SUPPORTING INFORMATION

Synthesis of Substituted Piperidines by Enantioselective Desymmetrizing Intramolecular aza-Michael Reactions

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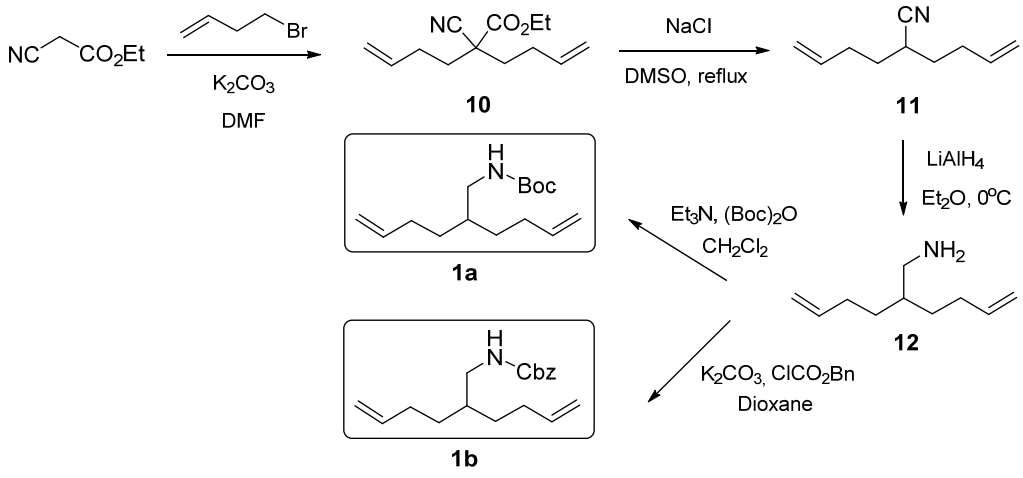
GENERAL REMARKS

Reactions involving moisture-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under nitrogen atmosphere. The following solvents were purified prior to use: THF, diethyl ether and toluene were distilled from sodium/benzophenone, CH_2Cl_2 was distilled from calcium hydride. All other solvents and reagents were used as received. The reactions were monitored with the aid of thin-layer chromatography (TLC) on 0.25 mm precoated silica gel plates. Visualization was carried out with UV light and aqueous ceric ammonium molybdate solution or potassium permanganate stains. Flash column chromatography was performed with the indicated solvents on silica gel 60 (particle size 0.040-0.063 mm). ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts are given in ppm (δ), with reference to the residual proton resonances of the solvents. Coupling constants (*J*) are given in Hertz (Hz). The letters m, s, d, t, and q stand for multiplet, singlet, doublet, triplet and quartet, respectively. The letters br indicate that the signal is broad. High-resolution mass spectra were carried out on VGmAutospec (VG Analytical, Micromass Instruments) by the Universidad de Valencia Mass Spectrometry Service. Microwave reactions were carried out at 0.1M solution in a 0.5-2 mL vial with an Initiator™ 2.0, by Biotage. The solutions were pre-stirred before the irradiation was started. The absorbance of the solvent was set as "normal" and 4-5 bars at 100ºC were reached. The reaction time was initiated as soon the system reached the input temperature, although approximately two minutes were needed to reach it. Enantiomeric ratios were determined with the aid of HPLC analysis with an appropriate chiral column (25 cm x 0.46 cm) with mixtures of *n*-hexane: *i*-propanol as eluents.

SYNTHESIS OF *N*-PROTECTED DIOLEFINIC AMINES 10, 11

The starting diolefinic amines **1**, **2**, protected as carbamates, were synthesized following the literature procedures summarized below.



Synthesis of 5-cyano-1,8-nonadiene (11)

To a solution of ethyl cyanoacetate (2.5 g, 22.1 mmol) in dry DMF (100 mL), K_2CO_3 (12.2 g, 88.4 mmol) was added. After stirring for 5 min at room temperature, a solution of 4-bromo-1-butene (6.7 mL, 66.3 mmol) in dry DMF (20 mL) was added dropwise. The reaction mixture was stirred at room temperature for 20h, when TLC analysis showed complete disappearance of ethyl cyanoacetate. The mixture containing ethyl α,α-dihomoallylcyanoacetate (**10**) was diluted with water (150 mL) and extracted with ether (3 x 30 mL). The combined organic layers were washed with brine, dried with Na_2SO_4, and concentrated under reduced pressure. Then, the crude product was dissolved in DMSO (100 mL), NaCl (5.2 g, 88.4 mmol) was added, and the suspension was heated at 150ºC for 8h, when TLC analysis showed the decarboxylation was complete. The reaction mixture was cooled to room temperature, diluted with water (150 mL) and the product was extracted into ether (3 x 30 mL). The combined organic layers were washed with brine, dried with Na_2SO_4 and filtered. After removal of the solvents, the crude mixture was purified by flash column chromatography with 6:1 *n*-hexane: ethyl acetate to afford compound **11** as a colorless oil (2.6 g, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.58-1.80 (m, 4H), 2.14-2.35 (m, 4H), 2.53-2.63 (m, 1H), 5.02-5.13 (m, 4H), 5.69-5.83 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 30.2, 31.1, 31.3, 116.3, 121.8, 136.4 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{10}H_{15}N$ (M^++H): 150.1204; found: 150.1201.

Synthesis of 5-aminomethyl-1,8-nonadiene (12)

A solution of nitrile **11** (3 g, 20 mmol) in diethyl ether (20 mL) was slowly added to a suspension of $LiAlH_4$ (6 g, 40 mmol) in ether (80 mL) at 0ºC. The mixture was allowed to stir for 3h at room temperature. Then, $Na_2SO_4 \cdot 10H_2O$ was added with vigorous stirring until aluminum salts turned white. The suspension was filtered through a pad of Celite® washing with small portions of diethyl ether. The filtrate was dried with Na_2SO_4, filtered and concentrated under vacuum, obtaining a colorless oil (crude **12**) that was employed without purification for the *N*-protection.

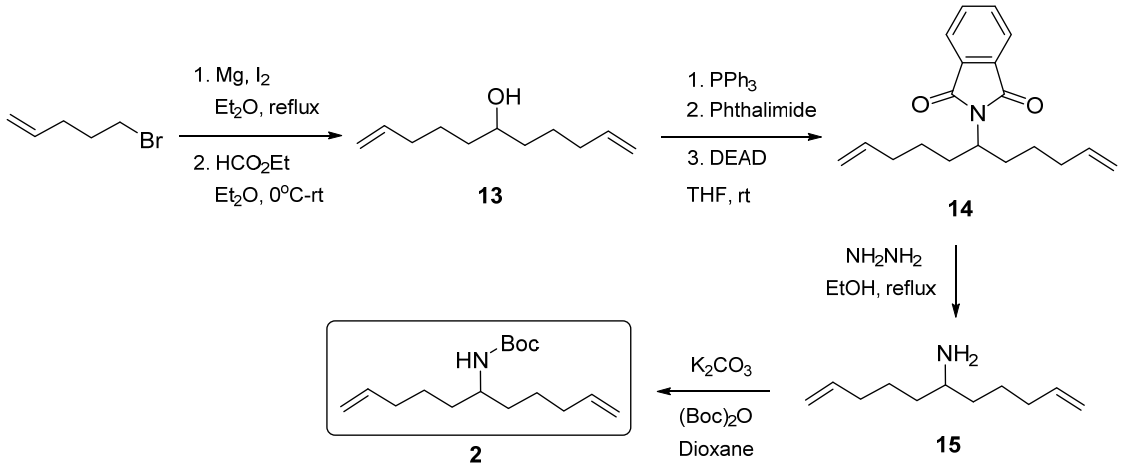
Synthesis of 5-*tert*-butoxycarbonylaminomethyl-1,8-nonadiene (1a)

Et_3N (2.73 mL, 19.56 mmol) and a catalytic amount of DMAP (30 mg) were added to a solution of amine **12** (1 g, 6.52 mmol) in CH_2Cl_2 (30 mL). After 5 min, $(Boc)_2O$ (1.6 g, 7.2 mmol) was added to the resulting solution and the mixture was stirred at room temperature for 4 h. The solvent was then removed, the residue diluted with water (50 mL), acidified with 1M HCl until pH = 5, and extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After the solvent was removed, the crude mixture was purified by flash chromatography with 10:1 *n*-hexane: ethyl acetate to afford **1a** (1 g, 60% yield, two steps) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.32-

1.40 (m, 4H), 1.43 (s, 9H), 1.48-1.54 (m, 1H), 2.03-2.10 (m, 4H), 3.08 (t, J = 5.9 Hz, 2H), 4.50 (br s, 1H), 4.92-5.03 (m, 4H), 5.71-5.85 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 28.4, 30.8, 37.2, 43.4, 79.0, 114.5, 138.7, 156.1 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{15}H_{27}NO_2$ (M^++H): 254.2042; found: 254.2039.

Synthesis of 5-benzyloxycarbonylaminomethyl-1,8-nonadiene (1b)

To a solution of amine **12** (1 g, 6.52 mmol) in dioxane (33 mL) $K_2CO_3$was added (1.4 g, 9.78 mmol). To this suspension, $ClCO_2Bn$ (1.85 mL, 13.04 mmol) was added dropwise and the mixture was vigorously stirred for 1 h. Then, solvent was removed under reduced pressure and the residue was diluted with 1M HCl (30 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After solvent was removed, the crude mixture was purified by flash column chromatography with 5:1 *n*-hexane: ethyl acetate to afford **1b** (1 g, 56% yield, two steps) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.34-1.41 (m, 4H), 1.54-1.58 (m, 1H), 2.04-2.11 (m, 4H), 3.18 (t, J = 5.9 Hz, 2H), 4.71 (br s, 1H), 4.94-5.04 (m, 4H), 5.10 (s, 2H), 5.74-5.85 (m, 2H), 7.31-7.37 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 30.7, 30.8, 37.1, 43.9, 66.7, 114.7, 128.1, 128.5, 136.6, 138.5, 156.5 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{18}H_{25}NO_2$ (M^++H): 288.1958; found: 288.1953.



Undeca-1,10-dien-6-ol **13** was prepared in 82% yield according to the procedure previously described.[1] Mitsunobu substitution of alcohol **13** with phthalimide was also described and it afforded diene **14** in 91% yield.[2]

Synthesis of 6-*tert*-butoxycarbonylamino-1,10-undecadiene (2).

To a solution of phthalimide **14** (3 g, 10.1 mmol) in ethanol (50 mL), hydrazine hydrate (1.1 g, 21.21 mmol) was added and the mixture was heated at reflux for 12h. After cooling to

[1] C. Gignoux, A. F. Newton, A. Barthelme, W. Lewis, M. L. Alcaraz, R. A. Stockman, *Org. Biomol. Chem.,* 2012, **10**, 67.
[2] M. Rejzek, R. A. Stockman, D. L. Hughes, *Org. Biomol. Chem.*, 2005, **3**, 73.

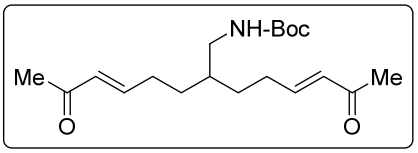
room temperature, solvent was concentrated under vacuum. The residue was diluted with diethyl ether and acidified with conc. HCl. Then, water was added and the solution was washed with diethyl ether (3 x 20 mL). The aqueous layer was treated with NaOH until pH 12 and a white precipitate appeared, which was filtered through a pad of Celite® washing with ether. The combined organic layers were dried with Na_2SO_4 and solvents were removed at reduced pressure. The resulting oil was employed in the next reaction without purification.

The crude amine **15** (1.7 g, 10.1 mmol) was dissolved in dioxane (50 mL). K_2CO_3 (2.1 g, 15.15 mmol) and a catalytic amount of DMAP (50 mg) were added and, after 5 min, $(Boc)_2O$ (2.4 g, 11.11 mmol). The mixture was stirred at room temperature for 8 h. Then solvent was concentrated under vacuum, the residue was diluted with water and the product was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After solvent was removed, the crude mixture was purified by flash column chromatography with 8:1 *n*-hexane: ethyl acetate to afford compound **2** (1.6 g, 59% yield, two steps) as a colorless oil. NMR data agree with those previously reported in the literature.[3]

GENERAL PROCEDURE FOR THE CROSS-METATHESIS REACTON. SYNTHESIS OF SYMMETRICAL BIS-ENONES 3, 4

The corresponding vinyl ketone (5.0 equiv) and second generation Hoveyda-Grubbs catalyst (10 mol%) were successively added to a stirred solution of the corresponding *N*-protected diolefinic amine **1**, **2** (1.0 equiv) in dichloromethane (0.2 M) under nitrogen atmosphere. The resulting mixture was stirred for 24 h at room temperature and then concentrated to dryness and purified by means of flash column chromatography on silica gel using mixtures of *n*- hexane and ethyl acetate as eluents.

(3*E*,10*E*)-7-*tert*-butoxycarbonylaminomethyltrideca-3,10-diene-2,12-dione (3a)



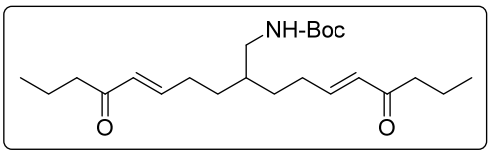
3a

By means of the general procedure described above, compound **3a** (231 mg, 58% yield) was obtained as a brown oil starting from 300 mg (1.18 mmol) of **1a** after flash chromatography with 2:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.43 (s, 9H), 1.43-1.49 (m, 4H), 1.52-1.58 (m, 1H), 2.23-2.29 (m, 10H), 3.11 (t, J = 5.9 Hz, 2H), 4.54 (br s, 1H), 6.08 (dt, J_1 = 16.2 Hz, J_2 = 1.4 Hz, 2H), 6.77 (dt, J_1 = 15.9 Hz, J_2 = 6.9 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 26.9, 28.3, 29.4, 29.8, 37.7, 42.9, 79.3, 131.4, 147.6,

[3] M. Díaz-Gavilán, W. R. J. D. Galloway, K. M. G. O'Connell, J. T. Hodkingson, D. R. Spring, *Chem. Commun.*, 2010, **46**, 776.

156.0, 198.5 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{19}H_{31}NO_4$ (M^++H): 338.2326; found: 338.2326.

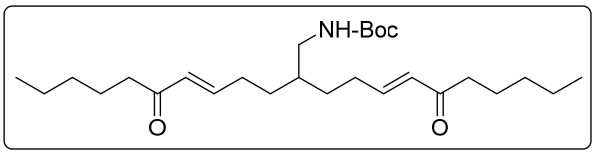
(5*E*,12*E*)-9-*tert*-butoxycarbonylaminomethylheptadeca-5,12-diene-4,14-dione (3b)



3b

By means of the general procedure described above, compound **3b** (293 mg, 63% yield) was obtained as a brown oil starting from 300 mg (1.18 mmol) of **1a** after flash chromatography with 3:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.91 (t, *J* = 7.4 Hz, 6H), 1.42 (s, 9H), 1.40-1.46 (m, 4H), 1.57-1.67 (m, 5H), 2.19-2.26 (m, 4H), 2.48 (t, *J* = 7.4 Hz, 4H), 3.09 (t, *J* = 5.7 Hz, 2H), 4.57 (br s, 1H), 6.08 (dt, J_1 = 15.9, J_2 = 1.5 Hz, 2H), 6.77 (dt, J_1 = 15.9, J_2 = 6.8 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.8, 17.6, 28.4, 29.4, 29.9, 37.7, 42.1, 43.0, 79.4, 130.5, 146.2, 156.1, 200.6 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{23}H_{39}NO_4$ (M^++H): 394.2952; found: 394.2947.

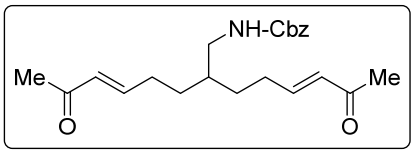
(7*E*,14*E*)-11-*tert*-butoxycarbonylaminomethylhenicosa-7,14-diene-6,16-dione (3c)



3c

By means of the general procedure described above, compound **3c** (329 mg, 62% yield) was obtained as a brown oil starting from 300 mg (1.18 mmol) of **1a** after flash chromatography with 4:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.88 (t, *J* = 6.9 Hz, 6H), 1.24-1.32 (m, 9H), 1.40-1.47 (m, 3H),1.43 (s, 9H), 1.54-1.64 (m, 5H), 2.19-2.27 (m, 4H), 2.50 (t, *J* = 7.5 Hz, 4H), 3.10 (t, *J* = 5.7 Hz, 2H), 4.54 (br s, 1H), 6.09 (dt, J_1 = 15.9 Hz, J_2 = 1.3 Hz, 2H), 6.78 (dt, J_1 = 15.6 Hz, J_2 = 6.8 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 22.4, 23.9, 28.3, 29.4, 29.9, 31.4, 37.7, 40.2, 43.0, 79.3, 130.5, 146.2, 156.0, 200.7 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{27}H_{47}NO_4$ (M^++H): 450.3578; found: 450.3572.

(3*E*,10*E*)-7-benzyloxycarbonylaminomethyltrideca-3,10-diene-2,12-dione (3d)

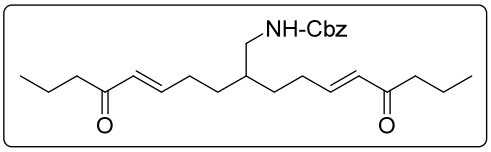


3d

By means of the general procedure described above, compound **3d** (305 mg, 79% yield) was obtained as a brown oil starting from 300 mg (1.04 mmol) of **1b** after flash

chromatography with 2:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.41-1.48 (m, 4H), 1.53-1.59 (m, 1H), 2.14-2.28 (m, 10H), 3.18 (t, *J* = 5.9 Hz, 2H), 4.94 (br s, 1H), 5.08 (s, 2H), 6.06 (d, *J* = 15.9 Hz, 2H), 6.74 (dt, J_1 = 15.9, J_2 = 6.9 Hz, 2H), 7.33 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 26.9, 29.4, 29.7, 37.6, 43.4, 66.7, 128.0, 128.1, 128.5, 131.4, 136.4, 147.4, 156.5, 198.4 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{22}H_{29}NO_4$ (M^++H): 372.2169; found: 372.2171.

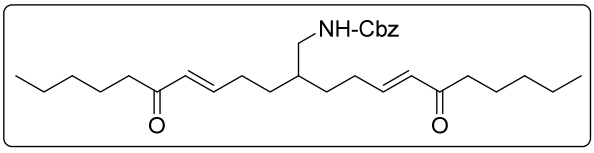
(5*E*,12*E*)-9-*tert*-benzyloxycarbonylaminomethylheptadeca-5,12-diene-4,14-dione (3e)



3e

By means of the general procedure described above, compound **3e** (369 mg, 83% yield) was obtained as a brown oil starting from 300 mg (1.04 mmol) of **1b** after flash chromatography with 3:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.91 (t, *J* = 7.5 Hz, 6H), 1.40-1.47 (m, 4H), 1.55-1.67 (m, 5H), 2.18-2.25 (m, 4H), 2.47 (t, *J* = 7.4 Hz, 4H), 3.17 (t, *J* = 5.9 Hz, 2H), 4.92 (br s, 1H), 5.08 (s, 2H), 6.08 (d, *J* = 15.9 Hz, 2H), 6.76 (dt, J_1 = 15.9, J_2 = 6.9 Hz, 2H), 7.32 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.7, 17.6, 29.3, 29.8, 37.6, 42.0, 43.4, 66.7, 127.9, 128.0, 128.4, 130.5, 136.4, 146.0, 156.5, 200.5 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{26}H_{37}NO_4$ (M^++H): 428.2795; found: 428.2782.

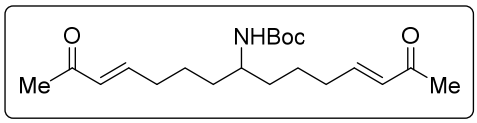
(7*E*,14*E*)-11-benzyloxycarbonylaminomethylhenicosa-7,14-diene-6,16-dione (3f)



3f

By means of the general procedure described above, compound **3f** (3827 mg, 76% yield) was obtained as a brown oil starting from 300 mg (1.04 mmol) of **1b** after flash chromatography with 3:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.89 (t, *J* = 6.9 Hz, 6H), 1.25-1.33 (m, 9H), 1.41-1.48 (m, 4H), 1.55-1.65 (m, 4H), 2.20-2.27 (m, 4H), 2.50 (t, *J* = 7.5 Hz, 4H), 3.18 (t, *J* = 5.9 Hz, 2H), 4.79 (br s, 1H), 5.09 (s, 2H), 6.09 (d, *J* = 15.9 Hz, 2H), 6.77 (dt, J_1 = 15.6, J_2 = 6.9 Hz, 2H), 7.34 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 22.4, 23.9, 29.4, 29.9, 31.4, 37.7, 40.3, 43.5, 66.8, 128.1, 128.2, 128.5, 130.5, 136.4, 146.0, 156.5, 200.6. HRMS (EI^+) (*m/z)*: calcd. for $C_{30}H_{45}NO_4$ (M^++H): 484.3421; found: 484.3420.

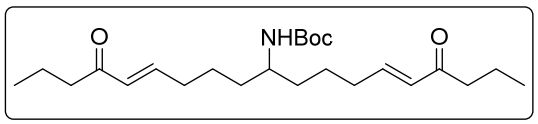
(3*E*,12*E*)-7-*tert*-butoxycarbonylaminopentadeca-3,12-diene-2,14-dione (4a)



4a

By means of the general procedure described above, compound **4a** (283 mg, 72% yield) was obtained as a brown oil starting from 300 mg (1.12 mmol) of **2** after flash chromatography with 2:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.29-1.36 (m, 1H), 1.44 (s, 9H), 1.47-1.53 (m, 5H), 1.62 (br s, 2H), 2.16-2.30 (m, 10H), 3.57 (br s, 1H), 4.22 (d, J = 8.4 Hz, 1H), 6.07 (d, J = 15.9 Hz, 2H), 6.77 (dt, J_1 = 15.9, J_2 = 6.9 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 24.5, 26.9, 28.4, 32.2, 35.3, 50.0, 79.2, 131.5, 147.7, 155.7, 198.6 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{20}H_{33}NO_4$ (M^++H): 352.2482; found: 352.2471.

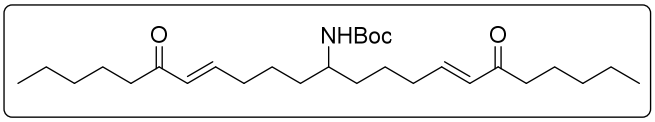
(5*E*,14*E*)-10-*tert*-butoxycarbonylaminononadeca-5,14-diene-4,16-dione (4b)



4b

By means of the general procedure described above, compound **4b** (310 mg, 68% yield) was obtained as a brown oil starting from 300 mg (1.12 mmol) of **2** after flash chromatography with 3:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.91 (t, J = 7.4 Hz, 6H), 1.27-1.37 (m, 2H), 1.42 (s, 9H), 1.42-1.52 (m, 6H), 1.58-1.68 (m, 4H), 2.16-2.25 (m, 4H), 2.49 (t, J = 7.4 Hz, 4H), 3.57 (br s, 1H), 4.24 (d, J = 9.3 Hz, 1H), 6.07 (d, J = 15.9 Hz, 2H), 6.77 (dt, J_1 = 15.9, J_2 = 6.9 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.8, 17.6, 24.5, 28.4, 32.1, 35.2, 42.1, 50.0, 79.1, 130.6, 146.4, 155.7, 200.7 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{24}H_{41}NO_4$ (M^++H): 408.3108; found: 408.3095.

(7*E*,16*E*)-12-*tert*-butoxycarbonylaminotricosa-7,16-diene-6,18-dione (4c)



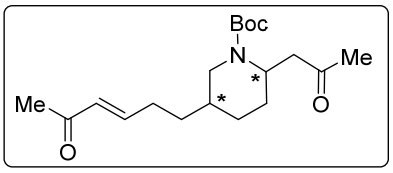
4c

By means of the general procedure described above, compound **4c** (327 mg, 63% yield) was obtained as a brown oil starting from 300 mg (1.12 mmol) of **2** after flash chromatography with 4:1 *n*-hexanes: ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.87 (t, J = 6.8 Hz, 6H); 1.26-1.32 (m, 10H) 1.42 (s, 9H), 1.42-1.63 (m, 10H), 2.15-2.25 (m, 4H), 2.49 (t, J = 7.4 Hz, 4H), 3.56 (br s, 1H), 4.23 (d, J = 9.3 Hz, 1H), 6.07 (d, J = 15.9 Hz, 2H), 6.77 (dt, J_1 = 15.9 Hz, J_2 = 6.9 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 22.4, 23.9, 24.5, 28.4, 31.4, 32.1, 35.3, 40.2, 50.0, 79.1, 130.5, 146.4, 155.7, 200.8 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{28}H_{49}NO_4$ (M^++H): 464.3734; found: 464.3715.

GENERAL PROCEDURE FOR THE INTRAMOLECULAR AZA-MICHAEL REACTION. SYNTHESIS OF DISUBSTITUTED PIPERIDINES 5, 6

In a 10 mL round bottomed flask, the corresponding bis-enone **3**, **4** (1.0 equiv) was dissolved in chloroform (0.1 M). Catalyst **I** (20 mol%) and trifluoroacetic acid (TFA) (20 or 10 mol%) were added and the resulting solution was stirred at room temperature during the time specified in Tables 1-3. Then, the crude reaction mixture was subjected to flash column chromatography on silica gel using mixtures of *n*-hexane: ethyl acetate as eluents to afford the corresponding piperidines **5** and **6**. The enantiomeric ratios were determined by means of HPLC analysis with an appropriate chiral column. In the cases specified in Tables 2 and 3, reactions were conducted in a sealed vial under microwave irradiation at 60ºC.

N-tert-butoxycarbonyl-5-[(*E*)-5-oxohex-3-en-1-yl)]-2-(2-oxopropyl) piperidine (5a)



(*trans*+*cis*)-**5a**

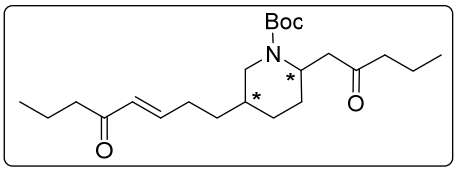
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, disubstituted piperidine **5a** (28 mg, 82% yield) was obtained from **3a** (0.1 mmol) as a non-separable 2:1 mixture of diastereoisomers, with 76:24 *er* and 95:5 *er* for the major diastereoisomer (*trans*-**5a**) and minor diastereoisomer (*cis*-**5a**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5a** (23 mg, 68% yield) was obtained from **3a** (0.1 mmol) as a non-separable 5:1 mixture of diastereoisomers, with 94:6 *er* and 56:44 *er* for the major diastereoisomer (*trans*-**5a**) and minor diastereoisomer (*cis*-**5a**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 95:5); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5a**): t_{major}= 17.2 min, t_{minor}=18.6 min; minor diastereoisomer (*cis*-**5a**): t_{major}= 29.1 min, t_{minor}= 46.0 min.

Data for the mixture of diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.24-1.31 (m, 3H), 1.35 (s, 9H), 1.49-1.72 (m, 4H), 2.09 (s, 3H), 2.14-2.15 (m, 5H), 2.51-2.62 (m, 2H), 2.91 (dd, J_1 = 14.0 Hz, J_2 = 2.9 Hz, 1H), 3.70 (d, J = 14.1 Hz, 0.8H), 3.97 (br s, 0.2H), 4.55-4.59 (m, 0.8H), 4.70 (br s, 0.2H), 6.48 (dt, J_1 = 15.9 Hz, J_2 = 1.4 Hz, 1H), 6.64-6.75 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 23.5, 23.7, 25.4, 26.7, 28.2, 28.5, 29.2, 29.8, 30.1, 32.2, 32.4, 35.2, 41.8, 43.9, 44.5, 47.4, 79.5, 131.2, 147.4, 147.7, 154.3, 154.9, 198.3, 206.7 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{19}H_{31}NO_4$ (M^++Na): 360.2145; found: 360.2145.

***N-tert*-butoxycarbonyl-5-[(*E*)-5-oxooct-3-en-1-yl)]-2-(2-oxopentyl) piperidine (5b)**



(*trans*+*cis*)-**5b**

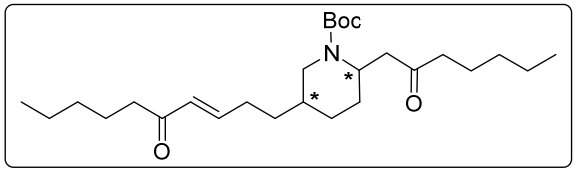
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, disubstituted piperidine **5b** (64.5 mg, 82% yield) was obtained from **3b** (0.2 mmol) as a non-separable 2:1 mixture of diastereoisomers, with 83:17 *er* and 92:8 *er* for the major diastereoisomer (*trans*-**5b**) and minor diastereoisomer (*cis*-**5b**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5b** (44 mg, 56% yield) was obtained from **3b** (0.2 mmol) as a non-separable 2.4:1 mixture of diastereoisomers, with 96:4 *er* and 56:44 *er* for the major diastereoisomer (*trans*-**5b**) and minor diastereoisomer (*cis*-**5b**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 95:5); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5b**): t_{major}= 9.0 min, t_{minor}=10.0 min; minor diastereoisomer (*cis*-**5b**): t_{major}= 16.3 min, t_{minor}= 19.2 min.

Data for the mixture of diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.88-0.95 (m, 6H), 1.32-1.44 (m, 3H), 1.44 (s, 9H), 1.54-1.64 (m, 7H), 1.75-1.84 (m, 1H), 2.18-2.30 (m, 2H), 2.39-2.52 (m, 4H), 2.63-2.66 (m, 2H), 3.00 (dd, J_1 = 13.8 Hz, J_2 = 3.0 Hz, 1H), 3.78 (d, J = 13.8 Hz, 1H), 4.64 (br s, 1H), 6.10 (dt, J_1 = 15.6 Hz, J_2 = 1.4 Hz, 1H), 6.74-6.85 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.8, 13.9, 17.2, 17.7, 17.8, 23.8, 24.1, 25.8, 28.5, 28.8, 29.5, 30.4, 32.6, 32.8, 35.6, 42.2, 43.2, 43.9, 44.9, 47.8, 79.9, 130.6, 146.5, 146.8, 154.7, 155.3, 200.9, 209.3 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{23}H_{39}NO_4$ (M^++Na): 416.2771; found: 416.2765.

***N-tert*-butoxycarbonyl-5-[(*E*)-5-oxodec-3-en-1-yl)]-2-(2-oxoheptyl) piperidine (5c)**



(*trans*+*cis*)-**5c**

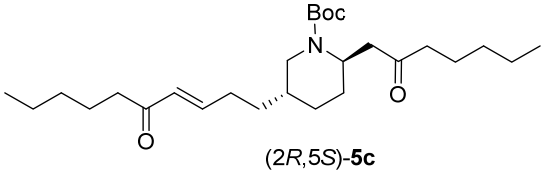
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,5-disubstituted piperidine **5c** (78 mg, 87% yield) was obtained from **3c** (0.2 mmol) as a non-separable 2:1 mixture of diastereoisomers, with 88:12 *er* and 98:2 *er* for the major diastereoisomer (*trans*-**5c**) and minor diastereoisomer (*cis*-**5c**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5c** (54 mg, 60% yield) was obtained from **3c** (0.2 mmol) as a non-separable 4:1 mixture of diastereoisomers, with

96:4 *er* and 84:16 *er* for the major diastereoisomer (*trans*-**5c**) and minor diastereoisomer (*cis*-**5c**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 95:5); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5c**): t_{major}= 7.7 min, t_{minor}= 9.1 min; minor diastereoisomer (*cis*-**5c**): t_{major}= 12.9 min, t_{minor}= 16.0 min.

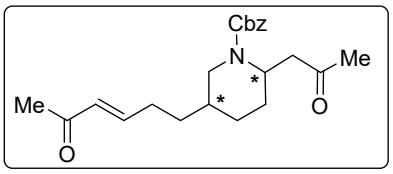
Data for major diastereoisomer:



(2*R*,5*S*)-**5c**

The mixture of diastereoisomers (*trans*+*cis*)-**5c** was separated by semi-preparative chiral HPLC using a Chiralpak IC column (hexane: 2-propanol, 98:2; flow rate 4 mL/ min). $[\alpha]_D^{25}$ $_{\text{major enantiomer}}$= +21.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.85-0.90 (m, 6H), 1.24-1.36 (m, 10H), 1.43 (s, 9H), 1.52-1.62 (m, 7H), 1.74-1.84 (m, 2H), 2.18-2.29 (m, 2H), 2.40-2.53 (m, 4H), 2.60-2.71 (m, 2H), 2.99 (dd, J_1 = 14.0 Hz, J_2 = 2.9 Hz, 1H), 3.78 (d, J = 14.4 Hz, 1H), 4.63 (br s, 1H), 6.10 (dt, J_1 = 15.9 Hz, J_2 = 1.4 Hz, 1H), 6.80 (dt, J_1 = 15.9 Hz, J_2 = 6.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.8, 13.9, 22.5, 23.4, 23.7, 24.0, 28.4, 28.8, 30.2, 31.3, 31.5, 32.7, 40.2, 42.1, 42.9, 43.8, 47.7, 79.7, 130.4, 146.6, 155.1, 200.8, 209.2 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{27}H_{47}NO_4$ (M^++H): 450.3505; found: 450.3498.

***N*-benzyloxycarbonyl-5-[(*E*)-5-oxohex-3-en-1-yl)]-2-(2-oxopropyl) piperidine (5d)**



(*trans*+*cis*)-**5d**

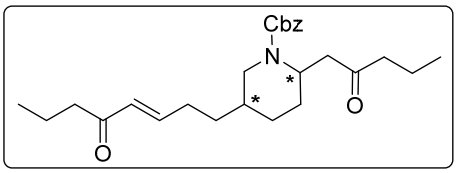
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,5-disubstituted piperidine **5d** (48 mg, 65% yield) was obtained from **3d** (0.2 mmol) as a non-separable 3:1 mixture of diastereoisomers, with 93:7 *er* and 99:1 *er* for the major diastereoisomer (*trans*-**5d**) and minor diastereoisomer (*cis*-**5d**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5d** (19 mg, 25% yield) was obtained from **3d** (0.2 mmol) as a non-separable 5:1 mixture of diastereoisomers, with 98:2 *er* and 56:44 *er* for the major diastereoisomer (*trans*-**5d**) and minor diastereoisomer (*cis*-**5d**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 75:25); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5d**): t_{major}= 12.0 min, t_{minor}= 14.8 min; minor diastereoisomer (*cis*-**5d**): t_{major}= 18.1 min, t_{minor}= 24.1 min.

Data for the mixture of diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.34-1.41 (m, 3H), 1.55-1.82 (m, 4H), 2.05-2.12 (m, 3H), 2.16-2.21 (m, 5H), 2.62-2.76 (m, 2H), 3.07 (dd, J_1 = 13.9 Hz, J_2 = 3.2 Hz, 1H), 3.82 (d, J = 13.8 Hz, 0.7H), 3.96-4.14 (m, 0.3H), 4.65-4.71 (m, 0.7H), 4.78-4.86 (m, 0.3H), 5.03-5.17 (m, 2H), 5.97-6.08 (m, 1H), 6.65-6.74 (m, 1H), 7.31-7.34 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 23.7, 23.8, 25.5, 26.8, 26.9, 28.6, 29.3, 30.0, 30.2, 32.6, 42.6, 44.0, 44.6, 44.7, 47.0, 48.0, 67.1, 127.9, 128.0, 128.4, 131.3, 136.6, 147.4, 147.7, 155.1, 155.6, 198.5, 206.7 ppm. HRMS (EI$^+$) (*m/z*): calcd. for $C_{22}H_{29}NO_4$ (M^++H): 372.2169; found: 372.2171.

***N*-benzyloxycarbonyl-5-[(*E*)-5-oxooct-3-en-1-yl)]-2-(2-oxopentyl) piperidine (5e)**



(*trans*+*cis*)-**5e**

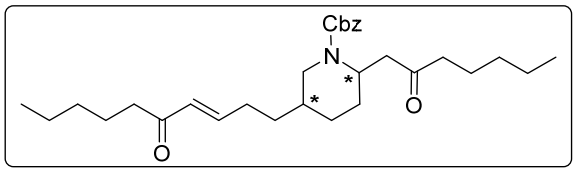
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,5-disubstituted piperidine **5e** (59 mg, 69% yield) was obtained from **3e** (0.2 mmol) as a non-separable 1.5:1 mixture of diastereoisomers, with 94:6 *er* and >99:1 *er* for the major diastereoisomer (*trans*-**5e**) and minor diastereoisomer (*cis*-**5e**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5e** (30 mg, 35% yield) was obtained from **3e** (0.2 mmol) as a non-separable 3:1 mixture of diastereoisomers, with 99:1 *er* and 56:44 *er* for the major diastereoisomer (*trans*-**5e**) and minor diastereoisomer (*cis*-**5e**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 92:8); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5e**): t_{major}= 19.2 min, t_{minor}= 26.8 min; minor diastereoisomer (*cis*-**5e**): t_{major}= 31.5 min, t_{minor}= 45.2 min.

Data for the mixture of diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.83-0.95 (m, 6H), 1.34-1.41 (m, 3H), 1.50-1.65 (m, 6.5H), 1.74-1.84 (m, 1.5H), 2.10-2.23 (m, 2H), 2.34-2.39 (m, 2H), 2.45-2.49 (m, 2H), 2.61-2.68 (m, 2H), 3.07 (dd, J_1 = 13.9 Hz, J_2 = 3.2 Hz, 1H), 3.82 (d, J = 13.8 Hz, 0.8H), 3.96-4.13 (m, 0.2H), 4.63-4.70 (m, 0.8H), 4.78 (br s, 0.2H), 5.03-5.16 (m, 2H), 6.00-6.10 (m, 1H), 6.68-6.79 (m, 1H), 7.30-7.34 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.6, 13.8, 17.0, 17.6, 23.7, 23.8, 25.5, 28.7, 29.3, 30.1, 32.6, 42.0, 42.1, 42.6, 43.0, 43.6, 44.8, 47.1, 48.1, 67.1, 127.8, 127.9, 128.0, 128.4, 130.4, 130.5, 136.6, 146.4, 155.6, 200.6, 208.8 ppm. HRMS (EI$^+$) (*m/z*): calcd. for $C_{26}H_{37}NO_4$ (M^++H): 428.2795; found: 428.2787.

***N*-benzyloxycarbonyl-5-[(*E*)-5-oxodec-3-en-1-yl)]-2-(2-oxoheptyl) piperidine (5f)**



(*trans*+*cis*)-**5f**

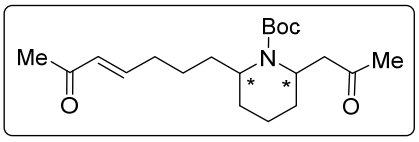
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,5-disubstituted piperidine **5f** (72 mg, 74% yield) was obtained from **3f** (0.2 mmol) as a non-separable 2:1 mixture of diastereoisomers, with 91:9 *er* and >99:1 *er* for the major diastereoisomer (*trans*-**5f**) and minor diastereoisomer (*cis*-**5f**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **5f** (29 mg, 30% yield) was obtained from **3f** (0.2 mmol) as a non-separable 1.8:1 mixture of diastereoisomers, with 98:2 *er* and 63:37 *er* for the major diastereoisomer (*trans*-**5f**) and minor diastereoisomer (*cis*-**5f**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 95:5); flow rate = 1.0 mL/min; major diastereoisomer (*trans*-**5f**): t_{major}= 28.1 min, t_{minor}= 44.8 min; minor diastereoisomer (*cis*-**5f**): t_{major}= 48.7 min, t_{minor}= 72.9 min.

Data for the mixture of diastereoisomers: ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.85-0.92 (m, 6H), 1.21-1.42 (m, 11.5H), 1.47-1.86 (m, 8.5H), 2.13-2.24 (m, 1.5H), 2.39 (t, J = 7.2 Hz, 2H), 2.49 (t, J = 7.3 Hz, 2H), 2.68 (d, J = 7.2 Hz, 1.5H), 3.08 (dd, J_1 = 13.9 Hz, J_2 = 3.2 Hz, 1H), 3.83 (d, J = 12.3 Hz, 0.7H), 3.98-4.15 (m, 0.3H), 4.64-4.70 (m, 0.7H), 4.80 (br s, 0.3H), 5.04-5.17 (m, 2H), 6.01-6.11 (m, 1H), 6.68-6.80 (m, 1H), 7.32-7.35 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 22.4, 22.5, 23.4, 23.7, 23.8, 23.9, 25.5, 28.8, 29.4, 30.2, 31.3, 31.5, 32.6, 40.2, 40.3, 42.7, 43.0, 43.6, 44.9, 47.1, 48.1, 67.1, 127.8, 128.0, 128.5, 130.5, 136.7, 146.4, 155.7, 200.8, 209.0 ppm. HRMS (EI^+) (*m/z*): calcd. for $C_{30}H_{45}NO_4$ (M^++H): 484.3421; found: 484.3430.

***N-tert*-butoxycarbonyl-6-[(*E*)-6-oxohept-4-en-1-yl)] 2-(2-oxopropyl) piperidine (6a)**



(*cis*+*trans*)-**6a**

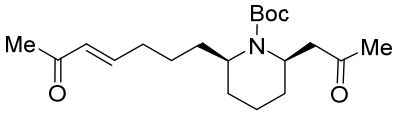
By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,6-disubstituted piperidine **6a** (56 mg, 80% yield) was obtained from **4a** (0.2 mmol) as a 2.4:1 mixture of diastereoisomers, with 88:12 *er* and 84:16 *er* for the major diastereoisomer (*cis*-**6a**) and minor diastereoisomer (*trans*-**6a**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **6a** (45 mg, 64% yield) was obtained from **4a** (0.2 mmol) as a 1.7:1 mixture of diastereoisomers, with 87:13 *er* and

57:43 *er* for the major diastereoisomer (*cis*-**6a**) and minor diastereoisomer (*trans*-**6a**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel AD column (hexane: 2-propanol, 97:3); flow rate = 1.0 mL/min; minor diastereoisomer (*trans*-**6a**): t_{major}= 11.2 min, t_{minor}= 12.4 min; major diastereoisomer (*cis*-**6a**): t_{major}= 15.5 min, t_{minor}= 17.7 min.

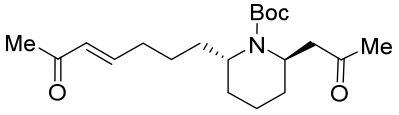
Data for major diastereoisomer:



(2*R*,6*R*)-**6a**

Piperidine (2*R*,6*R*)-**6a** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.43 (s, 9H), 1.46-1.56 (m, 10H), 2.16 (s, 3H), 2.20 (s, 3H), 2.22-2.28 (m, 2H), 2.49-2.69 (m, 2H), 4.07 (br s, 1H), 4.58-4.62 (m, 1H), 6.07 (dt, J_1 = 15.9 Hz, J_2 = 1.5 Hz, 1H), 6.78 (dt, J_1 = 15.9 Hz, J_2 = 6.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 25.8, 26.9, 27.2, 28.0, 28.4, 30.0, 32.2, 34.0, 46.1, 48.5, 49.7, 79.6, 131.4, 147.8, 155.0, 198.6, 206.8 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{20}H_{33}NO_4$ (M^++H): 352.2482; found: 352.2474.

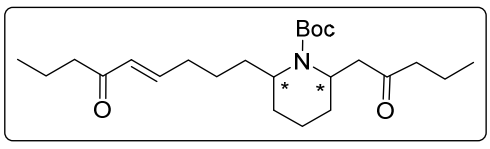
Data for minor diastereoisomer:



(2*R*,6*S*)-**6a**

Piperidine (2*R*,6*S*)-**6a** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 1.43 (s, 9H), 1.45-1.79 (m, 10H), 2.15 (s, 3H), 2.24 (s, 3H), 2.22-2.29 (m, 2H), 2.60 (dd, J_1 = 16.3 Hz, J_2 = 8.3 Hz, 1H), 3.03 (dd, J_1 = 16.4 Hz, J_2 = 5.3 Hz, 1H), 3.91 (br s, 1H), 4.04 (br s, 1H), 6.08 (d, J = 15.0 Hz, 1H), 6.81 (dt, J_1 = 15.0 Hz, J_2 = 6.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 15.9, 25.2, 26.6, 26.8, 28.5, 30.1, 30.9, 32.3, 32.5, 47.6, 48.3, 52.4, 79.4, 131.5, 148.2, 155.3, 198.7, 207.0 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{20}H_{33}NO_4$ (M^++H): 352.2482; found: 352.2466.

***N-tert*-butoxycarbonyl-6-[(*E*)-6-oxonon-4-en-1-yl)] 2-(2-oxopentyl) piperidine (6b)**



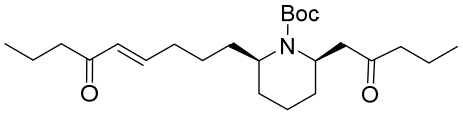
(*cis*+*trans*)-**6b**

By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,6-disubstituted piperidine **6b** (64 mg, 78% yield) was obtained from **4b** (0.2 mmol) as a 3.5:1 mixture of diastereoisomers, with 76:24 *er* and 94:6 *er* for the major diastereoisomer (*cis*-**6b**) and minor diastereoisomer (*trans*-**6b**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **6b** (49 mg, 60% yield) was obtained from **4b** (0.2 mmol) as a 1.6:1 mixture of diastereoisomers, with 90:10 *er* and 59:41 *er* for the major diastereoisomer (*cis*-**6b**) and minor diastereoisomer (*trans*-**6b**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 99:1); flow rate = 1.0 mL/min; minor diastereoisomer (*trans*-**6b**): t_{minor}= 21.3 min, t_{major}=24.0 min; major diastereoisomer (*cis*-**6b**): t_{major}= 31.0 min, t_{minor}= 36.0 min.

