Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Synthesis of Multi-substituted 1,2,4-triazoles Utilising the Ambiphilic Reactivity of Hydrazones

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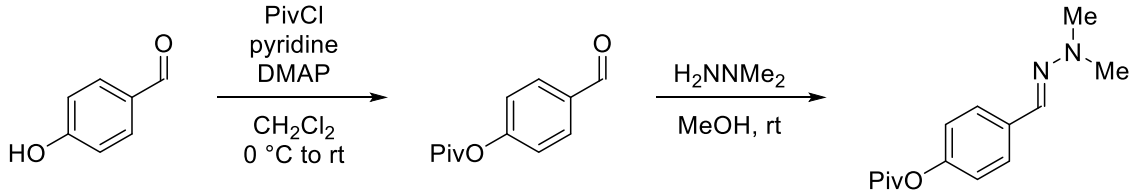
1. General Information

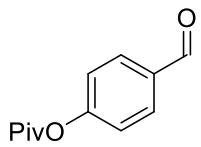
Flash column chromatography were performed using Silicycle silica gel (SiliaFlash® F60, 40-63 μm) or performed on Yamazen Automated Liquid Chromatography System Smart Flash EPCLC-AI-580S using ULTRAPACK SI-40B or Biotage Automated Liquid Chromatography System Isolera One using Biotage SNAP KP-Sil 25g or 50g or 100g silica gel cartridges. NMR spectra were recorded at 300 MHz/75 MHz (^{1}H NMR/^{13}C NMR), 500 MHz/125 MHz (^{1}H NMR/^{13}C NMR) or 600 MHz/150 MHz (^{1}H NMR/^{13}C NMR) using Varian MERCURY plus 300 (300 MHz), Varian NMR system AS-500 (500 MHz), or Bruker Avance III HD 600 (600 MHz) spectrometers. Chemical shifts (δ) are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, td = triplet of doublets, m = multiplet), coupling constants, and integration. Infrared (IR) spectra were recorded on a Perkin-Elmer SpectrumOne A spectrometer. The high-resolution mass spectra (HRMS) were obtained using Thermo Fischer Scientific Exactive Orbitrap mass spectrometer by ESI technique. Melting points (uncorrected) were determined on BÜCHI M-565 apparatus. Preparative TLC separations (PTLC) were carried out on precoated silica gel plates (E. Merck 60F254). *N*-Chlorosuccinimide (NCS), $BF_3 \cdot OEt_2$ were purchased from Nacalai Tesque, Inc. Hydrazones **1a**[1a], **1b**[1b], **1c**[1a], **1e**[1c], **1f**[1d], **1g**[1d], **1h**[1a], **1i**[1d], **1j**[1c], **1k**[1e], **1l**[1f], **1m**[1g], **1n**[1g], **1o**[1a], **1p**[1g], **1q**[1a], **1u**[1h], **1v**[1i] were prepared according to literatures[1], respectively. The spectra data of these known compounds were identical with those reported in the literatures, respectively.

2. Experimental Section

2.1 Experimental procedure for the preparation of hydrazone (1d)



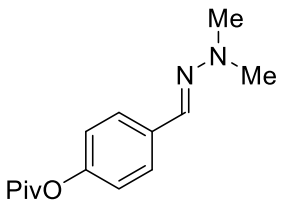
2,2-Dimethylpropionic acid 4-formylphenyl ester (S2)



To a solution of 4-hydroxybenzaldehyde (**S1**) (733 mg, 6.0 mmol) in CH_2Cl_2 (7.3 mL) were added pyridine (823 μL, 10.2 mmol), DMAP (73 mg, 0.60 mmol) at 0 ℃ and then slowly added pivaloyl chloride (1.1 mL, 9.0 mmol) at the same temperature. After being stirred at room temperature for 1 h, the reaction mixture was quenched with H_2O (10 mL) and extracted with $CHCl_3$ (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 5/1) to afford pivalate **S2** as a colorless oil (1.40 g,

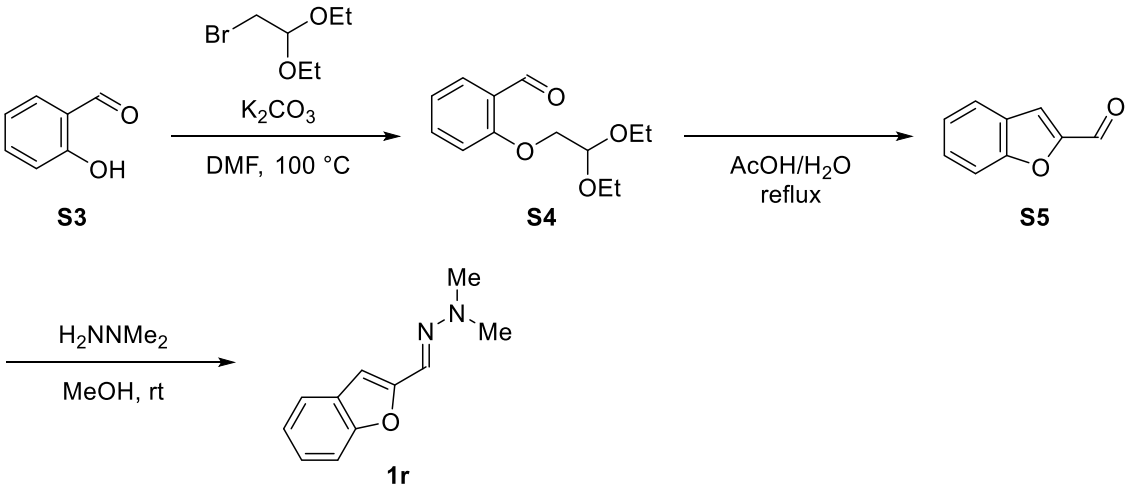
quant.). The spectra data matched those previously reported in the literature[2].

(*E*)-2,2-Dimethylpropionic acid 4-[(2,2-dimethylhydrazinylidene)methyl]phenyl ester (1d)

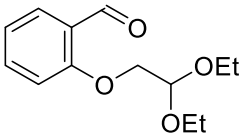


To a solution of **S2** (1.4 g, 6.0 mmol) in MeOH (12 mL) was added *N*,*N*-dimethylhydrazine (486 μL, 7.2 mmol) at room temperature. After being stirred for 1.5 h, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 10/1) to afford hydrazone **1d** (1.33 g, 89%) as white crystals; **Mp**: 72-74 ℃ (Hexane); **IR** (KBr): 1744, 1563 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.56 (d, *J* = 8.7 Hz, 2H), 7.21 (s, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 2.95 (s, 6H), 1.35 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 176.9, 150.2, 134.4, 131.8, 126.3, 121.4, 42.8, 39.0, 27.1; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{14}H_{21}O_2N_2$ 249.1598; Found 249.1596.

2.2 Experimental procedure for the preparation of hydrazone (1r)

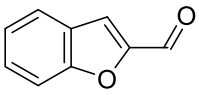


2-(2,2-Diethoxyethoxy)benzaldehyde (S4)



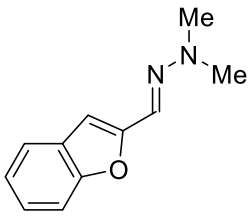
To a solution of salicylaldehyde (**S3**) (5.2 mL, 50 mmol) in DMF (50 mL) were added bromoacetaldehyde diethyl acetal (8.1 mL, 52.5 mmol), K_2CO_3 (14 g, 100 mmol) at room temperature. The reaction mixture was stirred at 100 ℃. After being stirred for 23 h, the reaction mixture was diluted with EtOAc (30 mL) and then filtered through celite. The filtrate was concentrated under reduced pressure. The residue was dissolved in Et_2O (30 mL) and H_2O (20 mL) and extracted with Et_2O (30 mL × 3). The organic phase was washed with H_2O (20 mL × 3), brine (20 mL) and dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 10/1) to give 2-(2,2-diethoxyethoxy)benzaldehyde (**S4**) (10.6 g, 89%) as a yellow oil. The spectra data matched those previously reported in the literature[3].

2-Benzofurancarboxaldehyde (S5)



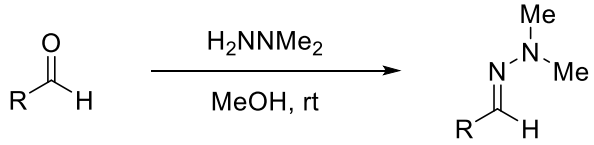
A solution of aldehyde **S4** (11 g, 44 mmol) in AcOH (18 mL) and H_2O (2.4 mL) was stirred at reflux. After being stirred for 48 h at the same temperature, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in Et_2O (120 mL) and washed with sat. $NaHCO_3$ aq. (24 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 20/1 to 10/1) to give 2-benzofurancarboxaldehyde (**S5**) (1.04 g, 16%) as a pale yellow oil. The spectra data matched those previously reported in the literature[3].

(*E*)-2-Benzofurancarboxaldehyde dimethyl hydrazone (1r)



To a solution of 2-benzofurancarboxaldehyde (**S5**) (1.0 g, 7.1 mmol) in MeOH (14 mL) was added *N*,*N*-dimethylhydrazine (648 μL, 8.5 mmol) at room temperature. After being stirred for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in MeOH (1.0 mL) and then added sat. $NaHSO_3$ aq. (5.0 mL) and shaken for approximately 30 sec and extracted with hexanes (20 mL). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure to give the hydrazones **1r** (997.5 mg, 75%) as a yellow oil; **IR** (neat): 1595 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.50 (d, *J* = 9.0 Hz, 2H), 7.23 (m, 2H), 7.14 (s, 1H), 6.64 (s, 1H), 3.05 (s, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 154.6, 154.0, 128.8, 124.1, 122.8, 121.3, 120.5, 111.2, 103.2, 42.6; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{13}ON_2$ 189.1022; Found 189.1022. The crude product **1r** was used without the further purification.

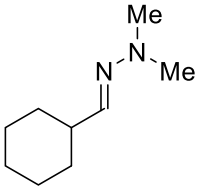
2.3 General procedure for the preparation of hydrazones (1s, 1t)



To a solution of corresponding aldehydes **S6** (10 mmol) in MeOH (20 mL) was added *N*,*N*-dimethylhydrazine (1.1 mL, 15 mmol) at room temperature. After being stirred for several hours, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography to give the corresponding hydrazones **1s** and **1t**.

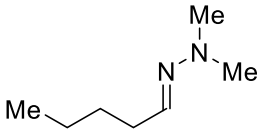
(*E*)-Cyclohexanecarboxaldehyde 2,2-dimethylhydrazone (1s)

1.47 g, 96% yield; Reaction time: 3 h; Purification by flash column chromatography (Yamazen Smart Flash EPCLC-AI-580S using ULTRAPACK SI-40B) (Hexane/EtOAc = 19/1 to 47/13); A



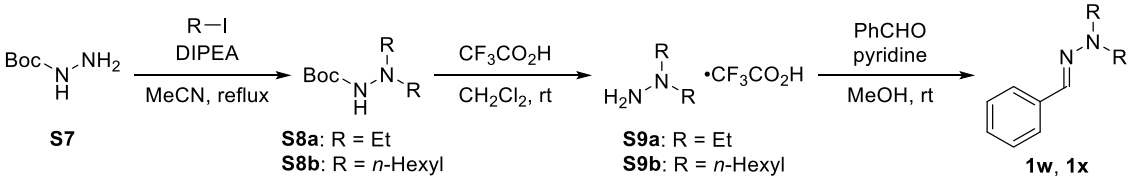
colorless oil; **IR** (neat): 1607 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 6.51 (d, *J* = 6.0 Hz, 1H), 2.70 (s, 6H), 2.23-2.14 (m, 1H), 1.79-1.64 (m, 5H), 1.34-1.16 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 144.0, 43.2, 41.2, 31.3, 25.9, 25.6; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_9H_{19}N_2$ 155.1543; Found 155.1542.

(*E*)-Pentanal 2,2-dimethylhydrazone (1t)

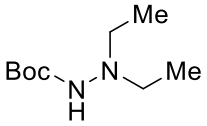


641 mg, 50% yield; Reaction time: 3.5 h; Purification by flash column chromatography (Hexane/EtOAc = 5/1); A pale yellow oil; **IR** (neat): 1620 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 6.66 (t, *J* = 5.6 Hz, 1H), 2.72 (s, 6H), 2.23 (td, *J* = 7.8, 5.6, Hz, 2H), 1.46 (quint, *J* = 7.4 Hz, 2H), 1.36 (sext, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 139.7, 43.3, 32.7, 29.8, 22.2, 13.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_7H_{17}N_2$ 129.1386; Found 129.1388.

2.4 General procedure for the preparation of hydrazones (1w, 1x)

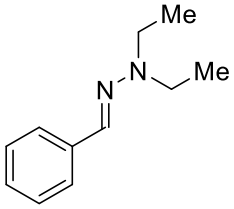


2,2-Diethylhydrazinecarboxylic acid 1,1-dimethylethyl ester (S8a)



To a solution of *tert*-butyl carbazate (**S7**) (4.0 g, 30 mmol) in MeCN were added iodoethane (6.1 mL, 75 mmol), DIPEA (16 mL, 90 mmol) at room temperature. After being stirred at reflux for 6 h, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 2/1) to give the 2,2-diethylhydrazine **S8a** (4.60 g, 82%) as a white solid; **Mp**: 53-57 ℃ (Hexane); **IR** (KBr) 3240, 1712 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.23 (br s, 1H), 2.72 (q, *J* = 7.2 Hz, 4H), 1.46 (s, 9H), 1.09 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 155.2, 79.3, 51.9, 28.2, 11.8; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_9H_{20}O_2N_2Na$ 211.1417; Found 211.1416.

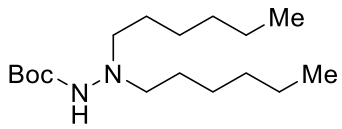
(*E*)-Benzaldehyde 2,2-diethylhydrazone (1w)



To a solution of 2,2-diethylhydrazine **S8a** (1.9 g, 10 mmol) in CH_2Cl_2 (20 mL) was added trifluoroacetic acid (5.0 mL) at room temperature. After being stirred for 1.5 h, the reaction mixture was concentrated under reduced pressure. The crude product **S9a** dissolved in MeOH (20 mL) and then added benzaldehyde (1.0 mL, 10 mmol), pyridine (1.2 mL, 15 mmol) at room temperature. After being stirred for 1 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (20 mL) and washed with 1 M HCl aq. (10 mL), sat.

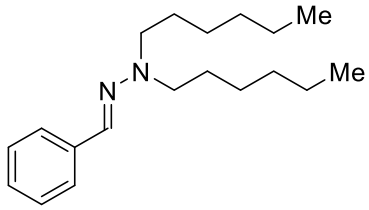
$NaHCO_3$ aq. (10 ml), brine (10 ml). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 10/1) to give the hydrazone **1w** (585 mg, 33%) as a yellow oil; **IR** (neat): 1559 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.28 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H) 3.35 (q, *J* = 7.2 Hz, 4H), 1.17 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 137.4, 130.1, 128.3, 126.7, 125.2, 46.6, 11.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{17}N_2$ 177.1386; Found 177.1384.

2,2-Dihexylhydrazinecarboxylic acid 1,1-dimethylethyl ester (S8b)



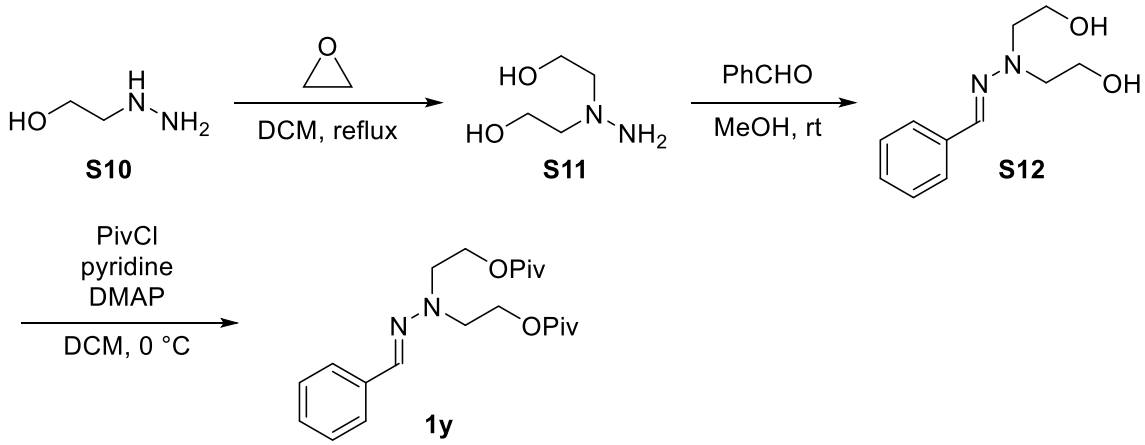
To a solution of *tert*-butyl carbazate (**S7**) (4.0 g, 30 mmol) in MeCN (30 mL) were added 1-iodohexane (15 mL, 105 mmol), DIPEA (16 mL, 90 mmol) at room temperature. After being stirred at reflux for 6 h, the reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 10/1) to give the 2,2-dihexylhydrazine **S8b** (7.96 g, 88%) as a white solid; **Mp**: 30-32 °C; **IR** (KBr): 3230, 1699 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.22 (br s, 1H), 2.64 (br m, 4H), 1.48-1.22 (m, 25H), 0.88 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 155.1, 79.4, 58.3, 31.7, 28.3, 26.9, 26.8, 22.6, 14.0; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{17}H_{36}O_2N_2Na$ 323.2669; Found 323.2668.

(*E*)-Benzaldehyde 2,2-dihexylhydrazone (1x)



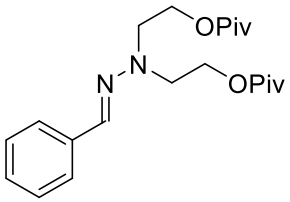
To a solution of 2,2-dihexylhydrazine **S8b** (3.0 g, 10 mmol) in CH_2Cl_2 (20 mL) was added trifluoroacetic acid (5.0 mL) at room temperature. After being stirred for 3 h, the reaction mixture was concentrated under reduced pressure. The crude product **S9b** dissolved in MeOH (20 mL) and then added benzaldehyde (683 μL, 6.7 mmol), pyridine (1.6 mL, 20 mmol) at room temperature. After being stirred for 3 h, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in EtOAc (20 mL) and washed with 1 M HCl aq. (10 mL), sat. $NaHCO_3$ aq. (10 ml), brine (10 ml). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/Et_2O = 20/1) to give the hydrazone **1x** (1.75 g, 90%) as a yellow oil; **IR** (neat): 1560 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.52 (d, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.19 (s, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 3.26 (br m, 4H), 1.59 (br quint, *J* = 7.2 Hz, 4H), 1.35-1.30 (m, 12H), 0.90 (t, *J* = 6.8 Hz, 6H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 137.7, 128.5, 128.3, 126.4, 125.1, 53.5, 31.7, 26.9, 26.8, 22.6, 14.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{19}H_{33}N_2$ 289.2638; Found 289.2636.

2.5 Experimental procedure for the preparation of hydrazone 1y



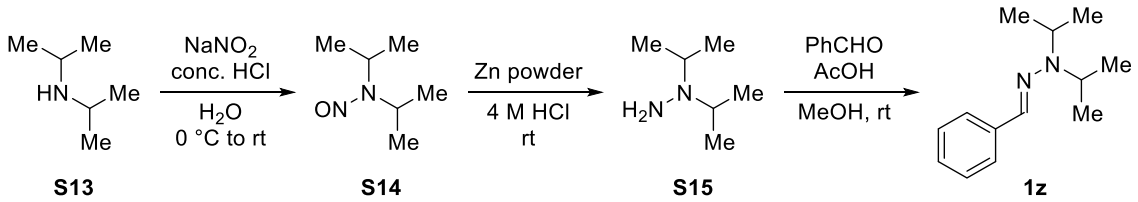
To a suspension of 2-hydrazinoethanol (**S10**) (850 μL, 10 mmol) in DCM (10 mL) was added ethylene oxide in DCM (1.0 M, 10 mL, 10 mmol) at room temperature. The reaction mixture was stirred at reflux. After being stirred for 15 h, the reaction mixture was concentrated under reduced pressure. The crude product **S11** dissolved in MeOH (16 mL) and then added benzaldehyde (790 μL, 7.8 mmol) at room temperature. After being stirred for 2 h, the reaction mixture was concentrated under reduced pressure. The crude product **S12** was used without the further purification.

(*E*)-2,2-Dimethylpropanoic acid 1,1'-(2-benzylidenenaminimino)bis(2,1-ethanediyl) ester (1y)



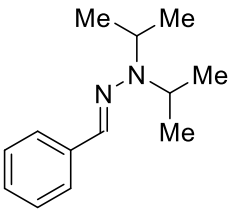
To a suspension of hydrazone **S12** in DCM (18 mL) were slowly added pyridine (2.4 mL, 30 mmol), DMAP (220 mg, 1.8 mmol), pivaloyl chloride (3.2 mL, 26 mmol) at 0 ℃ and then stirred at the same temperature. After being stirred for 1 h, pivaloyl chloride (2.2 mL, 18 mmol) was slowly added to the reaction mixture. After additional 30 min, the reaction mixture was quenched with H_2O (10 mL) and extracted with $CHCl_3$ (20 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was dissolved in $CHCl_3$ (20 mL) and basified by 1.0 M NaOH aq. (20 mL) and then extracted with $CHCl_3$ (20 mL × 2). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 20/1) to afford hydrazone **1y** (1.31 g, 44%, 3 steps) an yellow oil; **IR** (neat): 1744, 1563 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 7.2 Hz, 2H), 7.37 (s, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.23-7.18 (m, 1H), 4.28 (t, *J* = 6.0 Hz, 4H), 3.63 (t, *J* = 6.0 Hz, 4H), 1.20 (s, 18H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 178.4, 136.6, 130.9, 128.4, 127.3, 125.5, 61.7, 52.6, 38.7, 27.2; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{32}O_4N_2Na$ 399.2254; Found 399.2248.

2.6 Experimental procedure for the preparation of hydrazone 1z



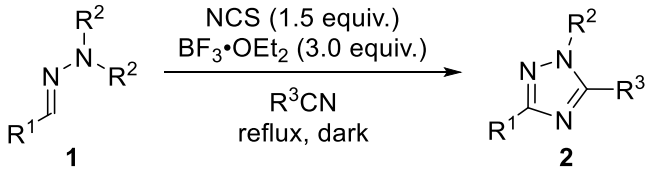
Diisopropylamine **S13** (2.8 mL, 20 mmol) was added to conc. HCl (2.0 mL, 24 mmol) at 0 ℃. Then, to the resulting mixture was added $NaNO_2$ (1.7 g, 25 mmol) in H_2O (4.0 mL) at the same temperature and stirred at room temperature. After being stirred for 30 min, the reaction mixture was diluted with Et_2O (20 mL) and extracted with Et_2O (20 mL × 3). The organic phase was washed with brine (10 mL) and dried over $MgSO_4$ and concentrated under reduced pressure. The residue was dissolved in 4 M HCl aq. (59 mL) and Zn powder (1.6 g, 25 mmol) was added at room temperature. After being stirred at the same temperature for 4 h, Zn powder (8.0 g, 125 mmol) was added and then stirred for 30 min. The reaction mixture was filtered through celite. Then, the filtrate was basified with 4 M NaOH aq. (60 mL) and extracted with $CHCl_3$ (50 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product **S15** was used without the further purification.

(*E*)-Benzaldehyde 2,2-di(1-methylethyl)hydrazone (1z)



To a solution of benzaldehyde (1.4 mL, 14 mmol) in MeOH (28 mL) was added 2,2-diisopropylhydrazine (**S15**) (2.0 g, 17 mmol) at room temperature. After being stirred for 1 h, AcOH (81 μL, 1.42 mmol) was added and then stirred for 2.5 h. The reaction mixture was concentrated under reduced pressure. The crude product was purified by flash column chromatography (Hexane/EtOAc = 40/1) to give the hydrazone **1z** (1.77 g, 61%) as a yellow oil; **IR** (neat): 1558 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.23 (s, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 3.89 (sept, *J* = 6.4 Hz, 2H), 1.21 (d, *J* = 6.4 Hz, 12H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 138.6, 128.3, 126.0, 125.9, 124.7, 47.4, 21.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{21}N_2$ 205.1699; Found 205.1700.

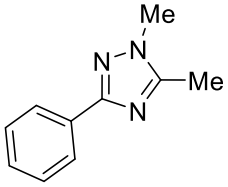
2.7 General procedure for synthesis of triazoles 2



To a solution of hydrazones **1** (0.20 mmol) in dry nitriles (4.0 mL) were added NCS (40 mg, 0.30

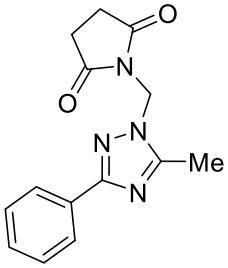
mmol) and BF_3•OEt_2 (76 μL, 0.6 mmol). The reaction mixture was stirred at reflux in the dark. After being stirred for several hours, the reaction mixture was basified with 1 M NaOH aq. (4.0 mL) and extracted with $CHCl_3$ (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by preparative TLC or flash column chromatography to afford the corresponding triazoles **2**.

1,5-Dimethyl-3-phenyl-1*H*-1,2,4-triazole (2aa)



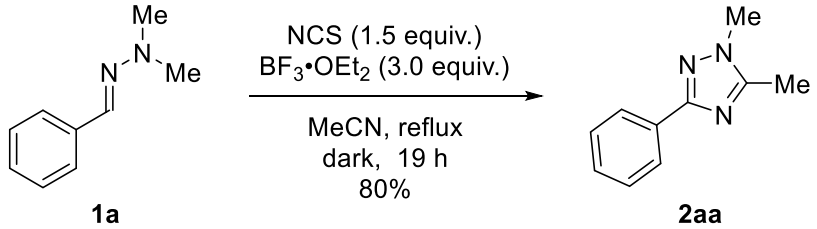
31.2 mg, 90% yield; **Reaction time**: 14 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 116-117 ℃ (EtOAc); **IR** (KBr): 1527 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.1 Hz, 2H), 7.40-7.27 (m, 3H), 3.59 (s, 3H), 2.28 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.5, 152.2, 130.6, 128.2, 127.9, 125.3, 34.4, 11.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{12}N_3$ 174.1026; Found 174.1030.

1-[(5-Methyl-3-phenyl-1*H*-1,2,4-triazol-1-yl)methyl]-2,5-pyrrolidinedione (4)



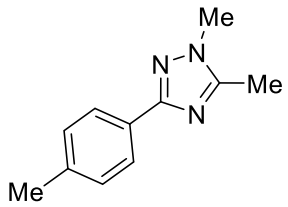
8.6 mg, 9% yield; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A colorless oil; **IR** ($CHCl_3$): 1723, 1524 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.4 Hz, 2H), 7.41-7.35 (m, 3H), 5.72 (s, 2H), 2.80 (s, 4H), 2.72 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 175.6, 161.7, 154.7, 130.5, 129.3, 128.4, 126.4, 48.4, 28.1, 12.1; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{14}H_{14}O_2N_4Na$ 293.1009; Found 293.1008.

Scalable synthesis of triazole 2aa (6.8 mmol scale)



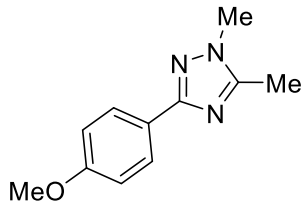
To a solution of hydrazones **1a** (1.0 g, 6.8 mmol) in dry MeCN (68 mL) were added NCS (1.4 g, 10 mmol) and BF_3•OEt_2 (2.6 mL, 20 mmol) in the dark. The reaction mixture was stirred at reflux in the dark. After being stirred for 19 h, the reaction mixture was basified with 1 M NaOH aq. (25 mL) and extracted with $CHCl_3$ (50 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Yamazen Smart Flash EPCLC-AI-580S using ULTRAPACK SI-40B) ($CHCl_3$ to $CHCl_3$/MeOH = 97/3) to afford the triazole **2aa** (993 mg, 80%) as a white solid.

1,5-Dimethyl-3-(4-methylphenyl)-1*H*-1,2,4-triazole (2ba)



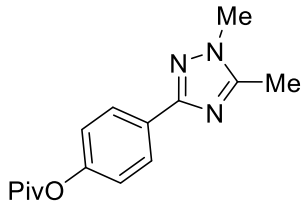
Hydrazone **1b** (37.4 mg, 0.23 mmol) was used. 42.4 mg, 98% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 204-205 ℃ (Hexane/EtOAc); **IR** (KBr): 1536 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 3.82 (s, 3H), 2.47 (s, 3H), 2.37 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.6, 152.7, 138.8, 129.2, 128.2, 125.9, 35.1, 21.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}N_3$ 188.1182; Found 188.1184.

1,5-Dimethyl-3-(4-methoxyphenyl)-1*H*-1,2,4-triazole (2ca)



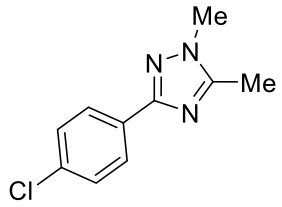
Hydrazone **1c** (50.0 mg, 0.28 mmol) was used. 39.9 mg, 68% yield; **Reaction time**: 24 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 117-119 ℃ (Hexane/EtOAc); **IR** (KBr): 1538 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 8.7 Hz, 2H), 6.93 (d, *J* = 8.7 Hz, 2H), 3.82 (s, 3H), 3.79 (s, 3H), 2.45 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.2, 160.1, 152.5, 127.3, 123.6, 113.7, 55.1, 35.0, 11.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}ON_3$ 204.1131; Found 204.1135.

2,2-Dimethylpropionic acid 4-(1,5-dimethyl-1*H*-1,2,4-triazol-3-yl)phenyl ester (2da)



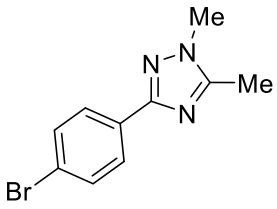
28.6 mg, 52% yield; **Reaction time**: 17.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 184-185 ℃ (Hexane/EtOAc); **IR** (KBr): 1736 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.7 Hz, 2H), 7.12 (d, *J* = 9.0 Hz, 2H), 3.82 (s, 3H), 2.47 (s, 3H), 1.36 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 176.8, 159.8, 152.8, 151.6, 128.5, 127.0, 121.5, 39.0, 35.1, 27.0, 11.8; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{19}O_2N_3Na$ 296.1370; Found 296.1366.

3-(4-Chlorophenyl)-1,5-dimethyl-1*H*-1,2,4-triazole (2ea)



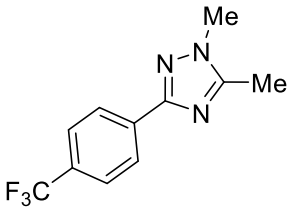
Hydrazone **1e** (41.5 mg, 0.23 mmol) was used. 40.7 mg, 85% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 176 ℃ (decomposed) (Hexane/EtOAc); **IR** (KBr): 1526 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.98 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.6, 153.0, 134.7, 129.6, 128.7, 127.3, 35.2, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_3{}^{35}Cl$ 208.0636; Found 208.0636.

3-(4-Bromophenyl)-1,5-dimethyl-1*H*-1,2,4-triazole (2fa)



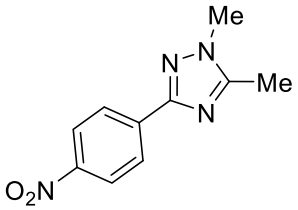
35.4 mg, 70% yield; **Reaction time**: 22 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow solid; **Mp**: 194-196 ℃ (Hexane/EtOAc); **IR** (KBr): 1524 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.6, 153.0, 131.6, 130.0, 127.5, 123.0, 35.2, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_3{}^{79}Br$ 252.0131; Found 252.0129.

1,5-Dimethyl-3-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole (2ga)



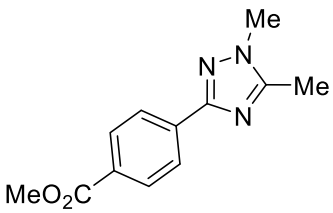
34.3 mg, 71% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow solid; **Mp**: 167-169 ℃ (EtOAc); **IR** (KBr): 1620 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.98 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.1, 153.2, 134.4, 131.2 (C-F, $^2J_{C\text{-}F}$ = 32.2 Hz), 130.7 (C-F, $^2J_{C\text{-}F}$ = 32.2 Hz), 130.3 (C-F, $^2J_{C\text{-}F}$ = 32.2 Hz), 129.9 (C-F, $^2J_{C\text{-}F}$ = 32.2 Hz), 129.5 (C-F, $^1J_{C\text{-}F}$ = 270.4 Hz), 126.2, 125.9 (C-F, $^1J_{C\text{-}F}$ = 270.4 Hz), 125.5 (C-F, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.42 (C-F, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.37 (C-F, $^3J_{C\text{-}F}$ = 3.8 Hz), 125.3 (C-F, $^3J_{C\text{-}F}$ = 3.8 Hz), 122.3 (C-F, $^1J_{C\text{-}F}$ = 270.4 Hz), 118.7 (C-F, $^1J_{C\text{-}F}$ = 270.4 Hz), 35.2, 11.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{11}N_3F_3$ 242.0900; Found 242.0904.

1,5-Dimethyl-3-(4-nitrolphenyl)-1*H*-1,2,4-triazole (2ha)



Hydrazone **1h** (468 mg, 2.42 mmol) was used. 373.9 mg, 71% yield; **Reaction time**: 22 h; Purification by Biotage Isolera One using Biotage SNAP KP-Sil 50g ($CHCl_3$ to $CHCl_3$/MeOH = 24/1); A white solid; **Mp**: 286 ℃ (decomposed) (Hexane/EtOAc); **IR** (KBr): 1602, 1509 cm^{-1}; **^{1}H NMR** (300 MHz, THF-d_8) δ: 8.02 (d, *J* = 9.0 Hz, 2H), 7.37 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 2.41 (s, 3H); **^{13}C NMR** (75 MHz, THF-d_8) δ: 160.0, 154.1, 135.0, 132.0, 129.4, 128.3, 35.4, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}O_2N_4$ 219.0877; Found 219.0877.

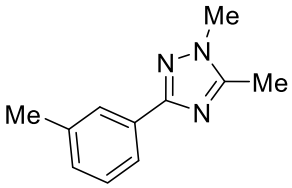
4-(1,5-Dimethyl-1*H*-1,2,4-triazol-3-yl)benzoic acid methyl ester (2ia)



30.5 mg, 66% yield; **Reaction time**: 16.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 20/1); A yellow solid; **Mp**: 190-192 ℃ (Hexane/EtOAc); **IR** (KBr): 1728 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.13 (d, *J* = 8.4 Hz, 2H), 8.09 (d, *J* = 8.7 Hz, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 2.50 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 166.8,

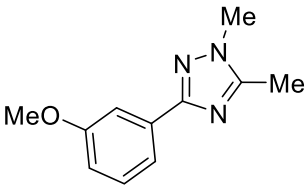
159.6, 153.2, 135.2, 130.2, 129.8, 125.8, 52.1, 35.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}O_2N_3$ 232.1081; Found 232.1081.

1,5-Dimethyl-3-(3-methylphenyl)-1*H*-1,2,4-triazole (2ja)



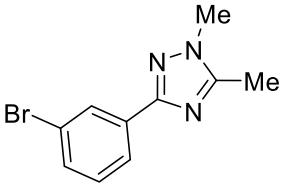
35.5 mg, 95% yield; **Reaction time**: 17.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 110-112 ℃ (Hexane/EtOAc); **IR** (KBr): 1529 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.88 (s, 1H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 3.83 (s, 3H), 2.48 (s, 3H), 2.39 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.6, 152.7, 138.1, 130.8, 129.7, 128.4, 126.6, 123.1, 35.1, 21.3, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}N_3$ 188.1182; Found 118.1182.

1,5-Dimethyl-3-(3-methoxyphenyl)-1*H*-1,2,4-triazole (2ka)



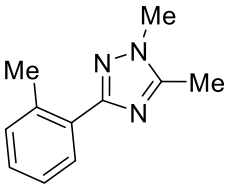
Hydrazone **1k** (50.0 mg, 0.28 mmol) was used. 48.5 mg, 85% yield; **Reaction time**: 21 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A white solid; **Mp**: 104-105 ℃ (Hexane/EtOAc); **IR** (KBr): 1614 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.1 Hz, 1H), 7.59 (s, 1H), 7.32 (t, *J* = 8.1 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 2.50 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.5, 159.8, 152.8, 132.4, 129.6, 118.6, 115.7, 110.5, 55.4, 35.2, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}ON_3$ 204.1131; Found 204.1135.

3-(3-Bromophenyl)-1,5-dimethyl-1*H*-1,2,4-triazole (2la)



31.9 mg, 63% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow solid; **Mp**: 97-99 ℃ (Hexane/EtOAc); **IR** (KBr): 1601 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.22 (s, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.28 (t, *J* = 8.1 Hz, 1H), 3.84 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.1, 153.0, 133.0, 131.8, 130.0, 129.0, 124.5, 122.7, 35.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_3{}^{79}Br$ 252.0131; Found 252.0131.

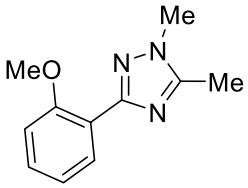
1,5-Dimethyl-3-(2-methylphenyl)-1*H*-1,2,4-triazole (2ma)



19.4 mg, 52% yield; **Reaction time**: 16 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1530 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.84 (d, *J* = 8.1 Hz, 1H), 7.26-7.22 (m, 3H), 3.83 (s, 3H), 2.59 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 161.2, 151.9, 136.7,

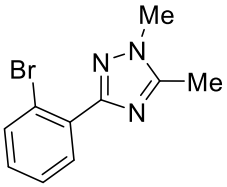
130.9, 130.4, 129.2, 128.4, 125.5, 35.1, 21.4, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}N_3$ 188.1182; Found 118.1180.

1,5-Dimethyl-3-(2-methoxyphenyl)-1*H*-1,2,4-triazole (2na)



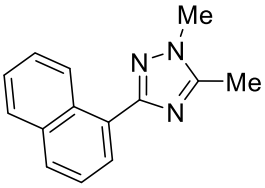
Hydrazone **1n** (50.0 mg, 0.28 mmol) was used. 31.4 mg, 55% yield; **Reaction time**: 19 h; Purification by preparative TLC ($CHCl_3$/MeOH = 10/1); A colorless oil; **IR** (neat): 1585 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 7.8 Hz, 1H), 7.33 (dd, *J* = 7.8, 5.1 Hz, 1H), 7.02-6.96 (m, 2H), 3.90 (s, 3H), 3.84 (s, 3H), 2.48 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 158.5, 156.8, 151.8, 130.3, 129.9, 120.3, 119.8, 111.2, 55.9, 35.3, 12.0; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{11}H_{13}ON_3Na$ 226.0951; Found 226.0951.

3-(2-Bromophenyl)-1,5-dimethyl-1*H*-1,2,4-triazole (2oa)



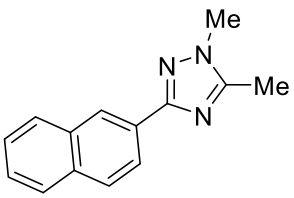
30.4 mg, 60% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1524 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 8.1 Hz, 1H), 3.87 (s, 3H), 2.51 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 159.9, 152.3, 133.6, 132.3, 131.4, 129.9, 127.1, 121.7, 35.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}N_3{}^{79}Br$ 252.0131; Found 252.0131.

1,5-Dimethyl-3-(1-naphthalenyl)-1*H*-1,2,4-triazole (2pa)



Hydrazone **1p** (50.0 mg, 0.25 mmol) was used. 45.8 mg, 81% yield; **Reaction time**: 14.5 h; Purification by preparative TLC (EtOAc); A white solid; **Mp**: 139-141 °C (Hexane/EtOAc); **IR** (KBr): 1530 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.99 (d, *J* = 8.7 Hz, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.59-7.47 (m, 3H), 3.91 (s, 3H), 2.55 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.9, 152.3, 133.9, 130.9, 129.5, 128.3, 128.2, 127.5, 126.6, 126.3, 125.7, 125.1, 35.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}N_3$ 224.1182; Found 224.1183.

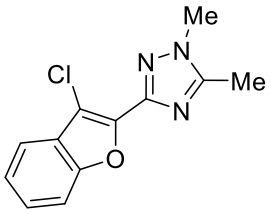
1,5-Dimethyl-3-(2-naphthalenyl)-1*H*-1,2,4-triazole (2qa)



Hydrazone **1q** (57.6 mg, 0.29 mmol) was used. 57.2 mg, 88% yield; **Reaction time**: 14.5 h; Purification by preparative TLC (EtOAc); A white solid; **Mp**: 140-142 °C (EtOAc); **IR** (KBr): 1530 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.56 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.93-7.83 (m, 3H), 7.50-7.47 (m, 2H), 3.89 (s, 3H), 2.54 (s, 3H); **^{13}C NMR** (75

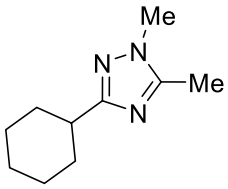
MHz, $CDCl_3$) δ: 160.3, 152.7, 133.5, 133.2, 128.3, 128.2, 128.0, 127.5, 126.1, 126.0, 125.1, 123.6, 35.4, 12.2; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{14}H_{14}N_3$ 224.1182; Found 224.1183.

3-(3-Chlorobenzofran-2-yl)-1,5-dimethyl-1*H*-1,2,4-triazole (2ra)



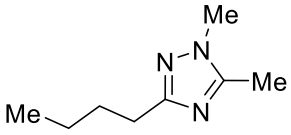
24.5 mg, 49% yield; **Reaction time**: 17.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A pale yellow solid; **Mp**: 159-161 ℃ (Hexane/EtOAc); **IR** (KBr): 1517 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.65 (d, *J* = 8.4 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.42-7.31 (m, 2H), 3.93 (s, 3H), 2.56 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 153.2, 153.1, 152.6, 142.5, 127.1, 126.2, 123.6, 119.3, 111.9, 110.6, 35.6, 11.9; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{12}H_{10}ON_3{}^{35}ClNa$ 270.0405; Found 270.0403.

3-Cyclohexyl-1,5-dimethyl-1*H*-1,2,4-triazole (2sa)



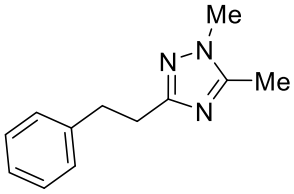
23.8 mg, 66% yield; **Reaction time**: 16.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 20/1); A colorless oil; **IR** (neat): 1509 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 3.75 (s, 3H), 2.66 (tt, *J* = 11.4, 3.3 Hz, 1H), 2.41 (s, 3H), 1.98 (d, *J* = 11.7 Hz, 2H), 1.81 (d, *J* = 12.3 Hz, 2H), 1.71, (d, *J* = 10.8 Hz, 1H), 1.54 (q, *J* = 12.6 Hz, 2H), 1.42-1.24 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 167.0, 151.8, 37.5, 34.8, 31.9, 26.1, 25.9, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{10}H_{18}N_3$ 180.1495; Found 180.1497.

3-Butyl-1,5-dimethyl-1*H*-1,2,4-triazole (2ta)



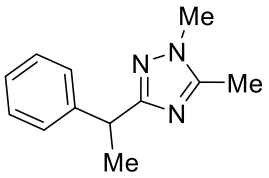
19.1 mg, 62% yield; **Reaction time**: 18 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1515 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 3.75 (s, 3H), 2.64 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.70 (quint, *J* = 7.8 Hz, 2H), 1.39 (sext, *J* = 7.2 Hz, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 163.1, 152.0, 34.7, 30.5, 27.8, 22.4, 13.7, 11.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_8H_{16}N_3$ 154.1339; Found 154.1341.

1,5-Dimethyl-3-(2-phenylethyl)-1*H*-1,2,4-triazole (2ua)



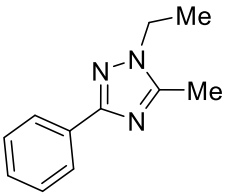
19.6 mg, 49% yield; **Reaction time**: 17.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1515 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.32-7.16 (m, 5H), 3.74 (s, 3H), 3.08-3.01 (m, 2H), 2.98-2.91 (m, 2H), 2.42 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 162.2, 152.2, 141.4, 128.3, 128.2, 125.9, 34.8, 34.6, 30.2, 11.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}N_3$ 202.1339; Found 202.1338.

