

Supporting information for Palladium-catalyzed Cross Coupling of Secondary and Tertiary Alkyl Bromides with a Nitrogen Nucleophile

D. Matthew Peacock, Casey B. Roos, and John F. Hartwig
Department of Chemistry, University of California, Berkeley, California 94720, United States.

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General experimental details

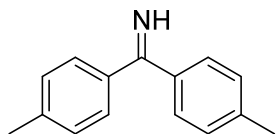
All reactions were performed under a nitrogen atmosphere, unless otherwise specified. Anhydrous *tert*-amyl alcohol was purchased from Sigma Aldrich and used as received. Dry THF, pentane, and diethyl ether were collected from a solvent purification system containing a 0.33 m column of activated alumina under nitrogen prior to use in reactions. Benzophenone imine (97%) purchased from Acros Organics was used in coupling reactions. Benzophenone imine (95%) purchased from Sigma Aldrich was used for the preparation of authentic imines by condensation reactions. All other chemicals were purchased from commercial suppliers and used as received.

Column chromatography was performed with 230-400 mesh silica gel from Fisher Scientific. TLC plates with fluorescent indicators were purchased from Silicycle or EMD and visualized under a 254 nm UV lamp unless otherwise noted. "Prebasified" silica refers to silica gel and TLC plates which have been soaked with 2-5% triethylamine in hexanes prior to use. "Untreated" silica refers to silica gel and TLC plates used as received. Special precautions taken to minimize hydrolysis are noted for relevant compounds.

GC spectra were obtained on an Agilent 7890 GC equipped with an HP-5 column (25 m x 0.20 mm x 0.33 μ m film) and an FID detector. NMR spectra were obtained on 500 MHz or 600 MHz Bruker Avance series instruments at the University of California, Berkeley NMR facility. Chemical shifts are reported relative to the residual solvent signals (CDCl_3 7.26 ppm for ^1H , 77.16 ppm for ^{13}C ; C_6D_6 7.16 ppm for ^1H , 128.06 ppm for ^{13}C). ESI high resolution mass spectrometry (HRMS) was performed by the QB3 Mass Spectrometry Facility or the LBNL Catalysis Center at the University of California, Berkeley. EIMS (positive ionization) was performed on an Agilent 7890A/5975C GC-MS. Elemental analysis was performed by the UC Berkeley Microanalytical Laboratory.

Preparation of benzophenone imine derivatives

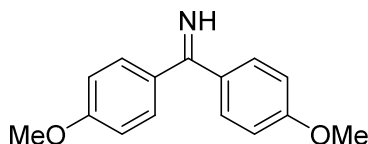
Note: The imines prepared below are sensitive to hydrolysis and contain small amounts of the corresponding ketones as impurities. The percent imine was measured by NMR spectroscopy and noted. To prevent further hydrolysis, these compounds were stored in a nitrogen-filled glovebox.



4,4'-Dimethylbenzophenone imine (2b). Dry magnesium turnings (365 mg, 15.0 mmol, 1.50 equiv), dry THF (20 ml), and a magnetic stir bar were placed in a nitrogen-filled flask, and the flask was connected to a reflux condenser. 4-Bromotoluene (1.84 ml, 2.57 g, 15.0 mmol, 1.50 equiv) was dissolved in THF (3 ml), and a small amount of this solution was transferred to the reaction flask.

The reaction was initiated with a single iodine crystal. The remaining aryl bromide solution was slowly transferred to the reaction flask, the syringe was rinsed with THF (3 ml), and the mixture was stirred at ambient temperature for 2.5 h at which time the majority of the magnesium was visibly consumed. The reaction mixture was then cooled to 0 °C, a solution of *p*-tolunitrile (1.20 ml, 1.17 g, 9.99 mmol) in THF (7 ml) was added to the flask, and the syringe rinsed with THF (3 ml). The reaction mixture was heated at reflux for 20 h, then cooled to 0 °C, and then quenched with dry methanol (3 ml). The reaction mixture was diluted with hexanes (30 ml), filtered through a pad of Celite, and concentrated at reduced pressure. The yellow oil was purified by column chromatography (5 to 10% ethyl acetate gradient and 5% triethylamine in hexanes on prebasified silica) to give the title compound as a pale yellow oil (1.82 g, 8.68 mmol, 87% yield, 97% imine by ¹H NMR spectroscopy). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.¹

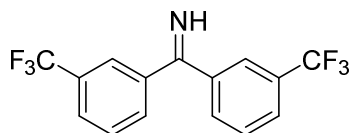
EIMS 209.1 (M⁺), 194.1 (base peak).



4,4'-Dimethoxybenzophenone imine (2c). A solution of 4-methoxyphenylmagnesium bromide (16 ml, 1.0M, 16 mmol, 1.1 equiv) in THF was transferred to a 100 ml nitrogen-filled flask fitted with a reflux condenser, and the solution was cooled to 0 °C. A solution of 4-methoxybenzonitrile (2.00 g, 15.0 mmol) in dry THF (9 ml) was added

to the flask, and the syringe rinsed with THF (3 ml). The reaction mixture was heated at reflux for 17 h, then cooled to 0 °C, and then quenched with dry methanol (3 ml). The reaction mixture was diluted with hexanes (20 ml), filtered through a pad of Celite, and concentrated at reduced pressure. The yellow solid was purified by column chromatography (0 to 50% ethyl acetate gradient and 5% triethylamine in hexanes on prebasified silica) to give the title compound as an off-white powder (2.48 g, 10.3 mmol, 69% yield, 96% imine by ¹H NMR spectroscopy). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.²

EIMS 241.1 (M⁺), 210.1 (base peak).

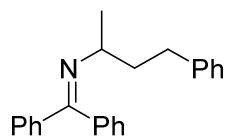


3,3'-Bis(trifluoromethyl)benzophenone imine (2d). Dry magnesium turnings (370 mg, 15.2 mmol, 1.49 equiv), dry THF (10 ml), and a magnetic stir bar were placed in a nitrogen-filled flask, and the flask was connected to a reflux condenser. 3-Bromobenzotrifluoride (2.10 ml, 3.38 g, 15.0 mmol, 1.47 equiv) was dissolved in THF (3 ml), and a small amount of this solution was transferred to the reaction flask. The reaction was initiated with a single iodine crystal. The remaining aryl bromide solution was slowly transferred to the reaction flask, the syringe was rinsed with THF (3 ml), and the mixture was heated at reflux until the majority of the magnesium was visibly consumed. The reaction mixture was then cooled to 0 °C, a solution of 3-trifluoromethylbenzonitrile (1.37 ml, 1.75 g, 10.2 mmol) in THF (2 ml) was added to the flask, and the syringe rinsed twice with THF (2 ml). The reaction mixture was heated at reflux for 4 h, then cooled to 0 °C, and then quenched with dry methanol (2 ml). The reaction mixture was diluted with hexanes (50 ml), neutralized with sodium bicarbonate, filtered through a pad of Celite, and concentrated at reduced pressure. The red oil was purified by kugelrohr distillation (150 °C, ~0.5 Torr) to give the title compound as a pale yellow oil (2.52 g, 7.94 mmol, 79% yield, >98% imine by ¹H NMR spectroscopy). This procedure has also been run on larger scale with 15.8 g of 3-trifluoromethylbenzonitrile. All masses and volumes were scaled accordingly, and 12.0 g (73% yield) of the title compound was obtained after purification by short path distillation (vapor temp 85-96 °C at approximately 0.20 Torr).

Note: when characterized in wet CDCl₃, the NMR signals were broad. Therefore, this compound was characterized in anhydrous CDCl₃ stored under nitrogen.

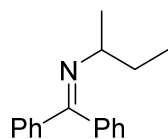
¹H NMR (500 MHz, CDCl₃) δ 10.05 (s, 1H), 8.05 (s, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 2H), 7.67 (s, 1H), 7.64 – 7.53 (m, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 175.7, 140.5, 138.5, 132.5, 131.7 (q, *J* = 32.8 Hz), 131.3 (q, *J* = 32.8 Hz), 130.8, 129.6, 129.1, 127.8, 127.2, 126.0, 124.4, 124.0 (q, *J* = 272.1 Hz), 123.8 (q, *J* = 272.4 Hz). **¹⁹F NMR** (565 MHz, CDCl₃) δ -63.7. **ESI⁺** calc'd 318.0712 (M+H⁺), found 318.0709.

Preparation of authentic products

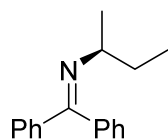


***N*-(4-phenylbutan-2-yl)benzophenone imine (3a).** Benzophenone imine (181 mg, 1.00 mmol), 1-methyl-3-phenylpropylamine (179 mg, 1.20 mmol, 1.20 equiv), and dry DCM (1 ml) were mixed in a 1 dram vial and stirred for 4 days at ambient temperature. The volatile materials were evaporated at reduced pressure, and the crude product was purified by kugelrohr distillation (0.5 to 1.0 Torr, 180 °C) to give the title compound as a colorless glass (286 mg, 0.912 mmol, 91% yield).

¹H NMR (600 MHz, CDCl₃) δ 7.62 (d, *J* = 7.4 Hz, 2H), 7.45 - 7.39 (m, 3H), 7.37 (t, *J* = 7.1 Hz, 1H), 7.33 (t, *J* = 7.4 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.17 - 7.10 (m, 5H), 3.50 - 3.43 (m, 1H), 2.60 (ddd, *J* = 13.7, 11.2, 5.4 Hz, 1H), 2.44 (ddd, *J* = 13.8, 11.1, 5.6 Hz, 1H), 2.02 - 1.93 (m, 1H), 1.85 - 1.77 (m, 1H), 1.20 (d, *J* = 6.2 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 166.5, 142.7, 140.4, 137.6, 129.8, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 127.9, 125.7, 57.3, 40.2, 33.2, 22.4. **ESI⁺** calc'd 314.1903 (M+H⁺), found 314.1899.



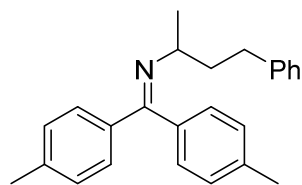
***N*-(*sec*-butyl)benzophenone imine (20).** Benzophenone imine (182 mg, 1.00 mmol), *sec*-butylammonium chloride (115 mg, 1.05 mmol, 1.05 equiv), and dry DCM (2 ml) were mixed in a 1 dram vial and stirred for 14 h at ambient temperature. The reaction mixture was filtered through a plug of Celite, which was rinsed with DCM (2 ml). The volatile materials were evaporated at reduced pressure, and the crude product was purified by column chromatography (2% triethylamine in hexanes on prebasified silica) to give the title compound as a clear and colorless oil (183 mg, 0.771 mmol, 77% yield). The ¹H and ¹³C NMR spectra matched those of (*S*)-**20**.



(*S*)-*N*-(*sec*-butyl)benzophenone imine ((*S*)-20). Benzophenone imine (363 mg, 2.00 mmol), (*S*)-*sec*-butylamine (184 mg, 2.51 mmol, 1.25 equiv), and dry DCM (2 ml) were mixed in a 1 dram vial and stirred for 7 days at ambient temperature. The volatile materials were evaporated at reduced pressure, and the crude product was purified by kugelrohr distillation (0.5 to 1.0 Torr, 120 °C) and column chromatography (5% triethylamine in hexanes on prebasified silica; R_f 0.85) to give the title compound as a clear and colorless oil (357 mg, 1.50 mmol, 75% yield).

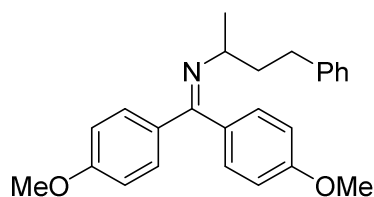
¹H NMR (500 MHz, CDCl₃) δ 7.62 - 7.57 (m, 2H), 7.47 - 7.38 (m, 3H), 7.38 - 7.29 (m, 3H), 7.15 (dd, *J* = 7.9, 1.4 Hz, 2H), 3.36 - 3.22 (m, 1H), 1.68 - 1.57 (m, 1H), 1.55 - 1.45 (m, 1H), 1.15 (d, *J* = 6.2 Hz, 3H), 0.79 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 166.2, 140.5, 137.8, 129.7, 128.5 (2C), 128.1 (2C), 127.9, 59.1, 31.3, 22.1, 11.3. **ESI⁺** calc'd 238.1590 (M+H⁺), found 238.1588.

(*S*)-*N*-(*sec*-butyl)benzophenone imine ((*S*)-**20**) and (*S*)-*N*-(*sec*-butyl)benzamide ((*S*)-**21**) were prepared from the same sample of (*S*)-*sec*-butylamine. Therefore, the sample of (*S*)-**20** is also presumed to have 97% ee.



***N*-(4-phenylbutan-2-yl)-4,4'-dimethylbenzophenone imine (3b).** 4,4'-Dimethylbenzophenone imine (208 mg, 0.993 mmol), 1-methyl-3-phenylpropylamine (179 mg, 1.20 mmol, 1.20 equiv), and dry DCM (1 ml) were mixed in a 1 dram vial and stirred for 5 days at ambient temperature. The volatile materials were evaporated at reduced pressure, and the crude product was purified by column chromatography (2% triethylamine in hexanes on prebasified silica, Rf 0.41) to give the title compound as a clear and colorless oil which solidified into a white solid on standing (259 mg, 0.758 mmol, 76% yield).

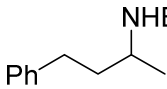
¹H NMR (500 MHz, CDCl₃) δ 7.51 (d, J = 8.2 Hz, 2H), 7.25 – 7.20 (m, 4H), 7.17 – 7.10 (m, 5H), 7.01 (d, J = 7.9 Hz, 2H), 3.47 (dq, J = 8.3, 6.2, 4.3 Hz, 1H), 2.59 (ddd, J = 13.7, 11.1, 5.4 Hz, 1H), 2.47 – 2.38 (m, 4H), 2.36 (s, 3H), 1.96 (dddd, J = 13.5, 11.0, 8.3, 5.4 Hz, 1H), 1.85 – 1.73 (m, 1H), 1.19 (d, J = 6.2 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 166.6, 142.8, 139.8, 138.0, 137.8, 134.8, 129.1, 128.8, 128.5, 128.5, 128.3, 127.8, 125.6, 77.4, 77.2, 57.2, 40.3, 33.3, 22.4, 21.5, 21.4. **ESI⁺** calc'd 342.2216 (M+H⁺), found 342.2212.



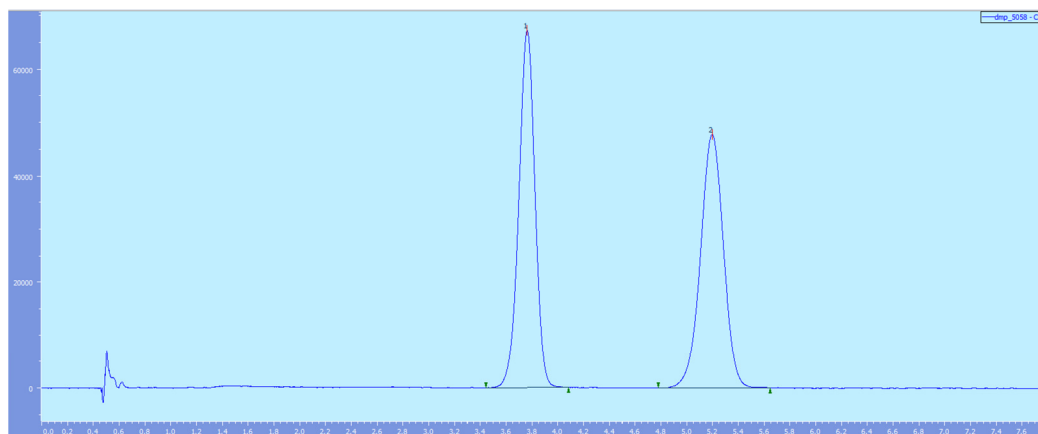
***N*-(4-phenylbutan-2-yl)-4,4'-dimethoxybenzophenone imine (3c).** 4,4'-Dimethoxybenzophenone imine (241 mg, 0.999 mmol), 1-methyl-3-phenylpropylamine (179 mg, 1.20 mmol, 1.20 equiv), and dry DCM (1 ml) were mixed in a 1 dram vial and stirred for 4 days at ambient temperature. The volatile materials were evaporated at reduced pressure, and the crude product was purified by column chromatography (10% ethylacetate and 5% triethylamine in hexanes on prebasified silica, Rf 0.44) to give the title compound as a clear and colorless oil (270 mg, 0.723 mmol, 72% yield).

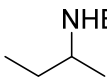
¹H NMR (500 MHz, Chloroform-d) δ 7.56 (d, J = 8.9 Hz, 2H), 7.23 (t, J = 7.4 Hz, 2H), 7.16 – 7.10 (m, 3H), 7.04 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 3.87 (s, 3H), 3.82 (s, 3H), 3.47 (dq, J = 8.3, 6.2, 4.3 Hz, 1H), 2.58 (ddd, J = 13.8, 11.0, 5.5 Hz, 1H), 2.42 (ddd, J = 13.8, 10.9, 5.7 Hz, 1H), 1.94 (dddd, J = 13.6, 10.9, 8.3, 5.5 Hz, 1H), 1.83 – 1.74 (m, 1H), 1.19 (d, J = 6.2 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 165.8, 161.1, 159.4, 142.8, 133.7, 130.1, 129.9, 129.3, 128.5, 128.3, 125.6, 113.8, 113.4, 77.4, 77.2, 77.0, 57.0, 55.5, 55.4, 40.3, 33.2, 22.5. **ESI⁺** calc'd 374.2115 (M+H⁺), found 374.2110.

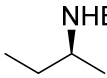
General procedure for the preparation of benzamides: The amine (0.50 mmol), triethylamine (84 μ l, 61 mg, 0.60 mmol, 1.2 equiv), and dry DCM (2 ml) were mixed in a 1 dram vial. The reaction mixture was cooled to 0 °C, and the vial was flushed with nitrogen. Benzoyl chloride (70 μ l, 85 mg, 0.60 mmol, 1.2 equiv) was slowly added through a septum cap. The reaction mixture was stirred at ambient temperature for 4 h. The reaction was quenched with 0.5 M HCl_(aq) (2 ml). The layers were separated, and the aqueous layer extracted twice more with DCM (2 ml). The combined organic layers were filtered through a plug of MgSO₄. The volatile materials were evaporated at reduced pressure. The crude products were purified by column chromatography (25% ethyl acetate in hexanes).

 **N-(4-phenylbutan-2-yl)benzamide (19).** Prepared by the general procedure above with 1-methyl-3-phenylpropylamine (74.5 mg, 0.499 mmol) to give the title compound as a white powder (126 mg, 0.497 mmol, 99% yield). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.³

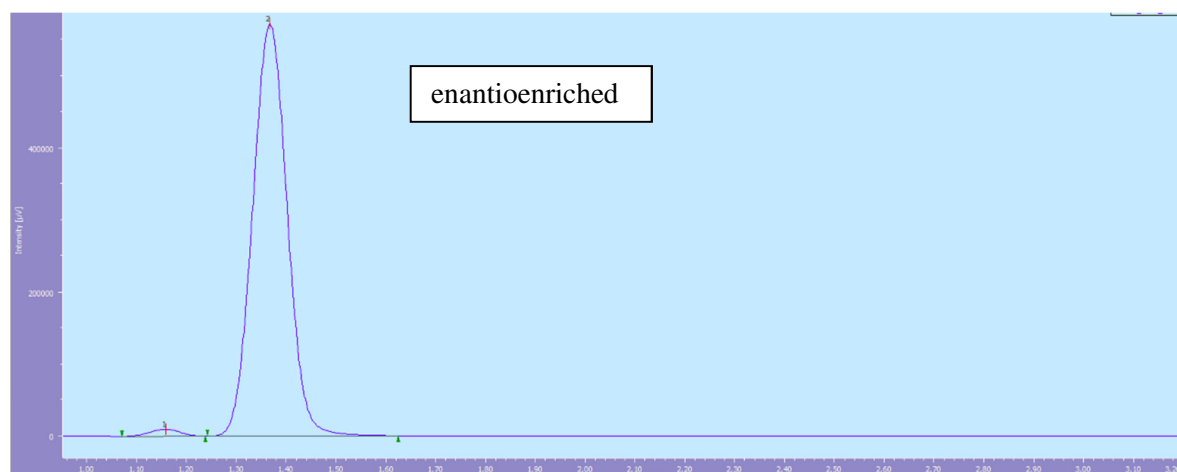
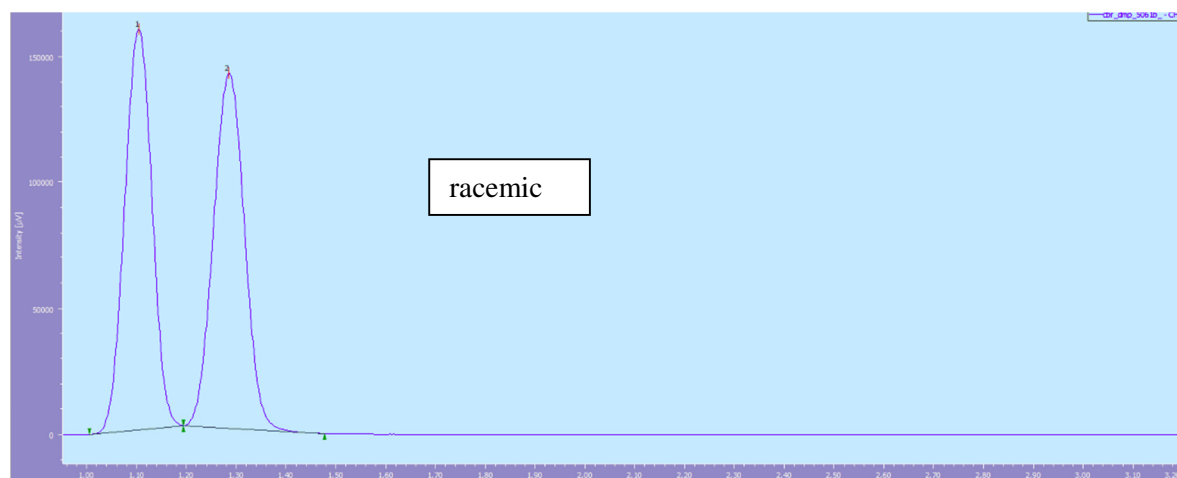
Chiral SFC Analysis: 0% ee, Chiracel OD-H column, 15% *i*-PrOH, 2.5 ml/min flow rate, *t* = 3.76, 5.19 min.



 **N-(*sec*-butyl)benzamide (21).** Prepared by the general procedure above with (rac)-*sec*-butylamine (36.6 mg, 0.500 mmol) to give the title compound as a white powder (85.4 mg, 0.482 mmol, 96% yield). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.⁴

 **(*S*)-N-(*sec*-butyl)benzamide ((*S*)-21).** Prepared by the general procedure above with (*S*)-*sec*-butylamine (38.4 mg, 0.525 mmol) to give the title compound as a white powder (84.8 mg, 0.478 mmol, 91% yield, 97% ee by SFC). The ¹H NMR spectrum matched that of the racemic sample.

Chiral SFC Analysis: 97% ee, Chiracel AS-H column, 15% *i*-PrOH, 2.5 ml/min flow rate, *t*_R (minor) = 1.16 min, *t*_R (major) = 1.37 min.



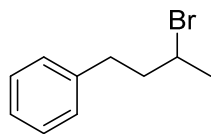
Preparation of alkyl bromides

The following alkyl bromides were prepared according to published procedures:

Methyl 4-bromohexanoate,⁵ 3-bromo-3-methyl-1-phenylbutane,⁶ 3-bromo-3-methylbutyl benzoate,⁷ 2-(2-bromo-2-methylpropyl)-1,3-dioxane,⁸ 5-bromo-1-chloro-5-methylhexane,⁹ *trans*-3-bromo-2-((3-methylbut-2-en-1-yl)oxy)tetrahydro-2H-pyran,¹⁰ and (Z)-5-bromocyclooct-1-ene.¹¹

The following alkyl bromides were prepared with minor modifications from published procedures:

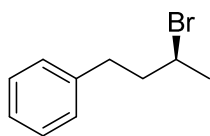
Endo-2-bromonorbornane¹² was purified by filtering through silica with hexanes, followed by kugelrohr distillation; the compound was determined to be 98% *endo* by ¹H NMR spectroscopy. *N*-(3-bromo-3-methylbutyl)phthalimide¹³ was purified by column chromatography and recrystallized from hexanes prior to use.



3-Bromo-1-phenylbutane (1). 4-Phenyl-2-butanol (2.98 g, 19.8 mmol) was dissolved in dry DCM (50 ml) in a 100 ml flask. The flask was cooled to 0 °C and flushed with nitrogen. Triphenylphosphine (6.56 g, 25.0 mmol, 1.25 equiv) and carbon tetrabromide (8.30 g, 25.0 mmol, 1.25 equiv) were added slowly in that order.

The reaction mixture was stirred at ambient temperature for 2 h. The volume was lowered at reduced pressure. The reaction mixture was diluted with hexanes (50 ml) and filtered through silica, which was rinsed twice with hexanes (50 ml). The volatile materials were evaporated at reduced pressure. The crude product was purified by kugelrohr distillation (0.5 to 1.0 Torr, 86 °C) to give the title compound as a clear and colorless oil (3.39 g, 15.9 mmol, 80% yield). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.¹⁴

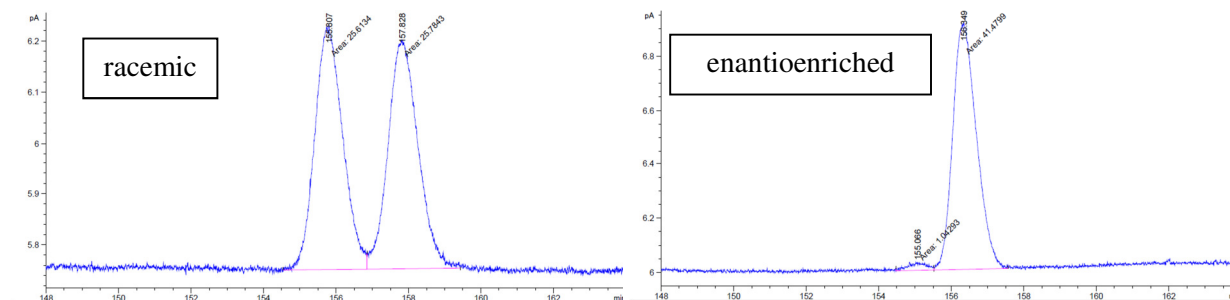
EIMS 214.0 (M⁺, ⁸¹Br), 212.0 (M⁺, ⁷⁹Br), 91.1 (base peak).



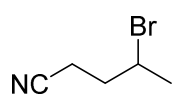
(S)-3-Bromo-1-phenylbutane ((S)-1). (*R*)-4-Phenyl-2-butanol (254 mg, 1.69 mmol) was dissolved in dry DCM (4 ml) in a 25 ml flask. The flask was cooled to 0 °C and flushed with nitrogen. Triphenylphosphine (554 mg, 2.11 mmol, 1.25 equiv) and carbon tetrabromide (700 mg, 2.11 mmol, 1.25 equiv) were slowly added in that order. The reaction mixture was stirred at ambient temperature for 2 h. The reaction

mixture was diluted to 10 ml with DCM and washed with 0.5 M HCl (10 ml). The aqueous layer was extracted twice more with DCM (10 ml). The combined organic layers were dried with MgSO₄. The volatile materials were evaporated at reduced pressure. The crude product was purified by kugelrohr distillation (0.5 to 0.8 Torr, 72 °C) to give the title compound as a clear and colorless oil (337 mg, 1.58 mmol, 94% yield). The ¹H NMR spectrum and EIMS matched that of the racemic sample.

Chiral GC Analysis: 95% ee, CycloSil-B column (30 m length, 0.25 mm diameter, 0.25 μm film), 85 °C to 93.5 °C ramp at 0.06 °C/min, *t_R* (minor) = 154 min, *t_R* (major) = 156 min.

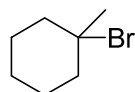


Note: chiral GC retention times for 3-bromo-1-phenylbutane (**1**) varied between 117 and 157 minutes due to variations in column conditions over time.



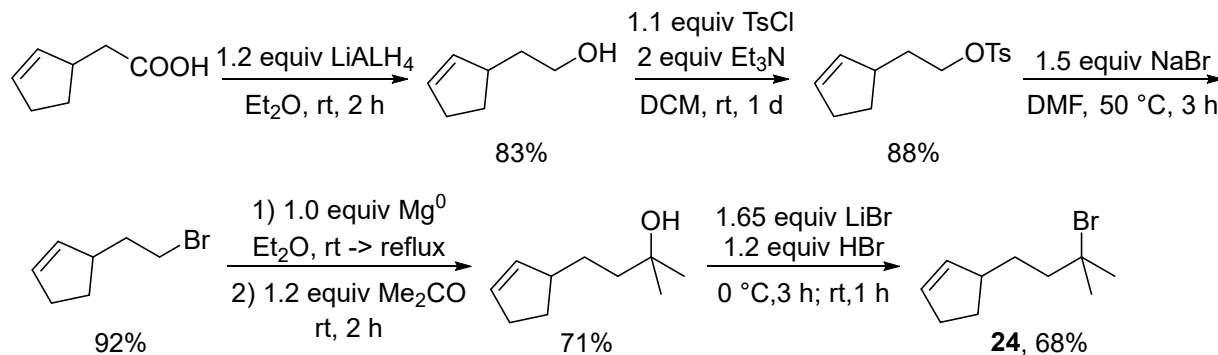
4-Bromopentanenitrile. A 20 dram vial was charged with 1,3-dibromobutane (2.16 g, 10.0 mmol), sodium cyanide (646 mg, 13.2 mmol, 1.32 equiv), ethanol (3 ml), and a magnetic stir bar. The vial was flushed with nitrogen and sealed with a Teflon-lined cap. The reaction mixture was heated at 80 °C for 26 h. The mixture was diluted with ether (approximately 50 ml), washed twice with water (~20 ml) and twice with brine (~20 ml). The organic layers were dried with MgSO₄, and the volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (0 to 25% ethyl acetate gradient in hexanes) followed by kugelrohr distillation (~120 °C, ~28 Torr), followed by column chromatography (0 to 10% ethyl acetate in hexanes gradient) to give the title compound as a clear and colorless oil (639 mg, 3.94 mmol, 39% yield).

¹H NMR (400 MHz, CDCl₃) δ 4.19 (dqd, *J* = 10.3, 6.7, 3.7 Hz, 1H), 2.65 – 2.53 (m, 2H), 2.22 – 2.11 (m, 1H), 2.11 – 2.00 (m, 1H), 1.77 (d, *J* = 6.7 Hz, 3H). **EIMS** 162.9 (M⁺, ⁸¹Br), 160.9 (M⁺, ⁷⁹Br), 82.1 (base peak).



1-Bromo-1-methylcyclohexane. 1-methylcyclohexan-1-ol (983 mg, 8.61 mmol) and a magnetic stir bar were placed in a 10 ml flask under air. HBr_(aq) (48%) was added slowly to the flask with stirring, and the mixture was stirred at ambient temperature for 20 h. The mixture was then diluted to approximately 40 ml with water and extracted twice with ether (~40 ml). The combined organic layers were washed twice with NaHCO_{3(aq)} (~40 ml) and dried with MgSO₄. The volatile materials were evaporated at reduced pressure. The crude product was purified by filtering through silica with pentanes, followed by kugelrohr distillation (85 °C, ~40 Torr) to give the title compound as a pale yellow oil (305 mg, 1.72 mmol, 20% yield). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.¹⁵

EIMS M⁺ not observed, 97.0 (base peak), 55.0.



2-(Cyclopent-2-en-1-yl)ethan-1-ol. 2-Cyclopentene-1-acetic acid (3.28 g, 26.0 mmol) was dissolved in dry Et_2O (200 ml) in a 500 ml flask. The reaction mixture was cooled to $0^\circ C$, and the flask flushed with nitrogen. $LiAlH_4$ (1.18 g, 31.1 mmol, 1.20 equiv) was added slowly. The reaction mixture was stirred at ambient temperature for 2 h. The reaction was then quenched at $0^\circ C$ with water (1 ml), 15% $NaOH_{(aq)}$ (1 ml), and water (3 ml). The mixture was stirred at ambient temperature until white, dried with $MgSO_4$, and filtered through Celite. The volatile materials were evaporated at reduced pressure. The crude product was purified by kugelrohr distillation ($120^\circ C$, 45 Torr) to give the title compound as a clear and colorless oil (2.43 g, 21.7 mmol, 83% yield). The 1H NMR spectrum was consistent with the spectrum reported in the literature.¹⁶

2-(Cyclopent-2-en-1-yl)ethyl 4-methylbenzenesulfonate. 2-(Cyclopent-2-en-1-yl)ethan-1-ol (3.38 g, 30.1 mmol) and triethylamine (8.5 ml, 6.2 g, 61 mmol, 2.0 equiv) were mixed in dry DCM (80 ml) in a 250 ml flask. The reaction mixture was cooled to $0^\circ C$, and the flask was flushed with nitrogen. $TsCl$ (6.32 g, 33.1 mmol, 1.10 equiv) was added slowly to the flask, and the reaction mixture was stirred at ambient temperature for 1 d. The reaction mixture was washed with 0.5 M $HCl_{(aq)}$ (100 ml). The aqueous layer was extracted twice more with DCM (30 ml). The combined organic layers were washed with 5% $NaOH_{(aq)}$ (100 ml), which was extracted twice more with DCM (30 ml). The organic layers were dried with $MgSO_4$. The volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (0 to 33% ethyl acetate gradient in hexanes) to give the title compound as a pale yellow oil (7.08 g, 26.6 mmol, 88% yield). The 1H NMR spectrum was consistent with the spectrum reported in the literature.¹⁷

3-(2-Bromoethyl)cyclopent-1-ene. 2-(Cyclopent-2-en-1-yl)ethyl 4-methylbenzenesulfonate (7.08 g, 26.6 mmol) was dissolved in dry DMF (30 ml) in a 50 ml flask. $NaBr$ (4.10 g, 39.8 mmol, 1.50 equiv) was added to flask, and the flask was flushed with nitrogen. The reaction mixture was heated at $50^\circ C$ for 3 h. The reaction mixture was diluted with water (100 ml), and the aqueous layer was extracted with pentane (100 ml). The organic layer was washed again with water (100 ml). The combined aqueous layers were extracted with pentane (100 ml), which was washed with water (100 ml) before combining organic layers. The combined organic layers were dried with $MgSO_4$. The volatile materials were evaporated at reduced pressure. The crude product was purified by filtering through a plug of silica (60 ml pentane to elute) to give the title compound as a clear and colorless oil (4.28 g, 24.5, 92% yield).

1H NMR (500 MHz, $CDCl_3$) δ 5.79 – 5.74 (m, 1H), 5.69 – 5.63 (m, 1H), 3.49 – 3.35 (m, 2H), 2.90 – 2.79 (m, 1H), 2.40 – 2.23 (m, 2H), 2.08 (dtd, $J = 13.0, 8.5, 5.0$ Hz, 1H), 1.97 (dtd, $J = 14.1, 7.7, 6.7, 6.7$ Hz, 1H), 1.84 (dtd, $J = 14.0, 7.7, 6.4$ Hz, 1H), 1.41 (ddt, $J = 12.8, 9.0, 6.4$ Hz, 1H). **EIMS** 176.0 (M^+ , ^{81}Br), 174.0 (M^+ , ^{79}Br), 67.1 (base peak).

4-(Cyclopent-2-en-1-yl)-2-methylbutan-2-ol. Dry magnesium turnings (304 mg, 12.5 mmol, 1.04 equiv) and dry Et₂O (4 ml) were placed in a 25 ml flask under nitrogen. 3-(2-Bromoethyl)cyclopent-1-ene (2.11 g, 12.1 mmol) was dissolved in dry Et₂O (6 ml). A few drops of this solution were added to the reaction flask, and the reaction was initiated with a single iodine crystal. The rest of the solution of alkyl bromide was added slowly over 45 min, and the syringe was rinsed with Et₂O (4 ml). The reaction mixture was heated at reflux until the majority of the magnesium was visibly consumed. The reaction mixture was cooled to 0 °C, and acetone (1.0 ml) mixed with Et₂O (6 ml) was slowly added. The reaction mixture was stirred at ambient temperature for 2 h, and then quenched at 0 °C with NH₄Cl_(aq) (2 ml). The reaction mixture was diluted to approximately 40 ml with ether and washed with NH₄Cl_(aq) (40 ml). The aqueous layer was extracted twice more with Et₂O (30 ml), and the combined organic layers were dried with MgSO₄. The volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (20 to 33% ether gradient in pentanes; KMnO₄ to visualize) to give the title compound as a clear and colorless oil (1.33 g, 8.62 mmol, 71% yield).

¹H NMR (500 MHz, CDCl₃) δ 5.74 – 5.70 (m, 1H), 5.69 – 5.66 (m, 1H), 2.67 – 2.55 (m, 1H), 2.41 – 2.21 (m, 2H), 2.04 (dtd, *J* = 13.0, 8.6, 4.6 Hz, 1H), 1.53 – 1.29 (m, 5H), 1.22 (s, 1H), 1.21 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 135.1, 130.6, 71.1, 46.0, 42.2, 32.1, 30.8, 29.9, 29.4, 29.4. **EIMS** 139.0 (M⁺ - 15), 80.0 (base peak).

3-(3-Bromo-3-methylbutyl)cyclopent-1-ene (24). 4-(Cyclopent-2-en-1-yl)-2-methylbutan-2-ol (1.13 g, 7.35 mmol) was placed in a 1 dram vial at 0 °C. LiBr (1.05 g, 12.1 mmol, 1.65 equiv) and HBr (47% in H₂O; 1.5 ml, 8.7 mmol, 1.2 equiv) were added, and the reaction mixture was stirred for 3 h at 0 °C and then at ambient temperature for 1 h. The reaction mixture was diluted with pentane (15 ml) and washed twice with NaHCO_{3(aq)} (15 ml). The combined aqueous layers were extracted with pentane (15 ml), which was washed again with NaHCO_{3(aq)} (15 ml) before combining. The combined organic layers were dried with MgSO₄ and filtered through a plug of silica, which was rinsed with pentane (100 ml). The volatile materials were evaporated at reduced pressure. The crude product was purified by kugelrohr distillation (70 °C, approximately 0.5 Torr) to give the title compound as a clear and colorless oil (1.08 g, 4.99 mmol, 68% yield).

¹H NMR (500 MHz, CDCl₃) δ 5.76 – 5.71 (m, 1H), 5.70 – 5.65 (m, 1H), 2.70 – 2.60 (m, 1H), 2.41 – 2.22 (m, 2H), 2.05 (dtd, *J* = 12.9, 8.6, 4.6 Hz, 1H), 1.88 – 1.77 (m, 2H), 1.76 (s, 3H), 1.75 (s, 3H), 1.66 – 1.58 (m, 1H), 1.53 – 1.37 (m, 2H). **¹³C NMR** (151 MHz, CDCl₃) δ 134.8, 130.9, 68.7, 45.9, 45.5, 34.4, 34.4, 32.6, 32.2, 29.8. **EIMS** 217.9 (M⁺, ⁸¹Br), 215.9 (M⁺, ⁷⁹Br), 67.0 (base peak).

Note: This alkyl bromide was stored cold.

Preparation of L₂PdHBr complexes.

The preparations of L₂PdHBr complexes were adapted with minor modifications from a literature procedure for the preparation of (Cy₃P)₂PdHBr.¹⁸

(Cy₂*t*-BuP)₂PdHBr. (COD)PdBr₂ (749 mg, 2.00 mmol) was suspended in degassed, dry toluene (4 ml) in a 50 ml flask under nitrogen. The reaction mixture was cooled to approximately -5 °C and stirred. NaOH (168 mg, 4.20 mmol, 2.10 equiv) was dissolved in dry methanol (2 ml) and slowly added to the reaction mixture. After the orange color dissipated, Cy₂*t*-BuP (1.07 g, 4.20 mmol, 2.10 equiv) dissolved in degassed, dry toluene (7 ml) was added to the reaction mixture. The reaction mixture was stirred at 0 °C for 2 h, then warmed to ambient temperature. Dry MeOH (20 ml) was added to precipitate the product. The mixture was cooled to 0 °C and stirred for 30 min. The crude product was collected by filtration and purified by recrystallization (warm ether layered with pentane, 3 crops) to give the title compound as colorless, blocky crystals (943 mg, 1.35 mmol, 68%).

¹H NMR (600 MHz, C₆D₆) δ 2.45 – 2.32 (m, 8H), 2.02 (d, J = 12.9 Hz, 4H), 1.80 – 1.57 (m, 20H), 1.45 – 1.16 (m, 30H), -13.52 (t, J = 7.0 Hz, 1H). ¹³C NMR (151 MHz, C₆D₆) δ 35.2 (4C), 33.8 (2C), 32.4 (4C), 30.9 (6C), 29.7 (4C), 27.8 (4C), 27.5 (4C), 26.8 (4C). ³¹P NMR (243 MHz, C₆D₆) δ 55.5. **Analysis** calc'd for C₃₂H₆₃BrP₂Pd: C 55.21, H 9.12; found C 55.61, H 8.99.

(1-Ad)₂MeP. (1-Ad)₂CIP (672 mg, 1.99 mmol) was dissolved in dry ether (10 ml) in a 25 ml Schlenk flask under N₂. The reaction mixture was cooled to -78 °C, and a solution of MeLi (1.5 ml, 1.6 M in Et₂O, 2.4 mmol, 1.2 equiv) was slowly added to the reaction flask with stirring. The reaction mixture was stirred at -78 °C for approximately 10 minutes, then at ambient temperature for one hour. The reaction mixture was put under static vacuum and moved to a nitrogen-filled glovebox. The mixture was carefully filtered through a plug of silica, which was rinsed with ether (approximately 15 ml). The volatile materials were evaporated at reduced pressure to give the title compound as a white powder (586 mg, 1.85 mmol, 93% yield). The ¹H NMR and ³¹P spectra were consistent with the spectra reported in the literature.¹⁹

[(1-Ad)₂MeP]₂PdHBr. (COD)PdBr₂ (240 mg, 0.641 mmol) was suspended in degassed, dry toluene (1 ml) in a 10 ml flask under nitrogen. The reaction mixture was cooled to approximately -5 °C and stirred. NaOH (54 mg, 1.35 mmol, 2.11 equiv) was dissolved in dry methanol (0.5 ml) and slowly added to the reaction mixture. After the orange color dissipated, (1-Ad)₂MeP (426 mg, 1.35 mmol, 2.11 equiv) dissolved in degassed, dry toluene (2.5 ml) was added to the reaction mixture. The reaction mixture was stirred at 0 °C for 3 h, then warmed to ambient temperature. Dry MeOH (5 ml) was added to precipitate the product. The mixture was cooled to 0 °C and stirred for 15 min. The crude product was collected by filtration and moved to a nitrogen-filled glovebox. The crude product was dissolved in dry toluene (approximately 10 ml) and filtered through a plug of Celite, which was rinsed with toluene (3x2 ml). The solvent was evaporated at reduced pressure. The solid residue was washed twice with cold ether (4 ml) and once with pentane (4 ml). The white powder was dried under vacuum (404 mg, 0.493 mmol, 77% yield).

¹H NMR (600 MHz, C₆D₆) δ 2.07 (q, J = 12.7 Hz, 24H), 1.94 – 1.85 (m, 12H), 1.72 (t, J = 2.4 Hz, 6H), 1.67 – 1.57 (m, 24H), -12.49 (t, J = 7.3 Hz, 1H). **¹³C NMR** (151 MHz, C₆D₆) δ 40.5 (12C), 37.8 (4C), 37.2 (12C), 29.0 (12C), 3.0 (2C). **³¹P NMR** (243 MHz, C₆D₆) δ 49.6. **Analysis** calc'd for C₄₂H₆₇BrP₂Pd: C 61.50, H 8.23; found C 62.38, H 8.46.

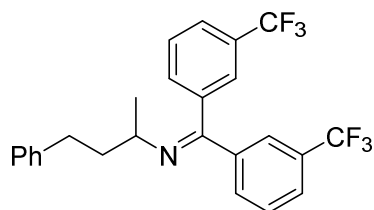
Note: The solid L₂PdHBr complexes are stable to brief handling in air, but solutions of the compounds should not be exposed to air. These compounds were stored cold in a nitrogen-filled glovebox.

Preparation of *N*-alkyl imines by palladium-catalyzed coupling (Table 3, Scheme 3, and Scheme 4)

General notes about product stability and purification: Isolation and purification of most *N*-alkyl imines is complicated due to hydrolysis and streaking during column chromatography. Isolation of the 3,3'-bis(trifluoromethyl)-substituted *N*-alkyl imines is much more straightforward. Stability to silica was determined by two-dimensional TLC (Prebasified: 5% triethylamine + varying % ethyl acetate in hexanes. Untreated: 10 or 25% ethyl acetate in hexanes). The starting 3,3'-bis(trifluoromethyl)benzophenone imine undergoes hydrolysis slowly on prebasified silica and readily on untreated silica. This compound also streaks significantly on untreated columns. However, no hydrolysis of the *N*-alkyl imine products listed below was detected on prebasified silica, and only faint hydrolysis was detected on untreated silica (varies some between compounds). These compounds do not streak significantly on either prebasified or untreated columns. Because the relative *R_f* values for nitrogen-containing compounds change significantly between prebasified and untreated silica, a combination of these two systems was often used to purify the *N*-alkyl imine products. *R_f* values on prebasified TLC plates are not well reproduced from trial to trial. With extended exposure, untreated silica gel can induce a selective hydrolysis of 3,3'-bis(trifluoromethyl)benzophenone imine in the presence of the *N*-alkyl imine products.

General procedure for Pd-catalyzed cross coupling of alkyl bromides with 2d (Table 3). In a nitrogen-filled glovebox, a 1 dram vial was charged with the alkyl bromide (0.300 mmol), 3,3'-bis(trifluoromethyl)benzophenone imine (**2d**) (1.5 or 3.0 equiv), (Cy₂*t*-BuP)₂PdHBr (11 mg, 0.016 mmol, 5.3 mol %), cesium carbonate (1.50 or 3.0 equiv), *tert*-amyl alcohol (0.40 ml; total volume approximately 0.6-0.7 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 3 or 20 h in an aluminum block. The product was isolated by column chromatography. Purification details are noted for each compound. Reaction times, equivalents of **2d**, and equivalents of Cs₂CO₃ are denoted with the letter codes A-C for each compound.

- A) **2d** (143 mg, 0.451 mmol, 1.50 equiv); Cs₂CO₃ (147 mg, 0.451 mmol, 1.50 equiv); 20 h
B) **2d** (286-288 mg, 0.90 mmol, 3.0 equiv); Cs₂CO₃ (293 mg, 0.899 mmol, 3.00 equiv); 20 h
C) **2d** (286 mg, 0.902 mmol, 3.00 equiv); Cs₂CO₃ (147 mg, 0.451 mmol, 1.50 equiv); 3 h

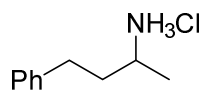


***N*-(4-Phenylbutan-2-yl)- 3,3'-bis(trifluoromethyl)benzophenone imine (**3d**).** Prepared by general procedure A with 3-phenyl-1-bromobutane (63.9 mg, 0.300 mmol). Purified by column chromatography (2% triethylamine in hexanes on prebasified silica, *R_f* 0.46; 5% ethyl acetate in hexanes, *R_f* 0.25) to give the title compound as a colorless oil (trial 1: 122 mg, 0.271 mmol, 90% yield) (trial 2: 120 mg, 0.267 mmol, 89% yield).

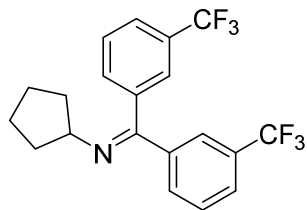
Glovebox-free procedure: prepared as described above, with the modification that all components were weighed and mixed under air. The 1 dram vial was then flushed with funnel connected to a nitrogen line prior to sealing and heating. The title compound was isolated as a very pale yellow oil (104 mg, 0.231 mmol, 77% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.96 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.64 (t, *J* = 8.8 Hz, 2H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.38 (s, 1H), 7.28 (d, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 7.3 Hz, 2H), 3.36 (m, 1H), 2.58 (ddd, *J* = 13.9, 10.4, 5.8 Hz, 1H), 2.46

(ddd, $J = 13.8, 10.1, 6.1$ Hz, 1H), 2.05 – 1.93 (m, 1H), 1.91 – 1.80 (m, 1H), 1.20 (d, $J = 6.2$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 163.3, 142.1, 140.3, 137.3, 131.8, 131.4 (q, $J = 32.8$ Hz), 131.2, 131.0 (q, $J = 32.5$ Hz), 129.5, 128.9, 128.5, 128.4, 126.8, 125.9, 125.6, 124.9, 124.5, 124.1 (q, $J = 272.3$ Hz), 123.9 (q, $J = 272.6$ Hz), 57.6, 39.8, 33.1, 22.1. ^{19}F NMR (565 MHz, CDCl_3) δ -63.5, -63.6. ESI^+ calc'd 450.1651 ($\text{M}+\text{H}^+$), found 450.1649.

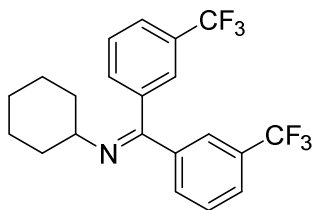


(4-Phenylbutan-2-yl)ammonium chloride. Under air, *N*-(4-Phenylbutan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (**3d**) (104 mg, 0.231 mmol) was dissolved in methanol (3 ml). $\text{HCl}_{(\text{aq})}$ (0.35 ml, 1.0 M, 0.35 mmol, 1.5 equiv) was added dropwise to the reaction mixture with stirring. After 60 min, the reaction mixture was diluted with ether (~5 ml) and filtered through a plug of glass wool, which was rinsed with ether (3x1 ml). The volatile materials were evaporated at reduced pressure. Ether and water (~5 ml each) were added to residue, the organic layer was removed, the aqueous layer was washed again with ether (2 ml), and the combined organic layers were extracted with water (2 ml). The volatile materials were removed from the combined aqueous layers at reduced pressure. The crude ammonium chloride salt was dissolved in DCM (3 ml) and filtered through a plug of Na_2SO_4 . Addition of hexanes (~8 ml) at 0 °C caused a precipitate to form, which was collected by filtration, washed with cold hexanes (2x2 ml), and dried under vacuum to give the title compound as a white powder (38.6 mg, 0.208 mmol, 90% yield). The ^1H NMR spectrum was consistent with that reported in the literature.²⁰



***N*-Cyclopentyl-3,3'-bis(trifluoromethyl)benzophenone imine (6).** Prepared by general procedure A with bromocyclopentane (44.8 mg, 0.299 mmol). Purified by column chromatography (1 to 3% ethyl acetate gradient in hexanes, R_f 0.24 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, R_f 0.50) to give the title compound as a very pale yellow oil (trial 1: 88.5 mg, 0.230 mmol, 77% yield) (trial 2: 90.0 mg; 0.234 mmol, 78% yield).

