

Supporting Information

Synthesis of a fully protected long-chain polyamine subunit of
aculeine B using photoremovable NPEC group

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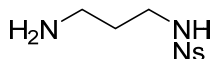
[SYNTHETIC PROCEDURES FOR ALL REACTIONS]

General methods

For photoirradiation, a JAXMAN® U1 Nichia (365 nm, 3 W) LED flashlight or an AHH400S (435 W) high-pressure Hg lamp was used.

IR spectra were recorded on a JASCO FT/IR-400 spectrometer. ¹H and ¹³C NMR spectra were recorded on a Bruker AVANCE III HD 400 spectrometer. Chemical shift values were reported in δ (ppm) with reference to internal residual solvent [¹H NMR, CDCl₃ (7.24), C₆D₆ (7.15), C₅D₅N (7.21); ¹³C NMR, CDCl₃ (77.0), C₆D₆ (128.0)]. The following abbreviations are used to designate the multiplicities; s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. ESI mass spectra were recorded on a Thermo Fisher Scientific Q Exactive Focus mass spectrometer or a Sciex TripleTOF 5600+ mass spectrometer. Analytical thin-layer chromatography (TLC) was performed using a Merck silica gel 60 F254 plate (0.25 mm thickness). Flash column chromatography was carried out using Fuji Silysia silica gel BW-300 (200-400 mesh), Kanto chemical silica gel 60N (40-50 mesh), or Yamazen silica gel HiFlash (SiOH-30μ Premium, 30 μm, 60 Å) with automated flash column system EPCLC-Wprep2XY-10VW (Yamazen Corporation). All reactions susceptible to moisture and air were carried out in an atmosphere of argon gas, using the glassware oven-dried over 3 h. CH₂Cl₂ and THF were purified by Glass Contour Solvent Dispensing System (Nikko Hansen). All other reagents were purchased at the highest commercial grade and used directly.

***N*-(3-Aminopropyl)-2-nitrobenzenesulfonamide (4)**

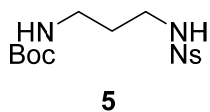


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To a stirred solution of 1,3-diaminopropane (**3**, 1.10 g, 0.0149 mol) in ethanol (25 mL) at 0 °C was added 2-nitrobenzenesulfonyl chloride (1.10 g, 0.00496 mol) in eleven portions over 40 min. After 30 min, a solution of sodium ethoxide (337 mg, 0.00496 mmol) in ethanol (50 mL) was added, and the mixture was diluted with ethanol (30 mL).

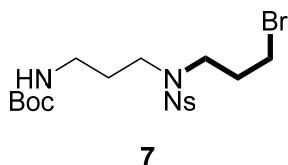
After filtration of the mixture through a pad of Celite, the filtrate was concentrated under reduced pressure. Coevaporation with benzene (30 mL) gave a residue, which was purified by silica gel column chromatography (60N, 60 g, MeOH/ⁱPrNH₂/CH₂Cl₂ = 5:5:190) to give *N*-*N*s amine **4** (1.31 g, 99%) as a white powder. The spectroscopic data were identical to those reported.¹

***tert*-Butyl (3-((2-nitrophenyl)sulfonamido)propyl)carbamate (5)**



To a stirred solution of amine **4** (7.21 g, 27.8 mmol) in CH₂Cl₂ (185 mL) at rt were added Et₃N (4.65 mL, 33.4 mmol) and Boc₂O (7.29 g, 33.4 mmol). After 3 h, hydrochloric acid (1 M, 36 mL) was added to the mixture. Organic layer was separated, and aqueous layer was extracted with CHCl₃ (100 mL). Combined organic layer was washed with brine (40 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 135 g, EtOAc/hexane = 1:1) to give *N*-Boc amine **5** (9.47 g, 94%) as a white solid. The spectroscopic data were identical to those reported.¹

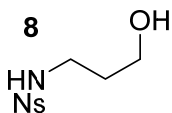
***tert*-Butyl (3-((*N*-(3-bromopropyl)-2-nitrophenyl)sulfonamido)propyl)carbamate (7)**



To a stirred mixture of K₂CO₃ (18.20 g, 131.7 mmol) and 1,3-dibromopropane (**6**, 16.96 g, 79.0 mmol) at 60 °C was added a solution of *N*-*N*s amine **5** (9.47 g, 26.3 mmol) in DMF (44 mL) over 15 min. After 40 min, the mixture was cooled to rt, and water (44 mL) was added. The mixture was extracted with Et₂O (3 × 60 mL). The combined extracts were washed with brine (40 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 135 g, EtOAc/hexane = 1:1) to give

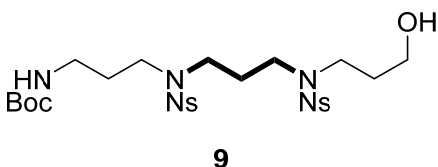
secondary amine **7** (10.7 g, 85%) as a colorless oil. The spectroscopic data were identical to those reported.¹

***N*-(3-Hydroxypropyl)-2-nitrobenzenesulfonamide (8)**



To a stirred solution of 3-aminopropanol (2.94 g, 39.2 mmol) in CH₂Cl₂ (100 mL) at 0 °C were added 2-nitrobenzenesulfonyl chloride (6.94 g, 31.3 mmol) and pyridine (2.96 mL, 31.3 mmol). After 2 h, hydrochloric acid (1 M, 48 mL) was added. Organic layer was separated, and aqueous layer was extracted with CH₂Cl₂ (2 × 50 mL). Combined organic layer was washed with brine (50 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 135 g, EtOAc/hexane = 1:1) to give *N*-Ns amine **8** (6.28 g, 87%) as a colorless oil. The spectroscopic data were identical to those reported.¹

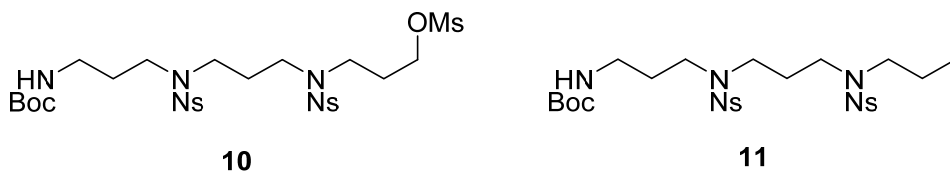
***tert*-Butyl (3-((*N*-(3-((*N*-(3-hydroxypropyl)-2-nitrophenyl)sulfonamido)propyl)-2-nitrophenyl)sulfonamido)propyl)carbamate (9)**



To a stirred solution of bromide **7** (3.41 g, 7.10 mmol) and *N*-Ns amine **8** (923 mg, 3.55 mmol) in CH₃CN (12 mL) at rt were added Cs₂CO₃ (5.78 g, 17.7 mmol) and Bu₄NI (655 mg, 1.77 mmol). After stirring at 60 °C for 90 min, brine (40 mL) was added, and the mixture was extracted with CH₂Cl₂ (3 × 40 mL). Combined layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 135 g, EtOAc/hexane = 1:1) to give 3-mer triamine **9** (1.96 g, 83%) as a white foam. The spectroscopic data were identical to those reported.¹

2,2-Dimethyl-9,13-bis((2-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13-

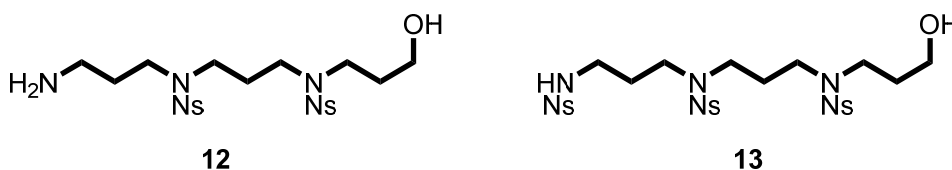
triazahexadecan-16-yl methanesulfonate (**10**), and
tert-butyl (3-((*N*-(3-((*N*-(3-iodopropyl)-2-
 nitrophenyl)sulfonamido)propyl)-2-
 nitrophenyl)sulfonamido)propyl)carbamate (**11**)



To a stirred solution of alcohol **9** (780 mg, 1.18 mmol) in CH₂Cl₂ (4.0 mL) at 0 °C were added Et₃N (0.330 mL, 2.36 mmol) and MsCl (0.182 mL, 2.36 mmol). After stirring at rt for 3.5 h, to the mixture were added hydrochloric acid (1 M, 1 mL) and water (5 mL). Organic layer was separated, and aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). Combined organic layer was washed with brine (5 mL), dried over Na₂SO₄, and concentrated under reduced pressure to give crude mesylate **10** (872 mg) which was used for the next reaction without purification.

To a stirred solution of crude mesylate **10**, thus obtained above, in 2-butanone (8.0 mL) at rt was added NaI (532 mg, 3.55 mmol). After stirring at 60 °C for 80 min, water (5 mL) was added and the mixture was extracted with Et₂O (3 × 20 mL). Combined extracts were washed with brine (10 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 16 g, EtOAc/hexane = 1:1) to give iodide **11** (849 mg, 93%) as a colorless oil. The spectroscopic data were identical to those reported.¹

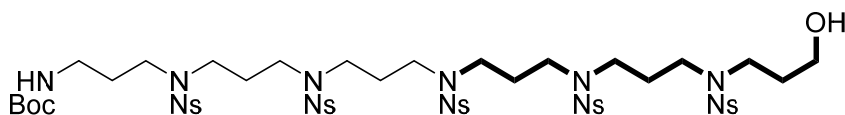
N-(3-Aminopropyl)-*N*-(3-((*N*-(3-hydroxypropyl)-2-
 nitrophenyl)sulfonamido)propyl)-2-nitrobenzenesulfonamide (**12**), and
N-(3-hydroxypropyl)-2-nitro-*N*-(3-((2-nitro-*N*-(3-((2-
 nitrophenyl)sulfonamido)propyl)phenyl)sulfonamido)propyl)benzenesul
 fonamide (**13**)



To a stirred solution of *N*-Boc amine **9** (612 mg, 0.927 mmol) in CH₂Cl₂ (2.1 mL) and MeOH (4.1 mL) at 0 °C was added SOCl₂ (0.606 mL, 8.35 mmol). After 1 h, the mixture was concentrated under reduced pressure to remove volatile materials, to give primary amine **12** (567 mg) as a colorless oil which was used for the next reaction without purification.

The crude amine **12**, thus obtained above, was dissolved in CH₂Cl₂ (9.2 mL) and Et₃N (0.257 mL, 1.85 mmol), and 2-nitrobenzenesulfonyl chloride (226 mg, 1.02 mmol) was added at 0 °C. After 1.5 h, hydrochloric acid (1 M, 4 mL) was added at rt, and the mixture was extracted with CH₂Cl₂ (3 × 15 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 16 g, MeOH/CHCl₃ = 3:97) to give tri-*N*-Ns amine **13** (653 mg, 94%) as a yellow oil: IR (neat) 3428, 2104, 1640, 1541, 1461, 1440, 1342, 1217, 1162, 1124, 1060 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.09 (m, 1H), 8.02–7.94 (m, 2H), 7.84 (m, 1H), 7.78–7.66 (m, 6H), 7.65–7.57 (m, 2H), 5.60 (t, *J* = 6.3 Hz, 1H), 3.68–3.63 (m, 2H), 3.40 (t, *J* = 7.1 Hz, 2H), 3.36 (t, *J* = 7.0 Hz, 2H), 3.29 (t, *J* = 7.3 Hz, 2H), 3.27 (t, *J* = 7.3 Hz, 2H), 3.12 (q, *J* = 6.5 Hz, 2H), 1.93–1.71 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 148.0, 147.9 (×2), 133.9, 133.8, 133.7, 133.3, 132.9, 132.7, 132.5, 132.1, 132.0, 130.9, 130.7, 130.6, 125.4, 124.3, 124.2, 59.2, 45.6, 45.5, 45.3, 45.0, 40.8, 31.0, 28.8, 27.6; HRMS calcd for C₂₇H₃₃N₆O₁₃S₃⁺ [(M+H)⁺] 745.1262, found 745.1255.

tert-Butyl (23-hydroxy-4,8,12,16,20-pentakis((2-nitrophenyl)sulfonyl)-4,8,12,16,20-pentaazatricosyl)carbamate (**14**)



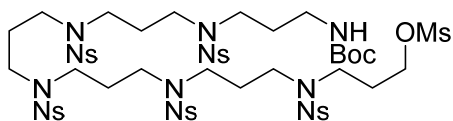
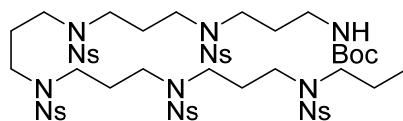
14 (6-mer polyamine)

To a stirred solution of tri-*N*-Ns amine **13** (85.0 mg, 0.114 mmol) in CH₃CN (0.160 mL) at 60 °C were added a solution of iodide **11** (152 mg,

0.198 mmol) in CH₃CN (0.600 mL) and Cs₂CO₃ (111 mg, 0.342 mmol). After 1 h, brine (3 mL) was added at rt, and the mixture was extracted with CH₂Cl₂ (3 × 2 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 16 g, MeOH/CHCl₃ = 3:97) to give 6-mer polyamine **14** (149 mg, 94%) as a colorless oil: IR (neat) 3439, 3096, 3020, 2976, 2935, 1703, 1591, 1543, 1459, 1440, 1368 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.99–7.89 (m, 5H), 7.74–7.65 (m, 10H), 7.64–7.55 (m, 5H), 4.82 (brs, 1H), 3.62 (t, *J* = 5.8 Hz, 1H), 3.40 (t, *J* = 7.1 Hz, 1H), 3.34–3.18 (m, 18H), 3.12–3.04 (m, 2H), 1.92–1.63 (m, 12H), 1.40 (s, 9H).

2,2-Dimethyl-9,13,17,21,25-pentakis((2-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17,21,25-hexaazaocacosan-28-yl methanesulfonate (15), and

tert-butyl (23-iodo-4,8,12,16,20-pentakis((2-nitrophenyl)sulfonyl)-4,8,12,16,20-pentaazatricosyl)carbamate (16)

**15****16**

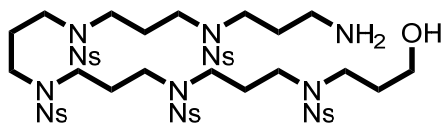
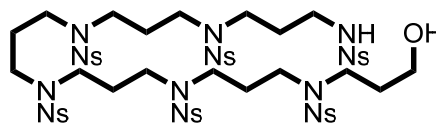
To a stirred solution of 6-mer alcohol **14** (199 mg, 0.140 mmol) in CH₂Cl₂ (0.480 mL) at 0 °C were added Et₃N (0.025 mL, 0.17 mmol) and MsCl (0.014 mL, 0.17 mmol). After 50 min, hydrochloric acid (1 M, 3 mL) was added at rt, and the mixture was extracted with CH₂Cl₂ (3 × 3 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure to give crude mesylate **15** (236.0 mg) as a pale yellow oil.

To a stirred solution of the crude mesylate **15**, thus obtained above, in 2-butanone (1.30 mL) at 60 °C was added NaI (65.0 mg, 0.430 mmol). After 1.5 h, water (2 mL) was added at rt and the mixture was extracted with CH₂Cl₂ (3 × 3 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 16 g, MeOH/CHCl₃ = 6:94) to give

iodide **16** (177 mg, 83%) as a pale yellow oil: IR (ATR) 2941, 1704, 1541, 1439, 1342, 1265, 1157, 1059, 851, 730, 651 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.03–7.91 (m, 5H), 7.75–7.66 (m, 10H), 7.65–7.58 (m, 5H), 4.81 (brs, 1H), 3.37–3.16 (m, 20H), 3.13–3.01 (m, 4H), 2.06–1.94 (m, 2H), 1.89–1.74 (m, 8H), 1.72–1.62 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.0, 148.0, 147.9, 147.9 ($\times 3$), 133.9 ($\times 4$), 133.8, 132.7, 132.5 ($\times 2$), 132.4, 132.2, 132.1, 132.1, 132.1, 132.0, 130.8, 130.6 ($\times 3$), 130.4, 124.3, 124.3, 124.2 ($\times 2$), 124.2, 79.1, 48.3, 45.7, 45.3 ($\times 7$), 45.3, 37.3, 31.8, 28.6, 28.4 ($\times 4$), 27.4, 27.3 ($\times 3$).

***N*-(19-Amino-4,8,12,16-tetrakis((2-nitrophenyl)sulfonyl)-4,8,12,16-tetraazanonadecyl)-*N*-(3-hydroxypropyl)-2-nitrobenzenesulfonamide (17), and**

***N*-(19-hydroxy-4,8,12,16-tetrakis((2-nitrophenyl)sulfonyl)-4,8,12,16-tetraazanonadecyl)-2-nitro-*N*-(3-(2-nitrophenylsulfonamido)propyl)benzenesulfonamide (18)**

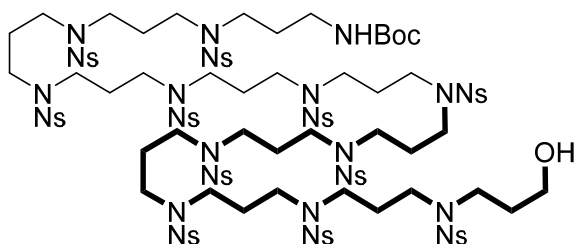
**17****18**

To a stirred solution of 6-mer *N*-Boc amine **14** (103 mg, 0.0740 mmol) in CH_2Cl_2 (0.174 mL) at 0 °C was added a solution of SOCl_2 (0.051 mL, 0.71 mmol) in MeOH (0.350 mL). After 1 h, the mixture was concentrated under reduced pressure to remove volatile materials, to give primary amine **17** (100.0 mg) as a colorless oil.

The amine, thus obtained above, was dissolved in CH_2Cl_2 (0.742 mL). To the stirred solution at 0 °C were added Et_3N (0.021 mL, 0.15 mmol) and NsCl (18.0 mg, 0.082 mmol). After 1 h, the mixture was allowed to warm to rt, and hydrochloric acid (1 M, 2 mL) was added. The mixture was extracted with CH_2Cl_2 (3 \times 3 mL). Combined organic layer was washed with brine (2 \times 3 mL), dried over Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 16 g, MeOH/ CHCl_3 = 8:92) to give 6-mer tetra-*N*-Ns amine **18** (68.0 mg, 62%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 8.08 (m, 1H), 8.00–7.92 (m, 5H), 7.82 (m, 1H), 7.74–

7.66 (m, 12H), 7.63-7.58 (m, 5H), 5.66 (t, $J = 6.3$ Hz, 1H), 3.65-3.61 (m, 2H), 3.40 (t, $J = 7.1$ Hz, 2H), 3.35 (t, $J = 7.1$ Hz, 2H), 3.32-3.21 (m, 16H), 3.15-3.08 (m, 2H), 1.91-1.71 (m, 13H).

tert-Butyl (47-hydroxy-4,8,12,16,20,28,32,36,40,44-decakis((2-nitrophenyl)sulfonyl)-24-((4-nitrophenyl)sulfonyl)-4,8,12,16,20,24,28,32,36,40,44-undecaazaheptatetracontyl)carbamate (2a)

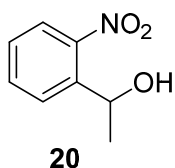


2a (12-mer LCPA subunit)

To a stirred solution of 6-mer *N*-Ns amine **18** (63.0 mg, 0.0430 mmol) in CH₃CN (0.100 mL) at 60 °C were added a solution of 6-mer iodide **16** (128 mg, 0.0860 mmol) in CH₃CN (0.290 mL) and Cs₂CO₃ (42.0 mg, 0.130 mmol). After 3 h, brine (2 mL) was added at rt, and the mixture was extracted with CH₂Cl₂ (5 × 2 mL). Combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure to give an inseparable mixture (180.0 mg) of 12-mer LCPA subunit **2a** and iodide **16** as a white powder. The ratio was not determined since ¹H signals are broad.

Selected data for 12-mer polyamine **2a**: ¹H NMR (400 MHz, pyridine-d₅) δ 8.27-8.05 (m, 11H), 7.98-7.81 (m, 11H), 7.82-7.65 (m, 22H), 4.14-4.00 (m, 2H), 4.00-3.71 (m, 6H), 3.71-3.44 (m, 38H), 3.42-3.23 (m, 2H), 2.21-1.87 (m, 24H), 1.52 (s, 9H).

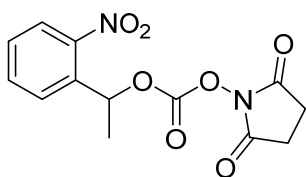
1-(2-Nitrophenyl)ethanol (20)



To a stirred solution of 2'-nitroacetophenone (**19**, 1.70 mL, 12.7

mmol) in THF (63 mL) at 0 °C was added sodium borohydride (958 mg, 25.3 mmol). After 21 h, water (30 mL) was added, and the mixture was extracted with CH₂Cl₂ (4 × 20 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure to give alcohol **20** (2.12 g, 99%) as a yellow oil which was sufficiently pure and used for the next reaction (**19** → **20**) without purification. The spectroscopic data of alcohol **20** were in good agreement with those of the reported one.²

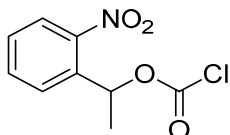
2,5-Dioxopyrrolidin-1-yl (1-(2-nitrophenyl)ethyl) carbonate (21)



21 (NPEC-OSu)

To a stirred solution of alcohol **20** (521 mg, 3.12 mmol) in CH₃CN (15.6 mL) at rt were added di(*N*-succinimidyl) carbonate (1.60 g, 6.24 mmol) and Et₃N (0.87 mL, 6.24 mmol). After 2.5 h, the mixture was diluted with EtOAc (40 mL), washed successively with water (15 mL) and brine (10 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (BW-300, 37 g, EtOAc/hexane = 40:60) to give NPEC-OSu **21** (993 mg, 94%) as a colorless oil. The spectroscopic data of NPEC-OSu **21** were in good agreement with those of the reported one.²⁻³

1-(2-Nitrophenyl)ethyl carbonochloridate (22)

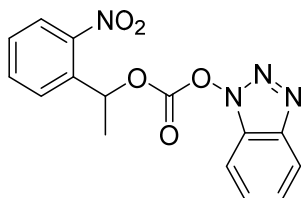


22 (NPEC-Cl)

To a stirred solution of alcohol **20** (2.02 g, 12.1 mmol) in THF (40 mL) at rt were added Na₂CO₃ (1.54 g, 14.5 mmol) and triphosgene (7.16 g, 24.1 mmol). After 23 h, water (40 mL) was added at 0 °C, and the mixture was extracted with CH₂Cl₂ (4 × 15 mL). Combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure, to give an inseparable mixture of NPEC-Cl **22** (2.59 g, 93% conversion

yield) and alcohol **20** (208 mg) as a black yellow oil which was used for the next reactions without purification.

1H-Benzo[d][1,2,3]triazol-1-yl (1-(2-nitrophenyl)ethyl) carbonate (23)

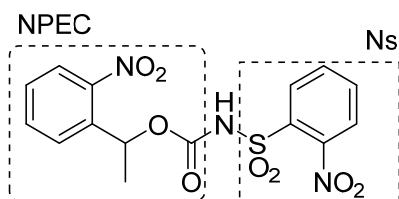


23 (NPEC-OBt)

1-Hydroxybenzotriazole monohydrate (HOBt•H₂O, 100.0 mg, 0.740 mmol) was azeotropically dehydrated with EtOH (3 × 3 mL) and toluene (3 × 3 mL), dried in vacuo at 60 °C for 2 h, and then dissolved in THF (1.6 mL). To the stirred solution of HOBt in THF at rt were added Et₃N (0.124 mL, 0.888 mmol) and a solution of NPEC-Cl (**21**, 187.0 mg, 0.814 mmol, containing alcohol **20**) in THF (1.0 mL). After 30 min, to the reaction mixture was added saturated aqueous NH₄Cl (2 × 4 mL) and the mixture was extracted with CHCl₃ (3 × 3 mL). Combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by trituration with EtOAc (30 mL) to give NPEC-OBt **23** (152 mg, 63%) as a white powder: IR (ATR) 3087, 1763, 1520, 1462, 1429, 1341, 1287, 1221, 1185, 1037, 858 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.17 (d, *J* = 8.5 Hz, 1H), 8.03 (dd, *J* = 8.3, 1.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.73 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.69 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.57–7.45 (m, 2H), 6.75 (q, *J* = 6.4 Hz, 1H), 1.87 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 147.3, 146.4, 136.2, 134.3, 133.5, 132.9, 132.7, 129.2, 127.5, 126.5, 124.7, 115.7, 115.1, 73.4, 22.2; HRMS (ESI, positive) calcd for C₁₅H₁₂N₄O₅Na⁺ [(M+Na)⁺] 351.0700, found 351.0700.

1-(2-Nitrophenyl)ethyl (2-nitrophenyl)sulfonylcarbamate (24)

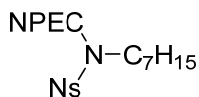
(NsNH(NPEC)) (Table 1, run 2)



24
"NPEC-NHNs"

To a stirred solution of NPEC-Cl **22** (2.59 g, 11.3 mmol) in CH₂Cl₂ (78 mL) at rt were added 2-nitrobenzenesulfonamide (1.59 g, 7.84 mmol), Et₃N (6.54 mL, 47.0 mmol), and DMAP (96.0 mg, 0.784 mmol). After 1.5 h, hydrochloric acid (1 M, 50 mL) was added. Organic layer was separated and aqueous layer was extracted with CH₂Cl₂ (3 × 15 mL). Combined organic layer was dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by trituration with PhH (80 mL) to give *N*-NPEC-*N*-Ns amine **24** (2.62 g, 85%) as a white powder: IR (ATR) 3239, 1752, 1517, 1448, 1356, 1225, 1163, 1055, 843, 740, 655 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.29 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.97–7.90 (m, 2H), 7.86 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.79 (dt, *J* = 1.7, 7.7 Hz, 1H), 7.74 (dt, *J* = 1.5, 7.5 Hz, 1H), 7.66–7.57 (m, 2H), 7.44 (ddd, *J* = 8.6, 6.8, 2.0 Hz, 1H), 6.29 (q, *J* = 6.5 Hz, 1H), 1.63 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 148.9, 148.1, 147.2, 136.6, 135.1, 134.0, 133.4, 132.7, 131.4, 128.9, 126.9, 125.2, 124.7, 71.7, 22.0; HRMS (ESI, positive) calcd for C₁₅H₁₃N₃O₈SNa⁺ [(M+Na)⁺] 418.0316, found 418.0318.

1-(2-Nitrophenyl)ethyl heptyl((2-nitrophenyl)sulfonyl)carbamate (25)

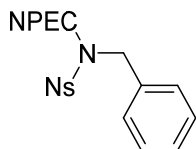


25

To a stirred solution of NPEC-NHNs **24** (41.6 mg, 0.104 mmol) in DMF (0.320 mL) at 80 °C were added K₂CO₃ (72.8 mg, 0.528 mmol), 1-bromoheptane (0.0250 mL, 0.160 mmol), and TBAI (7.8 mg, 0.021 mmol). After 3 h, to the reaction mixture was added hydrochloric acid (1 M,

2 mL), and the mixture extracted with EtOAc (4 × 2 mL). Combined organic layer was washed with brine (2 × 2 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 1.8 g, EtOAc/hexane = 3:7) to give heptylamine **4d** (35.0 mg, 77%) as a yellow oil: IR (ATR) 2930, 2858, 1735, 1525, 1442, 1365, 1265, 1172, 1057, 991, 854 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.28 (d, *J* = 7.6 Hz, 1H), 7.93 (d, 1H), 7.77–7.66 (m, 3H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 6.27 (q, *J* = 6.5 Hz, 1H), 3.82 (dd, *J* = 9.1, 7.7 Hz, 2H), 1.72 (tt, *J* = 7.4, 7.4 Hz, 2H), 1.52 (d, *J* = 6.4 Hz, 3H), 1.38–1.15 (m, 8H), 0.86 (t, *J* = 6.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 150.7, 147.8, 147.2, 136.9, 134.5, 133.9, 133.6, 133.1, 131.7, 128.8, 126.8, 124.7, 124.5, 72.1, 48.5, 31.7, 30.2, 28.8, 26.5, 22.5, 21.8, 14.0; HRMS (ESI, positive) calcd for C₂₂H₂₇N₃O₈SNa⁺ [(M+Na)⁺] 516.1411, found 517.1414.

1-(2-Nitrophenyl)ethyl benzyl((2-nitrophenyl)sulfonyl)carbamate (26)



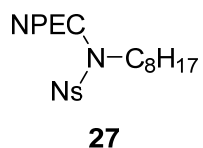
26

With the same procedure for the synthesis of **25** (see above), benzylamine **26** (62.0 mg, 98%) was obtained as a yellow oil starting from benzyl bromide (0.024 mL, 0.20 mmol), NPEC-NHNS **24**, TBAI, and K₂CO₃.

Data for benzylamine **26**: IR (ATR) 2932, 2859, 1733, 1542, 1442, 1265, 1173, 1057, 993, 700, 613 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.33 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.93 (m, 1H), 7.85–7.72 (m, 3H), 7.50–7.34 (m, 7H), 6.85 (m, 1H), 6.25 (q, *J* = 6.5 Hz, 1H), 5.19 and 5.02 (AB, *J* = 16.2 Hz, 2H), 1.51 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 150.8, 147.9, 147.1, 137.0, 136.9, 134.7, 134.4, 134.0, 132.5, 132.0, 128.8 (×2), 128.6, 127.8, 127.5 (×2), 126.8, 124.6, 124.6, 72.1, 51.4, 21.8; HRMS (ESI, positive) calcd for C₁₆H₁₆N₂O₄Na⁺ [(M+Na)⁺] 323.1002,

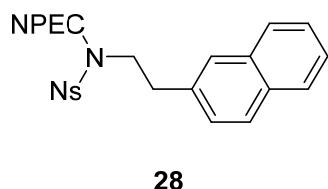
found 323.1003.

1-(2-Nitrophenyl)ethyl (2-nitrophenyl)sulfonyl(octyl)carbamate (27)



To a stirred solution of NPEC-NHNs **24** (550 mg, 1.36 mmol) in benzene (9.0 mL) at rt were added 1-octanol (0.423 mL, 2.68 mmol), triphenylphosphine (715 mg, 2.68 mmol), and a solution of diethyl azodicarboxylate in toluene (2.2 M, 1.25 mL, 2.68 mmol). After 16 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 30 g, MeOH/CHCl₃ = 1:19) to give octylamine **27** (627 mg, 92%) as a pale yellow oil: IR (ATR) 2928, 2856, 1732, 1526, 1442, 1364, 1265, 1170, 1139, 1057, 993 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.29 (d, *J* = 7.4 Hz, 1H), 7.94 (dd, *J* = 8.2, 1.3 Hz, 1H), 7.77–7.66 (m, 3H), 7.60 (ddd, *J* = 8.2, 7.8, 1.0 Hz, 1H), 7.48 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.42 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 1H), 6.27 (q, *J* = 6.4 Hz, 1H), 3.82 (dd, *J* = 8.6, 6.6 Hz, 2H), 1.72 (tt, *J* = 7.6, 7.6 Hz, 2H), 1.56–1.50 (m, 7H), 1.39–1.19 (m, 6H), 0.91–0.81 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 150.7, 147.8, 147.2, 136.9, 134.5, 133.9, 133.6, 133.0, 131.7, 128.8, 126.8, 124.7, 124.5, 72.0, 48.5, 31.7, 30.2, 29.1, 29.1, 26.6, 22.6, 21.8, 14.0; HRMS (ESI, positive) calcd for C₁₇H₂₆N₂O₄Na⁺ [(M+Na)⁺] 345.1785, found 345.1784.

1-(2-Nitrophenyl)ethyl (2-(naphthalen-2-yl)ethyl)((2-nitrophenyl)sulfonyl)carbamate (28)

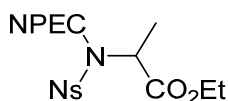


With the same procedure for the synthesis of **27** (see above), naphthalenylethylamine **28** (41.0 mg, 95%) was obtained as a pale yellow oil starting from 2-naphthaleneethanol (27.0 mg, 0.150 mmol),

NPEC-NHNs **24**, triphenylphosphine, and a solution of diethyl azodicarboxylate in toluene.

