SUPPORTING INFORMATION

Synthesis of Highly Enantioenriched 3,4-Dihydroquinolin-2-ones by 6-*Exo-trig* Radical Cyclizations of Axially Chiral α-Halo-*o*-Alkenyl Anilides

David B. Guthrie, Stephen J. Geib and Dennis P. Curran

Department of Chemistry, University of Pittsburgh, Pittsburgh PA, 15260

email: curran@pitt.edu

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General Methods

All reactions were performed in oven-dried glassware under an argon atmosphere, except where noted. Chemicals and solvents were purchased from commercial suppliers and used as received, excepting as follows. Dichloromethane, THF, ether, and toluene were dried by passing through an activated alumina column. When necessary, benzene was degassed by the freeze-pump-thaw method (at least 5 cycles). Trimethylsilyl chloride (TMSCl) was distilled over CaH_2 before use. Solutions of BuLi were titrated regularly against diphenylacetic acid in THF.

All reactions were followed by TLC to completion, unless stated otherwise. TLC analysis was performed by illumination with a UV lamp (254 nm) or staining with $KMnO_4$ and heating. All flash chromatography was performed with 230-400 mesh silica gel purchased from Sorbent Technologies as the stationary phase. "Gradient column chromatography" refers to packing the column with the initial eluent, and initially filling the solvent reservoir with ~4 column volumes of the initial eluent. After elution of one column volume, the solvent reservoir is refilled with the second eluent. This process is continued after every eluted column volume until the final compound has completely eluted.

^{1}H NMR spectra were measured on a Bruker Avance 300 MHz instrument in $CDCl_3$, and chemical shifts were measured relative to residual solvent peak (δ 7.27). The following abbreviations were used to describe coupling: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ^{13}C NMR spectra were measured on Bruker Avance instruments at 75 MHz with chemical shifts relative to residual solvent peak (δ 77.0). In ^{13}C spectra, a notation of (*x*C) is used to denote *x* equivalent carbons for a multi-carbon signal. IR spectra were recorded

as thin films ($CHCl_3$) or neat on NaCl plates on an ATI Mattson Genesis Series FTIR spectrometer. All quoted optical rotation values are corrected for 100% ee samples.

Melting ranges were determined using a Mel-Temp II apparatus and are uncorrected. Compounds listed as having a melting point at a single temperature had a sharp melting range of < 0.5 °C. Optical rotations were measured on a Perkin-Elmer 241 Polarimeter using a 1 dm cell length. All quoted optical rotation values are corrected for 100% ee samples, and have the units (deg cm^2 g^{-1}). Mass spectra were obtained on a VG-7070 or Fisons Autospec high-resolution magnetic sector mass spectrometer.

Analytical chiral HPLC analysis was conducted using either an (*S*,*S*)-Whelk-O 1 column (Pirkle, 250 mm x 4.6 mm ID) or a Chiralcel OD column (Daicel, 250 mm x 4.6 mm ID) typically eluting with hexanes:*i*-PrOH at 1.0 mL/min, 10-20 μg per injection. Preparatory chiral HPLC resolutions were performed on either an (*S*,*S*)-Whelk-O 1 column (Pirkle, 25 cm x 21.1 mm ID) or a Chiralcel OD column (Daicel, 250 mm x 20.0 mm ID) eluting with hexanes:iPrOH at 10.0 mL/min, 40-150 mg per injection. All HPLC injections were monitored with a Waters model 440 UV detector at wavelength 254 nm, when the solvent system was hexane:*i*-PrOH. In the cases where a hexane:EtOAc solvent system was used, the injections were monitored at wavelength 270 nm.

Gas chromatography analysis was performed with an Agilent 6850 GC under the following conditions: Initial oven temp. 100 °C, first ramp 10 °C/min to 250 °C, second ramp 15 °C/min to 315 °C, held at this temperature for 8 min. All GC yields were determined by calculation of response factors, using a straight-chain alkane internal standard. For each compound analyzed, three standard mixtures of a measured amount of the compound and a

known amount of internal standard from a stock solution were analyzed by GC. Response factors were calculated using the equation:[1]

$$RF_X = \frac{M_{IS} \cdot A_X}{A_{IS} \cdot M_X}$$

RF_X = response factor of compound X

M_{IS} = moles of internal standard

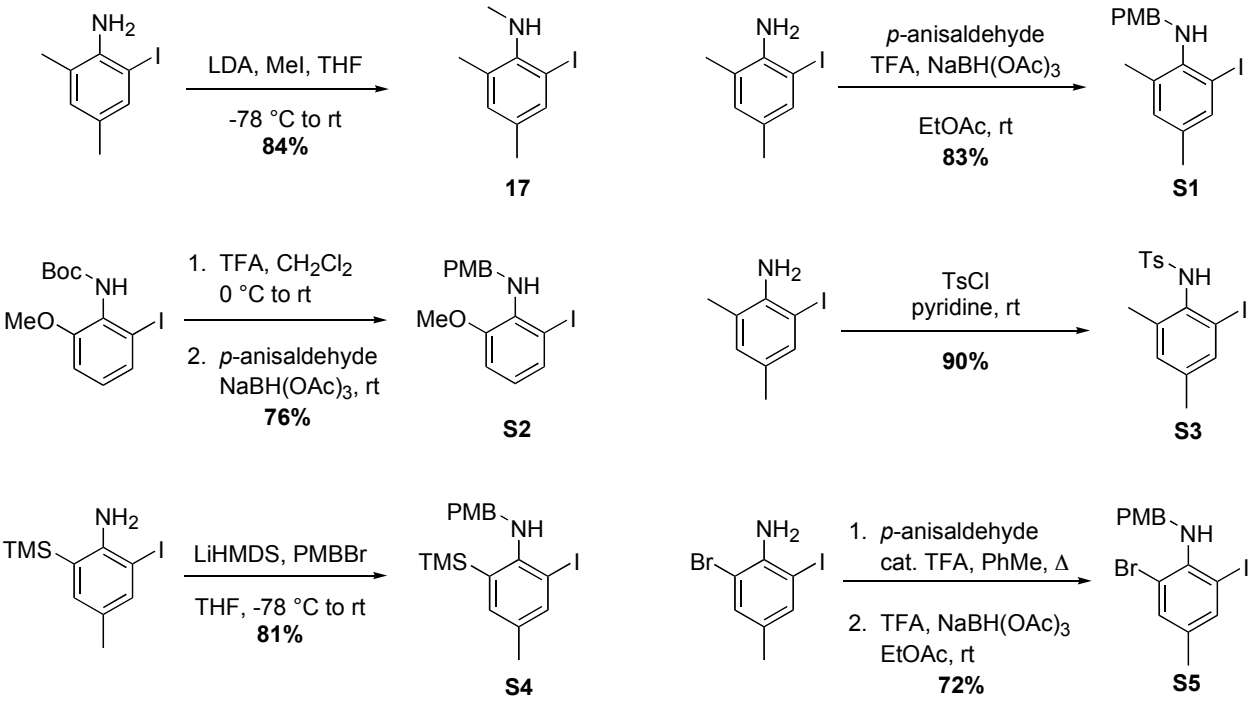
M_X = moles of compound X

A_{IS} = area of internal standard GC peak

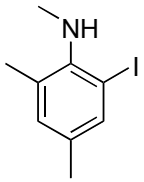
A_X = area of compound X GC peak

For each compound X, the three trials were graphed with the M_{IS}/M_X value on the y-axis, and the corresponding A_{IS}/A_X value on the x-axis. The slope of the line was taken to be the RF_X value. All compounds gave excellent linear plots with intercepts ≈ 0, showing that the response factor for each compound was consistent over varying molar ratios of compound to internal standard.

N-Substitution of *o*-Iodoanilines

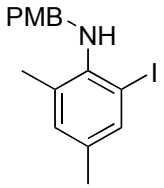


Scheme S.1 Preparation of *N*-Substituted Anilines



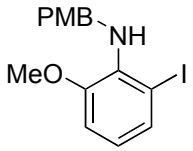
2-Iodo-*N*-4,6-trimethylaniline (17): LDA was made by dissolving *N*,*N*-diisopropylamine (2.43 g, 24.0 mmol) in THF (10 mL) at −78 °C with stirring, and adding a hexanes solution of BuLi (15.7 mL, 22.0 mmol) dropwise. The reaction mixture was stirred at this temperature for 40 min, warmed to 0 °C and stirred for 10 min. The resulting solution of LDA was then added dropwise over 10 min to a stirred solution of 2-iodo-4,6-dimethylaniline[2,3] (4.94 g, 20.0 mmol) in THF (150 mL) at −78 °C, and the mixture was stirred for an additional 20 min. Methyl iodide (2.98 g, 21.0 mmol) was added dropwise via syringe, the reaction mixture was warmed to room

temperature, and stirred for 1 h. The mixture was quenched with saturated aqueous NH_4Cl solution (200 mL) and diluted with Et_2O (250 mL). The organic layer was separated and washed with saturated aqueous NH_4Cl (3 x 250 mL) and brine (250 mL) solutions, dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Flash chromatography (25:1 pentane:Et_2O) afforded the title compound (4.40 g, 84%) as a red-brown, acrid-smelling liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (s, 1H), 6.93 (s, 1H), 3.31 (br s, 1H), 2.73 (s, 3H), 2.35 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.8, 136.8, 133.6, 132.5, 130.8, 95.3, 35.3, 19.9, 19.5; FTIR (neat, cm^{-1}) 3348, 2949, 2917, 2860, 1481, 1411, 1277, 1108, 1028, 852, 790, 726; LRMS (EI) *m/z* 261 (M^+, 75), 246 (32), 134 (29), 118 (27), 105 (45), 91 (100), 78 (87), 76 (99); HRMS (EI) calcd for $C_9H_{12}IN$: 261.0015, found: 261.0019.



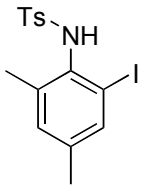
2-Iodo-*N*-(4-methoxybenzyl)-4,6-dimethylaniline (S1): To a stirred solution of 2-iodo-4,6-dimethylaniline[2,3] (6.18 g, 25.0 mmol) and *p*-anisaldehyde (3.57 g, 26.3 mmol) in EtOAc (75 mL) was added trifluoroacetic acid (5.70 g, 50.0 mmol). The mixture was stirred at room temperature for 30 min, and solid $NaBH(OAc)_3$ (9.54 g, 45.0 mmol) was added portionwise over 5 min. The reaction mixture was stirred for 3 h, cooled to 0 °C, and quenched with 10% w/w aqueous NaOH solution (*very* slowly at first, until gas production stopped) until two distinct layers formed. The organic layer was separated and washed with brine (2 x 100 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (10:1 hexanes:EtOAc) afforded the title compound (7.59 g, 83%) as an off-white solid, mp 69-70 °C:

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.36 (d, J = 8.7 Hz, 2H), 6.95 (s, 1H), 6.90 (d, J = 8.7 Hz, 2H), 4.02 (s, 2H), 3.83 (s, 3H), 3.44 (br s, 1H), 2.37 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.7, 145.2, 137.0, 133.9, 132.3, 131.6, 131.3, 129.3 (2C), 113.7 (2C), 96.2, 55.0, 52.1, 19.9, 19.4; FTIR (thin film, $CHCl_3$, cm^{-1}) 3326, 2928, 2832, 1509, 1471, 1462, 1275, 1179, 1055, 1029, 831, 820, 738; LRMS (EI) *m/z* 368 (26), 367 (M^+, 82), 238 (37), 122 (65), 121 (100), 91 (32), 77 (40); HRMS (EI) calcd for $C_{16}H_{18}INO$: 367.0433, found: 367.0430.

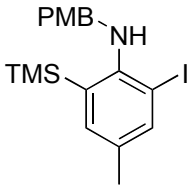


2-Iodo-6-methoxy-*N*-(4-methoxybenzyl)aniline (S2): To a stirred solution of *t*-butyl 2-iodo-6-methoxyphenylcarbamate[4] (4.36 g, 12.5 mmol) in CH_2Cl_2 (60 mL) at 0 °C was added trifluoroacetic acid (14.25 g, 125 mmol) in one portion via syringe. The reaction mixture was warmed to room temperature and stirred for 1.5 h, at which time *p*-anisaldehyde (1.79 g, 13.1 mmol) was added in one portion via syringe. The reaction was stirred for 10 min, and solid $NaBH(OAc)_3$ (7.95 g, 37.5 mmol) was added portionwise over 10 min. The mixture was stirred for 1 h, cooled to 0 °C, and quenched (*very* slowly at first, until gas production stopped) with 10% w/w aqueous NaOH solution (50 mL). The organic layer was separated and washed with brine (50 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (6:1 pentane:Et_2O) afforded the title compound (3.36 g, 76%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (dd, J = 8.1 Hz, 1.2 Hz, 1H), 7.30 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.81 (dd, J = 8.1 Hz, 1.2 Hz, 1H), 6.64 (t, J = 8.1 Hz, 1H), 4.32 (s, 2H), 4.02 (br s, 1H), 3.82 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6, 151.2, 139.0, 132.1, 131.2 (2C), 129.3, 123.1, 113.6 (2C), 111.4, 92.3, 55.7, 55.1, 51.4; FTIR (neat, cm^{-1}) 3347, 2934,

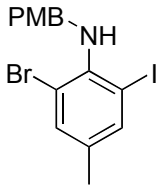
2833, 1611, 1582, 1512, 1463, 1247, 1175, 1031, 830, 760, 726; LRMS (EI) *m/z* 369 (M^+, 25), 240 (5), 121 (100), 91 (6), 77 (7); HRMS (EI) calcd for $C_{15}H_{16}INO_2$: 369.0226, found: 369.0227.



***N*-(2-Iodo-4,6-dimethylphenyl)-4-methylbenzenesulfonamide (S3):** To a stirred solution of 2-iodo-4,6-dimethylaniline[2,3] (2.47 g, 10.0 mmol) in pyridine (10 mL) was added *p*-toluenesulfonyl chloride (2.29 g, 12.0 mmol) all at once. The reaction mixture was stirred at room temperature for 5 h, at which point saturated aqueous NH_4Cl solution (40 mL) was added to quench the reaction. The mixture was extracted with CH_2Cl_2 (4 x 40 mL), and the combined organic layers were washed with 1 N HCl (3 x 40 mL) and brine (3 x 40 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (4:1 hexanes:EtOAc) afforded the title compound (3.63 g, 90%) as a white solid, mp 157-158 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, J = 8.1 Hz, 2H), 7.39 (s, 1H), 7.25 (d, J = 8.1 Hz, 2H), 7.07 (s, 1H), 6.04 (s, 1H), 2.49 (s, 3H), 2.44 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 139.4, 139.2, 137.5, 137.2, 133.2, 132.7, 129.5 (2C), 127.9 (2C), 100.2, 21.6, 20.7, 20.3; FTIR (thin film, $CHCl_3$, cm^{-1}) 3270 (broad), 2922, 1598, 1465, 1387, 1330, 1162, 1091, 891, 813, 756, 709; HRMS (ESI) calcd for $C_{15}H_{16}INNaO_2S$ $[M + Na]^+$: 423.9844, found: 423.9849.

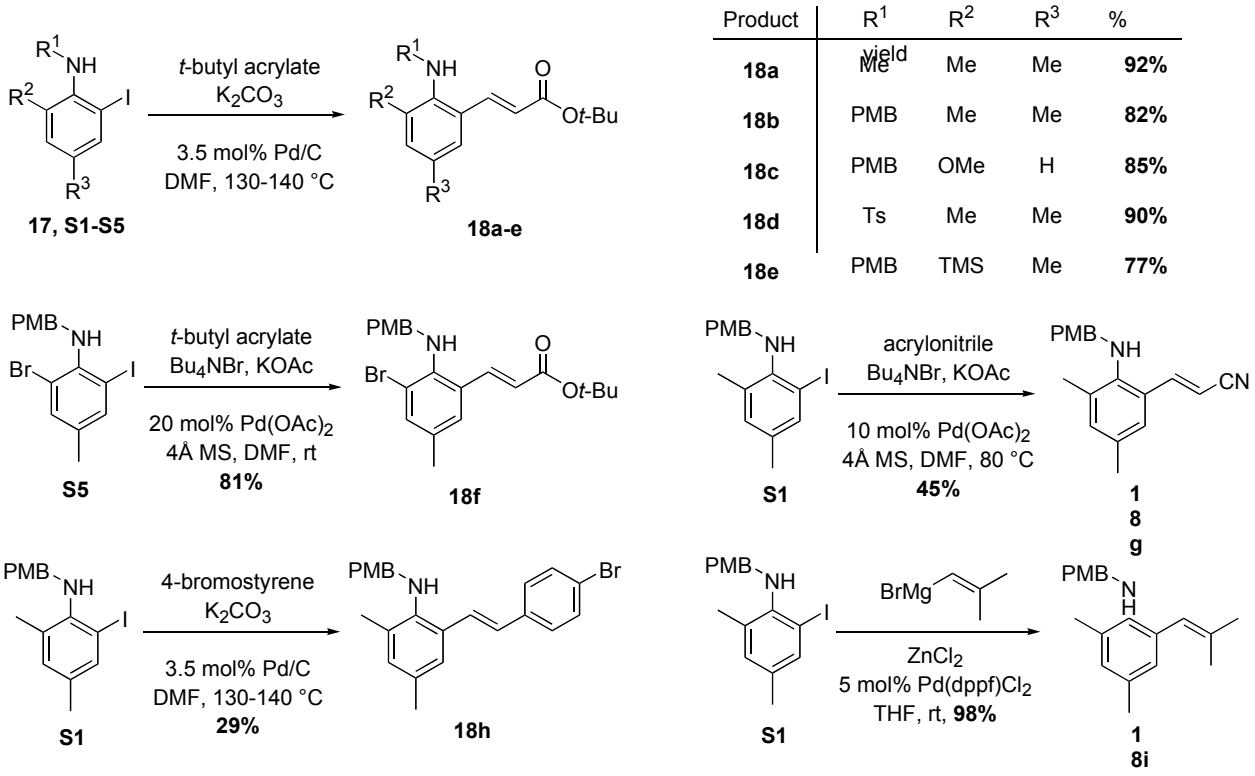


2-Iodo-*N*-(4-methoxybenzyl)-4-methyl-6-(trimethylsilyl)aniline (S4): To a stirred solution of 2-iodo-4-methyl-6-(trimethylsilyl)aniline[3] (5.26 g, 17.2 mmol) in THF (85 mL) at −78 °C was added a hexanes solution of LiHMDS (19.0 mL, 19.0 mmol) dropwise via syringe. The reaction mixture was warmed to room temperature, stirred for 30 min, and recooled to −78 °C. A solution of 4-methoxybenzyl bromide (4.16 g, 20.7 mmol) in THF (15 mL) was added to the reaction mixture dropwise via syringe, the mixture was warmed to room temperature and stirred for 3 h. Saturated aqueous NH_4Cl solution (100 mL) was added, and the mixture was extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (98:2 pentane:Et_2O) furnished the title compound (5.94 g, 81%) as an orange oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 1.8 Hz, 0.6 Hz, 1H), 7.44 (d, *J* = 8.7 Hz, 2H), 7.24 (d, *J* = 1.5 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 4.05 (d, *J* = 6.9 Hz, 2 H), 3.84 (s, 3H), 3.26 (br t, *J* = 6.9 Hz, 1H), 2.29 (s, 3H), 0.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 151.7, 141.3, 136.6, 136.2, 134.9, 131.6, 129.1 (2C), 113.8 (2C), 98.9, 55.2, 54.6, 20.2, 0.4 (3C); FTIR (neat, cm^{-1}) 3297, 2952, 2899, 2833, 1611, 1584, 1513, 1426, 1301, 1247, 1173, 1074, 1037, 905, 839, 766; HRMS (ESI) calcd for $C_{18}H_{25}INOSi$ $[M + H]^+$: 426.0750, found: 426.0788.



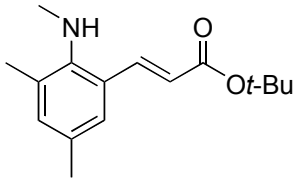
2-Bromo-6-iodo-*N*-(4-methoxybenzyl)-4-methylaniline (S5): A solution of 2-bromo-6-iodo-4-methylaniline[3,5] (3.12 g, 10.0 mmol), *p*-anisaldehyde (1.36 g, 10.0 mmol), and trifluoroacetic acid (.228 g, 2.00 mmol) in toluene (10 mL) was stirred in a round-bottom flask fitted with a Dean-Stark trap and a reflux condenser. The reaction mixture was refluxed for 12 h with azeotropic removal of water, cooled to room temperature, and solvent was removed by rotary evaporation. The crude residue was redissolved in EtOAc (30 mL) with stirring, trifluoroacetic acid (2.28 g, 20.0 mmol) was added, and the mixture was stirred for 30 min. Solid $NaBH(OAc)_3$ (4.24 g, 20.0 mmol) was added portionwise over 5 min, and the reaction mixture was stirred for 2 h at room temperature. The mixture was cooled to 0 °C, and quenched with 10% w/w aqueous NaOH solution (*very* slowly at first, until gas production stopped) until two distinct layers formed. The organic layer was separated and washed with brine (2 x 20 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (20:1 pentane:Et_2O) afforded the title compound (3.12 g, 72%) as a pink solid, mp 41-42 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.39 (d, J = 8.7 Hz, 2H), 7.37 (s, 1H), 6.89 (d, J = 8.7 Hz, 2H), 4.22 (s, 2H, 3.82 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.9, 144.5, 139.5, 135.6, 134.1, 131.3, 129.6 (2C), 117.0, 113.8 (2C), 94.6, 55.2, 52.1, 19.7; FTIR (thin film, $CHCl_3$, cm^{-1}) 3332, 2993, 2958, 2927, 2831, 1610, 1584, 1510, 1455, 1244, 1173, 1034, 852, 826, 745, 714; LRMS (EI) *m/z* 433 (M^+ (^{81}Br), 7), 431 (M^+ (^{79}Br), 7), 313 (5), 311 (5), 121 (100); HRMS (EI) calcd for $C_{15}H_{15}{}^{79}BrINO$: 430.9382, found: 430.9379.

Installation of Radical Acceptor Groups



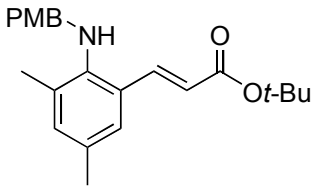
Product	R^1	R^2	R^3	% yield
18a	Me	Me	Me	**92%**
18b	PMB	Me	Me	**82%**
18c	PMB	OMe	H	**85%**
18d	Ts	Me	Me	**90%**
18e	PMB	TMS	Me	**77%**

Scheme S.2 Installation of Radical Acceptor Groups



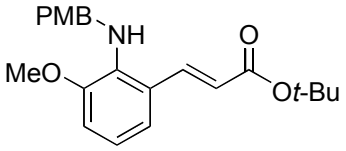
(*E*)-*tert*-Butyl 3-(3,5-dimethyl-2-(methylamino)phenyl)acrylate (18a): In a round-bottom flask fitted with a reflux condenser were combined **17** (1.31 g, 5.00 mmol), K_2CO_3 (1.04 g, 7.50 mmol), *tert*-butyl acrylate (0.961 g, 7.50 mmol), and 10% Pd/C (0.186 g, 0.175 mmol) in DMF (10 mL). The stirred mixture was heated at 140 °C for 2 h, cooled to room temperature, and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (100 mL). The combined filtrates were washed with water (3 x 100 mL) and brine (100 mL), dried over $MgSO_4$, filtered,

and concentrated by rotary evaporation. Column chromatography (5:1 hexanes:EtOAc) afforded the title compound (1.20 g, 92%) as a bright yellow solid, mp 76 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 15.9 Hz, 1H), 7.17 (s, 1H), 6.98 (s, 1H), 6.29 (d, *J* = 15.9 Hz, 1H), 3.17 (br s, 1H), 2.81 (3H, s), 2.26 (s, 3H), 2.25 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 146.2, 141.3, 132.9, 130.7, 129.1, 126.4, 126.0, 119.4, 79.9, 37.3, 28.1 (3C), 20.4, 17.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 3390, 2976, 2931, 1705, 1628, 1480, 1367, 1332, 1278, 1151, 984, 757, 714; LRMS (EI) *m/z* 262 ($M+H^+$, 1), 206 (65), 188 (100), 173 (66), 160 (96), 145 (41); HRMS (EI) calcd for $C_{16}H_{24}NO_2$ $[M + H]^+$: 262.1807, found: 262.1794.



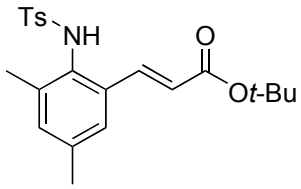
(*E*)-*tert*-Butyl 3-(2-(4-methoxybenzylamino)-3,5-dimethylphenyl)acrylate (18b): In a round-bottom flask fitted with a reflux condenser were combined **S1** (3.67 g, 10.0 mmol), K_2CO_3 (2.07 g, 15.0 mmol), *tert*-butyl acrylate (1.92 g, 15.0 mmol), and 10% Pd/C (0.372 g, 0.350 mmol) in DMF (20 mL). The stirred mixture was heated at 130 °C for 4 h, cooled to room temperature, diluted with Et_2O (200 mL), and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (50 mL). The filtrate was washed with water (3 x 200 mL) and brine (200 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (10:1 hexanes:EtOAc) gave the title compound (3.02 g, 82%) as a bright yellow-green solid, mp 68-70 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 15.9 Hz, 1H), 7.25 (d, *J* = 9.3 Hz, 2H), 7.21 (s, 1H), 6.97 (s, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.31 (d, *J* = 15.9 Hz, 1H), 4.04 (s, 2H), 3.81 (s, 2H), 3.27 (br s, 1H), 2.28 (s, 3H), 2.14 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6,

158.8, 144.4, 141.3, 133.0, 132.2, 131.4, 129.8 (2C), 129.2, 127.2, 126.1, 119.8, 113.8 (2C), 80.0, 55.2, 54.7, 28.2 (3C), 20.6, 17.8; FTIR (thin film, $CHCl_3$, cm^{-1}) 3368, 2975, 2933, 2835, 1703, 1628, 1611, 1512, 1476, 1278, 1248, 1153, 1036, 983, 854, 823, 757; LRMS (EI) *m/z* 367 (M^+, 14), 310 (6), 256 (9), 146 (11), 121 (100), 69 (55); HRMS (EI) calcd for $C_{23}H_{29}NO_3$: 367.2147, found: 367.2144.

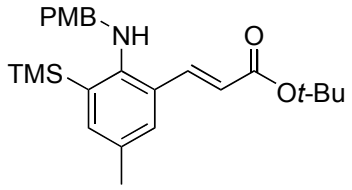


(*E*)-*tert*-Butyl 3-(3-methoxy-2-(4-methoxybenzylamino)phenyl)acrylate (18c): In a round-bottom flask fitted with a reflux condenser were combined **S2** (3.32 g, 9.00 mmol), K_2CO_3 (1.87 g, 13.5 mmol), *tert*-butyl acrylate (1.73 g, 13.5 mmol), and 10% Pd/C (0.335 g, 0.315 mmol) in DMF (18 mL). The stirred mixture was heated at 130 °C for 4 h, cooled to room temperature, and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (180 mL). Water (180 mL) was added to the filtrate, the organic layer was removed, and the aqueous layer was extracted with Et_2O (3 x 180 mL). The combined organic layers were washed with water (3 x 180 mL) and brine (180 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (3:1 hexanes:EtOAc) afforded the title compound (2.83 g, 85%) as a bright yellow-green solid, mp 67-68 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 15.9 Hz, 1H), 7.27 (d, *J* = 9.0 Hz, 2H), 7.09 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.88 (t, *J* = 8.1 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.81 (dd, *J* = 7.8 Hz, 1.2 Hz, 1H), 6.30 (d, *J* = 15.9 Hz, 1H), 4.29 (br s, 1H), 4.16 (s, 2H), 3.81 (s, 3H), 3.79 (s, 3H), 1.53 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.3, 158.6, 150.9, 141.0, 138.5, 132.1, 128.9 (2C), 125.9, 120.8, 119.8, 119.5, 113.6 (2C), 111.0, 79.9, 55.6, 54.9, 54.2, 28.0 (3C); FTIR (thin film, $CHCl_3$, cm^{-1}) 3359, 2976, 2935, 2835,

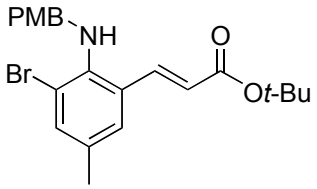
1701, 1628, 1581, 1513, 1456, 1243, 1147, 1078, 1036, 983, 852, 824, 759; HRMS (ESI) calcd for $C_{22}H_{27}NNaO_4$ $[M + Na]^+$: 392.1838, found: 392.1832.



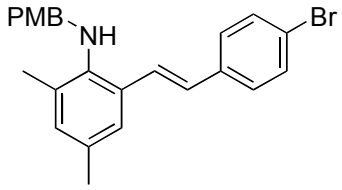
(*E*)-*tert*-Butyl 3-(3,5-dimethyl-2-(4-methylphenylsulfonamido)phenyl)acrylate (18d): In a round-bottom flask fitted with a reflux condenser were combined **S3** (2.01 g, 5.00 mmol), K_2CO_3 (1.04 g, 7.50 mmol), *tert*-butyl acrylate (0.961 g, 7.50 mmol), and 10% Pd/C (0.186 g, 0.175 mmol) in DMF (10 mL). The stirred mixture was heated at 140 °C for 1 h, cooled to room temperature and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (100 mL). Water (100 mL) was added to the filtrate, the organic layer was removed, and the aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (100 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (3:1 hexanes:EtOAc) afforded the title compound (1.80 g, 90%) as a white solid, mp 150-152 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 15.9 Hz, 2H), 7.18 (s, 1H), 7.17 (d, J = 7.8 Hz, 2H), 7.09 (s, 1H), 6.49 (s, 1H), 5.99 (d, J = 15.9 Hz, 2H), 2.38 (s, 3H), 2.31 (s, 3H), 2.28 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 143.5, 139.3, 139.0, 137.9, 136.3, 133.9, 133.6, 130.5, 129.6 (2C), 127.5 (2C), 125.2, 120.5, 80.3, 28.1 (3C), 21.6, 21.0, 18.8; FTIR (thin film, $CHCl_3$, cm^{-1}) 3256 (broad), 2978, 2928, 1691, 1633, 1331, 1258, 1160, 1092, 982, 899, 855, 814, 756; HRMS (ESI) calcd for $C_{22}H_{27}NNaO_4S$ $[M + Na]^+$: 424.1559, found: 424.1542.



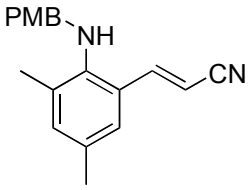
(*E*)-*tert*-Butyl-3-(2-(4-methoxybenzylamino)-5-methyl-3-(trimethylsilyl)phenyl)acrylate (18e): In a round-bottom flask fitted with a reflux condenser were combined **S4** (3.40 g, 8.00 mmol), K_2CO_3 (1.54 g, 12.0 mmol), *tert*-butyl acrylate (1.54 g, 12.0 mmol), and 10% Pd/C (0.298 g, 0.280 mmol) in DMF (16 mL). The stirred mixture was heated at 130 °C for 8 h, cooled to room temperature and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (160 mL). Water (160 mL) was added to the filtrate, the organic layer was removed, and the aqueous layer was extracted with Et_2O (3 x 160 mL). The combined organic layers were washed with water (3 x 160 mL) and brine (160 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (10:1 pentane:Et_2O) afforded the title compound (2.62 g, 77%) as a bright yellow-green oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 16.2 Hz, 1H), 7.38 (d, J = 8.7 Hz, 2H), 7.37 (s, 1H), 7.21 (d, J = 1.5 Hz, 1H), 6.31 (d, J = 16.2 Hz, 1H), 4.02 (br d, J = 5.1 Hz, 2H), 3.83 (s, 3H), 3.37 (br m, 1H), 2.32 (s, 3H), 1.53 (s, 9H), 0.30 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 158.9, 151.1, 141.8, 137.5, 131.8, 131.6, 131.4, 129.9, 129.4 (2C), 127.5, 119.8, 113.9 (2C), 80.0, 56.0, 55.2, 28.2 (3C), 20.7, 0.2 (3C); FTIR (neat, cm^{-1}) 3391, 2955, 2836, 1705, 1629, 1514, 1455, 1320, 1250, 1152, 1037, 910, 883, 837, 734; LRMS (EI) *m/z* 425 (M^+, 15), 369 (12), 309 (8), 216 (8), 121 (100); HRMS (EI) calcd for $C_{25}H_{35}NO_3Si$: 425.2386, found: 425.2389.



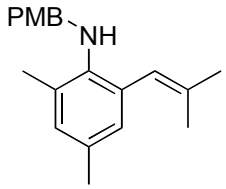
(*E*)-*tert*-Butyl 3-(3-bromo-2-(4-methoxybenzylamino)-5-methylphenyl)acrylate (18f): To a stirred solution of *o*-iodoaniline **S5** (1.73 g, 4.00 mmol) in DMF (20. mL) were added Bu_4NBr (1.29 g, 4.00 mmol), KOAc (1.18 g, 12.0 mmol), $Pd(OAc)_2$ (0.180 g, 0.80 mmol), and crushed activated 4Å molecular sieves (~2 g). Finally, *tert*-butyl acrylate (2.56 g, 20.0 mmol) was added, and the reaction mixture was stirred at room temperature for 2 days. The mixture was vacuum filtered through a Celite pad, and the pad was rinsed with Et_2O (200 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ solution (200 mL), water (3 x 200 mL), and brine (200 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Gradient column chromatography (hexanes to 10:1 hexanes:EtOAc) furnished the title compound (1.40 g, 81%) as a bright yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J = 15.9 Hz, 1H), 7.34 (d, J = 1.5 Hz, 1H), 7.29 (d, J = 8.4 Hz, 2H), 7.25 (s, 1H), 6.87 (d, J = 8.7 Hz, 2H), 6.31 (d, J = 15.9 Hz, 1H), 4.07 (d, J = 6.6 Hz, 2H), 3.97 (br t, J = 6.6 Hz, 1H), 3.82 (s, 3H), 2.28 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 158.9, 143.5, 140.9, 134.0, 132.7, 131.5, 129.4 (2C), 128.4, 128.0, 120.8, 118.1, 113.8 (2C), 80.4, 55.2, 54.6, 28.2 (3C), 20.3; FTIR (neat, cm^{-1}) 3344, 2975, 2932, 2835, 1705, 1631, 1611, 1513, 1460, 1321, 1249, 1150, 1036, 980, 854, 828, 736; HRMS (ESI) calcd for $C_{22}H_{26}{}^{79}BrNNaO_3$ $[M + Na]^+$: 454.0994, found: 454.0996.



(*E*)-2-(4-Bromostyryl)-*N*-(4-methoxybenzyl)-4,6-dimethylaniline (18g): In a round-bottom flask fitted with a reflux condenser were combined **S1** (1.84 g, 5.00 mmol), K_2CO_3 (1.04 g, 7.50 mmol), 4-bromostyrene (1.37 g, 7.50 mmol), and 10% Pd/C (0.186 g, 0.175 mmol) in DMF (10 mL). The stirred mixture was heated at 130 °C for 2 h, cooled to room temperature and filtered through a pad of Celite, followed by rinsing the pad with Et_2O (100 mL). Water (100 mL) was added to the filtrate, the organic layer was removed, and the aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (100 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Gradient column chromatography (hexanes to 6:1 hexanes:EtOAc) gave the title compound (0.602 g, 29%) as a bright yellow solid, mp 63-65 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 15.9 Hz, 1H), 7.35 (d, J = 8.7 Hz, 2H), 7.29 (s, 1H), 7.26 (d, J = 8.7 Hz, 2H), 6.95 (d, J = 16.2 Hz, 1H), 6.95 (s, 1H), 6.89 (d, J = 8.4 Hz, 2H), 4.13 (s, 2H), 3.82 (s, 3H), 2.35 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.8, 143.2, 136.9, 131.6 (2C), 131.5, 131.1, 129.9, 129.7, 129.0 (2C), 127.8 (2C), 127.3, 127.2, 125.3, 120.8, 113.9 (2C), 55.2, 54.1, 20.8, 17.9; FTIR (thin film, $CHCl_3$, cm^{-1}) 3363, 3001, 2912, 2834, 1610, 1511, 1487, 1246, 1175, 1072, 1035, 1007, 977, 908, 811, 732; HRMS (ESI) calcd for $C_{24}H_{25}NO^{79}Br$ $[M + H]^+$: 422.1120, found: 422.1133.

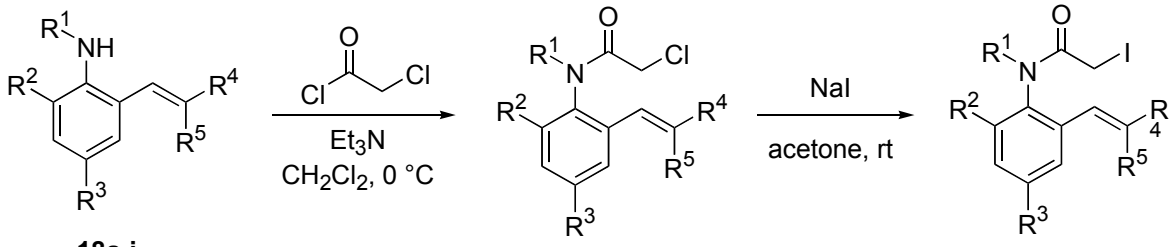


(*E*)-3-(2-(4-Methoxybenzylamino)-3,5-dimethylphenyl)acrylonitrile (18h): To a stirred solution of **S1** (1.84 g, 5.00 mmol) in DMF (25 mL) were added Bu_4NBr (1.61 g, 5.00 mmol), KOAc (1.47 g, 15.0 mmol), $Pd(OAc)_2$ (0.112 g, 0.50 mmol), and crushed activated 4Å molecular sieves (~2.5 g). Finally, acrylonitrile (1.33 g, 25.0 mmol) was added, and the reaction mixture was heated at 80 °C for 8 h. The mixture was cooled to room temperature, diluted with Et_2O (250 mL), and filtered through Celite, rinsing with Et_2O (25 mL). The filtrate was washed with saturated aqueous $NaHCO_3$ solution (250 mL), water (3 x 250 mL), and brine (250 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (4:1 hexanes:EtOAc) afforded the title compound (0.660 g, 45%) as a bright yellow-green oil, containing ~5% of an inseparable impurity by ^{1}H NMR: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 16.8 Hz, 1H), 7.17 (d, J = 8.7 Hz, 2H), 7.10 (s, 1H), 7.02 (s, 1H), 6.87 (d, J = 8.7 Hz, 2H), 5.86 (d, J = 16.8 Hz, 1H), 4.01 (br s, 2H), 3.82 (s, 3H), 3.27 (br s, 1H), 2.29 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 148.8, 144.5, 134.1, 131.9, 131.8, 130.4, 129.1 (2C), 126.4, 125.6, 119.0, 114.1 (2C), 95.1, 55.3, 55.2, 20.6, 17.7; FTIR (neat, cm^{-1}) 3362, 3011, 2933, 2836, 2214, 1610, 1512, 1475, 1248, 1175, 1033, 982, 822, 755; HRMS (ESI) calcd for $C_{19}H_{21}N_2O$ [M + H]$^+$: 293.1654, found: 293.1678.



***N*-(4-Methoxybenzyl)-2,4-dimethyl-6-(2-methylprop-1-enyl)aniline (18i):** To a stirred solution of 2-methyl-1-propenylmagnesium bromide (7.17 g, 45.0 mmol) in THF (90. mL) at room temperature was added $ZnCl_2$ (6.13 g, 45.0 mmol) dropwise via syringe over 15 min. The mixture was stirred for 2 h, solid $Pd(dppf)Cl_2 \bullet CH_2Cl_2$ (0.184 g, 0.225 mmol) was added all at once, and the mixture was stirred an additional 5 min. **S1** (1.65 g, 4.50 mmol) in THF (20 mL) was added dropwise via syringe, the reaction mixture was stirred for 2.5 h at rt, cooled to 0 °C, and saturated aqueous NH_4Cl solution (200 mL) was added to quench the reaction. The mixture was extracted with Et_2O (3 x 200 mL), and the combined organic layers were washed with brine (200 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (10:1 hexanes:EtOAc) afforded the title compound (1.30 g, 98%) as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 6.85 (s, 1H), 6.79 (s, 1H), 6.15 (s, 1H), 4.03 (s, 2H), 3.81 (s, 3H), 3.33 (br s, 1H), 2.26 (s, 3H), 2.25 (s, 3H), 1.88 (d, J = 1.5 Hz, 3H), 1.73 (d, J = 1.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 142.8, 135.3, 132.7, 130.3, 129.9, 129.8, 128.9 (2C), 128.7, 128.5, 122.9, 113.5 (2C), 54.8, 52.2, 25.8, 20.5, 19.2, 18.2; FTIR (neat, cm^{-1}) 3369, 2911, 1611, 1512, 1475, 1247, 1174, 1036, 861, 823, 737; LRMS (EI) *m/z* 295 (M^+, 10), 252 (9), 174 (37), 121 (100); HRMS (EI) calcd for $C_{20}H_{25}NO$: 295.1936, found: 295.1925.

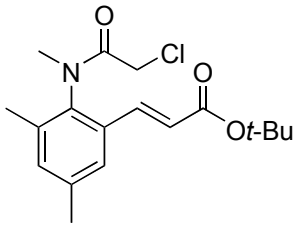
Preparation of α-Haloacetamide Precursors



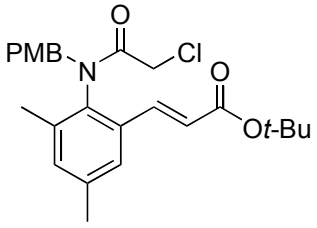
substrate	R^1	R^2	R^3	R^4	R^5	α-Cl amide	% yield[a]	α-I amide	% yield[a]
18a	Me	Me	Me	CO_2t-Bu	H	**19a**	90	**15a**	93
18b	PMB	Me	Me	CO_2t-Bu	H	**19b**	97	**15b**	92
18c	PMB	OMe	H	CO_2t-Bu	H	**19c**	85	**15c**	98
18d	Ts	Me	Me	CO_2t-Bu	H	**19d**	89	**15d**	78
18e	PMB	TMS	Me	CO_2t-Bu	H	**19e**	99	**15e**	96[b]
18f	PMB	Br	Me	CO_2t-Bu	H	**19f**	90	**15f**	91
18g	PMB	Me	Me	4-BrC_6H_4	H	**19g**	89	**15g**	86
18h	PMB	Me	Me	CN	H	**19h**	74	**15h**	86
18i	PMB	Me	Me	Me	Me	**19i**	98	**15i**	88

[a] Yield of racemate after isolation by column chromatography. [b] The reaction mixture was refluxed for 40 h and reaction progress was monitored by GC.

General acylation procedure (compounds 19a-i): To a stirred solution of **18a-i** (1.0 equiv.) in CH_2Cl_2 (10 mL/mmol = *X* mL) at 0 °C was added Et_3N (2.0 equiv.) all at once, followed by chloroacetyl chloride (1.5 equiv.) dropwise via syringe. The mixture was stirred at 0 °C until completion, at which point saturated aqueous NH_4Cl solution (*X* mL) was added. The mixture was extracted with CH_2Cl_2 (3 x *X* mL), and the combined organic layers were washed with brine (*X* mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude residue was subjected to column chromatography, using the appropriate eluent, to furnish the desired α-Cl amide **19a-i**.

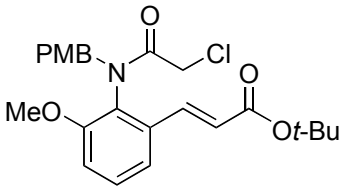


***rac*-(*E*)-*tert*-Butyl 3-(2-(2-chloro-*N*-methylacetamido)-3,5-dimethylphenyl)acrylate (19a):** Aniline **18a** (1.05 g, 4.00 mmol) was reacted according to the general procedure, and the reaction was complete after 2 h. After workup, column chromatography (2:1 hexanes:EtOAc) provided the title compound (1.21 g, 90%) as a white solid, mp 87 °C, as a mixture of amide rotamers in a 19:1 ratio: ^{1}H NMR (300 MHz, $CDCl_3$) Major rotamer δ 7.48 (d, *J* = 15.9 Hz, 1H), 7.35 (s, 1H), 7.16 (s, 1H), 6.36 (d, *J* = 15.9 Hz, 1H), 3.69 (d, *J* = 13.5 Hz, 1H), 3.64 (d, *J* = 13.5 Hz, 1H), 3.21 (s, 3H), 2.36 (s, 3H), 2.22 (s, 3H), 1.52 (s, 9H); minor rotamer δ 7.52 (d, *J* = 15.9 Hz, 1H), 7.35 (s, 1H), 7.12 (s, 1H), 6.35 (d, *J* = 15.9 Hz, 1H), 4.31 (d, *J* = 12.0 Hz, 1H), 4.23 (d, *J* = 12.0 Hz, 1H), 3.34 (s, 3H), 2.33 (s, 3H), 2.19 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 165.2, 138.9, 137.22, 137.17, 136.0, 133.8, 132.3, 125.8, 123.4, 80.6, 41.3, 36.0, 27.9 (3C), 20.8, 17.2; FTIR (thin film, $CHCl_3$, cm^{-1}) 2978, 2931, 1712, 1475, 1368, 1330, 1256, 1154, 1110, 983, 855, 755; HRMS (ESI) calcd for $C_{18}H_{24}ClNNaO_3$ $[M + Na]^+$: 360.1342, found: 360.1325.



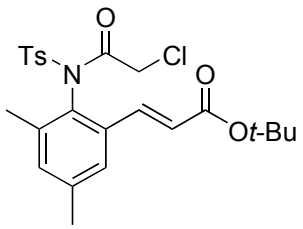
***rac*-(*E*)-*tert*-Butyl-3-(2-(2-chloro-*N*-(4-methoxybenzyl)acetamido)-3,5-dimethylphenyl) acrylate (19b):** Aniline **18b** (1.84 g, 7.00 mmol) was reacted according to the general procedure, and the reaction was complete after 3 h. After workup, column chromatography (3:1

hexanes:EtOAc) provided the title compound (3.01 g, 97%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 15.9 Hz, 2H), 7.09 (s, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.14 (d, *J* = 15.9 Hz, 2H), 4.87 (d, *J* = 13.8 Hz, 1H), 4.58 (d, *J* = 13.5 Hz, 1H), 3.76 (s, 3H), 3.69 (d, *J* = 13.8 Hz, 1H), 3.64 (d, *J* = 13.8 Hz, 1H), 2.35 (s, 3H), 1.93 (s, 3H), 1.49 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 164.7, 159.0, 138.6, 137.4, 136.3, 135.1, 133.6, 132.8, 131.1 (2C), 127.1, 125.4, 122.2, 113.3 (2C), 80.0, 54.6, 52.0, 41.6, 27.6 (3C), 20.7, 17.2; FTIR (neat, cm^{-1}) 2977, 2933, 2837, 1708, 1667, 1513, 1469, 1327, 1248, 1152, 1035, 984, 851, 792, 733; HRMS (ESI) calcd for $C_{25}H_{30}ClNNaO_4$ $[M + Na]^+$: 466.1761, found: 466.1730.

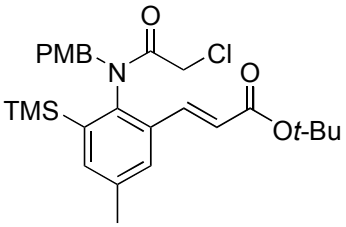


***rac*-(*E*)-*t*-Butyl 3-(2-(2-chloro-*N*-(4-methoxybenzyl)acetamido)-3-methoxyphenyl) acrylate (19c):** Aniline **18c** (1.35 g, 3.65 mmol) was reacted according to the general procedure, and the reaction was complete after 1 h. After workup, column chromatography (2:1 hexanes:EtOAc) provided the title compound (1.39 g, 85%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (t, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 16.8 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 2H), 6.18 (d, *J* = 15.9 Hz, 1H), 4.85 (d, *J* = 13.8 Hz, 1H), 4.63 (d, *J* = 13.8 Hz, 1H), 3.76 (d, *J* = 15.3 Hz, 1H), 3.74 (s, 3H), 3.71 (d, *J* = 14.7 Hz, 1H), 3.64 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 165.1, 159.0, 155.5, 137.3, 134.6, 131.2 (2C), 129.9, 127.8, 127.6, 123.3, 118.8, 113.3 (2C), 112.7, 80.7, 55.7, 55.0, 51.8, 42.5, 27.8 (3C); FTIR (neat, cm^{-1}) 2977, 2937, 2838, 2249, 1708, 1674, 1578, 1513, 1476, 1392,

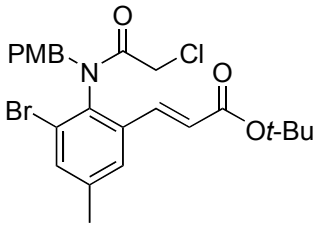
1249, 1153, 1070, 1035, 984, 913, 849, 790, 733; HRMS (ESI) calcd for $C_{24}H_{28}ClNNaO_5$ [M + Na]$^+$: 468.1554, found: 468.1530.



***rac*-(*E*)-*tert*-Butyl 3-(2-(2-chloro-*N*-tosylacetamido)-3,5-dimethylphenyl)acrylate (19d):** Aniline **18d** (1.20 g, 3.00 mmol) was reacted according to the general procedure, and the reaction was complete after 1 h. After workup, column chromatography (4:1 hexanes:EtOAc) provided the title compound (1.27 g, 89%) as a white solid, mp 170 °C (decomp.): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 8.4 Hz, 2H), 7.43 (s, 1H), 7.34 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 15.9 Hz, 1H), 7.24 (s, 1H), 6.38 (d, J = 15.9 Hz, 1H), 3.66 (s, 2H), 2.46 (s, 3H), 2.404 (s, 3H), 2.396 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.0, 164.7, 145.5, 140.8, 139.4, 137.2, 134.3, 134.1 (2C, accidental isochrony), 130.6, 130.2 (2C), 129.3 (2C), 125.9, 123.9, 80.6, 43.2, 27.8 (3C), 21.6, 21.1, 18.7; FTIR (thin film, $CHCl_3$, cm^{-1}) 2979, 1709, 1367, 1307, 1264, 1170, 1085, 983, 886, 814, 757; HRMS (ESI) calcd for $C_{24}H_{28}ClNNaO_5S$: [M + Na]$^+$: 500.1274, found: 500.1273.

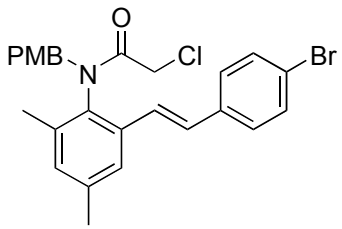


***rac*-(*E*)-*t*-Butyl 3-(2-(2-chloro-*N*-(4-methoxybenzyl)acetamido)-5-methyl-3-(trimethylsilyl) phenyl)acrylate (19e):** Aniline **18e** was reacted according to the general procedure, and the reaction was complete after 7 h. After workup, column chromatography (5:1 hexanes:EtOAc) provided the title compound (2.50 g, 99%) as a white solid, mp 69-71 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 1.8 Hz, 1H), 7.34 (s, 1H), 7.03 (d, J = 8.4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 15.9 Hz, 1H), 5.92 (d, J = 15.9 Hz, 1H), 5.76 (d, J = 13.5 Hz, 1H), 3.76 (d, J = 11.7 Hz, 3.74 (s, 3H), 3.73 (d, J = 14.1 Hz, 1H), 3.67 (d, J = 13.8 Hz, 1H), 2.39 (s, 3H), 1.44 (s, 9H), 0.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.1, 164.5, 159.1, 140.8, 139.3, 139.2, 138.1, 137.5, 133.6, 131.3 (2C), 128.5, 126.7, 121.9, 113.5 (2C), 79.9, 54.7, 54.1, 42.2, 27.7 (3C), 20.9, 0.1 (t, $J_{Si\text{-}C}$ = 26.3 Hz, 3C); FTIR (thin film, $CHCl_3$, cm^{-1}) 2977, 1707, 1670, 1512, 1437, 1320, 1252, 1155, 982, 874, 839, 757; HRMS (ESI) calcd for $C_{27}H_{36}ClNNaO_4Si$ $[M + Na]^+$: 524.2000, found: 524.1974.



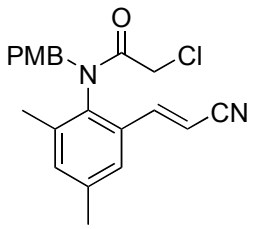
***rac*-(*E*)-*tert*-Butyl 3-(3-bromo-2-(2-chloro-*N*-(4-methoxybenzyl)acetamido)-5-methylphenyl) acrylate (19f):** Aniline **18f** (2.34 g, 5.50 mmol) was reacted according to the general procedure, and the reaction was complete after 2 h. After workup, column chromatography (3:1

hexanes:EtOAc) provided the title compound (2.51 g, 90%) as a white solid, mp 117 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.2 Hz, 1H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 15.9 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 2H), 6.01 (d, *J* = 15.9 Hz, 1H), 5.38 (d, *J* = 13.8 Hz, 1H), 4.21 (d, *J* = 14.1 Hz, 1H), 3.78 (d, *J* = 13.8 Hz, 1H), 3.75 (s, 3H), 3.66 (d, *J* = 14.1 Hz, 1H), 2.38 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 164.5, 159.3, 140.8, 136.9, 135.9, 135.4, 134.9, 131.5 (2C), 127.0, 126.7, 124.6, 123.3, 113.6 (2C), 80.6, 54.9, 51.9, 42.3, 27.9 (3C), 20.8; FTIR (thin film, $CHCl_3$, cm^{-1}) 3007, 2978, 2934, 1709, 1513, 1459, 1323, 1249, 1152, 1036, 983, 851, 826, 756; HRMS (ESI) calcd for $C_{24}H_{27}{}^{79}BrClNNaO_4$ [M + Na]$^{+}$: 530.0710, found: 530.0761.

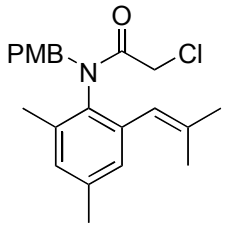


***rac*-(*E*)-*N*-(2-(4-Bromostyryl)-4,6-dimethylphenyl)-2-chloro-*N*-(4-methoxybenzyl)acetamide (19g):** Aniline **18g** (0.472 g, 1.12 mmol) was reacted according to the general procedure, and the reaction was complete after 2 h. After workup, column chromatography (4:1 hexanes:EtOAc) provided the title compound (0.498 g, 89%) as a yellow solid, mp 130-131 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.33 (s, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.06 (s, 1H), 6.99 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 16.2 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 2H), 6.41 (d, *J* = 16.2 Hz, 2H), 5.24 (d, *J* = 13.5 Hz, 1H), 4.24 (d, *J* = 13.5 Hz, 1H), 3.68 (s, 2H), 3.65 (s, 3H), 2.38 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 159.3, 138.8,136.1, 135.6, 135.4, 134.9, 132.0, 131.54 (2C), 131.50 (2C), 129.8, 128.2, 128.1 (2C), 124.5, 124.1, 121.7, 113.7 (2C), 55.0, 52.6, 42.3, 21.2, 17.8; FTIR (thin film, $CHCl_3$, cm^{-1}) 3001, 2932, 2835, 1667, 1512, 1488, 1394, 1325,

1303, 1247, 1176, 1035, 1008, 965, 910, 849, 810, 732; HRMS (ESI) calcd for $C_{26}H_{25}{}^{79}BrClNNaO_2$ $[M + Na]^+$: 520.0655, found: 520.0690.

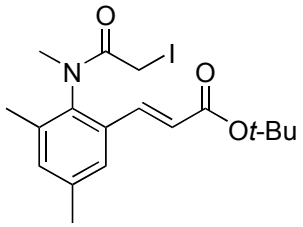


***rac*-(*E*)-2-Chloro-*N*-(2-(2-cyanovinyl)-4,6-dimethylphenyl)-*N*-(4-methoxybenzyl)acetamide (19h):** Aniline **18h** (0.731 g, 2.50 mmol) was reacted according to the general procedure, and the reaction was complete after 5 h. After workup, column chromatography (2:1 hexanes:EtOAc) provided the title compound (0.687 g, 74%) as a white solid, mp 159-160 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22 (s, 1H), 7.16 (s, 1H), 7.06 (d, J = 8.4 Hz, 2H), 6.80 (d, J = 8.7 Hz, 2H), 6.70 (d, J = 16.5 Hz, 1H), 5.56 (d, J = 16.8 Hz, 1H), 5.31 (d, J = 13.5 Hz, 1H), 4.13 (d, J = 13.5 Hz, 1H), 3.83 (s, 3H), 3.64 (d, J = 13.2 Hz, 1H), 3.59 (d, J = 13.5 Hz, 1H), 2.37 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0, 159.7, 144.8, 139.4, 136.9, 135.2, 135.1, 132.2, 131.4 (2C), 127.0, 124.6, 117.4, 114.0 (2C), 97.8, 55.2, 52.2, 41.6, 21.0, 17.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 3012, 2936, 2837, 2218, 1669, 1612, 1513, 1467, 1392, 1249, 1176, 1111, 1033, 966, 849, 761; LRMS (EI) *m/z* 368 (M^+, 8), 304 (12), 291 (15), 183 (10), 169 (15), 155 (18), 121 (100), 91 (37), 84 (50); HRMS (EI) calcd for $C_{21}H_{21}ClN_2O_2$: 368.1292, found: 368.1295.

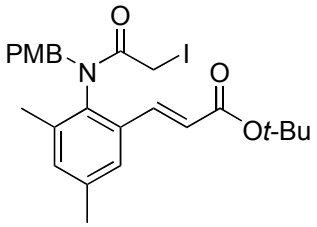


***rac*-2-Chloro-*N*-(2,4-dimethyl-6-(2-methylprop-1-enyl)phenyl)-*N*-(4-methoxybenzyl) acetamide (19i):** Aniline **18i** (0.886 g, 3.00 mmol) was reacted according to the general procedure, and the reaction was complete after 90 min. After workup, column chromatography (4:1 hexanes:EtOAc) provided the title compound (1.09 g, 98%) as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, J = 8.4 Hz, 2H), 6.90 (s, 2H), 6.75 (d, J = 8.4 Hz, 2H), 5.60 (s, 1H), 4.74 (d, J = 13.8 Hz, 1H), 4.62 (d, J = 13.8 Hz, 1H), 3.78 (s, 3H), 3.67 (d, 2H), 2.32 (s, 3H), 1.84 (s, 3H), 1.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 158.9, 137.7, 137.4, 136.5, 135.5, 134.7, 131.1 (2C), 130.1, 129.5, 128.4, 121.2, 113.3 (2C), 54.9, 51.7, 41.9, 26.2, 20.8, 19.0, 17.4; FTIR (neat, cm^{-1}) 2933, 2836, 1667, 1512, 1441, 1247, 1176, 1110, 1035, 915, 849, 822, 791, 733; HRMS (ESI) calcd for $C_{22}H_{26}ClNNaO_2$ $[M + Na]^+$: 394.1550, found: 394.1529.

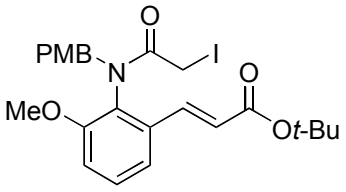
General procedure for Finkelstein reactions (Compounds 15a-i): To a solution of α-Cl amide **19a-i** (1.0 equiv.) in acetone (10 mL/mmol = X mL) was added NaI (10.0 equiv.) all at once, and the reaction mixture was stirred at room temperature overnight (16-20 h). The mixture was diluted with Et_2O (10X mL) and washed with 10% aqueous $Na_2S_2O_3$ (3 x X mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. The crude residue was subjected to column chromatography, using the appropriate eluent, to furnish the desired product.



(*E*)-*t*-Butyl 3-(2-(2-iodo-*N*-methylacetamido)-3,5-dimethylphenyl)acrylate (15a): Chloride *rac*-**19a** (1.01 g, 3.00 mmol) was reacted according to the general procedure. Column chromatography (2:1 hexanes:EtOAc) furnished *rac*-**15a** (1.20 g, 93%) as a yellow oil in a 14:1 ratio of amide rotamers. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 80:20 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ –153, 85/15 er (*c* 6.7 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ +131, 98.5/1.5 er (*c* 4.7 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) major rotamer δ 7.55 (d, *J* = 15.9 Hz, 1H), 7.36 (s, 1H), 7.15 (s, 1H), 6.35 (d, *J* = 15.9 Hz, 1H), 3.48 (d, *J* = 10.2 Hz, 1H), 3.44 (d, *J* = 10.2 Hz, 1H), 3.17 (s, 3H), 2.36 (s, 3H), 2.26 (s, 3H), 1.52 (s, 9H); minor rotamer δ 7.55 (d, *J* = 15.9 Hz, 1H), 7.31 (s, 1H), 7.09 (s, 1H), 6.34 (d, *J* = 15.9 Hz, 1H), 3.96 (d, *J* = 9.6 Hz, 1H), 3.88 (d, *J* = 9.6 Hz, 1H), 3.28 (s, 3H), 2.32 (s, 3H), 2.26 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) major rotamer only δ 167.7, 165.1, 138.6, 137.6, 135.6, 133.7, 131.9, 125.7, 123.1, 80.3, 36.2, 27.9, 27.9 (3C), 20.8, 17.5, −3.7; FTIR (neat, cm^{-1}) 2977, 2930, 2246, 1708, 1662, 1474, 1427, 1367, 1329, 1300, 1253, 1153, 1096, 983, 916, 855, 732; HRMS (ESI) calcd for $C_{18}H_{24}INNaO_3$ $[M + Na]^+$: 452.0699, found: 452.0661.

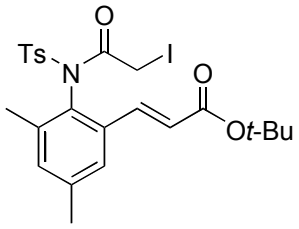


(*E*)-*tert*-Butyl 3-(2-(2-iodo-*N*-(4-methoxybenzyl)acetamido)-3,5-dimethylphenyl)acrylate (15b): Chloride *rac*-**19b** (2.00 g, 4.50 mmol) was reacted according to the general procedure. Column chromatography (2:1 hexanes:EtOAc) furnished *rac*-**15b** (2.22 g, 92%) as a yellow oil. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 70:30 hexanes:iPrOH), first eluting enantiomer $[\alpha]_D^{23}$ –16, 100/0 er (*c* 16.7 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ +15, 100/0 er (*c* 9.5 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.19 (d, *J* = 15.9 Hz, 1H), 7.10 (s, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2H), 6.13 (d, *J* = 15.9 Hz, 1H), 3.76 (s, 3H), 3.47 (s, 2H), 2.35 (s, 3H), 1.98 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 165.2, 159.2, 138.6, 138.3, 136.5, 136.4, 133.8, 132.9, 131.4 (2C), 127.5, 125.7, 122.4, 113.6 (2C), 80.4, 55.0, 52.4, 28.0 (3C), 21.0, 18.0, −2.5; FTIR (thin film, $CHCl_3$, cm^{-1}) 2977, 2933, 2836, 1707, 1655, 1512, 1469, 1368, 1326, 1303, 1249, 1158, 1036, 984, 912, 852, 732; HRMS (ESI) calcd for $C_{25}H_{30}INNaO_4$ $[M + Na]^+$: 558.1117, found: 558.1071.



