Conjugate Hydrotrifluoromethylation of α,β–Unsaturated Acyl–Oxazolidinones: Synthesis of Chiral Fluorinated Amino Acids

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Electronic Supplementary Information

Experimental Section

General Procedures. All syntheses involving air- and moisture-sensitive compounds were carried out using standard Schlenk-type glassware (or in a glove box) under an atmosphere of argon. Solvents were dried with the solvent purification system MB-SPS 800 from M. Braun or predistilled according to standard laboratory methods. Unless stated otherwise all chemicals were purchased from *Acros* or *Aldrich* and used without further purification.

3.1.1 The following instruments were used for physical characterization of the compounds: ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded at room temperature using a Bruker AC 250, JEOL ECX 400, JEOL Eclipse 500 or Bruker Advance 3 (700 MHz). ^{1}H NMR and ^{13}C NMR: chemical shift δ are referenced against the internal solvent ($CDCl_3$, δ ^{1}H = 7.26 ppm, ^{13}C = 77.0, $(CD_3)_2CO$, δ ^{1}H = 2.05 ppm, ^{13}C = 29.84). ^{19}F NMR: chemical shift δ is given relative to $CFCl_3$ (external reference). The order of citation in parentheses is a) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), b) coupling constants, c) number of protons and d) assignment. Coupling constants (*J*) are reported in Hertz (Hz). The attributions of the chemical shifts were determined by means of COSY, HSQC, HMQC, and NOE experiments. Melting points (m.p.) were determined using a Büchi 510 apparatus and are uncorrected. High resolution mass spectra (HRMS) were determined on an Agilent 6210 ESI-TOF MS instrument with a flow rate of 4 µL/min, spray voltage 4 kV, and the desolvation gas set to 15 psi. All other parameters were optimized for maximal abundance of $[M+H]^+$ or $[M+Na]^+$. IR spectra were recorded using a Jasco 6200 FTIR spectrometer. The following abbreviations were used to distinguish between the signals: vs: very strong, s: strong, m: medium, w: weak, br: broad. Elemental analyses were performed on a *Elementar Vario EL*. The specific rotation of optically active compounds was determined with a *241 Perkin-Elmer* polarimeter using a cell with 10.0 cm diameter and a capacity of 1 ml. Measurements were performed at room temperature using a Na-lamp with a wavelength of λ = 589.3 nm. Chloroform was used as the solvent. X-Ray Data sets were collected with a Smart-CCD diffractometer. For structure solution and refinement the programs of the SHELXS-97 series were used (G. M. Sheldrick, *Acta Cryst.*, 1990, **A46**, 467-473; G. M. Sheldrick, *Acta Cryst.*, 2008, **A64**, 112-122). For the visualization the programs Diamond and Mercury were used. All reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F254 (0.25 mm thickness). Flash chromatography was carried out using

Merck silica gel 60 (0.040−0.063 mm). 2,4,6-triisopropylbenzenesulfonyl azide[1] and 1,1,3,3-tetramethylguanidinium azide (TMGA)[2] were synthesized according to literature procedures.

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[1] M. Regitz, J. Hocker and A. Liedhegener, *Organic Synthesis*, 1973, **5**, 179.

[2] A. J. Papa, *J. Org. Chem.*, 1966, **31**, 1426.

1. *N*-Acylations of (*S*)-4-benzyloxazolidin-2-one

General procedure A:

The appropriate acid (1.00 equiv.) and triethylamine (1.30 equiv.) were dissolved in dry tetrahydrofuran (3.5 mL/mmol) and cooled to -78 °C. At this temperature trimethylacetyl chloride (1.05 equiv.) was added dropwise. The resulting suspension was stirred for 20 minutes at this temperature and afterwards for one hour at room temperature. The reaction mixture was then again cooled to -78 °C. In a second flask (*S*)-4-benzyloxazolidin-2-one (1.20 equiv.) was dissolved in dry tetrahydrofuran (3.0 mL/mmol) and cooled to -78 °C before *n*-butyllithium (1.15 equiv., 2.5 M in hexane) was added dropwise. After the yellow solution was stirred for ten minutes at that temperature it was transferred to the flask containing the mixed anhydride via cannula. The reaction mixture was then allowed to warm to room temperature overnight and was quenched by addition of water. The aqueous layer was extracted with diethyl ether, the combined organic phases were washed with water and brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel.

General procedure B:

(*S*)-4-Benzyloxazolidin-2-one (1.00 equiv.) was dissolved in dry tetrahydrofuran (2.0 mL/mmol) and cooled to -78 °C. At this temperature *n*-butyllithium (1.00 equiv., 2.5 M in hexane) was added dropwise. After stirring for 30 minutes at this temperature the appropriate freshly destilled acid chloride (1.10 equiv.), dissolved in dry tetrahydrofuran (1.0 mL/mmol) was slowly added. The resulting mixture was stirred at -78 °C between two and four hours. The resulting yellow suspension was then allowed to warm to room temperature. Stirring was continued for another ten minutes before saturated ammonium chloride solution was added. The aqueous layer was extracted with diethyl ether and the combined organic phases were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel.

1.1 Synthesis of (*S*)-3-acryloyl-4-benzyloxazolidin-2-one[3] (18)

To a solution of acrylic acid (0.70 mL, 10.2 mmol) in dry tetrahydrofuran (33.0 ml) at -20 °C was added triethylamine (2.60 mL, 18.5 mmol) followed by acryloyl chloride (0.81 mL, 9.52 mmol). The reaction mixture was stirred at that temperature for 2.5 h. LiCl (0.37 mg, 8.76

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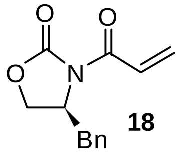
[3] D. Xiao, M. D. Vera, B. Liang and M. M. Joullié, *J. Org. Chem.*, 2001, **66**, 2734.

mmol) was added followed by (*S*)-4-benzyloxazolidin-2-one (1.30 g, 7.34 mmol). The reaction mixture was then allowd to warm to room temperature overnight. The reaction was quenched by addition of 0.2 N HCl and THF was removed *in vacuo*. The residue was partitioned between ethyl acetate and 0.2 N HCl. The organic layer was washed with half-saturated $NaHCO_3$ and brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (hexane/ethyl acetate 4:1) to afford **18** as a colourless solid. **Yield**: 1.22 g (5.19 mmol, 79%).



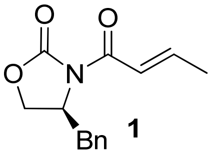
18

^{1}H NMR (400 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.52 (dd, *J* = 17.0 Hz, *J* = 10.5 Hz, 1H, CH=C*H*$_2$), 7.36-7.21 (m, 5H, Ph), 6.61 (dd, *J* = 17.0 Hz, *J* = 1.8 Hz, 1H, CH=C*H*$_2$), 5.94 (dd, *J* = 10.5 Hz, *J* = 1.8 Hz, 1H, C*H*=CH$_2$), 4.74 (m$_c$, 1H, NCH), 4.26-4.18 (m, 2H, OCH$_2$), 3.35 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.81 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph).

^{13}C{^{1}H} NMR (100 MHz, 298 K, $CDCl_3$): δ [ppm] = 164.9 (N*C*OC), 153.3 (O*C*ON), 135.2 (*i*-Ph), 131.9 (CH=*C*H$_2$), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 127.4 (*C*H=CH$_2$), 66.3 (OCH$_2$), 55.3 (NCH), 37.8 (*C*H$_2$Ph).

1.2 Synthesis of (*S*,*E*)-4-benzyl-3-(but-2-enoyl)oxazolidin-2-one[4] (1)

According to general procedure B, (*S*)-4-benzyloxazolidin-2-one (2.30 g, 13.0 mmol) was acylated with *n*-butyllithium (5.16 mL, 12.9 mmol, 2.5 M in hexane), and (*E*)-crotonyl chloride (1.36 mL, 14.2 mmol) for 2 hours. After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1 to 2:1) to afford **1** as a colourless solid. **Yield**: 2.42 g (9.88 mmol, 76%).



1

^{1}H NMR (400 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.20 (m, 7H, Ph, COCH, C*H*Me), 4.74 (m$_c$, 1H, NCH), 4.25-4.17 (m, 2H, OCH$_2$), 3.34 (dd, *J* = 13.3 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.82 (dd, *J* = 13.3 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph), 1.99 (d, *J* = 5.2 Hz, 3H, Me).

^{13}C{^{1}H} NMR (100 MHz, 298 K, $CDCl_3$): δ [ppm] = 164.9 (N*C*OC), 153.4 (O*C*ON), 146.9 (*C*HMe), 135.3 (*i*-Ph), 129.4 (*m*-Ph), 128.8 (*o*-Ph), 127.2 (*p*-Ph), 121.7 (CO*C*H), 66.0 (OCH$_2$), 55.2 (NCH), 37.8 (*C*H$_2$Ph), 18.5 (Me).

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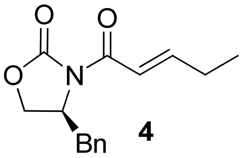
[4] D. A. Evans, K. T. Chapman and J. Bisaha, *J. Am. Chem. Soc.*, 1988, **110**, 1238.

1.3 Synthesis of (*S*,*E*)-4-benzyl-3-(pent-2-enoyl)oxazolidin-2-one[5] (4)

According to general procedure B, (*S*)-4-benzyloxazolidin-2-one (2.50 g, 14.1 mmol) was acylated with *n*-butyllithium (5.60 mL, 14.1 mmol, 2.5 M in hexane), and (*E*)-pent-2-enoyl chloride (1.80 g, 15.5 mmol) for 3 hours. After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1 to 2:1) to afford **4** as a colourless solid. **Yield**: 2.43 g (9.37 mmol, 65%).



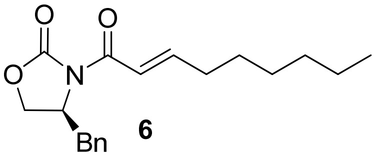
4

^{1}H NMR (400 MHz, 298 K, CDCl$_3$): δ [ppm] = 7.35-7.21 (m, 7H, Ph, C*H*=C*H*CH$_2$CH$_3$), 4.73 (m$_c$, 1H, NCH), 4.23-4.15 (m, 2H, OCH$_2$), 3.34 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.79 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph), 2.33 (m$_c$, 2H, CH=CHC*H*$_2$CH$_3$), 1.13 (t, *J* = 7.4 Hz, 3H, CH=CHCH$_2$C*H*$_3$).

^{13}C{^{1}H} NMR (100 MHz, 298 K, CDCl$_3$): δ [ppm] = 165.2 (N*C*OC), 153.4 (O*C*ON), 153.2 (CH=*C*H$_2$CH$_3$), 135.4 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.3 (*p*-Ph), 119.5 (*C*H=CHCH$_2$CH$_3$), 66.1 (OCH$_2$), 55.3 (NCH), 37.9 (*C*H$_2$Ph), 25.9 (CH=CH*C*H$_2$CH$_3$), 12.4 (CH=CHCH$_2$*C*H$_3$).

1.4 Synthesis of (*S*,*E*)-4-benzyl-3-(non-2-enoyl)oxazolidin-2-one (6)

According to general procedure A, (*S*)-4-benzyloxazolidin-2-one (2.70 g, 15.4 mmol) was acylated with (*E*)-non-2-enoic acid (2.00 g, 12.8 mmol), triethylamine (2.30 mL, 16.6 mmol), trimethylacetyl chloride (1.70 mL, 13.4 mmol), and *n*-butyllithium (6.70 mL, 14.7 mmol, 2.5 M in hexane). After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1) to afford **6** as a colourless solid. **Yield**: 2.50 g (7.93 mmol, 63%).



6

^{1}H NMR (500 MHz, 298 K, CDCl$_3$): δ [ppm] = 7.35-7.21 (m, 7H, Ph, COCH, CH=C*H*CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 4.75-4.70 (m, 1H, NCH), 4.22-4.14 (m, 2H, OCH$_2$), 3.33 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.79 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph), 2.32-2.28 (2H), 1.53-1.47 (2H), 1.37-1.27 (6H) (each m, CH=CHC*H*$_2$C*H*$_2$C*H*$_2$C*H*$_2$C*H*$_2$CH$_3$), 0.89 (t, *J* = 6.9 Hz, 3H, CH=CHCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H*$_3$).

^{13}C{^{1}H} NMR (126 MHz, 298 K, CDCl$_3$): δ [ppm] = 165.2 (N*C*OC), 153.4 (O*C*ON), 152.0 (CH=*C*HCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 135.4 (*i*-Ph), 129.5 (*m*-Ph), 128.9 (*o*-Ph), 127.3 (*p*-Ph),

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[5] K. Rück and H. Kunz, *Synthesis*, 1993, **10**, 1018.

120.3 (COCH), 66.1 (OCH_2), 55.3 (NCH), 37.9 (CH_2Ph), 32.7, 31.6, 28.9, 28.1, 22.5 ($CH{=}CHCH_2CH_2CH_2CH_2CH_2CH_3$), 14.0 ($CH{=}CHCH_2CH_2CH_2CH_2CH_2CH_3$).

HRMS(ESI): found *m/z*: 338.1716, calcd. for $[C_{19}H_{25}NNaO_3]^+$: 338.1727.

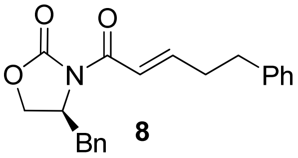
Optical Rotation: $[\alpha]_D^{22} = +60.8$ (c = 1.0, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2927 (w), 1780 (s), 1682 (m), 1634 (m), 1455 (w), 1386 (w), 1353 (m), 1289 (w), 1209 (m), 1104 (w), 1052 (w), 750 (w), 701 (w).

Melting Point: 54-57 °C.

1.5 Synthesis of (*S*,*E*)-4-benzyl-3-(5-phenylpent-2-enoyl)oxazolidin-2-one (8)

According to general procedure A, (*S*)-4-benzyloxazolidin-2-one (0.60 g, 3.41 mmol) was acylated with (*E*)-5-phenylpent-2-enoic acid (0.50 g, 2.84 mmol), triethylamine (0.50 mL, 3.69 mmol), trimethylacetyl chloride (0.40 mL, 2.98 mmol), and *n*-butyllithium (1.30 mL, 3.27 mmol, 2.5 M in hexane). After workup the crude product was purified by column chromatography (hexane/ethyl acetate 6:1) to afford **8** as a colourless solid. **Yield**: 0.70 g (2.09 mmol, 78%).



8

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.34-7.21 (m, 12H, Ph, COC*H*=CH, COCH=C*H*), 4.73 (m_c, 1H, NCH), 4.22-4.16 (m, 2H, OCH_2), 3.33 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, CH_2Ph), 2.85-2.78 (m, 3H, CH_2CH_2Ph, CH_2Ph), 2.66-2.62 (m, 2H, CH_2CH_2Ph).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 164.9 (NCOC), 153.4 (OCON), 150.5 (COCH=CH), 140.7 (*i*-Ph), 135.3 (*i*-Ph), 129.4, 128.9, 128.5, 128.4, 127.3, 126.2 (*m*-Ph, *o*-Ph, *p*-Ph), 120.9 (COCH=CH), 66.1 (OCH_2), 55.3 (NCH), 37.9 (CH_2Ph), 34.33, 34.32 (CH_2CH_2Ph).

HRMS(ESI): found *m/z*: 358.1415, calcd. for $[C_{21}H_{21}NNaO_3]^+$: 358.1414.

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3026 (w), 2921 (w), 1777 (vs), 1682 (s), 1634 (m), 1496 (w), 1387 (w), 1355 (s), 1288 (w), 1110 (w), 1053 (w), 751 (w), 700 (m).

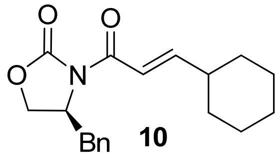
Optical Rotation: $[\alpha]_D^{22} = +59.5$ (c = 1.0, $CHCl_3$).

Melting Point: 52-56 °C.

1.6 Synthesis of (*S*,*E*)-4-benzyl-3-(3-cyclohexylacryloyl)oxazolidin-2-one (10)

According to general procedure A, (*S*)-4-benzyloxazolidin-2-one (2.06 g, 12.4 mmol) was acylated with (*E*)-3-cyclohexylacrylic acid (1.50 g, 9.73 mmol), triethylamine (1.75 mL, 12.6 mmol), trimethylacetyl chloride (1.26 mL, 10.2 mmol), and *n*-butyllithium (5.08 mL, 11.2

mmol, 2.5 M in hexane). After workup the crude product was purified by column chromatography (hexane/ethyl acetate 5:1) to afford **10** as a colourless solid. **Yield**: 1.64 g (5.23 mmol, 54%).


10

^{1}**H NMR** (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.13 (m, 7H, Ph, COC*H*=CH, COCH=C*H*), 4.75-4.70 (m, 1H, NCH), 4.22-4.14 (m, 2H, OCH_2), 3.35 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, CH_2Ph), 2.78 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, CH_2Ph), 2.24 (dtt, *J* = 10.3 Hz, *J* = 6.6 Hz, *J* = 3.3 Hz, 1H, Cy^{CH}), 1.85-1.74 (4H), 1.73-1.65 (1H), 1.35-1.27 (2H), 1.25-1.16 (3H) (each m, Cy^{CH2}).

^{13}**C{^{1}H} NMR** (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 165.5 (N*C*OC), 156.7 (O*C*ON), 153.4 (COCH=*C*H), 135.5 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.3 (*p*-Ph), 118.0 (CO*C*H=CH), 66.0 (OCH_2), 55.4 (NCH), 41.0 ($\mathrm{Cy}^{\mathrm{CH}}$), 37.9 (*C*$H_2$Ph), 31.70, 31.66, 26.3, 25.9, 25.6 ($\mathrm{Cy}^{\mathrm{CH2}}$).

HRMS(ESI): found *m/z*: 336.1575, calcd. for $[C_{19}H_{23}NNaO_3]^+$: 336.1570.

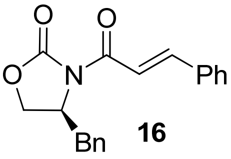
Optical Rotation: $[\alpha]_D^{22}$ = +68.6 (c = 1.0, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2925 (s), 2852 (m), 1779 (vs), 1681 (s), 1631 (m), 1450 (w), 1351(s), 1281(w), 1197 (m), 1108 (w), 1053 (w), 1004 (w), 761 (w), 701 (m), 504 (w).

Melting Point: 100-104 °C.

1.7 Synthesis of (*S*)-4-benzyl-3-(6-(benzyloxy)hex-2-enoyl)oxazolidin-2-one[6] (16)

According to general procedure B, (*S*)-4-benzyloxazolidin-2-one (2.00 g, 11.3 mmol) was acylated with *n*-butyllithium (4.52 mL, 11.3 mmol, 2.5 M in hexane), (*E*)-cinnamoyl chloride (2.06 g, 12.4 mmol) for 2 hours. After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1 to 2:1) to afford **16** as a colourless solid. **Yield**: 2.36 g (7.68 mmol, 68%).


16

^{1}**H NMR** (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.94-7.92 (m, 2H, Ph), 7.67-7.63 (m, 2H, Ph), 7.42-7.24 (m, 7H, COC*H*=CH, COCH=C*H*, Ph), 4.81 (m_c, 1H, NCH), 4.28-4.19 (m, 2H, OCH_2), 3.38 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, CH_2Ph), 2.86 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, CH_2Ph).

^{13}**C{^{1}H} NMR** (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 165.4 (N*C*OC), 153.7 (O*C*ON), 146.6 (COCH=*C*H), 135.5, 134.7 (*i*-Ph), 130.9, 129.6 (*m*-Ph), 129.2, 129.0 (*o*-Ph), 128.8, 127.5 (*p*-Ph), 117.2 (CO*C*H=CH), 66.3 (OCH_2), 55.6 (NCH), 38.1 (*C*H_2Ph).

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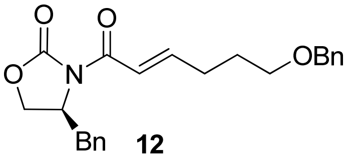
[6] H. Sakaguchi, H. Tokuyama and T. Fukuyama, *Org. Lett.*, 2007, **9**, 1635.

1.8 Synthesis of (*S*,*E*)-4-benzyl-3-(6-(benzyloxy)hex-2-enoyl)oxazolidin-2-one (12)

According to general procedure A, (*S*)-4-benzyloxazolidin-2-one (1.45 g, 8.17 mmol) was acylated with (*E*)-6-(benzyloxy)hex-2-enoic acid (1.50 g, 6.81 mmol), triethylamine (1.20 mL, 8.85 mmol), trimethylacetyl chloride (0.88 mL, 7.15 mmol), and *n*-butyllithium (3.56 mL, 7.83 mmol, 2.5 M in hexane). After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1) to afford **12** as a colourless oil. **Yield**: 739 mg (1.95 mmol, 28%).



12

^{1}H NMR (500 MHz, 298 K, CDCl$_3$): δ [ppm] = 7.35-7.19 (m, 12H, Ph, COC*H*=CH, COCH=C*H*), 4.72 (m$_c$, 1H, NCH), 4.51 (s, 2H, OC*H*$_2$Ph), 4.21-4.15 (m, 2H, OCH$_2$), 3.52 (t, *J* = 6.3 Hz, 2H, CH$_2$CH$_2$C*H*$_2$O), 3.33 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.79 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.42 (m$_c$, 2H, C*H*$_2$CH$_2$CH$_2$O), 1.84 (m$_c$, 2H, CH$_2$C*H*$_2$CH$_2$O).

^{13}C{^{1}H} NMR (125 MHz, 298 K, CDCl$_3$): δ [ppm] = 165.1 (N*C*OC), 153.5 (O*C*ON), 151.2 (COCH=*C*H), 138.5 (*i*-Ph), 135.5 (*i*-Ph), 129.6, 129.1, 128.5, 127.8, 127.7, 127.4 (Ph), 120.8 (COCH=*C*H), 73.1 (O*C*H$_2$Ph), 69.5 (CH$_2$CH$_2$*C*H$_2$O), 66.2 (OCH$_2$), 55.4 (NCH), 38.0 (*C*H$_2$Ph), 29.6 (*C*H$_2$CH$_2$CH$_2$O), 28.4 (CH$_2$*C*H$_2$CH$_2$O).

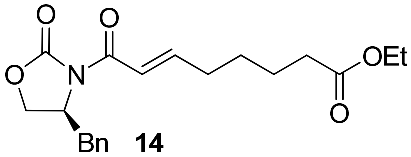
HRMS(ESI): found *m/z*: 402.1721, calcd. for [C$_{23}$H$_{25}$NNaO$_4$]$^+$: 402.1676.

Optical Rotation: $[\alpha]_D^{22}$ = +60.6 (c = 1.0, CHCl$_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2857 (w), 1778 (vs), 1682 (s), 1634 (m), 1495 (w), 1454 (w), 1387 (w), 1355 (s), 1290 (w), 1211 (s), 1101 (s), 1027 (w), 737 (w), 700 (m), 507 (w).

1.9 Synthesis of (*S*,*E*)-ethyl-8-(4-benzyl-2-oxooxazolidin-3-yl)-8-oxooct-6-enoate (14)

According to general procedure A, (*S*)-4-benzyloxazolidin-2-one (1.59 g, 8.99 mmol) was acylated with (*E*)-8-ethoxy-8-oxooct-2-enoic acid (1.50 g, 7.49 mmol), triethylamine (1.35 mL, 9.74 mmol), trimethylacetyl chloride (0.97 mL, 7.86 mmol), and *n*-butyllithium (3.90 mL, 8.61 mmol, 2.5 M in hexane). After workup the crude product was purified by column chromatography (hexane/ethyl acetate 4:1) to afford **14** as a colourless oil. **Yield**: 824 mg (2.29 mmol, 31%).



14

^{1}H NMR (500 MHz, 298 K, CDCl$_3$): δ [ppm] = 7.33-7.14 (m, 7H, Ph, COCH=C*H*, COC*H*=CH), 4.71 (m$_c$, 1H, NCH), 4.21-4.14 (m, 2H, OCH$_2$), 4.11 (q, *J* = 7.1 Hz, 2H, OC*H*$_2$CH$_3$), 3.31 (dd, *J* = 13.4 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 2.78 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 2.34-4.28 (4H), 1.71-4.65 (2H), 1.57-4.51 (2H) (each m_c, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{COO}$), 1.24 (t, *J* = 7.1 Hz, 3H, $\mathrm{OCH_2C}\mathit{H}_3$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 173.5 ($\mathit{C}\mathrm{OOCH_2CH_3}$), 165.1 ($\mathrm{N}\mathit{C}\mathrm{OC}$), 153.5 ($\mathrm{O}\mathit{C}\mathrm{ON}$), 151.1 ($\mathrm{COCH{=}}\mathit{C}\mathrm{H}$), 135.5 (*i*-Ph), 129.6 (*m*-Ph), 129.0 (*o*-Ph), 127.4 (*p*-Ph), 120.8 ($\mathrm{CO}\mathit{C}\mathrm{H{=}CH}$), 66.1 ($\mathrm{OCH_2}$), 60.4 ($\mathrm{O}\mathit{C}\mathrm{H_2CH_3}$), 55.4 (NCH), 38.0 ($\mathit{C}\mathrm{H_2Ph}$), 34.1, 32.4, 27.6, 24.6 ($\mathit{C}\mathrm{H_2}\mathit{C}\mathrm{H_2}\mathit{C}\mathrm{H_2}\mathit{C}\mathrm{H_2COO}$), 14.4 ($\mathrm{OCH_2}\mathit{C}\mathrm{H_3}$).

HRMS(ESI): found *m/z*: 382.1659, calcd. for $[C_{20}H_{25}NNaO_5]^+$: 382.1625.

Optical Rotation: $[\alpha]_D^{22}$ = +58.0 (c = 1.0, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2980 (w), 2936 (w), 2864 (w), 1778 (vs), 1682 (s), 1635(s), 1497 (w), 1454 (m), 1388 (w), 1355 (s), 1278 (w), 1211 (s), 1112 (m), 1077 (w), 914 (w), 848 (w), 761 (m), 702 (m), 595 (w), 507 (w).

2. Synthesis of trifluoromethyl substituted oxazolidinones

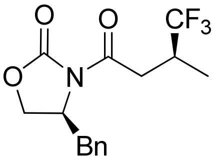
General procedure C

In a *Schlenk* tube Ytterbium(III) trifluoromethanesulfonate hydrate (2.00 equiv.) was dissolved in tetrahydrofuran (5.0 mL/mmol substrate) and dichloromethane (5.0 mL/mmol substrat). After addition of the substrate (1.00 equiv.), the reaction mixture was stirred for 30 minutes at room temperature and was then cooled to -78 °C and stirred for an additional 30 minutes. Trifluoroiodomethane (9.00 equiv.) and triethylborane (5.00 equiv., 1.0 M in hexane) were then added. Finally oxygen (10.0 mL O_2 / 1.00 mmol Et_3B) was added via syringe over 1.5 hours in intervals of 15 minutes. After stirring at -78 °C for an additional 15 minutes, trifluoroiodomethane (9.00 equiv.) and triethylborane (5.00 equiv., 1.0 M in hexane) were added. Oxygen (10.0 mL O_2 / 1.00 mmol Et_3B) was added via syringe over 1.5 hours in intervals of 15 minutes. After stirring at -78 °C for an additional 15 minutes, trifluoroiodomethane (9.00 equiv.) and triethylborane (5.00 equivalents, 1.0 M in hexane) were added. Oxygen (10.0 mL O_2 / 1.00 mmol Et_3B) was added via syringe over 1.5 hours in intervals of 15 minutes. The reaction mixture was stirred over night at -78 °C before it was quenched by addition of 0.1 M HCl solution. After stirring for an addtional 2 hours at room temperature, the aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel.

2.1 Synthesis of (*S*)-4-benzyl-3-((*S*)-4,4,4-trifluoro-3-methylbutanoyl)oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-4,4,4-trifluoro-3-methylbutanoyl)oxazolidin-2-one (2a,b)

Compound **1** (200 mg, 0.82 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.04 g, 1.63 mmol), trifluoroiodomethane (165 mL, 7.34 mmol), and triethylborane (4.07 mL, 4.07 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **2**. **Yield**: 180 mg (0.57 mmol, 70%).

The diastereoisomers were separated by column chromatography (hexane : ethyl acetate 4:1) to afford **2a** (86.0 mg, 0.27 mmol, 34%) as a colourless solid and **2b** (87.0 mg, 0.28 mmol, 34%) as a colourless oil.



2a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.38-7.16 (m, 5H, Ph), 4.70 (m$_c$, 1H, NCH), 4.26-4.18 (m, 2H, OCH_2), 3.30 (dd, *J* = 13.4 Hz, *J* = 3.5 Hz, 1H, CH_2Ph), 3.24 (dd, *J* = 17.7 Hz, *J* = 4.2 Hz, 1H, $COCH_2$), 3.05 (dd, *J* = 17.7 Hz, *J* = 8.5 Hz, 1H, $COCH_2$), 2.96 (m$_c$, 1H, $CHCF_3$), 2.78 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, CH_2Ph), 1.23 (d, *J* = 6.8 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.2 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.9 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 66.4 (OCH_2), 55.2 (NCH), 37.9 (*C*H_2Ph), 36.0 (q, *J* = 2.7 Hz, CO*C*H_2), 34.0 (q, *J* = 27.6 Hz, *C*HCH_3), 13.3 (q, *J* = 2.7 Hz, CH_3).

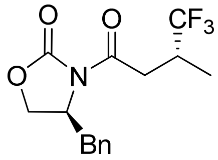
^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −73.2 (d, *J* = 8.7 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 338.0977, calcd. for $[C_{15}H_{16}F_3NNaO_3]^+$: 338.0975.

Optical Rotation: $[\alpha]_D^{22}$ = +23.2 (c = 1.06, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3540 (w), 2989 (m), 2927 (m), 1781 (vs), 1702 (s), 1467 (m), 1320 (w), 1227 (m), 1173 (m), 1132 (m), 1016 (w), 749 (w), 702 (w), 619 (w), 554 (w).

Melting Point: 61-63 °C.



2b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.39-7.19 (m, 5H, Ph), 4.69 (m$_c$, 1H, NCH), 4.25-4.18 (m, 2H, OCH_2), 3.35-3.29 (m, 2H, CH_2Ph, $COCH_2$), 3.03-2.94 (m, 2H, $COCH_2$, $CHCF_3$), 2.77 (dd, *J* = 13.3 Hz, *J* = 9.6 Hz, 1H, CH_2Ph), 1.21 (d, *J* = 6.5 Hz, 3H, CH_3).

$^{13}C\{^1H\}$ NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.1 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.8 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 66.4 (OCH_2), 55.2 (NCH), 37.8 (*C*H_2Ph), 36.0 (q, *J* = 2.7 Hz, CO*C*H_2), 34.0 (q, *J* = 27.6 Hz, *C*HCH_3), 13.3 (q, *J* = 2.7 Hz, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −73.3 (d, *J* = 8.7 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 338.0953, calcd. for $[C_{15}H_{16}F_3NNaO_3]^+$: 338.0975.

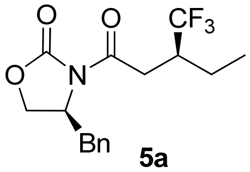
Optical Rotation: $[\alpha]_D^{22}$ = +62.3 (c = 0.45, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3550 (w), 3064 (w), 2923 (w), 1783 (vs), 1701 (s), 1604 (w), 1481 (w), 1388 (m), 1268 (m), 1132 (s), 1016 (m), 930 (w), 829 (w), 761 (w), 627 (w), 555 (w).

2.2 Synthesis of (*S*)-4-benzyl-3-((*S*)-3-(trifluoromethyl)pentanoyl)oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-3-(trifluoromethyl)pentanoyl)oxazolidin-2-one (5a,b)

Compound **4** (300 mg, 1.16 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.48 g, 2.31 mmol), trifluoroiodomethane (234 mL, 10.4 mmol), and triethylborane (5.80 mL, 5.80 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **5**. **Yield**: 195 mg (0.59 mmol, 51%).

The diastereoisomers were separated by column chromatography (hexane : ethyl acetate 4:1) to afford **5a** (94.0 mg, 0.29 mmol, 25%) and **5b** (96.0 mg, 0.29 mmol, 25%) as a colourless oils.



5a

^1H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.19 (m, 5H, Ph), 4.69 (m_c, 1H, NCH), 4.24-4.18 (m, 2H, OCH_2), 3.31 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, C*H*$_2$Ph), 3.22 (dd, *J* = 18.1 Hz, *J* = 6.1 Hz, 1H, $COCH_2$), 3.07 (dd, *J* = 18.1 Hz, *J* = 6.3 Hz, 1H, $COCH_2$), 2.89 (m_c, 1H, $CHCF_3$), 2.76 (dd, *J* = 13.4 Hz, *J* = 9.7 Hz, 1H, C*H*$_2$Ph), 1.77 (m_c, 1H, C*H*$_2$$CH_3$), 1.54 ($m_c$, 1H, C*H*$_2$$CH_3$), 1.03 (t, *J* = 7.5 Hz, 3H, CH_2C*H*$_3$).

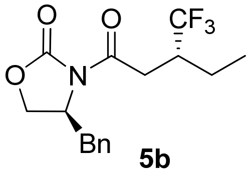
$^{13}C\{^1H\}$ NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 128.7 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 66.4 (OCH_2), 55.3 (NCH), 39.8 (q, *J* = 26.1 Hz, *C*HCF_3), 37.9 (*C*H_2Ph), 34.2 (q, *J* = 2.9 Hz, CO*C*H_2), 21.6 (m, *C*$H_2$$CH_3$), 11.2 ($CH_2$*C*$H_3$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.6 (d, *J* = 9.1 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 352.1124, calcd. for $[C_{16}H_{18}F_3NNaO_3]^+$: 352.1131.

Optical Rotation: $[\alpha]_D^{22}$ = +53.8 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2971 (w), 1783 (s), 1702 (m), 1455 (w), 1389 (m), 1256 (m), 1168 (m), 1133 (m), 1049 (w), 955 (w), 761 (w), 701 (m), 668 (w), 507 (w).



5b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.19 (m, 5H, Ph), 4.69 (m_c, 1H, NCH), 4.23-4.17 (m, 2H, OCH_2), 3.33 (dd, *J* = 18.1 Hz, *J* = 5.7 Hz, 1H, $COCH_2$), 3.29 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, CH_2Ph), 3.00 (dd, *J* = 18.1 Hz, *J* = 6.6 Hz, 1H, $COCH_2$), 2.95-2.87 (m, 1H, $CHCF_3$), 2.78 (dd, *J* = 13.4 Hz, *J* = 9.5 Hz, 1H, CH_2Ph), 1.77 (m_c, 1H, CH_2CH_3), 1.53 (m_c, 1H, CH_2CH_3), 1.02 (t, *J* = 7.5 Hz, 3H, CH_2CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (NCOC), 153.2 (OCON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 128.9 (*o*-Ph), 128.6 (q, *J* = 278 Hz, CF_3), 127.3 (*p*-Ph), 66.3 (OCH_2), 55.2 (NCH), 39.7 (q, *J* = 26.0 Hz, $CHCF_3$), 37.6 (CH_2Ph), 34.4 (q, *J* = 2.5 Hz, $COCH_2$), 21.5 (m, CH_2CH_3), 11.1 (CH_2CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.5 (d, *J* = 8.8 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 352.1139, calcd. for $[C_{16}H_{18}F_3NNaO_3]^+$: 352.1131.

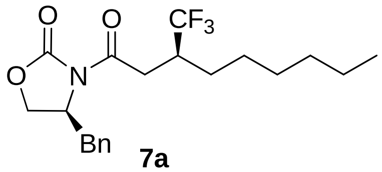
Optical Rotation: $[\alpha]_D^{22}$ = +44.5 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3087 (w), 2972 (m), 2884 (w), 1788 (s), 1704 (s), 1497 (m), 1327 (w), 1213 (m), 1169 (m), 1134 (m), 1049 (w), 956 (m), 747 (w), 702 (m), 667 (w), 551 (w).

2.3 Synthesis of (*S*)-4-benzyl-3-((*S*)-(trifluoromethyl)nonanoyl)oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-(trifluoromethyl)nonanoyl)oxazolidin-2-one (7a,b)

Compound **6** (284 mg, 0.90 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.15 g, 1.80 mmol), trifluoroiodomethane (181 mL, 8.10 mmol), and triethylborane (4.50 mL, 4.50 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **7**. **Yield**: 194 mg (0.50 mmol, 56%).

The diastereoisomers were separated by HPLC (1% isopropanol / hexane) to afford **7a** (90.0 mg, 0.25 mmol, 27%) and **7b** (85.0 mg, 0.22 mmol, 25%) as corlourless oils.



7a

^{1}H NMR (700 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.20 (m, 5H, Ph), 4.71-4.68 (m, 1H, NCH), 4.24-4.19 (m, 2H, OCH_2), 3.35 (dd, J = 19.9 Hz, J = 7.8 Hz, 1H, $COCH_2$), 3.30 (dd, J = 13.5 Hz, J = 9.6 Hz, 1H, CH_2Ph), 2.99-2.95 (m, 2H, $COCH_2$, $CHCF_3$), 2.77 (dd, J = 13.5 Hz, J = 9.6 Hz, 1H, CH_2Ph), 1.73-1.69 (m, 1H, $CH_2(CH_2)_4CH_3$), 1.47-1.25 (3H), 1.34-1.25 (6H) (each m, $CH_2(CH_2)_4CH_3$), 0.89 (t, J = 7.1 Hz, 3H, $CH_2(CH_2)_4CH_3$).

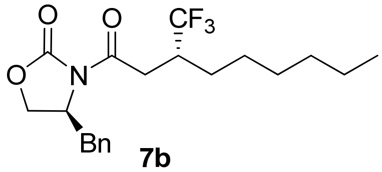
^{13}C{^{1}H} NMR (176 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.5 (NCOC), 153.3 (OCON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 128.0 (q, J = 280 Hz, CF_3), 127.4 (*p*-Ph), 66.3 (OCH_2), 55.3 (NCH), 38.5 (q, J = 26.1 Hz, $CHCF_3$), 37.7 (CH_2Ph), 34.5 (q, J = 2.3 Hz, $COCH_2$), 31.5, 29.2, 28.5 (m), 26.6, 22.5 ($CH_2(CH_2)_4CH_3$), 14.0 ($CH_2(CH_2)_4CH_3$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.8 (d, J = 9.0 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 408.1749, calcd. for $[C_{20}H_{26}F_3NNaO_3]^+$: 408.1757.

Optical Rotation: $[\alpha]_D^{22}$ = +41.3 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2929 (m), 1785 (s), 1703 (s), 1455 (w), 1388 (m), 1253 (m), 1162 (m), 1134 (m), 1051 (w), 762 (w), 748 (m), 668 (w), 627 (w).



7b

^{1}H NMR (700 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.21 (m, 5H, Ph), 4.70-4.68 (m, 1H, NCH), 4.25-4.18 (m, 2H, OCH_2), 3.32 (dd, J = 13.4 Hz, J = 3.5 Hz, 1H, CH_2Ph), 3.24 (dd, J = 18.0 Hz, J = 6.0 Hz, 1H, $COCH_2$), 3.05 (dd, J = 18.0 Hz, J = 6.0 Hz, 1H, $COCH_2$), 3.00-2.93 (m, 1H, $CHCF_3$), 2.77 (dd, J = 13.4 Hz, J = 9.7 Hz, 1H, CH_2Ph), 1.75-1.71 (m, 1H, $CH_2(CH_2)_4CH_3$), 1.49-1.38 (3H), 1.36-1.27 (6H) (each m, $CH_2CH_2CH_2CH_2CH_2CH_3$) 0.91 (t, J = 7.1 Hz, 3H, $CH_2(CH_2)_4CH_3$)

^{13}C{^{1}H} NMR (176 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.5 (NCOC), 153.4 (OCON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 128.0 (q, J = 280 Hz, CF_3), 127.5 (*p*-Ph), 66.4 (OCH_2), 55.3 (NCH), 38.5 (q, J = 26.1 Hz, $CHCF_3$), 37.8 (CH_2Ph), 34.5 (q, J = 2.3 Hz, $COCH_2$), 31.5, 29.2, 28.5 (m), 26.6, 22.5 ($CH_2CH_2CH_2CH_2CH_2CH_3$), 14.0 ($(CH_2)_5CH_3$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.8 (d, J = 8.6 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 408.1749, calcd. for $[C_{20}H_{26}F_3NNaO_3]^+$: 408.1757.