Data for naphthalenylethylamine **28**: IR (ATR) 3057, 1732, 1542, 1443, 1365, 1264, 1200, 1171, 1139, 1057, 854 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.26 (d, $J = 7.8$ Hz, 1H), 7.91 (d, $J = 7.6$ Hz, 1H), 7.82-7.75 (m, 3H), 7.73 (d, $J = 4.2$ Hz, 2H), 7.71-7.63 (m, 2H), 7.51-7.33 (m, 5H), 7.27 (d, $J = 7.5$ Hz, 1H), 6.20 (q, $J = 6.4$ Hz, 1H), 4.16 (dt, $J = 7.4, 3.3$ Hz, 2H), 3.20 (t, $J = 7.6$ Hz, 2H), 1.44 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 150.7, 147.8, 147.1, 136.7, 135.1, 134.6, 133.9, 133.7, 133.6, 132.9, 132.4, 131.8, 128.7, 128.3, 127.7, 127.7, 127.6, 127.4, 126.7, 126.1, 125.6, 124.6, 124.5, 72.3, 49.3, 36.9, 21.7; HRMS (ESI, positive) calcd for $\text{C}_{27}\text{H}_{23}\text{N}_3\text{O}_8\text{SNa}^+$ [(M+Na) $^+$] 572.1098, found 572.1099.

Ethyl **2-(2-nitro-N-((1-(2-nitrophenyl)ethoxy)carbonyl)phenylsulfonamido)propanoate (29)**



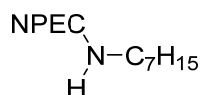
29

With the same procedure for the synthesis of **27** (see above), alanine ester **29** (34.0 mg, 85%, dr = 57:43) was obtained as a pale yellow oil starting from ethyl *rac*-lactate (0.0200 mL, 0.160 mmol), NPEC-NHNs **24**, triphenylphosphine, and a solution of diethyl azodicarboxylate in toluene.

Data for alanine ester **29**: IR (ATR) 2982, 1738, 1545, 1527, 1444, 1368, 1265, 1181, 1057, 909, 853 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.48 and 8.44 (two double doublets, $J = 6.7, 2.0$ Hz, 1H total), 7.94 (d, $J = 8.3$ Hz, 1H), 7.80-7.67 (m, 3H), 7.62 (m, 1H), 7.50 (m, 1H), 7.42 (t, $J = 7.8$ Hz, 1H), 6.34-6.24 (two multiplets, 1H total), 5.11 and 5.09 (two quartets, $J = 6.5$ Hz, 1H total), 4.24-4.05 (two multiplets, 2H total), 1.73 and 1.70 (two doublets, $J = 6.5$ Hz, 3H total), 1.52 and 1.45 (two doublets, $J = 6.3$ Hz, 3H total), 1.20 and 1.14 (two triplets, $J = 7.2$ Hz, 3H total); ^{13}C NMR (100 MHz, CDCl_3) δ 169.7,

169.6, 150.7, 150.4, 150.2, 148.2, 148.1, 147.3, 147.1, 147.0, 136.8, 136.4, 134.5, 134.5, 134.1, 134.0, 133.5, 132.9, 132.5, 132.1, 132.0, 128.8, 128.8, 127.3, 124.6, 124.6, 124.5, 124.5, 72.8, 72.1, 62.0, 62.0, 56.0, 55.9, 21.8, 21.8, 16.7, 16.5, 14.0, 13.9; HRMS (ESI, positive) calcd for $C_{20}H_{21}N_3O_{10}SNa^+$ [(M+Na)⁺] 518.0840, found 518.0844.

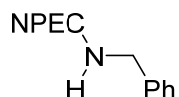
1-(2-Nitrophenyl)ethyl heptylcarbamate (**25a**)



25a

To a stirred solution of *N*-NPEC-*N*-Ns heptylamine **25** (18.0 mg, 0.0360 mmol) in CH_3CN (0.670 mL) at 0 °C were added thiophenol (0.010 mL, 0.10 mmol) and Cs_2CO_3 (33.0 mg, 0.100 mmol). After 1.5 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (2 mL), and the mixture was extracted with CH_2Cl_2 (1 × 2 mL, 4 × 1 mL). Combined organic layer was washed with brine (2 × 2 mL), dried over Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 600 mg, EtOAc/hexane = 2:8) to give des-*N*-Ns product **25a** (9.7 mg, 88%) as a yellow oil: IR (ATR) 3345, 2929, 2856, 1703, 1523, 1446, 1346, 1253, 1200, 1133, 1063 cm^{-1} ; 1H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 8.2 Hz, 1H), 7.62–7.57 (m, 2H), 7.39 (m, 1H), 6.21 (q, J = 6.5 Hz, 1H), 4.69 (brs, 1H), 3.23–2.98 (m, 2H), 1.59 (d, J = 6.5 Hz, 3H), 1.53–1.36 (m, 2H), 1.34–1.14 (m, 8H), 0.85 (t, J = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 147.7, 138.8, 133.3, 128.1, 127.0, 124.4, 68.5, 41.0, 31.7, 29.9, 28.9, 26.6, 22.5, 22.2, 14.0; HRMS (ESI, positive) calcd for $C_{16}H_{25}N_2O_4^+$ [(M+H)⁺] 309.1809, found 309.1808.

1-(2-Nitrophenyl)ethyl benzylcarbamate (**26a**)



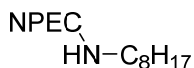
26a

With the same procedure for the synthesis of **25a** (see above), des-*N*-Ns product **26a** (8.0 mg, 89%) was obtained as a yellow oil starting

from *N*-NPEC-*N*-Ns benzylamine **26** (15.0 mg, 0.0310 mmol), thiophenol, and Cs₂CO₃.

Data for des-*N*-Ns product **26a**: IR (ATR) 3330, 3063, 2934, 1700, 1610, 1578, 1454, 1344, 1243, 1200, 1128 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 8.2 Hz, 1H), 7.66–7.55 (m, 2H), 7.40 (m, 1H), 7.35–7.19 (m, 5H), 6.28 (q, *J* = 6.5 Hz, 1H), 5.03 (brs, 1H), 4.43–4.21 (m, 2H), 1.61 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.2, 147.6, 138.6, 138.2, 133.4, 128.7 (×3), 128.2, 127.6 (×2), 127.0, 124.4, 68.9, 45.1, 22.2; HRMS (ESI, positive) calcd for C₁₆H₁₆N₂O₄Na⁺ [(M+Na)⁺] 323.1002, found 323.1003.

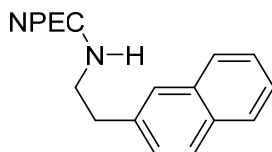
1-(2-Nitrophenyl)ethyl octylcarbamate (**27a**)



27a

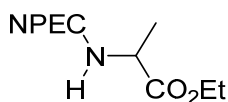
With the same procedure for the synthesis of **25a** (see above), des-*N*-Ns product **27a** (9.8 mg, 91%) was obtained as a yellow oil starting from *N*-NPEC-*N*-Ns octylamine **27** (17.0 mg, 0.0330 mmol), thiophenol, and Cs₂CO₃.

Data for des-*N*-Ns product **27a**: IR (ATR) 3341, 2926, 2855, 1700, 1523, 1445, 1346, 1247, 1133, 1063, 856 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, *J* = 8.2 Hz, 1H), 7.62–7.54 (m, 2H), 7.38 (m, 1H), 6.21 (q, *J* = 6.5 Hz, 1H), 4.69 (brs, 1H), 3.23–2.98 (m, 2H), 1.59 (d, *J* = 6.5 Hz, 3H), 1.49–1.37 (m, 2H), 1.32–1.15 (m, 10H), 0.85 (t, *J* = 6.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.2, 147.7, 138.8, 133.3, 128.1, 127.0, 124.4, 68.5, 41.0, 31.7, 29.9, 29.2, 29.2, 26.7, 22.6, 22.2, 14.1; HRMS (ESI, positive) calcd for C₁₇H₂₆N₂O₄Na⁺ [(M+Na)⁺] 345.1785, found 345.1784.

1-(2-Nitrophenyl)ethyl (2-(naphthalen-2-yl)ethyl)carbamate (28a)**28a**

With the same procedure for the synthesis of **25a** (see above), des-*N*-Ns product **28a** (8.8 mg, 88%) was obtained as a yellow oil starting from *N*-NPEC-*N*-Ns naphthalenylethylamine **28** (16.0 mg, 0.029 mmol), thiophenol, and Cs₂CO₃.

Data for des-*N*-Ns product **28a**: IR (ATR) 3416, 3053, 2934, 1705, 1522, 1445, 1345, 1242, 1130, 1060, 1007 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, *J* = 8.1 Hz, 1H), 7.84–7.73 (m, 3H), 7.59 (s, 1H), 7.56–7.49 (m, 2H), 7.49–7.41 (m, 2H), 7.37 (m, 1H), 7.28 (d, *J* = 8.4 Hz, 1H), 6.23 (q, *J* = 6.5 Hz, 1H), 4.74 (brs, 1H), 3.47 (dt, *J* = 6.8, 6.8 Hz, 2H), 2.93 (t, *J* = 6.8 Hz, 2H), 1.57 (d, *J* = 6.5 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 155.2, 147.6, 138.7, 136.1, 133.5, 133.4, 132.3, 128.3, 128.1, 127.6, 127.5, 127.2, 127.1, 126.9, 126.2, 125.5, 124.4, 68.6, 41.9, 36.1, 22.2; HRMS (ESI, positive) calcd for C₂₁H₂₀N₂O₄Na⁺ [(M+Na)⁺] 387.1315, found 387.1316.

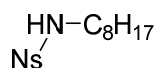
Ethyl 2-(((1-(2-nitrophenyl)ethoxy)carbonyl)amino)propanoate (29a)**29a**

With the same procedure for the synthesis of **25a** (see above), des-*N*-Ns product **29a** (10.0 mg, 90%, dr = 57:43) was obtained as a yellow oil starting from *N*-NPEC-*N*-Ns alanine ester **29** (18.0 mg, 0.0360 mmol), thiophenol, and Cs₂CO₃.

Data for des-*N*-Ns product **29a**: IR (ATR) 3359, 2983, 1448, 1343, 1203, 1065, 855, 787, 734, 702, 674 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.92 and 7.90 (two doublets, *J* = 7.1 Hz, 1H total), 7.66–7.55 (two multiplets, 2H total), 7.39 (two multiplets, 1H total), 6.24 (q, *J* = 6.5 Hz, 1H),

5.33 and 3.16 (brs, 1H total), 4.30-4.08 (m, 3H), 1.60 (d, $J = 6.5$ Hz, 3H), 1.38 and 1.33 (two doublets, $J = 7.2$ Hz, 3H total), 1.29-1.17 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 172.9 ($\times 2$), 155.1, 154.4, 147.5 ($\times 2$), 138.7, 138.5, 133.6, 133.5, 133.4, 128.2, 128.2, 128.1, 127.1, 124.4, 68.9 ($\times 2$), 61.5 ($\times 2$), 49.6, 22.3 ($\times 2$), 18.8, 18.7, 15.2, 14.1 ($\times 2$); HRMS (ESI, positive) calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_6\text{Na}^+$ [(M+Na) $^+$] 333.1057, found 333.1058.

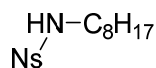
Typical procedure for photodeprotection of NPEC group of 27 with the LED light (365 nm, 3 W) (Table 3, run 5): 2-nitro-*N*-octylbenzenesulfonamide (27b)



27b

A solution of *N*-NPEC-*N*-Ns octylamine **27** (1.60 mg, 0.00315 mmol) in MeOH (1 mL) at rt under Ar bubbling was irradiated with the LED light (365 nm, 3 W). After 20 min, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 600 mg, EtOAc/hexane = 3:7) to give des-*N*-NPEC product **27b** (0.94 mg, 95%) as a brown oil: IR (ATR) 3293, 2925, 2856, 1593, 1539, 1414, 1362, 1340, 1265, 1163, 1124 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.12 (m, 1H), 7.84 (m, 1H), 7.76-7.68 (m, 2H), 5.22 (brs, 1H), 3.07 (dt, $J = 6.8, 6.8$ Hz, 2H), 1.54-1.44 (m, 2H), 1.31-1.13 (m, 10H), 0.84 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.1, 133.8, 133.4, 132.7, 131.1, 125.3, 43.9, 31.7, 29.5, 29.0, 28.9, 26.4, 22.6, 14.0; HRMS (ESI, positive) calcd for $\text{C}_{14}\text{H}_{23}\text{N}_2\text{O}_4\text{S}^+$ [(M+H) $^+$] 315.1373, found 315.1373.

Typical procedure for photodeprotection of NPEC group of 27 with high-pressure Hg lamp (435 W) (Table 3, run 11): 2-nitro-*N*-octylbenzenesulfonamide (27b)

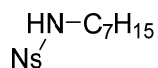


27b

A stirred solution of *N*-NPEC-*N*-Ns octylamine **27** (29.0 mg, 0.0571 mmol) in MeOH (40 mL) at rt under Ar bubbling was irradiated with

high pressure Hg lamp (435 W). After 1 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 600 mg, EtOAc/hexane = 3:7) to give des-*N*-NPEC product **27b** (16.0 mg, 94%) as a brown oil. For spectroscopic data of **27b**, see above.

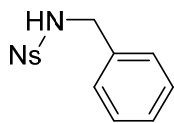
***N*-Heptyl-2-nitrobenzenesulfonamide (25b) (Table 4, run 1)**



25b

With the same procedure for the synthesis of **27b** (see the procedure above for Table 3, entry 5), *N*-NPEC-*N*-Ns amine **25** (5.8 mg) was irradiated with the LED light (365 nm, 3 W) in MeOH at rt to give **25b**.⁴

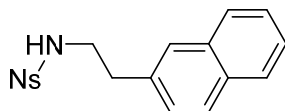
***N*-Benzyl-2-nitrobenzenesulfonamide (26b) (Table 4, run 2)**



26b

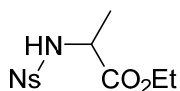
With the same procedure for the synthesis of **27b** (see the procedure above for Table 3, entry 5), *N*-NPEC-*N*-Ns amine **26** (6.3 mg) was irradiated with the LED light (365 nm, 3 W) in MeOH at rt to give **26b**.⁴

***N*-(2-(Naphthalen-2-yl)ethyl)-2-nitrobenzenesulfonamide (28b) (Table 4, run 3)**

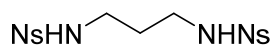


28b

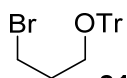
With the same procedure for the synthesis of **27b** (see the procedure above for Table 3, entry 5), *N*-NPEC-*N*-Ns amine **28** (5.3 mg) was irradiated with the LED light (365 nm, 3 W) in MeOH at rt to give **28b**.

Ethyl ((2-nitrophenyl)sulfonyl)alaninate (29b) (Table 4, run 4)**29b**

With the same procedure for the synthesis of **27b** (see the procedure above for Table 3, entry 5), *N*-NPEC-*N*-Ns amine **29** (5.2 mg) was irradiated with the LED light (365 nm, 3 W) in MeOH at rt to give **29b**.⁴

***N,N'*-(Propane-1,3-diyl)bis(2-nitrobenzenesulfonamide) (30)****30**

To a stirred solution of 1,3-diaminopropane (**3**, 1.14 mL, 13.5 mmol) in THF (67.0 mL) at rt were added 2-nitrobenzenesulfonyl chloride (5.68 g, 25.6 mmol) and K₂CO₃ (3.73 g, 27.0 mmol). After 23 h, the mixture was concentrated under reduced pressure, and to the residue were added CH₂Cl₂ (30 mL) and hydrochloric acid (1 M, 30 mL). Organic layer was separated and aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). Combined organic layer was washed with brine (2 × 20 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was washed with Et₂O (60 mL) to give *N*-Ns diamine **30** (4.80 g, 84%) as a brown powder: IR (ATR) 3326, 3292, 1532, 1414, 1336, 1160, 1117, 1063, 1025, 854, 782 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.16–8.12 (m, 2H), 7.88–7.85 (m, 2H), 7.79–7.70 (m, 4H), 5.62 (m, 2H), 3.22 (dt, *J* = 6.4, 6.4 Hz, 4H), 1.79 (p, *J* = 6.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 148.0 (×2), 135.6 (×2), 133.7 (×2), 133.0 (×2), 131.0 (×2), 125.5 (×2), 40.13 (×2), 30.4. The other spectroscopic data of **30** were in good agreement with those of the reported one.⁵

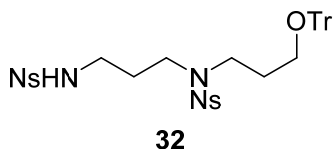
((3-Bromopropoxy)methanetriyl)tribenzene (31)**31**

To a stirred solution of 3-bromo-1-propanol (0.651 mL, 7.20 mmol) in

THF (14.0 mL) at rt were added trityl chloride (2.006 g, 7.20 mmol) and Et₃N (1.00 mL, 7.20 mmol). After 18 h, the reaction mixture was concentrated under reduced pressure, and to the residue were added CH₂Cl₂ (10 mL) and water (20 mL). Organic layer was separated and aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). Combined organic layer was washed with brine (2 × 15 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was washed with hexane (60 mL) to give an inseparable mixture of Tr ether **31** (1.545 g, 56%) and TrOH (191 mg, 10%) as a white powder, which was used for the next reaction (**30+31**→**32**) without purification.

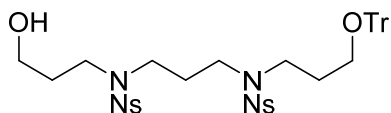
Data for Tr ether **31**: ¹H NMR (400 MHz, CDCl₃) δ 7.44–7.38 (m, 6H), 7.33–7.18 (m, 9H), 3.54 (t, *J* = 6.7 Hz, 2H), 3.20 (t, *J* = 5.9 Hz, 2H), 2.10 (tt, *J* = 6.3, 6.3 Hz, 2H). The other spectroscopic data of **31** were in good agreement with those of the reported one.⁶

2-Nitro-*N*-(3-(2-nitrophenylsulfonamido)propyl)-*N*-(3-(trityloxy)propyl)benzenesulfonamide (32)



To a stirred solution of *N*-Ns amine **31** (4.74 g, 10.7 mmol) in DMF (35.0 mL) at 60 °C were added a solution of bromide **31** (1.36 g, 3.57 mmol) in DMF (71 mL) and K₂CO₃ (2.95 g, 21.3 mmol). After 3.5 h, the reaction mixture was poured into water (120 mL) and EtOAc (50 mL). Organic layer was separated and aqueous layer was extracted with EtOAc (4 × 20 mL). Combined organic layer was washed with brine (2 × 30 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 120 g, acetone/CHCl₃ = 1:9) to give dimer diamine **32** (2.49 g, 94%) as a yellow oil: ¹H NMR (400 MHz, CDCl₃) δ 8.09 (m, 1H), 7.98 (ddd, *J* = 7.8, 6.1, 1.6 Hz, 1H), 7.82 (m, 1H), 7.76–7.50 (m, 5H), 7.37–7.31 (m, 5H), 7.30–7.17 (m, 10H), 5.56 (t, *J* = 6.3 Hz, 1H), 3.38–3.30 (m, 4H), 3.12 (dt, *J* = 6.3, 6.5 Hz, 2H), 3.07–3.01 (m, 2H), 1.83–1.68 (m, 4H).

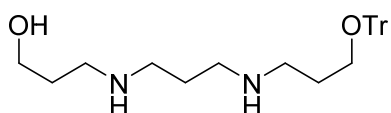
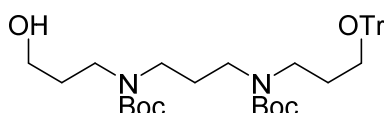
***N*-(3-Hydroxypropyl)-2-nitro-*N*-(3-(2-nitro-*N*-(3-(trityloxy)propyl)phenylsulfonamido)propyl)benzenesulfonamide (33)**

**33**

To a stirred solution of *N*-Ns amine **33** (2.49 g, 3.34 mmol) in DMF (30.0 mL) at 60 °C were added K₂CO₃ (2.95 g, 21.3 mmol) and 3-bromo-1-propanol (0.361 mL, 4.00 mmol). After 5 h, the reaction mixture was poured into water (50 mL), and the mixture was extracted with EtOAc (1 × 30 mL, 3 × 20 mL). Combined organic layer was washed with brine (2 × 30 mL), dried over Na₂SO₄, and concentrated in vacuo. The residue was purified by silica gel column chromatography (60N, 100 g, acetone/CHCl₃ = 2:8) to give trimer diamine **33** (1.80 g, 67%) as a pale yellow oil: IR (ATR) 3566, 3434, 2948, 2879, 1542, 1372, 1346, 1160, 1070, 766, 752 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.88 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.74 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.50–7.43 (m, 6H), 7.15–7.10 (m, 6H), 7.08–7.01 (m, 3H), 6.79–6.67 (m, 4H), 6.60–6.51 (m, 2H), 3.37–3.22 (m, 6H), 3.21–3.12 (m, 4H), 3.01 (t, *J* = 6.0 Hz, 2H), 1.75–1.59 (m, 4H), 1.49 (tt, *J* = 6.5, 6.5 Hz, 2H), 1.19 (brs, 1H); ¹³C NMR (100 MHz, C₆D₆) δ 148.4, 148.3, 144.6 (×3), 133.5, 133.3, 133.0, 133.0, 131.1, 131.1, 131.0, 130.9, 129.0 (×6), 128.1 (×6), 127.3 (×3), 123.9, 123.8, 87.1, 61.1, 59.2, 45.7, 45.5, 45.5, 45.1, 31.4, 29.3, 27.9; HRMS (ESI, positive) calcd for C₄₀H₄₂N₄O₁₀S₂Na [(M+Na)⁺] 825.2235, found 825.2233.

3-((3-((3-(Trityloxy)propyl)amino)propyl)amino)propan-1-ol (34), and

***tert*-butyl (3-((*tert*-butoxycarbonyl)(3-(trityloxy)propyl)amino)propyl)(3-hydroxypropyl)carbamate (35)**

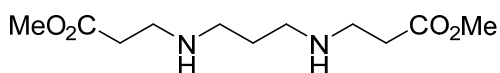
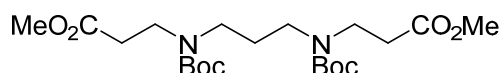
**34****35**

To a stirred solution of di-*N*-Ns amine **33** (49.0 mg, 0.0610 mmol) in

CH₃CN (0.670 mL) at 0 °C were added thiophenol (0.0200 mL, 0.180 mmol) and Cs₂CO₃ (60.0 mg, 0.180 mmol). After 2.5 h, the mixture was poured into saturated aqueous NaHCO₃ (5 mL), and the mixture was extracted with CH₂Cl₂ (1 × 3 mL, 3 × 2 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure to give diamine **34** (42.0 mg) as a yellow oil, which was used for the next reaction without purification.

To a stirred solution of the diamine **34** (42.0 mg), thus obtained above, in MeOH (0.610 mL) at rt was added Boc₂O (0.099 mL, 0.43 mmol). After 22 h, the mixture was poured into water (3 mL), and the mixture was extracted with CH₂Cl₂ (3 × 2 mL). Combined organic layer was washed with brine (2 × 3 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 16 g, MeOH/CHCl₃ = 6:94) to give di-*N*-Boc amine **35** (6.8 mg, 18%) as a pale yellow oil: IR (ATR) 3449, 2974, 1686, 1478, 1416, 1365, 1249, 1162, 1068, 736, 705 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 7.58–7.47 (m, 6H), 7.14–7.09 (m, 6H), 7.08–7.00 (m, 3H), 3.64–3.49 (m, 2H), 3.41–2.80 (m, 10H), 1.93–1.70 (m, 2H), 1.70–1.54 (m, 2H), 1.54–1.41 (m, 11H), 1.41–1.32 (m, 9H); ¹³C NMR (100 MHz, C₆D₆) δ 156.7, 155.3, 144.8 (×3), 129.0 (×6), 128.5 (×6), 127.2 (×3), 87.0, 79.6, 78.9, 61.7, 58.5, 45.3 (×2), 45.0 (×2), 43.2, 31.4, 29.9, 28.5 (×3), 28.4 (×3); HRMS (ESI, positive) calcd for C₃₈H₅₂N₂O₆Na [(M+Na)⁺] 655.3718, found 655.3718.

Dimethyl 3,3'-(propane-1,3-diylbis(azanediyl)dipropionate (37), and dimethyl 3,3'-(2,2,12,12-tetramethyl-4,10-dioxo-3,11-dioxa-5,9-diazatridecane-5,9-diyl)dipropionate (38)

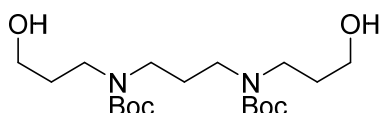
**37****38**

To a stirred solution of 1,3-diaminopropane (**3**, 1.14 mL, 6.41 mmol) in EtOH (6.40 mL) at 0 °C was added a solution of methyl acrylate (1.21 mL, 13.5 mmol) in EtOH (6.40 mL) in a dropwise manner over 30 min. After 1 h, the reaction mixture was concentrated under reduced

pressure to remove volatile materials, to give diester **37** (1.75 g) as a colorless oil, which was used for the next reaction (**37**→**38**) without purification.

To a stirred solution of the crude trimer diamine **37** (1.75 g), thus obtained above, in MeOH (21 mL) at rt was added Boc₂O (4.42 mL, 19.2 mmol). After 1.5 h, the reaction mixture was poured into water (20 mL), and the mixture was extracted with CH₂Cl₂ (1 × 20 mL, 3 × 10 mL). Combined organic layer was washed with brine (2 × 20 mL), dried over Na₂SO₄, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30μ Premium, 40 g, EtOAc/hexane = 4:6) to give *N*-Boc diamine **38** (2.29 g, 80%) as a colorless oil: IR (ATR) 2976, 1737, 1686, 1477, 1415, 1365, 1249, 1157, 1045, 865, 734 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.63 (s, 6H), 3.42 (t, *J* = 6.6 Hz, 4H), 3.15 (t, *J* = 6.8 Hz, 4H), 2.52 (t, *J* = 6.6 Hz, 4H), 1.69 (tt, *J* = 6.8, 6.8 Hz, 2H), 1.40 (brs, 18H); ¹³C NMR (100 MHz, CDCl₃) δ 172.2 (×2), 155.1 (×2), 79.7 (×2), 51.6 (×2), 45.5 (×2), 43.3 (×2), 33.5 (×2), 28.4 (×7); HRMS (ESI, positive) calcd for C₂₁H₃₈N₂O₈Na [(M+Na)⁺] 469.2520, found 469.2522.

Di-tert-butyl propane-1,3-diylbis((3-hydroxypropyl)carbamate) (39)

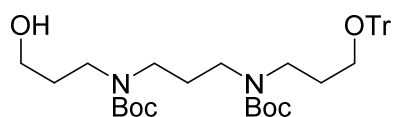


39

To a stirred suspension of lithium aluminum hydride (92.0 mg, 2.42 mmol) in THF (3.2 mL) at 0 °C was added a solution of diester **38** (111 mg, 0.242 mmol, including its ethyl ester) in THF (0.8 mL) in a dropwise manner over 10 min. After 2 h, saturated aqueous Rochelle's salt (14 drops) was added dropwise, and the mixture was vigorously stirred at rt for 14 h. The mixture was filtered through a pad of Celite®, and the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 1 g, MeOH/CHCl₃ = 10:90) to give diol **39** (83.0 mg, 88%) as a colorless oil: IR (ATR) 3416, 2976, 1665, 1479, 1416, 1365, 1297, 1250, 1162, 1058, 881 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.64–3.45 (m, 4H), 3.41–3.26

(m, 4H), 3.20–3.05 (m, 4H), 1.76 (tt, $J = 7.3, 7.3$ Hz, 2H), 1.71–1.61 (m, 4H), 1.44 (brs, 18H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.6 ($\times 2$), 80.1 ($\times 2$), 58.3 ($\times 2$), 44.9 ($\times 2$), 42.7 ($\times 2$), 30.7 ($\times 2$), 28.4 ($\times 6$), 27.7; HRMS (ESI, positive) calcd for $\text{C}_{19}\text{H}_{39}\text{N}_2\text{O}_6$ $[(\text{M}+\text{H})^+]$ 391.2803, found 391.2807.

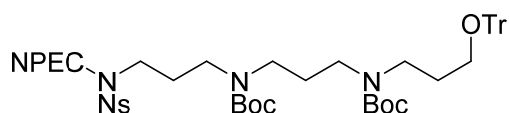
tert-Butyl (3-((*tert*-butoxycarbonyl)(3-(trityloxy)propyl)amino)propyl)(3-hydroxypropyl)carbamate (**35**)



35

To a stirred solution of diol **39** (1.01 g, 2.59 mmol) in CH_2Cl_2 (25 mL) at rt were added trityl chloride (1.08 g, 3.88 mmol), Et_3N (1.08 mL, 7.77 mmol), and DMAP (31.0 mg, 0.259 mmol). After 2 h, the mixture was poured into water (20 mL). Organic layer was separated and aqueous layer was extracted with CH_2Cl_2 (5 \times 10 mL). Combined organic layer was washed with brine (2 \times 20 mL), dried over Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 16 g, MeOH/ CHCl_3 = 8:92) to give monotrityl ether **35** (831 mg, 51%) as a pale yellow oil. Unreacted substrate **39** (383 mg, 38%) was also recovered. For spectroscopic data of **35**, see above (**34** \rightarrow **35**).

tert-Butyl (3-((*tert*-butoxycarbonyl)(3-(2-nitro-*N*-(1-(2-nitrophenyl)ethoxy)carbonyl)phenylsulfonamido)propyl)amino)propyl)(3-(2-nitro-*N*-(1-(2-nitrophenyl)ethoxy)carbonyl)phenylsulfonamido)propyl)carbamate (**36**)



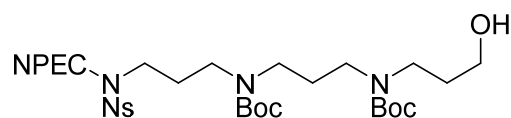
36

key 3-mer triamine building block

To a stirred solution of alcohol **35** (250 mg, 0.400 mmol) in benzene (1.0 mL) at rt were added a solution of NPEC-NHNs **24** (172 mg, 0.440 mmol) in benzene (3.0 mL), PPh_3 (207 mg, 0.790 mmol), and a solution of diethyl azodicarboxylate in toluene (2.2 M, 0.359 mL, 0.790 mmol).

After 2 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 23 g, acetone/CHCl₃ = 5:95) to give 3-mer triamine key building block **36** (314 mg, 78%) as a pale yellow oil: IR (ATR) 2977, 1734, 1684, 1544, 1417, 1365, 1265, 1170, 853, 731, 705 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.28 (m, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.77–7.65 (m, 5H), 7.61 (m, 1H), 7.43–7.37 (m, 5H), 7.30–7.16 (m, 10H), 6.27 (q, *J* = 6.2 Hz, 1H), 3.88–3.78 (m, 2H), 3.29–3.19 (m, 4H), 3.18–3.00 (m, 6H), 2.02–1.87 (m, 2H), 1.87–1.75 (m, 2H), 1.75–1.64 (m, 2H), 1.57–1.48 (m, 3H), 1.43 (s, 9H), 1.39 (s, 9H); ¹³C NMR (100 MHz, C₆D₆) δ 155.4 (×2), 151.1, 148.1, 147.7 (×2), 144.9 (×3), 137.0, 134.1 (×4), 132.9, 131.2, 129.1 (×6), 128.5 (×6), 127.2 (×3), 124.5, 123.9, 87.0, 79.2, 78.8, 72.2, 61.8, 46.6, 45.0 (×4), 29.9 (×2), 28.5 (×7), 21.5; HRMS (ESI, positive) calcd for C₅₃H₆₄N₅O₁₃S [(M+H)⁺] 1010.4216, found 1010.4216.