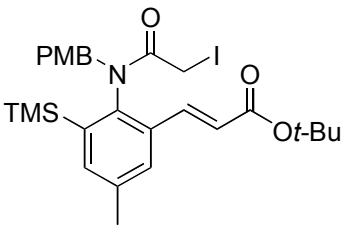
(*E*)-*t*-Butyl 3-(2-(2-Iodo-*N*-(4-methoxybenzyl)acetamido)-3-methoxyphenyl)acrylate (15c): Chloride *rac*-**19c** (0.981 g, 2.20 mmol) was reacted according to the general procedure. Column chromatography (2:1 hexanes:EtOAc) furnished *rac*-**15c** (1.16 g, 98%) as a yellow oil. The

racemate was submitted to preparative chiral HPLC separation (Chiralcel OD, 90:10 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ –27, 99/1 er (*c* 9.5 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ +28, 99/1 er (*c* 13.6 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 16.2 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.1 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 2H), 6.16 (d, *J* = 16.2 Hz, 1H), 4.87 (d, *J* = 13.8 Hz, 1H), 4.56 (d, *J* = 13.8 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.50 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 165.0, 158.8, 155.2, 137.6, 134.1, 131.0 (2C), 129.6, 128.5, 127.7, 122.7, 118.5, 113.1 (2C), 112.7, 80.3, 55.5, 54.9, 51.6, 27.9, –2.1; FTIR (neat, cm^{-1}) 2976, 2935, 2837, 1708, 1659, 1577, 1513, 1368, 1248, 1153, 1070, 1035, 983, 849, 913, 849, 800, 732; HRMS (ESI) calcd for $C_{24}H_{28}INNaO_5$ $[M + Na]^+$: 560.0910, found: 560.0901.

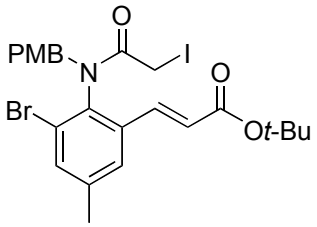


(*E*)-*tert*-Butyl 3-(2-(2-iodo-*N*-tosylacetamido)-3,5-dimethylphenyl)acrylate (15d): Chloride *rac*-**19d** (0.717 g, 1.50 mmol) was reacted according to the general procedure. Column chromatography (2:1 hexanes:EtOAc) furnished *rac*-**15d** (0.662 g, 78%) as a white solid, mp 205 °C (decomp.): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.1 Hz, 2H), 7.43 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 15.6 Hz, 1H), 7.25 (s, 1H), 6.37 (d, *J* = 15.9 Hz, 1H), 3.48 (s, 2H), 2.46 (2 overlapping s, 2 x 3H), 2.41 (s, 3H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7, 165.0, 145.5, 140.6, 139.6, 137.9, 134.5, 134.3, 134.1, 132.0, 130.4 (2C), 129.4 (2C), 125.9, 123.7, 80.6, 28.0 (3C), 21.8, 21.2, 19.3, −2.2; FTIR (thin film, $CHCl_3$, cm^{-1}) 2978, 1705, 1365, 1275,

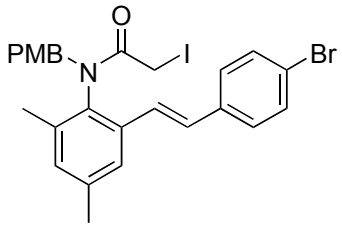
1171, 1083, 982, 885, 815, 758; HRMS (ESI) calcd for $C_{24}H_{28}INNaO_5S$ [M + Na]$^+$: 592.0631, found: 592.0616.



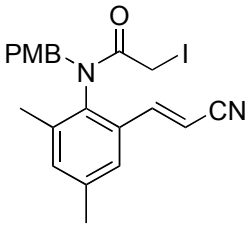
(*E*)-*t*-Butyl 3-(2-(2-iodo-*N*-(4-methoxybenzyl)acetamido)-5-methyl-3-(trimethylsilyl)phenyl) acrylate (15e): In a round bottom flask equipped with a reflux condenser, chloride *rac*-**19e** (1.51 g, 3.00 mmol) was mixed with NaI (4.50 g, 30.0 mmol) in acetone (30 mL). The stirred mixture was refluxed for 40 h until complete conversion had been achieved (monitored using GC). The mixture was cooled to room temperature, and was worked up according to the general procedure. Column chromatography (5:1 hexanes:EtOAc) furnished *rac*-**15e** (2.88 g, 96%) as a glassy yellow solid, mp 51-53 °C. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 70:30 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ +86, 100/0 er (*c* 8.8 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ –87, 100/0 er (*c* 12.2 mg/mL, $CHCl_3$.): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, *J* = 1.8 Hz, 1H), 7.35 (d, *J* = 1.8 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.78 (d, *J* = 15.9 Hz, 1H), 6.70 (d, *J* = 8.7 Hz, 2H), 5.92 (d, *J* = 15.9 Hz, 1H), 5.70 (d, *J* = 13.5 Hz, 1H), 3.77 (d, *J* = 13.5 Hz, 1H), 3.74 (s, 3H), 3.55 (d, *J* = 11.1 Hz, 1H), 3.51 (d, *J* = 11.4 Hz, 1H), 2.39 (s, 3H), 1.45 (s, 9H), 0.36 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 164.3, 158.9, 141.7, 138.9, 137.8, 137.6, 133.2, 131.1 (2C), 128.2, 126.5, 121.3, 113.3 (2C), 79.5, 54.5, 54.2, 27.6 (3C), 20.8, 0.18 (3C), −0.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 2976, 2836, 1706, 1659, 1512, 1437, 1367, 1320, 1250, 1161, 1109, 1036, 1007, 983, 874, 838, 757; HRMS (ESI) calcd for $C_{27}H_{36}INNaO_4Si$ [M + Na]$^+$: 616.1356, found: 616.1395.



(*E*)-*t*-Butyl 3-(3-bromo-2-(2-iodo-*N*-(4-methoxybenzyl)acetamido)-5-methylphenyl) acrylate (15f): Chloride *rac*-**19f** (2.20 g, 4.32 mmol) was reacted according to the general procedure. Column chromatography (3:1 hexanes:EtOAc) furnished *rac*-**15f** (2.35 g, 91%) as a sticky yellow semi-solid. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 70:30 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ +21, 99/1 er (*c* 14.4 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ –19, 100/0 er (*c* 10.9 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 1.2 Hz, 1H), 7.33 (s, 1H), 7.11 (d, *J* = 15.9 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.70 (d, *J* = 8.7 Hz, 2H), 6.01 (d, *J* = 15.9 Hz, 1H), 5.27 (d, *J* = 14.1 Hz, 1H), 4.26 (d, *J* = 13.8 Hz, 1H), 3.74 (s, 3H), 3.58 (d, *J* = 10.8 Hz, 1H), 3.44 (d, *J* = 10.5 Hz, 1H), 2.38 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 164.3, 159.0, 140.4, 137.3, 135.8, 135.3, 135.2, 131.2 (2C), 126.8, 126.6, 124.3, 122.7, 113.4 (2C), 80.2, 54.7, 51.8, 27.7 (3C), 20.7, −2.5; FTIR (thin film, $CHCl_3$, cm^{-1}) 2977, 2932, 2836, 1708, 1665, 1513, 1459, 1368, 1321, 1248, 1154, 1035, 982, 851, 822, 756; HRMS (ESI) calcd for $C_{24}H_{27}{}^{79}BrINNaO_4$ $[M + Na]^+$: 622.0066, found: 622.0031.

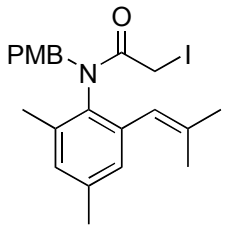


(*E*)-*N*-(2-(4-Bromostyryl)-4,6-dimethylphenyl)-2-iodo-*N*-(4-methoxybenzyl)acetamide (15g): Chloride *rac*-**19g** (0.399 g, 0.800 mmol) was reacted according to the general procedure. Column chromatography (4:1 hexanes:EtOAc) furnished *rac*-**15g** (0.408 g, 86%) as a yellow-orange solid, mp 97-98 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.34 (s, 1H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.05 (s, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 16.2 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 6.51 (d, *J* = 16.2 Hz, 1H), 5.14 (d, *J* = 13.5 Hz, 1H), 4.28 (d, *J* = 13.5 Hz, 1H), 3.64 (s, 3H), 3.50 (d, *J* = 10.2 Hz, 1H), 3.46 (d, *J* = 10.2 Hz, 1H), 2.38 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.1, 159.2, 138.6, 136.0, 135.9, 135.7, 135.0, 132.0, 131.5 (4C = two overlapping 2C), 129.4, 128.2, 128.1 (2C), 124.7, 124.5, 121.6, 113.7 (2C), 55.0, 52.6, 21.2, 18.1, −2.1; FTIR (thin film, $CHCl_3$, cm^{-1}) 3002, 2933, 2835, 1651, 1512, 1487, 1386, 1322, 1302, 1249, 1176, 1107, 1073, 1035, 1008, 909, 849, 810, 732; HRMS (ESI) calcd for $C_{26}H_{25}{}^{79}BrINNaO_2$ $[M + Na]^+$: 612.0011, found: 612.0002.



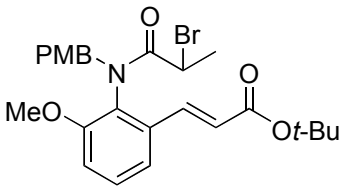
(*E*)-*N*-(2-(2-cyanovinyl)-4,6-dimethylphenyl)-2-iodo-*N*-(4-methoxybenzyl)acetamide (15h): To a solution of chloride *rac*-**19h** (0.619 g, 1.60 mmol) in acetone (65 mL) was added NaI (2.40 g, 16.0 mmol) all at once and the reaction mixture was stirred at room temperature overnight.

After 16 h, 10% aqueous $Na_2S_2O_3$ (65 mL) was added and the mixture was extracted with EtOAc (3 x 160 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (2:1 hexanes:EtOAc) furnished *rac*-**15h** (0.633 g, 86%) as a white solid, mp 144-145 °C. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 80:20 hexanes:EtOAc), first eluting enantiomer $[\alpha]_D^{23}$ –0.4, 99/1 er (*c* 11.2 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ +0.5, 99.5/0.5 er (*c* 43.9 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.21 (s, 1H), 7.04 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 16.8 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 2H), 5.56 (d, *J* = 16.5 Hz, 1H), 5.22 (d, *J* = 13.5 Hz, 1H), 4.16 (d, *J* = 13.8 Hz, 1H), 3.82 (s, 3H), 3.44 (d, *J* = 10.2 Hz, 1H), 3.39 (d, *J* = 10.2 Hz, 1H), 2.37 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 159.6, 145.3, 139.1, 136.7, 136.1, 135.2, 131.8, 131.3 (2C), 127.1, 124.6, 117.5, 113.9 (2C), 97.4, 55.2, 52.2, 21.0, 17.9, −3.2; FTIR (thin film, $CHCl_3$, cm^{-1}) 3004, 2934, 2217, 1655, 1512, 1385, 1304, 1250, 1176, 1107, 1033, 1007, 965, 849, 822, 755; HRMS (ESI) calcd for $C_{21}H_{21}IN_2NaO_2$ $[M + Na]^+$: 483.0545, found: 483.0533.



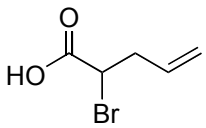
***N*-(2,4-Dimethyl-6-(2-methylprop-1-enyl)phenyl)-2-iodo-*N*-(4-methoxybenzyl)acetamide (15i):** Chloride *rac*-**19i** (0.744 g, 2.00 mmol) was reacted according to the general procedure. Column chromatography (4:1 hexanes:EtOAc) furnished *rac*-**15i** (0.816 g, 88%) as a white solid, mp 73-74 °C. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 80:20 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$–4.4, 99/1 er (*c* 2.8 mg/mL, $CHCl_3$),

second eluting enantiomer $[\alpha]_D^{23}$ +4.2, 100/0 er (*c* 5.2 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.7 Hz, 2H), 6.90 (br s, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 5.69 (s, 1H), 4.70 (d, *J* = 13.5 Hz, 1H), 4.61 (d, *J* = 13.8 Hz, 1H), 3.77 (s, 3H), 3.47 (s, 2H), 2.32 (s, 3H), 1.89 (s, 3H), 1.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 158.9, 137.4, 137.2, 136.3, 135.8, 135.3, 131.1 (2C), 130.1, 129.4, 128.4, 121.6, 113.3 (2C), 54.9, 51.7, 26.3, 20.9, 19.1, 17.8, −1.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 2931, 2857, 2835, 1655, 1612, 1512, 1440, 1385, 1303, 1247, 1176, 1107, 1035, 849, 835, 822, 756; HRMS (ESI) calcd for $C_{22}H_{26}INNaO_2$ $[M + Na]^+$: 486.0906, found: 486.0867.



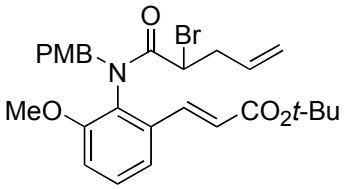
(*E*)-*t*-Butyl 3-(2-(2-bromo-*N*-(4-methoxybenzyl)propanamido)-3-methoxyphenyl) acrylate (**25a** and **25b**): To a stirred solution of **18c** (1.11 g, 3.00 mmol) and Et_3N (0.455 g, 4.50 mmol) in THF (6.0 mL) at 0 °C was added 2-bromopropionyl bromide (0.971 g, 4.50 mmol) dropwise via syringe. The mixture was stirred at 0 °C for 30 min, and saturated aqueous NH_4Cl (15 mL) was added. The mixture was extracted with Et_2O (3 x 30 mL), and the combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (3:1 hexanes:EtOAc) provided two diastereomers. The first eluting diastereomer, *rac*-**25a**, was isolated (0.497 g, 33%) as a clear, pale yellow oil. This racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 75:25 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ +47, 98/2 er (*c* 13.4 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ –48, 99/1 er (*c* 15.1 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, *J* = 8.1 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz,

2H), 6.90 (d, J = 15.9 Hz, 1H), 6.69 (d, J = 8.7 Hz, 1H), 5.43 (d, J = 15.9 Hz, 1H), 4.15 (d, J = 13.8 Hz, 1H), 4.01 (q, J = 6.6 Hz, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 1.69 (d, J = 6.6 Hz, 3H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 165.0, 159.1, 155.7, 137.3, 134.7, 131.3 (2C), 129.7, 128.0, 127.9, 123.2, 118.0, 113.5 (2C), 113.1, 80.5, 55.7, 55.0, 51.3, 39.1, 28.0 (3C), 22.1; FTIR (neat, cm^{-1}) 2975, 2936, 2838, 2249, 1708, 1666, 1612, 1578, 1513, 1477, 1394, 1272, 1248, 1175, 1154, 1072, 1036, 984, 912, 849, 800, 733; HRMS (ESI) calcd for $C_{25}H_{30}BrNNaO_5$ $[M + Na]^+$: 526.1205, found: 526.1214. The second eluting diastereomer, *rac*-**25b**, was isolated (0.983 g, 65%) as a clear, colorless oil. This racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 70:30 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ +66, 100/0 er (*c* 9.9 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ –67, 100/0 er (*c* 6.3 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 15.9 Hz, 1H), 7.31 (t, J = 8.1 Hz, 1H), 7.23 (d, J = 8.1 Hz, 1H), 6.98 (d, J = 8.7 Hz, 2H), 6.85 (d, J = 7.8 Hz, 1H), 6.68 (d, J = 8.4 Hz, 2H), 6.20 (d, J = 15.9 Hz, 1H), 4.82 (d, J = 13.8 Hz, 1H), 4.56 (d, J = 13.8 Hz, 1H), 4.11 (q, J = 6.6 Hz, 1H), 3.74 (s, 3H), 3.53 (s, 3H), 1.74 (d, J = 6.6 Hz, 3H), 1.51 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 165.2, 158.9, 155.3, 138.2, 134.4, 131.0 (2C), 129.5, 128.3, 127.9, 122.6, 119.0, 113.1 (2C), 112.3, 80.3, 55.5, 54.9, 51.7, 39.6, 27.9 (3C), 21.7; FTIR (neat, cm^{-1}) 2976, 2934, 2839, 1708, 1670, 1577, 1513, 1475, 1394, 1368, 1271, 1248, 1152, 1068, 984, 849, 801, 732; HRMS (ESI) calcd for $C_{25}H_{30}BrNNaO_5$ $[M + Na]^+$: 526.1205, found: 526.1206.



***rac*-2-Bromopent-4-enoic acid (S6):** To a stirred solution of NaBr (6.47 g, 62.9 mmol) in aqueous HBr (0.75 M, 60 mL) at −15 °C was added, in one portion, $NaNO_2$ (1.52 g, 22.1 mmol). After stirring at this temperature for 15 min, (±)-2-amino-4-pentenoic acid (1.96 g, 17.0 mmol)

was added in one portion. The reaction mixture was stirred at −15 °C for 1 h, 0 °C for 1 h, and at room temperature for 2 h, and was then extracted with EtOAc (3 x 125 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (50:50:1 hexanes:EtOAc:AcOH) provided the title compound (1.75 g, 58%) as a mobile red liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 16.8 Hz, 10.2 Hz, 6.9 Hz, 1H), 5.23 (d, *J* = 16.5 Hz, 1H), 5.22 (d, *J* = 10.5 Hz, 1H), 4.28 (t, *J* = 7.2 Hz, 1H), 2.89 (dt, *J* = 14.4 Hz, 7.2 Hz, 1H), 2.76 (dd, *J* = 14.4 Hz, 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3, 132.5, 119.5, 43.7, 38.6; FTIR (neat, cm^{-1}) 3083, 3000 (broad), 1720, 1430, 1253, 1201, 1171, 993, 927; HRMS (EI) calcd for $C_5H_7{}^{79}BrO_2$ $[M]^+$: 177.9629, found: 177.9626.



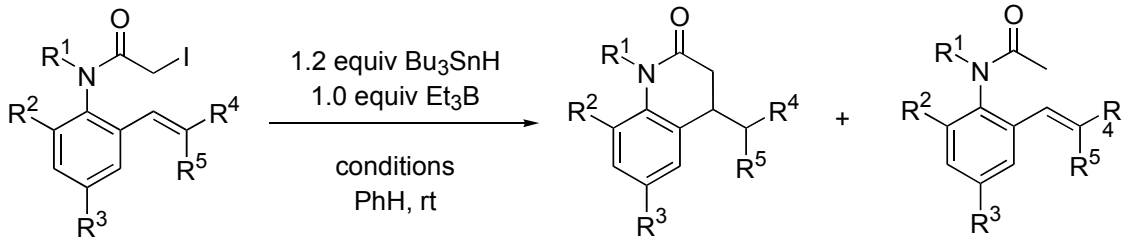
(*E*)-*t*-Butyl 3-(2-(2-bromo-*N*-(4-methoxybenzyl)pent-4-enamido)-3-methoxyphenyl) acrylate (**27a** and **27b**): To a stirred solution of *rac*-**S6** (0.896 g, 5.00 mmol) in CH_2Cl_2 (20 mL) at 0 °C was added oxalyl chloride (0.635 g, 5.00 mmol) via syringe, followed by catalytic DMF (~1 drop). The mixture was warmed to room temperature and stirred for 2 h. This mixture containing the crude acid chloride was transferred dropwise over 10 min via syringe to a stirred solution of **18c** (0.739 g, 2.00 mmol) in CH_2Cl_2 at 0 °C. After 10 min of stirring, Et_3N (0.202 g, 2.00 mmol) was added to this mixture via syringe, and the mixture was stirred at room temperature for 1 h. Saturated aqueous NH_4Cl (35 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 x 35 mL). The combined organic layers were washed with brine (35 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (4:1 hexanes:EtOAc) provided two diastereomers. The first eluting

diastereomer, *rac*-**27a**, was isolated (0.370 g, 35%) as a clear, colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, *J* = 8.1 Hz, 1H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.95 (d, *J* = 15.9 Hz, 1H), 6.70 (d, *J* = 8.4 Hz, 2H), 6.06 (d, *J* = 15.9 Hz, 1H), 5.60 (ddt, *J* = 14.1 Hz, 9.9 Hz, 7.2 Hz, 1H), 5.40 (d, *J* = 13.8 Hz, 1H), 5.10-5.01 (m, 2H), 4.20 (d, *J* = 14.1 Hz, 1H), 3.83 (s, 3H), 3.79 (t, *J* = 7.2 Hz, 1H), 3.73 (s, 3H), 2.86 (dt, 14.1 Hz, 7.2 Hz, 1H), 2.62 (dt, *J* = 14.1 Hz, 7.2 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.7, 164.9, 159.0, 155.7, 137.7, 134.6, 133.6, 131.1 (2C), 129.7, 127.9, 127.8, 123.0, 118.8, 117.9, 113.4 (2C), 113.0, 80.3, 55.6, 54.9, 51.3, 43.1, 39.7, 27.9 (3C); FTIR (neat, cm^{-1}) 2977, 2936, 2837, 1708, 1666, 1612, 1578, 1513, 1476, 1439, 1393, 1271, 1248, 1152, 1071, 1035, 983, 929, 849, 798; HRMS (ESI) calcd for $C_{27}H_{32}{}^{79}BrNNaO_5$ $[M + Na]^+$: 552.1362, found: 552.1337. The second eluting diastereomer, *rac*-**27b**, was isolated (0.413 g, 39%) as a clear, colorless oil. The racemate was submitted to preparative chiral HPLC separation ((*S*,*S*)-Whelk-O1, 80:20 hexanes:*i*-PrOH), first eluting enantiomer $[\alpha]_D^{23}$ +84, 100/0 er (*c* 3.4 mg/mL, $CHCl_3$), second eluting enantiomer $[\alpha]_D^{23}$ –83, 100/0 er (*c* 4.1 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 15.9 Hz, 1H), 7.31 (t, *J* = 8.1 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 2H), 6.18 (d, *J* = 16.2 Hz, 1H), 5.67 (dddd, *J* = 16.8 Hz, 10.2 Hz, 7.5 Hz, 6.6 Hz, 1H), 5.06 (d, *J* = 17.1 Hz, 1H), 5.05 (d, *J* = 9.9 Hz, 1H), 4.77 (d, *J* = 13.8 Hz, 1H), 4.64 (d, *J* = 13.8 Hz, 1H), 3.89 (t, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 3.54 (s, 3H), 2.89 (dt, *J* = 14.4 Hz, 6.9 Hz, 1H), 2.68 (dt, *J* = 14.4 Hz, 7.5 Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 165.2, 158.9, 155.1, 138.3, 134.5, 134.1, 131.1 (2C), 129.6, 128.1, 127.9, 122.5, 118.8, 117.7, 113.1 (2C), 112.1, 80.3, 55.2, 54.9, 51.7, 43.6, 39.4, 28.0 (3C); FTIR (neat, cm^{-1}) 2977, 2934, 2837, 1707, 1670, 1577, 1513, 1475, 1438, 1394, 1270, 1247,

1152, 1070, 1035, 984, 921, 848, 800, 732; HRMS (ESI) calcd for $C_{27}H_{32}{}^{79}BrNNaO_5$ $[M + Na]^+$: 552.1362, found: 552.1349.

Radical Cyclizations of Substrates

Table S.1 Cyclizations of Racemic α-Iodoamides 15a-i

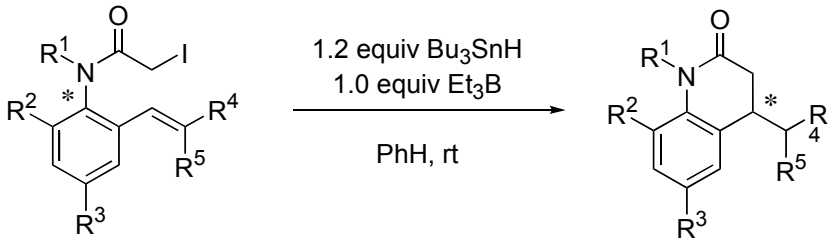


rac-**15a-i** *rac*-**14a-i** *rac*-**20a-i**

entry	α-I	R^1	R^2	R^3	R^4	R^5	cond.[a]	cyc. product	% yield[b]
1	**15a**	Me	Me	Me	CO_2t-Bu	H	B	**14a**	55[d]
2	**15a**	Me	Me	Me	CO_2t-Bu	H	A	**14a**	83
3	**15b**	PMB	Me	Me	CO_2t-Bu	H	B	**14b**	72[d]
4	**15b**	PMB	Me	Me	CO_2t-Bu	H	A	**14b**	85
5	**15c**	PMB	OMe	H	CO_2t-Bu	H	A	**14c**	97
6	**15d**	Ts	Me	Me	CO_2t-Bu	H	A	**14d**	nd[c,d]
7	**15e**	PMB	TMS	Me	CO_2t-Bu	H	A	**14e**	93
8	**15f**	PMB	Br	Me	CO_2t-Bu	H	A	**14f**	61
9	**15g**	PMB	Me	Me	4-BrC_6H_4	H	B	**14g**	nd[c]
10	**15g**	PMB	Me	Me	4-BrC_6H_4	H	A	**14g**	nd[c]
11	**15h**	PMB	Me	Me	CN	H	A	**14h**	< 71
12	**15h**	PMB	Me	Me	CN	H	C	**14h**	70
13	**15i**	PMB	Me	Me	Me	Me	A	**14i**	51[d]

[a] Conditions A: Bu_3SnH and Et_3B in 20 mL PhH were added over 2 h via syringe pump to a stirred 10 mM PhH solution of iodide. B: neat Bu_3SnH and Et_3B were added sequentially in one portion to a stirred PhH solution of iodide with $[Bu_3SnH]_i$ = 10 mM. C: Same as B with $[Bu_3SnH]_i$ = 5 mM. [b] Yield of racemic **14a-i** after isolation by column chromatography on 10% w/w KF/silica gel. [c] nd = not determined. [d] Directly reduced **20a-i** was detected in crude reaction mixture by TLC or ^{1}H NMR.

Table S.2 Chirality Transfer in Cyclizations of α-Iodoamides 15a-i



15a-i **14a-i**

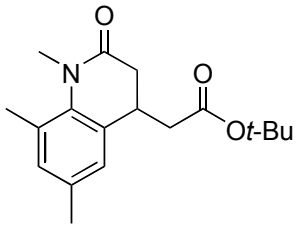
entry	precursor	R^1	R^2	R^3	R^4	R^5	er	cond.[a]	product	% yield[b]	er	% ct[d]
1	(+)-**15a**	Me	Me	Me	CO_2t-Bu	H	98.5/1.5	A	(–)-**14a**	79	91/9	92
2	(–)-**15a**	Me	Me	Me	CO_2t-Bu	H	85/15	A	(+)-**14a**	81	84/16	99
3	(+)-**15b**	PMB	Me	Me	CO_2t-Bu	H	100/0	A	(–)-**14b**	87	95/5	95
4	(–)-**15b**	PMB	Me	Me	CO_2t-Bu	H	100/0	A	(+)-**14b**	85	96/4	96
5	(+)-**15c**	PMB	OMe	H	CO_2t-Bu	H	99/1	A	(–)-**14c**	94	93/7	94
6	(–)-**15c**	PMB	OMe	H	CO_2t-Bu	H	99/1	A	(+)-**14c**	96	93/7	94
7	(+)-**15e**	PMB	TMS	Me	CO_2t-Bu	H	100/0	A	(+)-**14e**	95	95/5	95
8	(–)-**15e**	PMB	TMS	Me	CO_2t-Bu	H	100/0	A	(–)-**14e**	93	94/6	96
9	(*P*)-**15f**[c]	PMB	Br	Me	CO_2t-Bu	H	99/1	A	(*S*)-**14f**[c]	63	95/5	96
10	(*M*)-**15f**[c]	PMB	Br	Me	CO_2t-Bu	H	0/100	A	(*R*)-**14f**[c]	66	94/6	94
11	(+)-**15h**	PMB	Me	Me	CN	H	99.5/0.5	C	(–)-**14h**	71	93/7	93
12	(–)-**15h**	PMB	Me	Me	CN	H	99/1	C	(+)-**14h**	68	96/4	97
13	(+)-**15i**	PMB	Me	Me	Me	Me	99/1	A	(+)-**14i**	57	80/20	81
14	(–)-**15i**	PMB	Me	Me	Me	Me	0/100	A	(–)-**14i**	55	80/20	80

[a] Conditions A: Bu_3SnH and Et_3B in 20 mL PhH were added over 2 h via syringe pump to a stirred 10 mM PhH solution of iodide. C: neat Bu_3SnH and Et_3B were added sequentially in one portion to a stirred PhH solution of iodide with $[Bu_3SnH]_i$ = 5 mM. [b] Yield of **14a-i** after isolation by column chromatography on 10% w/w KF/silica gel. [c] Absolute stereochemistry determined by X-ray crystallography. [d] Percent chirality transfer.

General procedure "A" for radical cyclizations: Bu_3SnH (0.122 g, 0.42 mmol) and Et_3B (0.35 mL of a 1.0 M hexane solution, 0.35 mmol) were dissolved in degassed benzene (20 mL). This solution was added via syringe pump over a period of 2 h to a stirred solution of the appropriate α-halo amide (0.35 mmol) in benzene (35 mL). Upon completion of the reaction, solvent was removed by rotary evaporation, and the crude residue was directly subjected to flash chromatography on 10% w/w KF/silica gel[6] using the appropriate eluent.

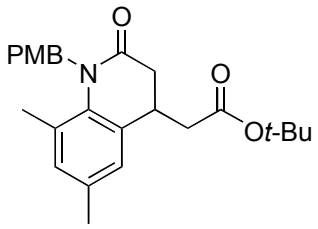
General procedure "B" for radical cyclizations: Bu_3SnH (0.122 g, 0.42 mmol) and the appropriate a-halo amide (0.35 mmol) were dissolved in a stirred solution of non-degassed benzene (35 mL, 10 mM in Bu_3SnH). Et_3B (0.35 mL of a 1.0 M hexane solution, 0.35 mmol) was added all at once via syringe. Upon completion of the reaction, solvent was removed by rotary evaporation, and the crude residue was directly subjected to flash chromatography on 10% w/w KF/silica gel using the appropriate eluent.

General procedure "C" for radical cyclizations: Bu_3SnH (0.122 g, 0.42 mmol) and the appropriate a-halo amide (0.35 mmol) were dissolved in a stirred solution of non-degassed benzene (70 mL, 5 mM in Bu_3SnH). Et_3B (0.35 mL of a 1.0 M hexane solution, 0.35 mmol) was added all at once via syringe. Upon completion of the reaction, solvent was removed by rotary evaporation, and the crude residue was directly subjected to flash chromatography on 10% w/w KF/silica gel using the appropriate eluent.



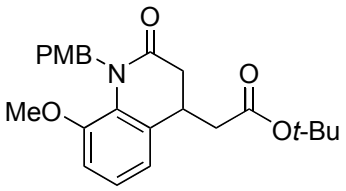
***t*-Butyl 2-(1,6,8-trimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)acetate (14a):** According to general procedure A, **14a** was prepared from the reaction of **15a** and chromatographed eluting with 3:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (75:25 hexanes:*i*-PrOH). *rac*-**15a** yielded *rac*-**14a** as a clear, colorless oil (0.088 g, 83%). The atropisomer (–)-**15a** yielded (+)-**14a** as a clear, colorless oil (0.086 g, 81%), $[\alpha]_D^{23}$ +6.3 (*c* 9.6 mg/mL, $CHCl_3$), 84/16 er, first eluting enantiomer. The atropisomer (+)-**15a** yielded

(–)-**14a** as a clear, colorless oil (0.084 g, 79%), $[\alpha]_D^{23}$ –6.0 (*c* 8.5 mg/mL, $CHCl_3$), 91/9 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (s, 1H), 6.88 (s, 1H), 3.34 (s, 3H), 3.29 (tt, *J* = 7.5 Hz, 4.8 Hz, 1H), 2.67 (dd, *J* = 15.3 Hz, 4.8 Hz, 1H), 2.54 (dd, *J* = 15.3 Hz, 4.5 Hz, 1H), 2.44 (dd, *J* = 15.3 Hz, 7.5 Hz, 1H), 2.38 (dd, *J* = 15.6 Hz, 7.2 Hz, 1H), 2.33 (s, 3H), 2.27 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 170.7, 138.3, 133.6, 132.3, 131.8, 127.6, 125.3, 80.9, 38.9, 37.8, 35.7, 33.4, 28.0 (3C), 20.6, 20.4; FTIR (neat, cm^{-1}) 2976. 2929, 1728, 1674, 1482, 1426, 1366, 1309, 1256, 1148, 1082, 1039, 961, 859, 844, 733; HRMS (ESI) calcd for $C_{18}H_{25}NNaO_3$ $[M + Na]^+$: 326.1732, found: 326.1756.



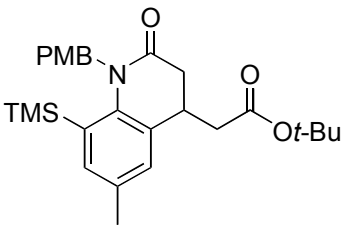
***t*-Butyl 2-(1-(4-methoxybenzyl)-6,8-dimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl) acetate (14b):** According to general procedure A, **14b** was prepared from the reaction of **15b** and chromatographed eluting with 3:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (80:20 hexanes:*i*-PrOH). *rac*-**15b** yielded *rac*-**14b** as a clear, pale yellow oil (0.126 g, 88%). The atropisomer (+)-**15b** yielded (+)-**14b** as a clear, pale yellow oil (0.122 g, 85%), $[\alpha]_D^{23}$ +64 (*c* 9.5 mg/mL, $CHCl_3$), 96/4 er, first eluting enantiomer. The atropisomer (–)-**15b** yielded (–)-**14b** as a clear, pale yellow oil (0.126 g, 87%), $[\alpha]_D^{23}$ –64 (*c* 16.7 mg/mL, $CHCl_3$), 95/5 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.4 Hz, 2H), 6.90 (s, 1H), 6.82 (s, 1H), 6.75 (d, *J* = 8.7 Hz, 2H), 5.15 (d, *J* = 14.7 Hz, 1H), 4.87 (d, *J* = 14.7 Hz, 1H), 3.75 (s, 3H), 3.17 (tt, *J* = 7.5 Hz, 5.1 Hz, 1H), 2.63 (dd, *J* = 15.0 Hz, 5.1 Hz, 1H), 2.46 (dd, *J* = 15.0 Hz, 5.1 Hz, 1H), 2.34 (s, 3H), 2.26 (s, 3H), 2.08 (dd, *J* = 15.6 Hz, 7.8

Hz, 1H), 2.01 (dd, J = 15.6 Hz, 7.5 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 170.8, 158.6, 137.1, 133.7, 133.5, 131.8, 129.5, 129.4 (2C), 127.9, 125.5, 113.5 (2C), 80.5, 55.0, 48.6, 38.2, 33.5, 27.9 (3C), 21.0, 20.5, missing peak due to accidental isochrony; FTIR (neat, cm^{-1}) 2976, 2932, 2836, 1727, 1674, 1611, 1513, 1479, 1368, 1248, 1147, 1035, 911, 845, 733; HRMS (ESI) calcd for $C_{25}H_{31}NNaO_4$ $[M + Na]^+$: 432.2151, found: 432.2142.

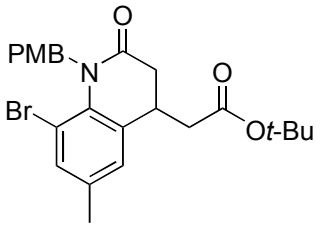


***tert*-Butyl 2-(8-methoxy-1-(4-methoxybenzyl)-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)acetate (14c):** According to general procedure A, **14c** was prepared from the reaction of **15c** and chromatographed eluting with 2:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (50:50 hexanes:*i*-PrOH). *rac*-**15c** yielded *rac*-**14c** as a clear, colorless oil (0.140 g, 97%). The atropisomer (–)-**15c** yielded (+)-**14c** as a clear, colorless oil (0.138 g, 96%), $[\alpha]_D^{23}$ +86 (*c* 4.1 mg/mL, $CHCl_3$), 93/7 er, first eluting enantiomer. The atropisomer (+)-**15c** yielded (–)-**14c** as a clear, colorless oil (0.136 g, 94%), $[\alpha]_D^{23}$ –87 (*c* 7.3 mg/mL, $CHCl_3$), 93/7 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, J = 8.7 Hz, 2H), 7.01 (t, J = 7.8 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 6.74 (d, J = 8.7 Hz, 2H), 5.38 (d, J = 14.4 Hz, 1H), 5.22 (d, J = 14.7 Hz, 1H), 3.81 (s, 3H), 3.74 (s, 3H), 3.27 (m, 1H), 2.70 (dd, J = 15.0 Hz, 5.1 Hz, 1H), 2.54 (dd, J = 15.0 Hz, 4.8 Hz, 1H), 2.22 (dd, J = 15.9 Hz, 7.8 Hz, 1H), 2.17 (dd, J = 16.2 Hz, 7.8 Hz, 1H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.7, 158.4, 149.9, 133.9, 130.4, 129.3 (2C), 128.1, 124.7, 119.6, 113.3 (2C), 111.5, 80.7, 55.5, 55.0, 46.7, 38.2, 37.7, 33.4, 28.0 (3C); FTIR (neat, cm^{-1}) 2976, 2936, 2837,

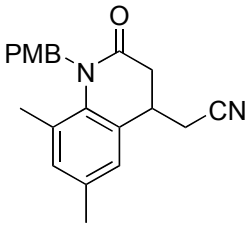
2248, 1727, 1674, 1612, 1589, 1513, 1484, 1462, 1368, 1248, 1148, 1102, 1033, 912, 845, 784, 733; HRMS (ESI) calcd for $C_{24}H_{29}NNaO_5$ $[M + Na]^+$: 434.1943, found: 434.1945.



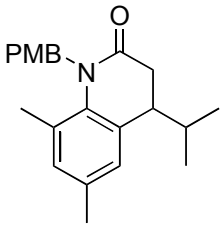
***tert*-Butyl 2-(1-(4-methoxybenzyl)-6-methyl-2-oxo-8-(trimethylsilyl)-1,2,3,4-tetrahydroquinolin-4-yl) acetate (14e):** According to general procedure A, **14e** was prepared from the reaction of **15e** and chromatographed eluting with 3:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (80:20 hexanes:*i*-PrOH). *rac*-**15e** yielded *rac*-**14e** as a clear, colorless oil (0.152 g, 93%). The atropisomer (+)-**15e** yielded (+)-**14e** as a clear, colorless oil (0.155 g, 95%), $[\alpha]_D^{23}$ +122 (*c* 4.8 mg/mL, $CHCl_3$), 95/5 er, first eluting enantiomer. The atropisomer (–)-**15e** yielded (–)-**14e** as a clear, colorless oil (0.152 g, 93%), $[\alpha]_D^{23}$ –120 (*c* 15.2 mg/mL, $CHCl_3$), 94/6 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, *J* = 1.8 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 1.8 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 2H), 5.34 (d, *J* = 13.5 Hz, 1H), 4.69 (d, *J* = 13.5 Hz, 1H), 3.73 (s, 3H), 3.08 (m, 1H), 2.59 (dd, *J* = 15.0 Hz, 5.1 Hz, 1H), 2.41 (dd, *J* = 15.0 Hz, 4.2 Hz, 1H), 2.31 (s, 3H), 1.73 (m, 2H), 0.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.9, 158.9, 143.5, 136.0, 133.1, 132.6, 130.3, 130.2 (2C), 129.1, 129.0, 113.5 (2C), 80.3, 55.0, 51.7, 37.9, 37.8, 33.4, 27.9 (3C), 20.7, 0.6 (3C); FTIR (thin film, $CHCl_3$, cm^{-1}) 2975, 2836, 1727, 1675, 1611, 1513, 1452, 1368, 1249, 1151, 1112, 1037, 922, 864, 838, 757; HRMS (ESI) calcd for $C_{27}H_{37}NNaO_4Si$ $[M + Na]^+$: 490.2390, found: 490.2409.



***tert*-Butyl 2-(8-bromo-1-(4-methoxybenzyl)-6-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl) acetate (14f):** According to general procedure A, **14f** was prepared from the reaction of **15f** and chromatographed eluting with 3:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (70:30 hexanes:*i*-PrOH). *rac*-**15f** yielded *rac*-**14f** as a clear, colorless oil (0.102 g, 61%). The atropisomer (+)-**15f** yielded (+)-**14f** as a white solid (0.104 g, 63%), $[\alpha]_D^{23}$ +100 (*c* 7.0 mg/mL, $CHCl_3$), 95/5 er, first eluting enantiomer. The atropisomer (–)-**15f** yielded (–)-**14f** as a clear, colorless oil (0.109 g, 66%), $[\alpha]_D^{23}$ –100 (*c* 10.3 mg/mL, $CHCl_3$), 96/4 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (s, 1H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.93 (s, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 5.42 (d, *J* = 14.7 Hz, 1H), 5.34 (d, *J* = 15.3 Hz, 1H), 3.74 (s, 3H), 3.15 (m, 1H), 2.62 (dd, *J* = 15.0 Hz, 4.8 Hz, 1H), 2.47 (dd, *J* = 15.0 Hz, 5.1 Hz, 1H), 2.27 (s, 3H), 1.97 (d, *J* = 7.5 Hz, 2H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 170.5, 158.8, 136.3, 135.5, 133.9, 130.2 (2C), 129.3, 127.3, 113.5, 113.4 (2C), 80.7, 55.0, 47.5, 38.0, 37.7, 33.6, 27.9 (3C), 20.3, missing peak due to accidental isochrony; FTIR (neat, cm^{-1}) 2977, 2932, 2836, 1725, 1685, 1611, 1513, 1467, 1366, 1302, 1248, 1153, 1035, 917, 827, 761, 734; HRMS (ESI) calcd for $C_{24}H_{28}{}^{79}BrNNaO_4$ $[M + Na]^+$: 496.1099, found: 496.1104.

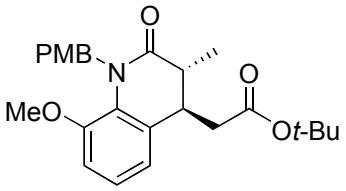


2-(1-(4-Methoxybenzyl)-6,8-dimethyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)acetonitrile (14h): According to general procedure C, **14f** was prepared from the reaction of **15f** and chromatographed eluting with 3:2 hexanes:EtOAc. The fractions containing the desired product were collected and concentrated, and a second flash column (silica gel only) was performed, eluting with 3:2 hexanes:EtOAc to remove residual impurities. The products were ~95% pure by ^{1}H NMR, containing trace unidentifiable impurities. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (80:20 hexanes:EtOAc). *rac*-**15h** yielded *rac*-**14h** as a white solid (0.082 g, 70%), mp 101-102 °C. The atropisomer (–)-**15h** yielded (+)-**14h** as a white solid (0.080 g, 68%), $[\alpha]_D^{23}$ +99 (*c* 19.8 mg/mL, $CHCl_3$), 96/4 er, first eluting enantiomer. The atropisomer (+)-**15h** yielded (–)-**14h** as a white solid (0.083 g, 71%), $[\alpha]_D^{23}$ –97 (*c* 4.5 mg/mL, $CHCl_3$), 93/7 er, second eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.87 (s, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 5.25 (d, *J* = 14.4 Hz, 1H), 4.73 (d, *J* = 14.4 Hz, 1H), 3.75 (s, 3H), 2.97 (m, 1H), 2.71 (dd, *J* = 15.3 Hz, 4.8 Hz, 1H), 2.50 (dd, *J* = 15.3 Hz, 4.2 Hz, 1H), 2.41 (s, 3H), 2.33 (s, 3H), 2.03 (dd, *J* = 16.8 Hz, 6.6 Hz, 1H), 1.75 (dd, *J* = 16.8 Hz, 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 159.0, 136.8, 134.5, 132.8, 130.7, 129.8 (2C), 129.1, 128.5, 125.9, 117.5, 113.7 (2C), 55.1, 48.6, 37.7, 34.0, 20.8, 20.6, 20.3; FTIR (thin film, $CHCl_3$, cm^{-1}) 3012, 2959, 2837, 1673, 1513, 1479, 1376, 1249, 1176, 1033, 859, 757; HRMS (ESI) calcd for $C_{21}H_{22}N_2NaO_2$ $[M + Na]^+$: 357.1579, found: 357.1612.

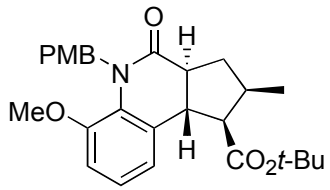


4-Isopropyl-1-(4-methoxybenzyl)-6,8-dimethyl-3,4-dihydroquinolin-2(1*H*)-one (14i):

According to general procedure A, **14i** was prepared from the reaction of **15i** and chromatographed eluting with 3:1 pentane:Et_2O. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (80:20 hexanes:*i*-PrOH). *rac*-**15i** yielded *rac*-**14i** as a clear, colorless oil (0.060 g, 51%). The atropisomer (–)-**15i** yielded (–)-**14i** as a clear, colorless oil (0.065 g, 55%), $[\alpha]_D^{23}$ –44 (*c* 6.3 mg/mL, $CHCl_3$), 80/20 er, second eluting enantiomer. The atropisomer (+)-**15i** yielded (+)-**14i** as a clear, colorless oil (0.067 g, 57%), $[\alpha]_D^{23}$ +44 (*c* 8.6 mg/mL, $CHCl_3$), 80/20 er, first eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, *J* = 8.7 Hz, 2H), 6.90 (s, 1H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.71 (s, 1H), 5.22 (d, *J* = 14.7 Hz, 1H), 4.74 (d, *J* = 14.7 Hz, 1H), 3.75 (s, 3H), 2.65 (dd, *J* = 15.0 Hz, 3.6 Hz, 1H), 2.54 (dd, *J* = 14.7 Hz, 4.8 Hz, 1H), 2.33 (s, 3H), 2.28 (s, 3H), 2.19 (dt, *J* = 9.3 Hz, 4.2 Hz, 1H), 1.06 (d of septets, *J* = 9.3 Hz, 6.6 Hz, 2.7 Hz, 1H), 0.84 (d, *J* = 6.6 Hz, 3H), 0.66 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 158.6, 137.3, 134.8, 133.2, 131.3, 129.7, 129.5 (2C), 128.1, 127.3, 113.3 (2C), 55.2, 48.6, 44.8, 36.3, 28.2, 21.5, 21.1, 20.6, 19.8; FTIR (neat, cm^{-1}) 2957, 2868, 2835, 1673, 1611, 1513, 1477, 1365, 1295, 1247, 1177, 1162, 1112, 1035, 860, 812; HRMS (ESI) calcd for $C_{22}H_{27}NNaO_2$ [M + Na]$^+$: 360.1939, found: 360.1911.



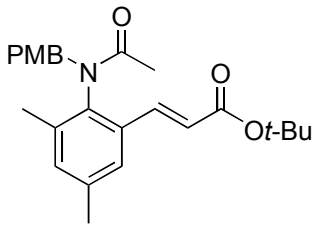
***trans-tert*-Butyl 2-(8-methoxy-1-(4-methoxybenzyl)-3-methyl-2-oxo-1,2,3,4-tetrahydroquinolin-4-yl)acetate (26):** According to general procedure A, **26** was prepared from the reaction of **25b** and chromatographed eluting with 2:1 hexanes:EtOAc. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (70:30 hexanes:*i*-PrOH). *rac*-**25b** yielded *rac*-**26** as a clear, colorless oil (0.145 g, 97%). The atropisomer (+)-**25b** yielded (–)-**26** as a clear, colorless oil (0.146 g, 98%), $[\alpha]_D^{23}$ –109 (*c* 13.2 mg/mL, $CHCl_3$), 99/1 er, second eluting enantiomer. The atropisomer (–)-**25b** yielded (+)-**26** as a clear, colorless oil (0.145 g, 97%), $[\alpha]_D^{23}$ +111 (*c* 20.4 mg/mL, $CHCl_3$), 99.5/0.5 er, first eluting enantiomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.7 Hz, 2H), 7.01 (t, *J* = 8.4 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.75 (d, *J* = 8.7 Hz, 2H), 5.41 (d, *J* = 14.4 Hz, 1H), 5.17 (d, *J* = 14.7 Hz, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 2.97 (m with clear d, *J* = 2.7 Hz, 1H), 2.68 (qd, *J* = 7.2 Hz, 2.7 Hz, 1H), 2.21 (dd, *J* = 15.6 Hz, 6.9 Hz, 1H), 2.10 (dd, *J* = 15.6 Hz, 8.1 Hz, 1H), 1.38 (s, 9H), 1.05 (d, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 170.7, 158.3, 149.5, 131.2, 130.6, 129.2 (2C), 127.1, 124.7, 121.5, 113.2 (2C), 111.7, 80.5, 55.4, 54.9, 46.7, 41.8, 40.4, 39.0, 27.9 (3C), 14.9; FTIR (thin film, $CHCl_3$, cm^{-1}) 2974, 2934, 2837, 1727, 1669, 1612, 1590, 1512, 1483, 1461, 1365, 1248, 1175, 1150, 1107, 1085, 1036, 976, 935, 846, 790, 740; HRMS (ESI) calcd for $C_{25}H_{31}NNaO_5$ [M + Na]$^+$: 448.2100, found: 448.2128.



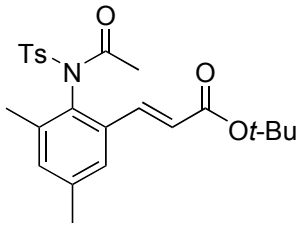
(±)-(1*S*,2*S*,3a*R*,9b*S*)-*t*-Butyl 6-methoxy-5-(4-methoxybenzyl)-2-methyl-4-oxo-2,3,3a,4,5,9b-hexahydro-1*H*-cyclopenta[*c*]quinoline-1-carboxylate (28): According to general procedure A,

28 was prepared from the reaction of **27a-b** (0.143 g, 0.270 mmol) and chromatographed eluting with 3:1 hexanes:EtOAc on 10% w/w KF/silica. A second flash column was run with 3:2 pentane:Et_2O on silica only to remove residual impurities. Chiral analysis was performed on the analytical (*S*,*S*)-Whelk-O1 column (60:40 hexanes:*i*-PrOH). *rac*-**27a** yielded *rac*-**28** as a clear, colorless solid (0.062 g, 51%, > 95% diastereomeric purity). The atropisomer (+)-**27b** yielded (–)-**28** as a clear, colorless oil (0.062 g, 51%, ~95% diastereomeric purity), $[\alpha]_D^{23}$ –113 (*c* 12.3 mg/mL, $CHCl_3$), 99/1 er, first eluting enantiomer. The atropisomer (–)-**27b** yielded (+)-**28** as a clear, colorless solid, (0.060 g, 49%, ~95% diastereomeric purity), $[\alpha]_D^{23}$ +110 (*c* 10.4 mg/mL, $CHCl_3$), 98/2 er, second eluting enantiomer: ^{1}H NMR (75 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.7 Hz, 2H), 7.00 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.8 Hz, 1H), 6.73 (d, *J* = 8.7 Hz, 2H), 6.53 (d, *J* = 7.5 Hz,1H), 5.51 (d, *J* = 15.0 Hz, 1H), 5.01 (d, *J* = 15.0 Hz, 1H), 3.77 (s, 3H), 3.73 (s, 3H), 3.30 (dd, *J* = 14.1 Hz, 10.8 Hz, 1H), 2.89 (t, *J* = 10.8 Hz, 1H), 2.69 (d of sextets, *J* = 10.5 Hz, 7.2 Hz, 1H), 2.40 (ddd, *J* = 14.4 Hz, 11.1 Hz, 7.2 Hz, 1H), 2.30 (dt, *J* = 12.6 Hz, 7.2 Hz, 1H), 1.68 (m, 1H), 1.51 (s, 9H), 1.10 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 172.4, 158.2, 149.9, 135.3, 130.9, 129.1, 128.4 (2C), 125.0, 116.2, 113.4 (2C), 111.1, 80.9, 55.4, 55.0, 50.7, 46.9, 46.8, 44.2, 35.1, 33.7, 28.1 (3C), 18.2; FTIR (thin film, $CHCl_3$, cm^{-1}) 2971, 2837, 1724, 1678, 1513, 1459, 1368, 1280, 1247, 1148, 1067, 1036, 800, 763; HRMS (ESI) calcd for $C_{27}H_{33}NNaO_5$ $[M + Na]^+$: 474.2256, found: 474.2293.

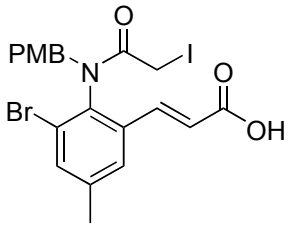
Synthesis of Other Compounds



(*E*)-*tert*-Butyl 3-(2-(*N*-(4-methoxybenzyl)acetamido)-3,5-dimethylphenyl)acrylate (20b): To a stirred solution of **18b** (0.147 g, 0.400 mmol) and Et_3N (0.080 g, 0.800 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C was added acetyl chloride (0.047 g, 0.600 mmol) dropwise via syringe. The mixture was stirred at this temperature for 15 min, and saturated aqueous NH_4Cl solution (5 mL) was added. The mixture was extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (2:1 hexanes:EtOAc) provided the title compound (0.150 g, 92%) as a clear, colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (s, 1H), 7.17 (d, J = 15.9 Hz, 1H), 7.07 (s, 1H), 7.05 (d, J = 8.7 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 6.13 (d, J = 15.9 Hz, 1H), 4.83 (d, J = 13.8 Hz, 1H), 4.55 (d, J = 13.5 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H), 1.91 (s, 3H), 1.72 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 165.4, 159.0, 138.4, 138.0, 137.5, 136.6, 133.6, 133.0, 131.3 (2C), 128.4, 125.5, 122.0, 113.5 (2C), 80.3, 55.0, 51.2, 28.0 (3C), 22.0, 21.0, 17.5; FTIR (neat, cm^{-1}) 2977, 2931, 2836, 1708, 1659, 1612, 1512, 1471, 1391, 1326, 1247, 1151, 1035, 984, 851, 731; HRMS (ESI) calcd for $C_{25}H_{31}NNaO_4$ $[M + Na]^+$: 432.2151, found: 432.2149.



***rac*-(*E*)-*tert*-Butyl 3-(3,5-dimethyl-2-(*N*-tosylacetamido)phenyl)acrylate (20d):** To a stirred solution of **18d** (0.402 g, 1.00 mmol) and Et_3N (0.202 g, 2.00 mmol) in CH_2Cl_2 (5.0 mL) at 0 °C was added AcCl (0.118 g, 1.50 mmol) dropwise via syringe. The reaction mixture was stirred at this temperature for 30 min, and saturated aqueous NH_4Cl solution (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 x 10 mL), and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated by rotary evaporation. Column chromatography (3:1 hexanes:EtOAc) furnished the title compound (0.400 g, 90%) as a flaky white solid, mp 144-145 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 16.2 Hz, 1H), 7.23 (s, 1H), 6.37 (d, J = 15.6 Hz, 1H), 2.45 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H), 1.78 (s, 3H), 1.47 (9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 164.8, 144.8, 139.8, 139.1, 137.8, 135.0, 133.7 (2C, accidental isochrony), 132.6, 129.9 (2C), 129.0 (2C), 125.5, 123.1, 80.2, 27.7 (3C), 23.9, 21.4, 20.9, 18.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 2978, 2929, 1709, 1635, 1366, 1332, 1258, 1169, 1086, 1011, 983, 881, 853, 814, 756; HRMS (ESI) calcd for $C_{24}H_{29}NNaO_5S$ $[M + Na]^+$: 466.1664, found: 466.1634.



(*P*)-(*E*)-3-(3-Bromo-2-(2-iodo-*N*-(4-methoxybenzyl)acetamido)-5-methylphenyl)acrylic acid (24): To a stirred solution of (+)-**15f** (0.284 g, 0.473 mmol, 99/1 er) in CH_2Cl_2 (2.0 mL) at room temperature was added trifluoroacetic acid (2.0 mL) via syringe all at once. The reaction mixture was stirred for 1 h, at which point solvent was removed by rotary evaporation. The crude residue was directly subjected to column chromatography (40:60:1 hexanes:EtOAc:AcOH) to furnish the title compound (0.183 g, 71%) as a pale yellow solid, mp 109-110 °C, $[\alpha]_D^{23}$ +21, 99/1 er (*c* 14.9 mg/mL, $CHCl_3$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.36 (s, 1H), 7.26 (d, *J* = 15.9 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.07 (d, *J* = 15.9 Hz, 1H), 5.38 (d, *J* = 14.1 Hz, 1H), 4.21 (d, *J* = 14.1 Hz, 1H), 3.75 (s, 3H), 3.60 (d, *J* = 10.5 Hz, 1H), 3.43 (d, *J* = 10.8 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 167.7, 159.4, 140.8 (2C, accidental isochrony), 136.1, 136.0, 135.0, 131.5 (2C), 127.2, 126.8, 124.7, 120.1, 113.8 (2C), 55.1, 52.1, 20.9, −2.6; FTIR (thin film, $CHCl_3$, cm^{-1}) 2999 (broad), 2836, 1693, 1662, 1512, 1461, 1383, 1320, 1283, 1250, 1176, 1106, 1034, 982, 910, 851, 822, 732; HRMS (ESI) calcd for $C_{20}H_{19}{}^{79}BrINNaO_4$ $[M + Na]^+$: 565.9440, found: 565.9465.

Analysis of *N*-Aryl Bond Rotation Barriers

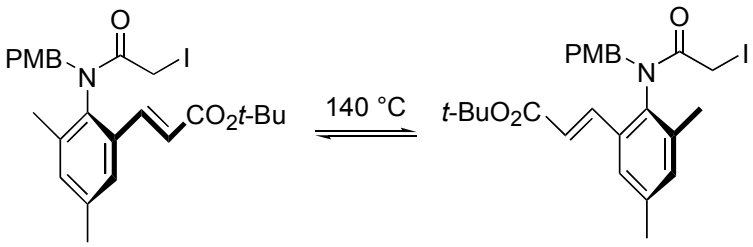
The appropriate compound (enantiomerically enriched in the second eluting enantiomer) was dissolved in a 9:1 hexanes:iPrOH solvent mixture to make a ~2 mg/mL solution in a sealable tube. The tube was sealed and placed in a pre-equilibrated oil bath with electronic temperature controller. At various time intervals, the sealed tube was removed briefly (1-2 minutes) from the bath, cracked, and a 10 μL aliquot was removed via syringe and injected onto the appropriate analytical HPLC column to measure the enantiomeric ratio. This ratio was plotted against time, and the barrier to rotation was calculated from the plot.[7] In the y-axis of the plot, "F" denotes the fraction of the first eluting enantiomer, and "S" denotes the fraction of the second eluting enantiomer. The half-life for racemization at ambient temperature is determined by first calculating the rate of racemization (k_{rac}) from the barrier to rotation at 25 °C, assuming that $\Delta G^{\ddagger}_{rot}$ is mostly constant over a large temperature range.

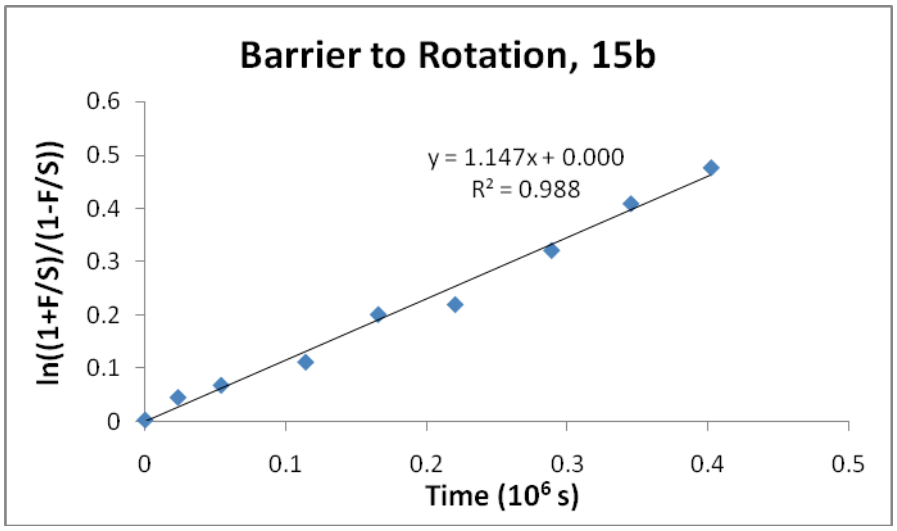
$$k_{rac} = 2k_{rot} = \frac{2k_B T}{h} e^{\left(\frac{-\Delta G^{\ddagger}_{rot}}{RT}\right)} \qquad t_{1/2} = \frac{\ln 2}{k_{rac}}$$

A sample full data treatment is shown for **15b**.