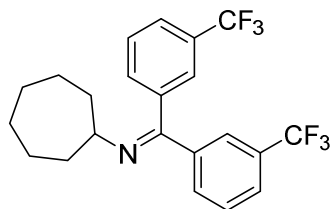
^1H NMR (500 MHz, CDCl_3) δ 7.95 (s, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.65 – 7.58 (m, 3H), 7.47 – 7.40 (m, 2H), 7.36 (d, $J = 7.6$ Hz, 1H), 3.62 (p, $J = 6.6$ Hz, 1H), 1.94 – 1.83 (m, 2H), 1.78 – 1.69 (m, 4H), 1.62 – 1.52 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 162.5, 140.5, 137.5, 131.8, 131.4, 131.4 (q, $J = 32.8$ Hz), 130.93 (q, $J = 32.4$ Hz), 129.4, 128.8, 126.6, 125.7, 124.9, 124.8, 124.2 (q, $J = 272.4$ Hz), 124.0 (q, $J = 272.5$ Hz), 63.8, 35.1, 25.3. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 386.1338 ($\text{M}+\text{H}^+$), found 386.1337.



***N*-Cyclohexyl-3,3'-bis(trifluoromethyl)benzophenone imine (7).** Prepared by general procedure A with bromocyclohexane (49.0 mg, 0.300 mmol). Purified by column chromatography (1 to 3% ethyl acetate gradient in hexanes, R_f 0.17 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, R_f 0.52) to give the title compound as a colorless oil (47.6 mg, 0.119 mmol, 40% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.94 (s, 1H), 7.74 (d, $J = 8.0$ Hz, 1H), 7.66 – 7.61 (m, 2H), 7.60 (d, $J = 7.7$ Hz, 1H), 7.43 (t, $J = 8.1$ Hz, 1H), 7.41 (s, 1H), 7.36 (d, $J = 7.6$ Hz, 1H), 3.13 (tt, $J = 9.5, 4.4$ Hz, 1H), 1.81 – 1.71 (m, 2H), 1.69 – 1.52 (m, 5H), 1.27 (qt, $J = 12.4, 3.4$ Hz, 1H), 1.15 (qt, $J = 12.3, 3.7$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 162.5, 140.5, 137.4, 131.8, 131.4 (q, $J = 32.8$ Hz), 131.2, 130.9 (q, $J = 32.4$

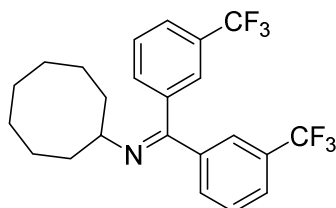
Hz), 129.5, 128.8, 126.7, 125.7, 124.9, 124.5, 124.2 (q, $J = 272.5$ Hz), 124.0 (d, $J = 272.6$ Hz), 62.0, 34.0, 25.7, 24.3. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 400.1494 ($\text{M}+\text{H}^+$), found 400.1489.



***N*-Cycloheptyl-3,3'-bis(trifluoromethyl)benzophenone imine (8).**

Prepared by general procedure A with bromocycloheptane (53.1 mg, 0.300 mmol). Purified by column chromatography (0 to 3% ethyl acetate gradient in hexanes, R_f 0.21 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, R_f 0.43) to give the title compound as a colorless oil (trial 1: 92.9 mg, 0.225 mmol, 75% yield) (trial 2: 99.4 mg, 0.240 mmol, 80% yield).

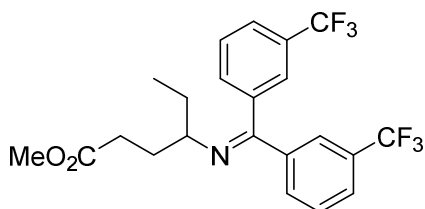
^1H NMR (500 MHz, CDCl_3) δ 7.93 (s, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.65 – 7.58 (m, 3H), 7.43 (t, $J = 7.8$ Hz, 1H), 7.40 (s, 1H), 7.35 (d, $J = 7.6$ Hz, 1H), 3.31 (tt, $J = 8.6, 4.4$ Hz, 1H), 1.82 – 1.70 (m, 4H), 1.66 – 1.47 (m, 6H), 1.40 – 1.30 (m, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.2, 140.58, 137.39, 131.83, 131.36 (q, $J = 32.7$ Hz), 131.22, 130.90 (d, $J = 32.4$ Hz), 129.42, 128.78, 126.6, 125.6, 124.9, 124.6, 124.2 (q, $J = 272.4$ Hz), 124.0 (q, $J = 272.5$ Hz), 63.6, 35.9, 28.8, 24.6. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 414.1651 ($\text{M}+\text{H}^+$), found 414.1650.



***N*-Cyclooctyl-3,3'-bis(trifluoromethyl)benzophenone imine (9).**

Prepared by general procedure A with bromocyclooctane (57.2 mg, 0.299 mmol). Purified by column chromatography (3% ethyl acetate in hexanes, R_f 0.17; 2% triethylamine in hexanes on prebasified silica, R_f 0.46) to give the title compound as a colorless oil (111 mg, 0.259 mmol, 86% yield).

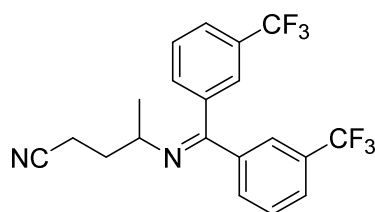
^1H NMR (500 MHz, CDCl_3) δ 7.93 (d, $J = 7.6$ Hz, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.66 – 7.60 (m, 3H), 7.46 – 7.40 (m, 2H), 7.35 (d, $J = 7.6$ Hz, 1H), 3.36 (tt, $J = 8.2, 3.7$ Hz, 1H), 1.88 – 1.72 (m, 4H), 1.64 – 1.47 (m, 6H), 1.47 – 1.32 (m, 4H), 1.32 – 1.22 (m, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.2, 140.5, 137.5, 131.8, 131.4 (q, $J = 32.6$ Hz), 131.2, 130.9 (q, $J = 32.3$ Hz), 129.4, 128.8, 126.6, 125.6, 124.9, 124.6, 124.2 (q, $J = 272.5$ Hz), 124.0 (q, $J = 272.4$ Hz), 62.5, 33.7, 27.3, 26.1, 24.0. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 428.1807 ($\text{M}+\text{H}^+$), found 428.1808.



Methyl 4-((bis(3-(trifluoromethyl)phenyl)methylene)amino)hexanoate (10).

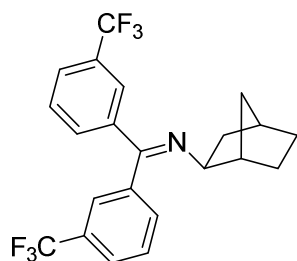
Prepared by general procedure A with methyl 4-bromohexanoate (62.7 mg, 0.300 mmol). Purified by column chromatography (1 to 10% ethyl acetate in hexanes, R_f 0.30 in 10% EA/Hex; 5% triethylamine in hexanes on prebasified silica, R_f 0.28) to give the title compound as a pale yellow oil (trial 1: 109 mg, 0.245 mmol, 82% yield) (trial 2: 105 mg, 0.236 mmol, 79% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.95 (s, 1H), 7.73 (d, $J = 7.9$ Hz, 1H), 7.67 – 7.59 (m, 3H), 7.45 (t, $J = 7.8$ Hz, 1H), 7.41 (s, 1H), 7.36 (d, $J = 7.6$ Hz, 1H), 3.57 (s, 3H), 3.15 (p, $J = 6.3$ Hz, 1H), 2.32 – 2.19 (m, 2H), 1.99 – 1.87 (m, 2H), 1.65 – 1.56 (m, 2H), 0.81 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.9, 164.1, 140.1, 137.3, 131.8, 131.4, 131.4 (q, $J = 32.7$ Hz), 130.9 (q, $J = 32.5$ Hz), 129.4, 128.9, 126.9, 125.6, 124.8 (2C), 124.1 (d, $J = 272.5$ Hz), 123.9 (d, $J = 272.4$ Hz), 63.0, 51.6, 31.0, 31.0, 29.2, 11.0. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 446.1549 ($\text{M}+\text{H}^+$), found 446.1549.



4-((Bis(3-(trifluoromethyl)phenyl)methylene)amino)pentanenitrile (11). Prepared by general procedure A with 4-bromopentanenitrile (48.6 mg, 0.300 mmol). Purified by column chromatography (1 to 25% ethyl acetate gradient in hexanes, very slowly to allow all 3,3'-bis(trifluoromethyl)benzophenone imine to hydrolyze, Rf 0.50 in 25% EA/Hex) to give the title compound as a pale yellow oil (trial 1: 90.4 mg, 0.227 mmol, 76% yield) (trial 2: 89.2 mg, 0.224 mmol, 75%).

¹H NMR (500 MHz, CDCl₃) δ 7.99 (s, 1H), 7.76 (d, *J* = 7.9 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 1H), 7.44 (s, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 3.47 (dq, *J* = 9.8, 6.3, 3.5 Hz, 1H), 2.41 – 2.27 (m, 2H), 2.08 – 2.00 (m, 1H), 1.91 – 1.81 (m, 1H), 1.16 (d, *J* = 6.3 Hz, 3H). **¹³C NMR** (151 MHz, CDCl₃) δ 165.3, 139.7, 136.6, 131.9, 131.7 (q, *J* = 32.8 Hz), 131.1, 131.1 (q, *J* = 32.5 Hz), 129.8, 129.0, 127.2, 126.0, 124.8, 124.3, 124.1 (q, *J* = 272.4 Hz), 123.8 (q, *J* = 272.5 Hz), 119.6, 56.0, 33.6, 21.6, 14.5. **¹⁹F NMR** (565 MHz, CDCl₃) δ -63.6, -63.7. **ESI⁺** calc'd 399.1290 (M+H⁺), found 399.1289.



Exo-2-((bis(3-(trifluoromethyl)phenyl)methylene)amino)norbornane (12). Prepared by general procedure A with *exo*-2-bromonorbornane or *endo*-2-bromonorbornane (52.5 mg, 0.300 mmol). Purified by column chromatography (0 to 3% ethyl acetate gradient in hexanes, Rf 0.21 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, Rf 0.46) to give the title compound as a colorless oil.

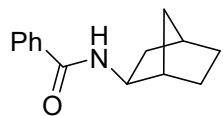
¹H NMR (600 MHz, CDCl₃) δ 7.93 (s, 1H), 7.73 (d, *J* = 7.9 Hz, 1H), 7.64 – 7.59 (m, 3H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.40 (s, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 3.16 (d, *J* = 7.4 Hz, 1H), 2.32 (s, 1H), 2.14 (s, 1H), 2.06 (d, *J* = 9.3 Hz, 1H), 1.52 – 1.44 (m, 3H), 1.40 (dd, *J* = 12.0, 7.6 Hz, 1H), 1.27 (d, *J* = 9.6 Hz, 1H), 1.05 (t, *J* = 8.3 Hz, 1H), 0.97 (t, *J* = 8.4 Hz, 1H). **¹³C NMR** (151 MHz, CDCl₃) δ 161.3, 140.5, 137.6, 131.8, 131.6, 131.3 (q, *J* = 32.7 Hz), 130.9 (q, *J* = 32.4 Hz), 129.3, 128.8, 126.6, 125.6, 125.0, 124.9, 124.2 (q, *J* = 272.4 Hz), 124.0 (d, *J* = 272.6 Hz), 65.8, 44.6, 41.0, 36.4, 36.1, 29.1, 26.5. **¹⁹F NMR** (565 MHz, CDCl₃) δ -63.6, -63.7. **ESI⁺** calc'd 412.1494 (M+H⁺), found 412.1490.

With *exo*-2-bromonorbornane: 48.6 mg, 0.118 mmol, 39% yield.

With *endo*-2-bromonorbornane; trial 1: 56.4 mg, 0.137 mmol, 46% yield; trial 2: 42.1 mg, 0.102 mmol, 34% yield.

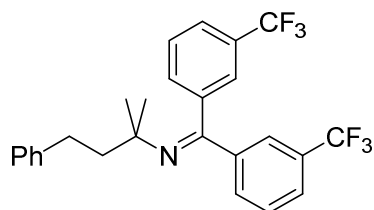
Note: The ¹H NMR spectrum obtained from every sample of *exo*-2-((bis(3-(trifluoromethyl)phenyl)methylene)amino)norbornane contains a set of small signals which are presumed to originate from the *endo* isomer of the compound. Integration of the signal at 3.51 ppm (expected to correspond to the C-2 hydrogen of the *endo* isomer) indicates that the samples contain approximately 2% of the *endo* compound (same in every sample).

Exo-stereochemistry of the major isomer was confirmed by conversion to the corresponding benzamide:



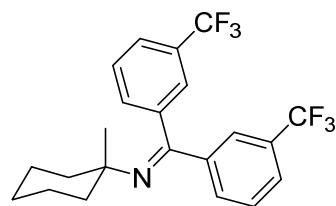
Exo-2-(benzoylamino)norbornane. *Exo*-2-((bis(3-(trifluoromethyl)phenyl)methylene)amino)norbornane (**12**) (126 mg, 0.306 mmol) and 0.5 M HCl_(aq) (6 ml) were mixed in a 20 ml vial. The vial was flushed with nitrogen and sealed with a Teflon-lined cap. The reaction mixture was heated at 80 °C with stirring for 4 h in an aluminum heating block. The mixture was washed twice with ether (4 ml). The organic layers were extracted with 0.5 M HCl_(aq), and the combined aqueous layers were basified with K₂CO₃ (2.0 g). The mixture was extracted four times with DCM (6 ml). The organic layers were filtered through a plug of Na₂SO₄ into a 20 ml vial. The volatile materials were evaporated at reduced pressure, and the vial flushed with nitrogen.

The crude amine was dissolved in dry DCM (8 ml). Triethylamine (0.13 ml, 93 mg, 0.92 mmol, 3.0 equiv) was added, and the reaction mixture cooled to 0 °C. BzCl (53 µl, 65 mg, 0.46 mmol, 1.5 equiv) was added slowly, and the reaction mixture was stirred at ambient temperature for 13 h. The mixture was diluted to approximately 10 ml with DCM, transferred to a separatory funnel, and washed with 0.5 M HCl_(aq) (approximately 8 ml). The aqueous layer was extracted thrice more with DCM (6 ml). The combined organic layers were dried with MgSO₄. The volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (1 to 25% ethyl acetate gradient in hexanes, R_f 0.43 in 25% EA/Hex) to give *exo*-2-(benzoylamino)norbornane as a white solid (50.8 mg, 0.236 mmol, 77% yield, 98% *exo*). The ¹H NMR spectrum was consistent with the spectrum reported in the literature.²¹ The % *exo* was determined by the relative integration of the C-2 ¹H NMR signals at 3.92 and 4.32 ppm for the *exo* and *endo* isomers, respectively.



N-(2-methyl-4-phenylbutan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (13). Prepared by general procedure B with 3-bromo-3-methyl-1-phenylbutane (68.1 mg, 0.300 mmol). Purified by column chromatography (1 to 3% ethyl acetate gradient in hexanes, R_f 0.23 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, R_f 0.32) to give the title compound as a pale yellow oil (109 mg, 0.235 mmol, 78% yield).

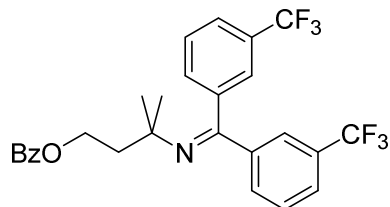
¹H NMR (500 MHz, CDCl₃) δ 7.98 (s, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.49 (s, 1H), 7.44 – 7.40 (m, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 7.3 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 2.81 – 2.73 (m, 2H), 1.96 – 1.87 (m, 2H), 1.09 (s, 6H). ¹³C NMR (151 MHz, CDCl₃) δ 160.6, 143.2, 142.0, 140.0, 131.8, 131.4, 131.0 (q, *J* = 32.7 Hz), 130.8 (q, *J* = 32.4 Hz), 128.9, 128.7, 128.5, 128.5, 126.5, 125.8, 125.4, 125.2, 124.6, 124.2 (q, *J* = 272.4 Hz), 124.0 (q, *J* = 272.6 Hz), 59.8, 48.6, 3.4, 28.8. ¹⁹F NMR (565 MHz, CDCl₃) δ -63.6, -63.7. ESI⁺ calc'd 464.1807 (M+H⁺), found 464.1807.



N-(1-methylcyclohexyl)-3,3'-bis(trifluoromethyl)benzophenone imine (14). Prepared by general procedure B with 1-bromo-1-methylcyclohexane (53.1 mg, 0.300 mmol). Purified by column chromatography (0 to 3% ethyl acetate gradient in hexanes, R_f 0.24 in 3% EA/Hex; 5% triethylamine in hexanes on prebasified silica, R_f 0.57) to give the title compound as a pale yellow oil (68.4 mg, 0.165 mmol, 55% yield).

¹H NMR (500 MHz, CDCl₃) δ 7.94 (s, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.53 (m, 3H), 7.47 (s, 1H), 7.44 – 7.37 (m, 2H), 1.73 – 1.64 (m, 2H), 1.64 – 1.49 (m, 3H), 1.49 – 1.38 (m, 2H), 1.36 – 1.23 (m, 3H), 1.01 (s, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 160.2, 142.0, 140.2, 131.3, 131.2, 130.7 (q, *J* = 32.5 Hz),

130.6 (q, $J = 32.2$ Hz), 128.6, 128.4, 126.2, 125.1, 124.7, 124.3, 124.0 (q, $J = 272.5$ Hz), 123.8 (q, $J = 272.5$ Hz), 59.2, 40.32, 28.1, 25.8, 22.8. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.8. ESI^+ calc'd 414.1651 ($\text{M}+\text{H}^+$), found 414.1646.

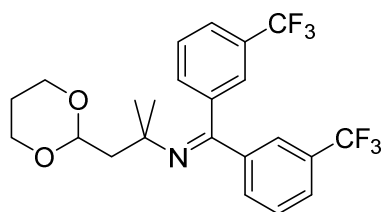


***N*-(1-(1,3-dioxan-2-yl)-2-methylpropan-2-yl)-3,3'-**

bis(trifluoromethyl)benzophenone imine (15). Prepared by general procedure B with 3-bromo-3-methylbutyl benzoate (81.4 mg, 0.300 mmol). Purified by column chromatography (5% triethylamine in hexanes on prebasified silica, R_f 0.37; 0 to 10% ethyl acetate gradient in hexanes, R_f 0.42 in 10% EA/Hex; 5% DCM in toluene, R_f 0.46) to give the title compound as a clear and colorless oil (115 mg, 0.227

mmol, 76% yield).

^1H NMR (500 MHz, CDCl_3) δ 8.01 (d, $J = 7.1$ Hz, 2H), 7.85 (s, 1H), 7.72 (d, $J = 7.9$ Hz, 1H), 7.62 – 7.56 (m, 3H), 7.53 (t, $J = 7.4$ Hz, 1H), 7.49 (s, 1H), 7.44 – 7.36 (m, 4H), 4.59 (t, $J = 7.0$ Hz, 2H), 2.11 (t, $J = 7.0$ Hz, 2H), 1.12 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.8, 161.1, 141.6, 139.8, 132.9, 131.7, 131.4, 131.0 (q, $J = 32.8$ Hz), 130.8 (q, $J = 32.3$ Hz), 130.6, 129.6, 129.0, 128.7, 128.4, 126.6, 125.5, 125.1, 124.6, 124.1 (q, $J = 272.5$ Hz), 123.9 (q, $J = 272.8$ Hz) 62.59, 59.04, 44.73, 29.18. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 508.1706 ($\text{M}+\text{H}^+$), found 508.1698.



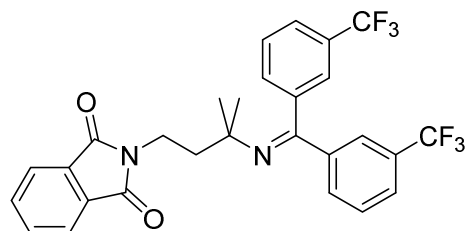
***N*-(1-(1,3-dioxan-2-yl)-2-methylpropan-2-yl)-3,3'-**

bis(trifluoromethyl)benzophenone imine (16). Prepared by general procedure B with 2-(2-bromo-2-methylpropyl)-1,3-dioxane (66.9 mg, 0.300 mmol). Purified by column chromatography (0/5/95 to 20/5/75 EA/TEA/Hex gradient on prebasified silica, R_f 0.62 in 20/5/75 EA/TEA/Hex; 0 to 25% ethyl acetate gradient in hexanes, R_f 0.59 in 25% EA/Hex) to give the title compound as a pale yellow oil (91.4 mg,

0.19 mmol, 66% yield).

Note: this compound hydrolyzed slightly during column chromatography on untreated silica, leading to a 2 mol% ketone impurity detected in the ^1H and ^{19}F NMR spectra.

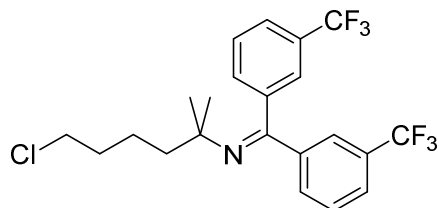
^1H NMR (600 MHz, CDCl_3) δ 8.00 (s, 1H), 7.71 (d, $J = 7.7$ Hz, 1H), 7.61 (d, $J = 7.5$ Hz, 1H), 7.58 (t, $J = 7.7$ Hz, 1H), 7.48 (s, 2H), 7.41 (q, $J = 7.5$ Hz, 2H), 4.88 (t, $J = 4.2$ Hz, 1H), 4.12 (dd, $J = 11.5, 4.6$ Hz, 2H), 3.81 (t, $J = 12.1$ Hz, 2H), 2.09 (qt, $J = 12.6, 5.0$ Hz, 1H), 1.92 (d, $J = 3.7$ Hz, 2H), 1.35 (d, $J = 13.4$ Hz, 1H), 1.06 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ 160.4, 142.0, 139.9, 131.7, 131.6, 130.9 (q, $J = 32.8$ Hz), 130.8 (q, $J = 32.4$ Hz), 128.9, 128.7, 126.4, 125.4, 125.2 (q, $J = 3.6$ Hz), 124.7, 124.2 (q, $J = 272.4$ Hz), 123.9 (q, $J = 272.5$ Hz), 101.4, 67.1, 58.5, 51.3, 29.6, 25.9. ^{19}F NMR (565 MHz, CDCl_3) δ -63.6, -63.7. ESI^+ calc'd 460.1706 ($\text{M}+\text{H}^+$), found 460.1696.



***N*-(3-((bis(3-(trifluoromethyl)phenyl)methylene)amino)-3-methylbutyl)phthalimide (17).** Prepared by general procedure C with *N*-(3-bromo-3-methylbutyl)phthalimide (88.8 mg, 0.300 mmol). Purified by column chromatography (0/5/95 to 20/5/75 EA/TEA/Hex gradient on prebasified silica, R_f 0.48 in 20/5/75 EA/TEA/Hex; 0 to 25% ethyl acetate gradient in hexanes, R_f 0.54) to give the title compound as a clear and colorless oil,

which solidified into a white solid on standing (119 mg, 0.223 mmol, 74% yield).

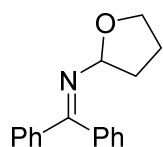
¹H NMR (600 MHz, CDCl₃) δ 7.73 (s, 1H), 7.72 – 7.67 (m, 3H), 7.62 – 7.54 (m, 4H), 7.53 – 7.46 (m, 3H), 7.28 (t, *J* = 8.4 Hz, 1H), 3.93 (t, *J* = 7.3 Hz, 2H), 2.04 (t, *J* = 7.3 Hz, 2H), 1.07 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 168.6, 161.1, 141.6, 139.7, 133.8, 132.3, 131.8, 131.3, 130.9 (q, *J* = 32.7 Hz), 130.5 (q, *J* = 32.3 Hz), 128.9, 128.5, 126.4, 125.4, 125.2, 124.5, 124.1 (q, *J* = 272.5 Hz), 123.9 (q, *J* = 272.6 Hz), 123.0, 59.3, 44.4, 34.8, 28.7. **¹⁹F NMR** (565 MHz, CDCl₃) δ -63.6, -63.7. **ESI⁺** calc'd 533.1658 (M+H⁺), found 533.1646.



***N*-(6-chloro-2-methylhexan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (18).** Prepared by general procedure C with 5-bromo-1-chloro-5-methylhexane (64.1 mg, 0.300 mmol). Purified by column chromatography (0 to 10% ethyl acetate gradient in hexanes, *R_f* 0.24 in 3% EA/Hex; 2% triethylamine in hexanes on prebasified silica, *R_f* 0.48) to give the title compound as a pale yellow oil (82.3 mg, 0.183 mmol, 61% yield).

Note: a side product resulting from elimination of the alkyl chloride was also detected in this reaction mixture, but it was removed by column chromatography.

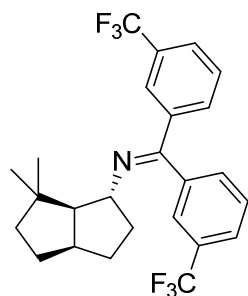
¹H NMR (500 MHz, CDCl₃) δ 7.90 (s, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.55 (m, 2H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.43 – 7.37 (m, 2H), 3.57 (t, *J* = 6.6 Hz, 2H), 1.82 – 1.72 (m, 2H), 1.62 – 1.50 (m, 4H), 1.04 (s, 6H). **¹³C NMR** (151 MHz, CDCl₃) δ 160.5, 142.0, 140.0, 131.7, 131.4, 130.9 (q, *J* = 32.4 Hz), 130.8 (q, *J* = 32.3 Hz), 128.9, 128.7, 126.5, 125.4, 125.2, 124.6, 124.2 (q, *J* = 272.4 Hz), 123.9 (q, *J* = 272.6 Hz), 59.8, 45.3, 45.2, 33.2, 28.9, 22.1. **¹⁹F NMR** (565 MHz, CDCl₃) δ -63.7, -63.7. **ESI⁺** calc'd 450.1418 (M+H⁺), found 450.1412.



***N*-(tetrahydrofuran-2-yl)benzophenone imine (23):** In a nitrogen-filled glovebox, a 20 ml vial was charged with benzophenone imine (**2a**) (54.4 mg, 0.300 mmol), *i*-PrBr (74 mg, 0.60 mmol, 2.0 equiv), [Cy₂(*t*-Bu)P]₂PdHBr (11 mg, 0.016 mmol, 5.3 mol %), cesium carbonate (147 mg, 0.451 mmol, 1.50 equiv), THF (6.0 ml; total volume approximately 6 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape.

The reaction mixture was heated at 80 °C with stirring for 48 h in an aluminum block. The product was isolated by column chromatography (5% triethylamine in hexanes on prebasified silica, *R_f* 0.43; 0 to 10% ethyl acetate gradient in hexanes, *R_f* 0.22 – some hydrolysis occurs on untreated silica) to give the title compound as a clear and colorless oil (33.0 mg, 0.131 mmol, 44% yield).

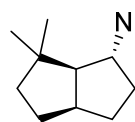
¹H NMR (500 MHz, CDCl₃) δ 7.64 (d, *J* = 7.2 Hz, 2H), 7.48 – 7.42 (m, 3H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.4 Hz, 2H), 7.19 (d, *J* = 7.7 Hz, 2H), 5.18 (dd, *J* = 6.3, 3.9 Hz, 1H), 4.22 (q, *J* = 7.2 Hz, 1H), 3.90 (td, *J* = 7.8, 7.4, 5.4 Hz, 1H), 2.22 – 2.10 (m, 1H), 2.01 – 1.94 (m, 1H), 1.89 – 1.78 (m, 2H). **¹³C NMR** (151 MHz, CDCl₃) δ 167.0, 139.5, 136.8, 130.4, 128.9, 128.7, 128.5, 128.1, 128.0, 91.9, 68.0, 34.2, 25.6. **ESI⁺** calc'd 252.1383 (M+H⁺), found 252.1381.



2-((Bis(3-(trifluoromethyl)phenyl)methylene)amino)-8,8-

dimethylbicyclo[3,3,0]octane (25). Prepared according to general procedure A for Pd-catalyzed radical amination with 3-(3-bromo-3-methylbutyl)cyclopent-1-ene (**24**) (65.1 mg, 0.300 mmol). The crude product was purified by column chromatography (1 to 3% ethyl acetate gradient in hexanes; R_f 0.30 in 3% EA/Hex) to give the title compound as a pale yellow oil (trial 1: 87.6 mg, 0.193 mmol, 64% yield) (trial 2: 86.5 mg, 0.191 mmol, 64% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.90 (s, 1H), 7.74 (d, $J = 7.9$ Hz, 1H), 7.66 – 7.60 (m, 3H), 7.47 – 7.41 (m, 2H), 7.37 (d, $J = 7.6$ Hz, 1H), 3.33 (dt, $J = 8.5, 6.4$ Hz, 1H), 2.86 – 2.73 (m, 1H), 2.29 (dd, $J = 9.4, 7.0$ Hz, 1H), 2.14 – 2.02 (m, 2H), 1.85 – 1.69 (m, 2H), 1.68 – 1.60 (m, 1H), 1.22 – 1.09 (m, 4H), 0.91 (s, 3H), 0.68 (s, 3H). **^{13}C NMR** (151 MHz, CDCl_3) δ 162.6, 140.6, 137.7, 131.7, 131.4, 131.3 (q, $J = 33.1$ Hz), 130.9 (q, $J = 32.4$ Hz), 129.3, 128.8, 126.6, 125.7, 124.9, 124.2 (q, $J = 272.6$ Hz), 124.0 (q, $J = 273.0$ Hz), 77.0, 66.7, 62.7, 43.3, 41.3, 39.9, 36.7, 33.2, 31.3, 29.7, 25.0. **^{19}F NMR** (565 MHz, CDCl_3) δ -63.6, -63.8. **ESI $^+$** calc'd 454.1964 ($\text{M}+\text{H}^+$), found 454.1963.

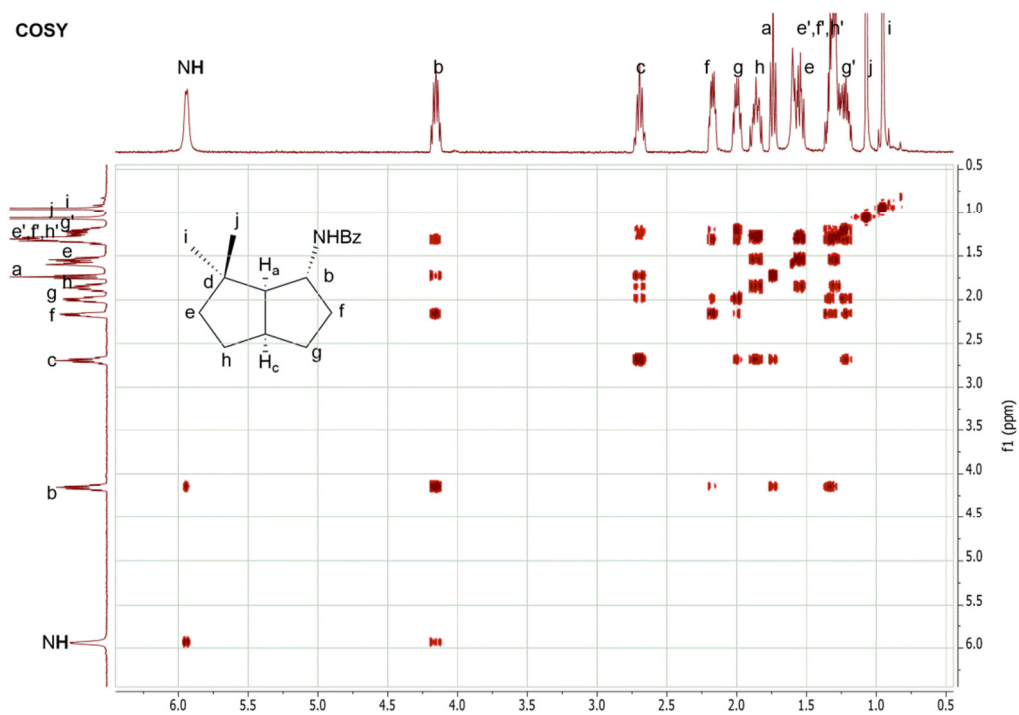
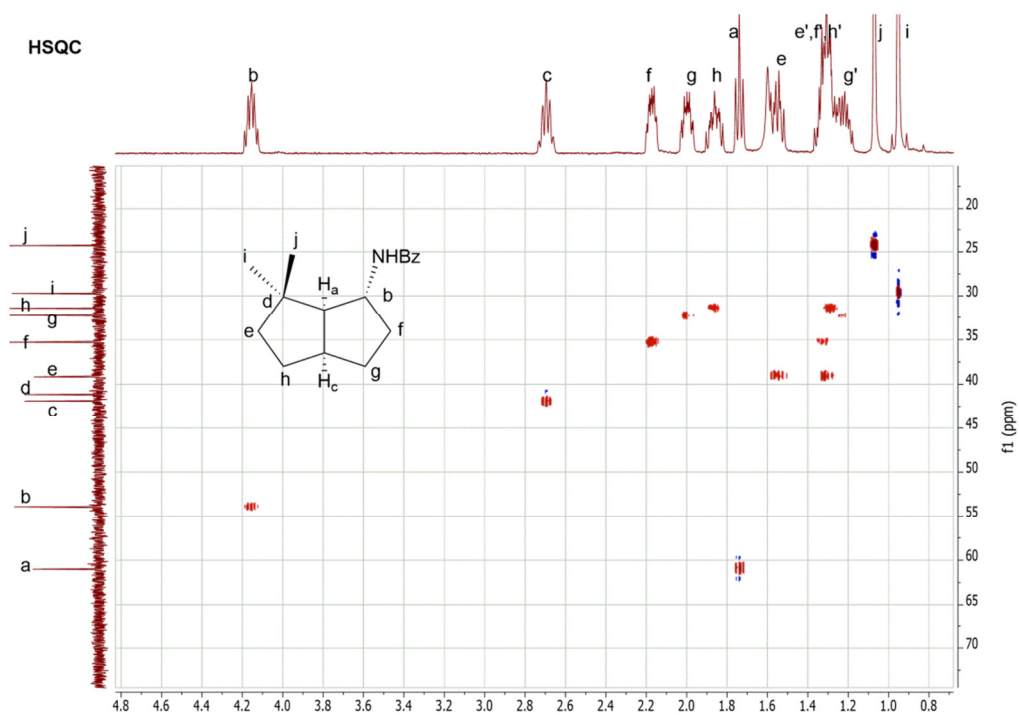


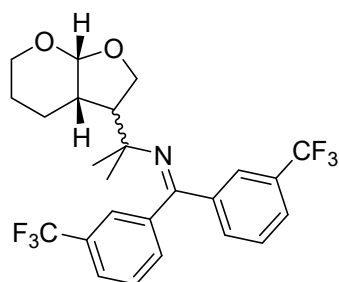
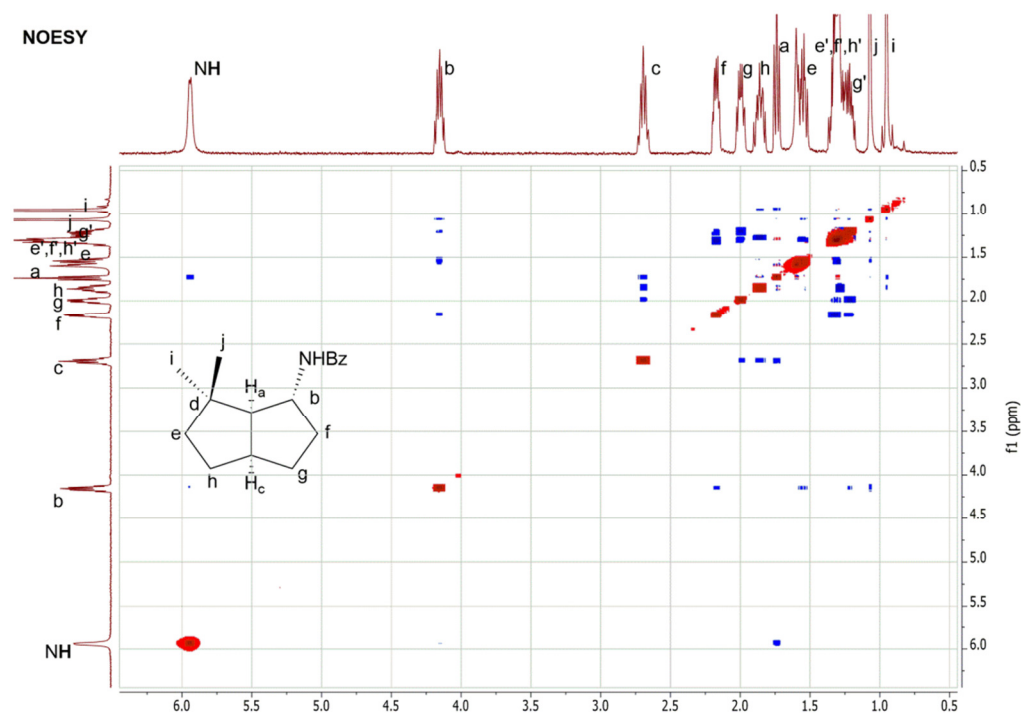
2-Benzamido-8,8-dimethylbicyclo[3,3,0]octane. *N*-(8,8-dimethylbicyclo[3,3,0]octan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (**25**) (130 mg, 0.287 mmol) and 0.5 M $\text{HCl}_{(\text{aq})}$ (6 ml) were mixed in a 20 ml vial. The vial was flushed with nitrogen and sealed with a Teflon-lined cap. The reaction mixture was heated at 80 °C with stirring for 4 h in an aluminum heating block. The mixture was washed twice with ether (4 ml). The organic layers were extracted with 0.5 M $\text{HCl}_{(\text{aq})}$ (4 ml), and the combined aqueous layers were basified with K_2CO_3 (2.0 g). The mixture was extracted four times with DCM (6 ml). The organic layers were filtered through a plug of Na_2SO_4 into a 25 ml flask. The volatile materials were evaporated at reduced pressure, and the flask refilled with nitrogen.

The crude amine was dissolved in dry DCM (8 ml). Triethylamine (0.12 ml, 87 mg, 0.86 mmol, 3.0 equiv) was added, and the reaction mixture cooled to 0 °C. BzCl (50 μl , 61 mg, 0.43 mmol, 1.5 equiv) was added slowly, and the reaction mixture was stirred at ambient temperature for 14 h. The mixture was diluted to approximately 10 ml with DCM, transferred to a separatory funnel, and washed with 0.5 M $\text{HCl}_{(\text{aq})}$ (approximately 8 ml). The aqueous layer was extracted thrice more with DCM (6 ml). The combined organic layers were dried with MgSO_4 . The volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (1 to 25% ethyl acetate gradient in hexanes, R_f 0.43 in 25% EA/Hex) to give the title compound as a white solid (56.3 mg, 0.219 mmol, 76% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.74 (d, $J = 7.0$ Hz, 2H), 7.49 (t, $J = 7.3$ Hz, 1H), 7.43 (t, $J = 7.4$ Hz, 2H), 5.94 (d, $J = 6.6$ Hz, 1H), 4.16 (qd, $J = 8.6, 6.1$ Hz, 1H), 2.77 – 2.63 (m, 1H), 2.17 (dtd, $J = 11.5, 5.8, 2.2$ Hz, 1H), 2.06 – 1.95 (m, 1H), 1.86 (dddd, $J = 12.9, 11.1, 9.3, 7.2$ Hz, 1H), 1.74 (t, $J = 9.1$ Hz, 1H), 1.55 (td, $J = 12.2, 7.8$ Hz, 1H), 1.40 – 1.16 (m, 4H), 1.07 (s, 3H), 0.95 (s, 3H). **^{13}C NMR** (151 MHz, CDCl_3) δ 166.9, 135.3, 131.4, 128.7, 126.9, 61.0, 53.9, 41.9, 41.1, 39.2, 35.3, 32.3, 31.4, 29.7, 24.3. **ESI $^+$** calc'd 258.1852 ($\text{M}+\text{H}^+$), found 258.1856; calc'd ($\text{M}+\text{Na}^+$) 280.1672, found 280.1670.

The relative configurations of this compound were assigned by 2D NMR spectroscopy, as shown below. The carbon skeleton was assigned unambiguously by HSQC and COSY NMR spectra. Strong NOESY correlations of H_a to H_c , H_i , and NH were observed. Only a weak NOESY correlation between H_a and H_b was observed, and no NOESY correlation between H_b and H_c was detected. These spectra are most consistent with the diastereomer drawn.





***N*-(2-(hexahydro-4H-furo[2,3-b]pyran-3-yl)propan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (27).**

In a nitrogen-filled glovebox, a 1 dram vial was charged with *trans*-3-bromo-2-((3-methylbut-2-en-1-yl)oxy)tetrahydro-2H-pyran (**26**) (99.7 mg, 0.400 mmol), 3,3'-bis(trifluoromethyl)benzophenone imine (**2d**) (192 mg, 0.605 mmol, 1.51 equiv), [(1-Ad)₂MeP]₂PdHBr (17 mg, 0.021 mmol, 5.2 mol %), cesium carbonate (195 mg, 0.599 mmol, 1.50 equiv), *tert*-amyl alcohol (3 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 h in an aluminum block. The reaction mixture was diluted to approximately 20 ml with ether, and the mixture was washed with NaHCO_{3(aq)} (~15 ml) and brine (~15 ml). The organic layer was filtered through a plug of Na₂SO₄. The volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (0 to 50% ethyl acetate gradient in hexanes, R_f 0.34 in 25% EA/Hex; 0/5/95 to 10/5/85 EA/TEA/Hex gradient on prebasified silica, R_f 0.48 in 10/5/85 EA/TEA/Hex) to give the title compound as a very viscous, clear, and colorless oil (142 mg, 0.293 mmol, 73% yield).

Note: This compound formed as a 2:3 mixture of diastereomers. NMR signals were assigned to either the major or minor isomer by their integrals, and these assignments were confirmed through HSQC and HMBC correlations.

¹H NMR (600 MHz, CDCl₃):

Aryl (major and minor overlap): δ 7.89(major) or 7.80(minor) (s, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.65 – 7.55 (m, 3H), 7.47 – 7.35 (m, 3H).

Aliphatic (major): δ 5.29 (d, *J* = 3.4 Hz, 1H), 4.54 (dd, *J* = 10.9, 7.6 Hz, 1H), 4.07 (t, *J* = 7.8 Hz, 1H), 3.89 – 3.82 (m, 1H), 3.72 – 3.65 (m, 1H), 2.38 – 2.29 (m, 1H), 2.07 (dddd, *J* = 12.2, 8.7, 6.1, 3.3 Hz, 1H), 1.99 – 1.91 (m, 1H), 1.66 – 1.60 (m, 1H), 1.58 – 1.49 (m, 2H), 1.05 (s, 3H), 0.97 (s, 3H).

Aliphatic (minor): δ 5.13 (d, $J = 3.8$ Hz, 1H), 4.26 (t, $J = 8.7$ Hz, 1H), 3.97 (dd, $J = 8.6, 6.3$ Hz, 1H), 3.93 (dtd, $J = 11.5, 4.0, 1.6$ Hz, 1H), 3.50 (td, $J = 10.7, 2.7$ Hz, 1H), 2.43 (td, $J = 8.6, 6.3$ Hz, 1H), 2.38 – 2.29 (m, 1H), 1.99 – 1.82 (m, 2H), 1.80 – 1.69 (m, 1H), 1.43 (dq, $J = 13.8, 3.9$ Hz, 1H), 1.03 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (151 MHz, CDCl_3):

CF_3 (only two signals observed; major and minor likely overlap): δ 124.1 (q, $J = 272.5$ Hz), 123.9 (d, $J = 272.7$ Hz).

$\text{C}-\text{CF}_3$ (unable to assign major and minor): δ 131.1 (q, $J = 32.7$ Hz), 131.1 (q, $J = 32.3$ Hz), 130.9 (q, $J = 32.4$ Hz), 130.8 (q, $J = 32.2$ Hz).

Other aryl (major): δ 159.8, 141.6, 140.0, 131.5, 131.3, 129.0, 128.9, 126.6, 125.6, 125.0, 124.6.

Aliphatic (major): δ 101.7, 65.7, 61.3, 59.7, 55.1, 37.1, 29.3, 28.3, 23.8, 21.0.

Other aryl (minor): δ 161.6, 141.6, 139.9, 131.7, 131.4, 129.0, 128.8, 126.7, 125.6, 125.1, 124.8.

Aliphatic (minor): δ 102.9, 70.2, 64.3, 61.1, 52.9, 40.0, 27.7, 27.4, 25.3, 21.3.

^{19}F NMR (565 MHz, CDCl_3) δ -63.7(major), -63.7(minor), -63.8(minor), -63.8(major).

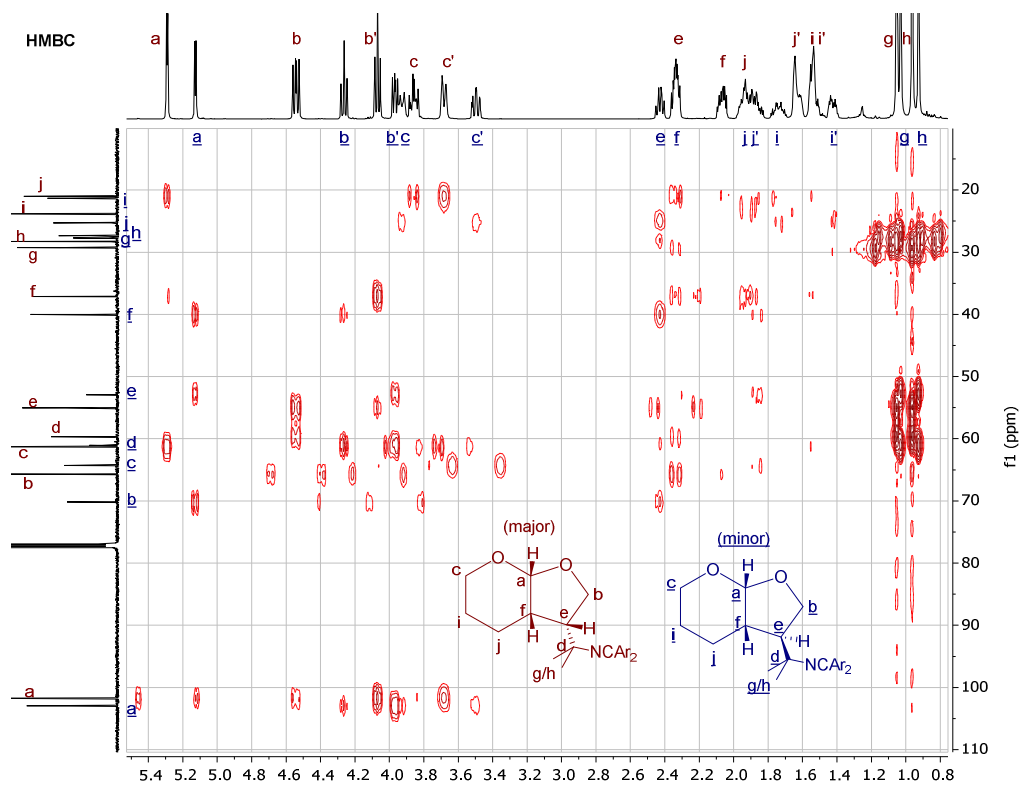
ESI^+ calc'd 486.1862 ($\text{M}+\text{H}^+$), found 486.1857.