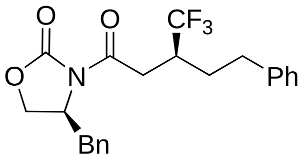
Optical Rotation: $[\alpha]_D^{22}$ = +46.5 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2955 (m), 2859 (w), 1785 (s), 1703 (s), 1497 (m), 1388 (w), 1213 (m), 1161 (m), 1134 (m), 1051 (w), 997 (m), 747 (w), 701 (m), 667 (w), 626 (w).

2.4 Synthesis of (*S*)-4-benzyl-3-((*S*)-5-phenyl-3-(trifluoromethyl)pentanoyl)oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-5-phenyl-3-(trifluoromethyl)pentanoyl)oxazolidin-2-one (9a,b)

Compound **8** (350 mg, 1.04 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.33 g, 2.08 mmol), trifluoroiodomethane (212 mL, 9.36 mmol), and triethylborane (5.20 mL, 5.20 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **9**. **Yield**: 170 mg (0.42 mmol, 40%)

The diastereoisomers were separated by HPLC (7.5% ethyl acetate / hexane; flow: 128 mL/min) to afford **9a** (82.0 mg, 0.20 mmol, 19%) and **9b** (79.0 mg, 0.20 mmol, 19%) as colourless oils.



9a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.20 (m, 10H, Ph), 4.69 (m_c, 1H, NCH), 4.24-4-18 (m, 2H, OCH_2), 3.34-3.12 (m, 2H, C*H*$_2$Ph, $COCH_2$), 3.11 (dd, *J* = 17.9 Hz, *J* = 6.4 Hz, 1H, $COCH_2$), 3.08-3.00 (m, 1H, $CHCF_3$), 2.79-2.75 (m, 3H, C*H*$_2$Ph, CH_2C*H*$_2$Ph), 2.11-2.03 (m, 1H, C*H*$_2$$CH_2$Ph), 1.85-1.77 (m, 1H, C*H*$_2$$CH_2$Ph).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.2 (N*C*OC), 153.3 (O*C*ON), 140.9 (*i*-Ph), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*m*-Ph), 128.6 (*o*-Ph), 128.3 (*o*-Ph), 127.5 (*p*-Ph), 126.3 (*p*-Ph), 66.5 (OCH_2), 55.3 (NCH), 38.4 (q, *J* = 26.3 Hz, *C*HCF_3), 37.9 (*C*H_2Ph), 34.4 (q, *J* = 1.8 Hz, CO*C*H_2), 33.1 (CH_2*C*H_2Ph), 30.4(q, *J* = 1.8 Hz, *C*H_2CH_2Ph) n.o. (CF_3).

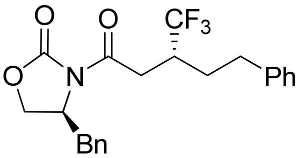
^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.6 (d, *J* = 8.9 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 428.1440, calcd. for $[C_{22}H_{22}F_3NNaO_3]^+$: 428.1444.

Optical Rotation: $[\alpha]_D^{22}$ = +31.6 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2926 (w), 1782 (s), 1702 (m), 1603 (w), 1455 (m), 1388 (m), 1249 (w), 1153 (m), 1113 (m), 1051 (w), 997 (w), 747 (m), 700 (m), 668 (w), 627 (w).

Melting Point: 78-80 °C.



9b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.20 (m, 10H, Ph), 4.68 (m_c, 1H, NCH), 4.24-4.18 (m, 2H, OCH_2), 3.40 (m_c, 1H, $COCH_2$), 3.30 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, C*H*$_2$Ph), 3.10-3.03 (m, 2H, $COCH_2$, $CHCF_3$), 2.79-2.75 (m, 3H, C*H*$_2$Ph, CH_2C*H*$_2$Ph), 2.10-2.03 (m, 1H, CH_2CH_2Ph), 1.86-1.78 (m, 1H, CH_2CH_2Ph).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.2 (N*C*OC), 153.3 (O*C*ON), 140.9 (*i*-Ph), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*m*-Ph), 128.5 (*o*-Ph), 128.3 (*o*-Ph), 127.4 (*p*-Ph), 126.2 (*p*-Ph), 66.3 (OCH_2), 55.2 (NCH), 38.9 (q, *J* = 26.3 Hz, $CHCF_3$), 37.7 (CH_2Ph), 34.5 (q, *J* = 2.5 Hz, $COCH_2$), 33.0 (CH_2CH_2Ph), 30.3 (q, *J* = 1.8 Hz, CH_2CH_2Ph) n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.5 (d, *J* = 8.5 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 428.1443, calcd. for $[C_{22}H_{22}F_3NNaO_3]^+$: 428.1444.

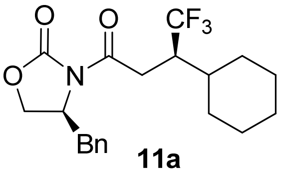
Optical Rotation: $[\alpha]_D^{22}$ = +56.7 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2928 (m), 2870 (w), 1788 (s), 1703 (s), 1481 (m), 1391 (m), 1327 (w), 1213 (m), 1153 (w), 1134 (m), 1051 (w), 951 (m), 747 (w), 700 (m), 668 (w).

2.6 Synthesis of (*S*)-4-benzyl-3-((*S*)-3-cyclohexyl-4,4,4-trifluorobutanoyl)oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-3-cyclohexyl-4,4,4-trifluorobutanoyl)oxazolidin-2-one (11a,b)

Compound **10** (300 mg, 0.96 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.22 g, 1.91 mmol), trifluoroiodomethane (194 mL, 8.61 mmol), and triethylborane (4.78 mL, 4.78 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **11**. **Yield**: 80.0 mg (0.21 mmol, 22%).

The diastereoisomers were separated by HPLC (12% ethyl acetate / hexane) to afford **11a** (39.0 mg, 0.10 mmol, 11%) and **11b** (39.0 mg, 0.10 mmol, 11%) as colourless oils.



11a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.20 (m, 5H, Ph), 4.69 (m$_c$, 1H, NCH), 4.25-4.18 (m, 2H, OCH_2), 3.32 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, CH_2Ph), 3.21 (dd, *J* = 18.2 Hz, *J* = 7.0 Hz, 1H, $COCH_2$), 3.10 (dd, *J* = 18.2 Hz, *J* = 5.0 Hz, 1H, $COCH_2$), 3.01-2.92 (m, 1H, $CHCF_3$), 2.77 (dd, *J* = 13.4 Hz, *J* = 9.7 Hz, 1H, CH_2Ph), 1.81-1.73 (m, 5H, Cy^{CH}, Cy^{CH2}), 1.68 (m, 1H, Cy^{CH2}), 1.33-1.12 (m, 5H, Cy^{CH2}).

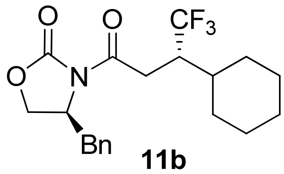
^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.9 (N*C*OC), 153.4 (O*C*ON), 135.1 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 128.6 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 66.4 (OCH_2), 55.4 (NCH), 43.3 (q, *J* = 24.9 Hz, $CHCF_3$), 37.8 (CH_2Ph), 37.4 (m,CF_3CHCH), 31.6 (q, *J* = 2.7 Hz, $COCH_2$) 30.6, 29.2, 26.6, 26.4, 26.0 (Cy^{CH2}).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −66.9 (d, *J* = 9.9 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 406.1601, calcd. for $[C_{20}H_{24}F_3NNaO_3]^+$: 406.1600.

Optical Rotation: $[\alpha]_D^{22}$ = +40.5 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2930 (w), 1784 (s), 1703 (m), 1453 (w), 1387 (m), 1280 (m), 1157 (m), 1104 (m), 1050 (w), 980 (w), 761 (w), 701 (m), 674 (w), 634 (w).



11b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.34-7.19 (m, 5H, Ph), 4.70 (m_c, 1H, NCH), 4.24-4.17 (m, 2H, OCH_2), 3.34-3.27 (m, 2H, CH_2Ph, $COCH_2$), 3.02 (dd, *J* = 18.5 Hz, *J* = 4.9 Hz, 1H, $COCH_2$), 2.96 (m_c, 1H, $CHCF_3$), 2.78 (dd, *J* = 13.5 Hz, *J* = 9.5 Hz, 1H, 1H, CH_2Ph), 1.79-1.70 (m, 5H, Cy$^{\text{CH,}}$ Cy$^{\text{CH2}}$), 1.68-1.66 (m, 1H, Cy$^{\text{CH2}}$), 1.28-1.11 (m, 5H, Cy$^{\text{CH2}}$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.9 (NCOC), 153.3 (OCON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 66.3 (OCH_2), 55.3 (NCH), 43.2 (q, *J* = 24.9 Hz, $CHCF_3$), 37.8 (CH_2Ph), 37.4 (m, CF_3CHCH), 31.6 (m, $COCH_2$), 30.5, 29.3, 26.5, 26.3, 26.0 (Cy$^{\text{CH2}}$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −66.9 (d, *J* = 9.7 Hz, 3F, CF_3).

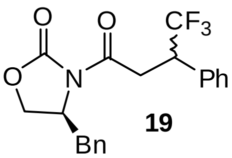
HRMS(ESI): found *m/z*: 406.1602, calcd. for $[C_{20}H_{24}F_3NNaO_3]^+$: 406.1600.

Optical Rotation: $[\alpha]_D^{22}$ = +34.7 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2930 (m), 2856 (w), 1787 (s), 1704 (s), 1454 (m), 1391 (s), 1351 (w), 1275 (m), 1156 (m), 1112 (s), 983 (m), 749 (w), 701 (m).

2.7 Attempted Synthesis of (*S*)-4-benzyl-3-((*R*)-4,4,4-trifluoro-3-phenylbutanoyl)-oxazolidin-2-one and (*S*)-4-benzyl-3-((*S*)-4,4,4-trifluoro-3-phenylbutanoyl)oxazolidin-2-one (19)

Compound **18** (200 mg, 0.65 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (839 mg, 1.30 mmol), trifluoroiodomethane (132 mL, 5.86 mmol), and triethylborane (3.25 mL, 3.25 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. The reaction was worked up according to the general procedure C.



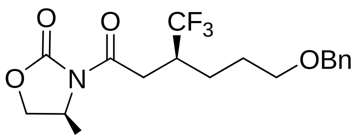
19

Subsequent NMR-data of the crude material showed no product formation, but remaining starting material.

2.8 Synthesis of (*S*)-4-benzyl-3-((*S*)-6-(benzyloxy)-3-(trifluoromethyl)hexanoyl)-oxazolidin-2-one and (*S*)-4-benzyl-3-((*R*)-6-(benzyloxy)-3-(trifluoromethyl)hexanoyl)-oxazolidin-2-one (13a,b)

Compound **12** (180 mg, 0.47 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (559 mg, 0.95 mmol), trifluoroiodomethane (95 mL, 4.27 mmol), and triethylborane (2.37 mL, 2.37 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2/toluene/Et_2O 2:1:0.1) to afford **13**. **Yield**: 81.0 mg (0.18 mmol, 38%)

The diastereoisomers were separated by column chromatography (CH_2Cl_2/toluene/Et_2O 4:2:1) to afford **13a** (40.0 mg, 89.1 µmol, 19%) and **13b** (36.0 mg 80.1 µmol, 17%) as colourless oils.



13a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.19 (m, 10H, Ph), 4.71-4.66 (m, 1H, NCH), 4.51 (s, 2H, $\mathrm{OC}\mathit{H}_2\mathrm{Ph}$), 4.24-4.17 (m, 2H, OCH_2), 3.50 (t, *J* = 6.1 Hz, 2H, $\mathrm{CH_2CH_2C}\mathit{H}_2\mathrm{OBn}$), 3.33-3.22 (m, 2H, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$, $COCH_2$), 3.08 (dd, *J* = 18.0 Hz, *J* = 6.2 Hz, 1H, $COCH_2$), 3.04-2.96 (m, 1H, $CHCF_3$), 2.72 (dd, *J* = 13.4 Hz, *J* = 9.8 Hz, 1H, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 1.90-1.82 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{CH_2CH_2OBn}$), 1.78-1.73 (m, 2H, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CH_2OBn}$), 1.62-1.56 (m, 1H, $\mathrm{C}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{CH_2OBn}$).

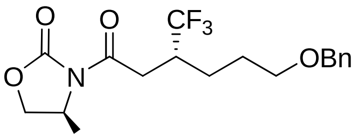
^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.3 (N*C*OC), 153.3 (O*C*ON), 138.4, 135.0 (*i*-Ph), 129.3, 128.4 (*m*-Ph), 129.0, 127.6 (*o*-Ph), 127.7, 127.5 (*p*-Ph), 73.0 ($\mathrm{O}\mathit{C}\mathrm{H_2Ph}$), 69.6 ($\mathrm{CH_2CH_2}\mathit{C}\mathrm{H_2OBn}$), 66.4 ($OCH_2$), 55.3 (NCH), 38.3 (q, *J* = 26.5 Hz, $\mathit{C}\mathrm{HCF_3}$), 37.8 ($\mathit{C}\mathrm{H_2Ph}$), 34.5 (q, *J* = 2.4 Hz, $\mathrm{CO}\mathit{C}\mathrm{H_2}$), 26.9 ($\mathrm{CH_2}\mathit{C}\mathrm{H_2CH_2OBn}$), 25.4 (m, $\mathit{C}\mathrm{H_2CH_2CH_2OBn}$) n.o. ($CF_3$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.7 (d, *J* = 8.8 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 472.1687, calcd. for $[C_{20}H_{26}F_3NNaO_4]^+$: 472.1706.

Optical Rotation: $[\alpha]_D^{22}$ = +27.6 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2928 (w), 1783 (s), 1703 (m), 1455 (w), 1388 (m), 1274 (m), 1162 (m), 1102 (m), 1052 (w), 913 (w), 760 (w), 700 (m).



13b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.19 (m, 10H, Ph), 4.67- 4.62 (m, 1H, NCH), 4.50 (s, 2H, OCH_2Ph), 4.21-4.17 (m, 2H, OCH_2), 3.50 (t, *J* = 6.2 Hz, 2H, $CH_2CH_2CH_2OBn$), 3.37-3.31 (dd, *J* = 20.2 Hz, *J* = 7.7 Hz, 1H, $COCH_2$) 3.31-3.27 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, CH_2Ph), 3.04-2.98 (m, 2H, $CHCF_3$, $COCH_2$), 2.76 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, CH_2Ph), 1.87-1.80 (m, 1H, $CH_2CH_2CH_2OBn$), 1.76-1.70 (m, 2H, $CH_2CH_2CH_2OBn$), 1.61-1.66 (m, 1H, $CH_2CH_2CH_2OBn$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.3 (NCOC), 153.3 (OCON), 138.4, 135.0 (*i*-Ph), 129.4, 128.4 (*m*-Ph), 129.0, 127.6 (*o*-Ph), 127.6, 127.4 (*p*-Ph), 72.9 (OCH_2Ph), 69.7 ($CH_2CH_2CH_2OBn$), 66.4 (OCH_2), 55.3 (NCH), 38.3 (q, *J* = 26.3 Hz, $CHCF_3$), 37.7 (CH_2Ph), 34.5 (q, *J* = 2.4 Hz, $COCH_2$), 26.9 ($CH_2CH_2CH_2OBn$), 25.4 (m, $CH_2CH_2CH_2OBn$) n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.7 (d, *J* = 8.3 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 472.1688, calcd. for $[C_{20}H_{26}F_3NNaO_4]^+$: 472.1706.

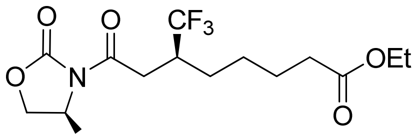
Optical Rotation: $[\alpha]_D^{22}$ = +34.2 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2926 (m), 2859 (w), 1782 (s), 1702 (s), 1455 (m), 1388 (s), 1353 (w), 1274 (m), 1162 (m), 1121 (s), 999 (w), 743 (w), 700 (m).

2.9 Synthesis of (*S*)-ethyl 8-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-8-oxo-6-(trifluoromethyl)octanoate and (*S*)-ethyl 8-((*R*)-4-benzyl-2-oxooxazolidin-3-yl)-8-oxo-6-(trifluoromethyl)octanoate (15a,b)

Compound **14** (219 mg, 0.61 mmol) was reacted according to general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (757 mg, 1.22 mmol), trifluoroiodomethane (123 mL, 5.44 mmol), and triethylborane (3.05 mL, 3.05 mmol). The addition of trifluoroiodomethane and triethylborane was repeated twice. After workup the crude product (dr = 1:1) was purified by column chromatography (CH_2Cl_2/toluene/Et_2O 2:1:0.1) to afford **15**. **Yield**: 108 mg (0.25 mmol, 42%).

The diastereoisomers were separated by column chromatography (CH_2Cl_2/toluene/Et_2O 2:1.0.1) to afford **15a** (49.5 mg, 0.12 mmol, 19%) and **15b** (53.0 mg, 0.12 mmol, 20%) as colourless oils.



15a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.20 (m, 5H, Ph), 4.71-4.65 (m, 1H, NCH), 4.25-4.18 (m, 2H,

OCH_2), 4.11 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 3.31 (dd, J = 13.4 Hz, J = 3.5 Hz, 1H, CH_2Ph), 3.24 (dd, J = 18.0 Hz, J = 6.1 Hz, 1H, $COCH_2$), 3.05 (dd, J = 18.0 Hz, J = 6.2 Hz, 1H, $COCH_2$), 2.98-2.92 (m, 1H, $CHCF_3$), 2.75 (dd, J = 13.4 Hz, J = 9.8 Hz, 1H, CH_2Ph), 2.32 (t, J = 7.1 Hz, 2H, $CH_2CH_2CH_2CH_2CO_2Et$), 1.77-1.71 (1H), 1.69-1.63 (2H), 1.53-1.42 (3H) (each m $CH_2CH_2CH_2CH_2CO_2Et$), 1.24 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

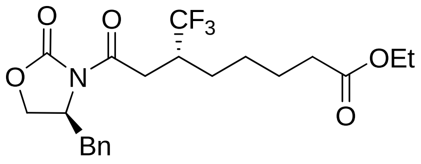
^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 173.4 ($CO_2CH2CH3$), 170.3 (NCOC), 153.43 (OCON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.3 (*o*-Ph), 127.4 (*p*-Ph), 66.4 (OCH_2), 60.3 (OCH_2CH_3), 55.3 (NCH), 38.4 (q, J = 26.0 Hz, $CHCF_3$), 37.8 (CH_2Ph), 34.5 (q, J = 2.9 Hz, $COCH_2$), 33.9 ($CH_2CH_2CH_2CH_2CO_2Et$), 28.5 (m, $CH_2CH_2CH_2CH_2CO_2Et$), 26.1, 24.8 ($CH_2CH_2CH_2CH_2CO_2Et$), 14.2 (OCH_2CH_3), n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.7 (d, J = 8.8 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 452.1637, calcd. for $[C_{21}H_{26}F_3NNaO_5]^+$: 452.1655.

Optical Rotation: $[\alpha]_D^{22}$ = +35.8 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2938 (m), 2871 (w), 1783 (s), 1703 (s), 1455 (m), 1388 (m), 1252 (w), 1166 (m), 1116 (m), 1051 (w), 944 (w), 762 (w), 702 (m), 667 (w), 628 (w), 505 (w).



15b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.19 (m, 5H, Ph), 4.71-4.67 (m, 1H, NCH), 4.26-4.18 (m, 2H, OCH_2), 4.12 (q, J = 7.1 Hz, 2H, OCH_2CH_3), 3.34-3.27 (m, 2H, $COCH_2$, CH_2Ph), 3.01-2.93 (m, 2H, $COCH_2$, $CHCF_3$), 2.77 (dd, J = 13.4 Hz, J = 9.6 Hz, 1H, CH_2Ph), 2.31 (t, J = 7.4 Hz, 2H, $CH_2CH_2CH_2CH_2CO_2Et$), 1.76-1.70 (1H), 1.69-1.61 (2H), 1.48-1.40 (3H) (each m, $CH_2CH_2CH_2CH_2CO_2Et$), 1.25 (t, J = 7.1 Hz, 3H, OCH_2CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 173.4 ($CO_2CH2CH3$), 170.3 (NCOC), 153.43 (OCON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.4 (*o*-Ph), 127.4 (*p*-Ph), 66.4 (OCH_2), 60.3 (OCH_2CH_3), 55.3 (NCH), 38.3 (q, J = 26.2 Hz, $CHCF_3$), 37.7 (CH_2Ph), 34.4 (q, J = 2.5 Hz, $COCH_2$), 33.9 ($CH_2CH_2CH_2CH_2CO_2Et$), 28.2 (m, $CH_2CH_2CH_2CH_2CO_2Et$), 26.1, 24.7 ($CH_2CH_2CH_2CH_2CO_2Et$), 14.2 (OCH_2CH_3), n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.7 (d, J = 8.4 Hz, 3F, CF_3).

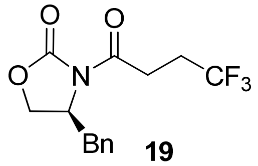
HRMS(ESI): found *m/z*: 452.1655, calcd. for $[C_{21}H_{26}F_3NNaO_3]^+$: 452.1629.

Optical Rotation: $[\alpha]_D^{22}$ = +42.6 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2935 (w), 1784 (s), 1703 (m), 1455 (w), 1389 (m), 1275 (m), 1152 (m), 1052 (w), 944 (w), 761 (w), 702 (m), 664 (w), 627 (w).

2.11 Synthesis of (*S*)-4-benzyl-3-(4,4,4-trifluorobutanoyl)oxazolidin-2-one (19)

Compound **18** (250 mg, 1.08 mmol) was reacted according to a modified general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.37 g, 2.15 mmol), trifluoroiodomethane (217 mL, 9.72 mmol), and triethylborane (5.40 mL, 5.40 mmol). After workup the crude product was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **19** as a light yellow oil. **Yield**: 110 mg (0.37 mmol, 34%).



19

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.19 (m, 5H, Ph), 4.68 (m_c, 1H, NCH), 4.25-4.19 (m, 2H, OCH_2), 3.31-3.16 (m, 3H, CH_2Ph, $COCH_2CH_2$), 2.79 (dd, J = 13.4 Hz, J = 9.6 Hz, 1H, CH_2Ph), 2.56 (m_c, 2H, $COCH_2CH_2$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.3 (NCOC), 153.3 (OCON), 134.9 (*i*-Ph), 129.9 (*m*-Ph), 129.0 (*o*-Ph), 128.4 (q, J = 278 Hz, CF_3), 127.5 (*p*-Ph), 66.5 (OCH_2), 55.2 (NCH), 37.8 (CH_2Ph), 28.8 (q, J = 2.7 Hz, $COCH_2CH_2$), 28.4 (q, J = 27.6 Hz, $COCH_2CH_2$).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −66.3 (t, J = 10.5 Hz, 3F, CF_3).

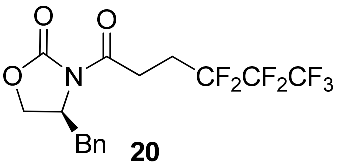
HRMS(ESI): found *m/z*: 324.0825, calcd. for $[C_{14}H_{14}F_3NNaO_3]^+$: 324.0818.

Optical Rotation: $[\alpha]_D^{22}$ = +43.9 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2924 (w), 1781 (vs), 1703 (s), 1481 (m), 1358 (m), 1225 (m), 1140 (m), 1016 (w), 746 (w), 701 (w), 621 (w), 561 (w).

2.10 Synthesis of (*S*)-4-benzyl-3-(4,4,5,5,6,6,6-heptafluorohexanoyl)oxazolidin-2-one (20)

Compound **18** (200 mg, 0.87 mmol) was reacted according to a modified general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.10 g, 1.73 mmol), heptafluoro-*n*-propyl iodide (2.30 g, 7.78 mmol, filtered over neutral alox), and triethylborane (4.32 mL, 4.32 mmol). After workup the crude product was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **20** as a colourless oil. **Yield**: 114 mg (0.28 mmol, 33%).



20

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.19 (m, 5H, Ph), 4.69 (m_c, 1H, NCH), 4.26-4.20 (m, 2H, OCH_2), 3.36-3.22 (m, 3H, CH_2Ph, $COCH_2CH_2$), 2.79 (dd, J = 13.4 Hz, J = 9.6 Hz, 1H, CH_2Ph), 2.55 (m_c, 2H, $COCH_2CH_2$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 66.5 (OCH_2), 55.2 (NCH), 37.8 ($\mathit{C}H_2Ph$), 27.2 (t, *J* = 3.5 Hz, $COCH_2CH_2$), 25.3 (t, *J* = 21.8 Hz, $COCH_2CH_2$), n.o. (CF_2, CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −80.4 (t, *J* = 9.8 Hz, 3F, $CF_2CF_2C\mathit{F}_3$), −115.3 (m$_c$, 2F, $CF_2C\mathit{F}_2CF_3$), −127.7 (m$_c$, 2F, $C\mathit{F}_2CF_2CF_3$).

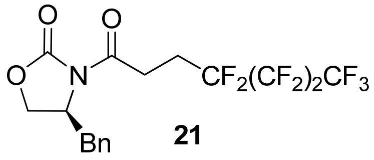
HRMS(ESI): found *m/z*: 424.0748, calcd. for $[C_{16}H_{14}F_7NNaO_3]^+$: 424.0754.

Optical Rotation: $[\alpha]_D^{22}$ = +40.5 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2924 (m), 1784 (s), 1703 (s), 1482 (w), 1390 (m), 1355 (s), 1290 (w), 1224 (s), 1179 (m), 1112 (s), 988 (w), 748 (w), 702 (m), 538 (w).

2.14 Synthesis of (*S*)-4-benzyl-3-(4,4,5,5,6,6,7,7,7-nonafluoroheptanoyl)oxazolidin-2-one (21)

Compound **18** (250 mg, 1.08 mmol) was reacted according to a modified general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.38 g, 2.16 mmol), perfluorobutyl iodide (3.36 g, 9.72 mmol, filtered over neutral alox), and triethylborane (5.50 mL, 5.50 mmol). After workup the crude product was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **21** as a colourless oil. **Yield**: 133 mg (0.29 mmol, 27%).



21

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.19 (m, 5H, Ph), 4.69 (m$_c$, 1H, NCH), 4.26-4.20 (m, 2H, OCH_2), 3.35-3.21 (m, 3H, $C\mathit{H}_2Ph$, $COC\mathit{H}_2CH_2$), 2.79 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, $C\mathit{H}_2Ph$), 2.57 (m$_c$, 2H, $COCH_2C\mathit{H}_2$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 66.5 (OCH_2), 55.2 (NCH), 37.8 ($\mathit{C}H_2Ph$), 27.2 (t, *J* = 3.5 Hz, $CO\mathit{C}H_2CH_2$), 25.5 (t, *J* = 22.0 Hz, $COCH_2\mathit{C}H_2$), n.o. (CF_2, CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −80.9 (m$_c$, 3F, CF_3), −114.5 (m$_c$, 2F, CF_2), −124.4 (m$_c$, 2F, CF_2), −126.0 (m$_c$, 2F, CF_2).

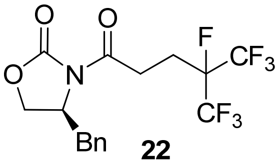
HRMS(ESI): found *m/z*: 474.0717 calcd. for $[C_{20}H_{24}F_3NNaO_3]^+$: 474.0722.

Optical Rotation: $[\alpha]_D^{22}$ = +38.5 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3030 (w), 2965 (w), 1784 (s), 1704 (s), 1498 (w), 1391 (m), 1354 (m), 1222 (s), 1133 (s), 1052 (w), 979 (m), 747 (w), 701 (m), 526 (w).

2.15 Synthesis of (*S*)-4-benzyl-3-(4,5,5,5-tetrafluoro-4-(trifluoromethyl)pentanoyl)-oxazolidin-2-one (22)

Compound **18** (200 mg, 0.87 mmol) was reacted according to a modified general procedure C with Ytterbium(III) trifluoromethanesulfonate hydrate (1.10 g, 1.73 mmol), heptafluoroisopropyl iodide (2.31 g, 7.79 mmol, filtered over neutral alox), and triethylborane (4.32 mL, 4.32 mmol). After workup the crude product was purified by column chromatography (CH_2Cl_2: toluene 2:1) to afford **22** as a colourless oil. **Yield**: 59.0 mg (0.15 mmol, 17%).



22

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.20 (m, 5H, Ph), 4.68 (m_c, 1H, NCH), 4.26-4.20 (m, 2H, OCH_2), 3.34-3-19 (m, 3H, CH_2Ph, $COCH_2CH_2$), 2.78 (dd, *J* = 13.4 Hz, *J* = 9.7 Hz, 1H, CH_2Ph), 2.63-2.51 (m, 2H, $COCH_2CH_2$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.5 (N*C*OC), 153.3 (O*C*ON), 135.0 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 66.5 (OCH_2), 55.2 (NCH), 37.8 (CH_2Ph), 28.5 (d, *J* = 4.9 Hz, $COCH_2CH_2$), 22.9 (d, *J* = 20.1 Hz, $COCH_2CH_2$), n.o. (CF, CF_3).
^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −76.5-76.4 (m, 6F, CF_3), −185.0 (m_c, 1F, F).
HRMS(ESI): found *m/z*: 424.0745 calcd. for $[C_{16}H_{14}F_7NNaO_3]^+$: 424.0754.
Optical Rotation: $[\alpha]_D^{22}$ = +36.4 (c = 1.00, $CHCl_3$).
IR (film): $\tilde{\nu}$ [cm^{-1}] = 3030 (w), 2924 (w), 1786 (s), 1704 (s), 1482 (w), 1391 (m), 1352 (m), 1222 (s), 1158 (m), 1054 (w), 934 (m), 749 (w), 702 (m), 534 (w).

3 Synthesis of enantiomerically pure β-trifluoromethyl substituted amino acids

3.1.1 Synthesis of Boc-protected chiral β-trifluoromethyl substituted *N*-acyloxazolidinones via direct azide transfer

General procedure D:

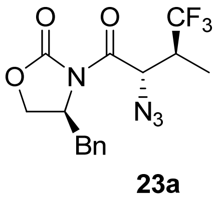
Potassium bis(trimethylsilyl)amide (KHMDS) (1.10 equiv., 0.5 M in toluene) was dissolved in tetrahydrofuran (3.0 mL / mmol substrate) at -78 °C. To the resulting solution was added via cannula a precooled (-78 °C) solution of the appropriate β-trifluoromethyl substituted *N*-acyloxazolidinone (1.00 equiv.) in tetrahydrofuran (3.0 mL / mmol substrate). The reaction mixture was stirred for 30 minutes at -78 °C. To the above solution was then added via cannula a precooled (-78 °C) solution of trisyl azide (1.23 equiv., 0.4 M in tetrahydrofuran). After a reaction time of 5.5 to 8.0 minutes glacial acetic acid (4.60 equiv.) was added and the cooling bath was removed. The reaction was stirred at room temperature for 12-14 h. Aqueous sodium chloride solution was added followed by extraction with dichloromethane. The combined organic phases were washed with saturated sodium bicarbonate solution, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was purified by column chromatography.

General procedure E:

Palladium on charcoal (10 weight% palladium) was suspended in ethyl acetate (9.0 mL / mmol substrate) and saturated with dihydrogen gas (1bar) for 30 minutes. Afterwards, di-tert-butyl dicarbonate (3.50 equiv.) and a solution of the appropriate β-trifluoromethyl substituted *N*-acyloxazolidinone azide (1.00 equiv.) in ethyl acetate (3.0 mL / mmol substrate) were added. The reaction mixture was stirred for two to four hours at room temperature under 1 bar (ballon) of dihydrogen gas. The reaction mixture was filtered over *Celite* and the clear solution concentrated *in vacuo*. The crude material was purified by column chromatography.

3.1.2 Synthesis of (*S*)-3-((2*S*,3*S*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyloxazolidin-2-one (23a)

According to general procedure D, compound **2a** (300 mg, 1.00 mmol) was reacted with KHMDS (2.09 mL, 1.05 mmol), and trisyl azide (2.42 mL, 1.17 mmol) for 6.5 minutes before glacial acetic acid (250 µL, 4.74 mmol) was added. After workup, the crude product (dr = 95:5) was purified by column chromatography (hexane / ethyl acetate 4:1) to afford **23a** as a colourless oil. **Yield**: 250 mg (0.70 mmol, 71%).



23a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.21(m, 5H, Ph), 5.44 (d, *J* = 6.1 Hz, CHN_3), 4.72 (m$_c$, 1H, NCH), 4.32-4.24 (m, 2H, OCH_2), 3.30 (dd, *J* = 10.1 Hz, *J* = 3.4 Hz, 1H, C*H*$_2$Ph), 3.00 (m$_c$, 1H, $CHCF_3$), 2.88 (dd, *J* = 10.1 Hz, *J* = 4.4 Hz, 1H, C*H*$_2$Ph), 1.32 (d, *J* = 7.1 Hz, 3H, CH_3). **^{13}C{^{1}H} NMR** (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.7 (N*C*OC), 152.8 (O*C*ON), 134.4 (*i*-Ph), 129.4 (*m*-Ph), 129.1 (*o*-Ph), 127.6 (*p*-Ph), 126.5 (q, *J* = 280 Hz, CF_3), 66.7 (OCH_2), 58.5 (q, *J* = 2.7 Hz, CHN_3), 55.4 (NCH), 39.3 (q, *J* = 27.3 Hz, *C*HCF_3), 37.5 (*C*H_2Ph), 9.1 (q, *J* = 6.1 Hz, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.6 (d, *J* = 9.2 Hz, 3F, CF_3).

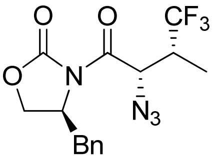
HRMS(ESI): found *m/z*: 379.0988, calcd. for $[C_{15}H_{15}F_3N_4NaO_3]^+$: 379.1016.

Optical Rotation: $[\alpha]_D^{22}$ = +93.0 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3445 (w), 2925 (w), 1782 (vs), 1706 (s), 1499 (w), 1455 (m), 1391 (s), 1366 (s), 1308 (m), 1236 (m), 1132 (s), 1028 (w), 913 (w), 736 (w), 640 (w).

3.1.3 Synthesis of (*S*)-3-((2*R*,3*R*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyloxazolidin-2-one and (*S*)-3-((2*S*,3*R*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyloxazolidin-2-one (epi-30b, 30b)

According to general procedure D, compound **2b** (546 mg, 1.78 mmol) was reacted with KHMDS (3.93 mL, 1.97 mmol), and trisyl azide (5.49 mL, 2.19 mmol) for 8 minutes before glacial acetic acid (447 µL, 8.22 mmol) was added. After workup, the crude product (dr: **epi-30b**:**30b** = 84:16) was purified by column chromatography (hexane / ethyl acetate 4:1 to 3:1) to afford the title compounds as colourless oils. **Yield**: **epi-30b**: 306 mg (0.86 mmol, 48%); **30b**: 67.4 mg (0.22 mmol, 12%).



epi-30b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.17 (m, 5H, Ph), 5.45 (d, *J* = 5.7 Hz, CHN_3), 4.72 (m_c, 1H, NCH), 4.30-4.21 (m, 2H, OCH_2), 3.36 (dd, *J* = 13.3 Hz, *J* = 3.4 Hz, 1H, C*H*$_2$Ph), 3.04 (m_c, 1H, $CHCF_3$), 2.71 (dd, *J* = 13.3 Hz, *J* = 10.1 Hz, 1H, C*H*$_2$Ph), 1.31 (d, *J* = 7.2 Hz, 3H, CH_3).

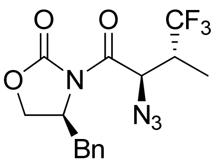
^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.8 (N*C*OC), 152.8 (O*C*ON), 134.6 (*i*-Ph), 129.3 (*m*-Ph), 129.1 (*o*-Ph), 127.6 (*p*-Ph), 126.6 (q, *J* = 278 Hz, CF_3), 66.8 (OCH_2), 58.7 (q, *J* = 2.2 Hz, CHN_3), 55.4 (NCH), 39.5 (q, *J* = 26.7 Hz, *C*HCF_3), 37.6 (*C*H_2Ph), 8.9 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.3 (d, *J* = 8.1 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 379.0999, calcd. for $[C_{15}H_{15}F_3N_4NaO_3]^+$: 379.0988.

Optical Rotation: $[\alpha]_D^{22}$ = +67.0 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2959 (w), 1786 (vs), 1710 (s), 1498 (w), 1455 (m), 1392 (s), 1358 (s), 1321 (m), 1261 (m), 1143 (s), 1021 (w), 992 (w), 735 (w), 701 (w).


30b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.21(m, 5H, Ph), 5.28 (d, *J* = 8.4 Hz, CHN_3), 4.72 (m_c, 1H, NCH), 4.30-4.25 (m, 2H, OCH_2), 3.29 (dd, *J* = 13.6 Hz, *J* = 3.3 Hz, 1H, $C\mathit{H_2}Ph$), 3.00 (m_c, 1H, $CHCF_3$), 2.91 (dd, *J* = 13.6 Hz, *J* = 9.0 Hz, 1H, $C\mathit{H_2}Ph$), 1.21 (d, *J* = 7.0 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.3 (N*C*OC), 152.8 (O*C*ON), 134.3 (*i*-Ph), 129.3 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 126.7 (q, *J* = 280 Hz, CF_3), 66.6 (OCH_2), 59.6 (q, *J* = 1.4 Hz, CHN_3), 55.3 (NCH), 39.0 (q, *J* = 26.7 Hz, *C*HCF_3), 37.2 (*C*H_2Ph), 11.0 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −68.7 (d, *J* = 7.6 Hz, 3F, CF_3).

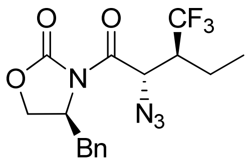
HRMS(ESI): found *m/z*: 379.0976, calcd. for $[C_{15}H_{15}F_3N_4NaO_3]^+$: 379.0976.

Optical Rotation: $[\alpha]_D^{22}$ = +107.1 (c = 2.10, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = $\tilde{\nu}$ [cm^{-1}] = 3030 (w), 2957 (w), 1781 (vs), 1708 (s), 1497 (w), 1455 (m), 1393 (s), 1356 (s), 1283 (m), 1212 (m), 1178 (m), 1017 (w), 913 (w), 748 (w), 647 (w), 555 (w).

3.1.4 Synthesis of (*S*)-3-((2*S*,3*S*)-2-azido-3-(trifluoromethyl)pentanoyl)-4-benzyl-oxazolidin-2-one (24a)

According to general procedure D, compound **5a** (711 mg, 2.16 mmol) was reacted with KHMDS (4.75 mL, 2.38 mmol), and trisyl azide (6.64 mL, 2.66 mmol) for 5.5 minutes before glacial acetic acid (557µL, 9.94 mmol) was added. After workup, the crude product (dr = 98:2) was purified by column chromatography (hexane / ethyl acetate 4:1) to afford **24a** as a light yellow oil. **Yield**: 603 mg (1.63 mmol, 75%).