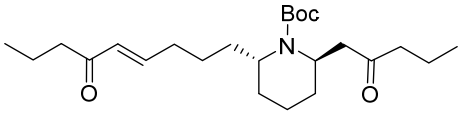
Data for major diastereoisomer:



(2*R*,6*R*)-**6b**

Piperidine (2*R*,6*R*)-**6b** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.89 (t, *J* = 7.4 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 1.43 (s, 9H), 1.45-1.65 (m, 14H), 2.20-2.26 (m, 2H), 2.45-2.50 (m, 1H), 2.41 (t, *J* = 7.4 Hz, 2H), 2.49 (t, *J* = 7.4 Hz, 2H), 2.59-2.67 (m, 1H), 4.07 (br s, 1H), 4.57-4.60 (m, 1H), 6.09 (dt, J_1 = 15.9 Hz, J_2 = 1.5 Hz, 1H), 6.80 (dt, J_1 = 15.9 Hz, J_2 = 6.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.6, 13.8, 13.9, 17.1, 17.7, 25.9, 27.2, 28.0, 28.4, 32.2, 34.0, 42.0, 44.7, 46.2, 47.5, 49.7, 79.5, 130.5, 146.5, 155.0, 200.6, 209.0 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{24}H_{41}NO_4$ (M^++H): 408.3108; found: 408.3100.

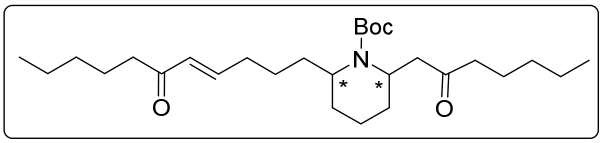
Data for minor diastereoisomer:



(2*R*,6*S*)-**6b**

Piperidine (2*R*,6*S*)-**6b** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.90 (t, *J* = 7.5 Hz, 3H), 0.93 (t, *J* = 7.5 Hz, 3H), 1.44 (s, 9H), 1.44-1.67 (m, 14H), 2.21-2.27 (m, 2H), 2.38-2.44 (m, 2H), 2.48-2.63 (m, 3H), 2.98 (dd, J_1 = 16.5 Hz, J_2 = 4.8 Hz, 1H), 3.90 (br s, 1H), 4.06 (br s, 1H), 6.10 (d, *J* = 15.9 Hz, 1H), 6.83 (dt, J_1 = 15.9 Hz, J_2 = 6.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.7, 13.8, 15.8, 17.2, 17.7, 25.3, 26.4, 28.5, 30.9, 32.2, 32.6, 42.0, 44.9, 47.3, 47.6, 52.4, 79.4, 130.5, 146.9, 155.3, 200.8, 209.3 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{24}H_{41}NO_4$ (M^++H): 408.3108; found: 408.3109.

***N-tert*-butoxycarbonyl-2-(2-oxoheptyl)-6-[(*E*)-6-oxoundec-4-en-1-yl)] piperidine (6c)**



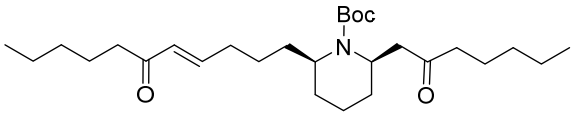
(*cis*+*trans*)-**6c**

By means of the general procedure described above employing a 20:20 mol% ratio of catalyst **I**/ TFA, 2,6-disubstituted piperidine **6c** (70 mg, 75% yield) was obtained from **4c** (0.2 mmol) as a 3.2:1 mixture of diastereoisomers, with 83:17 *er* and 93:7 *er* for the major diastereoisomer (*cis*-**6c**) and minor diastereoisomer (*trans*-**6c**), respectively.

Employing a 20:10 mol% ratio of catalyst **I**/ TFA, piperidine **6c** (65 mg, 70% yield) was obtained from **4c** (0.2 mmol) as a 2:1 mixture of diastereoisomers, with 88:12 *er* and 61:39 *er* for the major diastereoisomer (*cis*-**6c**) and minor diastereoisomer (*trans*-**6c**), respectively.

The *er* values were determined by HPLC analysis using a Chiracel OD-H column (hexane: 2-propanol, 99:1); flow rate = 1.0 mL/min; minor diastereoisomer (*trans*-**6c**): t_{minor}= 17.6 min, t_{major}= 19.0 min; major diastereoisomer (*trans*-**6c**): t_{major}= 24.8 min, t_{minor}= 28.6 min.

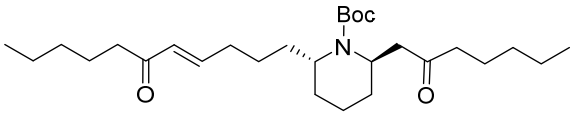
Data for major diastereoisomer:



(2*R*,6*R*)-**6c**

Piperidine (2*R*,6*R*)-**6c** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.03-0.07 (m. 4H), 0.84-0.89 (m, 6H), 1.24-1.31 (m, 8H), 1.43 (s, 9H), 1.43-1.64 (m, 10H), 2.20-2.27 (m, 2H), 2.39-2.52 (m, 5H), 2.59-2.68 (m, 1H), 4.08 (br s, 1H), 4.57-4.60 (m, 1H), 6.09 (dt, J_1 = 15.8 Hz, J_2 = 1.5 Hz, 1H), 6.80 (dt, J_1 = 15.8 Hz, J_2 = 6.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 1.0, 13.8, 13.9, 22.4, 23.4, 23.9, 25.9, 27.2, 28.0, 28.4, 29.6, 31.3, 31.5, 32.2, 34.1, 40.2, 42.8, 46.2, 47.4, 49.7, 79.6, 130.5, 146.5, 155.0, 200.8, 209.1 ppm. HRMS (EI$^+$) (*m/z)*: calcd. for $C_{28}H_{49}NO_4$ (M^++H): 464.3734; found: 464.3725.

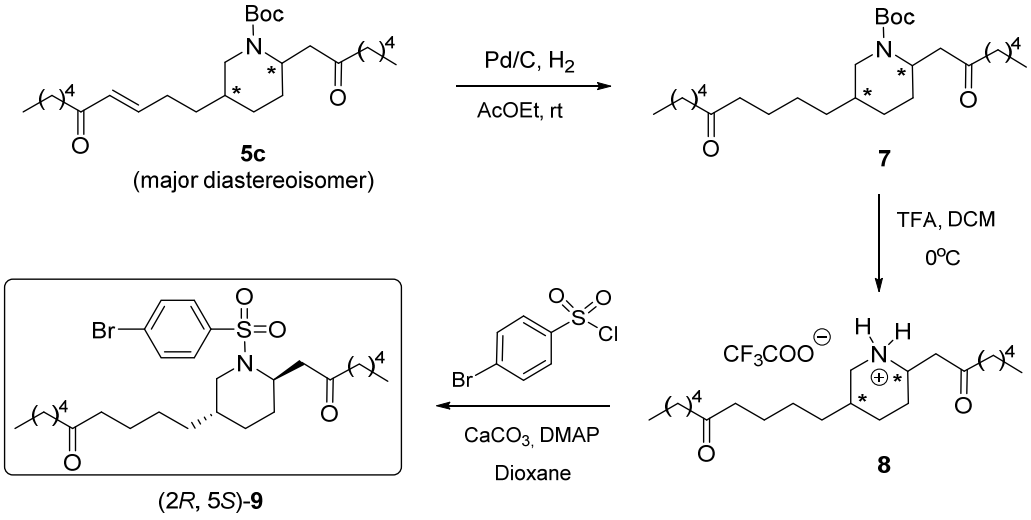
Data for minor diastereoisomer:



(2*R*,6*S*)-**6c**

Piperidine (2*R*,6*S*)-**6c** was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.85-0.91 (m, 6H), 1.26-1.31 (m, 8H), 1.44 (s, 9H), 1.46-1.65 (m, 14H), 2.21-2.27 (m, 2H), 2.39-2.45 (m, 2H), 2.48-2.64 (m, 3H), 2.98 (dd, J_1 = 16.1 Hz, J_2 = 4.8 Hz, 1H), 3.90 (br s, 1H), 4.06 (br s, 1H), 6.09 (d, J = 15.9 Hz, 1H), 6.82 (dt, J_1 = 15.8 Hz, J_2 = 6.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 15.8, 22.5, 23.4, 24.0, 25.3, 26.4, 28.5, 31.4, 31.5, 32.2, 32.6, 40.1, 43.0, 47.3, 47.6, 52.4, 79.4, 130.5, 147.0, 155.3, 201.0, 209.4 ppm. HRMS (EI$^+$) (*m/z)*: calcd. for $C_{28}H_{49}NO_4$ (M^++H): 464.3734; found: 464.3721.

SYNTHESIS OF 2,5-DISUBSTITUTED PIPERIDINE 9 FOR THE X-RAY ANALYSIS



Synthesis of (2*R*,5*S*)-1-[(4-bromophenyl)sulfonyl]-5-(5-oxodecyl)-2-(2-oxoheptyl)piperidine (9)

To a solution of 2,6-disubstituted piperidine **5c** (major diastereoisomer previously separated by semi-preparative chiral HPLC; 198 mg, 0.54 mmol) in EtOAc (5.5 mL) palladium on carbon (10% in Pd, 57.5 mg, 0.054 mmol) was added. A balloon filled with hydrogen was then connected and the resulting black suspension was stirred overnight at room temperature. The reaction mixture was filtered through a short pad of Celite®, washing with small portions of EtOAc and the filtrate was concentrated under reduced pressure. The crude product **7** (189 mg, 95% yield) was subsequently *N*-deprotected.

Trifluoroacetic acid (0.33 mL, 4.32 mmol) was dropwise added to a solution of piperidine **7** (189 mg, 0.54 mmol) in CH_2Cl_2 (5.5 mL) at 0°C. Upon disappearance of the starting material (30 min), the reaction mixture was basified with a saturated aqueous solution of K_2CO_3 and extracted with CH_2Cl_2 (3 x 5 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated under vacuum. To a solution of crude trifluoroacetate product **8** in dioxane (5.5 mL) $CaCO_3$ (162 mg, 1.62 mmol) and DMAP (10 mg, 0.081 mmol) were added. After stirring for 10 min, 4-bromobenzenesulfonyl chloride (690 mg, 2.7 mmol) was added and the mixture was stirred at room temperature overnight. Then, solvent was removed under reduced pressure, the residue was dissolved in CH_2Cl_2 (10 mL), water (10 mL was added) and the product was extracted into CH_2Cl_2 (3 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography with 2:1 *n*-hexanes: EtOAc as the eluent, affording piperidine **9** (215 mg, 82% yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ= 0.89 (t, J = 7.1 Hz, 6H), 1.14-1.38 (m 13H), 1.44-1.70 (m, 10H), 2.27-2.47 (m, 7H), 2.79 (dd, J_1 = 16.8 Hz, J_2 = 9.6 Hz, 1H), 3.09 (dd, J_1 = 13.21 Hz, J_2 = 3.0 Hz, 1H),

3.39 (t, J = 13.5 Hz, 1H), 4.38 (br s, 1H), 7.61-7.67 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ= 13.9, 13.9, 22.4, 22.5, 23.3, 23.4, 23.5, 23.6, 24.3, 26.9, 30.1, 31.3, 31.4, 32.8, 42.5, 42.7, 42.8, 43.4, 45.3, 49.4, 127.3, 128.6, 132.3, 139.6, 208.2, 211.4 ppm. HRMS (EI^+) (*m/z)*: calcd. for $C_{28}H_{44}BrNO_4S$ (M^++H): 570.2174; found: 570.2.

X-RAY STRUCTURE OF COMPOUND 9[4]

Crystal data for compound 9: $C_{28}H_{44}BrNO_4S$, M = 570.61, orthorhombic, a = 5.6897(3), b = 11.2486(5), c = 45.457(2), V = 2909.3(2) Å^3, space group $P2_12_12_1$, Z = 4, T = 120(2) K, λ = 0.71073 Å, Dcalcd = 1.303 gcm^{-3}, μ = 1.517 cm^{-1}, 18099 reflections measured, 7666 unique (R_{int} = 0.0405), colorless crystals obtained by *i*-PrOH evaporation, crystal structure solved dual-space methods with all non hydrogen atoms refined anisotropically on F^2 using the programs SHELXT[5] and SHELXL-2017/2,[6] methyl group hydrogen atoms were included as *rigid* and others using a *riding* model, absolute structure was determined with Flack x = 0.024(5),[7] GOF = 1.154, R (Fo, I > 2σ(I)) = 0.0663, Rw (Fo^2, all data) = 0.1170.

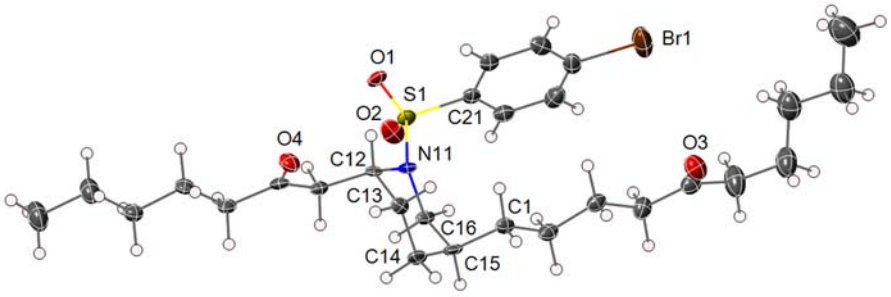


Figure S1. X-ray thermal ellipsoid plot for compound **9** (50% probability level). Torsion angle C(21)-S(1)···C(15)-C(1) 19.2(3)º.

[4] CCDC 1829500 contains the full supplementary crystallographic data for compound **9**. These data are provided free of charge by The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[5] G. M. Sheldrick, *Acta Cryst.*, 2015, **A71**, 3.
[6] G. M. Sheldrick, *Acta Cryst.*, 2015, **C71**, 3.
[7] S. Parsons, H. D. Flack, T. Wagner, *Acta Cryst.*, 2013, **B69**, 249.

STEREOCHEMICAL ASSIGNMENT OF 2,6-DISUBSTITUTED PIPERIDINES 6

The relative position of the substituents in piperidine **6a** (major diastereoisomer) was established by means of a NOESY experiment which showed an interaction between H_a at carbon 2 and H_b at carbon 6, indicating that both display a *cis* relationship. That interaction was not observed in the minor diastereoisomer.

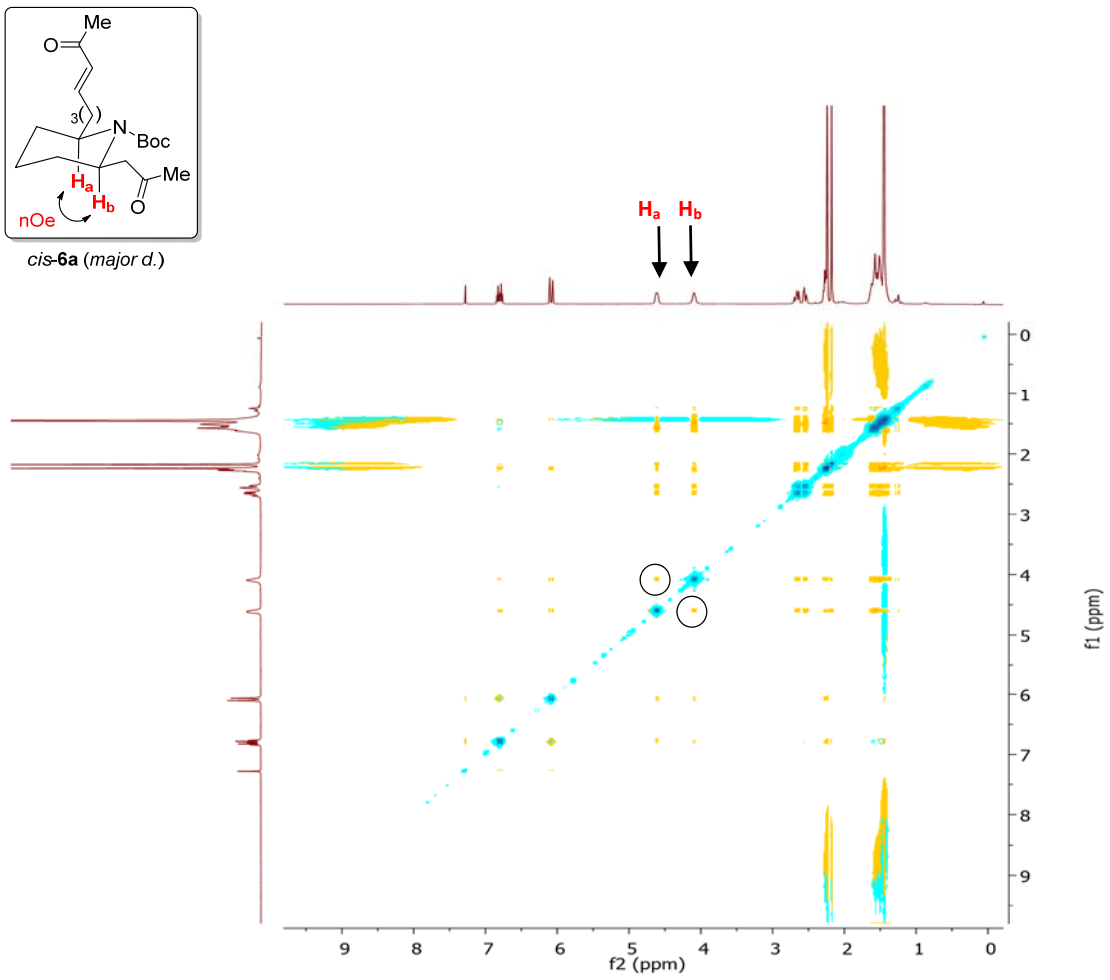


Figure S2. NOESY experiment on piperidine **6a** (major diastereoisomer)

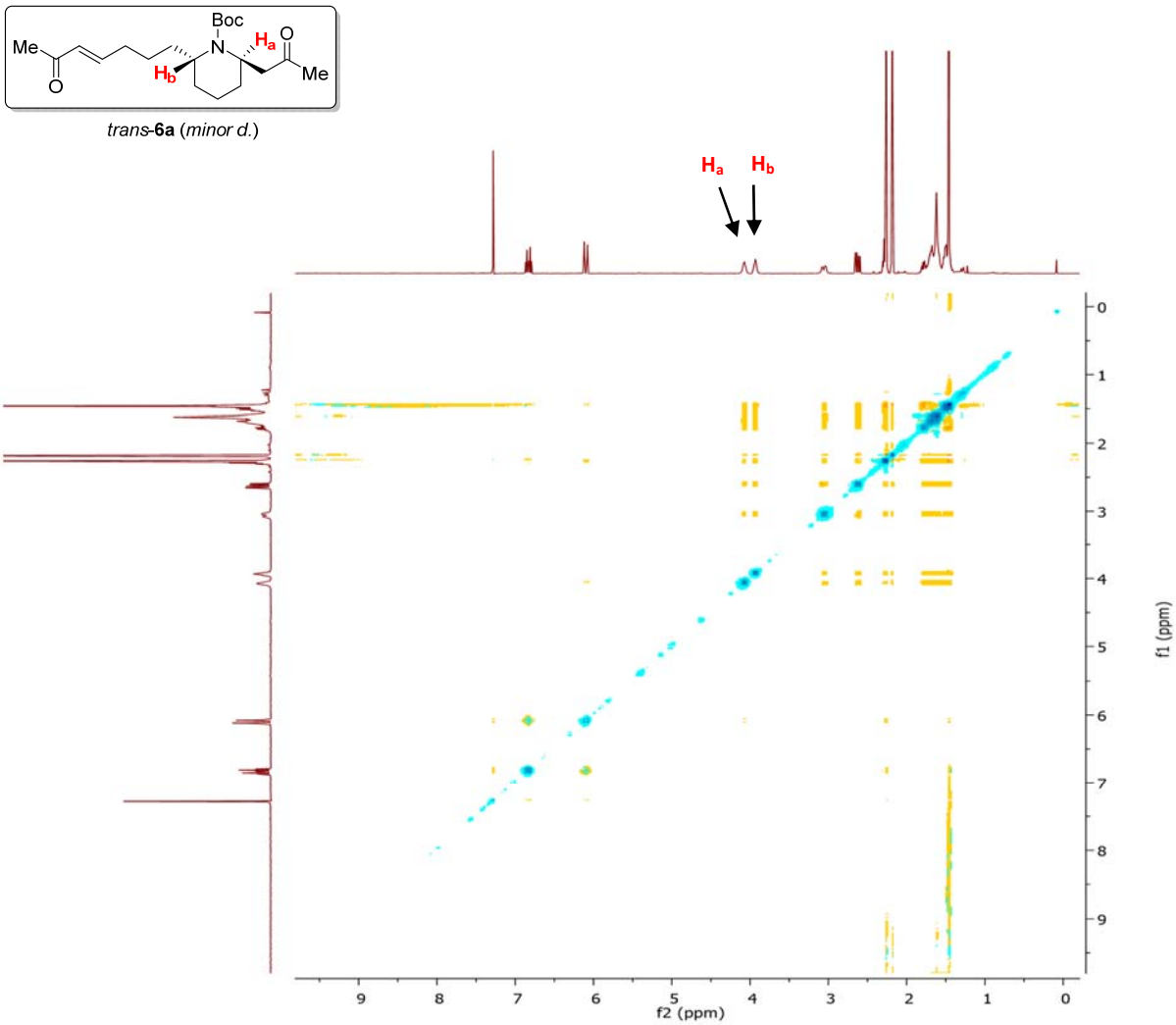


Figure S3. NOESY experiment on piperidine **6a** (minor diastereoisomer)

COMPUTATIONAL STUDY

All structures were initially optimized using density functional theory (DFT) with B3LYP[8] and the 6-31G(d,p) basis set as implemented in Gaussian 09.[9] Further optimizations were carried out at M06-2X/6-311+G(d,p) level of theory,[10] in a solvent model (IEFPCM, solvent=acetonitrile).[11] The stationary points were characterized by frequency calculations in order to verify that they have the right number of imaginary frequencies.

Cartesian Coordinates of the structures included in the Main Text:

TS1

G(M06-2x/6-311+G(d,p): -2217,042236 hartrees

Imaginary frequency: -252.6

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.316662	-1.295038	4.019988
2	6	0	-1.347252	2.100380	-2.215302
3	6	0	-1.322313	4.026086	1.800850
4	6	0	0.502306	1.570952	-3.763596
5	6	0	-0.695146	-0.056044	3.318892
6	7	0	-2.141842	1.030659	-0.224041
7	6	0	0.998615	3.183683	-0.826885
8	7	0	1.264496	1.839233	-1.141255
9	6	0	2.652153	1.478664	-1.542355
10	6	0	0.781169	5.292808	1.257587
11	6	0	-2.490410	-0.262115	1.786624
12	6	0	1.920847	1.024907	-3.900049

[8] (*a*) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B*, 1988, **37**, 785. (*b*) A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648. (*c*) W. Kohn, A. D. Becke, R. G. Parr, *J. Phys. Chem.*, 1996, **100**, 12974.

[9] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Menucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Jr. Montgomery, J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT, 2013.

[10] Y. Zhao, D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215.

[11] (*a*) E. Cancès, B. Mennucci, J. Tomasi, *J. Chem. Phys*., 1997, **107**, 3032. (*b*) M. Cossi, V. Barone, B. Mennuci, J. Tomasi, *Chem. Phys. Lett.* 1998, **286**, 253. (c) J. Tomasi, B. Mennucci, E. Cancès, *J. Mol. Struct. (Theochem)* 1999, **464**, 211.

13	7	0	-1.734513	0.704905	2.599549
14	6	0	-0.184747	1.336829	-2.442416
15	6	0	-3.681788	2.481385	-1.408451
16	6	0	-2.839670	-1.084307	4.090433
17	6	0	-3.191634	0.454373	0.618128
18	6	0	-2.332165	1.833953	-1.265694
19	6	0	-1.139219	5.245862	-0.389649
20	6	0	-0.383195	4.485034	0.693824
21	6	0	1.067063	-1.423206	-0.111939
22	6	0	0.756553	-2.670789	0.753967
23	6	0	-4.124107	-0.473412	-0.146864
24	6	0	-5.483097	-0.337160	-0.029904
25	6	0	-3.633206	-1.547886	-0.955009
26	6	0	-4.589450	-2.414547	-1.560711
27	6	0	-6.349838	-1.247585	-0.691074
28	6	0	-4.125430	-3.512796	-2.325716
29	6	0	-2.266013	-1.806284	-1.152737
30	6	0	-2.783082	-3.760541	-2.489601
31	6	0	-1.843099	-2.888115	-1.889801
32	6	0	0.055084	-4.191689	-2.529943
33	7	0	-5.937542	-2.248607	-1.425347
34	6	0	-2.613029	1.338233	3.593847
35	6	0	-3.099903	0.318256	4.656802
36	6	0	-3.422912	-1.119105	2.666993
37	1	0	2.222400	1.109275	-4.948620
38	1	0	-0.144627	0.317378	-2.051609
39	1	0	-0.240159	0.624738	4.047169
40	1	0	-1.794383	4.890793	2.274914
41	1	0	-0.149623	1.101943	-4.512173
42	1	0	-1.195598	0.708954	-0.009286
43	1	0	-3.660093	3.227721	-2.202191
44	1	0	-1.970945	4.641209	-0.761789
45	1	0	1.934518	-0.041952	-3.641951
46	1	0	0.496528	2.648457	-3.971558
47	1	0	-4.437103	1.729870	-1.657502
48	1	0	2.658827	0.390796	-1.417328
49	1	0	0.390788	6.169010	1.782628
50	1	0	-0.904249	-1.422050	5.026022
51	1	0	-1.530245	2.937348	-2.881622

52	1	0	-2.093348	3.363732	1.393113
53	1	0	-3.309417	-1.848810	4.715540
54	1	0	-3.987300	2.960815	-0.472450
55	1	0	-1.737635	-0.921535	1.346323
56	1	0	1.343864	4.685990	1.972740
57	1	0	-0.482535	5.504015	-1.220932
58	1	0	-0.769950	3.453501	2.549747
59	1	0	-1.084441	-2.204385	3.455001
60	1	0	-1.546962	6.166065	0.038524
61	1	0	1.450276	5.624542	0.462756
62	1	0	0.956291	1.180129	-0.401609
63	8	0	0.116123	3.218230	0.166055
64	8	0	1.472521	4.120479	-1.425569
65	8	0	1.935791	-1.549935	-0.972008
66	9	0	1.318705	-2.526823	1.969332
67	9	0	-0.563141	-2.840314	0.963718
68	8	0	0.401848	-0.398289	0.231530
69	9	0	1.223923	-3.800128	0.222020
70	1	0	-5.907890	0.463747	0.570464
71	1	0	-4.874813	-4.158279	-2.771110
72	1	0	-1.493936	-1.199047	-0.705892
73	1	0	-2.453458	-4.614071	-3.071138
74	1	0	-3.804015	1.270059	1.027360
75	8	0	-0.498334	-3.012226	-1.984337
76	1	0	-0.297493	-5.078471	-1.990795
77	1	0	-0.185148	-4.288903	-3.595300
78	1	0	1.131265	-4.088012	-2.398551
79	1	0	-7.426873	-1.124776	-0.591736
80	1	0	-3.464215	1.788011	3.069365
81	1	0	-2.064121	2.163778	4.058698
82	1	0	-4.164555	0.459481	4.871196
83	1	0	-2.557582	0.446627	5.600245
84	1	0	0.073227	-0.349085	2.600165
85	1	0	-4.447587	-0.722066	2.675637
86	1	0	-3.475283	-2.138935	2.272047
87	6	0	2.908871	1.776755	-3.012654
88	1	0	2.849491	2.856261	-3.194208
89	6	0	3.681748	2.108736	-0.594016
90	1	0	3.883770	3.136933	-0.913199

91	1	0	3.250189	2.167642	0.414907
92	6	0	4.980691	1.301160	-0.518194
93	1	0	5.345178	1.079447	-1.529900
94	1	0	5.757961	1.907726	-0.041087
95	6	0	4.825207	-0.008988	0.271547
96	1	0	4.521652	0.221107	1.299526
97	1	0	4.031130	-0.626178	-0.170231
98	6	0	6.100851	-0.791953	0.286337
99	1	0	6.450965	-1.146865	-0.684184
100	6	0	6.824926	-1.053704	1.377688
101	1	0	6.502874	-0.710029	2.358474
102	6	0	8.100793	-1.813065	1.383026
103	6	0	8.629524	-2.368953	0.074785
104	1	0	7.907477	-3.060214	-0.369271
105	1	0	8.804328	-1.564204	-0.645193
106	1	0	9.564269	-2.891246	0.274060
107	8	0	8.703754	-1.980777	2.424486
108	1	0	3.930914	1.459582	-3.245969

TS2

G(M06-2x/6-311+G(d,p): -2217, 037451 hartrees

Imaginary frequency: -253.5

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	5.367864	-4.066909	-0.682176
2	6	0	4.027462	-4.759306	-0.411845
3	6	0	3.337610	-5.006290	-1.764113
4	6	0	5.037421	-2.648683	-1.211810
5	6	0	3.352403	-3.668468	-2.553256
6	7	0	3.636561	-2.539483	-1.654794
7	6	0	3.159230	-3.802175	0.424089
8	6	0	2.714494	-2.646100	-0.506313
9	6	0	-2.112084	1.321143	-2.113387
10	6	0	0.194733	5.371246	0.149917
11	6	0	1.040261	-0.227404	3.537045
12	6	0	4.017609	3.805040	3.944481

13	6	0	2.118304	1.782904	4.382377
14	6	0	1.916259	-0.231474	2.414849
15	6	0	-0.058646	-2.093278	2.825427
16	6	0	2.135852	3.962295	0.889296
17	7	0	-0.724301	1.640340	-1.690889
18	6	0	-1.465654	1.125326	-4.554909
19	6	0	0.551471	0.838840	-3.009296
20	6	0	2.044385	4.774009	-1.481711
21	6	0	0.761760	-2.193386	1.670038
22	6	0	1.867660	1.143952	-2.635371
23	7	0	0.066673	-1.161034	3.732946
24	6	0	1.749569	-1.272016	1.446667
25	6	0	1.171474	0.796832	4.504590
26	6	0	2.885822	0.787368	2.309740
27	6	0	0.006588	1.437683	-4.281805
28	6	0	1.226402	4.330835	-0.273558
29	6	0	2.578292	-1.270928	0.170712
30	6	0	4.021566	0.779511	-1.439914
31	6	0	-2.412468	1.764616	-3.540312
32	6	0	2.554958	0.498283	-1.604274
33	6	0	2.990220	1.772978	3.266209
34	6	0	-0.340662	2.985770	-1.543287
35	7	0	1.950184	-0.342385	-0.771509
36	6	0	-1.321657	-1.136334	-0.131567
37	1	0	-2.110606	0.223832	-2.103875
38	1	0	5.944843	-4.637996	-1.418056
39	1	0	5.968297	-4.010229	0.231312
40	1	0	3.582559	-0.906885	0.404072
41	1	0	4.177228	-5.701750	0.122065
42	1	0	2.310358	-5.350800	-1.600453
43	1	0	3.857780	-5.793069	-2.319476
44	1	0	5.679007	-2.378219	-2.057530
45	1	0	5.213920	-1.900519	-0.431243
46	1	0	2.393041	-3.486163	-3.046658
47	1	0	4.125330	-3.677145	-3.329374
48	1	0	2.293192	-4.325890	0.836238
49	1	0	3.734372	-3.419401	1.278445
50	1	0	1.726858	-2.873752	-0.930767
51	1	0	4.313619	1.616285	-2.074143

52	1	0	4.285375	1.021680	-0.407562
53	1	0	-0.544637	1.114282	-0.817043
54	1	0	-0.849841	-2.824479	2.975910
55	1	0	4.585172	-0.106003	-1.744749
56	1	0	3.573904	0.832954	1.475384
57	1	0	0.958659	-0.585667	-0.934621
58	1	0	2.618338	5.667684	-1.221189
59	1	0	-0.441407	5.663025	-0.685425
60	1	0	-1.605273	0.036299	-4.550113
61	1	0	2.828212	3.167486	0.598760
62	1	0	0.174802	2.521769	-4.269294
63	1	0	2.716745	4.835068	1.200963
64	1	0	-2.366979	2.854670	-3.606534
65	1	0	4.268573	3.483334	4.961845
66	1	0	0.545255	-2.974098	0.950336
67	1	0	3.071266	4.359845	3.963067
68	1	0	0.157592	-0.145262	-2.743705
69	1	0	0.715582	6.256237	0.526477
70	1	0	0.488730	0.772745	5.346998
71	1	0	1.545582	3.601339	1.736766
72	1	0	0.624666	1.031744	-5.092487
73	1	0	2.383189	1.942066	-3.158995
74	1	0	-0.428077	4.970945	0.954962
75	1	0	1.401625	5.003566	-2.332465
76	1	0	-1.720396	1.471399	-5.561265
77	1	0	4.808392	4.454323	3.569149
78	1	0	2.745370	3.981544	-1.760573
79	1	0	2.192932	2.554395	5.139179
80	8	0	-0.733683	3.887265	-2.247996
81	8	0	3.953295	2.711663	3.054209
82	8	0	0.564364	3.062501	-0.573148
83	8	0	-1.340548	-0.046776	0.459015
84	8	0	-0.582544	-1.520806	-1.070660
85	6	0	-2.374410	-2.186005	0.307904
86	9	0	-1.803887	-3.364989	0.610790
87	9	0	-3.081111	-1.796148	1.372987
88	9	0	-3.250174	-2.419398	-0.688656
89	6	0	-3.123781	1.811459	-1.067001
90	1	0	-3.484448	2.811873	-1.334334

91	1	0	-2.603539	1.891161	-0.107508
92	6	0	-4.284005	0.824509	-0.891315
93	1	0	-5.079331	1.006632	-1.623255
94	1	0	-3.917919	-0.192138	-1.077569
95	6	0	-4.863100	0.851097	0.529441
96	1	0	-4.027365	0.687587	1.222857
97	1	0	-5.308095	1.827156	0.753064
98	6	0	-5.866848	-0.241773	0.720574
99	6	0	-7.160811	-0.063230	0.998568
100	1	0	-5.474445	-1.251933	0.597517
101	1	0	-7.578812	0.933631	1.123529
102	6	0	-8.140884	-1.165369	1.165767
103	8	0	-9.305732	-0.914382	1.406675
104	6	0	-7.660250	-2.597341	1.030719
105	1	0	-7.234467	-2.769746	0.037997
106	1	0	-6.878852	-2.812431	1.765234
107	1	0	-8.507443	-3.263532	1.188078
108	1	0	-3.443387	1.462232	-3.758210

TS3

G(M06-2x/6-311+G(d,p): -2217,037286 hartrees

Imaginary frequency: -213.2

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	1	0	2.855991	-2.755671	4.727740
2	1	0	4.212004	-2.927368	3.610140
3	1	0	2.892348	-1.867177	0.016594
4	1	0	4.301915	-0.632392	4.509036
5	1	0	2.224046	0.855017	4.164238
6	1	0	1.997766	-0.427691	5.352409
7	1	0	1.537975	-3.432458	2.882171
8	1	0	2.821590	-3.059316	1.739099
9	1	0	0.298276	-0.051543	3.134881
10	1	0	0.466584	-1.590785	3.981173
11	1	0	4.185555	0.615473	2.391368

12	1	0	4.583279	-1.049259	1.957350
13	1	0	2.005034	0.489121	1.645852
14	1	0	0.215997	-3.598043	-1.313066
15	1	0	-2.857766	-1.140383	-0.324078
16	1	0	1.931114	-3.165344	-1.354753
17	1	0	-1.685855	0.838473	0.064965
18	1	0	4.716528	3.177279	-1.218527
19	1	0	1.054115	-3.152953	0.192613
20	1	0	4.468083	-2.745116	-0.615003
21	1	0	1.075119	0.408707	-0.569500
22	1	0	-2.253576	5.687782	-2.891795
23	1	0	-3.498211	4.574294	-0.175104
24	1	0	-2.979103	-1.865829	-2.959148
25	1	0	0.307898	4.207947	-2.150760
26	1	0	-2.430023	1.119783	-3.422795
27	1	0	-0.167963	5.789577	-1.488744
28	1	0	-4.767176	0.452915	-2.086563
29	1	0	8.499054	-4.197886	-1.500089
30	1	0	2.867589	1.893376	-0.171503
31	1	0	7.715946	-4.351723	-3.099875
32	1	0	-0.425046	0.886940	-2.060000
33	1	0	-2.415645	5.980413	-0.247424
34	1	0	7.855267	0.269605	-2.611598
35	1	0	0.227897	4.434128	-0.398700
36	1	0	-1.586897	-0.207990	-4.206940
37	1	0	-1.168375	-2.108272	-2.053632
38	1	0	-1.973029	4.584177	0.753157
39	1	0	-3.401711	4.341357	-2.719477
40	1	0	-3.933329	-0.803548	-3.963333
41	1	0	7.486349	-5.617662	-1.867066
42	1	0	-1.825289	4.084354	-3.507788
43	1	0	8.218433	-2.178181	-2.581839
44	6	0	3.265710	-2.401934	3.775107
45	6	0	3.484068	-0.884626	3.828439
46	6	0	2.168673	-0.231832	4.289043
47	6	0	2.278895	-2.672888	2.610905
48	6	0	1.017140	-0.821156	3.429144
49	7	0	1.555765	-1.454105	2.210231
50	6	0	3.805647	-0.410355	2.399995

51	6	0	2.486880	-0.490935	1.596657
52	8	0	-3.853447	2.453181	-1.354503
53	8	0	6.433693	-3.945654	-1.511782
54	8	0	-1.623847	2.837410	-1.181260
55	6	0	-3.407366	-0.217109	-0.559068
56	6	0	-2.453479	4.889565	-0.180902
57	6	0	5.952281	0.189435	-1.637881
58	6	0	7.602846	-4.546227	-2.026890
59	6	0	7.313647	-1.757380	-2.160679
60	6	0	4.953625	-0.651665	-1.063380
61	6	0	4.781276	2.091750	-1.176025
62	6	0	-0.238343	4.707874	-1.346297
63	7	0	-2.344440	0.782663	-0.754458
64	6	0	-3.314556	-0.828132	-3.061090
65	6	0	-1.075685	0.017882	-2.170070
66	6	0	-2.347080	4.614262	-2.704744
67	6	0	3.723883	1.360757	-0.578929
68	6	0	-0.604368	-1.230897	-1.764409
69	7	0	5.853624	1.547505	-1.692952
70	6	0	3.791010	-0.009185	-0.528411
71	6	0	7.118540	-0.400341	-2.181468
72	6	0	5.176821	-2.048754	-1.048668
73	6	0	-2.100005	0.084197	-3.282392
74	6	0	-1.702034	4.286292	-1.362119
75	6	0	2.664727	-0.808514	0.104105
76	6	0	0.970797	-2.945234	-0.878357
77	6	0	-4.187871	-0.445740	-1.858964
78	6	0	0.590261	-1.501346	-1.068604
79	6	0	6.325542	-2.592381	-1.582050
80	6	0	-2.723020	2.094212	-1.108708
81	7	0	1.403570	-0.570731	-0.604181
82	9	0	0.213572	2.486378	3.530685
83	9	0	1.993737	2.810197	2.353225
84	8	0	-0.937086	1.311955	1.467090
85	8	0	0.753843	1.992494	0.131956
86	9	0	0.292848	4.132186	2.127891
87	6	0	0.649871	2.850267	2.322880
88	6	0	0.092012	1.953979	1.190124
89	6	0	-4.269810	0.135524	0.660741

90	1	0	-4.769823	1.092616	0.476216
91	1	0	-3.584667	0.289113	1.501626
92	6	0	-5.307658	-0.944779	1.002162
93	1	0	-4.972559	-1.921015	0.626563
94	1	0	-5.388901	-1.053397	2.089163
95	6	0	-6.704599	-0.636491	0.439050
96	1	0	-7.081376	0.269120	0.932086
97	1	0	-6.647245	-0.410251	-0.630270
98	6	0	-7.658879	-1.767316	0.665912
99	6	0	-8.236344	-2.476310	-0.307692
100	1	0	-7.854766	-2.028553	1.707113
101	1	0	-8.053500	-2.241052	-1.354539
102	6	0	-9.156933	-3.622369	-0.091307
103	8	0	-9.618046	-4.216216	-1.045314
104	6	0	-9.502576	-4.028685	1.327687
105	1	0	-8.600818	-4.306502	1.881010
106	1	0	-9.976971	-3.199837	1.860982
107	1	0	-10.183774	-4.877521	1.288441
108	1	0	-4.901564	-1.258880	-1.685338

TS4

G(M06-2x/6-311+G(d,p): -2217, 038416 hartrees

Imaginary frequency: -223.4

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-3.086057	2.836494	-0.260007
2	6	0	1.952805	-4.848282	0.057830
3	6	0	1.963136	-1.886344	3.506545
4	6	0	3.122380	-0.906584	3.748042
5	6	0	-0.710677	-2.557584	-2.537077
6	6	0	-3.947308	-2.970909	-0.210049
7	6	0	-5.611859	-1.318476	-1.066733
8	6	0	-5.013061	-1.504301	1.338114
9	6	0	0.934283	-1.376664	2.520673
10	6	0	3.987623	-0.608077	2.513173

11	7	0	-3.746302	-1.789616	0.649188
12	6	0	-4.164766	3.074022	0.624308
13	6	0	3.195915	-0.276209	1.240392
14	6	0	-0.205411	-2.025234	-1.175137
15	6	0	0.411013	-0.095393	2.713280
16	6	0	0.540947	-5.417640	-0.000068
17	7	0	-1.472497	-0.142891	1.200833
18	6	0	-6.557259	5.622344	1.556071
19	6	0	-4.826344	4.283395	0.629212
20	7	0	2.235489	-1.353034	0.948602
21	6	0	-1.013122	2.624329	-2.056858
22	6	0	-1.107167	1.866683	2.507312
23	6	0	-4.598513	-0.162125	-1.030295
24	6	0	2.802236	-5.619757	1.063458
25	6	0	-4.870405	-2.622288	-1.408520
26	6	0	-3.393799	5.106711	-1.122707
27	6	0	-6.203712	-1.458813	0.343022
28	6	0	-2.692307	3.876887	-1.151569
29	6	0	2.581966	-4.796813	-1.329923
30	6	0	2.754921	-2.643302	0.689990
31	6	0	-0.726111	0.466847	2.104756
32	6	0	-2.335768	1.618542	-0.309103
33	6	0	-4.436358	5.318146	-0.257766
34	6	0	-2.669326	0.432903	0.581457
35	6	0	-3.378277	-0.666209	-0.224503
36	6	0	-1.302722	1.526724	-1.207975
37	7	0	-1.666543	3.759333	-2.041101
38	1	0	-0.085471	-4.847938	-0.688514
39	1	0	-0.689601	0.630460	-1.271699
40	1	0	-2.641950	-1.058845	-0.932253
41	1	0	-5.059830	0.717946	-0.562313
42	1	0	2.348014	-2.854519	3.167712
43	1	0	2.557285	0.595973	1.442579
44	1	0	-5.903757	6.461303	1.822442
45	1	0	-0.875976	2.560762	1.693008
46	1	0	0.583364	-6.459825	-0.327661
47	1	0	0.076836	-5.377181	0.989168
48	1	0	-4.916689	-0.550006	1.868529
49	1	0	4.641375	-1.457236	2.299750

50	1	0	-0.556506	2.169188	3.396554
51	1	0	0.329053	-2.126728	2.009214
52	1	0	-0.198213	2.538982	-2.772920
53	1	0	-5.161286	-2.271749	2.103819
54	1	0	-4.521174	2.318470	1.315494
55	1	0	-6.397877	-1.114091	-1.799144
56	1	0	3.766076	-1.322740	4.529330
57	9	0	0.279135	-2.734385	-3.415587
58	1	0	1.973363	-4.174936	-1.993386
59	1	0	-4.277558	-2.488203	-2.321232
60	1	0	-6.868040	-0.618157	0.569522
61	1	0	-3.340888	0.751612	1.383265
62	1	0	-7.319277	5.502412	2.325152
63	1	0	-3.070382	5.876205	-1.815550
64	9	0	-1.367155	-3.720007	-2.424472
65	1	0	-4.953376	6.269870	-0.260115
66	1	0	1.442602	-2.072577	4.454078
67	1	0	1.552776	-1.122516	0.182298
68	1	0	-4.287033	0.134161	-2.036912
69	1	0	-5.585107	-3.429141	-1.600193
70	1	0	2.624587	-5.807048	-1.746041
71	1	0	2.357649	-5.543284	2.060810
72	1	0	-6.802611	-2.374369	0.406171
73	1	0	3.594638	-4.392532	-1.288137
74	9	0	-1.574295	-1.665797	-3.066345
75	1	0	-7.043019	5.832749	0.596072
76	1	0	2.727930	0.029219	4.157743
77	1	0	3.825071	-5.245896	1.096197
78	1	0	-1.224980	-1.095370	0.882075
79	1	0	0.918866	0.562975	3.406752
80	1	0	-2.968044	-3.321630	-0.539692
81	1	0	2.815793	-6.675982	0.779819
82	1	0	-4.393368	-3.752355	0.414793
83	1	0	-2.177900	1.956145	2.708453
84	8	0	-5.845696	4.403140	1.518982
85	8	0	3.930809	-2.929509	0.670915
86	8	0	1.736200	-3.478334	0.526084
87	8	0	0.704881	-1.171866	-1.261034
88	8	0	-0.810829	-2.448369	-0.173781

89	1	0	4.634922	0.244088	2.744039
90	6	0	4.068142	0.046544	0.023396
91	1	0	4.759982	-0.783433	-0.152609
92	1	0	3.409506	0.107681	-0.853319
93	6	0	4.839247	1.356765	0.167397
94	1	0	5.566881	1.288387	0.984154
95	1	0	4.146777	2.168934	0.429492
96	6	0	5.585249	1.723997	-1.122149
97	1	0	6.279458	0.920325	-1.391178
98	1	0	4.855495	1.806650	-1.938623
99	6	0	6.329072	3.016672	-0.987545
100	6	0	7.653057	3.150099	-1.098985
101	1	0	5.720760	3.893135	-0.758174
102	1	0	8.285834	2.293758	-1.323115
103	6	0	8.391029	4.429938	-0.937443
104	8	0	9.600047	4.449523	-1.052029
105	6	0	7.612306	5.693634	-0.628502
106	1	0	6.887943	5.904570	-1.420471
107	1	0	7.058104	5.585740	0.308432
108	1	0	8.315489	6.521029	-0.544853

