Supporting Information for

Development of a Triazinyluronium-Based Dehydrative Condensing Reagent with No Heteroatomic Bonds

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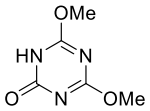
1. General information

NMR spectra were recorded on a JEOL JNM-ECS400 spectrometer [^{1}H NMR (400 MHz), ^{13}C{^{1}H} NMR (100 MHz)] or a JEOL JNM-ECZ600R [^{1}H NMR (600 MHz), ^{13}C{^{1}H} NMR (150 MHz)] at 20 °C unless otherwise noted. Chemical shifts for ^{1}H NMR are reported in parts per million (δ) relative to the residual solvent (CD_3CN, δ 1.94) tetramethylsilane (TMS) as the internal standard. Coupling constants (J) are reported in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Chemical shifts for ^{13}C{^{1}H} NMR are reported in parts per million (δ) relative to the solvent [$(CD_3)_2SO$, δ 39.52; CD_3OD, δ 49.00; CD_3CN, δ 1.32; or $CDCl_3$, δ 77.16]. Mass spectra were measured on a JMS-T100TD AccuTOF TLC (ESI-MS, JEOL) spectrometer and an LCMS-2050 spectrometer (ESI-MS, Shimadzu). DSC analysis was performed on a DSC7020 system (Hitachi) under nitrogen flow at a heating rate of 10 °C/min in a temperature range of 50–350 °C. The sample was placed in a sealed stainless steel pan (SUS303Cu). HPLC analysis was performed using an LC-2050C 3D system (Shimadzu). Measurements for single-crystal X-ray structure analysis were performed on a Rigaku R-AXIS RAPID diffractometer. The structures were solved by SHELXT[1] and were refined using SHELXL[2] on Yadokari-XG 2009[3]. Analytical thin layer chromatography (TLC) was performed using glass plates precoated with 0.25 mm silica gel impregnated with a fluorescent indicator (254 nm). Flash chromatography separations were performed on silica (Kanto Chemical Silica Gel 60 N, spherical, neutral, 40−100 mesh) or amine-functionalized silica (Chromatorex NH-DM2035, 60 μm, Fuji Silysia Chemical). $NaPF_6$-treated amine-functionalized silica was prepared by treatment of amine-functionalized silica with a solution of $NaPF_6$ in MeOH (5 w/v%) and washing with CH_2Cl_2. Reagents were commercial grades and were used without any purification unless otherwise noted. Dehydrated DMF, CH_2Cl_2, THF, MeOH, and MeCN were purchased from commercial sources. ^{i}Pr$_2$EtN, *N*-methylpyrrolidine, 2-phenylethylamine (**7a**), aniline (**7b**), diethylamine (**7c**), dibenzylamine (**7d**), and morpholine (**7e**) were purchased from commercial sources and distilled before use. All reactions sensitive to moisture were conducted under a N_2 atmosphere.

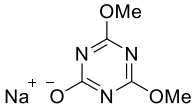
2. Experimental procedure and characterization data

4,6-Dimethoxy-1,3,5-triazin-2(1*H*)-one (2)[4]



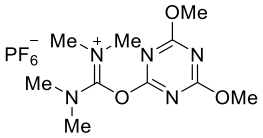
2-Chloro-4,6-dimethoxy-1,3,5-triazine (17.56 g, 100 mmol) was added to a solution of sodium acetate (16.41 g, 200 mmol), *N*-methylpyrrolidine (5.30 mL, 20 mmol) in THF/H_2O (1:1, 200 mL) at room temperature. The reaction mixture was heated to 60 °C for 1 h using an oil bath and then cooled to room temperature. The reaction mixture was treated with acetic acid (34.3 mL, 600 mmol) and concentrated under reduced pressure to approximately half its original volume. The precipitate was filtered and washed with H_2O to afford a white solid (13.7 g, 87%). ^{1}H NMR (400 MHz, CD_3OD): δ 4.00 (s, 6H); ^{13}C{^{1}H} NMR [100 MHz, $(CD_3)_2SO$]: δ 168.2 (br), 157.1, 55.2. MS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_5H_8N_3O_3$ 158; Found 158.

Sodium 4,6-dimethoxy-1,3,5-triazin-2-olate (4)[5]



Compound **2** (11.71 g, 74.5 mmol) was added to a solution of NaOH (2.98 g, 74.5 mmol) in H_2O (120 mL) at room temperature. After 10 min, the reaction mixture was concentrated under reduced pressure. The residue was recrystallized from EtOH to afford a white solid (9.31 g, 70%). ^{1}H NMR (400 MHz, CD_3OD): δ 3.84 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, CD_3OD): δ 174.4, 174.1, 54.5. MS (ESI) *m*/*z*: $[M - Na]^-$ Calcd for $C_5H_6N_3O_3$ 156; Found 156.

2-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (DMT-TU)



Synthesis on a 1 mmol scale: Salt **3** (179.1 mg, 1.0 mmol) was added to a solution of **4** (280.6 mg, 1.0 mmol) in MeCN (3.30 mL) at room temperature. After 1 h, the reaction mixture was filtered. Et_2O (24 mL) was added to the filtrate to induce precipitation. The precipitate was collected to afford a white solid (368.5 mg, 92%).

Synthesis on a 60 mmol scale: Salt **3** (16.80 g, 60 mmol) was added to a solution of **4** (10.74 g, 60 mmol) in MeCN (200 mL) at room temperature. After 1 h, the reaction mixture was filtered. Et_2O was added to the filtrate to induce precipitation. The precipitate was collected to afford a white solid (20.1 g, 84%).

Mp: 180 °C (decomp.). ^{1}H NMR (600 MHz, CD_3CN, 20 °C): δ 4.04 (s, 6H), 3.15 (br s, 12H),. ^{1}H NMR (600 MHz, CD_3CN, 70 °C): δ 4.07 (s, 6H), 3.16 (s, 12H). $^{13}C\{^1H\}$ NMR (150 MHz, CD_3CN, 70 °C): δ 175.7, 170.8, 159.4, 57.4, 41.7. HRMS (ESI-TOF) *m*/*z*: $[M - PF_6]^+$ Calcd for $C_{10}H_{18}N_5O_3$ 256.1405; Found: 256.1412. Anal. Calcd for $C_{10}H_{18}F_6N_5O_3P$: C, 29.93; H, 4.52; N, 17.45; Found: C, 29.37; H, 4.44; N, 17.05.

Table S1. Summary of crystal data for DMT-TU.

CCDC registry	2370150
Method for preparing crystals	vapor diffusion of $CHCl_3$ into MeCN solution at room temperature
Formula	$C_{10}H_{18}N_5O_3F_6P$
Formula Weight (g/mol)	401.26
Crystal Dimensions (mm)	0.23 × 0.16 × 0.09
Crystal System	triclinic
Space Group	P 1
Temperature (K)	123
a (Å)	8.1394(7)
b (Å)	8.1660(8)
c (Å)	8.2777(6)
α (°)	92.291(7)
β (°)	115.656(8)
γ (°)	118.213(8)
V (Å^3)	415.78(7)
Number of reflections to determine final unit cell	3283
Min and Max 2θ for cell determination (°)	5.74, 54.86
Z	1
F(000)	206
λ (Å, Mo Kα)	0.71075
μ (mm^{-1})	0.250
Max 2θ for data collection (°)	54.864
Measured fraction of data	0.997
Number of reflections measured	4082
Unique reflections measured	3084
R_{merge}	3.47%
Number of parameters in least-squares	232
R_1	0.0570
wR_2	0.1588
R_1 (all data)	0.0744
wR_2 (all data)	0.2156

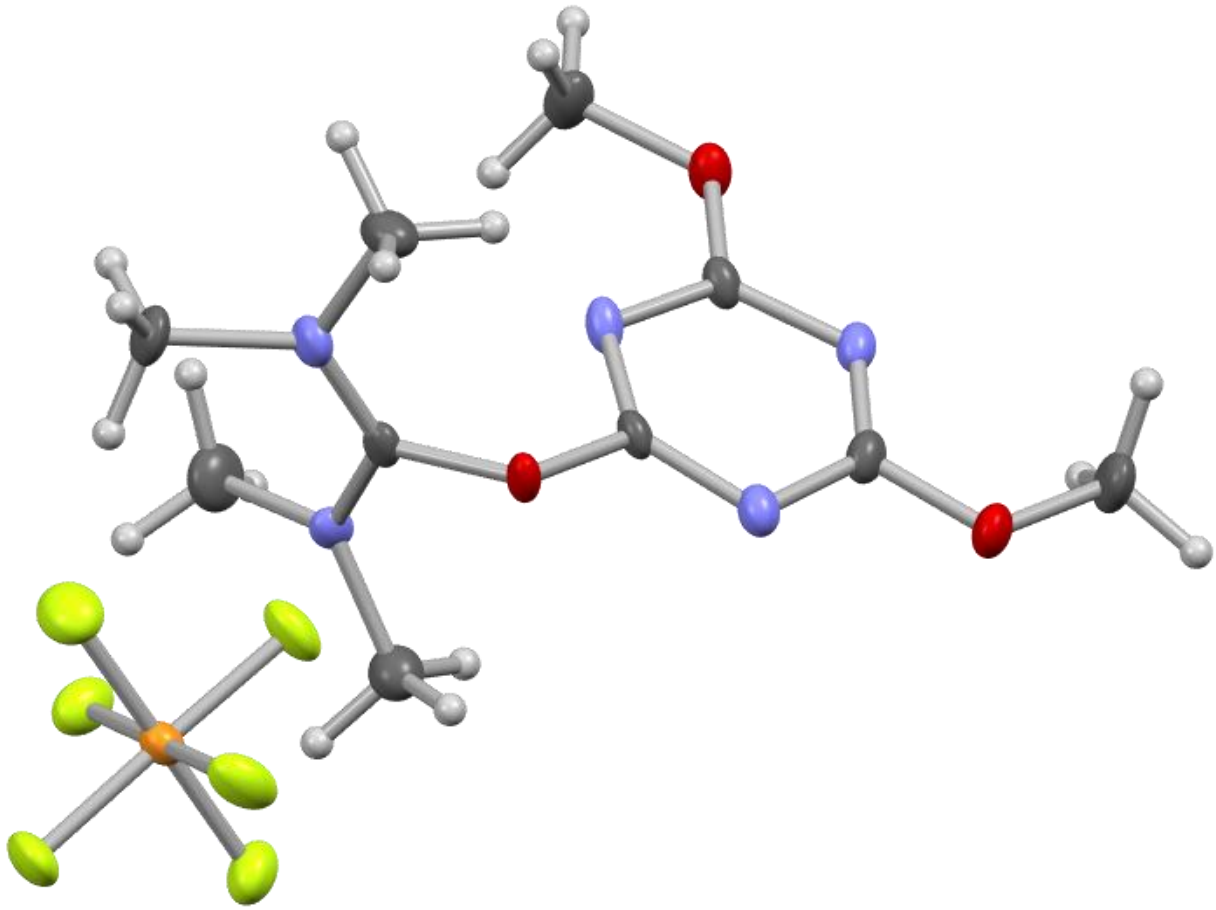
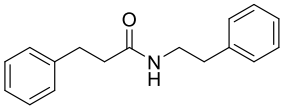


Figure S1. ORTEP diagram of DMT-TU with thermal ellipsoids drawn at 50% probability.

General procedure for dehydration condensing reactions using DMT-TU

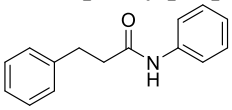
DMT-TU (1.2 equiv.) was added to a solution of carboxylic acid **6** (1 equiv.), amine **7** (1.2 equiv.), and $^{i}Pr_2EtN$ (1.2 equiv.) in MeCN (5 mL per 1 mmol of **6**) at room temperature. The reaction mixture was stirred until TLC monitoring indicated complete conversion. The reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography to afford amide **8**.

***N*-Phenethyl-3-phenylpropanamide (8aa)**[6]



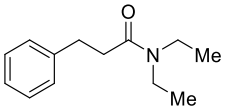
The general procedure was followed using DMT-TU (240.7 mg, 0.60 mmol), **6a** (75.1 mg, 0.50 mmol), **7a** (75.7 µL, 0.60 mmol), and $^{i}Pr_2EtN$ (103 µL, 0.60 mmol) in MeCN (2.50 mL) at room temperature. The reaction mixture was stirred for 3 h. Column chromatography (silica, hexane/EtOAc = 3:1) afforded a white solid (116.9 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.14 (m, 8H), 7.08 (d, J = 6.9 Hz, 2H), 5.32 (br s, 1H), 3.47 (dt, J = 6.8, 6.8 Hz, 2H), 2.94 (t, J = 7.7 Hz, 2H), 2.73 (t, J = 6.8 Hz, 2H), 2.42 (t, J = 7.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.1, 141.0, 139.0, 128.9, 128.7, 128.6, 128.5, 126.6, 126.4, 40.7, 38.7, 35.8, 31.8. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{19}NNaO$ 276; Found 276.

***N*,3-Diphenylpropanamide (8ab)**[6]



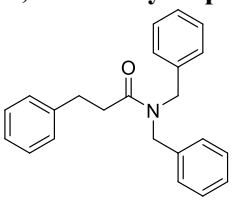
The general procedure was followed using DMT-TU (240.7 mg, 0.60 mmol), **6a** (75.1 mg, 0.50 mmol), **7b** (54.8 μL, 0.60 mmol), and $^{i}Pr_2EtN$ (103 μL, 0.60 mmol) in MeCN (2.50 mL) at room temperature. The reaction mixture was stirred for 23 h. Column chromatography (silica, hexane/THF =4:1) afforded a brown solid (105.6 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 7.7 Hz, 2H), 7.37–7.16 (m, 8H), 7.08 (dd, J = 7.7, 7.7 Hz, 1H), 3.03 (t, J = 7.6 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.6, 140.7, 137.8, 129.1, 128.8, 128.5, 126.5, 124.4, 120.1, 39.5, 31.7 MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{15}NNaO$ 248; Found 248.

_N_,_N_-Diethyl-3-phenylpropanamide (8ac)[7]



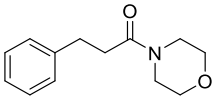
The general procedure was followed using DMT-TU (240.7 mg, 0.60 mmol), **6a** (75.1 mg, 0.50 mmol), **7c** (62.3 μL, 0.60 mmol), and $^{i}Pr_2EtN$ (103 μL, 0.60 mmol) in MeCN (2.50 mL) at room temperature. The reaction mixture was stirred for 4.5 h. Column chromatography (silica, hexane/acetone = 9:1 to hexane/THF = 9:1) afforded a colorless oil (93.6 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.11 (m, 5H), 3.38 (q, J = 7.2 Hz, 2H), 3.22 (q, J = 7.2 Hz, 2H), 2.98 (t, J = 8.0 Hz, 2H), 2.59 (t, J = 8.0 Hz, 2H), 1.16–1.04 (m, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.3, 141.7, 128.6, 128.5, 126.2, 42.0, 40.3, 35.2, 31.7, 14.4, 13.2. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{19}NNaO$ 228; Found 228.

_N_,_N_-Dibenzyl-3-phenylpropanamide (8ad)[8]



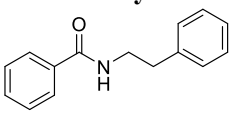
The general procedure was followed using DMT-TU (240.7 mg, 0.60 mmol), **8a** (75.1 mg, 0.50 mmol), **7d** (115 μL, 0.60 mmol), and $^{i}Pr_2EtN$ (103 μL, 0.60 mmol) in MeCN (2.50 mL) at room temperature. The reaction mixture was stirred for 3 h. Column chromatography (silica, hexane/acetone = 19:1) afforded a white solid (150.9 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.13 (m, 13H), 7.07 (d, J = 7.3 Hz, 2H), 4.60 (s, 2H), 4.36 (s, 2H), 3.05 (t, J = 7.8 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.8, 141.3, 137.4, 136.5, 129.0, 128.7, 128.62, 128.58, 128.4, 127.7, 127.5, 126.4, 126.3, 49.9, 48.4, 35,1, 31.7. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{23}NNaO$ 352; Found 352.

1-Morpholino-3-phenylpropan-1-one (8ae)[9]



The general procedure was followed using DMT-TU (3.37 g, 8.4 mmol), **6a** (1.05 g, 7.0 mmol), **7e** (725 μL, 8.4 mmol), and $^{i}Pr_2EtN$ (1.45 mL, 8.4 mmol) in MeCN (35.0 mL) at room temperature. The reaction mixture was stirred for 1 h. Column chromatography (silica, hexane/EtOAc = 1:1) afforded a clear colorless oil (1.27 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.15 (m, 5H), 3.62 (s, 4H), 3.51 (t, J = 4.8 Hz, 2H), 3.35 (t, J = 4.8 Hz, 2H), 2.98 (t, J = 7.8 Hz, 2H), 2.61 (t, J = 7.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.0, 141.2, 128.7, 128.6, 126.4, 67.0, 66.6, 46.1, 42.1, 34.9, 31.6. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{17}NNaO_2$ 242; Found 242.

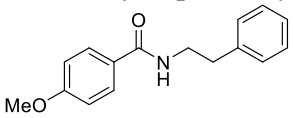
_N_-Phenethylbenzamide (8ba)[8]



The general procedure was followed using DMT-TU (240.7 mg, 0.60 mmol), **6b** (76.1 mg, 0.50 mmol), **7a** (75.7 μL, 0.60 mmol), and $^{i}Pr_2EtN$ (103 μL, 0.60 mmol) in MeCN (2.50 mL) at room temperature. The reaction mixture was stirred for 3 h. Column chromatography (silica, hexane/EtOAc = 2:1) afforded a white

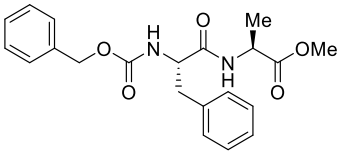
solid (104.5 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.64 (m, 2H), 7.53–7.43 (m, 1H), 7.43–7.34 (m, 2H), 7.34–7.28 (m, 2H), 7.28–7.17 (m, 3H), 6.29 (s, 1H), 3.70 (q, J = 6.8 Hz, 2H), 2.64 (t, J = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.6, 139.0, 134.7, 131.5, 128.9, 128.8, 128.6, 126.9, 126.7, 41.2, 35.8. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{15}NNaO$ 248; Found 248.

4-Methoxy-*N*-phenethylbenzamide (8ca)[8]



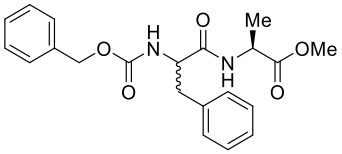
DMT-TU (240.7 mg, 0.60 mmol) was added to a solution of **6c** (76.1 mg, 0.50 mmol), **7a** (75.7 μL, 0.60 mmol), and ^{i}Pr$_2$EtN (103 μL, 0.60 mmol) in MeCN/THF (1:1, 5.00 mL) at room temperature. After 20 h, the reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (silica, hexane/EtOAc = 2:1 to 1:1) afforded a white solid (126.3 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73–7.60 (m, 2H), 7.37–7.16 (m, 5H), 6.95–6.80 (m, 2H), 6.27 (s, 1H), 3.81 (s, 3H), 3.68 (dt, J = 6.9 Hz, 2H), 2.91 (t, J = 6.9 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 167.1, 162.1, 139.1, 128.9, 128.8, 128.7, 127.0, 126.6, 113.8, 55.5, 41.2, 35.9. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{17}NNaO_2$ 278; Found 278.

Compound 8df[8]



DMT-TU (88.2 mg, 0.22 mmol) was added to a solution of **6d** (57.1 mg, 0.20 mmol), **7f-HCl** (30.7 mg, 0.22 mmol), and ^{i}Pr$_2$EtN (75.8 μL, 0.44 mmol) in MeCN (2.50 mL) at room temperature. After 1 h, the reaction mixture was diluted with $CHCl_3$ and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (silica, hexane/EtOAc = 1:1) afforded a white solid (68.7 mg, 89%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33–7.16 (m, 10H), 6.71 (br s, 1H), 5.70–5.32 (m, 1H), 5.10–4.97 (m, 2H), 4.56–4.44 (m, 2H), 3.69 (s, 3H), 3.06 (d, J = 4.2 Hz, 2H), 1.31 (d, J = 4.8 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 172.9, 170.7, 156.1, 136.4, 136.2, 129.4, 128.64, 128.55, 128.2, 128.0, 127.0, 67.0, 56.0, 52.5, 48.1, 38.6, 18.2. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{24}N_2NaO_5$ 407; Found 407.

Compound DL-8df[8]



DMT-TU (88.2 mg, 0.22 mmol) was added to a solution of *N*-(benzyloxy)carbonyl-DL-phenylalanine (57.1 mg, 0.20 mmol), **7f-HCl** (30.7 mg, 0.22 mmol), and ^{i}Pr$_2$EtN (75.8 μL, 0.44 mmol) in DMF (2.50 mL) at room temperature. After 1 h, the reaction mixture was diluted with $CHCl_3$ and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Recrystallization (hexane/CH_2Cl_2) afforded a white solid (53.4 mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.41–7.12 (m, 10H), 6.41–6.24 (m, 0.5H), 6.24–6.06 (m, 0.5H), 5.54–5.24 (m, 1H), 5.08 (s, 2H), 4.57–4.34 (m, 2H), 3.71 (s, 1.5H), 3.70 (s, 1.5H), 3.20–2.95 (m, 2H), 1.33 (d, J = 6.9 Hz, 1.5H), 1.21 (d, J = 7.3 Hz, 1.5H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 173.0, 172.9, 170.4, 170.3, 156.0, 136.3, 129.48, 129.45, 128.85, 128.81, 128.7, 128.3, 128.1, 127.2, 67.2, 56.3, 56.1, 52.6, 48.3, 48.0, 39.0, 38.6, 18.4, 18.2; MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{24}N_2NaO_5$ 407; Found 407.