Analysis of **15b**:

time (min)	% ee
0	99.7
39	95.6
90	93.4
190	89.5
276	81.8
367	80.3
481	72.5
575	66.4
670	62.1





Equation for racemization: $$\ln\left[\frac{1+[F-15b]/[S-15b]}{1-[F-15b]/[S-15b]}\right] = k_{rac}t + c = 2k_{rot}t + c$$

Corresponding plot: $$\ln\left[\frac{1+[F-15b]/[S-15b]}{1-[F-15b][S-15b]}\right]$$ vs. time, where slope = $2k_{rot}$

$$k_{rot} = \frac{slope}{2} = \frac{1.147\times10^{-5}\,s^{-1}}{2} = 5.735\times10^{-6}\,s^{-1}$$

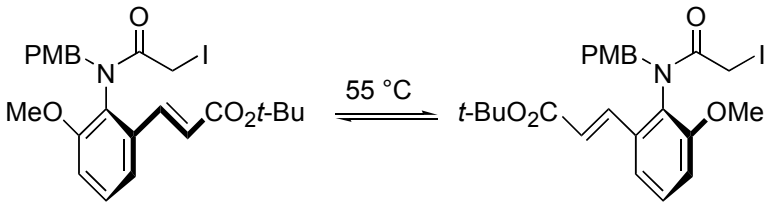
$$K^{\ddagger}_{rot} = \frac{k_{rot}h}{kT} = \frac{(5.735\times10^{-5}\,s^{-1})(6.626\times10^{-34}\,J\cdot s)}{(1.381\times10^{-23}\,J/K)(388K)} = 6.66\times10^{-19}$$

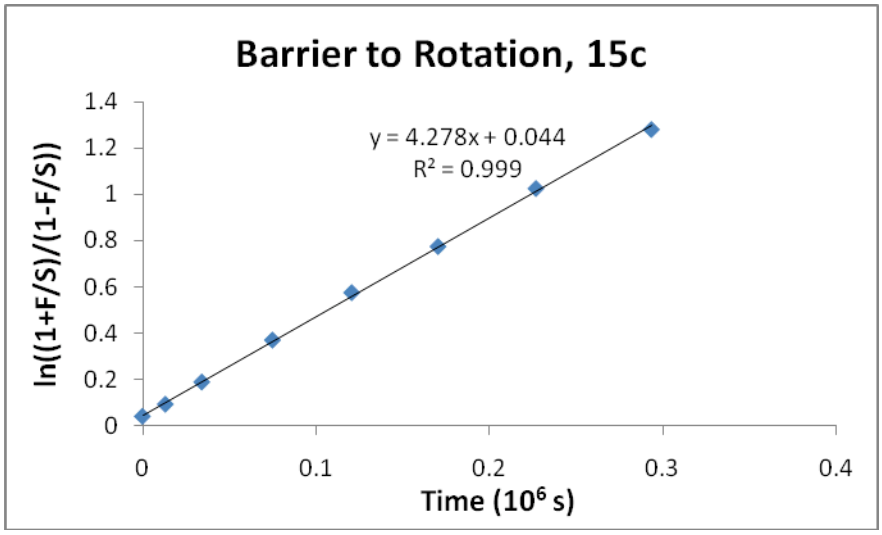
$$\Delta G^{\ddagger}_{rot} = -RT\ln K^{\ddagger}_{rot} = -(.0083145kJ/mol)(388K)\ln(6.66\times10^{-19}) = 143.72kJ/mol = 34.3kcal/mol$$

k_{rot} = 5.74 x 10^{-6} s^{-1}
$\Delta G^{\ddagger}_{rot}$ = 34.3 kcal/mol
$t_{1/2}$ at 25 °C = 27,500 years

Analysis of **15c**:

time (min)	% ee
0	96.2
22	91.3
57	82.9
125	69.1
201	56.2
284	46.1
378	35.8
489	27.7





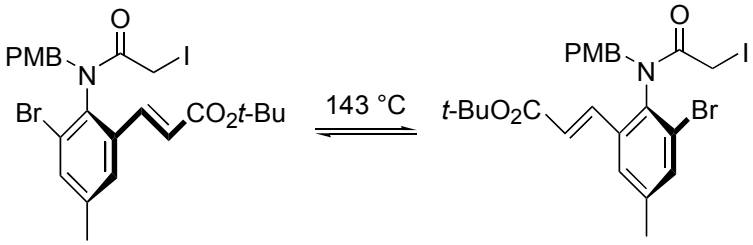
k_{rot} = 2.14 x 10^{-5} s^{-1}

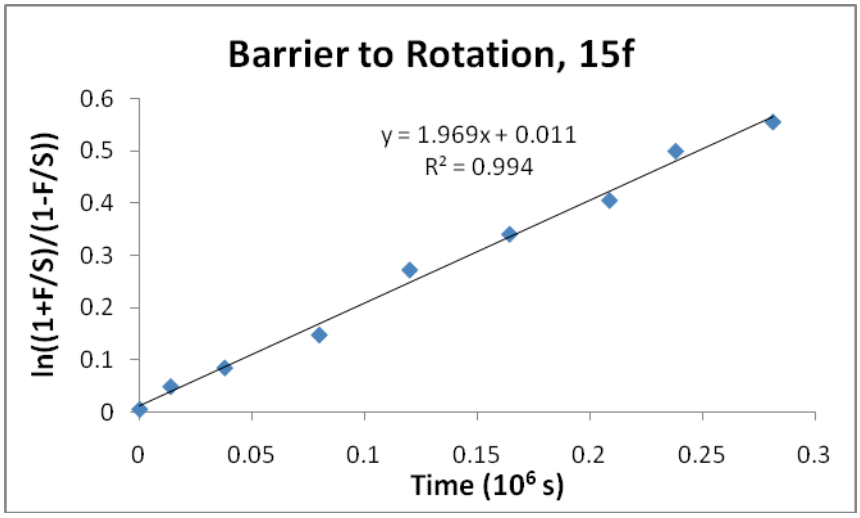
$\Delta G^{\ddagger}_{rot}$ = 26.3 kcal/mol

$t_{1/2}$ at 25 °C = 12 days

Analysis of **15f**:

time (min)	% ee
0	99.5
23	95.3
63	91.9
133	86.3
200	76.2
274	71.1
348	66.7
397	60.7
469	57.4





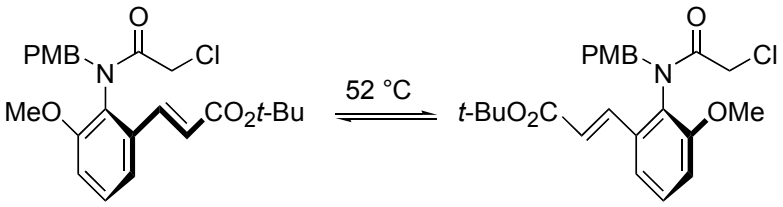
k_{rot} = 9.85 x 10^{-6} s^{-1}

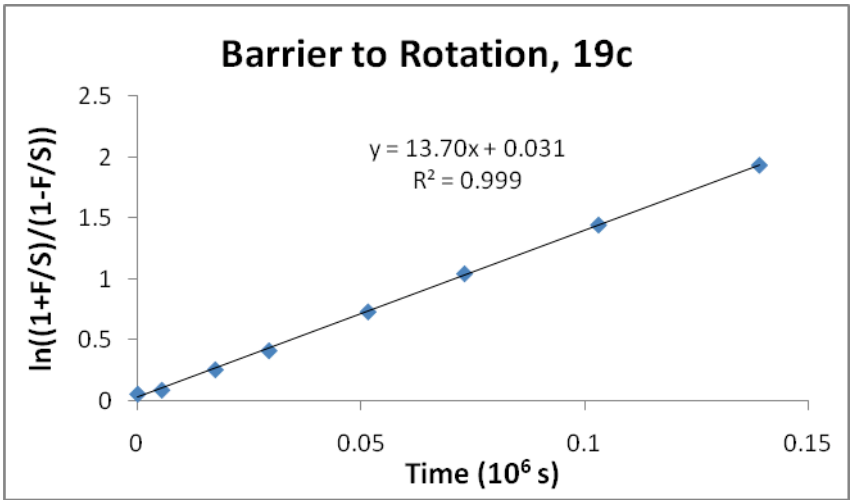
$\Delta G^{\ddagger}_{rot}$ = 34.2 kcal/mol

$t_{1/2}$ at 25 °C = 19,900 years

Analysis of **19c**:

time (min)	% ee
0	94.1
9	91.1
29	77.1
49	65.9
86	47.9
122	35.1
172	23.5
232	14.4





k_{rot} = 6.85 x 10^{-5} s^{-1}

$\Delta G^{\ddagger}_{rot}$ = 25.3 kcal/mol

$t_{1/2}$ at 25 °C = 2.2 days

References

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5. Petit, M.; Geib, S. J.; Curran, D. P. *Tetrahedron* **2004**, *60*, 7543-7552.
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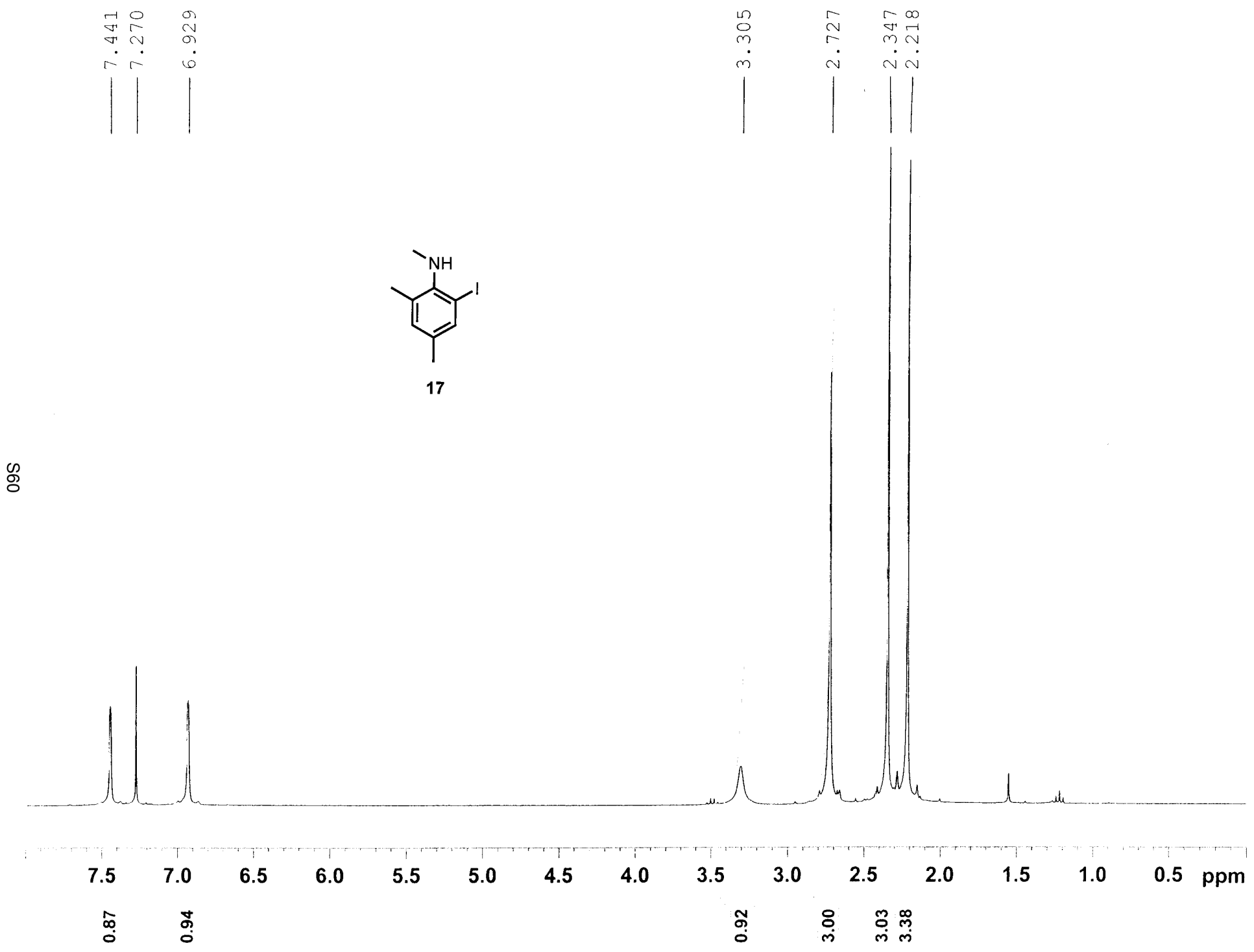
7. Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons, Inc.: New York, 1994.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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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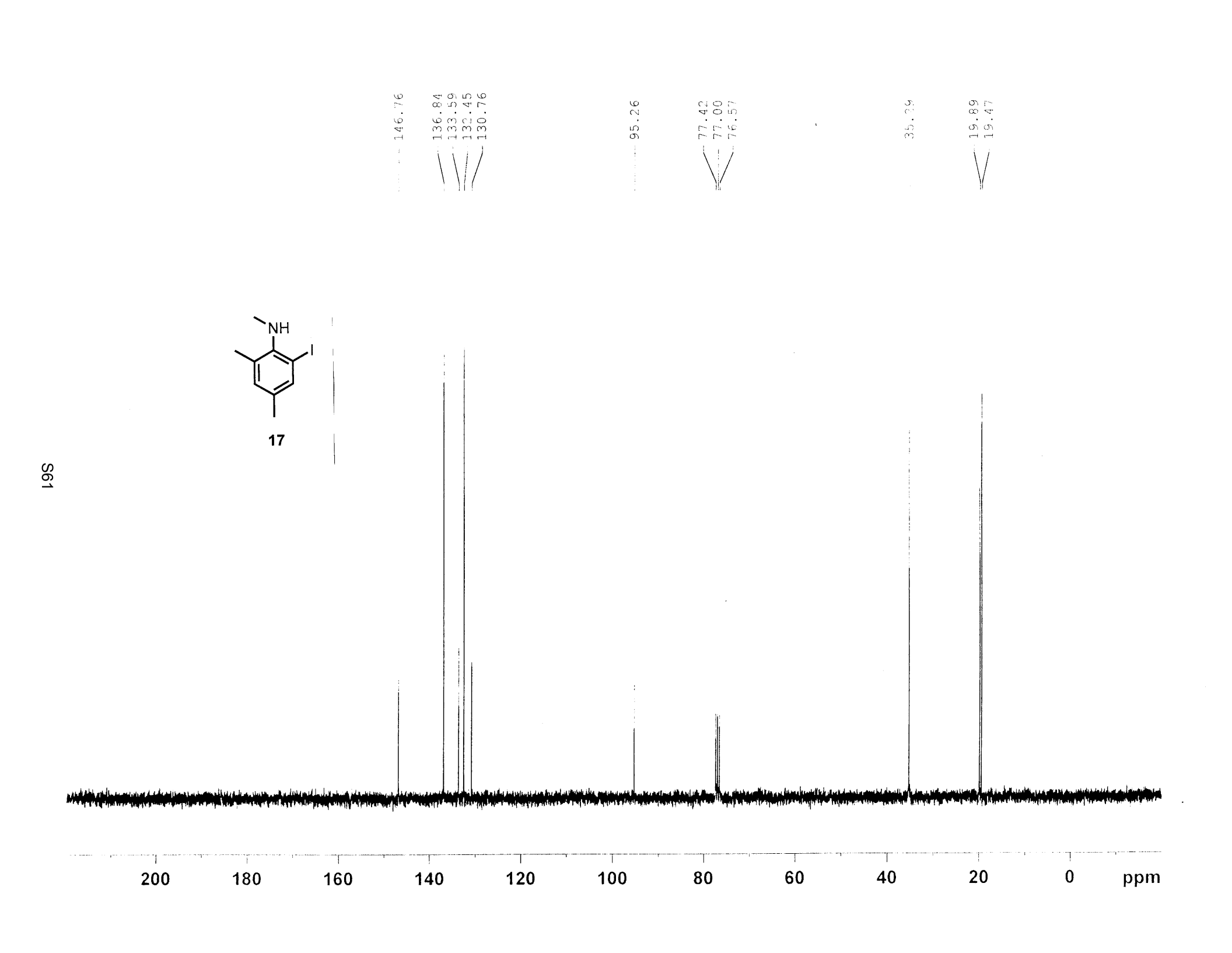
3.38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76.57
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I
17
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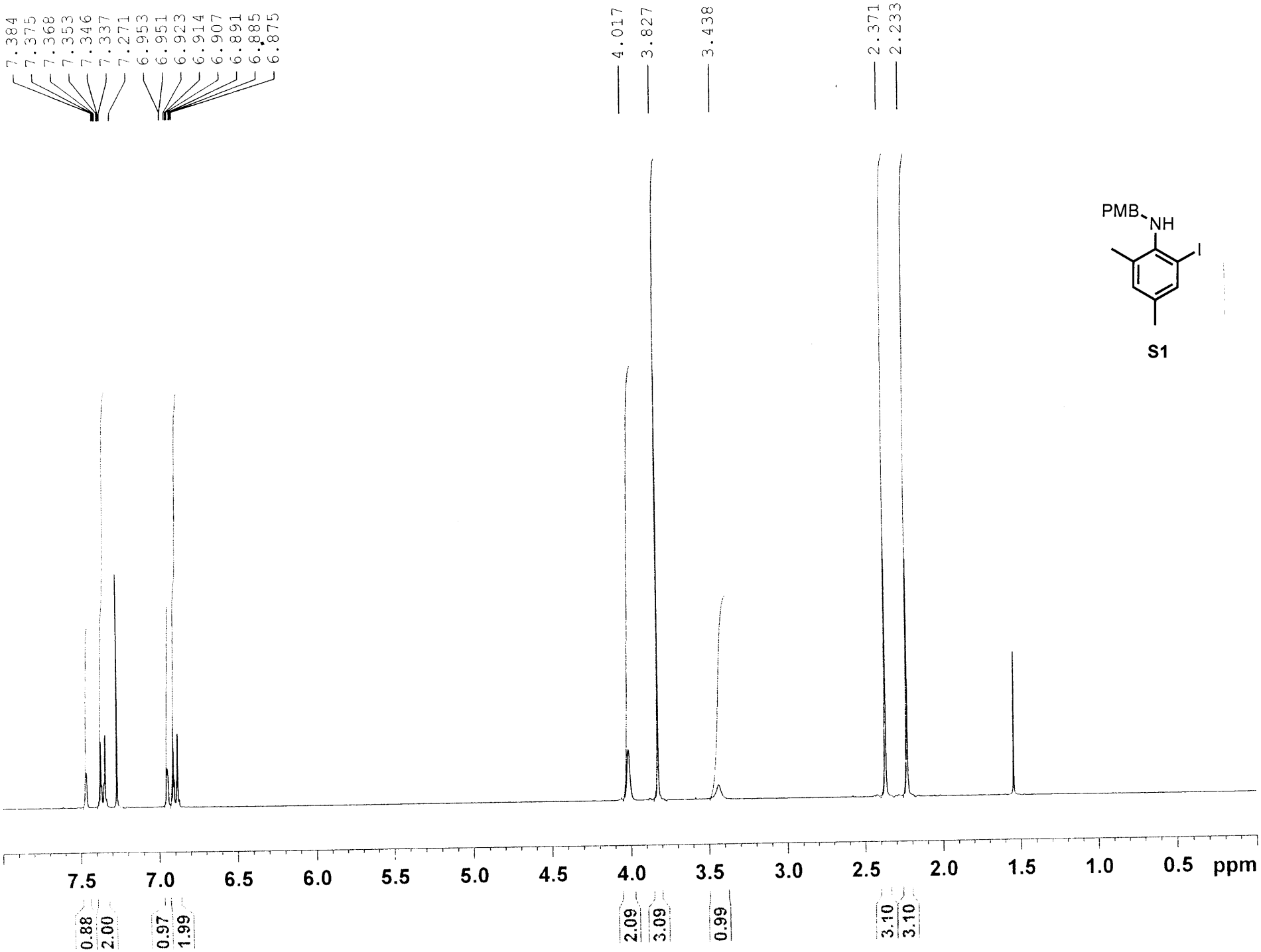
140
120
100
80
60
40
20
0
ppm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6.885
6.875
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3.827
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2.371
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NH
I
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5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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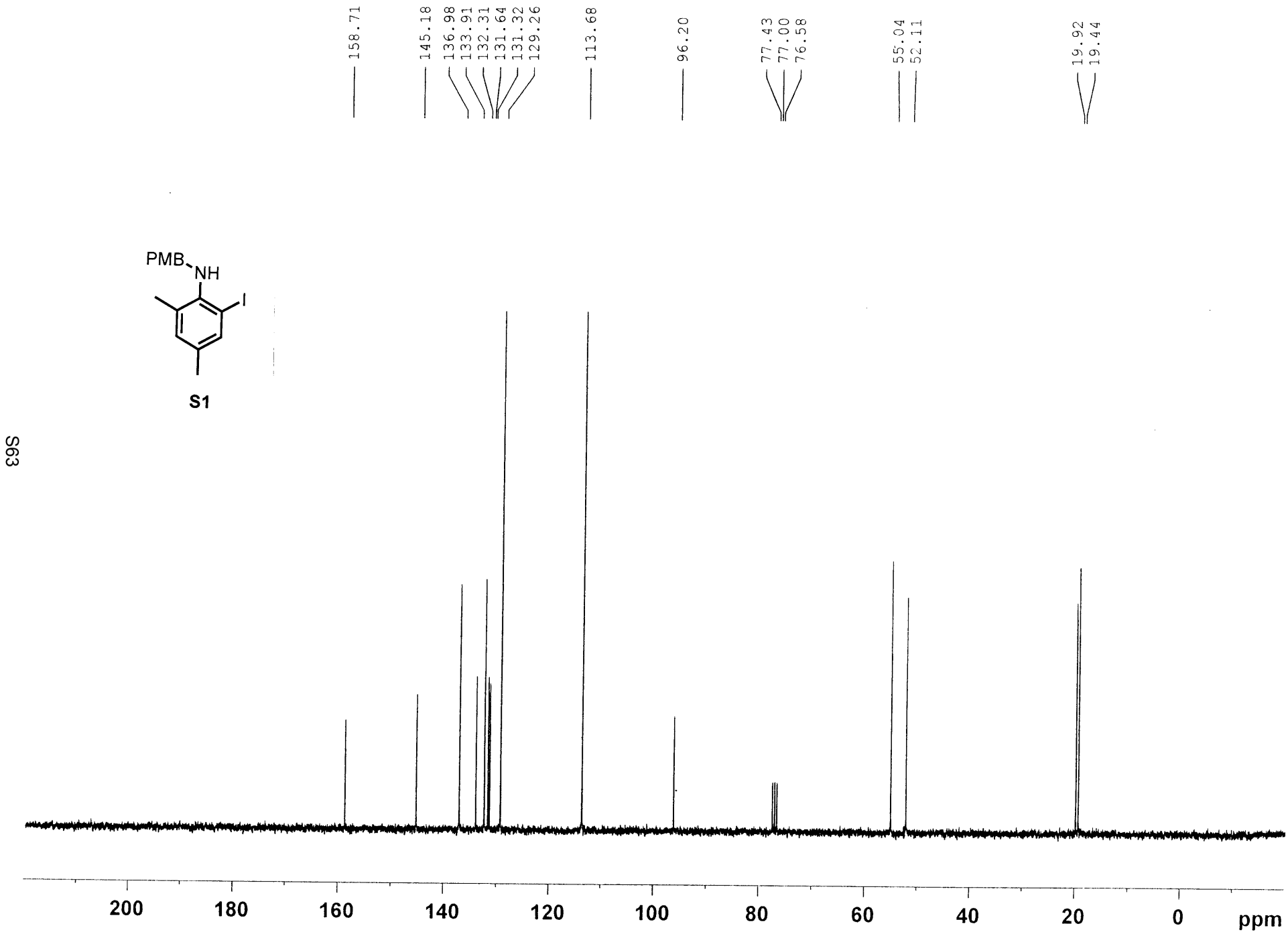
3.10
3.10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52.11
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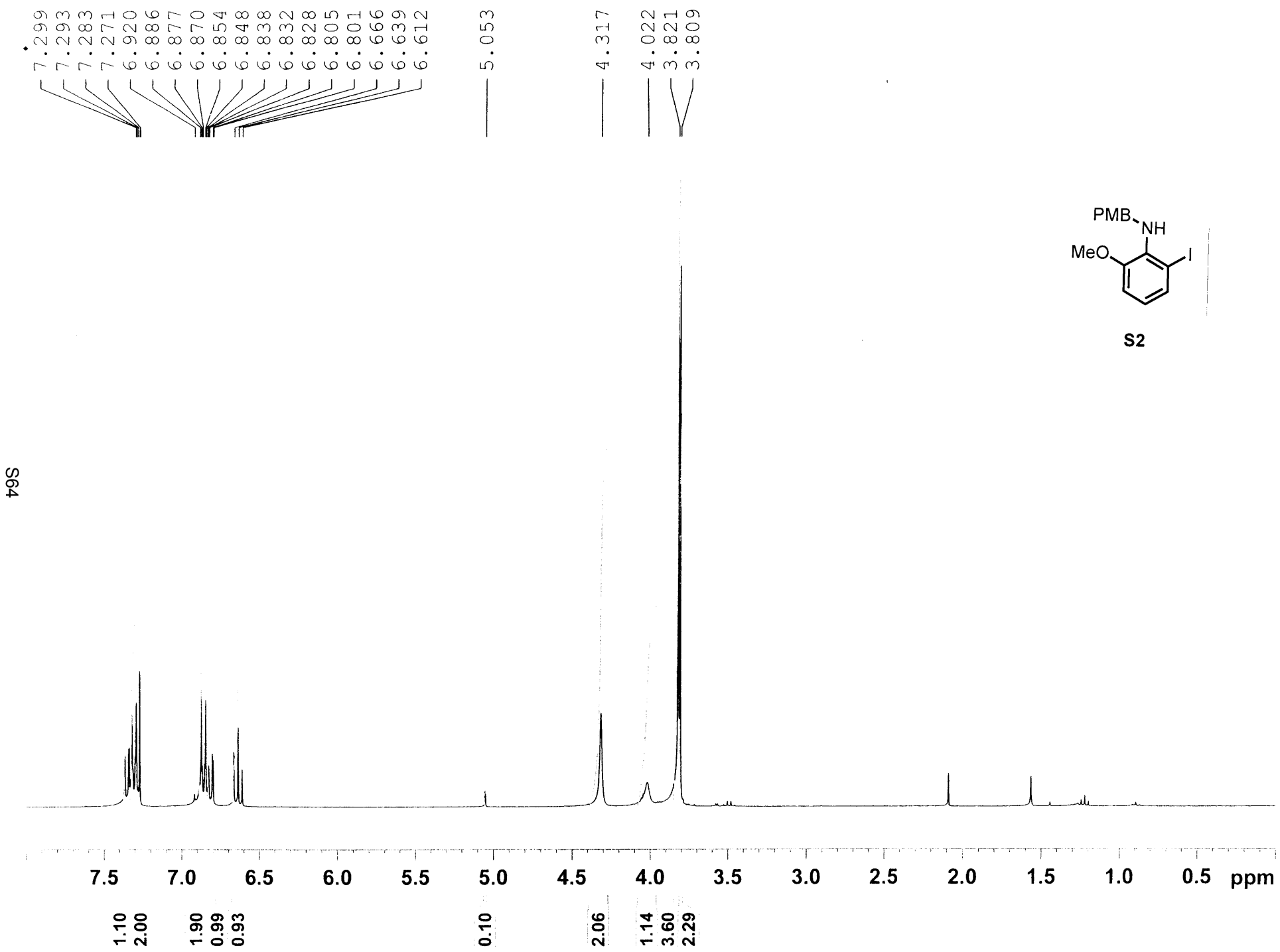
140
120
100
80
60
40
20
0
ppm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6.828
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6.801
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5.053
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I
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5.0
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3.0
2.5
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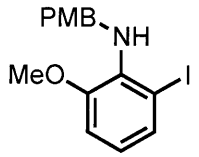
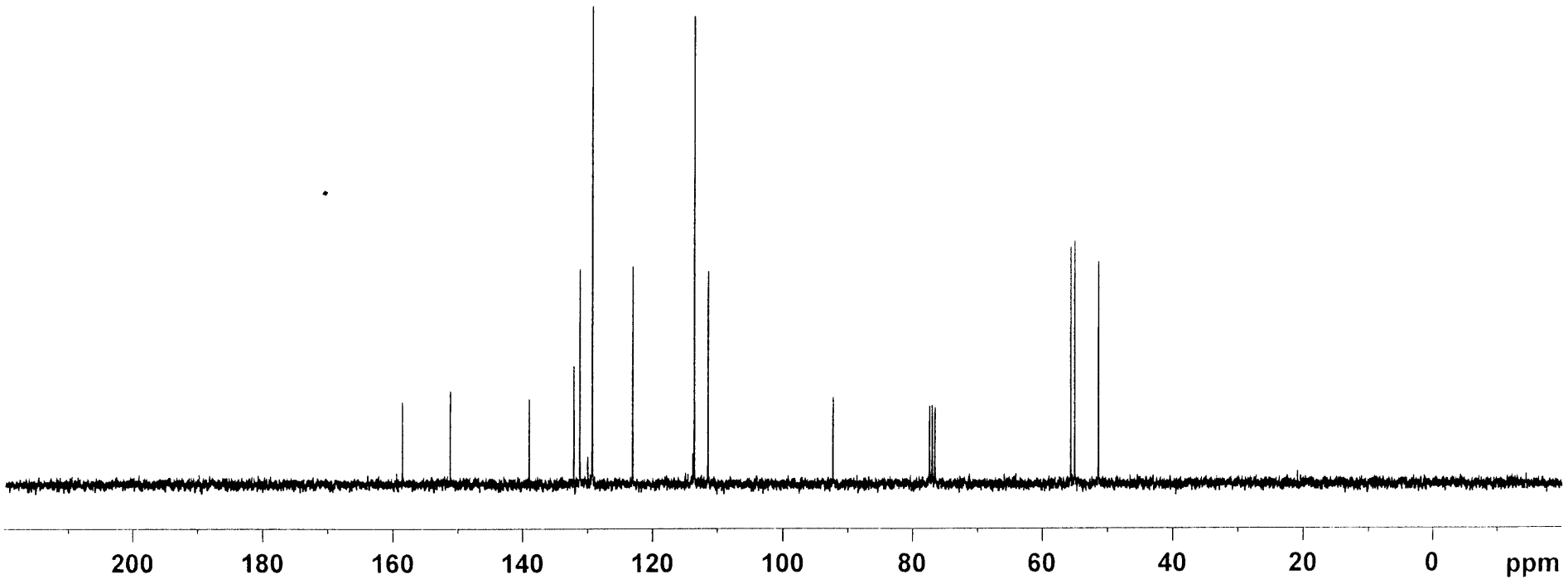
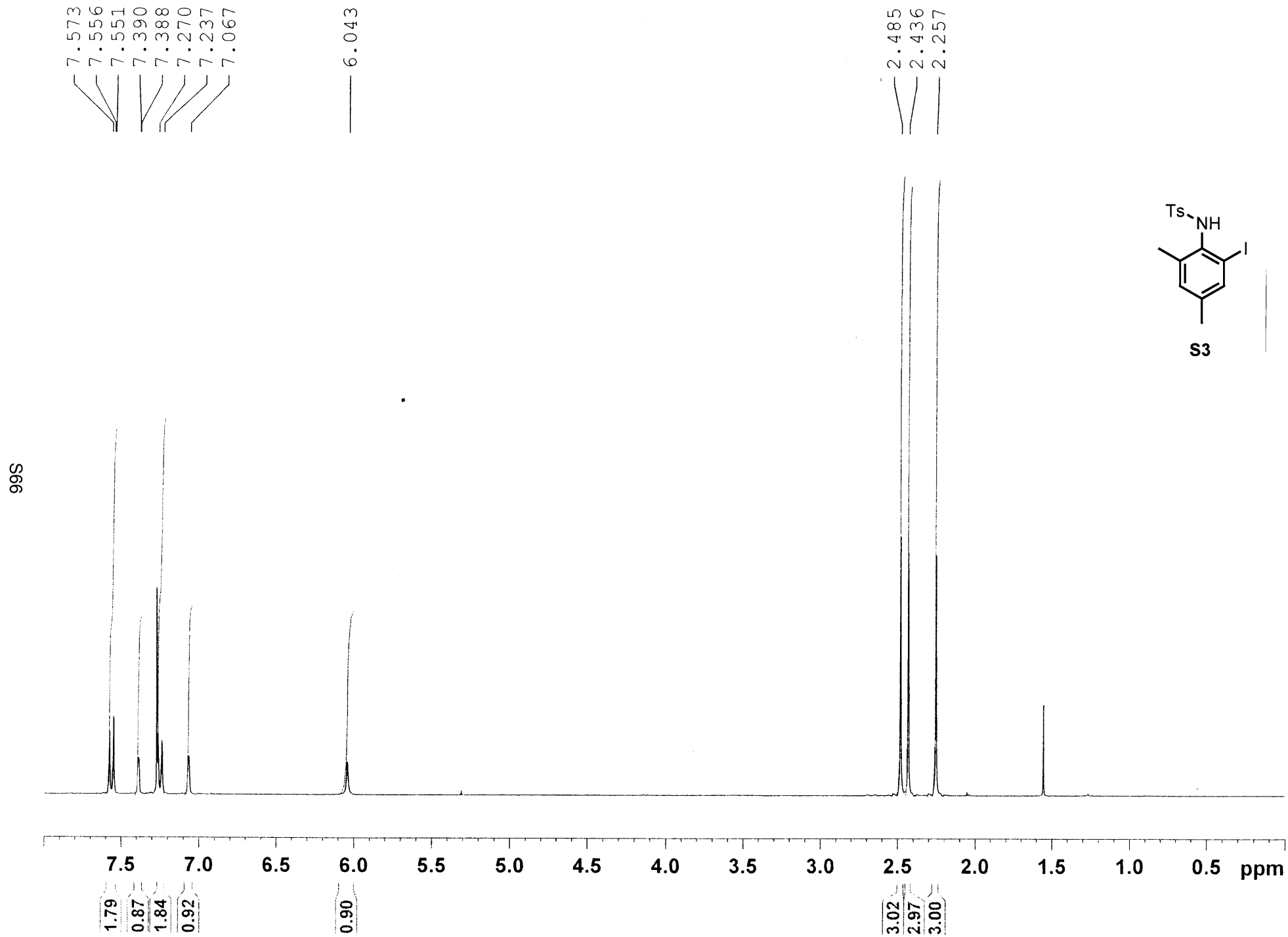


S2

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I
S3
S66
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6.5
6.0
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5.0
4.5
4.0
3.5
3.0
2.5
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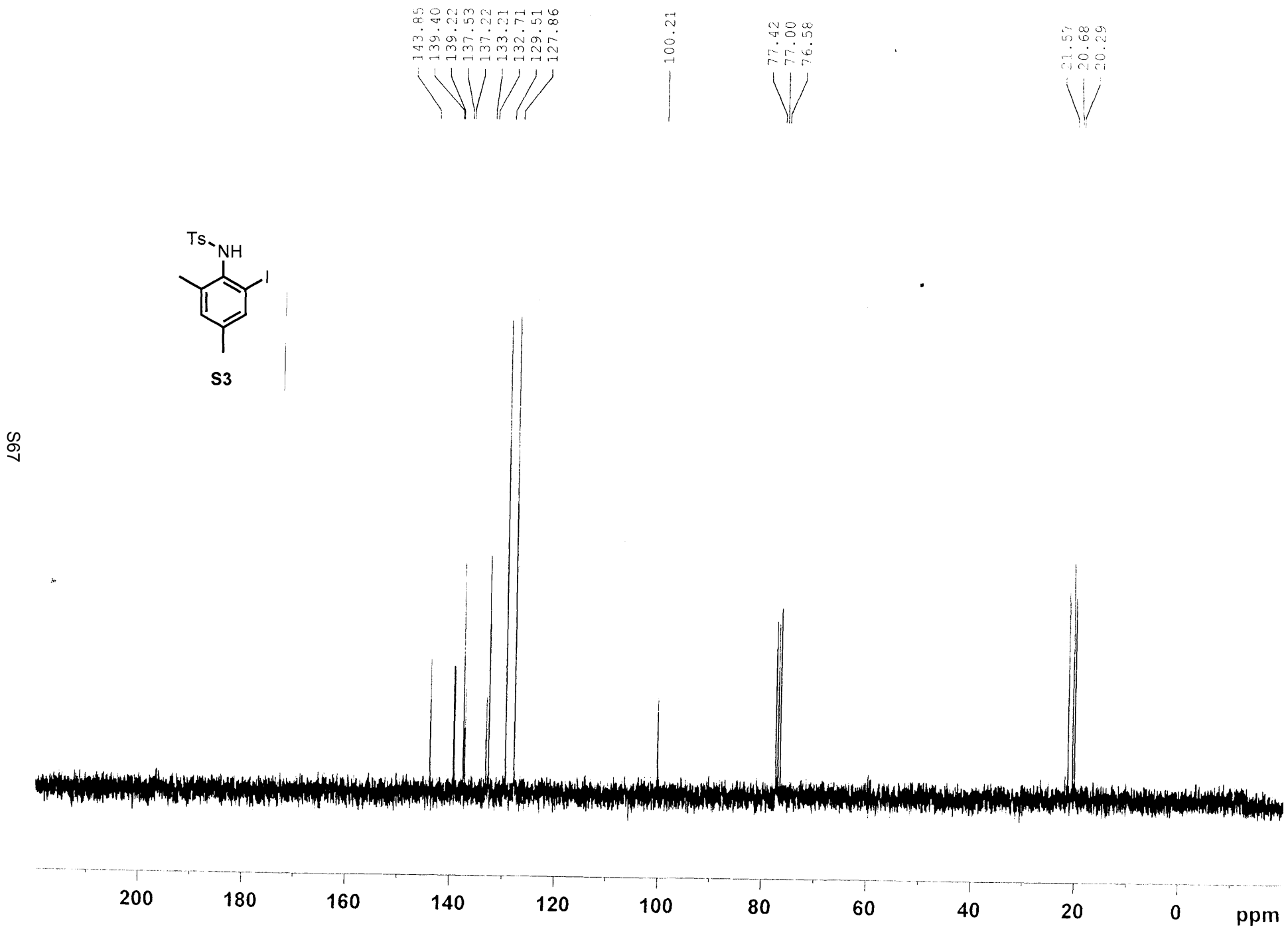
3.00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I
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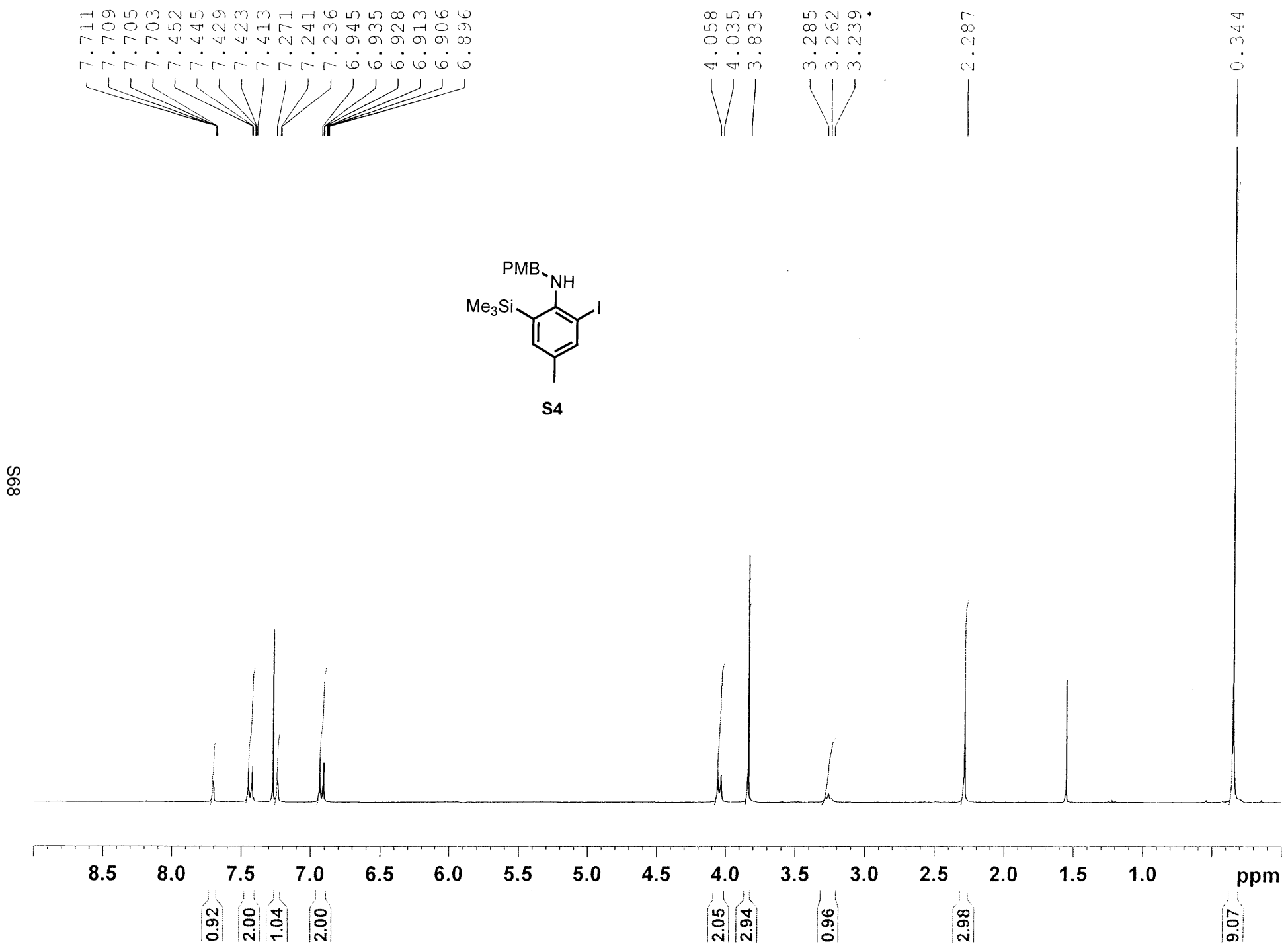
120
100
80
60
40
20
0
ppm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4.058
4.035
3.835
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I
S4
S68
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7.5
7.0
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
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ppm
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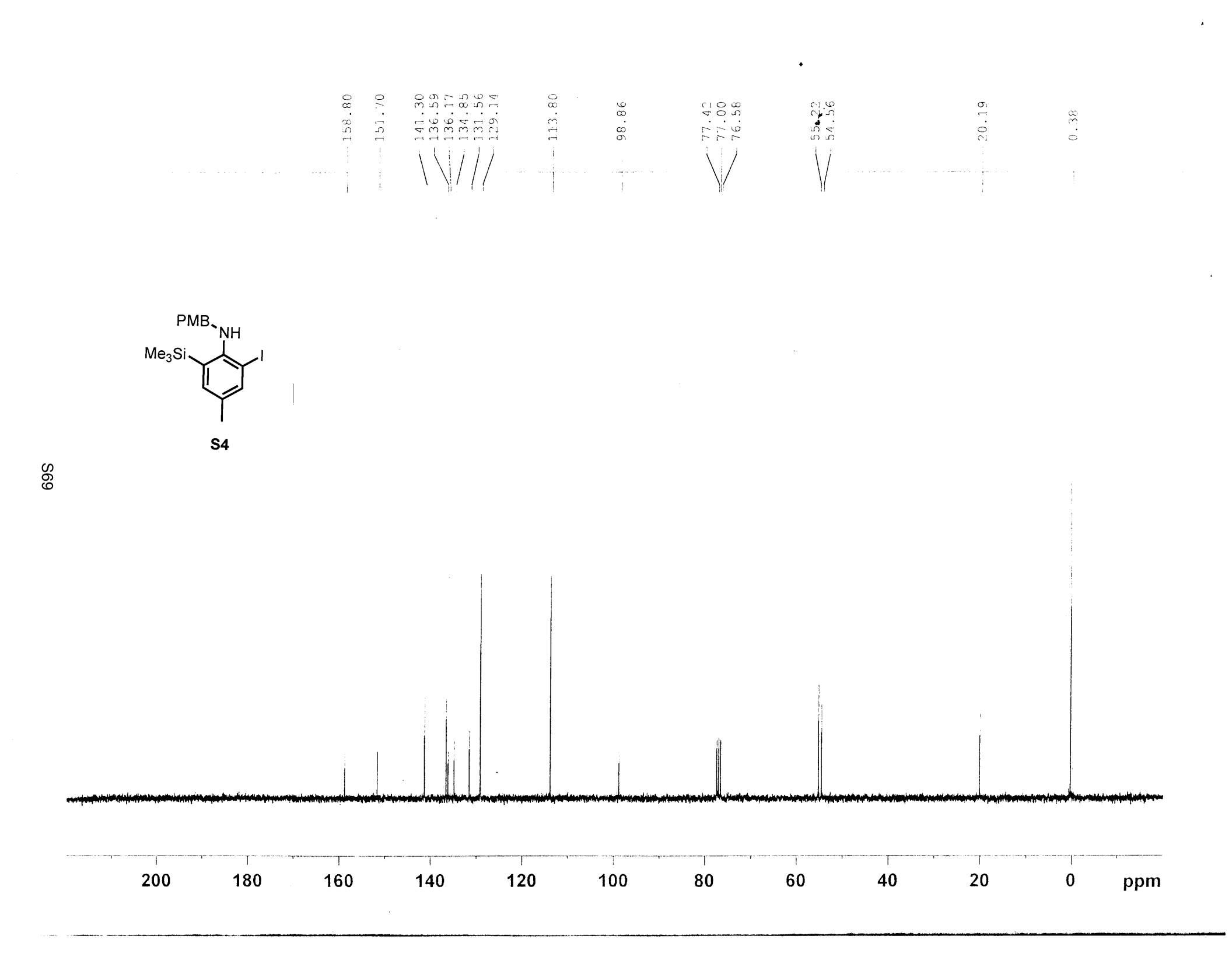
9.07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20.19
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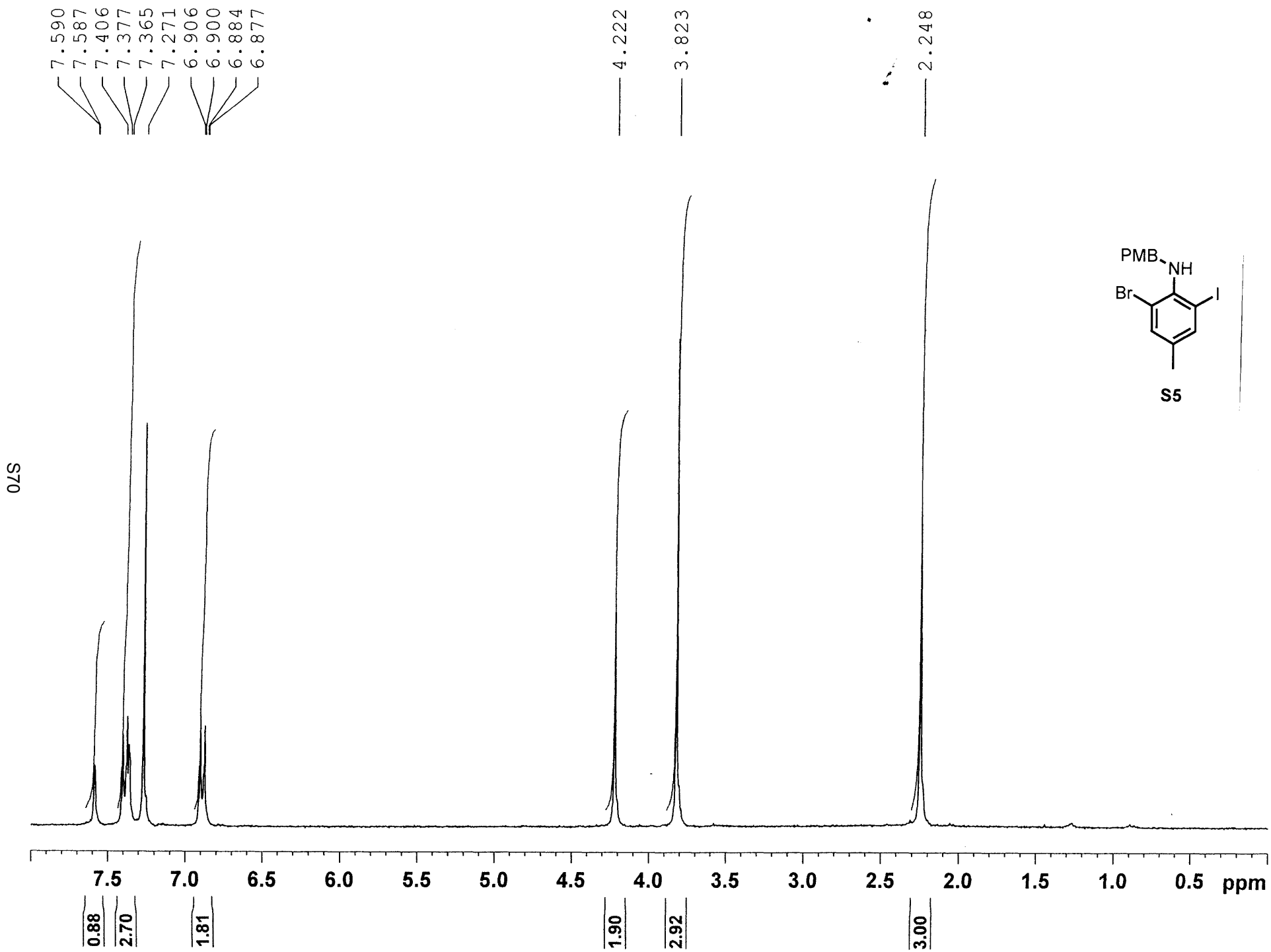
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S70
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5.0
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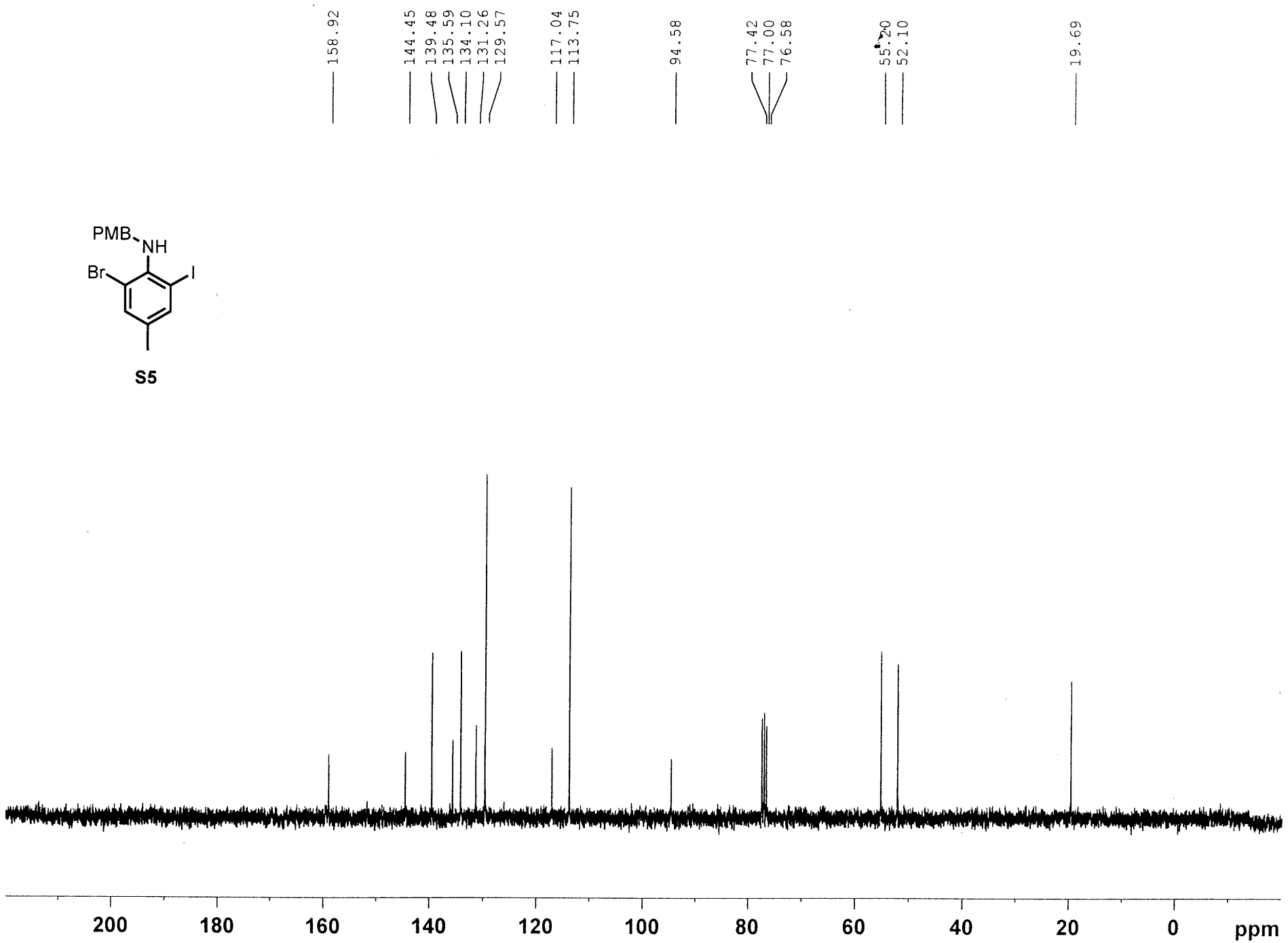
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55.20
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19.69
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NH
Br
I
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200
180
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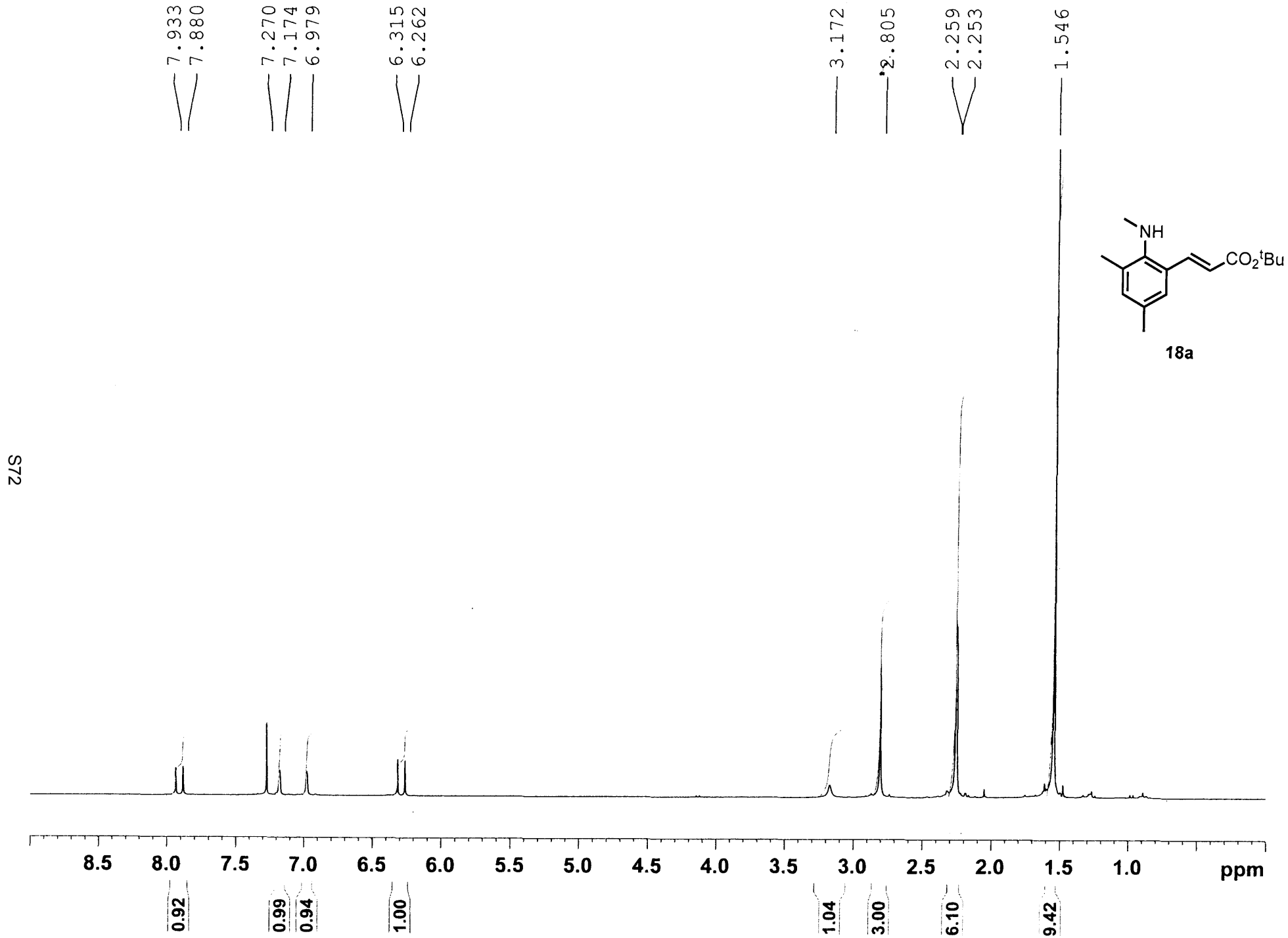
140
120
100
80
60
40
20
0
ppm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5.0
4.5
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3.0
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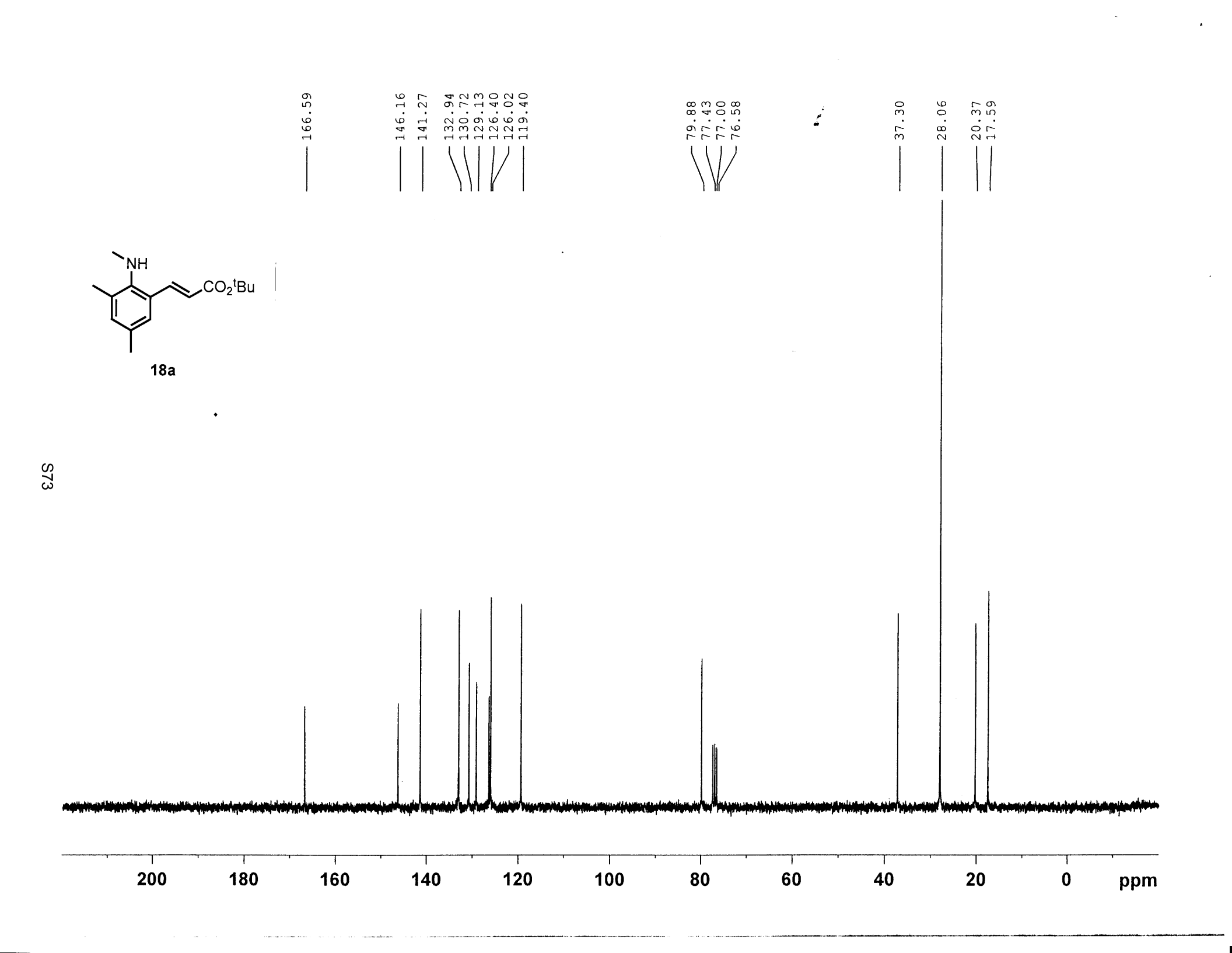
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28.06
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CO2tBu
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120
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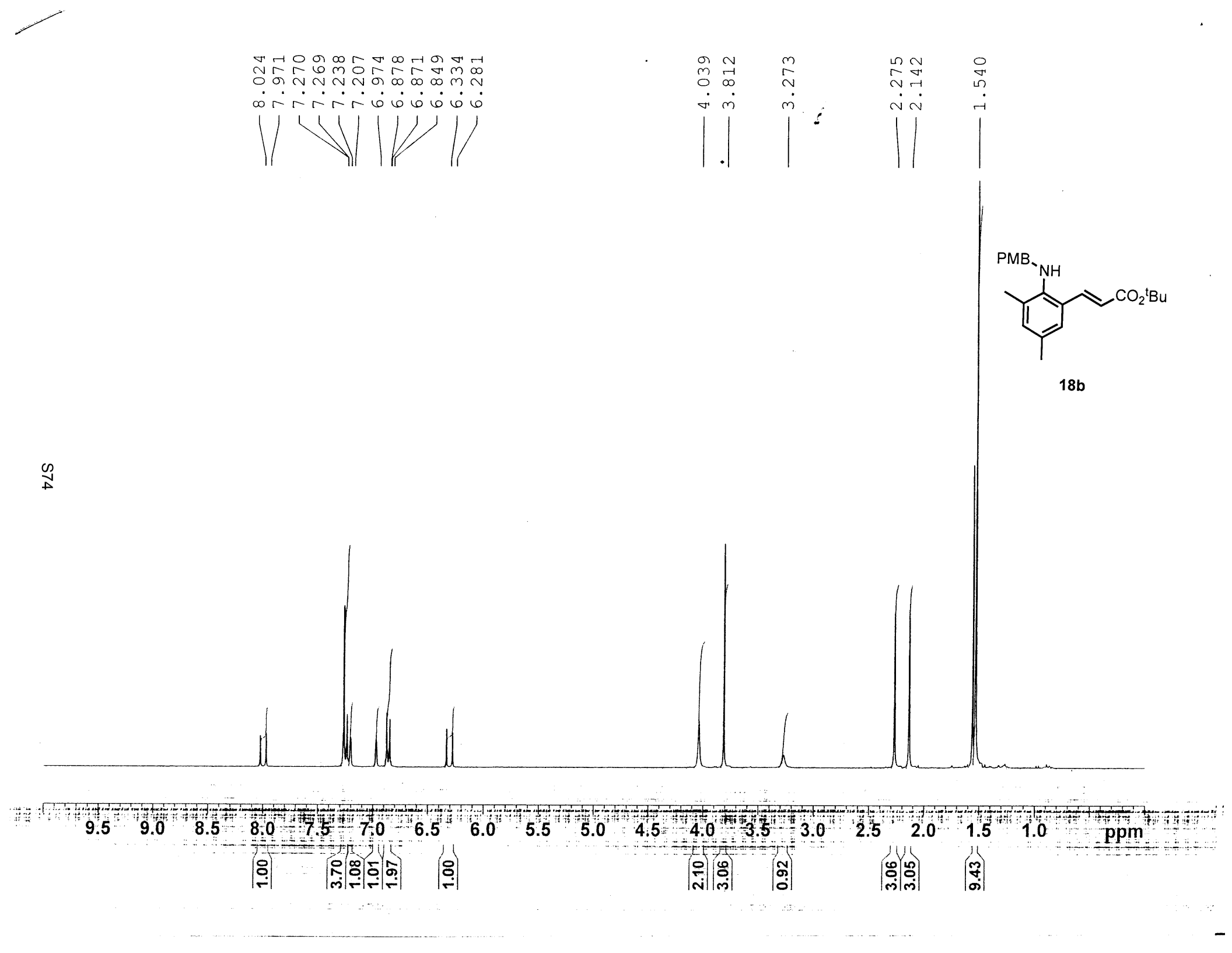
60
40
20
0
ppm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18b
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8.0
7.5
7.0
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6.0
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5.0
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4.0
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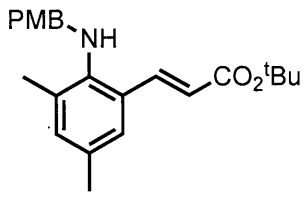
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18b

