Table of Contents

1. General Methods

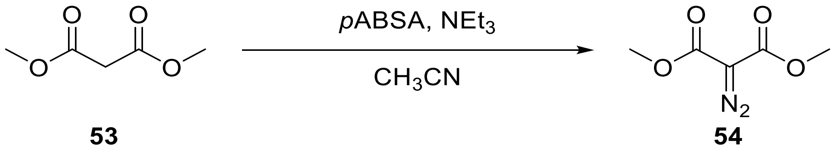
All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, Karl-Fischer titration). The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem, Fluorochem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ^{1}H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-*d*, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation). ^{19}F-NMR spectra were recorded on a Bruker DPX-400 376 MHz spectrometer in $CDCl_3$. ^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.

Photoredox catalyzed reactions were performed in test tubes (2, 5 and 10 mL), which were hold using a rack for test tubes placed at the center of a crystallization flask or regular clamps. On this flask were attached the blue LEDs (RUBAN LED 5MÈTRES - 60LED/M - 3528 BLEU - IP65 with Transformateur pour Ruban LED 24W/2A/12V, bought directly on RubanLED.com). The distance between the LEDs and the test tubes was approximatively 3 to 5 cm. Long irradiation resulted in temperature increasing up to 32 °C during overnight reactions.

2. Preparation of Starting Materials

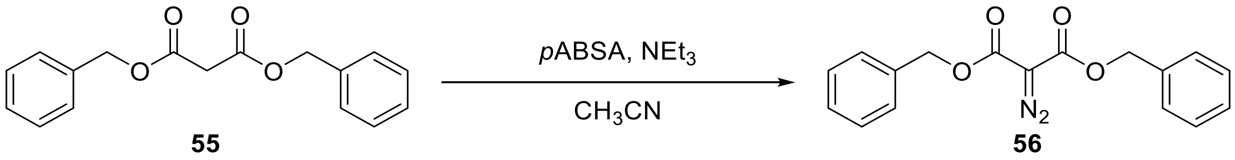
2.1 Synthesis of Diazo Compounds

Dimethyl 2-diazomalonate (54)



Following a modified procedure,[1] triethylamine (13.4 mL, 96.0 mmol, 2.4 equiv.) and dimethyl malonate (**53**) (4.60 mL, 40.0 mmol, 1.0 equiv.) were added to a solution of *p*ABSA (14.4 g, 60.0 mmol, 1.5 equiv.) in CH_3CN (160 mL) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (100 mL), the remaining solids were filtered off and the solvent was evaporated. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 95:5 to 90:10) to afford compound **54** (6.26 g, 39.6 mmol, 99 % yield) as a yellow oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 3.84 (s, 6H, C*H₃*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 161.2, 52.4. One carbon was not resolved. The characterization data is corresponding to the reported values.[1]

Dibenzyl 2-diazomalonate (56)



Following a modified procedure,[2] triethylamine (1.0 mL, 7.2 mmol, 2.4 equiv.) and dibenzyl malonate (**55**) (0.75 mL, 4.0 mmol, 1.0 equiv.) were added to a solution of *p*ABSA (1.08 g, 4.50 mmol, 1.5 equiv.) in CH_3CN (16.0 mL) at room temperature and the resulting mixture was stirred for 18 hours at room temperature. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (15 mL), the remaining solids were filtered off and the solvent was evaporated. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 95:5) to afford compound **56** (889 mg, 2.86 mmol, 95% yield) as a yellow oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.39- 7.34 (m, 10H, Ar*H*), 5.28 (s, 4H, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 160.9, 135.3, 128.8, 128.6, 128.5, 67.3. One carbon was not resolved. The characterization data correspond to the reported values.[2]

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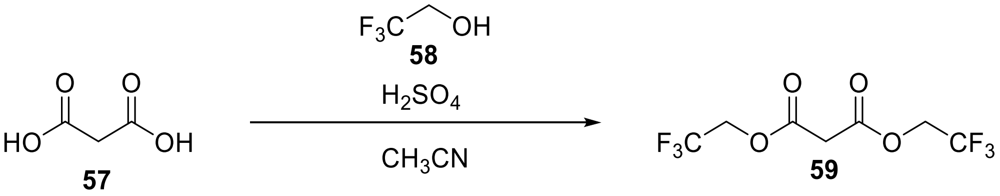
[1] F. de Nanteuil, J. Waser, *Angew. Chem. Int. Ed.* **2011**, *50*, 12075–12079.

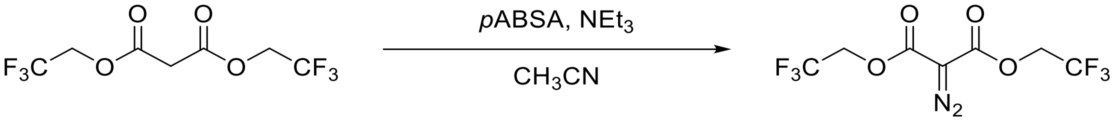
[2] F. de Nanteuil, J. Loup, J. Waser, *Org. Lett.* **2013**, *15*, 3738-3741.

Bis(2,2,2-trifluoroethyl) malonate (59)



Following a reported procedure,[2] H_2SO_4 (1.00 mL, 18.8 mmol, 0.25 equiv.) was added to a solution of trifluoroethanol (**58**) (29.9 mL, 415 mmol, 5.4 equiv.) and malonic acid **57** (8.00 g, 77.0 mmol, 1.0 equiv.) in toluene (40.0 mL) and the resulting mixture was heated to reflux for 8 hours. After cooling to room temperature, toluene (80.0 mL) was added and the mixture was washed with aq. NaOH (200 mL, 1 M), water (200 mL) and brine (200 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated under reduced pressure to afford the title compound **59** (6.80 g, 25.4 mmol, 33 % yield) as a colorless oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 4.55 (q, *J* = 8.2 Hz, 4H, OC*H₂*), 3.61 (s, 2H, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 164.4, 122.8 (q, *J* = 277.3 Hz), 61.4 (q, *J* = 37.0 Hz), 40.3. The characterization data correspond to the reported values.[2]

Bis(2,2,2-trifluoroethyl) 2-diazomalonate (60)

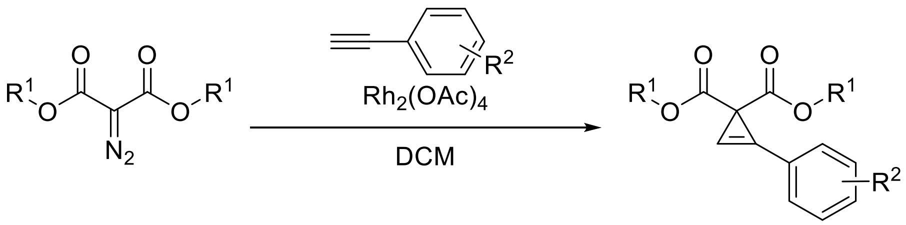


59 **60**

Following a modified procedure,[2] triethylamine (6.00 mL, 43.3 mmol, 2.4 equiv.) and bis(trifluorethyl)malonate (**59**) (4.84 g, 18.0 mmol, 1.0 equiv.) were added to a solution of *p*ABSA (6.50 g, 27.1 mmol, 1.5 equiv.) in CH_3CN (72.0 mL) at room temperature and the resulting mixture was stirred for 18 hours. Thereafter the mixture was filtered and the solvent was evaporated. The residue was triturated with CH_2Cl_2 (50 mL), the solids were filtered off and the solvent was evaporated. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 95:5 to 90:10) to afford compound **60** (5.26 g, 17.9 mmol, 99 % yield) as a yellow oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 4.62 (q, 4 H, *J* = 8.2 Hz, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 158.7, 122.6 (q, *J* = 277.3 Hz), 60.9 (q, *J* = 37.0 Hz). One carbon was not resolved. The characterization data correspond to the reported values.[2]

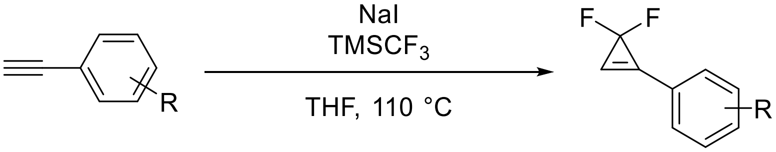
2.2 Synthesis of Cyclopropenes

General procedure A: Synthesis of cyclopropenes from diazo compounds.



Following a modified procedure,[3] the diazo compound was dissolved in DCM (0.5 M) and the resulting solution was added via syringe pump to a suspension of $Rh_2(OAc)_4$ (0.01 equiv.) in the indicated acetylene (3.0 equiv.) at room temperature over 10 hours. After the addition was complete, the reaction mixture was allowed to stir for another 10 hours. The reaction mixture was then filtered through a small pad of silica eluting with CH_2Cl_2 and the filtrate was concentrated under reduced pressure. The crude residue was purified by column chromatography with the indicated solvents.

General procedure B: Synthesis of difluorocyclopropenes.



Following a modified procedure,[4] a 20 mL microwave vial was charged with NaI (2.2 equiv.). The vial was sealed, evacuated and back-filled with nitrogen (3 times). Then THF (0.33 M), $TMSCF_3$ (2 equiv.) and the alkyne (1 equiv.), were added via syringe. The resulting reaction mixture was then stirred at 110 °C for 4 hours. The reaction was quenched by adding a saturated Na_2CO_3 solution, followed by extraction with Et_2O. The combined organic layers were dried over anhydrous K_2CO_3, filtered, and evaporated under reduced pressure. The crude residue was purified by column chromatography with the indicated solvents (the column should be previously deactivated with a 97:3 mixture of Pentane:Et_3N).

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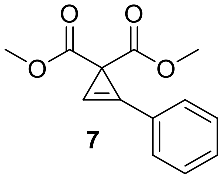
[3] S. Chuprakov, M. Rubin, V. Gevorgyan, *J. Am. Chem. Soc.* **2005**, *127*, 3714-3715.

[4] F. Wang, T. Luo, J. Hu, Y. Wang, H. S. Krishnan, P. V. Jog, S. K. Ganesh, G. K. Suryah Prakash, G. A. Olah, *Angew. Chem. Int. Ed.* **2011**, *50*, 7153 –7157.

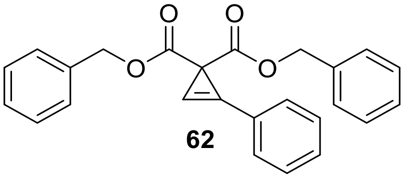
Dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (7)



7

Following the general procedure A, starting from dimethyl 2-diazomalonate (**54**) (5.10 g, 32.0 mmol, 1.0 equiv.) and phenylacetylene (**61)** (10.54 mL, 96.00 mmol, 3.0 equiv.), the title compound **7** was obtained after purification by column chromatography (SiO_2, Pentane:Et_2O 80:20) as a pale yellow solid (5.08 g, 21.9 mmol, 68 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.67 – 7.60 (m, 2H, Ar*H*), 7.48 – 7.41 (m, 3H, Ar*H*), 6.89 (s, 1H, C=C*H*), 3.74 (s, 6H, C*H*$_3$); **^{13}C NMR (101 MHz, Chloroform-*d*)** 171.3, 130.8, 130.4, 128.8, 123.5, 112.2, 95.1, 52.3, 32.8. The characterization data correspond to the reported values.[5]

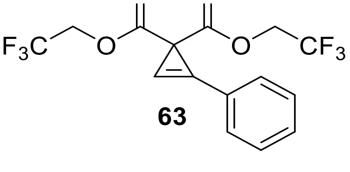
Dibenzyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (61)



62

Following the general procedure A, starting from dibenzyl 2-diazomalonate (**56**) (889 mg, 2.86 mmol, 1.0 equiv.) and phenylacetylene (**61)** (0.95 mL, 8.5 mmol, 3.0 equiv.), the title compound **62** was obtained after purification by column chromatography (SiO_2, Pentane:Et_2O 80:20 to 70:30) as a pale yellow solid (738 mg, 1.92 mmol, 67 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.64 – 7.58 (m, 2H, Ar*H*), 7.44 – 7.40 (m, 3H, Ar*H*), 7.31 – 7.26 (m, 10H, Ar*H*), 6.91 (s, 1H, C=C*H*), 5.18 (s, 4H, C*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.7, 135.9, 130.7, 130.5, 129.0, 128.6, 128.2, 128.0, 124.1, 112.5, 95.3, 67.0, 33.5. The characterization data correspond to the reported values.[6]

Bis(2,2,2-trifluoroethyl) 2-phenylcycloprop-2-ene-1,1-dicarboxylate (63)



63

Following the general procedure A, starting from bis(2,2,2-trifluoroethyl) 2-diazomalonate (**57**) (935 mg, 3.18 mmol, 1.0 equiv.) and phenylacetylene (**61**) (1.05 mL, 9.54 mmol, 3.0 equiv), the title compound **63** was obtained after purification by column chromatography (SiO_2, Pentane:Et_2O 90:10 to 80:20) as a pale yellow oil (542 mg, 1.47 mmol, 46 % yield). **R_f** 0.55

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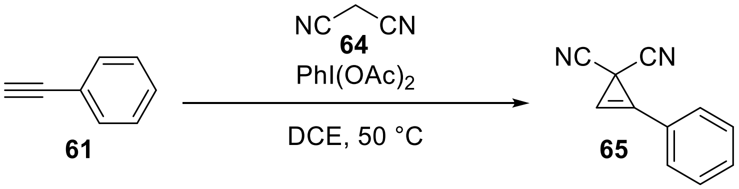
[5] L.-A. Liao, F. Zhang, N. Yan, J. A. Golen, J. M. Fox, *Tetrahedron* **2004**, *60*, 1803–1816.

[6] Y. Wang, E. A. F. Fordyce, F. Y. Chen, H. W. Lam, *Angew. Chem. Int. Ed.* **2008**, *47*, 7350 –7353.

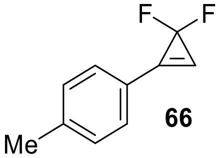
(Pentane:Et_2O 80:20). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.66 – 7.57 (m, 2H, Ar*H*), 7.51 – 7.44 (m, 3H, Ar*H*), 6.92 (s, 1H, C=C*H*), 4.53 (qd, *J* = 8.3, 6.3 Hz, 4H, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.6, 131.4, 130.5, 129.2, 123.0, 122.8 (q, *J* = 277.3 Hz), 111.7, 93.9, 61.1 (q, *J* = 37.0 Hz), 32.5; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -73.9 (t, *J* = 8.3 Hz); **IR $\tilde{\nu}_{max}$** 3663 (w), 2983 (m), 2899 (m), 1758 (m), 1452 (w), 1409 (m), 1288 (s), 1253 (s), 1228 (m), 1171 (s), 1084 (s), 976 (w), 882 (w), 847 (w); **HRMS (ESI)** calcd for $C_{15}H_{10}F_6NaO_4^+$ $[M+Na]^+$ 391.0375; found 391.0370.

2-Phenylcycloprop-2-ene-1,1-dicarbonitrile (65)



Following a reported procedure,[7] $PhI(OAc)_2$ (773 mg, 2.40 mmol, 1.2 equiv.) and malonitrile (**64**) (159 mg, 2.40 mmol, 1.2 equiv.) were charged in a 25 mL microwave vial. Then Phenylacetylene (**61**) (0.22 mL, 2.0 mmol, 1.0 equiv.) and DCE (8.0 mL) were added, and the resulting solution was stirred at 50 °C. After 3 hours, the reaction mixture was cooled to room temperature, quenched with water (25 mL), and extracted with DCM (3 x 20 mL). The combined organic layers were evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 90:10) affording the title compound **65** (82 mg, 0.49 mmol, 25 % yield) as an orange oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.76 – 7.70 (m, 2H, Ar*H*), 7.66 – 7.56 (m, 3H, Ar*H*), 7.08 (s, 1H, C=C*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 133.1, 130.7, 129.8, 120.5, 116.3, 112.2, 92.7, 3.9. The characterization data correspond to the reported values.[7]

1-(3,3-Difluorocycloprop-1-en-1-yl)-4-methylbenzene (66)



66

Following the general procedure B, starting from 1-ethynyl-4-methylbenzene (**67**) (0.51 mL, 4.0 mmol, 1.0 equiv.), the title compound **66** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a brown solid (584 mg, 3.51 mmol, 88 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.55 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.38 (t, *J* = 1.8 Hz, 1H, C=C*H*), 7.29 (d, *J* = 7.8 Hz, 2H, Ar*H*), 2.42 (s, 3H, C*H₃*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 142.4, 133.7 (t, *J* = 10.2 Hz), 130.2, 129.6, 120.4, 112.2 (t, *J* = 12.5 Hz), 101.7 (t, *J* = 268.1 Hz), 21.8. The characterization data correspond to the reported values.[8]

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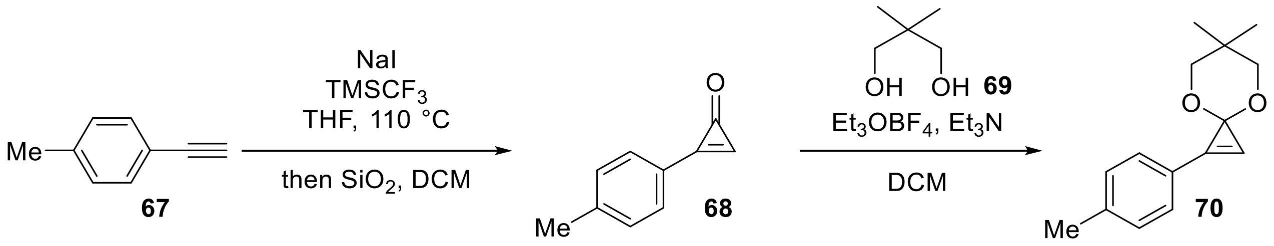
[7] S. Lin, M. Li, Z. Dong, F. Liang, J. Zhang, *Org. Biomol. Chem.* **2014**, *12*, 1341–1350.

[8] F. Wang, W. Zhang, J. Zhu, H. Li, K.-W. Huang, J. Hu, *Chem. Commun.* **2011**, *47*, 2411–2413.

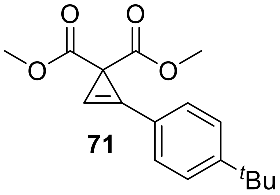
6,6-Dimethyl-1-(p-tolyl)-4,8-dioxaspiro[2.5]oct-1-ene (70)



A 20 mL microwave vial was charged with NaI (0.66 g, 4.4 mmol, 2.2 equiv.). The vial was sealed, evacuated and back-filled with nitrogen (3 times). Then THF (6 mL), $TMSCF_3$ (0.64 mL, 4.0 mmol, 2 equiv.) and 1-ethynyl-4-methylbenzene (**67**) (0.25 mL, 2.0 mmol, 1 equiv.), were added via syringe. The resulting reaction mixture was then stirred at 110 °C for 4 hours. The reaction was quenched by adding a saturated Na_2CO_3 solution, followed by extraction with Et_2O. The combined organic layers were dried over anhydrous K_2CO_3, filtered, and evaporated under reduced pressure. 3.50 g of SiO_2 and 10 mL of DCM were added to the previously obtained crude product, and the resulting mixture was left stirring overnight. The suspension was then filtered through a small pad of silica gel eluting with EtOAc, and the filtrate was concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 100 % Et_2O) affording compound **68** (262 mg, 1.82 mmol, 91 % yield) as a brown oil. **R_f** 0.25 (100% Et_2O) ; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.41 (s, 1H, C=C*H*), 7.75 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.35 (d, *J* = 7.8 Hz, 2H, Ar*H*), 2.45 (s, 3H, C*H3*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 161.8, 155.5, 144.8, 139.2, 131.4, 130.2, 120.7, 22.1; **IR $\tilde{\nu}_{max}$** 3052 (w), 1826 (s), 1609 (s), 1587 (s), 1567 (m), 1497 (m), 1451 (w), 1416 (w), 1214 (w), 1183 (w), 1114 (w), 812 (m); **HRMS (ESI)** calcd for $C_{10}H_9O^+$ $[M+H]^+$ 145.0648; found 145.0647.

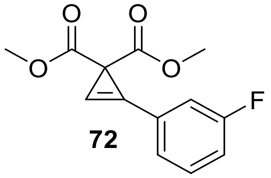
Et_3OBF_4 (0.285 g, 1.50 mmol, 1.5 equiv.) was added to a solution of 2-(p-tolyl)cycloprop-2-enone (**68**) (144 mg, 1.00 mmol, 1 equiv.) in DCM (1.6 mL) under vigorous stirring at room temperature. After 30 min, a solution of 2,2-dimethylpropane-1,3-diol (**69**) (0.208 g, 2.00 mmol, 2 equiv.) and Et_3N (0.278 mL, 2.00 mmol) in DCM (0.55 mL) was added dropwise. After 2 h, the reaction was treated with $NaHCO_3$ (10 mL), followed by extraction with DCM (2 x 10 mL). Combined organic layers were further washed with $NaHCO_3$ (20 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:Et_3N 98:2, the column should be previously eluted with Pentane:Et_3N 95:5) affording compound **70** (164 mg, 0.711 mmol, 71 % yield) as an orange solid. **R_f** 0.32 (Pentane:Et_2O 90:10); **m.p** = 63-64 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.60 (s, 1H, C=C*H*), 7.53 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.24 (d, *J* = 7.8 Hz, 2H, Ar*H*), 3.82 – 3.68 (m, 4H, OC*H2*), 2.39 (s, 3H, C_{Ar}-C*H3*), 1.14 (s, 3H, C*H3*), 1.08 (s, 3H, C*H3*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 140.4, 135.6, 129.8, 129.6, 123.2, 113.3, 83.3, 78.0, 30.6, 22.6, 22.4, 21.7; **IR $\tilde{\nu}_{max}$** 3106 (w), 3031 (w), 2952 (m), 2851 (m), 1721 (w), 1610 (w), 1508 (w), 1465 (w), 1269 (s), 1206 (m), 1173 (w), 1077 (s), 1023 (s), 995 (m), 925 (w), 823 (m), 750 (m), 650 (w), 618 (w); **HRMS (APPI)** calcd for $C_{15}H_{18}O_2^+$ $[M]^+$ 230.1301; found 230.1303.

Dimethyl 2-(4-(*tert*-butyl)phenyl)cycloprop-2-ene-1,1-dicarboxylate (71)


71

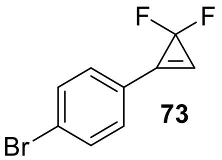
Following the general procedure A, starting from dimethyl 2-diazomalonate (**54**) (395 mg, 2.50 mmol, 1.0 equiv.) and 1-(*tert*-butyl)-4-ethynylbenzene (1.35 mL, 7.50 mmol, 3.0 equiv.), the title compound **71** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 95:5 to 90:10) as an orange solid (517 mg, 1.79 mmol, 72 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.58 – 7.54 (m, 2H, Ar*H*), 7.49 – 7.44 (m, 2H, Ar*H*), 6.82 (s, 1H, C=C*H*), 3.73 (s, 6H, OCH_3), 1.33 (s, 9H, *t*Bu); **^{13}C NMR (101 MHz, Chloroform-d)** δ 171.4, 154.3, 130.3, 126.1, 121.2, 112.1, 94.3, 52.5, 35.2, 32.8, 31.3. The characterization data correspond to the reported values.[9]

Dimethyl 2-(3-fluorophenyl)cycloprop-2-ene-1,1-dicarboxylate (72)


72

Following the general procedure A, starting from dimethyl 2-diazomalonate (**54**) (316 mg, 2.0 mmol, 1.0 equiv.) and 1-ethynyl-3-fluorobenzene (0.69 mL, 6.0 mmol, 3.0 equiv.), the title compound **72** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 90:10) as a pale yellow oil (282 mg, 1.13 mmol, 56 % yield). **R_f** 0.37 (Pentane:EtOAc 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.44 – 7.40 (m, 2H, Ar*H*), 7.33 (dd, *J* = 9.0, 2.5 Hz, 1H, Ar*H*), 7.18 – 7.11 (m, 1H, Ar*H*), 6.96 (s, 1H, C=C*H*), 3.75 (s, 6H, OCH_3); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 171.0, 162.9 (d, *J* = 248.0 Hz), 130.7 (d, *J* = 8.4 Hz), 126.3 (d, *J* = 3.1 Hz), 126.1 (d, *J* = 8.3 Hz), 117.9 (d, *J* = 21.2 Hz), 117.1 (d, *J* = 22.7 Hz), 111.7 (d, *J* = 3.4 Hz), 97.0, 52.7, 33.2; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -111.9; **IR $\tilde{\nu}_{max}$** 3149 (w), 2955 (w), 2924 (w), 2851 (w), 1736 (s), 1609 (w), 1586 (m), 1484 (w), 1436 (m), 1288 (s), 1244 (s), 1067 (s), 870 (m); **HRMS (ESI)** calcd for $C_{13}H_{11}FNaO_4^+$ $[M+Na]^+$ 273.0534; found 273.0534.

1-Bromo-4-(3,3-difluorocycloprop-1-en-1-yl)benzene (73)


73

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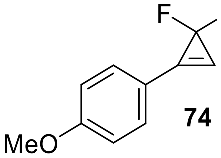
[9] Y. Liu, Q. Yu, S. Ma, *Eur. J. Org. Chem.* **2013**, 3033–3040.

Following the general procedure B, starting from 1-bromo-4-ethynylbenzene (0.36 g, 2.0 mmol, 1.0 equiv.), the title compound **73** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a light brown oil (360 mg, 1.56 mmol, 78 % yield). **R*f*** 0.35 (Pentane:Et_3N 96:4) ; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.67 – 7.60 (m, 2H, Ar*H*), 7.56 – 7.49 (m, 3H, Ar*H* & C=C*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 133.2 (t, *J* = 10.7 Hz), 132.6, 131.6, 126.5, 122.4, 114.4 (t, *J* = 12.4 Hz), 101.4 (t, *J* = 270.3 Hz); **^{19}F NMR (376 MHz, Chloroform-*d*) δ** -106.6; **IR $\tilde{\nu}_{max}$** 3134 (w), 1717 (w), 1586 (m), 1482 (m), 1402 (w), 1313 (s), 1286 (s), 1230 (w), 1180 (w), 1105 (w), 1071 (m), 1017 (s), 972 (w), 838 (m), 818 (s); **HRMS (APPI)** calcd for $C_9H_5{}^{79}BrF_2$ [M^+] 229.9537; found 229.9540.

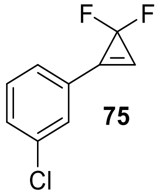
1-(3,3-Difluorocycloprop-1-en-1-yl)-4-methoxybenzene (74)



74

Following the general procedure B, starting from 1-ethynyl-4-methoxybenzene (0.39 mL, 3.0 mmol, 1.0 equiv.), the title compound **74** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a brown oil (519 mg, 2.85 mmol, 95 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.63 – 7.58 (m, 2H, Ar*H*), 7.28 (t, *J* = 1.9 Hz, 1H, C=C*H*), 7.02 – 6.96 (m, 2H, Ar*H*), 3.87 (s, 3H, OMe); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 162.3, 133.3 (t, *J* = 10.3 Hz), 132.1, 116.1, 114.7, 110.5 (t, *J* = 12.5 Hz), 102.1 (t, *J* = 269.4 Hz), 55.6. The characterization data correspond to the reported values.[10]

1-Chloro-3-(3,3-difluorocycloprop-1-en-1-yl)benzene (75)



75

Following the general procedure B, starting from 1-chloro-3-ethynylbenzene (0.25 mL, 2.0 mmol, 1.0 equiv.), the title compound **75** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a brown oil (263 mg, 1.41 mmol, 71 % yield).**R*f*** 0.32 (Pentane:Et_3N 96:4); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.65 (t, *J* = 1.7 Hz, 1H, C=C*H*), 7.57 – 7.52 (m, 2H, Ar*H*), 7.50 – 7.41 (m, 2H, Ar*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 135.3, 133.2 (t, *J* = 10.9 Hz), 131.8, 130.5, 130.1, 128.3, 125.1, 115.3 (t, *J* = 12.3 Hz), 101.3 (t, *J* = 270.7 Hz); **^{19}F NMR (376 MHz, Chloroform-*d*) δ** -106.4; **IR $\tilde{\nu}_{max}$** 3137 (w), 1723 (w), 1569 (w), 1471 (w), 1421 (w), 1303 (s), 1236 (w), 1026 (s), 976 (w), 890 (w), 828 (m); **HRMS (APPI)** calcd for $C_9H_5ClF^+$ [M^+] 167.0058; found 167.0057.

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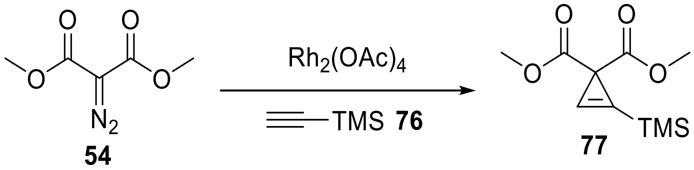
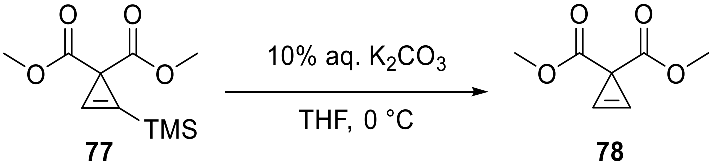
[10] X.-Y. Deng, J.-H. Lin, J. Zheng, J.-C. Xiao, *Chem. Commun.* **2015**, *51*, 8805-8808.

Dimethyl 2-(trimethylsilyl)cycloprop-2-ene-1,1-dicarboxylate (77)



Following a modified procedure,[11] a solution of dimethyl 2-diazomalonate (**54**) (0.79 g, 5.0 mmol, 1.0 equiv.) in ethynyltrimethylsilane (**76**) (2 mL) was added using a syringe pump over 18 hours to a refluxing stirred suspension of $Rh_2(OAc)_4$ (22 mg, 0.050 mmol, 0.01 equiv.) in ethynyltrimethylsilane (**76**) (10 mL). After the addition was complete, the reaction mixture was stirred at reflux for an additional 4 hours. The suspension was then filtered through a small pad of silica gel eluting with DCM, and the filtrate was evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 90:10) affording the title compound **77** (824 mg, 3.61 mmol, 72 % yield) as a colorless oil. **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.05 (s, 1H, C=C*H*), 3.70 (s, 6H, OC*H3*), 0.25 (s, 9H, TMS); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 172.4, 113.5, 110.8, 52.8, 30.8, -1.7. The characterization data correspond to the reported values.[11]

Dimethyl cycloprop-2-ene-1,1-dicarboxylate (78)



Following a reported procedure,[12] to a stirred solution of dimethyl 2-(trimethylsilyl)cycloprop-2-ene-1,1-dicarboxylate (**77**) (355 mg, 1.55 mmol, 1 equiv.) in THF (3 mL) was added dropwise a 10% aq. K_2CO_3 solution (2 mL). The reaction mixture was stirred for 30 min at 0 °C and 30 min at room temperature. Then brine (5 mL) was added and the phases were separated. The organic phase was further washed with brine (2 x 5 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 85:15) affording compound **78** (150 mg, 0.961 mmol, 62 % yield) as a colorless oil. **^{1}H NMR (400 MHz, Chloroform-d)** δ 6.90 (s, 2H, *H*C=C*H*), 3.73 (s, 6H, OC*H3*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 171.9, 102.5, 52.7, 30.3. The characterization data correspond to the reported values.[12]

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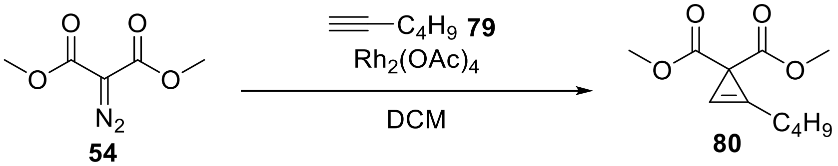
[11] S. Chuprakov, D. A. Malyshev, A. Trofimov, V. Gevorgyan, *J. Am. Chem. Soc.* **2007**, *129*, 14868-14869.

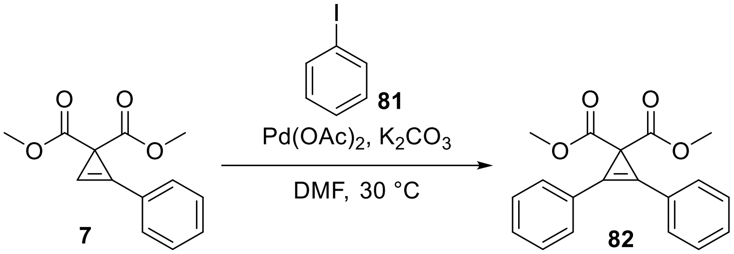
[12] K. Krämer, P. Leong, M. Lautens, *Org. Lett.* **2011**, *13*, 819-821.

Dimethyl 2-butylcycloprop-2-ene-1,1-dicarboxylate (80)



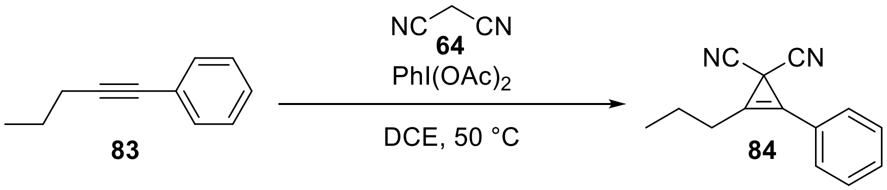
A solution of dimethyl 2-diazomalonate (**54**) (395 mg, 2.50 mmol, 1.0 equiv.) in DCM (1.75 mL) was added using a syringe pump over 15 hours to a stirred mixture of hex-1-yne (**79**) (1.15 mL, 10.0 mmol, 4.0 equiv.) and $Rh_2(OAc)_4$ (11.1 mg, 0.025 mmol, 0.01 equiv.) in DCM (2.0 mL). After the addition was complete, the mixture was stirred for additional 3 hours. The suspension was then filtered through a small pad of silica gel eluting with DCM, and the filtrate was evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 90:10) affording the title compound **80** (240 mg, 1.13 mmol, 45 % yield) as a pale yellow oil. **^{1}H NMR (400 MHz, Chloroform-d)** δ 6.35 (t, *J* = 1.4 Hz, 1H, C=C*H*), 3.71 (s, 6H, OCH_3), 2.55 (td, *J* = 7.4, 1.4 Hz, 2H, $CH_2CH_2CH_2CH_3$), 1.60 – 1.53 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.44 – 1.32 (m, 2H, $CH_2CH_2CH_2CH_3$), 0.91 (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_2CH_3$); **^{13}C NMR (101 MHz, Chloroform-*d*)** 172.5, 114.8, 93.8, 52.8, 32.4, 29.1, 24.5, 22.5, 14.2. The characterization data correspond to the reported values.[5]

Dimethyl 2,3-diphenylcycloprop-2-ene-1,1-dicarboxylate (82)



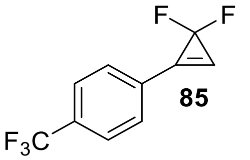
Following a reported procedure,[3] a 5 mL microwave vial was loaded with $Pd(OAc)_2$ (45 mg, 0.20 mmol, 0.1 equiv.), iodobenzene (**81**) (0.25 mL, 2.2 mmol, 1.1 equiv.), dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (0.464 g, 2.00 mmol, 1.0 equiv.) and K_2CO_3 (0.691 g, 5.00 mmol, 2.5 equiv.) under nitrogen atmosphere. DMF (2.0 mL) was added, and the reaction mixture was stirred at 30 °C for 18 hours. The reaction mixture was filtered through a short column of silica gel eluting with Et_2O, and the obtained ethereal solution was washed subsequently with a sat. NH_4Cl solution (15 mL), water (15 mL), and brine (15 mL). Combined organic layers were then dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Pentane:EtOAc 97:3 to 90:10) affording the title compound **82** (228 mg, 0.738 mmol, 37 % yield) as a pale yellow solid. **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.78 – 7.71 (m, 4H, Ar*H*), 7.52 – 7.46 (m, 4H, Ar*H*), 7.46 – 7.42 (m, 2H, Ar*H*), 3.73 (s, 6H, OCH_3); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.9, 130.3, 130.1, 129.2, 125.4, 106.6, 52.5, 35.1. The characterization data correspond to the reported values.[13]

2-phenyl-3-propylcycloprop-2-ene-1,1-dicarbonitrile (84)



Following a reported procedure,[7] PhI(OAc)$_2$ (1.16 g, 3.60 mmol, 1.2 equiv.) and malonitrile (**64**) (238 mg, 3.60 mmol, 1.2 equiv.) were charged in a 25 mL microwave vial. Then pent-1-yn-1-ylbenzene (**83**) (0.22 mL, 2.0 mmol, 1.0 equiv.) and DCE (12.0 mL) were added, and the resulting solution was stirred at 50 °C. After 3 hours, the reaction mixture was cooled to room temperature, quenched with water (25 mL), and extracted with DCM (3 x 20 mL). The combined organic layers were evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO$_2$, Pentane:EtOAc 95:5) affording the title compound **84** (212 mg, 1.02 mmol, 34 % yield) as an orange oil. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ = 7.61 (m, 2H, Ar*H*), 7.55 (m, 3H, Ar*H*), 2.82 (t, *J* = 7.28, 2H, CH_2CH$_2$CH$_3$), 1.90 (h, *J* = 7.35, 2H, CH$_2$CH_2CH$_3$), 1.13 (t, *J* = 7.40, 3H, CH$_2$CH$_2$CH_3); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 131.8, 129.5, 129.3, 121.7, 116.5, 106.1, 104.1, 26.1, 20.2, 13.8, 5.2. The characterization data correspond to the reported values.[7]

1-(3,3-Difluorocycloprop-1-en-1-yl)-4-(trifluoromethyl)benzene (85)



Following the general procedure B, starting from 1-ethynyl-4-(trifluoromethyl)benzene (0.41 mL, 2.5 mmol, 1.0 equiv.), the title compound **85** was obtained after purification by column chromatography (SiO$_2$, Pentane:Et$_3$N 96:4) as a brown oil (201 mg, 0.913 mmol, 37 % yield). **R*f*** 0.38 (Pentane:Et$_3$N 96:4) ; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.81 – 7.73 (m, 4H, Ar*H*), 7.65 (t, *J* = 1.6 Hz, 1H, C=C*H*) ; **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 133.4 (q, *J* = 32.7 Hz), 133.2 (t, *J* = 10.8 Hz), 130.5, 126.8, 126.3 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 272.5 Hz), 116.6 (t, *J* = 12.2 Hz), 101.1 (t, *J* = 271.0 Hz) ; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -63.1, -106.6; **IR $\tilde{\nu}_{max}$** 1721 (w), 1410 (m), 1325 (s), 1305 (s), 1292 (s), 1175 (s), 1129 (s), 1064 (s), 1030 (s), 1020 (s), 972 (w), 851 (m), 823 (s), 789 (m), 780 (m), 735 (m); **HRMS (APPI)** calcd for $C_{10}H_5F_4^+$ [M$^+$] 201.0322; found 201.0321.

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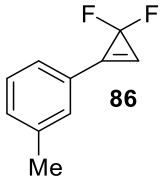
[13] D. C. Horwell, V. Sabin, **2000**, US Patent: US6020519.

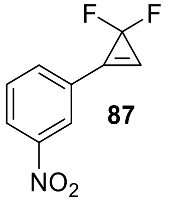
1-(3,3-Difluorocycloprop-1-en-1-yl)-3-methylbenzene (86)



86

Following the general procedure B, starting from 1-ethynyl-3-methylbenzene (0.26 mL, 2.0 mmol, 1.0 equiv.), the title compound **86** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a brown oil (260 mg, 1.57 mmol, 78 % yield). **R*f*** 0.43 (Pentane:Et_3N 96:4); **^{1}H NMR (400 MHz, Chloroform-*d*) δ** 7.47 (d, *J* = 7.6 Hz, 2H, Ar*H*), 7.43 (t, *J* = 1.7 Hz, 1H, C=C*H*), 7.37 (td, *J* = 7.3, 1.2 Hz, 1H, Ar*H*), 7.31 (d, *J* = 7.6 Hz, 1H, Ar*H*), 2.41 (s, 3H, CH_3); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 139.1, 134.2 (t, *J* = 10.4 Hz), 132.6, 130.9, 129.1, 127.4, 123.4, 113.3 (t, *J* = 12.3 Hz), 102.0 (t, *J* = 269.9 Hz), 21.3; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -106.4; **IR $\tilde{\nu}_{max}$** 3134 (w), 2928 (w), 2862 (w), 1717 (w), 1604 (w), 1584 (w), 1484 (w), 1463 (w), 1305 (s), 1188 (w), 1021 (s), 890 (w), 811 (m); **HRMS (ESI)** calcd for $C_{10}H_8F_2$ [M^+] 166.0589; found 166.0593.

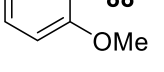
1-(3,3-Difluorocycloprop-1-en-1-yl)-3-nitrobenzene (87)



87

Following the general procedure B, starting from 1-ethynyl-3-nitrobenzene (0.29 g, 2.0 mmol, 1.0 equiv.), the title compound **87** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 96:4 to Pentane:Et_3N:EtOAc 90:5:5) as a brown solid (171 mg, 0.866 mmol, 43 % yield). **R*f*** 0.32 (Pentane:Et_3N:EtOAc 90:5:5) ; **m.p** = 41-44 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.51 (t, *J* = 1.9 Hz, 1H, C=C*H*), 8.37 (ddd, *J* = 8.4, 2.3, 1.1 Hz, 1H, Ar*H*), 7.98 (dt, *J* = 7.7, 1.3 Hz, 1H, Ar*H*), 7.76 – 7.67 (m, 2H, Ar*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 148.8, 135.7, 132.5 (t, *J* = 11.2 Hz), 130.5, 126.2, 125.1, 124.9, 117.3 (t, *J* = 12.2 Hz), 100.7 (t, *J* = 271.6 Hz); **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -106.4; **IR $\tilde{\nu}_{max}$** 3133 (w), 3092 (w), 1723 (w), 1613 (w), 1530 (s), 1474 (w), 1434 (w), 1356 (s), 1305 (s), 1283 (s), 1031 (s), 892 (w), 818 (m), 790 (m), 747 (s), 735 (s), 675 (m); **HRMS (APPI)** calcd for $C_9H_5F_2NO_2^+$ [M^+] 197.0288; found 197.0231.

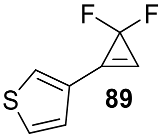
1-(3,3-difluorocycloprop-1-en-1-yl)-2-methoxybenzene (88)



88

Following the general procedure B, starting from 1-ethynyl-2-methoxybenzene (0.26 mL, 2.0 mmol, 1.0 equiv.), the title compound **88** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 90:10) as a brown oil (317 mg, 1.74 mmol, 87 % yield). **R*f*** 0.35 (Pentane:Et_3N 96:4); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.58 (dd, *J* = 7.6, 1.7 Hz, 1H, Ar*H*), 7.48 (ddd, *J* = 8.3, 7.5, 1.8 Hz, 1H, Ar*H*), 7.41 (t, *J* = 2.0 Hz, 1H, C=C*H*), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H, Ar*H*), 6.98 (d, *J* = 8.4 Hz, 1H, Ar*H*), 3.94 (s, 3H, OC*H*$_3$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 159.5, 133.5, 132.1, 130.2 (t, *J* = 10.5 Hz), 120.8, 113.9 (t, *J* = 12.2 Hz), 112.7, 111.2, 101.4 (t, *J* = 269.9 Hz), 55.9; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -105.3; **IR $\tilde{\nu}_{max}$** 1722 (w), 1599 (m), 1490 (m), 1469 (w), 1305 (s), 1273 (s), 1173 (w), 1018 (s), 826 (m), 785 (m), 755 (s), 728 (w); **HRMS (APPI)** calcd for $C_{10}H_8F_2O^+$ [M$^+$] 182.0538; found 182.0540.

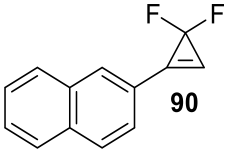
3-(3,3-Difluorocycloprop-1-en-1-yl)thiophene (89)



89

Following the general procedure B, starting from 1-ethynyl-2-methoxybenzene (0.20 mL, 2.0 mmol, 1.0 equiv.), the title compound **89** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 96:4) as a brown oil (225 mg, 1.42 mmol, 71 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.81 (d, *J* = 1.7 Hz, 1H, HetAr*H*), 7.43 (dd, *J* = 5.0, 2.9 Hz, 1H, HetAr*H*), 7.35 (dd, *J* = 5.1, 1.2 Hz, 1H, HetAr*H*), 7.28 (t, *J* = 1.8 Hz, 1H, C=C*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 130.9 (t, *J* = 1.4 Hz), 128.3 (t, *J* = 10.5 Hz), 127.8, 127.2, 124.4, 110.8 (t, *J* = 12.4 Hz), 100.9 (t, *J* = 269.8 Hz). The characterization data correspond to the reported values.[10]

2-(3,3-Difluorocycloprop-1-en-1-yl)naphthalene (90)

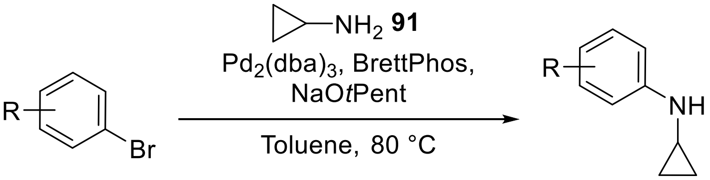


90

Following the general procedure B, starting from 2-ethynylnaphthalene (0.30 g, 2.0 mmol, 1.0 equiv.), the title compound **90** was obtained after purification by column chromatography (SiO_2, Pentane:Et_3N 95:5) as a light brown solid (379 mg, 1.87 mmol, 94 % yield). **R*f*** 0.28 (Pentane:Et_3N 96:4); **m.p** = 46-48 °C ; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.19 (s, 1H, C=C*H*), 7.96 – 7.91 (m, 2H, Ar*H*), 7.91 – 7.86 (m, 1H, Ar*H*), 7.69 (dd, *J* = 8.5, 1.7 Hz, 1H, Ar*H*), 7.63 – 7.53 (m, 3H, Ar*H*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 134.7, 134.2 (t, *J* = 10.6 Hz), 133.1, 131.4, 129.2, 128.9, 128.3, 128.1, 127.2, 126.0, 120.7, 113.8 (t, *J* = 12.3 Hz), 102.0 (t, *J* = 270.2 Hz); **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -106.4; **IR $\tilde{\nu}_{max}$** 3130 (w), 3060 (w), 1716 (w), 1631 (w), 1462 (w), 1289 (s), 1196 (w), 1139 (w), 1014 (s), 893 (w), 862 (w), 809 (m), 787 (m), 766 (m), 675 (w); **HRMS (APPI)** calcd for $C_{13}H_8F_2^+$ [M$^+$] 202.0589; found 202.0592.

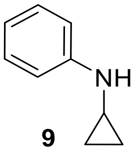
2.3 Synthesis of Cyclopropylanilines

General procedure C: Synthesis of cyclopropylanilines.



Following a modified procedure,[14] an oven-dried microwave vial was charged with $Pd_2(dba)_3$ (1 mol%) and BrettPhos (3 mol%). The vial was sealed, evacuated and back-filled with nitrogen (3 times). Then toluene (0.5 M), cyclopropylamine (**91**) (1.6 equiv.), the aromatic bromide (1 equiv.) and NaO^{t}Pent (45% solution in toluene, 1.5 equiv.) were added via syringe to the vial and it was heated at 80 °C for 18 h. The reaction mixture was then cooled to room temperature, diluted with Et_2O, and filtered through a small pad of silica gel. The filtrate was evaporated under reduced pressure, and the obtained crude residue was subjected to column chromatography with the indicated solvents.

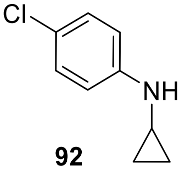
N-Cyclopropylaniline (9)



9

Following the general procedure C, starting from bromobenzene (3.16 mL, 30.0 mmol, 1.0 equiv.), the title compound **9** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a pale yellow oil (3.40 g, 25.5 mmol, 85 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.24 – 7.15 (m, 2H, Ar*H*), 6.84 – 6.77 (m, 2H, Ar*H*), 6.77 – 6.70 (m, 1H, Ar*H*), 4.21 (bs, 1H, N*H*), 2.43 (tt, *J* = 6.7, 3.6 Hz, 1H, NHC*H*), 0.77 – 0.70 (m, 2H, CH_2), 0.56 – 0.49 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 148.8, 129.2, 117.9, 113.3, 25.4, 7.5. The characterization data correspond to the reported values.[15]

4-Chloro-*N*-cyclopropylaniline (92)



92

Following the general procedure C, starting from 1-bromo-4-chlorobenzene (383 mg, 2.00 mmol, 1.0 equiv.), the title compound **92** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a yellow oil (221 mg, 1.32 mmol, 66 % yield). **^{1}H NMR (400**

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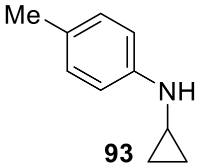
[14] S. Maity, M. Zhu, R. S. Shinabery, N. Zheng, *Angew. Chem. Int. Ed.* **2012**, *51*, 222 –226.

[15] T. V. Nykaza, J. Yang, A. T. Radosevich, *Tetrahedron* **2019**, *75*, 3248–3252.

MHz, Chloroform-*d*) δ 7.17 – 7.09 (m, 2H, Ar*H*), 6.75 – 6.66 (m, 2H, Ar*H*), 2.40 (tt, *J* = 6.7, 3.5 Hz, 1H, NHC*H*), 0.77 – 0.70 (td, *J* = 6.7, 4.7 Hz, 2H, CH_2), 0.53 – 0.46 (td, *J* = 6.7, 4.7 Hz, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 147.3, 129.1, 122.5, 114.4, 25.5, 7.6. The characterization data correspond to the reported values.[16]

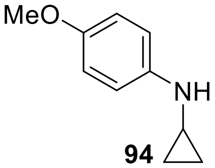
_N_-Cyclopropyl-4-methylaniline (93)



93

Following the general procedure C, starting from 1-bromo-4-methylbenzene (0.37 mL, 3.0 mmol, 1.0 equiv.), the title compound **93** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a yellow oil (242 mg, 1.64 mmol, 55 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.04 – 6.98 (d, *J* = 8.2 Hz, 2H, Ar*H*), 6.76 – 6.69 (d, *J* = 8.2 Hz, 2H, Ar*H*), 4.14 (brs, 1H, N*H*), 2.41 (tt, *J* = 6.7, 3.6 Hz, 1H, NHC*H*), 2.26 (s, 3H, CH_3), 0.75 – 0.67 (m, 2H, CH_2), 0.55 – 0.46 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 146.4, 129.7, 127.1, 113.4, 25.7, 20.6, 7.5. The characterization data correspond to the reported values.[17]

_N_-Cyclopropyl-4-methoxyaniline (94)



94

Following the general procedure C, starting from 1-bromo-4-methoxybenzene (0.25 mL, 2.0 mmol, 1.0 equiv.), the title compound **94** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a yellow oil (248 mg, 1.52 mmol, 76 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 6.84 – 6.72 (m, 4H, Ar*H*), 4.22 (bs, 1H, N*H*), 3.76 (s, 3H, OCH_3), 2.40 (tt, *J* = 6.7, 3.6 Hz, 1H, NHC*H*), 0.70 (m, 2H, CH_2), 0.54 – 0.48 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 152.6, 142.8, 114.9, 114.5, 56.0, 26.2, 7.4. The characterization data correspond to the reported values.[18]

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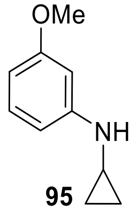
[16] R. N. Loeppky, S. Elomari, *J. Org. Chem.* **2000**, *65*, 96-103.
[17] Y. Kuang, Y. Ning, J. Zhu, Y. Wang, *Org. Lett.* **2018**, *20*, 2693−2697.
[18] T. H. Nguyen, S. Maity, N. Zheng, *Beilstein J. Org. Chem.* **2014,** *10*, 975–980.

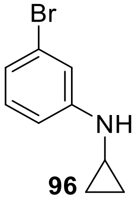
N-cyclopropyl-3-methoxyaniline (95)



95

Following the general procedure C, starting from 1-bromo-3-methoxybenzene (0.38 mL, 3.0 mmol, 1.0 equiv.), the title compound **95** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a white solid (434 mg, 2.66 mmol, 89 % yield).**^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.13 – 7.05 (m, 1H, Ar*H*), 6.42 – 6.35 (m, 2H, Ar*H*), 6.34 – 6.28 (m, 1H, Ar*H*), 3.79 (s, 3H, OC*H₃*), 2.42 (tt, *J* = 6.7, 3.6 Hz, 1H, NHC*H*), 0.76 – 0.69 (m, 2H, C*H₂*), 0.59 – 0.51 (m, 2H, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 160.7, 150.2, 129.8, 106.3, 102.6, 99.0, 54.8, 25.1, 7.3. The characterization data correspond to the reported values.17

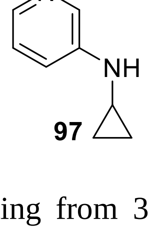
3-Bromo-*N*-cyclopropylaniline (96)



96

Following the general procedure C, starting from 1,3-dibromobenzene (0.30 mL, 2.5 mmol, 1.0 equiv.), the title compound **96** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 50:50) as a yellow oil (142 mg, 0.670 mmol, 27 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.02 (t, *J* = 8.0 Hz, 1H, Ar*H*), 6.95 (t, *J* = 2.1 Hz, 1H, Ar*H*), 6.85 (ddd, *J* = 7.8, 1.9, 1.0 Hz, 1H, Ar*H*), 6.66 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H, Ar*H*), 4.32 (bs, 1H, N*H*), 2.41 (tt, *J* = 6.7, 3.5 Hz, 1H, NHC*H*), 0.79 – 0.71 (m, 2H, C*H₂*), 0.55 – 0.48 (m, 2H, C*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 150.0, 130.5, 123.3, 120.7, 115.8, 112.2, 25.2, 7.6. The characterization data correspond to the reported values.[17]

N-Cyclopropylpyridin-3-amine (97)

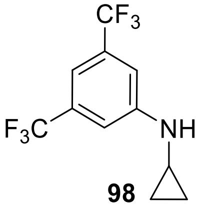


97

Following the general procedure C, starting from 3-bromopyridine (0.24 mL, 2.5 mmol, 1.0 equiv.), the title compound **97** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 50:50) as a yellow oil (206 mg, 1.54 mmol, 61 % yield). **^{1}H NMR (400 MHz,**

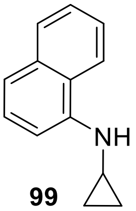
Chloroform-*d*) δ 8.18 – 8.10 (m, 1H, Ar*H*), 7.99 (dd, *J* = 3.7, 2.4 Hz, 1H, Ar*H*), 7.13 – 7.04 (m, 2H, Ar*H*), 4.23 (bs, 1H, N*H*), 2.43 (tt, *J* = 6.7, 3.5 Hz, 1H, NHC*H*), 0.82 – 0.72 (m, 2H, CH_2), 0.55 – 0.48 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 144.8, 139.2, 136.2, 123.8, 119.4, 25.0, 7.6. The characterization data correspond to the reported values.[19]

N-Cyclopropyl-3,5-bis(trifluoromethyl)aniline (98)


98

Following the general procedure C, starting from 1-bromo-3,5-bis(trifluoromethyl)benzene (0.35 mL, 2.0 mmol, 1.0 equiv.), the title compound **98** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a white solid (310 mg, 1.15 mmol, 58 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.18 (m, 1H, Ar*H*), 7.11 (m, 2H, Ar*H*), 2.48 (tt, *J* = 6.7, 3.6 Hz, 1H, NHC*H*), 0.88 – 0.80 (m, 2H, CH_2), 0.59 – 0.52 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 149.4, 132.4 (q, *J* = 32.7 Hz), 123.7 (q, *J* = 272.4 Hz), 112.6 – 112.1 (m), 110.8 (dt, *J* = 8.0, 4.2 Hz), 25.0, 7.8. The characterization data correspond to the reported values.[17]

N-cyclopropylnaphthalen-1-amine (99)


99

Following the general procedure C, starting from 1-bromonaphthalene (0.28 mL, 2.0 mmol, 1.0 equiv.), the title compound **99** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 98:2) as a white solid (328 mg, 1.79 mmol, 89 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.83 – 7.77 (m, 1H, Ar*H*), 7.76 – 7.70 (m, 1H, Ar*H*), 7.49 – 7.37 (m, 3H, Ar*H*), 7.29 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.08 (dd, *J* = 7.6, 1.1 Hz, 1H, Ar*H*), 4.89 (bs, 1H, N*H*), 2.59 (tt, *J* = 6.8, 3.6 Hz, 1H, NHC*H*), 0.90 – 0.81 (m, 2H, CH_2), 0.69 – 0.62 (m, 2H, CH_2); **^{13}C NMR (101 MHz, Chloroform-d)** δ 144.0, 134.3, 128.8, 126.7, 125.8, 124.8, 123.3, 119.8, 117.9, 106.0, 25.6, 7.7. The characterization data correspond to the reported values.[19,20]

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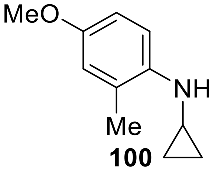
[19] W. Cui, R. N. Loeppky, *Tetrahedron* **2001**, *57*, 2953-2956.

[20] Our obtained signals were slightly shifted from the reported ones.

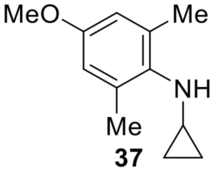
N-Cyclopropyl-4-methoxy-2-methylaniline (100)



100

Following the general procedure C, starting from 1-bromo-4-methoxy-2-methylbenzene (0.28 mL, 2.0 mmol, 1.0 equiv.), the title compound **100** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a yellow oil (250 mg, 1.41 mmol, 71 % yield). **R*f*** 0.25 (Pentane:EtOAc 95:5); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 6.99 (d, *J* = 8.6, 1H, Ar*H*), 6.74 (dd, *J* = 8.6, 3.0, 1H, Ar*H*), 6.69 (d, *J* = 2.9, 1H, Ar*H*), 3.76 (s, 3H, OC*H*$_3$), 2.41 (tt, *J* = 6.7, 3.6, 1H, NHC*H*), 2.10 (s, 3H, C*H*$_3$), 0.77 – 0.70 (m, 2H, C*H*$_2$), 0.56 – 0.49 (m, 2H, C*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 152.1, 141.0, 123.5, 116.9, 112.1, 111.7, 56.0, 26.0, 17.7, 7.5; **IR $\tilde{\nu}_{max}$** 3398 (w), 2996 (w), 2951 (w), 2830 (w), 1667 (w), 1612 (w), 1509 (s), 1455 (m), 1365 (m), 1284 (m), 1233 (s), 1208 (m), 1161 (m), 1050 (m), 852 (w), 805 (w); **HRMS (ESI)** calcd for $C_{11}H_{16}NO^+$ $[M+H]^+$ 178.1226; found 178.1227.

N-Cyclopropyl-4-methoxy-2,6-dimethylaniline (37)

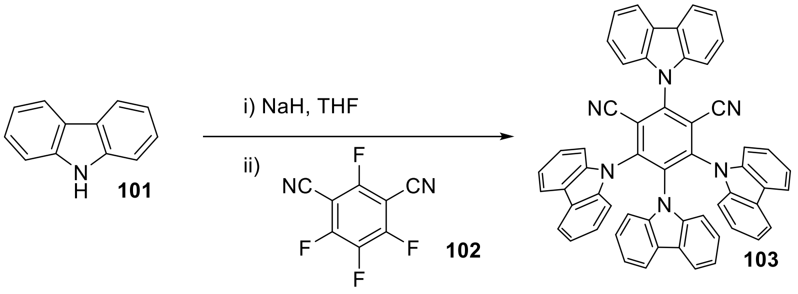


37

Following the general procedure C, starting from 2-bromo-5-methoxy-1,3-dimethylbenzene (1.8 g, 8.5 mmol, 1.0 equiv.), the title compound **37** was obtained after purification by column chromatography (SiO_2, Pentane:EtOAc 97:3) as a yellow oil (1.38 g, 7.19 mmol, 85 % yield). **R*f*** 0.3 (Pentane:EtOAc 95:5); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 6.57 (s, 2H, Ar*H*), 3.75 (s, 3H, OC*H*$_3$), 2.49 (tt, *J* = 6.8, 3.8 Hz, 1H, NHC*H*), 2.29 (s, 6H, C*H*$_3$), 0.62 – 0.53 (td, *J* = 6.8, 4.7 Hz, 2H, C*H*$_2$), 0.53 – 0.45 (td, *J* = 6.8, 4.7 Hz, 2H, C*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.5, 139.1, 131.1, 114.0, 55.5, 30.7, 19.6, 8.4; **IR $\tilde{\nu}_{max}$** 3365 (w), 2995 (w), 2947 (m), 2833 (w), 1609 (m), 1489 (s), 1358 (w), 1316 (m), 1256 (m), 1203 (m), 1149 (s), 1065 (s), 1019 (w), 999 (w), 855 (m), 836 (m); **HRMS (ESI)** calcd for $C_{12}H_{17}NO$ $[M]^+$ 191.1305; found 191.1308.

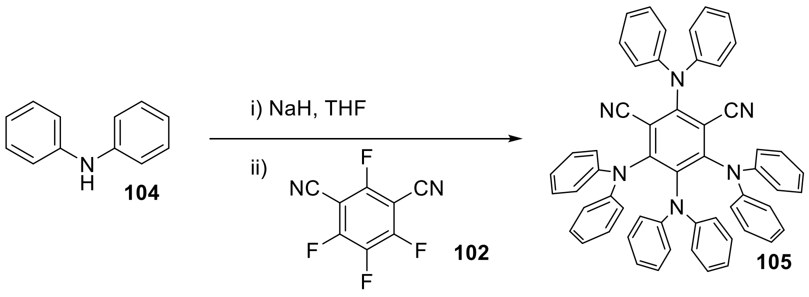
3. Synthesis of Organic Dyes

2,4,5,6-Tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN, 103)



Following a reported procedure,[21] sodium hydride (60% suspension in mineral oil, 0.60 g, 15 mmol, 7.5 equiv), was added slowly to a stirred solution of 9*H*-carbazole (**101**) (1.67 g, 10.0 mmol, 5.00 equiv) in dry THF (40 mL) under a nitrogen atmosphere at room temperature. After 45 min, 2,4,5,6-tetrafluoroisophthalo-nitrile (**102**) (0.40 g, 2.0 mmol, 1.0 equiv.) was added portionwise. After stirring at room temperature for 15 hours, 2 mL of water were added to the reaction mixture to quench the excess of NaH. The resulting mixture was then concentrated under reduced pressure. The obtained residue was purified by recrystallization from hexane/CH_2Cl_2 (1:1, 90 mL) affording the crude product as a yellow powder. Further purification by column chromatography (SiO_2, Pentane:DCM 50:50 to 40:60) afforded the title compound **103** as a bright yellow crystalline solid (1.14 g, 1.45 mmol, 73 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.2 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.8 – 7.6 (m, 8H, Ar*H*), 7.5 (ddd, *J* = 8.0, 6.6, 1.6 Hz, 2H, Ar*H*), 7.3 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.2 (dd, *J* = 8.4, 1.5 Hz, 4H, Ar*H*), 7.2 – 7.0 (m, 8H, Ar*H*), 6.8 (t, *J* = 7.8 Hz, 4H, Ar*H*), 6.6 (td, *J* = 7.6, 1.2 Hz, 2H, Ar*H*).**^{13}C NMR (101 MHz, Chloroform-*d*)** δ 145.2, 144.6, 140.0, 138.2, 136.9, 134.7, 127.0, 125.8, 124.9, 124.7, 124.5, 123.8, 122.4, 121.9, 121.4, 121.0, 120.4, 119.6, 116.3, 111.6, 109.9, 109.5, 109.4. The characterization data correspond to the reported values.[21]

2,4,5,6-Tetrakis(diphenylamino)isophthalonitrile (4DPAIPN, 105)



Following a slightly modified procedure,[21] sodium hydride (60% suspension in mineral oil, 0.65 g, 16 mmol, 8.0 equiv), was added slowly to a stirred solution diphenylamine (**104**) (2.03 g, 12.0 mmol, 6 equiv.) in dry DMF (20 mL). The resulting suspension was heated to 50 °C for 1 h. Then 2,4,5,6-tetrafluoroisophthalonitrile (**102**) (0.40 g, 2.0 mmol, 1.0 equiv.) was added portionwise,

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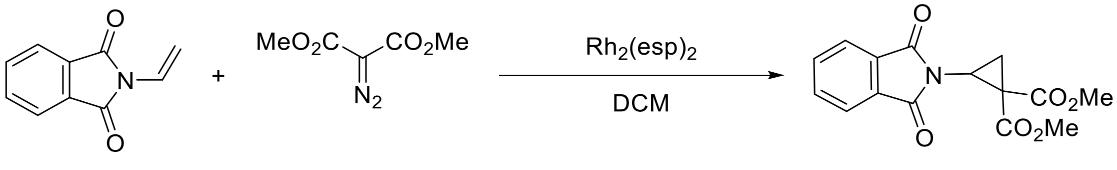
[21] M. Garreau, F. Le Vaillant, J. Waser, *Angew. Chem. Int. Ed.* **2019**, *58*, 8182–8186.

and the resulting reaction mixture was stirred at 50 °C for 4 h, and then at room temperature for 15 h. Water (5 mL) was added to quench the excess NaH, and the precipitate was filtered and purified by recrystallization from hexane/CH_2Cl_2 (1:2, 100 mL) to afford the title compound **105** as an orange crystalline solid (877 mg, 1.10 mmol, 55 % yield). **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 – 7.22 (m, 4H, ArH), 7.12 – 7.05 (m, 12H, ArH), 7.07 – 6.98 (m, 2H, ArH), 6.96 – 6.84 (m, 8H, ArH), 6.73 – 6.63 (m, 10H, ArH), 6.56 (d, J = 7.4 Hz, 4H, ArH). **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.2, 151.7, 145.5, 144.6, 143.1, 140.3, 129.4, 128.6, 127.5, 124.2, 123.9, 122.9, 122.6, 122.6, 121.1, 113.1, 113.0. The characterization data correspond to the reported values.[21]

4. Preliminary Attempts at the Lewis-Acid Catalysed [3+2] Annulation

4.1 Synthesis of the Donor-Acceptor Cyclopropane

Dimethyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (8)



106 **54** **8**

Following a modified procedure,[22] bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] (11 mg, 0.014 mmol, 0.1 mol%) was weighted in the glovebox. The flask was closed with a septum and put under N_2 atmosphere. A solution of *N*-vinyl-phthalimide (**106**) (2.5 g, 14 mmol, 1 equiv) in 30 mL of dry dichloromethane was added and the resulting green suspension was cooled down to 0 °C with an ice/water bath. A solution of dimethyl-2-diazomalonate (**54**) (2.5 g, 15 mmol, 1.1 equiv) in dichloromethane (20 mL) was then added over five minutes. When the addition was complete, the reaction wass allowed to warm to room temperature. After 5 hours at room temperature, the solvent wass removed under reduced pressure and the obtained crude residue was purified by column chromatography (SiO_2, Hexane:EtOAc 90:10 to 70:30) to afford compound **8** (3.4 g, 11 mmol, 78% yield) as a colorless solid. **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.86 (m, 2H, Phth), 7.75 (m, 2H, Phth), 3.85 (s, 3H, OCH_3), 3.72 (dd, 1H, *J* = 8.5, 6.6 Hz, NC*H*), 3.64 (s, 3H, OCH_3), 2.73 (dd, 1H, *J* = 6.5, 6.5 Hz, CH_2), 2.06 (dd, 1 H, J = 8.5, 6.4 Hz, CH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.5, 167.8, 166.9, 134.3, 131.4, 123.5, 53.1, 53.0, 34.9, 33.1, 19.6. The characterization data is corresponding to the reported values.[22]

4.2 Preliminary Cycloaddition Attempts

General method for the lewis acid catalyzed annulation:

A 5 mL microwave vial was charged in a glove box with the Lewis acid (10 mol%). The vial was sealed and put under N_2 atmosphere. A solution of 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (23 mg, 0.10 mmol, 1.0 equiv.) and dimethyl 2-(1,3-dioxoisoindolin-2-yl)cyclopropane-1,1-dicarboxylate (**8**) (36 mg, 0.12 mmol, 1.2 equiv.) in DCM was then added. The resulting reaction mixture was left stirring overnight at the indicated temperature. The reaction mixture was then filtered through a small pad of silica gel eluting with EtOAc, and the filtrate was concentrated under reduced pressure.

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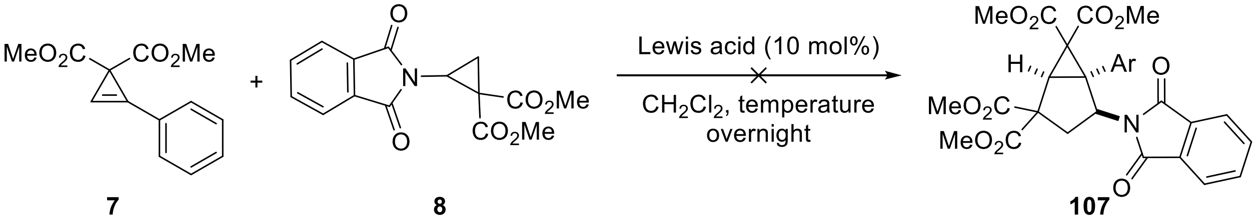
[22] F. Gonzalez-Bobes, M. D. B. Fenster, S. Kiau, L. Kolla, S. Kolotuchin, M. Soumeillant, *Adv. Synth. Catal.* **2008**, *350*, 813-816.

Table S1: [3+2] cycloaddition with donor-acceptor aminocyclopropane 8



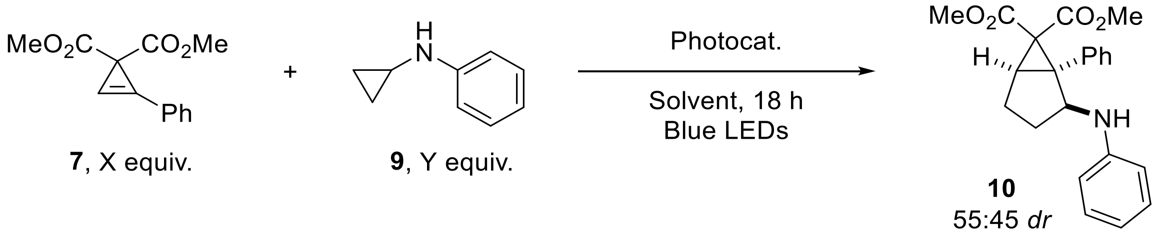
Entry	Lewis acid	Dilution	Temperature	Outcome
1	$Yb(OTf)_3$	1 M	RT	Complex mixture
2	$Hf(OTf)_4$	0.1 M	RT	Complex mixture
3	$SnCl_4$	0.1 M	-78 °C	Complex mixture

5. Optimizations

General method for the optimization:

A 2 mL test tube was charged with the photocatalyst, the cyclopropene (0.1 mmol, 1 equiv.) and the cyclopropylaniline. The tube was sealed, evacuated and back-filled with nitrogen (3 times). Then degassed solvent (3 freeze pump thaw cycles) was added via syringe and the resulting mixture was irradiated at room temperature for 18 h with Blue LEDs, positioned at 4 to 5 cm of the reaction vessel. The reaction mixture was then filtered through a small pad of silica gel eluting with Et_2O, and the filtrate was concentrated under reduced pressure. The obtained crude residue was then subjected to preparative TLC, leading to the isolation of the desired cycloadduct.

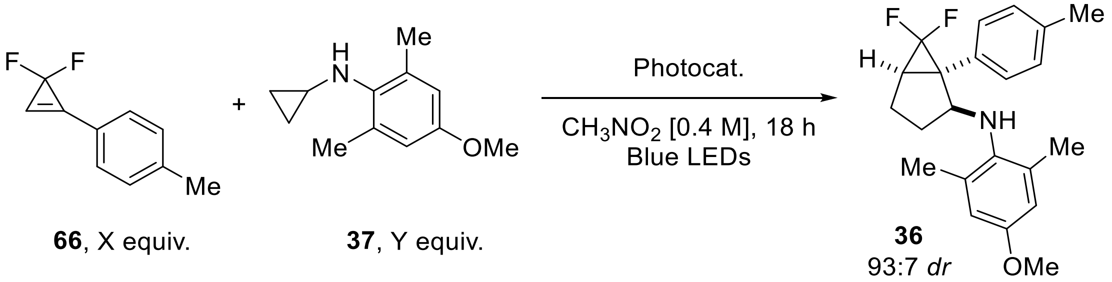
Table S2: Optimization of the general [3+2] cycloaddition



Entry	X	Y	Photocat. (mol %)	Solvent [M]	Isolated Yield
1	2.5	1.0	$Ru(bpz)_3(PF_6)_2$ (2)	CH_3NO_2 [0.1]	52%
2	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	CH_3NO_2 [0.1]	49%
3	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	CH_3CN [0.1]	38%
4	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	MeOH [0.1]	28%
5	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	DMF [0.1]	11%
6	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	THF [0.1]	24%
7	1.0	1.2	$Ru(bpz)_3(PF_6)_2$ (2)	DCE [0.1]	32%
8	1.0	1.5	$Ru(bpz)_3(PF_6)_2$ (2)	CH_3NO_2 [0.1]	53%
9	1.0	1.5	4CzIPn (5)	CH_3NO_2 [0.1]	60%
10	1.0	1.5	4CzIPn (5)	CH_3NO_2 [0.2]	70%
11	1.0	1.5	4CzIPn (5)	CH_3NO_2 [0.4]	82%
12	1.0	1.8	4CzIPn (5)	CH_3NO_2 [0.4]	86%
13	1.0	1.8	4DPAIPN (5)	CH_3NO_2 [0.4]	87% (87%[a])
14	1.0	1.8	$[Ir(dtbbpy)(ppy)_2][PF_6]$ (2)	CH_3NO_2 [0.4]	85%
15	1.0	2.5	$[Ir(dtbbpy)(ppy)_2][PF_6]$ (2)	CH_3NO_2 [0.4]	89%

[a] Isolated yield on 0.3 mmol.

Table S3: Optimization of the diastereoselective [3+2] cycloaddition

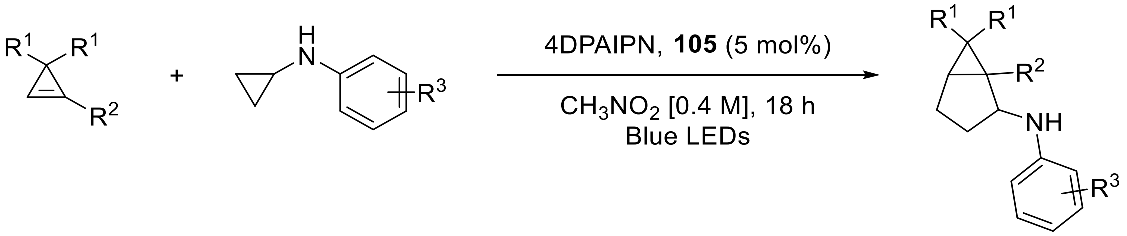


Entry	X	Y	Photocat. (mol %)	Isolated Yield
1	1.0	1.8	4CzIPn (5)	54%
2	2.5	1.0	4CzIPn (5)	47%
3	1.0	1.8	Ru(bpy)$_3$(PF$_6$)$_2$ (2)	52%
4	1.0	1.8	[Ir(dF-CF$_3$-ppy)$_2$(dtbpy)]PF$_6$ (2)	57%
5	2.5	1.0	4CzIPn (5)	56%
6	1.8	1.0	Ir(ppy)$_3$ (2)	26%
7	1.8	1.0	DCA (5)	9%
8	1.8	1.0	Ru(bpz)$_3$(PF$_6$)$_2$ (2)	32%
9	1.8	1.0	Rose Bengal (5)	39%
10	1.8	1.0	DPAIPN (5)	60% (57%)
11	1.8	1.0	[Ir(dtbbpy)(ppy)$_2$][PF$_6$] (2)	64%
12	2.5	1.0	DPAIPN (5)	67%
13	2.5	1.0	[Ir(dtbbpy)(ppy)$_2$][PF$_6$] (2)	72% (73%)

[a] Isolated yield on 0.3 mmol.

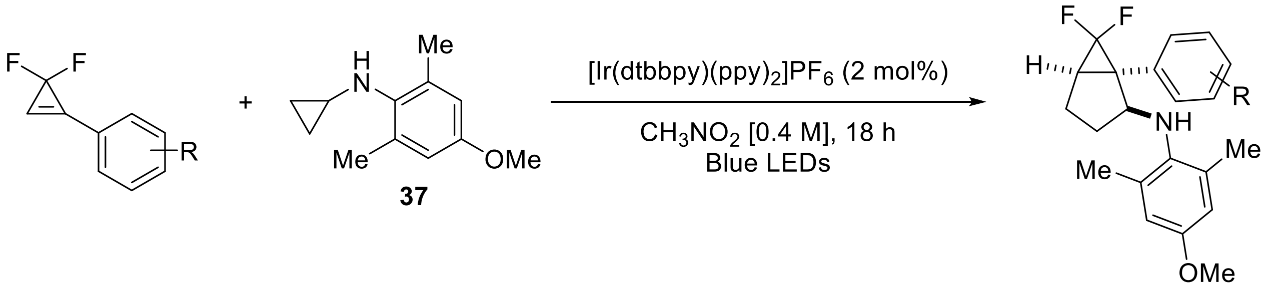
6. Photoredox Mediated [3+2] Cycloaddition

General procedure D



A 5 mL test tube was charged with 2,4,5,6-tetrakis(diphenylamino)isophthalonitrile (4-DPAIPN, **105**) (12 mg, 0.015 mmol, 0.05 equiv.), the cyclopropene (0.30 mmol, 1.0 equiv.) and the cyclopropylaniline (0.54 mmol, 1.8 equiv.). The tube was sealed, evacuated and back-filled with nitrogen (3 times). Then 0.75 mL of degassed nitromethane (3 freeze pump thaw cycles) was added via syringe and the resulting mixture was irradiated at room temperature for 18 hours with Blue LEDs, positioned at 4 to 5 cm of the reaction vessel. The reaction mixture was then filtered through a small pad of silica gel eluting with Et_2O, and the filtrate was concentrated under reduced pressure. The obtained crude residue was then subjected to column chromatography using the indicated solvents.

General procedure E

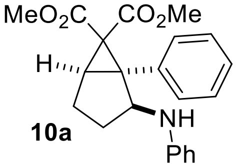


A 5 mL test tube was charged with $[Ir(dtbbpy)(ppy)_2]PF_6$ (5.5 mg, 6.0 µmol, 0.02 equiv.), the difluorocyclopropene (0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methoxy-2,6-dimethylaniline (**37**) (0.14 g, 0.75 mmol, 2.5 equiv.). The tube was sealed, evacuated and back-filled with nitrogen (3 times). Then 0.75 mL of degassed nitromethane (3 freeze pump thaw cycles) was added via syringe and the resulting mixture was irradiated at room temperature for 18 hours with Blue LEDs, positioned at 4 to 5 cm of the reaction vessel. The reaction mixture was then filtered through a small pad of silica gel eluting with Et_2O, and the filtrate was concentrated under reduced pressure. The obtained crude residue was then subjected to column chromatography using the indicated solvents.

The stereochemistry of the major diastereoisomer for the cycloadducts was assigned by analogy with compound **10a**, for which product modification led to **50**, confirming its proposed relative configuration. The stereochemistry of the minor diastereoisomer was assigned by analogy with compound **16b**, for which a crystal structure could be obtained by X-Ray diffraction.

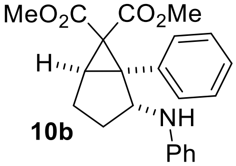
Dimethyl 1-phenyl-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (10)

Following the general procedure D, starting from dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **10** (55:45 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10).



10a

10a, major diastereoisomer, colorless oil (52 mg, 0.14 mmol, 47 % yield). **R*f*** 0.35 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.33 - 7.27 (m, 2H, Ar*H*), 7.24 - 7.14 (m, 3H, Ar*H*), 7.05 - 6.99 (m, 2H, Ar*H*), 6.55 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.45 (d, *J* = 7.4 Hz, 2H, Ar*H*), 5.23 (d, *J* = 10.4 Hz, 1H, N*H*), 4.42 (td, *J* = 10.3, 9.7, 7.0 Hz, 1H, C*H*NH), 3.86 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 2.65 (d, *J* = 4.6 Hz, 1H, C*H*CH$_2$), 2.35 - 2.12 (m, 3H, NHCHCH_2 and NHCHCH$_2$CH_2), 0.96 - 0.84 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.1, 167.8, 148.2, 137.8, 129.1, 129.0, 128.3, 127.4, 116.9, 113.2, 63.5, 53.4, 52.8, 50.5, 42.0, 34.8, 28.1, 24.5; **IR $\tilde{\nu}_{max}$** 3383 (w), 3055 (w), 3028 (w), 2955 (w), 1731 (s), 1602 (s), 1511 (s), 1436 (m), 1313 (s), 1236 (s), 1196 (m), 1124 (m), 1076 (m), 1011 (w), 934 (w); **HRMS (ESI)** calcd for $C_{22}H_{24}NO_4^+$ [M+H]$^+$ 366.1700; found 366.1700.



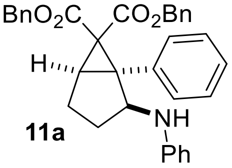
10b

10b, minor diastereoisomer, colorless oil (44 mg, 0.12 mmol, 40 % yield). **R*f*** 0.25 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.41 - 7.35 (m, 1H, Ar*H*), 7.36 - 7.28 (m, 2H, Ar*H*), 7.26 - 7.21 (m, 2H, Ar*H*), 7.11 - 7.02 (m, 2H, Ar*H*), 6.63 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.37 (d, *J* = 7.3 Hz, 2H, Ar*H*), 4.35 (d, *J* = 5.7 Hz, 1H, C*H*NH), 3.88 (s, 3H, OCH_3), 3.52 (bs, 1H, N*H*), 3.36 (s, 3H, OCH_3), 2.92 (d, *J* = 4.3 Hz, 1H, C*H*CH$_2$), 2.41 - 2.28 (m, 1H, NHCHCH$_2$CH_2), 2.14 (dd, *J* = 13.5, 8.3 Hz, 1H, NHCHCH$_2$CH_2), 1.92 (dd, *J* = 14.9, 9.4 Hz, 1H, NHCHCH_2), 1.46 - 1.33 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.1, 167.4, 146.9, 134.8, 129.8, 129.1, 128.9, 128.0, 117.6, 113.5, 58.8, 53.1, 52.7, 51.0, 42.5, 36.5, 30.1, 24.8; **IR $\tilde{\nu}_{max}$** 3407 (w), 3055 (w), 3028 (w), 2953 (w), 1735 (s), 1602 (s), 1504 (m), 1434 (m), 1315 (m), 1259 (s), 1211 (m), 1178 (m), 1121 (m), 1073 (w), 1013 (w); **HRMS (ESI)** calcd for $C_{22}H_{24}NO_4^+$ [M+H]$^+$ 366.1700; found 366.1698.

Dibenzyl 1-phenyl-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (11)

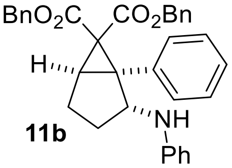
Following the general procedure D, starting from dibenzyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**62**) (0.12 g, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54

mmol, 1.8 equiv.), the title compound **11** (58:42 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 85:15).



11a

11a, major diastereoisomer, pale yellow oil (65 mg, 0.13 mmol, 42 % yield). **R$_f$** 0.40 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.39 – 7.33 (m, 5H, Ar*H*), 7.29 – 7.24 (m, 5H, Ar*H*), 7.16 (dp, *J* = 3.6, 2.0 Hz, 3H, Ar*H*), 7.06 – 7.01 (m, 2H, Ar*H*), 7.02 – 6.95 (m, 2H, Ar*H*), 6.54 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.32 (d, *J* = 7.3 Hz, 2H, Ar*H*), 5.25 (app. d, *J* = 2.5 Hz, 2H, C*H*$_2$Ph), 5.14 (d, *J* = 10.6 Hz, 1H, N*H*), 4.89 (d, *J* = 12.3 Hz, 1H, C*H*$_2$Ph), 4.71 (d, *J* = 12.2 Hz, 1H, C*H*$_2$Ph), 4.40 (td, *J* = 10.3, 7.4 Hz, 1H, C*H*NH), 2.65 (d, *J* = 4.2 Hz, 1H, C*H*CH$_2$), 2.30 – 2.10 (m, 3H, NHCHC*H*$_2$ and NHCHCH$_2$C*H*$_2$), 0.89 (td, *J* = 7.5, 6.6, 3.7 Hz, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 169.3, 167.3, 148.1, 137.7, 135.2, 134.9, 129.1, 129.0, 128.9, 128.5, 128.3, 128.3, 127.3, 116.8, 113.2, 68.4, 67.5, 63.7, 50.7, 42.2, 35.0, 28.0, 24.5; 3 aromatic carbons were not resolved. **IR $\tilde{\nu}_{max}$** 3385 (w), 3064 (w), 3031 (w), 2960 (w), 1729 (s), 1602 (m), 1513 (m), 1453 (w), 1401 (w), 1378 (w), 1312 (m), 1277 (m), 1254 (m), 1221 (s), 1187 (m), 1119 (m), 1075 (m), 911 (m); **HRMS (ESI)** calcd for $C_{34}H_{32}NO_4^+$ [M+H]$^+$ 518.2326; found 518.2332.

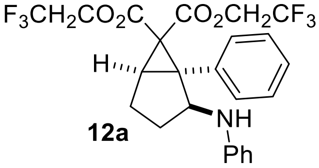


11b

11b, minor diastereoisomer, pale yellow oil (62 mg, 0.12 mmol, 40 % yield). **R$_f$** 0.35 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.46 – 7.40 (m, 2H, Ar*H*), 7.41 – 7.35 (m, 3H, Ar*H*), 7.34 – 7.30 (m, 1H, Ar*H*), 7.28 – 7.24 (m, 5H, Ar*H*), 7.19 (tt, *J* = 7.1, 1.7, 1H, Ar*H*), 7.13 (t, *J* = 7.5, 1H, Ar*H*), 7.08 – 6.95 (m, 4H, Ar*H*), 6.61 (t, *J* = 7.3, 1H, Ar*H*), 6.24 (d, *J* = 7.5, 2H, Ar*H*), 5.37 (d, *J* = 12.0, 1H, C*H*$_2$Ph), 5.20 (d, *J* = 12.0, 1H, C*H*$_2$Ph), 4.85 (d, *J* = 12.3, 1H, C*H*$_2$Ph), 4.67 (d, *J* = 12.4, 1H, C*H*$_2$Ph), 4.26 (d, *J* = 5.8, 1H, C*H*NH), 3.51 (bs, 1H, N*H*), 2.91 (d, *J* = 4.3, 1H, C*H*CH$_2$), 2.34 – 2.21 (m, 1H, NHCHCH$_2$C*H*$_2$), 2.10 (dd, *J* = 13.5, 8.3, 1H, NHCHCH$_2$C*H*$_2$), 1.75 (dd, *J* = 14.9, 9.4, 1H, NHCHC*H*$_2$), 1.31 – 1.26 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 167.2, 166.9, 146.9, 135.4, 135.2, 134.6, 130.0, 129.7, 129.1, 129.0, 128.8, 128.7, 128.5, 128.2, 128.1, 128.0, 127.9, 117.5, 113.4, 67.8, 67.3, 58.8, 51.1, 42.6, 36.6, 29.9, 24.7. **IR $\tilde{\nu}_{max}$** 3409 (w), 3057 (m), 3033 (m), 2960 (m), 2928 (m), 1731 (s), 1604 (s), 1500 (s), 1455 (m), 1430 (w), 1375 (w), 1309 (m), 1286 (s), 1257 (s), 1203 (s), 1180 (s), 1117 (s), 1071 (m), 1026 (w), 1003 (w), 982 (w), 907 (s); **HRMS (ESI)** calcd for $C_{34}H_{32}NO_4^+$ [M+H]$^+$ 518.2326; found 518.2327.

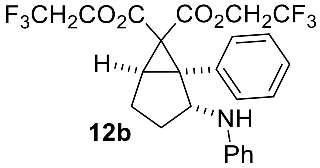
Bis(2,2,2-trifluoroethyl) 1-phenyl-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (12)

Following the general procedure D, starting from bis(2,2,2-trifluoroethyl) 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**63**) (0.11 g, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **12** (66:34 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 90:10 to 85:15).



12a

12a, major diastereoisomer, colorless oil (81 mg, 0.16 mmol, 54 % yield). **R*f*** 0.42 (Pentane:Et_2O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.31 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 3H, Ar*H*), 7.07 – 6.99 (m, 2H, Ar*H*), 6.59 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.44 (d, *J* = 7.4 Hz, 2H, Ar*H*), 5.07 (bs, 1H, N*H*) 4.77 (dq, *J* = 12.6, 8.3 Hz, 1H, CH_2CF_3), 4.59 – 4.45 (m, 2H, CH_2CF_3 and C*H*NH), 4.24 (dq, *J* = 12.7, 8.3 Hz, 1H, CH_2CF_3), 4.12 (dq, *J* = 12.6, 8.3 Hz, 1H, CH_2CF_3), 2.77 (d, *J* = 4.3 Hz, 1H, C*H*CH_2), 2.40 – 2.28 (m, 2H, $NHCHCH_2CH_2$ and $NHCHCH_2$), 2.24 (dd, *J* = 12.6, 8.7 Hz, 1H, $NHCHCH_2CH_2$), 1.03 – 0.90 (m, 1H, $NHCHCH_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 167.7, 165.4, 147.8, 136.6, 129.2, 128.9, 128.6, 127.8, 122.8 (q, *J* = 277.1 Hz), 122.5 (q, *J* = 276.9 Hz), 117.2, 113.2, 63.7, 61.9 (q, *J* = 37.0 Hz), 61.3 (q, *J* = 37.2 Hz), 52.1, 41.4, 36.2, 28.0, 24.3; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -73.4 (t, *J* = 8.3 Hz), -74.0 (t, *J* = 8.2 Hz); **IR $\tilde{\nu}_{max}$** 3414 (w), 3064 (w), 3028 (w), 2972 (w), 1752 (m), 1602 (m), 1513 (m), 1442 (w), 1413 (m), 1286 (s), 1250 (m), 1219 (m), 1171 (s), 1119 (m), 1084 (w), 971 (m), 911 (m); **HRMS (ESI)** calcd for $C_{24}H_{22}F_6NO_4^+$ $[M+H]^+$ 502.1448; found 502.1466.



12b

12b, minor diastereoisomer, colorless oil (36 mg, 0.072 mmol, 24 % yield). **R*f*** 0.36 (Pentane:Et_2O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.38 – 7.30 (m, 3H, Ar*H*), 7.26 – 7.23 (m, 2H, Ar*H*), 7.13 – 7.03 (m, 2H, Ar*H*), 6.67 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.38 (d, *J* = 7.2 Hz, 2H, Ar*H*), 4.65 (qd, *J* = 8.4, 1.2 Hz, 2H, CH_2CF_3), 4.41 (d, *J* = 5.9 Hz, 1H, C*H*NH), 4.20 (dq, *J* = 12.6, 8.3 Hz, 1H, CH_2CF_3), 4.05 (dq, *J* = 12.6, 8.3 Hz, 1H, CH_2CF_3), 3.03 (d, *J* = 4.4 Hz, 1H, C*H*CH_2), 2.50 – 2.37 (m, 1H, $NHCHCH_2CH_2$), 2.18 (dd, *J* = 13.8, 8.4 Hz, 1H, $NHCHCH_2CH_2$), 1.99 (dd, *J* = 15.2, 9.6 Hz, 1H, $NHCHCH_2$), 1.46 (dddd, *J* = 14.8, 10.8, 8.5, 5.9 Hz, 1H, $NHCHCH_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 165.4, 165.0, 146.4, 133.6, 129.7, 129.2, 128.4, 128.3, 122.9 (q, *J* = 277.3), 122.4 (q, *J* = 277.3), 118.2, 113.7, 61.4 (q, *J* = 37.0 Hz), 61.3 (q, *J* = 37.1 Hz) 59.0, 52.4, 41.9, 37.8, 29.9, 24.8; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -73.35 (t, *J* = 8.2 Hz), -74.03 (t, *J* = 8.2 Hz); **IR $\tilde{\nu}_{max}$** 3407 (w), 3058 (w), 3030 (w), 2974 (w), 1754 (m),

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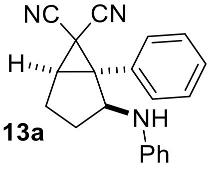
[23] N*H* was not resolved.

1602 (m), 1502 (m), 1411 (w), 1288 (s), 1250 (m), 1167 (s), 1117 (m), 1080 (w), 1026 (w), 982 (m), 909 (w); **HRMS (ESI)** calcd for $C_{24}H_{22}F_6NO_4^+$ $[M+H]^+$ 502.1448; found 502.1454.

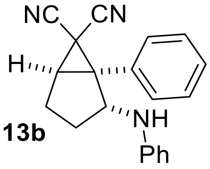
1-Phenyl-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarbonitrile (13)

Following the general procedure D, starting from 2-phenylcycloprop-2-ene-1,1-dicarbonitrile (**65**) (50 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **13** (70:30 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 70:30).



13a

13a, major diastereoisomer, brown oil (46 mg, 0.15 mmol, 51 % yield). **R*f*** 0.44 (Pentane:Et$_2$O 65:35); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.44 – 7.39 (m, 2H, Ar*H*), 7.38 – 7.33 (m, 3H, Ar*H*), 7.07 – 6.99 (m, 2H, Ar*H*), 6.67 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.34 (d, *J* = 7.6 Hz, 2H, Ar*H*), 4.65 (q, *J* = 9.3 Hz, 1H, C*H*NH), 4.09 (d, *J* = 9.1 Hz, 1H, N*H*), 2.79 (d, *J* = 3.5 Hz, 1H, C*H*CH$_2$), 2.56 – 2.41 (m, 3H, NHCHC*H$_2$* and NHCHCH$_2$C*H$_2$*), 1.90 – 1.79 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 146.8, 133.9, 129.5, 129.3, 128.9, 118.6, 114.7, 113.6, 113.6, 63.6, 55.9, 42.0, 30.1, 24.9, 12.9; **IR $\tilde{\nu}_{max}$** 3405 (m), 2970 (s), 2900 (s), 2245 (m), 1638 (s), 1603 (s), 1498 (s), 1441 (m), 1400 (s), 1315 (m), 1262 (s), 1175 (m), 1071 (s), 914 (s), 739 (s), 698 (s); **HRMS (ESI)** calcd for $C_{20}H_{18}N_3^+$ $[M+H]^+$ 300.1495; found 300.1503.

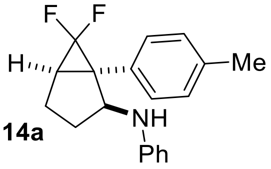


13b

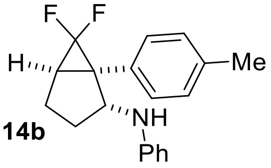
13b, minor diastereoisomer, brown oil (22 mg, 0.073 mmol, 25 % yield). **R*f*** 0.32 (Pentane:Et$_2$O 65:35); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.43 (dd, *J* = 4.3, 1.8 Hz, 5H, Ar*H*), 7.18 – 7.11 (m, 2H, Ar*H*), 6.76 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.45 (d, *J* = 7.4 Hz, 2H, Ar*H*), 4.46 (dd, *J* = 6.7, 2.0 Hz, 1H, C*H*NH), 3.06 (d, *J* = 4.7 Hz, 1H, C*H*CH$_2$), 2.68 – 2.55 (m, 1H, NHCHCH$_2$C*H$_2$*), 2.45 (dtd, *J* = 15.1, 8.7, 6.6 Hz, 1H, NHCHCH$_2$C*H$_2$*), 2.31 (ddd, *J* = 14.3, 8.9, 2.4 Hz, 1H, NHCHC*H$_2$*), 2.11 (ddt, *J* = 15.1, 10.8, 2.4 Hz, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 145.7, 130.9, 130.1, 129.5, 129.4, 119.0, 114.0, 113.3, 113.1, 58.6, 55.3, 42.1, 31.8, 25.2, 15.9; **IR $\tilde{\nu}_{max}$** 3395 (w), 3058 (w), 2932 (w), 2249 (m), 1603 (s), 1498 (s), 1439 (w), 1313 (m), 1258 (w), 1178 (w), 1031 (w), 912 (m), 737 (s), 694 (s); **HRMS (ESI)** calcd for $C_{20}H_{18}N_3^+$ $[M+H]^+$ 300.1495; found 300.1499.

6,6-Difluoro-*N*-phenyl-1-(p-tolyl)bicyclo[3.1.0]hexan-2-amine (14)

Following the general procedure D, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-methylbenzene (**66**) (50 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **14** (68:32 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 98:2 to 95:5).


14a

14a, major diastereoisomer, pale brown oil (56 mg, 0.19 mmol, 62 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 95:5); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.16 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.04 – 6.96 (m, 4H, Ar*H*), 6.57 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.42 (d, *J* = 7.7 Hz, 2H, Ar*H*), 4.44 (td, *J* = 8.9, 6.2 Hz, 1H, C*H*NH), 2.44 – 2.32 (m, 1H, CF$_2$CHC*H*$_2$), 2.29 – 2.18 (m, 5H, CF$_2$CHC*H*$_2$, NHCHC*H*$_2$ and C*H*$_3$), 2.09 (dd, *J* = 14.4, 5.0 Hz, 1H, C*H*CF$_2$), 1.54 – 1.43 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 147.5, 137.3, 132.1, 129.3, 128.7, 117.8, 116.8 (dd, *J* = 303.4, 281.6 Hz), 113.7, 63.9, 44.5 (dd, *J* = 11.7, 8.5 Hz), 33.6 (dd, *J* = 12.3, 9.0 Hz), 31.3 (d, *J* = 7.4 Hz), 24.5, 21.3; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.7 (dd, *J* = 161.0, 14.8 Hz), -138.5 (d, *J* = 160.4 Hz); **IR $\tilde{\nu}_{max}$** 3418 (w), 3025 (w), 2953 (m), 1733 (w), 1603 (s), 1511 (s), 1447 (s), 1315 (m), 1280 (m), 1245 (m), 1196 (s), 1155 (m), 1060 (m), 984 (s), 918 (m), 813 (m), 748 (s), 694 (m); **HRMS (ESI)** calcd for $C_{19}H_{20}F_2N^+$ [M+H]$^+$ 300.1558; found 300.1559.


14b

14b, minor diastereoisomer, pale brown oil (23 mg, 0.077 mmol, 26 % yield). **R*f*** 0.35 (Pentane:Et$_2$O 95:5); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.16 (d, *J* = 1.3 Hz, 4H, Ar*H*), 7.14 – 7.09 (m, 2H, Ar*H*), 6.69 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.46 (d, *J* = 7.8 Hz, 2H, Ar*H*), 4.22 (d, *J* = 4.4 Hz, 1H, C*H*NH), 2.42 (dd, *J* = 14.2, 5.3 Hz, 1H, C*H*CF$_2$), 2.37 – 2.29 (m, 4H, C*H*$_3$ and CF$_2$CHC*H*$_2$), 2.15 – 1.99 (m, 3H, CF$_2$CHC*H*$_2$ and NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 146.6, 138.0, 129.6, 129.5, 129.3, 128.9, 118.0, 115.5 (dd, *J* = 305.0, 276.3 Hz), 113.7, 57.6, 46.2 – 45.7 (m), 32.5 (dd, *J* = 11.4, 9.4 Hz), 31.8 (d, *J* = 9.7 Hz), 24.0, 21.3; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -125.5 (ddd, *J* = 158.3, 14.4, 4.9 Hz), -141.3 (d, *J* = 158.3 Hz); **IR $\tilde{\nu}_{max}$** 3405 (w), 3031 (w), 2932 (w), 2878 (w), 1602 (s), 1503 (s), 1431 (s), 1321 (m), 1251 (m), 1208 (m), 1082 (w), 993 (m), 923 (m), 820 (w), 752 (s), 690 (m); **HRMS (ESI)** calcd for $C_{19}H_{20}F_2N^+$ [M+H]$^+$ 300.1558; found 300.1561.

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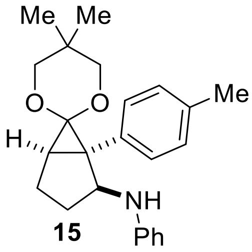
[24] One carbon was not resolved.

5',5'-Dimethyl-*N*-phenyl-1-(p-tolyl)spiro[bicyclo[3.1.0]hexane-6,2'-[1,3]dioxan]-2-amine (15)

Following the general procedure D, starting from 6,6-dimethyl-1-(*p*-tolyl)-4,8-dioxaspiro[2.5]oct-1-ene (**70**) (69 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **15** (> 95:5 *dr* in the crude ^{1}H NMR, putative minor diastereoisomer could not be detected) was obtained as a single diastereoisomer after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 98:2 to 95:5), and as a pale yellow oil (49 mg, 0.14 mmol, 45 % yield).

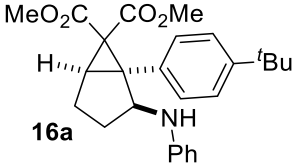


15

R*f* 0.55 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.31 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.14 – 7.05 (m, 4H, Ar*H*), 6.64 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.57 (d, *J* = 7.3 Hz, 2H, Ar*H*), 4.53 – 4.35 (m, 2H, C*H*NH & N*H*), 3.73 (d, *J* = 10.6 Hz, 1H, OC*H$_2$*), 3.61 (d, *J* = 10.6 Hz, 1H, OC*H$_2$*), 3.57 – 3.46 (m, 2H, OC*H$_2$*), 2.45 – 2.35 (m, 1H, CH), 2.31 (s, 3H, C$_{Ar}$-C*H$_3$*), 2.28 – 2.19 (m, 1H, NHCHCH$_2$C*H$_2$*), 2.13 (dd, *J* = 13.5, 9.0 Hz, 1H, NHCHCH$_2$C*H$_2$*), 1.89 (d, *J* = 5.3 Hz, 1H, NHCHC*H$_2$*), 1.69 – 1.56 (m, 1H, NHCHC*H$_2$*), 1.29 (s, 3H, C*H$_3$*), 0.82 (s, 3H, C*H$_3$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 148.5, 136.1, 135.5, 129.1, 128.8, 128.7, 116.8, 113.5, 94.1, 76.9, 76.3, 63.4, 46.0, 34.5, 32.5, 31.0, 25.4, 23.0, 22.1, 21.3; **IR $\tilde{\nu}_{max}$** 3399 (w), 3050 (w), 3026 (w), 2952 (m), 2863 (m), 1906 (w), 1601 (m), 1504 (m), 1464 (w), 1392 (w), 1308 (w), 1278 (w), 1241 (w), 1143 (m), 1115 (m), 1062 (m), 1012 (m), 969 (w), 908 (s), 811 (m), 728 (s), 691 (m), 646 (w); **HRMS (ESI)** calcd for $C_{24}H_{29}NNaO_2^+$ [M + Na]$^+$ 386.2090; found 386.2094.

Dimethyl 1-(4-(*tert*-butyl)phenyl)-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (16)

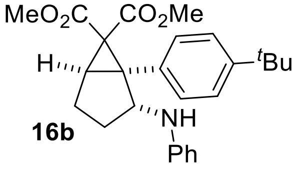
Following the general procedure D, starting from dimethyl 2-(4-(*tert*-butyl)phenyl)cycloprop-2-ene-1,1-dicarboxylate (**71**) (78 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **16** (54:46 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10).



16a

16a, major diastereoisomer, pale yellow oil (61 mg, 0.15 mmol, 48 % yield). **R*f*** 0.38 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.20 – 7.14 (m, 4H, Ar*H*), 7.06 – 7.00 (m, 2H, Ar*H*), 6.59 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.50 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.42 (dd, *J* =

10.1, 8.0 Hz, 1H, C*H*NH), 3.87 (s, 3H, OC*H*$_3$), 3.41 (s, 3H, OC*H*$_3$), 2.63 (d, *J* = 4.5 Hz, 1H, C*H*CH$_2$), 2.36 – 2.16 (m, 3H, NHCHC*H*$_2$ and NHCHCH$_2$C*H*$_2$), 1.24 (s, 9H, ^{t}Bu), 0.95 – 0.87 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.3, 167.7, 150.0, 147.5, 134.5, 129.1, 128.5, 125.1, 117.5, 113.9, 64.0, 53.4, 52.8, 49.9, 42.2, 34.9, 34.6, 31.4, 28.0, 24.5; **IR $\tilde{\nu}_{max}$** 3386 (w), 3028 (w), 2964 (m), 2875 (w), 1732 (s), 1604 (s), 1521 (s), 1438 (m), 1310 (s), 1246 (s), 1144 (m), 1010 (w), 908 (s), 735 (s); **HRMS (ESI)** calcd for $C_{26}H_{32}NO_4^+$ [M+H]$^+$ 422.2326; found 422.2332.