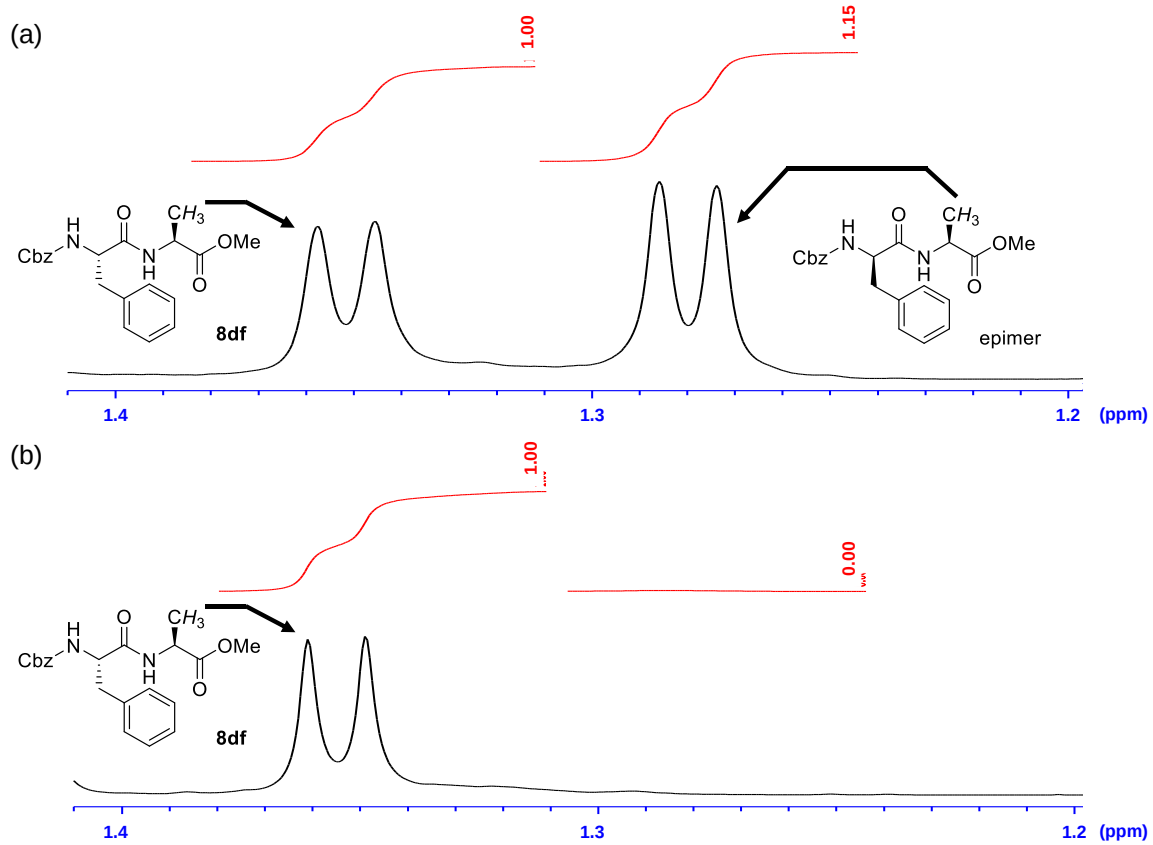
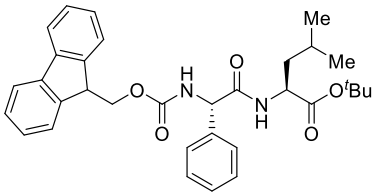


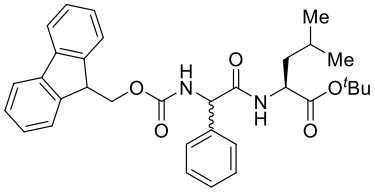
Figure S2. Comparison of ^{1}H NMR spectra ($CDCl_3$, 400 MHz) of (a) the crude mixture of **DL-8df** and (b) the crude mixture of **8df**.

Compound 8eg[10]



DMT-TU (192.5 mg, 0.48 mmol) was added to a solution of **6e** (149.4 mg, 0.40 mmol), **7g-HCl** (107.4 mg, 0.48 mmol), and $^{i}Pr_2EtN$ (151 µL, 0.88 mmol) in MeCN (4.00 mL) at room temperature. After 3 h, the reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (twice; silica, hexane/EtOAc = 3:1 for the first chromatography; amine-functionalized silica, hexane/EtOAc = 4:1 for the second chromatography) afforded a white solid [172.0 mg, 79%, dr = 95:5 as indicated by HPLC analysis (Figure S3)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 7.7 Hz, 2H), 7.61–7.50 (m, 2H), 7.42–7.21 (m, 9H), 6.22 (d, J = 6.0 Hz, 1H), 6.10 (d, J = 7.8 Hz, 1H), 5.26 (d, J = 6.0 Hz, 1H), 4.45 (ddd, J = 7.8, 7.3, 7.3 Hz, 1H), 4.35 (d, J = 7.1 Hz, 2H), 4.18 (dd, J = 7.1, 7.1 Hz, 1H), 1.75–1.40 (m, 3H), 1.34 (s, 9H), 0.93 (d, J = 6.4 Hz, 6H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 171.2, 169.5, 155.8, 143.9, 143.8, 141.3, 137.9, 129.0, 128.5, 127.7, 127.3, 127.1, 125.23, 125.18, 120.0, 81.9, 67.3, 58.5, 52.0, 47.1, 41.7, 27.9, 24.9, 22.7, 22.2. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{33}H_{38}N_2NaO_5$ 565; Found 565.

Compound DL-8eg[10]



DMT-TU (192.5 mg, 0.48 mmol) was added to a solution of [(9-fluorenylmethyloxy)carbonyl]-DL-phenylglycine (147.6 mg, 0.40 mmol), **7g-HCl** (107.4 mg, 0.48 mmol), and $^{i}Pr_2EtN$ (151 μL, 0.88 mmol) in MeCN (4.00 mL) at room temperature. After 3 h, the reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (twice; silica, CH_2Cl_2/MeOH = 97:3 for the first chromatography; amine-functionalized silica, hexane/EtOAc = 4:1 for the second chromatography) afforded a white solid [166.6 mg, 78%, dr = 53:47 as indicated by HPLC analysis (Figure S3)]. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 7.3 Hz, 2H), 7.63–7.49 (m, 2H), 7.46–7.17 (m, 9H), 6.41–6.12 (m, 2H), 5.30 (d, J = 5.5 Hz, 1H), 4.55–4.26 (m, 3H), 4.23–4.10 (m, 1H), 1.70–1.40 (m, 3H), 1.44 (s, 4.5H), 1.33 (s, 4.5H), 0.92 (d, J = 6.4 Hz, 3H), 0.74 (d, J = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ 171.8, 171.2, 169.5, 169.4, 155.8, 155.6, 143.95, 143.92, 143.8, 141.3, 138.4, 137.9, 129.10, 129.07, 128.8, 128.6, 128.5, 127.7, 127.3, 127.2, 127.1, 125.2, 120.0, 82.2, 82.0, 67.3, 67.2, 58.7, 58.6, 52.0, 51.7, 47.1, 41.7, 41.5, 28.0, 27.9, 24.9, 24.7, 22.74, 22.71, 22.2, 21.9. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{33}H_{38}N_2NaO_5$ 565; Found 565.

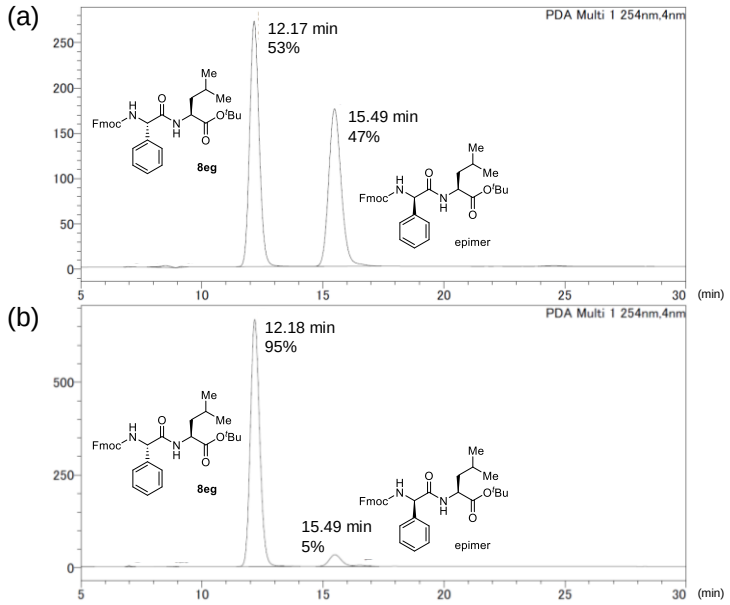
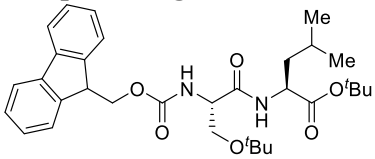


Figure S3. HPLC analysis of (a) **DL-8eg** and (b) **8eg**. Conditions: Chiralpak IC-3 (4.0 × 10 mm), hexane/^{i}PrOH = 9:1, flow rate = 1.0 mL/min, detection at 245 nm.

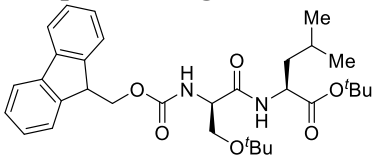
Compound 8fg[10]



DMT-TU (96.3 mg, 0.24 mmol) was added to a solution of **6f** (76.7 mg, 0.20 mmol), **7g-HCl** (53.7 mg, 0.24 mmol), and $^{i}Pr_2EtN$ (75.8 μL, 0.44 mmol) in MeCN (2.0 mL) at room temperature. After 3 h, the reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (silica, hexane/EtOAc = 4:1) afforded a white solid [98.3 mg, 89%, dr = 98.3:1.7 as indicated by HPLC analysis (Figure S4)]. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.76 (d, J = 7.5, 2H), 7.64–7.56 (m, 2H), 7.40 (dd, J = 7.5, 7.4 Hz, 2H), 7.31 (dd, J = 7.5, 7.4 Hz, 2H), 7.23 (d, J = 6.9, 1H), 5.78 (d, J = 4.7, 1H),

4.52–4.44 (m, 1H), 4.44–4.36 (m, 2H), 4.29–4.20 (m, 2H), 3.83 (dd, J = 8.3 Hz, 1H), 3.47–3.37 (m, 1H), 1.73–1.60 (m, 2H), 1.59–1.50 (m, 1H), 1.46 (s, 9H), 1.23 (s, 9H), 0.95 (d, J = 6.6 Hz, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 171.8, 170.0, 156.2, 144.1, 143.9, 141.4, 127.8, 127.2, 125.3, 120.1, 81.8, 74.4, 67.2, 61.9, 54.3, 51.8, 47.3, 42.0, 28.1, 27.5, 25.0, 23.0, 22.3. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{44}N_2NaO_6$ 575; Found 575.

Compound D-8fg[10]



DMT-TU (96.3 mg, 0.24 mmol) was added to a solution of **D-6f** (76.7 mg, 0.20 mmol), **7g-HCl** (53.7 mg, 0.24 mmol), and $^{i}Pr_2EtN$ (75.8 μL, 0.44 mmol) in MeCN (2.0 mL) at room temperature. After 3 h, the reaction mixture was diluted with EtOAc and washed with aqueous HCl (1 M), saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure. Column chromatography (silica, hexane/EtOAc = 4:1) afforded a white solid [106.7 mg, 97%, dr = 98.8:1.2 as indicated by HPLC analysis (Figure S4)]. ^1H NMR (600 MHz, $CDCl_3$): δ 7.76 (d, J = 7.5 Hz, 2H), 7.60 (d, J = 7.5, 2H), 7.40 (dd, J = 7.5, 7.5 Hz, 2H), 7.31 (dd, J = 7.5, 7.5 Hz, 2H), 6.99 (d, J = 7.2 Hz, 1H), 5.80 (br s, 1H), 4.56–4.49 (m, 1H), 4.38 (d, J = 6.9 Hz, 2H), 4.29–4.20 (m, 1H), 3.88–3.77 (m, 1H), 3.37 (dd, J = 8.3, 8.3 Hz, 1H), 1.73–1.59 (m, 2H), 1.59–1.50 (m, 1H), 1.47 (s, 9H), 1.22 (s, 9H), 0.99–0.90 (m, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 171.9, 169.8, 156.2, 144.0, 143.9, 141.43, 141.42, 127.8, 127.2, 125.3, 120.1, 82.0, 74.4, 67.2, 61.9, 54.6, 51.7, 47.3, 42.2, 28.1, 27.5, 25.0, 22.9, 22.2. MS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{44}N_2NaO_6$ 575; Found 575.

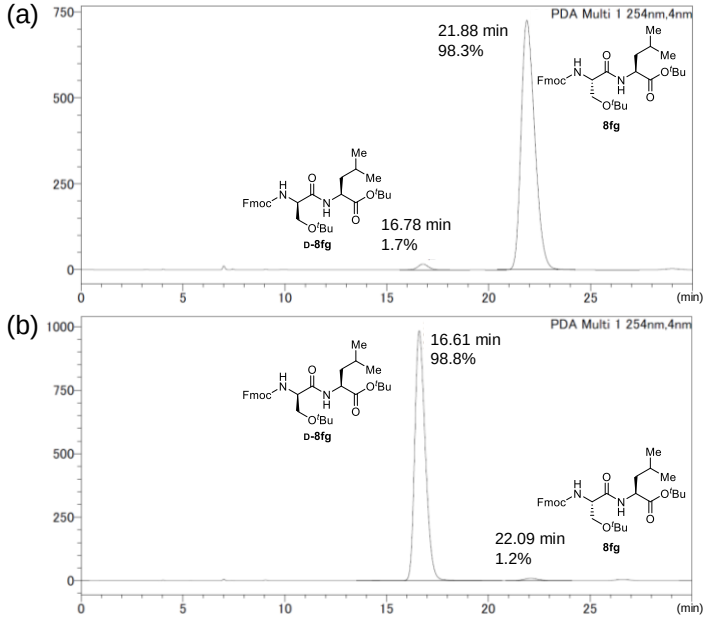


Figure S4. HPLC analysis of (a) **8fg** and (b) **D-8fg**. Conditions: Chiralpak IC-3 (4.0 × 10 mm), hexane/^{i}PrOH = 9:1, flow rate = 1.0 mL/min, detection at 254 nm.

Monitoring of the reaction intermediates of DMT-TU

Using DMT-TU (1.2 equiv.): A solution of **6b** (8.2 mg, 0.067 mmol) in CD_3CN (500 µL) was added dropwise to a solution of DMT-TU (32.0 mg, 0.080 mmol) and $^{i}Pr_2EtN$ (27.6 µL, 0.16 mmol) in CD_3CN (500 µL) at room temperature. After 2 h, an aliquot (600 µL) was transferred to an NMR tube and immediately used for a ^1H NMR measurement (600 MHz, 20 °C). After an additional 0.5 h, **7a** (10.1 µL, 0.080 mmol) was added to the solution in the NMR tube at room temperature. After an additional 15 min, trifluoroacetic acid (TFA, 20.5 µL, 0.27 mmol) was added to acidify the reaction mixture. The yield of **8ba** (71%) was calculated by ^1H quantitative NMR spectroscopic analysis using 1,3,5-trimethoxybenzene (5.4 mg) as the internal standard.

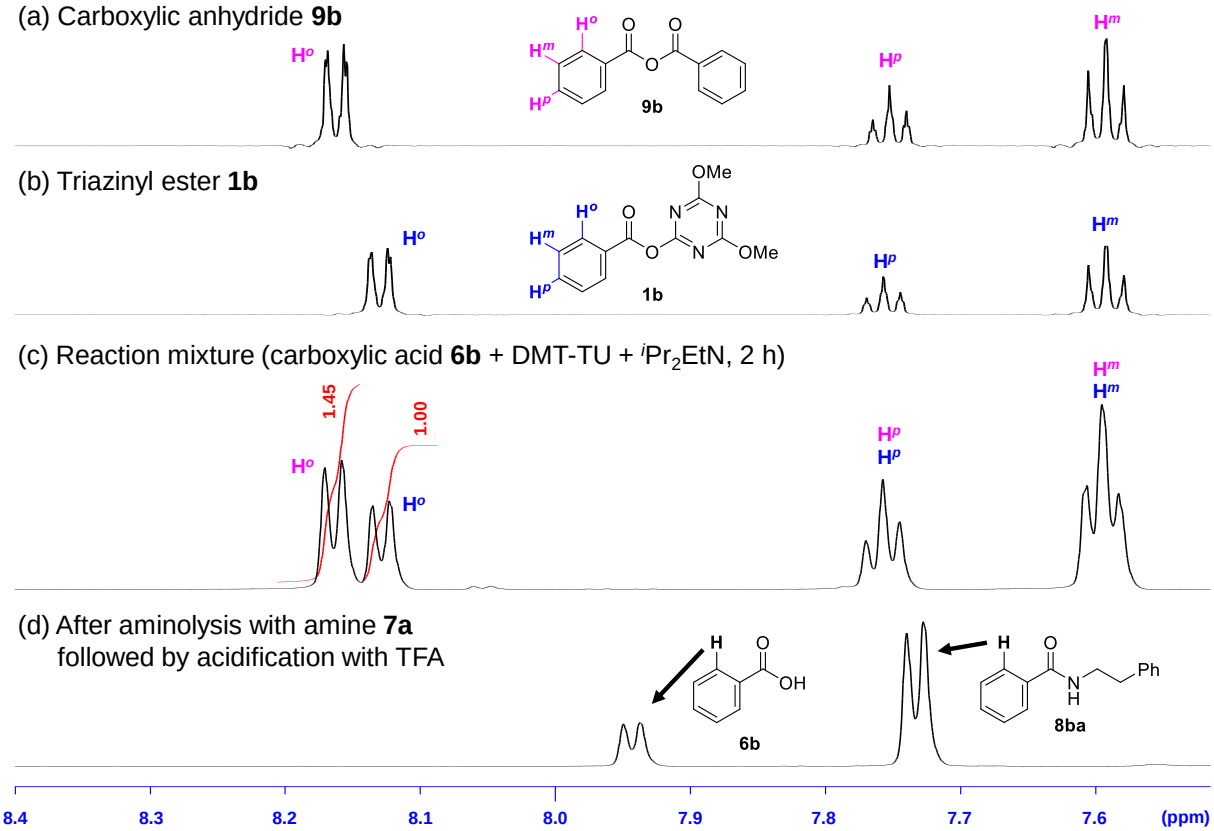


Figure S5. Comparison of ^1H NMR spectra (CD_3CN, 600 MHz) of (a) carboxylic anhydride **9b**, (b) triazinyl ester **1b**, (c) the reaction mixture (2 h) of carboxylic acid **6b** (1 equiv.), DMT-TU (1.2 equiv.), and $^{i}Pr_2EtN$ (2.4 equiv.), and (d) the reaction mixture quenched by the addition of amine **7a** (1.2 equiv.) followed by TFA.

Using DMT-TU (2 equiv.): A solution of **6b** (8.2 mg, 0.067 mmol) in CD_3CN (500 µL) was added dropwise to a solution of DMT-TU (53.7 mg, 0.13 mmol) and $^{i}Pr_2EtN$ (27.6 µL, 0.16 mmol) in CD_3CN (500 µL) at room temperature. After 2 h, an aliquot (600 µL) was transferred to an NMR tube and immediately used for a ^1H NMR measurement (600 MHz, 20 °C). After an additional 0.5 h, **7a** (16.9 µL, 0.13 mmol) was added to the solution in the NMR tube at room temperature. After an additional 15 min, trifluoroacetic acid (TFA, 20.5 µL, 0.27 mmol) was added to acidify the reaction mixture. The yield of **8ba** (96%) was calculated by ^1H quantitative NMR spectroscopic analysis using 1,3,5-trimethoxybenzene (5.4 mg) as the internal standard.

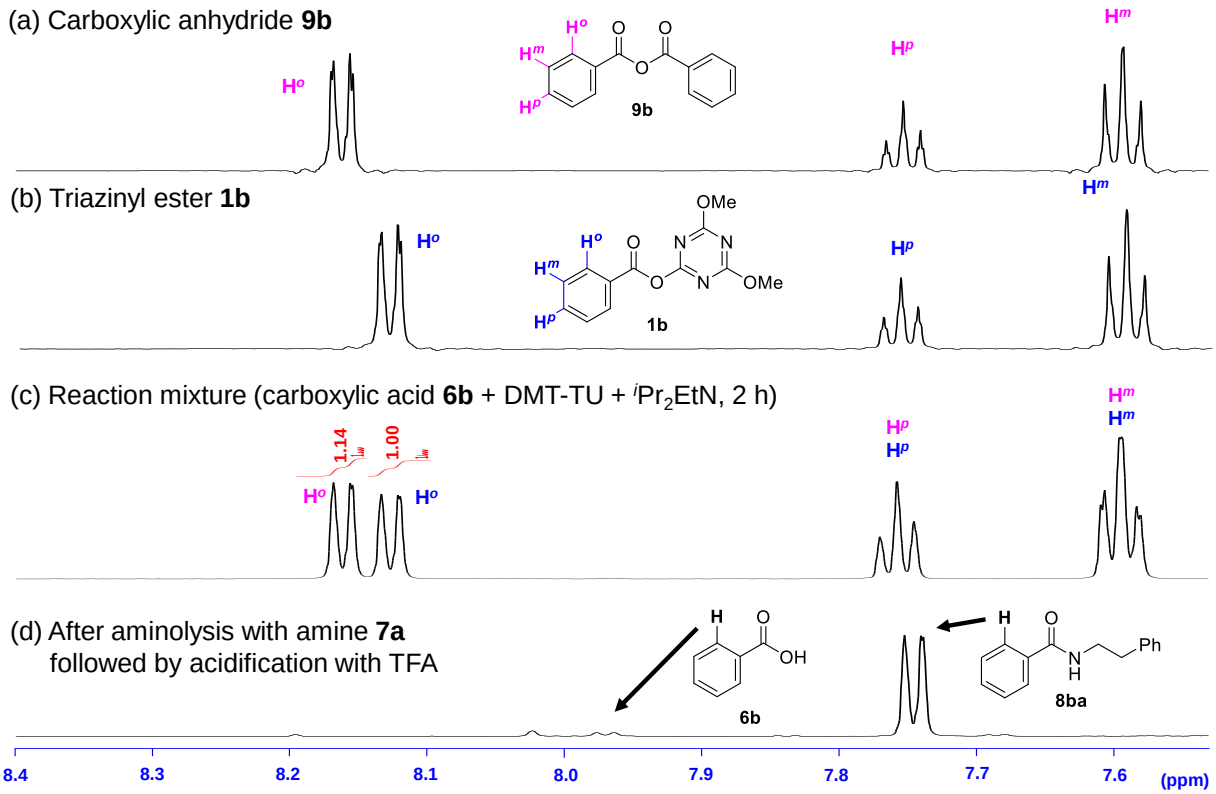
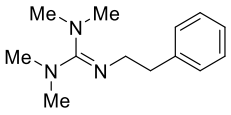


Figure S6. Comparison of ^1H NMR spectra (CD_3CN, 600 MHz) of (a) carboxylic anhydride **9b**, (b) triazinyl ester **1b**, (c) the reaction mixture (2 h) of carboxylic acid **6b** (1 equiv.), DMT-TU (2 equiv.), and $^{i}Pr_2EtN$ (2.4 equiv.), and (d) the reaction mixture quenched by the addition of amine **7a** (2 equiv.) followed by TFA.