1,5-Dimethyl-3-(1-phenylethyl)-1*H*-1,2,4-triazole (2va)



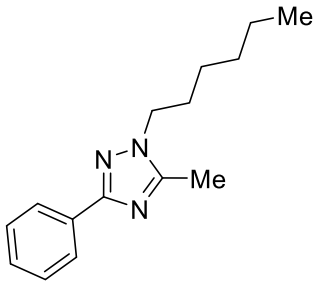
21.0 mg, 52% yield; **Reaction time**: 17.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1508 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 7.37-7.26 (m, 4H), 7.18 (t, *J* = 7.2 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 2.38 (s, 3H), 1.67 (d, *J* = 7.5Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 165.6, 152.2, 144.3, 128.4, 127.4, 126.3, 39.4, 34.9, 20.7, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}N_3$ 202.1339; Found 202.1338.

1-Ethyl-5-methyl-3-phenyl-1*H*-1,2,4-triazole (2wa)



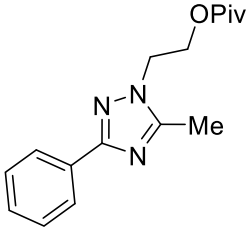
24.0 mg, 64% yield; **Reaction time**: 15.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1518 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 9.0 Hz, 2H), 7.43-7.34 (m, 3H), 4.14 (q, *J* = 9.0 Hz, 2H), 2.50 (s, 3H), 1.48 (t, *J* = 9.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 160.6, 151.9, 131.2, 128.8, 128.5, 126.1, 43.4, 15.1, 11.8; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}N_3$ 188.1182; Found 188.1177.

1-Hexyl-5-methyl-3-phenyl-1*H*-1,2,4-triazole (2xa)



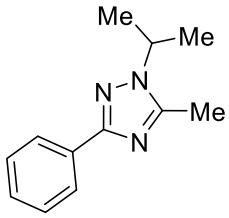
28.3 mg, 58% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1518 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.0 Hz, 2H), 7.42-7.34 (m, 3H), 4.06 (t, *J* = 7.0 Hz, 2H), 2.49 (s, 3H), 1.87 (quint, *J* = 7.0 Hz, 2H), 1.33 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 160.5, 152.3, 131.2, 128.8, 128.4, 126.1, 48.5, 31.3, 29.8, 26.2, 22.4, 13.9, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}N_3$ 244.1808; Found 244.1812.

2,2-Dimethylpropionic acid 2-(5-methyl-3-phenyl-1*H*-1,2,4-triazol-1-yl)ethyl ester (2ya)



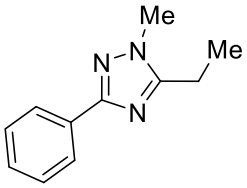
34.7 mg, 58% yield; **Reaction time**: 17 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1731, 1518 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.1 Hz, 2H), 7.45-7.37 (m, 3H), 4.47 (t, *J* = 5.4 Hz, 2H), 4.35 (t, *J* = 5.4 Hz, 2H), 2.53 (s, 3H), 1.14 (s, 9H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 178.1, 161.0, 153.2, 130.9, 129.0, 128.4, 126.0, 62.4, 47.0, 38.6, 27.0, 11.9; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{16}H_{21}O_2N_3Na$ 310.1526; Found 310.1523.

5-Methyl-1-(1-methylethyl)-3-phenyl-1*H*-1,2,4-triazole (2za)



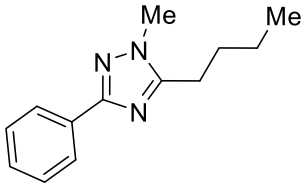
21.3 mg, 53% yield; **Reaction time**: 22 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1512 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.07 (d, *J* = 8.1 Hz, 2H), 7.44-7.31 (m, 3H), 4.45 (sept, *J* = 6.6 Hz, 1H), 2.48 (s, 3H), 1.52 (d, *J* = 6.6 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.3, 151.1, 131.5, 128.6, 128.4, 126.0, 50.0, 22.3, 11.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}N_3$ 202.1339; Found 202.1339.

5-Ethyl-1-methyl-3-phenyl-1*H*-1,2,4-triazole (2ab)



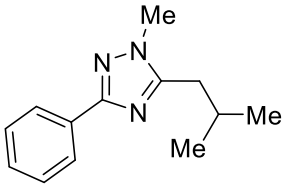
Propionitrile (4.0 mL) was used. 28.6 mg, 76% yield; **Reaction time**: 21 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1518 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.1 Hz, 2H), 7.44-7.33 (m, 3H), 3.84 (s, 3H), 2.80 (q, *J* = 7.5 Hz, 2H), 1.38 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 160.5, 157.5, 131.2, 128.8, 128.4, 126.1, 35.0, 19.4, 12.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{11}H_{14}N_3$ 188.1182; Found 188.1185.

5-Butyl-1-methyl-3-phenyl-1*H*-1,2,4-triazole (2ac)



Valeronitrile (4.0 mL) was used. 34.0 mg, 79% yield; **Reaction time**: 19.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1518 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.1 Hz, 2H), 7.44-7.35 (m, 3H), 3.83 (s, 3H), 2.76 (t, *J* = 7.8 Hz, 2H), 1.76 (quint, *J* = 7.8 Hz, 2H), 1.44 (sext, *J* = 7.5 Hz, 2H), 0.96 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.5, 156.7, 131.1, 128.8, 128.4, 126.0, 35.0, 29.8, 25.7, 22.4, 13.7; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}N_3$ 216.1495; Found 216.1495.

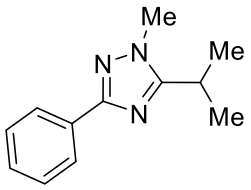
1-Methyl-5-(2-methylpropyl)- 3-phenyl-1*H*-1,2,4-triazole (2ad)



Isovaleronitrile (4.0 mL) was used. 31.7 mg, 74% yield; **Reaction time**: 18.5 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1518 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 7.8 Hz, 2H), 7.45-7.36 (m, 3H), 3.84 (s, 3H), 2.65 (d, *J* = 7.5 Hz, 2H), 2.19 (sept, *J* = 6.9 Hz, 1H), 1.00 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.5, 156.0, 131.1, 128.8, 128.4, 126.0, 35.2, 34.7, 28.3, 22.3; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{13}H_{18}N_3$ 216.1495; Found 216.1495.

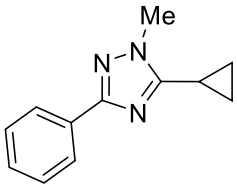
1-Methyl-5-(1-methylethyl)- 3-phenyl-1*H*-1,2,4-triazole (2ae)

Isobutyronitrile (4.0 mL) was used. 33.1 mg, 82% yield; **Reaction time**: 15.5 h; Purification by



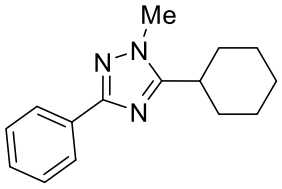
preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1513 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.1 Hz, 2H), 7.44-7.32 (m, 3H), 3.85 (s, 3H), 3.09 (sept, *J* = 6.9 Hz, 1H), 1.39 (d, *J* = 6.9 Hz, 6H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 161.1, 160.5, 131.3, 128.7, 128.4, 126.2, 34.9, 25.8, 20.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{16}N_3$ 202.1339; Found 202.1339.

5-Cyclopropyl-1-methyl-3-phenyl-1*H*-1,2,4-triazole (2af)



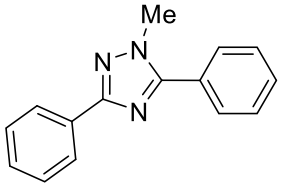
Cyclopropyl cyanide (4.0 mL) was used. 29.5 mg, 74% yield; **Reaction time**: 16 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1540 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.02 (d, *J* = 8.1 Hz, 2H), 7.42-7.34 (m, 3H), 3.92 (s, 3H), 1.89-1.80 (m, 1H), 1.18-1.04 (m, 4H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.3, 158.0, 131.2, 128.7, 128.4, 126.1, 34.8, 7.9, 6.2; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{12}H_{14}N_3$ 200.1182; Found 200.1184.

5-Cyclohexyl-1-methyl-3-phenyl-1*H*-1,2,4-triazole (2ag)



Cyclohexanecarbonitrile (4.0 mL) was used. 34.7 mg, 72% yield; **Reaction time**: 16 h; Purification by preparative TLC ($CHCl_3$/MeOH = 50/1); A yellow oil; **IR** (neat): 1500 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.06 (d, *J* = 8.4 Hz, 2H), 7.43-7.32 (m, 3H), 3.85 (s, 3H), 2.78-2.68 (tt, *J* = 11.7, 3.3 Hz, 1H), 1.94-1.89 (m, 4H), 1.80-1.67 (m, 3H), 1.43-1.31 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.5, 160.3, 131.3, 128.7, 128.4, 126.1, 35.4, 34.9, 31.0, 26.0, 25.5; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}N_3$ 242.1652; Found 242.1651.

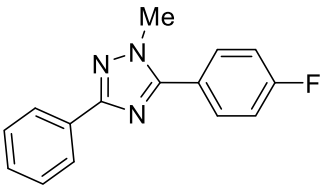
3,5-Diphenyl-1-methyl-1*H*-1,2,4-triazole (2ah)



Benzonitrile (4.0 mL) was used. 41.7 mg, 89% yield; **Reaction time**: 16 h; Purification by Biotage Isolera One using Biotage SNAP KP-Sil 25g (Hexane/EtOAc = 17/1 to 5/2); A white solid; **Mp**: 80-81 °C (Hexane/Et_2O); **IR** (KBr): 1473 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.51-7.50 (m, 3H), 7.45-7.38 (m, 3H), 3.99 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 161.1, 155.6, 131.0, 130.0, 129.0, 128.8, 128.7, 128.5, 128.0, 126.3, 36.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{14}N_3$ 236.1182; Found 236.1182.

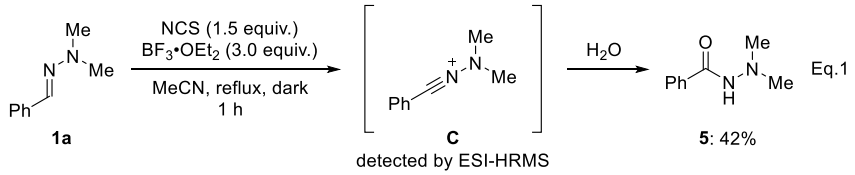
5-(4-Fluorophenyl)-1-methyl-3-phenyl-1*H*-1,2,4-triazole (2ai)

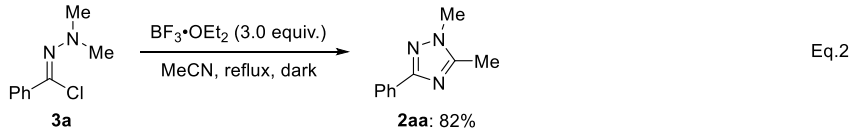
4-Fluorobenzonitrile (4.0 mL) was used. 32.2 mg, 64% yield; **Reaction time**: 19.5 h; Purification by

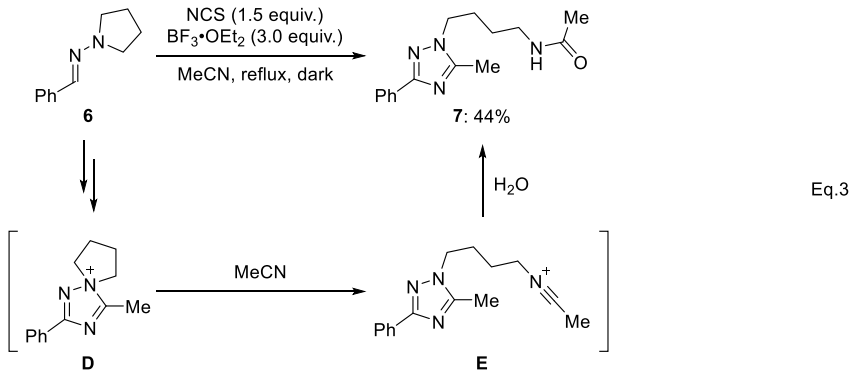


Biotage Isolera One using Biotage SNAP KP-Sil 100g (Hexane/EtOAc = 17/1 to 3/2); A yellow solid; **Mp**: 107-111 ℃ (Hexane); **IR** (KBr): 1608 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 8.4 Hz, 2H), 7.72 (dd, *J* = 9.0, 5.4 Hz, 2H), 7.47-7.39 (m, 3H), 7.21 (t, *J* = 8.4 Hz, 2H), 3.99 (s, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 165.3 (C-F, $^1J_{C\text{-}F}$ = 249.5 Hz), 162.0 (C-F, $^1J_{C\text{-}F}$ = 249.5 Hz), 161.1, 154.7, 130.8 (C-F, $^3J_{C\text{-}F}$ = 8.6 Hz), 130.7 (C-F, $^3J_{C\text{-}F}$ = 8.6 Hz), 129.1, 128.5, 126.2, 124.2 (C-F, $^4J_{C\text{-}F}$ = 3.5 Hz), 124.1 (C-F, $^4J_{C\text{-}F}$ = 3.5 Hz), 116.2 (C-F, $^2J_{C\text{-}F}$ = 21.8 Hz), 115.9 (C-F, $^2J_{C\text{-}F}$ = 21.8 Hz), 36.9; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{15}H_{13}N_3F$ 254.1088; Found 254.1088.

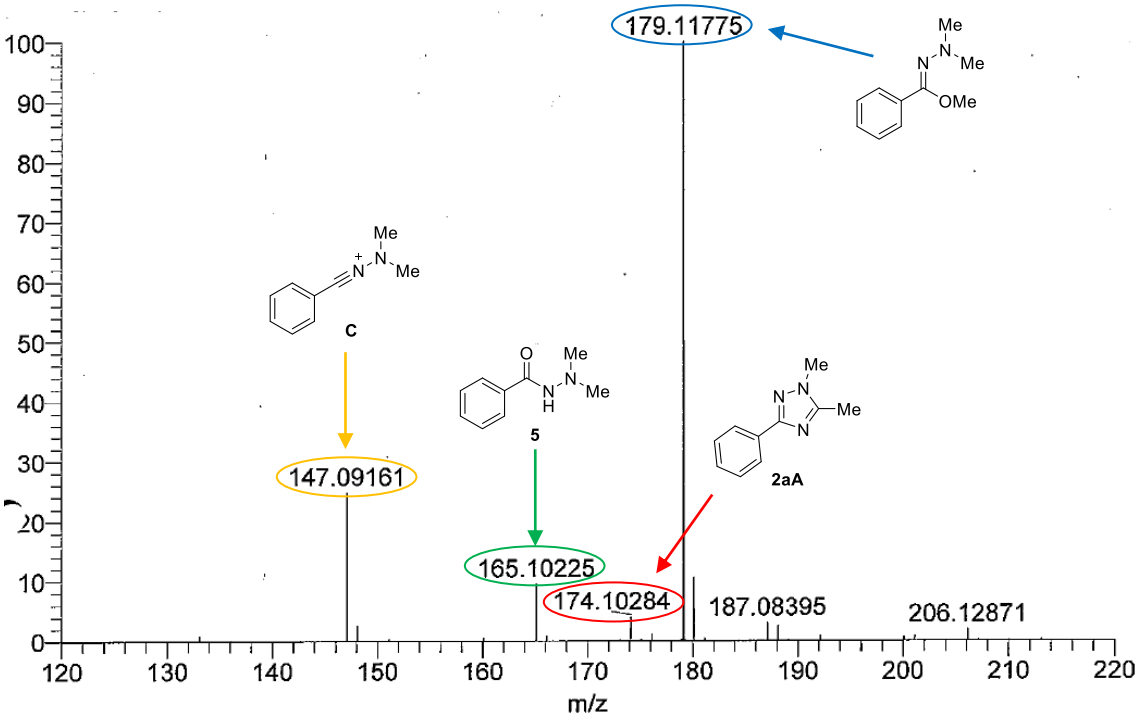
2.8 Control experiments







Eq. 1

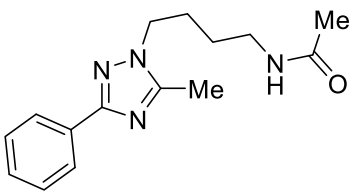


To a solution of hydrazone **1a** (30 mg, 0.20 mmol) in dry CH_3CN (4.0 mL) were added NCS (40 mg, 0.30 mmol) and BF_3•OEt_2 (76 μL, 0.60 mmol) in the dark. The mixture was stirred at reflux for 1 h. The ESI (+)-MS spectrum of reaction mixture showed a peak of m/z 147.09161 which indicated the Intermediate **C**. The reaction mixture was basified with 1 M NaOH aq. (4.0 mL) and extracted with $CHCl_3$ (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by preparative TLC ($CHCl_3$/MeOH = 49/1) or flash column chromatography to afford the hydrazide **5** (13.9 mg, 42%) as a pale yellow solid. The spectra data matched those previously reported in the literature[4].

Eq. 2

To a solution of hydrazonoyl chloride **3a**[5] (37 mg, 0.20 mmol) in dry MeCN (4.0 mL) was added BF_3•OEt_2 (76 μL, 0.60 mmol) in the dark. The reaction mixture was stirred at reflux in the dark. After being stirred for 17 h, the reaction mixture was basified with 1 M NaOH aq. (4.0 mL) and extracted with $CHCl_3$ (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by preparative TLC ($CHCl_3$/MeOH = 50/1) to afford the triazole **2aa** (28.3 mg, 82%).

Eq. 3; *N*-[4-(5-Methyl-3-phenyl-1*H*-1,2,4-triazol-1-yl)butyl]acetamide (7)

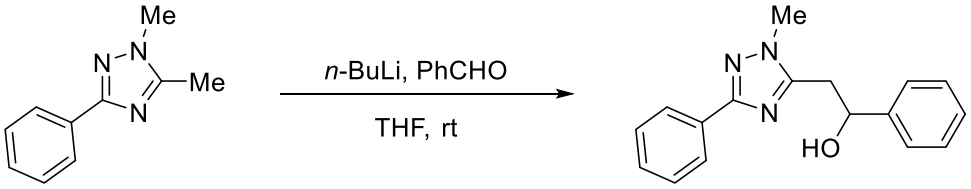


To a solution of hydrazone **6** (35 mg, 0.20 mmol) in dry MeCN (4.0 mL) were added NCS (40 mg, 0.30 mmol), BF_3•OEt_2 (76 μL, 0.60 mmol) in the dark. The reaction mixture was stirred at reflux in the dark. After being stirred for 18 h, the reaction mixture was

basified with 1 M NaOH aq. (4.0 mL) and extracted with $CHCl_3$ (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by preparative TLC ($CHCl_3$/MeOH = 50/1) to afford the triazole **7** (23.7 mg, 44%) as a yellow oil; **IR** (neat): 3287, 1655, 1553 cm^{-1}; **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 8.04 (d, *J* = 8.0 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 1H), 5.77 (br s, 1H), 4.12, (t, *J* = 7.0 Hz, 2H), 3.28 (q, *J* = 6.5 Hz, 2H), 2.50 (s, 3H), 1.96 (s, 3H), 1.92 (quint, *J* = 7.5 Hz, 2H), 1.56 (quint, *J* = 7.5 Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ: 170.2, 160.6, 152.5, 131.0, 129.0, 128.5, 126.0, 47.7, 38.9, 27.1, 26.4, 23.3, 12.0; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}N_4Na$ 295.1529; Found 295.1529.

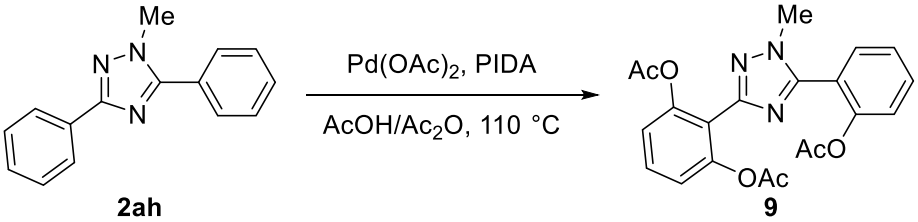
2.9 Experimental procedure for the transformation of triazoles 2

α,3-Diphenyl-1-methyl-1*H*-1,2,4-triazole-5-ethanol (8)



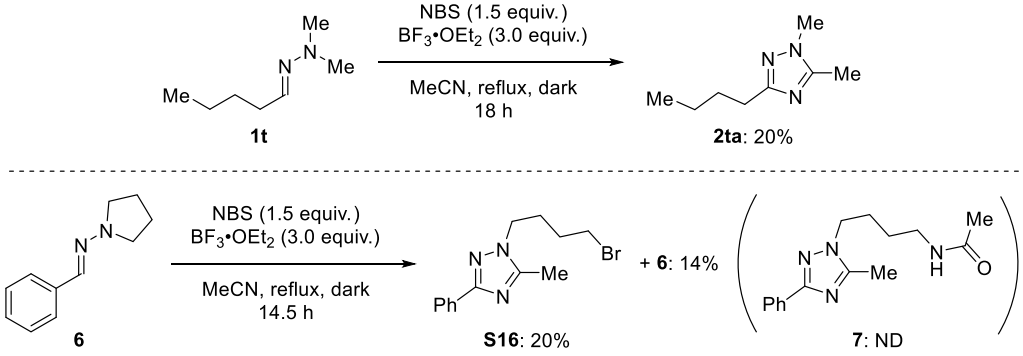
To a solution of triazole 2**aa** (35 mg, 0.20 mmol) in dry THF (2.0 mL) was slowly added *n*-BuLi in hexane (1.6 M, 188 μL, 0.30 mmol) at room temperature under argon atmosphere. The reaction mixture was stirred at the same temperature for 1 h. Subsequently, benzaldehyde (30 μL, 0.30 mmol) was slowly added at the same temperature. The reaction mixture was stirred for 2.5 h. The reaction mixture was quenched with sat. NH_4Cl aq. (4.0 mL) and extracted with Et_2O (10 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Biotage Isolera One using Biotage SNAP KP-Sil 25g) (Hexane/EtOAc = 7/1 to 1/19) to afford the alcohol **8** (31.8 mg, 57%) as a white solid; **Mp**: 161 °C (decomposed) (Hexane/EtOAc); **IR** (KBr): 3152, 1492 cm^{-1}; **^{1}H NMR** (300 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.1 Hz, 2H), 7.45-7.27 (m, 8H), 5.23 (t, *J* = 6.6 Hz, 1H), 4.89 (br s, 1H), 3.64 (s, 3H), 3.06 (d, *J* = 6.6 Hz, 2H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ: 160.4, 154.0, 142.8, 130.6, 129.1, 128.6, 128.5, 127.8, 126.1, 125.5, 71.6, 35.5, 35.0; **HRMS (ESI)** m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}ON_3$ 280.1444; Found 280.1444.

2-[5-(2-Acetoxyphenyl)-1-methyl-1*H*-1,2,4-triazol-3-yl]-1,3-benzenediol 1,3-diacetate (9)



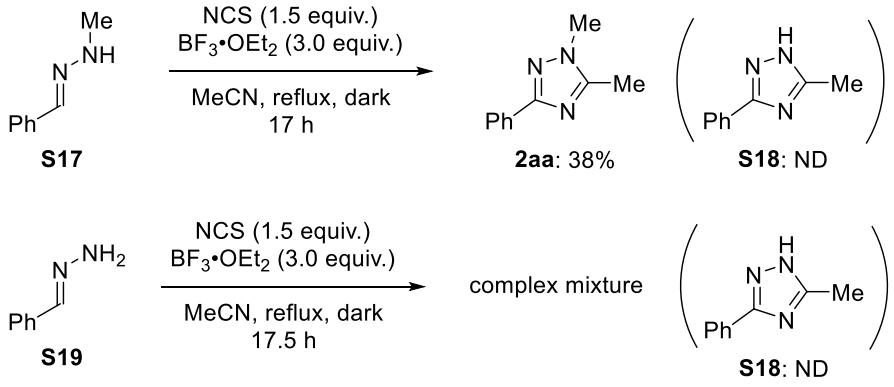
To a solution of triazole **2ah** (47 mg, 0.20 mmol) in AcOH (2.0 mL) and Ac_2O (2.0 mL) were added $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), PIDA (644 mg, 2.0 mmol). The reaction mixture was stirred at 110 °C. After being stirred for 2 h, the reaction mixture was poured into sat. $NaHCO_3$ aq. (20 mL) and extracted with EtOAc (20 mL × 2). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (Biotage Isolera One using Biotage SNAP KP-Sil 25g) (Hexane/EtOAc = 7/1 to 1/16) to afford the triacetoxylated triazole **9** (44.3 mg, 54%) as a yellow oil; **IR** (neat): 1769, 1462 cm^{-1}; **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 7.56 (t, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 1H), 7.08 (t, *J* = 8.4 Hz, 2H), 3.83 (s, 3H), 2.25 (s, 6H), 2.12 (s, 3H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ: 169.8, 169.1, 155.0, 151.0, 149.8, 149.0, 131.6, 130.7, 129.6, 126.1, 123.4, 121.8, 121.5, 118.2, 36.4, 21.1, 20.6; **HRMS (ESI)** m/z: $[M + Na]^+$ Calcd for $C_{21}H_{19}O_6N_3Na$ 432.1166; Found 432.1162.

2.10 Unsuccess results utilizing NBS instead of NCS

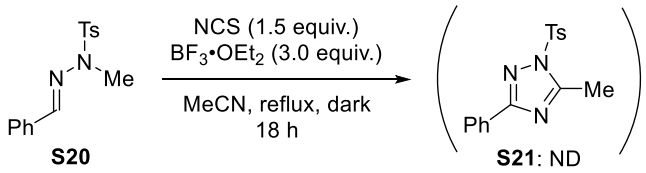


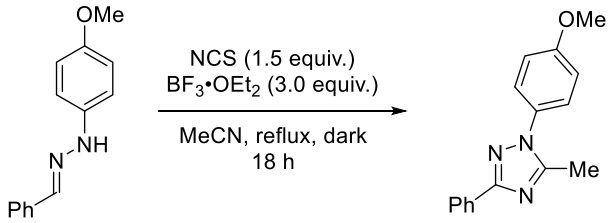
The reaction of *N*,*N*-dimethylhydrazone **1t** with NBS under optimized conditions gave triazole **2ta** in 20% yield. The use of hydrazone **6** with NBS led to the formation of alkyl-tethered triazole **S16** with bromo group in 20% yield.

2.11 Substituent effects on nitrogen atom



The reaction of *N*-monomethyl hydrazone **S17** under optimized conditions gave triazole **2aa** in 38% yield with no formation of 5-methyl-3-phenyl-1*H*-1,2,4-triazole **S18**. Additionally, the use of simple hydrazone **S19** led to the complex mixture.





The reaction of *N*-methyl-*N*-tosyl hydrazone **S20** under optimized conditions did not give triazole **S21**. Moreover, the use of *N*-(4-methoxyphenyl) hydrazone **S22** led to the formation of triazole **S23**[6] in 3% yield.

3. References

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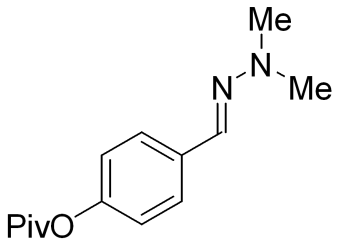
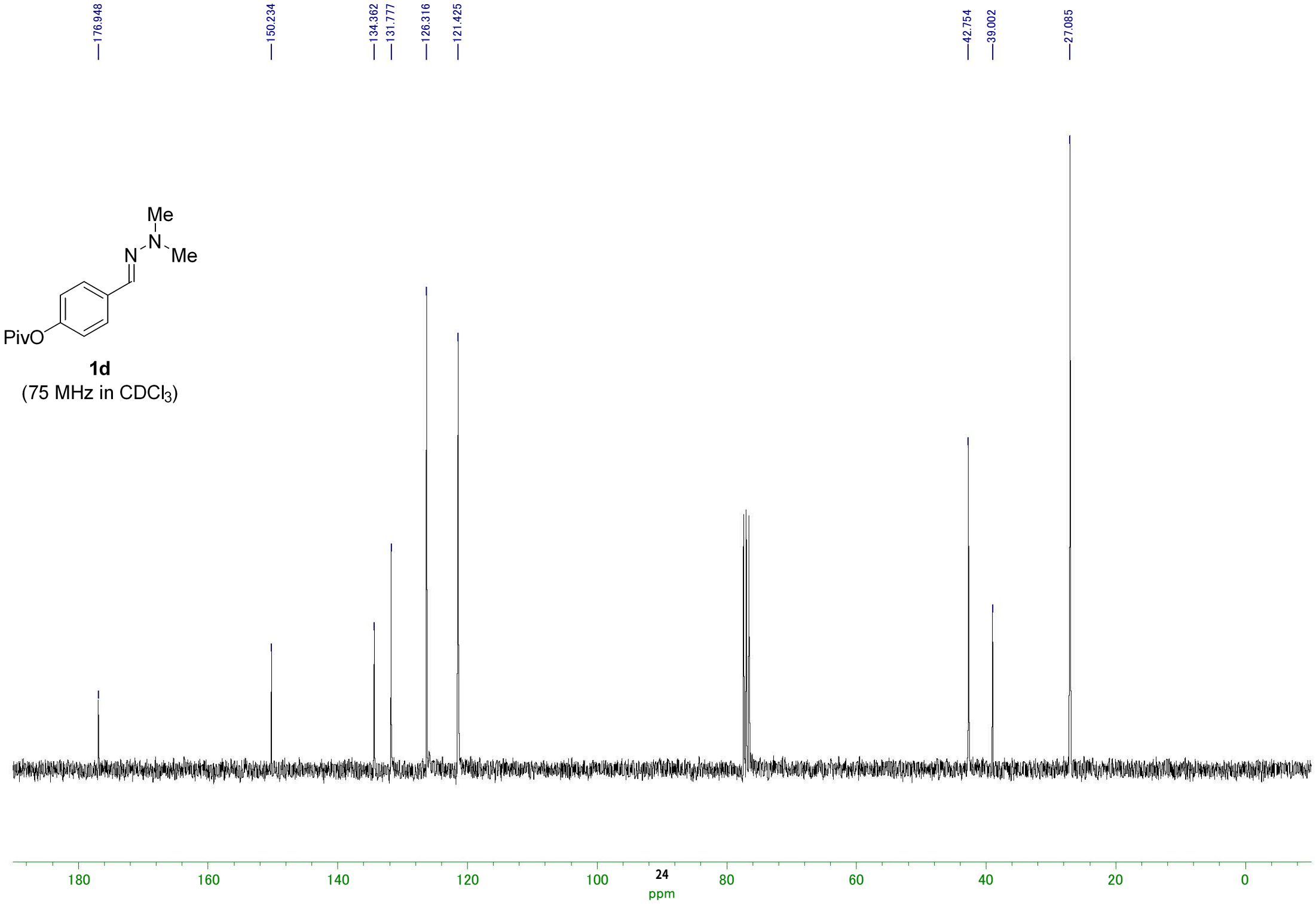
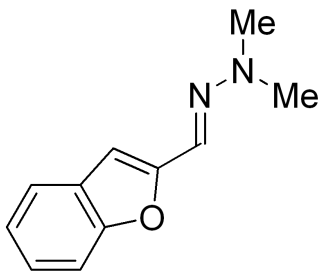


1d

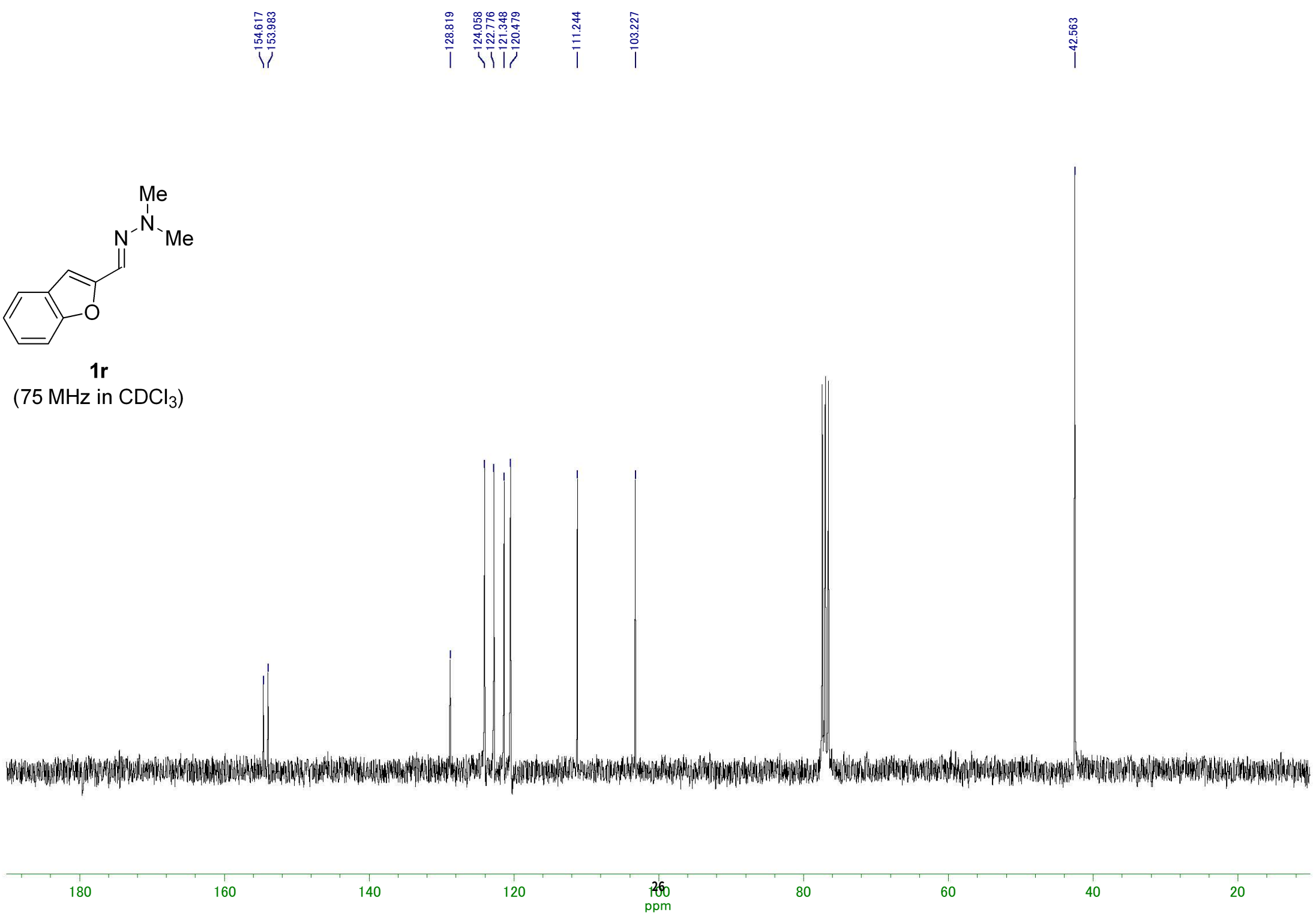
(300 MHz in $CDCl_3$)


176.948
150.234
134.362
131.777
126.316
121.425
42.754
39.002
27.085
Me
N
N
Me
PivO
1d
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



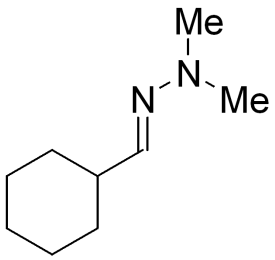
1r

(300 MHz in $CDCl_3$)



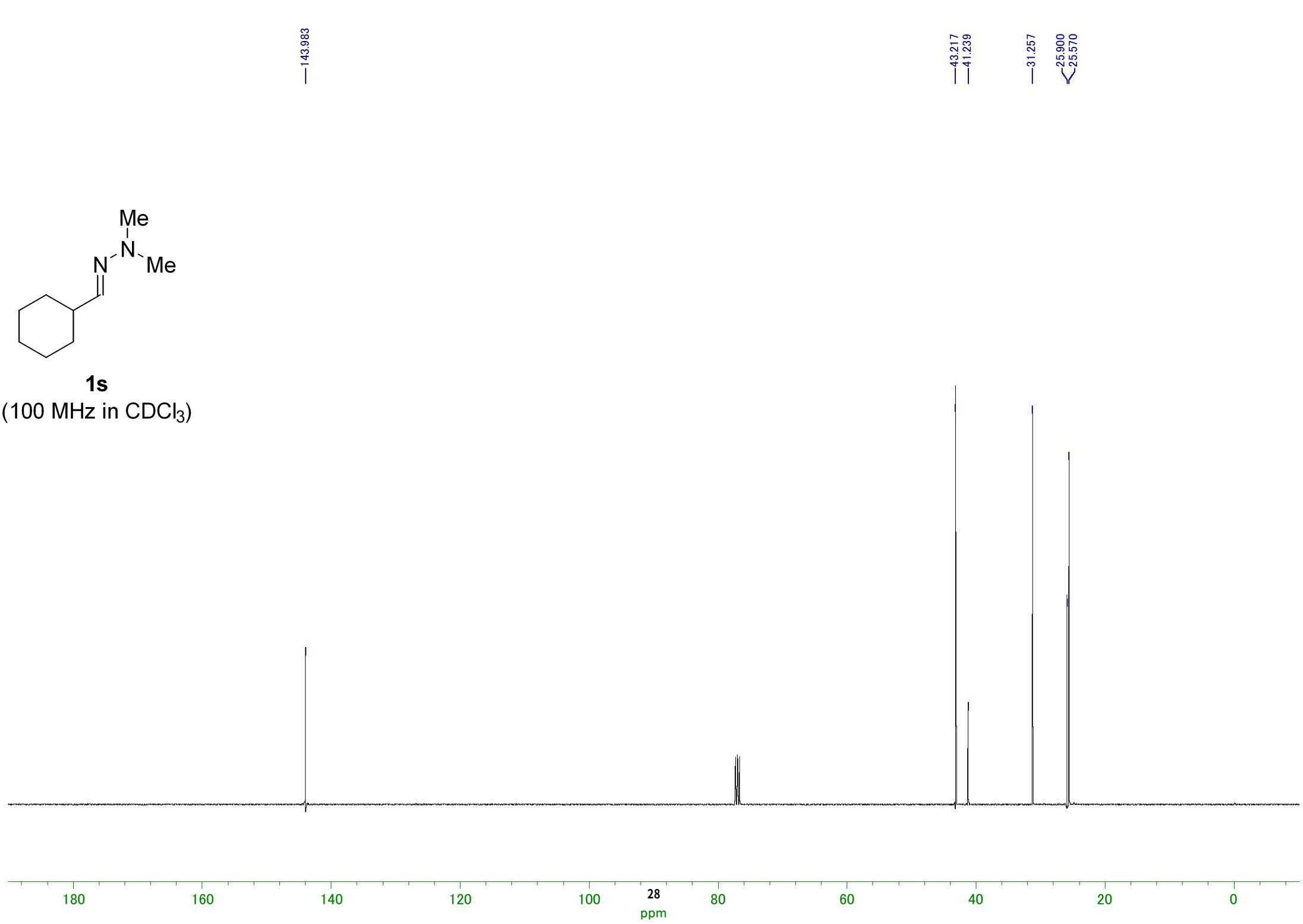
1r

(75 MHz in $CDCl_3$)



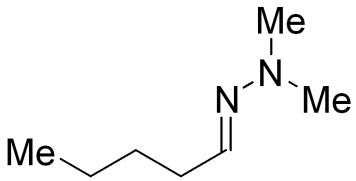
1s

(400 MHz in $CDCl_3$)



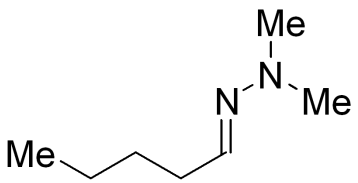
1s

(100 MHz in $CDCl_3$)



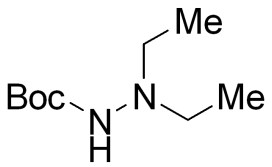
1t

(400 MHz in $CDCl_3$)

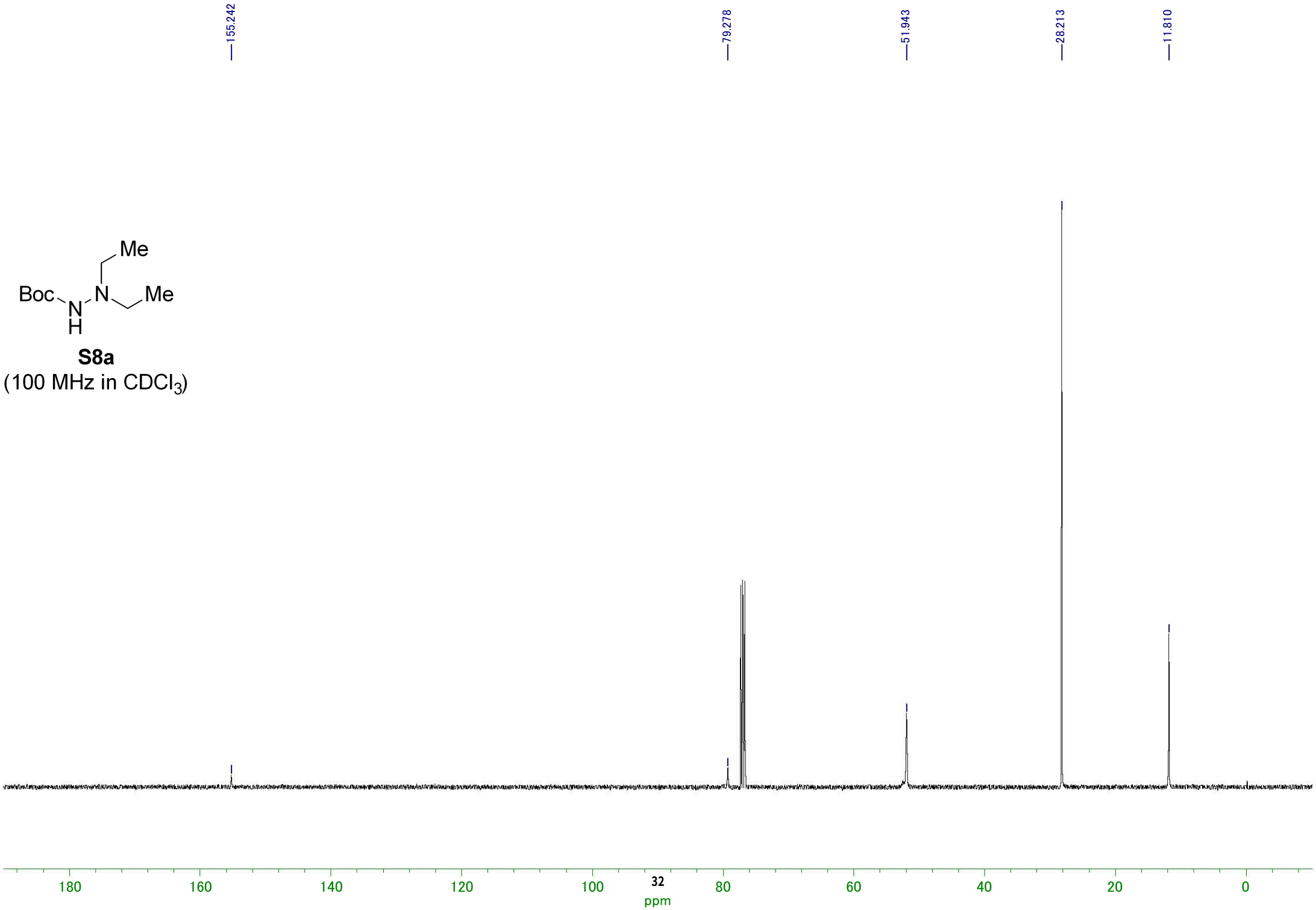


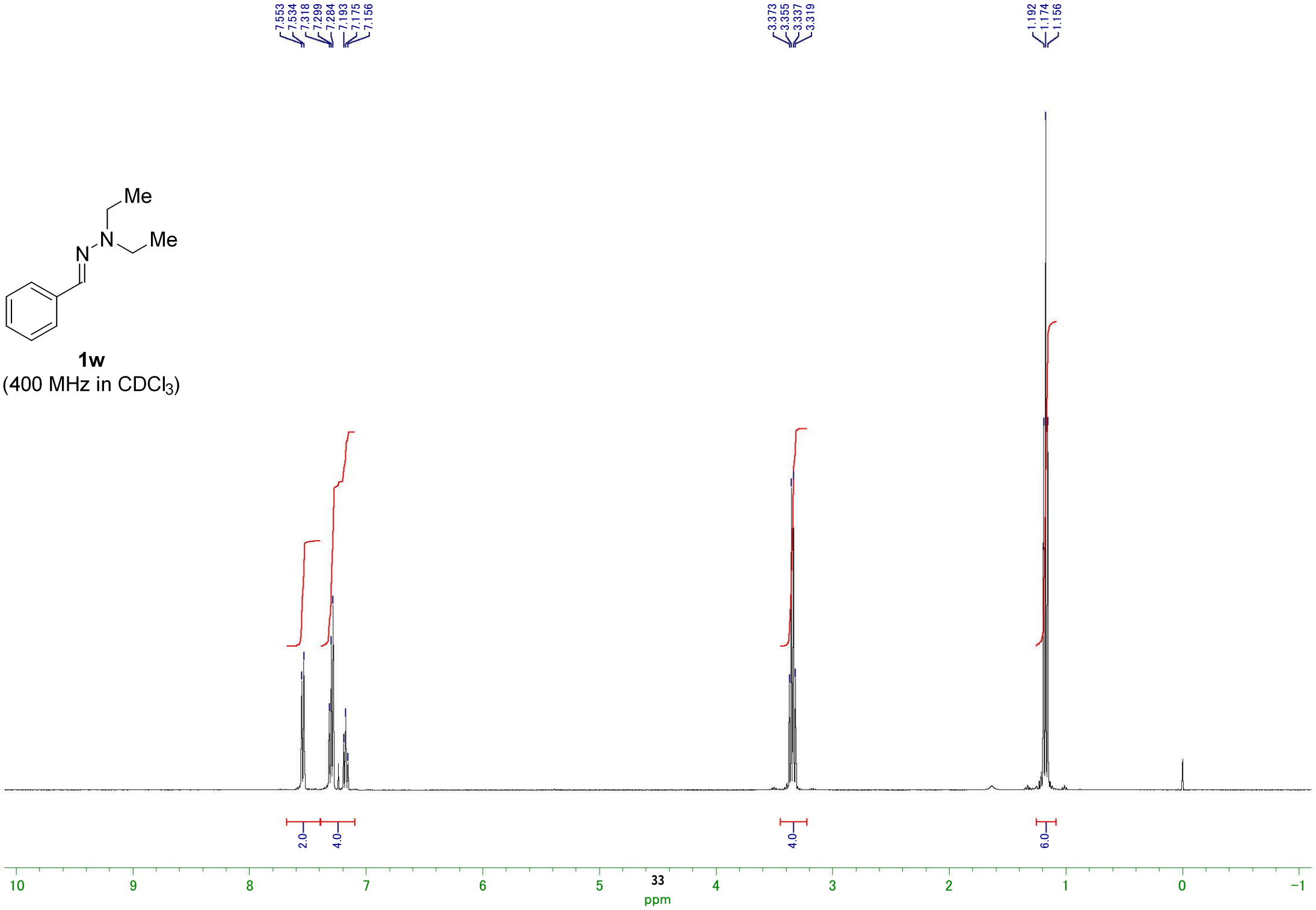
1t

(100 MHz in $CDCl_3$)