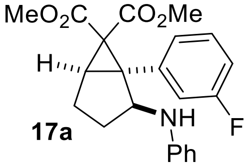


16b

16b, minor diastereoisomer, pale yellow solid (55 mg, 0.13 mmol, 44 % yield). **R*f*** 0.32 (Pentane:Et$_2$O 80:20); **m.p** = 59-62 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.34 – 7.26 (m, 2H, Ar*H*), 7.24 – 7.19 (m, 2H, Ar*H*), 7.10 – 7.03 (m, 2H, Ar*H*), 6.65 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.41 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.33 (d, *J* = 5.8 Hz, 1H, C*H*NH), 3.87 (s, 3H, OC*H*$_3$), 3.33 (s, 3H, OC*H*$_3$), 2.91 (d, *J* = 4.4 Hz, 1H, C*H*CH$_2$), 2.44 – 2.29 (m, 1H, NHCHCH$_2$C*H*$_2$), 2.12 (dd, *J* = 13.4, 8.3 Hz, 1H, NHCHCH$_2$C*H*$_2$), 1.94 (dd, *J* = 14.9, 9.4 Hz, 1H, NHCHC*H*$_2$), 1.44 – 1.35 (m, 1H, NHCHC*H*$_2$), 1.27 (s, 9H, ^{t}Bu); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.1, 167.4, 150.8, 146.5, 131.3, 129.6, 129.3, 129.1, 126.0, 124.7, 118.0, 114.0, 59.2, 53.1, 52.6, 50.5, 42.6, 36.3, 34.7, 31.4, 29.9, 24.8; **IR $\tilde{\nu}_{max}$** 3398 (w), 2964 (m), 2875 (w), 1732 (s), 1604 (m), 1502 (m), 1438 (m), 1259 (s), 1208 (m), 1125 (m), 914 (s), 735 (s), 697 (m); **HRMS (ESI)** calcd for $C_{26}H_{32}NO_4^+$ [M+H]$^+$ 422.2326; found 422.2321.

Dimethyl 1-(3-fluorophenyl)-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (17)

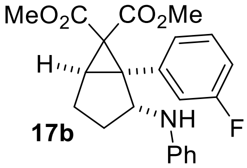
Following the general procedure D, starting from dimethyl 2-(3-fluorophenyl)cycloprop-2-ene-1,1-dicarboxylate (**72**) (75 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **17** (56:44 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 85:15).



17a

17a, major diastereoisomer, pale yellow oil (57 mg, 0.15 mmol, 50 % yield). **R*f*** 0.45 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.17 (td, *J* = 7.9, 5.9 Hz, 1H, Ar*H*), 7.13 – 6.98 (m, 4H, Ar*H*), 6.88 (tdd, *J* = 8.4, 2.7, 1.1 Hz, 1H, Ar*H*), 6.60 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.6 Hz, 2H, Ar*H*), 5.35 (bs, 1H, N*H*), 4.44 (dd, *J* = 10.1, 7.6 Hz, 1H, C*H*NH), 3.88 (s, 3H, OC*H*$_3$), 3.47 (s, 3H, OC*H*$_3$), 2.65 (d, *J* = 4.1 Hz, 1H, C*H*CH$_2$), 2.38 – 2.15 (m, 3H, NHCHC*H*$_2$ and NHCHCH$_2$C*H*$_2$), 0.96 – 0.86 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 169.9, 167.6, 162.6 (d, *J* = 246.0 Hz), 147.7, 140.3 (d, *J* = 7.7 Hz), 129.7 (d, *J*

= 8.4 Hz), 129.2, 124.8 (d, *J* = 2.9 Hz), 117.4, 116.0 (d, *J* = 21.6 Hz), 114.4 (d, *J* = 21.0 Hz), 113.5, 63.5, 53.5, 52.9, 49.9, 42.1, 35.1, 28.0, 24.4; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -113.4 (td, *J* = 8.8, 6.0 Hz); **IR $\tilde{\nu}_{max}$** 3373 (m), 3028 (w), 2958 (m), 1725 (s), 1604 (s), 1508 (m), 1432 (s), 1309 (s), 1235 (s), 1190 (s), 1149 (s), 1075 (m), 992 (w), 912 (s), 867 (m), 789 (m), 733 (s), 692 (s), 651 (w); **HRMS (ESI)** calcd for $C_{22}H_{23}FNO_4^+$ $[M+H]^+$ 384.1606; found 384.1606.

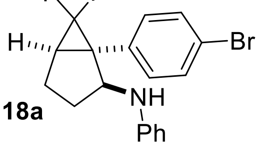


17b

17b, minor diastereoisomer, pale yellow oil (47 mg, 0.12 mmol, 41 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*, 1:1 mixture of rotamers (A/B))** δ 7.25 – 7.19 (m, 0.5H, Ar*H* (A)), 7.13 – 7.07 (m, 1H, Ar*H* (A+B)), 7.04 – 6.96 (m, 3H, Ar*H* (A+B)), 6.96 – 6.91 (m, 0.5H, Ar*H* (B)), 6.88 – 6.78 (m, 1H, Ar*H* (A+B)), 6.57 (t, *J* = 7.2 Hz, 1H, Ar*H* (A+B)), 6.32 (dd, *J* = 8.2, 3.4 Hz, 2H, Ar*H* (A+B)), 4.30 (dd, *J* = 12.8, 5.9 Hz, 1H, C*H*NH (A+B)), 3.80 (s, 3H, OC*H*$_3$ (A+B)), 3.47 (s, 1H, N*H* (A+B)), 3.36 (s, 1.5H, OC*H*$_3$ (A)), 3.32 (s, 1.5H, OC*H*$_3$ (B)), 2.82 (dd, *J* = 7.8, 4.4 Hz, 1H, C*H*CH$_2$ (A+B)), 2.26 (dddd, *J* = 14.0, 10.9, 9.4, 4.5 Hz, 1H, NHCHCH$_2$C*H*$_2$ (A+B)), 2.06 (dd, *J* = 13.6, 8.3 Hz, 1H, NHCHCH$_2$C*H*$_2$ (A+B)), 1.83 (dd, *J* = 15.0, 9.4 Hz, 1H, NHCHC*H*$_2$ (A+B)), 1.34 (ddq, *J* = 14.6, 9.3, 5.4 Hz, 1H, NHCHC*H*$_2$ (A+B)); **^{13}C NMR (101 MHz, Chloroform-*d*, 1:1 mixture of rotamers)** δ 167.2, 162.9 (d, *J* = 247.4 Hz), 162.3 (d, *J* = 246.7 Hz), 146.6, 146.5, 137.6 (t, *J* = 7.5 Hz), 130.3 (d, *J* = 8.3 Hz), 129.6 (d, *J* = 8.5 Hz), 129.2, 125.6 (d, *J* = 3.1 Hz), 117.8, 117.8, 117.1 (d, *J* = 21.5 Hz), 116.6 (d, *J* = 21.2 Hz), 115.2 (d, *J* = 21.2 Hz), 114.8 (d, *J* = 20.8 Hz), 113.5, 113.5, 59.0, 58.9, 53.2, 52.9, 52.8, 50.4, 50.4, 42.7, 42.5, 36.8, 36.6, 30.2, 30.0, 24.6; Not all carbon were resolved. **^{19}F NMR (376 MHz, Chloroform-d, 1:1 mixture of rotamers (A/B)**) δ -112.7 (q, *J* = 8.4 Hz (A)), -113.2 (q, *J* = 7.2 Hz (B)); **IR $\tilde{\nu}_{max}$** 3411 (m), 3060 (m), 2964 (m), 1735 (s), 1601 (m), 1498 (m), 1433 (m), 1243 (s), 1212 (s), 1180 (s), 1120 (m), 1073 (w), 1017 (w), 959 (m), 908 (s), 731 (s), 694 (s), 651 (m); **HRMS (ESI)** calcd for $C_{22}H_{23}FNO_4^+$ $[M+H]^+$ 384.1606; found 384.1603.

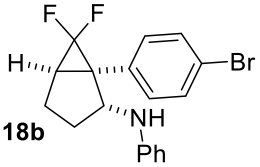
1-(4-Bromophenyl)-6,6-difluoro-*N*-phenylbicyclo[3.1.0]hexan-2-amine (18)

Following the general procedure D, starting from 1-bromo-4-(3,3-difluorocycloprop-1-en-1-yl)benzene (**73**) (69 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **18** (67:33 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 98:2 to 95:5).



18a

18a, major diastereoisomer, pale orange oil (65 mg, 0.18 mmol, 60 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.41 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.23 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.13 – 7.05 (m, 2H, Ar*H*), 6.68 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.2 Hz, 2H, Ar*H*), 4.53 (td, *J* = 8.8, 6.0 Hz, 1H, C*H*NH), 4.04 (bs, 1H, N*H*), 2.52 – 2.40 (m, 1H, NHCHC*H₂*), 2.38 – 2.22 (m, 2H, CF_2CHC*H₂*), 2.18 (dd, *J* = 14.3, 4.9 Hz, 1H, C*H*CF_2), 1.64 – 1.50 (m, 1H, NHCHC*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 147.2, 134.3, 131.7, 130.6, 129.4, 121.7, 118.1, 116.4 (dd, *J* = 303.5, 281.3 Hz), 113.7, 63.7, 44.3 (dd, *J* = 11.9, 8.2 Hz), 33.7 (dd, *J* = 12.6, 9.1 Hz), 31.3 (d, *J* = 7.4 Hz), 24.4; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.7 (dd, *J* = 161.6, 13.8 Hz), -138.6 (d, *J* = 161.5 Hz); **IR $\tilde{\nu}_{max}$** 3405 (w), 3053 (w), 2951 (m), 2875 (w), 1603 (s), 1509 (s), 1496 (s), 1443 (m), 1396 (w), 1309 (m), 1284 (m), 1243 (m), 1206 (s), 1194 (s), 1151 (m), 1060 (m), 1013 (m), 986 (s), 910 (s), 820 (m), 729 (s), 692 (s), 653 (m); **HRMS (ESI)** calcd for $C_{18}H_{17}BrF_2N^+$ $[M+H]^+$ 364.0507; found 364.0502.

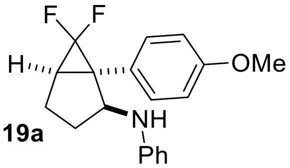


18b

18b, minor diastereoisomer, pale orange oil (32 mg, 0.088 mmol, 29 % yield). **R*f*** 0.34 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.49 – 7.43 (m, 2H, Ar*H*), 7.17 – 7.08 (m, 4H, Ar*H*), 6.70 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.46 (d, *J* = 7.7 Hz, 2H, Ar*H*), 4.28 (d, *J* = 5.0 Hz, 1H, C*H*NH), 3.53 (bs, 1H, N*H*) 2.44 (dd, *J* = 14.3, 5.3 Hz, 1H, C*H*CF_2), 2.38 – 2.25 (m, 1H, CF_2CHC*H₂*), 2.16 – 1.99 (m, 3H, CF_2CHC*H₂* and NHCHC*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 146.2, 131.8, 131.2, 129.2, 122.0, 118.1, 114.9 (dd, *J* = 305.0, 276.6 Hz), 113.5, 57.3, 45.7 (dd, *J* = 12.4, 9.3 Hz), 32.6 (dd, *J* = 11.7, 9.1 Hz), 31.9 (d, *J* = 9.4 Hz), 23.7; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -125.4 (ddd, *J* = 159.2, 14.3, 4.6 Hz), -141.3 (d, *J* = 159.3 Hz); **IR $\tilde{\nu}_{max}$** 3417 (w), 3053 (w), 2945 (m), 2862 (w), 1725 (w), 1604 (s), 1502 (s), 1425 (s), 1310 (m), 1247 (m), 1208 (m), 1075 (m), 994 (s), 906 (s), 822 (s), 727 (s), 694 (s), 649 (m); **HRMS (ESI)** calcd for $C_{18}H_{17}BrF_2N^+$ $[M+H]^+$ 364.0507; found 364.0502.

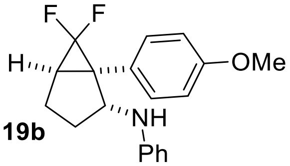
6,6-Difluoro-1-(4-methoxyphenyl)-*N*-phenylbicyclo[3.1.0]hexan-2-amine (19)

Following the general procedure D, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-methoxybenzene (**74**) (55 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **19** (68:32 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 98:2 to 95:5).



19a

19a, major diastereoisomer, yellow oil (45 mg, 0.14 mmol, 48 % yield). **R*f*** 0.40 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 – 7.27 (m, 2H, Ar*H*), 7.12 – 7.06 (m, 2H, Ar*H*), 6.87 – 6.81 (m, 2H, Ar*H*), 6.66 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.7 Hz, 2H, Ar*H*), 4.52 (td, *J* = 8.8, 6.1 Hz, 1H, C*H*NH), 3.97 (bs, 1H, N*H*), 3.78 (s, 3H, C*H₃*), 2.53 – 2.40 (m, 1H, NHCHC*H*$_2$), 2.39 – 2.23 (m, 2H, CF$_2$CHC*H*$_2$), 2.16 (dd, *J* = 14.3, 5.0 Hz, 1H, C*H*CF$_2$), 1.64 – 1.50 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 159.1, 147.7, 129.9, 129.3, 127.2, 117.6, 116.9 (hidden dd, one peak was not found due to overlapping), 114.0, 113.5, 63.9, 55.4, 44.3 (dd, *J* = 11.7, 8.3 Hz), 33.6 (dd, *J* = 12.4, 9.0 Hz), 31.3 (d, *J* = 7.5 Hz), 24.4; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.7 (dd, *J* = 160.2, 14.3 Hz), -138.7 (d, *J* = 159.6 Hz); **IR $\tilde{\nu}_{max}$** 3405 (w), 3041 (w), 2945 (m), 2836 (w), 1604 (s), 1515 (s), 1444 (m), 1291 (m), 1246 (s), 1188 (m), 1180 (m), 1151 (m), 1066 (m), 1038 (m), 1021 (m), 984 (s), 943 (w), 912 (s), 828 (s), 807 (m), 752 (s), 731 (s), 694 (s); **HRMS (ESI)** calcd for $C_{19}H_{20}F_2NO^+$ [M+H]$^+$ 316.1507; found 316.1511.

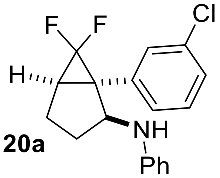


19b

19b, minor diastereoisomer, yellow oil (19 mg, 0.060 mmol, 20 % yield). **R*f*** 0.34 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.23 – 7.17 (m, 2H, Ar*H*), 7.16 – 7.08 (m, 2H, Ar*H*), 6.91 – 6.85 (m, 2H, Ar*H*), 6.69 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.46 (d, *J* = 7.6 Hz, 2H, Ar*H*), 4.20 (d, *J* = 4.6 Hz, 1H, C*H*NH), 3.80 (s, 3H, C*H*$_3$), 3.62 (bs, 1H, N*H*), 2.39 (dd, *J* = 14.1, 5.3 Hz, 1H, C*H*CF$_2$), 2.36 – 2.25 (m, 1H, CF$_2$CHC*H*$_2$), 2.17 – 1.98 (m, 3H, CF$_2$CHC*H*$_2$ and NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 159.4, 146.7, 130.8, 129.3, 123.9, 117.8, 115.5 (dd, *J* = 304.6, 276.1 Hz), 114.3, 113.5, 57.4, 55.4, 45.7 (dd, *J* = 12.2, 9.5 Hz), 32.7 (dd, *J* = 11.8, 8.9 Hz), 32.0 (d, *J* = 9.5 Hz), 24.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -125.6 (ddd, *J* = 158.1, 14.2, 4.9 Hz), -141.5 (d, *J* = 156.7 Hz); **IR $\tilde{\nu}_{max}$** 3053 (w), 2951 (m), 3398 (w), 2849 (w), 1732 (w), 1601 (s), 1515 (s), 1505 (s), 1426 (s), 1299 (m), 1252 (s), 1206 (m), 1180 (s), 1108 (m), 1075 (m), 1036 (m), 992 (s), 922 (m), 908 (m), 832 (m), 746 (s), 692 (s); **HRMS (ESI)** calcd for $C_{19}H_{20}F_2NO^+$ [M+H]$^+$ 316.1507; found 316.1514.

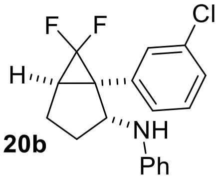
1-(3-Chlorophenyl)-6,6-difluoro-*N*-phenylbicyclo[3.1.0]hexan-2-amine (20)

Following the general procedure D, starting from 1-chloro-3-(3,3-difluorocycloprop-1-en-1-yl)benzene (**75**) (56 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **20** (67:33 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 98:2 to 95:5).



20a

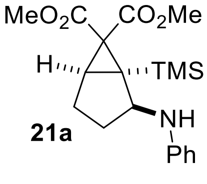
20a, major diastereoisomer, pale yellow oil (52 mg, 0.16 mmol, 54 % yield). **R*f*** 0.46 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.35 – 7.31 (m, 1H, Ar*H*), 7.29 – 7.26 (m, 1H, Ar*H*), 7.25 – 7.18 (m, 2H, Ar*H*), 7.12 – 7.06 (m, 2H, Ar*H*), 6.67 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.49 (d, *J* = 7.4 Hz, 2H, Ar*H*), 4.54 (td, *J* = 8.9, 6.1 Hz, 1H, C*H*NH), 3.92 (bs, 1H, N*H*), 2.46 (m, 1H, NHCHCH_2), 2.39 – 2.26 (m, 2H, CF$_2$CHCH_2), 2.20 (dd, *J* = 14.4, 5.0 Hz, 1H, C*H*CF$_2$), 1.63 – 1.49 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 147.4, 137.3, 134.3, 129.8, 129.3, 128.9 (d, *J* = 2.7 Hz), 127.9, 127.4, 118.0, 116.3 (dd, *J* = 303.4, 281.5 Hz), 113.7, 63.7, 44.5 (dd, *J* = 12.0, 8.3 Hz), 33.8 (dd, *J* = 12.5, 9.1 Hz), 31.3 (d, *J* = 7.4 Hz), 24.4; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.4 (dd, *J* = 161.4, 14.1 Hz), -138.4 (d, *J* = 161.6 Hz); **IR $\tilde{\nu}_{max}$** 3411 (m), 3060 (m), 2951 (m), 2875 (w), 1604 (s), 1502 (s), 1444 (m), 1311 (m), 1284 (m), 1243 (s), 1208 (s), 1198 (s), 1153 (s), 1064 (m), 988 (s), 949 (w), 912 (m), 879 (w), 785 (m), 750 (s), 694 (s); **HRMS (ESI)** calcd for $C_{18}H_{17}ClF_2N^+$ $[M+H]^+$ 320.1012; found 320.0998.


20b

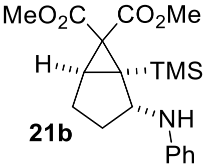
20b, minor diastereoisomer, pale yellow oil (29 mg, 0.091 mmol, 30 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.27 – 7.24 (m, 3H, Ar*H*), 7.19 – 7.15 (m, 1H, Ar*H*), 7.14 – 7.08 (m, 2H, Ar*H*), 6.69 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.46 (d, *J* = 7.6 Hz, 2H, Ar*H*), 4.30 (d, *J* = 4.6 Hz, 1H, C*H*NH), 3.54 (bs, 1H, N*H*), 2.45 (dd, *J* = 14.4, 5.3 Hz, 1H, C*H*CF$_2$), 2.38 – 2.25 (m, 1H, CF$_2$CHCH_2), 2.16 – 1.98 (m, 3H, CF$_2$CHCH_2 and NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 146.3, 134.6, 134.4 (d, *J* = 3.7 Hz), 130.0, 129.7 (d, *J* = 2.7 Hz), 129.3, 128.4, 128.0, 118.1, 115.0 (dd, *J* = 304.9, 276.8 Hz), 113.6, 57.4, 46.0 (dd, *J* = 12.5, 9.2 Hz), 32.7 (dd, *J* = 11.8, 9.0 Hz), 32.0 (d, *J* = 9.5 Hz), 23.8; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -125.2 (ddd, *J* = 159.4, 14.5, 5.0 Hz), -141.2 (d, *J* = 158.3 Hz); **IR $\tilde{\nu}_{max}$** 3405 (m), 3047 (m), 2958 (m), 2881 (m), 1601 (s), 1568 (m), 1505 (s), 1426 (s), 1315 (m), 1247 (s), 1208 (s), 1169 (m), 1089 (m), 1001 (s), 931 (s), 879 (m), 791 (s), 748 (s), 690 (s); **HRMS (ESI)** calcd for $C_{18}H_{17}ClF_2N^+$ $[M+H]^+$ 320.1012; found 320.1007.

Dimethyl 2-(phenylamino)-1-(trimethylsilyl)bicyclo[3.1.0]hexane-6,6-dicarboxylate (21)

Following the general procedure D, starting from dimethyl 2-(trimethylsilyl)cycloprop-2-ene-1,1-dicarboxylate (**77**) (69 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **21** (59:41 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10).


21a

21a, major diastereoisomer, colorless oil (28 mg, 0.077 mmol, 26 % yield). **R*f*** 0.35 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.19 – 7.10 (m, 2H, Ar*H*), 6.65 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.58 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.24 (bs, 1H, N*H*), 4.34 (t, *J* = 8.8 Hz, 1H, C*H*NH), 3.78 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 2.27 – 2.09 (m, 3H, C*H*CH$_2$, NHCHCH_2 and NHCHCH$_2$CH_2), 2.08 – 1.96 (m, 1H, NHCHCH$_2$CH_2), 0.56 (dtd, *J* = 13.7, 10.2, 8.4 Hz, 1H, NHCHC*H₂*), 0.11 (s, 9H, TMS); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 171.0, 170.6, 147.8, 129.3, 117.0, 113.3, 60.4, 53.3, 53.0, 39.8, 36.8, 35.9, 26.1, -0.5; **IR $\tilde{\nu}_{max}$** 3028 (w), 2958 (m), 2894 (w), 3373 (w), 1729 (s), 1603 (m), 1513 (m), 1435 (m), 1309 (m), 1182 (m), 1130 (m), 1075 (w), 978 (w), 908 (m), 844 (s), 754 (m), 692 (m); **HRMS (ESI)** calcd for $C_{19}H_{28}NO_4Si^+$ $[M+H]^+$ 362.1782; found 362.1773.

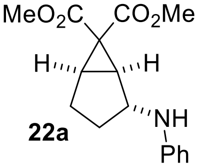


21b

21b, minor diastereoisomer, colorless oil (25 mg, 0.069 mmol, 23 % yield). **R*f*** 0.25 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.23 – 7.12 (m, 2H, Ar*H*), 6.72 (t, *J* = 7.3 Hz, 1H, Ar*H*), 6.58 (d, *J* = 7.6 Hz, 2H, Ar*H*), 4.22 (d, *J* = 5.4 Hz, 1H, C*H*NH), 3.76 (s, 3H, OC*H₃*), 3.70 (s, 3H, OC*H₃*), 2.61 (d, *J* = 4.0 Hz, 1H, C*H*CH₂), 2.20 – 1.96 (m, 2H, NHCHCH₂C*H₂*), 1.55 – 1.51 (m, 1H, NHCHC*H₂*), 1.14 – 1.03 (m, 1H, NHCHC*H₂*), 0.10 (s, 9H, TMS); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 169.4, 169.0, 146.1, 129.5, 118.1, 114.1, 60.1, 53.0, 53.0, 41.2, 36.7, 29.3, 24.7, 0.9; **IR $\tilde{\nu}_{max}$** 3383 (w), 2924 (m), 2853 (s), 1734 (s), 1604 (m), 1551 (w), 1503 (m), 1441 (m), 1307 (m), 1247 (s), 1208 (m), 1169 (m), 1123 (m), 1072 (w), 1010 (w), 915 (m), 849 (m), 745 (m), 696 (s); **HRMS (ESI)** calcd for $C_{19}H_{28}NO_4Si^+$ $[M+H]^+$ 362.1782; found 362.1777.

Dimethyl 2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (22)

Following the general procedure D, starting from dimethyl cycloprop-2-ene-1,1-dicarboxylate (**78**) (47 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylaniline (**9**) (72 mg, 0.54 mmol, 1.8 equiv.), the title compound **22** (69:31 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 90:10 to 80:20).



22a

22a, major diastereoisomer,[25] colorless oil (22 mg, 0.076 mmol, 25 % yield). **R*f*** 0.42 (Pentane:Et_2O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.24 – 7.16 (m, 2H, Ar*H*), 6.76 (t, *J* = 7.4 Hz, 1H, Ar*H*), 6.69 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.12 (d, *J* = 6.6 Hz, 1H, C*H*NH), 3.80 (s, 3H, OC*H₃*), 3.71 (s, 3H, OC*H₃*), 2.31 – 2.24 (m, 2H, NHCHC*H* & C_{quat}C*H*), 2.22 – 2.11 (m, 1H, NHCHCH₂C*H₂*), 2.07 (dd, *J* = 13.8, 8.7 Hz, 1H, NHCHCH₂C*H₂*), 1.74 (dd, *J* = 15.3, 9.3 Hz, 1H, NHCHC*H₂*), 1.34 – 1.26 (m, 1H, NHCHC*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.2, 167.8, 146.1, 129.5, 118.5, 114.1, 55.0, 53.1, 53.0, 38.2, 36.3, 34.1, 29.7, 24.6; **IR $\tilde{\nu}_{max}$** 3398 (w), 2951 (m), 1725 (s), 1605 (s), 1507 (m), 1435 (s), 1326 (s), 1252 (s), 1196 (m), 1161 (s), 1114

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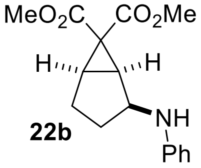
[25] Relative stereochemistry attributed by analogy with compounds **16b**, based on ^{1}H NMR chemical shifts and couplings.

(m), 1064 (w), 994 (w), 908 (m), 731 (s), 694 (m); **HRMS (ESI)** calcd for $C_{16}H_{19}NNaO_4^+$ [M+Na]$^+$ 312.1206; found 312.1212.

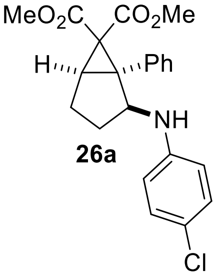


22b

22b, minor diastereoisomer,[26] pale yellow oil (8 mg, 0.03 mmol, 9 % yield). **R*f*** 0.30 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.20 – 7.15 (m, 2H, Ar*H*), 6.72 – 6.65 (m, 3H, Ar*H*), 4.70 (bs, 1H, N*H*), 4.47 (ddd, *J* = 10.3, 8.3, 4.4 Hz, 1H, C*H*NH), 3.84 (s, 3H, OC*H$_3$*), 3.70 (s, 3H, OC*H$_3$*), 2.43 (dd, *J* = 6.7, 4.3 Hz, 1H, NHCHC*H*), 2.21 – 2.01 (m, 4H, C$_{quat}$C*H*, NHCHCH$_2$C*H$_2$* and NHCHC*H$_2$*), 0.78 – 0.63 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.3, 169.7, 147.9, 129.5, 117.7, 113.8, 55.9, 53.2, 53.1, 37.1, 36.1, 32.1, 27.4, 25.0; **IR $\tilde{\nu}_{max}$** 3379 (w), 3034 (w), 2951 (m), 2856 (w), 1732 (s), 1603 (s), 1515 (s), 1435 (m), 1313 (s), 1247 (s), 1202 (m), 1163 (m), 1114 (w), 916 (w), 752 (s), 696 (m); **HRMS (ESI)** calcd for $C_{16}H_{20}NO_4^+$ [M+H]$^+$ 290.1387; found 290.1388.

Dimethyl 2-((4-chlorophenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (26)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and 4-chloro-*N*-cyclopropylaniline (**92**) (91 mg, 0.54 mmol, 1.8 equiv.), the title compound **26** (56:44 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10).



26a

26a, major diastereoisomer, pale yellow oil (48 mg, 0.12 mmol, 40 % yield). **R*f*** 0.38 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 – 7.28 (m, 2H, Ar*H*), 7.26 – 7.20 (m, 3H, Ar*H*), 6.97 (d, *J* = 8.8, 2H, Ar*H*), 6.38 (d, *J* = 8.9, 2H, Ar*H*), 5.38 (s, 1H, N*H*), 4.40 (dd, *J* = 10.3, 7.6, 1H, C*H*NH), 3.90 (s, 3H, OC*H$_3$*), 3.44 (s, 3H, OC*H$_3$*), 2.68 (d, *J* = 4.3, 1H, C*H*CH$_2$), 2.34 – 2.18 (m, 3H, NHCHC*H$_2$* and NHCHCH$_2$C*H$_2$*), 0.93 (dtd, *J* = 16.9, 8.3, 7.9, 3.4, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.3, 167.7, 146.6, 137.6, 128.9, 128.9, 128.3, 127.5, 121.4, 114.4, 63.8, 53.5, 52.8, 50.3, 42.1, 34.9, 28.1, 24.5; **IR $\tilde{\nu}_{max}$** 3384 (w), 3030 (w), 2953 (m), 1727 (s), 1600 (m), 1504 (s), 1434 (m), 1402 (w), 1296 (s), 1236 (s), 1196 (m), 1176 (m), 1121 (m), 1090 (m), 1007 (w), 911 (s), 817 (m); **HRMS (ESI)** calcd for $C_{22}H_{23}ClNO_4^+$ [M+H]$^+$ 400.1310; found 400.1308.

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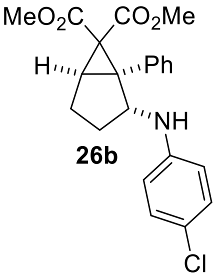
[26] Relative stereochemistry attributed by analogy with compounds **9a**, based on ^{1}H NMR chemical shifts and couplings.

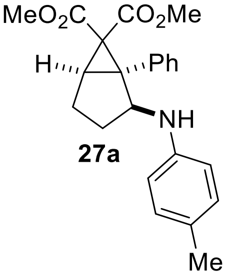


26b

26b, minor diastereoisomer, pale yellow oil (41 mg, 0.10 mmol, 34 % yield). **R*f*** 0.30 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.40 – 7.26 (m, 3H, Ar*H*), 7.23 (m, 2H, Ar*H*), 6.99 (d, *J* = 8.9, 2H, Ar*H*), 6.30 (d, *J* = 8.7, 2H, Ar*H*), 4.31 (d, *J* = 5.9, 1H, C*H*NH), 3.87 (s, 3H, OC*H$_3$*), 3.36 (s, 3H, OC*H$_3$*), 2.92 (d, *J* = 4.4, 1H, C*H*CH$_2$), 2.35 (dddd, *J* = 13.9, 10.8, 9.5, 4.5, 1H, NHCHCH$_2$C*H$_2$*), 2.13 (dd, *J* = 13.6, 8.2, 1H, NHCHCH$_2$C*H$_2$*), 1.88 (dd, *J* = 14.9, 9.5, 1H, NHCHC*H$_2$*), 1.44 – 1.36 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.0, 167.3, 145.1, 134.5, 129.8, 129.7, 128.9, 128.1, 128.1, 114.8, 59.3, 53.2, 52.8, 50.8, 42.6, 36.4, 30.0, 24.7; **IR $\tilde{\nu}_{max}$** 3409 (w), 2956 (m), 2905 (m), 1735 (s), 1602 (m), 1500 (s), 1436 (m), 1398 (w), 1317 (m), 1259 (s), 1209 (m), 1178 (m), 1124 (m), 1071 (m), 913 (m), 818 (m); **HRMS (ESI)** calcd for $C_{22}H_{22}ClNNaO_4^+$ $[M+Na]^+$ 422.1130; found 422.1141.

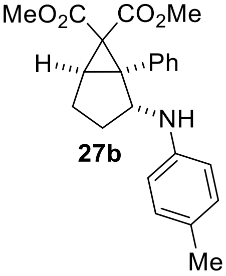
Dimethyl 1-phenyl-2-(*p*-tolylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (27)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methylaniline (**93**) (79 mg, 0.54 mmol, 1.8 equiv.), the title compound **27** (55:45 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10).



27a

27a, major diastereoisomer, pale yellow oil (55 mg, 0.15 mmol, 48 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.34 – 7.28 (m, 2H, Ar*H*), 7.25 – 7.14 (m, 3H, Ar*H*), 6.85 (d, *J* = 7.9, 2H, Ar*H*), 6.40 (d, *J* = 8.3, 2H, Ar*H*), 5.15 (bs, 1H, N*H*), 4.40 (dd, *J* = 10.1, 7.4, 1H, C*H*NH), 3.87 (s, 3H, OC*H$_3$*), 3.42 (s, 3H, OC*H$_3$*), 2.65 (d, *J* = 4.1, 1H, C*H*CH$_2$), 2.35 – 2.18 (m, 3H, NHCHC*H$_2$* and NHCHCH$_2$C*H$_2$*), 2.17 (s, 3H, C*H$_3$*), 0.88 (ddt, *J* = 13.7, 8.2, 4.0, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.1, 167.8, 145.7, 137.8, 129.6, 129.0, 128.2, 127.3, 126.2, 113.5, 64.0, 53.4, 52.8, 50.5, 42.0, 34.8, 28.0, 24.5, 20.4; **IR $\tilde{\nu}_{max}$** 3375 (w), 3027 (w), 2956 (w), 1730 (m), 1619 (m), 1518 (m), 1434 (m), 1305 (m), 1238 (m), 1189 (m), 1126 (m), 1078 (w), 920 (w), 806 (m), 735 (m), 701 (m); **HRMS (ESI)** calcd for $C_{23}H_{26}NO_4^+$ $[M+H]^+$ 380.1856; found 380.1868.

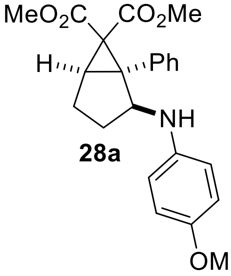


27b

27b, minor diastereoisomer, pale yellow oil (45 mg, 0.12 mmol, 40 % yield). **R*f*** 0.34 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.42 – 7.29 (m, 3H, Ar*H*), 7.25 – 7.17 (m, 2H, Ar*H*), 6.89 (d, *J* = 8.0, 2H, Ar*H*), 6.34 (d, *J* = 8.5, 2H, Ar*H*), 4.32 (d, *J* = 5.8, 1H, C*H*NH), 3.87 (s, 3H, OC*H$_3$*), 3.36 (s, 3H, OC*H$_3$*), 2.92 (d, *J* = 4.4, 1H, C*H*CH$_2$), 2.44 – 2.30 (m, 1H, NHCHCH$_2$C*H$_2$*), 2.18 (s, 3H, C*H$_3$*), 2.13 (dd, *J* = 13.6, 8.4, 1H, NHCHCH$_2$C*H$_2$*), 1.94 (dd, *J* = 14.8, 9.3, 1H, NHCHC*H$_2$*), 1.43 – 1.32 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.1, 167.4, 144.2, 134.6, 129.8, 129.7, 128.9, 128.0, 128.0, 114.1, 59.6, 53.1, 52.7, 50.9, 42.5, 36.5, 29.8, 24.8, 20.5; **IR $\tilde{\nu}_{max}$** 3401 (w), 3025 (w), 2949 (m), 2872 (w), 1737 (s), 1731 (s), 1620 (m), 1518 (s), 1436 (m), 1254 (s), 1212 (s), 1126 (s), 1072 (w), 1013 (w), 913 (m), 808 (m), 737 (m), 703 (s); **HRMS (ESI)** calcd for $C_{23}H_{26}NO_4^+$ [M+H]$^+$ 380.1856; found 380.1849.

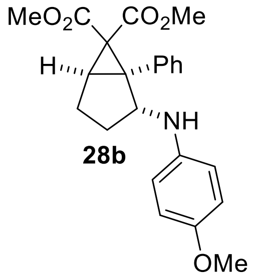
Dimethyl 2-((4-methoxyphenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (28)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methoxyaniline (**94**) (88 mg, 0.54 mmol, 1.8 equiv.), the title compound **28** (52:48 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 80:20).



28a

28a, major diastereoisomer, yellow oil (53 mg, 0.13 mmol, 45 % yield). **R*f*** 0.35 (Pentane:Et$_2$O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 – 7.26 (m, 2H, Ar*H*), 7.24 – 7.13 (m, 3H, Ar*H*), 6.63 (d, *J* = 8.9 Hz, 2H, Ar*H*), 6.43 (d, *J* = 8.8 Hz, 2H, Ar*H*), 5.01 (bs, 1H, N*H*), 4.41 – 4.30 (m, 1H, C*H*NH), 3.87 (s, 3H, COOC*H*$_3$), 3.68 (s, 3H, OC*H*$_3$), 3.42 (s, 3H, COOC*H*$_3$), 2.64 (d, *J* = 4.8 Hz, 1H, C*H*CH$_2$), 2.34 – 2.13 (m, 3H, NHCHC*H$_2$* and NHCHCH$_2$C*H$_2$*), 0.96 – 0.83 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 170.2, 167.8, 151.9, 142.2, 137.9, 129.0, 128.2, 127.3, 114.9, 64.8, 56.0, 53.4, 52.8, 50.5, 42.1, 34.9, 28.1, 24.5; **IR $\tilde{\nu}_{max}$** 3366 (w), 3028 (w), 2958 (m), 1732 (s), 1515 (s), 1444 (m), 1310 (m), 1234 (s), 1182 (m), 1131 (m), 1074 (w), 1036 (m), 908 (m), 822 (m), 733 (s), 702 (m); **HRMS (ESI)** calcd for $C_{23}H_{26}NO_5^+$ [M+H]$^+$ 396.1805; found 396.1802.

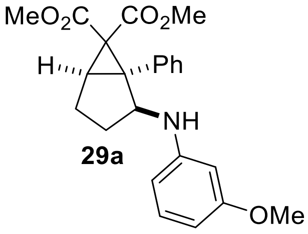


28b

28b, minor diastereoisomer, pale yellow oil (47 mg, 0.12 mmol, 40 % yield). **R*f*** 0.30 (Pentane:Et$_2$O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)**^{23} δ ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.28 (m, 3H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 6.67 (d, *J* = 8.5 Hz, 2H, Ar*H*), 6.36 (d, *J* = 8.4 Hz, 2H, Ar*H*), 4.27 (d, *J* = 5.7 Hz, 1H, C*H*NH), 3.87 (s, 3H, COOC*H*$_3$), 3.69 (s, 3H, OC*H*$_3$), 3.36 (s, 3H, COOC*H*$_3$), 2.91 (d, *J* = 4.3 Hz, 1H, C*H*CH$_2$), 2.43 – 2.30 (m, 1H, NHCHCH$_2$C*H*$_2$), 2.13 (dd, *J* = 13.5, 8.3 Hz, 1H, NHCHCH$_2$C*H*$_2$), 1.90 (dd, *J* = 14.9, 9.4 Hz, 1H, NHCHC*H*$_2$), 1.42 – 1.33 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.1, 167.4, 152.5, 141.1, 134.8, 129.8 (d, *J* = 3.5 Hz), 128.9, 128.0 (d, *J* = 9.7 Hz), 115.1, 114.8, 59.9, 55.9, 53.1, 52.7, 51.1, 42.5, 36.4, 30.0, 24.8; **IR $\tilde{\nu}_{max}$** 3398 (w), 3028 (w), 2951 (m), 2843 (w), 1732 (s), 1511 (s), 1435 (m), 1243 (s), 1186 (m), 1124 (m), 1071 (w), 1036 (m), 912 (s), 826 (m), 731 (s), 700 (m); **HRMS (ESI)** calcd for $C_{23}H_{26}NO_5^+$ [M+H]$^+$ 396.1805; found 396.1807.

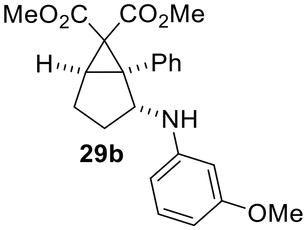
Dimethyl 2-((3-methoxyphenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (29)

Following the general procedure D, starting from dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-3-methoxyaniline (**95**) (88 mg, 0.54 mmol, 1.8 equiv.), the title compound **29** (56:44 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 80:20).



29a

29a, major diastereoisomer, pale yellow oil (57 mg, 0.14 mmol, 48 % yield). **R*f*** 0.35 (Pentane:Et$_2$O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 – 7.28 (m, 2H, Ar*H*), 7.23 – 7.17 (m, 3H, Ar*H*), 6.94 (t, *J* = 8.1 Hz, 1H, Ar*H*), 6.14 (dd, *J* = 8.1, 1.9 Hz, 1H, Ar*H*), 6.10 (dd, *J* = 8.0, 1.7 Hz, 1H, Ar*H*), 5.99 (t, *J* = 2.3 Hz, 1H, Ar*H*), 5.36 (bs, 1H, N*H*), 4.41 (dd, *J* = 10.1, 7.6 Hz, 1H, C*H*NH), 3.87 (s, 3H, COOC*H*$_3$), 3.67 (s, 3H, OC*H*$_3$), 3.42 (s, 3H, COOC*H*$_3$), 2.65 (d, *J* = 4.1 Hz, 1H, C*H*CH$_2$), 2.34 – 2.18 (m, 3H, NHCHC*H*$_2$ and NHCHCH$_2$C*H*$_2$), 0.95 – 0.86 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.2, 167.7, 160.8, 149.3, 137.7, 129.9, 129.0, 128.3, 127.4, 106.5, 102.5, 99.1, 63.6, 55.1, 53.4, 52.8, 50.4, 42.1, 34.9, 28.1, 24.5; **IR $\tilde{\nu}_{\mathbf{max}}$** 3366 (w), 3015 (w), 2951 (m), 1725 (s), 1604 (s), 1508 (m), 1432 (m), 1297 (s), 1227 (s), 1163 (s), 1119 (m), 1074 (w), 1042 (w), 908 (m), 838 (w), 731 (s), 702 (m); **HRMS (ESI)** calcd for $C_{23}H_{26}NO_5^+$ $[M+H]^+$ 396.1805; found 396.1806.

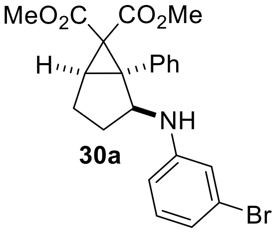


29b

29b, minor diastereoisomer, colorless oil (48 mg, 0.12 mmol, 41 % yield). **R*f*** 0.30 (Pentane:Et$_2$O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.33 – 7.23 (m, 3H, Ar*H*), 7.18 – 7.13 (m, 2H, Ar*H*), 6.90 (t, *J* = 8.1 Hz, 1H, Ar*H*), 6.15 (dd, *J* = 8.0, 2.0 Hz, 1H, Ar*H*), 5.94 (dd, *J* = 8.2, 1.8 Hz, 1H, Ar*H*), 5.89 (t, *J* = 2.1 Hz, 1H, Ar*H*), 4.26 (d, *J* = 5.8 Hz, 1H, C*H*NH), 3.80 (s, 3H, COOC*H*$_3$), 3.64 (s, 3H, OC*H*$_3$), 3.29 (s, 3H, COOC*H*$_3$), 2.85 (d, *J* = 4.4 Hz, 1H, C*H*CH$_2$), 2.36 – 2.20 (m, 1H, NHCHCH$_2$C*H*$_2$), 2.06 (dd, *J* = 13.7, 8.1 Hz, 1H, NHCHCH$_2$C*H*$_2$), 1.87 (dd, *J* = 15.0, 9.4 Hz, 1H, NHCHC*H*$_2$), 1.33 – 1.27 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.0, 167.3, 160.7, 147.7, 134.6, 129.9, 129.0, 128.1, 128.0, 107.1, 103.0, 100.1, 59.3, 55.3, 53.2, 52.7, 50.8, 42.6, 36.4, 30.0, 24.8; **IR $\tilde{\nu}_{\mathbf{max}}$** 3405 (w), 2955 (m), 2850 (w), 1737 (s), 1607 (s), 1500 (m), 1443 (m), 1258 (s), 1212 (s), 1169 (m), 1118 (m), 1050 (w), 912 (m), 834 (w), 729 (s), 696 (m); **HRMS (ESI)** calcd for $C_{23}H_{25}NNaO_5^+$ $[M+Na]^+$ 418.1625; found 418.1632.

Dimethyl 2-((3-bromophenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (30)

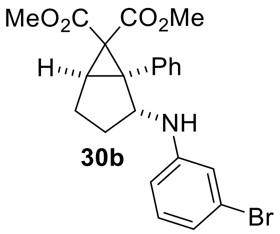
Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and 3-bromo-*N*-cyclopropylaniline (**96**) (115 mg, 0.54 mmol, 1.8 equiv.), the title compound **30** (56:44 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 85:15).



30a

30a, major diastereoisomer, yellow oil (62 mg, 0.14 mmol, 47 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.30 – 7.26 (m, 2H, Ar*H*), 7.25 – 7.16 (m, 3H, Ar*H*), 6.85 (t, *J* = 8.0 Hz, 1H, Ar*H*), 6.66 (ddd, *J* = 7.8, 1.8, 0.9 Hz, 1H, Ar*H*), 6.55 (t, *J* = 2.1 Hz, 1H, Ar*H*), 6.36 (ddd, *J* = 8.2, 2.3, 0.9 Hz, 1H, Ar*H*), 5.37 (bs, 1H, N*H*), 4.38 (dd, *J* = 10.1, 7.4 Hz, 1H, C*H*NH), 3.87 (s, 3H, COOC*H*$_3$), 3.42 (s, 3H, COOC*H*$_3$), 2.70 – 2.64 (d, *J* = 5.1 Hz, 1H, C*H*CH$_2$), 2.36 – 2.14 (m, 3H, NHCHC*H*$_2$ and NHCHCH$_2$C*H*$_2$), 0.99 – 0.83 (m, 1H, NHCHC*H*$_2$);

^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.2, 167.6, 149.4, 137.5, 130.3, 128.9, 128.4, 127.5, 123.2, 119.6, 115.7, 112.0, 63.4, 53.5, 52.8, 50.3, 42.1, 34.9, 28.0, 24.5; **IR $\tilde{\nu}_{max}$** 3668 (w), 3379 (m), 2959 (m), 2898 (m), 1723 (s), 1595 (s), 1510 (s), 1480 (m), 1434 (m), 1288 (s), 1231 (s), 1197 (m), 1120 (m), 1079 (s), 985 (m), 908 (s), 760 (s), 731 (s), 700 (s), 681 (m); **HRMS (ESI)** calcd for $C_{22}H_{23}{}^{79}BrNO_4^+$ [M + H]$^+$ 444.0805; found 444.0812.

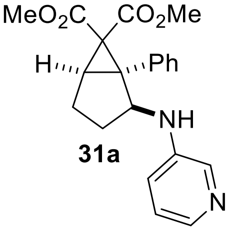


30b

30b, minor diastereoisomer, yellow oil (39 mg, 0.088 mmol, 29 % yield). **R*f*** 0.35 (Pentane:Et_2O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.41 – 7.29 (m, 2H, Ar*H*), 7.27 – 7.22 (m, 3H, Ar*H*), 6.89 (t, *J* = 8.0 Hz, 1H, Ar*H*), 6.73 (ddd, *J* = 7.9, 1.8, 0.9 Hz, 1H, Ar*H*), 6.50 (t, *J* = 2.1 Hz, 1H, Ar*H*), 6.27 (ddd, *J* = 8.3, 2.3, 1.0 Hz, 1H, Ar*H*), 4.33 (d, *J* = 5.8 Hz, 1H, C*H*NH), 3.89 (s, 3H, COOCH_3), 3.62 (bs, 1H, N*H*), 3.37 (s, 3H, COOCH_3), 2.92 (d, *J* = 4.4 Hz, 1H, C*H*CH_2), 2.40 – 2.26 (m, 1H, NHCHCH_2CH_2), 2.15 (dd, *J* = 13.5, 8.3 Hz, 1H, NHCHCH_2CH_2), 1.88 (dd, *J* = 14.9, 9.4 Hz, 1H, NHCHCH_2), 1.46 – 1.37 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.0, 167.3, 148.0, 134.5, 130.4, 129.8, 129.6, 129.0, 128.1, 128.1, 123.1, 120.3, 115.9, 112.1, 58.7, 53.2, 52.8, 50.7, 42.6, 36.3, 30.0, 24.7; **IR $\tilde{\nu}_{max}$** 3405 (w), 3031 (w), 2952 (m), 2858 (w), 1733 (s), 1595 (s), 1489 (m), 1434 (m), 1317 (m), 1255 (s), 1211 (s), 1122 (m), 1074 (w), 987 (m), 914 (m), 839 (w), 732 (s), 702 (s); **HRMS (ESI)** calcd for $C_{22}H_{22}BrNNaO_4^+$ [M + Na]$^+$ 466.0624; found 466.0624.

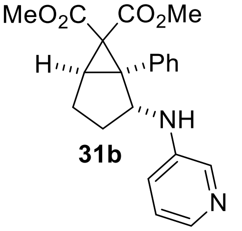
Dimethyl 1-phenyl-2-(pyridin-3-ylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (31)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylpyridin-3-amine (**97**) (73 mg, 0.54 mmol, 1.8 equiv.), the title compound **31** (56:44 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:EtOAc 85:15 to 80:20).



31a

31a, major diastereoisomer, yellow oil (54 mg, 0.15 mmol, 49 % yield). **R*f*** 0.25 (Pentane:EtOAc 30:70); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.90 (d, *J* = 2.9 Hz, 1H, HetAr*H*), 7.80 (d, *J* = 4.7 Hz, 1H, HetAr*H*), 7.31 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.14 (m, 3H, Ar*H*), 6.89 (dd, *J* = 8.4, 4.6 Hz, 1H, HetAr*H*), 6.62 (d, *J* = 8.1 Hz, 1H, HetAr*H*), 5.34 (d, *J* = 10.7 Hz, 1H, N*H*), 4.43 (td, *J* = 10.1, 7.4 Hz, 1H, C*H*NH), 3.89 (s, 3H, COOCH_3), 3.43 (s, 3H, COOCH_3), 2.68 (d, *J* = 4.2 Hz, 1H, C*H*CH$_2$), 2.37 – 2.15 (m, 3H, NHCHC*H$_2$* and NHCHCH$_2$C*H$_2$*), 1.03 – 0.91 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.3, 167.6, 144.1, 138.2, 137.5, 136.4, 128.9, 128.4, 127.6, 123.6, 119.0, 63.3, 53.5, 52.8, 50.3, 42.1, 35.0, 28.1, 24.5; **IR $\tilde{\nu}_{max}$** 3369 (w), 3032 (w), 2954 (w), 1730 (s), 1587 (s), 1515 (m), 1438 (m), 1306 (s), 1237 (s), 1189 (m), 1129 (m), 1121 (m), 1077 (w), 1009 (w), 916 (m), 791 (m), 730 (s), 702 (s), 645 (w); **HRMS (ESI)** calcd for $C_{21}H_{23}N_2O_4^+$ [M+H]$^+$ 367.1652; found 367.1649.

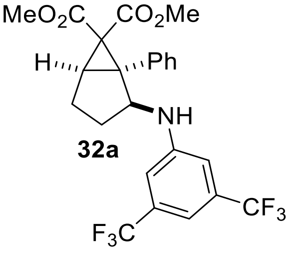


31b

31b, minor diastereoisomer, yellow oil (36 mg, 0.098 mmol, 33 % yield). **R*f*** 0.20 (Pentane:EtOAc 30:70); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.86 (dd, *J* = 4.7, 1.3 Hz, 1H, HetAr*H*), 7.75 (d, *J* = 2.9 Hz, 1H, HetAr*H*), 7.39 – 7.26 (m, 3H, Ar*H*), 7.24 – 7.18 (m, 2H, Ar*H*), 6.95 (dd, *J* = 8.3, 4.7 Hz, 1H, HetAr*H*), 6.66 (ddd, *J* = 8.7, 2.9, 1.4 Hz, 1H, HetAr*H*), 4.36 (t, *J* = 6.0 Hz, 1H, C*H*NH), 3.88 (s, 3H, COOC*H$_3$*), 3.62 (d, *J* = 5.4 Hz, 1H, N*H*), 3.37 (s, 3H, COOC*H$_3$*), 2.92 (d, *J* = 4.4 Hz, 1H, CHC*H$_2$*), 2.41 – 2.29 (m, 1H, NHCHCH$_2$C*H$_2$*), 2.16 (dd, J = 13.6, 8.4 Hz, 1H, NHCHCH$_2$C*H$_2$*), 1.86 (dd, *J* = 15.0, 9.4 Hz, 1H, NHCHC*H$_2$*), 1.52 – 1.39 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 167.9, 167.2, 142.9, 138.7, 136.4, 134.5, 129.8, 128.9, 128.1, 123.6, 119.3, 58.7, 53.2, 52.8, 50.9, 42.6, 36.4, 30.2, 24.8; **IR $\tilde{\nu}_{max}$** 3396 (w), 3262 (w), 3036 (w), 2954 (w), 1736 (s), 1583 (s), 1480 (m), 1434 (m), 1306 (s), 1253 (s), 1203 (s), 1117 (s), 1070 (w), 1014 (w), 910 (m), 794 (m), 735 (s), 702 (s), 644 (w); **HRMS (ESI)** calcd for $C_{21}H_{23}N_2O_4^+$ [M+H]$^+$ 367.1652; found 367.1647.

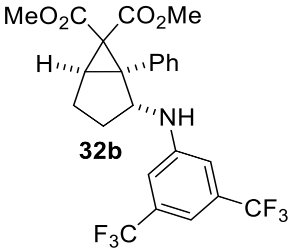
Dimethyl 2-((3,5-bis(trifluoromethyl)phenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (32)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-3,5-bis(trifluoromethyl)aniline (**98**) (0.15 g, 0.54 mmol, 1.8 equiv.), the title compound **32** (58:42 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 85:15).



32a

32a, major diastereoisomer, colorless oil (69 mg, 0.14 mmol, 46 % yield). **R*f*** 0.42 (Pentane:Et$_2$O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.29 – 7.25 (m, 2H, Ar*H*), 7.24 – 7.18 (m, 3H, Ar*H*), 6.97 (s, 1H, Ar*H*), 6.70 (s, 2H, Ar*H*), 5.78 (d, *J* = 10.5 Hz, 1H, N*H*), 4.49 (q, *J* = 9.5 Hz, 1H, C*H*NH), 3.90 (s, 3H, OCH_3), 3.44 (s, 3H, OCH_3), 2.70 (d, *J* = 4.5 Hz, 1H, C*H*CH_2), 2.39 – 2.19 (m, 3H, NHCHCH_2 and NHCHCH_2CH_2), 1.08 – 0.94 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.6, 167.5, 148.8, 137.2, 132.2 (q, *J* = 32.6 Hz), 128.8, 128.6, 127.8, 123.6 (q, *J* = 272.5 Hz), 112.6 – 112.1 (m), 109.7 (p, *J* = 4.1 Hz), 63.4, 53.6, 52.9, 50.2, 42.2, 35.3, 28.1, 24.5; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -63.3; **IR $\tilde{\nu}_{max}$** 3377 (w), 3031 (w), 2957 (w), 1725 (m), 1622 (m), 1529 (w), 1478 (w), 1439 (m), 1394 (m), 1276 (s), 1178 (s), 1122 (s), 994 (w), 912 (m), 861 (m), 733 (s), 700 (s), 682 (m), 639 (w); **HRMS (ESI)** calcd for $C_{24}H_{22}F_6NO_4^+$ $[M+H]^+$ 502.1448; found 502.1451.

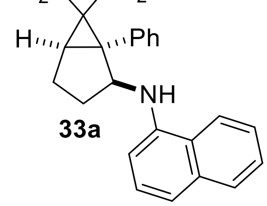


32b

32b, minor diastereoisomer, yellow oil (38 mg, 0.076 mmol, 25 % yield). **R*f*** 0.28 (Pentane:Et_2O 75:25); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.40 – 7.34 (m, 1H, Ar*H*), 7.33 – 7.27 (m, 1H, Ar*H*), 7.26 – 7.19 (m, 3H, Ar*H*), 7.03 (s, 1H, Ar*H*), 6.66 (s, 2H, Ar*H*), 4.44 (d, *J* = 6.1 Hz, 1H, C*H*NH), 3.95 (bs, 1H, N*H*), 3.90 (s, 3H, OCH_3), 3.39 (s, 3H, OCH_3), 2.93 (d, *J* = 4.4 Hz, 1H, C*H*CH_2), 2.34 (dddd, *J* = 14.0, 10.9, 9.4, 4.6 Hz, 1H, NHCHCH_2CH_2), 2.19 (dd, *J* = 13.7, 8.4 Hz, 1H, NHCHCH_2CH_2), 1.85 (dd, *J* = 15.1, 9.4 Hz, 1H, NHCHCH_2), 1.56 – 1.49 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 167.9, 167.1, 147.3, 134.3, 132.2 (q, *J* = 32.6 Hz), 129.9, 129.7, 129.0, 128.3, 128.2, 123.6 (q, *J* = 272.6 Hz), 112.9 – 112.3 (m), 110.4 (p, *J* = 3.9 Hz), 58.8, 53.3, 52.9, 50.7, 42.7, 36.3, 30.1, 24.8; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -63.2; **IR $\tilde{\nu}_{max}$** 3393 (w), 3033 (w), 2955 (w), 1731 (m), 1622 (w), 1521 (w), 1478 (w), 1439 (w), 1396 (m), 1276 (s), 1171 (s), 1124 (s), 1005 (w), 912 (w), 861 (w), 729 (w), 700 (m), 682 (w); **HRMS (ESI)** calcd for $C_{24}H_{21}F_6NNaO_4^+$ $[M+Na]^+$ 524.1267; found 524.1277.

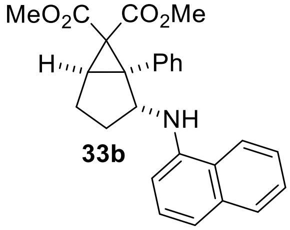
Dimethyl 2-(naphthalen-1-ylamino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (33)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropylnaphthalen-1-amine (**99**) (99 mg, 0.54 mmol, 1.8 equiv.), the title compound **33** (61:39 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 95:5 to 90:10).



33a

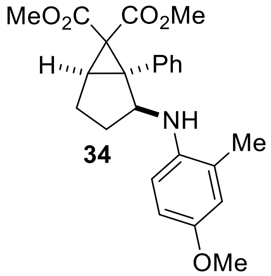
33a, major diastereoisomer, colorless oil (59 mg, 0.14 mmol, 47 % yield). **R*f*** 0.44 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 8.11 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.74 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.51 (ddd, *J* = 8.4, 6.8, 1.5 Hz, 1H, Ar*H*), 7.44 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1H, Ar*H*), 7.37 (dt, *J* = 6.0, 1.6 Hz, 2H, Ar*H*), 7.23 – 7.07 (m, 5H, Ar*H*), 6.31 (d, *J* = 7.5 Hz, 1H, Ar*H*), 4.63 (dd, *J* = 10.2, 8.2 Hz, 1H, C*H*NH), 3.89 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 2.73 (d, *J* = 4.5 Hz, 1H, C*H*CH$_2$), 2.51 (dt, *J* = 14.4, 8.5 Hz, 1H, NHCHCH$_2$CH_2), 2.42 – 2.24 (m, 2H, NHCHCH_2 and NHCHCH$_2$CH_2), 1.04 – 0.91 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.5, 167.8, 143.3, 137.7, 134.5, 129.0, 128.6, 128.3, 127.4, 126.5, 125.8, 124.9, 123.9, 120.8, 116.8, 104.3, 63.5, 53.6, 52.9, 50.6, 42.3, 34.9, 27.9, 24.8; **IR $\tilde{\nu}_{max}$** 3391 (s), 3052 (s), 2955 (s), 1731 (s), 1580 (s), 1534 (s), 1490 (s), 1440 (s), 1407 (s), 1306 (s), 1233 (s), 1128 (s), 1080 (s), 1015 (s), 911 (s), 772 (s), 730 (s), 699 (s); **HRMS (ESI)** calcd for $C_{26}H_{26}NO_4^+$ [M+H]$^+$ 416.1856; found 416.1858.



33b

33b, minor diastereoisomer, colorless oil (36 mg, 0.087 mmol, 29 % yield). **R*f*** 0.40 (Pentane:Et$_2$O 80:20); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] δ 7.71 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.53 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.49 – 7.42 (m, 2H, Ar*H*), 7.36 (ddd, *J* = 8.0, 6.7, 1.2 Hz, 1H, Ar*H*), 7.31 – 7.27 (m, 2H, Ar*H*), 7.24 (d, *J* = 1.7 Hz, 2H, Ar*H*), 7.21 – 7.17 (m, 2H, Ar*H*), 6.52 (d, *J* = 7.5 Hz, 1H, Ar*H*), 4.48 (d, *J* = 5.7 Hz, 1H, C*H*NH), 3.92 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 3.01 (d, *J* = 4.4 Hz, 1H, C*H*CH$_2$), 2.51 – 2.36 (m, 1H, NHCHCH$_2$CH_2), 2.20 (dd, *J* = 13.5, 8.3 Hz, 1H, NHCHCH$_2$CH_2), 2.08 (dd, *J* = 14.9, 9.5 Hz, 1H, NHCHCH_2), 1.51 – 1.41 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.1, 167.5, 141.8, 134.8, 134.3, 129.9, 129.7, 129.3, 128.7, 128.3, 128.3, 126.4, 125.8, 124.9, 124.0, 119.7, 117.9, 105.6, 59.1, 53.2, 52.8, 51.1, 42.4, 36.8, 29.5, 25.1; **IR $\tilde{\nu}_{max}$** 3420 (w), 3060 (w), 2953 (m), 1733 (s), 1580 (m), 1526 (m), 1476 (m), 1440 (m), 1407 (m), 1254 (s), 1210 (m), 1126 (m), 1019 (w), 908 (m), 770 (m), 735 (s), 703 (m); **HRMS (ESI)** calcd for $C_{26}H_{25}NNaO_4^+$ [M+Na]$^+$ 438.1676; found 438.1680.

Dimethyl 2-((4-methoxyphenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (34)



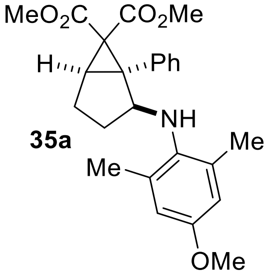
34

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methoxy-2-

methylaniline (**100**) (96 mg, 0.54 mmol, 1.8 equiv.), the title compound **34** (57:43 *dr* in the crude ^{1}H NMR) was obtained as an inseparable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O:DCM 85:10:5) and as a yellow oil (87 mg, 0.21 mmol, 71% yield). **R*f*** 0.40 (Pentane:Et$_2$O:DCM 70:20:10); **^{1}H NMR (400 MHz, Chloroform-*d*)**[23] major diastereoisomer δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.23 – 7.13 (m, 3H, Ar*H*), 6.66 – 6.63 (m, 1H, Ar*H*), 6.48 (d, *J* = 3.0 Hz, 1H, Ar*H*), 6.25 (d, *J* = 8.8 Hz, 1H, Ar*H*), 4.37 (t, *J* = 9.1 Hz, 1H, C*H*NH), 3.86 (s, 3H, COOCH_3), 3.68 (s, 3H, OCH_3), 3.42 (s, 3H, COOCH_3), 2.65 (d, *J* = 4.4 Hz, 1H, C*H*CH$_2$), 2.46 – 2.35 (m, 1H, NHCHCH$_2$CH_2), 2.27 (s, 3H, CH_3), 2.23 (dd, *J* = 9.3, 1.7 Hz, 1H, NHCHCH_2), 2.20 – 2.11 (m, 1H, NHCHCH$_2$CH_2), 0.97 – 0.80 (m, 1H, NHCHCH_2); minor diastereoisomer δ 7.43 – 7.35 (m, 3H, Ar*H*), 7.32 – 7.30 (m, 2H, Ar*H*), 6.64 – 6.62 (m, 1H, Ar*H*), 6.57 (d, *J* = 2.8 Hz, 1H, Ar*H*), 6.50 (d, *J* = 3.0 Hz, 1H, Ar*H*), 4.22 (d, *J* = 5.7 Hz, 1H, C*H*NH), 3.88 (s, 3H, COOCH_3), 3.70 (s, 3H, OCH_3), 3.39 (s, 3H, COOCH_3), 2.94 (d, *J* = 4.3 Hz, 1H, C*H*CH$_2$), 2.39 – 2.34 (m, 1H, NHCHCH$_2$CH_2), 2.24 – 2.21 (m, 1H, NHCHCH$_2$CH_2), 2.01 – 1.90 (m, 1H, NHCHCH_2), 1.63 (s, 3H, CH_3), 1.43 – 1.31 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** major diastereoisomer δ 170.3, 167.8, 137.8, 130.0, 129.8, 129.4, 128.9, 128.3, 128.2, 127.3, 117.0, 111.6, 64.5, 55.9, 53.5, 52.8, 51.0, 42.4, 36.9, 28.2, 24.6, 18.2; minor diastereoisomer δ 168.0, 167.4, 137.8, 130.0, 129.3, 129.1, 128.9, 128.3, 128.2, 127.3, 117.2, 111.4, 64.5, 55.9, 53.1, 52.7, 50.5, 42.1, 34.9, 29.8, 25.0, 17.3; **IR $\tilde{\nu}_{max}$** 3391 (w), 2953 (m), 2844 (w), 1727 (s), 1511 (s), 1435 (m), 1225 (s), 1120 (s), 1054 (w), 910 (m), 733 (s), 700 (m); **HRMS (ESI)** calcd for $C_{24}H_{28}NO_5^+$ [M+H]$^+$ 410.1962; found 410.1957.

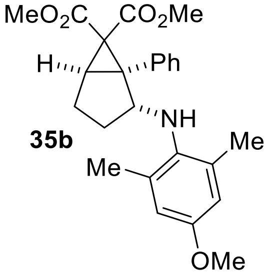
Dimethyl 2-((4-methoxy-2,6-dimethylphenyl)amino)-1-phenylbicyclo[3.1.0]hexane-6,6-dicarboxylate (35)

Following the general procedure D, starting from dimethyl dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (70 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methoxy-2,6-dimethylaniline (**37**) (0.10 g, 0.54 mmol, 1.8 equiv.), the title compound **35** (84:16 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 85:15).



35a

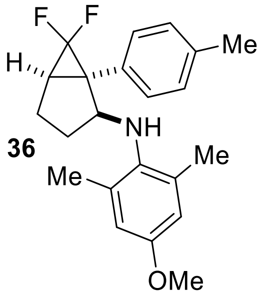
35a, major diastereoisomer, pale yellow oil (29 mg, 0.068 mmol, 23 % yield). **R$_f$** 0.42 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.35 – 7.26 (m, 2H, Ar*H*), 7.23 – 7.18 (m, 2H, Ar*H*), 7.17 – 7.12 (m, 1H, Ar*H*), 6.35 (s, 2H, Ar*H*), 4.15 (bs, 1H, N*H*), 3.84 (s, 4H, COOCH_3 & C*H*NH), 3.60 (s, 3H, OCH_3), 3.37 (s, 3H, COOCH_3), 2.55 – 2.50 (m, 1H, C*H*CH$_2$), 2.11 – 2.02 (m, 2H, NHCHCH$_2$CH_2), 1.81 (m, 7H, NHCHCH_2 & CH_3), 1.07 – 0.87 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 170.5, 168.1, 154.2, 138.9, 138.3, 131.4, 129.5, 128.0, 127.2, 114.1, 68.5, 55.4, 53.4, 52.8, 50.7, 41.8, 34.5, 28.5, 24.2, 18.8; **IR $\tilde{\nu}_{max}$** 3376 (w), 2952 (m), 2842 (w), 1727 (s), 1602 (w), 1485 (s), 1434 (s), 1306 (s), 1219 (s), 1194 (m), 1150 (m), 1123 (s), 1064 (s), 1003 (w), 910 (m), 850 (w), 762 (m), 731 (s), 700 (s), 649 (w); **HRMS (ESI)** calcd for $C_{25}H_{30}NO_5^+$ $[M + H]^+$ 424.2118; Found 424.2114.



35b

35b, minor diastereoisomer, pale yellow oil (4 mg, 0.009 mmol, 3 % yield). **R*f*** 0.37 (Pentane:Et_2O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)**^{23} δ 7.57 – 7.51 (m, 1H, Ar*H*), 7.33 – 7.29 (m, 2H, Ar*H*), 7.26 – 7.22 (m, 2H, Ar*H*), 6.49 (s, 2H, Ar*H*), 4.18 (d, *J* = 5.9 Hz, 1H, C*H*NH), 3.78 (s, 3H, COOC*H*3), 3.70 (s, 3H, OC*H*3), 3.35 (s, 3H, COOC*H*3), 2.95 (d, *J* = 4.2 Hz, 1H, C*H*CH2), 2.52 – 2.38 (m, 1H, NHCHCH2C*H2*), 2.12 (m, 7H, NHCHCH2C*H2* & C*H3*), 1.65 – 1.57 (m, 1H, NHCHC*H2*), 1.05 – 0.91 (m, 1H, NHCHC*H2*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 168.2, 167.5, 133.3, 130.3, 129.7, 128.8, 128.4, 127.9, 127.7, 114.1, 62.5, 55.4, 53.0, 52.7, 51.6, 42.6, 36.1, 27.6, 24.9, 19.3; **IR $\tilde{\nu}_{max}$** 3362 (w), 2951 (m), 2871 (w), 1739 (s), 1602 (w), 1481 (m), 1442 (m), 1314 (m), 1248 (s), 1212 (s), 1150 (m), 1124 (m), 1065 (m), 1011 (w), 914 (m), 854 (w), 731 (m), 702 (m), 611 (w); **HRMS (ESI)** calcd for $C_{25}H_{30}NO_5^+$ $[M + H]^+$ 424.2118; Found 424.2120.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(p-tolyl)bicyclo[3.1.0]hexan-2-amine (36)

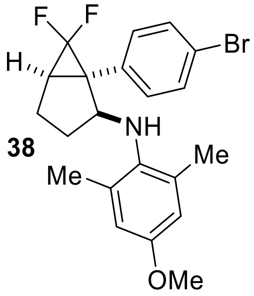


36

Following the general procedure D, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-methylbenzene (**66**) (50 mg, 0.30 mmol, 1.0 equiv.) and *N*-cyclopropyl-4-methoxy-2,6-dimethylaniline (**37**) (0.10 g, 0.54 mmol, 1.8 equiv.), the title compound **36** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 95:5 to 90:10) as a yellow oil and as a mixture of diastereoisomers (61 mg, 0.14 mmol, 57% yield). **R*f*** 0.45 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.22 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.07 (d, *J* = 7.7 Hz, 2H, Ar*H*), 6.44 (s, 2H, Ar*H*), 4.20 (dd, *J* = 16.4, 8.0 Hz, 1H, C*H*NH), 3.70 (s, 3H, OMe), 3.23 (bs, 1H, N*H*), 2.32 (s, 3H, C*H*3), 2.24 – 2.18 (m, 2H, CF2CHC*H2*), 2.09 – 2.07 (m, 1H, CF2C*H*), 2.06 (s, 6H, C*H3*), 2.06 – 2.02 (m, 1H, NHCHC*H2*), 1.70 – 1.59 (m, 1H, NHCHC*H2*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.4, 138.1, 137.0, 132.5, 130.6, 129.1, 128.9, 115.7 (Hidden dd, one measurable constant: J = 281.8 Hz), 114.1, 67.8, 55.5, 44.8 (dd, J = 11.9, 8.1 Hz), 34.4 (dd, J = 12.6, 9.0 Hz), 31.4 (d, J = 7.5 Hz), 24.2, 21.3, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.3 (dd, J = 160.8, 14.1 Hz, *Major diastereoisomer*), -124.8 (dd, J = 157.3, 18.5 Hz, *Minor diasteroisomer*), -137.6 (d, J = 160.0 Hz, *Major diastereoisomer*), -141.3 (d, J = 157.6 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3382 (w), 2946 (m), 2251 (w), 1902 (w), 1728 (w), 1607 (m), 1517 (m), 1484 (s), 1440 (s), 1378 (w), 1317 (m), 1223 (s), 1194 (s), 1149 (s), 1106 (m), 1065 (s), 1029 (m), 984 (s), 984 (s), 939 (m), 912 (s), 855 (m), 812 (s), 734 (s), 693 (m), 669 (w), 650 (m); **HRMS (ESI)** calcd for $C_{22}H_{26}F_2NO^+$ [M+H]$^+$ 358.1977; found 358.1984.

Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-methylbenzene (**63**) (50 mg, 0.30 mmol, 1.0 equiv), the title compound **35** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a yellow oil and as a mixture of diastereoisomers (78 mg, 0.22 mmol, 73% yield). With this procedure the characterization was the same as described above.

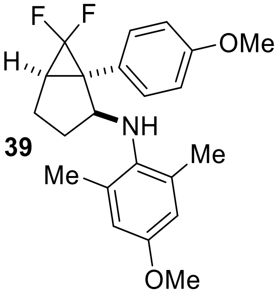
1-(4-Bromophenyl)-6,6-difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)bicyclo[3.1.0]hexan-2-amine (38)



38

Following the general procedure E, starting from 1-bromo-4-(3,3-difluorocycloprop-1-en-1-yl)benzene (**73**) (69 mg, 0.30 mmol, 1.0 equiv.), the title compound **38** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a colorless oil and as a single diastereoisomer (100 mg, 0.24 mmol, 79 % yield). **R*f*** 0.37 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.36 (d, J = 8.4 Hz, 2H, Ar*H*), 7.16 (d, J = 8.4 Hz, 2H, Ar*H*), 6.43 (s, 2H, Ar*H*), 4.20 (dt, J = 9.5, 7.2 Hz, 1H, C*H*NH), 3.70 (s, 3H, OMe), 3.28 (bs, 1H, N*H*), 2.27 – 2.10 (m, 3H, CF$_2$CHC*H$_2$* & NHCHC*H$_2$*), 2.06 (m, 7H, CF$_2$C*H* & C*H$_3$*), 1.70 – 1.58 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.6, 137.8, 134.7, 131.3, 130.9, 130.5, 121.3, 116.7 (dd, J = 302.8, 281.9 Hz), 114.2, 67.6, 55.5, 44.6 (dd, J = 12.1, 7.8 Hz), 34.6 (dd, J = 12.6, 9.0 Hz), 31.4 (d, J = 7.7 Hz), 24.2, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.1 (dd, J = 161.7, 13.9 Hz), -137.7 (d, J = 161.3 Hz); **IR $\tilde{\nu}_{max}$** 3373 (w), 2951 (m), 2830 (w), 1604 (w), 1489 (s), 1313 (m), 1287 (m), 1227 (s), 1196 (s), 1153 (s), 1106 (m), 1062 (s), 1013 (m), 986 (s), 945 (w), 912 (w), 822 (s), 741 (m); **HRMS (ESI)** calcd for $C_{21}H_{23}{}^{79}BrF_2NO^+$ [M+H]$^+$ 422.0926; found 422.0928.

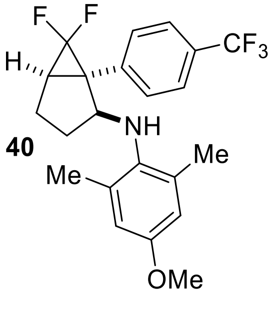
6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(4-methoxyphenyl)bicyclo[3.1.0]hexan-2-amine (39)



39

Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-methoxybenzene (**74**) (55 mg, 0.30 mmol, 1.0 equiv.), the title compound **39** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a yellow oil and as a single diastereoisomer (68 mg, 0.18 mmol, 61 % yield). **R$_f$** 0.28 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.24 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.80 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.44 (s, 2H, Ar*H*), 4.18 (dt, *J* = 9.3, 7.3 Hz, 1H, C*H*NH), 3.78 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.25 (bs, 1H, N*H*), 2.25 – 2.17 (m, 2H, CF$_2$CHC*H$_2$* & NHCHC*H$_2$*), 2.15 – 2.09 (m, 1H, CF$_2$CHC*H$_2$*), 2.08 – 2.00 (m, 7H, CF$_2$C*H* & C*H$_3$*), 1.67 – 1.56 (m, 1H, NHCHC*H$_2$*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 158.9, 154.4, 138.2, 130.6, 130.4, 127.6, 117.3 (dd, *J* = 302.4, 281.9 Hz), 114.1, 113.7, 67.9 (d, *J* = 2.1 Hz), 55.5, 55.4, 44.6 (dd, *J* = 11.9, 8.5 Hz), 34.4 (dd, *J* = 12.5, 8.9 Hz), 31.4 (d, *J* = 7.6 Hz), 24.2, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.3 (dd, *J* = 159.6, 13.6 Hz), -137.8 (d, *J* = 159.8 Hz); **IR $\tilde{\nu}_{max}$** 3379 (w), 2958 (m), 2913 (w), 2836 (w), 1727 (w), 1614 (m), 1517 (s), 1484 (s), 1301 (m), 1247 (s), 1194 (s), 1151 (s), 1110 (w), 1066 (s), 1029 (m), 986 (m), 910 (m), 830 (m), 737 (m), 587 (w); **HRMS (ESI)** calcd for $C_{22}H_{26}F_2NO_2^+$ [M+H]$^+$ 374.1926; found 374.1929.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(4-(trifluoromethyl)phenyl)bicyclo[3.1.0] hexan-2-amine (40)

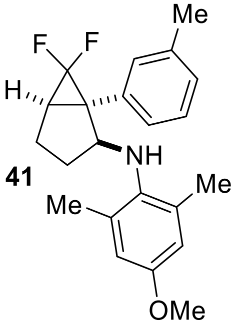


40

Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-4-(trifluoromethyl)benzene (**85**) (66 mg, 0.30 mmol, 1.0 equiv.), the title compound **40** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a pale yellow oil and as a single diastereoisomer (95 mg, 0.23 mmol, 77 % yield). **R$_f$** 0.20 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400**

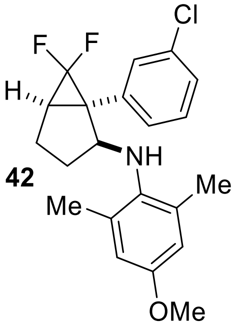
MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.39 (d, *J* = 8.1 Hz, 2H, Ar*H*), 6.41 (s, 2H, Ar*H*), 4.26 (dt, *J* = 9.6, 6.9 Hz, 1H, C*H*NH), 3.68 (s, 3H, OC*H₃*), 3.28 (bs, 1H, N*H*), 2.30 – 2.15 (m, 3H, NHCHC*H₂* & CF_2CHC*H₂*), 2.10 (dd, *J* = 14.5, 3.9 Hz, 1H, CF_2C*H*), 2.07 (s, 6H, C*H₃*), 1.73 – 1.59 (m, 1H, NHCHC*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.7, 139.8, 137.8, 130.4, 129.6, 129.3 (q, *J* = 32.8 Hz), 125.0 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.1 Hz), 116.5 (dd, *J* = 303.0, 282.2 Hz), 114.1, 67.6, 55.4, 44.9 (dd, *J* = 12.3, 7.7 Hz), 34.9 (dd, *J* = 12.8, 9.2 Hz), 31.4 (d, *J* = 7.7 Hz), 24.2, 18.9; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -62.6, -122.9 (dd, *J* = 162.6, 14.4 Hz), -137.6 (d, *J* = 162.0 Hz); **IR $\tilde{\nu}_{max}$** 3384 (w), 2950 (m), 2844 (w), 1611 (m), 1486 (s), 1448 (m), 1325 (s), 1201 (m), 1158 (s), 1126 (s), 1059 (s), 1017 (m), 985 (m), 949 (w), 913 (m), 837 (m), 734 (m), 702 (m); **HRMS (ESI)** calcd for $C_{22}H_{23}F_5NO^+$ $[M+H]^+$ 412.1694; found 412.1705.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(m-tolyl)bicyclo[3.1.0]hexan-2-amine (41)



Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-3-methylbenzene (**86**) (50 mg, 0.30 mmol, 1.0 equiv.), the title compound **41** (94:6 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 95:5 to 90:10) as a pale yellow oil and as a mixture of diastereoisomers (80 mg, 0.22 mmol, 75 % yield). **R*f*** 0.38 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.17 – 7.01 (m, 4H, Ar*H*), 6.43 (s, 2H, Ar*H*), 4.24 (dt, *J* = 9.8, 6.9 Hz, 1H, C*H*NH), 3.70 (s, 3H, OMe), 3.26 (bs, 1H, N*H*), 2.27 (s, 3H, C*H₃*), 2.24 – 2.11 (m, 3H, CF_2CHC*H₂* & NHCHC*H₂*), 2.09 – 2.03 (m, 7H, CF_2C*H* & C*H₃*), 1.70 – 1.60 (m, 1H, NHCHC*H₂*); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.4, 138.1, 137.7, 135.5, 133.0, 130.5, 130.1, 128.1, 126.1 (d, *J* = 2.5 Hz), 117.2 (dd, *J* = 302.6, 282.2 Hz), 114.1, 67.8, 55.4, 45.2 (dd, *J* = 11.8, 8.1 Hz), 34.6 (dd, *J* = 12.6, 9.1 Hz), 31.6 (d, *J* = 7.7 Hz), 24.2, 21.4, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.1 (dd, *J* = 160.6, 15.3 Hz, *Major diastereoisomer*), -124.7 (d, *J* = 158.0 Hz, *Minor diasteroisomer*), -137.5 (d, *J* = 160.9 Hz, *Major diastereoisomer*), -141.2 (d, *J* = 157.6 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3379 (w), 3041 (w), 2945 (m), 1610 (m), 1486 (s), 1449 (s), 1319 (m), 1194 (s), 1157 (m), 1103 (w), 1068 (s), 1031 (m), 986 (m), 914 (m), 852 (m), 787 (m), 739 (m), 704 (s), 643 (w). **HRMS (ESI)** calcd for $C_{22}H_{26}F_2NO^+$ $[M+H]^+$ 358.1977; found 358.1983.

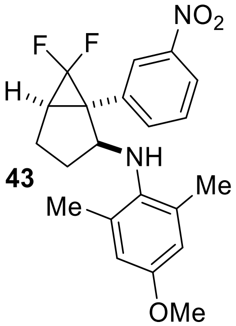
1-(3-Chlorophenyl)-6,6-difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)bicyclo[3.1.0]hexan-2-amine (42)



42

Following the general procedure E, starting from 1-chloro-3-(3,3-difluorocycloprop-1-en-1-yl)benzene (**75**) (56 mg, 0.30 mmol, 1.0 equiv.), the title compound **42** (92:8 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et_2O 95:5 to 90:10) as a yellow oil and as a mixture of diastereoisomers (94 mg, 0.25 mmol, 83 % yield). **R*f*** 0.35 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.26 – 7.24 (m, 1H, Ar*H*), 7.22 – 7.14 (m, 3H, Ar*H*), 6.43 (s, 2H, Ar*H*), 4.22 (q, *J* = 8.1 Hz, 1H, C*H*NH), 3.70 (s, 3H, OMe), 3.23 (bs, 1H, N*H*), 2.29 – 2.15 (m, 3H, CF_2CHCH_2 & $NHCHCH_2$), 2.09 – 2.03 (m, 7H, CF_2CH & CH_3), 1.70 – 1.60 (m, 1H, $NHCHCH_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.6, 137.8, 137.7, 133.9, 130.5, 129.4 (d, *J* = 2.3 Hz), 129.4, 127.5, 127.5 (d, *J* = 2.3 Hz), 116.6 (dd, *J* = 302.8, 283.1 Hz), 114.2, 67.6 (d, *J* = 2.0 Hz), 55.4, 44.8 (dd, *J* = 12.1, 7.8 Hz), 34.8 (dd, *J* = 12.7, 9.2 Hz), 31.5 (d, *J* = 7.6 Hz), 24.1, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.1 (dd, *J* = 161.8, 14.6 Hz, *Major diastereoisomer*), -124.6 (ddd, *J* = 158.7, 14.2, 5.0 Hz, *Minor diasteroisomer*), -137.6 (d, *J* = 161.4 Hz, *Major diastereoisomer*), -141.1 (d, *J* = 158.0 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3386 (w), 3047 (w), 2945 (m), 2843 (w), 1731 (w), 1599 (m), 1486 (s), 1322 (m), 1196 (s), 1153 (s), 1101 (m), 1071 (s), 1027 (w), 988 (m), 912 (m), 848 (m), 785 (m), 733 (s), 694 (m); **HRMS (ESI)** calcd for $C_{21}H_{23}ClF_2NO^+$ $[M+H]^+$ 378.1431; found 378.1430.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(3-nitrophenyl)bicyclo[3.1.0]hexan-2-amine (43)

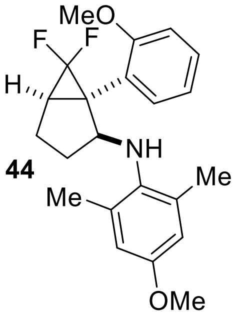


43

Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-3-nitrobenzene (**87**) (59 mg, 0.30 mmol, 1.0 equiv.), the title compound **43** (91:9 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge

KP-SIL 25 g, Pentane:Et$_2$O 90:10 to 80:20) as a yellow oil and as a mixture of diastereoisomers (87 mg, 0.22 mmol, 75 % yield). **R*f*** 0.25 (Pentane:Et$_2$O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 8.09 – 8.00 (m, 2H, Ar*H*), 7.58 (dt, *J* = 7.8, 1.3 Hz, 1H, Ar*H*), 7.37 (t, *J* = 7.9 Hz, 1H, Ar*H*), 6.37 (s, 2H, Ar*H*), 4.28 (dt, *J* = 9.7, 7.4 Hz, 1H, C*H*NH), 3.66 (s, 3H, OCH_3), 3.26 (bs, 1H, N*H*), 2.33 – 2.20 (m, 3H, NHCHCH_2 & CF$_2$CHCH_2), 2.16 – 2.12 (m, 1H, CF$_2$C*H*), 2.07 (s, 6H, CH_3), 1.74 – 1.64 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.6, 148.0, 137.9, 137.5, 135.5, 130.3, 129.0, 124.1 (d, *J* = 2.6 Hz), 122.3, 116.2 (dd, *J* = 302.8, 281.9 Hz), 114.1, 67.5, 55.4, 44.7 (dd, *J* = 12.5, 7.6 Hz), 35.2 (dd, *J* = 12.7, 9.1 Hz), 31.3 (d, *J* = 7.7 Hz), 24.1, 18.9; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -122.8 (dd, *J* = 162.8, 14.6 Hz, *Major diastereoisomer*), -124.4 (ddd, *J* = 159.2, 14.5, 4.6 Hz, *Minor diasteroisomer*), -137.9 (d, *J* = 162.8 Hz, *Major diastereoisomer*), -141.0 (d, *J* = 158.7 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3377 (w), 3081 (w), 2951 (m), 1720 (w), 1603 (w), 1529 (s), 1486 (s), 1447 (m), 1349 (s), 1314 (m), 1197 (m), 1151 (s), 1102 (m), 1065 (s), 1032 (w), 989 (m), 915 (w), 857 (w), 809 (w), 737 (m), 687 (m); **HRMS (ESI)** calcd for $C_{21}H_{23}F_2N_2O_3^+$ [M+H]$^+$ 389.1671; found 389.1677.

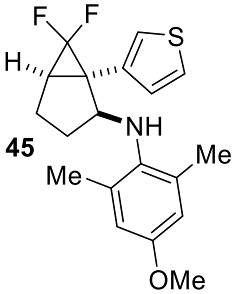
6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(2-methoxyphenyl)bicyclo[3.1.0]hexan-2-amine (44)



44

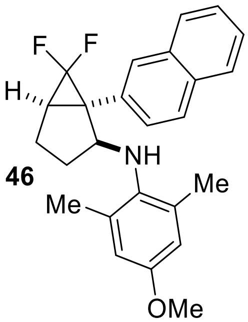
Following the general procedure E, starting from 1-(3,3-difluorocycloprop-1-en-1-yl)-2-methoxybenzene (**88**) (55 mg, 0.30 mmol, 1.0 equiv.), the title compound **44** (94:6 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a pale yellow oil and as a mixture of diastereoisomers (83 mg, 0.22 mmol, 74 % yield). **R*f*** 0.28 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.25 – 7.16 (m, 2H, Ar*H*), 6.87 – 6.80 (m, 2H, Ar*H*), 6.41 (s, 2H, Ar*H*), 4.33 (dd, *J* = 16.5, 7.9 Hz, 1H, C*H*NH), 3.84 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.25 (bs, 1H, N*H*), 2.30 – 2.15 (m, 2H, CF$_2$CHCH_2), 2.12 – 2.06 (m, 1H, NHCHCH_2), 2.03 (s, 6H, CH_3), 1.96 (dd, *J* = 14.9, 5.2 Hz, 1H, CF$_2$C*H*), 1.64 – 1.54 (m, 1H, NHCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 158.5, 154.2, 138.6, 131.9, 130.5, 128.7, 123.5, 120.3, 117.8 (dd, *J* = 302.7, 282.8 Hz), 114.0, 110.4, 65.7, 55.5, 55.4, 41.6 (dd, *J* = 12.6, 7.3 Hz), 35.1 (dd, *J* = 12.5, 8.8 Hz), 31.4 (d, *J* = 7.9 Hz), 24.2, 18.7; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -122.7 (dd, *J* = 160.7, 17.3 Hz, *Major diastereoisomer*), -127.3 (ddd, *J* = 158.9, 14.0, 3.5 Hz, *Minor diasteroisomer*), -137.9 (d, *J* = 159.5 Hz, *Major diastereoisomer*), -141.8 (dd, *J* = 336.1, 156.5 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3386 (w), 2947 (m), 2840 (m), 1606 (m), 1485 (s), 1435 (s), 1317 (m), 1241 (s), 1194 (s), 1148 (s), 1119 (m), 1065 (s), 1029 (s), 981 (s), 910 (s), 850 (m), 795 (w), 754 (s); **HRMS (ESI)** calcd for $C_{22}H_{26}F_2NO_2^+$ [M+H]$^+$ 374.1926; Found 374.1930.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(thiophen-3-yl)bicyclo[3.1.0]hexan-2-amine (45)


45

Following the general procedure E, starting from 3-(3,3-difluorocycloprop-1-en-1-yl)thiophene (**89**) (47 mg, 0.30 mmol, 1.0 equiv.), the title compound **45** (95:5 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 98:2 to 95:5) as a pale yellow oil and as a mixture of diastereoisomers (43 mg, 0.12 mmol, 41 % yield). **R$_f$** 0.52 (Pentane:Et$_2$O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.18 (dd, *J* = 5.0, 3.0 Hz, 1H, HetAr*H*), 7.10 (dd, *J* = 3.1, 1.3 Hz, 1H, HetAr*H*), 6.96 (dt, *J* = 5.2, 1.2 Hz, 1H, HetAr*H*), 6.48 (s, 2H, Ar*H*), 4.33 (dt, *J* = 9.6, 6.7 Hz, 1H, C*H*NH), 3.72 (s, 3H, OC*H*$_3$), 3.27 (bs, 1H, N*H*), 2.22 – 2.04 (m, 10H, NHCHC*H*$_2$, CF$_2$CHC*H*$_2$ & CF$_2$C*H*), 1.69 – 1.59 (m, 1H, NHCHC*H*$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 154.5, 138.2, 135.9, 130.6, 127.8, 125.1, 123.1, 117.2 (hidden dd, one peak was not found due to overlapping), 114.2, 66.4, 55.5, 41.5 (dd, *J* = 12.3, 8.0 Hz), 35.5 (dd, *J* = 12.2, 9.0 Hz), 31.4 (d, *J* = 8.0 Hz), 23.9, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.4 (dd, *J* = 160.6, 15.5 Hz, *Major diastereoisomer*), -125.6 (ddd, *J* = 157.4, 13.5, 5.0 Hz, *Minor diasteroisomer*), -138.1 (d, *J* = 161.4 Hz, *Major diastereoisomer*), -141.8 (d, *J* = 157.0 Hz, *Minor diasteroisomer*); **IR $\tilde{\nu}_{max}$** 3385 (w), 3105 (w), 2947 (m), 2842 (w), 1603 (m), 1486 (s), 1376 (w), 1319 (m), 1225 (s), 1191 (m), 1151 (s), 1101 (m), 1065 (s), 1031 (w), 987 (m), 911 (m), 853 (m), 781 (m), 733 (m), 687 (w), 646 (w); **HRMS (ESI)** calcd for $C_{19}H_{22}F_2NOS^+$ $[M+H]^+$ 350.1385; found 350.1388.

6,6-Difluoro-*N*-(4-methoxy-2,6-dimethylphenyl)-1-(naphthalen-2-yl)bicyclo[3.1.0]hexan-2-amine (46)

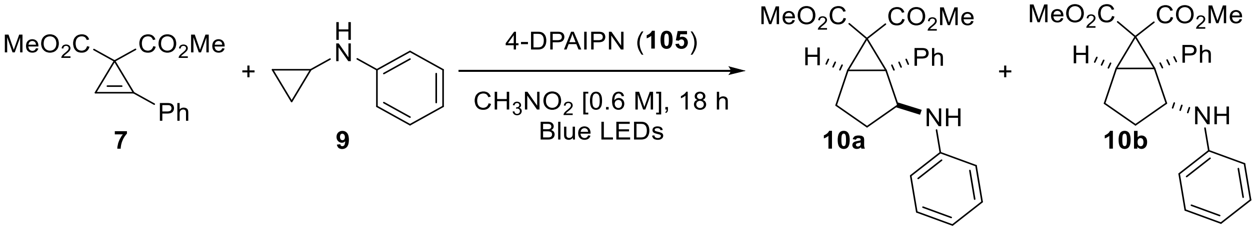

46

Following the general procedure E, starting from 2-(3,3-difluorocycloprop-1-en-1-yl)naphthalene (**90**) (61 mg, 0.30 mmol, 1.0 equiv.), the title compound **46** (93:7 *dr* in the crude ^{19}F NMR) was obtained after purification by column chromatography on Biotage (SNAP cartridge KP-SIL 25 g, Pentane:Et$_2$O 95:5 to 90:10) as a pale yellow oil and as a single diastereoisomer (81 mg, 0.21

mmol, 69 % yield). **R*f*** 0.32 (Pentane:Et_2O 90:10); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.82 – 7.76 (m, 1H, Ar*H*), 7.76 – 7.71 (m, 3H, Ar*H*), 7.49 – 7.40 (m, 3H, Ar*H*), 6.37 (s, 2H, Ar*H*), 4.35 (dd, *J* = 16.5, 7.9 Hz, 1H, C*H*NH), 3.60 (s, 3H, OMe), 3.35 (bs, 1H, N*H*), 2.34 – 2.25 (m, 2H, CF_2CHCH_2), 2.18 (m, 2H, CF_2CH & $NHCHCH_2$), 2.05 (s, 6H, CH_3), 1.76 – 1.64 (m, 1H, $NHCHCH_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)**[24] δ 154.4, 138.1, 133.2, 133.0, 132.6, 130.5, 128.4, 128.0, 127.8, 127.7, 126.0, 125.9, 117.2 (dd, *J* = 302.7, 282.4 Hz), 114.1, 67.6, 55.4, 45.4 (dd, *J* = 11.9, 8.0 Hz), 34.7 (dd, *J* = 12.6, 9.0 Hz), 31.7 (d, *J* = 7.6 Hz), 24.3, 19.0; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -123.0 (dd, *J* = 161.3, 15.8 Hz), -137.3 (d, *J* = 160.5 Hz); **IR $\tilde{\nu}_{max}$** 3373 (w), 3053 (w), 1610 (m), 1486 (s), 1443 (m), 1317 (m), 1231 (m), 1194 (m), 1151 (m), 1066 (s), 1025 (w), 988 (m), 908 (s), 861 (m), 820 (m), 731 (s), 649 (w); **HRMS (ESI)** calcd for $C_{25}H_{26}F_2NO^+$ $[M+H]^+$ 394.1977; found 394.1969.

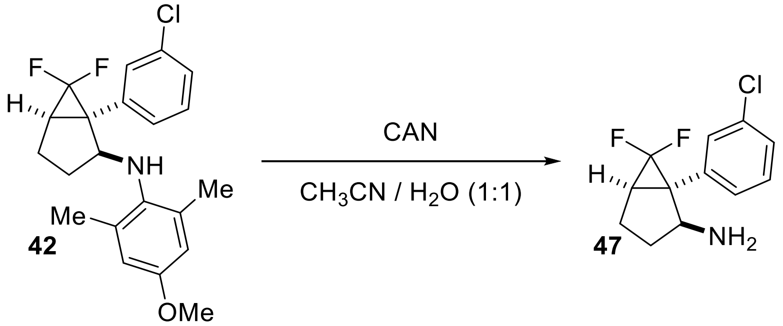
7. Gram-scale Synthesis of 9 and Product Modifications

Procedure for the gram scale 3+2 cycloaddition



A 10 mL test tube was charged with 2,4,5,6-tetrakis(diphenylamino)isophthalonitrile (4-DPAIPN, **105**) (69 mg, 0.086 mmol, 0.02 equiv.), dimethyl 2-phenylcycloprop-2-ene-1,1-dicarboxylate (**7**) (1.00 g, 4.31 mmol, 1 equiv.) and *N*-cyclopropylaniline (**9**) (1.03 g, 7.75 mmol, 1.8 equiv.). The tube was sealed, evacuated and back-filled with nitrogen (3 times). Then 7.2 mL of degassed nitromethane (3 freeze pump thaw cycles) was added via syringe and the resulting mixture was irradiated at room temperature for 18 hours with Blue LEDs, positioned at 4 to 5 cm of the reaction vessel. The reaction mixture was then filtered through a small pad of silica gel eluting with Et_2O, and the filtrate was concentrated under reduced pressure. The desired product (55:45 *dr* in the crude ^{1}H NMR) was obtained as a separable mixture of two diastereoisomers after purification by column chromatography (SiO_2, Pentane:Et_2O 95:5 to 90:10) affording **10a** (755 mg, 2.07 mmol, 48 % yield) and **10b** (677 mg, 1.85 mmol, 43 % yield).

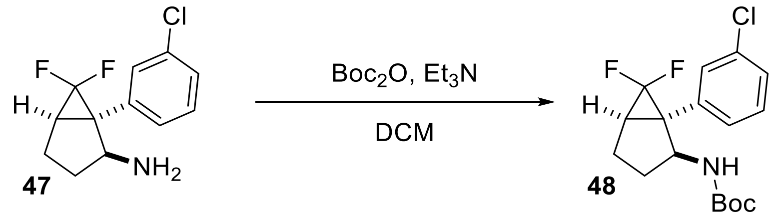
1-(3-Chlorophenyl)-6,6-Difluorobicyclo[3.1.0]hexan-2-amine (47)



To a solution of **42** (92:8 dr, 94 mg, 0.25 mmol, 1.0 equiv.) in CH_3CN (5 mL) was added dropwise at room temperature, a solution of CAN (546 mg, 0.995 mmol, 4.0 equiv.) in H_2O (5 mL). After 30 mins, TLC monitoring (pentane:Et_2O 9:1) indicated full conversion of the starting material. The reaction mixture was quenched with 1 M aq. NaOH until pH = 11 was reached, followed by extraction with EtOAc (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, DCM:MeOH 98:2 to 95:5) affording the title compound **47** (0.041 g, 0.168 mmol, 68 % yield) as a colorless oil and as a 93:7 mixture of diastereoisomers (based on ^{19}F NMR integrations). **R_f** 0.55 (DCM:MeOH 95:5); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.35 – 7.32 (m, 1H, Ar*H*), 7.32 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.22 (m, 1H, Ar*H*), 3.77 (dt, *J* = 9.8, 7.3 Hz, 1H, C*H*NH$_2$), 2.31 – 2.17 (m, 3H, CF$_2$CHC*H$_2$* & NH$_2$CHC*H$_2$*), 2.09 (dd, *J* = 14.6, 4.8 Hz, 1H, CF$_2$C*H*), 1.67 (bs, 2H, N*H$_2$*), 1.63 – 1.52 (m, 1H, NH$_2$CHC*H$_2$*); **^{13}C NMR**

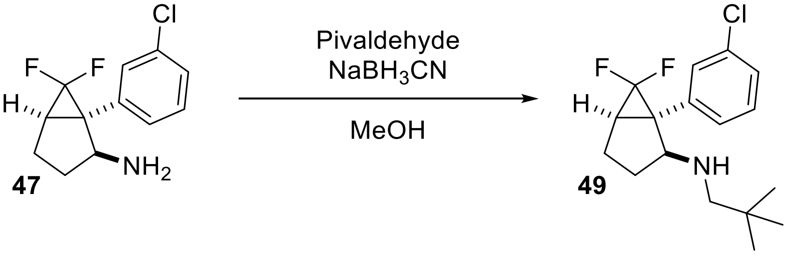
(101 MHz, Chloroform-*d*) δ 137.7, 134.6, 130.1, 129.2 (d, *J* = 2.6 Hz), 128.0, 127.4, 116.4 (dd, *J* = 303.4, 280.1 Hz), 63.3, 46.2 (dd, *J* = 11.8, 7.4 Hz), 34.9 (dd, *J* = 12.6, 9.2 Hz), 32.8 (d, *J* = 8.2 Hz), 24.4; **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -122.9 (dd, *J* = 161.9, 14.8, *Major diastereoisomer*), -125.1 (d, *J* = 162.0, *Minor diastereoisomer*), -140.4 (d, *J* = 161.9, *Major diastereoisomer*), -141.4 (d, *J* = 159.3, *Minor diastereoisomer*); **IR $\tilde{\nu}_{max}$** 3381 (w), 3060 (w), 3033 (w), 2956 (m), 2882 (w), 1717 (w), 1598 (m), 1572 (m), 1477 (m), 1446 (m), 1303 (w), 1255 (m), 1203 (s), 1072 (m), 1023 (w), 987 (s), 946 (w), 915 (w), 874 (w), 783 (s), 733 (m), 697 (s), 603 (w); **HRMS (ESI)** calcd for $C_{12}H_{13}ClF_2N^+$ $[M+H]^+$ 244.0699; found 244.0699.

Tert-butyl (-1-(3-chlorophenyl)-6,6-difluorobicyclo[3.1.0]hexan-2-yl)carbamate (48)



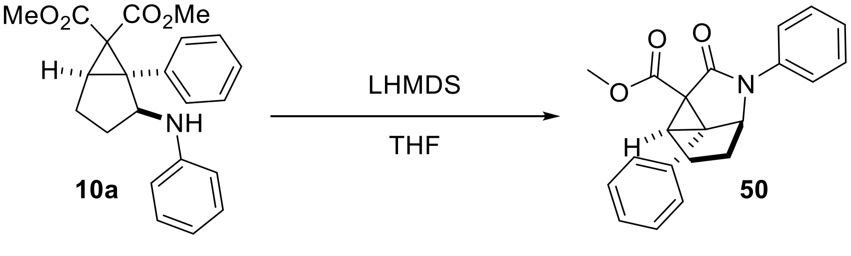
To a solution of **47** (93:7 dr, 21 mg, 0.086 mmol, 1.0 equiv.) in DCM (0.4 mL) was added Boc_2O (26 mg, 0.12 mmol, 1.4 equiv.) and trimethylamine (32 µL, 0.23 mmol, 2.7 equiv.), and the resulting mixture was left stirring overnight at room temperature. The solution was then washed with aqueous citric acid (0.1 M, 1.5 mL). The aqueous layer was extracted with DCM (3 x 5 mL), and the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 5 mL) and brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC (Pentane:EtOAc 85:15) affording compound **48** (22 mg, 0.064 mmol, 74 % yield) as a colorless oil and as a 95:5 mixture of diastereoisomers (based on ^{19}F NMR integrations). **R_f** 0.45 (Pentane:EtOAc 80:20); **^{1}H NMR (400 MHz, Acetonitrile-d_3)** δ 7.40 – 7.27 (m, 4H, Ar*H*), 5.44 (d, *J* = 9.0, 1H, N*H*), 4.61 (qd, *J* = 9.6, 6.6, 1H, NHC*H*), 2.39 – 2.24 (m, 2H, NHCHCH_2), 2.19 – 2.14 (m, 2H, NHCHCH$_2$CH_2 & CF$_2$C*H*), 1.56 – 1.46 (m, 1H, NHCHCH$_2$CH_2), 1.35 (s, 9H, Boc); **^{13}C NMR (101 MHz, Acetonitrile-d_3)** δ 156.3, 138.3, 134.6, 131.0, 130.0, 128.6, 128.5, 117.3 (dd, *J* = 303.6, 277.9 Hz), 79.6, 60.6, 45.2 – 44.7 (m), 34.3 (t, *J* = 10.8 Hz), 30.6 (d, *J* = 8.5 Hz), 28.5, 24.4; **^{19}F NMR (376 MHz, Acetonitrile-d_3)** δ -124.4 (d, *J* = 161.2, *Minor diastereoisomer*), -125.3 (dd, *J* = 160.8, 15.5, *Major diastereoisomer*), -139.9 (d, *J* = 163.0, *Major diastereoisomer*), -142.6 (d, *J* = 159.0, *Minor diastereoisomer*); **IR $\tilde{\nu}_{max}$** 3443 (m), 3339 (m), 2976 (m), 1704 (s), 1567 (w), 1496 (s), 1448 (m), 1369 (m), 1286 (m), 1241 (m), 1167 (s), 1052 (m), 986 (m), 948 (w), 871 (w), 781 (m), 693 (m); **HRMS (ESI)** calcd for $C_{17}H_{20}ClF_2NNaO_2^+$ $[M+Na]^+$ 366.1043; found 366.1048.