24a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.22 (m, 5H, Ph), 5.47 (d, *J* = 6.4 Hz, CHN_3), 4.73-4.68 (m, 1H, NCH), 4.30-4.24 (m, 2H, OCH_2), 3.29 (dd, *J* = 13.6 Hz, *J* = 3.3 Hz, 1H, $C\mathit{H_2}Ph$), 2.88 (dd, *J* = 13.6 Hz, *J* = 9.2 Hz, 1H, $C\mathit{H_2}Ph$), 2.86-2.78 (m, 1H, $CHCF_3$), 1.87-1.77 (m, 2H, $C\mathit{H_2}CH_3$), 1.10 (t, *J* = 7.4 Hz, 3H, $CH_2C\mathit{H_3}$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 168.0 (N*C*OC), 152.7 (O*C*ON), 134.4 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 127.6 (q, *J* = 280 Hz, CF_3), 66.6 (OCH_2), 58.3 (q, *J* = 2.7 Hz, CHN_3), 55.4 (NCH), 45.2 (q, *J* = 24.9 Hz, *C*HCF_3), 37.4 (*C*H_2Ph), 18.1 (m_c, *C*H_2CH_3), 11.8 (CH_2*C*H_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −67.1 (d, *J* = 8.5 Hz, 3F, CF_3).

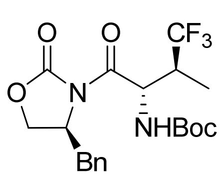
HRMS(ESI): found *m/z*: 393.1138, calcd. for $[C_{16}H_{17}F_3N_4NaO_3]^+$: 393.1145.

Optical Rotation: $[\alpha]_D{}^{22}$ = +40.9 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2972 (w), 1783 (vs), 1708 (s), 1497 (w), 1455 (m), 1392 (s), 1362 (s), 1252 (m), 1132 (s), 1031 (w), 914 (w), 735 (w), 647 (w), 506 (w).

3.1.5 Synthesis of *tert*-butyl-((2*S*,3*S*)-1-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-4,4,4-trifluoro-3-methyl-1-oxobutan-2-yl)carbamate (25a)

According to general procedure E, compound **23a** (429 mg, 1.20 µmol) was reacted with Palladium on charcoal (128 mg, 0.12 mmol), and di-tert-butyl dicarbonate (919 mg, 0.42 mmol) for 1.5 hours under 1 bar of dihydrogen gas. After workup the crude product was purified by column chromatography (hexane / ethyl acetate 4:1 to 3:1) to afford **25a** as a colourless solid. **Yield**: 435 mg (1.01 mmol, 84%).



25a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.34-7.19 (m, 5H, Ph), 5.83 (br s, 1H, NH), 5.35 (d, *J* = 8.9 Hz, COC*H*NHBoc), 4.66-4.61 (m, 1H, NCH), 4.26-4.18 (m, 2H, OCH_2), 3.31 (dd, *J* = 13.4 Hz, *J* = 3.2 Hz, 1H, C*H*$_2$Ph), 2.80 (m_c, 1H, $CHCF_3$), 2.79 (dd, *J* = 13.4 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph), 1.45 (s, 9H, COOC(C*H*$_3$)$_3$), 1.15 (d, *J* = 7.2 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (N*C*OC), 154.8 (*C*OOC(CH_3)$_3$), 152.5 (O*C*ON), 134.8 (*i*-Ph), 129.3 (*m*-Ph), 128.9 (*o*-Ph), 127.3 (*p*-Ph), 126.5 (q, *J* = 280 Hz, CF_3), 80.3 (COO*C*(CH_3)$_3$), 66.5 (OCH_2), 55.5 (NCH), 51.6 (m, CO*C*HNHBoc) 38.8 (q, *J* = 25.9 Hz, *C*HCF$_3$), 37.2 (*C*H$_2$Ph), 28.1 (COOC(*C*H$_3$)$_3$), 8.1 (br m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.4 (d, *J* = 7.3 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 453.1626, calcd. for $[C_{20}H_{25}F_3N_2NaO_5]^+$: 453.1608.

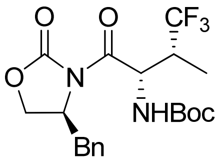
Optical Rotation: $[\alpha]_D{}^{22}$ = +42.3 (c = 0.975, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2979 (w), 1787 (vs), 1703 (s), 1499 (w), 1455 (m), 1391 (s), 1366 (s), 1261 (m), 1172 (s), 1021 (w), 992 (w), 761 (w), 702 (w).

Melting Point: 138-142 °C.

3.1.6 Synthesis of *tert*-butyl-((2*S*,3*R*)-1-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-4,4,4-trifluoro-3-methyl-1-oxobutan-2-yl)carbamate (25b)

According to general procedure E, compound **epi-30b** (321 mg, 900 µmol) was reacted with Palladium on charcoal (95.4 mg, 90.0 µmol), and di-tert-butyl dicarbonate (687 mg, 3.15 mmol) for 4 hours under 1 bar of dihydrogen gas. After workup, the crude product was purified by column chromatography (hexane / ethyl acetate 5:1) to afford **25b** as a colourless solid. **Yield**: 302 mg (0.70 mmol, 78%).



25b

^{1}**H NMR** (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.34-7.19 (m, 5H, Ph), 5.57 (dd, *J* = 10.1 Hz, *J* = 4.2 Hz, 1H, COC*H*NHBoc), 5.39 (d, *J* = 10.1 Hz, 1H, NH), 4.62 (m_c, 1H, NCH), 4.26-4.20 (m, 2H, OCH_2), 3.32 (dd, *J* = 13.5 Hz, *J* = 2.7 Hz, 1H, C*H*$_2$Ph), 2.98 (br m, 1H, $CHCF_3$), 2.80 (dd, *J* = 13.5 Hz, *J* = 9.6 Hz, 1H, C*H*$_2$Ph), 1.46 (s, 9H, COOC(C*H*$_3$)$_3$), 1.28 (d, *J* = 7.0 Hz, 3H, CH_3).

^{13}**C{^{1}H} NMR** (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.2 (N*C*OC), 155.6 (*C*OOC(CH_3)$_3$), 152.9 (O*C*ON), 134.8 (*i*-Ph), 129.4 (*m*-Ph), 128.9 (*o*-Ph), 127.4 (*p*-Ph), 127.1 (q, *J* = 278 Hz, CF_3) 80.4 (COO*C*(CH_3)$_3$), 66.7 (OCH_2), 55.9 (NCH), 53.8 (m, CO*C*HNHBoc), 39.8 (q, *J* = 25.1 Hz, *C*HCF_3), 37.3 (*C*H$_2$Ph), 28.1 (COOC(*C*H$_3$)$_3$), 11.4 (m_c, CH_3).

^{19}**F NMR** (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −67.4 (d, *J* = 7.8 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 453.1608, calcd. for $[C_{20}H_{25}F_3N_2NaO_5]^+$: 453.1608.

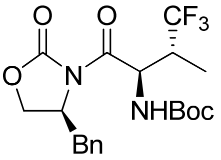
Optical Rotation: $[\alpha]_D^{22}$ = +117.0 (c = 1.78, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2980 (w), 1784 (vs), 1708 (s), 1499 (w), 1455 (m), 1391 (s), 1367 (s), 1239 (m), 1164 (s), 1134 (m), 1075 (w), 992 (w), 763 (w), 702 (w).

Melting Point: 111-113 °C.

3.1.7 Synthesis of *tert*-butyl-((2*R*,3*R*)-1-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-4,4,4-trifluoro-3-methyl-1-oxobutan-2-yl)carbamate (epi-25b)

According to general procedure E, compound **30b** (95.0 mg, 267 μmol) was reacted with Palladium on charcoal (28.2 mg, 26.7 μmol), and di-tert-butyl dicarbonate (204 mg, 0.93 mmol) for 2 hours under 1 bar of dihydrogen gas. After workup, the crude product was purified by column chromatography (hexane / ethyl acetate 4:1) to afford **epi-25b** as a colourless oil. **Yield**: 90.0 mg (0.21 mmol, 78%).



epi-25b

^{1}**H NMR** (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.19 (m, 5H, Ph), 5.81 (d, *J* = 8.1 Hz, 1H, NH), 5.30-5.27 (m, 1H, COC*H*NHBoc), 4.72 (m_c, 1H, NCH), 4.30-4.20 (m, 2H, OCH_2), 3.27 (dd, *J* = 13.3 Hz, *J* = 3.6 Hz, 1H, C*H*$_2$Ph), 2.89 (m_c, 1H, $CHCF_3$), 2.74 (dd, *J* = 13.3 Hz, *J* = 9.8 Hz, 1H, C*H*$_2$Ph), 1.44 (s, 9H, COOC(C*H*$_3$)$_3$), 1.12 (d, *J* = 7.3 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.2 (N*C*OC), 154.9 (*C*OOC(CH_3)$_3$), 152.6 (O*C*ON), 134.7 (*i*-Ph), 129.2 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 126.5 (q, *J* = 278 Hz, CF_3) 80.4 (COO*C*(CH_3)$_3$), 66.8 (OCH_2), 55.1 (NCH), 51.5 (m, CO*C*HNHBoc), 38.6 (q, *J* = 25.1 Hz, *C*HCF_3), 38.0 (*C*H_2Ph), 28.2 (COOC(*C*H_3)$_3$), 7.6 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.4 (d, *J* = 6.7 Hz, 3F, CF_3).

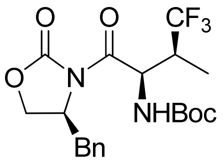
HRMS(ESI): found *m/z*: 453.1608, calcd. for $[C_{20}H_{25}F_3N_2NaO_5]^+$: 453.1608.

Optical Rotation: $[\alpha]_D^{22}$ = +47.0 (c = 1.78, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2980 (w), 1787 (vs), 1701 (s), 1499 (w), 1456 (m), 1391 (s), 1365 (s), 1239 (m), 1173 (s), 1131 (m), 1075 (w), 998 (w), 763 (w), 701 (w).

3.1.8 Synthesis of *tert*-butyl-((2*R*,3*S*)-1-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-4,4,4-trifluoro-3-methyl-1-oxobutan-2-yl)carbamate (epi-25a)

According to general procedure E, compound **30a** (232 mg, 651 µmol) was reacted with Palladium on charcoal (68.9 mg, 65.1 µmol), and di-tert-butyl dicarbonate (497 mg, 2.28 mmol) for 3 hours under 1 bar of dihydrogen gas. After workup, the crude product was purified by column chromatography (hexane / ethyl acetate 5:1) to afford **epi-25a** as a colourless oil. **Yield**: 203 mg (0.47 mmol, 73%).



epi-25a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.34-7.20 (m, 5H, Ph), 5.48 (dd, *J* = 10.3 Hz, *J* = 3.5 Hz, 1H, COC*H*NHBoc), 5.38 (d, *J* = 10.3 Hz, 1H, NH), 4.72 (m$_c$, 1H, NCH), 4.26-4.18 (m, 2H, OCH_2), 3.36 (dd, *J* = 13.3 Hz, *J* = 3.3 Hz, 1H, C*H*$_2$Ph), 3.24-3.11 (m, 1H, CHCF_3), 2.60 (dd, *J* = 13.3 Hz, *J* = 10.5 Hz, 1H, C*H*$_2$Ph), 1.45 (s, 9H, COOC(C*H*$_3$)$_3$), 1.33 (d, *J* = 7.0 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.0 (N*C*OC), 155.8 (*C*OOC(CH_3)$_3$), 153.0 (O*C*ON), 135.0 (*i*-Ph), 129.2 (*m*-Ph), 128.9 (*o*-Ph), 128.6 (q, *J* = 278 Hz, CF_3), 127.3 (*p*-Ph), 80.4 (COO*C*(CH_3)$_3$), 66.9 (OCH_2), 55.2 (NCH), 54.1 (m, CO*C*HNHBoc), 39.9 (q, *J* = 24.7 Hz, *C*HCF_3), 37.5 (*C*H_2Ph), 28.1 (COOC(*C*H_3)$_3$), 11.3 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −66.8 (d, *J* = 9.1 Hz, 3F, CF_3).

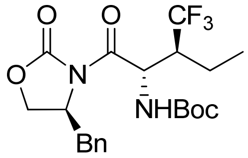
HRMS(ESI): found *m/z*: 453.1608, calcd. for $[C_{20}H_{25}F_3N_2NaO_5]^+$: 453.1608.

Optical Rotation: $[\alpha]_D^{22}$ = +6.0 (c = 0.666, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2979 (w), 1782 (vs), 1708 (s), 1500 (w), 1456 (m), 1391 (s), 1366 (s), 1237 (m), 1173 (s), 1131 (m), 1075 (w), 913 (w), 763 (w), 703 (w).

3.1.9 Synthesis of *tert*-butyl-((2*S*,3*S*)-1-((*S*)-4-benzyl-2-oxooxazolidin-3-yl)-1-oxo-3-(trifluoromethyl)pentan-2-yl)carbamate (26a)

According to general procedure E, compound **24a** (550 mg, 1.48 mmol) was reacted with Palladium on charcoal (157 mg, 0.15 mmol), and di-tert-butyl dicarbonate (1.13 g, 5.20 mmol) for 3.5 hours under 1 bar of dihydrogen gas. After workup, the crude product was purified by column chromatography (hexane / ethyl acetate 4.5:1 to 3:1) to afford **26a** as a colourless solid. **Yield**: 475 mg (1.06 mmol, 72%).



26a

^{1}**H NMR** (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.35-7.21 (m, 5H, Ph), 5.84 (br m, 1H, COC*H*NHBoc), 5.29 (br m, 1H, NH), 4.64 (m_c, 1H, NCH), 4.26-4.20 (m, 2H, OCH_2), 3.33 (dd, *J* = 13.5 Hz, *J* = 3.1 Hz, 1H, CH_2Ph), 2.79 (dd, *J* = 13.5 Hz, *J* = 9.7 Hz, 1H, CH_2Ph), 2.65 (br m, 1H, $CHCF_3$), 1.74-1.58 (m, 2H, CH_2CH_3), 1.46 (s, 9H, $COOC(CH_3)_3$), 1.02 (t, *J* = 7.5 Hz, 3H, CH_2CH_3).

^{13}**C{^{1}H} NMR** (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.8 (N*C*OC), 154.9 (*C*OOC$(CH_3)_3$), 152.6 (O*C*ON), 134.9 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.4 (q, *J* = 278 Hz, CF_3), 127.4 (*p*-Ph), 80.4 (COO*C*$(CH_3)_3$), 66.6 (OCH_2), 55.8 (NCH), 51.7 (m, CO*C*HNHBoc), 45.5 (m, *C*HCF_3), 37.3 (*C*H$_2$Ph), 28.2 (COOC(*C*H$_3$)$_3$), 17.0 (m, *C*H$_2$CH$_3$), 12.2 (CH$_2$*C*H$_3$).

^{19}**F NMR** (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −67.0 (br m, 3F, CF_3).

HRMS(ESI): found *m/z*: 467.1762, calcd. for $[C_{21}H_{27}F_3N_2NaO_5]^+$: 467.1764.

Optical Rotation: $[\alpha]_D^{22}$ = +55.1 (c = 1.0, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3427 (m), 2980 (w), 1783 (s), 1713 (s), 1499 (m), 1455 (w), 1393 (m), 1369 (s), 1294 (w), 1169 (m), 1133 (w), 1115 (w), 913 (w), 763 (w), 701 (w), 553 (w).

Melting Point: 148-152 °C.

3.2 Synthesis of α-azido-β-trifluoromethyl-substituted *N*-acyloxazolidinones via the bromo derivative

General procedure F:

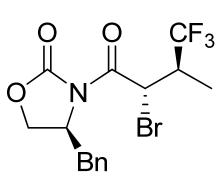
The β-trifluoromethyl-substituted *N*-acyloxazolidinone (1.00 equiv.) was dissolved in dichloromethane (10.0 mL / mmol substrate) and cooled to -78 °C. Freshly distilled *N*,*N*-diisopropylethylamine (1.20 equiv.) was slowly added followed by dropwise addition of dibutylboryl triflate (1.05 equiv., 1 M in dichloromethane). The resulting solution was stirred for 15 minutes at -78 °C and then at 0 °C for one hour. The solution was cooled to -78°C and added via cannula to a precooled (-78 °C) suspension of *N*-bromosuccinimide (1.10 equiv.) in dichloromethane (3.0 mL / mmol NBS). The reaction mixture was stirred for 2 hours at -78 °C and was then allowed to warm to room temperature. The reaction is queched by pouring into an aqueous sodium bisulfate-brine-solution (0.5 N). The aqueous phase was extracted with ethyl acetate. The combined organic phases were washed with aqueous sodium thiosulfate-brine (0.5 N) and brine, dried over sodiumsulfate, filtert and concentrated *in vacuo*. The crude material was purified by column chromatography.

General procedure G:

The α-brominated substrate (1.00 equiv.) was dissolved in dichloromethane (10.0 mL / mmol substrate) and cooled to 0 °C. At this temperature, trimethylguanidimin azide (TMGA) (5.00 equiv.) was added in one portion. The solution was stirred for 19 hours at 0 °C and was quenched by addition of saturated aqueous sodium hydrogensulfate. The aqueous phase was extracted with dichloromethane. The combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by column chromatography.

3.2.1 Synthesis of (*S*)-4-benzyl-3-((2*S*,3*R*)-2-bromo-4,4,4-trifluoro-3-methylbutanoyl)-oxazolidin-2-one (29a)

According to general procedure F, the boron enolate formed from compound **2a** (124 mg, 0.39 mmol), *N*,*N*-diisopropylethylamine (80.3 µl, 0.47 mmol), and dibutylboryl triflate (0.413 ml, 0.413 mmol, 1 M in CH_2Cl_2) was reacted with *N*-bromosuccinimide (77.0 mg, 0.43 mmol). After workup, the crude product (dr: 95:5) was purified by column chromatography (hexane / ethyl acetate 5:1) to afford **29a** as yellowish oil. **Yield**: 113 mg (0.29 mmol, 73%).



29a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.23 (m, 5H, Ph), 5.91 (d, *J* = 8.7 Hz, CHBr), 4.72 (m$_c$, 1H, NCH), 4.29-4.20 (m, 2H, OCH_2), 3.31 (dd, *J* = 13.5 Hz, *J* = 3.4 Hz, 1H, CH_2Ph), 3.19 (m$_c$, 1H, $CHCF_3$), 2.81 (dd, *J* = 13.5 Hz, *J* = 9.5 Hz, 1H, CH_2Ph), 1.47 (d, *J* = 7.0 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.9 (N*C*OC), 152.3 (O*C*ON), 134.6 (*i*-Ph), 129.5 (*m*-Ph), 129.1 (*o*-Ph), 127.5 (*p*-Ph), 66.3 (OCH_2), 55.3 (NCH), 41.5 (q, *J* = 2.3 Hz, CHBr), 49.8 (q, *J* = 26.4 Hz, *C*HCF_3), 36.9 (*C*H_2Ph), 13.0 (m, CH_3) n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.1 (d, *J* = 7.9 Hz, 3F, CF_3).

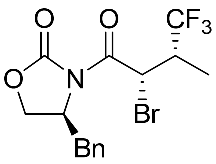
HRMS(ESI): found *m/z*: 416.0115, calcd. for $[C_{15}H_{15}BrF_3NNaO_3]^+$: 416.0086.

Optical Rotation: $[\alpha]_D^{22}$ = +29.3 (c = 0.833, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3028 (w), 2923 (w), 1782 (vs), 1705 (s), 1497 (w), 1455 (m), 1391 (s), 1353 (s), 1304 (m), 1256 (m), 1212 (m), 1104 (s), 913 (w), 748 (w), 606 (w).

3.2.2 Synthesis of (*S*)-4-benzyl-3-((2*S*,3*S*)-2-bromo-4,4,4-trifluoro-3-methylbutanoyl) oxazolidin-2-one and (*S*)-4-benzyl-3-((2*R*,3*S*)-2-bromo-4,4,4-trifluoro-3-methylbutanoyl)oxazolidin-2-one (29b, epi-29b)

According to general procedure F, the boron enolate formed from compound **2b** (330 mg, 1.04 mmol), *N*,*N*-diisopropylethylamine (213 µl, 1.26 mmol), and dibutylboryl triflate (1.10 mL, 1 M in CH_2Cl_2) was reacted with *N*-bromosuccinimide (205 mg, 1.15 mmol). After workup, the crude product (dr: **29b**:**epi-29b** = 78:22) was purified by column chromatography (hexane / ethyl acetate 5:1) to afford the title compounds as colourless oils. **Yield**: **29b**: 192 mg (0.49 mmol, 47%); **epi-29b**: 55.1 mg (0.14 mmol, 13%).



29b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.24 (m, 5H, Ph), 5.96 (d, *J* = 7.9 Hz, CHBr), 4.73 (m_c, 1H, NCH), 4.28-4.21 (m, 2H, OCH_2), 3.31 (dd, *J* = 13.5 Hz, *J* = 3.3 Hz, 1H, CH_2Ph), 3.09 (m_c, 1H, $CHCF_3$), 2.81 (dd, *J* = 13.5 Hz, *J* = 9.5 Hz, 1H, CH_2Ph), 1.37 (d, *J* = 7.0 Hz, 3H, CH_3).

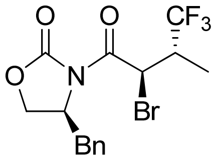
^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 166.9 (N*C*OC), 152.3 (O*C*ON), 134.5 (*i*-Ph), 129.4 (*m*-Ph), 129.0 (*o*-Ph), 127.5 (*p*-Ph), 126.1 (q, *J* = 280 Hz, CF_3), 66.2 (OCH_2), 55.3 (NCH), 42.1 (q, *J* = 26.9 Hz, *C*HCF_3), 38.8 (m, CHBr), 36.7 (*C*H_2Ph), 11.7 (q, *J* = 2.9 Hz, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −68.4 (d, *J* = 7.7 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 418.0086, calcd. for $[C_{15}H_{15}BrF_3NNaO_3]^+$: 416.0080.

Optical Rotation: $[\alpha]_D^{22}$ = +108.9 (c = 2.18, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2923 (w), 1781 (vs), 1703 (s), 1497 (w), 1455 (m), 1395 (s), 1354 (s), 1297 (m), 1258 (m), 1235 (m), 1108 (s), 1014 (m), 913 (m), 748 (w), 651 (w), 507 (w);



epi-29b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.36-7.21 (m, 5H, Ph), 5.94 (d, *J* = 8.8 Hz, CHBr), 4.70 (m_c, 1H, NCH), 4.28-4.19 (m, 2H, OCH_2), 3.35 (dd, *J* = 13.4 Hz, *J* = 3.4 Hz, 1H, CH_2Ph), 3.22 (m_c, 1H, $CHCF_3$), 2.70 (dd, *J* = 13.4 Hz, *J* = 10.1 Hz, 1H, CH_2Ph), 1.46

(d, J = 7.0 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.9 (N*C*OC), 152.4 (O*C*ON), 134.8 (*i*-Ph), 129.3 (*m*-Ph), 129.1 (*o*-Ph), 127.5 (*p*-Ph), 66.3 (OCH_2), 55.8 (NCH), 41.3 (m, CHBr), 40.0 (q, J = 26.4 Hz, *C*HCF_3), 37.5 (*C*H_2Ph), 12.8 (m, CH_3) n.o. (CF_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −69.8 (d, J = 7.7 Hz, 3F, CF_3).

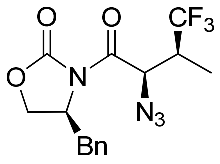
HRMS(ESI): found *m/z*: 418.0086, calcd. for $[C_{15}H_{15}BrF_3NNaO_3]^+$: 416.0086.

Optical Rotation: $[\alpha]_D^{22}$ = +49.1 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3029 (w), 2923 (w), 1781 (vs), 1703 (s), 1455 (m), 1395 (s), 1354 (s), 1297 (m), 1258 (m), 1235 (m), 1108 (s), 1014 (m), 913 (m), 748 (w), 651 (w), 507 (w).

3.2.3 Synthesis of (*S*)-3-((2*S*,3*S*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyl-oxazolidin-2-one and (*S*)-3-((2*R*,3*S*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyl-oxazolidin-2-one (30a, 23a)

According to general procedure G, compound **29a** (357 mg, 0.91 mmol) was reacted with TMGA (716 mg, 4.53 mmol). After workup, the crude product (dr: **30a**:**23a** = 88:12) was purified by column chromatography (hexane / ethyl acetate 5:1) to afford the title compounds as colourless oil. **Yield**: **30a**: 244 mg (0.68 mmol, 76%); **23a**: 34.0 mg (95.4 µmol, 10%). Analytical data for **23a** are consistent with **23a** (cf. 3.1.2).



30a

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.37-7.22 (m, 5H, Ph), 5.21 (d, J = 7.3 Hz, CHN_3), 4.77 (m$_c$, 1H, NCH), 4.32-4.23 (m, 2H, OCH_2), 3.41 (dd, J = 13.3 Hz, J = 3.5 Hz, 1H, C*H*$_2$Ph), 3.09 (m$_c$, 1H, $CHCF_3$), 2.65 (dd, J = 13.3 Hz, J = 10.3 Hz, 1H, C*H*$_2$Ph), 1.28 (d, J = 7.0 Hz, 3H, CH_3).

^{13}C{^{1}H} NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 167.8 (N*C*OC), 153.0 (O*C*ON), 134.6 (*i*-Ph), 129.3 (*m*-Ph), 129.1 (*o*-Ph), 128.8 (q, J = 280 Hz, CF_3), 127.6 (*p*-Ph), 66.9 (OCH_2), 59.8 (m, CHN_3), 55.5 (NCH), 39.6 (q, J = 27.0 Hz, *C*HCF_3), 37.7 (*C*H_2Ph), 11.3 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, $CDCl_3$): δ [ppm] = −68.3 (d, J = 8.7 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 379.0993, calcd. for $[C_{15}H_{15}F_3N_4NaO_3]^+$: 379.0989.

Optical Rotation: **a:** $[\alpha]_D^{22}$ = +31.7 (c = 1.05, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3030 (w), 2925 (w), 1781 (vs), 1711 (s), 1497 (w), 1455 (m), 1392 (s), 1353 (s), 1285 (m), 1238 (m), 1116 (m), 913 (m), 746 (w), 648 (w), 629 (w).

3.2.4 Synthesis of (*S*)-3-((2*S*,3*R*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyl-oxazolidin-2-one and (*S*)-3-((2*R*,3*R*)-2-azido-4,4,4-trifluoro-3-methylbutanoyl)-4-benzyl-oxazolidin-2-one (30b, epi-30b)

According to general procedure G, compound **29b** (200 mg, 0.51 mmol) was reacted with TMGA (402 mg, 2.54 mmol). After workup, the crude product (dr: **30b**:**epi-30** = 63:27) was purified by column chromatography (hexane / ethyl acetate 5:1) to afford the title compounds as colourless oil. **Yield**: **30b**: 93.0 mg (262 µmol, 51%); **epi-30b**: 40.0 mg (112 µmol, 22%). Analytical data for **30b** and **epi-30b** are consistent with **30b** and **epi30b** (cf. 3.1.3).

3.3 Removal of the auxiliary and *N*-Boc-deprotection

General procedure H:

The Boc-protected β-trifluoromethyl substituted *N*-Acyloxazolidinone (1.00 equiv.) was dissolved in a mixture (3:1) of tetrahydrofuran and water (10.0 mL / mmol substrate) and cooled to 0 °C. Lithium hydroxide (3.00 equiv.) and hydrogen peroxide (6.00 equiv., 30 %) were dissolved in a separate flask in a mixture (3:1) of tetrahydrofuran and water (10.0 mL / mmol substrate) at 0 °C. The resulting solution was then transferred to the *N*-Acyloxazolidinone solution at 0 °C. The resulting reaction was stirred between 40 minutes to two hours at this temperature, aqueous Na_2SO_3 (6.60 equiv., 0.68 M) was then added, stirring was continued for an additional 5 min at 0 °C. After removal of the tetrahydrofuran, the aqueous residue was extracted with dichloromethane (recovery of chiral auxiliary). The aqueous solution was acidified with HCl (2 N) until pH ~3 and extracted with ethyl acetate. The combined organic phases were dried over sodium sulfate, filtered, and concentrated *in vacuo*.

General procedure I:

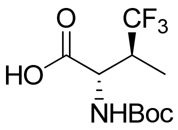
The Boc-protected amino acid (1.00 equiv.) was dissolved in dichloromethane (2.0 mL / 0.1 mmol substrate) and trifluoroacetic acid (18.0 equiv.) was added dropwise at room temperature. The mixture was stirred overnight and then concentrated *in vacuo.*

General procedure J:

The final Boc protected amino acids were stirred in a 1:1 mixture of DCM / TFA for three hours at room temperature. DCM and TFA were removed under reduced pressure. The remaining brownish oil was dissolved in 10% Na_2CO_3 and Dioxane. The mixture was cooled to 0°C and 1.1 eq. Fmoc-OSu was added. The reaction was stirred for three hours at 0°C and over night at room temperature. The reaction was quenched with water and acidified with HCl to pH = 2. The aqueous phase was extracted with DCM (4 x 50.0 mL). The combined organic phases dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by reversed-phase preparative HPLC using linear CH_3CN/H_2O gradients containing 0.1% trifluoroacetic acid (TFA) and identified by ESI-ToF MS.

3.3.1 Synthesis of (2*S*,3*S*)-2-((tert-butoxycarbonyl)amino)-4,4,4-trifluoro-3-methyl-butanoic acid (27a)

According to general procedure H, compound **25a** (239 mg, 0.56 mmol) was reacted with Lithium hydroxide (69.9 mg, 1.66 mmol) and hydrogen peroxide (103 µL, 3.33 mmol) for 45 minutes before Na_2SO_3 was added. Subsequent workup afforded **27a** as a colourless solid. **Yield**: 139 mg (0.50 mmol, 93%, 1% epimerization at the α-carbon was observed as determined by ^{19}F-NMR spectroscopic analysis).



27a

^{1}H NMR (500 MHz, 298 K, C_3D_6O): δ [ppm] = 6.37 (d, *J* = 9.8 Hz, 1H, NH), 4.79 (dd, *J* = 9.8 Hz, *J* = 2.9 Hz, 1H, C*H*CO_2H), 2.01 (m_c, 1H, $CHCF_3$), 1.40 (s, 9H, COOC(C*H*$_3$)$_3$), 1.20 (d, *J* = 7.2 Hz, 3H, CH_3) n.o. (COOH).

^{13}C{^{1}H} NMR (125 MHz, 298 K, C_3D_6O): δ [ppm] = 171.7 (COOH), 156.1 (*C*OOC(CH_3)$_3$), 128.1 (q, *J* = 280 Hz, CF_3), 79.5 (COO*C*(CH_3)$_3$), 52.7 (m, *C*HCO_2H), 40.1 (q, *J* = 26.3 Hz, *C*HCF_3), 28.3 (COOC(*C*H$_3$)$_3$), 8.6 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, C_3D_6O): δ [ppm] = −71.3 (d, *J* = 8.6 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 270.0934, calcd. for $[C_{10}H_{15}F_3NO_4]^-$: 270.0959.

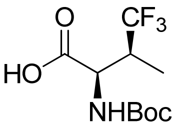
Optical Rotation: $[\alpha]_D^{22}$ = -7.8 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3306 (w), 2969 (w), 1730 (s), 1651 (s), 1478 (w), 1367 (m), 1317 (m), 1293 (m), 1239 (m), 1186 (s), 1091 (m), 979 (w), 848 (w), 666 (w).

Melting Point: 141-143 °C.

3.3.2 Synthesis of (2*R*,3*S*)-2-((tert-butoxycarbonyl)amino)-4,4,4-trifluoro-3-methyl-butanoic acid (31a)

According to general procedure H, compound **epi-25a** (129 mg, 0.30 mmol) was reacted with Lithium hydroxide (37.7 mg, 899 µmol) and hydrogen peroxide (55.6 µL, 1.79 mmol) for 40 minutes before Na_2SO_3 was added. Subsequent workup afforded **31a** as a colourless solid. **Yield**: 67.4 mg (0.25 mmol, 83%, 4% epimerization at the α-carbon was observed as determined by ^{19}F-NMR spectroscopic analysis).



31a

^{1}H NMR (500 MHz, 298 K, C_3D_6O): δ [ppm] = 6.05 (br d, *J* = 8.6 Hz, 1H, NH), 4.54-4.51 (m, 1H, C*H*CO_2H), 3.11-2.98 (m, 1H, $CHCF_3$), 1.42 (s, 9H, COOC(CH_3)$_3$), 1.24 (d, *J* = 7.2 Hz, 3H, CH_3) n.o. (COOH).

^{13}C{^{1}H} NMR (125 MHz, 298 K, C_3D_6O): δ [ppm] = 171.5 (COOH), 156.4 (*C*OOC(CH_3)$_3$), 128.3 (q, *J* = 283 Hz, CF_3), 79.9 (COO*C*(CH_3)$_3$), 54.1 (m, *C*HCO_2H), 40.9 (q, *J* = 25.6 Hz, *C*HCF_3), 28.4 (COOC(*C*H_3)$_3$), 11.2 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, C_3D_6O): δ [ppm] = −69.3 (d, *J* = 9.0 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 270.0964, calcd. for $[C_{10}H_{15}F_3NO_4]^-$: 270.0959.

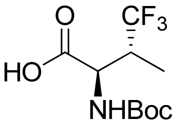
Optical Rotation: $[\alpha]_D^{22}$ = -12.8 (c = 0.80, $CHCl_3$); {lit.[7] $[\alpha]_D^{22}$ = -13.2 (c = 0.80, $CHCl_3$)}.

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3455 (w), 2983 (w), 1723 (vs), 1514 (s), 1458 (w), 1396 (m), 1371 (m), 1283 (s), 1256 (s), 1165 (s), 1080 (m), 989 (w), 854 (w), 637 (w).

Melting Point: 80-83 °C, {lit.[7] mp 85-86}.

3.3.3 Synthesis of (2*R*,3*R*)-2-((tert-butoxycarbonyl)amino)-4,4,4-trifluoro-3-methyl-butanoic acid (31b)

According to general procedure H, compound **epi-25b** (73.0 mg, 169 µmol) was reacted with Lithium hydroxide (21.3 mg, 507 µmol) and hydrogen peroxide (31.4 µL, 1.01 mmol) for 2 hours before Na_2SO_3 was added. Subsequent workup afforded **31b** as a colourless solid. **Yield**: 40.2 mg (0.15 mmol, 87%, 1% epimerization at the α-carbon was observed as determined by ^{19}F-NMR spectroscopic analysis).



31b

^{1}H NMR (500 MHz, 298 K, C_3D_6O): δ [ppm] = 6.37 (d, *J* = 9.8 Hz, 1H, NH), 4.79 (dd, *J* = 9.8 Hz, *J* = 2.9 Hz, 1H, C*H*CO_2H), 3.01 (m_c, 1H, $CHCF_3$), 1.41 (s, 9H, COOC(CH_3)$_3$), 1.20 (d, *J* = 7.2 Hz, 3H, CH_3) n.o. (COOH).

^{13}C{^{1}H} NMR (125 MHz, 298 K, C_3D_6O): δ [ppm] = 171.9 (COOH), 156.3 (*C*OOC(CH_3)$_3$), 128.4 (q, *J* = 280 Hz, CF_3), 79.8 (COO*C*(CH_3)$_3$), 52.9 (m, *C*HCO_2H), 40.3 (q, *J* = 26.3 Hz, *C*HCF_3), 28.6 (COOC(*C*H_3)$_3$), 8.7 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, D_2O): δ [ppm] = −71.3 (d, *J* = 8.6 Hz, CF_3).

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[7] Q. Chen, X.-L. Qui and F.-L. Qing, *J. Org. Chem.*, 2006, **71**, 3763.

HRMS(ESI): found *m/z*: 270.0972, calcd. for $[C_{10}H_{15}F_3NO_4]^-$: 270.0959.

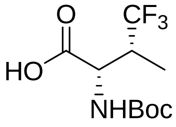
Optical Rotation: $[\alpha]_D{}^{22} = +2.2$ (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3254 (w), 2984 (w), 2417 (w), 1731 (vs), 1632 (s), 1419 (s), 1306 (m), 1258 (s), 1178 (m), 1087 (m), 1007 (m), 943 (w), 774 (w), 637 (w), 598 (w).

Melting Point: 142-146 °C.

3.3.4 Synthesis of (2*S*,3*R*)-2-((tert-butoxycarbonyl)amino)-4,4,4-trifluoro-3-methyl-butanoic acid (27b)

According to general procedure H, compound **25b** (102 mg, 236 µmol) was reacted with Lithium hydroxide (29.8 mg, 709 µmol) and hydrogen peroxide (43.8 µL, 1.42 mmol) for 45 minutes before Na_2SO_3 was added. Subsequent workup afforded **27b** as a colourless oil. **Yield**: 53.1 mg (0.12 mmol, 83%, 8% epimerization at the α-carbon was observed as determined by ^{19}F-NMR spectroscopic analysis).



27b

^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.26 (m, 1H, NH), 4.49 (d, *J* = 4.7 Hz, 1H, C*H*CO_2H), 3.04 (m_c, 1H, $CHCF_3$), 1.39 (s, 9H, $COOC(CH_3)_3$), 1.21 (d, *J* = 7.1 Hz, 3H, CH_3) n.o. (COOH).

$^{13}C\{^1H\}$ NMR (125 MHz, 298 K, $CDCl_3$): δ [ppm] = 170.4 (COOH), 155.8 (*C*$OOC(CH_3)_3$), 127.5 (q, *J* = 280 Hz, CF_3), 79.0 (COO*C*$(CH_3)_3$), 53.3 (m, *C*HCO_2H), 40.1 (q, *J* = 26.3 Hz, *C*HCF_3), 27.6 (COOC(*C*$H_3)_3$), 10.3 (CH_3).

^{19}F NMR (470 MHz, 298 K, D_2O): δ [ppm] = −69.3 (d, *J* = 8.6 Hz, CF_3).

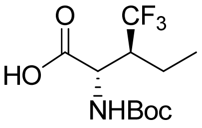
HRMS(ESI): found *m/z*: 270.0976, calcd. for $[C_{10}H_{15}F_3NO_4]^-$: 270.0959.

Optical Rotation: $[\alpha]_D{}^{22} = +11.7$ (c = 1.00, $CHCl_3$), {lit.[7] for enantiomer $[\alpha]_D{}^{22} = -13.2$ (c = 0.80, $CHCl_3$)}.

IR (film): $\tilde{\nu}$ [cm^{-1}] = 2982 (w), 2554 (w), 1724 (vs), 1514 (m), 1457 (s), 1396 (m), 1257 (s), 1167 (m), 1081 (m), 1025 (m), 988 (w), 783 (w), 636 (w), 505 (w).

3.3.5 Synthesis of (2*S*,3*S*)-2-((tert-butoxycarbonyl)amino)-3-(trifluoromethyl)pentanoic acid (28a)

According to general procedure H, compound **26a** (230 mg, 0.52 mmol) was reacted with Lithium hydroxide (65.1 mg, 155 µmol) and hydrogen peroxide (95.9 µL, 3.10 mmol) for 45 minutes before Na_2SO_3 was added. Subsequent workup afforded **28a** as a colourless solid. **Yield**: 134 mg (0.47 mmol, 90%).


28a

^{1}H NMR (500 MHz, 298 K, C_3D_6O): δ [ppm] = 10.84 (v br, 1H, OH), 6.29 (d, *J* = 9.8 Hz, 1H, NH), 4.80 (dd, *J* = 9.8 Hz, *J* = 2.9 Hz, 1H, C*H*CO_2H), 2.83 (m_c, 1H, $CHCF_3$), 1.73 (m_c, 2H, C*H*$_2CH_3$), 1.39 (s, 9H, COOC(C*H*$_3$)$_3$), 1.01 (t, *J* = 7.6 Hz, 3H, CH_2C*H*$_3$).