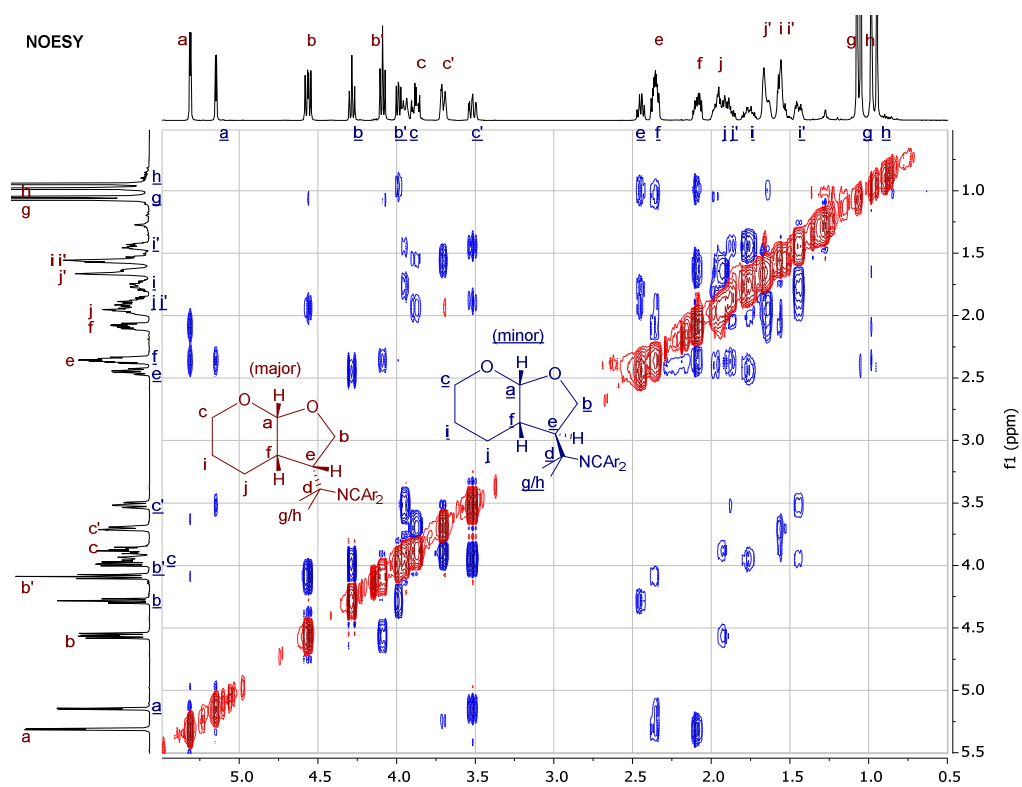
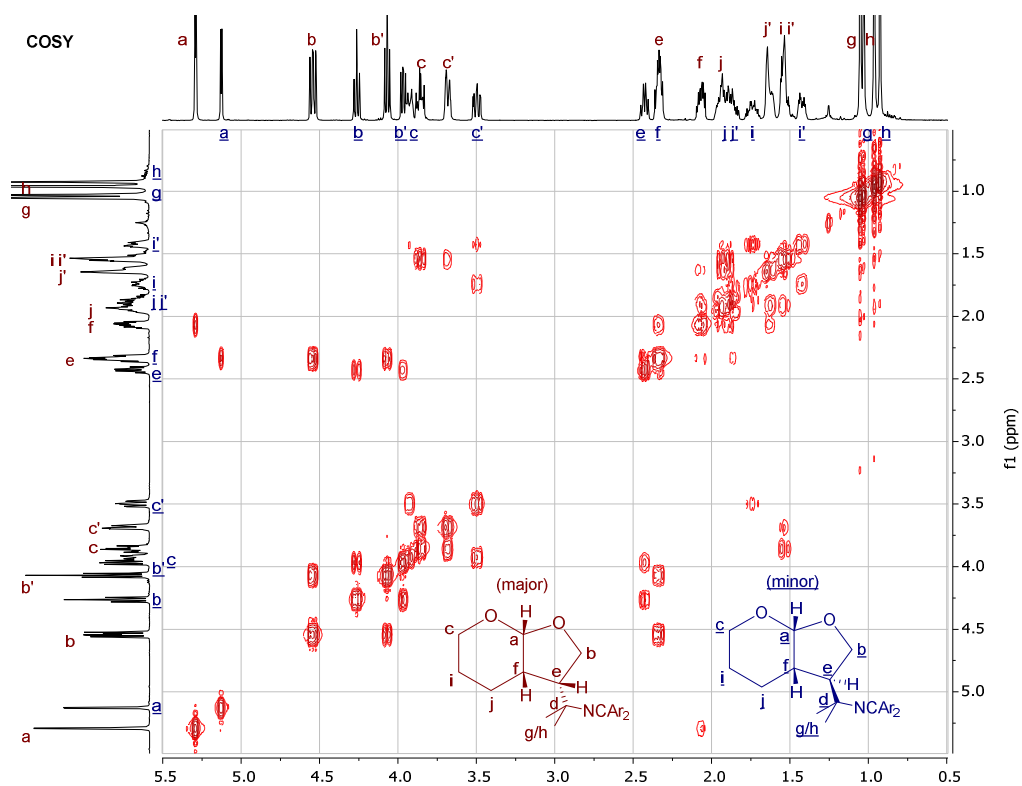
The relative configurations for both isomers of this compound were assigned by 2D NMR spectroscopy as shown below. The aliphatic carbon skeleton was assigned unambiguously by HSQC, HMBC, and COSY NMR spectra. Structurally relevant NOESY correlations are summarized in the following tables (qualitative):

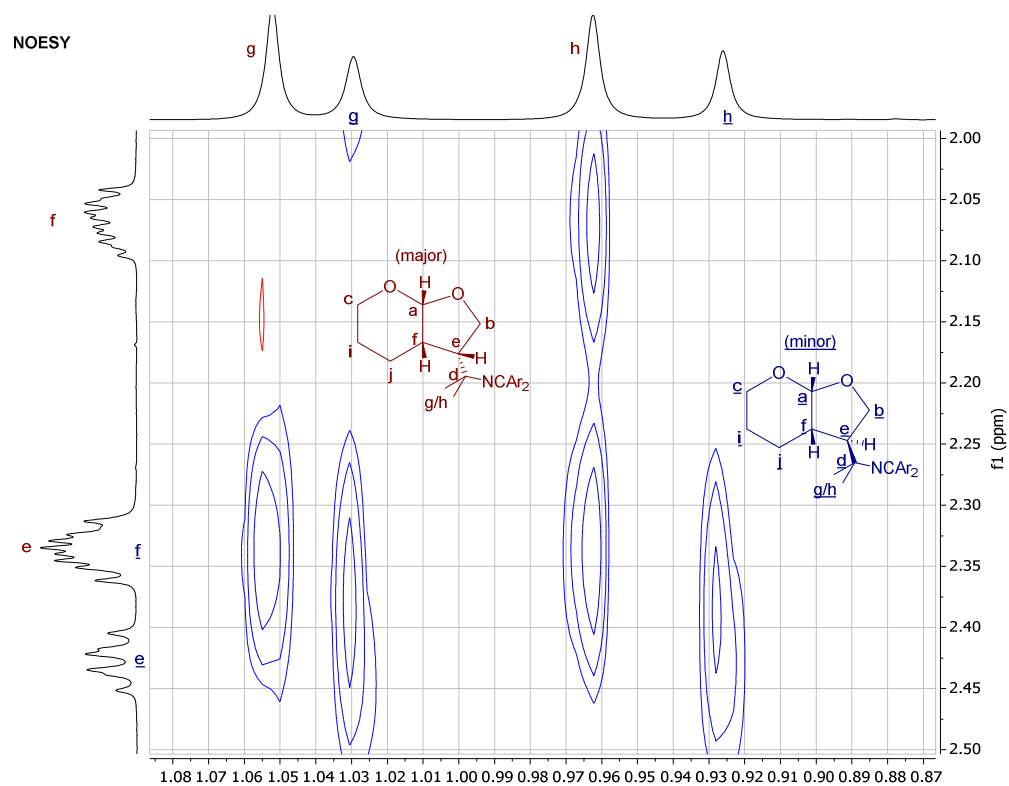
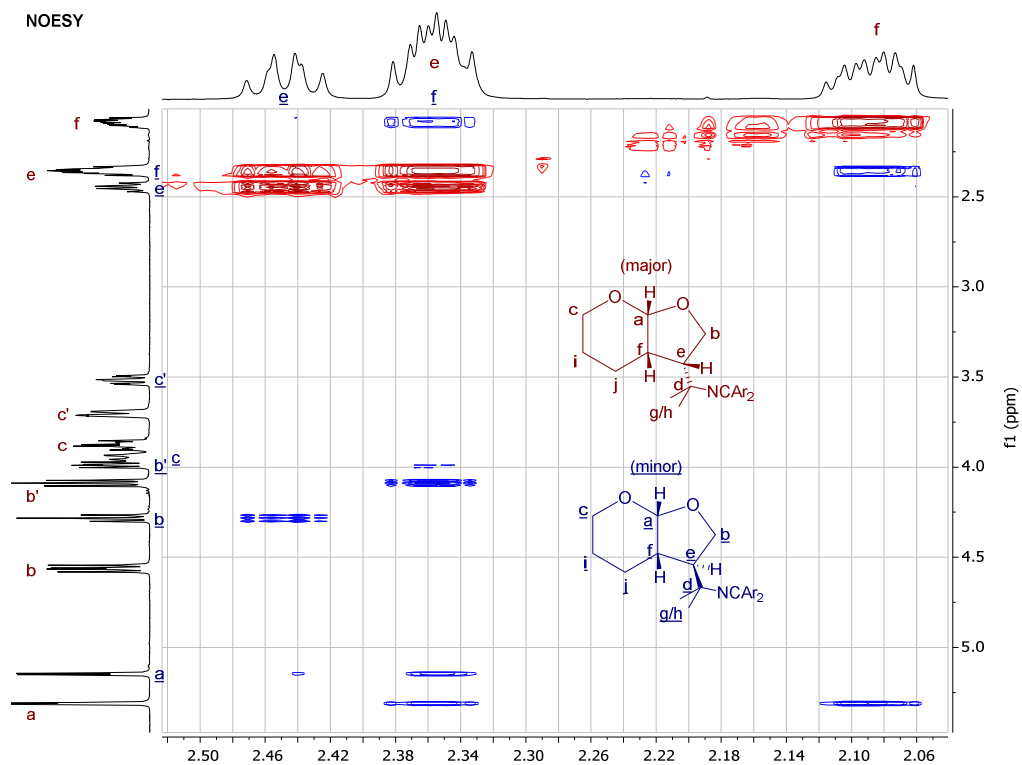
| | | | | |
|--------------|--------------|--------------|--------------|--------------|
| major | | H_a | H_e | H_f |
| | H_e | strong | | |
| | H_f | strong | strong | |
| | H_g | n.d. | strong | med |
| | H_h | n.d. | strong | n.d. |

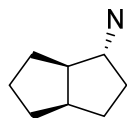
| | | | | |
|--------------|--------------|--------------|--------------------------|--------------|
| minor | | H_a | H_e | H_f |
| | H_e | weak | | |
| | H_f | strong | $\Delta\delta$ too small | |
| | H_g | n.d. | strong | strong |
| | H_h | n.d. | strong | strong |

In the major diastereomer: H_a , H_f , and H_e are all likely on the same face of the 5-ring, such as in the *endo* isomer drawn. In the minor diastereomer: H_a and H_f are likely on the same face, and H_f is close in space to the methyl groups (g) and (h), such as in the *exo* isomer drawn.





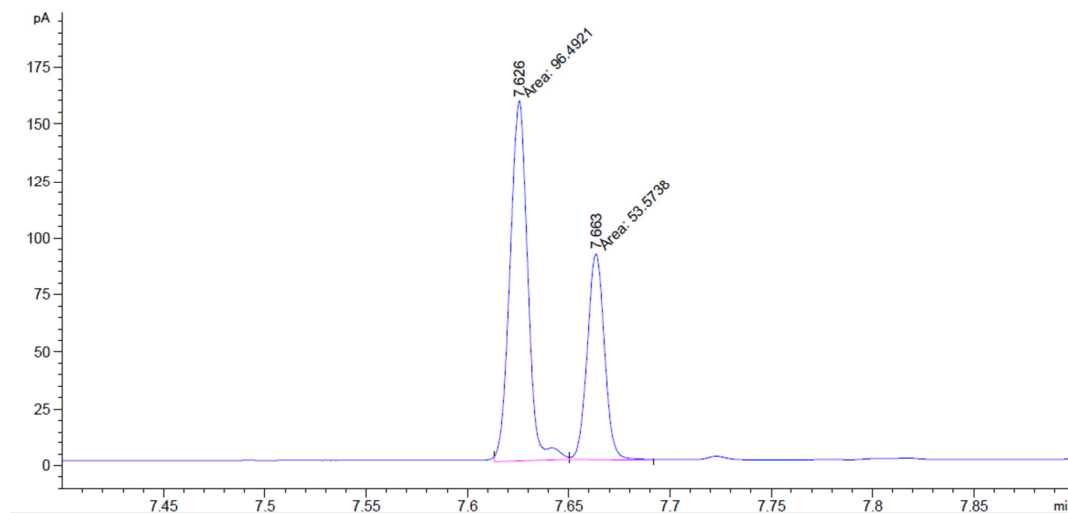




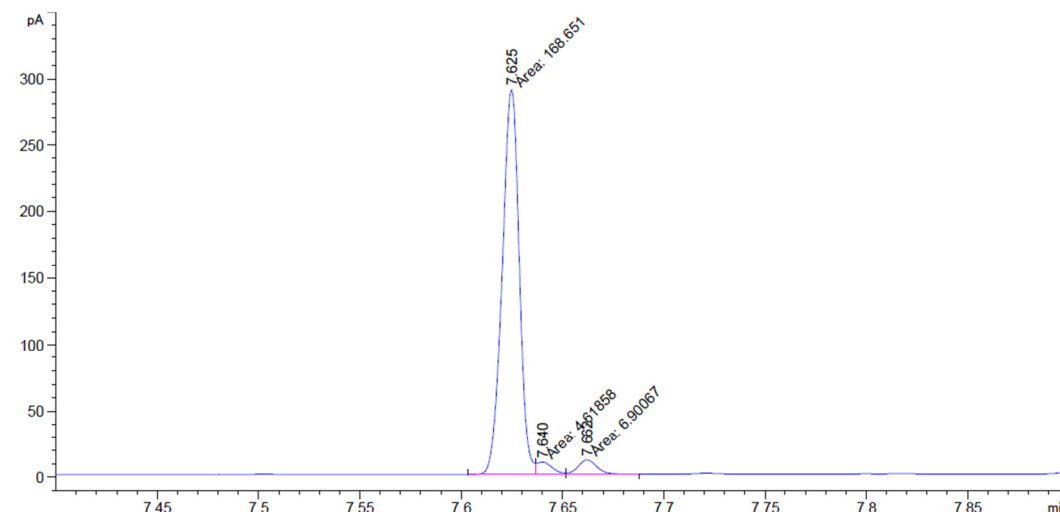
2-Benzamido-bicyclo[3,3,0]octane (29). In a nitrogen-filled glovebox, a 20 ml vial was charged with (Z)-5-bromocyclooct-1-ene (75.6 mg, 0.400 mmol) (**28**), 3,3'-bis(trifluoromethyl)benzophenone imine (**2d**) (190 mg, 0.599 mmol, 1.50 equiv), [(1-Ad)₂MeP]₂PdHBr (16.4 mg, 0.0200 mmol, 5.00 mol %), cesium carbonate (198 mg, 0.608 mmol, 1.52 equiv), *tert*-amyl alcohol (12 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 h in an aluminum block. The reaction mixture was diluted to approximately 20 ml with ether and filtered through a pad of Celite, which was rinsed with ether (3 x approximately 10 ml). The volatile materials were evaporated at reduced pressure. The residue was dissolved in approximately 1 ml of 2% triethylamine in hexanes and filtered through a plug of basified silica (2-3 ml), which was rinsed with 2% triethylamine in hexanes (approximately 10 ml). The volatile materials were evaporated at reduced pressure to give the crude *N*-alkyl imine product.

Note: The crude imine product contains both the *endo* isomer and direct coupling product as impurities (tentative assignment). Crude GC traces are shown below of: (a) the reaction run at 0.50 M catalyzed by 5.3% (Cy₂*t*-BuP)₂PdHBr and (b) the reaction run at 0.03 M catalyzed by 5% [(1-Ad)₂MeP]₂PdHBr. The peak at 7.63 minutes is the major product. The small shoulder at 7.64 minutes is presumed to originate from the *endo* isomer (overlap complicates integration, but <5% in both cases). The peak at 7.66 minutes is presumed to be the direct coupling product, and its formation is greatly suppressed when the reaction is run at dilute concentrations. The change of phosphine ligand does not have a significant effect on either ratio. To remove these impurities, the crude imine product (an oil) was carried on to the corresponding benzamide (**29**), which was recrystallized.

a) [**28**] = 0.50 M, (Cy₂*t*-BuP)₂PdHBr cat



b) $[28] = 0.03 \text{ M}$, $[(1\text{-Ad})_2\text{MeP}]_2\text{PdHBr}$ cat



The crude imine and 0.5 M $\text{HCl}_{(\text{aq})}$ (6 ml) were mixed in a 20 ml vial. The vial was flushed with nitrogen and sealed with a Teflon-lined cap. The reaction mixture was heated at 80 °C with stirring for 4 h in an aluminum heating block. The mixture was washed twice with ether (4 ml). The organic layers were extracted with 0.5 M $\text{HCl}_{(\text{aq})}$ (4 ml), and the combined aqueous layers were basified with K_2CO_3 (1.5 g). The mixture was extracted four times with ether (4 ml). The organic layers were filtered through a plug of Na_2SO_4 into a 25 ml flask. The volatile materials were evaporated at reduced pressure to give the crude primary amine product. The crude amine was dissolved in dry DCM (2 ml) and filtered through a second plug of Na_2SO_4 , which was rinsed twice more with DCM (2 ml), into a 25 ml flask under nitrogen.

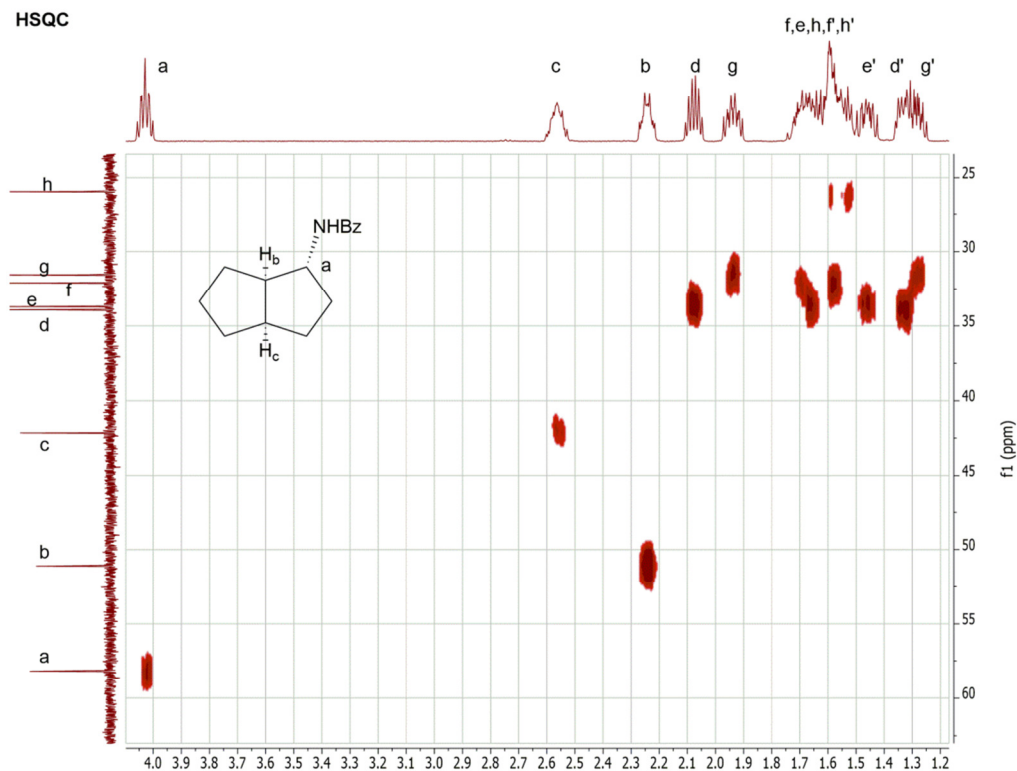
The solution was cooled to 0 °C, and triethylamine (170 μl , 120 mg, 1.2 mmol, 3.0 equiv) and benzoyl chloride (93 μl , 110 mg, 0.80 mmol, 2.0 equiv) were added with stirring. The reaction mixture was stirred for 12 h at ambient temperature. The mixture was diluted to approximately 10 ml with DCM, and the resulting solution was transferred to a separatory funnel and washed with 0.5 M $\text{HCl}_{(\text{aq})}$ (approximately 15 ml). The aqueous layer was extracted thrice more with DCM (approximately 8 ml), and the combined organic layers were dried with MgSO_4 . The volatile materials were evaporated at reduced pressure, and the crude product was purified by column chromatography (0 to 25% ethyl acetate gradient in hexanes, Rf 0.41 in 25% EA/Hex) followed by recrystallization (DCM/Hex, 3 crops) to give the title compound as a fluffy white solid (49.4 mg, 0.215 mmol, 54% yield).

^1H NMR (500 MHz, CDCl_3) δ 7.79 – 7.72 (m, 2H), 7.49 (t, $J = 7.3 \text{ Hz}$, 1H), 7.43 (t, $J = 7.4 \text{ Hz}$, 2H), 6.05 (broad, NH), 4.03 (ddd, $J = 13.7, 7.7, 6.0 \text{ Hz}$, 1H), 2.62 – 2.52 (m, 1H), 2.24 (tdd, $J = 9.1, 6.0, 3.3 \text{ Hz}$, 1H), 2.08 (dq, $J = 11.8, 5.8 \text{ Hz}$, 1H), 1.94 (dddd, $J = 13.4, 8.7, 6.6, 5.0 \text{ Hz}$, 1H), 1.75 – 1.50 (m, 5H), 1.50 – 1.42 (m, 1H), 1.37 – 1.24 (m, 2H). **^{13}C NMR** (151 MHz, CDCl_3) δ 167.29, 135.19, 131.38, 128.66, 126.97, 58.18, 51.11, 42.15, 33.93, 33.72, 32.11, 31.56, 25.93. **ESI $^+$** calc'd ($\text{M} + \text{Na}^+$) 252.1359, found 252.1354.

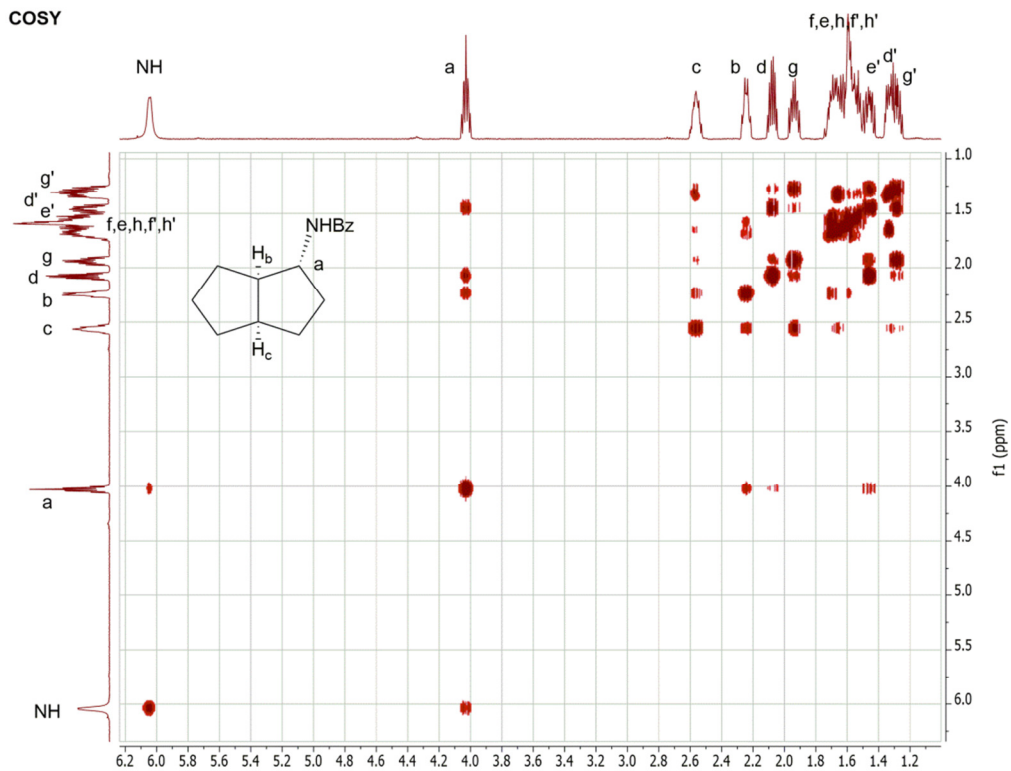
The ^1H NMR spectrum of this compound contains a set of small signals, which integrate to approximately 3% relative to the major compound. These small signals are presumed to originate from an isomer of the product; either the direct coupling product or the *endo* diastereomer of the major compound.

The relative configurations of the major compound were assigned by 2D NMR spectroscopy, as shown below. Many CH_2 ^1H and ^{13}C signals were closely spaced or overlapping, and the COSY spectrum was

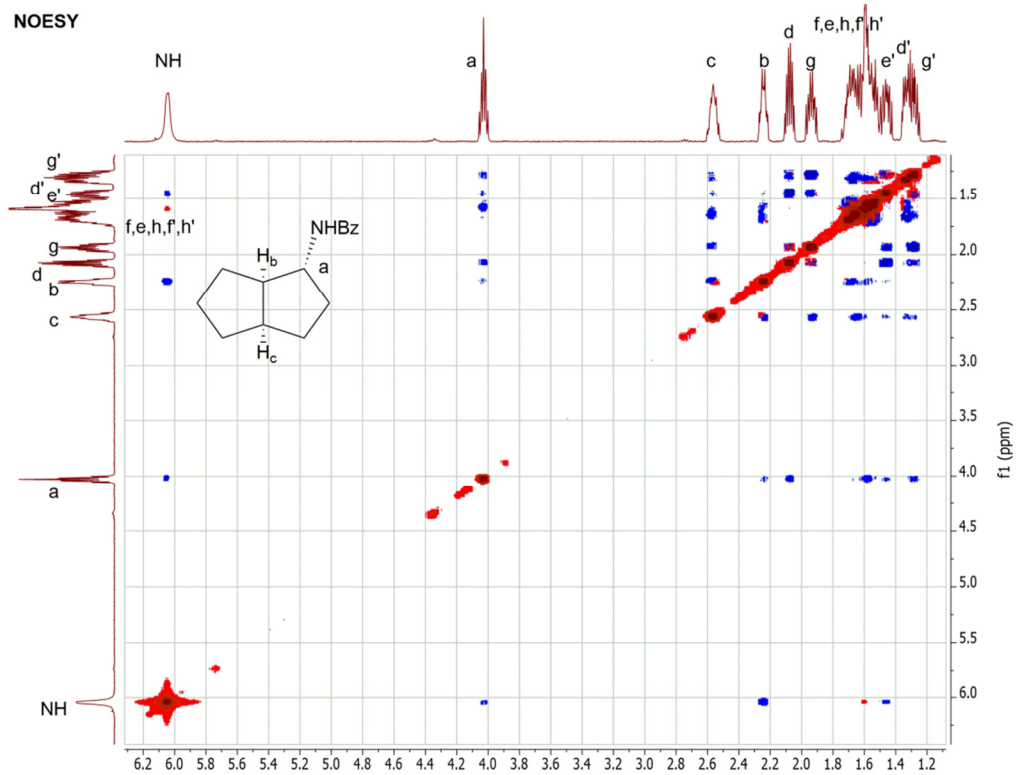
complicated by long-range coupling. Therefore, CH₂ signals were not assigned to the structure drawn below. However, the NH and CH signals were assigned unambiguously. Strong NOESY correlations of H_b to H_c and NH were observed. Only a weak NOESY correlation between H_a and H_b was observed, and no NOESY correlation between H_a and H_c was detected. These spectra are most consistent with the diastereomer drawn.



COSY

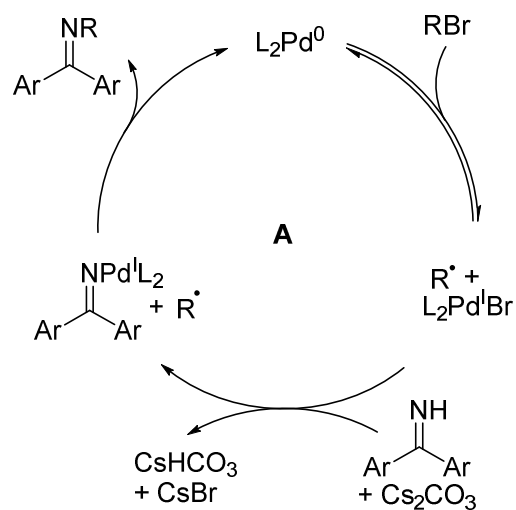


NOESY

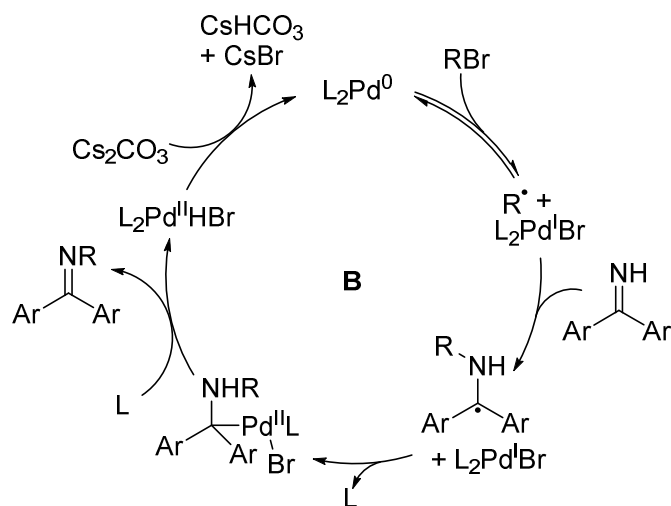


Plausible mechanisms for Pd-catalyzed *N*-alkylation of imines

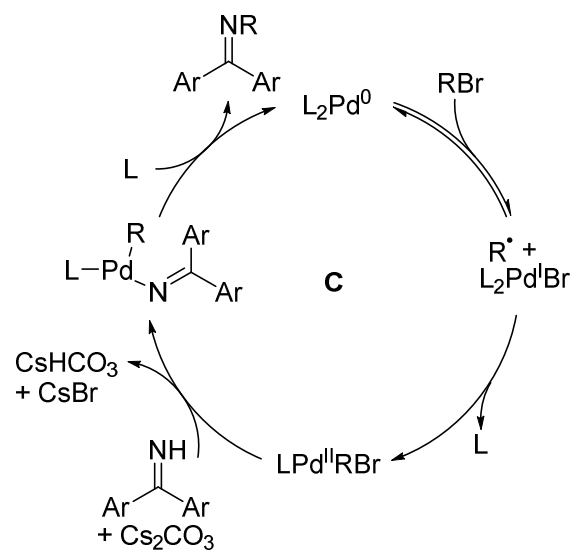
Three mechanisms consistent with our studies are drawn below:



A. C–N bond formed *via* radical addition to a palladium-bound methyleneamido group.



B. C–N bond formed *via* radical addition to a free benzophenone imine.



C. C-N bond formed *via* reductive elimination from an alkylpalladium(II)methyleneamido complex.

Although many variations on each of these mechanisms are possible, those shown above present three distinct mechanisms of C-N bond formation.

GC response factors

All GC yields (integration relative to a 1.0 equiv 1,3,5-trimethoxybenzene internal standard) were corrected with the following response factors determined with authentic compounds:

3-bromo-1-phenylbutane (**1**): 0.685

N-(4-phenylbutan-2-yl)benzophenone imine (**3a**): 0.249

N-(4-phenylbutan-2-yl)-4,4'-dimethylbenzophenone imine (**3b**): 0.246

N-(4-phenylbutan-2-yl)-4,4'-dimethoxybenzophenone imine (**3c**): 0.257

N-(4-phenylbutan-2-yl)-3,3'-bis(trifluoromethyl)benzophenone imine (**3d**): 0.252

4-phenylbutene (**4**): 0.669. *Note*: a mixture of 4 isomers was identified by GC/MS. The response factor was determined with commercially available 4-phenyl-1-butene and assumed to apply equally to the combined mixture of isomers.

1-phenylbutane (**5**): 0.645

N-(*sec*-butyl)benzophenone imine (**20**): 0.362. *Note*: this response factor was assumed to apply equally to a mixture of *N*-(*sec*-butyl)benzophenone imine and *N*-(*tert*-butyl)benzophenone imine.

Experimental details for Table 1

General procedure: In a nitrogen-filled glovebox, a 2 ml volumetric flask was charged with 3-bromo-1-phenylbutane (**1**) (426 mg, 2.00 mmol), benzophenone imine (**2a**) (399 mg, 2.20 mmol, 1.10 equiv), palladium allyl chloride dimer (22.0 mg, 0.0601 mmol, 3.01%), and 1,3,5-trimethoxybenzene (336 mg, 2.00 mmol, 1.00 equiv). The mixture was diluted to the mark with *t*-amyl alcohol, then diluted to double volume. A 0.30 ml (0.15 mmol alkyl bromide) sample of this mixture was transferred to a vial with the noted phosphine ligand (0.018 mmol, 12%), cesium carbonate (73 mg, 0.23 mmol, 1.5 equiv), and a magnetic stir bar. The vials were sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~2 ml), and a sample taken for GC analysis after filtration through a plug of silica.

Entry 1: no ligand

Entry 2: Cy₂PhP (4.9 mg)

Entry 3: *t*-Bu₂PhP (4.0 mg)

Entry 4: Ph₃P (4.8 mg)

Entry 5: Ph₂EtP (4.1 mg)

Entry 6: 1,2-(dicyclohexylphosphino)ethane (3.9 mg, 6%)

Entry 7: Cy₃P (5.0 mg)

Entry 8: *t*-Bu₃P (3.7 mg)

Entry 9: *t*-Bu₂CyP (4.2 mg)

Entry 10: *t*-Bu₂MeP (3.1 mg)

Entry 11: Ad₂MeP (5.7 mg)

Entry 12: Cy₂*t*-BuP (4.7 mg)

Table S-1. Effect of additional reaction parameters

Reaction scheme: 3-bromo-1-phenylbutane (**1**) + benzophenone imine (**2a**) (1.1 equiv) $\xrightarrow[80\text{ }^{\circ}\text{C}, 20\text{ h}]{5\% (\text{Cy}_2t\text{-BuP})_2\text{PdHBr}, 1.5\text{ equiv Cs}_2\text{CO}_3, t\text{-amyl alcohol (0.5 M)}}$ 3a + 4 + 5

| entry | variation | % conv 1 | % yield 3a | % yield 4 | % yield 5 |
|-------|--|-----------------|-------------------|------------------|------------------|
| 1 | as written | 96 | 46 | 3 | 13 |
| 2 | no cat | 19 | ~1 | 12 | nd |
| 3 | 6% NiCl ₂ /glyme + 12% Cy ₂ <i>t</i> -BuP as cat | 39 | ~1 | 23 | nd |
| 4 | [1] = 0.25 M | 81 | 37 | 5 | 11 |
| 5 | <i>i</i> -PrOH as solvent | >99 | 36 | 10 | 27 |
| 6 | LiOt-Bu as base | 67 | 32 | 6 | 8 |
| 7 | Cy ₂ MeN as base | 21 | 5 | 9 | 1 |

General procedure (entries 1-4, 6, and 7): In a nitrogen-filled glovebox, a 2 ml volumetric flask was charged with 3-bromo-1-phenylbutane (**1**) (213 mg, 0.999 mmol), benzophenone imine (**2a**) (200 mg, 1.10 mmol, 1.10 equiv), and 1,3,5-trimethoxybenzene (168 mg, 0.999 mmol, 1.00 equiv). The mixture was diluted to the mark with *t*-amyl alcohol, and 0.30 ml (0.15 mmol alkyl bromide) of this mixture was transferred to a vial with the noted catalyst, cesium carbonate (73 mg, 0.23 mmol, 1.5 equiv), and a magnetic stir bar. The vials were sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~2 ml), and a sample taken for GC analysis after filtration through a plug of silica.

Entry 1: As described above with 5.5 mg (Cy₂*t*-BuP)₂PdHBr

Entry 2: As described above, with no metal catalyst

Entry 3: As described above with 4.1 mg NiCl₂/glyme and 2.0 mg Cy₂*t*-BuP.

Entry 4: As described above with 5.5 mg (Cy₂*t*-BuP)₂PdHBr; an additional 0.30 ml *t*-amyl alcohol was added.

Entry 6: As described above with 5.5 mg (Cy₂*t*-BuP)₂PdHBr and 18.1 mg LiOt-Bu and no Cs₂CO₃.

Entry 7: As described above with 5.5 mg (Cy₂*t*-BuP)₂PdHBr and 44.4 mg Cy₂MeN and no Cs₂CO₃.

Entry 5: In a nitrogen-filled glovebox, a 4 ml vial was charged with 3-bromo-1-phenylbutane (64.3 mg, 0.302 mmol), benzophenone imine (59.5 mg, 0.328 mmol, 1.09 equiv), 1,3,5-trimethoxybenzene (49.5 mg, 0.295 mmol, 0.976 equiv), (Cy₂*t*-BuP)₂PdHBr (11.0 mg, 0.0158 mmol, 5.27%), cesium carbonate (146 mg, 0.448 mmol, 1.48 equiv), *i*-PrOH (0.40 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~2 ml), and a sample taken for GC analysis after filtration through a plug of silica. Data reported for this entry are an average of two experiments.

Table S-2. Full data and experimental details for Table 2

Reaction scheme: 3-bromo-1-phenylbutane (**1**) + imine (**2a-d**) $\xrightarrow[80\text{ }^{\circ}\text{C}, 20\text{ h}]{5\% (\text{Cy}_2t\text{-BuP})_2\text{PdHBr}, 1.5\text{ equiv Cs}_2\text{CO}_3, t\text{-amyl alcohol (0.5 M)}}$ product (**3a-d**) + byproducts (**4** and **5**)

| entry | Ar | equiv 2a-d | % conv 1 | % yield 3a-d | % 4 | % 5 |
|-------|---|-------------------|-----------------|---------------------|------------|------------|
| 1 | Ph (2a) | 1.1 | 88 | 46 | 3 | 14 |
| 2 | <i>p</i> -Tol (2b) | 1.1 | 96 | 39 | 3 | 25 |
| 3 | (4-OMe) C_6H_4 (2c) | 1.1 | 93 | 35 | 4 | 20 |
| 4 | (3-CF ₃) C_6H_4 (2d) | 1.1 | 96 | 74 | 2 | 7 |
| 5 | “ | 1.2 | 99 | 78 | 2 | 6 |
| 6 | “ | 1.5 | >99 | 83 | 1 | 5 |

General procedure: In a nitrogen-filled glovebox, a 2 ml volumetric flask was charged with 3-bromo-1-phenylbutane (**1**) (213 mg, 0.999 mmol), (Cy₂t-BuP)₂PdHBr (37.0 mg, 0.0532 mmol, 5.32%), and 1,3,5-trimethoxybenzene (168 mg, 0.999 mmol, 1.00 equiv). The mixture was diluted to the mark with *t*-amyl alcohol, and 0.30 ml (0.15 mmol alkyl bromide) of this mixture was transferred to a vial with the noted imine (**2a-d**), cesium carbonate (73 mg, 0.23 mmol, 1.5 equiv), and a magnetic stir bar. The vials were sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~2 ml), and a sample taken for GC analysis after filtration through a plug of silica. The reported data are averages of two experiments for each entry.

Entry 1: Benzophenone imine (**2a**) (30.0 mg, 0.166 mmol, 1.11 equiv)

Entry 2: 4,4'-Dimethylbenzophenone imine (**2b**) (34.6 mg, 0.165 mmol, 1.10 equiv)

Entry 3: 4,4'-Dimethoxybenzophenone imine (**2c**) (39.7 mg, 0.165 mmol, 1.10 equiv)

Entry 4: 3,3'-Bis(trifluoromethyl)benzophenone imine (**2d**) (52.4 mg, 0.165 mmol, 1.10 equiv)

Entry 5: 3,3'-Bis(trifluoromethyl)benzophenone imine (**2d**) (57.2 mg, 0.180 mmol, 1.20 equiv)

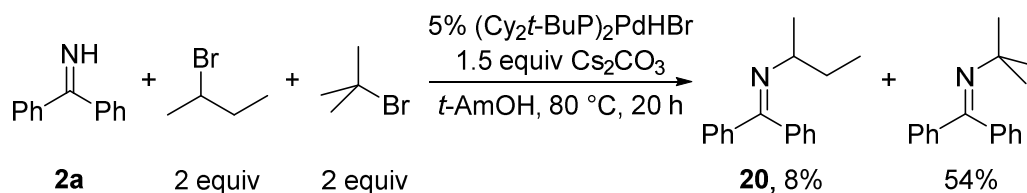
Entry 6: 3,3'-Bis(trifluoromethyl)benzophenone imine (**2d**) (71.2 mg, 0.224 mmol, 1.49 equiv)

General procedure: In a nitrogen-filled glovebox, a 2 ml volumetric flask was charged with 3,3'-bis(trifluoromethyl)benzophenone imine (**2d**) (952 mg, 3.00 mmol, 1.50 equiv), (Cy₂*t*-BuP)₂PdHBr (73.8 mg, 0.106 mmol, 5.30%), and 1,3,5-trimethoxybenzene (337 mg, 2.00 mmol, 1.00 equiv). The mixture was diluted to the mark with *t*-amyl alcohol, the resulting solution was then diluted 2x with *t*-amyl alcohol, and 0.30 ml (0.15 mmol TMB) of the final mixture was transferred to a vial with the noted electrophile, cesium carbonate (73 mg, 0.23 mmol, 1.5 equiv), and a magnetic stir bar. The vials were sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~2 ml), and a sample taken for GC analysis after filtration through a plug of silica.

Entry 2: 3-Iodo-1-phenylbutane (39.1 mg, 0.150 mmol, 1.00 equiv)

Entry 3: 4-Phenylbutan-2-yl 4-methylbenzenesulfonate (45.7 mg, 0.150 mmol, 1.00 equiv)

Scheme S-1. Competitive alkylation of benzophenone imine with a mixture of *s*-BuBr and *t*-BuBr



In a nitrogen-filled glovebox, a 1 dram vial was charged with benzophenone imine (**2a**) (33.6 μ l, 36.2 mg, 0.200 mmol), *sec*-butylbromide (43.6 μ l, 54.9 mg, 0.400 mmol, 2.00 equiv), *tert*-butylbromide (45.0 μ l, 54.9 mg, 0.400 mmol, 2.00 equiv), (Cy₂*t*-BuP)₂PdHBr (7.0 mg, 0.010 mmol, 5.0 mol %), cesium carbonate (98 mg, 0.30 mmol, 3.0 equiv), *tert*-amyl alcohol (0.30 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 h in an aluminum block. The reaction mixture was then diluted with ether and water (2 ml each). The organic layer was removed, and the aqueous layer was extracted thrice more with ether (2 ml). The organic layers were passed through a plug of silica into a vial containing 1,3,5-trimethoxybenzene (33.6 mg, 0.200 mmol, 1.00 equiv). An aliquot of this solution was then removed for ¹H NMR spectroscopy and GC analysis. Yields were determined by corrected GC integration against TMB and are an average of two trials.

Yield *N*-(*sec*-butyl)benzophenone imine: 8%

Yield *N*-(*tert*-butyl)benzophenone imine: 54%

N-(*tert*-butyl)benzophenone imine to *N*-(*sec*-butyl)benzophenone imine product ratio: 7.1

Experimental details for Scheme 2a

General procedure: In a nitrogen-filled glovebox, a 4 ml vial was charged with benzophenone imine (**2a**) (36.1 mg, 0.199 mmol), (*S*)-3-bromo-1-phenylbutane ((*S*)-**1**) (85.1 mg, 0.399 mmol, 2.01 equiv), [Cy₂(*t*-Bu)P]₂PdHBr (10.0 mg, 0.0144 mmol, 7.22 mol%), cesium carbonate (98.6 mg, 0.303 mmol, 1.52 equiv), *t*-amyl alcohol (0.26 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for *x* hours in an aluminum block. The reaction mixture was diluted with ether (2 ml) and filtered through a small plug of Celite into a 20 ml vial. A small aliquot was removed for GC/MS and chiral GC analysis at this stage. The volatile materials were evaporated at reduced pressure.

HCl_(aq) (4 ml, 0.5 M) was added to the vial, and the mixture was heated at 80 °C with stirring for 4 h. The mixture was washed with ether (4 ml, 2x 2 ml). The organic layer was extracted with HCl_(aq) (2 ml, 0.5 M), and the resulting mixture was washed with ether (2x 2 ml). The combined aqueous layers were transferred to a separatory funnel, and the vial was rinsed with H₂O (1 ml). The mixture was basified with K₂CO₃ (1.0 g) and extracted with DCM (3x 4 ml). The combined organic layers were dried with Na₂SO₄ and filtered through cotton. The volatile materials were evaporated at reduced pressure.

The vial was flushed with nitrogen and cooled to 0 °C. Dry DCM (3 ml), triethylamine (42 µl, 30 mg, 0.30 mmol, 1.5 equiv) then benzoyl chloride (35 µl, 42 mg, 0.30 mmol, 1.5 equiv) were added to the vial. The reaction mixture was stirred at ambient temperature for 5 h. The mixture was diluted to approximately 10 ml with DCM, transferred to a separatory funnel, and washed with HCl_(aq) (10 ml, 0.5 M). The aqueous layer was extracted further with DCM (2x 10 ml). The combined organic layers were dried with MgSO₄ and the volatile materials were evaporated at reduced pressure. The crude product was purified by column chromatography (25% EA/hexanes) to give (rac)-*N*-(4-phenylbutan-2-yl)benzamide (**19**). The ¹H NMR spectrum matched that of the authentic sample.

Note: To more accurately measure the ee of unconverted alkyl bromide (*S*)-**1**, the chiral GC data was fit to the following function *y*(*t*) by the method of least squares:

$$y(t) = p_1(t) + p_2(t) + b(t)$$

$$p_1(t) = a_1 * (1 / (\sigma_1 * \text{SQRT}(2 * \pi))) * \text{EXP}(-((t - \mu_1)^2 / (2 * \sigma_1^2)))$$

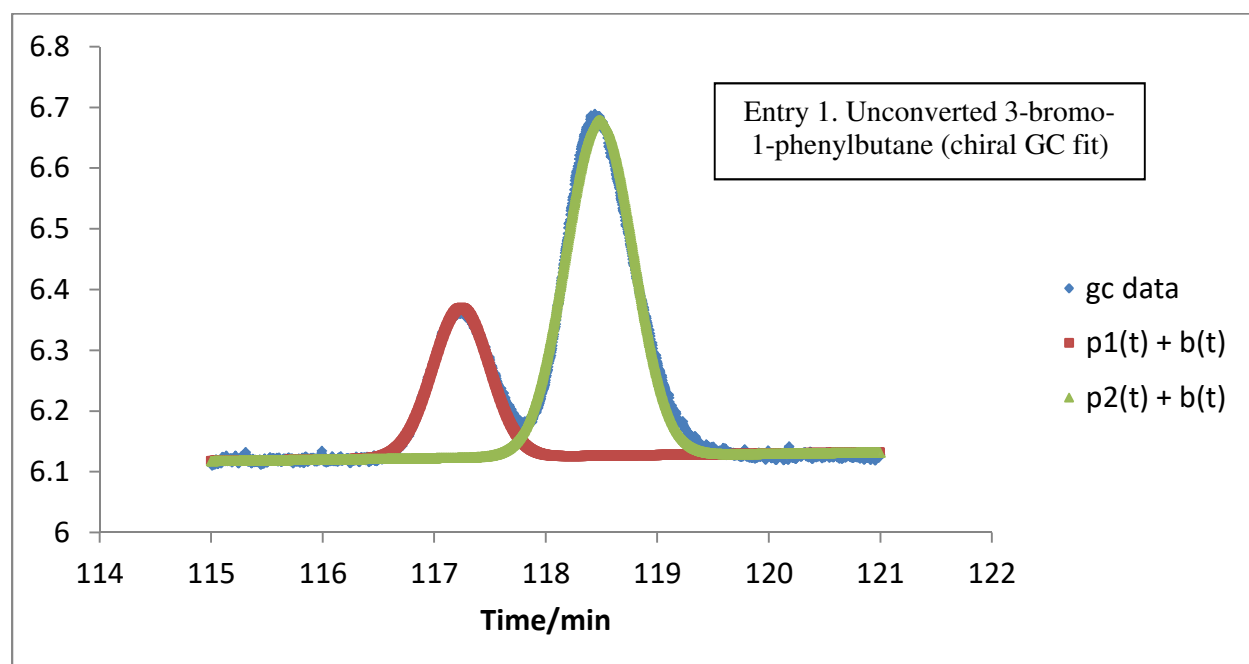
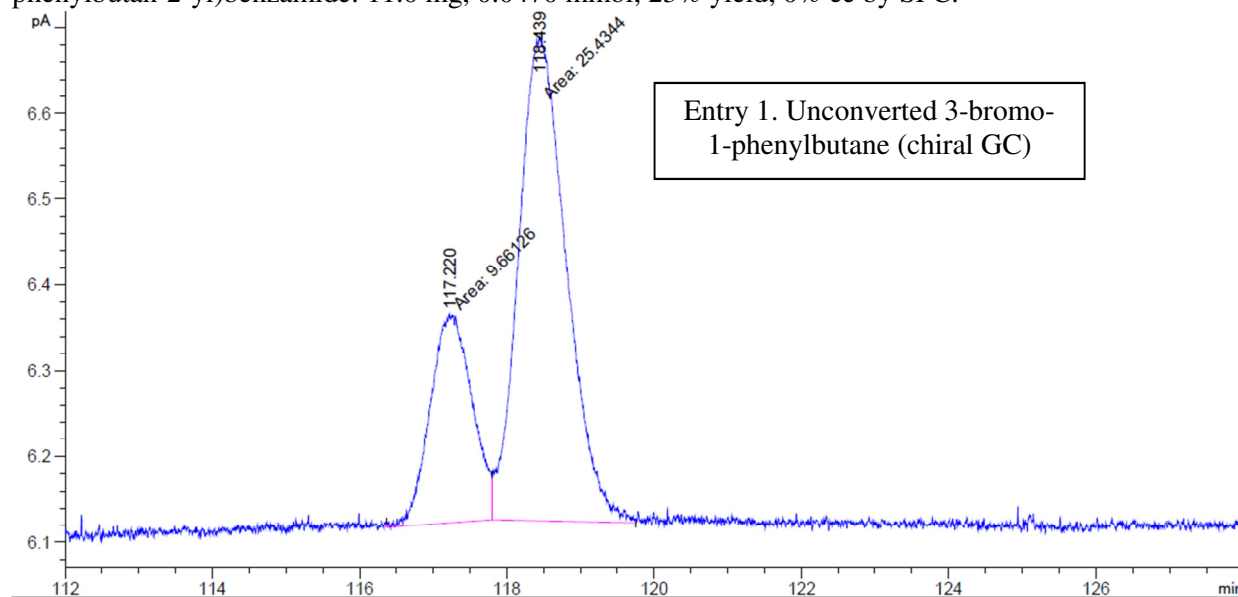
$$p_2(t) = a_2 * (1 / (\sigma_2 * \text{SQRT}(2 * \pi))) * \text{EXP}(-((t - \mu_2)^2 / (2 * \sigma_2^2)))$$

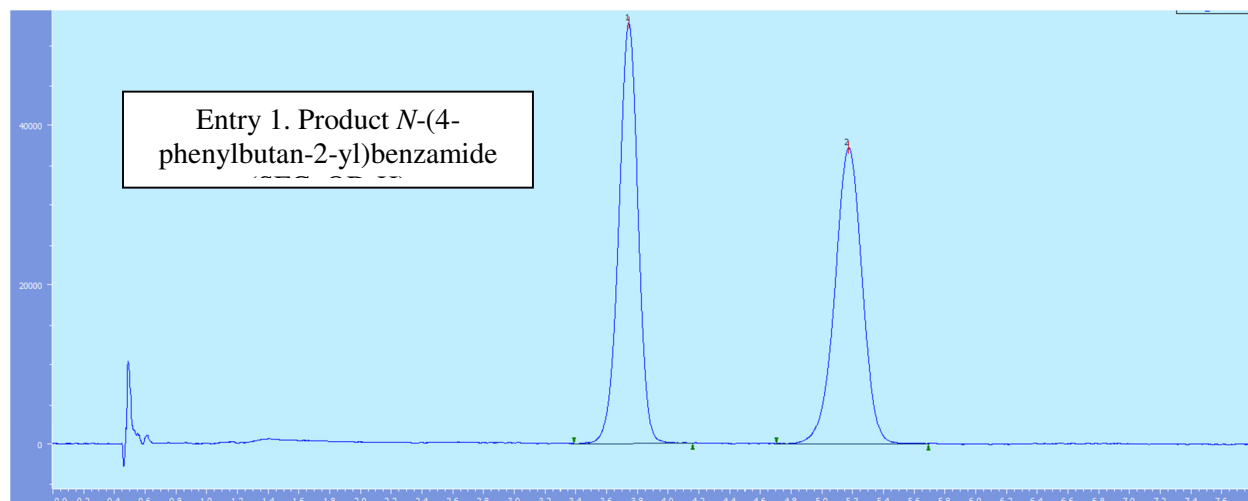
$$b(t) = m * t + c$$

p_i(*t*) is a Gaussian probability distribution with area *a_i*, mean *μ_i*, and standard deviation *σ_i* to approximate the shape of a GC peak

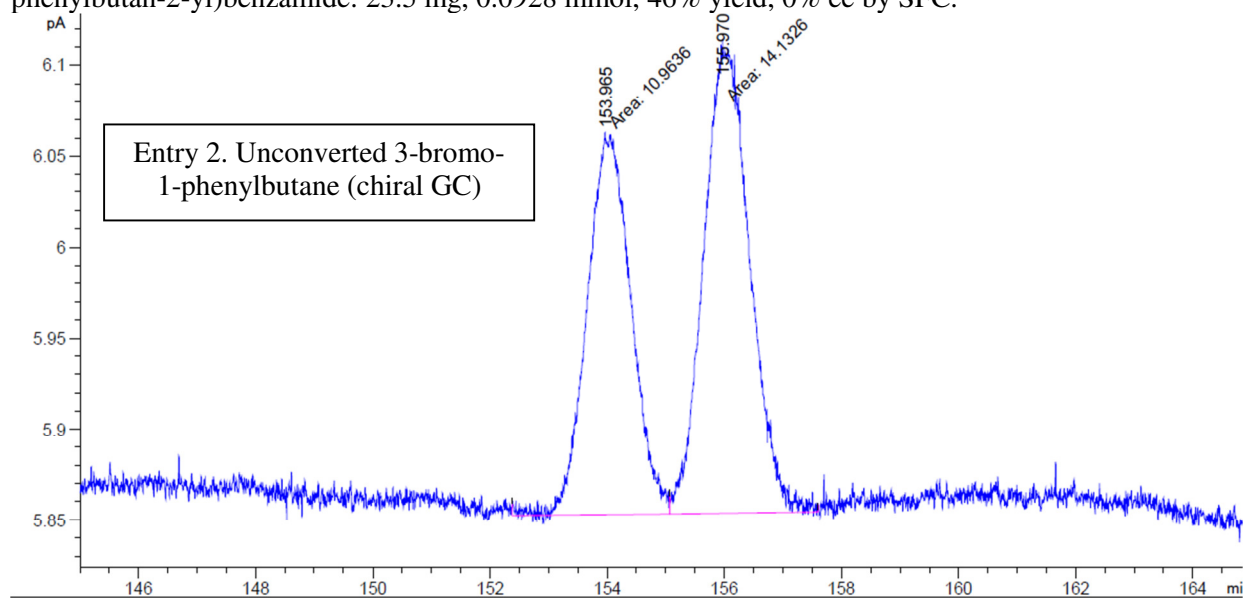
b(*t*) is a linear function to correct the GC baseline

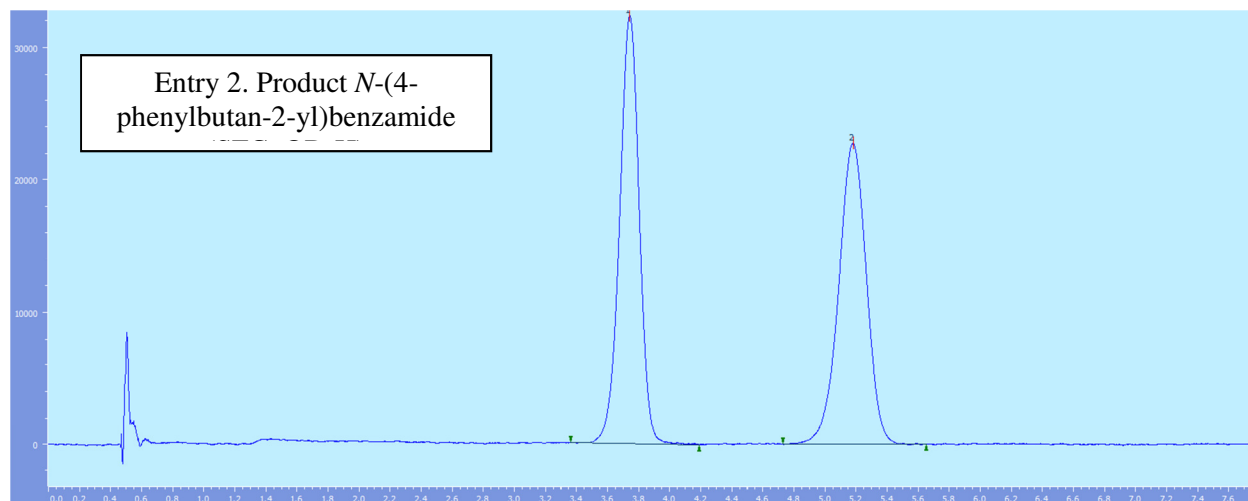
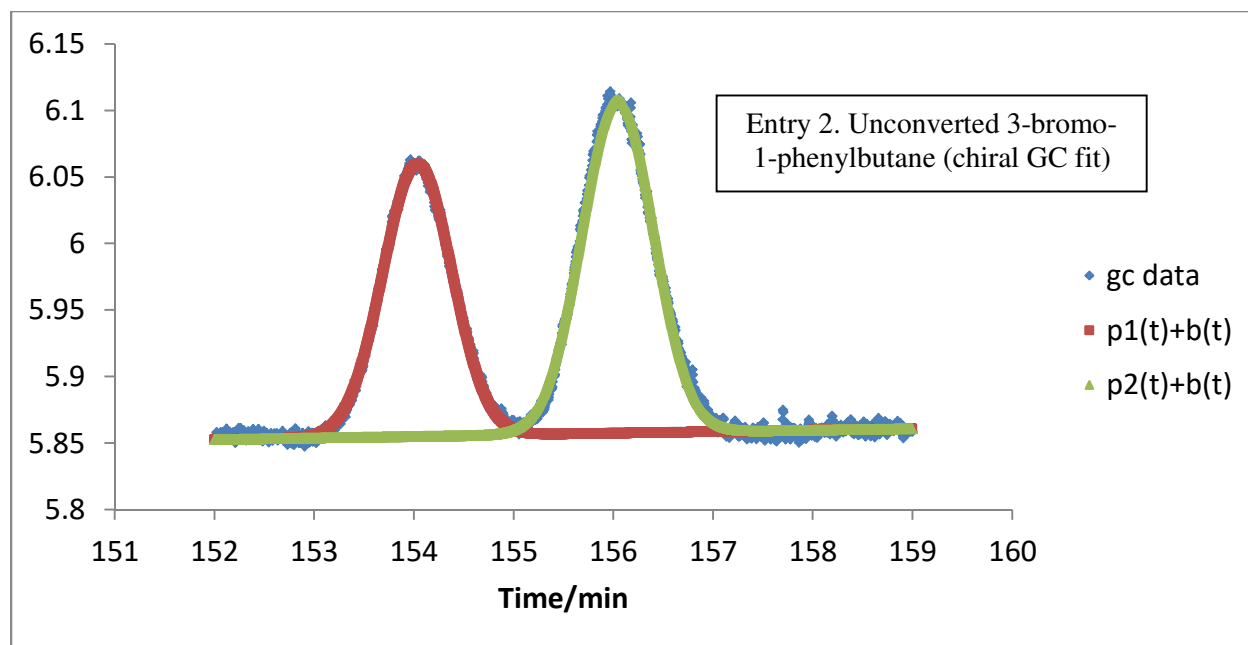
Entry 1: Reaction time = 1 h. Unconverted 3-bromo-1-phenylbutane: 45% ee by chiral GC. *N*-(4-phenylbutan-2-yl)benzamide: 11.0 mg, 0.0470 mmol, 23% yield, 0% ee by SFC.