1-(3-Chlorophenyl)-6,6-difluoro-*N*-neopentylbicyclo[3.1.0]hexan-2-amine (49)



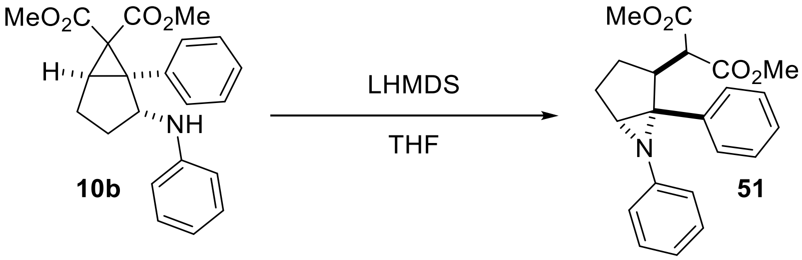
To a solution of **47** (93:7 dr, 21 mg, 0.086 mmol, 1.0 equiv.) in MeOH (0.8 mL) was added $NaBH_3CN$ (8.1 mg, 0.13 mmol, 1.5 equiv.) and pivaldehyde (19 µL, 0.17 mmol, 2.0 equiv.) and the resulting mixture was left stirring overnight at room temperature. The solution was then acidified using aqueous hydrochloric acid (0.1 M, 2.0 mL), followed by extracting with Et_2O (2 x 5 mL). The aqueous layer was then basified with aqueous sodium hydroxide (0.1 M, 4.5 mL), and extracted with DCM (3 x 5 mL). The DCM fractions were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by preparative TLC (Pentane:EtOAc 98:2) affording compound **49** (13 mg, 0.041 mmol, 48 % yield) as a pale yellow oil and as a 92:8 mixture of diastereoisomers (based on ^{19}F NMR integrations). **R_f** 0.58 (Pentane:EtOAc 98:2); **^1H NMR (400 MHz, Chloroform-*d*)** δ 7.47 (m, 1H, Ar*H*), 7.27 – 7.21 (m, 1H, Ar*H*), 7.19 – 7.16 (m, 2H, Ar*H*), 3.52 (dt, *J* = 10.3, 7.0 Hz, 1H, NHC*H*), 2.36 (dd, *J* = 11.4, 0.7 Hz, 1H, NHCH_2), 2.19 – 1.99 (m, 5H, NHCH_2 & NHCHCH_2 & NHCHCH$_2$CH_2 & CF$_2$C*H*), 1.41 – 1.36 (m, 1H, NHCHCH$_2$CH_2), 0.79 (s, 9H, (CH_3)$_3$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 138.4, 134.1, 129.4, 129.3 (d, *J* = 2.3 Hz), 127.4, 127.1, 116.6 (dd, *J* = 305.4, 279.8 Hz), 69.3, 60.9, 44.6 (dd, *J* = 12.4, 8.1 Hz), 33.2 (dd, *J* = 12.5, 9.1 Hz), 31.8, 31.1 (d, *J* = 7.1 Hz), 27.7, 24.2. **^{19}F NMR (376 MHz, Chloroform-*d*)** δ -124.6 (dd, *J* = 159.2, 14.9 Hz, *Major diastereoisomer*), -125.1 (dd, *J* = 157.6, 16.8 Hz, *Minor diastereoisomer*), -137.2 (d, *J* = 159.8 Hz, *Major diastereoisomer*), -141.3 (d, *J* = 158.3 Hz, *Minor diastereoisomer*); **IR $\tilde{\nu}_{max}$** 2953 (s), 2874 (m), 1736 (w), 1598 (m), 1572 (m), 1473 (s), 1364 (m), 1296 (m), 1251 (m), 1201 (s), 1144 (s), 1091 (m), 1067 (m), 988 (m), 912 (m), 830 (w), 786 (m), 735 (s), 694 (s); **HRMS (ESI)** calcd for $C_{17}H_{23}ClF_2N^+$ $[M+H]^+$ 314.1482; found 314.1488.

Methyl 3-oxo-2a^1,4-diphenylhexahydro-4-azacyclopropa[*cd*]pentalene-2b(1*H*)-carboxylate (50)



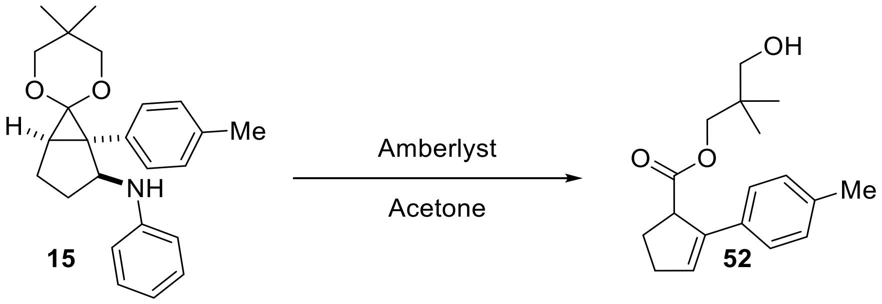
To a stirred solution of compound **10a** (73 mg, 0.20 mmol, 1 equiv.) in THF (3.0 mL) was added dropwise LHMDS (1.0 M solution in THF, 0.22 mL, 0.22 mmol, 1.1 equiv.). After 20 min stirring at room temperature, TLC monitoring indicated full conversion of the starting material. The reaction mixture was therefore quenched by filtration over a small pad of silica gel eluting with EtOAc, and the filtrate was evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO_2 previously deactivated with Et_3N, Pentane:Et_2O 60:40) affording the title compound **50** (0.058 g, 0.17 mmol, 87 % yield) as a pale yellow oil. **R*f*** 0.25 (Pentane:Et_2O 50:50); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.66 – 7.59 (m, 2H, Ar*H*), 7.41 – 7.29 (m, 7H, Ar*H*), 7.18 (t, *J* = 7.4 Hz, 1H, Ar*H*), 4.74 (d, *J* = 3.1 Hz, 1H, C*H*N), 3.56 (s, 3H, OCH_3), 3.30 (dd, *J* = 6.7, 1.5 Hz, 1H, C*H*CH_2), 2.47 – 2.34 (m, 1H, NCHCH_2), 2.14 – 1.99 (m, 2H, NCHCH_2CH_2), 1.97 – 1.86 (m, 1H, NCHCH_2); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 167.0, 165.9, 138.0, 134.2, 129.3, 128.8, 128.7, 128.5, 125.4, 121.8, 69.3, 55.7, 52.6, 49.4, 38.0, 37.1, 23.9; **IR $\tilde{\nu}_{max}$** 3057 (w), 2956 (w), 2871 (w), 1734 (s), 1694 (s), 1597 (w), 1496 (s), 1254 (s), 1219 (w), 1175 (w), 1138 (w), 1086 (m), 973 (w), 913 (m), 828 (w), 730 (s), 696 (m), 645 (w); **HRMS (ESI)** calcd for $C_{21}H_{20}NO_3^+$ $[M+H]^+$ 334.1438; found 334.1442.

Dimethyl 2-(1,6-diphenyl-6-azabicyclo[3.1.0]hexan-2-yl)malonate (51)



To a stirred solution of compound **10b** (73 mg, 0.20 mmol, 1 equiv.) in THF (3.0 mL) was added dropwise LHMDS (1.0 M solution in THF, 0.22 mL, 0.22 mmol, 1.1 equiv.). After 20 min stirring at room temperature, TLC monitoring indicated full conversion of the starting material. The reaction mixture was therefore quenched by filtration over a small pad of silica gel eluting with EtOAc, and the filtrate was evaporated under reduced pressure to afford the pure title compound **51** without further purification (0.069 g, 0.19 mmol, 95 % yield) as a pale yellow oil. NMR experiments were performed in $CDCl_3$ that was previously eluted through basic alumina, due to the observed acid sensitivity of **51**. **R*f*** 0.45 (Pentane:Et_2O 70:30); **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.31 – 7.24 (m, 4H, Ar*H*), 7.22 – 7.17 (m, 1H, Ar*H*), 7.12 (t, *J* = 7.7 Hz, 2H, Ar*H*), 6.87 – 6.81 (m, 3H, Ar*H*), 3.61 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.51 (d, *J* = 5.9 Hz, 1H, C*H*CHCOOCH_3), 3.49 (d, *J* = 2.4 Hz, 1H, C*H*COOCH_3), 3.38 (ddd, *J* = 8.9, 5.6, 1.4 Hz, 1H, NC*H*), 2.18 – 2.06 (m, 2H, NCHCH_2CH_2), 1.74 (ddt, *J* = 14.4, 8.4, 1.7 Hz, 1H, NCHC$H_2$$CH_2$), 1.50 – 1.39 (m, 1H, NCHC$H_2$$CH_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 169.3, 168.9, 148.1, 134.9, 130.1, 128.8, 128.3, 127.9, 121.5, 119.9, 59.9, 53.6, 52.5, 52.2, 48.5, 41.6, 26.3, 25.6; **IR $\tilde{\nu}_{max}$** 3026 (w), 2950 (m), 2858 (w), 1739 (s), 1597 (m), 1491 (m), 1442 (m), 1388 (w), 1367 (w), 1254 (s), 1199 (m), 1161 (m), 1029 (w), 930 (w), 766 (m), 698 (m); **HRMS (ESI)** calcd for $C_{22}H_{24}NO_4^+$ $[M+H]^+$ 366.1700; found 366.1694.

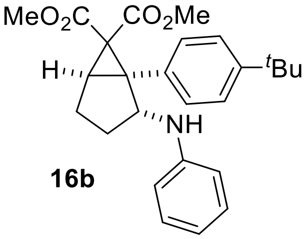
3-ydroxy-2,2-dimethylpropyl 2-(p-tolyl)cyclopent-2-ene-1-carboxylate (52)



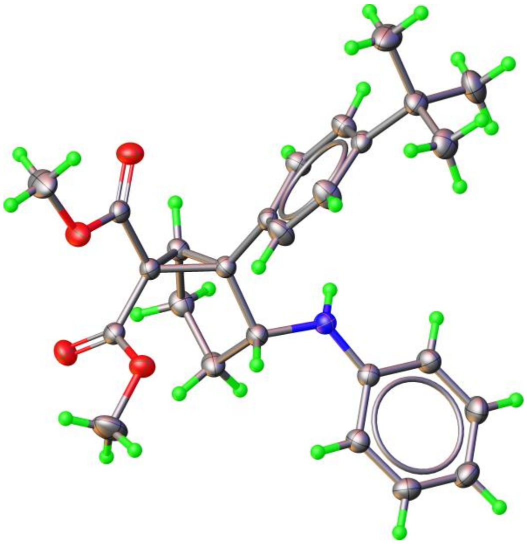
To a stirred solution of **15** (49.0 mg, 0.135 mmol, 1 equiv.) in acetone (4 mL) was added Amberlyst 15 (100 mg). The resulting suspension was stirred at room temperature for 24 h, and then filtered through celite. The filtrate was evaporated under reduced pressure. The crude residue was purified by preparative TLC (Pentane:EtOAc 80:20) affording the title compound **52** (29 mg, 0.099 mmol, 73 % yield) as a white solid. **R*f*** 0.35 (Pentane:EtOAc 80:20); **m.p** = 49-50 °C; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.32 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.11 (d, *J* = 7.9 Hz, 2H, Ar*H*), 6.28 (td, *J* = 2.7, 1.6 Hz, 1H, C=C*H*), 4.00 (dddt, *J* = 9.4, 4.2, 2.8, 1.4 Hz, 1H, C*H*CO), 3.85 (q, *J* = 11.0 Hz, 2H, COOCH_2), 3.06 (s, 2H, CH_2OH), 2.77 – 2.64 (m, 1H, C=CHCH_2CH$_2$), 2.62 – 2.50 (m, 1H, C=CHCH_2CH$_2$), 2.41 – 2.33 (m, 1H, C=CHCH$_2$CH_2), 2.32 (s, 3H, C$_{Ar}$CH_3), 2.30 – 2.21 (m, 1H, C=CHCH$_2$CH_2), 0.78 (s, 6H, (CH$_3$)$_2$); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 176.1, 141.0, 137.4, 132.7, 129.3, 129.3, 125.9, 69.8, 68.2, 51.5, 36.5, 32.7, 29.5, 21.5, 21.3; **IR $\tilde{\nu}_{max}$** 3485 (m), 2958 (s), 1725 (s), 1617 (w), 1513 (w), 1468 (m), 1375 (m), 1331 (m), 1268 (m), 1170 (s), 1044 (s), 962 (w), 810 (m), 740 (w); **HRMS (ESI)** calcd for $C_{18}H_{24}NaO3^+$ [M+Na]$^+$ 311.1618; found 311.1621.

8. Crystal Structure of 16b

Dimethyl 1-(4-(*tert*-butyl)phenyl)-2-(phenylamino)bicyclo[3.1.0]hexane-6,6-dicarboxylate (16b)



16b



Experimental. Single clear colourless plate-shaped crystals of **16b** were obtained by recrystallisation from DCM/Pentane at room temperature. A suitable crystal of 0.29×0.11×0.06 mm^3 was selected and mounted on a suitable support on a SuperNova, Dual, Cu at home/near, Atlas diffractometer. The crystal was kept at a steady T = 140.00(10) K during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) structure solution program using the dual solution method and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with version 2018/3 of **ShelXL** (Sheldrick, 2015) using full matrix least squares on $|F|^2$ minimisation.

Crystal Data. $C_{26}H_{31}NO_4$, M_r = 421.52, orthorhombic, *Pbca* (No. 61), a = 16.11470(19) Å, b = 12.70487(14) Å, c = 22.6264(2) Å, $\alpha = \beta = \gamma = 90^\circ$, V = 4632.42(9) Å^3, T = 140.00(10) K, Z = 8, Z' = 1, $\mu(\mathrm{Cu}K\alpha)$ = 0.647, 33970 reflections measured, 4653 unique (R_{int} = 0.0368) which were used in all calculations. The final wR_2 was 0.0953 (all data) and R_1 was 0.0350 (I > 2(I)).

Compound	bm3-459-pb (16b)
Formula	$C_{26}H_{31}NO_4$
$D_{calc.}$/ g cm^{-3}	1.209
μ/mm^{-1}	0.647
Formula Weight	421.52
Colour	clear colourless
Shape	plate
Size/mm^3	0.29×0.11×0.06
T/K	140.00(10)
Crystal System	orthorhombic
Space Group	*Pbca*
a/Å	16.11470(19)
b/Å	12.70487(14)
c/Å	22.6264(2)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
V/Å^3	4632.42(9)
Z	8
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu$K\alpha$
$\Theta_{min}/^\circ$	3.907
$\Theta_{max}/^\circ$	73.601
Measured Refl.	33970
Independent Refl.	4653
Reflections with I > 2(I)	3975
R_{int}	0.0368
Parameters	290
Restraints	0
Largest Peak/e Å^{-3}	0.352
Deepest Hole/e Å^{-3}	-0.169
GooF	1.022
wR_2 (all data)	0.0953
wR_2	0.0891
R_1 (all data)	0.0425
R_1	0.0350

A clear colourless plate-shaped crystal with dimensions of 0.29×0.11×0.06 mm^3 was mounted on a suitable support. Data were collected using a SuperNova, Dual, Cu at home/near, Atlas diffractometer operating at T = 140.00(10) K.

Data were measured using ω scans using Cu$K\alpha$ radiation. The total number of runs and images was based on the strategy calculation from the program **CrysAlisPro** (Rigaku, V1.171.40.20a, 2018) The maximum resolution achieved was Θ = 73.601° (0.80 Å).

The diffraction pattern was indexed. The total number of runs and images was based on the strategy calculation from the program **CrysAlisPro** (Rigaku, V1.171.40.20a, 2018) and the unit cell was refined using **CrysAlisPro** (Rigaku, V1.171.40.20a, 2018) on 10757 reflections, 32% of the observed reflections.

Data reduction, scaling and absorption corrections were performed using **CrysAlisPro** (Rigaku, V1.171.40.20a, 2018). The final completeness is 100.00 % out to 73.601° in Θ. A Gaussian absorption correction was performed using CrysAlisPro 1.171.40.20a (Rigaku Oxford Diffraction, 2018). Numerical absorption correction based on Gaussian integration over a multifaceted crystal model. Empirical absorption correction using spherical harmonics as implemented in SCALE3 ABSPACK scaling algorithm. The absorption coefficient μ of this material is 0.647 mm^{-1} at this wavelength (λ = 1.542Å) and the minimum and maximum transmissions are 0.687 and 1.000.

The structure was solved and the space group *Pbca* (# 61) determined by the **ShelXT** (Sheldrick, 2015) structure solution program using dual and refined by full matrix least squares on $|F|^2$ using version 2018/3 of **ShelXL** (Sheldrick, 2015). All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent C-atom (1.5 U_{eq} for the methyl groups), but hydrogen on nitrogen atom (N1) was found in a difference map and refined freely.

There is a single molecule in the asymmetric unit, which is represented by the reported sum formula. In other words: Z is 8 and Z' is 1.

Table 3: Fractional Atomic Coordinates ($\times10^4$) and Equivalent Isotropic Displacement Parameters (Å$^2\times10^3$) for **16b**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
O1	4552.8(6)	5092.8(7)	4125.0(4)	30.0(2)
O2	5377.9(6)	3665.4(7)	4127.5(4)	29.3(2)
O3	5393.3(6)	2921.6(7)	2813.8(4)	29.1(2)
O4	6560.3(5)	3705.7(7)	3125.0(4)	26.52(19)
N1	6243.3(6)	6845.1(8)	2311.9(4)	23.8(2)
C1	6157.0(7)	5757.2(9)	2499.5(5)	23.2(2)
C2	5611.1(7)	5741.8(9)	3061.0(5)	20.9(2)
C3	4772.6(7)	5337.2(9)	2877.8(5)	22.9(2)
C4	4765.4(8)	5139.6(10)	2218.2(5)	28.0(3)
C5	5686.3(8)	5079.7(10)	2039.1(5)	27.7(3)
C6	5786.2(7)	6567.6(9)	3514.8(5)	20.6(2)
C7	6504.2(8)	6499.7(10)	3849.2(6)	29.6(3)
C8	6748.5(8)	7318.2(10)	4217.5(6)	32.0(3)
C9	6280.8(7)	8233.4(9)	4270.2(5)	22.4(2)
C10	5530.2(8)	8256.0(9)	3965.3(5)	25.5(2)
C11	5285.9(7)	7445.5(10)	3591.6(5)	25.0(2)

Atom	x	y	z	U_{eq}
C12	6572.9(8)	9176.3(10)	4640.5(5)	28.4(3)
C13	6142.5(10)	9149.7(13)	5243.1(6)	43.4(4)
C14	6360.4(10)	10211.4(11)	4322.6(7)	39.6(3)
C15	7515.8(9)	9154.2(11)	4733.5(6)	34.2(3)
C16	5326.6(7)	4641.1(9)	3256.0(5)	21.0(2)
C17	5038.3(7)	4519.7(9)	3882.9(5)	22.4(2)
C18	5112.7(11)	3425.2(12)	4723.2(6)	42.2(4)
C19	5744.0(7)	3662.4(9)	3033.9(5)	21.9(2)
C20	7012.1(10)	2778.9(12)	2944.5(8)	46.0(4)
C21	6773.9(7)	7125.4(9)	1857.8(5)	22.3(2)
C22	6709.9(8)	8144.9(9)	1619.5(6)	27.5(3)
C23	7268.0(9)	8498.5(10)	1201.4(6)	32.6(3)
C24	7911.5(8)	7855.6(11)	1007.4(6)	32.7(3)
C25	7969.3(8)	6841.5(10)	1229.5(5)	28.8(3)
C26	7405.2(7)	6469.3(9)	1644.1(5)	24.8(2)

Table 4: Anisotropic Displacement Parameters (×10^4) **16b.** The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2} \times U_{11} + \ldots + 2hka^* \times b^* \times U_{12}]$

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	32.2(5)	31.3(5)	26.3(4)	-3.2(3)	5.8(4)	2.8(4)
O2	39.8(5)	26.0(4)	22.1(4)	3.4(3)	4.9(4)	2.3(4)
O3	33.6(5)	22.8(4)	30.9(4)	-5.4(3)	0.8(4)	-3.8(3)
O4	23.3(4)	27.8(4)	28.4(4)	-2.2(3)	1.4(3)	3.6(3)
N1	24.9(5)	21.6(5)	24.8(5)	2.1(4)	3.2(4)	2.2(4)
C1	26.7(6)	21.5(5)	21.3(5)	0.5(4)	1.9(4)	-0.4(4)
C2	23.1(5)	20.0(5)	19.4(5)	0.5(4)	-0.2(4)	0.1(4)
C3	24.1(5)	21.7(5)	22.8(5)	-1.9(4)	-1.6(4)	-0.1(4)
C4	33.9(6)	26.8(6)	23.2(6)	-2.2(5)	-6.1(5)	-1.4(5)
C5	38.1(7)	25.8(6)	19.1(5)	-1.3(4)	1.8(5)	-3.4(5)
C6	23.3(5)	20.1(5)	18.4(5)	0.9(4)	0.8(4)	-2.9(4)
C7	28.9(6)	24.1(6)	35.8(7)	-5.1(5)	-7.5(5)	5.3(5)
C8	28.8(6)	30.5(7)	36.8(7)	-5.4(5)	-12.5(5)	2.9(5)
C9	26.4(6)	23.2(6)	17.7(5)	0.5(4)	1.9(4)	-3.8(4)
C10	29.4(6)	22.5(6)	24.5(5)	-2.2(4)	-1.8(5)	3.9(5)
C11	24.5(6)	26.8(6)	23.8(5)	-1.8(4)	-4.3(4)	1.7(5)
C12	32.8(6)	27.6(6)	24.9(6)	-4.8(5)	0.6(5)	-5.0(5)
C13	50.8(9)	48.1(9)	31.4(7)	-15.7(6)	9.8(6)	-13.5(7)
C14	43.2(8)	24.7(6)	50.9(8)	-4.4(6)	-7.0(6)	-5.3(5)
C15	35.0(7)	35.1(7)	32.5(6)	-5.0(5)	-6.2(5)	-8.7(5)
C16	21.9(5)	20.2(5)	21.0(5)	-1.0(4)	1.0(4)	-1.5(4)
C17	23.0(5)	21.5(5)	22.7(5)	-2.4(4)	0.4(4)	-4.2(4)
C18	67.1(10)	35.4(7)	23.9(6)	6.7(5)	10.9(6)	2.2(7)
C19	24.4(5)	22.4(5)	18.9(5)	1.8(4)	1.7(4)	-0.6(4)
C20	36.9(8)	42.2(8)	58.8(9)	-13.4(7)	3.9(7)	15.6(6)
C21	23.5(5)	23.6(5)	19.7(5)	0.1(4)	-1.9(4)	-1.4(4)
C22	29.1(6)	24.8(6)	28.7(6)	2.9(5)	1.8(5)	3.8(5)
C23	40.6(7)	25.5(6)	31.5(6)	6.0(5)	3.7(5)	-1.1(5)
C24	33.0(7)	36.2(7)	28.8(6)	2.6(5)	7.5(5)	-5.0(5)
C25	25.8(6)	35.2(7)	25.4(6)	-2.6(5)	1.2(5)	3.5(5)
C26	27.9(6)	23.9(6)	22.6(5)	0.6(4)	-0.8(5)	2.3(4)

Table 5: Bond Lengths in Å for **16b**.

Atom	Atom	Length/Å
O1	C17	1.2011(15)
O2	C17	1.3357(15)
O2	C18	1.4466(15)
O3	C19	1.2055(15)
O4	C19	1.3326(15)
O4	C20	1.4434(16)
N1	C1	1.4526(15)
N1	C21	1.3834(15)
C1	C2	1.5454(15)
C1	C5	1.5497(16)
C2	C3	1.5038(15)
C2	C6	1.4949(15)
C2	C16	1.5363(15)
C3	C4	1.5134(16)
C3	C16	1.5204(16)
C4	C5	1.5402(18)
C6	C7	1.3851(17)
C6	C11	1.3872(17)
C7	C8	1.3895(18)
C8	C9	1.3908(17)
C9	C10	1.3929(17)
C9	C12	1.5358(16)
C10	C11	1.3894(17)
C12	C13	1.5302(18)
C12	C14	1.5376(19)
C12	C15	1.5342(19)
C16	C17	1.5004(15)
C16	C19	1.5004(16)
C21	C22	1.4068(16)
C21	C26	1.4012(17)
C22	C23	1.3805(18)
C23	C24	1.391(2)
C24	C25	1.3860(19)
C25	C26	1.3892(17)

Table 6: Bond Angles in ° for **16b**.

Atom	Atom	Atom	Angle/°
C17	O2	C18	115.88(10)
C19	O4	C20	114.86(10)
C21	N1	C1	121.41(10)
N1	C1	C2	107.87(9)
N1	C1	C5	112.27(9)
C2	C1	C5	105.48(9)
C3	C2	C1	106.81(9)
C3	C2	C16	60.00(7)
C6	C2	C1	116.64(9)
C6	C2	C3	126.79(10)
C6	C2	C16	119.85(9)
C16	C2	C1	114.68(9)
C2	C3	C4	109.59(10)
C2	C3	C16	61.06(7)

Atom	Atom	Atom	Angle/˚
C4	C3	C16	117.59(10)
C3	C4	C5	105.09(9)
C4	C5	C1	105.50(9)
C7	C6	C2	119.30(10)
C7	C6	C11	117.85(10)
C11	C6	C2	122.72(10)
C6	C7	C8	121.18(11)
C7	C8	C9	121.57(11)
C8	C9	C10	116.45(11)
C8	C9	C12	122.20(11)
C10	C9	C12	121.36(11)
C11	C10	C9	122.16(11)
C6	C11	C10	120.49(11)
C9	C12	C14	110.10(10)
C13	C12	C9	109.27(10)
C13	C12	C14	109.56(12)
C13	C12	C15	109.05(11)
C15	C12	C9	111.35(10)
C15	C12	C14	107.48(11)
C3	C16	C2	58.94(7)
C17	C16	C2	117.23(9)
C17	C16	C3	114.21(9)
C19	C16	C2	121.63(9)
C19	C16	C3	123.83(9)
C19	C16	C17	111.73(9)
O1	C17	O2	124.78(11)
O1	C17	C16	124.80(11)
O2	C17	C16	110.39(9)
O3	C19	O4	123.99(11)
O3	C19	C16	125.12(11)
O4	C19	C16	110.88(10)
N1	C21	C22	118.44(11)
N1	C21	C26	123.50(11)
C26	C21	C22	117.96(11)
C23	C22	C21	120.96(12)
C22	C23	C24	120.72(12)
C25	C24	C23	118.78(12)
C24	C25	C26	121.15(12)
C25	C26	C21	120.37(11)

Table 7: Torsion Angles in ˚ for **16b**.

Atom	Atom	Atom	Atom	Angle/˚
N1	C1	C2	C3	105.41(10)
N1	C1	C2	C6	-42.95(13)
N1	C1	C2	C16	169.56(9)
N1	C1	C5	C4	-91.34(11)
N1	C21	C22	C23	174.43(12)
N1	C21	C26	C25	-173.31(11)
C1	N1	C21	C22	167.58(11)
C1	N1	C21	C26	-16.23(17)
C1	C2	C3	C4	-2.18(12)
C1	C2	C3	C16	109.22(10)
C1	C2	C6	C7	-71.69(14)

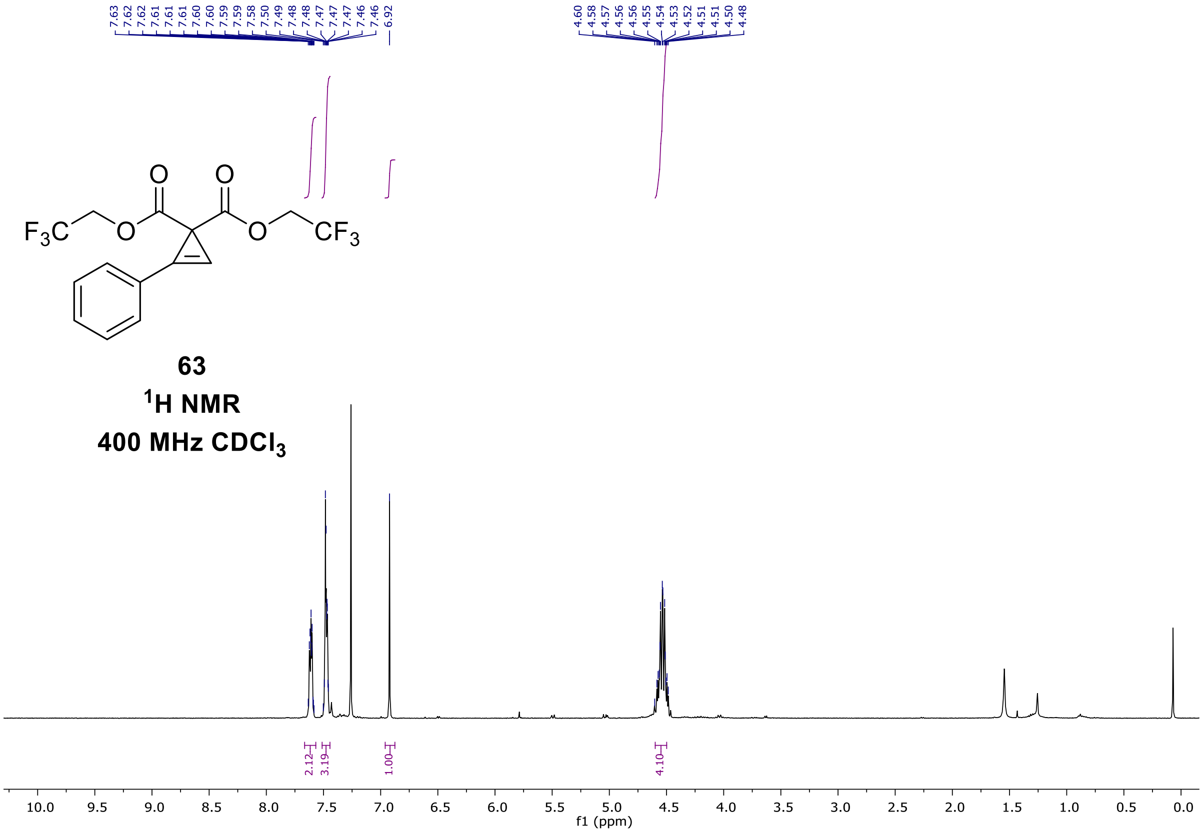
Atom	Atom	Atom	Atom	Angle/°
C1	C2	C6	C11	103.95(13)
C1	C2	C16	C3	-95.87(10)
C1	C2	C16	C17	160.93(10)
C1	C2	C16	C19	17.23(15)
C2	C1	C5	C4	25.88(12)
C2	C3	C4	C5	18.32(13)
C2	C3	C16	C17	108.35(10)
C2	C3	C16	C19	-109.47(12)
C2	C6	C7	C8	171.18(12)
C2	C6	C11	C10	-171.72(11)
C2	C16	C17	O1	48.11(16)
C2	C16	C17	O2	-133.82(10)
C2	C16	C19	O3	-128.14(12)
C2	C16	C19	O4	53.38(13)
C3	C2	C6	C7	147.14(12)
C3	C2	C6	C11	-37.22(17)
C3	C2	C16	C17	-103.20(11)
C3	C2	C16	C19	113.10(12)
C3	C4	C5	C1	-27.09(12)
C3	C16	C17	O1	-18.00(16)
C3	C16	C17	O2	160.07(9)
C3	C16	C19	O3	-56.61(16)
C3	C16	C19	O4	124.92(11)
C4	C3	C16	C2	98.25(11)
C4	C3	C16	C17	-153.40(10)
C4	C3	C16	C19	-11.22(16)
C5	C1	C2	C3	-14.76(12)
C5	C1	C2	C6	-163.12(10)
C5	C1	C2	C16	49.39(12)
C6	C2	C3	C4	141.98(11)
C6	C2	C3	C16	-106.62(12)
C6	C2	C16	C3	117.77(12)
C6	C2	C16	C17	14.57(15)
C6	C2	C16	C19	-129.13(11)
C6	C7	C8	C9	0.6(2)
C7	C6	C11	C10	3.97(17)
C7	C8	C9	C10	4.09(19)
C7	C8	C9	C12	-175.55(12)
C8	C9	C10	C11	-4.78(18)
C8	C9	C12	C13	-99.20(15)
C8	C9	C12	C14	140.43(13)
C8	C9	C12	C15	21.32(16)
C9	C10	C11	C6	0.80(18)
C10	C9	C12	C13	81.18(15)
C10	C9	C12	C14	-39.19(16)
C10	C9	C12	C15	-158.30(11)
C11	C6	C7	C8	-4.66(19)
C12	C9	C10	C11	174.86(11)
C16	C2	C3	C4	-111.40(10)
C16	C2	C6	C7	74.04(14)
C16	C2	C6	C11	-110.32(13)
C16	C3	C4	C5	-48.51(13)
C17	C16	C19	O3	86.38(14)
C17	C16	C19	O4	-92.10(11)
C18	O2	C17	O1	1.42(18)

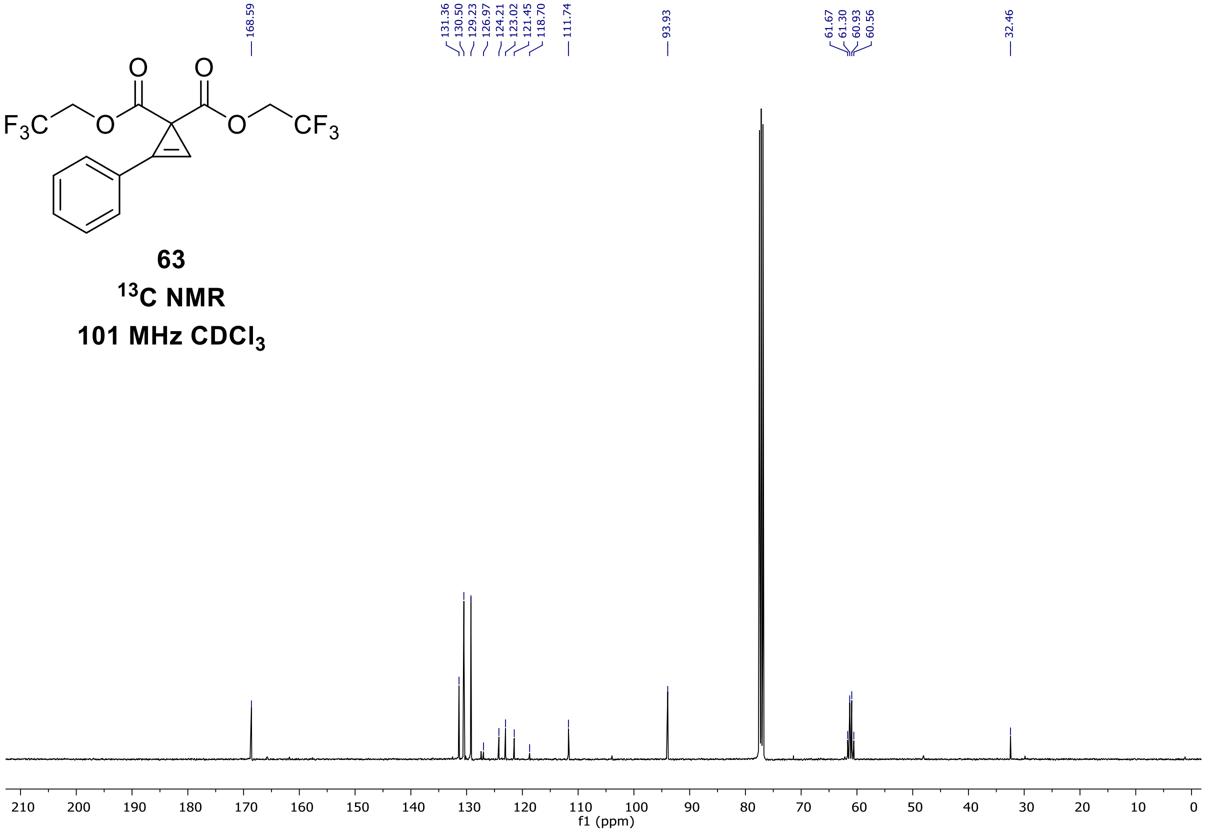
Atom	Atom	Atom	Atom	Angle/°
C18	O2	C17	C16	-176.65(11)
C19	C16	C17	O1	-164.75(11)
C19	C16	C17	O2	13.32(13)
C20	O4	C19	O3	-0.65(17)
C20	O4	C19	C16	177.85(11)
C21	N1	C1	C2	172.76(10)
C21	N1	C1	C5	-71.44(14)
C21	C22	C23	C24	-0.3(2)
C22	C21	C26	C25	2.89(17)
C22	C23	C24	C25	1.8(2)
C23	C24	C25	C26	-0.8(2)
C24	C25	C26	C21	-1.54(19)
C26	C21	C22	C23	-1.97(18)

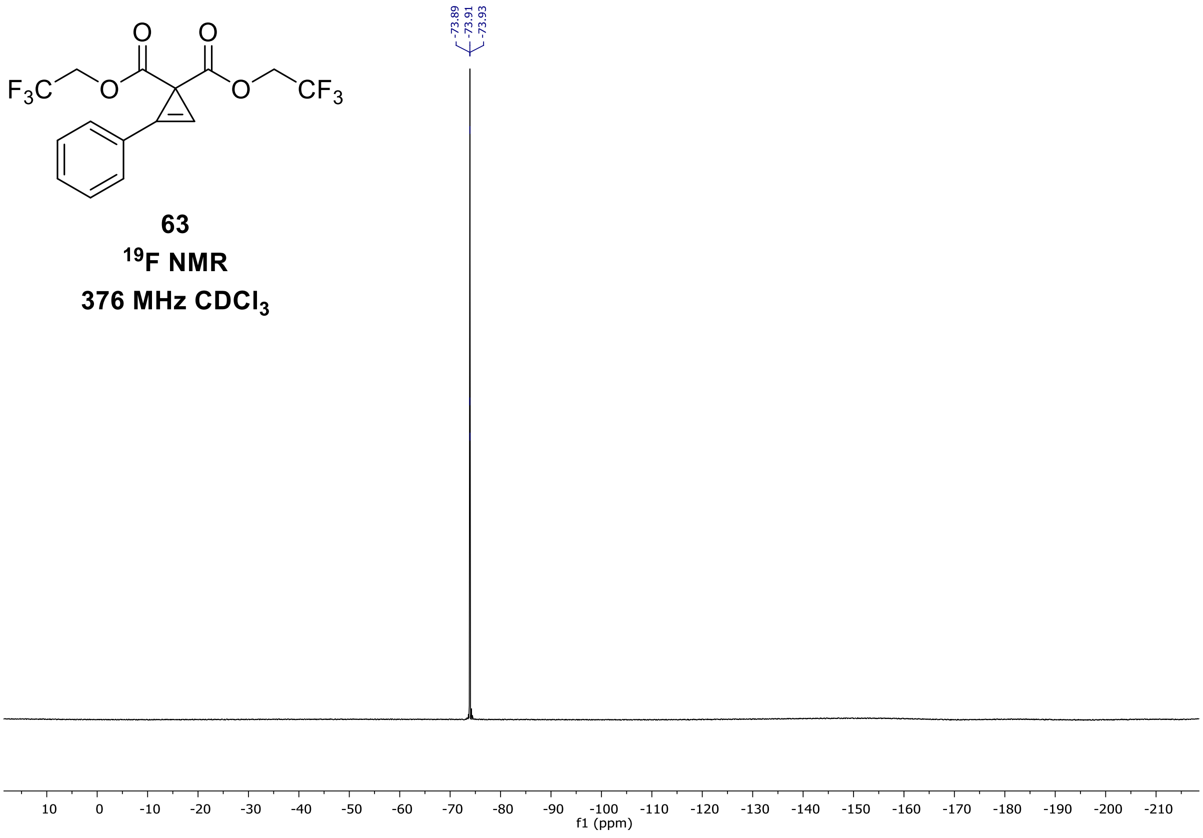
Table 8: Hydrogen Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters ($Å^2×10^3$) for **16b**. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{ij}.

Atom	x	y	z	U_{eq}
H1	5797(11)	7204(13)	2322(7)	33(4)
H1A	6702.75	5450.98	2582.72	28
H3	4278.74	5649.28	3059.94	27
H4A	4488.29	5709.33	2012.09	34
H4B	4483.11	4484.83	2127.79	34
H5A	5766.17	5357.62	1643.89	33
H5B	5880.87	4357.39	2048.49	33
H7	6828.49	5895.56	3826.89	36
H8	7236.4	7252.4	4433.96	38
H10	5181.03	8832.5	4013.48	31
H11	4783.13	7491.86	3391.42	30
H13A	6317.61	9744.07	5473.56	65
H13B	6287.71	8511.75	5445.59	65
H13C	5552.15	9176.73	5188.35	65
H14A	6618.34	10218.52	3940.13	59
H14B	6560.53	10794.94	4551.36	59
H14C	5769.63	10267.05	4277.68	59
H15A	7661.87	8552.87	4968.44	51
H15B	7686.73	9784.78	4933.06	51
H15C	7788.85	9111.04	4357.18	51
H18A	4518.18	3382.9	4735.37	63
H18B	5298.19	3969.75	4986.07	63
H18C	5345.84	2763.73	4843.57	63
H20A	6899.16	2633.98	2535.95	69
H20B	6841.61	2190.23	3181.14	69
H20C	7596.13	2896.17	2996.35	69
H22	6285.37	8587.14	1745.57	33
H23	7213.22	9173.86	1047.8	39
H24	8295.87	8101.67	733.67	39
H25	8393.12	6402.64	1098.71	35
H26	7446.73	5780.83	1780.52	30

9. Spectra of New Compounds



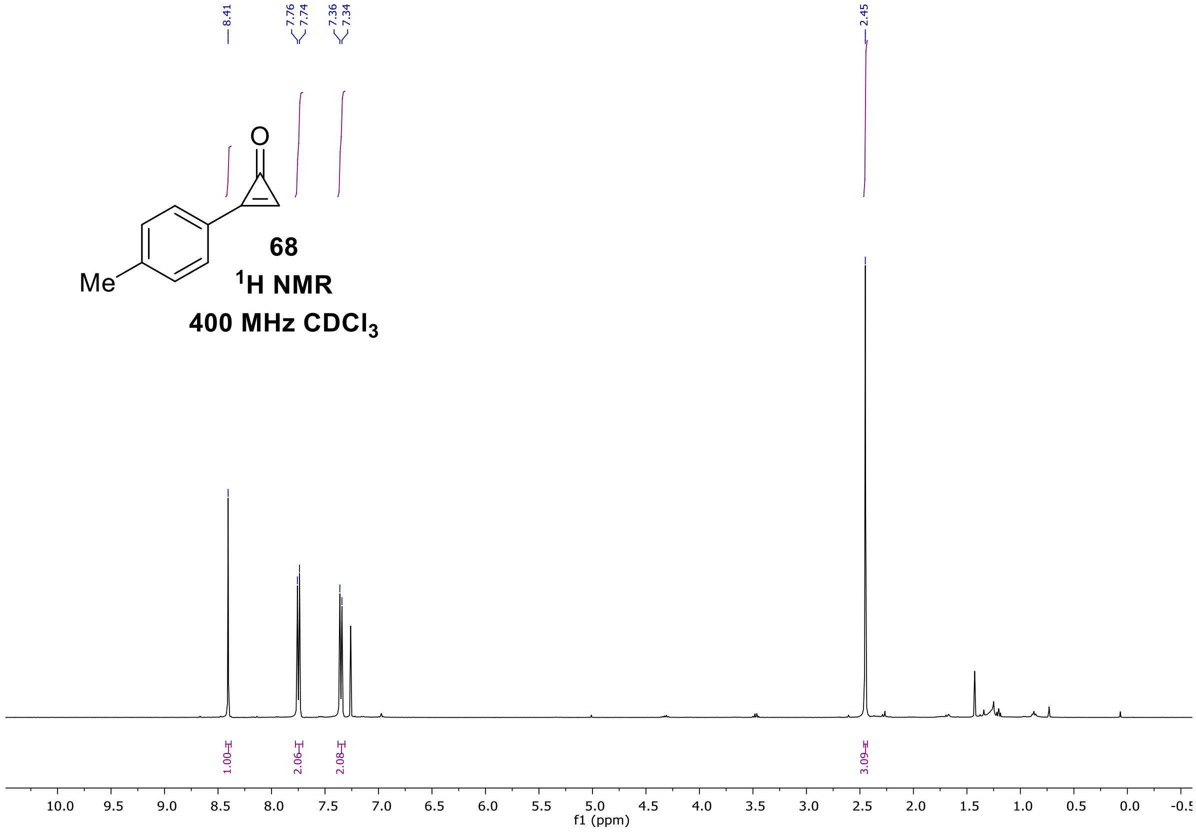


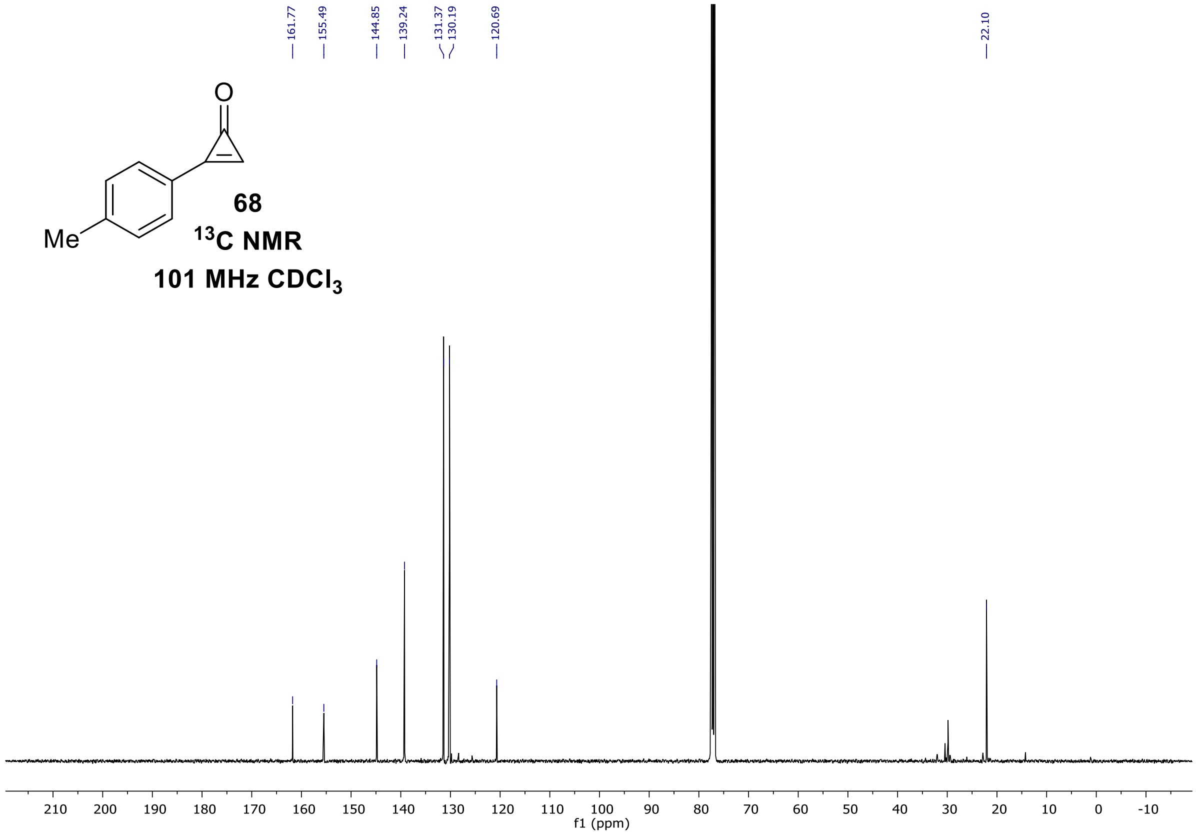


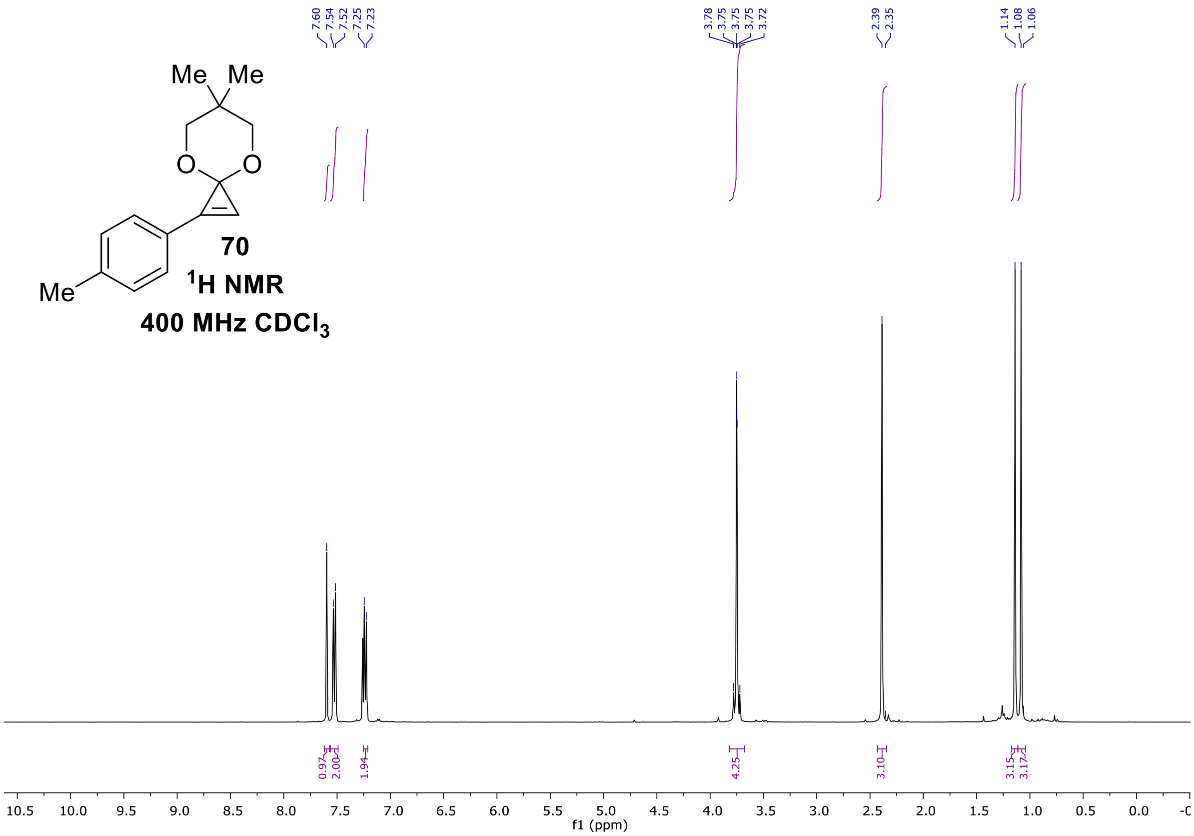
63

^{19}F NMR

376 MHz $CDCl_3$


8.41
7.76
7.74
7.36
7.34
2.45
O
Me
68
^{1}H NMR
400 MHz CDCl$_3$
1.00
2.06
2.08
3.09
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)

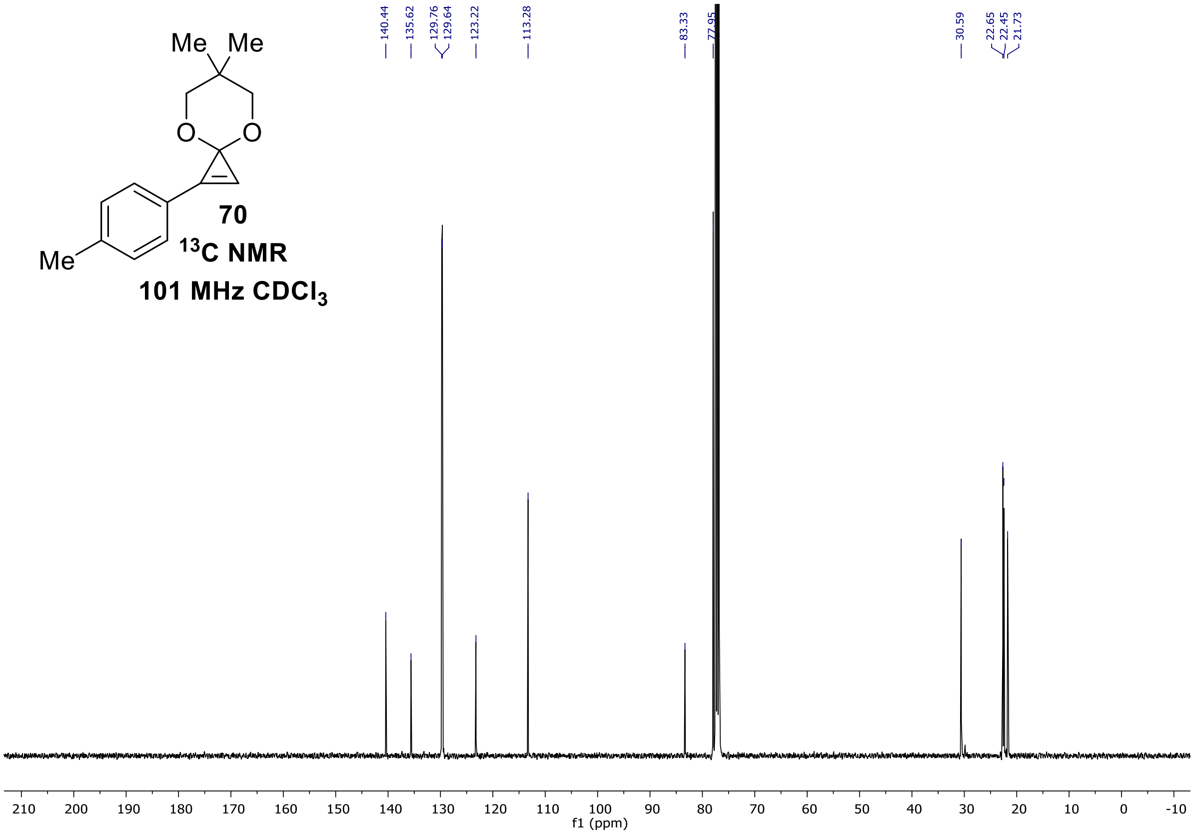

161.77
155.49
144.85
139.24
131.37
130.19
120.69
22.10
O
Me
68
^{13}C NMR
101 MHz CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



70

^{1}H NMR

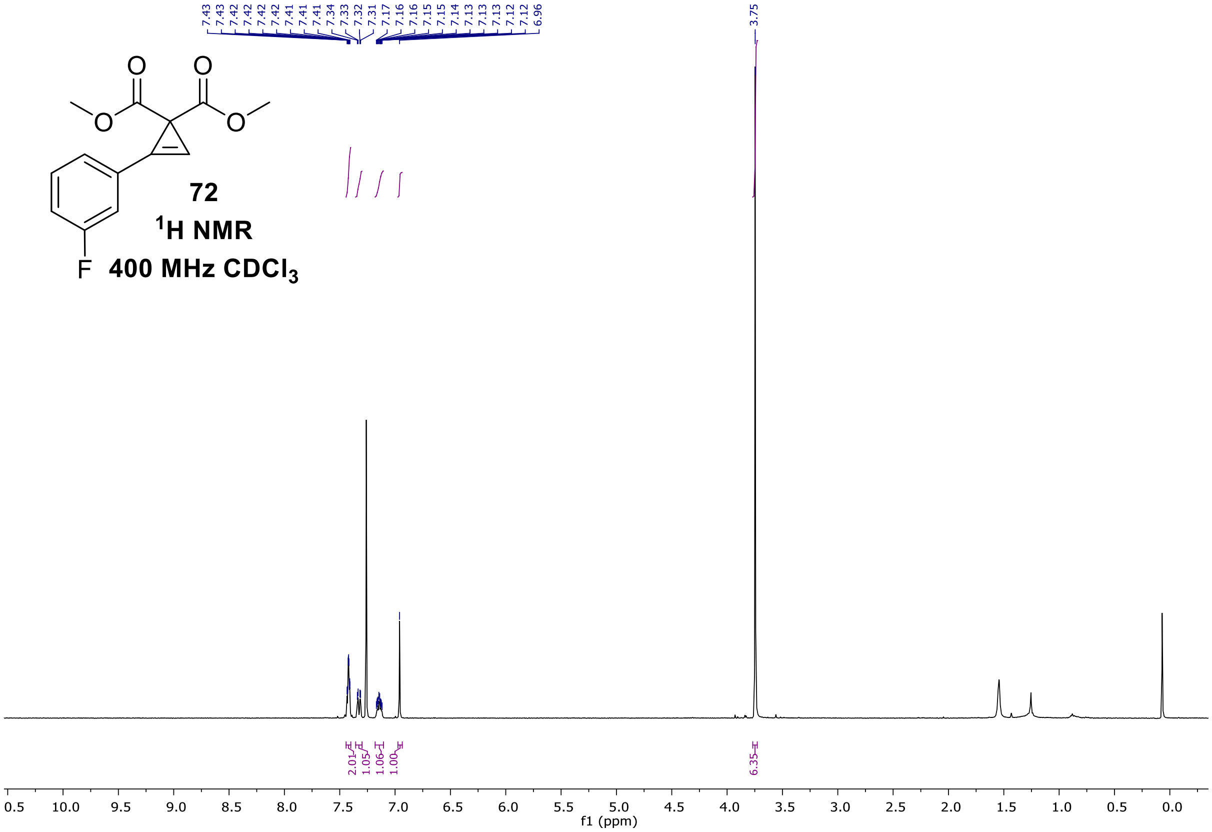
400 MHz CDCl$_3$



70

^{13}C NMR

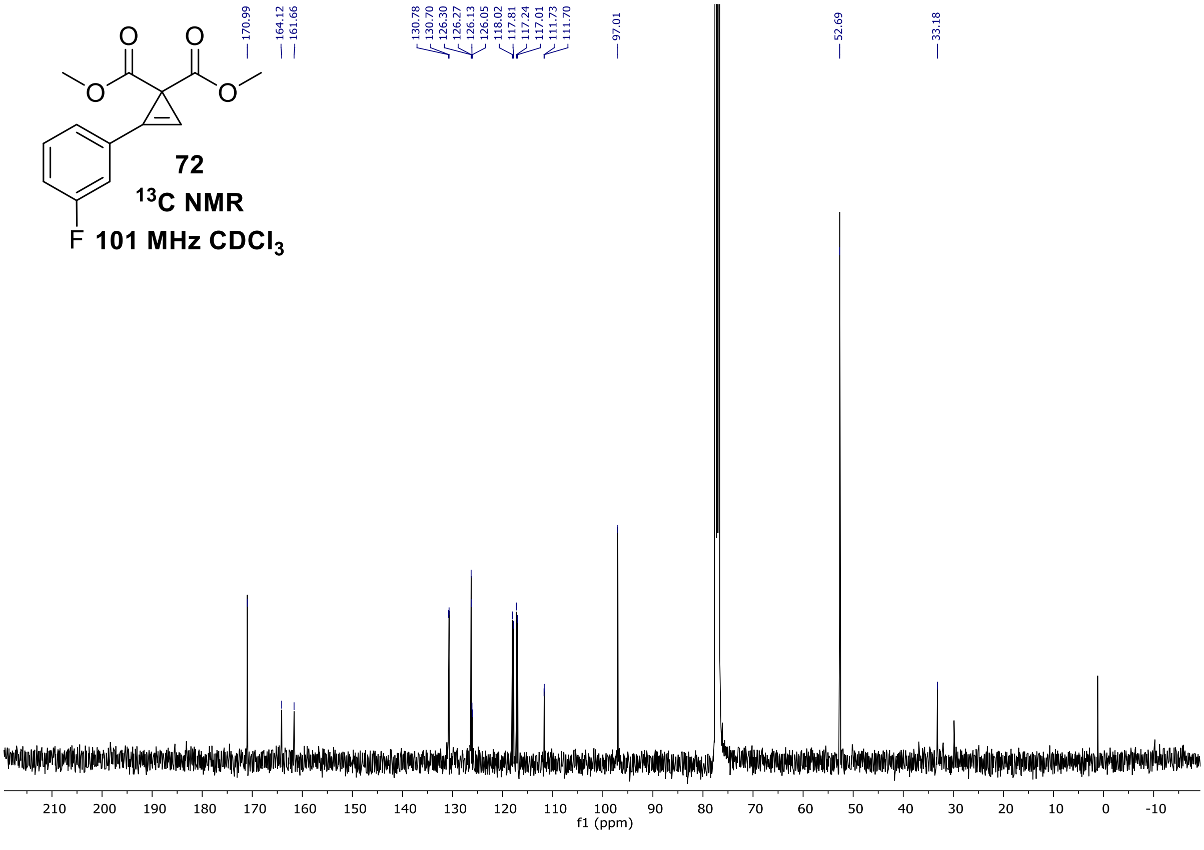
101 MHz CDCl$_3$



72

^{1}H NMR

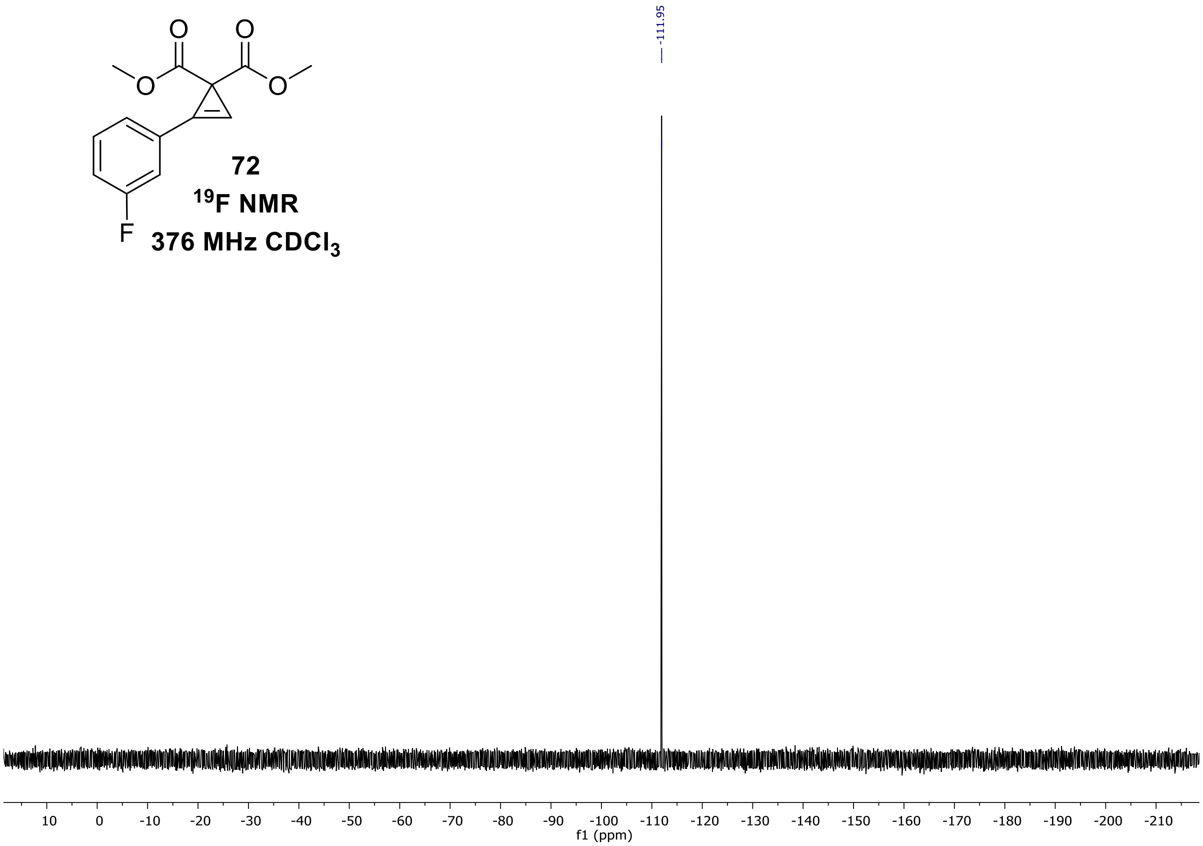
400 MHz CDCl$_3$



72

^{13}C NMR

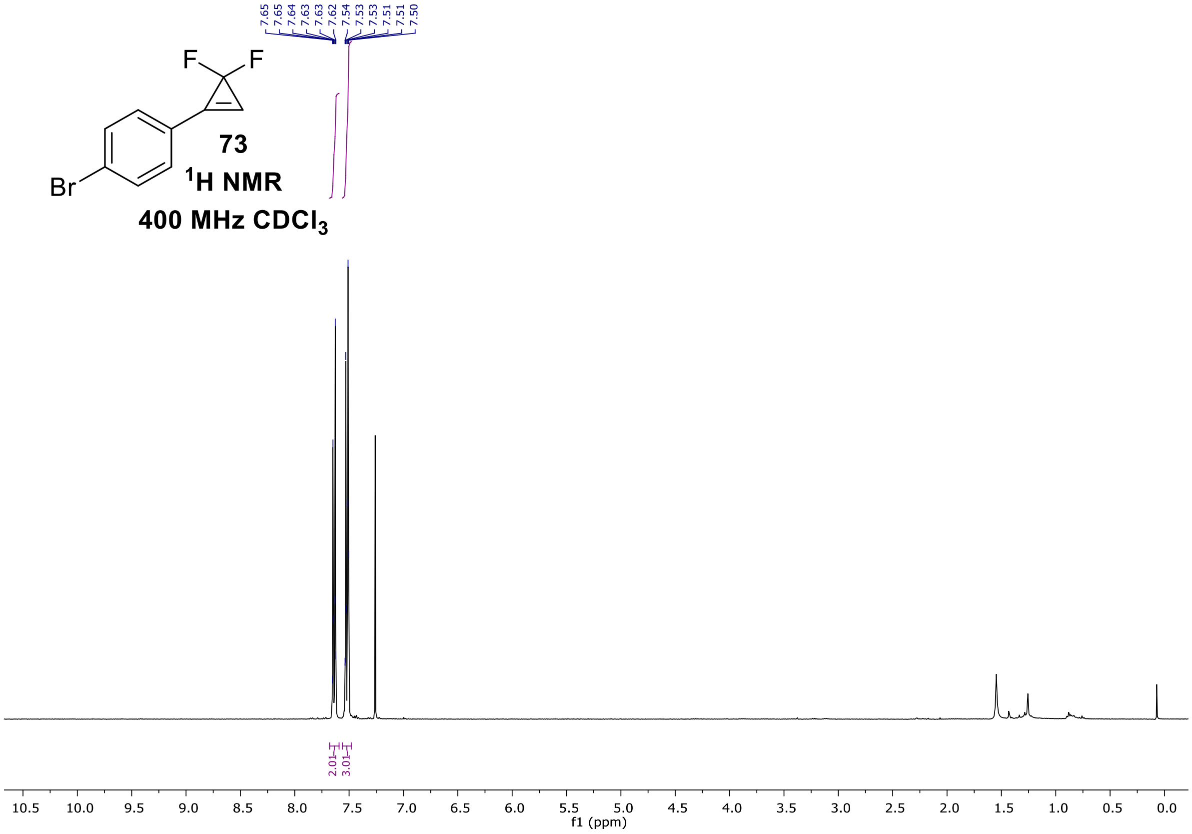
101 MHz CDCl$_3$

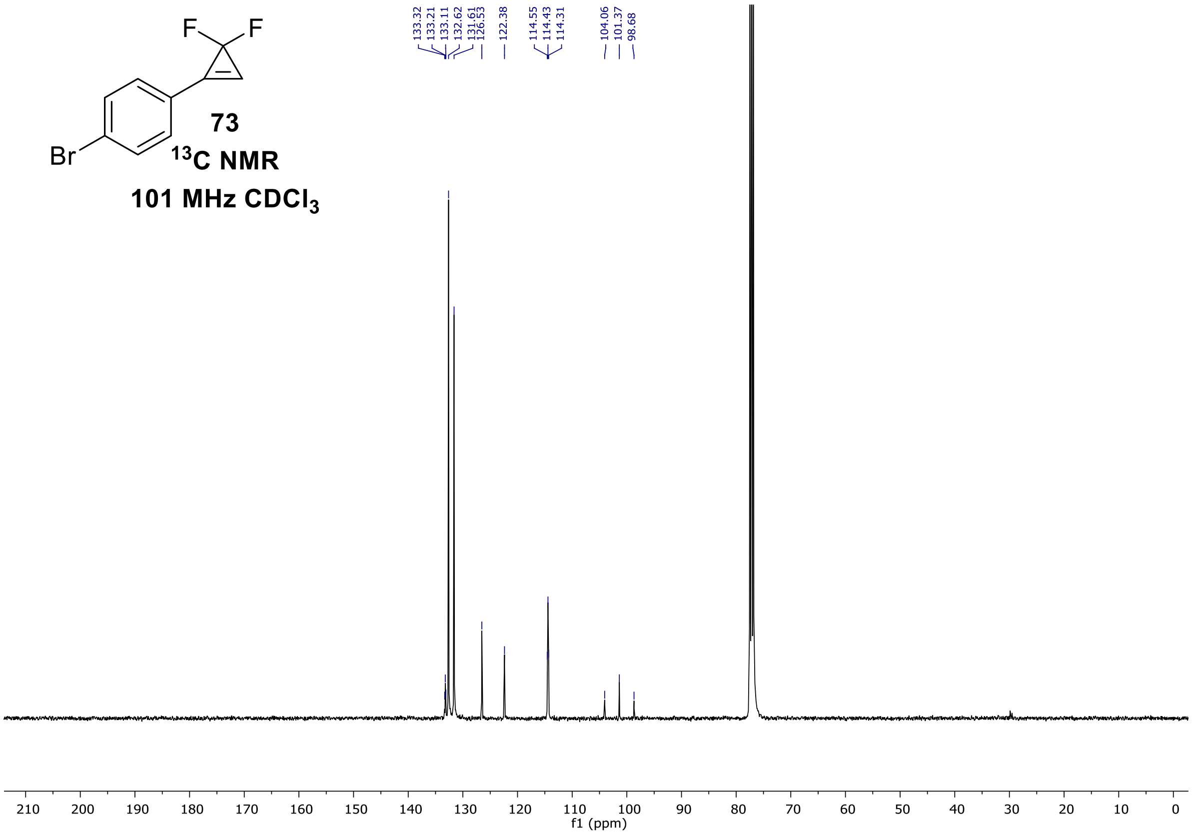


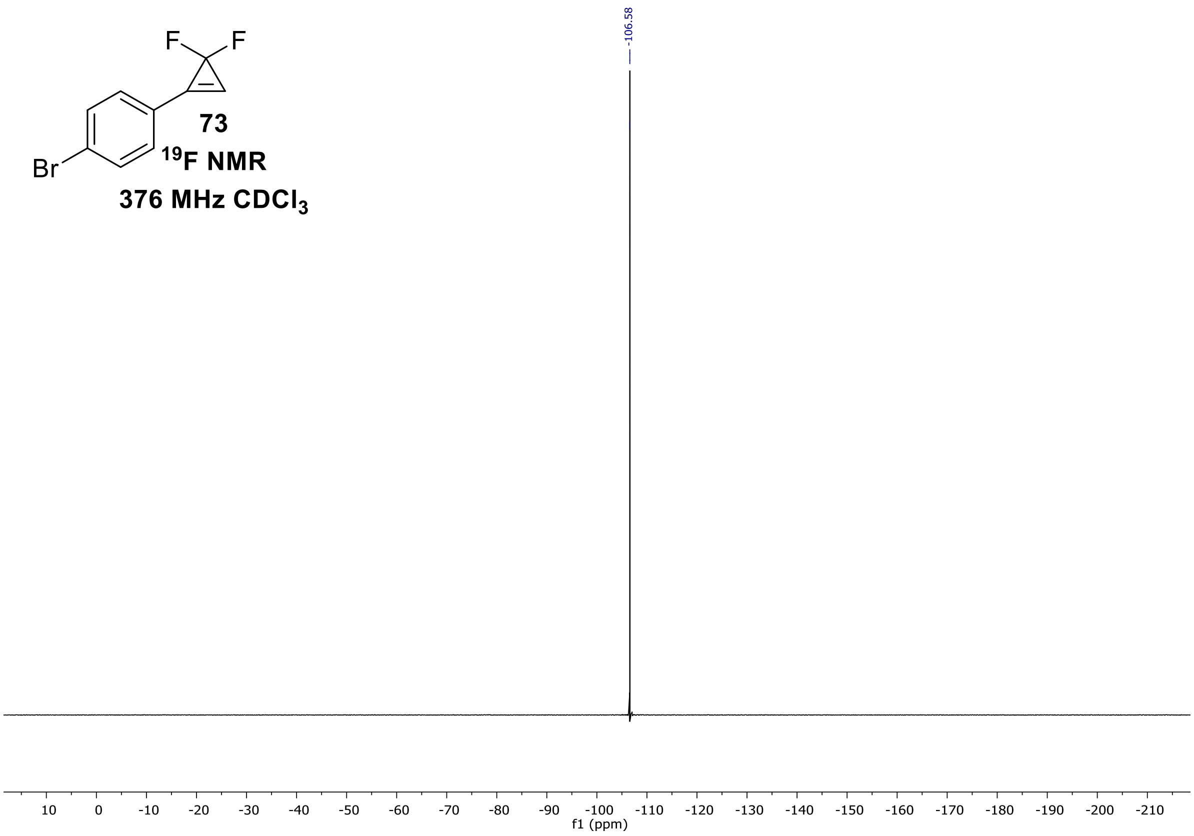
72

^{19}F NMR

376 MHz $CDCl_3$


7.65
7.65
7.64
7.63
7.63
7.62
7.54
7.53
7.53
7.51
7.51
7.50
F
F
Br
73
^{1}H NMR
400 MHz CDCl$_3$
2.01
3.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

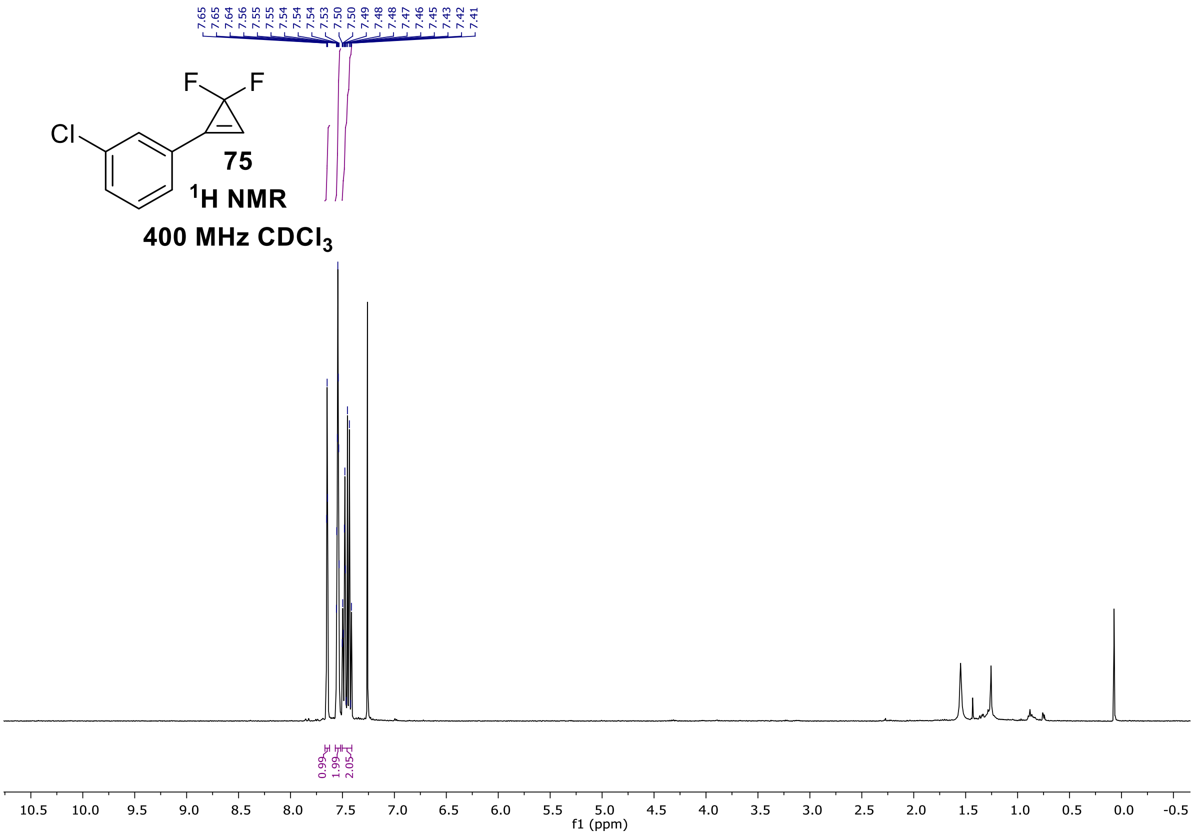

133.32
133.21
133.11
132.62
131.61
126.53
122.38
114.55
114.43
114.31
104.06
101.37
98.68
F
F
Br
73
^{13}C NMR
101 MHz CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

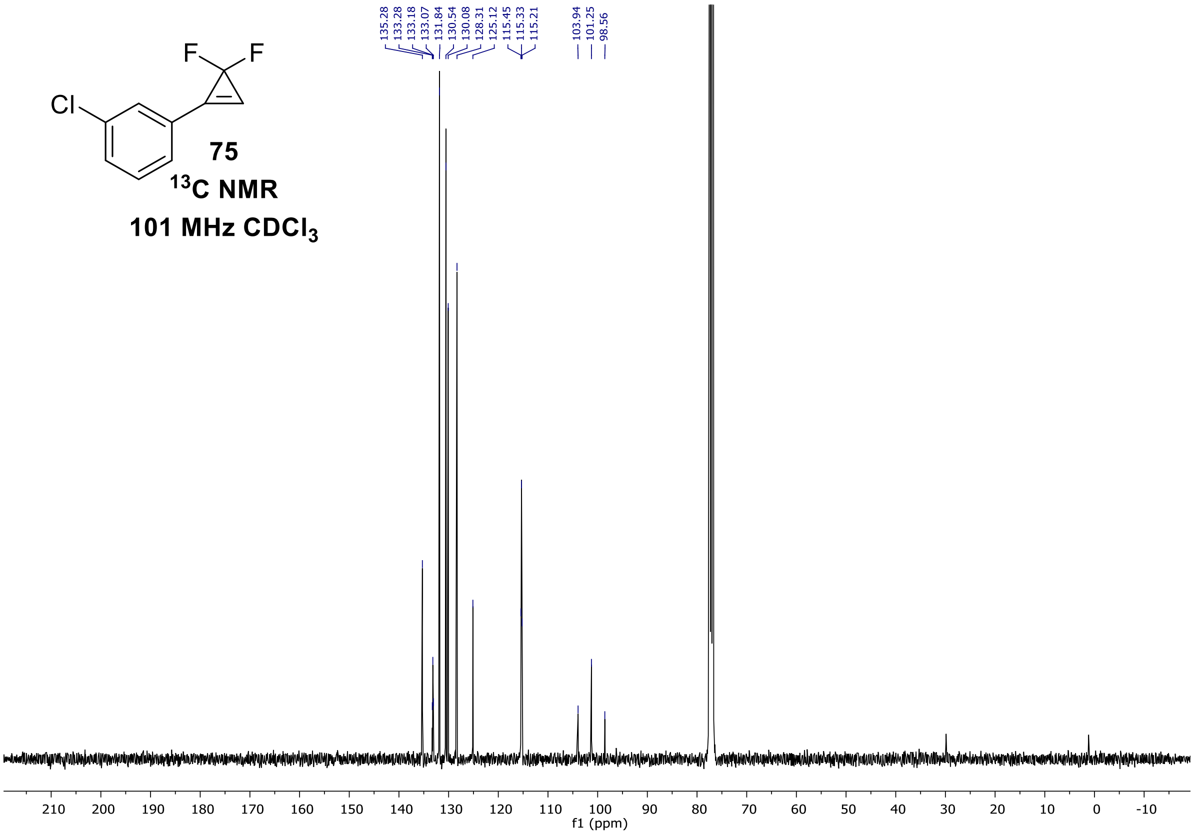


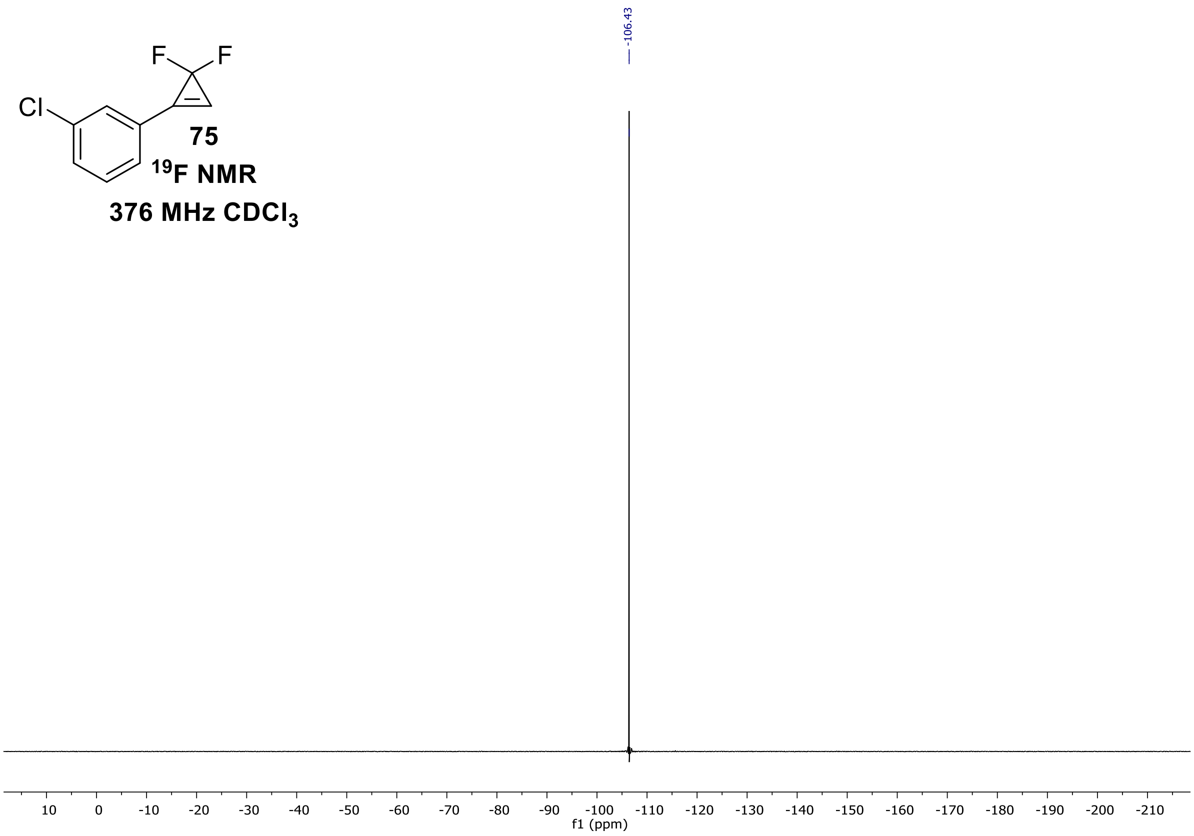
73

^{19}F NMR

376 MHz CDCl$_3$


7.65
7.65
7.64
7.56
7.55
7.55
7.54
7.54
7.54
7.53
7.50
7.50
7.49
7.48
7.48
7.47
7.46
7.45
7.43
7.42
7.41
F
F
Cl
75
1H NMR
400 MHz CDCl3
0.99
1.99
2.05
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

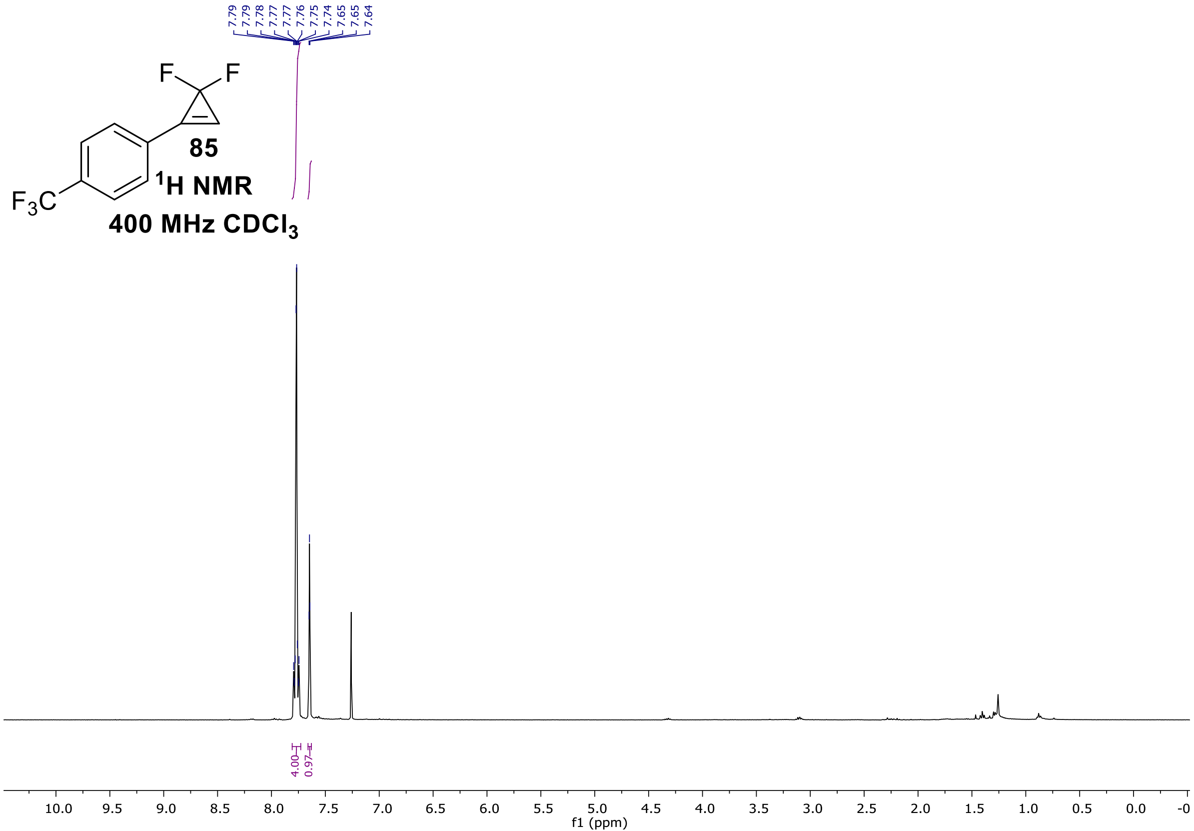

135.28
133.28
133.18
133.07
131.84
130.54
130.08
128.31
125.12
115.45
115.33
115.21
103.94
101.25
98.56
F
F
Cl
75
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

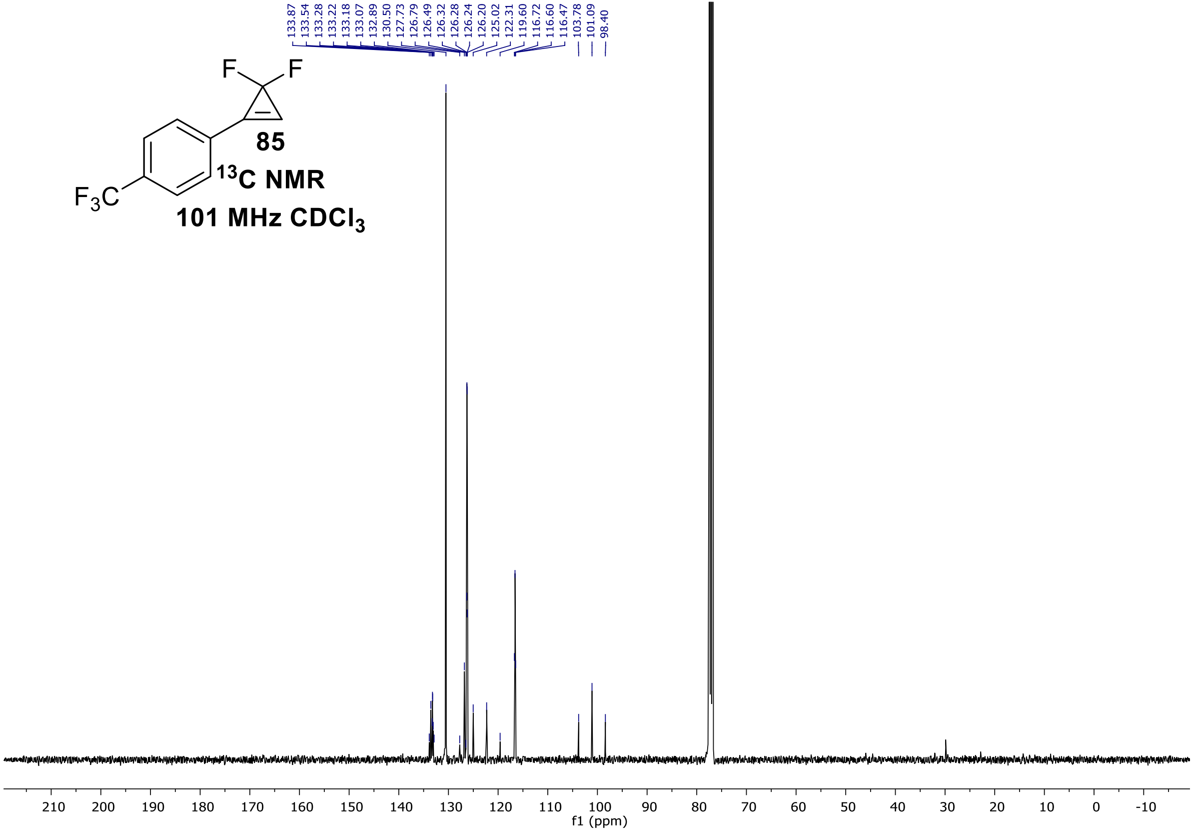


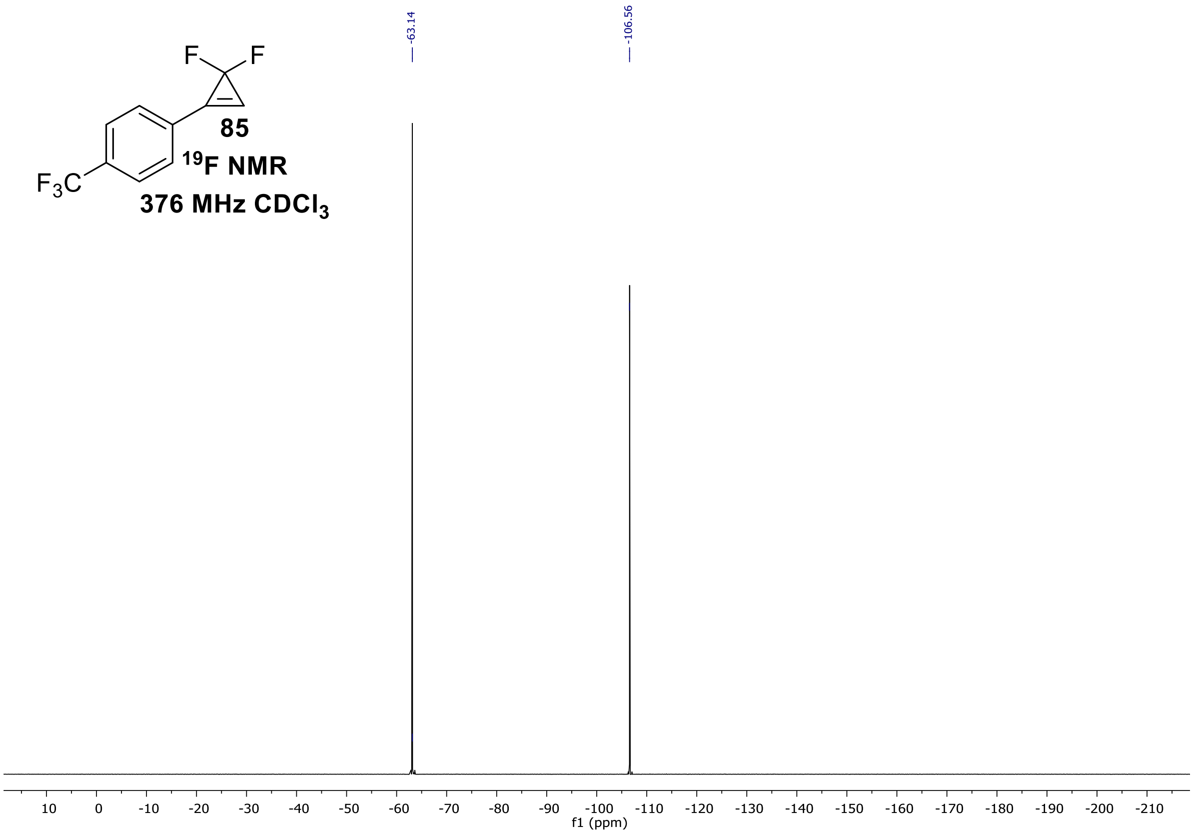
75

^{19}F NMR

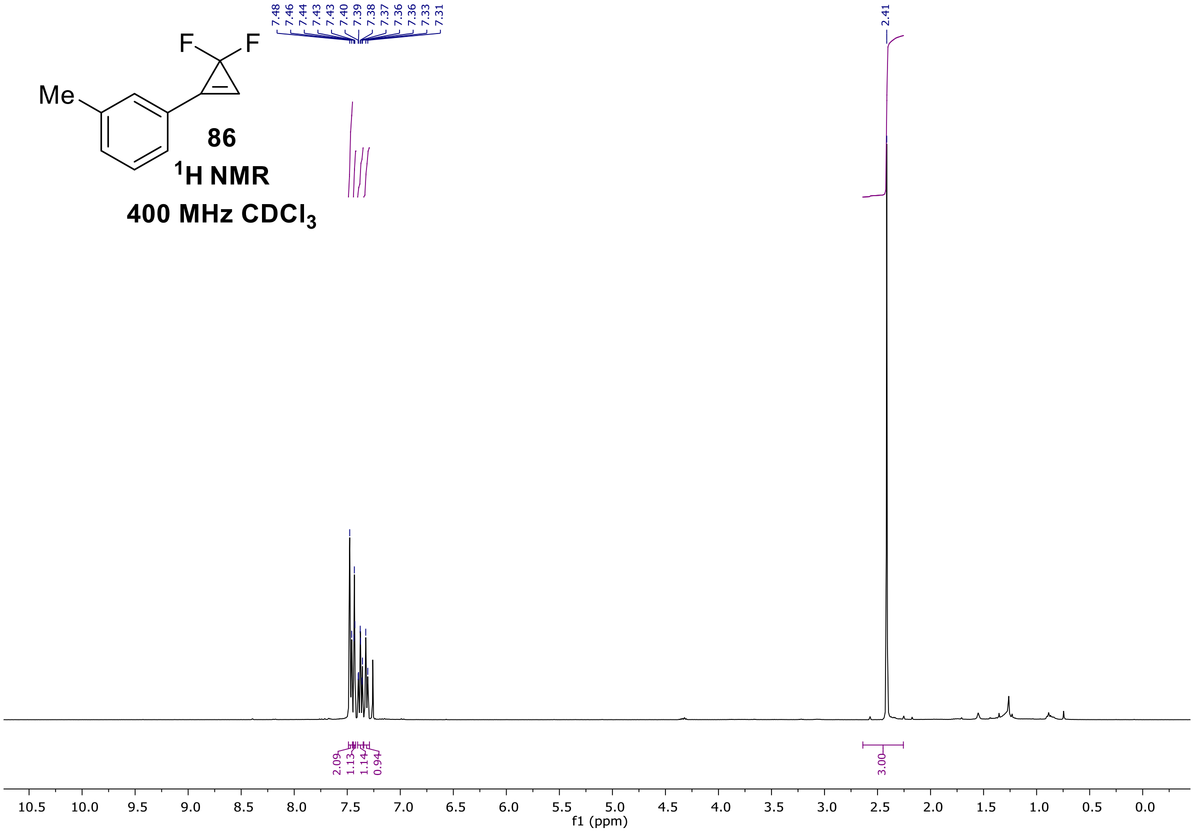
376 MHz $CDCl_3$

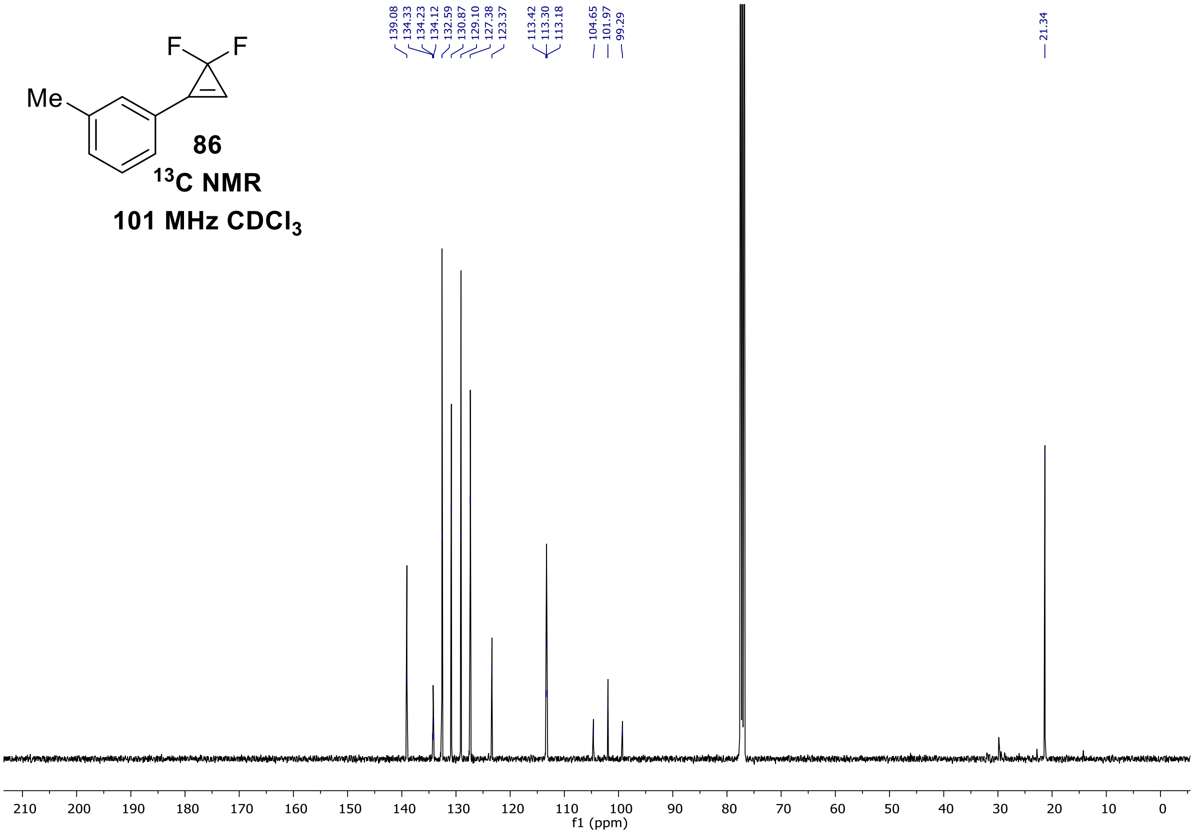

7.79
7.79
7.78
7.77
7.77
7.76
7.75
7.74
7.65
7.65
7.64
F
F
85
F3C
1H NMR
400 MHz CDCl3
4.00
0.97
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

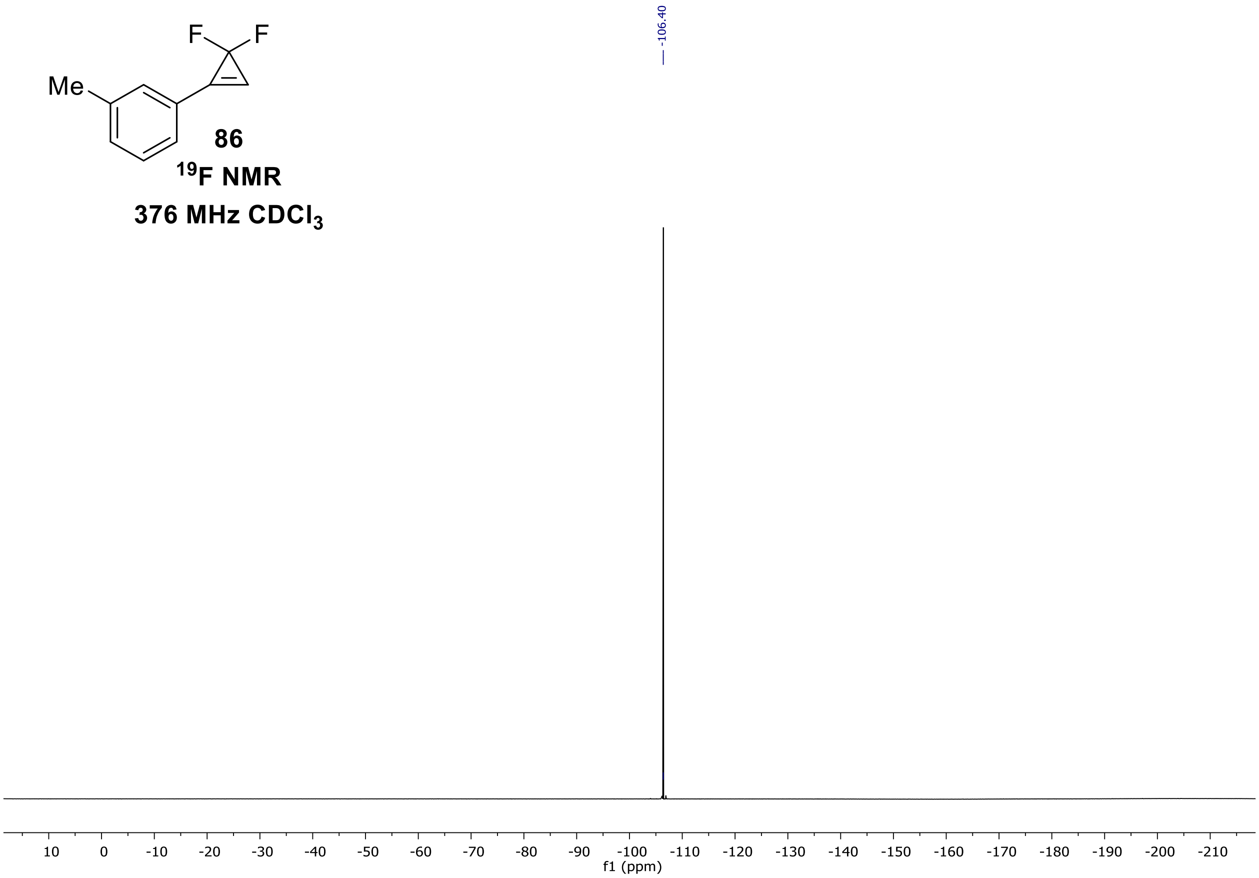

133.87
133.54
133.28
133.22
133.18
133.07
132.89
130.50
127.73
126.79
126.49
126.32
126.28
126.24
126.20
125.02
122.31
119.60
116.72
116.60
116.47
103.78
101.09
98.40
F
F
85
F3C
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



85
^{19}F NMR
376 MHz $CDCl_3$
-63.14
-106.56
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


F
F
Me
86
^{1}H NMR
400 MHz CDCl$_3$
7.48
7.46
7.44
7.43
7.40
7.39
7.38
7.37
7.36
7.36
7.33
7.31
2.41
2.09
1.13
1.14
0.94
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

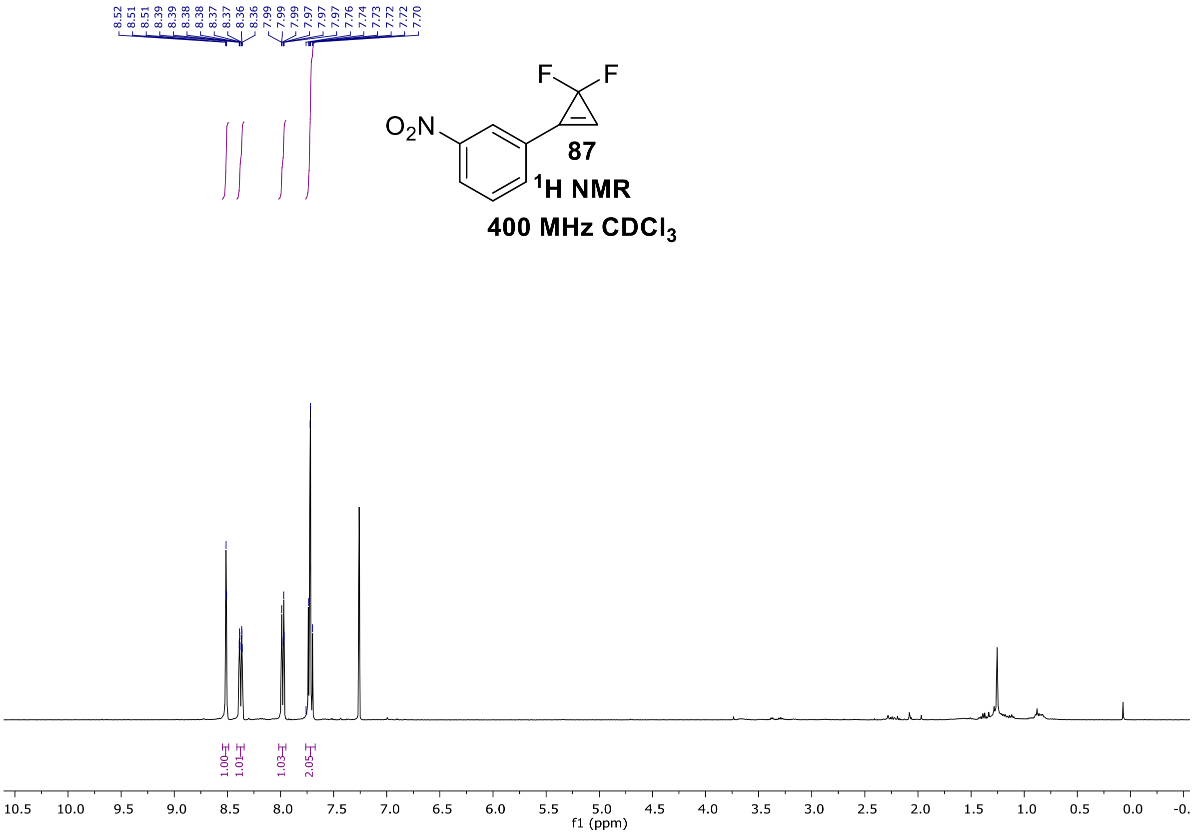

F
F
Me
86
^{13}C NMR
101 MHz CDCl$_3$
139.08
134.33
134.23
134.12
132.59
130.87
129.10
127.38
123.37
113.42
113.30
113.18
104.65
101.97
99.29
21.34
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