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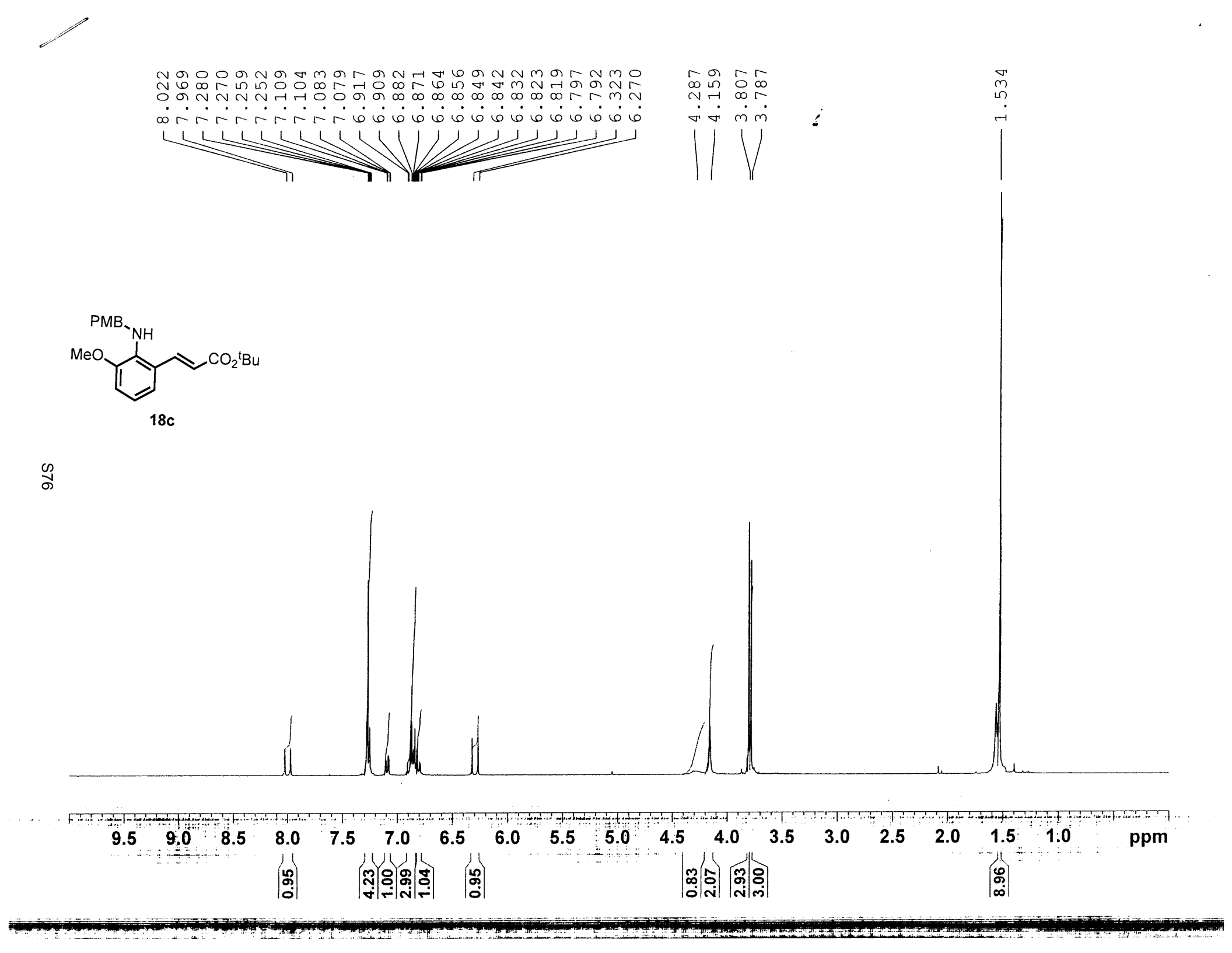
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6.864
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NH
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CO2tBu
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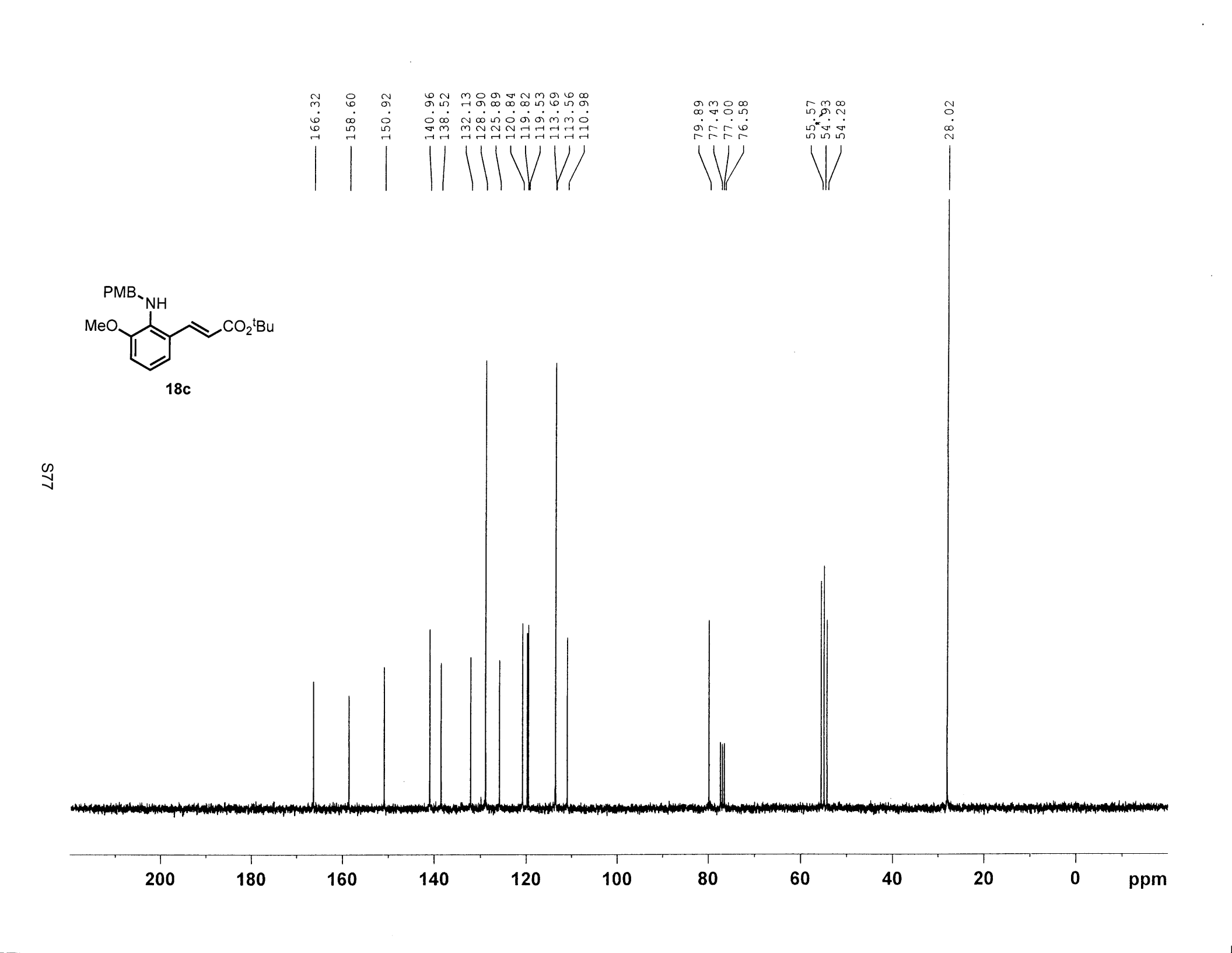
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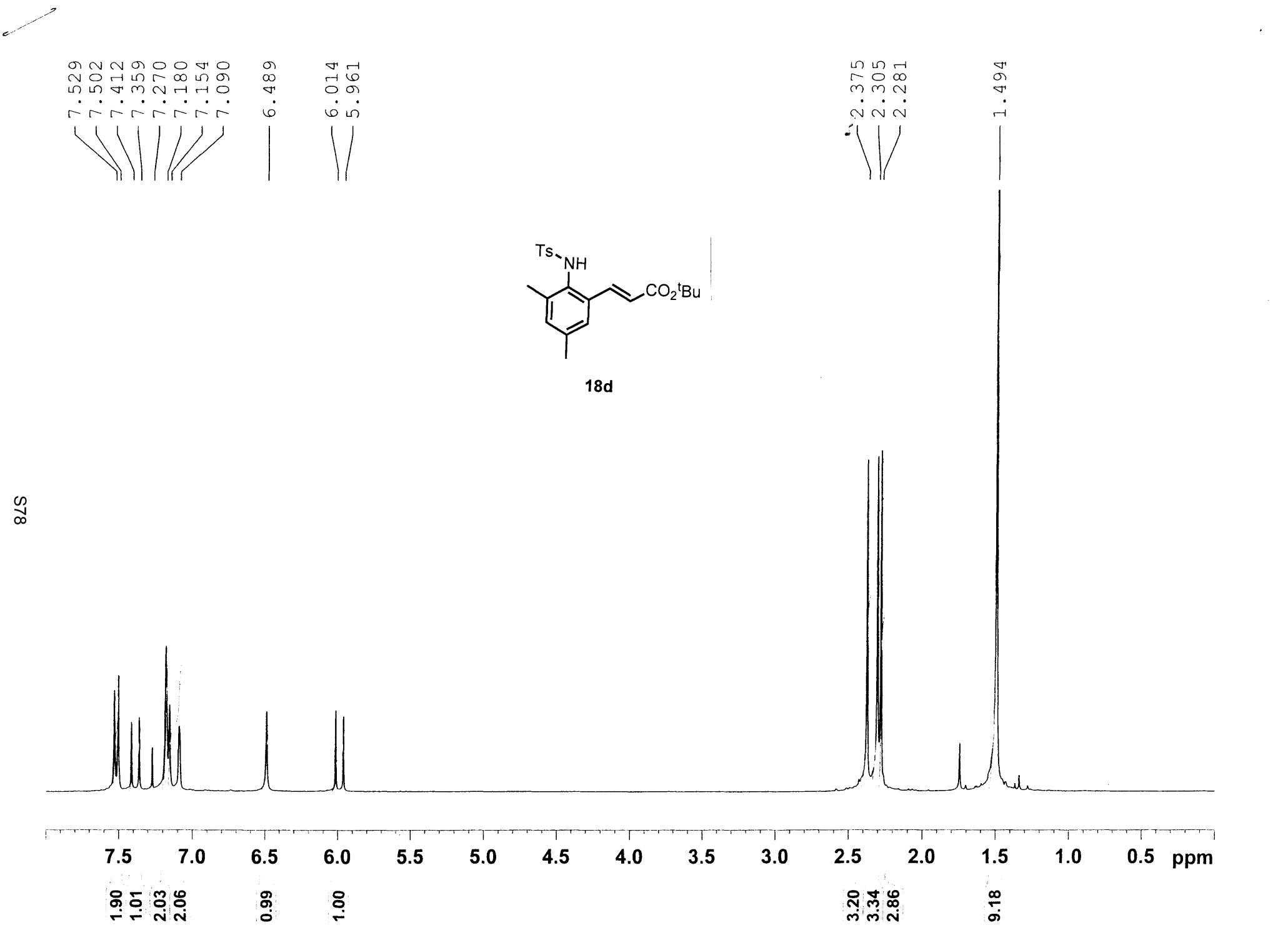
113.56
110.98
79.89
77.43
77.00
76.58
55.57
54.93
54.28
28.02
PMB
NH
MeO
CO2tBu
18c
200
180
160
140
120
100
80
60
40
20
0
ppm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2.281
1.494
Ts
NH
CO2tBu
18d
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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1.00
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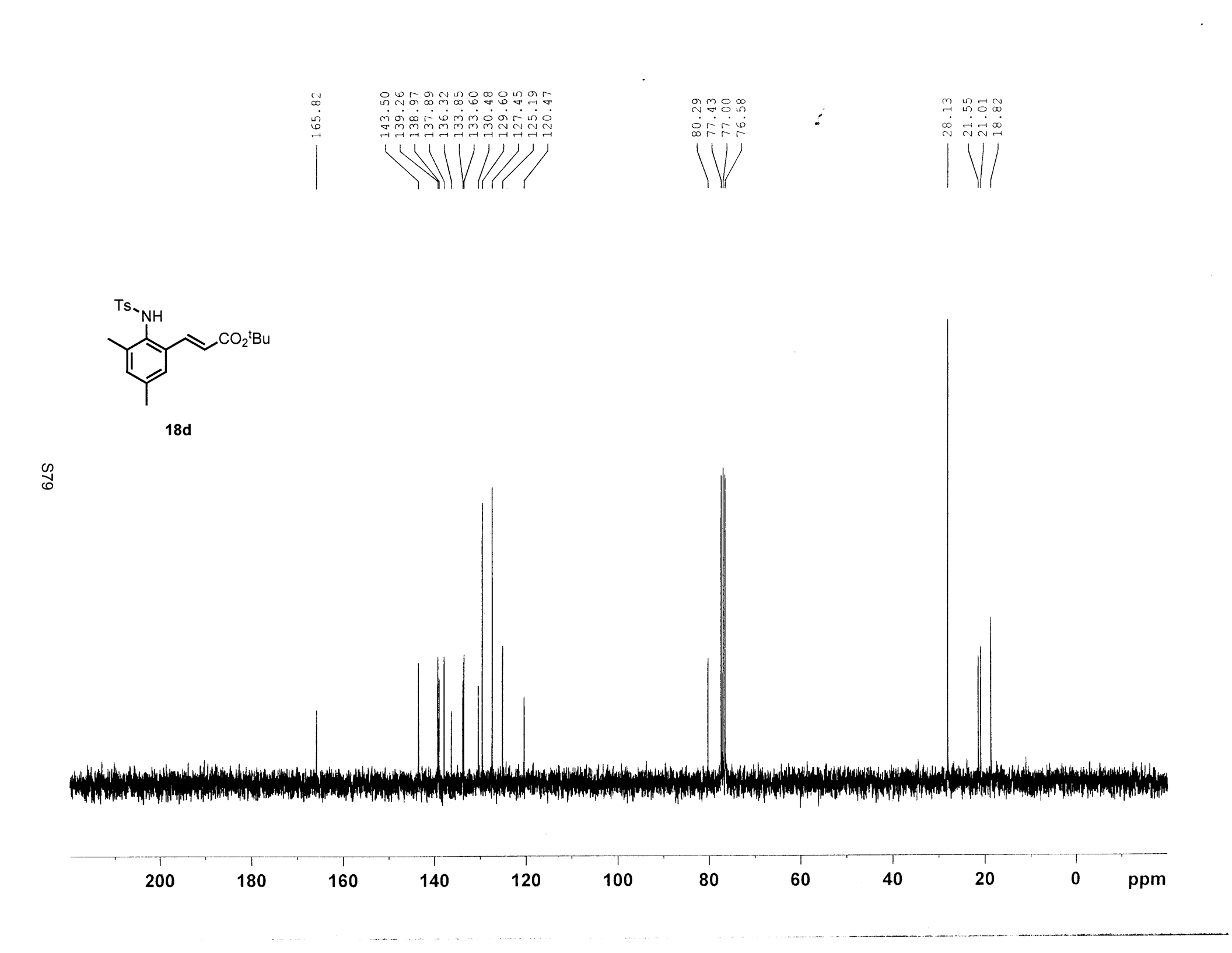
2.86
9.18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127.45
125.19
120.47
80.29
77.43
77.00
76.58
28.13
21.55
21.01
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NH
CO2tBu
18d
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120
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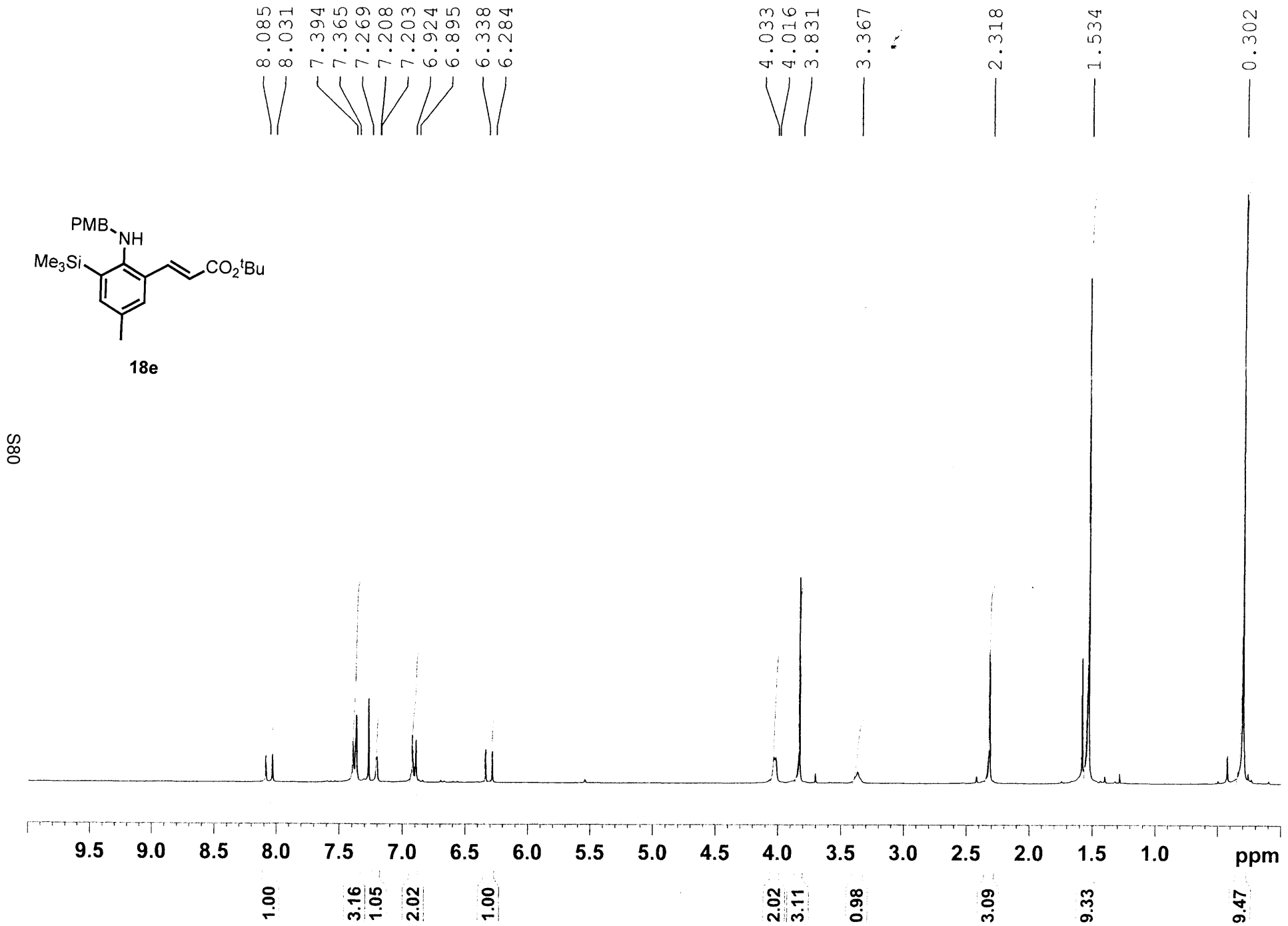
40
20
0
ppm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6.284
4.033
4.016
3.831
3.367
2.318
1.534
0.302
PMB
NH
Me3Si
CO2tBu
18e
S80
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
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1.05
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1.00
2.02
3.11
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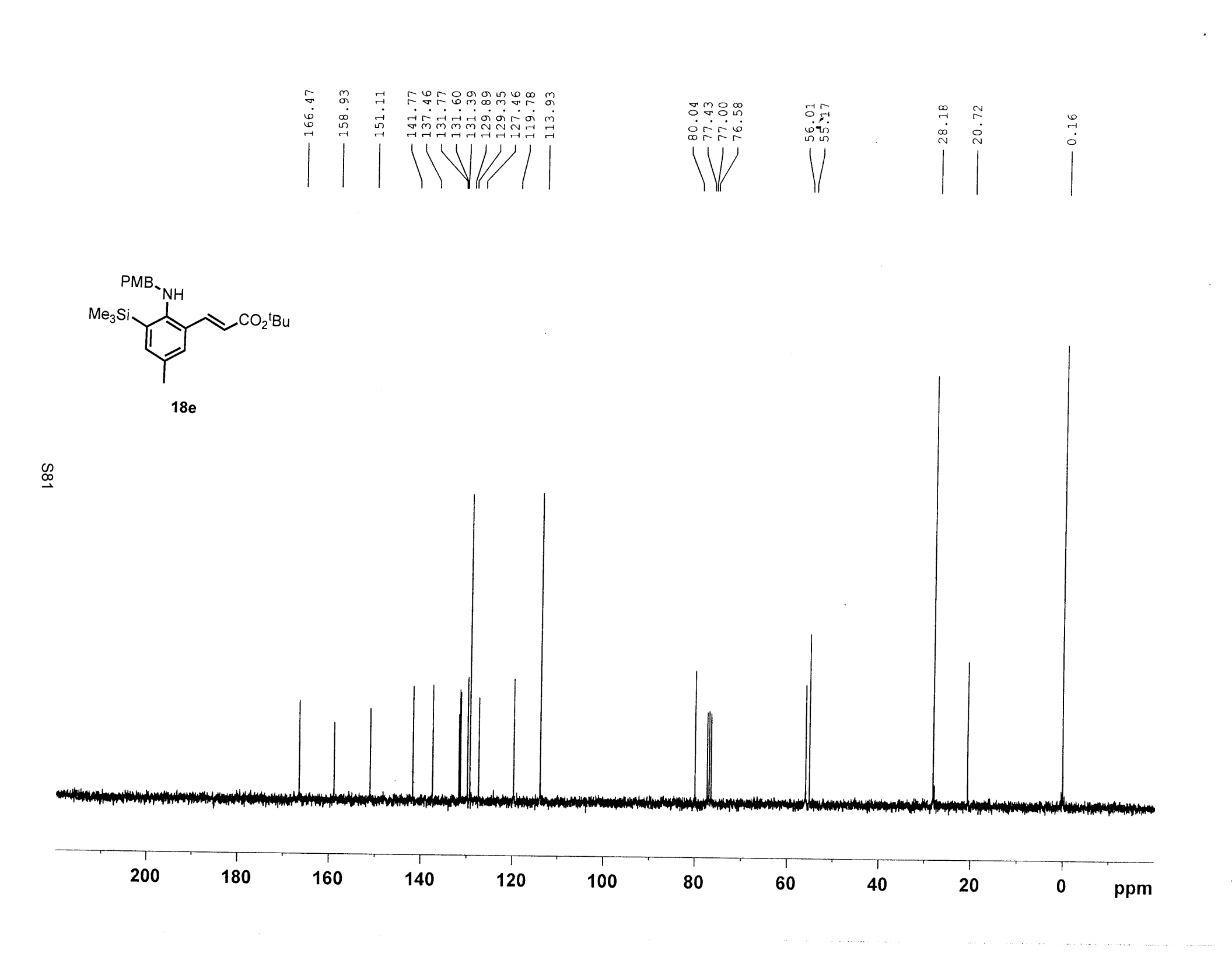
3.09
9.33
9.47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113.93
80.04
77.43
77.00
76.58
56.01
55.17
28.18
20.72
0.16
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CO2tBu
18e
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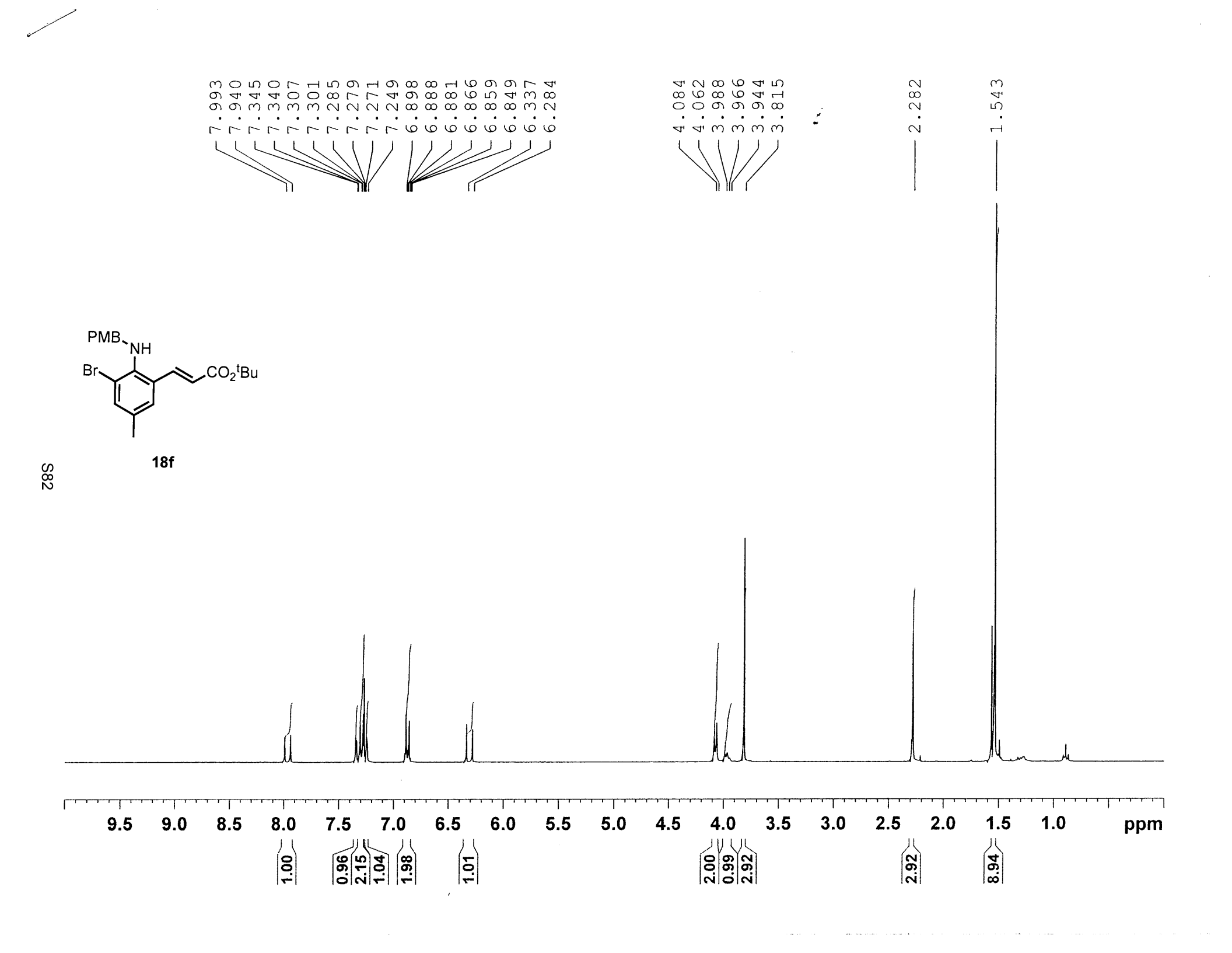
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7.279
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6.888
6.881
6.866
6.859
6.849
6.337
6.284
4.084
4.062
3.988
3.966
3.944
3.815
2.282
1.543
PMB
NH
Br
CO2tBu
18f
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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2.00
0.99
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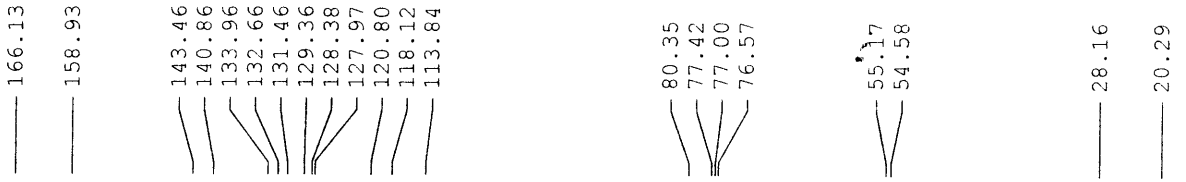
2.92
8.94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118.12
113.84
80.35
77.42
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76.57
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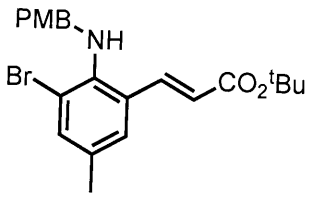
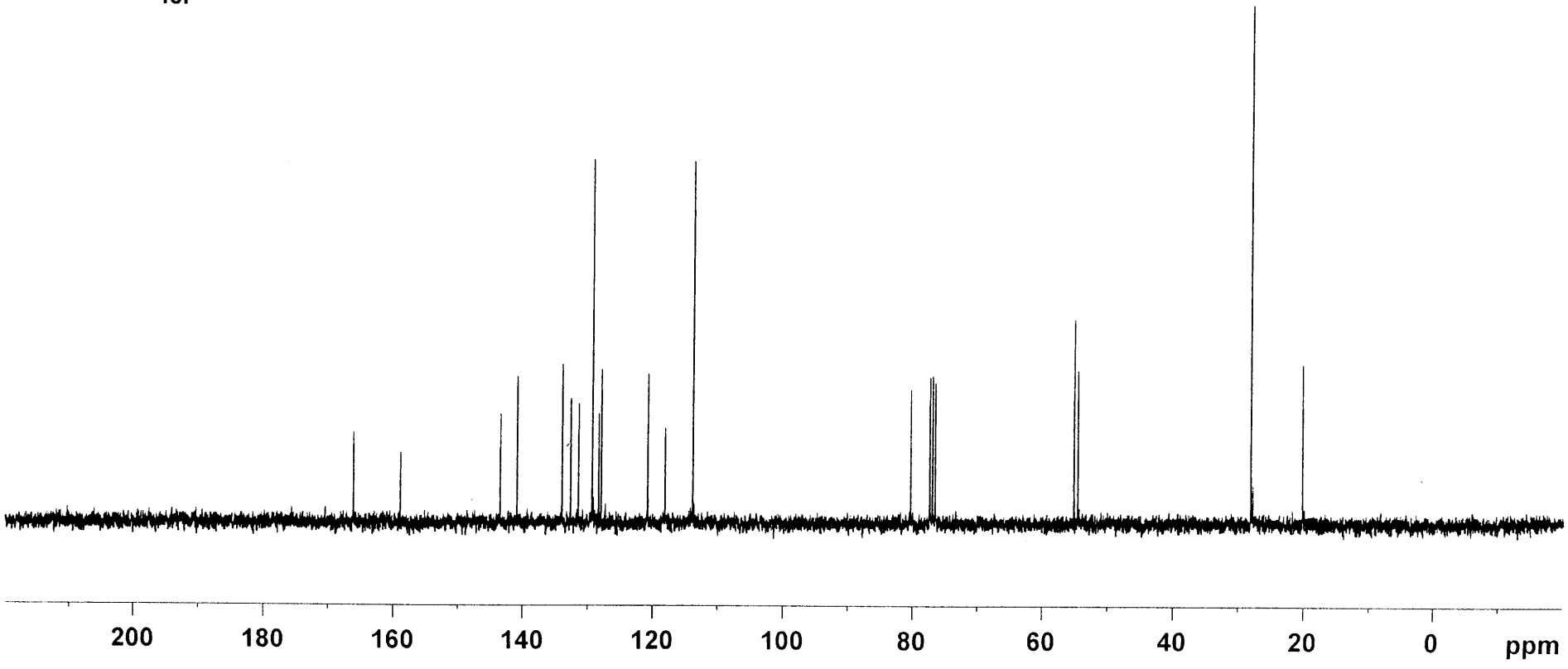
54.58
28.16
20.29


PMB
NH
Br
CO2tBu

18f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160
140
120
100
80
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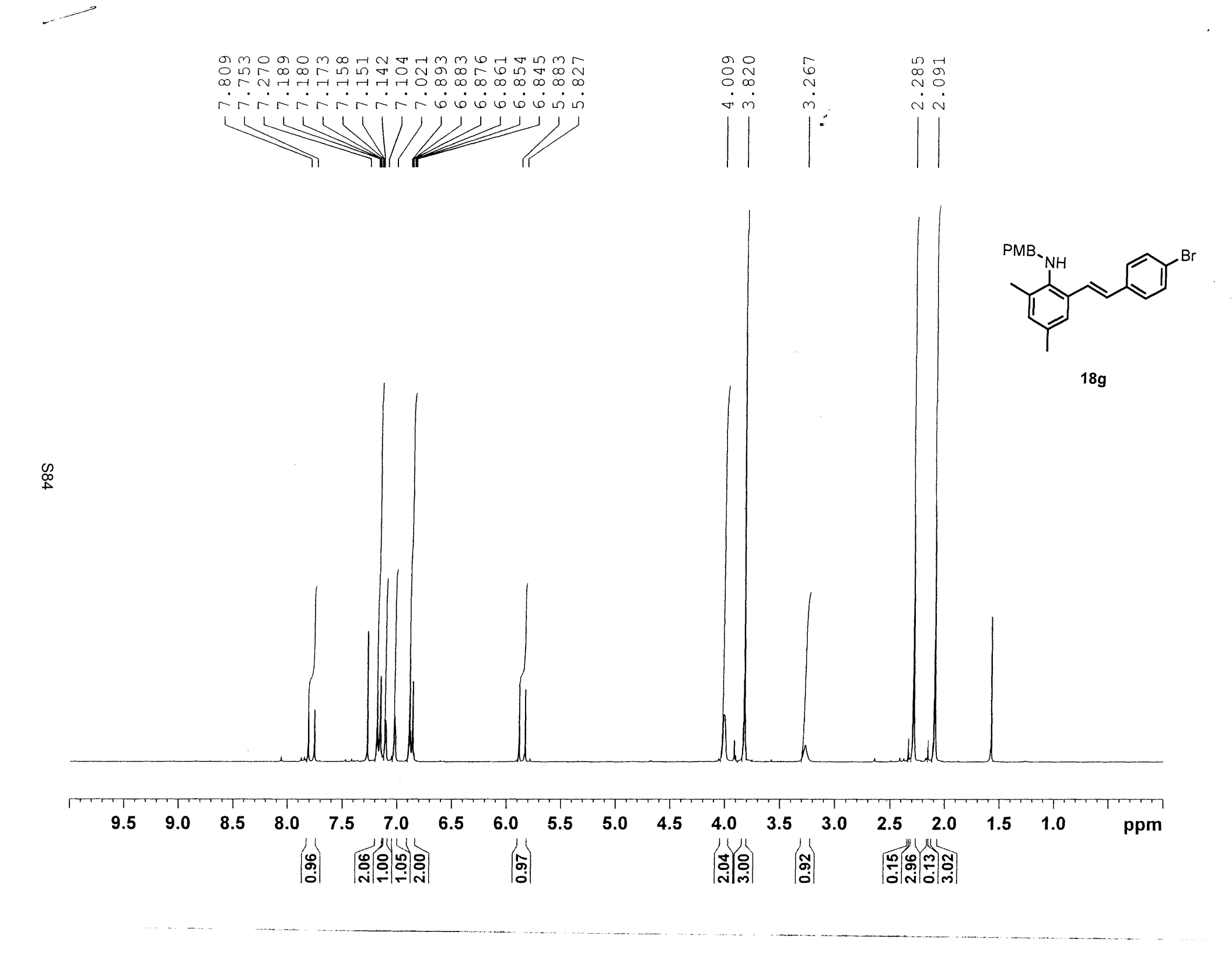
40
20
0
ppm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7.158
7.151
7.142
7.104
7.021
6.893
6.883
6.876
6.861
6.854
6.845
5.883
5.827
4.009
3.820
3.267
2.285
2.091
PMB
NH
Br
18g
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.96
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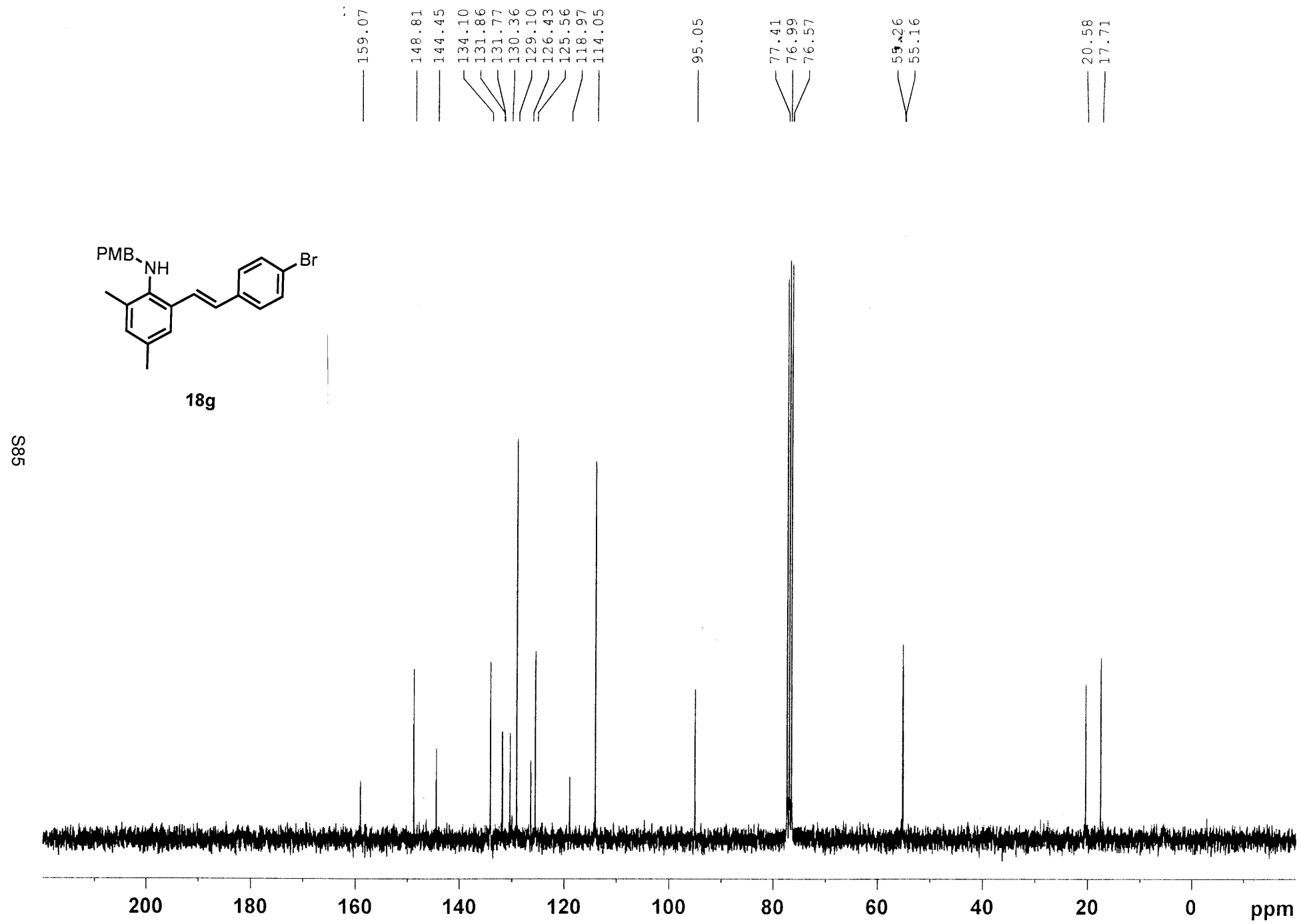
1.00
1.05
2.00
0.97
2.04
3.00
0.92
0.15
2.96
0.13
3.02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131.77
130.36
129.10
126.43
125.56
118.97
114.05
95.05
77.41
76.99
76.57
55.26
55.16
20.58
17.71
PMB
NH
Br
18g
200
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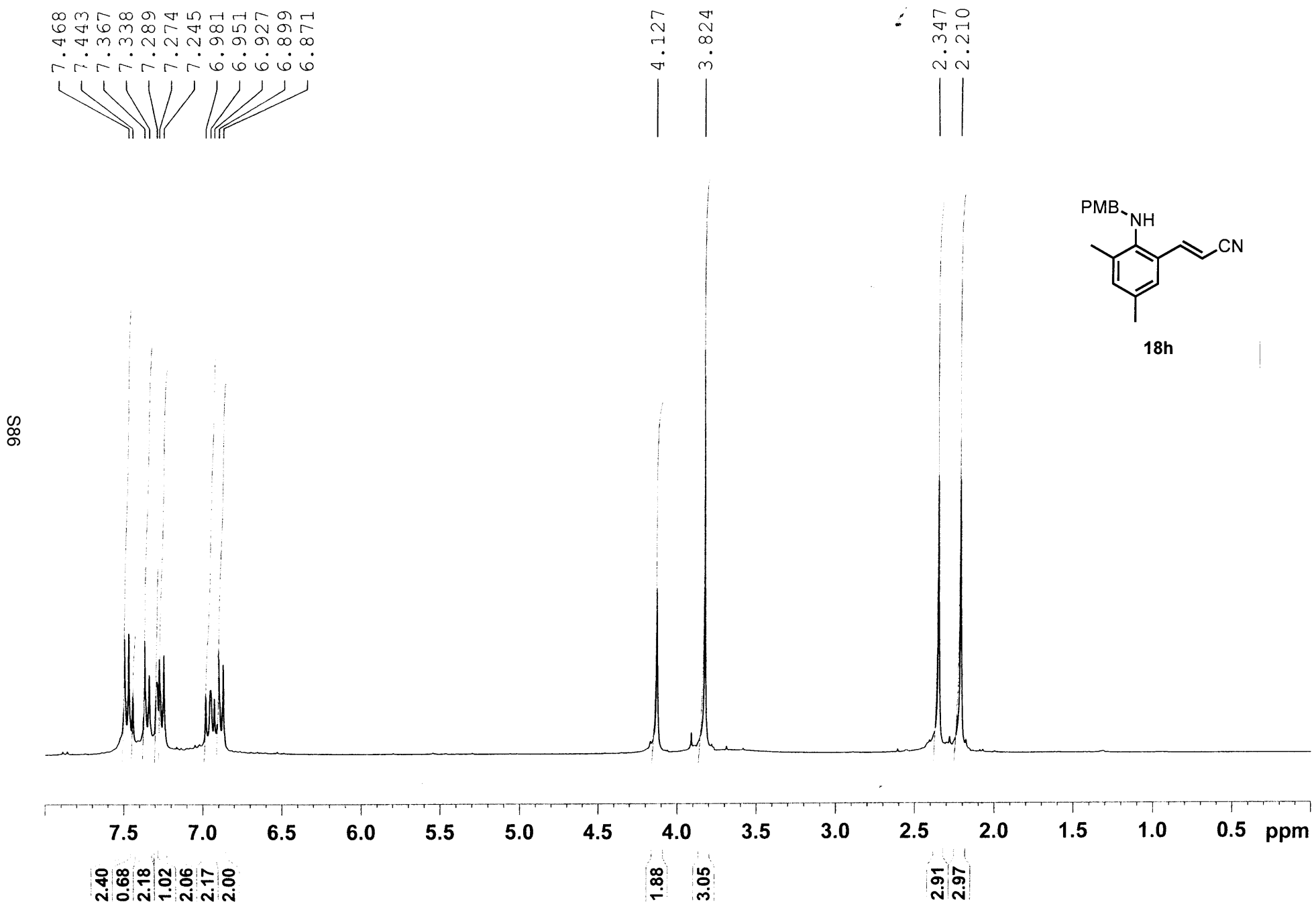
160
140
120
100
80
60
40
20
0
ppm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7.245
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6.951
6.927
6.899
6.871
4.127
3.824
2.347
2.210
PMB
NH
CN
18h
S86
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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2.00
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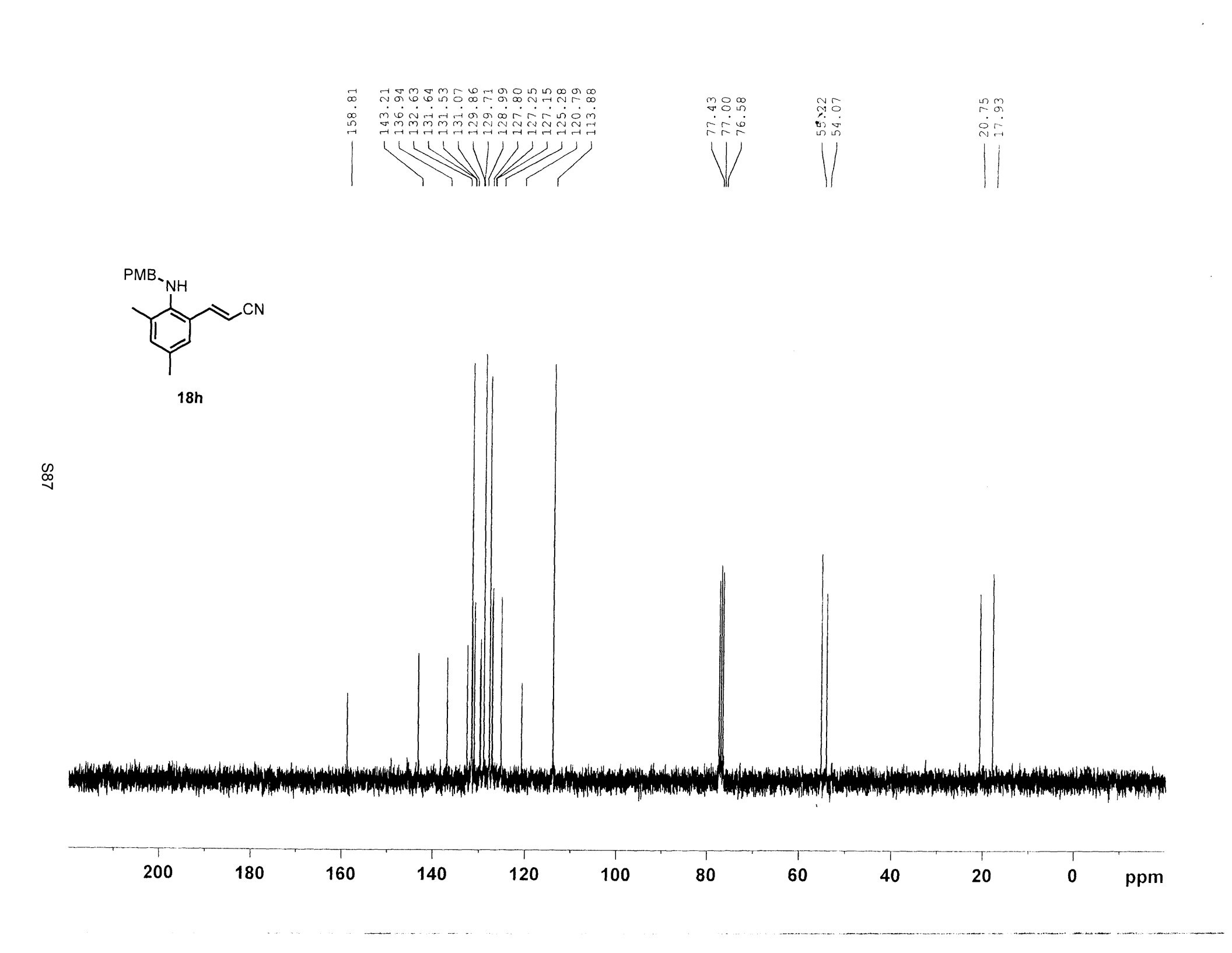
3.05
2.91
2.97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132.63
131.64
131.53
131.07
129.86
129.71
128.99
127.80
127.25
127.15
125.28
120.79
113.88
77.43
77.00
76.58
55.22
54.07
20.75
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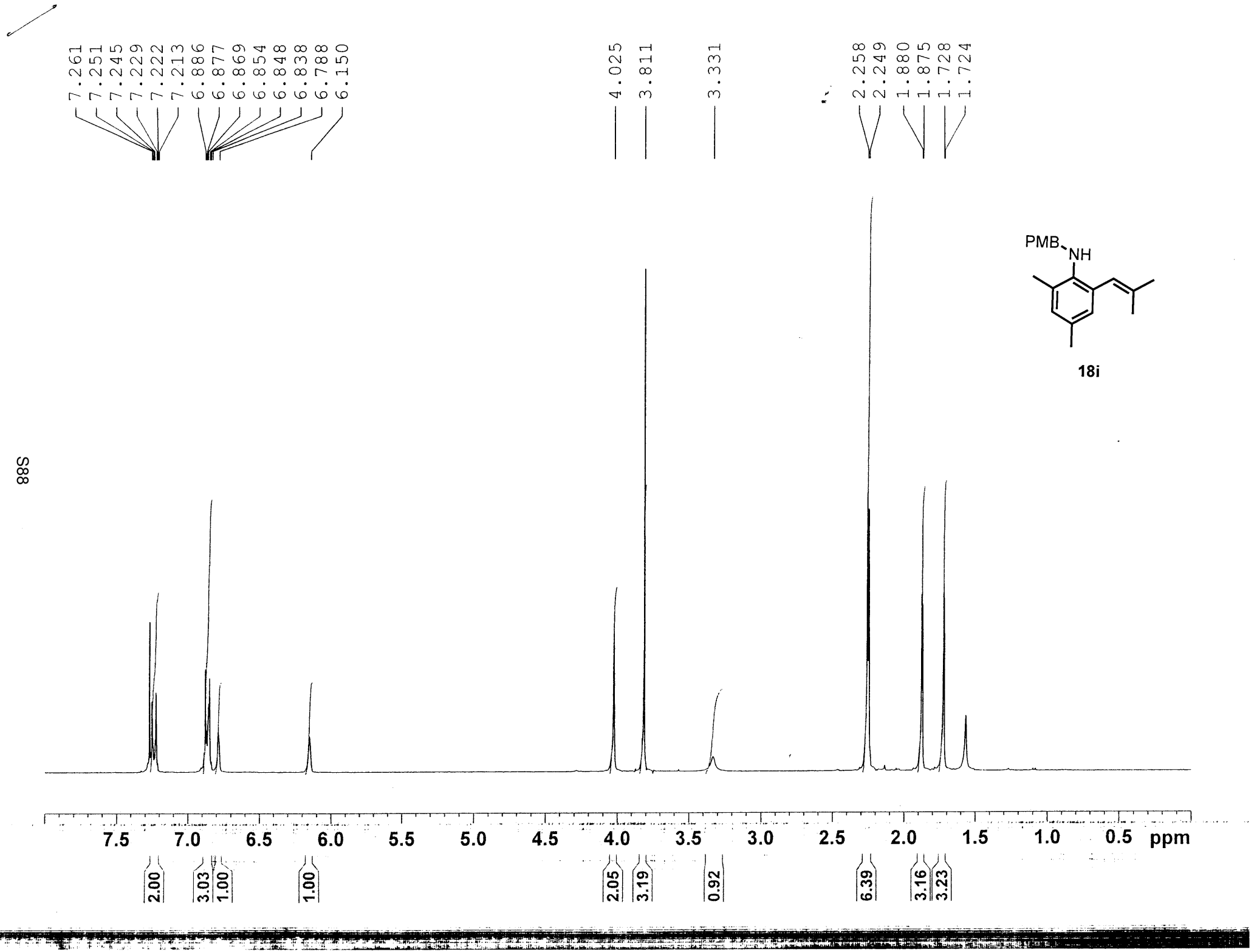
NH
CN
18h
200
180
160
140
120
100
80
60
40
20
0
ppm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7.213
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6.854
6.848
6.838
6.788
6.150
4.025
3.811
3.331
2.258
2.249
1.880
1.875
1.728
1.724
PMB
NH
18i
S88
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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1.00
1.00
2.05
3.19
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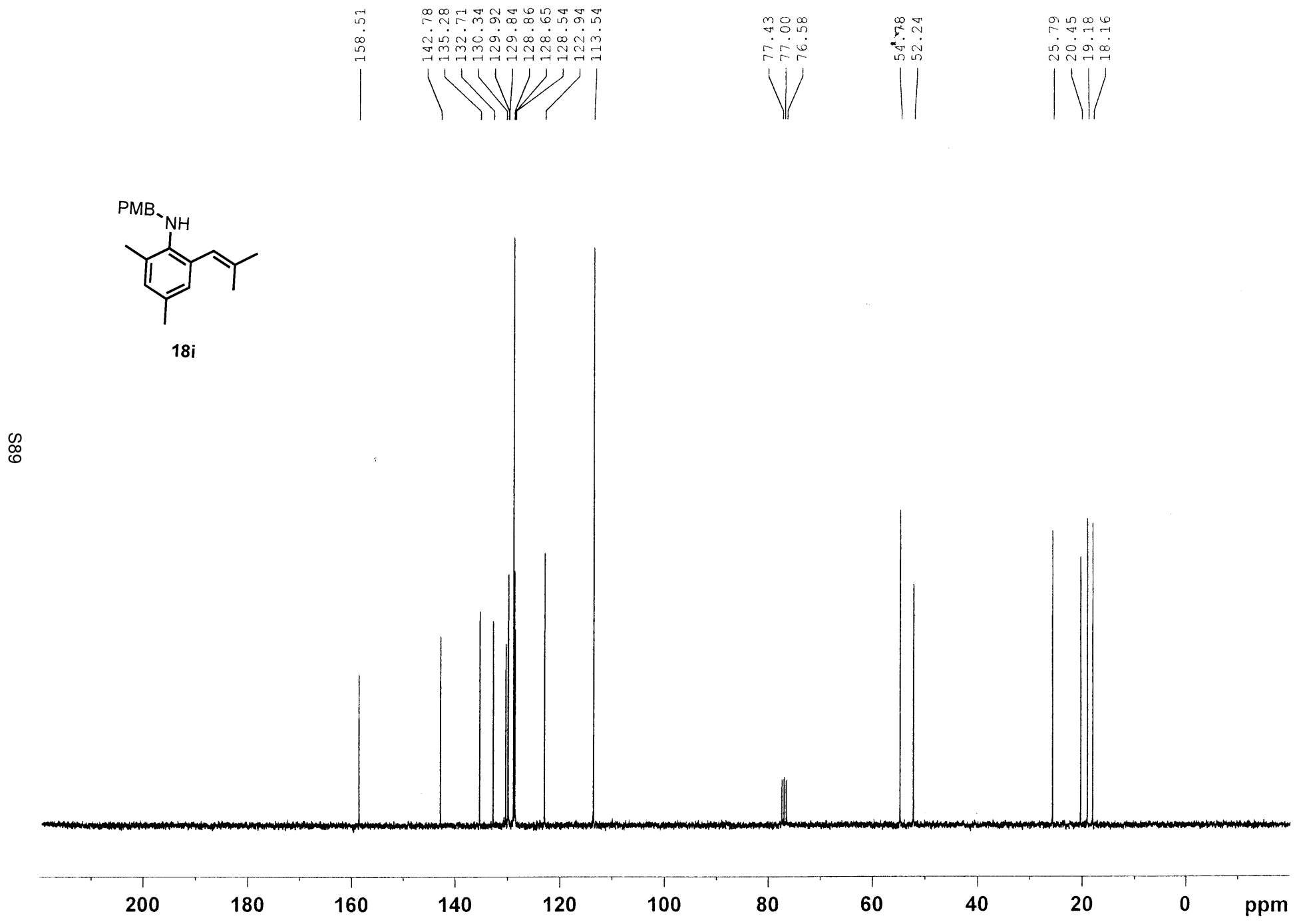
3.16
3.23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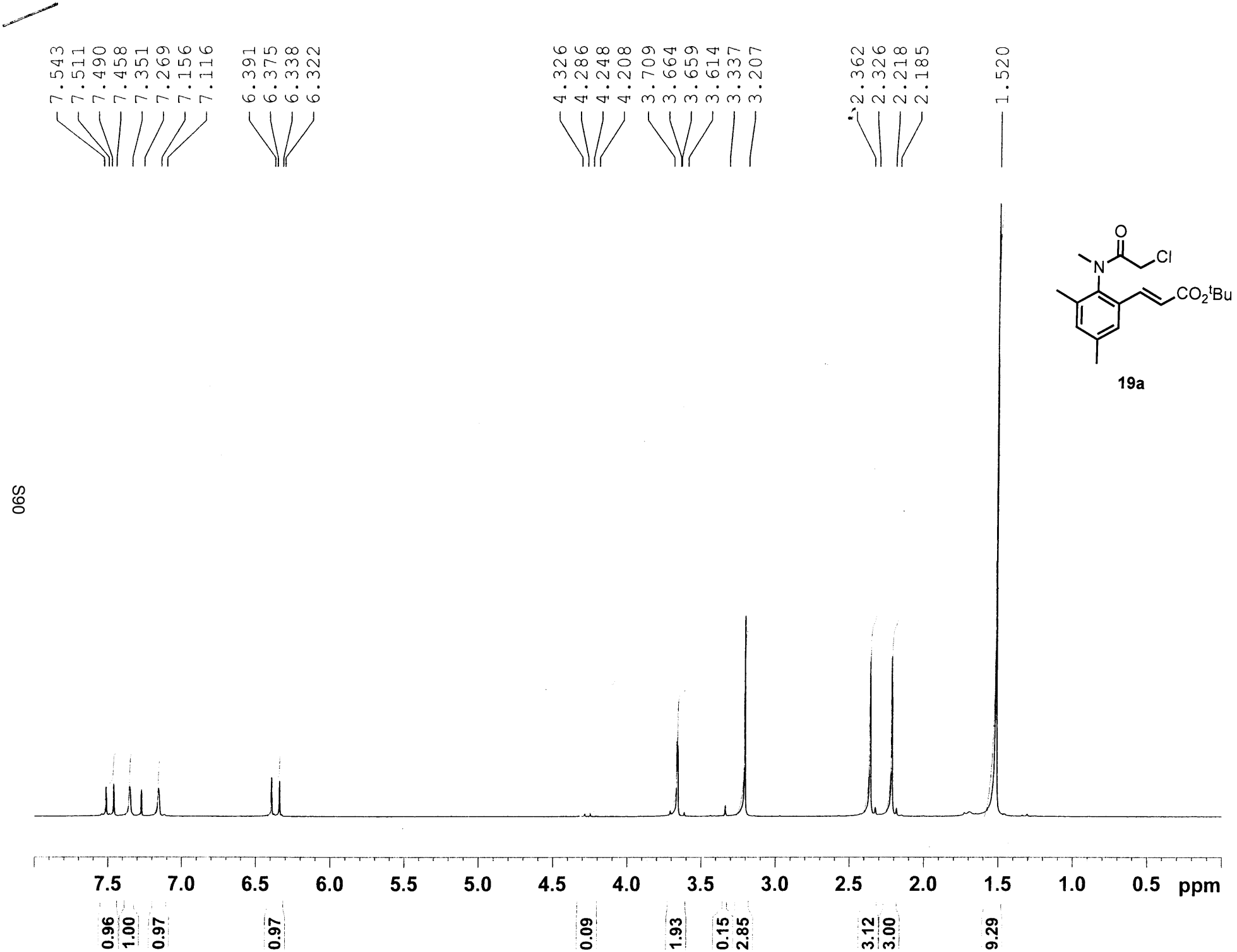
129.84
128.86
128.65
128.54
122.94
113.54
77.43
77.00
76.58
54.78
52.24
25.79
20.45
19.18
18.16
PMB
NH
18i
200
180
160
140
120
100
80
60
40
20
0
ppm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6.375
6.338
6.322
4.326
4.286
4.248
4.208
3.709
3.664
3.659
3.614
3.337
3.207
2.362
2.326
2.218
2.185
1.520
O
N
Cl
CO2tBu
19a
S90
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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0.97
0.97
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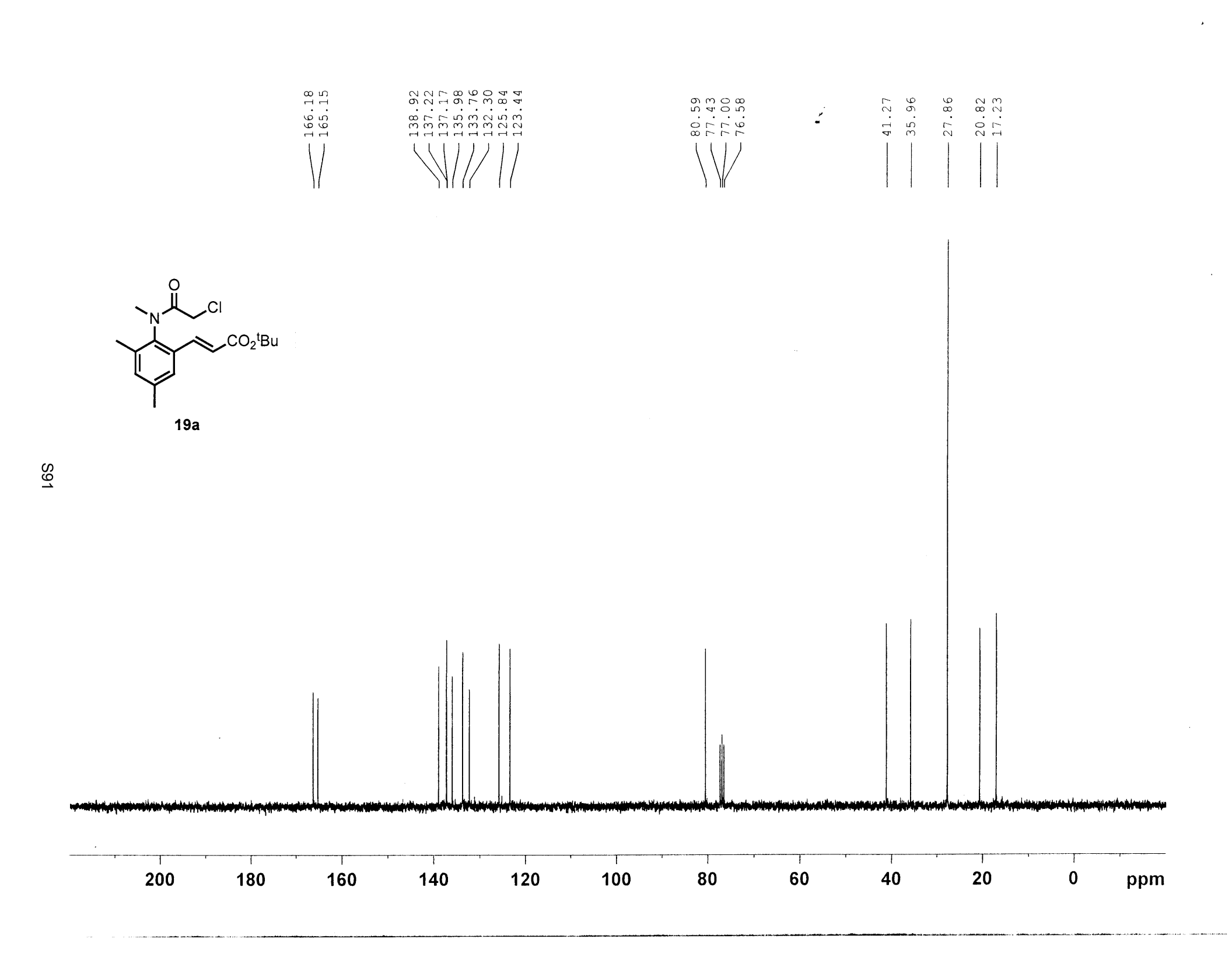
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137.17
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133.76
132.30
125.84
123.44
80.59
77.43
77.00
76.58
41.27
35.96
27.86
20.82
17.23
O
N
Cl
CO2tBu
19a
200
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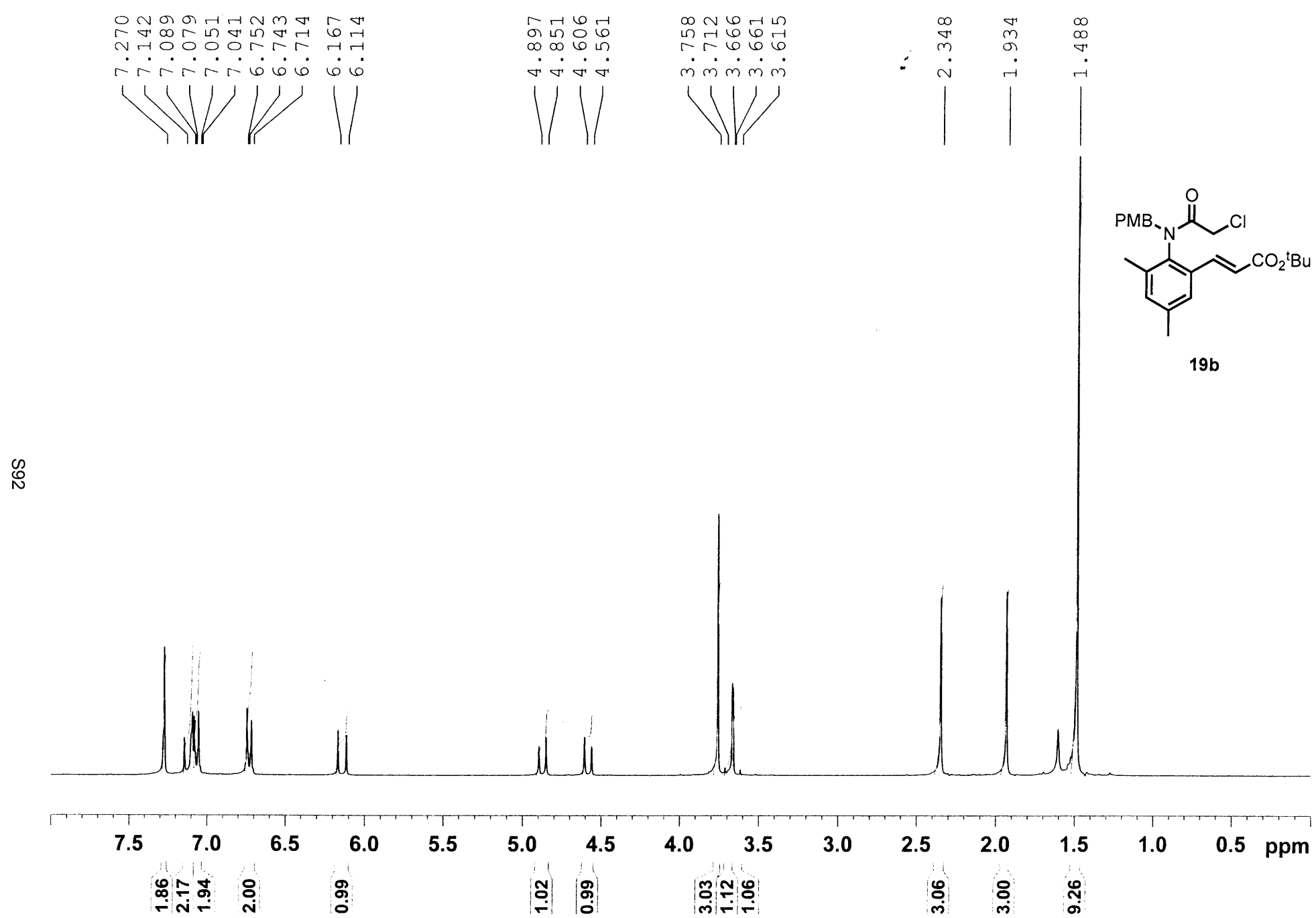
160
140
120
100
80
60
40
20
0
ppm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4.851
4.606
4.561
3.758
3.712
3.666
3.661
3.615
2.348
1.934
1.488
PMB
N
O
Cl
CO2tBu
19b
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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1.02
0.99
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1.12
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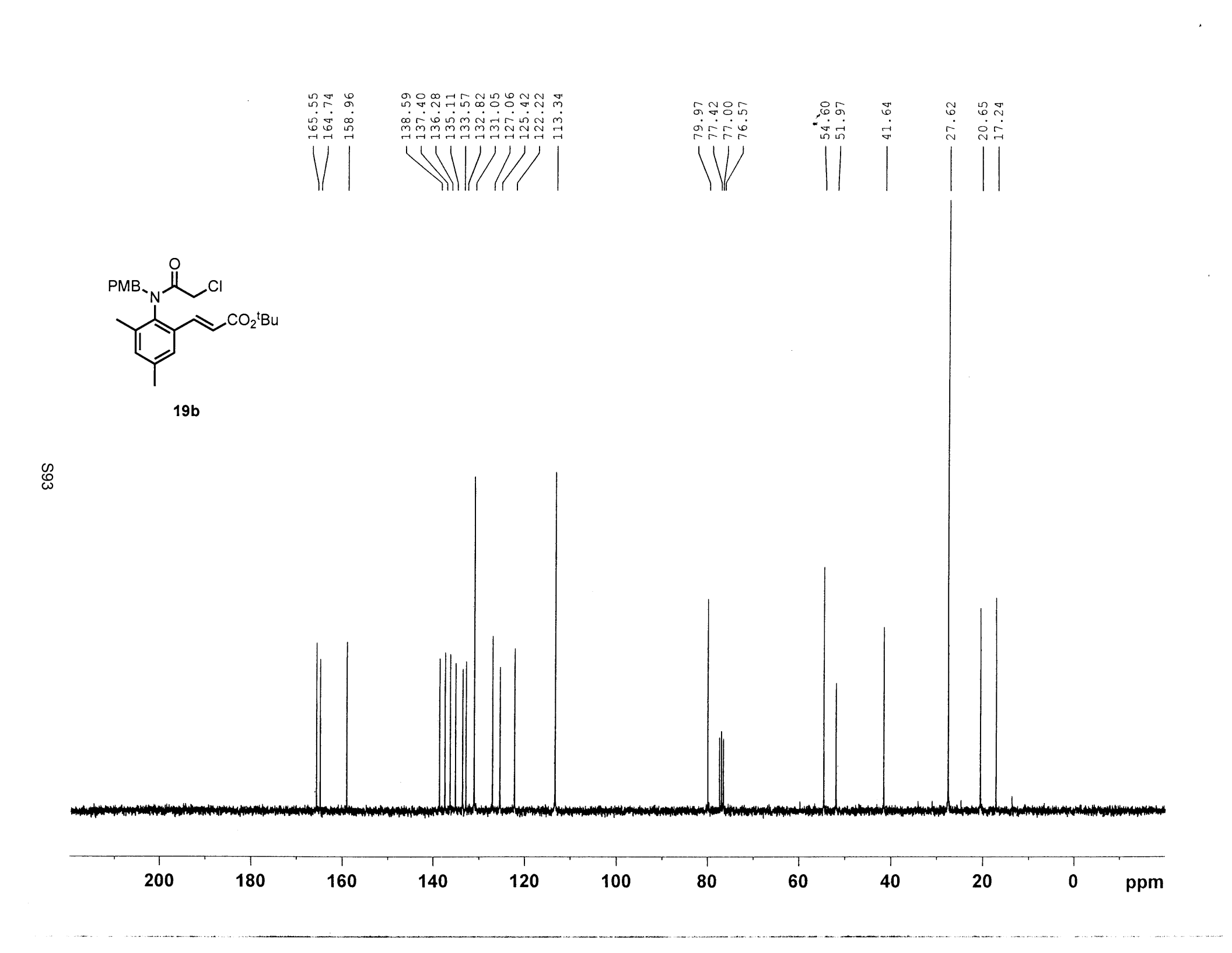
3.06
3.00
9.26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133.57
132.82
131.05
127.06
125.42
122.22
113.34
79.97
77.42
77.00
76.57
54.60
51.97
41.64
27.62
20.65
17.24
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O
Cl
CO2tBu
19b
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120
100
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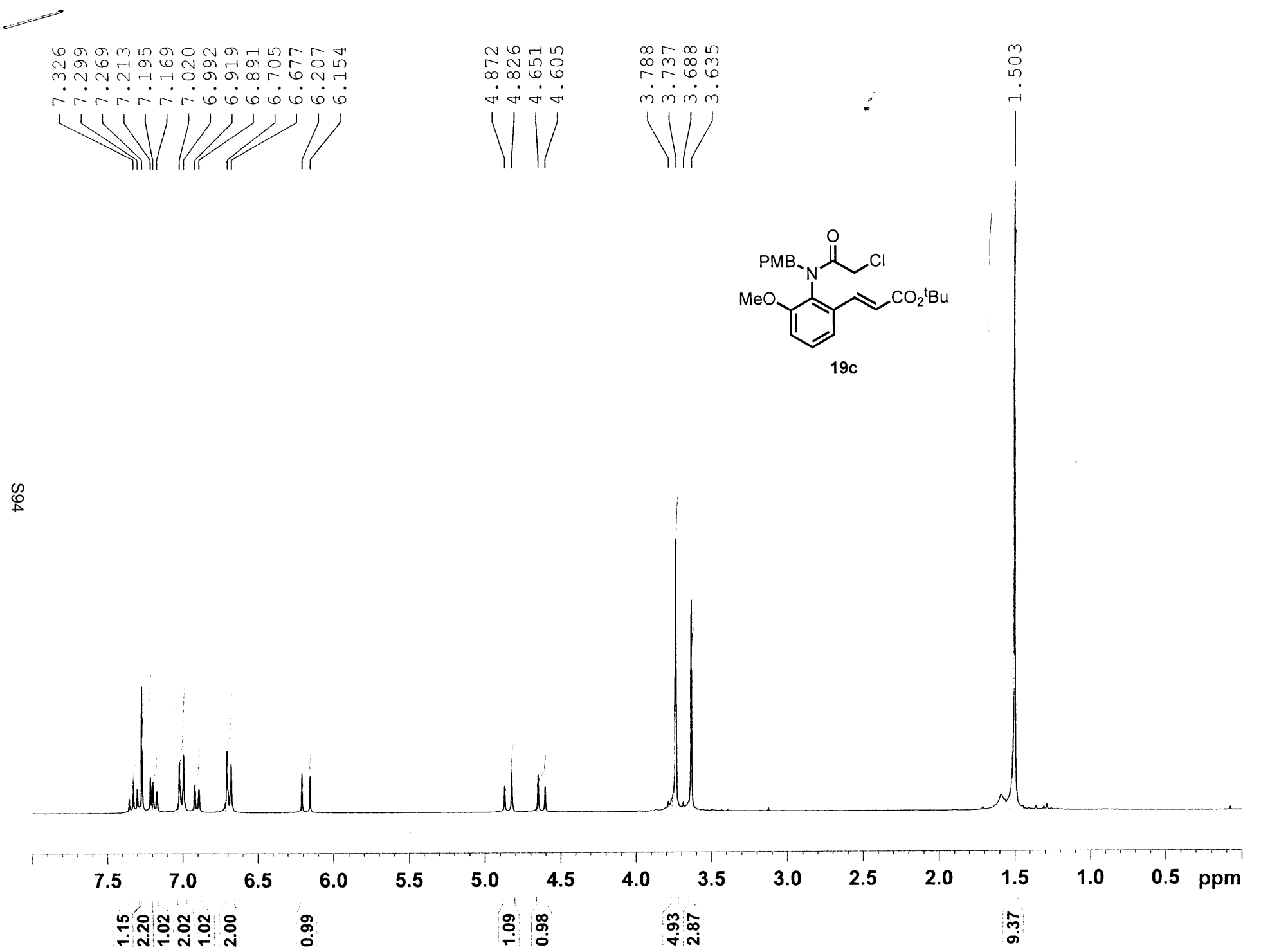
60
40
20
0
ppm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6.207
6.154
4.872
4.826
4.651
4.605
3.788
3.737
3.688
3.635
1.503
PMB
N
O
Cl
MeO
CO2tBu
19c
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.20
1.02
2.02
1.02
2.00
0.99
1.09
0.98
4.93
2.87
9.37