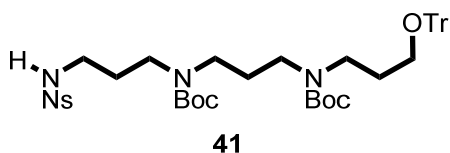
1-(2-Nitrophenyl)ethyl (3-((tert-butoxycarbonyl)(3-((tert-butoxycarbonyl)(3-hydroxypropyl)amino)propyl)amino)propyl)((2-nitrophenyl)sulfonyl)carbamate (40)

**40**

A solution of trimer Tr ether **36** (148 mg, 0.146 mmol) in 2,2,2-trifluoroethanol (1.46 mL) was stirred at reflux. After 41 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 5 g, EtOAc/hexane = 8:2) to give trimer alcohol **40** (99.0 mg, 88%) as a pale yellow oil: IR (ATR) 3423, 2977, 1736, 1683, 1544, 1478, 1419, 1365, 1265, 1166, 1057 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 8.10 (d, *J* = 7.4 Hz, 1H), 7.62–7.28 (m, 2H), 7.16 (m, 1H), 6.85 (m, 1H), 6.75–6.51 (m, 3H), 6.29 (q, *J* = 6.3 Hz, 1H), 4.15–3.96 (m, 2H), 3.67–3.45 (m, 2H), 3.39–2.80 (m, 8H), 2.15–1.88 (m, 2H), 1.78–1.46 (m, 13H), 1.45–1.38 (m, 9H), 1.29–1.18 (m, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 156.9, 155.4, 151.0, 148.1, 147.7, 136.8, 134.2, 133.9, 132.8 (×2), 131.3, 128.7, 126.8, 128.5, 124.6, 124.1, 79.7, 79.4, 72.2, 58.4, 46.6, 45.2, 44.8 (×2), 43.1, 31.4, 30.0, 28.5 (×3), 28.4 (×3), 21.4; HRMS (ESI, positive) calcd

for $C_{34}H_{49}N_5O_{13}SNa$ [(M+Na)⁺] 790.2940, found 790.2923.

tert-Butyl (3-((*tert*-butoxycarbonyl)(3-(trityloxy)propyl)amino)propyl)(3-(2-nitrophenylsulfonamido)propyl)carbamate (**41**)



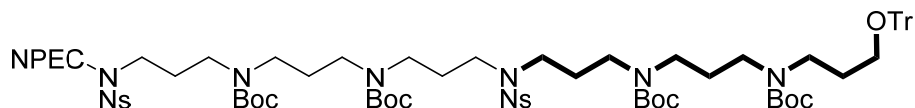
Reaction by the LED light (365 nm, 3 W). A stirred solution of NPEC-*N*-Ns amine **36** (7.5 mg, 0.0075 mmol) in MeOH (2.50 mL) at rt was irradiated with the LED light (365 nm, 3 W). After 20 min, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 0.1 g, EtOAc/PhH = 1:9) to give des-*N*-NPEC product **41** (6.1 mg, 99%) as a pale yellow oil.

Reaction by High pressure Hg lamp (435 W). A stirred solution of trimer *N*-NPEC-*N*-Ns amine **36** (93.0 mg, 0.0920 mmol) in MeOH (40 mL) at rt with Ar bubbling was irradiated with high-pressure Hg lamp (435 W). After 30 min, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 16 g, EtOAc/hexane = 1:1) to give des-*N*-NPEC product **41** (65.0 mg, 94%) as a yellow oil.

Data for des-*N*-NPEC product **41**: IR (ATR) 3242, 2978, 1682, 1542, 1478, 1417, 1363, 1265, 1164, 1069, 853 cm^{-1} ; 1H NMR (400 MHz, C_6D_6) δ 7.84 (d, J = 7.7 Hz, 1H), 7.58–7.50 (m, 6H), 7.14–7.09 (m, 6H), 7.09–7.00 (m, 3H), 6.93 (d, J = 8.0 Hz, 1H), 6.67 (m, 1H), 6.52 (m, 1H), 3.41–2.72 (m, 12H), 1.92–1.70 (m, 2H), 1.65–1.48 (m, 2H), 1.46–1.42 (m, 9H), 1.41–1.29 (m, 11H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.3 ($\times 2$), 148.5, 144.8 ($\times 3$), 132.5, 131.7 ($\times 2$), 130.6, 129.0 ($\times 6$), 128.5 ($\times 6$), 127.2 ($\times 3$), 124.6, 87.0, 79.6, 79.0, 61.7, 45.1 ($\times 3$), 43.7, 40.8, 29.9, 29.1, 28.5 ($\times 3$), 28.4 ($\times 3$), 28.0; HRMS (ESI, positive) calcd for $C_{44}H_{57}N_4O_9S$ [(M+H)⁺] 817.3841, found 817.3835.

tert-Butyl (9,13-bis(*tert*-butoxycarbonyl)-2-(2-nitrophenyl)-5,17-

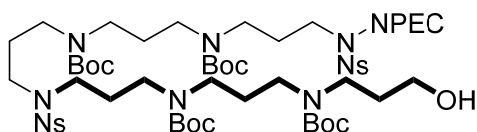
bis((2-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17-tetraazaicosan-20-yl)(3-((tert-butoxycarbonyl)(3-(trityloxy)propyl)amino)propyl)carbamate (42)



42 (6-mer polyamine)

To a stirred solution of trimer alcohol **40** (404 mg, 0.526 mmol) and trimer *N*-Ns amine **41** (405 mg, 0.533 mmol) in benzene (5.30 mL) at rt were added PPh₃ (276 mg, 1.05 mmol) and a solution of diethyl azodicarboxylate in toluene (2.2 M, 0.478 mL, 1.05 mmol). After 2 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (SiOH-30 μ Premium, 40 g, EtOAc/hexane = 6:4) to give hexamer polyamine **42** (675 mg, 82%) as a pale yellow oil: IR (ATR) 2977, 1684, 1544, 1478, 1417, 1365, 1265, 1157, 1058, 853, 733 cm⁻¹; ¹H NMR (400 MHz, C₆D₆) δ 8.14 (m, 1H), 7.84 (s, 1H), 7.62–7.51 (m, 5H), 7.48–7.38 (m, 2H), 7.27–7.11 (m, 7H), 7.10–7.02 (m, 3H), 6.92–6.81 (m, 2H), 6.77 (d, *J* = 7.2 Hz, 1H), 6.73–6.55 (m, 4H), 6.49 (m, 1H), 6.31 (m, 1H), 4.16–3.96 (m, 4H), 3.48–2.85 (m, 20H), 2.21–1.95 (m, 2H), 1.95–1.59 (m, 10H), 1.59–1.39 (m, 36H), 1.25 (d, *J* = 5.9 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 155.4 (\times 4), 151.1, 148.4, 148.1, 147.7, 144.9, 136.9, 134.0 (\times 2), 133.8, 133.0, 132.8, 131.2, 131.2, 131.0 (\times 2), 129.1 (\times 6), 128.5 (\times 7), 127.2 (\times 3), 124.6 (\times 2), 123.9 (\times 4), 87.0, 79.3, 79.2 (\times 2), 78.8, 72.2, 61.8, 46.6, 45.1 (\times 8), 44.9 (\times 2), 30.1 (\times 2), 28.5 (\times 12), 27.6 (\times 4), 21.5; HRMS (ESI, positive) calcd for C₇₈H₁₀₃N₉O₂₁S₂Na [(M+Na)⁺] 1588.6602, found 1588.6619.

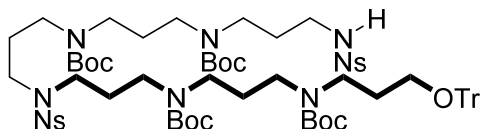
tert-Butyl (9,13-bis(tert-butoxycarbonyl)-2-(2-nitrophenyl)-5,17-bis((2-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17-tetraazaicosan-20-yl)(3-((tert-butoxycarbonyl)(3-hydroxypropyl)amino)propyl)carbamate (43)



43

A solution of hexamer Tr ether **42** (43.7 mg, 0.0279 mmol) in 2,2,2-trifluoroethanol (1.80 mL) was stirred at reflux. After 6 h, the mixture was concentrated under reduced pressure. The residue was purified by recycling preparative HPLC to give hexamer alcohol **43** (36.0 mg, 97%) as a pale yellow oil: IR (ATR) 2978, 2937, 1738, 1687, 1546, 1477, 1418, 1366, 1253, 1165, 1059 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 8.13 (m, 1H), 7.81 (m, 1H), 7.42 (d, $J = 8.2$ Hz, 1H), 6.91–6.79 (m, 3H), 6.76 (m, 1H), 6.71–6.55 (m, 4H), 6.47 (m, 1H), 6.31 (q, $J = 6.2$ Hz, 1H), 4.15–4.00 (m, 2H), 3.67–3.47 (m, 2H), 3.44–2.86 (m, 21H), 2.19–1.92 (m, 2H), 1.92–1.59 (m, 10H), 1.59–1.38 (m, 36H), 1.24 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.4 ($\times 3$), 155.4 ($\times 2$), 151.1, 148.4, 148.1, 147.8 ($\times 2$), 136.9, 134.1, 134.0 ($\times 2$), 133.7, 133.1, 132.9, 131.2, 131.2, 130.9, 124.6, 124.0, 123.9, 79.3 ($\times 4$), 72.3, 46.6, 45.3 ($\times 3$), 44.9 ($\times 4$), 44.8 ($\times 3$), 43.2, 31.4, 30.0, 28.5 ($\times 9$), 28.4 ($\times 3$), 27.9 ($\times 4$), 21.5; HRMS (ESI, positive) calcd for $\text{C}_{59}\text{H}_{89}\text{N}_9\text{O}_{21}\text{S}_2\text{Na}$ [(M+Na) $^+$] 1346.5507, found 1346.5495.

tert-Butyl (3-((*tert*-butoxycarbonyl)(3-(trityloxy)propyl)amino)propyl)(9-(*tert*-butoxycarbonyl)-2,2-dimethyl-13-((2-nitrophenyl)sulfonyl)-5-(3-(2-nitrophenylsulfonamido)propyl)-4-oxo-3-oxa-5,9,13-triazahexadecan-16-yl)carbamate (**44**)

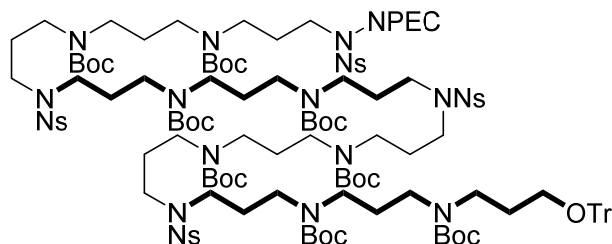
**44**

Reaction by the LED light (365 nm, 3 W). A stirred solution of hexamer *N*-NPEC-*N*-Ns polyamine **42** (13.3 mg, 0.00847 mmol) in MeOH (0.800 mL) at rt was irradiated with the LED light (365 nm, 3 W). After 20 min, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 0.3 g, EtOAc/PhH = 2:3) to give hexamer *N*-Ns amine **44** (11.3 mg, 97%) as a pale yellow oil.

Reaction by High pressure Hg lamp (435 W). A stirred solution of hexamer *N*-NPEC-*N*-Ns polyamine **42** (7.0 mg, 0.0045 mmol) in MeOH (8.0

mL) at rt with Ar bubbling was irradiated with high-pressure Hg lamp (435 W). After 10 min, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 600 mg, EtOAc/hexane = 7:3) to give hexamer *N*-Ns amine **44** (4.9 mg, 81%) as a yellow oil: IR (ATR) 2976, 2930, 1686, 1545, 1479, 1418, 1366, 1252, 1164, 1070, 748 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 7.90–7.77 (m, 2H), 7.60–7.51 (m, 6H), 7.22–7.10 (m, 6H), 7.10–7.02 (m, 3H), 7.00–6.96 (m, 1H), 6.88–6.78 (m, 2H), 6.77–6.61 (m, 3H), 6.55 (m, 1H), 4.10–3.94 (m, 2H), 3.45–2.75 (m, 22H), 1.95–1.56 (m, 12H), 1.52–1.37 (m, 36H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.4 ($\times 4$), 148.5, 148.4, 144.8 ($\times 4$), 133.6, 133.1, 132.7, 131.8, 131.2, 130.9, 130.7, 129.1 ($\times 6$), 128.5 ($\times 6$), 127.2 ($\times 3$), 124.7, 123.9, 87.0, 79.6, 79.3, 79.2, 78.9, 61.8, 45.2 ($\times 9$), 44.0, 41.0, 29.2, 28.5 ($\times 9$), 28.4 ($\times 3$), 28.0 ($\times 4$), 27.7; HRMS (ESI, positive) calcd for $\text{C}_{69}\text{H}_{96}\text{N}_8\text{O}_{17}\text{S}_2\text{Na}$ [(M+Na) $^+$] 1395.6227, found 1395.6227.

tert-Butyl (6,10-bis(*tert*-butoxycarbonyl)-14-((2-nitrophenyl)sulfonyl)-1,1,1-triphenyl-2-oxa-6,10,14-triazaheptadecan-17-yl)(9,13,21,25,33-pentakis(*tert*-butoxycarbonyl)-2-(2-nitrophenyl)-17-((2-nitrophenyl)sulfonyl)-5,29-bis((4-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17,21,25,29,33-octaazahexatriacontan-36-yl)carbamate (**45**)

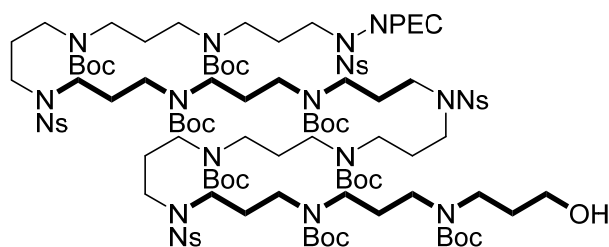


45 (12-mer polyamine)

To a stirred solution of hexamer alcohol **43** (16.0 mg, 0.0120 mmol) and hexamer *N*-Ns amine **44** (17.0 mg, 0.0124 mmol) in benzene (0.600 mL) at rt were added PPh_3 (7.0 mg, 0.024 mmol) and a solution of diethyl azodicarboxylate in toluene (2.2 M, 0.011 mL, 0.024 mmol). After 5 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 2 g, EtOAc/hexane = 9:1) to give 12-mer polyamine **45** (25.0 mg, 78%) as a

pale yellow oil: IR (ATR) 2974, 1683, 1543, 1477, 1416, 1364, 1248, 1154, 1058, 852, 734 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 8.14 (m, 1H), 7.94–7.76 (m, 3H), 7.60–7.51 (m, 5H), 7.48–7.39 (m, 2H), 7.27–7.11 (m, 5H), 7.10–7.02 (m, 3H), 7.02–6.84 (m, 8H), 6.84–6.71 (m, 4H), 6.71–6.58 (m, 3H), 6.51 (m, 1H), 6.31 (m, 1H), 4.15–3.96 (m, 4H), 3.51–2.83 (m, 44H), 2.19–1.96 (m, 2H), 1.95–1.61 (m, 22H), 1.61–1.39 (m, 72H), 1.29–1.22 (m, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.4 ($\times 8$), 151.1, 148.4 ($\times 4$), 148.1 ($\times 2$), 147.8 ($\times 3$), 144.9 ($\times 3$), 136.9, 134.2 ($\times 2$), 133.9 ($\times 2$), 133.7 ($\times 2$), 133.2 ($\times 2$), 132.9, 131.3 ($\times 4$), 130.9 ($\times 2$), 129.1 ($\times 6$), 128.5 ($\times 6$), 127.2 ($\times 3$), 124.6, 124.0 ($\times 4$), 87.0, 79.2 ($\times 7$), 78.9, 72.3, 61.8, 46.6, 45.4 ($\times 16$), 44.9 ($\times 6$), 30.1, 28.6 ($\times 25$), 27.8 ($\times 10$), 21.5; HRMS (ESI, positive) calcd for $\text{C}_{128}\text{H}_{183}\text{N}_{17}\text{O}_{37}\text{S}_4\text{Na}_2$ [$\text{M}+2\text{Na}$] $^{2+}$ 1362.0814, found 1362.0880.

tert-Butyl (9,13,21-tris(tert-butoxycarbonyl)-2-(2-nitrophenyl)-17-((2-nitrophenyl)sulfonyl)-5-((4-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17,21-pentaazatetracosan-24-yl)(9,17,21-tris(tert-butoxycarbonyl)-5-(3-hydroxypropyl)-2,2-dimethyl-13-((2-nitrophenyl)sulfonyl)-25-((4-nitrophenyl)sulfonyl)-4-oxo-3-oxa-5,9,13,17,21,25-hexaazaoctacosan-28-yl)carbamate (2b)



2b
12-mer LCPA subunit

A solution of 12-mer Tr ether **45** (25.0 mg, 0.00932 mmol) in 2,2,2-trifluoroethanol (0.932 mL) was stirred at rt. After 18 h, the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (60N, 600 mg, EtOAc/hexane = 9:1) to give 12-mer alcohol **2b** (110 mg, 40%) as a pale yellow oil. Unreacted substrate **45** (88.0 mg, 56%) was also recovered.

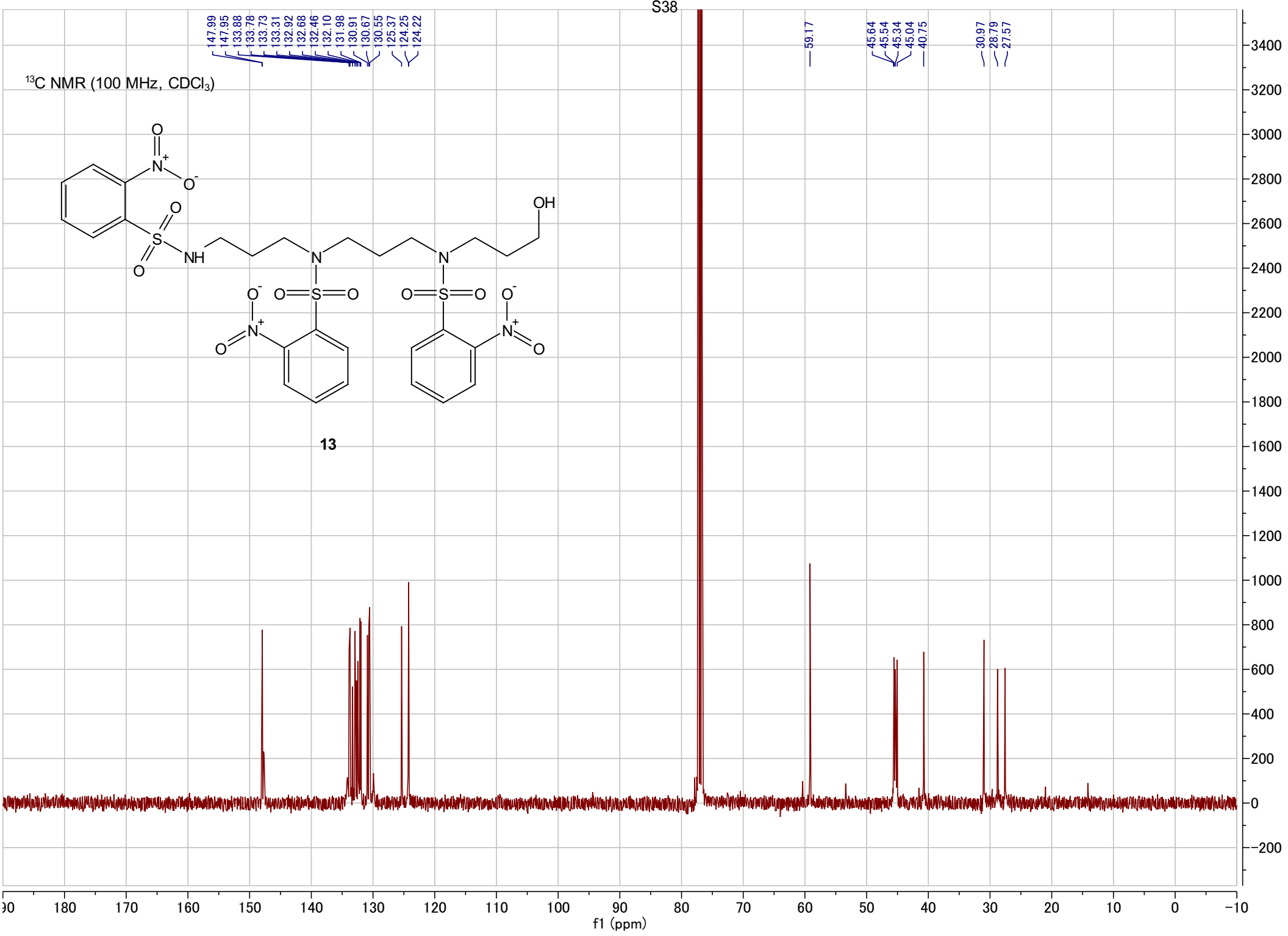
Data for 12-mer alcohol **2b**: IR (ATR) 2927, 1682, 1544, 1477, 1417,

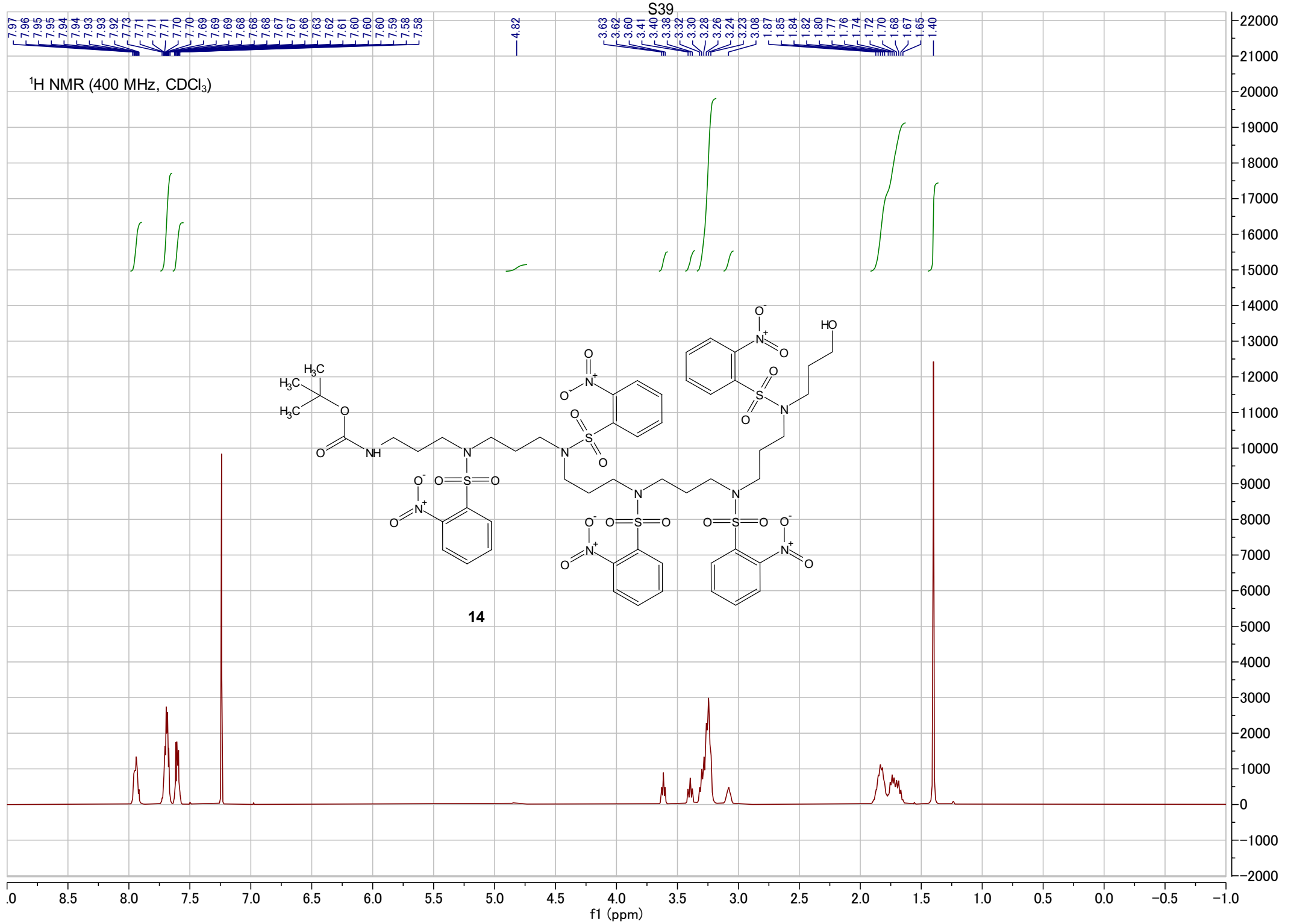
1365, 1250, 1156, 1058, 852, 732 cm^{-1} ; ^1H NMR (400 MHz, C_6D_6) δ 8.14 (m, 1H), 7.94-7.75 (m, 4H), 7.45 (d, $J = 8.2$ Hz, 1H), 7.04-6.87 (m, 7H), 6.87-6.73 (m, 4H), 6.73-6.61 (m, 2H), 6.55 (m, 1H), 6.31 (m, 1H), 4.14-3.99 (m, 2H), 3.67-3.50 (m, 2H), 3.48-2.90 (m, 44H), 2.18-1.95 (m, 2H), 1.92-1.62 (m, 22H), 1.55-1.46 (m, 63H), 1.45 (s, 9H), 1.26 (d, $J = 6.1$ Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 155.4 ($\times 9$), 148.4 ($\times 6$), 148.1 ($\times 3$), 147.8, 134.2 ($\times 2$), 133.9 ($\times 2$), 133.6 ($\times 2$), 133.2 ($\times 3$), 131.3 ($\times 4$), 130.9 ($\times 2$), 124.6, 124.0 ($\times 4$), 79.2 ($\times 8$), 72.3, 45.3 ($\times 16$), 44.9 ($\times 8$), 28.6 ($\times 24$), 28.5 ($\times 12$), 21.5; HRMS (ESI, positive) calcd for $\text{C}_{109}\text{H}_{169}\text{N}_{17}\text{O}_{37}\text{S}_4\text{Na}_2$ $[(\text{M}+2\text{Na})^{2+}]$ 1241.0266, found 1241.0257.

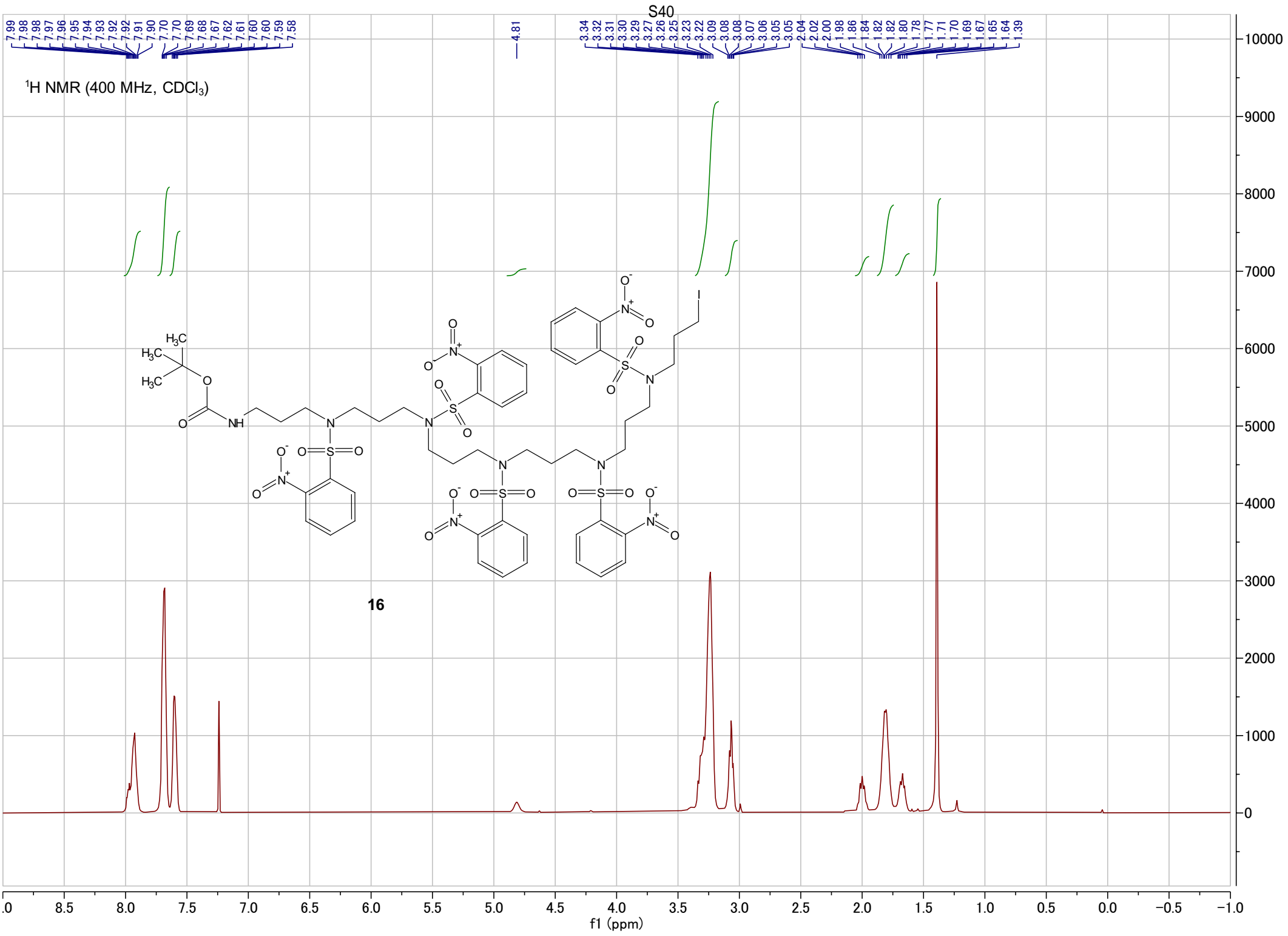
[REFERENCES AND NOTES]

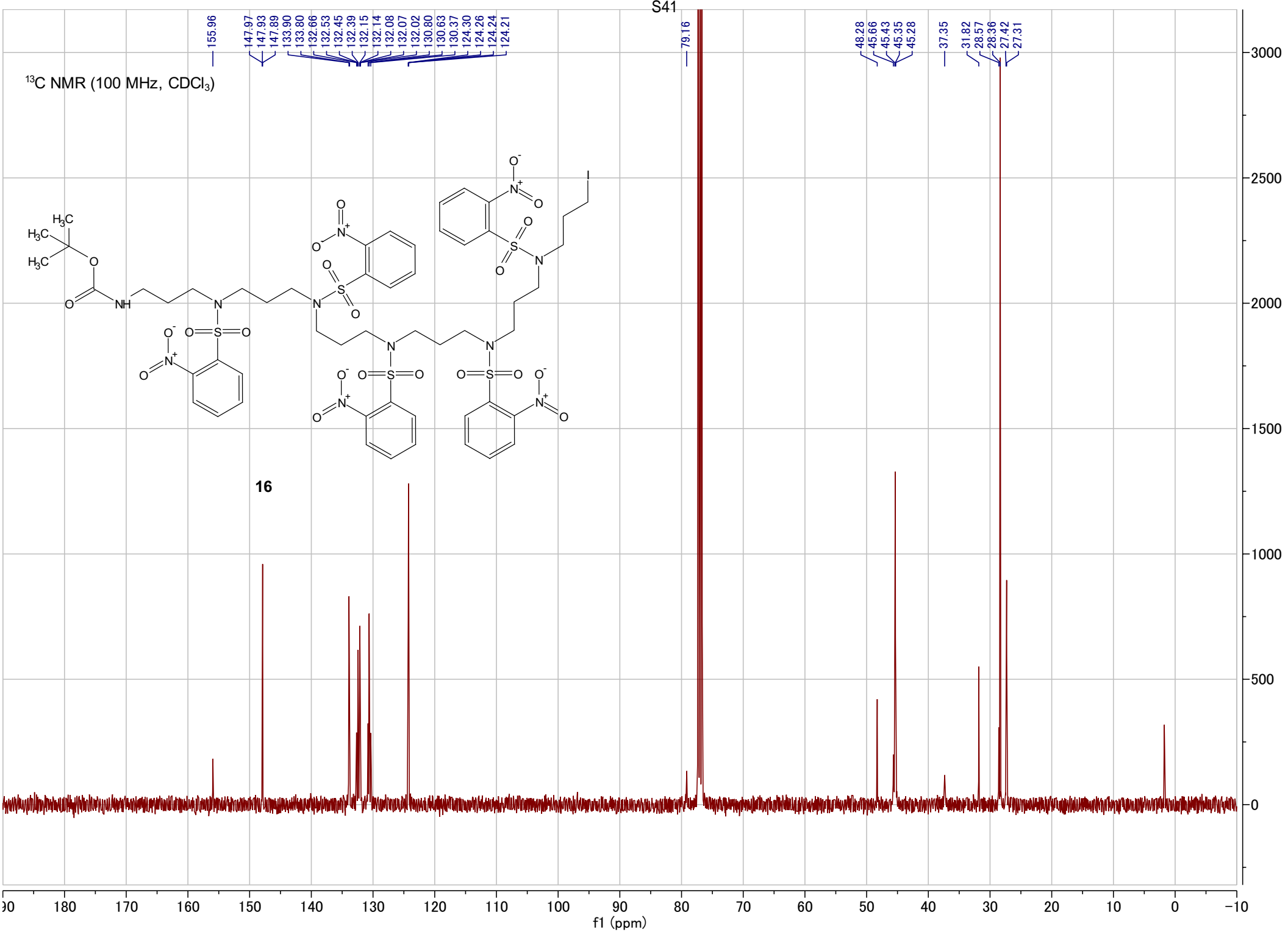
1. Y. Hidai, T. Kan and T. Fukuyama, *Chem. Pharm. Bull.*, 2000, **48**, 1570-1576.
2. F. Thuaud, F. Rohrbacher, A. Zwickly and J. W. Bode, *Helv. Chim. Acta*, 2016, **99**, 868-894.
3. (a) Y. Kikuchi, J. Nakanishi, T. Shimizu, H. Nakayama, S. Inoue, K. Yamaguchi, H. Iwai, Y. Yoshida, Y. Horiike, T. Takarada and M. Maeda, *Langmuir*, 2008, **24**, 13084-13095; (b) Y. Kawada, T. Kodama, K. Miyashita, T. Imanishi and S. Obika, *Org. Biomol. Chem.*, 2012, **10**, 5102-5108.
4. T. Fukuyama, M. Cheung and T. Kan, *Synlett*, 1999, 1301-1303.
5. M. R. Heinrich, Y. Kashman, P. Spiteller and W. Steglich, *Tetrahedron*, 2001, **57**, 9973-9978.
6. T. Niittymäki, U. Kaukinen, P. Virta, S. Mikkola and H. Lönnberg, *Bioconjugate Chem.*, 2004, **15**, 174-184.