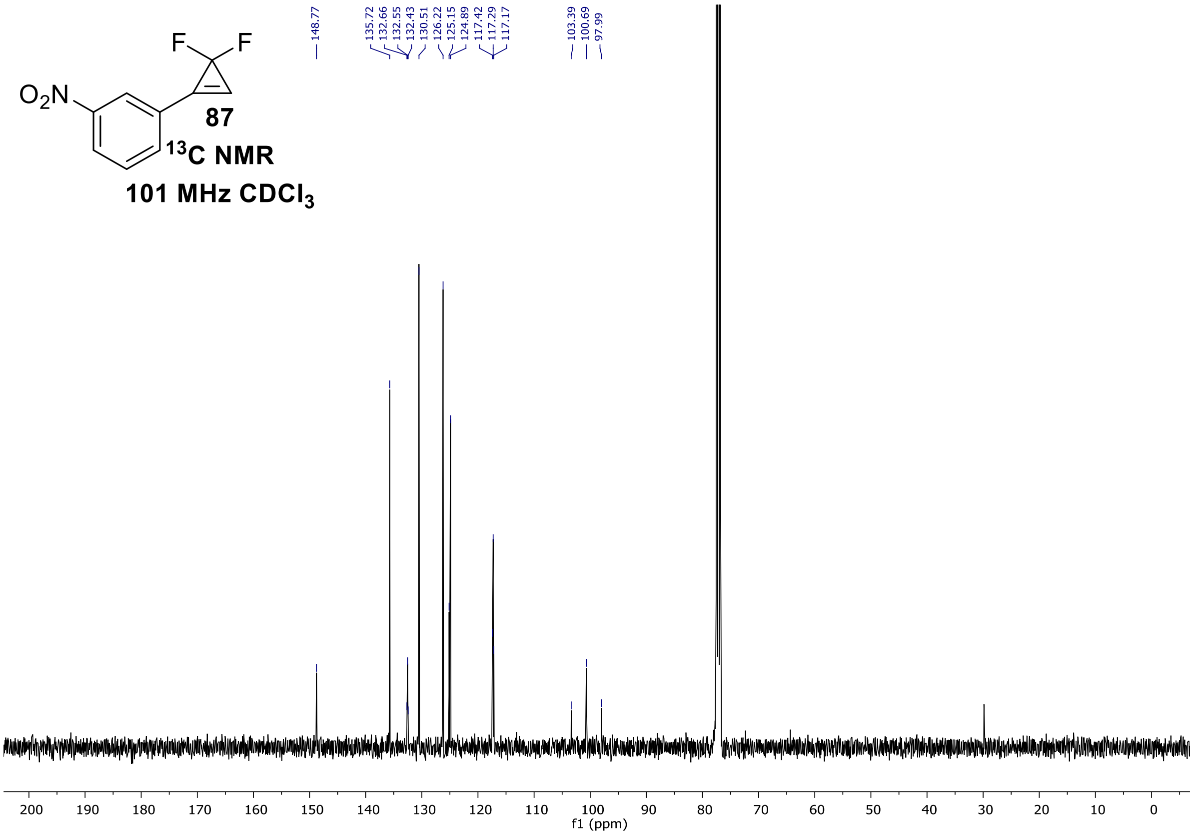


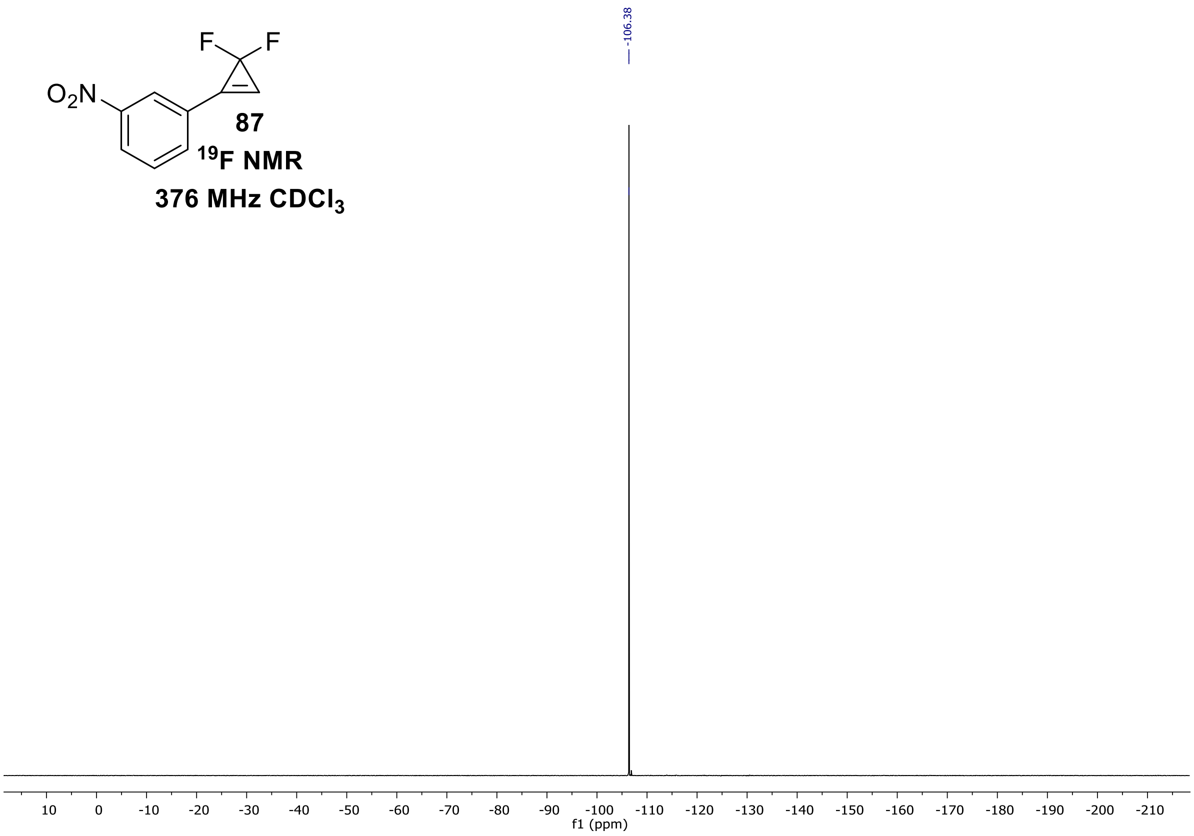
86

^{19}F NMR

376 MHz CDCl$_3$


8.52
8.51
8.51
8.39
8.39
8.38
8.38
8.37
8.37
8.36
8.36
7.99
7.99
7.99
7.97
7.97
7.97
7.76
7.74
7.73
7.72
7.72
7.70
F
F
O2N
87
1H NMR
400 MHz CDCl3
1.00
1.01
1.03
2.05
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)

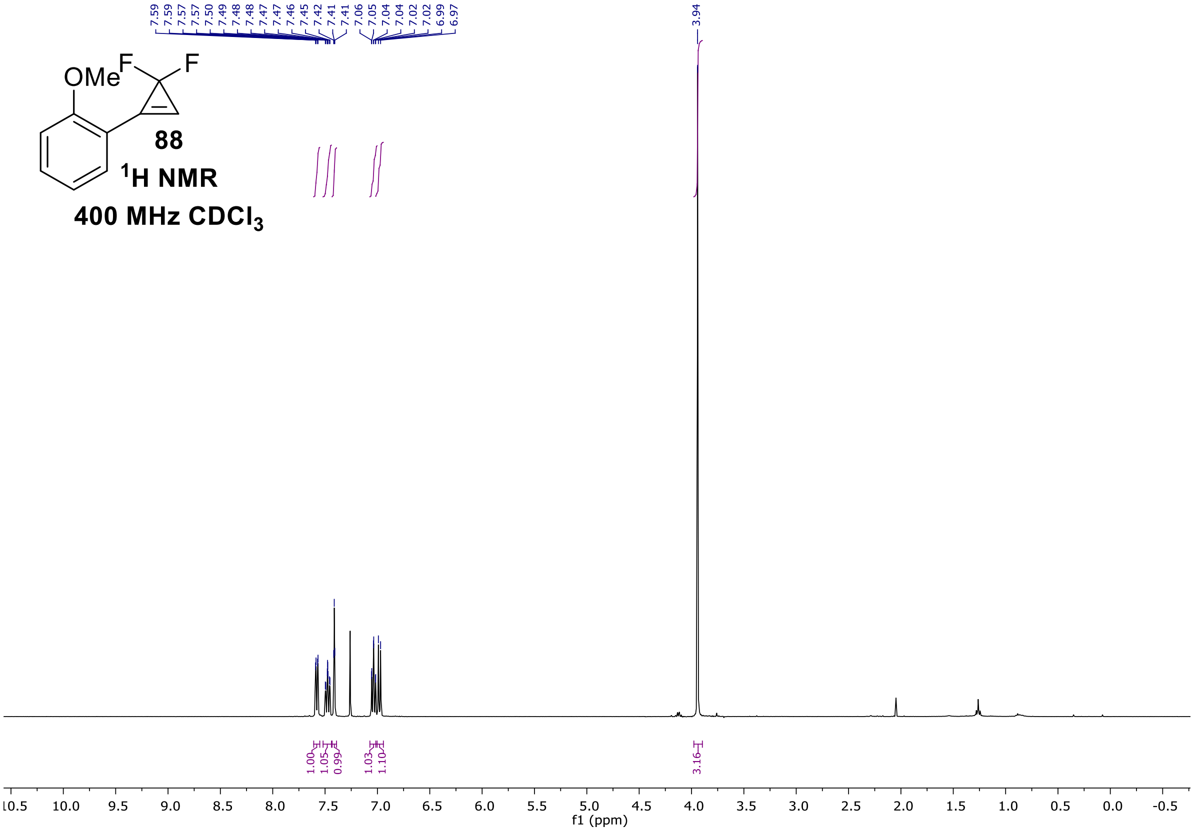

148.77
135.72
132.66
132.55
132.43
130.51
126.22
125.15
124.89
117.42
117.29
117.17
103.39
100.69
97.99
F
F
O2N
87
13C NMR
101 MHz CDCl3
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

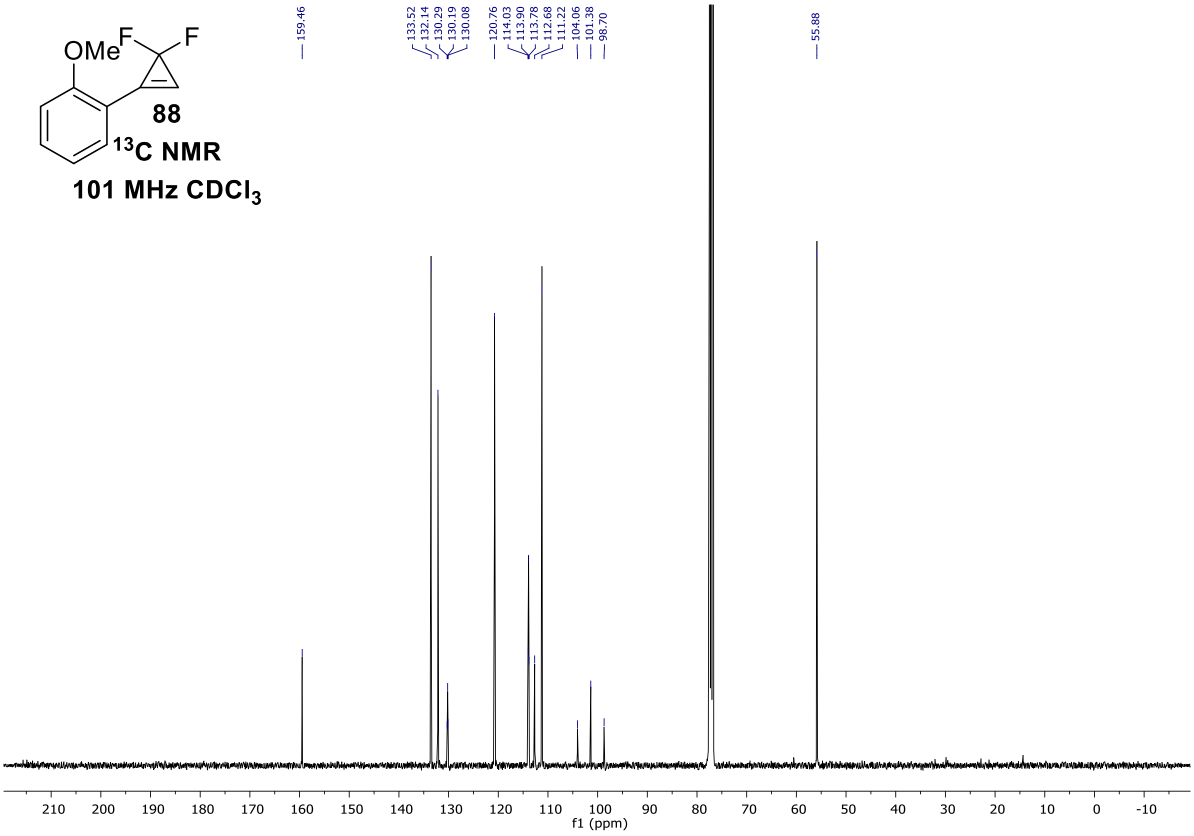


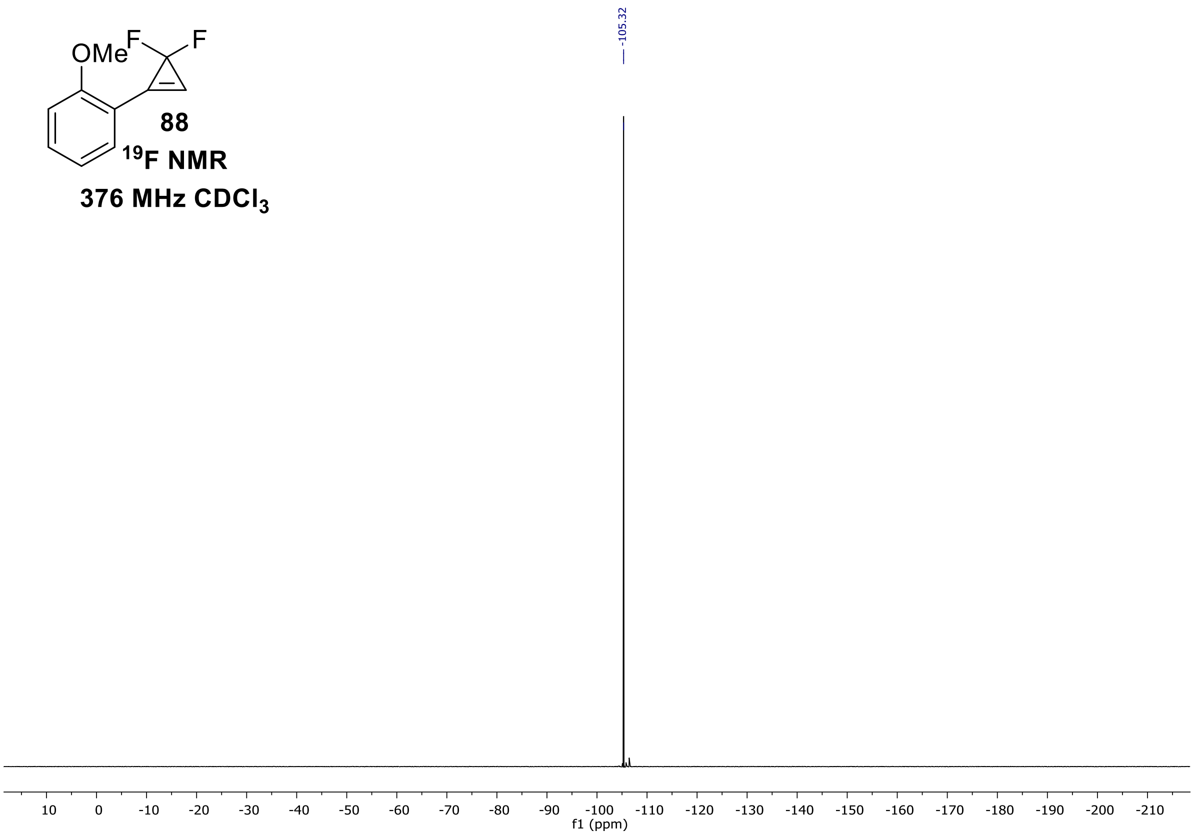
87

^{19}F NMR

376 MHz $CDCl_3$


7.59
7.59
7.57
7.57
7.50
7.49
7.48
7.48
7.47
7.47
7.46
7.45
7.42
7.41
7.41
7.06
7.05
7.04
7.04
7.02
7.02
6.99
6.97
3.94
OMe
F
F
88
^{1}H NMR
400 MHz CDCl$_3$
1.00
1.05
0.99
1.03
1.10
3.16
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

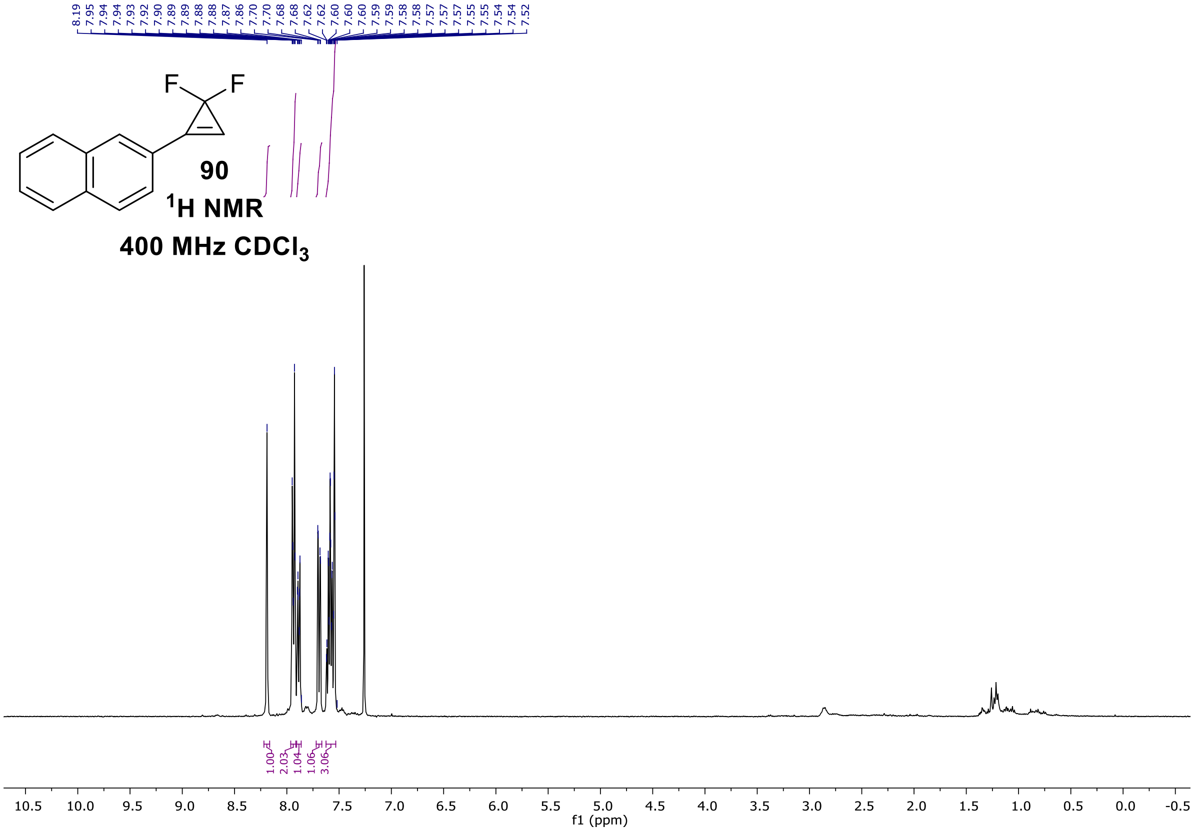

159.46
133.52
132.14
130.29
130.19
130.08
120.76
114.03
113.90
113.78
112.68
111.22
104.06
101.38
98.70
55.88
OMe
F
F
88
^{13}C NMR
101 MHz CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



88

^{19}F NMR

376 MHz $CDCl_3$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7.93
7.92
7.90
7.89
7.89
7.88
7.87
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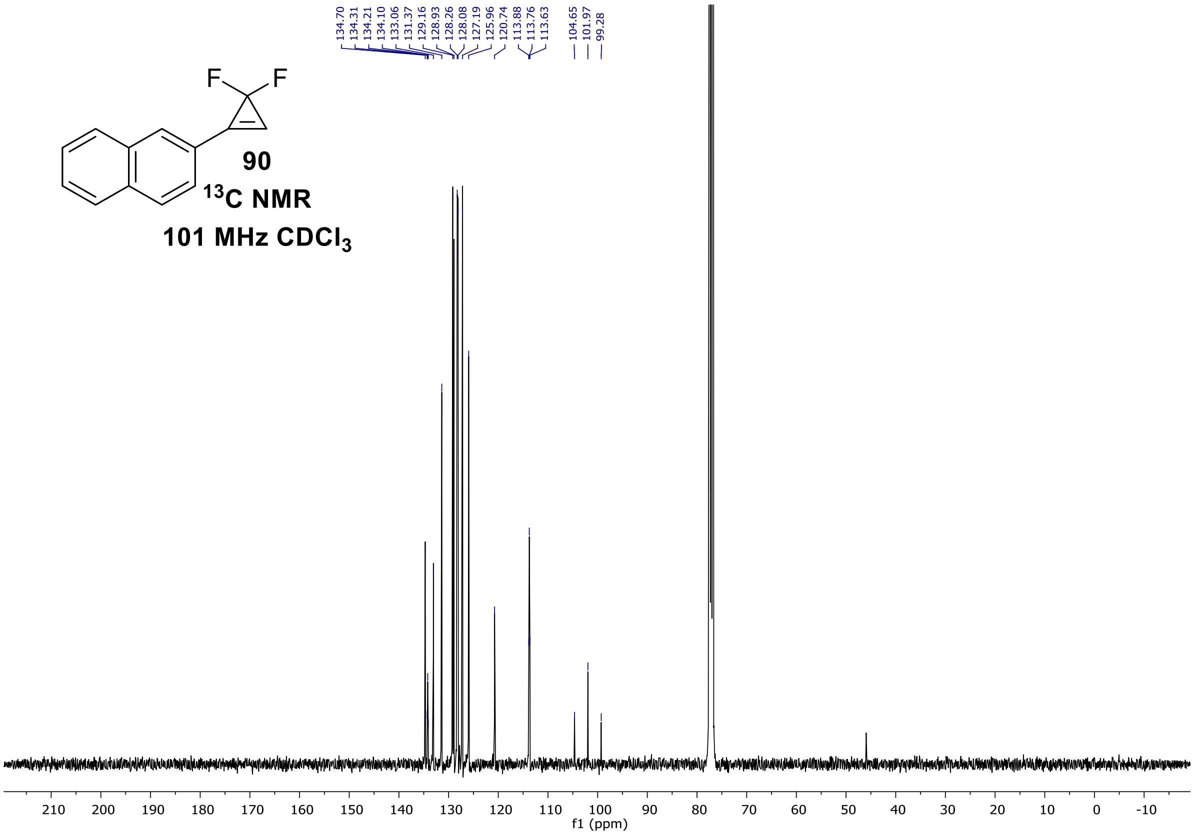
7.68
7.62
7.62
7.60
7.60
7.59
7.59
7.58
7.58
7.57
7.57
7.57
7.55
7.55
7.54
7.54
7.52
F
F
90
^{1}H NMR
400 MHz CDCl$_3$
1.00
2.03
1.04
1.06
3.06
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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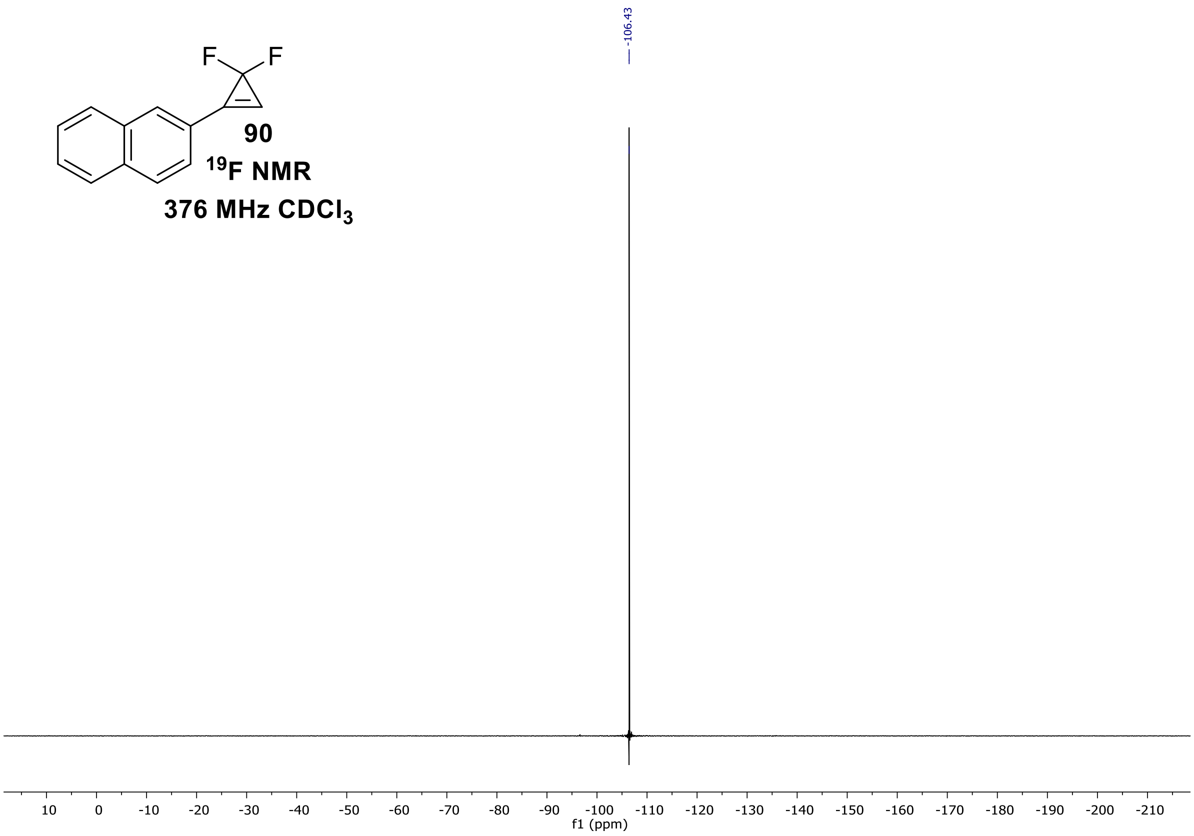
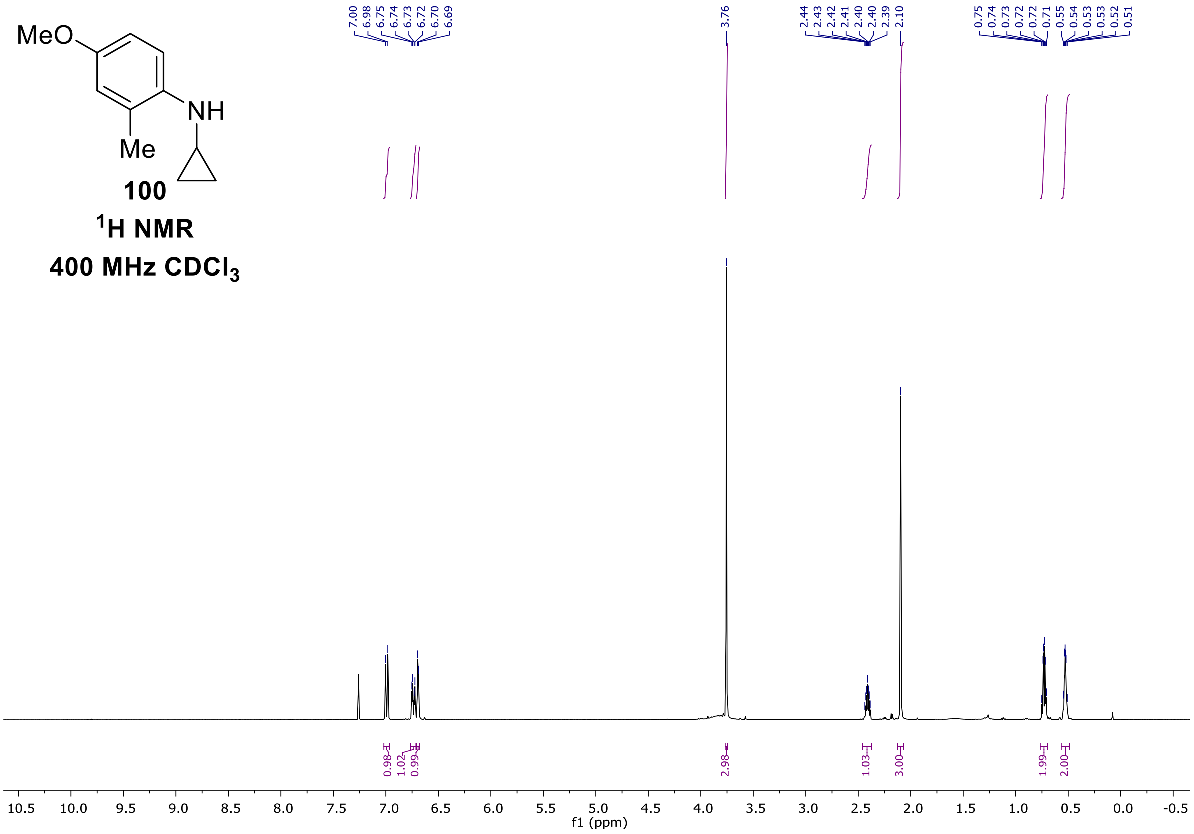
134.10
133.06
131.37
129.16
128.93
128.26
128.08
127.19
125.96
120.74
113.88
113.76
113.63
104.65
101.97
99.28
F
F
90
^{13}C NMR
101 MHz CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



90

^{19}F NMR

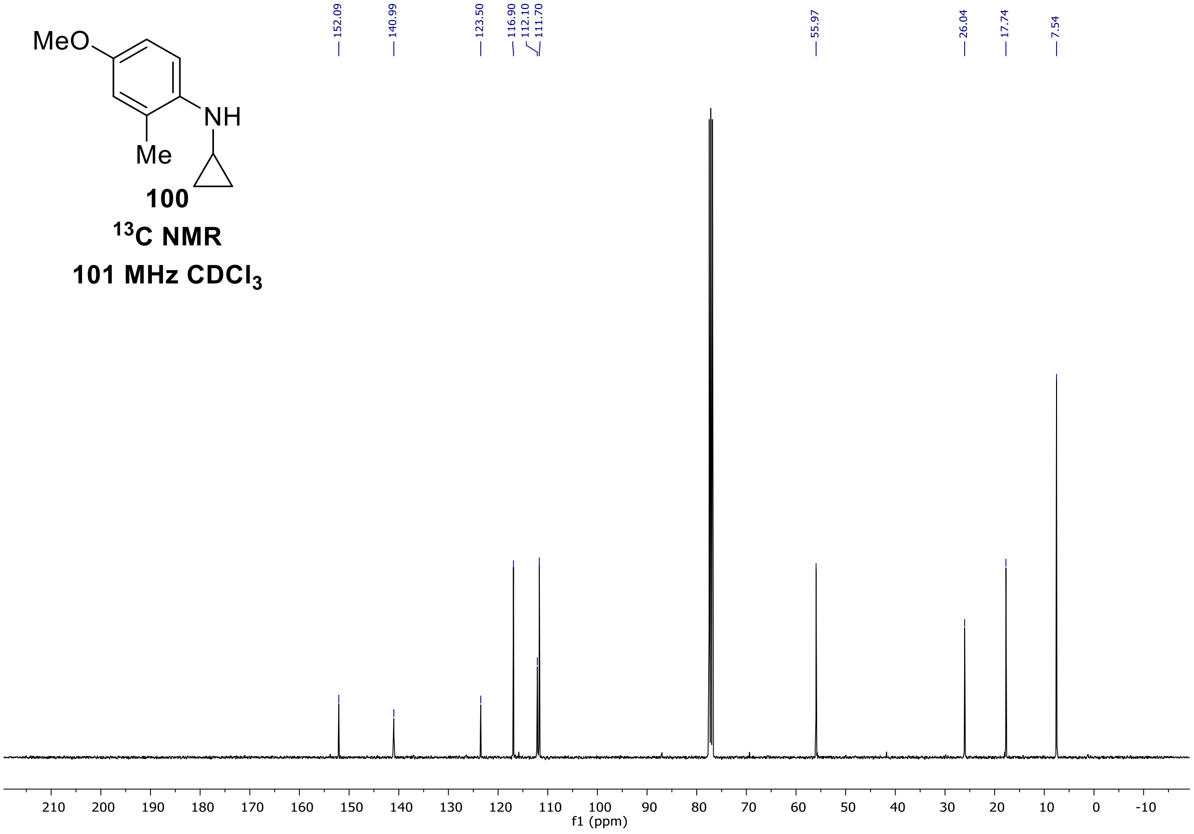
376 MHz $CDCl_3$



100

^{1}H NMR

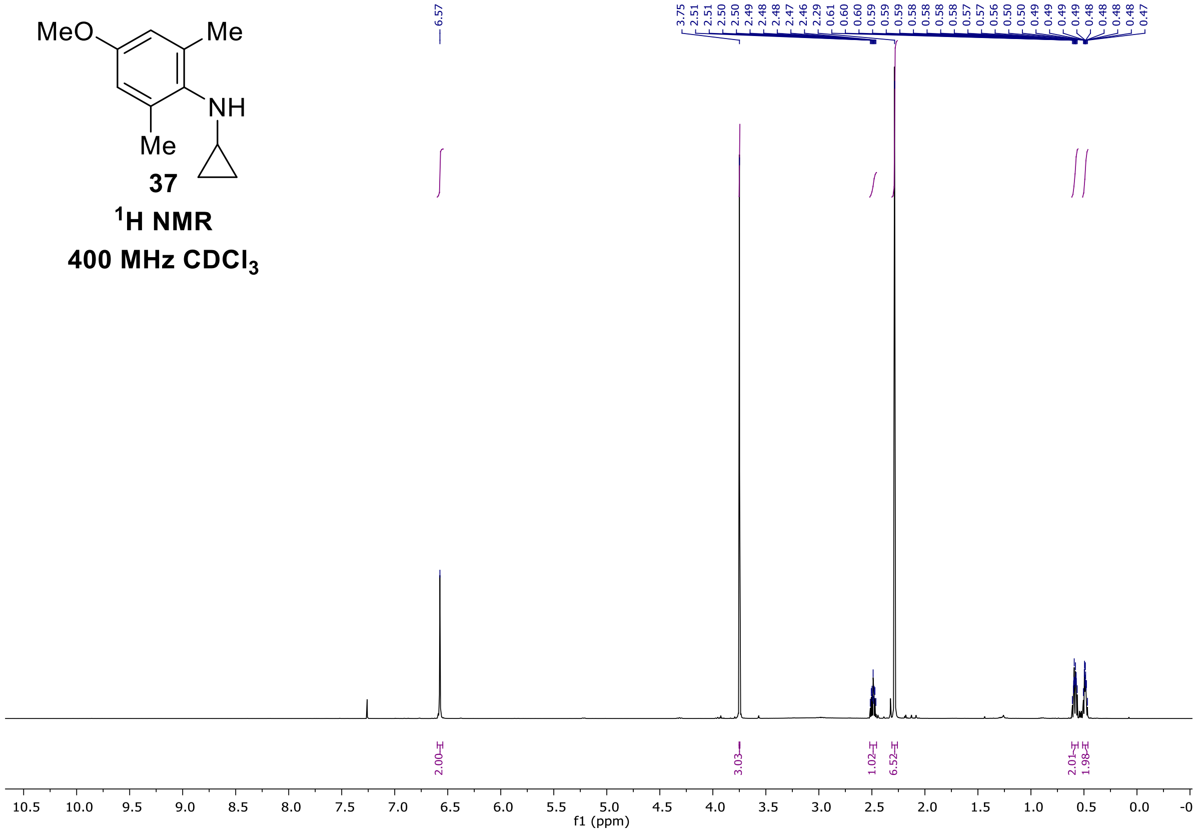
400 MHz $CDCl_3$



100

^{13}C NMR

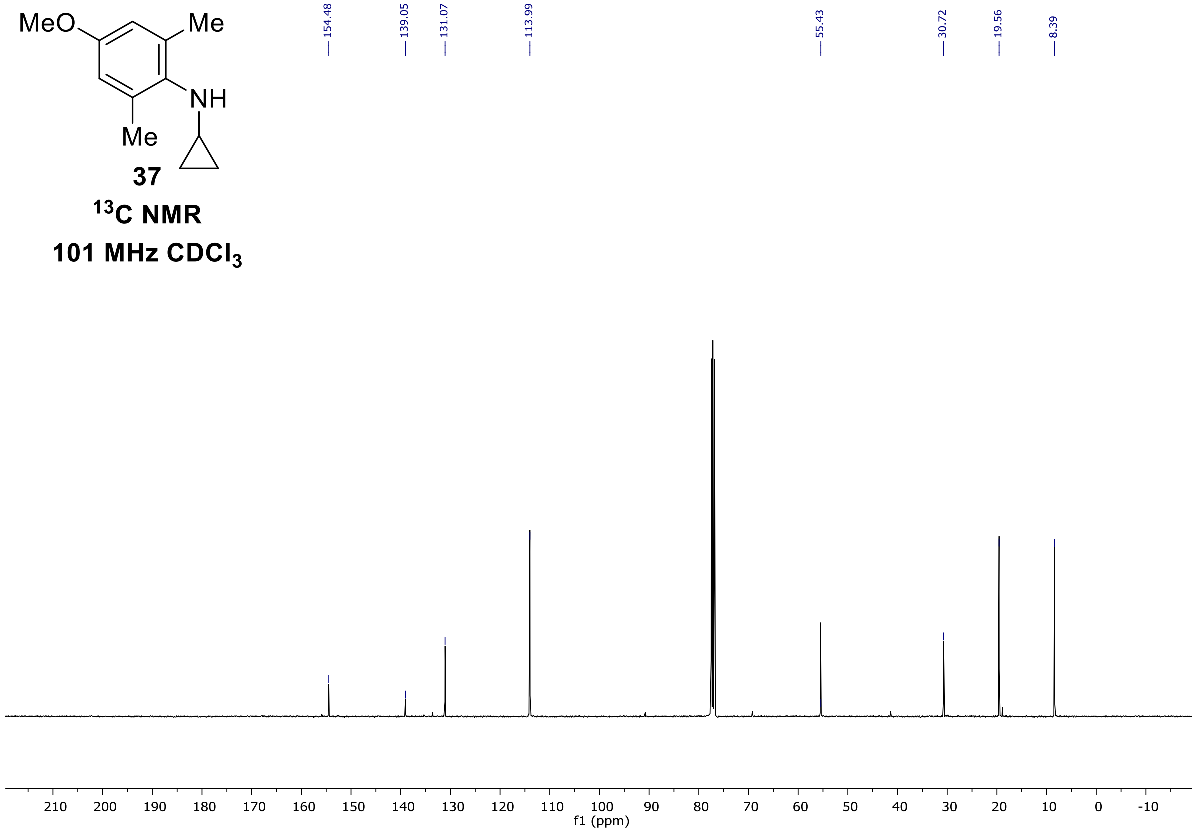
101 MHz $CDCl_3$



37

^{1}H NMR

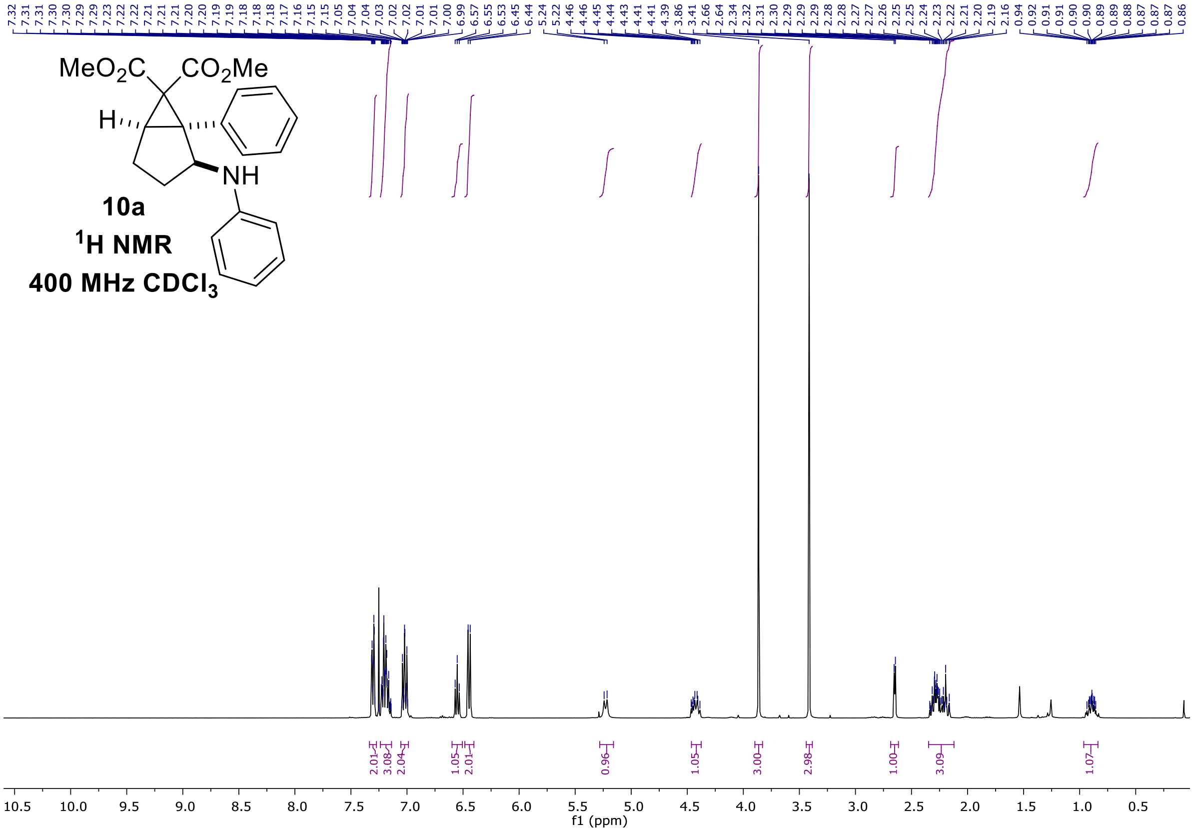
400 MHz CDCl$_3$



37

^{13}C NMR

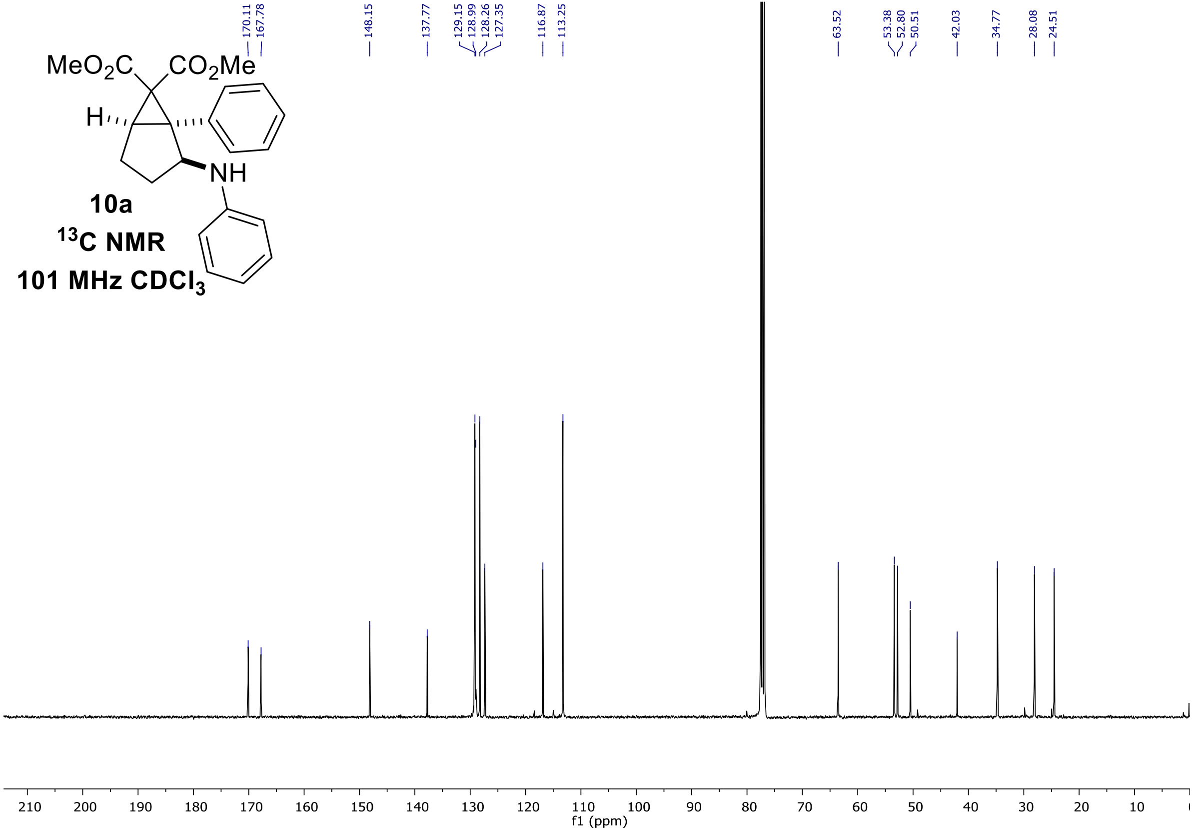
101 MHz CDCl$_3$



10a

^{1}H NMR

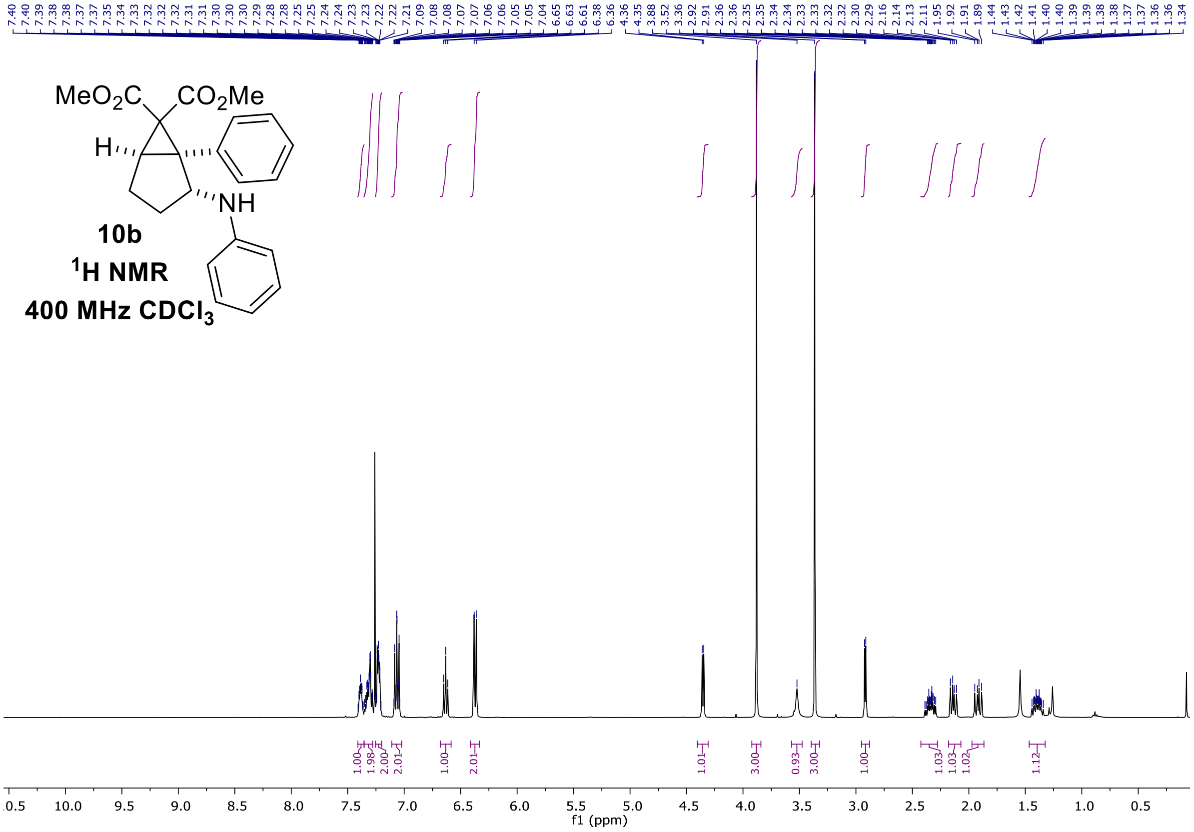
400 MHz CDCl$_3$



10a

^{13}C NMR

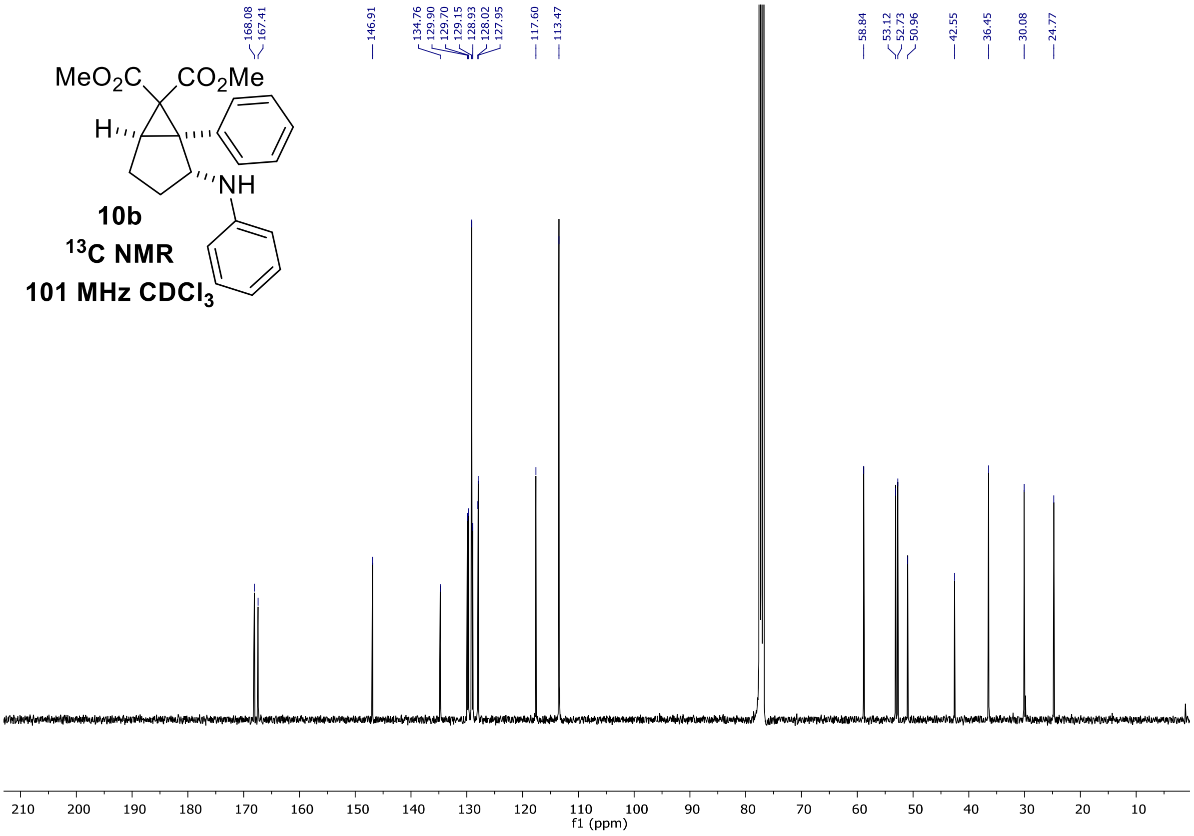
101 MHz CDCl$_3$



10b

^{1}H NMR

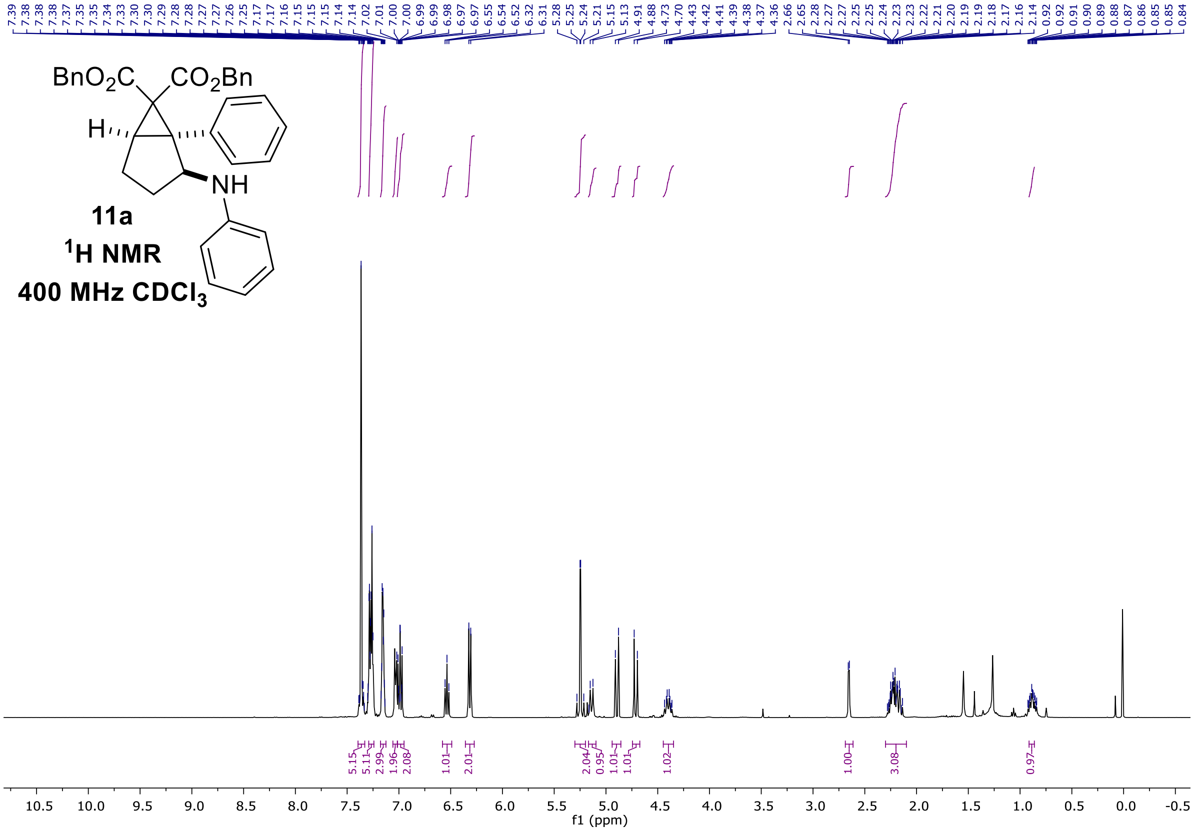
400 MHz CDCl$_3$



10b

^{13}C NMR

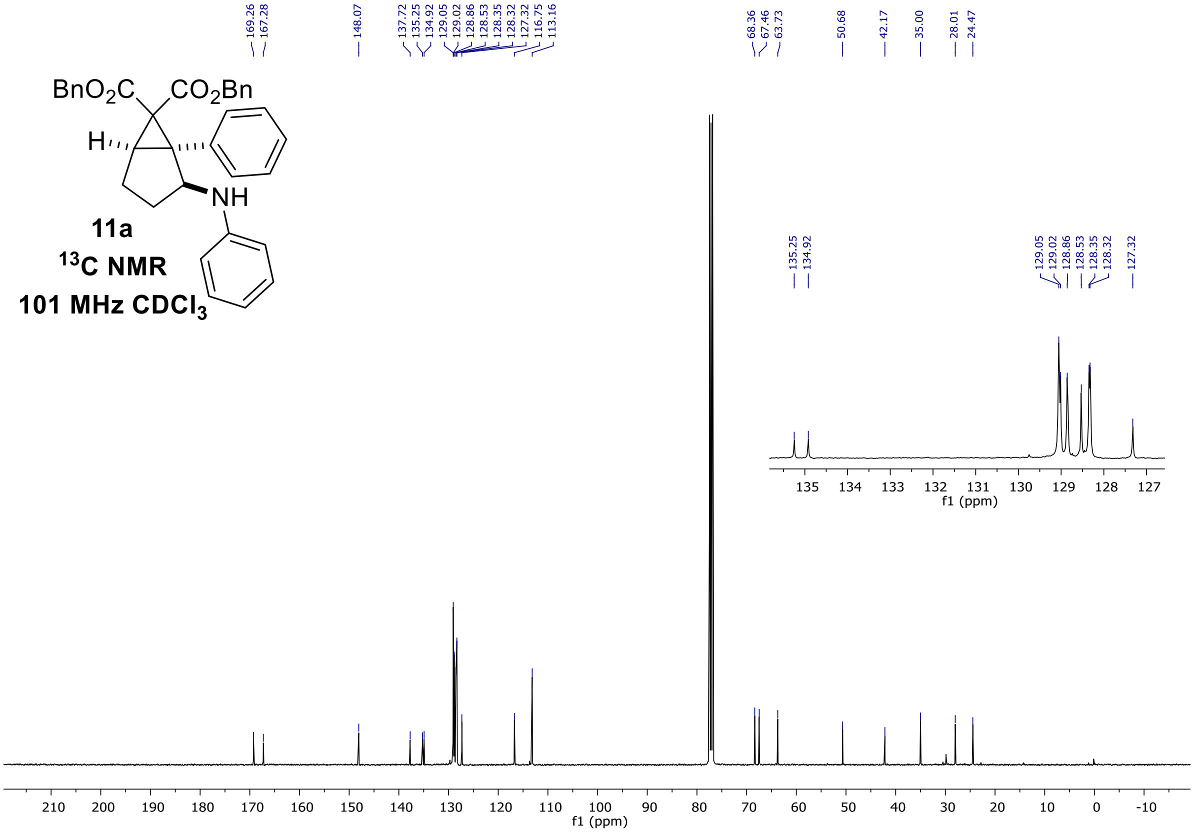
101 MHz CDCl$_3$



11a

^{1}H NMR

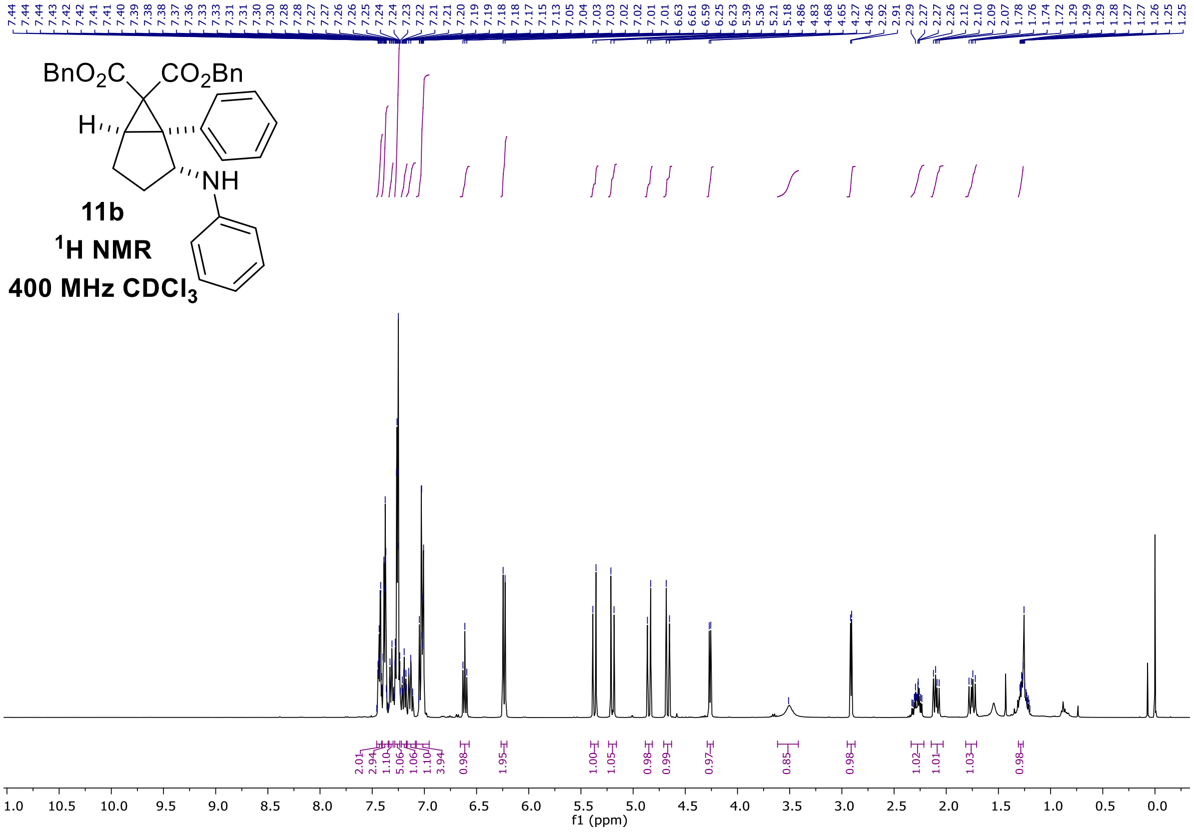
400 MHz $CDCl_3$



11a

^{13}C NMR

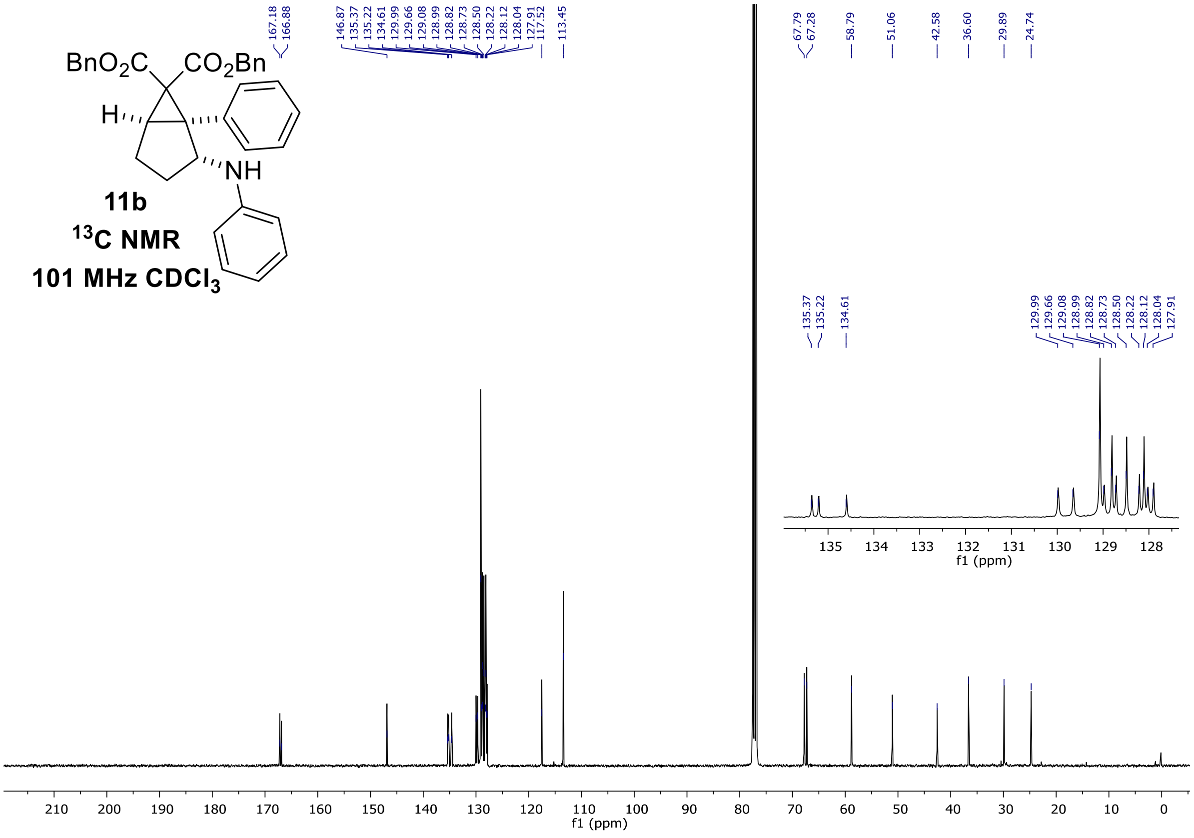
101 MHz $CDCl_3$



11b

^{1}H NMR

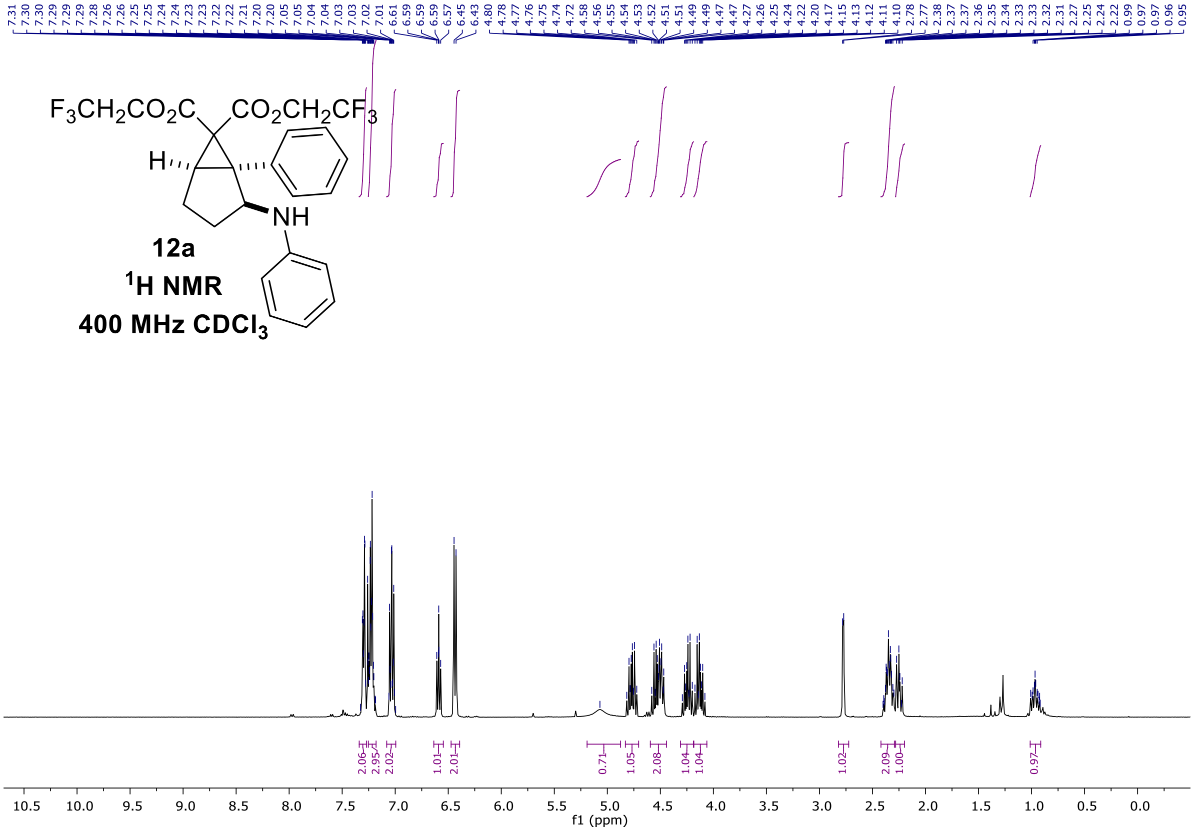
400 MHz CDCl$_3$



11b

^{13}C NMR

101 MHz CDCl$_3$


7.31
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7.29
7.29
7.28
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7.26
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7.25
7.24
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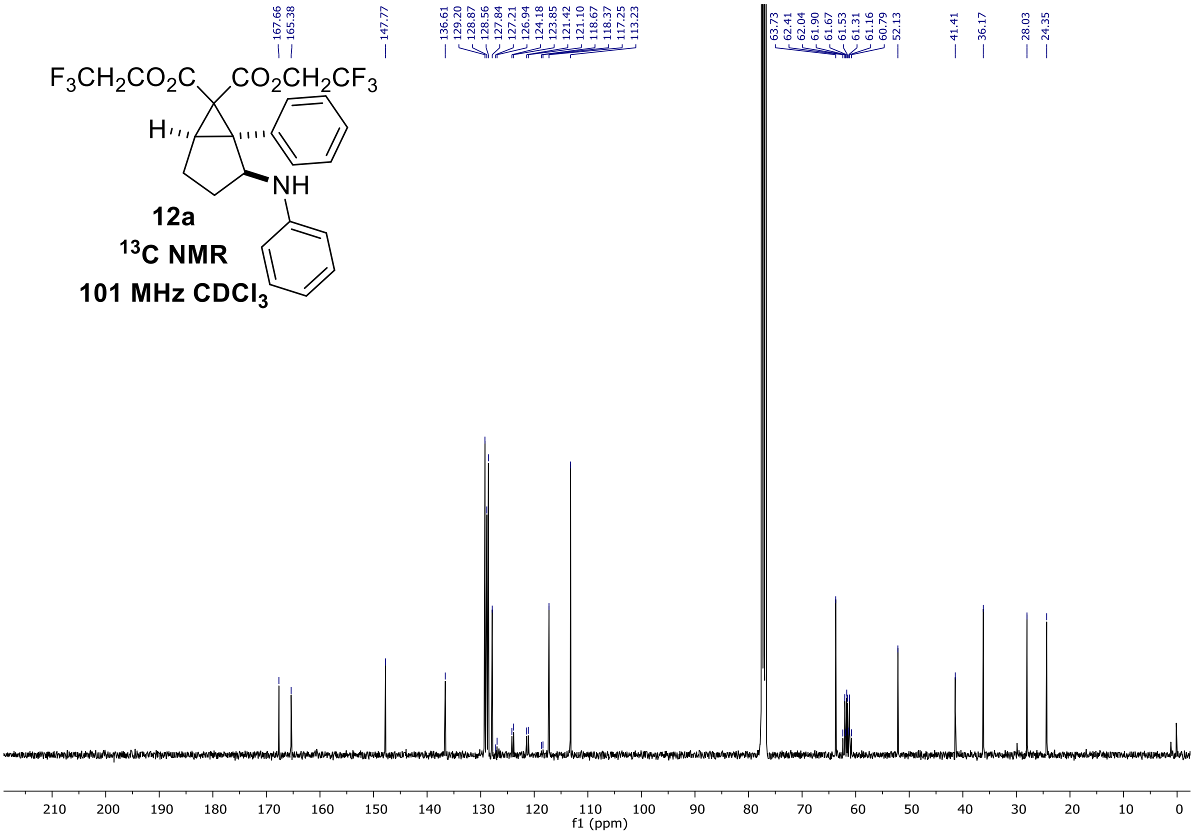
7.23
7.23
7.22
7.22
7.21
7.20
7.20
7.05
7.05
7.04
7.04
7.03
7.03
7.02
7.01
6.61
6.59
6.59
6.59
6.57
6.45
6.43
4.80
4.78
4.77
4.76
4.75
4.74
4.72
4.58
4.56
4.55
4.54
4.53
4.52
4.51
4.51
4.49
4.49
4.47
4.47
4.27
4.26
4.25
4.24
4.22
4.20
4.17
4.15
4.13
4.12
4.11
4.10
2.78
2.77
2.38
2.37
2.37
2.36
2.35
2.34
2.33
2.33
2.32
2.31
2.27
2.25
2.24
2.22
0.99
0.97
0.97
0.96
0.95
F3CH2CO2C
CO2CH2CF3
H
NH
12a
1H NMR
400 MHz CDCl3
2.06
2.95
2.02
1.01
2.01
0.71
1.05
2.08
1.04
1.04
1.02
2.09
1.00
0.97
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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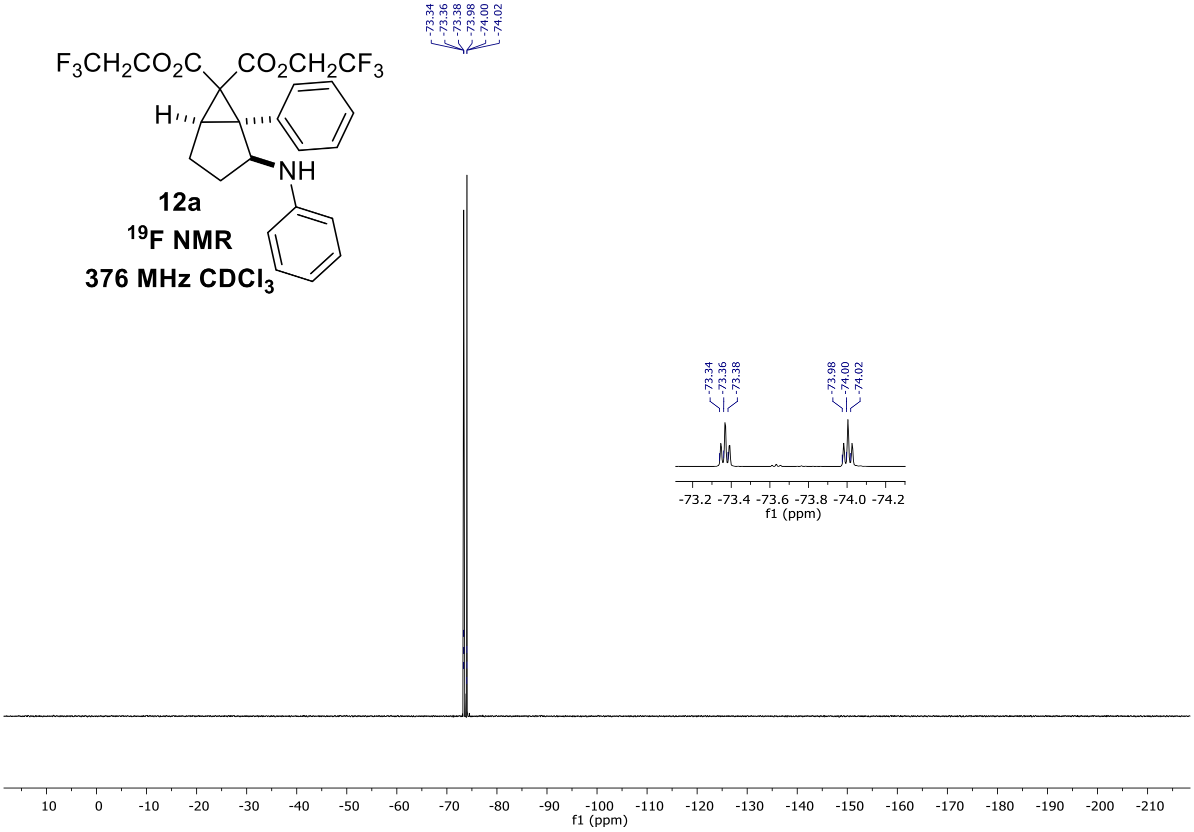
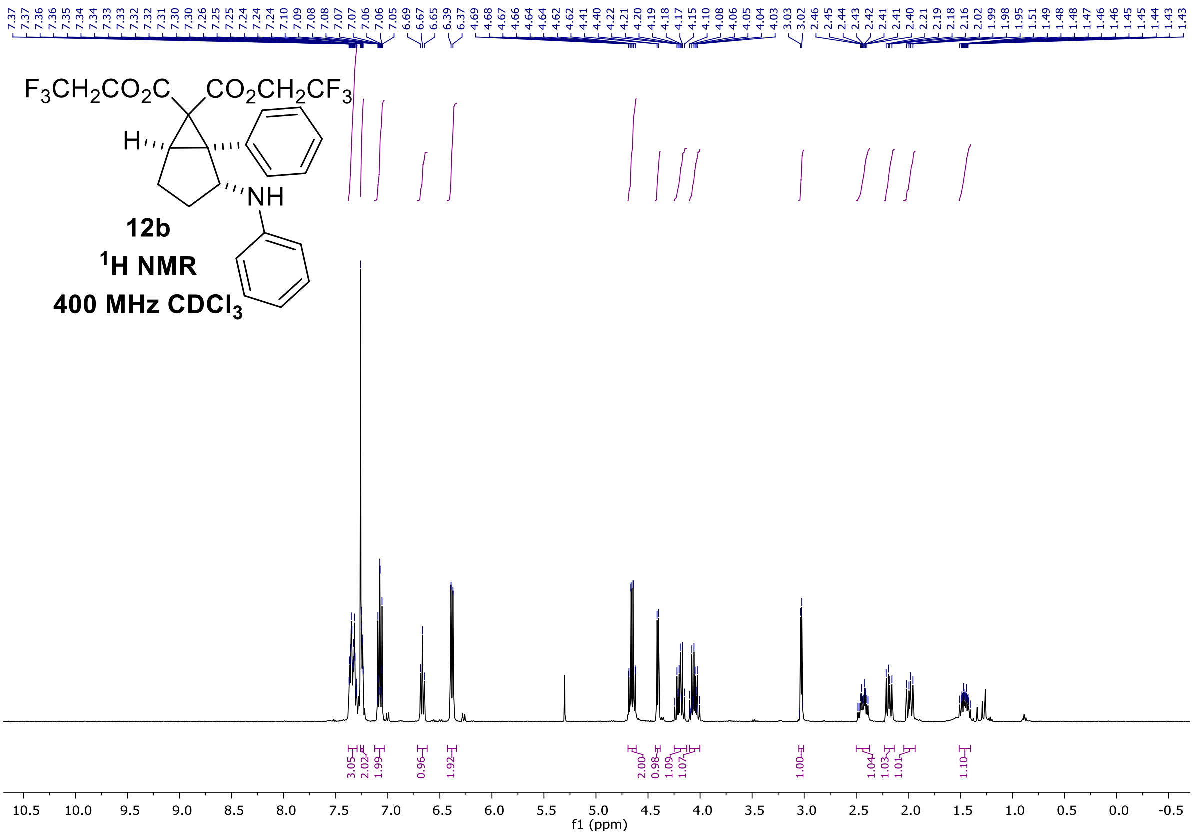
124.18
123.85
121.42
121.10
118.67
118.37
117.25
113.23
63.73
62.41
62.04
61.90
61.67
61.53
61.31
61.16
60.79
52.13
41.41
36.17
28.03
24.35
F3CH2CO2C
CO2CH2CF3
H
NH
12a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



12a

^{19}F NMR

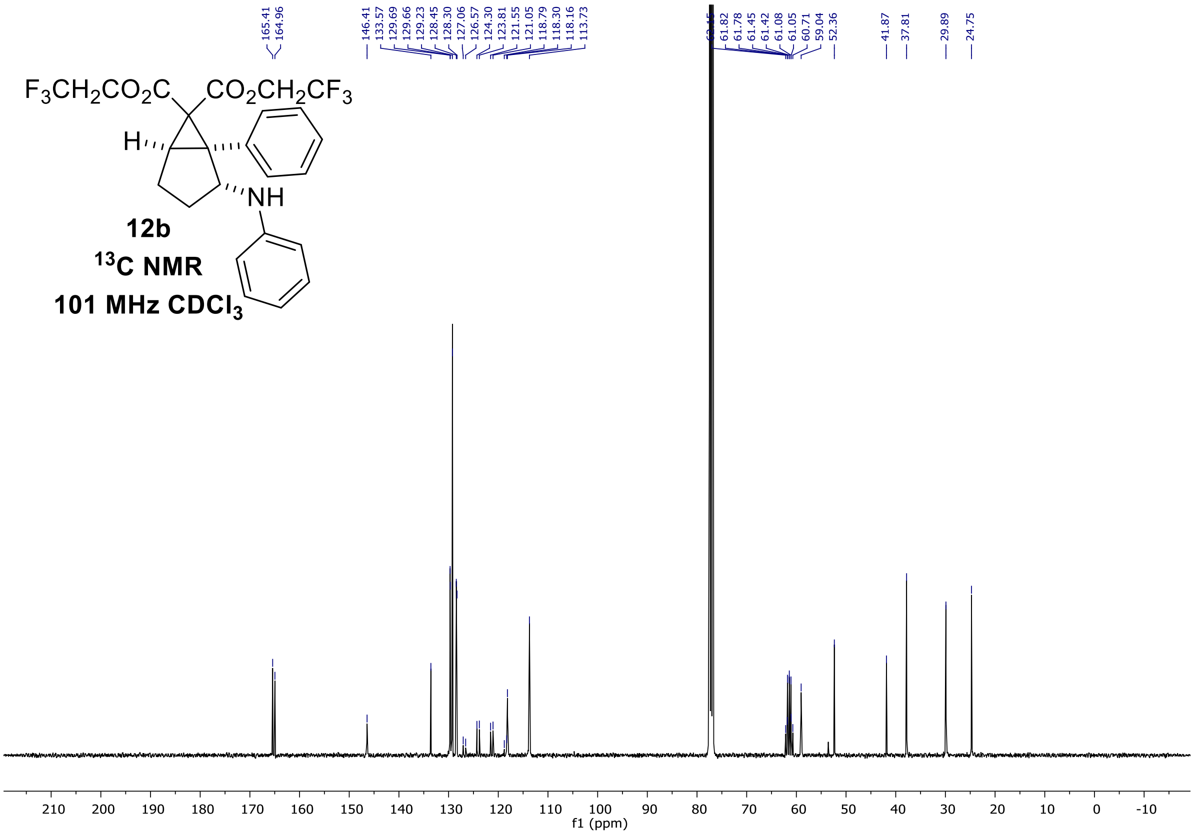
376 MHz $CDCl_3$



12b

^{1}H NMR

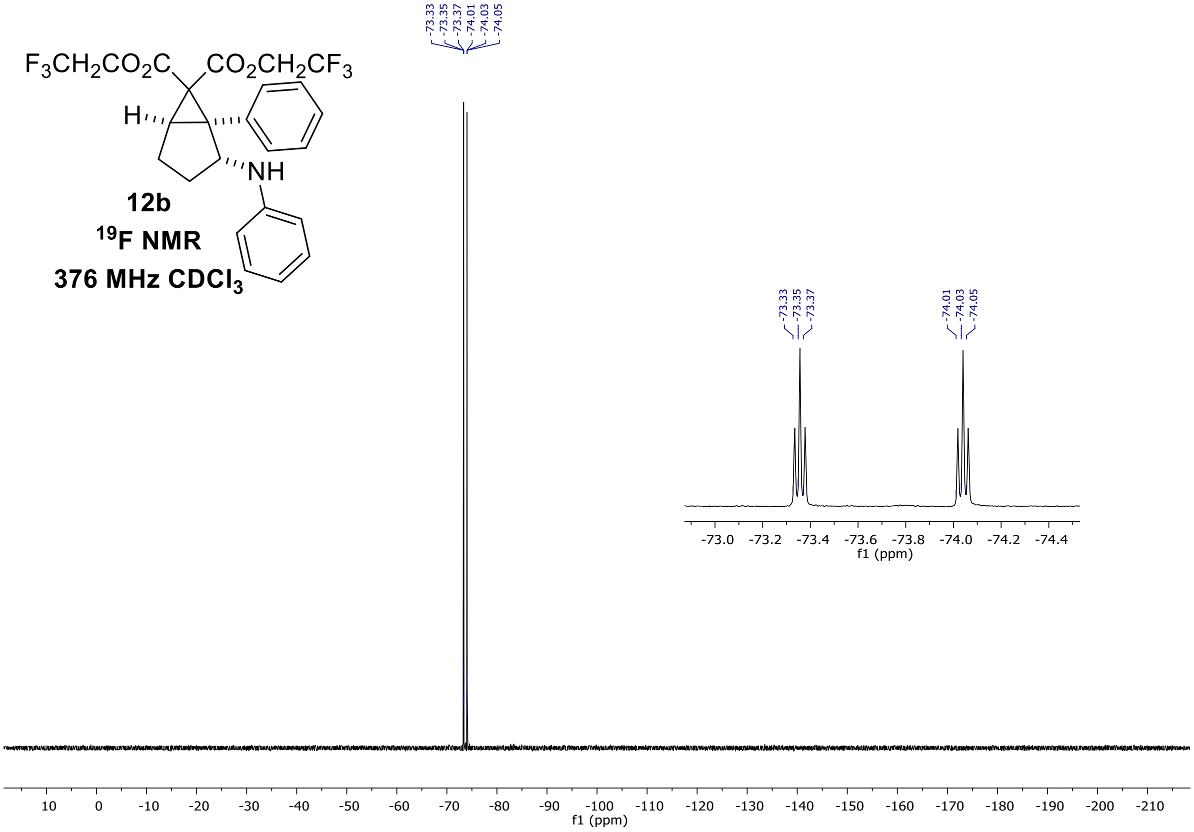
400 MHz $CDCl_3$



12b

^{13}C NMR

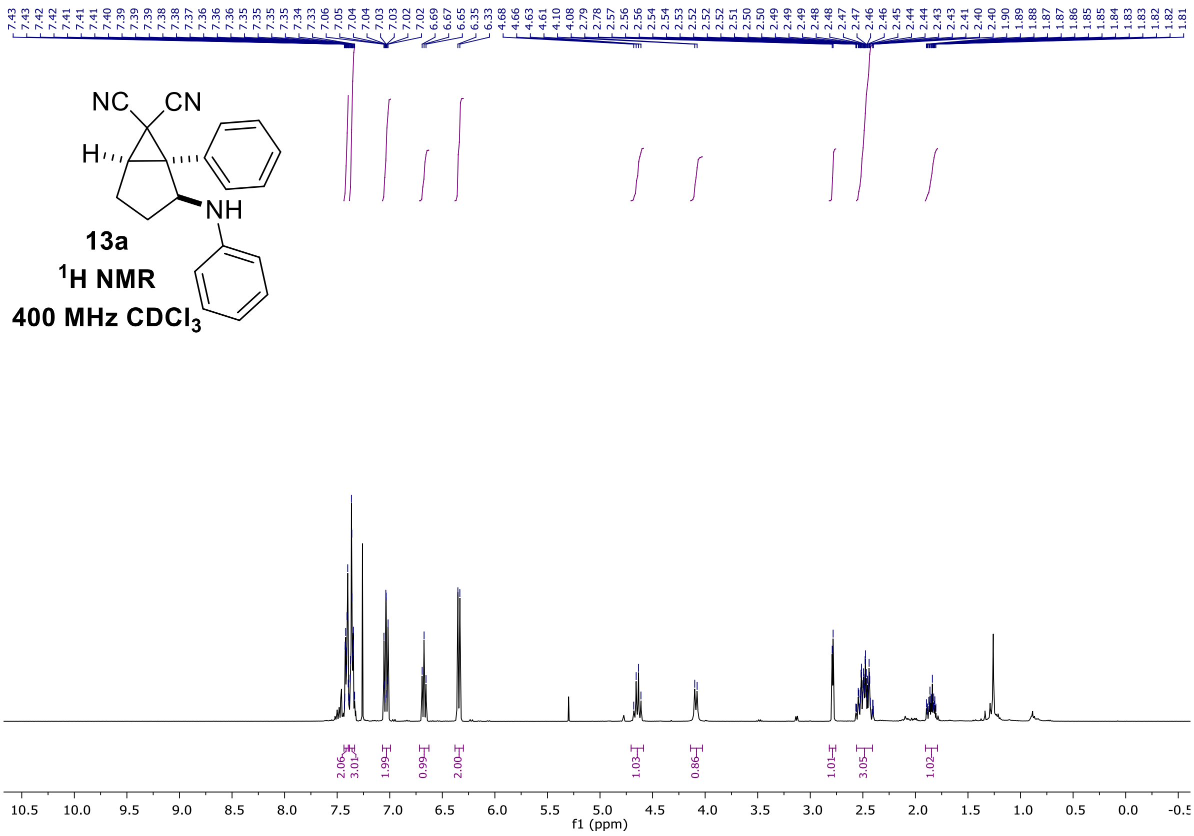
101 MHz $CDCl_3$



12b

^{19}F NMR

376 MHz $CDCl_3$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7.39
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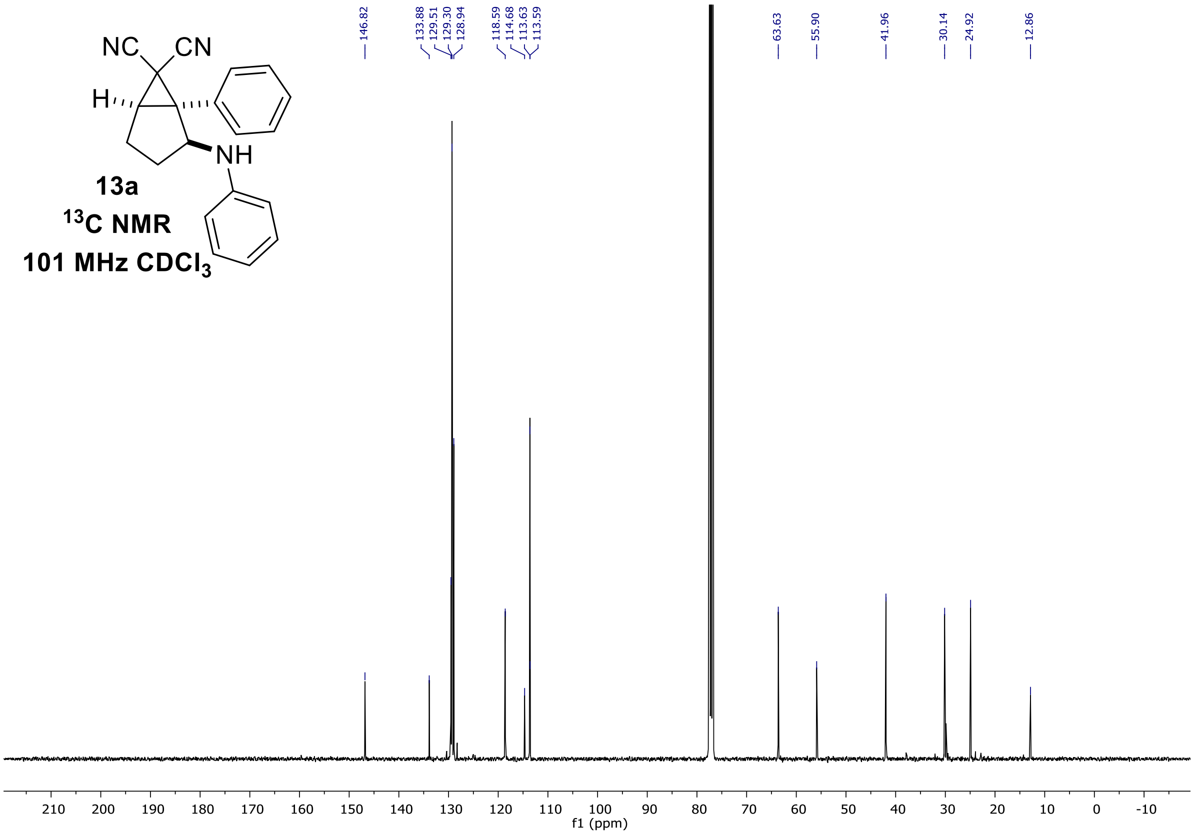
7.38
7.37
7.36
7.36
7.36
7.35
7.35
7.35
7.35
7.34
7.33
7.06
7.05
7.04
7.04
7.03
7.03
7.02
7.02
6.69
6.67
6.65
6.35
6.33
4.68
4.66
4.63
4.61
4.10
4.08
2.79
2.78
2.57
2.56
2.56
2.54
2.54
2.53
2.52
2.52
2.52
2.51
2.50
2.50
2.49
2.49
2.49
2.48
2.48
2.47
2.47
2.46
2.46
2.45
2.44
2.44
2.43
2.43
2.41
2.40
2.40
1.90
1.89
1.88
1.87
1.87
1.86
1.85
1.85
1.84
1.83
1.83
1.82
1.82
1.81
NC
CN
H
NH
13a
^{1}H NMR
400 MHz CDCl$_3$
2.06
3.01
1.99
0.99
2.00
1.03
0.86
1.01
3.05
1.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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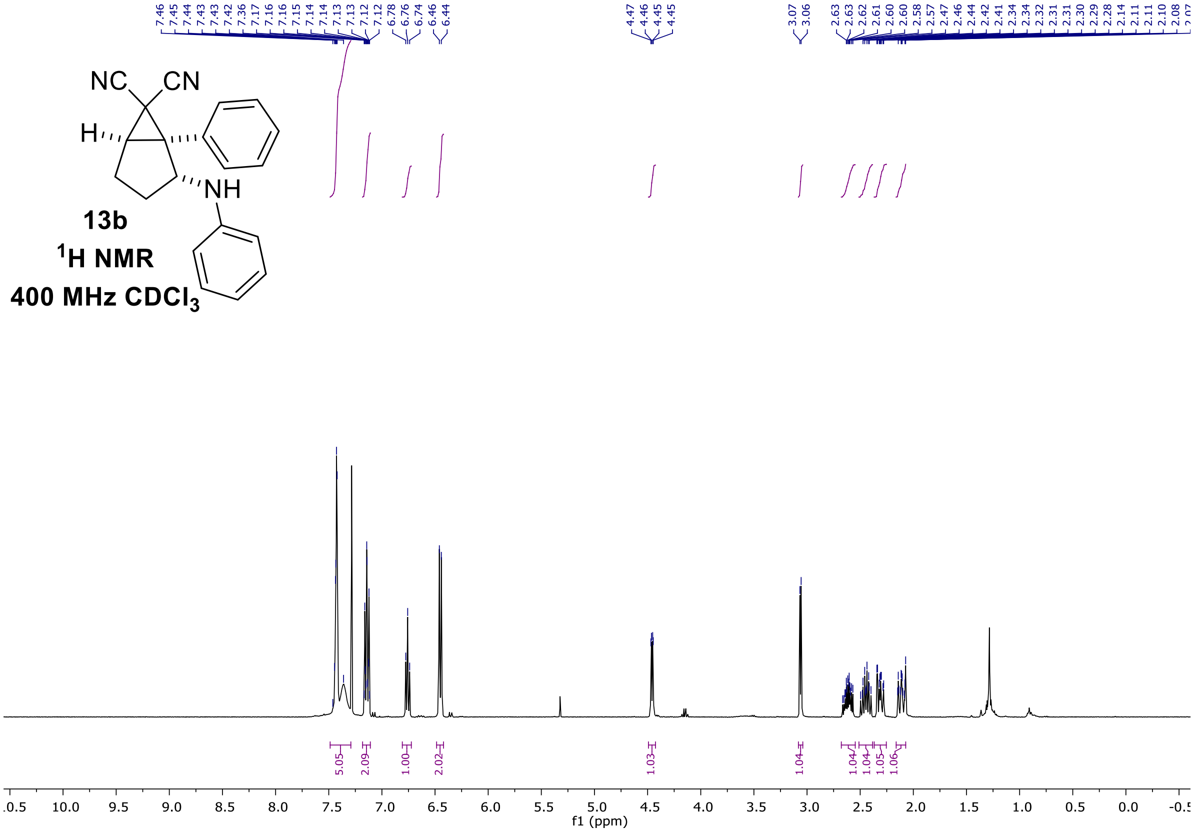
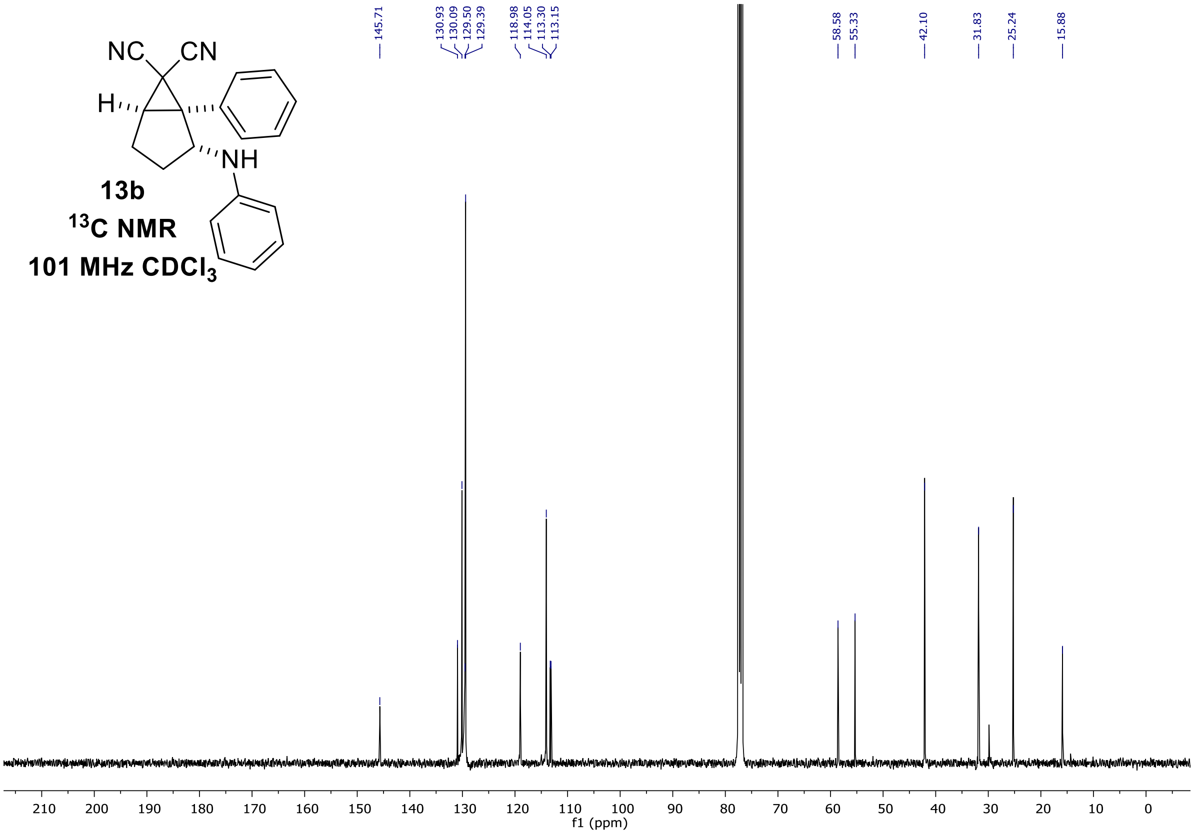
133.88
129.51
129.30
128.94
118.59
114.68
113.63
113.59
63.63
55.90
41.96
30.14
24.92
12.86
NC
CN
H
NH
13a
^{13}C NMR
101 MHz CDCl$_3$
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


