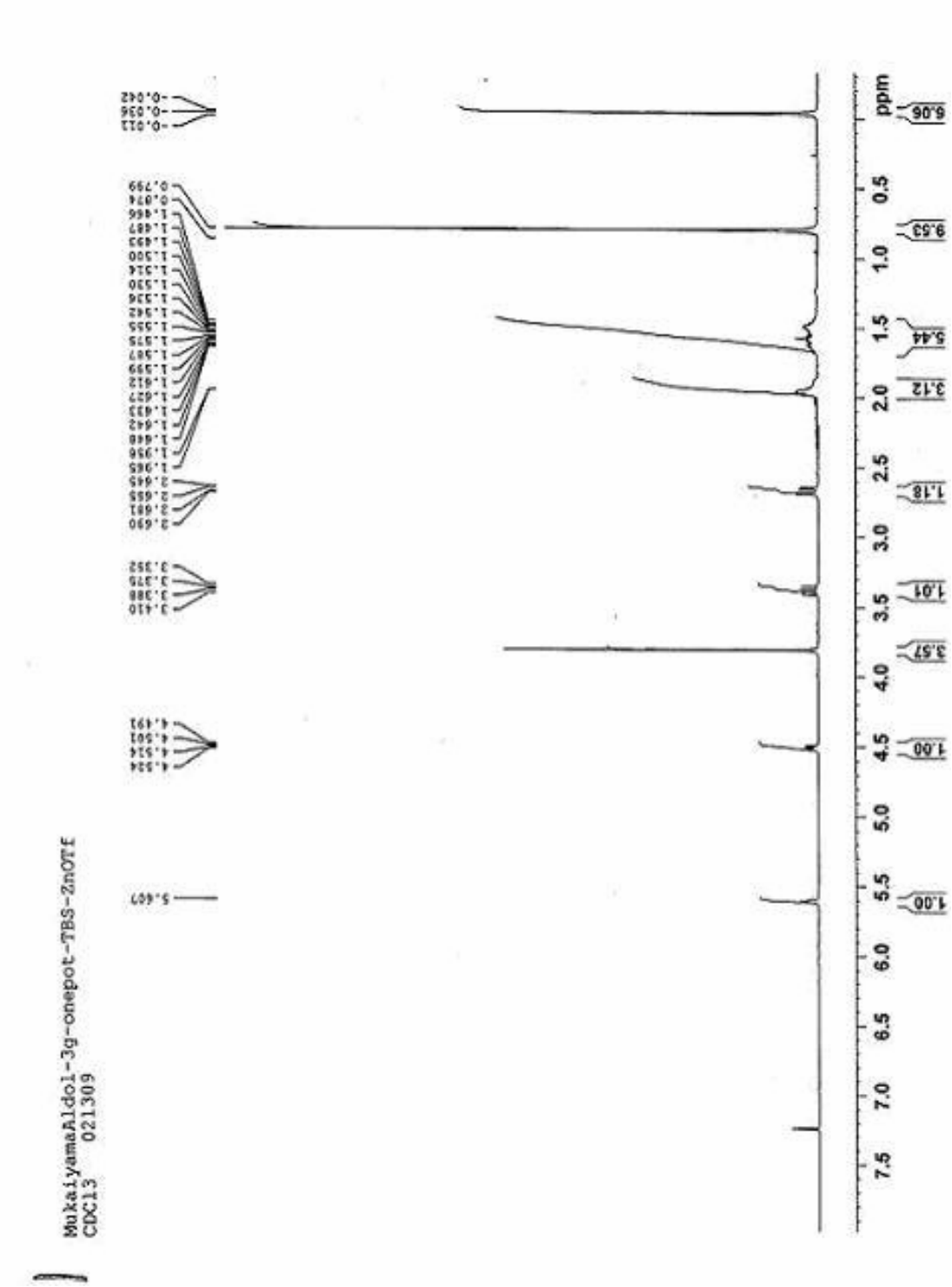
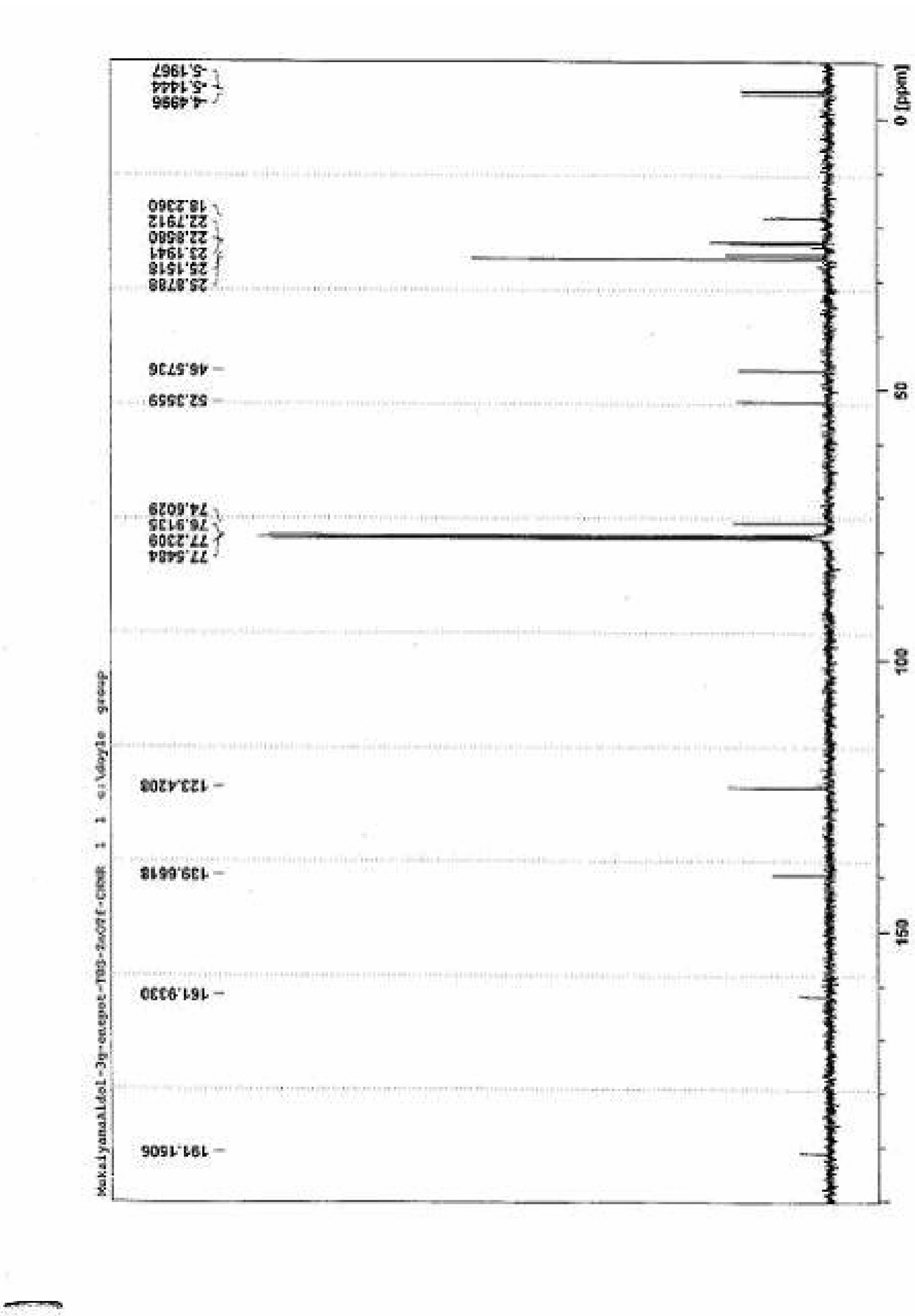
100
150

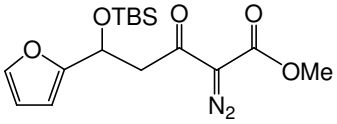
3g

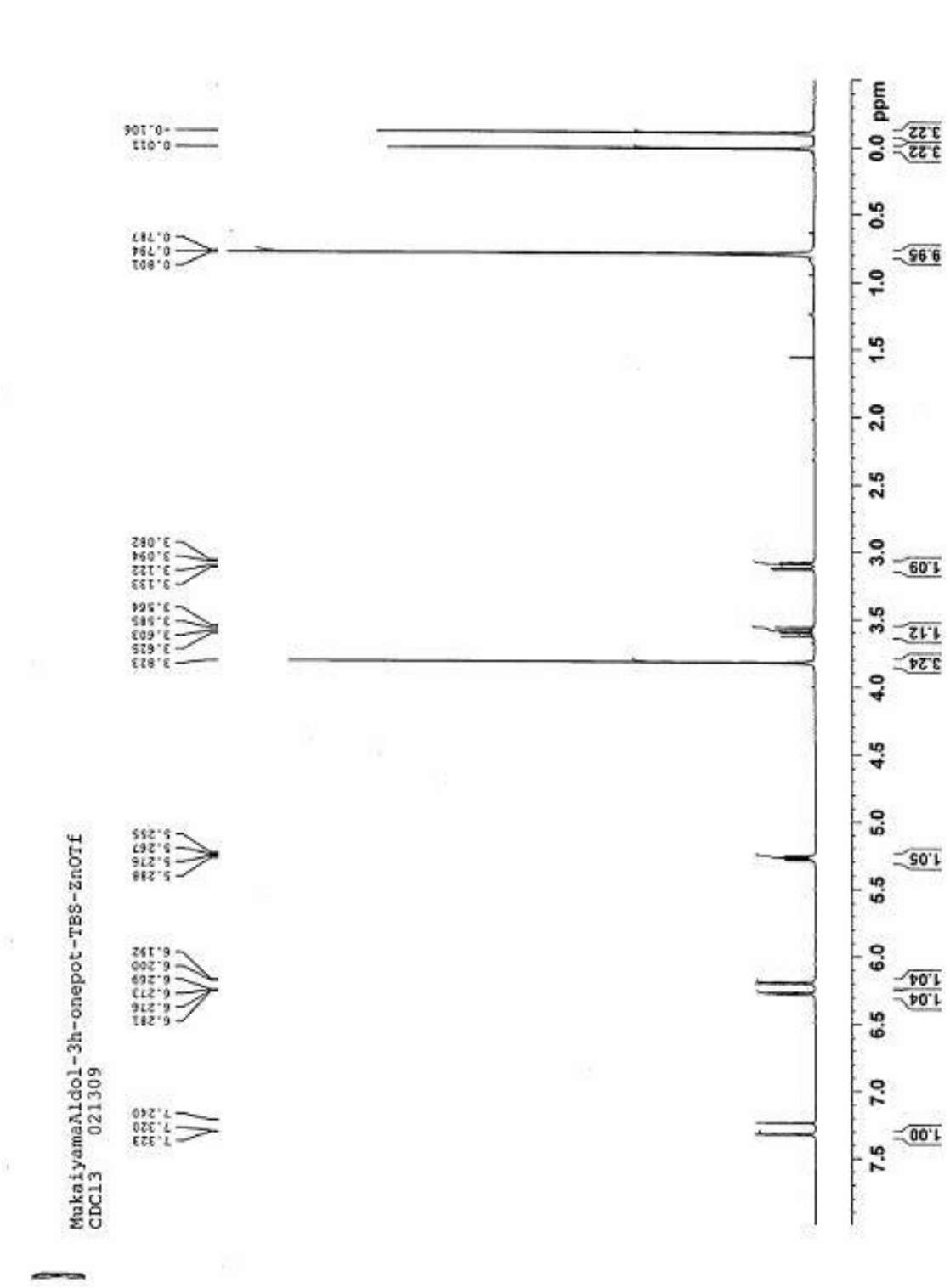

OTBS
O
O
OMe
N2

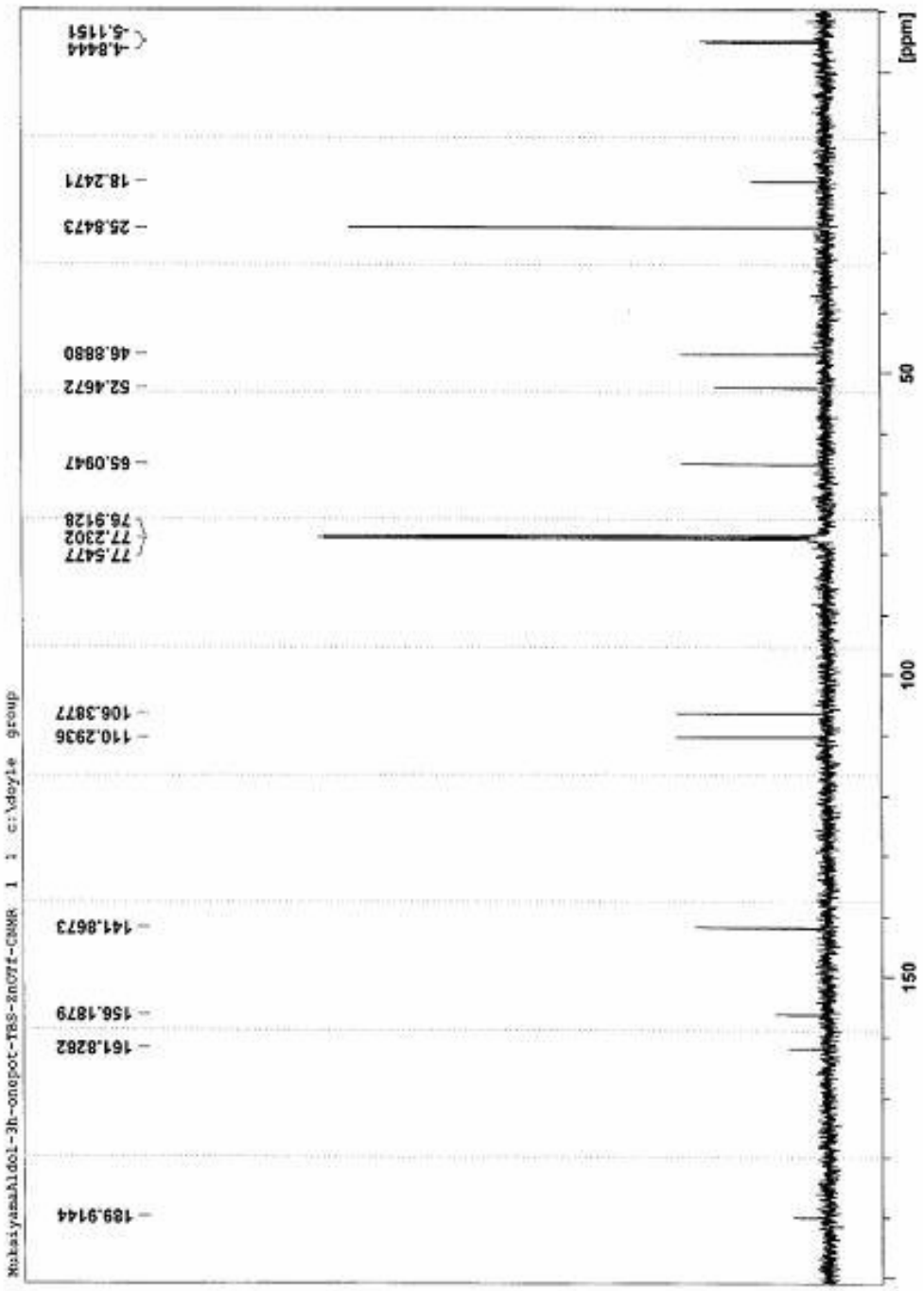

MukaiyamaAldol-3g-onepot-TBS-ZnOTf
CDCl3 021309
ppm


-5.1967
-5.1444
-4.4996
18.2360
22.7912
22.8580
23.1941
25.1518
25.8788
46.5736
52.3559
74.6029
76.9135
77.2309
77.5484
123.4208
139.6618
161.9330
191.1506
0 [ppm]
50
100
150