Entry 2: Reaction time = 4 h. Unconverted 3-bromo-1-phenylbutane: 12% ee by chiral GC. *N*-(4-phenylbutan-2-yl)benzamide: 23.5 mg, 0.0928 mmol, 46% yield, 0% ee by SFC.





Experimental details for Scheme 2b

In a nitrogen-filled glovebox, a 4 ml vial was charged with benzophenone imine (**2a**) (36.2 mg, 0.200 mmol), (*S*)-3-bromo-1-phenylbutane (**(S)-1**) (85.1 mg, 0.399 mmol, 2.00 equiv), [Cy₂(*t*-Bu)P]₂PdHBr (10.0 mg, 0.0144 mmol, 7.22 mol%), cesium carbonate (97.9 mg, 0.300 mmol, 1.50 equiv), (*S*)-*N*-(*sec*-butyl)benzophenone imine (**20**) (48.1 mg, 0.203 mmol, 1.02 equiv), *t*-amyl alcohol (0.26 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 24 hours in an aluminum block. The reaction mixture was diluted with ether (2 ml) and filtered through a small plug of Celite into a 20 ml vial. A small aliquot was removed for GC/MS and chiral GC analysis at this stage (unconverted alkyl bromide was racemic by chiral GC). The volatile materials were evaporated at reduced pressure.

HCl_(aq) (4 ml, 0.5 M) was added to the vial, and the mixture was heated with stirring at 80 °C for 4 h. The mixture was washed with ether (4 ml, 2x 2 ml). The organic layer was extracted with HCl_(aq) (2 ml, 0.5 M), which was washed with ether (2x 2 ml). The combined aqueous layers were transferred to a separatory funnel, and the vial was rinsed with H₂O (1 ml). DCM (4 ml) was added, and the mixture was basified with K₂CO₃ (1.0 g). The organic layer was transferred to a cold vial, the aqueous layer was extracted with DCM (2x 2ml), and the combined organic layers were dried with Na₂SO₄ and filtered through cotton into another cold vial containing a stir bar.

The vial was flushed with nitrogen. Triethylamine (84 µl, 61 mg, 0.60 mmol, 3.0 equiv), followed by benzoyl chloride (70 µl, 85 mg, 0.60 mmol, 3.0 equiv), were then added to the vial. The reaction mixture was stirred at ambient temperature for 4.5 h. The mixture was washed with HCl_(aq) (8 ml, 0.5 M), and the aqueous layer extracted further with DCM (2x 8 ml). The combined organic layers were dried with MgSO₄, and the volatile materials were evaporated at reduced pressure. The crude mixture was purified by column chromatography (25% EA/hexanes) to give a mixture of (*S*)-*N*-(*sec*-butyl)benzamide (**21**) (0.062 mmol, 30% yield, 97% ee by SFC: AS-H) and (rac)-*N*-(4-phenylbutan-2-yl)benzamide (**19**) (0.133 mmol, 67% yield, 0% ee by SFC: AS-H).

The combined mass of amides was 44.7 mg. ¹H NMR spectroscopy indicated a molar ratio of 1.0 *N*-(*sec*-butyl)benzamide to 2.15 *N*-(4-phenylbutan-2-yl)benzamide. The yield of each compound was, therefore, determined by solving the equation: $x(2.15 \times 253.35 + 177.25) = 44.7$; in which x = mmol *N*-(*sec*-butyl)benzamide and $2.15 \times x$ = mmol *N*-(4-phenylbutan-2-yl)benzamide.

The low isolated yield of *N*-(*sec*-butyl)benzamide is likely due to the high solubility of *sec*-butylamine in aqueous solutions.

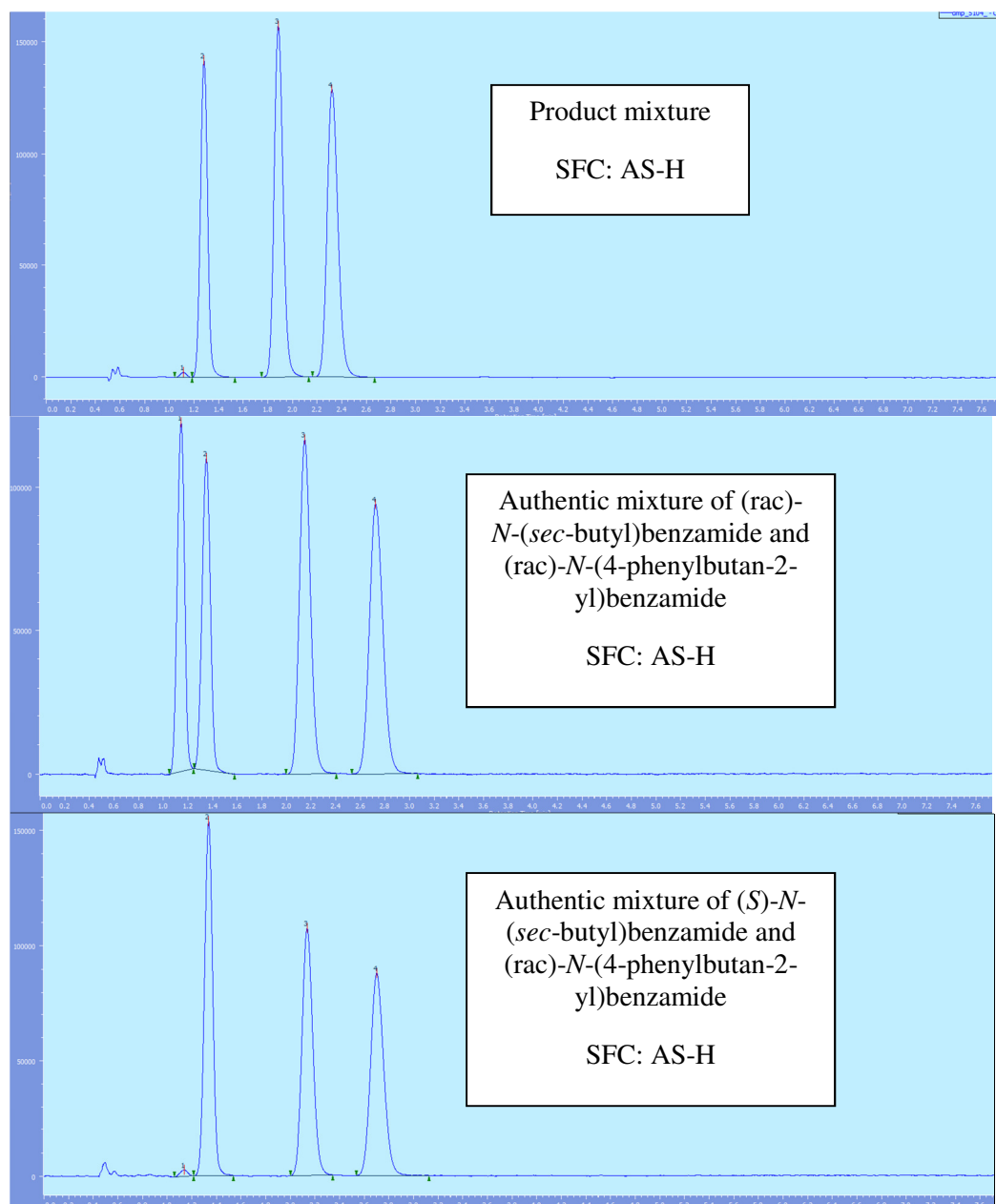
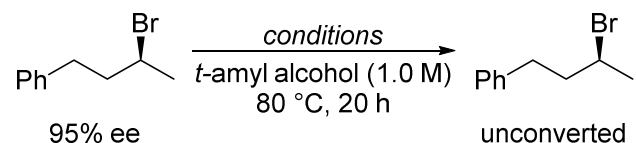


Table S-4. Racemization of (S)-1

| entry | conditions | ee unconverted RBr (%) |
|-------|---|------------------------|
| 1 | 4% [Cy ₂ (<i>t</i> -Bu)P] ₂ PdHBr | 93 |
| 2 | 0.5 equiv CsBr | 95 |
| 3 | 4% [Cy ₂ (<i>t</i> -Bu)P] ₂ PdHBr + 0.5 equiv CsBr | 89 |
| 4 | 0.75 equiv Cs ₂ CO ₃ | 91 |
| 5 | 4% [Cy ₂ (<i>t</i> -Bu)P] ₂ PdHBr + 0.75 equiv Cs ₂ CO ₃ | < 2 |

General procedure: In a nitrogen filled glovebox, a 1.0 M solution of (*S*)-3-bromo-1-phenylbutane ((*S*)-1) (95% ee by chiral GC) was prepared. A 200 μ l sample (0.20 mmol RBr) of this solution was added to a vial containing the noted compounds and a magnetic stir bar. The vials were sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 20 hours in an aluminum block. The reaction mixture was then diluted with ethyl acetate (~ 2 ml), and an aliquot was removed for GC analysis after filtration through a plug of silica. Ee values are averages of two experiments.

Entry 1: (Cy₂*t*-BuP)₂PdHBr (5.0 mg, 0.0072 mmol, 3.6%)

Entry 2: CsBr (21.3 mg, 0.100 mmol, 0.500 equiv)

Entry 3: (Cy₂*t*-BuP)₂PdHBr (5.0 mg, 0.0072 mmol, 3.6%) and CsBr (21.3 mg, 0.100 mmol, 0.500 equiv)

Entry 4: Cs₂CO₃ (48.8 mg, 0.150 mmol, 0.750 equiv)

Entry 5: (Cy₂*t*-BuP)₂PdHBr (5.0 mg, 0.0072 mmol, 3.6%) and Cs₂CO₃ (48.8 mg, 0.150 mmol, 0.750 equiv). Significant formation of *n*-butylbenzene was detected in this reaction mixture.

Experimental details for Scheme 3

0.5 M reaction: In a nitrogen-filled glovebox, a 1 dram vial was charged with benzophenone imine (**2a**) (54.4 mg, 0.300 mmol), *i*-PrBr (74 mg, 0.60 mmol, 2.0 equiv), [Cy₂(*t*-Bu)P]₂PdHBr (11 mg, 0.016 mmol, 5.3 mol %), cesium carbonate (147 mg, 0.451 mmol, 1.50 equiv), THF (0.46 ml; total volume approximately 0.6 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 48 h in an aluminum block. The mixture was diluted with ether (2 ml) and filtered through a plug of Celite, which was then rinsed with ether (3 x 2 ml). The volatile materials were evaporated at reduced pressure. The crude product was dissolved in 5% triethylamine in hexanes (approximately 1 ml) and filtered through a plug of basified silica, which was rinsed with 5% triethylamine in hexanes (3 x 2 ml), into a vial containing 1,3,5-trimethoxy benzene (50.5 mg, 0.300 mmol, 1.00 equiv). The volatile materials were removed at reduced pressure. Yields were determined by integrating the ¹H NMR spectroscopy peaks of the product relative to those of trimethoxybenzene (d1=12 s).

N-*iso*-propylbenzophenone imine (**22**): 75%

N-(tetrahydrofuran-2-yl)benzophenone imine (**23**): 14%

0.05 M reaction: In a nitrogen-filled glovebox, a 20 ml vial was charged with benzophenone imine (**2a**) (54.4 mg, 0.300 mmol), *i*-PrBr (74 mg, 0.60 mmol, 2.0 equiv), [Cy₂(*t*-Bu)P]₂PdHBr (11 mg, 0.016 mmol, 5.3 mol %), cesium carbonate (147 mg, 0.451 mmol, 1.50 equiv), THF (6.0 ml; total volume approximately 6 ml), and a magnetic stir bar. The vial was sealed with a Teflon-lined cap and Teflon tape. The reaction mixture was heated at 80 °C with stirring for 48 h in an aluminum block. The mixture was filtered through a plug of Celite, which was then rinsed with ether (3 x 2 ml). The volatile materials were evaporated at reduced pressure. The crude product was dissolved in 5% triethylamine in hexanes (approximately 1 ml) and filtered through a plug of basified silica, which was rinsed with 5% triethylamine in hexanes (3 x 2 ml), into a vial containing 1,3,5-trimethoxy benzene (50.5 mg, 0.300 mmol, 1.00 equiv). The volatile materials were removed at reduced pressure. Yields were determined by integrating the ¹H NMR spectroscopy peaks of the product relative to those of trimethoxybenzene (d1=12 s).

N-*iso*-propylbenzophenone imine (**22**): 22%

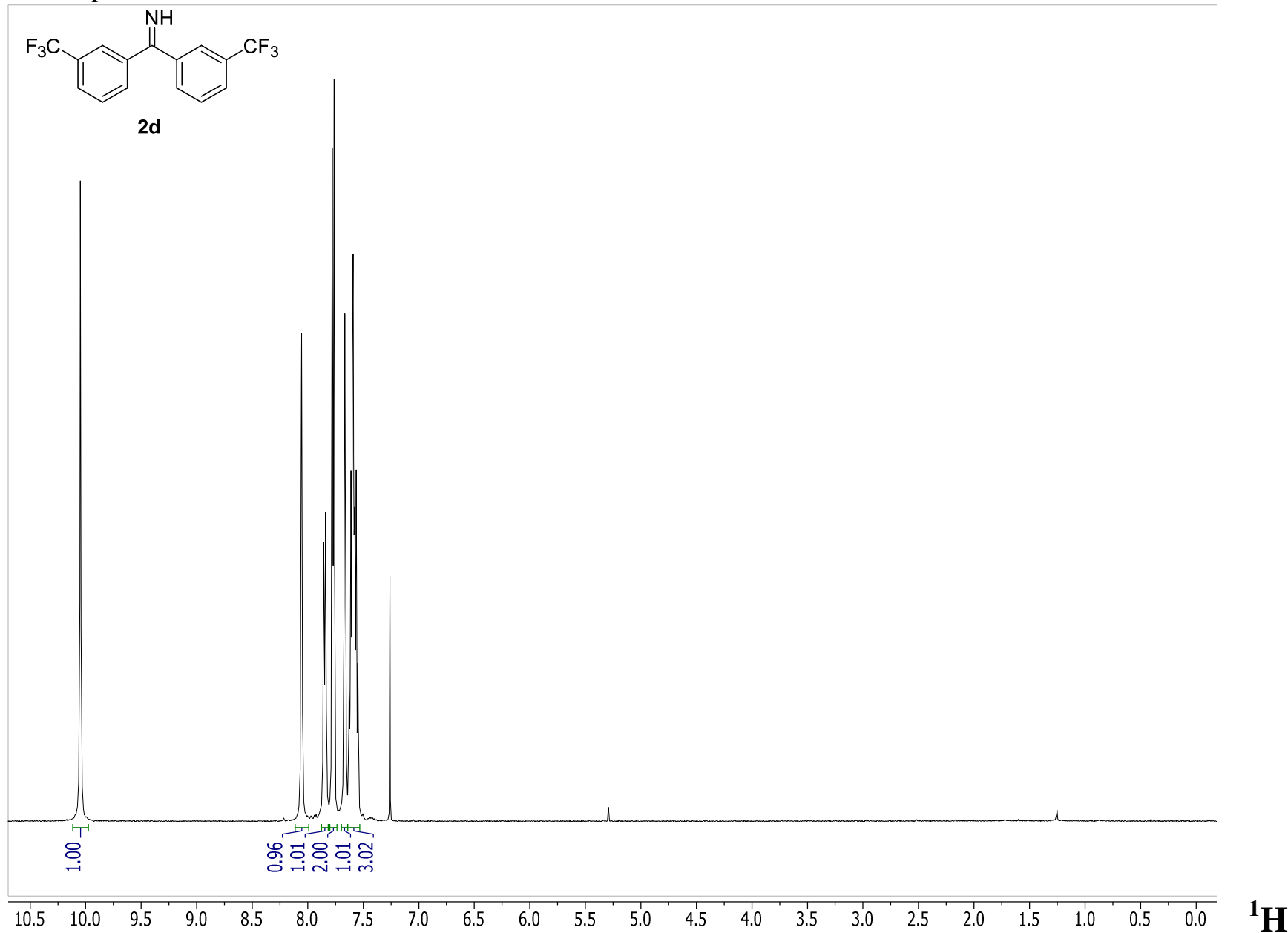
N-(tetrahydrofuran-2-yl)benzophenone imine (**23**): 60%

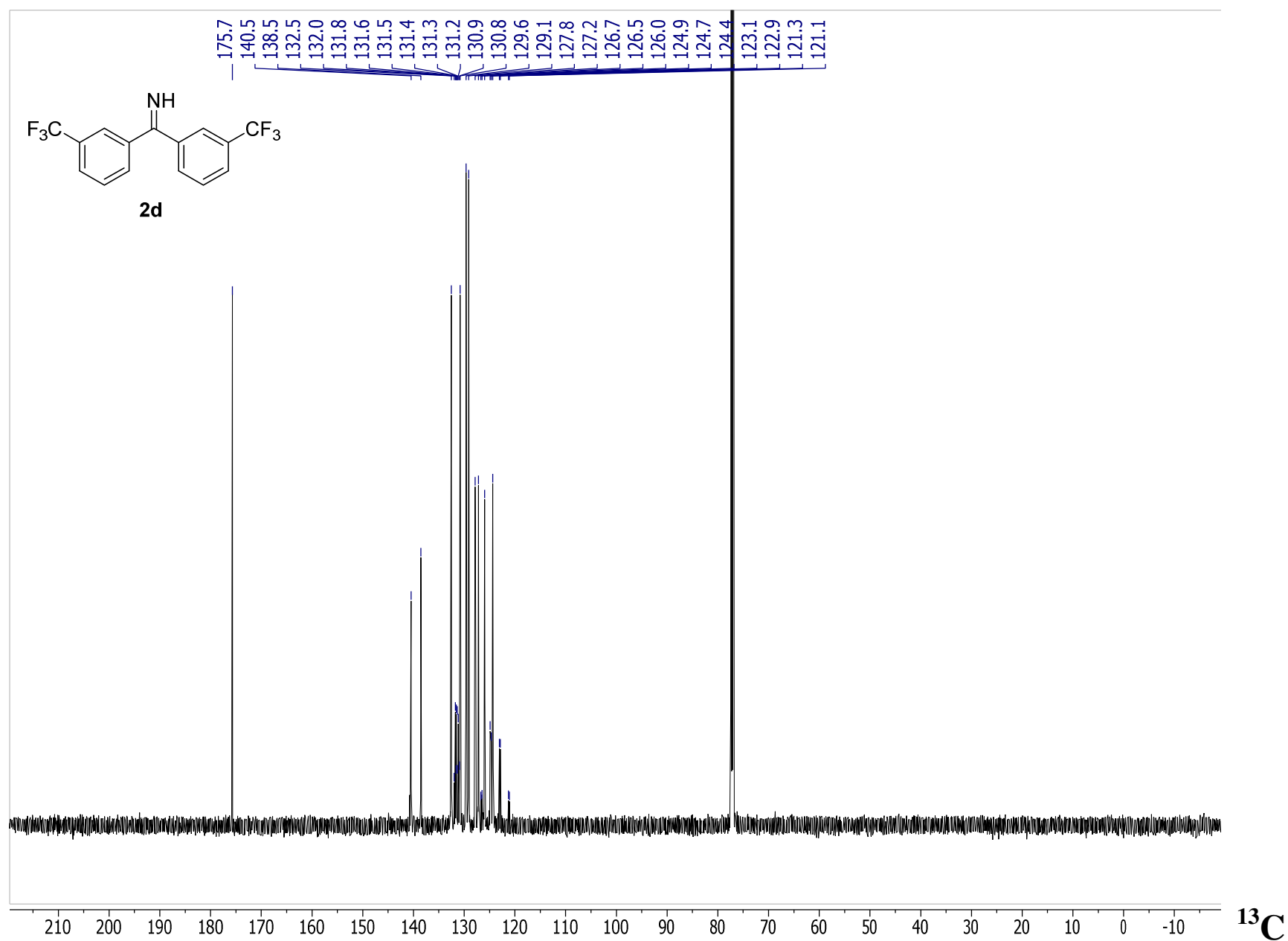
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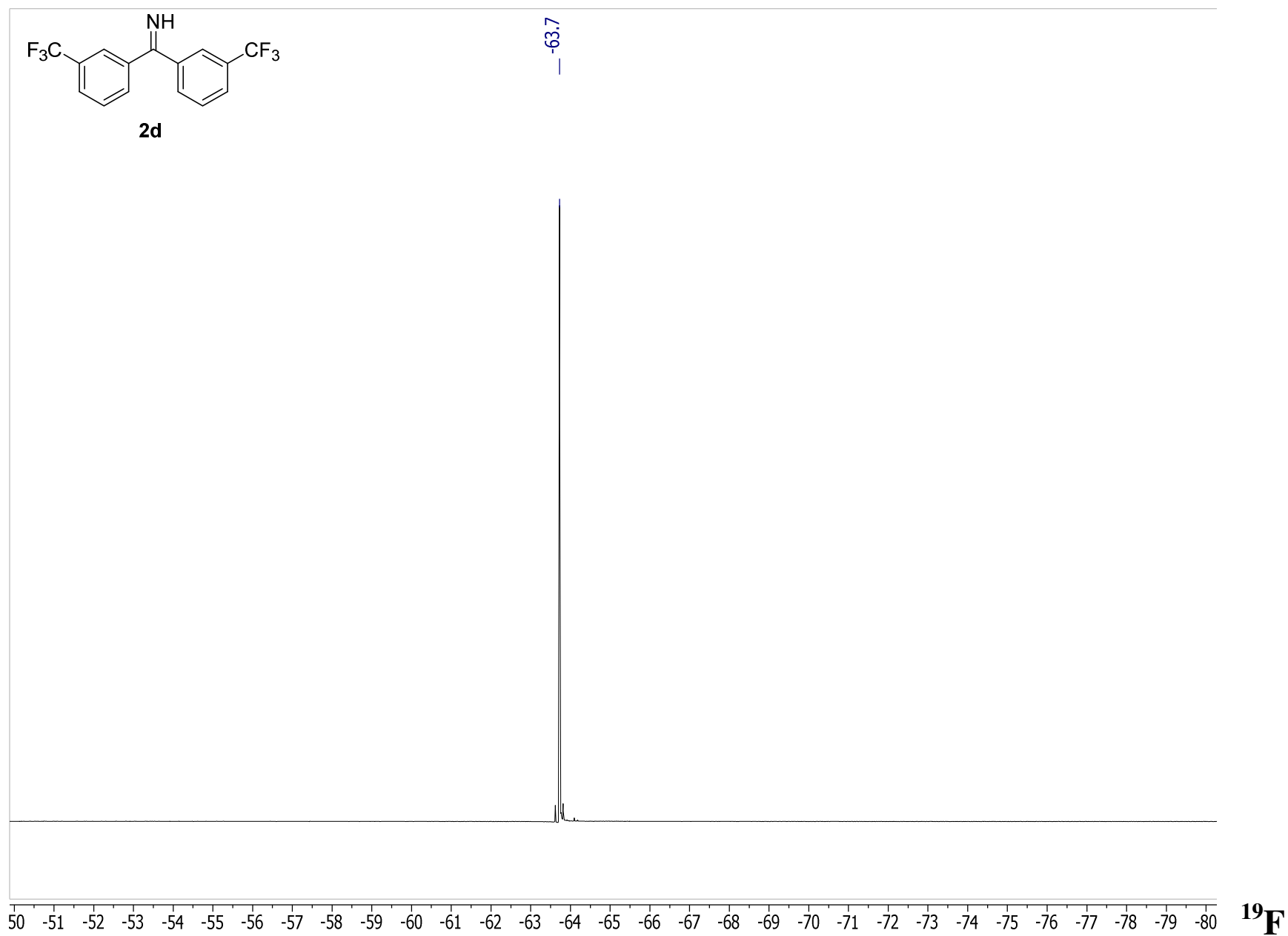
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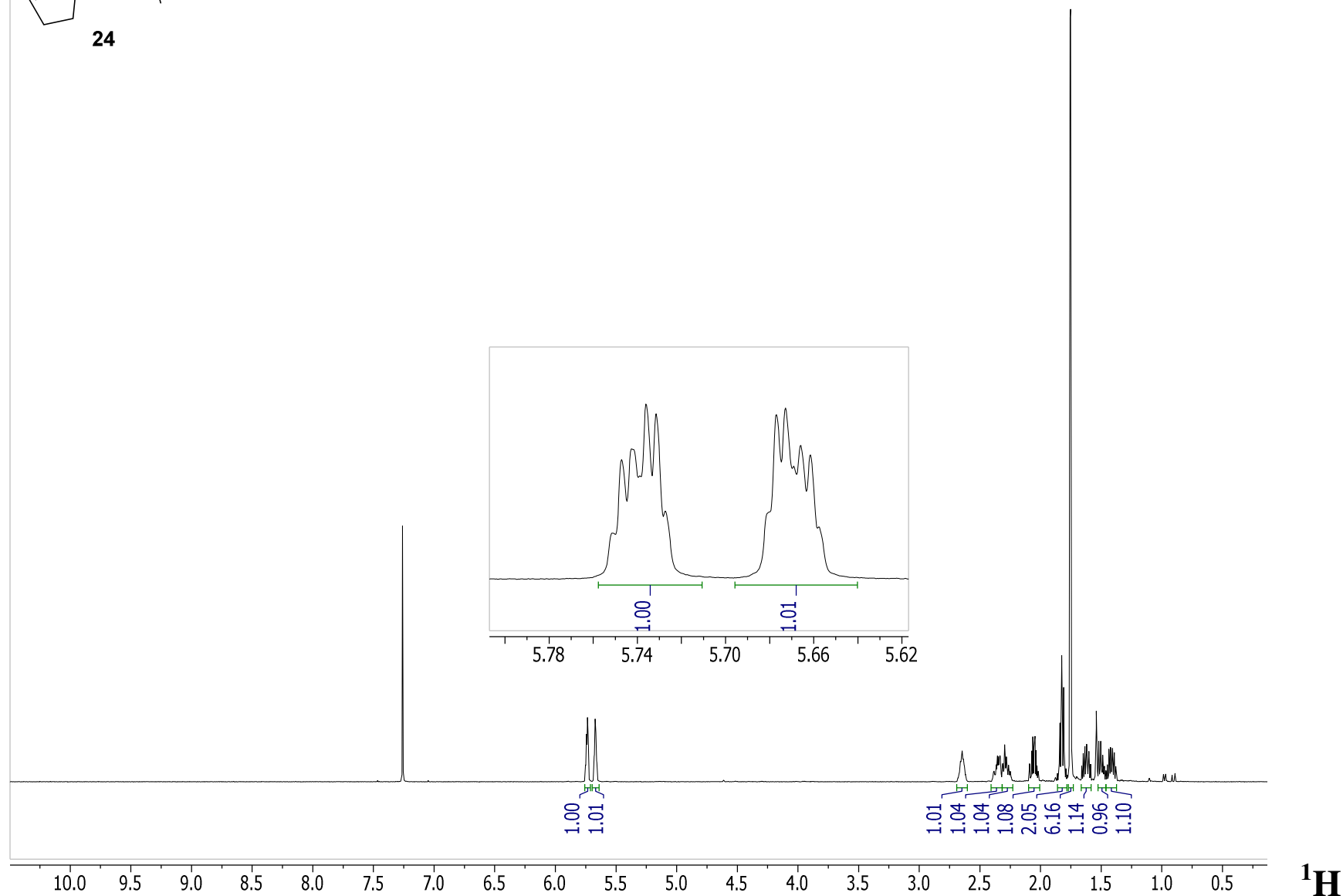
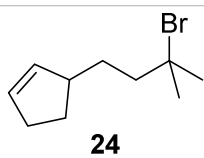
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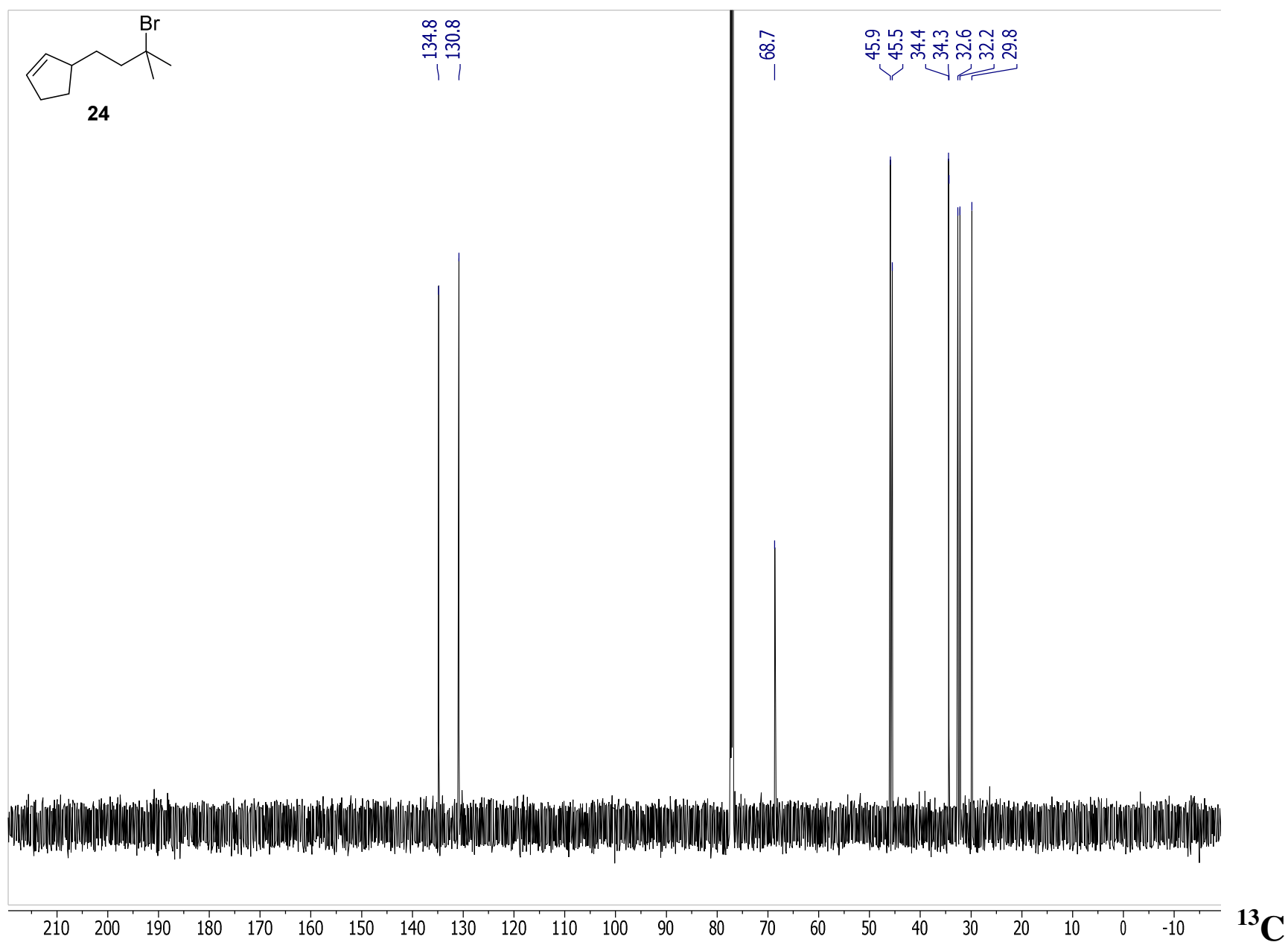
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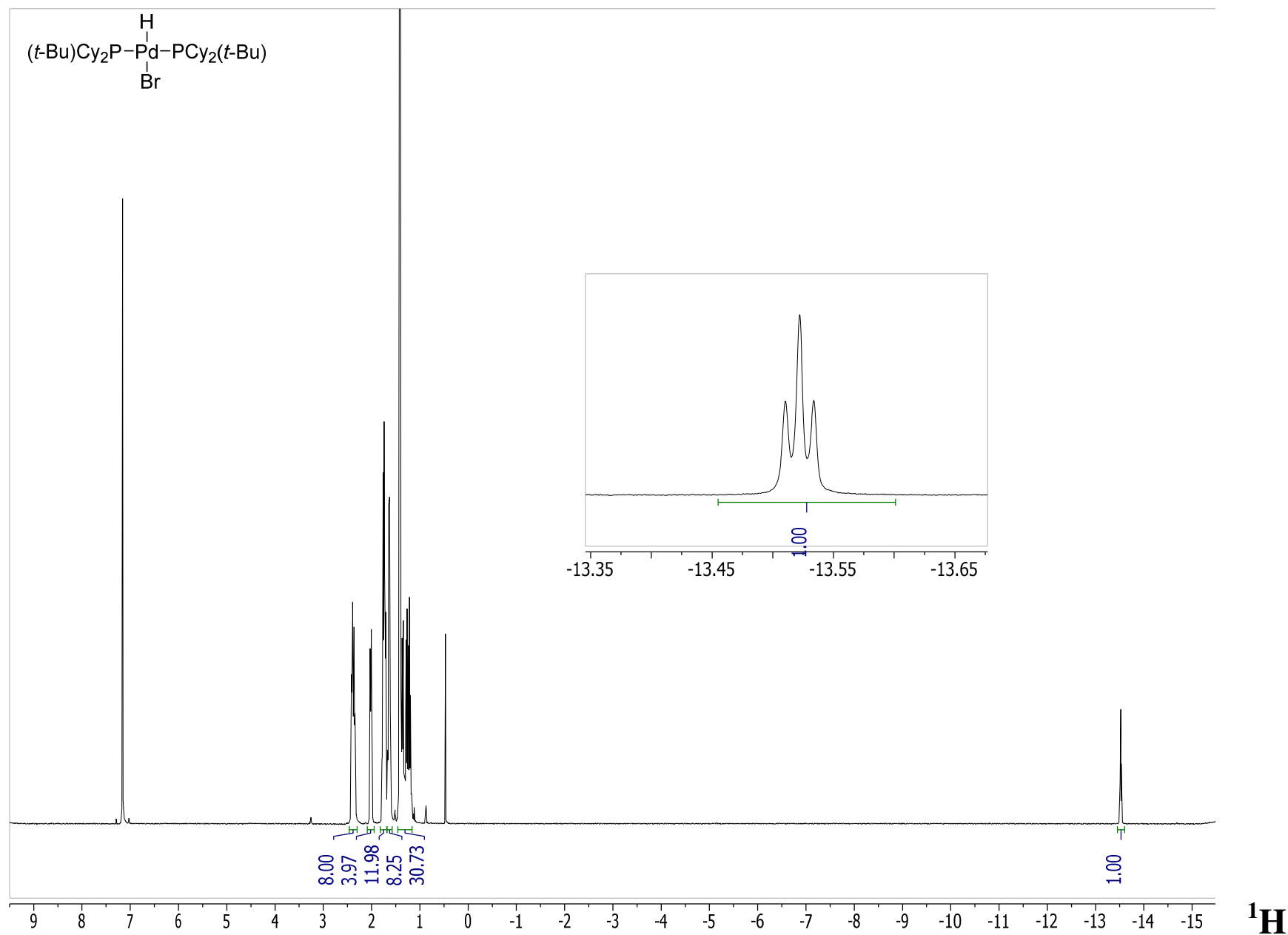