13b

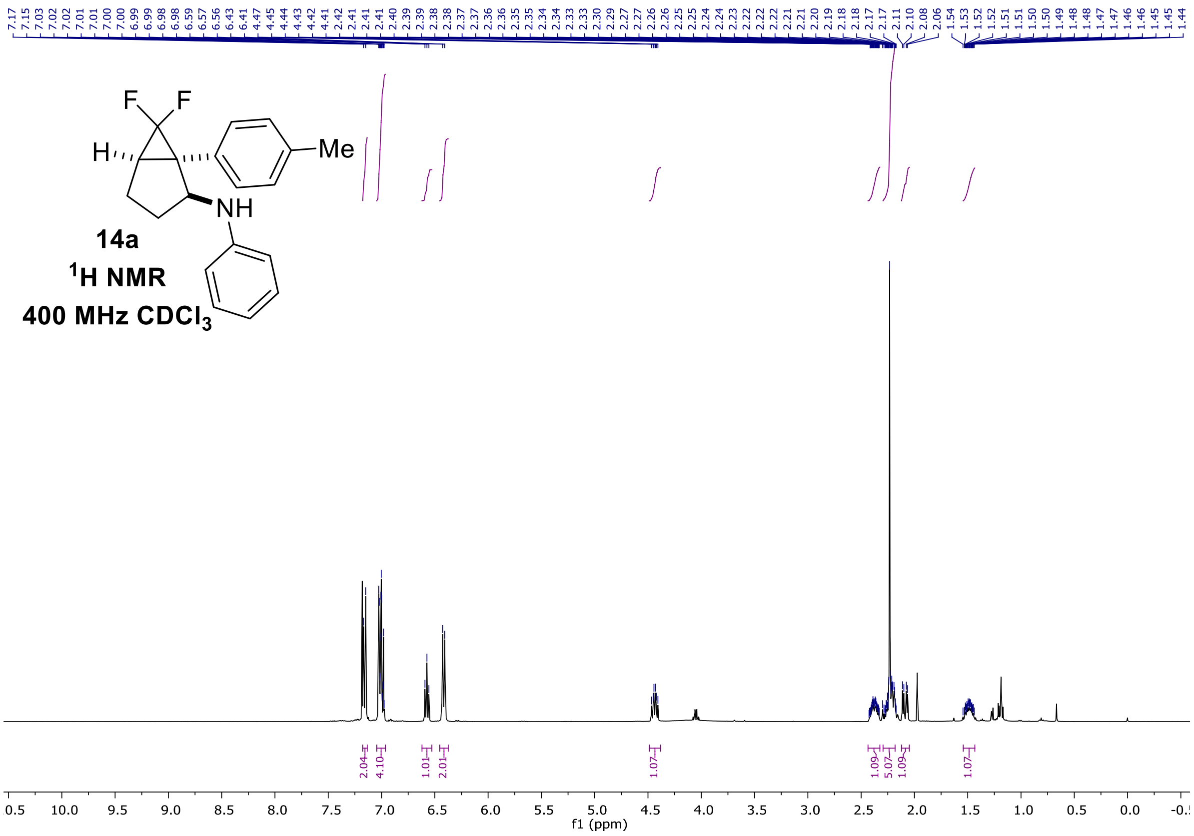
^{1}H NMR

400 MHz $CDCl_3$


13b

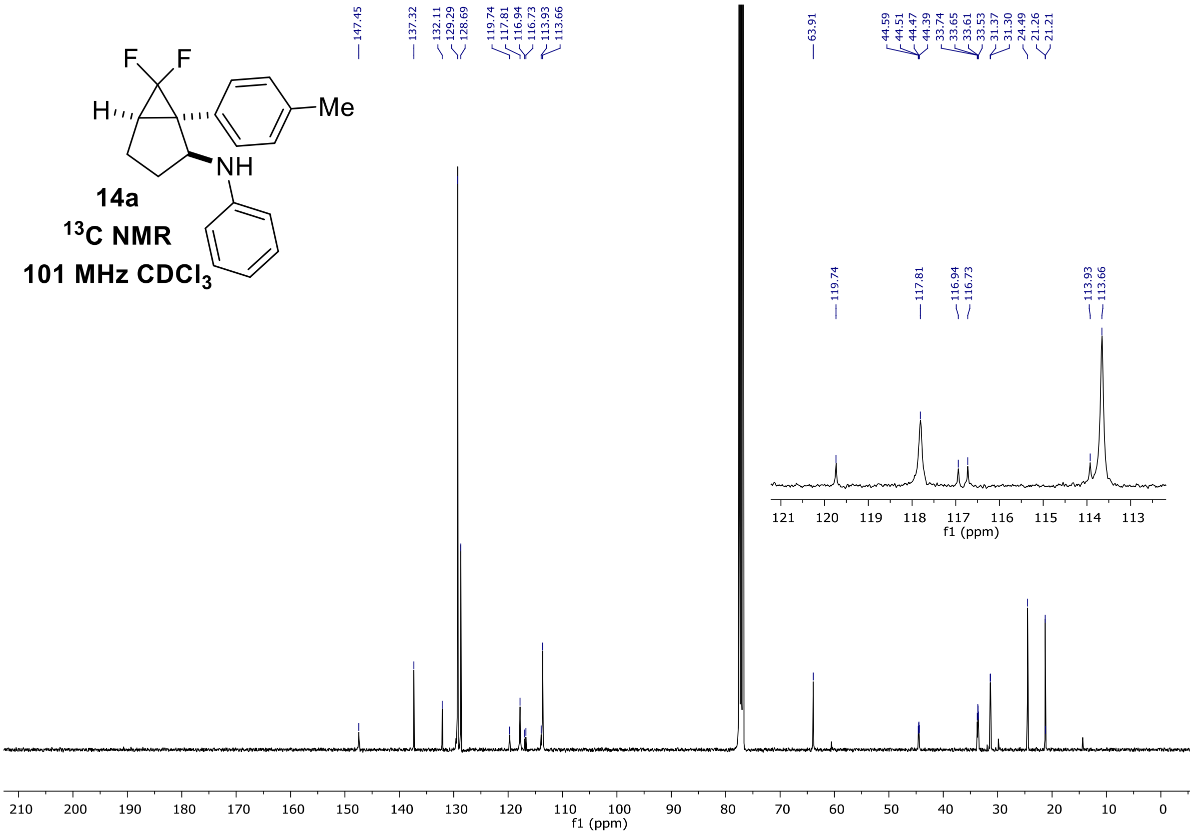
^{13}C NMR

101 MHz $CDCl_3$


14a

^{1}H NMR

400 MHz $CDCl_3$


14a

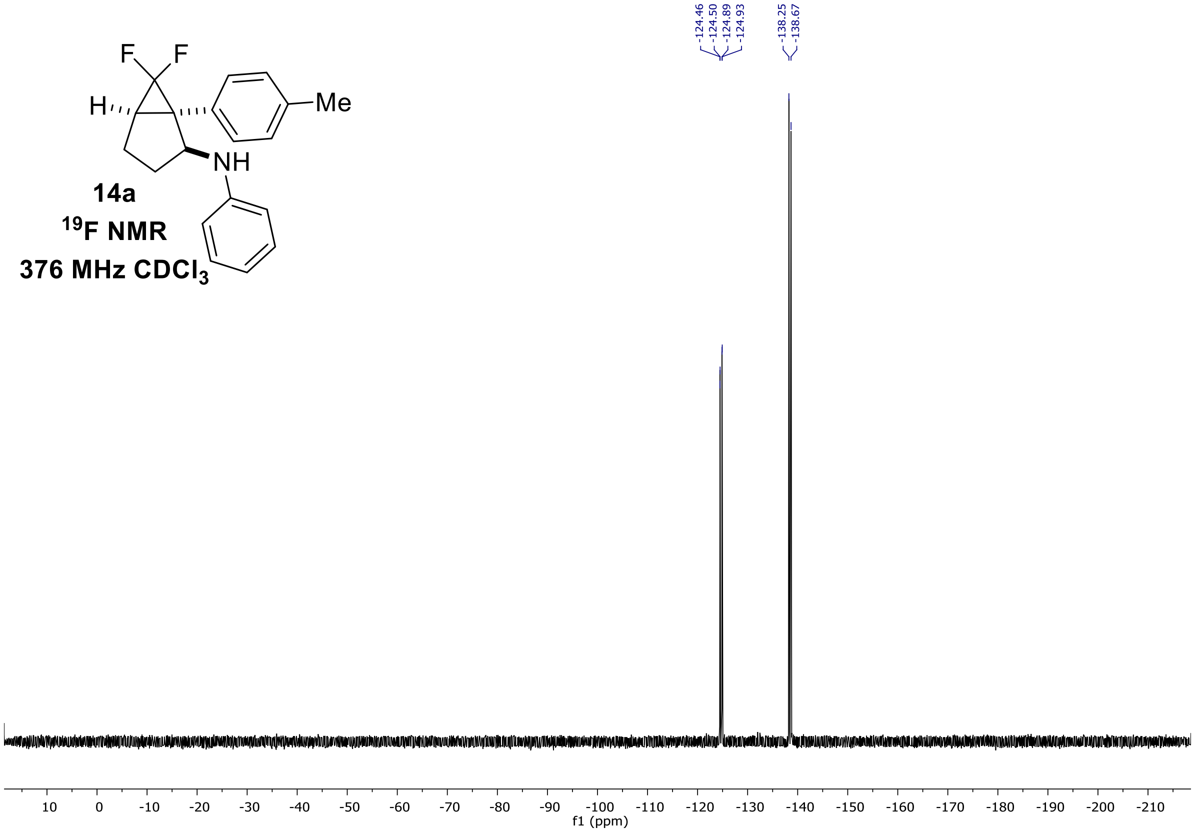
^{13}C NMR

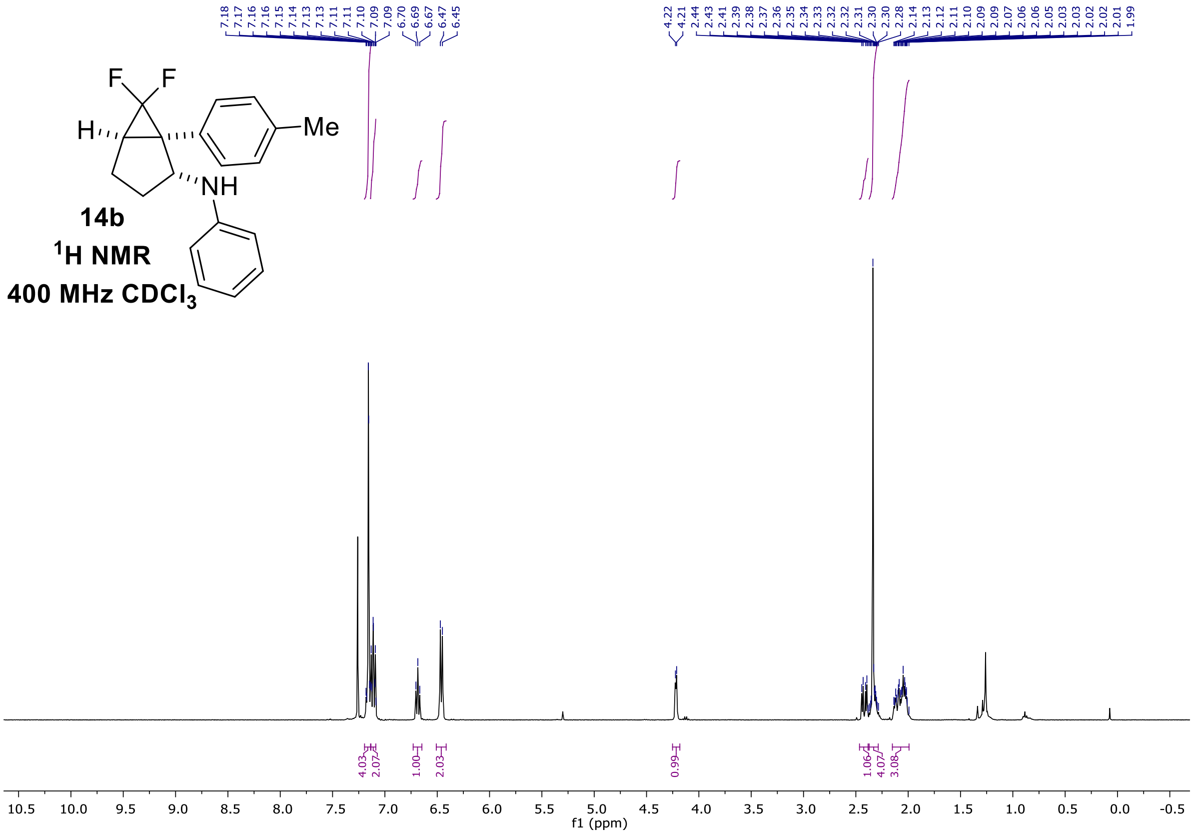
101 MHz $CDCl_3$

14a

^{19}F NMR

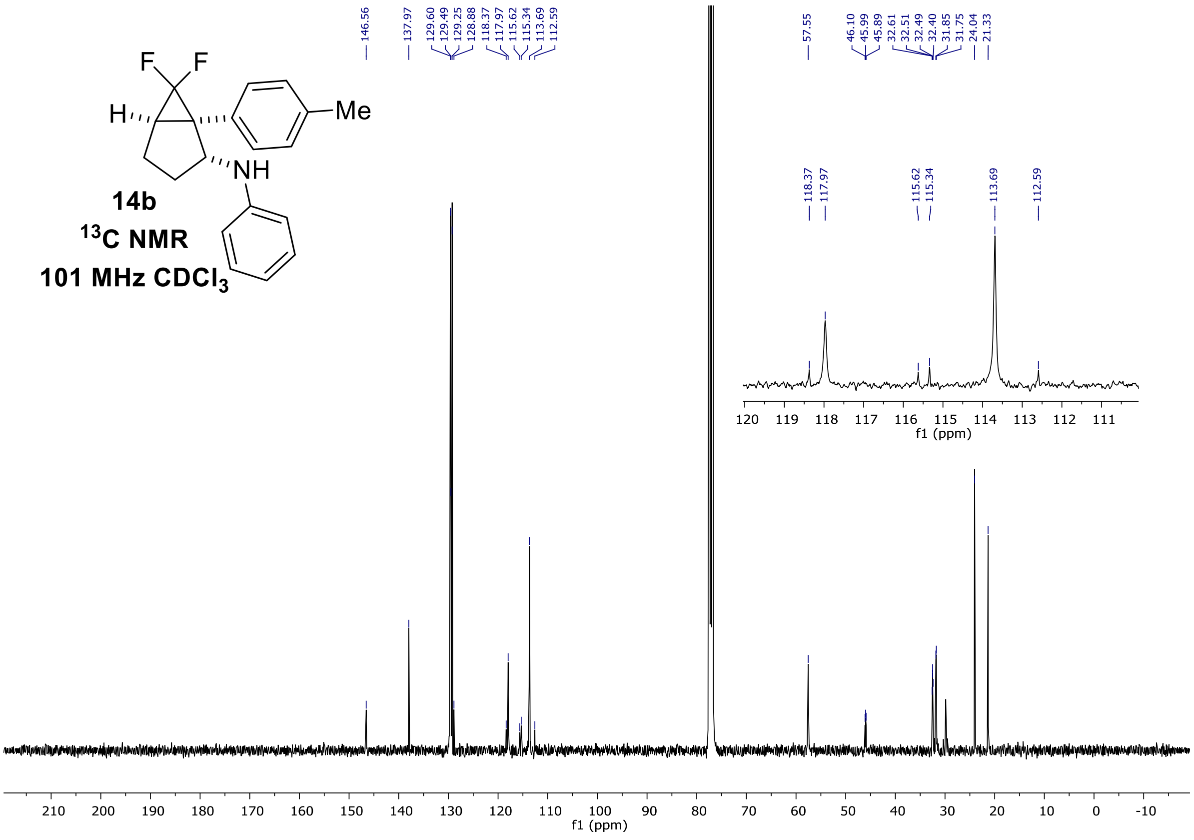
376 MHz $CDCl_3$




14b

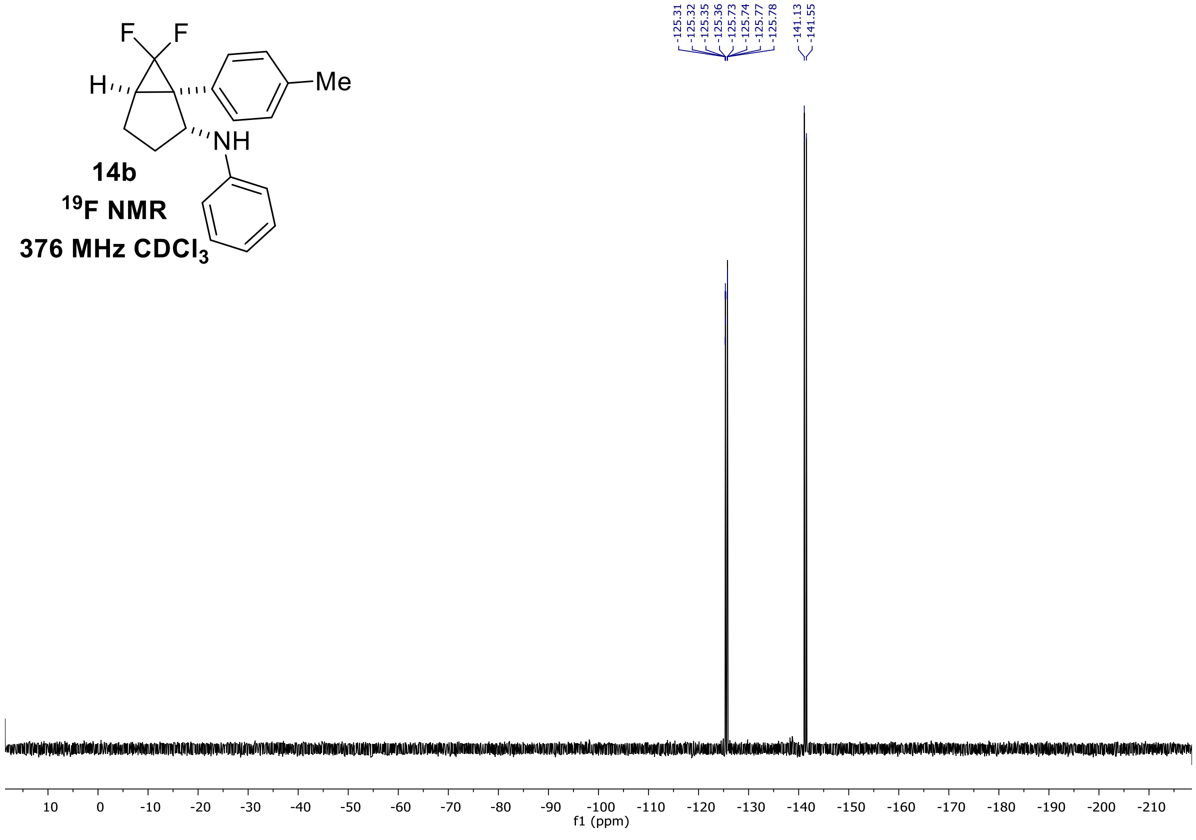
^{1}H NMR

400 MHz $CDCl_3$


14b

^{13}C NMR

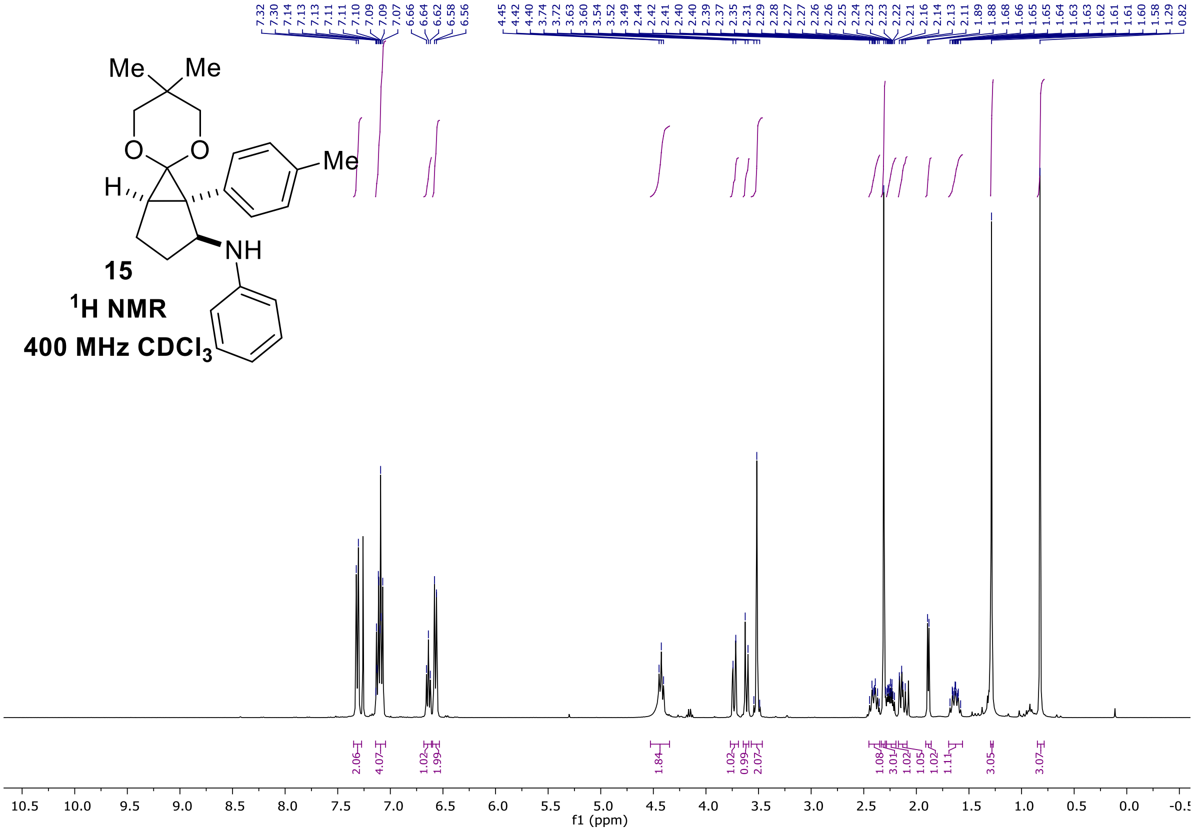
101 MHz $CDCl_3$



14b

^{19}F NMR

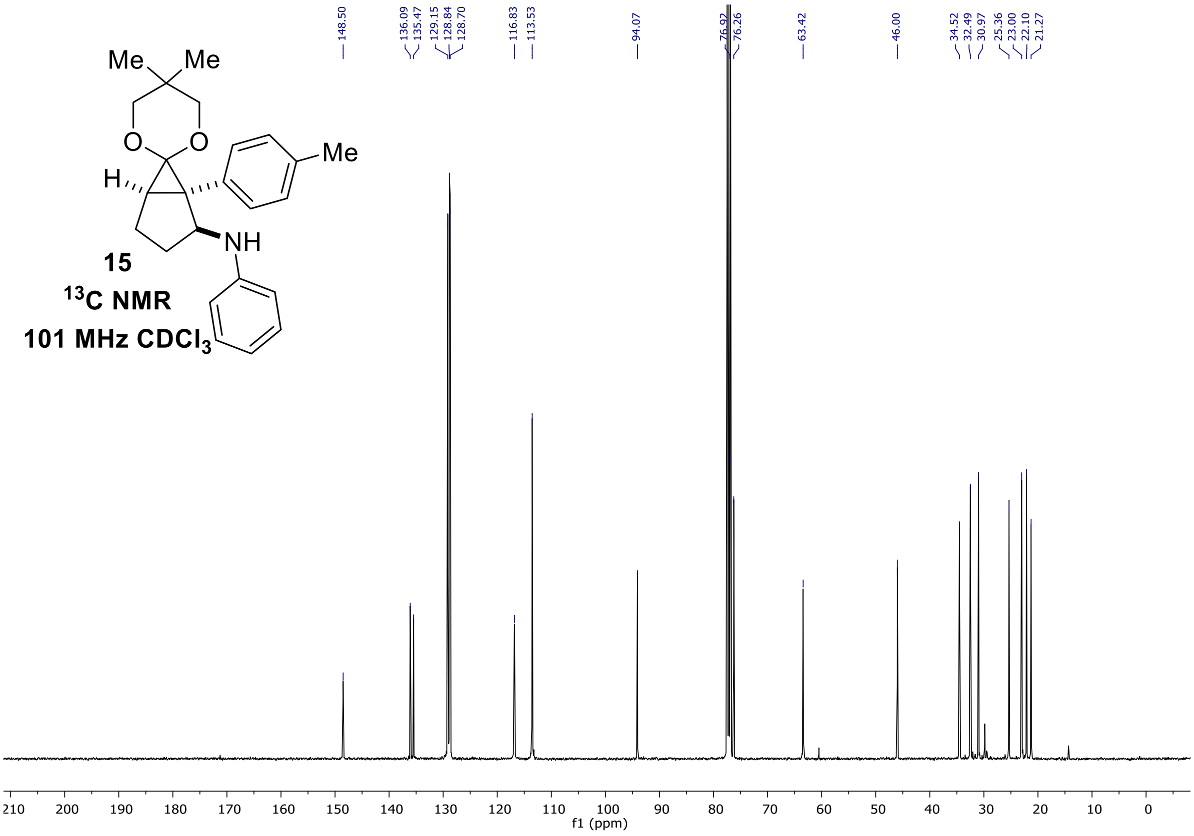
376 MHz $CDCl_3$



15

^{1}H NMR

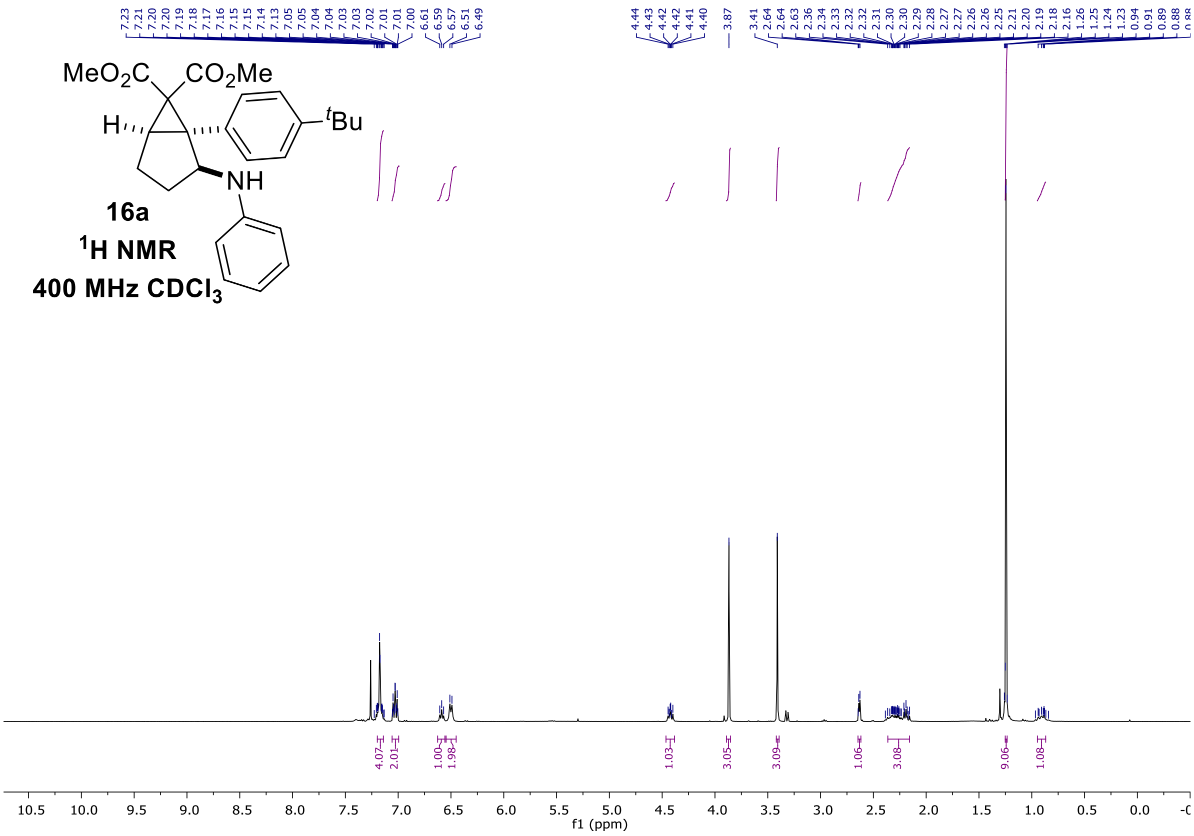
400 MHz $CDCl_3$



15

^{13}C NMR

101 MHz $CDCl_3$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7.18
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7.16
7.15
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7.14
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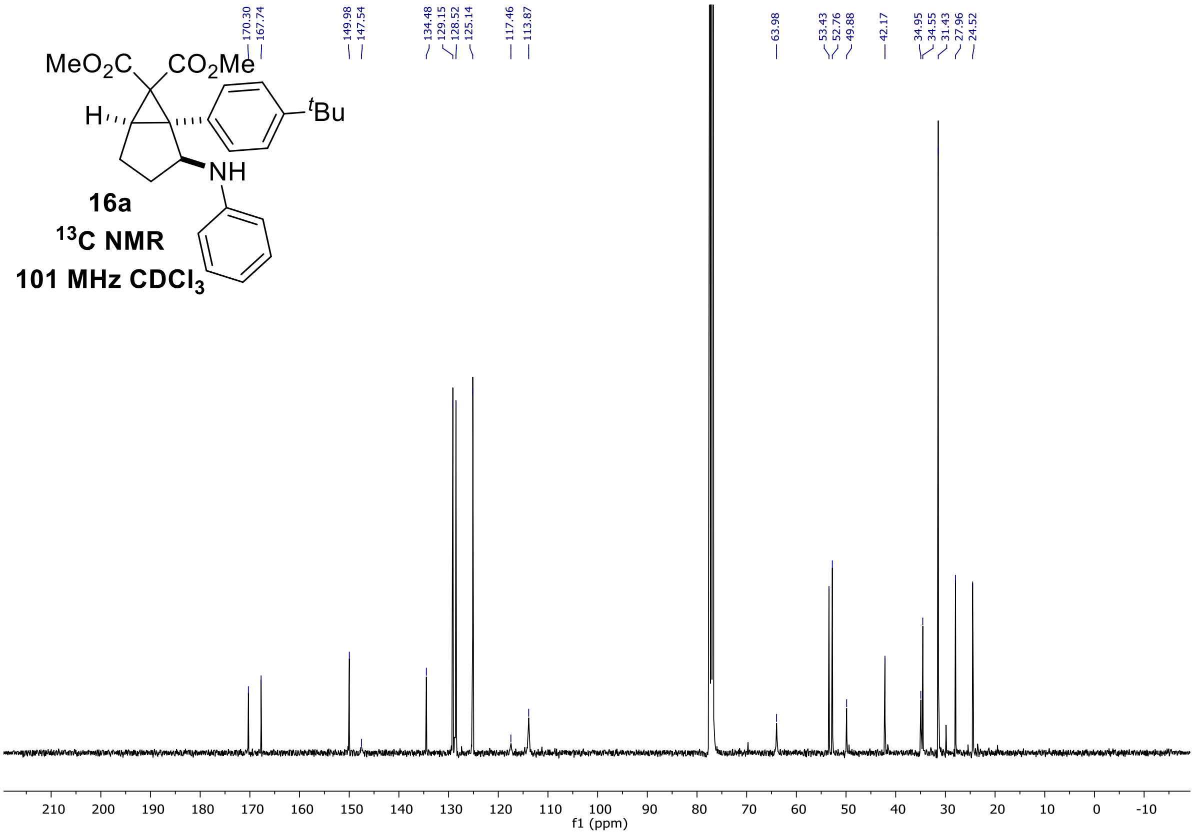
7.05
7.05
7.04
7.04
7.03
7.03
7.02
7.01
7.01
7.00
6.61
6.59
6.57
6.51
6.49
4.44
4.43
4.42
4.42
4.41
4.40
3.87
3.41
2.64
2.64
2.63
2.36
2.34
2.33
2.32
2.32
2.31
2.30
2.30
2.29
2.28
2.27
2.27
2.26
2.26
2.25
2.21
2.20
2.19
2.18
2.16
1.26
1.25
1.24
1.23
0.94
0.91
0.89
0.88
MeO2C
CO2Me
H
tBu
NH
16a
1H NMR
400 MHz CDCl3
4.07
2.01
1.00
1.98
1.03
3.05
3.09
1.06
3.08
9.06
1.08
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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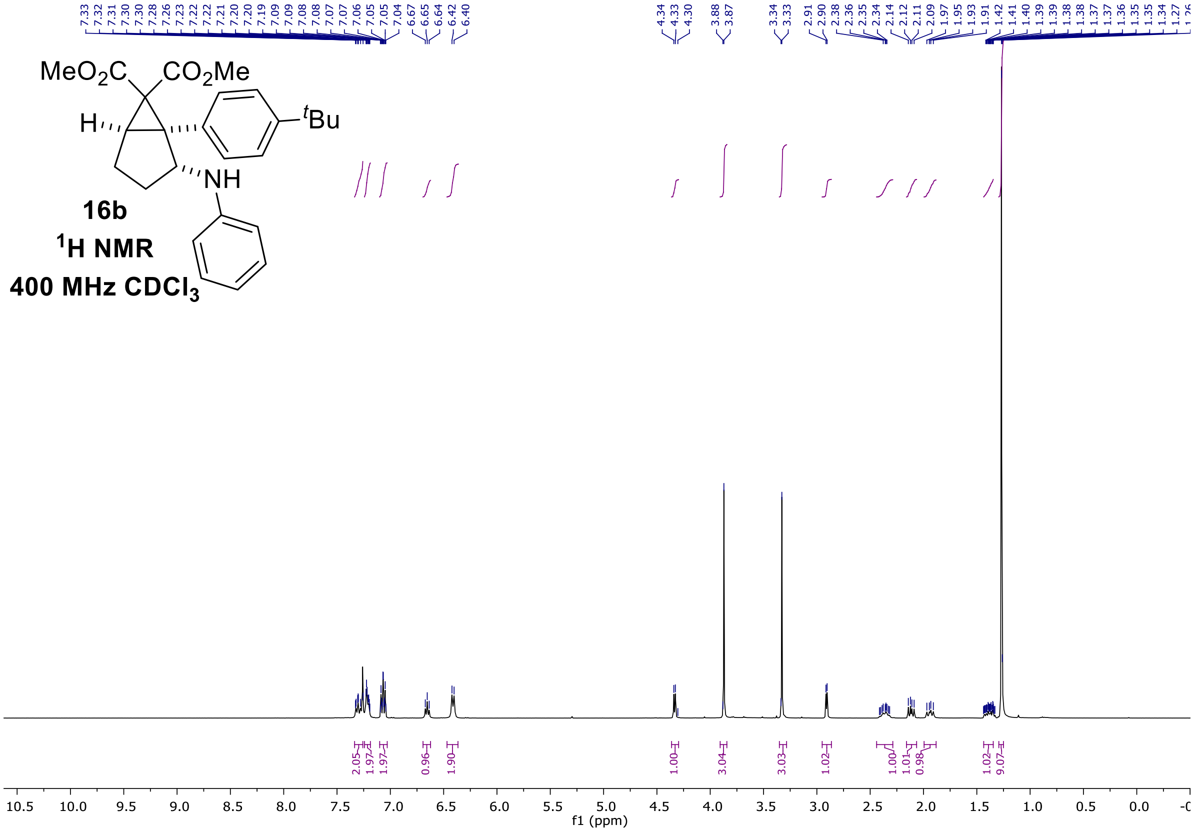
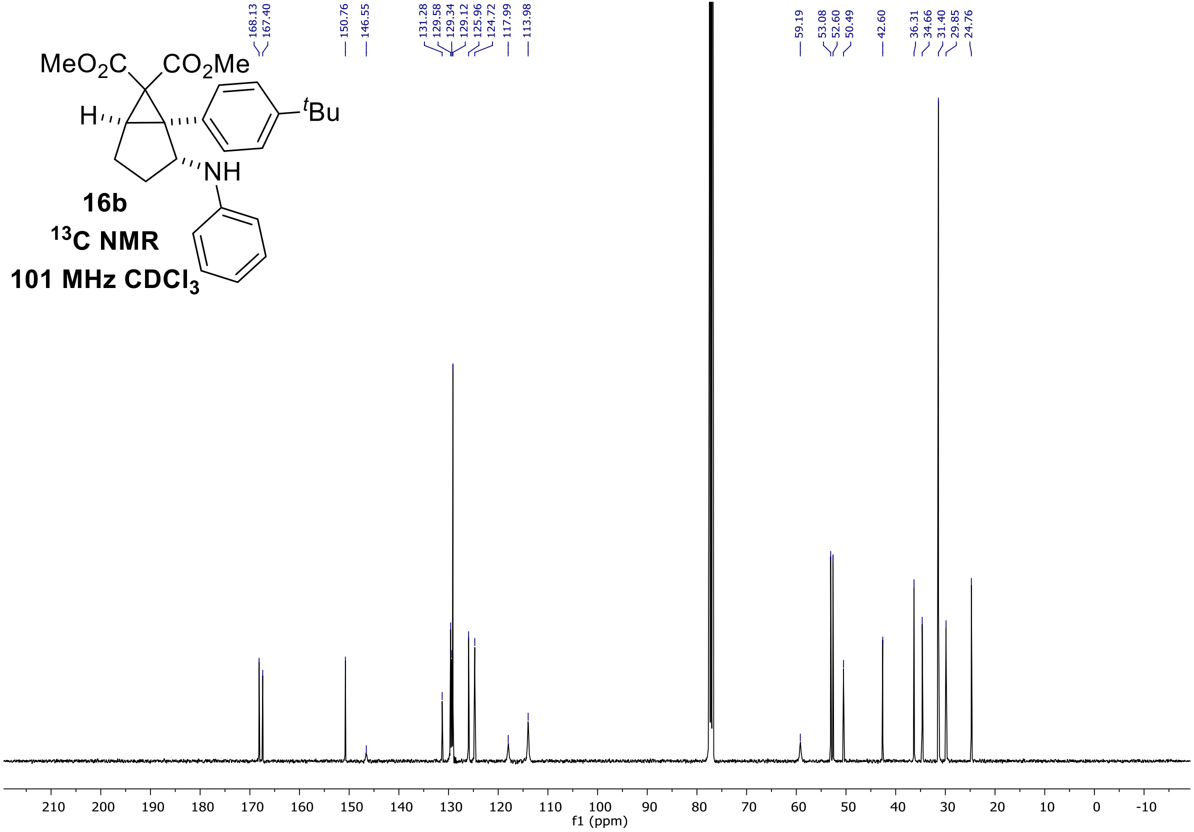
125.14
117.46
113.87
63.98
53.43
52.76
49.88
42.17
34.95
34.55
31.43
27.96
24.52
MeO2C
CO2Me
H
tBu
NH
16a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



16b

^{1}H NMR

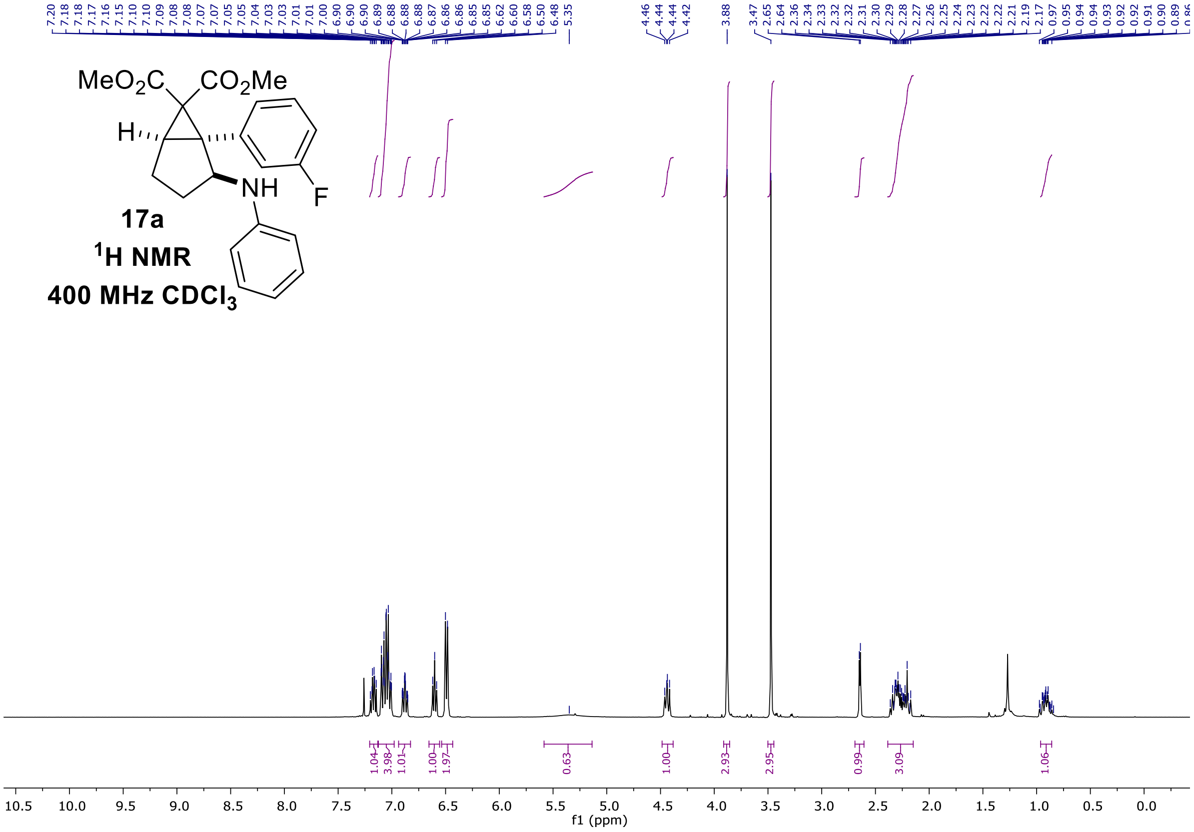
400 MHz $CDCl_3$



16b

^{13}C NMR

101 MHz $CDCl_3$


7.20
7.18
7.18
7.17
7.16
7.15
7.10
7.10
7.09
7.08
7.08
7.07
7.07
7.05
7.05
7.04
7.03
7.03
7.01
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7.00
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6.88
6.88
6.87
6.86
6.86
6.85
6.62
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6.50
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5.35
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3.47
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2.64
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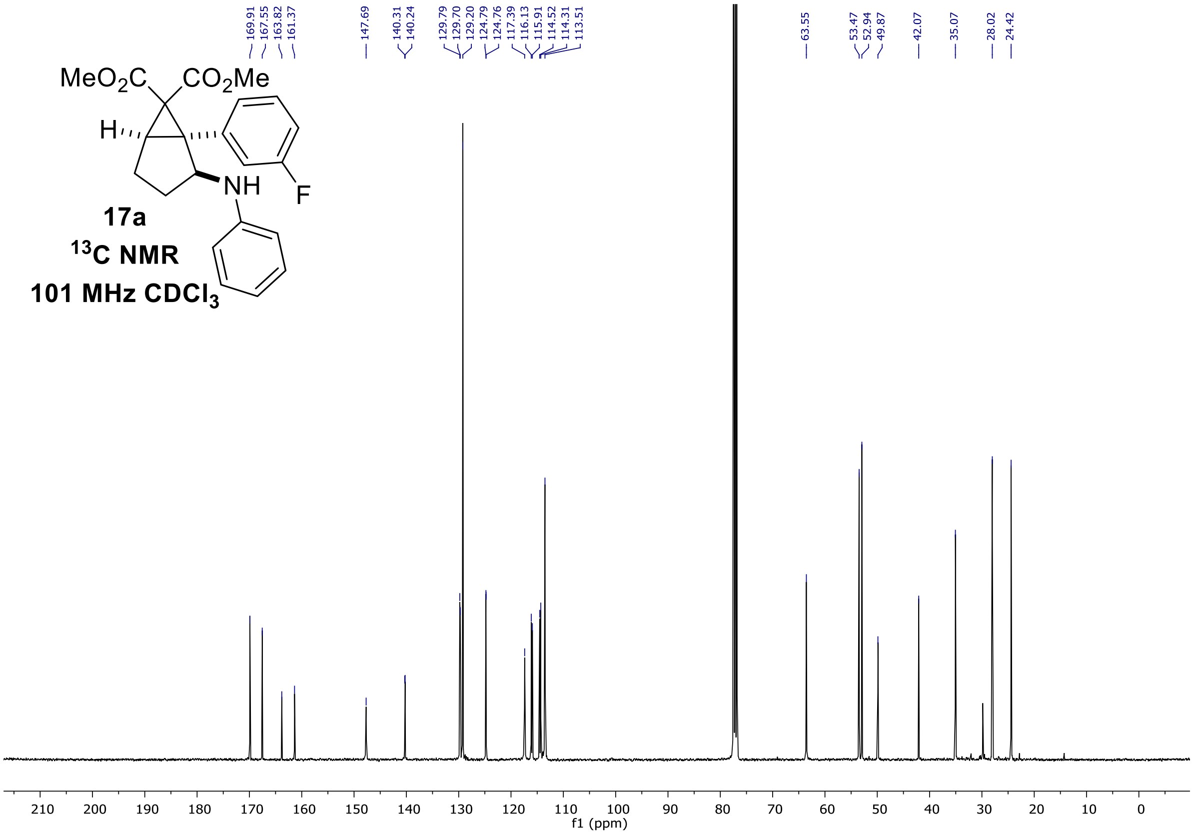
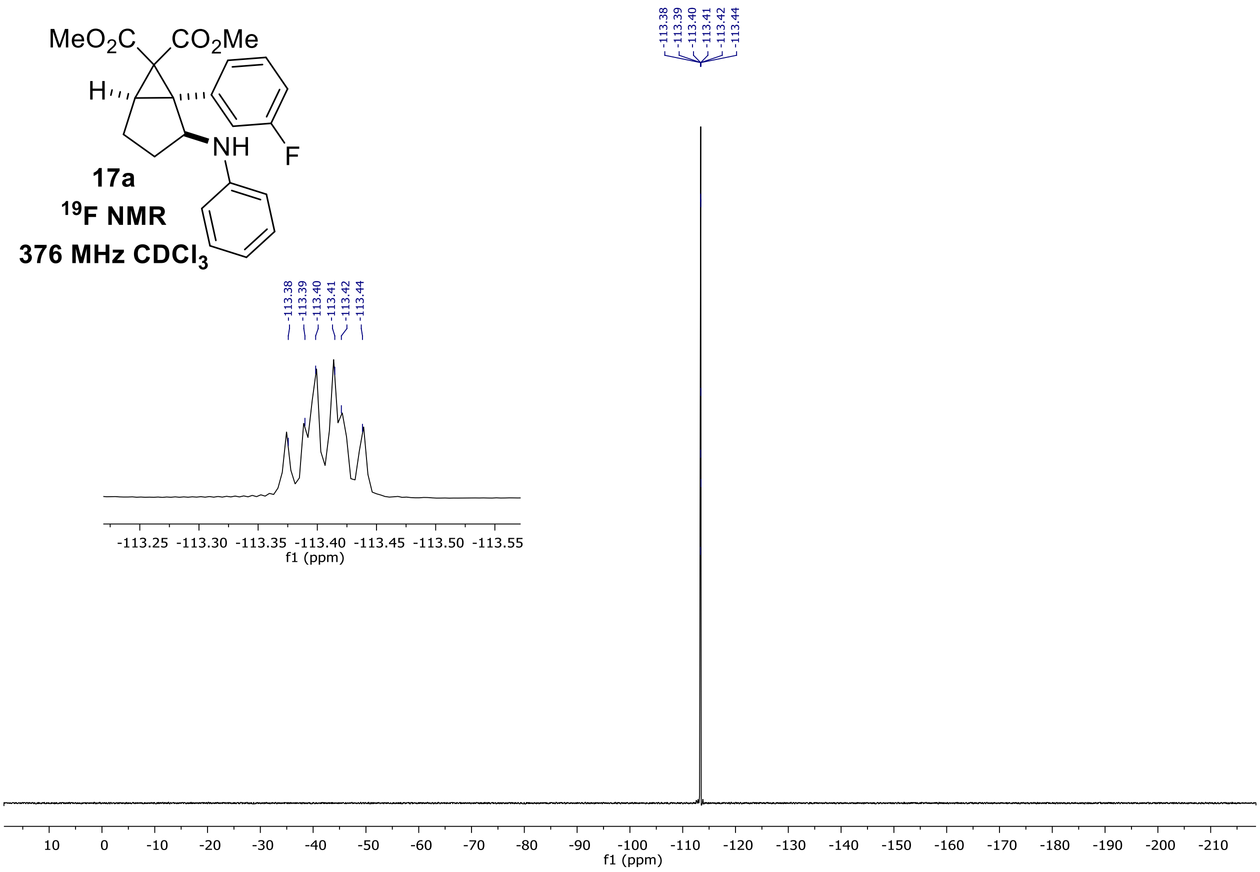
2.29
2.28
2.27
2.26
2.25
2.24
2.23
2.22
2.22
2.21
2.19
2.17
0.97
0.95
0.94
0.94
0.93
0.92
0.92
0.91
0.90
0.89
MeO2C
CO2Me
H
NH
F
17a
1H NMR
400 MHz CDCl3
1.04
3.98
1.01
1.00
1.97
0.63
1.00
2.93
2.95
0.99
3.09
1.06
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

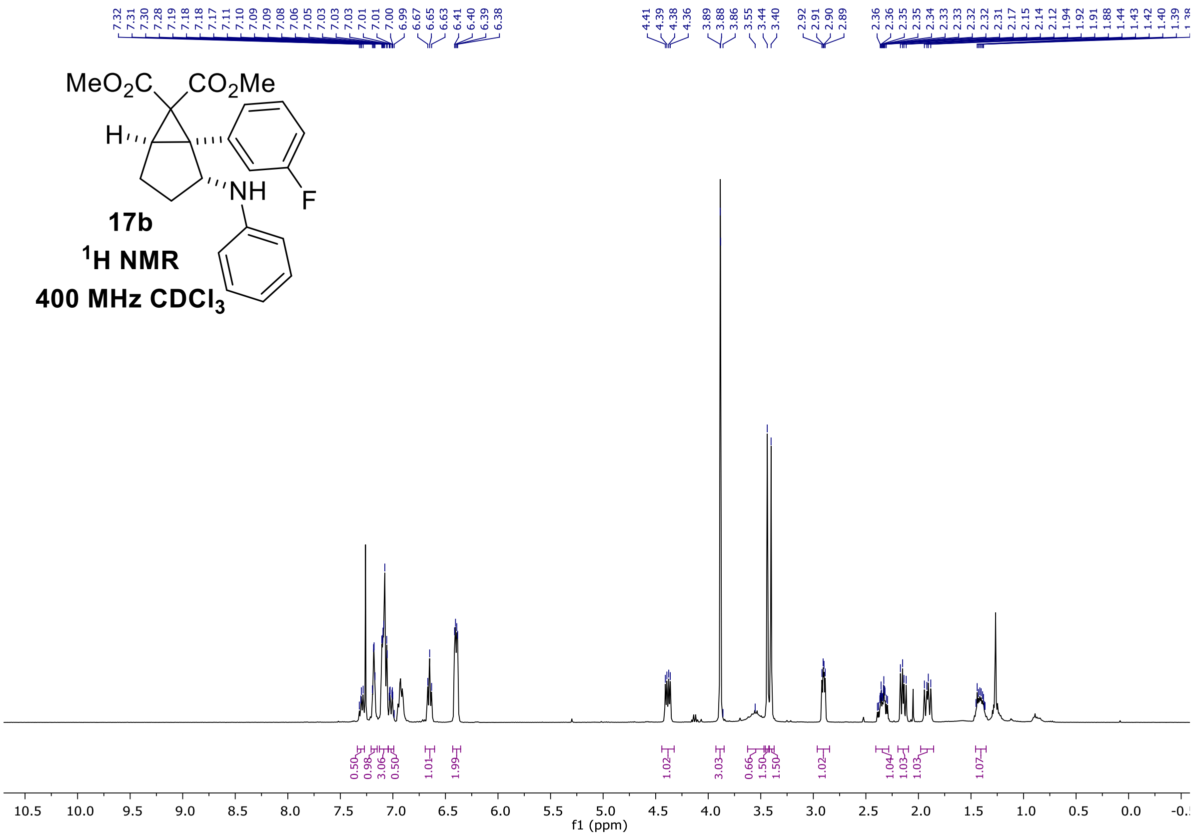

169.91
167.55
163.82
161.37
147.69
140.31
140.24
129.79
129.70
129.20
124.79
124.76
117.39
116.13
115.91
114.52
114.31
113.51
63.55
53.47
52.94
49.87
42.07
35.07
28.02
24.42
MeO2C
CO2Me
H
NH
F
17a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

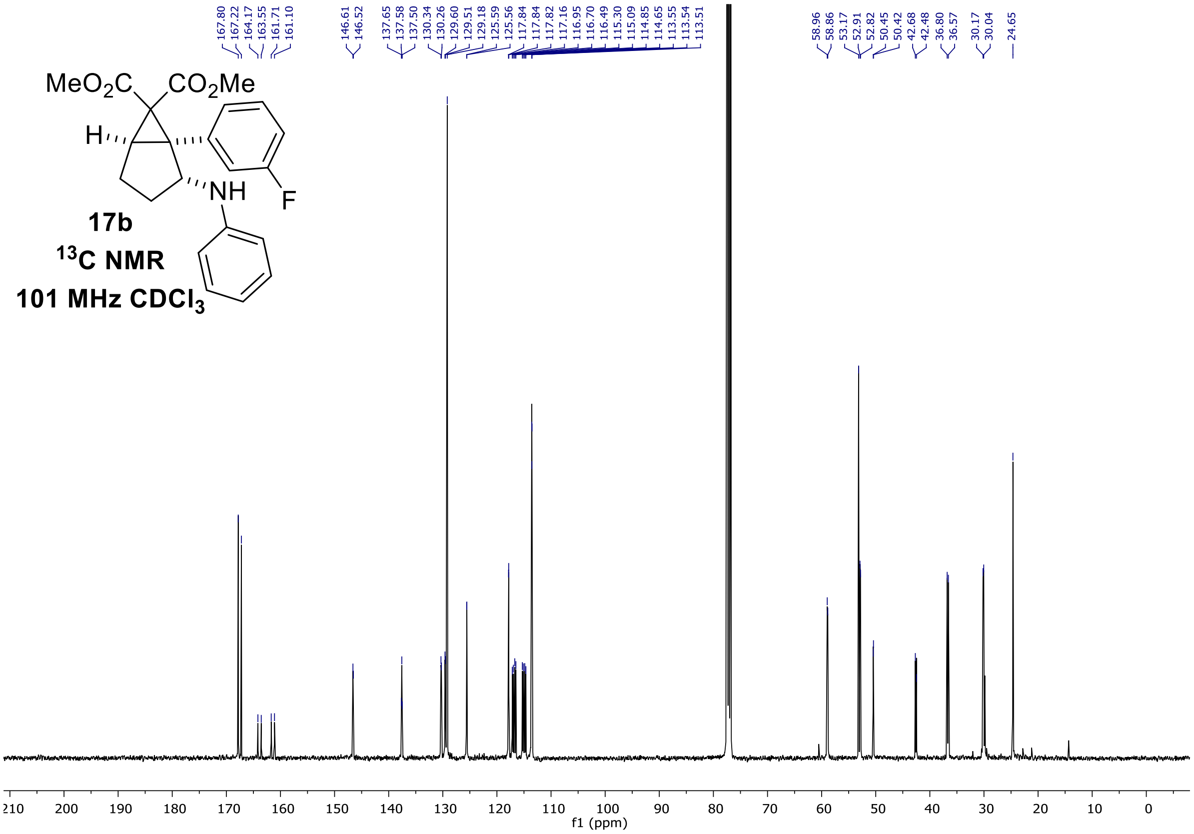


17a

^{19}F NMR

376 MHz CDCl$_3$

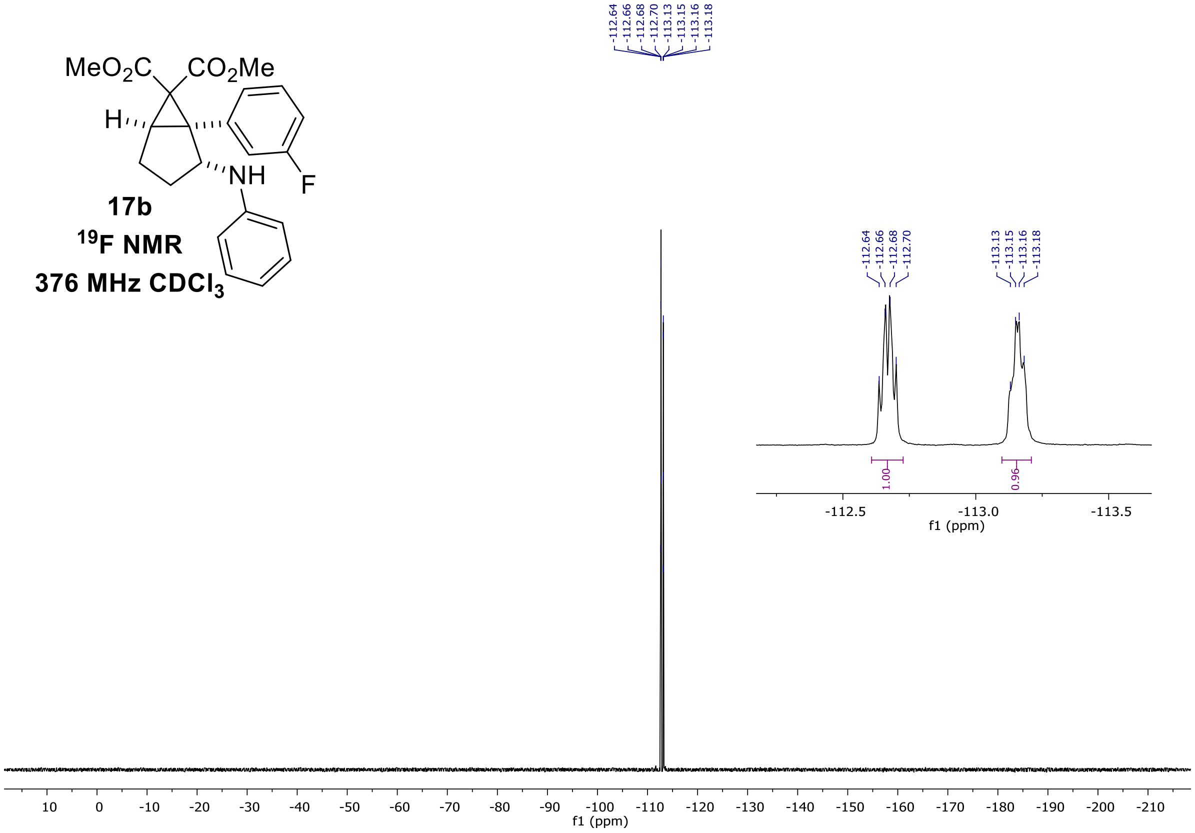

MeO2C
CO2Me
H
NH
F
17b
1H NMR
400 MHz CDCl3
7.32 7.31 7.30 7.28 7.19 7.18 7.17 7.11 7.10 7.09 7.09 7.08 7.06 7.05 7.03 7.03 7.01 7.01 7.00 6.99 6.67 6.65 6.63 6.41 6.40 6.39 6.38
4.41 4.39 4.38 4.36 3.89 3.88 3.86 3.55 3.44 3.40 2.92 2.91 2.90 2.89
2.36 2.36 2.35 2.34 2.33 2.33 2.32 2.31 2.17 2.15 2.14 2.12 1.94 1.92 1.91 1.88 1.44 1.43 1.42 1.40 1.39
0.50 0.98 3.06 0.50 1.01 1.99 1.02 3.03 0.66 1.50 1.50 1.02 1.04 1.03 1.03 1.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


MeO2C
CO2Me
H
NH
F
17b
13C NMR
101 MHz CDCl3
167.80 167.22 164.17 163.55 161.71 161.10
146.61 146.52
137.65 137.58 137.50 130.34 130.26 129.60 129.51 129.18 125.59 125.56 117.84 117.82 117.16 116.95 116.70 116.49 115.30 115.09 114.85 114.65 113.55 113.54 113.51
58.96 58.86 53.17 52.91 52.82 50.45 50.42 42.68 42.48 36.80 36.57 30.17 30.04 24.65
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