TS5

G(M06-2x/6-311+G(d,p): -2217, 042802 hartrees

Imaginary frequency: -302.1

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.295595	1.146449	-2.521559
2	6	0	-3.173096	0.203858	3.919038
3	6	0	-1.373266	4.332082	0.245979
4	6	0	1.772796	-0.148902	-2.941344
5	6	0	-2.088900	1.064087	3.215483
6	7	0	-1.933873	1.000083	-0.776408
7	6	0	1.577795	2.525621	-0.759933
8	7	0	1.695591	1.133859	-0.540851
9	6	0	3.083602	0.669895	-0.281356

10	6	0	0.976272	5.205462	0.402889
11	6	0	-3.223408	0.505013	1.209925
12	6	0	2.992144	-0.800387	-2.299920
13	7	0	-2.610254	1.619610	1.951647
14	6	0	0.686808	0.275119	-1.987469
15	6	0	-2.626520	1.955330	-2.896929
16	6	0	-4.536185	0.568563	3.305521
17	6	0	-3.304240	0.832241	-0.294074
18	6	0	-1.575884	1.337000	-2.015918
19	6	0	-0.067730	4.759467	-1.860149
20	6	0	0.006855	4.340685	-0.395873
21	6	0	0.522499	-1.392817	1.204253
22	6	0	-0.216784	-2.304736	2.214689
23	6	0	-4.080080	-0.231256	-1.056712
24	6	0	-5.340129	0.035060	-1.526587
25	6	0	-3.560970	-1.549716	-1.261946
26	6	0	-4.397307	-2.496374	-1.922893
27	6	0	-6.085496	-0.980214	-2.182097
28	6	0	-3.919493	-3.817120	-2.106907
29	6	0	-2.287479	-1.958858	-0.828149
30	6	0	-2.676039	-4.200644	-1.664135
31	6	0	-1.851262	-3.250299	-1.015285
32	6	0	-0.122284	-4.823041	-0.520628
33	7	0	-5.649039	-2.197788	-2.377675
34	6	0	-3.621019	2.635776	2.278501
35	6	0	-4.661707	2.098261	3.295901
36	6	0	-4.571528	0.095858	1.841730
37	1	0	3.603751	-1.253338	-3.088370
38	1	0	0.357108	-0.503879	-1.297832
39	1	0	-1.788722	1.911268	3.842328
40	1	0	-1.770973	5.349465	0.290787
41	1	0	1.287759	-0.856100	-3.626294
42	1	0	-1.209572	0.745657	-0.100787
43	1	0	-2.173644	2.349710	-3.806463
44	1	0	-0.731520	4.085684	-2.409670
45	1	0	2.672079	-1.602879	-1.621977
46	1	0	2.076273	0.716393	-3.544308
47	1	0	-3.372133	1.205724	-3.177996
48	1	0	2.984627	-0.174632	0.404952

49	1	0	0.610789	6.235908	0.417964
50	1	0	-3.179540	0.388905	4.997981
51	1	0	-0.058983	1.648769	-3.454188
52	1	0	-2.056679	3.701667	-0.331976
53	1	0	-5.353120	0.115018	3.873749
54	1	0	-3.150619	2.764640	-2.377619
55	1	0	3.616666	1.488694	0.210328
56	1	0	-2.526009	-0.331446	1.315155
57	1	0	1.034193	4.846015	1.433936
58	1	0	0.917437	4.749908	-2.327331
59	1	0	-1.316419	3.908980	1.251237
60	1	0	-2.964867	-0.861835	3.771774
61	1	0	-0.478313	5.771562	-1.918756
62	1	0	1.972333	5.192844	-0.041303
63	1	0	1.054189	0.785116	0.208898
64	8	0	0.411428	2.939566	-0.286599
65	8	0	2.425080	3.176836	-1.321617
66	8	0	1.545929	-1.829584	0.685483
67	9	0	-0.074329	-1.816490	3.460407
68	9	0	-1.541431	-2.355646	1.974730
69	8	0	-0.028756	-0.255128	1.071257
70	9	0	0.240368	-3.556908	2.215560
71	1	0	-5.778166	1.022166	-1.400852
72	1	0	-4.579279	-4.516998	-2.608473
73	1	0	-1.619833	-1.291681	-0.304073
74	1	0	-2.334293	-5.218958	-1.810825
75	1	0	-3.846232	1.782181	-0.411656
76	8	0	-0.605636	-3.496889	-0.548295
77	1	0	-0.785258	-5.472634	0.062502
78	1	0	-0.009043	-5.228161	-1.533128
79	1	0	0.849822	-4.761015	-0.033754
80	1	0	-7.084297	-0.753754	-2.551025
81	1	0	-4.109933	2.951532	1.349482
82	1	0	-3.103901	3.517872	2.670884
83	1	0	-5.674988	2.403828	3.014491
84	1	0	-4.468176	2.494613	4.298995
85	1	0	-1.196294	0.478320	2.987421
86	1	0	-5.417620	0.565554	1.321047
87	1	0	-4.708383	-0.987734	1.765576

88	6	0	3.836020	0.209076	-1.523440
89	1	0	4.030528	1.082824	-2.162202
90	6	0	5.175206	-0.412361	-1.115585
91	1	0	4.988605	-1.315803	-0.520127
92	1	0	5.694097	-0.740186	-2.025667
93	6	0	6.096889	0.531844	-0.329669
94	1	0	6.161125	1.489418	-0.865879
95	1	0	5.682181	0.743804	0.661046
96	6	0	7.472102	-0.041620	-0.174882
97	1	0	8.004420	-0.255868	-1.103055
98	6	0	8.056241	-0.316926	0.993719
99	1	0	7.548433	-0.119025	1.935466
100	6	0	9.416450	-0.896872	1.143532
101	6	0	10.214210	-1.232161	-0.101496
102	1	0	9.681350	-1.962986	-0.716673
103	1	0	10.373981	-0.337656	-0.710568
104	1	0	11.175366	-1.642430	0.205212
105	8	0	9.871247	-1.093383	2.252397

TS6

G(M06-2x/6-311+G(d,p): -2217,035181 hartrees

Imaginary frequency: -301.1

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	5.338418	-3.473035	-2.299801
2	6	0	4.722336	-4.121227	-1.054003
3	6	0	3.498533	-4.939650	-1.501174
4	6	0	4.324105	-2.415455	-2.805442
5	6	0	2.616663	-4.025477	-2.397120
6	7	0	2.987424	-2.612601	-2.220783
7	6	0	4.253238	-2.993690	-0.118009
8	6	0	3.008075	-2.346403	-0.769234
9	6	0	-3.133832	0.475026	0.188509
10	6	0	-0.470210	4.822544	0.255881
11	6	0	-6.740695	0.038627	-1.150297

12	6	0	3.723464	1.172521	2.644584
13	6	0	6.147858	4.785073	0.120064
14	6	0	4.949680	3.203669	2.103733
15	6	0	3.735096	0.792615	1.270443
16	6	0	2.565537	-0.690386	3.273810
17	6	0	-5.523881	0.003794	-0.216100
18	6	0	1.718227	3.631077	-0.094575
19	7	0	-1.769598	0.800357	-0.286656
20	6	0	-3.787178	-0.585590	-1.981750
21	6	0	-1.244319	-0.196978	-1.883814
22	6	0	0.223234	4.058285	-2.060851
23	6	0	2.506916	-1.159030	1.936340
24	6	0	-0.109601	0.390682	-2.484836
25	7	0	3.138424	0.430892	3.628367
26	6	0	3.062230	-0.422610	0.924216
27	6	0	4.338921	2.388990	3.023904
28	6	0	4.394099	1.630811	0.343710
29	6	0	-2.513127	-0.149669	-2.699329
30	6	0	0.278248	3.777352	-0.563077
31	6	0	2.865608	-0.836195	-0.524018
32	6	0	2.312150	0.738946	-2.944728
33	6	0	-4.205737	0.398472	-0.891999
34	6	0	1.207732	0.206762	-2.074171
35	6	0	4.979499	2.813117	0.742408
36	6	0	-1.532309	2.162461	-0.584600
37	7	0	1.530680	-0.412079	-0.943333
38	6	0	-0.565619	-1.669471	1.571687
39	6	0	-8.005216	-0.290071	-0.417153
40	6	0	-9.053548	0.528175	-0.298952
41	6	0	-10.300755	0.201873	0.441467
42	6	0	-10.418961	-1.146737	1.123080
43	1	0	-3.036985	-0.496146	0.684726
44	1	0	5.526553	-4.234949	-3.064671
45	1	0	6.299490	-3.006158	-2.061222
46	1	0	3.600770	-0.325205	-1.145493
47	1	0	5.450661	-4.761232	-0.548305
48	1	0	2.937983	-5.279552	-0.623287
49	1	0	3.815965	-5.832559	-2.049074
50	1	0	4.222464	-2.447735	-3.895446

51	1	0	4.669674	-1.406689	-2.551974
52	1	0	1.555386	-4.137240	-2.155808
53	1	0	2.742964	-4.271650	-3.457005
54	1	0	4.008946	-3.378118	0.876465
55	1	0	5.056475	-2.255116	0.014825
56	1	0	2.100212	-2.812568	-0.364485
57	1	0	-3.414188	1.204625	0.956759
58	1	0	1.895389	1.281165	-3.793183
59	1	0	-6.606054	-0.691360	-1.958063
60	1	0	2.973547	1.412145	-2.390555
61	1	0	-1.108294	0.442927	0.444857
62	1	0	2.093634	-1.276861	4.058818
63	1	0	2.903777	-0.100524	-3.322159
64	1	0	4.457068	1.384863	-0.710204
65	1	0	0.783123	-0.864773	-0.395238
66	1	0	0.727562	5.006990	-2.265041
67	1	0	-5.422674	-1.002468	0.214969
68	1	0	-1.504500	4.917391	-0.076563
69	1	0	-3.645466	-1.582183	-1.538852
70	1	0	2.210965	2.827466	-0.647310
71	1	0	-2.637584	0.865242	-3.098161
72	1	0	2.268214	4.560868	-0.265785
73	1	0	-4.320637	1.393598	-1.339600
74	1	0	6.968355	4.645303	0.833487
75	1	0	-5.713920	0.683629	0.623585
76	1	0	1.983723	-2.084954	1.726585
77	1	0	5.409711	5.472594	0.550525
78	1	0	-1.095450	-1.099587	-1.286053
79	1	0	0.027315	5.789770	0.142627
80	1	0	4.306573	2.651757	4.075831
81	1	0	1.762611	3.380570	0.969422
82	1	0	-2.330190	-0.805193	-3.559489
83	1	0	-0.273235	1.039071	-3.339292
84	1	0	-0.453359	4.549069	1.314398
85	1	0	-0.806015	4.122122	-2.416044
86	1	0	-4.582573	-0.679909	-2.727567
87	1	0	6.542761	5.212374	-0.801139
88	1	0	0.744247	3.264912	-2.605081
89	1	0	-6.825771	1.027007	-1.615890

90	1	0	5.407538	4.131012	2.426164
91	8	0	-2.364936	2.888018	-1.075597
92	8	0	5.558688	3.554586	-0.240845
93	8	0	-0.275585	2.451308	-0.287214
94	8	0	-0.801835	-0.484809	1.866207
95	8	0	-0.169834	-2.153461	0.486800
96	1	0	-8.035056	-1.271276	0.059185
97	1	0	-9.050472	1.514524	-0.758583
98	8	0	-11.203172	1.012948	0.491663
99	1	0	-10.313490	-1.957807	0.396785
100	1	0	-9.634011	-1.269626	1.874951
101	1	0	-11.395566	-1.208007	1.601164
102	6	0	-0.742042	-2.706310	2.708250
103	9	0	0.468192	-3.106274	3.159337
104	9	0	-1.414597	-2.223188	3.750808
105	9	0	-1.380296	-3.798713	2.275064

TS7

G(M06-2x/6-311+G(d,p): -2217, 041304 hartrees

Imaginary frequency: -283.5

Standard orientation:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.068873	1.902647	-2.486859
2	6	0	2.780281	1.621935	-0.653132
3	6	0	4.971206	0.343664	-0.688759
4	6	0	-3.422789	-1.485494	3.359671
5	6	0	-3.779392	3.297048	0.659554
6	6	0	1.398300	2.254320	-2.699112
7	6	0	-3.093437	-0.068286	2.815229
8	7	0	-2.203562	0.376696	-1.050219
9	6	0	-0.285878	3.639240	-0.195942
10	7	0	0.567730	2.530385	-0.179873
11	6	0	2.010891	2.772009	-0.007702
12	6	0	-2.336110	5.279449	1.201470
13	6	0	-3.079555	-1.086287	0.676821

14	6	0	2.748632	1.746139	-2.181037
15	7	0	-3.573585	0.076092	1.429779
16	6	0	0.215827	1.643112	-1.990745
17	6	0	-3.357644	1.058660	-3.077028
18	6	0	-4.482610	-2.111469	2.436416
19	6	0	-3.074700	-0.777962	-0.828782
20	6	0	-2.170692	1.112797	-2.157383
21	6	0	-2.892595	4.722693	-1.205545
22	6	0	-2.625566	4.173300	0.192092
23	6	0	4.192377	1.520386	-0.085625
24	6	0	6.212457	0.034379	0.087791
25	6	0	7.451459	0.051784	-0.410298
26	6	0	8.681759	-0.239770	0.369804
27	6	0	8.554212	-0.585082	1.840245
28	6	0	0.818902	-0.057947	1.868615
29	6	0	0.556308	-1.364835	2.657941
30	6	0	-2.666491	-1.976160	-1.675664
31	6	0	-3.594968	-2.604550	-2.465181
32	6	0	-1.340792	-2.518997	-1.652836
33	6	0	-1.090168	-3.687730	-2.428861
34	6	0	-3.232079	-3.752790	-3.218351
35	6	0	0.197317	-4.277594	-2.380243
36	6	0	-0.292412	-1.982643	-0.881379
37	6	0	1.200922	-3.751126	-1.603063
38	6	0	0.944703	-2.583301	-0.845569
39	6	0	2.994641	-2.706645	0.372114
40	7	0	-2.037825	-4.285531	-3.208666
41	6	0	-5.041509	0.099776	1.449291
42	6	0	-5.618568	-1.094441	2.255687
43	6	0	-3.858382	-2.365110	1.052772
44	1	0	3.536941	2.432423	-2.516714
45	1	0	0.367013	0.666513	-1.526757
46	1	0	-3.583642	0.708873	3.412911
47	1	0	-4.696075	3.890989	0.713158
48	1	0	1.296307	2.033561	-3.767424
49	1	0	-1.557628	0.592132	-0.288067
50	1	0	2.272377	0.694183	-0.356920
51	1	0	-3.238293	1.777828	-3.886740
52	1	0	-3.094176	3.900270	-1.898662

53	1	0	2.965091	0.769481	-2.628947
54	1	0	1.316234	3.344595	-2.603597
55	1	0	-3.453444	0.058716	-3.512278
56	1	0	4.101098	1.375656	0.997158
57	1	0	2.223431	2.805827	1.064912
58	1	0	4.746717	2.453961	-0.253669
59	1	0	-3.231192	5.895189	1.326901
60	1	0	-3.798834	-1.431759	4.386342
61	1	0	-1.194268	2.666833	-3.247043
62	1	0	-3.925382	2.459565	-0.029564
63	1	0	-4.863790	-3.044929	2.859833
64	1	0	-4.281376	1.279062	-2.531728
65	1	0	2.257355	3.738905	-0.456512
66	1	0	-2.039089	-1.209481	0.987407
67	1	0	-2.082661	4.840087	2.170293
68	1	0	-2.042580	5.300075	-1.570769
69	1	0	-3.561625	2.868604	1.641175
70	1	0	-2.520512	-2.105750	3.375128
71	1	0	5.228034	0.538580	-1.735669
72	1	0	-3.773905	5.369636	-1.172695
73	1	0	4.308793	-0.534124	-0.675596
74	1	0	-1.514572	5.914130	0.868292
75	1	0	0.233529	1.759312	0.457497
76	8	0	-1.505144	3.236970	0.159690
77	8	0	0.046396	4.743870	-0.560212
78	8	0	1.929960	0.443390	1.997437
79	9	0	-0.037120	-1.079158	3.831776
80	9	0	-0.264053	-2.213706	2.010392
81	8	0	-0.191947	0.362249	1.221109
82	9	0	1.681145	-2.032038	2.927202
83	1	0	6.059730	-0.201616	1.142316
84	1	0	7.632114	0.291213	-1.456382
85	8	0	9.767030	-0.198514	-0.174713
86	1	0	7.951041	-1.488068	1.973192
87	1	0	8.062055	0.224556	2.386627
88	1	0	9.551634	-0.748826	2.245797
89	1	0	-4.616113	-2.234419	-2.516526
90	1	0	0.356671	-5.169214	-2.977194
91	1	0	-0.423519	-1.121657	-0.242619

92	1	0	2.174786	-4.226783	-1.573246
93	1	0	-4.095434	-0.505975	-1.125900
94	8	0	1.865341	-1.966687	-0.054711
95	1	0	2.690257	-3.661548	0.814536
96	1	0	3.693278	-2.886972	-0.453737
97	1	0	3.470147	-2.089067	1.134389
98	1	0	-3.979080	-4.236634	-3.845111
99	1	0	-5.405338	0.083313	0.415285
100	1	0	-5.357416	1.059773	1.872157
101	1	0	-6.465433	-1.547710	1.729658
102	1	0	-5.982178	-0.765507	3.235510
103	1	0	-2.019199	0.126089	2.825309
104	1	0	-4.648299	-2.584417	0.320613
105	1	0	-3.181618	-3.225752	1.064917

TS8

G(M06-2x/6-311+G(d,p): -2217,03836 hartrees

Imaginary frequency: -338.5

Standard orientation:

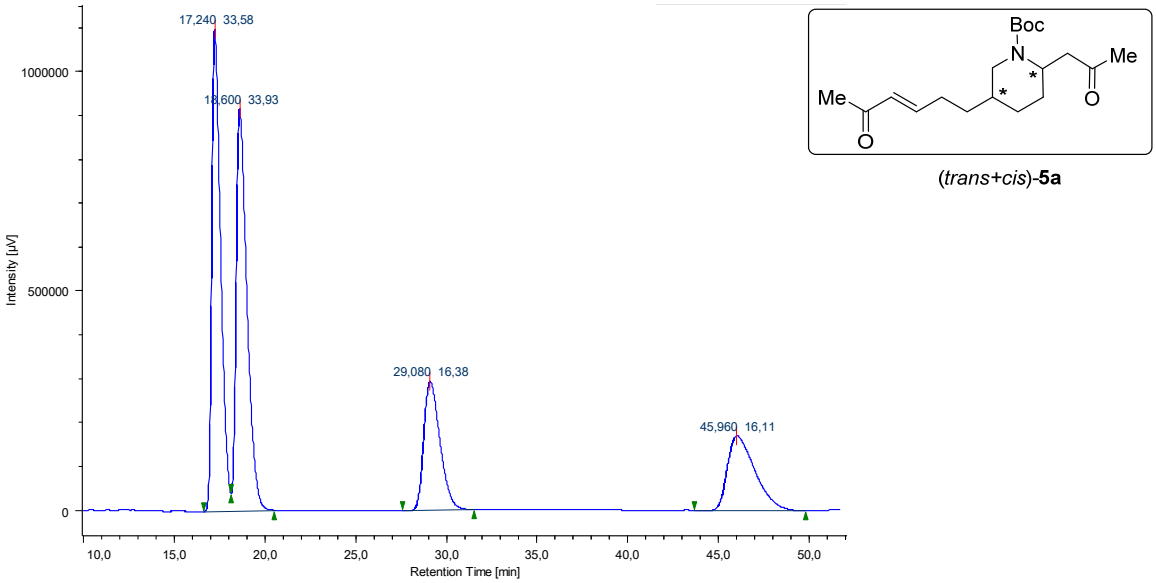
Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.170344	-1.735108	-2.345133
2	6	0	3.712729	-1.195399	-0.662770
3	6	0	5.960766	0.002784	-0.815028
4	6	0	-2.440642	4.668041	-2.058225
5	6	0	-2.793802	-3.045589	1.000993
6	6	0	2.309979	-2.080007	-2.606172
7	6	0	-1.991749	4.697779	-0.590527
8	6	0	-2.175023	0.406643	1.811751
9	7	0	-1.227853	-0.078442	-1.001819
10	6	0	0.679671	-3.215773	0.037650
11	7	0	1.482550	-2.060789	-0.114282
12	6	0	2.933230	-2.245043	0.121090
13	6	0	-1.189877	-4.854579	1.686365
14	6	0	-0.454201	4.760244	-0.561013
15	6	0	-6.524269	-0.156918	-0.225321

16	6	0	-4.809279	-0.281932	1.996712
17	6	0	-1.551570	2.265692	-0.509741
18	6	0	-2.923673	0.495587	0.664198
19	6	0	3.667099	-1.511010	-2.164645
20	6	0	-7.015198	-0.609481	1.025641
21	6	0	-2.449298	3.383450	0.065029
22	6	0	-6.168784	-0.662562	2.102916
23	6	0	-5.204857	0.218074	-0.362530
24	6	0	-4.311916	0.159942	0.734062
25	6	0	1.139260	-1.419735	-1.918500
26	6	0	-2.601810	-1.207705	-2.656597
27	6	0	-1.979904	3.309211	-2.648916
28	6	0	-8.653756	-0.425861	-1.242690
29	6	0	-2.786391	-0.012449	3.018396
30	6	0	-2.245283	0.901935	-0.634898
31	6	0	-1.284371	-0.991175	-1.965611
32	6	0	-1.844506	-4.567239	-0.744805
33	6	0	-1.585867	-3.873663	0.588906
34	6	0	5.129405	-1.074816	-0.107139
35	7	0	-4.045732	-0.358878	3.122878
36	6	0	0.085095	3.650020	-1.504725
37	7	0	-0.967007	2.664521	-1.800627
38	6	0	7.268641	0.228525	-0.121740
39	6	0	8.468635	0.021051	-0.669262
40	6	0	9.762885	0.224945	0.031521
41	6	0	9.750663	0.705458	1.469164
42	6	0	1.852198	0.848376	1.557276
43	6	0	1.625266	2.299087	2.052237
44	1	0	1.299490	-0.384751	-1.606427
45	1	0	-2.424113	5.557032	-0.070324
46	1	0	-1.113292	0.638361	1.800178
47	1	0	-3.668663	-3.692411	1.106730
48	1	0	2.178192	-1.954019	-3.685912
49	1	0	-0.358418	0.047396	-0.484644
50	1	0	-8.769487	-1.478290	-0.958063
51	1	0	-6.514597	-0.996264	3.075354
52	1	0	3.218911	-0.233093	-0.477760
53	1	0	-2.546799	-2.077373	-3.311288
54	1	0	-8.050228	-0.907502	1.139406

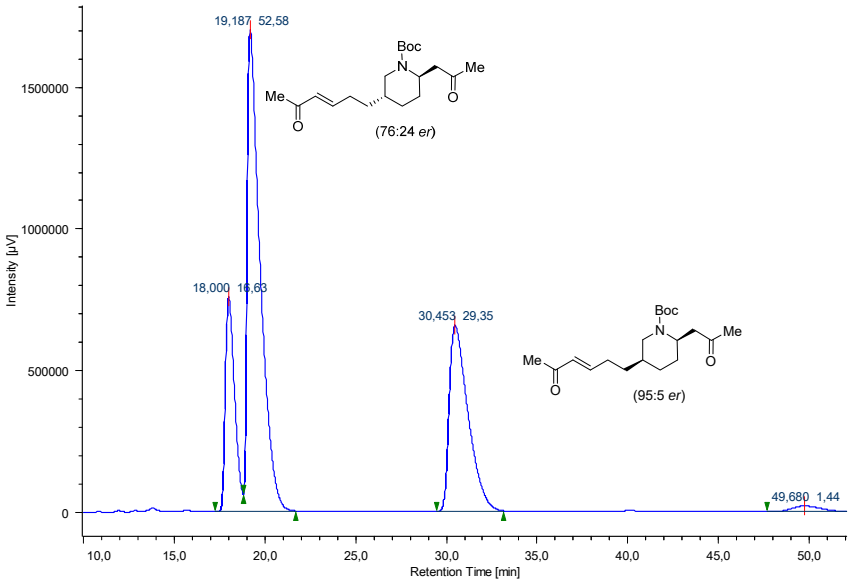
55	1	0	-2.086630	-3.824005	-1.509751
56	1	0	3.884987	-0.601093	-2.734639
57	1	0	2.246136	-3.157794	-2.410829
58	1	0	-2.847979	-0.335632	-3.272490
59	1	0	5.047898	-0.822432	0.956733
60	1	0	0.426483	4.067760	-2.458074
61	1	0	-0.089335	4.598337	0.458933
62	1	0	3.113640	-2.119315	1.192412
63	1	0	5.647526	-2.040856	-0.182254
64	1	0	4.453594	-2.235375	-2.412293
65	1	0	-3.527623	4.776790	-2.134381
66	1	0	-0.318876	-2.583516	-3.003988
67	1	0	-3.006249	-2.286682	0.242328
68	1	0	-1.555278	3.431538	-3.650186
69	1	0	-9.185682	0.204702	-0.520773
70	1	0	-0.106319	5.747798	-0.880399
71	1	0	-2.831153	2.625934	-2.751494
72	1	0	-3.414137	-1.349110	-1.936137
73	1	0	3.200872	-3.260763	-0.182188
74	1	0	-2.188447	-0.068443	3.926072
75	1	0	-0.705306	2.116634	0.170754
76	1	0	-0.951895	-4.310902	2.604648
77	1	0	-4.892841	0.565983	-1.340737
78	1	0	-0.982500	-5.149793	-1.069393
79	1	0	-9.079407	-0.273755	-2.233894
80	1	0	-2.616155	-2.537239	1.951917
81	1	0	-1.990196	5.505400	-2.603067
82	1	0	6.140596	-0.266503	-1.861581
83	1	0	-2.976468	0.955377	-1.441155
84	1	0	-2.702138	-5.236470	-0.632067
85	1	0	5.384987	0.938961	-0.810529
86	1	0	-2.032300	-5.520770	1.892048
87	1	0	-0.330023	-5.455713	1.389176
88	1	0	-2.349174	3.420598	1.153966
89	1	0	-3.510357	3.199347	-0.158237
90	1	0	1.146053	-1.225898	0.416360
91	1	0	0.928572	3.126846	-1.045910
92	8	0	-0.531846	-2.862836	0.440628
93	8	0	1.073567	-4.322700	-0.241423

94	8	0	-7.292657	-0.063418	-1.341934
95	8	0	2.859149	0.269055	1.943894
96	9	0	0.322974	2.537282	2.310885
97	9	0	1.993340	3.177277	1.098272
98	8	0	0.946051	0.451245	0.760026
99	9	0	2.314674	2.581740	3.151923
100	1	0	7.201216	0.567097	0.913014
101	1	0	8.564978	-0.321692	-1.697570
102	8	0	10.807063	0.006956	-0.549973
103	1	0	9.259194	1.679698	1.546080
104	1	0	9.200681	0.006952	2.106380
105	1	0	10.779926	0.786132	1.815910

HPLC TRACES OF ENANTIOENRICHED PIPERIDINES 5 AND 6



(*trans*+*cis*)-**5a**



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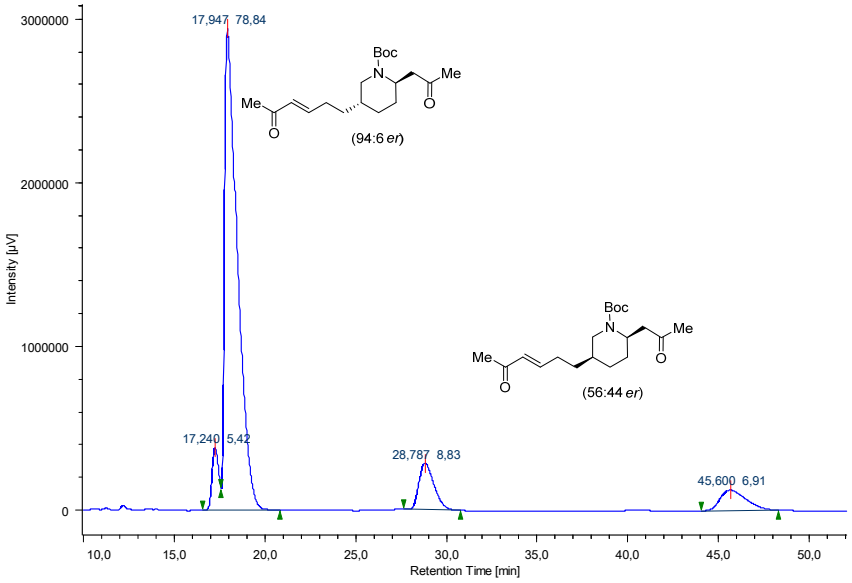
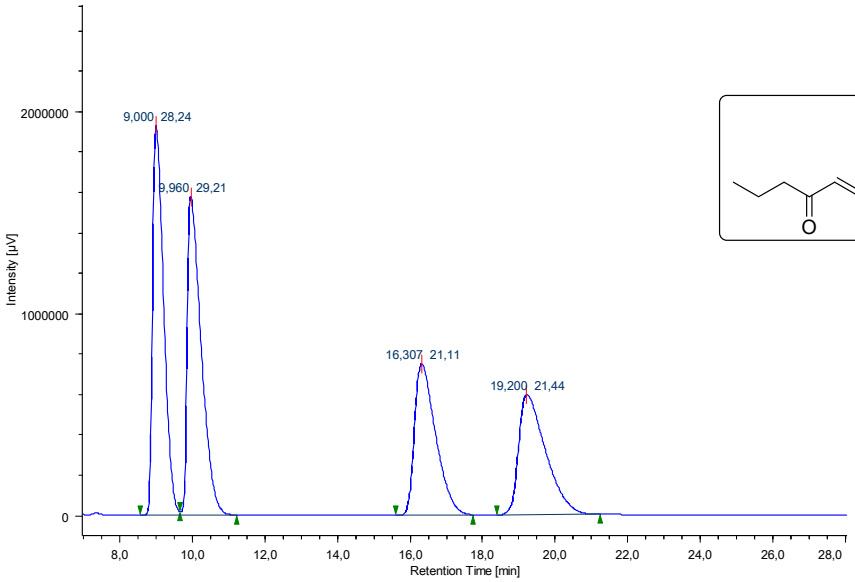
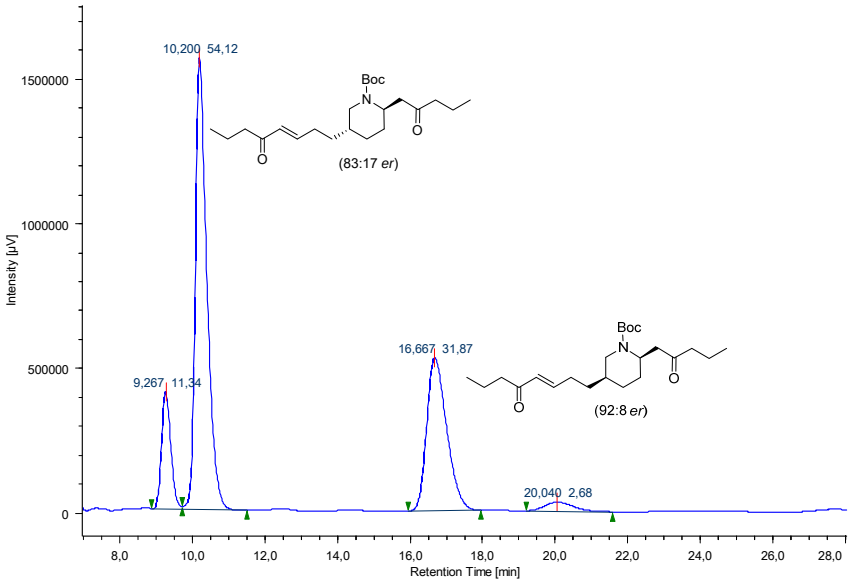


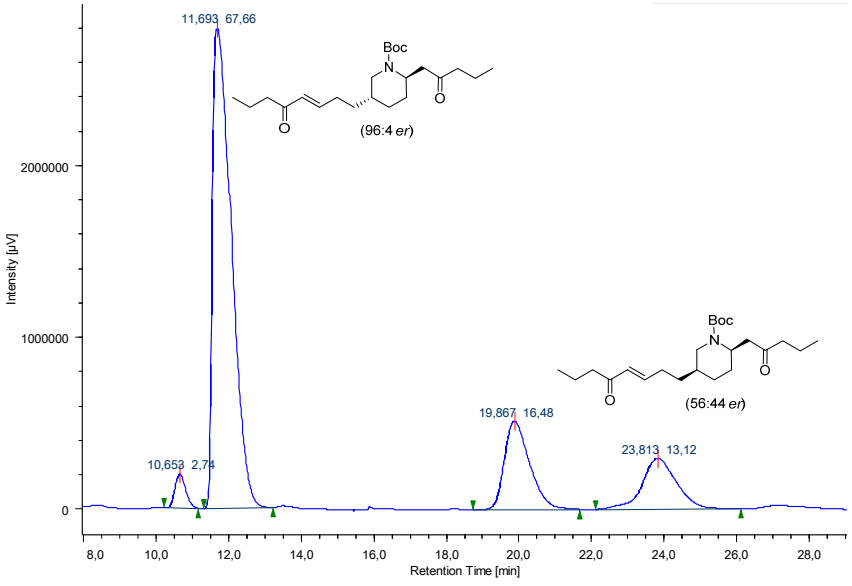
<u>20:10</u> cat. **I**/ TFA



(*trans*+*cis*)-**5b**



<u>20:20</u> cat. **I**/ TFA



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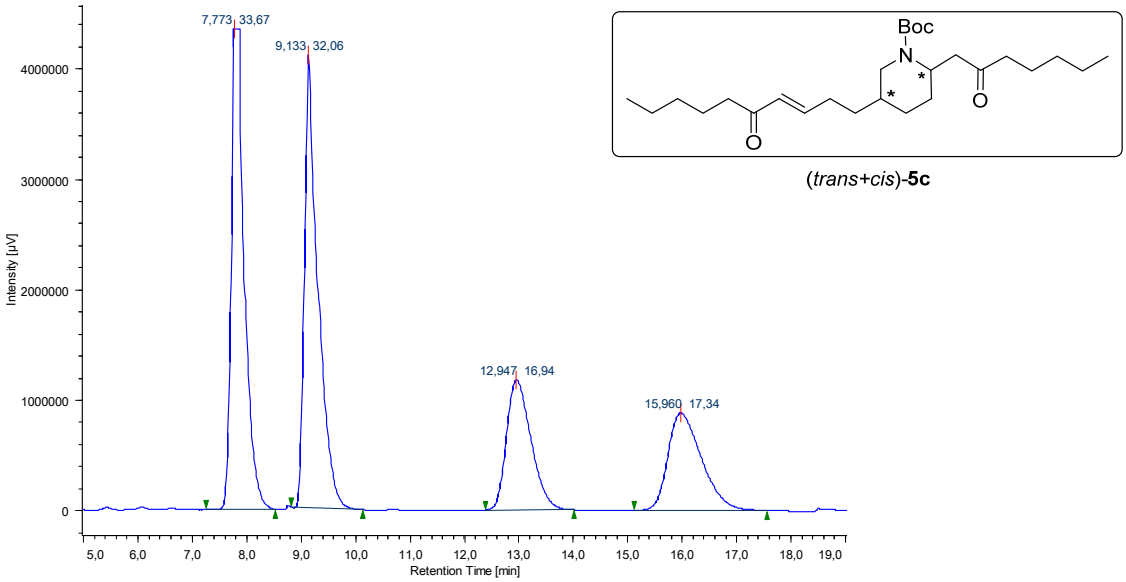
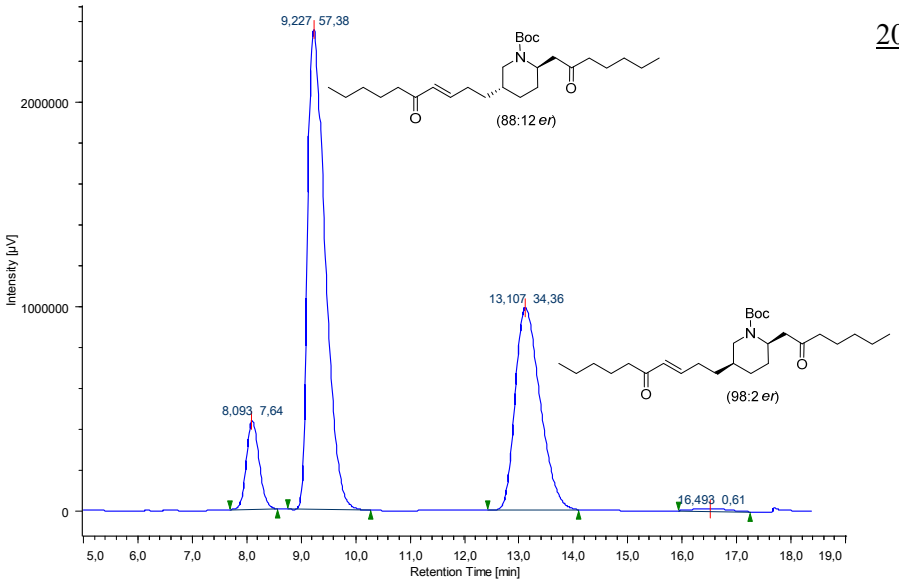


(*trans*+*cis*)-**5c**



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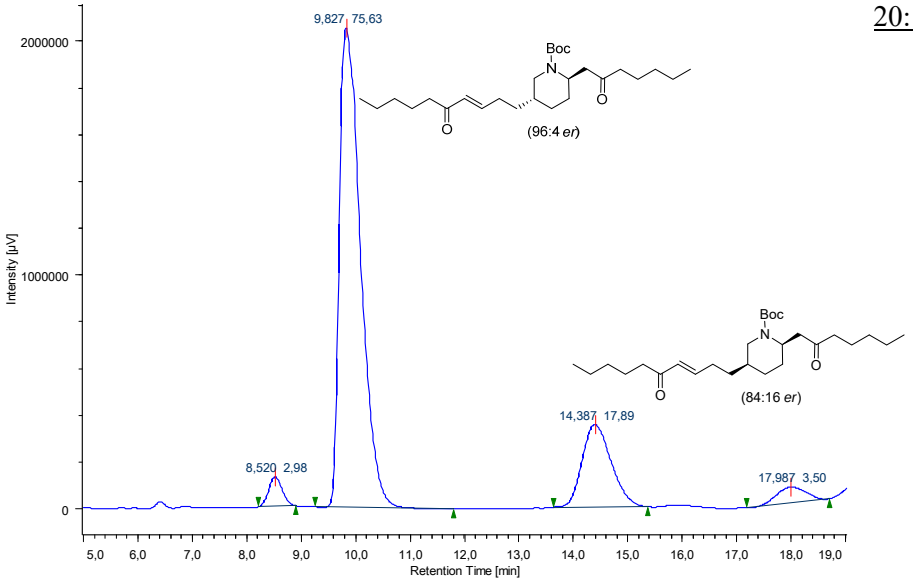

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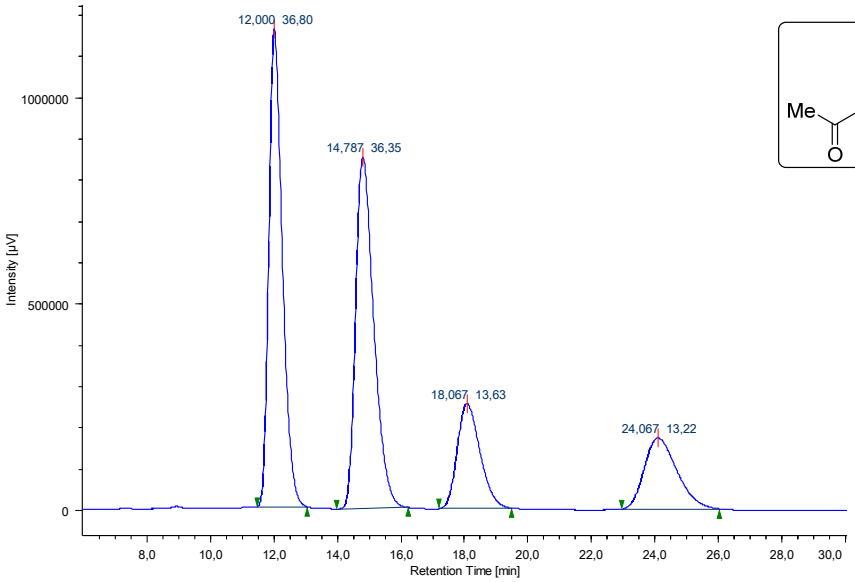
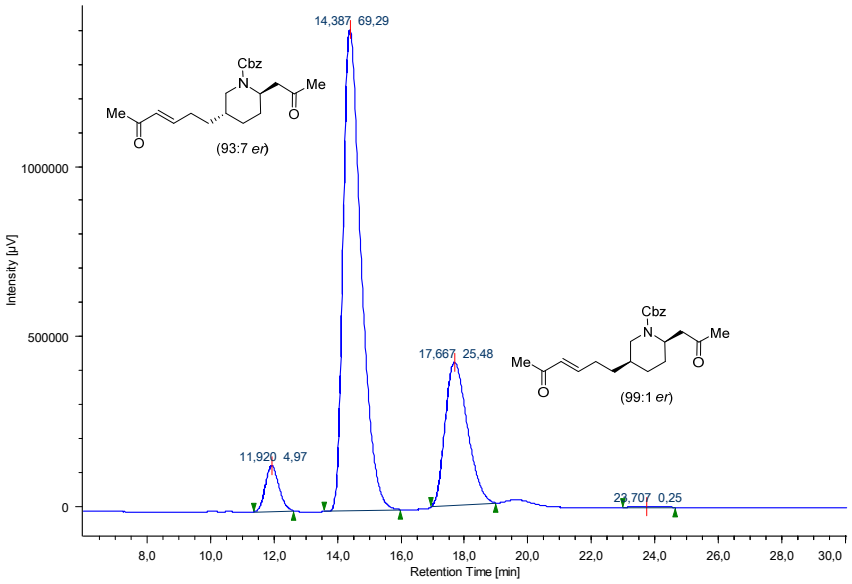
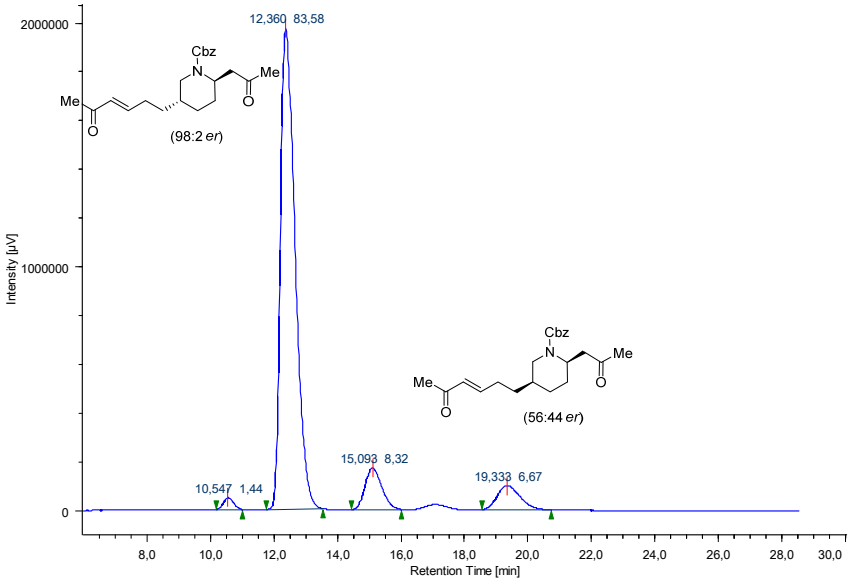