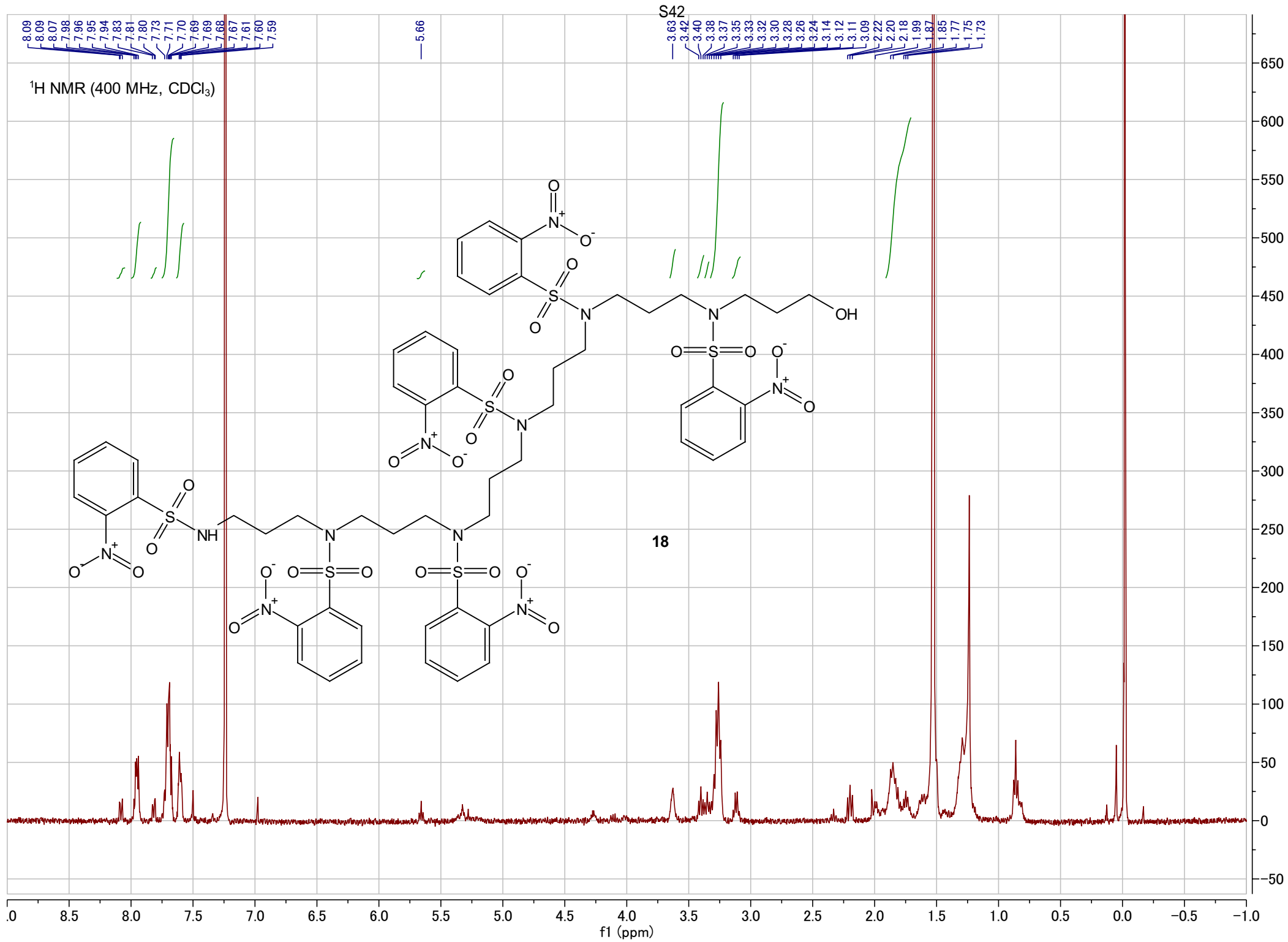
[NMR SPECTRA OF ALL NEW COMPOUNDS]

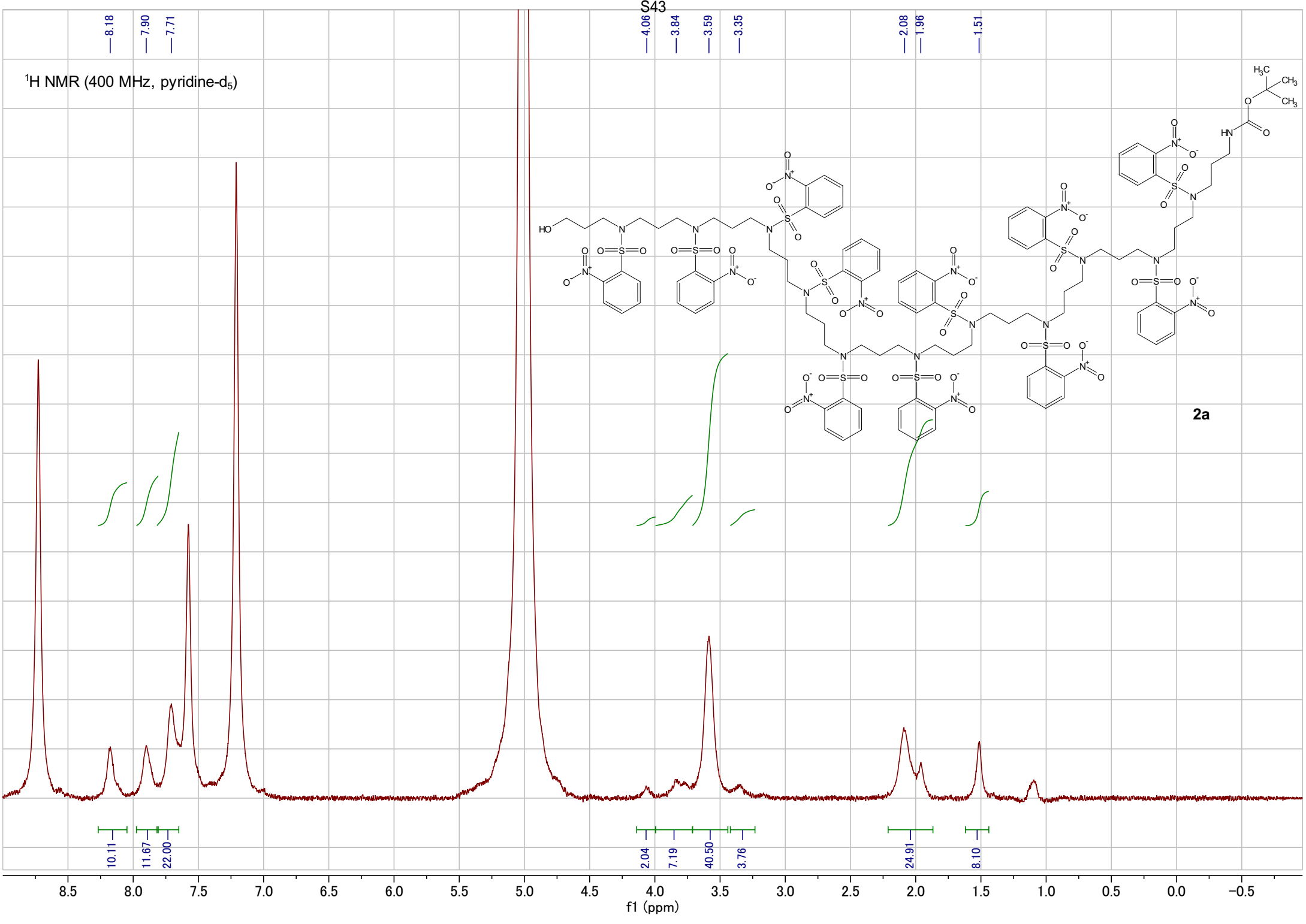




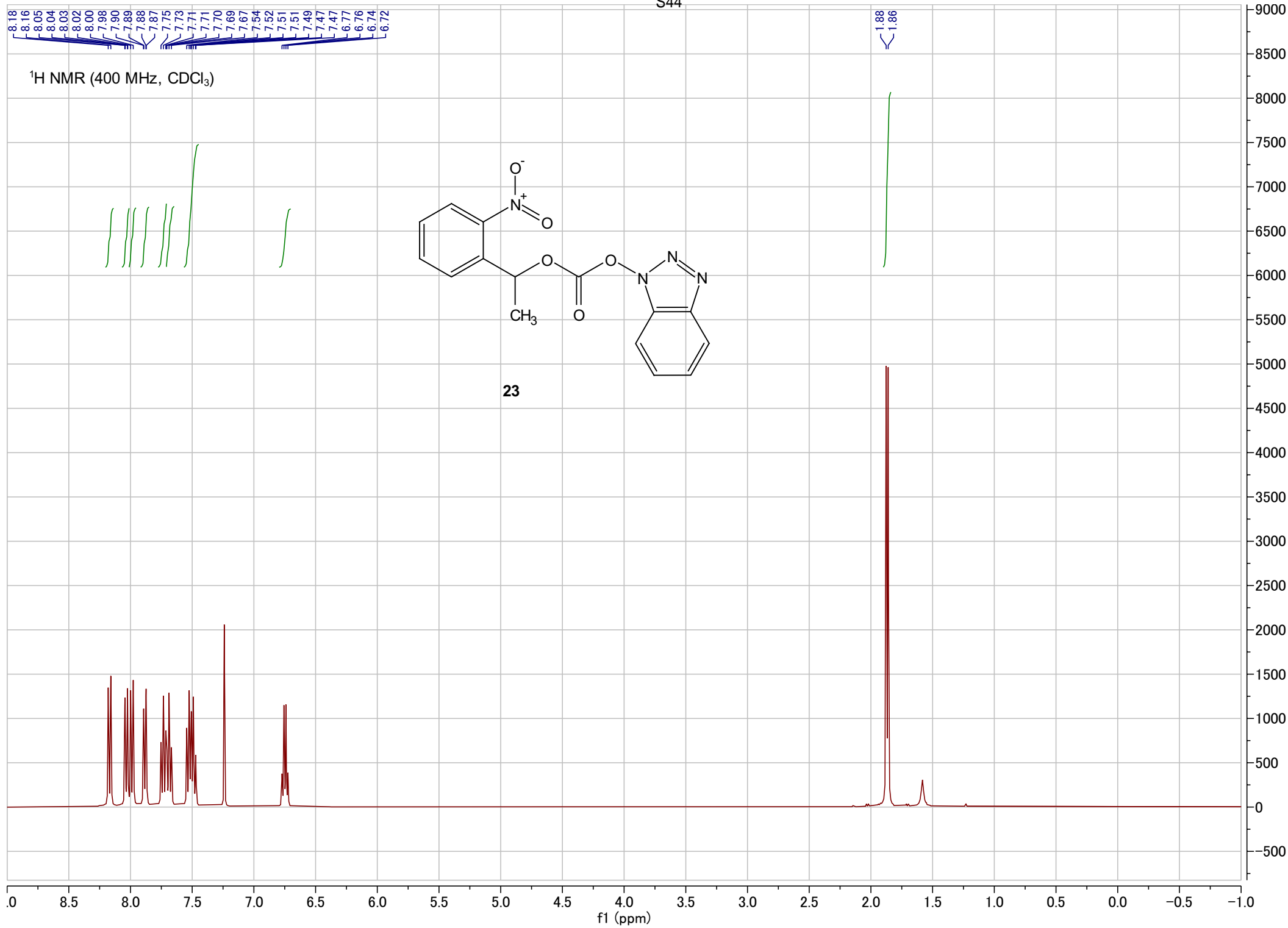








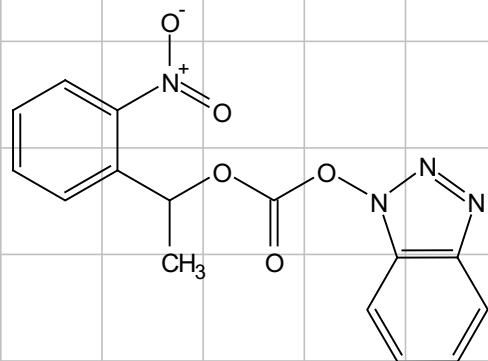
S44



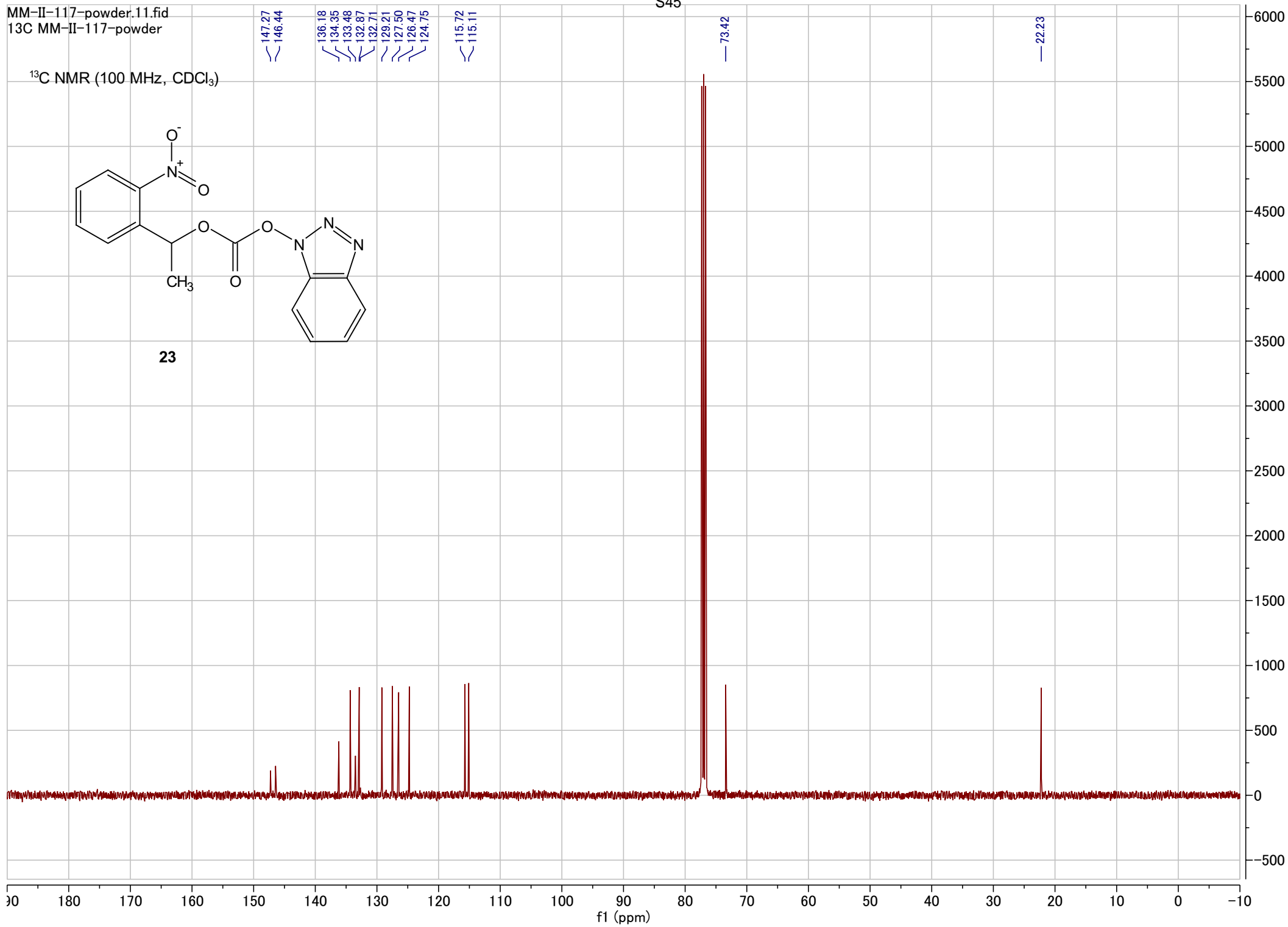
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13C MM-II-117-powder

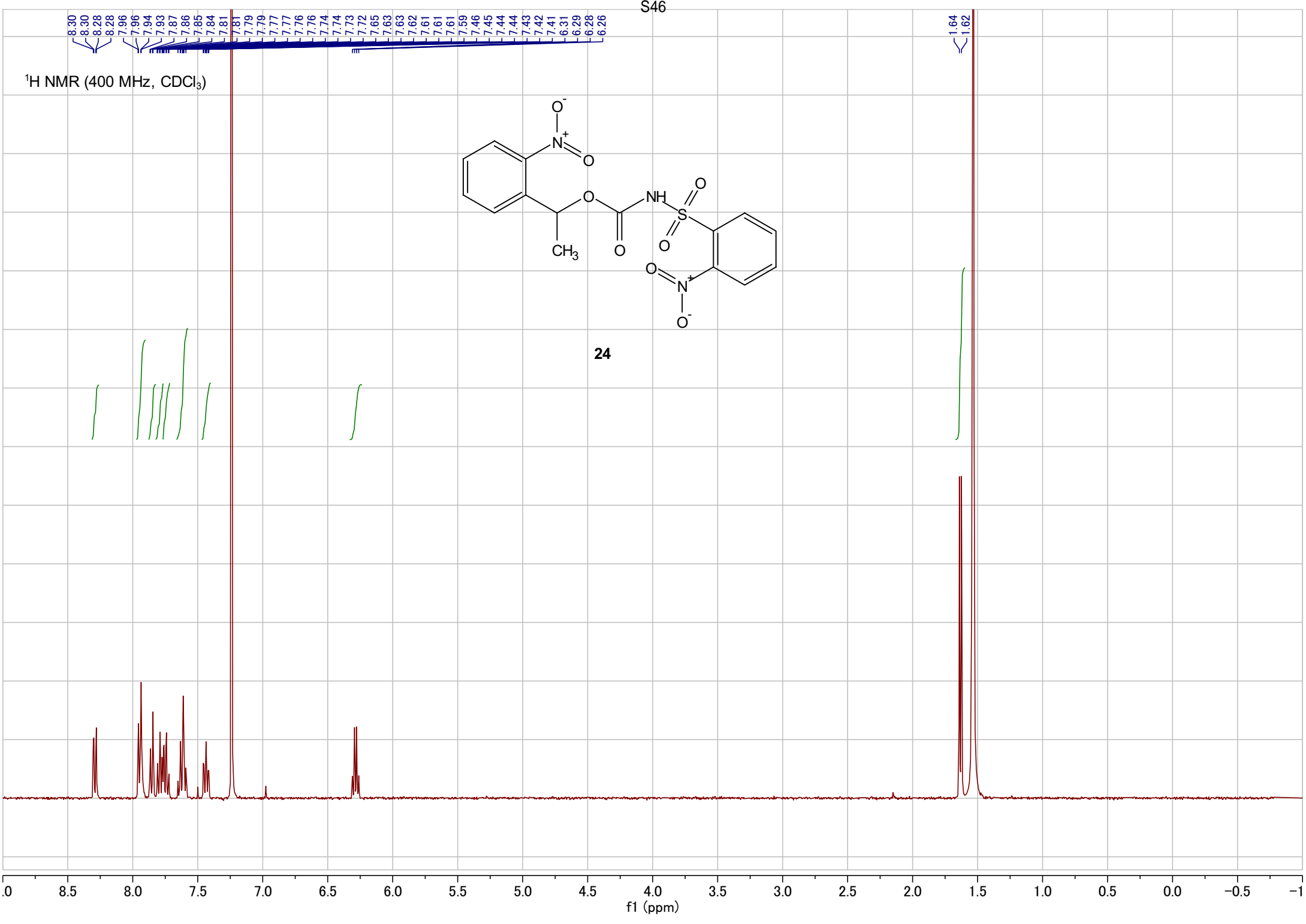
S45

¹³C NMR (100 MHz, CDCl₃)



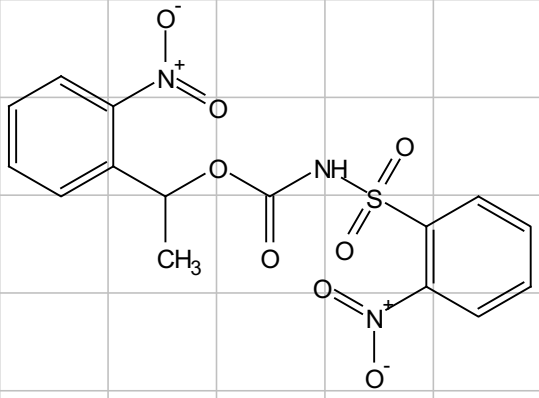
23





S46

¹H NMR (400 MHz, CDCl₃)



24

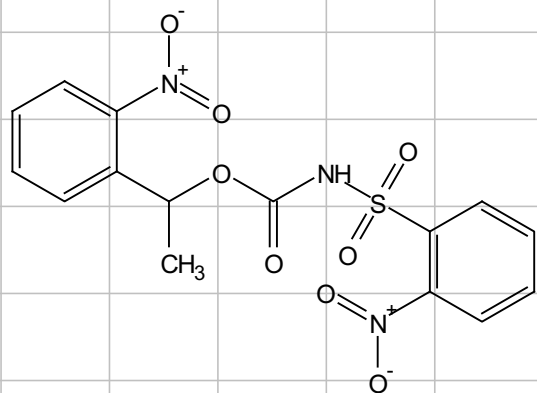
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8.28
8.28
7.96
7.94
7.93
7.87
7.86
7.85
7.84
7.81
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7.79
7.79
7.77
7.77
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7.74
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7.73
7.72
7.65
7.63
7.63
7.62
7.61
7.61
7.61
7.59
7.46
7.45
7.44
7.44
7.43
7.42
7.41
6.31
6.28
6.28
6.26

1.64
1.62

f1 (ppm)

S47

^{13}C NMR (100 MHz, CDCl_3)



24

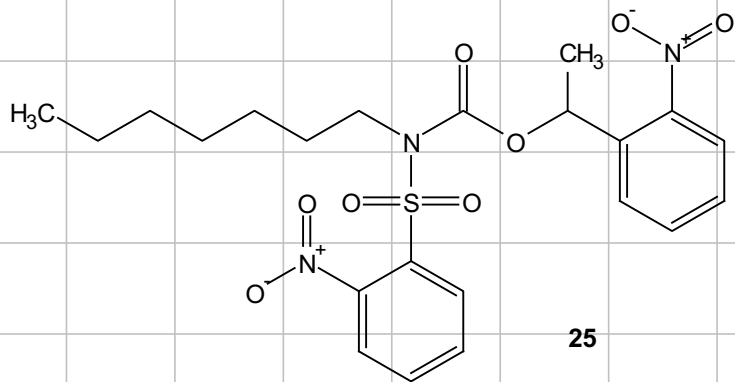
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71.75

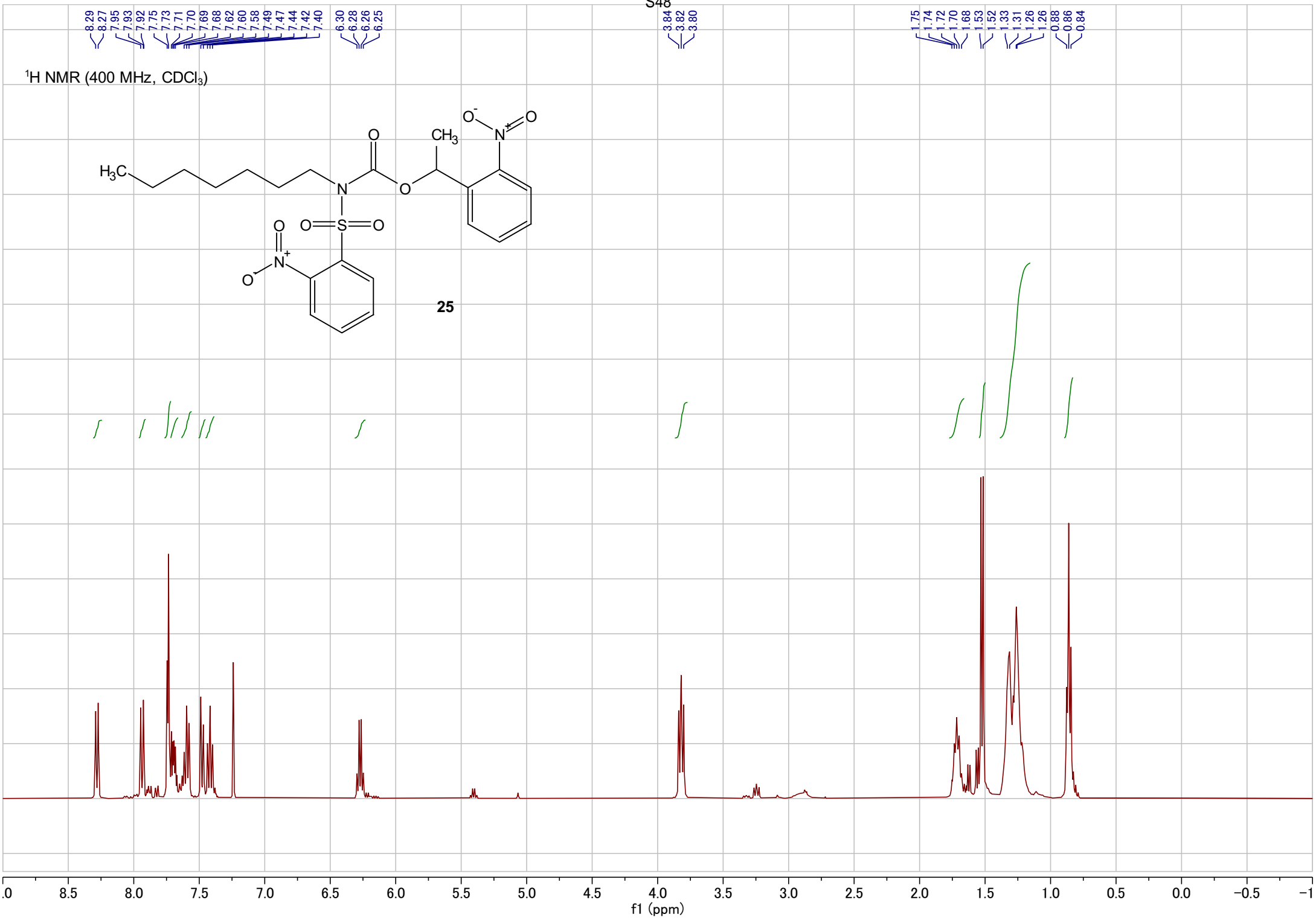
21.95

180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

¹H NMR (400 MHz, CDCl₃)

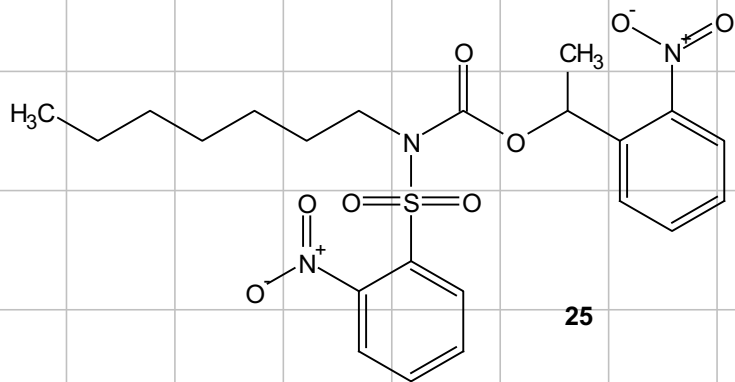


S48



S49

^{13}C NMR (100 MHz, CDCl_3)



150.73
147.80
147.24
136.90
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133.92
133.64
133.06
131.74
128.75
126.78
124.71
124.46

31.66
30.19
28.80
26.51
22.52
21.81

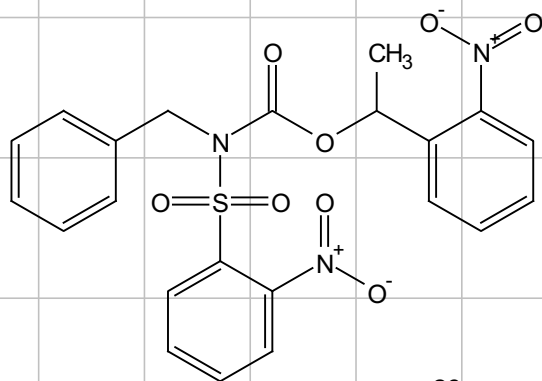
14.03

72.07

48.47

90 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

¹³C NMR (100 MHz, CDCl₃)



26

150.78
147.91
147.05
137.02
136.86
134.70
134.41
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128.58
127.76
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124.60
124.58

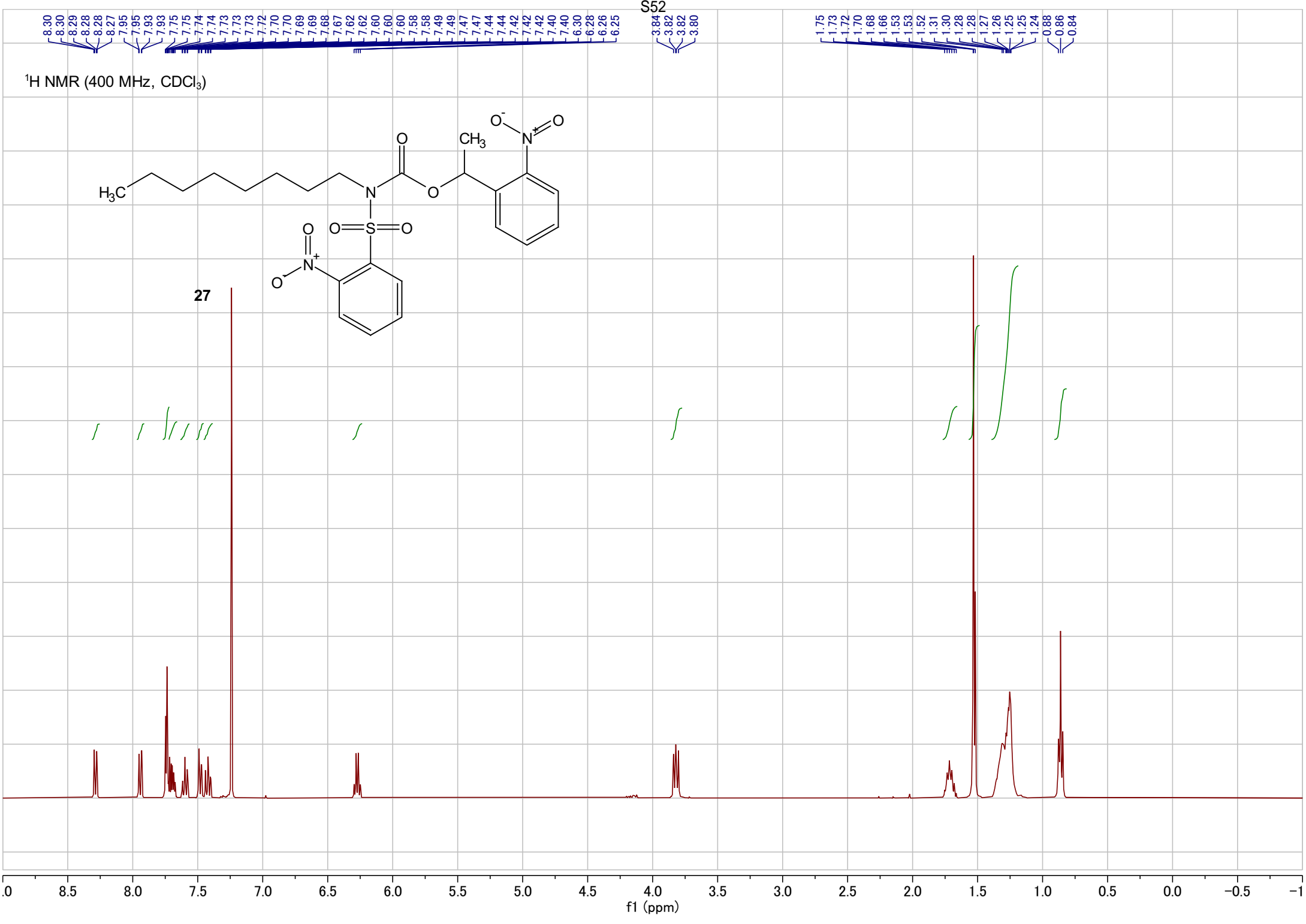
S51

72.08

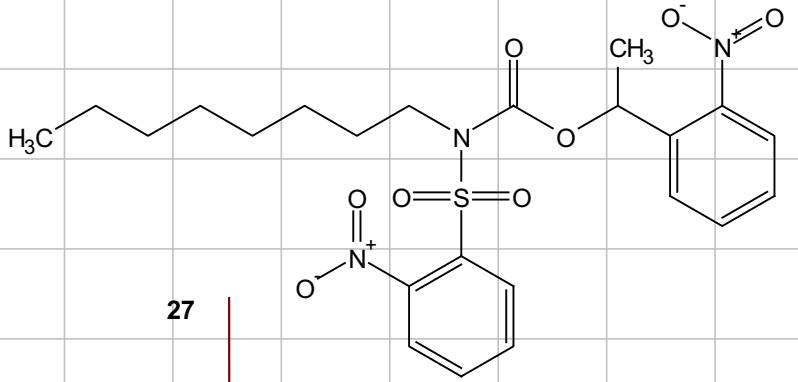
51.36

21.83

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



¹H NMR (400 MHz, CDCl₃)