1,1,3,3-Tetramethyl-2-phenethylguanidine (10)[11]



DMT-TU (80.2 mg, 0.20 mmol) was added to a solution of **7a** (27.8 µL, 0.22 mmol) and $^{i}Pr_2EtN$ (37.9 µL, 0.22 mmol) in MeCN (1.00 mL) at room temperature. After 2 h, the reaction mixture was passed through a pad of $NaPF_6$-treated amine-functionalized silica (CH_2Cl_2/MeOH = 19:1 as eluent). The eluent was concentrated under reduced pressure. The residue was dissolved in Et_2O and washed with aqueous NaOH (1 M) and brine. The organic layer was dried (Na_2SO_4) and filtrated. The filtrate was concentrated under reduced pressure to afford the product. (37.5 mg, 86%). ^1H NMR (600 MHz, $CDCl_3$): δ 7.30–7.20 (m, 4H), 7.20–7.15 (m, 1H), 3.40 (t, J = 7.5 Hz, 2H), 2.86 (t, J = 7.5 Hz, 2H), 2.72 (s, 6H), 2.66 (s, 6H). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$): δ 160.6, 141.1, 129.1, 128.3, 126.0, 51.0, 39.8, 39.0. MS (ESI) m/z: $[M + H]^+$ Calcd for $C_{13}H_{22}N_3$ 220; Found 220.

3. References

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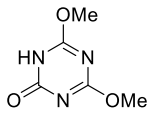
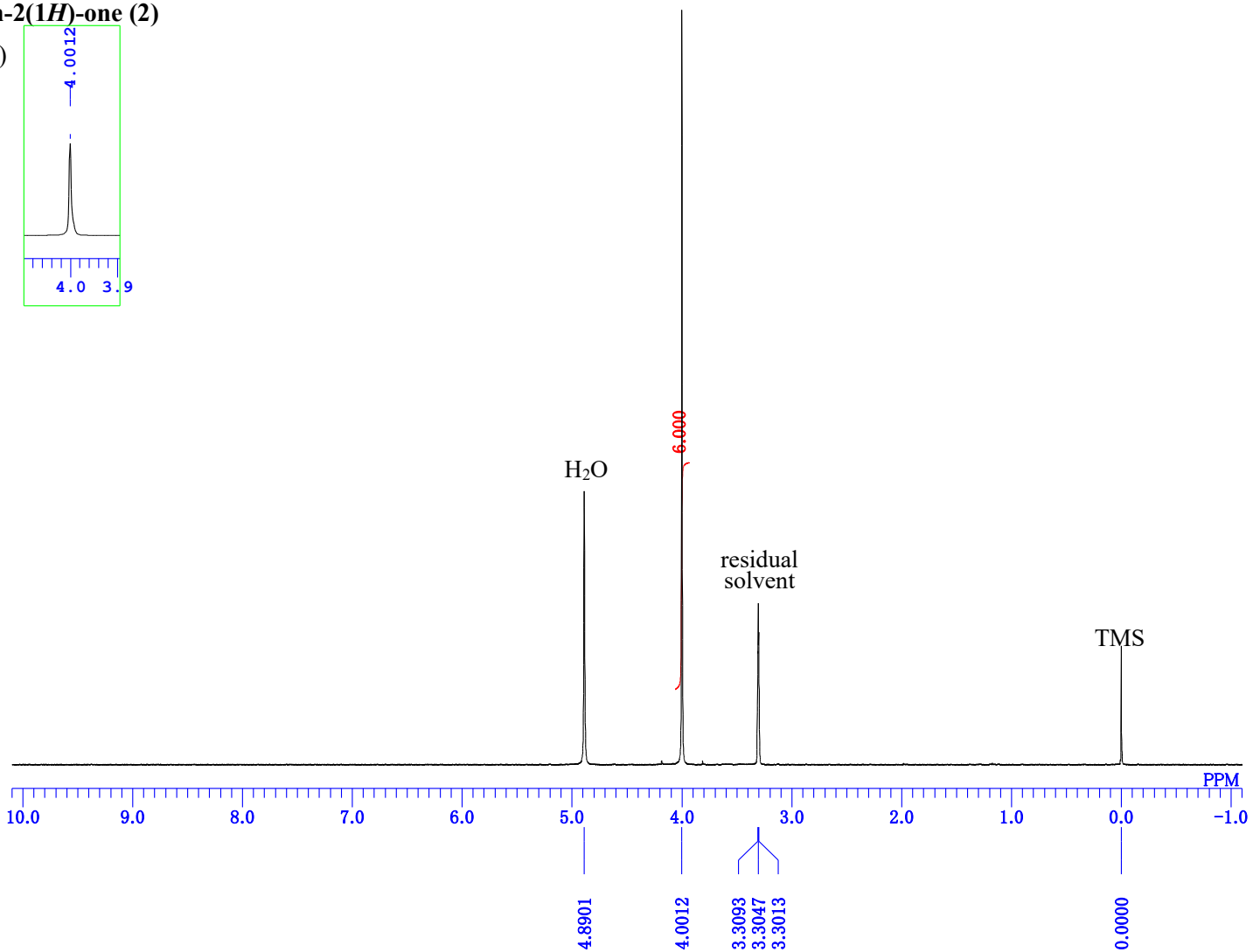
4. ^{1}H and ^{13}C NMR spectra

4,6-Dimethoxy-1,3,5-triazin-2(1*H*)-one (2)

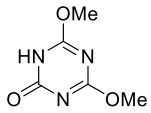
^{1}H NMR (400 MHz, CD_3OD)

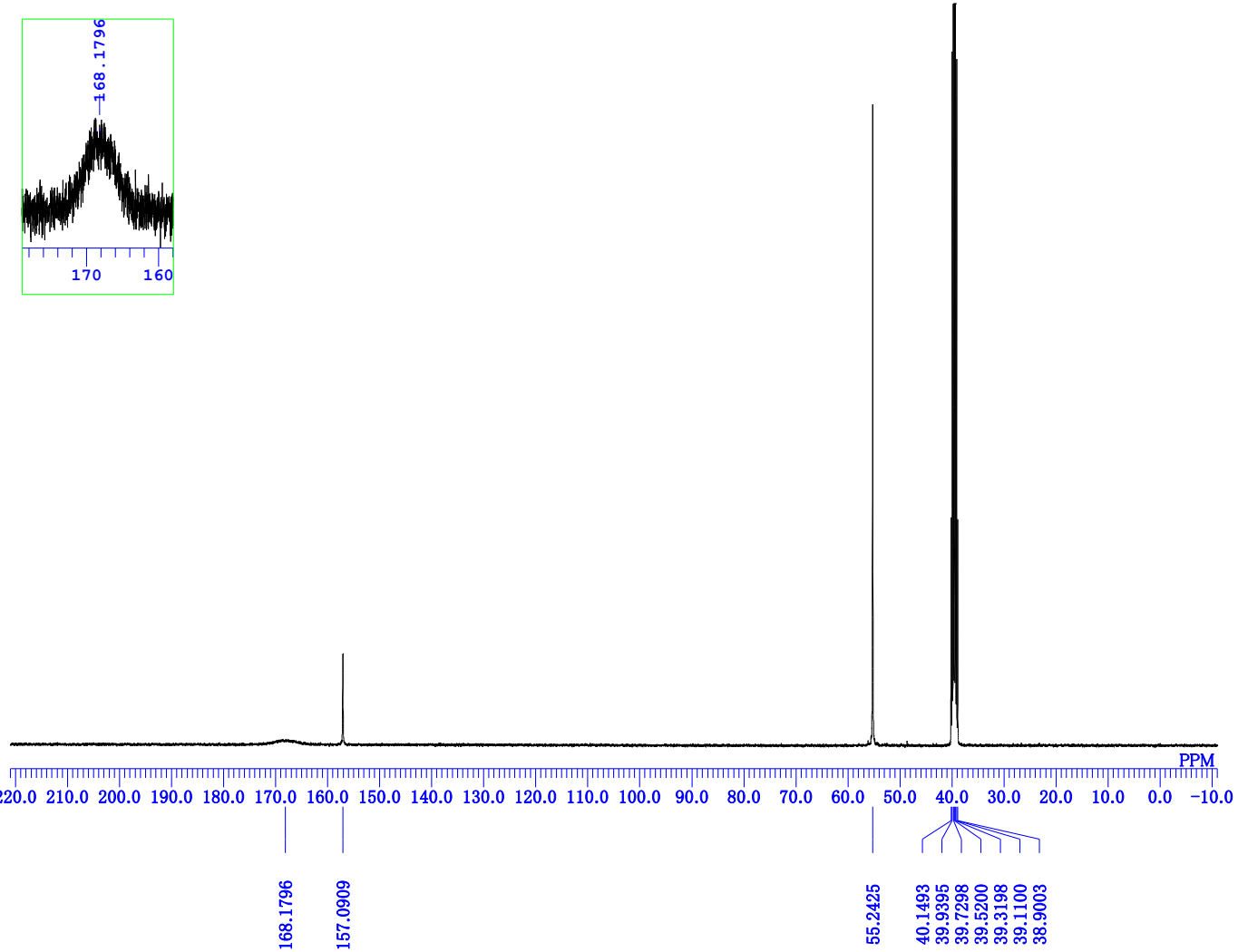




4,6-Dimethoxy-1,3,5-triazin-2(1*H*)-one (2)

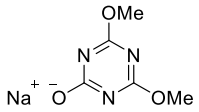
$^{13}C\{^{1}H\}$ NMR [100 MHz, $(CD_3)_2SO$]

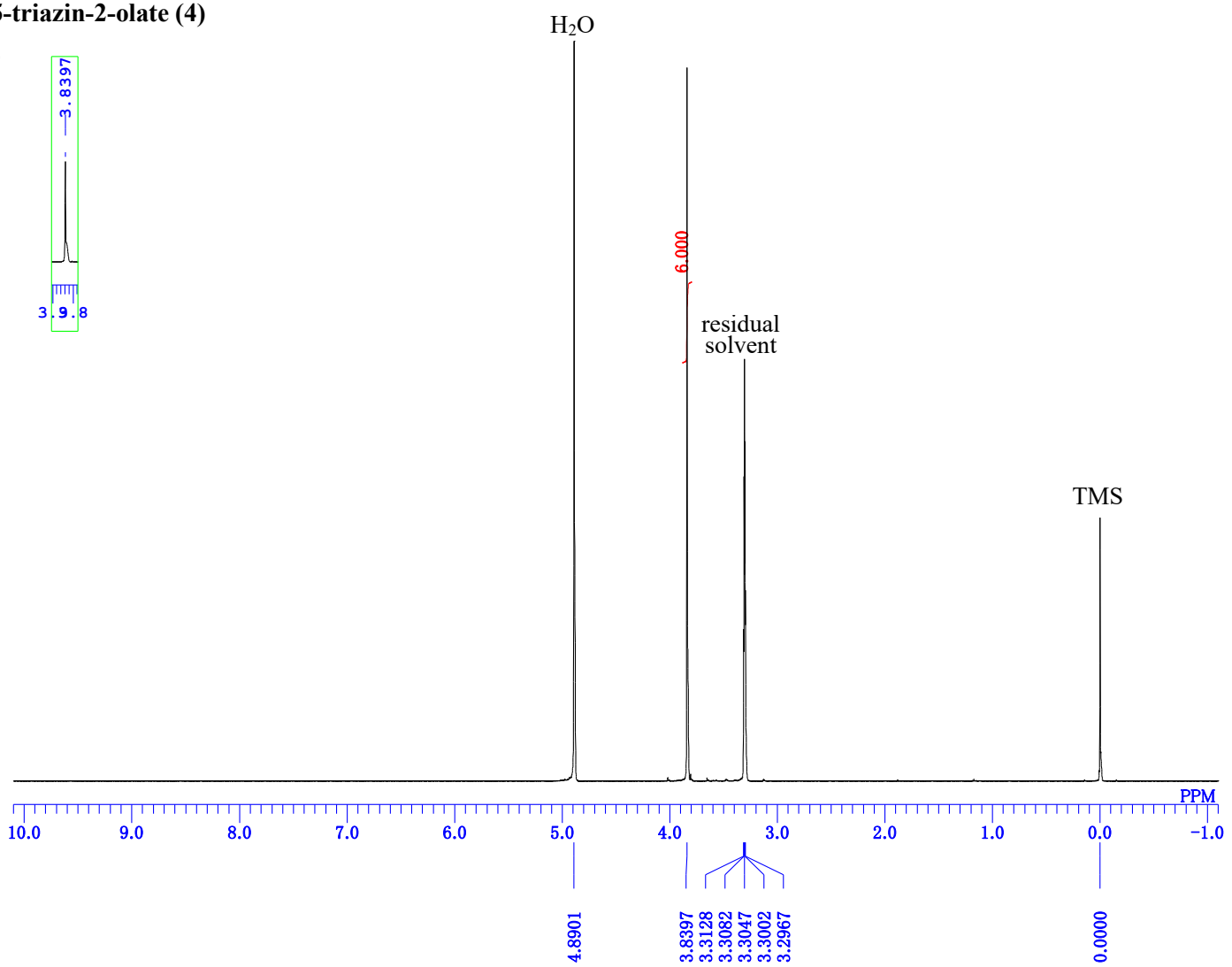




Sodium 4,6-dimethoxy-1,3,5-triazin-2-olate (4)

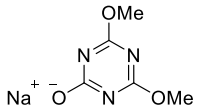
^{1}H NMR (400 MHz, CD_3OD)

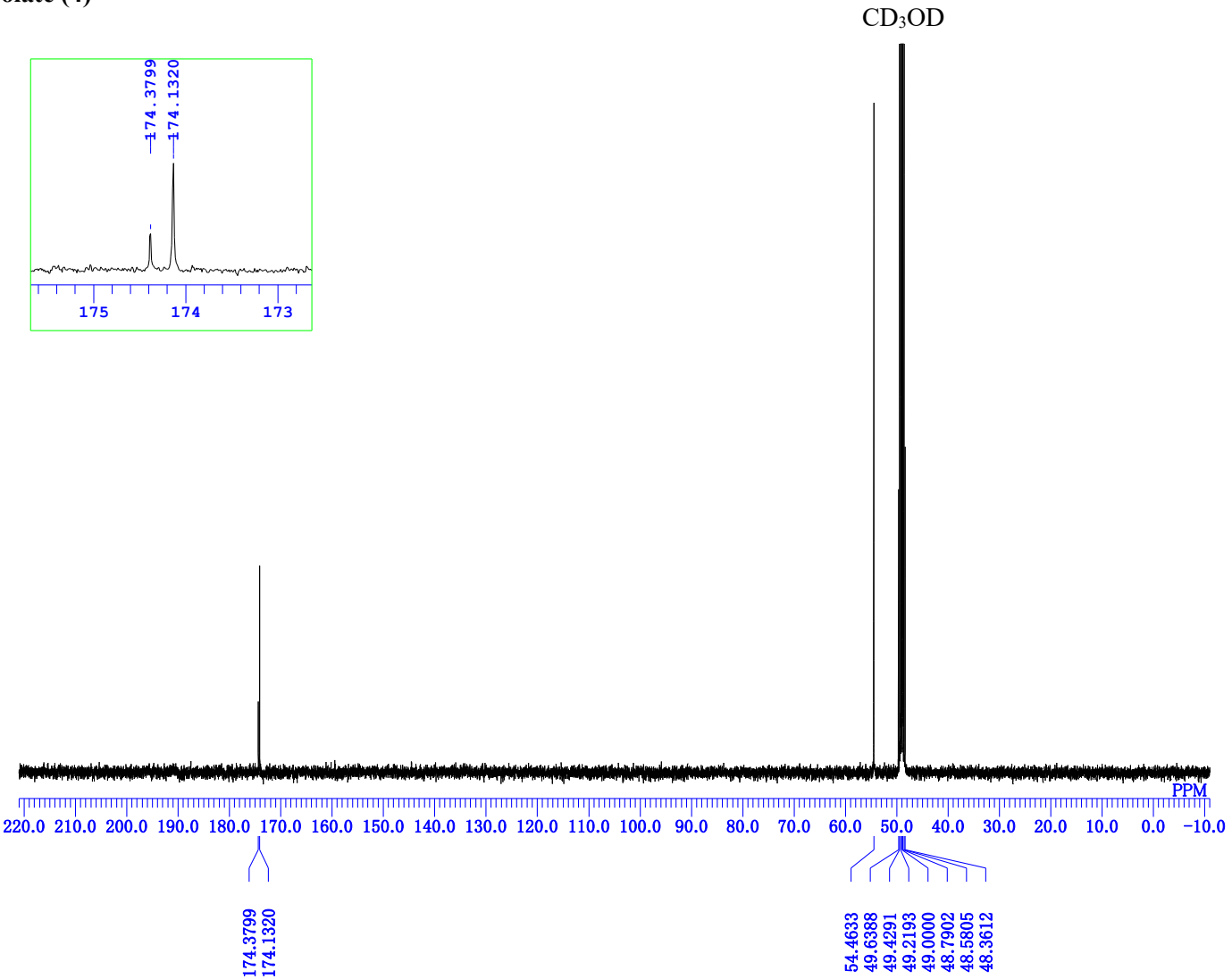




Sodium 4,6-dimethoxy-1,3,5-triazin-2-olate (4)

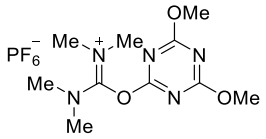
$^{13}C\{^{1}H\}$ NMR (100 MHz, CD_3OD)

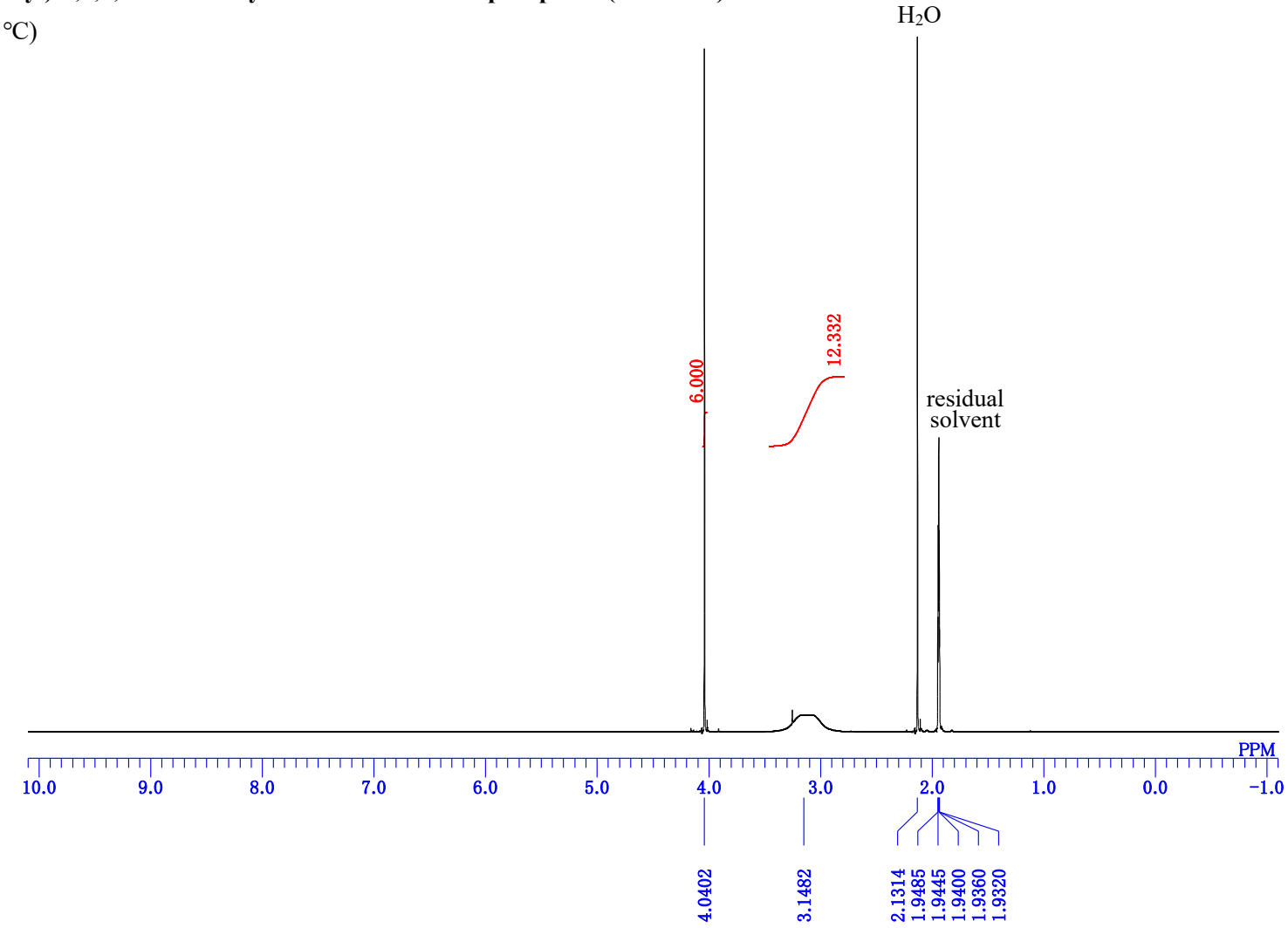




2-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (DMT-TU)

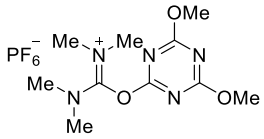
^{1}H NMR (600 MHz, CD_3CN, 20 °C)