(*trans*+*cis*)-**5d**



<u>20:20</u> cat. **I**/ TFA



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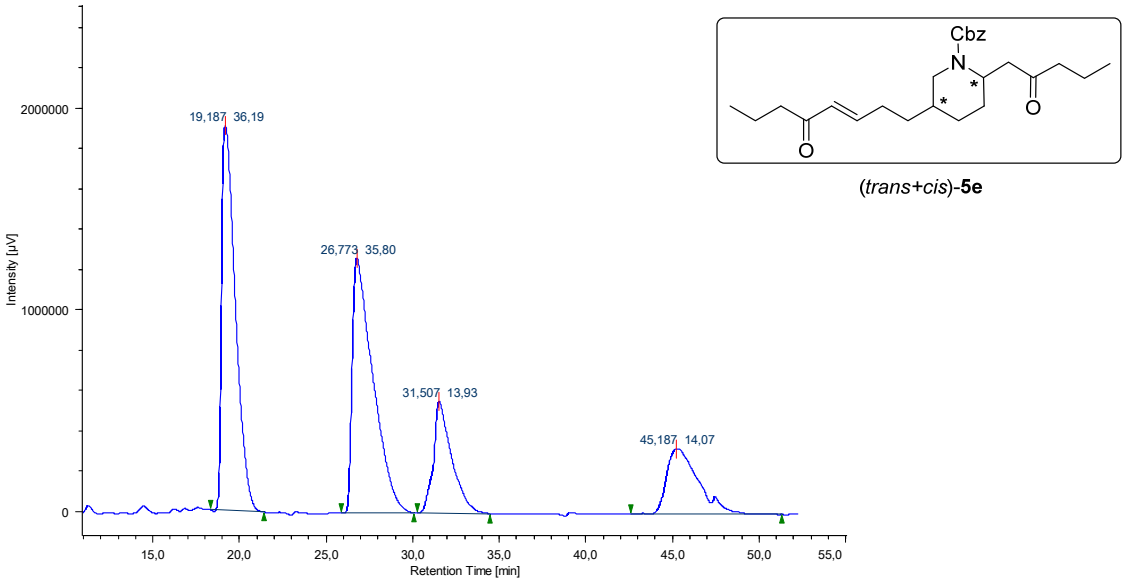
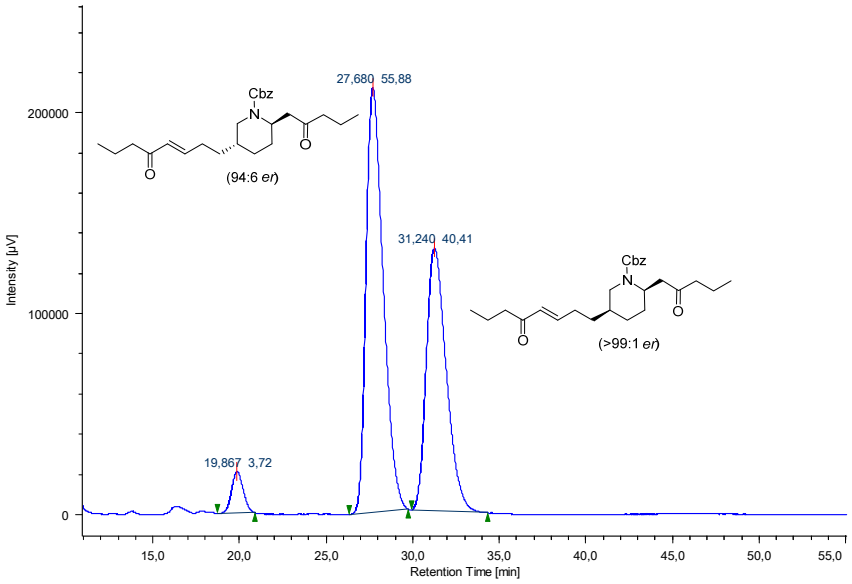


(*trans*+*cis*)-**5e**



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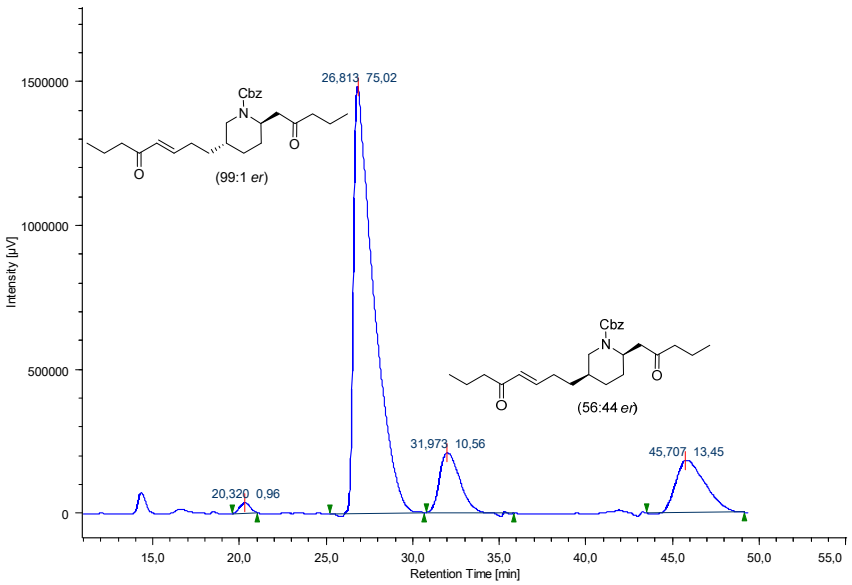

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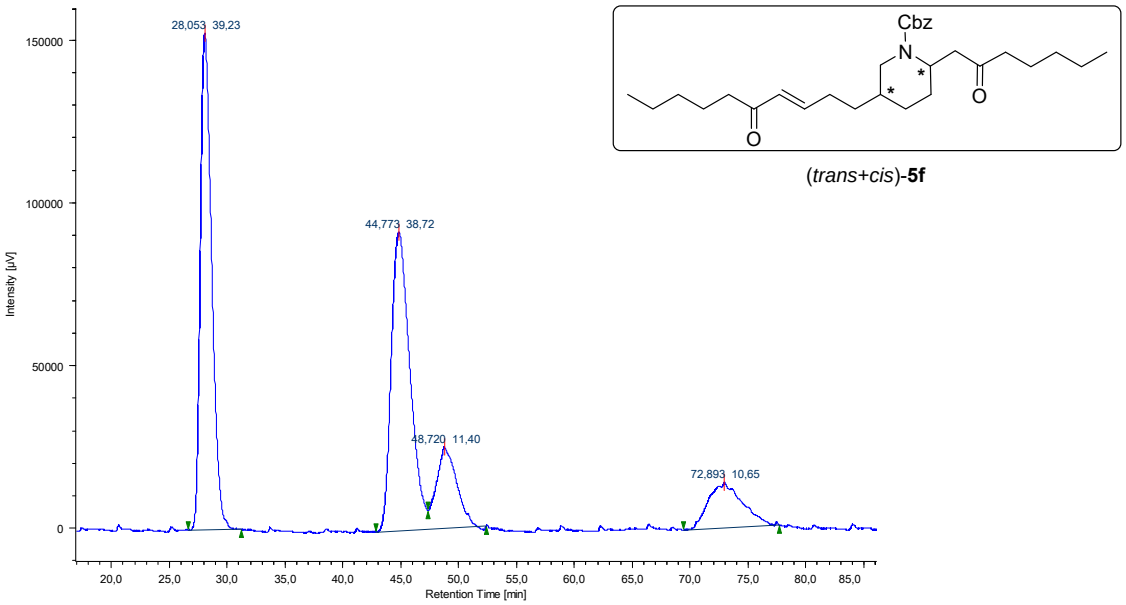
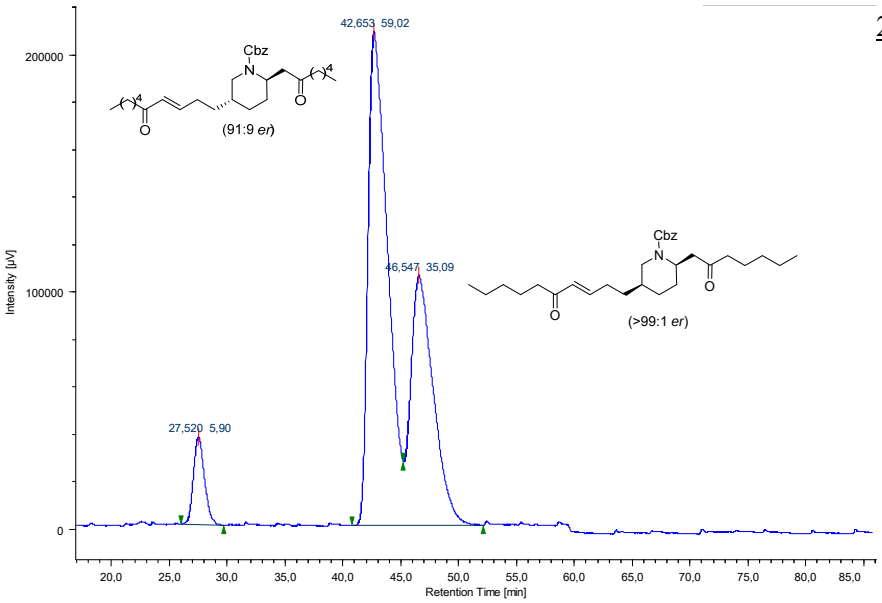


(*trans*+*cis*)-**5f**



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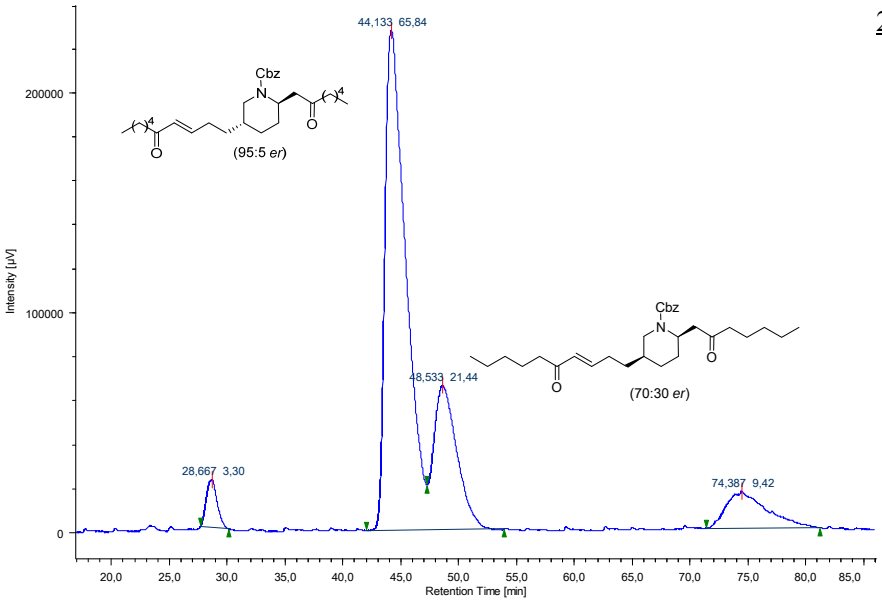

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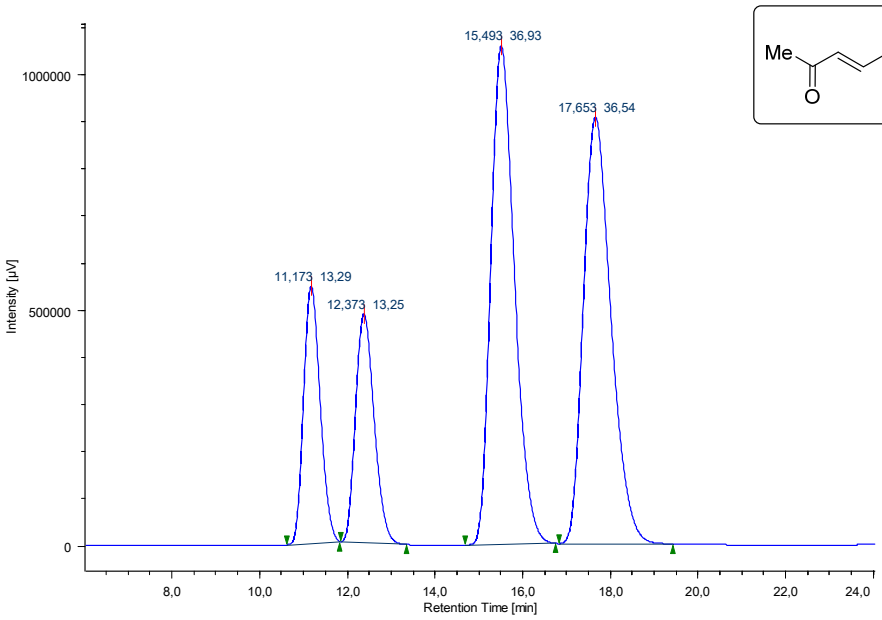

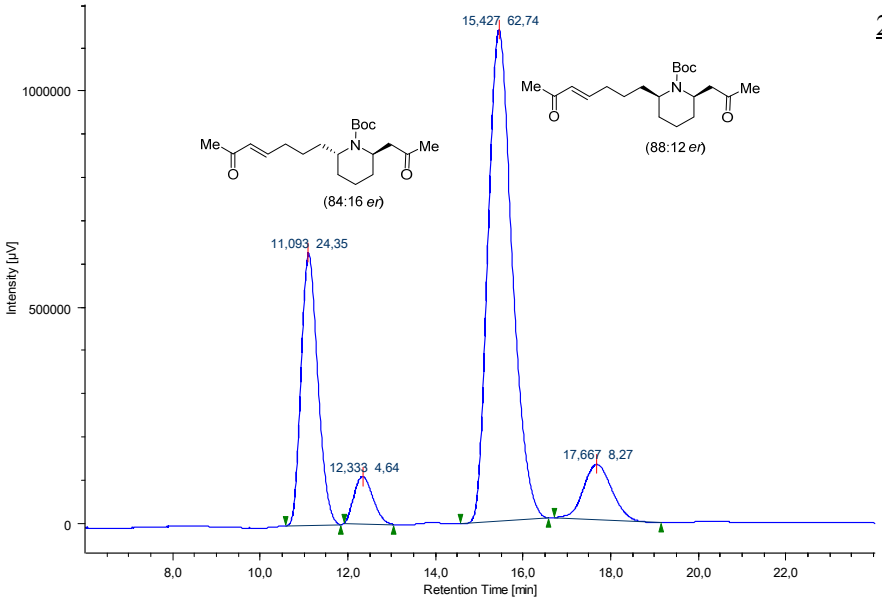

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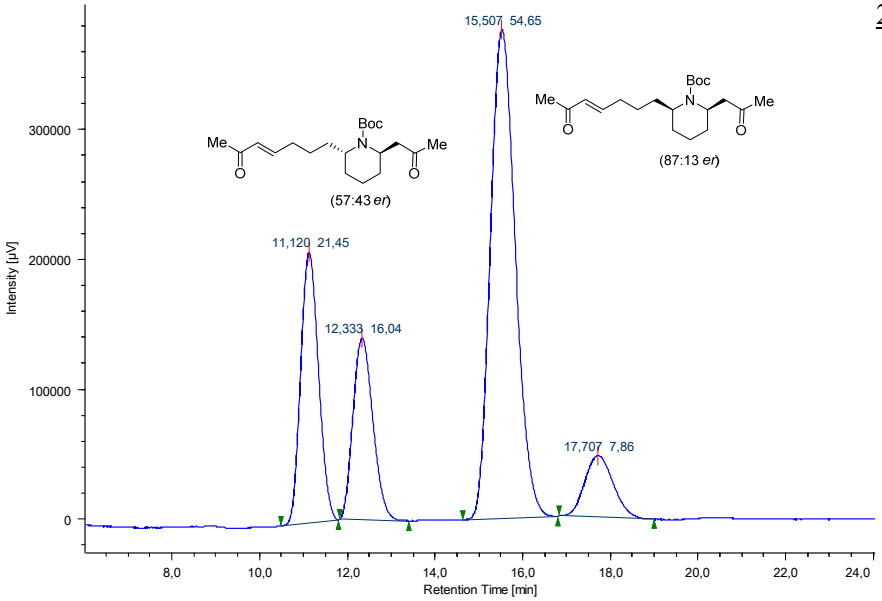

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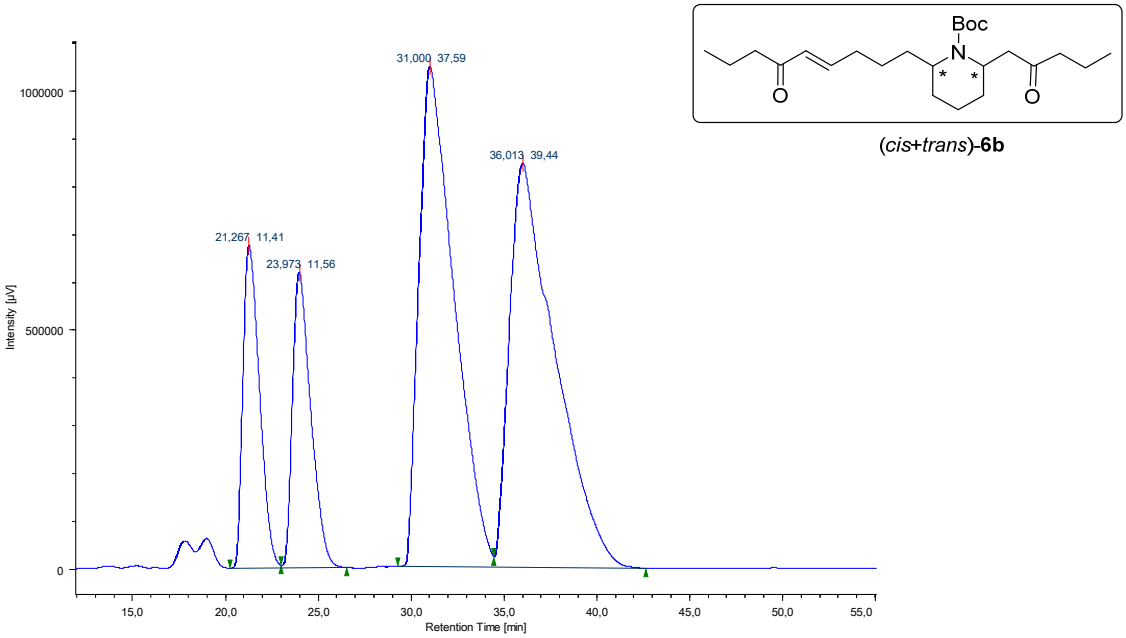
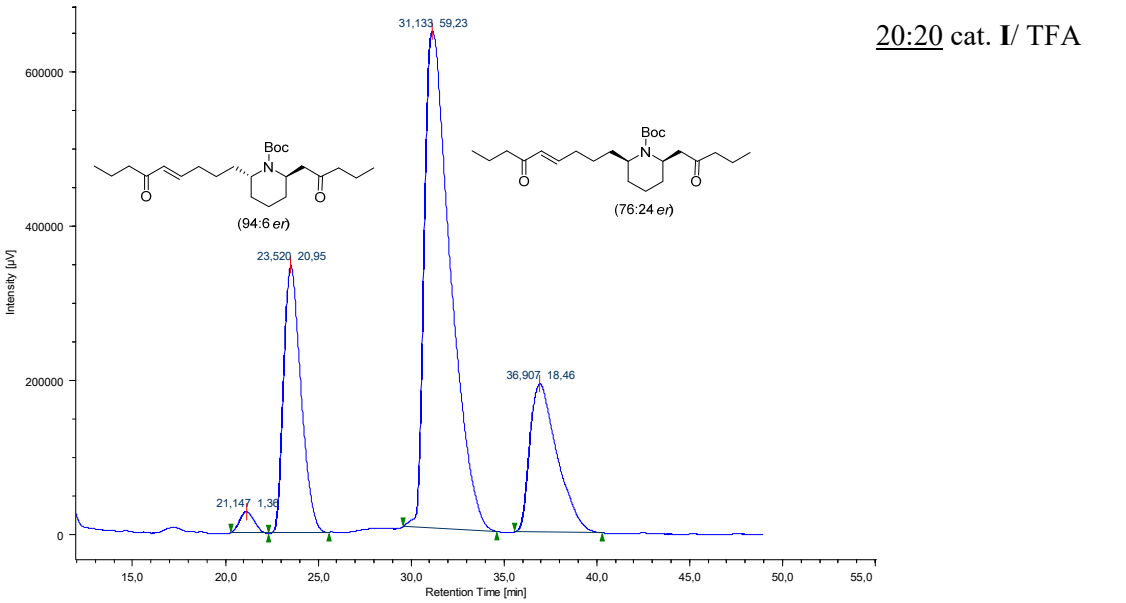
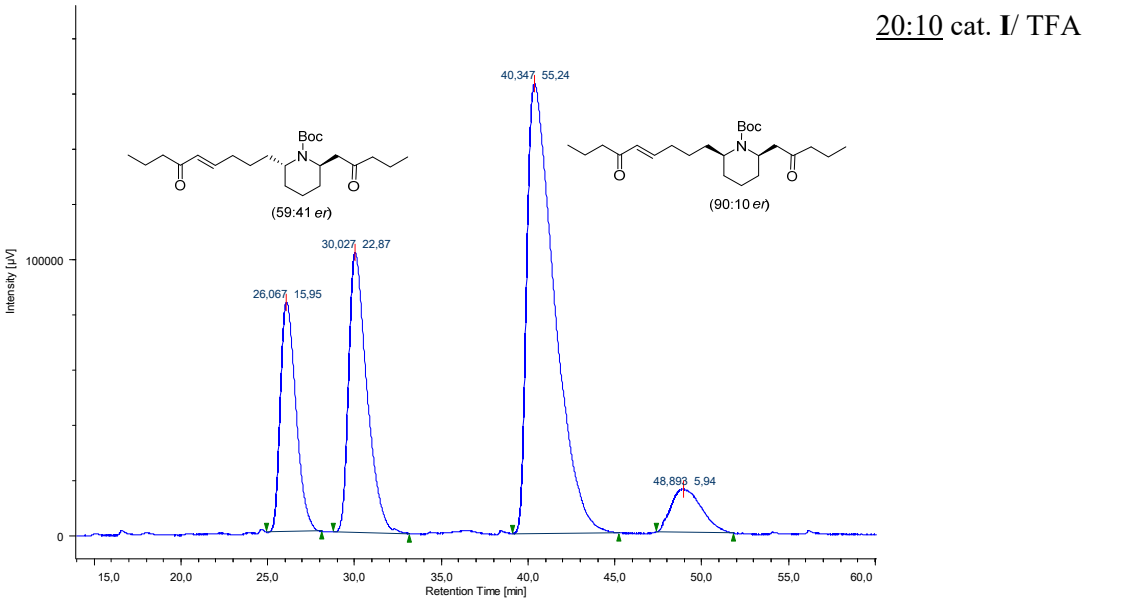
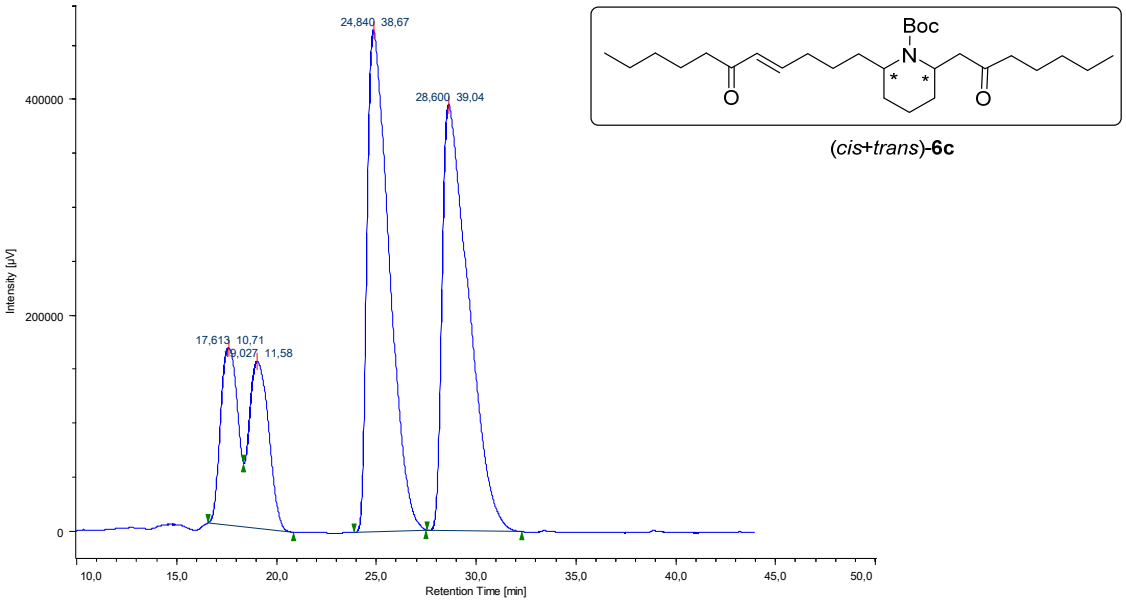
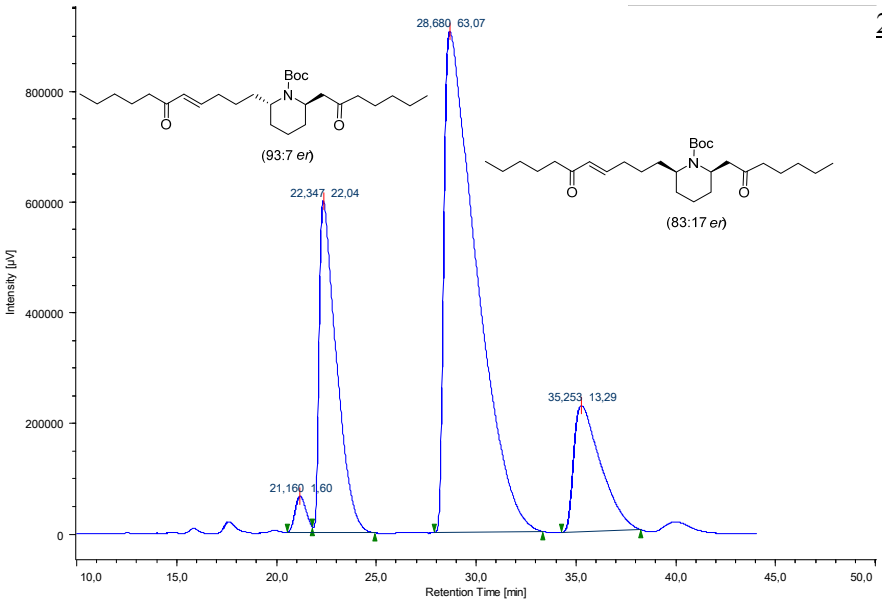
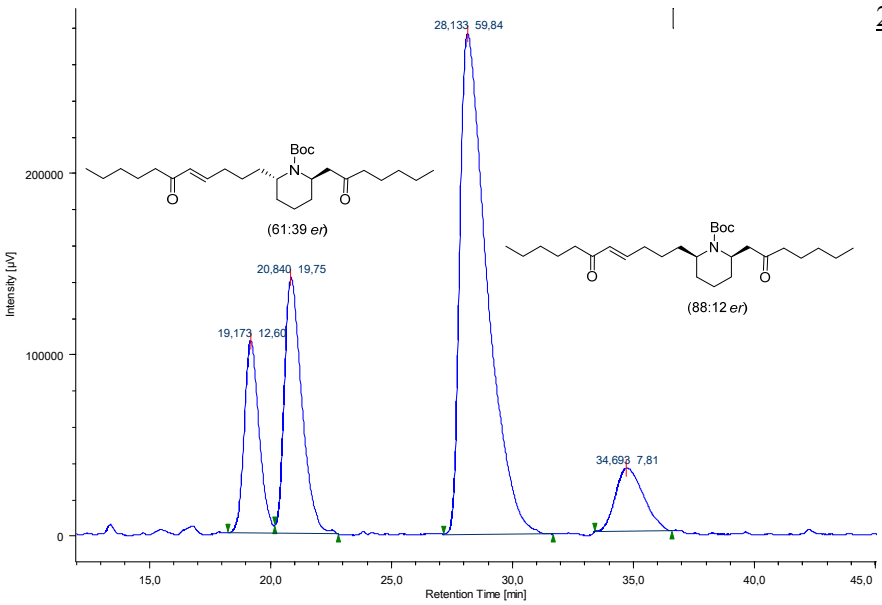

Boc
N
O
O
(*cis*+*trans*)-**6b**
31,000 37,59
36,013 39,44
21,267 11,41
23,973 11,56
Intensity [µV]
1000000
500000
0
15,0
20,0
25,0
30,0
35,0
40,0
45,0
50,0
55,0
Retention Time [min]

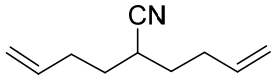

20:20 cat. **I**/ TFA
31,133 59,23
Boc
(94:6 *er*)
Boc
(76:24 *er*)
23,520 20,95
36,907 18,46
21,147 1,36
Intensity [µV]
600000
400000
200000
0
15,0
20,0
25,0
30,0
35,0
40,0
45,0
50,0
55,0
Retention Time [min]


20:10 cat. **I**/ TFA
40,347 55,24
Boc
(59:41 *er*)
Boc
(90:10 *er*)
30,027 22,87
26,067 15,95
48,893 5,94
Intensity [µV]
100000
0
15,0
20,0
25,0
30,0
35,0
40,0
45,0
50,0
55,0
60,0
Retention Time [min]


Boc
N
O
O
(cis+trans)-6c
24,840 38,67
28,600 39,04
17,613 10,71
19,027 11,58
Intensity [µV]
Retention Time [min]

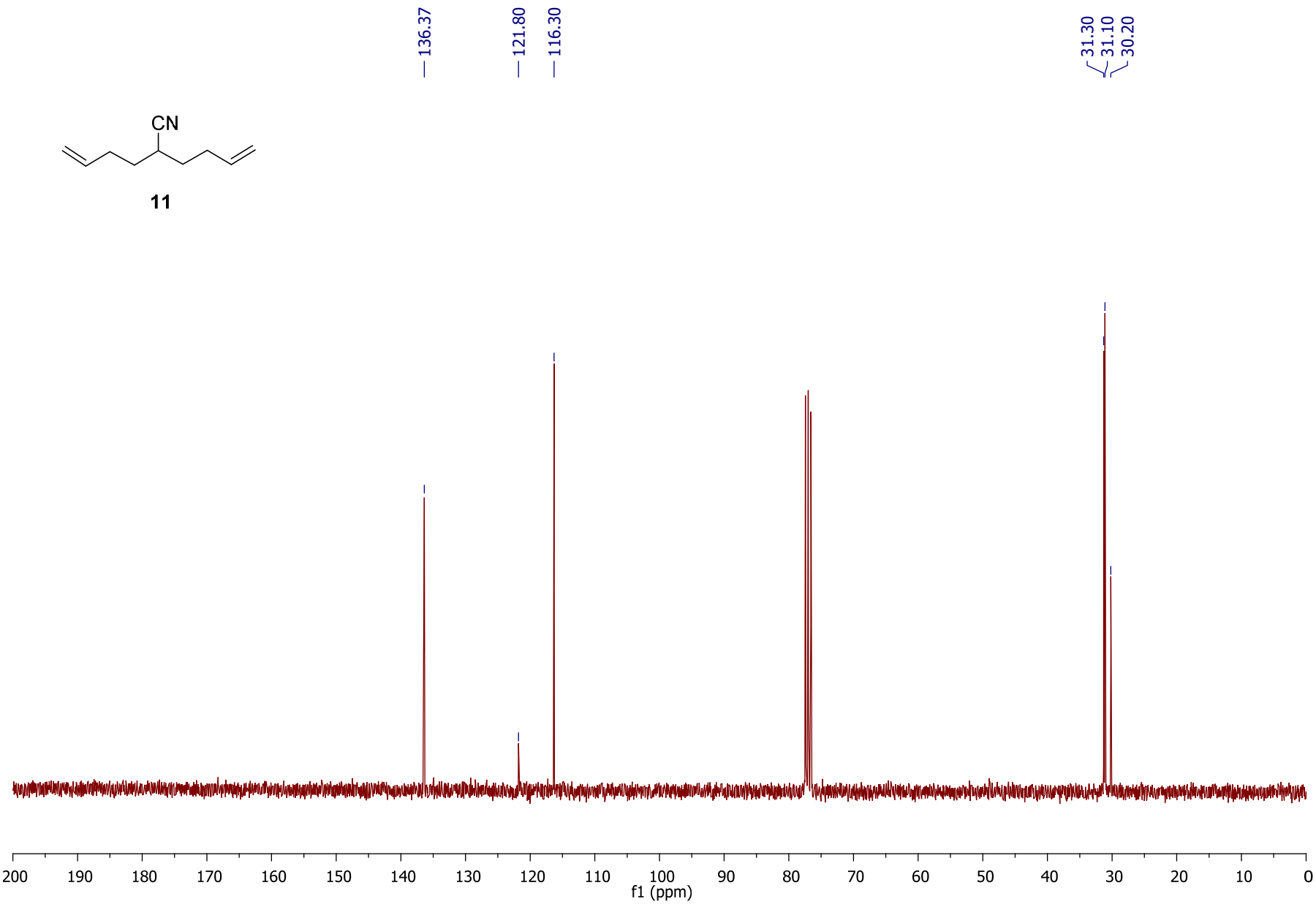

20:20 cat. I/ TFA
28,680 63,07
Boc
(93:7 er)
Boc
(83:17 er)
22,347 22,04
35,253 13,29
21,160 1,60
Intensity [µV]
Retention Time [min]

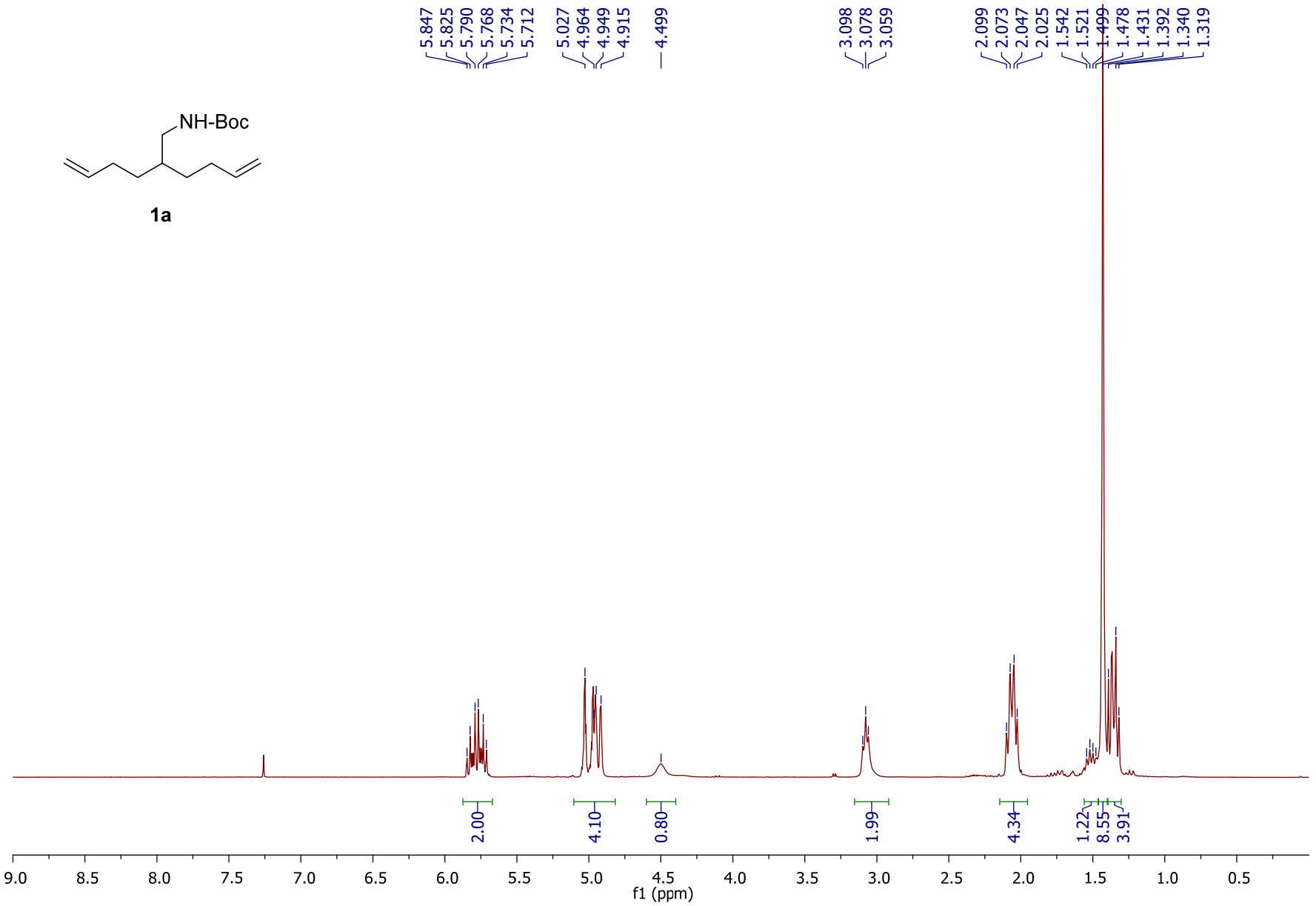

20:10 cat. I/ TFA
28,133 59,84
Boc
(61:39 er)
Boc
(88:12 er)
20,840 19,75
19,173 12,60
34,693 7,81
Intensity [µV]
Retention Time [min]

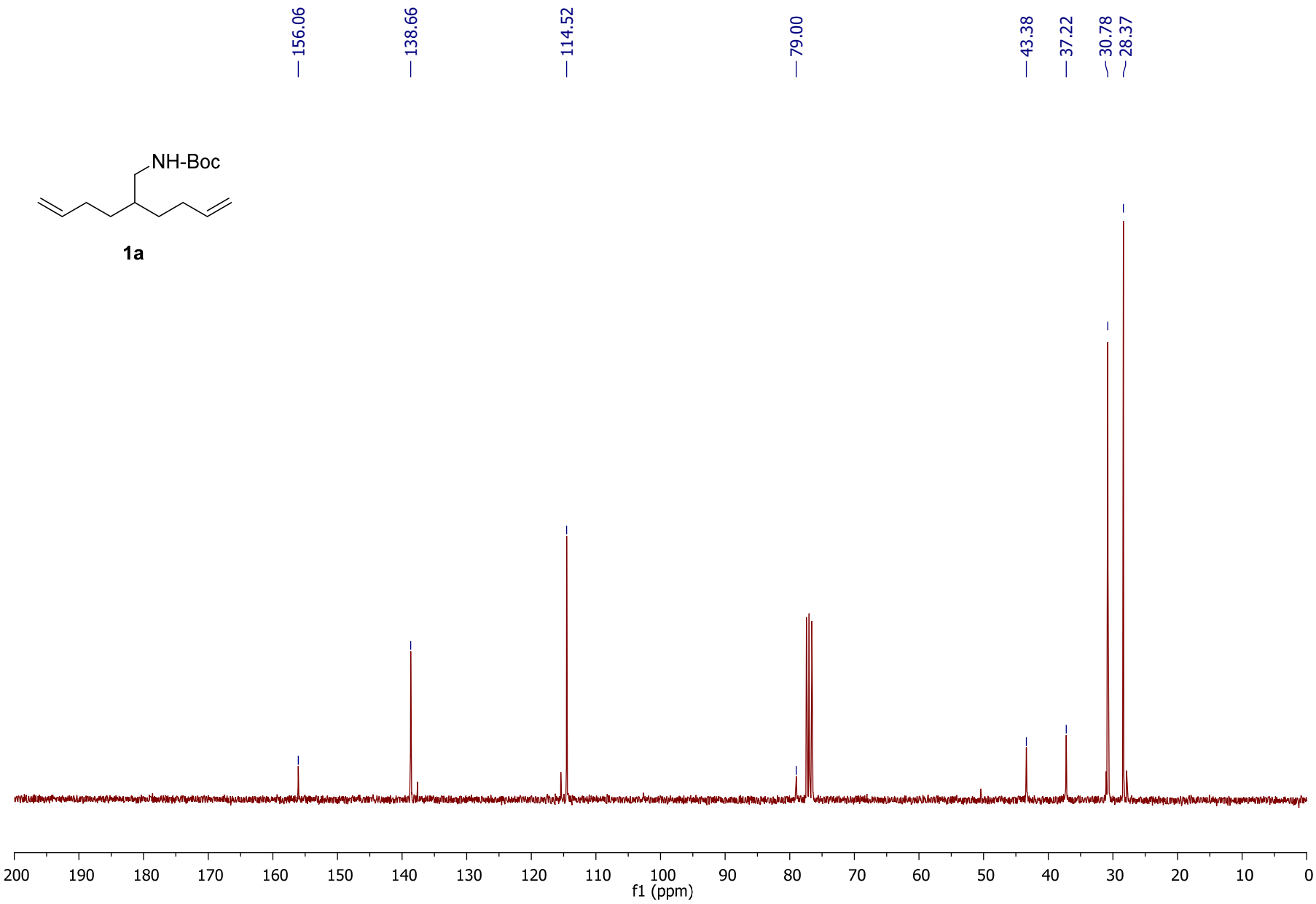

CN

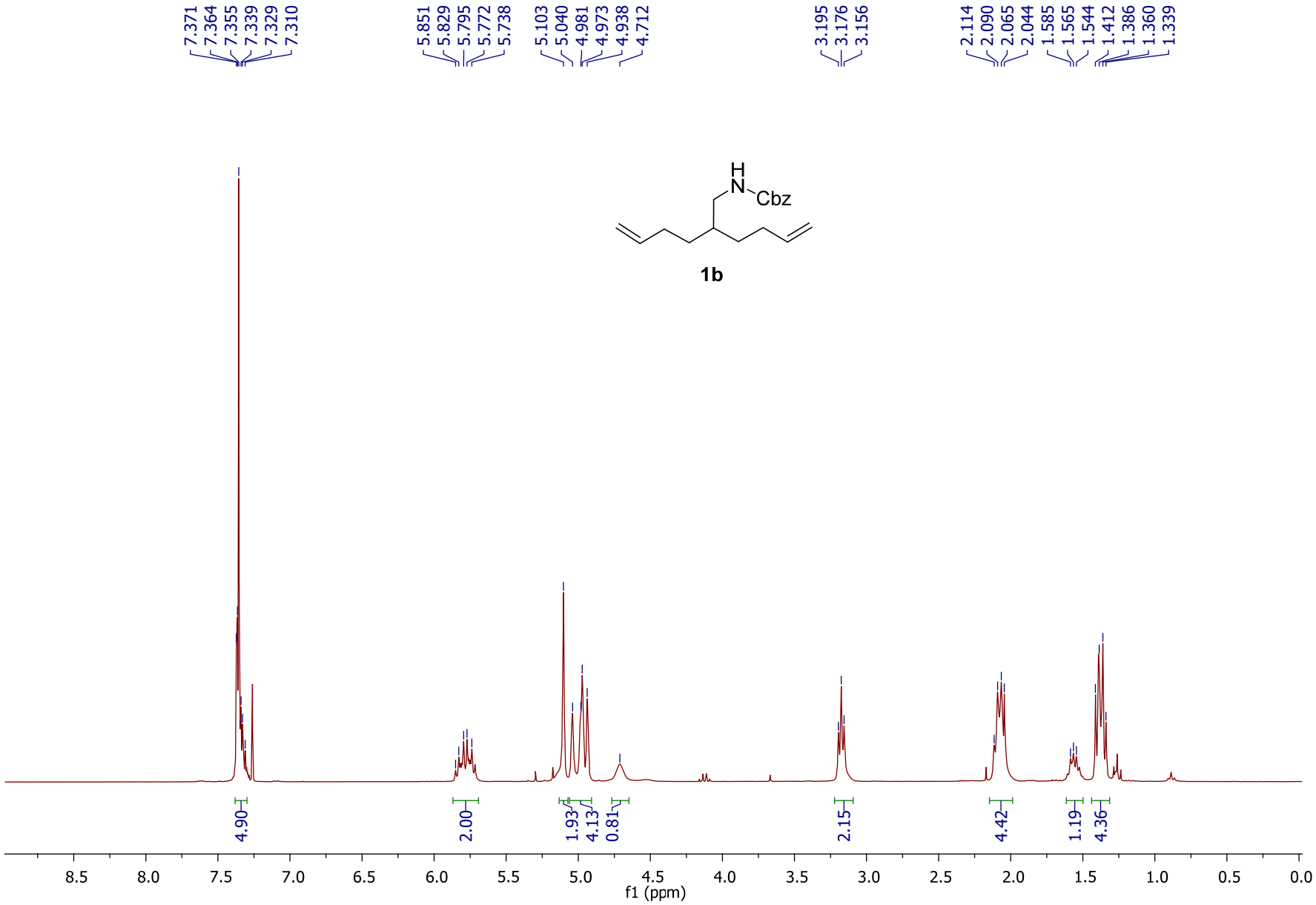
11

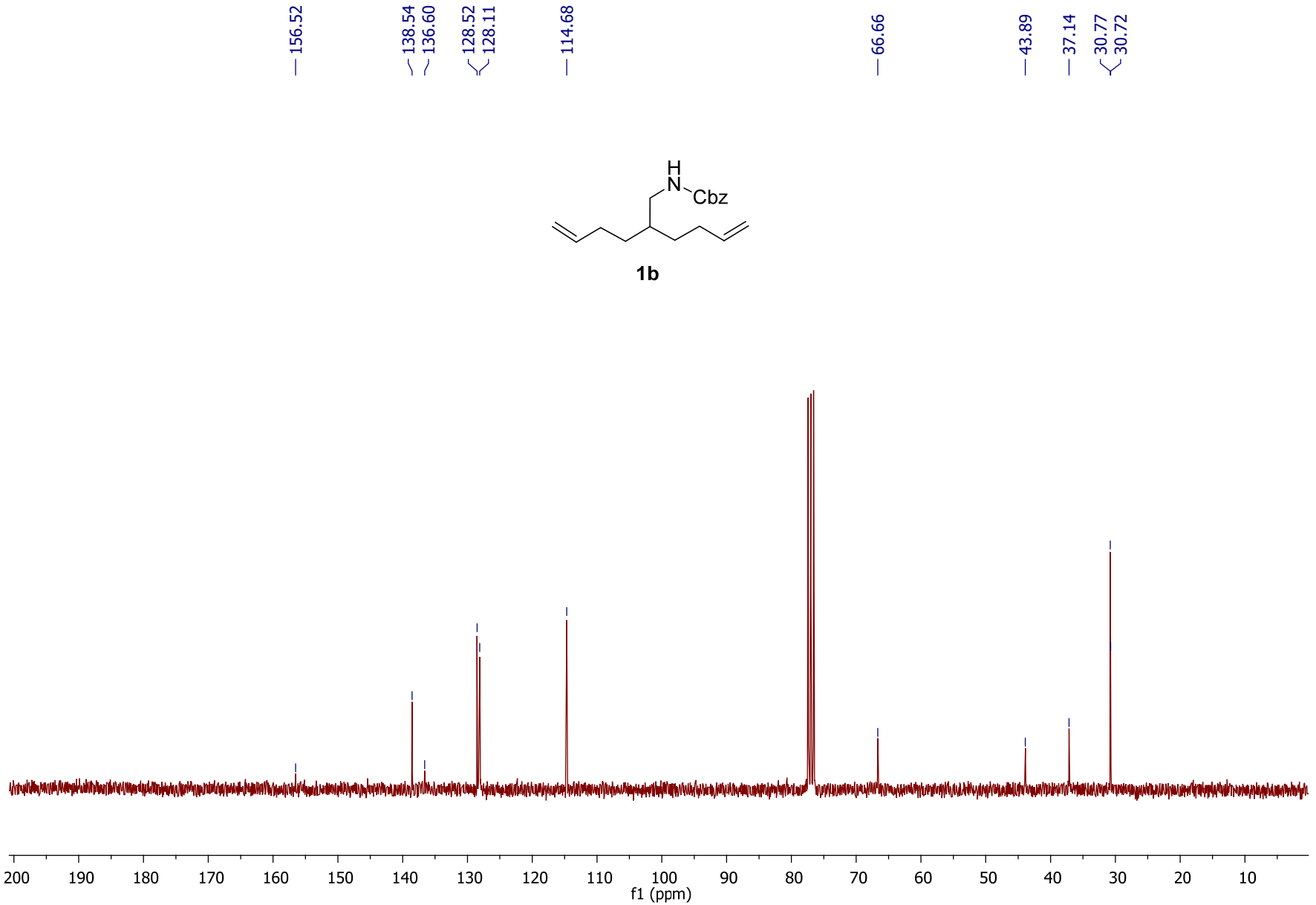
5.830
5.796
5.773
5.752
5.729
5.716
5.695
5.133
5.127
5.122
5.061
5.060
5.028
5.022
5.018
2.630
2.599
2.581
2.562
2.532
2.354
2.305
2.277
2.237
2.208
2.184
2.164
2.136
1.801
1.755
1.698
1.670
1.627
1.562
2.00
4.08
1.07
4.35
4.34
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