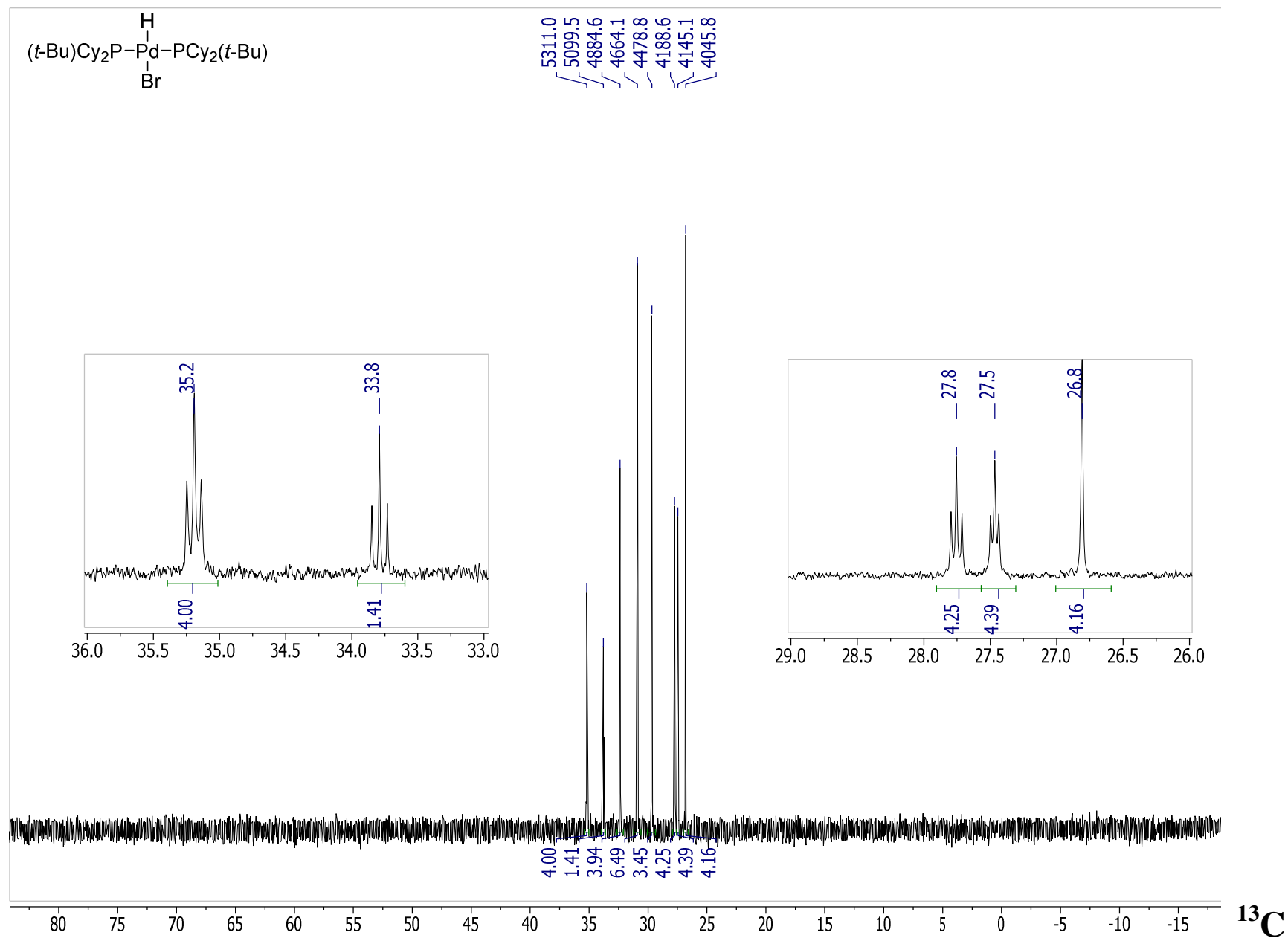


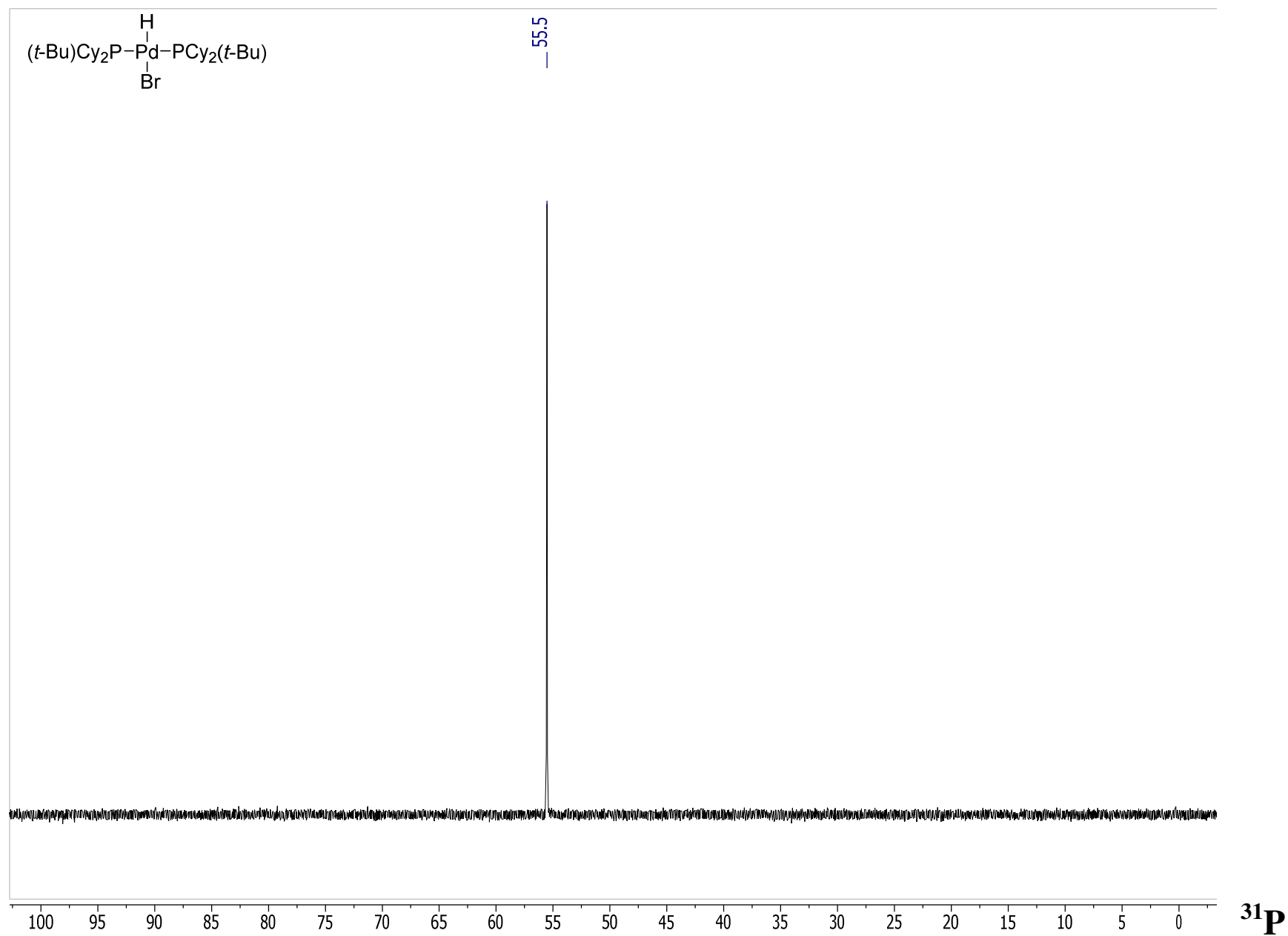


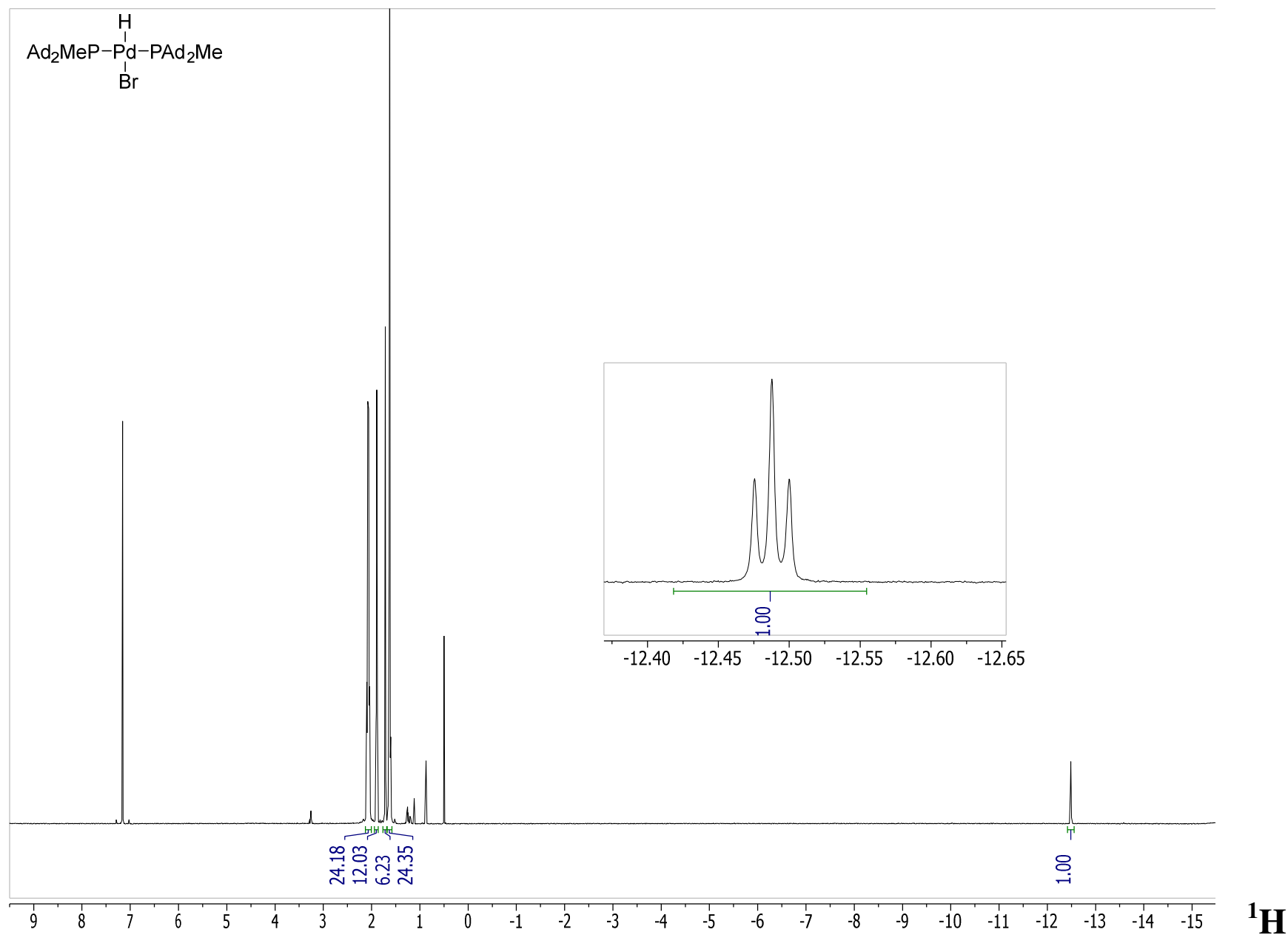


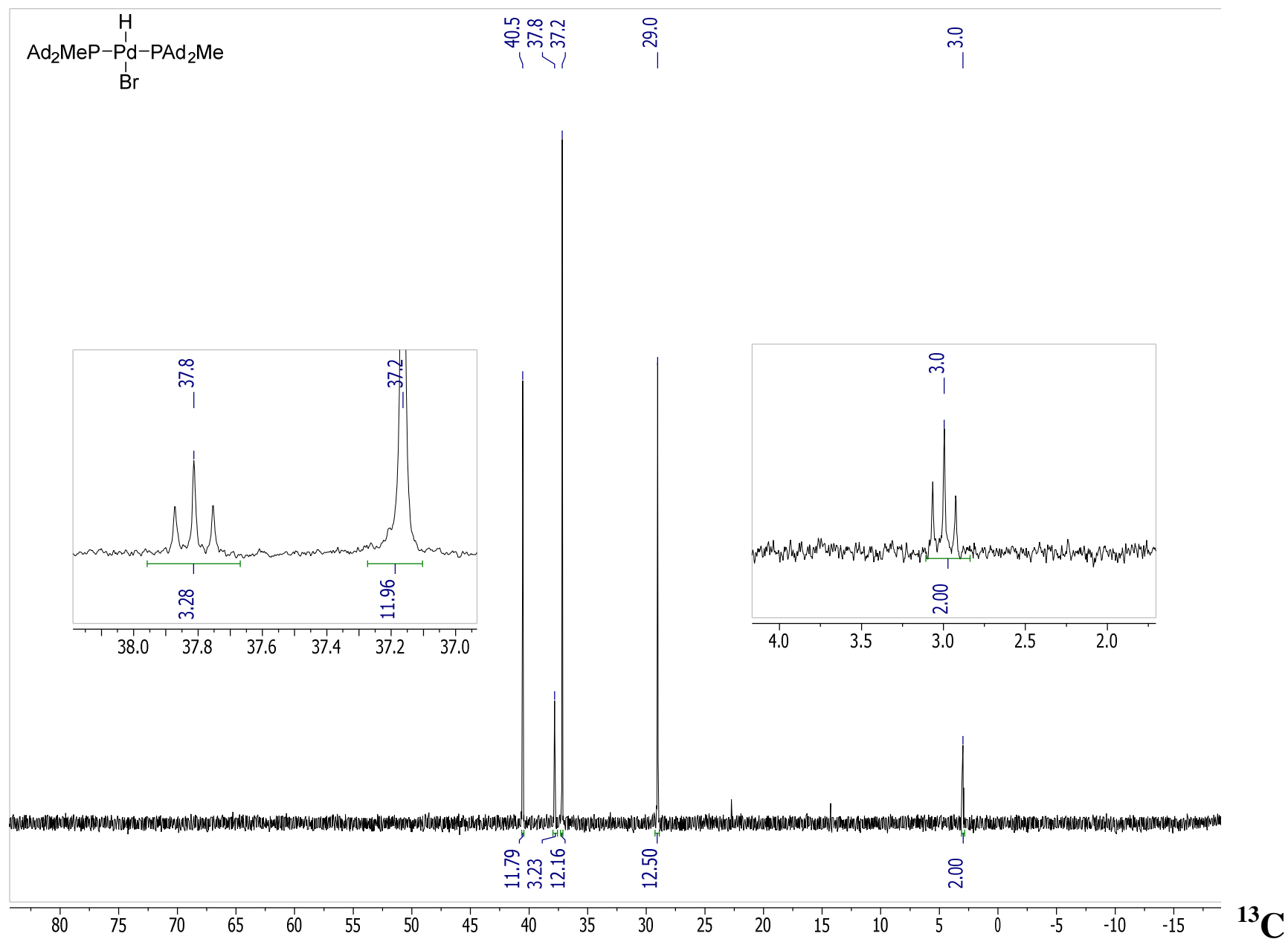


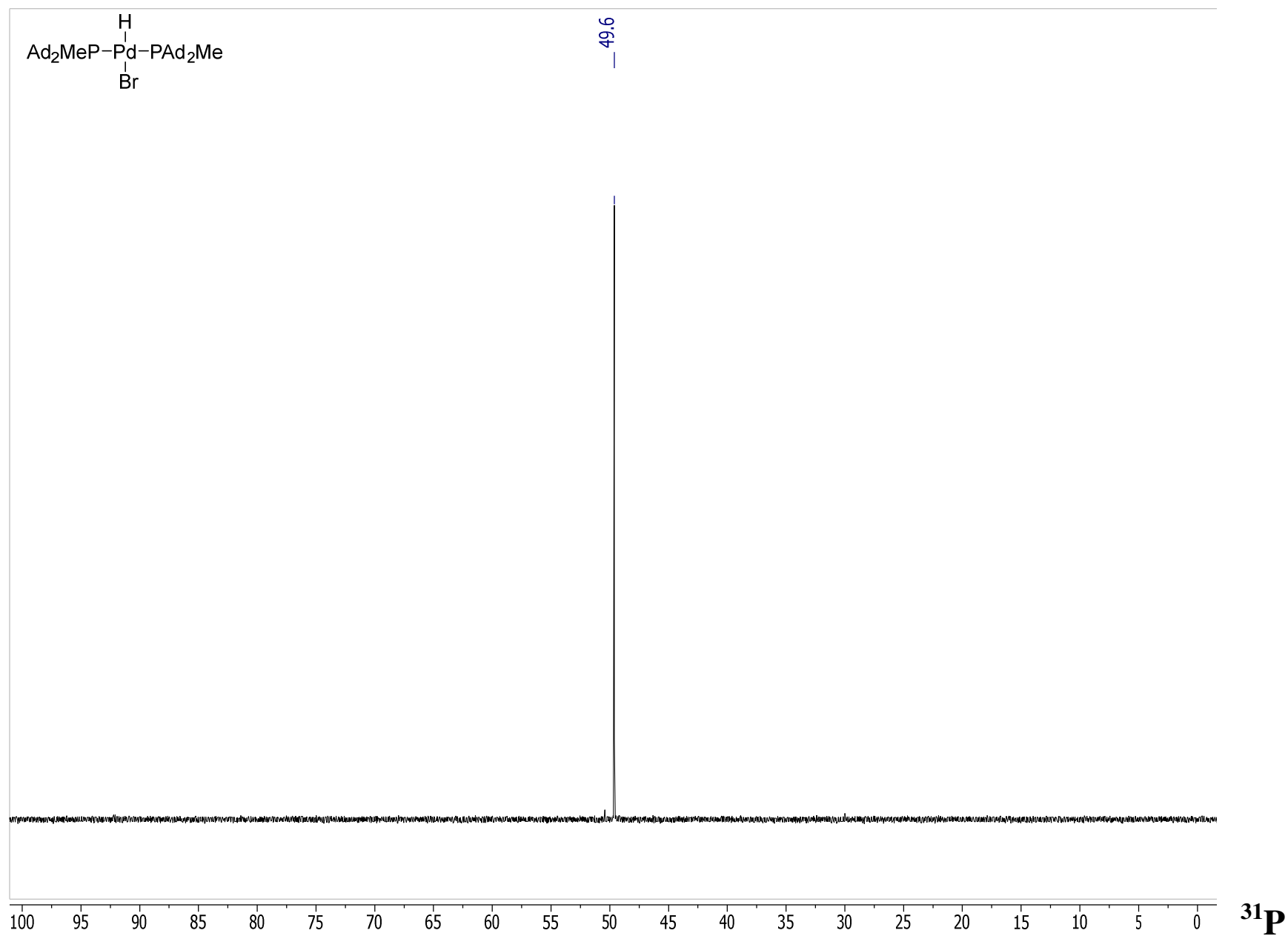


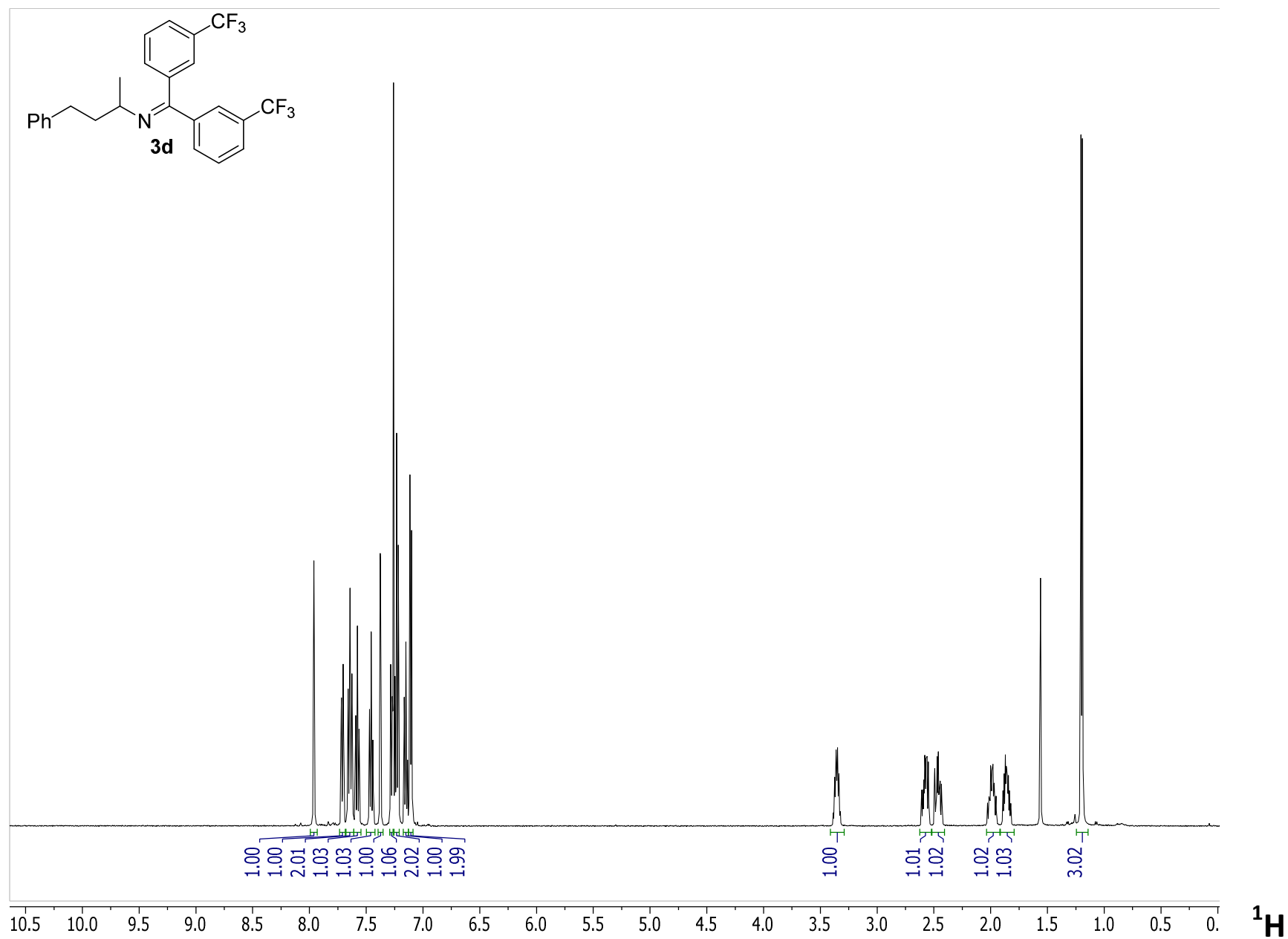


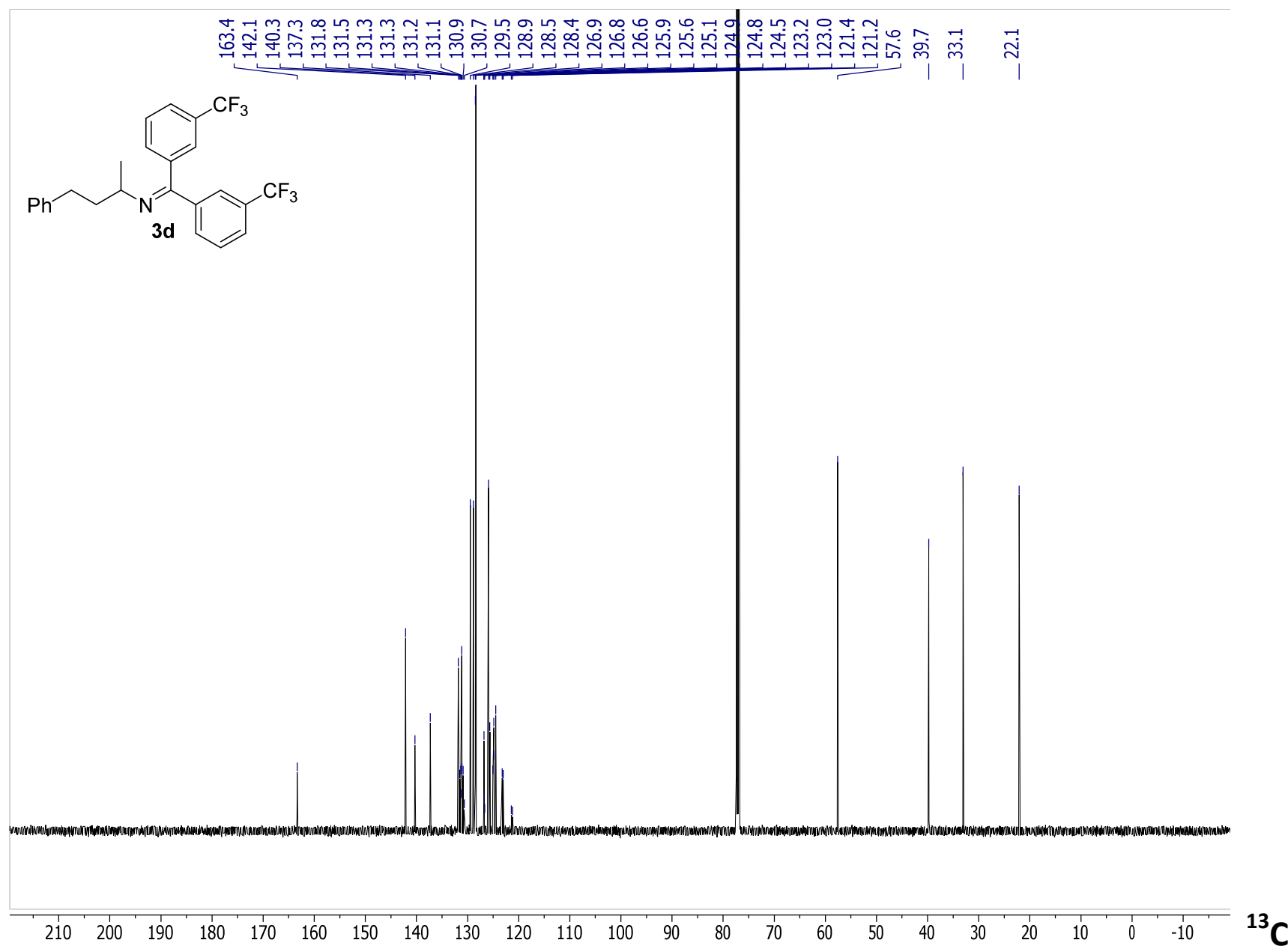


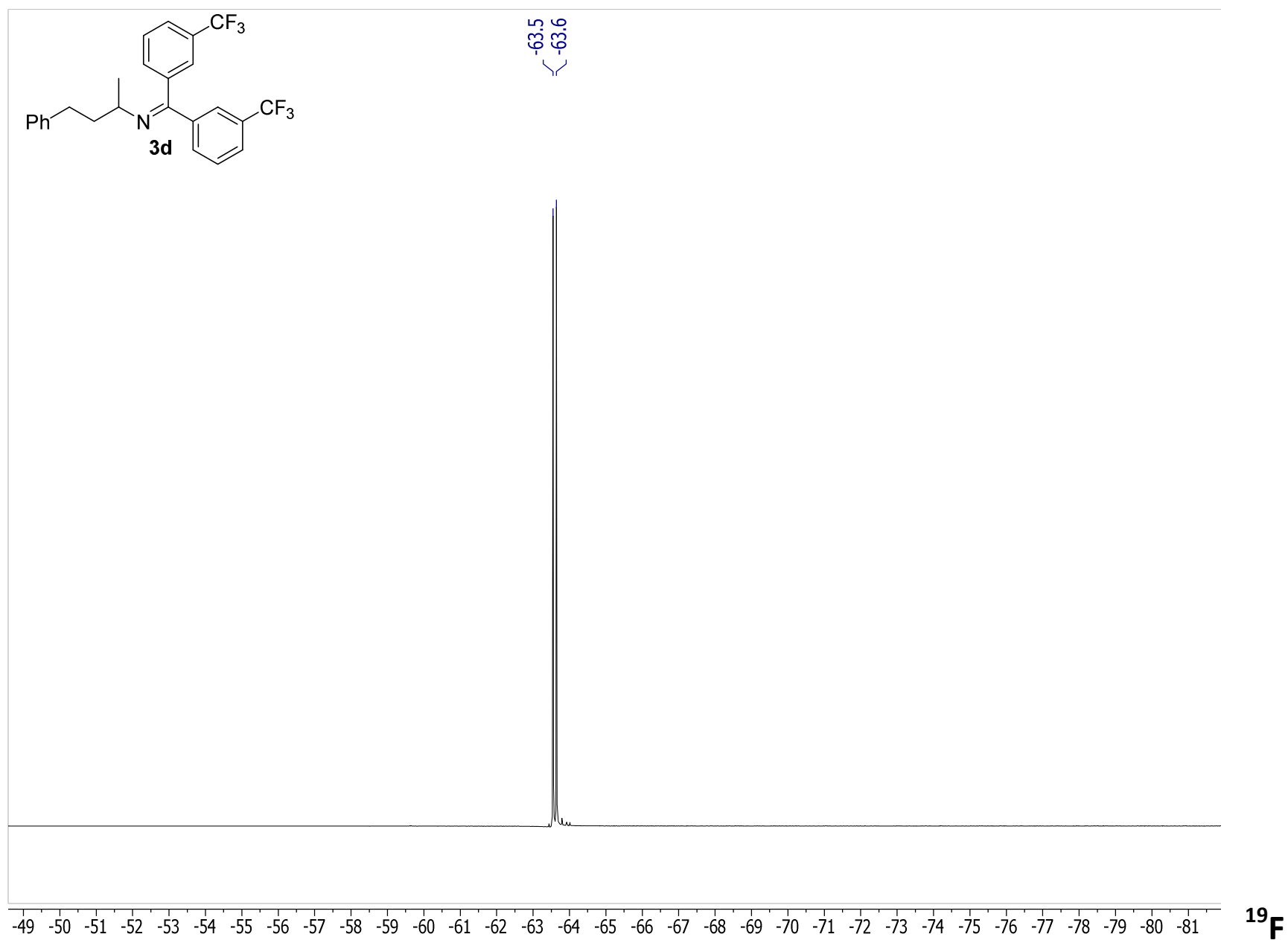


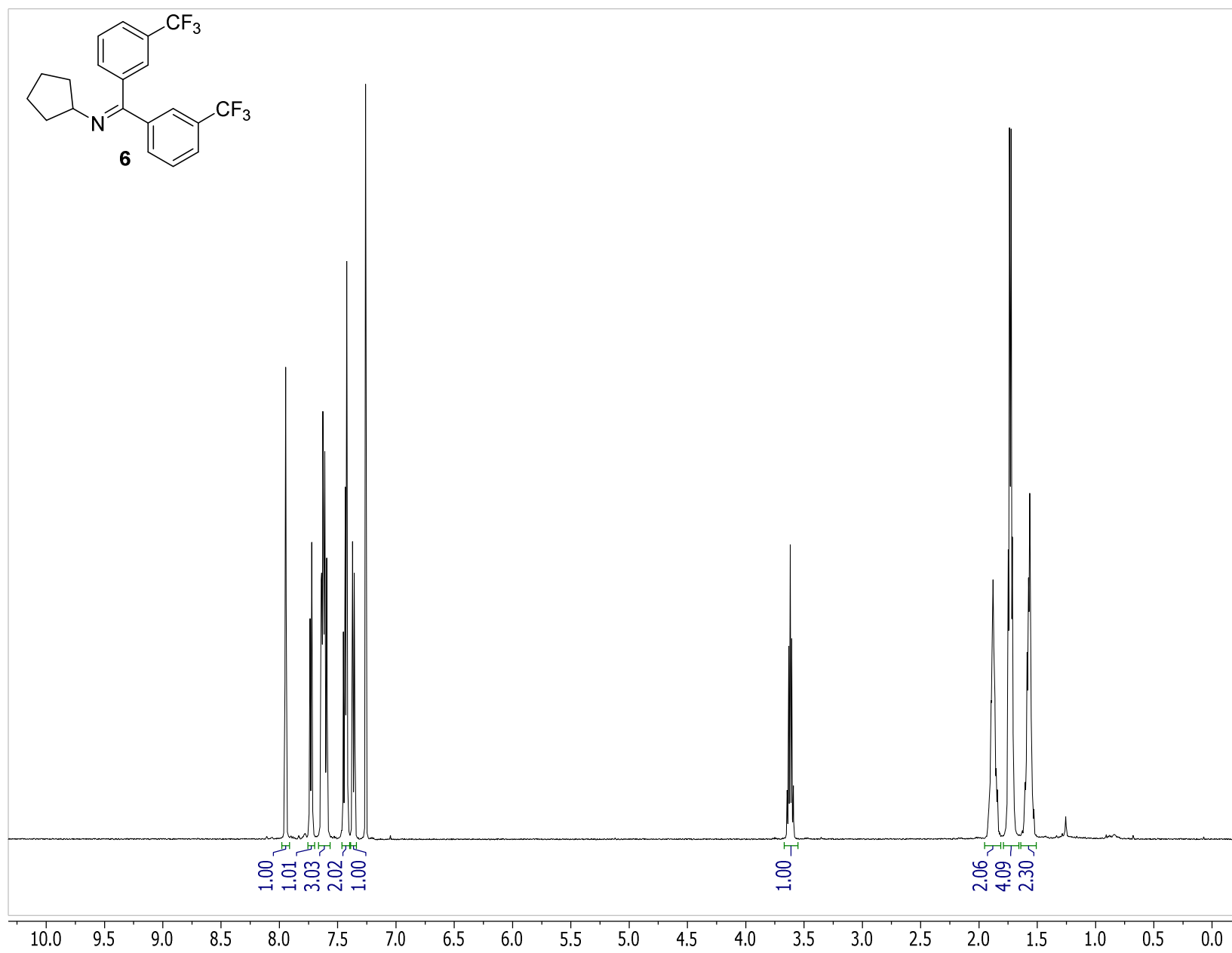


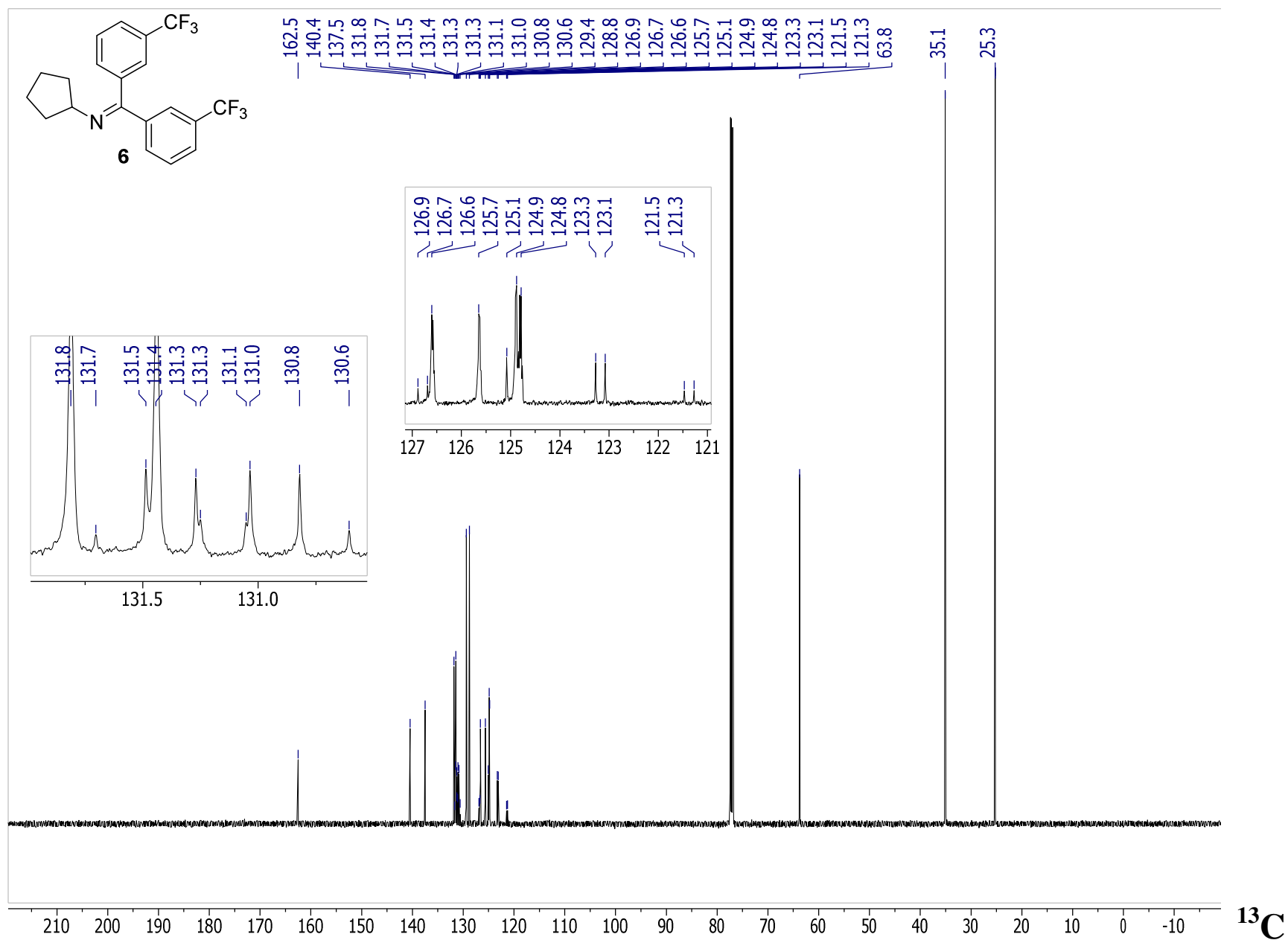


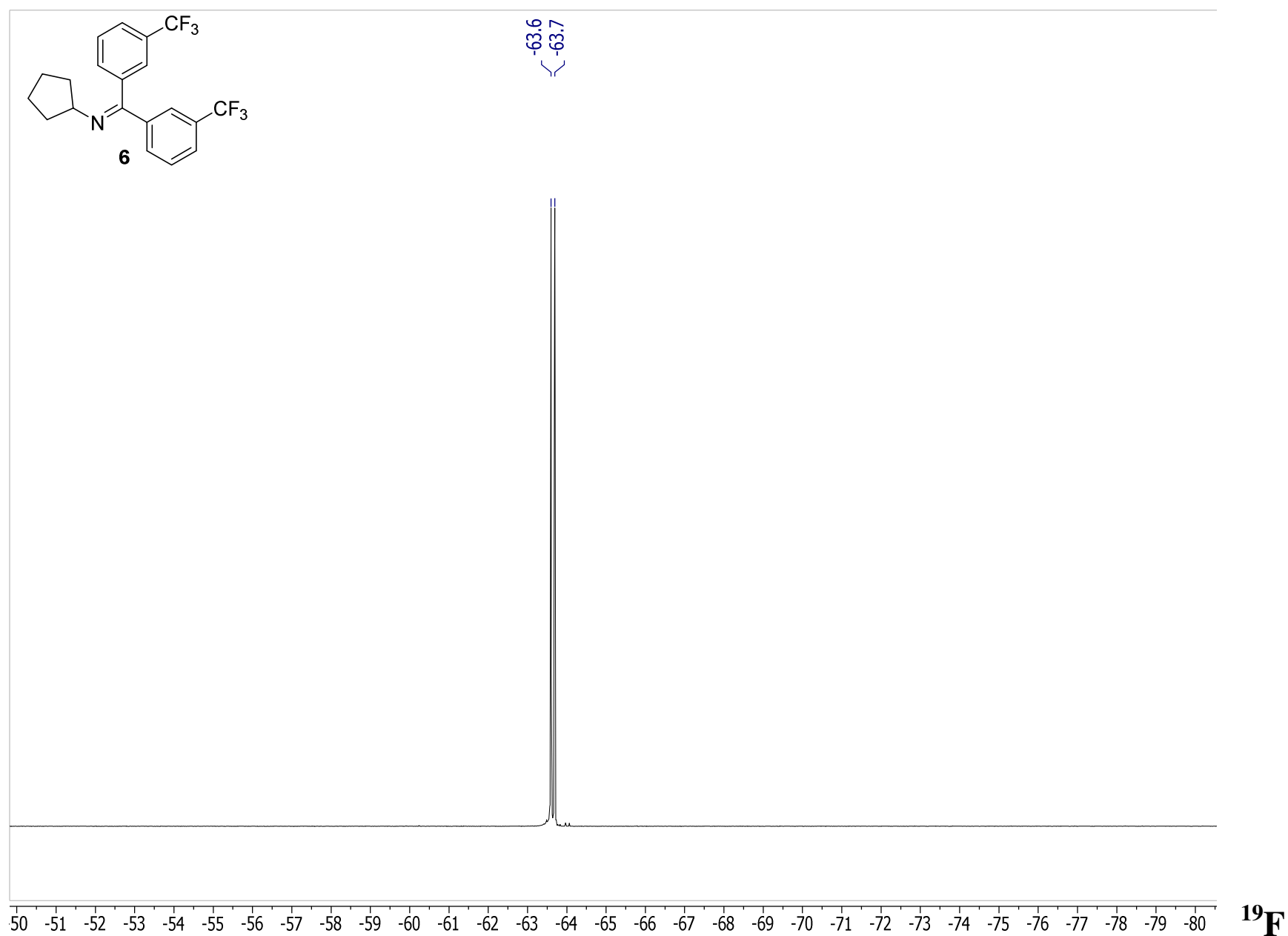


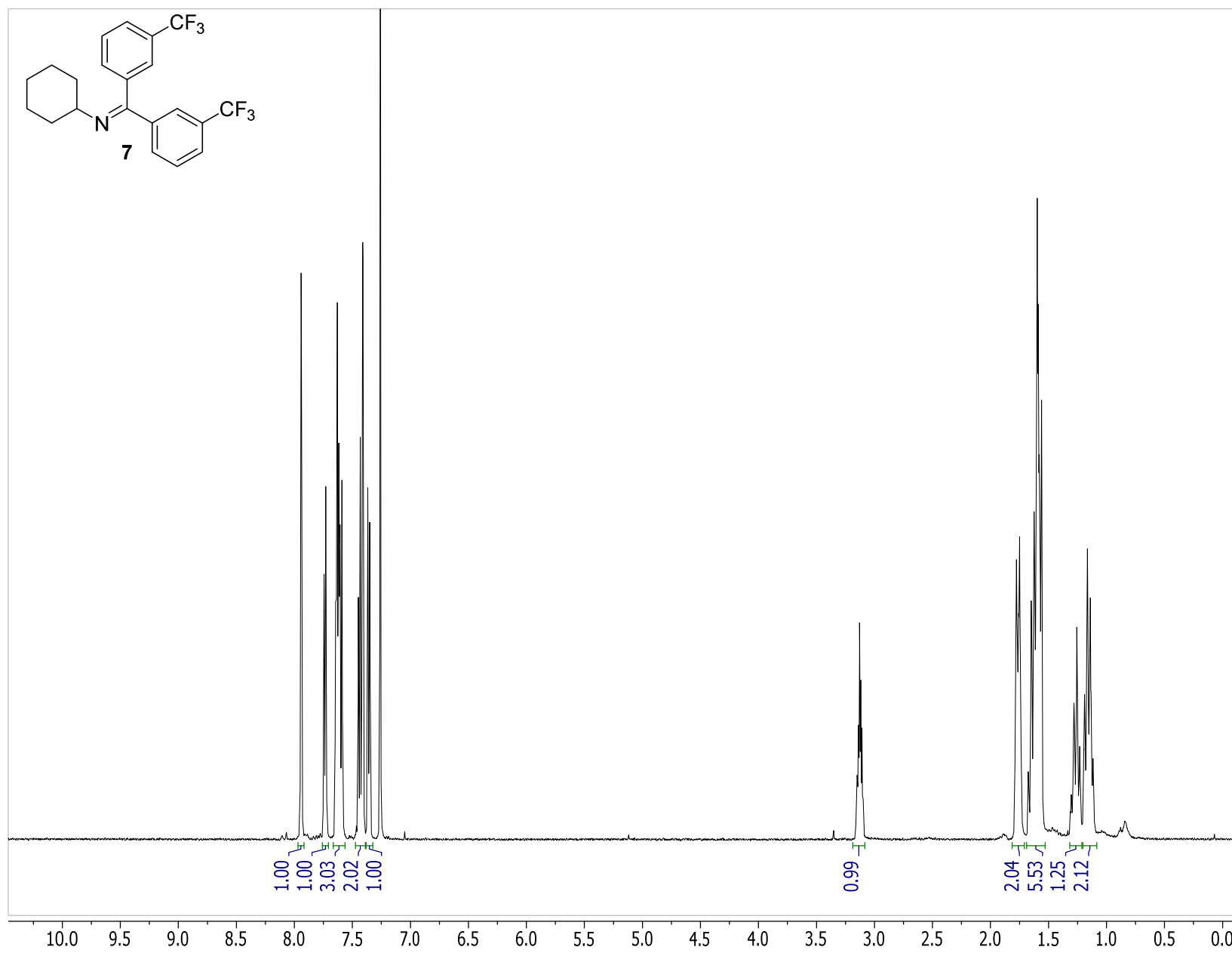


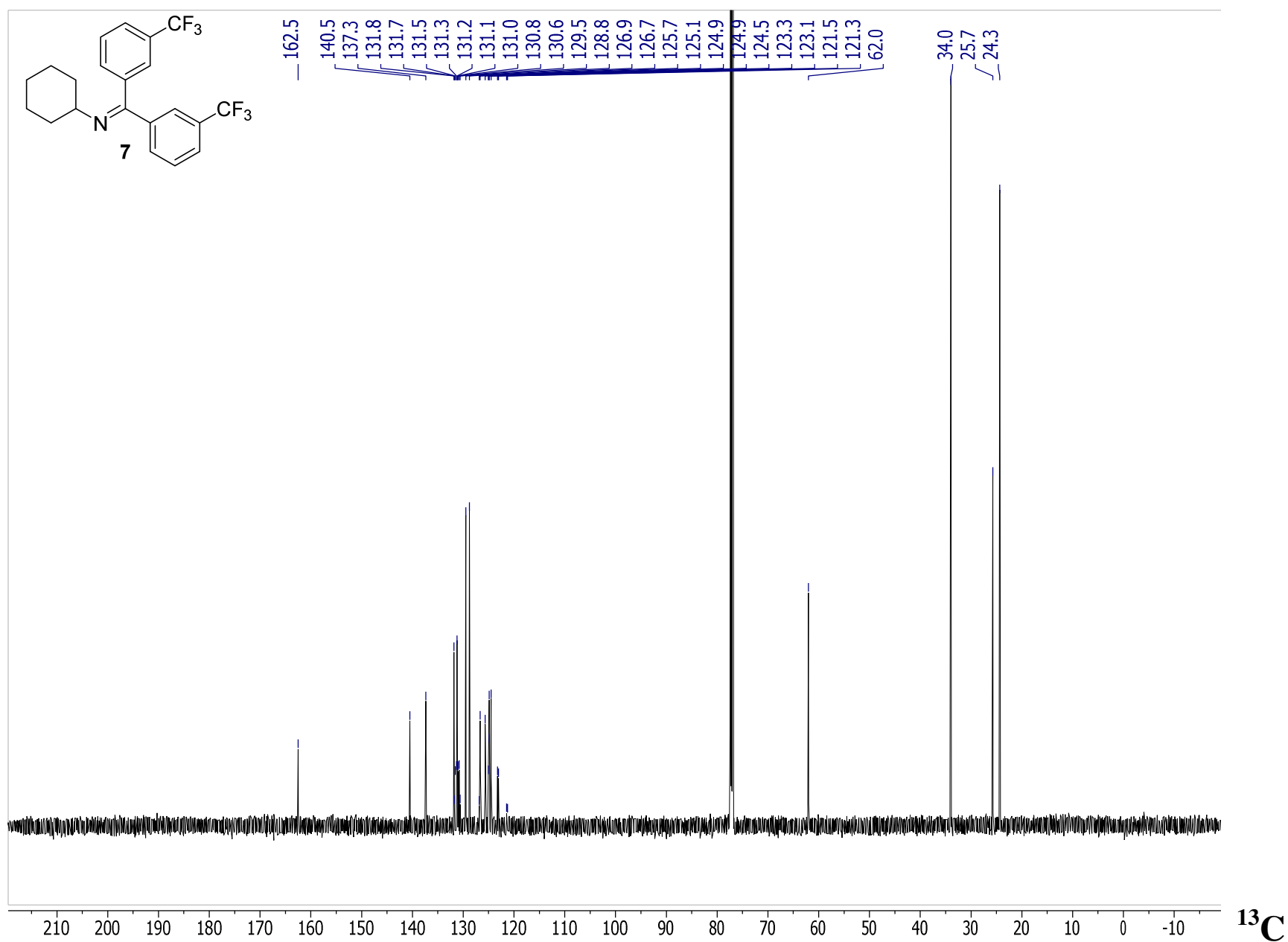


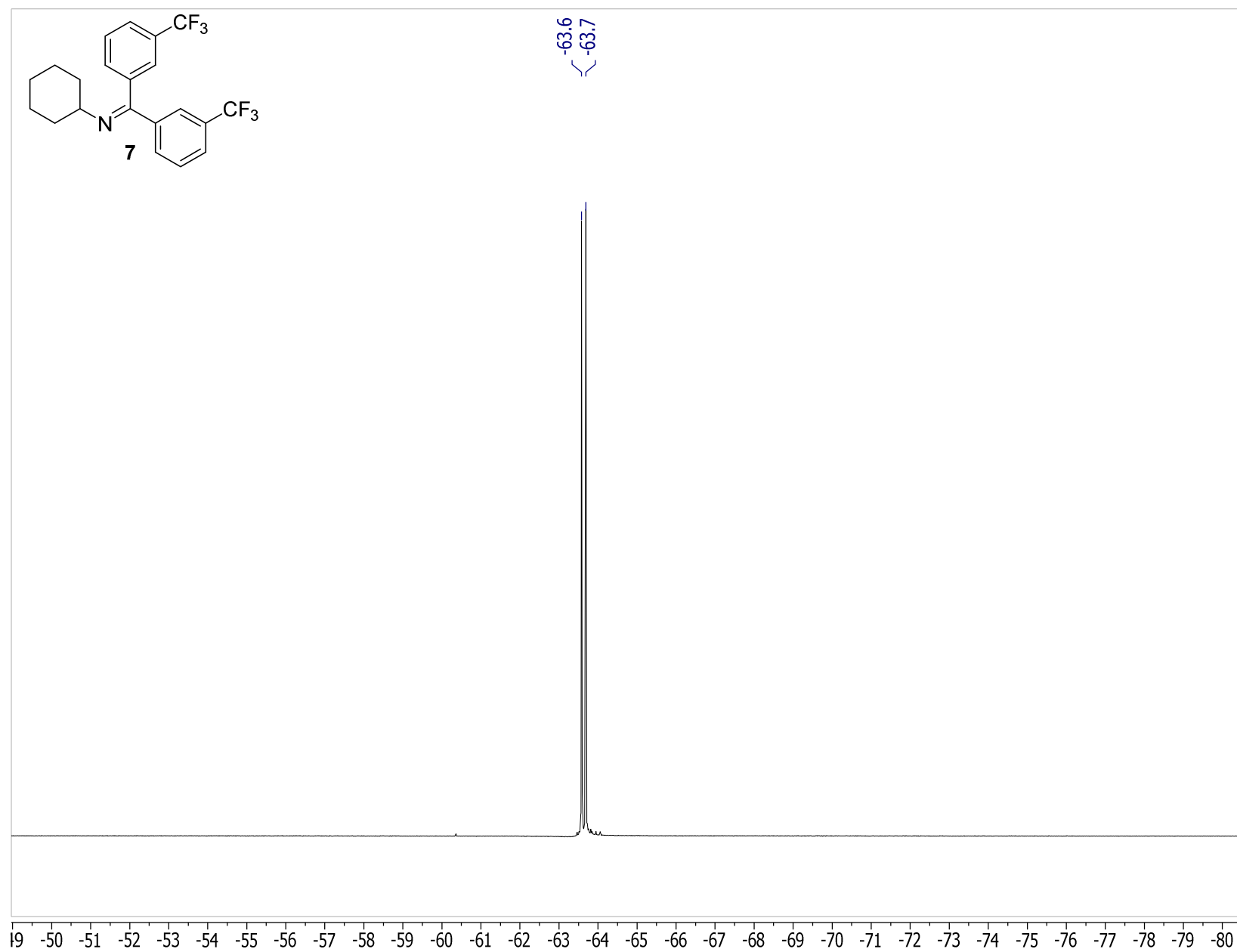