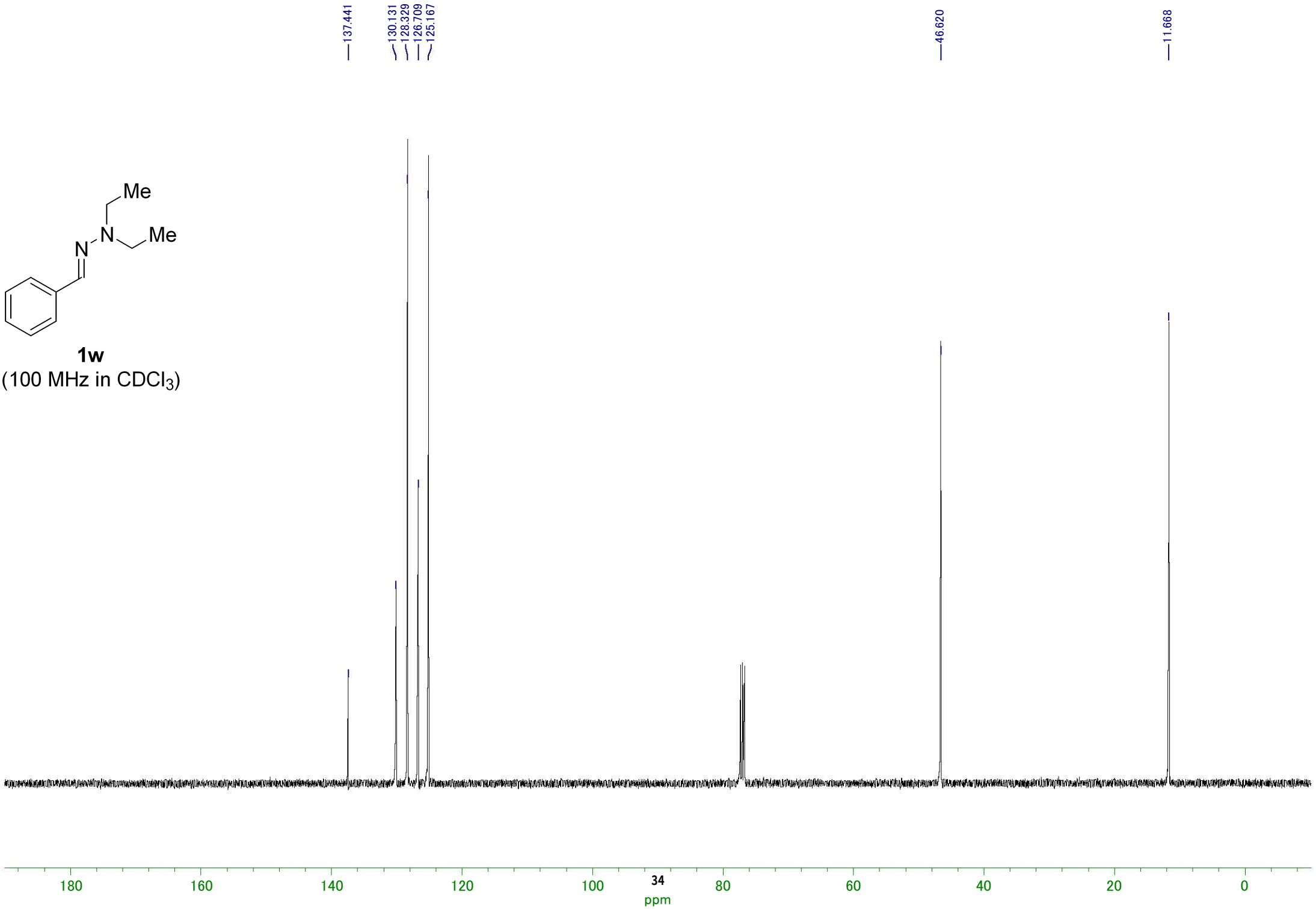


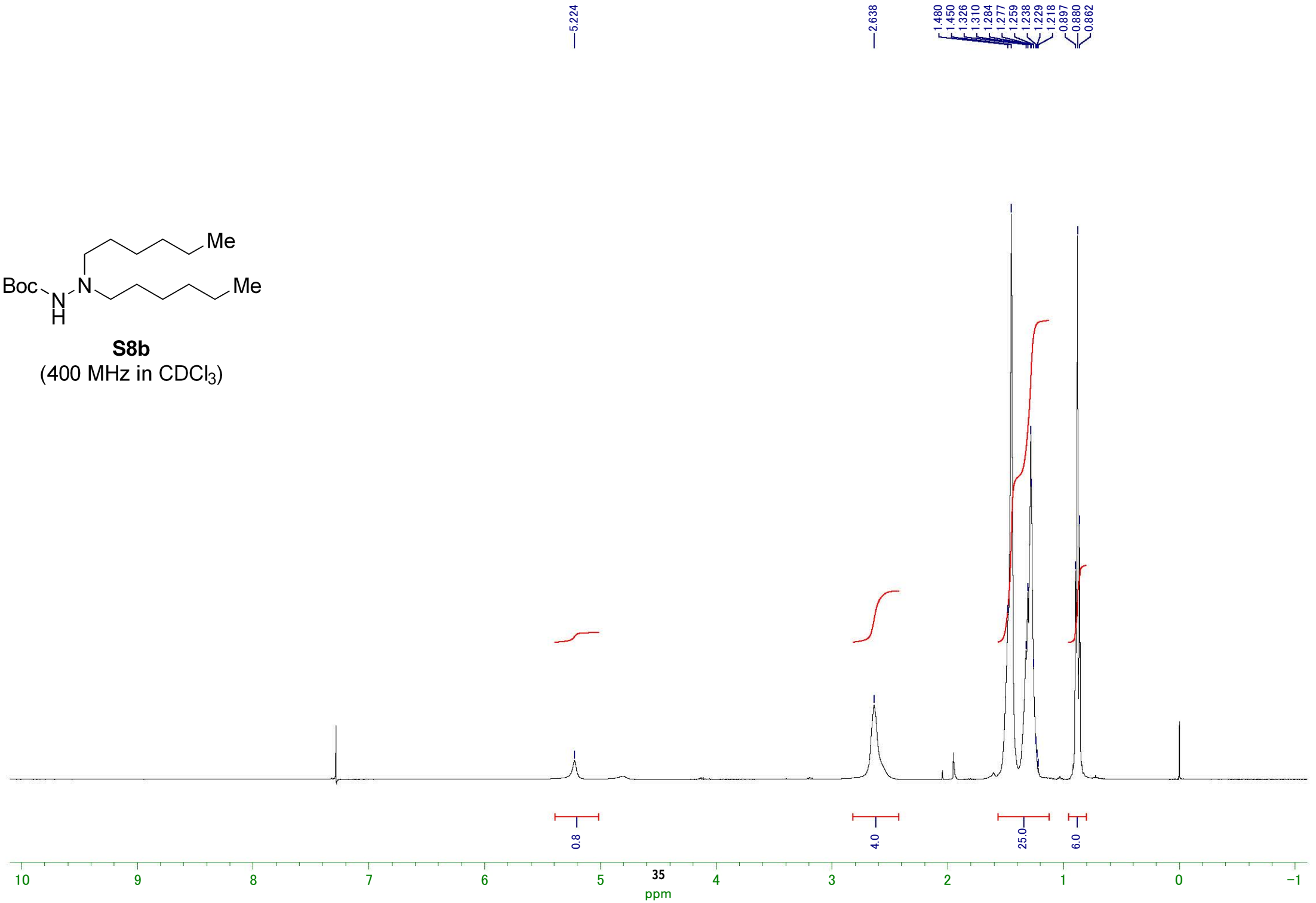
S8a
(400 MHz in $CDCl_3$)


155.242
79.278
51.943
28.213
11.810
Me
Boc
N
N
Me
H
S8a
(100 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



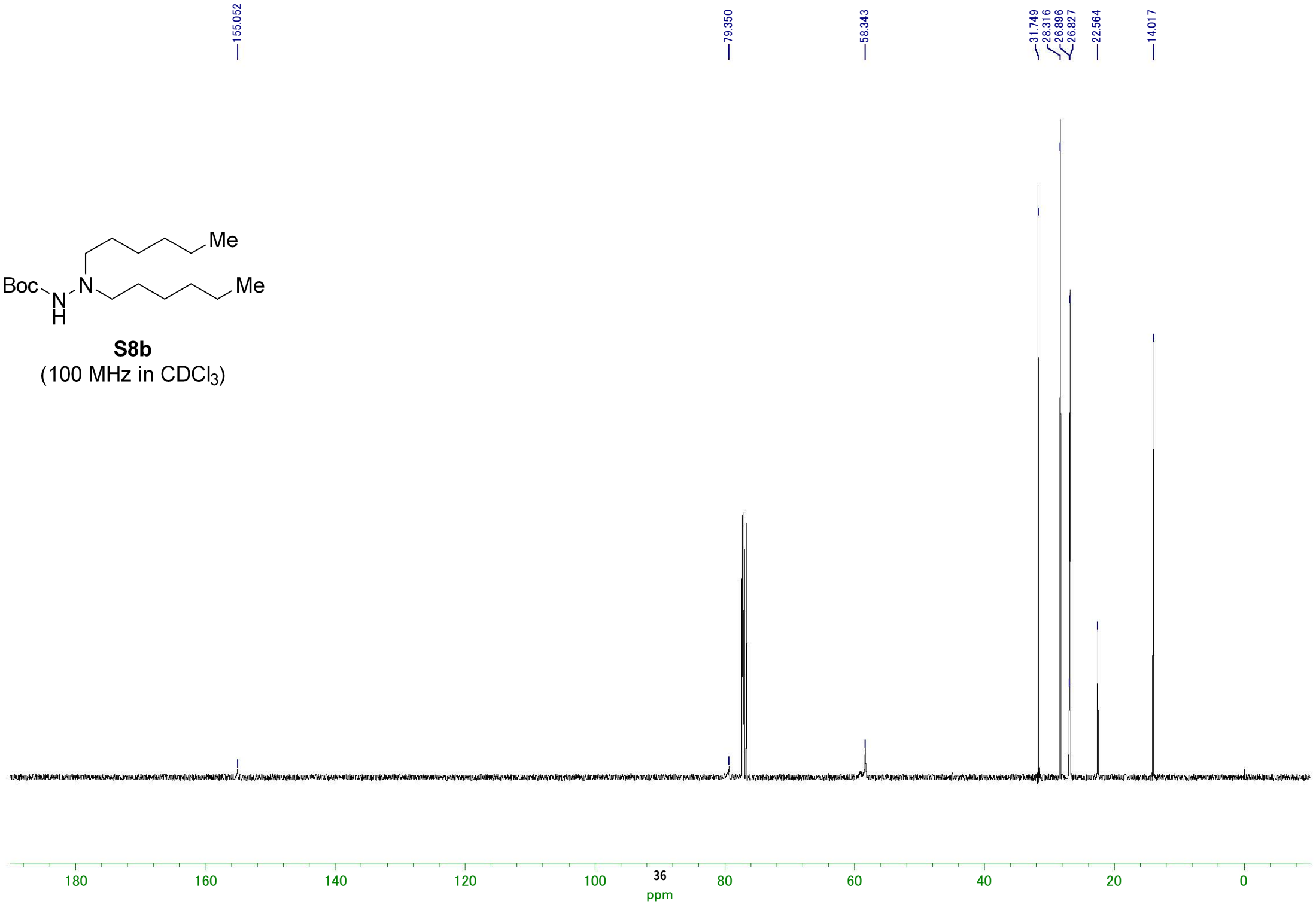
1w
(400 MHz in $CDCl_3$)


137.441
130.131
128.329
126.709
125.167
46.620
11.668
Me
N
N
Me
1w
(100 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



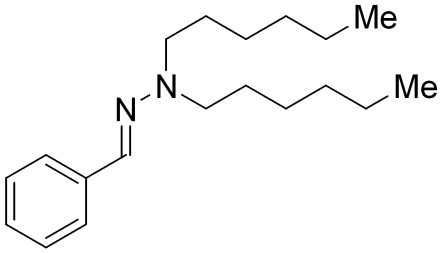
S8b

(400 MHz in $CDCl_3$)

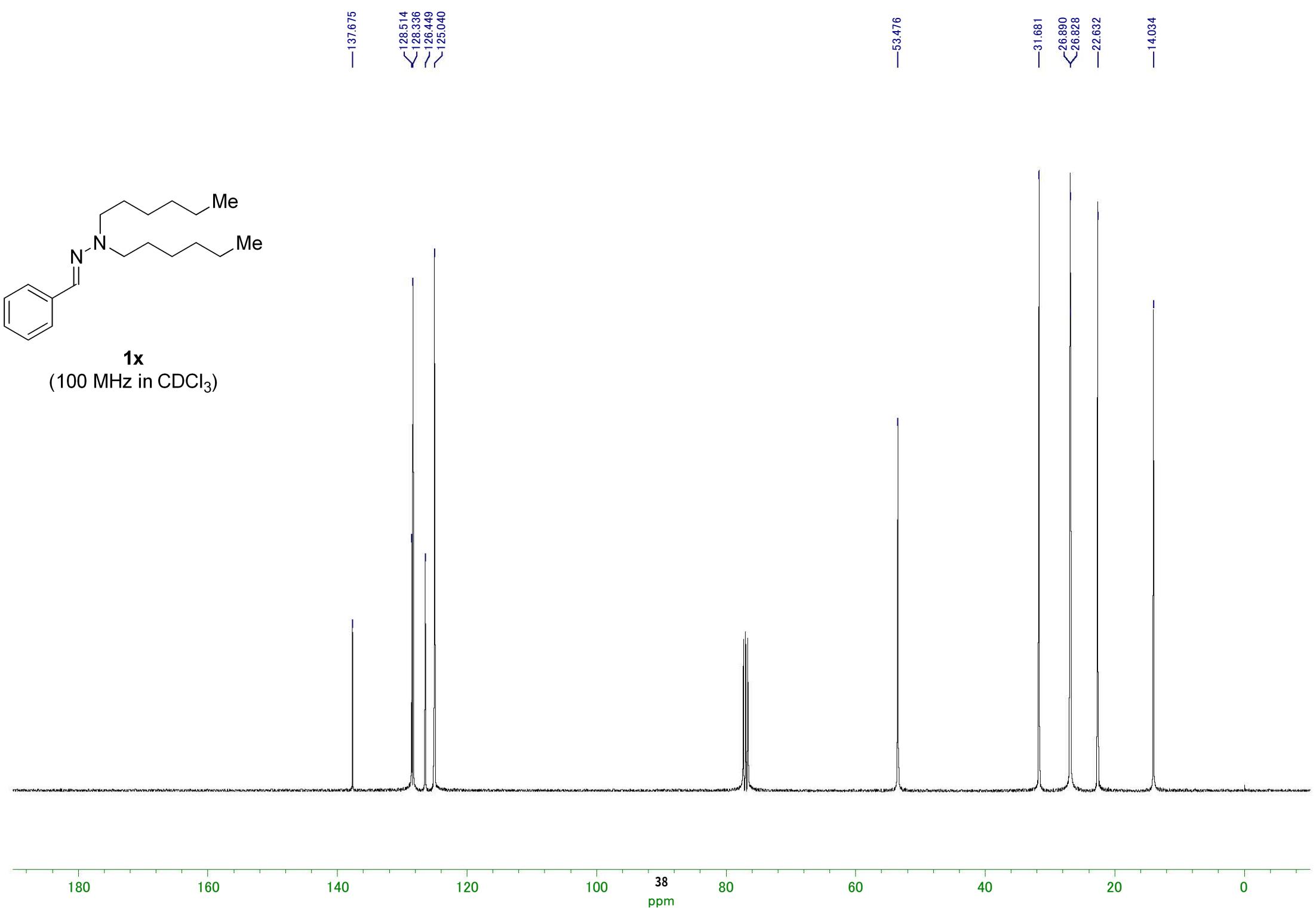


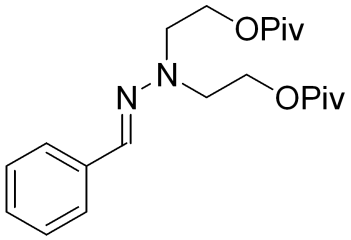
S8b

(100 MHz in $CDCl_3$)

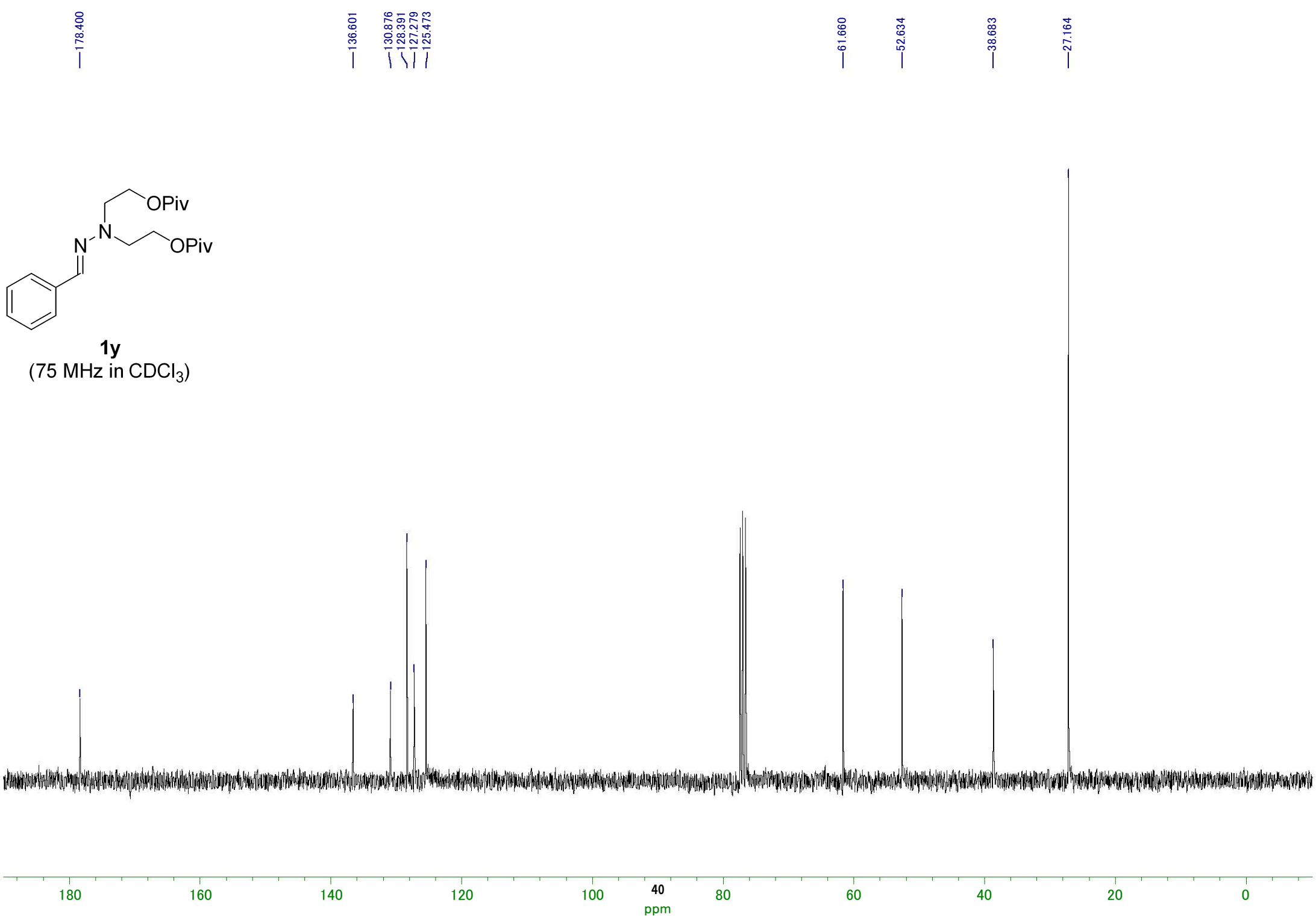


1x
(400 MHz in $CDCl_3$)

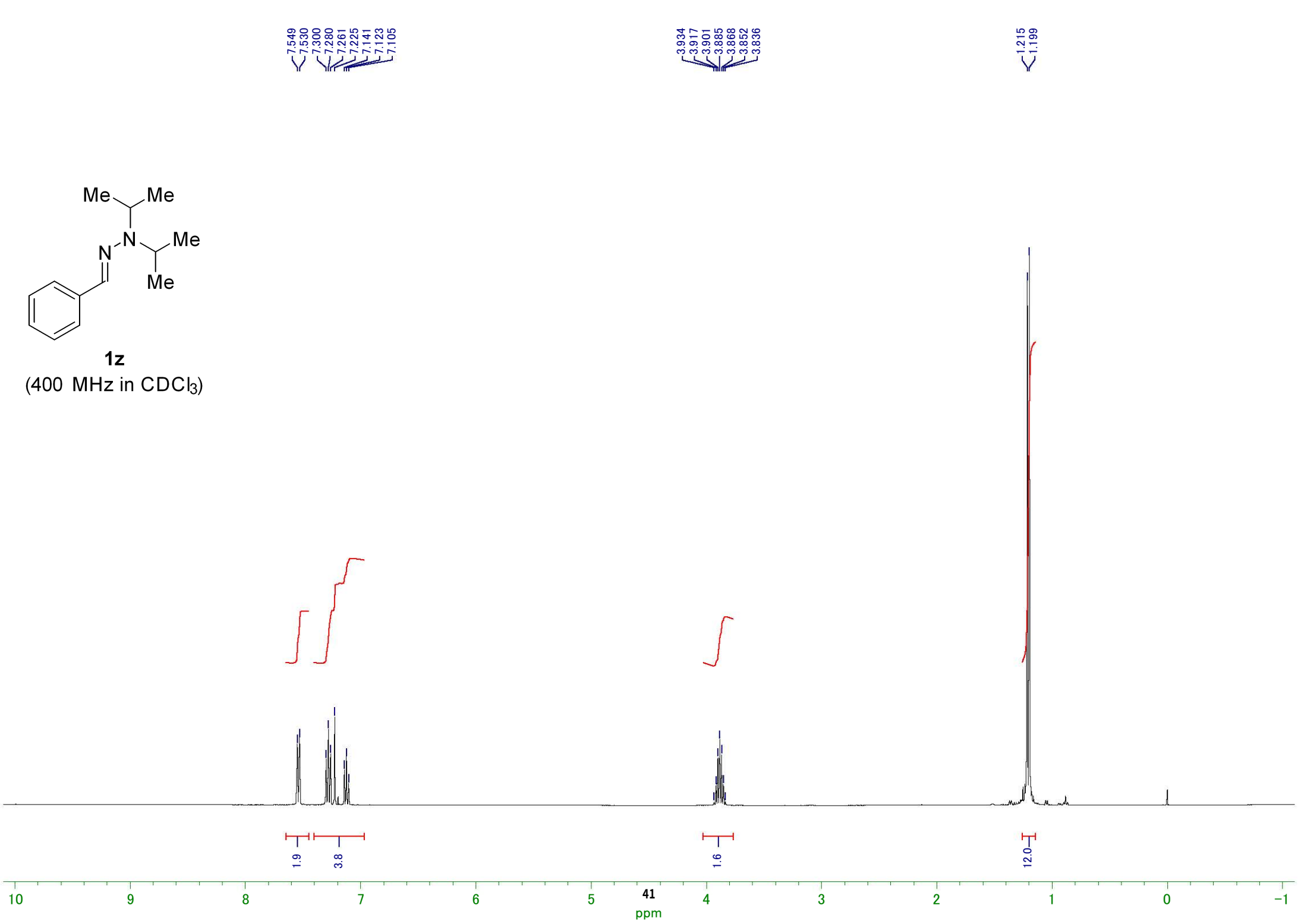

137.675
128.514
128.336
126.449
125.040
53.476
31.681
26.890
26.828
22.632
14.034
Me
N
N
Me
1x
(100 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

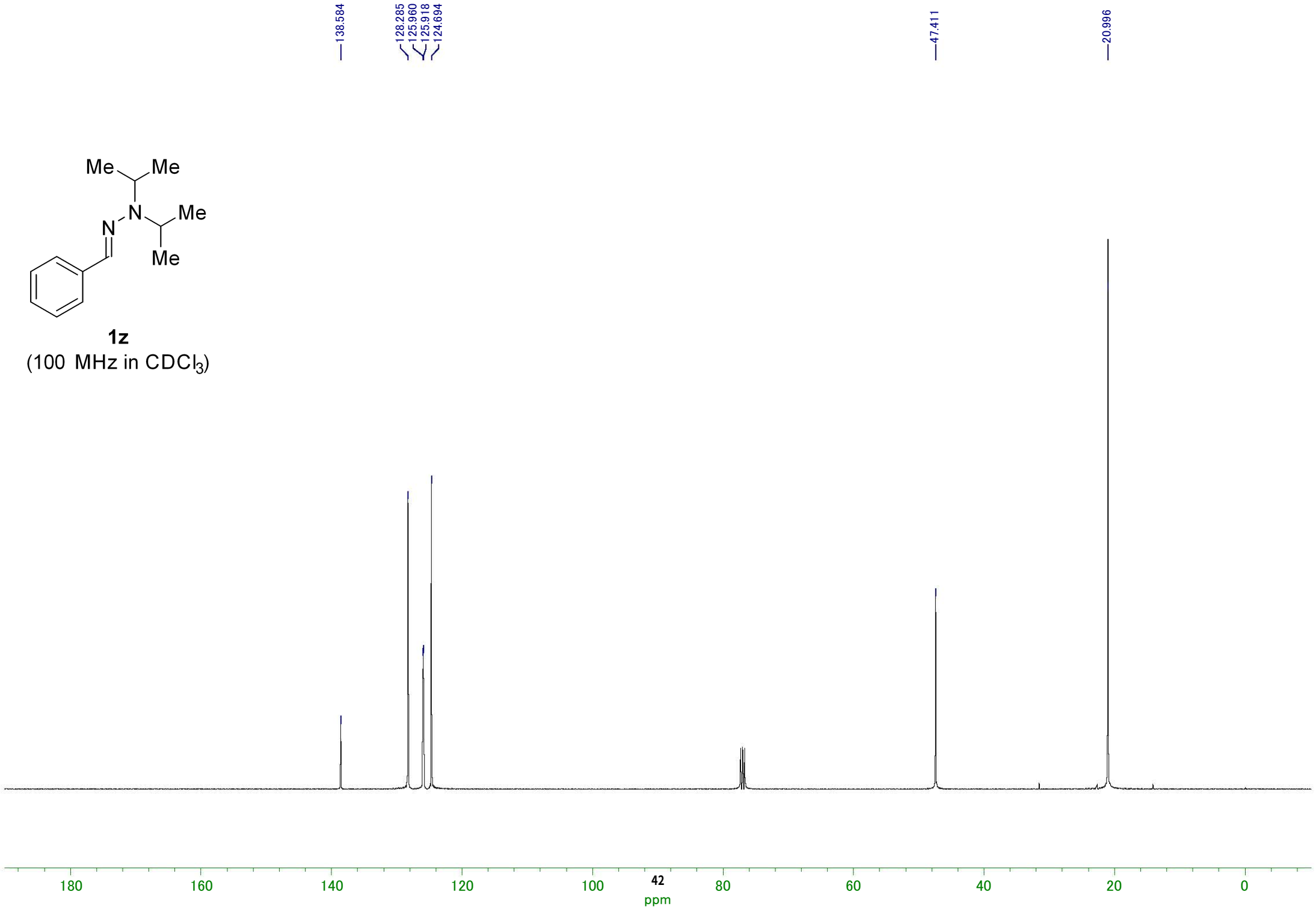


1y
(300 MHz in $CDCl_3$)



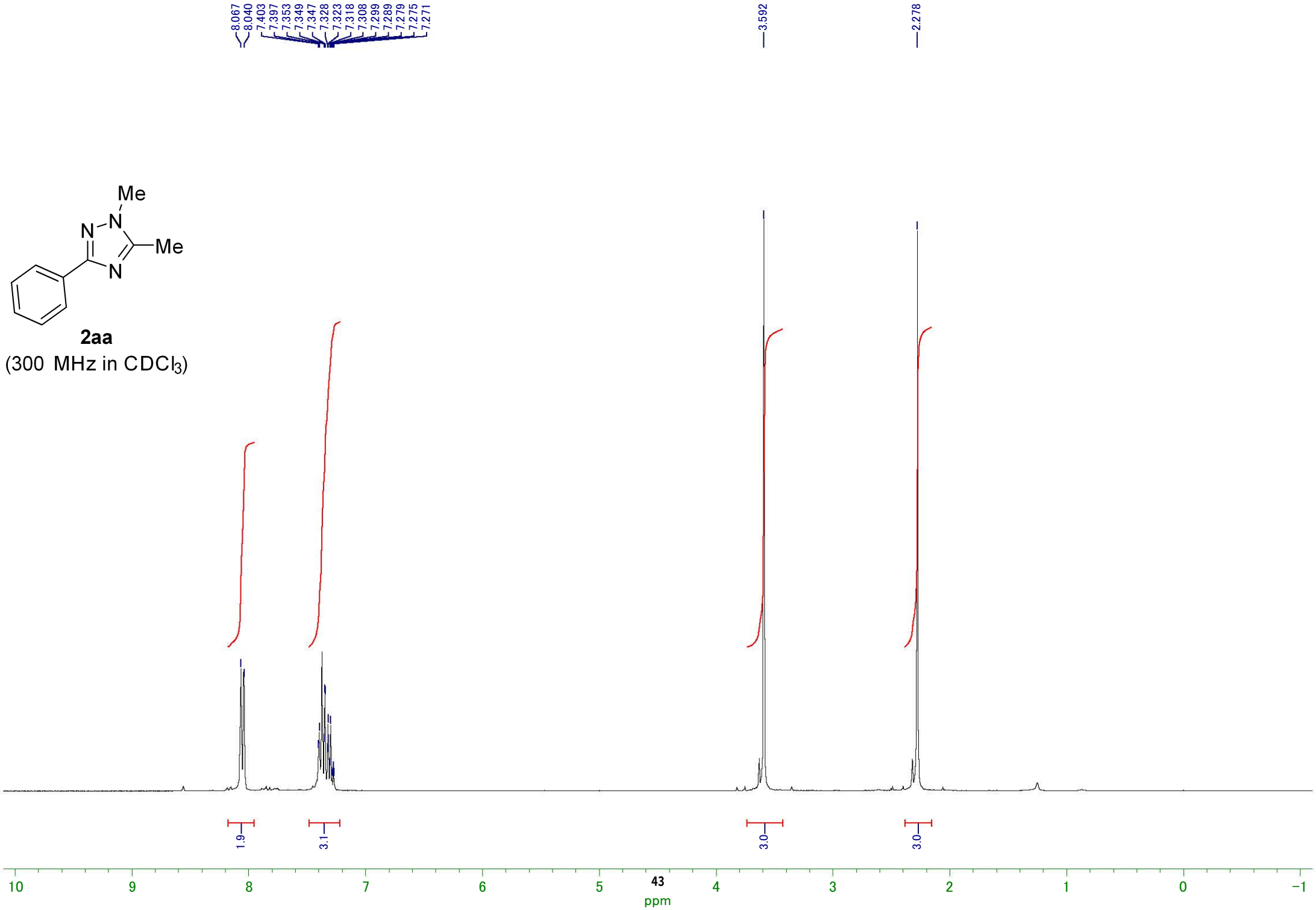
1y
(75 MHz in $CDCl_3$)

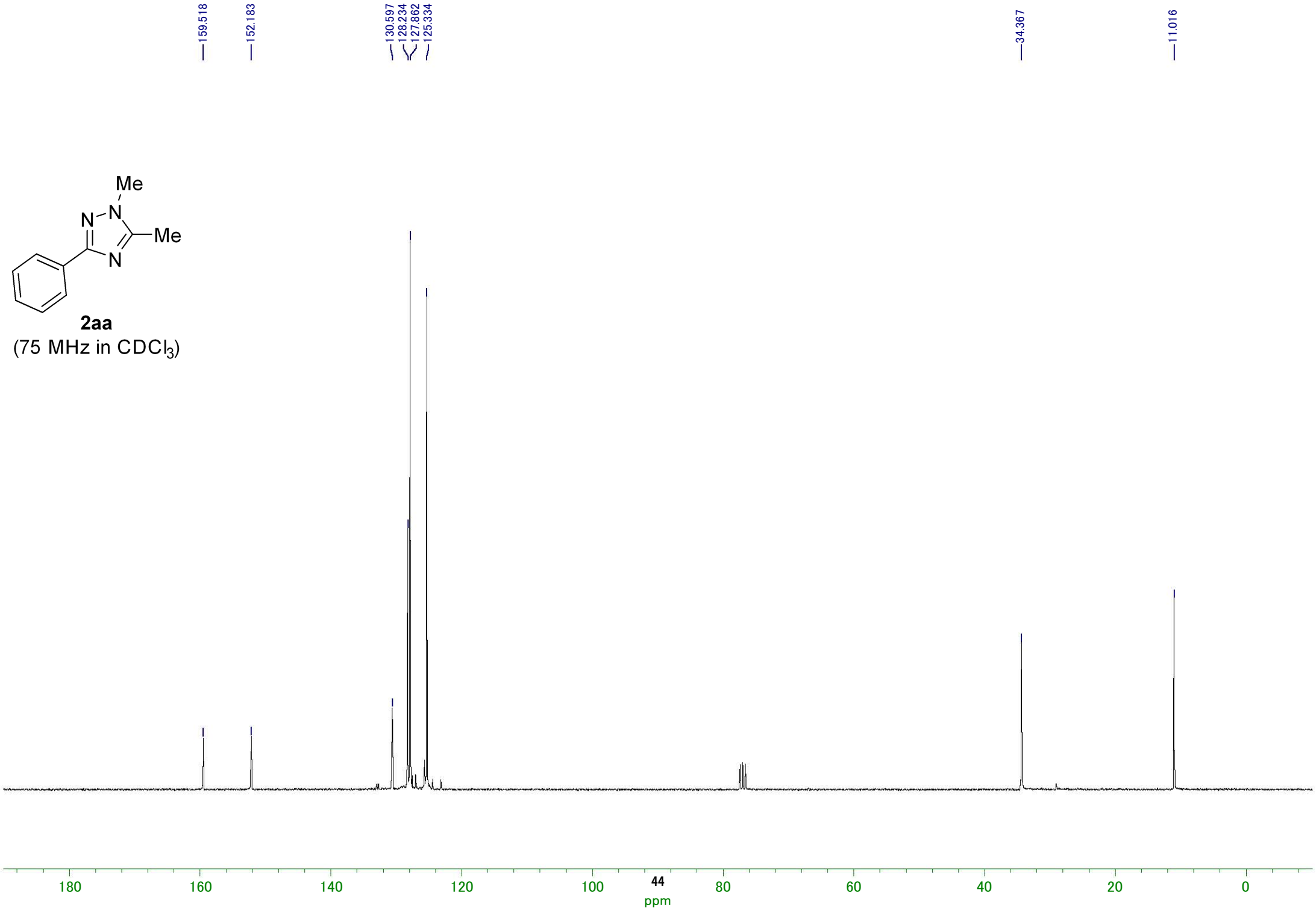

7.549
7.530
7.300
7.280
7.261
7.225
7.141
7.123
7.105
3.934
3.917
3.901
3.885
3.868
3.852
3.836
1.215
1.199
Me
Me
N
N
Me
Me
1z
(400 MHz in CDCl3)
1.9
3.8
1.6
12.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

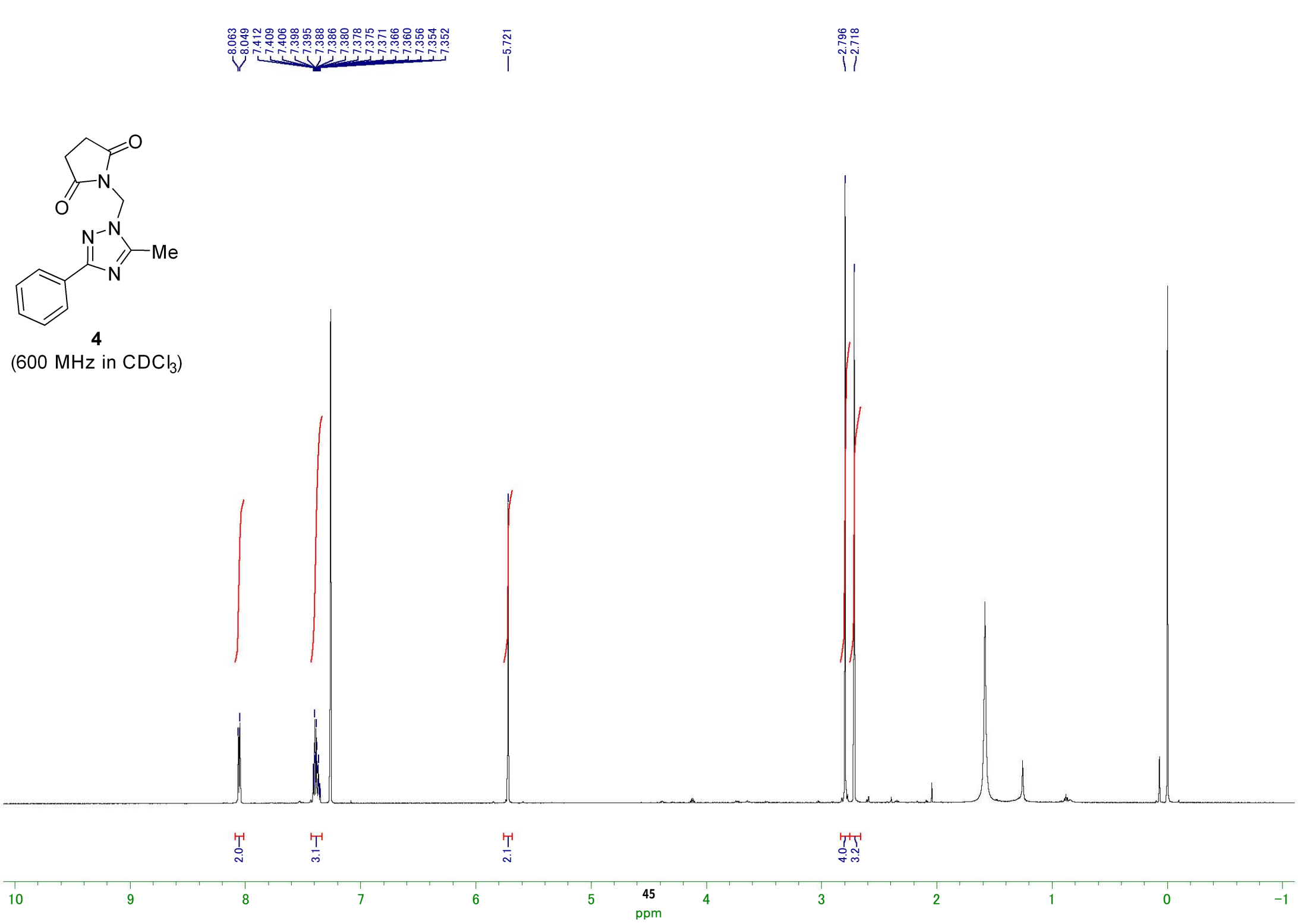


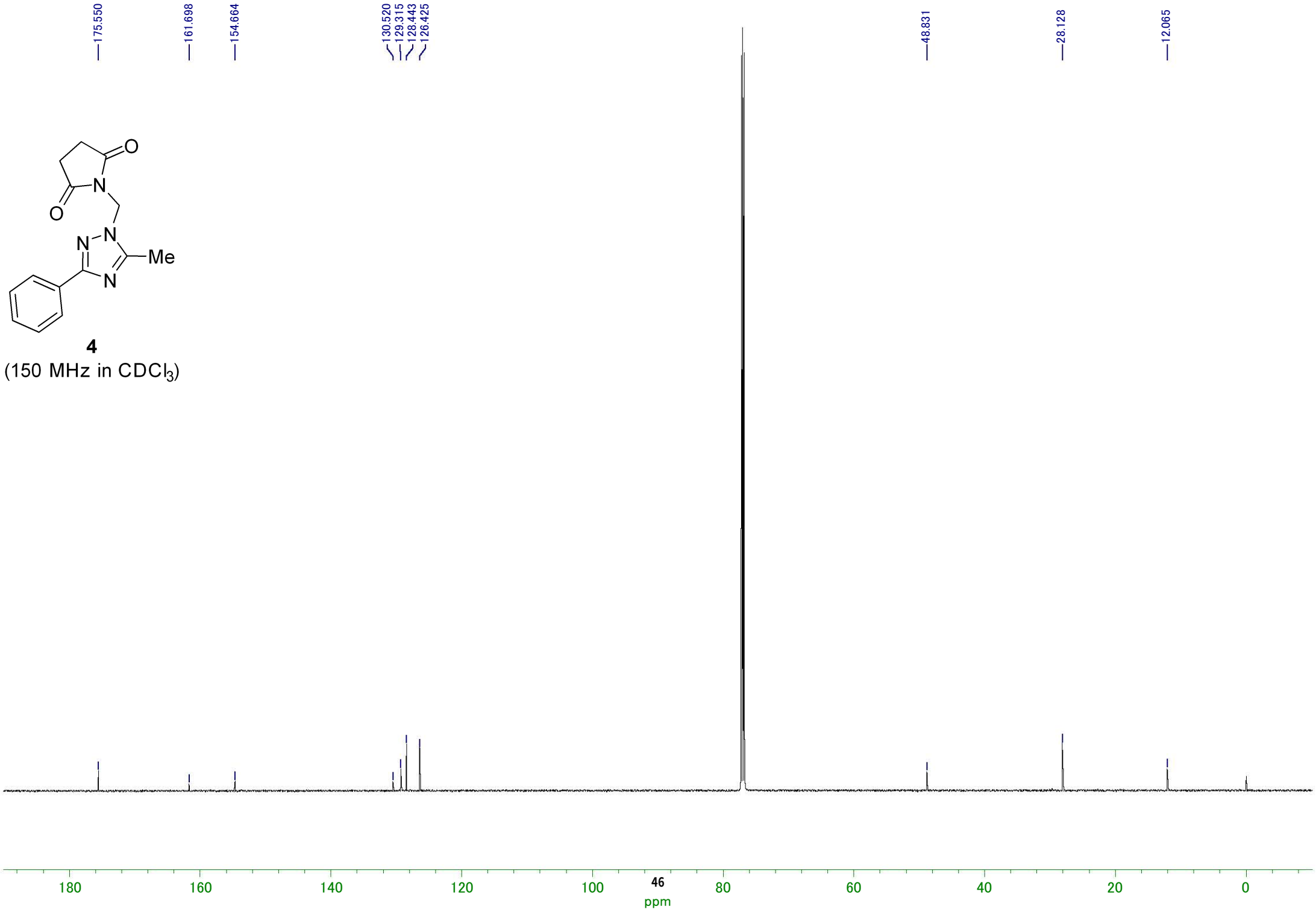
1z

(100 MHz in $CDCl_3$)