166.69
165.14
158.99
155.52
137.31
134.63
131.20
129.85
127.75
127.64
123.27
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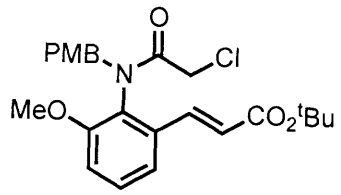
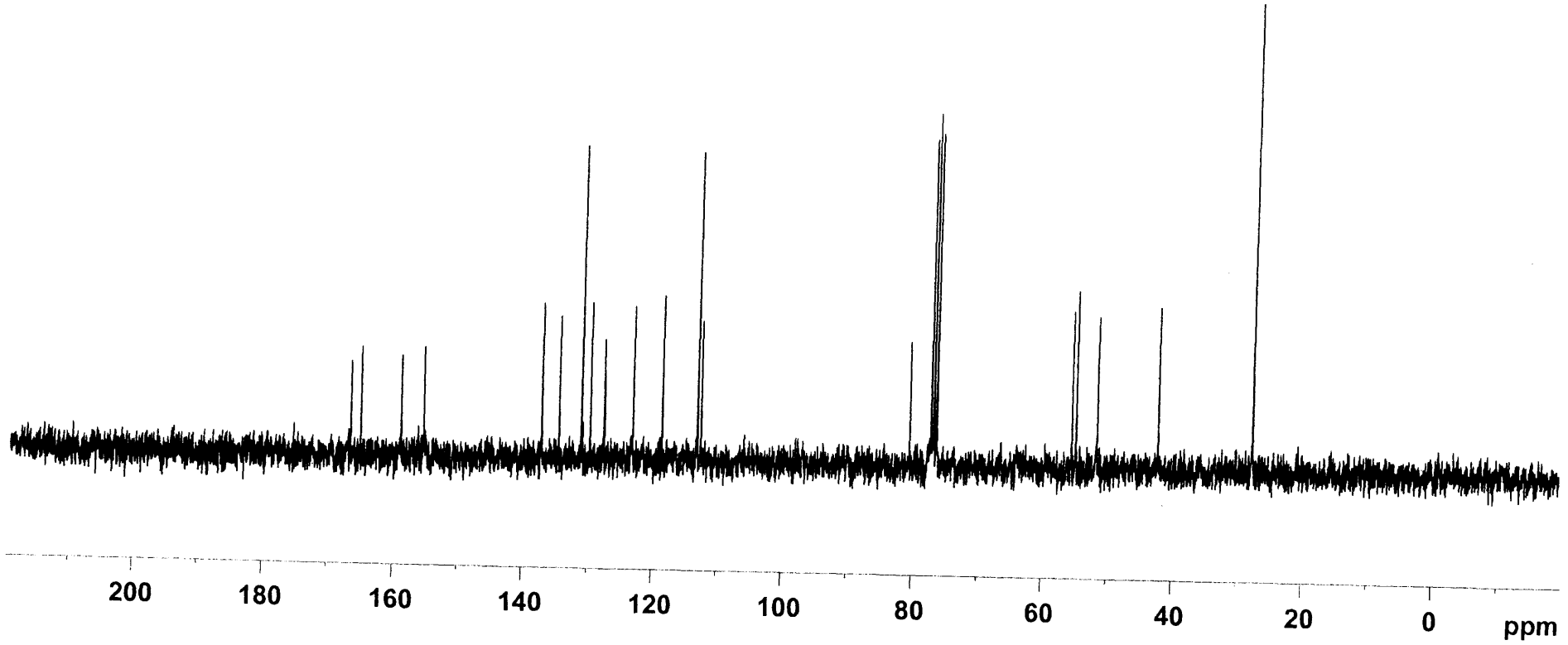
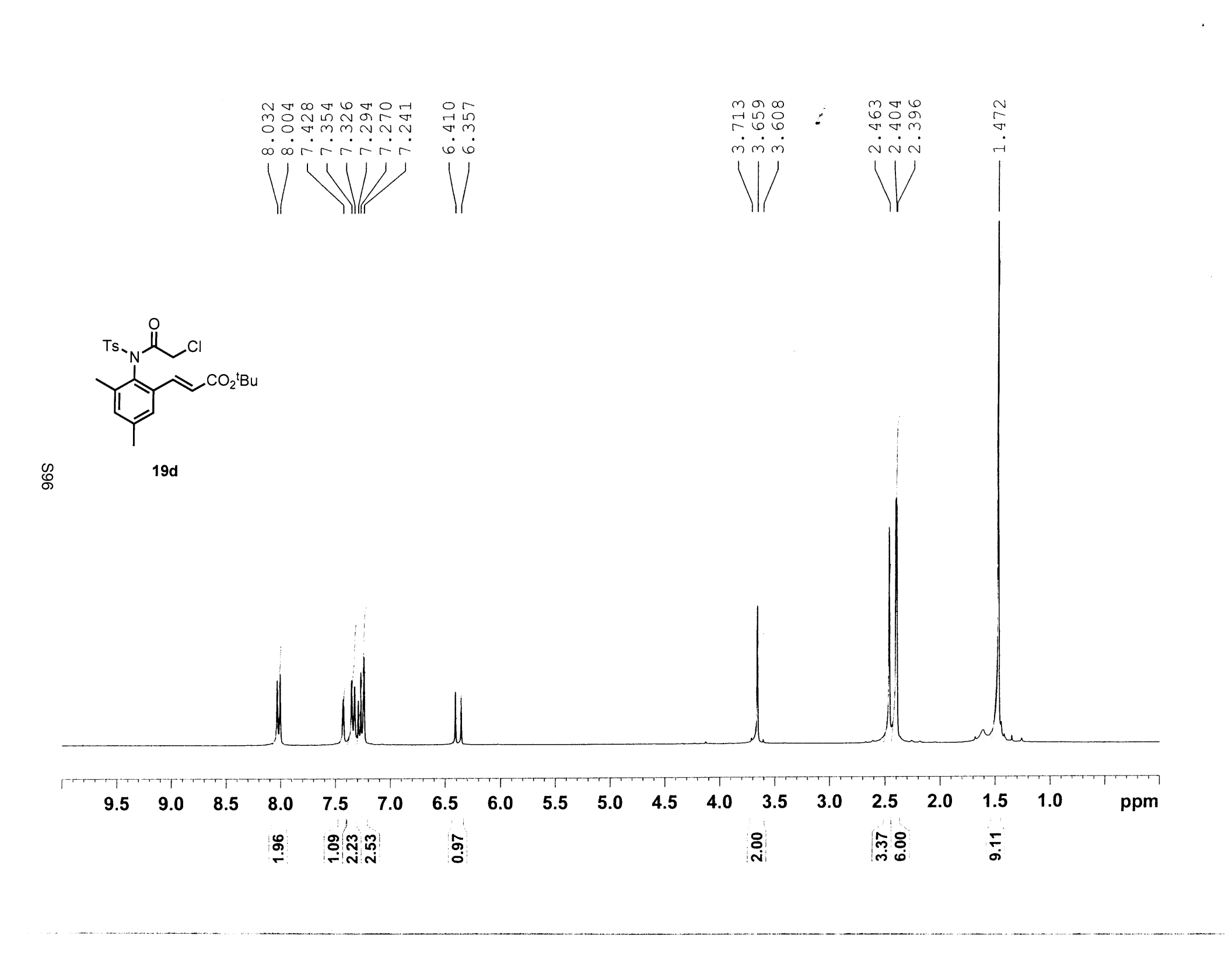
55.01
51.80
42.46
27.96



19c

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3.659
3.608
2.463
2.404
2.396
1.472
Ts
N
O
Cl
CO2tBu
19d
S96
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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ppm
1.96
1.09
2.23
2.53
0.97
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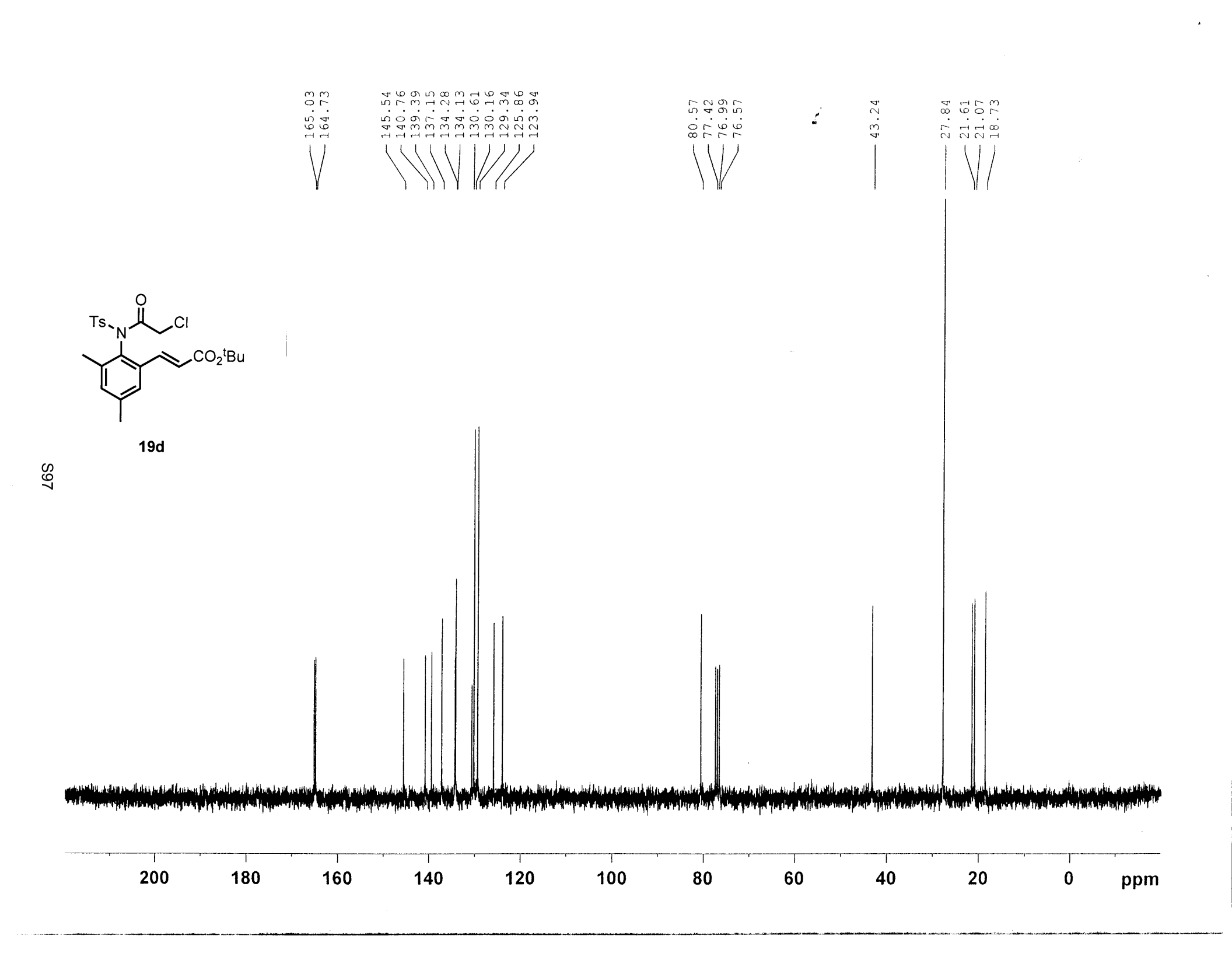
3.37
6.00
9.11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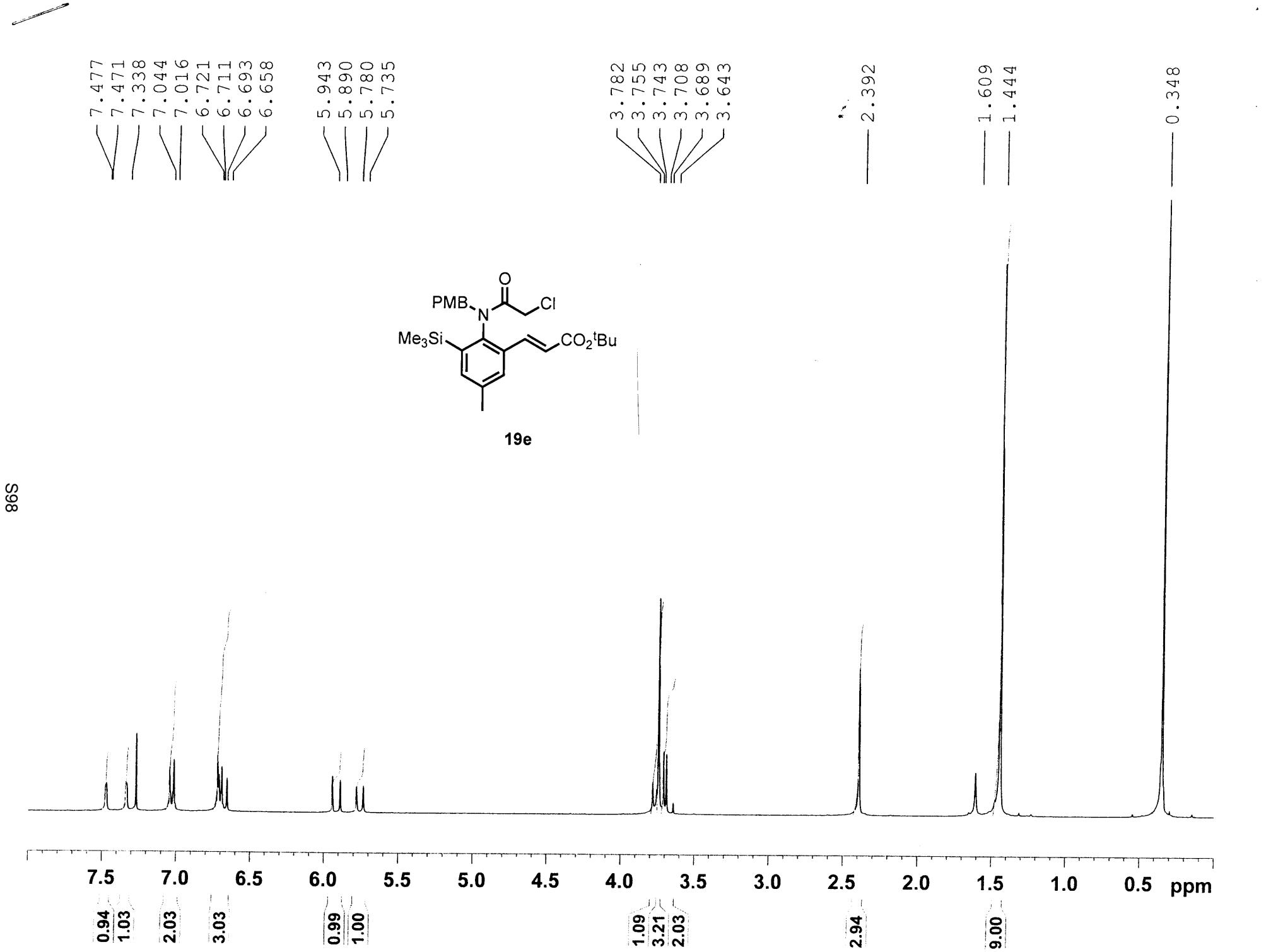
134.13
130.61
130.16
129.34
125.86
123.94
80.57
77.42
76.99
76.57
43.24
27.84
21.61
21.07
18.73
Ts
N
O
Cl
CO2tBu
19d
200
180
160
140
120
100
80
60
40
20
0
ppm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5.780
5.735
3.782
3.755
3.743
3.708
3.689
3.643
2.392
1.609
1.444
0.348
PMB
N
O
Cl
Me3Si
CO2tBu
19e
86S
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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ppm
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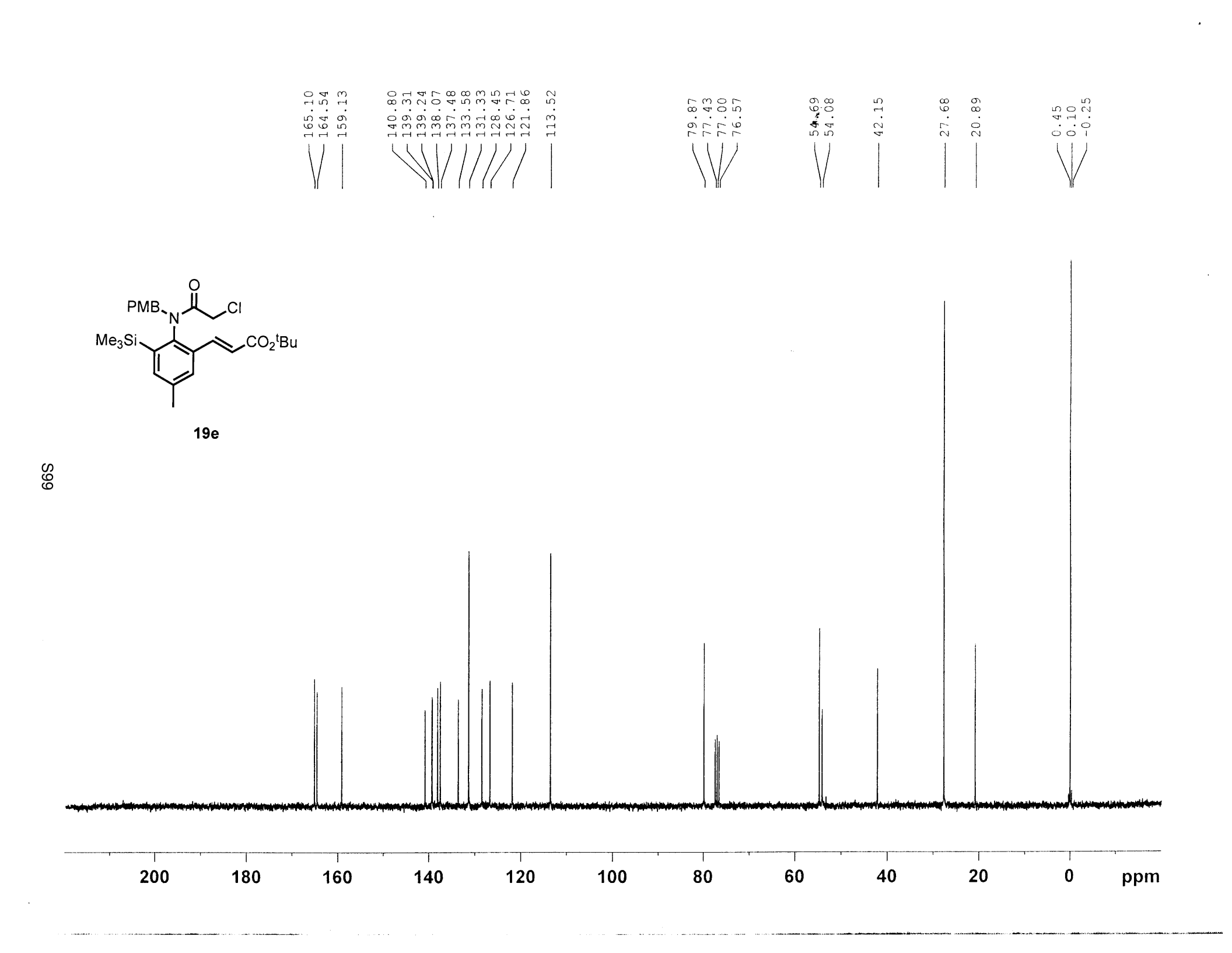
2.03
3.03
0.99
1.00
1.09
3.21
2.03
2.94
9.00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131.33
128.45
126.71
121.86
113.52
79.87
77.43
77.00
76.57
54.69
54.08
42.15
27.68
20.89
0.45
0.10
-0.25
O
PMB
N
Cl
Me3Si
CO2tBu
19e
S99
200
180
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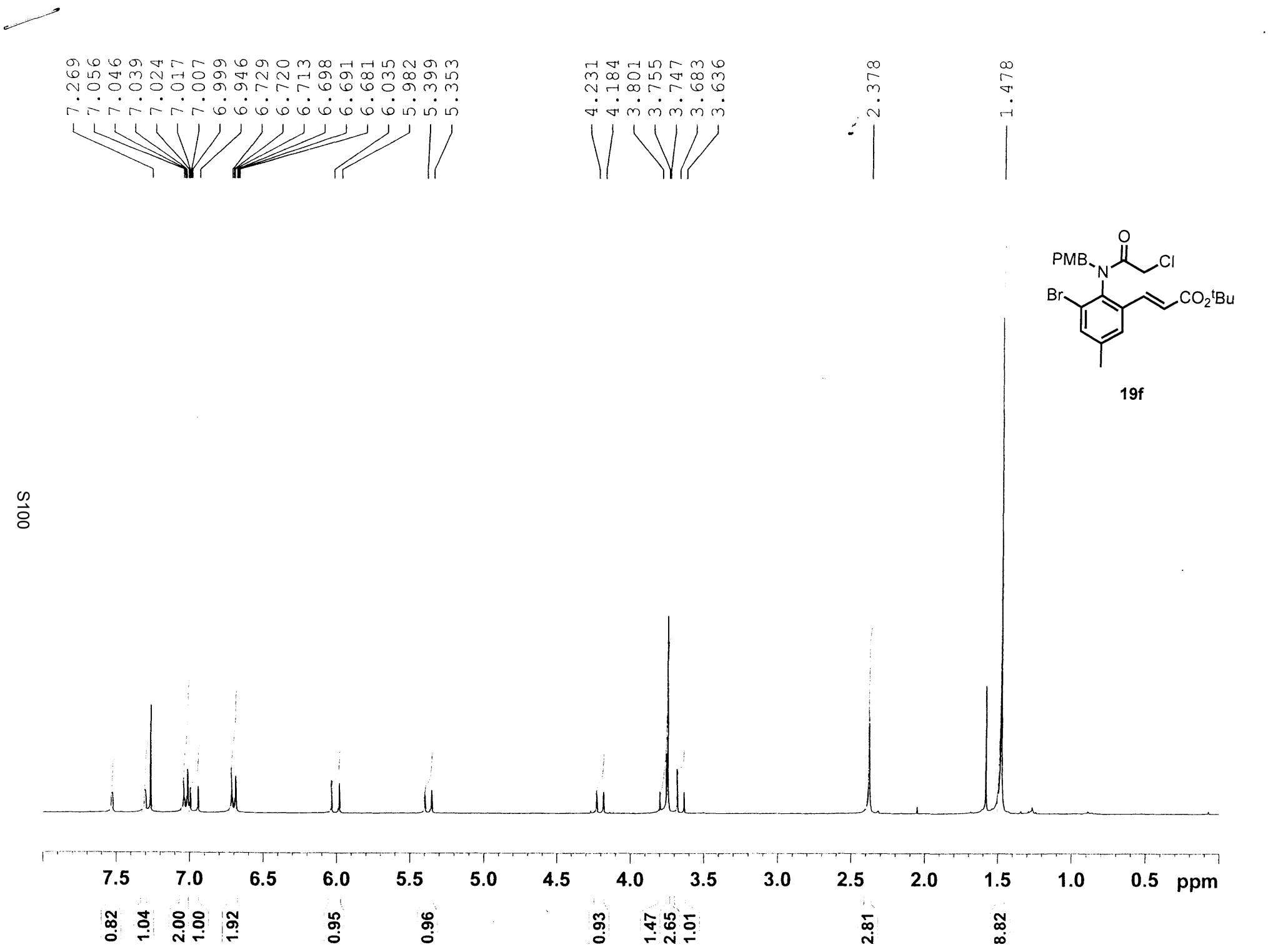
140
120
100
80
60
40
20
0
ppm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6.698
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5.982
5.399
5.353
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4.184
3.801
3.755
3.747
3.683
3.636
2.378
1.478
PMB
N
O
Cl
Br
CO2tBu
19f
S100
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.0
0.5
ppm
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1.00
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0.95
0.96
0.93
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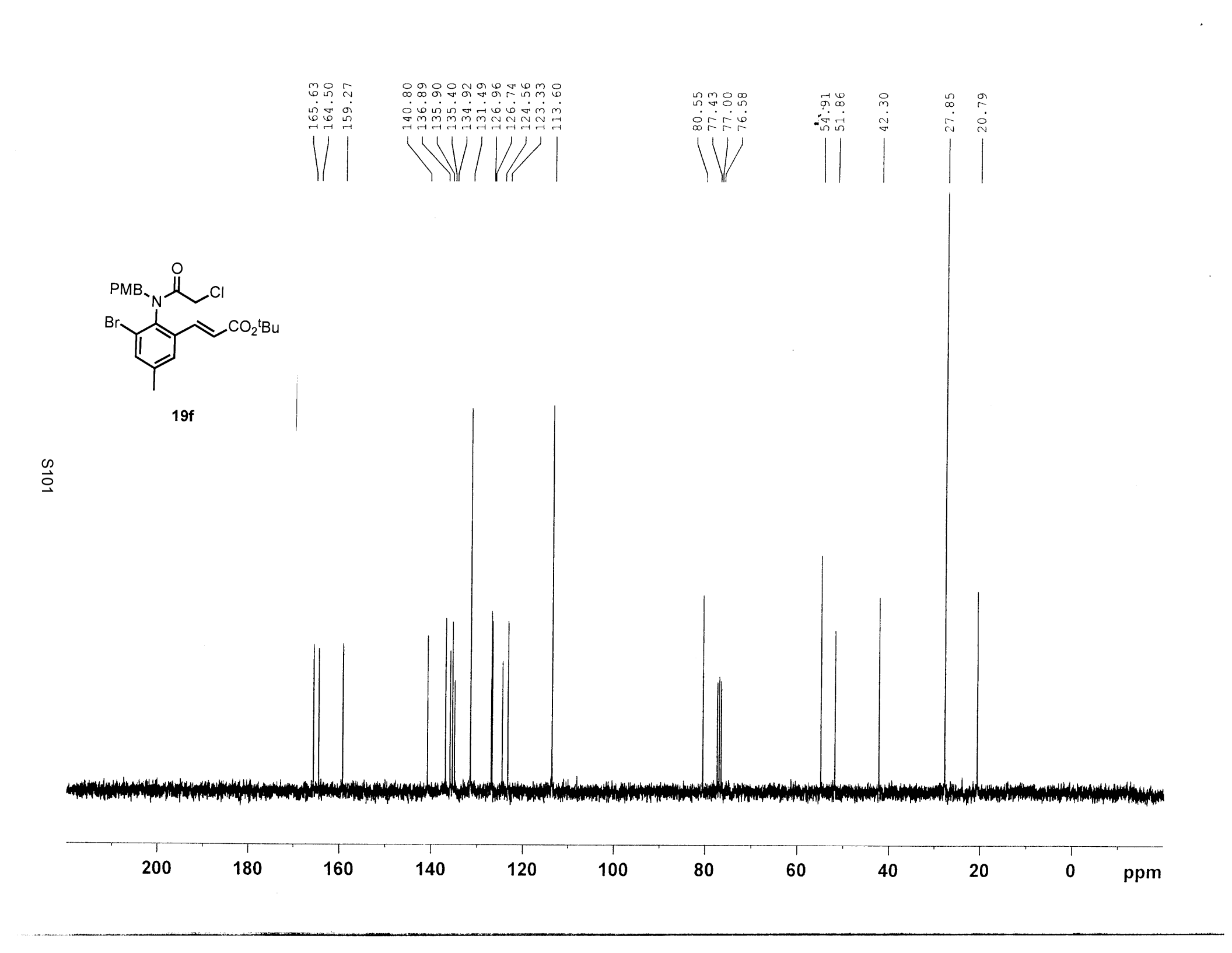
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76.58
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O
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Br
CO2tBu
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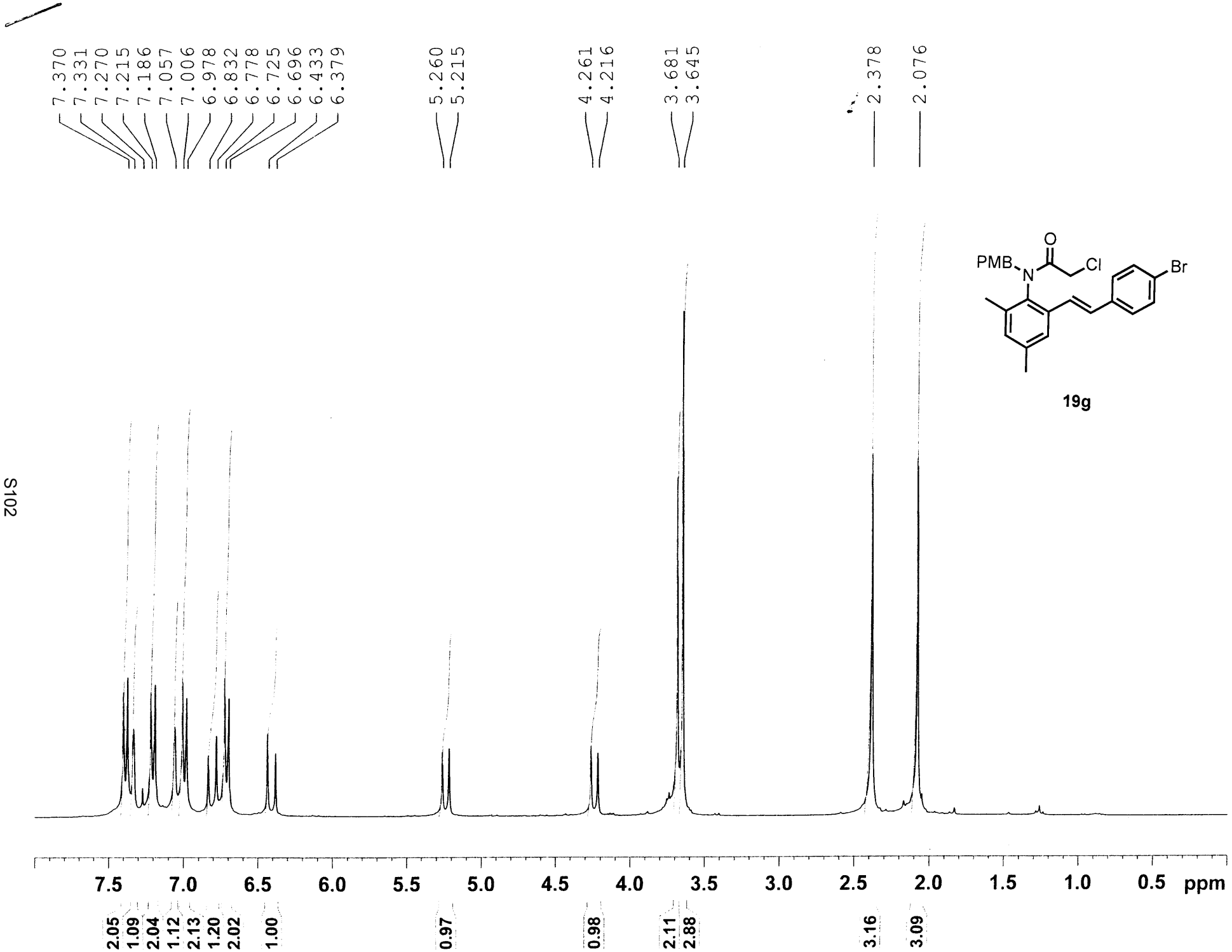
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5.215
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4.216
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3.645
2.378
2.076
PMB
N
O
Cl
Br
19g
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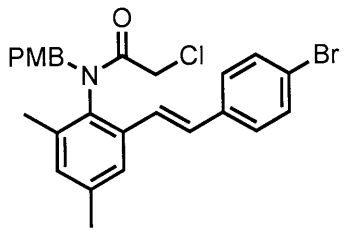
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Br

19g

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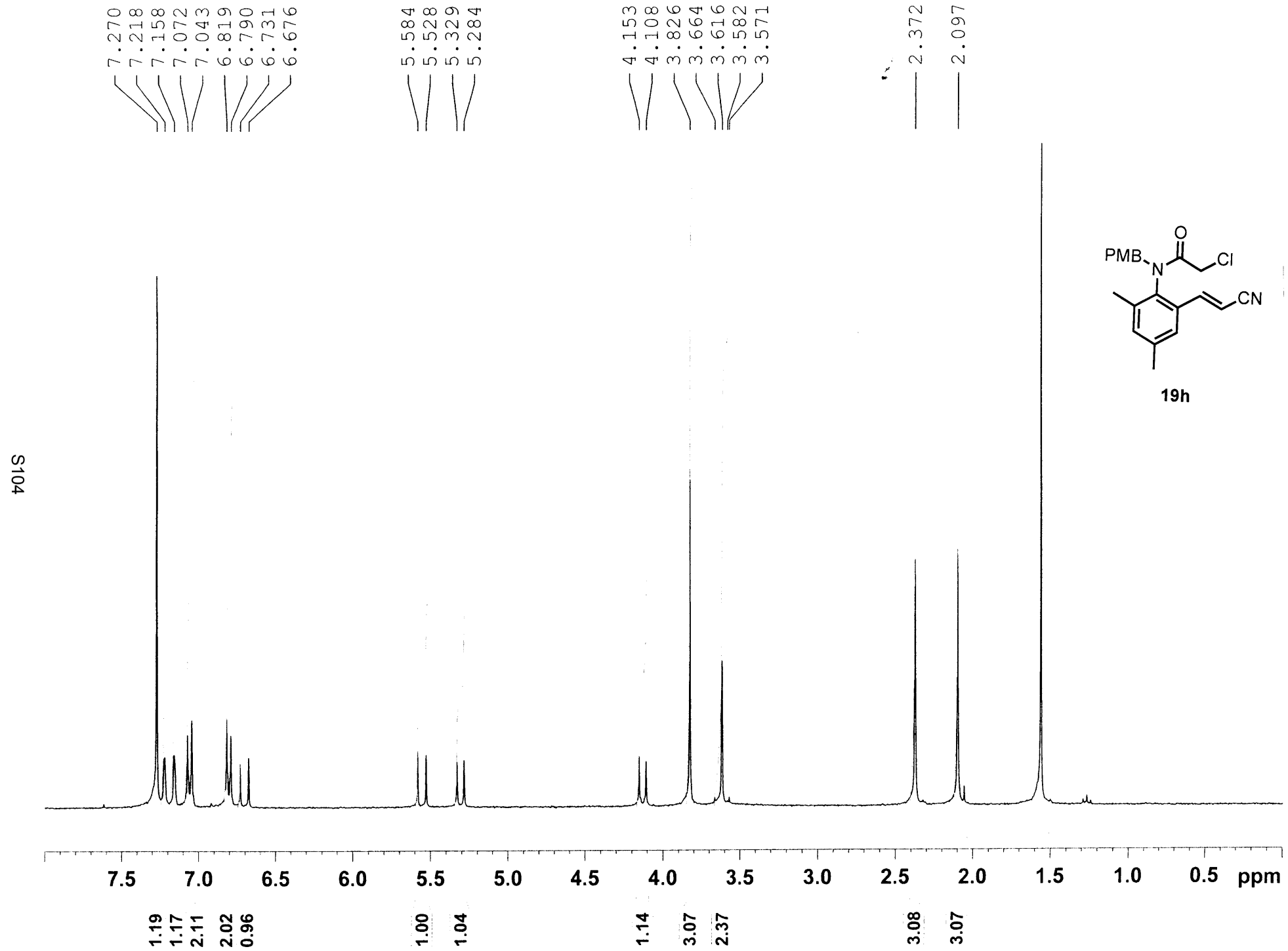
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4.153
4.108
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3.664
3.616
3.582
3.571
2.372
2.097
PMB
N
O
Cl
CN
19h
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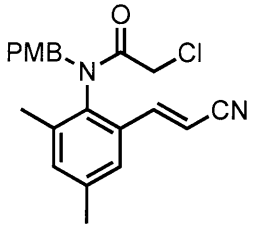
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Cl
CN