136.37
121.80
116.30
31.30
31.10
30.20
CN
11
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

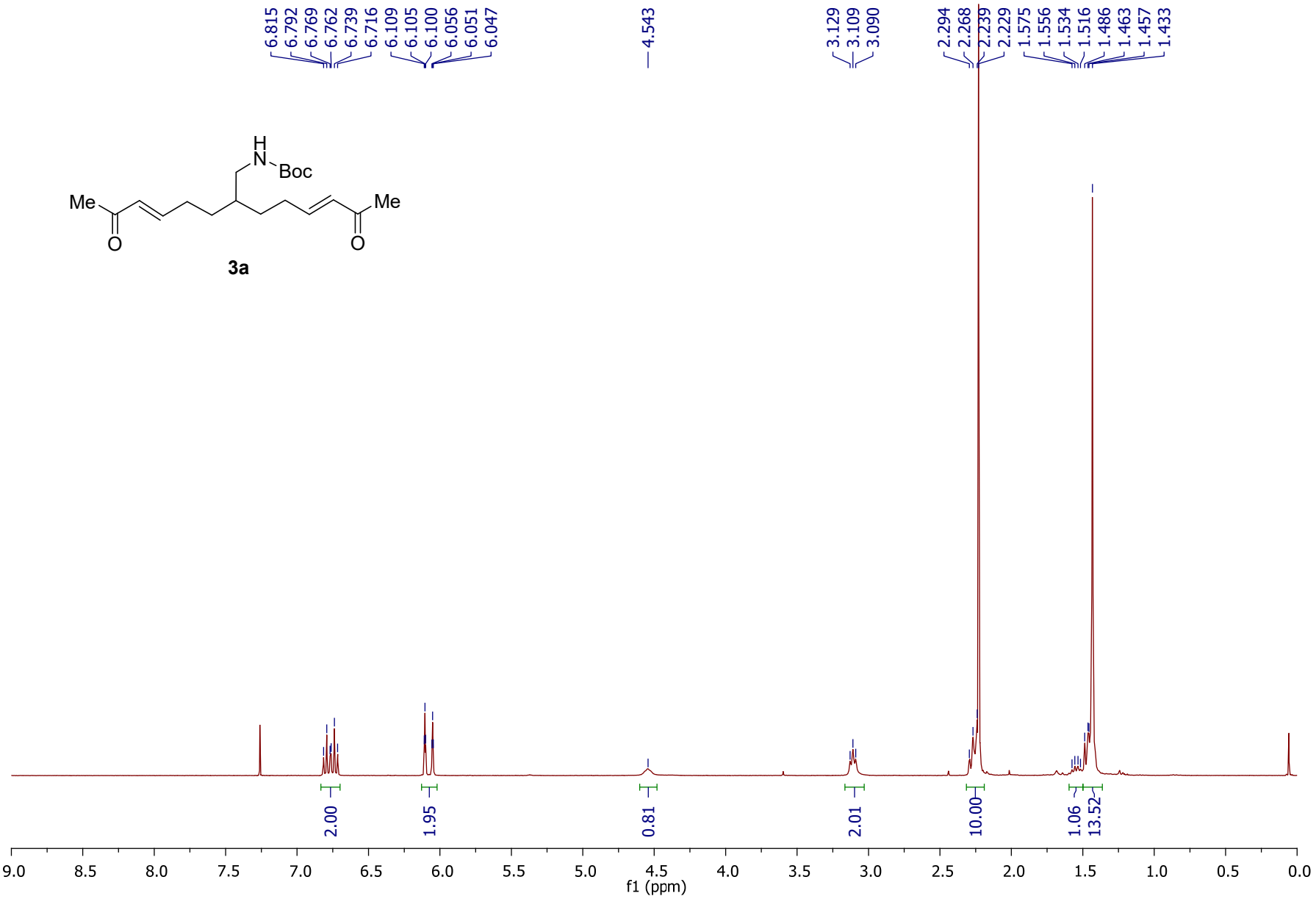

NH-Boc
1a
5.847
5.825
5.790
5.768
5.734
5.712
5.027
4.964
4.949
4.915
4.499
3.098
3.078
3.059
2.099
2.073
2.047
2.025
1.542
1.521
1.499
1.478
1.431
1.392
1.340
1.319
2.00
4.10
0.80
1.99
4.34
1.22
8.55
3.91
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

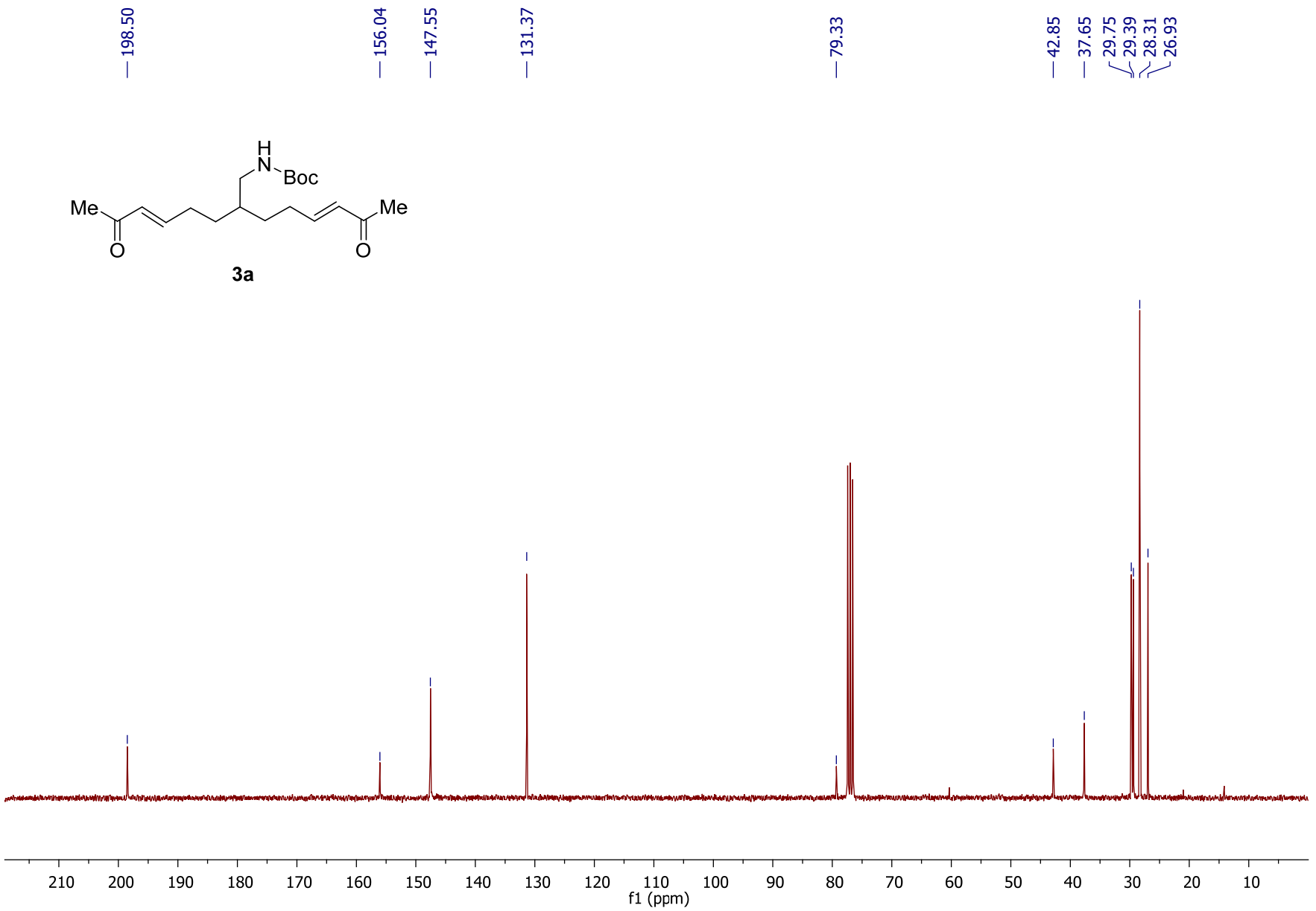

156.06
138.66
114.52
79.00
43.38
37.22
30.78
28.37
NH-Boc
1a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

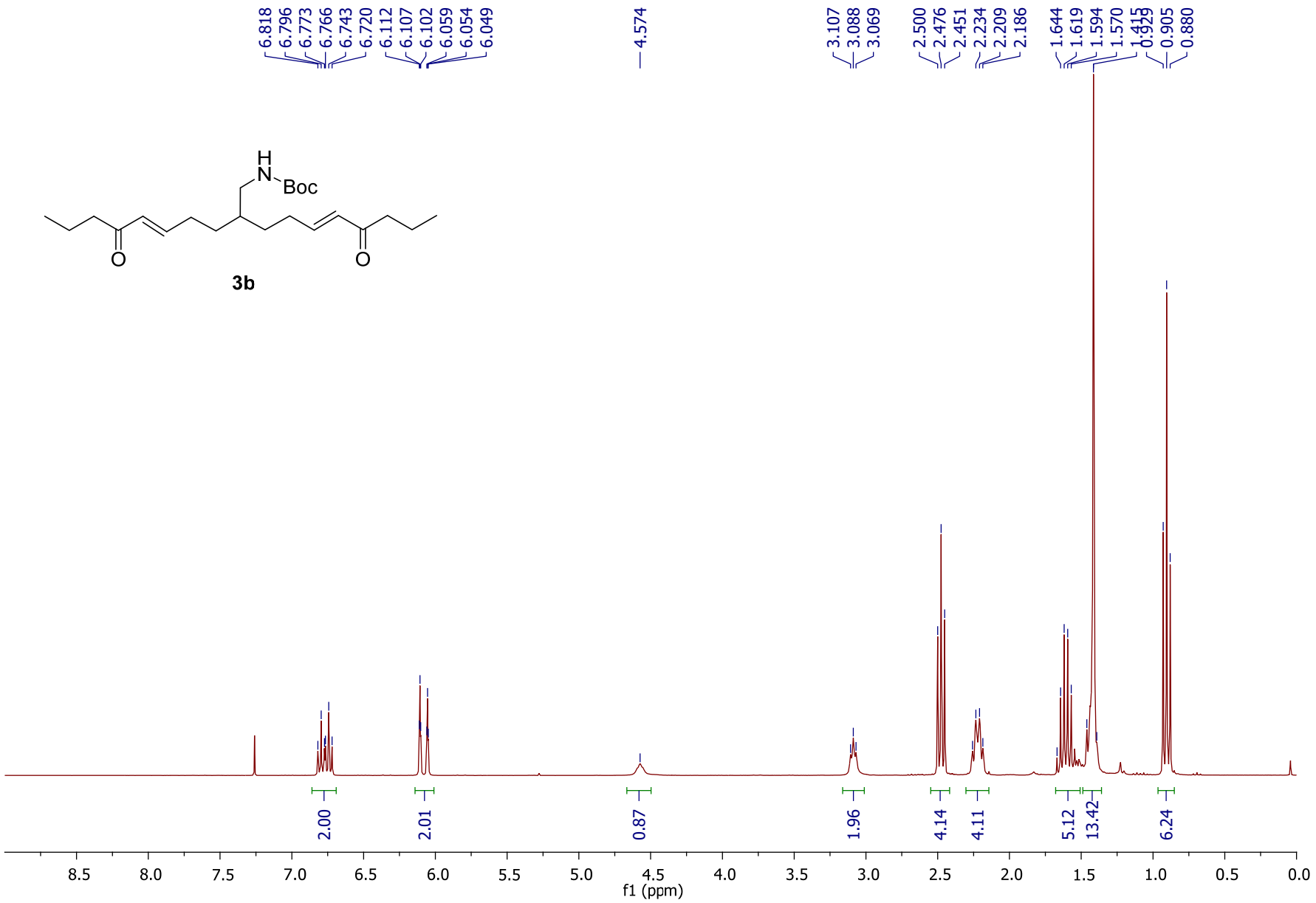

7.371
7.364
7.355
7.339
7.329
7.310
5.851
5.829
5.795
5.772
5.738
5.103
5.040
4.981
4.973
4.938
4.712
3.195
3.176
3.156
2.114
2.090
2.065
2.044
1.585
1.565
1.544
1.412
1.386
1.360
1.339
H
N
Cbz
1b
4.90
2.00
1.93
4.13
0.81
2.15
4.42
1.19
4.36
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

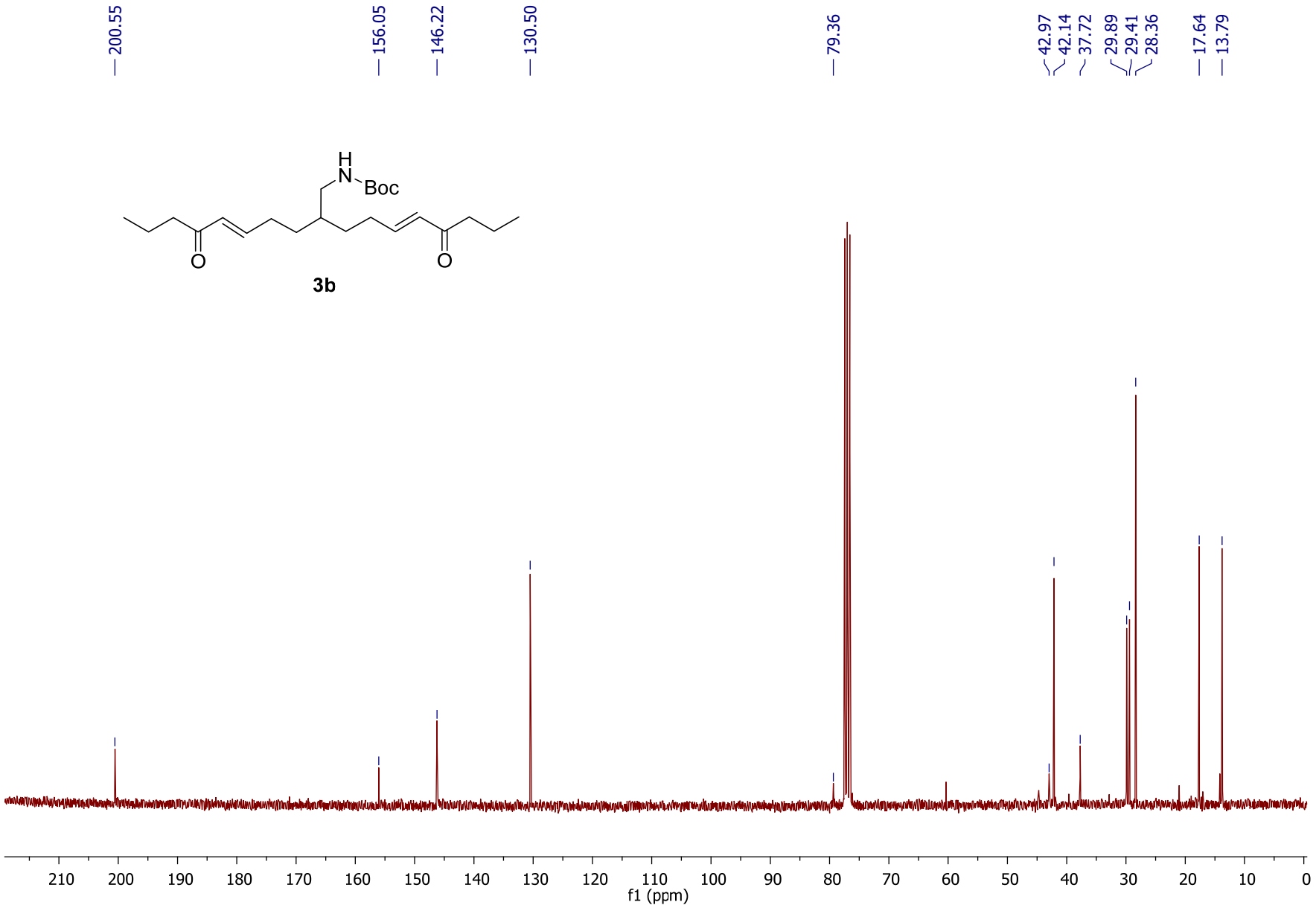

156.52
138.54
136.60
128.52
128.11
114.68
66.66
43.89
37.14
30.77
30.72
H
N
Cbz
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

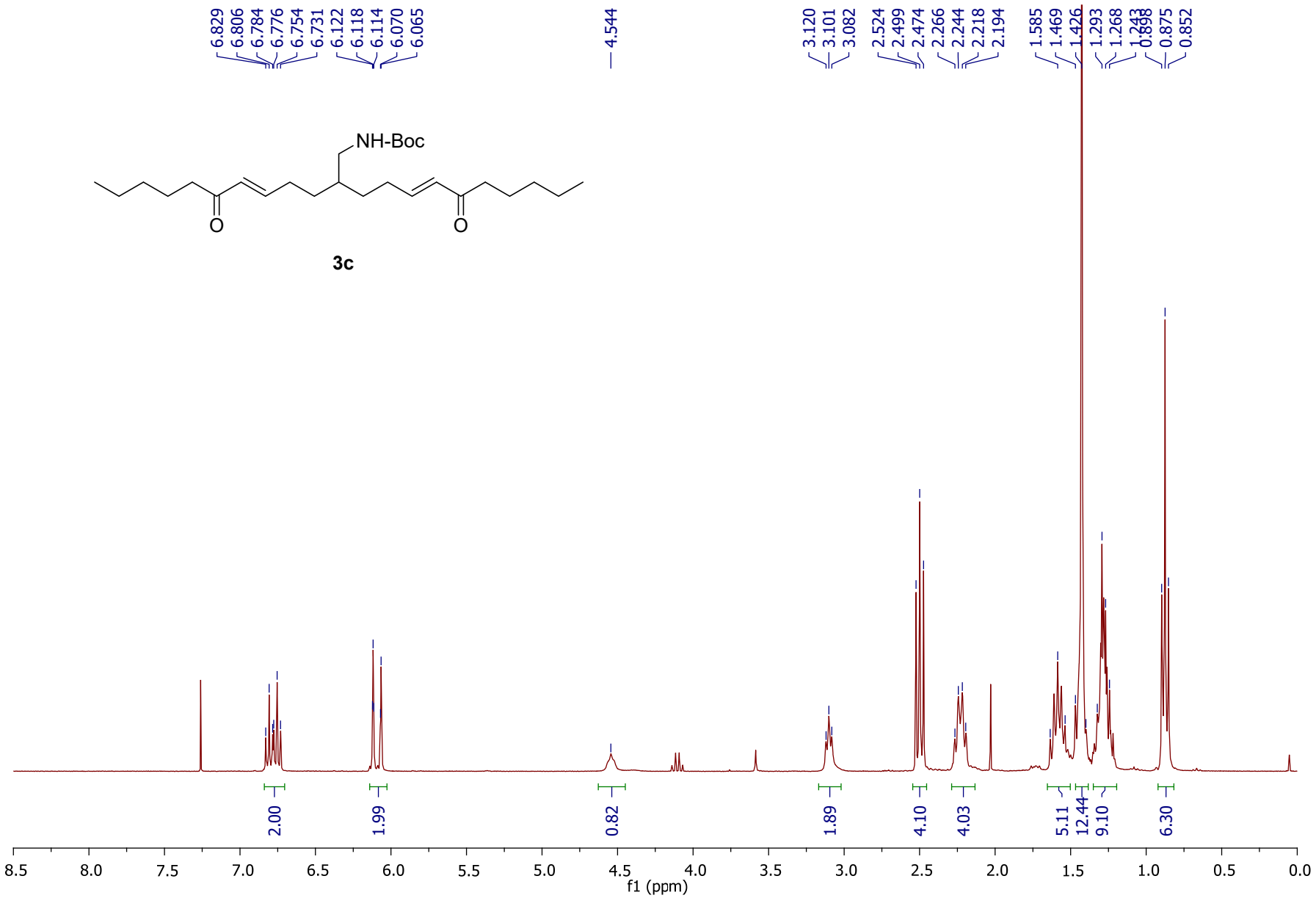
1b

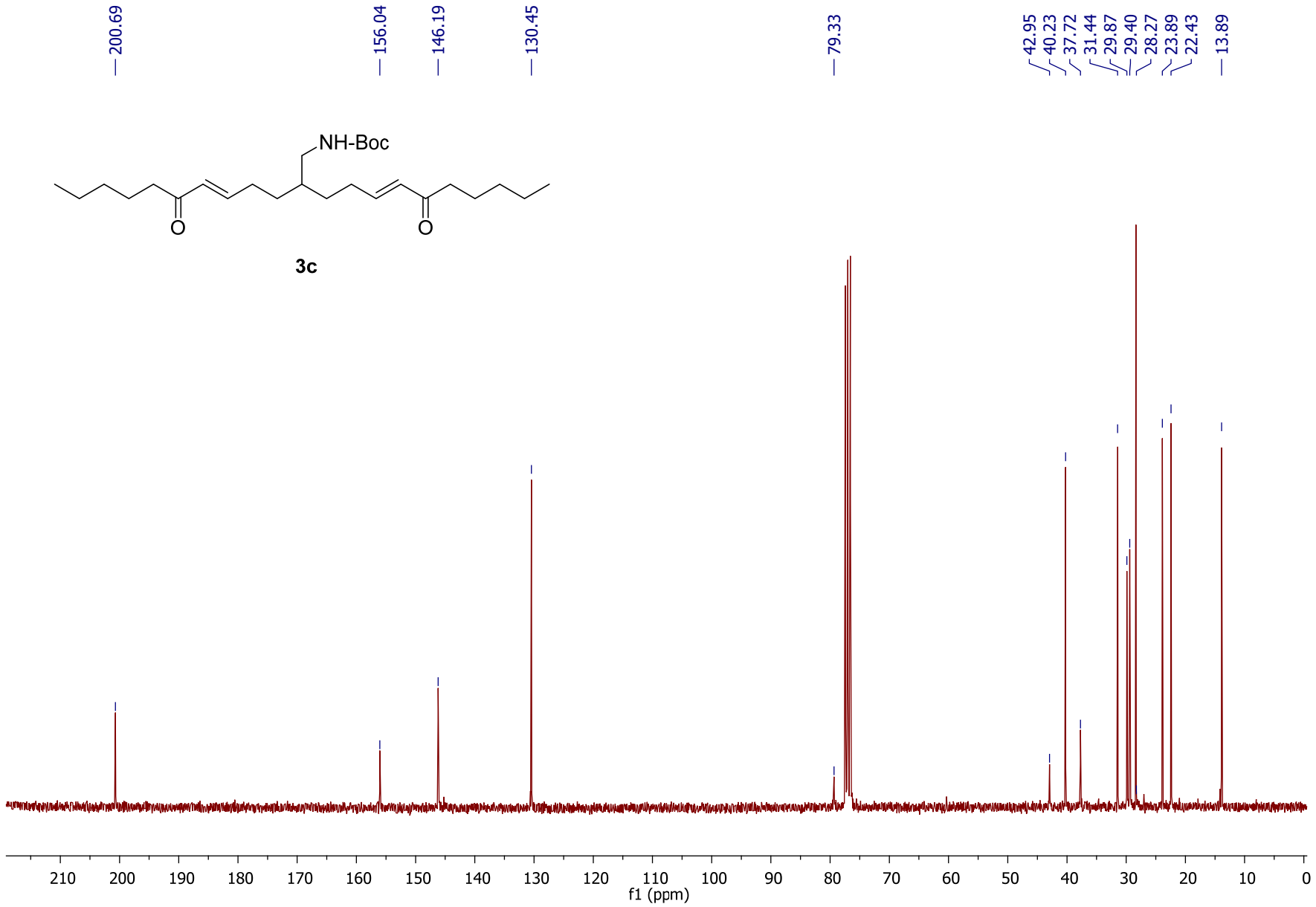

6.815
6.792
6.769
6.762
6.739
6.716
6.109
6.105
6.100
6.056
6.051
6.047
4.543
3.129
3.109
3.090
2.294
2.268
2.239
2.229
1.575
1.556
1.534
1.516
1.486
1.463
1.457
1.433
H
N
Boc
Me
Me
O
O
3a
2.00
1.95
0.81
2.01
10.00
1.06
13.52
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

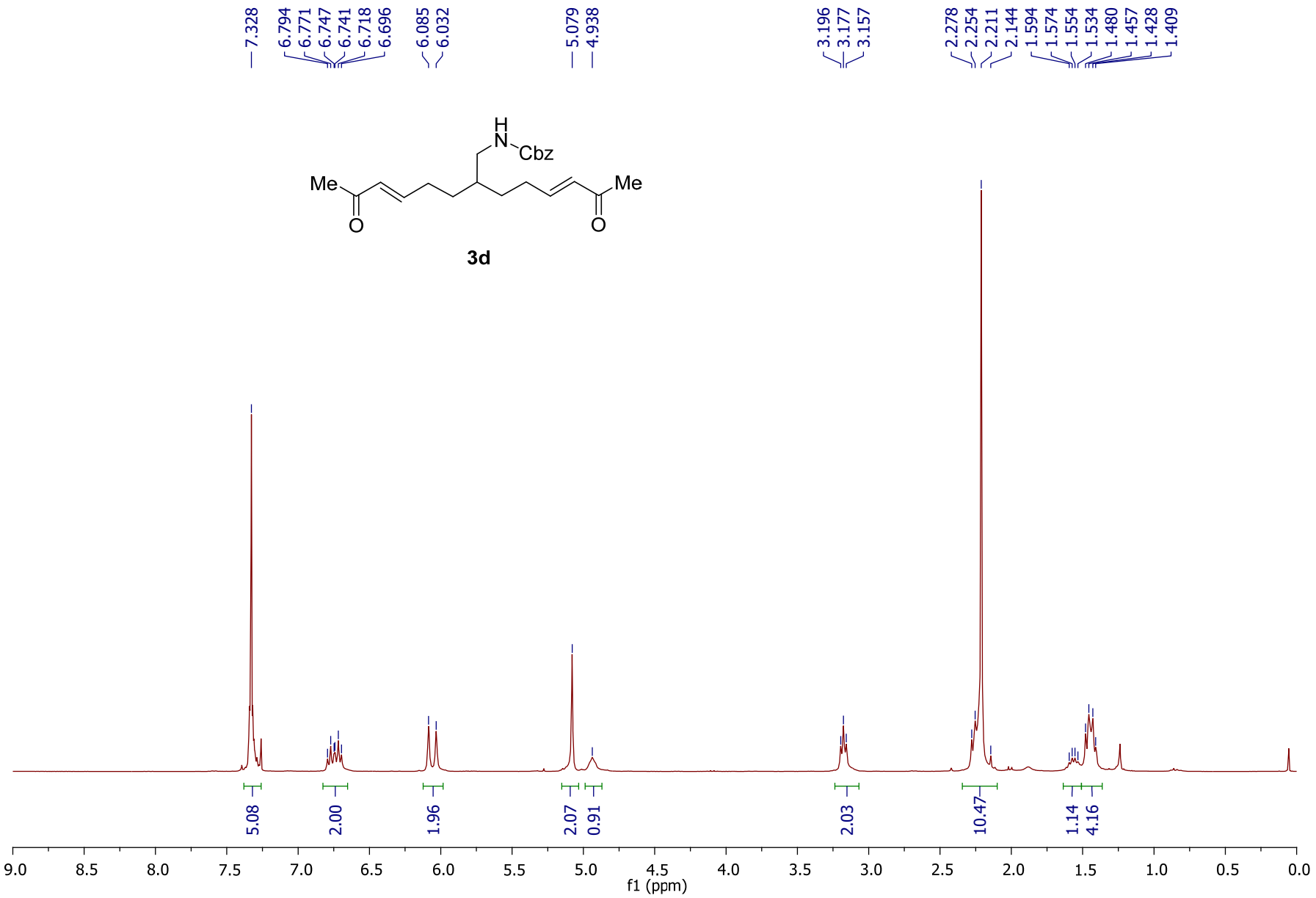

198.50
156.04
147.55
131.37
79.33
42.85
37.65
29.75
29.39
28.31
26.93
H
N
Boc
Me
Me
O
O
3a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

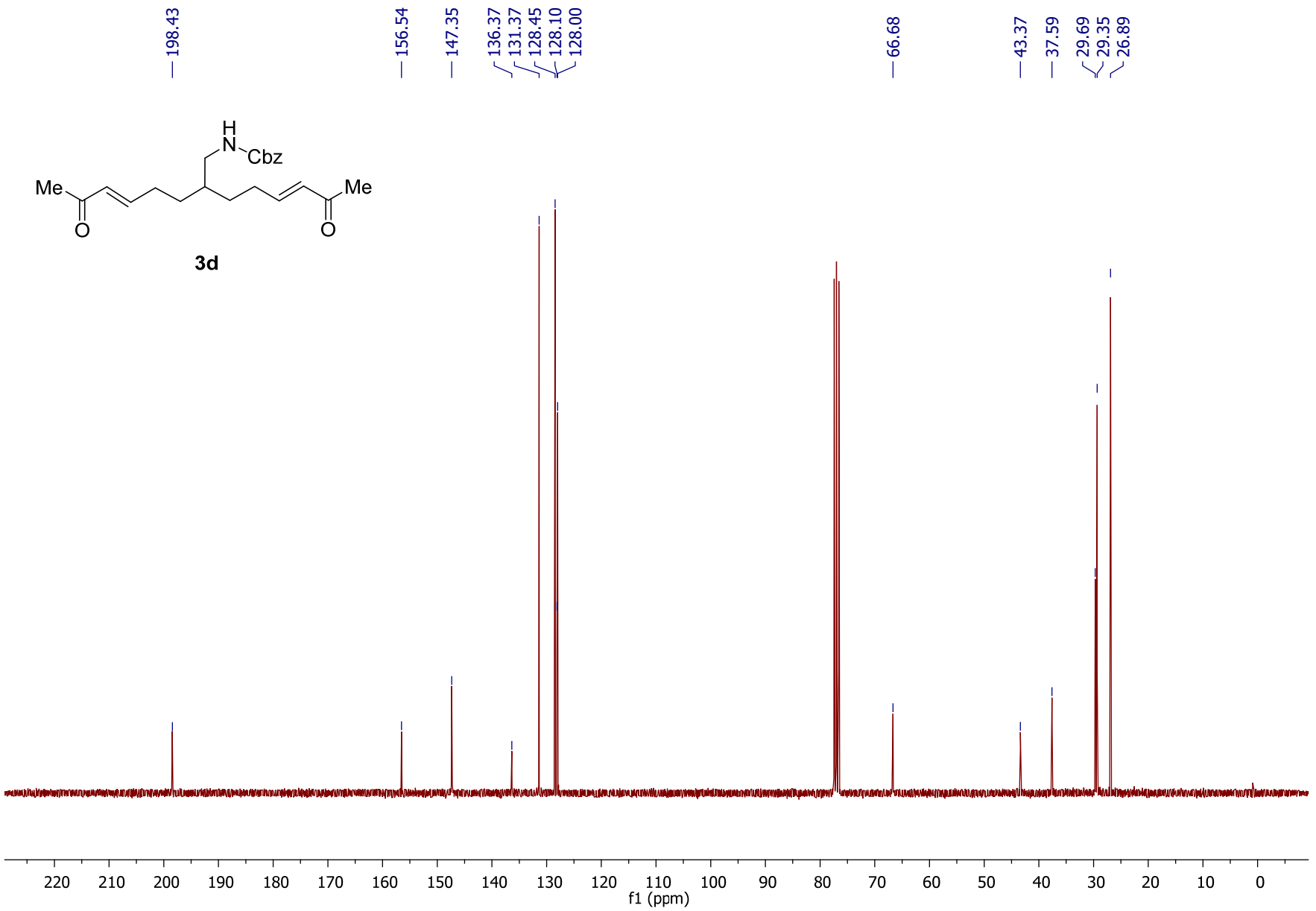

6.818
6.796
6.773
6.766
6.743
6.720
6.112
6.107
6.102
6.059
6.054
6.049
4.574
3.107
3.088
3.069
2.500
2.476
2.451
2.234
2.209
2.186
1.644
1.619
1.594
1.570
1.415
0.929
0.905
0.880
H
N
Boc
O
O
3b
2.00
2.01
0.87
1.96
4.14
4.11
5.12
13.42
6.24
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

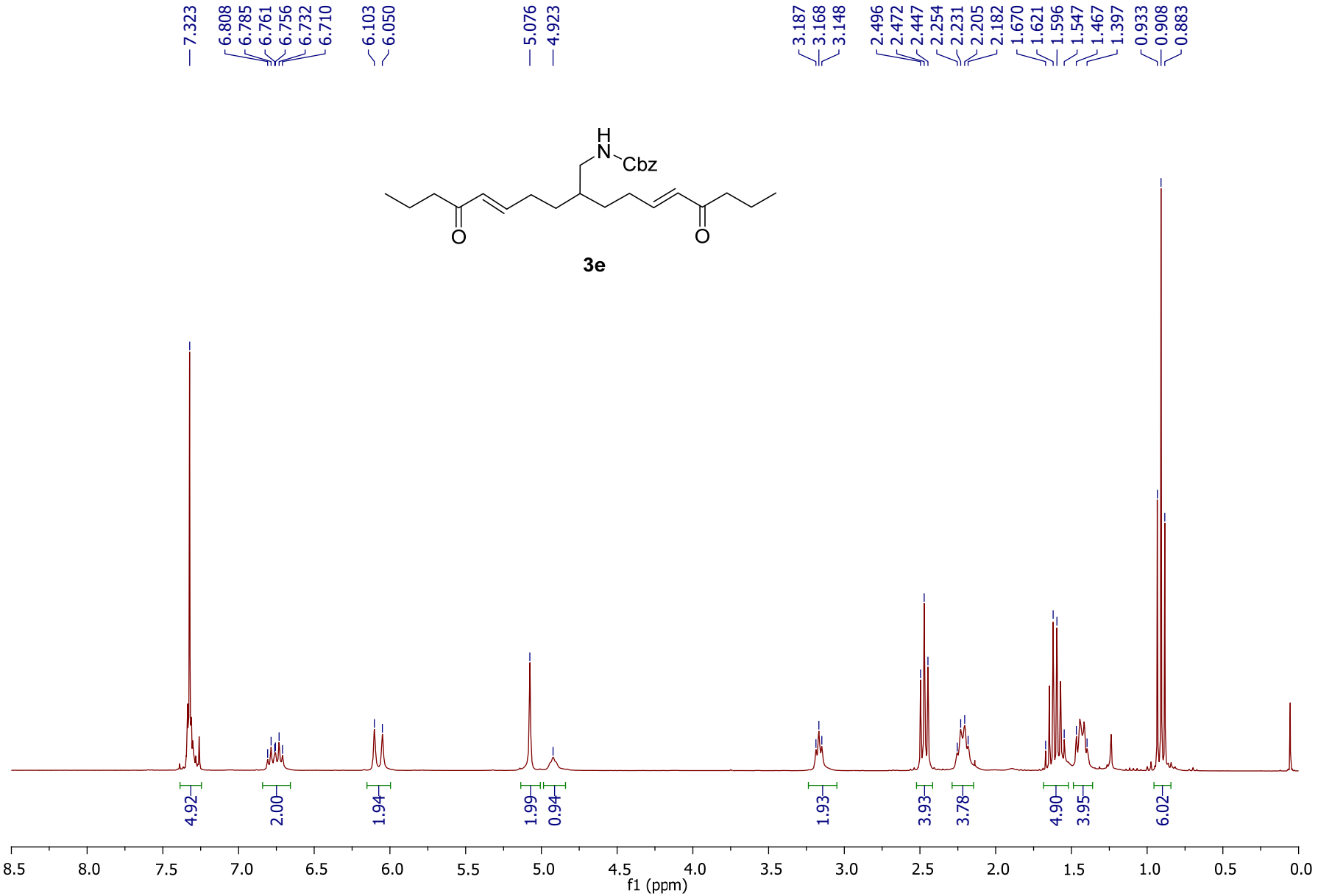

200.55
156.05
146.22
130.50
79.36
42.97
42.14
37.72
29.89
29.41
28.36
17.64
13.79
H
N
Boc
O
O
3b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

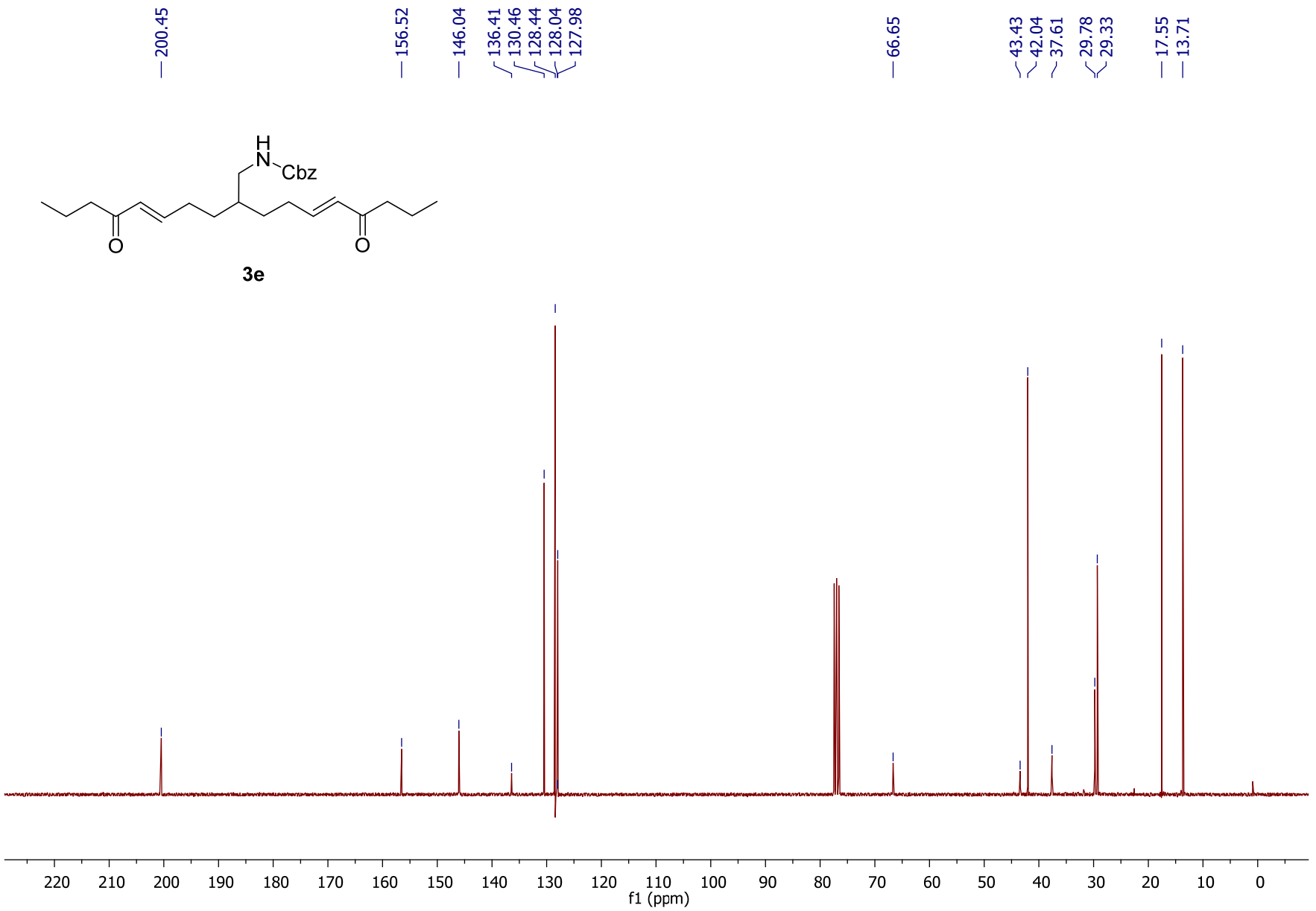

6.829
6.806
6.784
6.776
6.754
6.731
6.122
6.118
6.114
6.070
6.065
4.544
3.120
3.101
3.082
2.524
2.499
2.474
2.266
2.244
2.218
2.194
1.585
1.469
1.426
1.293
1.268
1.243
0.898
0.875
0.852
NH-Boc
O
O
3c
2.00
1.99
0.82
1.89
4.10
4.03
5.11
12.44
9.10
6.30
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

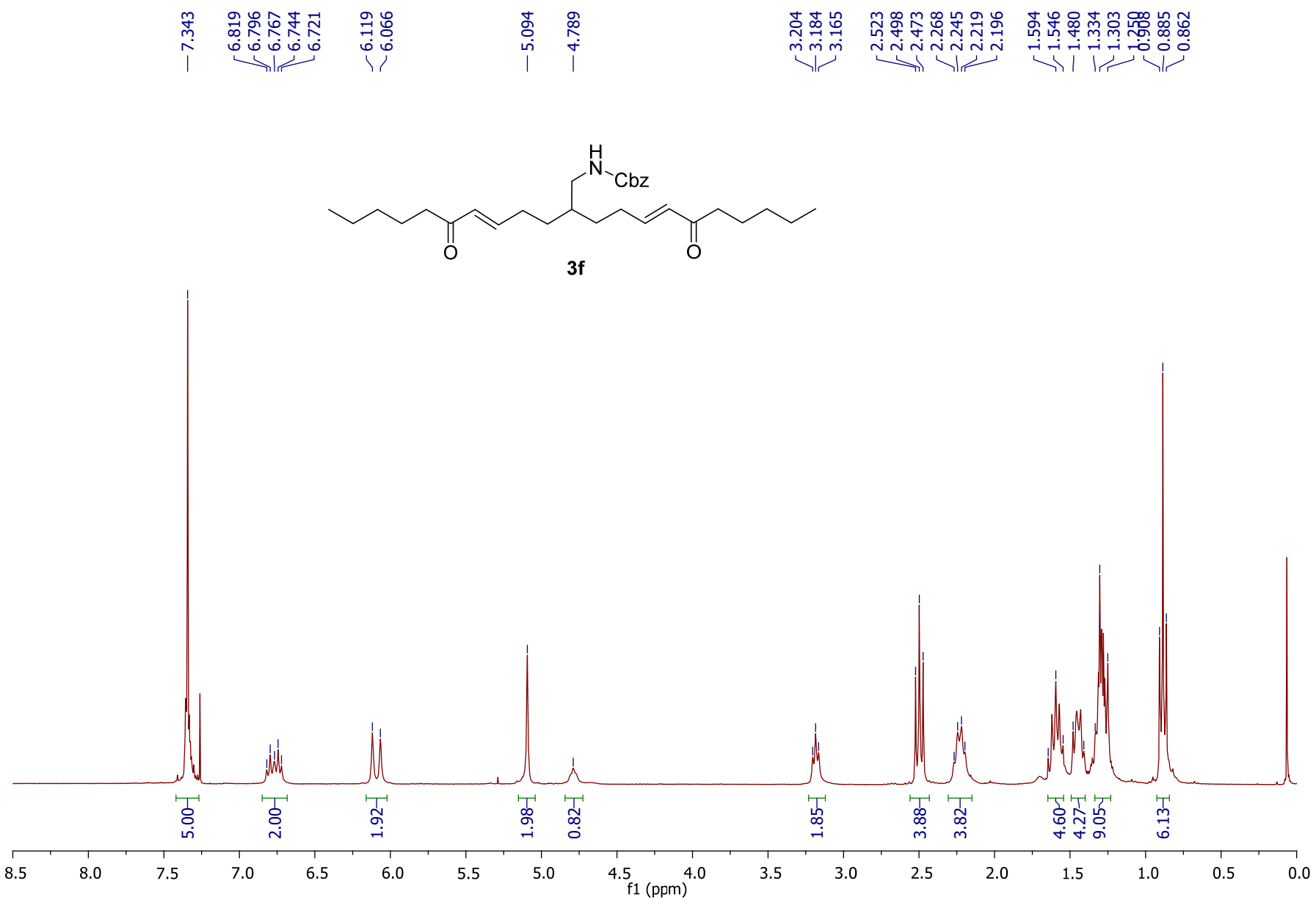

200.69
156.04
146.19
130.45
79.33
42.95
40.23
37.72
31.44
29.87
29.40
28.27
23.89
22.43
13.89
NH-Boc
O
O
3c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