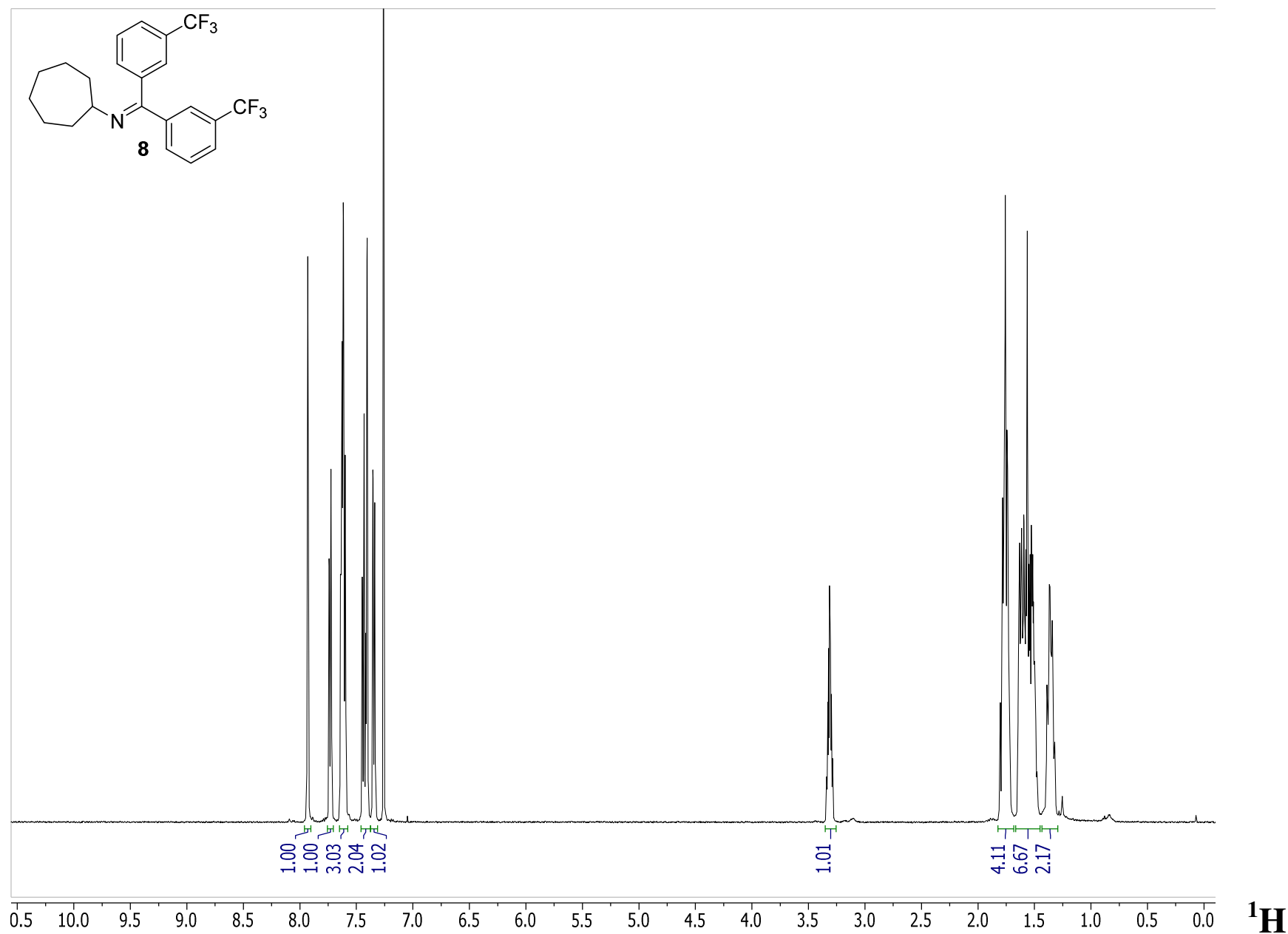


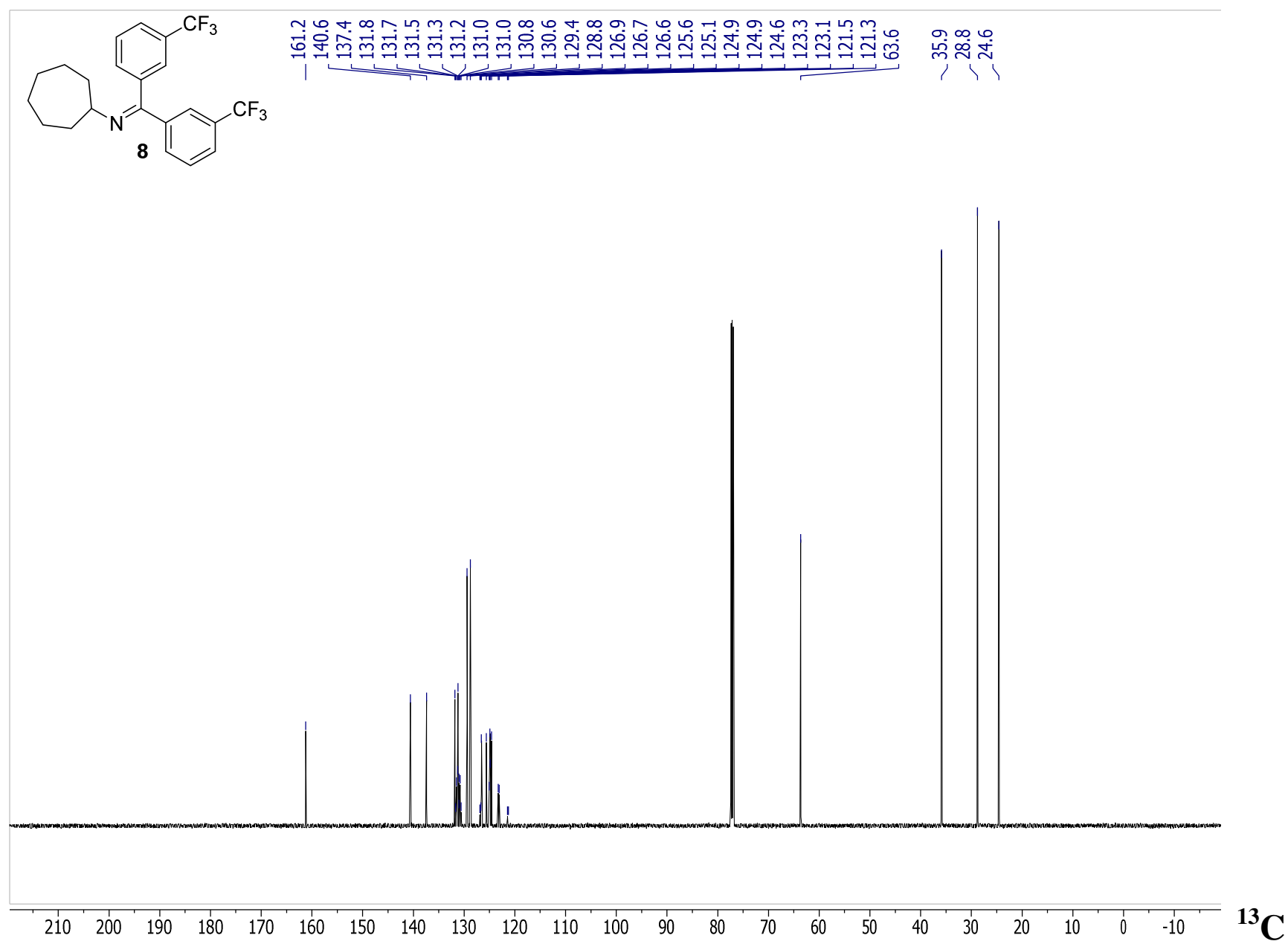


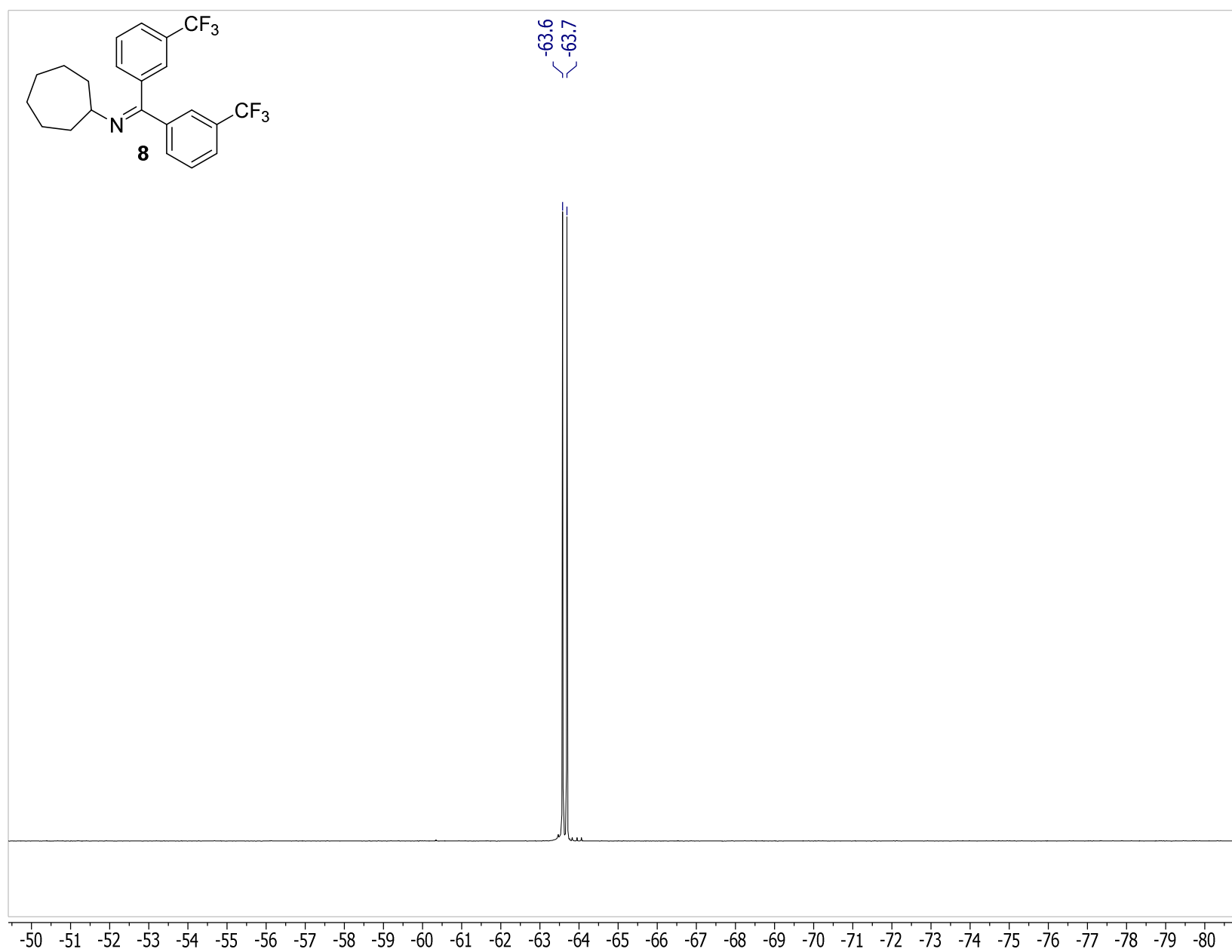


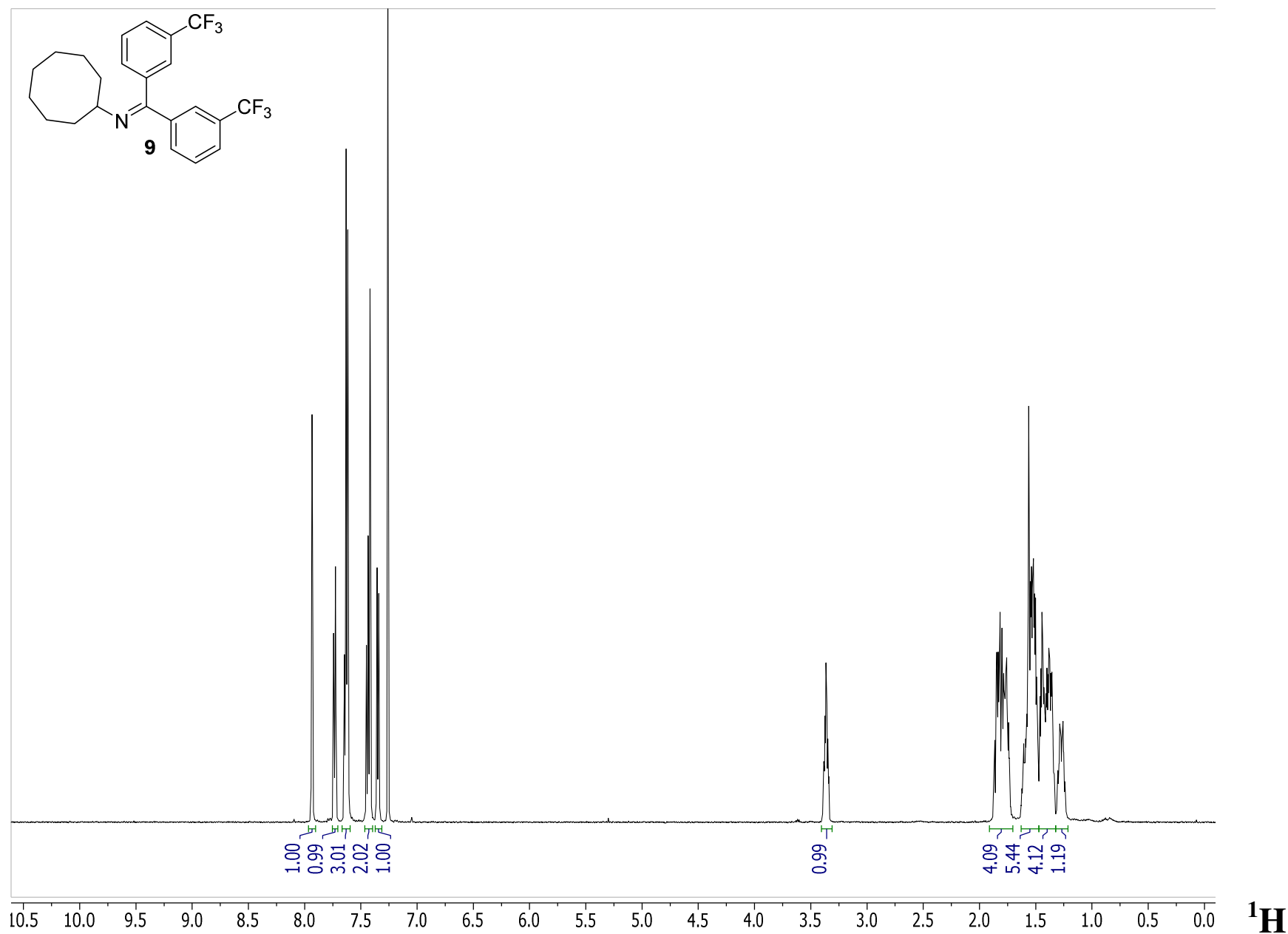


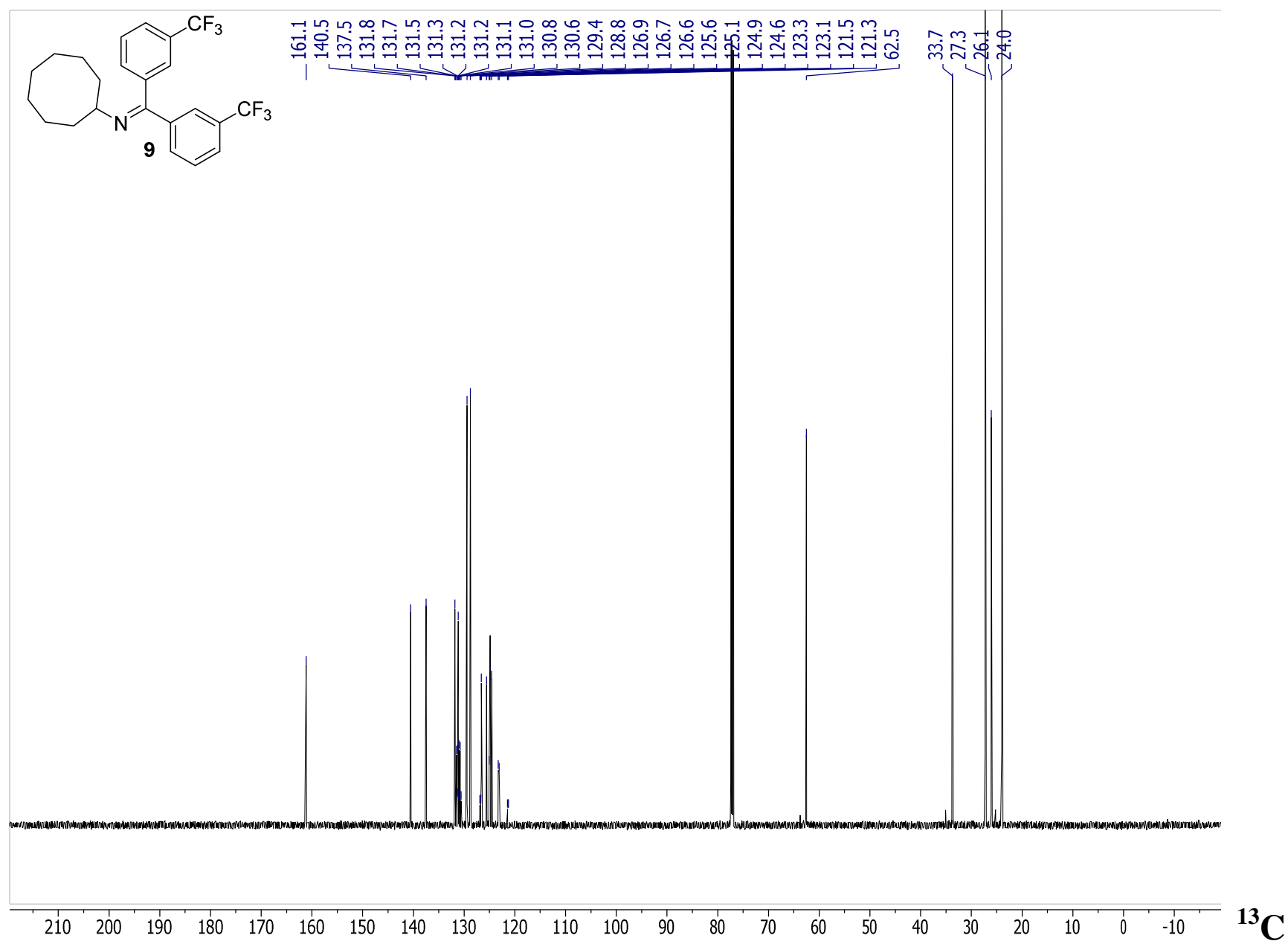


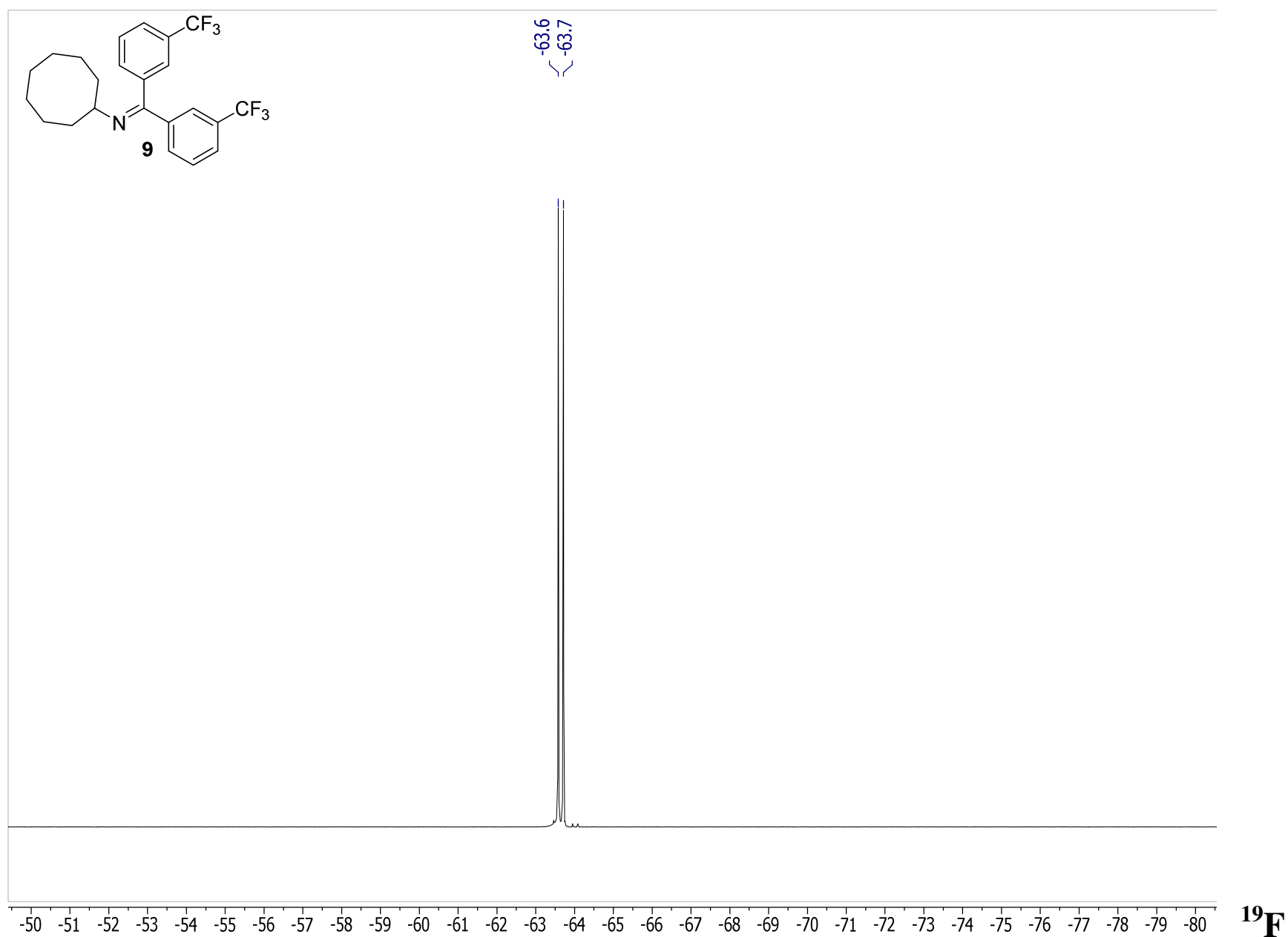


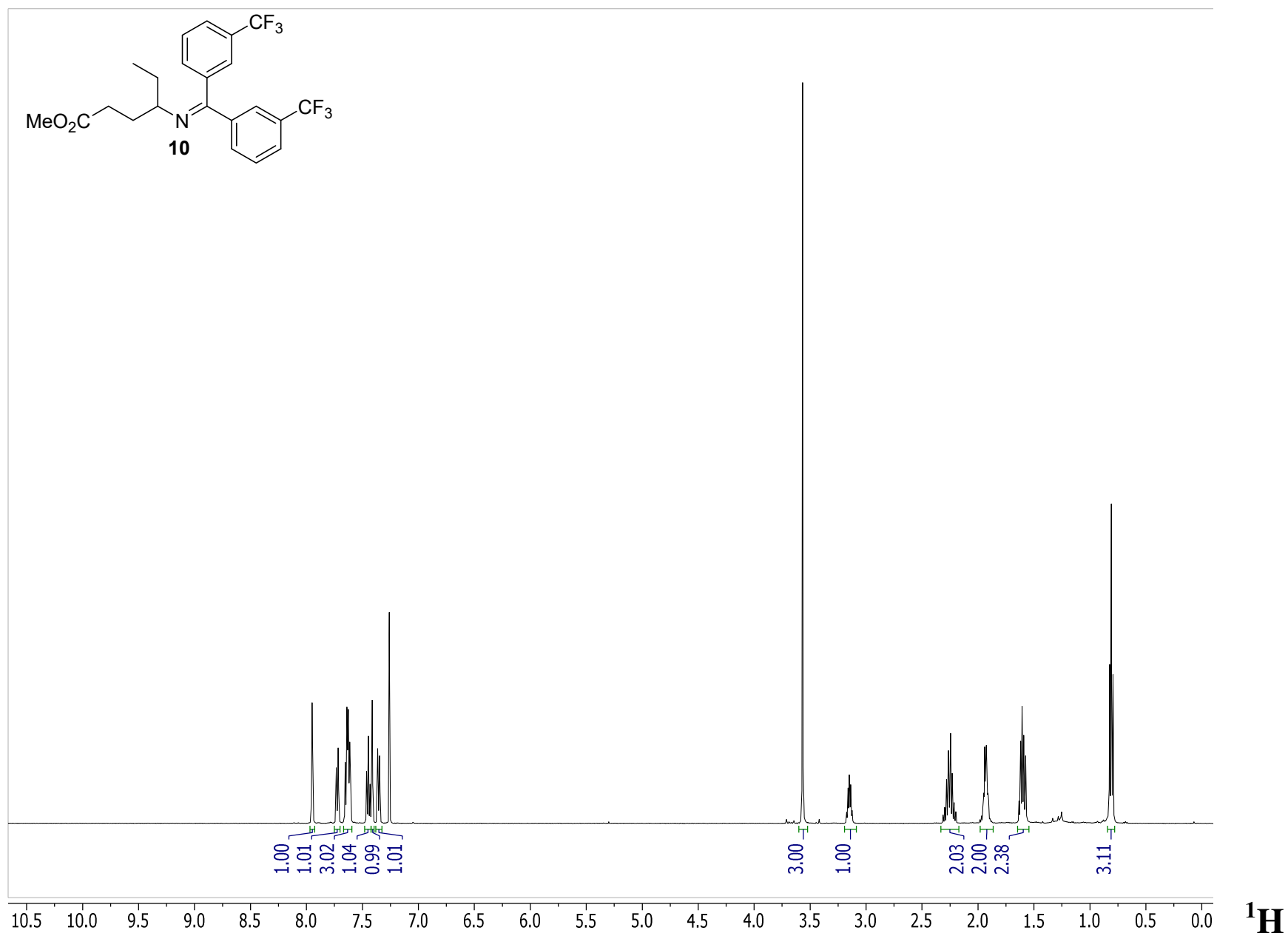


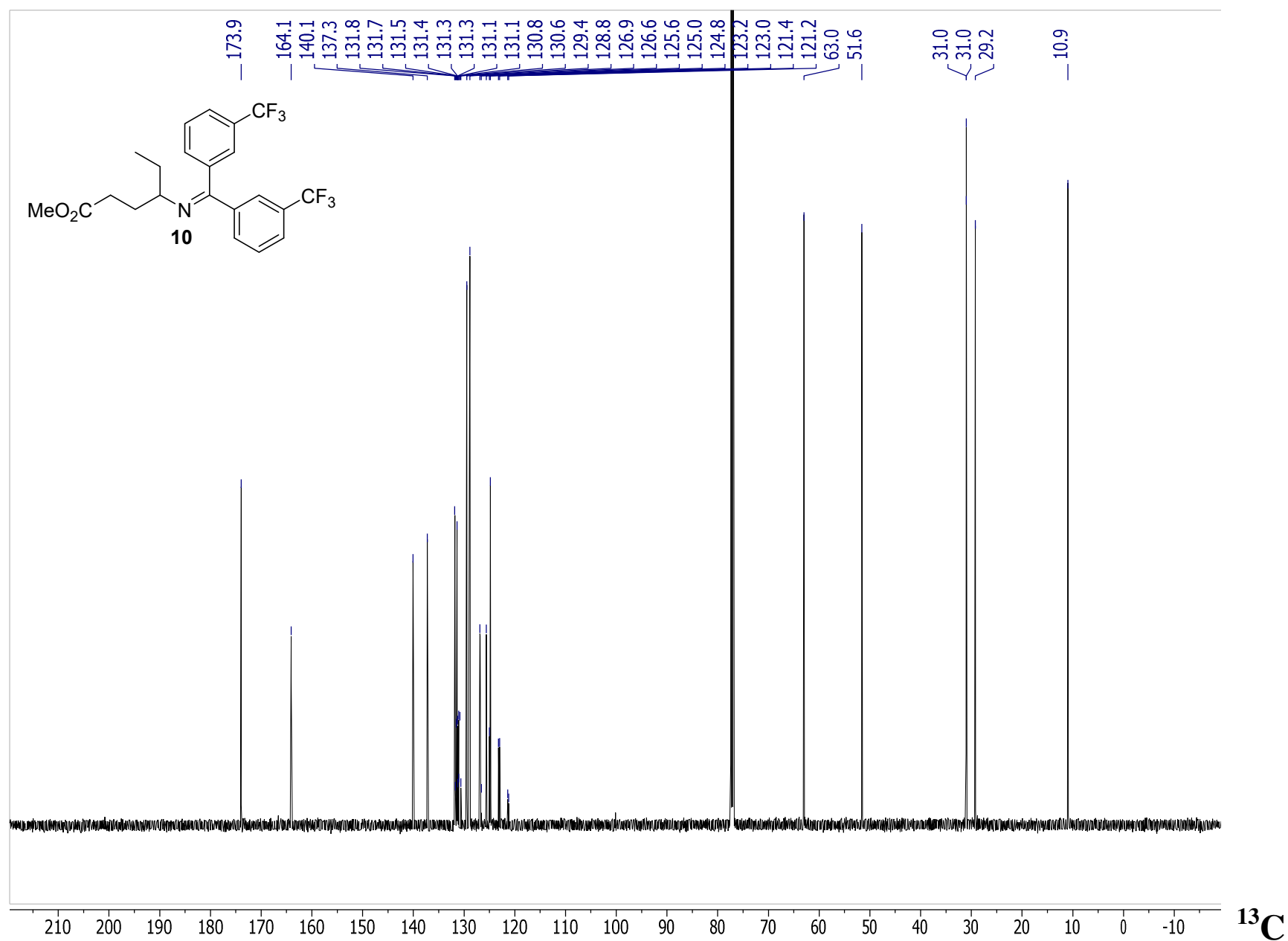


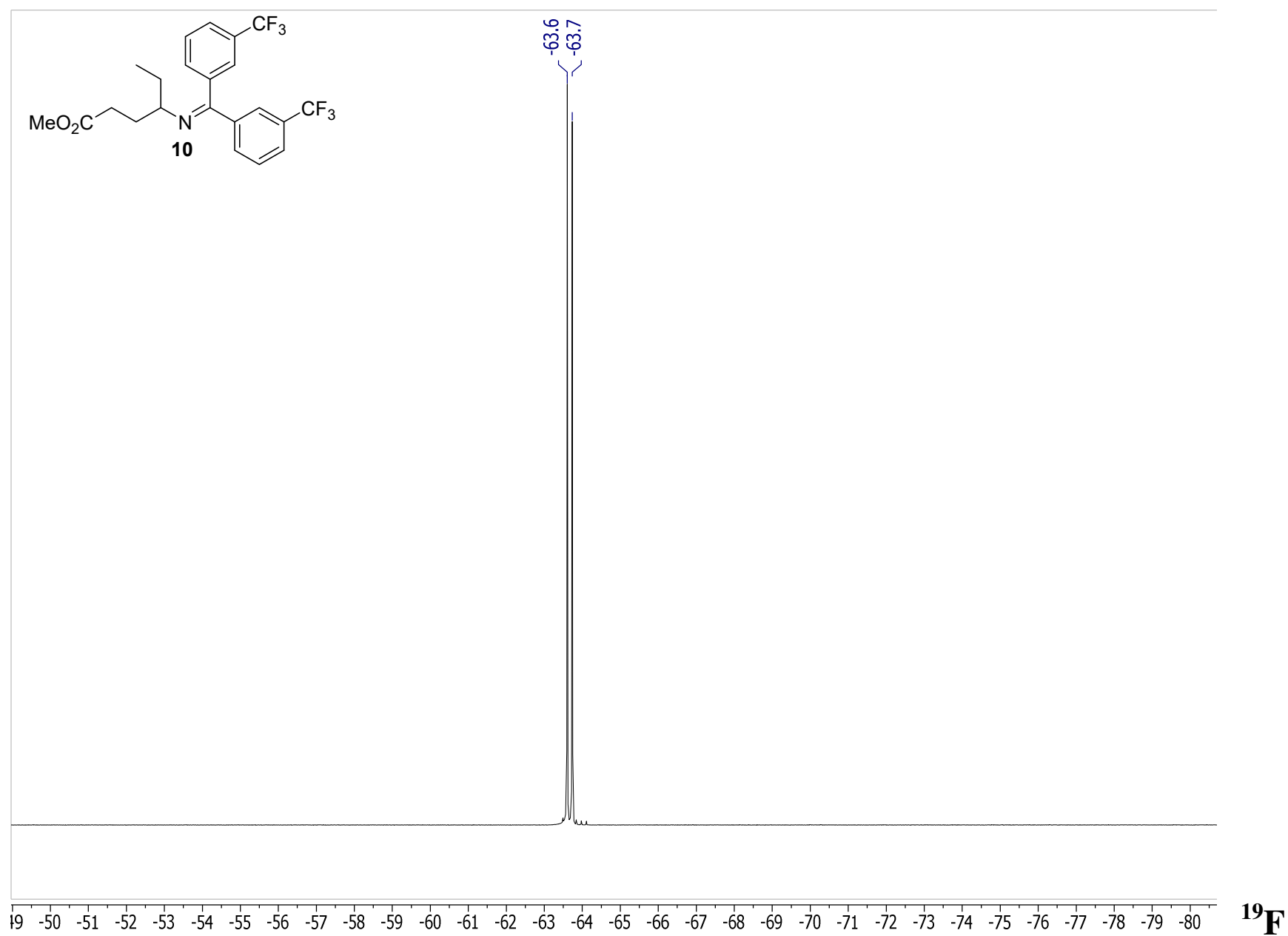


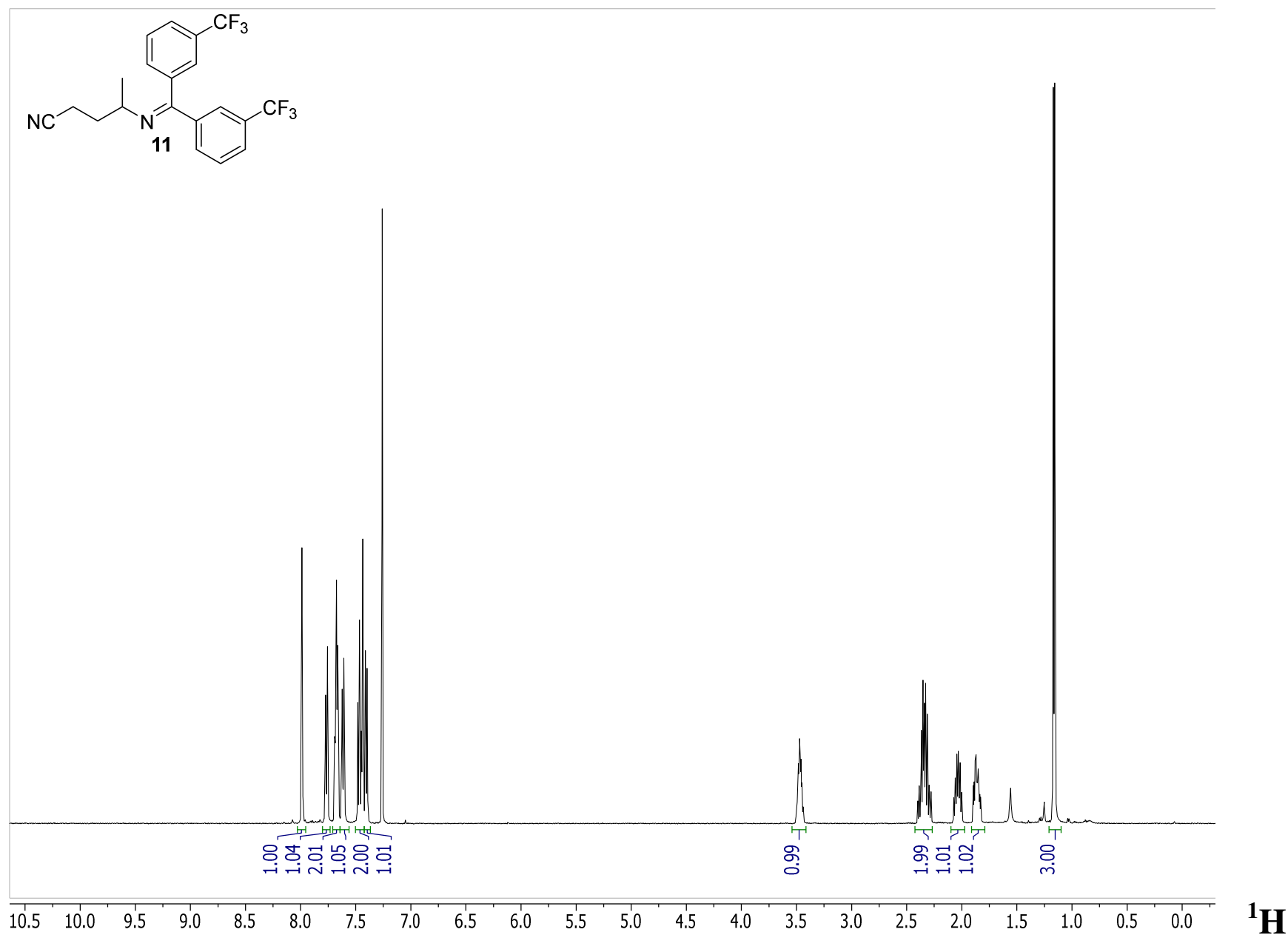


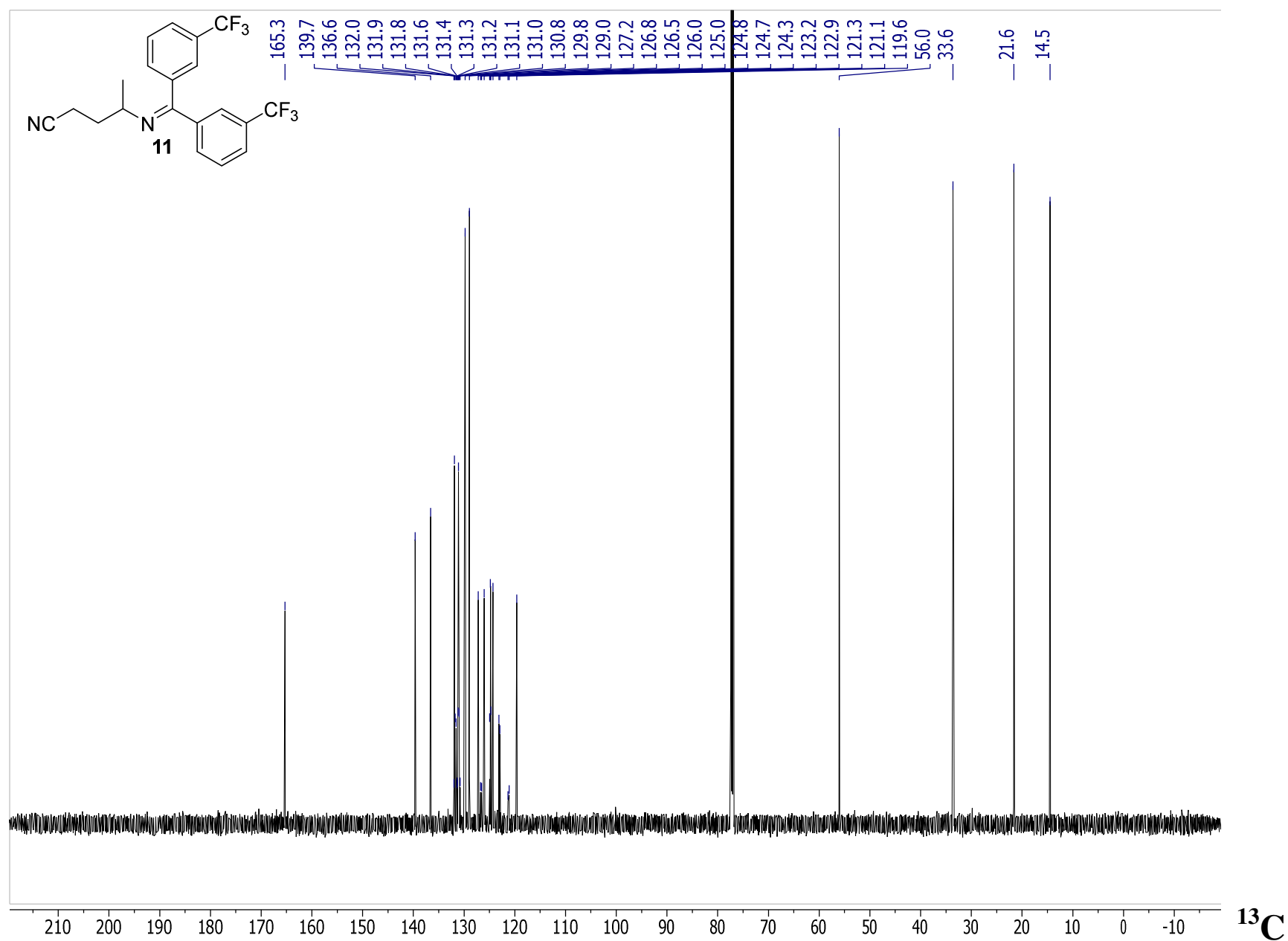


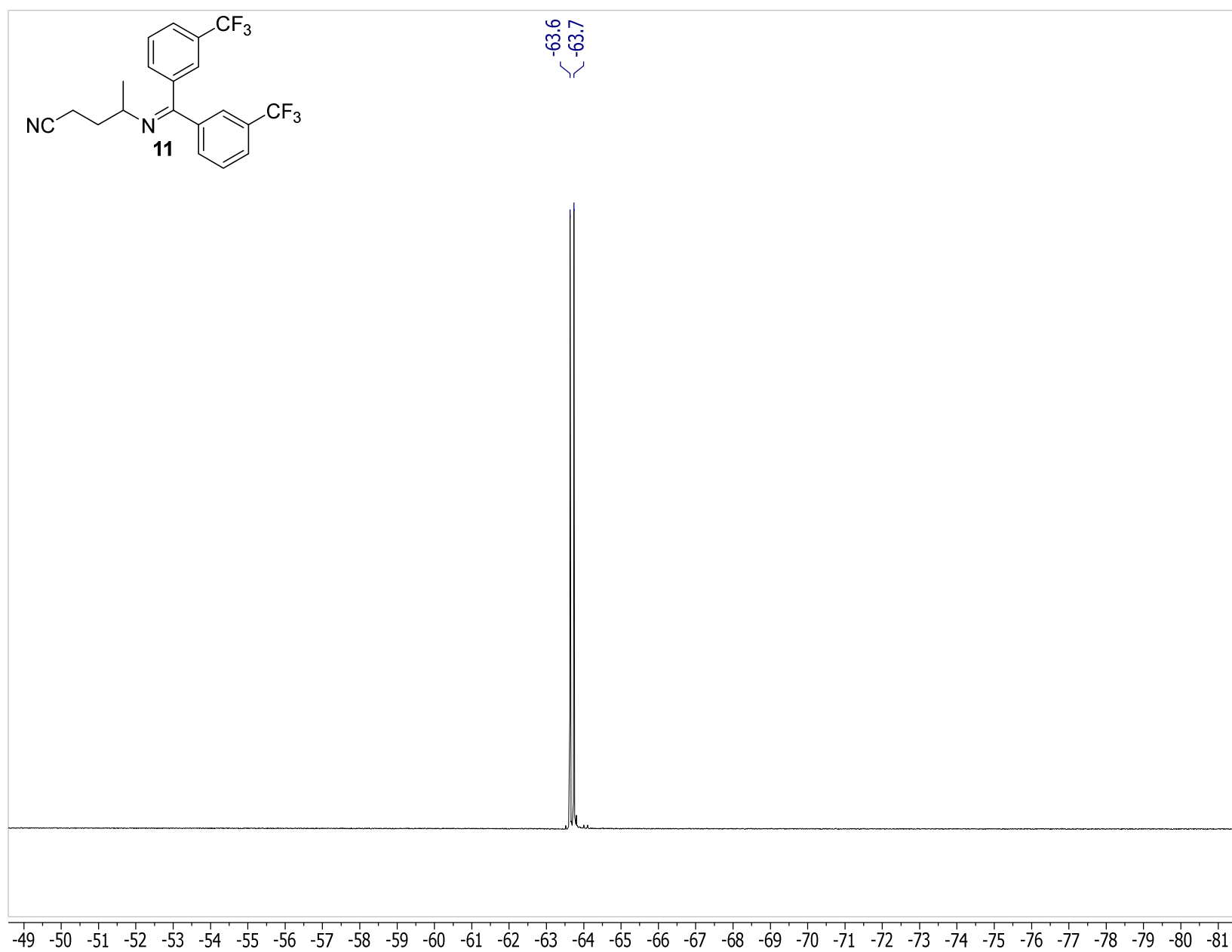


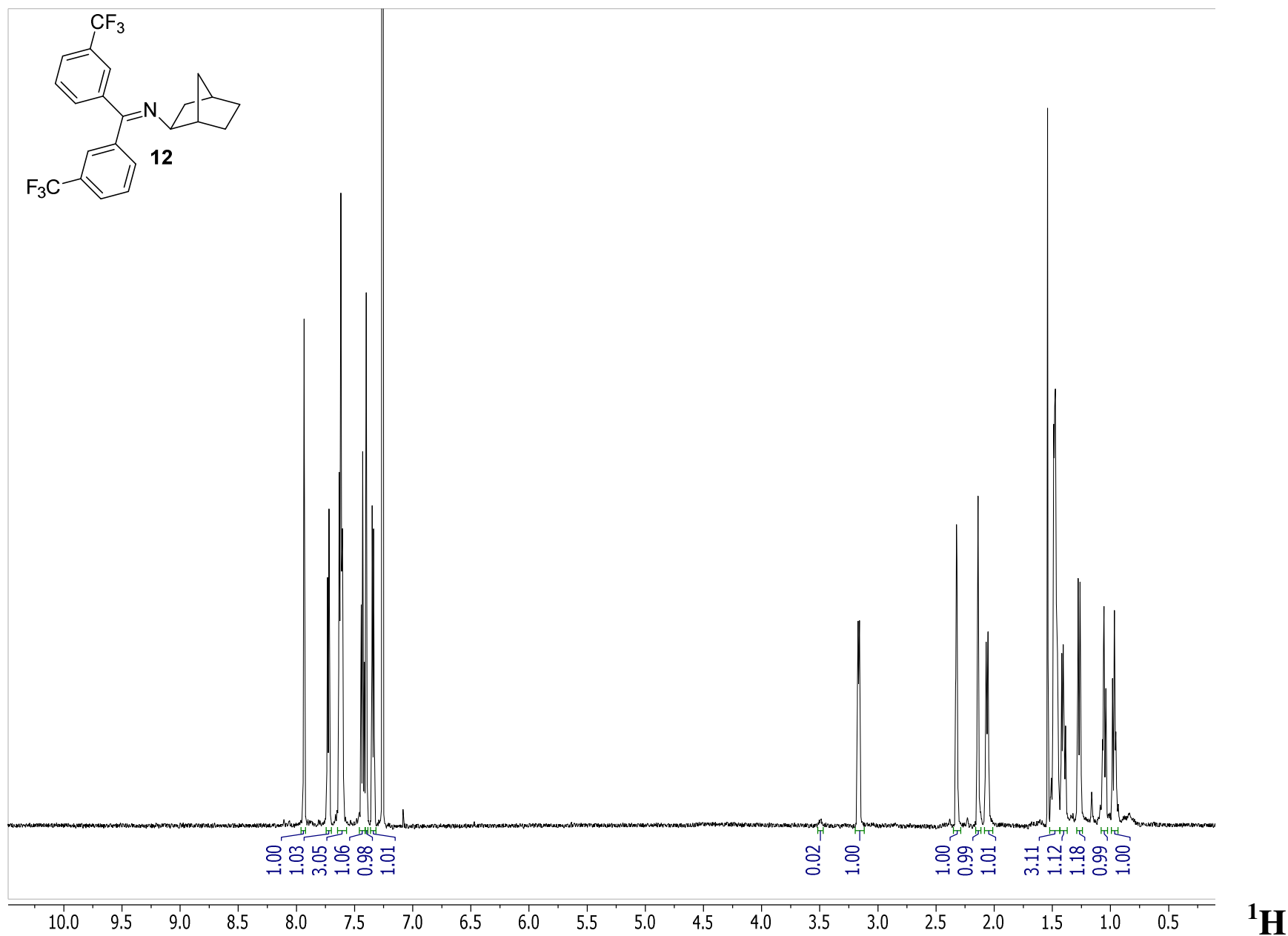