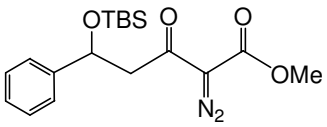
3h

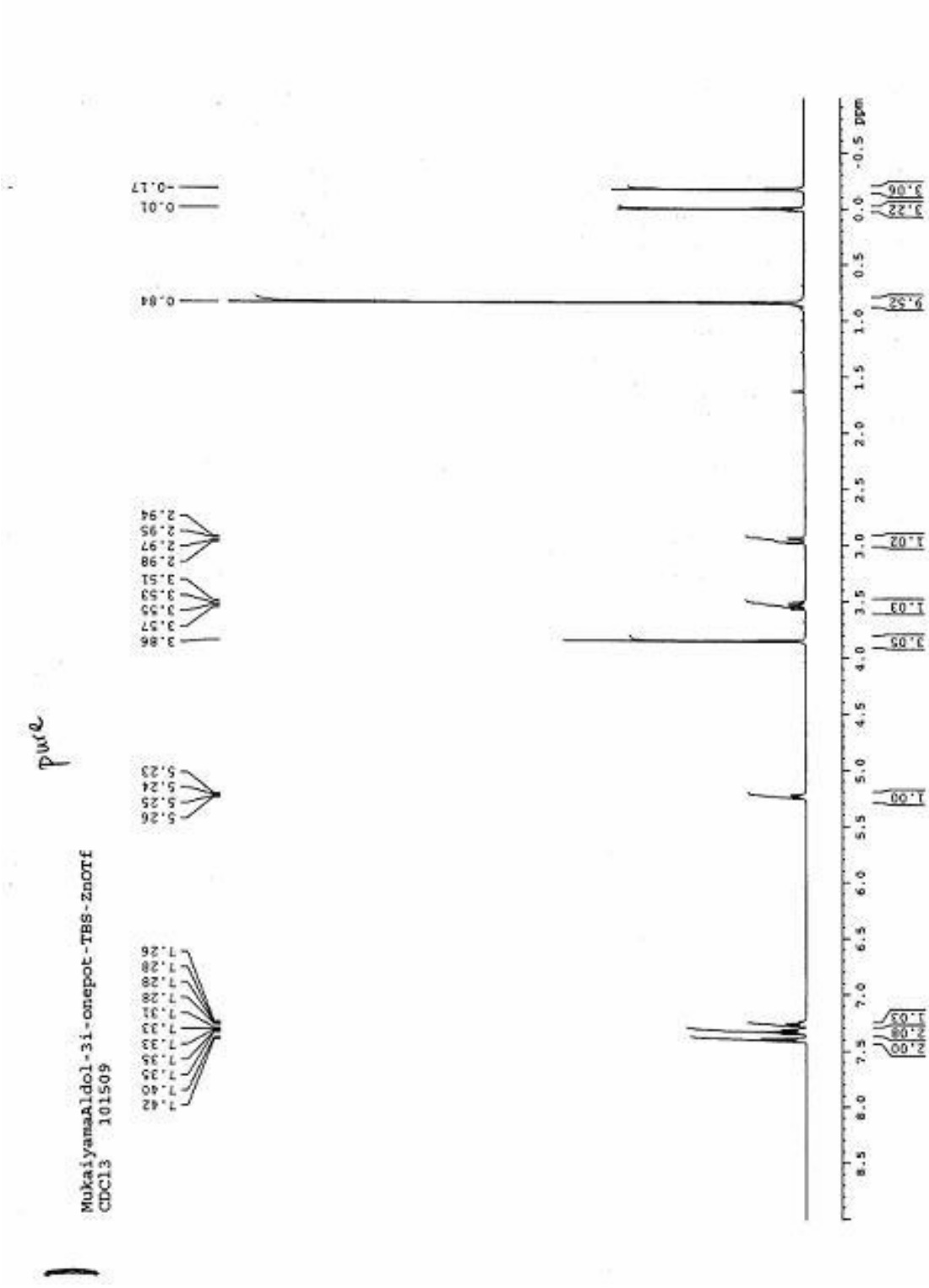

OTBS
O
O
O
OMe
N2

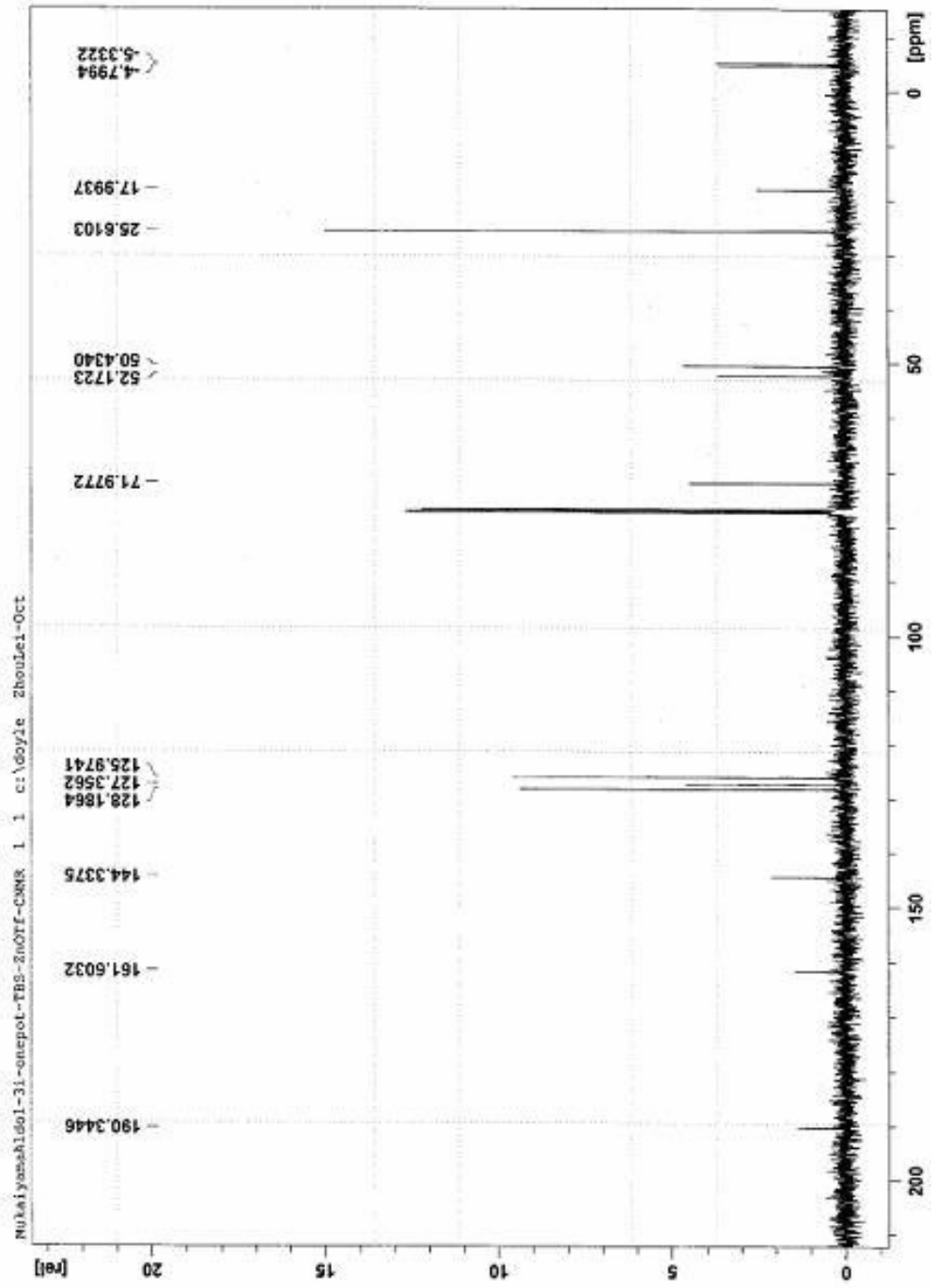

MukaiyamaAldol-3h-onepot-TBS-ZnOTf
CDCl3 021309
0.106
0.013
0.801
0.794
0.787
3.082
3.094
3.122
3.133
3.664
3.585
3.603
3.625
3.823
5.288
5.276
5.267
5.255
6.281
6.276
6.273
6.269
6.200
6.192
7.323
7.320
7.260
0.0 ppm
3.22
3.22
9.95
1.09
1.12
3.24
1.05
1.04
1.04
1.00


Mukaiyamaaldol-3h-onepot-TBS-80ff-CNMR 1 1 c:\doyle group
189.9144
161.8282
156.1879
141.8673
110.2936
106.3877
77.5477
77.2302
76.9128
65.0947
52.4672
46.8880
25.8473
18.2471
-4.8444
-5.1151
[ppm]
150
100
50

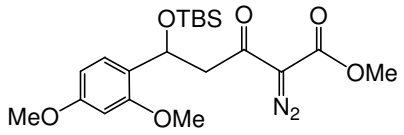
3i

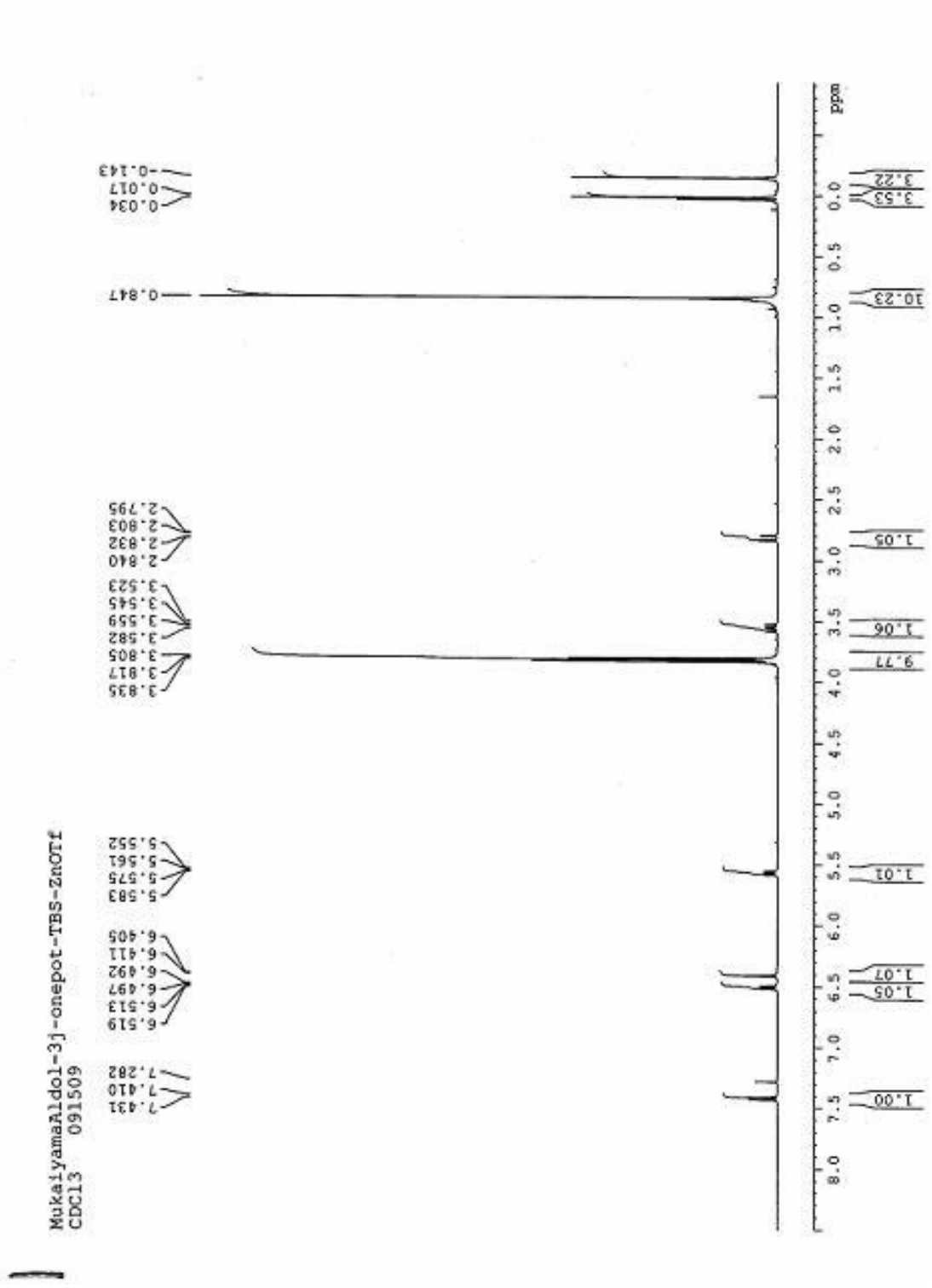

OTBS
O
O
OMe
N2

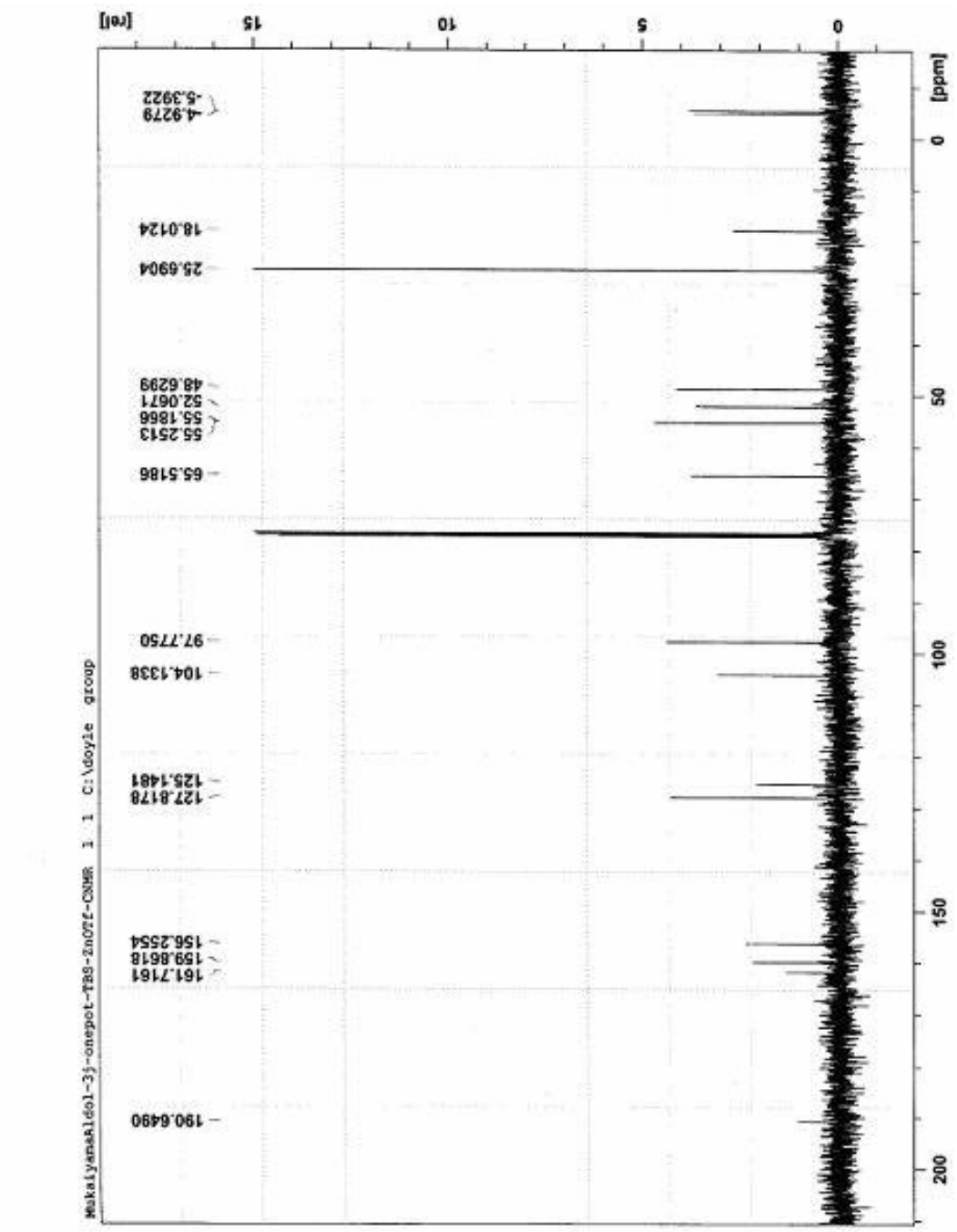

MukaiyamaAldol-31-onepot-TBS-ZnOTf
CDCl3 101509
pure
-0.17
0.01
0.84
2.94
2.95
2.97
2.98
3.51
3.53
3.55
3.57
3.86
5.23
5.24
5.25
5.26
7.26
7.28
7.28
7.28
7.31
7.33
7.33
7.35
7.35
7.60
7.62
3.06
3.22
9.52
1.02
1.03
3.05
1.00
1.03
2.08
2.00
-0.5 ppm


NukaiyamaAldol-31-onepot-TBS-ZnOTf-CNMR 1 1 c:\doyle ZhouLei-Oct
190.3446
161.6032
144.3375
128.1864
127.3562
125.9741
71.9772
52.1723
50.4340
25.6103
17.9937
-4.7994
-5.3322
[rel]
[ppm]