27

552

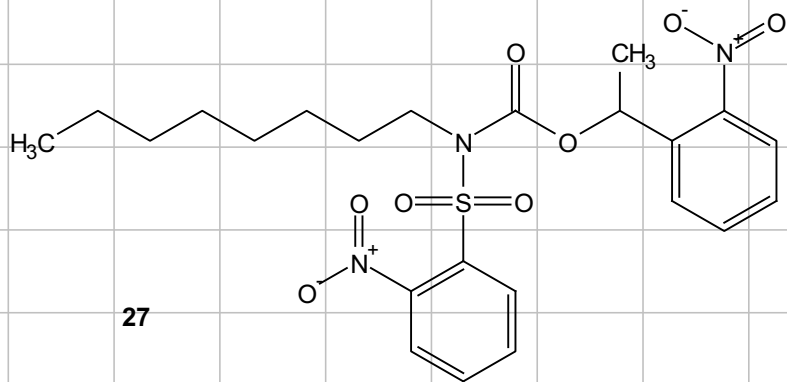
f1 (ppm)

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8.28
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6.30
6.28
6.26
6.25

3.84
3.82
3.82
3.80

1.75
1.73
1.72
1.70
1.68
1.66
1.53
1.53
1.52
1.31
1.30
1.28
1.28
1.27
1.26
1.25
1.24
0.88
0.86
0.84

0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

^{13}C NMR (100 MHz, CDCl_3)

150.72
147.79
147.23

136.88
134.47
133.92
133.62
133.04
131.74

128.75
126.78
124.70
124.46

72.06

48.46

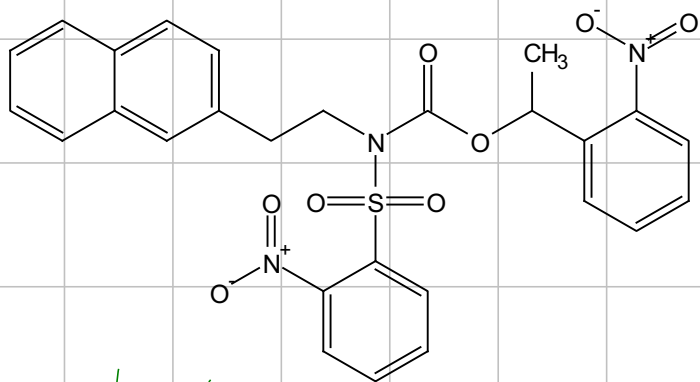
31.72
30.18
29.12
29.09
26.55
22.59
21.80

14.04

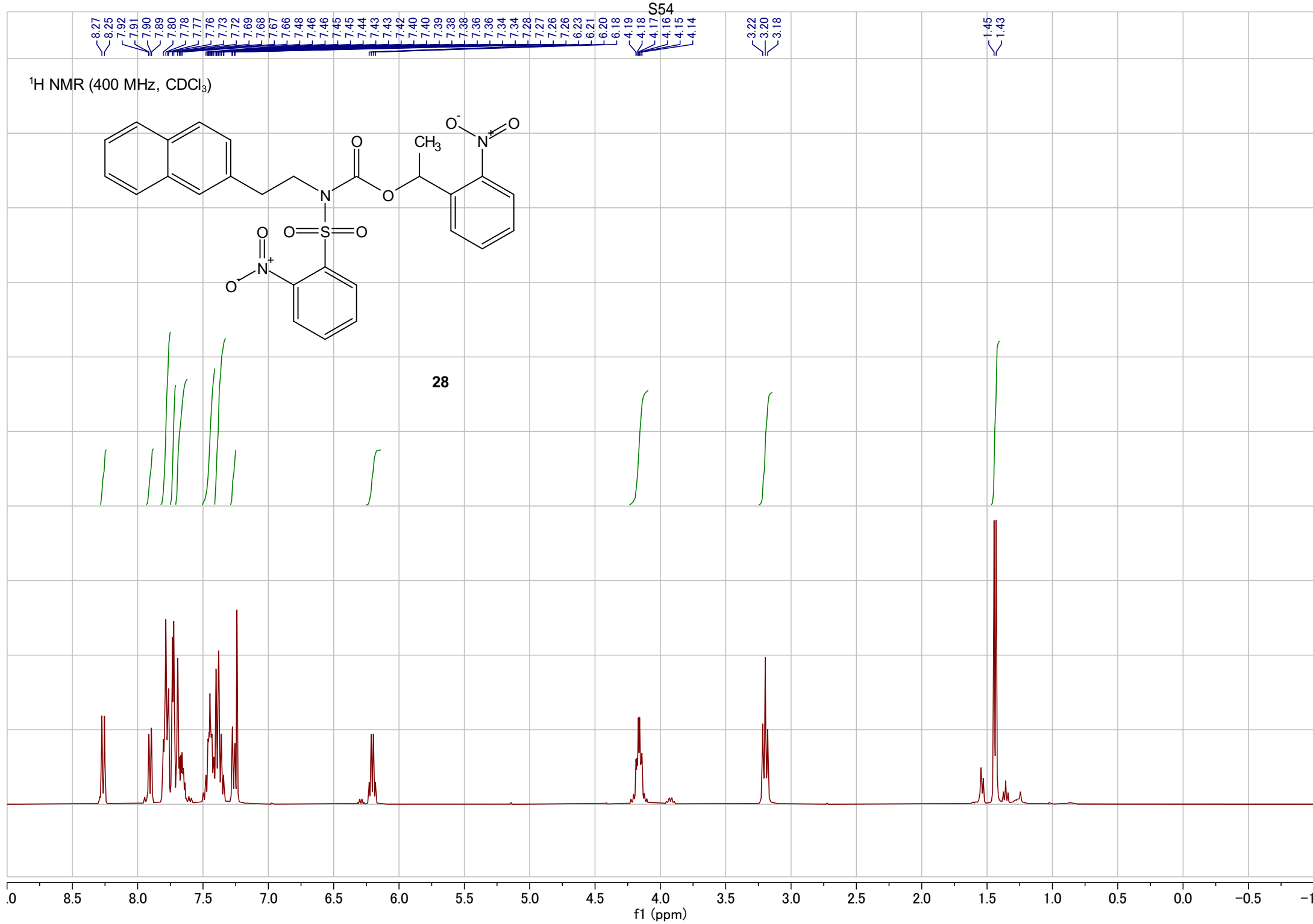
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

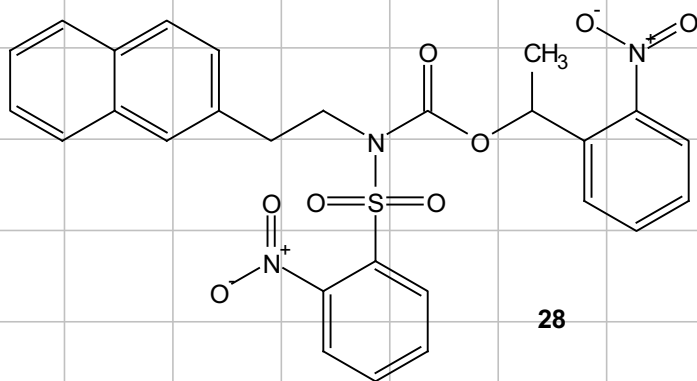
f1 (ppm)

¹H NMR (400 MHz, CDCl₃)



28



^{13}C NMR (100 MHz, CDCl_3)

28

150.67
147.82
147.08
136.66
135.12
134.58
133.90
133.74
133.55
132.91
132.87
131.77
128.70
128.25
127.69
127.65
127.57
127.38
126.70
126.10
125.59
124.63
124.49
124.44

72.28

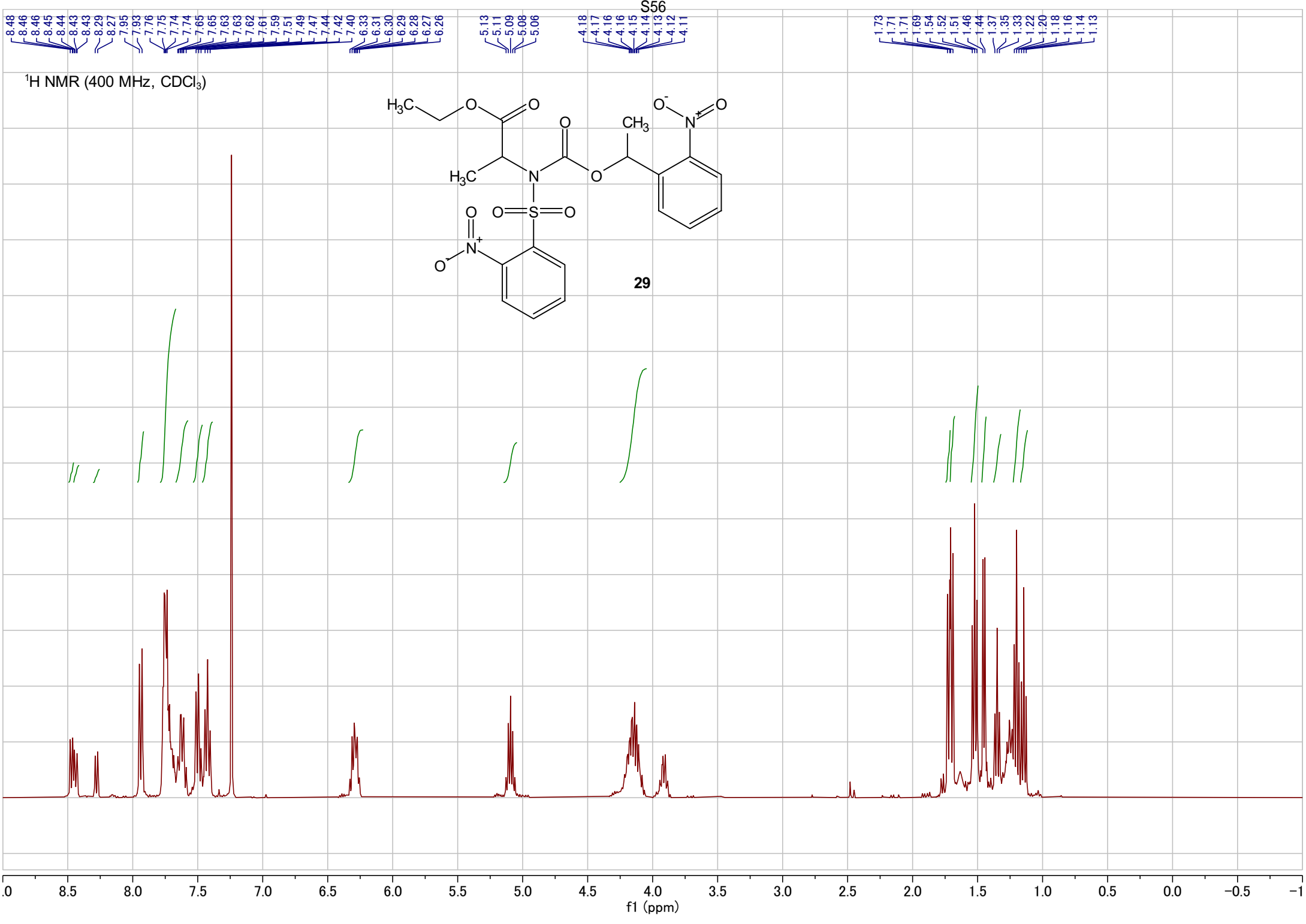
49.32

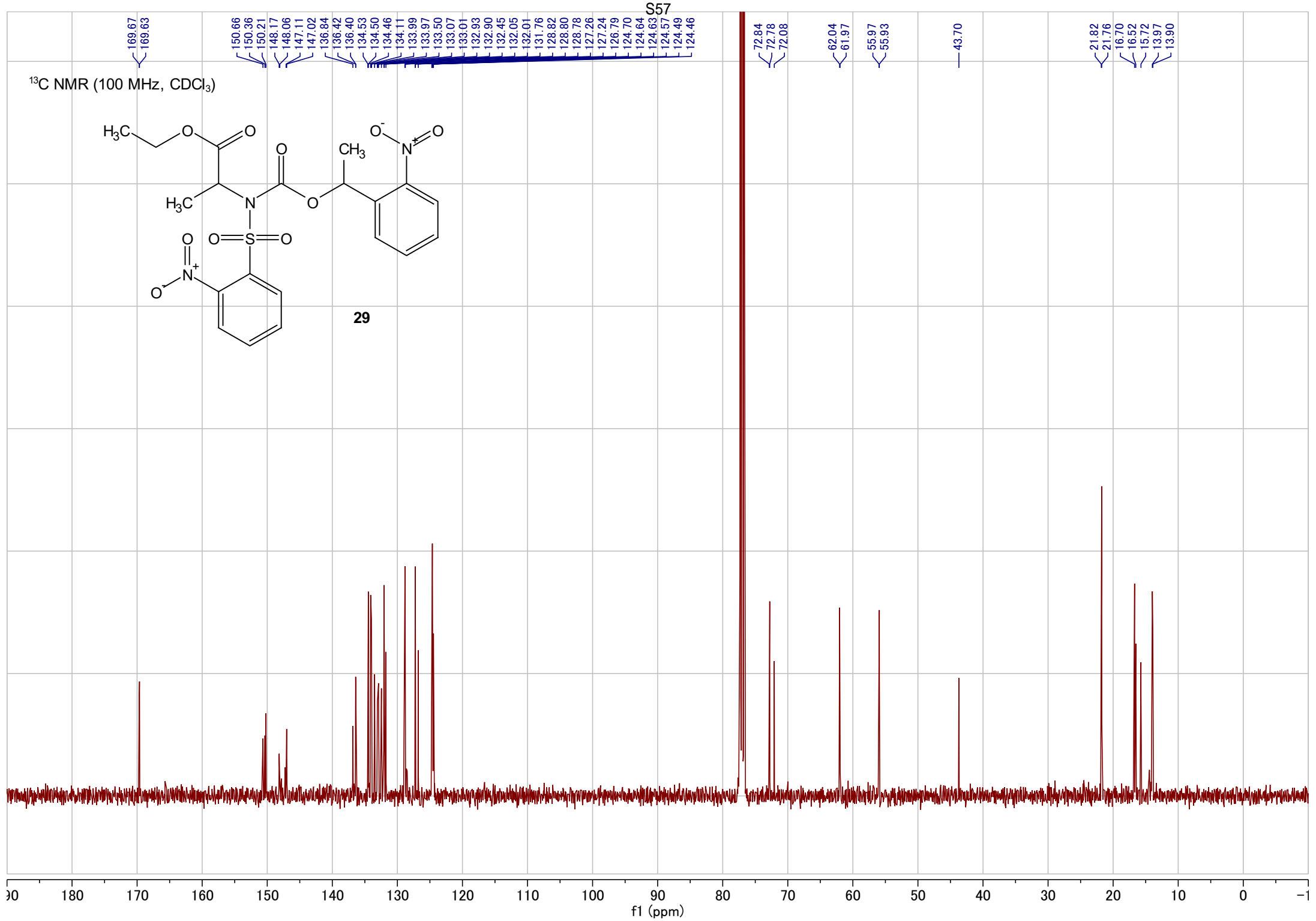
36.85

21.67

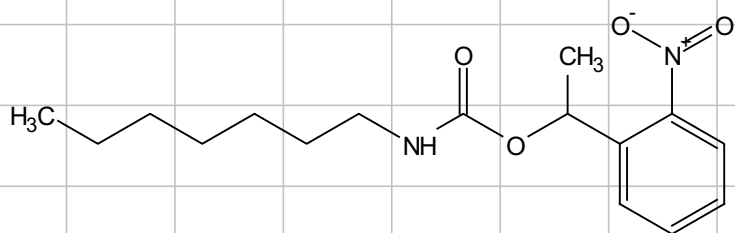
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

f1 (ppm)

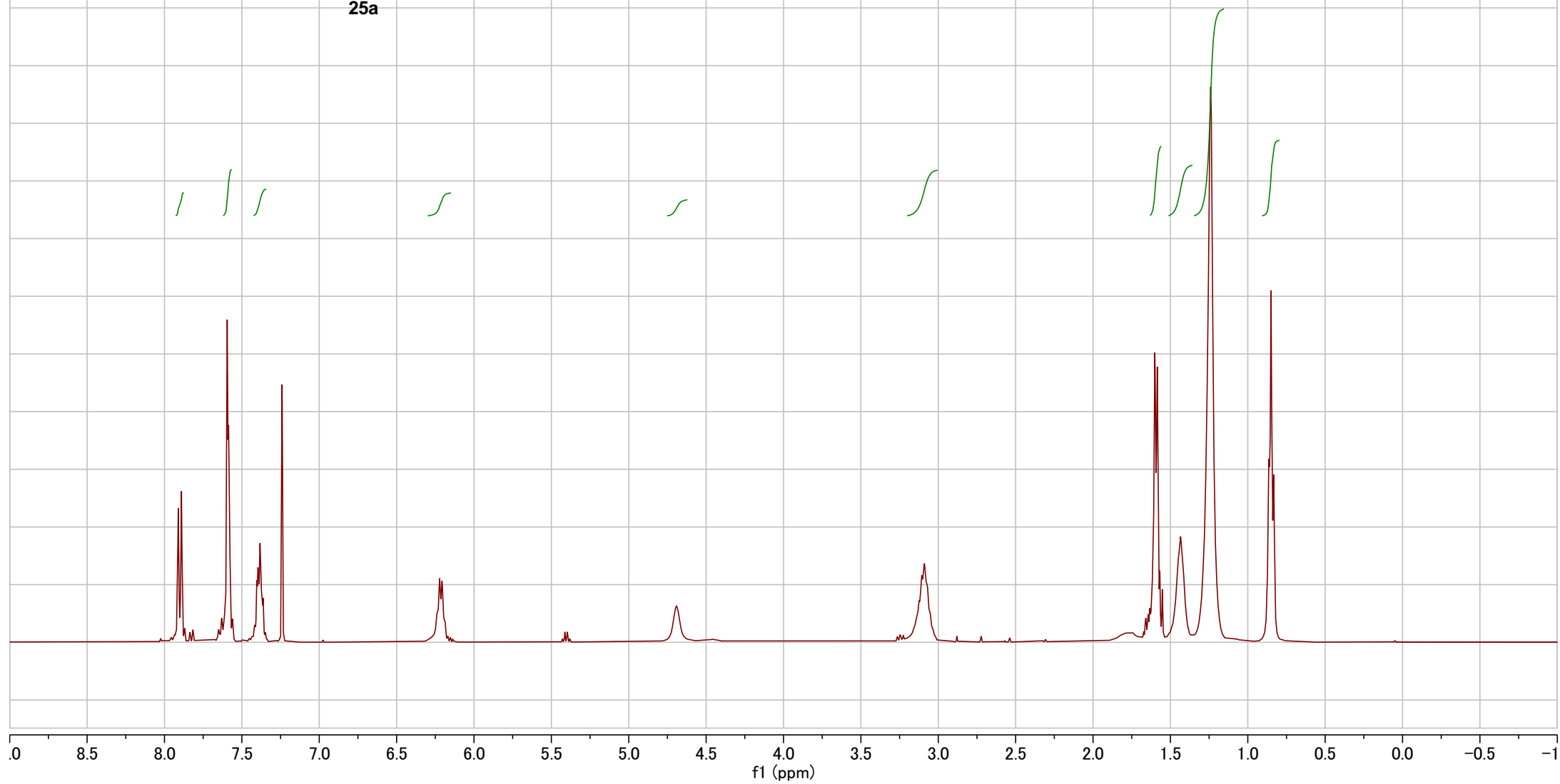


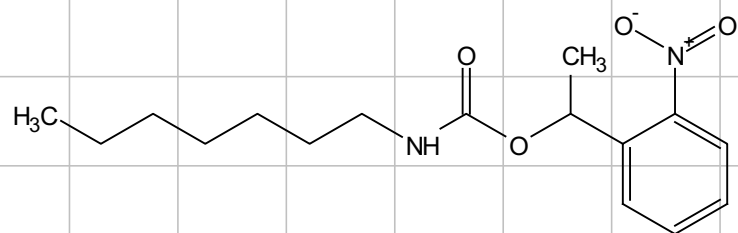


S58

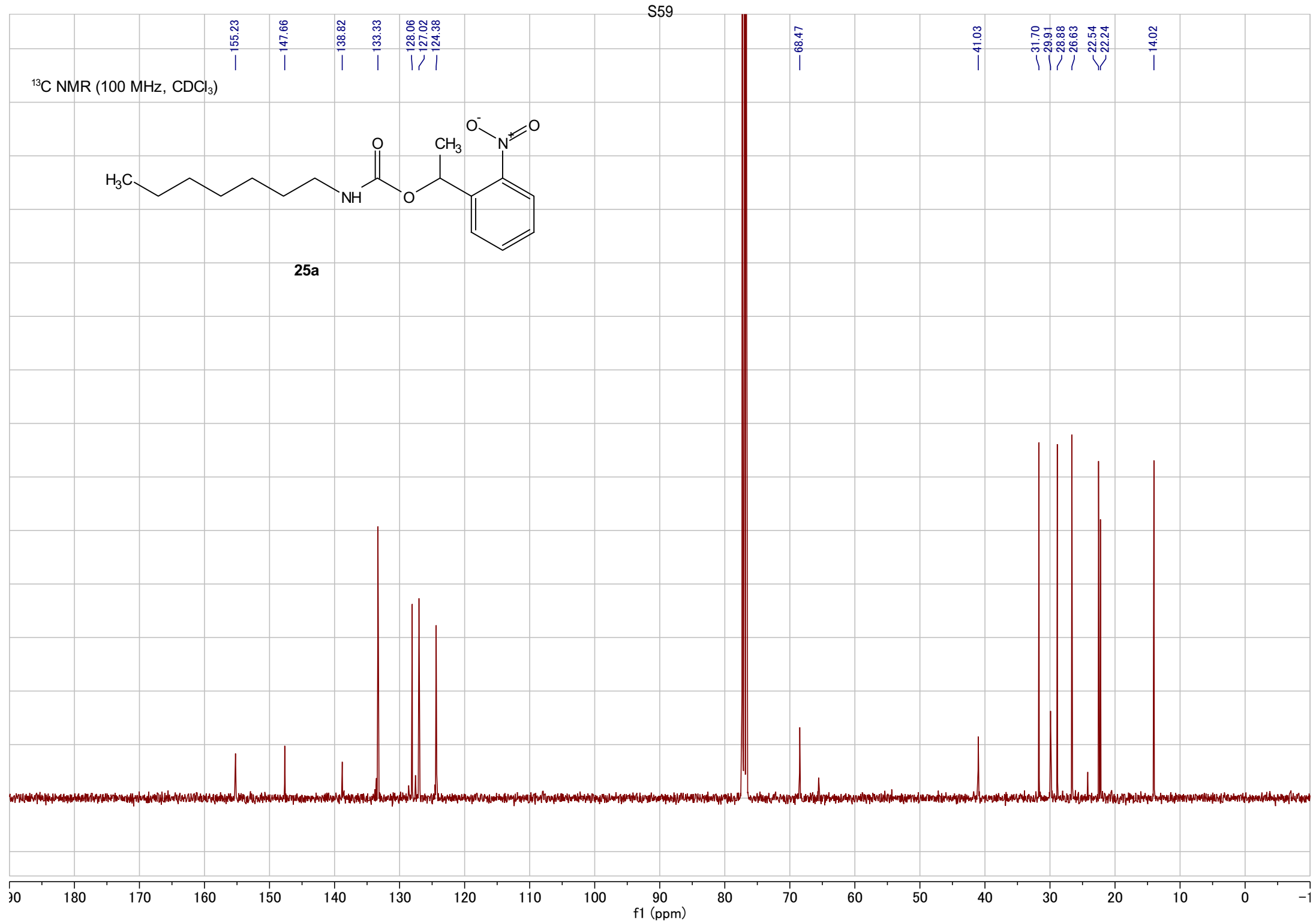
¹H NMR (400 MHz, CDCl₃)

25a

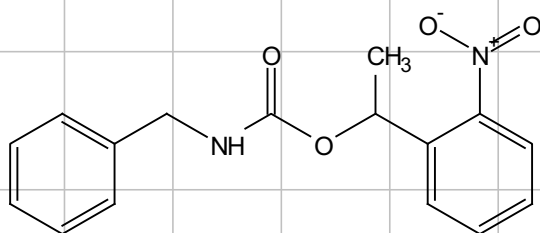


^{13}C NMR (100 MHz, CDCl_3)

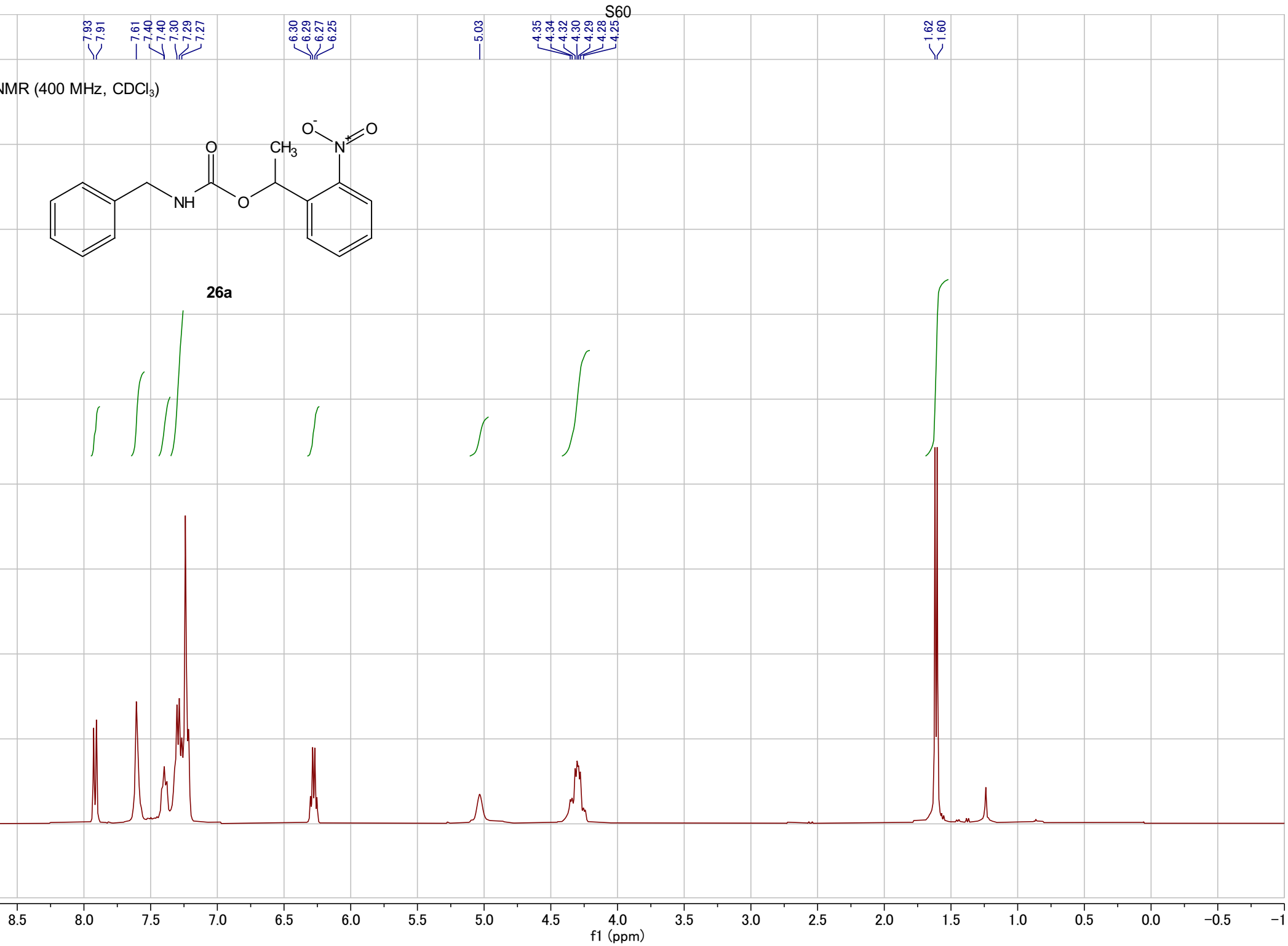
25a

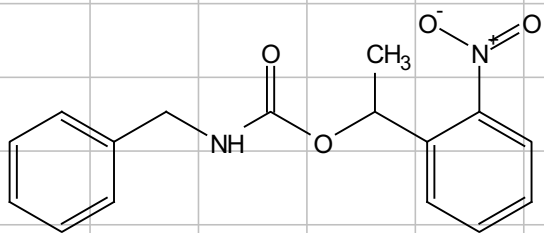


¹H NMR (400 MHz, CDCl₃)

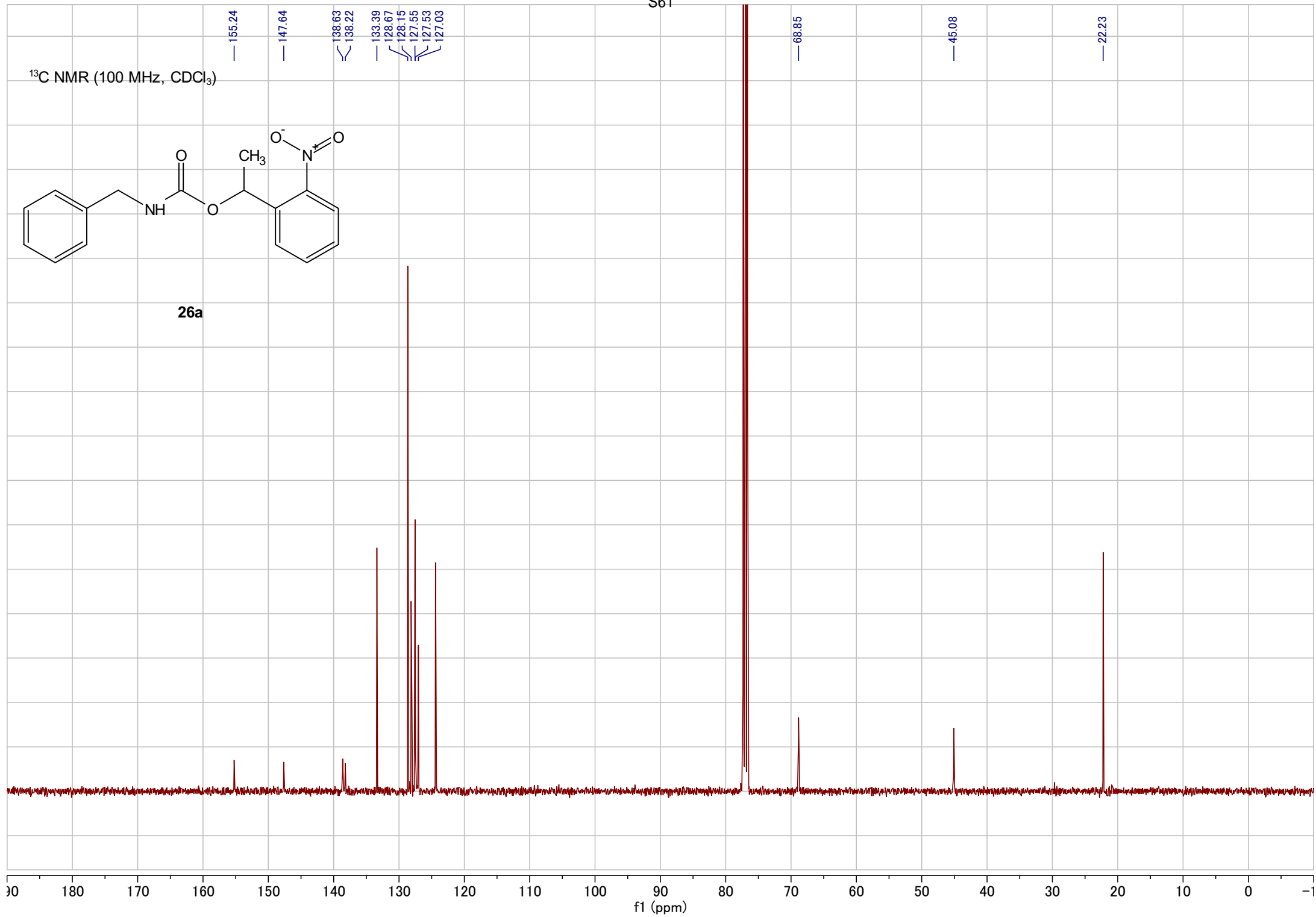


26a

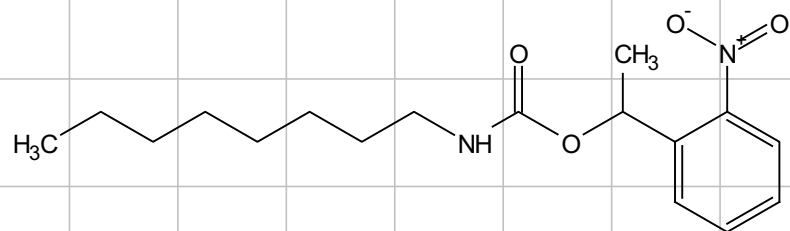


^{13}C NMR (100 MHz, CDCl_3)