8.067
8.040
7.403
7.397
7.353
7.349
7.347
7.328
7.323
7.318
7.308
7.299
7.289
7.279
7.275
7.271
3.592
2.278
Me
N
N
Me
N
2aa
(300 MHz in CDCl3)
1.9
3.1
3.0
3.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

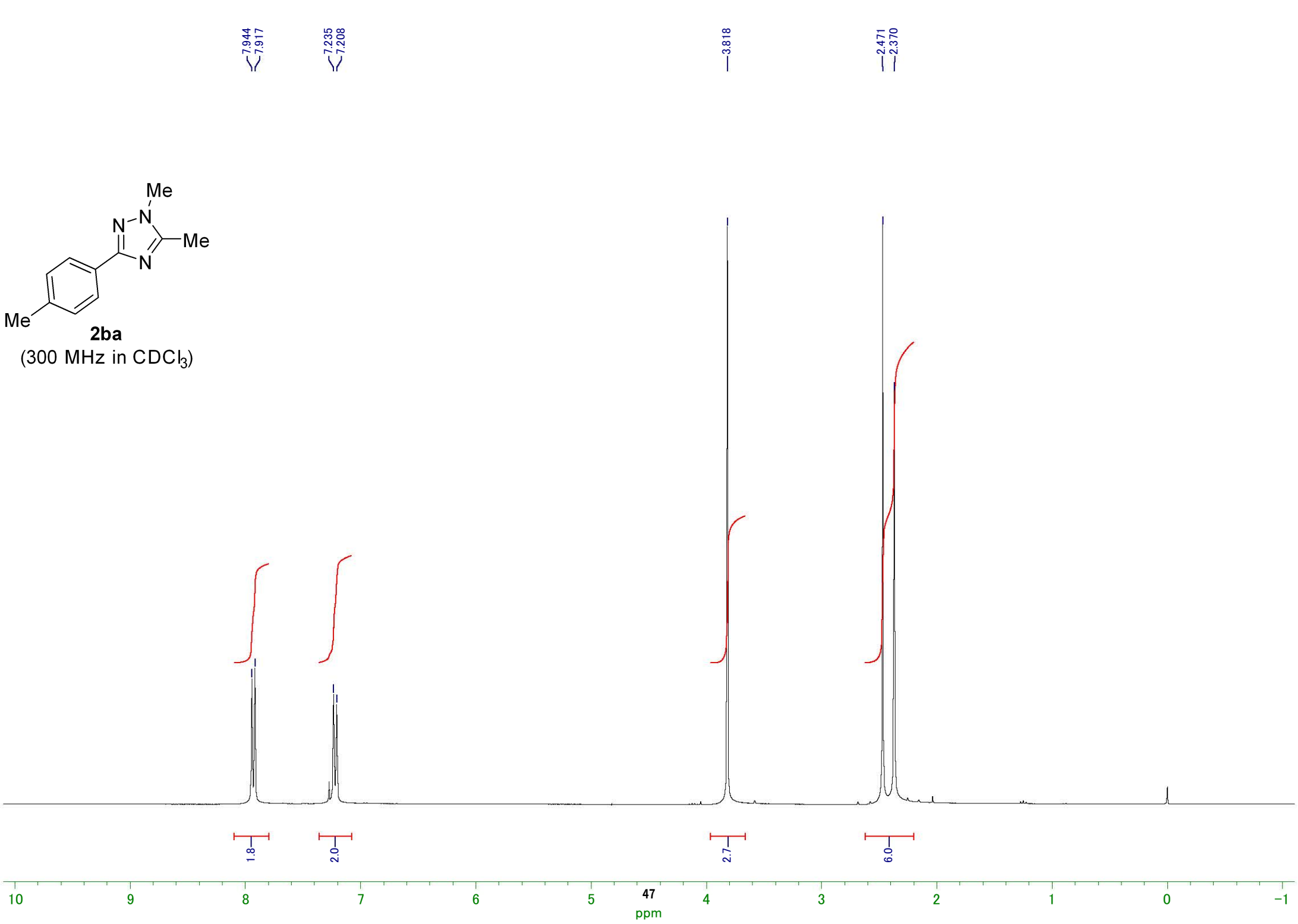

159.518
152.183
130.597
128.234
127.862
125.334
34.367
11.016
Me
N
N
Me
N
2aa
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

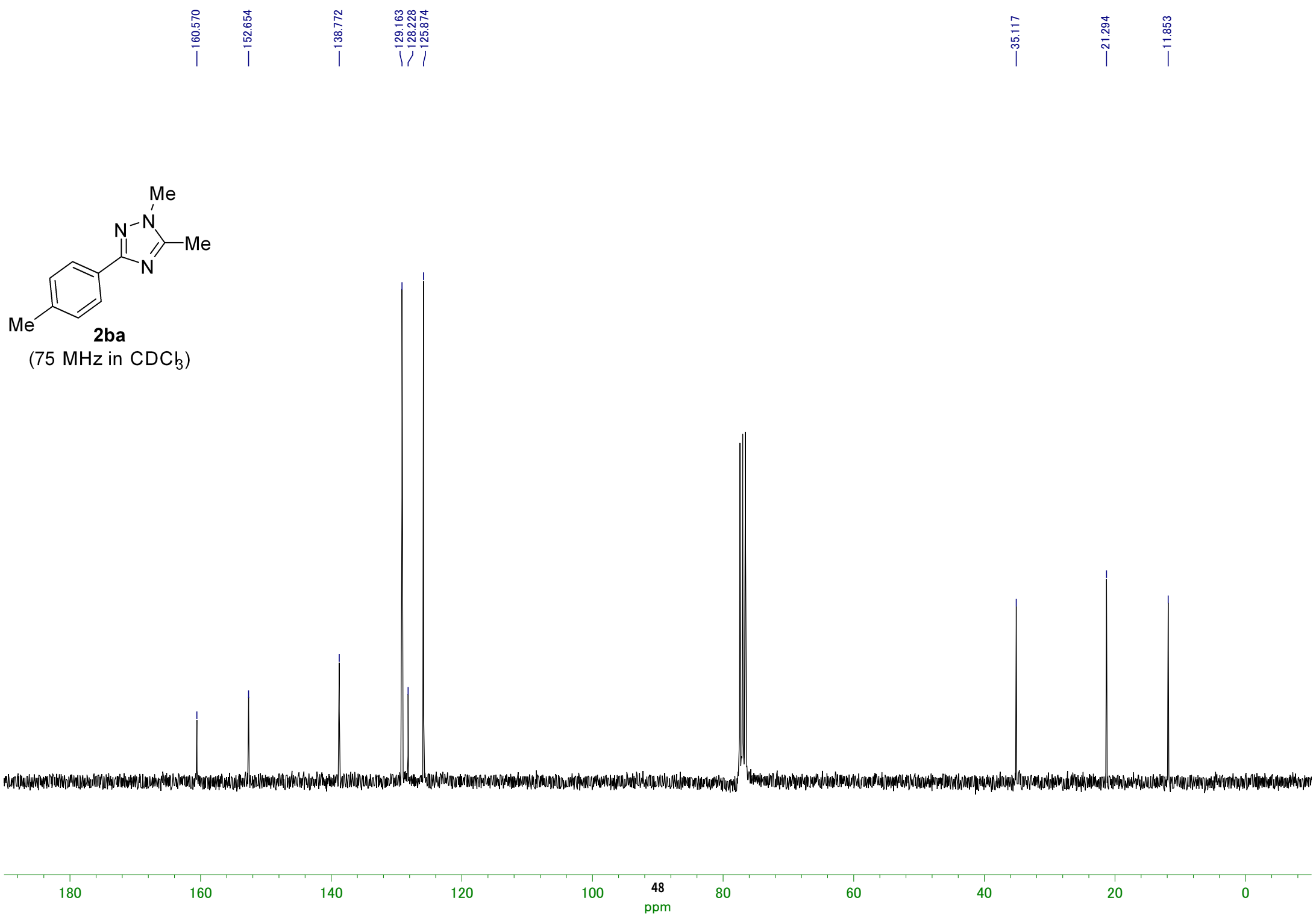

8.063
8.049
7.412
7.409
7.406
7.398
7.395
7.388
7.386
7.380
7.378
7.375
7.371
7.366
7.360
7.356
7.354
7.352
5.721
2.796
2.718
O
O
N
N
N
N
Me
4
(600 MHz in CDCl3)
2.0
3.1
2.1
4.0
3.2
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

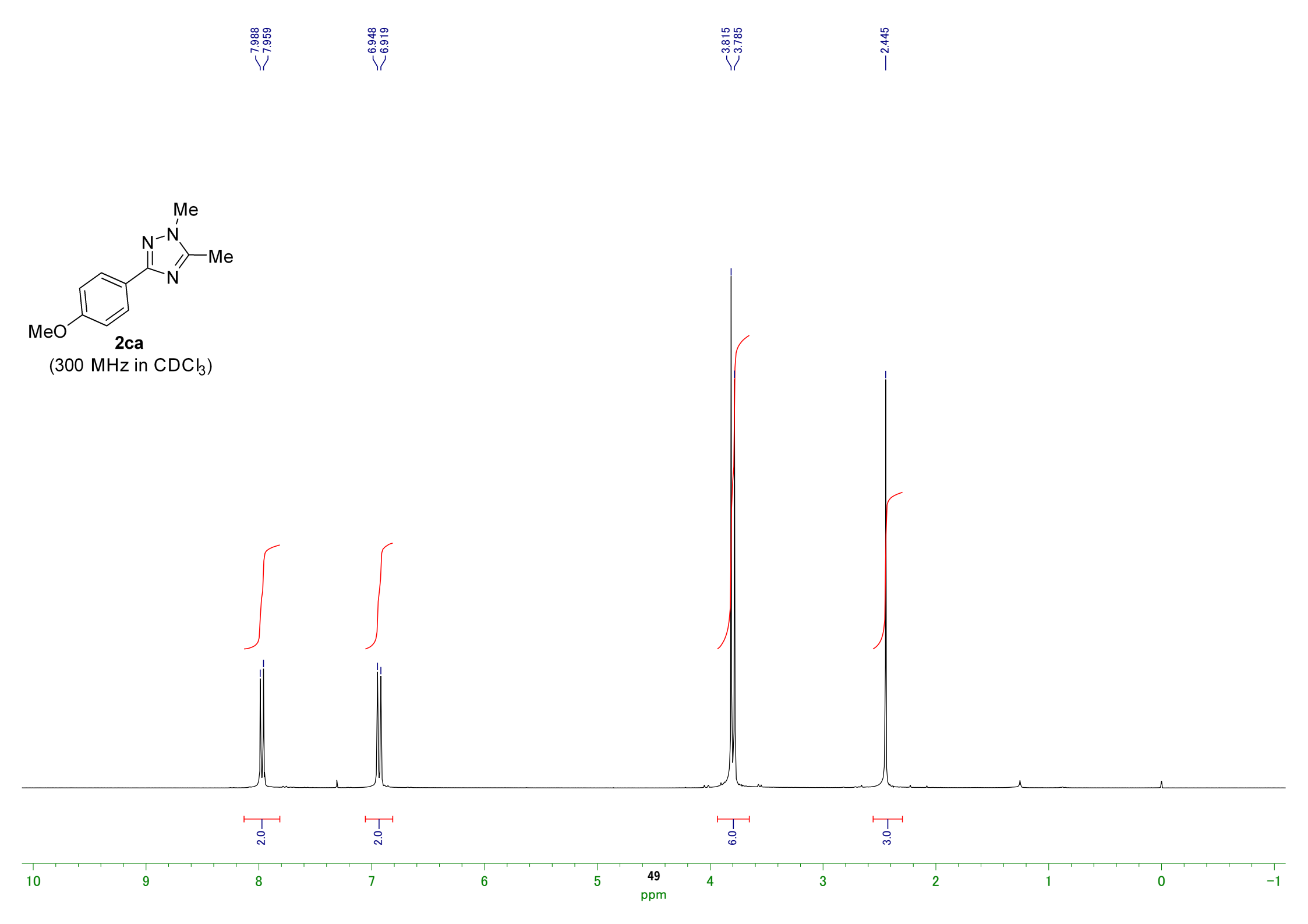


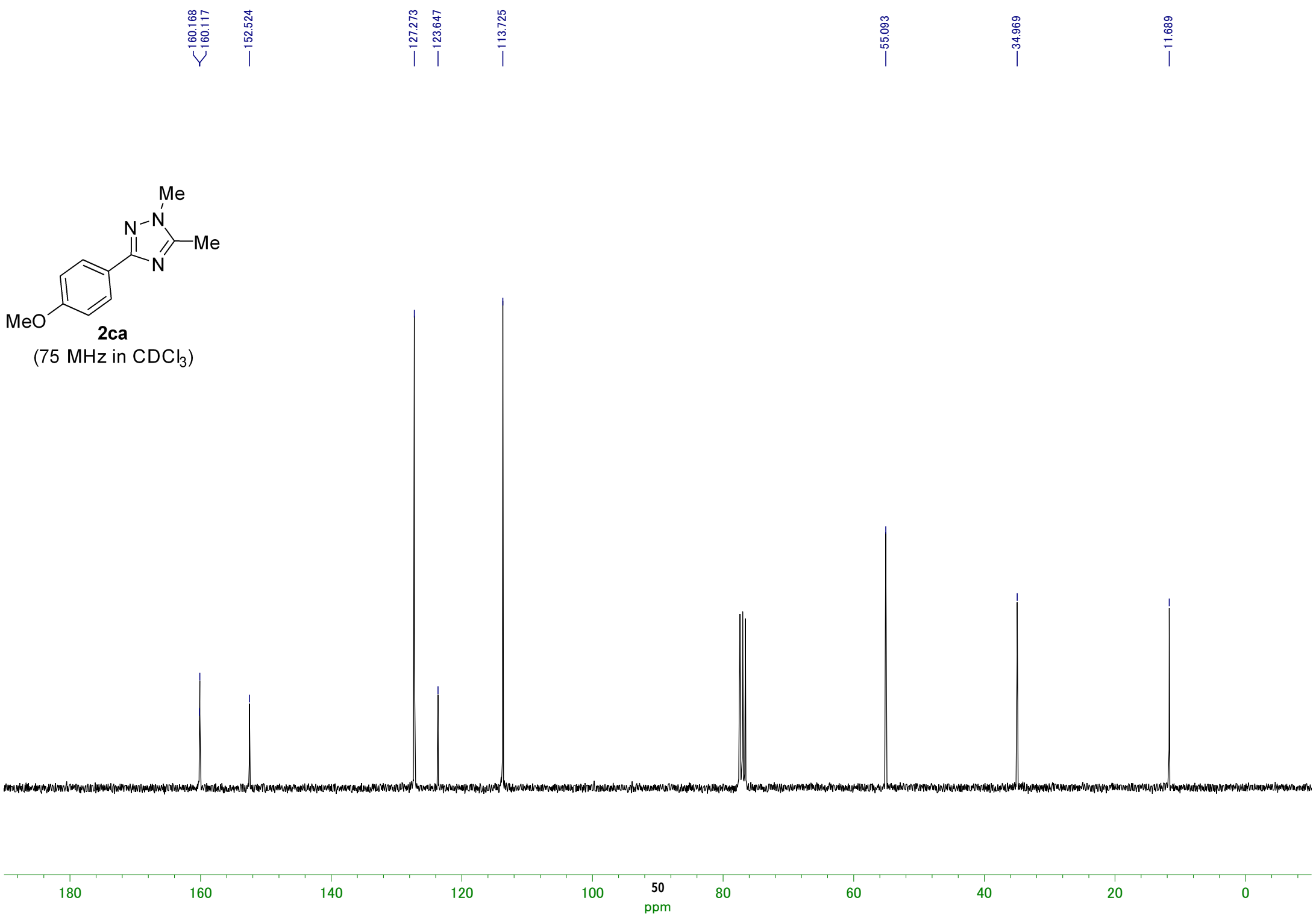
4

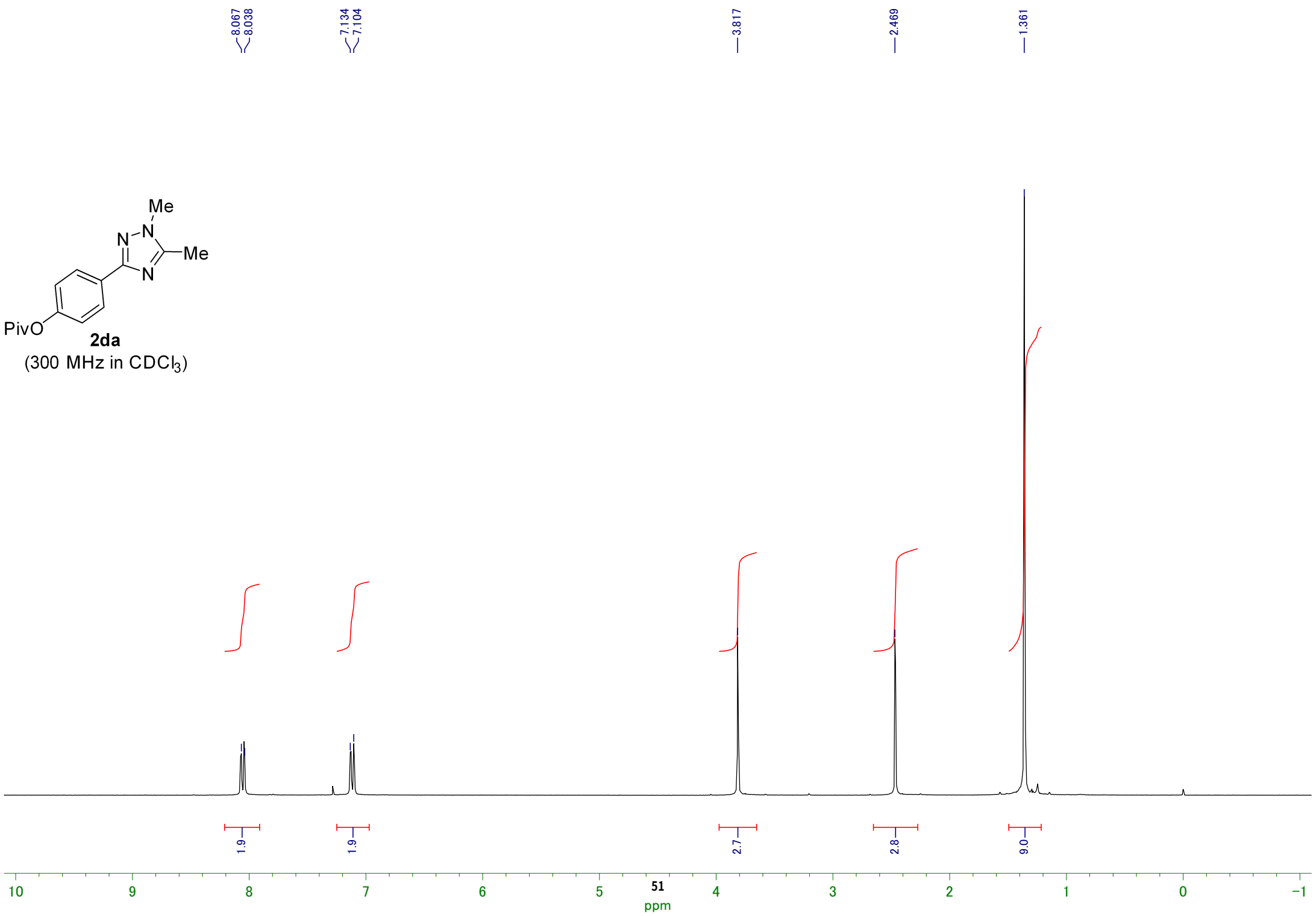
(150 MHz in $CDCl_3$)

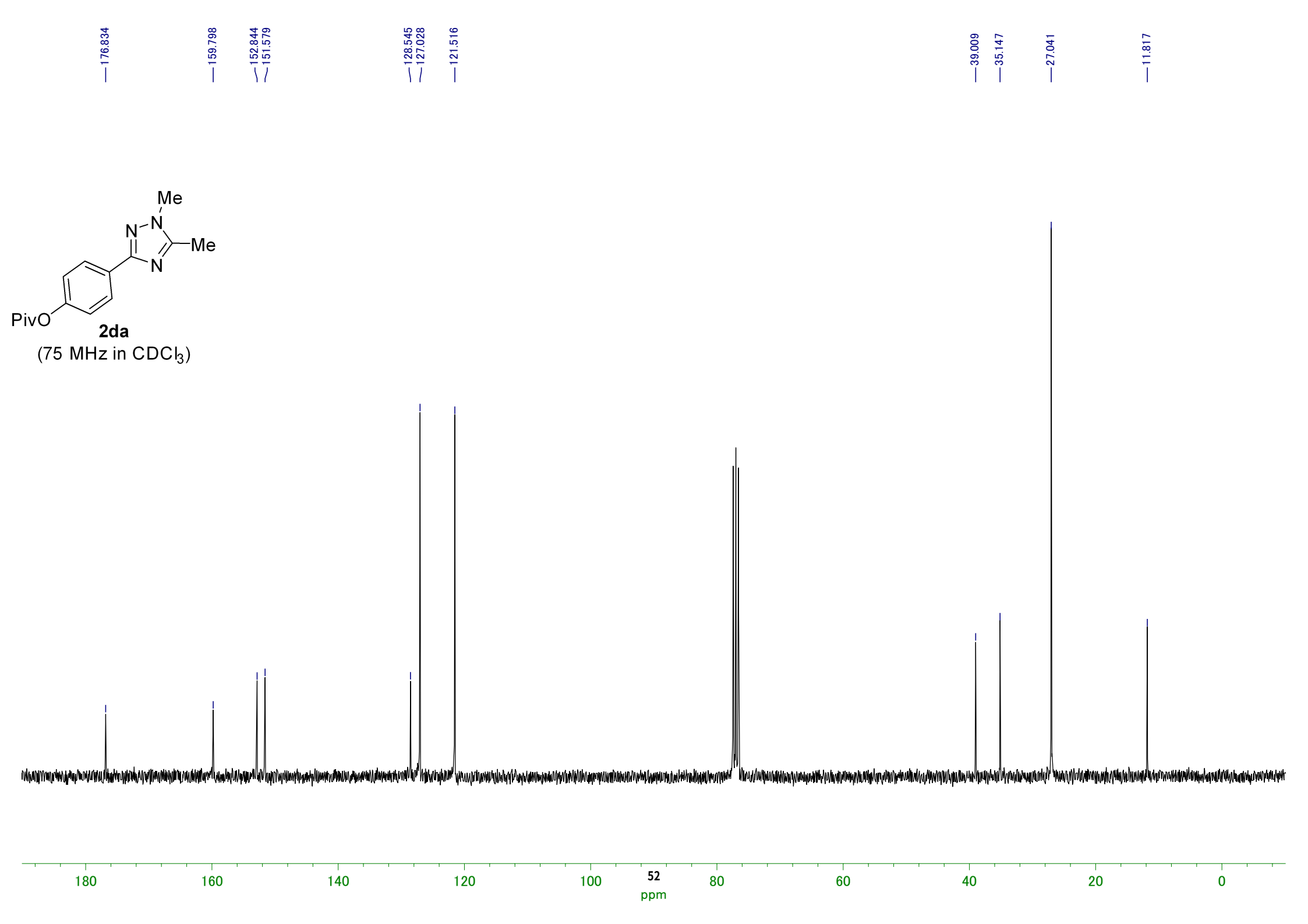

7.944
7.917
7.235
7.208
3.818
2.471
2.370
Me
N
N
Me
N
Me
2ba
(300 MHz in CDCl3)
1.8
2.0
2.7
6.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

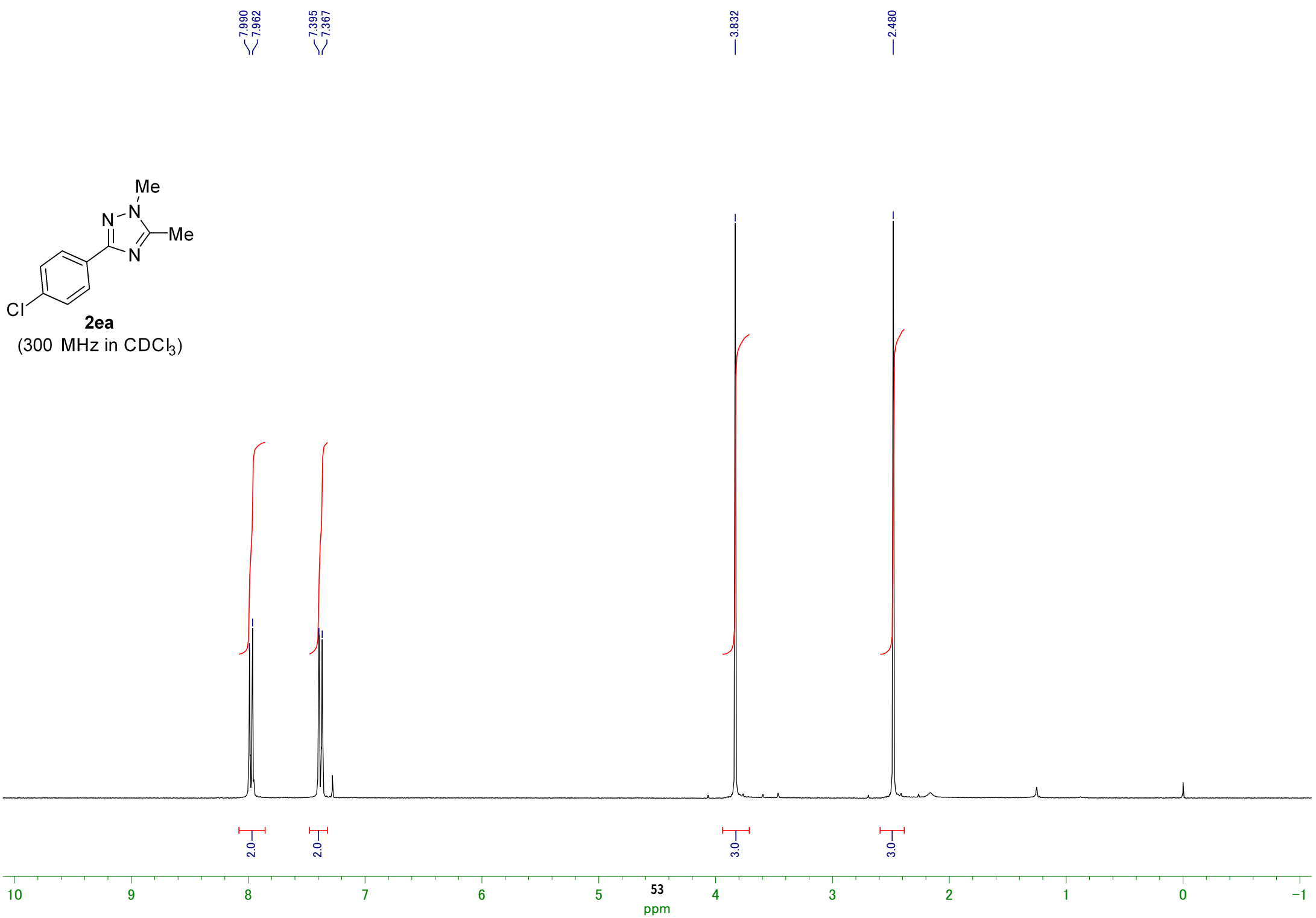

160.570
152.654
138.772
129.163
128.228
125.874
35.117
21.294
11.853
Me
N
N
Me
N
Me
2ba
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

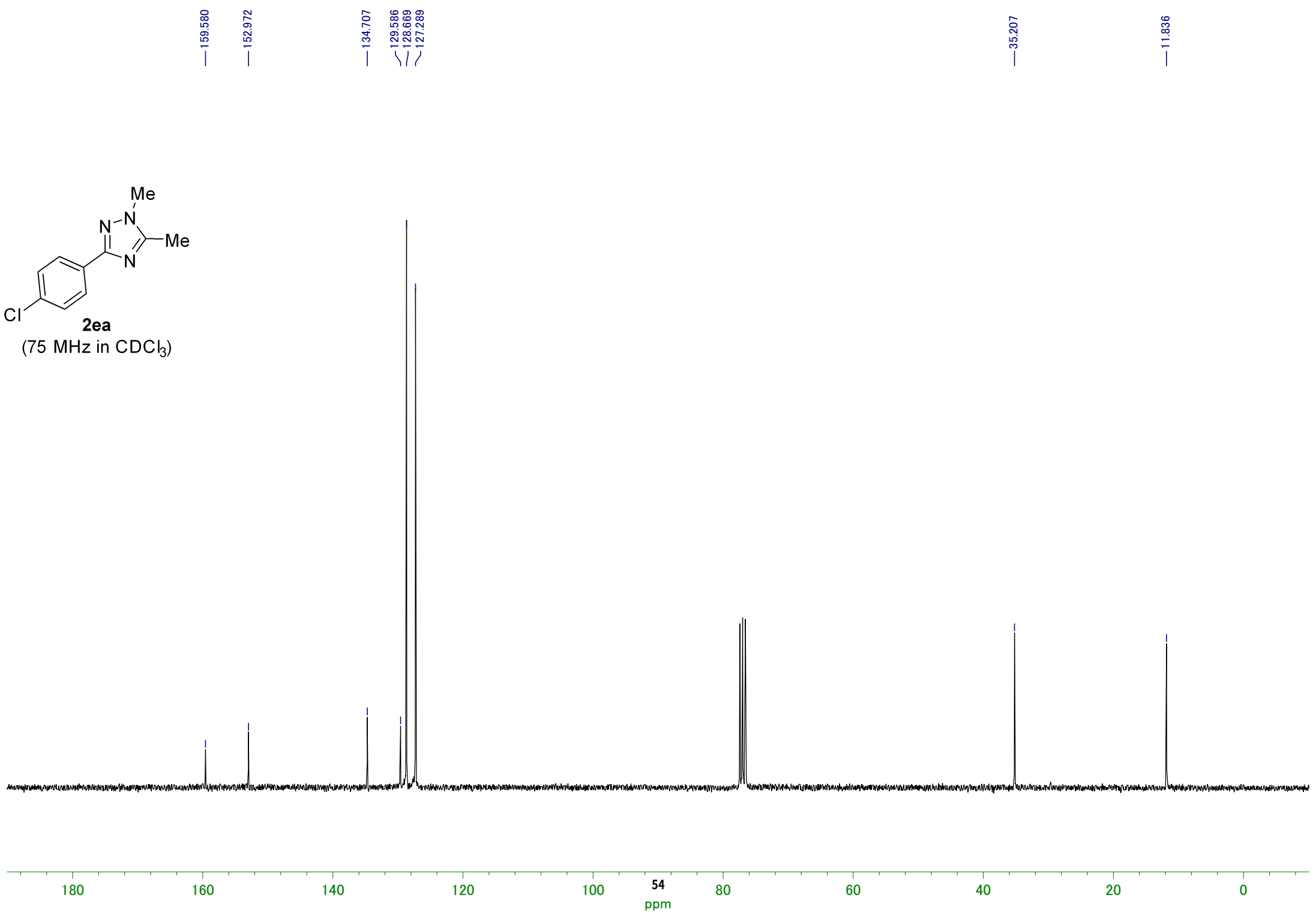

7.988
7.959
6.948
6.919
3.815
3.785
2.445
Me
N
N
Me
N
MeO
2ca
(300 MHz in CDCl3)
2.0
2.0
6.0
3.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

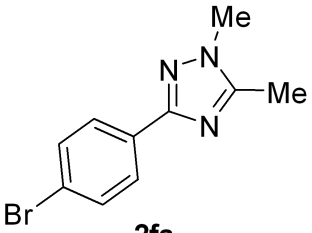

160.168
160.117
152.524
127.273
123.647
113.725
55.093
34.969
11.689
Me
N
N
Me
N
MeO
2ca
(75 MHz in CDCl3)
180
160
140
120
100
50
80
60
40
20
0
ppm


8.067
8.038
7.134
7.104
3.817
2.469
1.361
Me
N
N
Me
N
PivO
2da
(300 MHz in CDCl3)
1.9
1.9
2.7
2.8
9.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm


176.834
159.798
152.844
151.579
128.545
127.028
121.516
39.009
35.147
27.041
11.817
Me
N
N
Me
N
PivO
2da
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

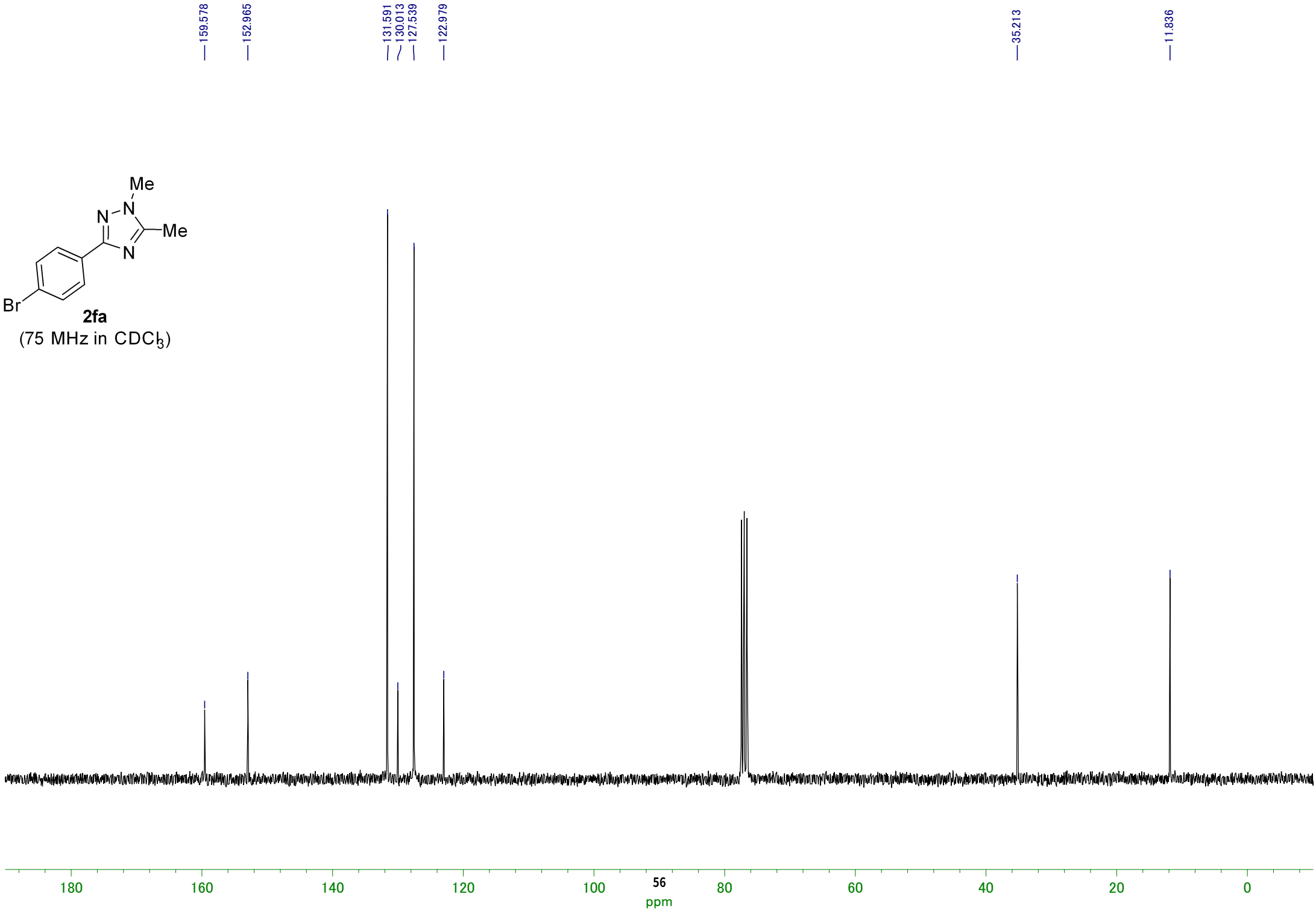

7.990
7.962
7.395
7.367
3.832
2.480
Me
N
N
Me
N
Cl
2ea
(300 MHz in CDCl3)
2.0
2.0
3.0
3.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

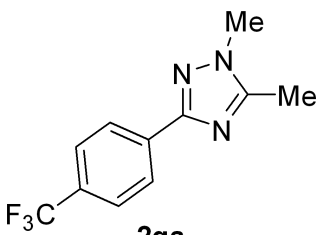

159.580
152.972
134.707
129.586
128.669
127.289
35.207
11.836
Me
N
N
Me
N
Cl
2ea
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



2fa

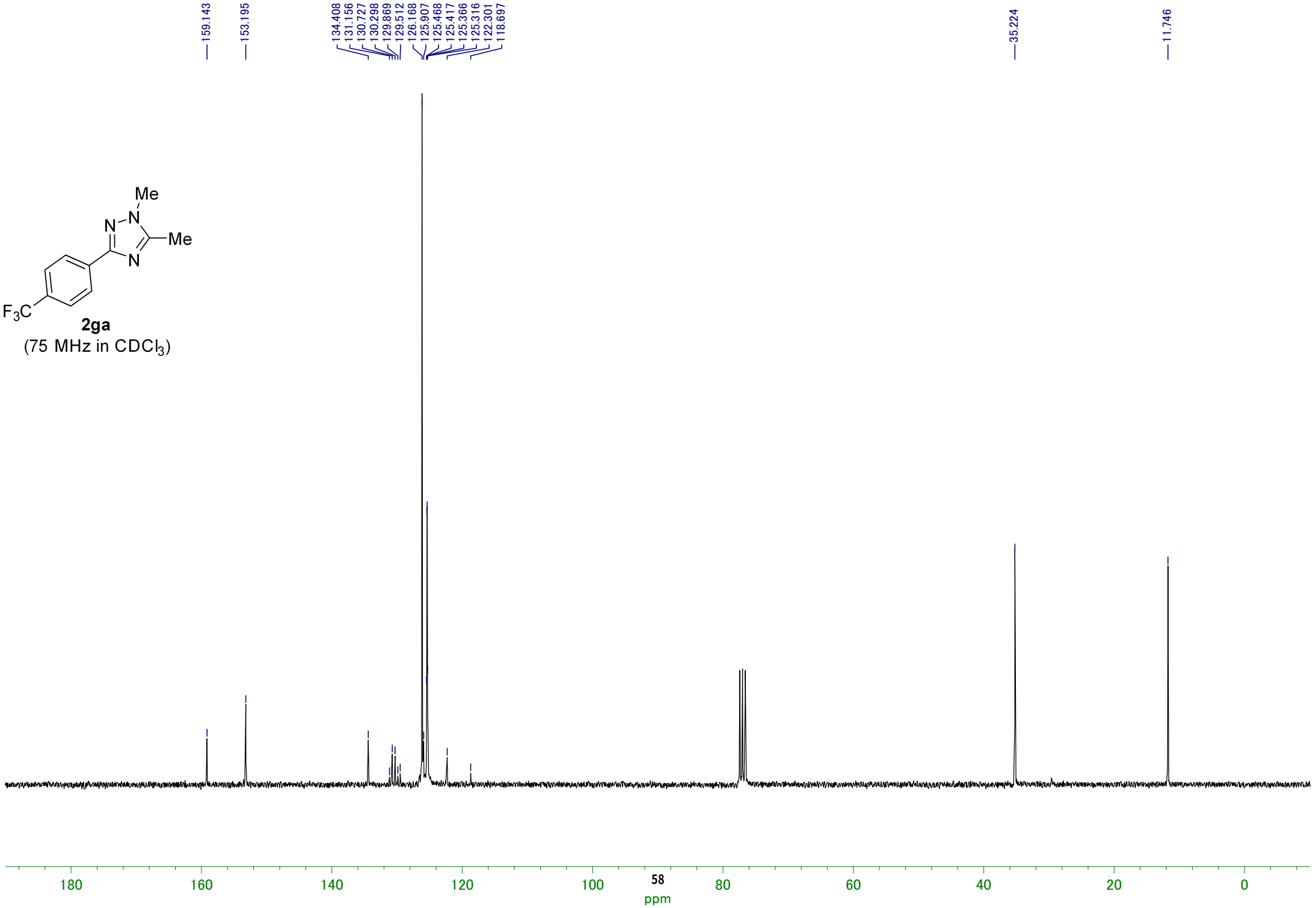
(300 MHz in $CDCl_3$)

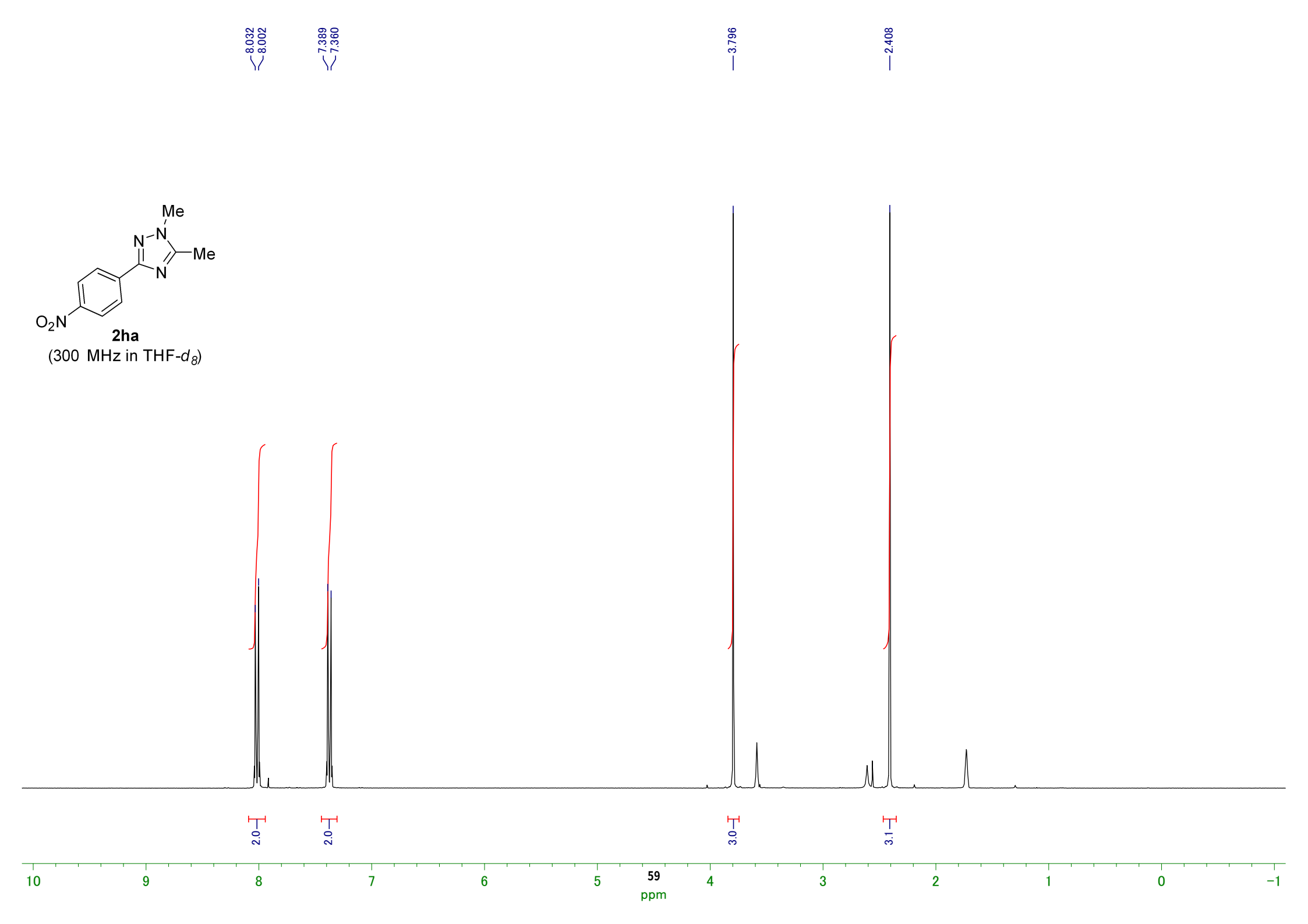

159.578
152.965
131.591
130.013
127.539
122.979
35.213
11.836
Me
N
N
Me
N
Br
2fa
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