17b

^{19}F NMR

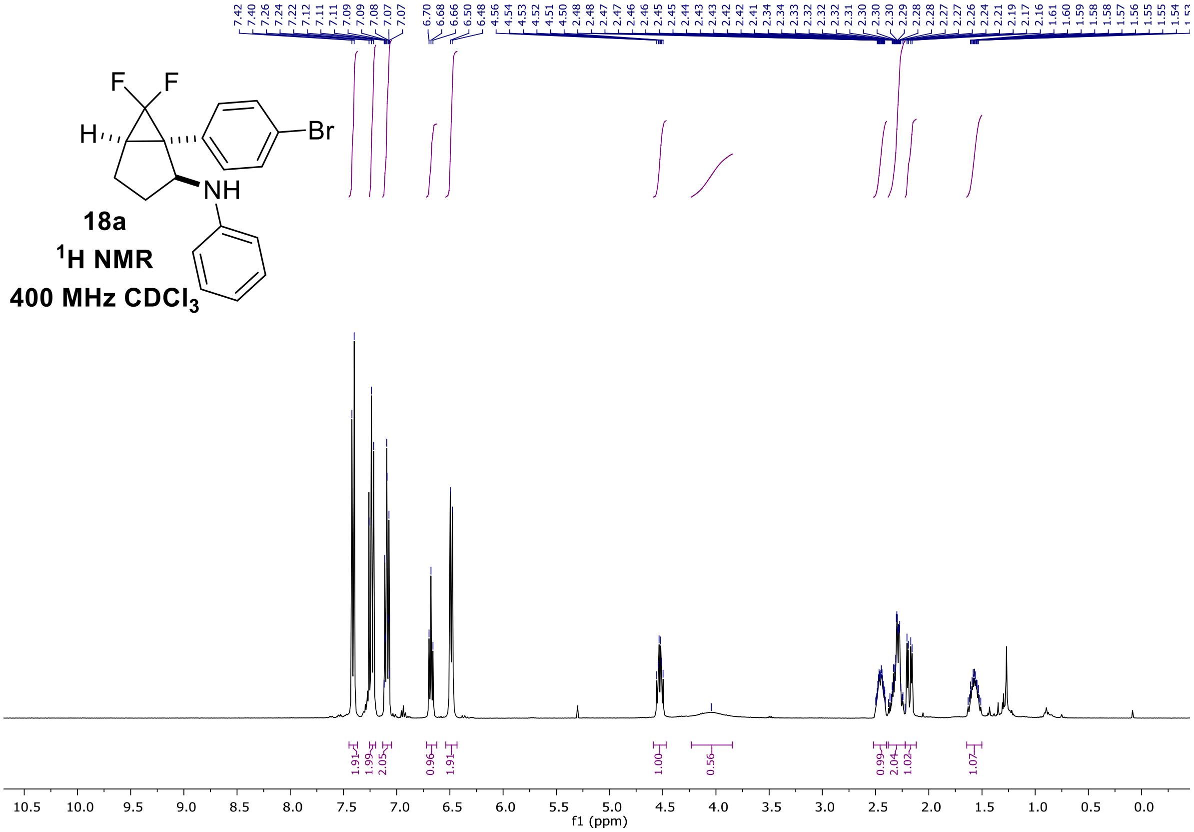
376 MHz CDCl$_3$



18a

^{1}H NMR

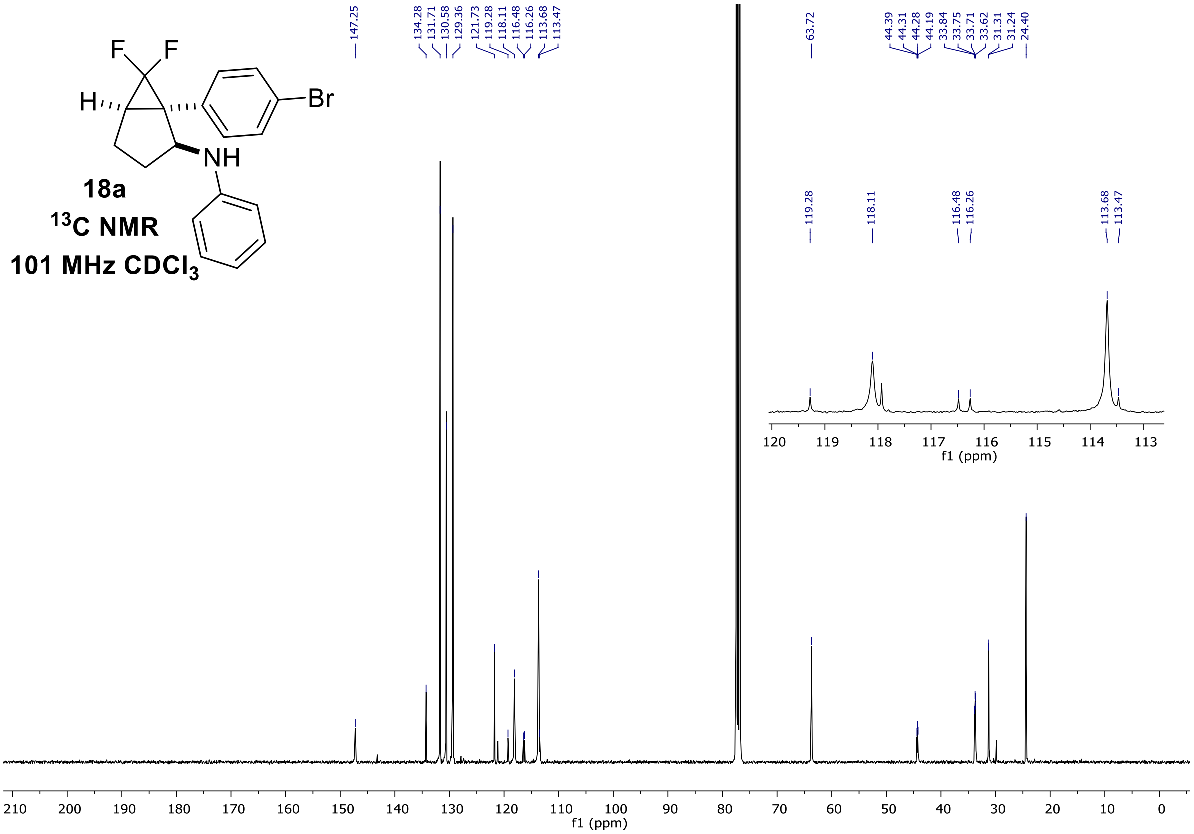
400 MHz CDCl$_3$

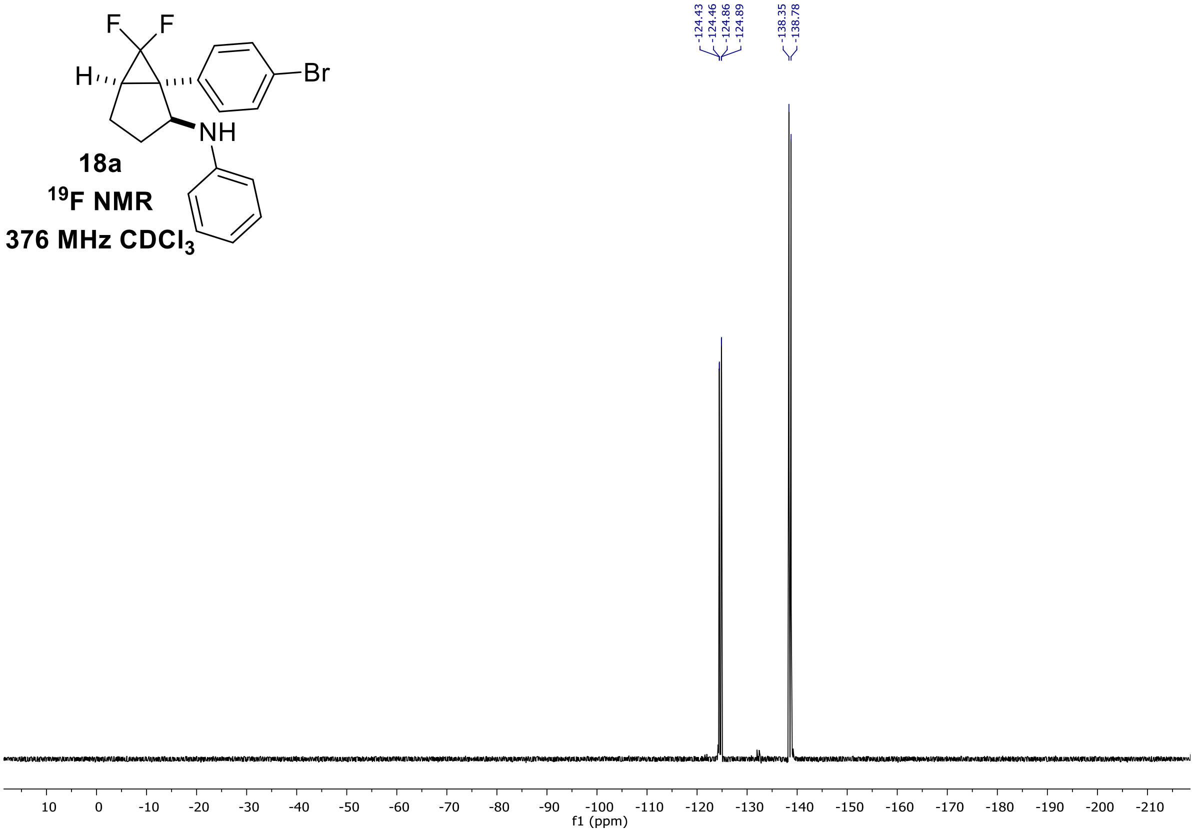


18a

^{13}C NMR

101 MHz CDCl$_3$

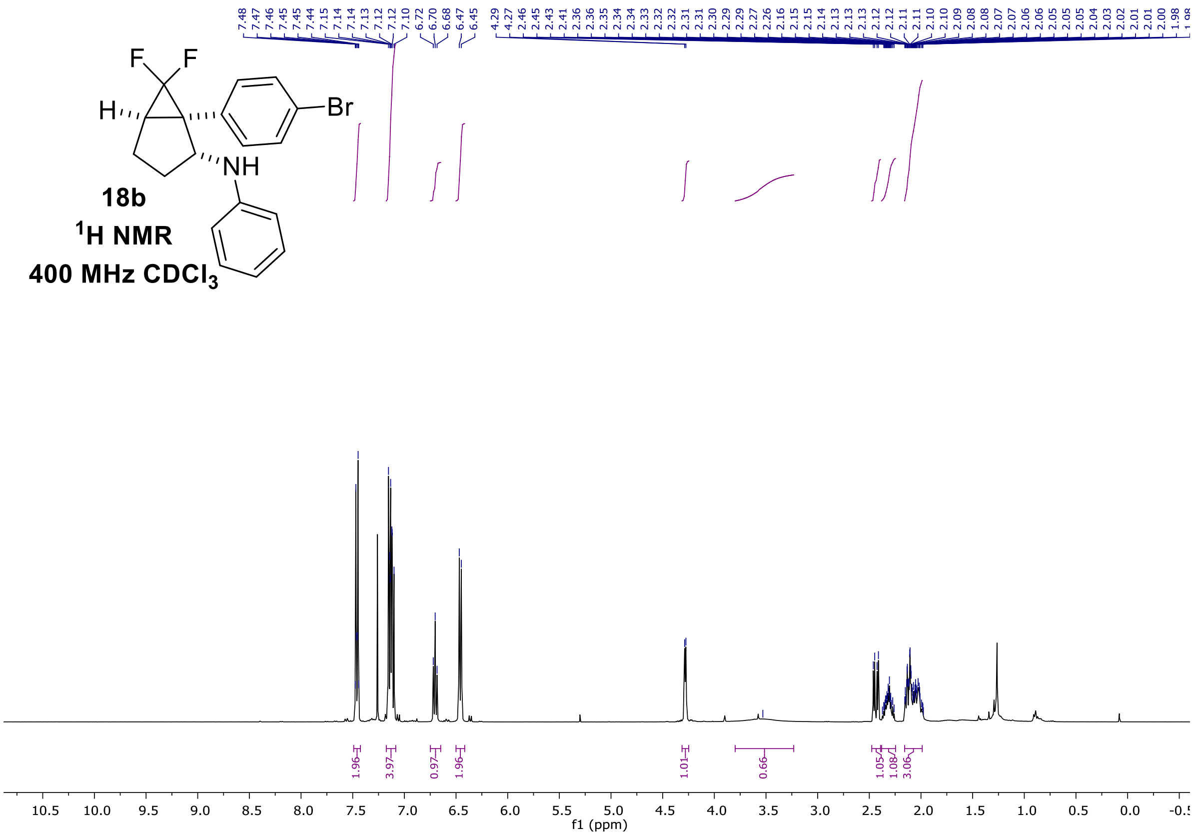




18a

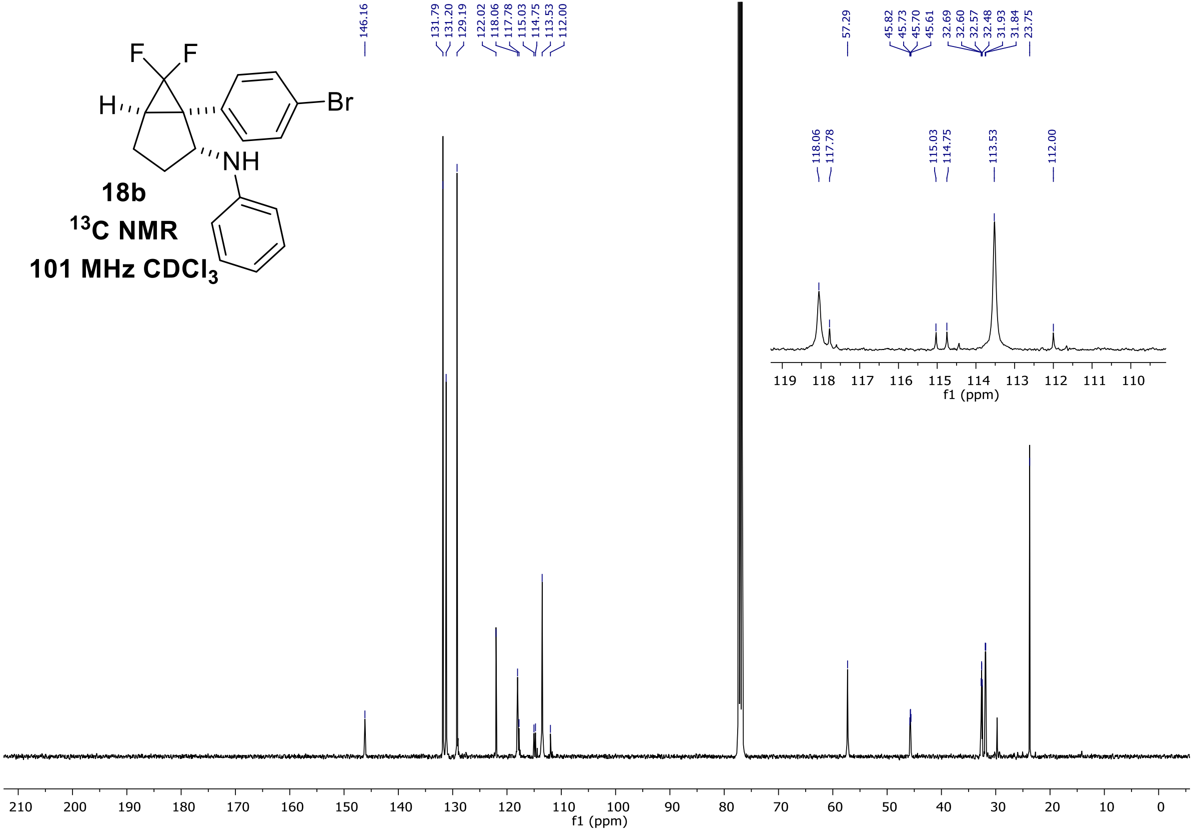
^{19}F NMR

376 MHz $CDCl_3$


18b

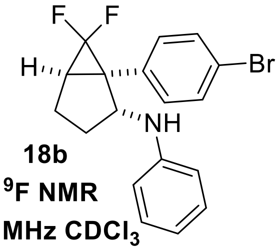
^{1}H NMR

400 MHz CDCl$_3$


18b

^{13}C NMR

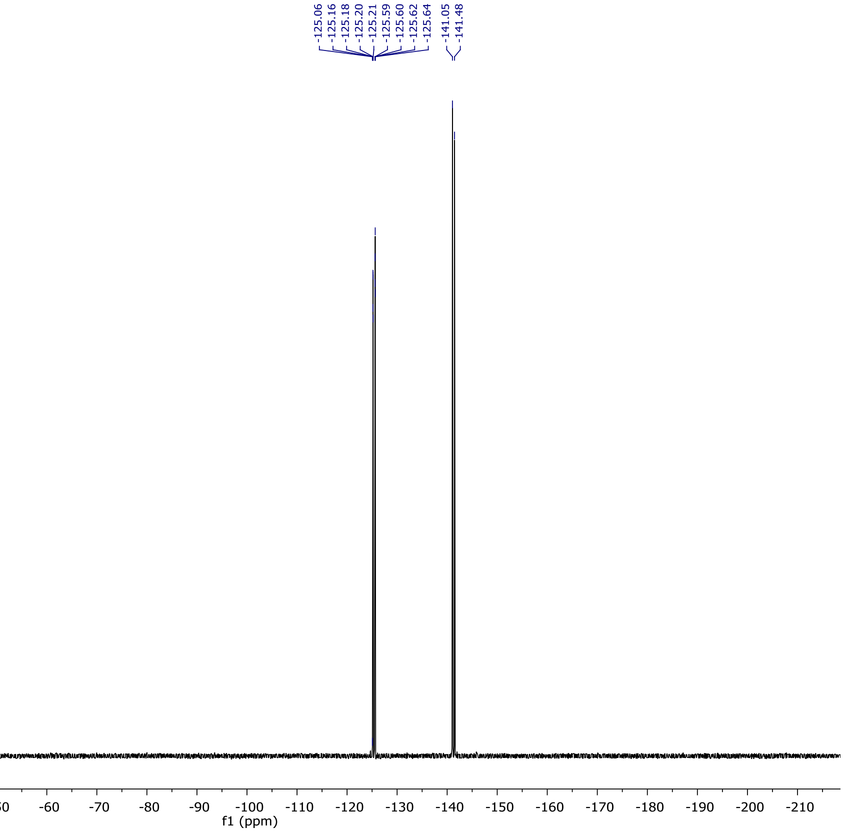
101 MHz CDCl$_3$

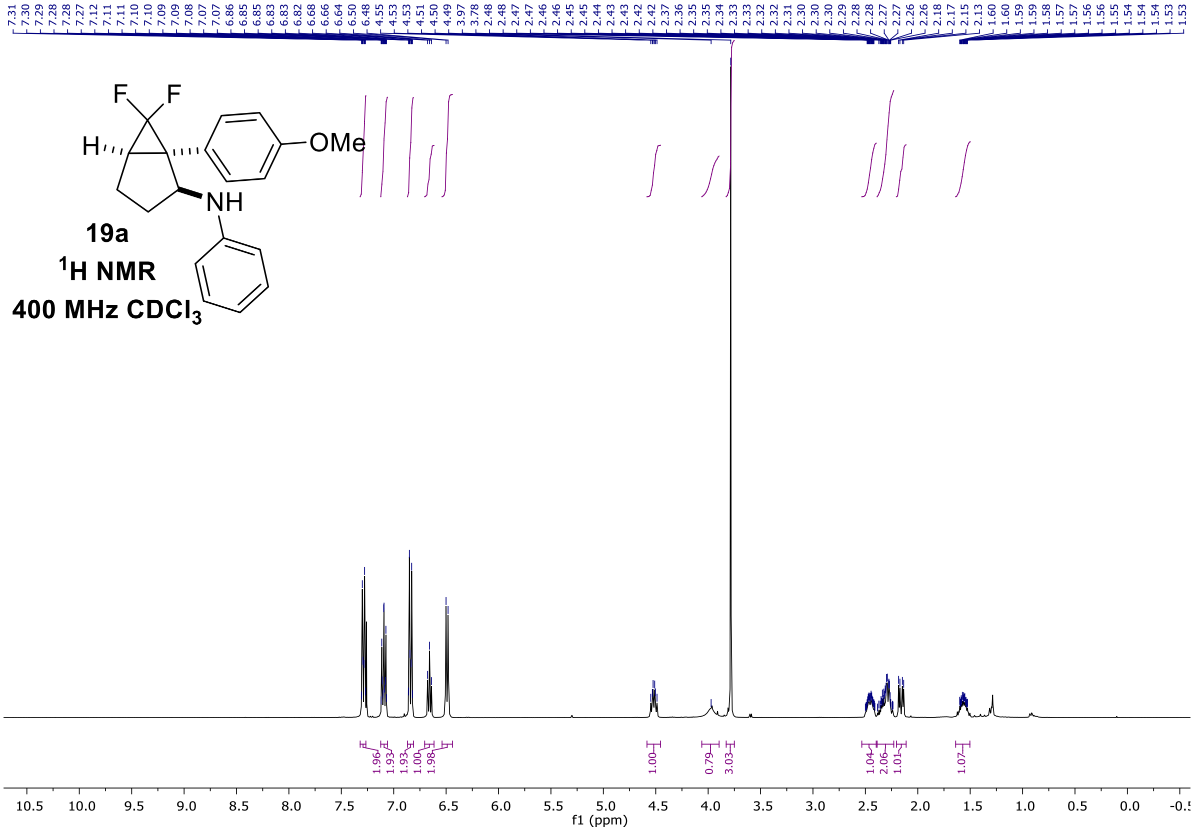


18b

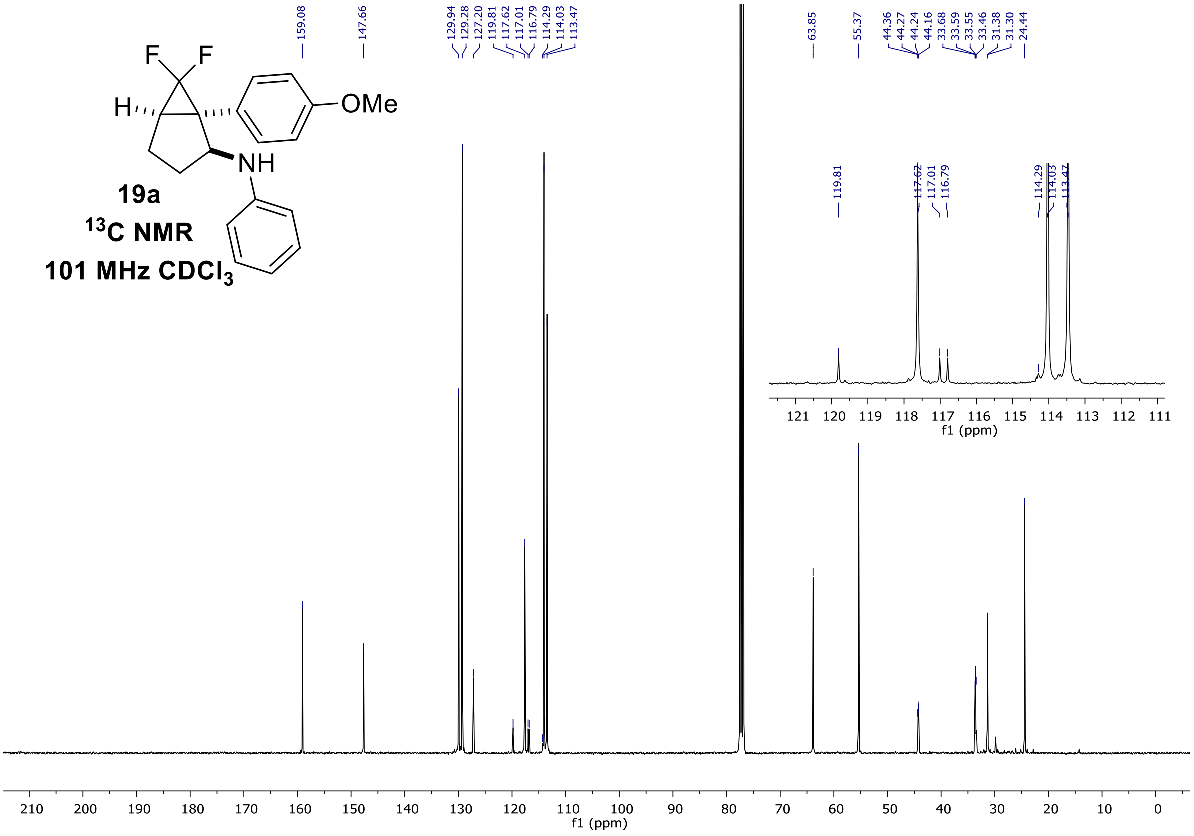
^{19}F NMR

376 MHz $CDCl_3$

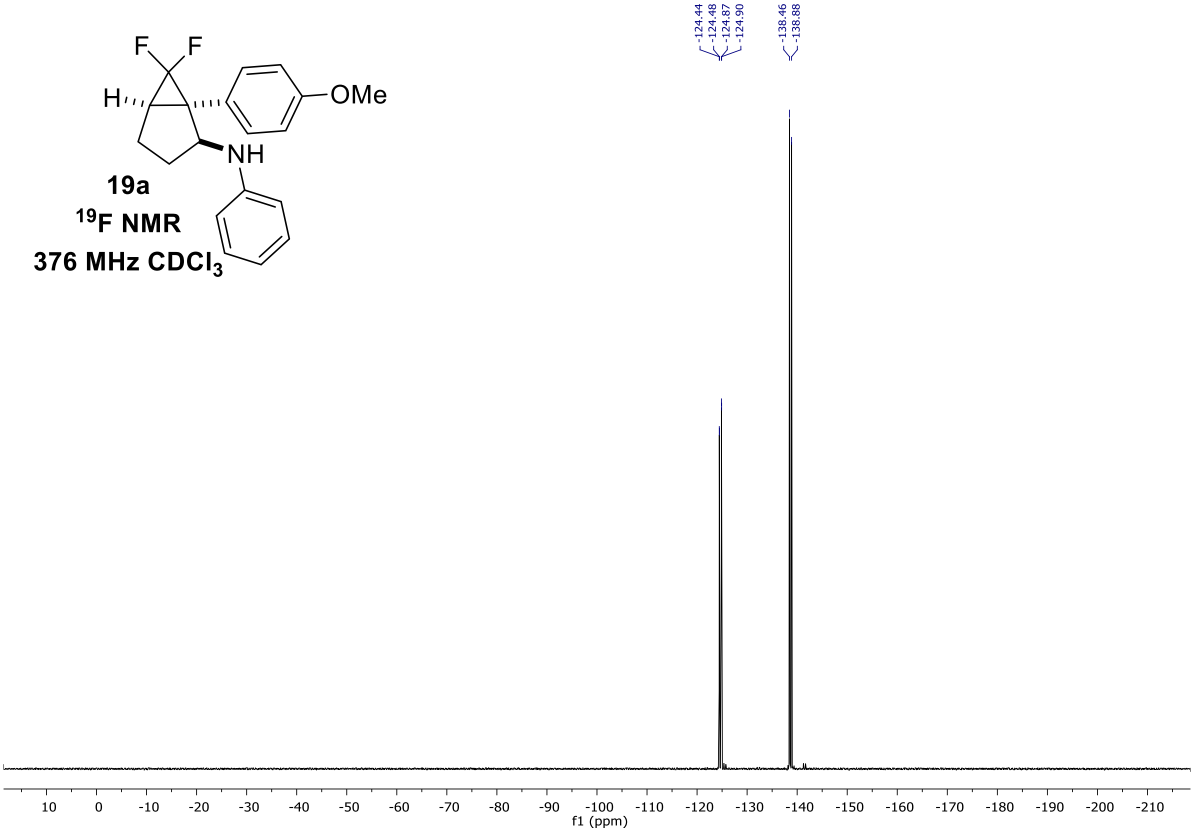




19a
^{1}H NMR
400 MHz CDCl$_3$



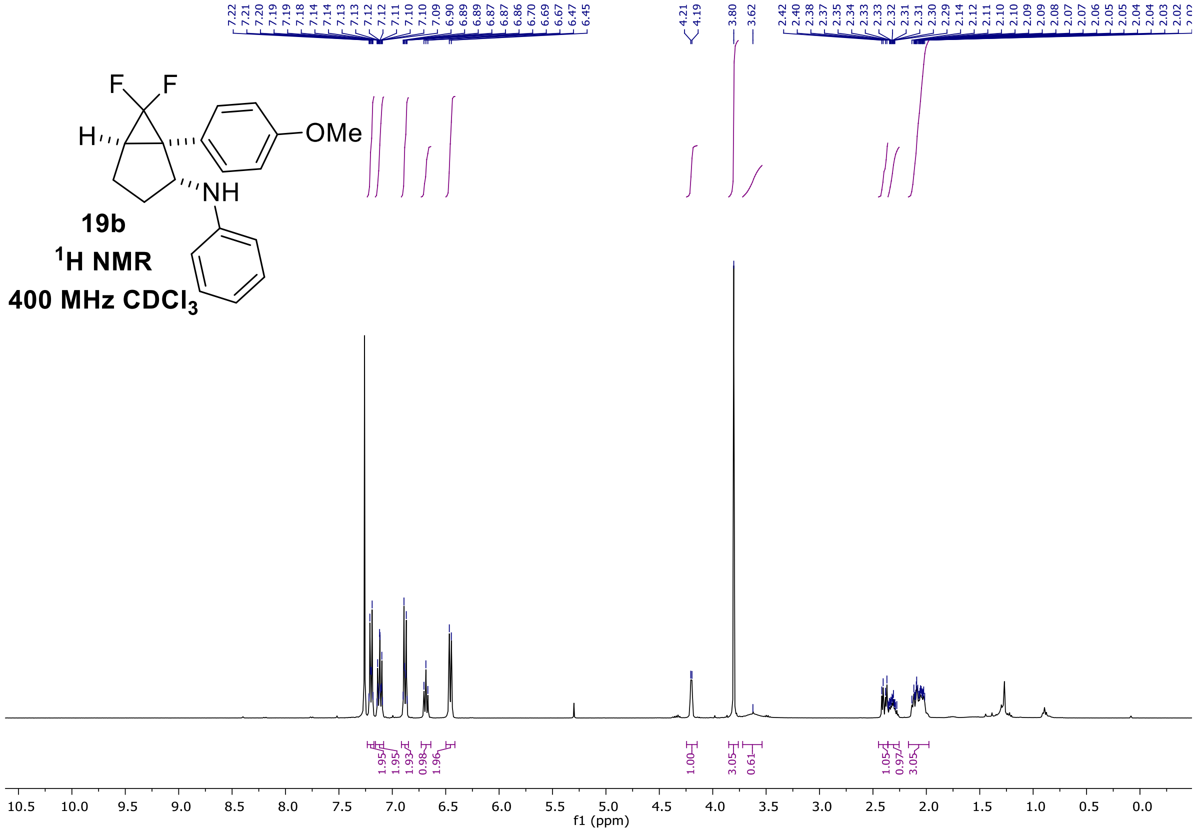
19a
^{13}C NMR
101 MHz CDCl$_3$



19a

^{19}F NMR

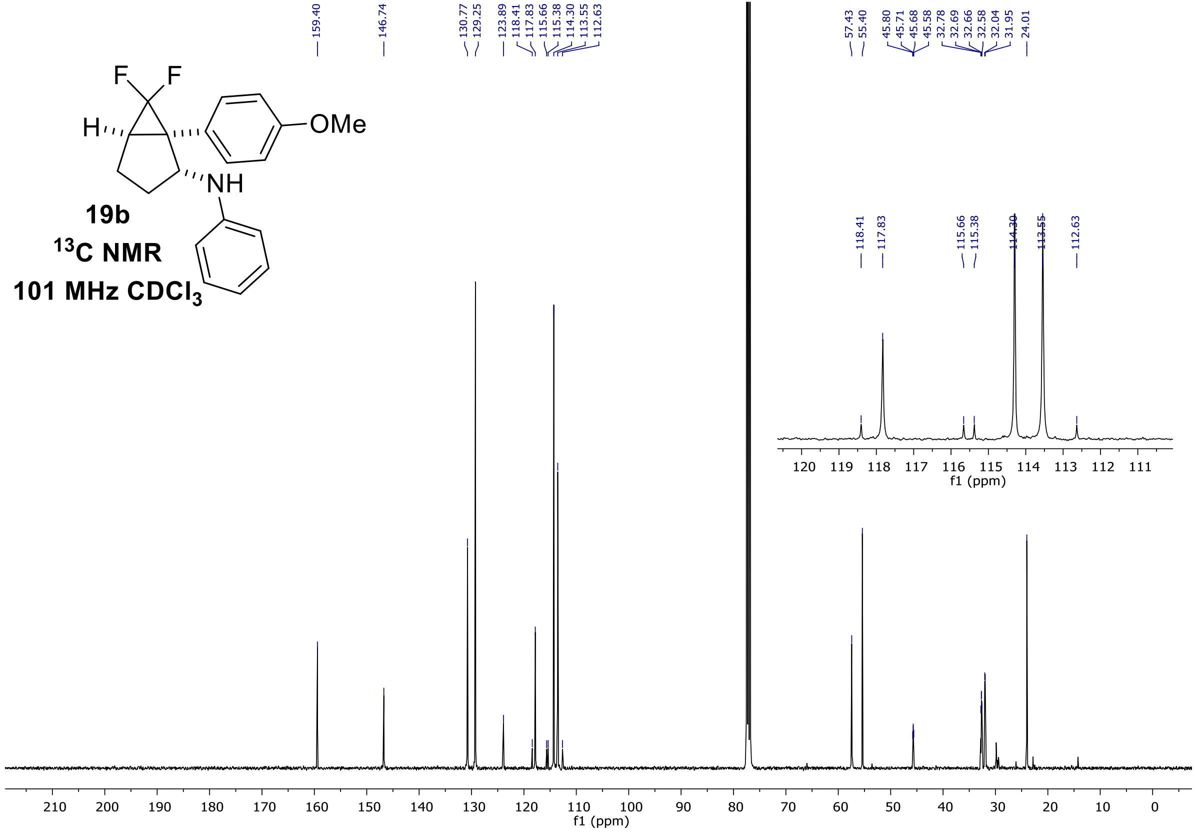
376 MHz CDCl$_3$



19b

^{1}H NMR

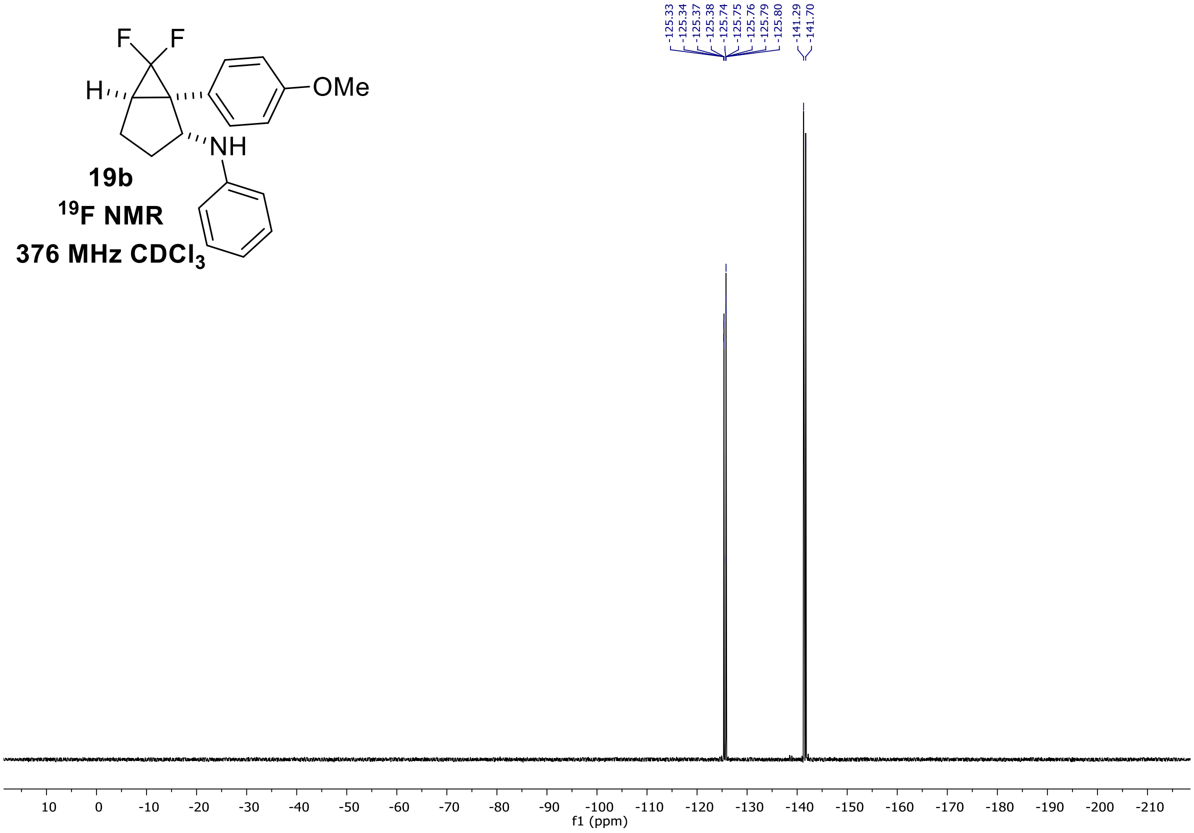
400 MHz $CDCl_3$



19b

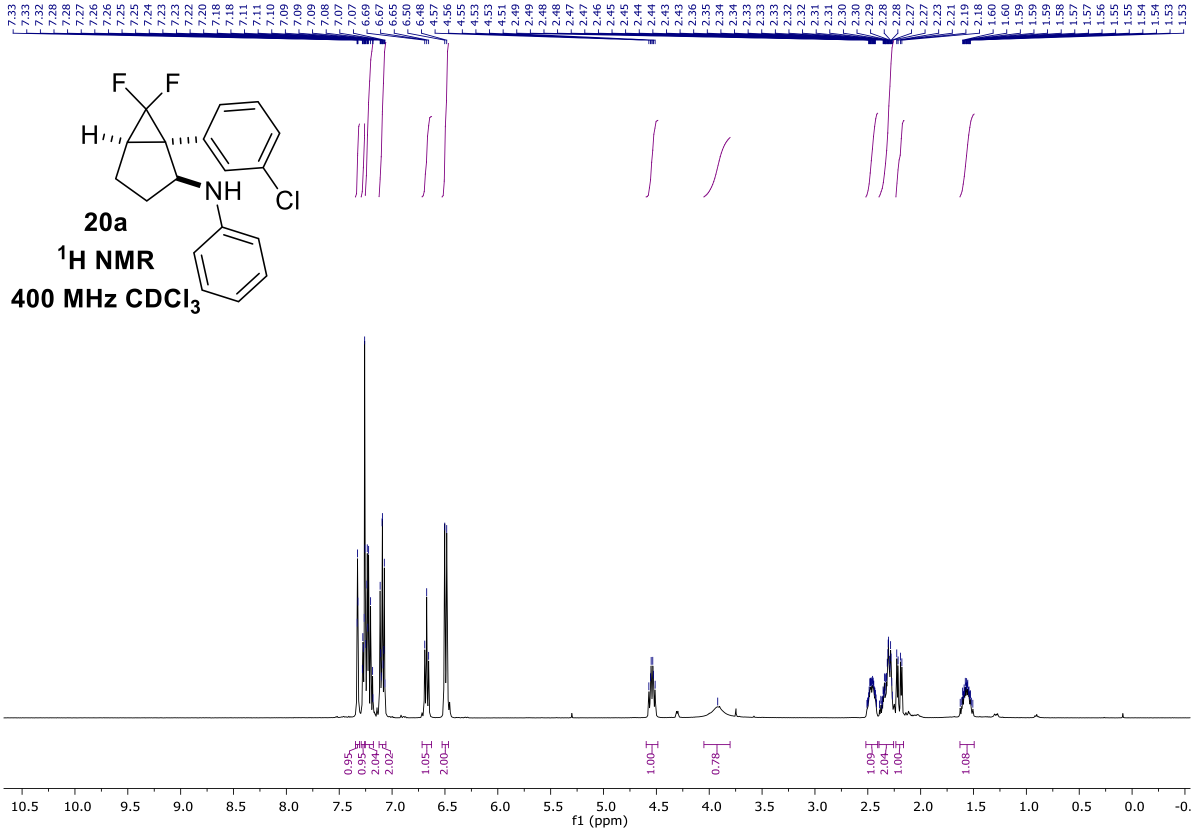
^{13}C NMR

101 MHz $CDCl_3$


19b

^{19}F NMR

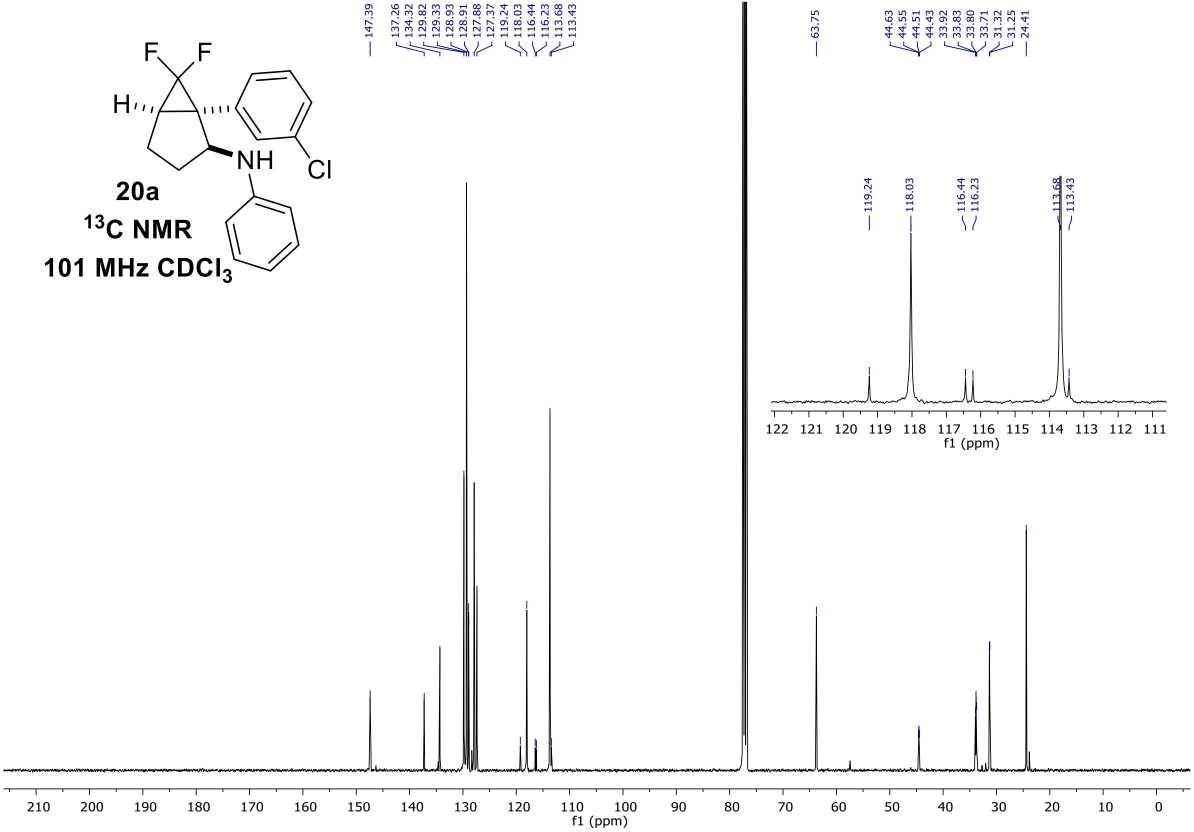
376 MHz $CDCl_3$



20a

^{1}H NMR

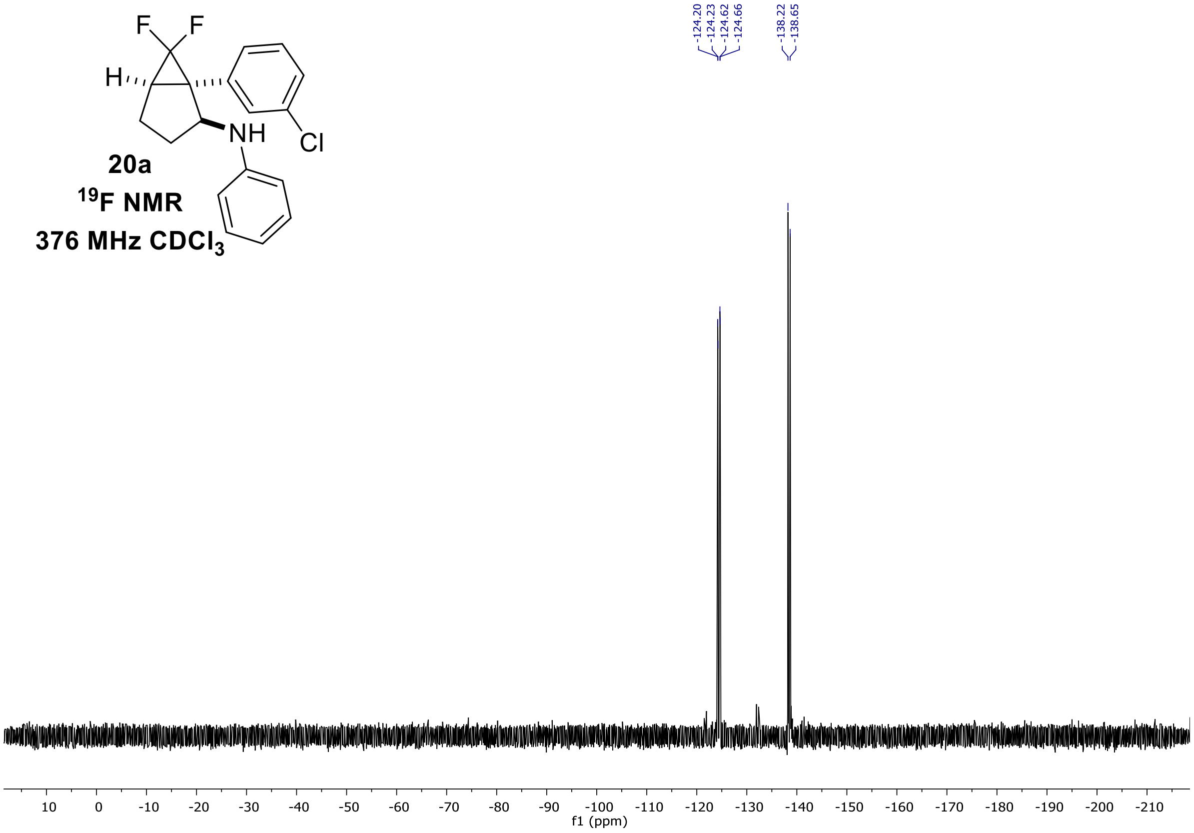
400 MHz $CDCl_3$



20a

^{13}C NMR

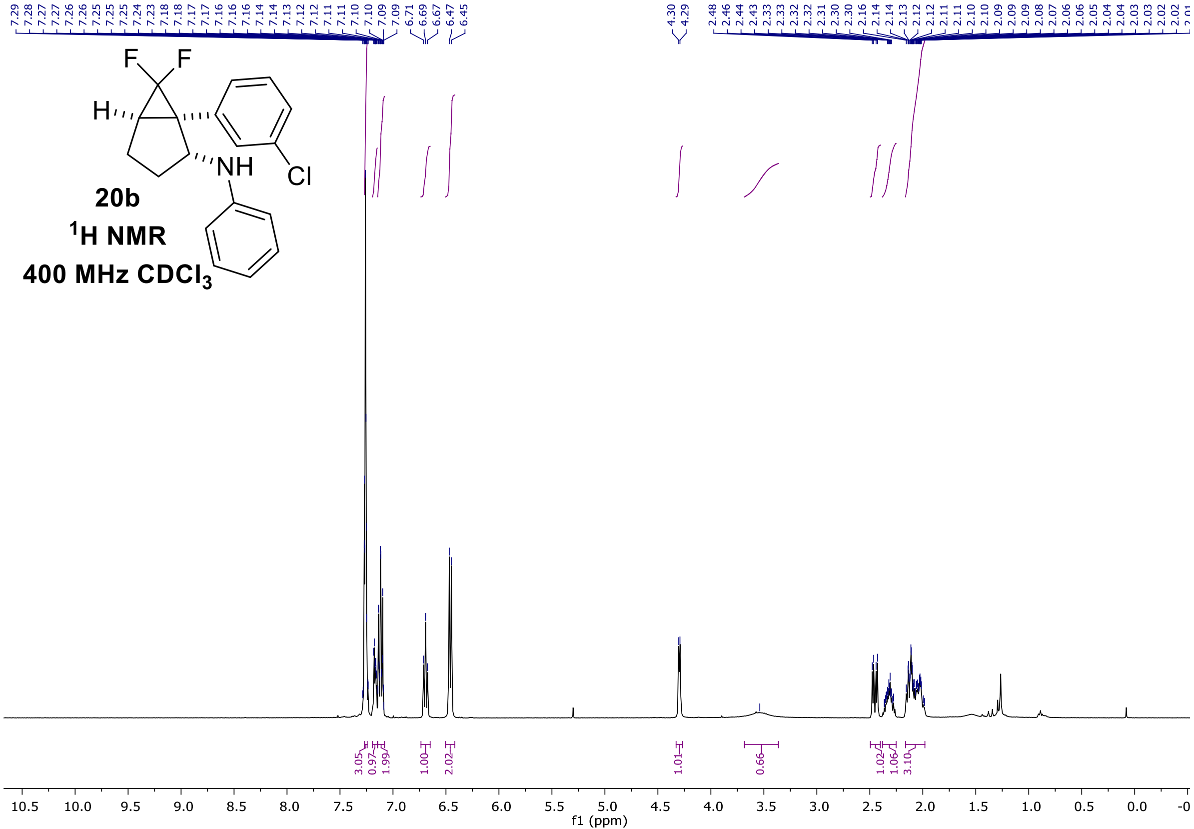
101 MHz $CDCl_3$



20a

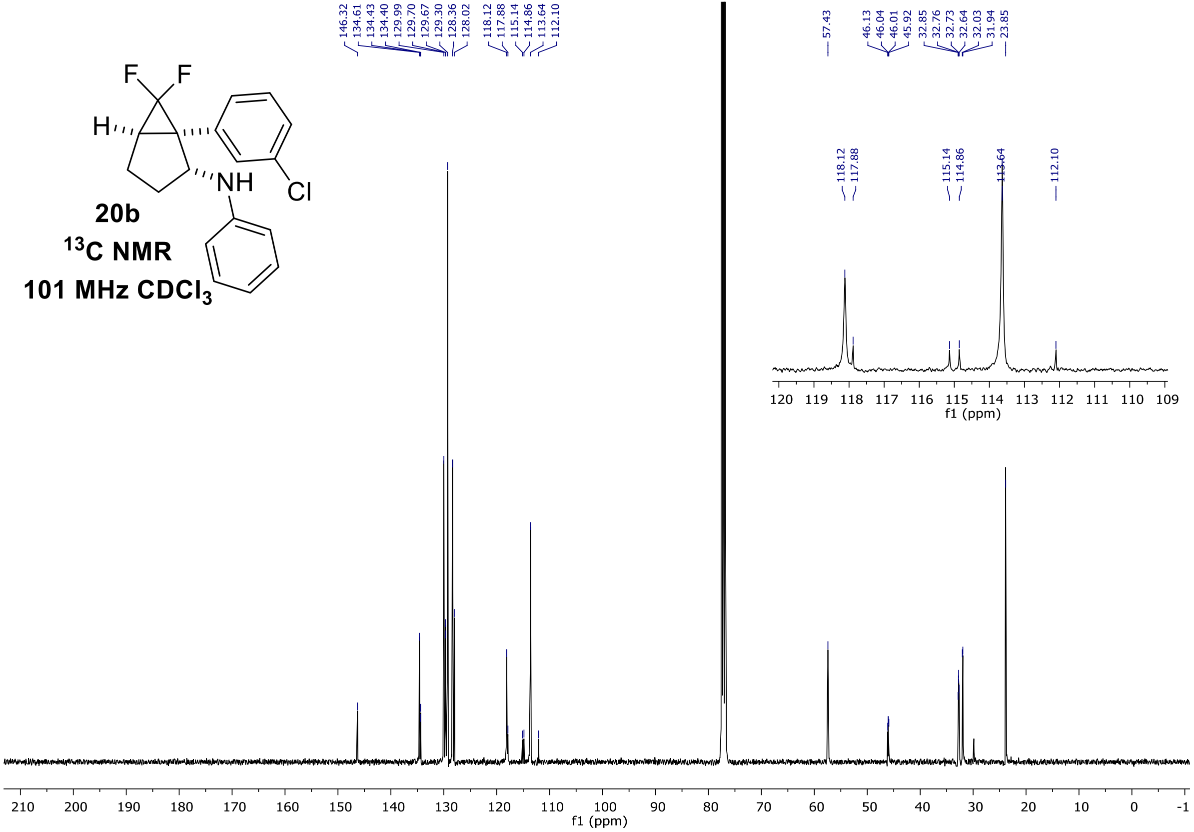
^{19}F NMR

376 MHz $CDCl_3$


20b

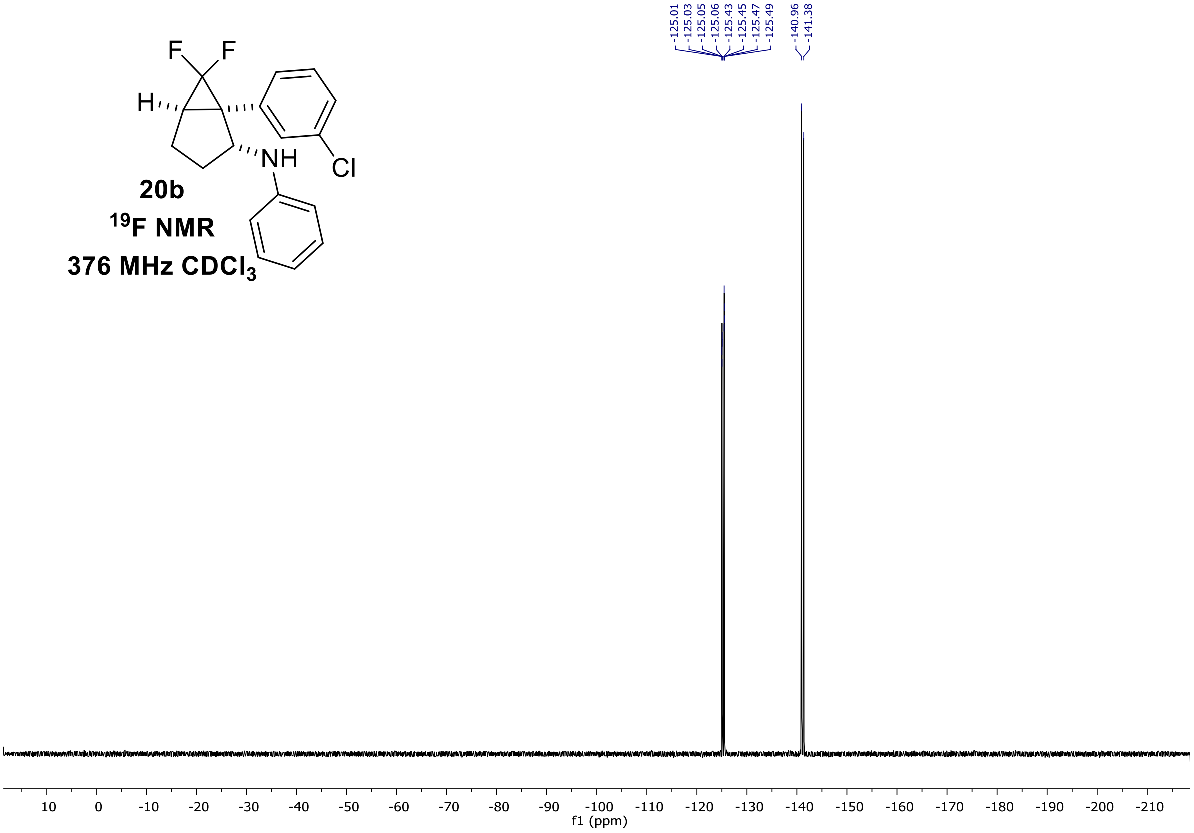
^{1}H NMR

400 MHz $CDCl_3$


20b

^{13}C NMR

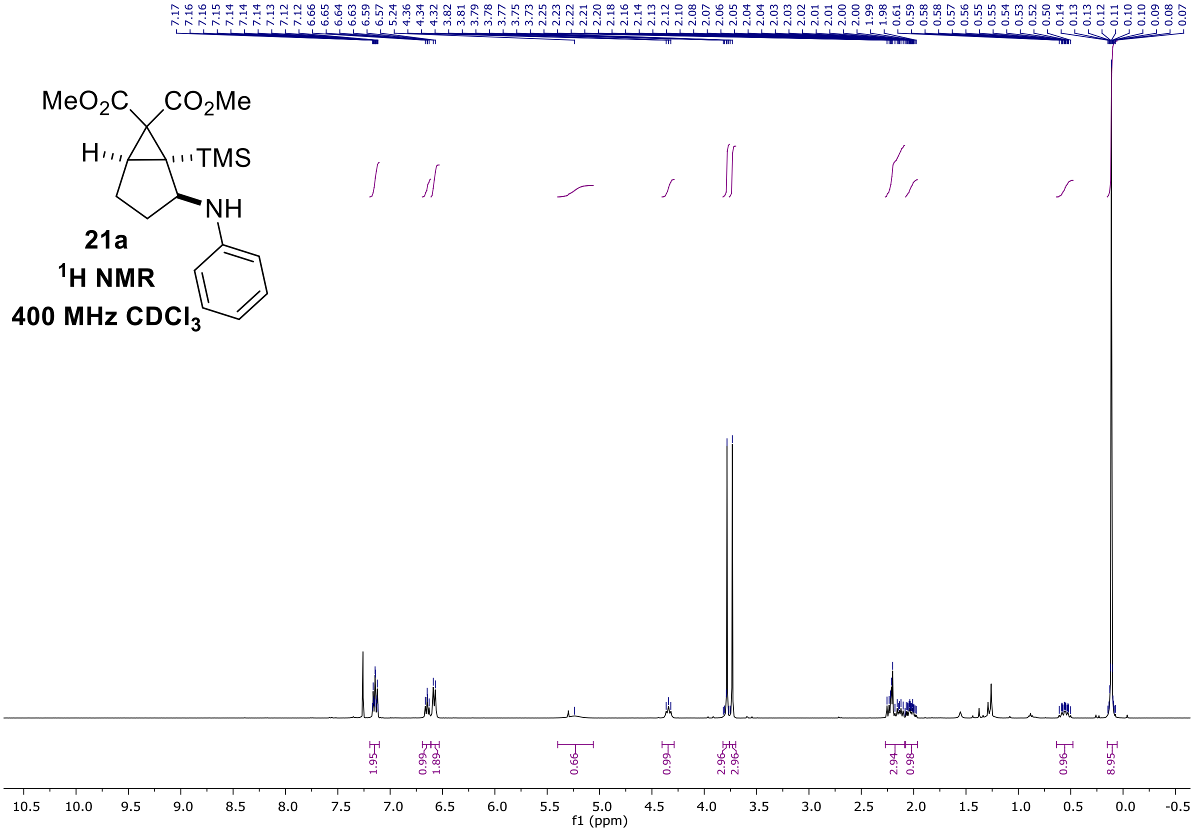
101 MHz $CDCl_3$



20b

^{19}F NMR

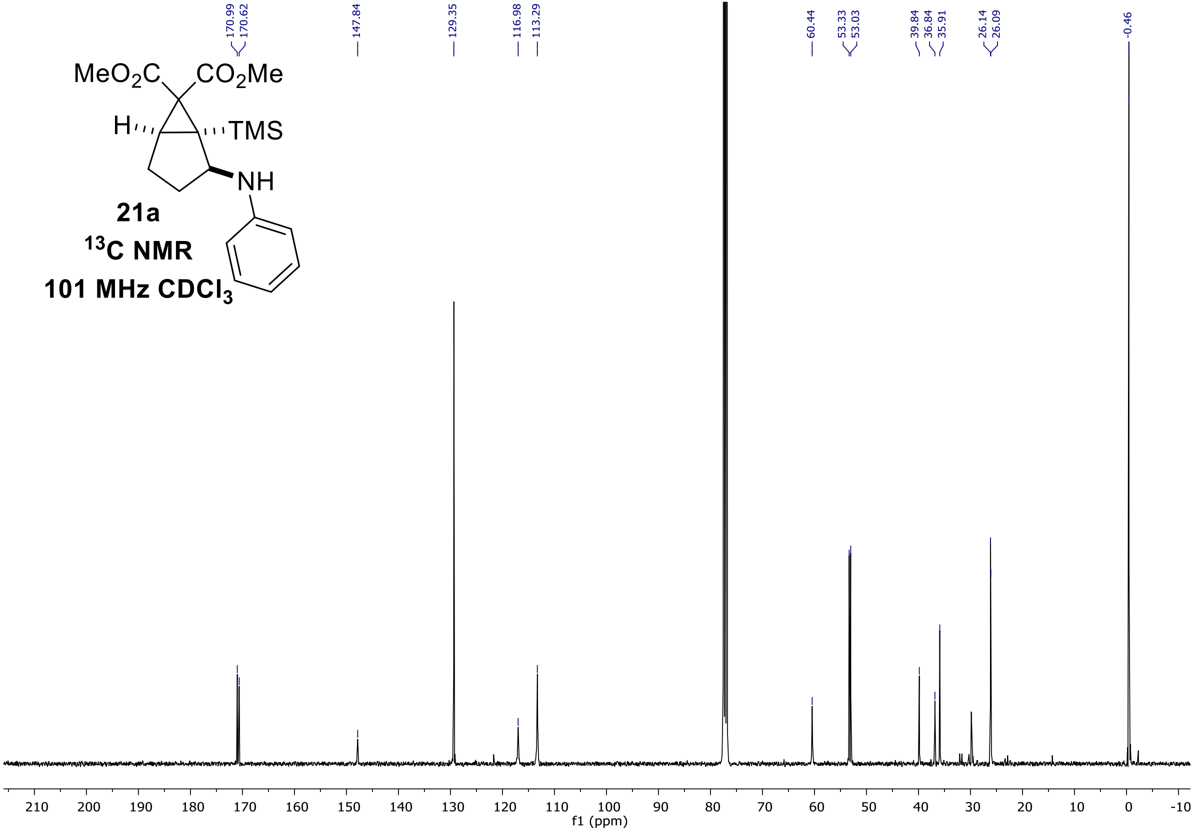
376 MHz $CDCl_3$



21a

^{1}H NMR

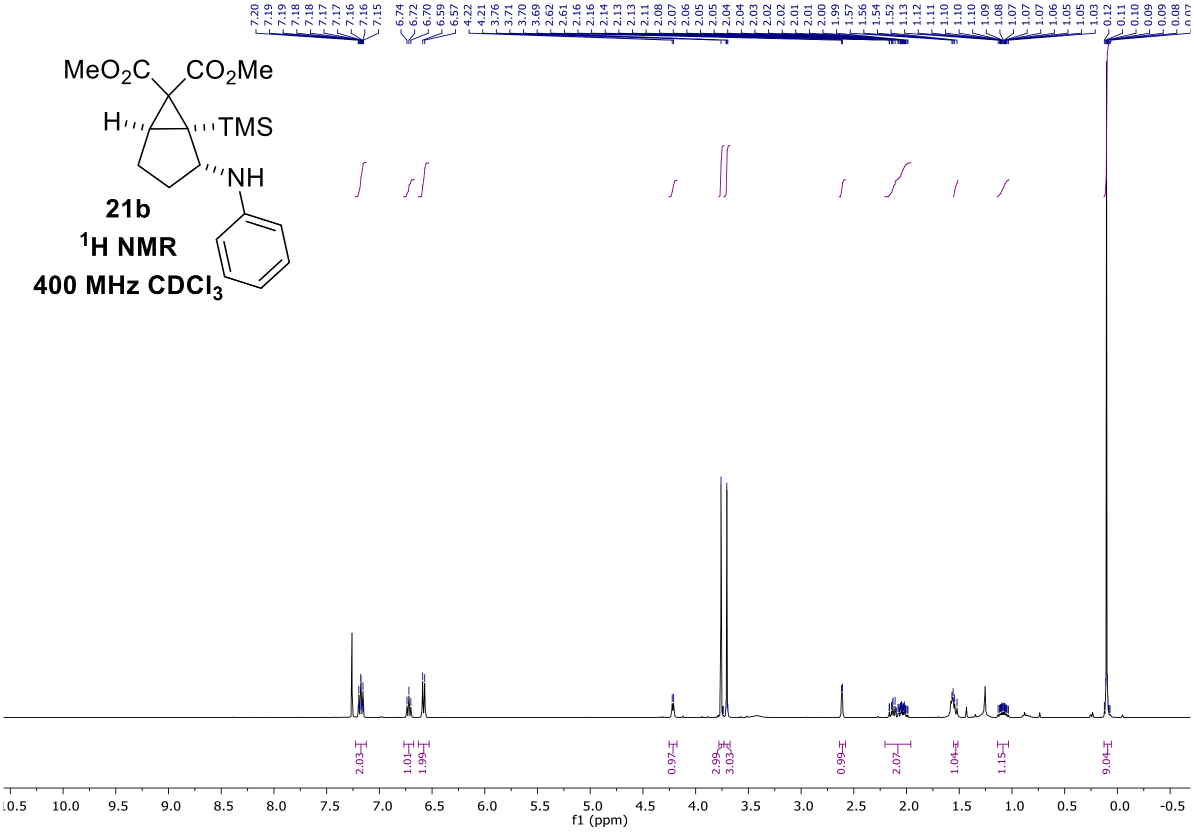
400 MHz $CDCl_3$



21a

^{13}C NMR

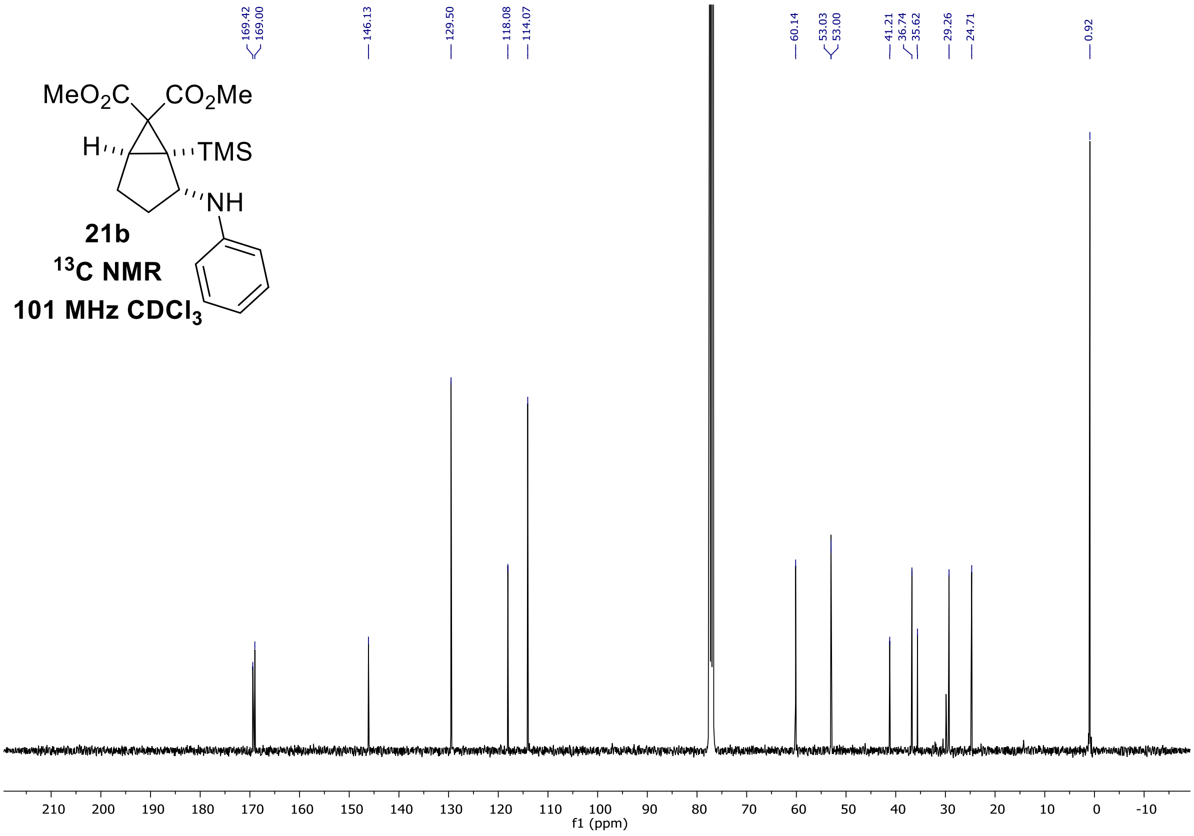
101 MHz $CDCl_3$



21b

^{1}H NMR

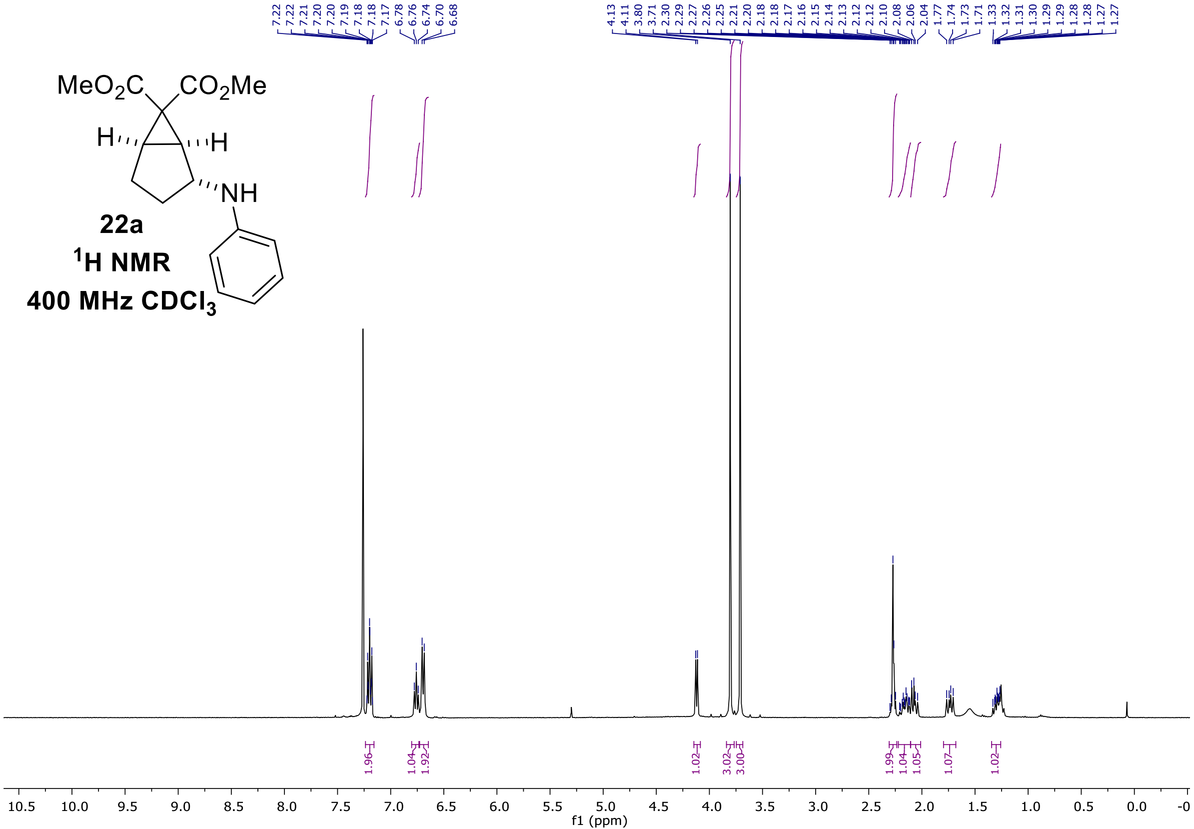
400 MHz $CDCl_3$

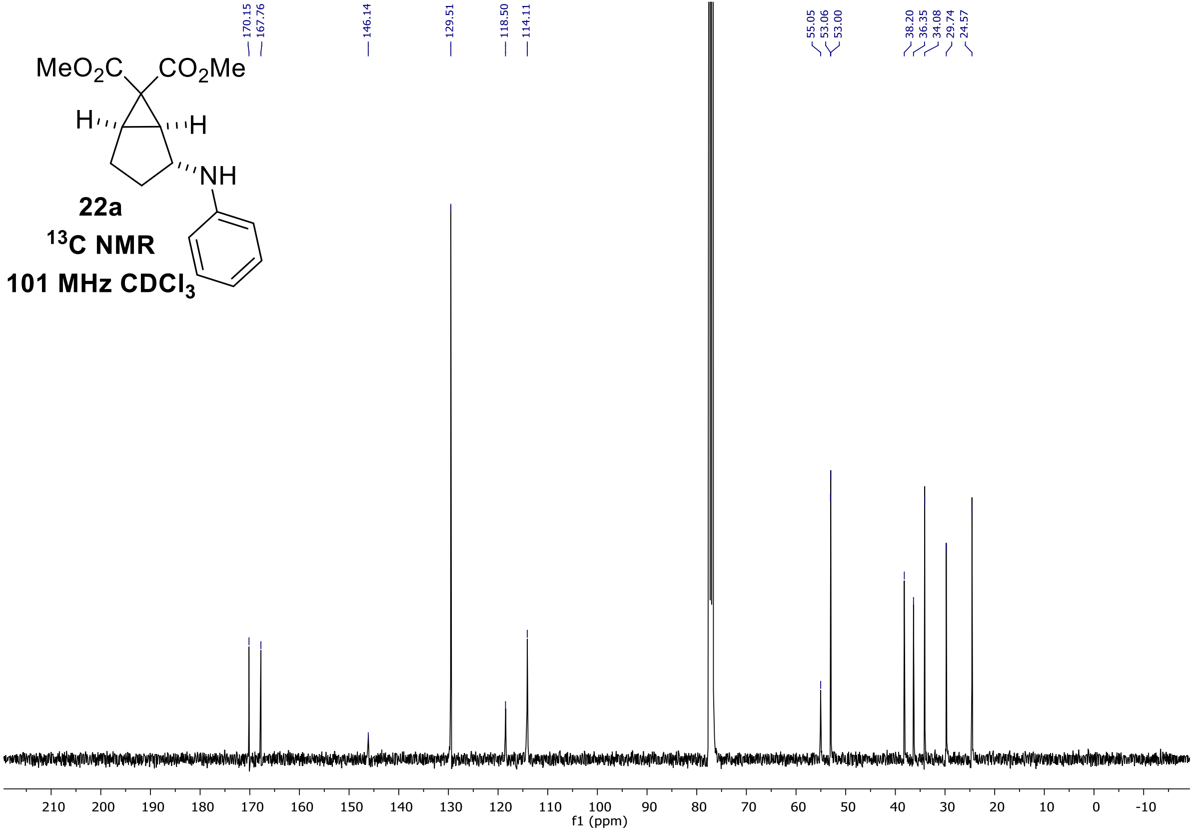


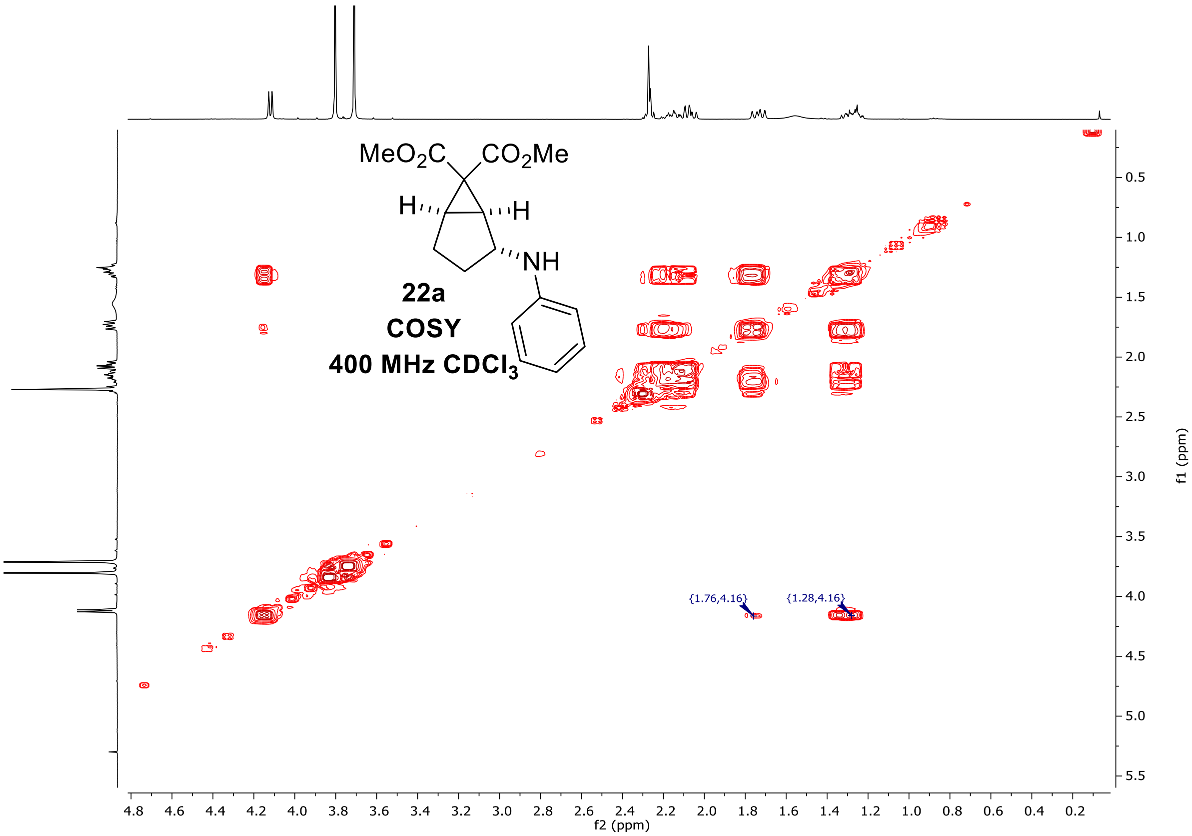
21b

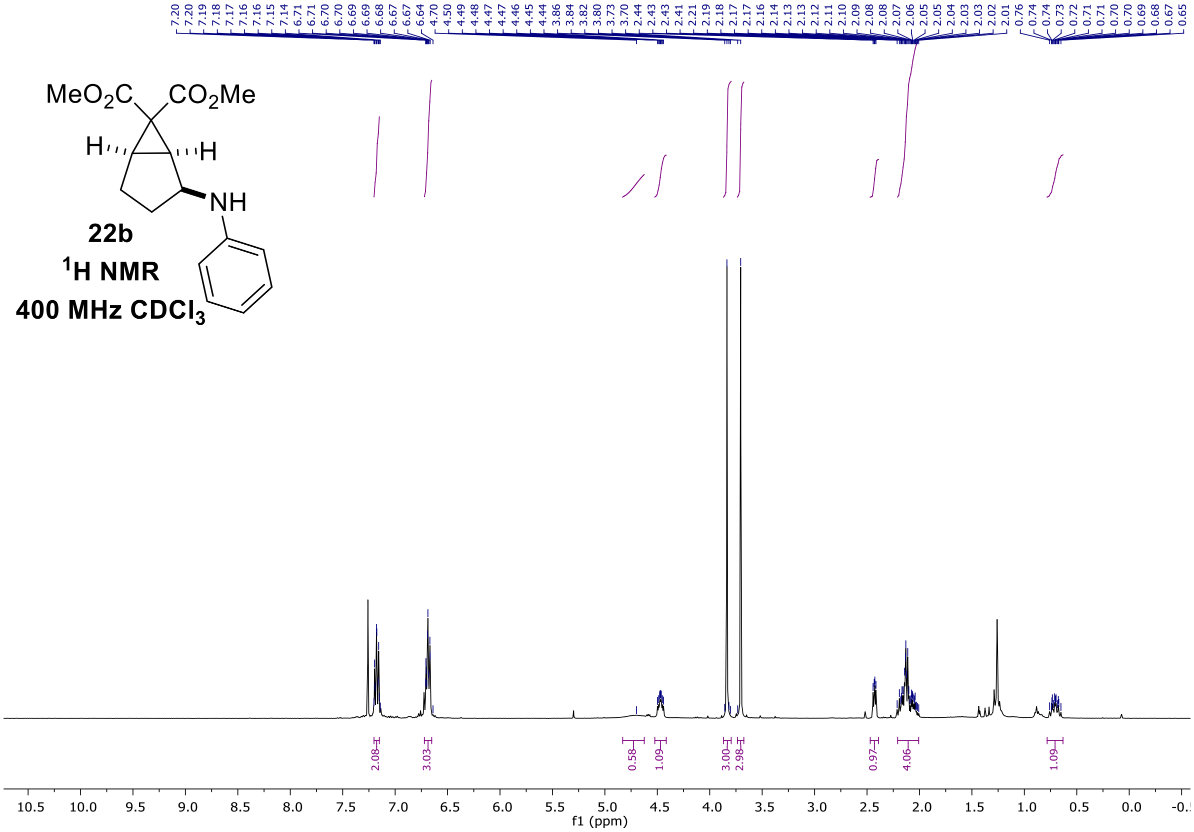
^{13}C NMR

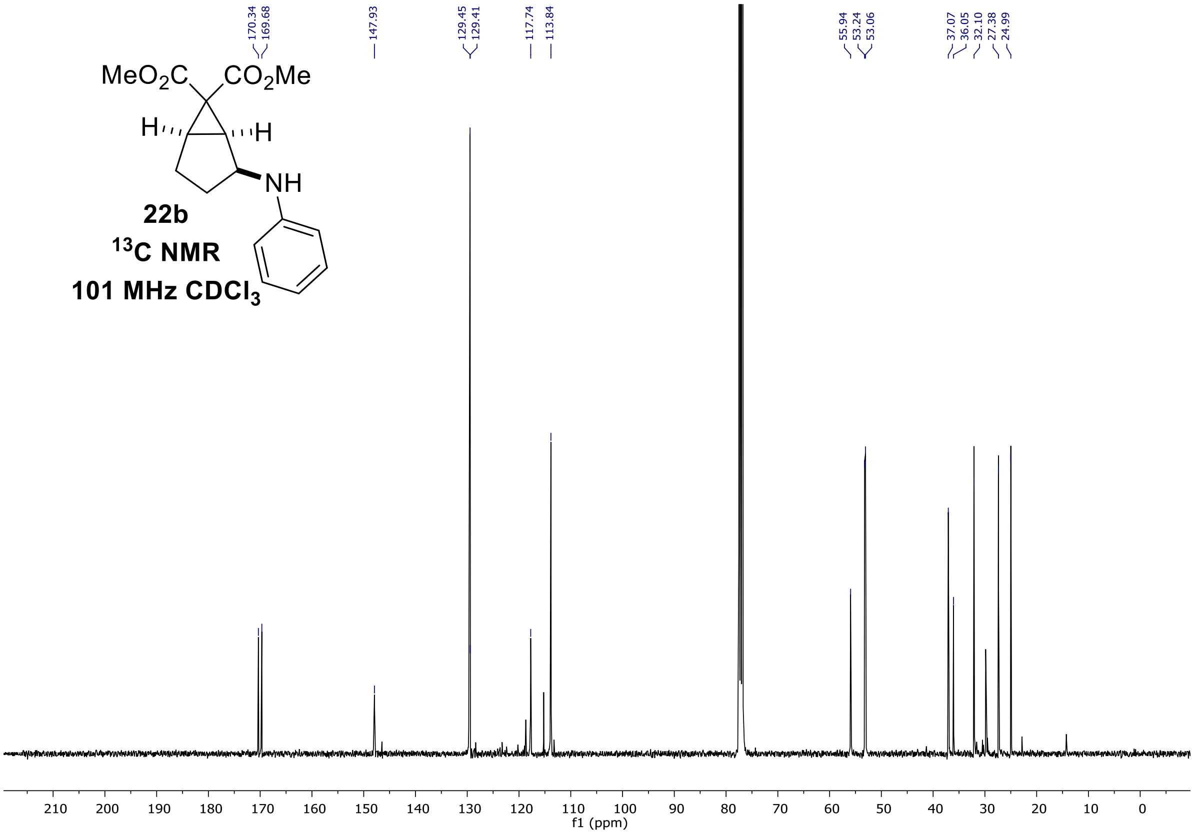
101 MHz $CDCl_3$

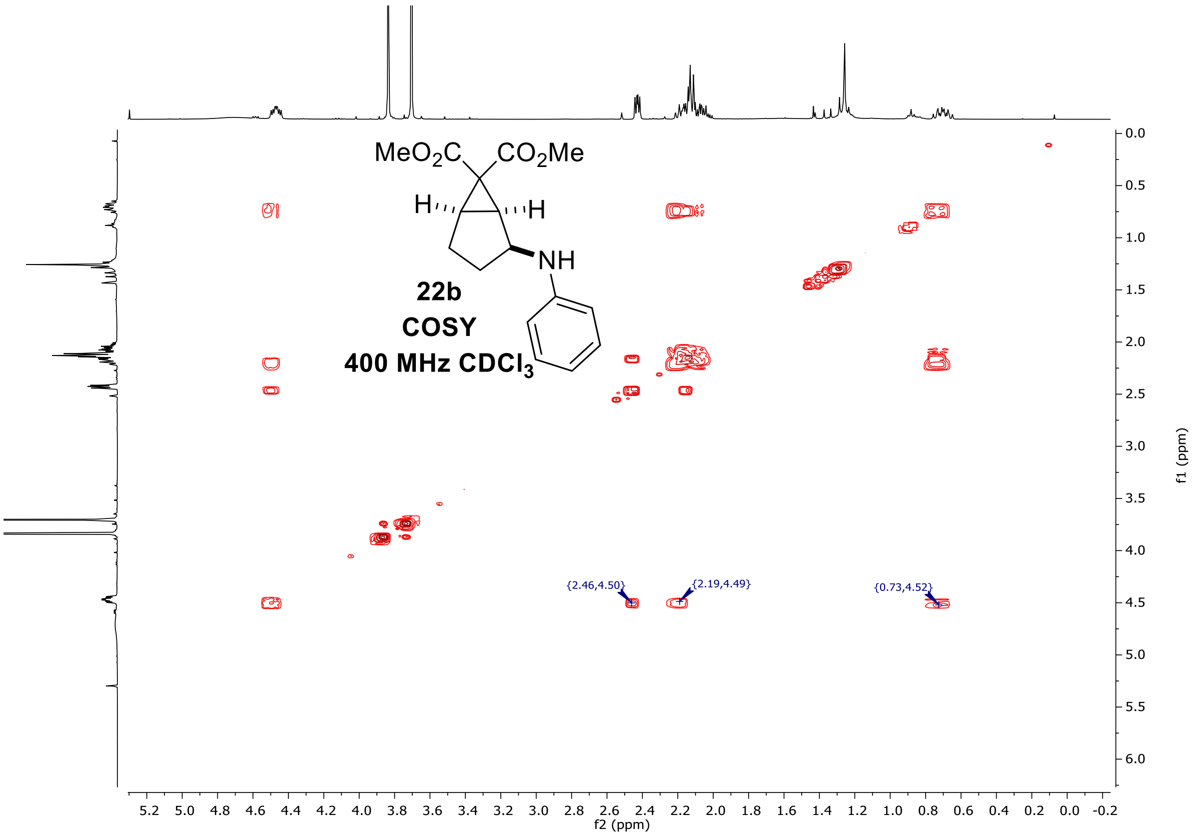

MeO2C
CO2Me
H
H
NH
22a
1H NMR
400 MHz CDCl3
7.22
7.22
7.21
7.20
7.20
7.19
7.18
7.18
7.17
6.78
6.76
6.74
6.70
6.68
4.13
4.11
3.80
3.71
2.30
2.29
2.27
2.26
2.25
2.21
2.20
2.18
2.18
2.17
2.16
2.15
2.14
2.13
2.12
2.12
2.10
2.08
2.06
2.04
1.77
1.74
1.73
1.71
1.33
1.32
1.31
1.30
1.29
1.29
1.28
1.28
1.27
1.27
1.96
1.04
1.92
1.02
3.02
3.00
1.99
1.04
1.05
1.07
1.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0
f1 (ppm)

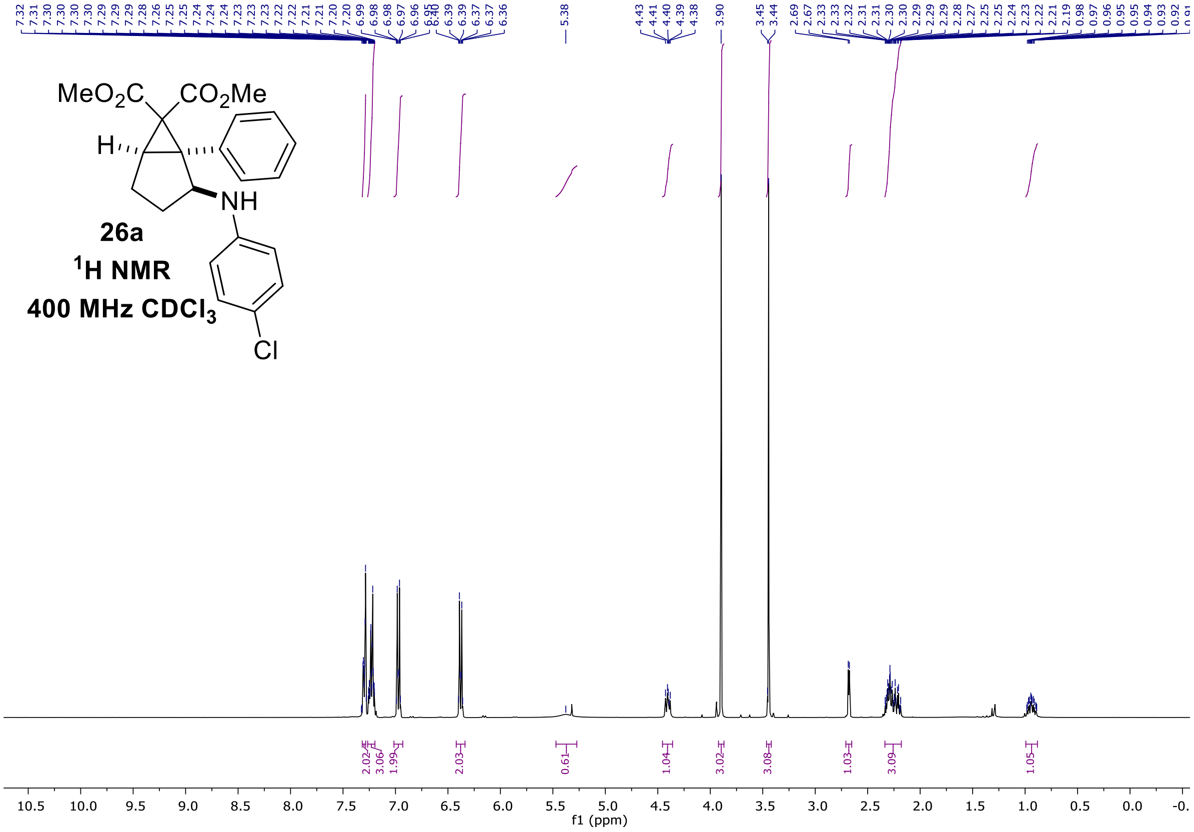

MeO2C
CO2Me
H
H
NH
22a
13C NMR
101 MHz CDCl3
170.15
167.76
146.14
129.51
118.50
114.11
55.05
53.06
53.00
38.20
36.35
34.08
29.74
24.57
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


MeO2C
CO2Me
H
H
NH
22a
COSY
400 MHz CDCl3
{1.76,4.16}
{1.28,4.16}
f2 (ppm)
f1 (ppm)
4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2
0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5


7.20 7.20 7.19 7.18 7.17 7.16 7.16 7.15 7.14 6.71 6.71 6.70 6.70 6.69 6.69 6.68 6.67 6.67 6.64 4.70 4.50 4.49 4.48 4.47 4.47 4.46 4.45 4.44 3.86 3.84 3.82 3.80 3.73 3.70 2.44 2.43 2.43 2.41 2.21 2.19 2.18 2.17 2.17 2.16 2.14 2.13 2.13 2.12 2.11 2.10 2.09 2.08 2.08 2.07 2.06 2.05 2.05 2.04 2.03 2.03 2.02 2.01 0.76 0.74 0.74 0.73 0.72 0.71 0.71 0.70 0.70 0.69 0.68 0.67 0.65
MeO2C
CO2Me
H
H
NH
22b
1H NMR
400 MHz CDCl3
2.08
3.03
0.58
1.09
3.00
2.98
0.97
4.06
1.09
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


170.34 169.68
147.93
129.45 129.41
117.74
113.84
55.94 53.24 53.06
37.07 36.05 32.10 27.38 24.99
MeO2C
CO2Me
H
H
NH
22b
13C NMR
101 MHz CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

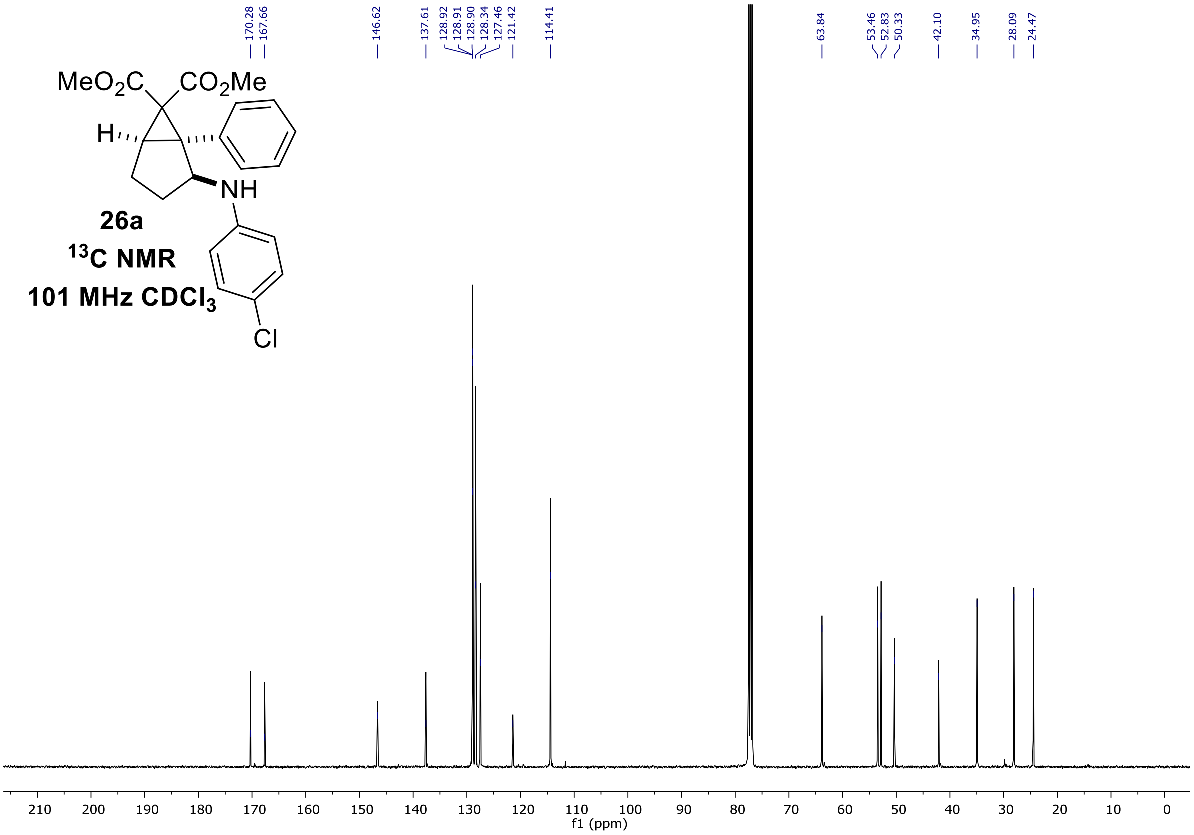

MeO2C
CO2Me
H
H
NH
22b
COSY
400 MHz CDCl3
{2.46,4.50}
{2.19,4.49}
{0.73,4.52}
5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0 -0.2
f2 (ppm)
0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0
f1 (ppm)