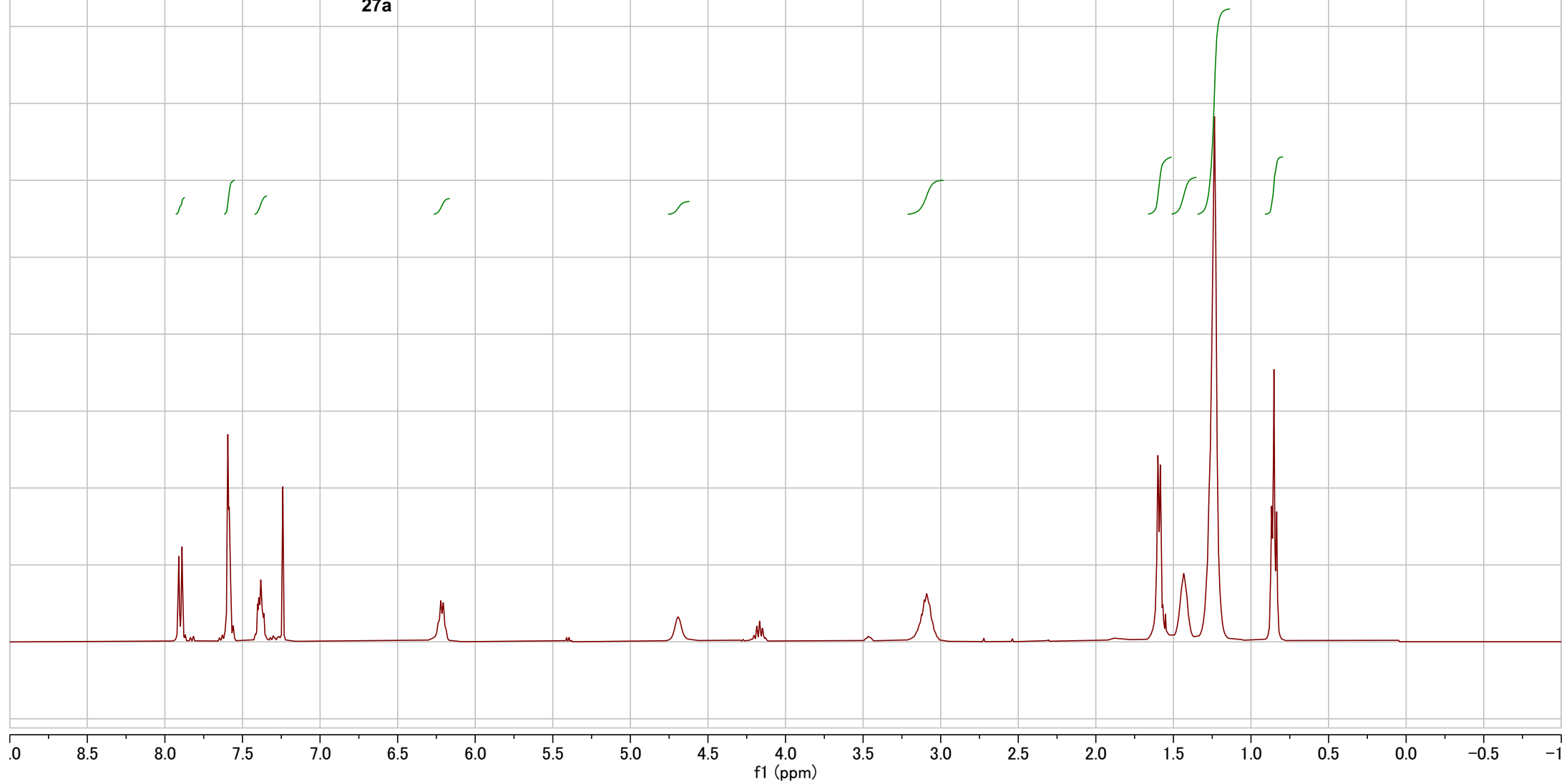
26a



S62

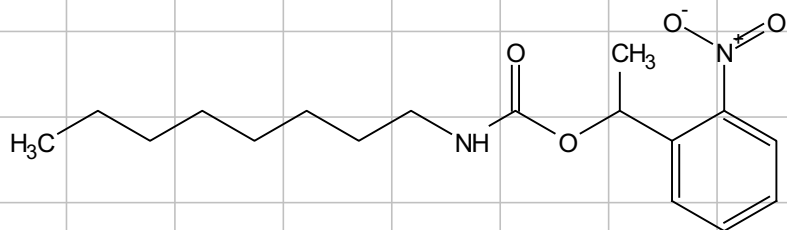
 $^1\text{H NMR}$ (400 MHz, CDCl_3)

27a



S63

¹³C NMR (100 MHz, CDCl₃)



27a

155.23

147.66

138.82

133.34

128.06

127.02

124.38

68.47

41.03

31.74

29.91

29.18

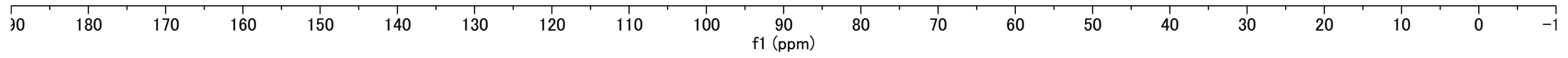
29.16

26.68

22.60

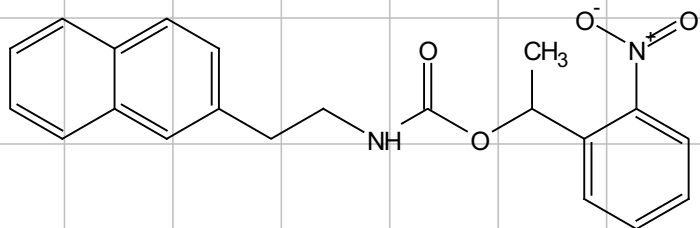
22.24

14.05

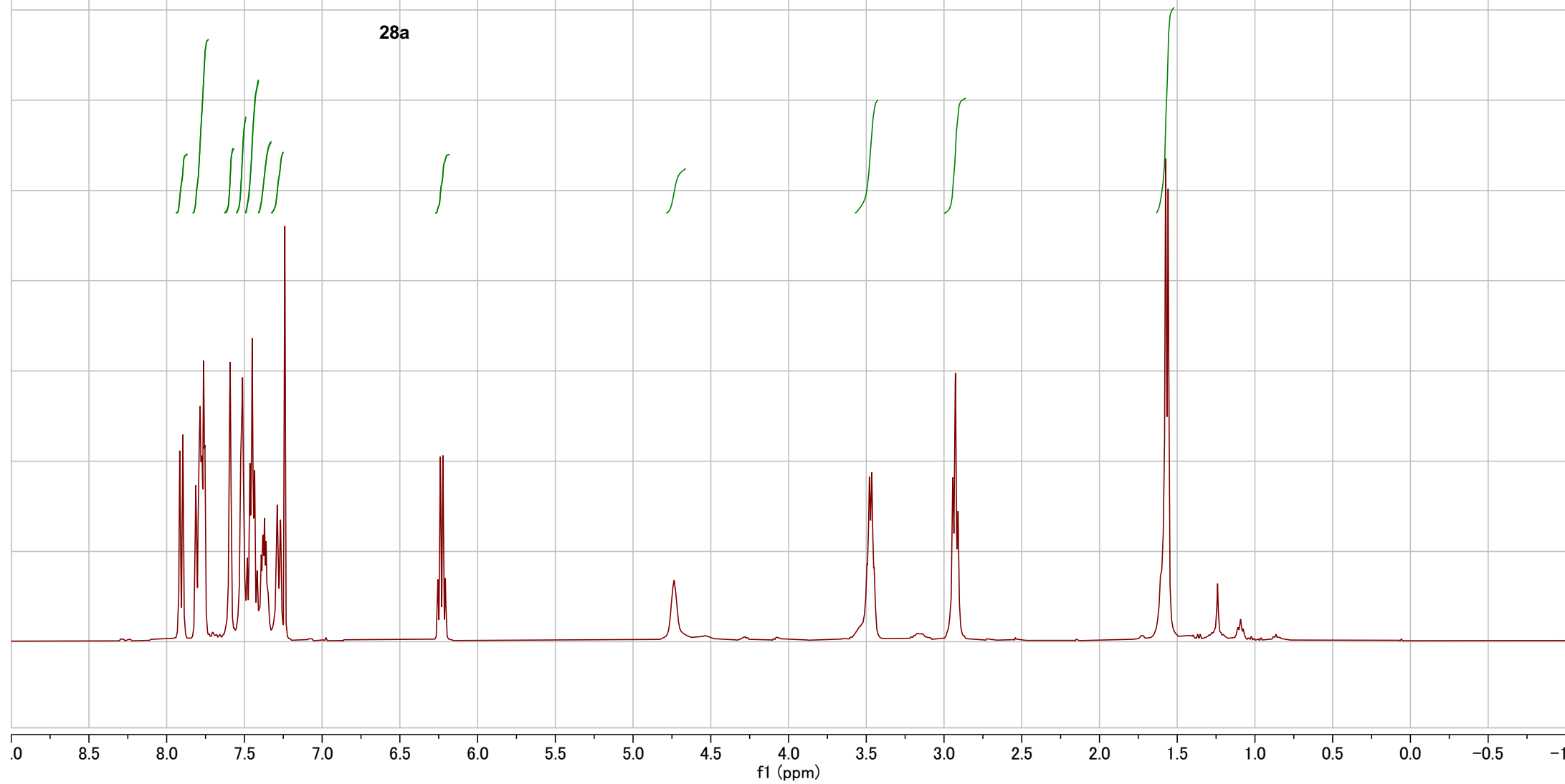


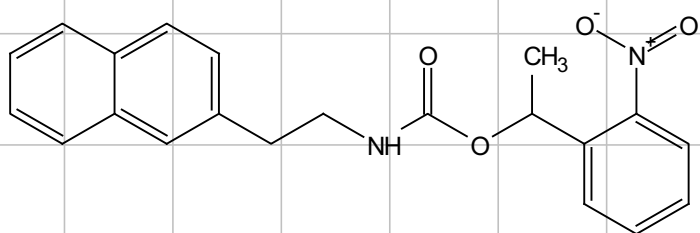
S64

¹H NMR (400 MHz, CDCl₃)

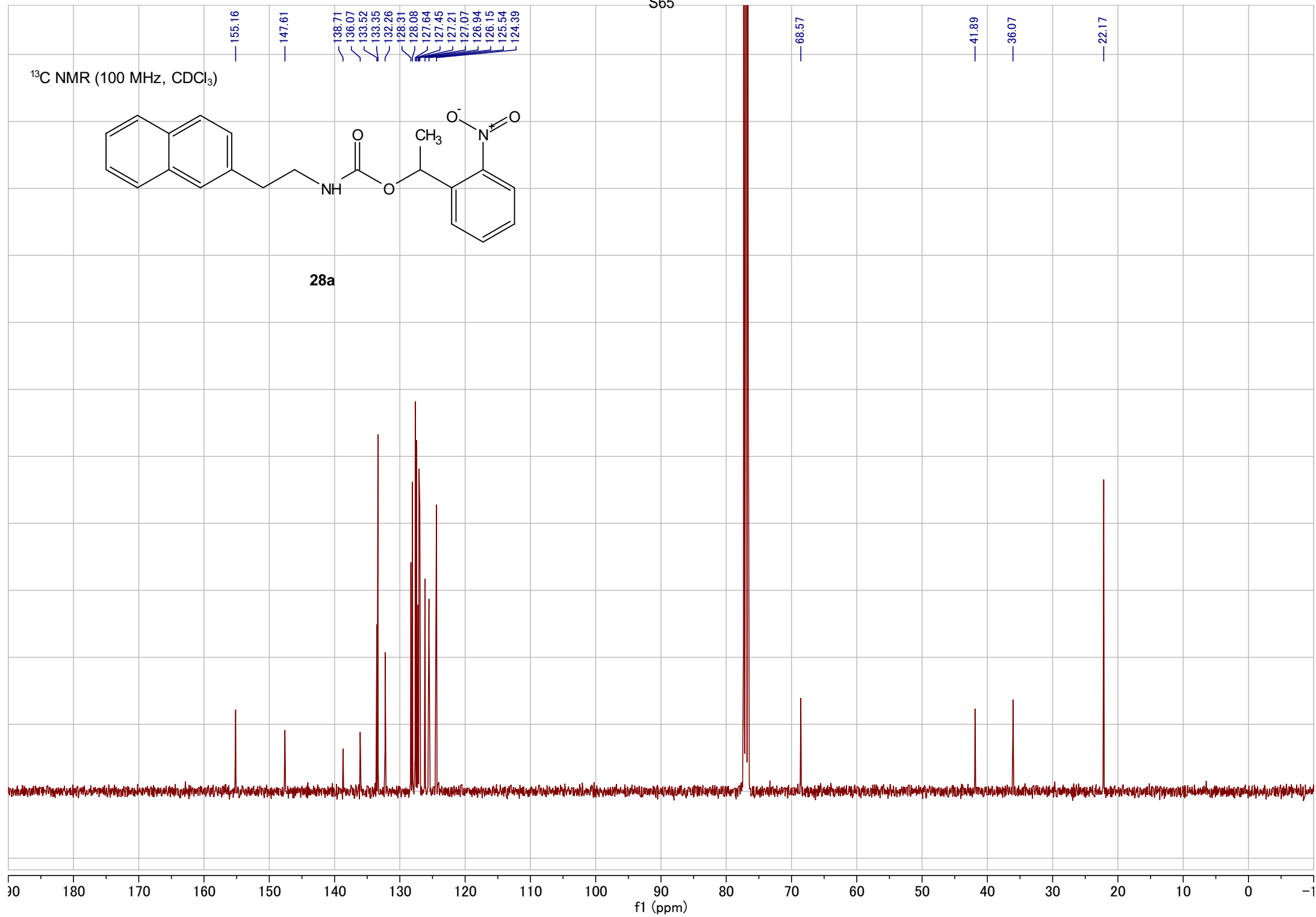


28a

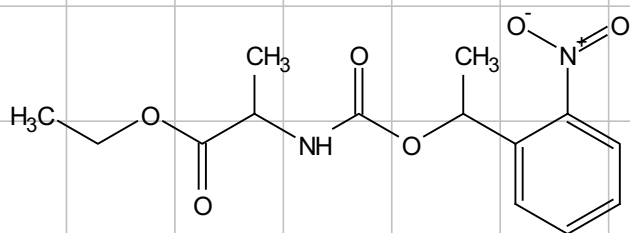


^{13}C NMR (100 MHz, CDCl_3)

28a



¹H NMR (400 MHz, CDCl₃)



29a

7.92
7.90
7.89
7.62
7.60
7.41
7.39
7.38
7.37

6.26
6.25
6.23
6.21

5.32

4.27
4.25
4.25
4.24
4.23
4.21
4.19
4.17
4.15
4.13

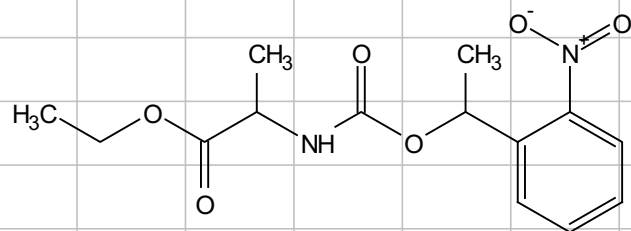
3.15

1.61
1.60
1.39
1.37
1.33
1.32
1.27
1.25
1.23
1.21
1.20

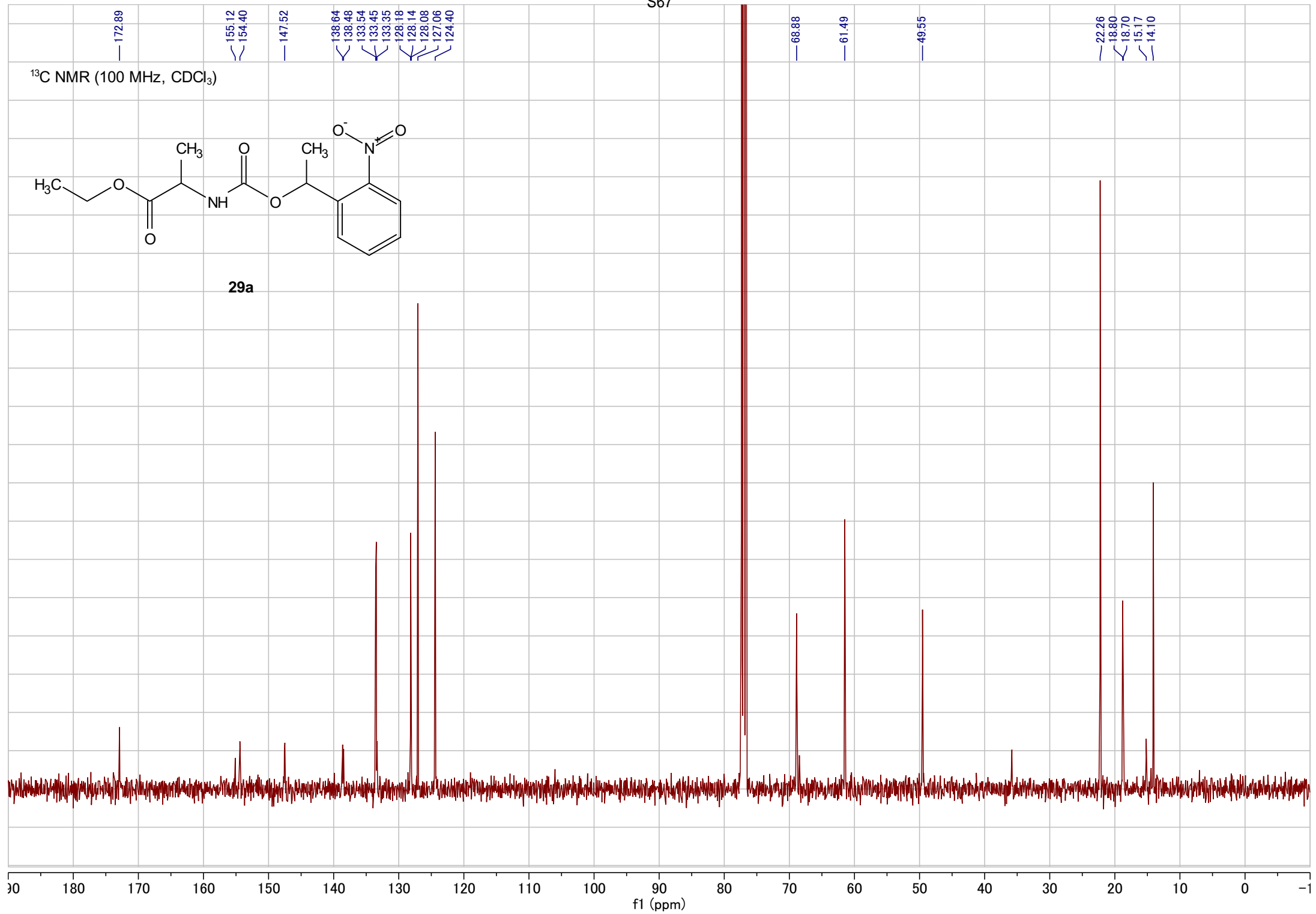
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

f1 (ppm)

S67

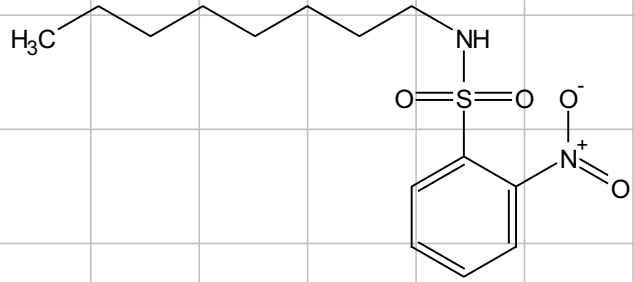
 ^{13}C NMR (100 MHz, CDCl_3)

29a



S68

¹H NMR (400 MHz, CDCl₃)



27b

8.13
8.12
8.11
7.85
7.83
7.82
7.74
7.73
7.72
7.70
7.69

5.22

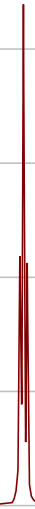
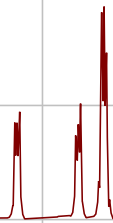
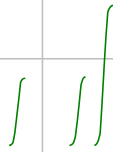
3.09
3.08
3.06
3.04

1.53
1.51
1.49
1.47
1.45
1.25
1.23

0.86
0.84
0.82

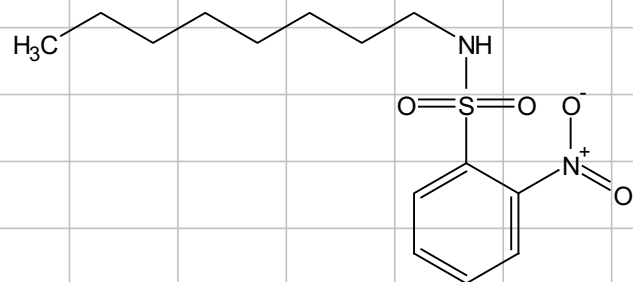
0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1

f1 (ppm)

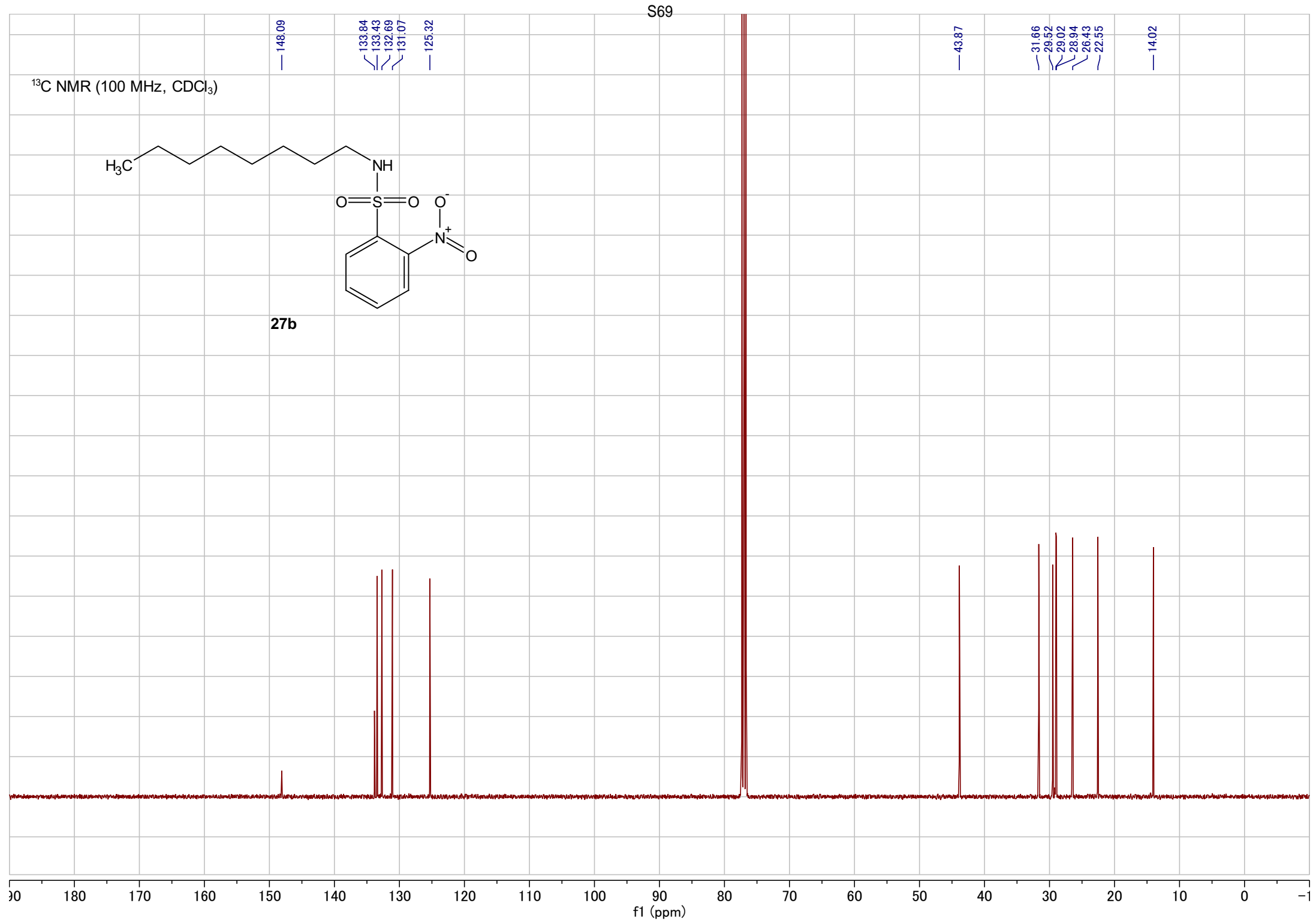


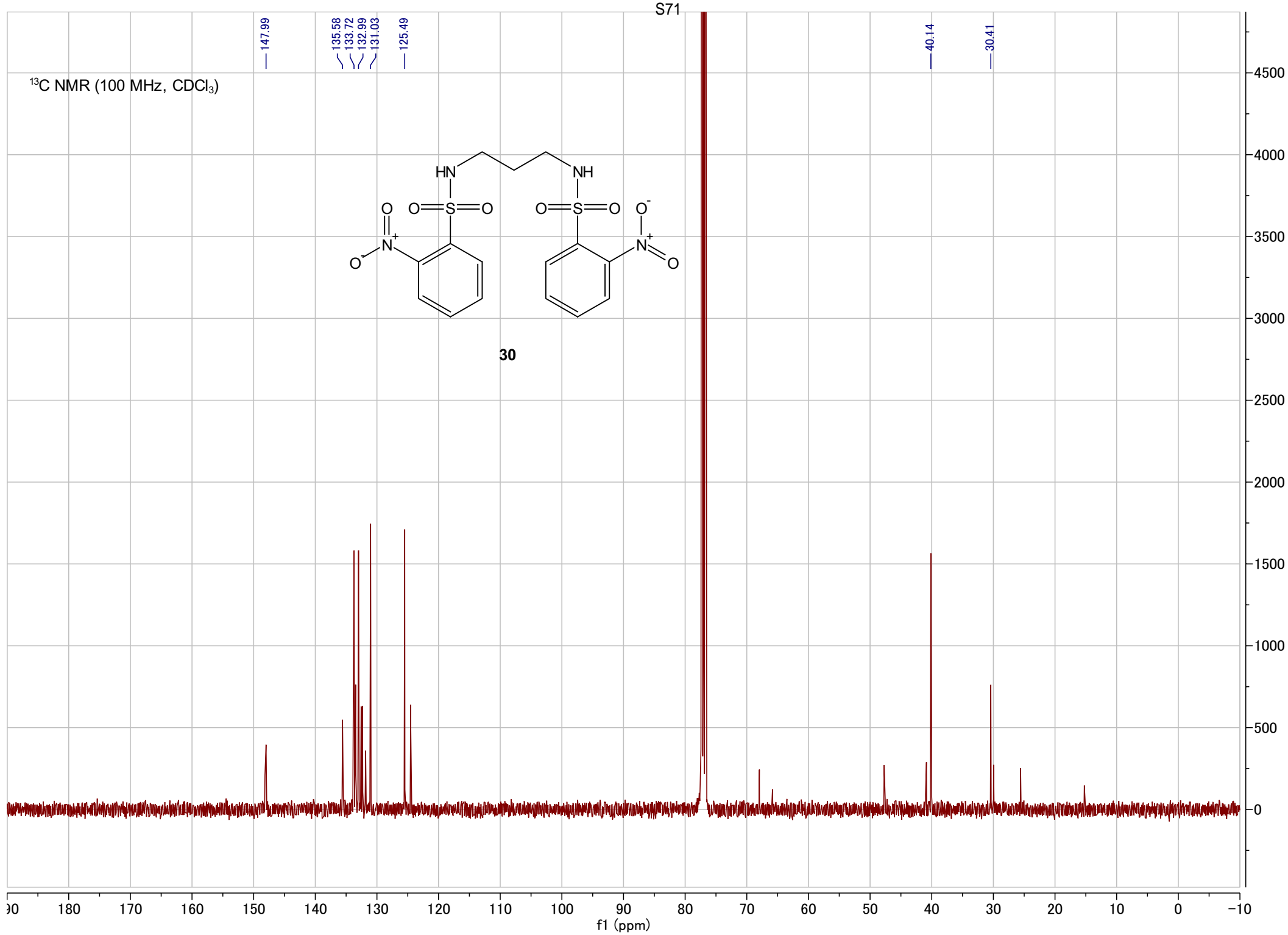
S69

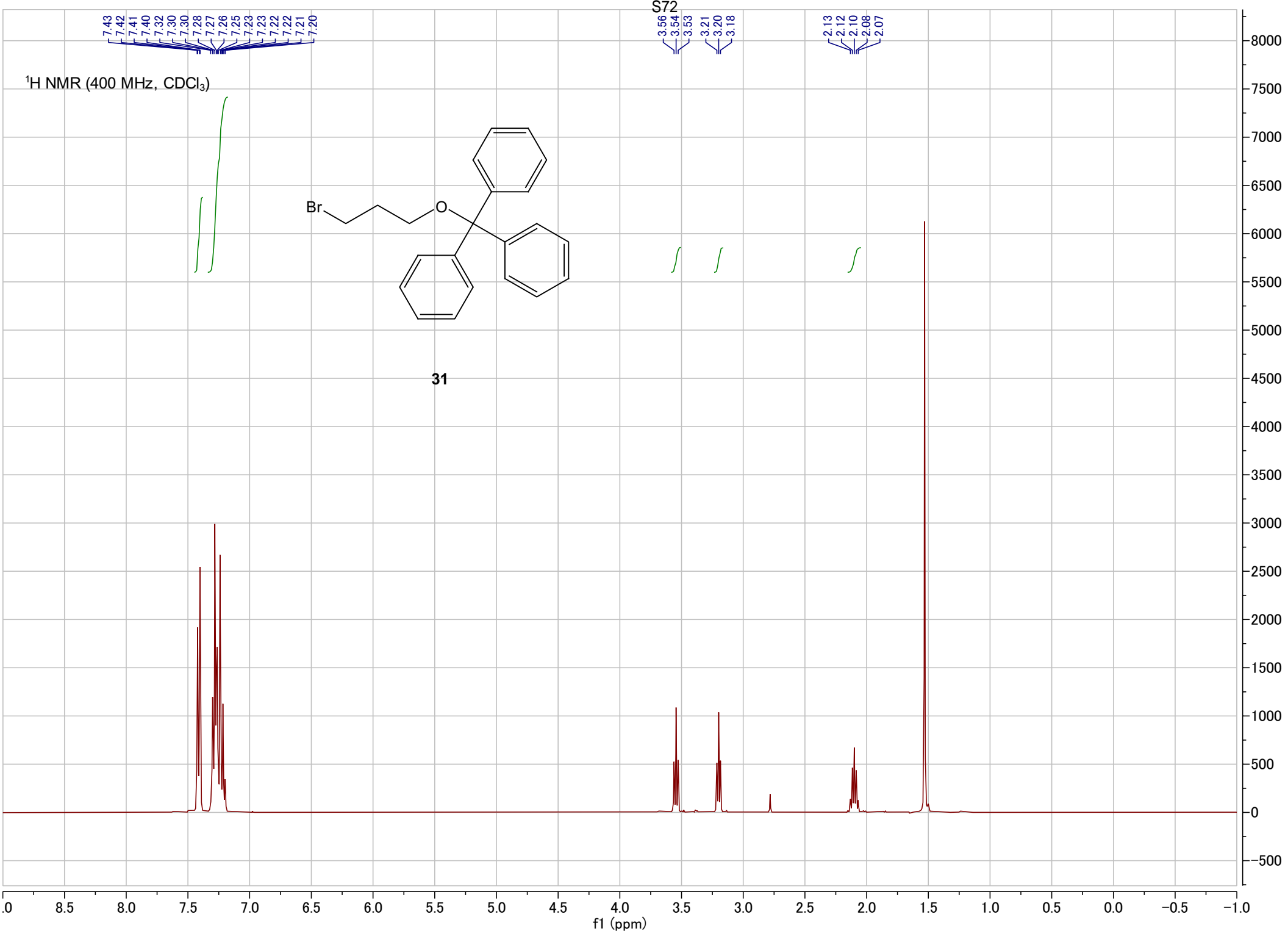
¹³C NMR (100 MHz, CDCl₃)