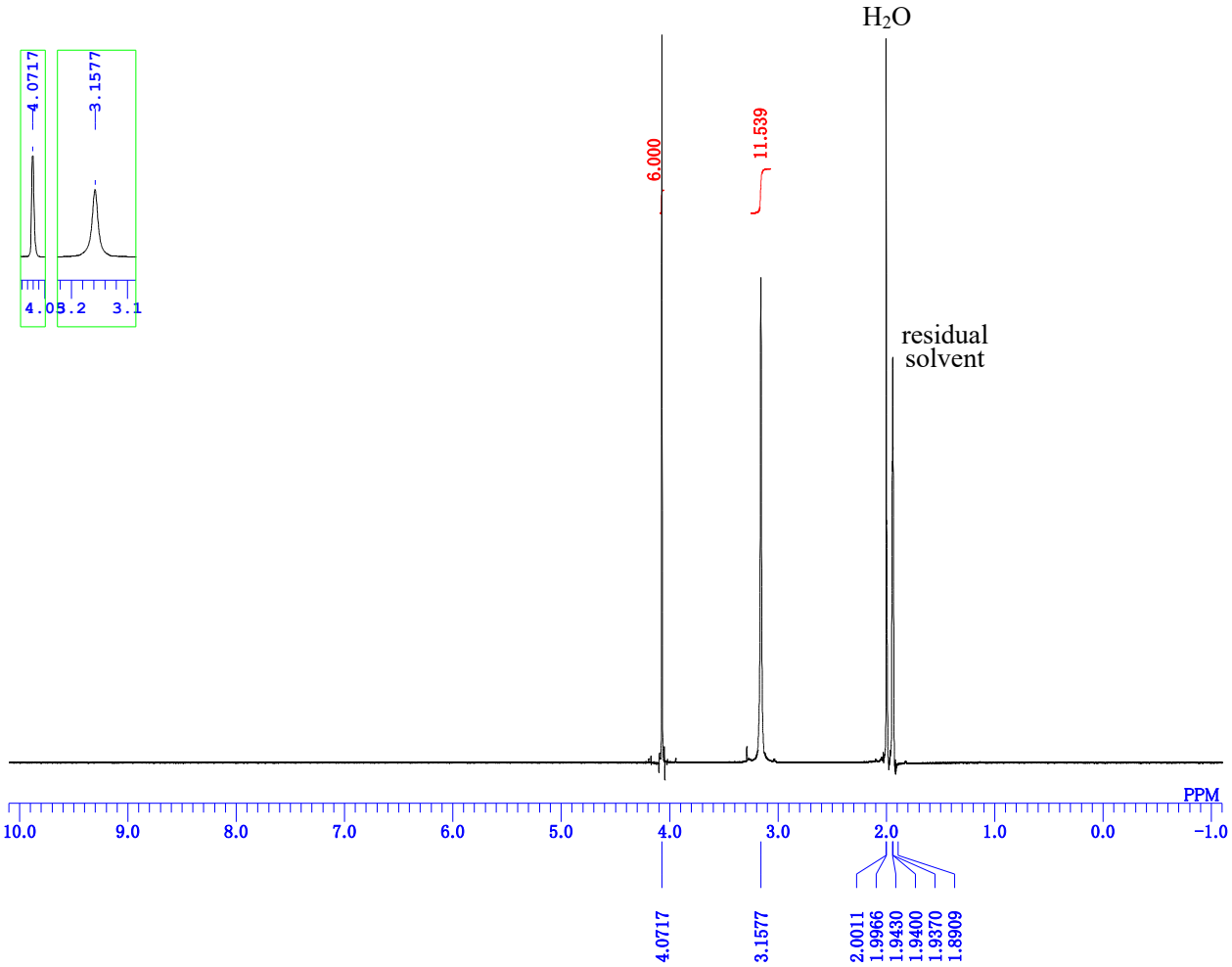




2-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (DMT-TU)

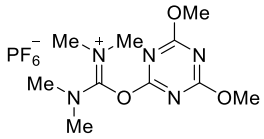
^{1}H NMR (600 MHz, CD_3CN, 70 °C)

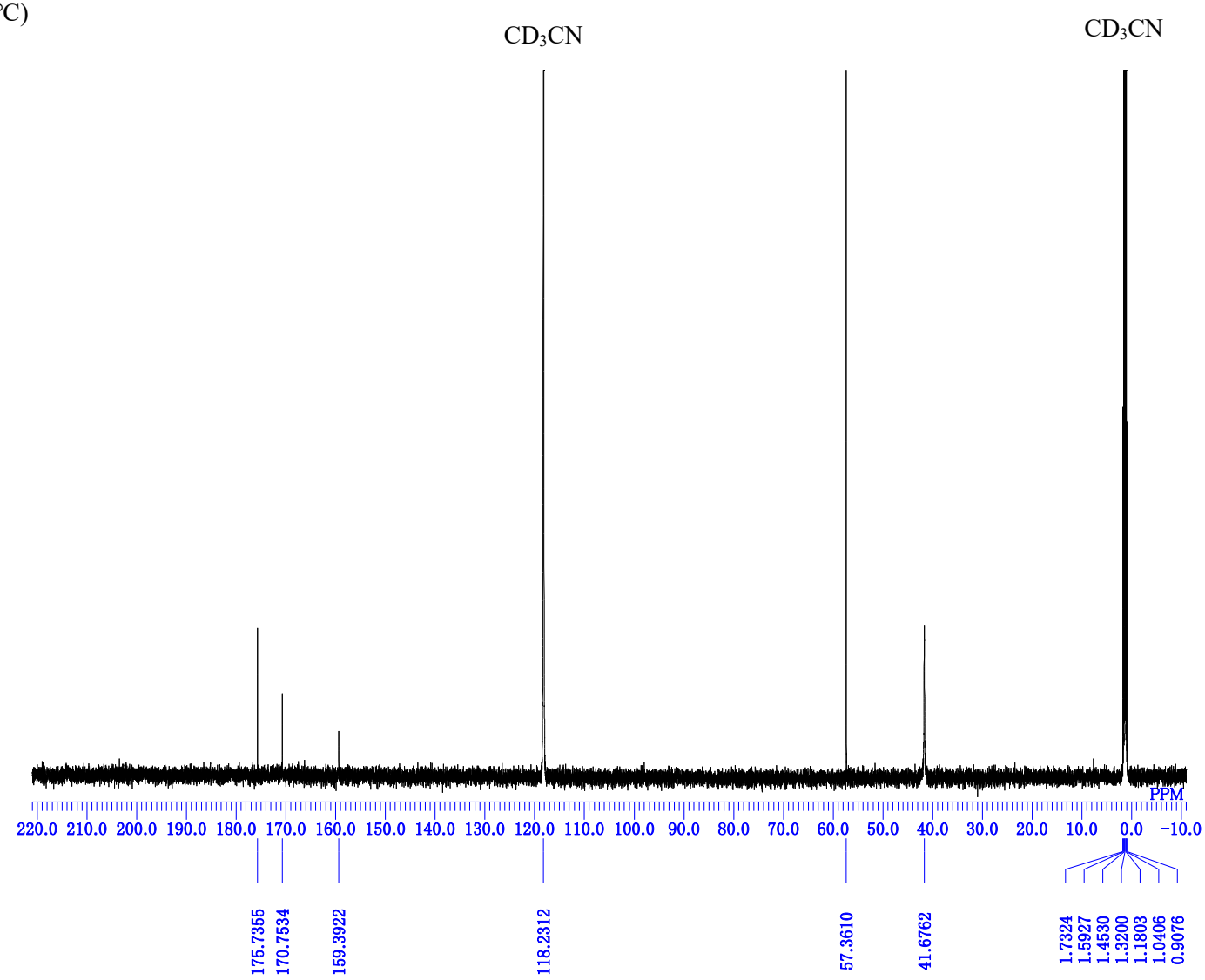




2-(4,6-Dimethoxy-1,3,5-triazin-2-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (DMT-TU)

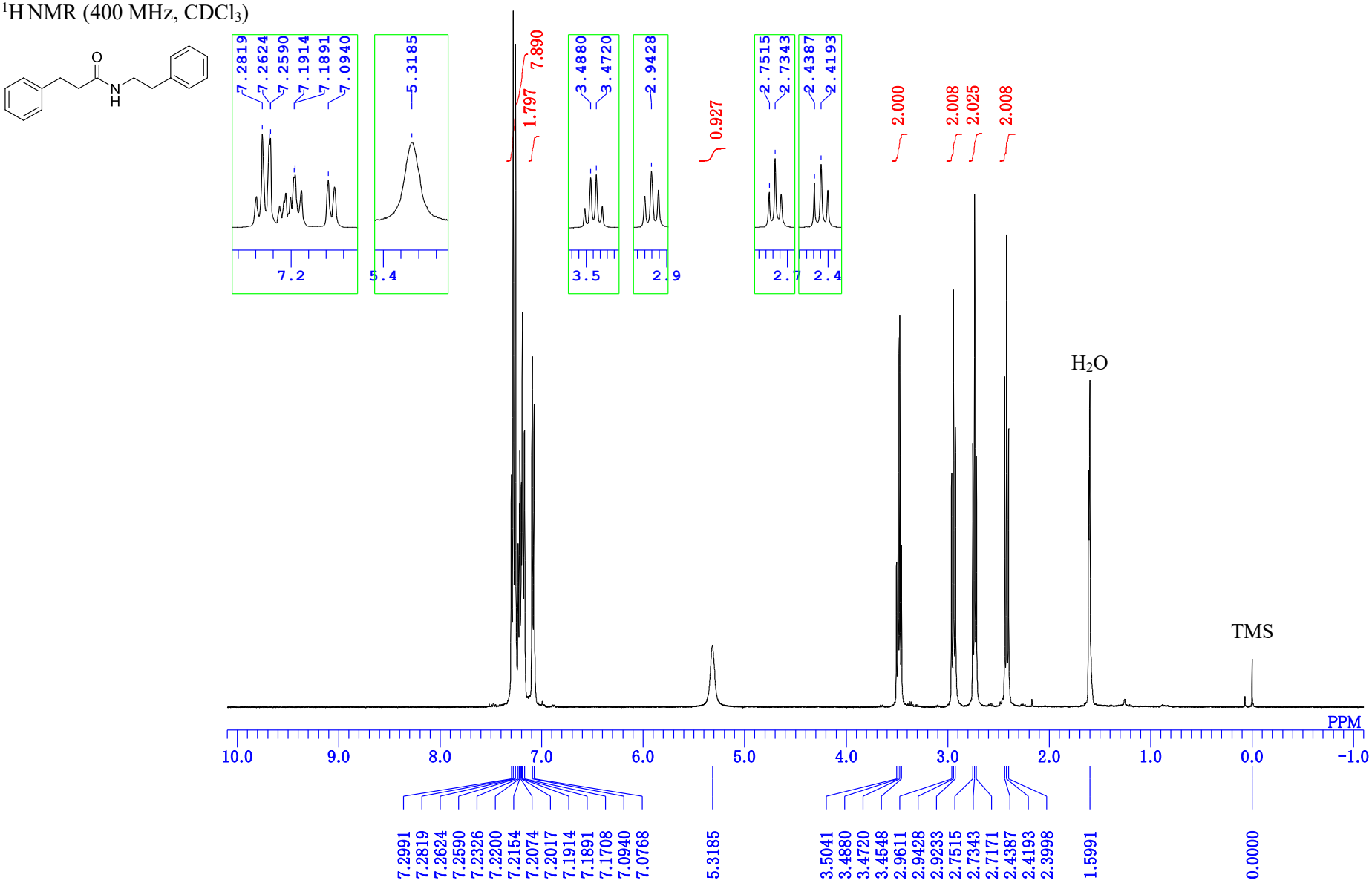
$^{13}C\{^{1}H\}$ NMR (150 MHz, CD_3CN, 70 ℃)





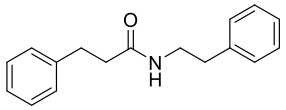
_N_-Phenethyl-3-phenylpropanamide (8aa)

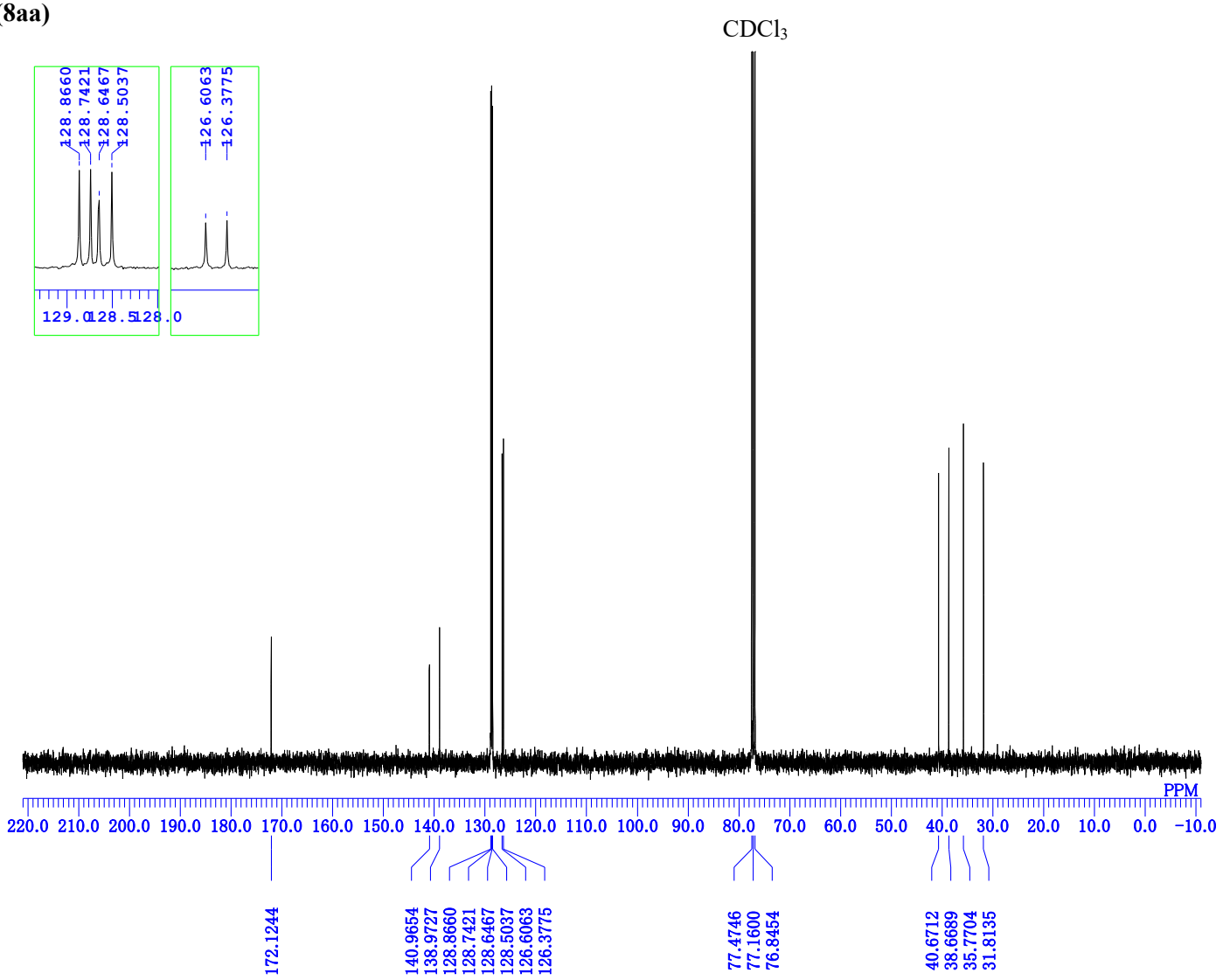
^{1}H NMR (400 MHz, $CDCl_3$)



_N_-Phenethyl-3-phenylpropanamide (8aa)

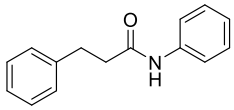
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

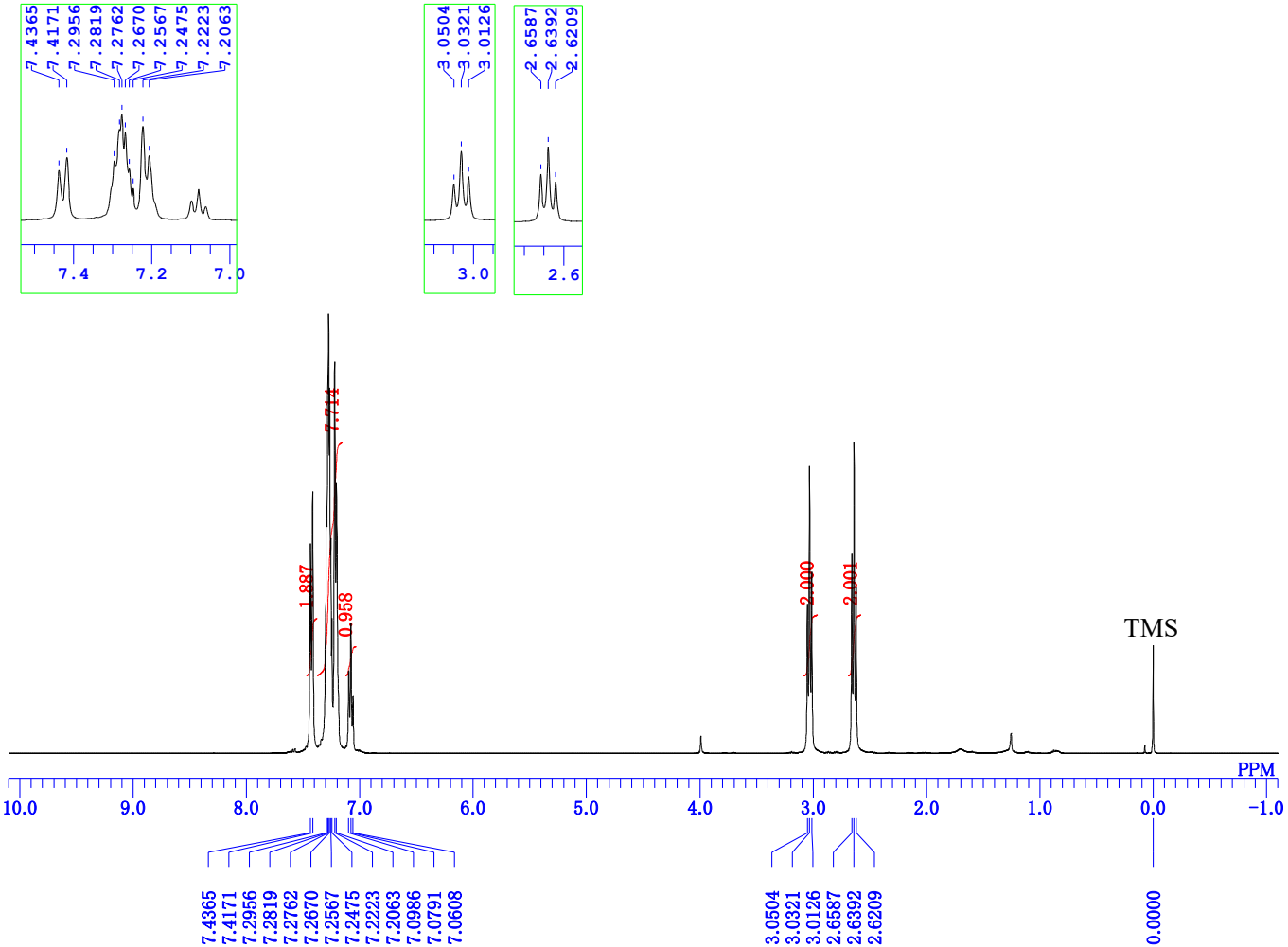




_N_,3-Diphenylpropanamide (8ab)

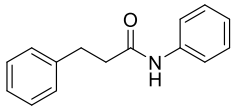
^{1}H NMR (400 MHz, $CDCl_3$)

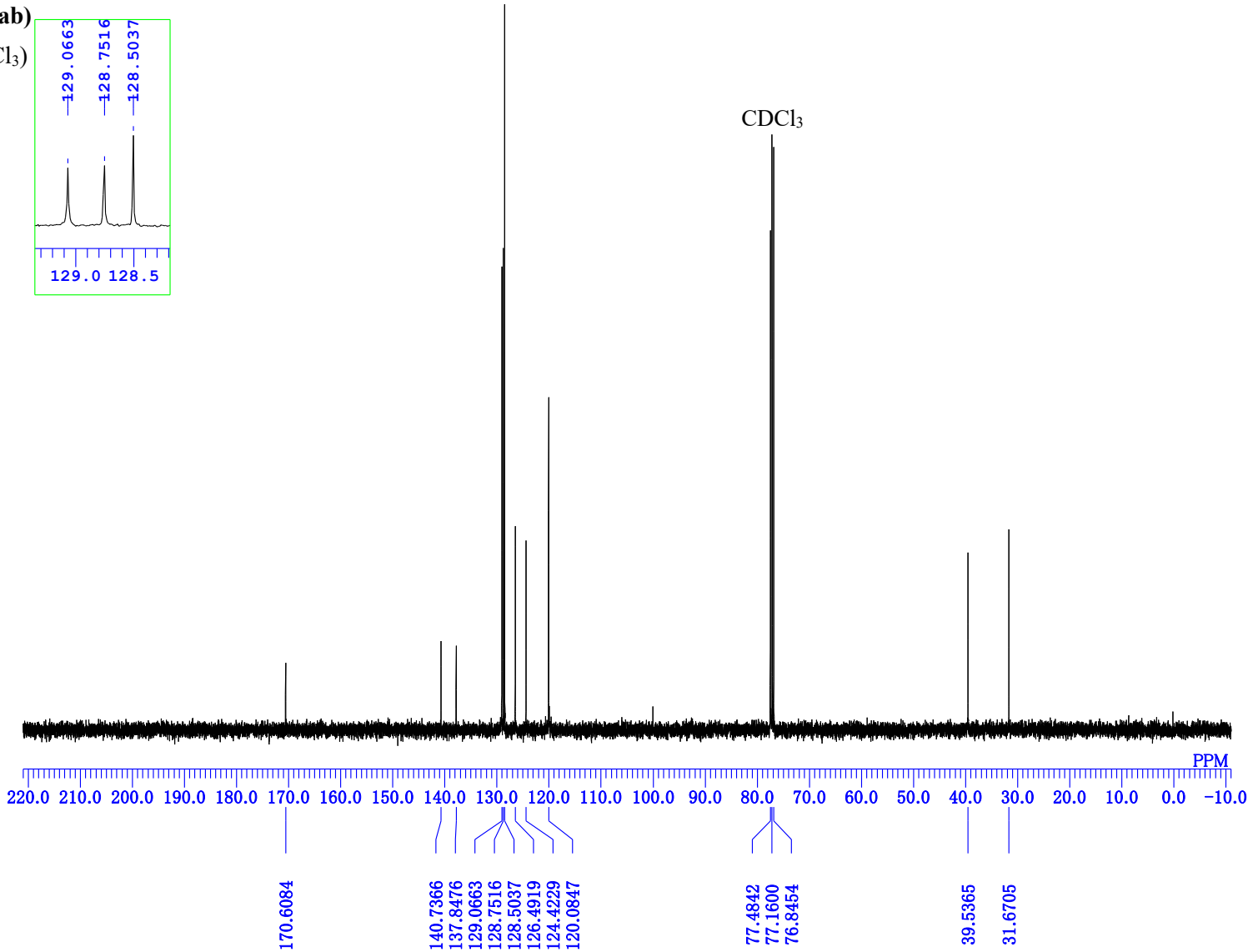




***N*,3-Diphenylpropanamide (8ab)**

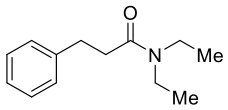
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