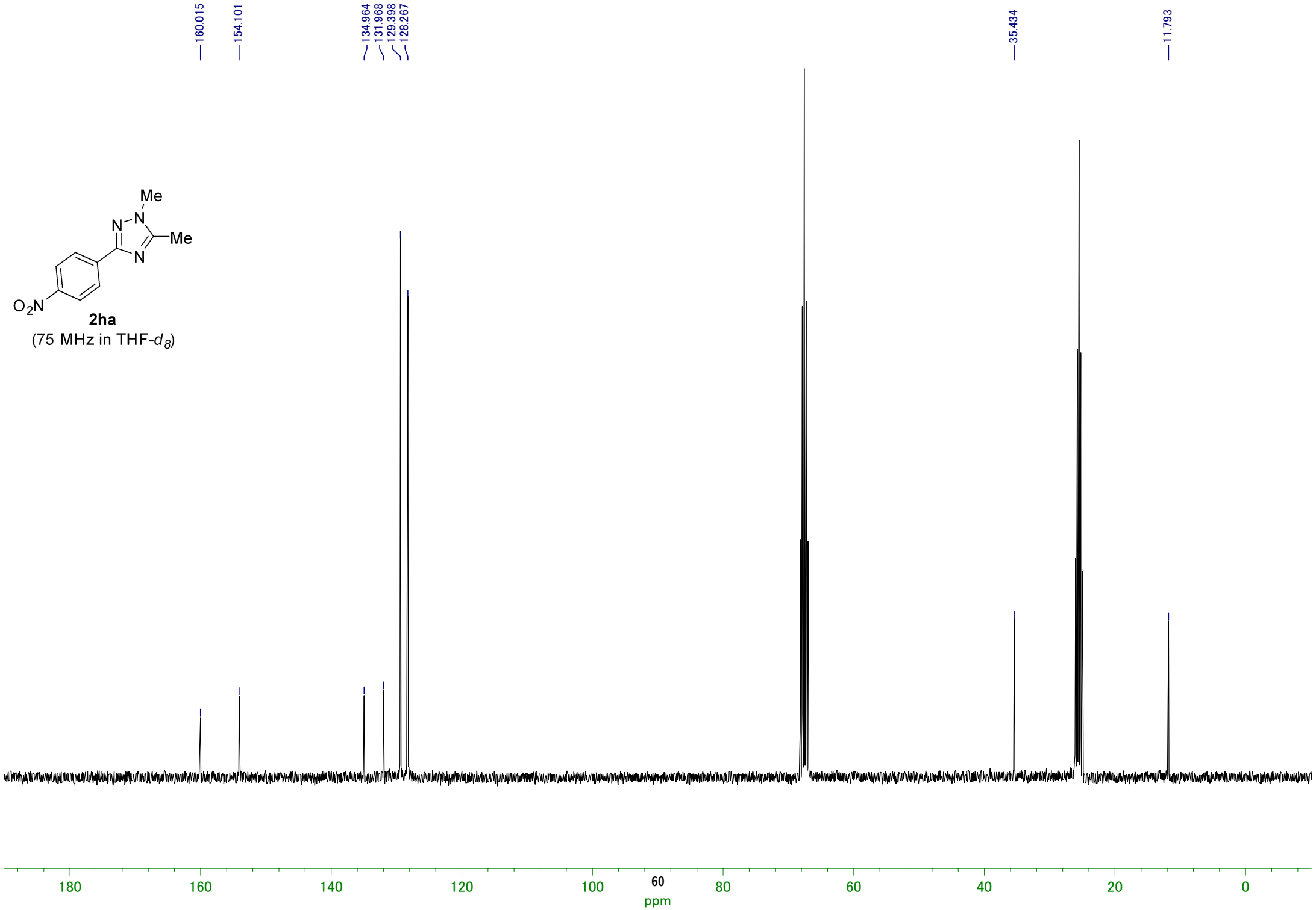


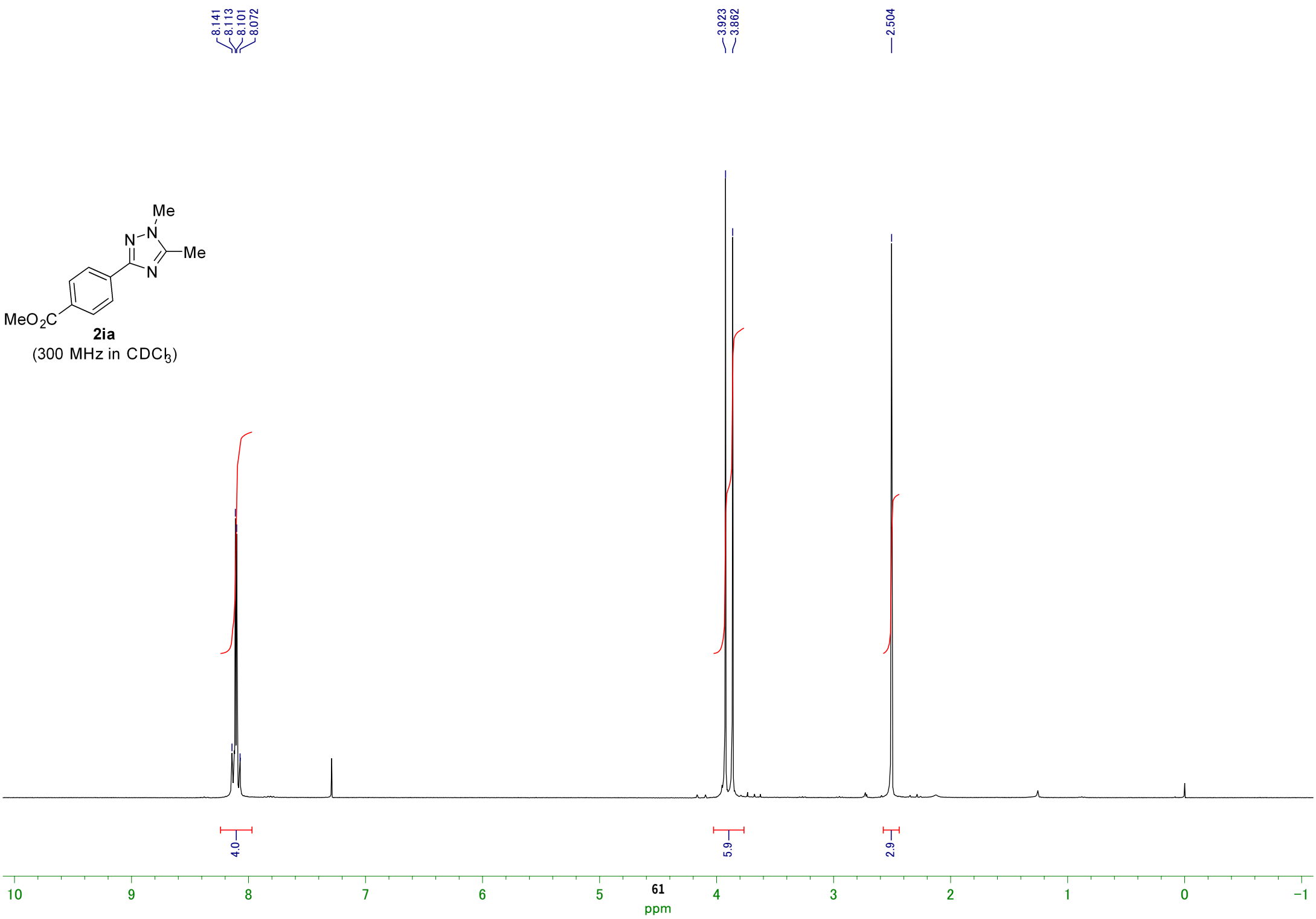
2ga

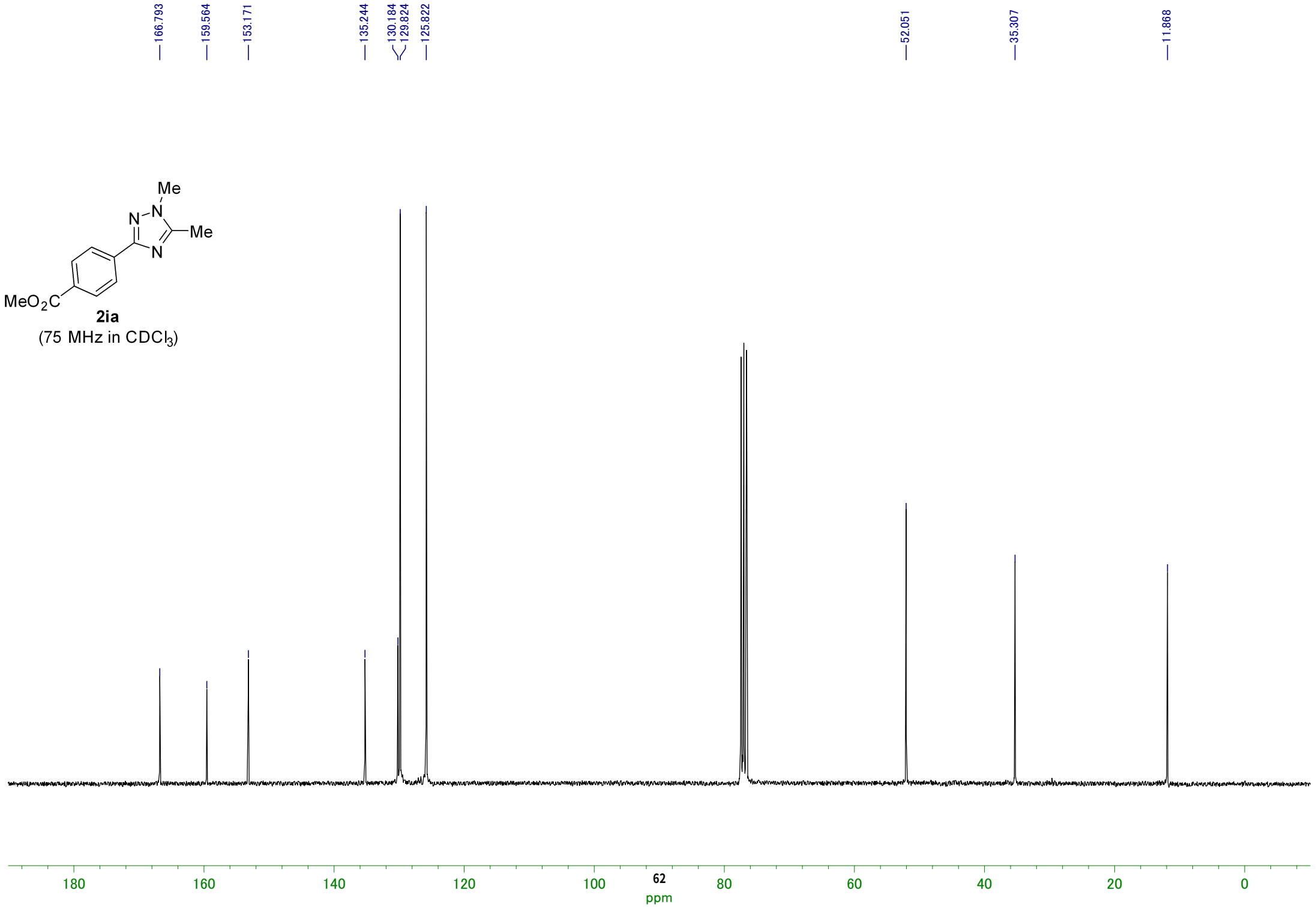
(300 MHz in $CDCl_3$)

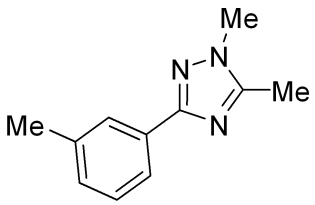

159.143
153.195
134.408
131.156
130.727
130.298
129.869
129.512
126.168
125.907
125.468
125.417
125.366
125.316
122.301
118.697
35.224
11.746
Me
N
N
Me
N
F3C
2ga
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm


8.032
8.002
7.389
7.360
3.796
2.408
Me
N
N
Me
N
O_2N
2ha
(300 MHz in THF-d_8)
2.0
2.0
3.0
3.1
10
9
8
7
6
5
4
3
2
1
0
−1
ppm


160.015
154.101
134.964
131.968
129.398
128.267
35.434
11.793
Me
N
N
Me
N
O2N
2ha
(75 MHz in THF-d8)
180
160
140
120
100
80
60
40
20
0
ppm

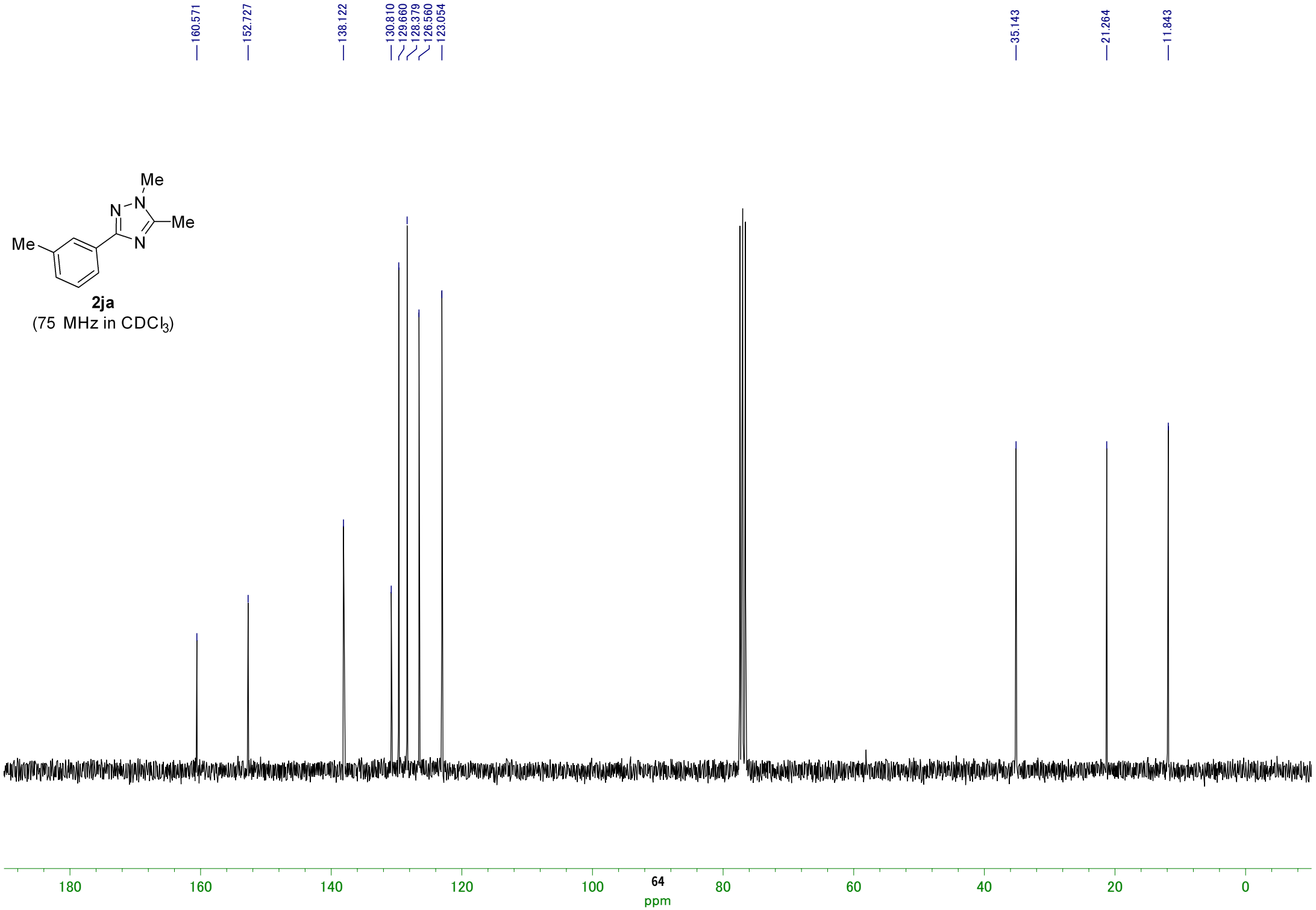

8.141
8.113
8.101
8.072
3.923
3.862
2.504
Me
N
N
Me
N
MeO2C
2ia
(300 MHz in CDCl3)
4.0
5.9
2.9
10
9
8
7
6
5
4
3
2
1
0
−1
61
ppm

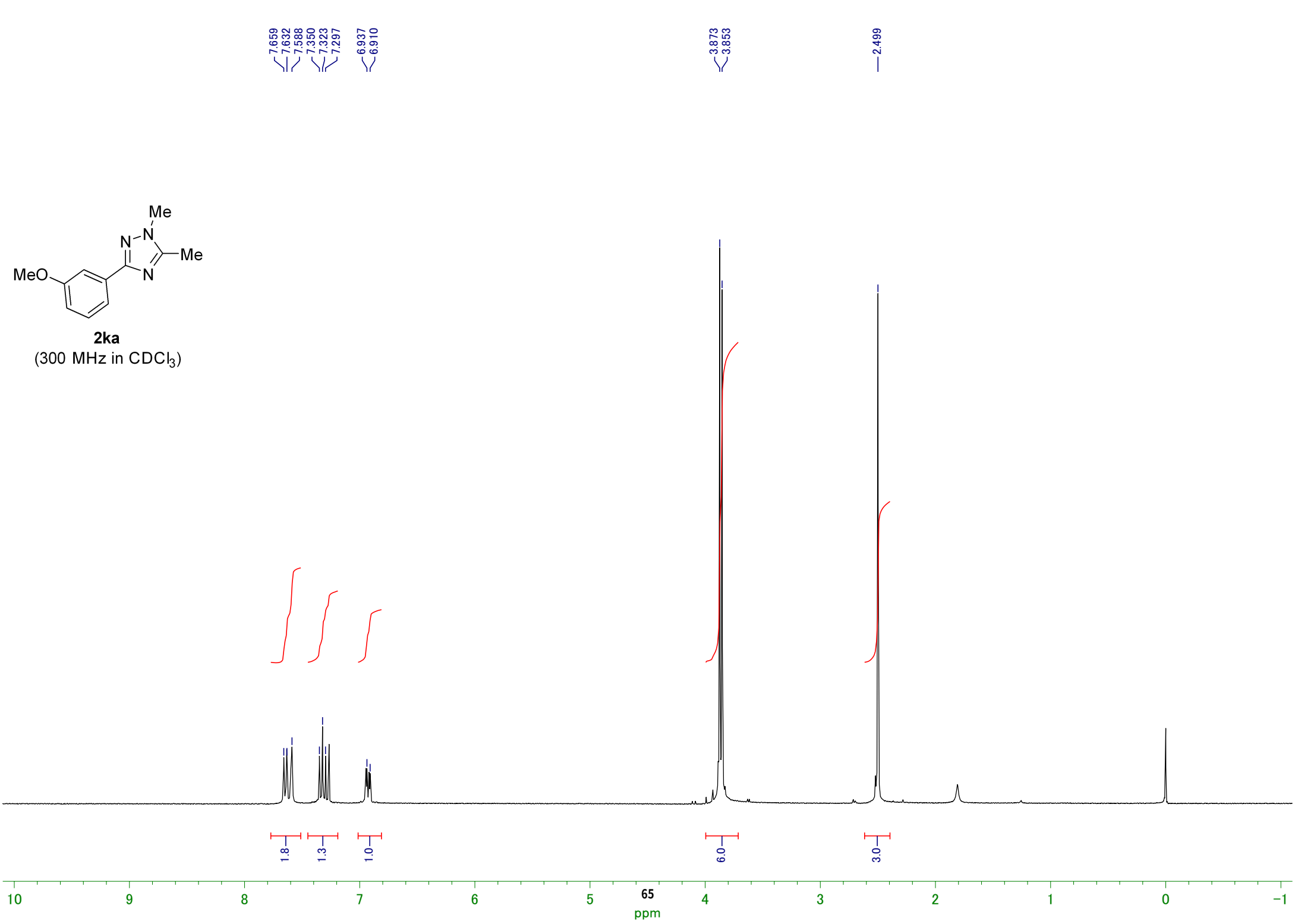

166.793
159.564
153.171
135.244
130.184
129.824
125.822
52.051
35.307
11.868
Me
N
N
Me
N
MeO2C
2ia
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



2ja

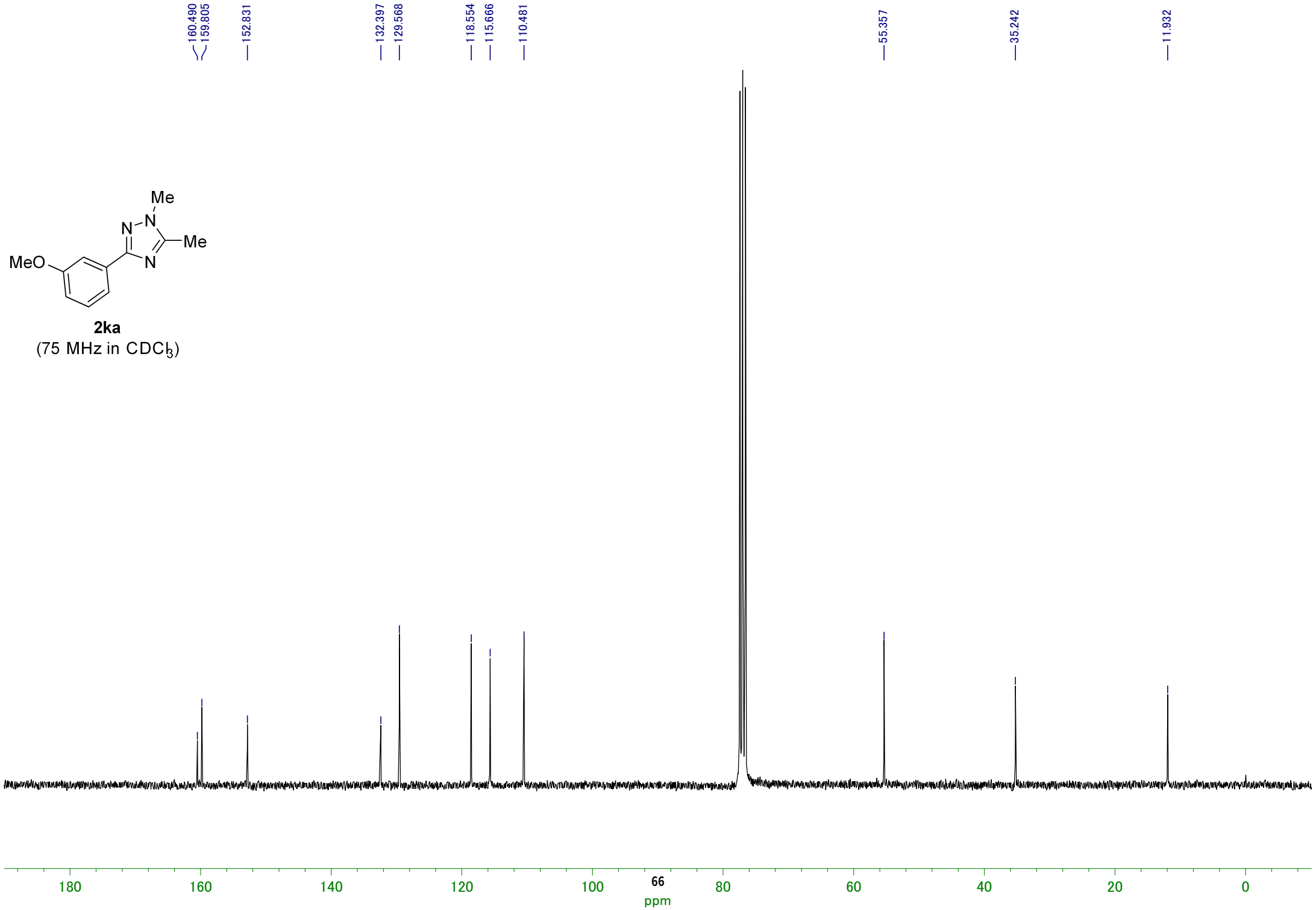
(300 MHz in $CDCl_3$)


160.571
152.727
138.122
130.810
129.660
128.379
126.560
123.054
35.143
21.264
11.843
Me
N
N
Me
Me
N
2ja
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

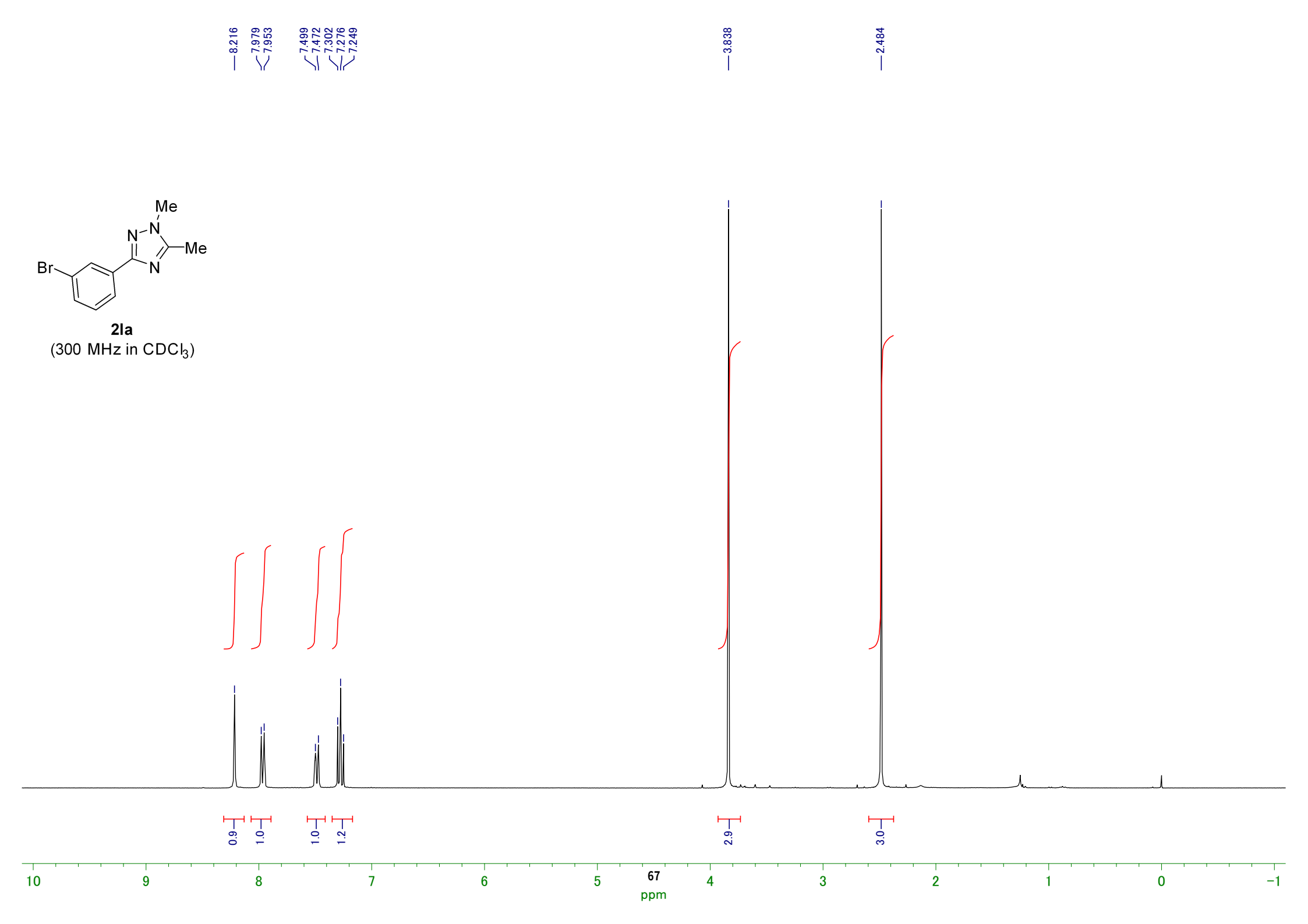


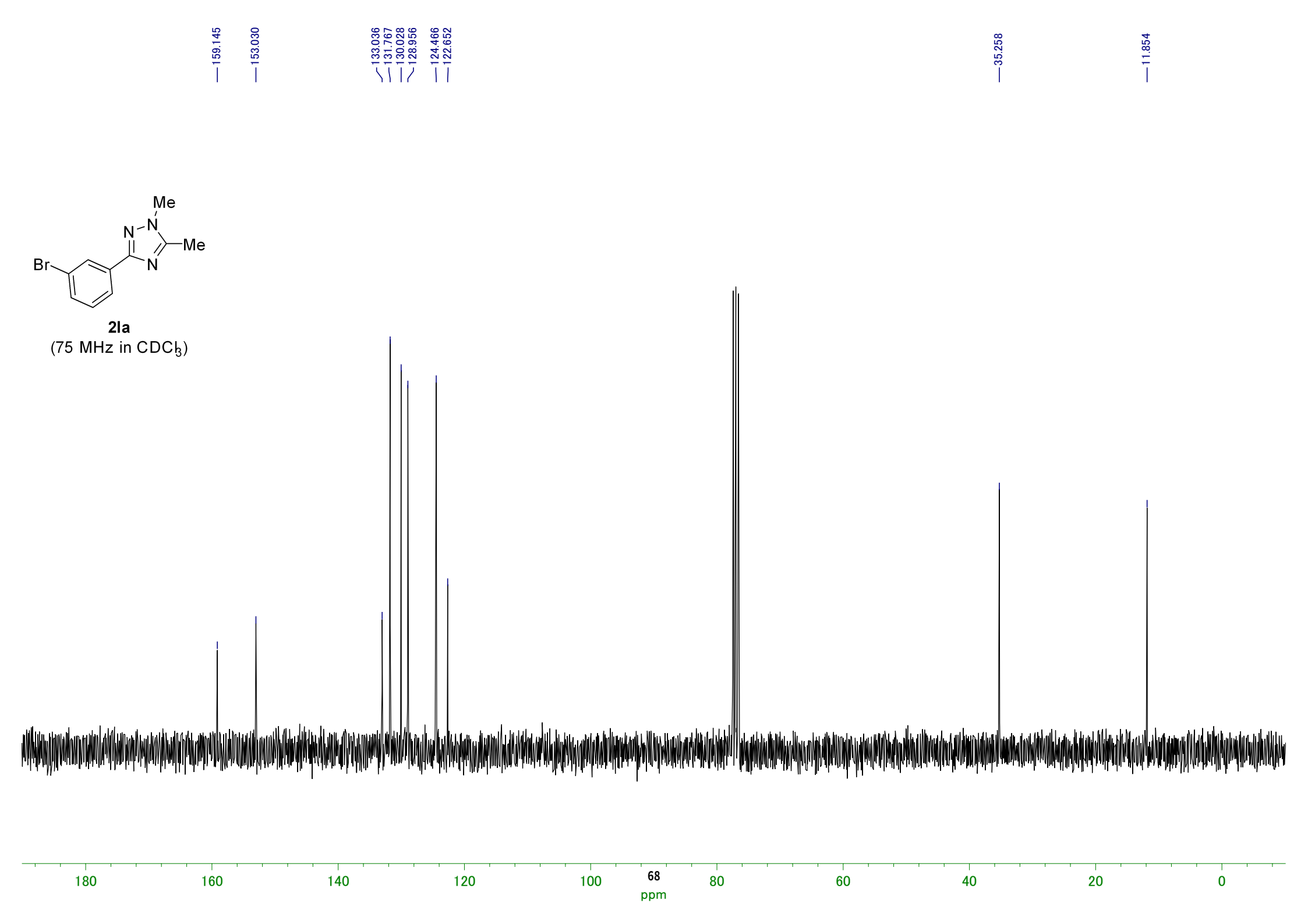
2ka

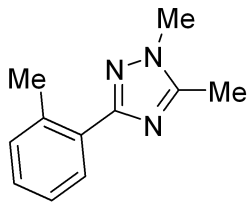
(300 MHz in $CDCl_3$)



2ka
(75 MHz in $CDCl_3$)

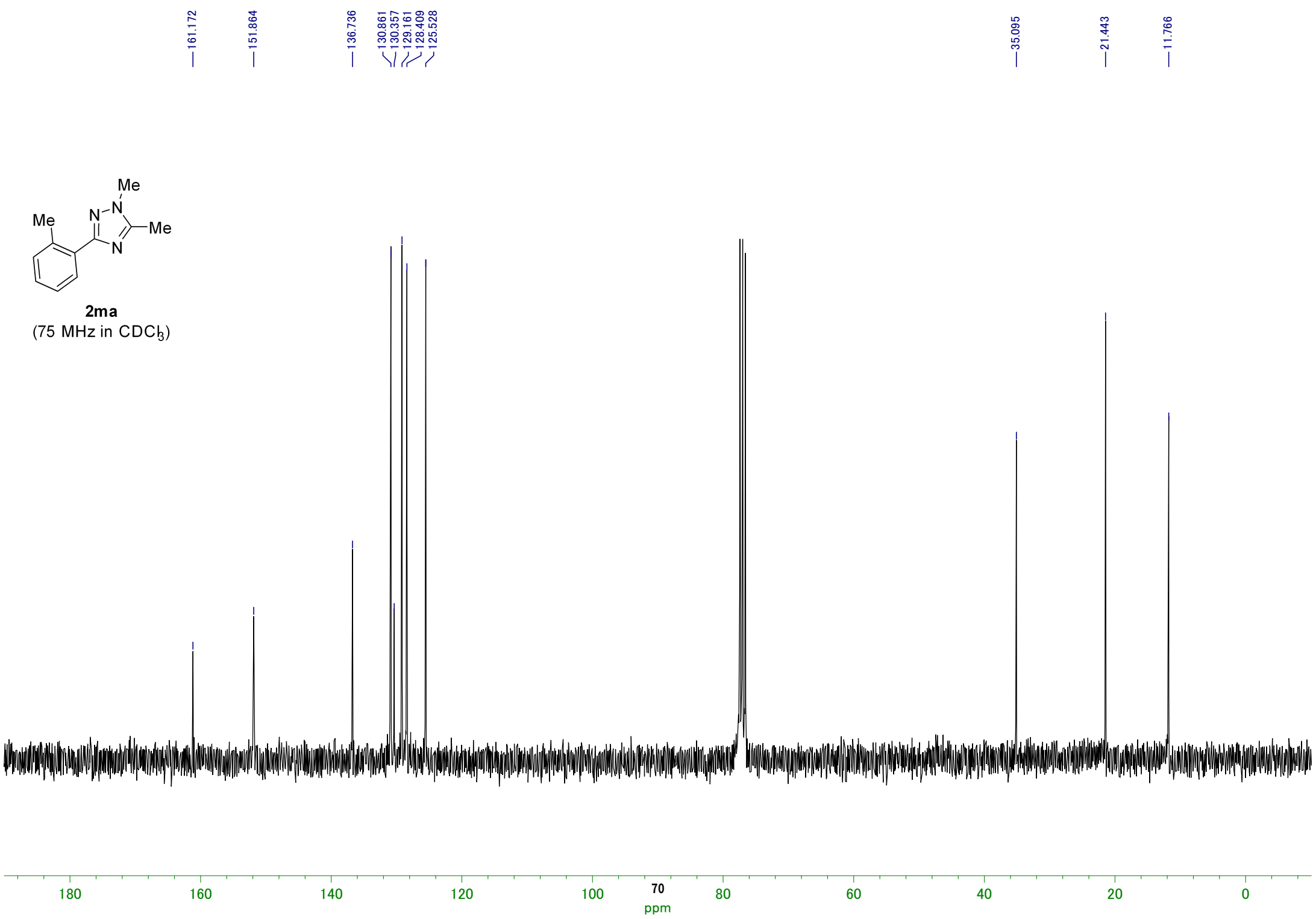

8.216
7.979
7.953
7.499
7.472
7.302
7.276
7.249
3.838
2.484
Me
N
N
Me
Br
N
2Ia
(300 MHz in CDCl3)
0.9
1.0
1.0
1.2
2.9
3.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

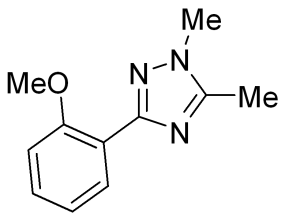

159.145
153.030
133.036
131.767
130.028
128.956
124.466
122.652
35.258
11.854
Me
N
N
Me
Br
N
2Ia
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



2ma

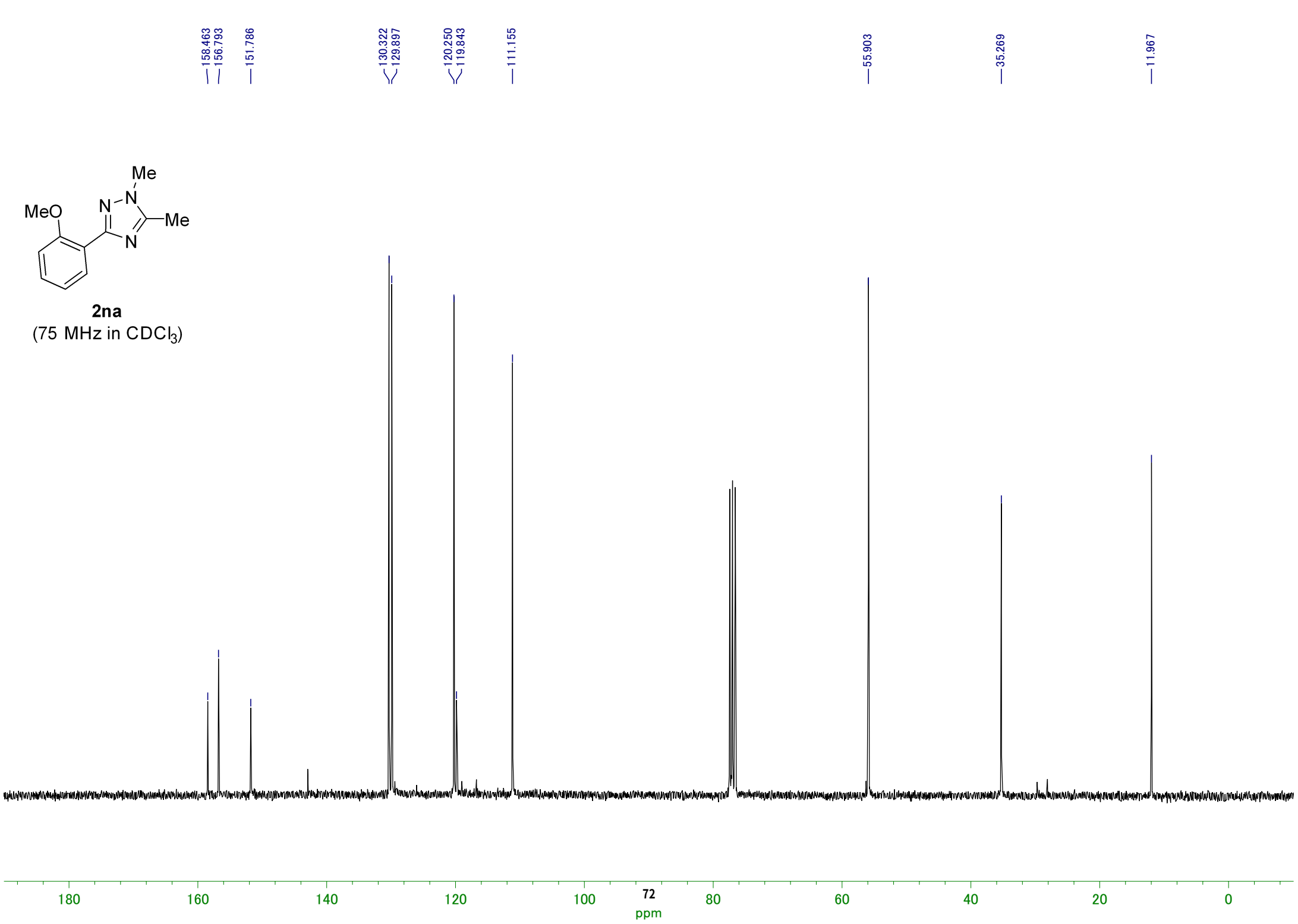
(300 MHz in $CDCl_3$)

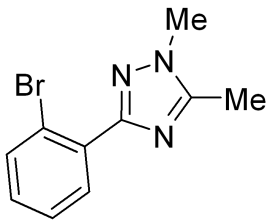

161.172
151.864
136.736
130.861
130.357
129.161
128.409
125.528
35.095
21.443
11.766
Me
N
N
Me
Me
N
2ma
(75 MHz in CDCl3)
180
160
140
120
100
70
ppm
80
60
40
20
0



2na

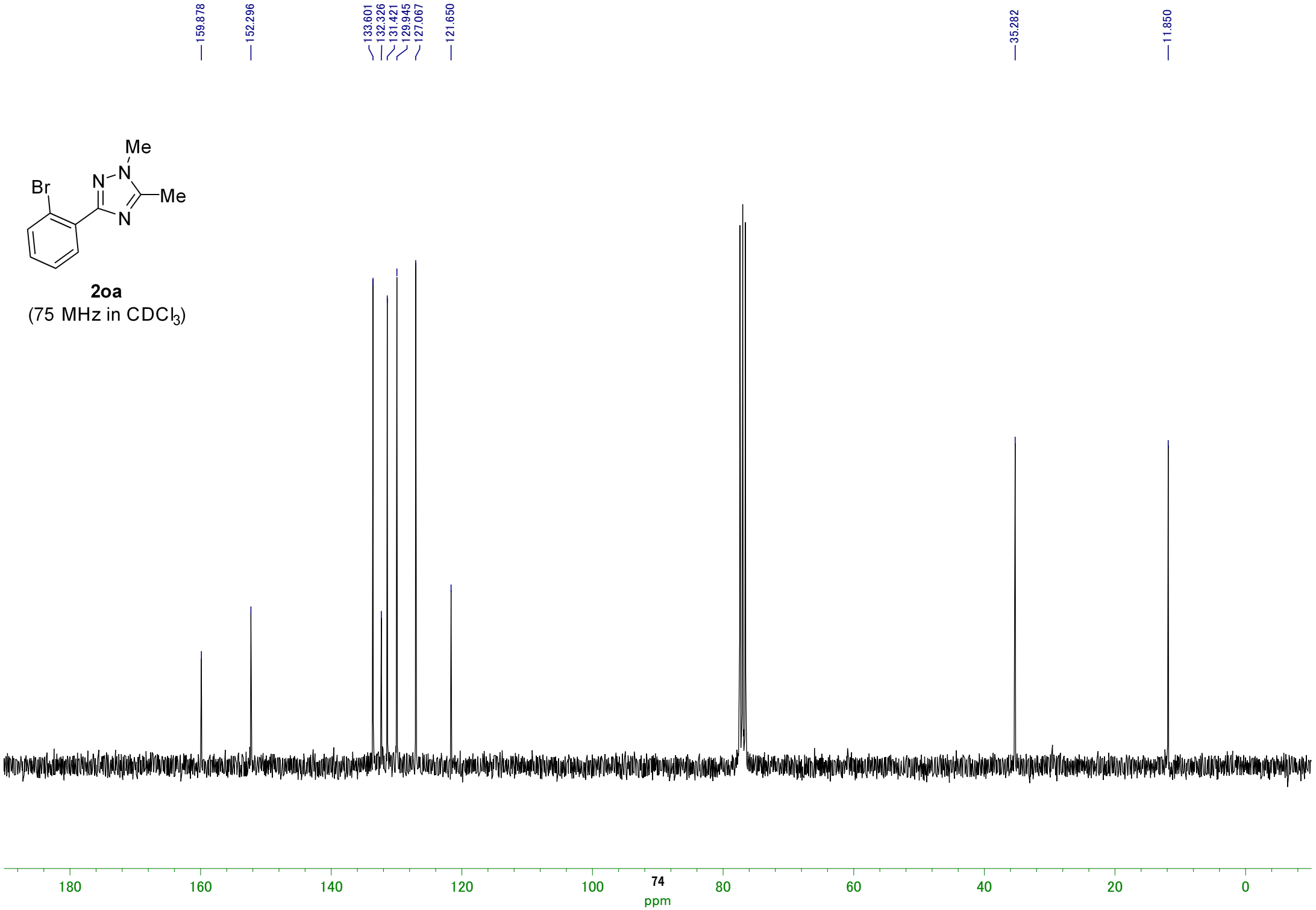
(300 MHz in $CDCl_3$)