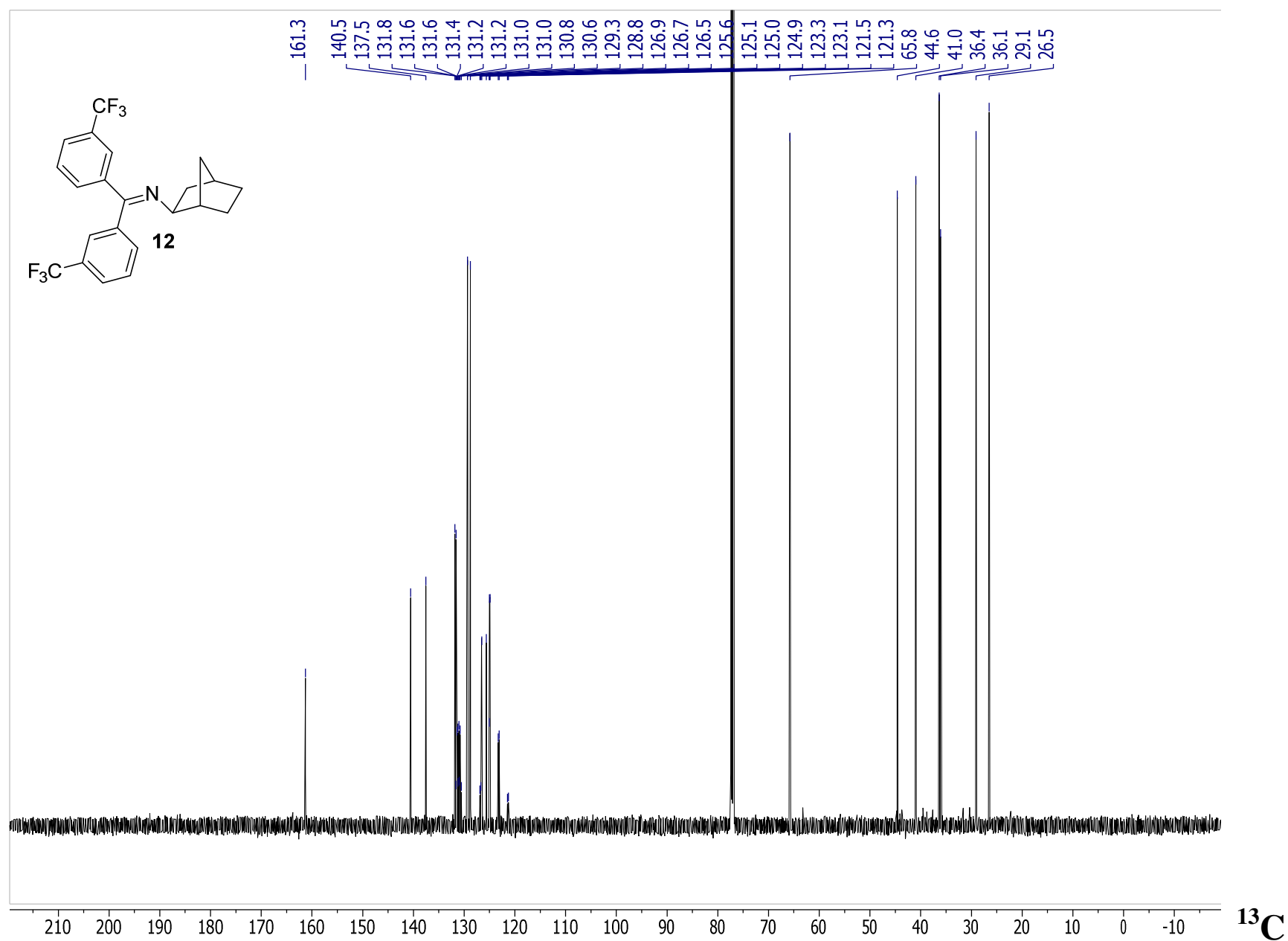


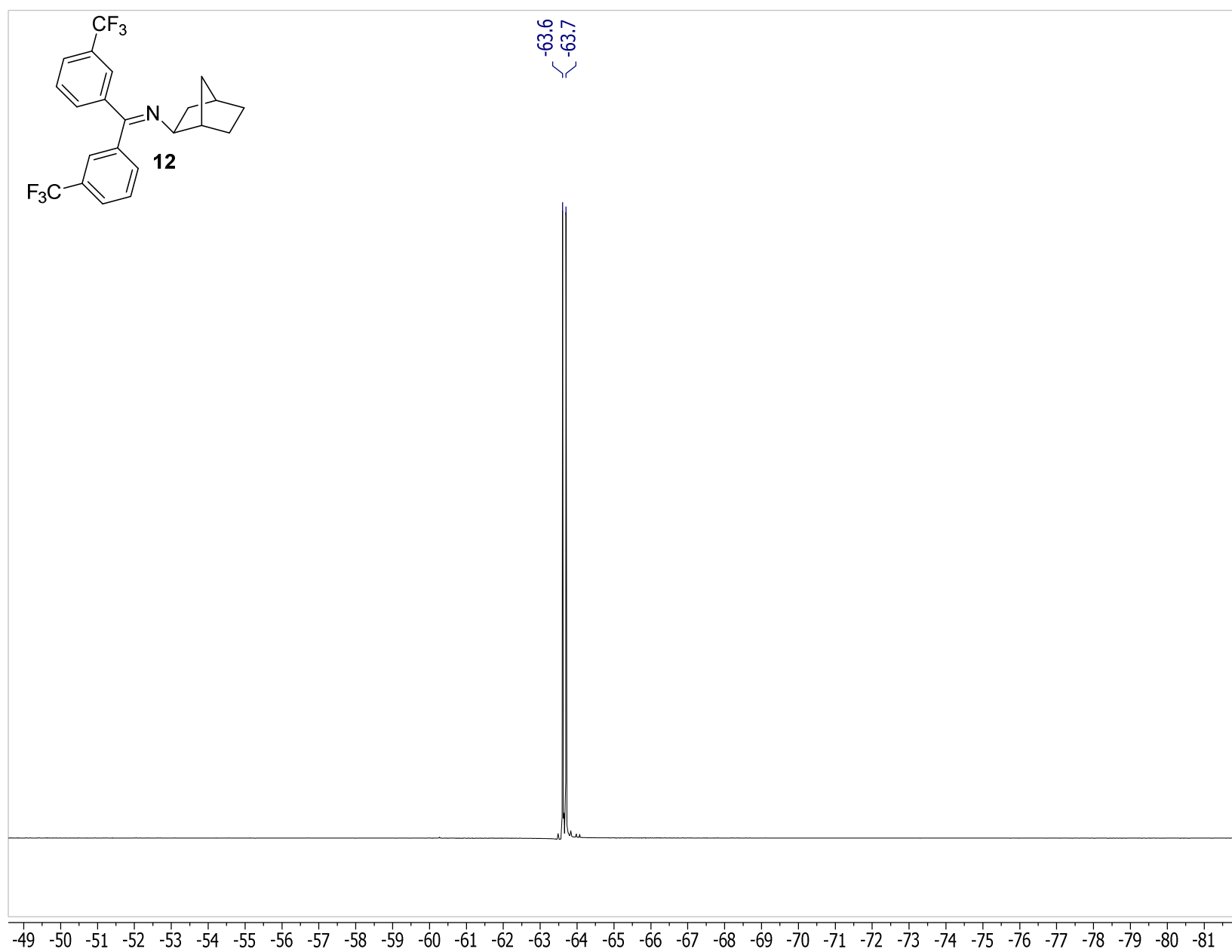


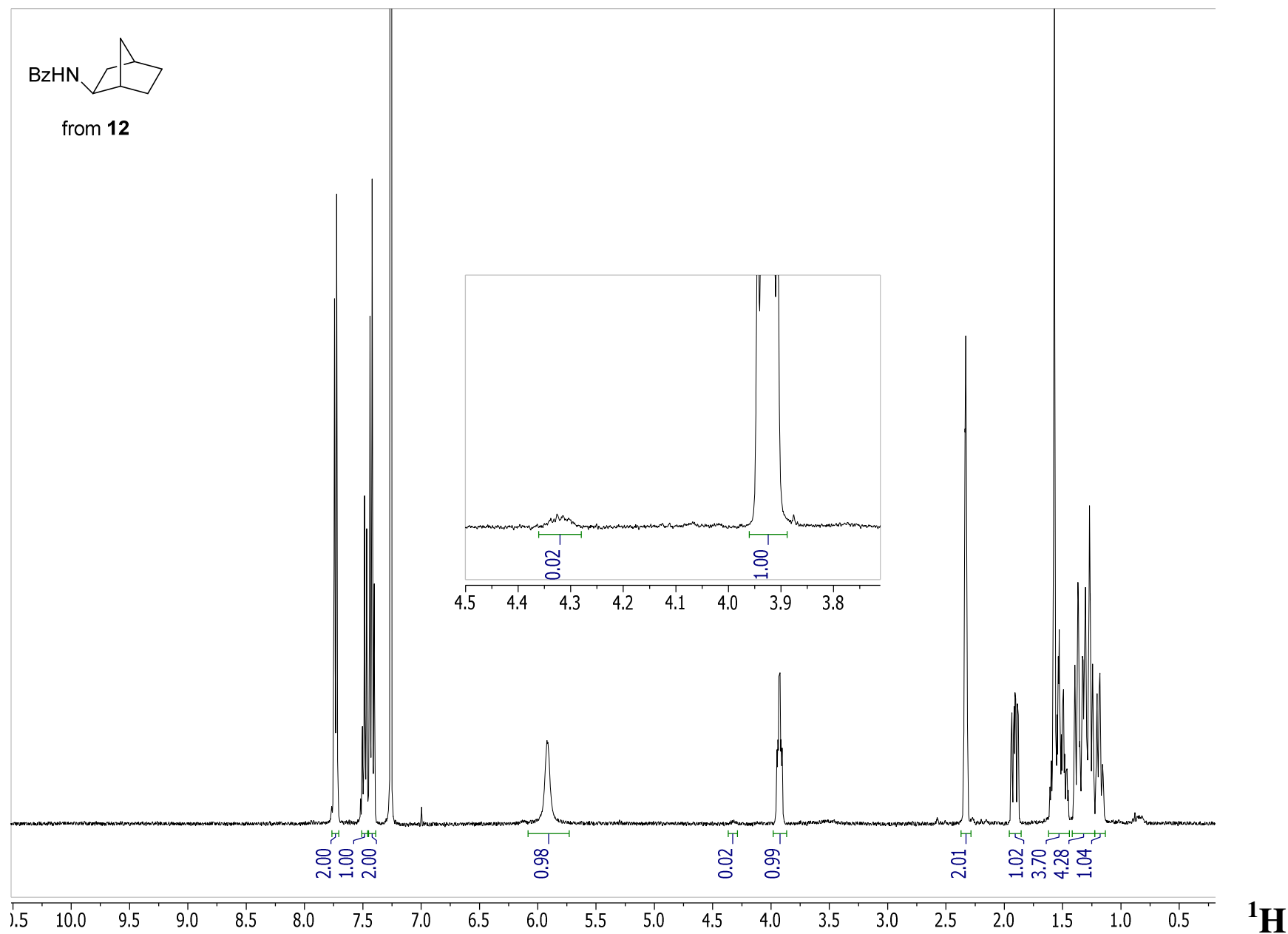


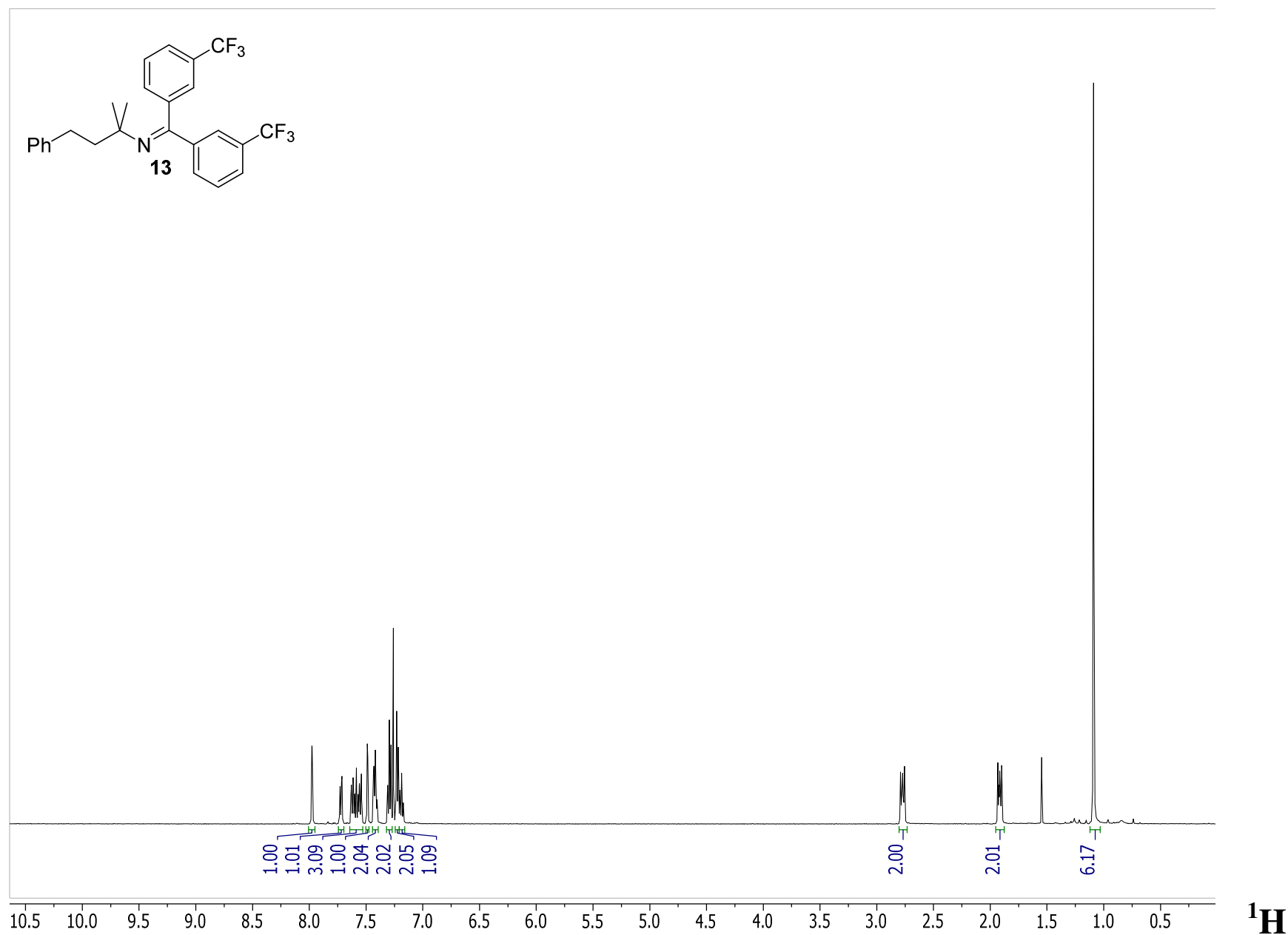


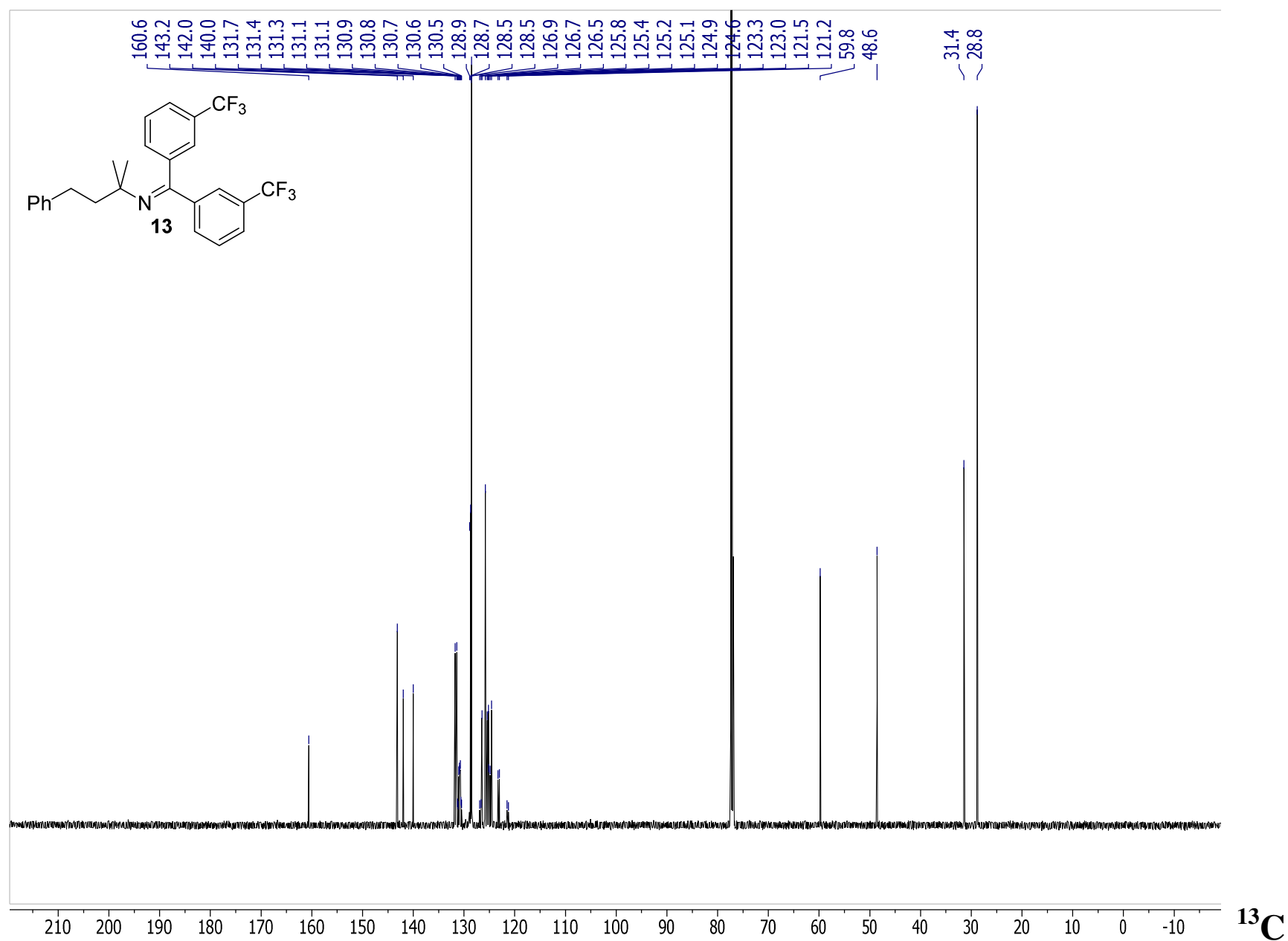


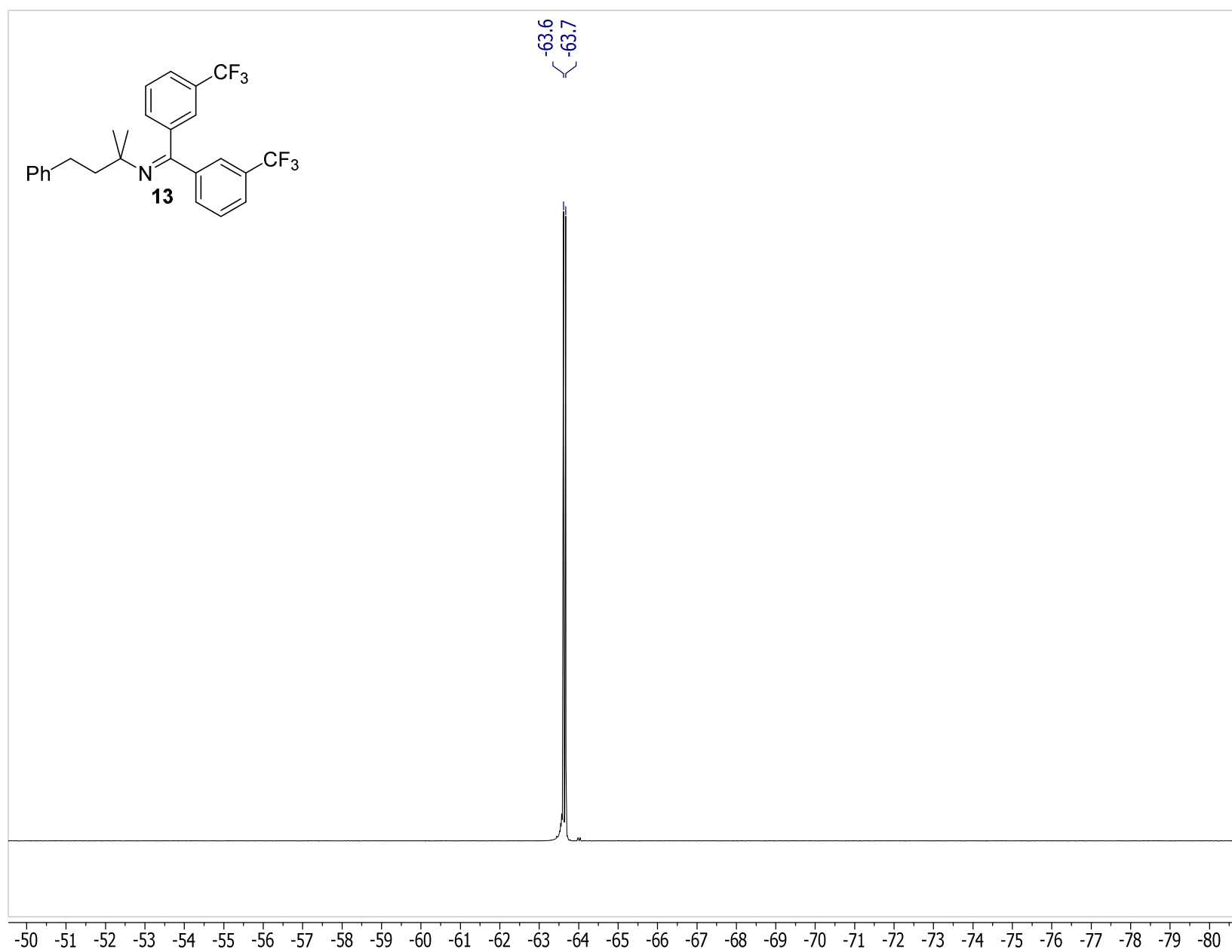


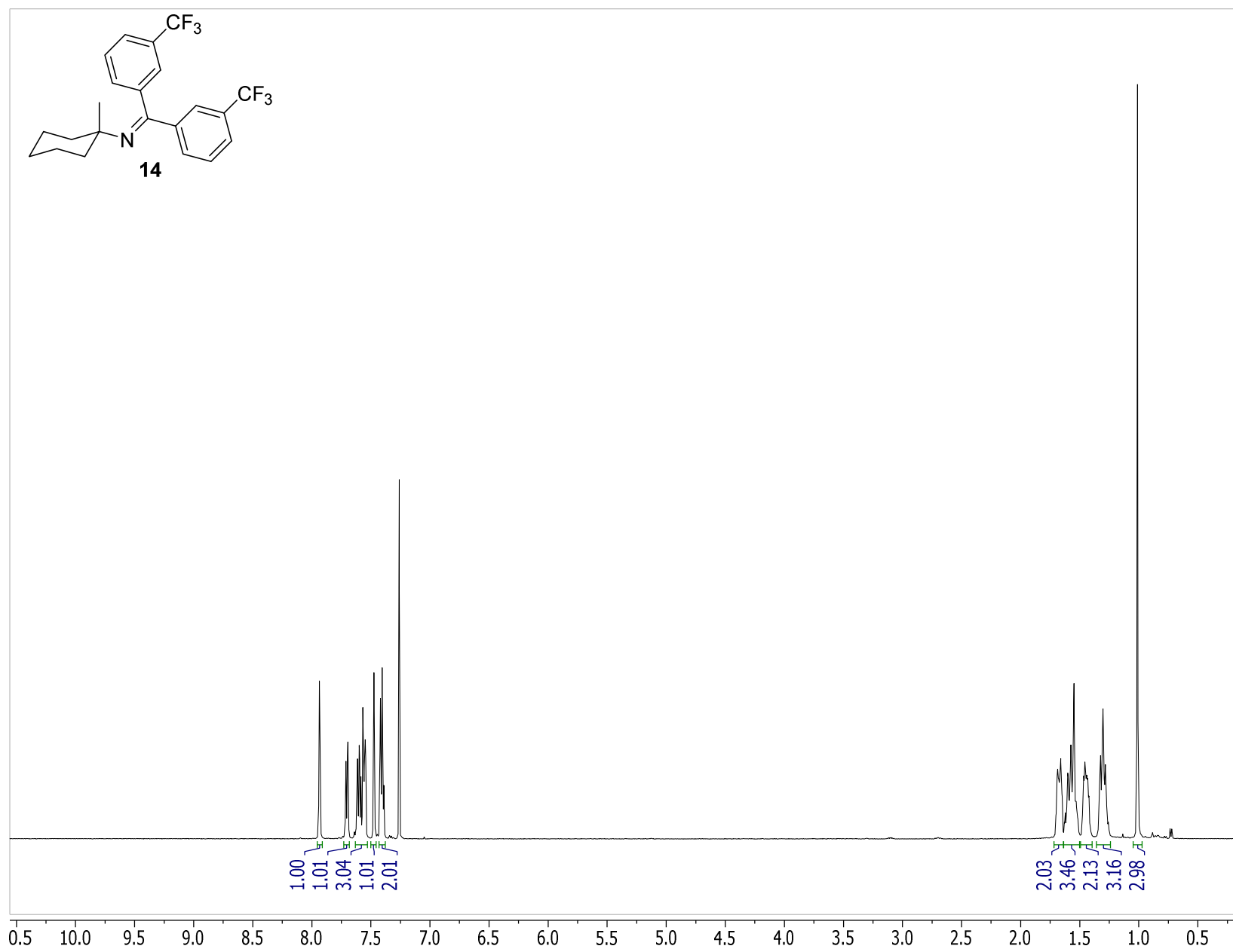


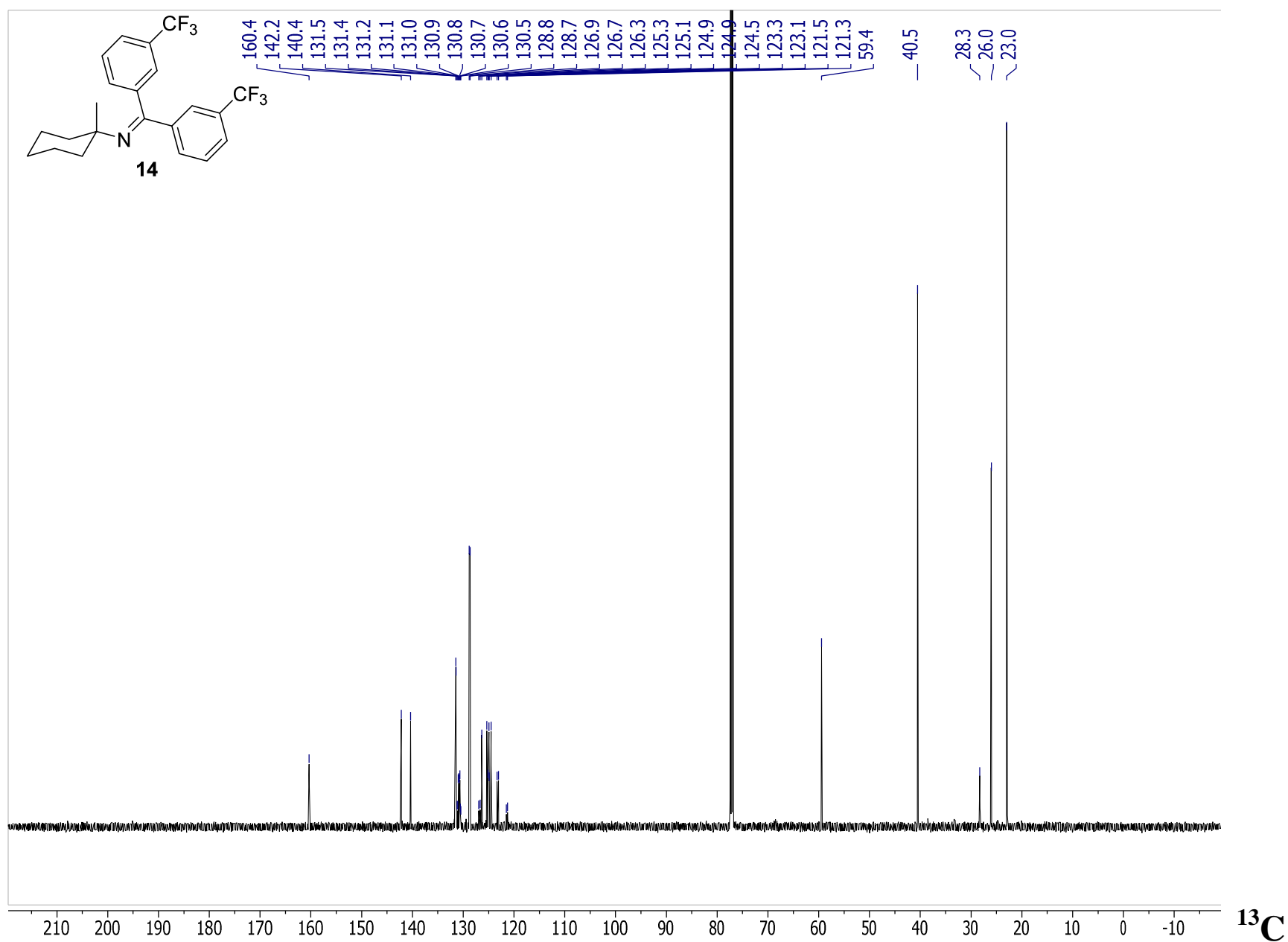


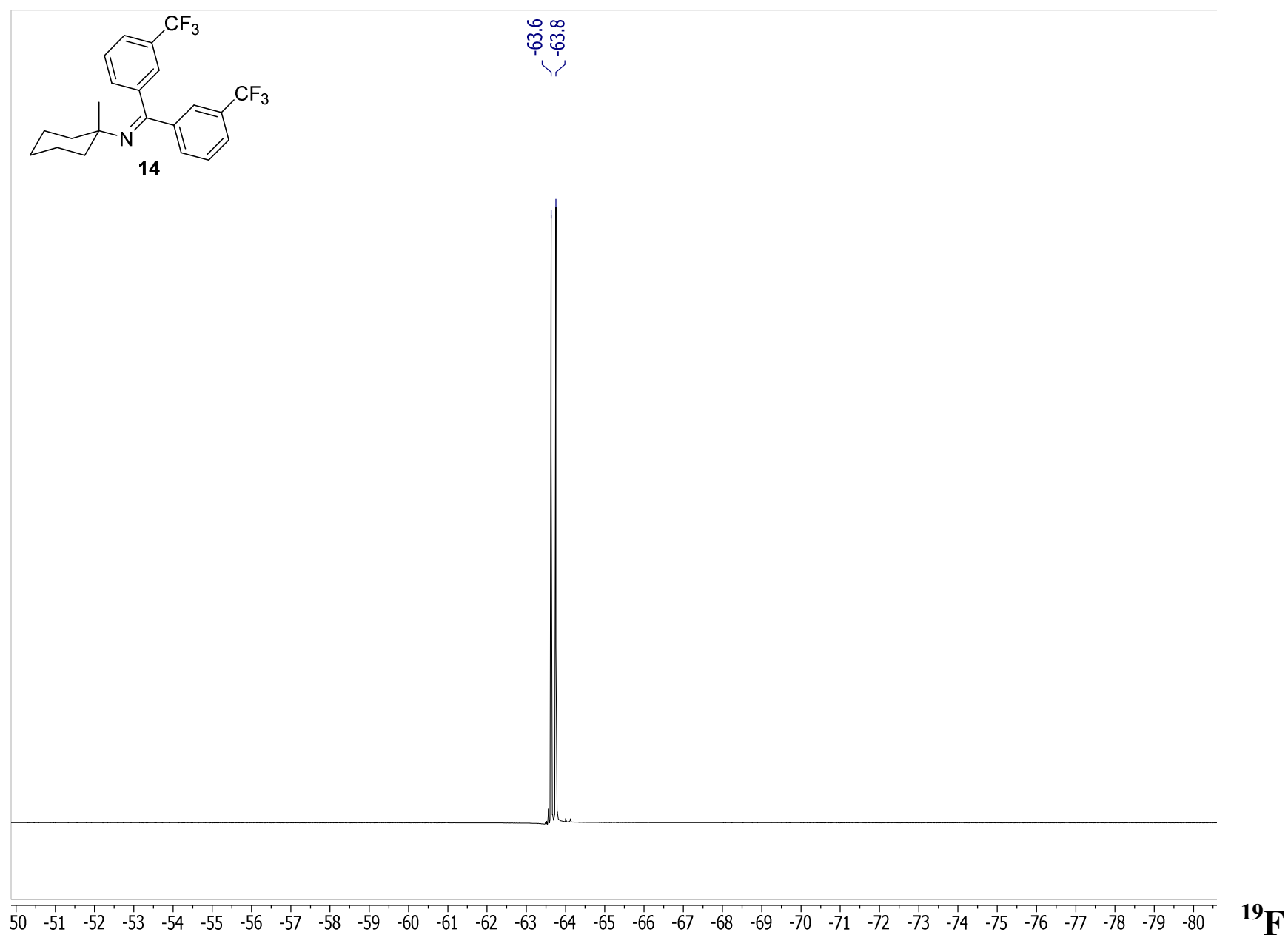


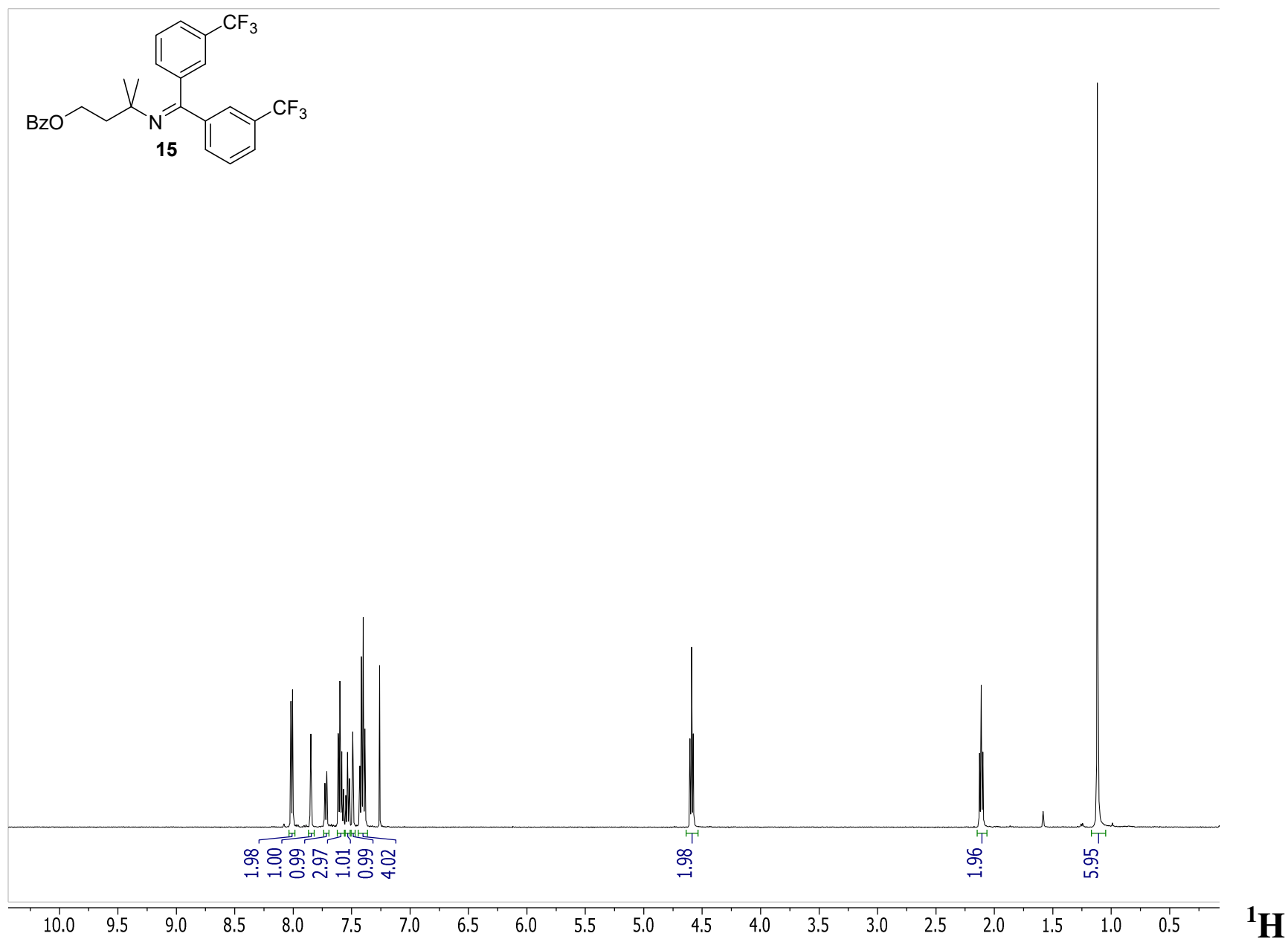


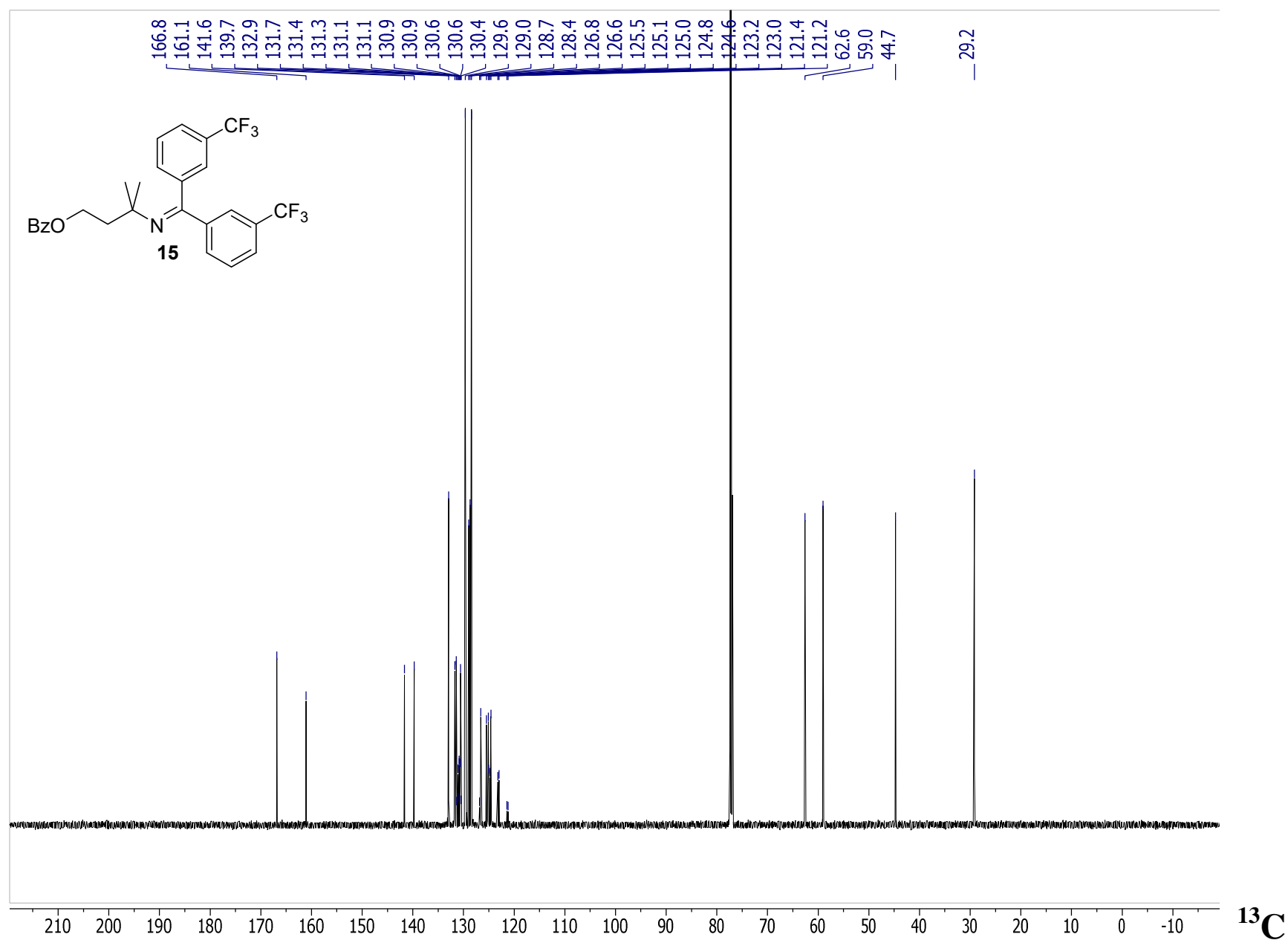


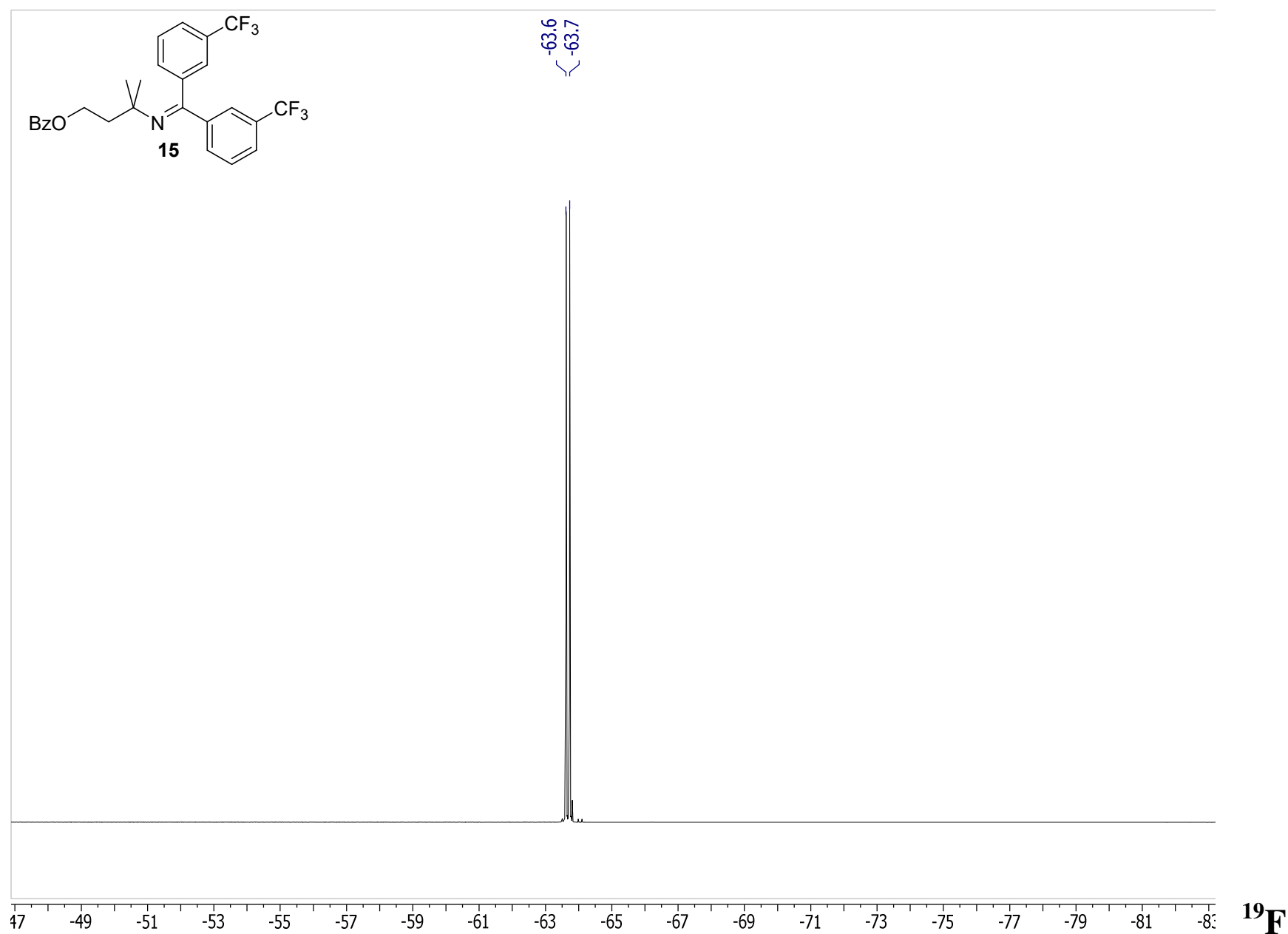


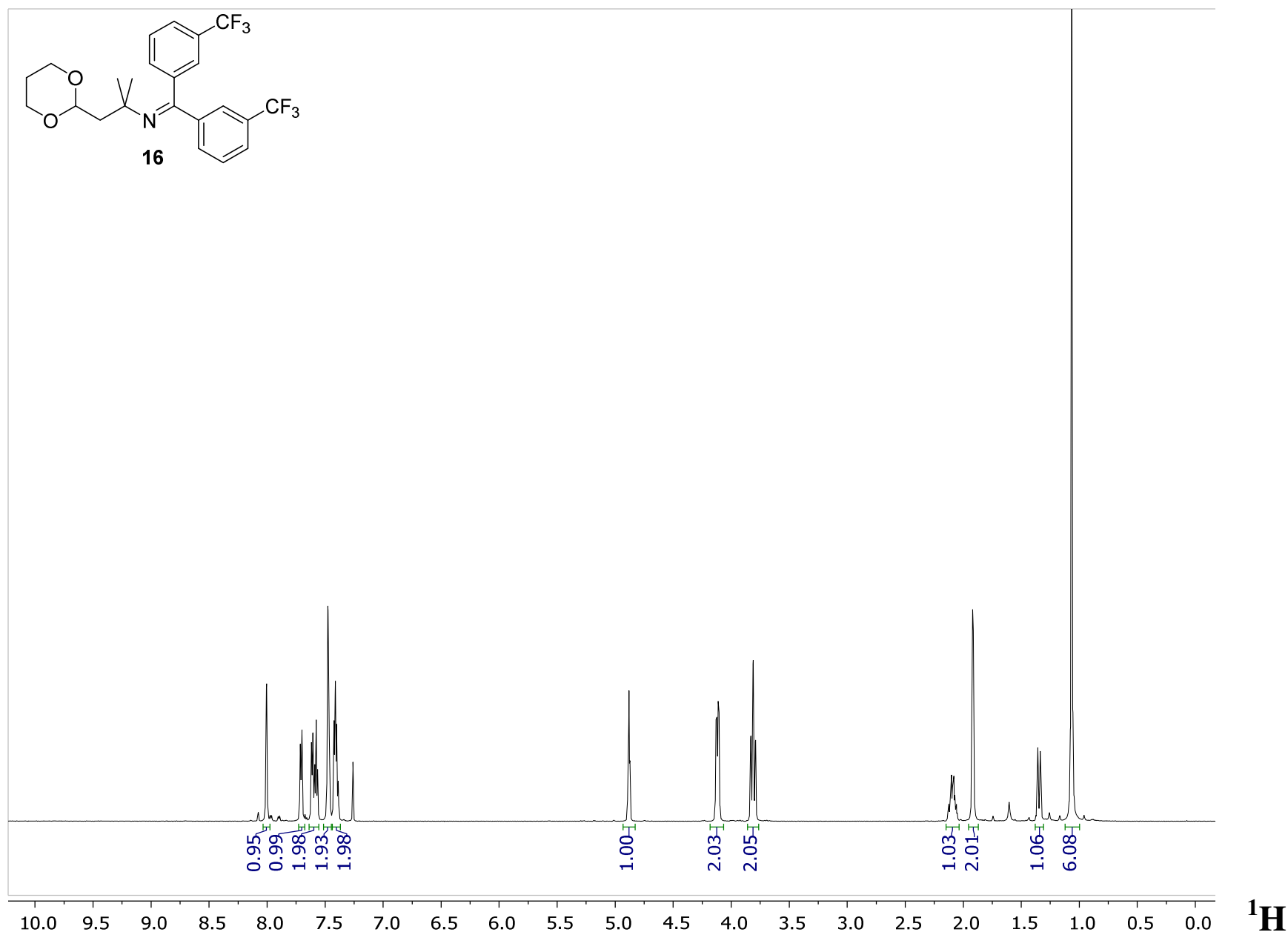
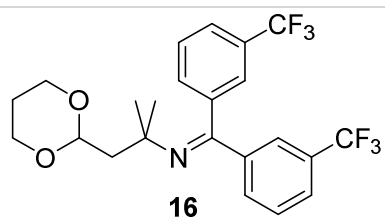