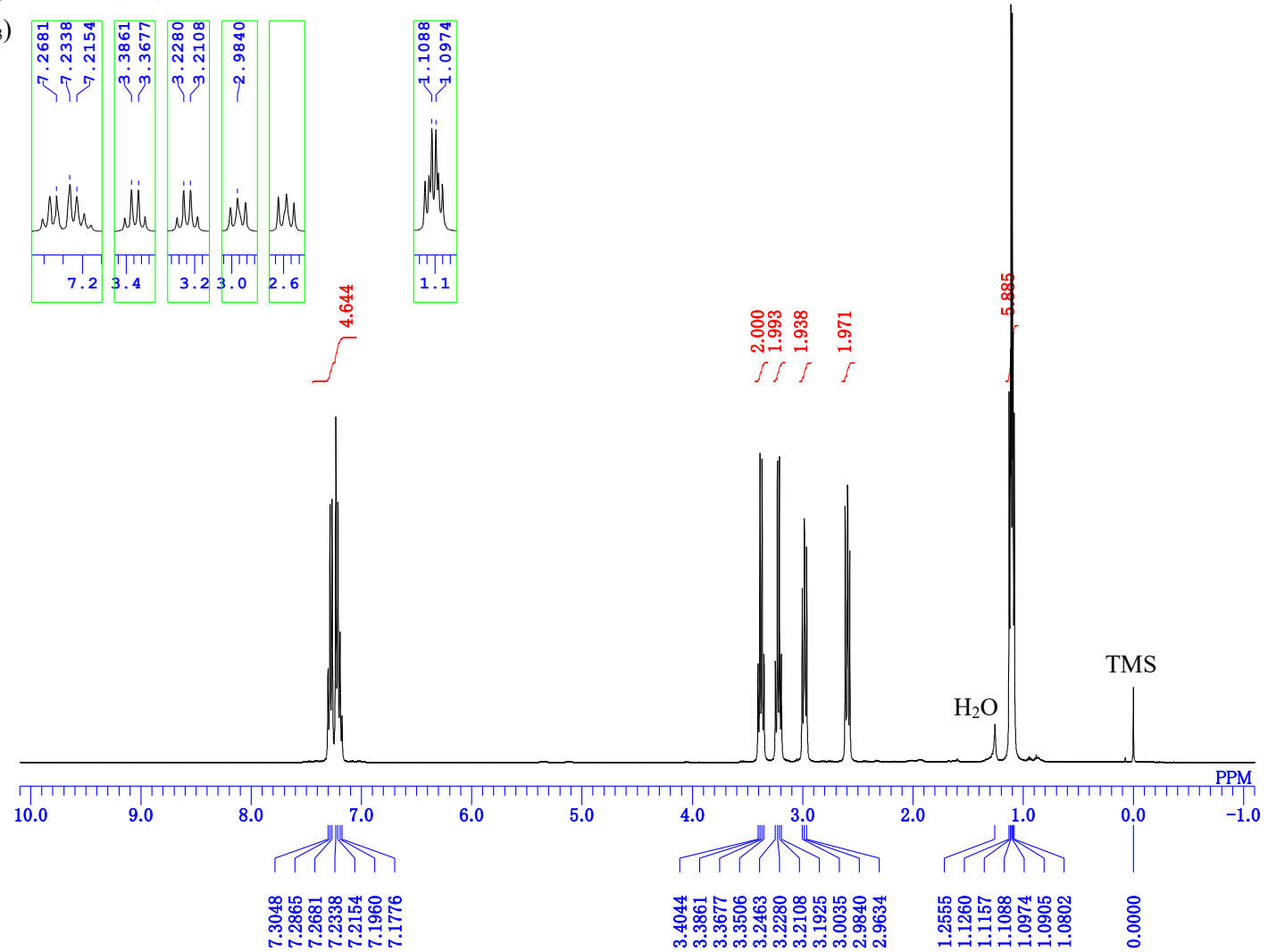




_N,N_-Diethyl-3-phenylpropanamide (8ac)

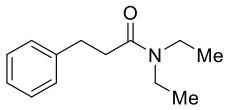
^{1}H NMR (400 MHz, $CDCl_3$)

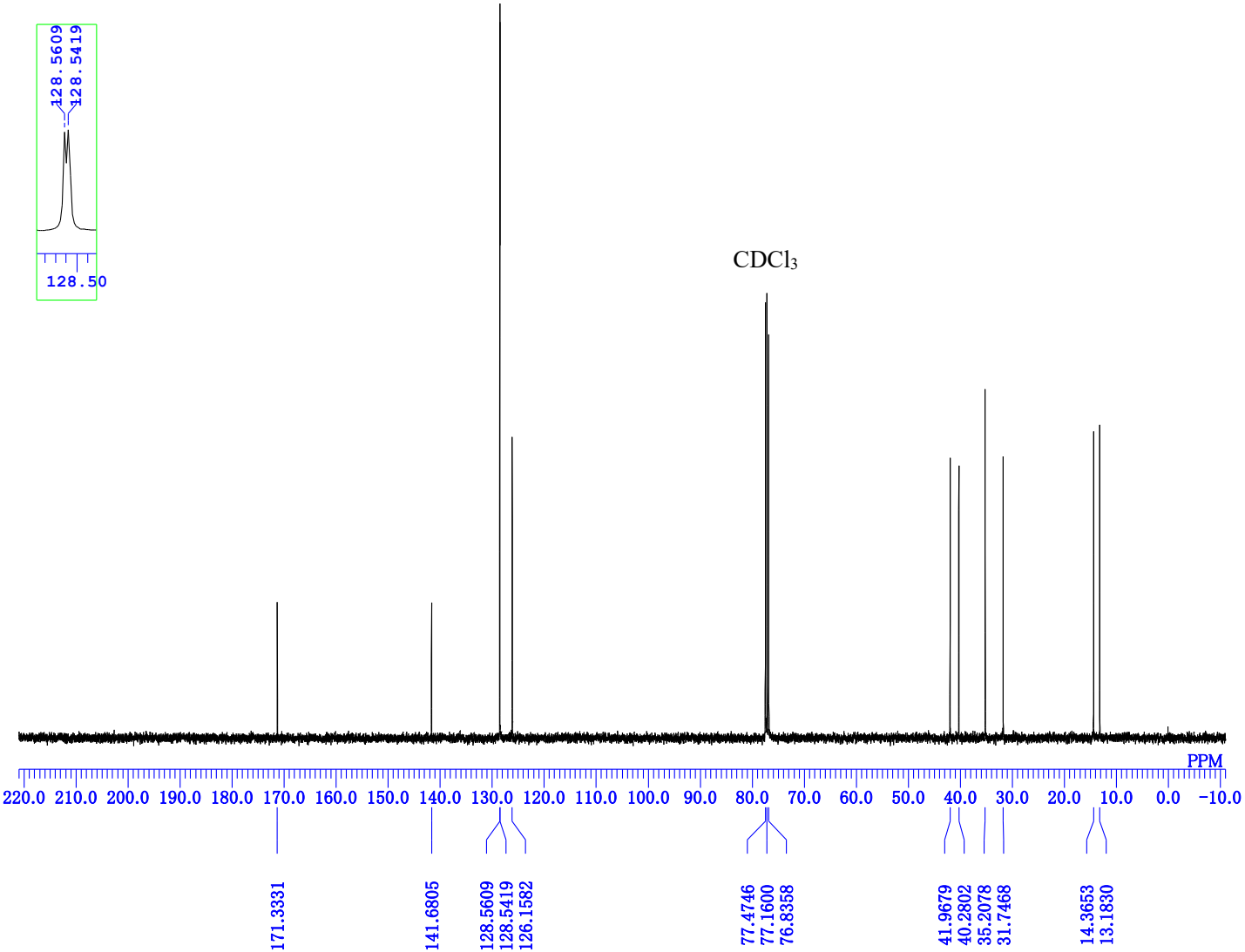




_N,N_-Diethyl-3-phenylpropanamide (8ac)

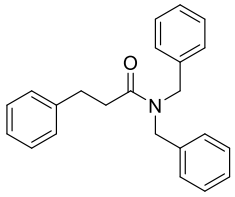
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

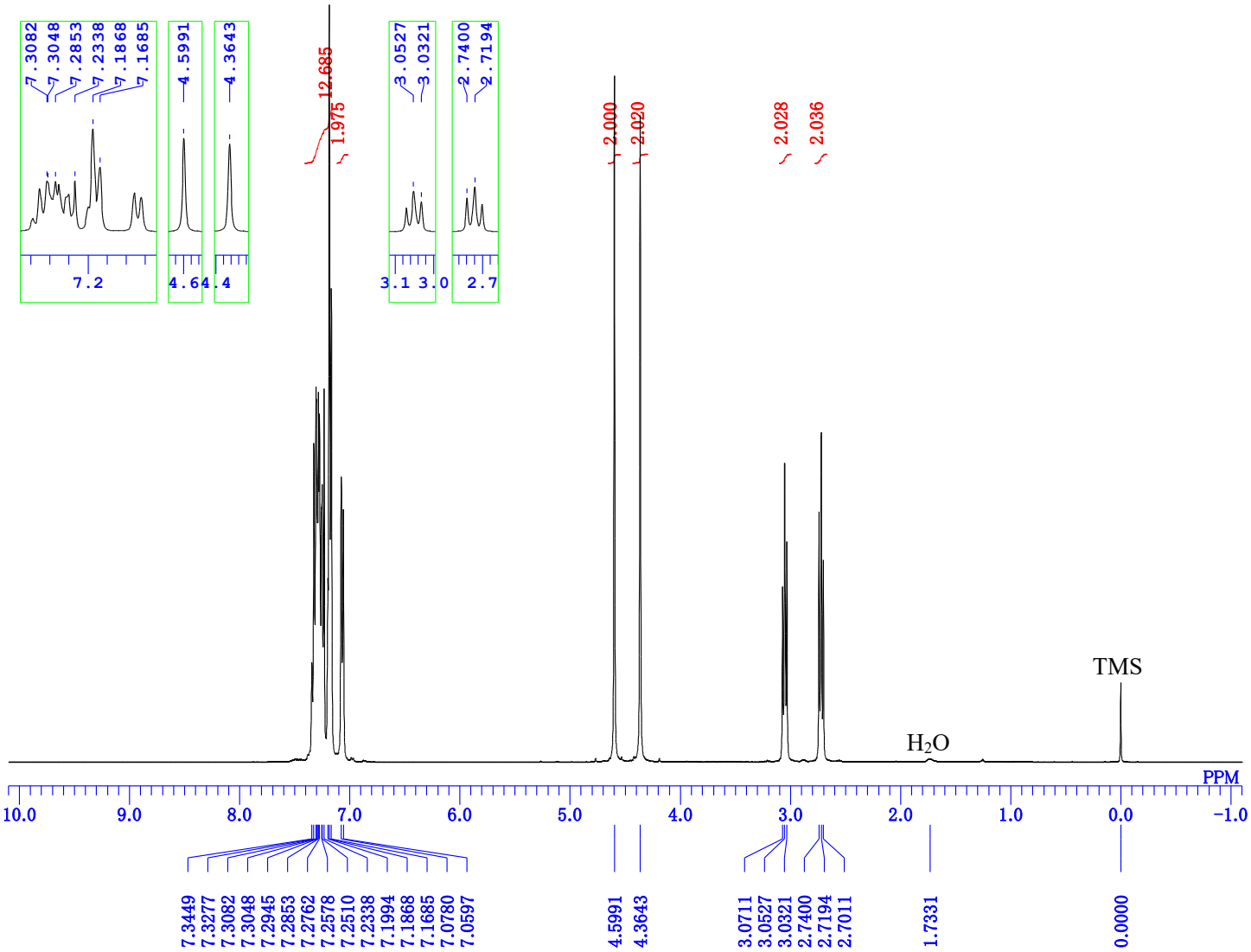




***N*,*N*-Dibenzyl-3-phenylpropanamide (8ad)**

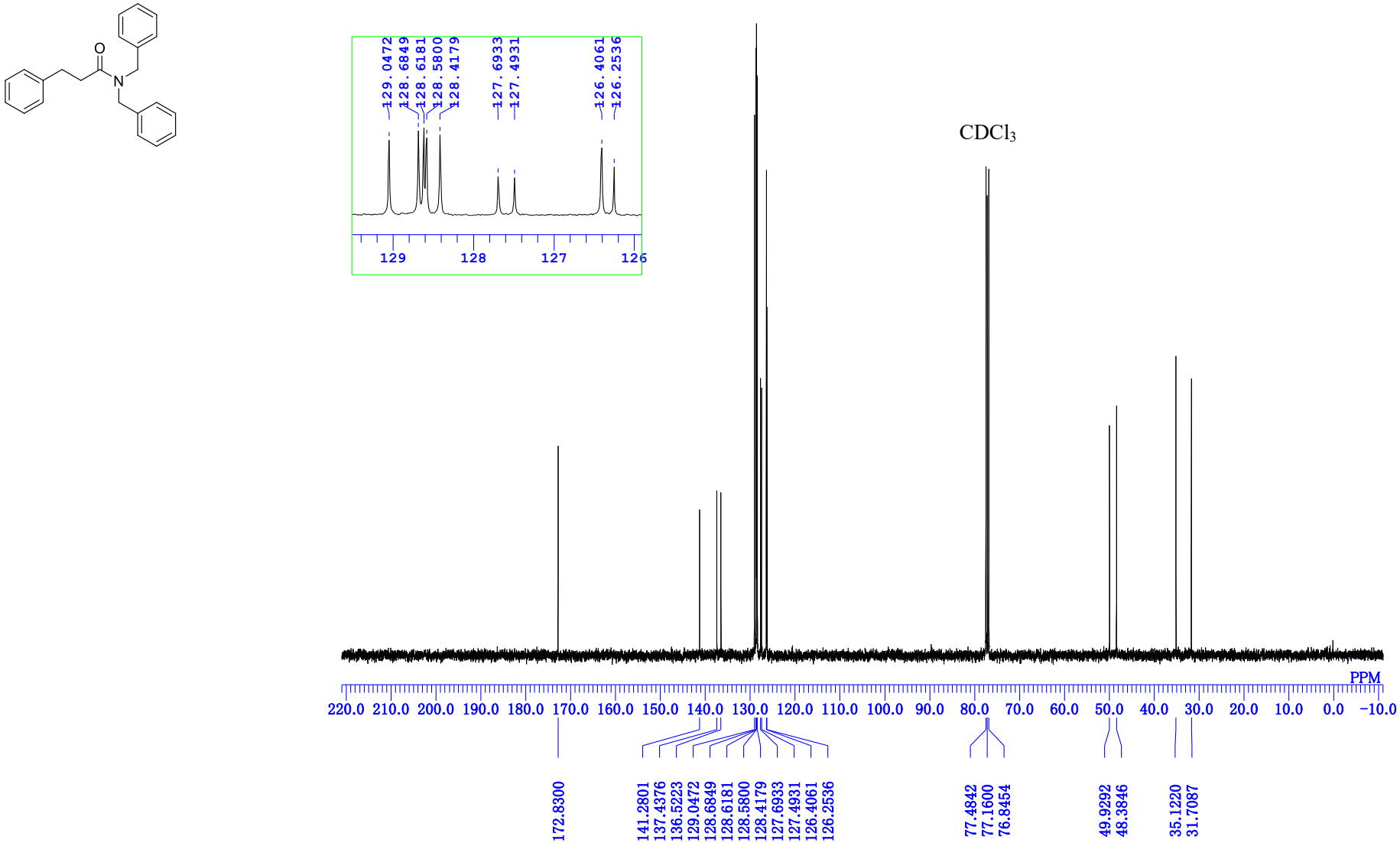
^{1}H NMR (400 MHz, $CDCl_3$)





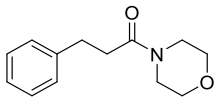
***N*,*N*-Dibenzyl-3-phenylpropanamide (8ad)**

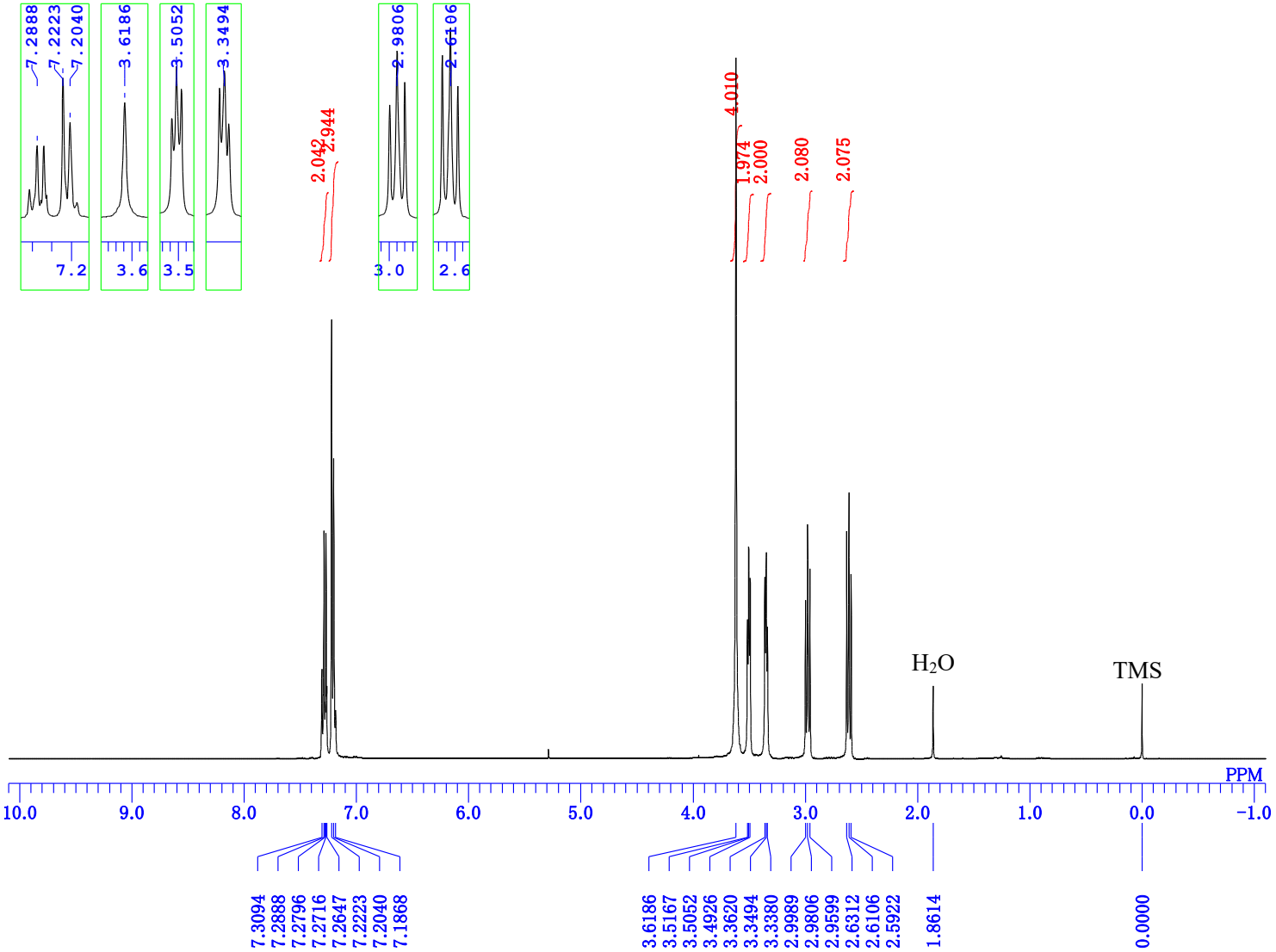
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



***N*-Morphonyl-3-phenylpropanamide(8ae)**

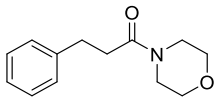
^{1}H NMR (400 MHz, $CDCl_3$)

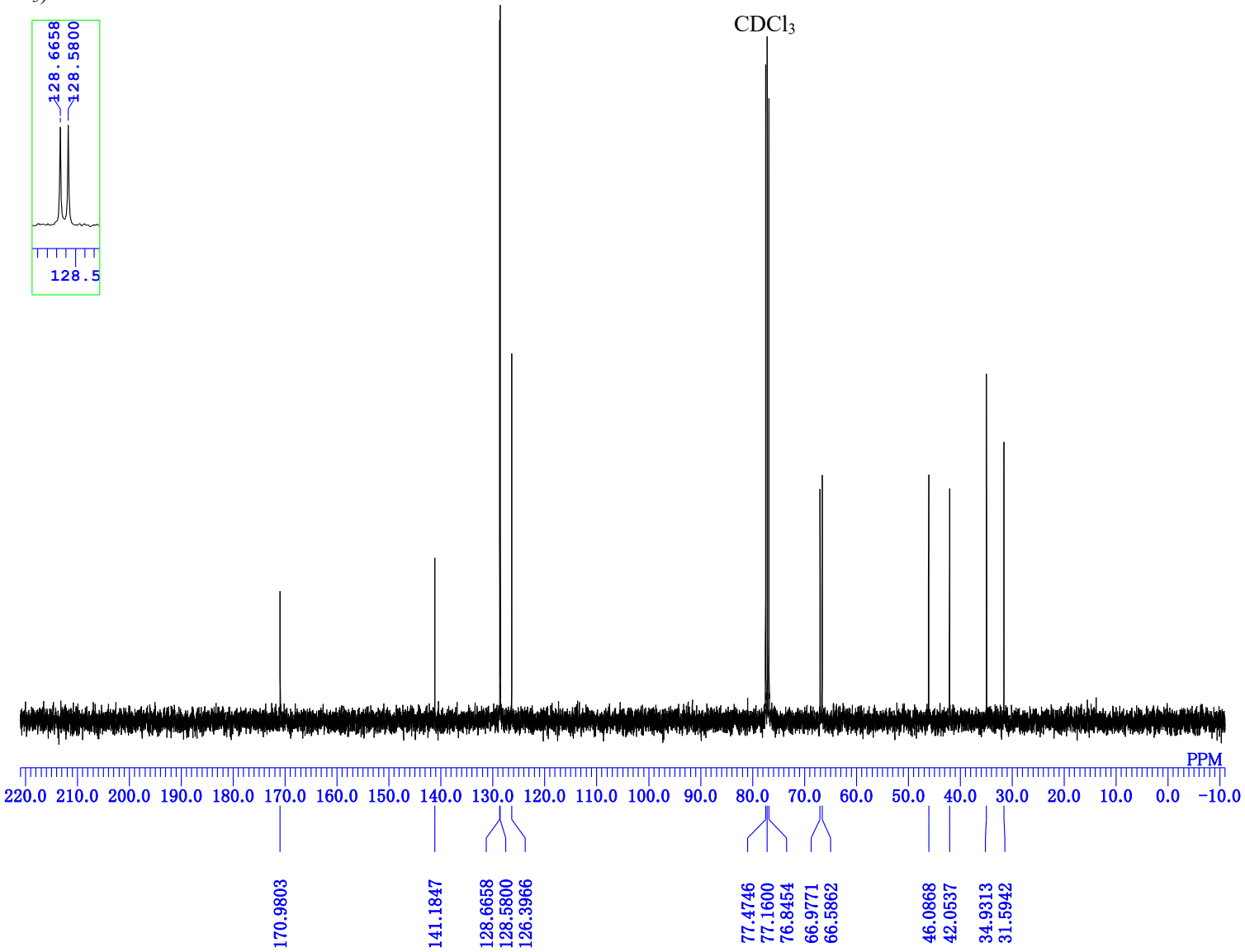




***N*-Morphonyl-3-phenylpropanamide(8ae)**

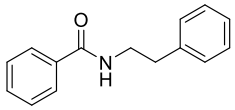
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