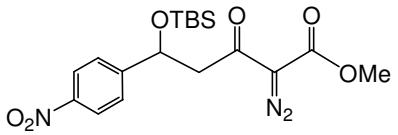
3j

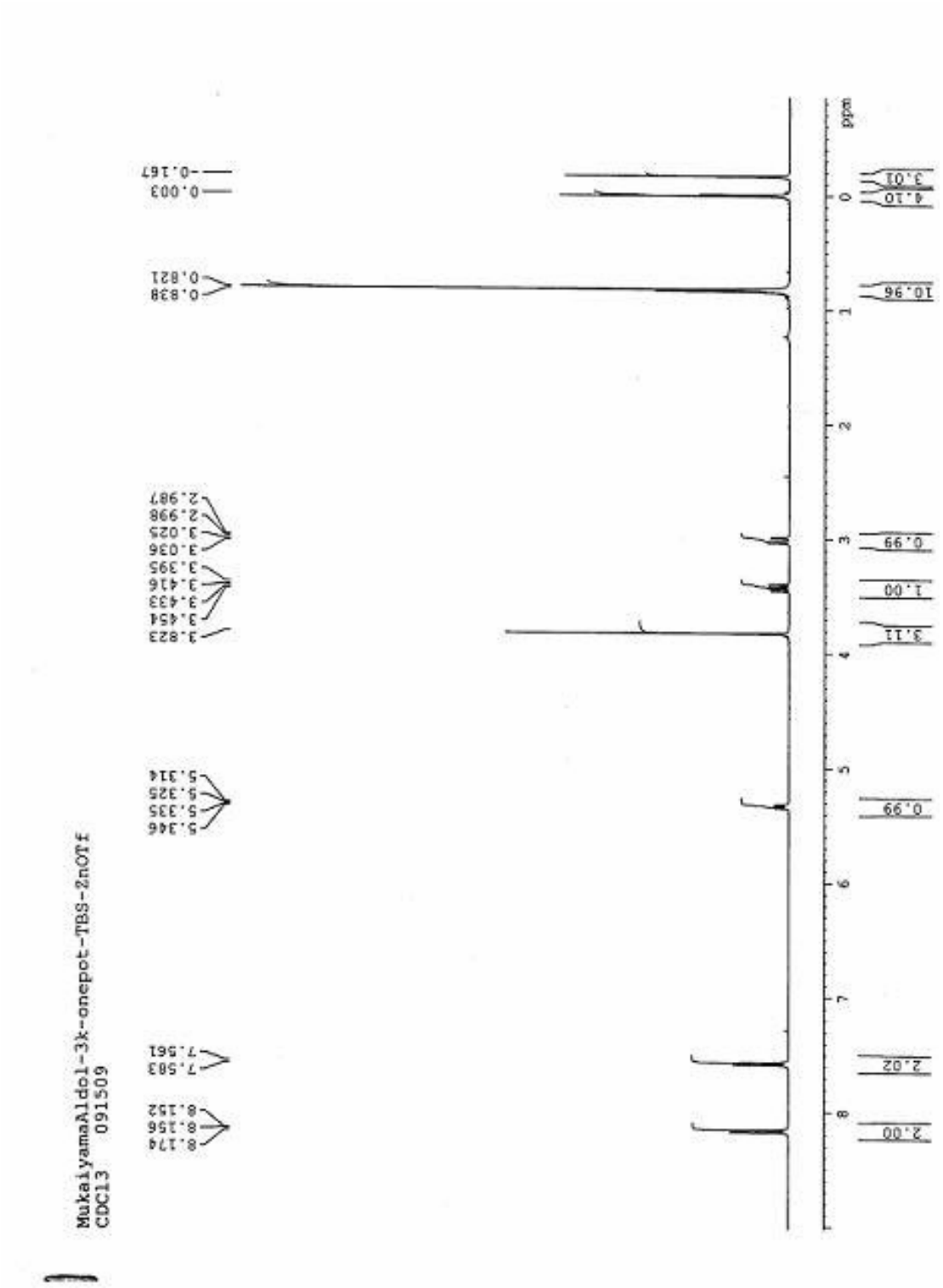

OTBS
O
O
OMe
N2
MeO
OMe

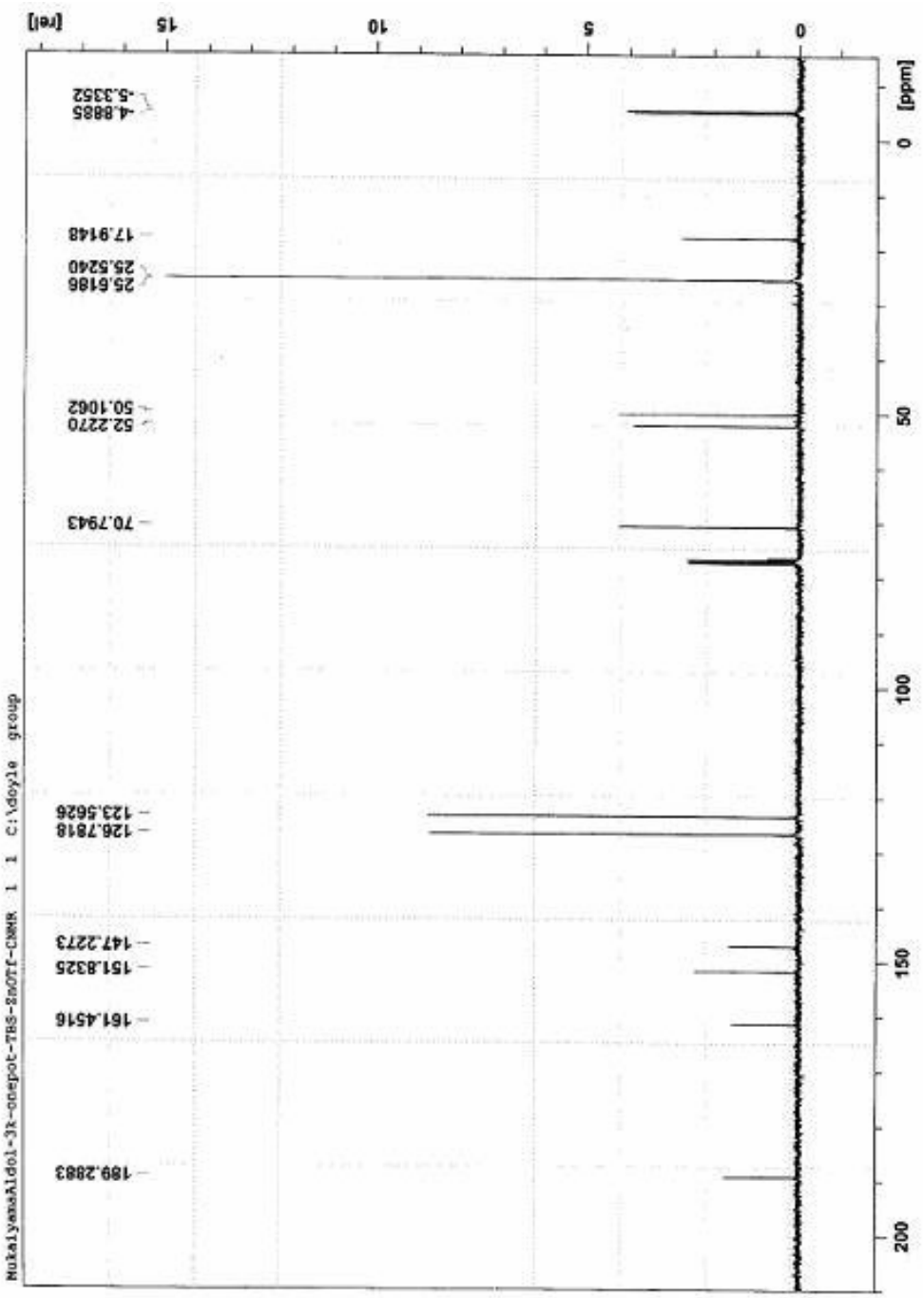

MukaiyamaAldol-3j-onepot-TBS-ZnOTf
CDCl3 091509
ppm


MakaiyamaAldol-3j-onepot-TBS-2nOff-CNMR 1 1 C:\doyle group
190.6490
161.7161
159.8618
156.2554
127.8178
125.1481
104.1338
97.7750
65.5186
55.2513
55.1866
52.0671
48.6299
25.6904
18.0124
-4.9279
-5.3922
[ppm]
[rel]

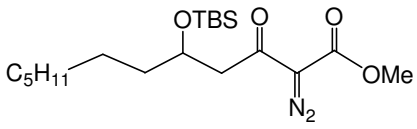
3k

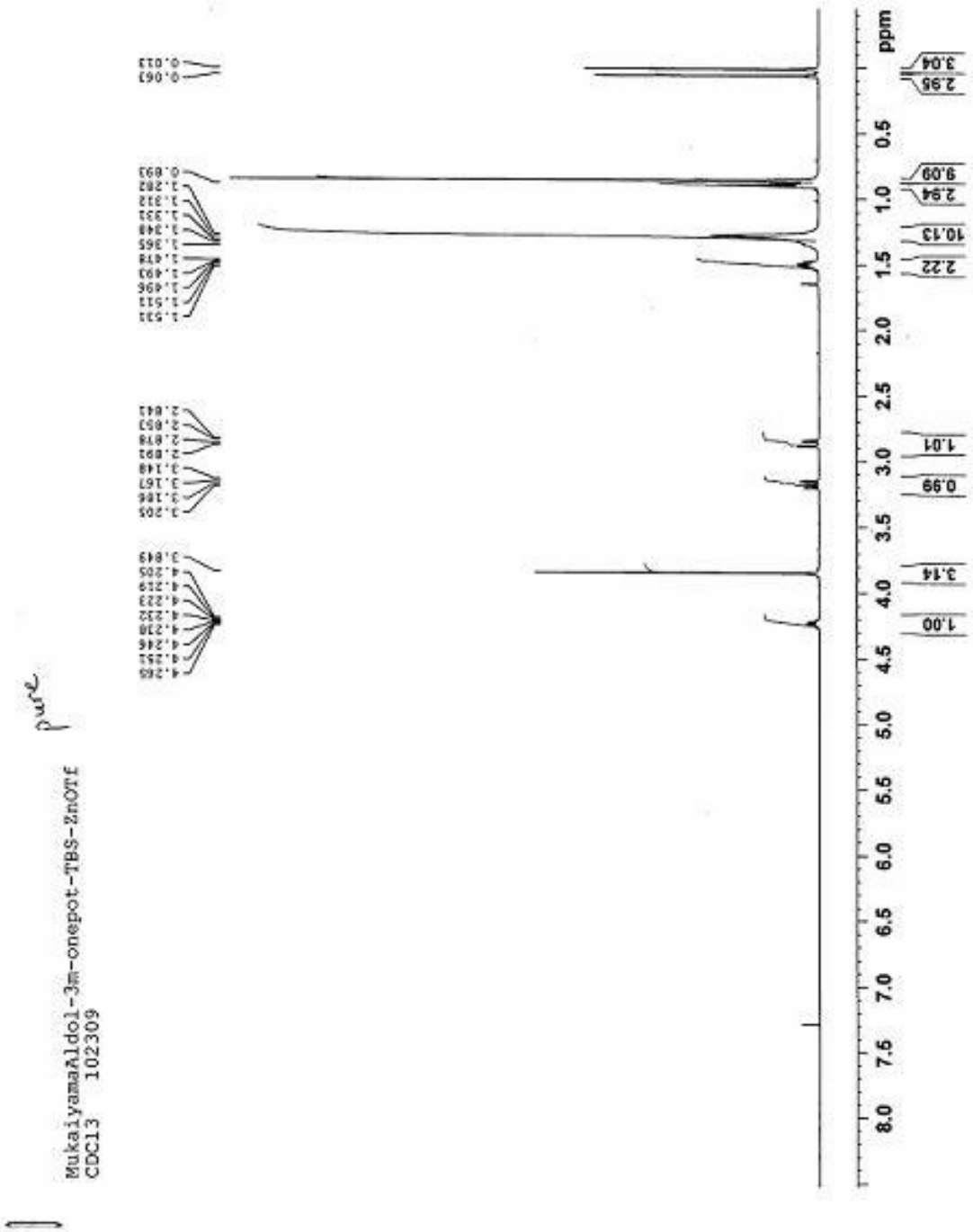

OTBS
O
O
OMe
O_2N
N_2

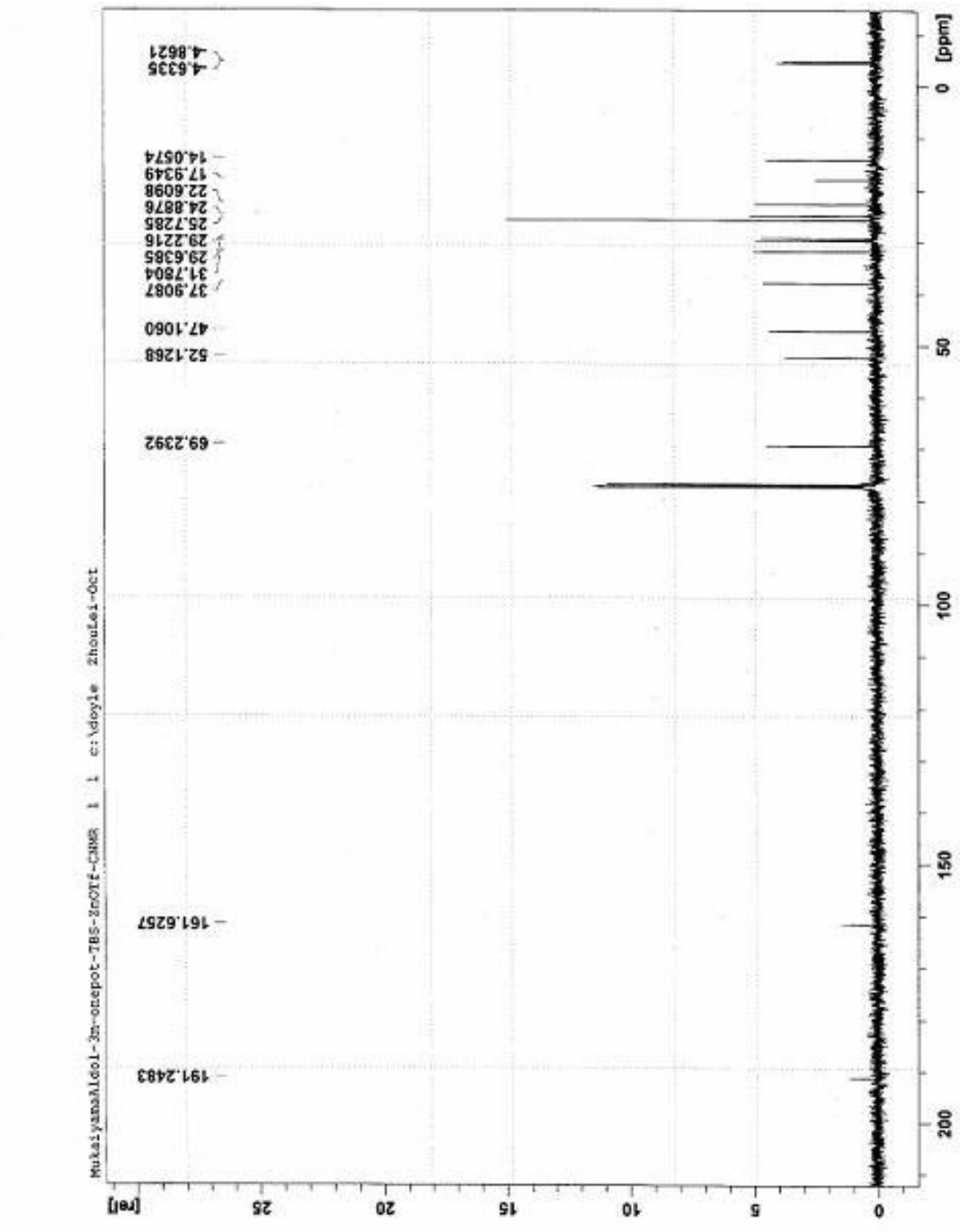

MukaiyamaAldol-3k-onepot-TBS-2nOTf
CDCl3 091509
ppm


Nukaiyamaaldol-3k-oxepot-TBS-2bOTf-CNMR 1 1 C:\doyle group
[ppm]
0
50
100
150
200
-4.8885
-5.3352
17.9148
25.5186
25.5240
50.1062
52.2270
70.7943
123.5626
126.7818
147.2273
151.8325
161.4516
189.2883