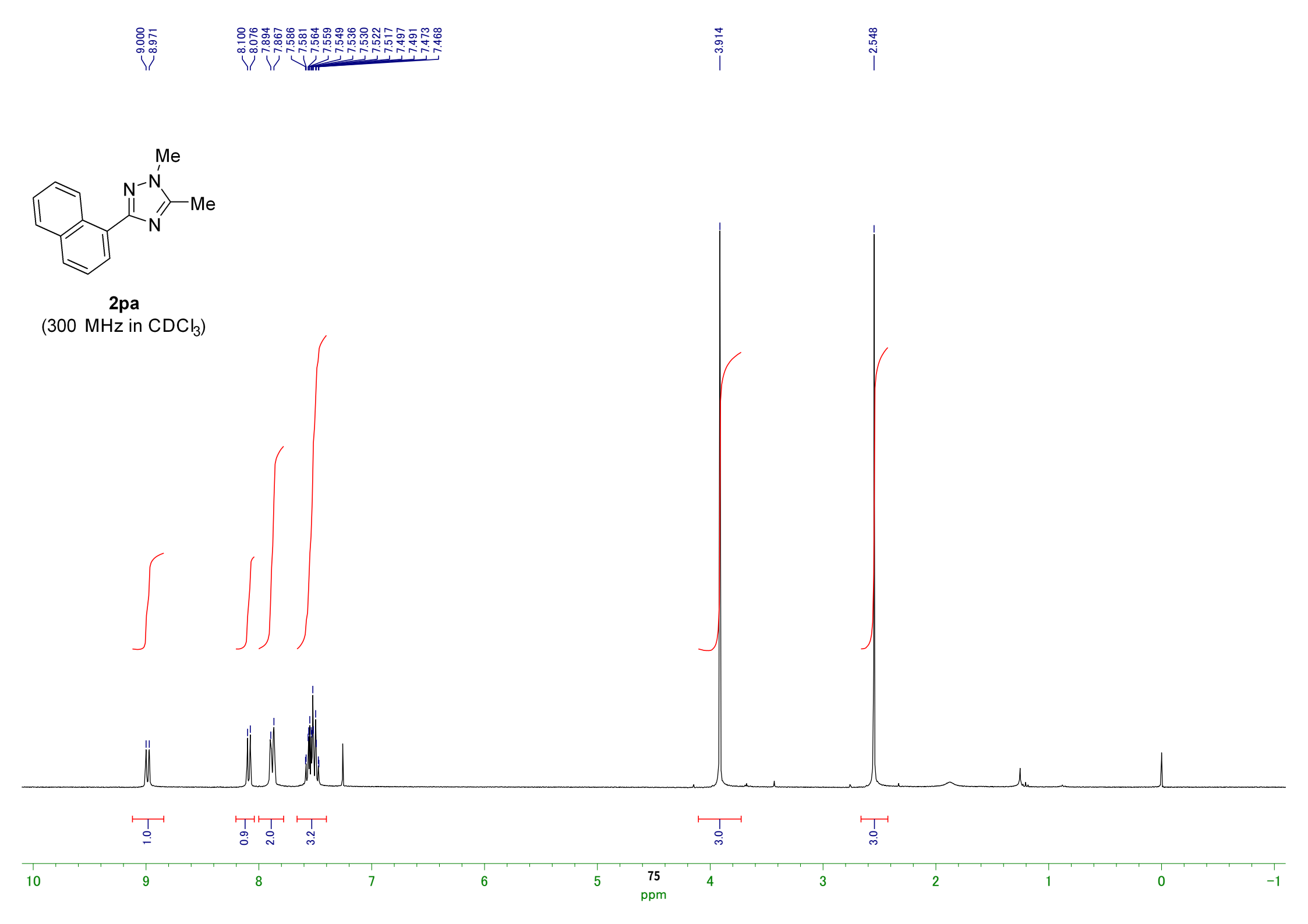

158.463
156.793
151.786
130.322
129.897
120.250
119.843
111.155
55.903
35.269
11.967
Me
N
N
MeO
Me
N
2na
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

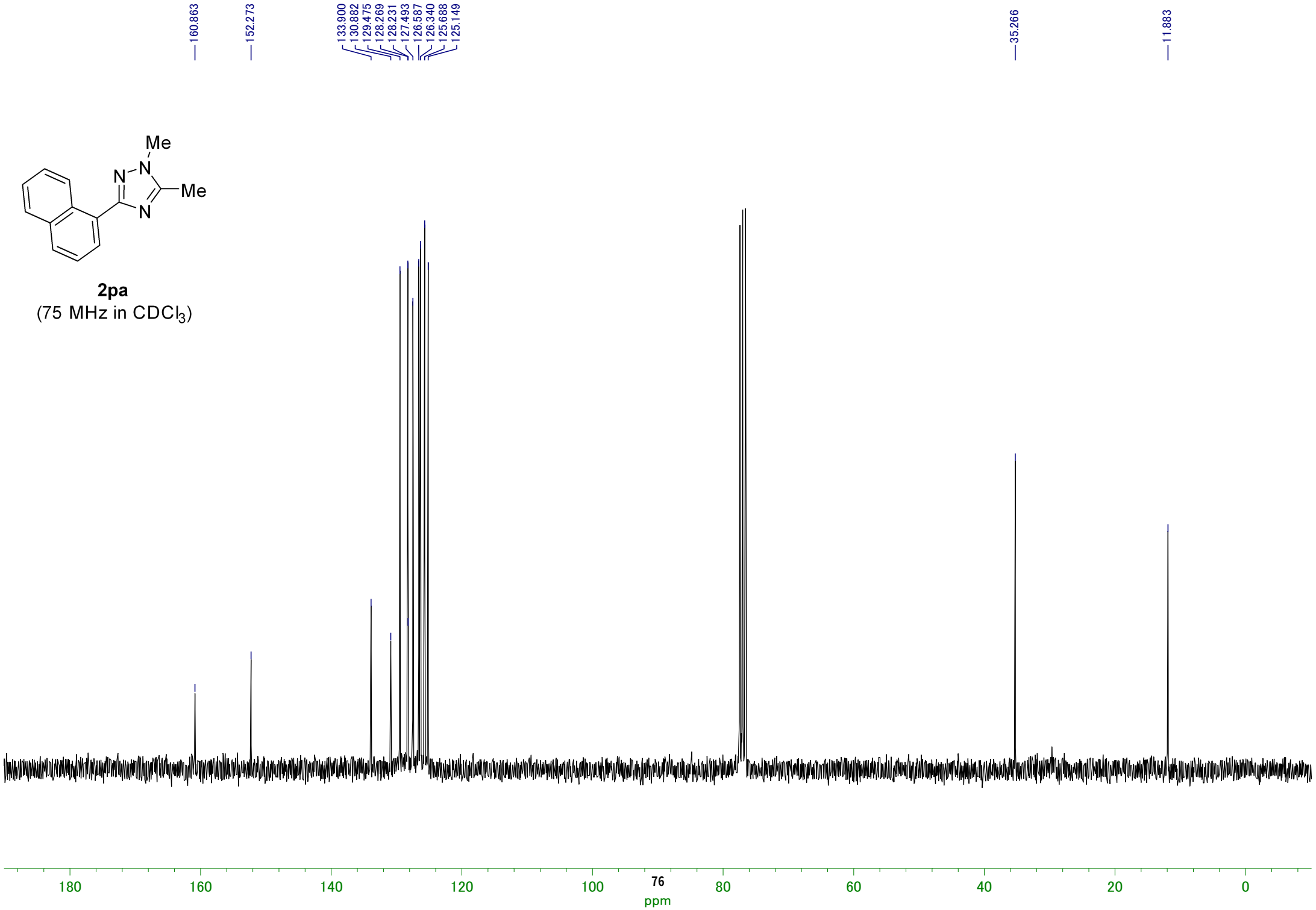


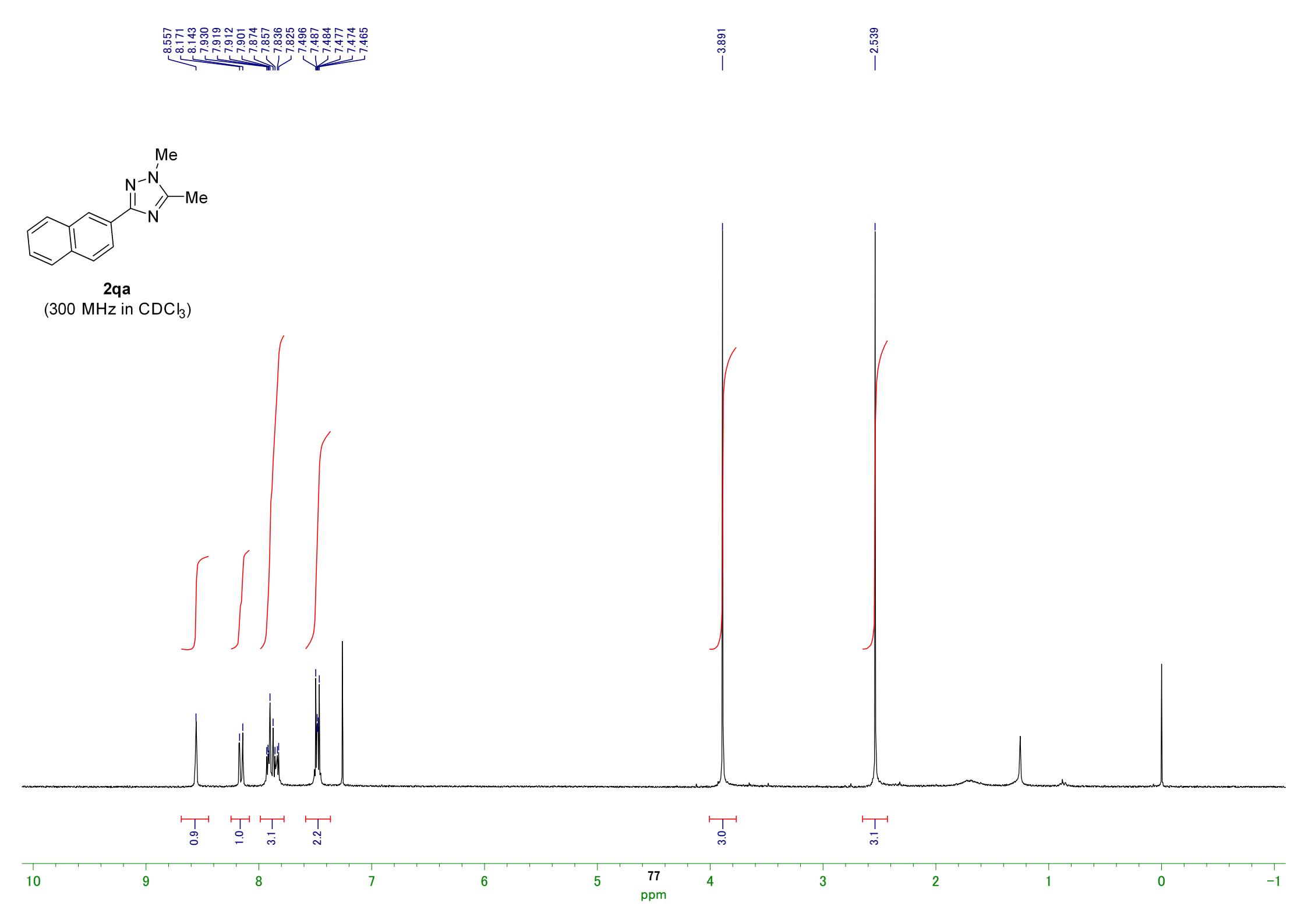
2oa

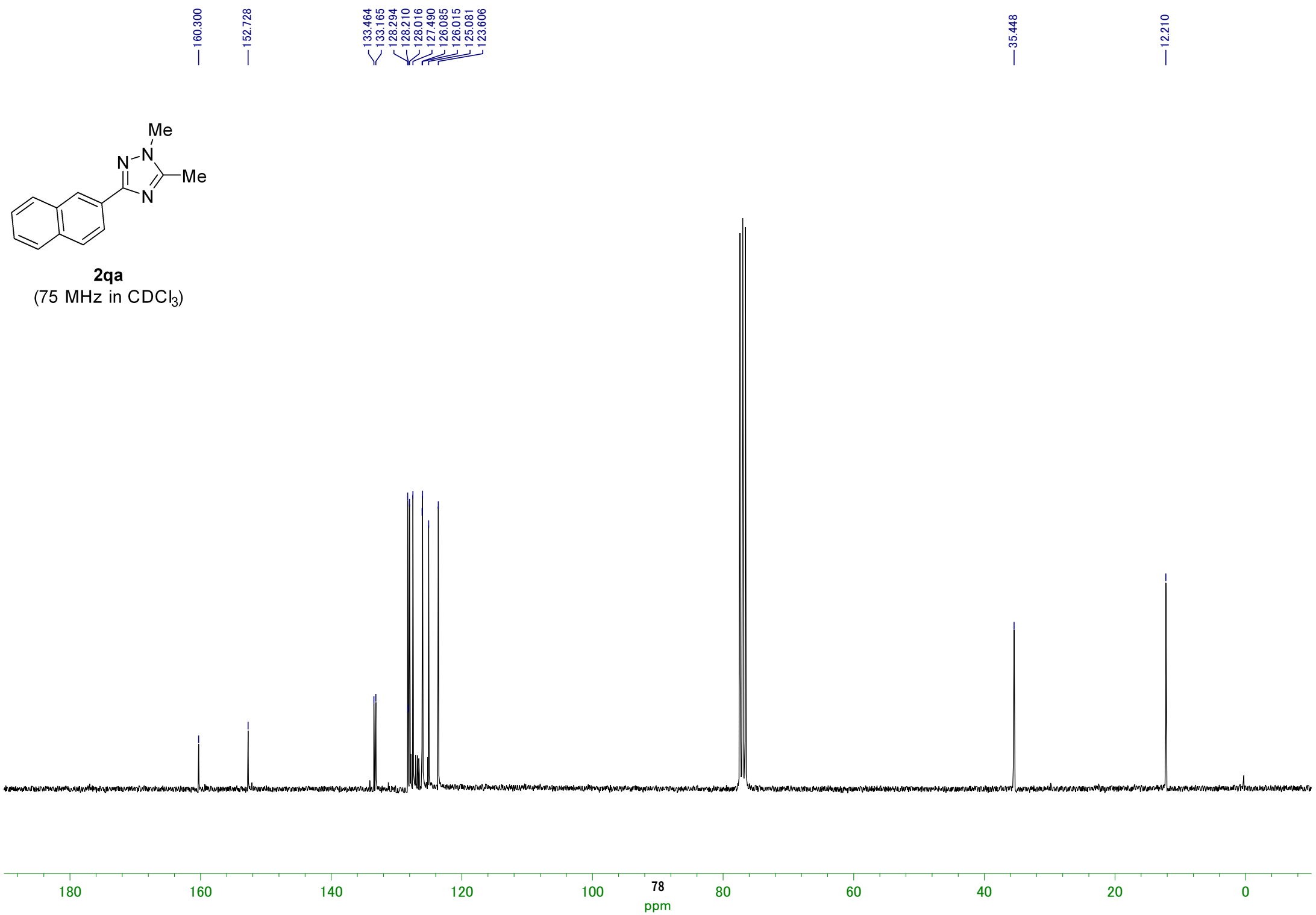
(300 MHz in $CDCl_3$)

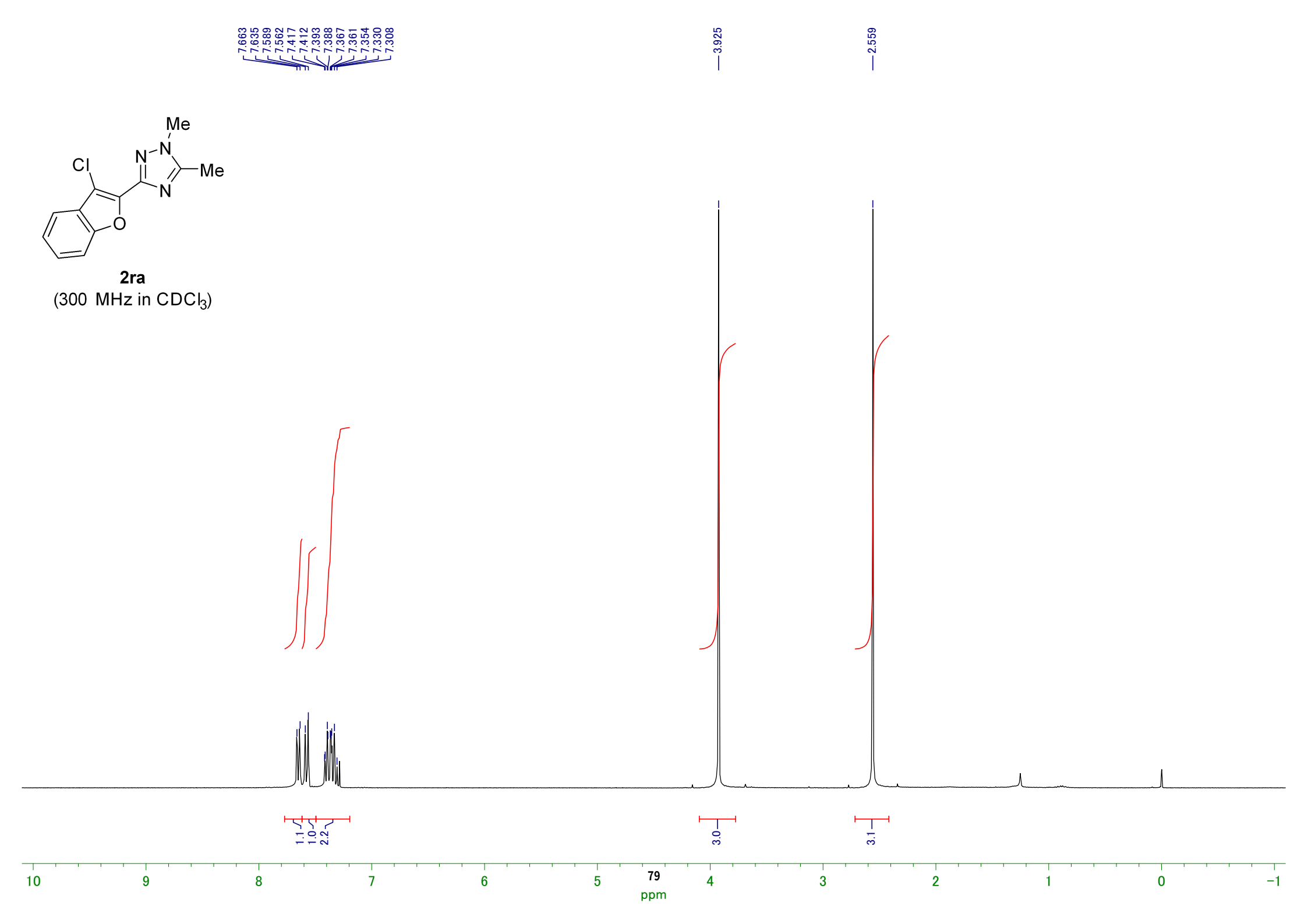

159.878
152.296
133.601
132.326
131.421
129.945
127.067
121.650
35.282
11.850
Me
N
N
Br
Me
N
2oa
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

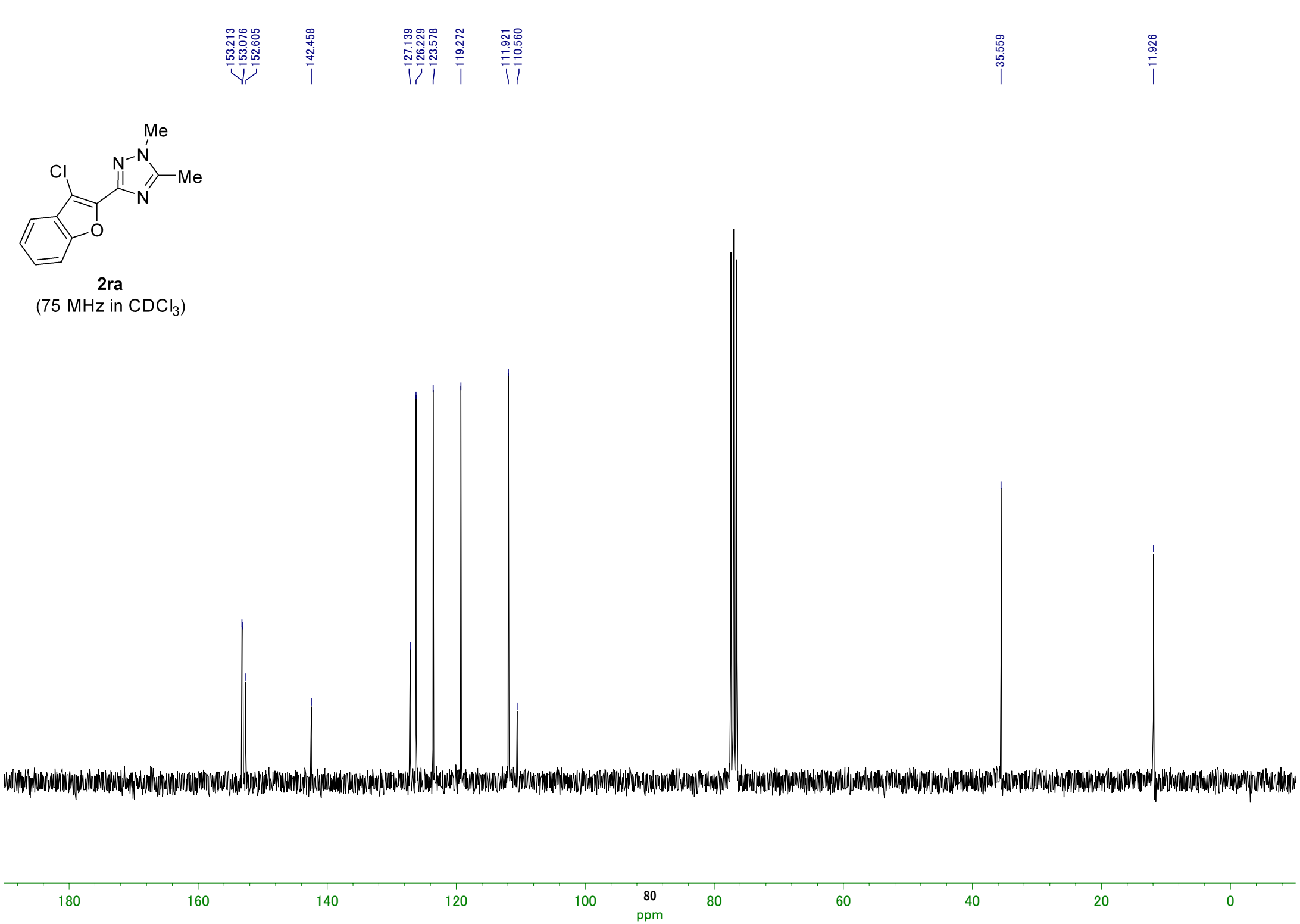

9.000
8.971
8.100
8.076
7.894
7.867
7.586
7.581
7.564
7.559
7.549
7.536
7.530
7.522
7.517
7.497
7.491
7.473
7.468
3.914
2.548
Me
N
N
Me
N
2pa
(300 MHz in CDCl3)
1.0
0.9
2.0
3.2
3.0
3.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

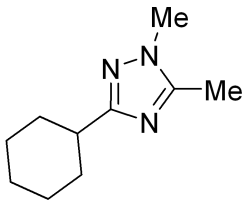

160.863
152.273
133.900
130.882
129.475
128.269
128.231
127.493
126.587
126.340
125.688
125.149
35.266
11.883
Me
N
N
Me
N
2pa
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm


8.557
8.171
8.143
7.930
7.919
7.912
7.901
7.874
7.857
7.836
7.825
7.496
7.487
7.484
7.477
7.474
7.465
3.891
2.539
Me
N
N
Me
N
2qa
(300 MHz in CDCl3)
0.9
1.0
3.1
2.2
3.0
3.1
10
9
8
7
6
5
4
3
2
1
0
−1
ppm


160.300
152.728
133.464
133.165
128.294
128.210
128.016
127.490
126.085
126.015
125.081
123.606
35.448
12.210
Me
N
N
Me
N
2qa
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

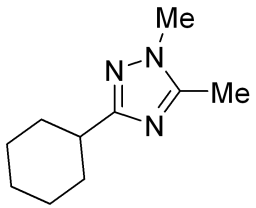

7.663
7.635
7.589
7.562
7.417
7.412
7.393
7.388
7.367
7.361
7.354
7.330
7.308
3.925
2.559
Me
N
N
Cl
Me
N
O
2ra
(300 MHz in CDCl3)
1.1
1.0
2.2
3.0
3.1
10
9
8
7
6
5
4
3
2
1
0
−1
ppm


153.213
153.076
152.605
142.458
127.139
126.229
123.578
119.272
111.921
110.560
35.559
11.926
Me
N
N
Me
Cl
N
O
2ra
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



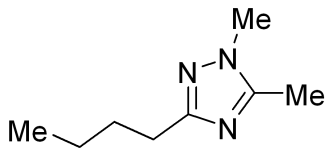
2sa

(300 MHz in $CDCl_3$)



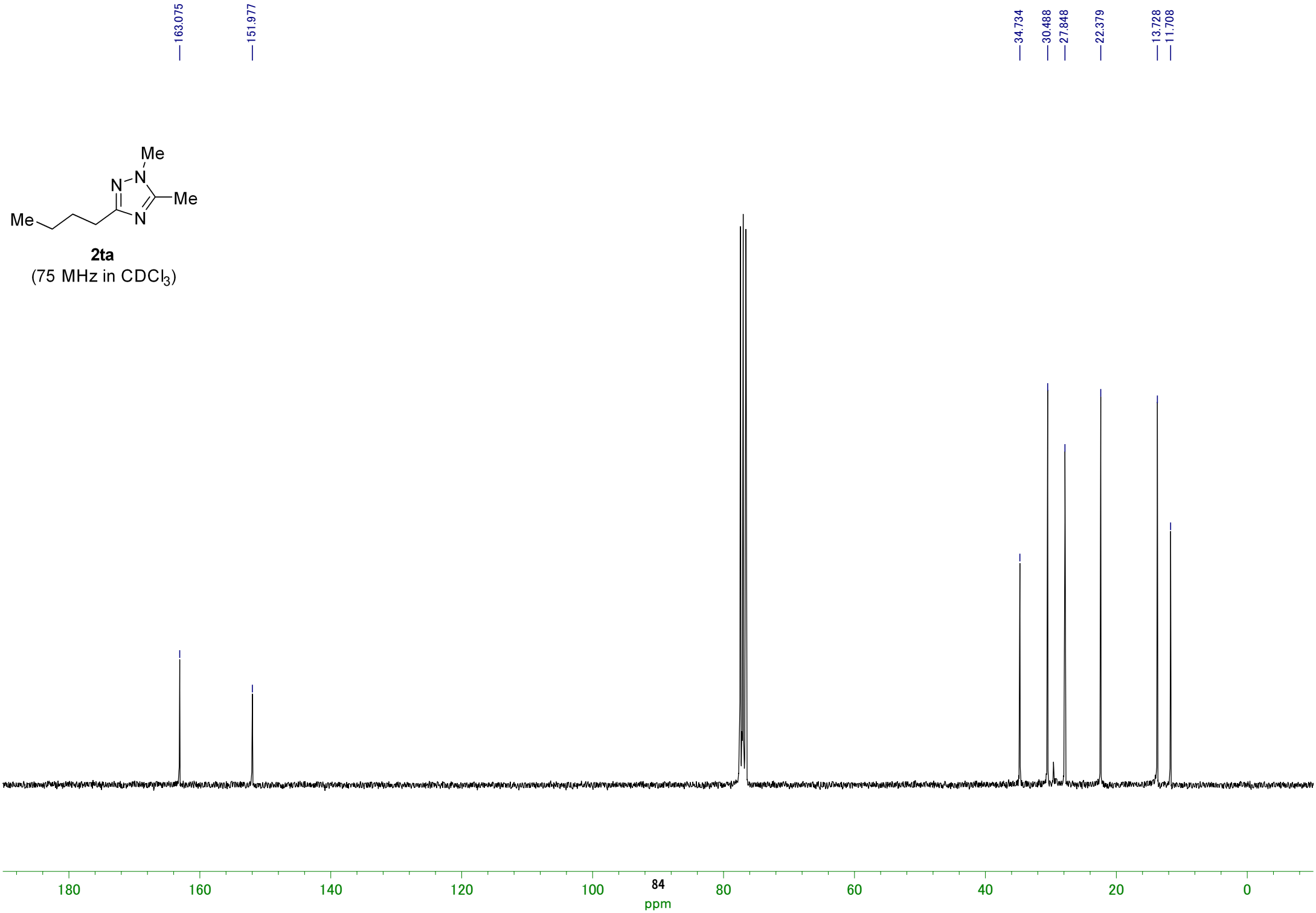
2sa

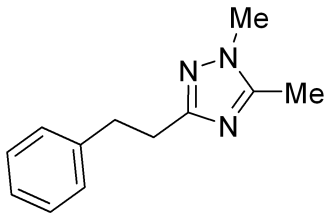
(75 MHz in $CDCl_3$)



2ta

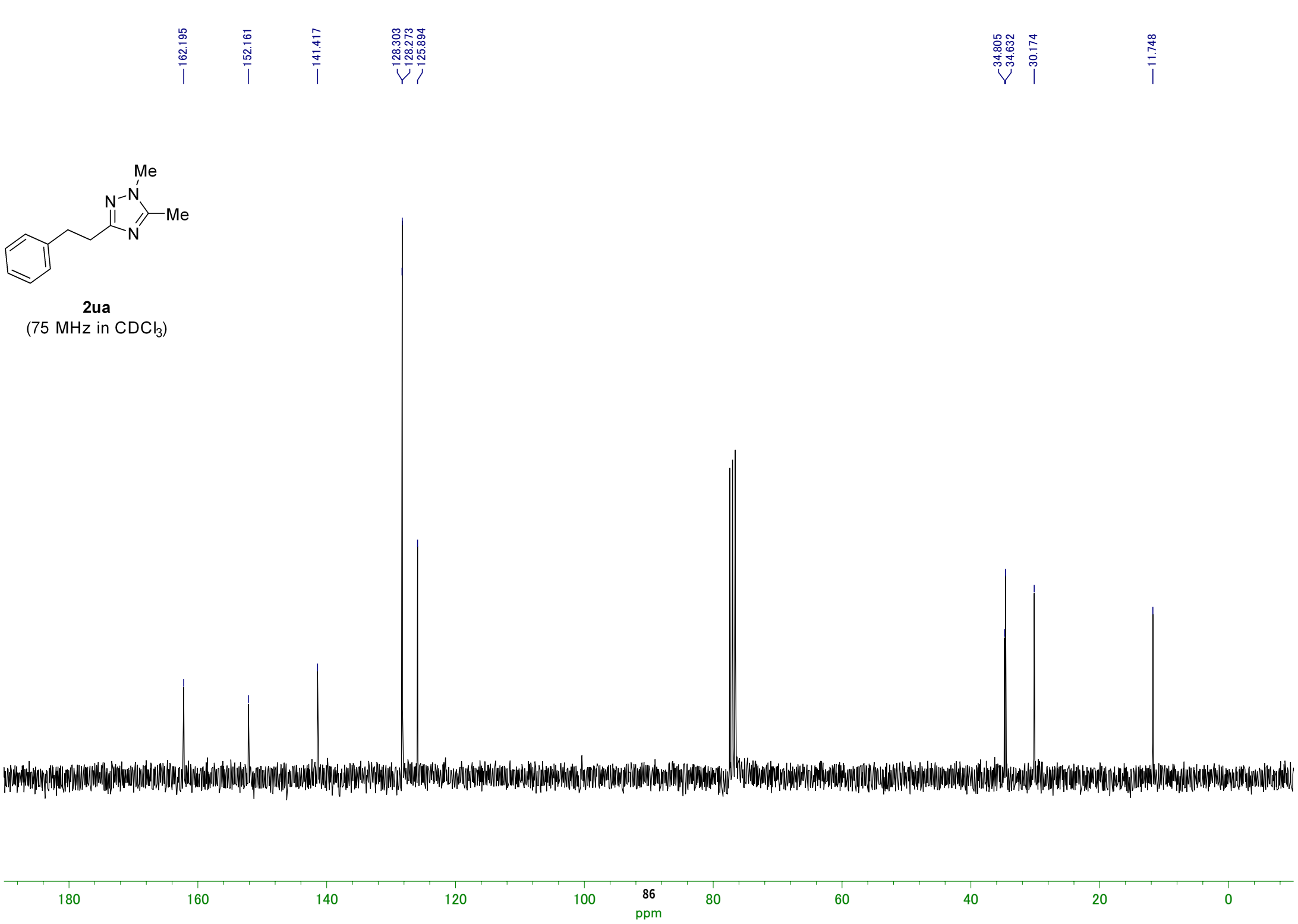
(300 MHz in $CDCl_3$)

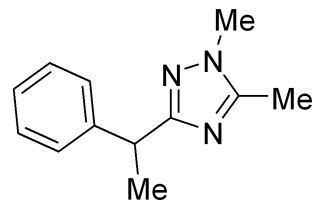

163.075
151.977
34.734
30.488
27.848
22.379
13.728
11.708
Me
N
N
Me
Me
N
2ta
(75 MHz in CDCl3)
180
160
140
120
100
84
ppm
80
60
40
20
0



2ua

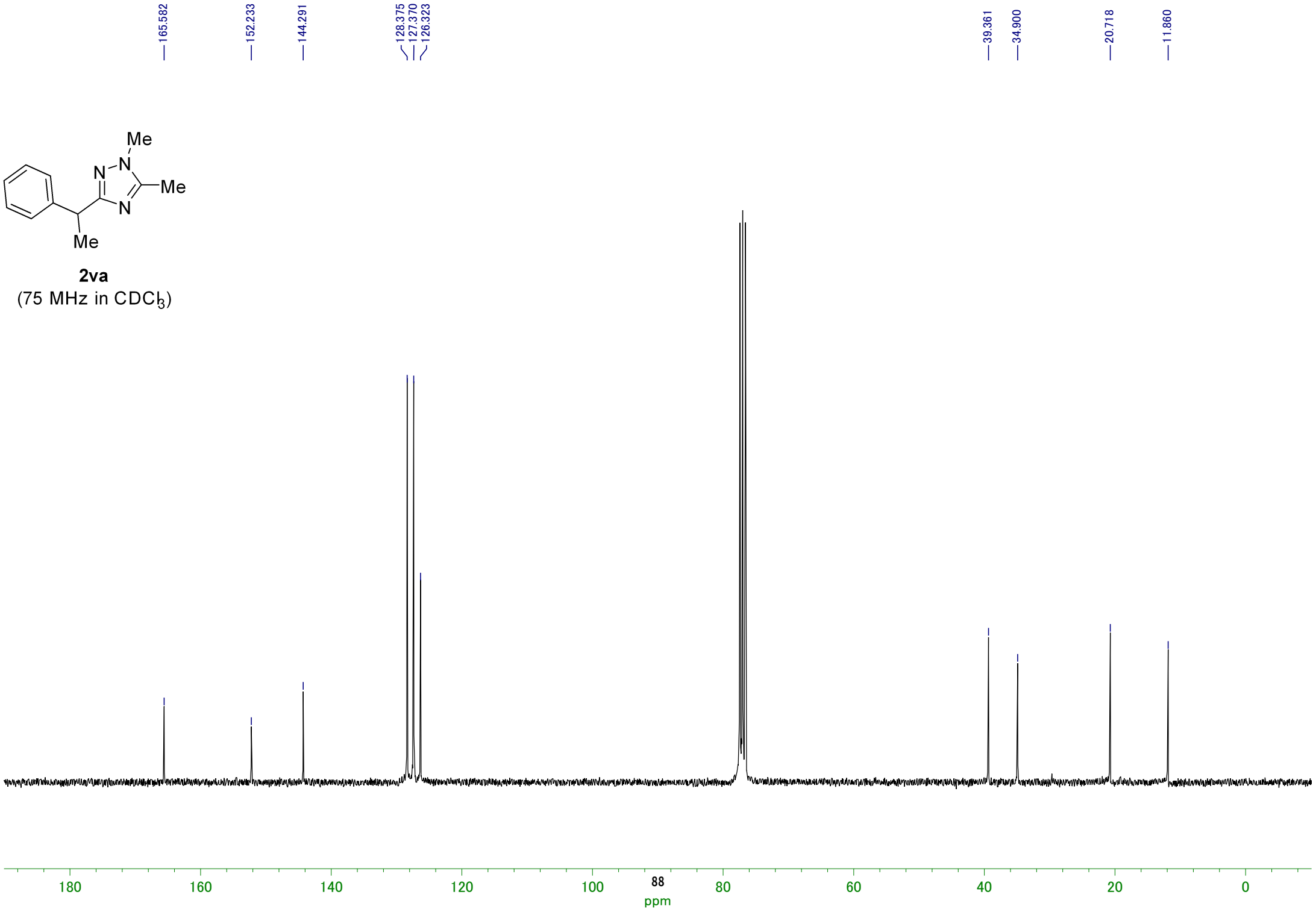
(300 MHz in $CDCl_3$)

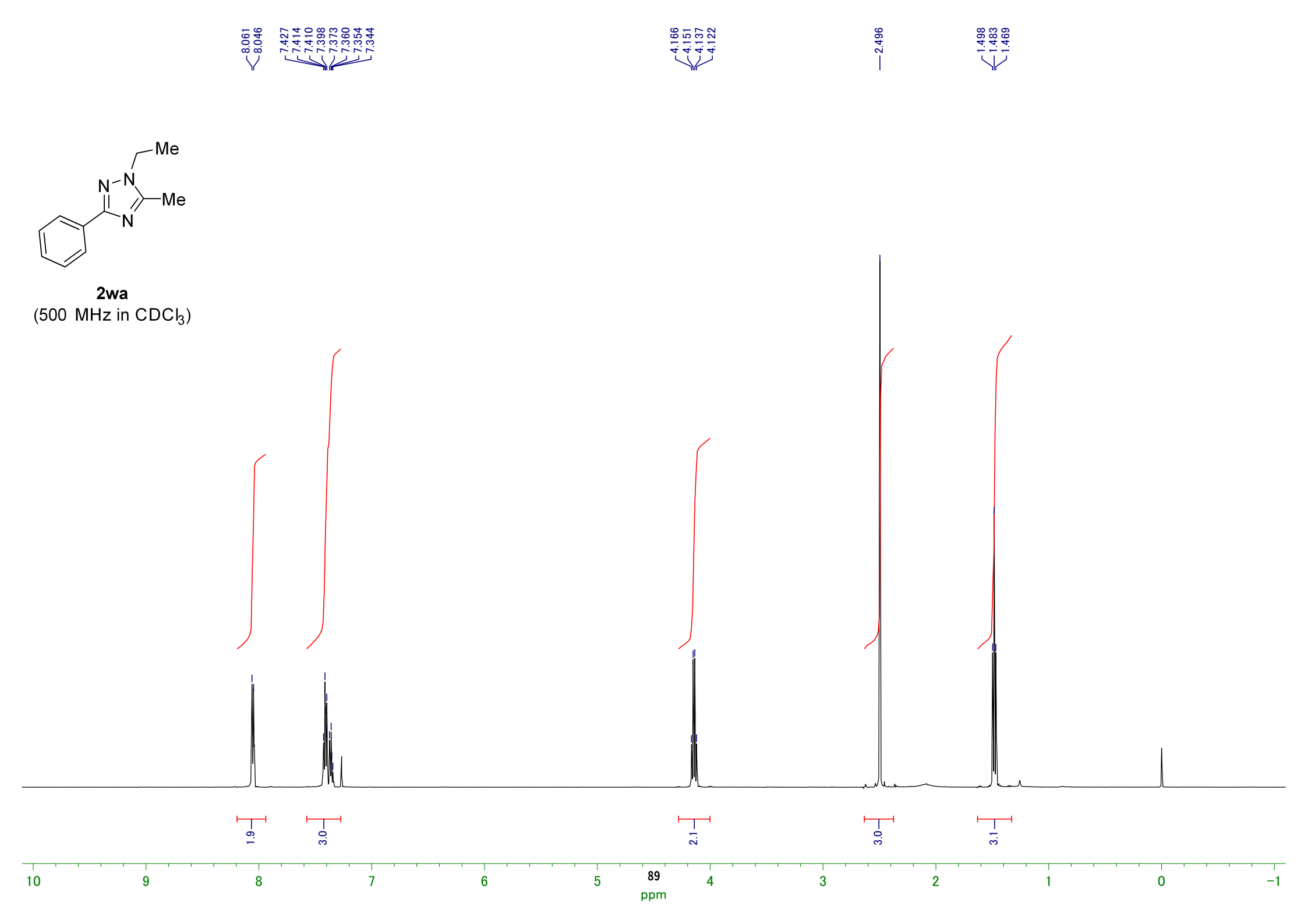

162.195
152.161
141.417
128.303
128.273
125.894
34.805
34.632
30.174
11.748
Me
N
N
Me
N
2ua
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

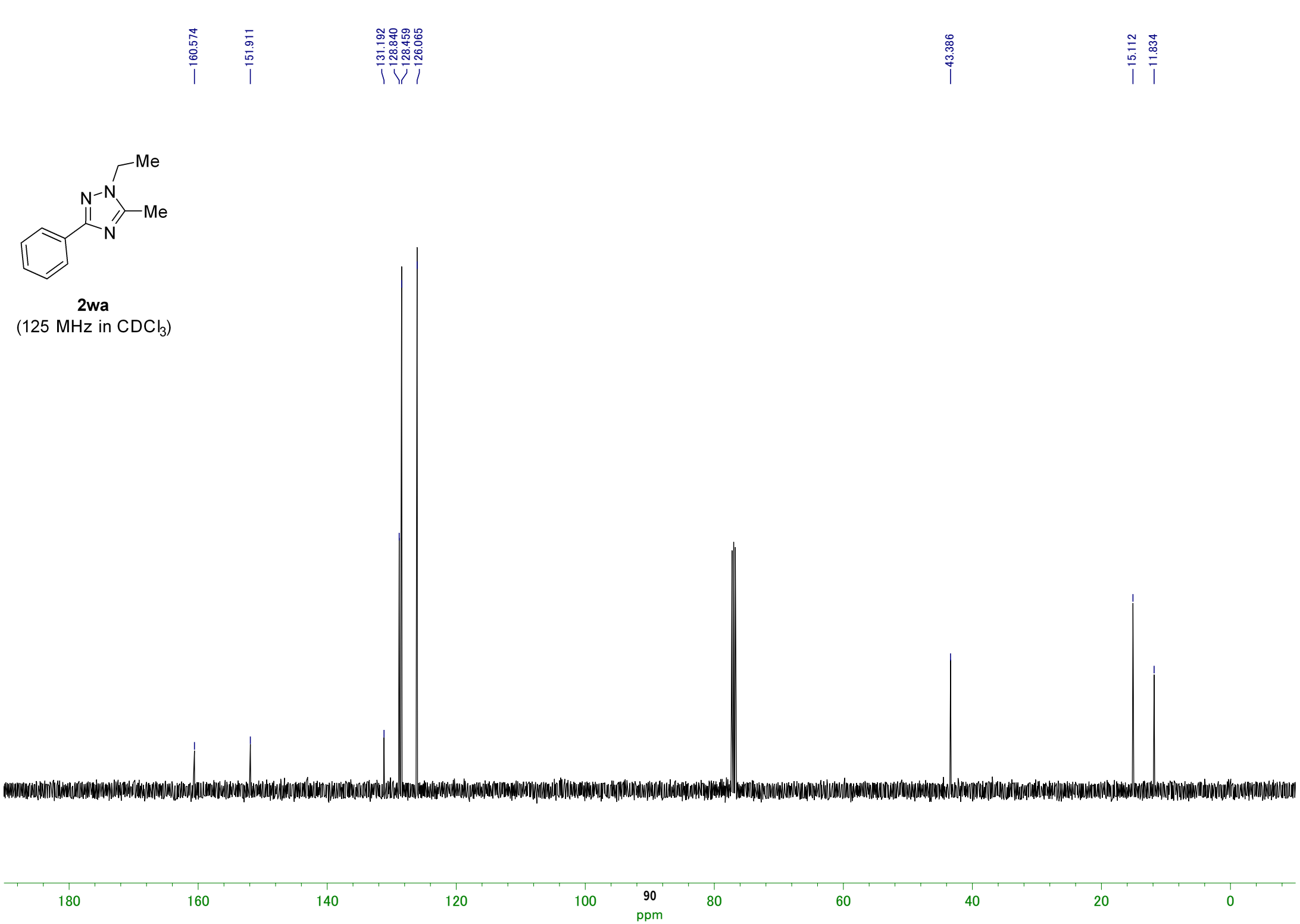


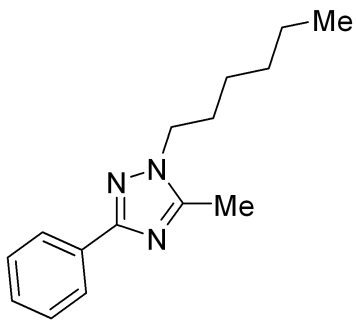
2va

(300 MHz in $CDCl_3$)