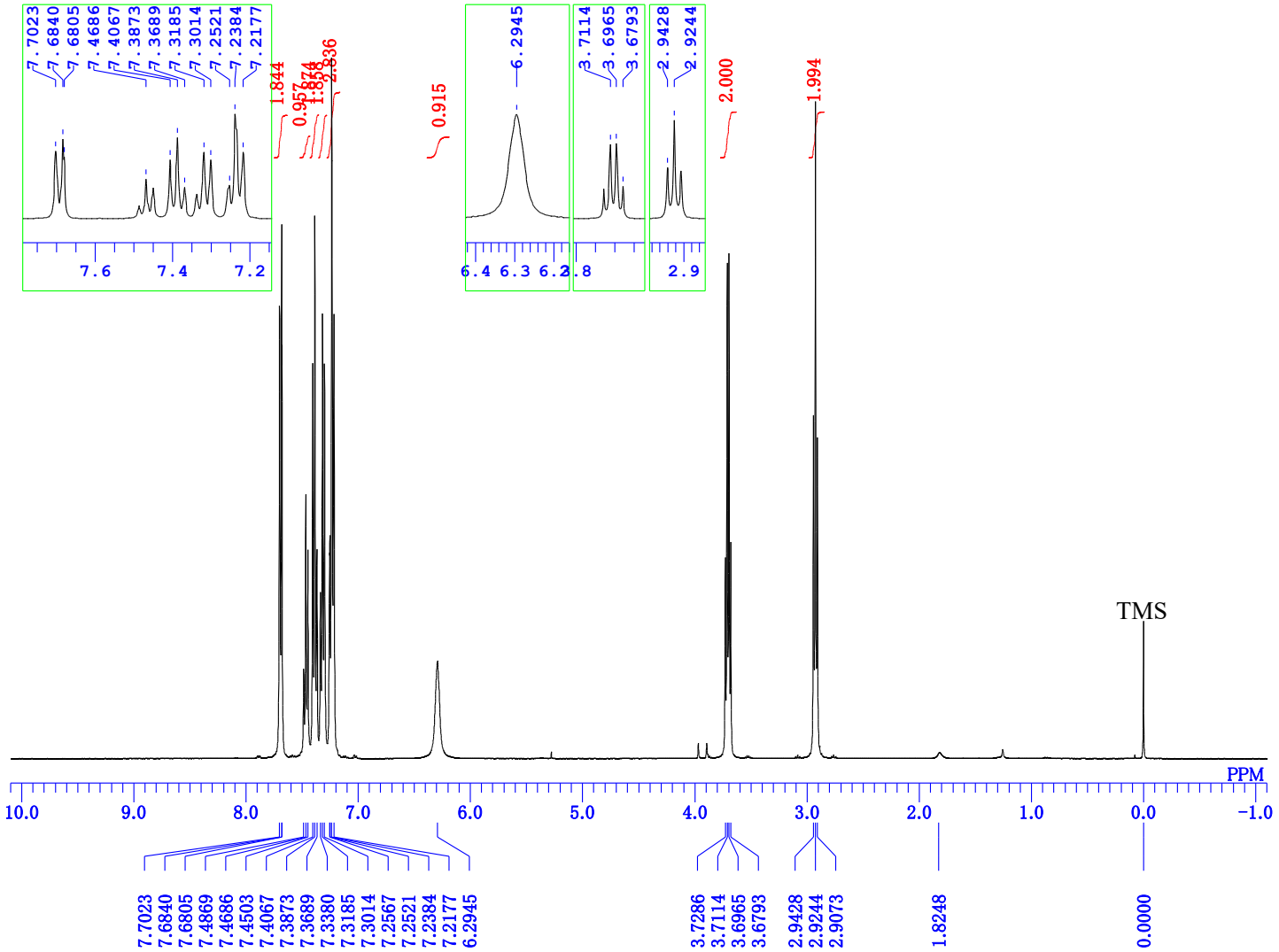




_N_-Phenethylbenzamide (8ba)

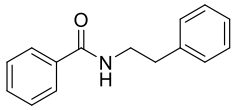
^{1}H NMR (400 MHz, $CDCl_3$)

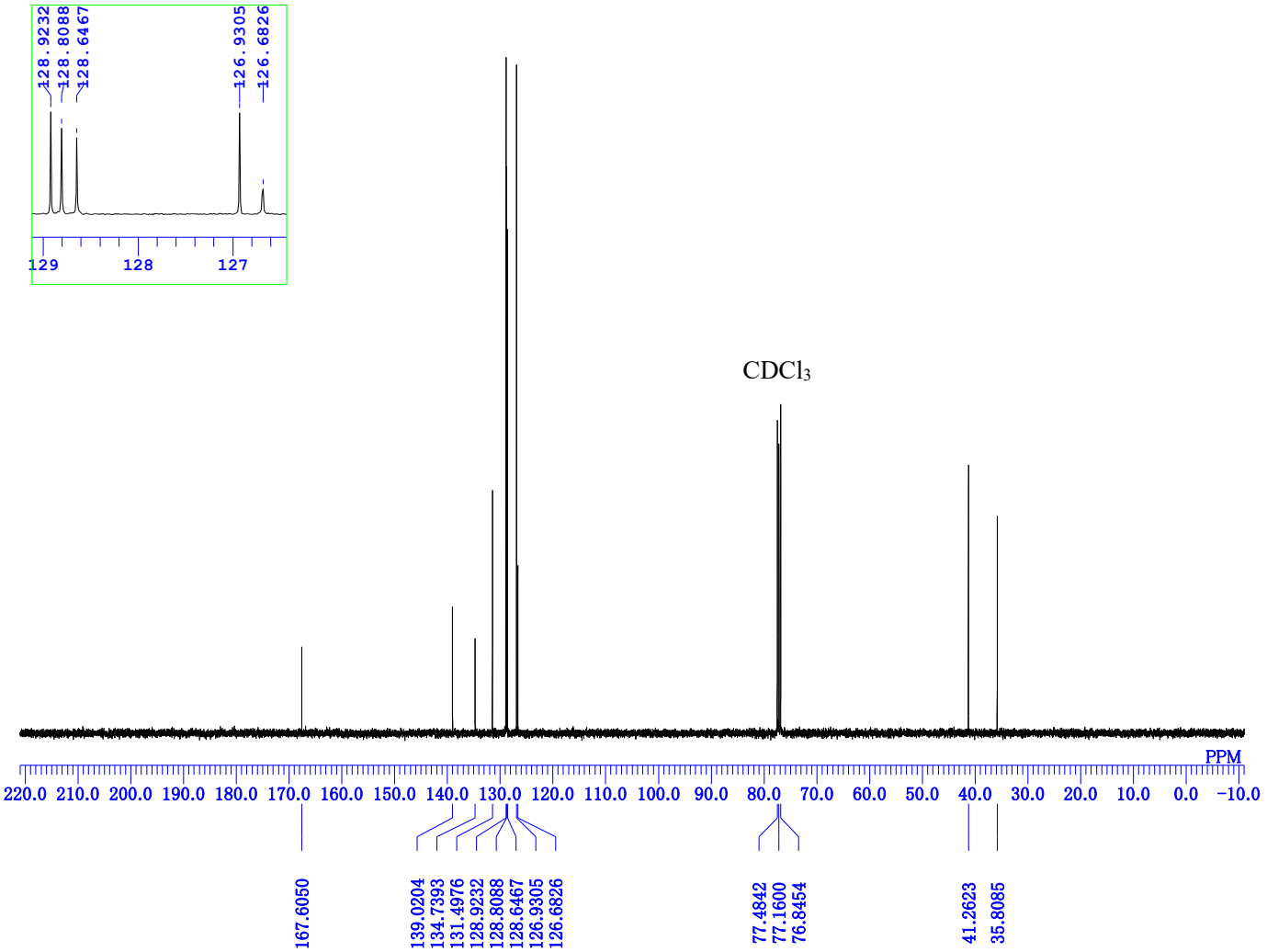




_N_-Phenethylbenzamide (8ba)

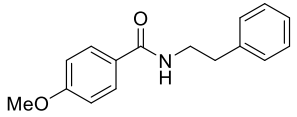
$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)

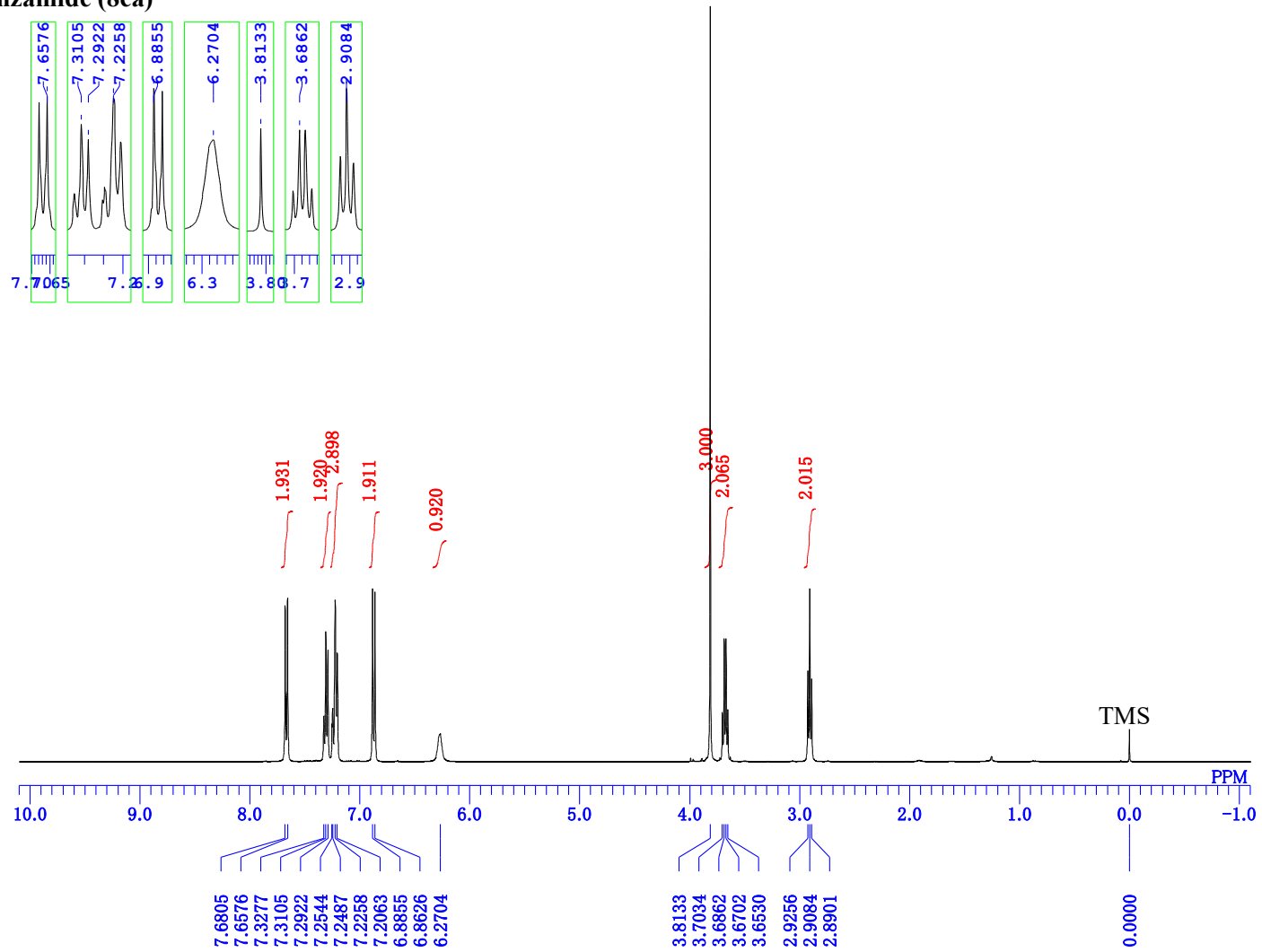




4-Methoxy-*N*-phenethylbenzamide (8ca)

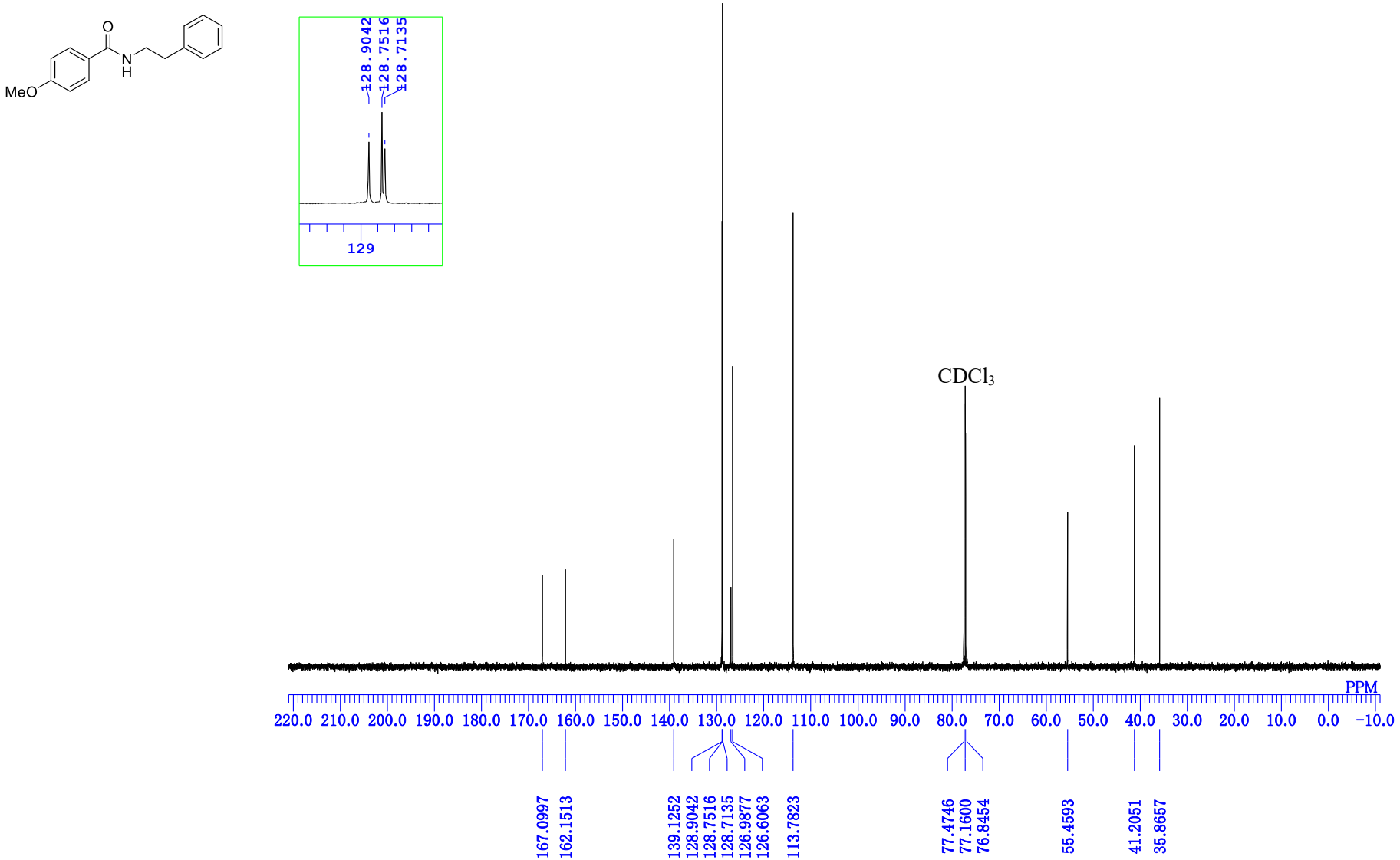
^{1}H NMR (400 MHz, $CDCl_3$)



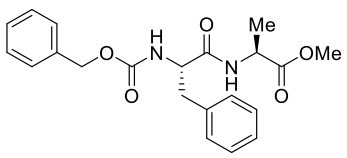


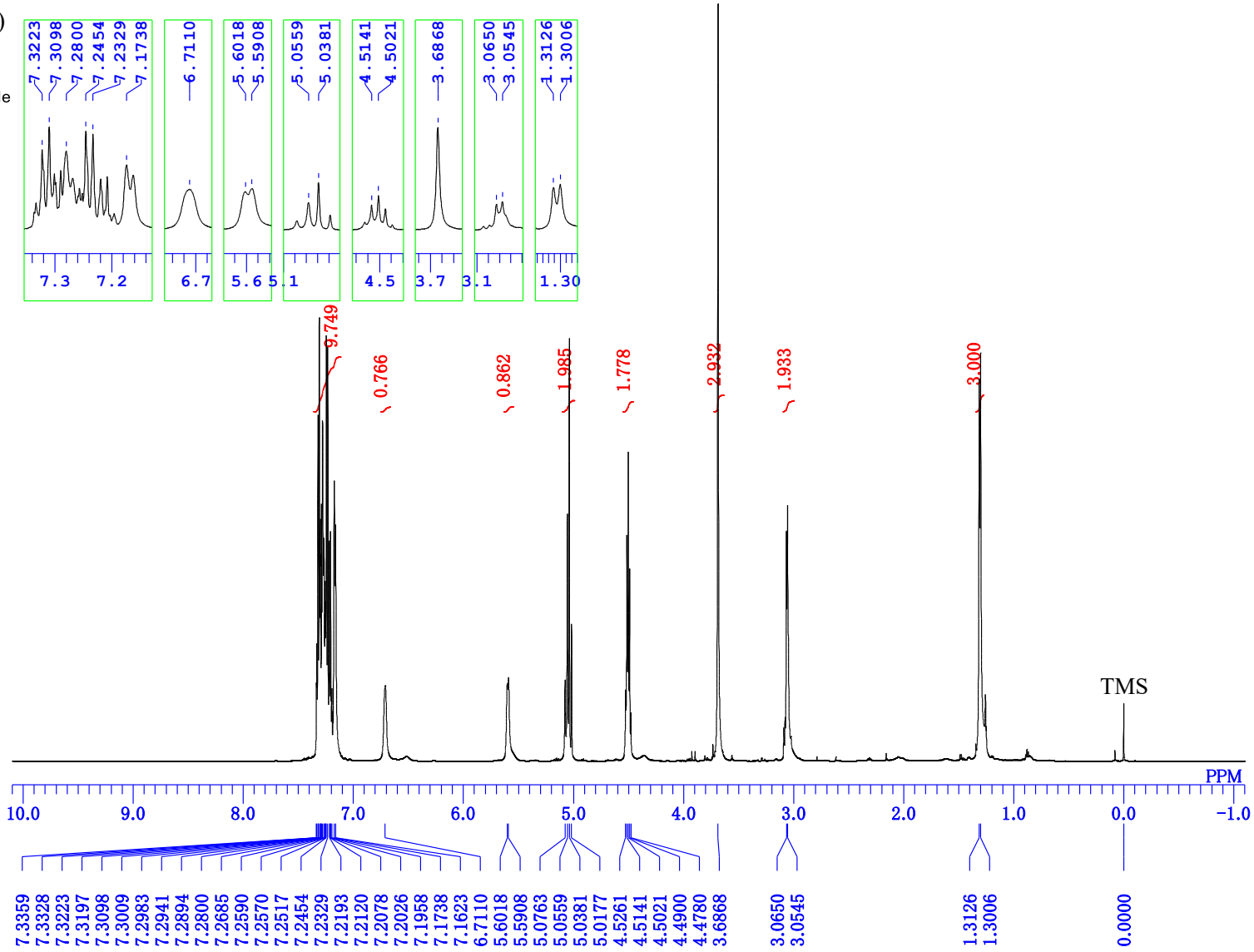
4-Methoxy-*N*-phenethylbenzamide (8ca)

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



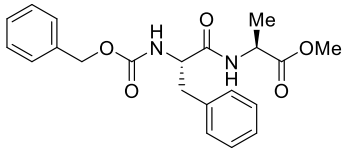
^{1}H NMR (400 MHz, $CDCl_3$)

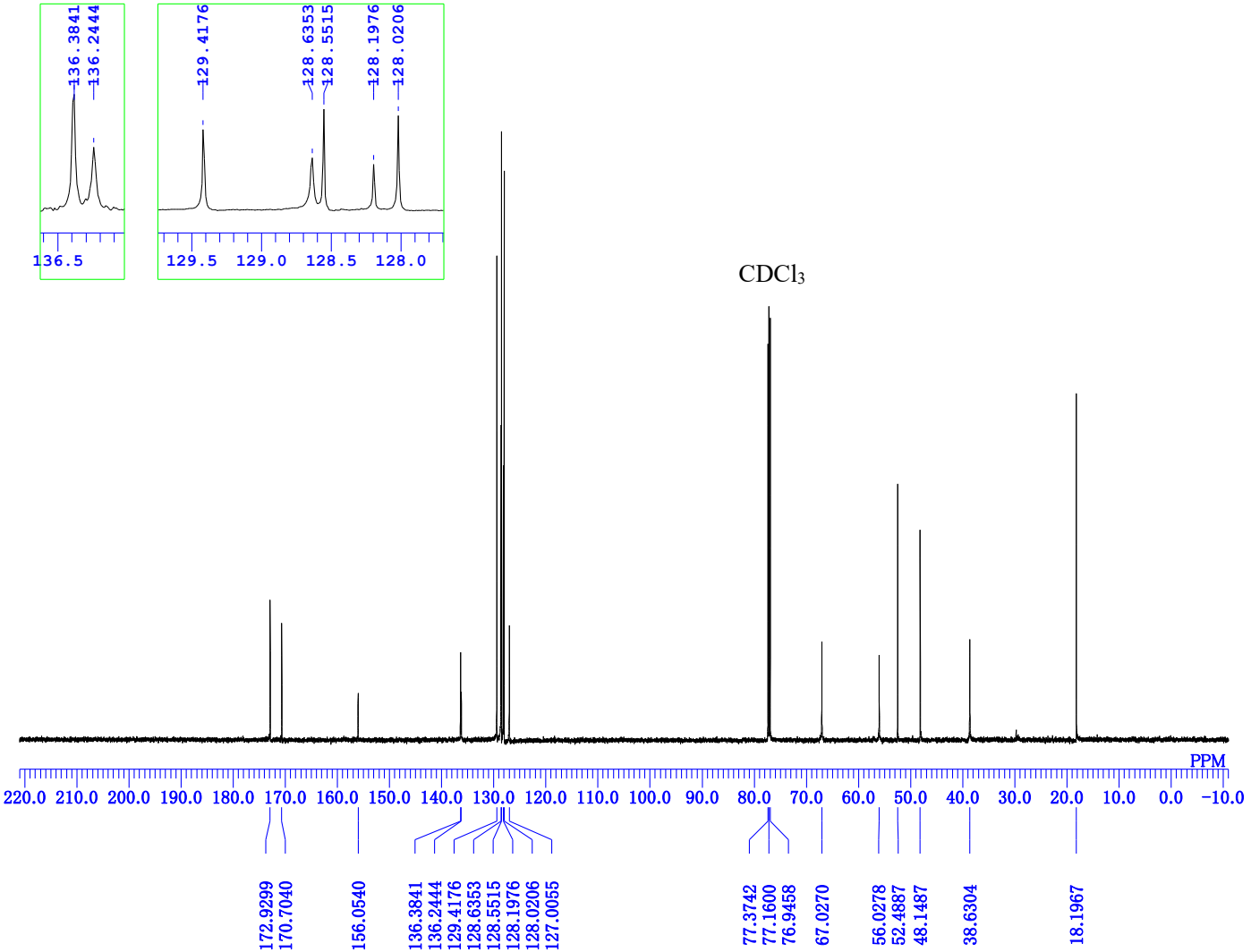




Compound 8df

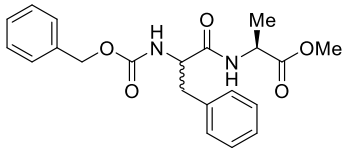
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