^{13}C{^{1}H} NMR (125 MHz, 298 K, C_3D_6O): δ [ppm] = 172.0 (COOH), 156.0 (*C*OOC(CH_3)$_3$), 128.7 (q, *J* = 280 Hz, CF_3), 79.4 (COO*C*(CH_3)$_3$), 51.8 (m, *C*HCO_2H), 46.7 (q, *J* = 26.3 Hz, *C*HCF_3), 28.1 (COOC(*C*H$_3$)$_3$), 18.1 (m, *C*H$_2CH_3$), 11.9 (CH_2*C*H$_3$).

^{19}F NMR (470 MHz, 298 K, C_3D_6O): δ [ppm] = −68.7 (d, *J* = 8.9 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 284.112, calcd. for $[C_{11}H_{17}F_3NO_4]^-$: 284.1115.

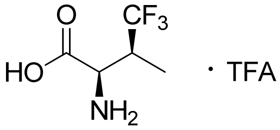
Optical Rotation: $[\alpha]_D^{22}$ = +24.4 (c = 1.00, $CHCl_3$).

IR (film): $\tilde{\nu}$ [cm^{-1}] = 3306 (w), 2969 (w), 2360 (w), 1730 (s), 1651 (s), 1478 (s), 1367 (m), 1239 (s), 1186 (m), 1050 (m), 1027 (m), 959 (w), 774 (w), 666 (w).

Melting Point: 121-124 °C.

3.3.6 Synthesis of (2*R*,3*S*)-2-amino-4,4,4-trifluoro-3-methylbutanoic acid[7]

According to general procedure I, compound **31a** (35.0 mg, 0.13 mmol) was treated with trifluoroacetic acid (0.18 mL, 2.34 mmol). After workup the product was obtained as a yellowish solid. **Yield**: 20.9 mg (0.12 mmol, 95%).



^{1}H NMR (500 MHz, 298 K, D_2O): δ [ppm] = 4.09 (d, *J* = 4.1 Hz, 1H, C*H*CO_2H), 3.10 (m_c, 1H, $CHCF_3$), 1.18 (d, *J* = 7.3 Hz, 3H, CH_3) n.o. (COOH, NH_2).

^{13}C{^{1}H} NMR (125 MHz, 298 K, D_2O): δ [ppm] = 170.1 (COOH), 127.6 (q, *J* = 280 Hz, CF_3), 53.4 (m, *C*HCO_2H), 38.8 (q, *J* = 27.6 Hz, *C*HCF_3), 10.0 (m, CH_3).

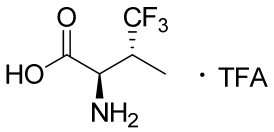
^{19}F NMR (470 MHz, 298 K, D_2O): δ [ppm] = −69.0 (d, *J* = 8.5 Hz, CF_3).

Optical Rotation: $[\alpha]_D^{22}$ = -3.40 (c = 0.3, 1 N HCl).

Melting Point: 147-152 °C

3.3.7 Synthesis of (2*R*,3*R*)-2-amino-4,4,4-trifluoro-3-methylbutanoic acid[8]

According to general procedure I, compound **31b** (34.0 mg, 0.13 mmol) treated with trifluoroacetic acid (0.17 mL, 2.27 mmol). After workup the product was obtained as a colourless solid. **Yield**: 21.3 mg (0.12 mmol, 99%).



^{1}H NMR (500 MHz, 298 K, D_2O): δ [ppm] = 4.09 (d, *J* = 2.5 Hz, 1H, C*H*CO_2H), 3.10 (m_c, 1H, $CHCF_3$), 1.09 (d, *J* = 7.4 Hz, 3H, CH_3) n.o. (COOH, NH_2).

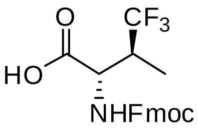
^{13}C{^{1}H} NMR (125 MHz, 298 K, D_2O): δ [ppm] = 170.9 (COOH), 127.8 (m, CF_3), 53.1 (m, *C*HCO_2H), 38.4 (m, *C*HCF_3), 7.4 (m, CH_3).

^{19}F NMR (470 MHz, 298 K, C_3D_6O): δ [ppm] = −70.7 (d, *J* = 8.7 Hz, 3F, CF_3).

Optical Rotation: $[\alpha]_D{}^{22}$ = -11.2 (c = 0.50, 1 N HCl).

3.3.8 Synthesis of (2*S*,3*S*)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4,4,4-trifluoro-3-methylbutanoic acid

According to general procedure J, the corresponding Boc-protected amino acid (120 mg, 0.44 mmol) was stirred in DCM / TFA (3.0 mL / 3.0 mL) for three hours at room temperature and the solvent was then removed *in vacuo*. The residue was dissolved in 10% Na_2CO_3 and dioxane, cooled to 0°C and Fmoc-OSu (164 mg, 0.49 mmol) was added. After stirring the reaction mixture overnight and subsequent workup the product was obtained as a corlourless solid. **Yield**: 63.4 mg (0.16 mmol, 36%).



^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.76 (d, *J* = 7.5 Hz, 2H, Ar (Fmoc)), 7.58 (d, *J* = 7.3 Hz, 2H, Ar (Fmoc)), 7.40 (t, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 7.31 (t, *J* = 7.5, 1.0 Hz, 2H, Ar (Fmoc)), 5.42 (d, *J* = 9.4 Hz, 1H, NH), 4.89 (dd, *J* = 9.2, 2.8 Hz, 1H, C*H*CO_2H), 4.63-4.34 (m, 2H, $COOCH_2$ (Fmoc)), 4.24 (t, *J* = 7.0 Hz, 1H, $COOCH_2C$*H* (Fmoc)), 3.02-2.85 (m, 1H, $CHCF_3$), 1.21 (d, *J* = 7.2 Hz, 3H, CH_3).

^{19}F NMR (376 MHz, 298 K, $CDCl_3$): δ [ppm] = −70.5 (d, *J* = 8.6 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 393.1197, calcd. for $[C_{20}H_{18}F_3NO_4]^-$: 393.1188.

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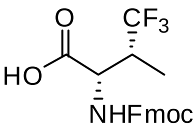
[8] J. A. Pigza, T. Quach and T. F. Molinski, *J. Org. Chem.*, 2009, **74**, 5510.

3.3.9 Synthesis of (2*S*,3*R*)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4,4,4-trifluoro-3-methylbutanoic acid

According to general procedure J, the corresponding Boc protected amino acid (150 mg, 0.55 mmol) was stirred in DCM / TFA (3.0 mL / 3.0 mL) for three hours at room temperature and the solvent was then removed in vacuo. The residue was dissolved in 10% Na_2CO_3 and dioxane, cooled to 0°C and Fmoc-OSu (205 mg, 0.61 mmol) was added. After stirring the reaction mixture overnight and subsequent workup the product was obtained as a colourless solid. **Yield**: 65.2 mg (0.17 mmol, 30%).



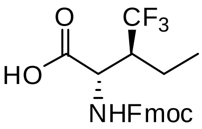
^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.76 (d, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 7.58 (d, *J* = 7.2, 2.6 Hz, 2H, Ar (Fmoc)), 7.40 (t, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 7.31 (t, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 5.36 (d, *J* = 9.7 Hz, 1H, NH), 4.68 (dd, *J* = 9.8, 3.7 Hz, 1H, C*H*CO_2H), 4.49-4.37 (m, 2H, $COOCH_2$ (Fmoc)), 4.24 (t, *J* = 7.0 Hz, 1H, $COOCH_2$C*H* (Fmoc)), 3.07 (m, 1H, $CHCF_3$), 1.27 (d, *J* = 7.2 Hz, 3H, CH_3).

^{19}F NMR (376 MHz, 298 K, D_2O): δ [ppm] = −68.1 (d, *J* = 8.8 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 393.1120, calcd. for $[C_{20}H_{18}F_3NO_4]^-$: 393.1188.

3.3.10 (2*R*,3*R*)-2-amino-4,4,4-trifluor-3-methylbutanoic acid

According to general procedure J the corresponding Boc protected amino acid (100 mg, 0.35 mmol) was stirred in DCM / TFA (3.0 mL / 3.0 mL) for three hours at room temperature and the solvent was then removed in vacuo. The residue was dissolved in 10% Na_2CO_3 and dioxane, cooled to 0°C and Fmoc-OSu (130 mg, 0.39 mmol) was added. After stirring the reaction mixture overnight and subsequent workup the product was obtained as a colourless solid. **Yield**: 117 mg (0.29 mmol, 82%).



^{1}H NMR (500 MHz, 298 K, $CDCl_3$): δ [ppm] = 7.76 (d, *J* = 7.5 Hz, 2H, Ar (Fmoc)), 7.57 (d, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 7.40 (t, *J* = 7.5 Hz, 2H, Ar (Fmoc)), 7.31 (t, *J* = 7.4 Hz, 2H, Ar (Fmoc)), 5.42 (d, *J* = 9.2 Hz, 1H, NH), 4.89 (dd, *J* = 9.3, 2.4 Hz, 1H, C*H*CO_2H), 4.43 (m, 2H, $COOCH_2$ (Fmoc)), 4.24 (t, *J* = 7.0 Hz, 1H, , $COOCH_2$C*H* (Fmoc)), 2.72 (m, 1H, $CHCF_3$), 1.81 (tt, *J* = 14.5, 7.4 Hz, 1H, CH_2CH_3), 1.66 (tt, *J* = 14.7, 7.4 Hz, 1H, CH_2CH_3), 1.09 (t, *J* = 7.4 Hz, 3H, CH_3).

^{19}F NMR (471 MHz, 298 K, $CDCl_3$): δ [ppm] = −67.8 (d, *J* = 8.3 Hz, 3F, CF_3).

HRMS(ESI): found *m/z*: 407.0975, calcd. for $[C_{21}H_{20}F_3NO_4]^-$: 407.1344.

4. Peptides

4.1 Peptide synthesis

Peptides were synthesized according to standard Fmoc strategy using a Multi-Syntech Syro XP peptide synthesizer (MultiSynTech GmbH, Witten, Germany). A NovaSyn®TGR-resin was preloaded with the first amino acid Fmoc-Lys(Boc)-OH (0.23 mmol/g, 0.03 mmol scale). C-terminal activation was carried out using TBTU/HOBt/DIEA (8 eq.). The fluorinated amino acid at the guest position Xaa and the following one were coupled manually using 2 eq. amino acid and HOBt/DIC activation. Fmoc deprotection was achieved by treatment of the resin with 2% piperidine and 2% DBU (4x5 min). For capping with acetic anhydride, a solution of Ac_2O (10 % (v/v)), DIEA (10 % (v/v)) in DMF (3 mL) was added to the resin. The reaction was shaken for 3x10 min. Peptides were cleaved from the resin by treatment with 2 mL of a solution containing triisopropylsilane (2,5 %, v/v), water (2,5%, v/v), and TFA (95 %, v/v), purified by reversed-phase preparative HPLC using linear CH_3CN/H_2O gradients containing 0.1% trifluoroacetic acid (TFA) and identified by ESI-ToF MS using an Agilent 6210 ESI-ToF LC–MS spectrometer (Agilent Technologies Inc., Santa Clara, CA, USA).

4.2 Sample preparation

The lyophilized peptide was dissolved in 1 M NaCl, 1 mM sodium phosphate, 1 mM sodium citrate, and 1 mM sodium borate buffer (pH 7.0). The concentration of peptide stock solutions was determined using the tyrosine absorbance in 6 M guanidinium chloride ($\varepsilon_{276\ nm}$ =1,455 $mol^{-1}cm^{-1}$ using a Varian Cary 50 spectrophotometer (Varian Medical Systems, Palo Alto, CA, USA) and PMMA cuvettes (10 mm path length, 1.5 mL, Plastibrand®, VWR International GmbH, Darmstadt, Germany). Stock solutions of 1 mM concentration were prepared for each peptide.

4.3 Circular dichroism

CD spectra were recorded with a Jasco J-810 spectropolarimeter at 0 °C. Quartz curettes (1.0 mm path length) were used. CD measurements were performed at peptide concentrations of 30, 50, and 80 µM. Each reported CD value represents the mean of at least 3 independent measurements. Data were collected from 250 to 200 nm at 0.2 nm intervals, 2 nm bandwidth, and 2 s response time. Spectra were background corrected by subtraction of the corresponding buffer spectra. The measured CD data in mdeg were converted into molar ellipticity per residue $[\theta]/\ (10^3 \cdot mdeg \cdot cm^2 \cdot dmol^{-1} \cdot residue^{-1})$. The mean residue molar ellipticity was independent of peptide concentration (30-80 µM) for all peptides. The fractional helical content of peptide (f_{helix}) was calculated from mean residue molar ellipticity at 222 nm and the number of backbone amides (N) 19 using the equation $f_{helix} = [\Theta]_{222} / (40000(1\text{-}2{,}5/N))$.

The helix propensity of the amino acid at the guest position was calculated from the f_{helix} of the corresponding peptide based on modified Lifson-Roig theory.[9]

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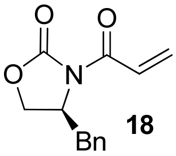
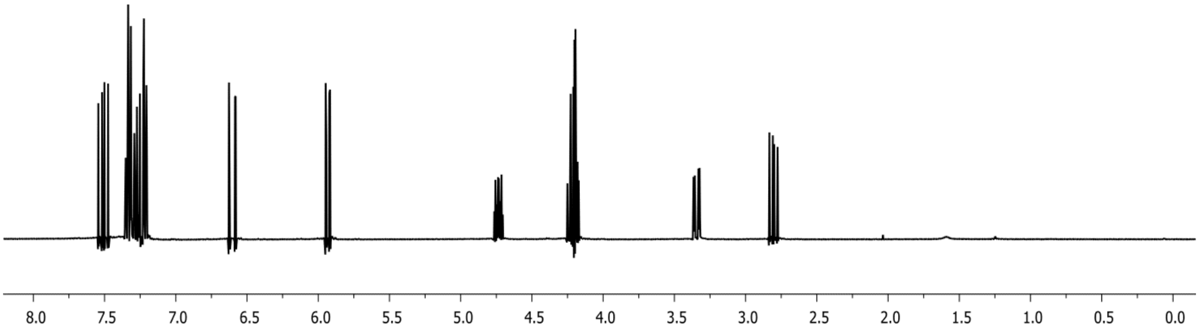
[9] A. Chakrabartty, T. Kortemme and R. L. Baldwin, *Protein Science*, 1994, **3**, 843.

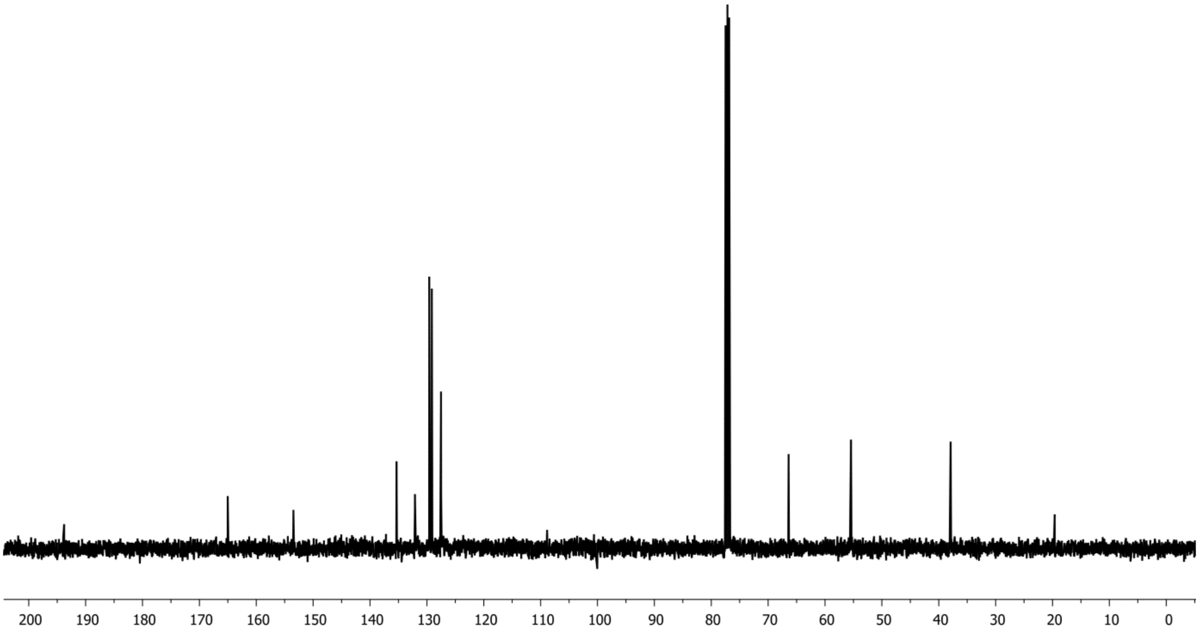
NMR Spectra

Compound 18



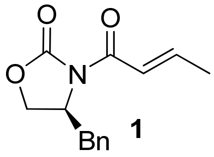


^{1}H NMR of compound **18** (500 MHz, $CDCl_3$, 298 K).

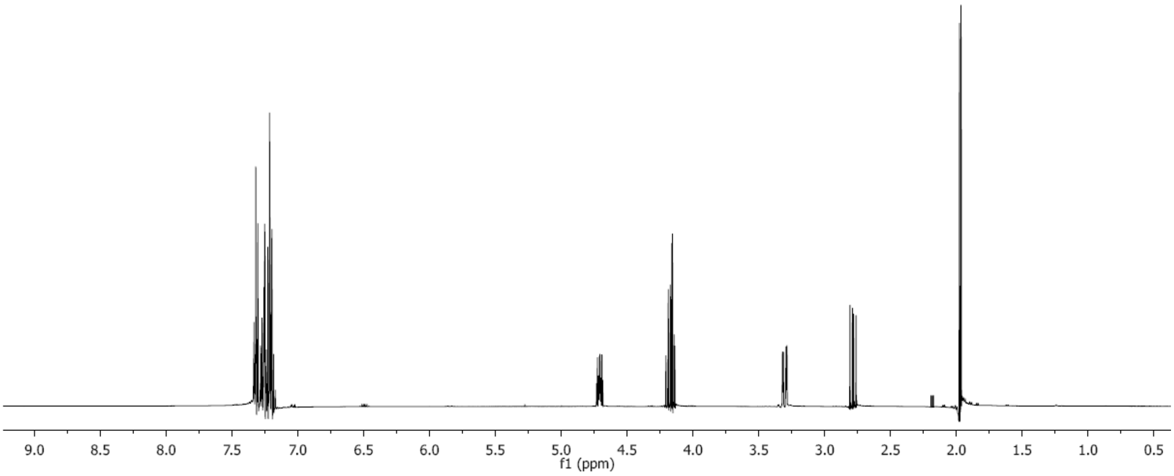


^{13}C NMR of compound **18** (125 MHz, $CDCl_3$, 298 K).

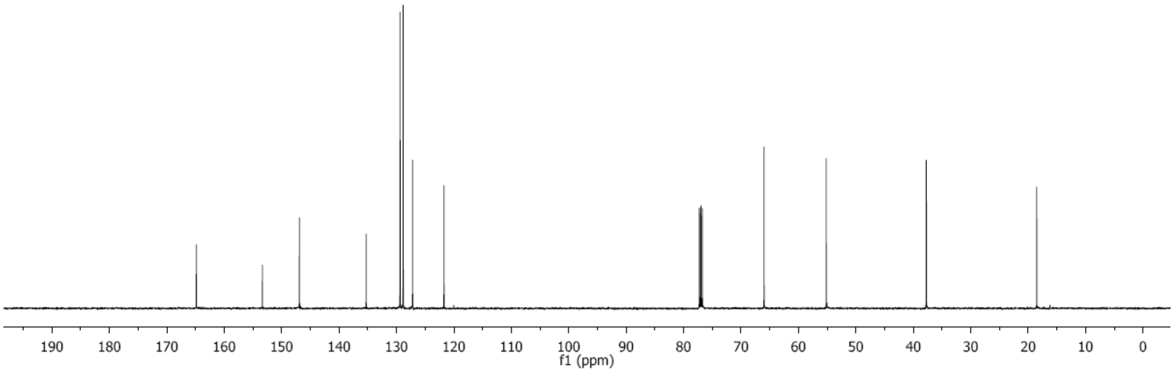
Compound 1



1

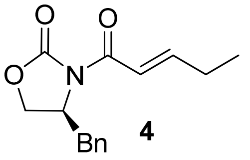


^{1}H NMR of compound **1** (500 MHz, $CDCl_3$, 298 K).

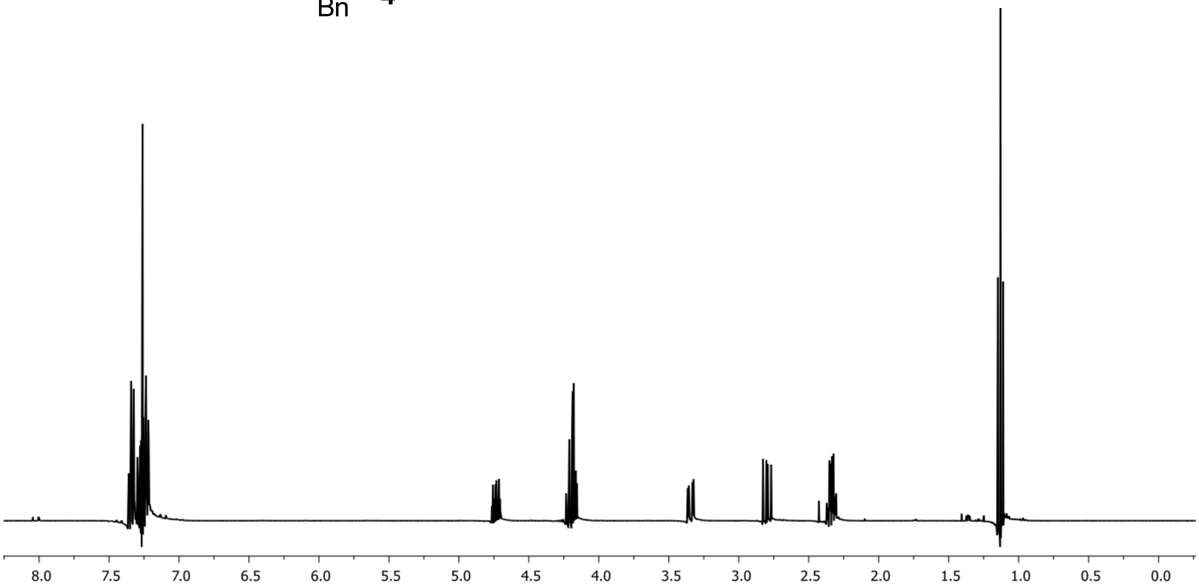


^{13}C NMR of compound **1** (125 MHz, $CDCl_3$, 298 K).

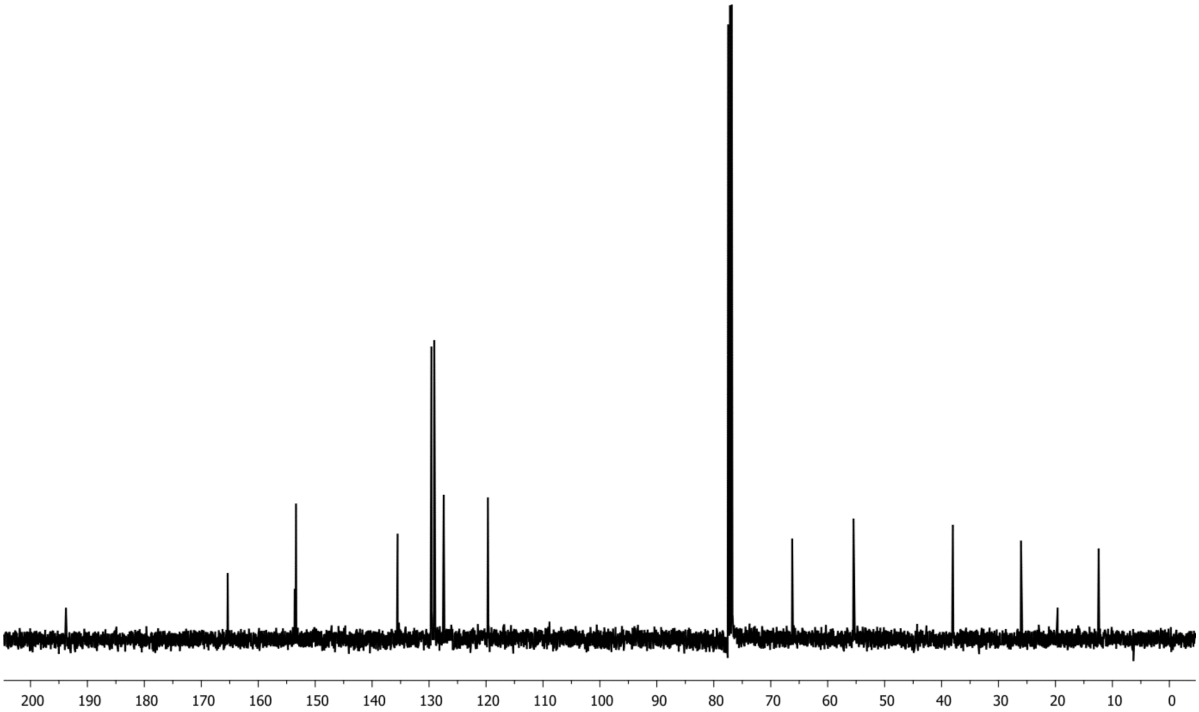
Compound 4



4

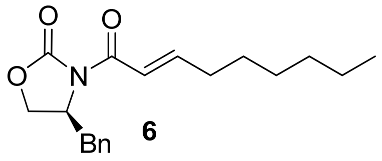


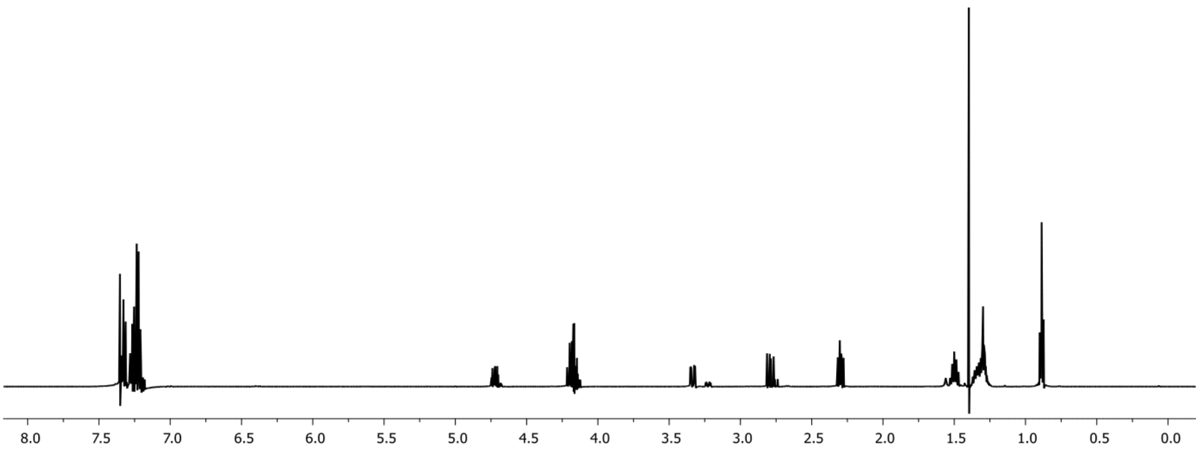
^{1}H NMR of compound **4** (500 MHz, $CDCl_3$, 298 K).



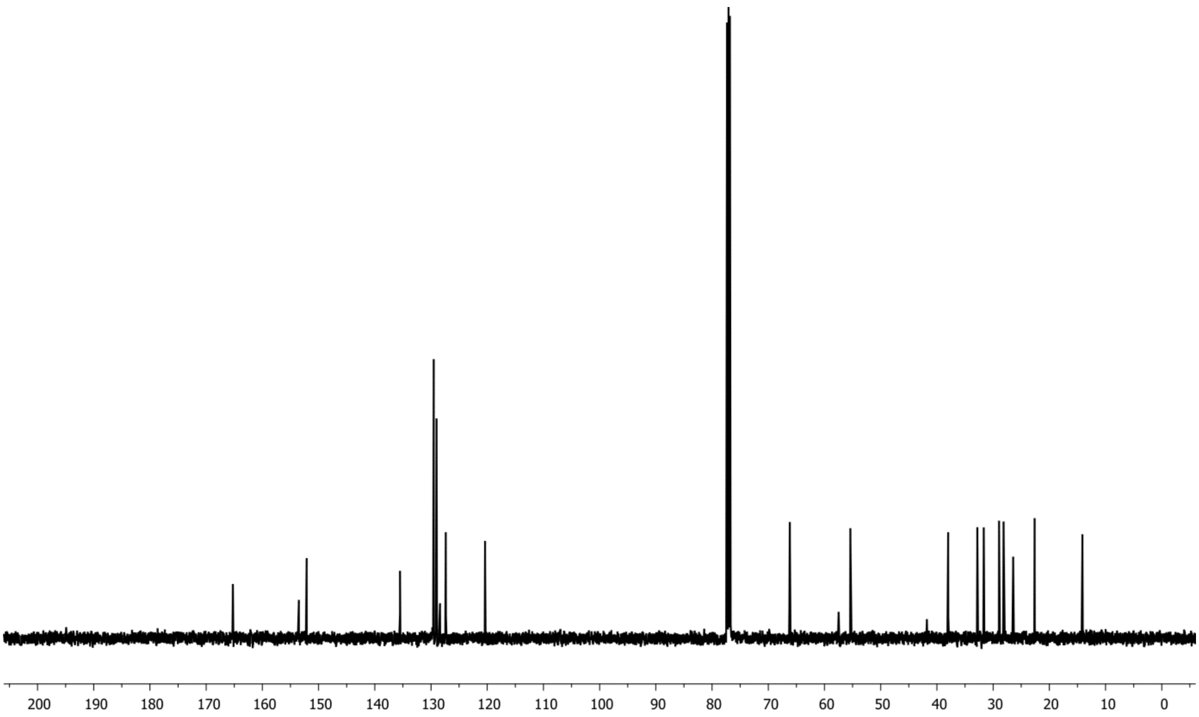
^{13}C NMR of compound **4** (125 MHz, $CDCl_3$, 298 K).

Compound 6



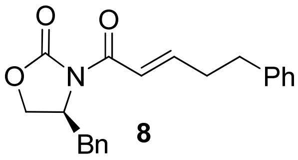


^{1}H NMR of compound **6** (500 MHz, $CDCl_3$, 298 K).

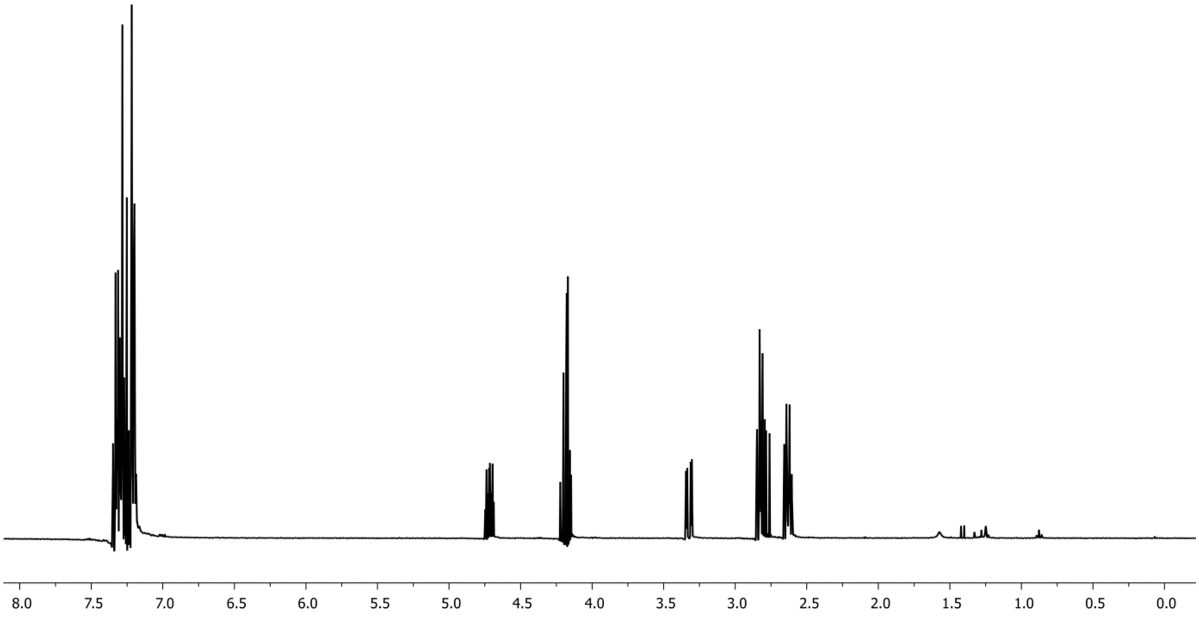


^{13}C NMR of compound **6** (125 MHz, $CDCl_3$, 298 K).

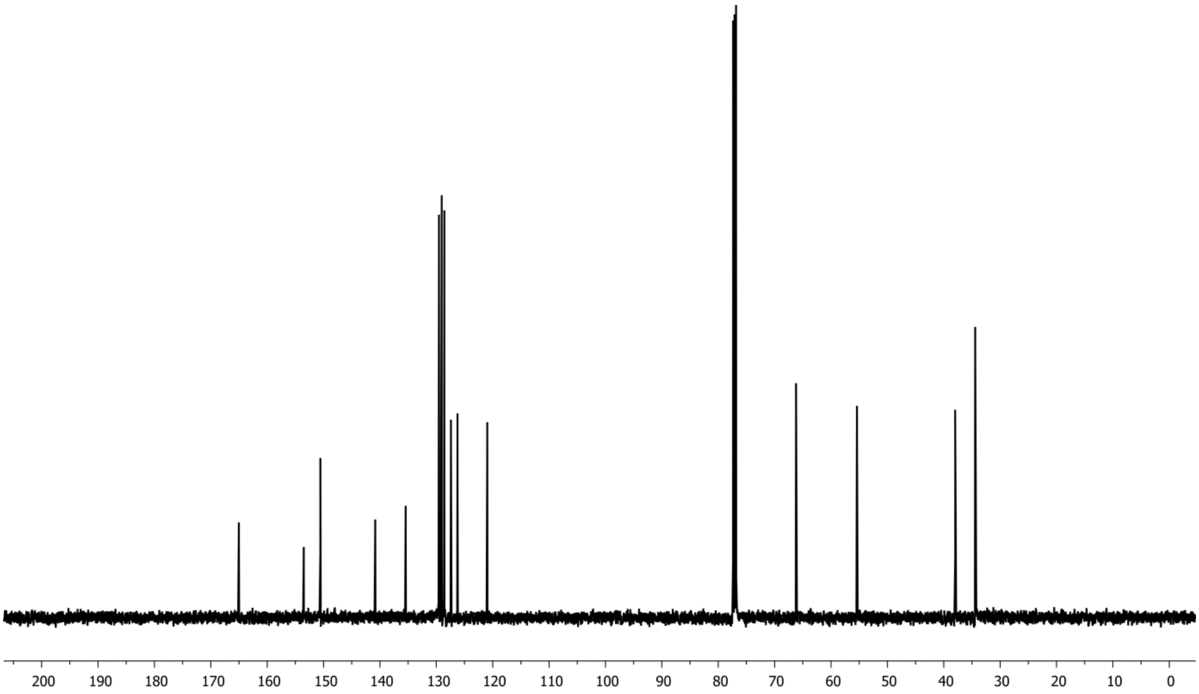
Compound 8



8

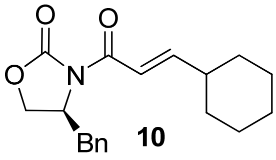


^{1}H NMR of compound **8** (500 MHz, CDCl$_3$, 298 K).



^{13}C NMR of compound **8** (125 MHz, CDCl$_3$, 298 K).

Compound 10



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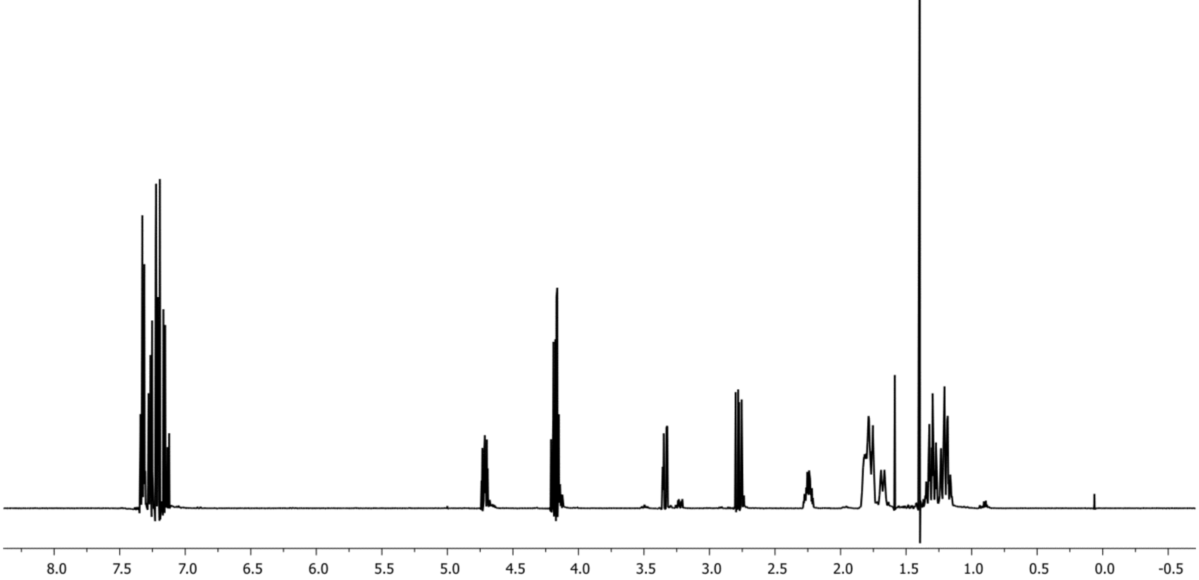
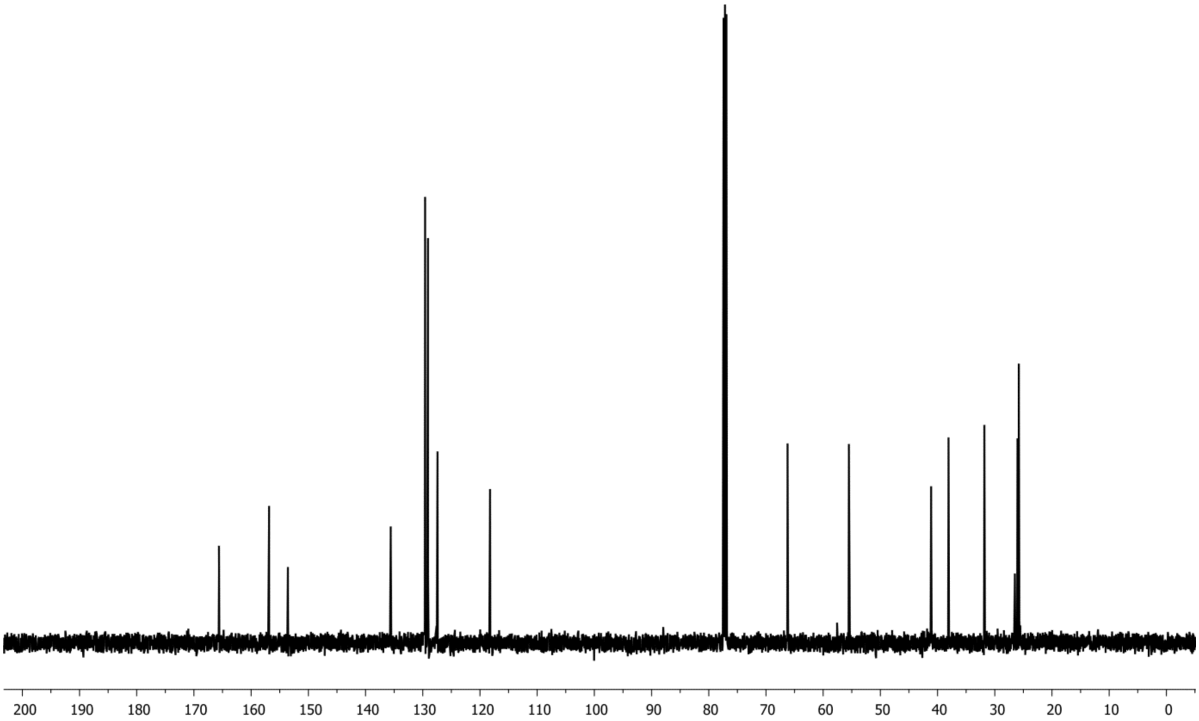
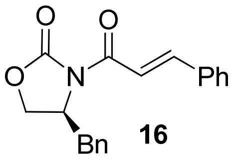


^{1}H NMR of compound **10** (500 MHz, CDCl$_3$, 298 K).