165.582
152.233
144.291
128.375
127.370
126.323
39.361
34.900
20.718
11.860
Me
N
N
Me
N
Me
2va
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

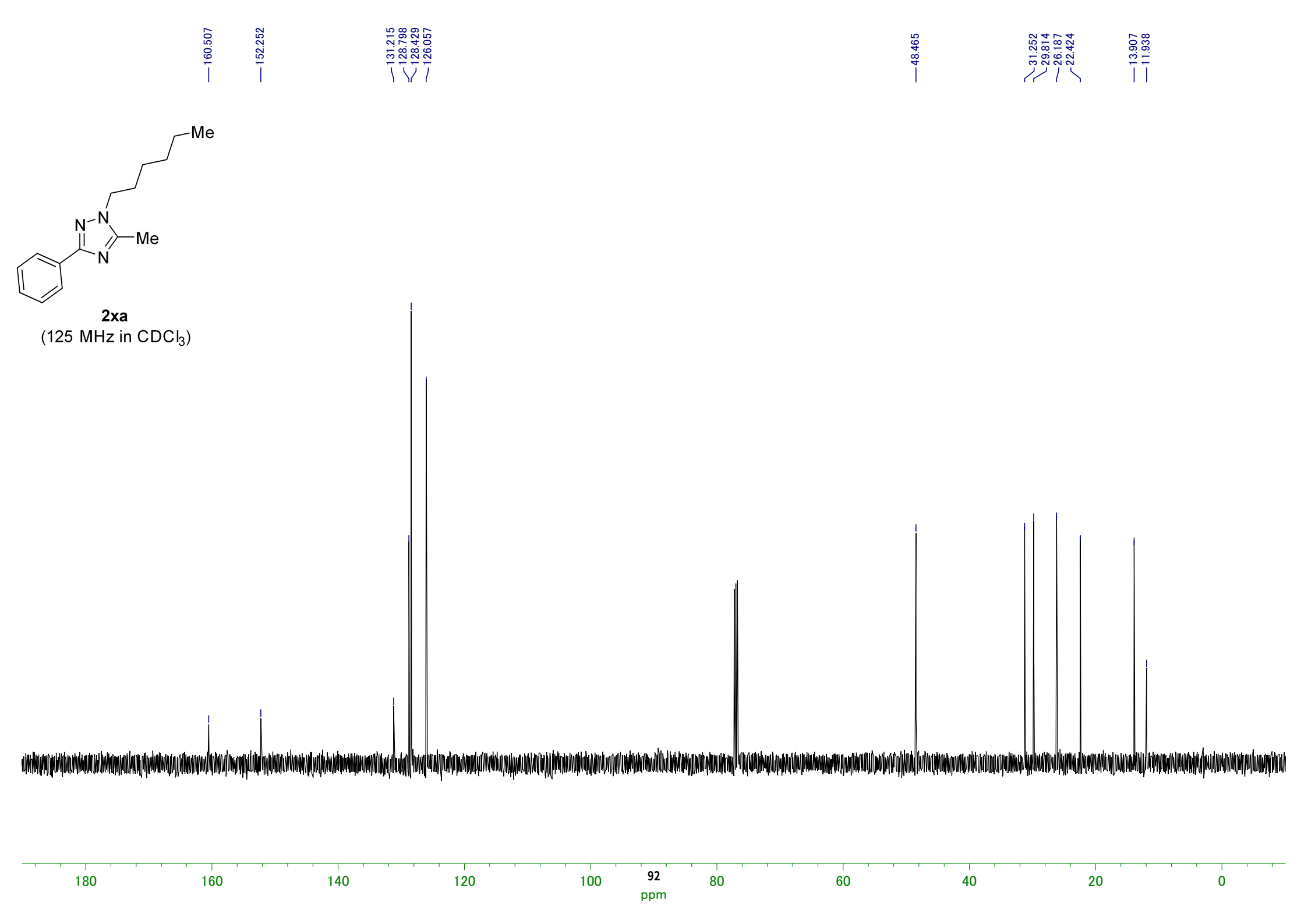

8.061
8.046
7.427
7.414
7.410
7.398
7.373
7.360
7.354
7.344
4.166
4.151
4.137
4.122
2.496
1.498
1.483
1.469
Me
N
N
Me
N
2wa
(500 MHz in CDCl3)
1.9
3.0
2.1
3.0
3.1
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

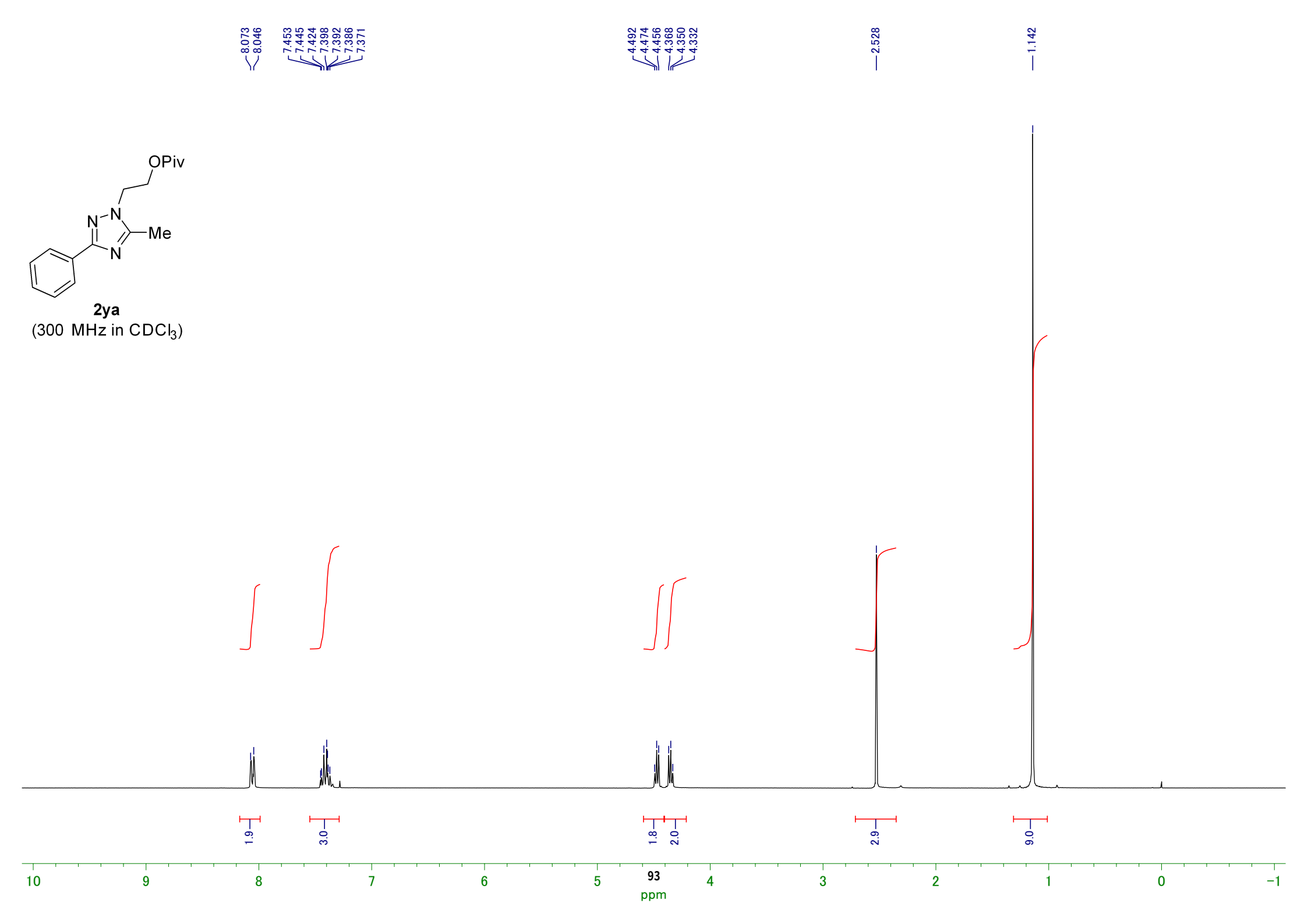

160.574
151.911
131.192
128.840
128.459
126.065
43.386
15.112
11.834
Me
N
N
Me
N
2wa
(125 MHz in CDCl3)
180
160
140
120
100
90
80
60
40
20
0
ppm

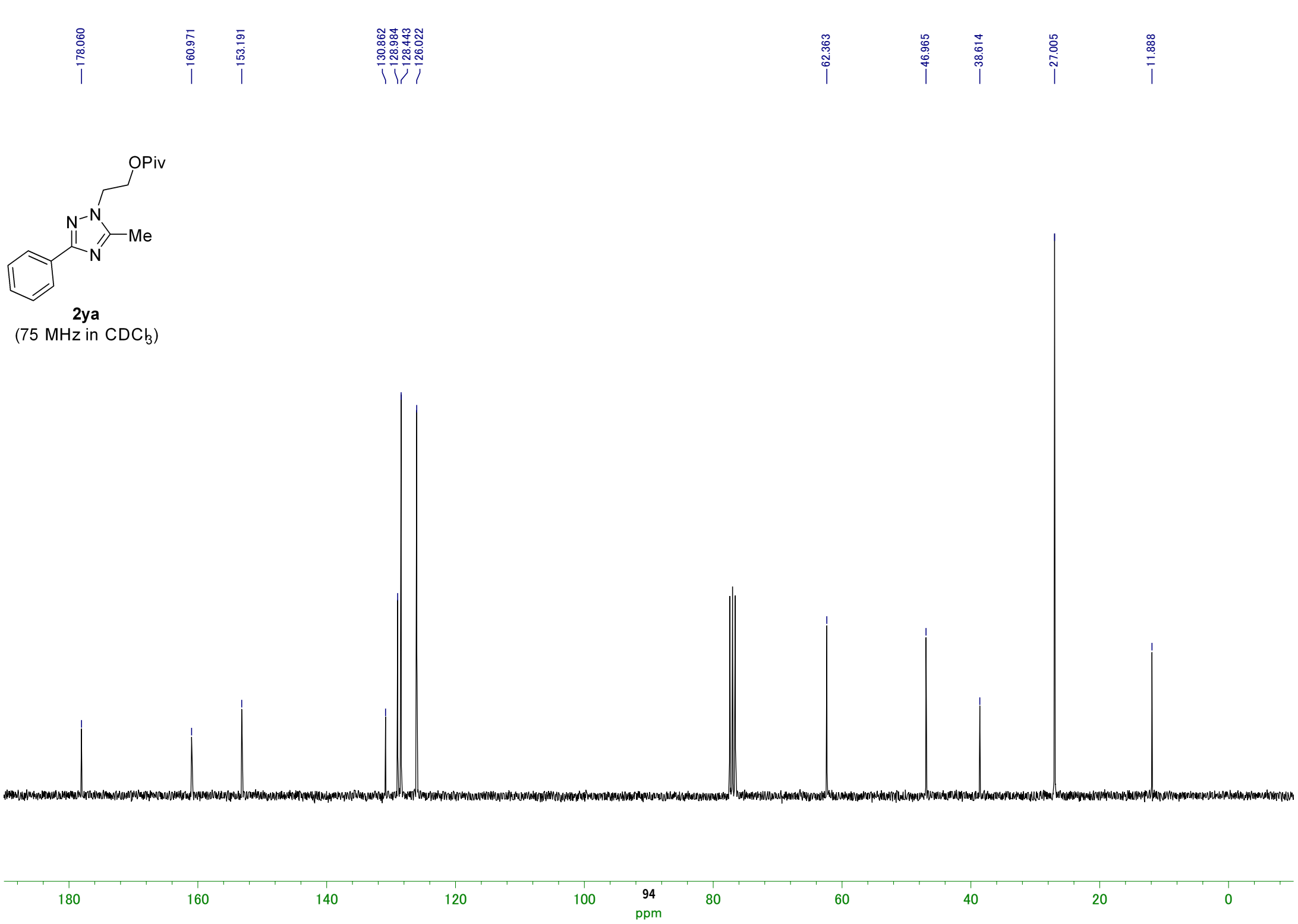


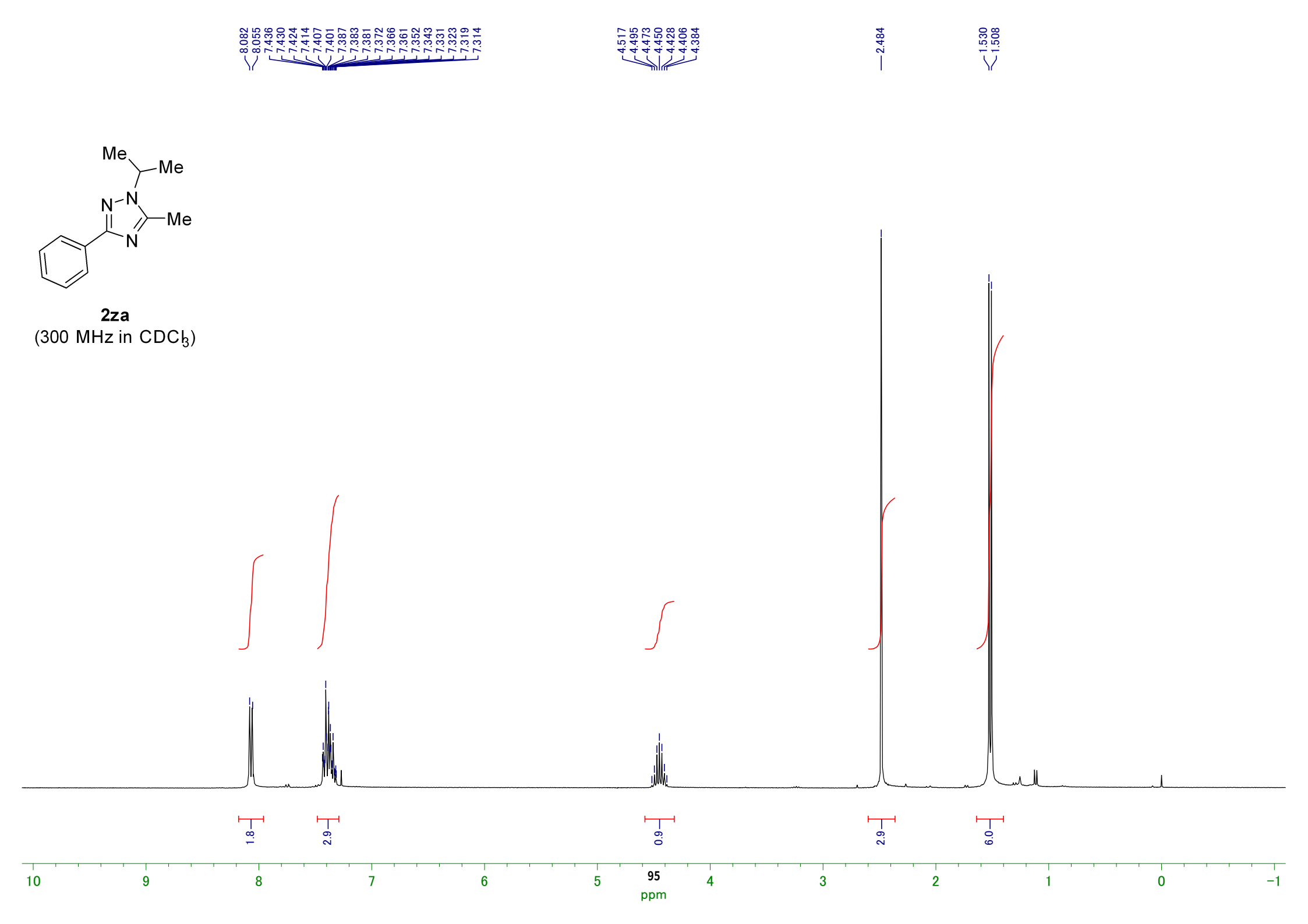
2xa

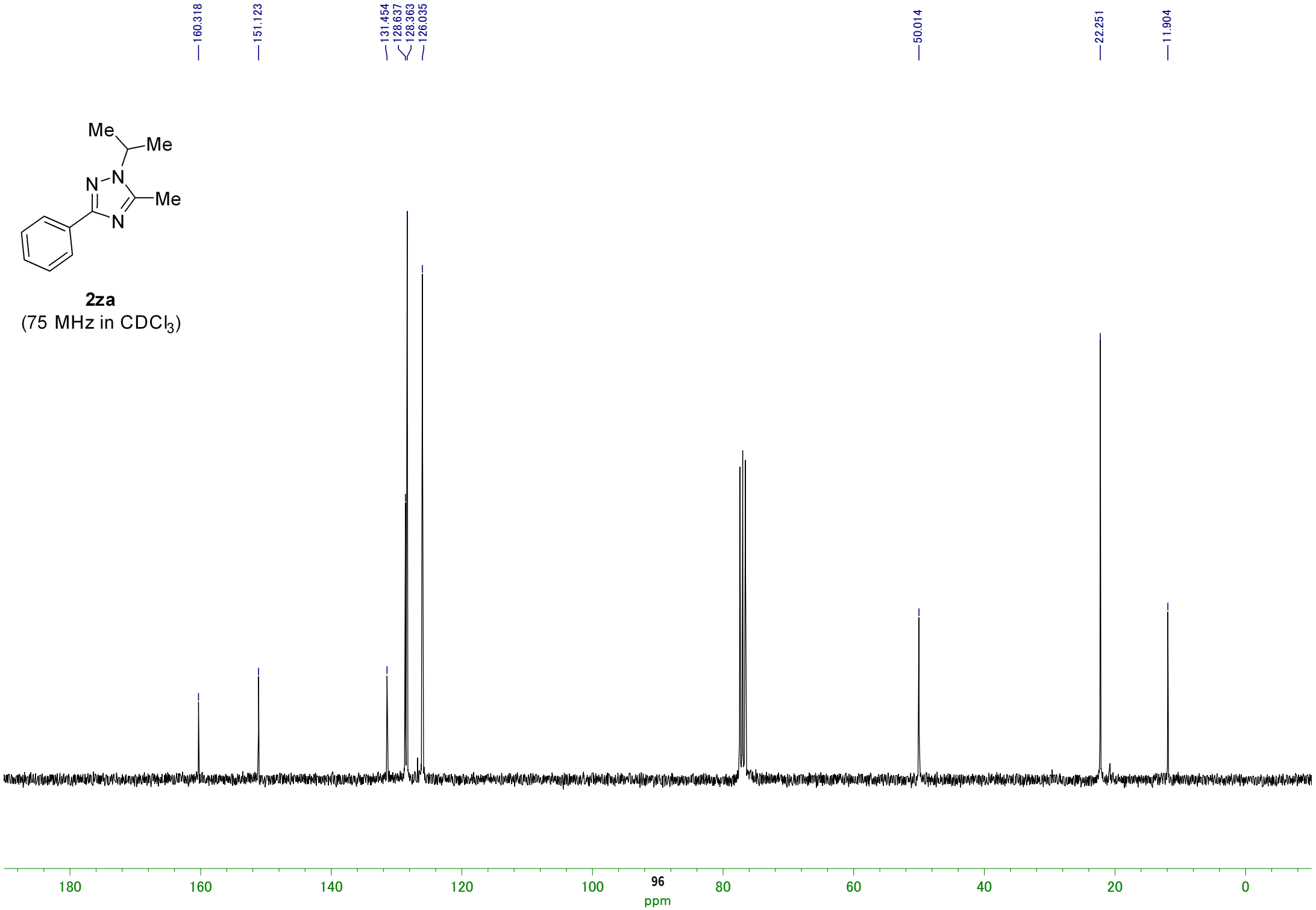
(500 MHz in $CDCl_3$)


160.507
152.252
131.215
128.798
128.429
126.057
48.465
31.252
29.814
26.187
22.424
13.907
11.938
Me
N
N
Me
N
2xa
(125 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm

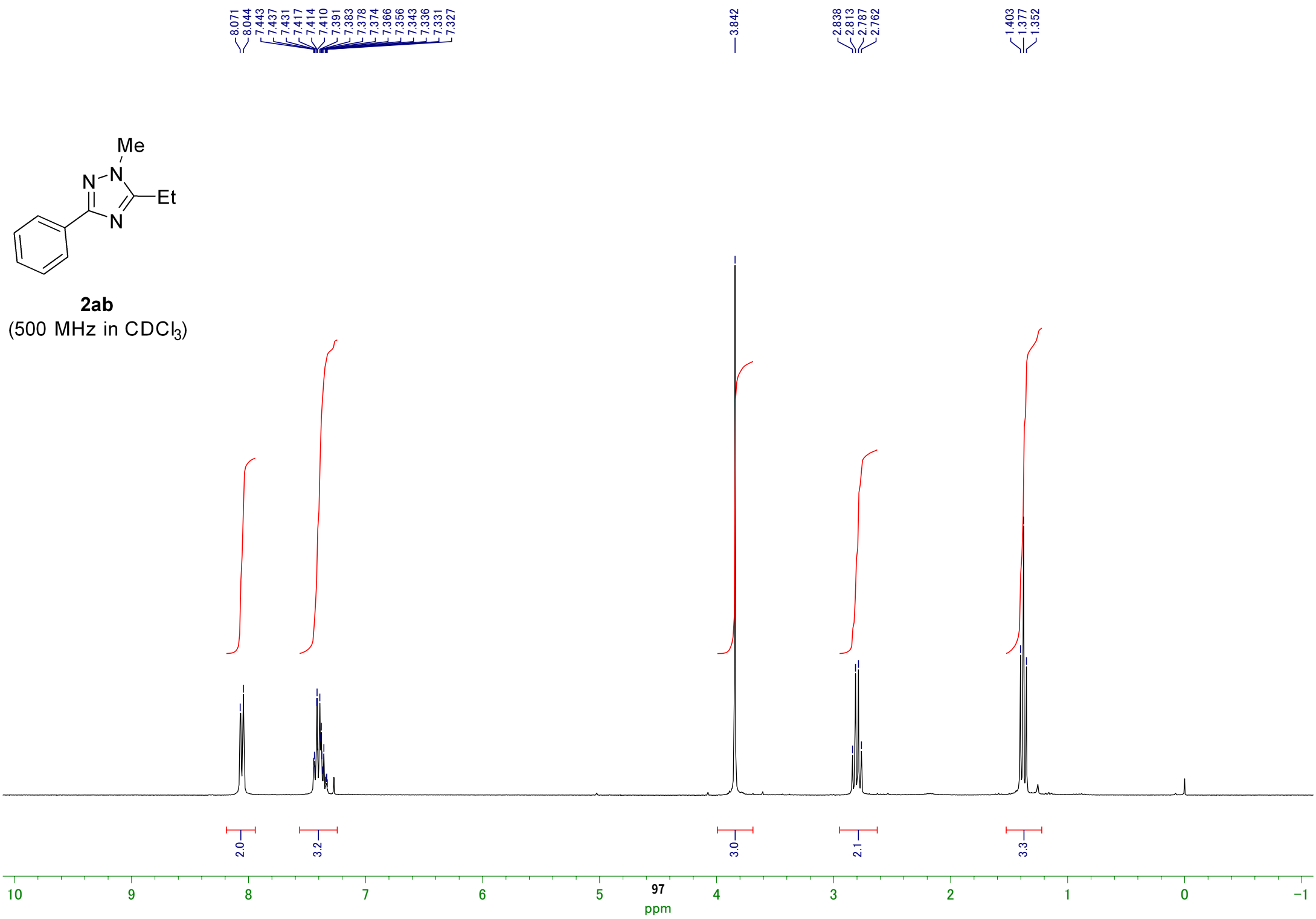

8.073
8.046
7.453
7.445
7.424
7.398
7.392
7.386
7.371
4.492
4.474
4.456
4.368
4.350
4.332
2.528
1.142
OPiv
N
N
Me
N
2ya
(300 MHz in CDCl3)
1.9
3.0
1.8
2.0
2.9
9.0
10
9
8
7
6
5
4
3
2
1
0
−1
93
ppm

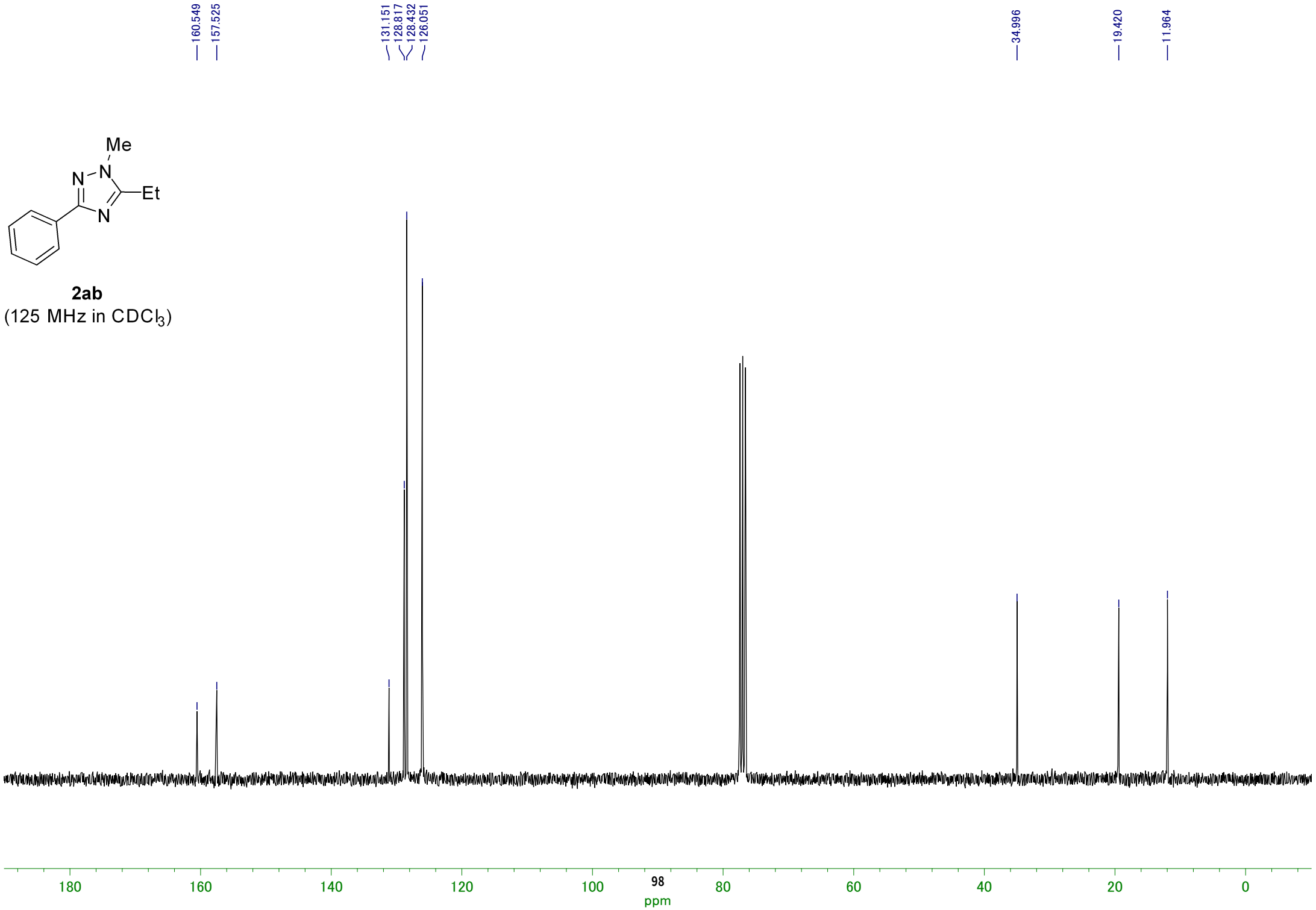

178.060
160.971
153.191
130.862
128.984
128.443
126.022
62.363
46.965
38.614
27.005
11.888
OPiv
N
N
Me
N
2ya
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm


8.082
8.055
7.436
7.430
7.424
7.414
7.407
7.401
7.387
7.383
7.381
7.372
7.366
7.361
7.352
7.343
7.331
7.323
7.319
7.314
4.517
4.495
4.473
4.450
4.428
4.406
4.384
2.484
1.530
1.508
Me
Me
N
N
Me
N
2za
(300 MHz in CDCl3)
1.8
2.9
0.9
2.9
6.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

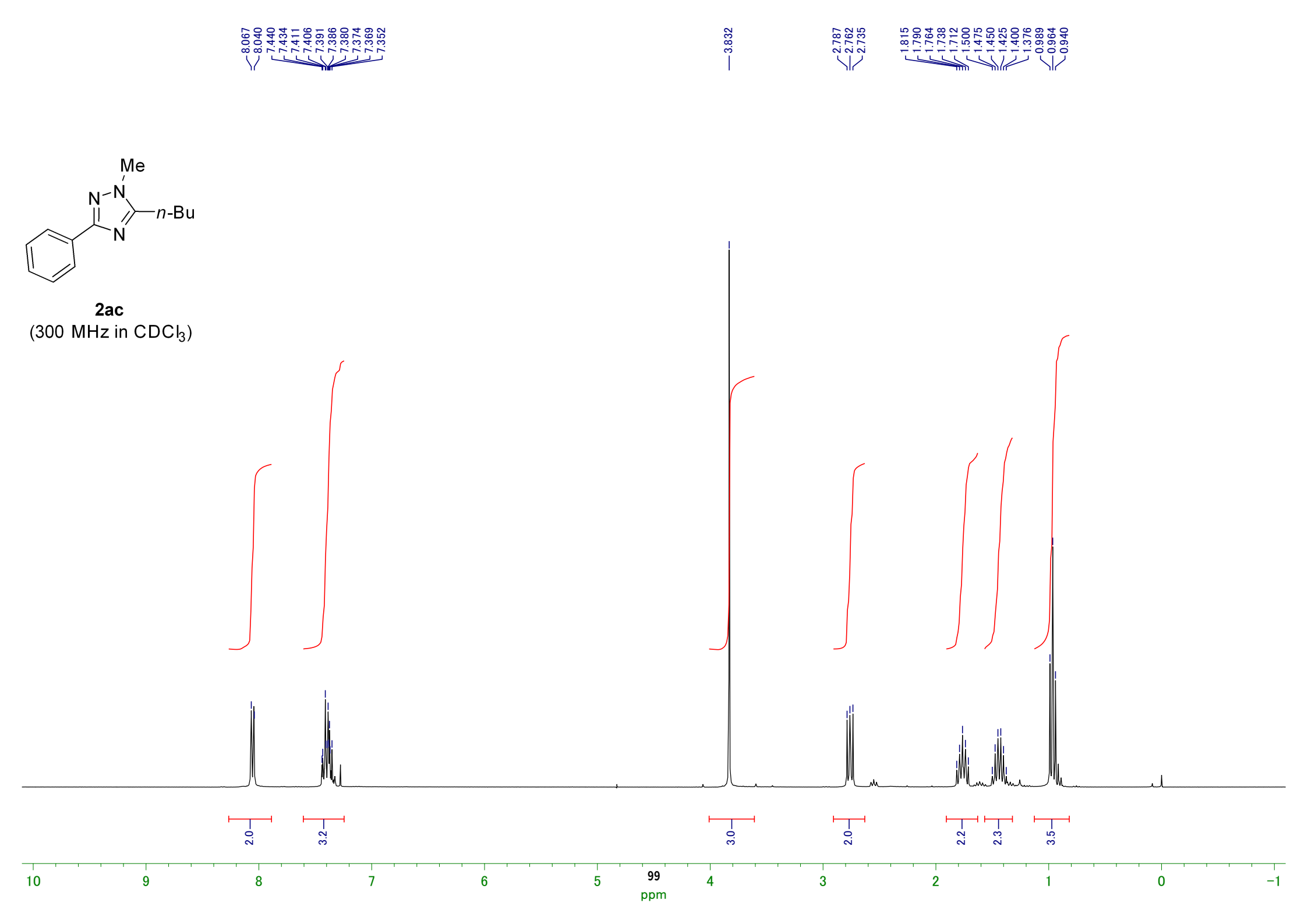


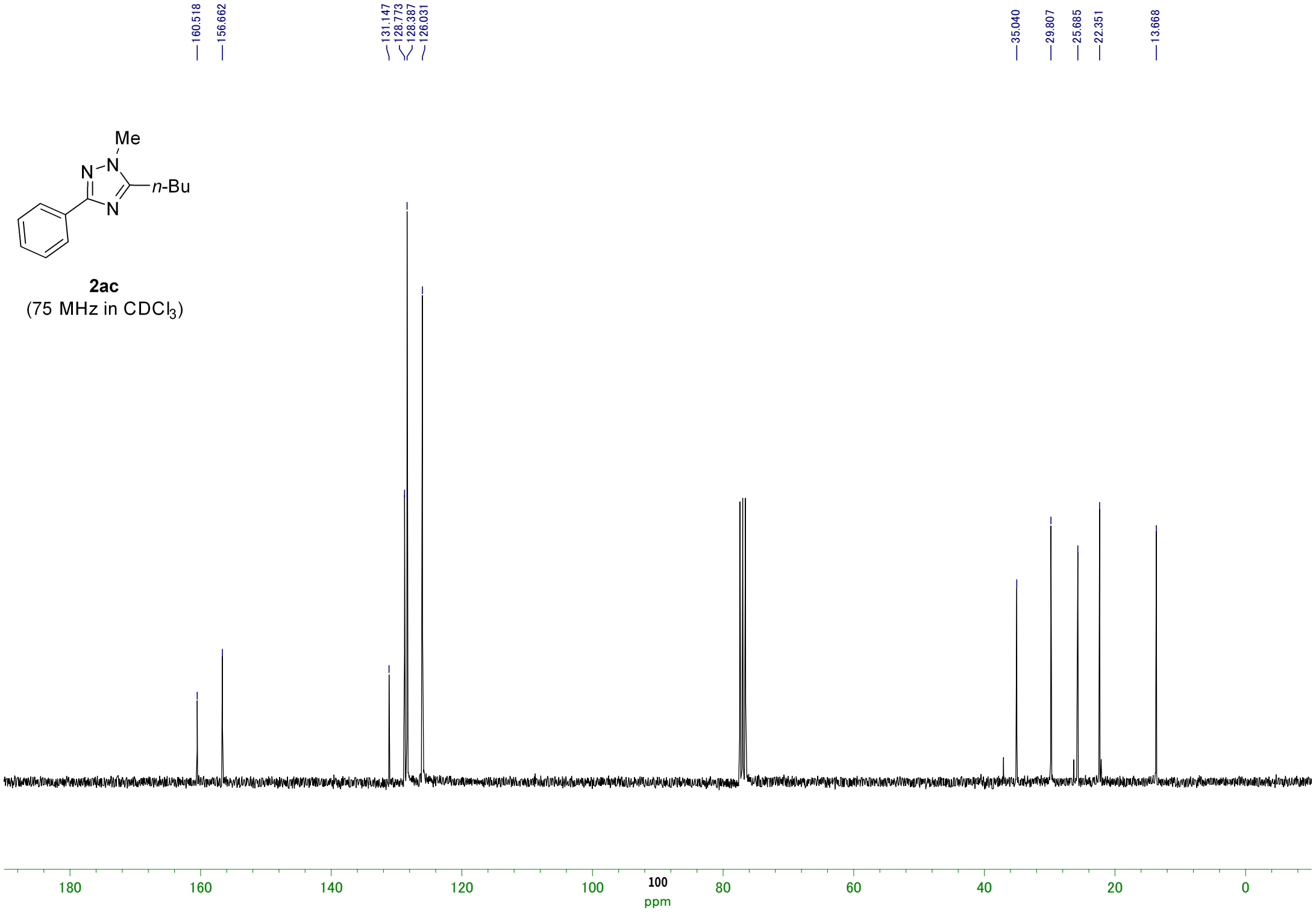
2za
(75 MHz in $CDCl_3$)

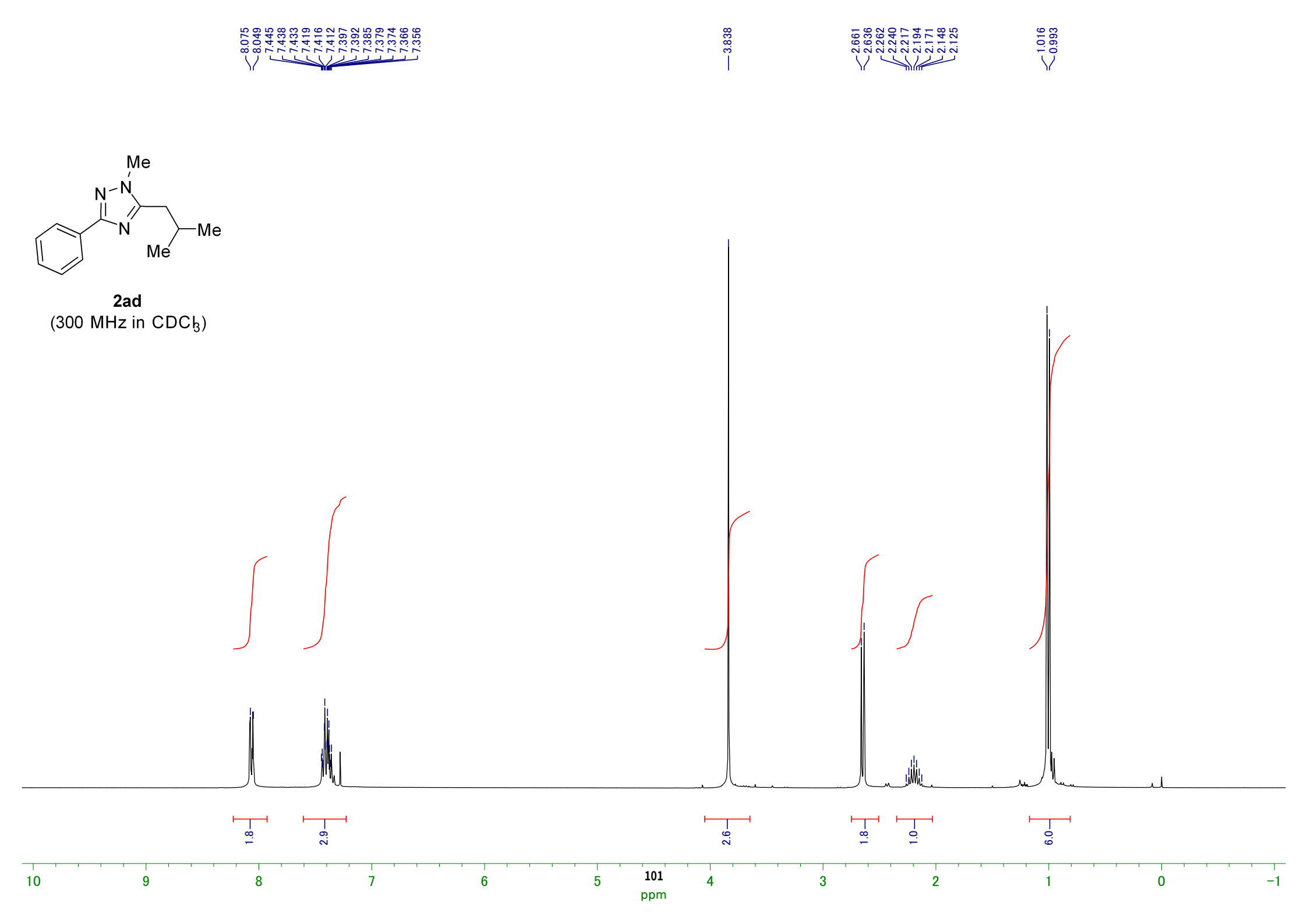

8.071
8.044
7.443
7.437
7.431
7.417
7.414
7.410
7.391
7.383
7.378
7.374
7.366
7.356
7.343
7.336
7.331
7.327
3.842
2.838
2.813
2.787
2.762
1.403
1.377
1.352
Me
N
N
Et
N
2ab
(500 MHz in CDCl3)
2.0
3.2
3.0
2.1
3.3
10
9
8
7
6
5
4
3
2
1
0
−1
97
ppm