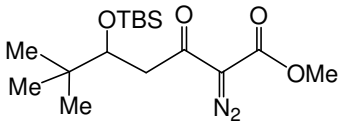
3l

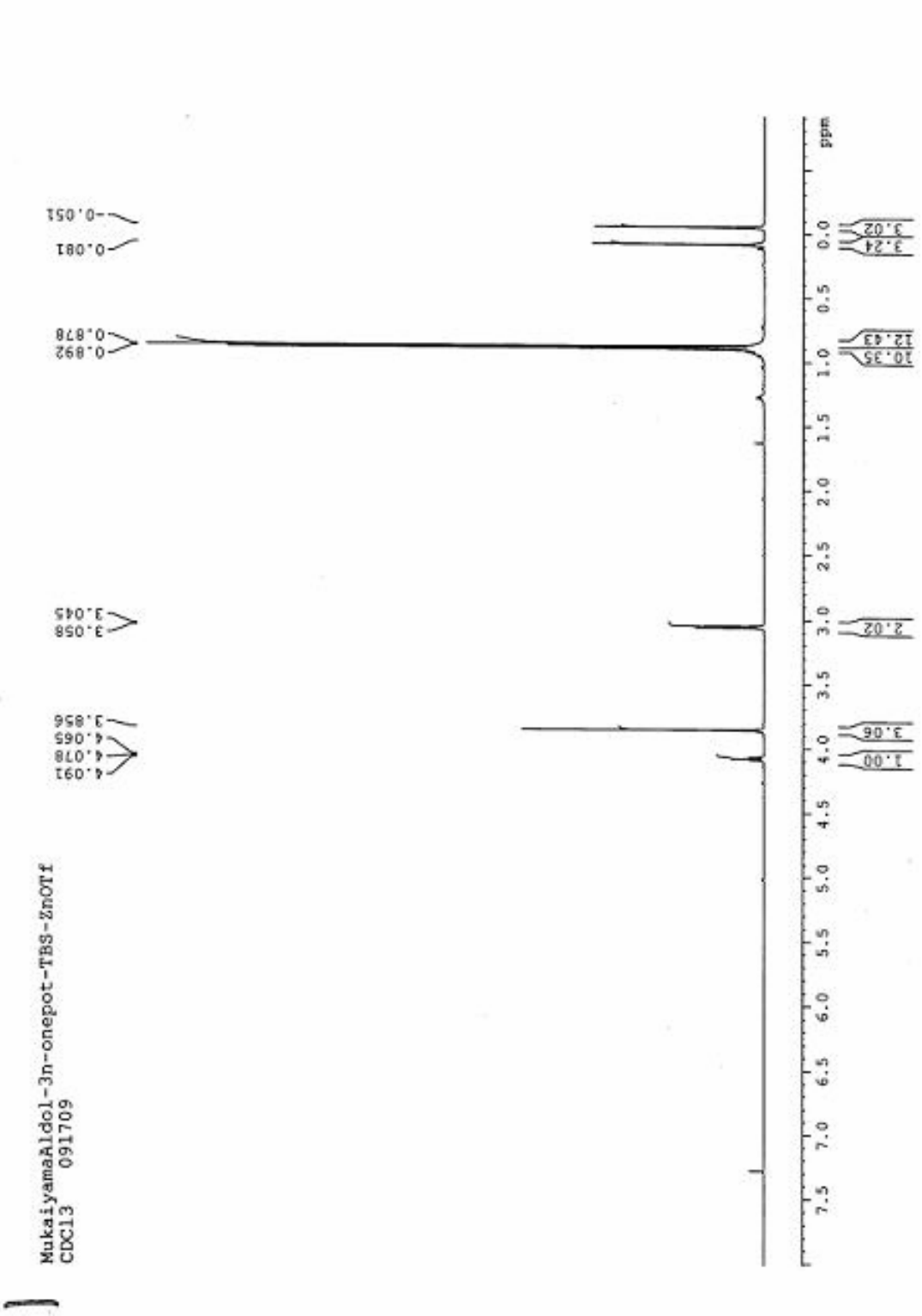

OTBS
O
O
C5H11
OMe
N2

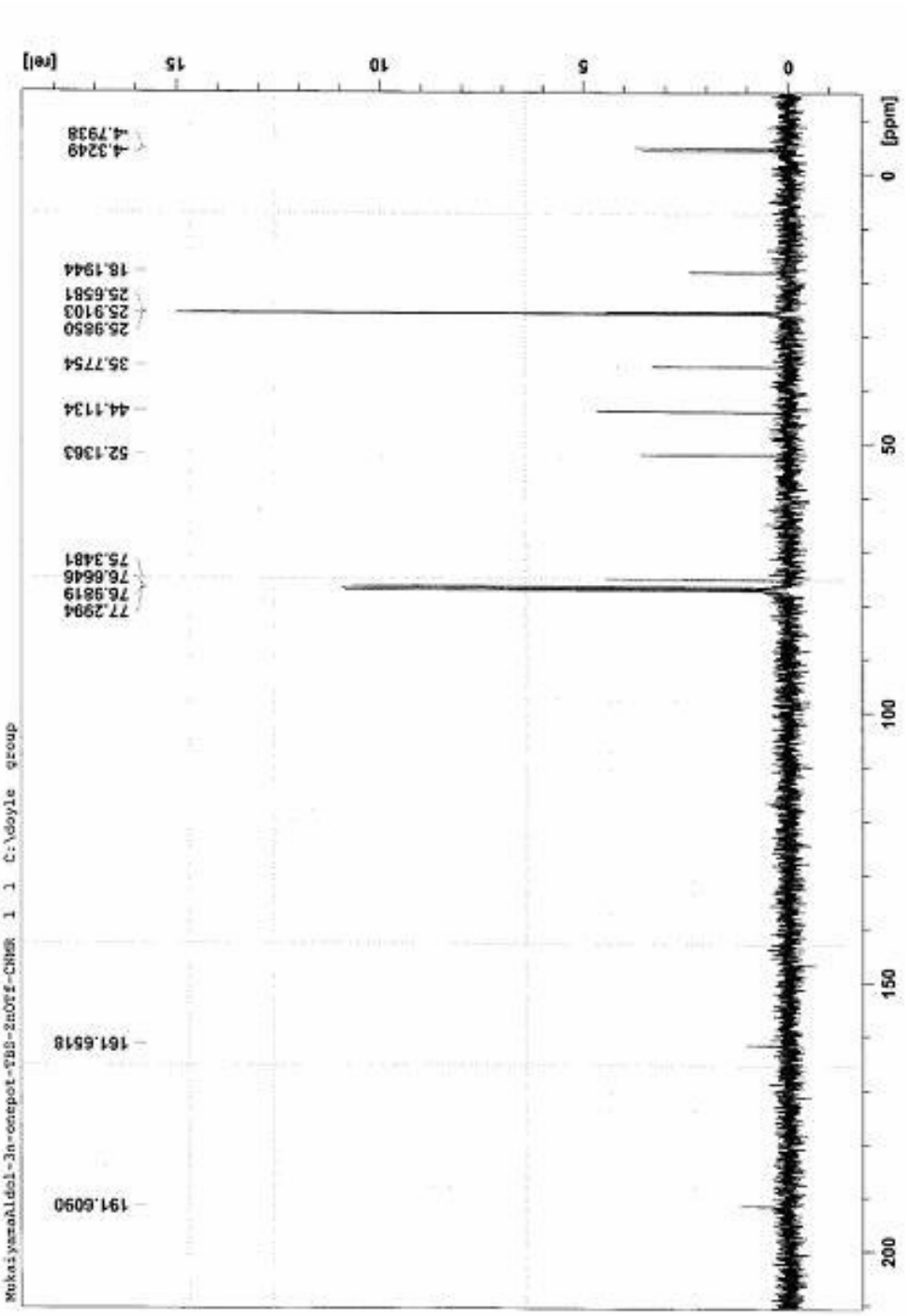

MukaiyamaAldol-3m-onepot-TBS-ZnOTf
CDCl3 102309
pure
ppm
3.04
2.95
9.09
2.94
10.13
2.22
1.01
0.99
3.14
1.00


Mukaiyamaaldol-3m-onepot-TBS-ZnOTf-CNMR 1 1 c:\doyle zhouLei-Oct
191.2483
161.6257
69.2392
52.1268
47.1060
37.9087
31.7804
29.6385
29.2216
25.7285
24.8876
22.6098
17.9349
14.0574
4.6335
4.8621
[rel]
0
5
10
15
20
25
[ppm]
0
50
100
150
200

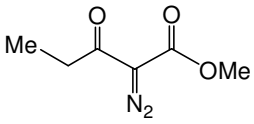
3m

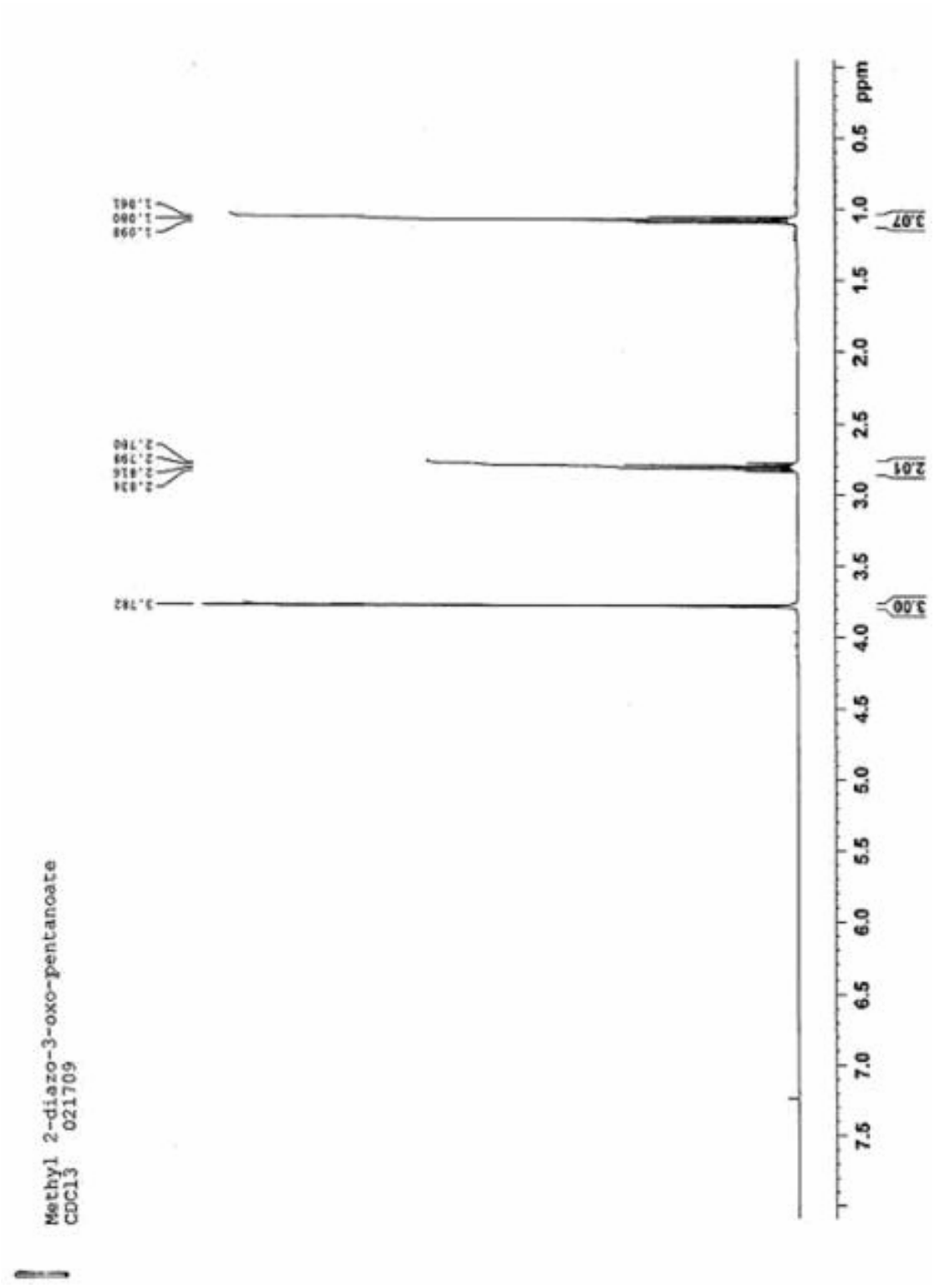

OTBS
O
O
Me
Me
Me
OMe
N2

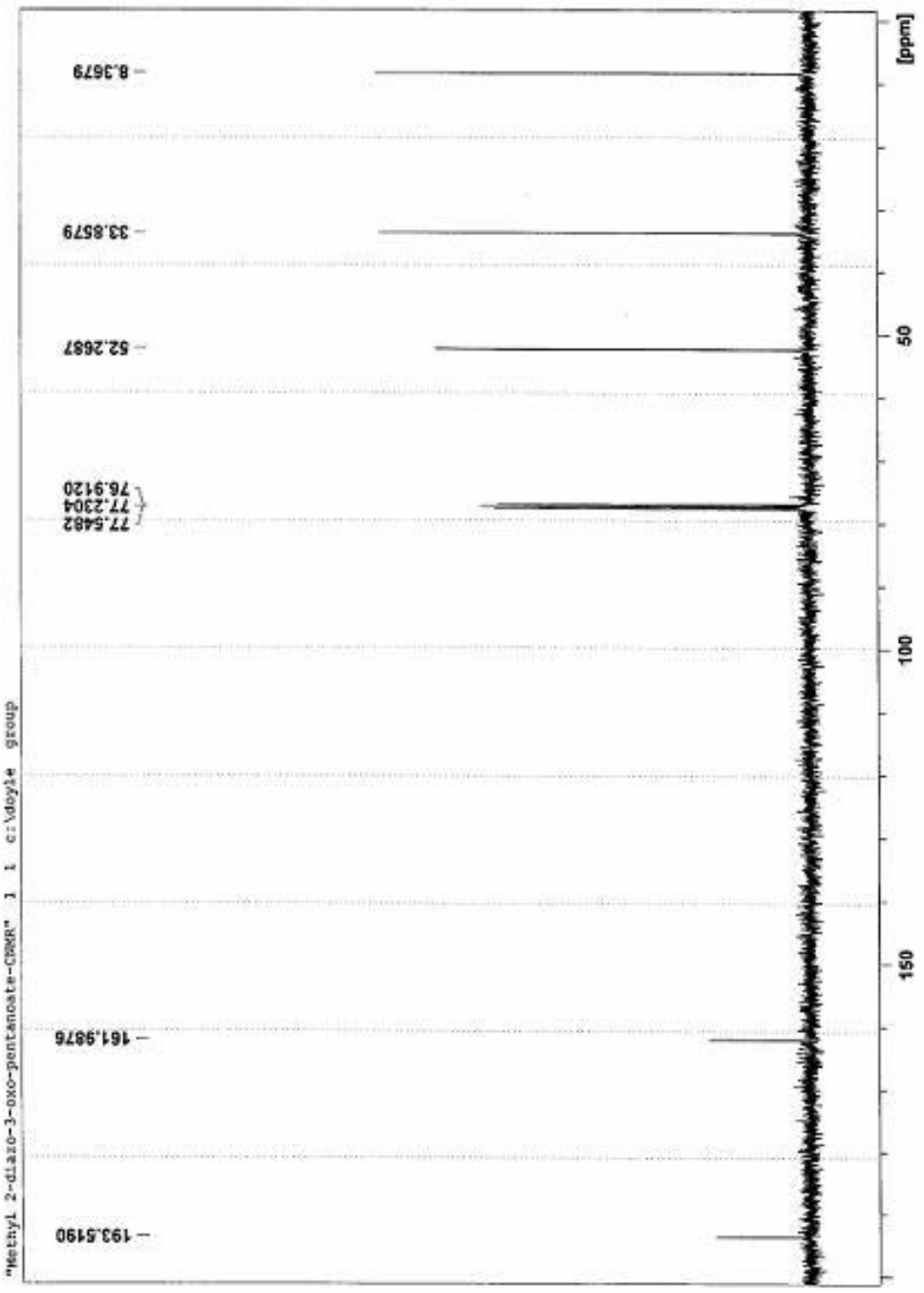

MukaiyamaAldol-3n-onepot-TBS-ZnOTf
CDCl3 091709
ppm


Mukaiyamaaldol-3n-onepot-TBS-2nOTf-CNMR 1 1 C:\doyle group
[rel]
15
10
5
0
[ppm]
0
50
100
150
200
4.7938
4.3249
18.1944
25.6581
25.9103
25.9850
35.7754
44.1134
52.1363
75.3481
76.6646
76.9819
77.2994
161.6518
191.6090