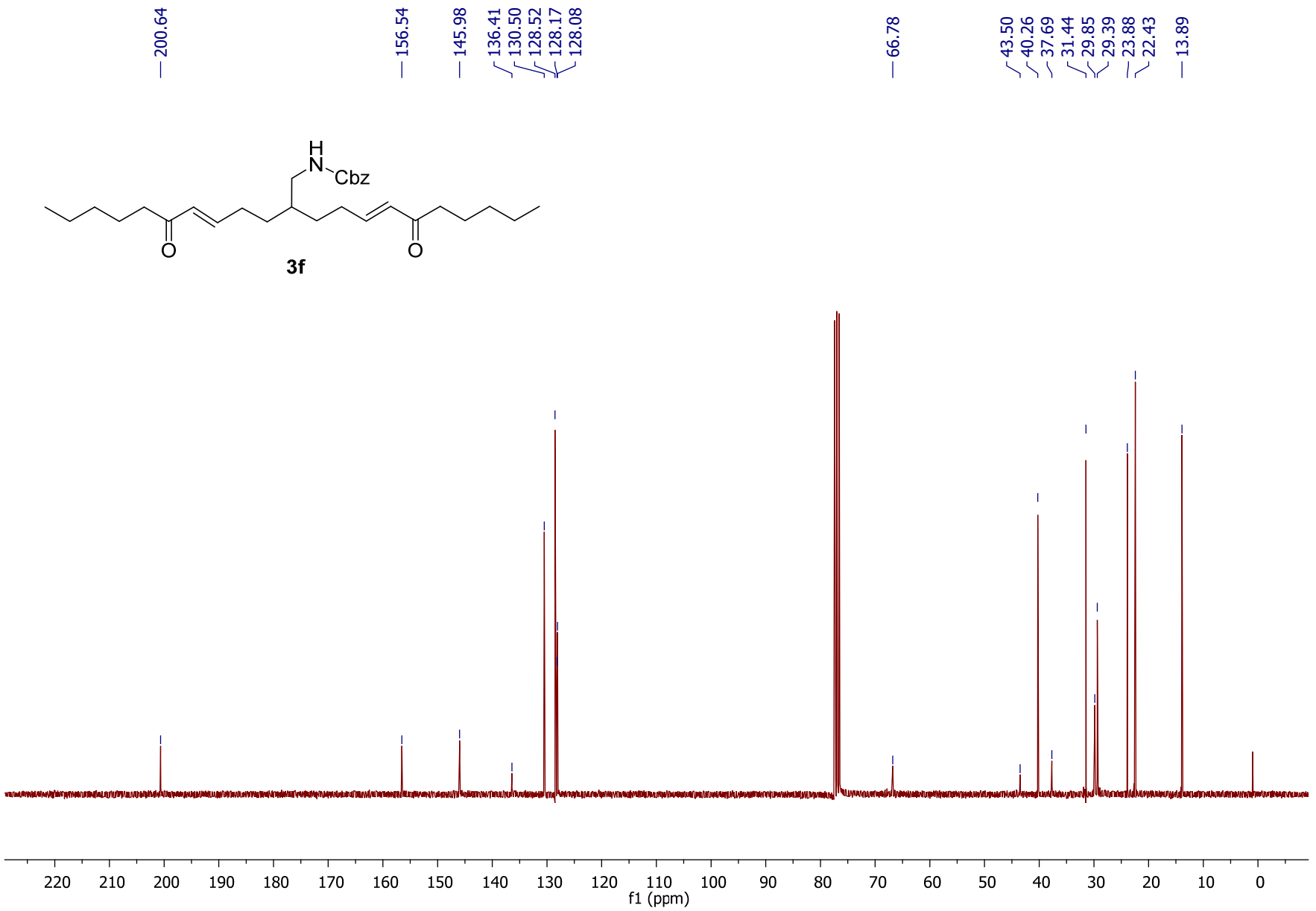

7.328
6.794
6.771
6.747
6.741
6.718
6.696
6.085
6.032
5.079
4.938
3.196
3.177
3.157
2.278
2.254
2.211
2.144
1.594
1.574
1.554
1.534
1.480
1.457
1.428
1.409
H
N
Cbz
Me
Me
O
O
3d
5.08
2.00
1.96
2.07
0.91
2.03
10.47
1.14
4.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

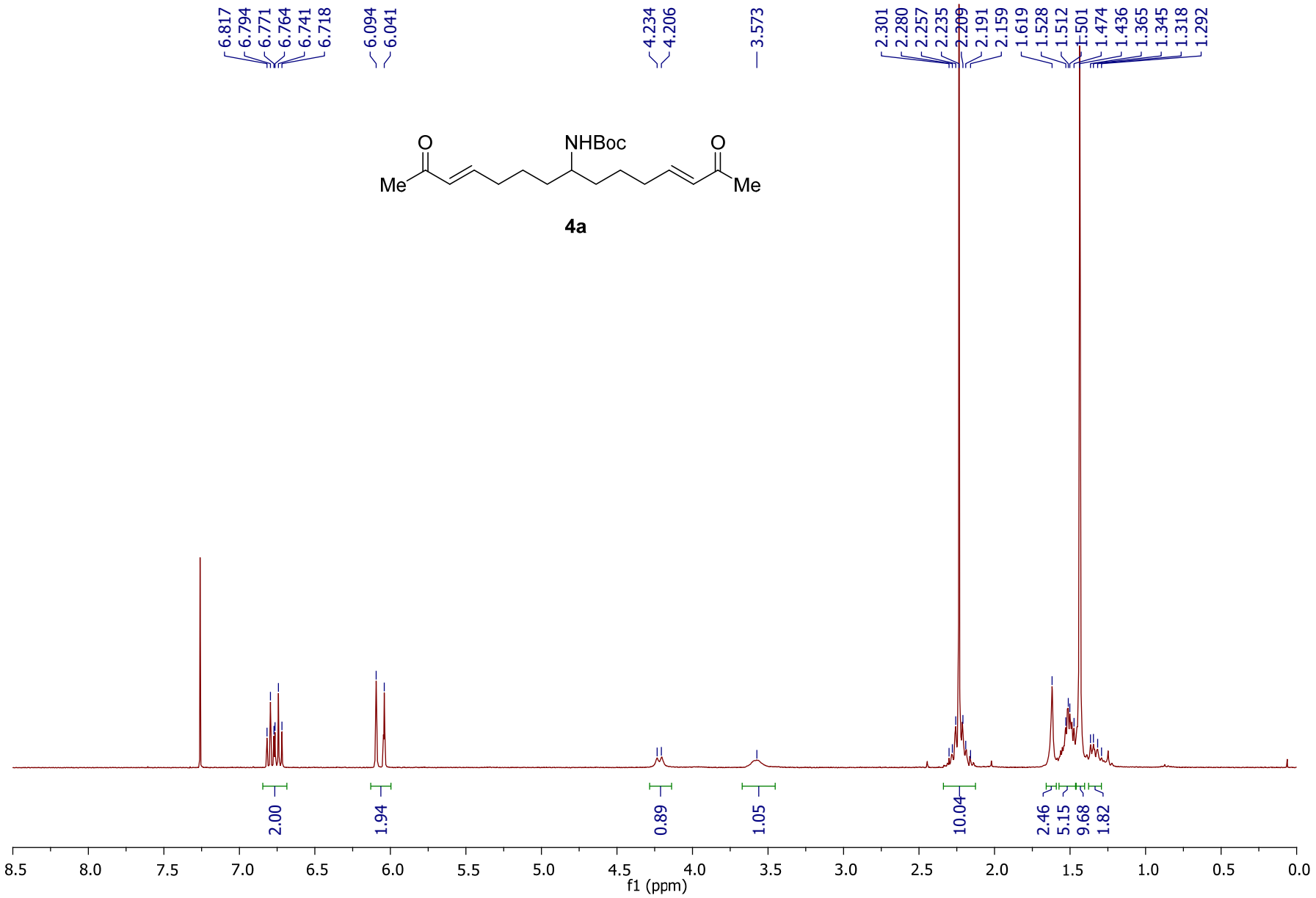

198.43
156.54
147.35
136.37
131.37
128.45
128.10
128.00
66.68
43.37
37.59
29.69
29.35
26.89
H
N
Cbz
Me
Me
O
O
3d
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.323
6.808
6.785
6.761
6.756
6.732
6.710
6.103
6.050
5.076
4.923
3.187
3.168
3.148
2.496
2.472
2.447
2.254
2.231
2.205
2.182
1.670
1.621
1.596
1.547
1.467
1.397
0.933
0.908
0.883
H
N
Cbz
O
O
3e
4.92
2.00
1.94
1.99
0.94
1.93
3.93
3.78
4.90
3.95
6.02
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
f1 (ppm)

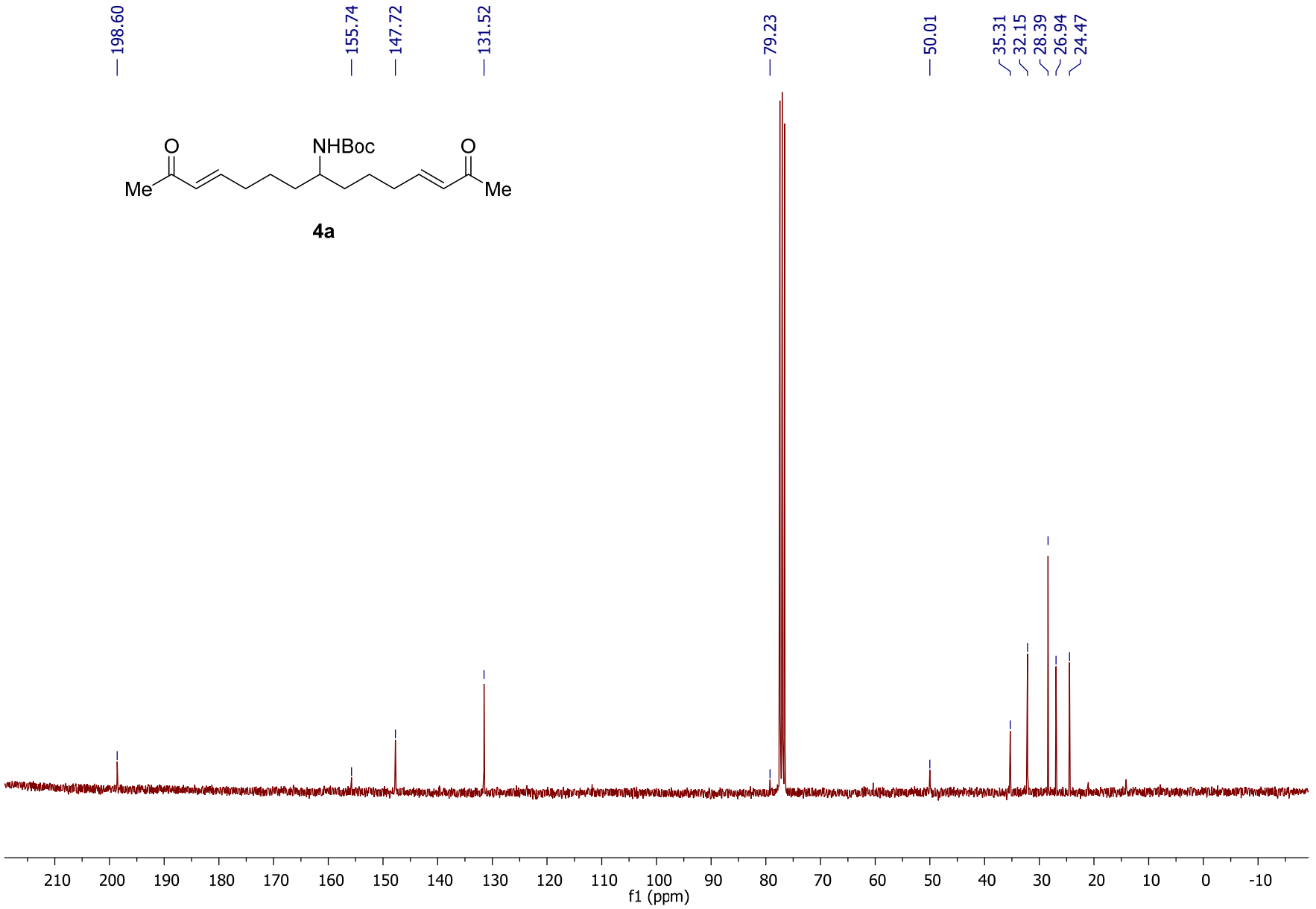

200.45
156.52
146.04
136.41
130.46
128.44
128.04
127.98
66.65
43.43
42.04
37.61
29.78
29.33
17.55
13.71
H
N
Cbz
O
O
3e
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

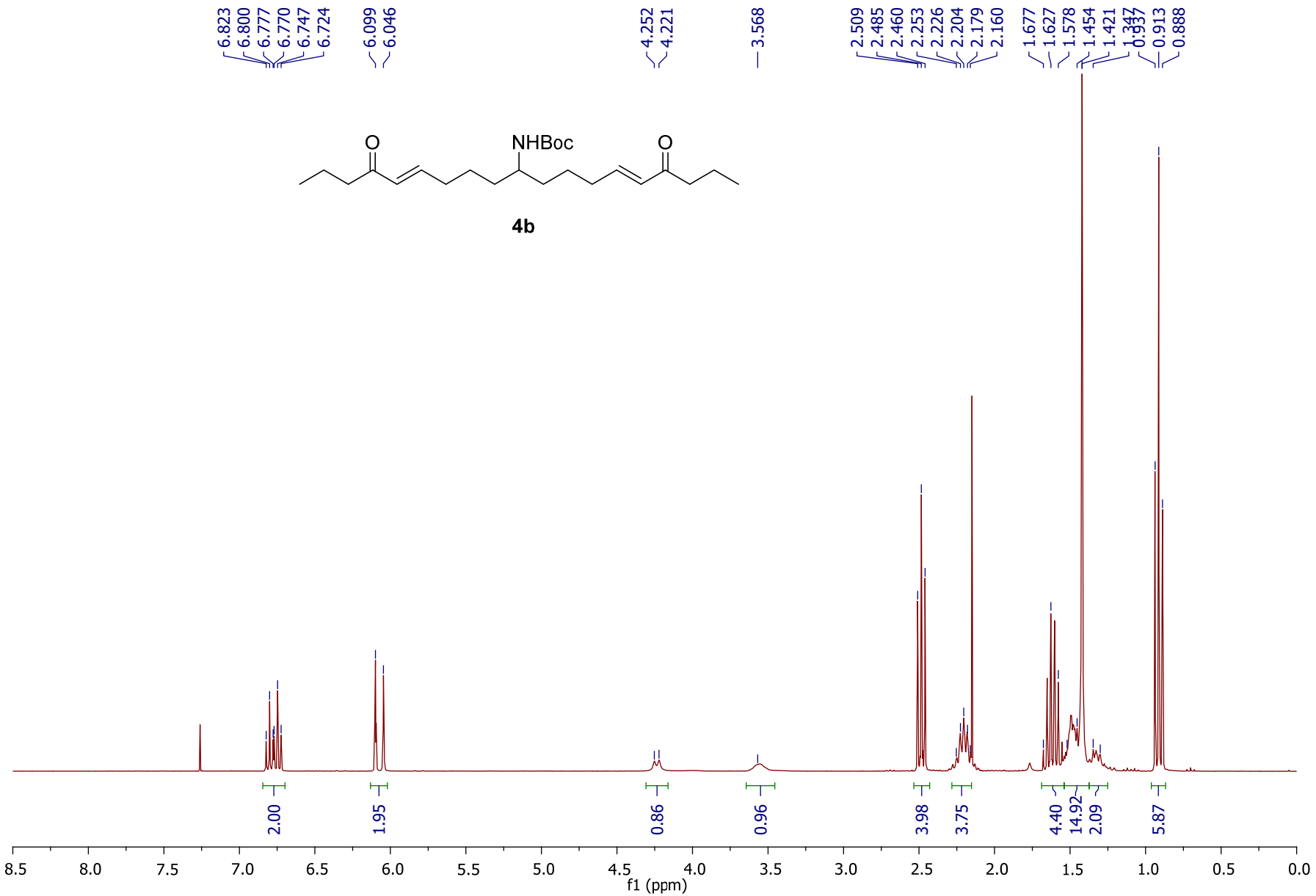

7.343
6.819
6.796
6.767
6.744
6.721
6.119
6.066
5.094
4.789
3.204
3.184
3.165
2.523
2.498
2.473
2.268
2.245
2.219
2.196
1.594
1.546
1.480
1.334
1.303
1.250
0.908
0.885
0.862
H
N
Cbz
O
O
3f
5.00
2.00
1.92
1.98
0.82
1.85
3.88
3.82
4.60
4.27
9.05
6.13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

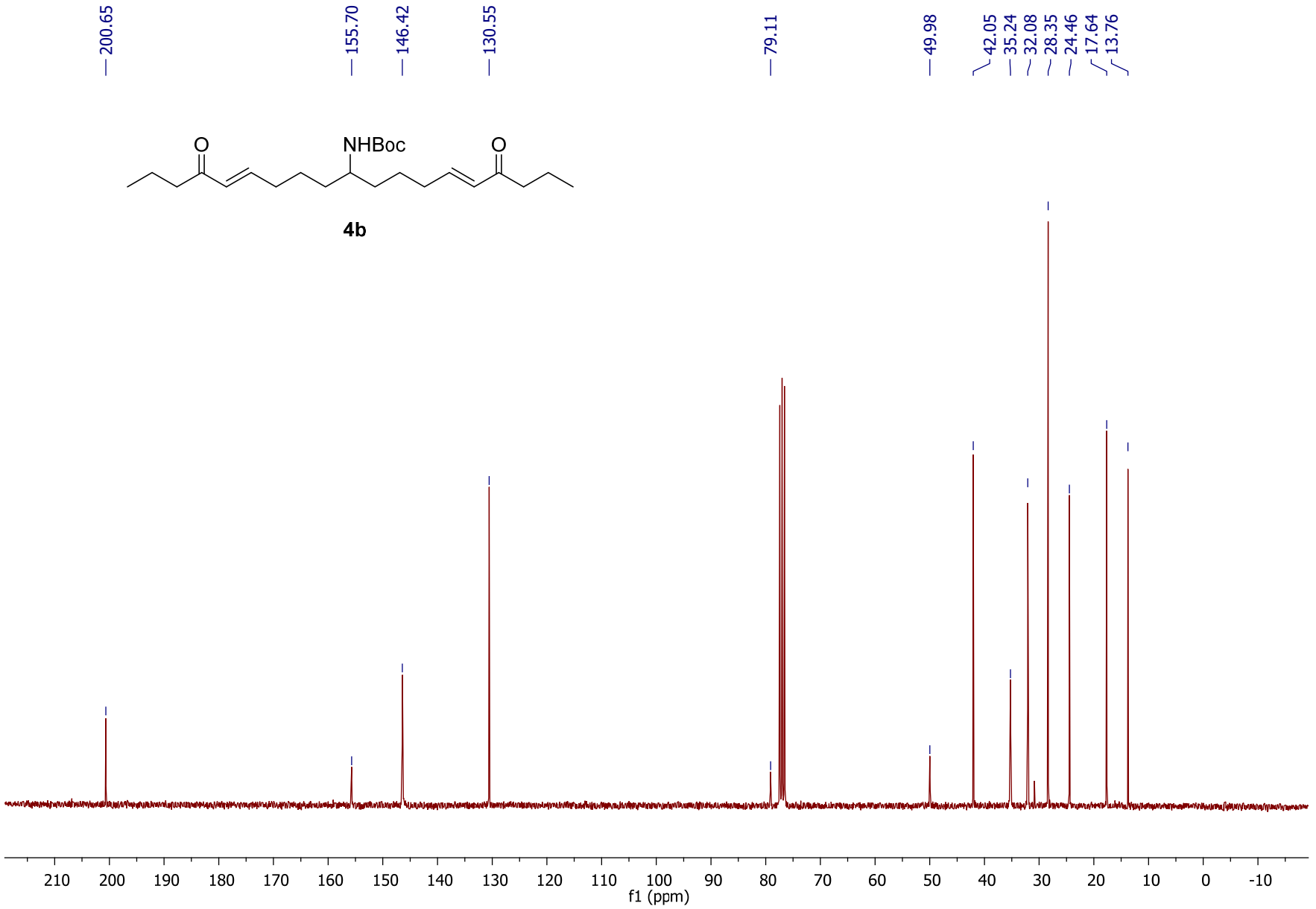

200.64
156.54
145.98
136.41
130.50
128.52
128.17
128.08
66.78
43.50
40.26
37.69
31.44
29.85
29.39
23.88
22.43
13.89
H
N
Cbz
O
O
3f
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

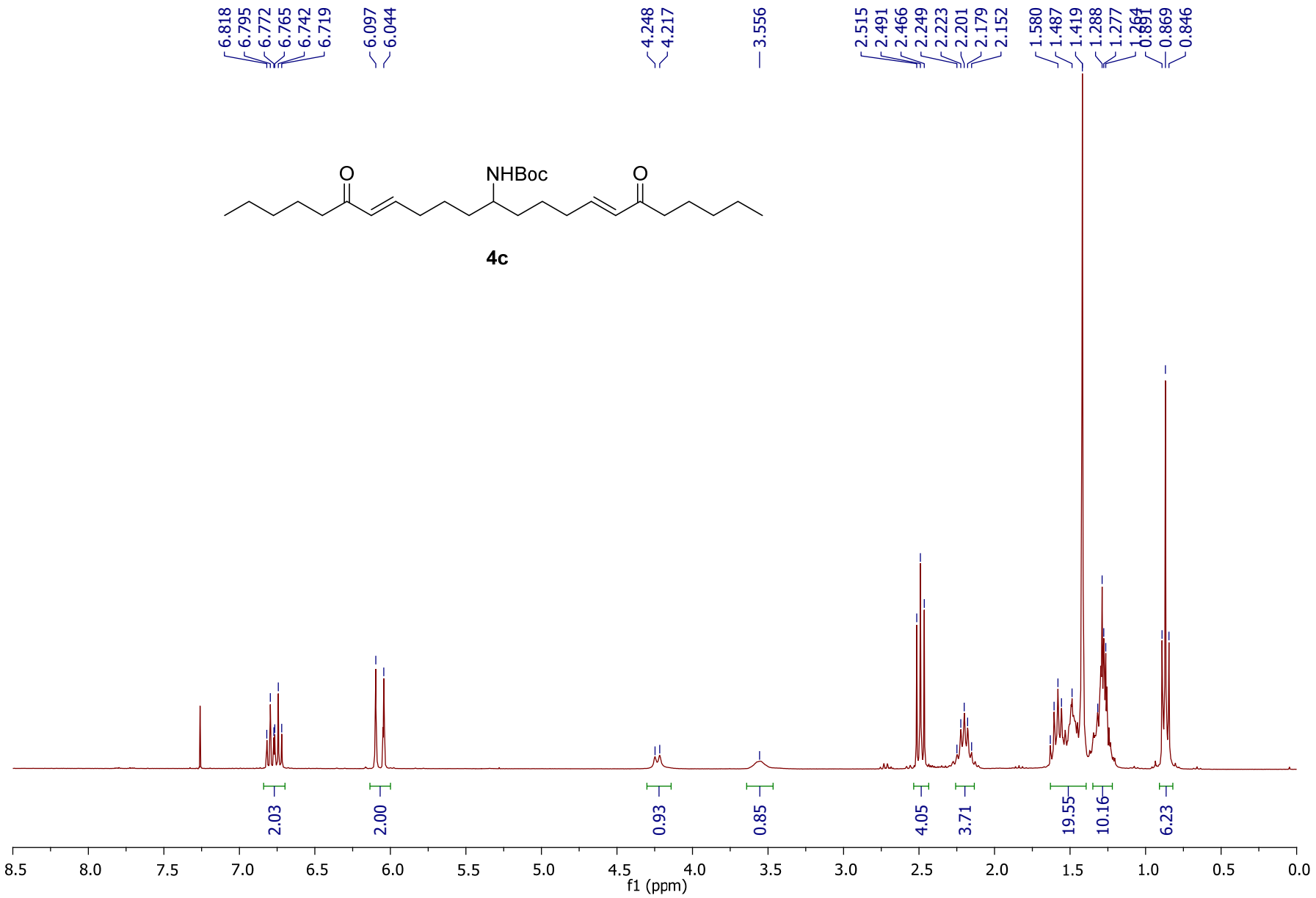

6.817
6.794
6.771
6.764
6.741
6.718
6.094
6.041
4.234
4.206
3.573
2.301
2.280
2.257
2.235
2.209
2.191
2.159
1.619
1.528
1.512
1.501
1.474
1.436
1.365
1.345
1.318
1.292
O
NHBoc
O
Me
Me
2.00
1.94
0.89
1.05
10.04
2.46
5.15
9.68
1.82
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

4a

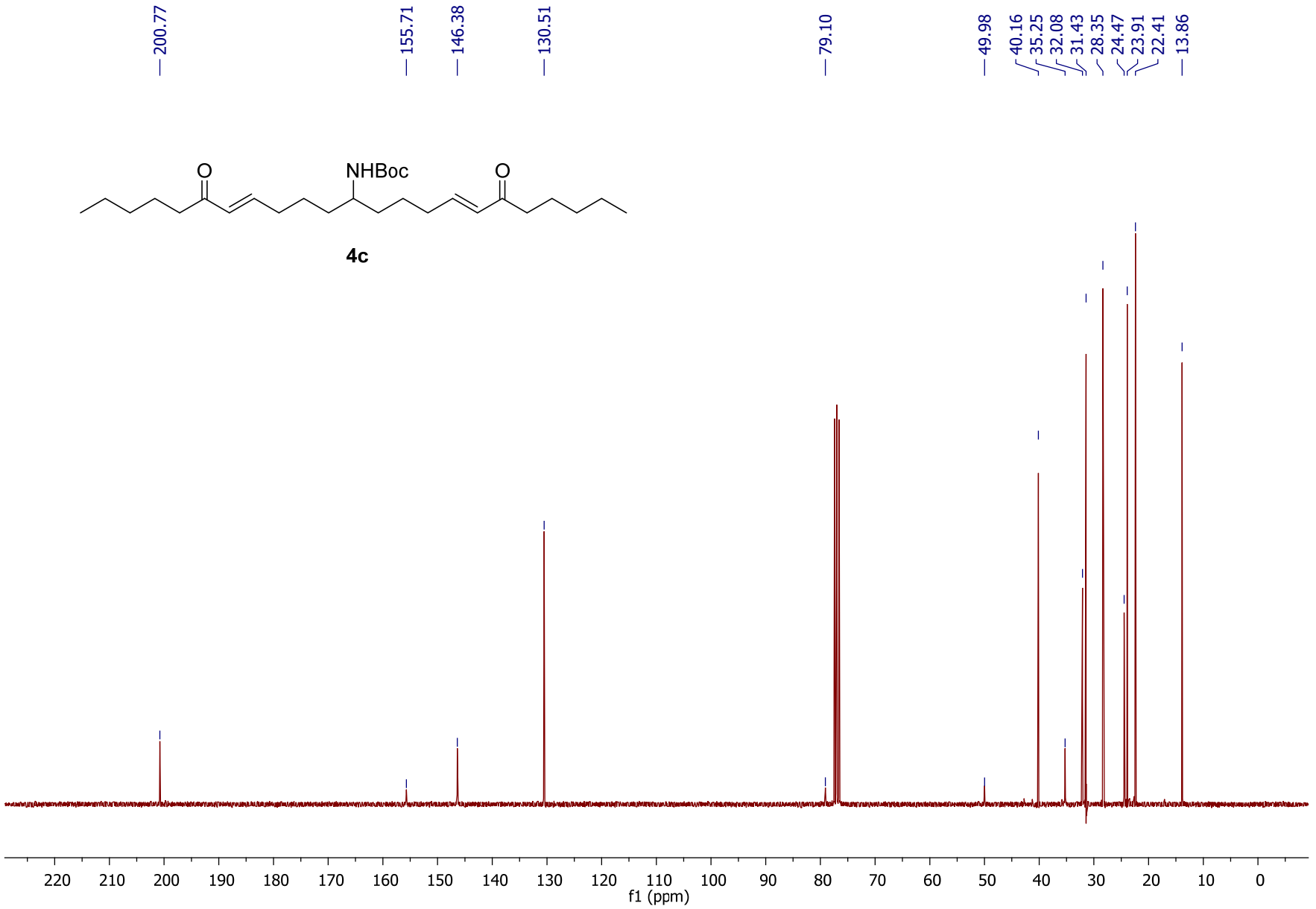

198.60
155.74
147.72
131.52
79.23
50.01
35.31
32.15
28.39
26.94
24.47
O
NHBoc
O
Me
Me
4a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

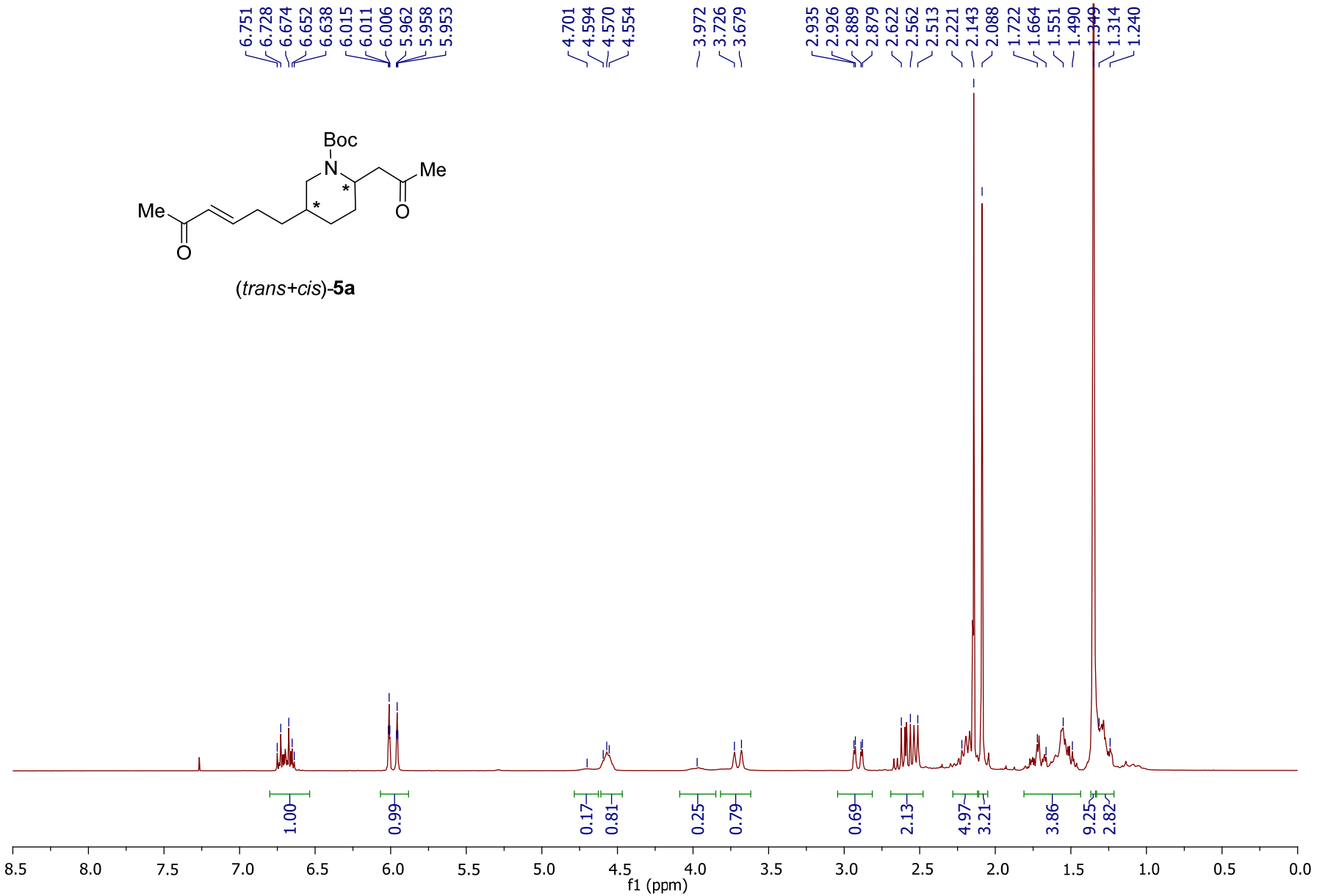

6.823
6.800
6.777
6.770
6.747
6.724
6.099
6.046
4.252
4.221
3.568
2.509
2.485
2.460
2.253
2.226
2.204
2.179
2.160
1.677
1.627
1.578
1.454
1.421
1.347
0.937
0.913
0.888
O
NHBoc
O
4b
2.00
1.95
0.86
0.96
3.98
3.75
4.40
14.92
2.09
5.87
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


200.65
155.70
146.42
130.55
79.11
49.98
42.05
35.24
32.08
28.35
24.46
17.64
13.76
O
NHBoc
O
4b
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

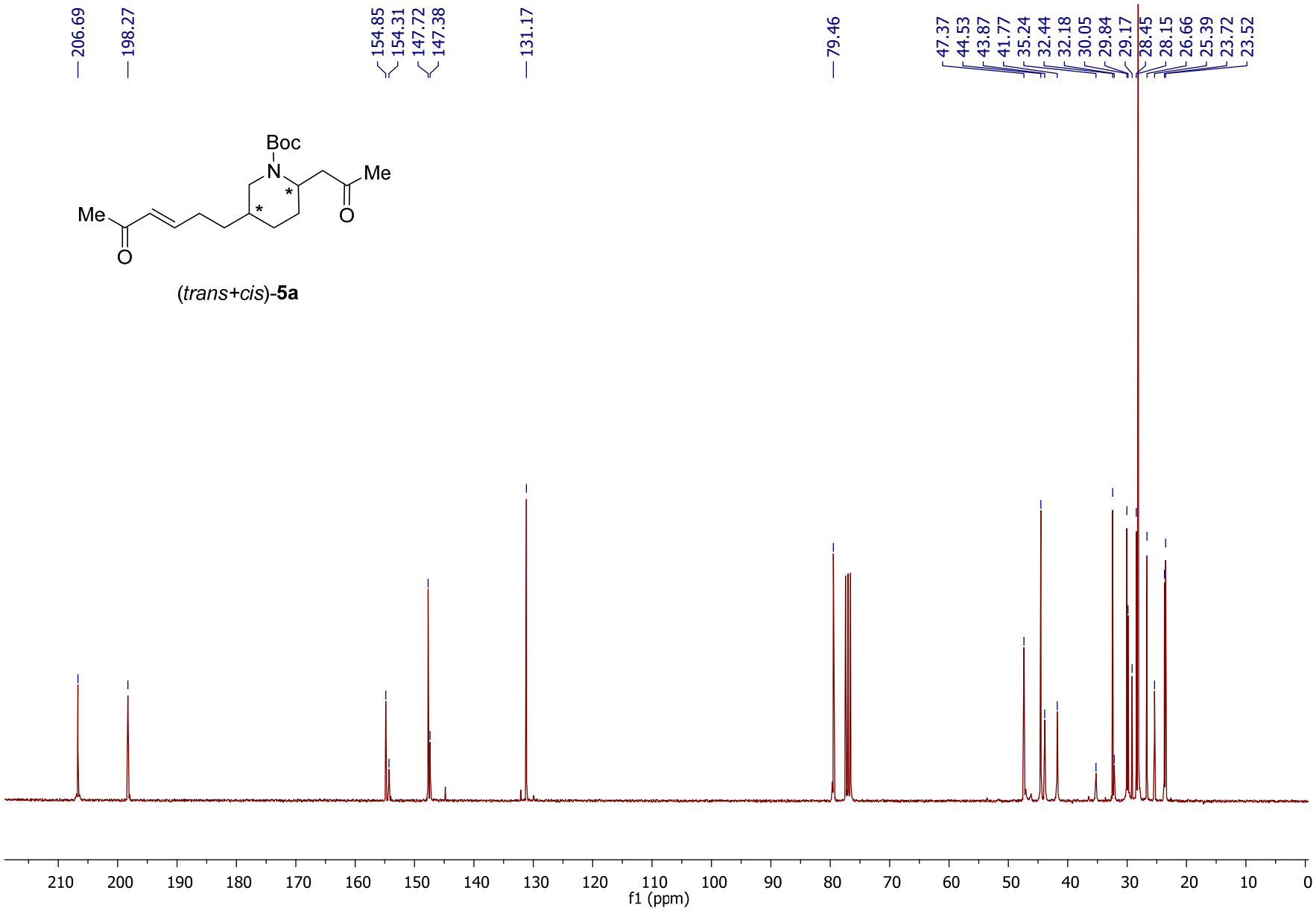

6.818
6.795
6.772
6.765
6.742
6.719
6.097
6.044
4.248
4.217
3.556
2.515
2.491
2.466
2.249
2.223
2.201
2.179
2.152
1.580
1.487
1.419
1.288
1.277
1.264
0.891
0.869
0.846
O
NHBoc
O
2.03
2.00
0.93
0.85
4.05
3.71
19.55
10.16
6.23
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

4c

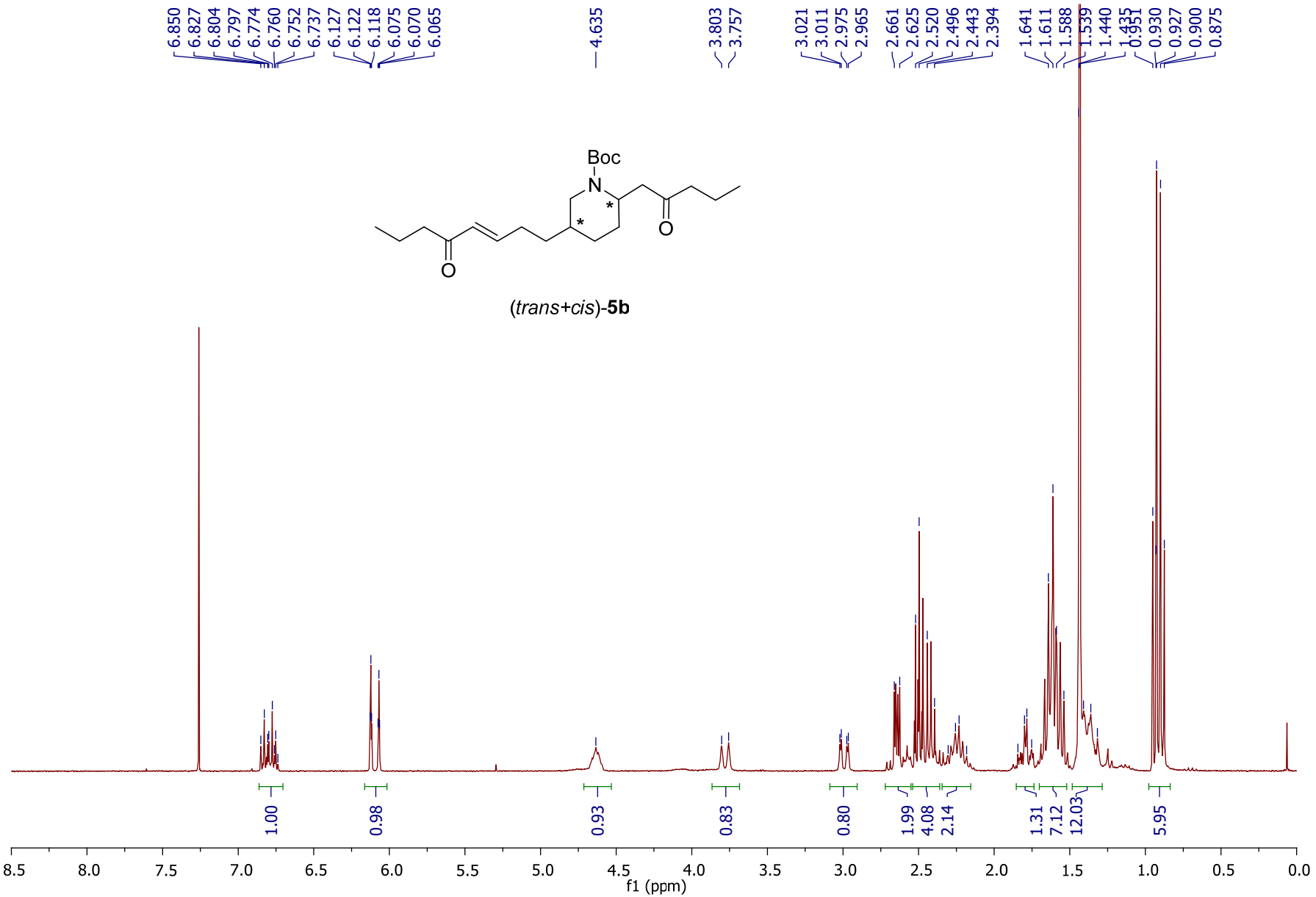

200.77
155.71
146.38
130.51
79.10
49.98
40.16
35.25
32.08
31.43
28.35
24.47
23.91
22.41
13.86
O
NHBoc
O
4c
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


6.751
6.728
6.674
6.652
6.638
6.015
6.011
6.006
5.962
5.958
5.953
4.701
4.594
4.570
4.554
3.972
3.726
3.679
2.935
2.926
2.889
2.879
2.622
2.562
2.513
2.221
2.143
2.088
1.722
1.664
1.551
1.490
1.349
1.314
1.240
Boc
N
Me
O
Me
O
1.00
0.99
0.17
0.81
0.25
0.79
0.69
2.13
4.97
3.21
3.86
9.25
2.82
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
f1 (ppm)

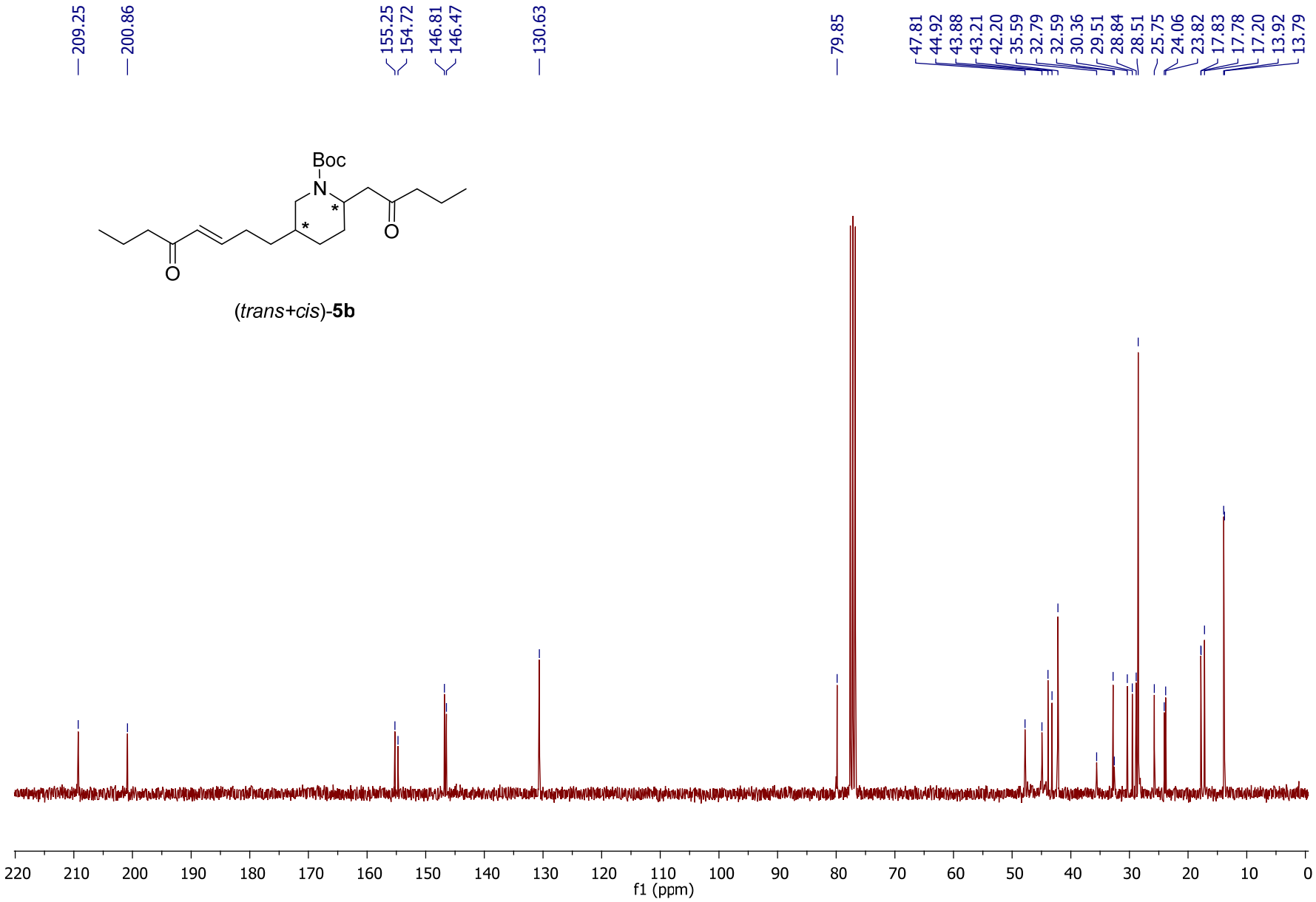
(*trans*+*cis*)-**5a**


206.69
198.27
154.85
154.31
147.72
147.38
131.17
79.46
47.37
44.53
43.87
41.77
35.24
32.44
32.18
30.05
29.84
29.17
28.45
28.15
26.66
25.39
23.72
23.52
Boc
N
Me
Me
O
O
*
*
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