26a

^{1}H NMR

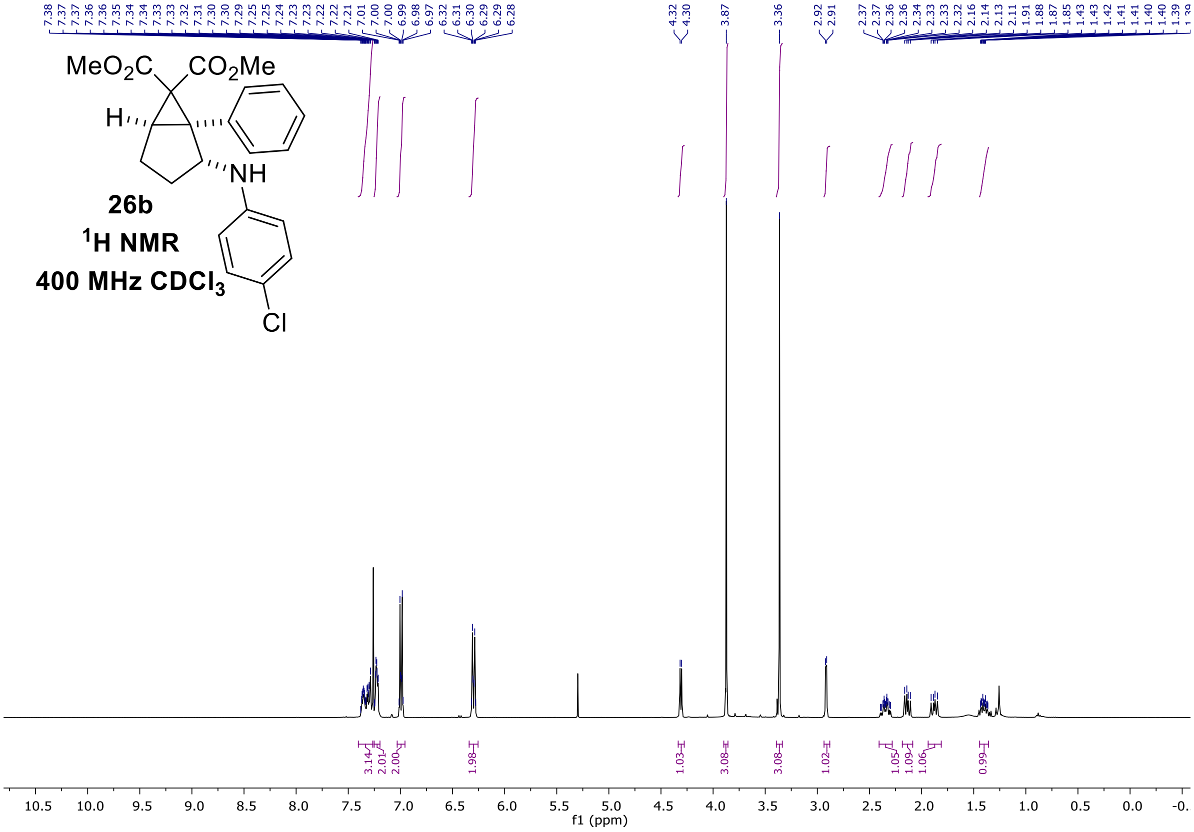
400 MHz $CDCl_3$



26a

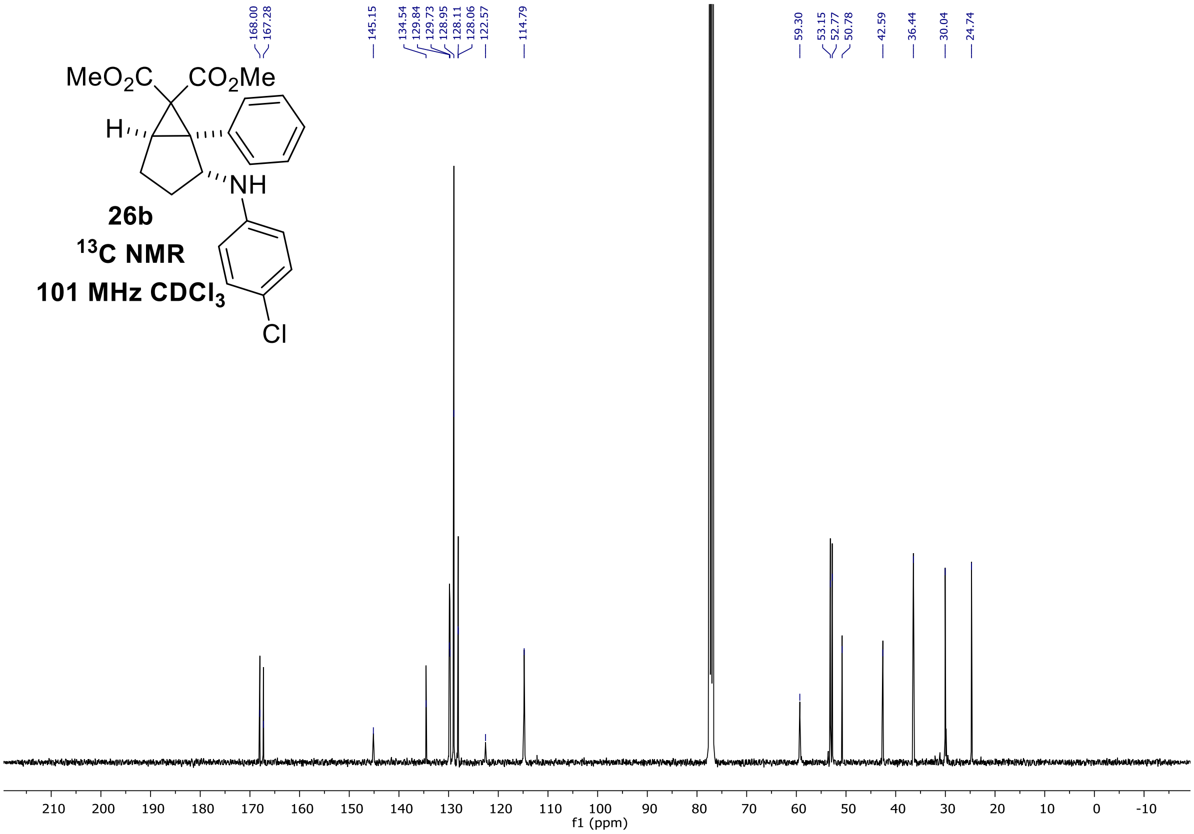
^{13}C NMR

101 MHz $CDCl_3$


26b

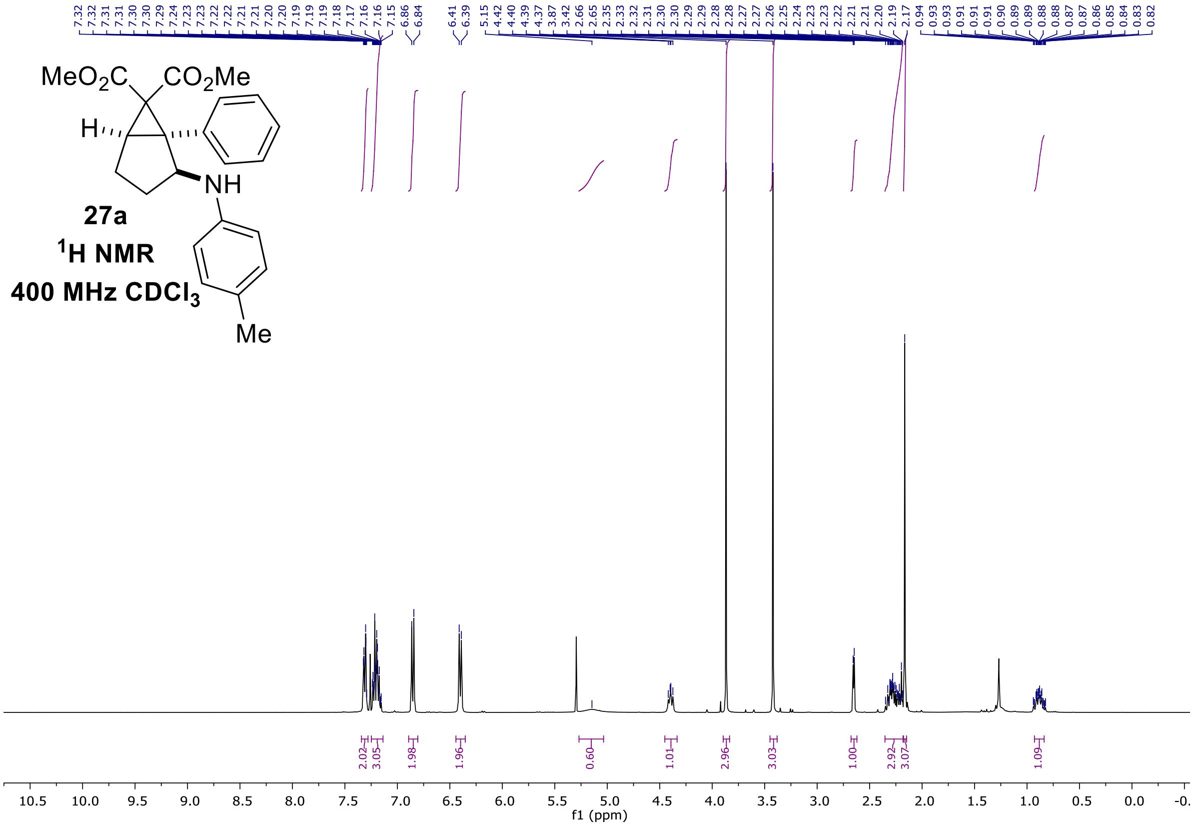
^1H NMR

400 MHz $CDCl_3$

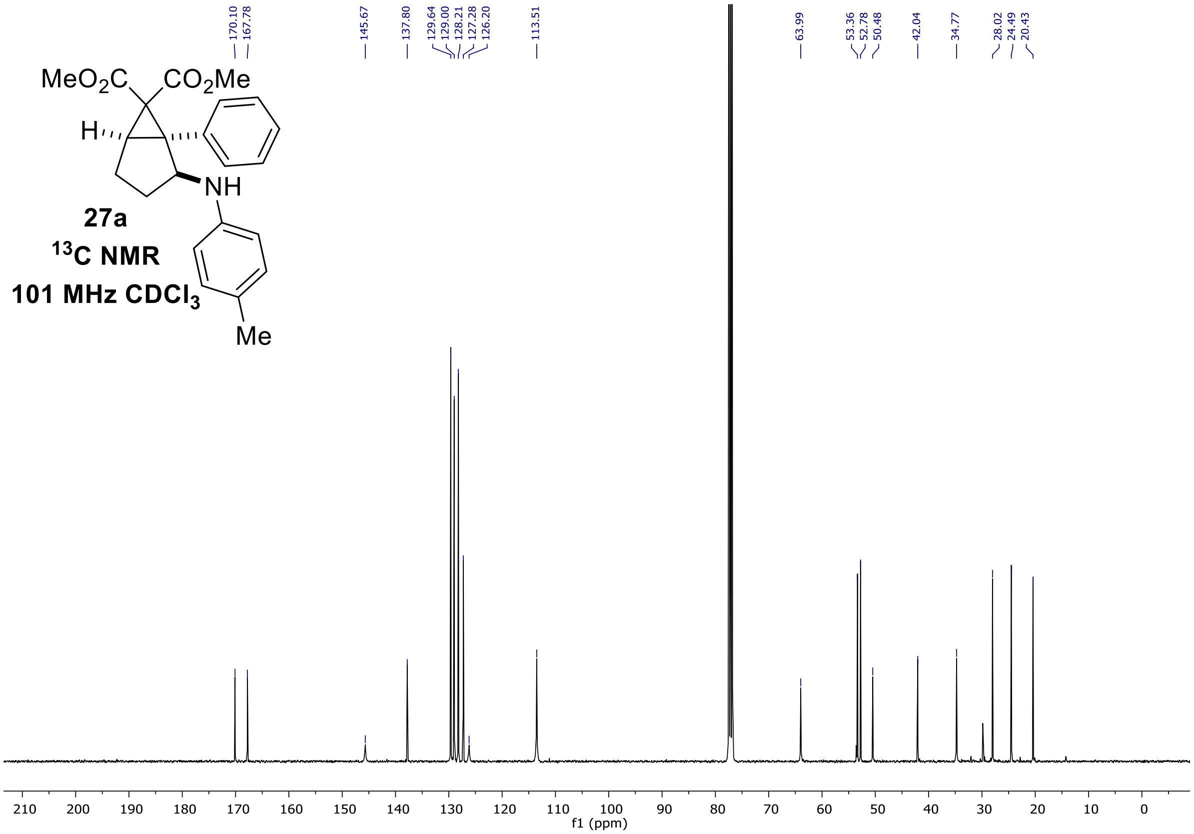

26b

^{13}C NMR

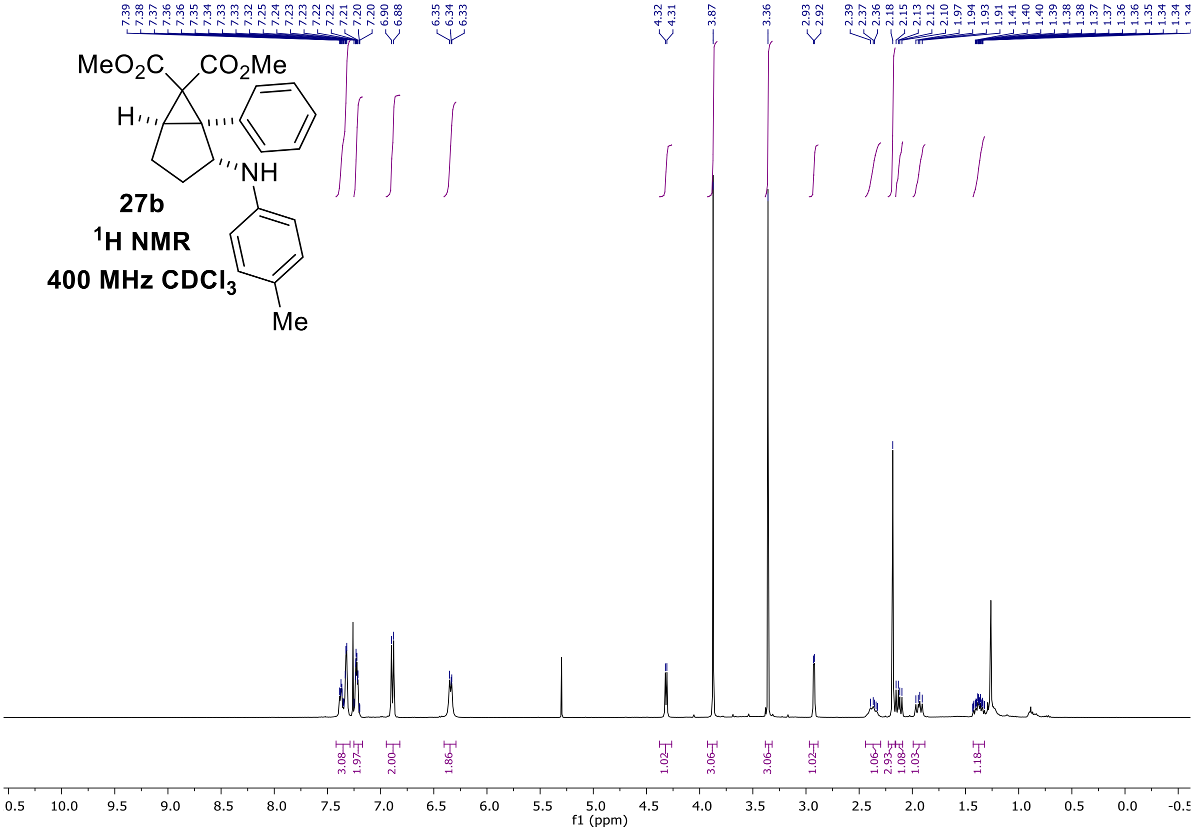
101 MHz $CDCl_3$



27a
^{1}H NMR
400 MHz CDCl$_3$



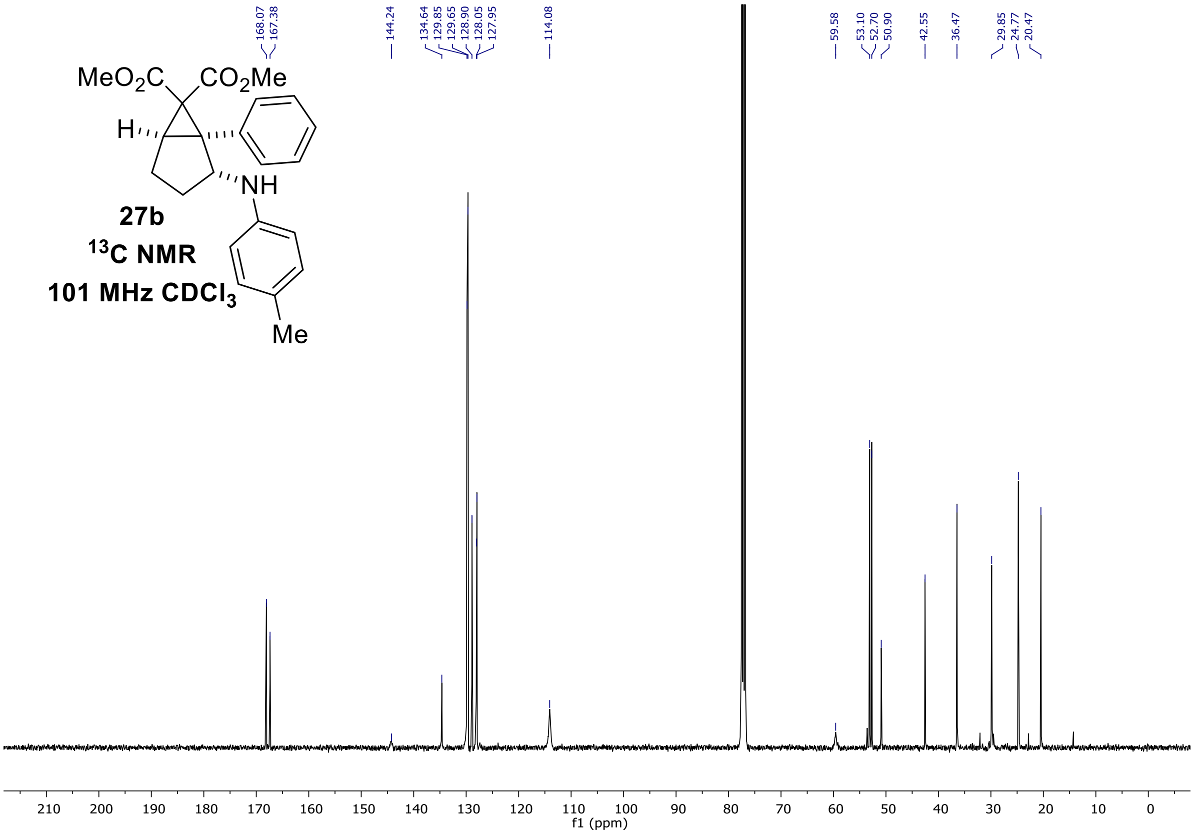
27a
^{13}C NMR
101 MHz CDCl$_3$



27b

^{1}H NMR

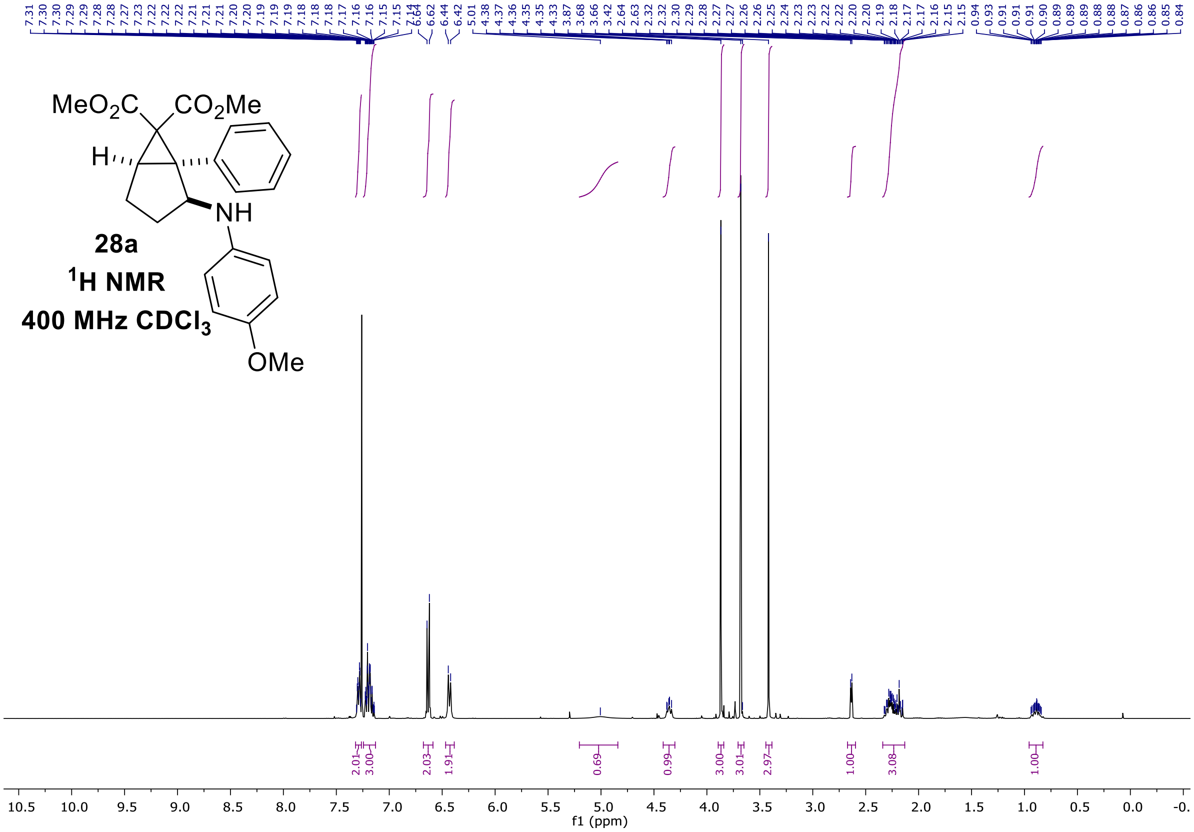
400 MHz $CDCl_3$



27b

^{13}C NMR

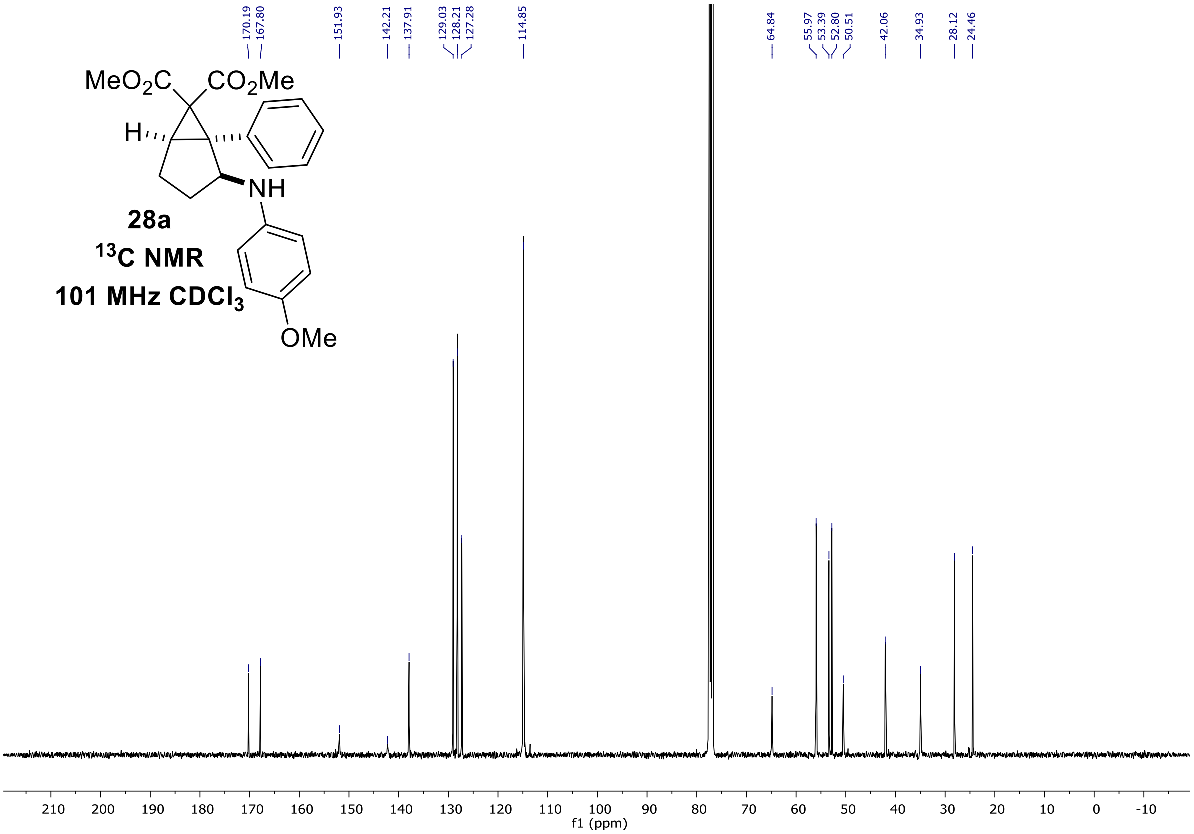
101 MHz $CDCl_3$



28a

^{1}H NMR

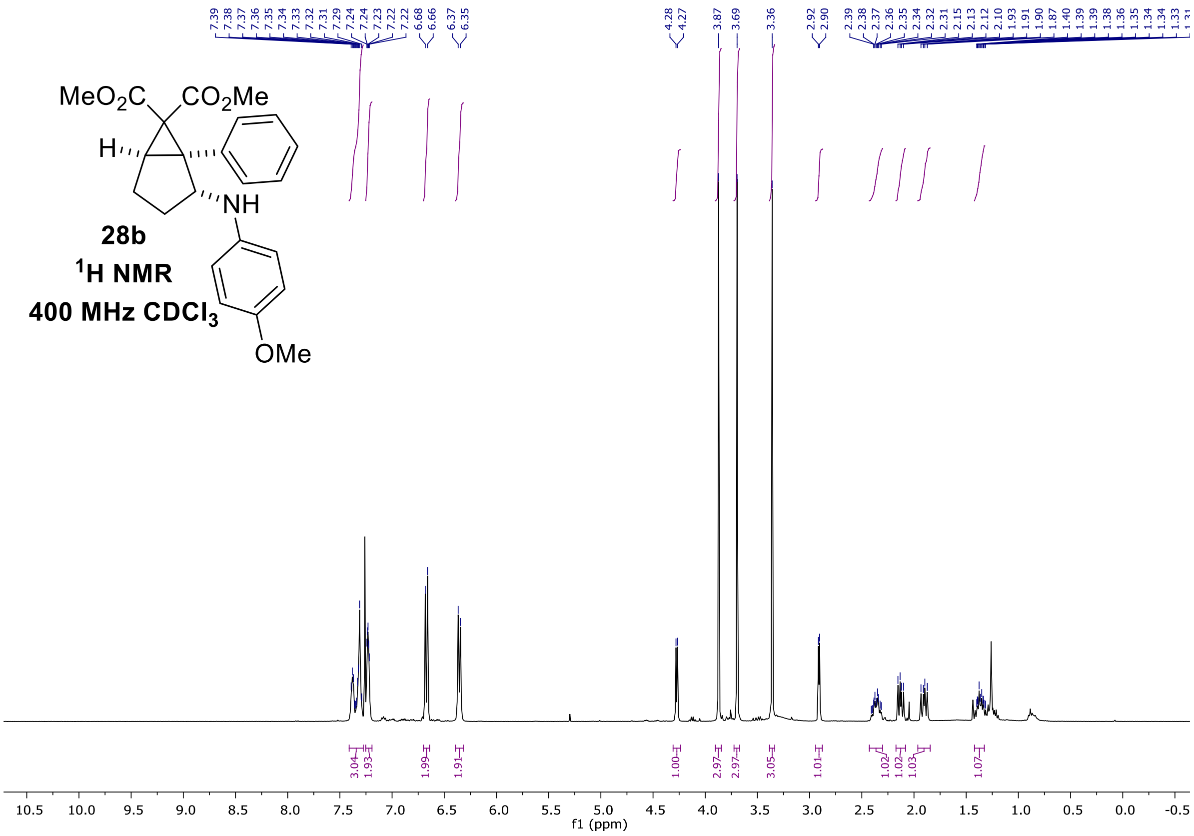
400 MHz $CDCl_3$



28a

^{13}C NMR

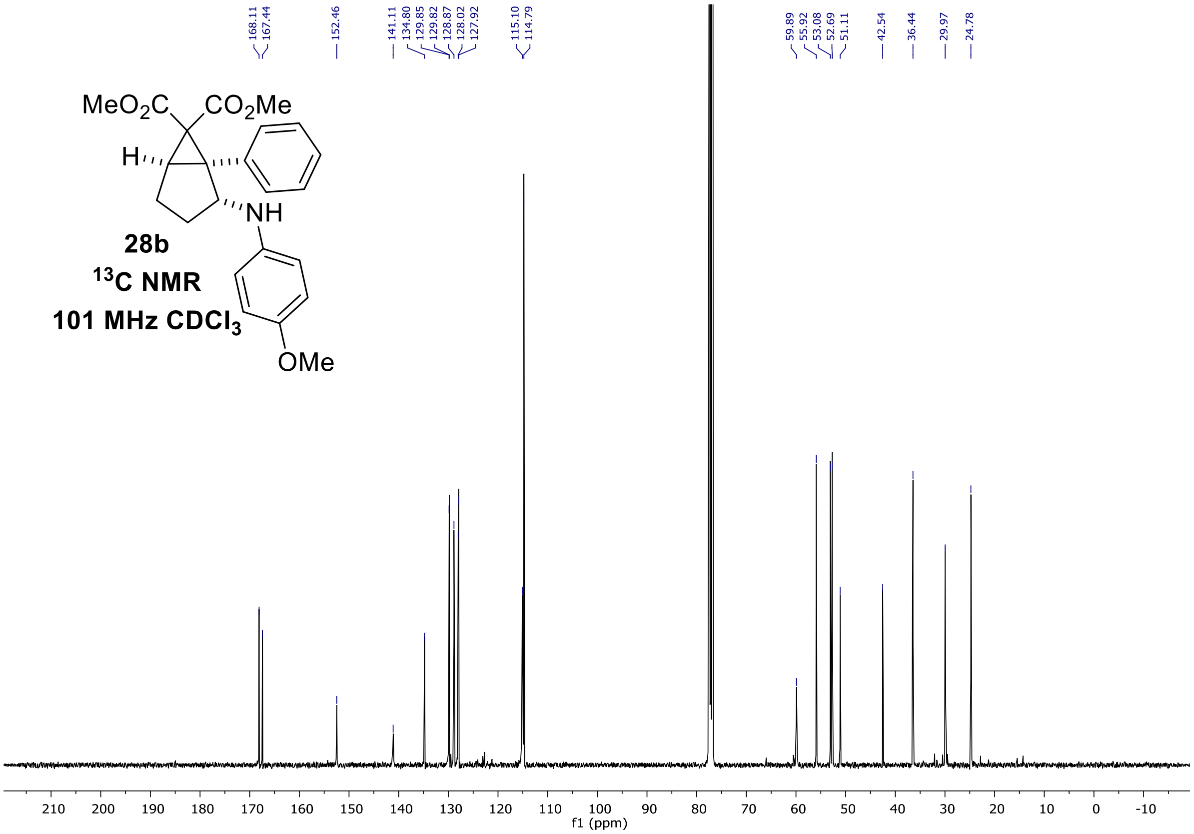
101 MHz $CDCl_3$



28b

^{1}H NMR

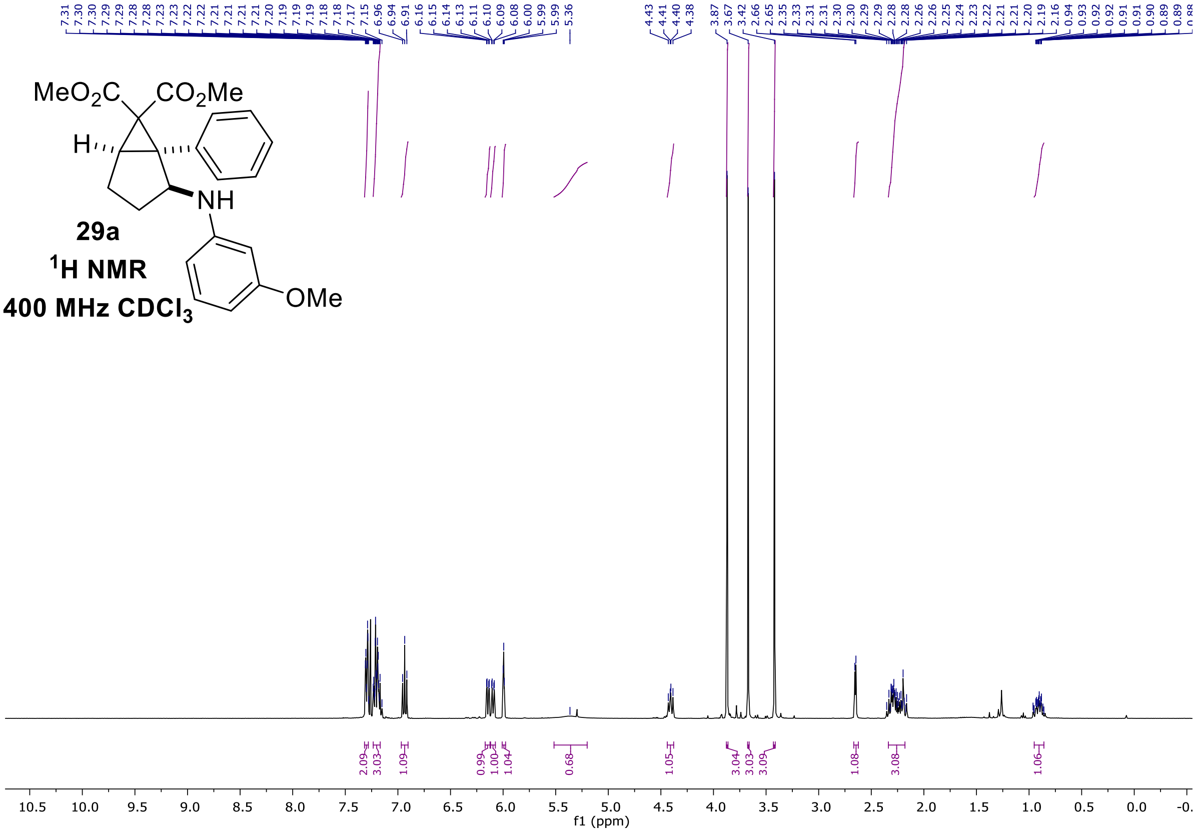
400 MHz CDCl$_3$



28b

^{13}C NMR

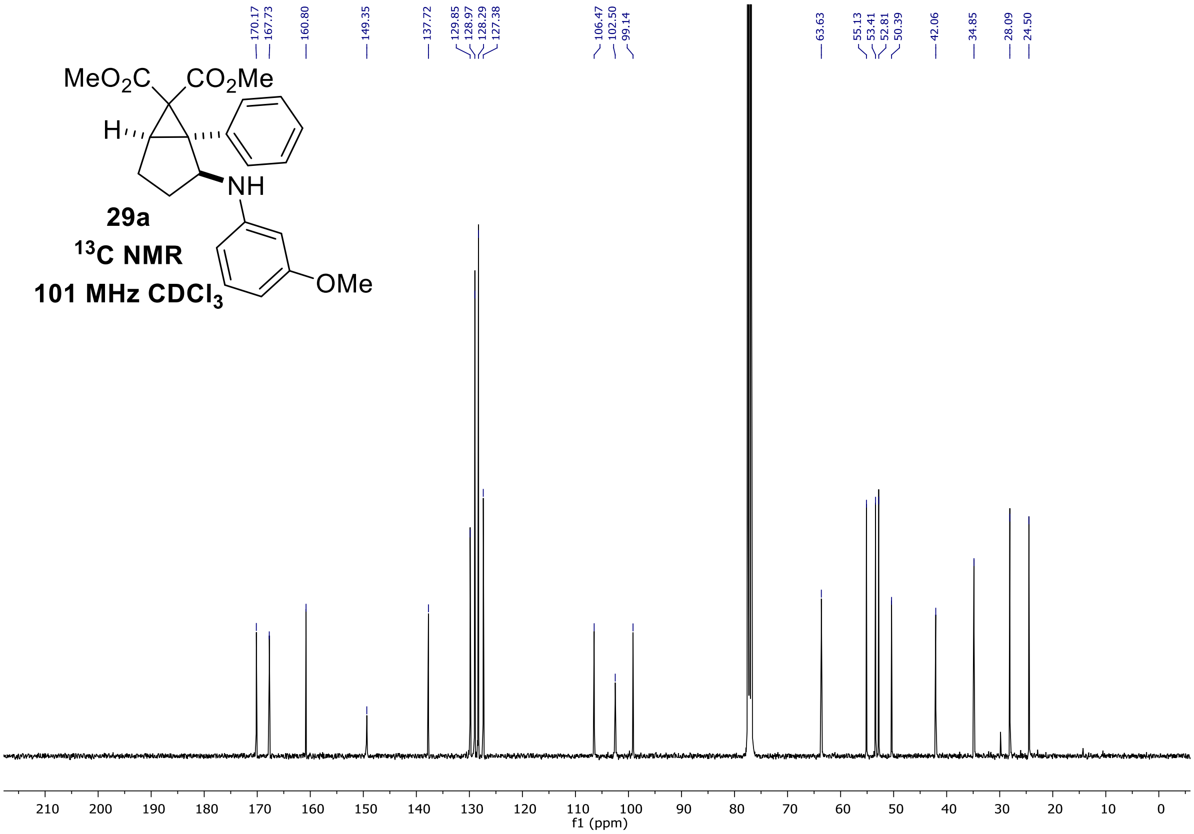
101 MHz CDCl$_3$



29a

^{1}H NMR

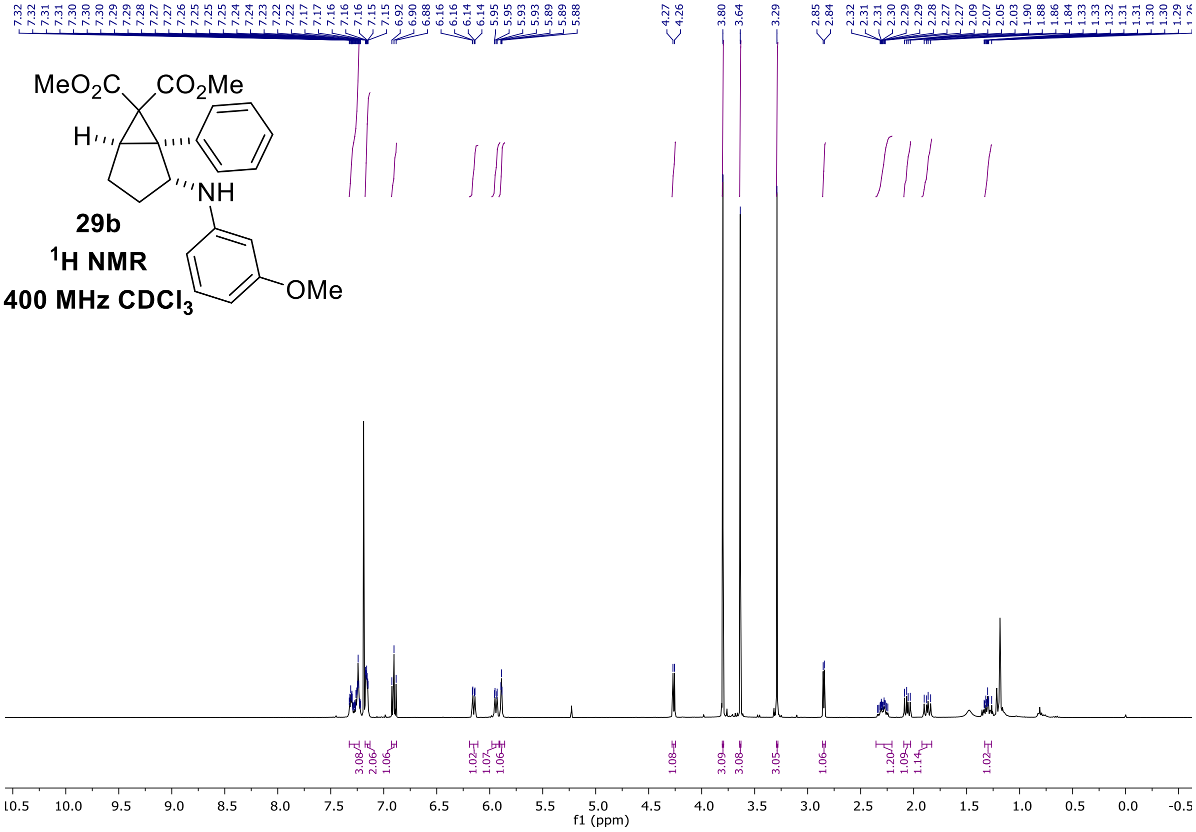
400 MHz CDCl$_3$



29a

^{13}C NMR

101 MHz CDCl$_3$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7.25
7.25
7.24
7.24
7.23
7.22
7.22
7.17
7.17
7.16
7.16
7.16
7.15
7.15
6.92
6.90
6.88
6.16
6.16
6.14
6.14
5.95
5.95
5.93
5.93
5.89
5.89
5.88
4.27
4.26
3.80
3.64
3.29
2.85
2.84
2.32
2.31
2.31
2.30
2.29
2.29
2.28
2.27
2.27
2.09
2.07
2.05
2.03
1.90
1.88
1.86
1.84
1.33
1.33
1.32
1.31
1.31
1.30
1.30
1.29
MeO2C
CO2Me
H
NH
OMe
29b
1H NMR
400 MHz CDCl3
3.08
2.06
1.06
1.02
1.07
1.06
1.08
3.09
3.08
3.05
1.06
1.20
1.09
1.14
1.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
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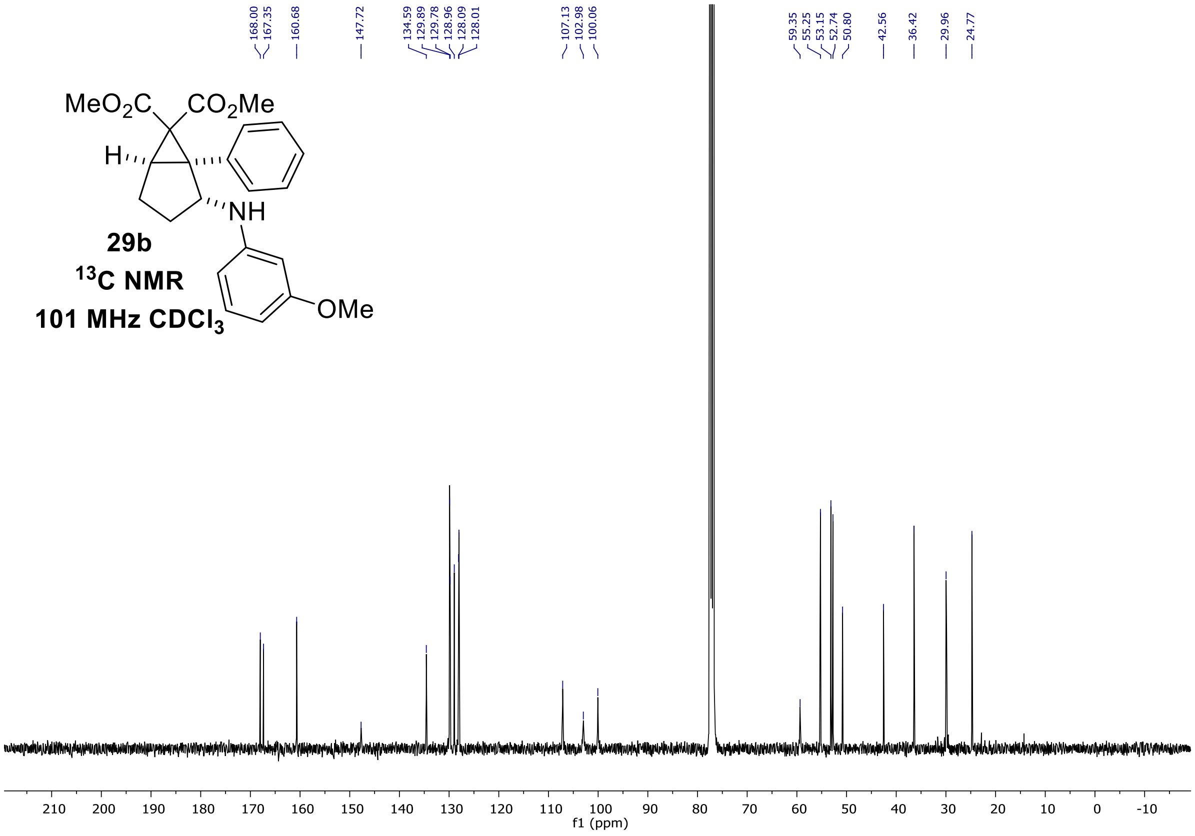
-0.5
f1 (ppm)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55.25
53.15
52.74
50.80
42.56
36.42
29.96
24.77
MeO2C
CO2Me
H
NH
OMe
29b
13C NMR
101 MHz CDCl3
210
200
190
180
170
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100
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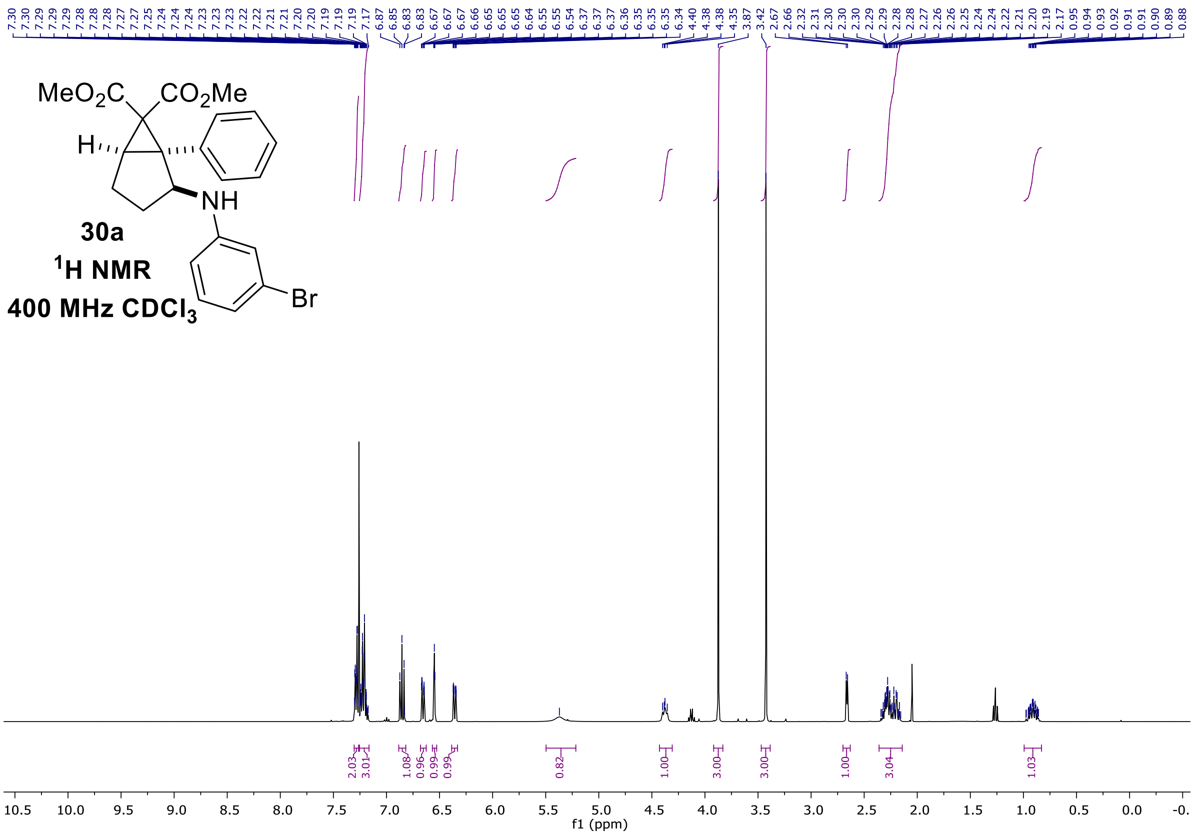
f1 (ppm)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7.19
7.19
7.17
6.87
6.85
6.83
6.83
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6.67
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6.66
6.65
6.65
6.65
6.64
6.55
6.55
6.54
6.37
6.37
6.37
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6.35
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6.35
6.34
4.40
4.38
4.38
4.35
3.87
3.42
2.67
2.66
2.32
2.31
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2.20
2.19
2.17
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0.94
0.93
0.92
0.91
0.91
0.90
0.89
0.88
MeO2C
CO2Me
H
NH
Br
30a
1H NMR
400 MHz CDCl3
2.03
3.01
1.08
0.96
0.99
0.99
0.82
1.00
3.00
3.00
1.00
3.04
1.03
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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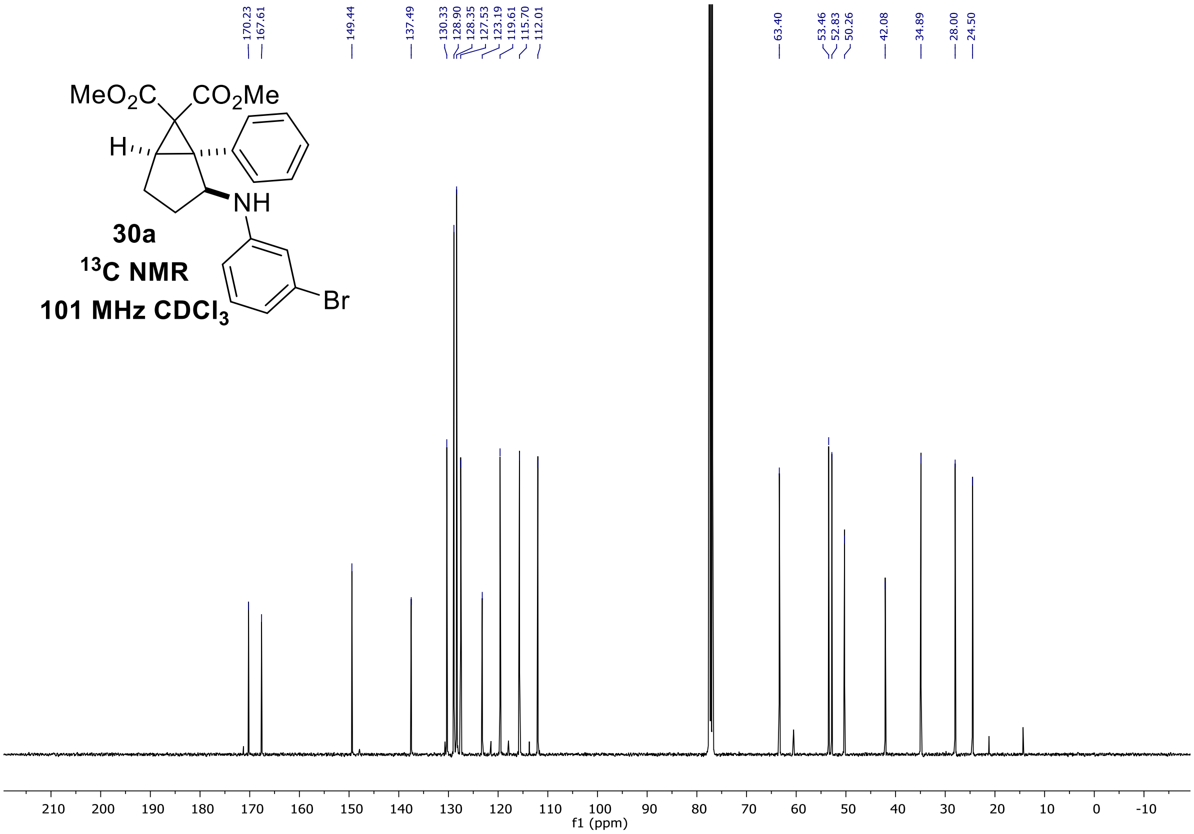
-0.
f1 (ppm)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123.19
119.61
115.70
112.01
63.40
53.46
52.83
50.26
42.08
34.89
28.00
24.50
MeO2C
CO2Me
H
NH
Br
30a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
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120
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100
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80
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30
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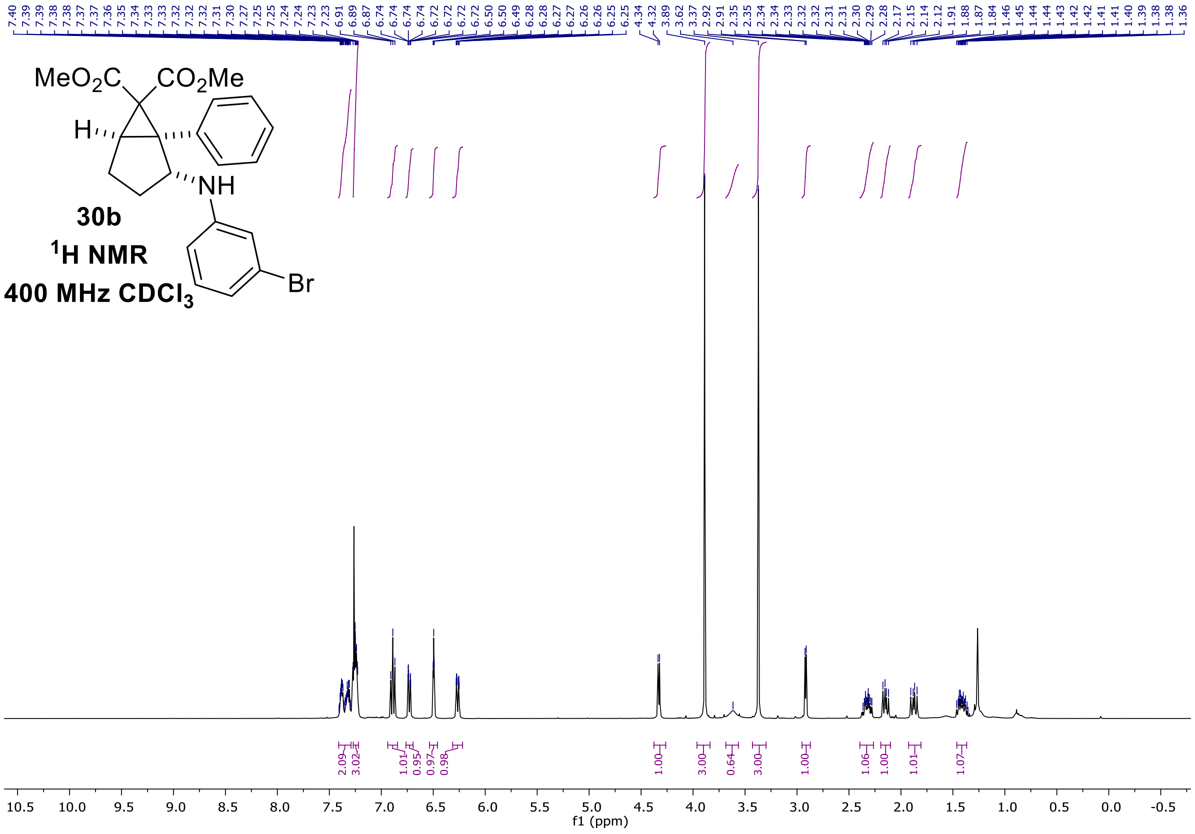
0
-10
f1 (ppm)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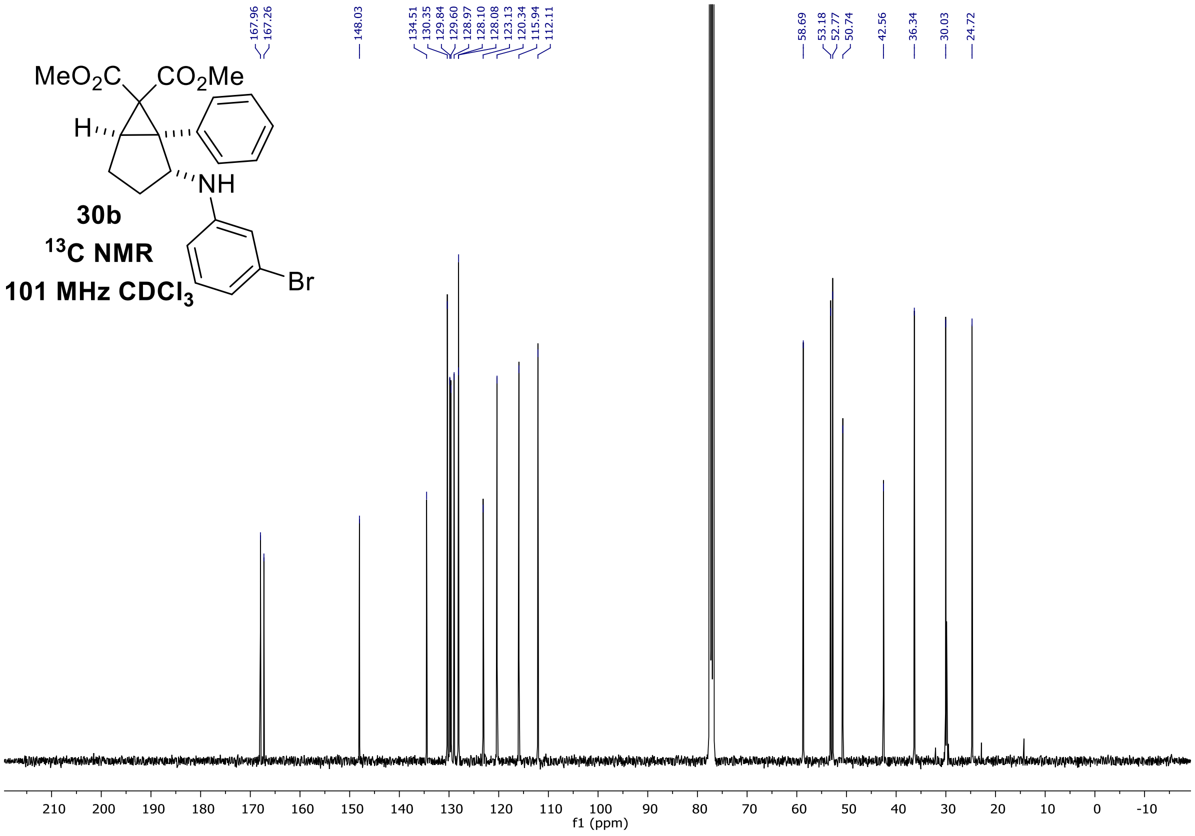
MeO_2C
CO_2Me
H
NH
Br
30b
^1H NMR
400 MHz $CDCl_3$
2.09 3.02 1.01 0.95 0.97 0.98 1.00 3.00 0.64 3.00 1.00 1.06 1.00 1.01 1.07
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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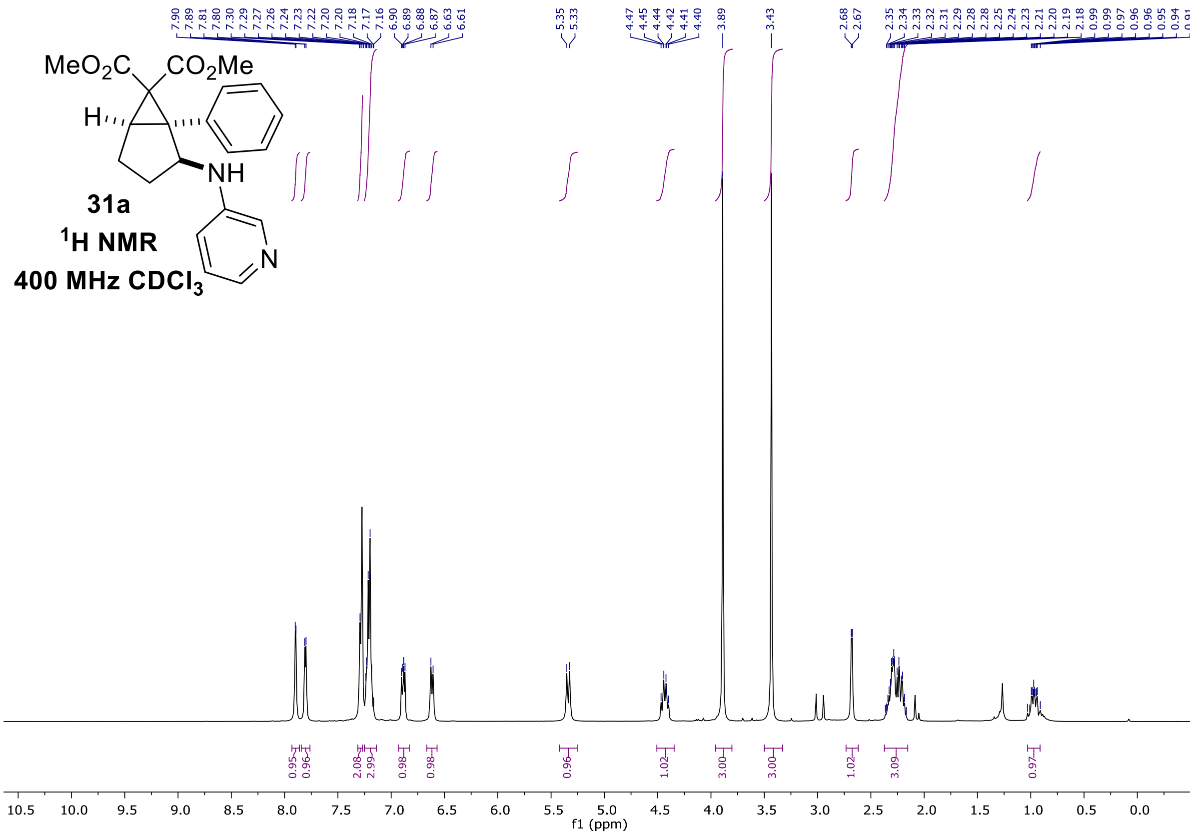
MeO_2C
CO_2Me
H
NH
Br
30b
^{13}C NMR
101 MHz $CDCl_3$
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.16
6.90
6.89
6.88
6.87
6.63
6.61
5.35
5.33
4.47
4.45
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2.24
2.23
2.21
2.20
2.19
2.18
0.99
0.99
0.97
0.96
0.96
0.95
0.94
MeO2C
CO2Me
H
NH
N
31a
1H NMR
400 MHz CDCl3
0.95
0.96
2.08
2.99
0.98
0.98
0.96
1.02
3.00
3.00
1.02
3.09
0.97
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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2.5
2.0
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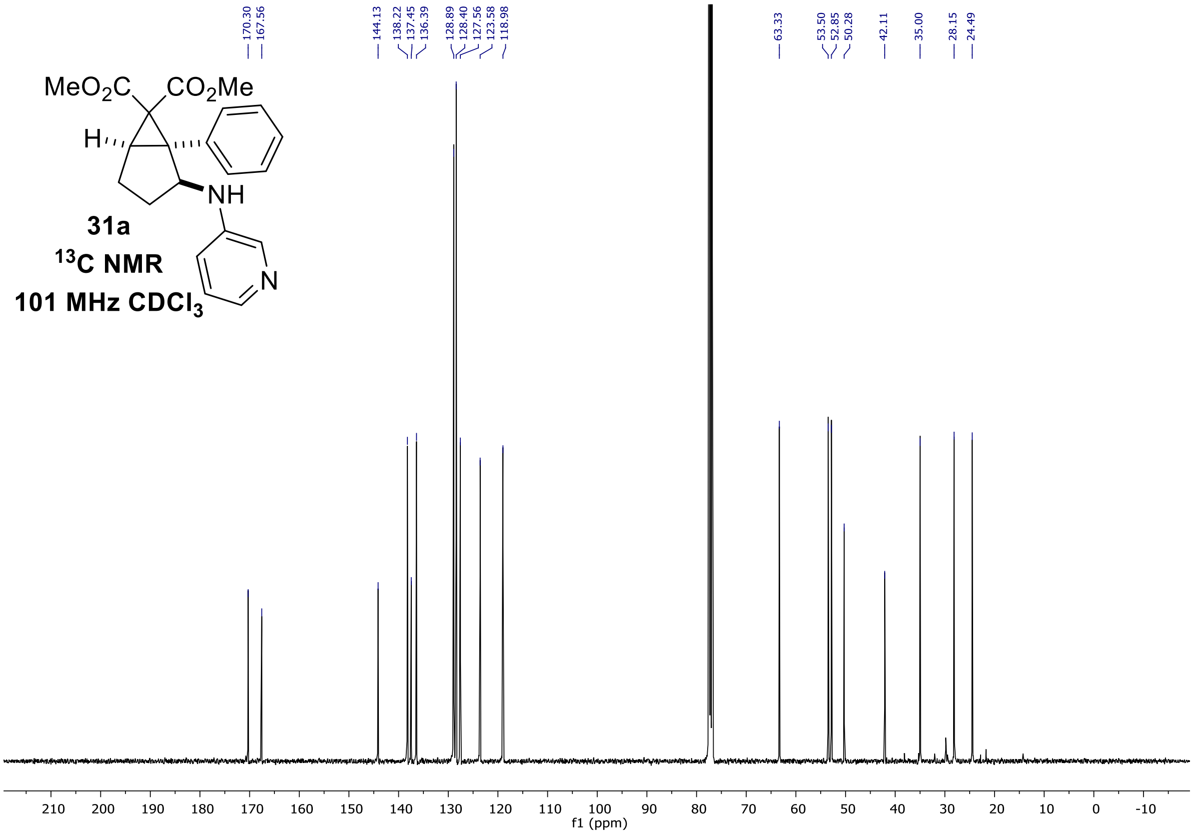
f1 (ppm)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52.85
50.28
42.11
35.00
28.15
24.49
MeO2C
CO2Me
H
NH
N
31a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
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140
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120
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100
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80
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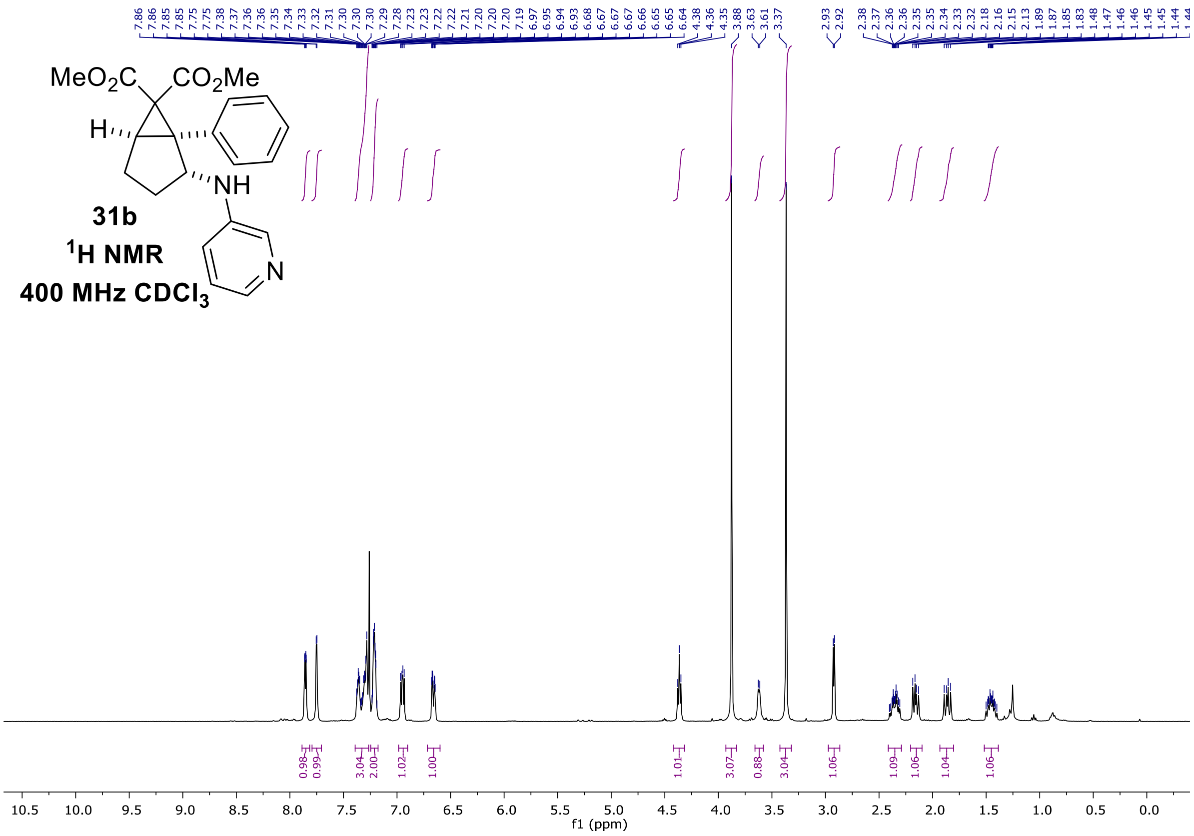
f1 (ppm)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2.33
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2.18
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2.15
2.13
1.89
1.87
1.85
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1.46
1.46
1.45
1.45
1.44
1.44
MeO2C
CO2Me
H
NH
N
31b
1H NMR
400 MHz CDCl3
0.98
0.99
3.04
2.00
1.02
1.00
1.01
3.07
0.88
3.04
1.06
1.09
1.06
1.04
1.06
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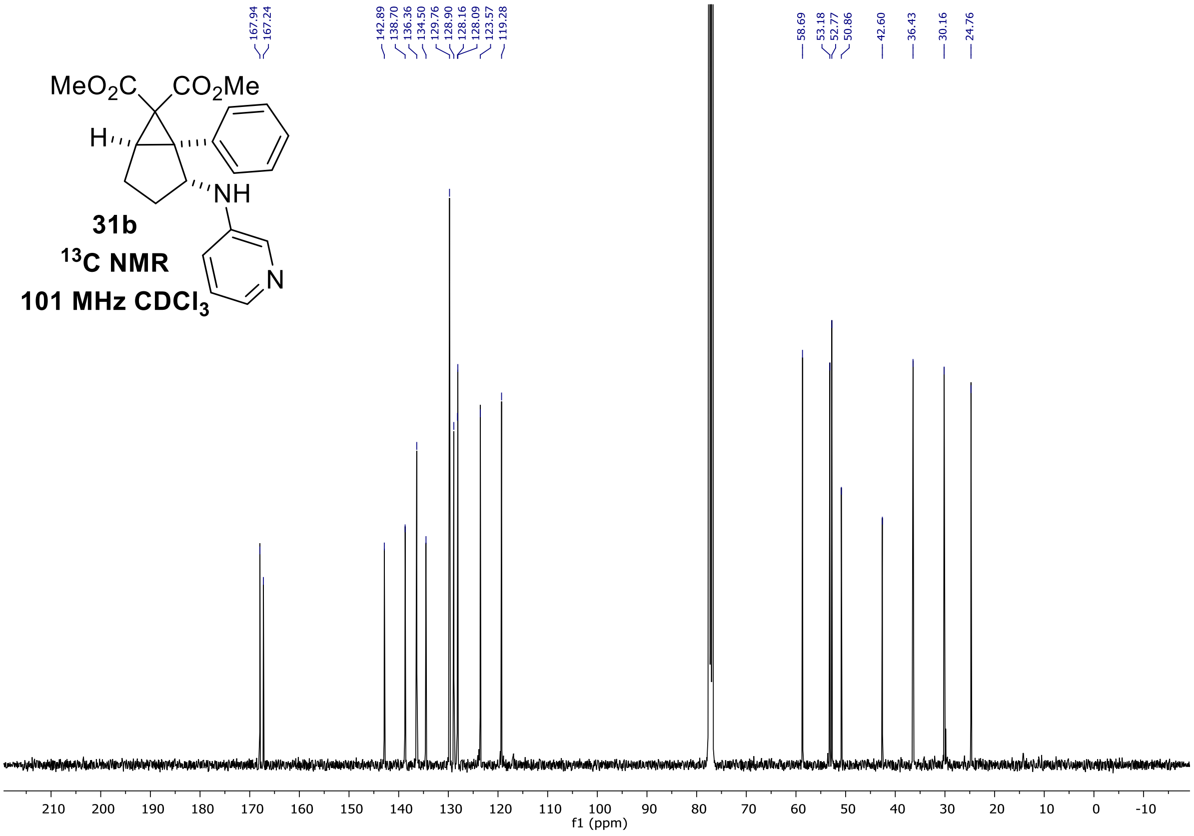
f1 (ppm)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53.18
52.77
50.86
42.60
36.43
30.16
24.76
MeO2C
CO2Me
H
NH
N
31b
13C NMR
101 MHz CDCl3
210
200
190
180
170
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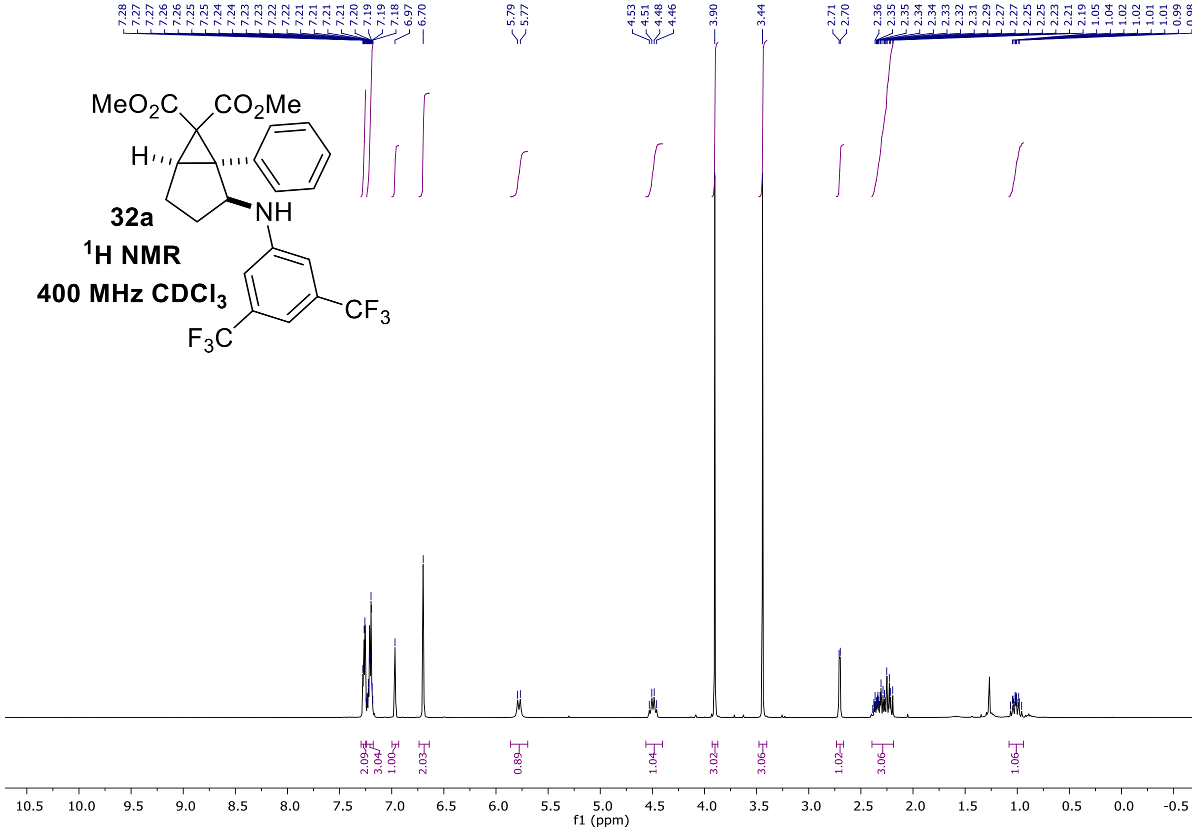
f1 (ppm)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5.77
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4.51
4.48
4.46
3.90
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2.32
2.31
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2.25
2.23
2.21
2.19
1.05
1.04
1.02
1.02
1.01
1.01
0.99
MeO2C
CO2Me
H
NH
CF3
F3C
32a
1H NMR
400 MHz CDCl3
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3.04
1.00
2.03
0.89
1.04
3.02
3.06
1.02
3.06
1.06
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2.0
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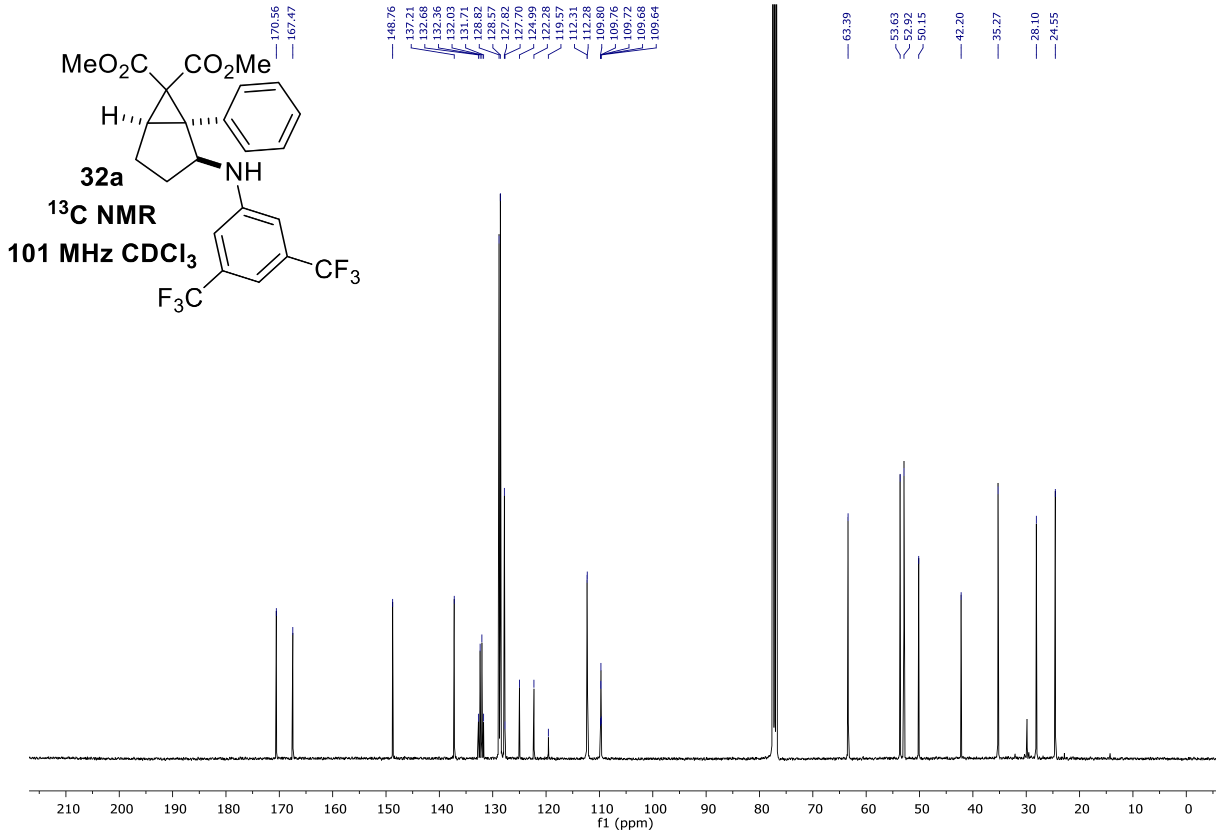
f1 (ppm)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35.27
28.10
24.55
MeO2C
CO2Me
H
NH
CF3
F3C
32a
13C NMR
101 MHz CDCl3
210
200
190
180
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90
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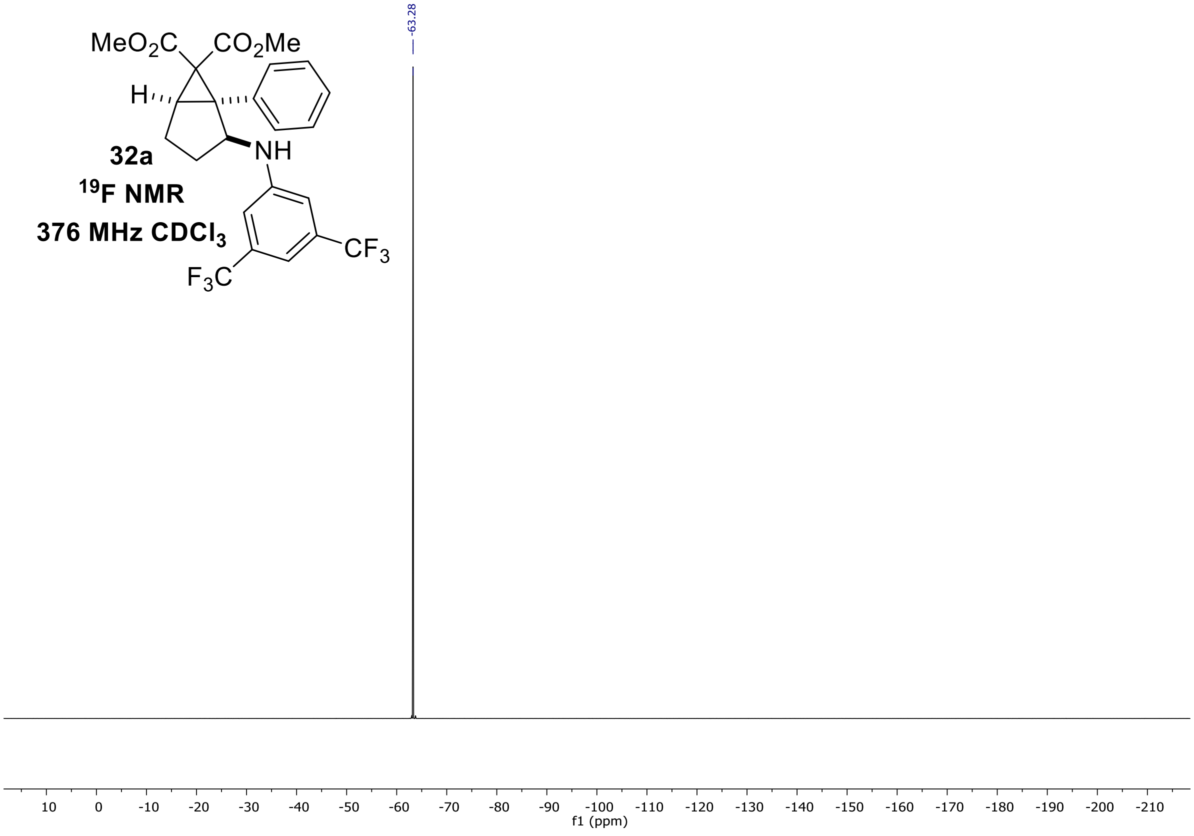
f1 (ppm)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-160
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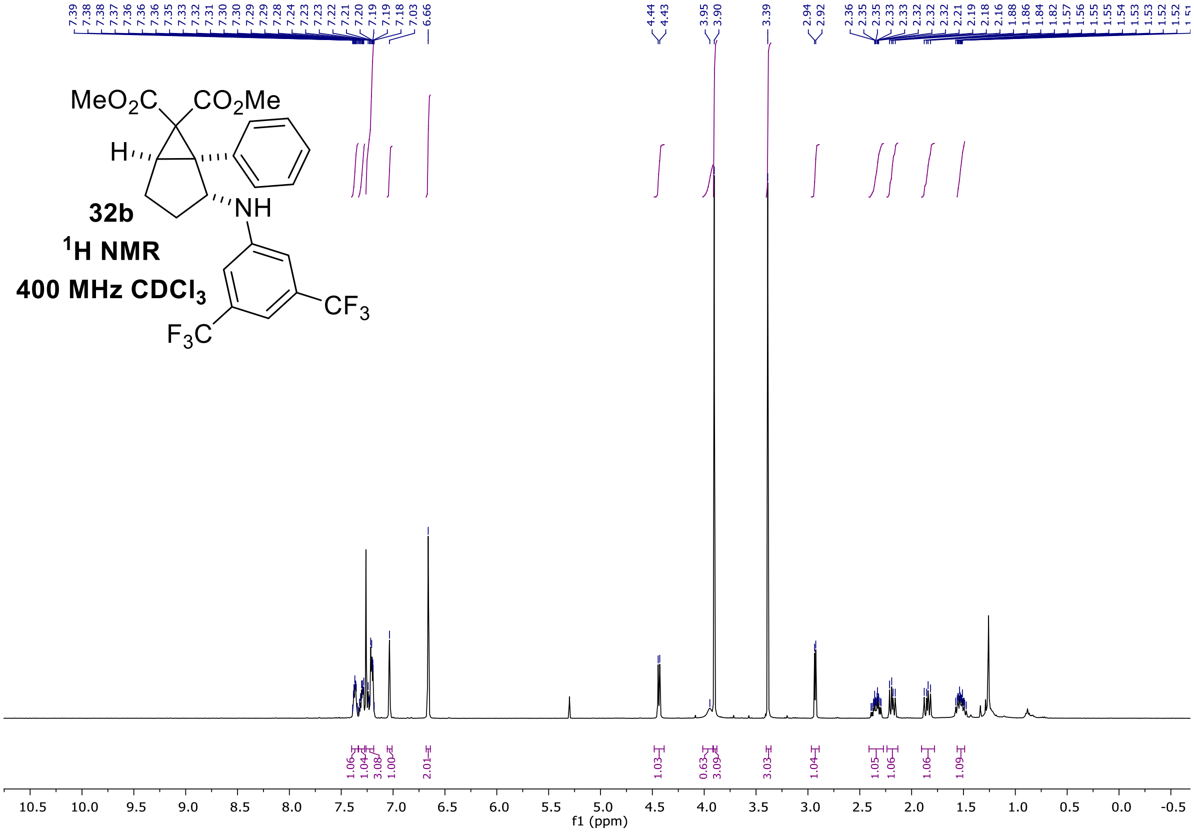
-190
-200
-210
f1 (ppm)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1.52
1.52
MeO2C
CO2Me
H
NH
CF3
F3C
32b
1H NMR
400 MHz CDCl3
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1.04
3.06
1.00
2.01
1.03
0.63
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3.03
1.04
1.05
1.06
1.06
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5.0
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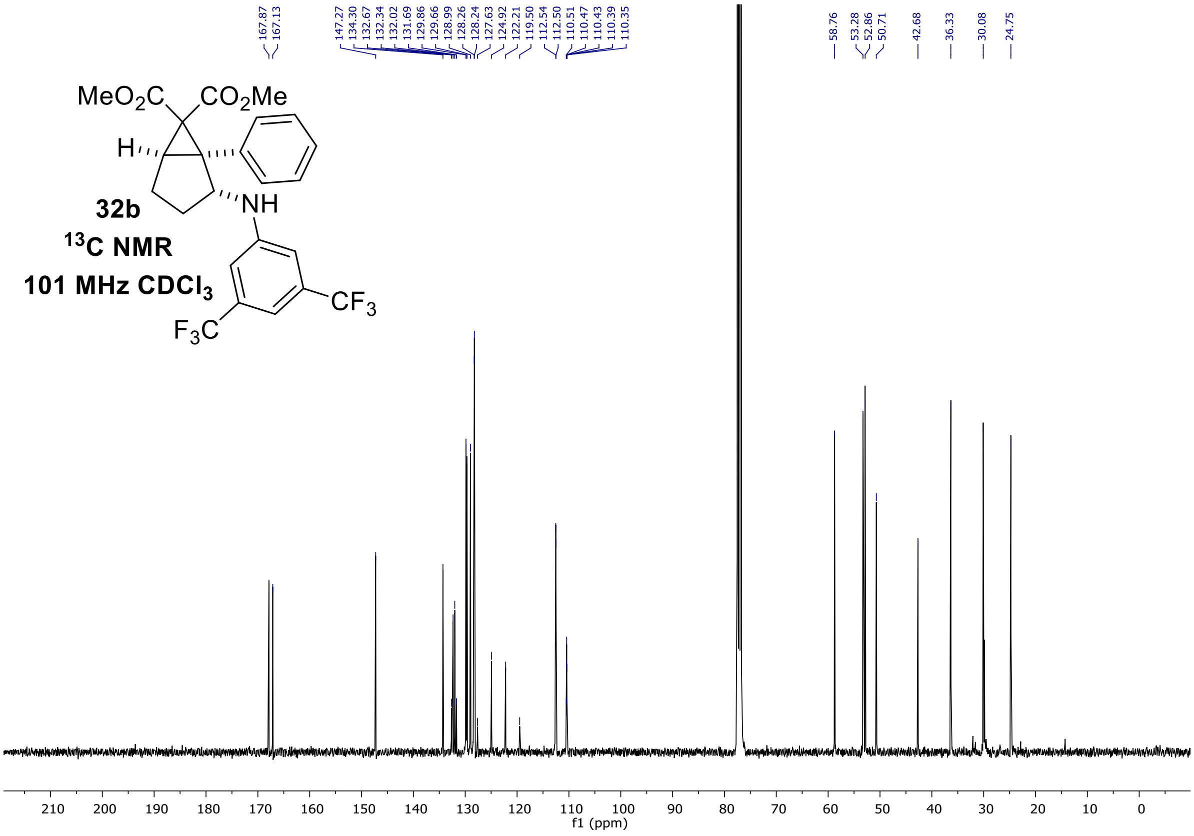
f1 (ppm)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112.50
110.51
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110.39
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50.71
42.68
36.33
30.08
24.75
MeO2C
CO2Me
H
NH
CF3
F3C
32b
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
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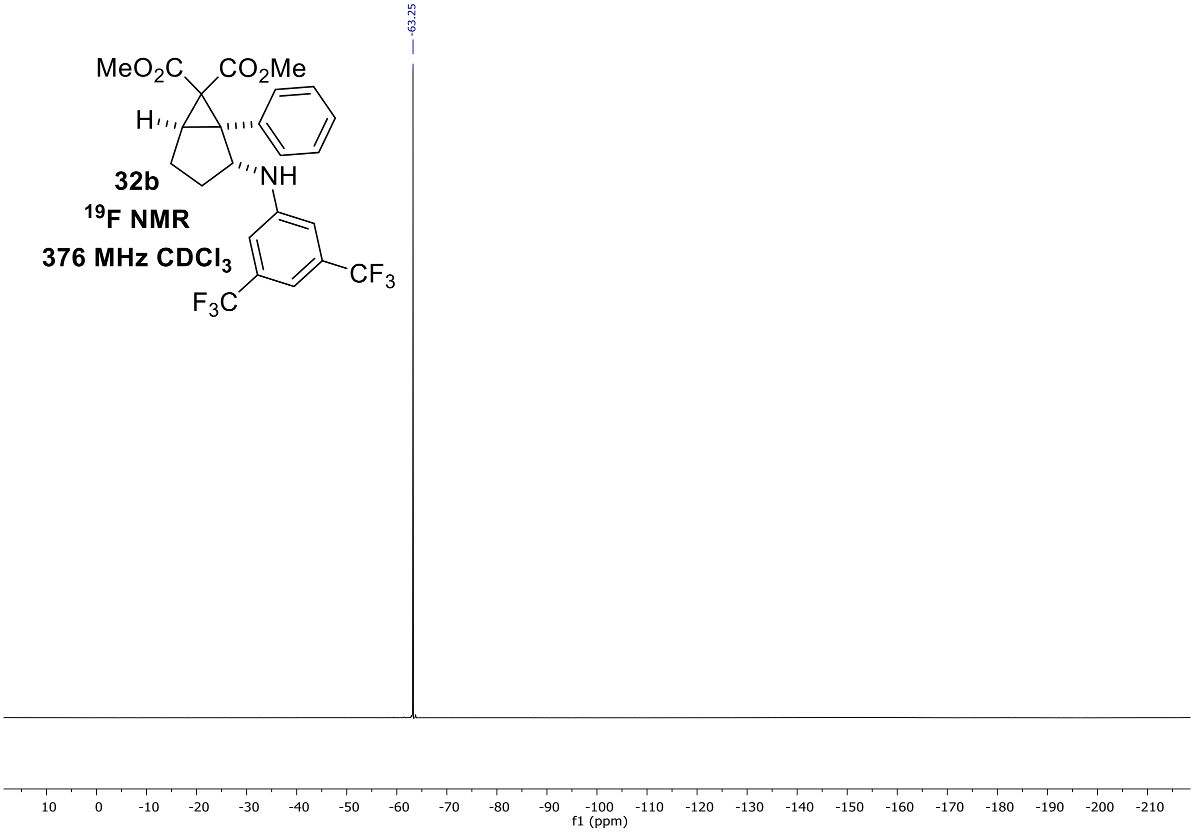
50
40
30
20
10
0
f1 (ppm)


-63.25
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CF3
F3C
32b
19F NMR
376 MHz CDCl3
10
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-50
-60
-70
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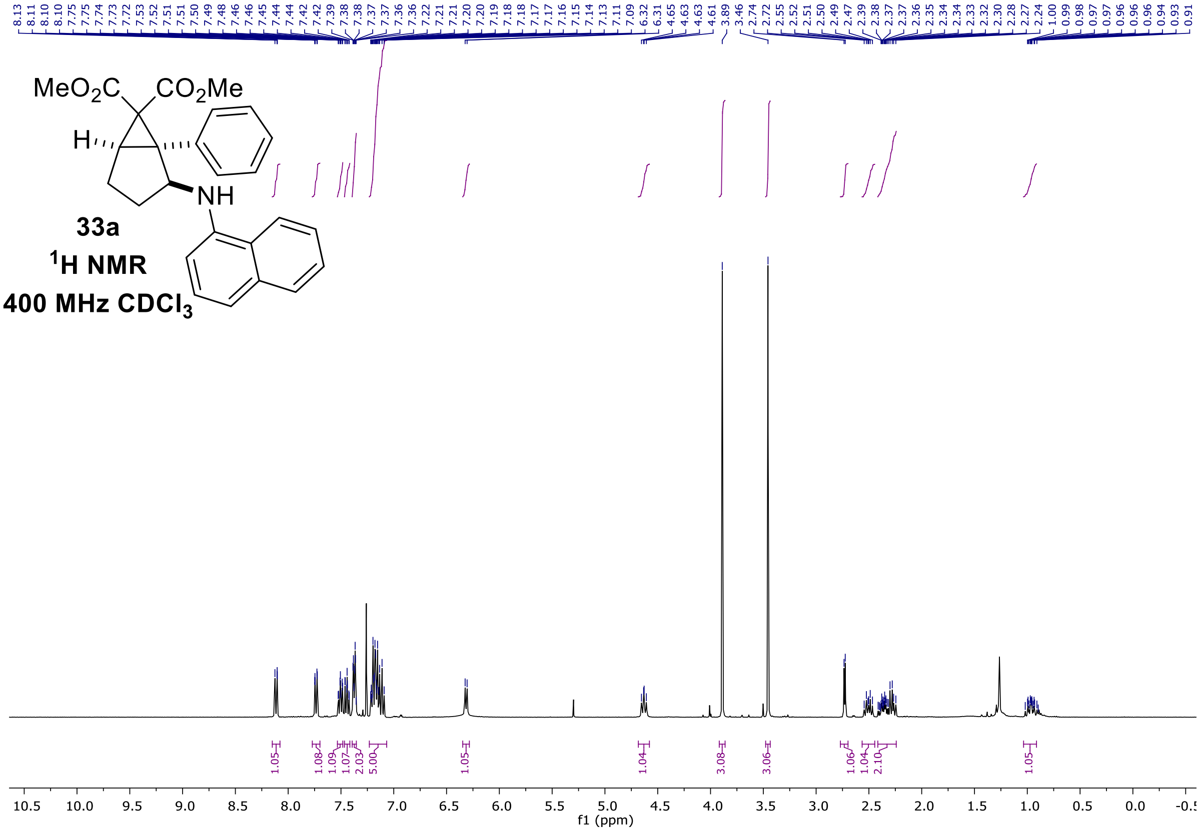
-200
-210
f1 (ppm)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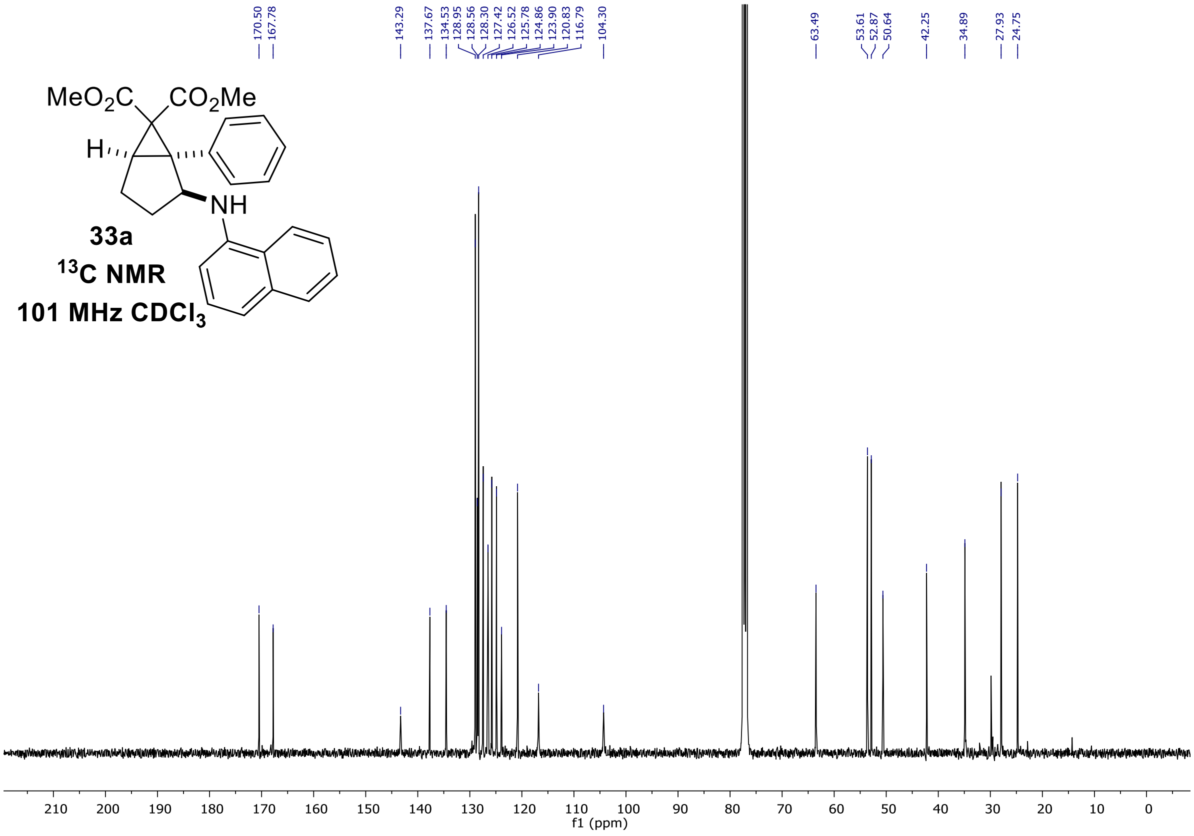
MeO2C
CO2Me
H
NH
33a
1H NMR
400 MHz CDCl3
1.05 1.08 1.09 1.07 2.03 5.00 1.05 1.04 3.08 3.06 1.06 1.04 2.10 1.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)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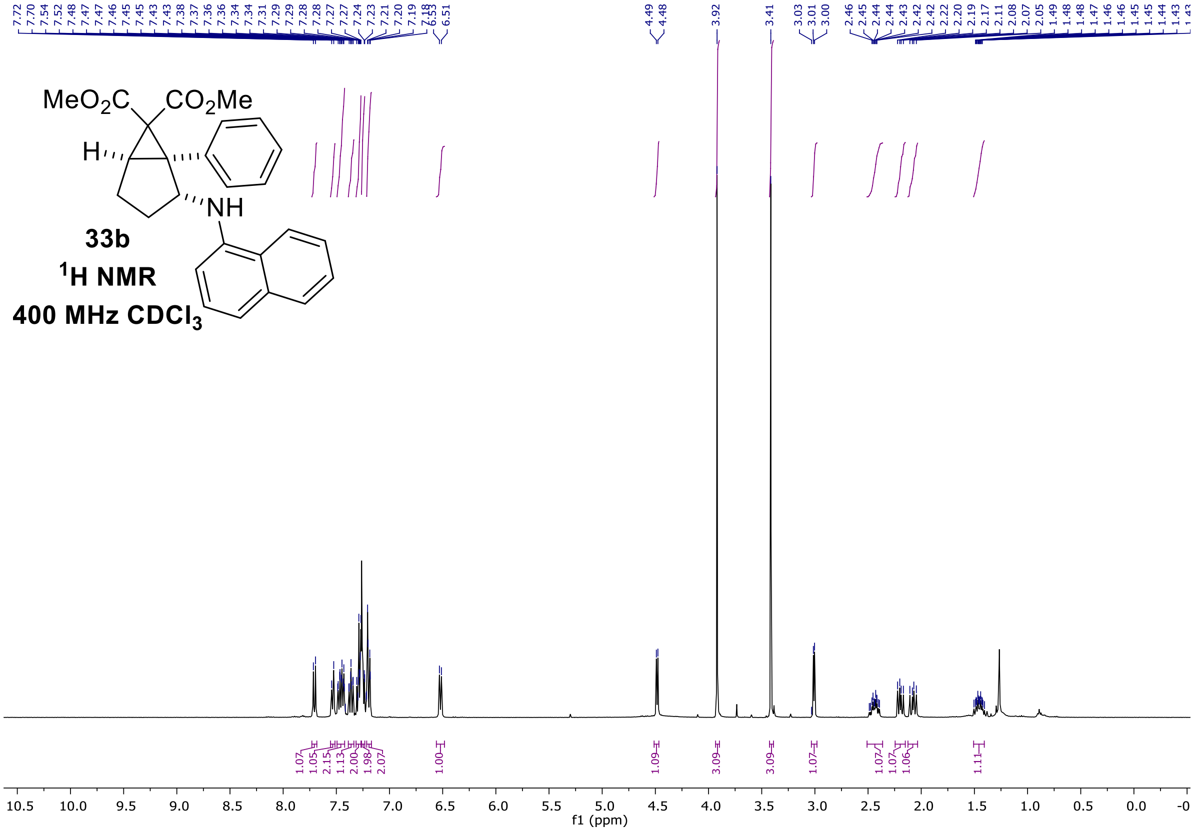
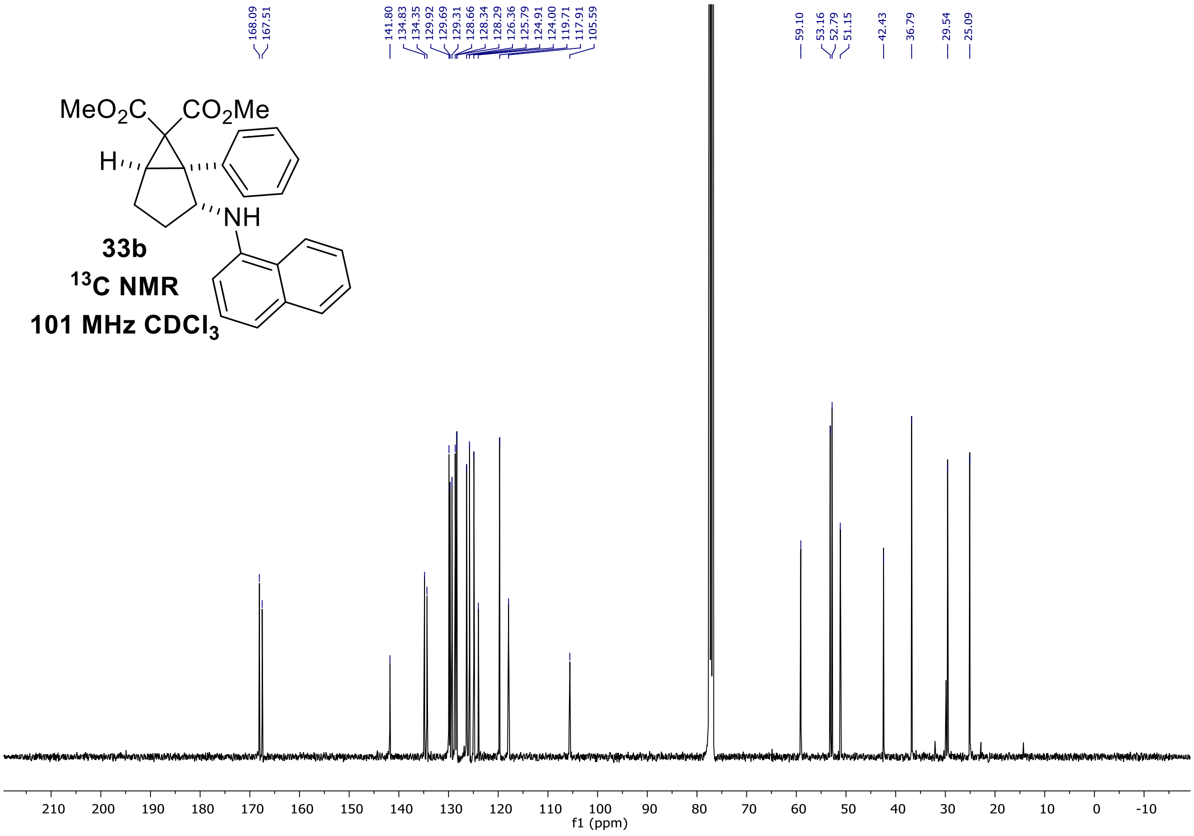
MeO2C
CO2Me
H
NH
33a
13C NMR
101 MHz CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



33b

^{1}H NMR

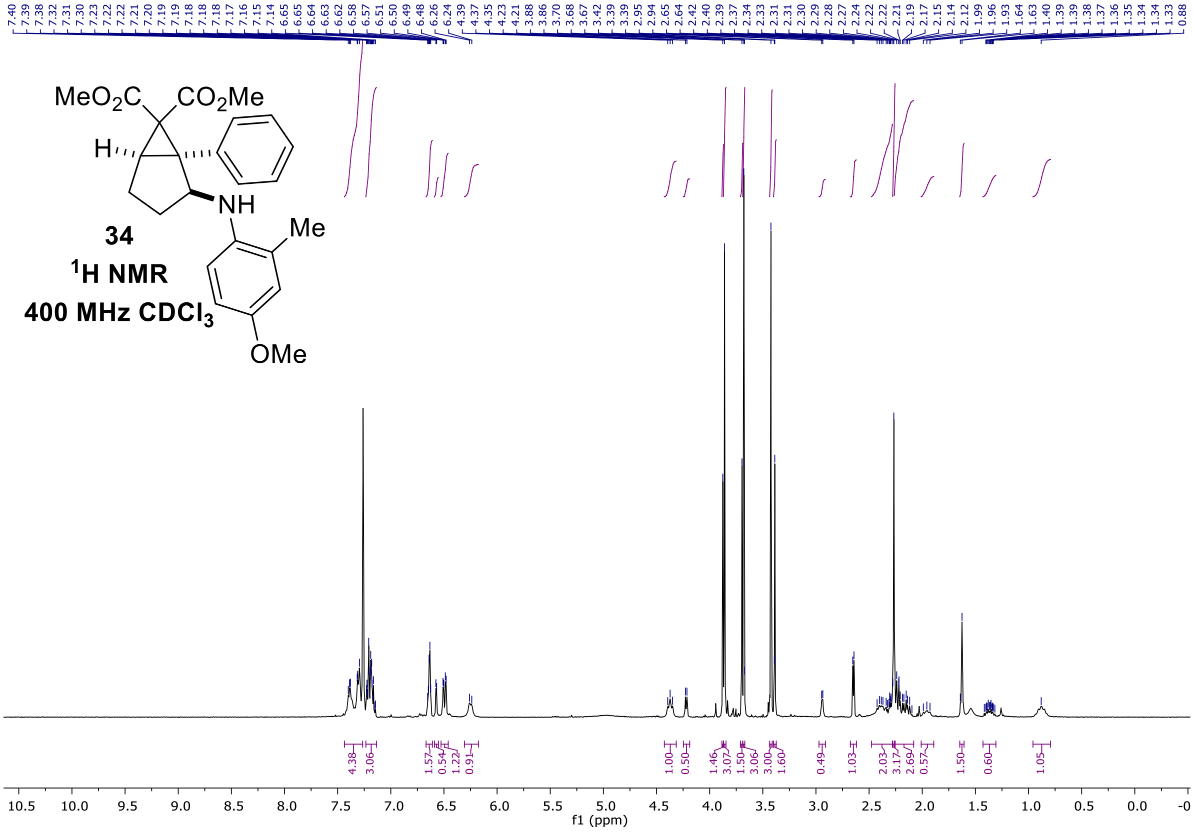
400 MHz CDCl$_3$

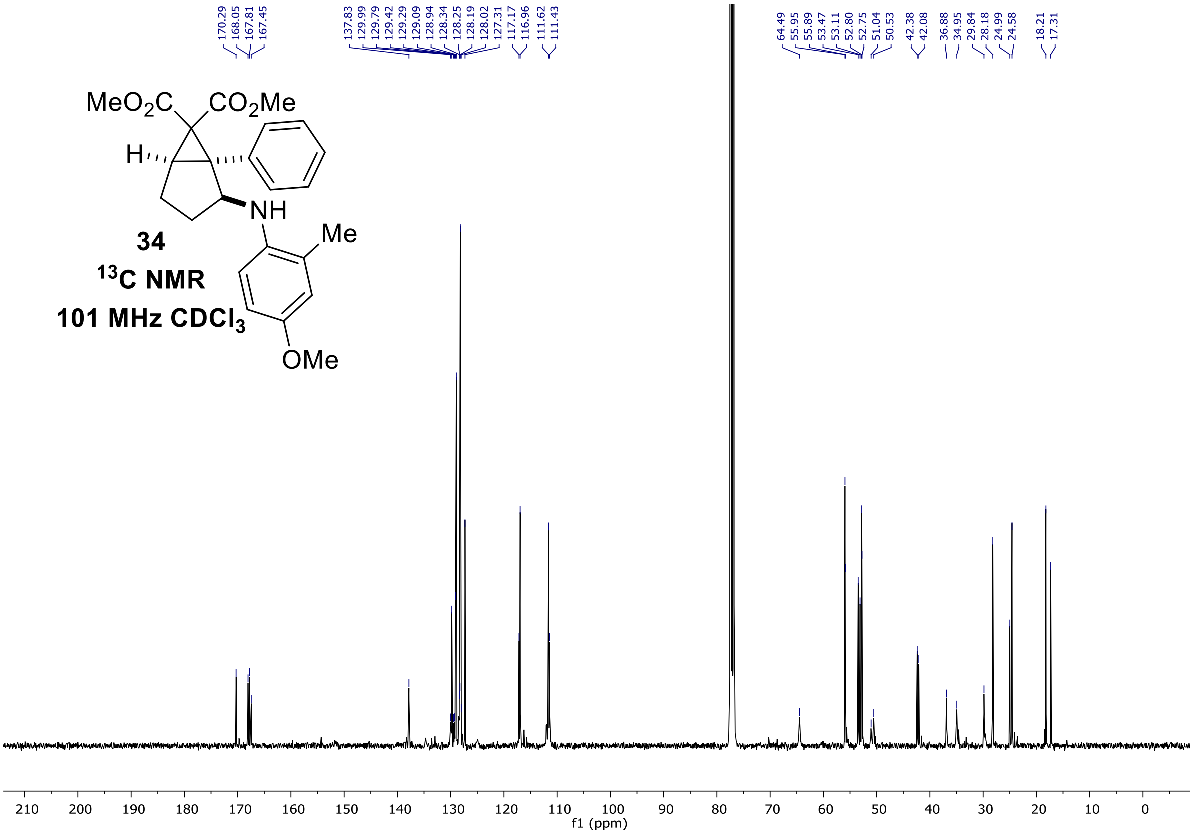


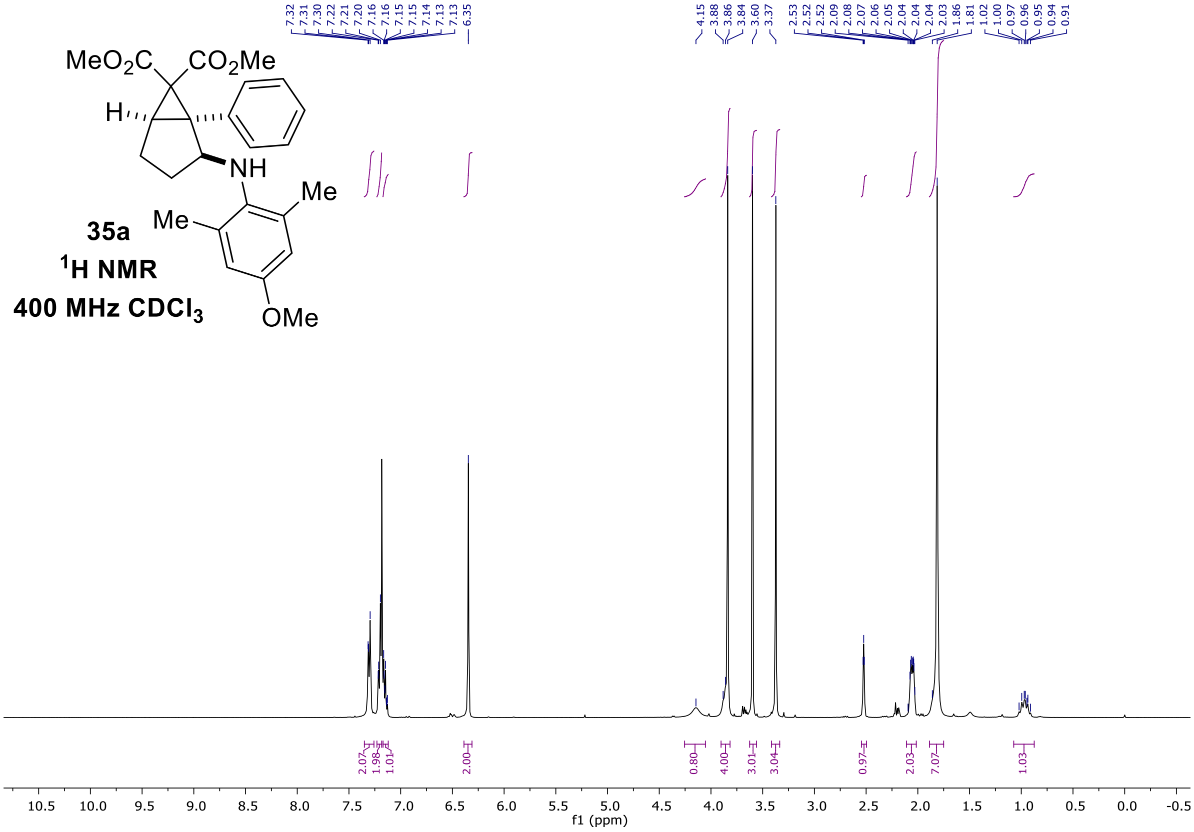
33b

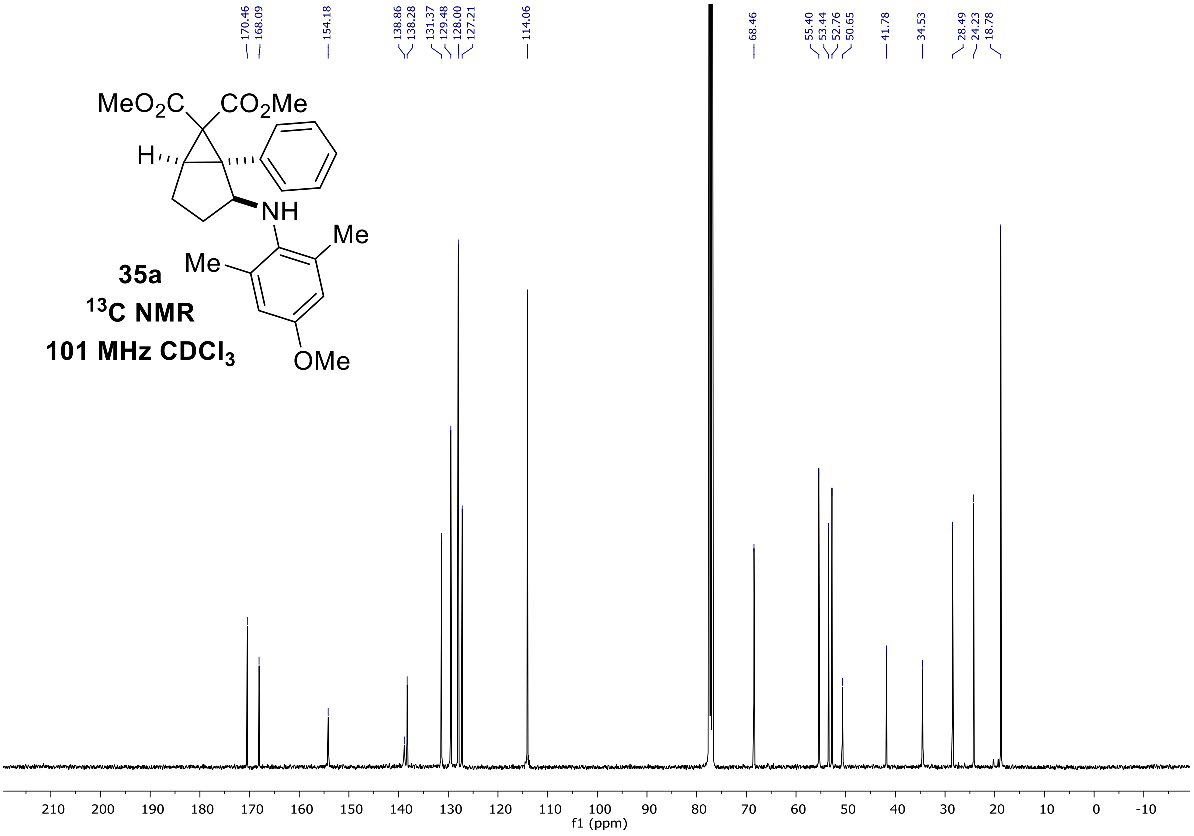
^{13}C NMR

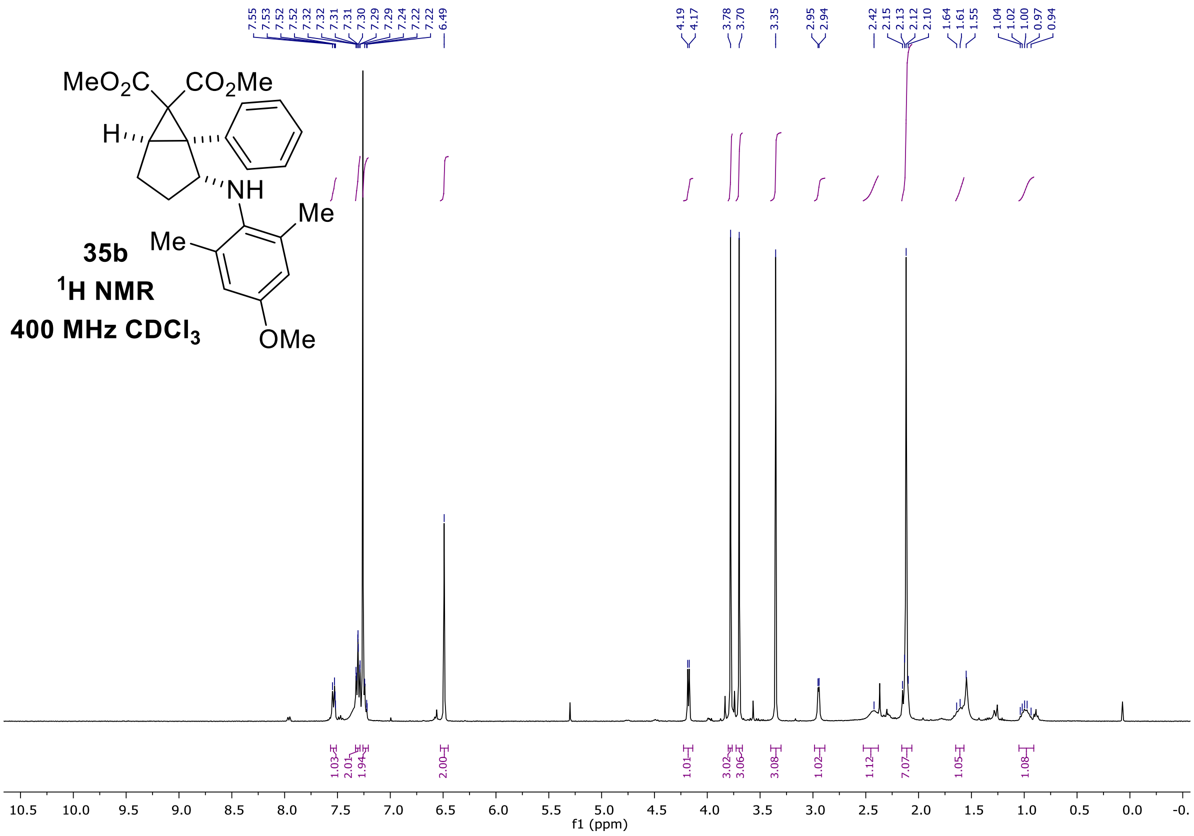
101 MHz CDCl$_3$

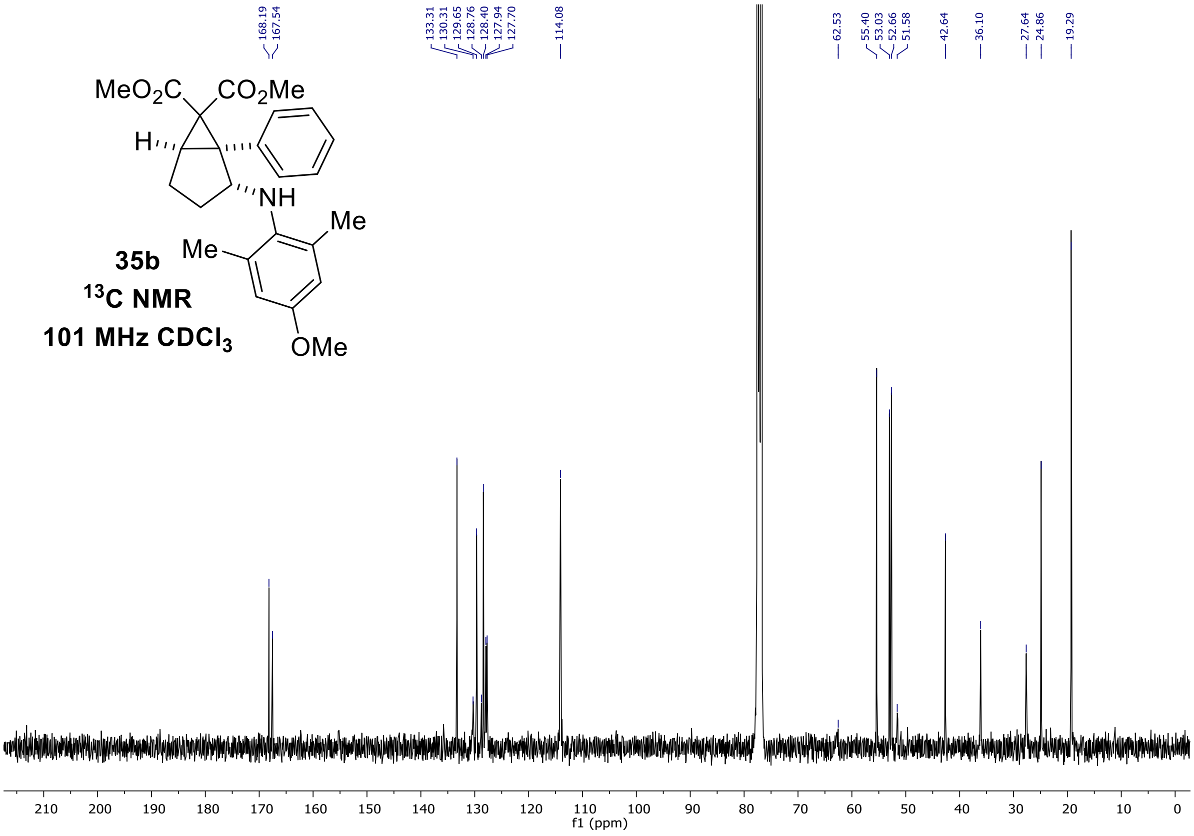

7.40 7.39 7.38 7.32 7.31 7.30 7.23 7.22 7.22 7.21 7.20 7.19 7.19 7.18 7.18 7.18 7.17 7.16 7.15 7.14 6.65 6.65 6.64 6.63 6.62 6.58 6.57 6.51 6.50 6.49 6.48 6.26 6.24 4.39 4.37 4.35 4.23 4.21 3.88 3.86 3.70 3.68 3.67 3.42 3.39 3.39 2.95 2.94 2.65 2.64 2.42 2.40 2.39 2.37 2.34 2.33 2.31 2.31 2.30 2.29 2.28 2.27 2.24 2.22 2.22 2.21 2.19 2.17 2.15 2.14 2.12 1.99 1.96 1.93 1.64 1.63 1.40 1.39 1.39 1.38 1.37 1.36 1.35 1.34 1.34 1.33 0.88
MeO2C
CO2Me
H
NH
Me
OMe
34
1H NMR
400 MHz CDCl3
4.38 3.06 1.57 0.54 1.22 0.91 1.00 0.50 1.46 3.07 1.50 3.06 3.00 1.60 0.49 1.03 2.03 3.17 2.69 0.57 1.50 0.60 1.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

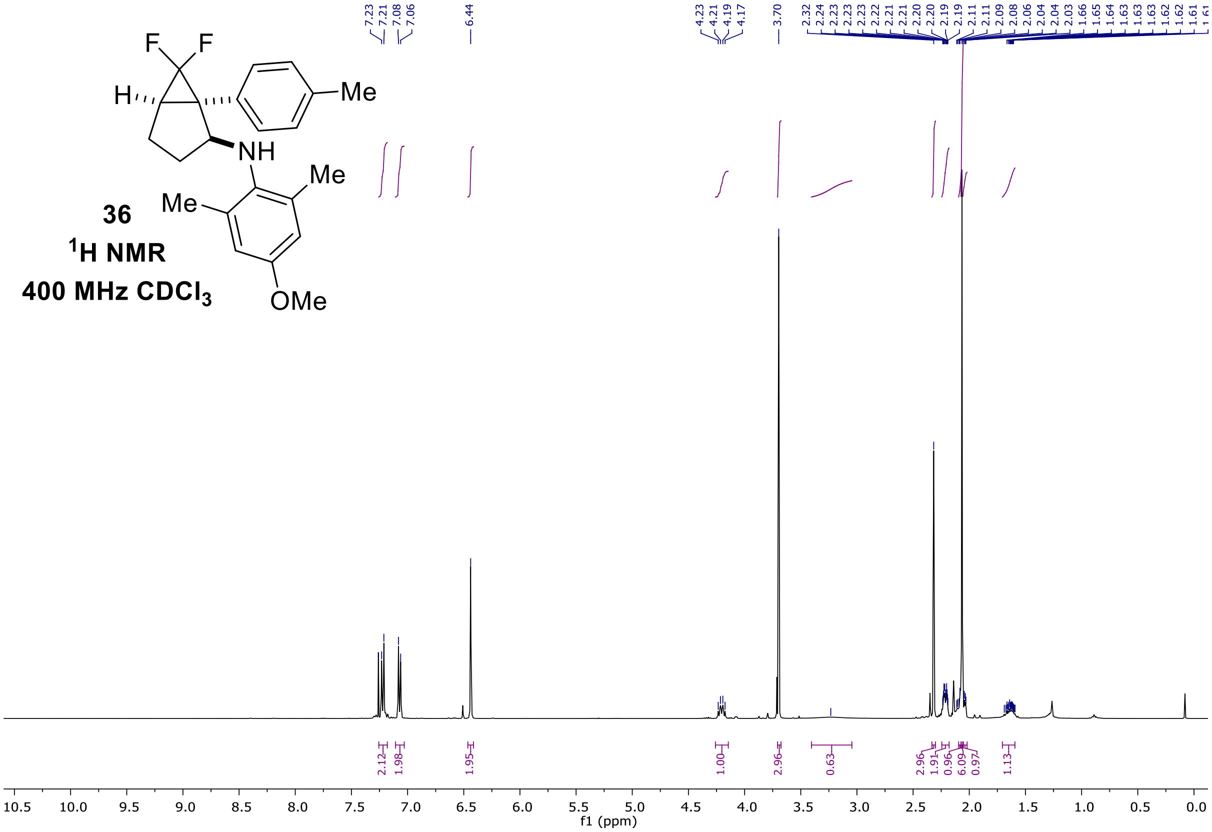

170.29 168.05 167.81 167.45 137.83 129.99 129.79 129.42 129.29 129.09 128.94 128.34 128.25 128.19 128.02 127.31 117.17 116.96 111.62 111.43 64.49 55.95 55.89 53.47 53.11 52.80 52.75 51.04 50.53 42.38 42.08 36.88 34.95 29.84 28.18 24.99 24.58 18.21 17.31
MeO2C
CO2Me
H
NH
Me
OMe
34
13C NMR
101 MHz CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.32
7.31
7.30
7.22
7.21
7.20
7.16
7.16
7.15
7.15
7.14
7.13
7.13
6.35
4.15
3.88
3.86
3.84
3.60
3.37
2.53
2.52
2.09
2.08
2.07
2.06
2.05
2.04
2.04
2.04
2.03
1.86
1.81
1.02
1.00
0.97
0.96
0.95
0.94
0.91
MeO2C
CO2Me
H
NH
Me
Me
OMe
35a
1H NMR
400 MHz CDCl3
2.07
1.98
1.01
2.00
0.80
4.00
3.01
3.04
0.97
2.03
7.07
1.03
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


170.46
168.09
154.18
138.86
138.28
131.37
129.48
128.00
127.21
114.06
68.46
55.40
53.44
52.76
50.65
41.78
34.53
28.49
24.23
18.78
MeO2C
CO2Me
H
NH
Me
Me
OMe
35a
13C NMR
101 MHz CDCl3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


35b
^{1}H NMR
400 MHz CDCl$_3$

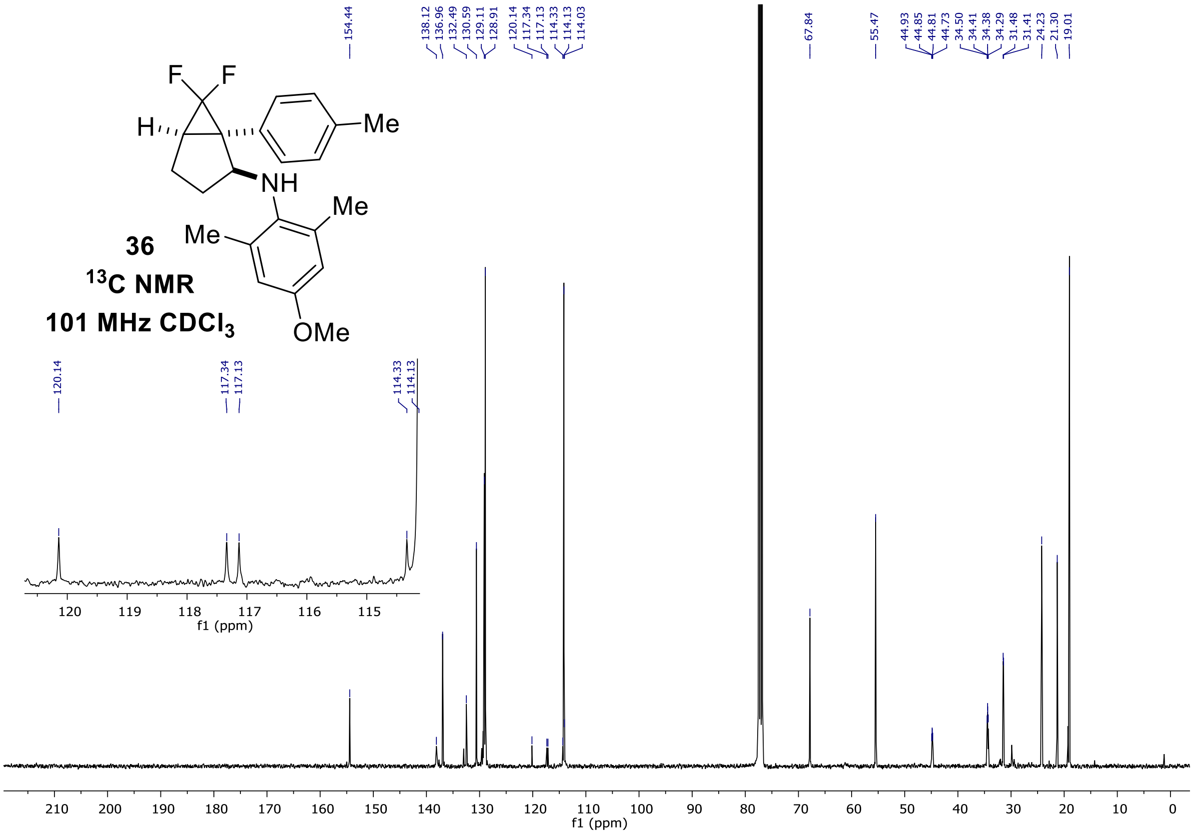

35b
^{13}C NMR
101 MHz CDCl$_3$



36

^{1}H NMR

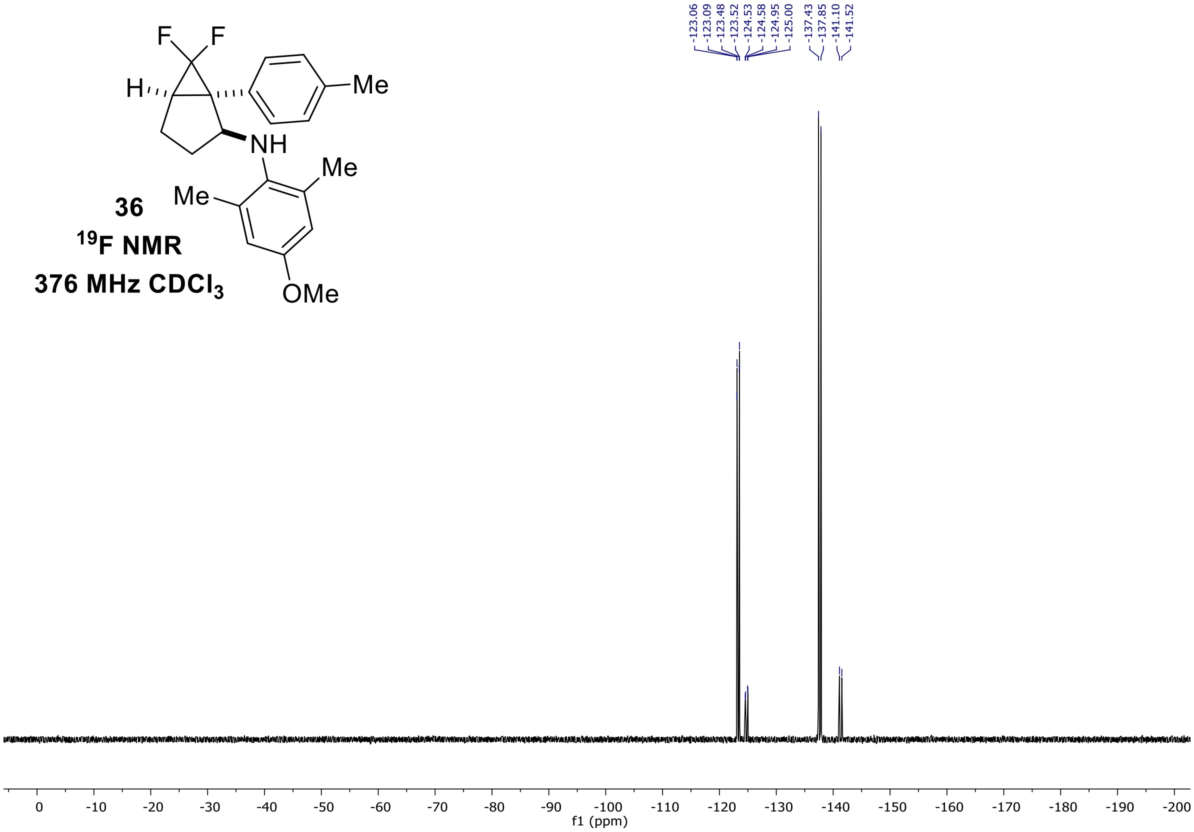
400 MHz $CDCl_3$



36

^{13}C NMR

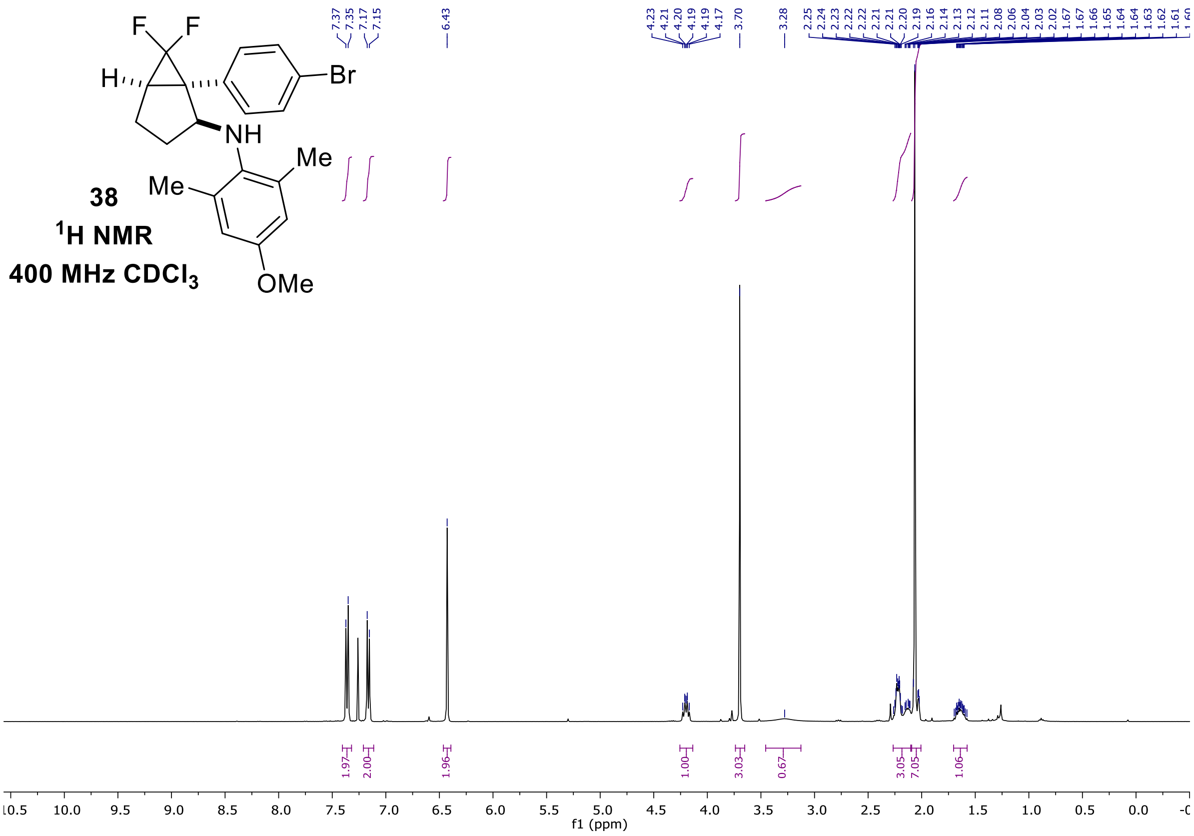
101 MHz $CDCl_3$

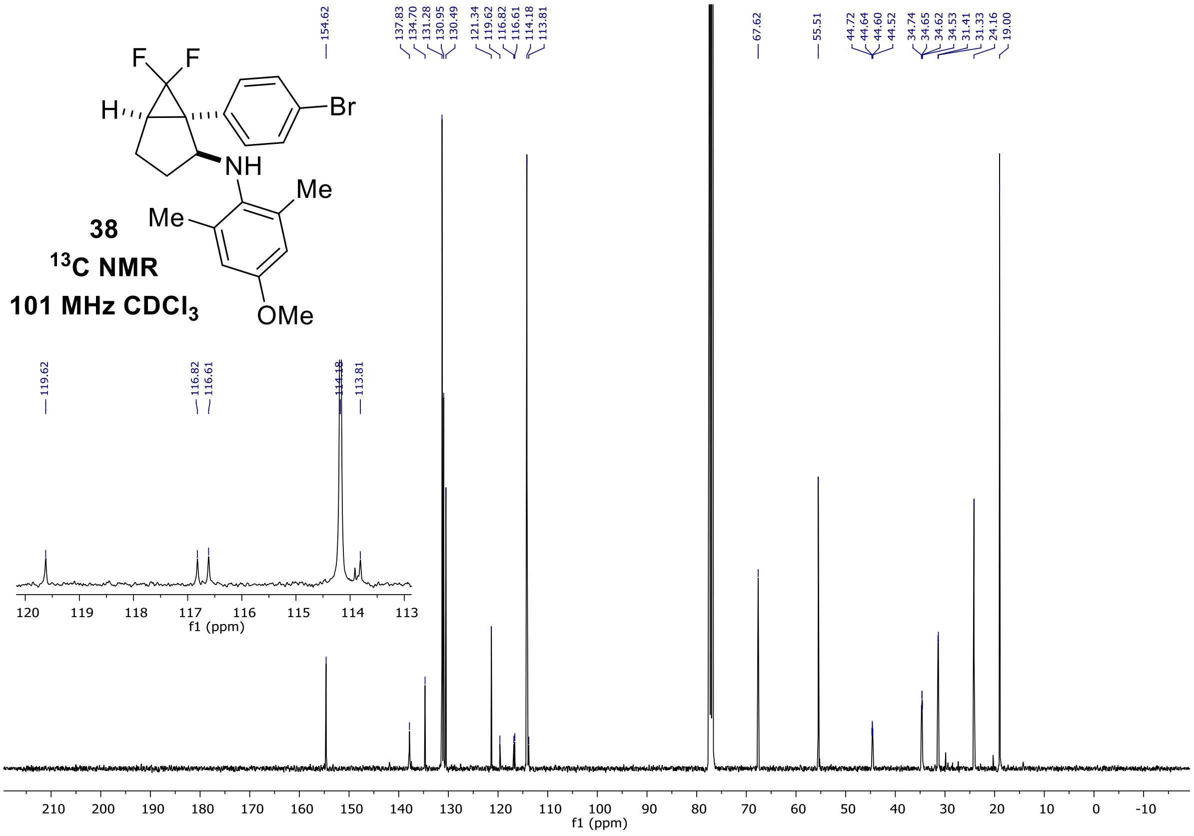


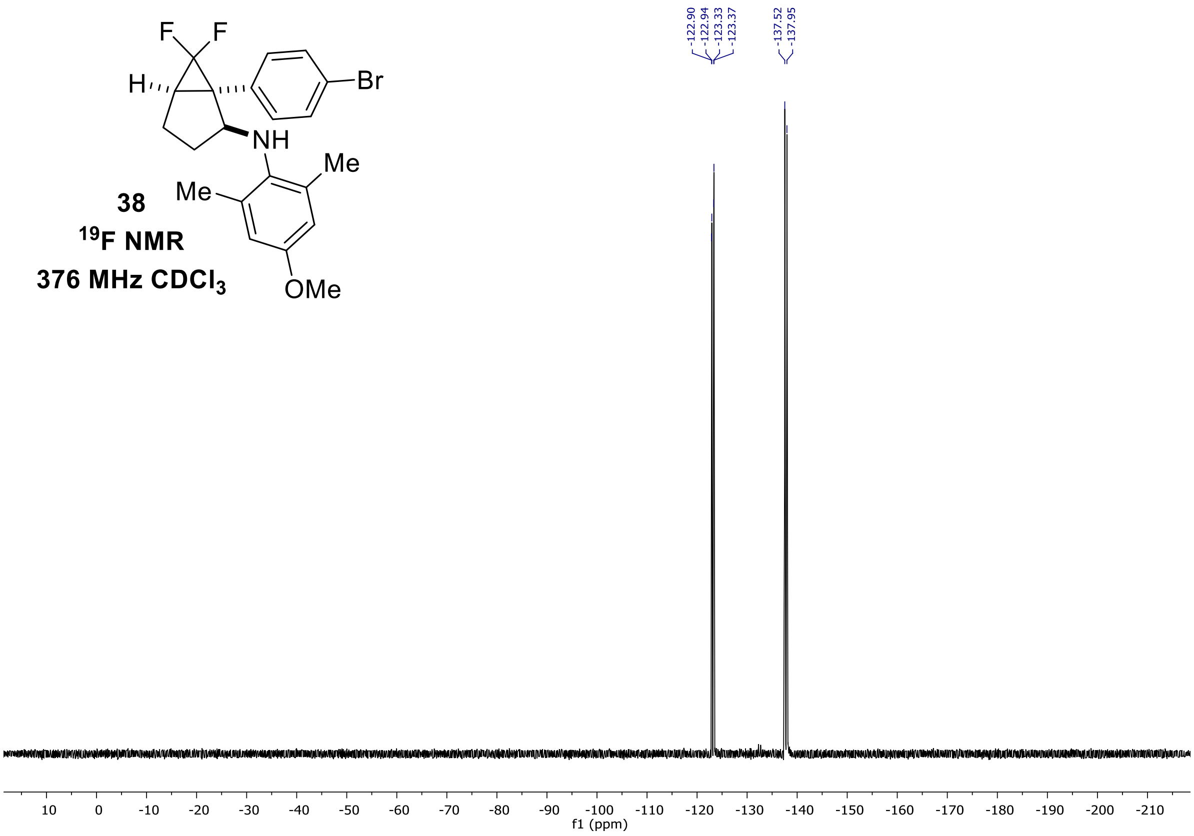
36

^{19}F NMR

376 MHz $CDCl_3$


38
^{1}H NMR
400 MHz CDCl$_3$
F F H Br NH Me Me OMe
7.37 7.35 7.17 7.15
6.43
4.23 4.21 4.20 4.19 4.19 4.17
3.70
3.28
2.25 2.24 2.23 2.22 2.22 2.21 2.21 2.20 2.19 2.16 2.14 2.13 2.12 2.11 2.08 2.06 2.04 2.03 2.02 1.67 1.67 1.66 1.65 1.64 1.64 1.63 1.62 1.61 1.6
1.97 2.00 1.96 1.00 3.03 0.67 3.05 7.05 1.06
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

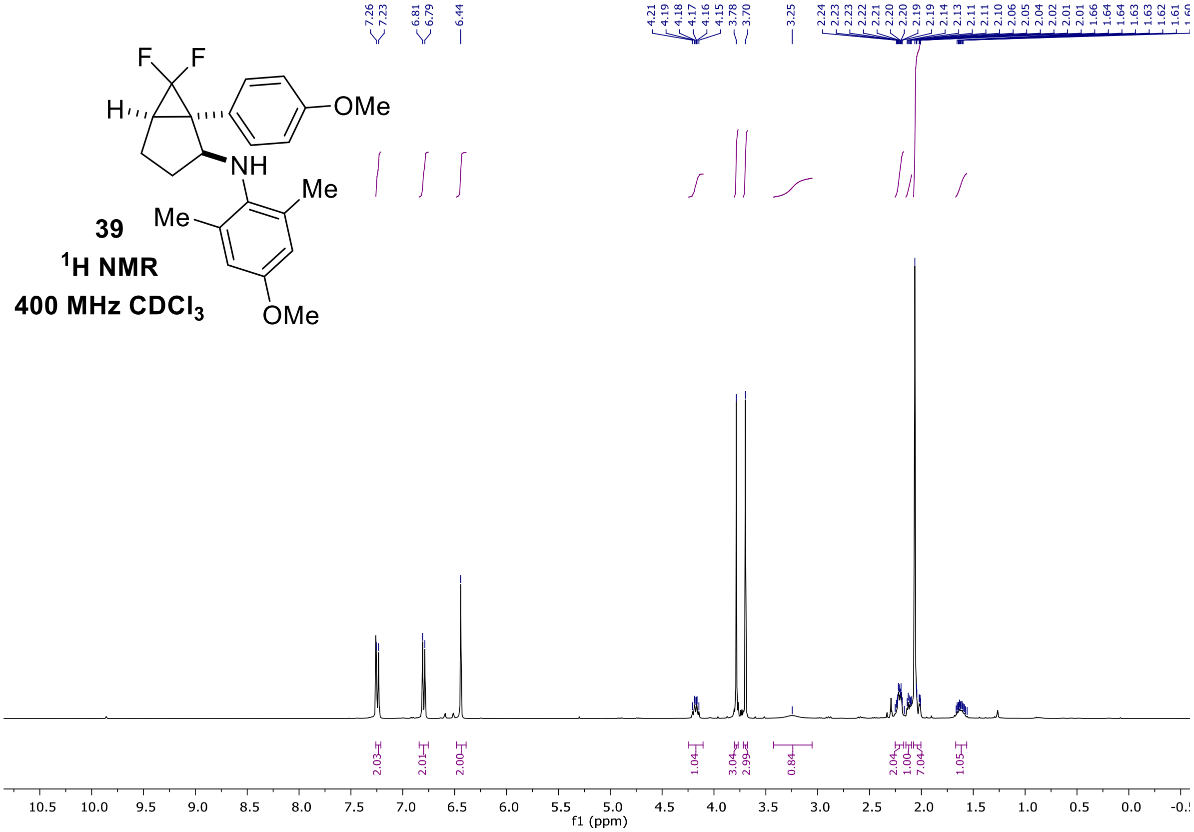

38
^{13}C NMR
101 MHz CDCl$_3$
F F H Br NH Me Me OMe
154.62
137.83 134.70 131.28 130.95 130.49 121.34 119.62 116.82 116.61 114.18 113.81
67.62
55.51
44.72 44.64 44.60 44.52 34.74 34.65 34.62 34.53 31.41 31.33 24.16 19.00
119.62 116.82 116.61 114.18 113.81
120 119 118 117 116 115 114 113
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