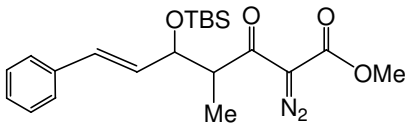
4

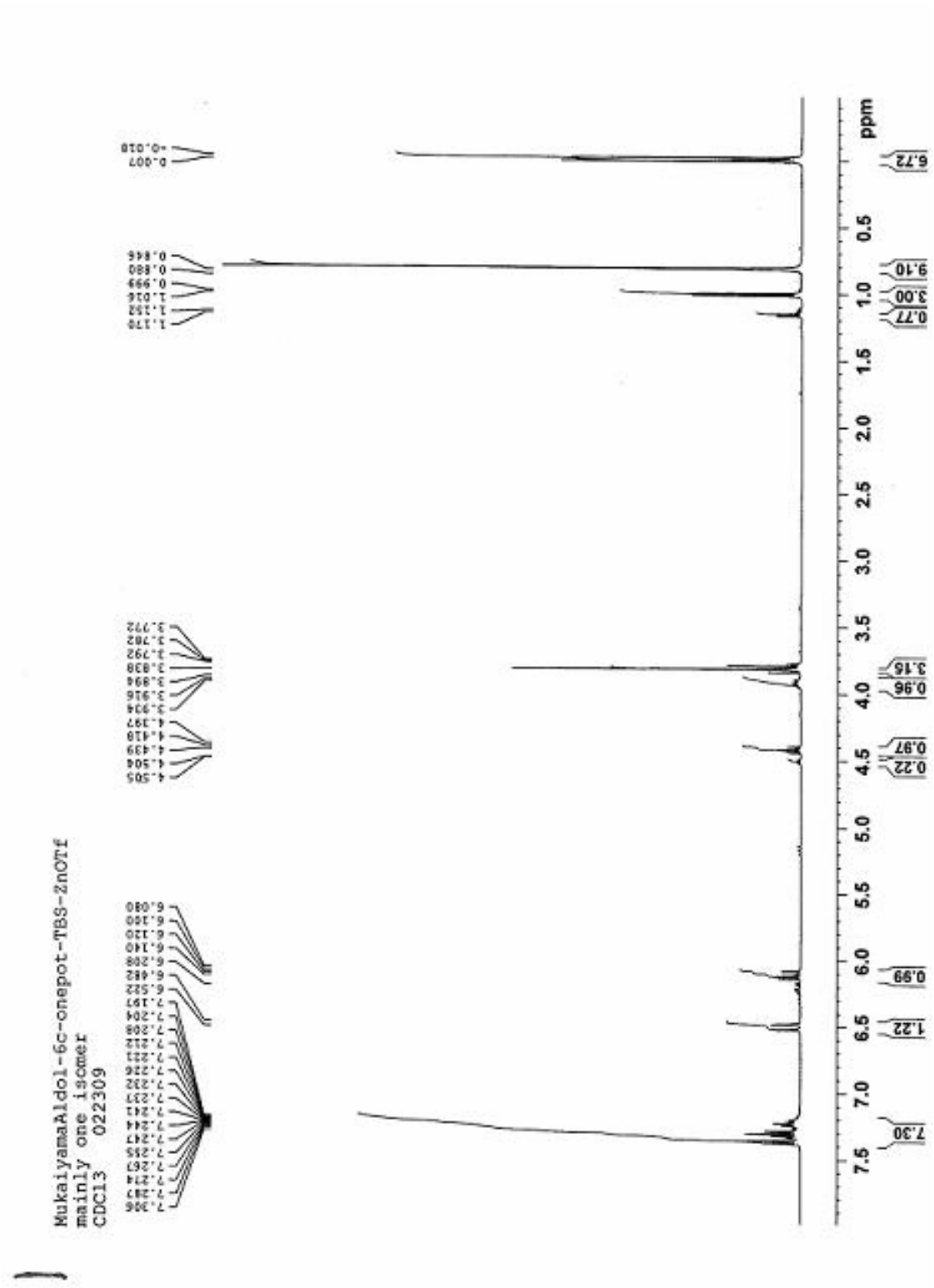

Me
O
O
OMe
N2

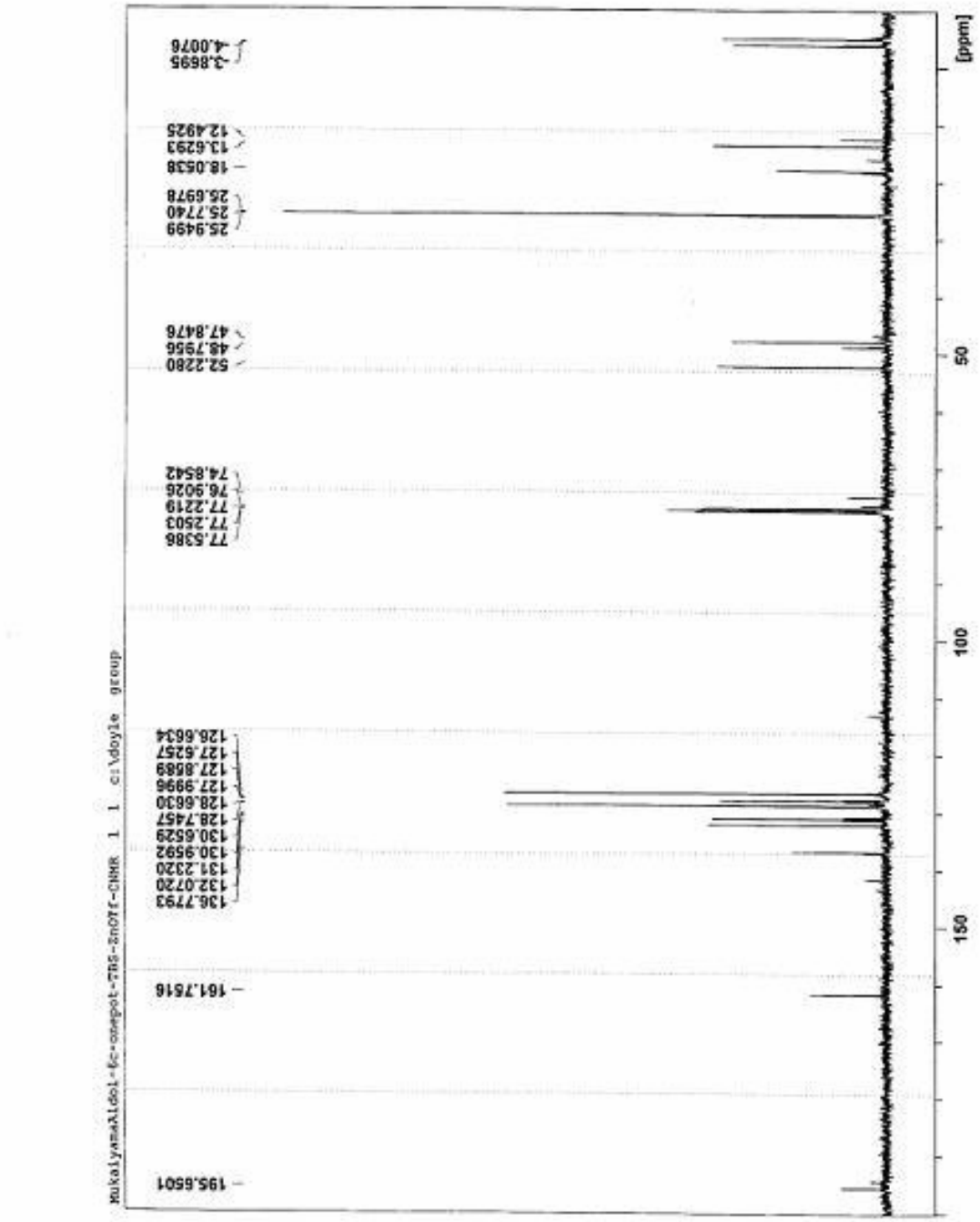

Methyl 2-diazo-3-oxo-pentanoate
CDCl3 021709
1.098
1.080
1.061
2.834
2.816
2.798
2.780
3.782
3.07
2.01
3.00
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5


"Methyl 2-diazo-3-oxo-pentanoate-CNMR" 1 1 c:\doyle group
193.5190
161.9876
77.5482
77.2304
76.9120
52.2687
33.8579
8.3679
150
100
50
[ppm]

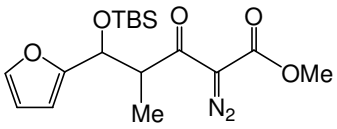
5c NMR after column chromatography

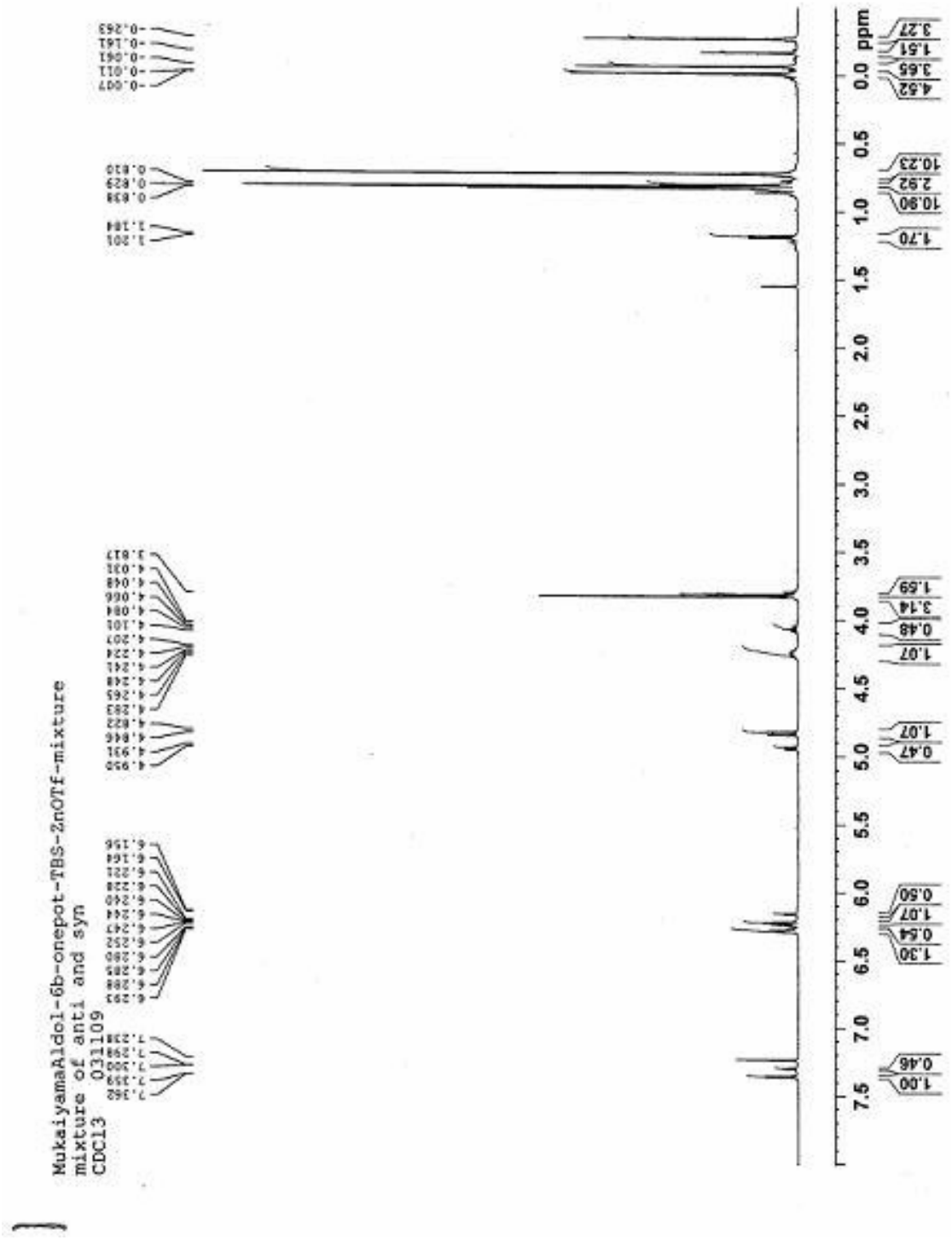


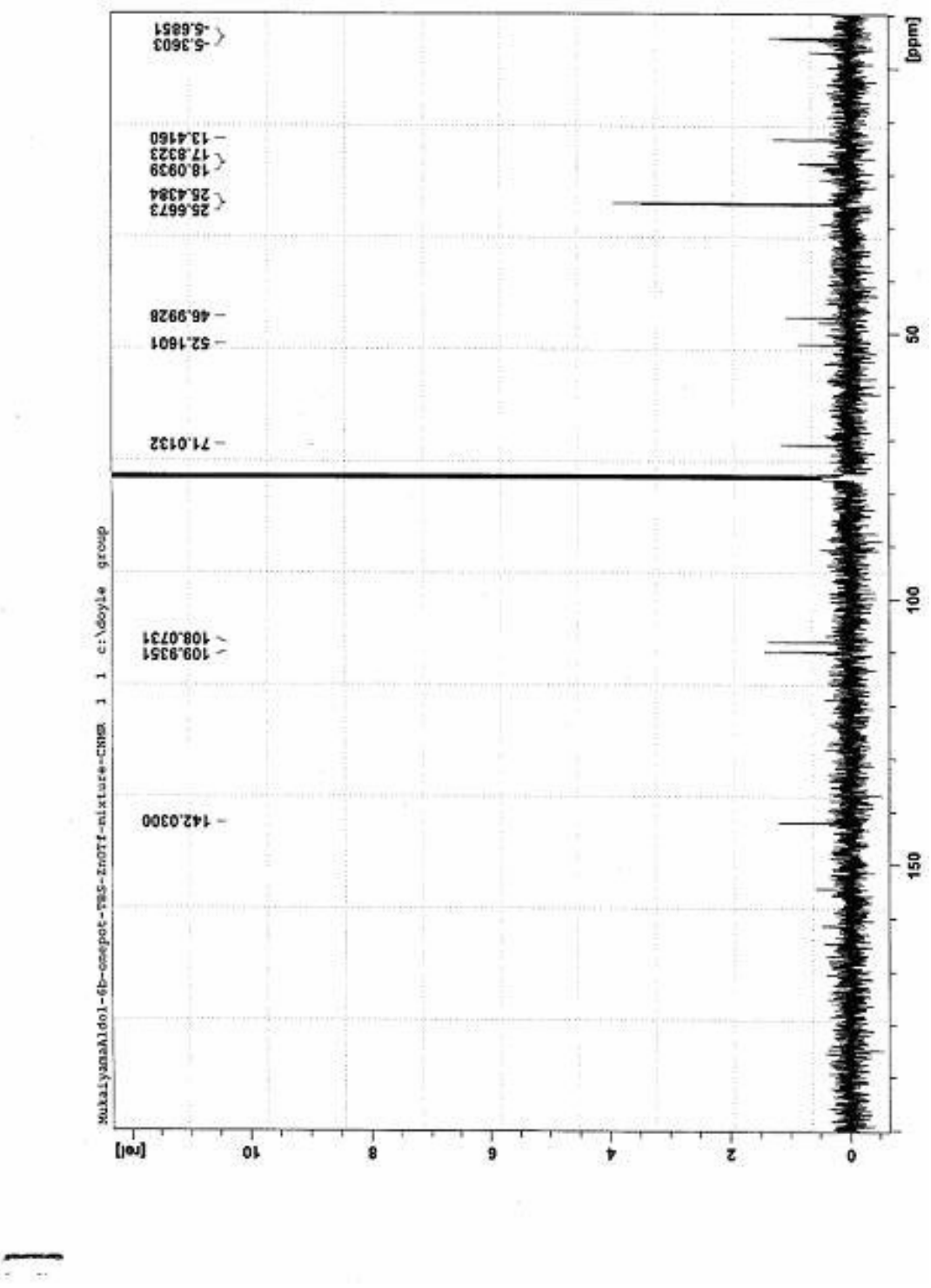



Mukaiyama Aldol-fc-compot-TMS-2n07f-CNMR 1 1 c:\doyle group
195.6501
161.7616
136.7793
132.0720
131.2320
130.9592
130.6529
128.7457
128.6630
127.9996
127.8689
127.6257
126.6614
77.5386
77.2503
77.2219
76.9026
74.8542
52.2280
48.7956
47.8476
25.9499
25.7740
25.6978
18.0538
13.6293
12.4925
-3.8695
-4.0076
[ppm]
150
100
50

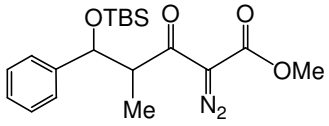
5h NMR after column chromatography

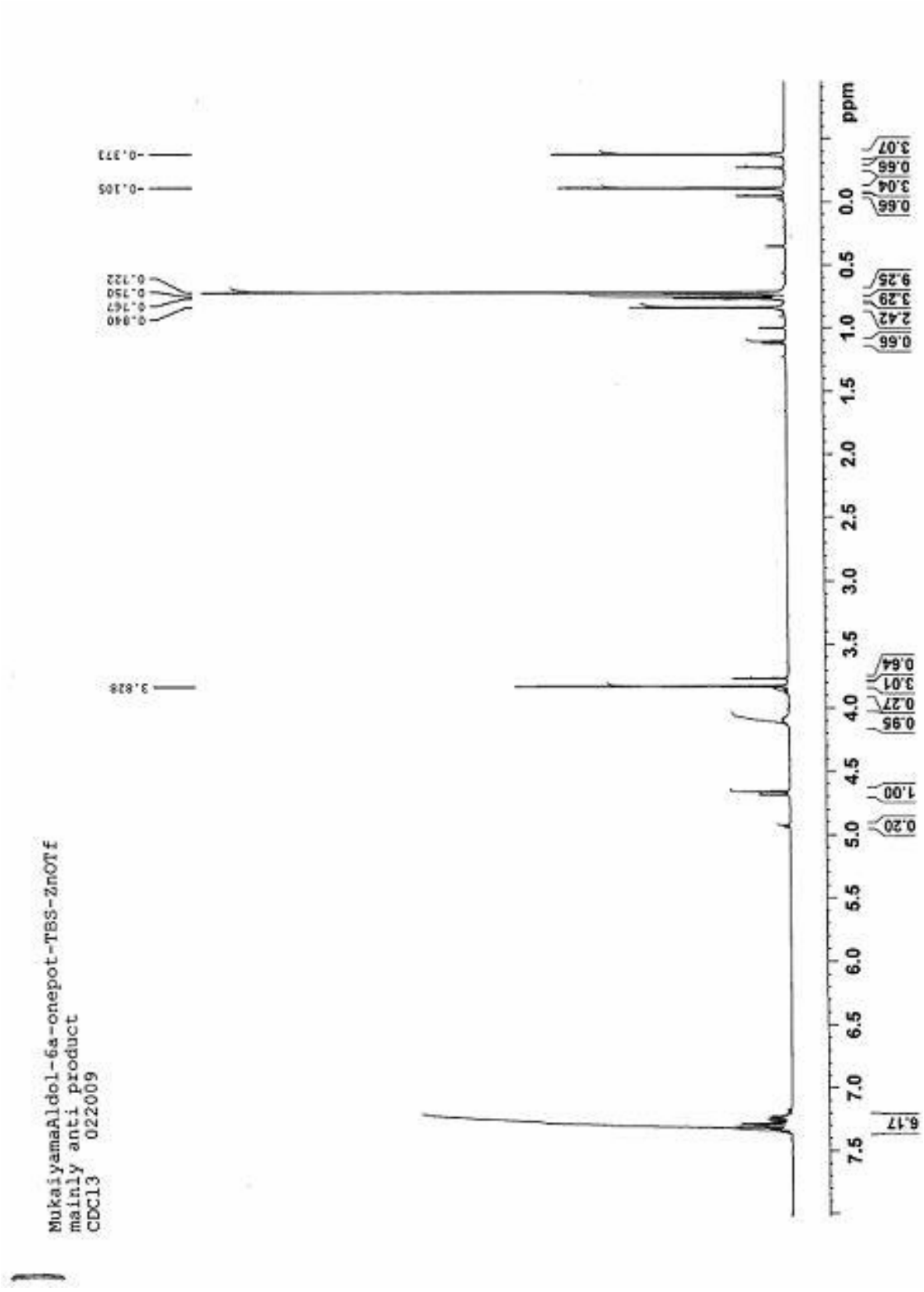


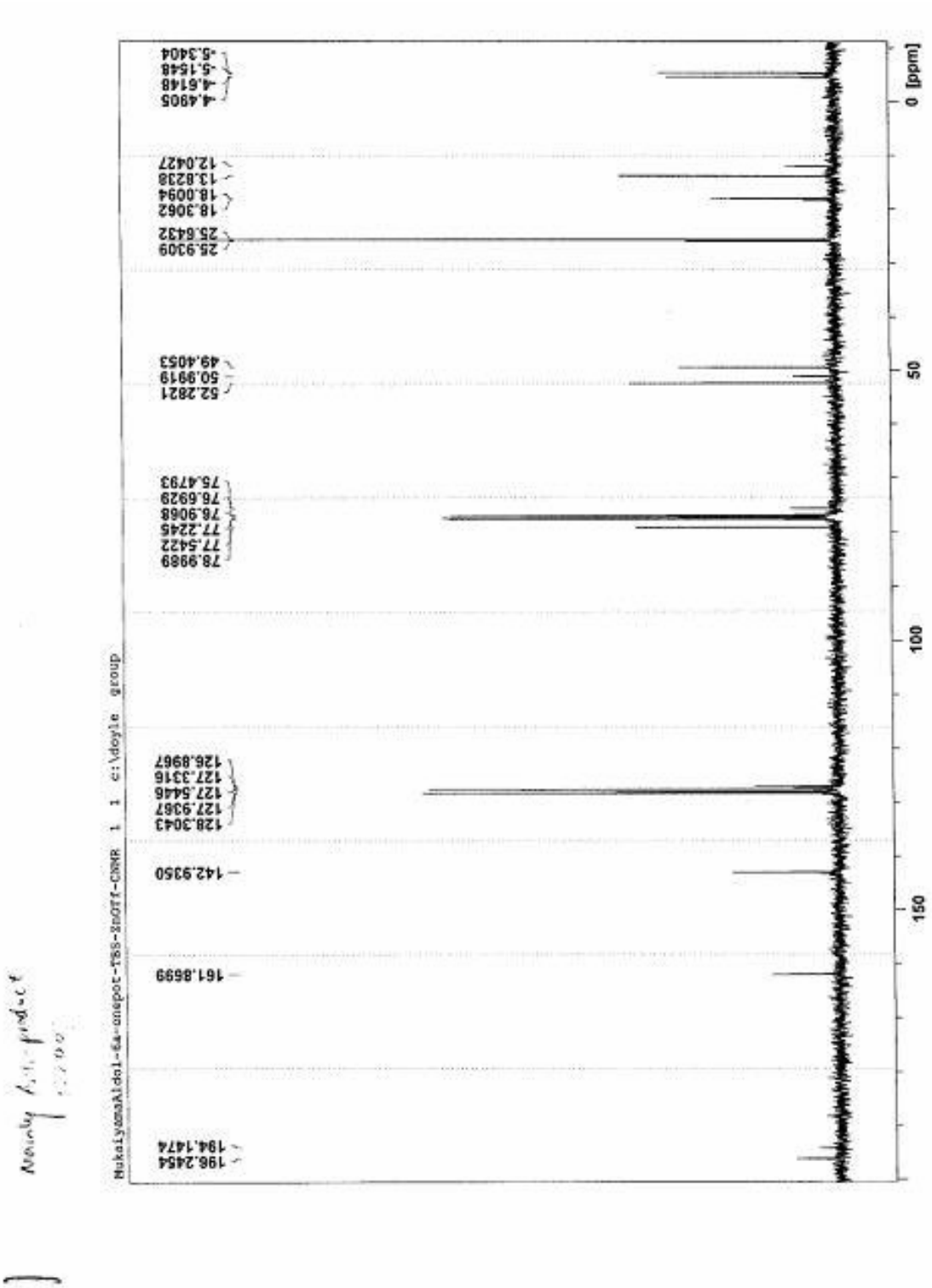



-5.3603
-5.6851
13.4160
17.8323
18.0939
25.6673
25.4384
46.9928
52.1601
71.0132
109.9351
108.0731
142.0300
[ppm]
[rel]
xukaiyanaAldol-6b-onepot-res-ZnOTf-mixture-CDCl3 1 1 c:\doyle group