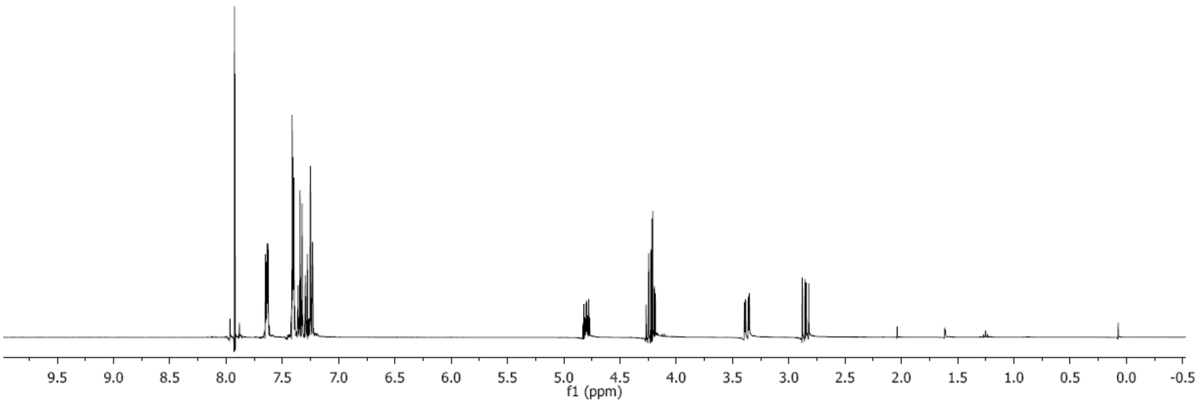


^{13}C NMR of compound **10** (125 MHz, CDCl$_3$, 298 K).

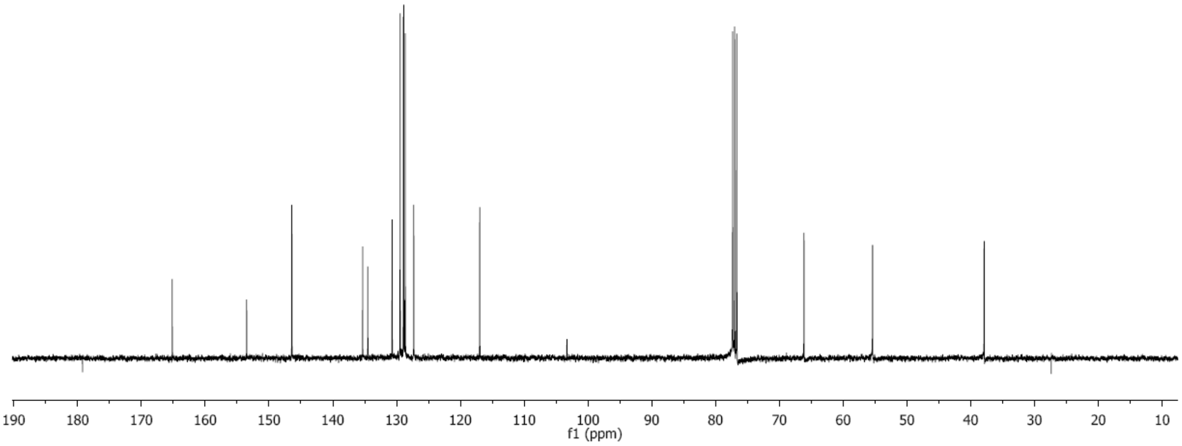
Compound 16



16

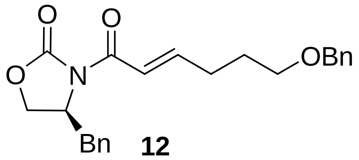


^{1}H NMR of compound **16** (500 MHz, $CDCl_3$, 298 K).

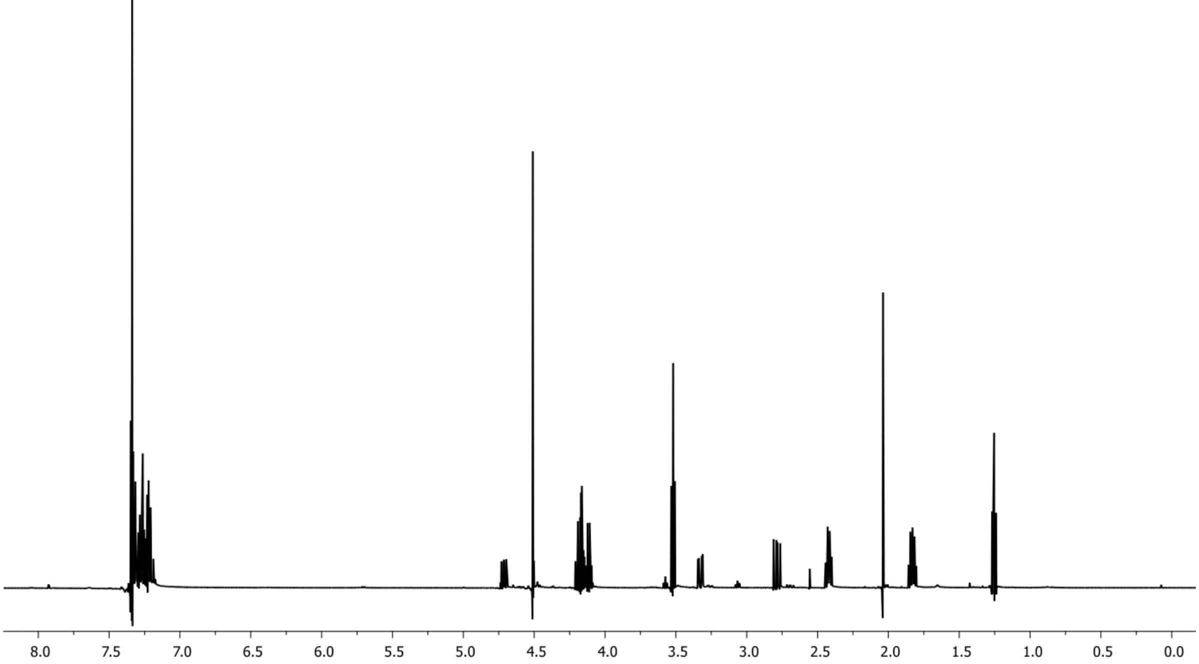


^{13}C NMR of compound **16** (125 MHz, $CDCl_3$, 298 K).

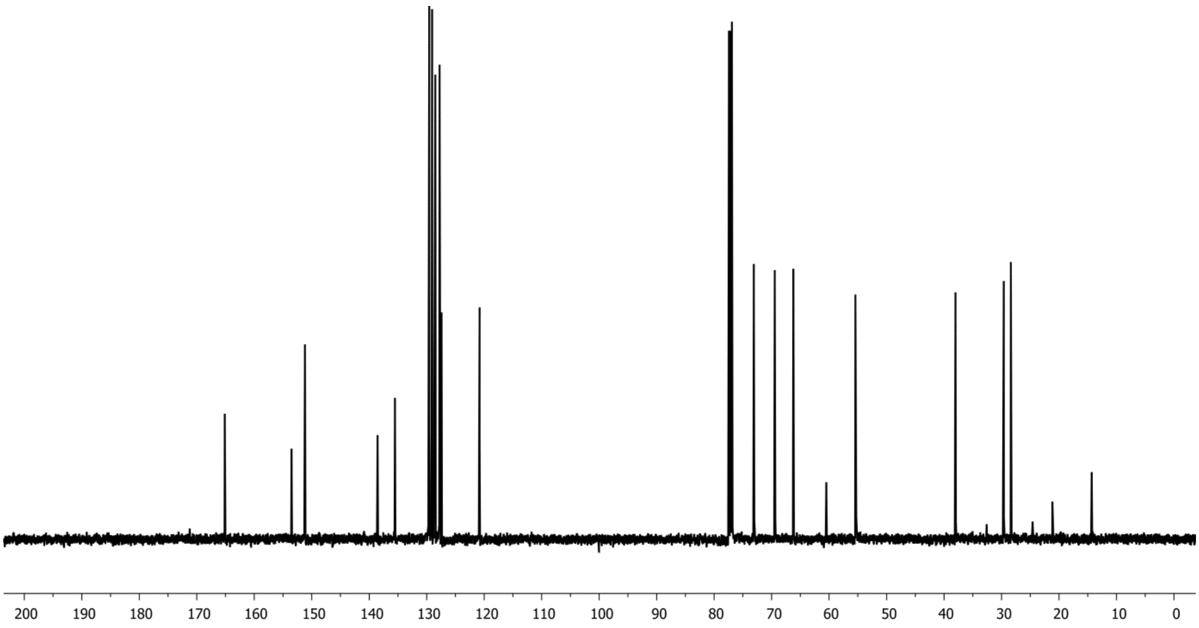
Compound 12



12

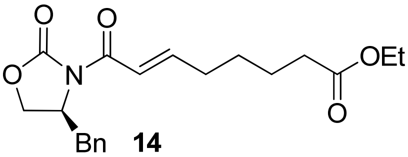


^{1}H NMR of compound **12** (500 MHz, $CDCl_3$, 298 K).

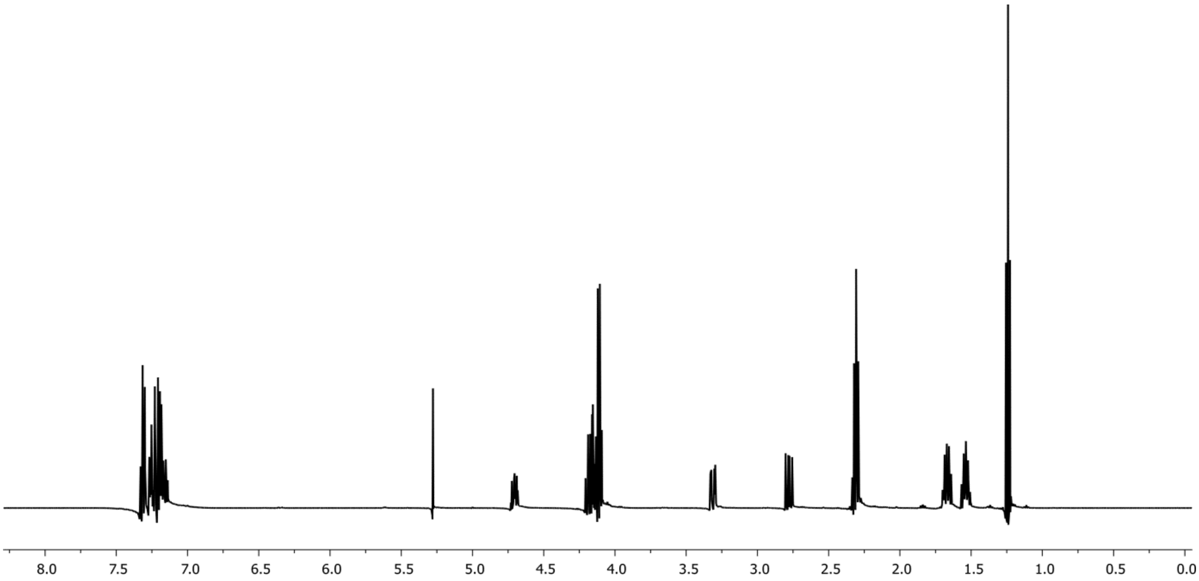


^{13}C NMR of compound **12** (125 MHz, $CDCl_3$, 298 K).

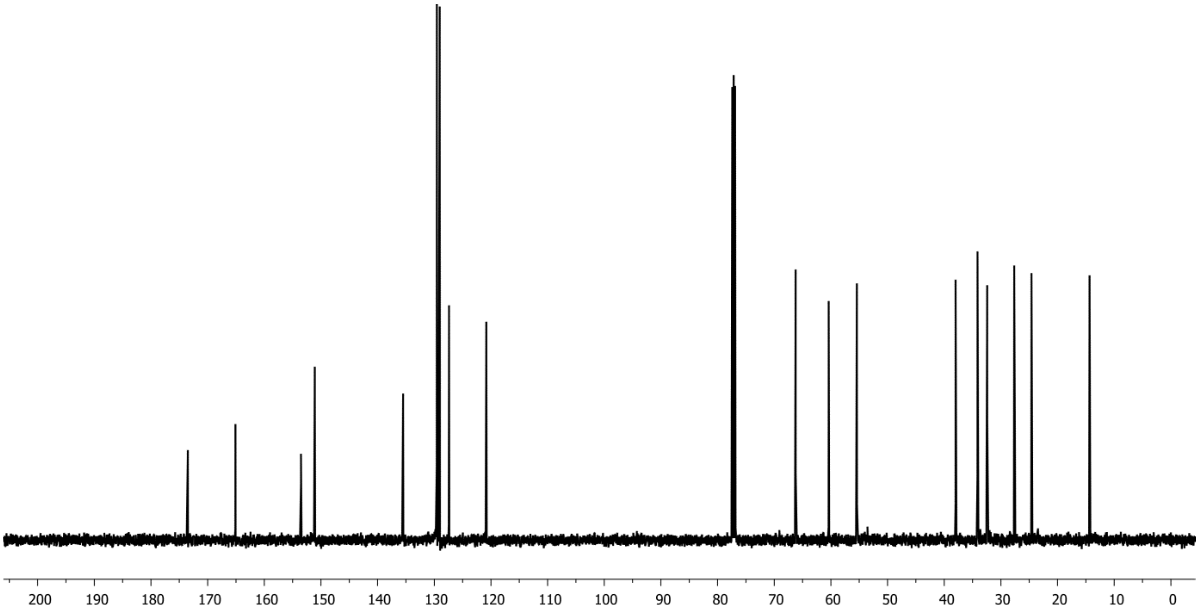
Compound 14



14

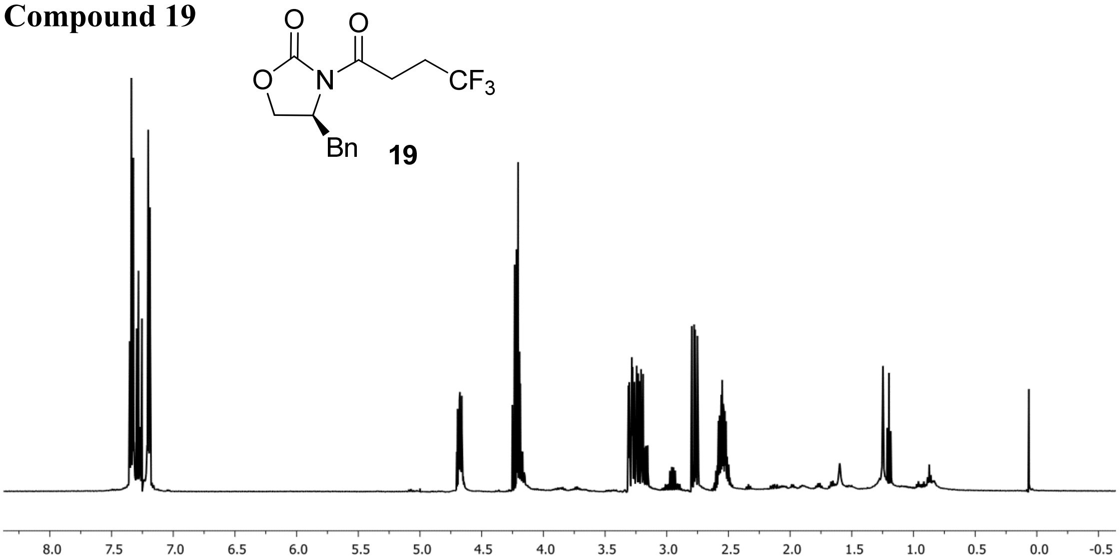


^{1}H NMR of compound **14** (500 MHz, $CDCl_3$, 298 K).

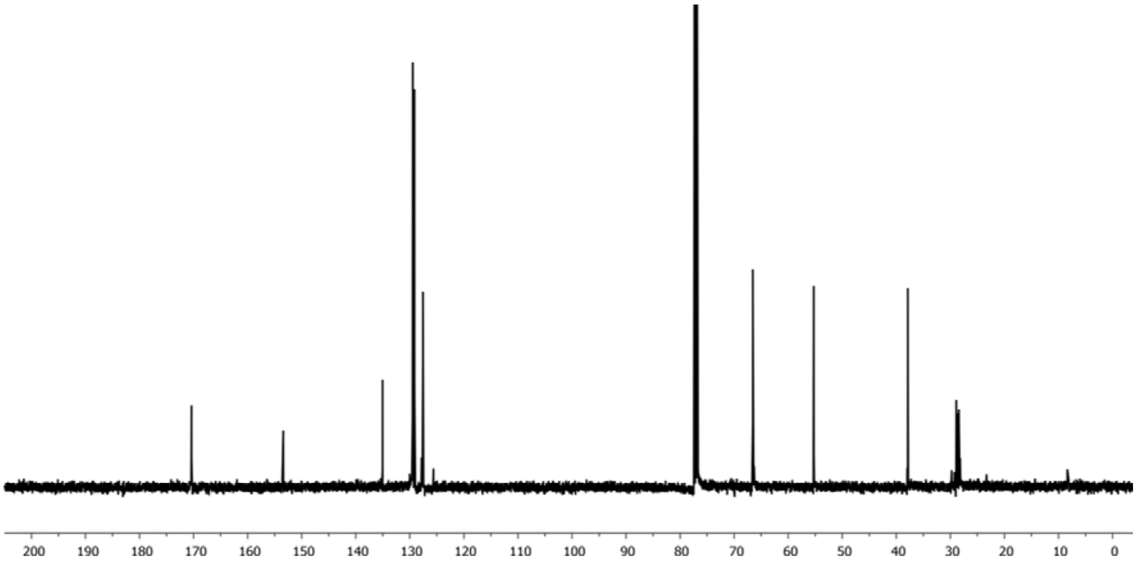


^{13}C NMR of compound **14** (125 MHz, $CDCl_3$, 298 K).

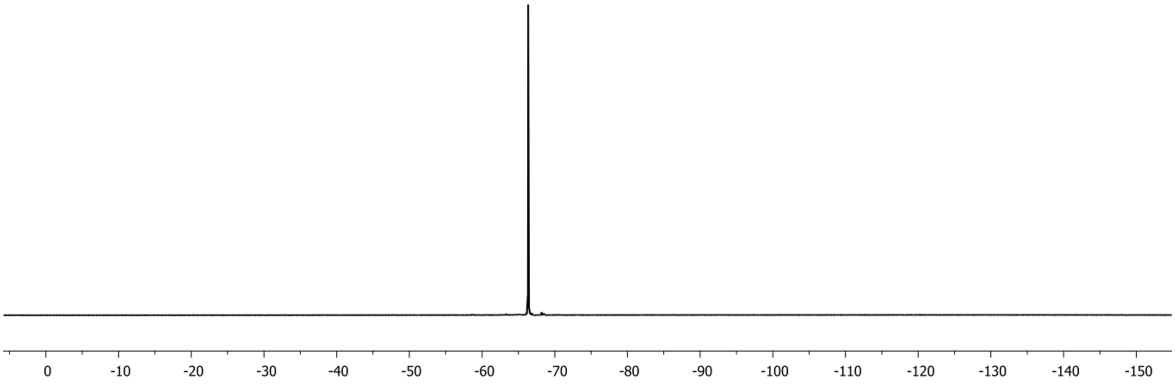
Compound 19



^{1}H NMR of compound **19** (500 MHz, $CDCl_3$, 298 K).

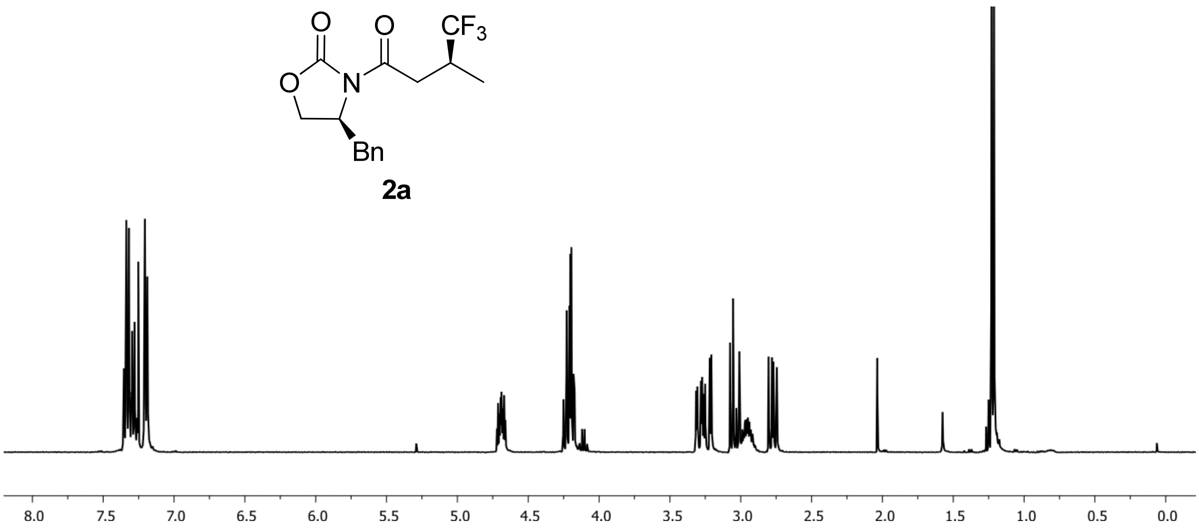


^{13}C NMR of compound **19** (125 MHz, $CDCl_3$, 298 K).



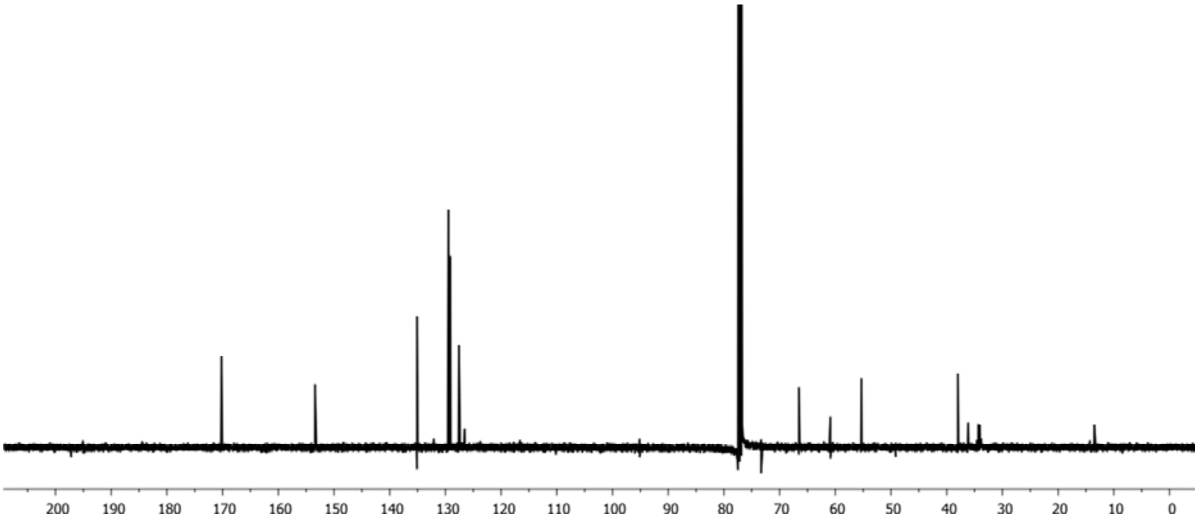
^{19}F NMR of compound **19** (470 MHz, $CDCl_3$, 298 K).

Compound 2a

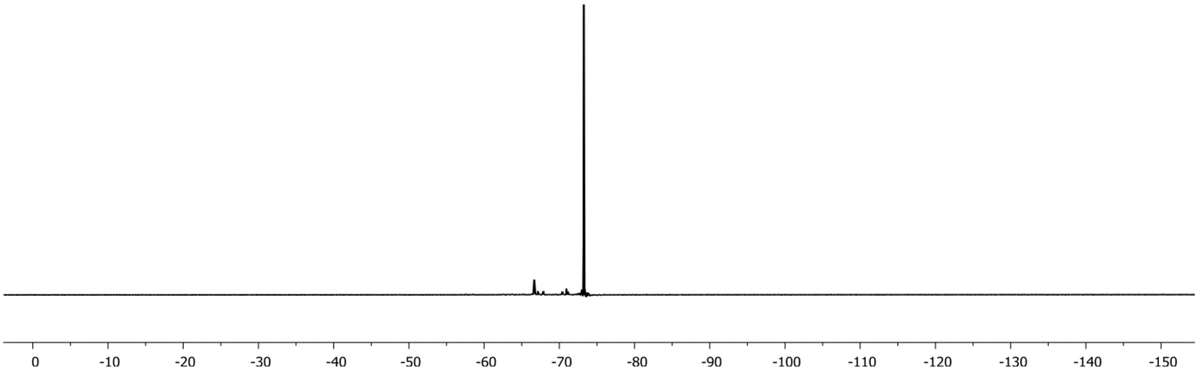


2a

^{1}H NMR of compound **2a** (500 MHz, $CDCl_3$, 298 K).

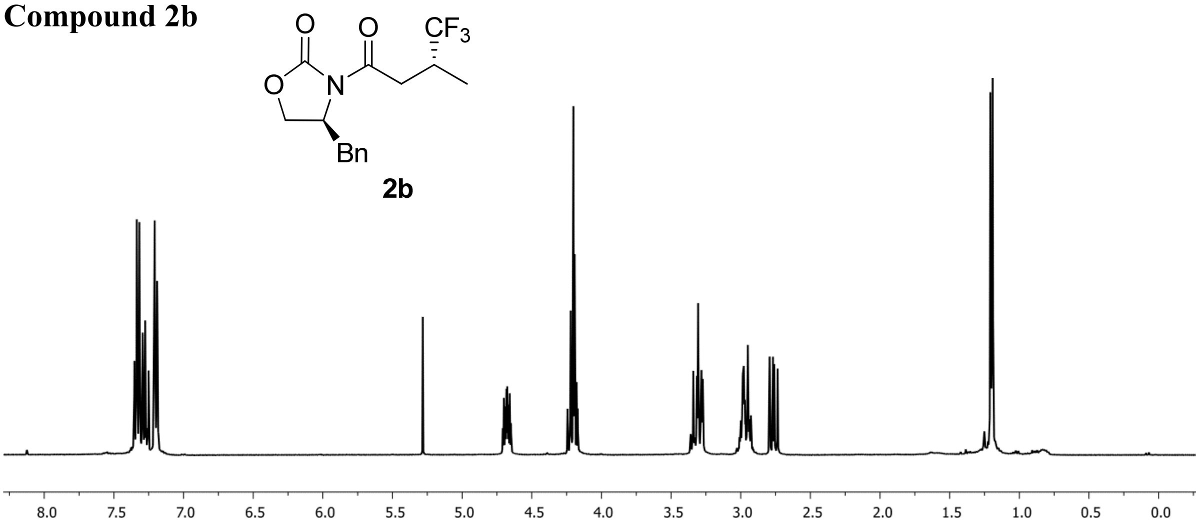


^{13}C NMR of compound **2a** (125 MHz, $CDCl_3$, 298 K).



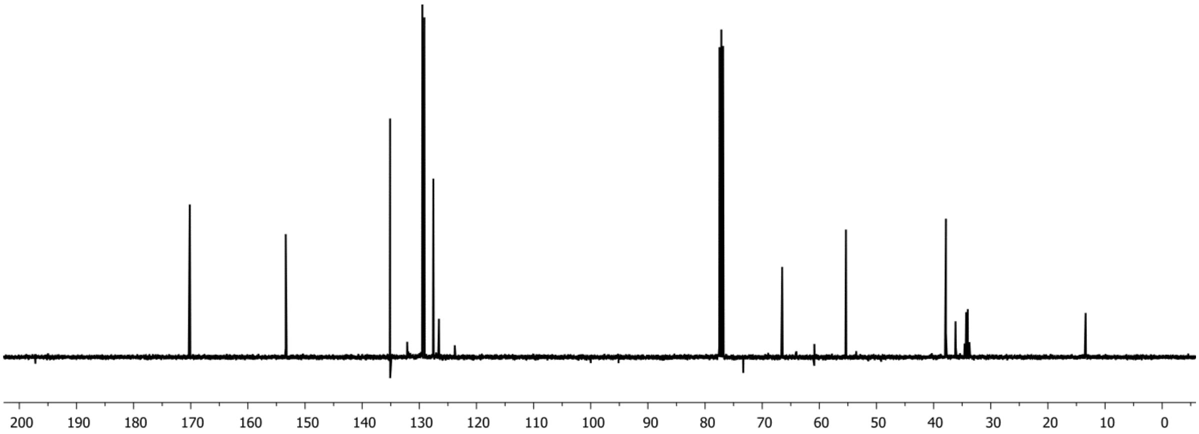
^{19}F NMR of compound **2a** (470 MHz, $CDCl_3$, 298 K).

Compound 2b

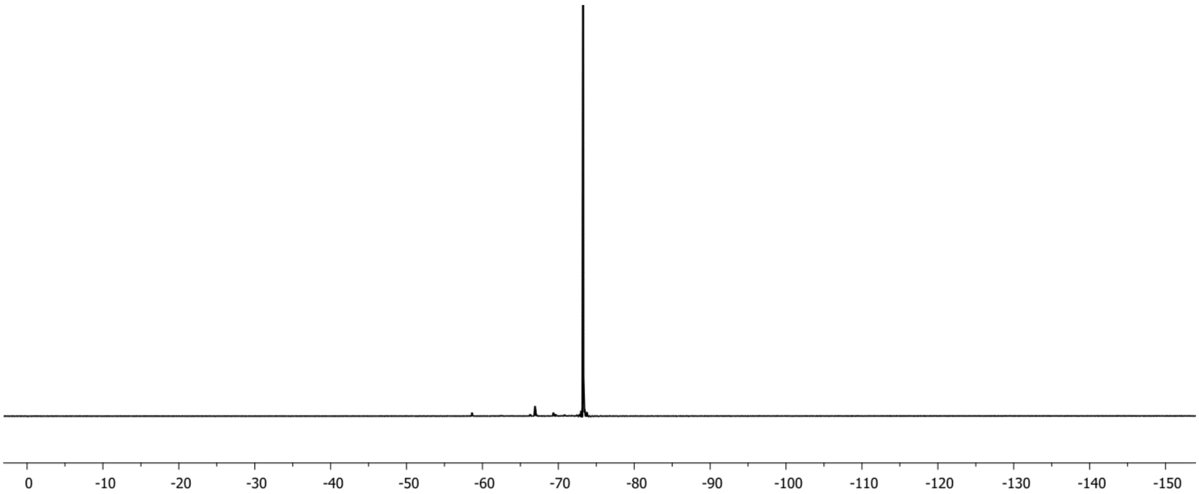


2b

^{1}H NMR of compound **2b** (500 MHz, $CDCl_3$, 298 K).



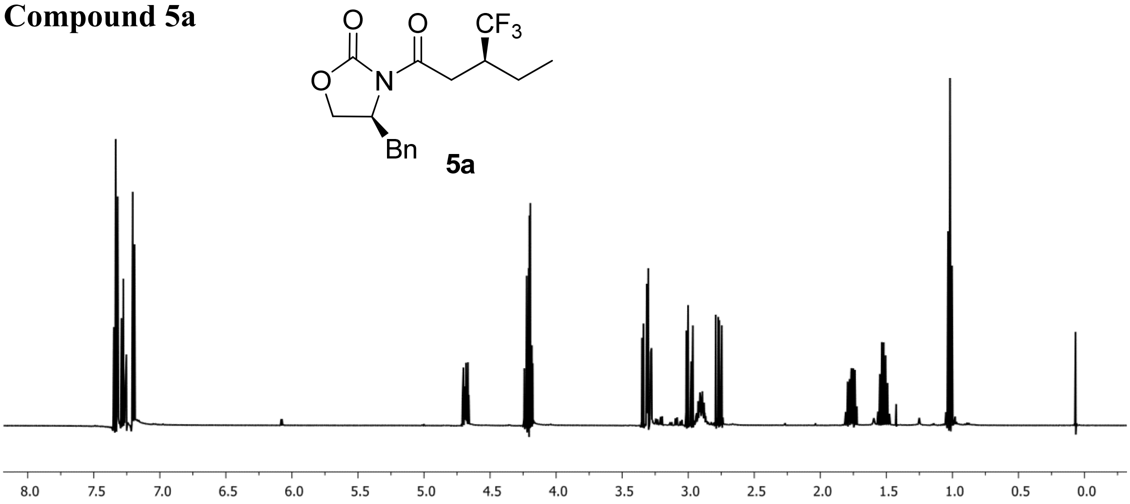
^{13}C NMR of compound **2b** (125 MHz, $CDCl_3$, 298 K).



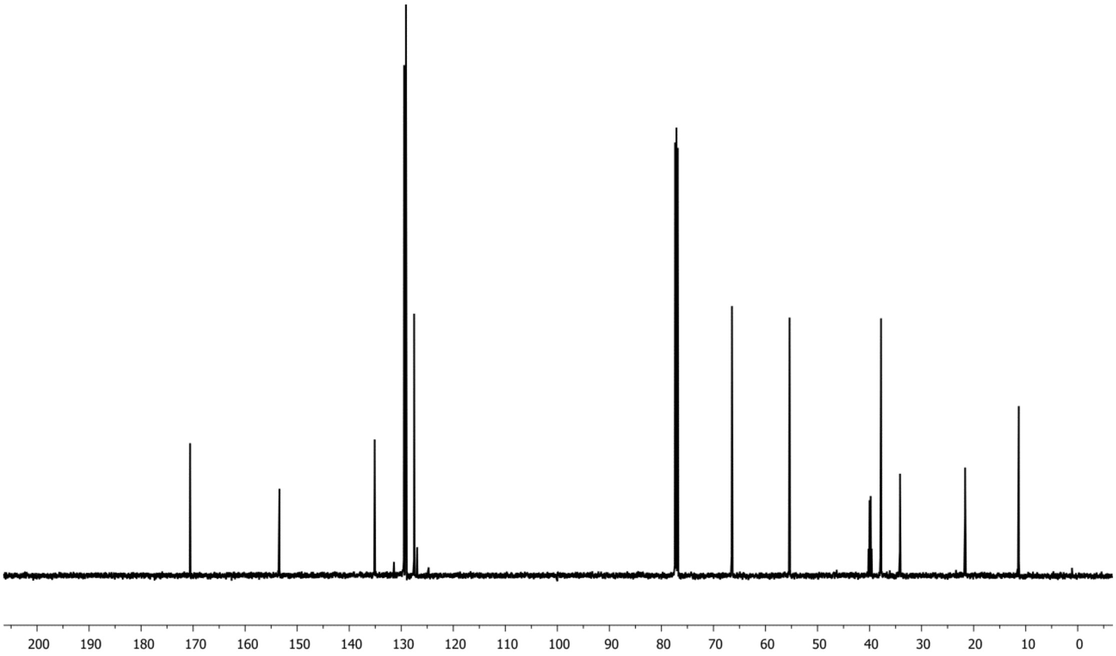
^{19}F NMR of compound **2b** (470 MHz, $CDCl_3$, 298 K).

Compound 5a

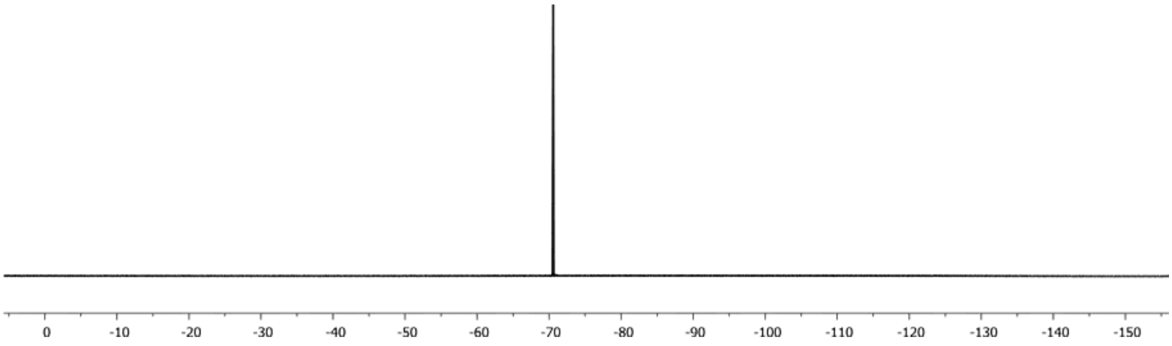
5a



^{1}H NMR of compound **5a** (500 MHz, $CDCl_3$, 298 K).

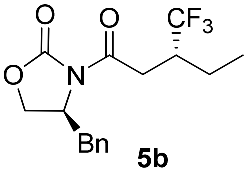


^{13}C NMR of compound **5a** (125 MHz, $CDCl_3$, 298 K).

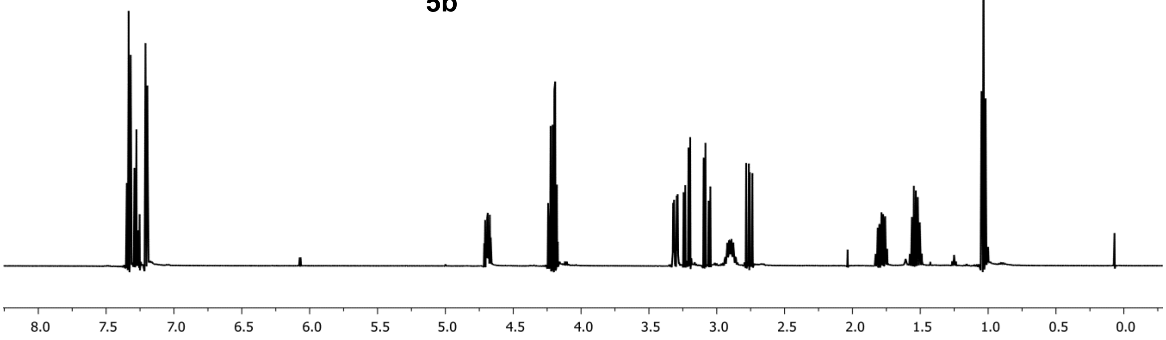


^{19}F NMR of compound **5a** (470 MHz, $CDCl_3$, 298 K).