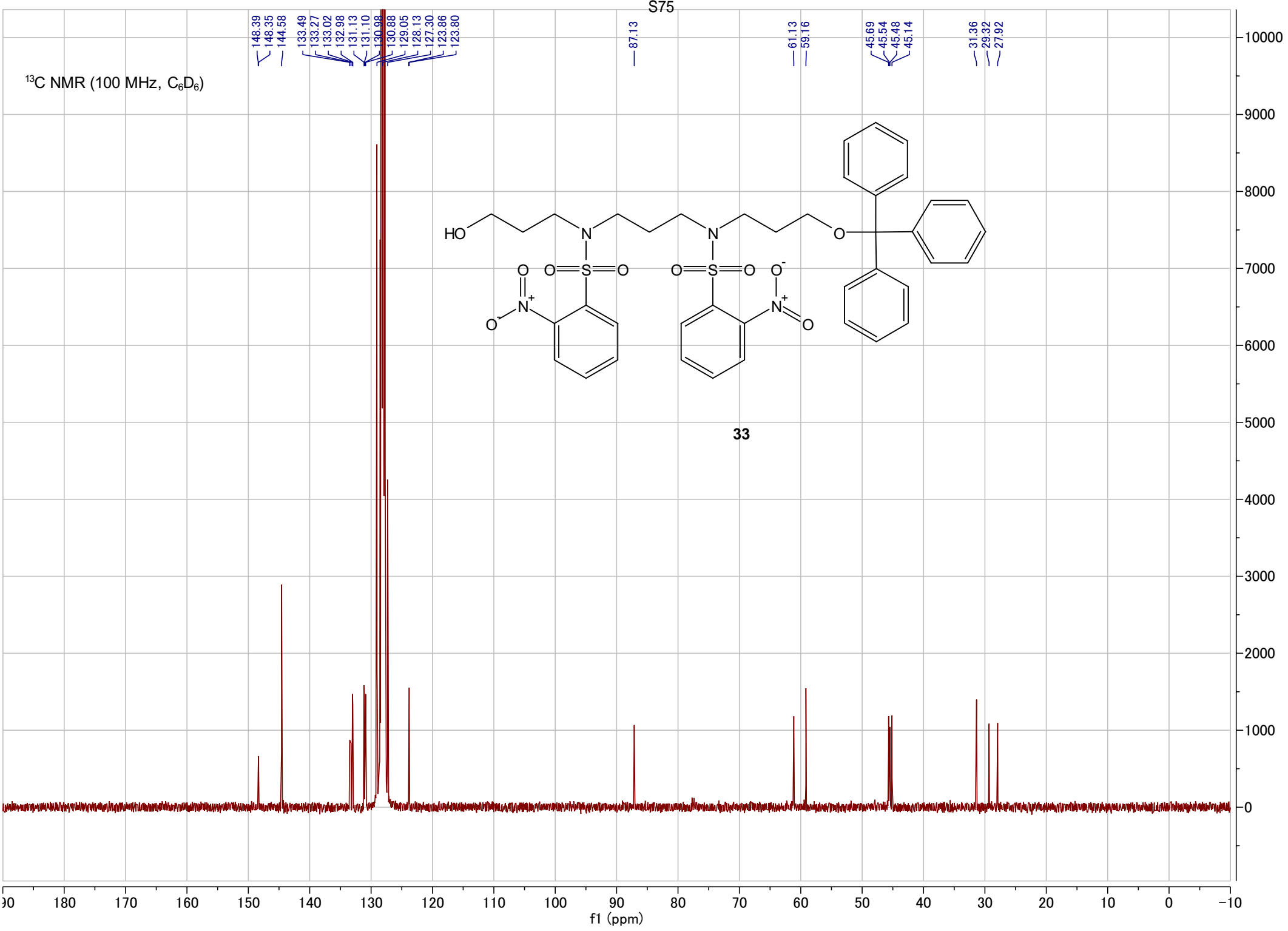


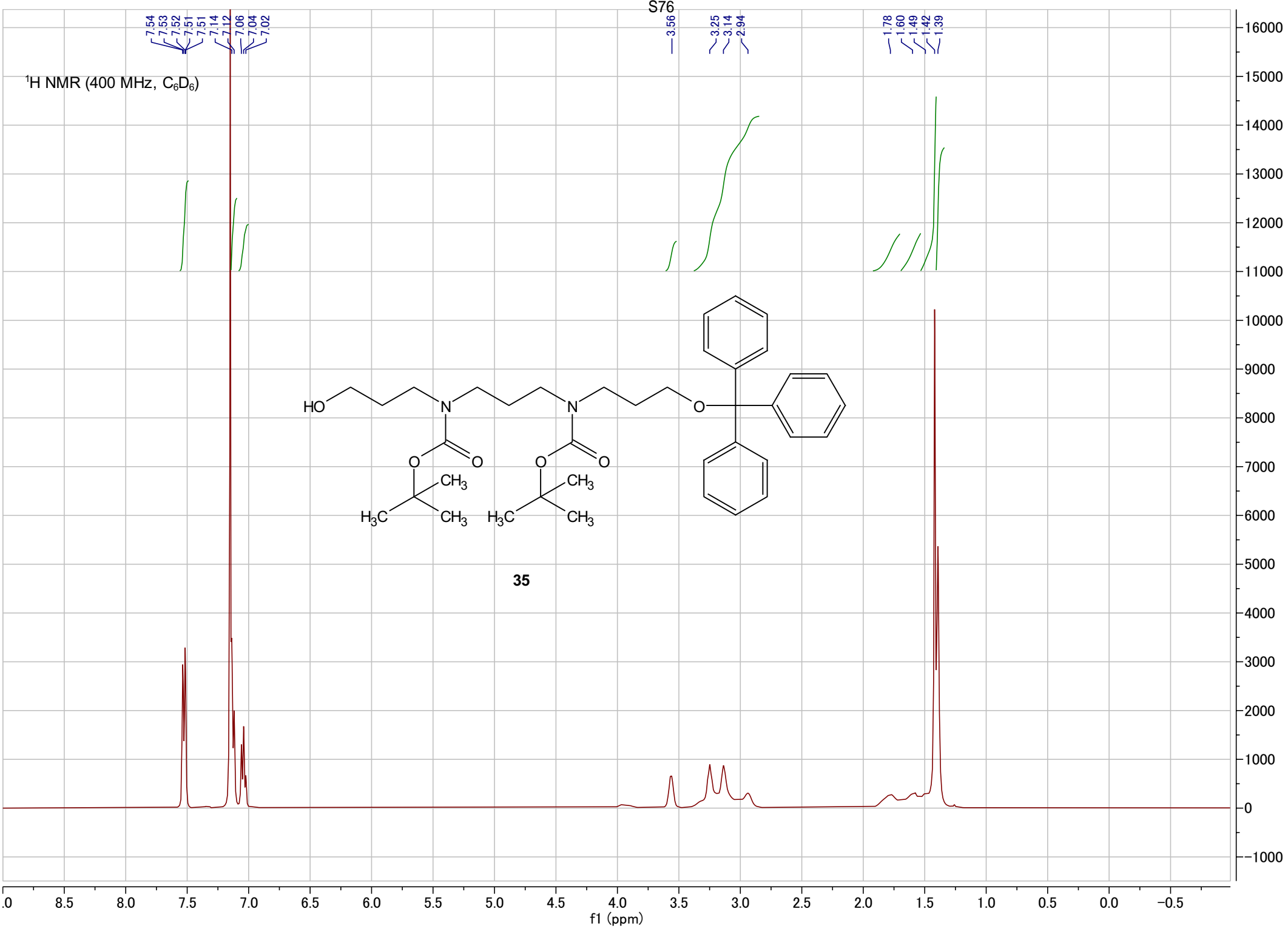
27b

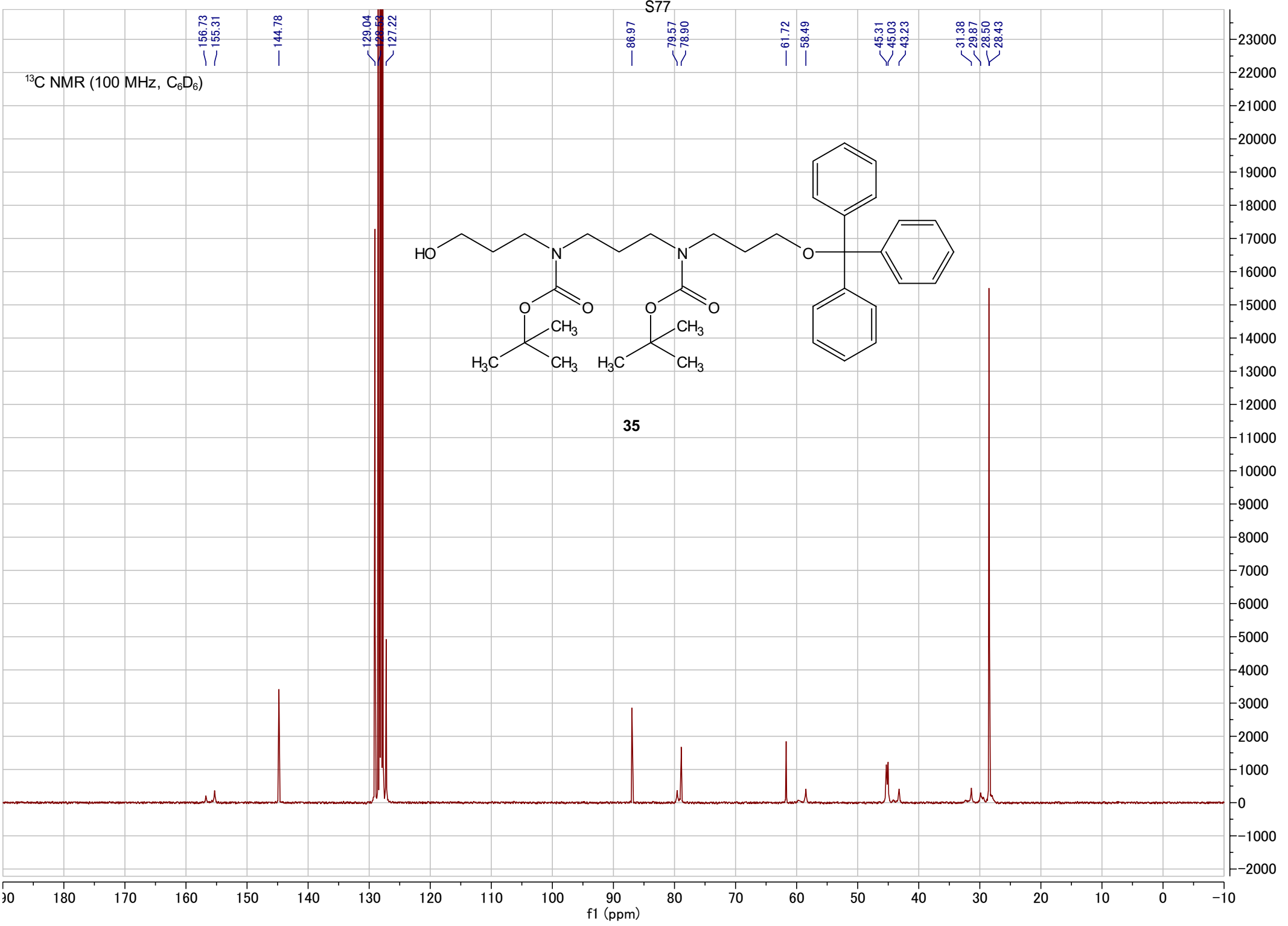




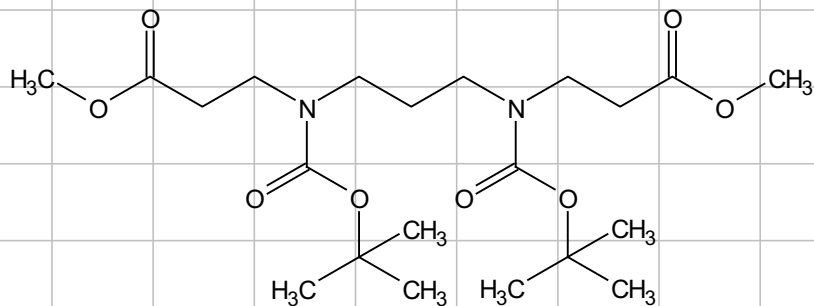








¹H NMR (400 MHz, CDCl₃)



38

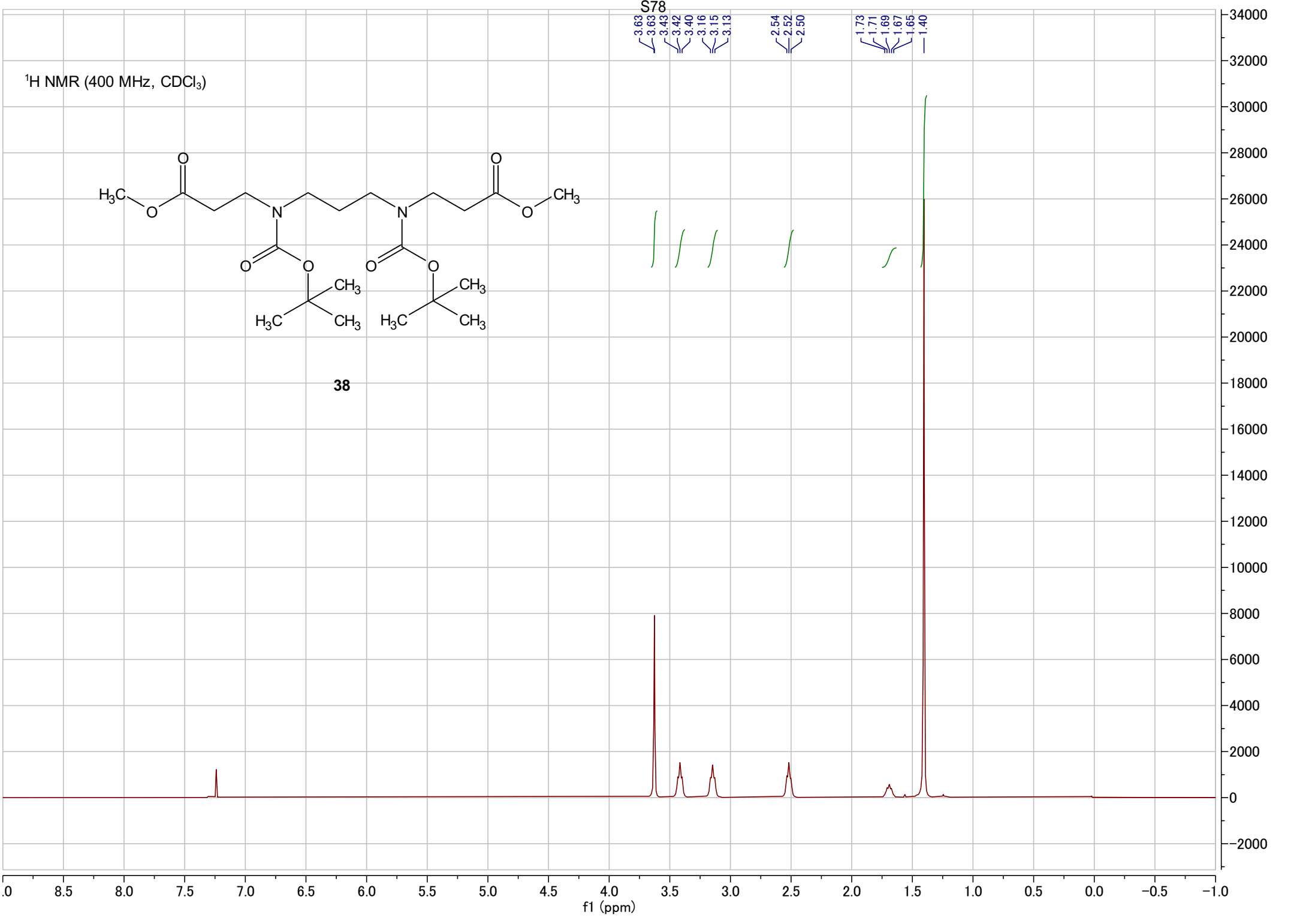
S78

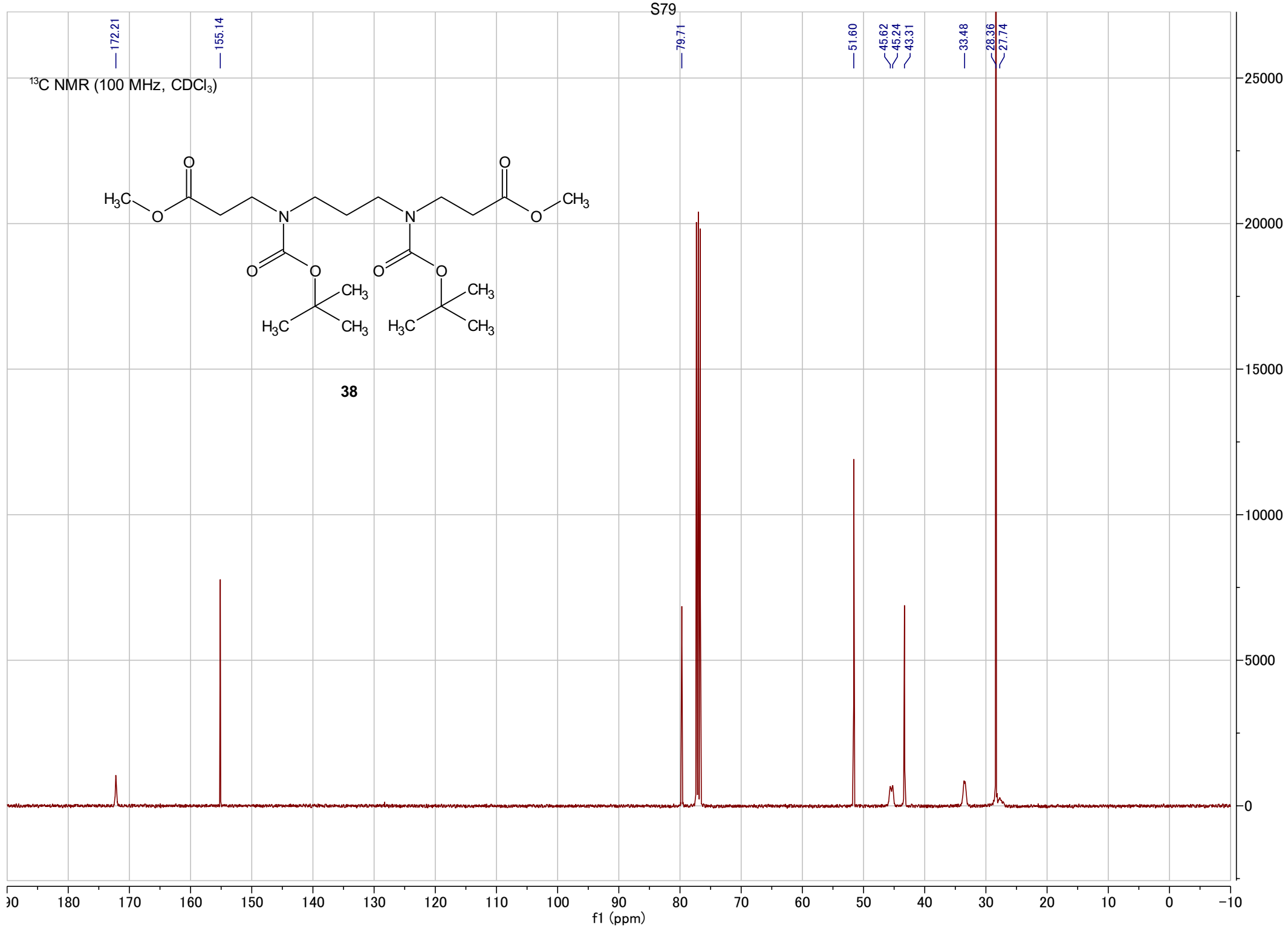
3.63
3.43
3.42
3.40
3.16
3.15
3.13

2.54
2.52
2.50

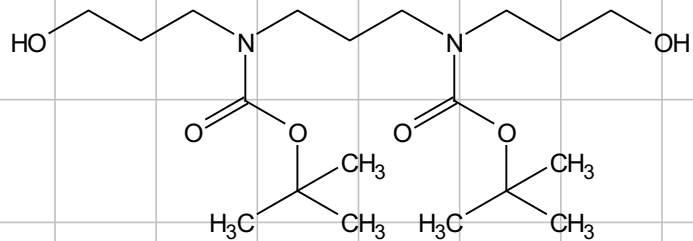
1.73
1.71
1.69
1.67
1.65

1.40





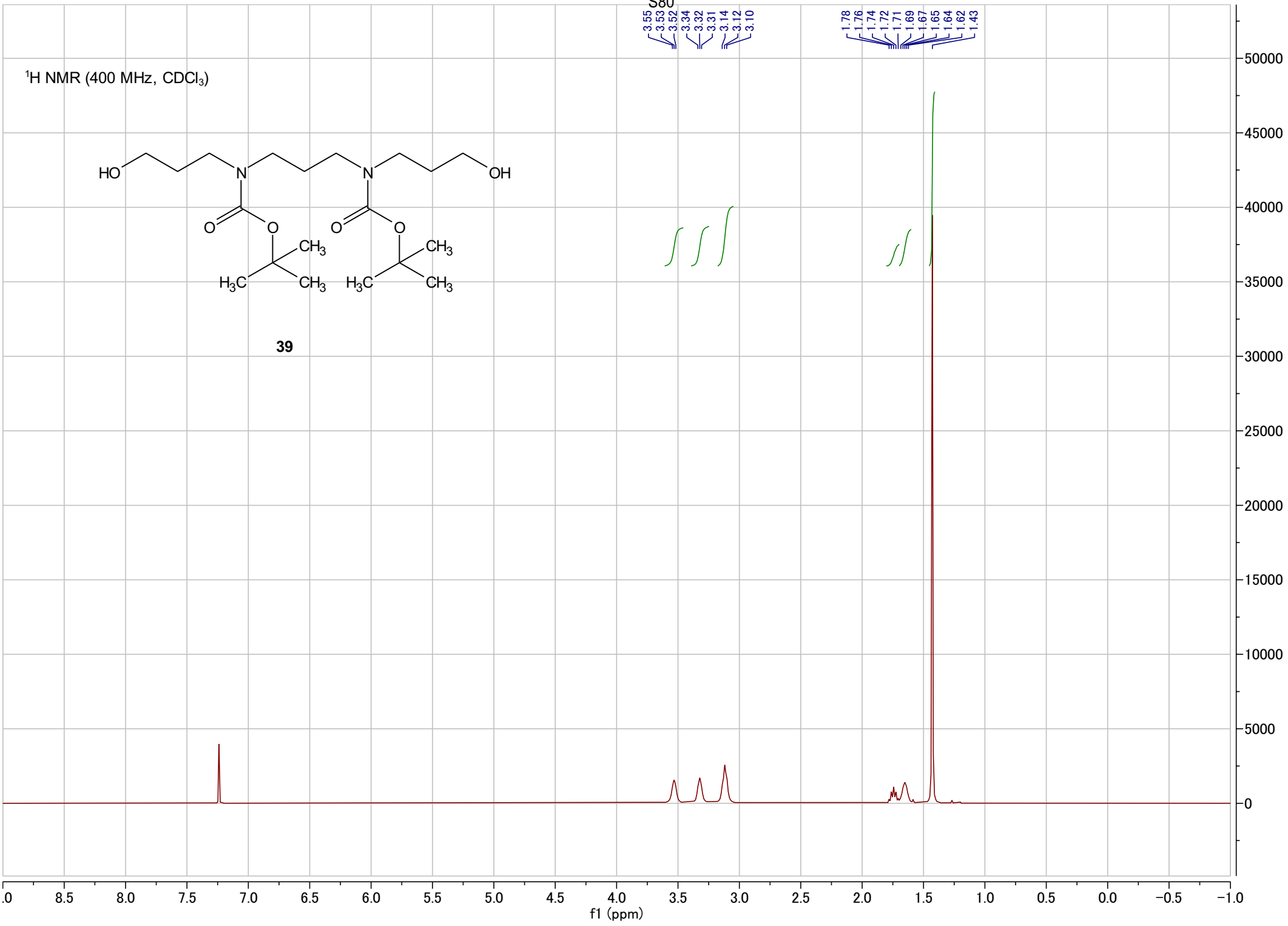
¹H NMR (400 MHz, CDCl₃)

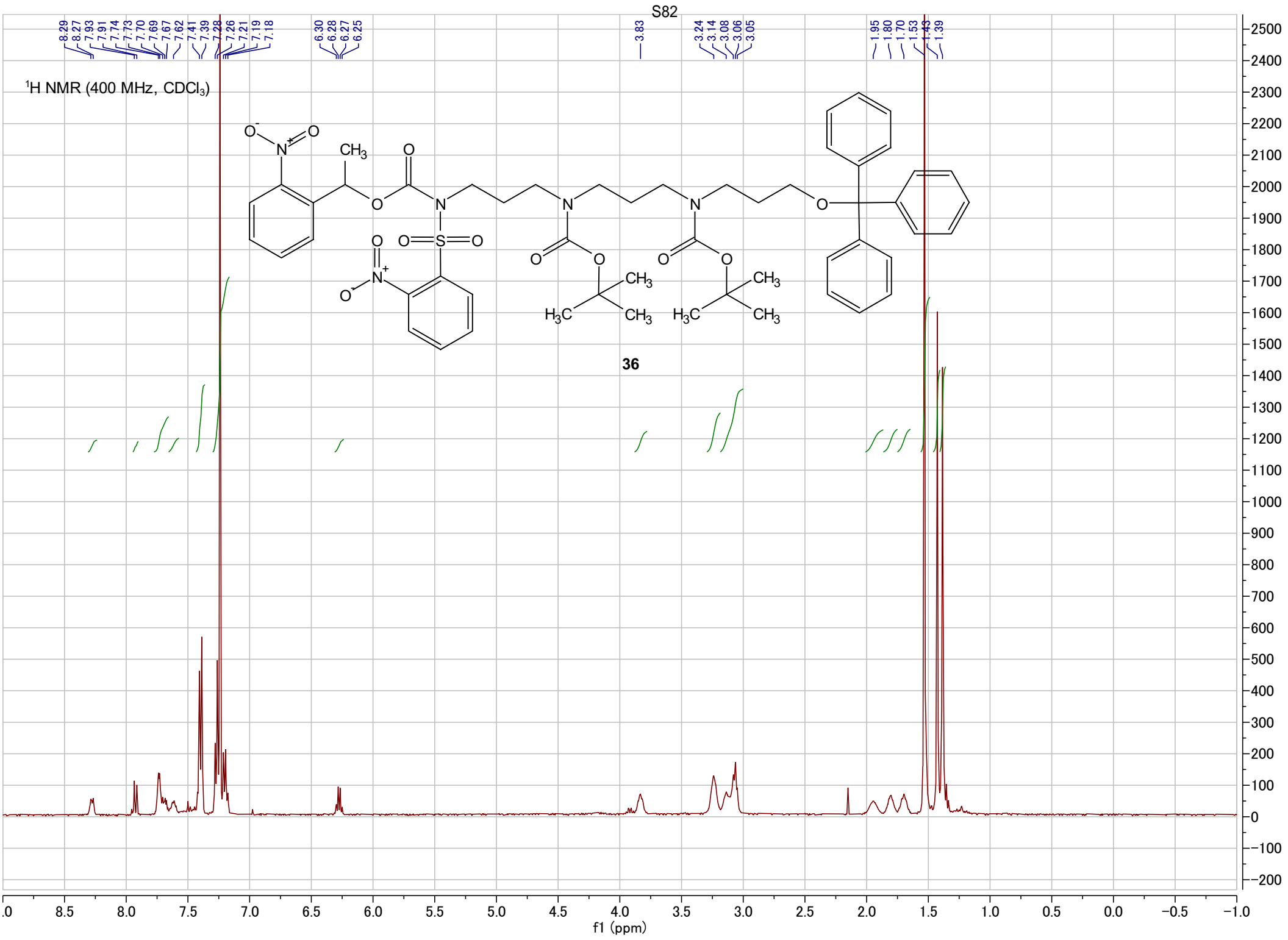


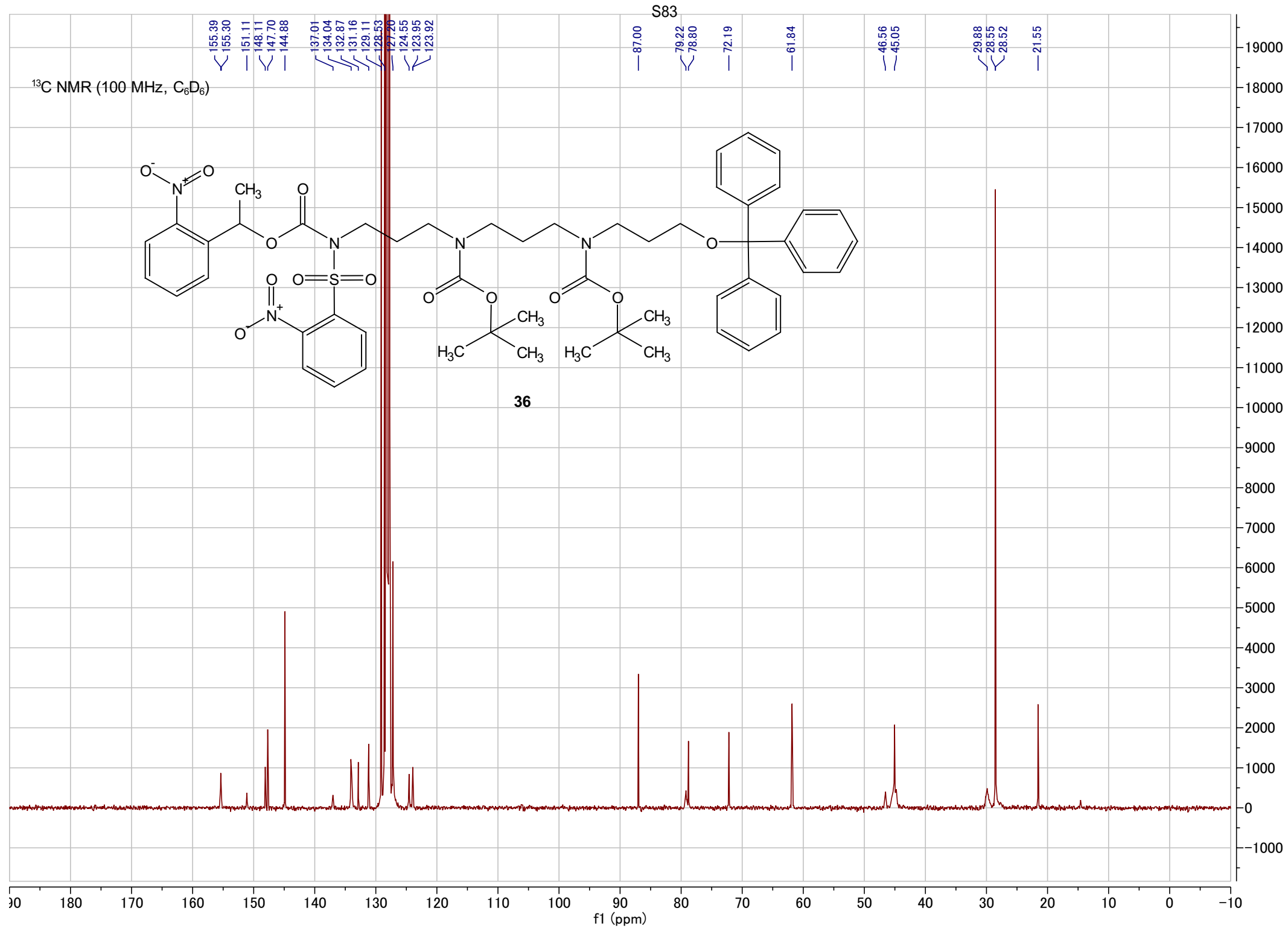
39

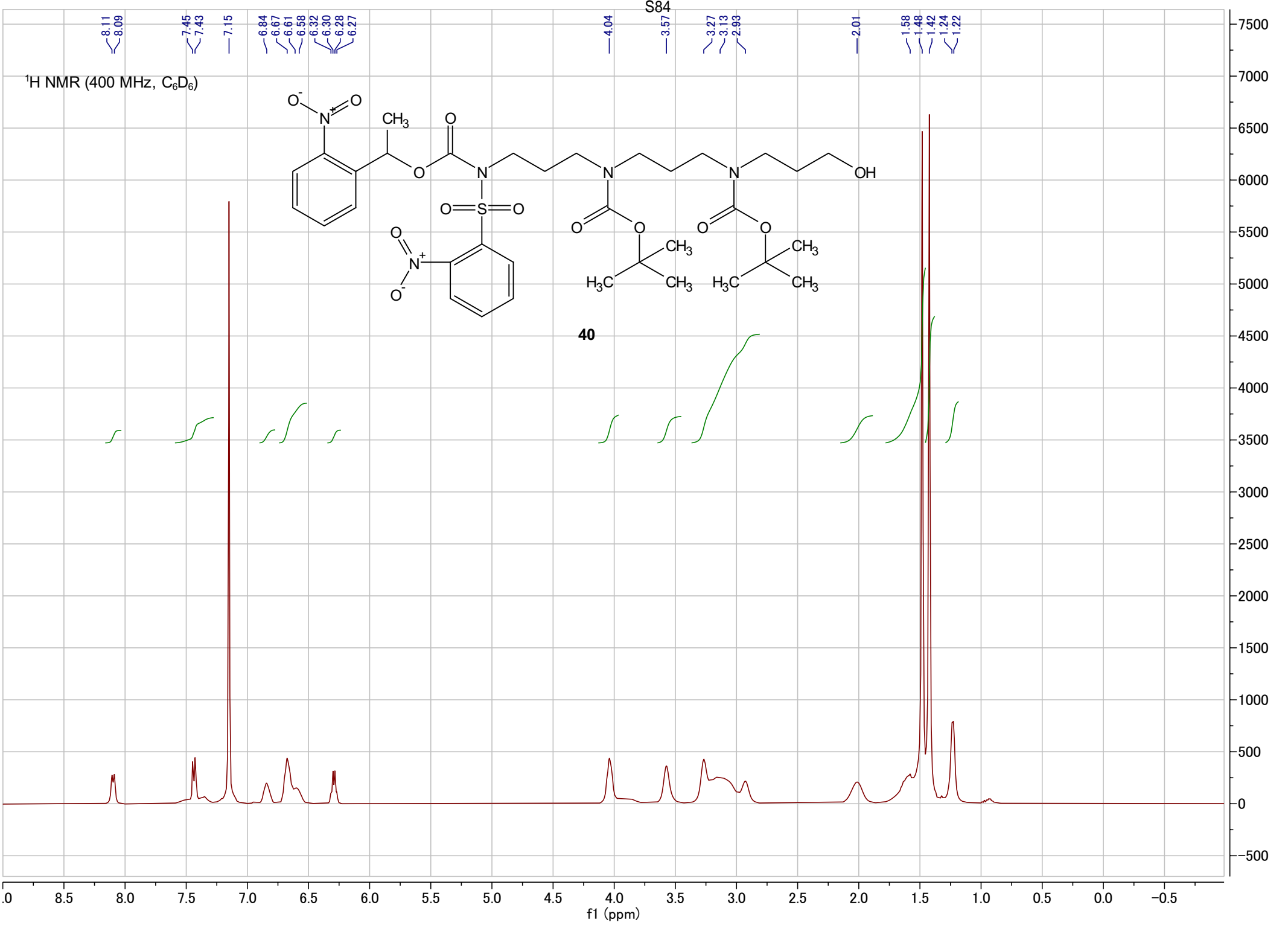
S80
3.55
3.53
3.52
3.34
3.32
3.31
3.14
3.12
3.10