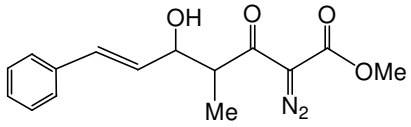
5i NMR after column chromatography

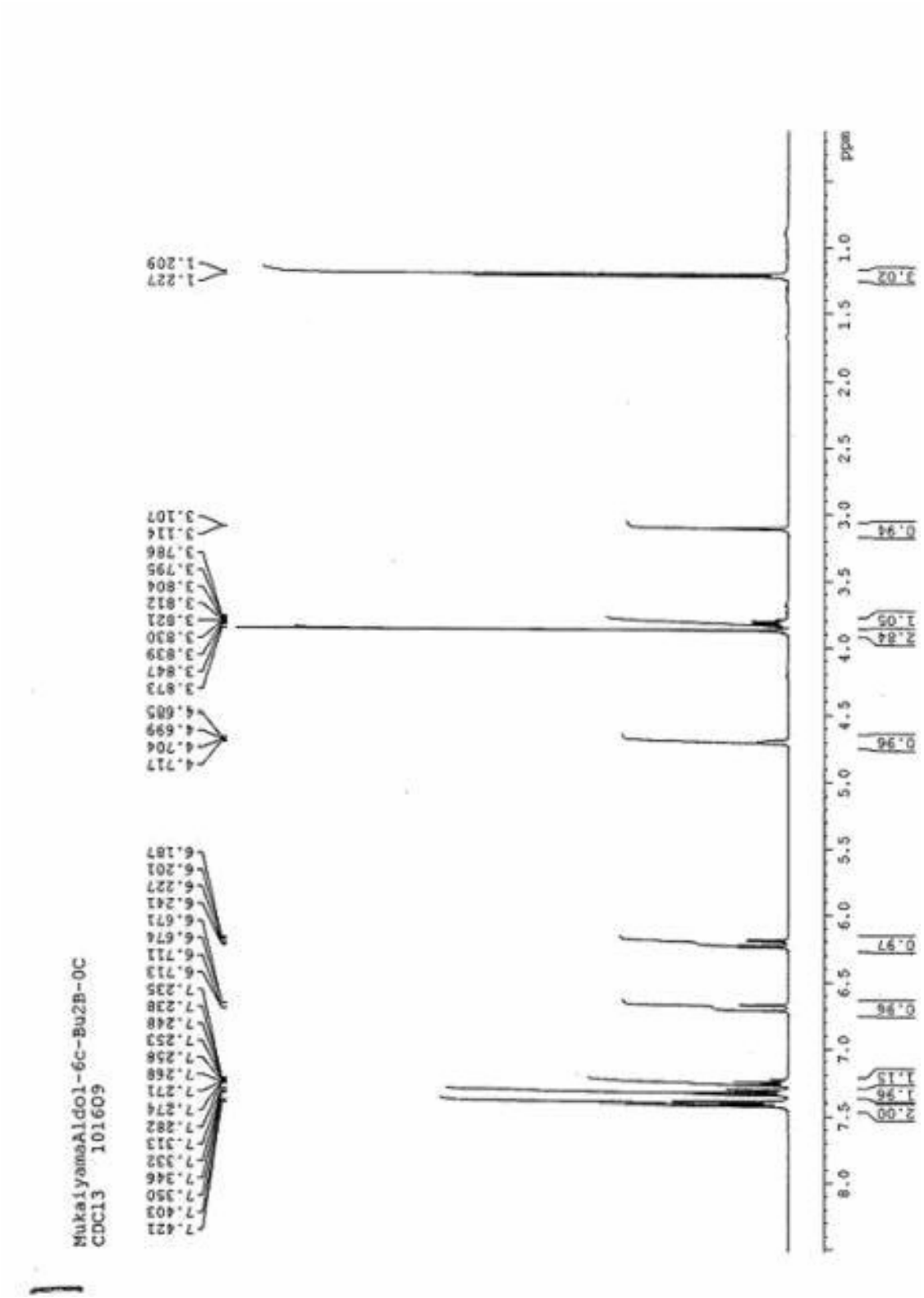


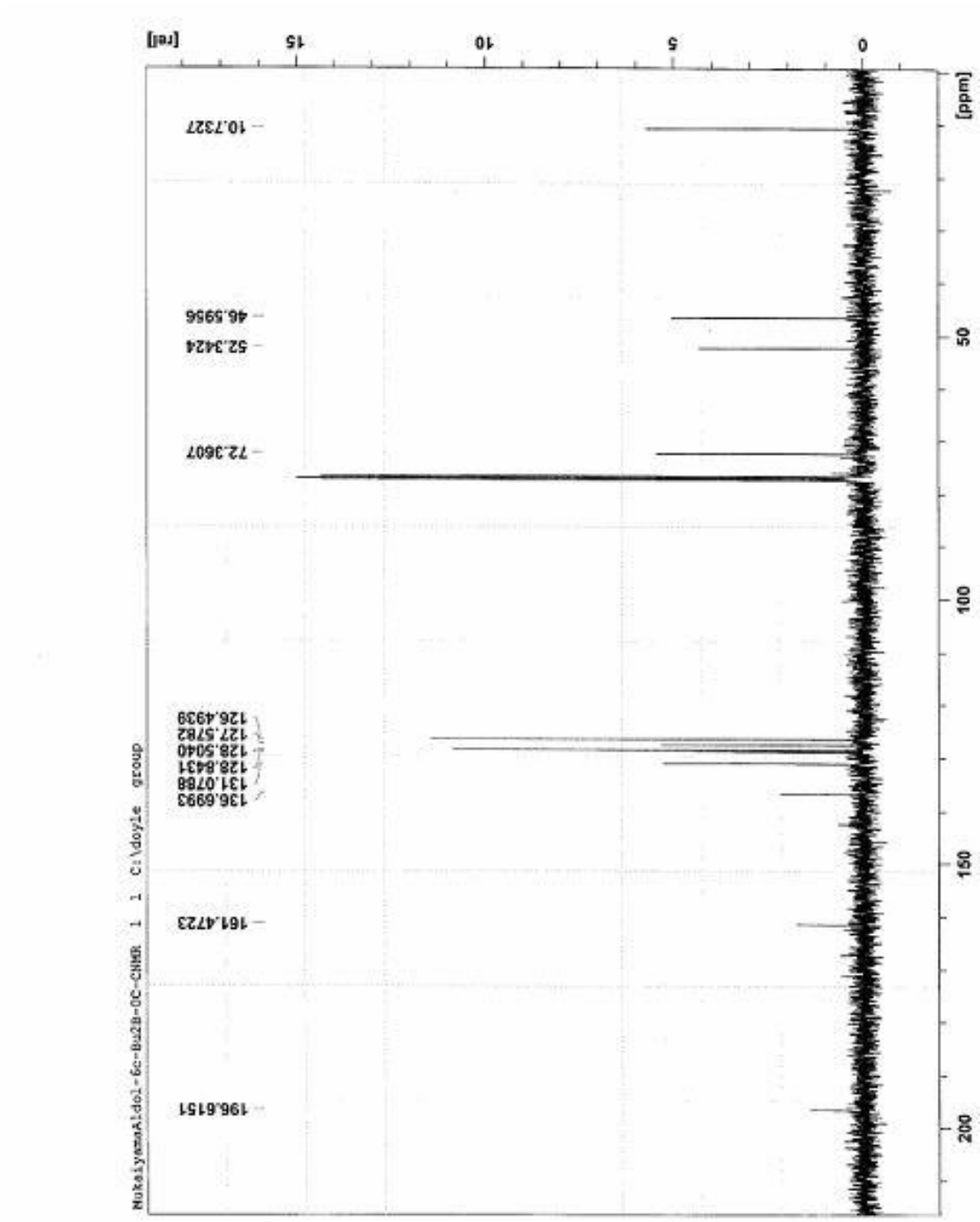



Nakiyama5Aldol-6a-onepot-TBS-2h0ff-CNMR 1 1 c:\doyle group
196.2454
194.1474
161.8699
142.9350
128.3043
127.9367
127.5446
127.3316
126.8967
78.9989
77.5422
77.2246
76.9068
76.6929
75.4793
52.2821
50.9919
49.4053
25.9309
25.6432
18.3062
18.0094
13.8238
12.0427
4.4805
4.6148
-5.1548
-5.3404
0 [ppm]
50
100
150

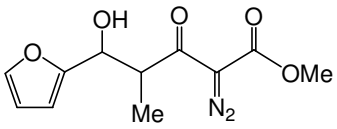
6c

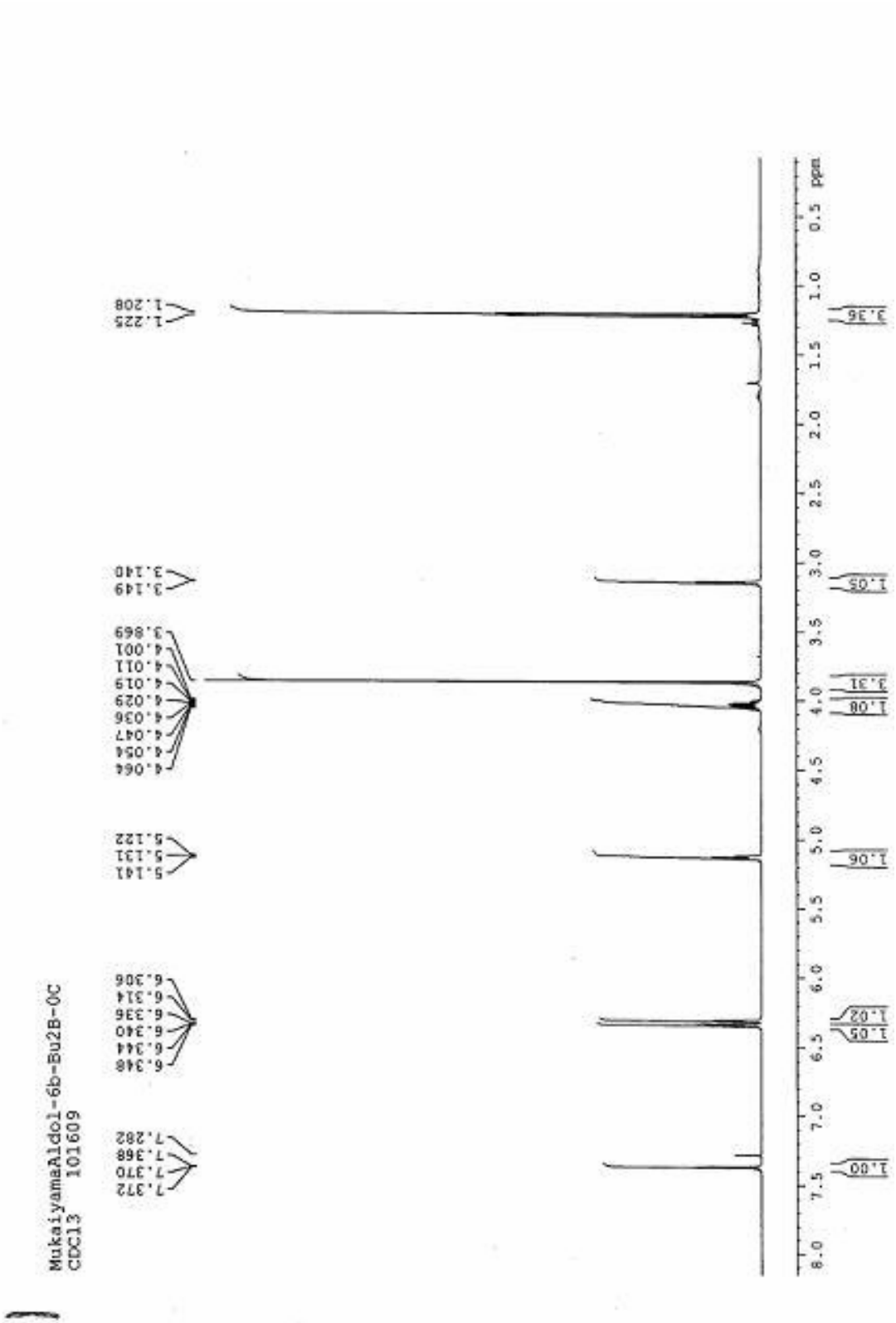

OH
O
O
OMe
Me
N2

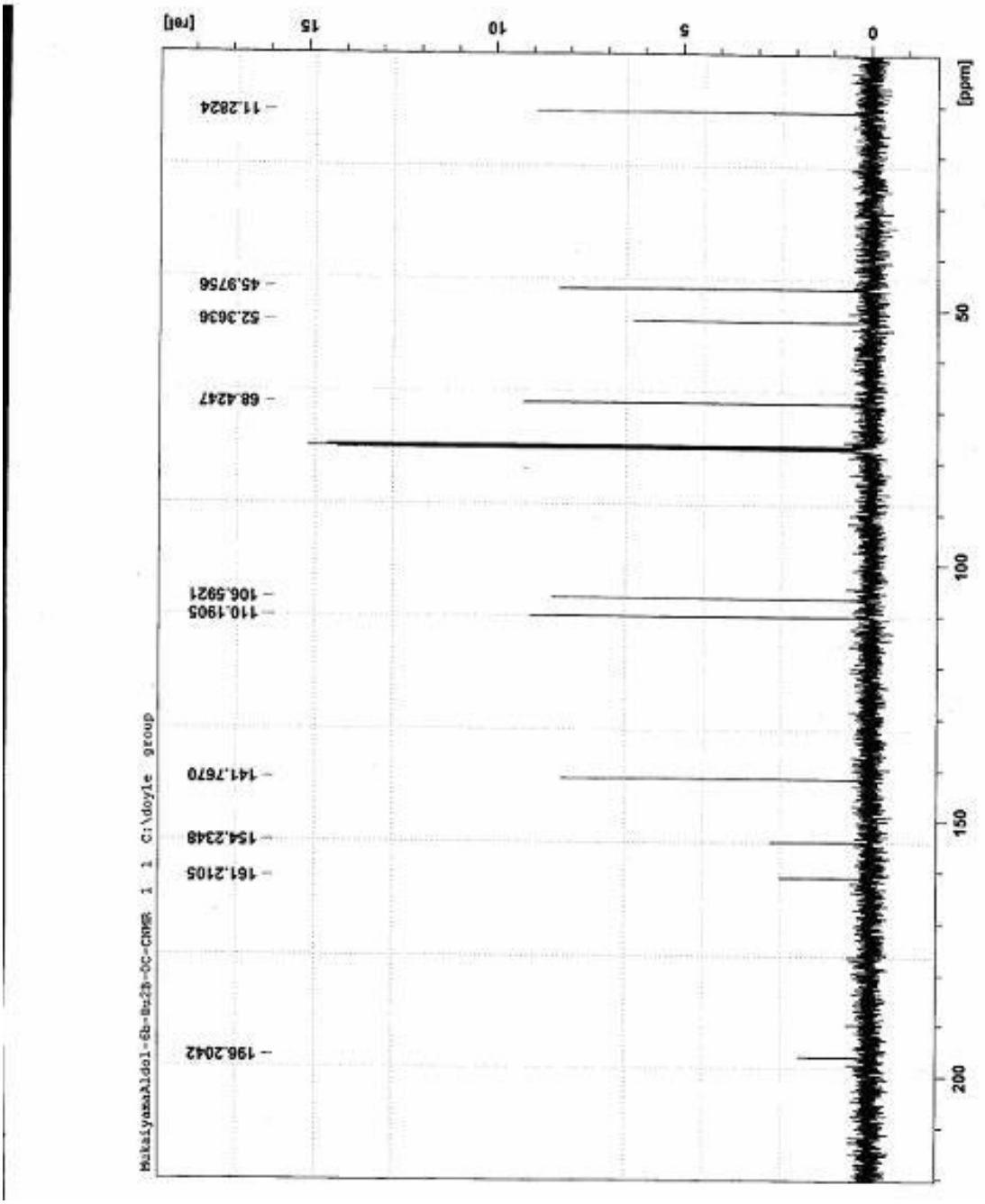

MukaiyamaAldol-6c-Bu2B-OC
CDCl3 101609
1.209
1.227
3.107
3.114
3.786
3.795
3.804
3.812
3.821
3.830
3.839
3.847
3.873
4.685
4.699
4.704
4.717
6.187
6.201
6.227
6.241
6.671
6.674
6.711
6.713
7.235
7.238
7.248
7.253
7.258
7.268
7.271
7.274
7.282
7.313
7.332
7.346
7.350
7.403
7.421
3.02
0.94
2.84
1.05
0.96
0.97
0.96
1.15
1.96
2.00
ppm