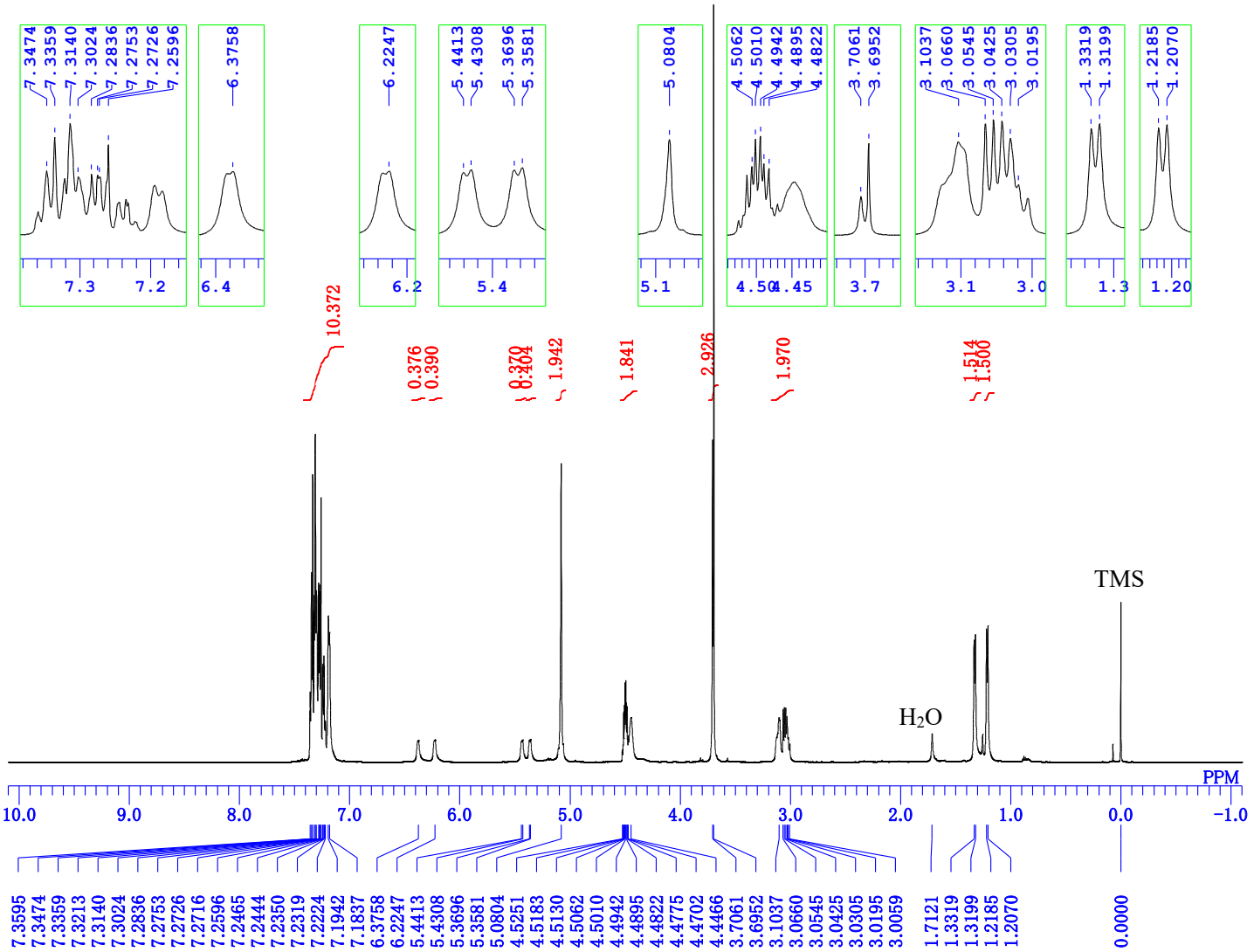




Compound DL-8df

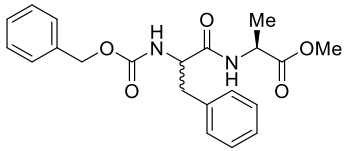
^{1}H NMR (400 MHz, $CDCl_3$)

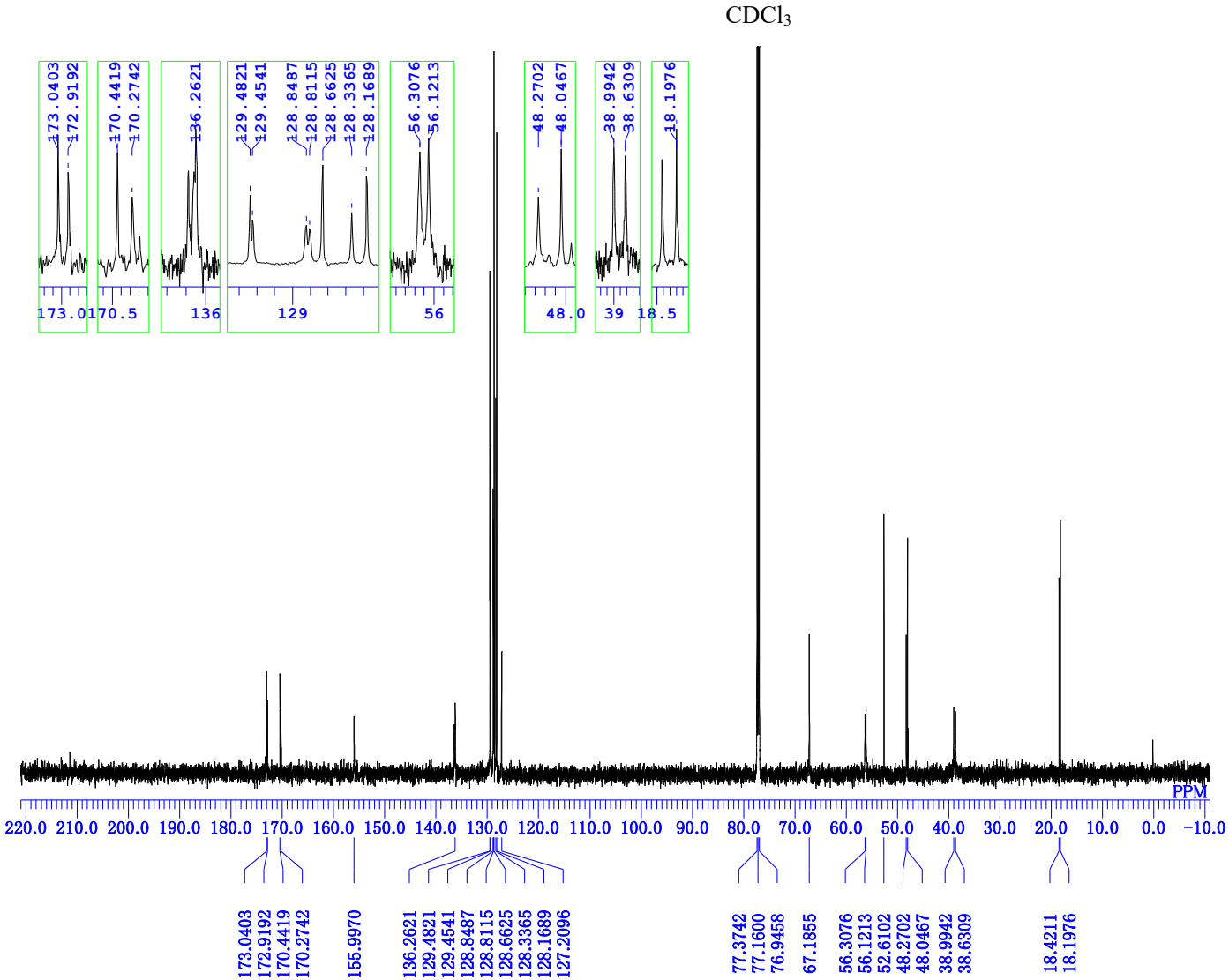




Compound DL-8df

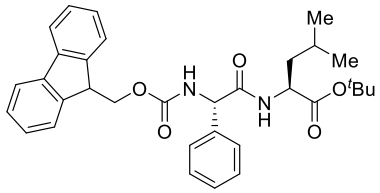
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

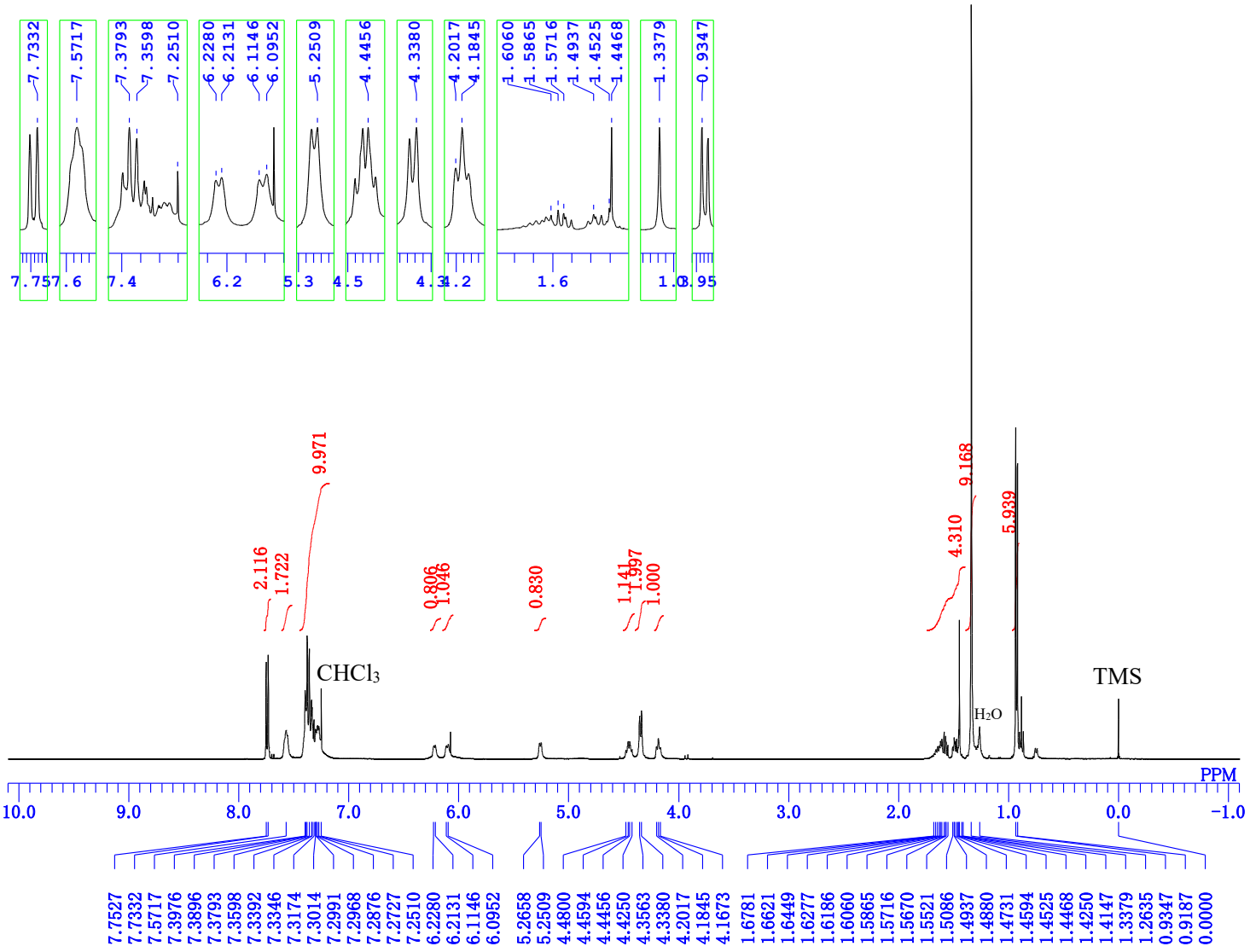




Compound 8eg

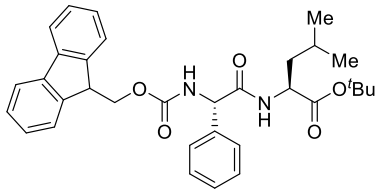
^{1}H NMR (600 MHz, $CDCl_3$)

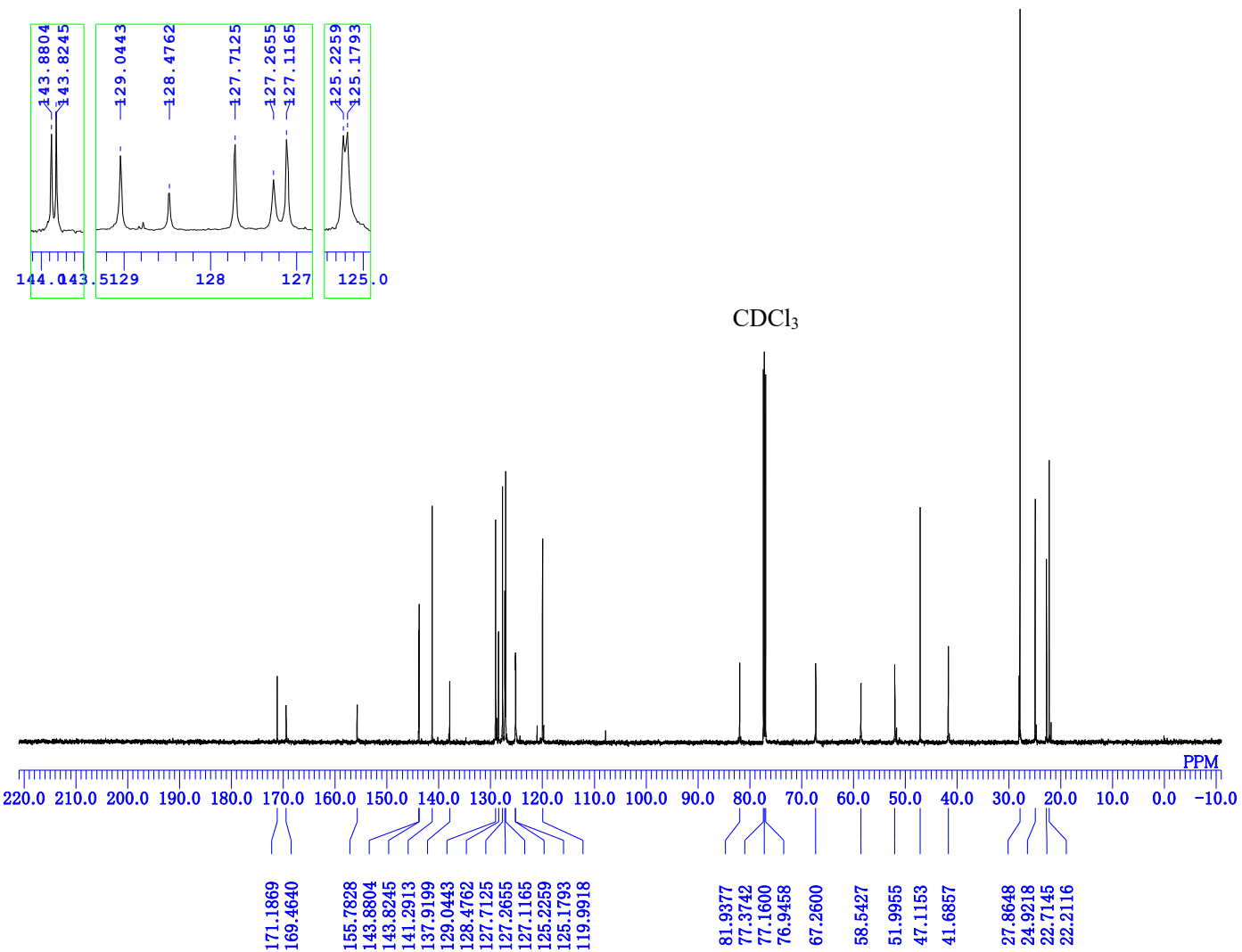




Compound 8eg

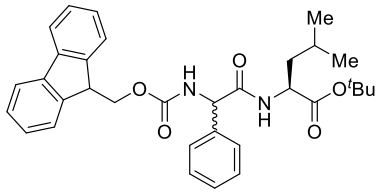
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

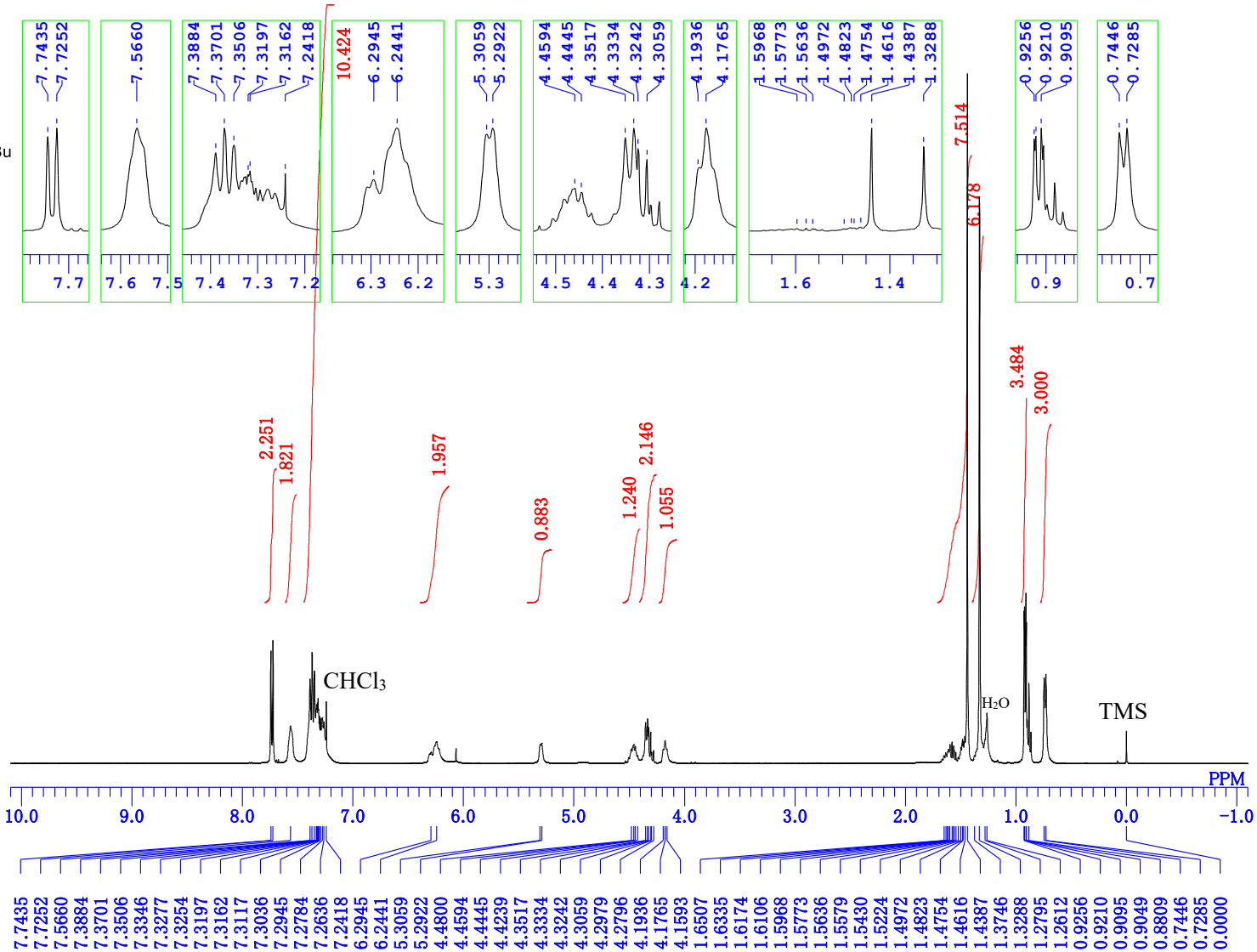




Compound DL-8eg

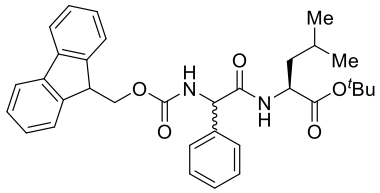
^{1}H NMR (600 MHz, $CDCl_3$)