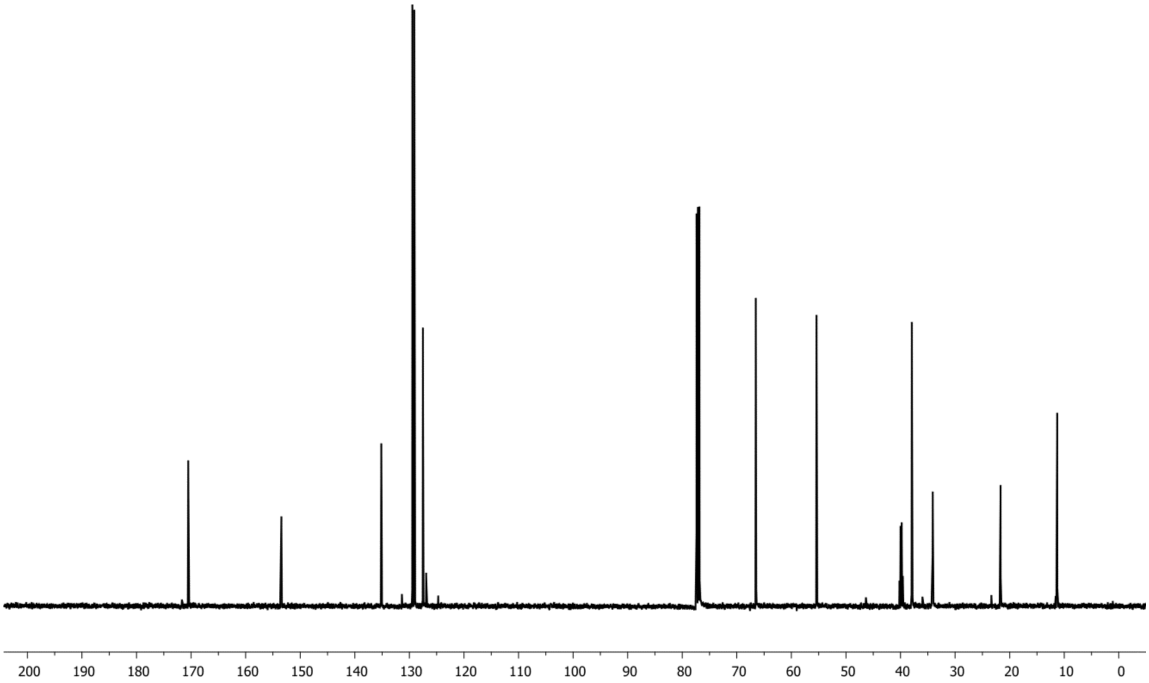
Compound 5b



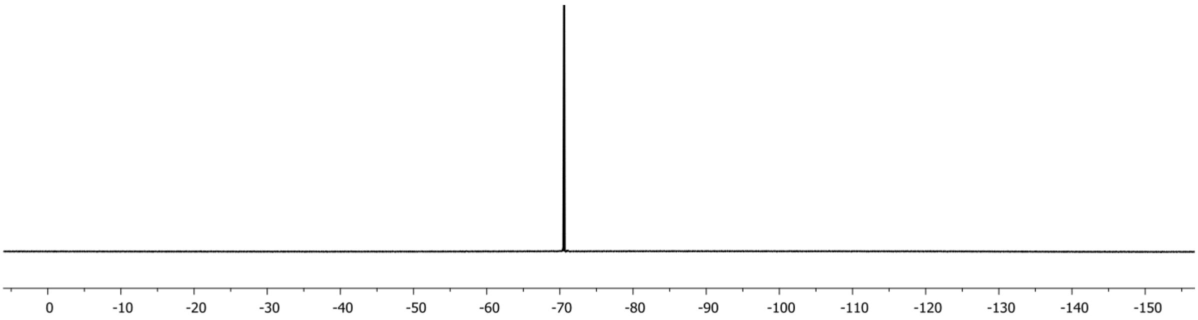
5b



^{1}H NMR of compound **5b** (500 MHz, $CDCl_3$, 298 K).

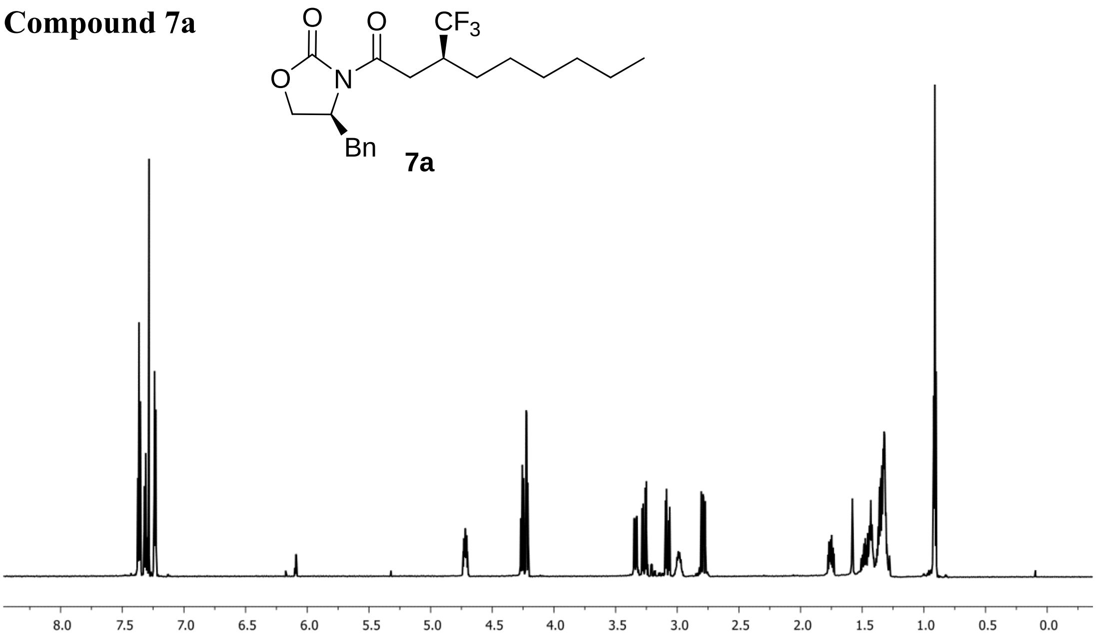


^{13}C NMR of compound **5b** (125 MHz, $CDCl_3$, 298 K).

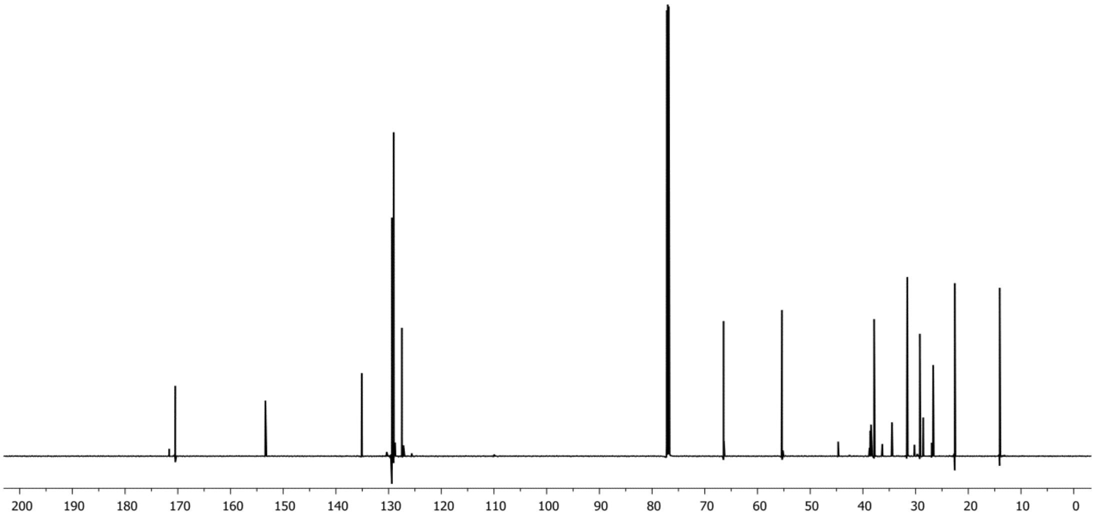


^{19}F NMR of compound **5b** (470 MHz, $CDCl_3$, 298 K).

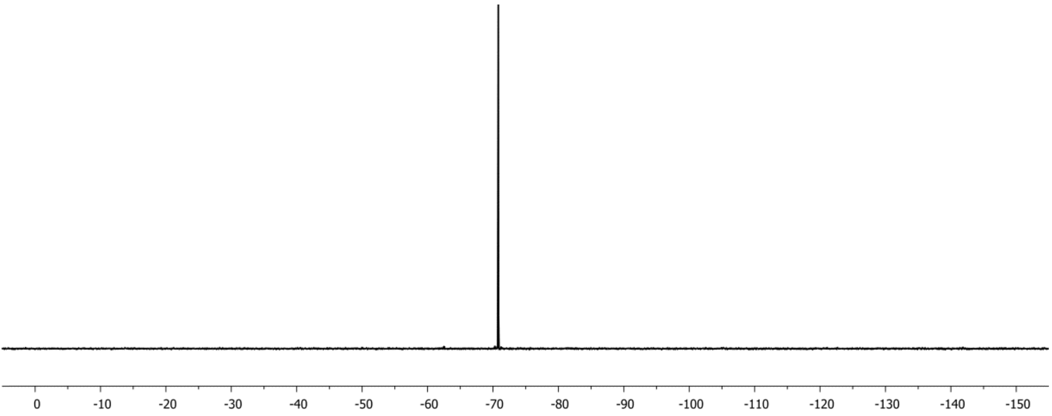
Compound 7a



^{1}H NMR of compound **7a** (700 MHz, CDCl$_3$, 298 K).

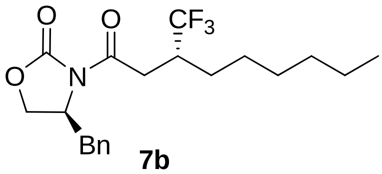


^{13}C NMR of compound **7a** (176 MHz, CDCl$_3$, 298
K).

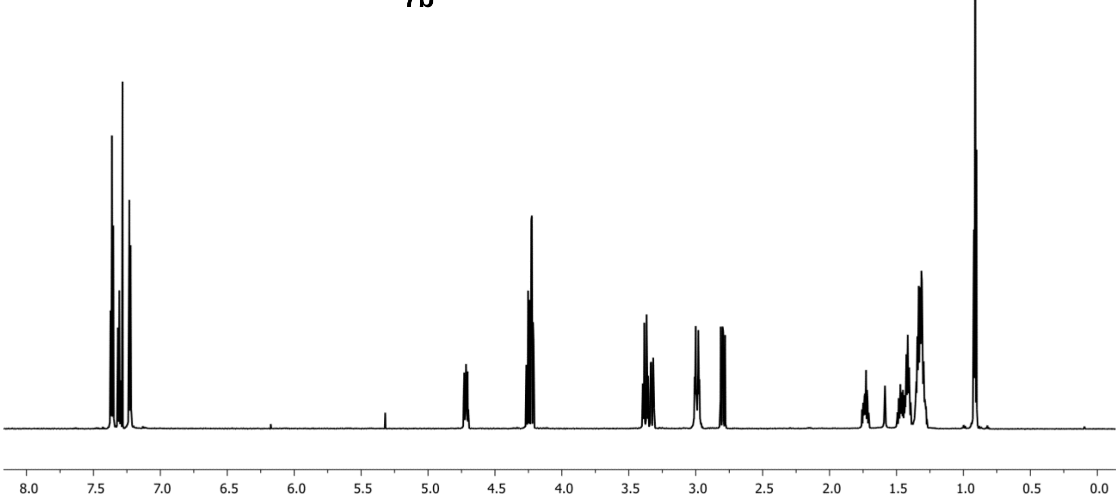


^{19}F NMR of compound **7a** (470 MHz, CDCl$_3$, 298 K).

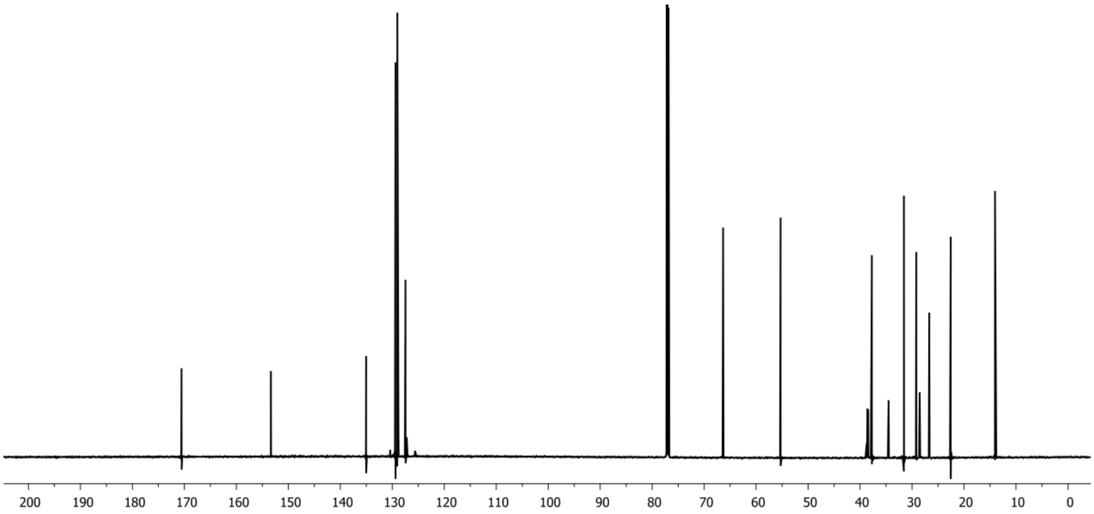
Compound 7b



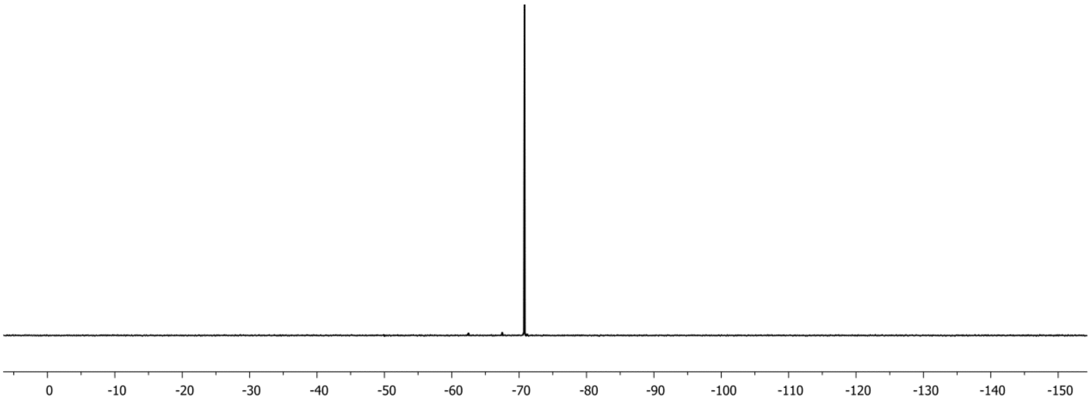
7b



^{1}H NMR of compound **7b** (700 MHz, CDCl$_3$, 298 K).

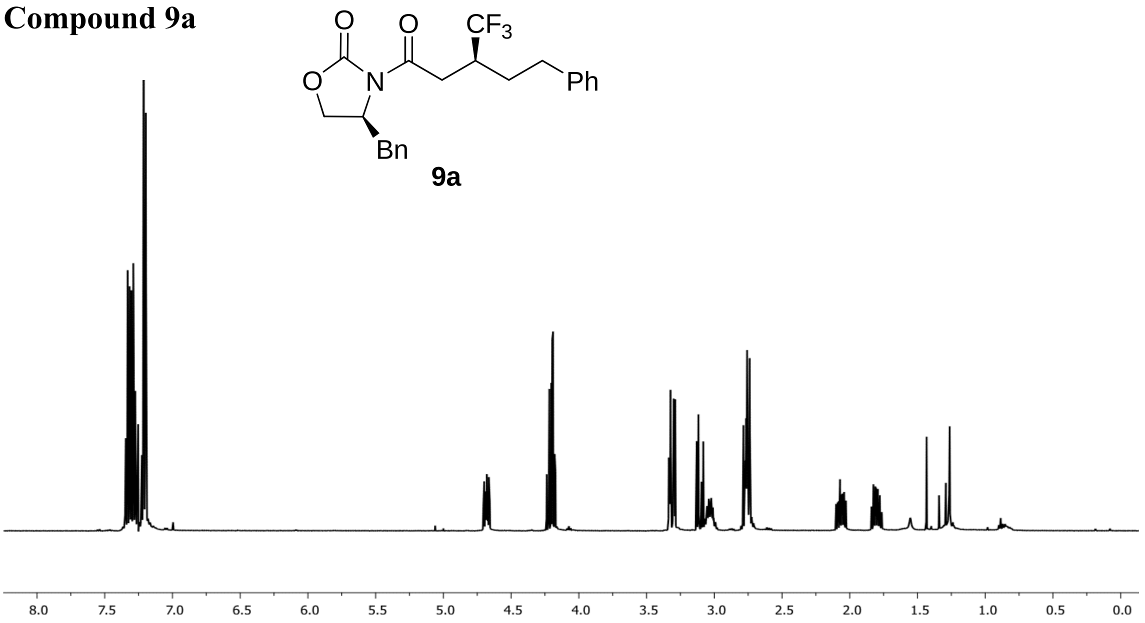


^{13}C NMR of compound **7b** (176 MHz, CDCl$_3$, 298 K).



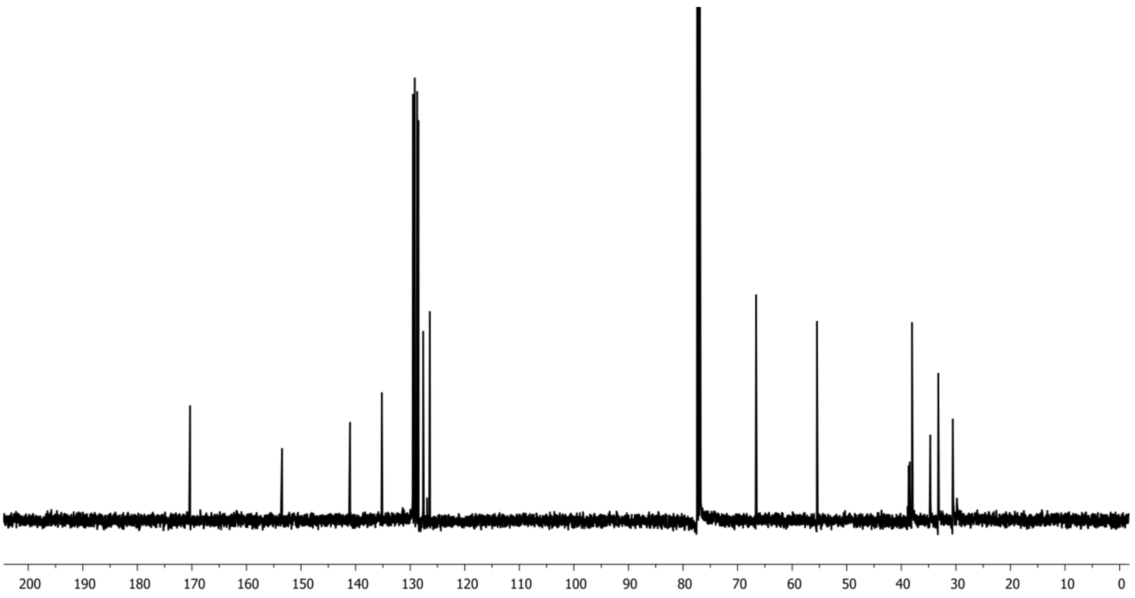
^{19}F NMR of compound **7b** (470 MHz, CDCl$_3$, 298 K).

Compound 9a

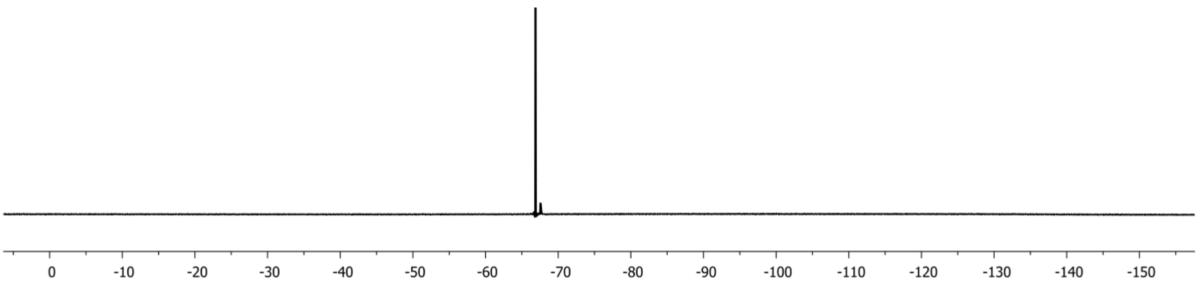


9a

^{1}H NMR of compound **9a** (500 MHz, $CDCl_3$, 298 K).

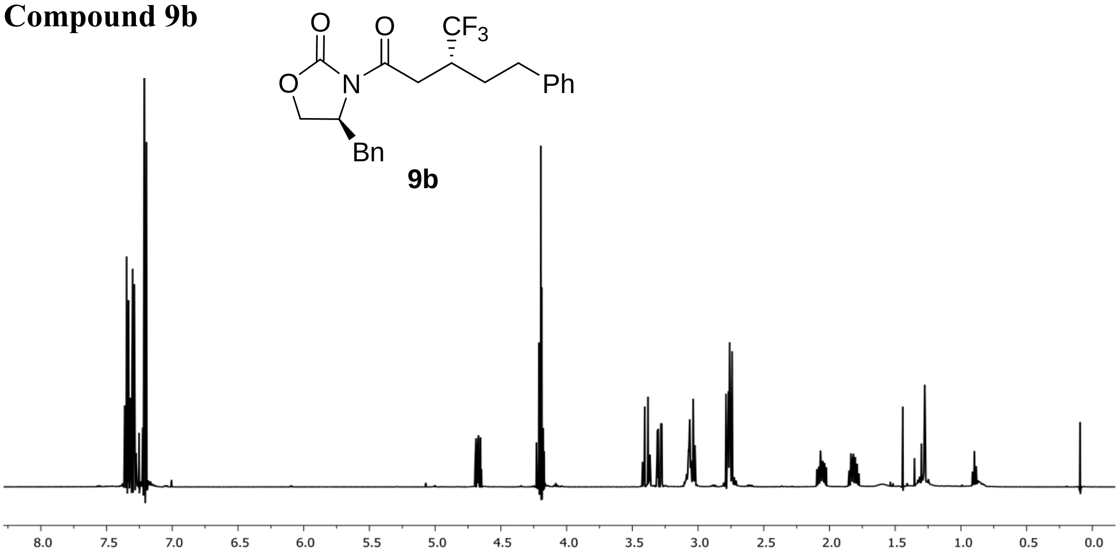


^{13}C NMR of compound **9a** (125 MHz, $CDCl_3$, 298 K).

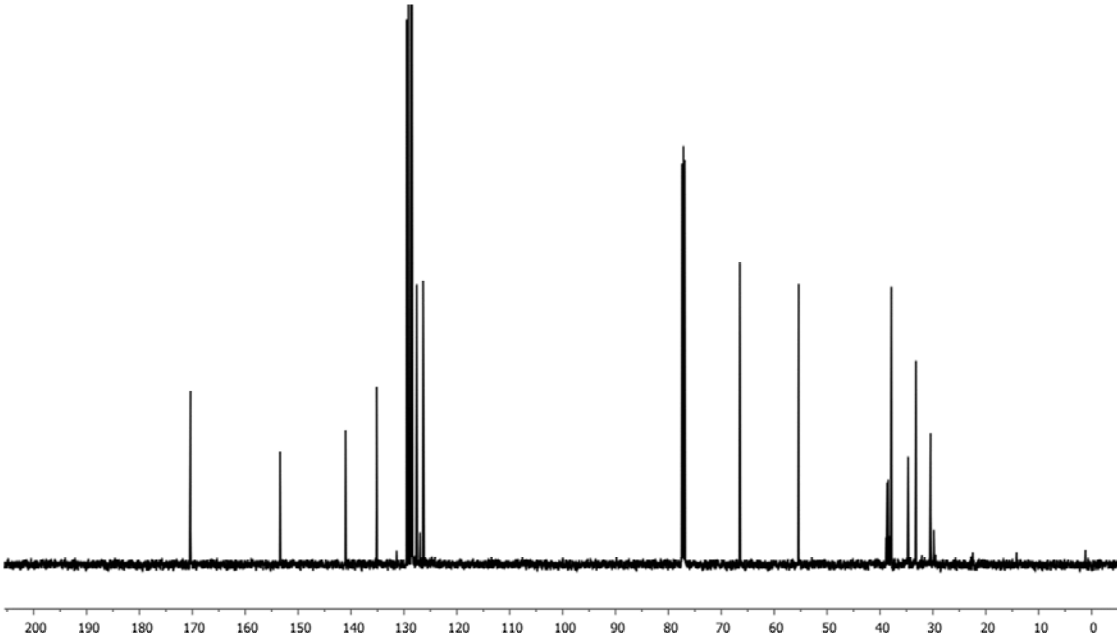


^{19}F NMR of compound **9a** (470 MHz, $CDCl_3$, 298 K).

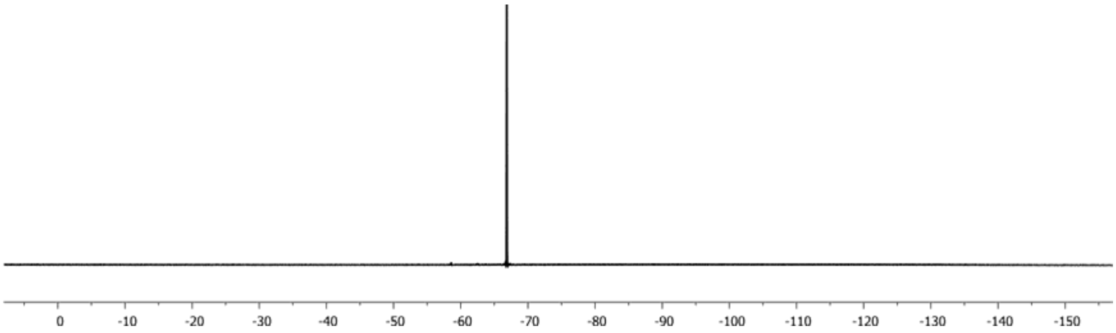
Compound 9b



^{1}H NMR of compound **9b** (500 MHz, $CDCl_3$, 298 K).

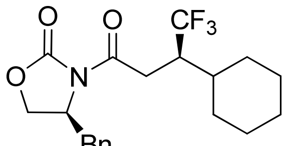


^{13}C NMR of compound **9b** (125 MHz, $CDCl_3$, 298 K).

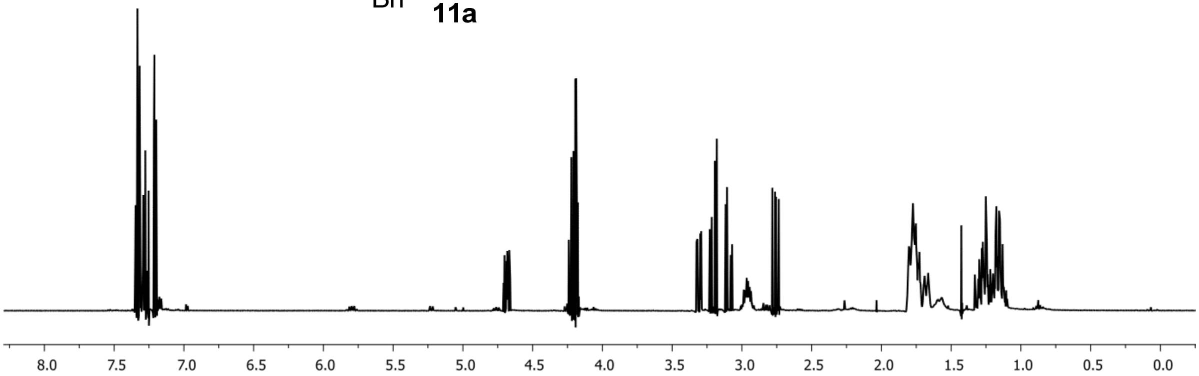


^{19}F NMR of compound **9b** (470 MHz, $CDCl_3$, 298 K).

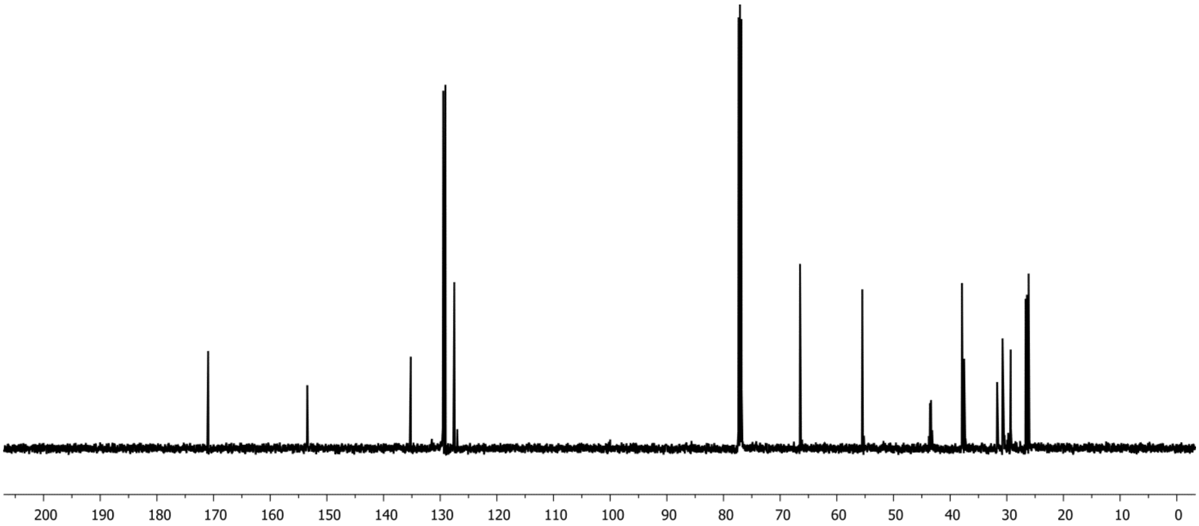
Compound 11a



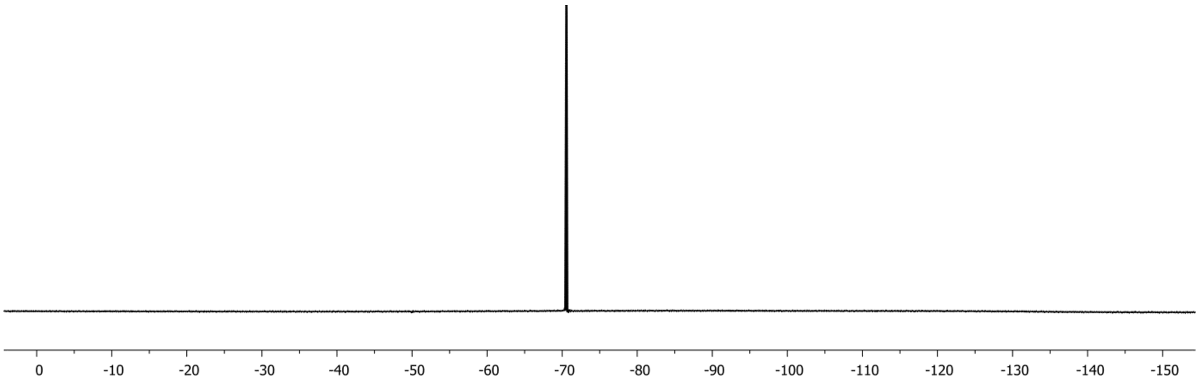
11a



^{1}H NMR of compound **11a** (500 MHz, $CDCl_3$, 298 K).

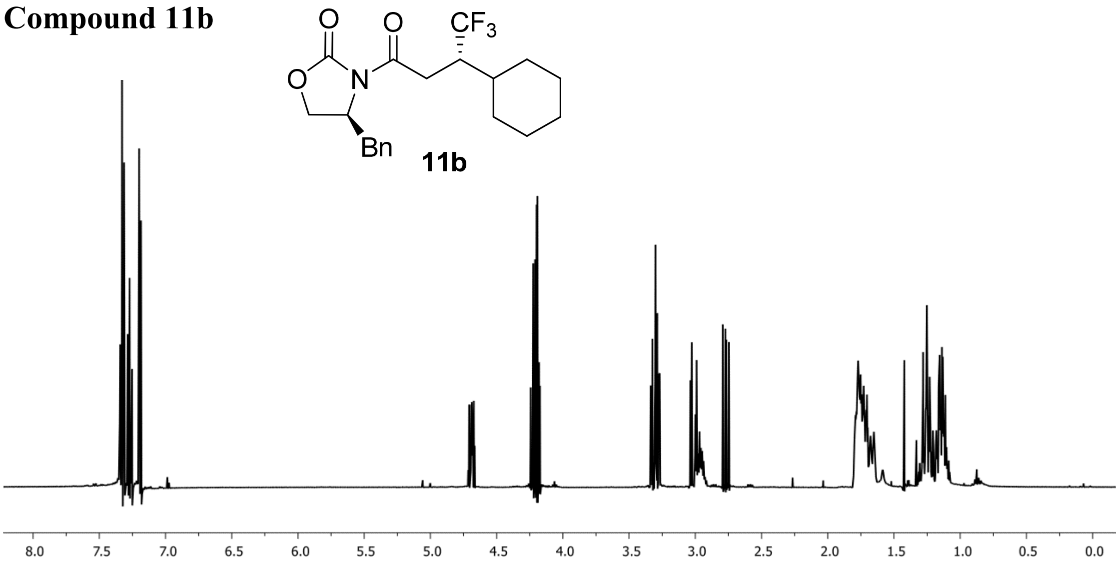


^{13}C NMR of compound **11a** (125 MHz, $CDCl_3$, 298 K).

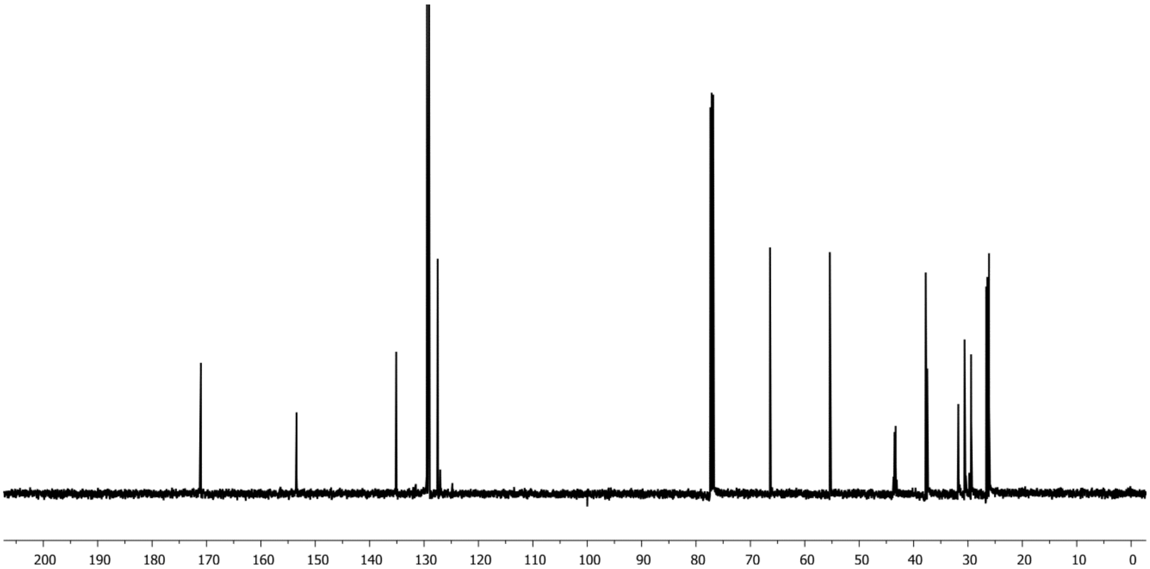


^{19}F NMR of compound **11a** (470 MHz, $CDCl_3$, 298 K).

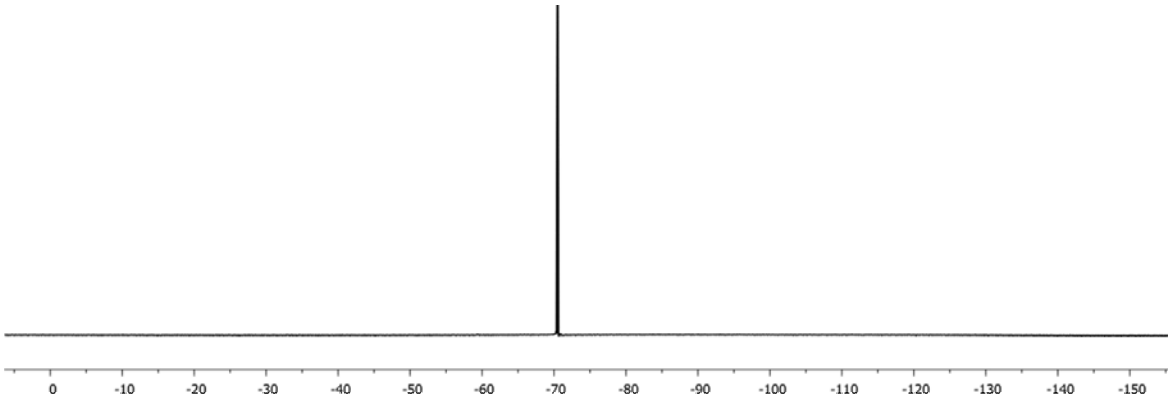
Compound 11b



^{1}H NMR of compound **11b** (500 MHz, $CDCl_3$, 298 K).

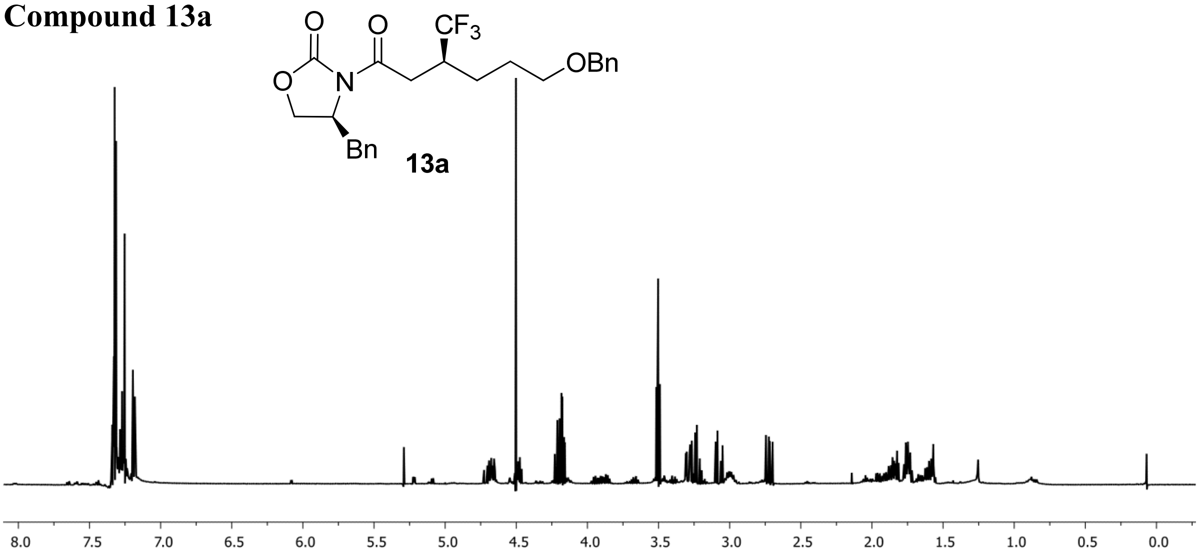


^{13}C NMR of compound **11b** (125 MHz, $CDCl_3$, 298 K).