[rel]
15
10
5
0
[ppm]
50
100
150
200
10.7327
46.5956
52.3424
72.3607
126.4939
127.5782
128.5040
128.8431
131.0788
136.6993
161.4723
196.6151
NakaiyamaAldol-6c-Bu2B-OC-CNMR 1 1 C:\doyle group

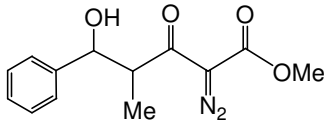
6h

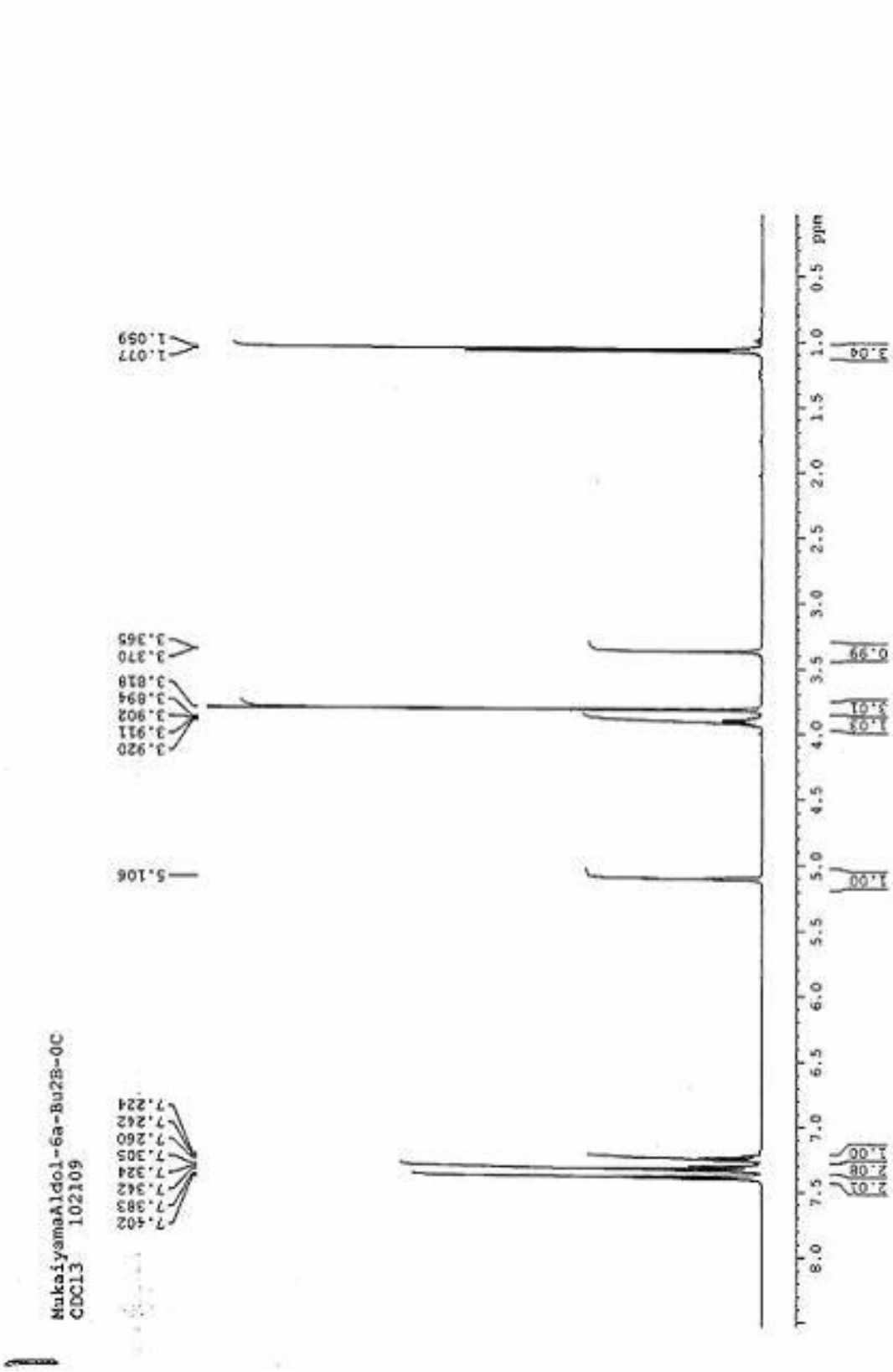

OH
O
O
O
OMe
Me
N2

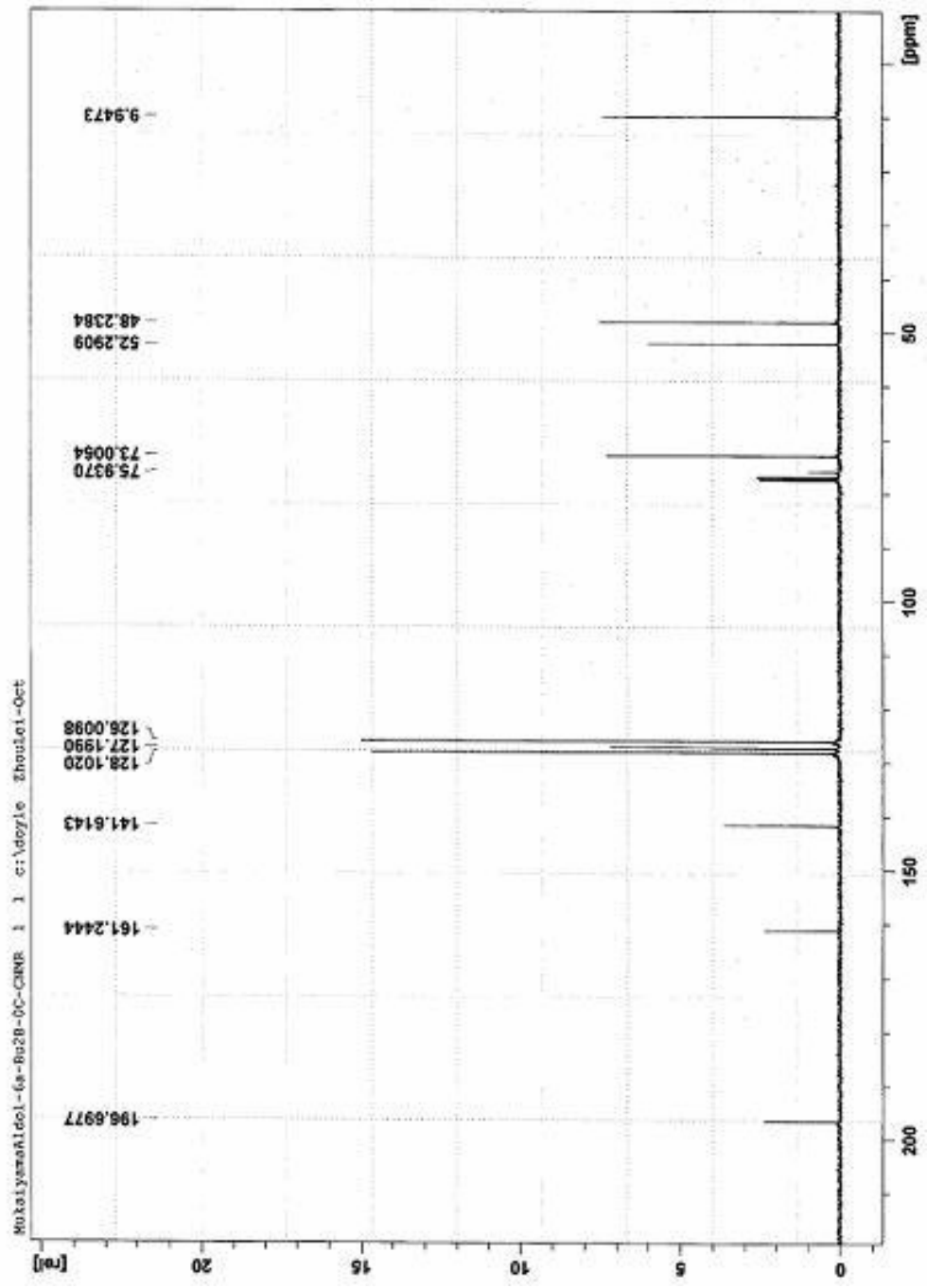

MukaiyamaAldol-6b-Bu2B-0C
CDCl3 101609
1.208
1.225
3.140
3.149
3.869
4.001
4.011
4.019
4.029
4.036
4.047
4.054
4.064
5.122
5.131
5.141
6.306
6.314
6.336
6.340
6.344
6.348
7.282
7.368
7.370
7.372
3.36
1.05
1.31
1.08
1.06
1.02
1.05
1.00
ppm


MakaiyamaAldol-6b-Bn2h-OC-CMMR 1 1 C:\doyle group
196.2042
161.2105
154.2348
141.7670
110.1905
106.5921
68.4247
52.3636
45.9756
11.2824
[rel]
15
10
5
0
[ppm]
50
100
150
200

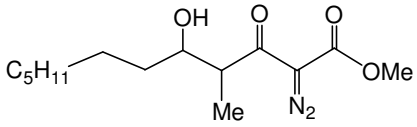
6i

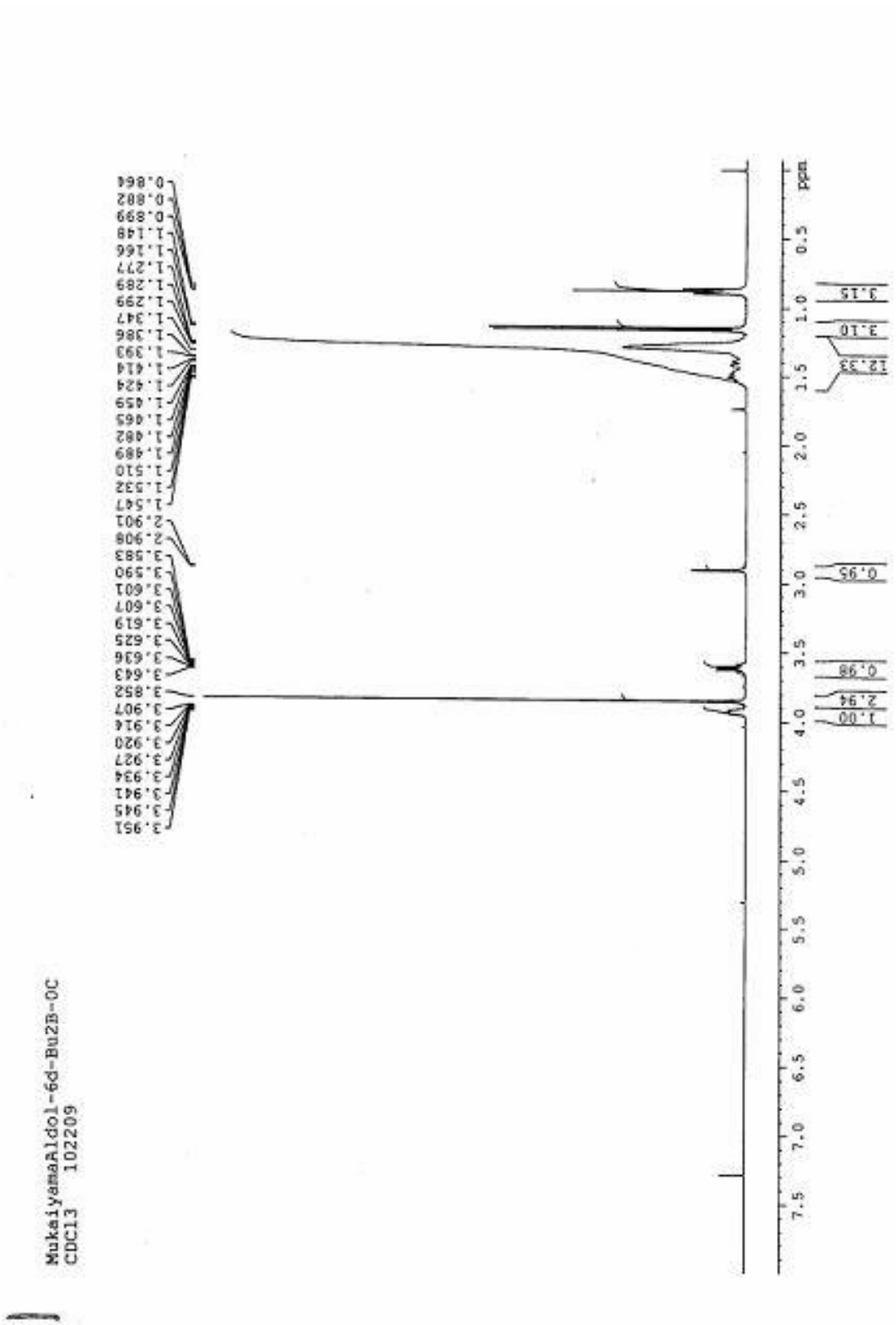

OH
O
O
OMe
Me
N2

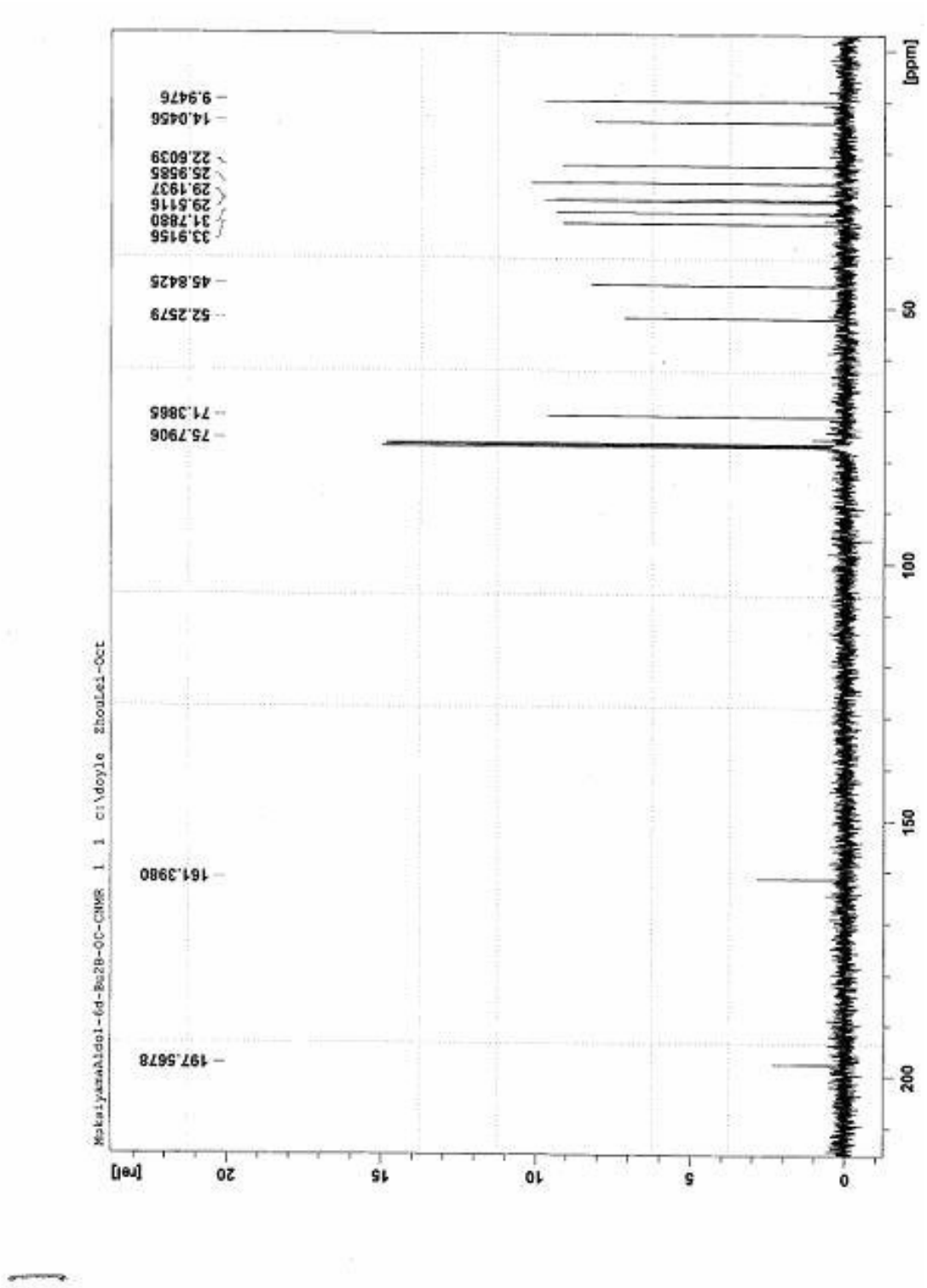

1.059
1.077
3.365
3.370
3.818
3.894
3.902
3.911
3.920
5.106
7.224
7.242
7.260
7.305
7.324
7.342
7.383
7.402
ppm
MukaiyamaAldol-6a-Bu2B-0C
CDCl3 102109