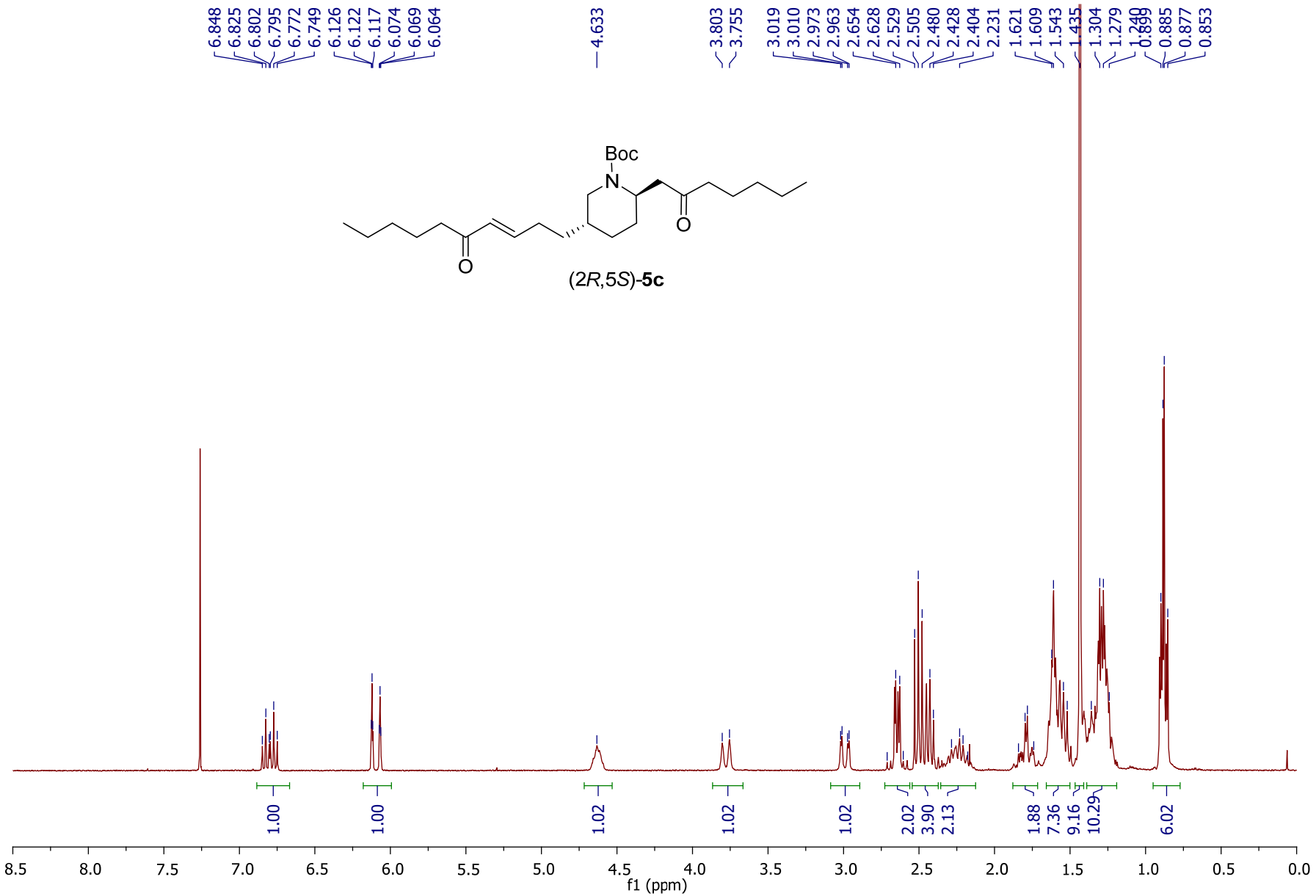
(*trans*+*cis*)-**5a**


6.850
6.827
6.804
6.797
6.774
6.760
6.752
6.737
6.127
6.122
6.118
6.075
6.070
6.065
4.635
3.803
3.757
3.021
3.011
2.975
2.965
2.661
2.625
2.520
2.496
2.443
2.394
1.641
1.611
1.588
1.539
1.440
1.435
0.951
0.930
0.927
0.900
0.875
Boc
N
O
O
1.00
0.98
0.93
0.83
0.80
1.99
4.08
2.14
1.31
7.12
12.03
5.95
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
f1 (ppm)

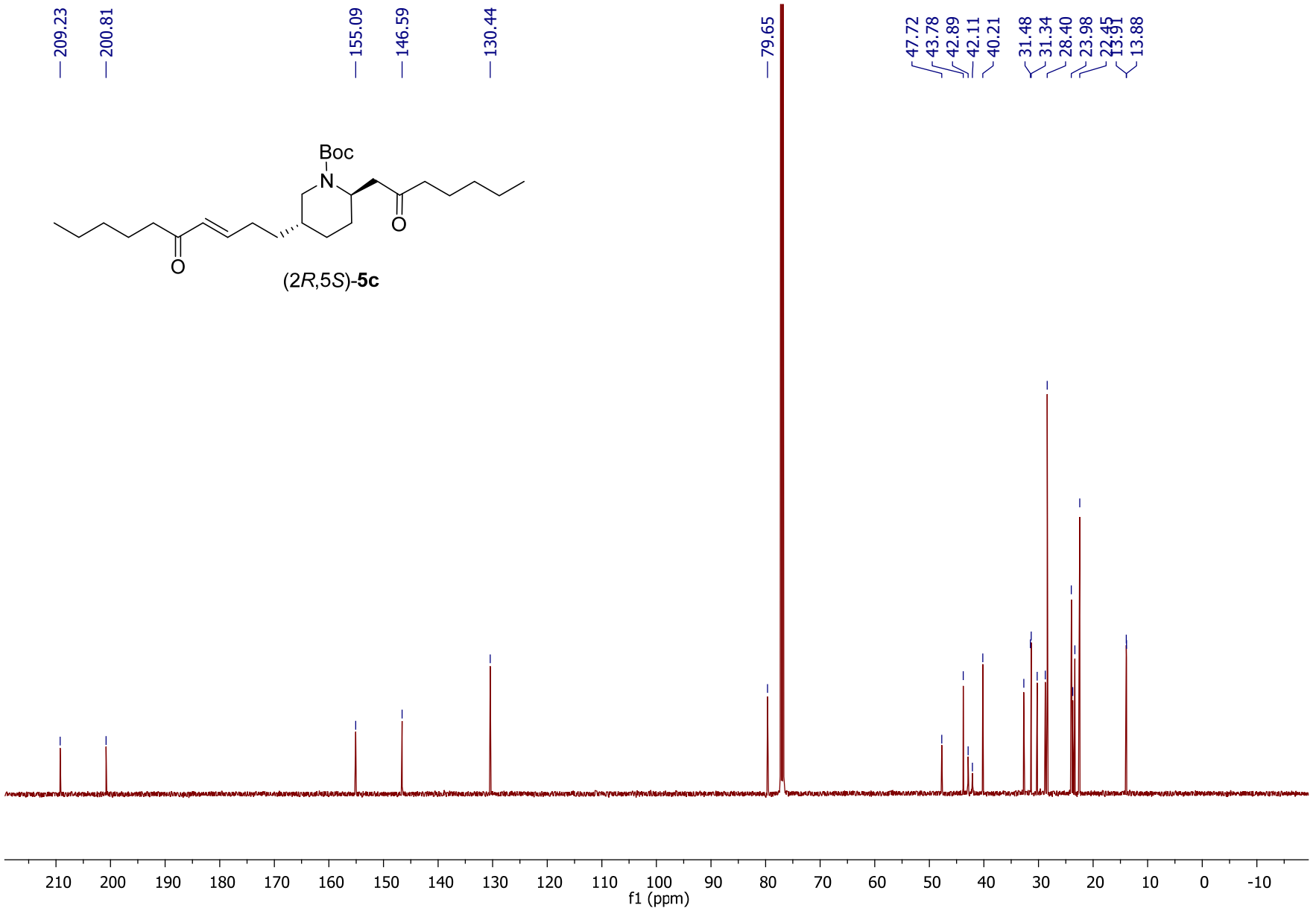
(*trans*+*cis*)-**5b**


209.25
200.86
155.25
154.72
146.81
146.47
130.63
79.85
47.81
44.92
43.88
43.21
42.20
35.59
32.79
32.59
30.36
29.51
28.84
28.51
25.75
24.06
23.82
17.83
17.78
17.20
13.92
13.79
Boc
N
O
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

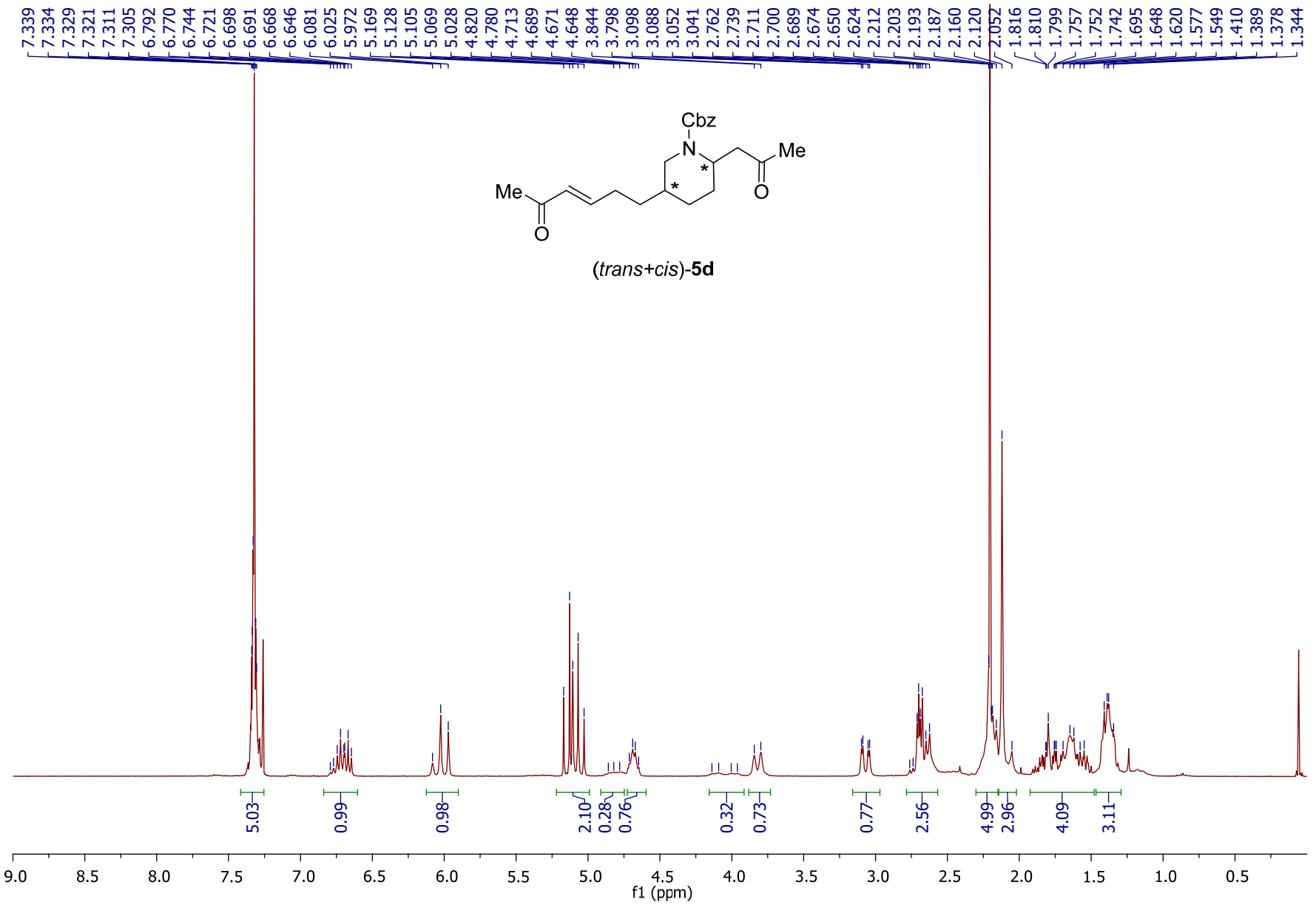
(*trans*+*cis*)-**5b**


6.848
6.825
6.802
6.795
6.772
6.749
6.126
6.122
6.117
6.074
6.069
6.064
4.633
3.803
3.755
3.019
3.010
2.973
2.963
2.654
2.628
2.529
2.505
2.480
2.428
2.404
2.231
1.621
1.609
1.543
1.435
1.304
1.279
1.240
0.899
0.885
0.877
0.853
Boc
N
O
O
1.00
1.00
1.02
1.02
1.02
2.02
3.90
2.13
1.88
7.36
9.16
10.29
6.02
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
f1 (ppm)

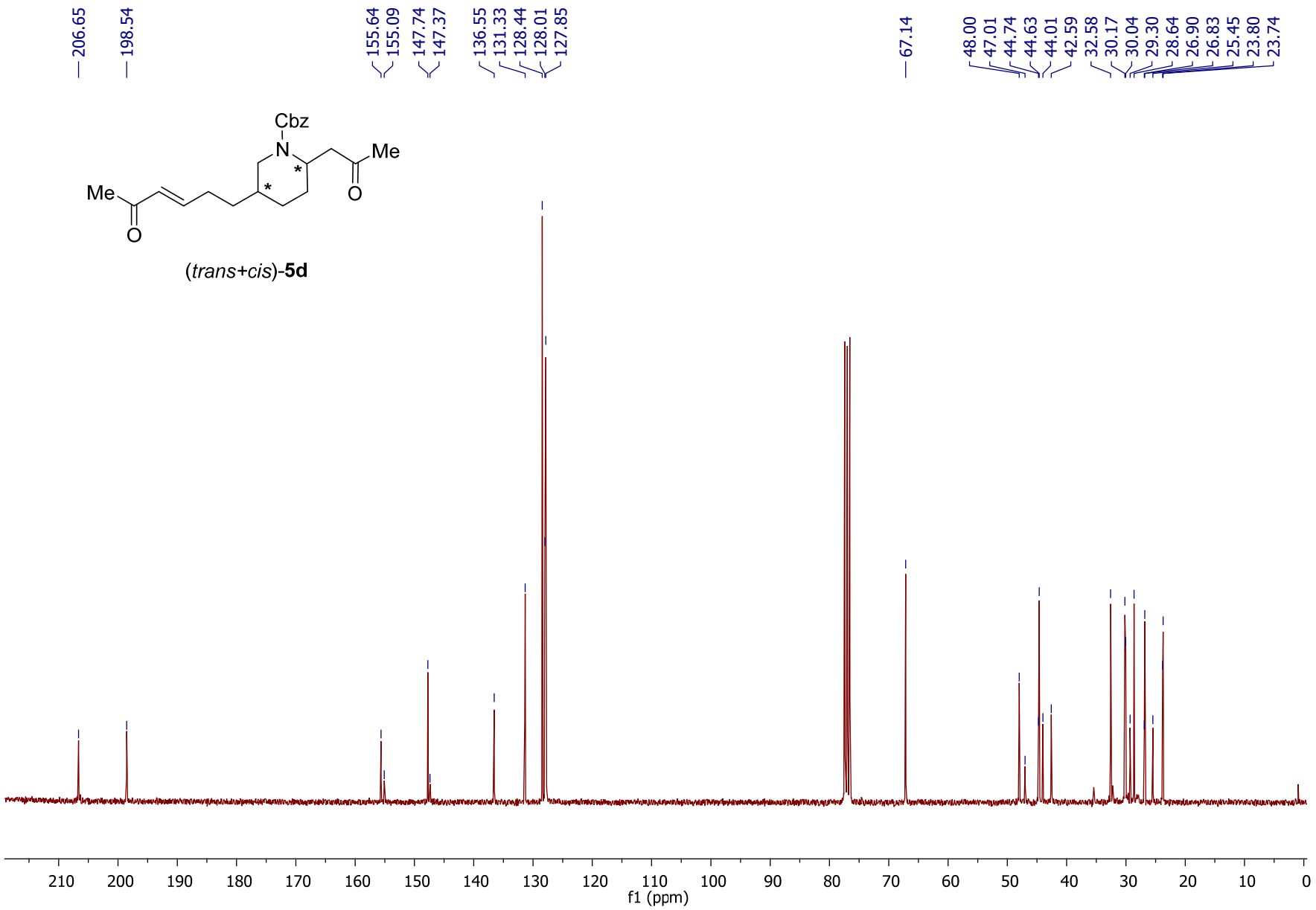
(2*R*,5*S*)-**5c**


209.23
200.81
155.09
146.59
130.44
79.65
47.72
43.78
42.89
42.11
40.21
31.48
31.34
28.40
23.98
22.45
13.91
13.88
Boc
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

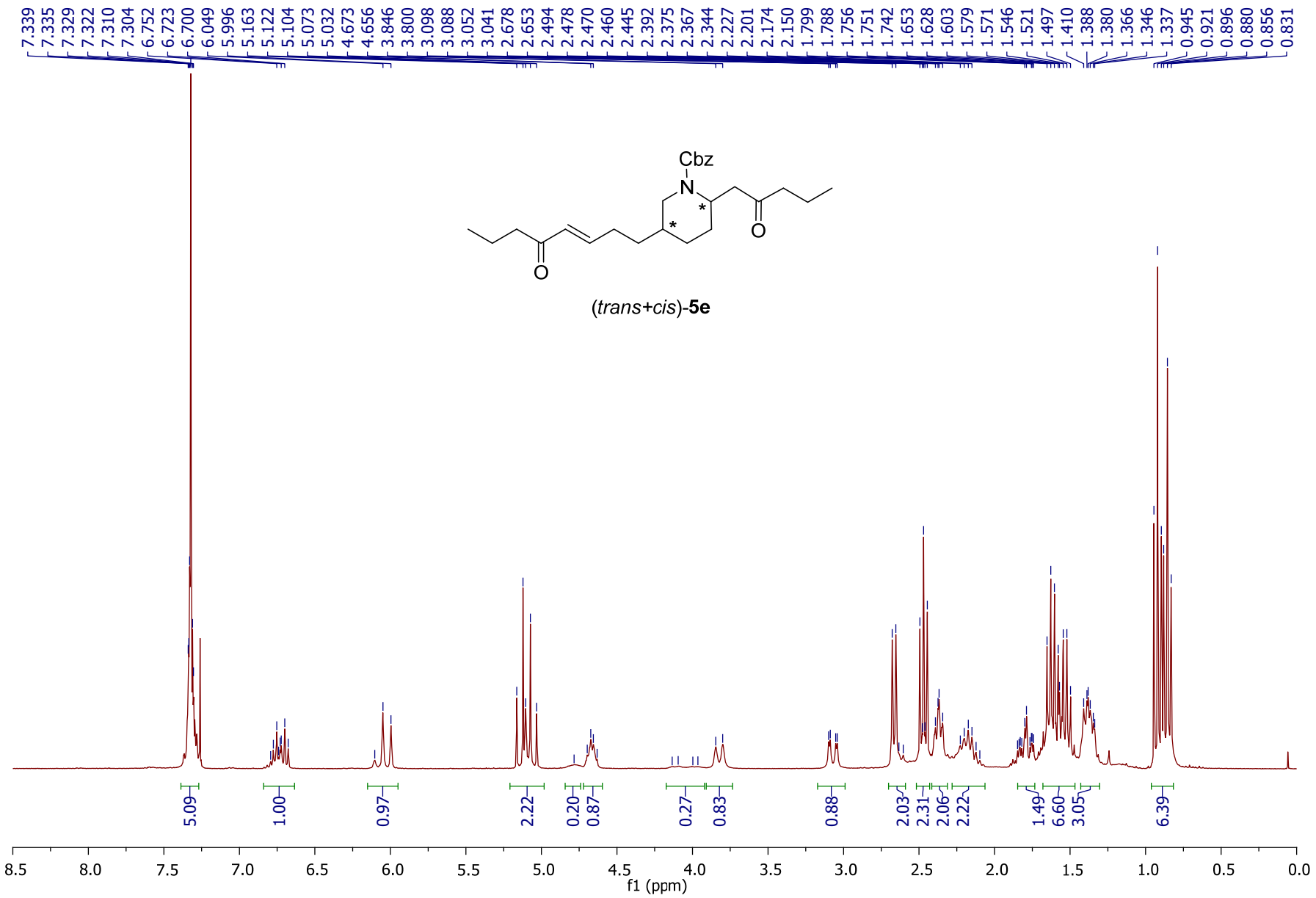
(2*R*,5*S*)-**5c**


7.339
7.334
7.329
7.321
7.311
7.305
6.792
6.770
6.744
6.721
6.698
6.691
6.668
6.646
6.081
6.025
5.972
5.169
5.128
5.105
5.069
5.028
4.820
4.780
4.713
4.689
4.671
4.648
3.844
3.798
3.098
3.088
3.052
3.041
2.762
2.739
2.711
2.700
2.689
2.674
2.650
2.624
2.212
2.203
2.193
2.187
2.160
2.120
2.052
1.816
1.810
1.799
1.757
1.752
1.742
1.695
1.648
1.620
1.577
1.549
1.410
1.389
1.378
1.344
Cbz
N
Me
Me
O
O
*
*
5.03
0.99
0.98
2.10
0.28
0.76
0.32
0.73
0.77
2.56
4.99
2.96
4.09
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

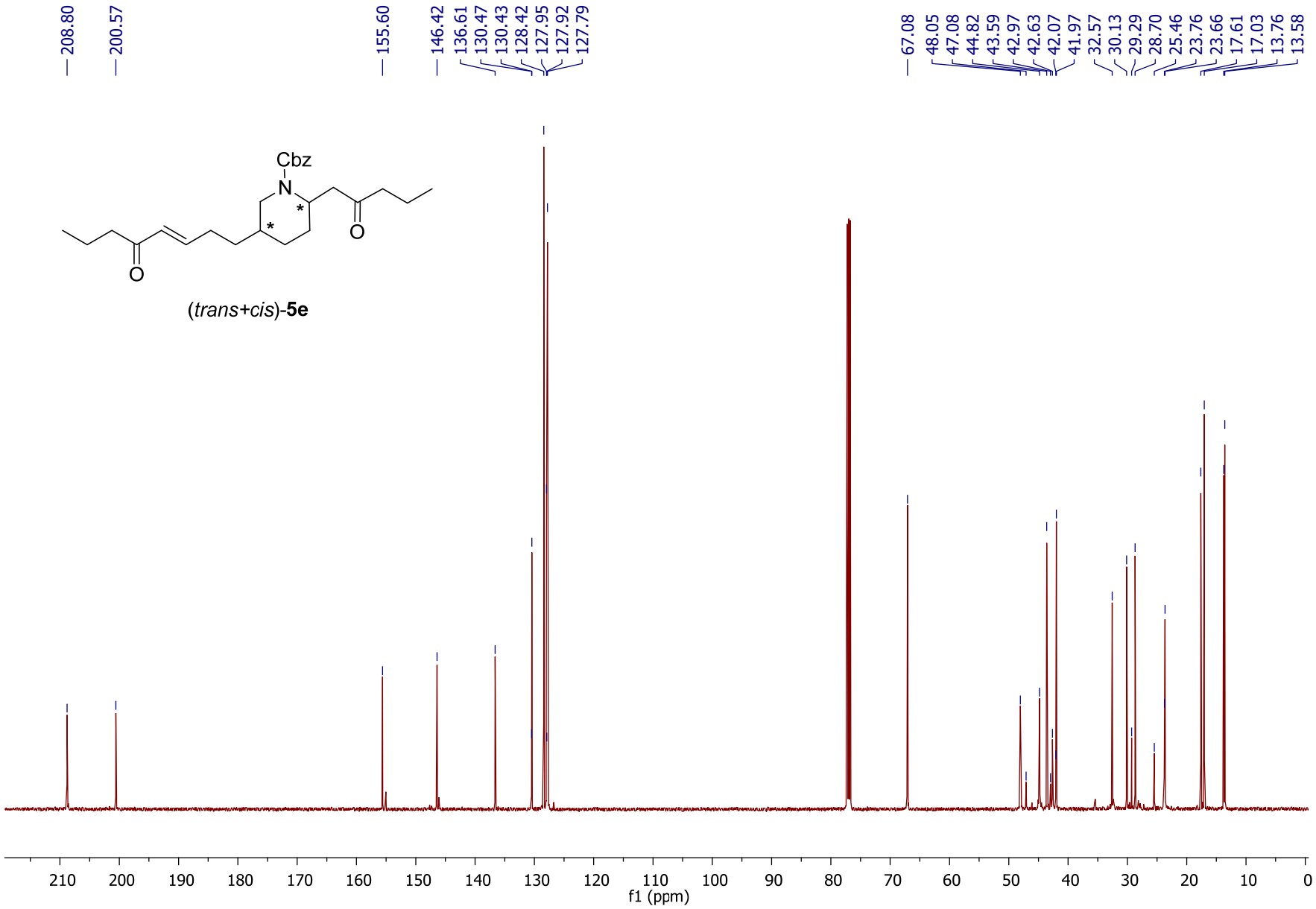
(*trans*+*cis*)-**5d**


206.65
198.54
155.64
155.09
147.74
147.37
136.55
131.33
128.44
128.01
127.85
67.14
48.00
47.01
44.74
44.63
44.01
42.59
32.58
30.17
30.04
29.30
28.64
26.90
26.83
25.45
23.80
23.74
Cbz
N
Me
O
Me
O
*
*
f1 (ppm)

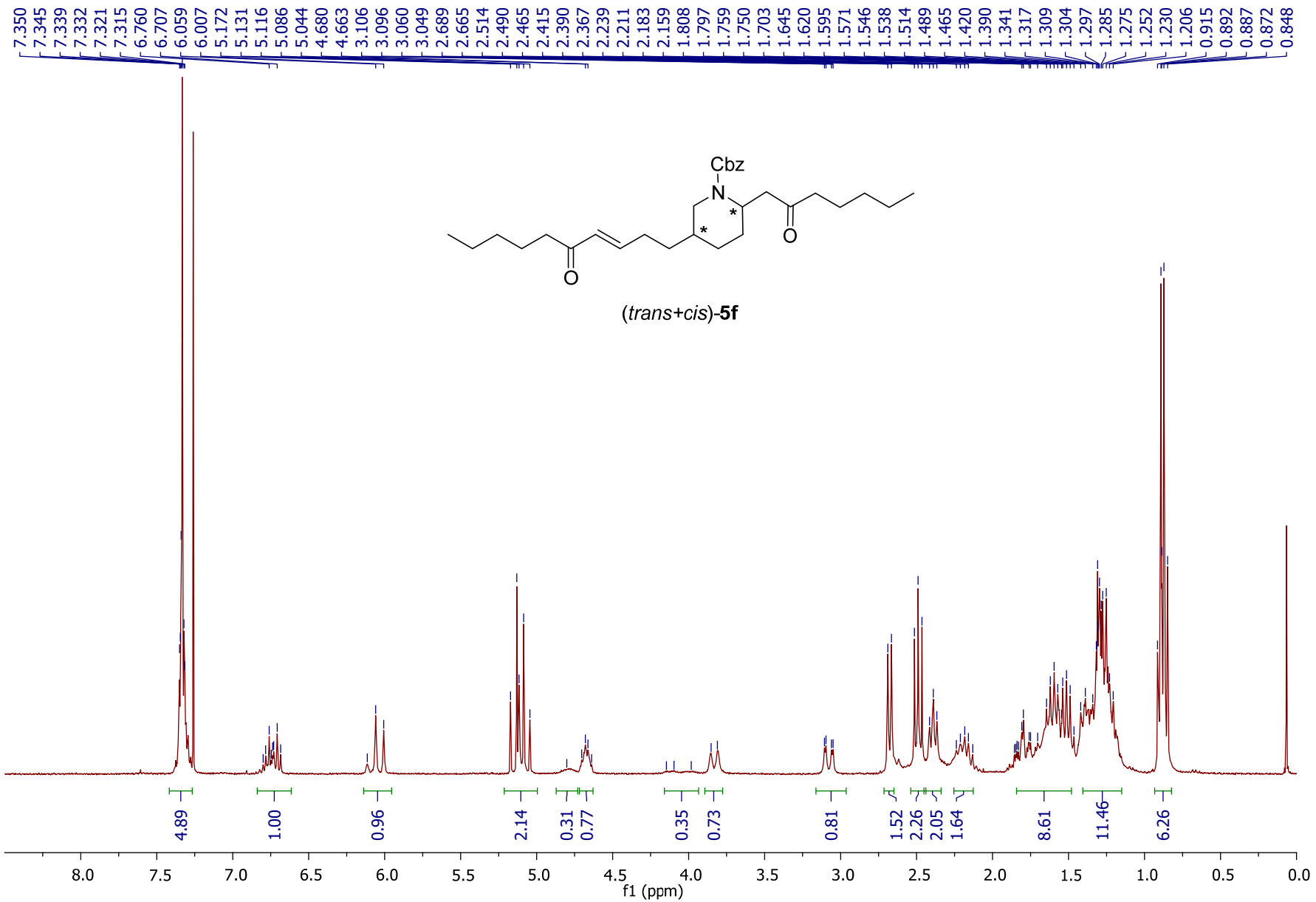
(*trans*+*cis*)-**5d**


7.339
7.335
7.329
7.322
7.310
7.304
6.752
6.723
6.700
6.049
5.996
5.163
5.122
5.104
5.073
5.032
4.673
4.656
3.846
3.800
3.098
3.088
3.052
3.041
2.678
2.653
2.494
2.478
2.470
2.460
2.445
2.392
2.375
2.367
2.344
2.227
2.201
2.174
2.150
1.799
1.788
1.756
1.751
1.742
1.653
1.628
1.603
1.579
1.571
1.546
1.521
1.497
1.410
1.388
1.380
1.366
1.346
1.337
0.945
0.921
0.896
0.880
0.856
0.831
Cbz
N
O
O
5.09
1.00
0.97
2.22
0.20
0.87
0.27
0.83
0.88
2.03
2.31
2.06
2.22
1.49
6.60
3.05
6.39
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
f1 (ppm)

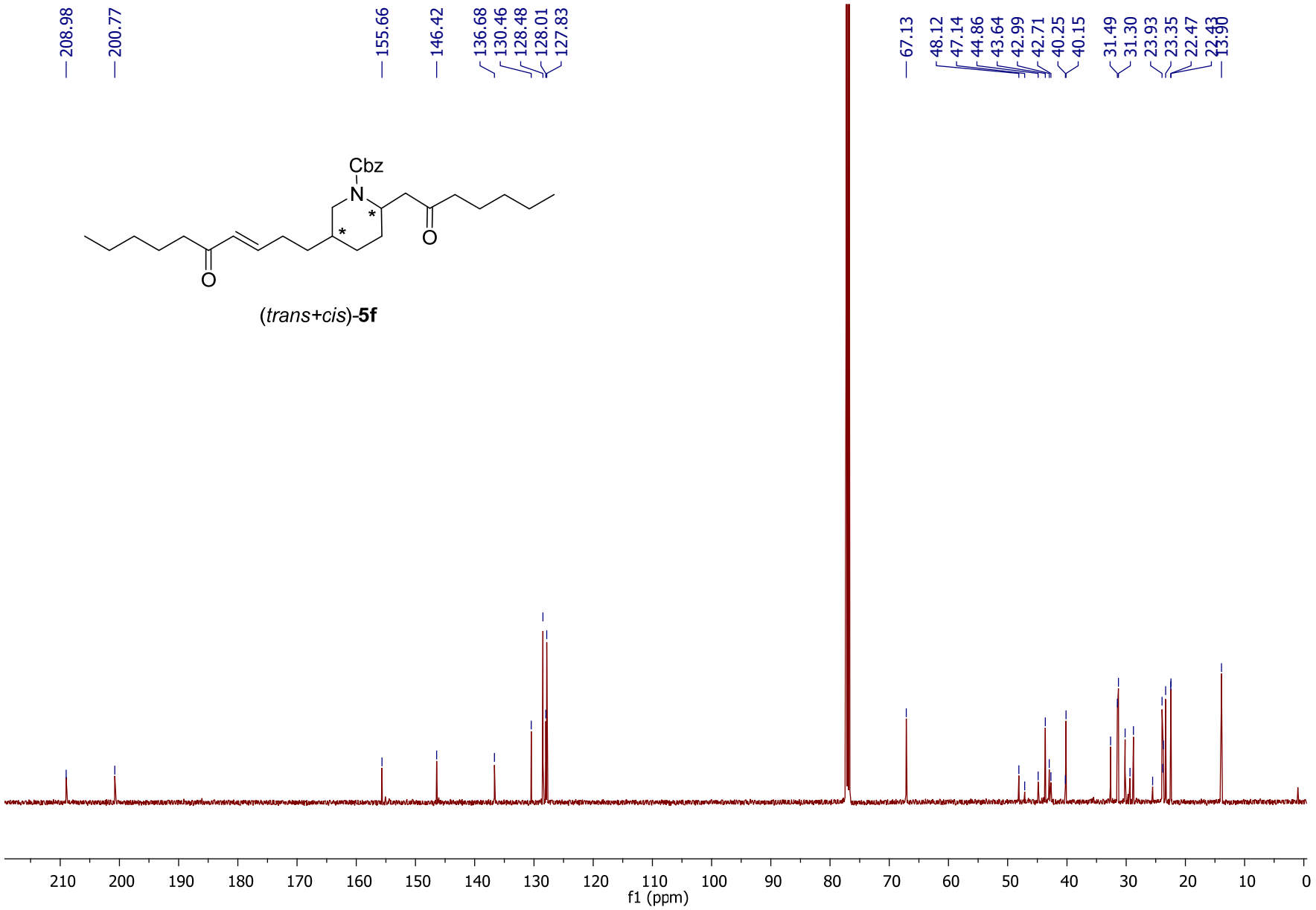
(*trans*+*cis*)-**5e**


208.80
200.57
155.60
146.42
136.61
130.47
130.43
128.42
127.95
127.92
127.79
67.08
48.05
47.08
44.82
43.59
42.97
42.63
42.07
41.97
32.57
30.13
29.29
28.70
25.46
23.76
23.66
17.61
17.03
13.76
13.58
Cbz
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

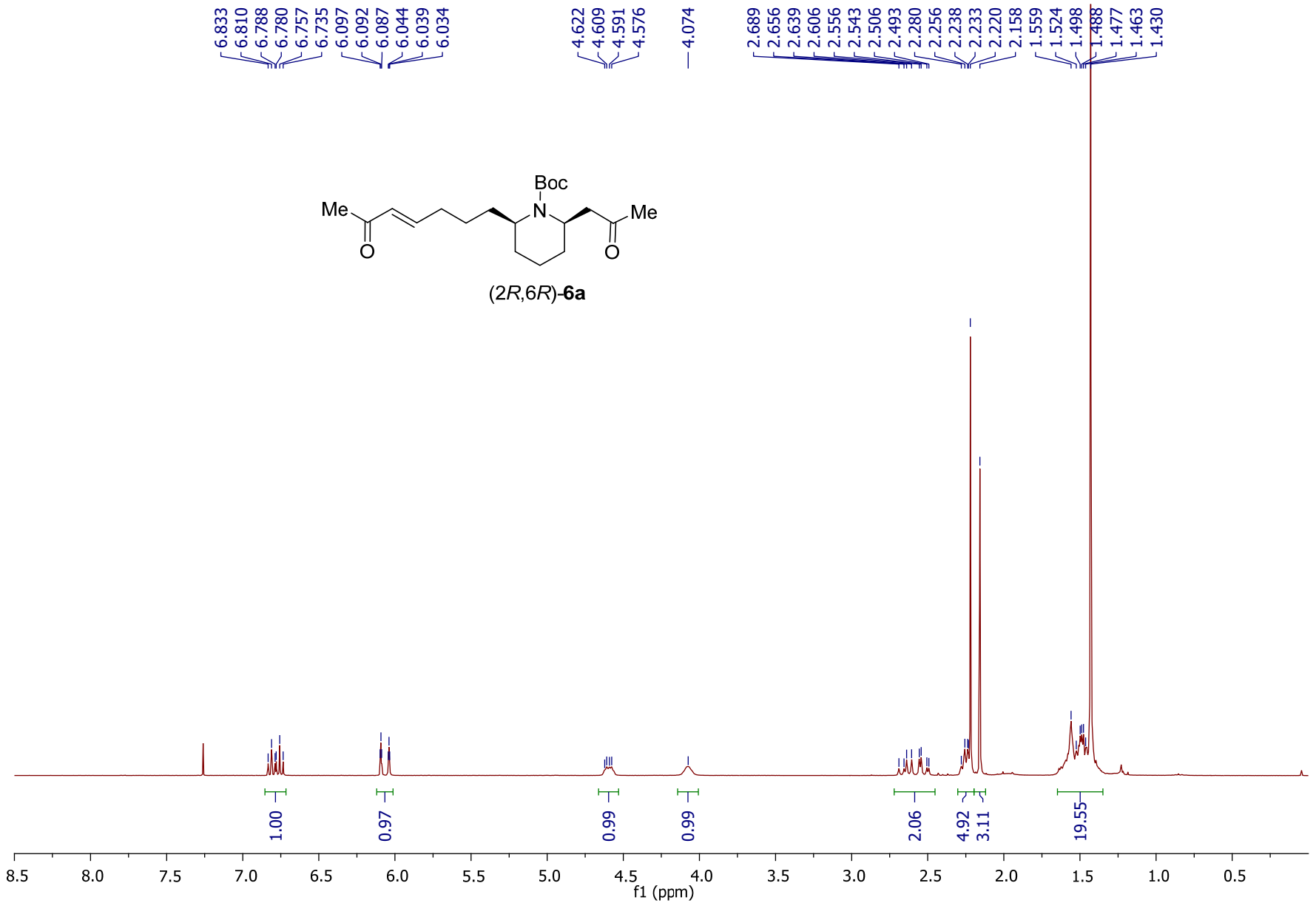
(*trans*+*cis*)-**5e**


7.350
7.345
7.339
7.332
7.321
7.315
6.760
6.707
6.059
6.007
5.172
5.131
5.116
5.086
5.044
4.680
4.663
3.106
3.096
3.060
3.049
2.689
2.665
2.514
2.490
2.465
2.415
2.390
2.367
2.239
2.211
2.183
2.159
1.808
1.797
1.759
1.750
1.703
1.645
1.620
1.595
1.571
1.546
1.538
1.514
1.489
1.465
1.420
1.390
1.341
1.317
1.309
1.304
1.297
1.285
1.275
1.252
1.230
1.206
0.915
0.892
0.887
0.872
0.848
Cbz
N
O
O
4.89
1.00
0.96
2.14
0.31
0.77
0.35
0.73
0.81
1.52
2.26
2.05
1.64
8.61
11.46
6.26
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
f1 (ppm)

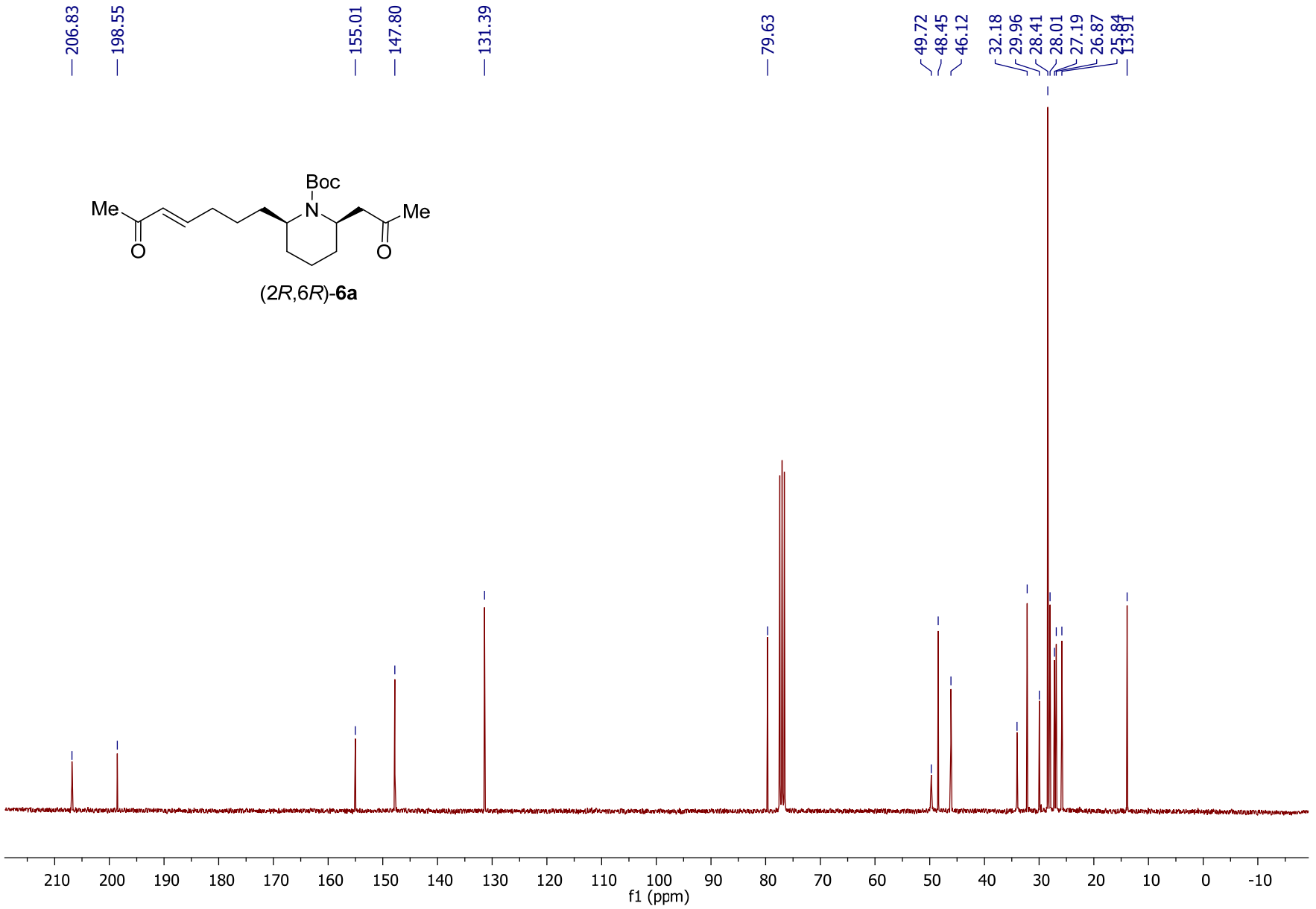
(*trans*+*cis*)-**5f**

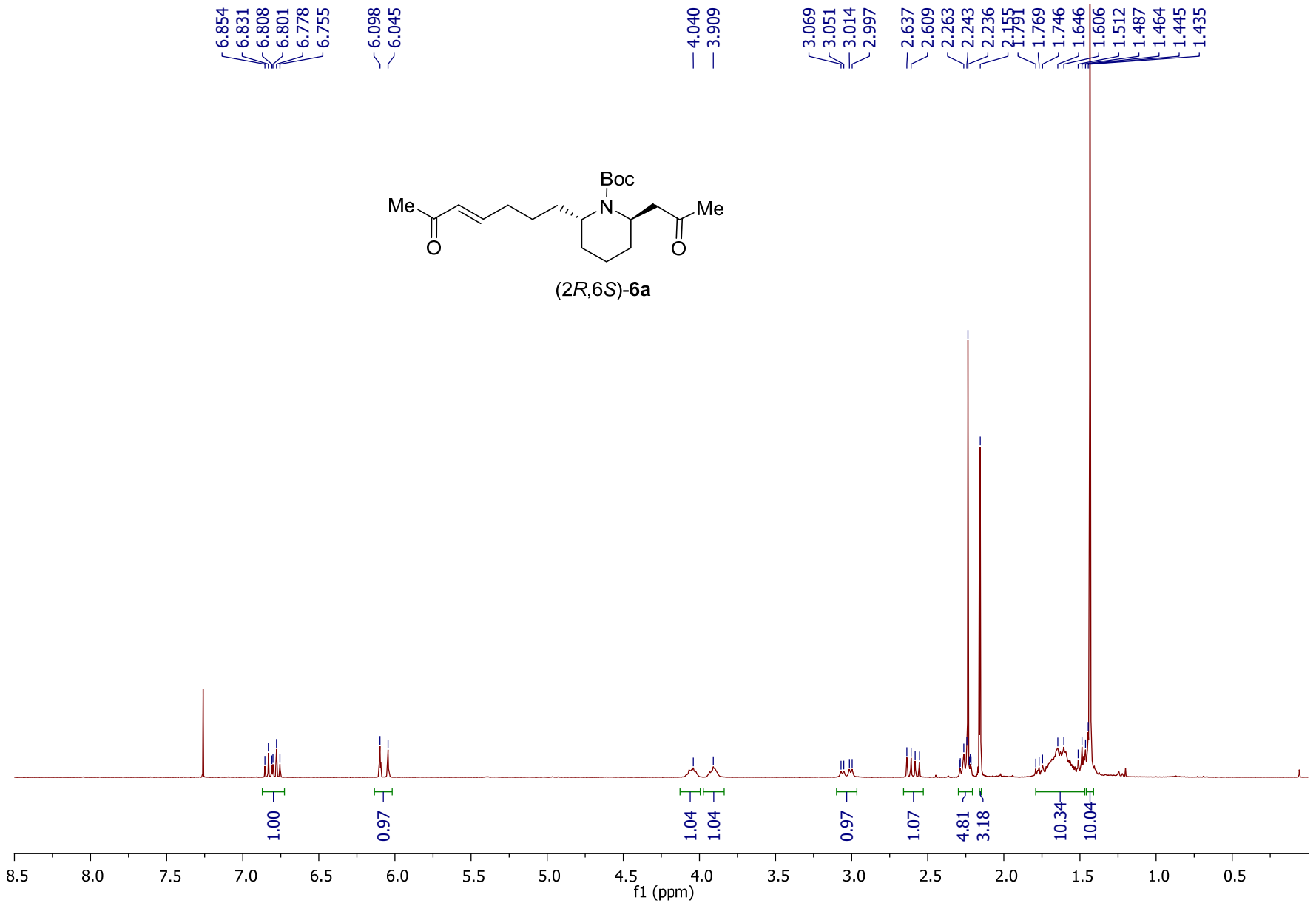

208.98
200.77
155.66
146.42
136.68
130.46
128.48
128.01
127.83
67.13
48.12
47.14
44.86
43.64
42.99
42.71
40.25
40.15
31.49
31.30
23.93
23.35
22.47
22.43
13.90
Cbz
N
O
O
*
*
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(*trans*+*cis*)-**5f**