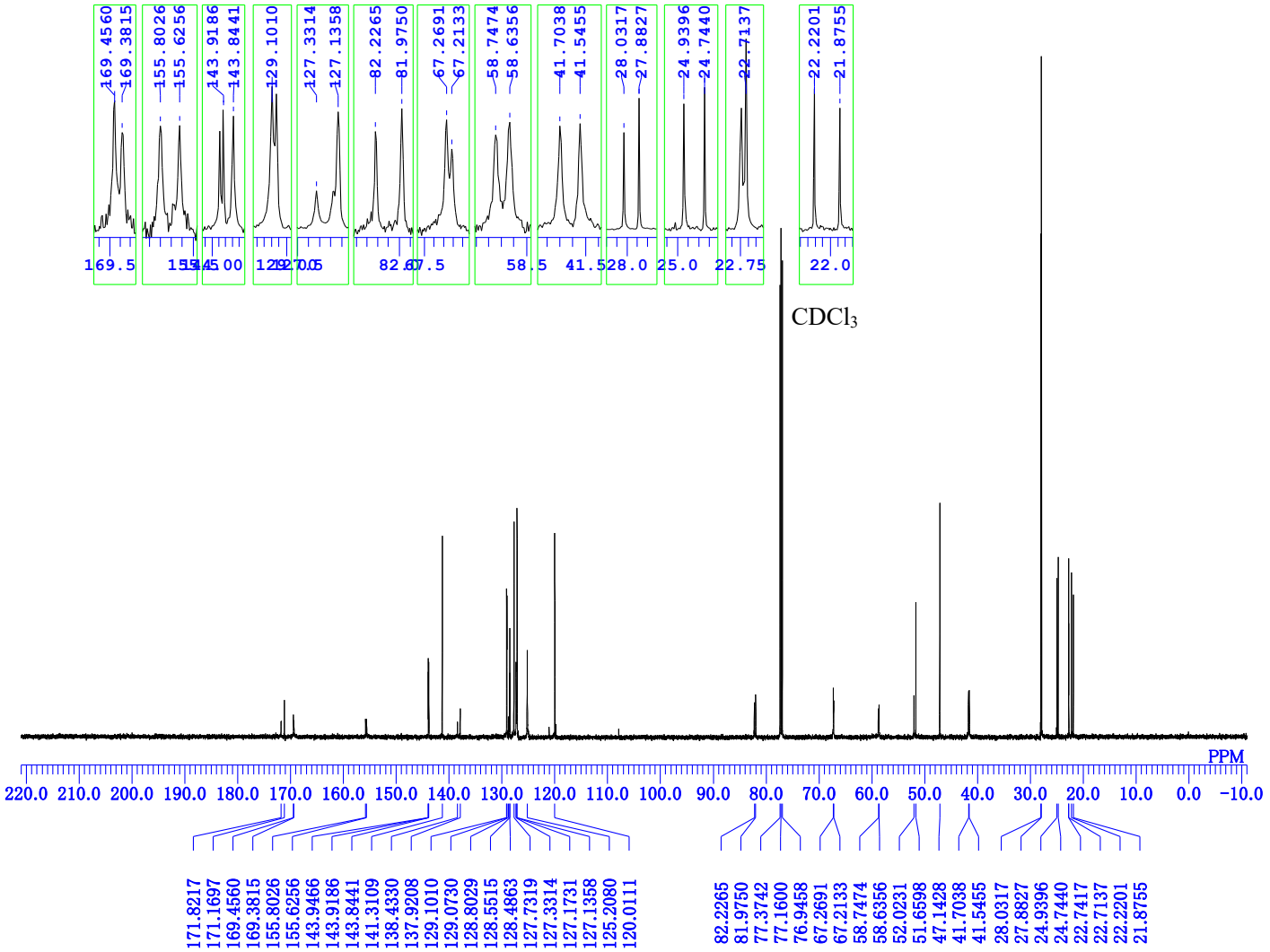




Compound DL-8eg

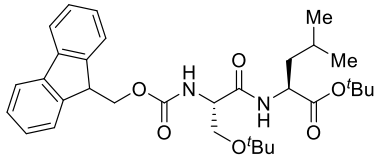
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)

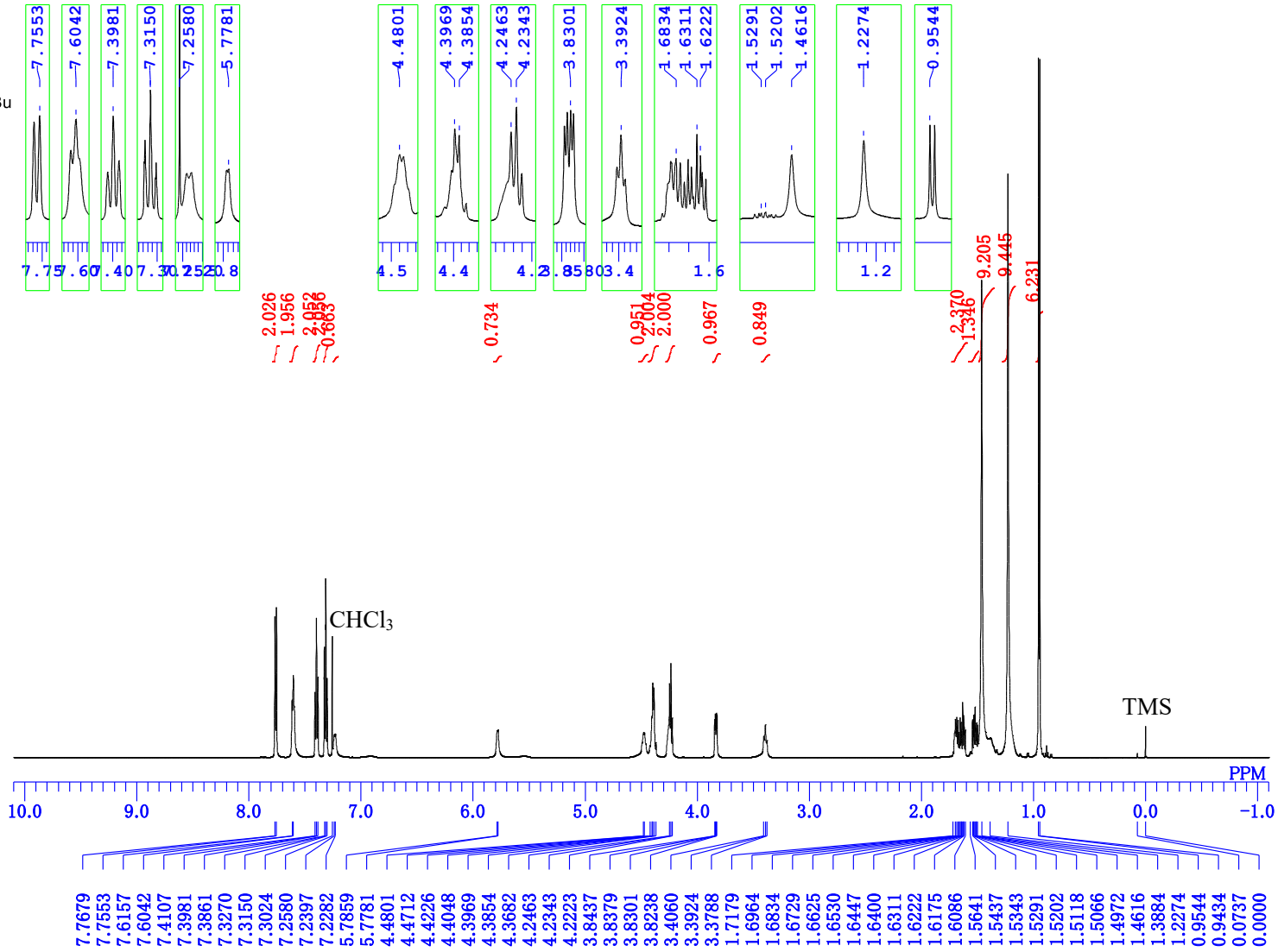




Compound 8fg

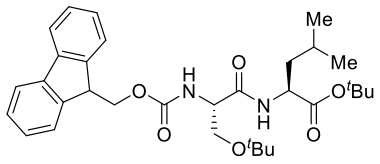
^{1}H NMR (600 MHz, $CDCl_3$)

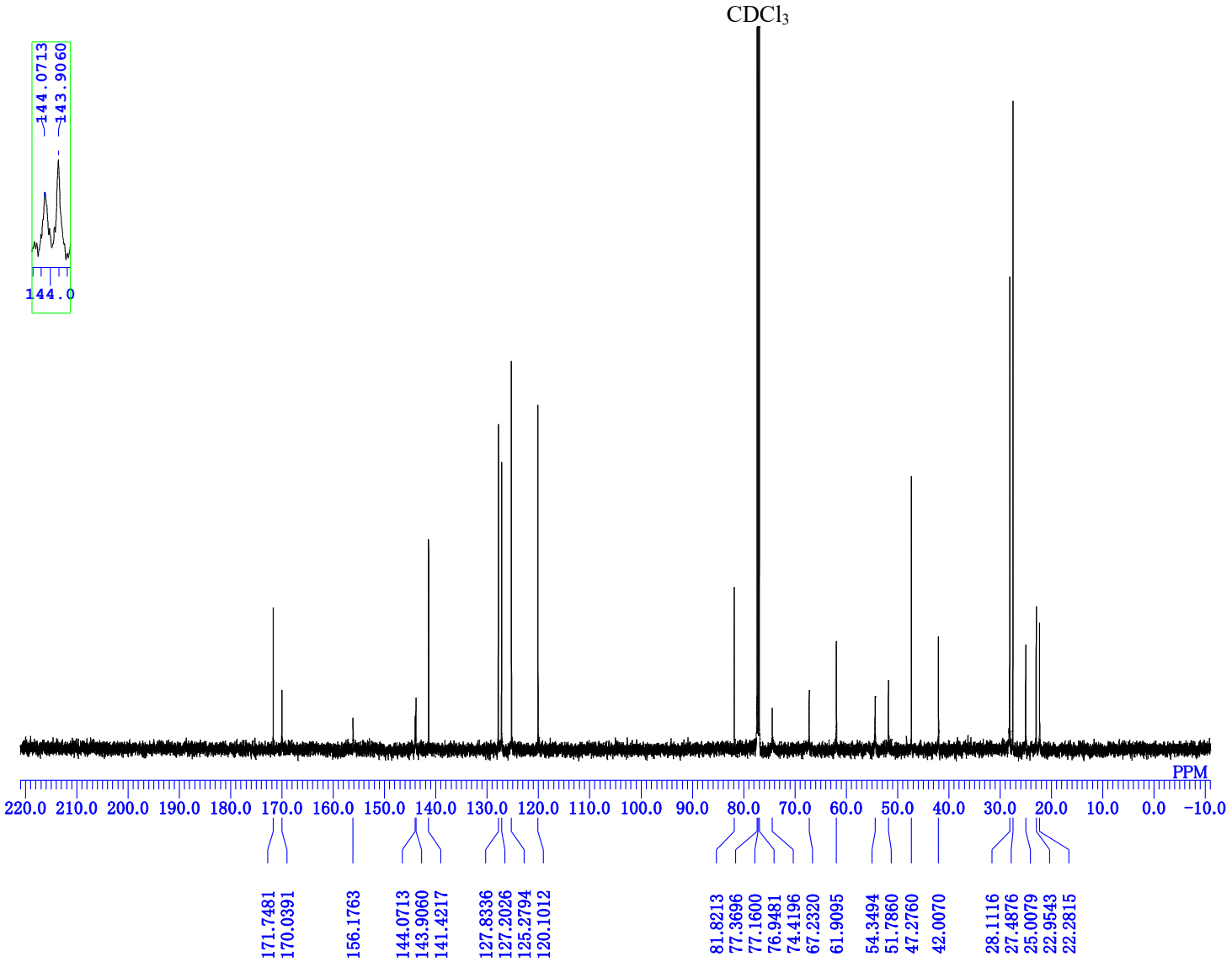




Compound 8fg

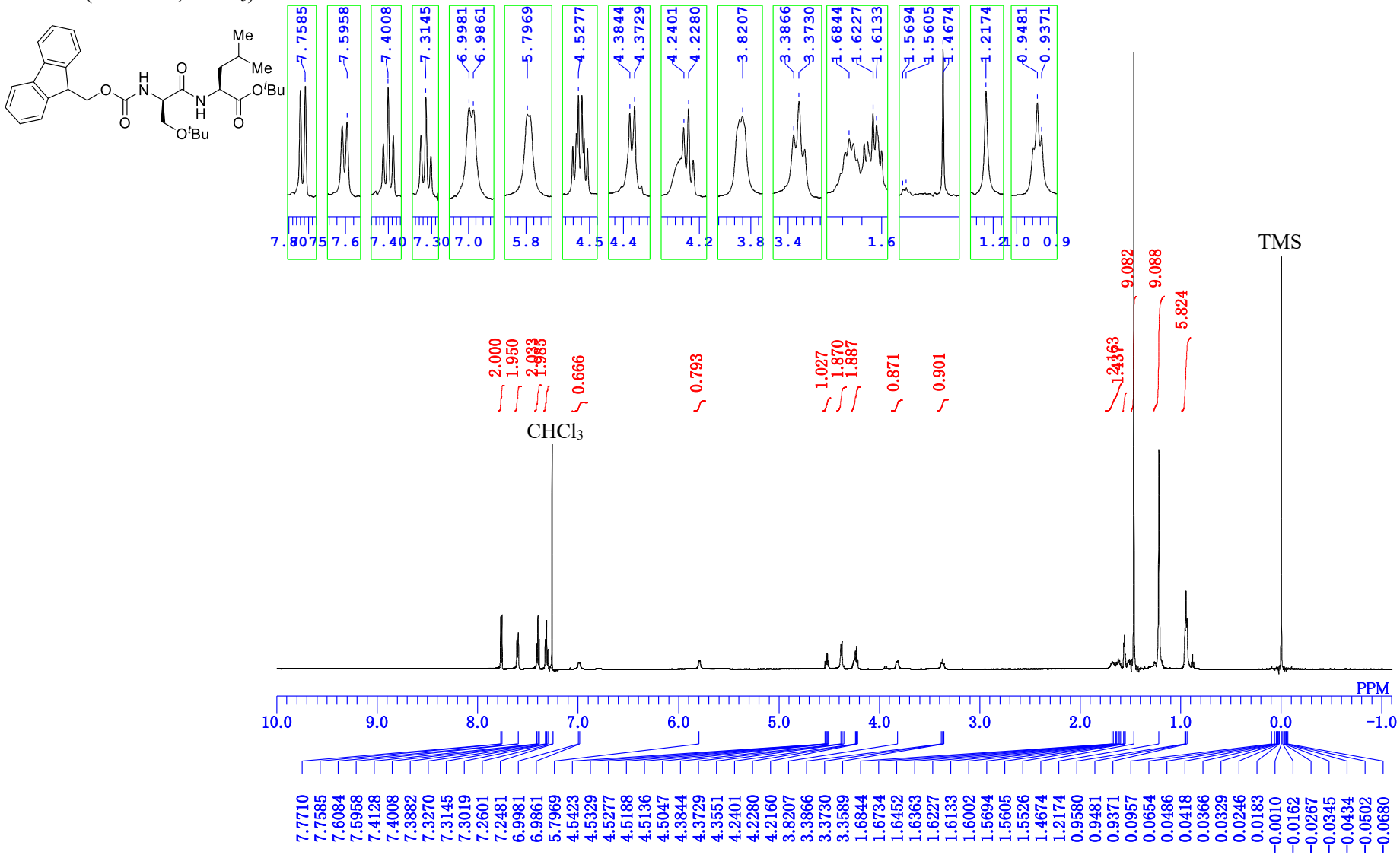
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)





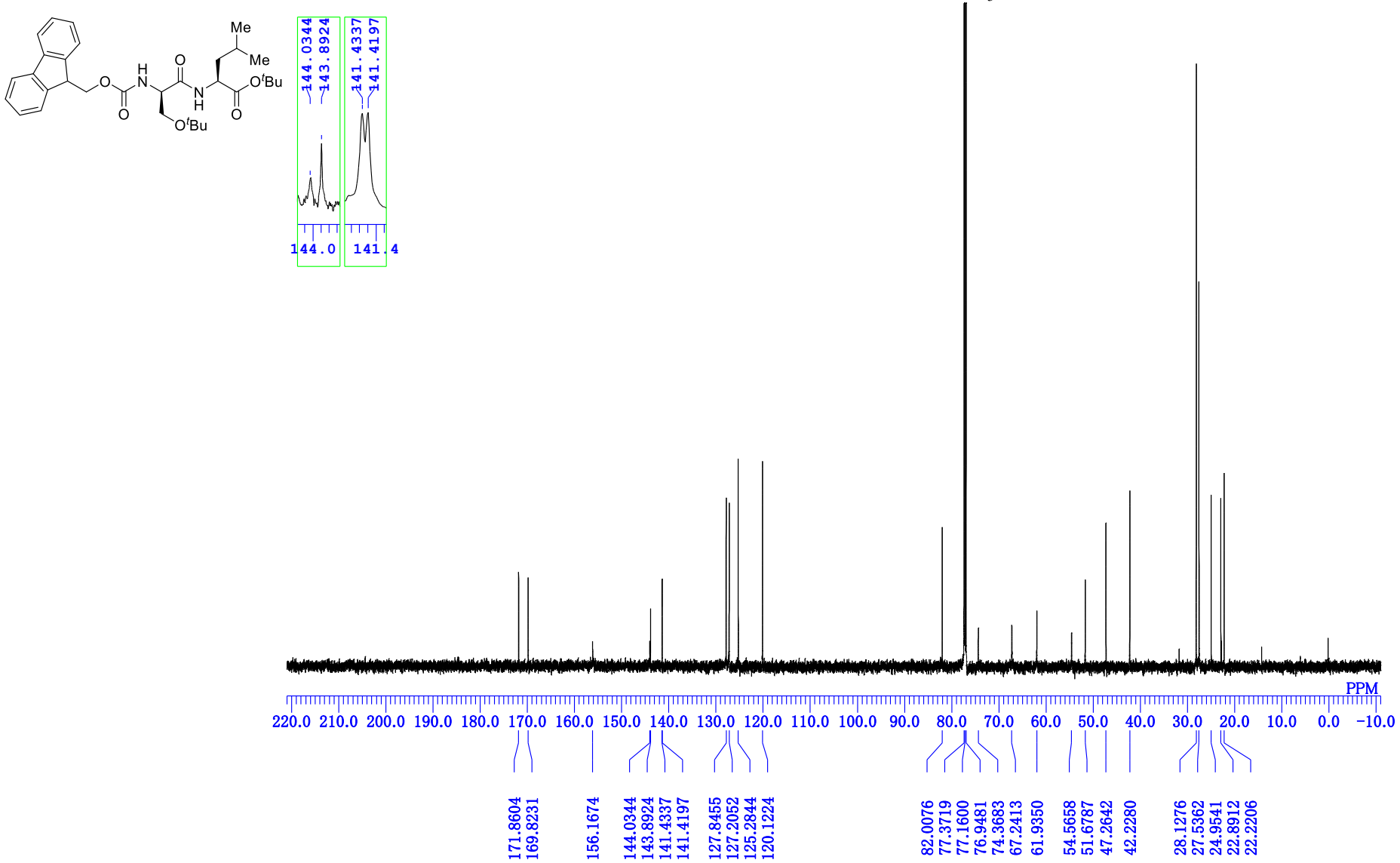
Compound D-8fg

^{1}H NMR (600 MHz, $CDCl_3$)



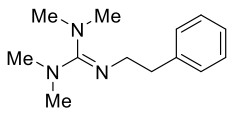
Compound D-8fg

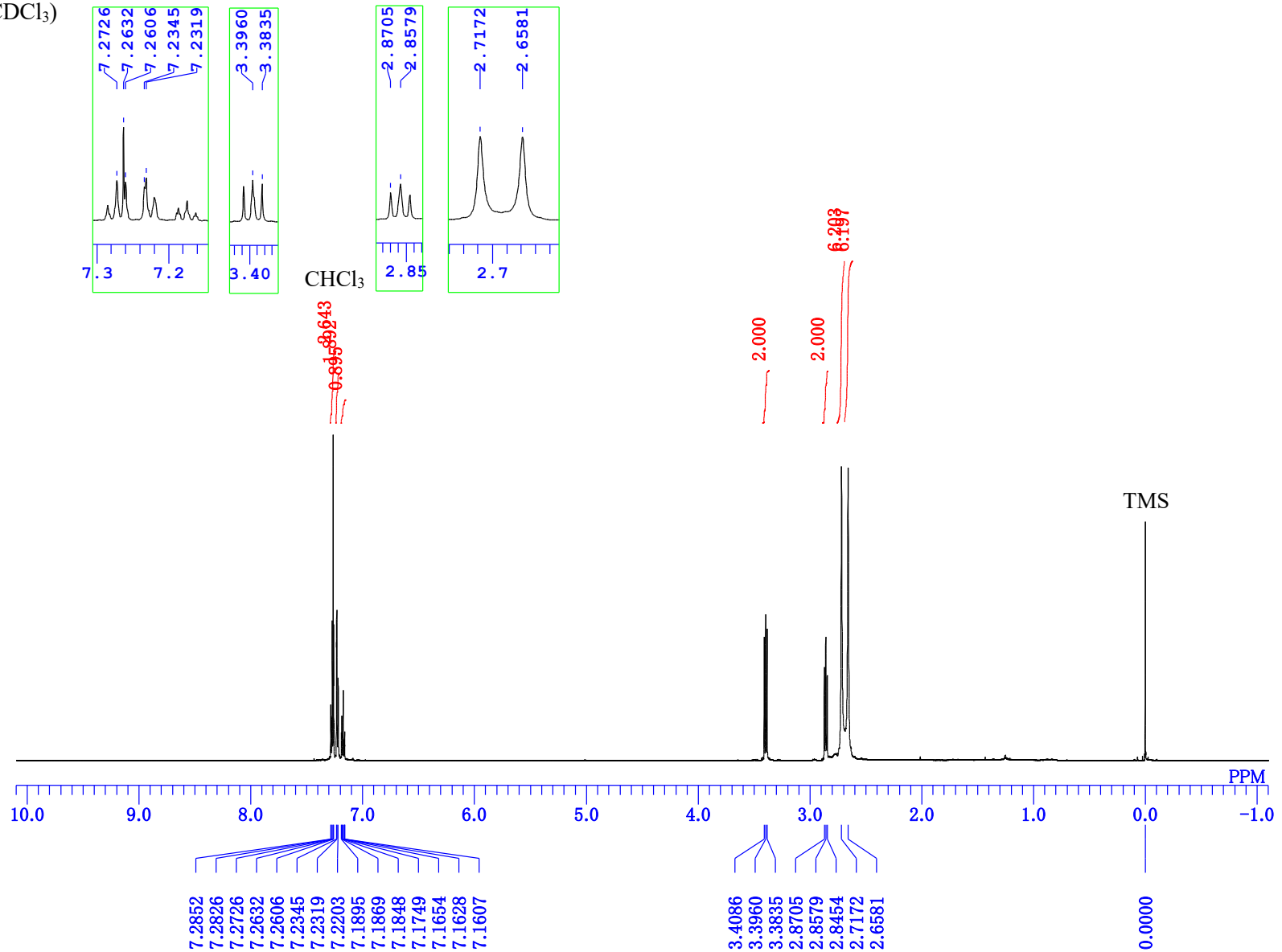
$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)



2-Benzyl-1,1,3,3-tetramethylguanidine (10)

^{1}H NMR (600 MHz, $CDCl_3$)





2-Benzyl-1,1,3,3-tetramethylguanidine (10)

$^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$)