19h

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77.42
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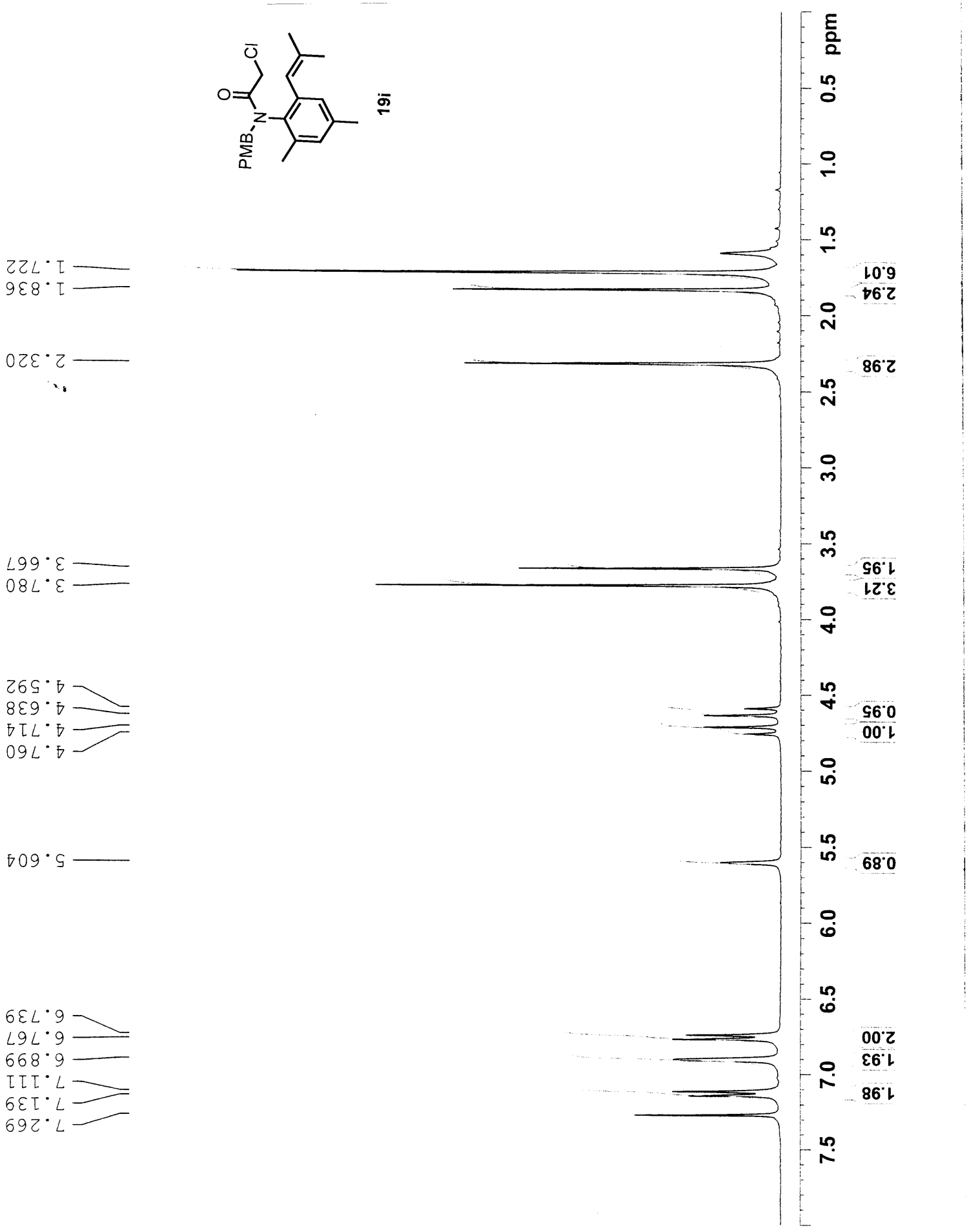
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Cl
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6.0
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1.00
0.89
2.00
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1.98
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1.836
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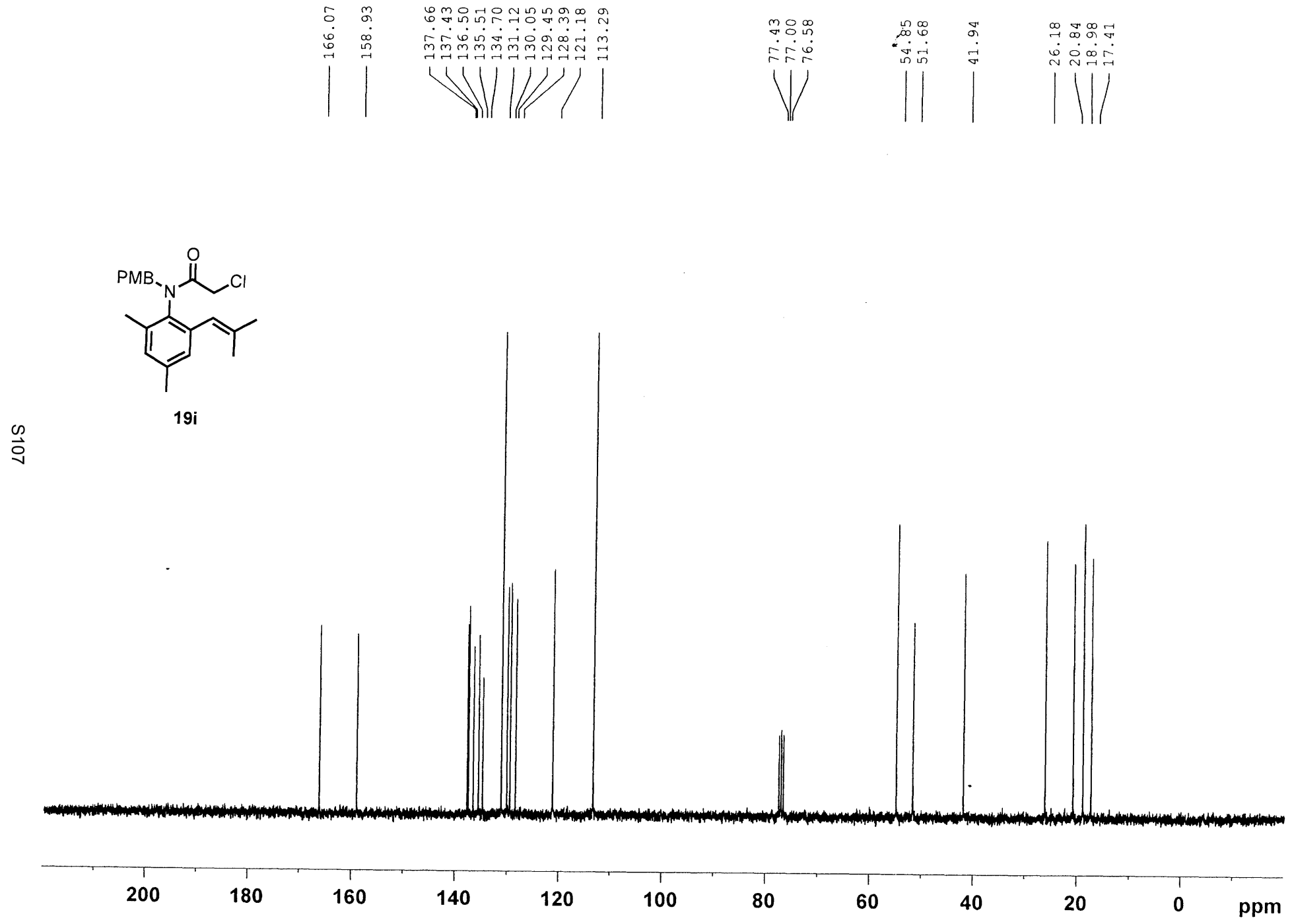
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113.29
77.43
77.00
76.58
54.85
51.68
41.94
26.18
20.84
18.98
17.41
PMB
N
O
Cl
19i
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140
120
100
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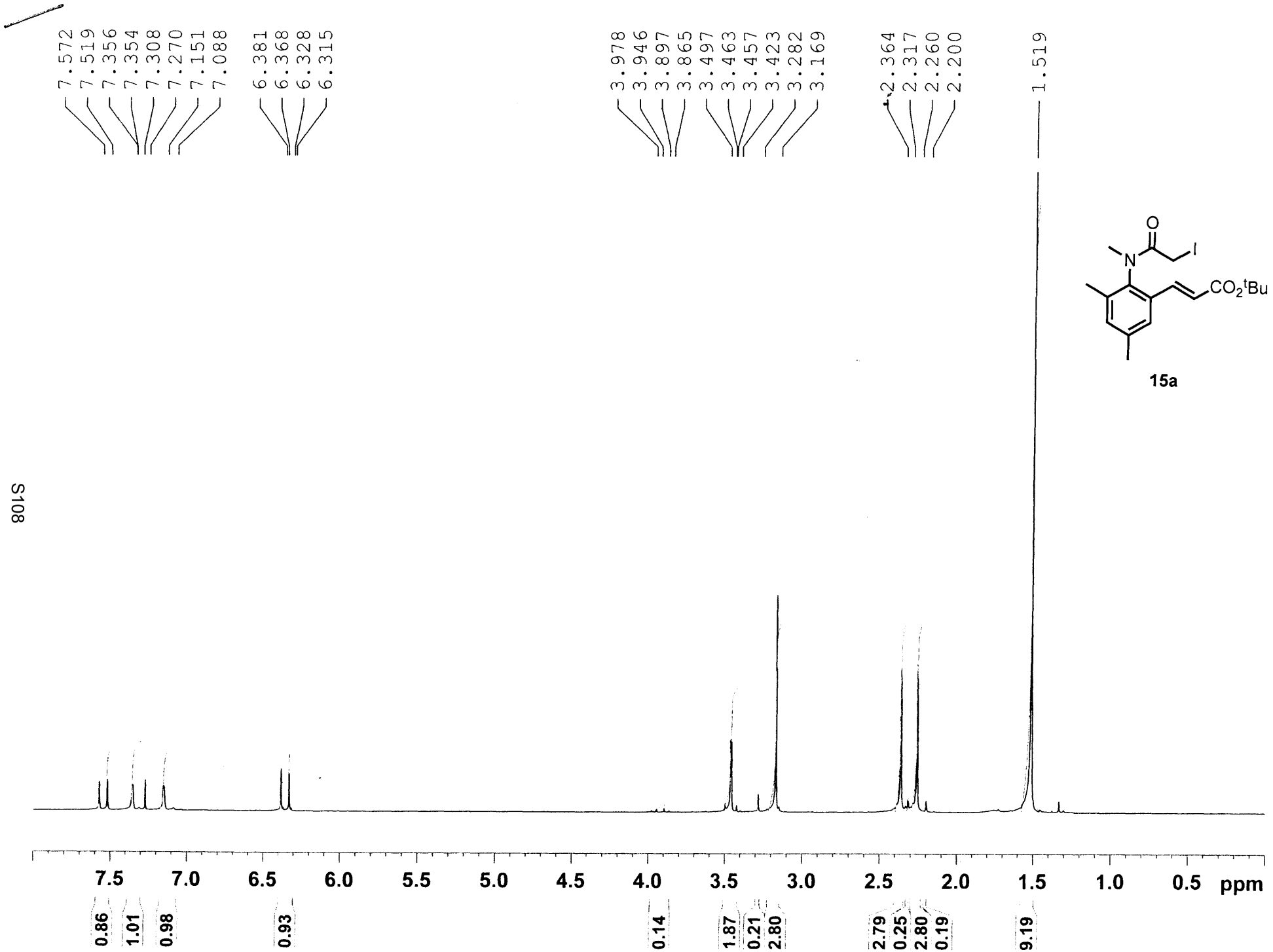
60
40
20
0
ppm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3.865
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3.463
3.457
3.423
3.282
3.169
2.364
2.317
2.260
2.200
1.519
O
N
I
CO2tBu
15a
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6.5
6.0
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5.0
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4.0
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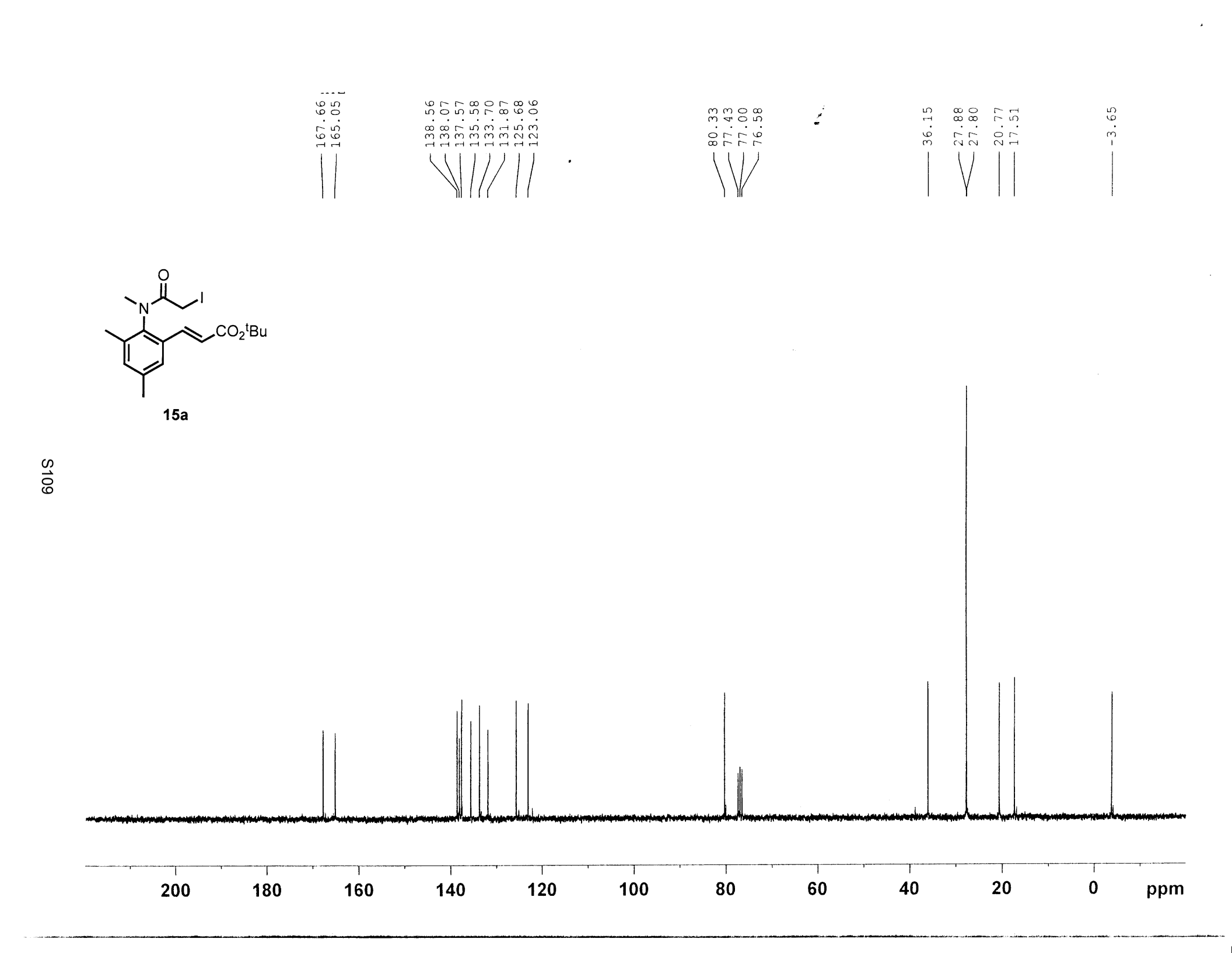
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27.88
27.80
20.77
17.51
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I
CO2tBu
15a
200
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140
120
100
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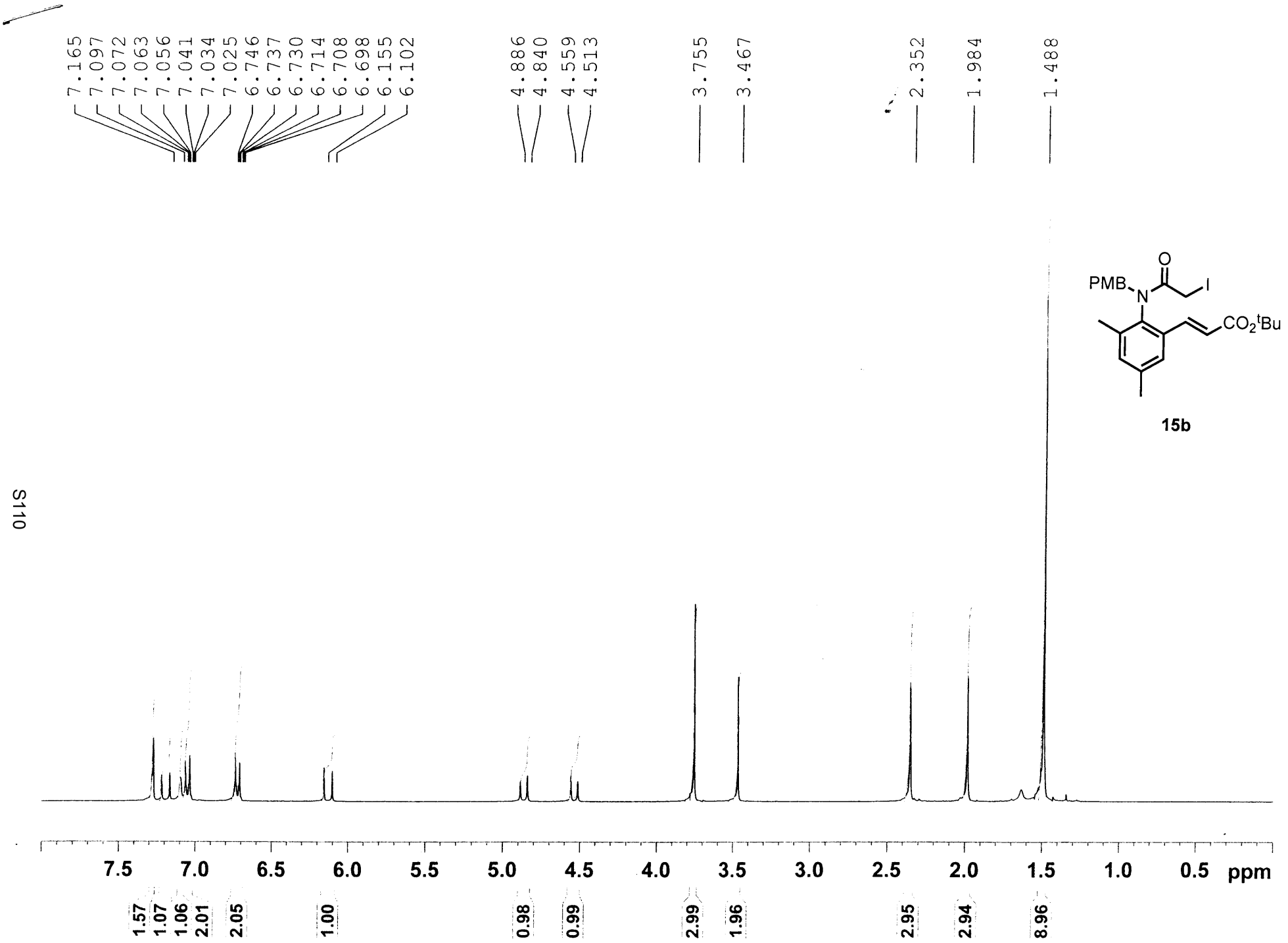
60
40
20
0
ppm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6.698
6.155
6.102
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4.840
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4.513
3.755
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2.352
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1.488
PMB
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O
I
CO2tBu
15b
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6.0
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5.0
4.5
4.0
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ppm
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2.94
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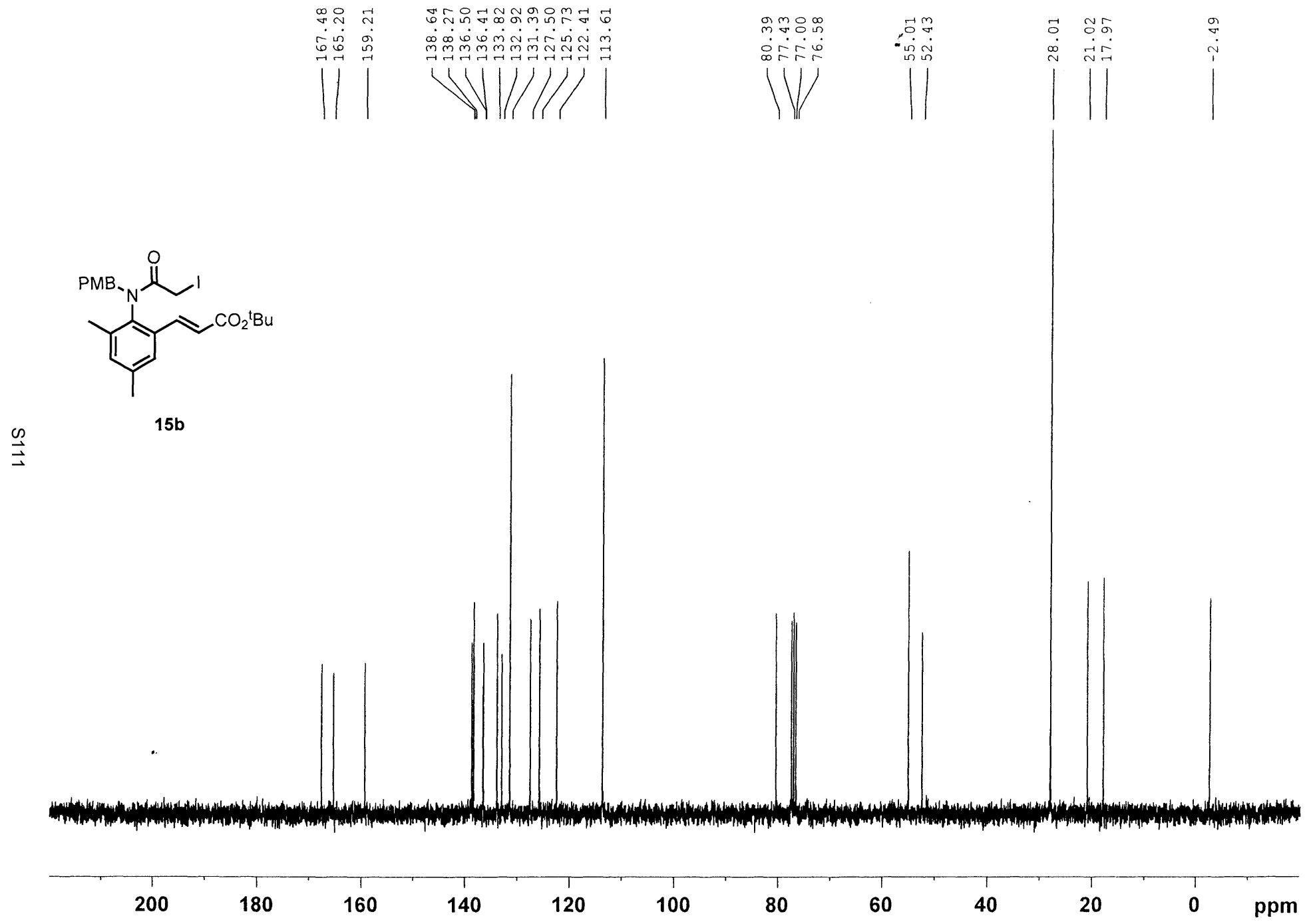
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80.39
77.43
77.00
76.58
55.01
52.43
28.01
21.02
17.97
-2.49
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I
CO2tBu
15b
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120
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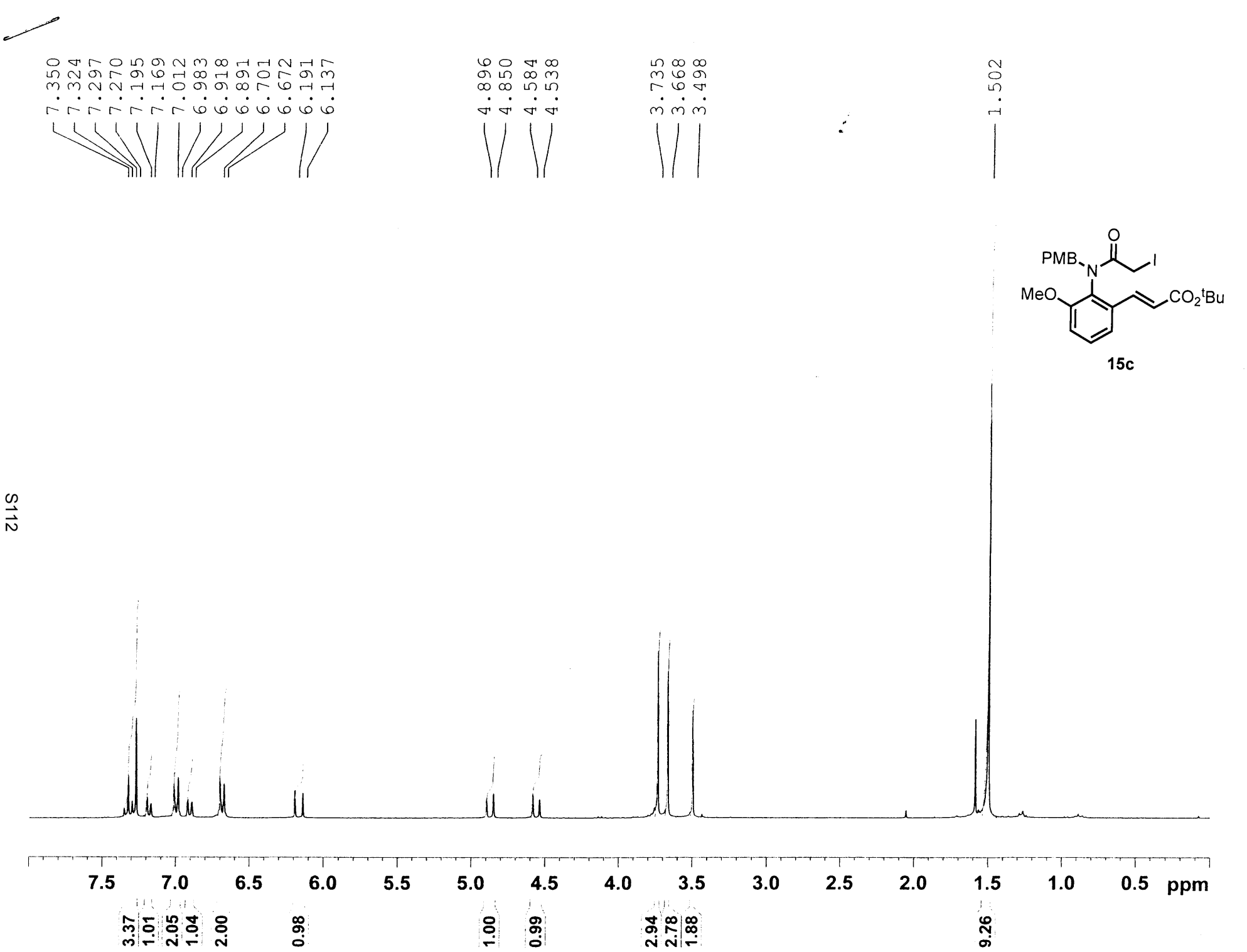
40
20
0
ppm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6.672
6.191
6.137
4.896
4.850
4.584
4.538
3.735
3.668
3.498
1.502
PMB
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O
I
MeO
CO2tBu
15c
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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1.0
0.5
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1.04
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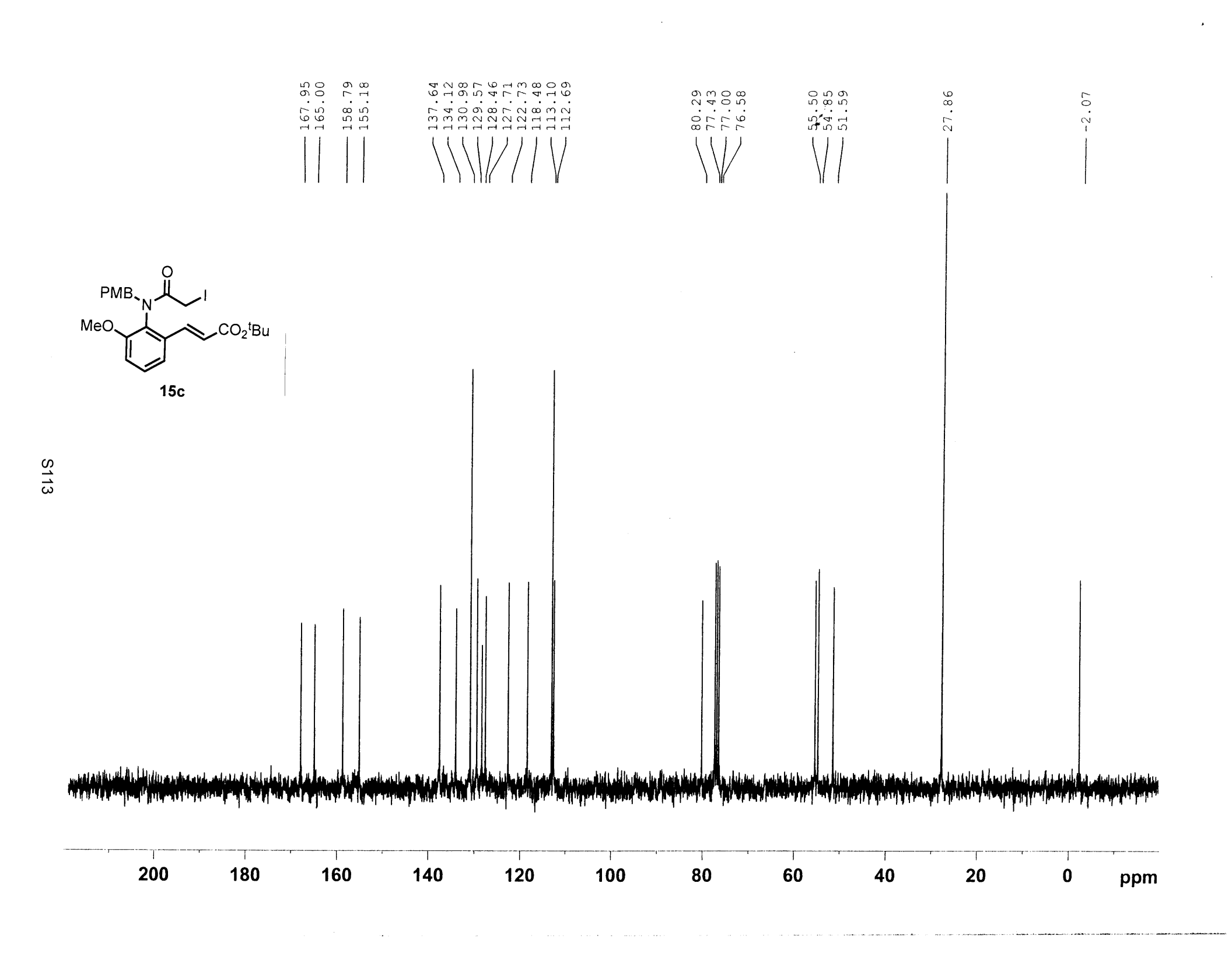
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112.69
80.29
77.43
77.00
76.58
55.50
54.85
51.59
27.86
-2.07
PMB
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MeO
CO2tBu
15c
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120
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20
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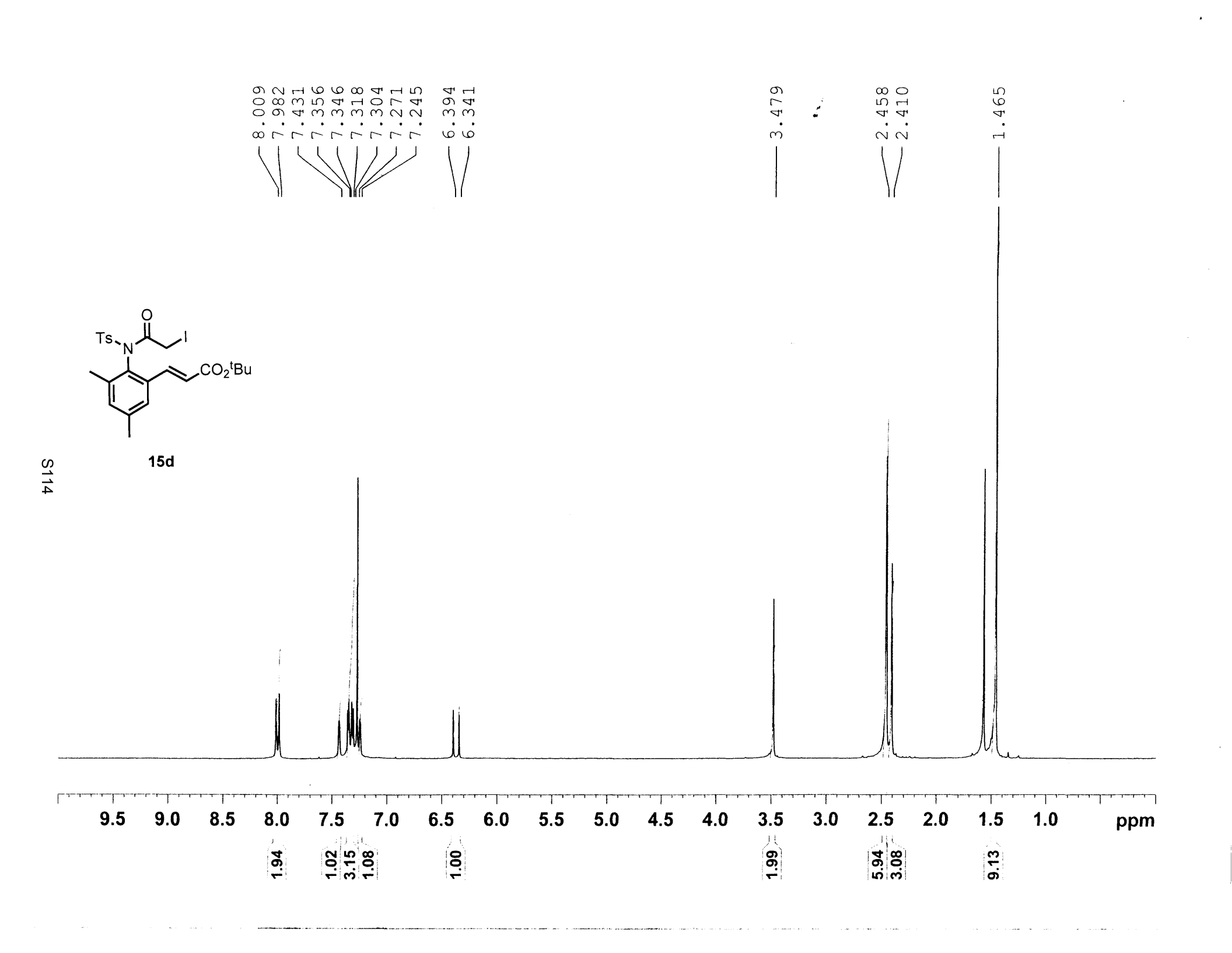
ppm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Ts
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O
I
CO2tBu
15d
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8.5
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7.0
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.00
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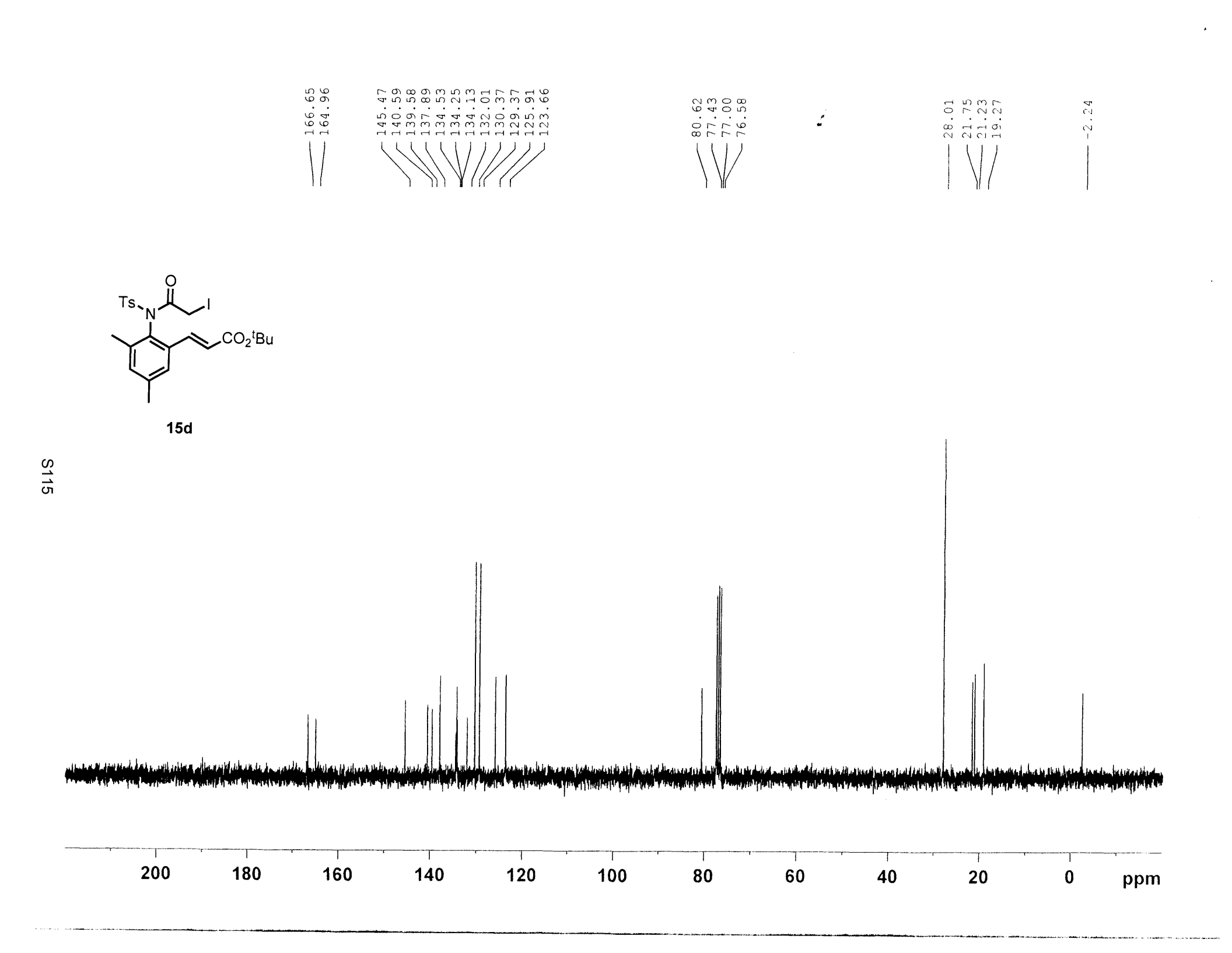
3.08
9.13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77.00
76.58
28.01
21.75
21.23
19.27
-2.24
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I
CO2tBu
15d
200
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120
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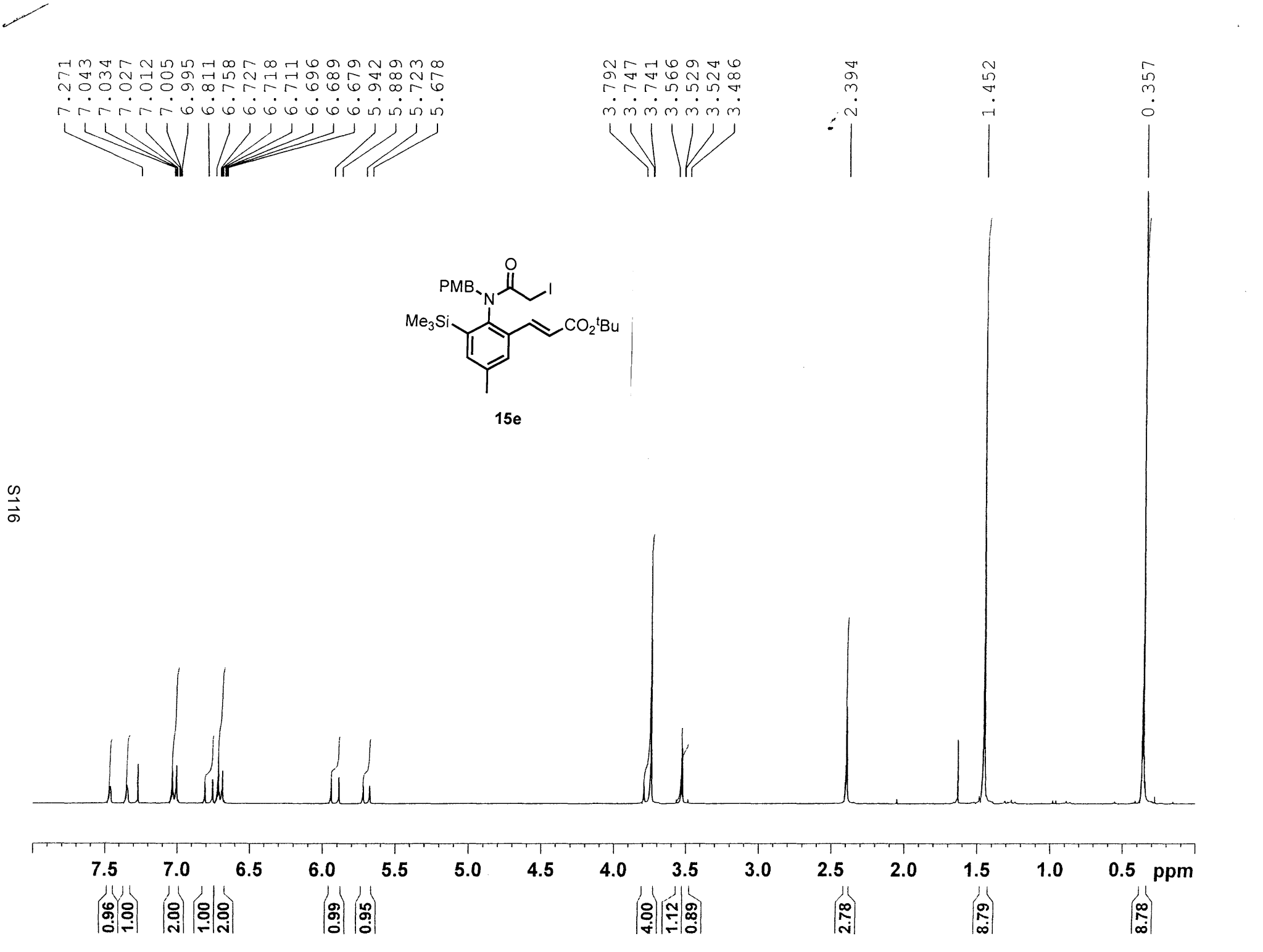
40
20
0
ppm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3.741
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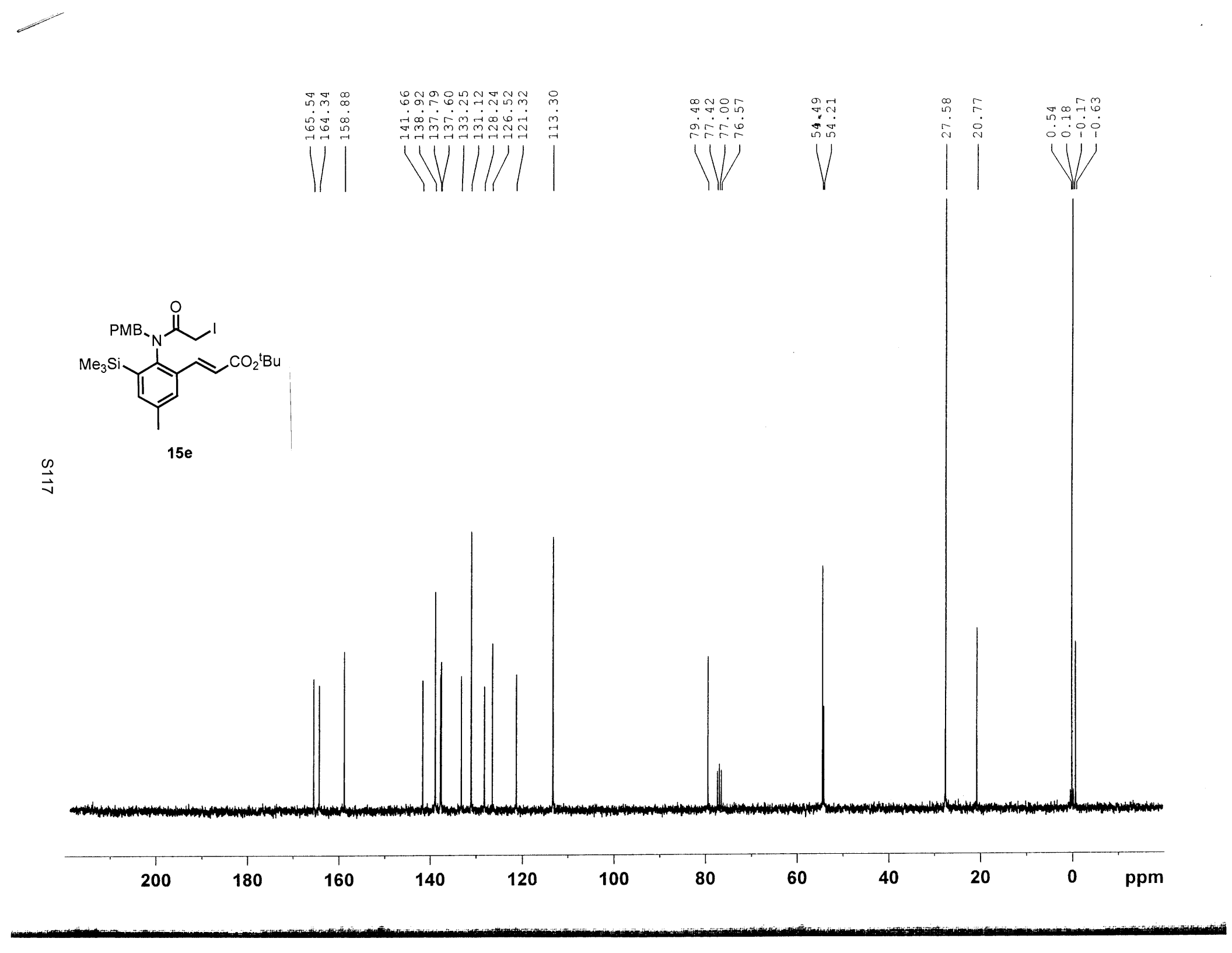
8.78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76.57
54.49
54.21
27.58
20.77
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0.18
-0.17
-0.63
O
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N
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Me3Si
CO2tBu
15e
200
180
160
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120
100
80
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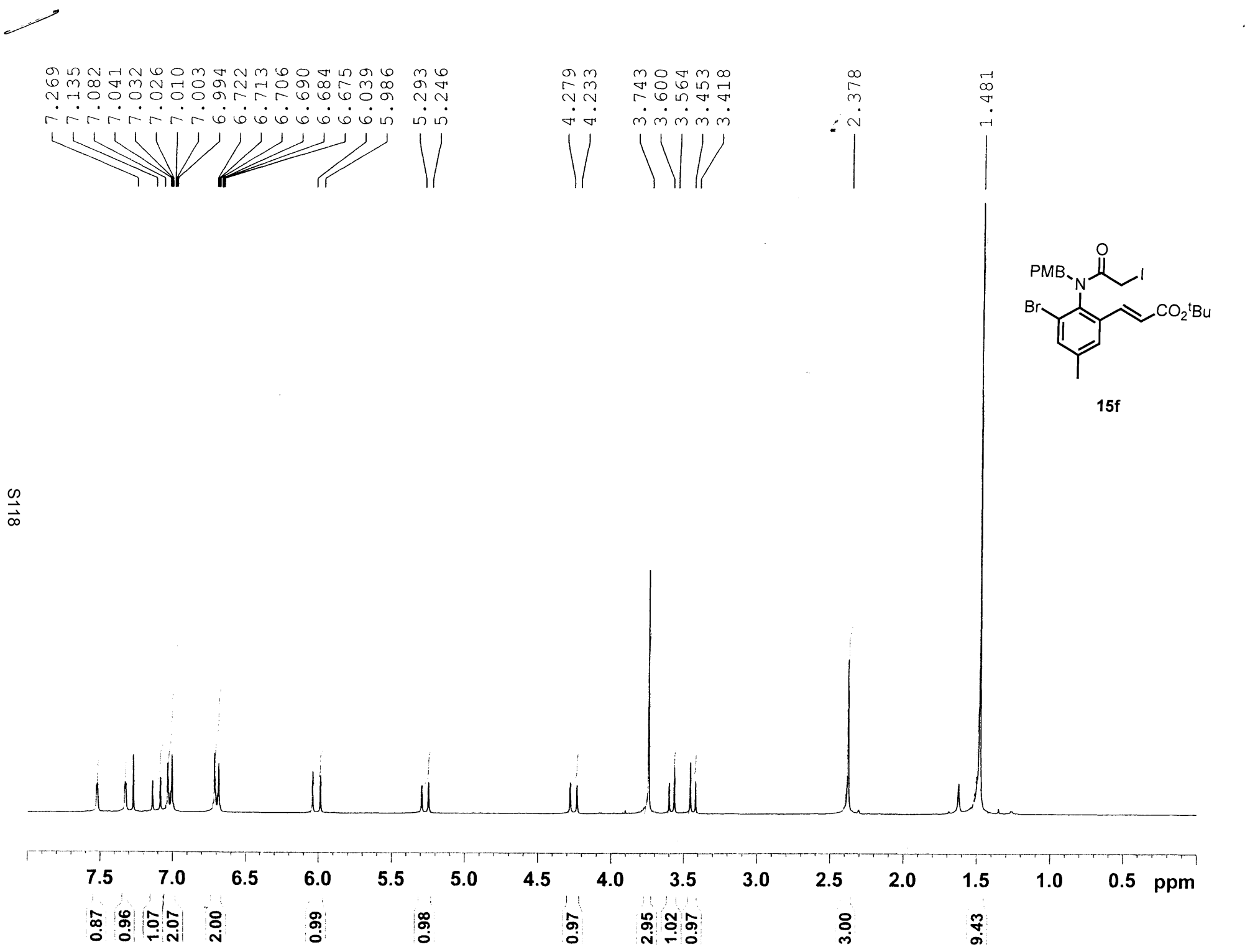
40
20
0
ppm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3.743
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3.564
3.453
3.418
2.378
1.481
PMB
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O
I
Br
CO2tBu
15f
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6.0
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5.0
4.5
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3.5
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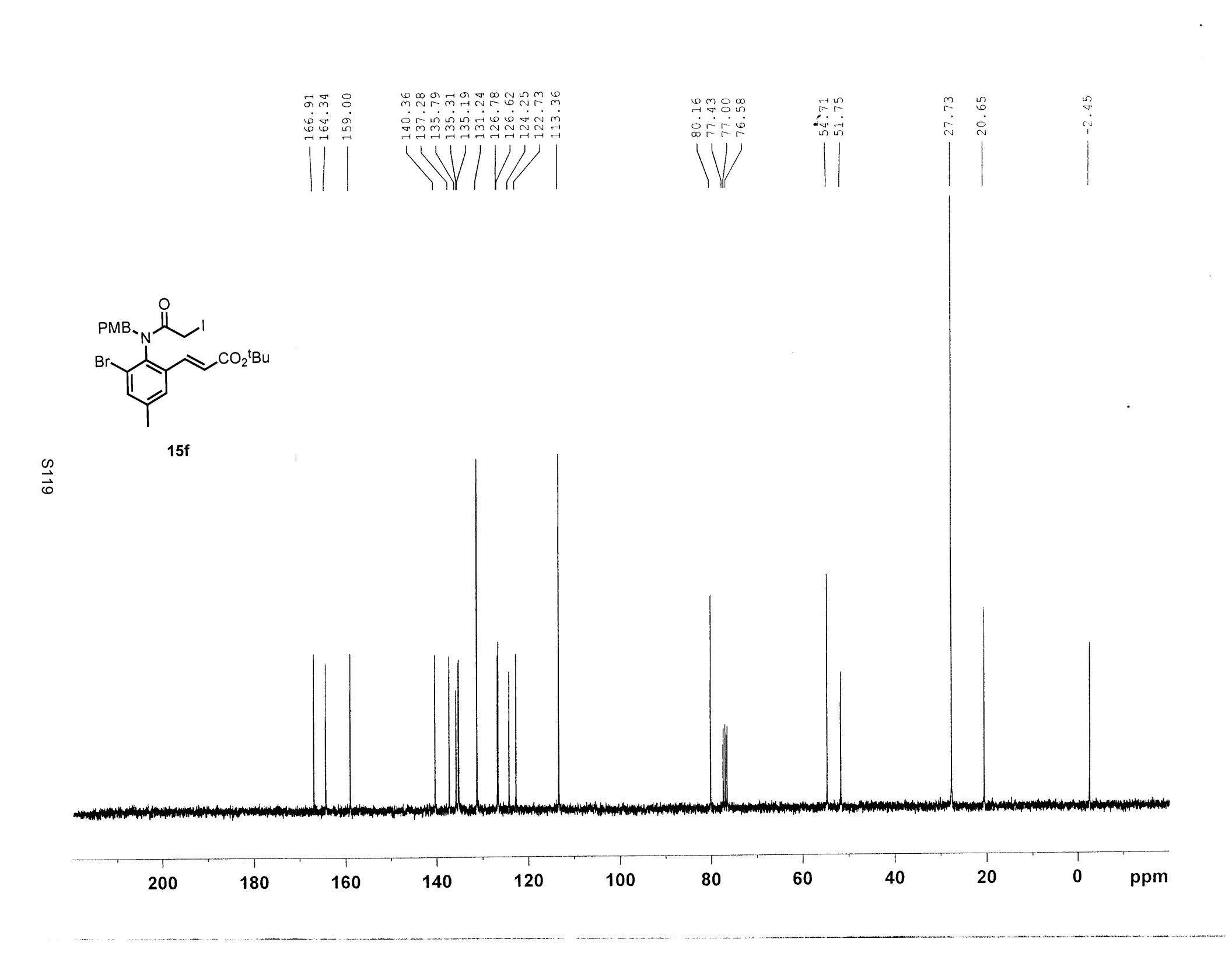
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76.58
54.71
51.75
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Br
CO2tBu
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120
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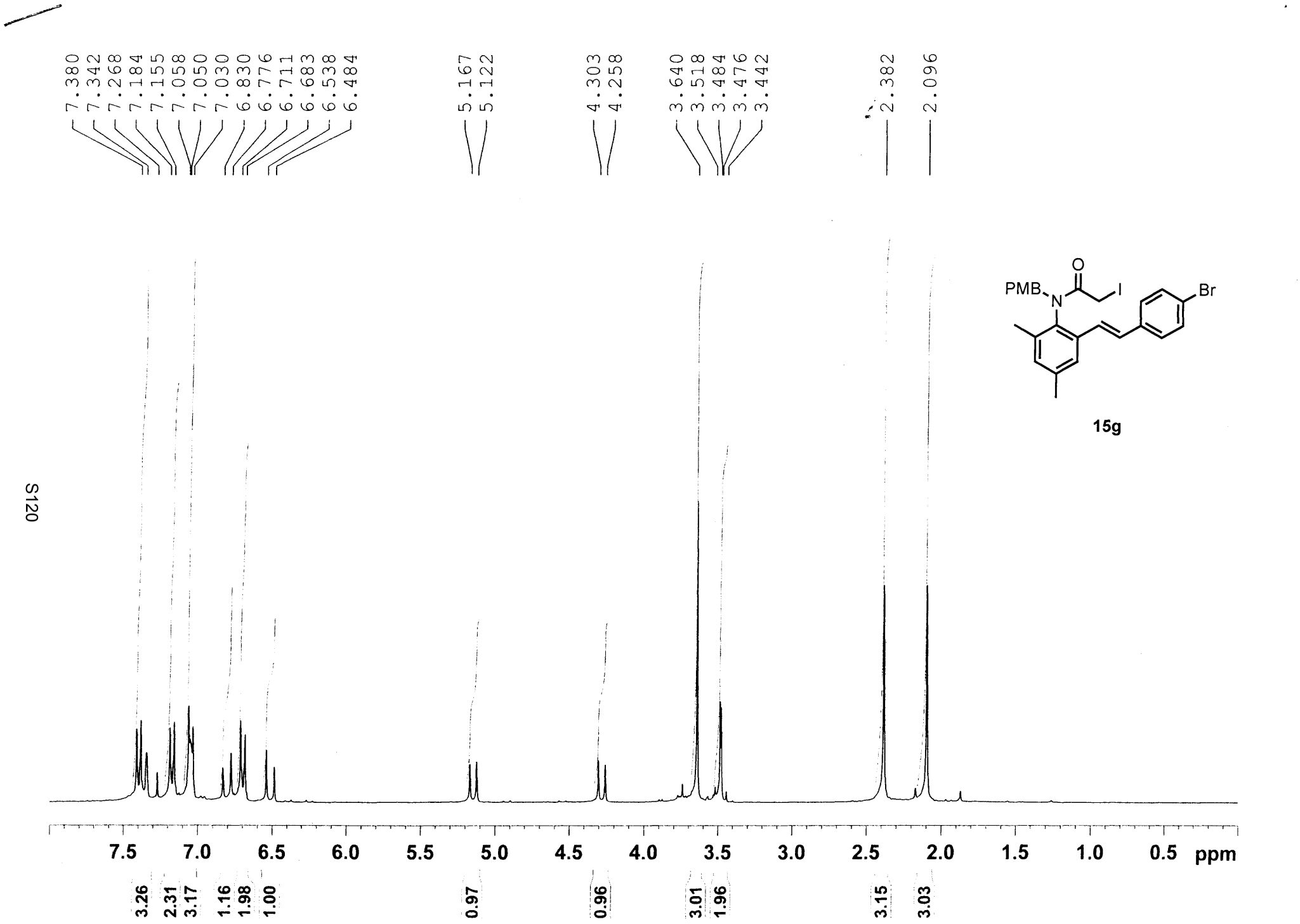
ppm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3.484
3.476
3.442
2.382
2.096
PMB
N
O
I
Br
15g
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6.5
6.0
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4.0
3.5
3.0
2.5
2.0
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1.0
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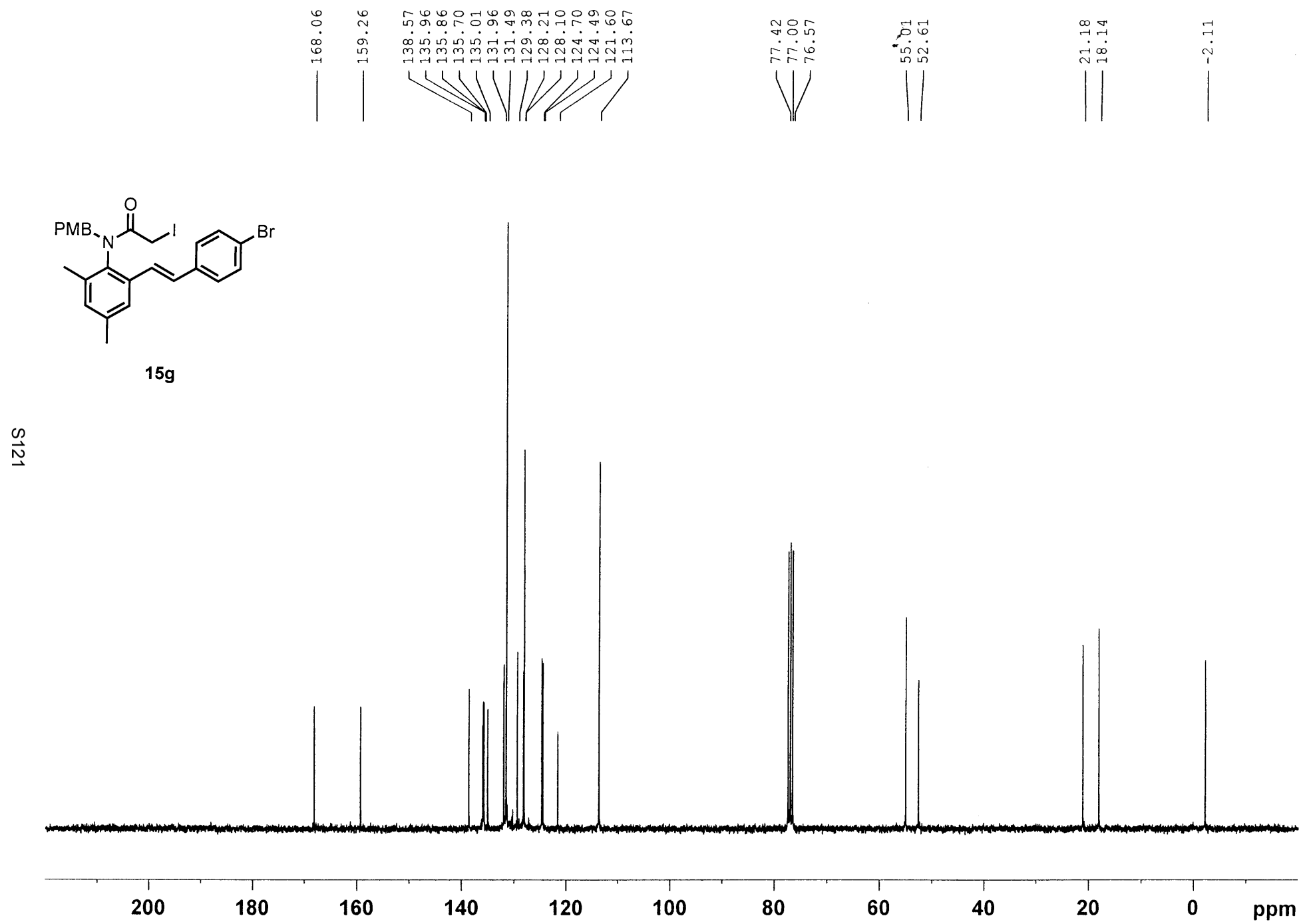
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18.14
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O
I
Br
15g
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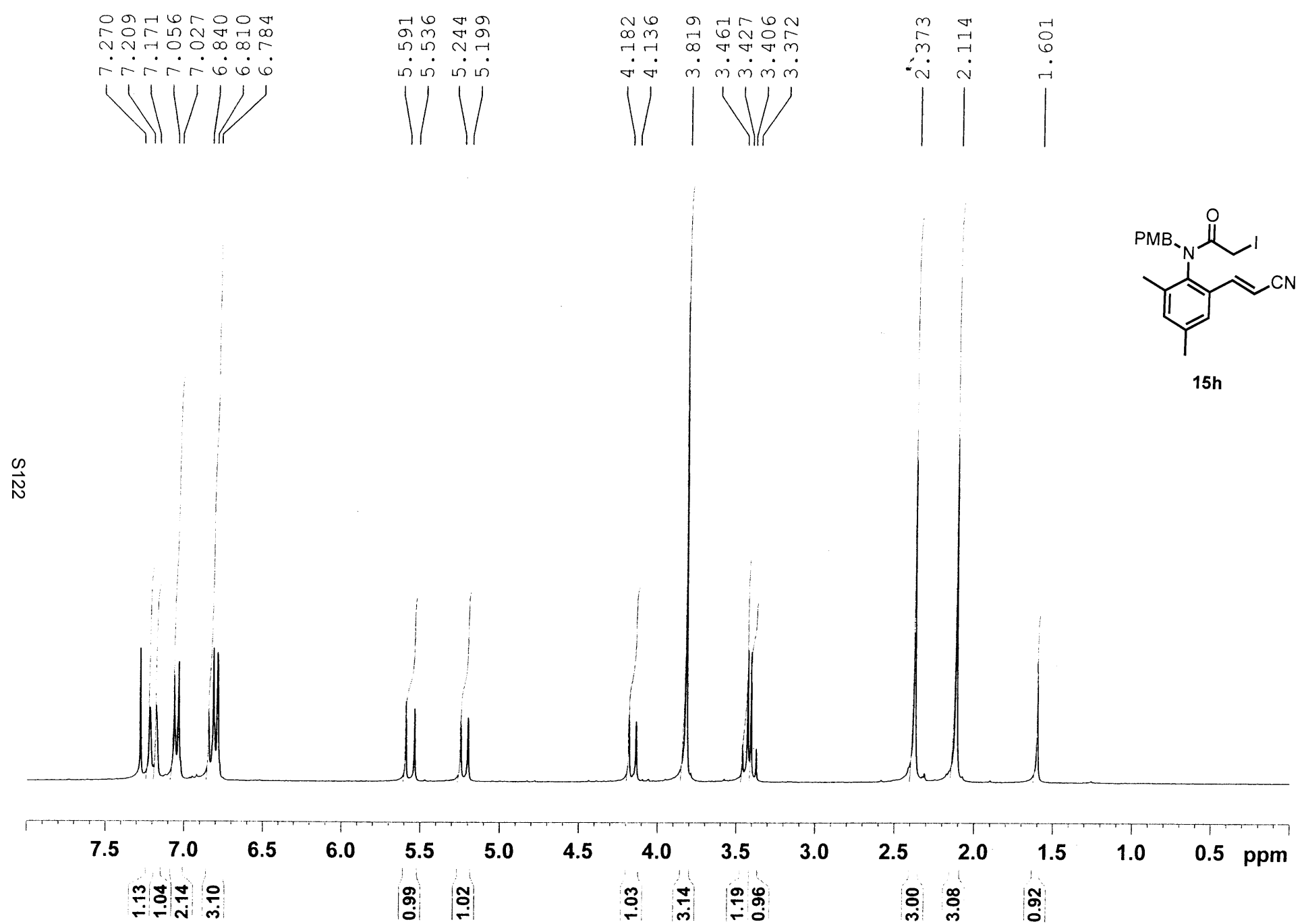
ppm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PMB
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I
CN
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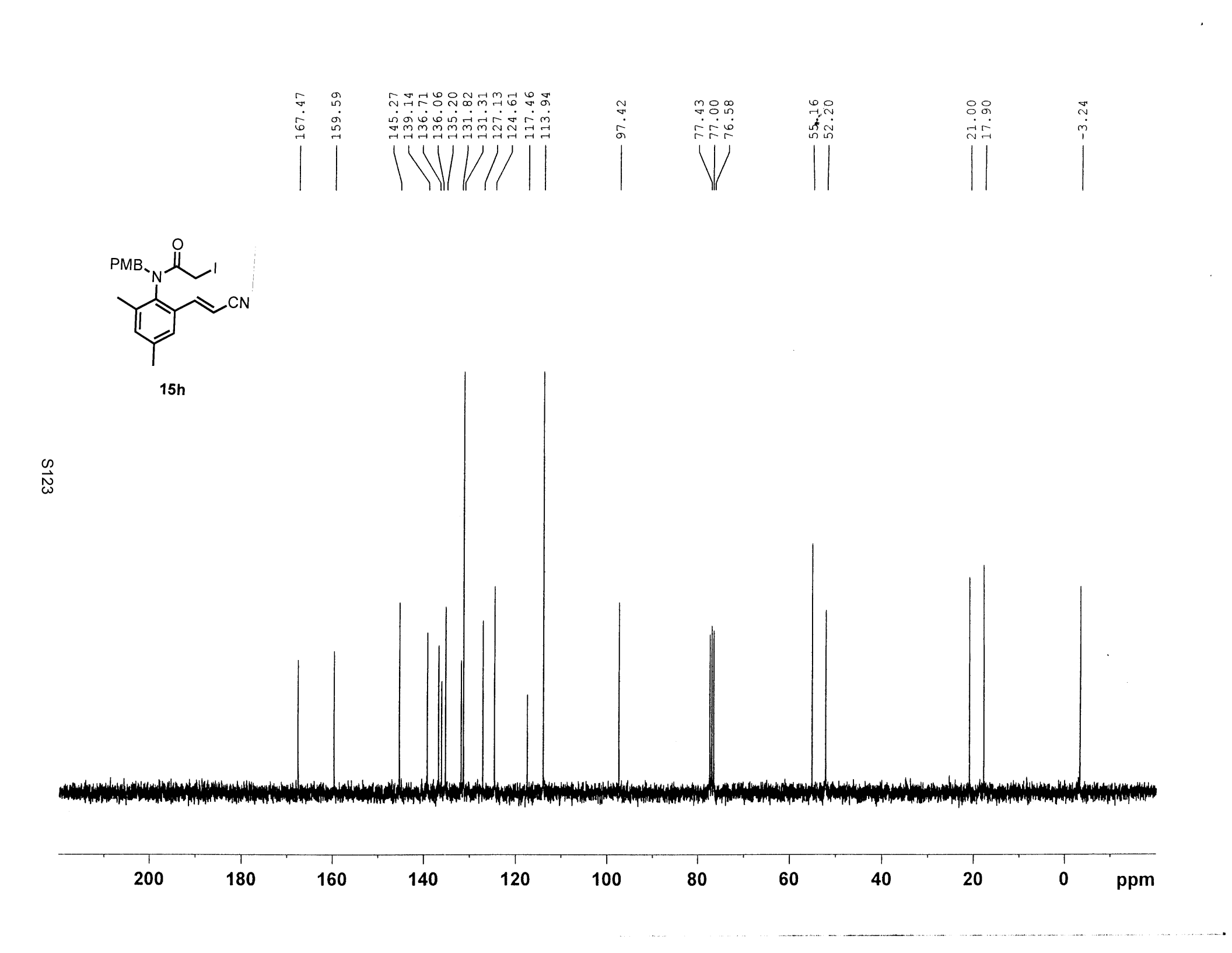
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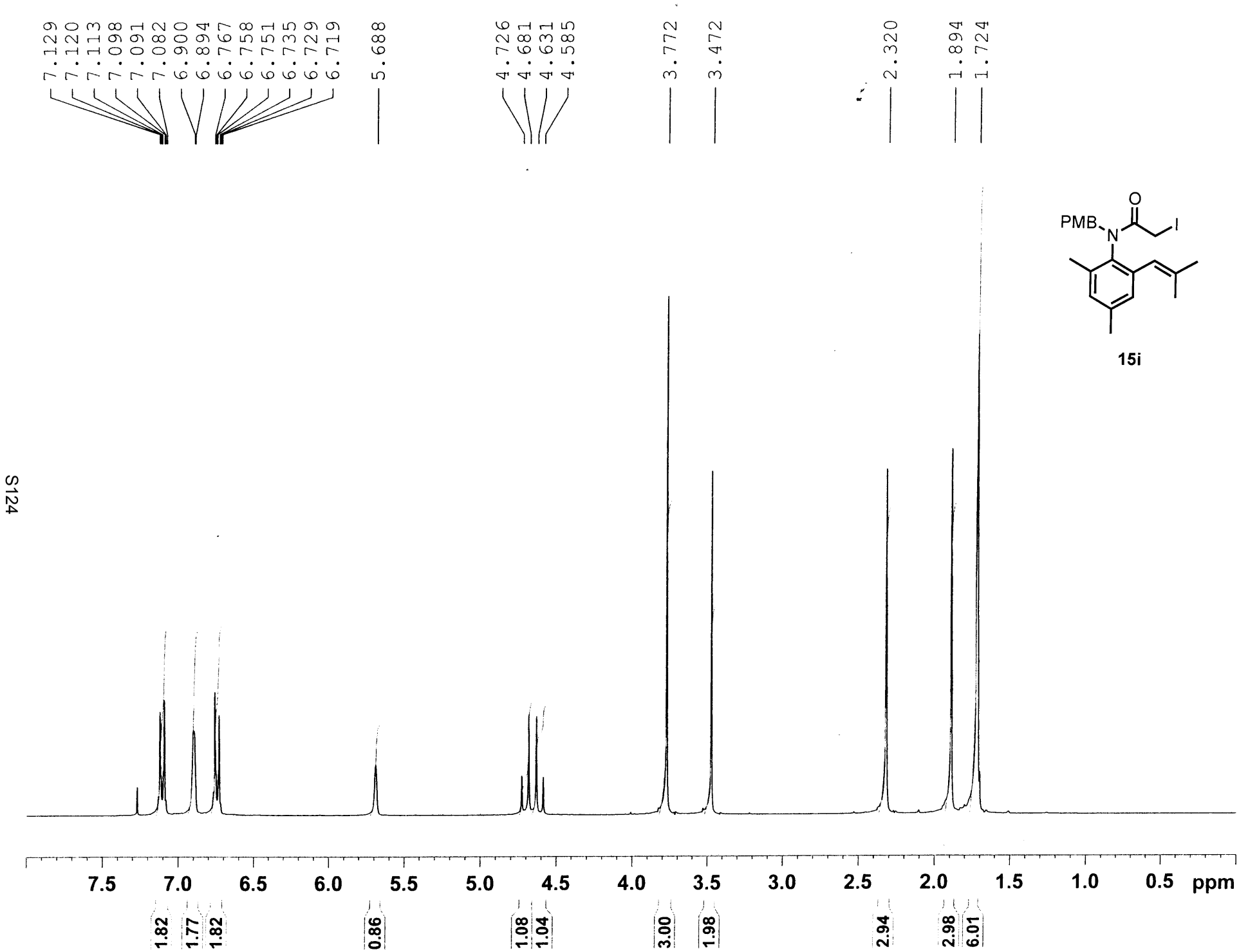
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1.724
PMB
N
O
I
15i
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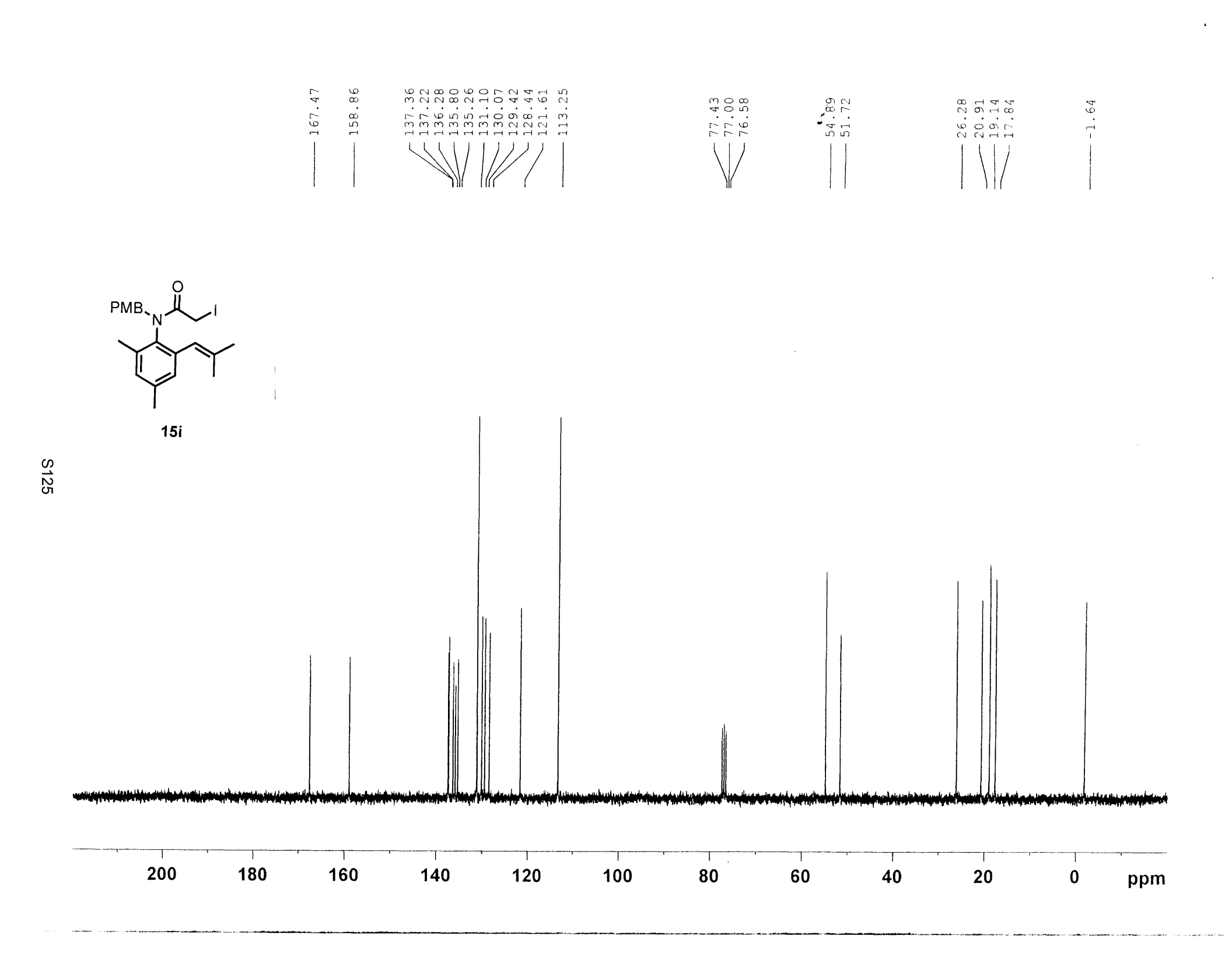
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I
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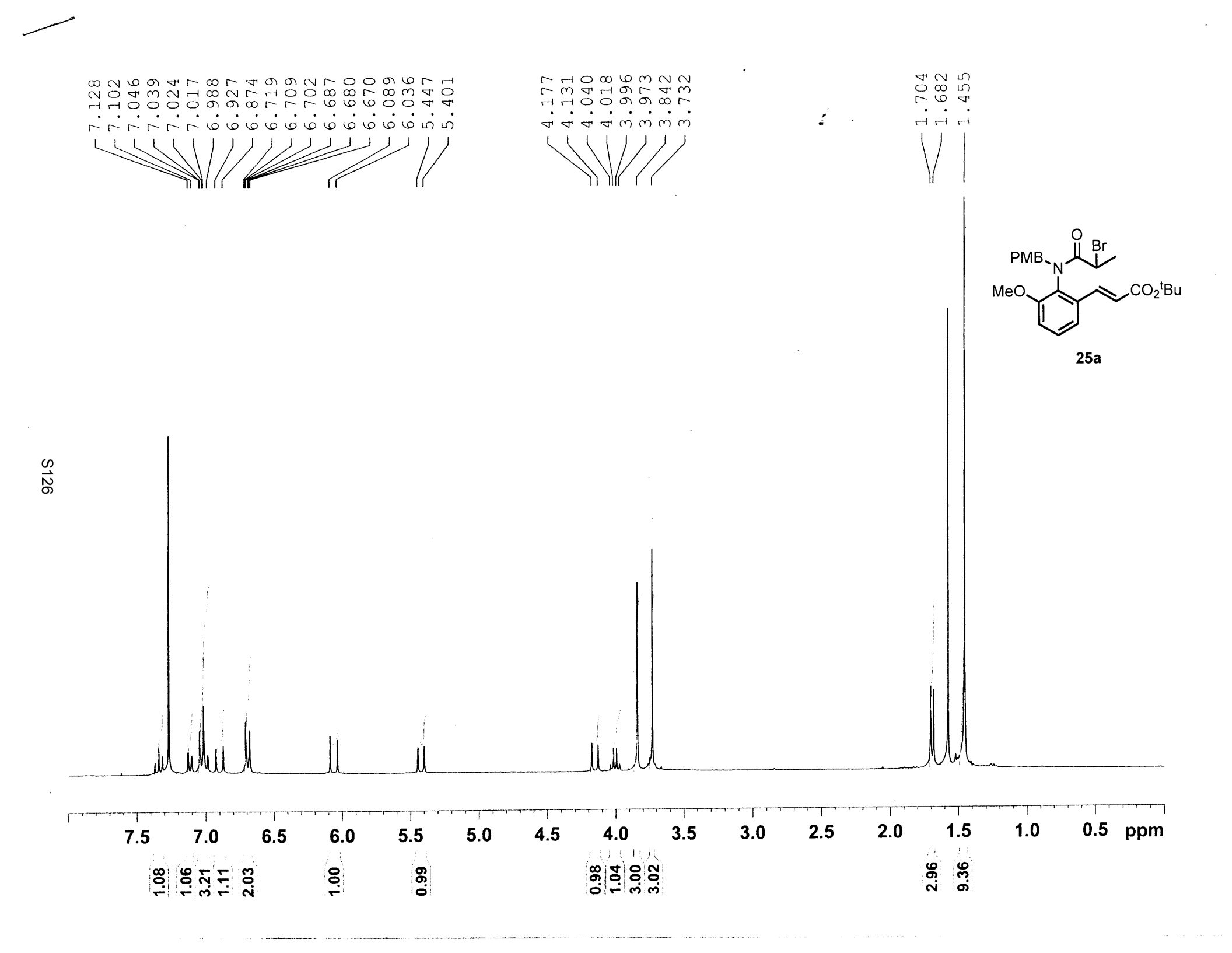
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3.732
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1.455
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Br
MeO
CO2tBu
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5.0
4.5
4.0
3.5
3.0
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2.0
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1.0
0.5
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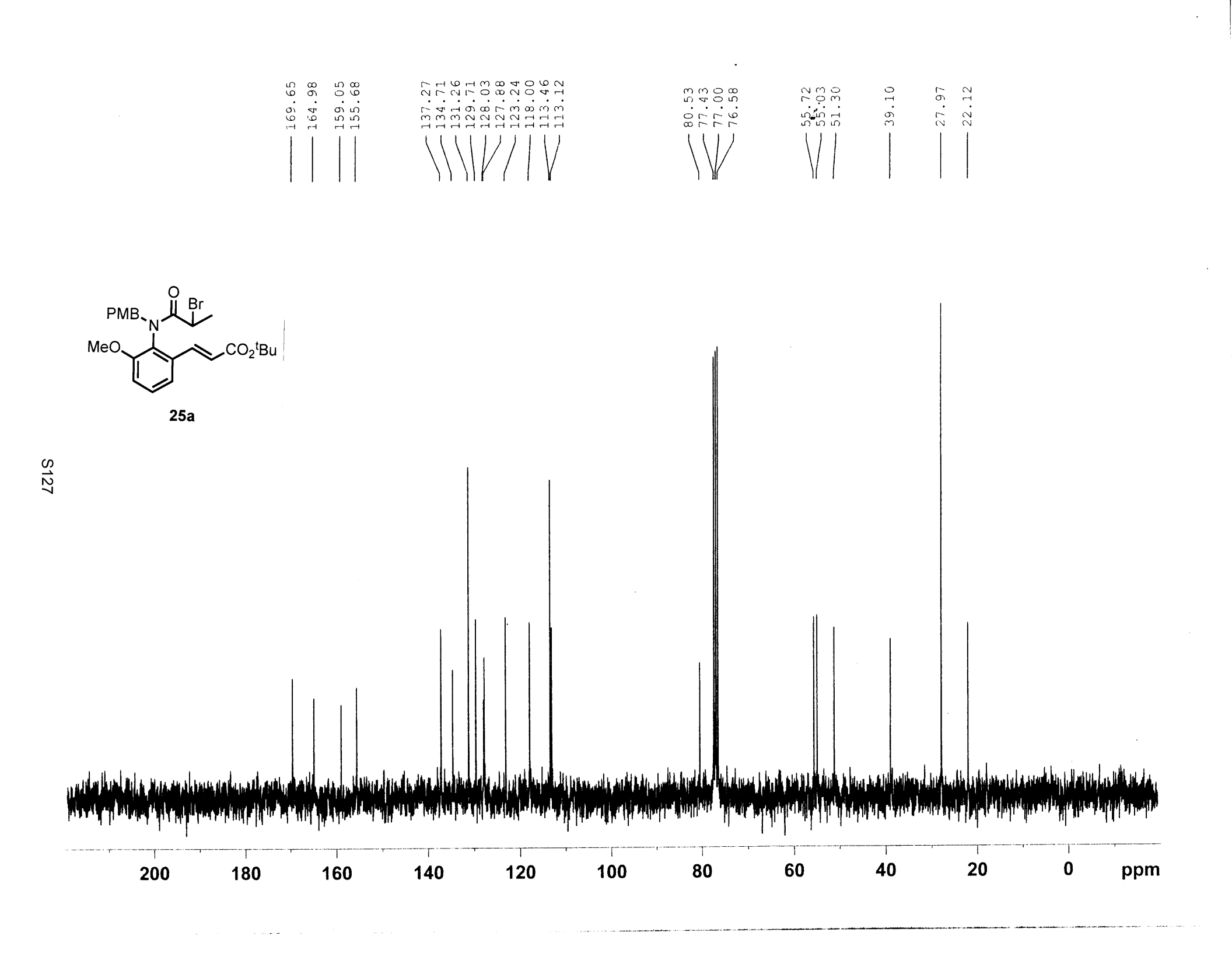
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77.00
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55.03
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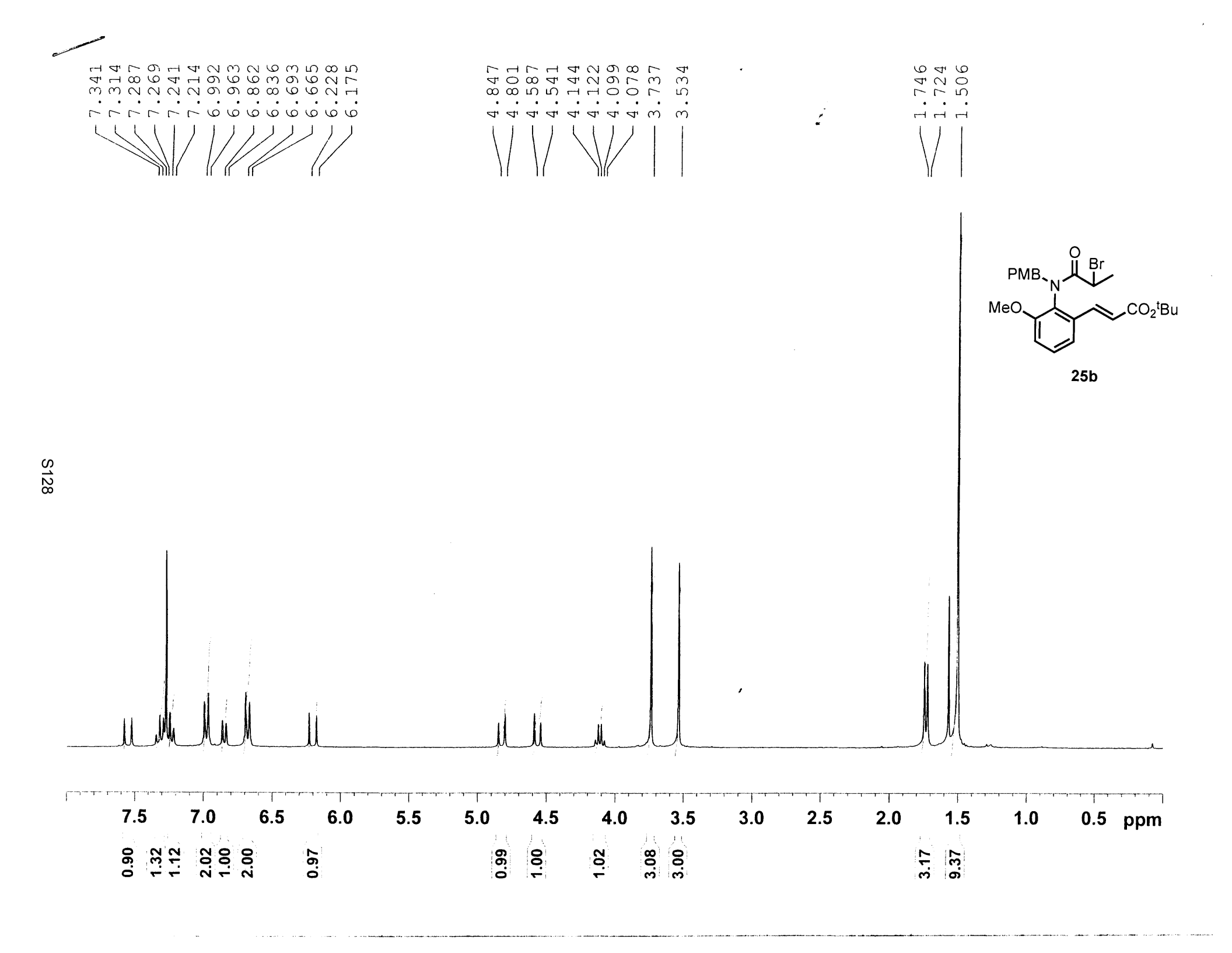
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3.534