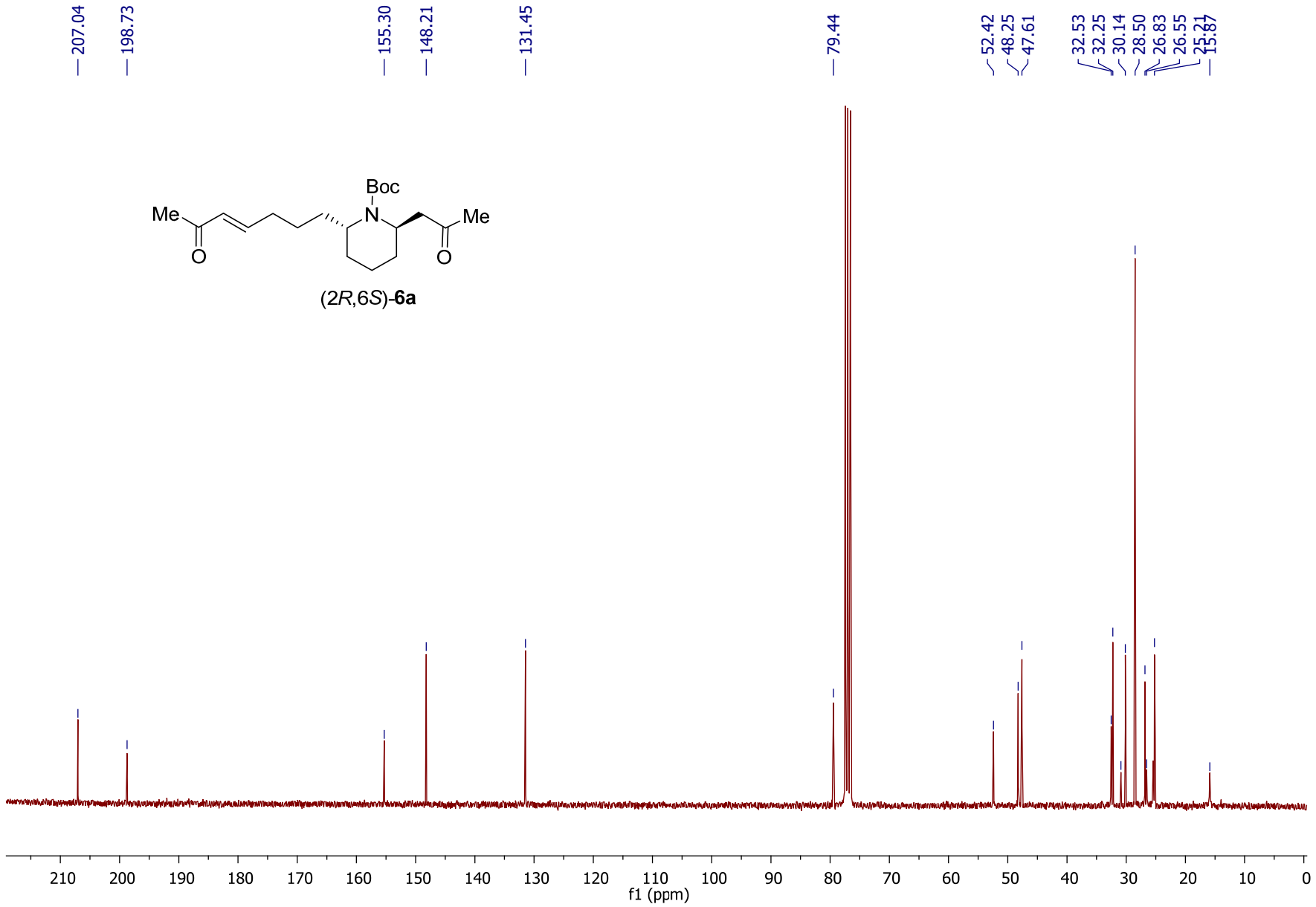

6.833
6.810
6.788
6.780
6.757
6.735
6.097
6.092
6.087
6.044
6.039
6.034
4.622
4.609
4.591
4.576
4.074
2.689
2.656
2.639
2.606
2.556
2.543
2.506
2.493
2.280
2.256
2.238
2.233
2.220
2.158
1.559
1.524
1.498
1.488
1.477
1.463
1.430
Boc
N
Me
Me
O
O
1.00
0.97
0.99
0.99
2.06
4.92
3.11
19.55
8.5
8.0
7.5
7.0
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
f1 (ppm)

(2*R*,6*R*)-**6a**

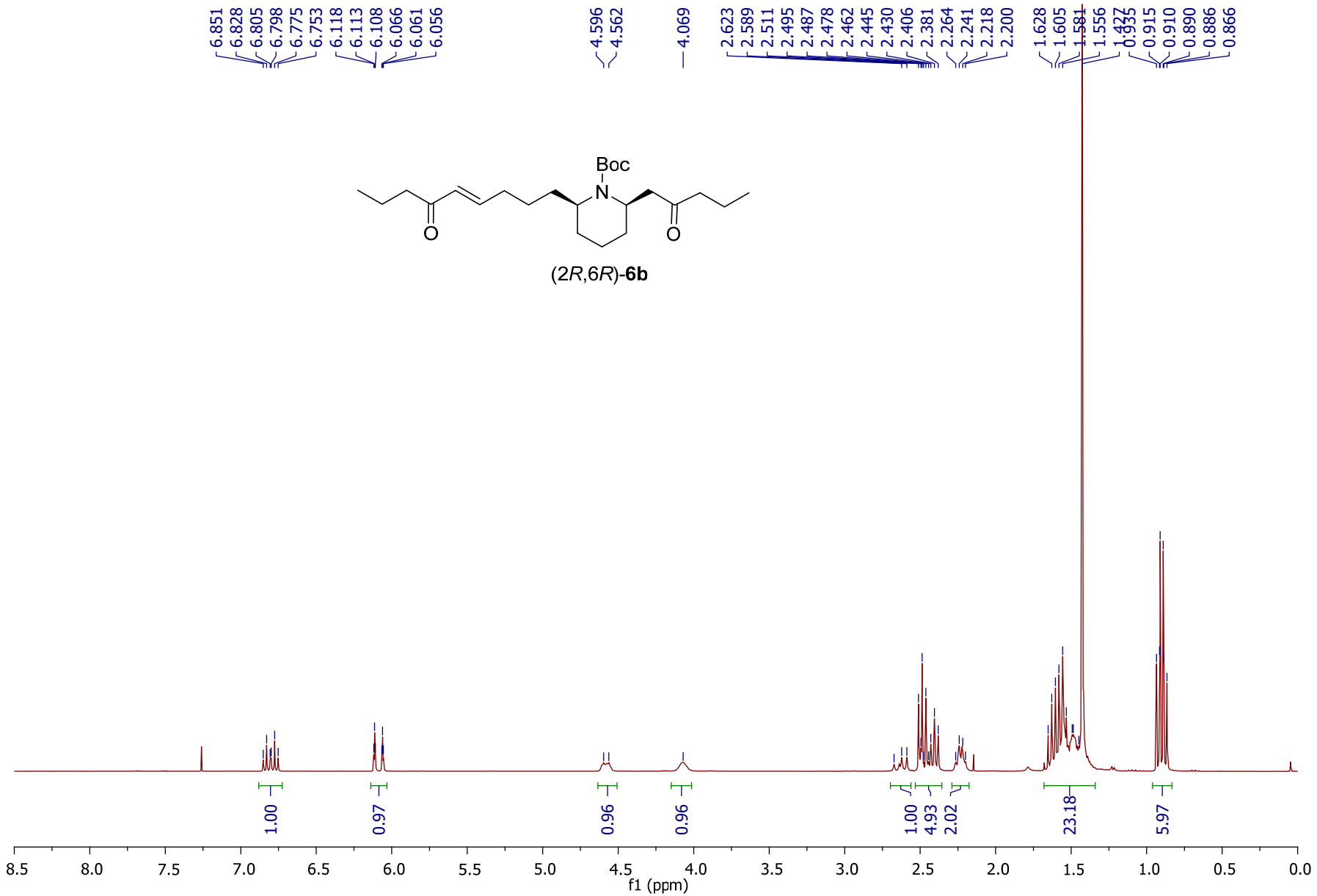

206.83
198.55
155.01
147.80
131.39
79.63
49.72
48.45
46.12
32.18
29.96
28.41
28.01
27.19
26.87
25.84
13.91
Boc
N
Me
Me
O
O
(2R,6R)-6a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


6.854
6.831
6.808
6.801
6.778
6.755
6.098
6.045
4.040
3.909
3.069
3.051
3.014
2.997
2.637
2.609
2.263
2.243
2.236
2.155
1.791
1.769
1.746
1.646
1.606
1.512
1.487
1.464
1.445
1.435
Boc
N
Me
Me
O
O
1.00
0.97
1.04
1.04
0.97
1.07
4.81
3.18
10.34
10.04
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
f1 (ppm)

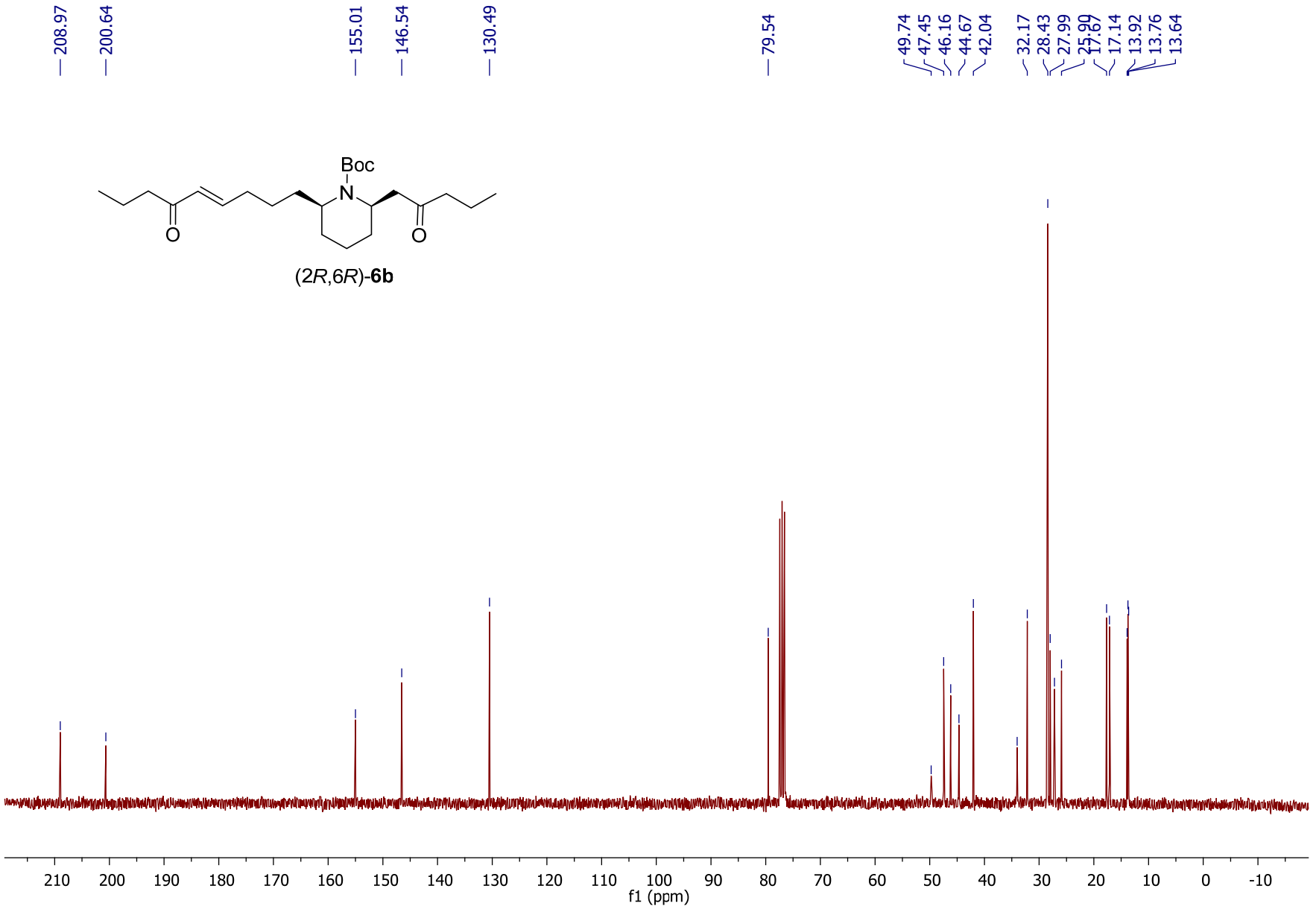
(2*R*,6*S*)-**6a**


207.04
198.73
155.30
148.21
131.45
79.44
52.42
48.25
47.61
32.53
32.25
30.14
28.50
26.83
26.55
25.21
15.87
Boc
N
Me
Me
O
O
f1 (ppm)

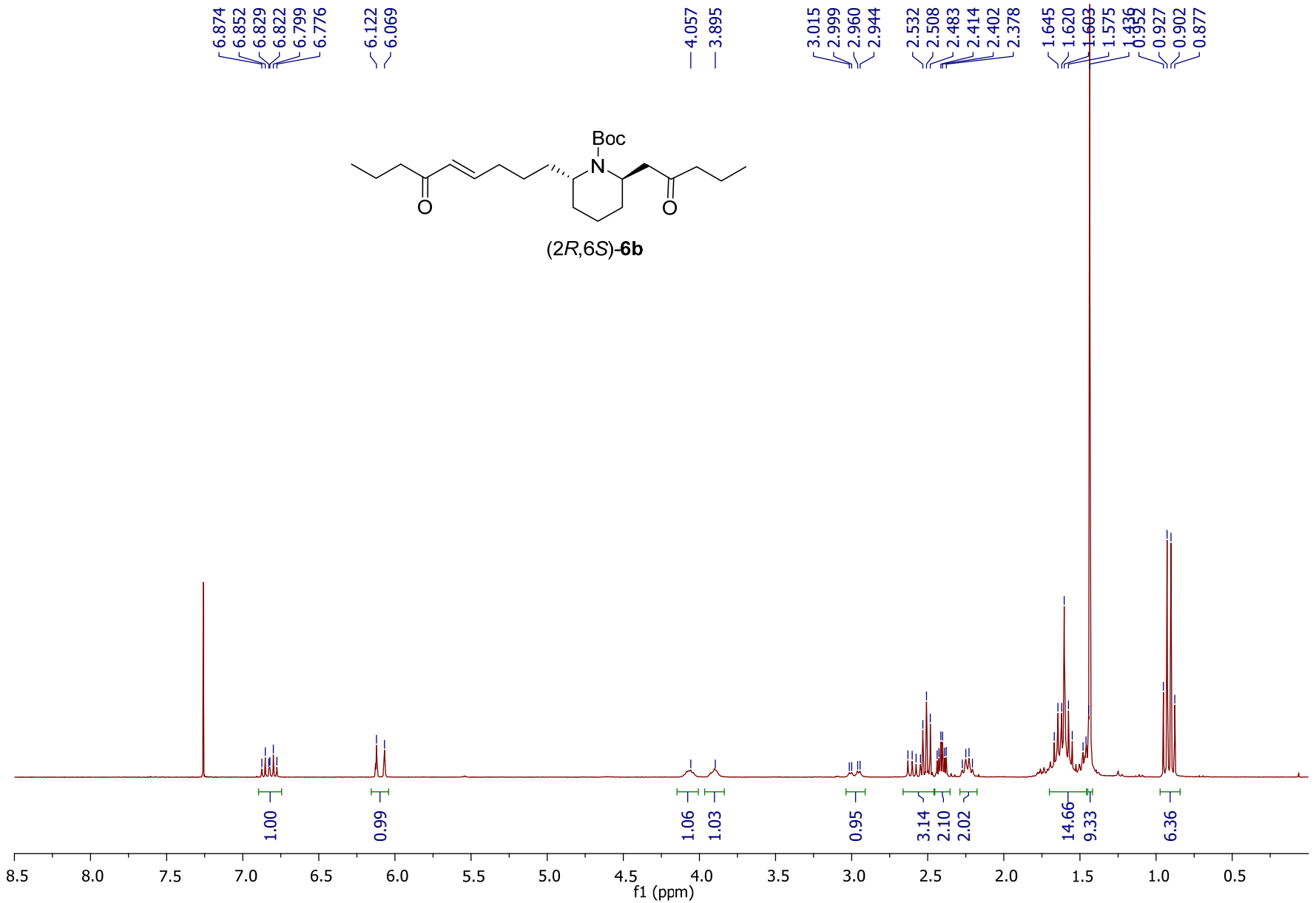
(2*R*,6*S*)-**6a**


6.851
6.828
6.805
6.798
6.775
6.753
6.118
6.113
6.108
6.066
6.061
6.056
4.596
4.562
4.069
2.623
2.589
2.511
2.495
2.487
2.478
2.462
2.445
2.430
2.406
2.381
2.264
2.241
2.218
2.200
1.628
1.605
1.581
1.556
1.427
0.935
0.915
0.910
0.890
0.886
0.866
Boc
N
O
O
1.00
0.97
0.96
0.96
1.00
4.93
2.02
23.18
5.97
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
f1 (ppm)

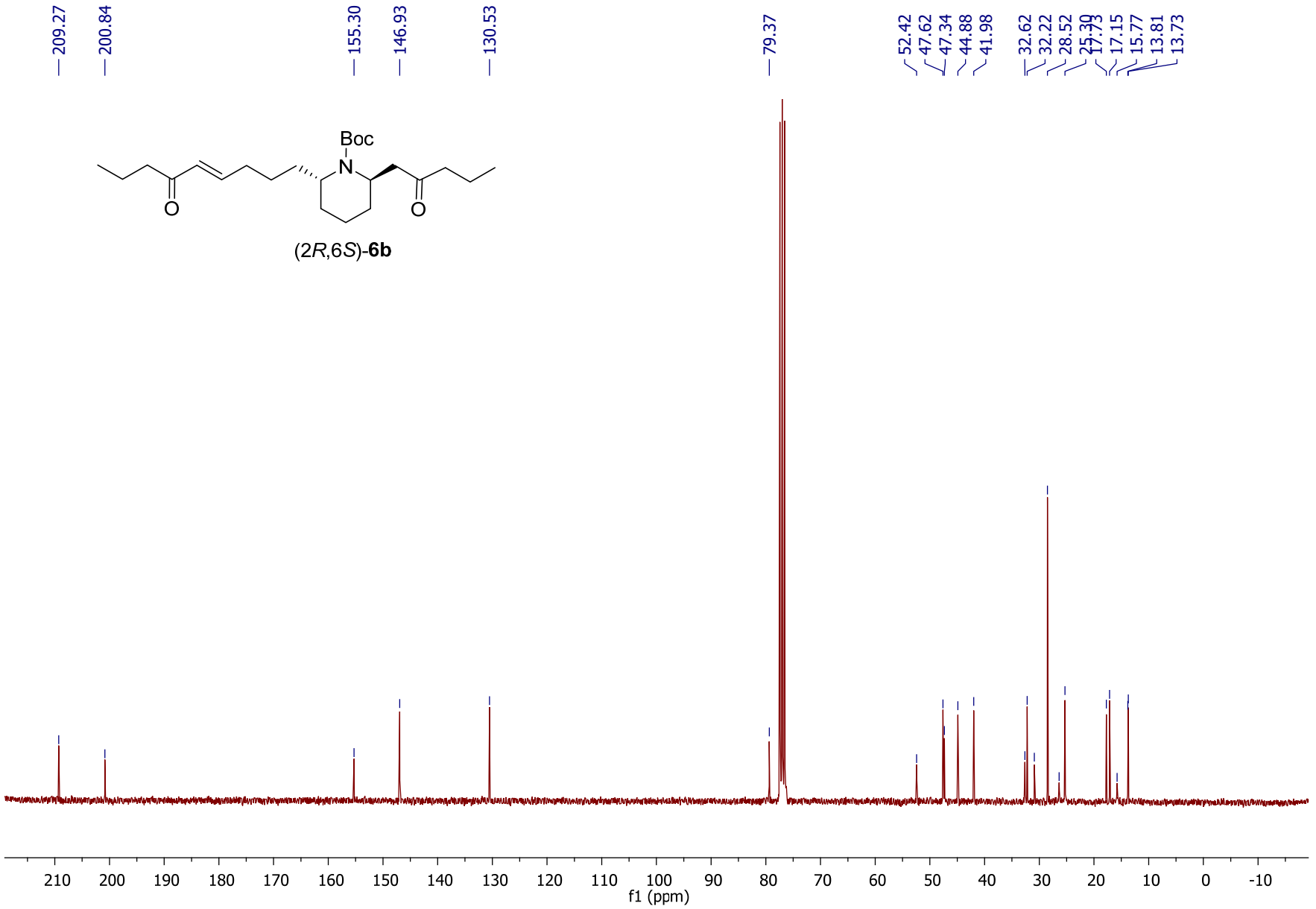
(2*R*,6*R*)-**6b**


208.97
200.64
155.01
146.54
130.49
79.54
49.74
47.45
46.16
44.67
42.04
32.17
28.43
27.99
25.99
17.67
17.14
13.92
13.76
13.64
Boc
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

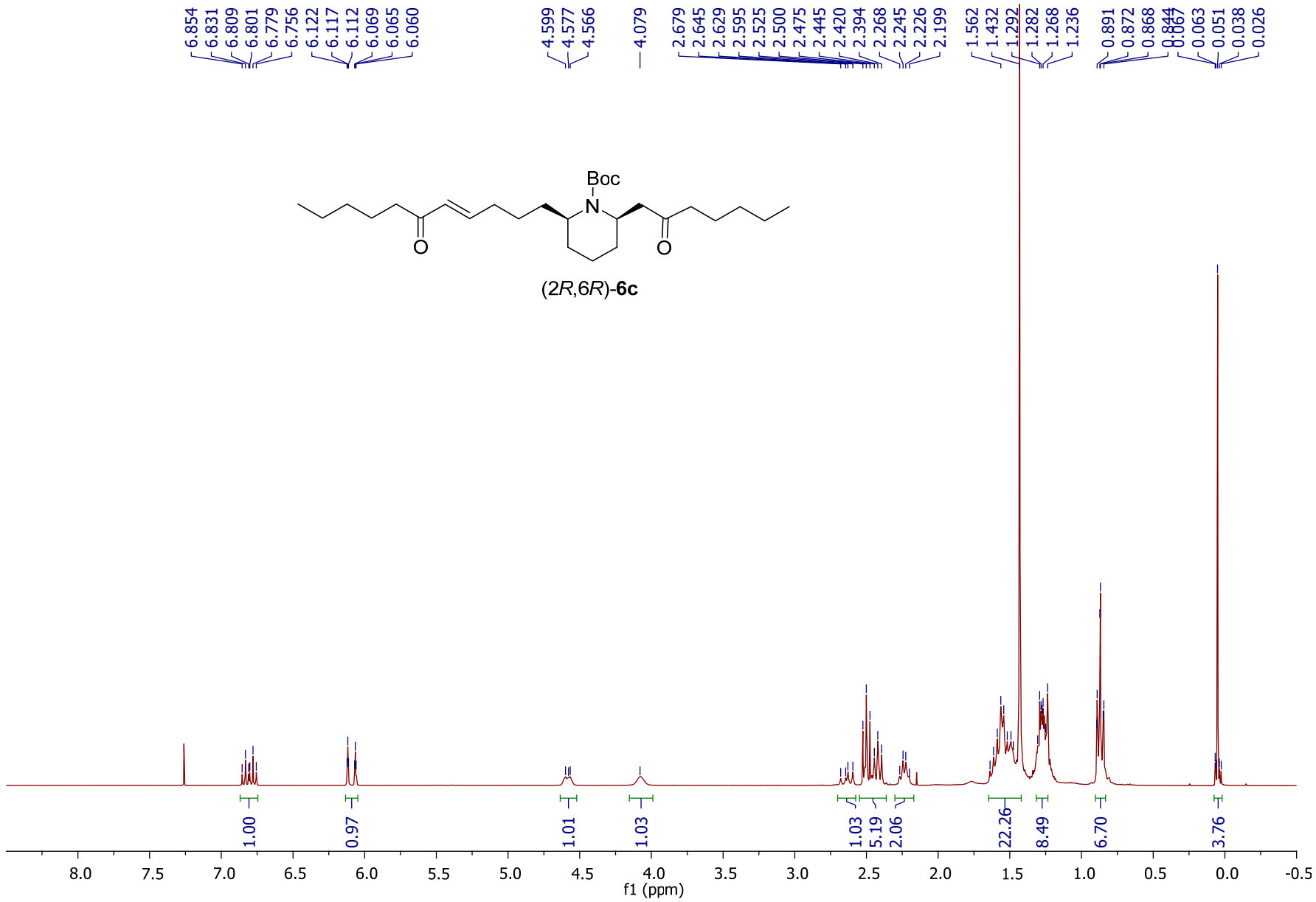
(2*R*,6*R*)-**6b**


6.874
6.852
6.829
6.822
6.799
6.776
6.122
6.069
4.057
3.895
3.015
2.999
2.960
2.944
2.532
2.508
2.483
2.414
2.402
2.378
1.645
1.620
1.603
1.575
1.436
0.952
0.927
0.902
0.877
Boc
N
O
O
1.00
0.99
1.06
1.03
0.95
3.14
2.10
2.02
14.66
9.33
6.36
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
f1 (ppm)

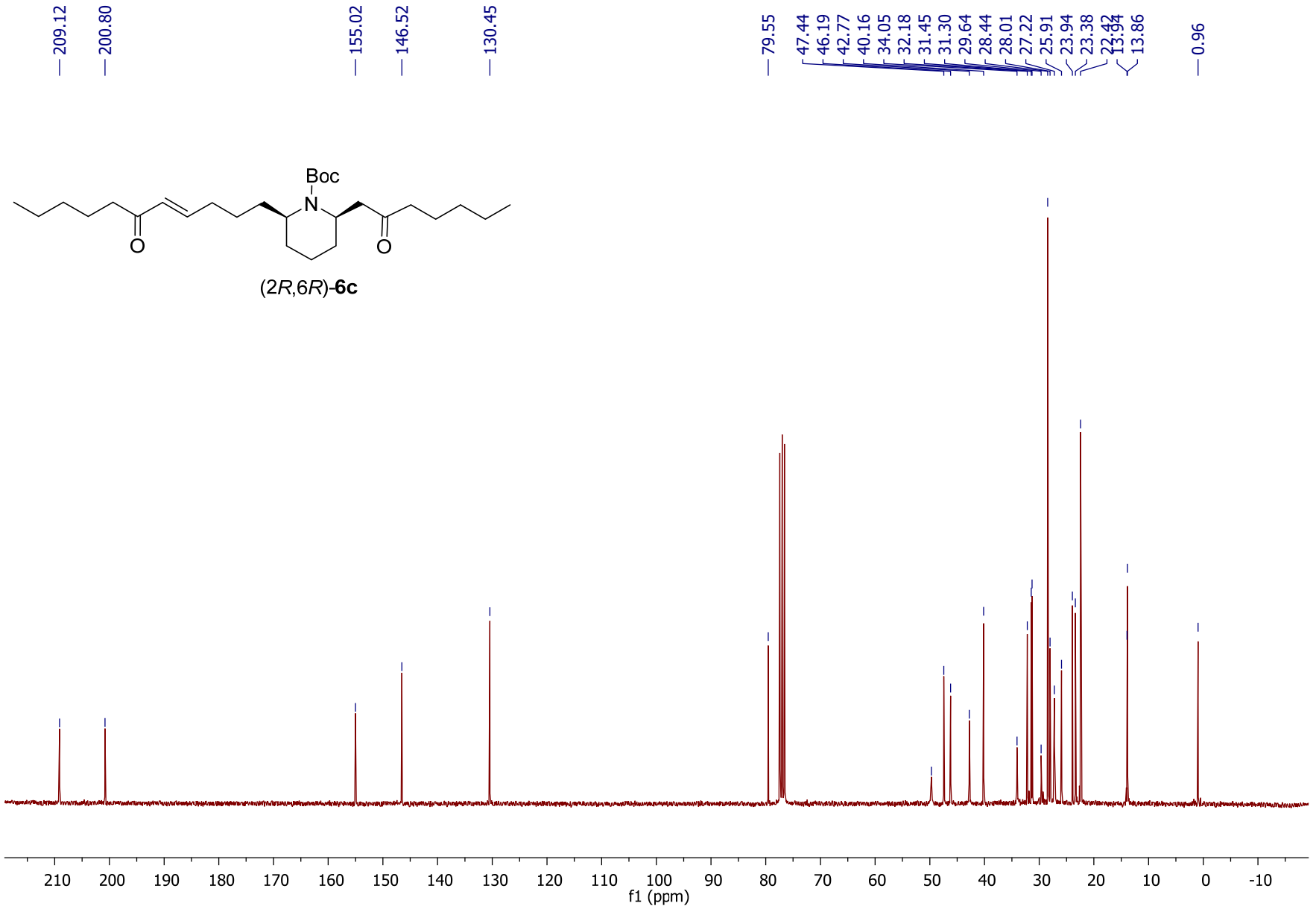
(2*R*,6*S*)-**6b**


209.27
200.84
155.30
146.93
130.53
79.37
52.42
47.62
47.34
44.88
41.98
32.62
32.22
28.52
25.39
17.73
17.15
15.77
13.81
13.73
Boc
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

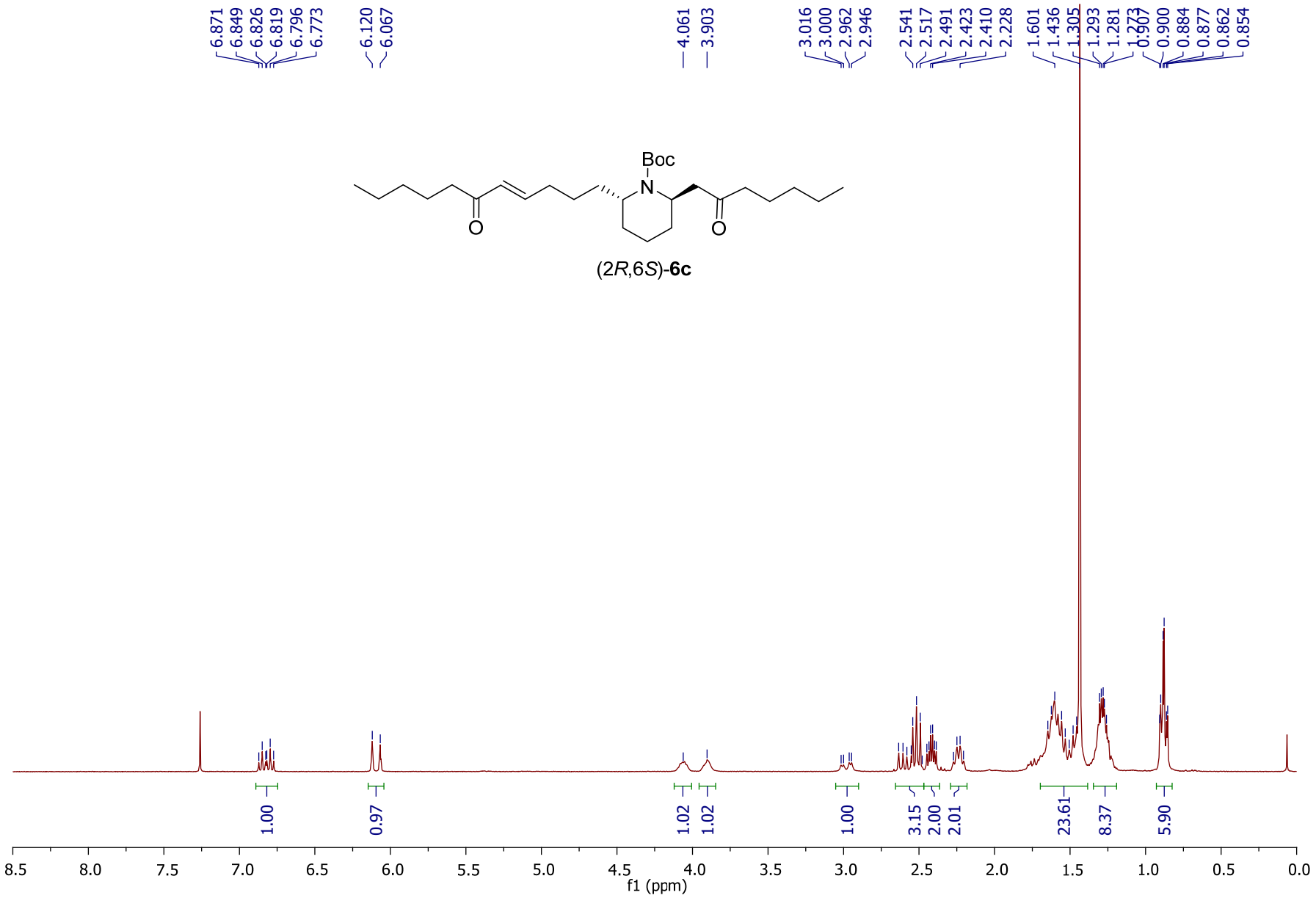
(2*R*,6*S*)-**6b**


6.854
6.831
6.809
6.801
6.779
6.756
6.122
6.117
6.112
6.069
6.065
6.060
4.599
4.577
4.566
4.079
2.679
2.645
2.629
2.595
2.525
2.500
2.475
2.445
2.420
2.394
2.268
2.245
2.226
2.199
1.562
1.432
1.292
1.282
1.268
1.236
0.891
0.872
0.868
0.063
0.051
0.038
0.026
Boc
N
O
O
1.00
0.97
1.01
1.03
1.03
5.19
2.06
22.26
8.49
6.70
3.76
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
f1 (ppm)

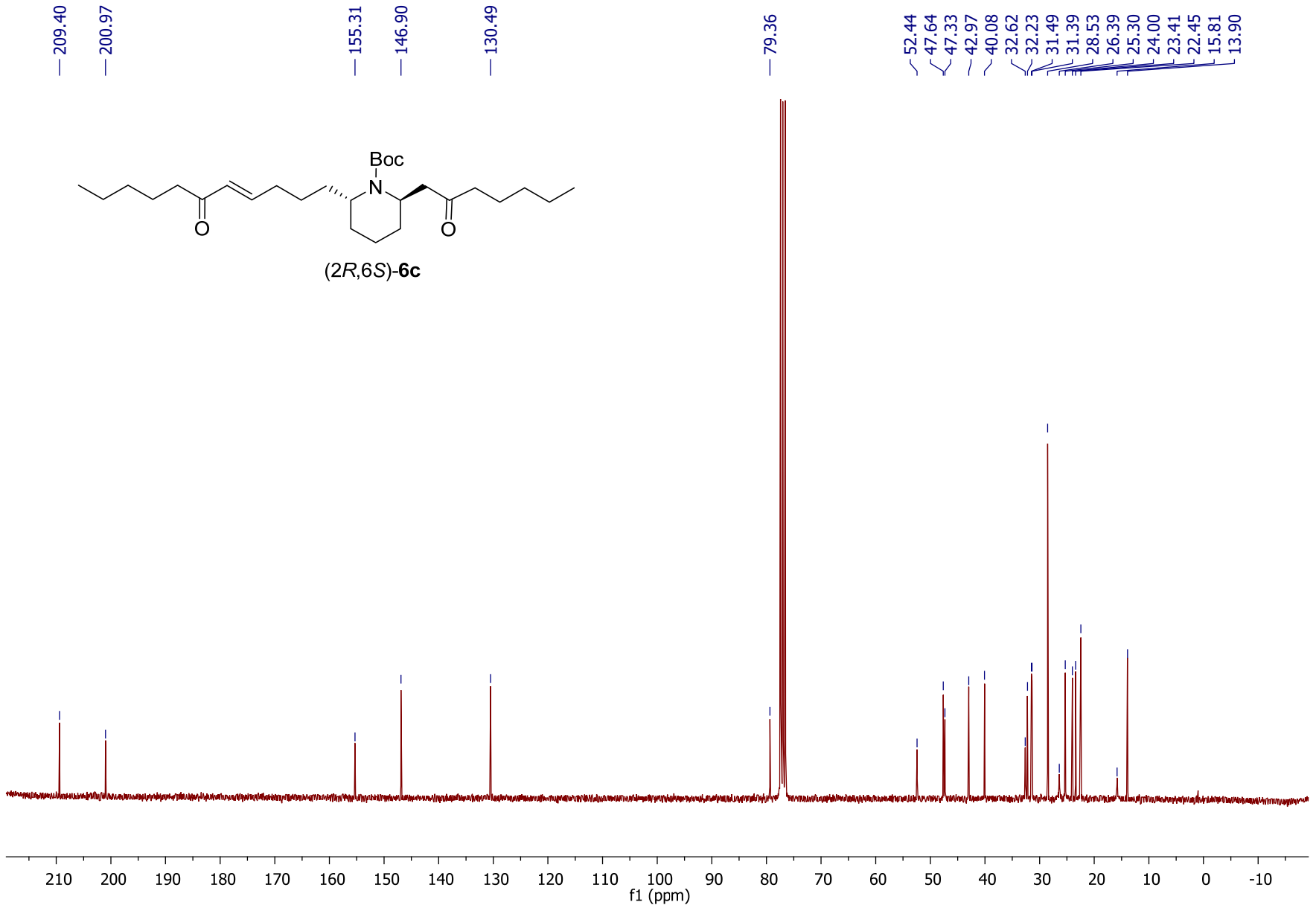
(2*R*,6*R*)-**6c**

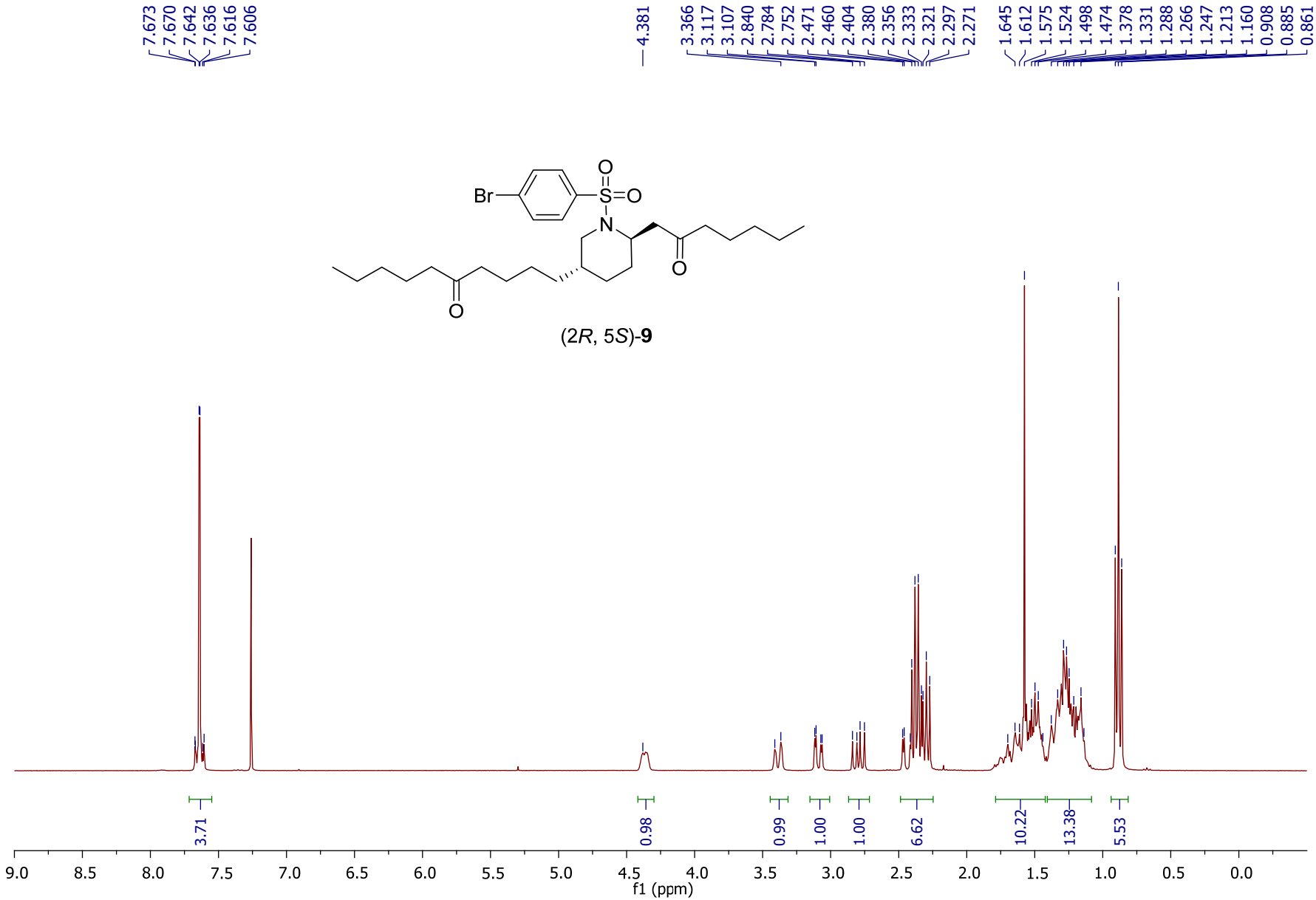

209.12
200.80
155.02
146.52
130.45
79.55
47.44
46.19
42.77
40.16
34.05
32.18
31.45
31.30
29.64
28.44
28.01
27.22
25.91
23.94
23.38
22.42
13.94
13.86
0.96
Boc
N
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

(2*R*,6*R*)-**6c**

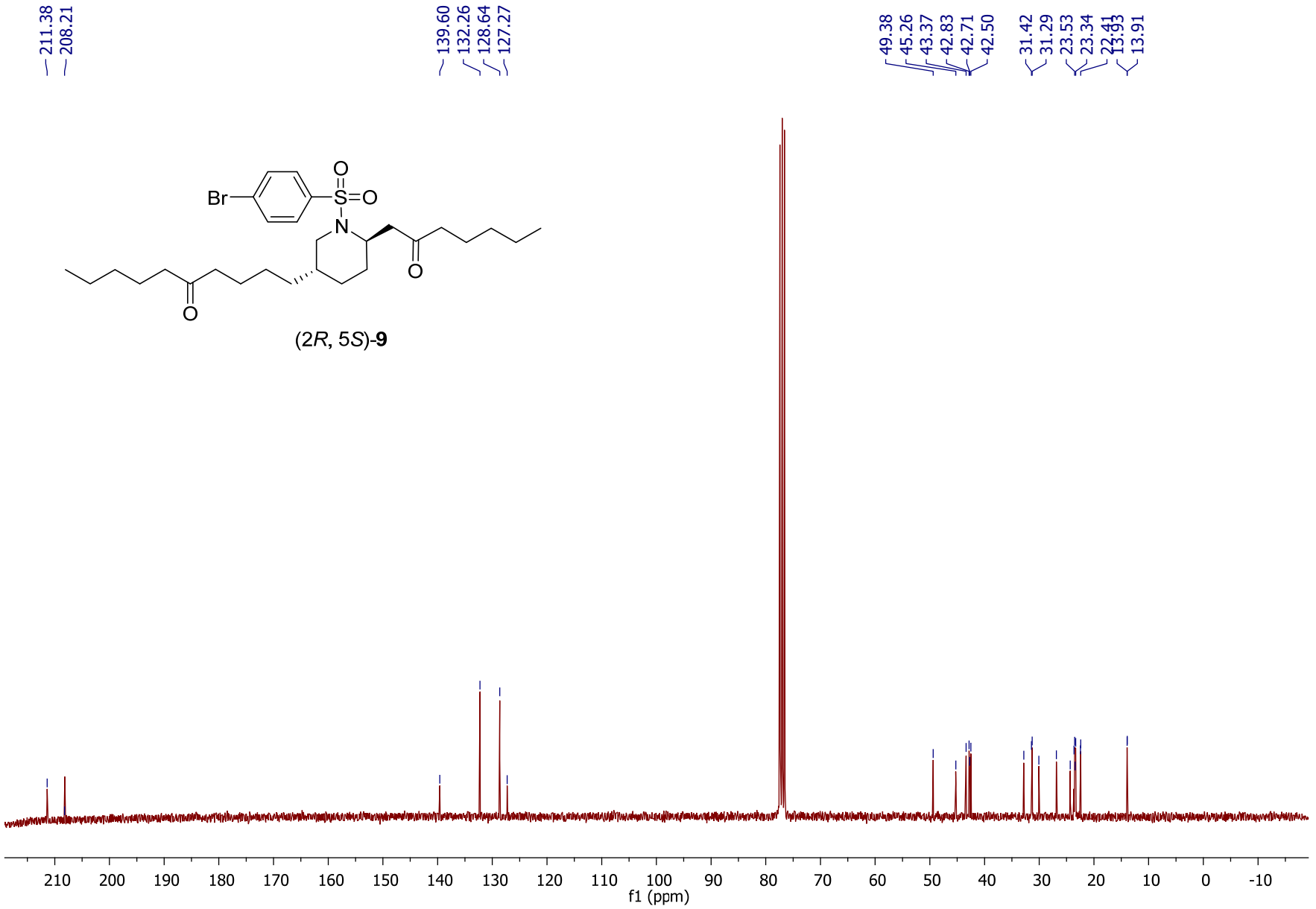

6.871
6.849
6.826
6.819
6.796
6.773
6.120
6.067
4.061
3.903
3.016
3.000
2.962
2.946
2.541
2.517
2.491
2.423
2.410
2.228
1.601
1.436
1.305
1.293
1.281
1.273
0.907
0.900
0.884
0.877
0.862
0.854
Boc
N
O
O
1.00
0.97
1.02
1.02
1.00
3.15
2.00
2.01
23.61
8.37
5.90
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

(2*R*,6*S*)-**6c**


209.40
200.97
155.31
146.90
130.49
79.36
52.44
47.64
47.33
42.97
40.08
32.62
32.23
31.49
31.39
28.53
26.39
25.30
24.00
23.41
22.45
15.81
13.90
Boc
N
O
O
(2R,6S)-6c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.673
7.670
7.642
7.636
7.616
7.606
4.381
3.366
3.117
3.107
2.840
2.784
2.752
2.471
2.460
2.404
2.380
2.356
2.333
2.321
2.297
2.271
1.645
1.612
1.575
1.524
1.498
1.474
1.378
1.331
1.288
1.266
1.247
1.213
1.160
0.908
0.885
0.861
Br
O
S
O
N
O
O
3.71
0.98
0.99
1.00
1.00
6.62
10.22
13.38
5.53
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

(2*R*, 5*S*)-**9**


211.38
208.21
139.60
132.26
128.64
127.27
49.38
45.26
43.37
42.83
42.71
42.50
31.42
31.29
23.53
23.34
22.41
13.93
13.91
Br
S
O
N
O
O
O
(2R, 5S)-9
f1 (ppm)