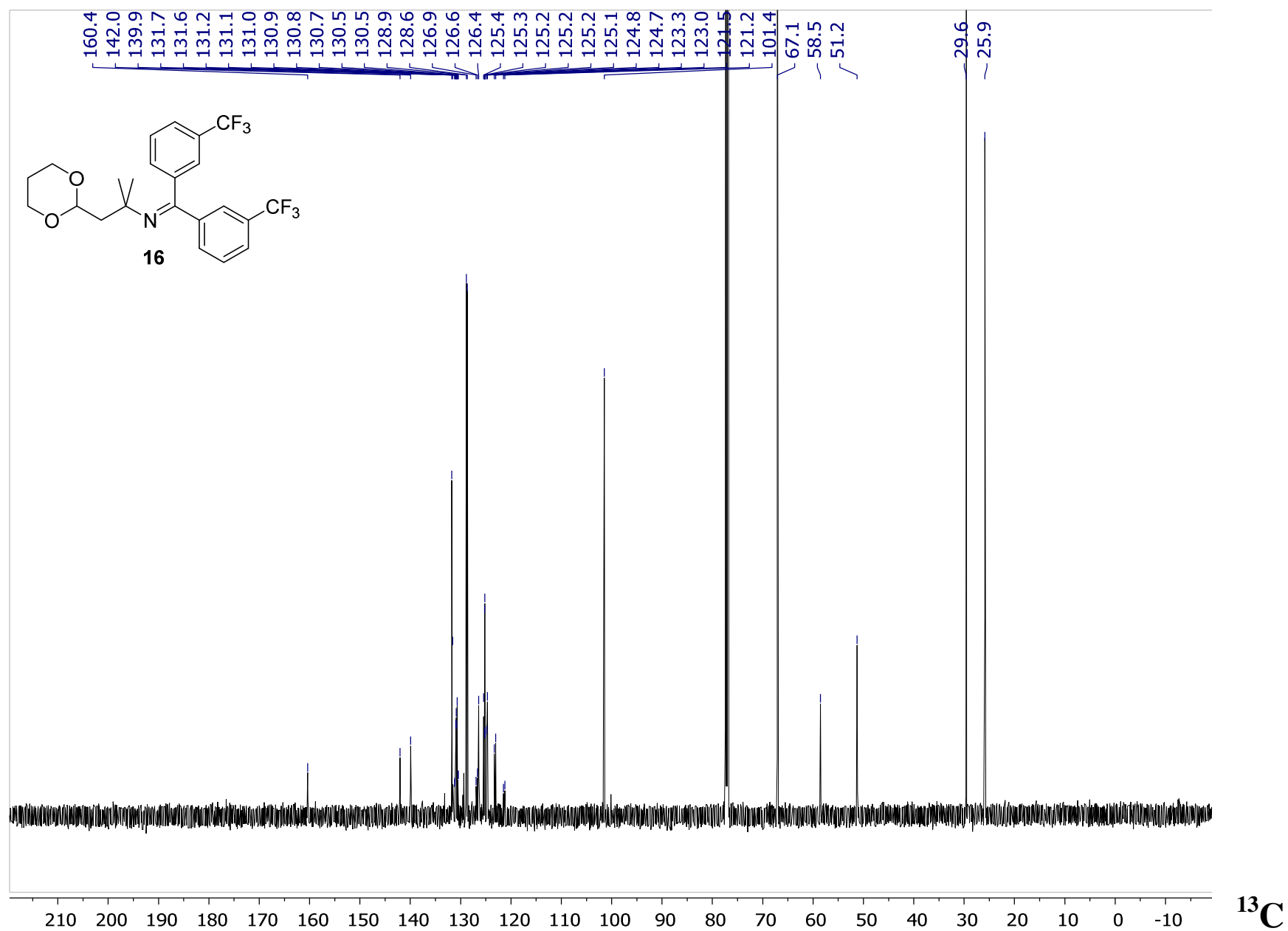


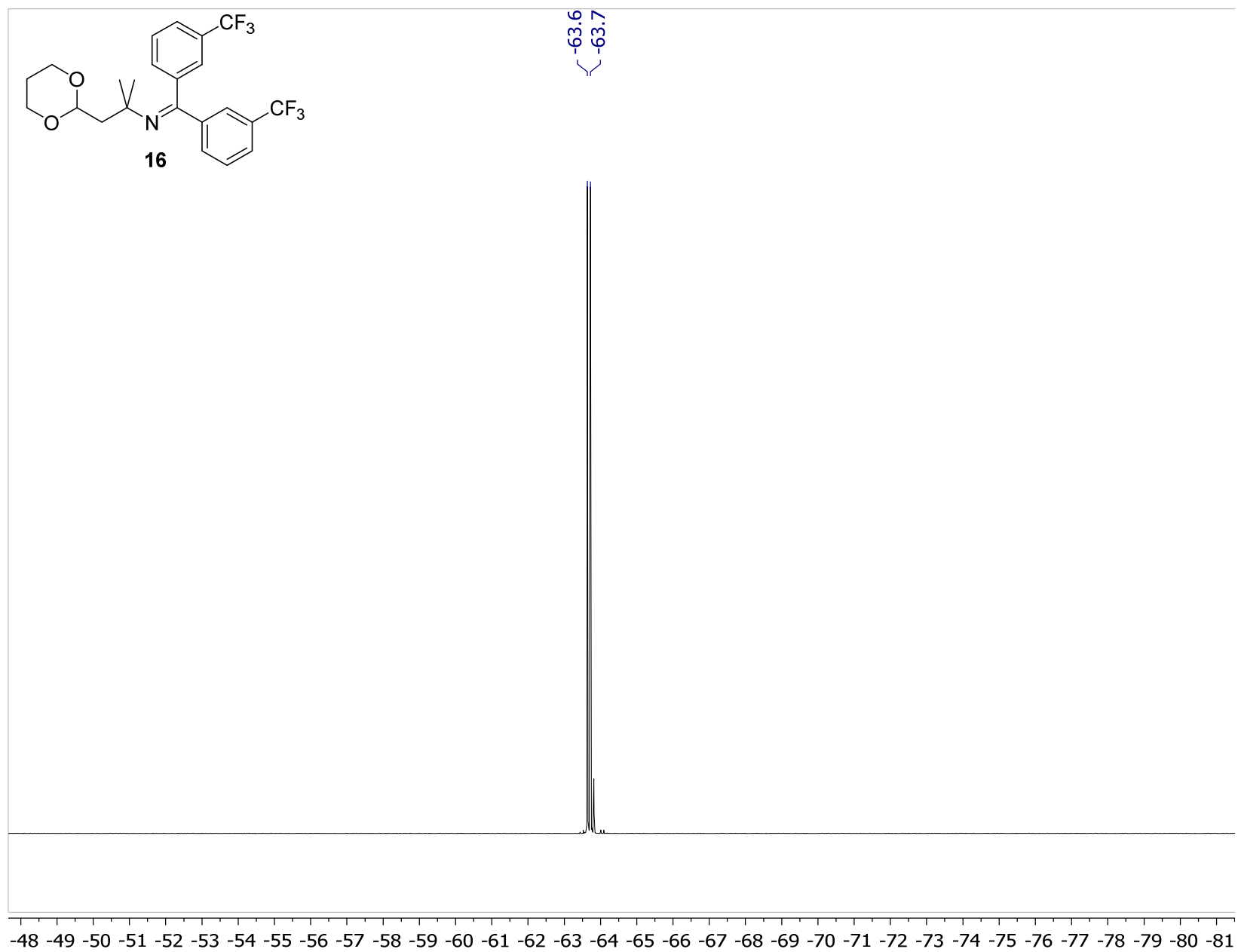


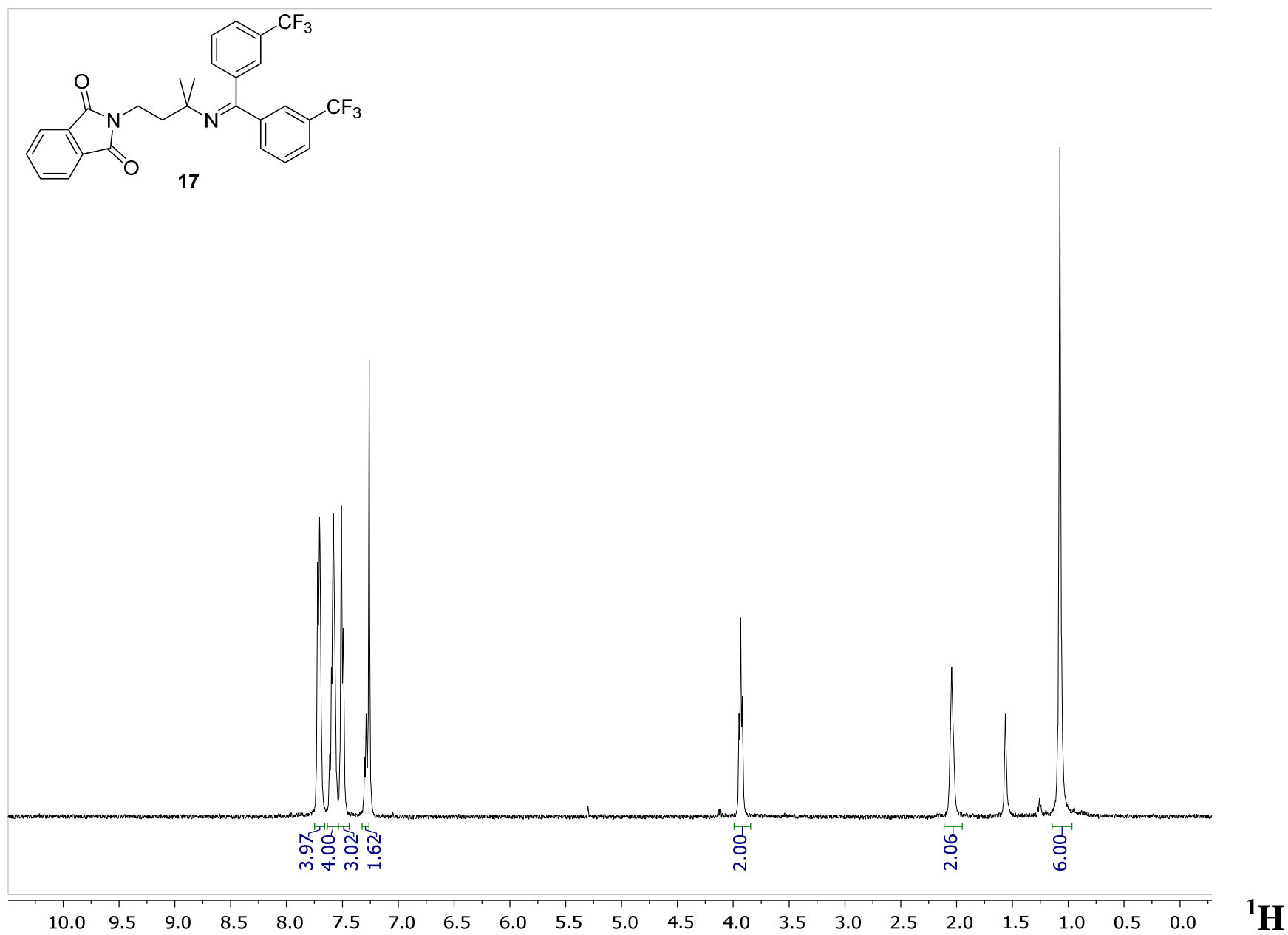


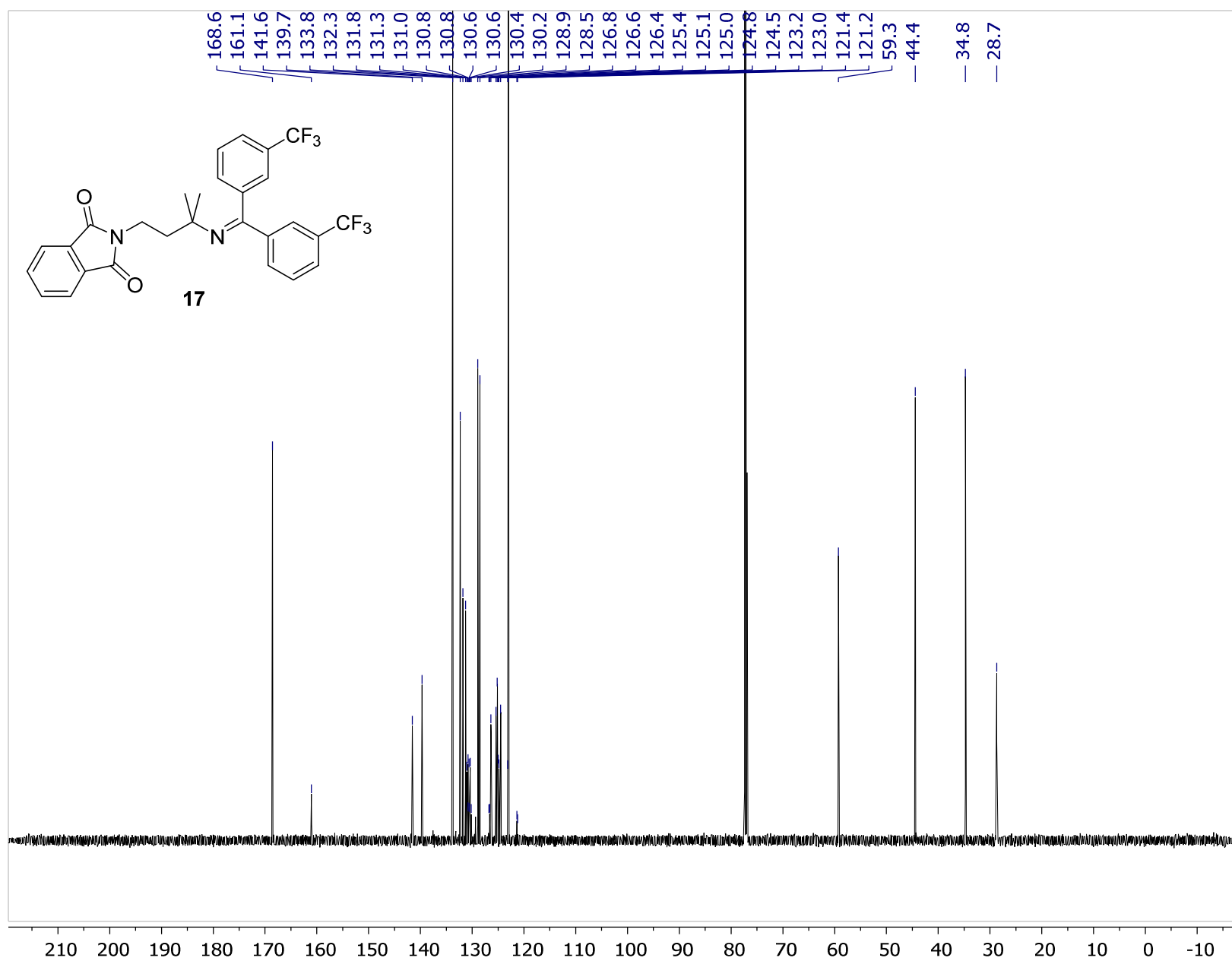


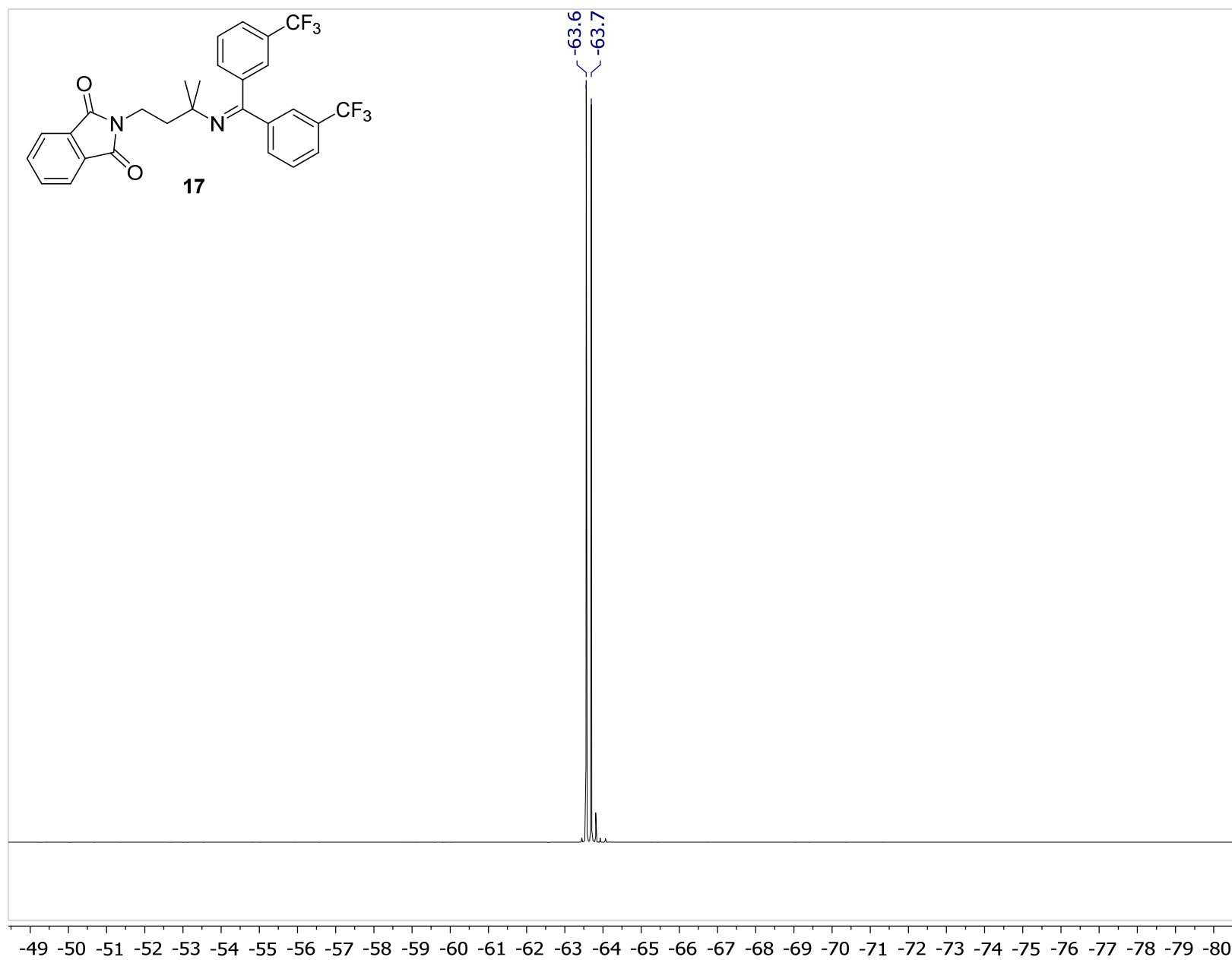


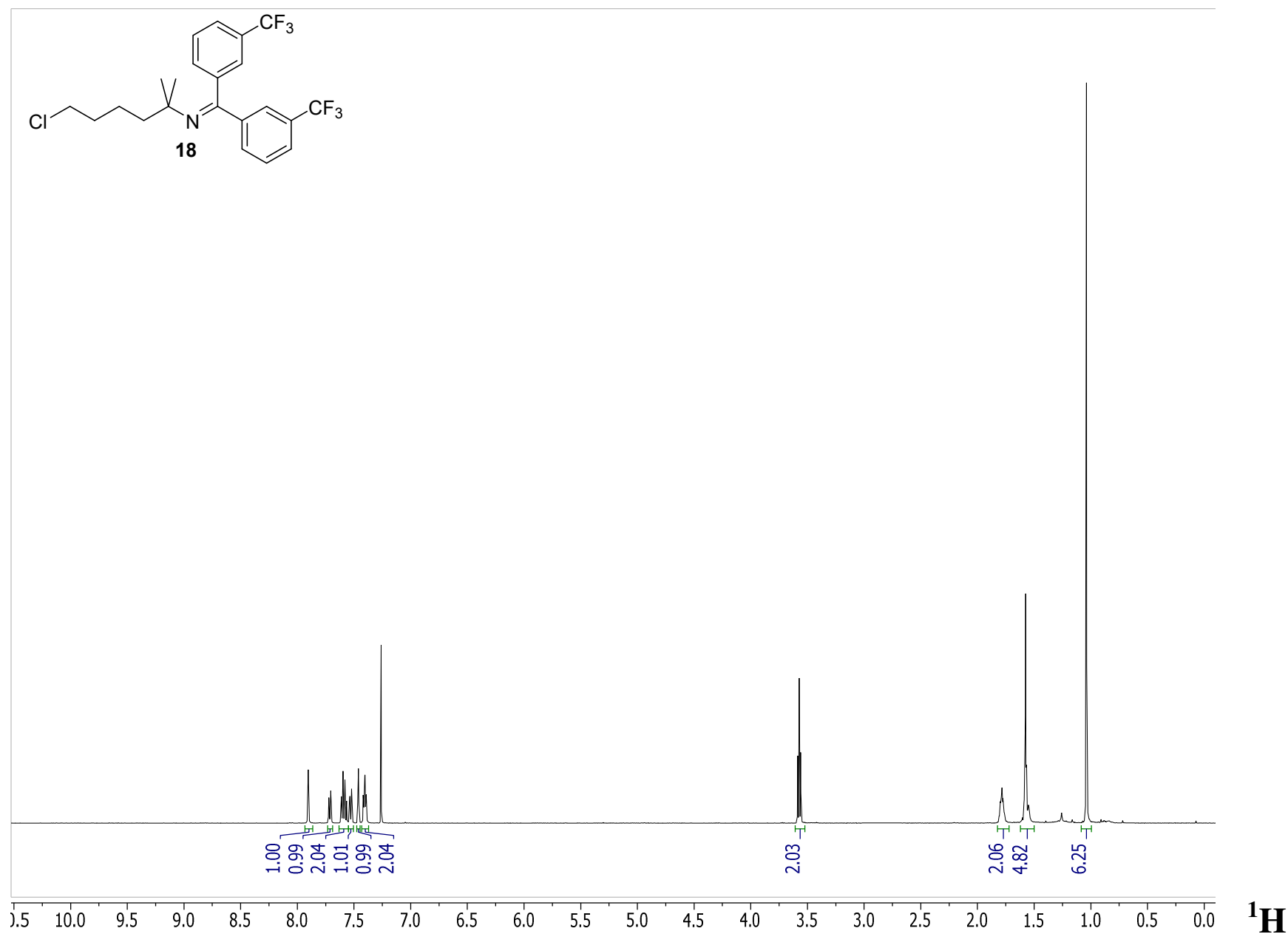


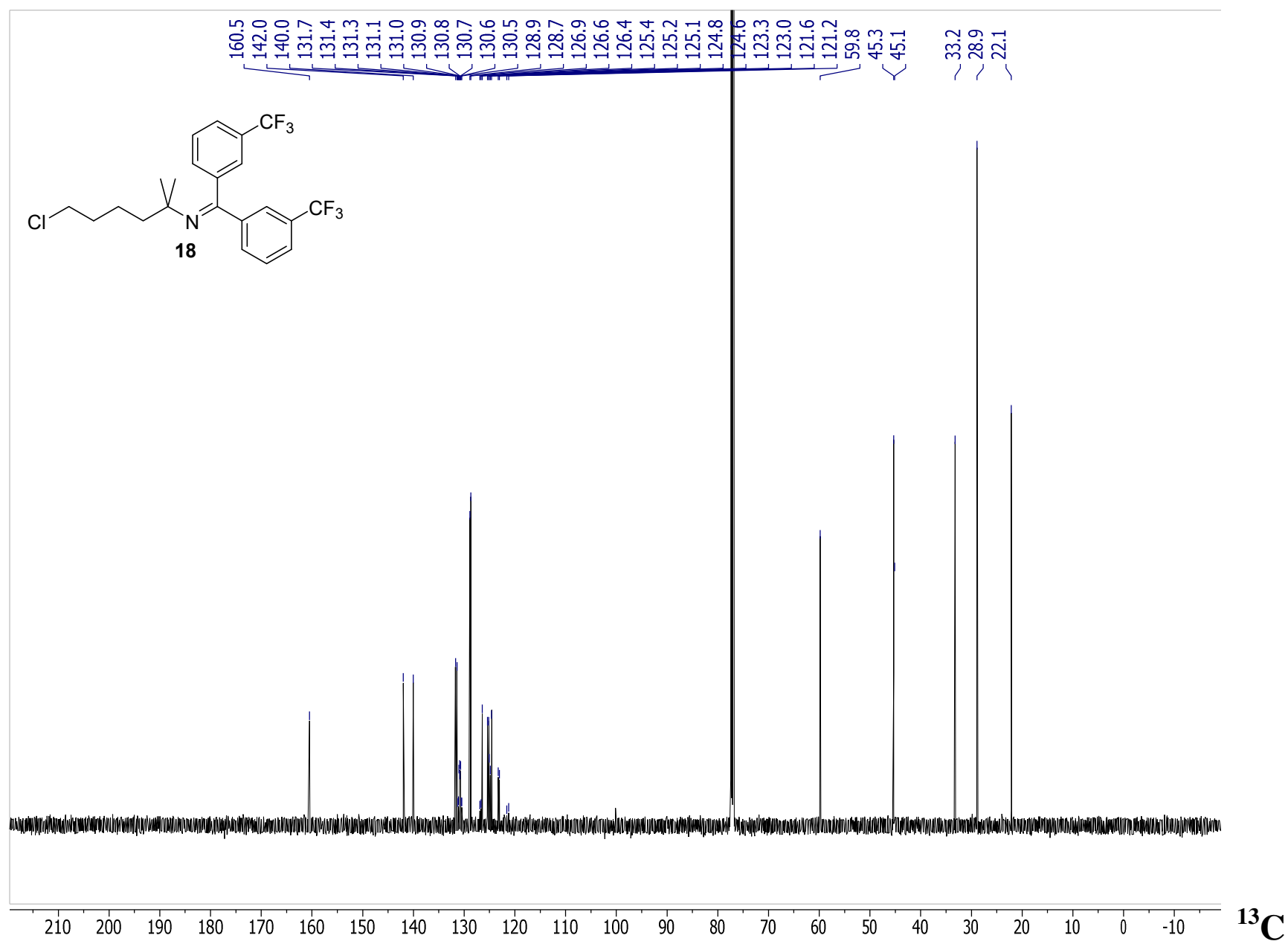


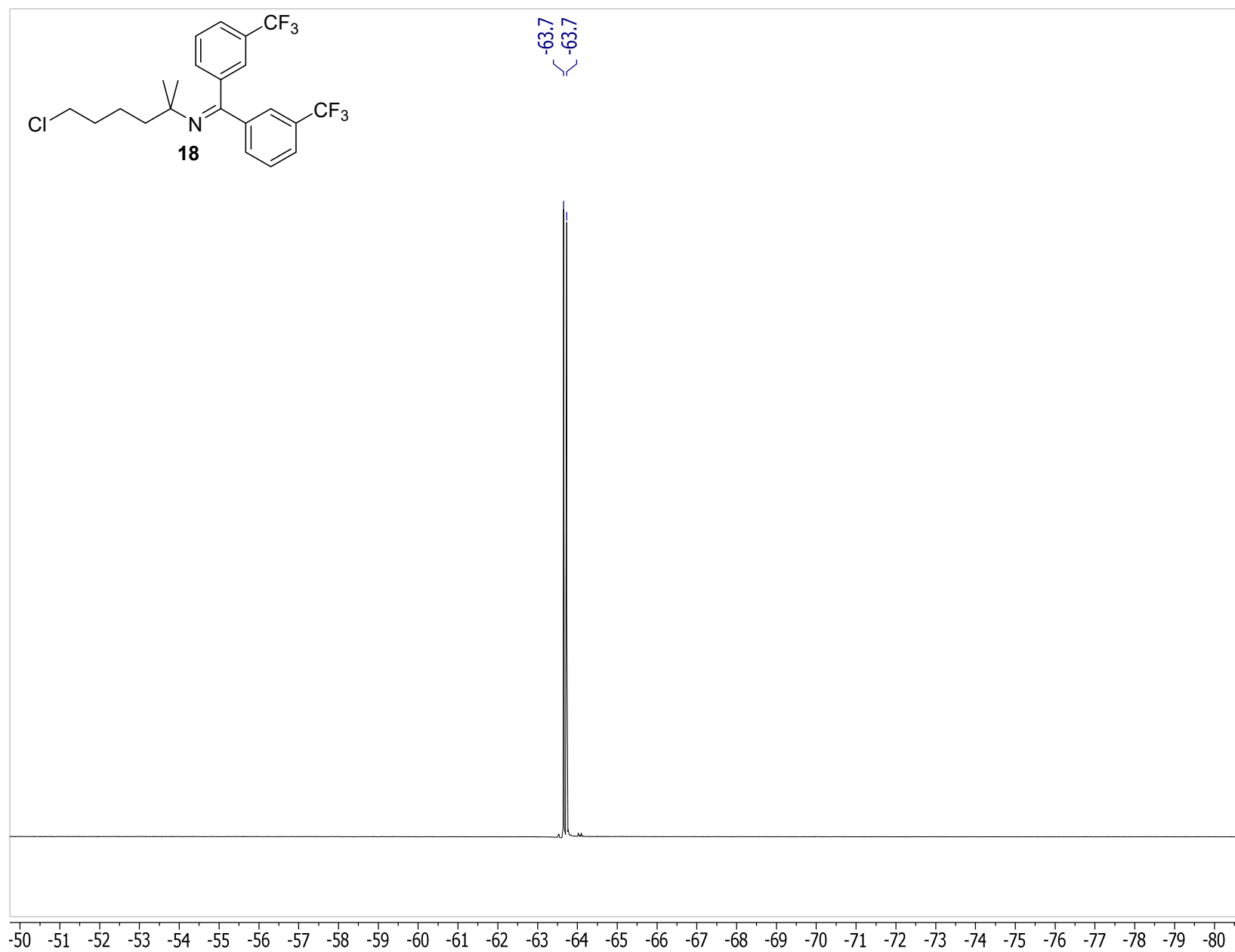


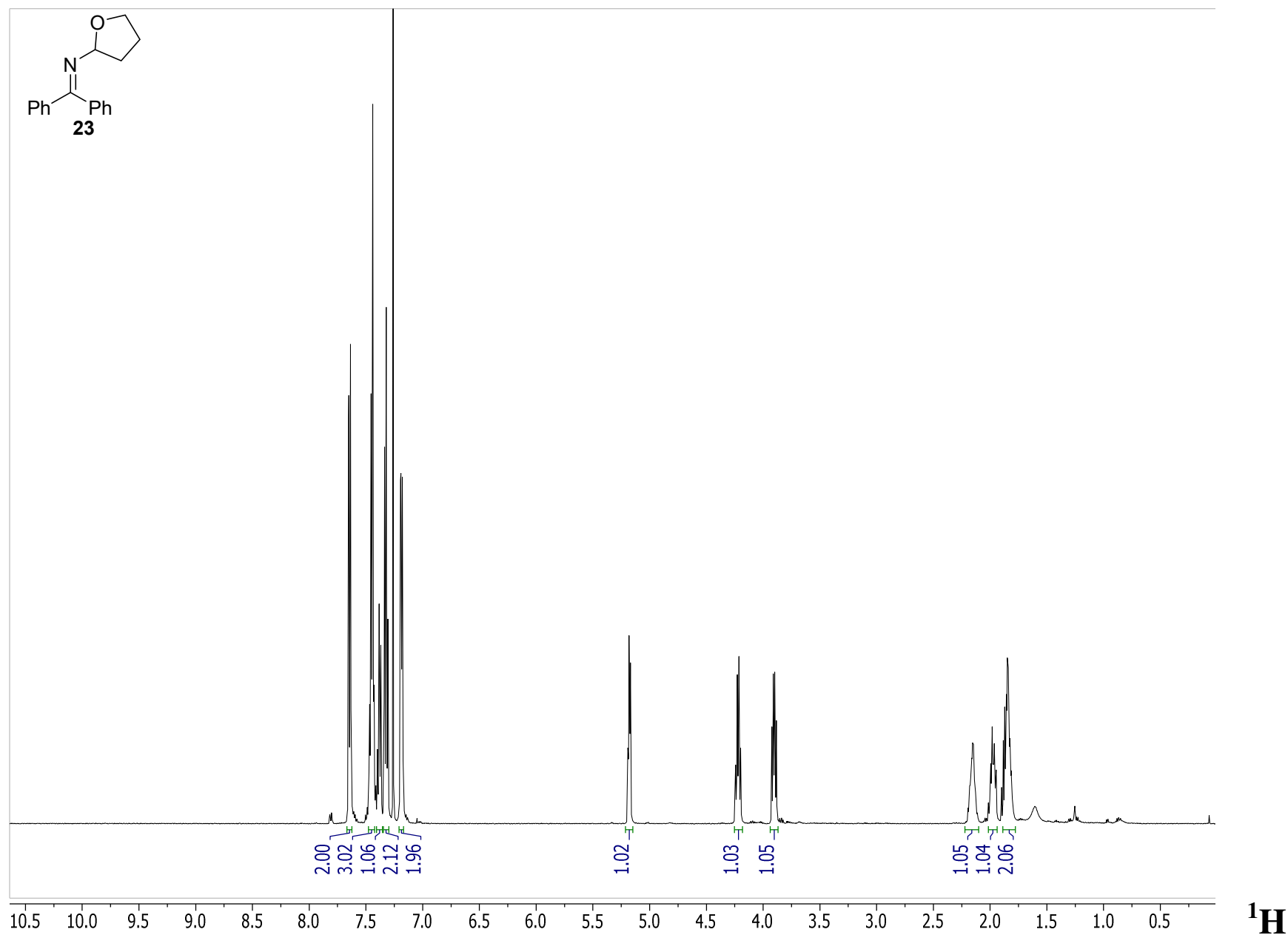


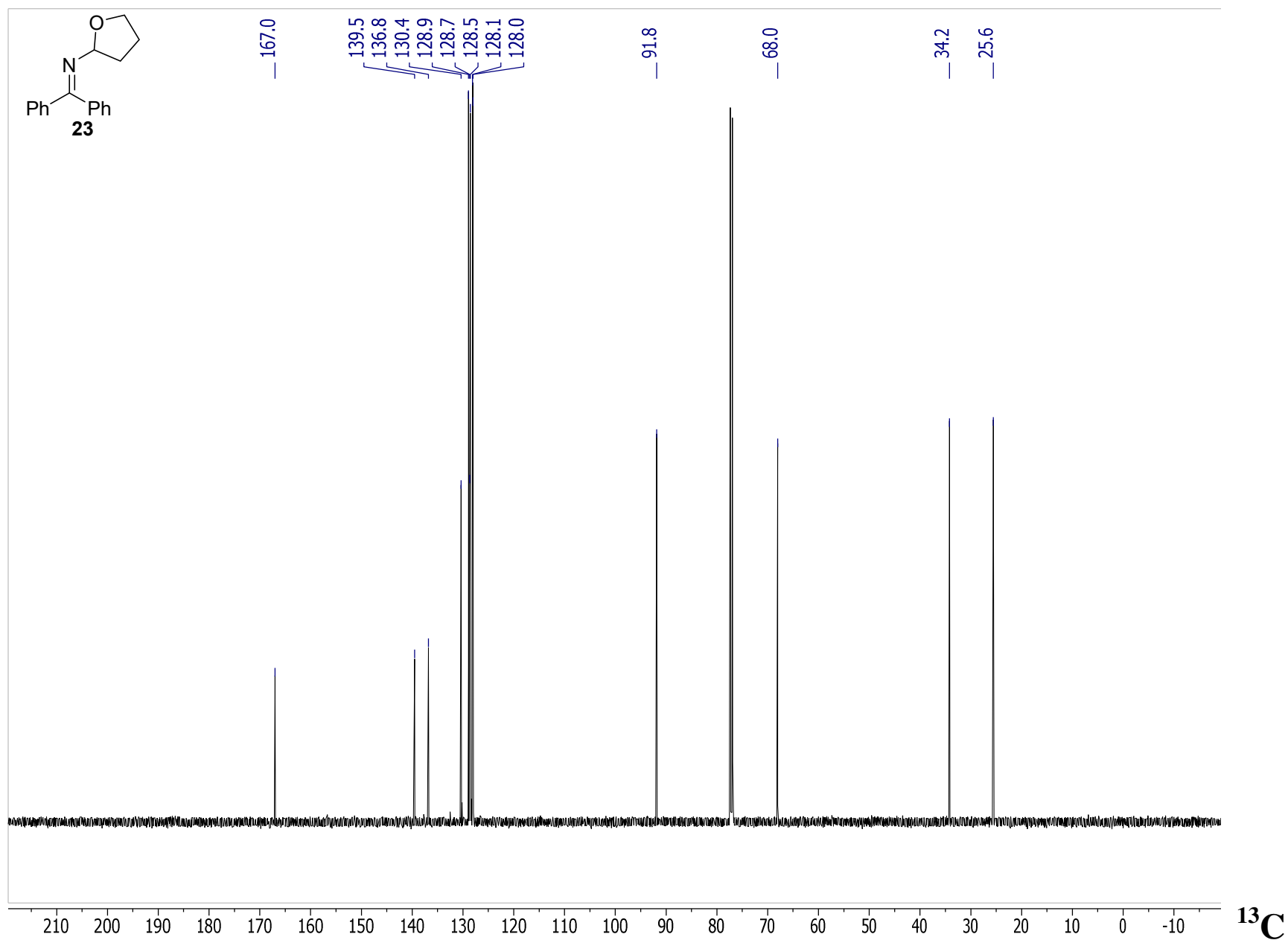


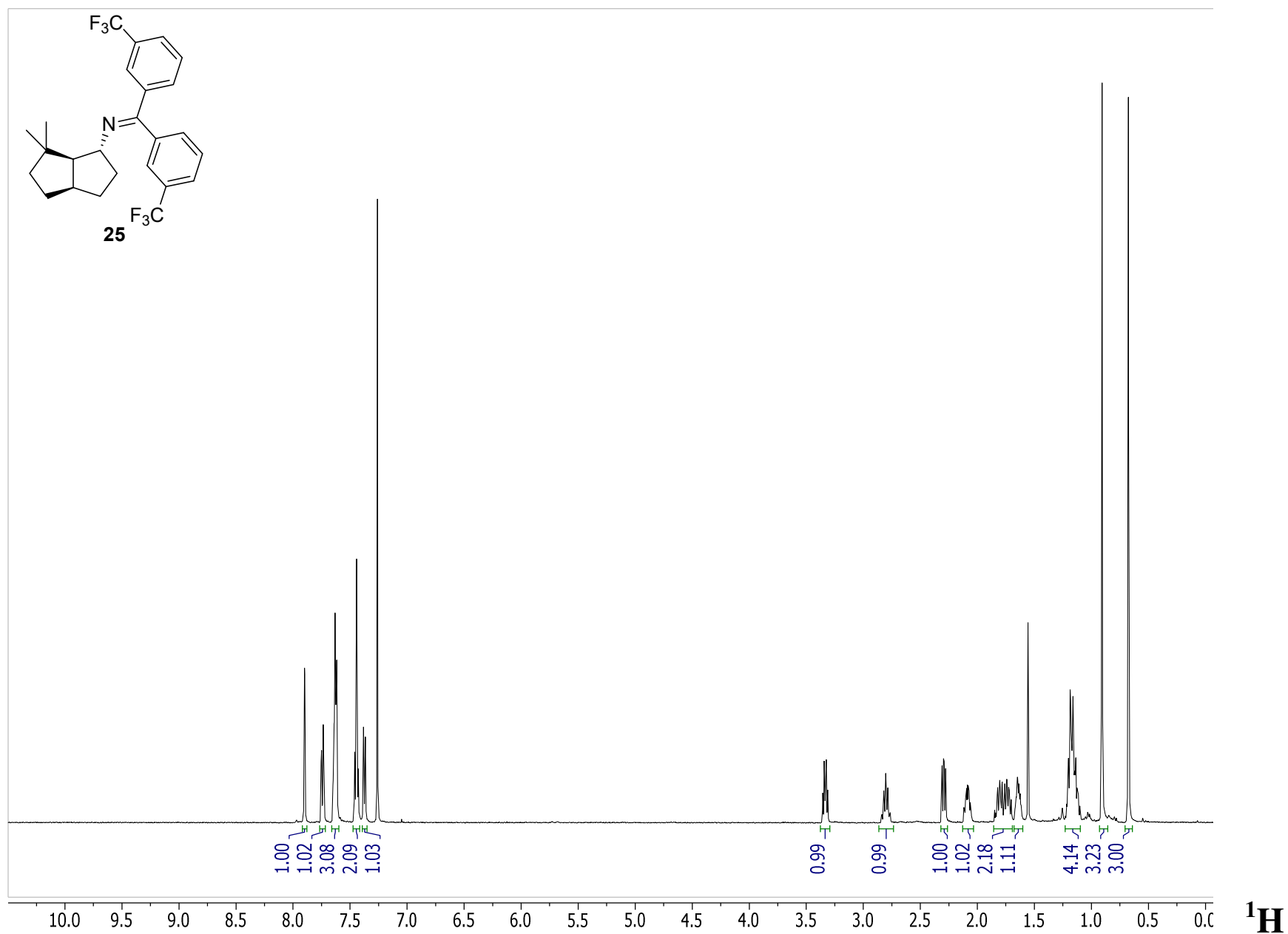


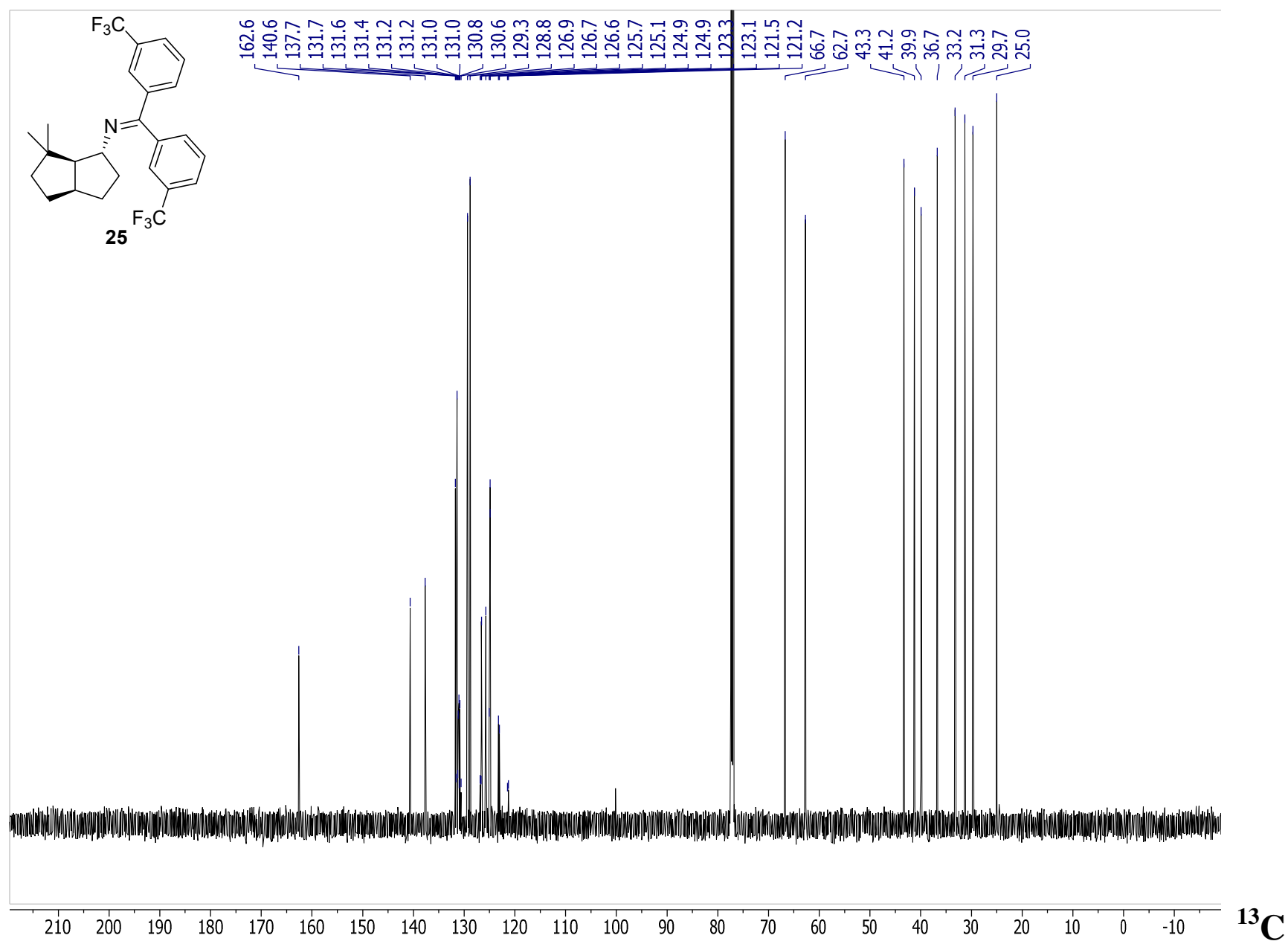


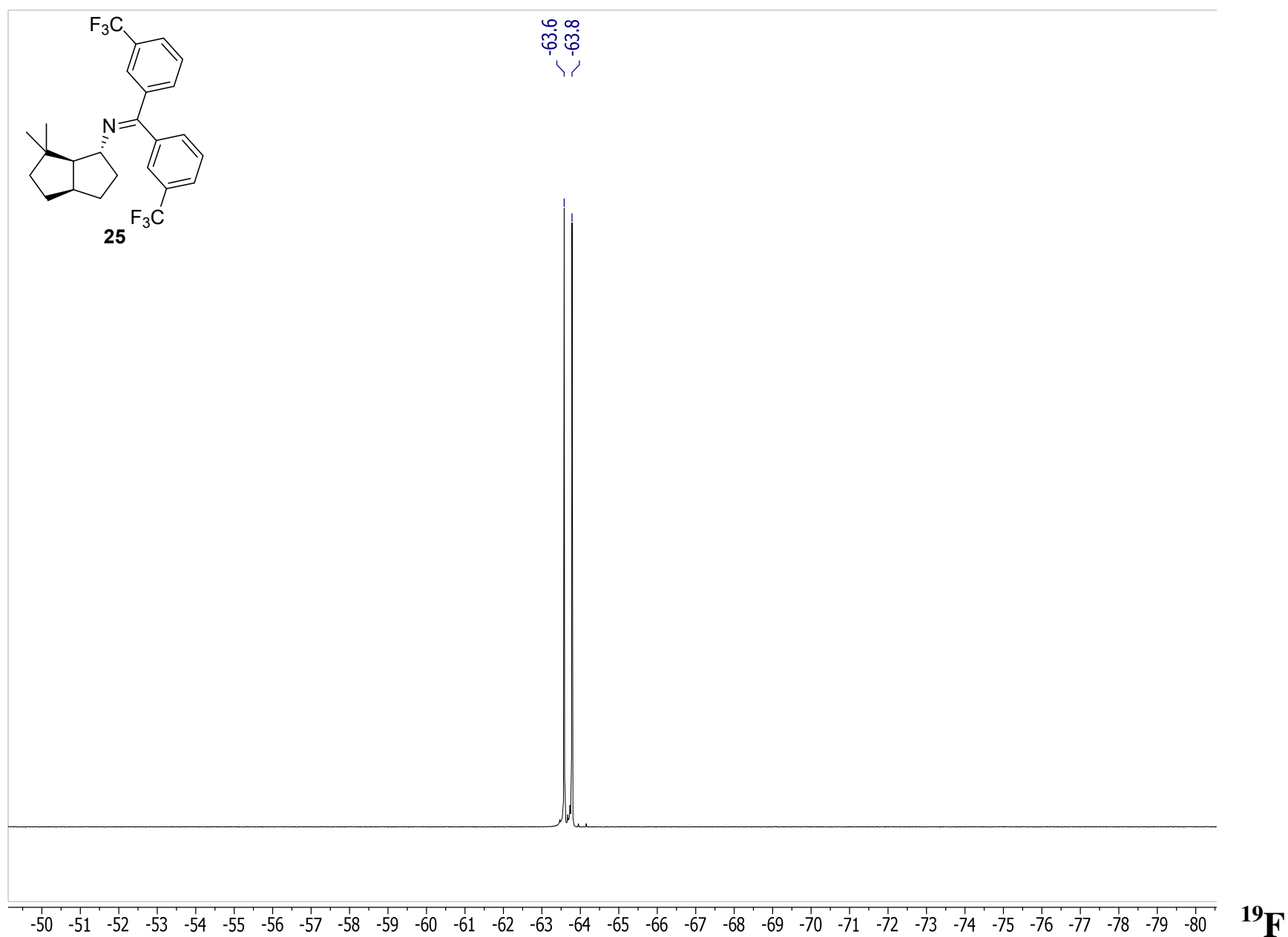


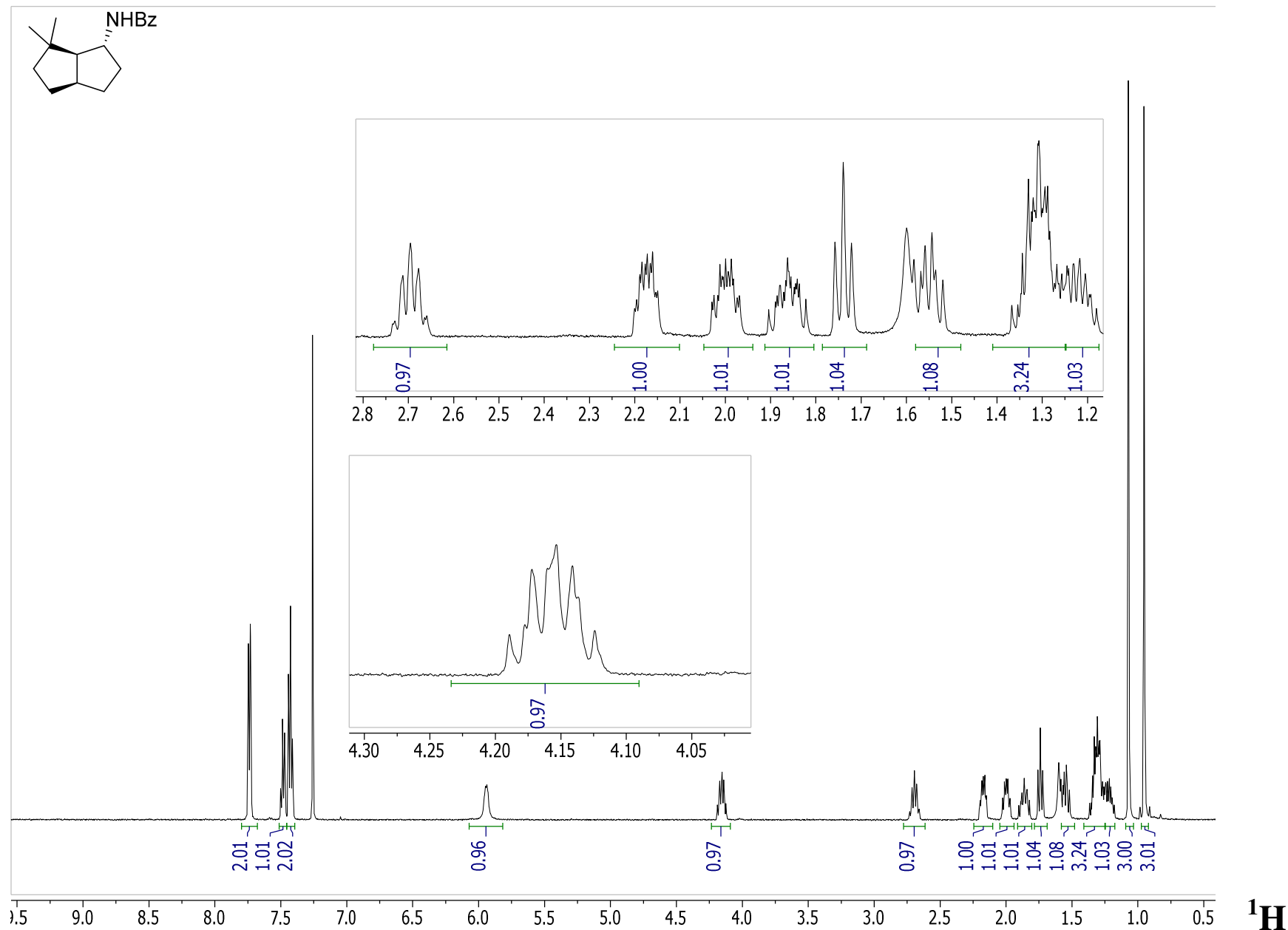


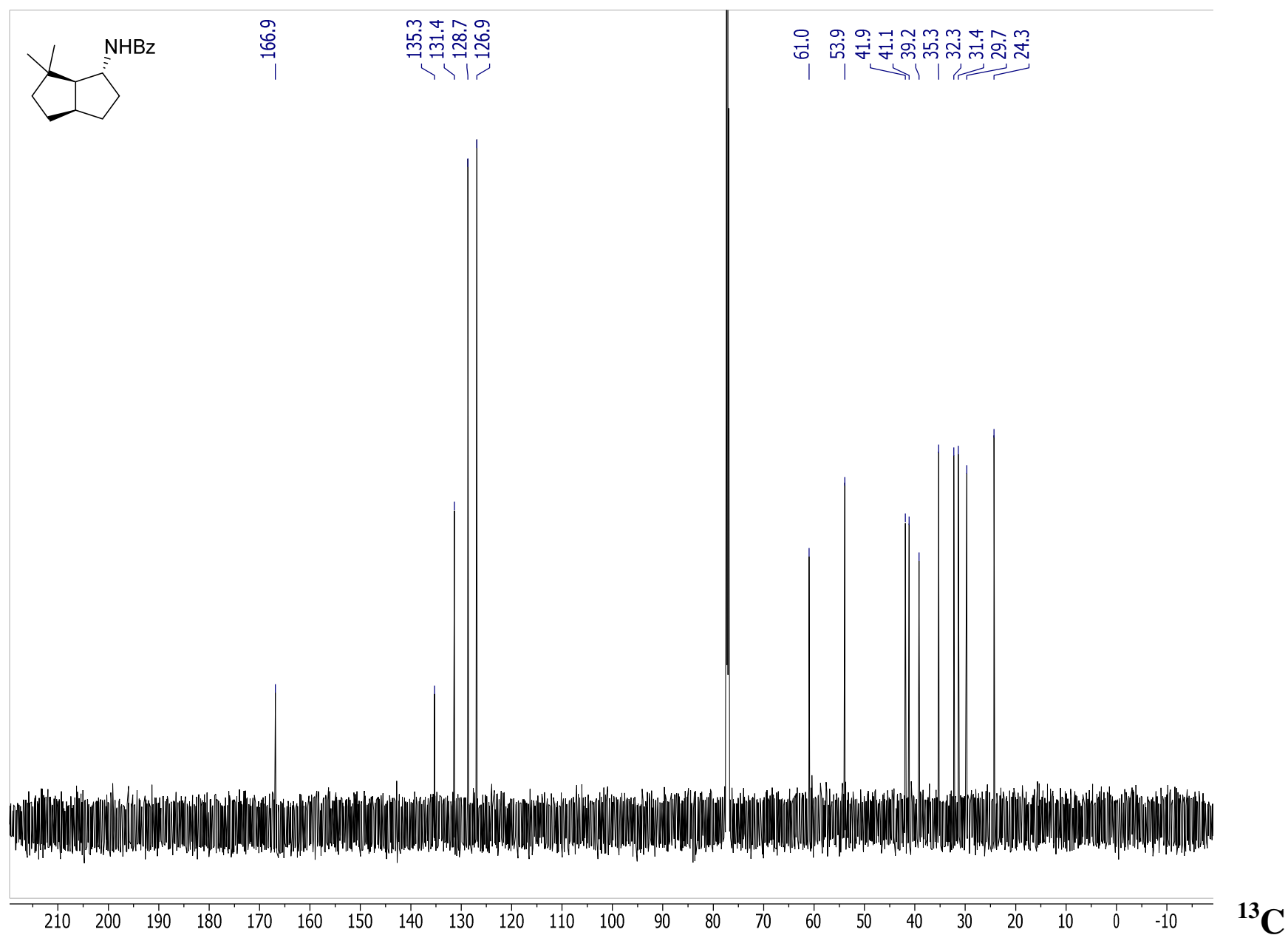


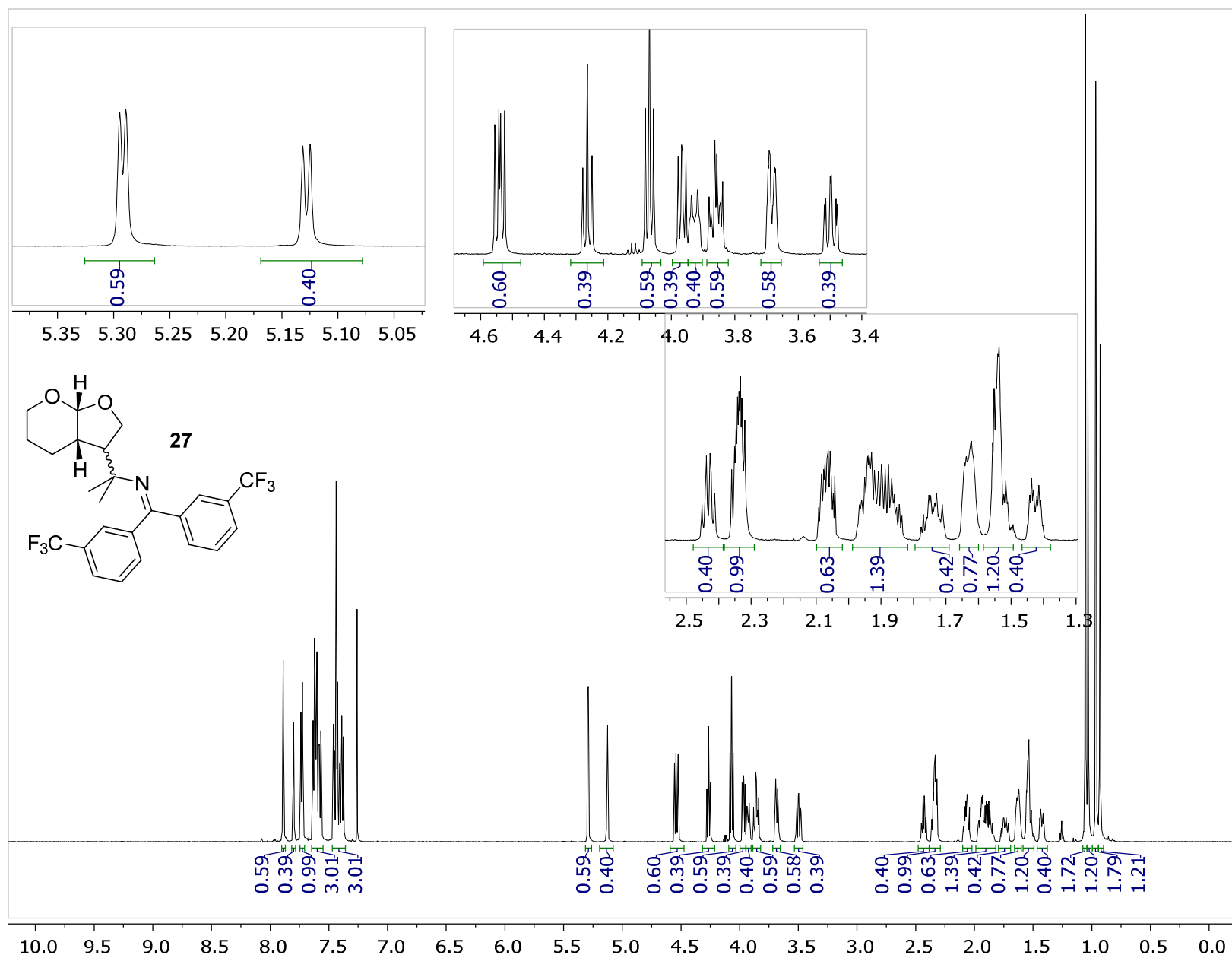


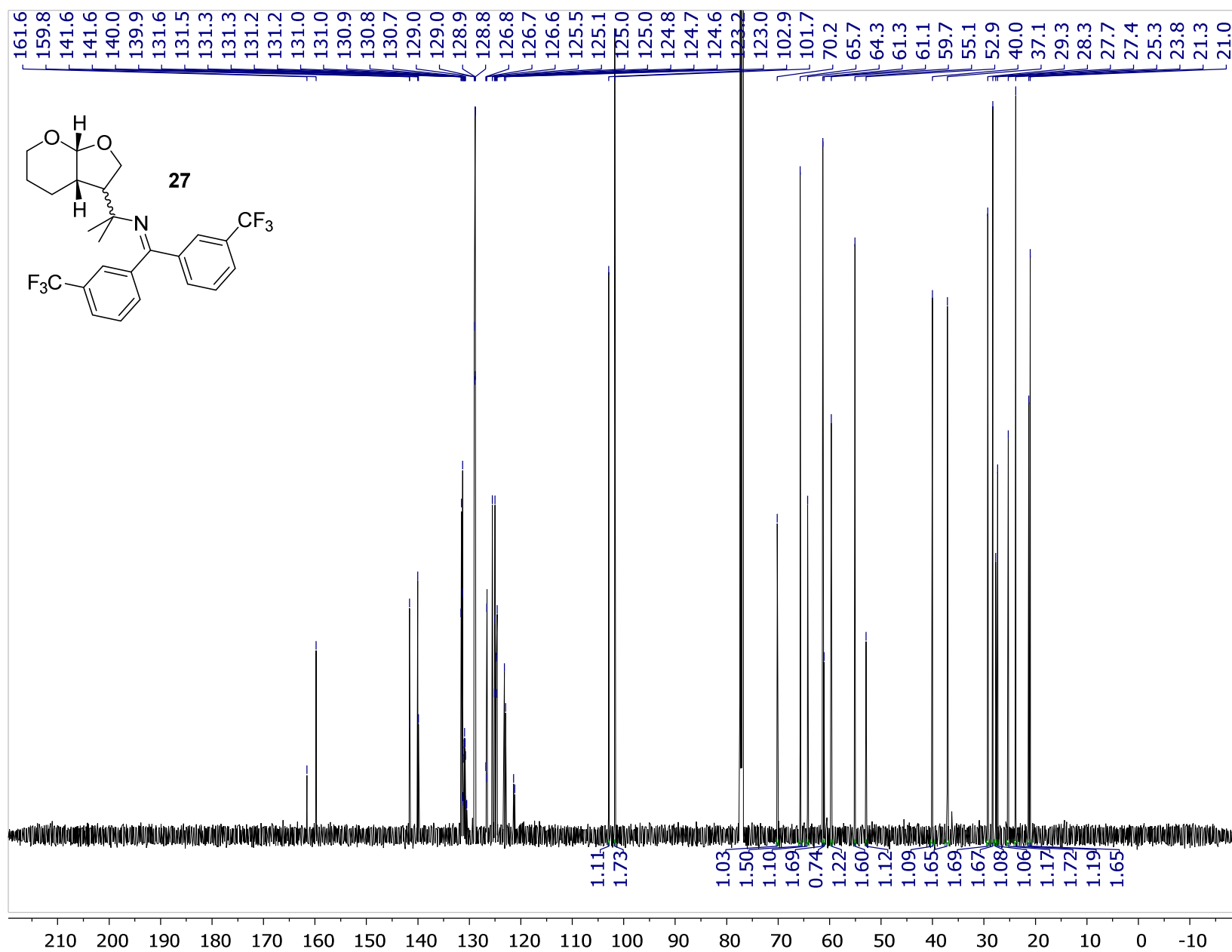


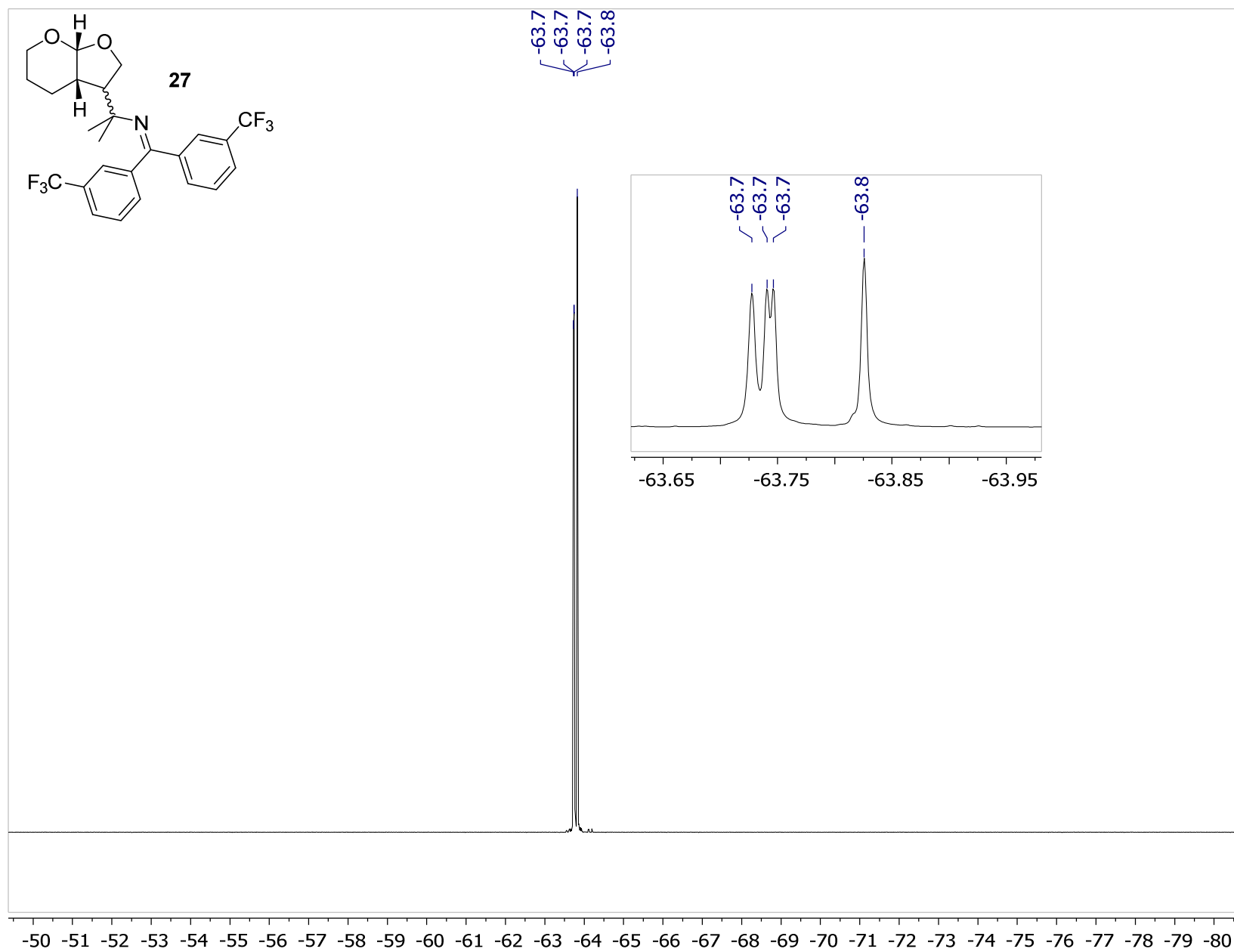












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