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1.724
1.506
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O
Br
MeO
CO2tBu
25b
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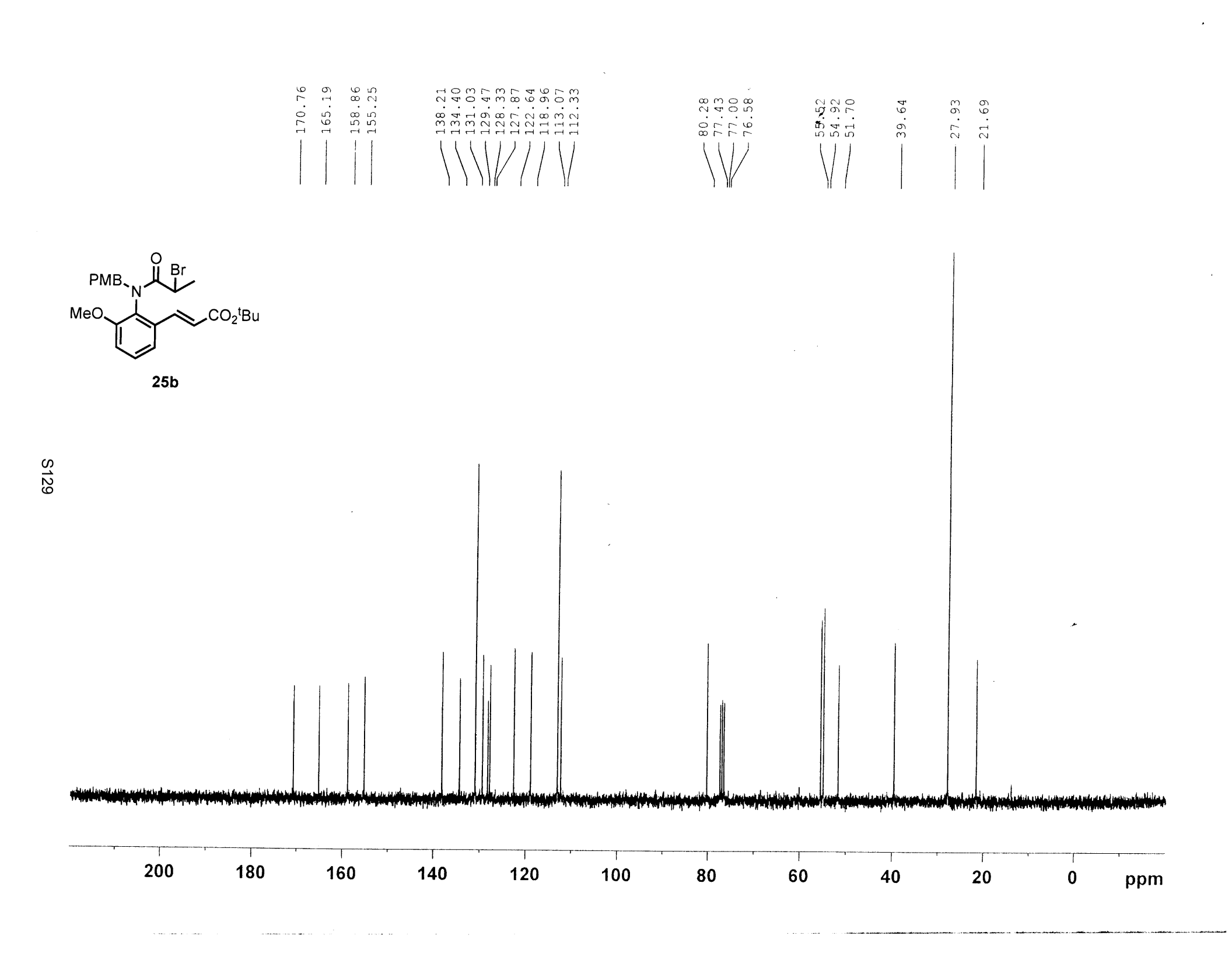
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113.07
112.33
80.28
77.43
77.00
76.58
55.52
54.92
51.70
39.64
27.93
21.69
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MeO
CO2tBu
25b
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40
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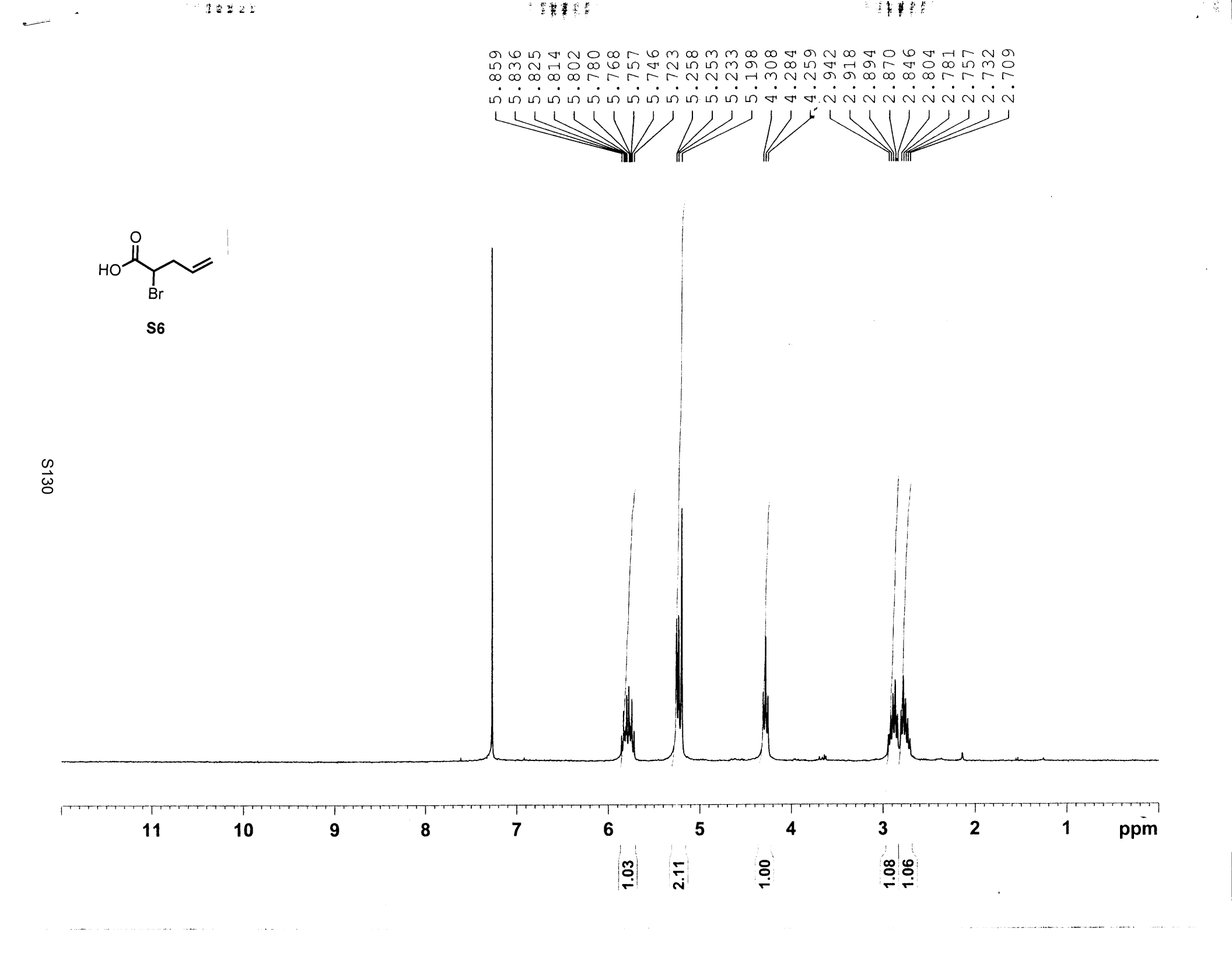
ppm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5.198
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4.284
4.259
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2.918
2.894
2.870
2.846
2.804
2.781
2.757
2.732
2.709
HO
O
Br
S6
S130
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7
6
5
4
3
2
1
ppm
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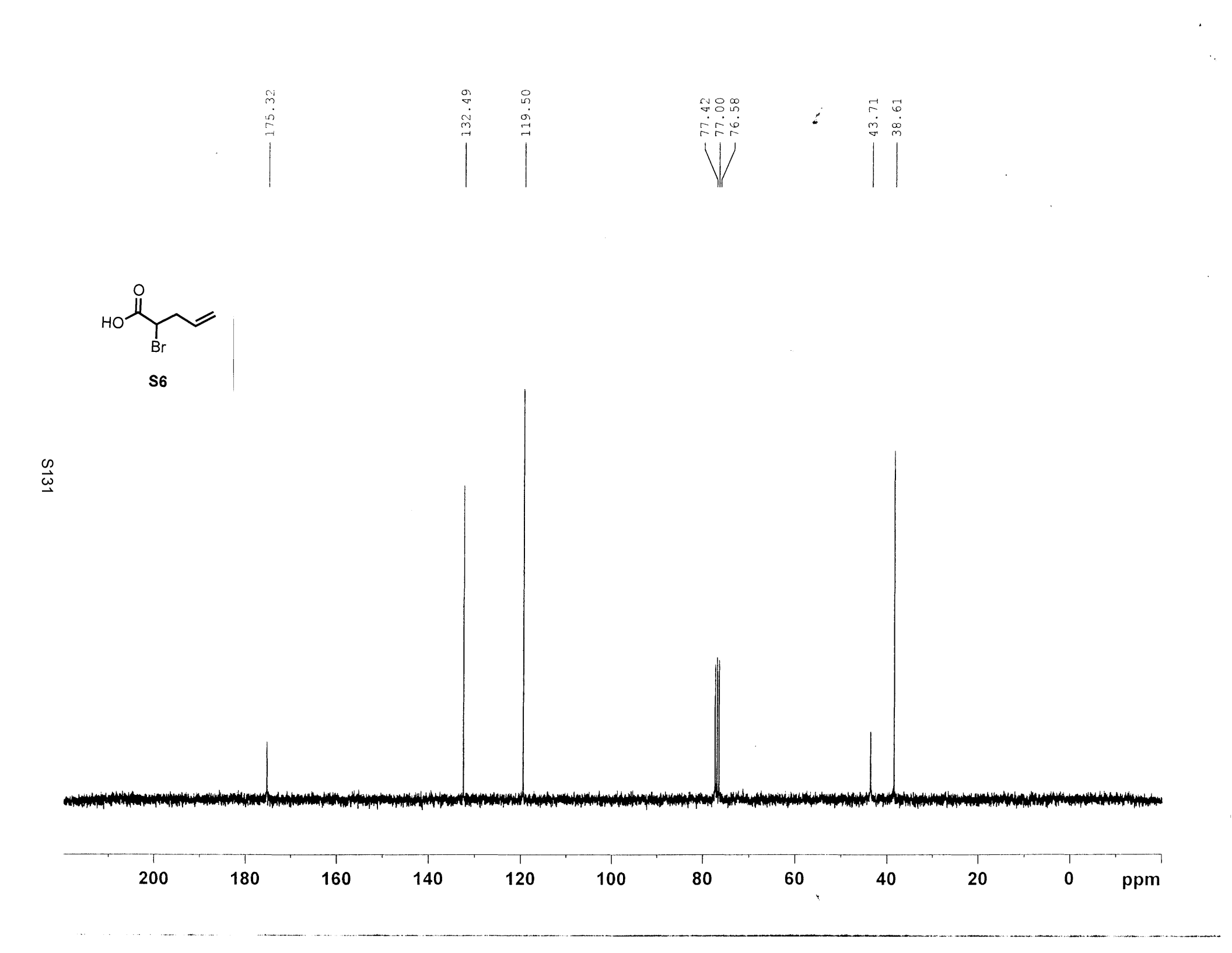
2.11
1.00
1.08
1.06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O
Br
S6
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120
100
80
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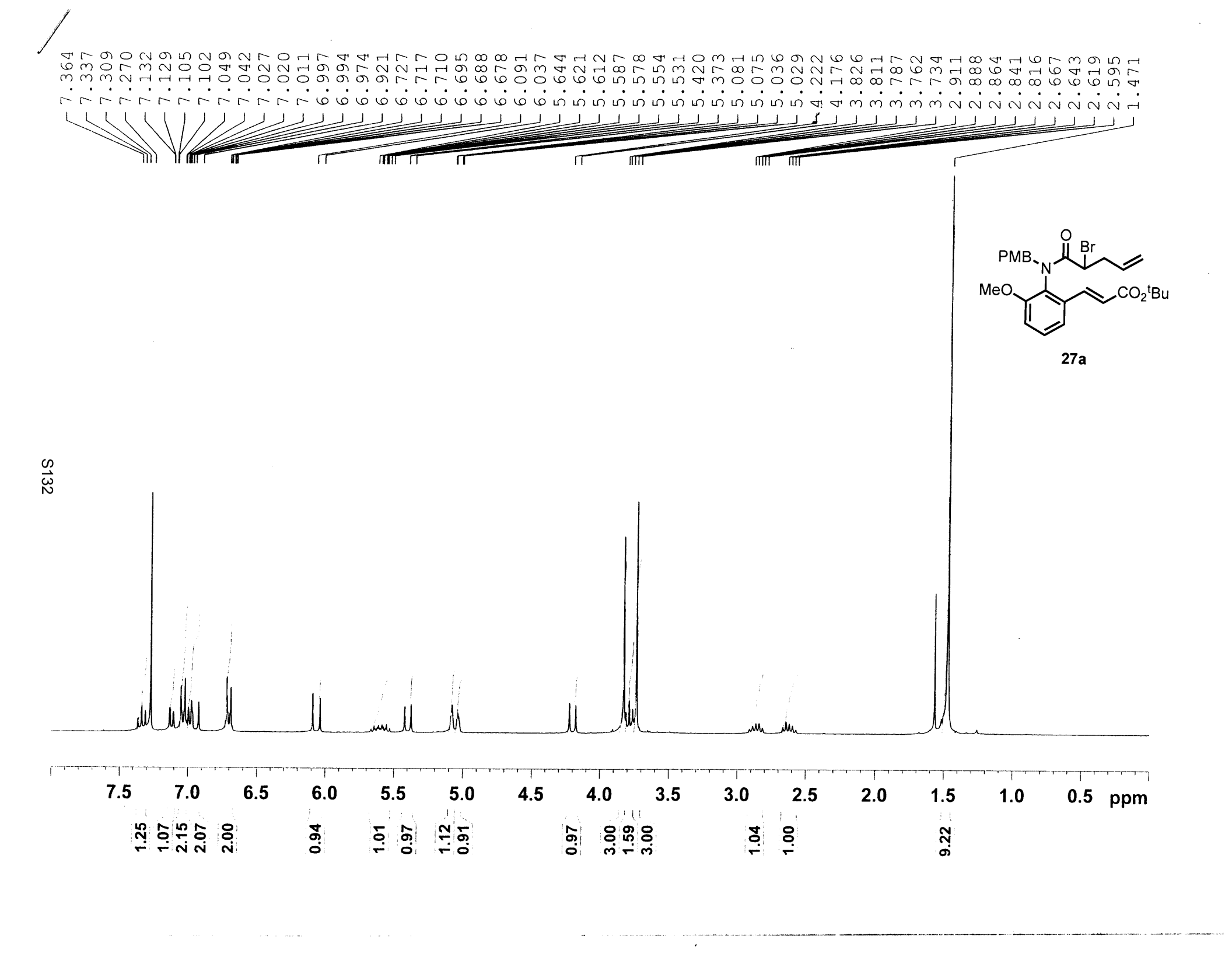
40
20
0
ppm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6.921
6.727
6.717
6.710
6.695
6.688
6.678
6.091
6.037
5.644
5.621
5.612
5.587
5.578
5.554
5.531
5.420
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5.075
5.036
5.029
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4.176
3.826
3.811
3.787
3.762
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2.911
2.888
2.864
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2.816
2.667
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2.619
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1.471
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O
Br
MeO
CO2tBu
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6.0
5.5
5.0
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4.0
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3.0
2.5
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1.0
0.5
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2.07
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1.00
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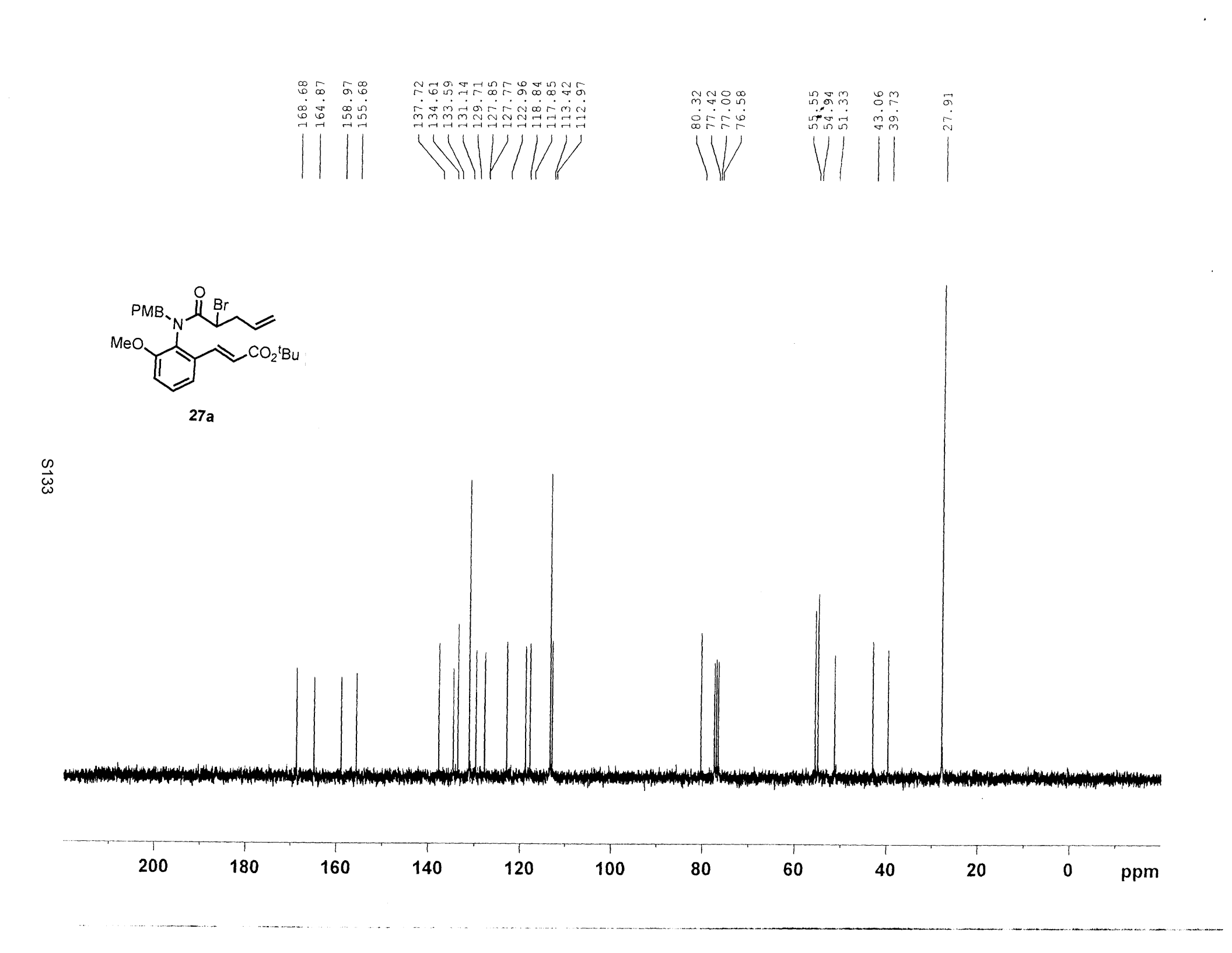
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77.00
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51.33
43.06
39.73
27.91
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O
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MeO
CO2tBu
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120
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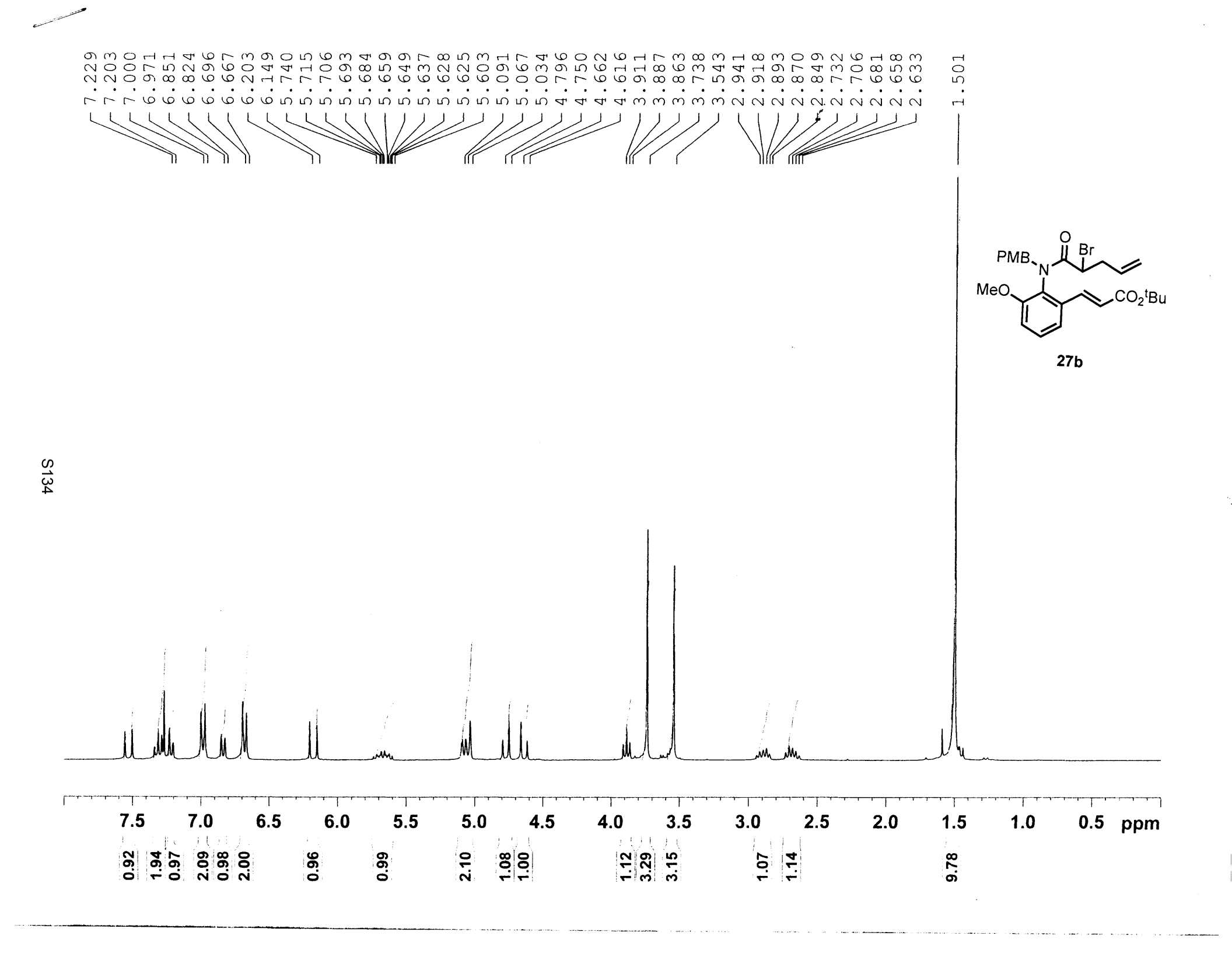
ppm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5.637
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5.625
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4.616
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3.887
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2.849
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2.706
2.681
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O
Br
MeO
CO2tBu
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6.0
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5.0
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4.0
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3.0
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ppm
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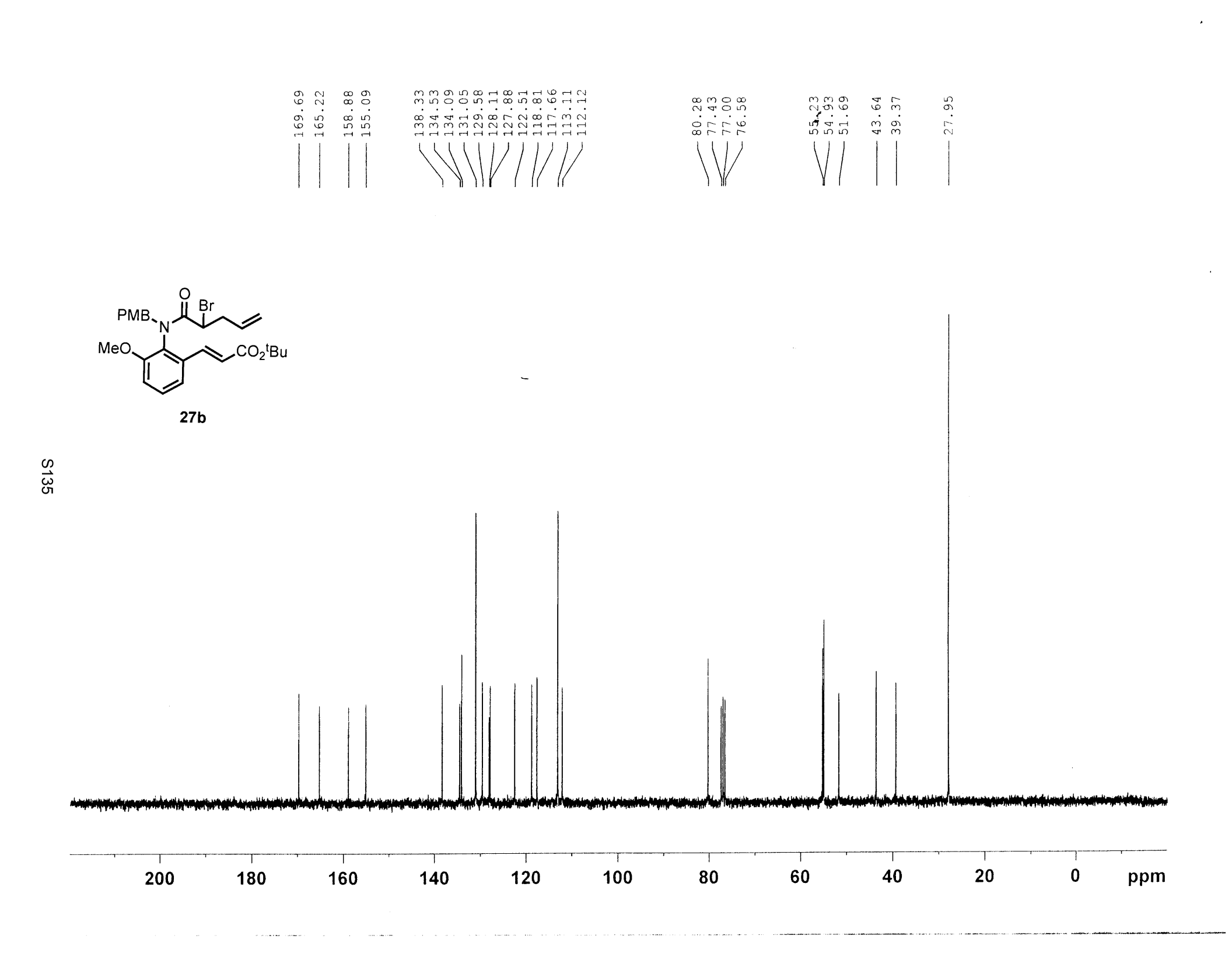
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112.12
80.28
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76.58
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54.93
51.69
43.64
39.37
27.95
PMB
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O
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MeO
CO2tBu
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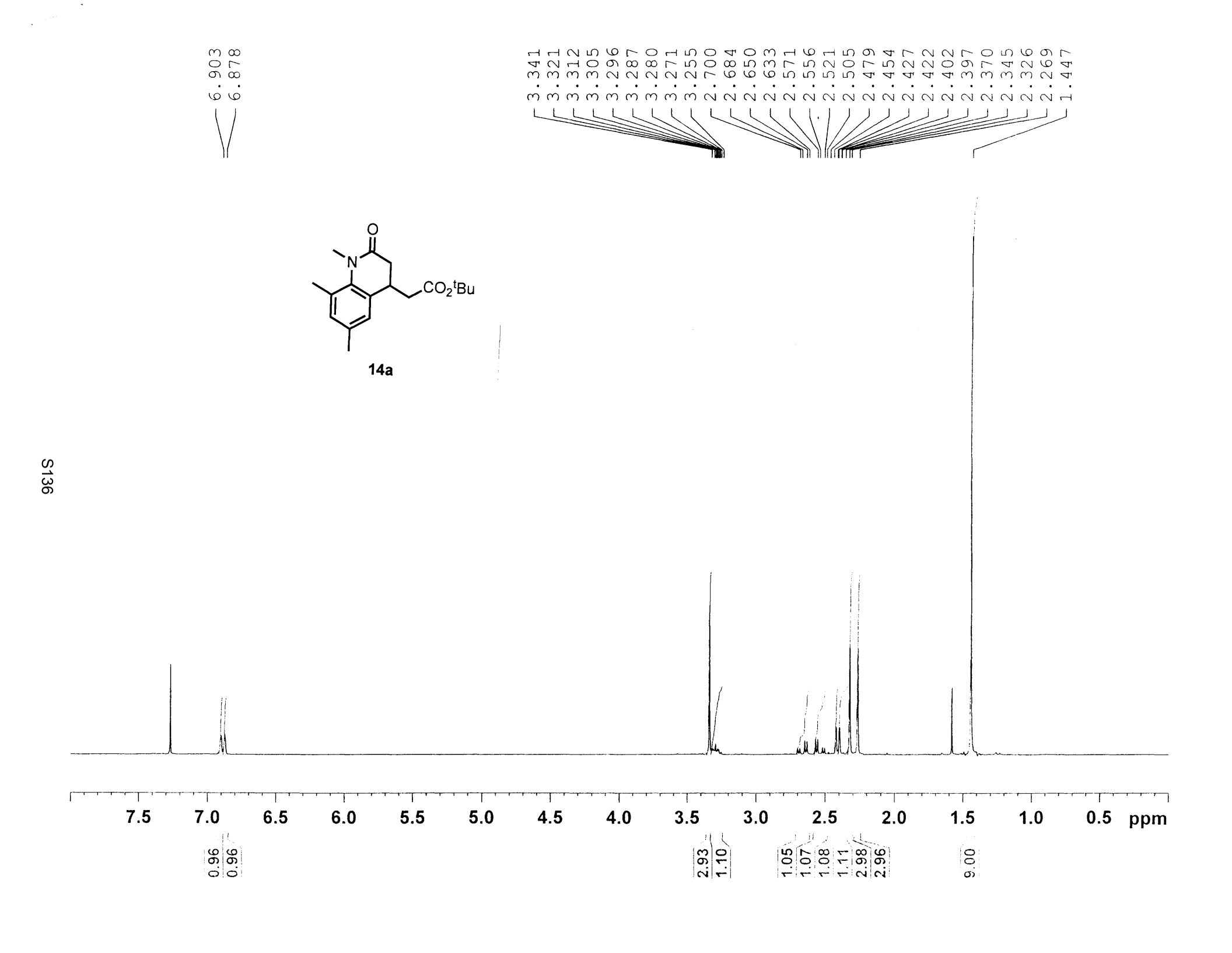
0
ppm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2.269
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O
N
CO2tBu
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5.0
4.5
4.0
3.5
3.0
2.5
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1.0
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1.08
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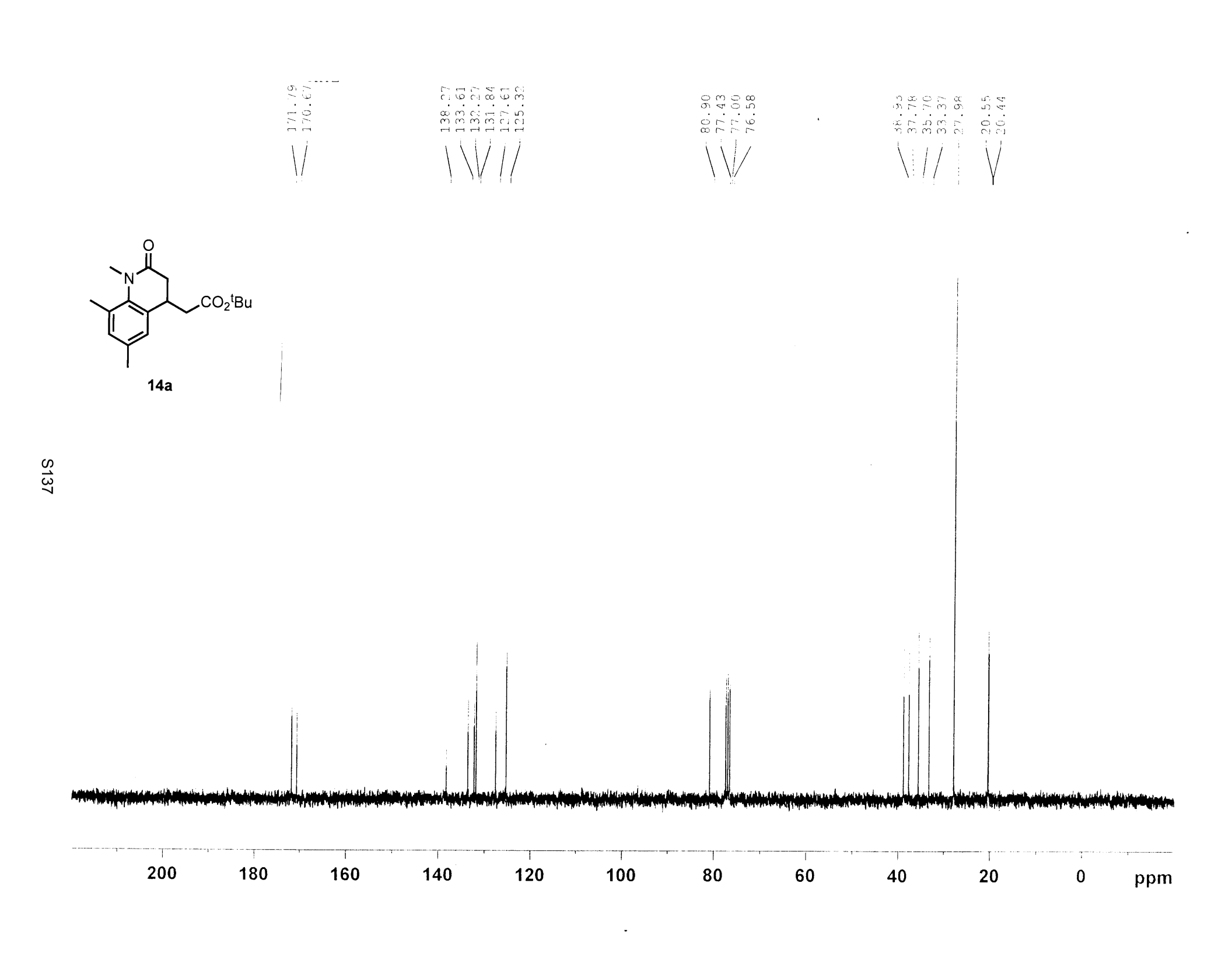
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0
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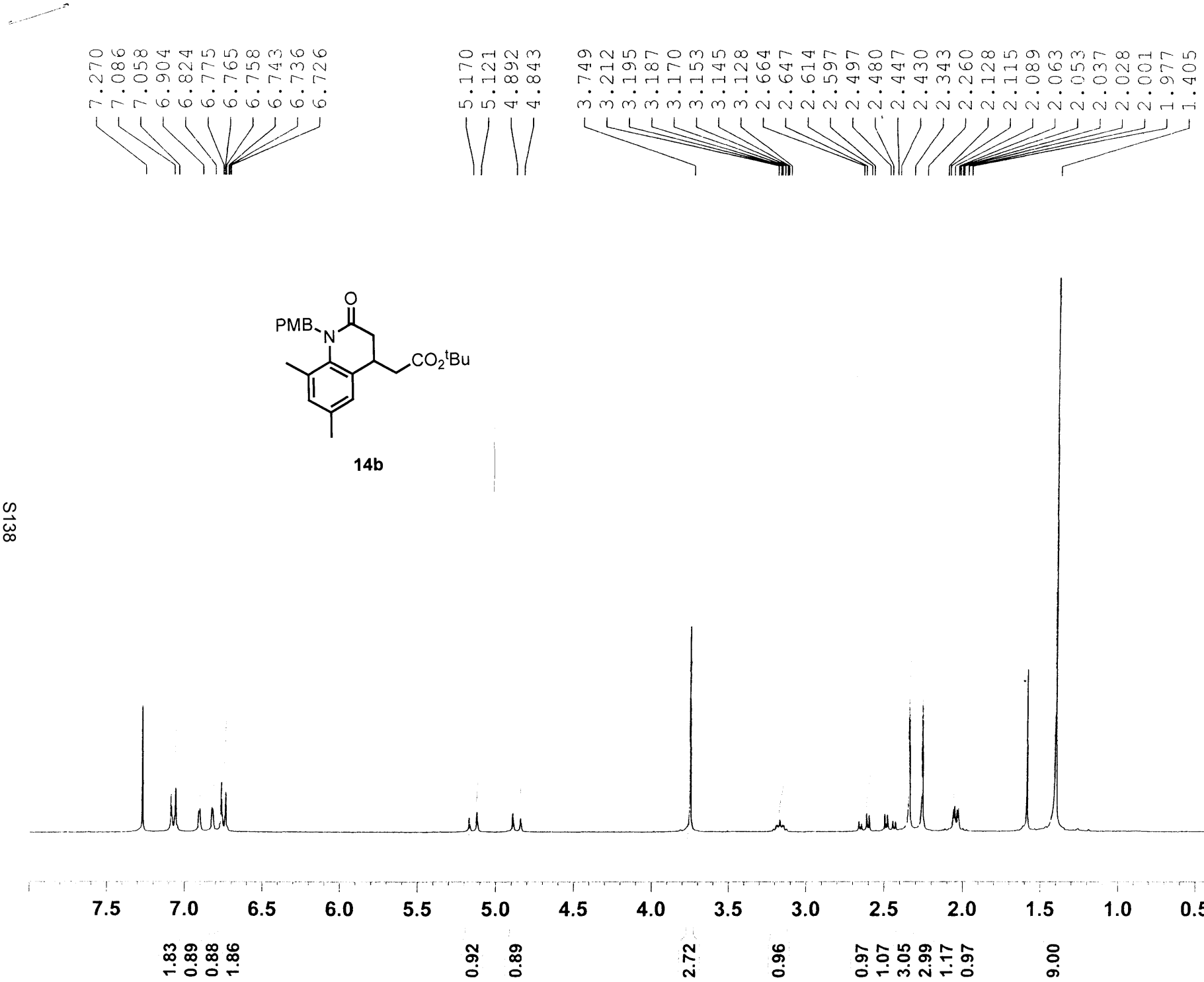
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3.187
3.170
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2.063
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2.037
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5.0
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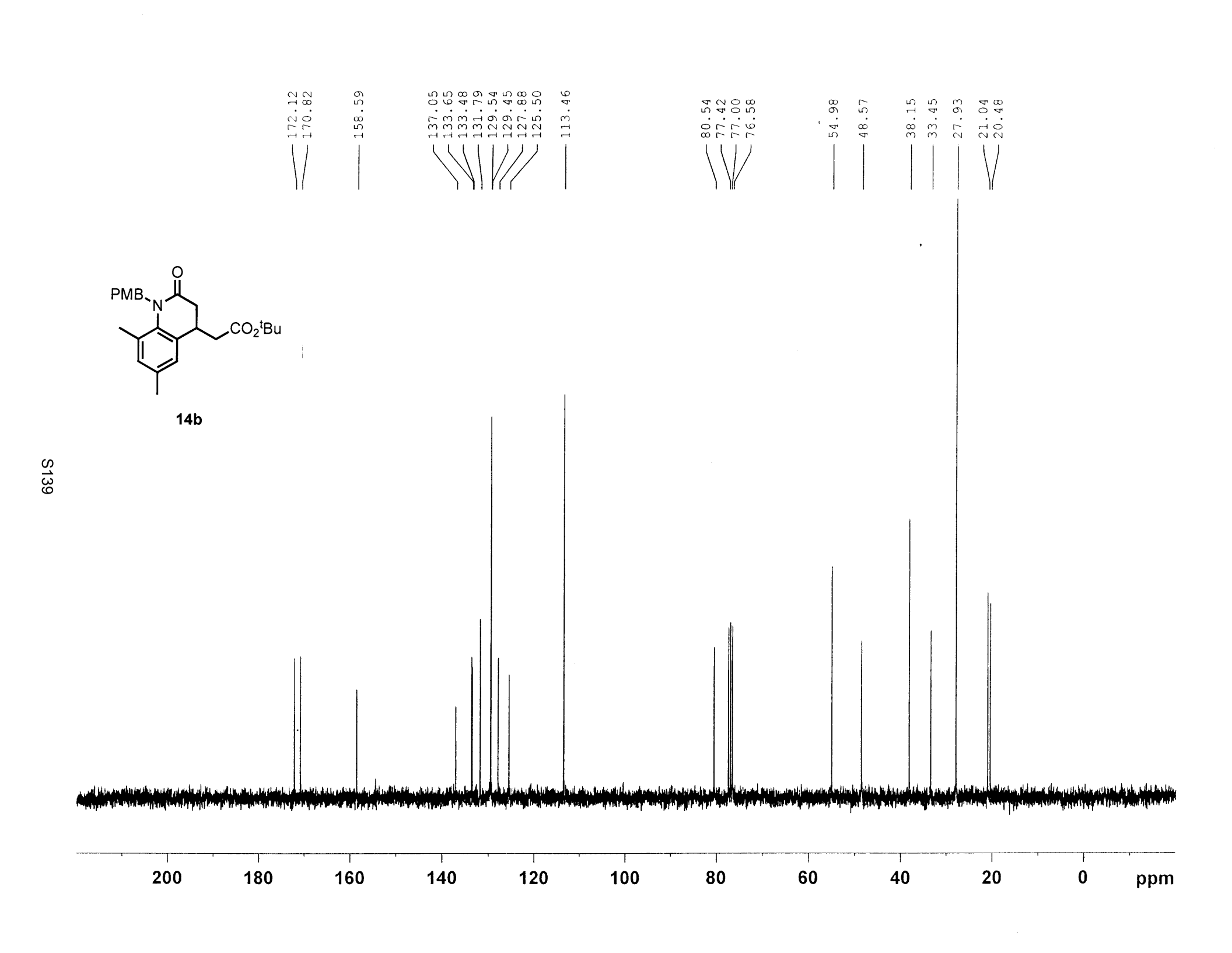
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38.15
33.45
27.93
21.04
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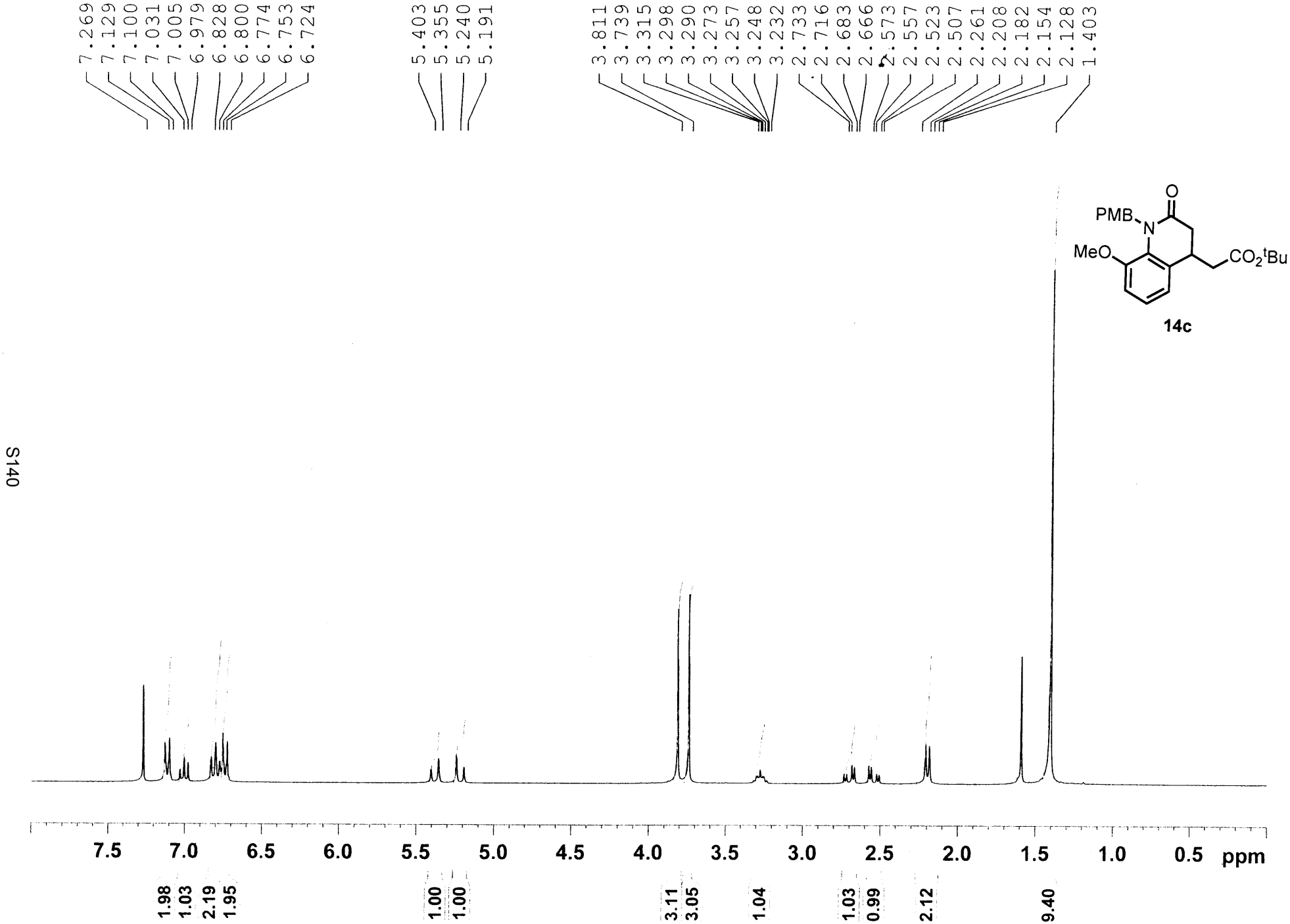
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2.128
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O
MeO
CO2tBu
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4.0
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2.5
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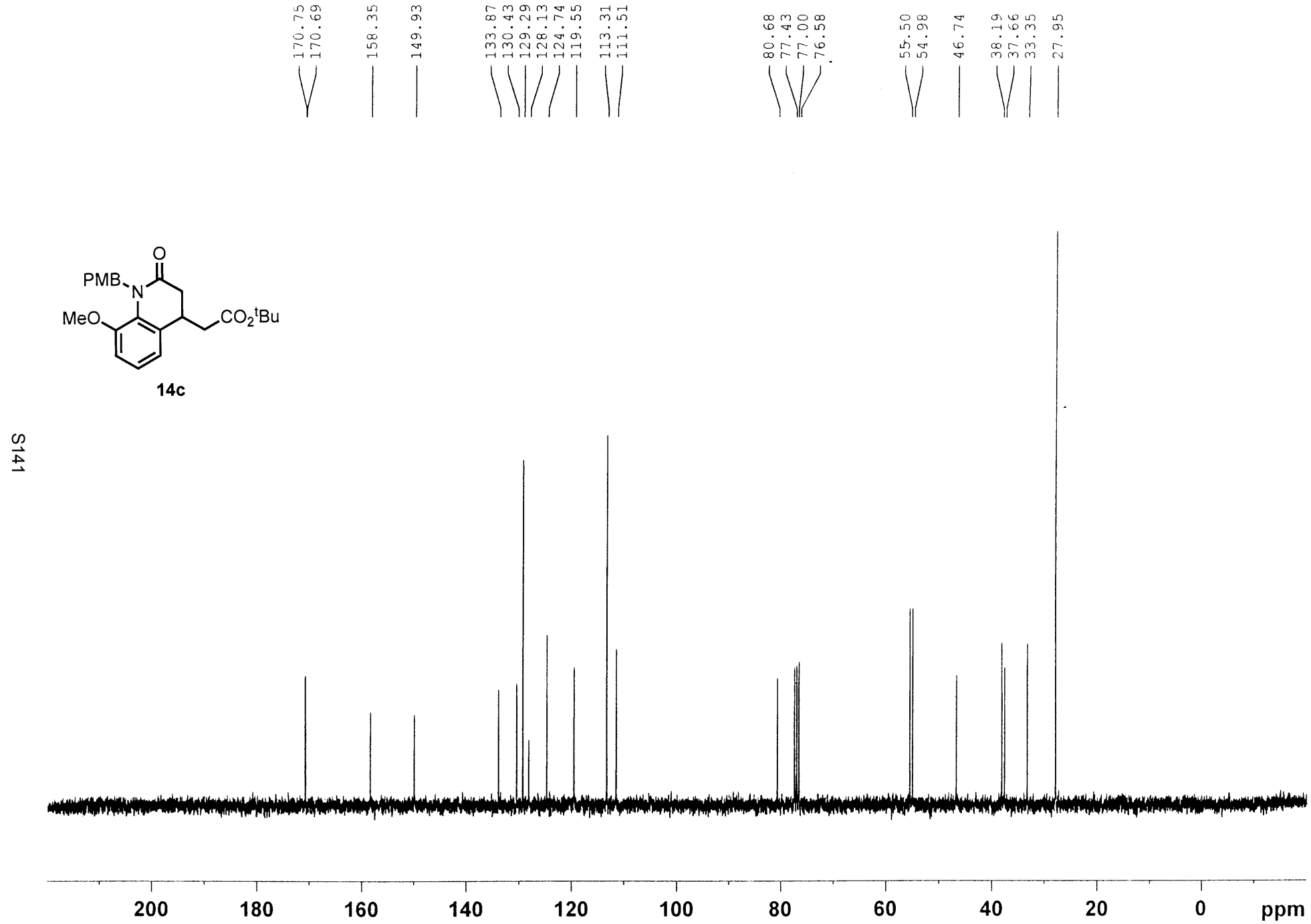
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77.00
76.58
55.50
54.98
46.74
38.19
37.66
33.35
27.95
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MeO
CO2tBu
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120
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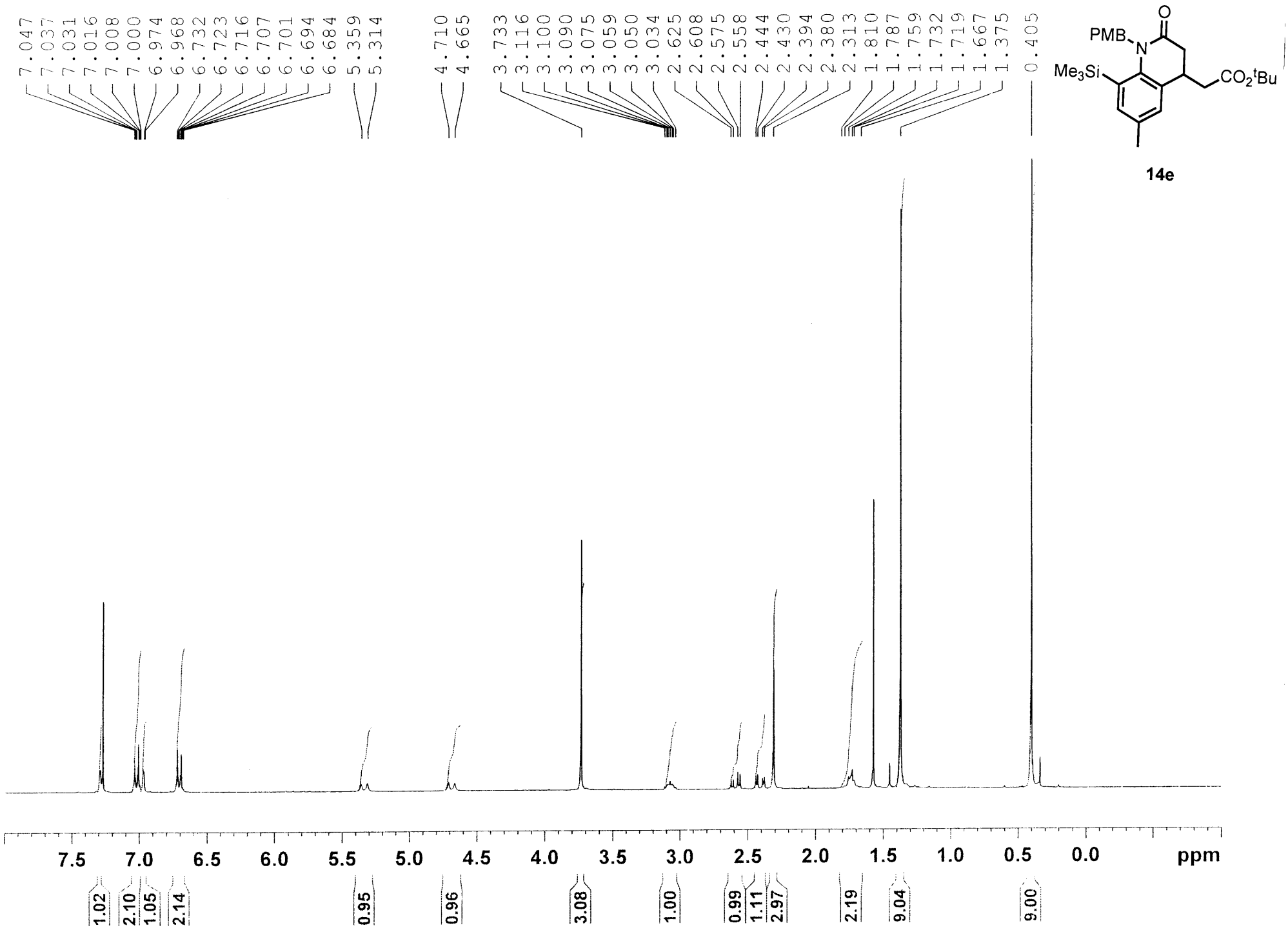
0
ppm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14e
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4.0
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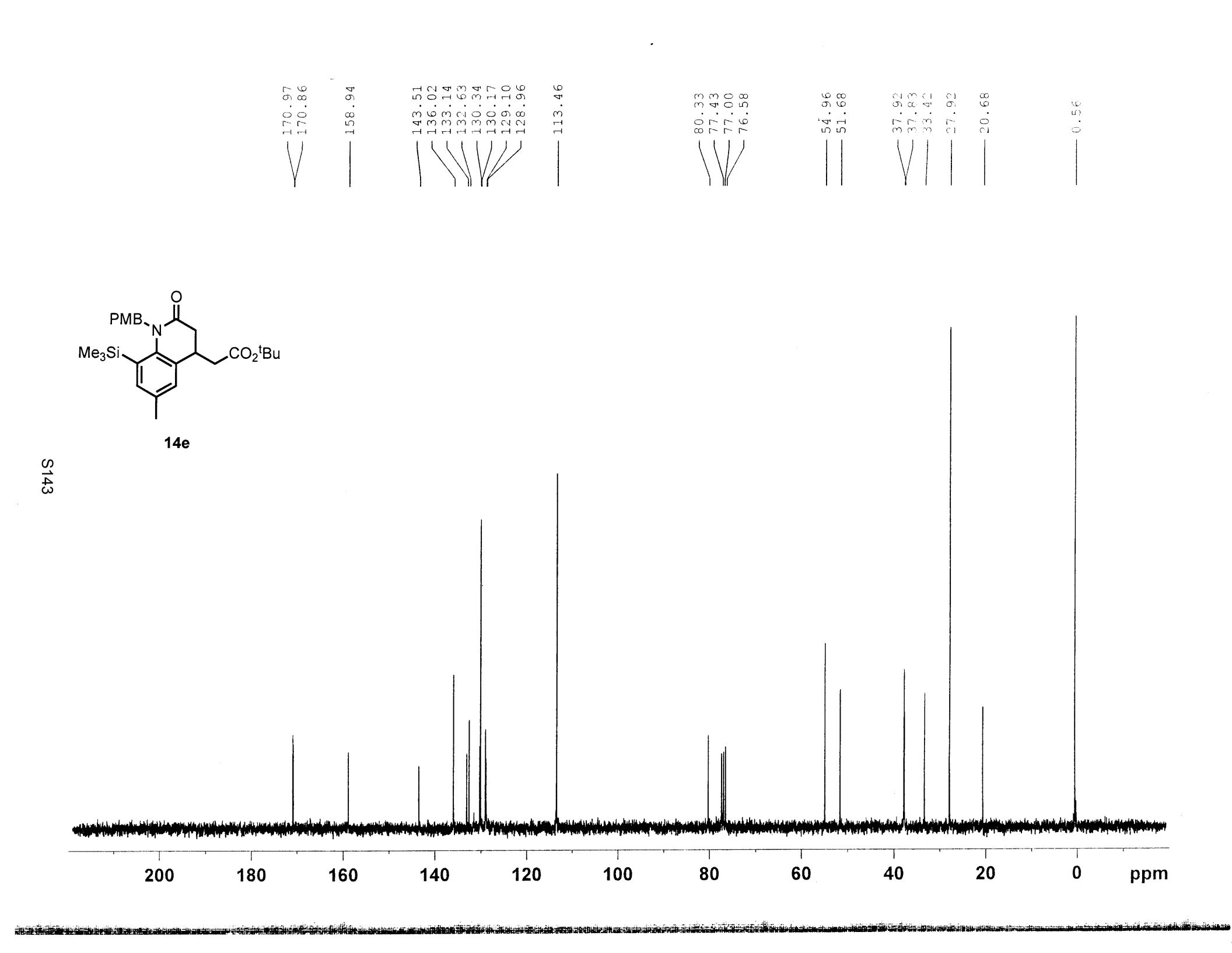
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77.00
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54.96
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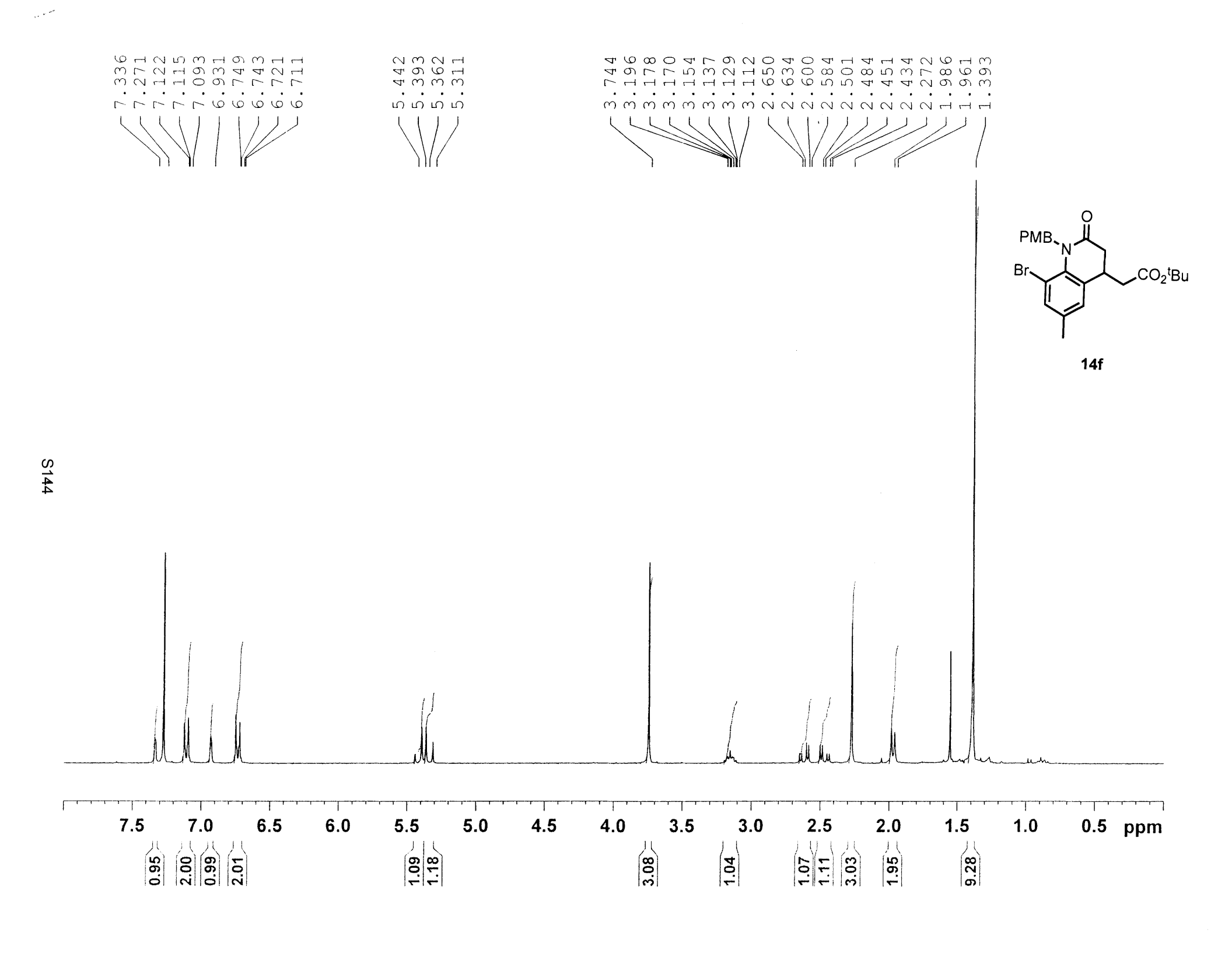
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PMB
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CO2tBu
14f
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.95
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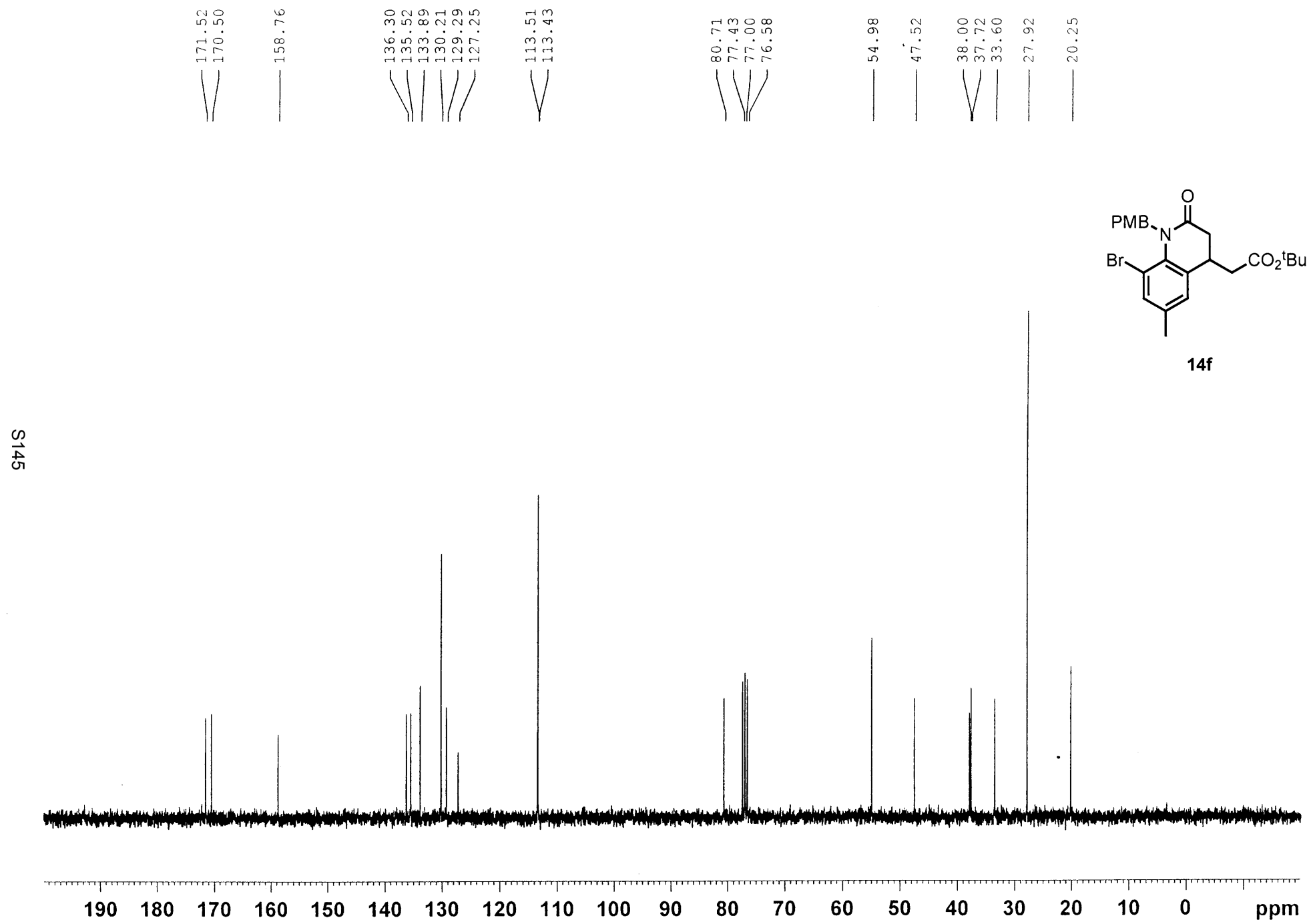
0.99
2.01
1.09
1.18
3.08
1.04
1.07
1.11
3.03
1.95
9.28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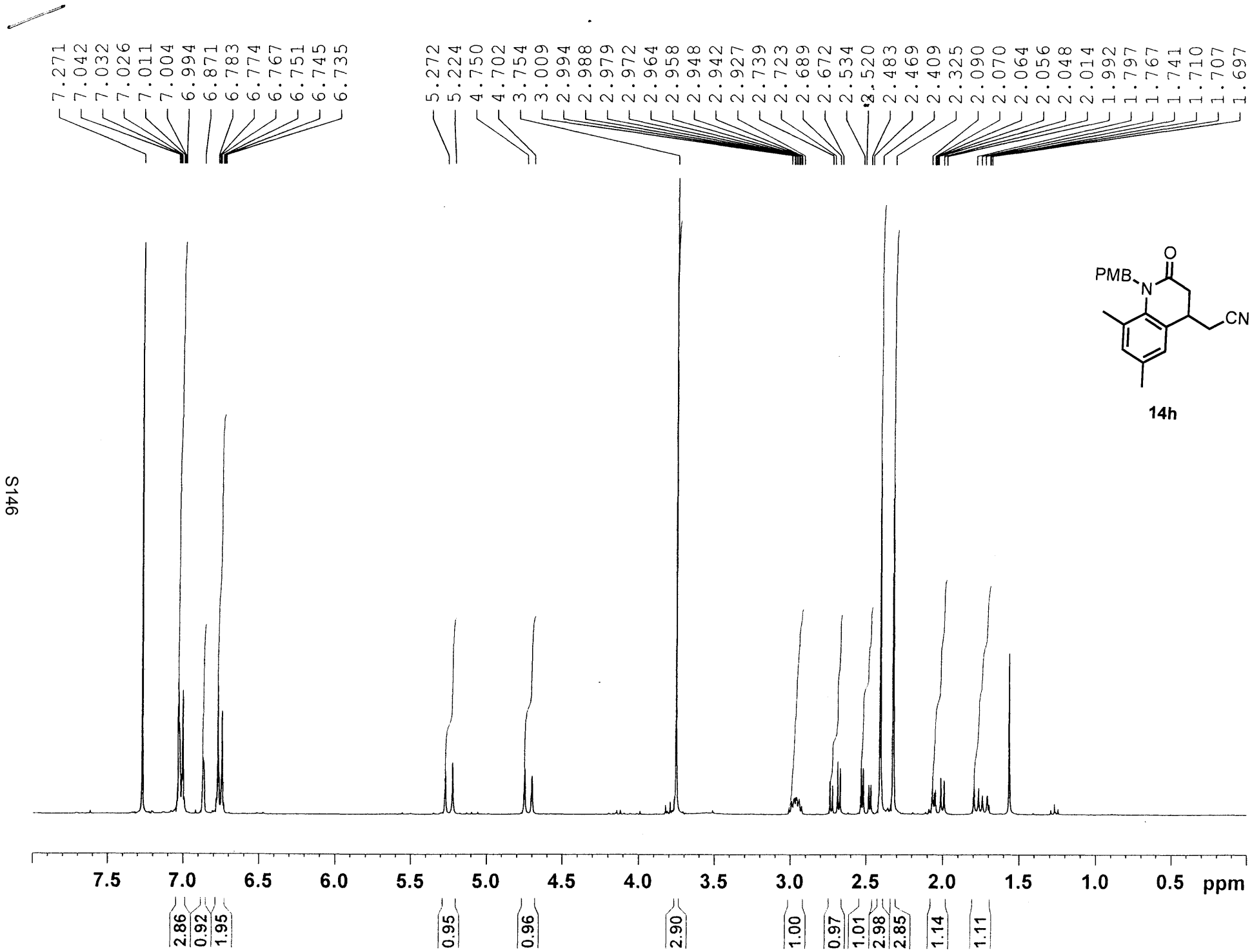
158.76
136.30
135.52
133.89
130.21
129.29
127.25
113.51
113.43
80.71
77.43
77.00
76.58
54.98
47.52
38.00
37.72
33.60
27.92
20.25
O
PMB
N
Br
CO2tBu
14f
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.032
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6.871
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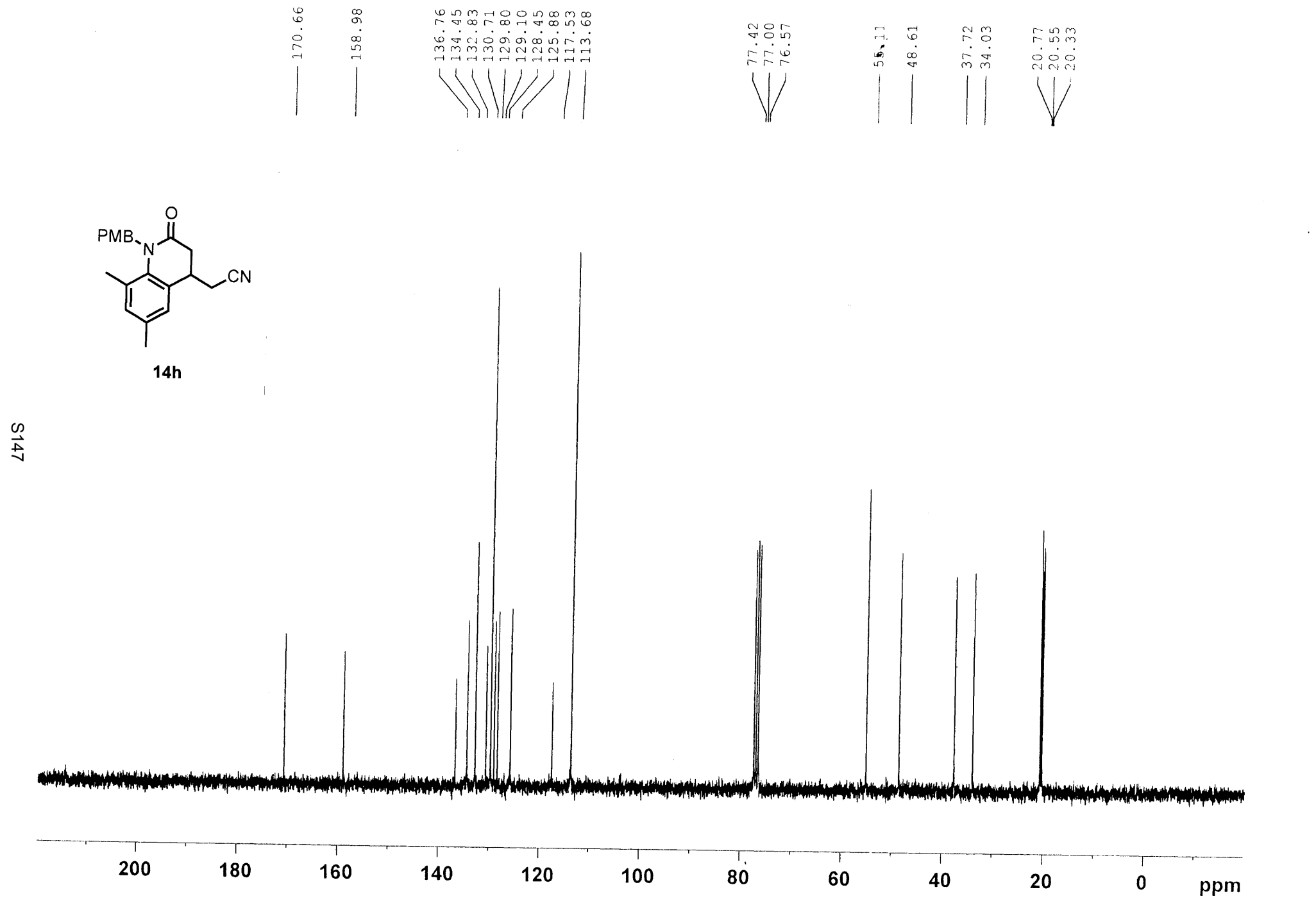
6.767
6.751
6.745
6.735
5.272
5.224
4.750
4.702
3.754
3.009
2.994
2.988
2.979
2.972
2.964
2.958
2.948
2.942
2.927
2.739
2.723
2.689
2.672
2.534
2.520
2.483
2.469
2.409
2.325
2.090
2.070
2.064
2.056
2.048
2.014
1.992
1.797
1.767
1.741
1.710
1.707
1.697
PMB
N
O
CN
14h
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.86
0.92
1.95
0.95
0.96
2.90
1.00
0.97
1.01
2.98
2.85
1.14
1.11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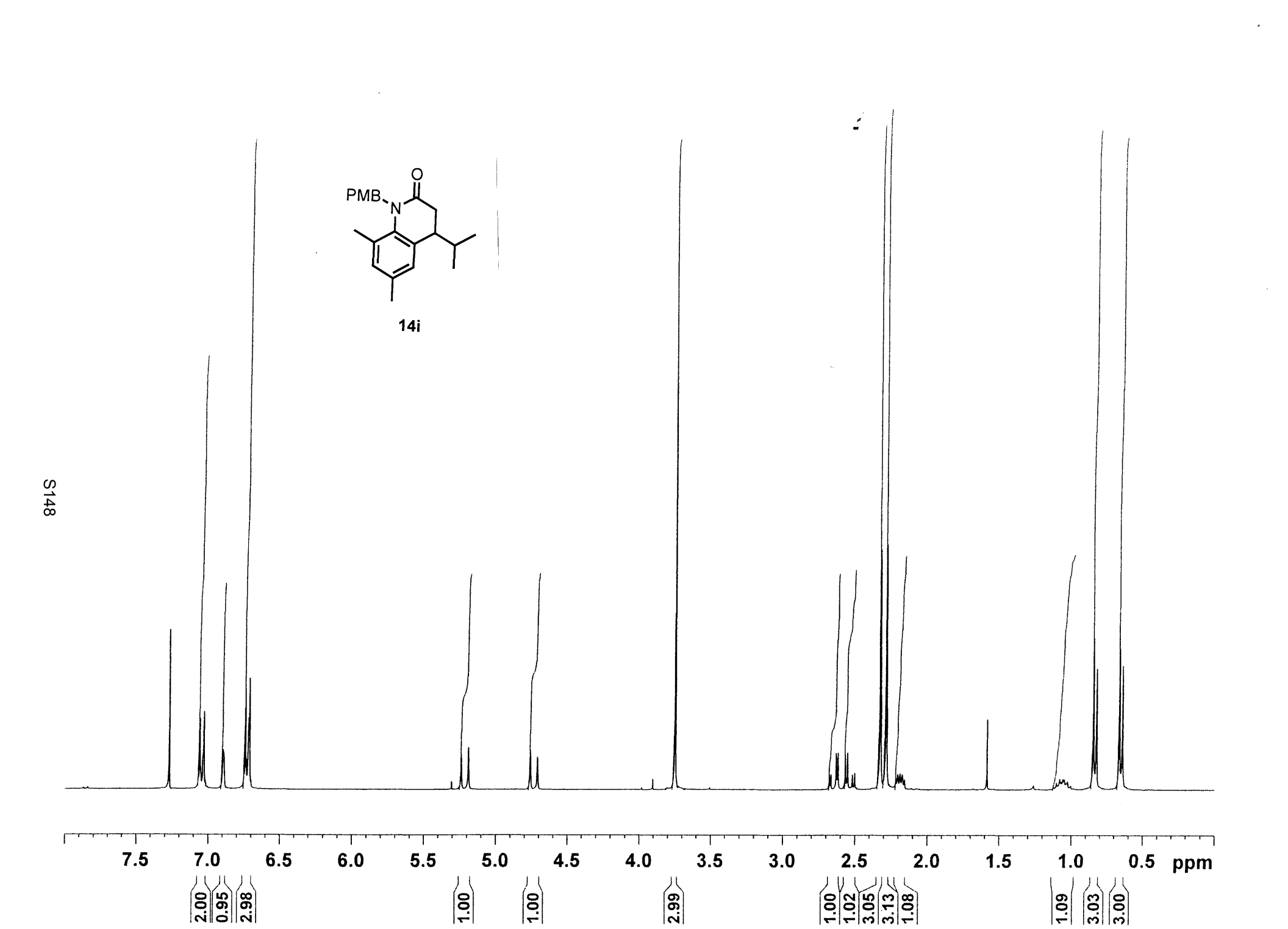
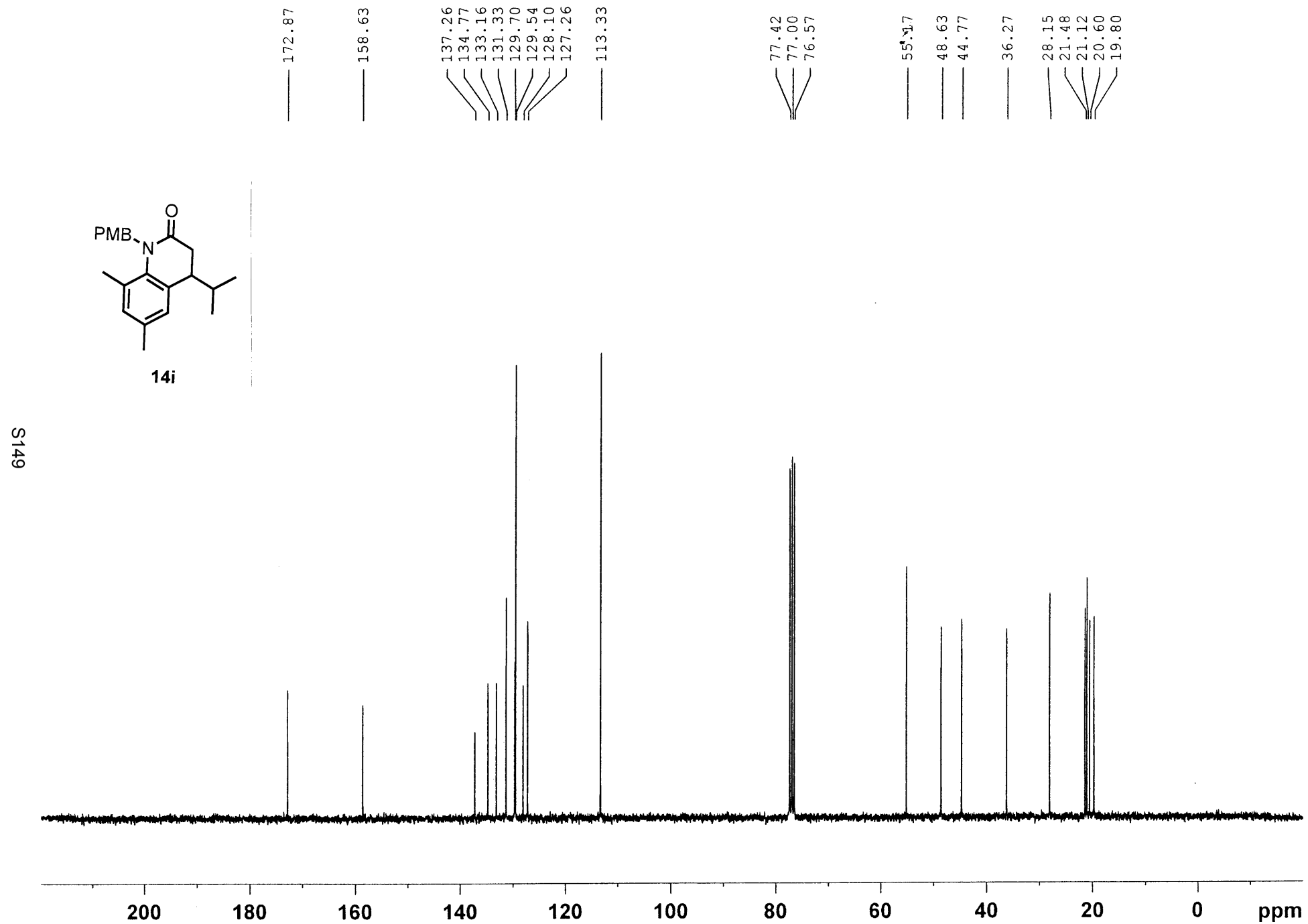
158.98
136.76
134.45
132.83
130.71
129.80
129.10
128.45
125.88
117.53
113.68
77.42
77.00
76.57
55.11
48.61
37.72
34.03
20.77
20.55
20.33
PMB
N
O
CN
14h
200
180
160
140
120
100
80
60
40
20
0
ppm