38

^{19}F NMR

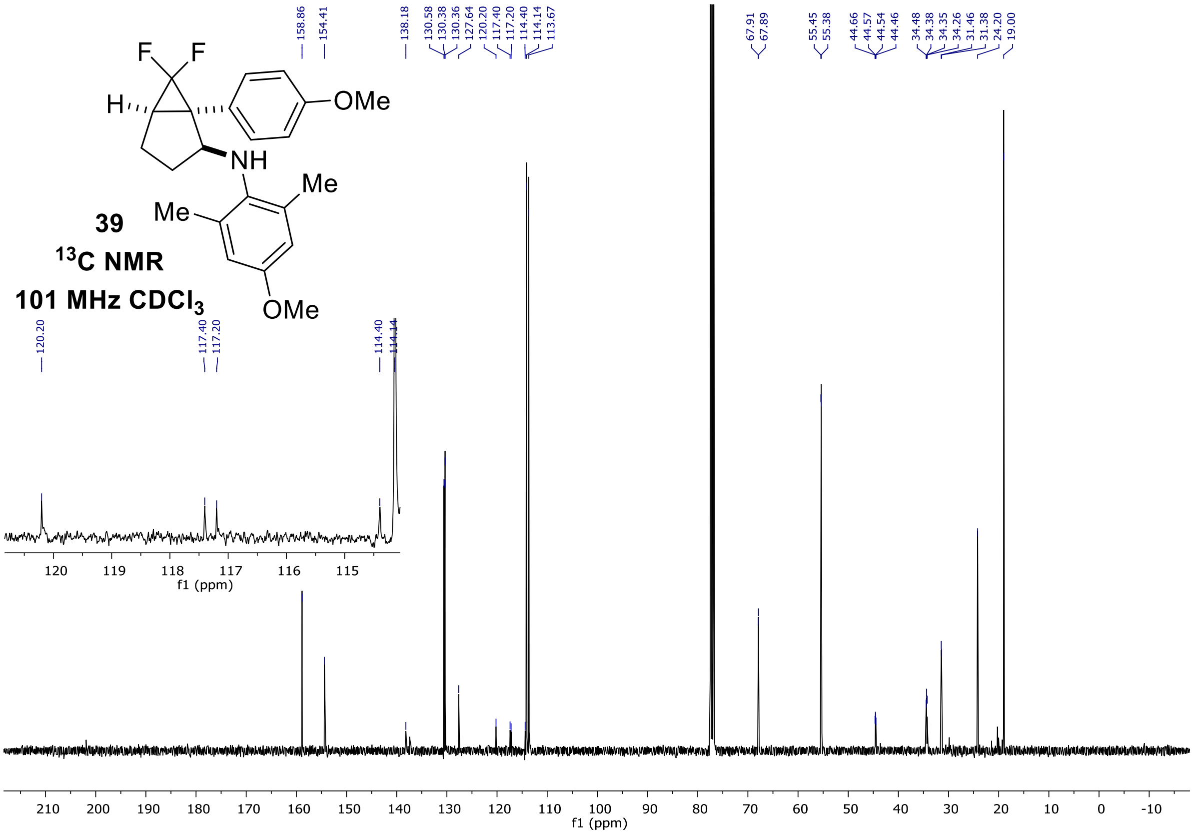
376 MHz $CDCl_3$



39

^{1}H NMR

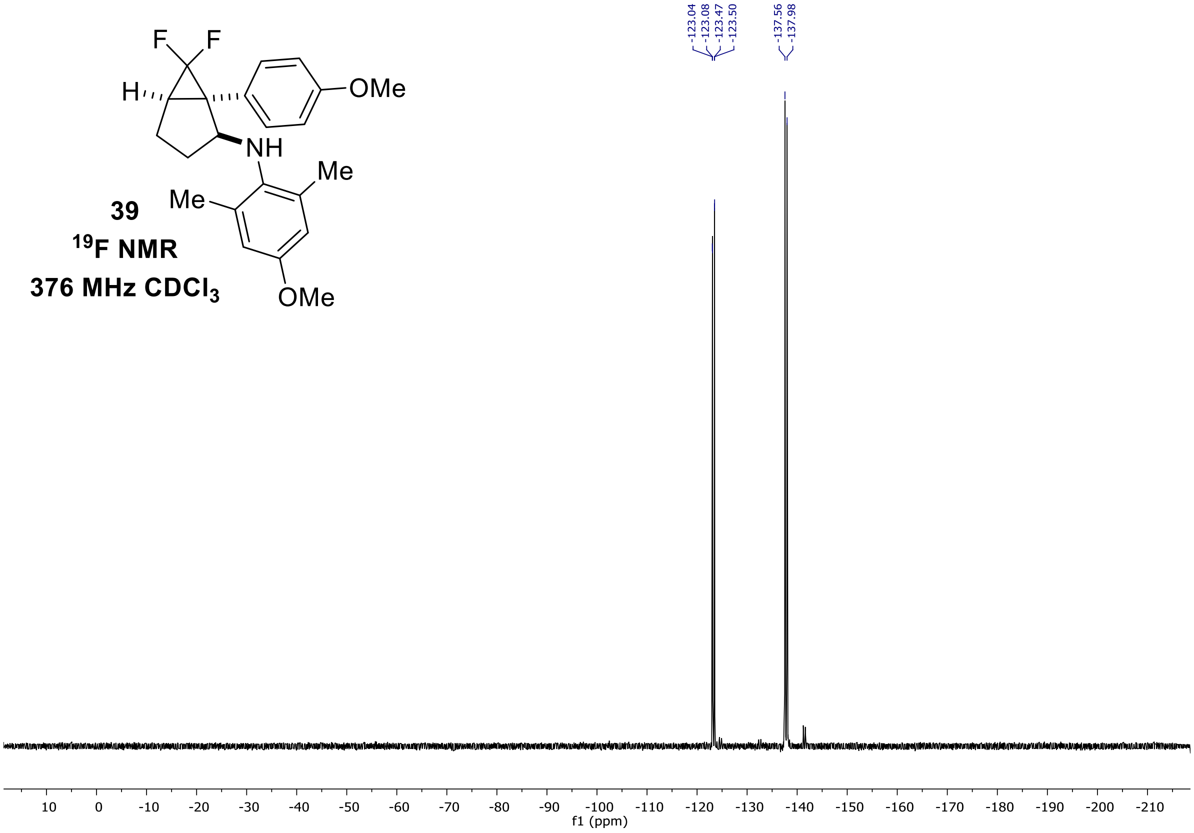
400 MHz CDCl$_3$



39

^{13}C NMR

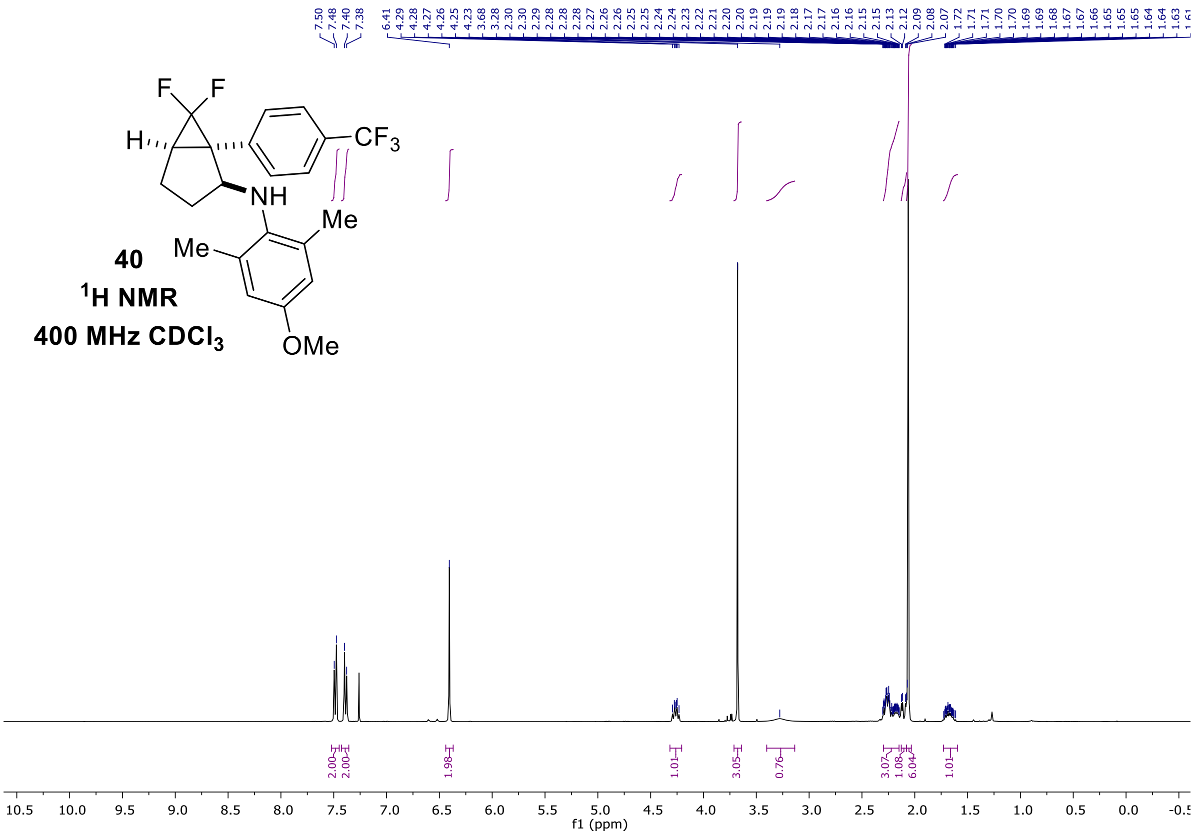
101 MHz CDCl$_3$



39

^{19}F NMR

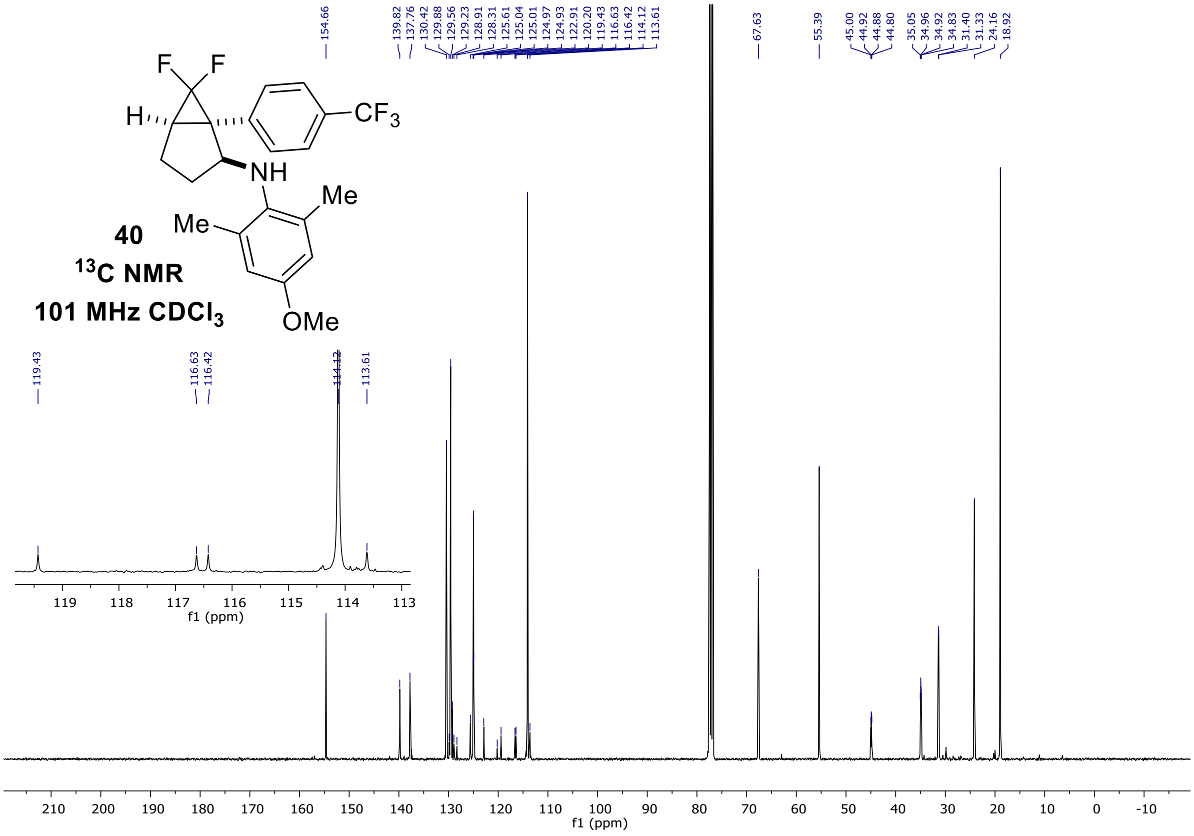
376 MHz $CDCl_3$



40

^{1}H NMR

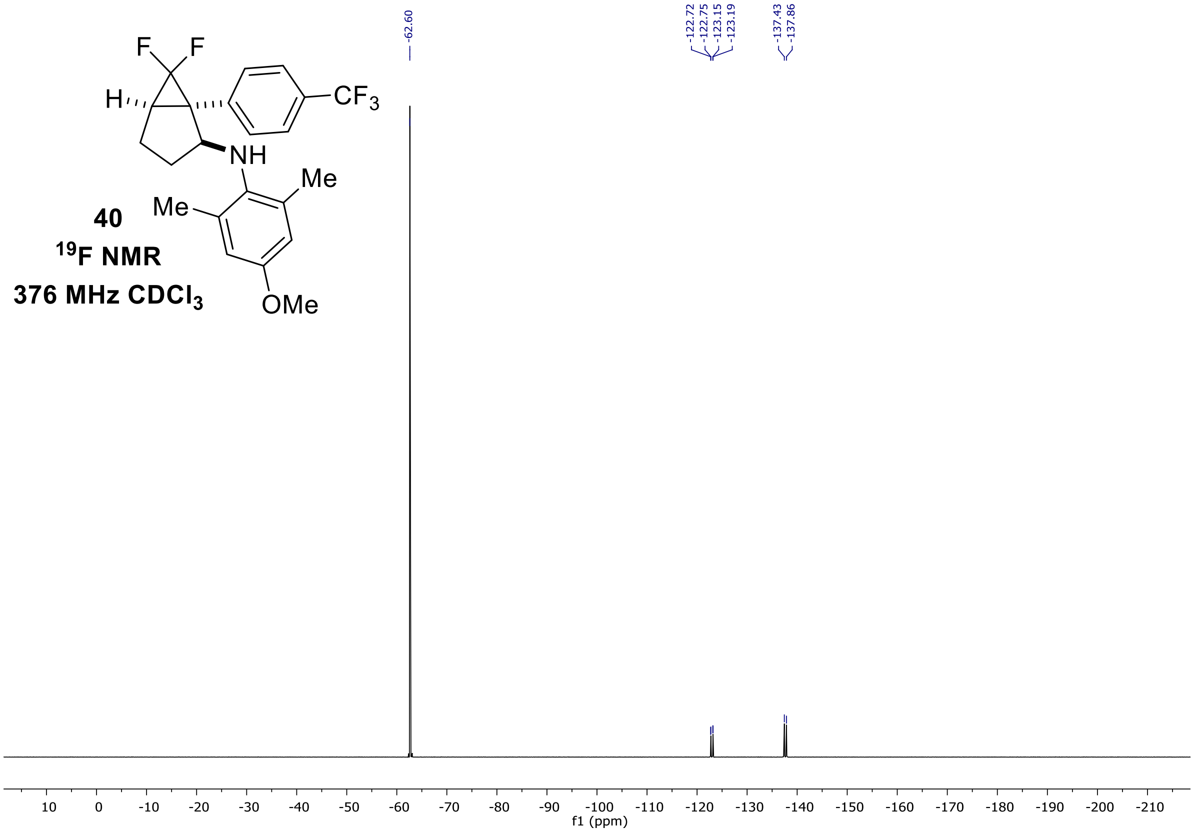
400 MHz $CDCl_3$



40

^{13}C NMR

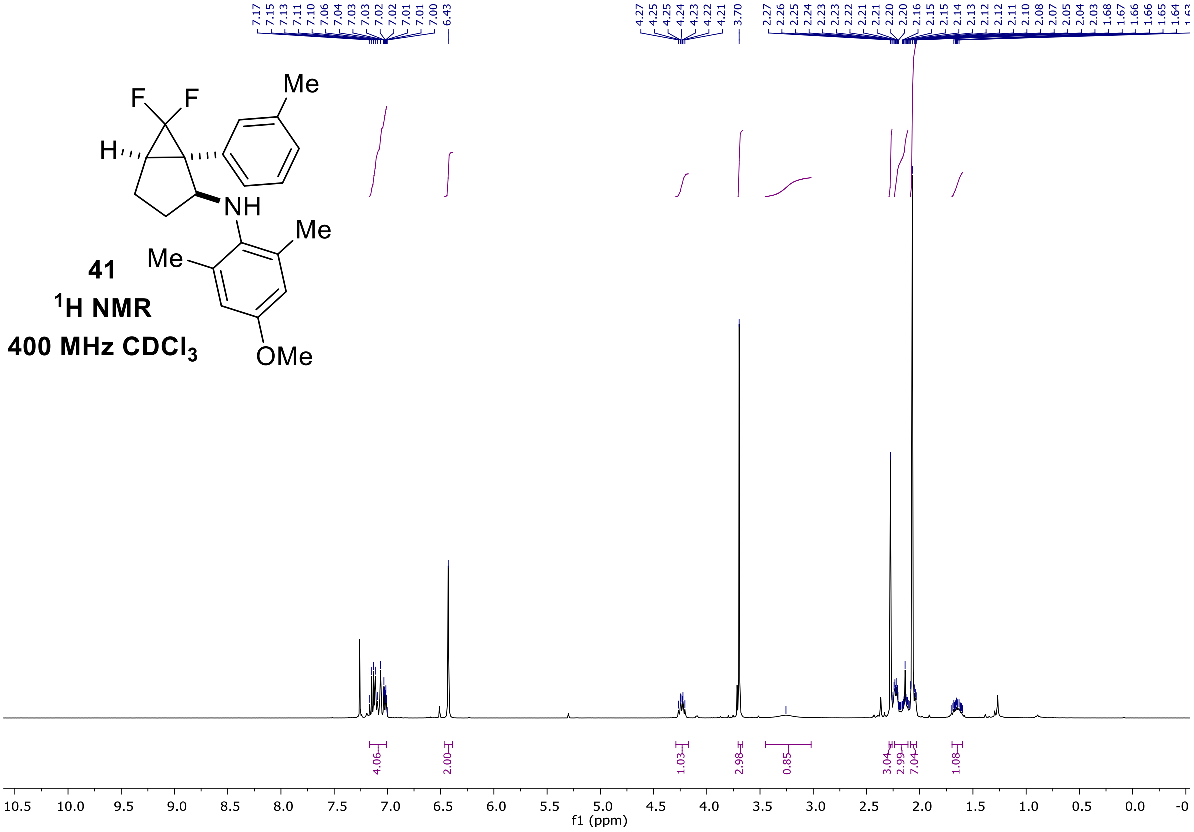
101 MHz $CDCl_3$



40

^{19}F NMR

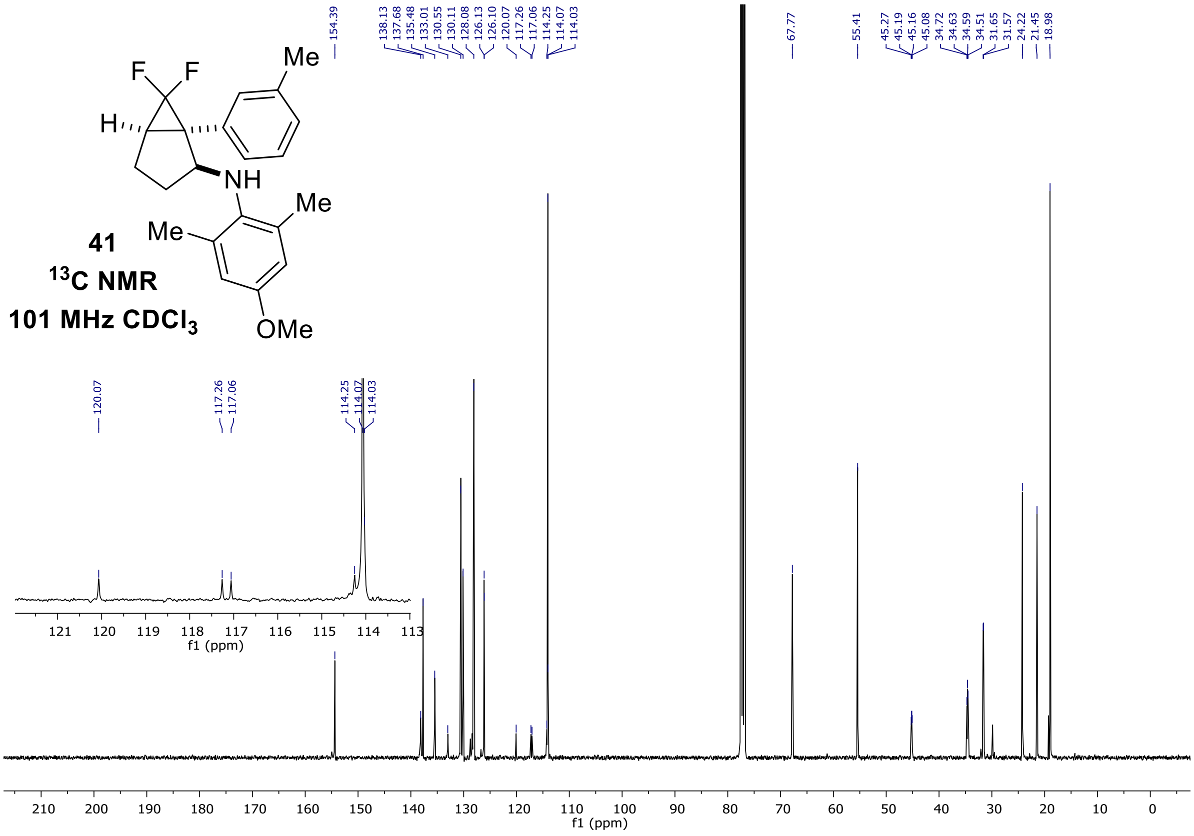
376 MHz $CDCl_3$



41

^{1}H NMR

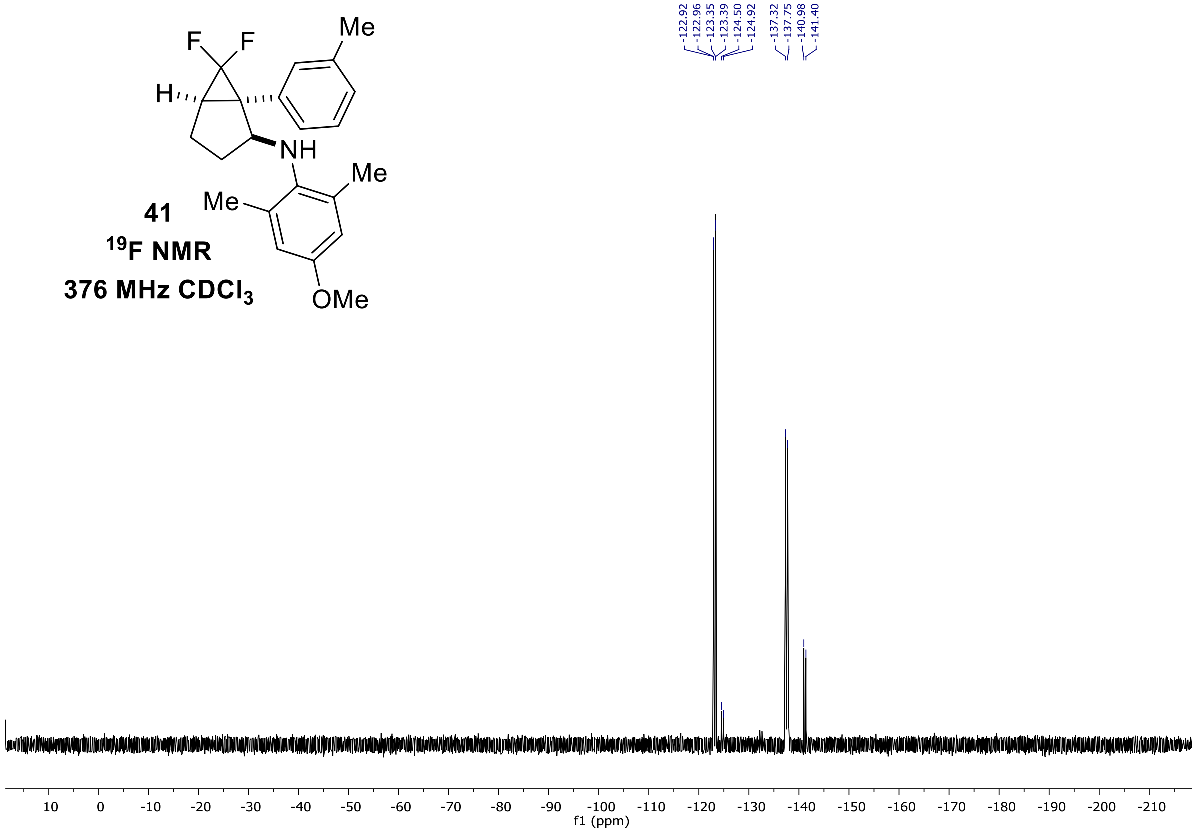
400 MHz CDCl$_3$



41

^{13}C NMR

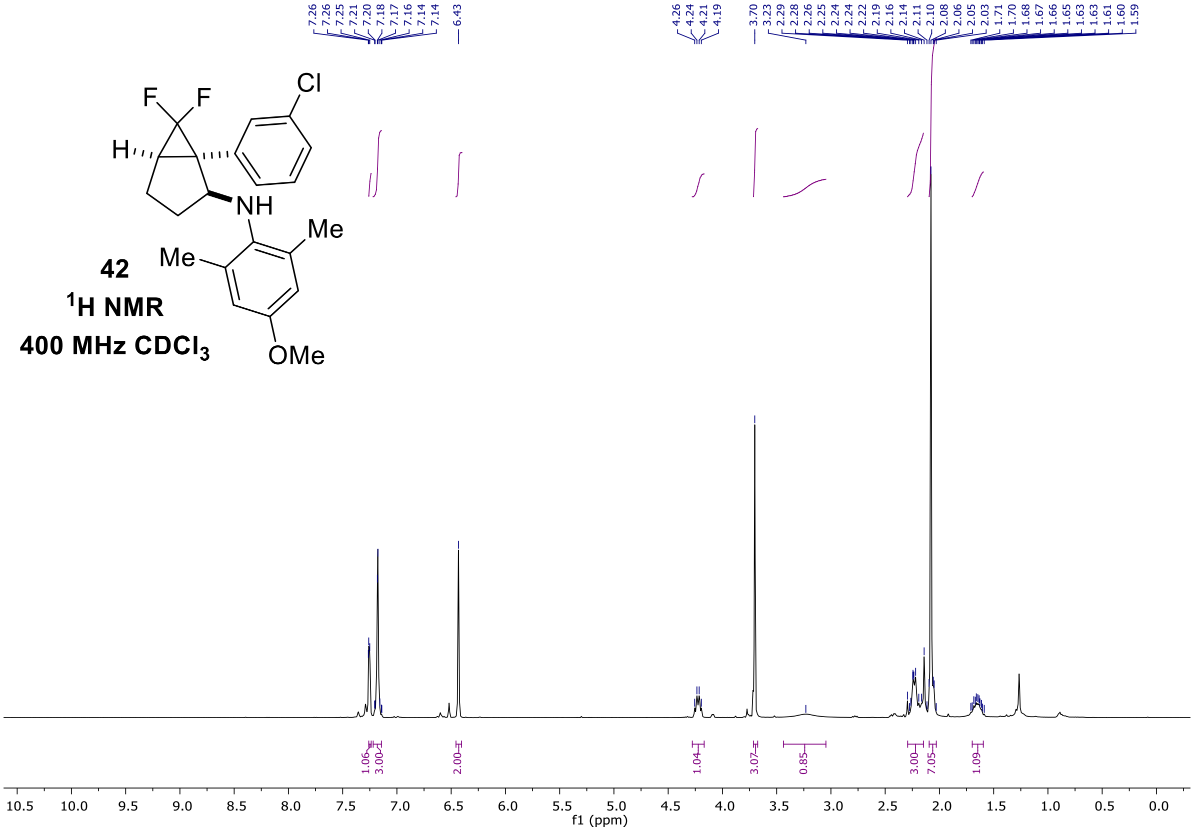
101 MHz CDCl$_3$



41

^{19}F NMR

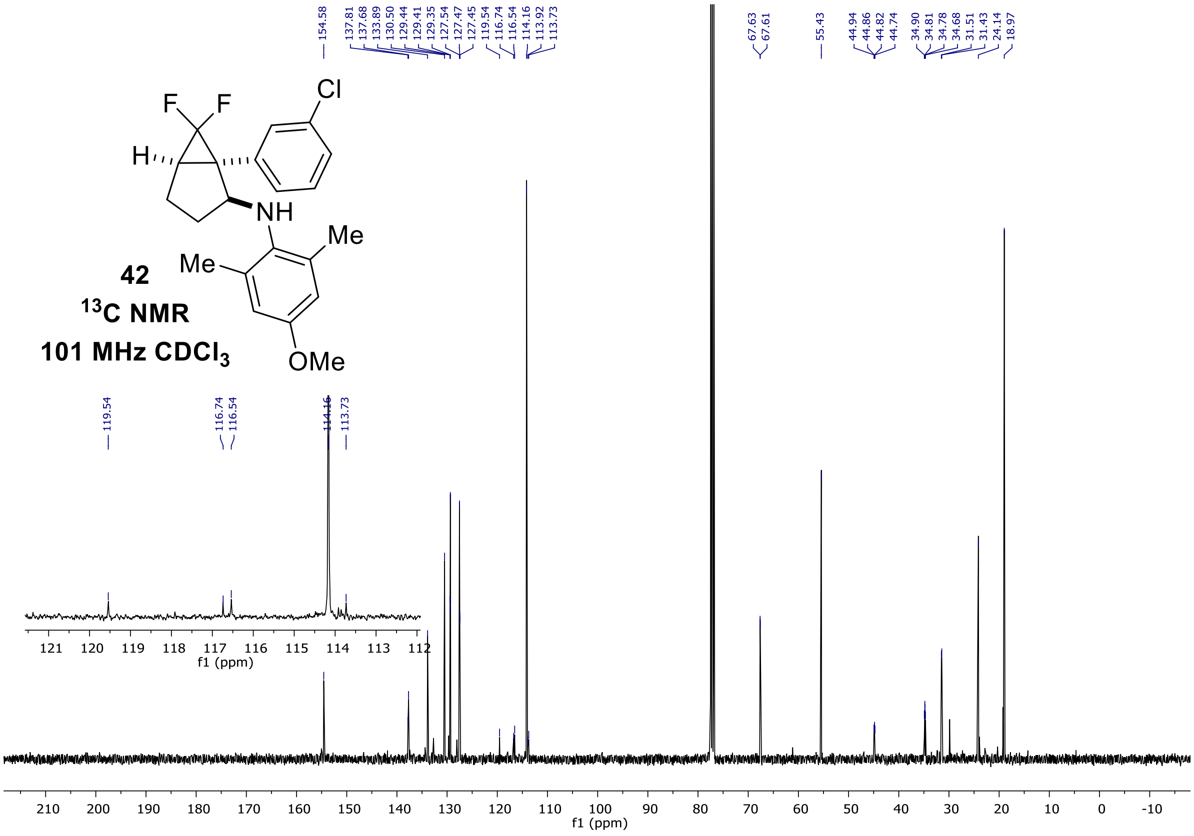
376 MHz $CDCl_3$



42

^{1}H NMR

400 MHz CDCl$_3$



42

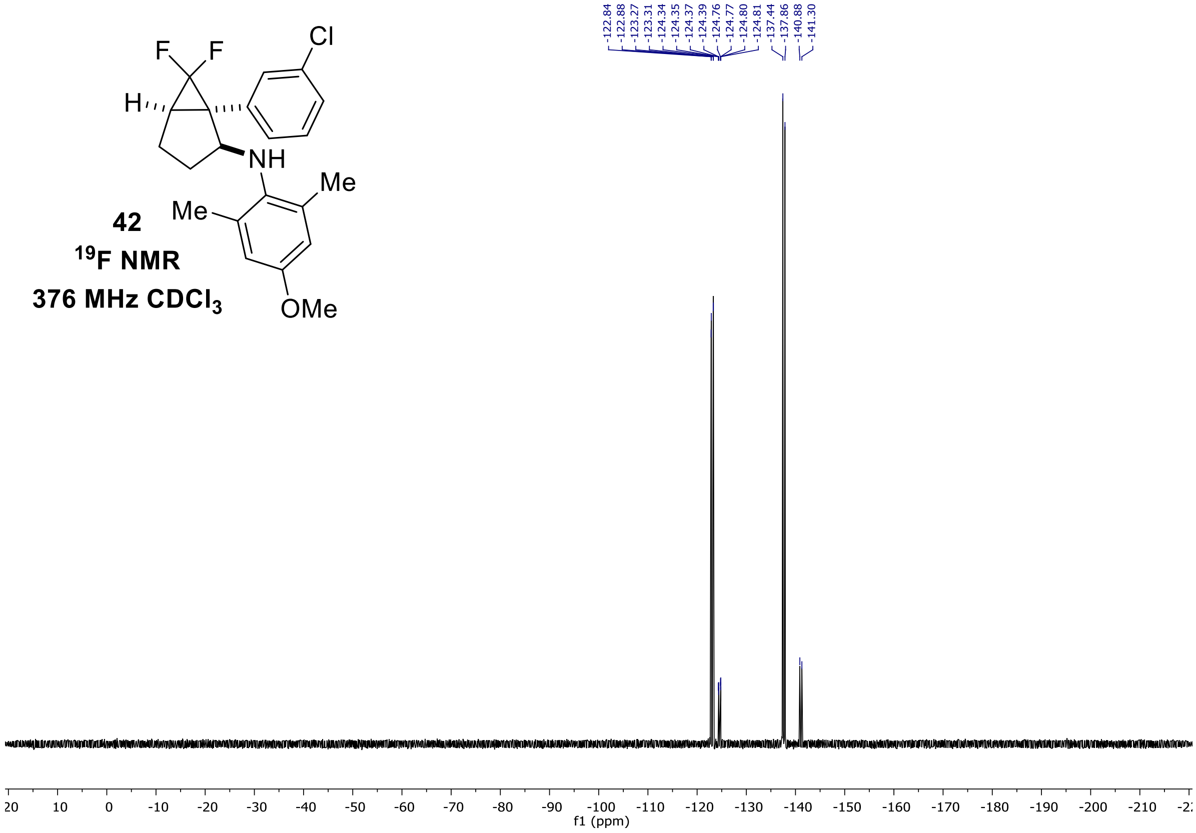
^{13}C NMR

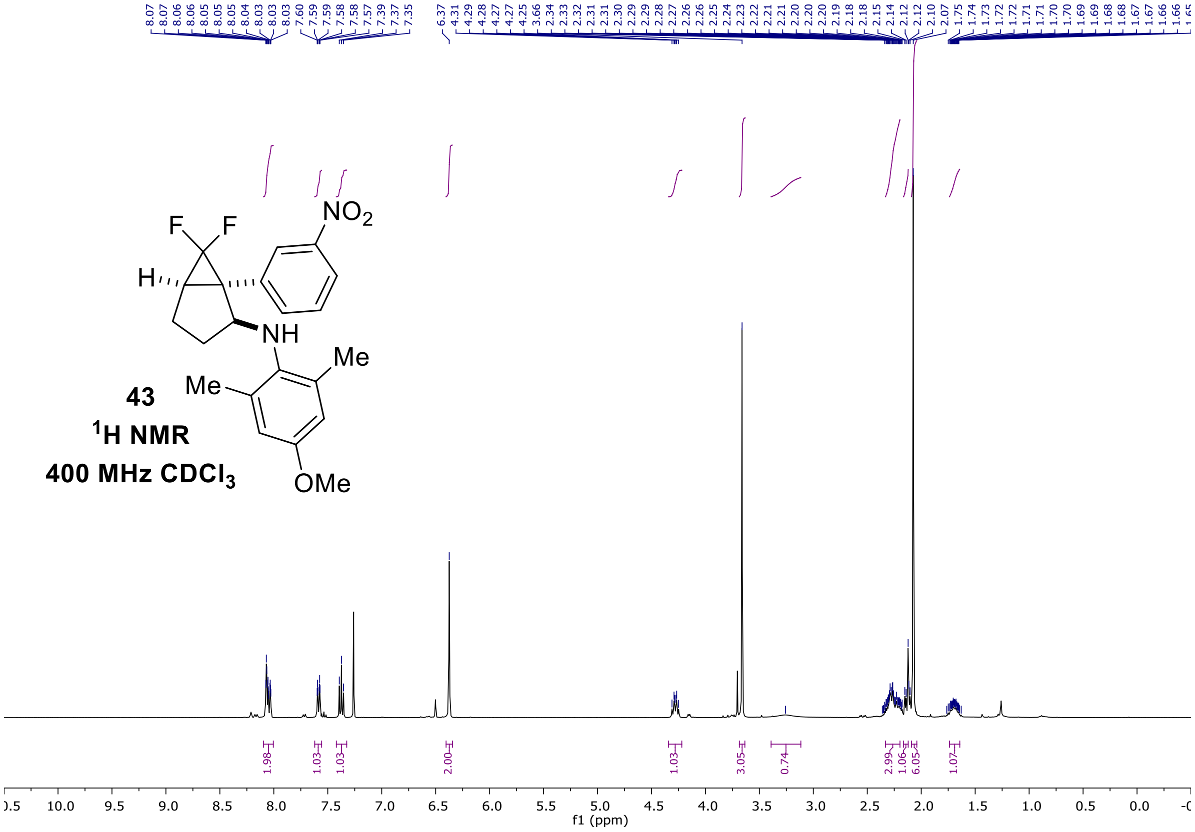
101 MHz CDCl$_3$

42

^{19}F NMR

376 MHz $CDCl_3$




8.07
8.07
8.06
8.06
8.05
8.05
8.04
8.03
8.03
8.03
7.60
7.59
7.59
7.58
7.58
7.57
7.39
7.37
7.35
6.37
4.31
4.29
4.28
4.27
4.27
4.25
3.66
2.34
2.33
2.32
2.31
2.31
2.30
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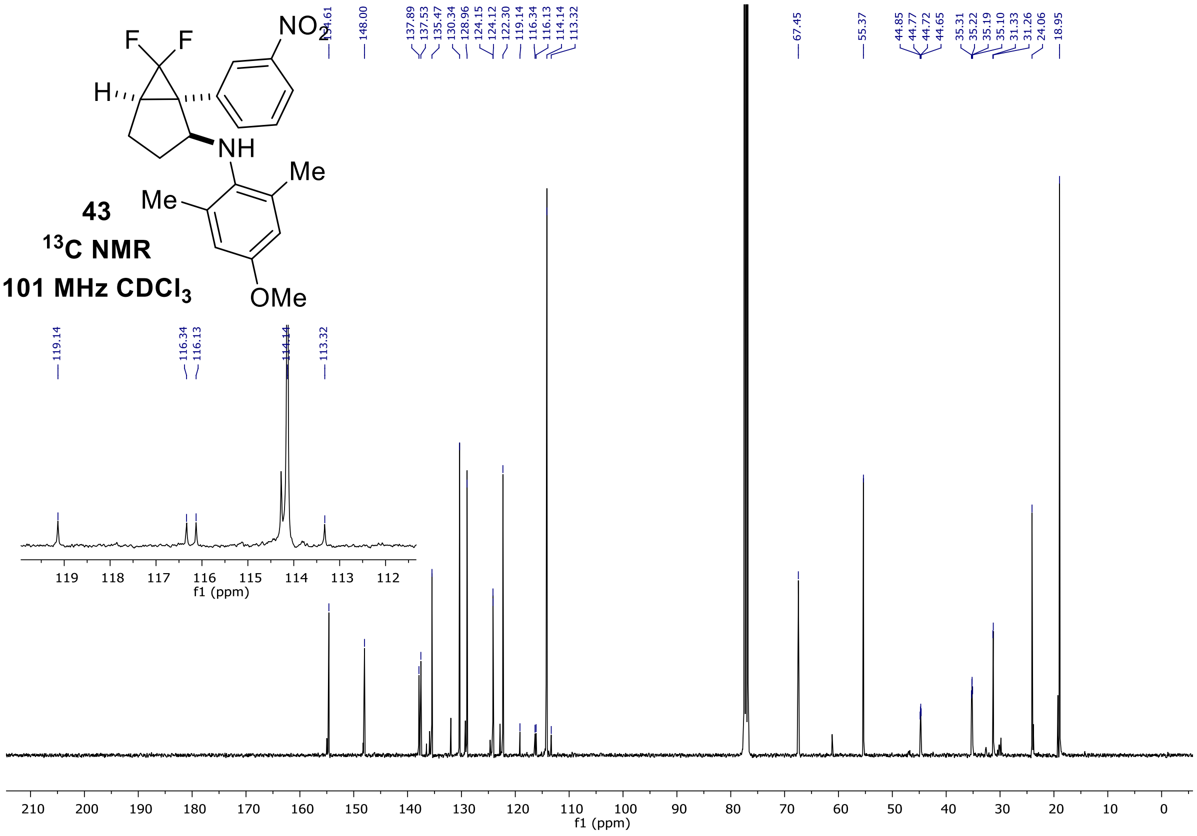
2.28
2.27
2.26
2.26
2.25
2.24
2.23
2.22
2.21
2.21
2.20
2.20
2.19
2.18
2.18
2.15
2.14
2.12
2.12
2.10
2.07
1.75
1.74
1.73
1.72
1.72
1.71
1.71
1.70
1.69
1.68
1.68
1.67
1.66
1.66
F
F
NO2
H
NH
Me
Me
OMe
43
1H NMR
400 MHz CDCl3
1.98
1.03
1.03
2.00
1.03
3.05
0.74
2.99
1.06
6.05
1.07
.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


154.61
148.00
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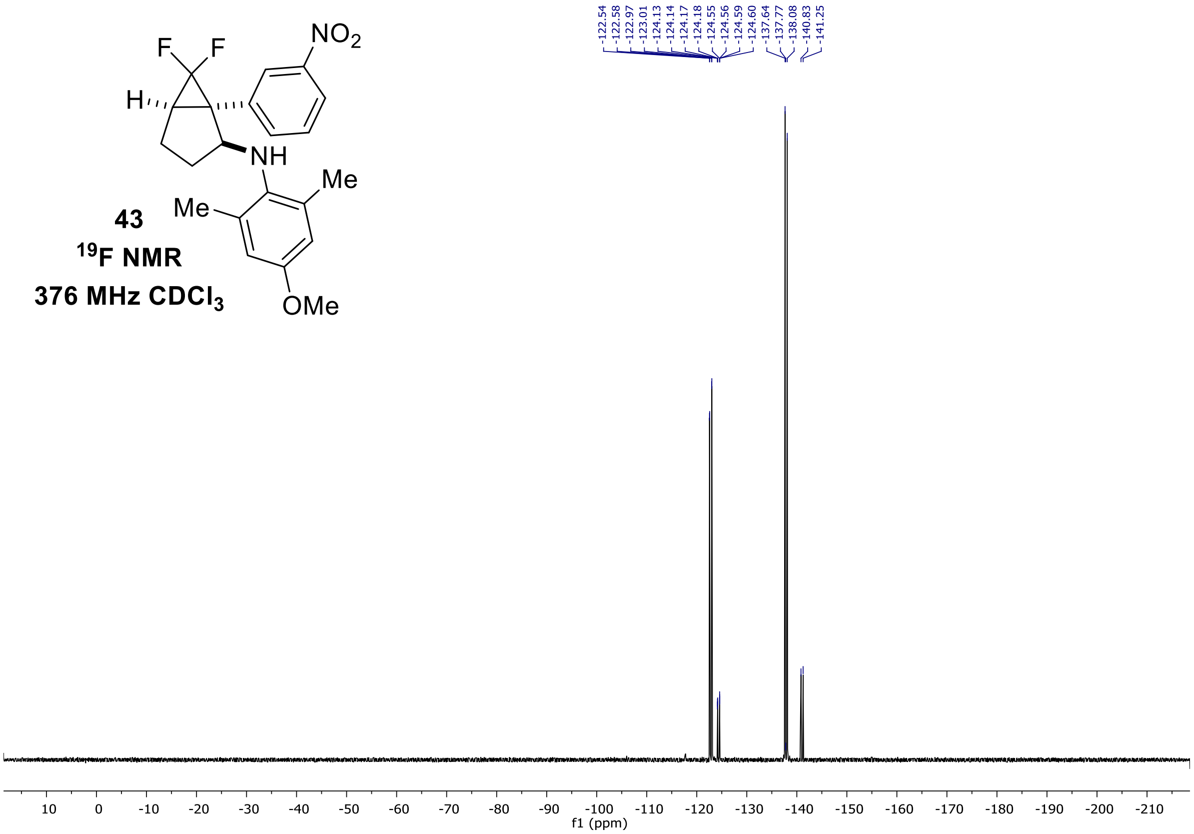
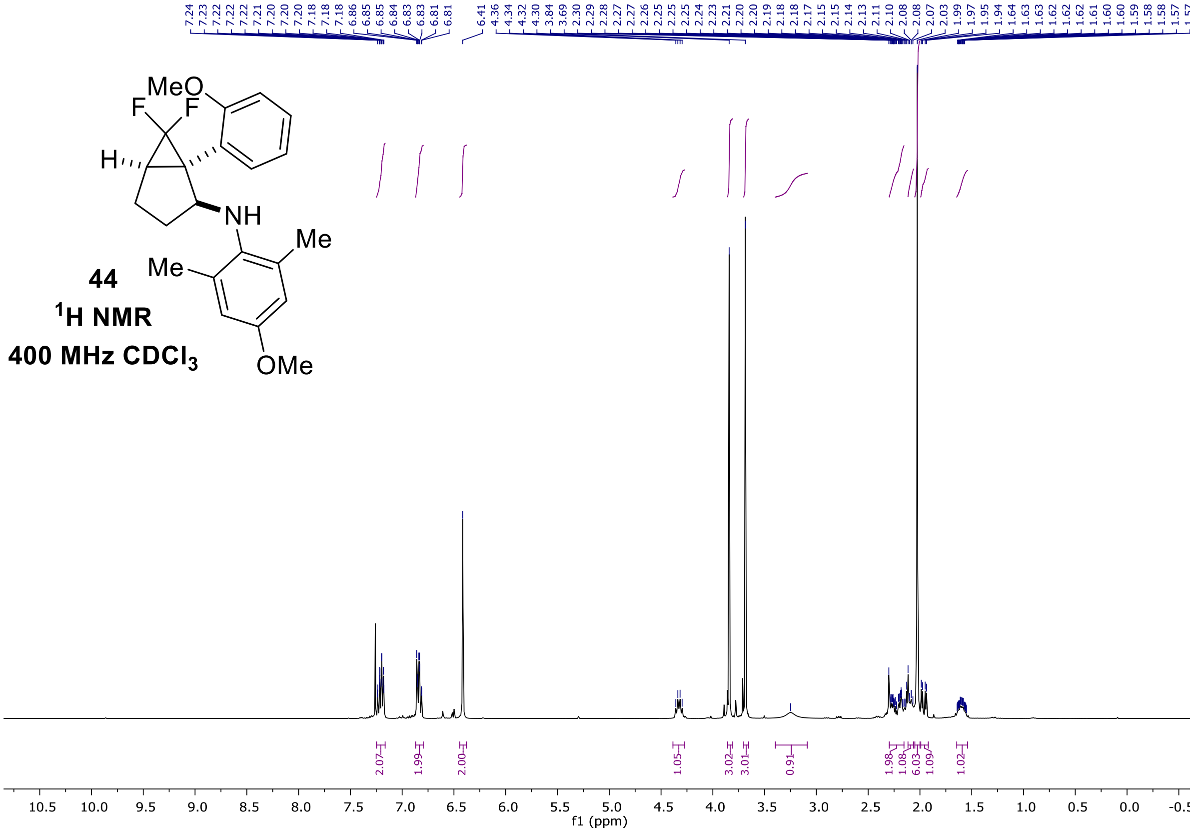
130.34
128.96
124.15
124.12
122.30
119.14
116.34
116.13
114.14
113.32
67.45
55.37
44.85
44.77
44.72
44.65
35.31
35.22
35.19
35.10
31.33
31.26
24.06
18.95
F
F
NO2
H
NH
Me
Me
OMe
43
13C NMR
101 MHz CDCl3
119.14
116.34
116.13
114.14
113.32
119
118
117
116
115
114
113
112
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



43

^{19}F NMR

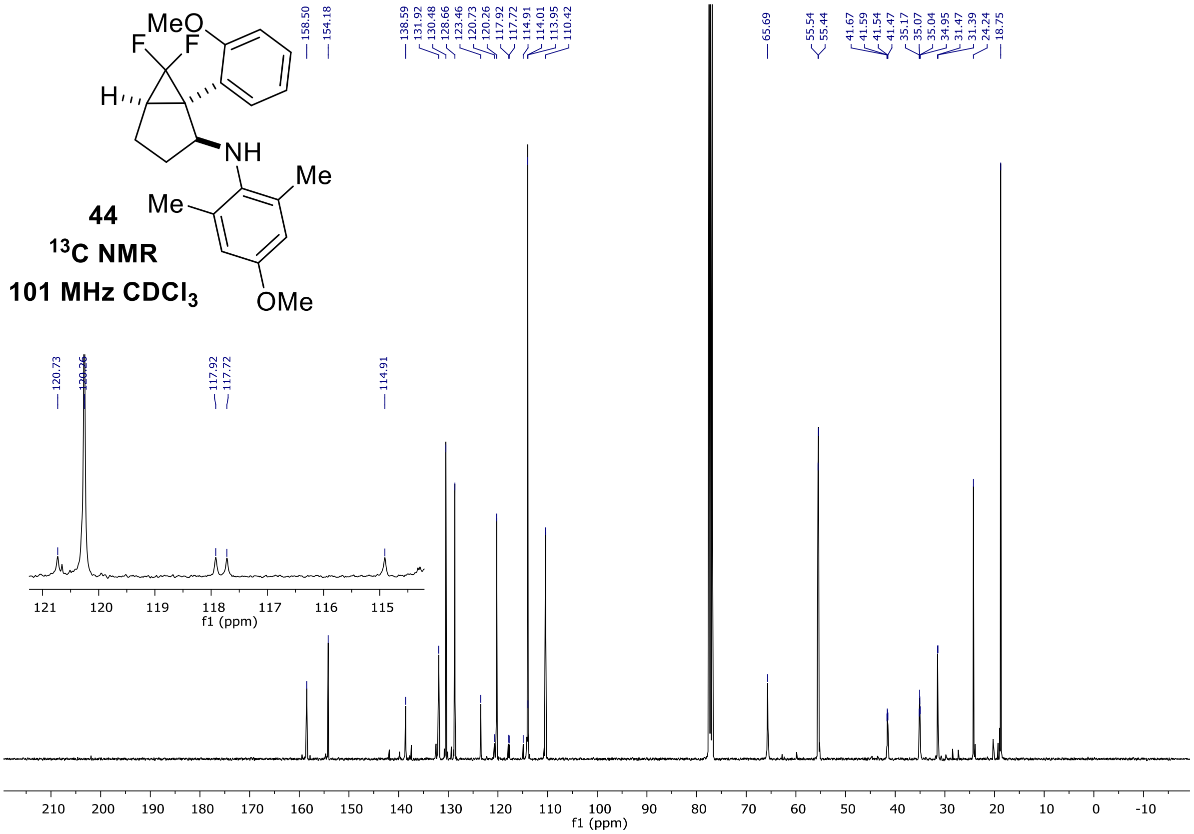
376 MHz $CDCl_3$



44

^{1}H NMR

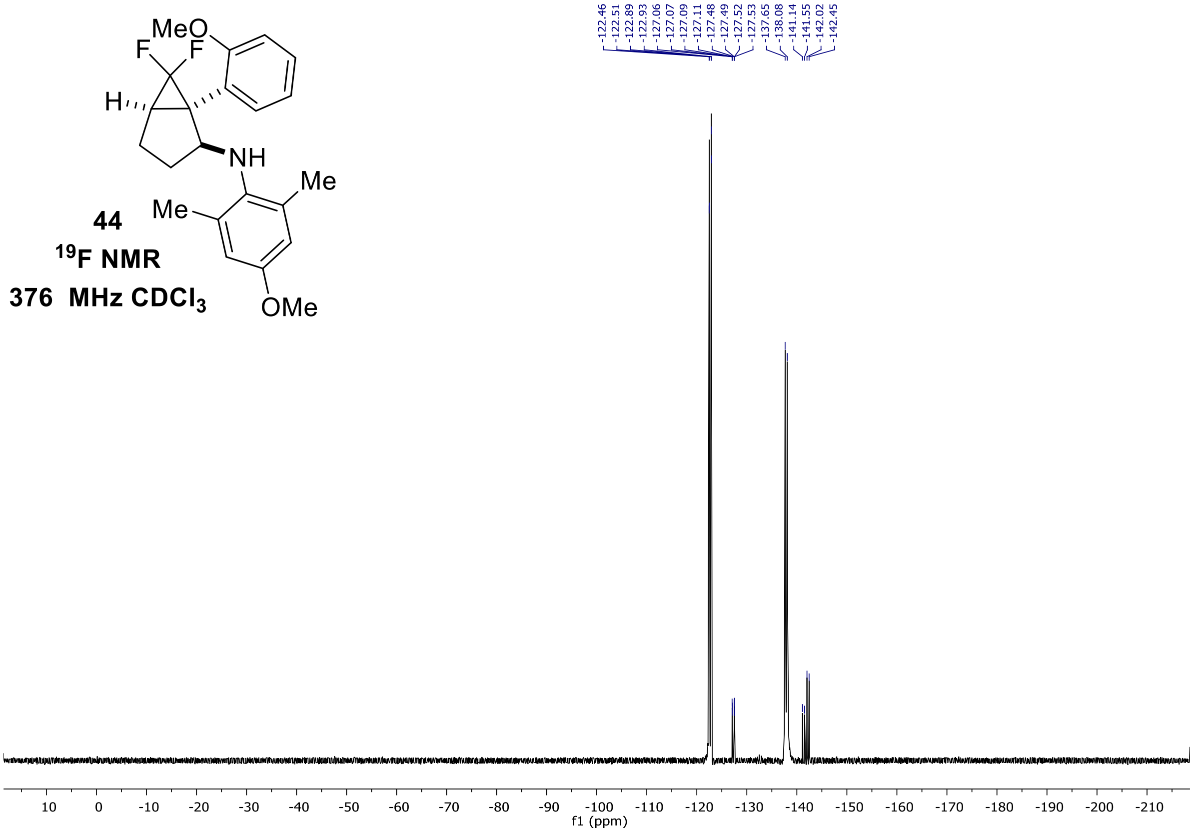
400 MHz CDCl$_3$



44

^{13}C NMR

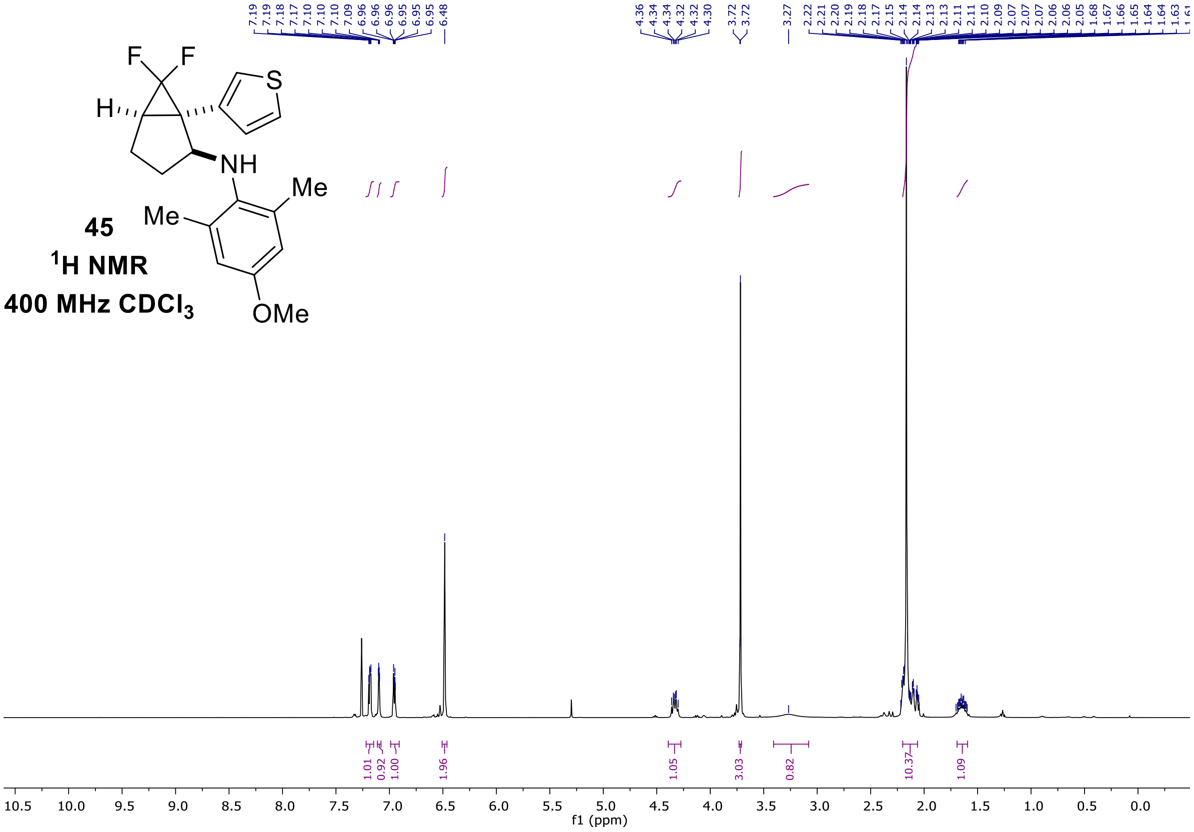
101 MHz CDCl$_3$



44

^{19}F NMR

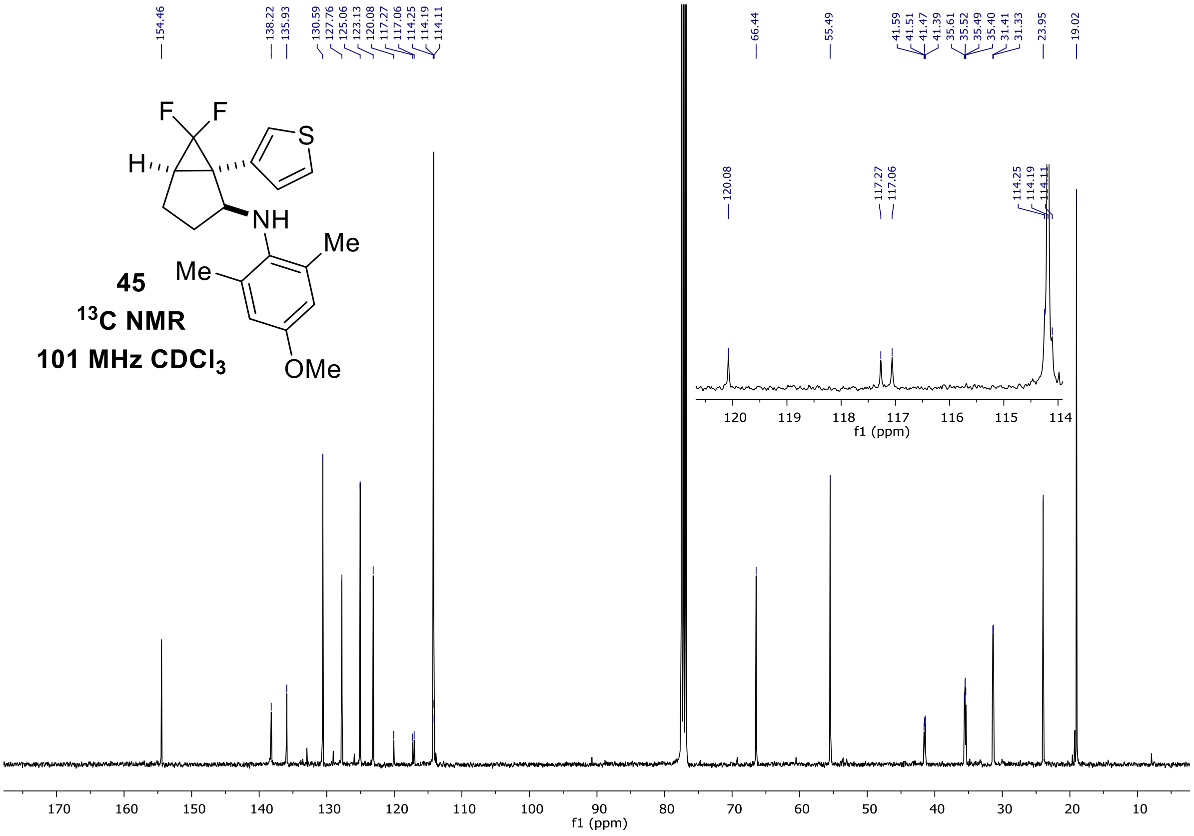
376 MHz $CDCl_3$



45

^{1}H NMR

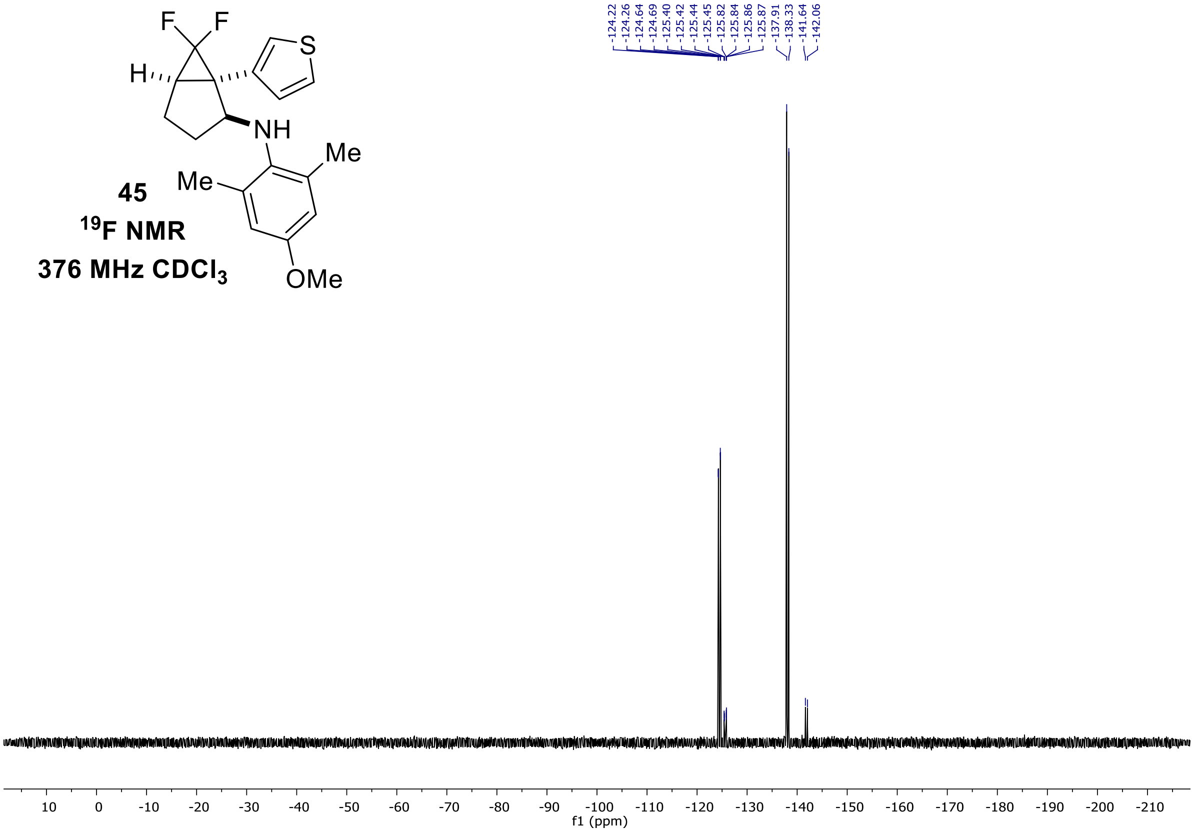
400 MHz CDCl$_3$



45

^{13}C NMR

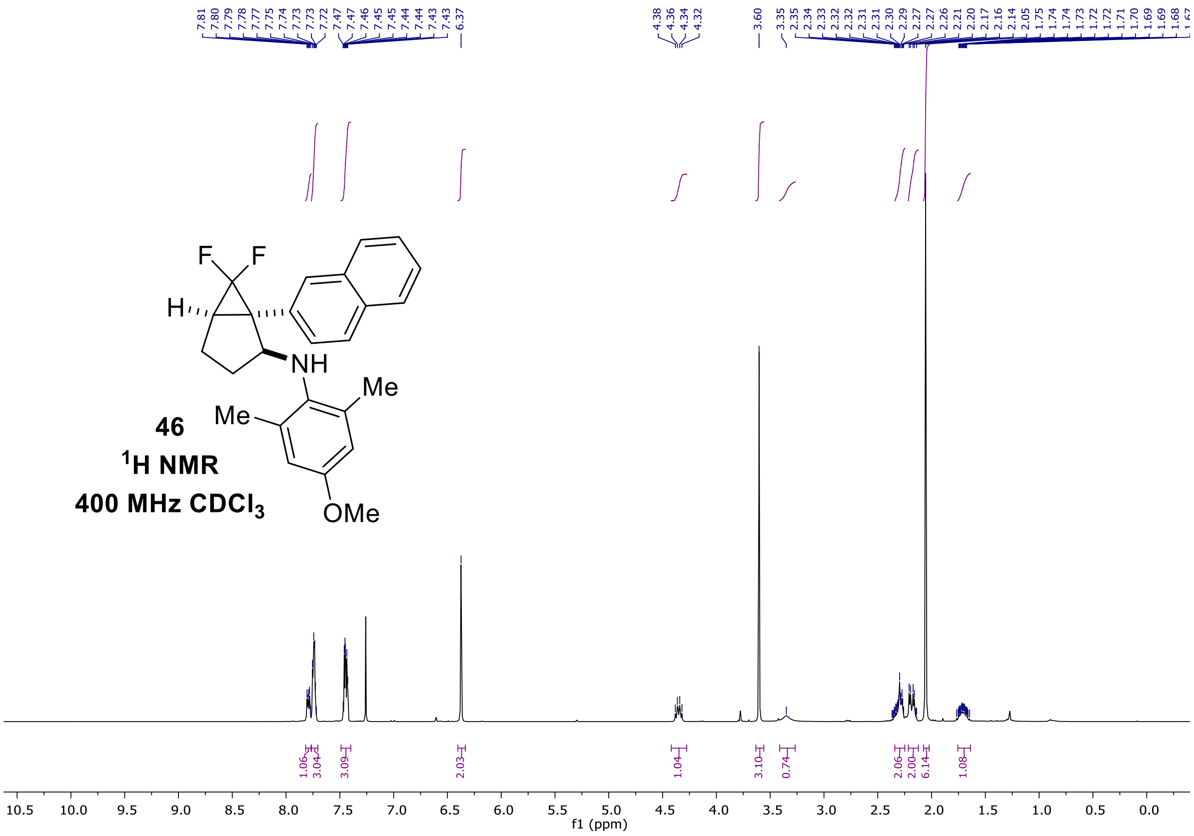
101 MHz CDCl$_3$

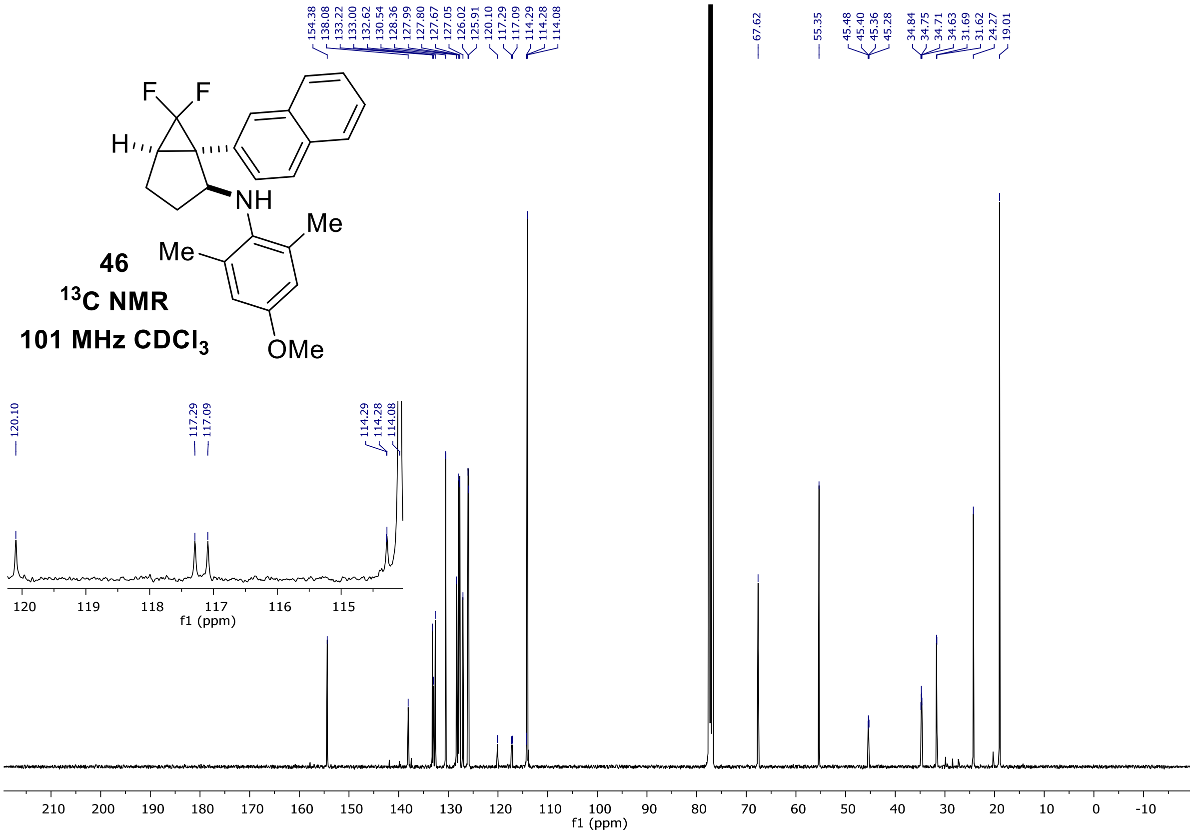


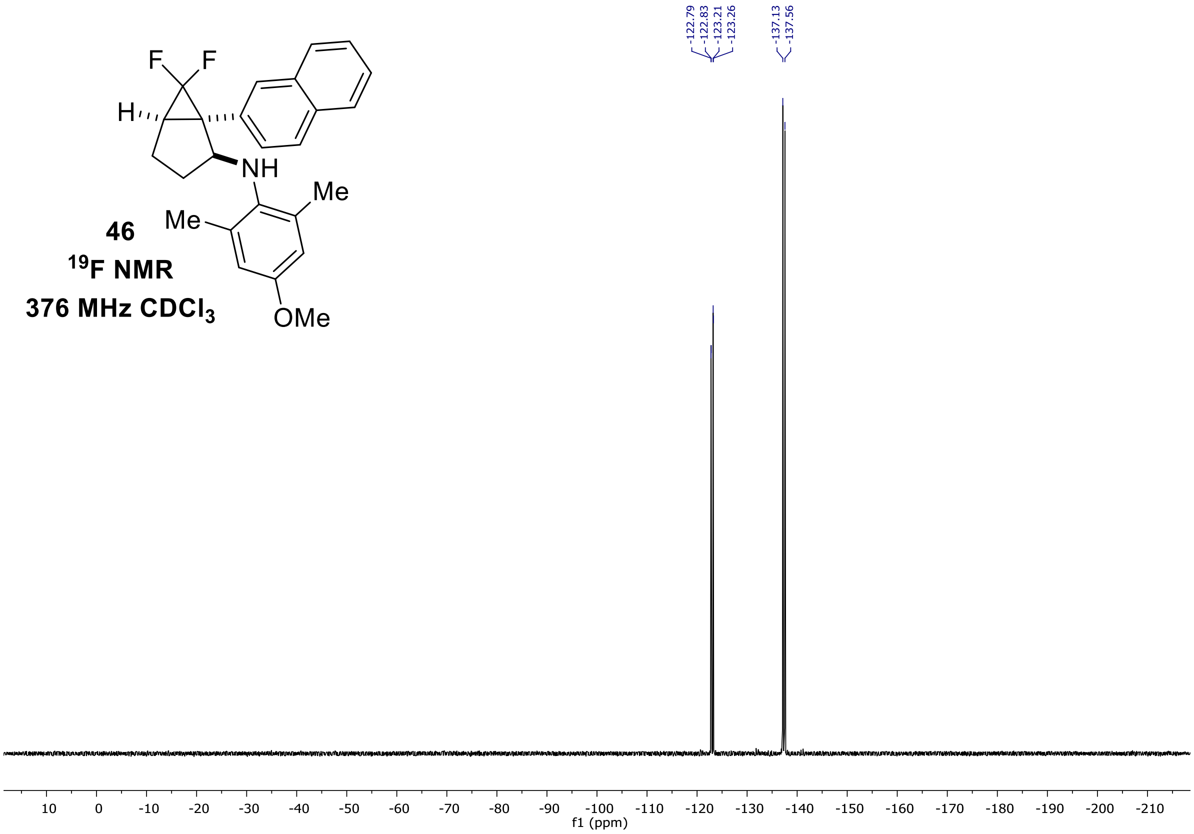
45

^{19}F NMR

376 MHz CDCl$_3$


46
^{1}H NMR
400 MHz $CDCl_3$

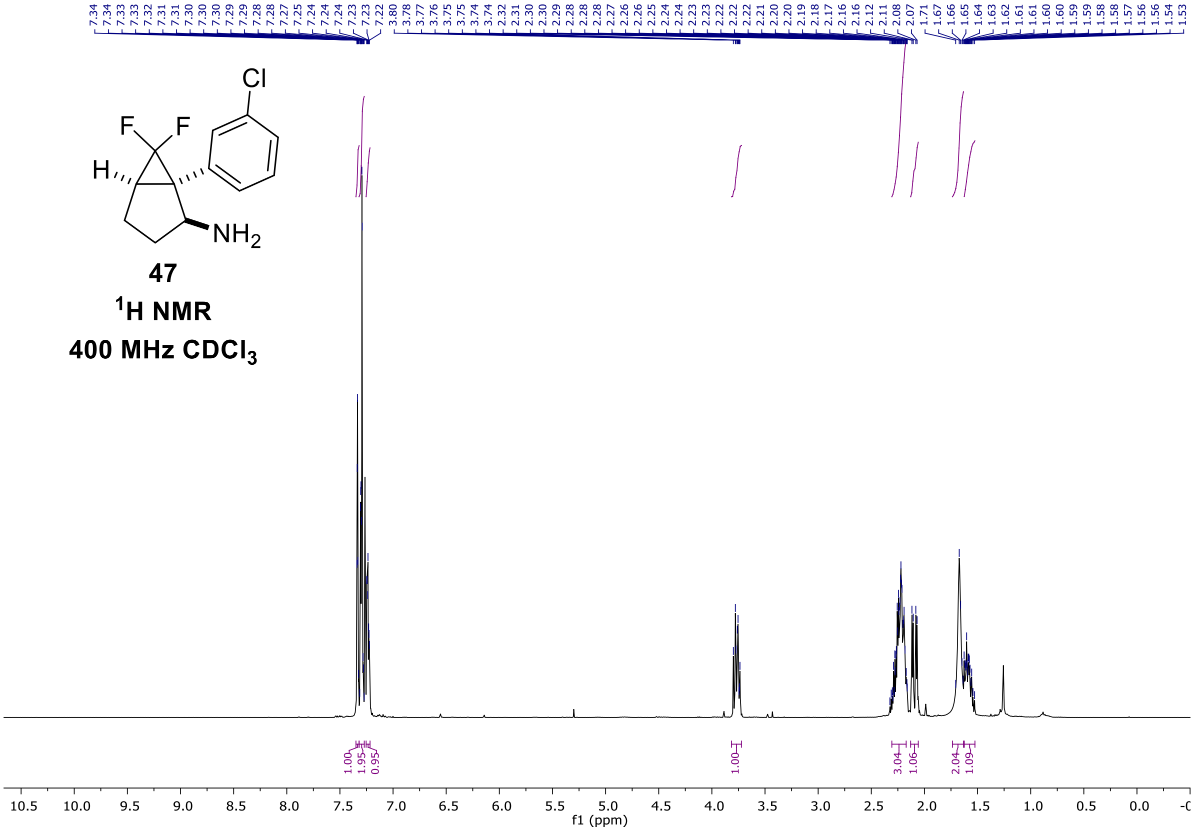

46
^{13}C NMR
101 MHz $CDCl_3$



46

^{19}F NMR

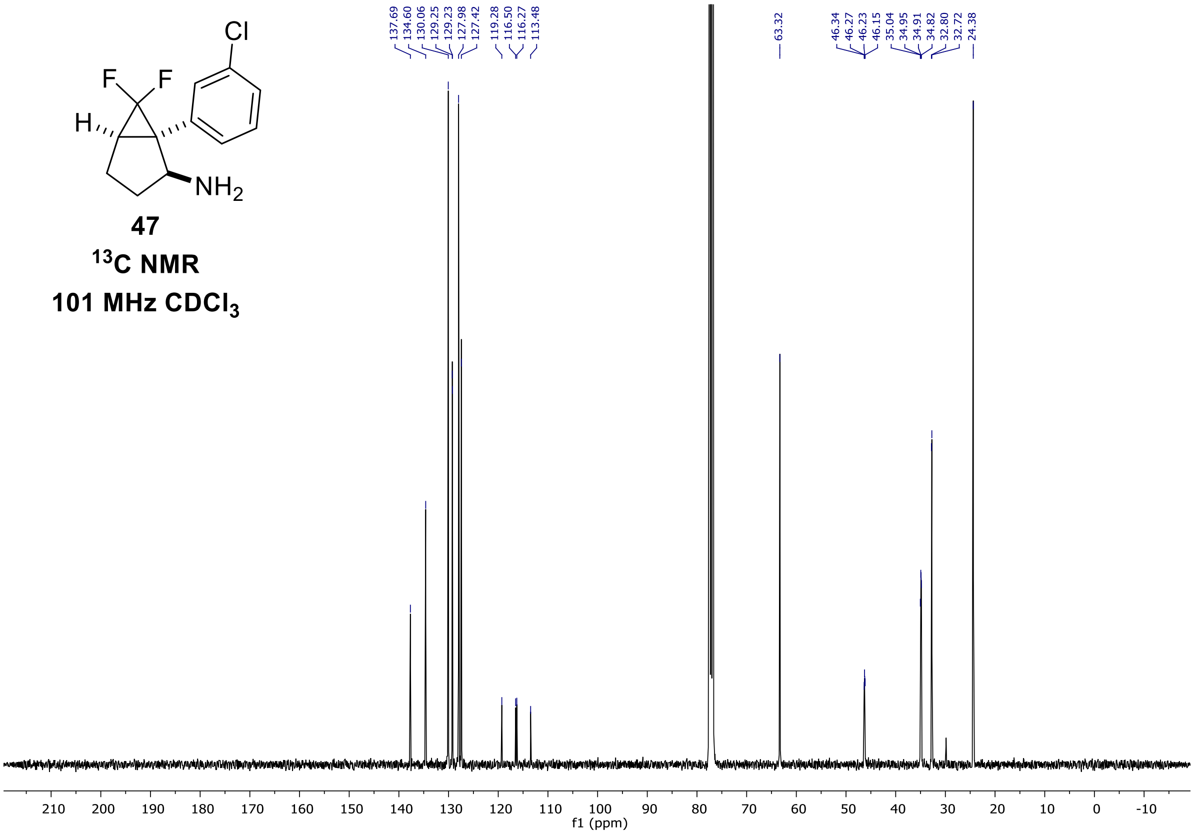
376 MHz CDCl$_3$



47

^{1}H NMR

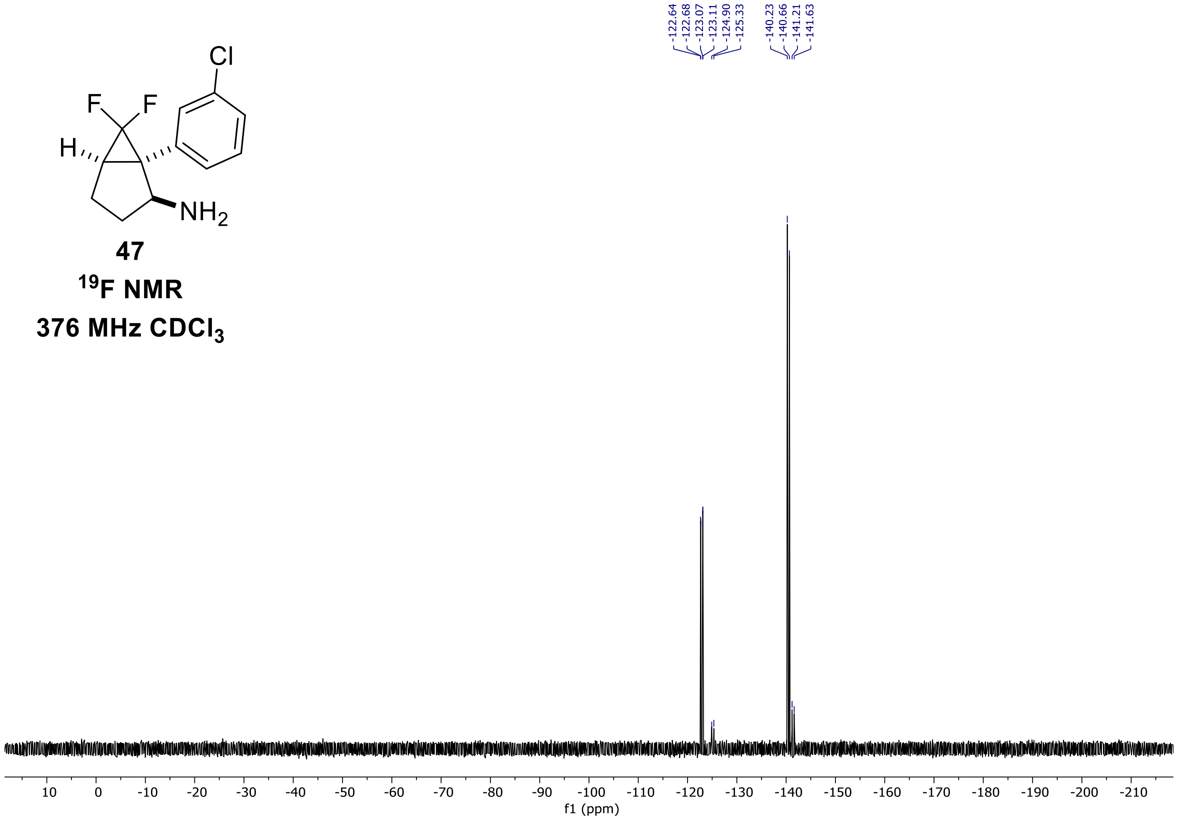
400 MHz $CDCl_3$



47

^{13}C NMR

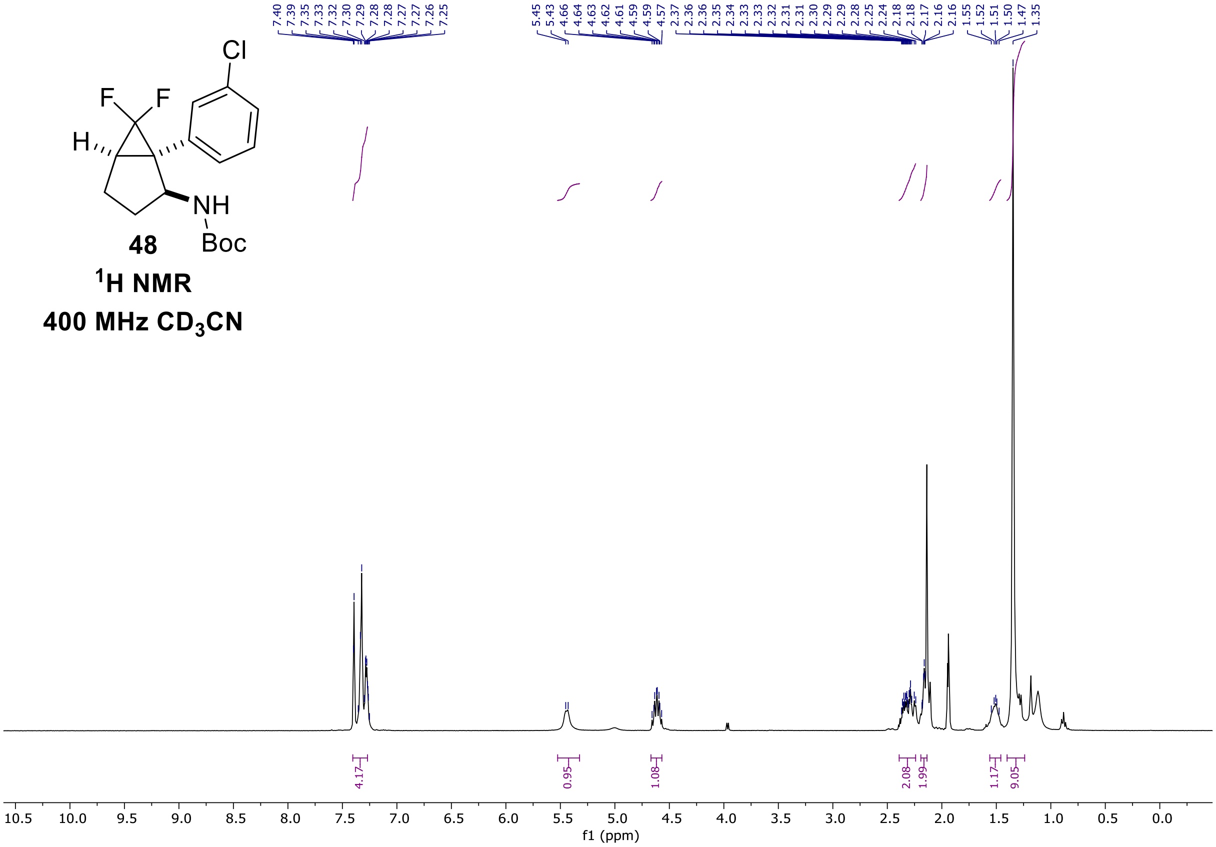
101 MHz $CDCl_3$



47

^{19}F NMR

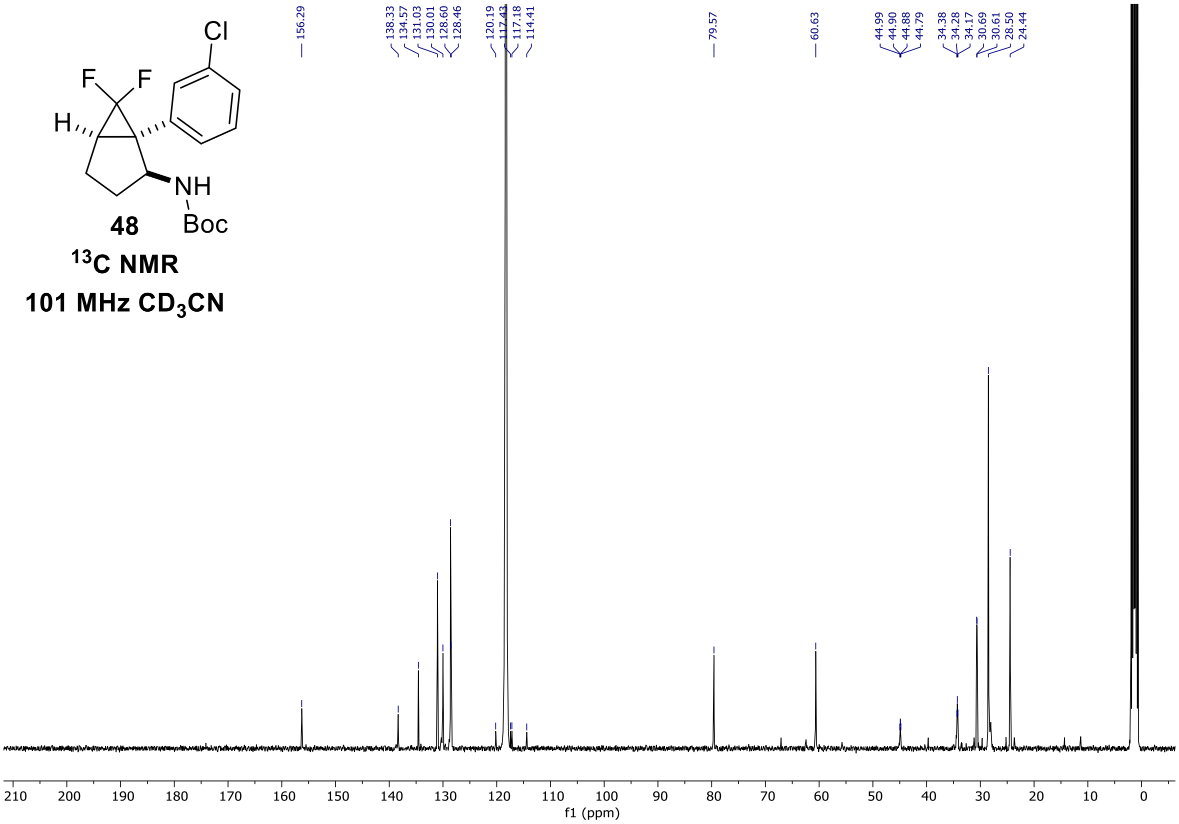
376 MHz $CDCl_3$



48

^{1}H NMR

400 MHz CD_3CN



48

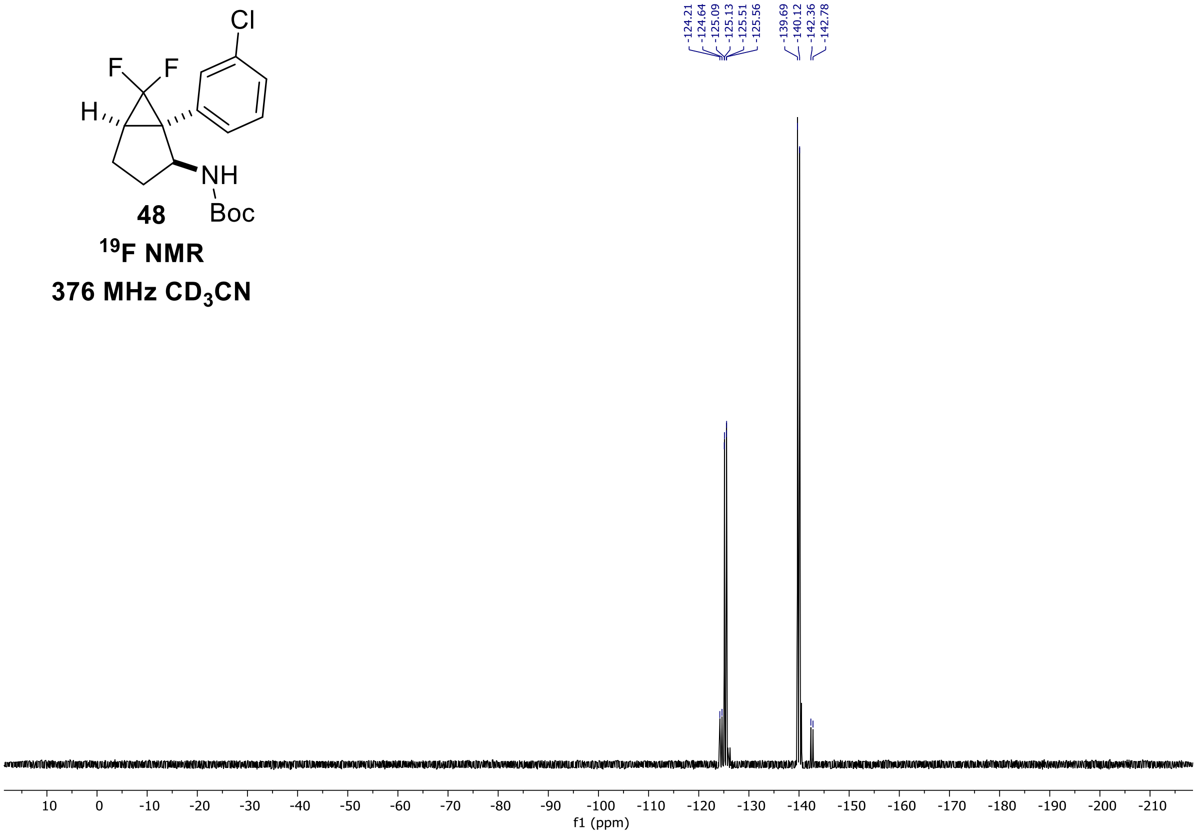
^{13}C NMR

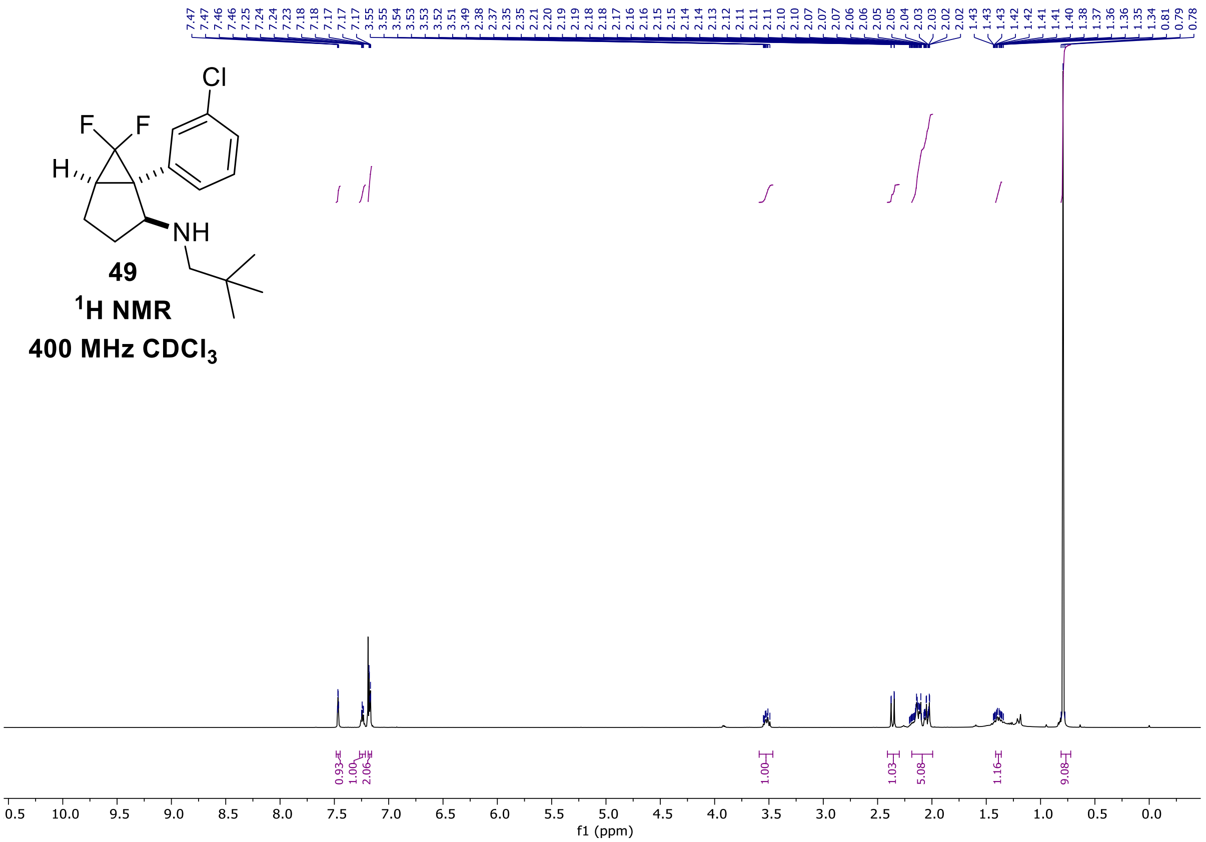
101 MHz CD_3CN

48

^{19}F NMR

376 MHz CD_3CN

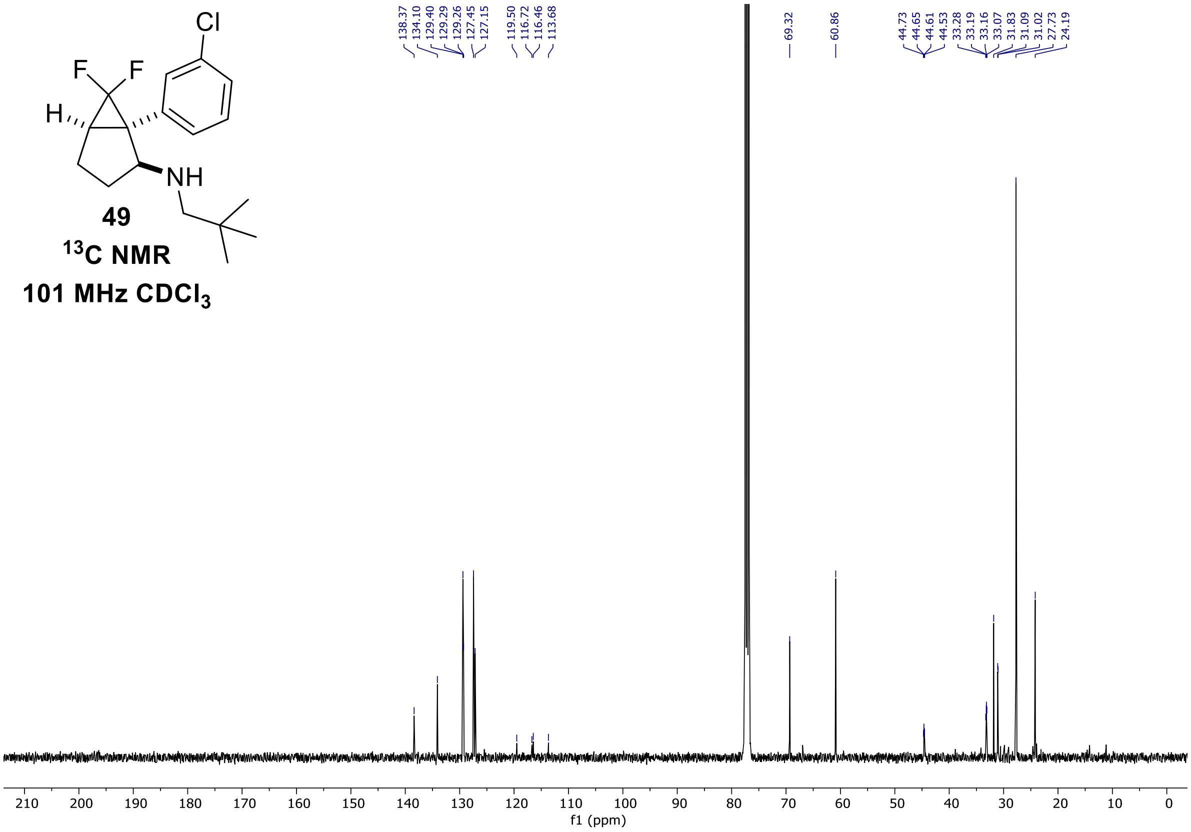




49

^{1}H NMR

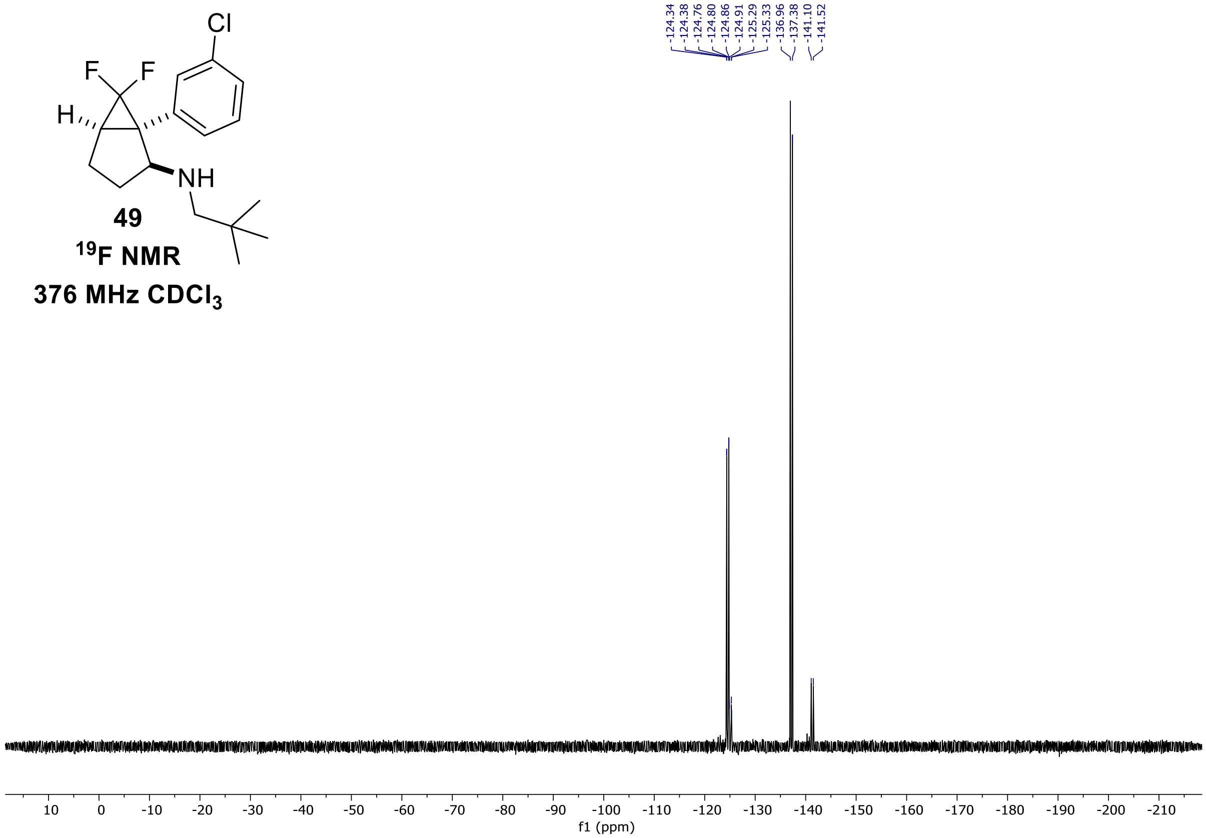
400 MHz $CDCl_3$



49

^{13}C NMR

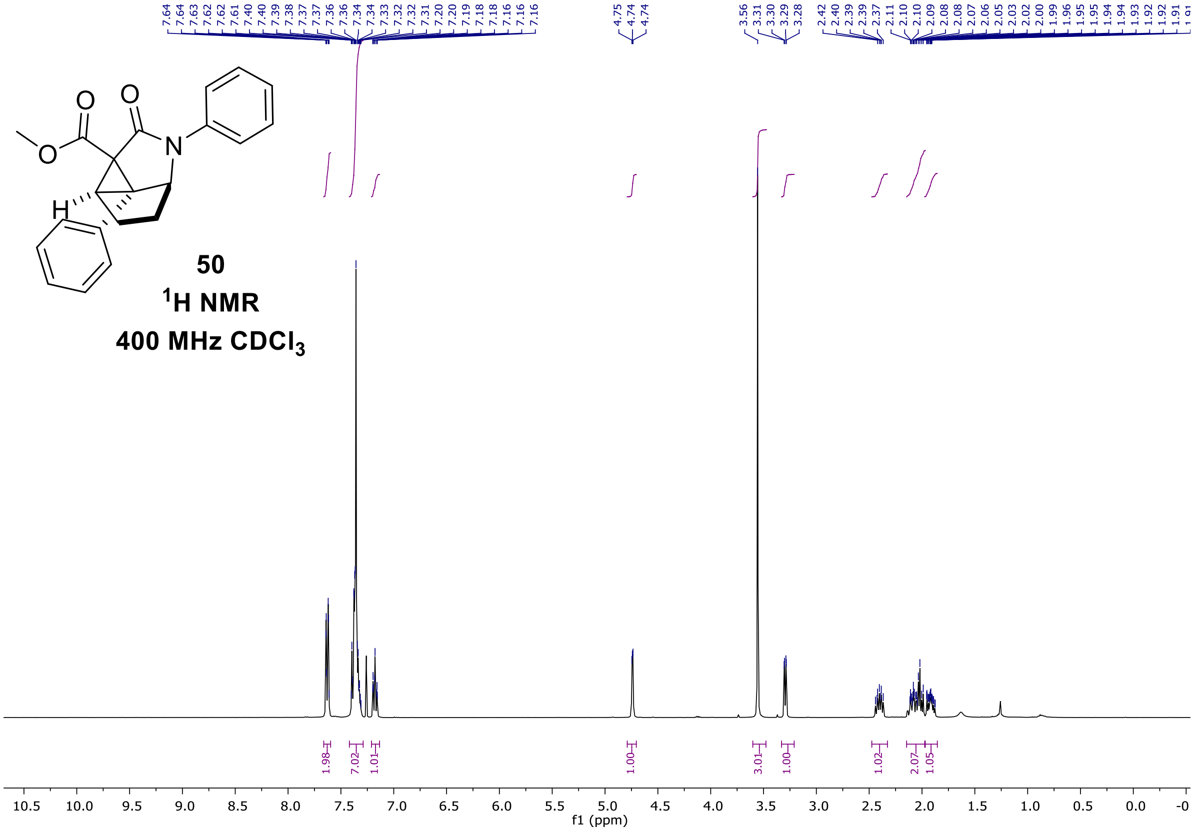
101 MHz $CDCl_3$



49

^{19}F NMR

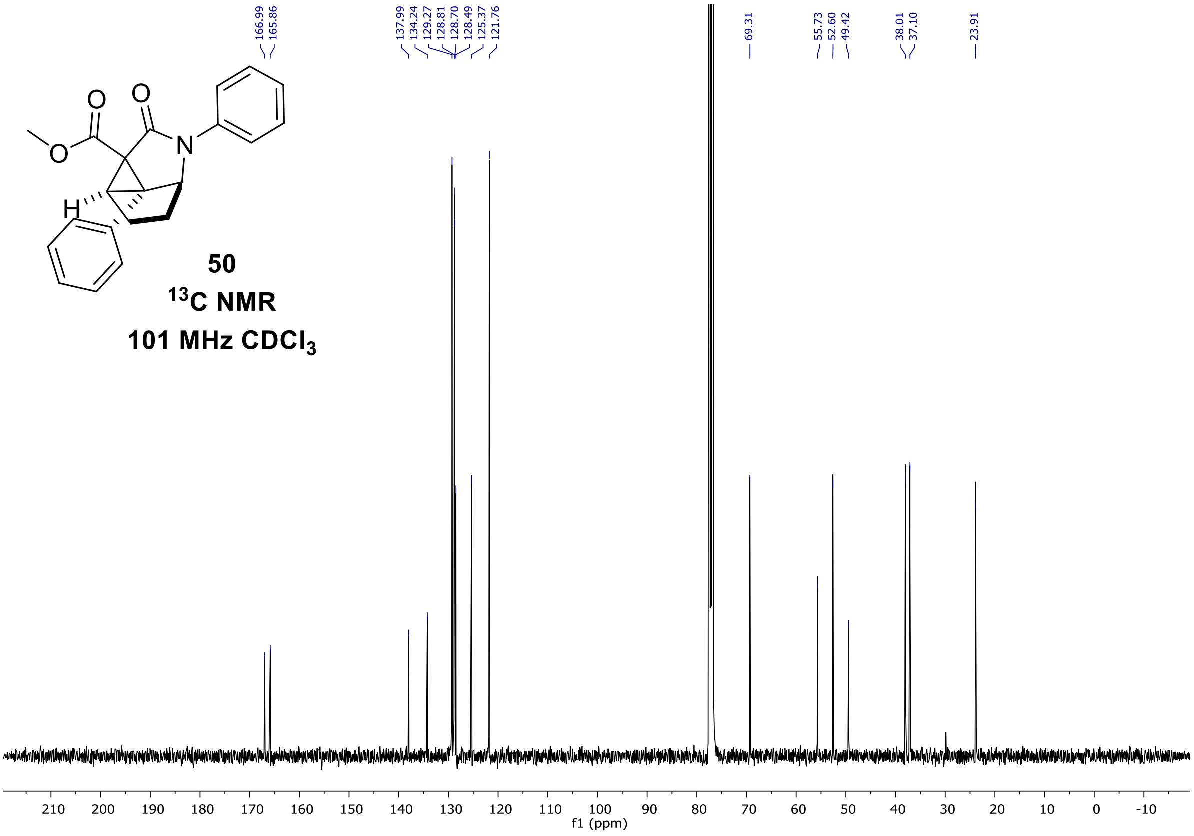
376 MHz $CDCl_3$



50

^{1}H NMR

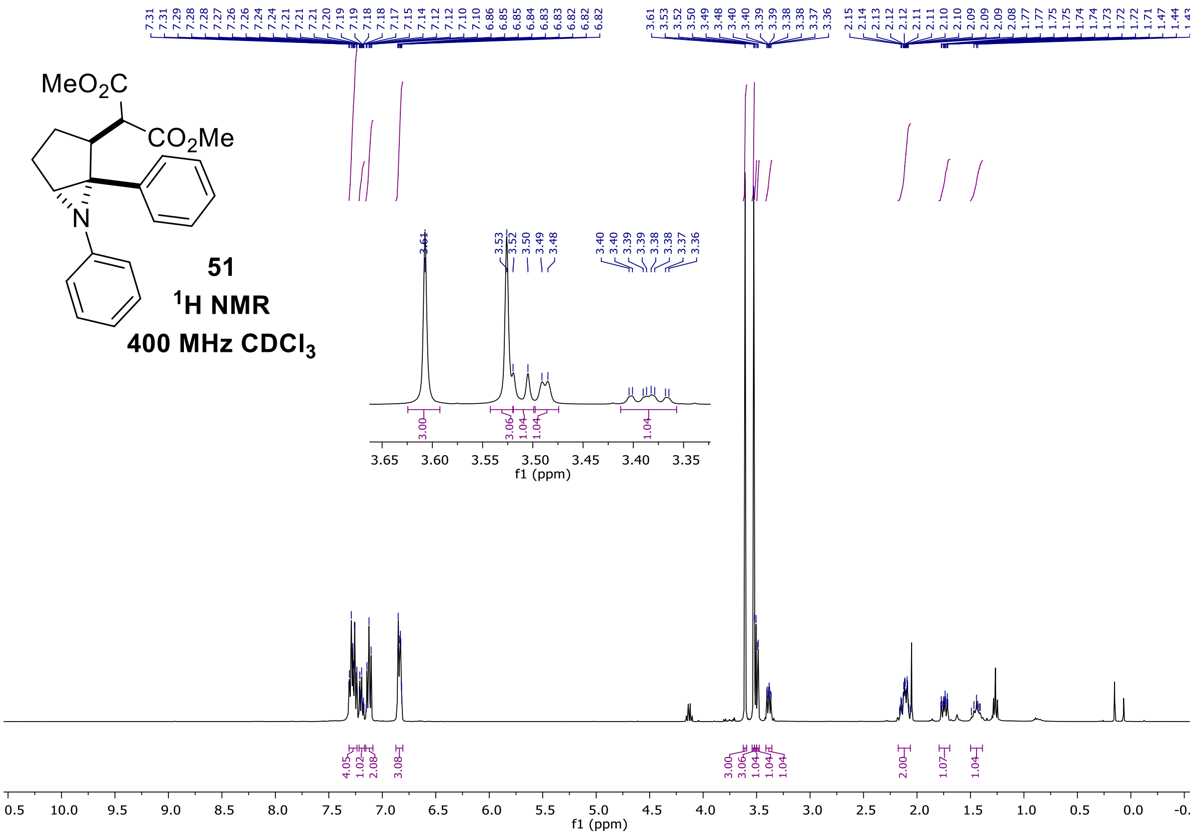
400 MHz $CDCl_3$



50

^{13}C NMR

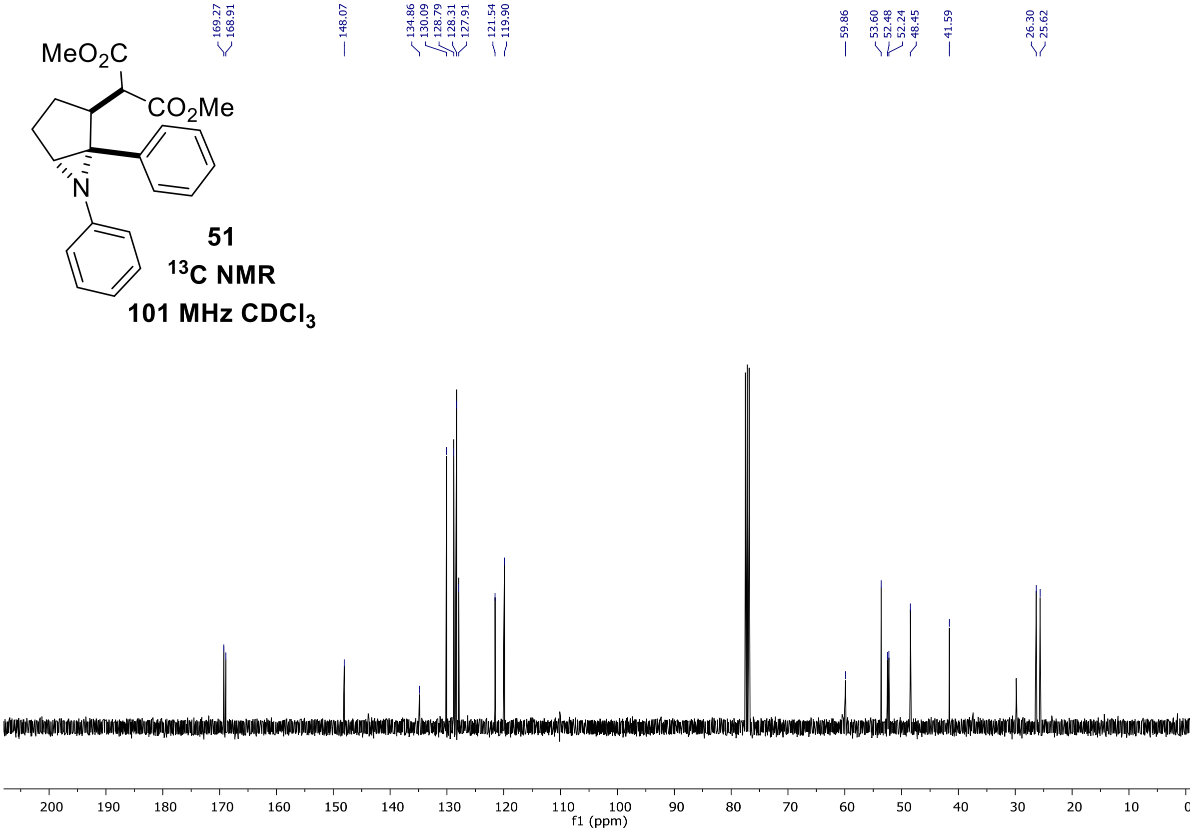
101 MHz $CDCl_3$



51

^{1}H NMR

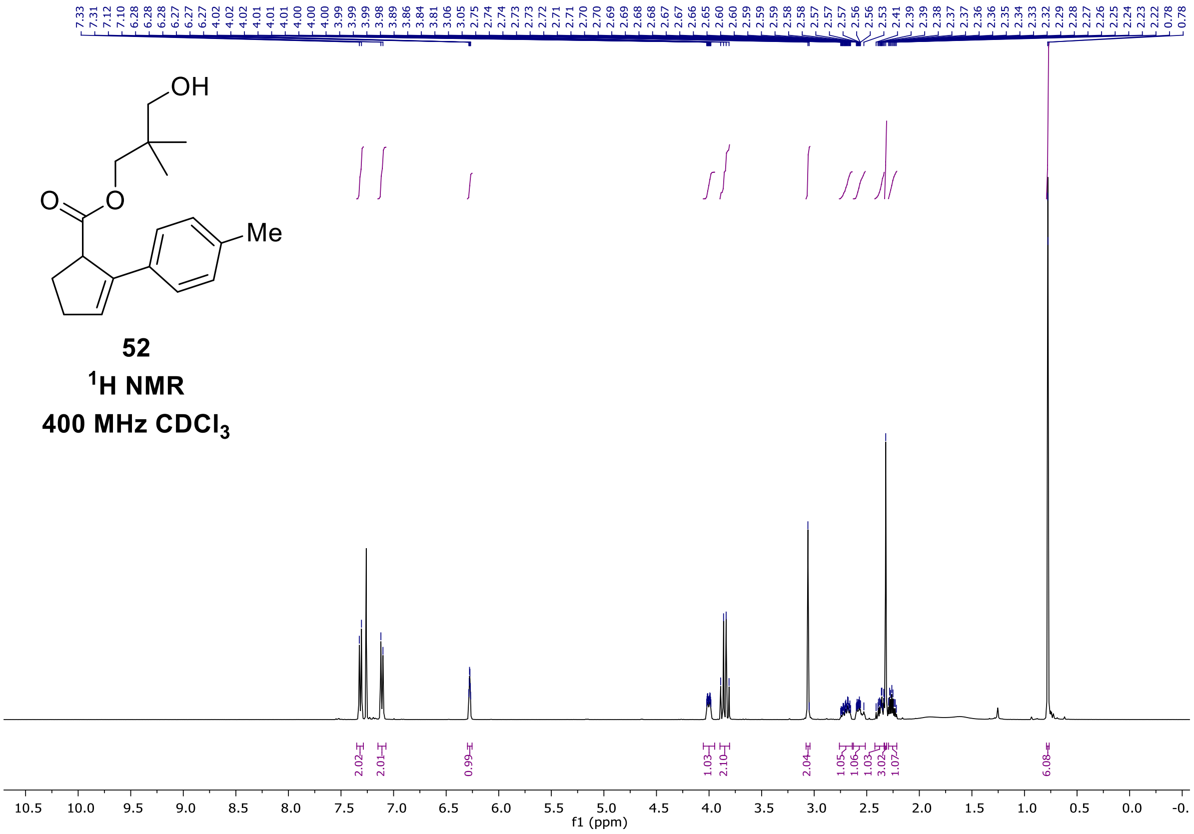
400 MHz CDCl$_3$



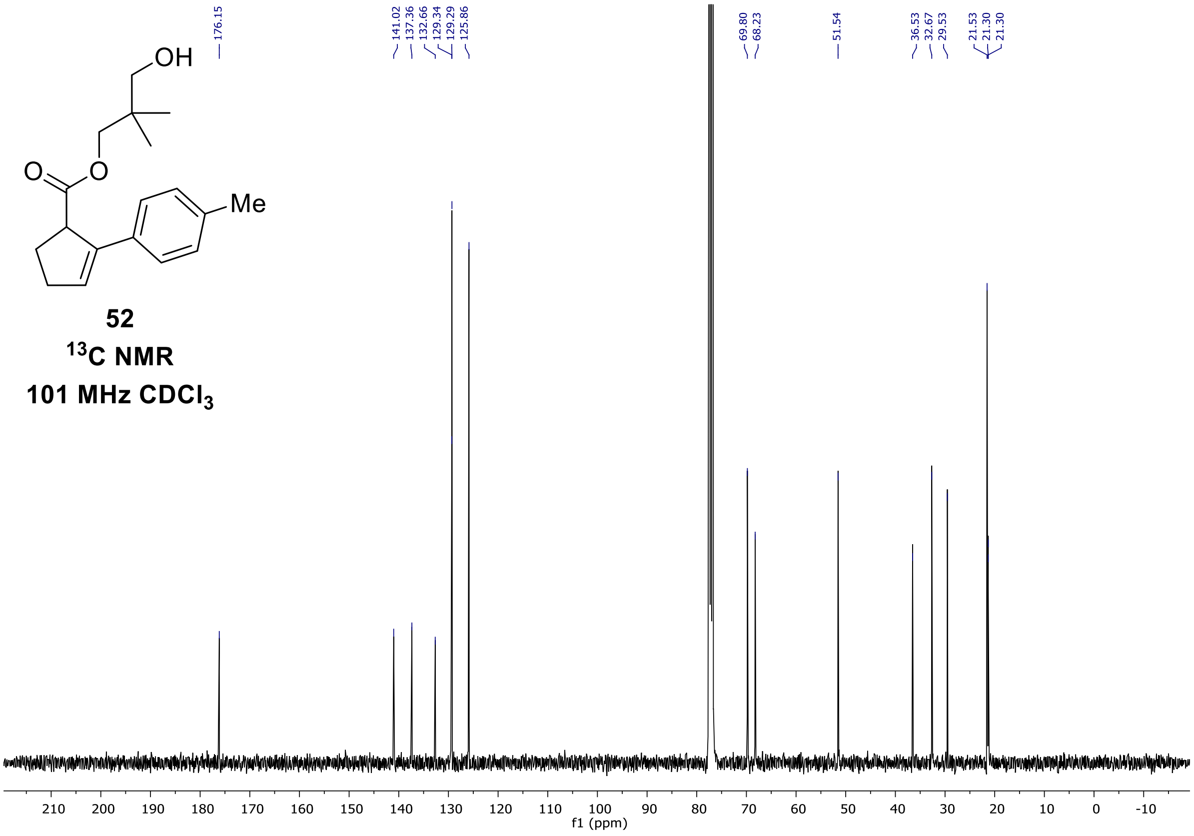
51

^{13}C NMR

101 MHz CDCl$_3$



52
^{1}H NMR
400 MHz $CDCl_3$



52
^{13}C NMR
101 MHz $CDCl_3$