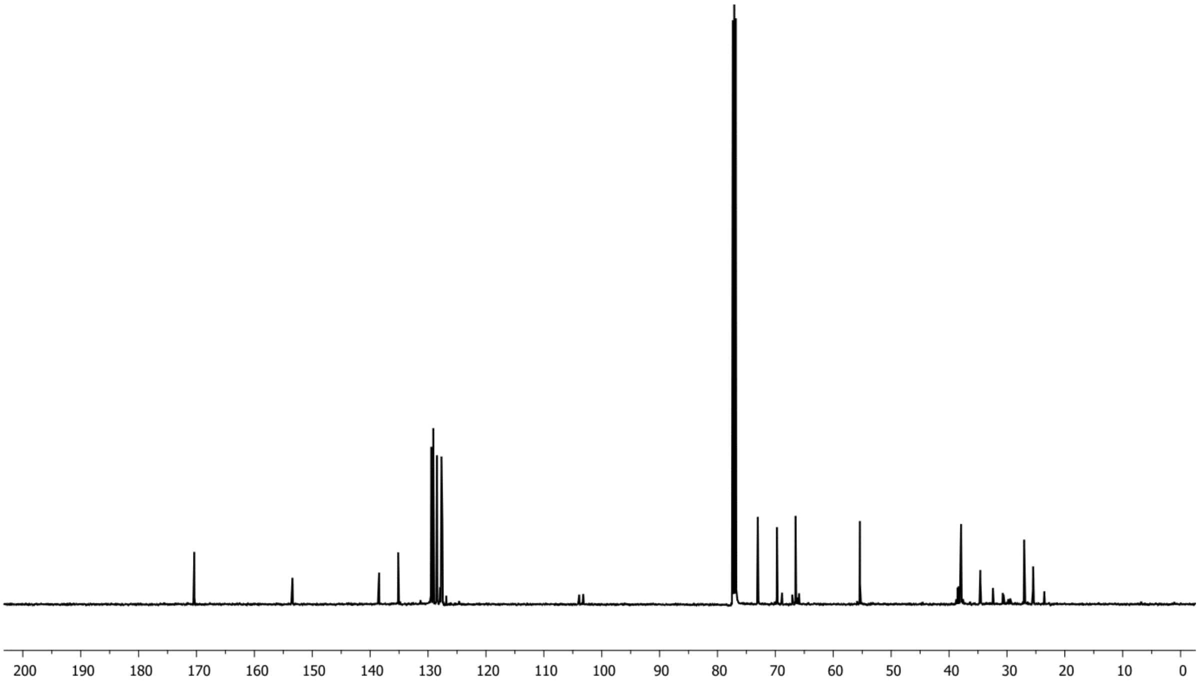


^{19}F NMR of compound **11b** (470 MHz, $CDCl_3$, 298 K).

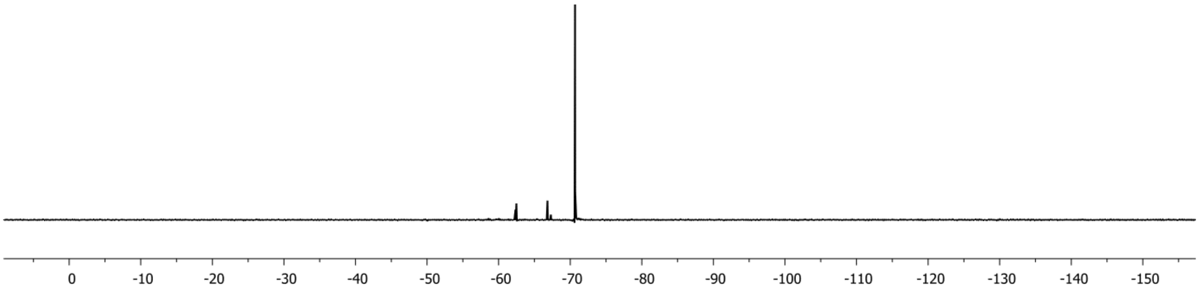
Compound 13a



^{1}H NMR of compound **13a** (500 MHz, CDCl$_3$, 298 K).

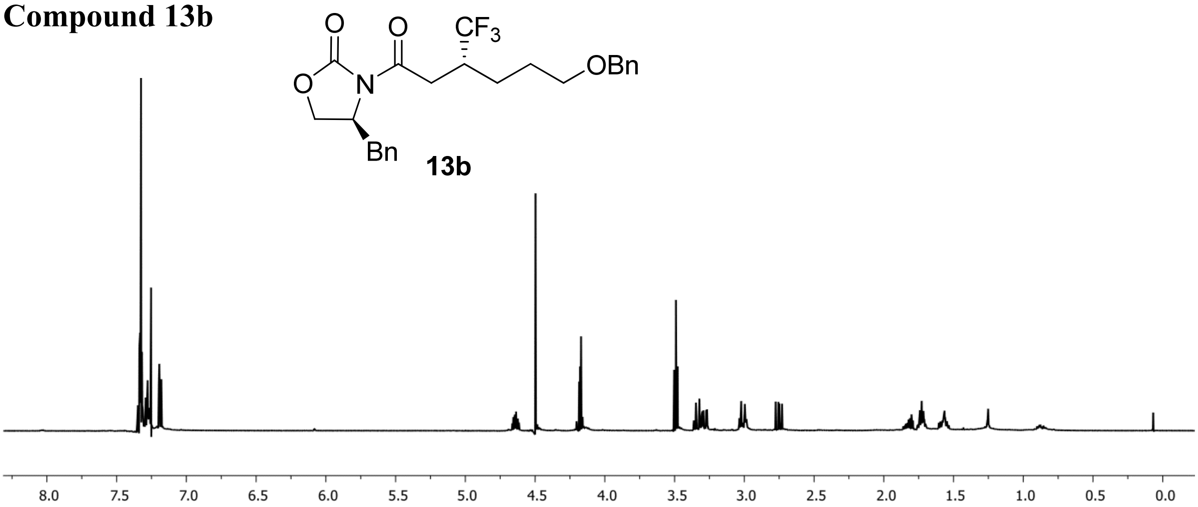


^{13}C NMR of compound **13a** (125 MHz, CDCl$_3$, 298 K).



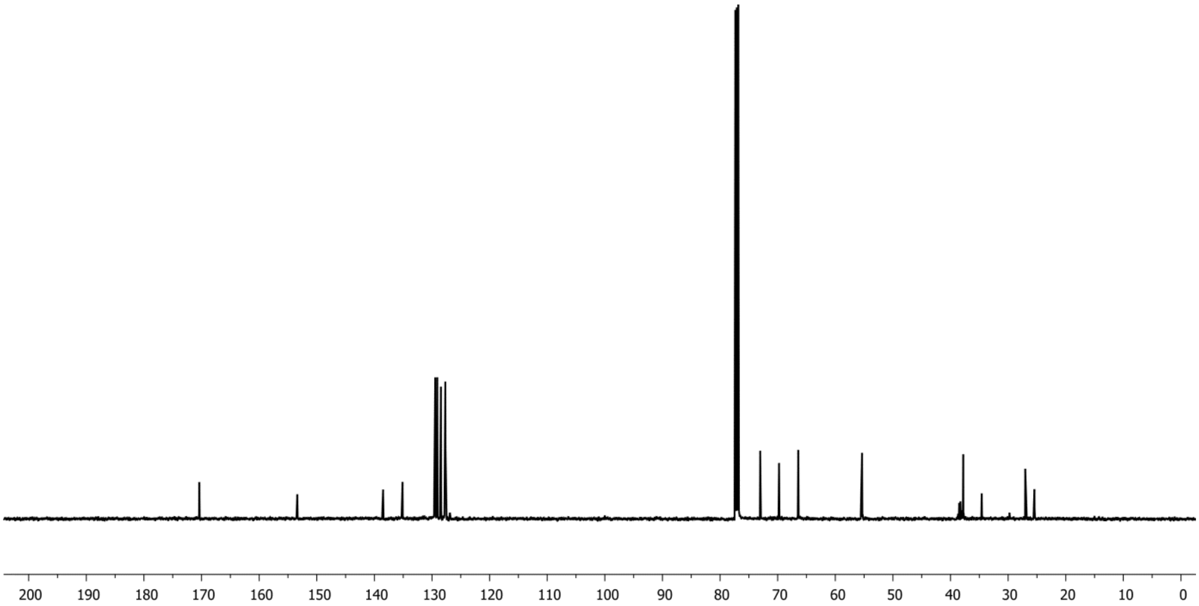
^{19}F NMR of compound **13a** (470 MHz, CDCl$_3$, 298 K).

Compound 13b

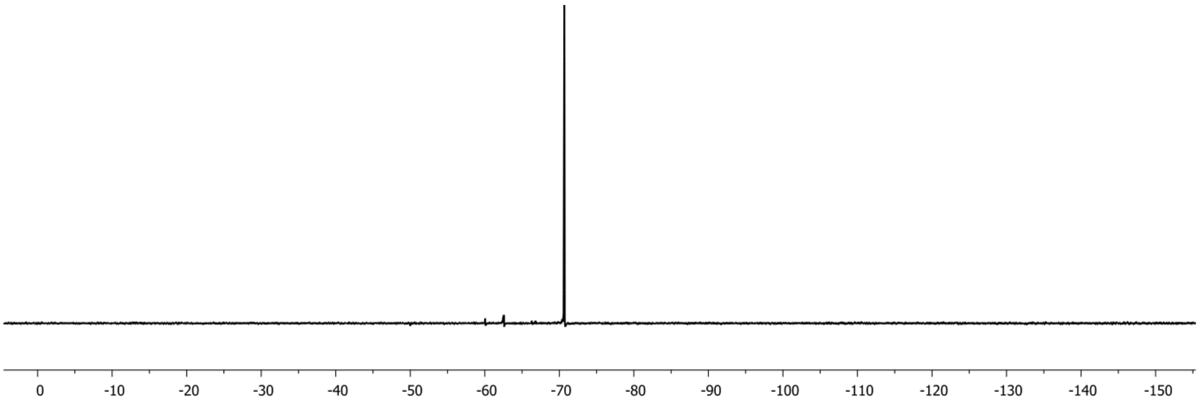


13b

[1]H NMR of compound **13b** (500 MHz, $CDCl_3$, 298 K).

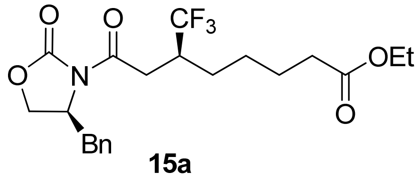


[13]C NMR of compound **13b** (125 MHz, $CDCl_3$, 298 K).

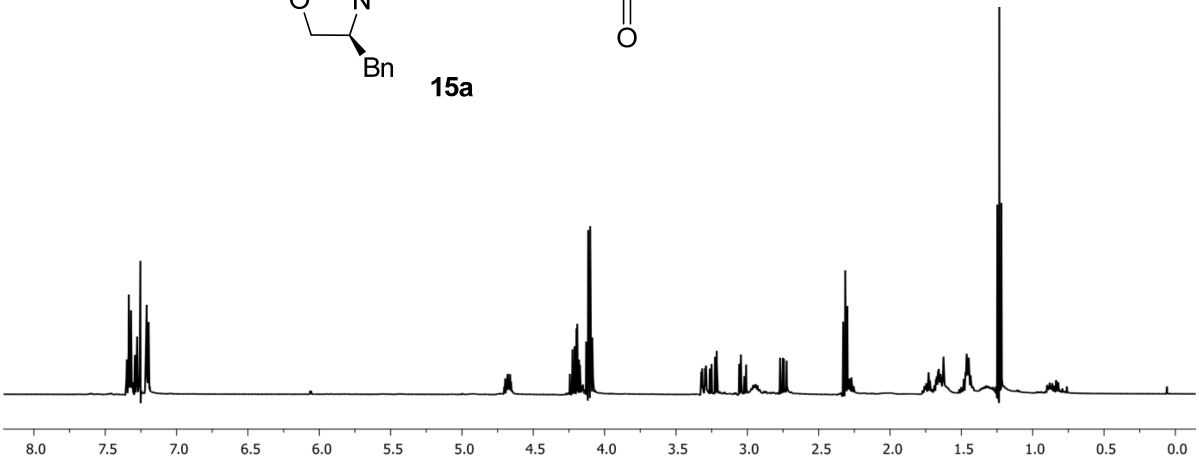


[19]F NMR of compound **13b** (470 MHz, $CDCl_3$, 298 K).

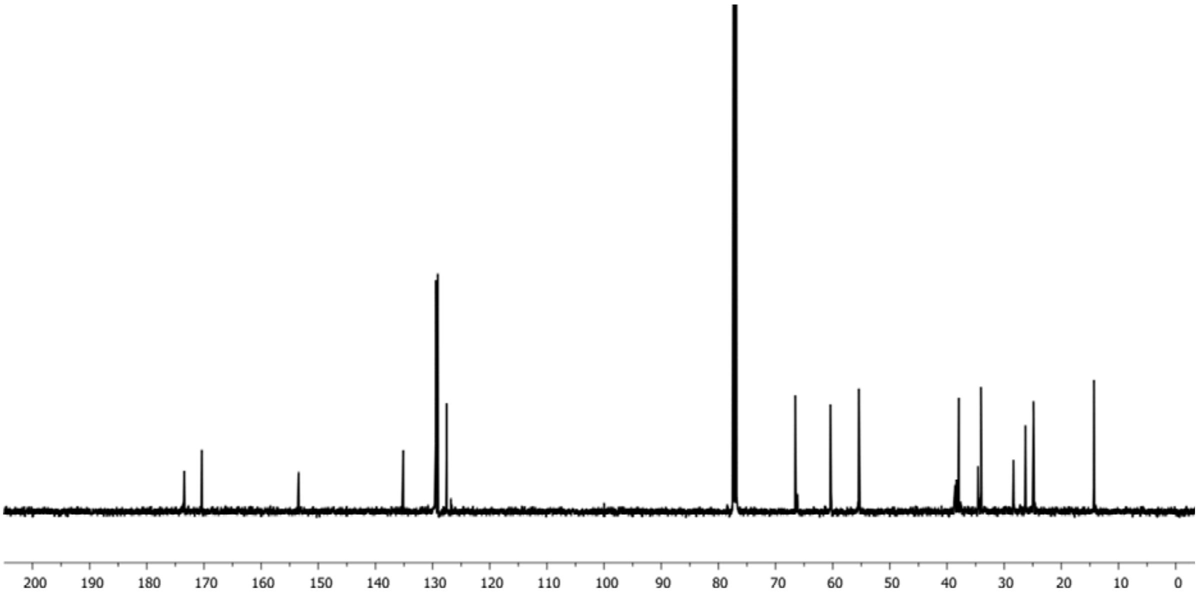
Compound 15a



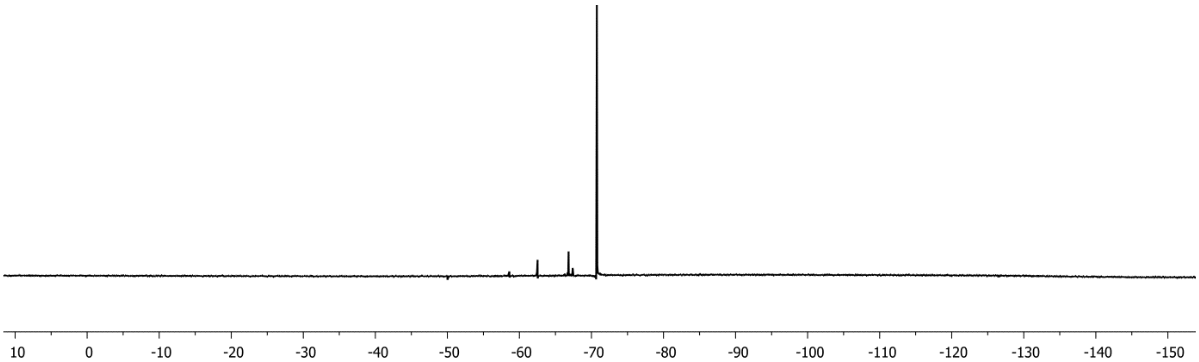
15a



^{1}H NMR of compound **15a** (500 MHz, CDCl$_3$, 298 K).

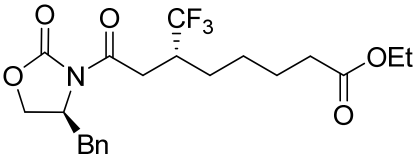


^{13}C NMR of compound **15a** (125 MHz, CDCl$_3$, 298 K).

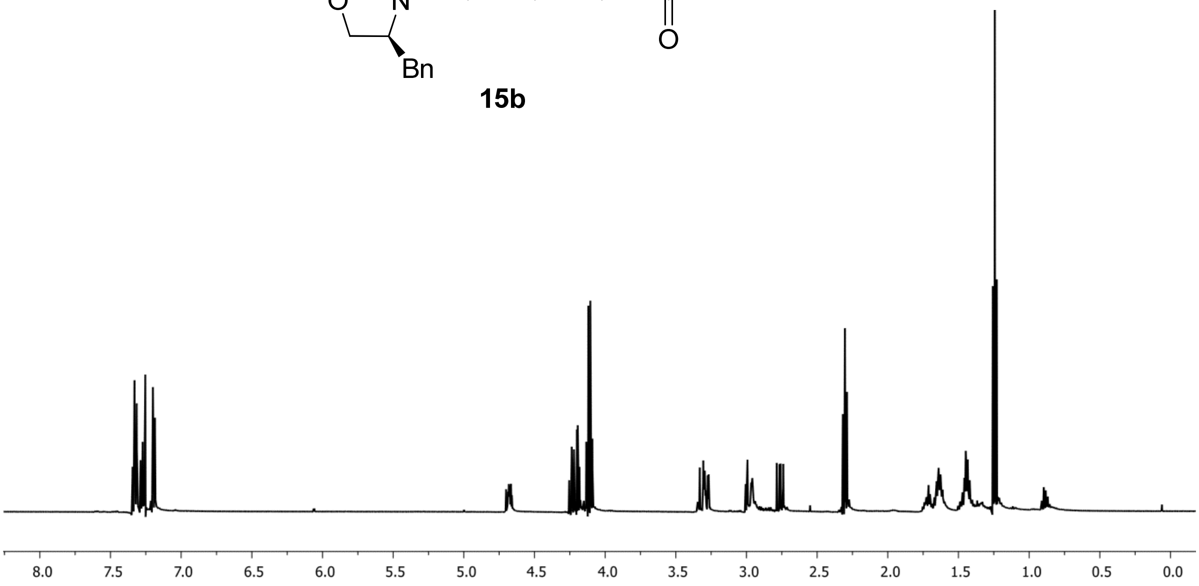


^{19}F NMR of compound **15a** (470 MHz, CDCl$_3$, 298 K).

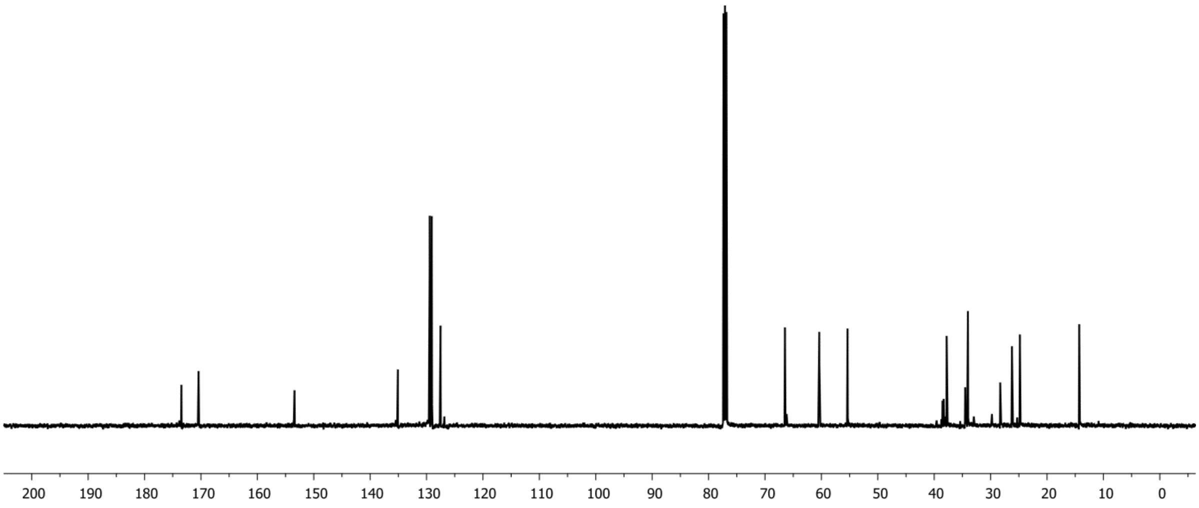
Compound 15b



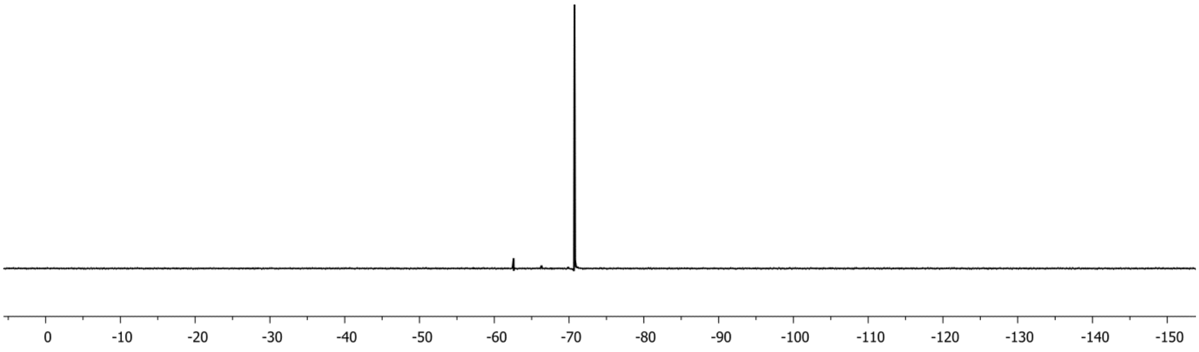
15b



^{1}H NMR of compound **15b** (500 MHz, $CDCl_3$, 298 K).

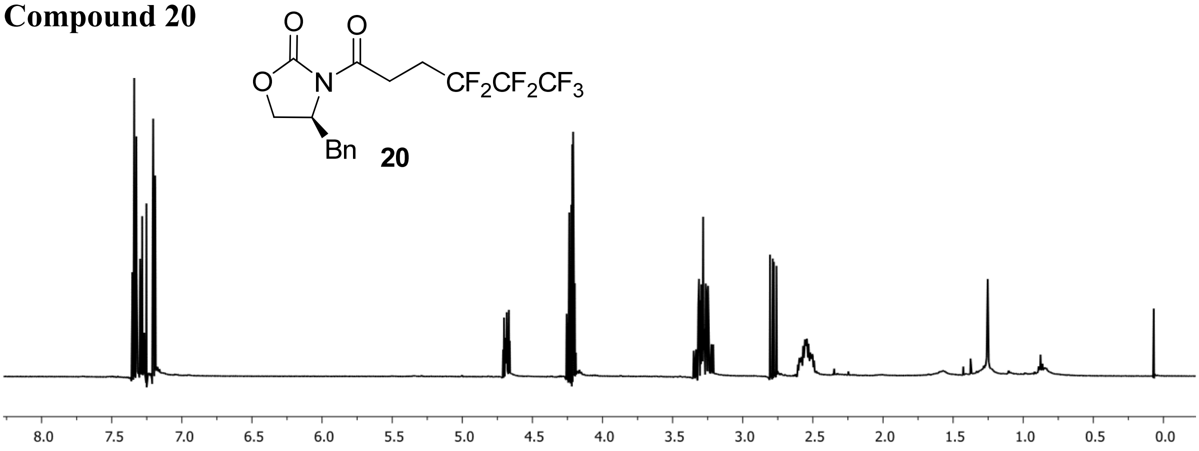


^{13}C NMR of compound **15b** (125 MHz, $CDCl_3$, 298 K).

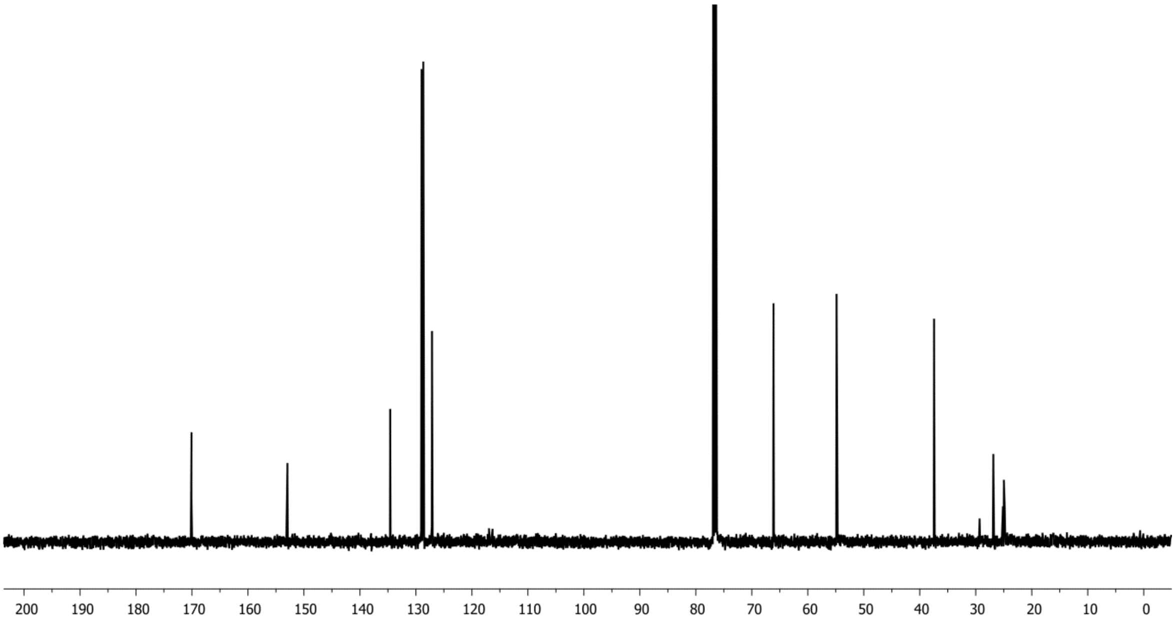


^{19}F NMR of compound **15b** (470 MHz, $CDCl_3$, 298 K).

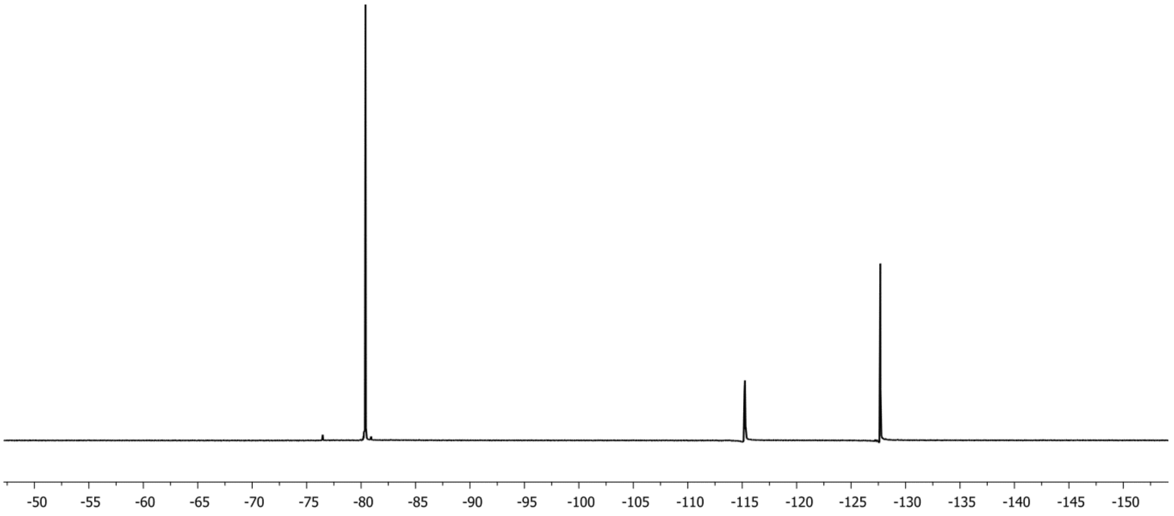
Compound 20



^{1}H NMR of compound **20** (500 MHz, $CDCl_3$, 298 K).

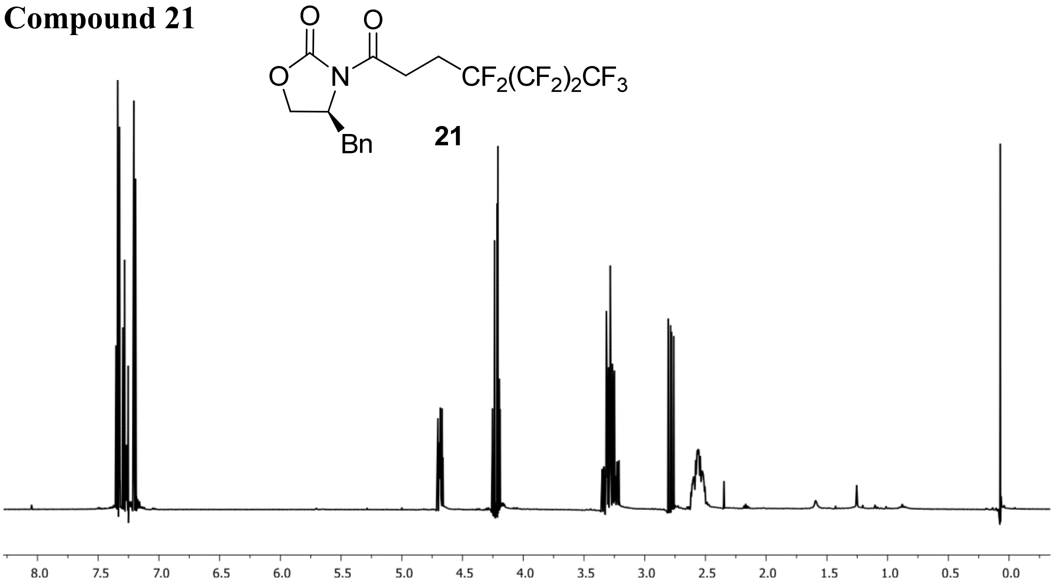


^{13}C NMR of compound **20** (125 MHz, $CDCl_3$, 298 K).

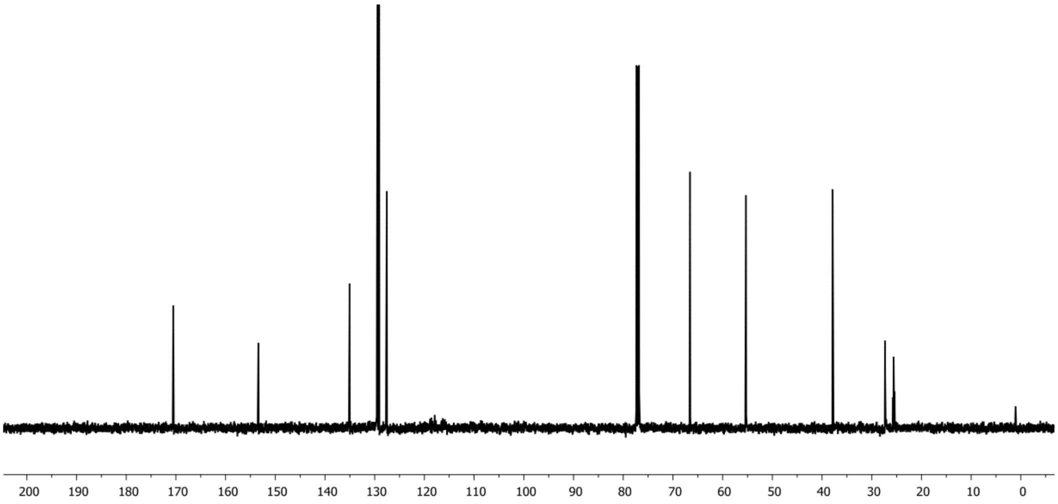


^{19}F NMR of compound **20** (470 MHz, $CDCl_3$, 298 K).

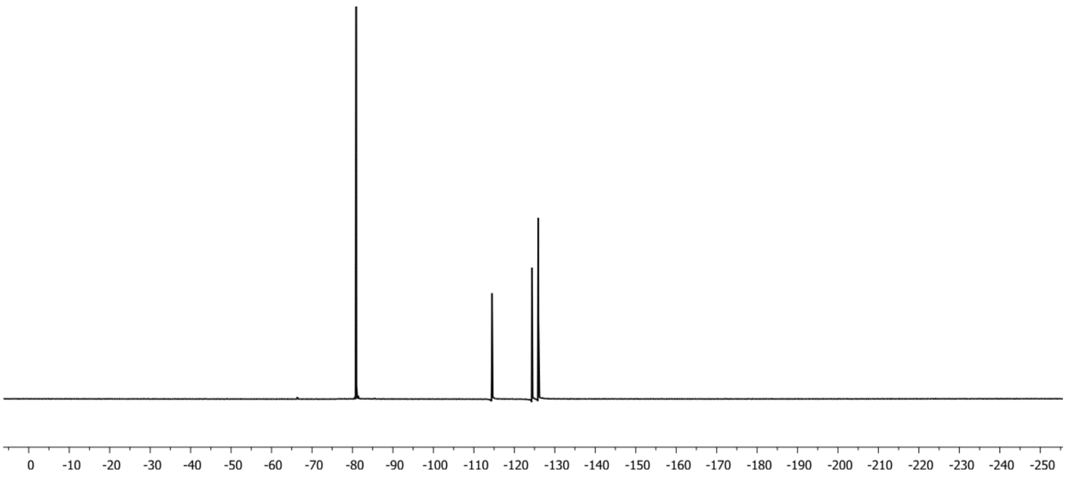
Compound 21



^{1}H NMR of compound **21** (500 MHz, $CDCl_3$, 298 K).

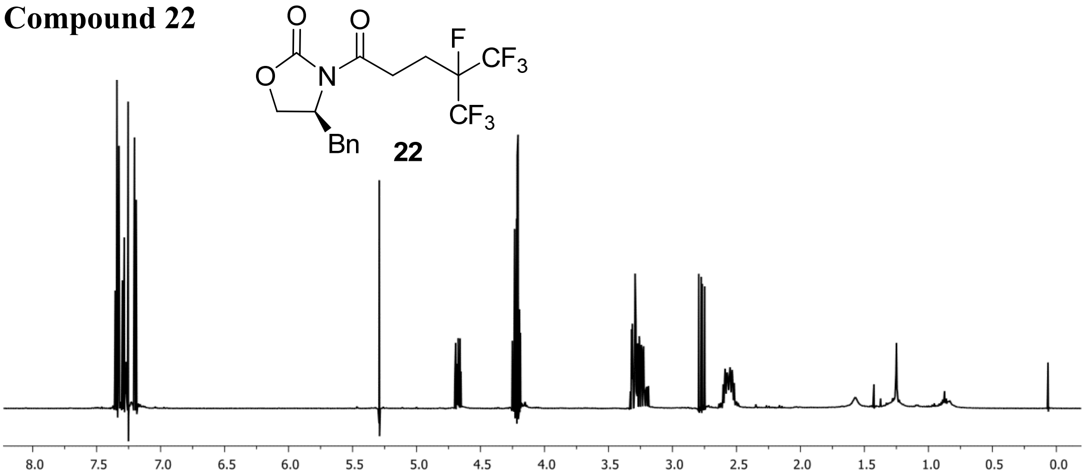


^{13}C NMR of compound **21** (125 MHz, $CDCl_3$, 298 K).

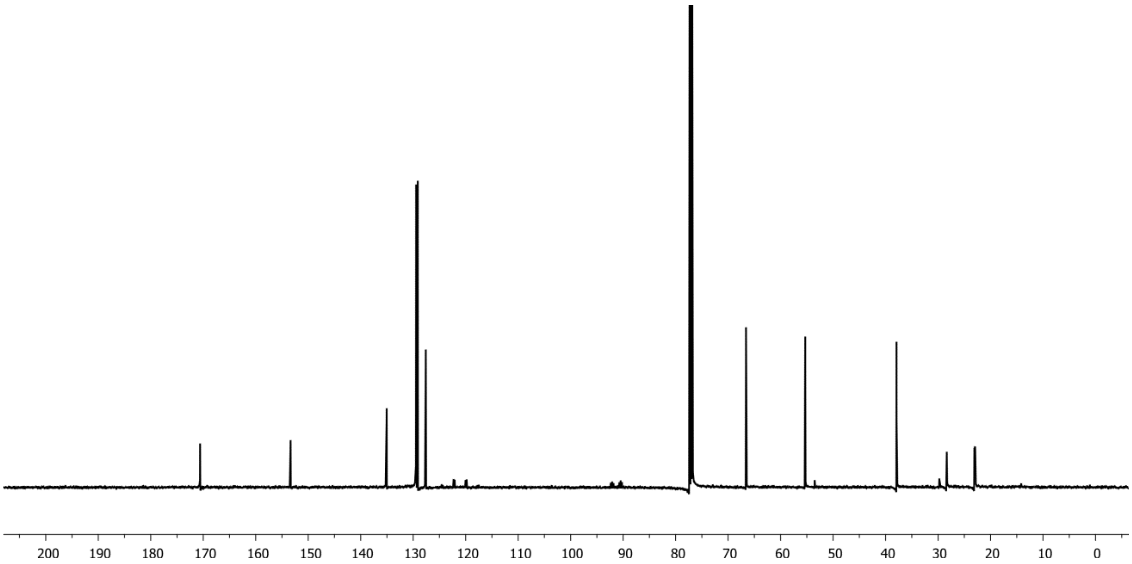


^{19}F NMR of compound **21** (470 MHz, $CDCl_3$, 298 K).

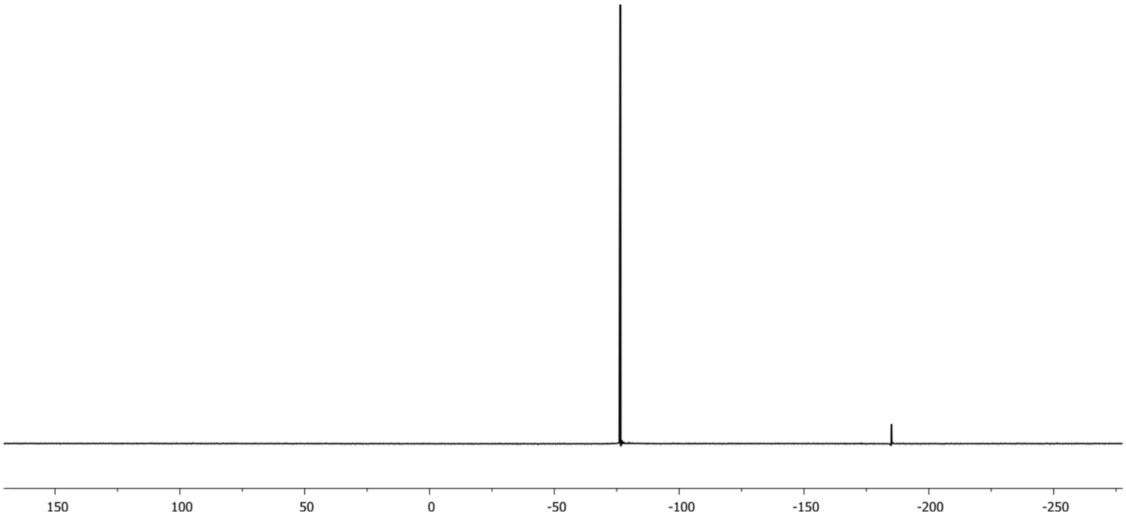
Compound 22



^{1}H NMR of compound **22** (500 MHz, $CDCl_3$, 298 K).