PMB
N
O
14i
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
0.95
2.98
1.00
1.00
2.99
1.00
1.02
3.05
3.13
1.08
1.09
3.03
3.00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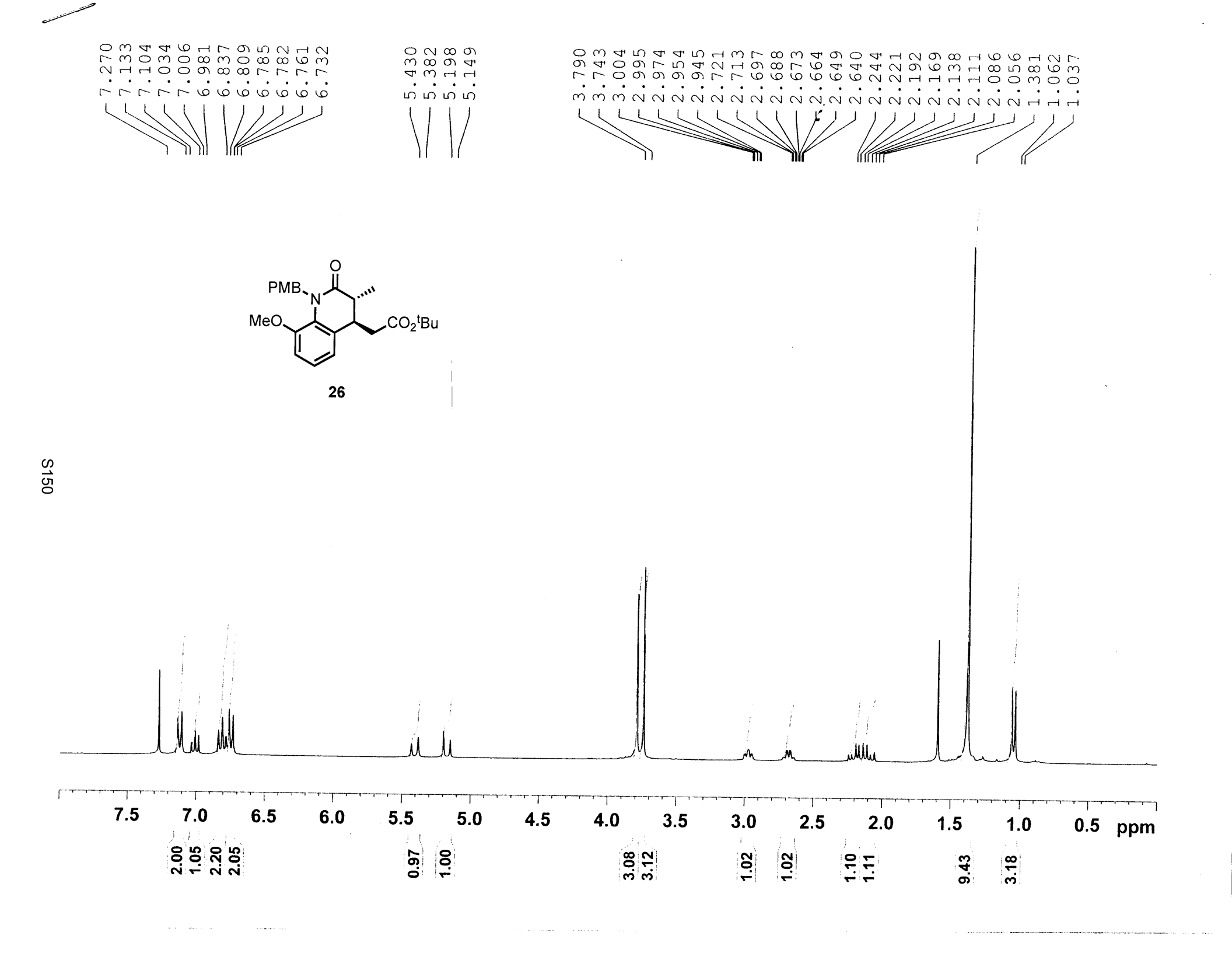
158.63
137.26
134.77
133.16
131.33
129.70
129.54
128.10
127.26
113.33
77.42
77.00
76.57
55.17
48.63
44.77
36.27
28.15
21.48
21.12
20.60
19.80
PMB
N
O
14i
200
180
160
140
120
100
80
60
40
20
0
ppm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7.133
7.104
7.034
7.006
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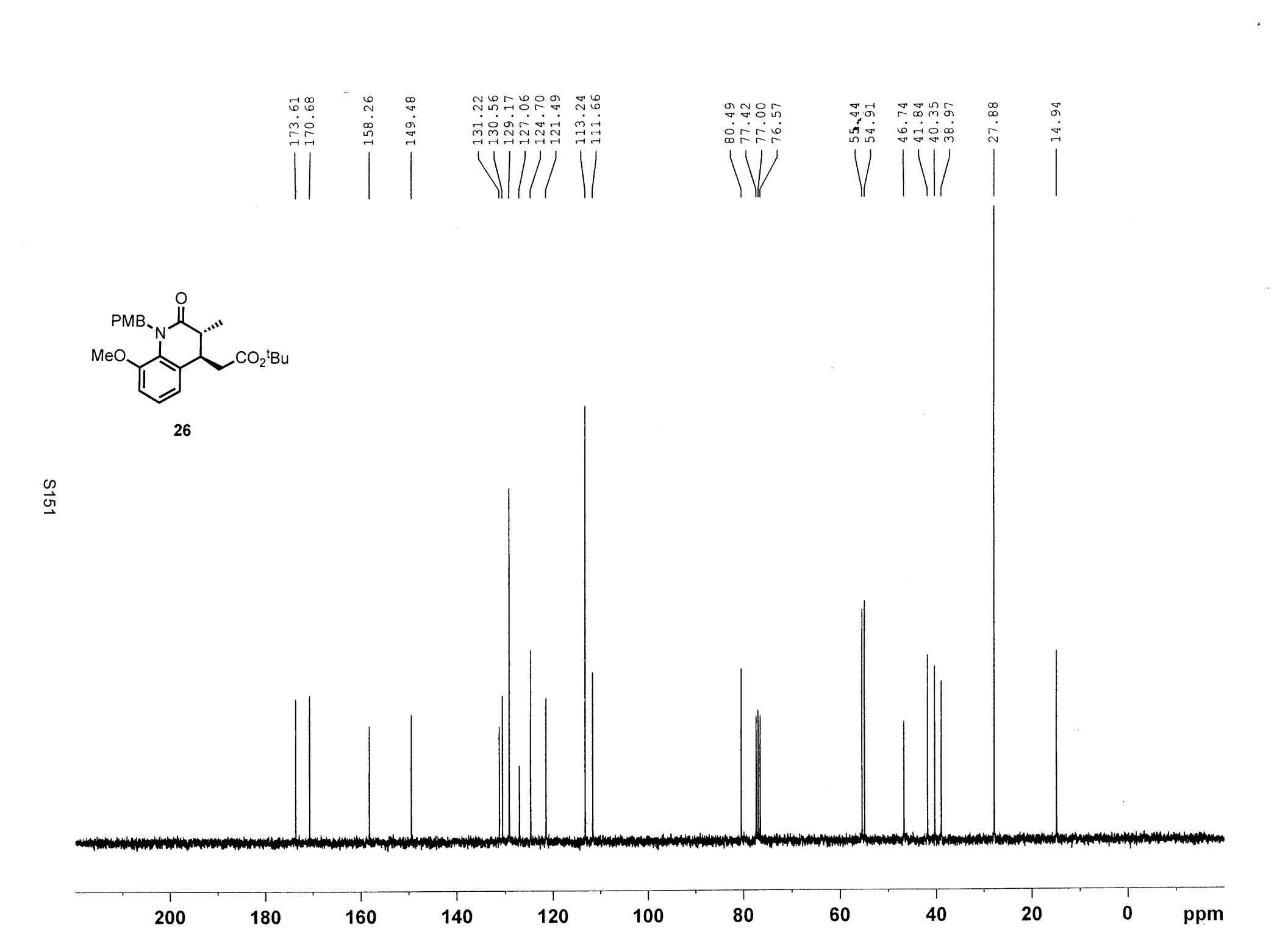
6.837
6.809
6.785
6.782
6.761
6.732
5.430
5.382
5.198
5.149
3.790
3.743
3.004
2.995
2.974
2.954
2.945
2.721
2.713
2.697
2.688
2.673
2.664
2.649
2.640
2.244
2.221
2.192
2.169
2.138
2.111
2.086
2.056
1.381
1.062
1.037
PMB
N
O
MeO
CO2tBu
26
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
1.05
2.20
2.05
0.97
1.00
3.08
3.12
1.02
1.02
1.10
1.11
9.43
3.18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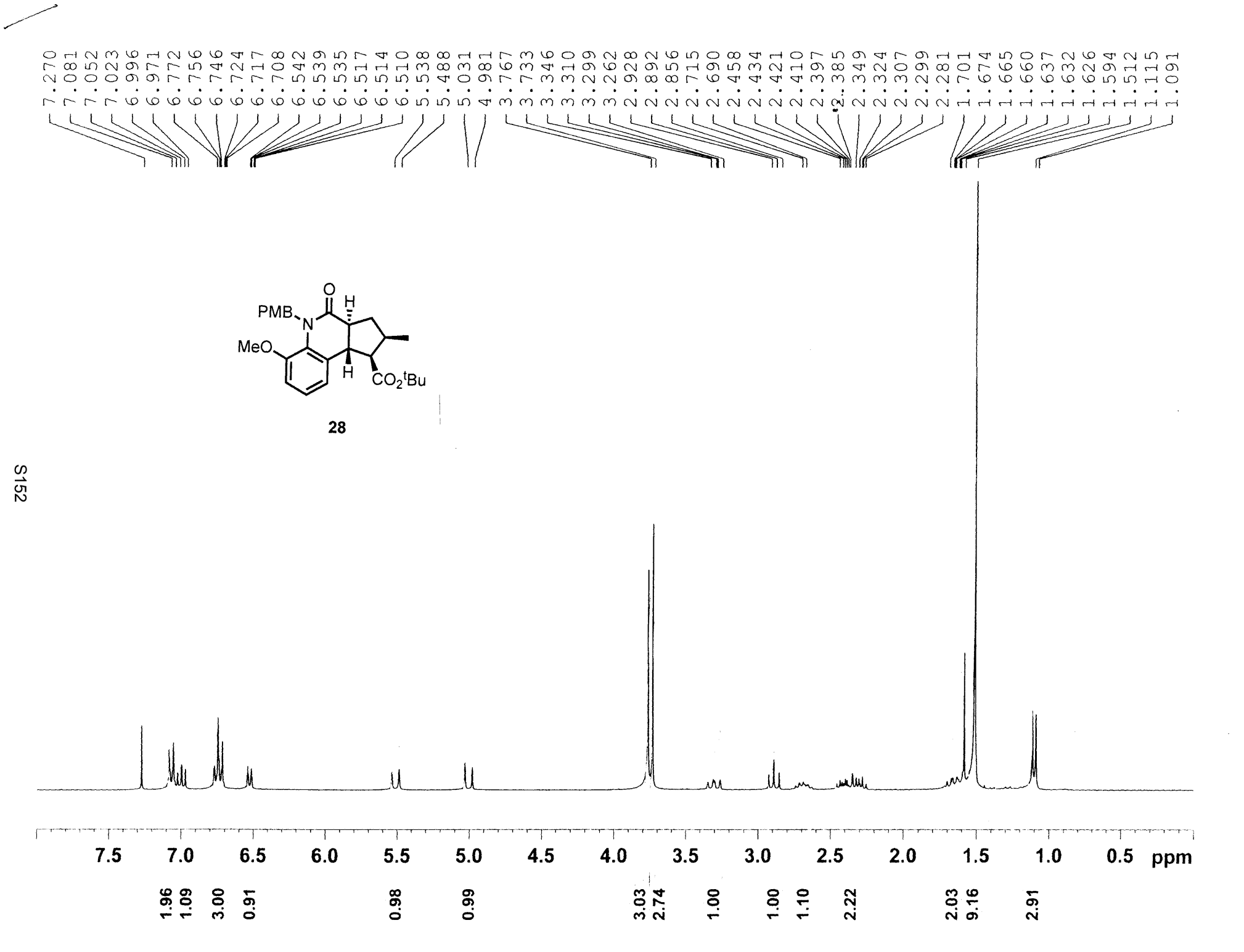
170.68
158.26
149.48
131.22
130.56
129.17
127.06
124.70
121.49
113.24
111.66
80.49
77.42
77.00
76.57
55.44
54.91
46.74
41.84
40.35
38.97
27.88
14.94
PMB
N
O
MeO
CO2tBu
200
180
160
140
120
100
80
60
40
20
0
ppm

26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6.971
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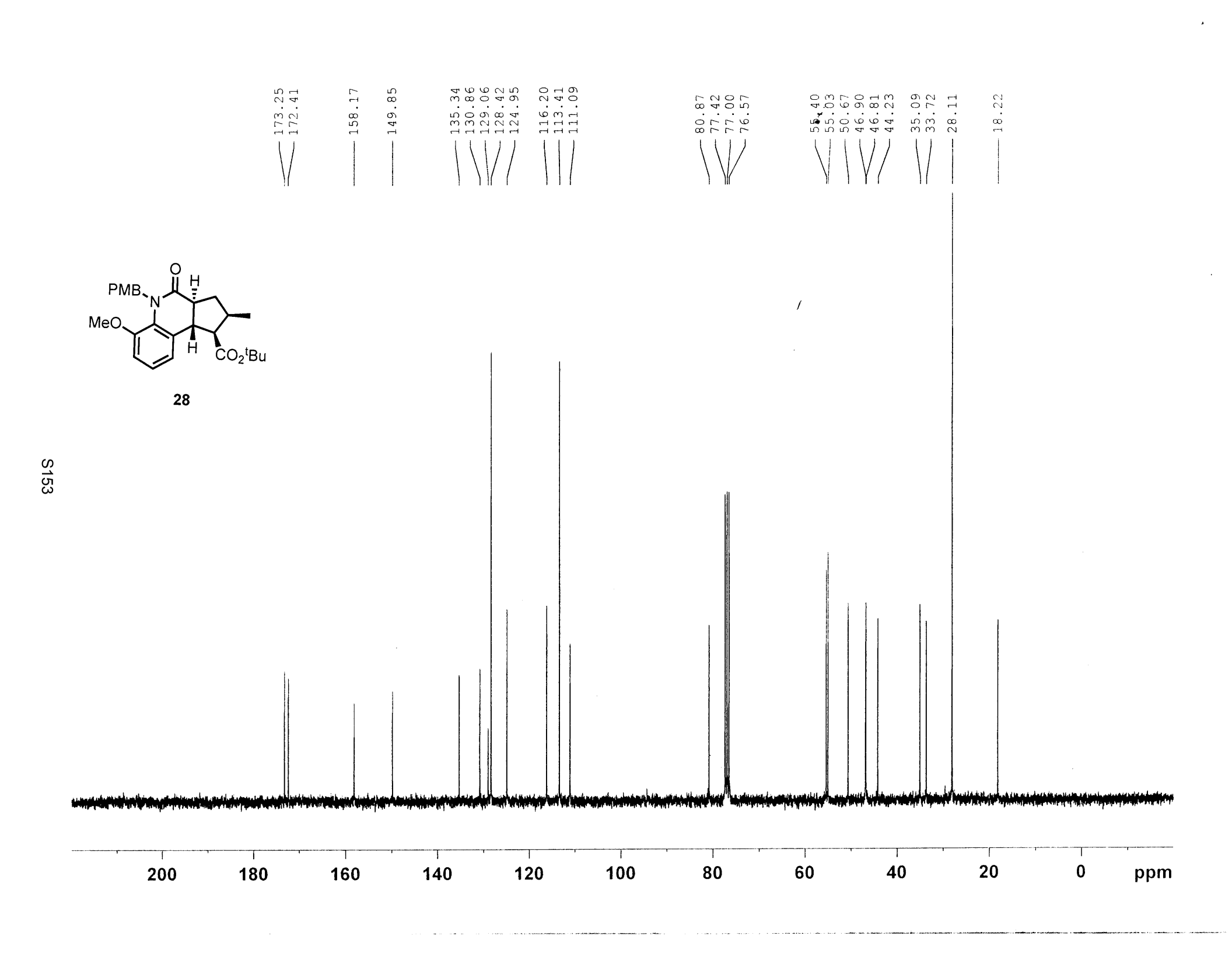
6.756
6.746
6.724
6.717
6.708
6.542
6.539
6.535
6.517
6.514
6.510
5.538
5.488
5.031
4.981
3.767
3.733
3.346
3.310
3.299
3.262
2.928
2.892
2.856
2.715
2.690
2.458
2.434
2.421
2.410
2.397
2.385
2.349
2.324
2.307
2.299
2.281
1.701
1.674
1.665
1.660
1.637
1.632
1.626
1.594
1.512
1.115
1.091
PMB
N
O
H
MeO
H
CO2tBu
28
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.96
1.09
3.00
0.91
0.98
0.99
3.03
2.74
1.00
1.00
1.10
2.22
2.03
9.16
2.91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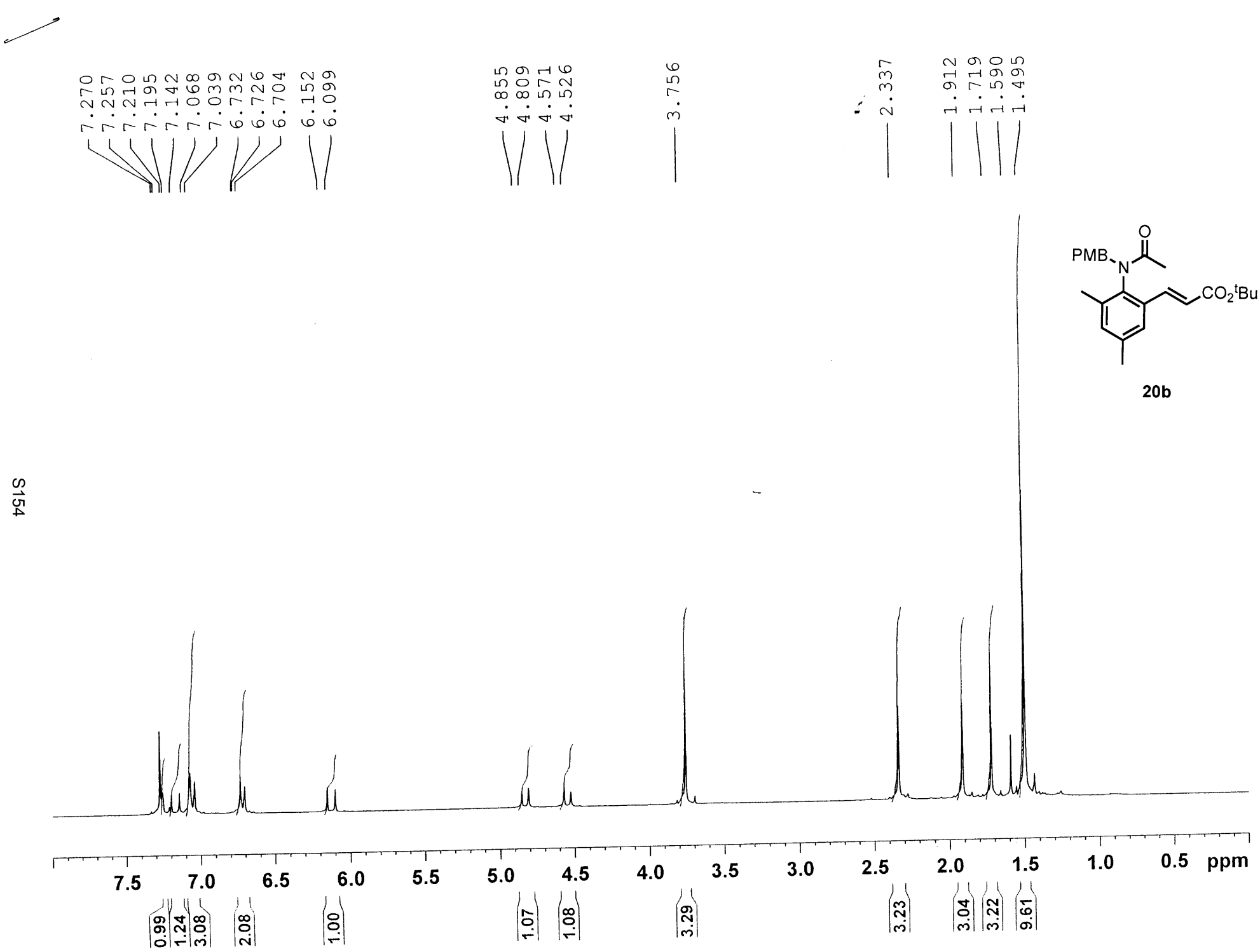
129.06
128.42
124.95
116.20
113.41
111.09
80.87
77.42
77.00
76.57
55.40
55.03
50.67
46.90
46.81
44.23
35.09
33.72
28.11
18.22
PMB
N
O
H
MeO
H
CO2tBu
28
200
180
160
140
120
100
80
60
40
20
0
ppm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6.099
4.855
4.809
4.571
4.526
3.756
2.337
1.912
1.719
1.590
1.495
PMB
N
O
CO2tBu
20b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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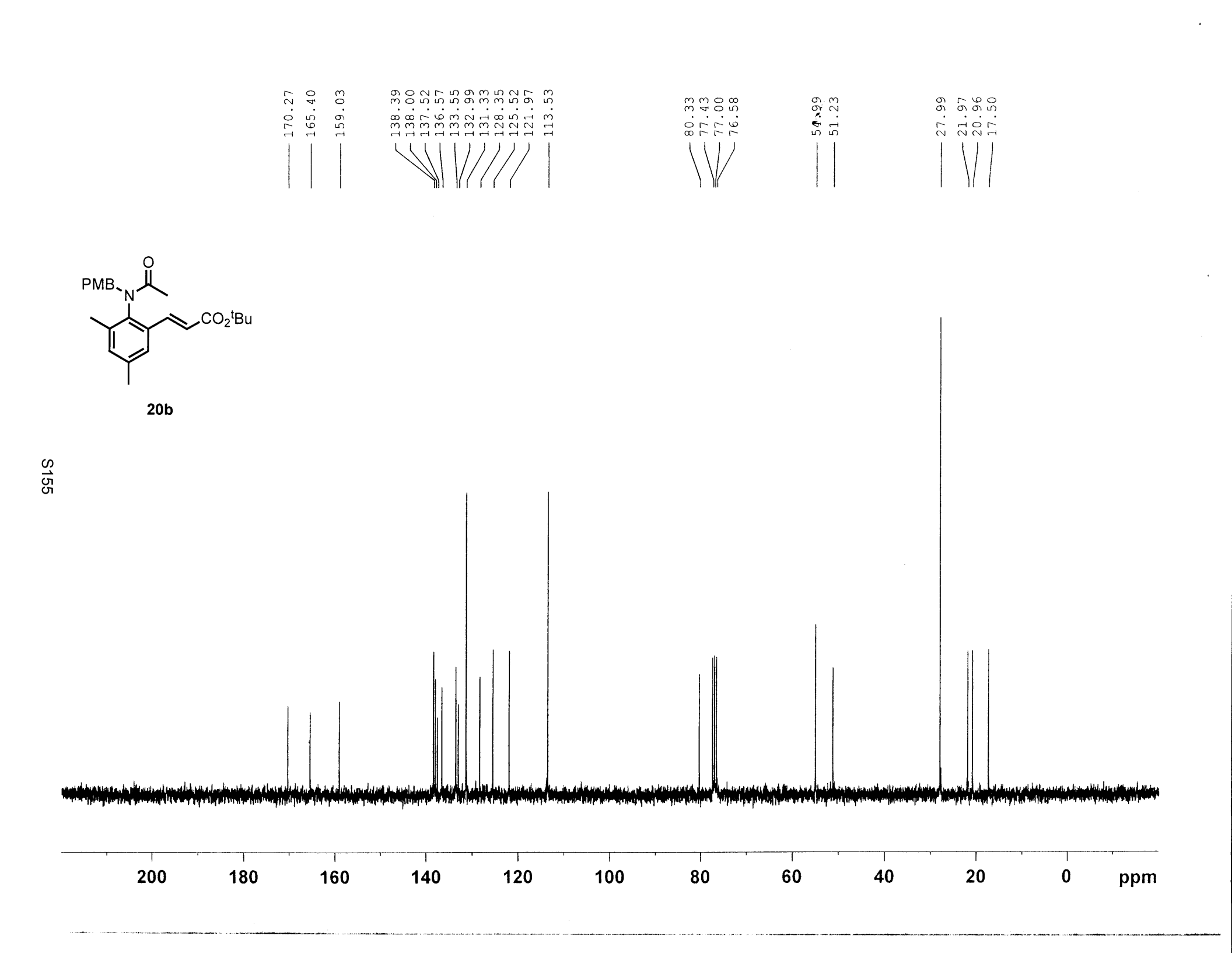
2.08
1.00
1.07
1.08
3.29
3.23
3.04
3.22
9.61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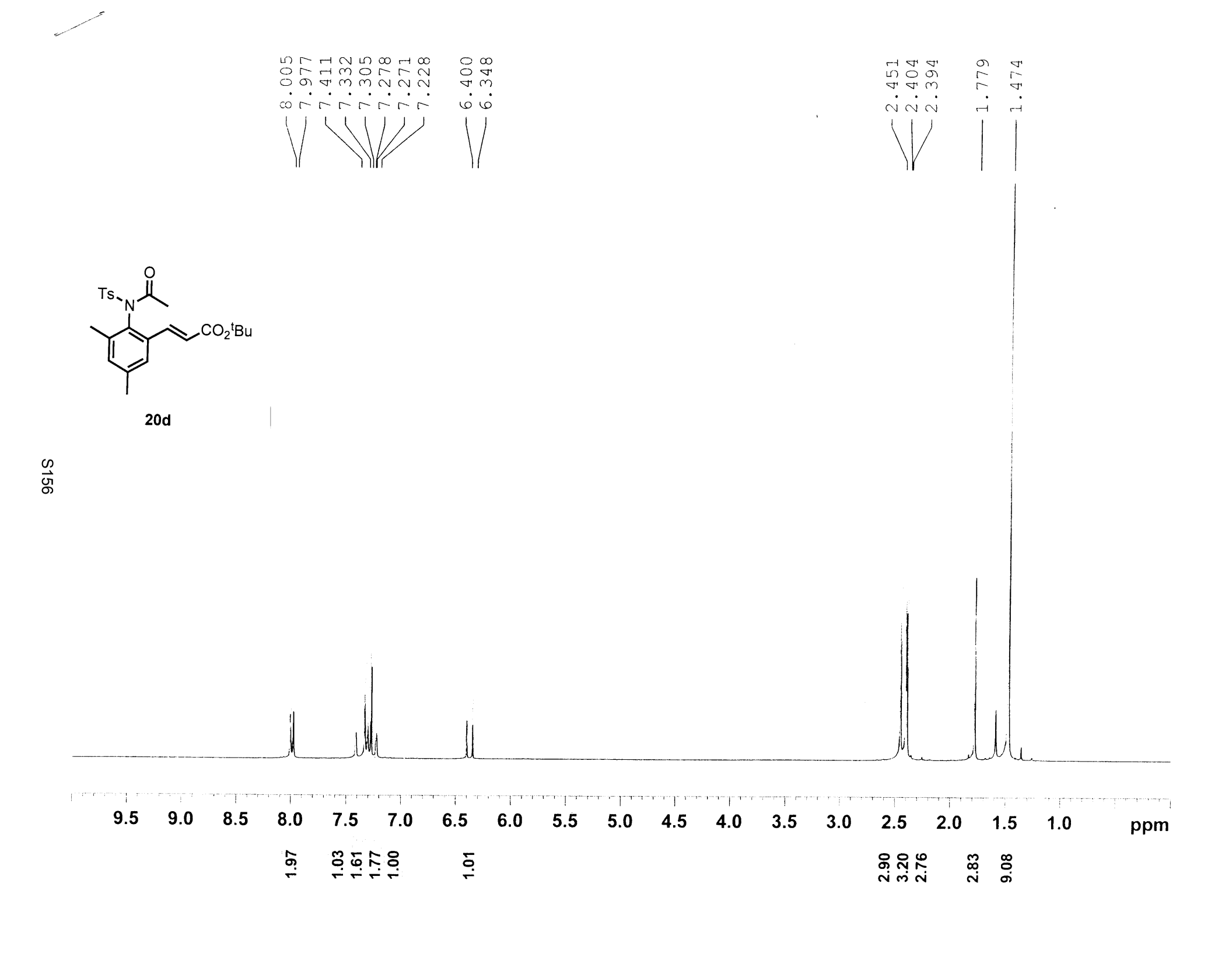
138.00
137.52
136.57
133.55
132.99
131.33
128.35
125.52
121.97
113.53
80.33
77.43
77.00
76.58
54.99
51.23
27.99
21.97
20.96
17.50
PMB
N
O
CO2tBu
20b
200
180
160
140
120
100
80
60
40
20
0
ppm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7.305
7.278
7.271
7.228
6.400
6.348
2.451
2.404
2.394
1.779
1.474
Ts
N
O
CO2tBu
20d
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
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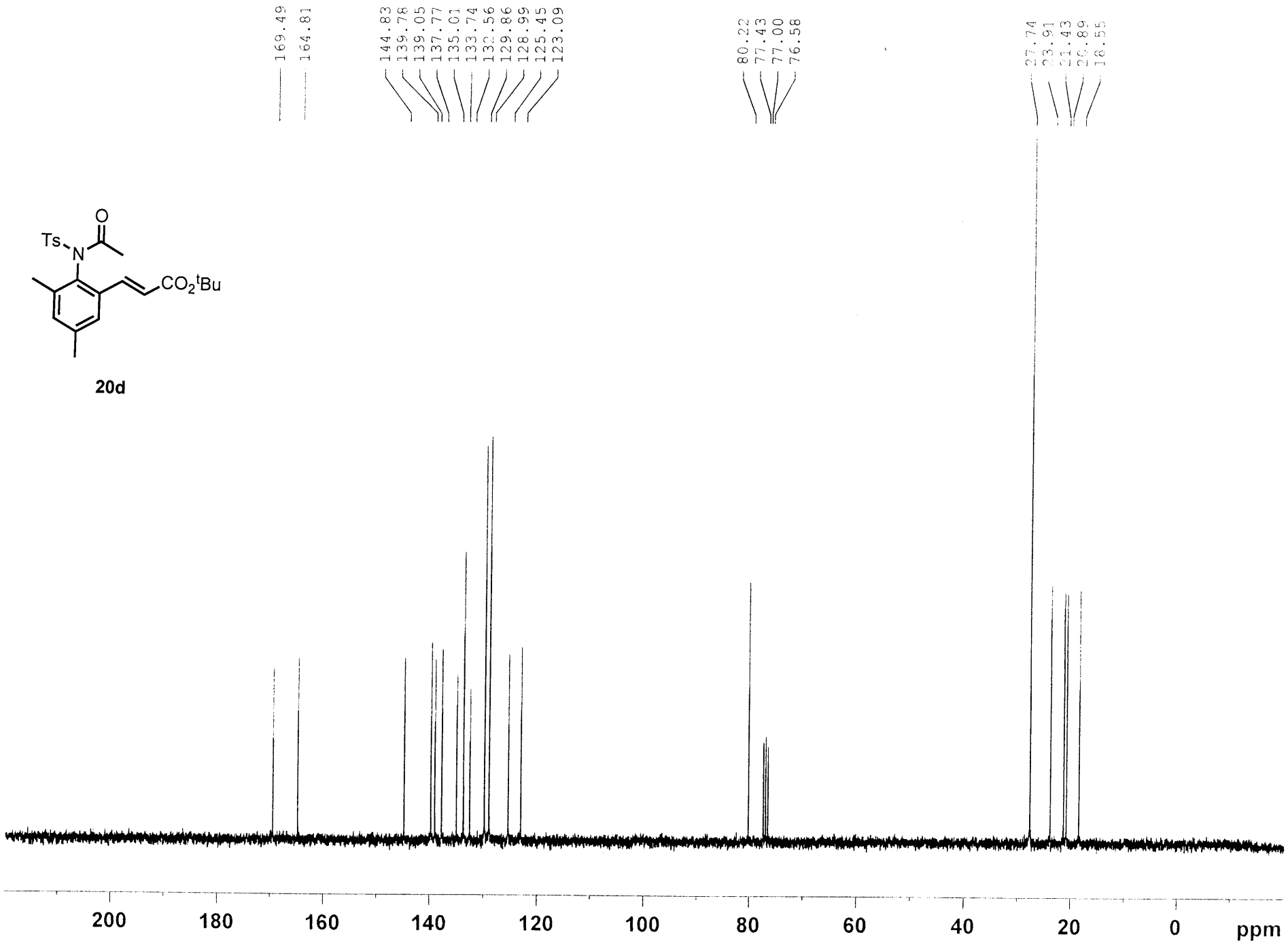
1.61
1.77
1.00
1.01
2.90
3.20
2.76
2.83
9.08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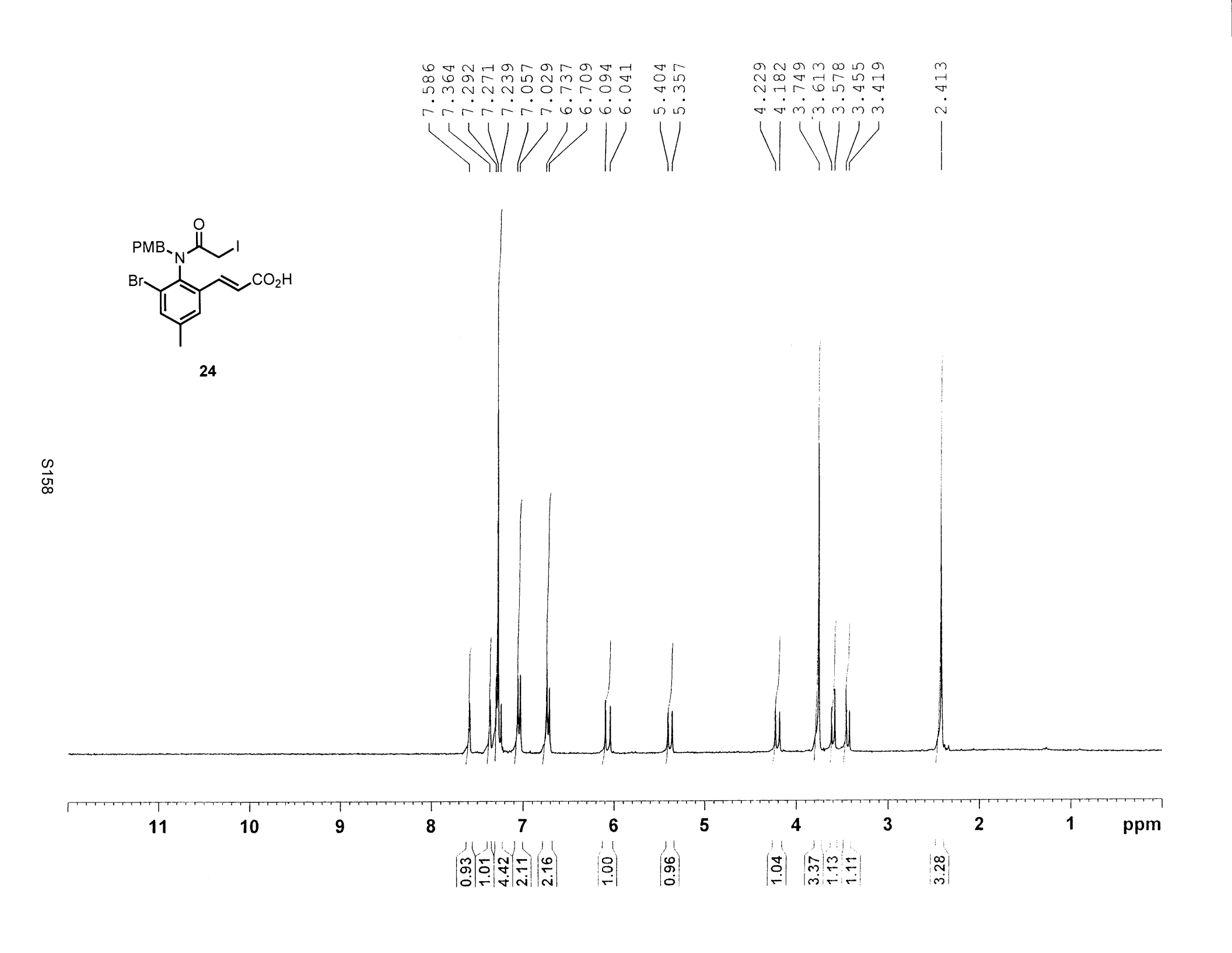
137.77
135.01
133.74
132.56
129.86
128.99
125.45
123.09
80.22
77.43
77.00
76.58
27.74
23.91
21.43
20.89
18.55
Ts
N
O
CO2tBu
200
180
160
140
120
100
80
60
40
20
0
ppm

20d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6.709
6.094
6.041
5.404
5.357
4.229
4.182
3.749
3.613
3.578
3.455
3.419
2.413
PMB
N
O
I
Br
CO2H
24
11
10
9
8
7
6
5
4
3
2
1
ppm
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2.11
2.16
1.00
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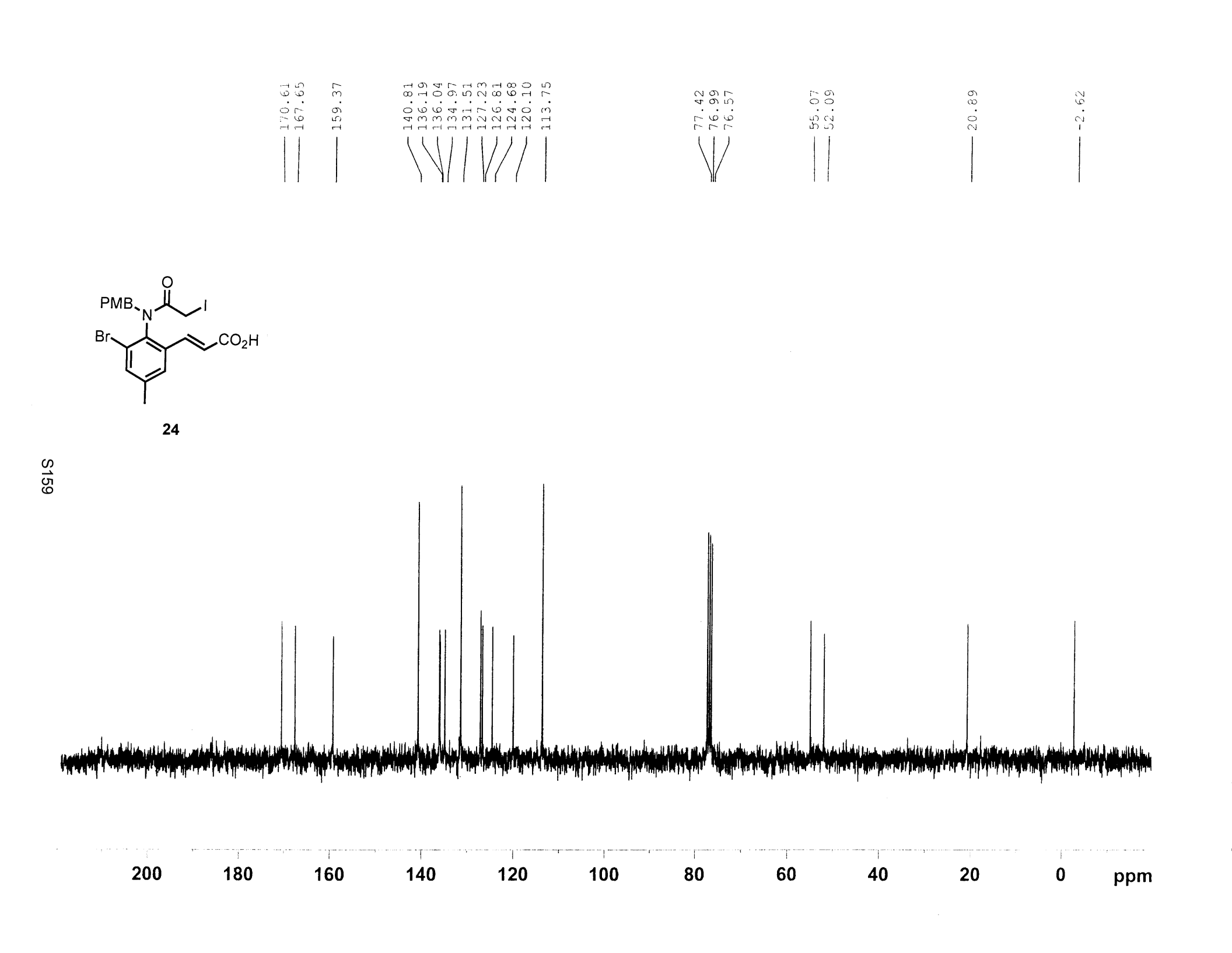
1.04
3.37
1.13
1.11
3.28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159.37
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136.19
136.04
134.97
131.51
127.23
126.81
124.68
120.10
113.75
77.42
76.99
76.57
55.07
52.09
20.89
-2.62
PMB
N
O
I
Br
CO2H
24
S159
200
180
160
140
120
100
80
60
40
20
0
ppm