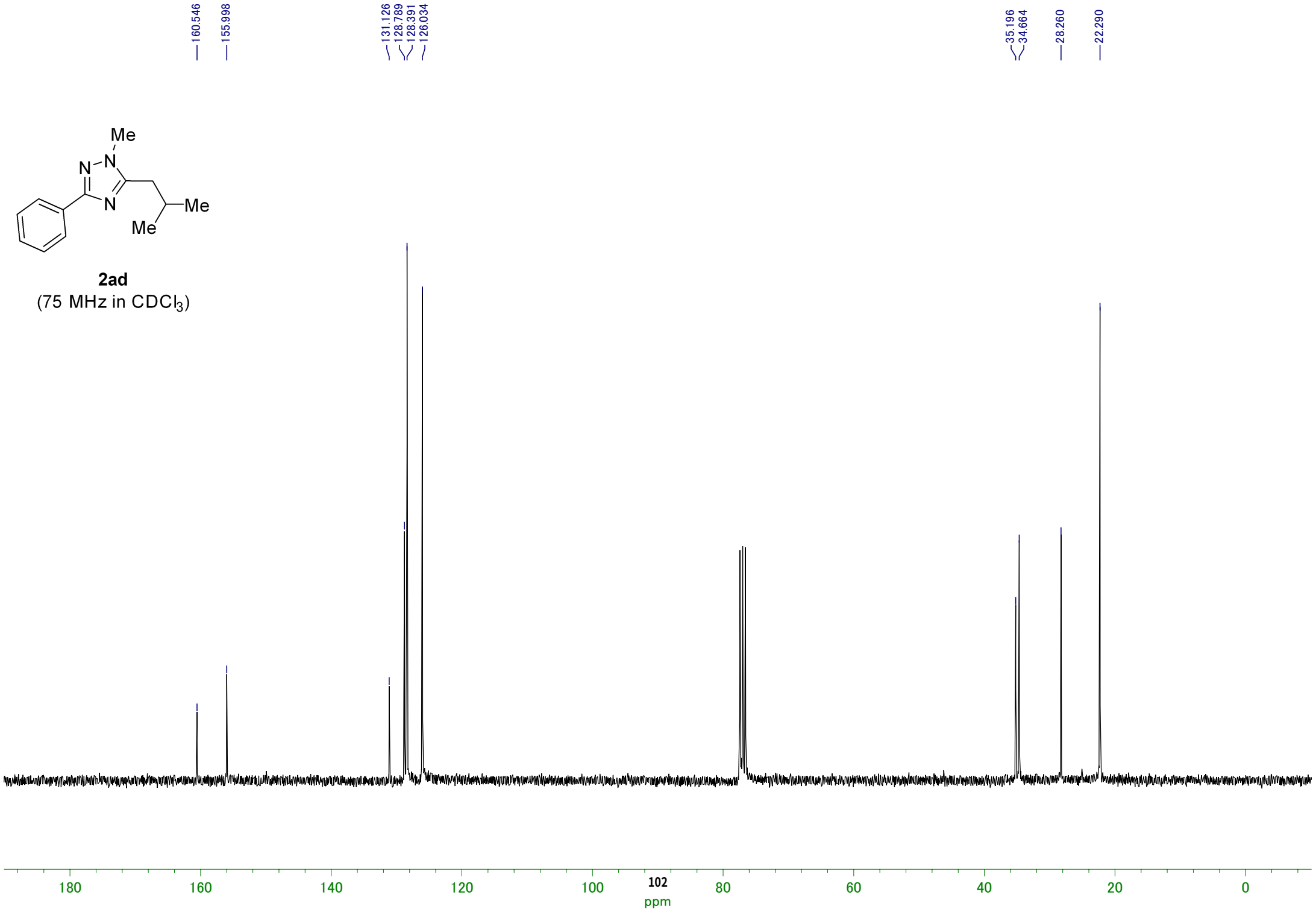


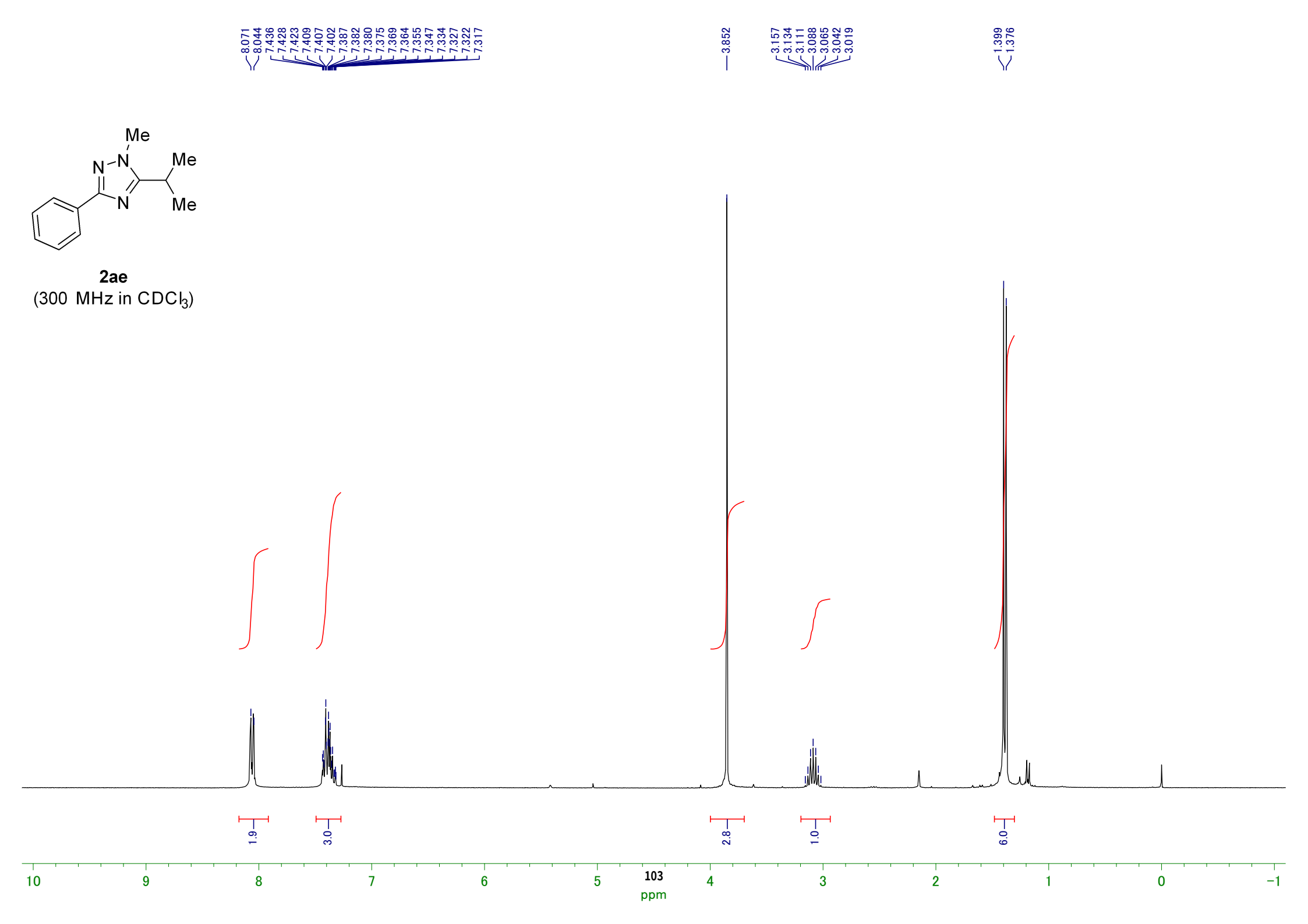
2ab
(125 MHz in $CDCl_3$)

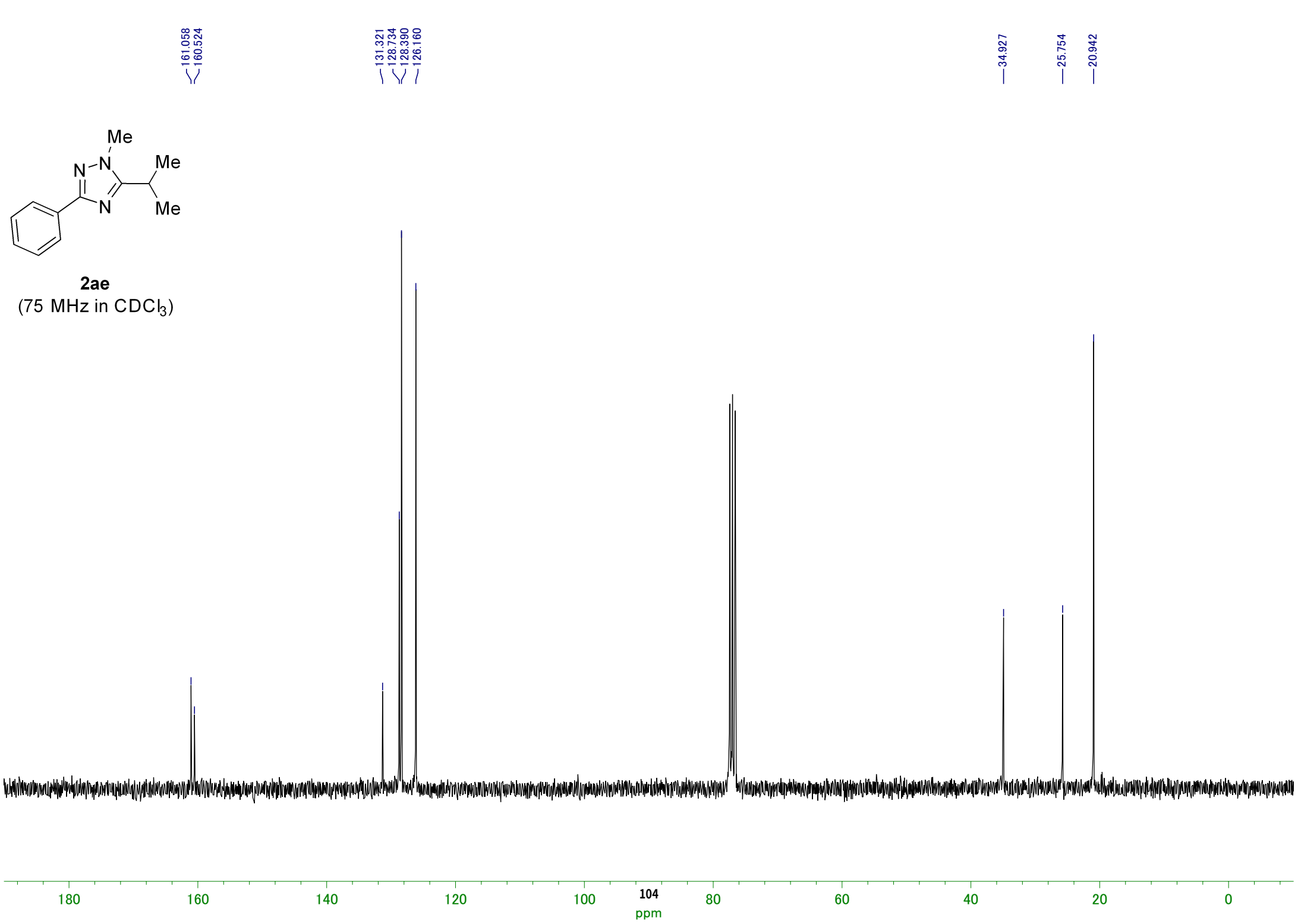

8.067
8.040
7.440
7.434
7.411
7.406
7.391
7.386
7.380
7.374
7.369
7.352
3.832
2.787
2.762
2.735
1.815
1.790
1.764
1.738
1.712
1.500
1.475
1.450
1.425
1.400
1.376
0.989
0.964
0.940
Me
N
N
n-Bu
N
2ac
(300 MHz in CDCl3)
2.0
3.2
3.0
2.0
2.2
2.3
3.5
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

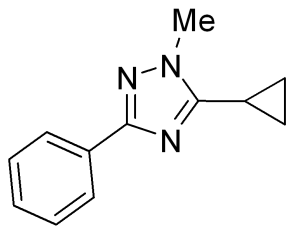

160.518
156.662
131.147
128.773
128.387
126.031
35.040
29.807
25.685
22.351
13.668
Me
N
N
N
n-Bu
2ac
(75 MHz in CDCl3)
180
160
140
120
100
100
ppm
80
60
40
20
0


8.075
8.049
7.445
7.438
7.433
7.419
7.416
7.412
7.397
7.392
7.385
7.379
7.374
7.366
7.356
3.838
2.661
2.636
2.262
2.240
2.217
2.194
2.171
2.148
2.125
1.016
0.993
Me
N
N
N
Me
Me
2ad
(300 MHz in CDCl3)
1.8
2.9
2.6
1.8
1.0
6.0
10
9
8
7
6
5
4
3
2
1
0
−1
101
ppm


160.546
155.998
131.126
128.789
128.391
126.034
35.196
34.664
28.260
22.290
Me
N
N
N
Me
Me
2ad
(75 MHz in CDCl3)
180
160
140
120
100
102
ppm
80
60
40
20
0

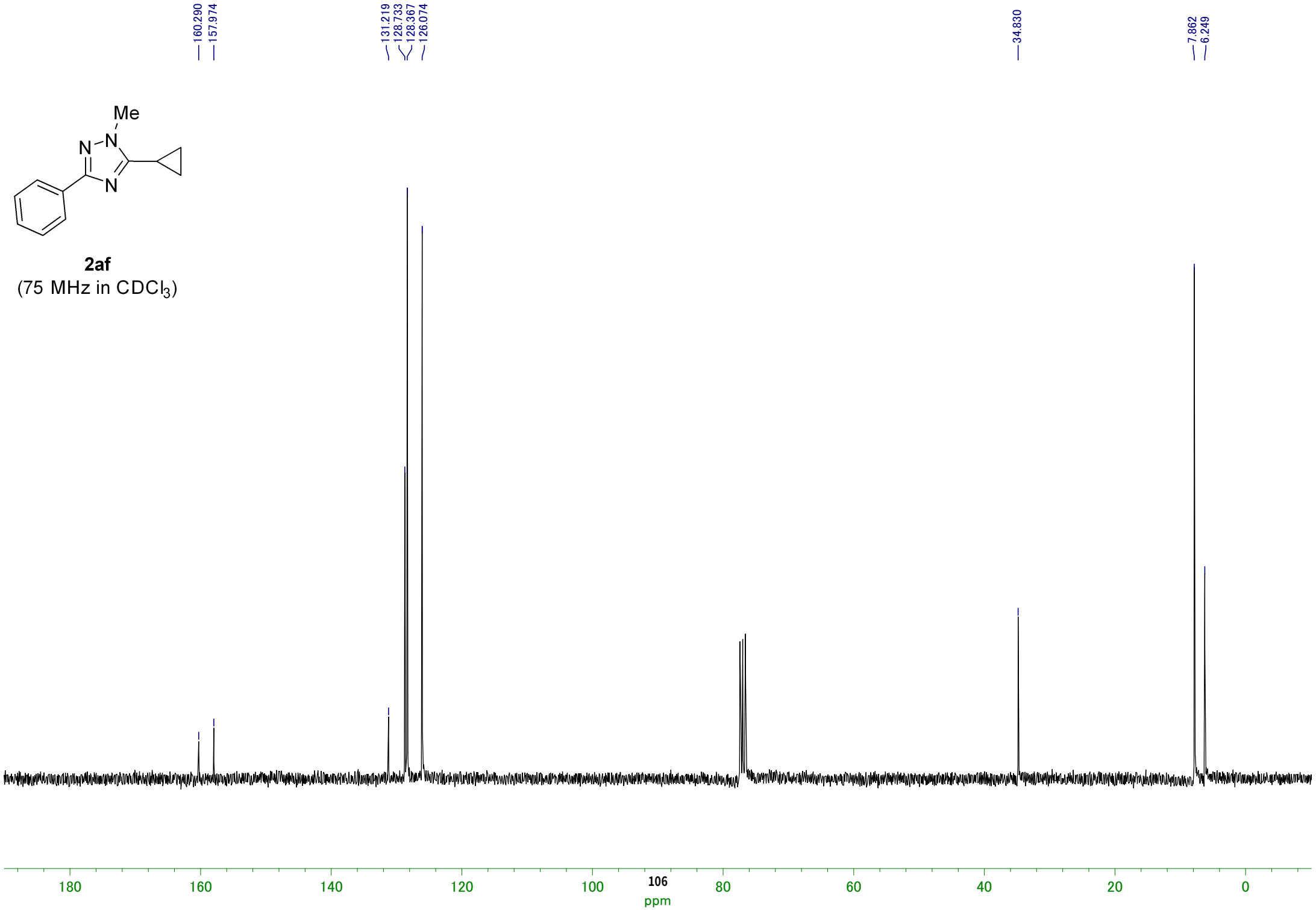

8.071
8.044
7.436
7.428
7.423
7.409
7.407
7.402
7.387
7.382
7.380
7.375
7.369
7.364
7.355
7.347
7.334
7.327
7.322
7.317
3.852
3.157
3.134
3.111
3.088
3.065
3.042
3.019
1.399
1.376
Me
N
N
Me
N
Me
2ae
(300 MHz in CDCl3)
1.9
3.0
2.8
1.0
6.0
10
9
8
7
6
5
4
3
2
1
0
−1
ppm

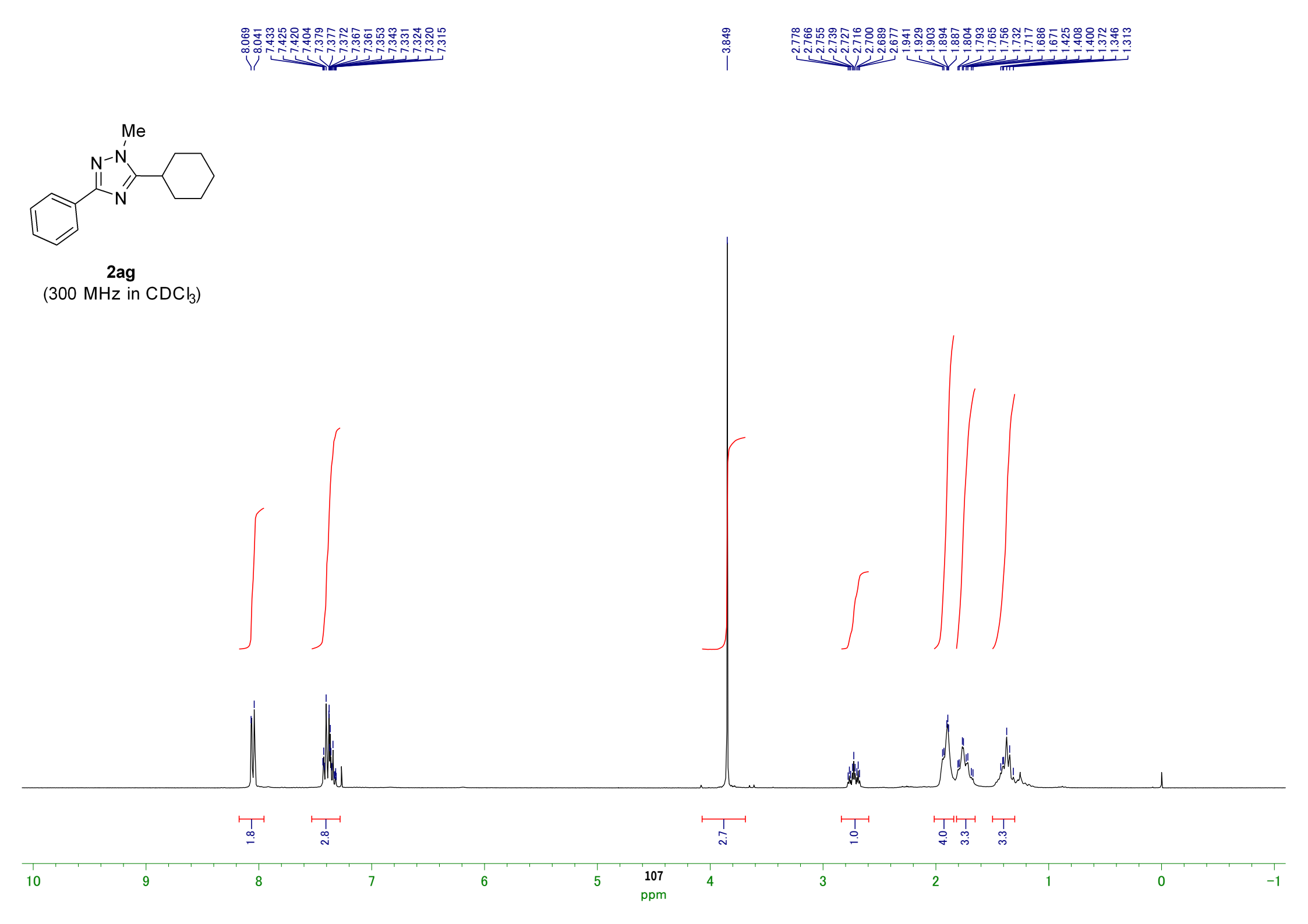

161.058
160.524
131.321
128.734
128.390
126.160
34.927
25.754
20.942
Me
N
N
Me
N
Me
2ae
(75 MHz in CDCl3)
180
160
140
120
100
104
ppm
80
60
40
20
0

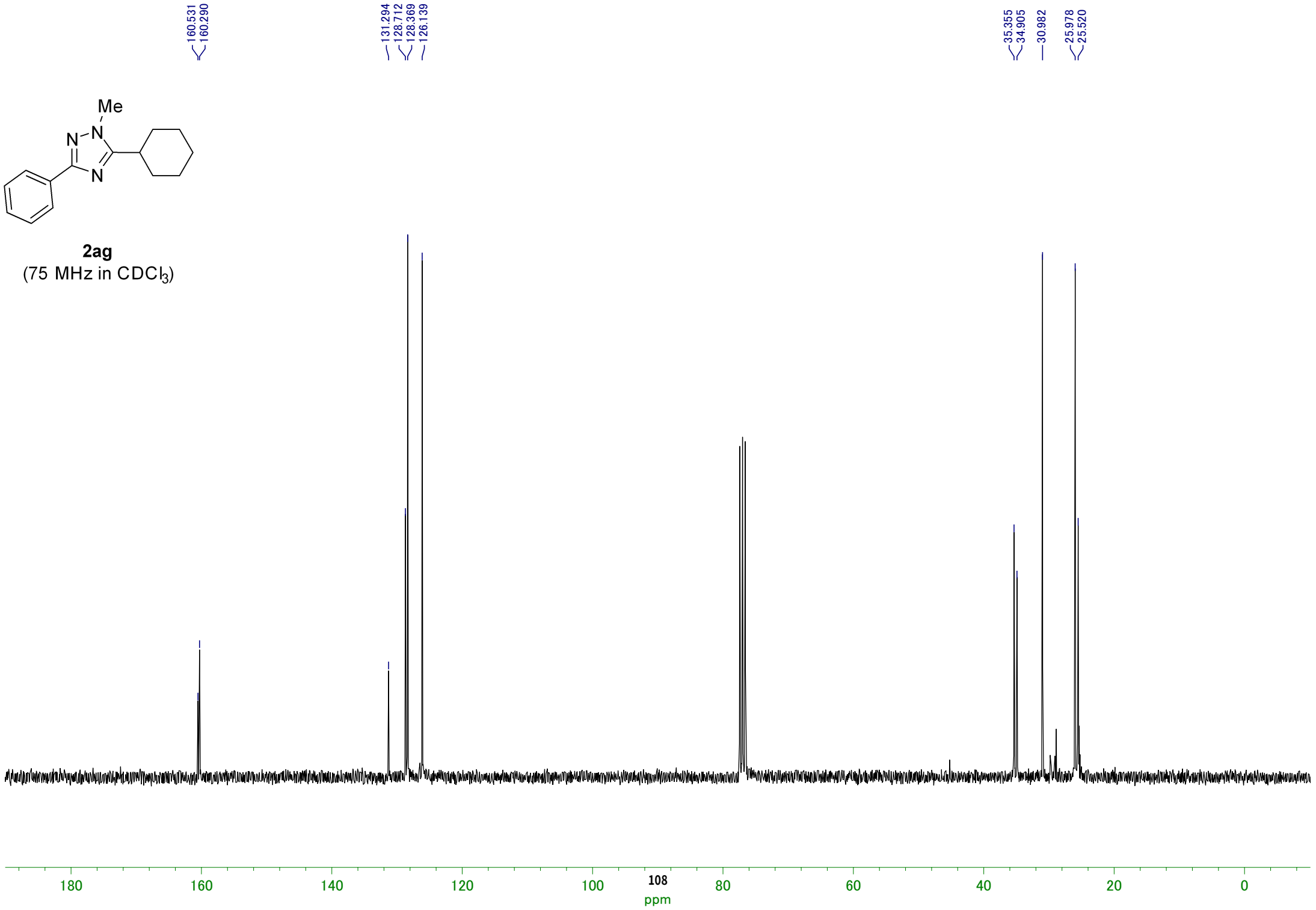


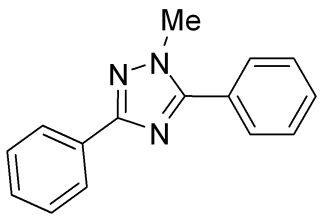
2af

(300 MHz in $CDCl_3$)

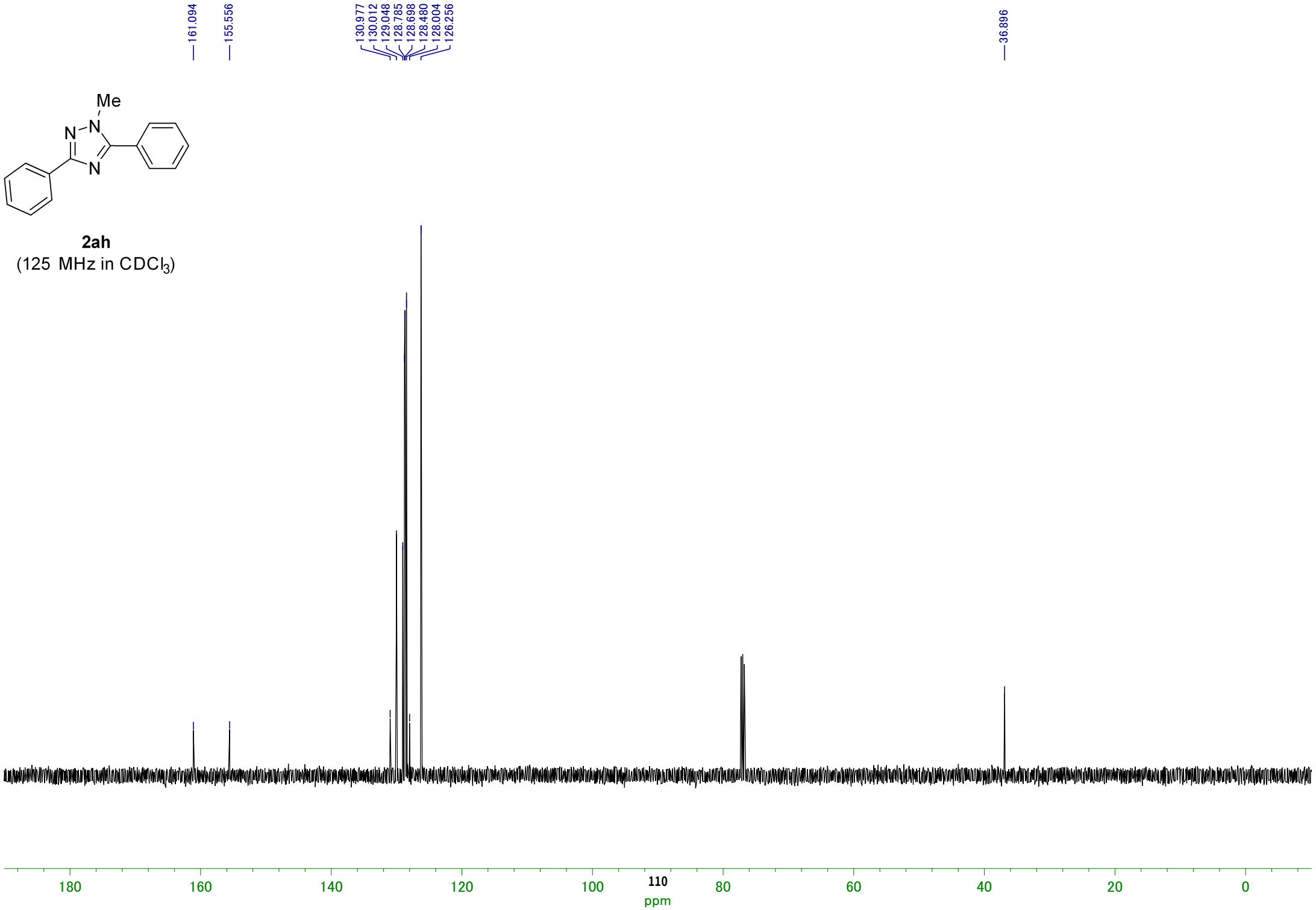

160.290
157.974
131.219
128.733
128.367
126.074
34.830
7.862
6.249
Me
N
N
N
2af
(75 MHz in CDCl3)
180
160
140
120
100
106
ppm
80
60
40
20
0

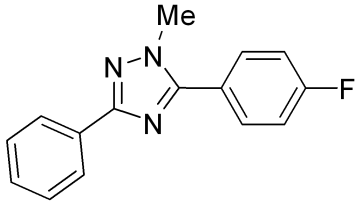

8.069
8.041
7.433
7.425
7.420
7.404
7.379
7.377
7.372
7.367
7.361
7.353
7.343
7.331
7.324
7.320
7.315
3.849
2.778
2.766
2.755
2.739
2.727
2.716
2.700
2.689
2.677
1.941
1.929
1.903
1.894
1.887
1.804
1.793
1.765
1.756
1.732
1.717
1.686
1.671
1.425
1.408
1.400
1.372
1.346
1.313
Me
N
N
N
2ag
(300 MHz in CDCl3)
1.8
2.8
2.7
1.0
4.0
3.3
3.3
10
9
8
7
6
5
4
3
2
1
0
−1
ppm


160.531
160.290
131.294
128.712
128.369
126.139
35.355
34.905
30.982
25.978
25.520
Me
N
N
N
2ag
(75 MHz in CDCl3)
180
160
140
120
100
108
ppm
80
60
40
20
0



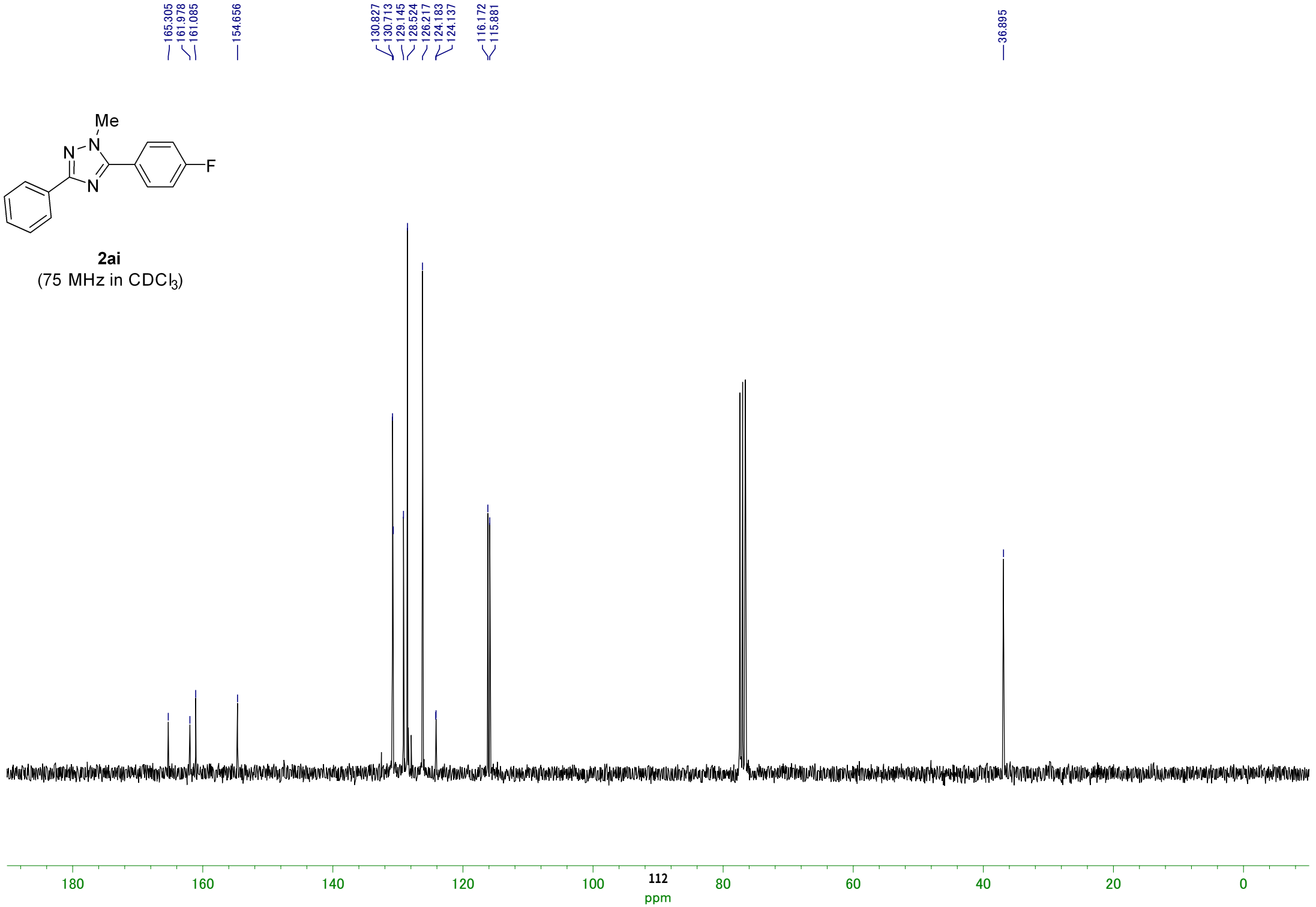
2ah
(500 MHz in $CDCl_3$)

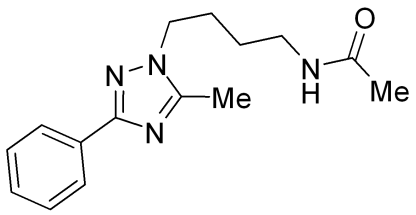

161.094
155.556
130.977
130.012
129.048
128.785
128.698
128.480
128.004
126.256
36.896
Me
N
N
N
2ah
(125 MHz in CDCl3)
180
160
140
120
100
110
80
60
40
20
0
ppm



2ai

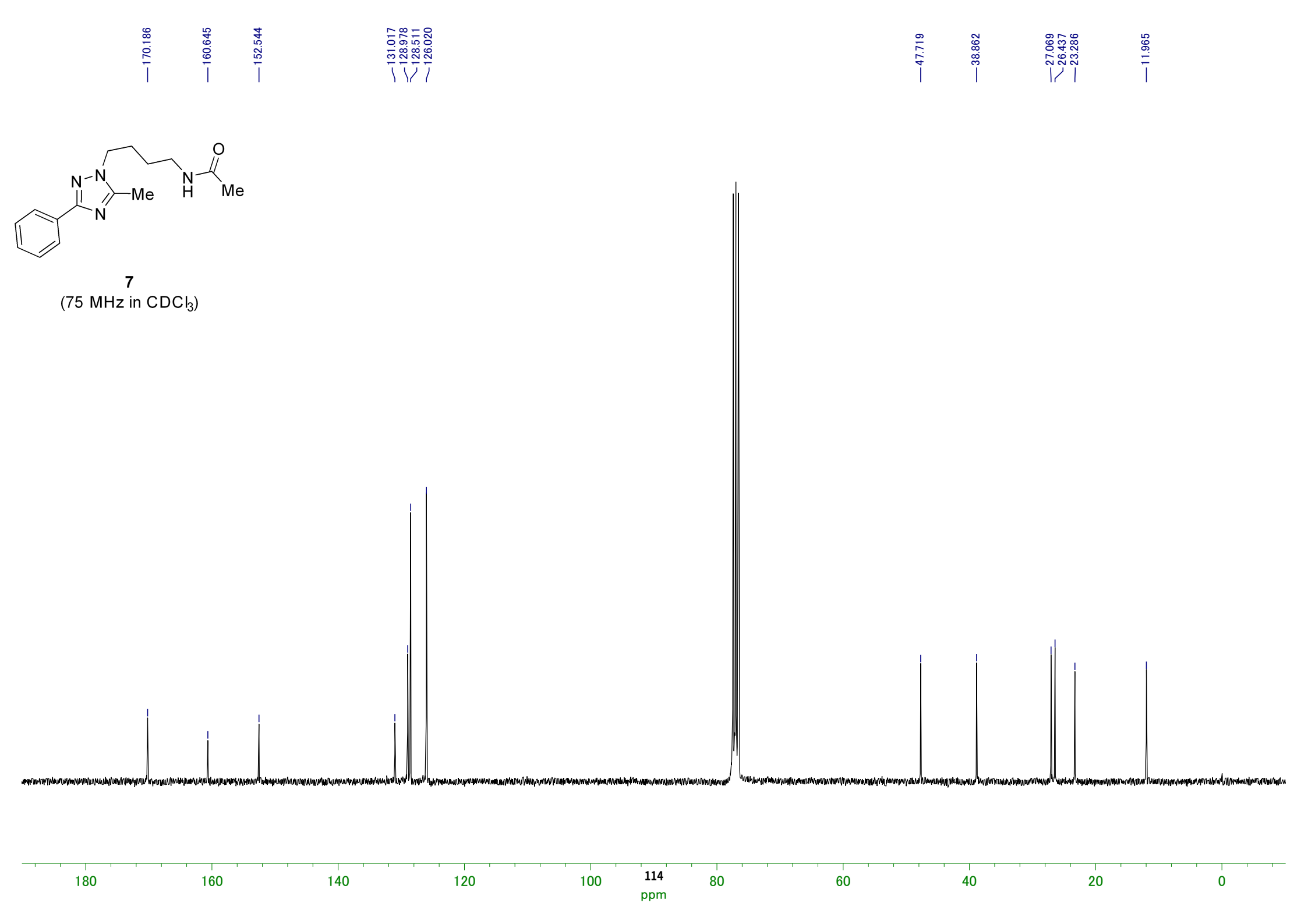
(300 MHz in $CDCl_3$)

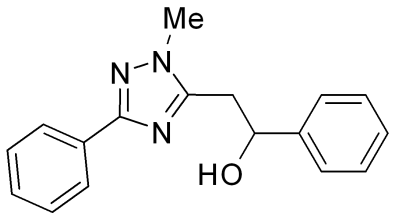

165.305
161.978
161.085
154.656
130.827
130.713
129.145
128.524
126.217
124.183
124.137
116.172
115.881
36.895
Me
N
N
N
F
2ai
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



7

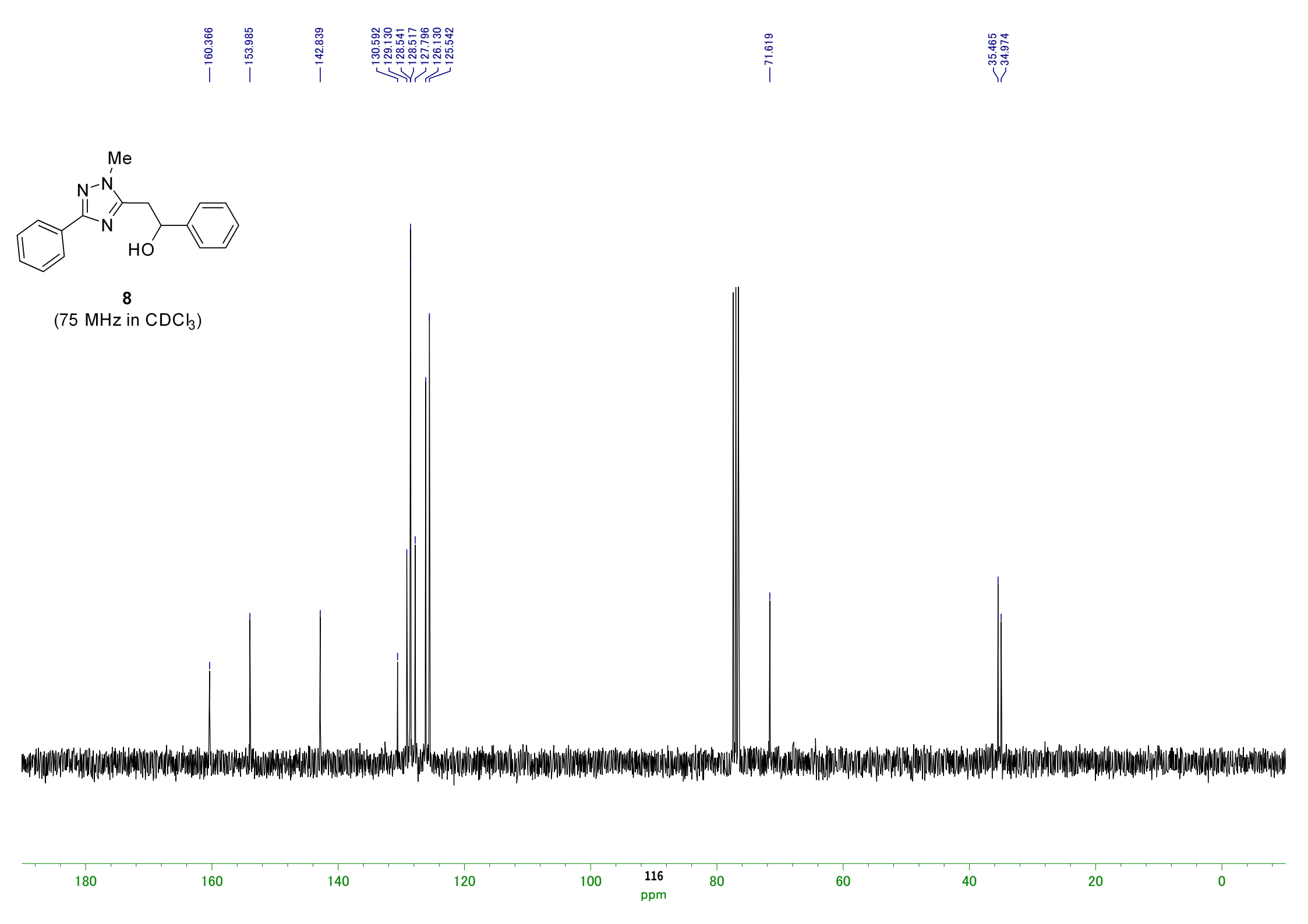
(300 MHz in $CDCl_3$)

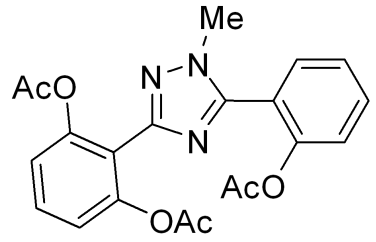

170.186
160.645
152.544
131.017
128.978
128.511
126.020
47.719
38.862
27.069
26.437
23.286
11.965
N
N
N
Me
N
H
O
Me
7
(75 MHz in CDCl3)
180
160
140
120
100
80
60
40
20
0
ppm



8

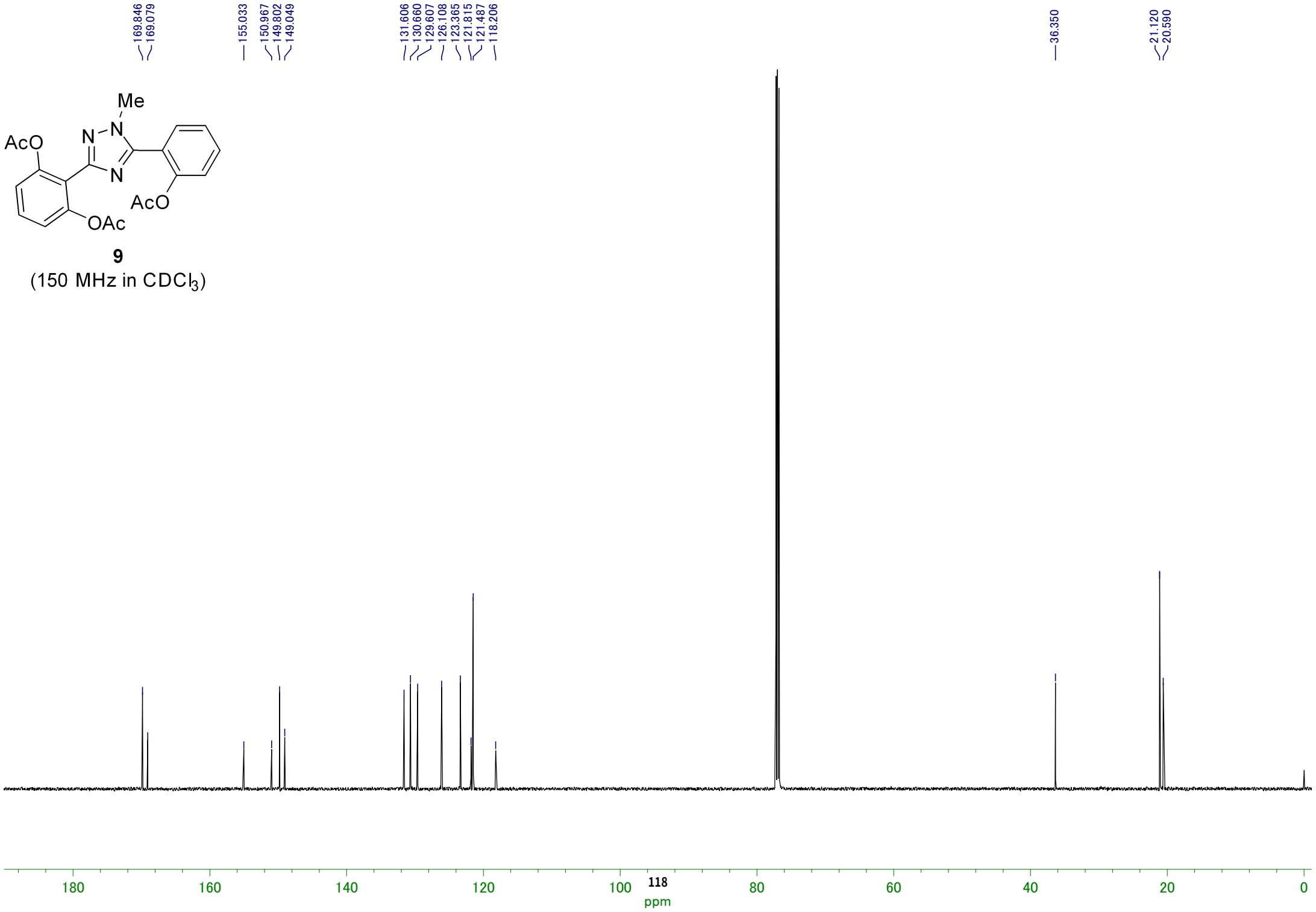
(300 MHz in $CDCl_3$)


160.366
153.985
142.839
130.592
129.130
128.541
128.517
127.796
126.130
125.542
71.619
35.465
34.974
Me
N
N
N
HO
8
(75 MHz in CDCl3)
180
160
140
120
100
116
ppm
80
60
40
20
0



9

(600 MHz in $CDCl_3$)


169.846
169.079
155.033
150.967
149.802
149.049
131.606
130.660
129.607
126.108
123.365
121.815
121.487
118.206
36.350
21.120
20.590
Me
N
N
N
AcO
AcO
OAc
9
(150 MHz in CDCl3)
180
160
140
120
100
118
80
60
40
20
0
ppm