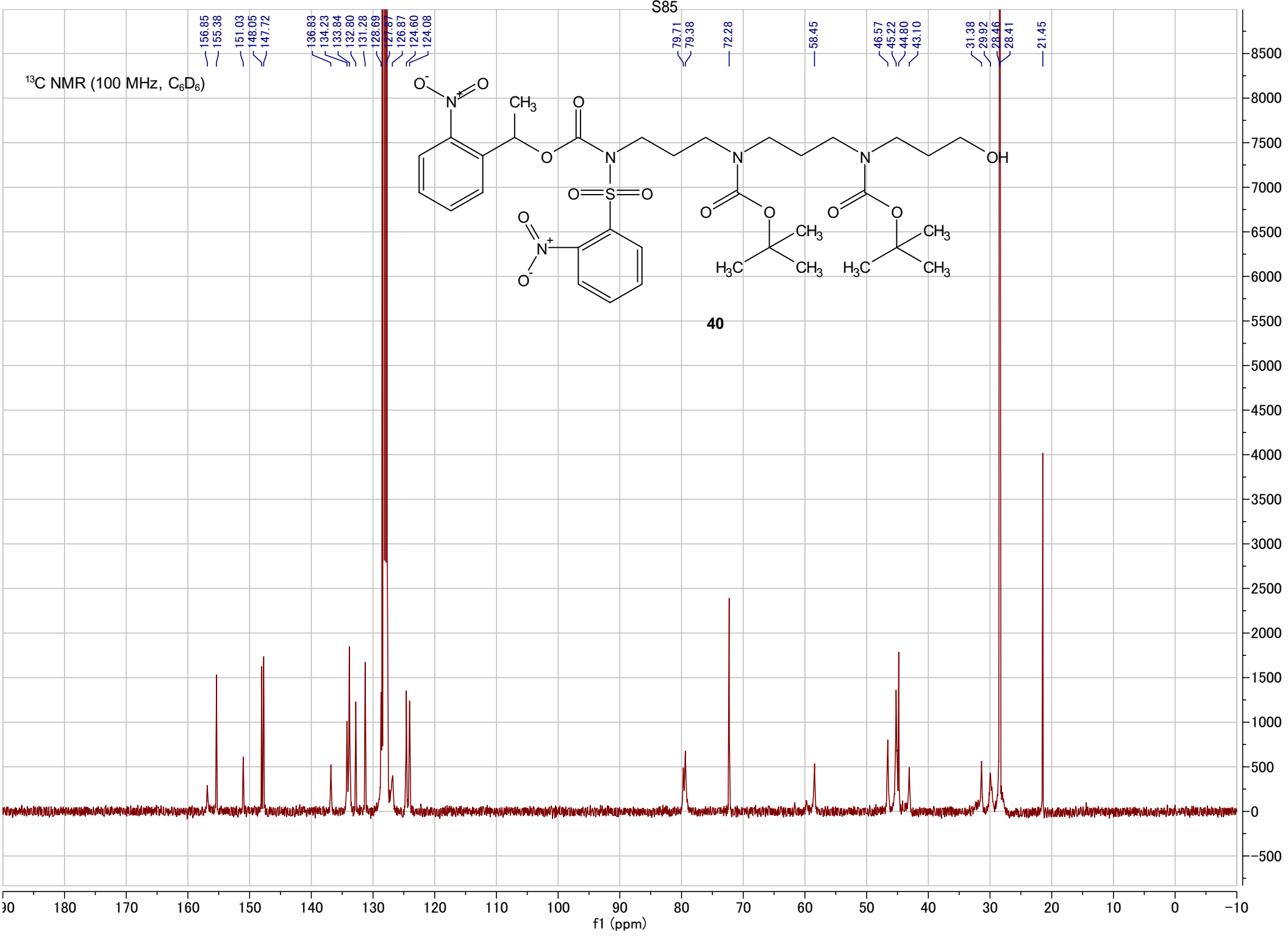
1.78
1.76
1.74
1.72
1.71
1.69
1.67
1.65
1.64
1.62
1.43

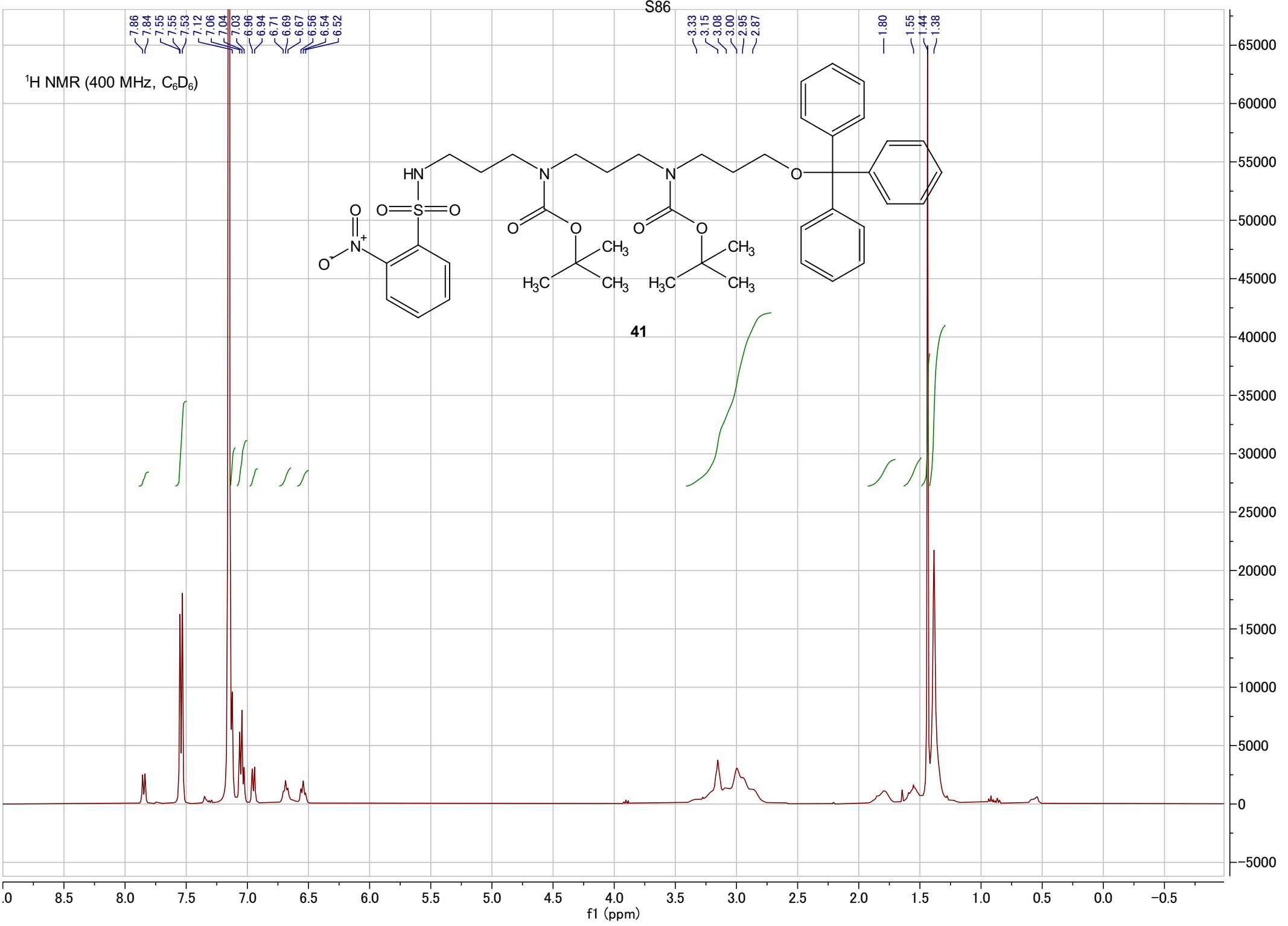


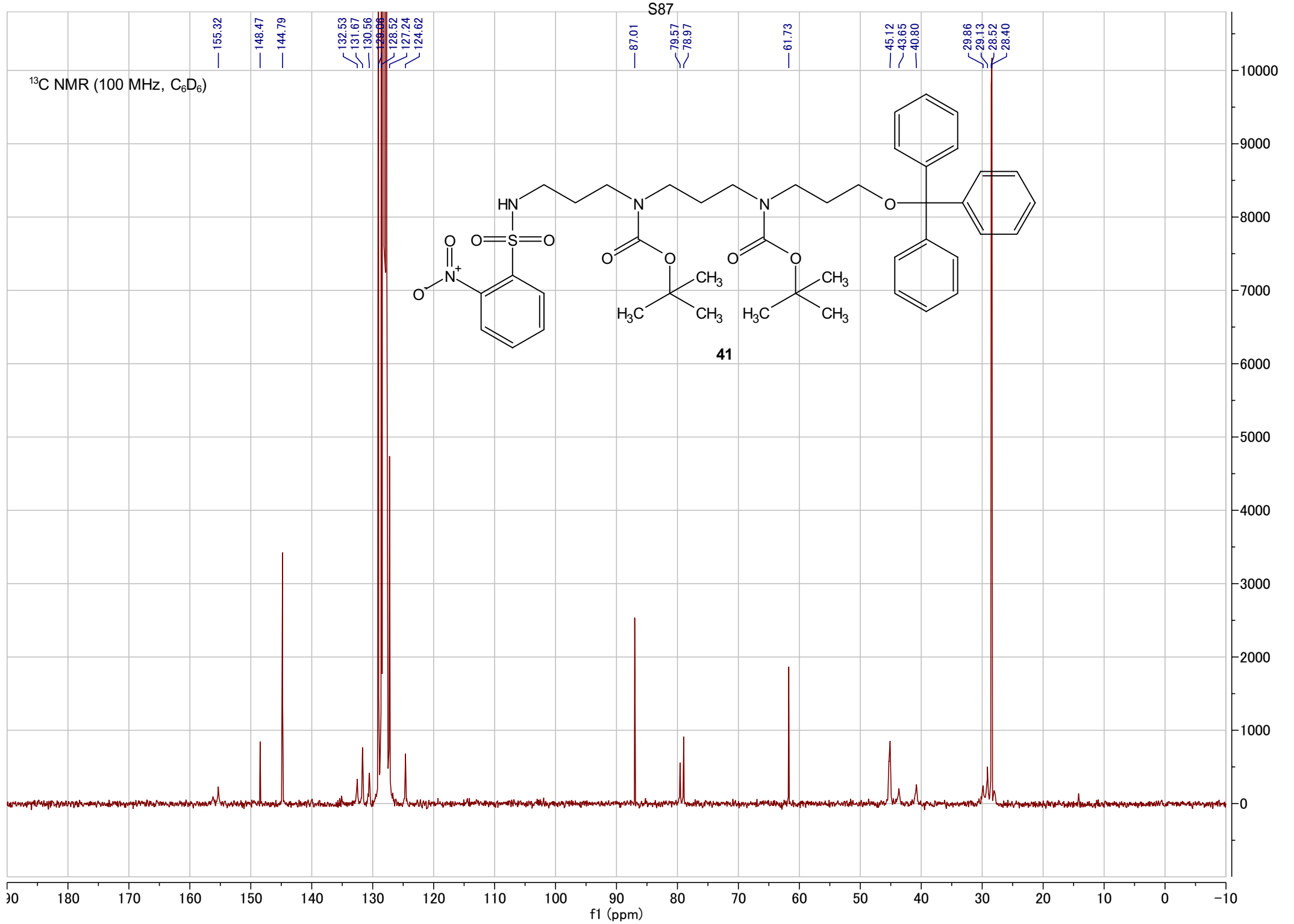


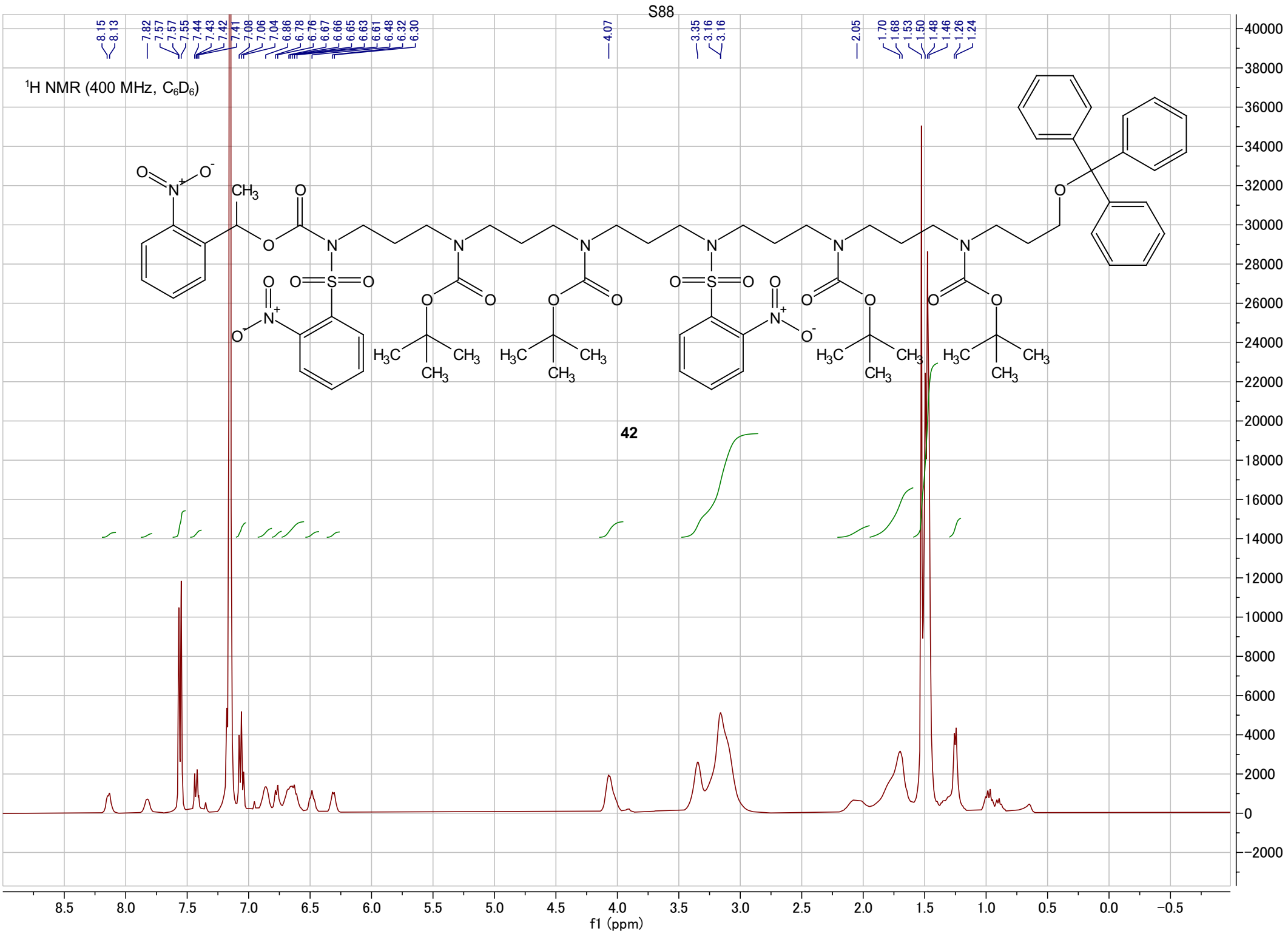


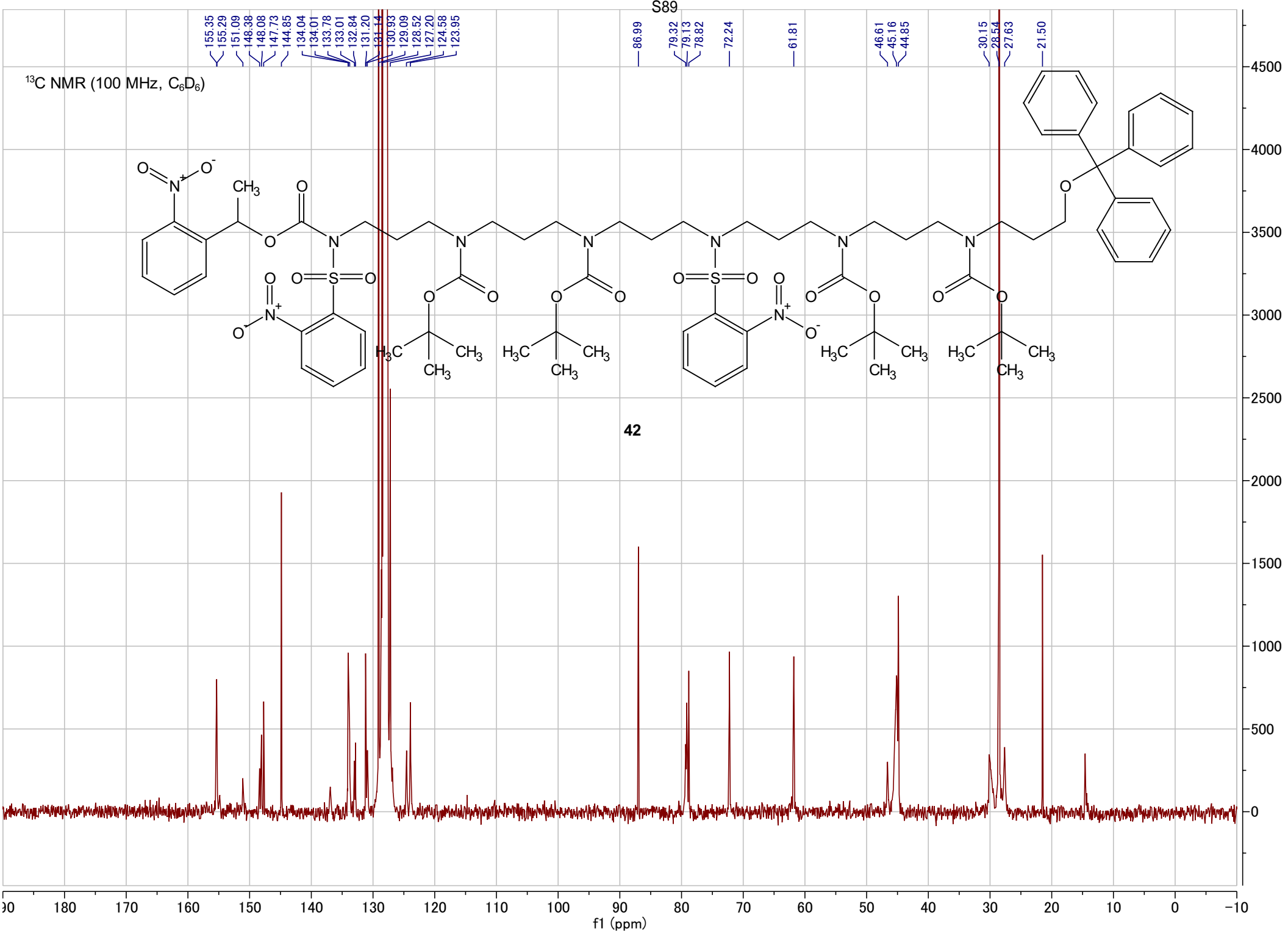


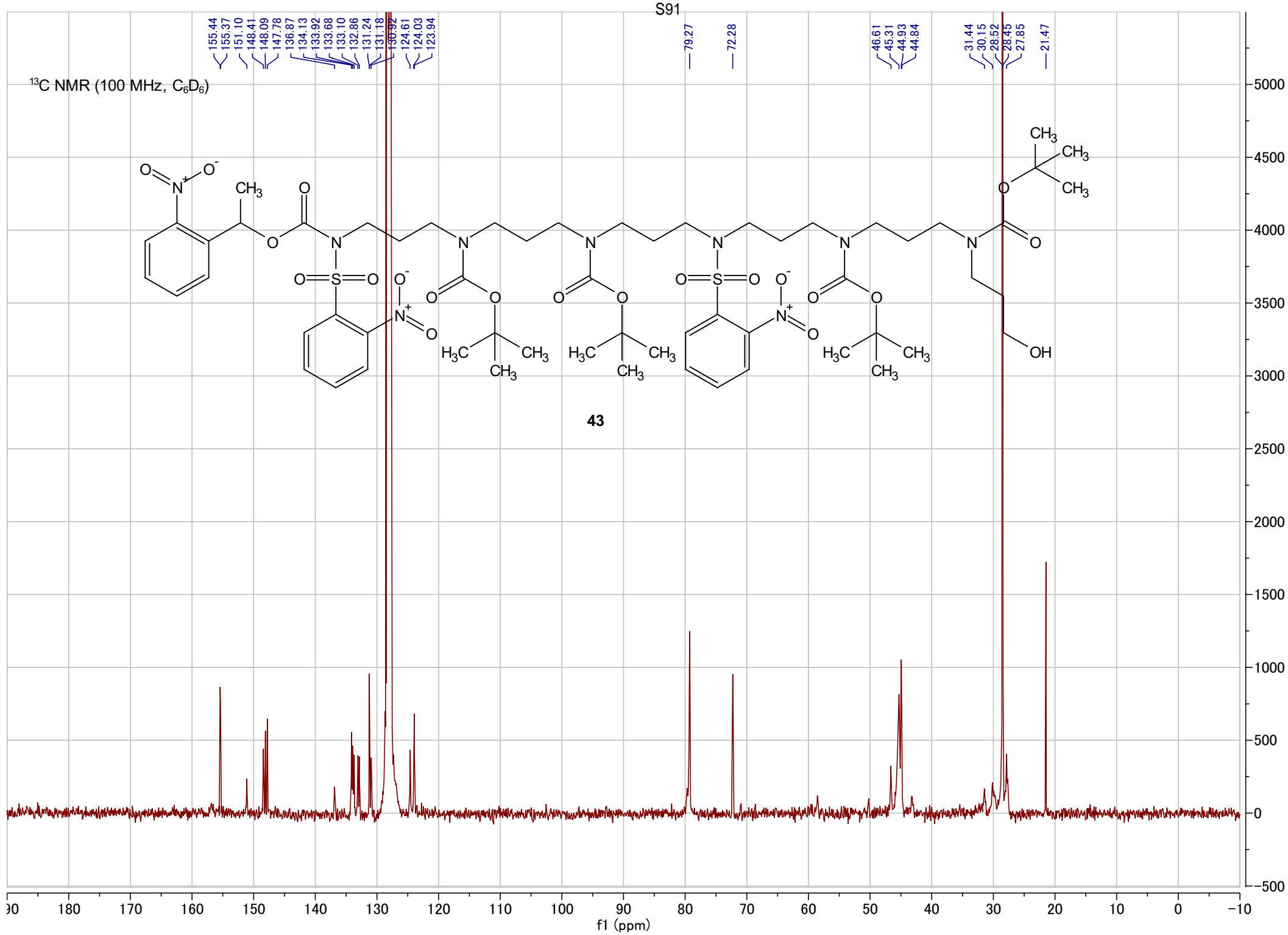


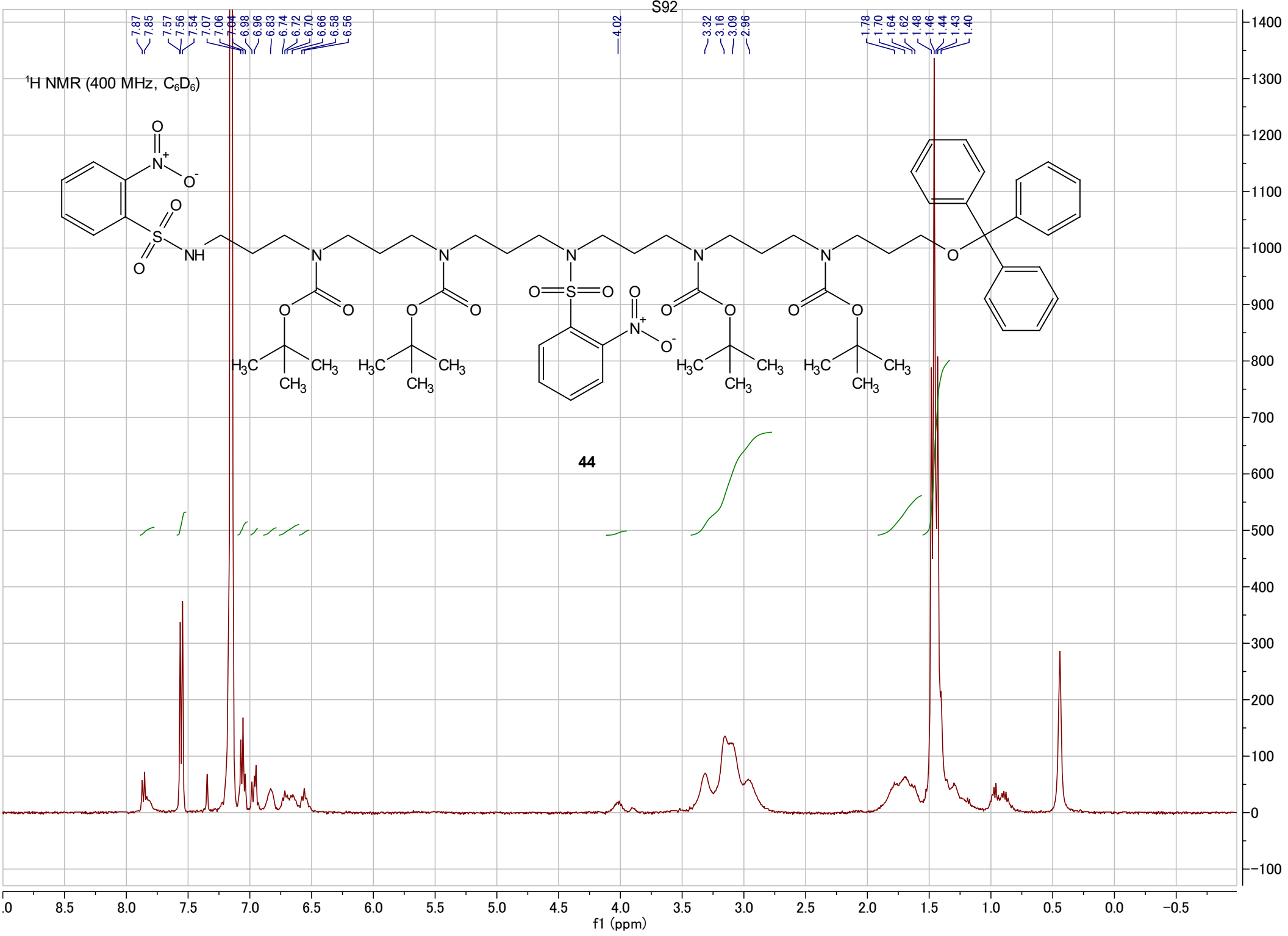






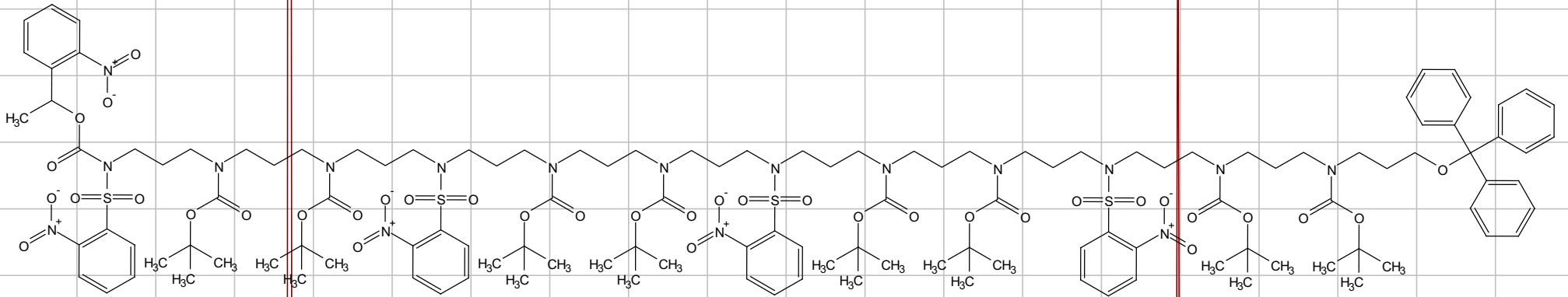






S94

¹H NMR (400 MHz, C₆D₆)



45