9.9473
48.2384
52.2909
73.0054
75.9370
126.0098
127.1990
128.1020
141.6143
161.2444
196.6977
[ppm]
[rel]

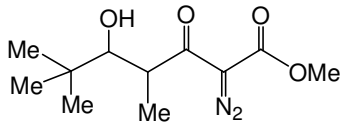
6l

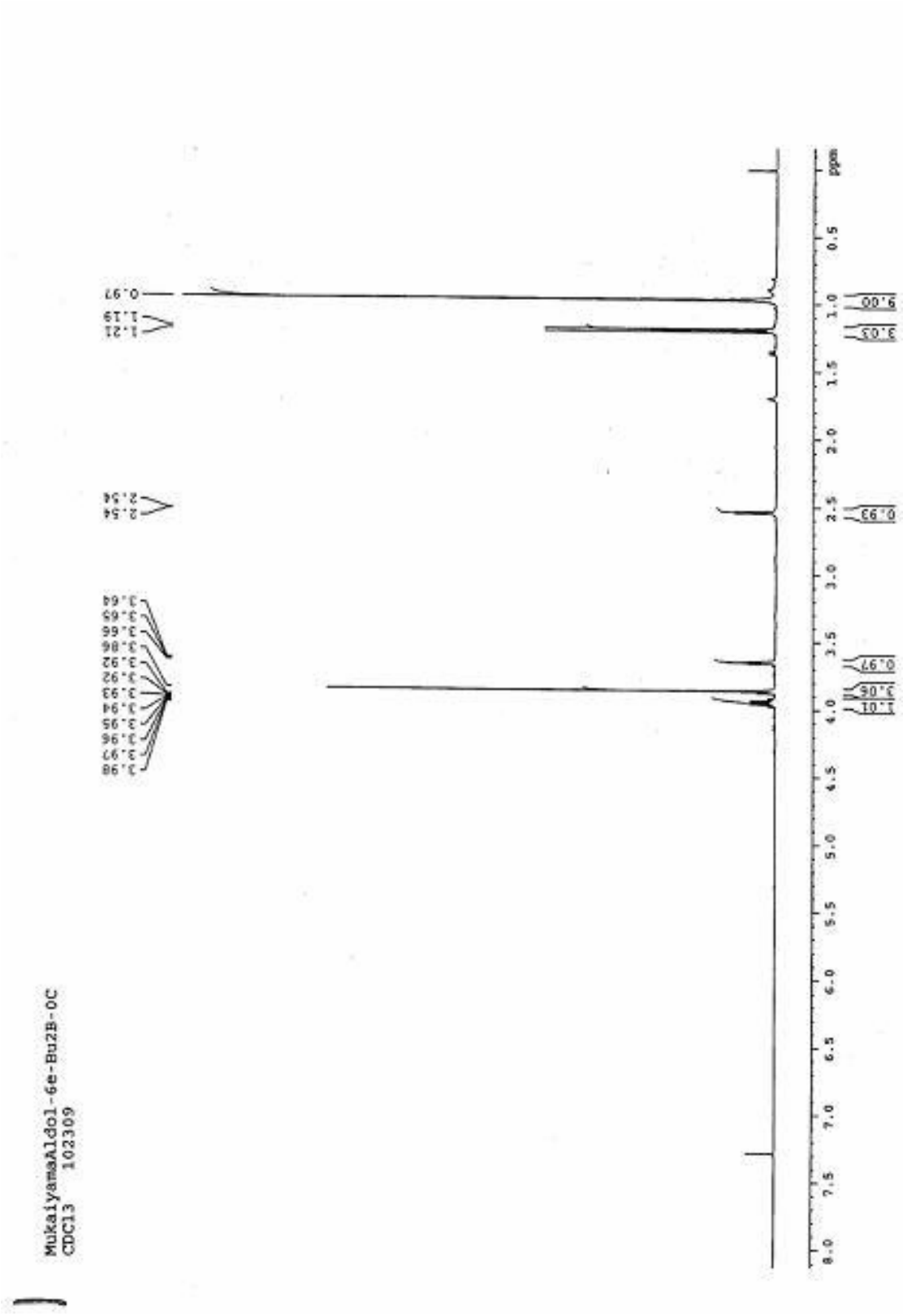

OH
O
O
C_5H_{11}
OMe
Me
N_2

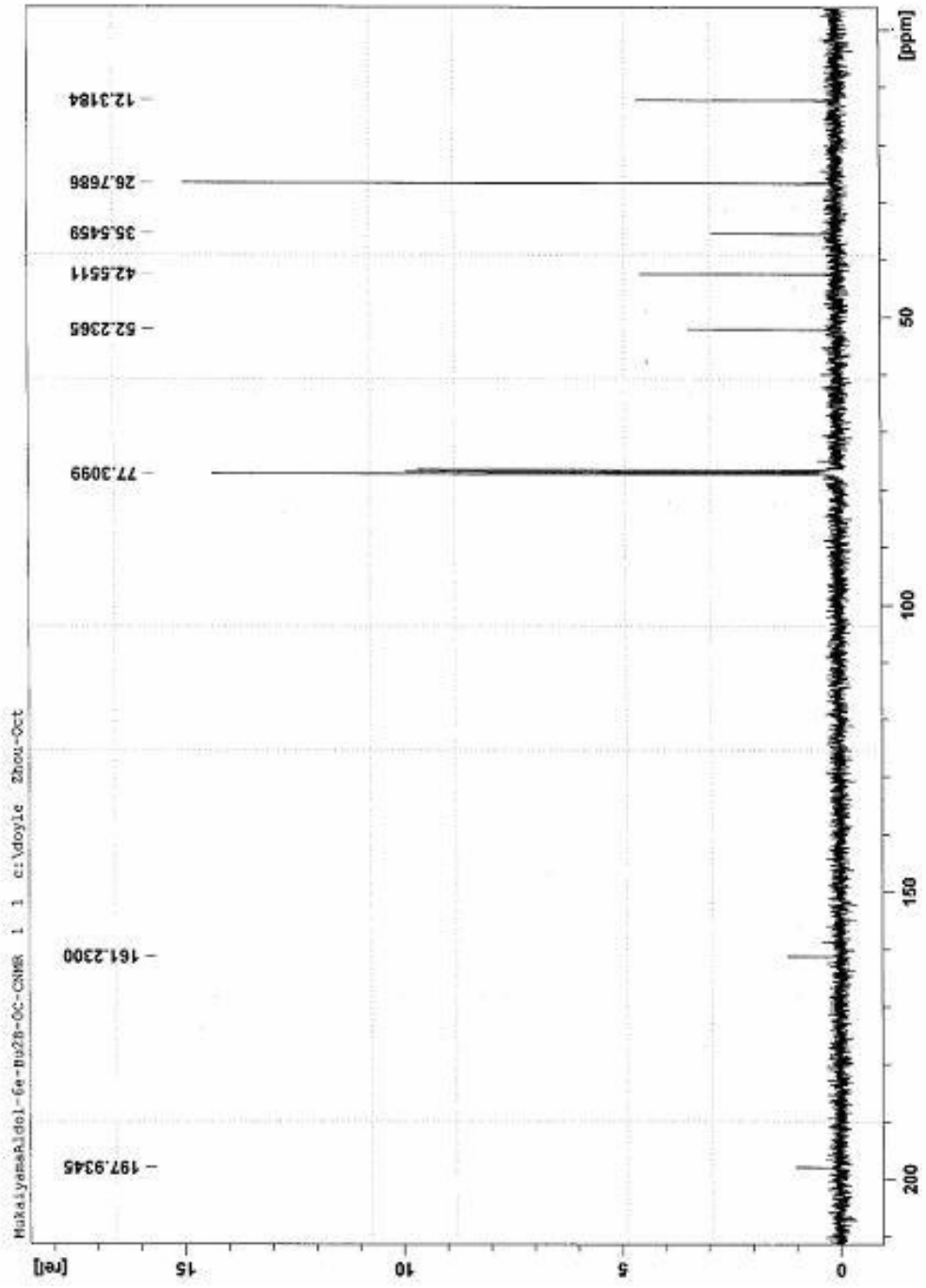

MukaiyamaAldol-6d-Bu2B-OC
CDCl3 102209
ppm
3.15
3.10
12.33
0.95
0.98
2.94
1.00


MakaiyaAaldol-6d-Bu2B-OC-CNMR 1 1 c:\doyle ZhouLei-Oct
197.5678
161.3980
75.7906
71.3865
52.2579
45.8425
33.9156
31.7880
29.5116
29.1937
25.9585
22.6039
14.0456
9.9476
[ppm]
200
150
100
50
0
5
10
15
20
[ppm]

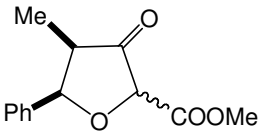
6m

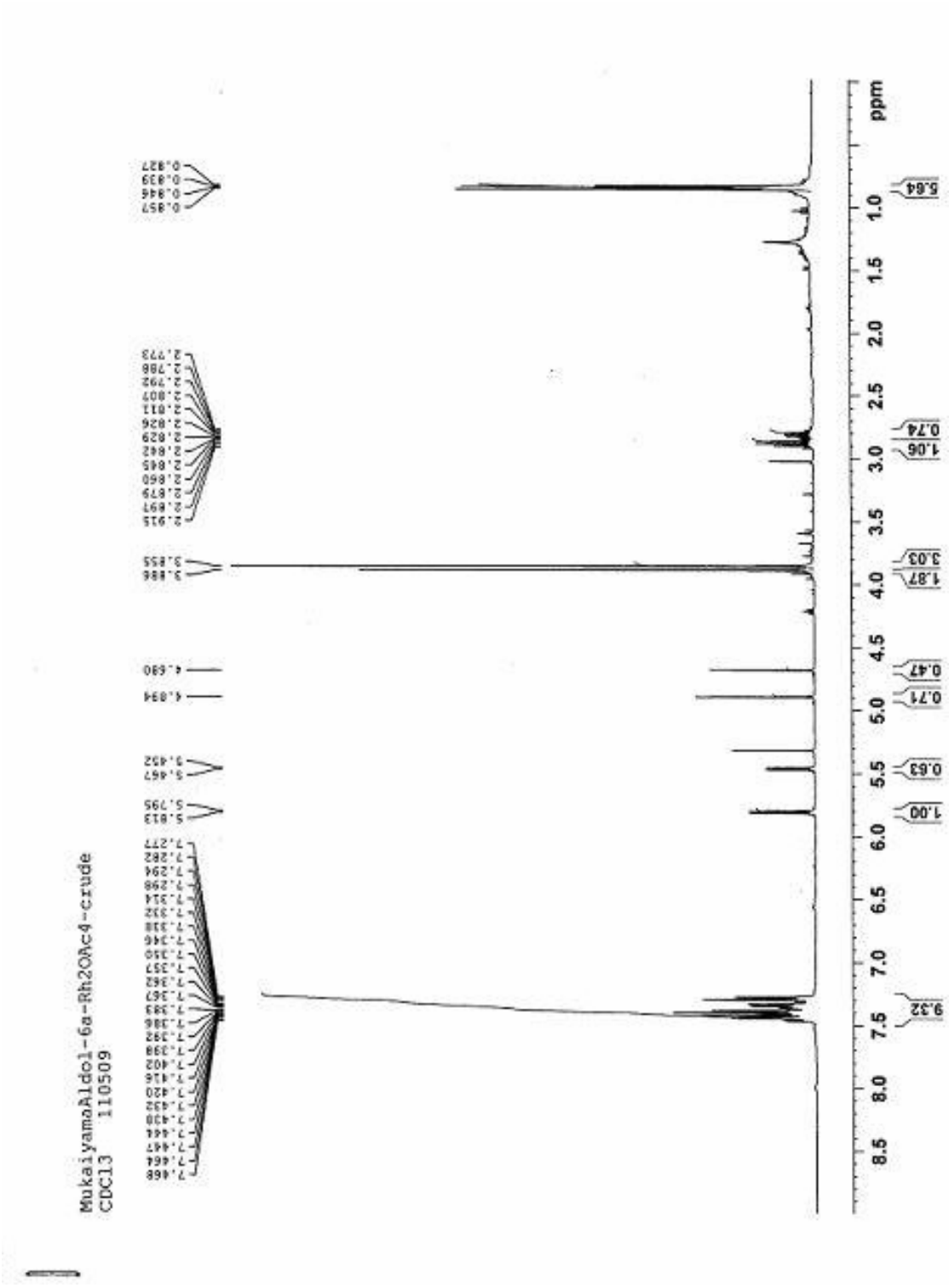

OH
O
O
Me
Me
Me
Me
OMe
N2

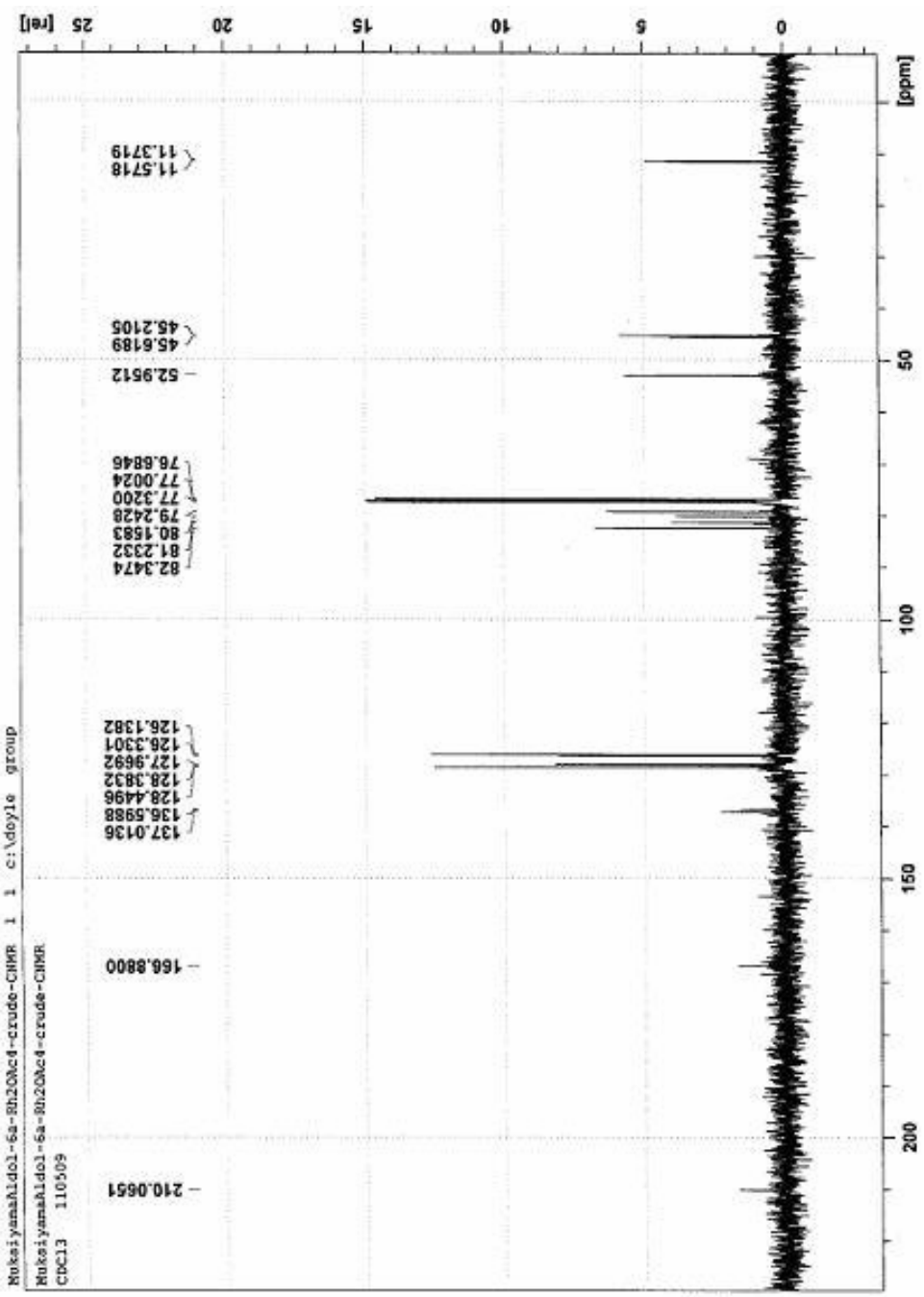

MukaiyamaAldol-6e-Bu2B-OC
CDCl3 102309
0.97
1.19
1.21
2.54
3.64
3.65
3.66
3.86
3.92
3.92
3.93
3.94
3.95
3.96
3.97
3.98
9.00
3.03
0.93
0.97
3.06
1.01
ppm


MukaiyamaAldol-6a-Bn2B-OC-CNMR 1 1 c:\doyle 2hou-Oct
197.9345
161.2300
77.3099
52.2365
42.5511
35.5459
26.7686
12.3184
[rel]
0
5
10
15
200
150
100
50
[ppm]

7 crude NMR: mixture of two diastereomers






Mukaiyamaaldol-6a-Rh2OAc4-crude-CNMR 1 1 c:\doyle group
Mukaiyamaaldol-6a-Rh2OAc4-crude-CNMR
CDCl3 110509
210.0651
166.8800
137.0136
136.5988
128.4496
128.3832
127.9692
126.3301
126.1382
82.3474
81.2332
80.1583
79.2428
77.3200
77.0024
76.6846
52.9512
45.6189
45.2105
11.5718
11.3719
[rel]
[ppm]