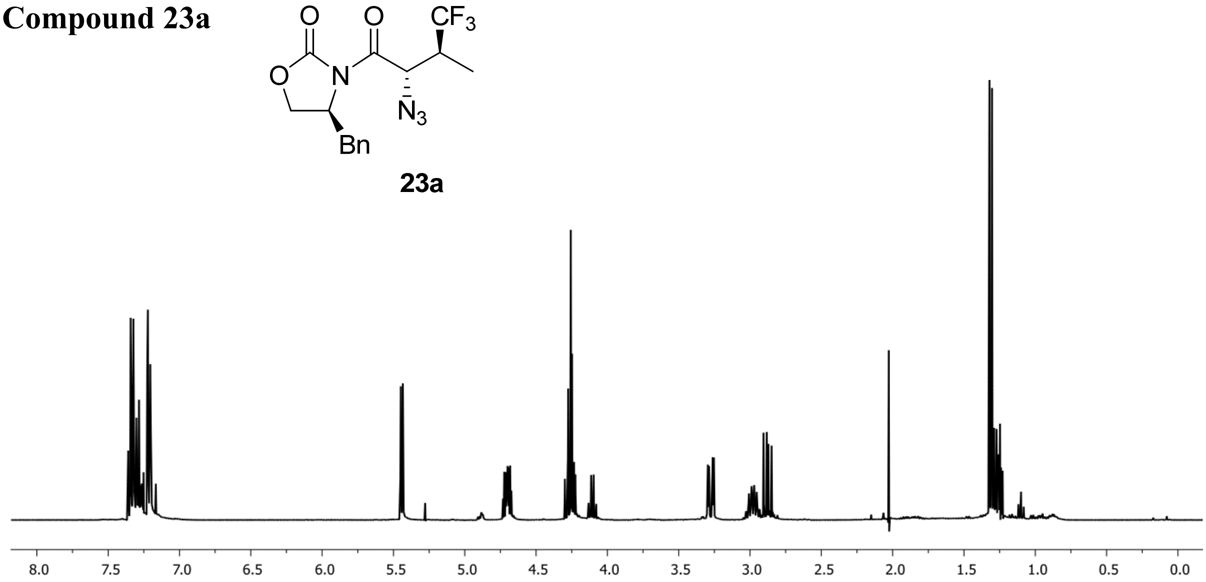


^{13}C NMR of compound **22** (125 MHz, $CDCl_3$, 298 K).



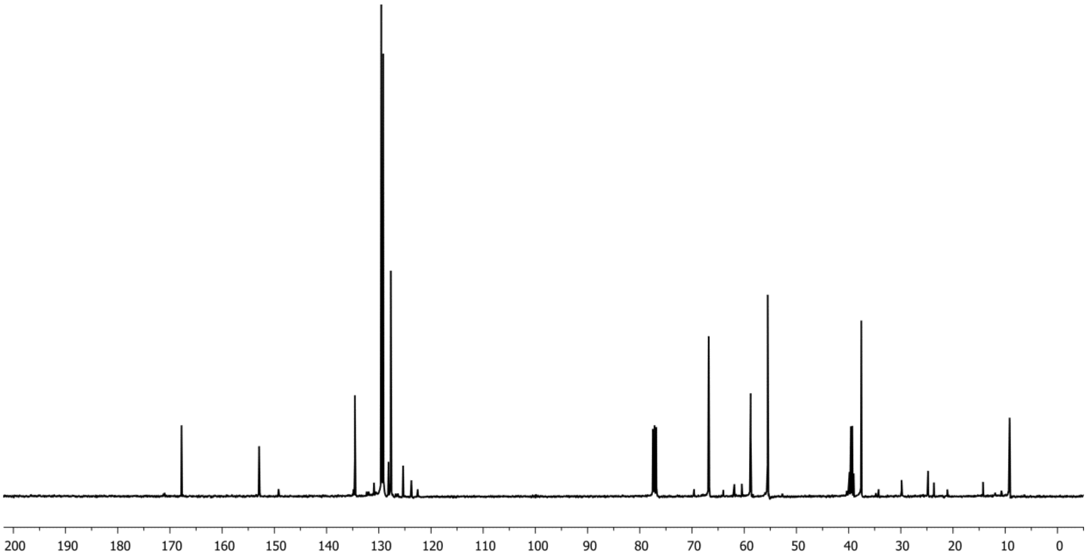
^{19}F NMR of compound **22** (470 MHz, $CDCl_3$, 298 K).

Compound 23a

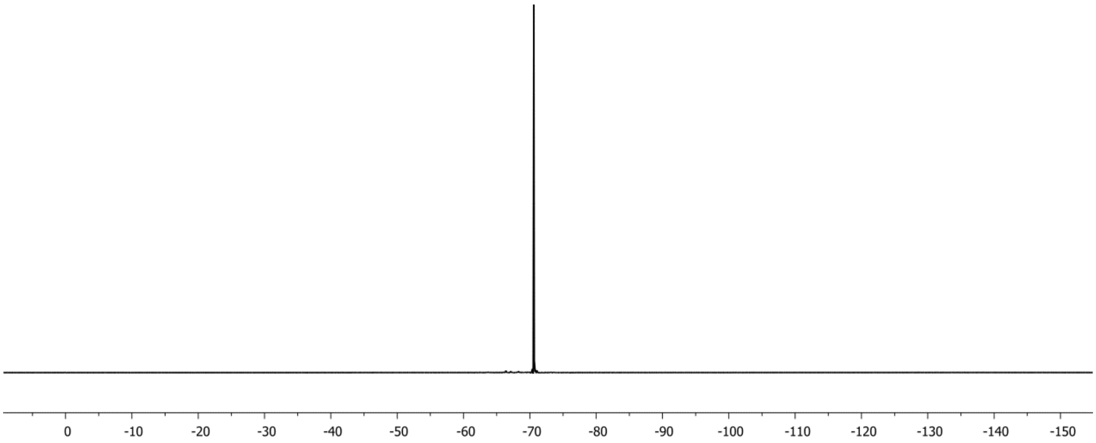


23a

^{1}H NMR of compound **23a** (500 MHz, CDCl$_3$, 298 K).

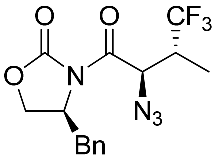


^{13}C NMR of compound **23a** (125 MHz, CDCl$_3$, 298 K).

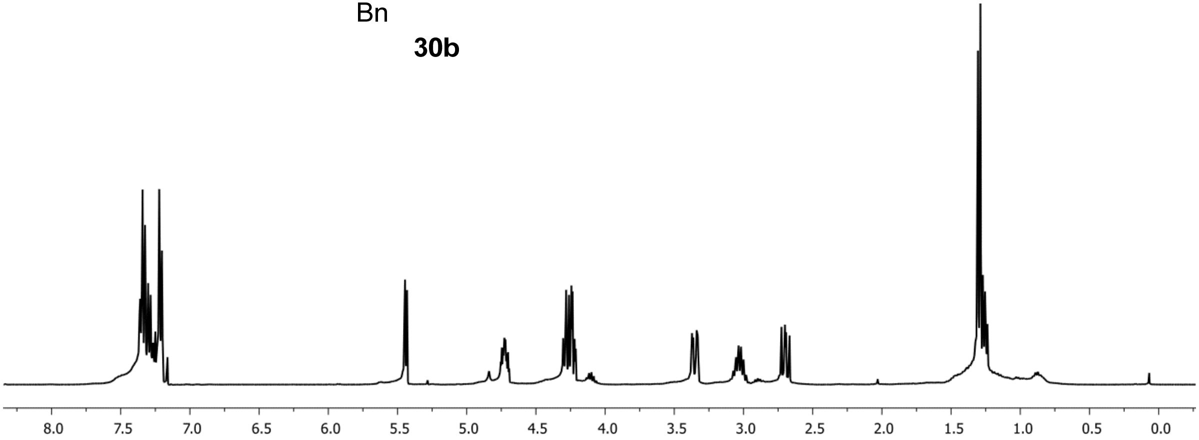


^{19}F NMR of compound **23a** (470 MHz, CDCl$_3$, 298 K).

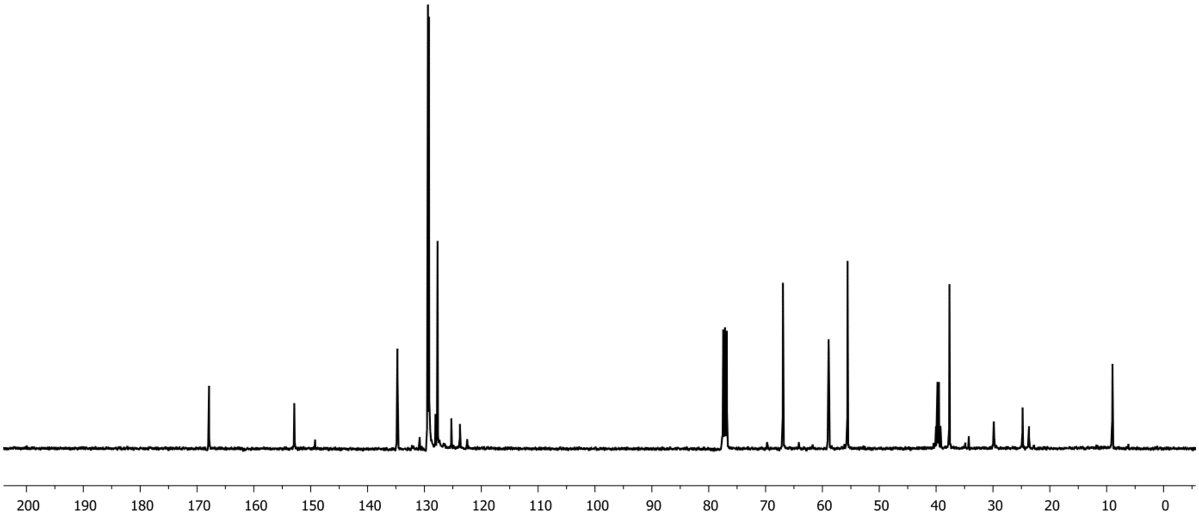
Compound 30b



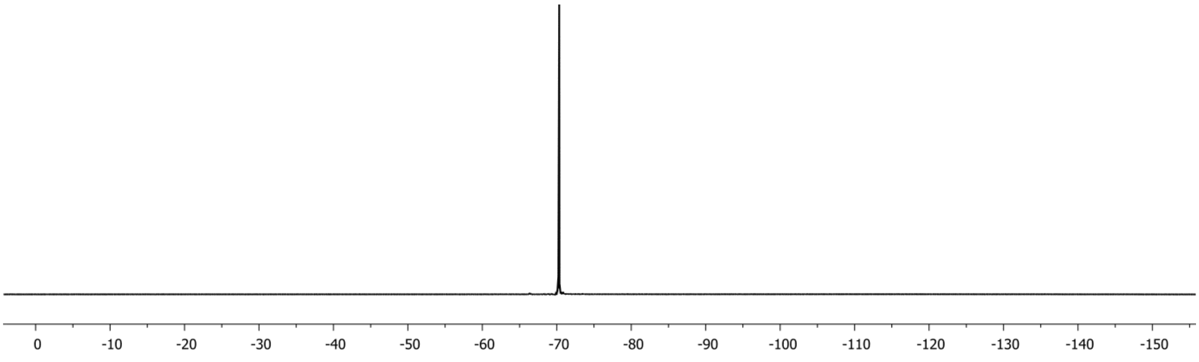
30b



^{1}H NMR of compound **30b** (500 MHz, $CDCl_3$, 298 K).

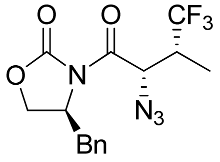


^{13}C NMR of compound **30b** (125 MHz, $CDCl_3$, 298 K).

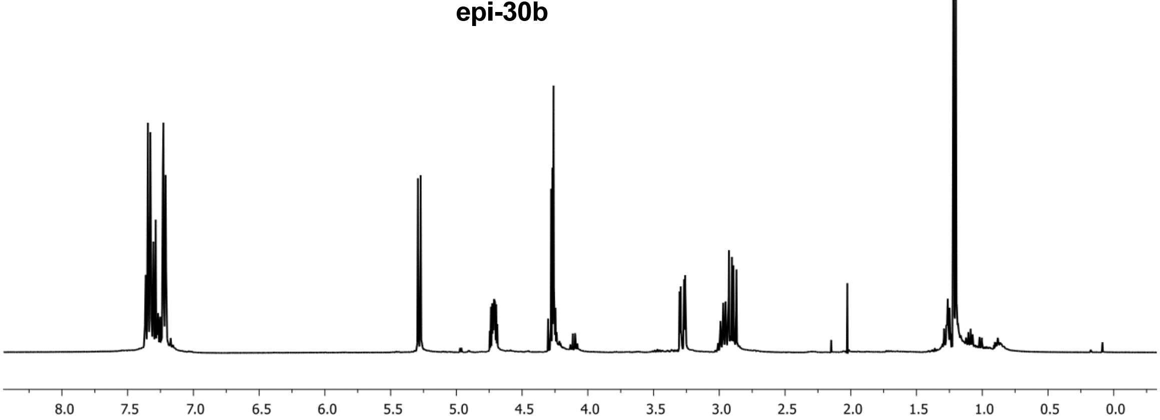


^{19}F NMR of compound **30b** (470 MHz, $CDCl_3$, 298 K).

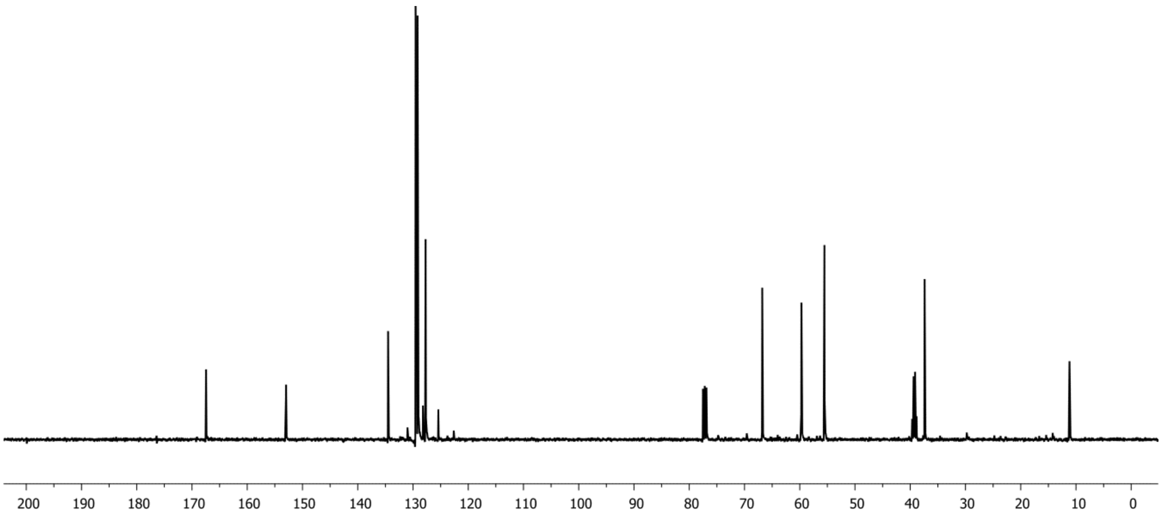
Compound epi-30b



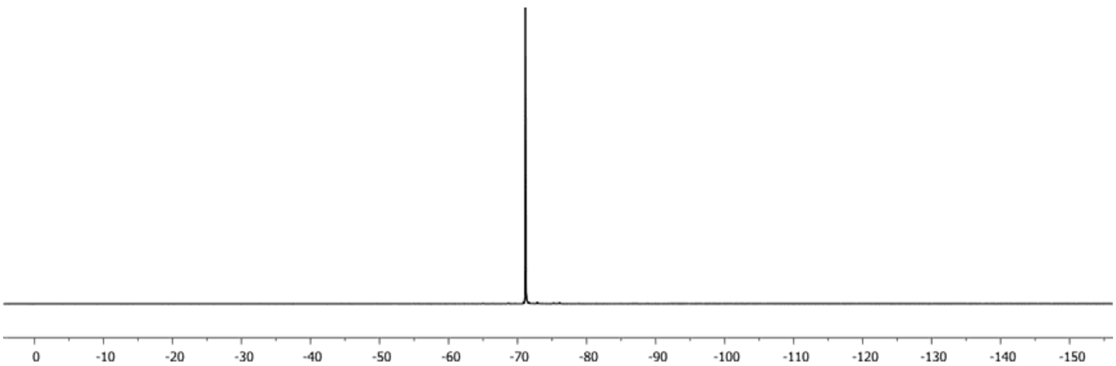
epi-30b



^{1}H NMR of compound **epi-30b** (500 MHz, $CDCl_3$, 298 K).

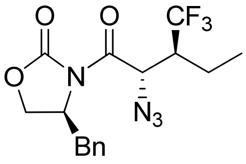


^{13}C NMR of compound **epi-30b** (125 MHz, $CDCl_3$, 298 K).

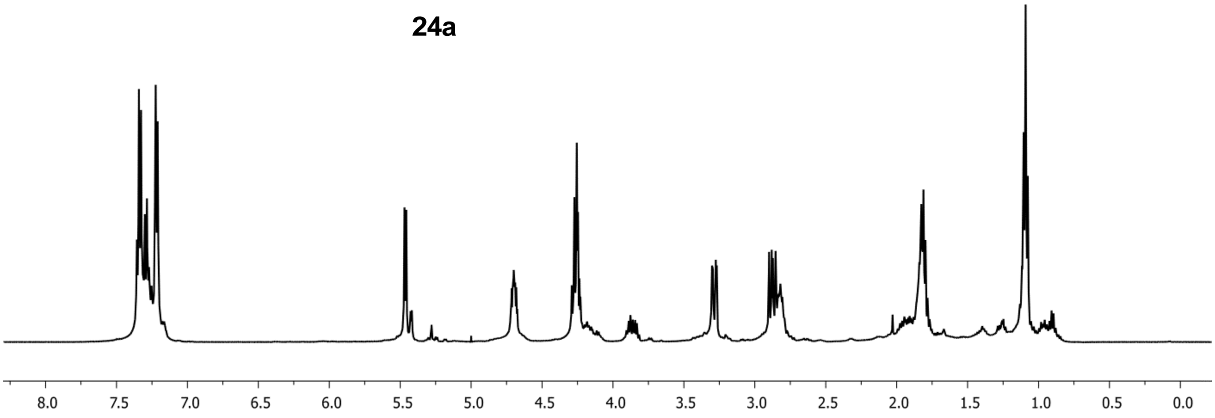


^{19}F NMR of compound **epi-30b** (470 MHz, $CDCl_3$, 298 K).

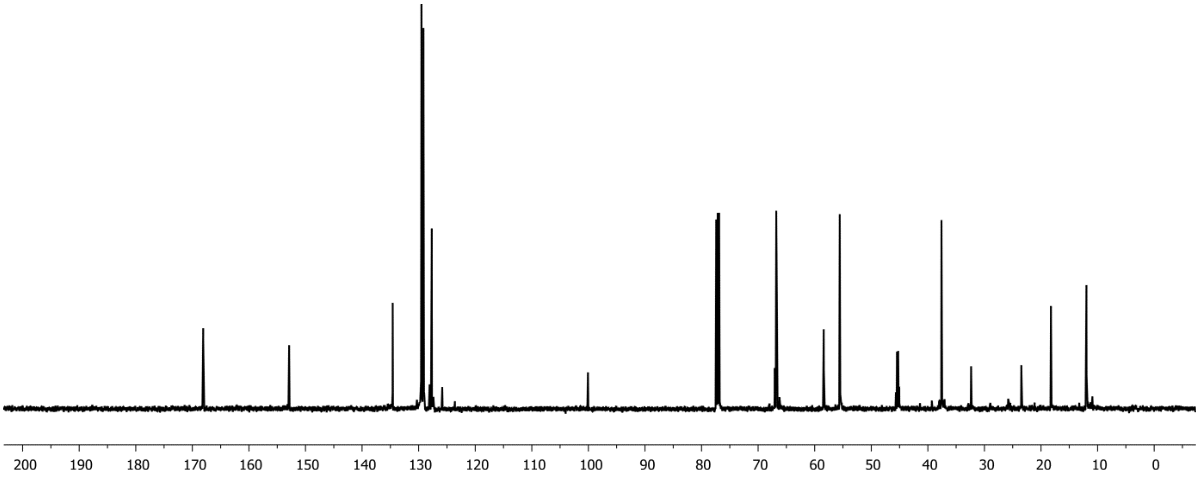
Compound 24a



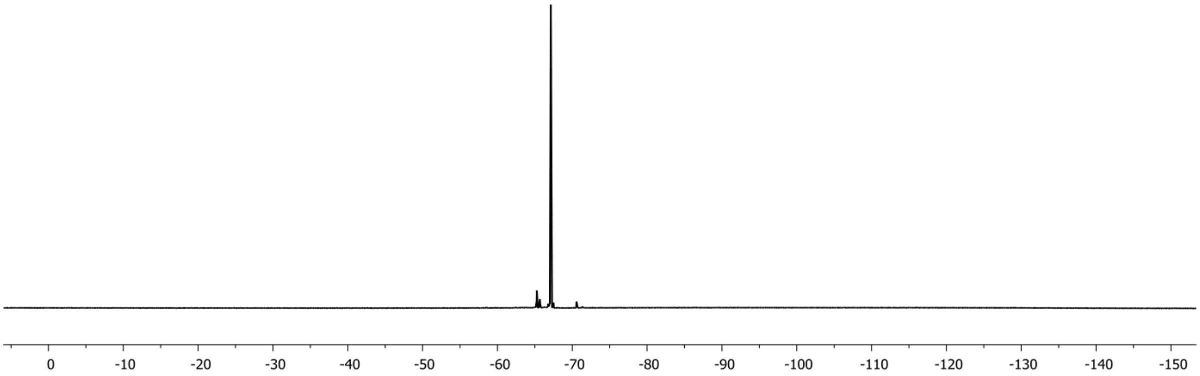
24a



^{1}H NMR of compound **24a** (500 MHz, CDCl$_3$, 298 K).

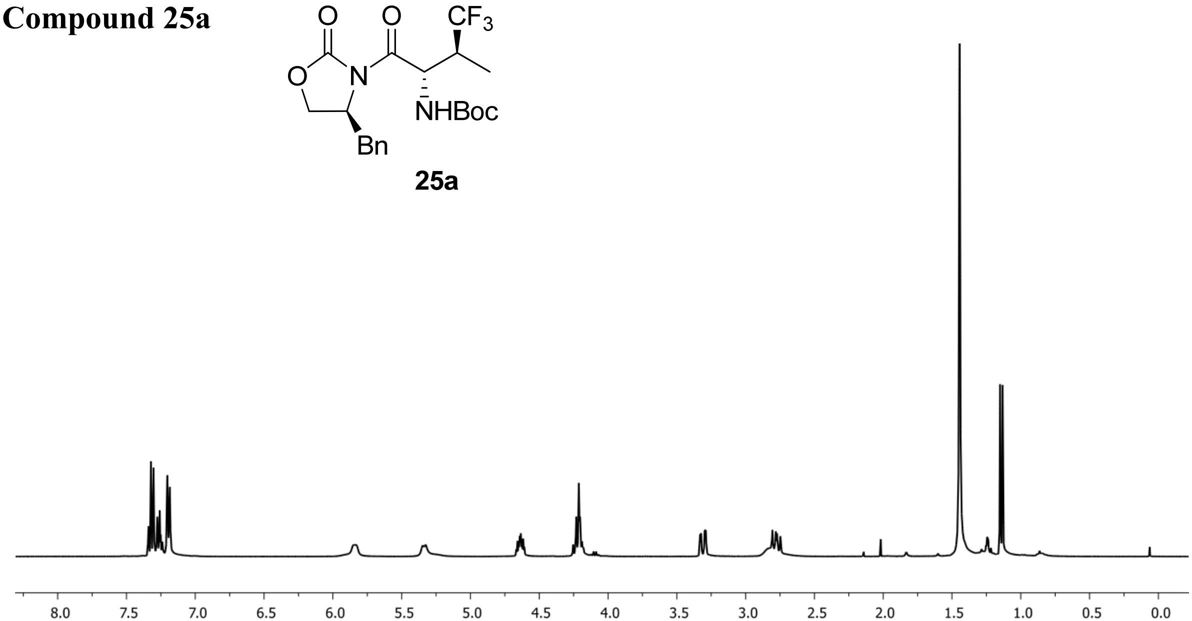


^{13}C NMR of compound **24a** (125 MHz, CDCl$_3$, 298 K).



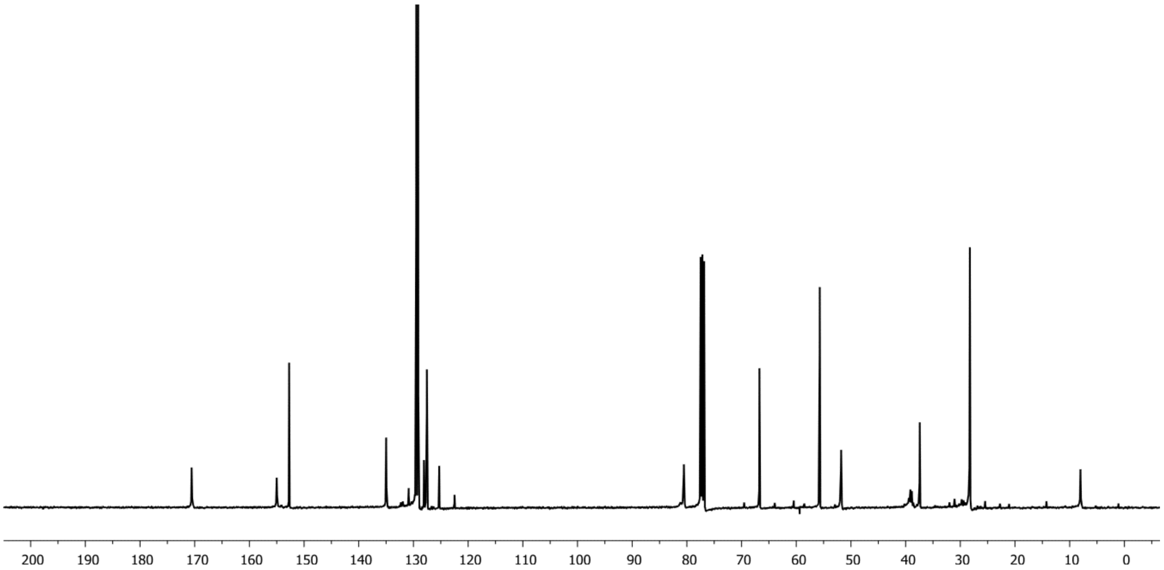
^{19}F NMR of compound **24a** (470 MHz, CDCl$_3$, 298 K).

Compound 25a

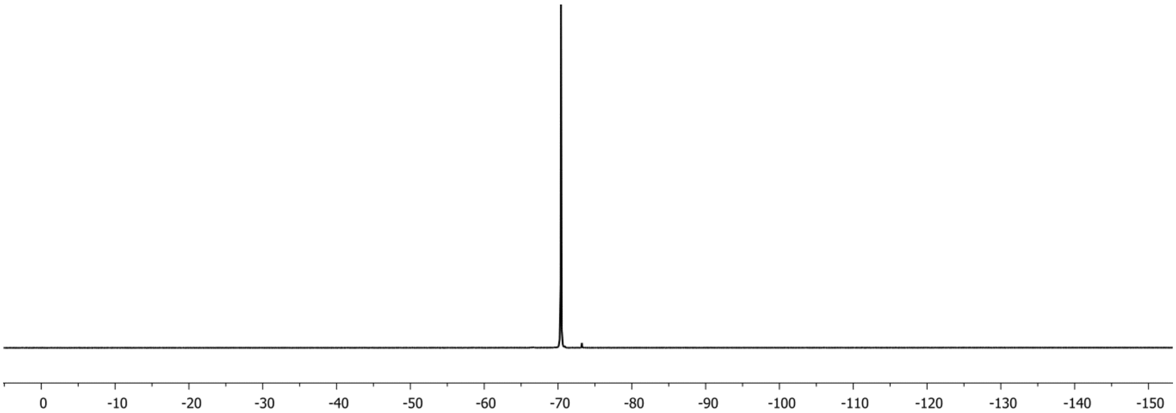


25a

^{1}H NMR of compound **25a** (500 MHz, CDCl$_3$, 298 K).

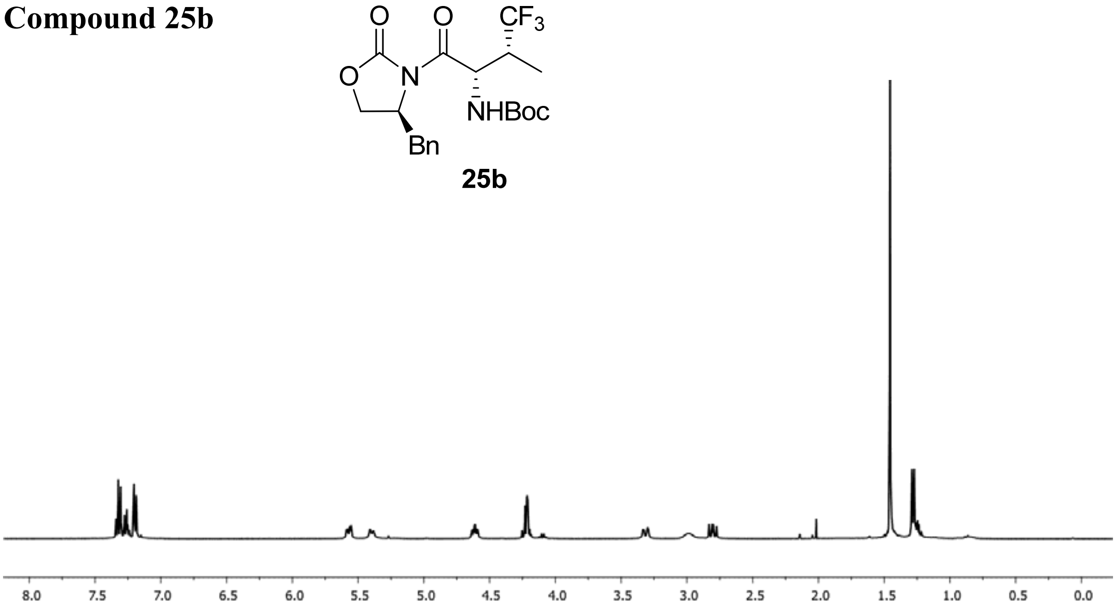


^{13}C NMR of compound **25a** (125 MHz, CDCl$_3$, 298 K).



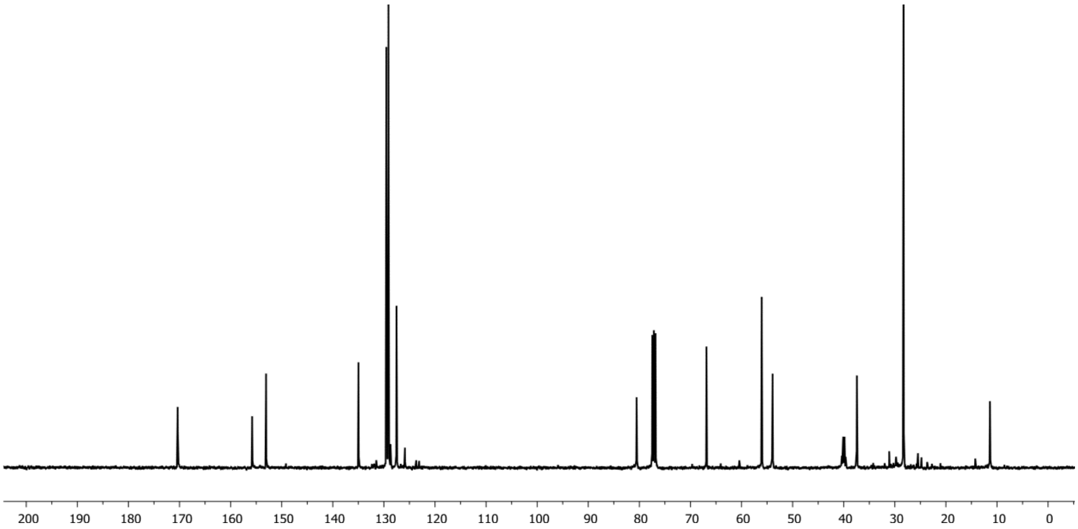
^{19}F NMR of compound **25a** (470 MHz, CDCl$_3$, 298 K).

Compound 25b

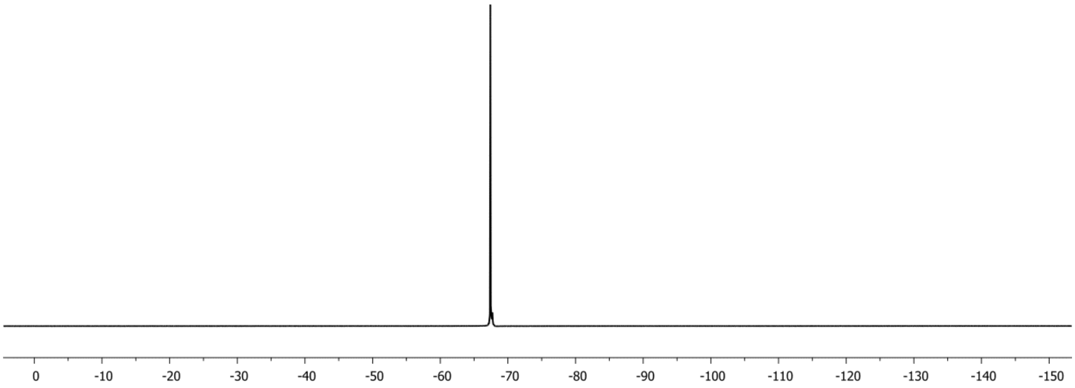


25b

^{1}H NMR of compound **25b** (500 MHz, $CDCl_3$, 298 K).



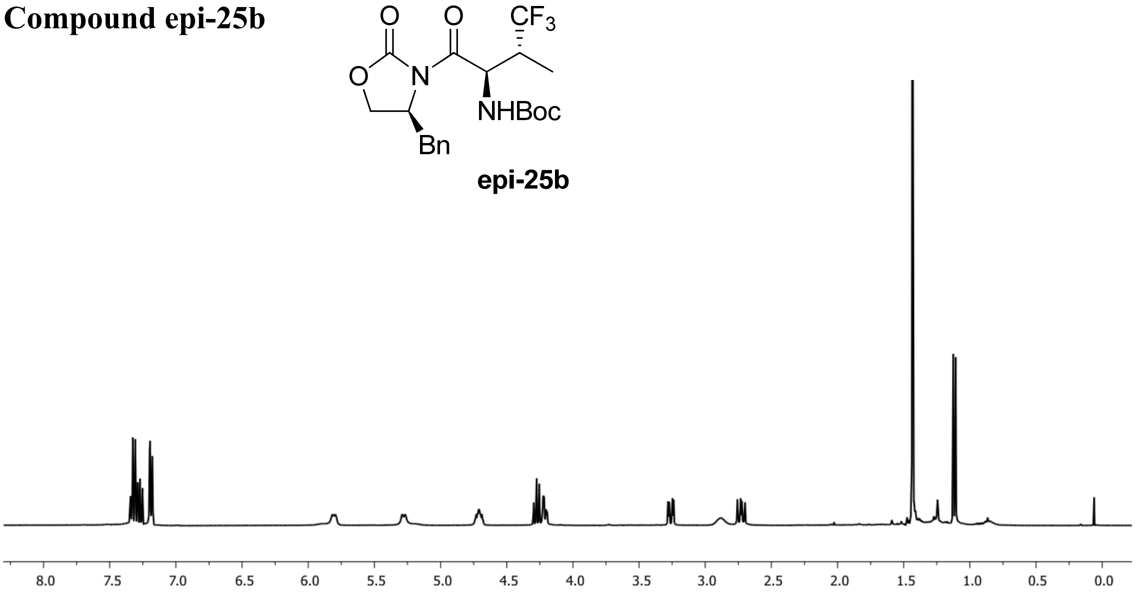
^{13}C NMR of compound **25b** (125 MHz, $CDCl_3$, 298 K).



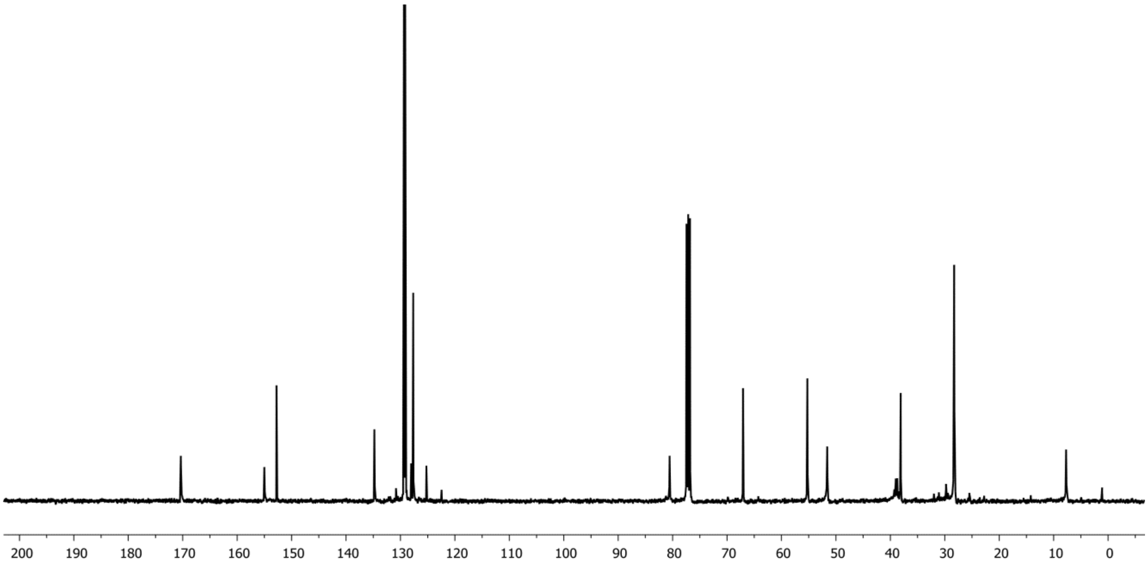
^{19}F NMR of compound **25b** (470 MHz, $CDCl_3$, 298 K).

Compound epi-25b

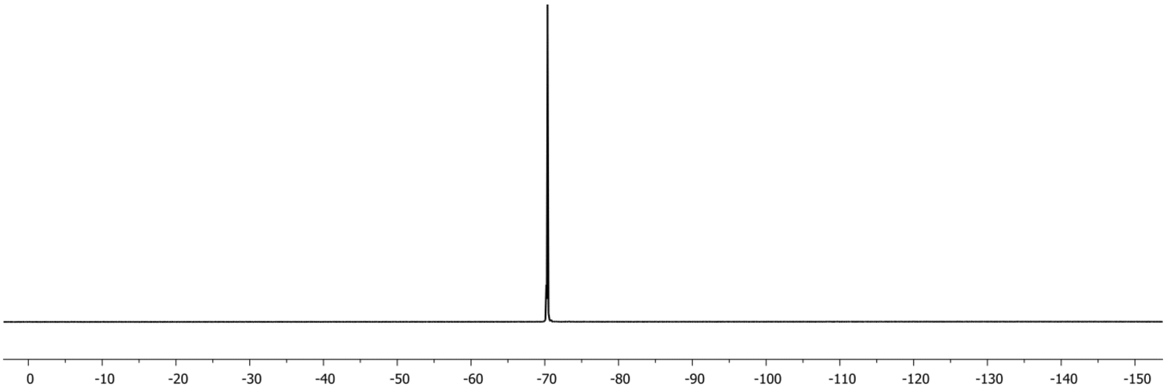
epi-25b



^{1}H NMR of compound **epi-25b** (500 MHz, CDCl$_3$, 298 K).

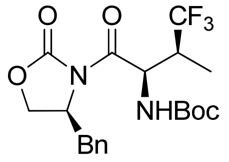


^{13}C NMR of compound **epi-25b** (125 MHz, CDCl$_3$, 298 K).

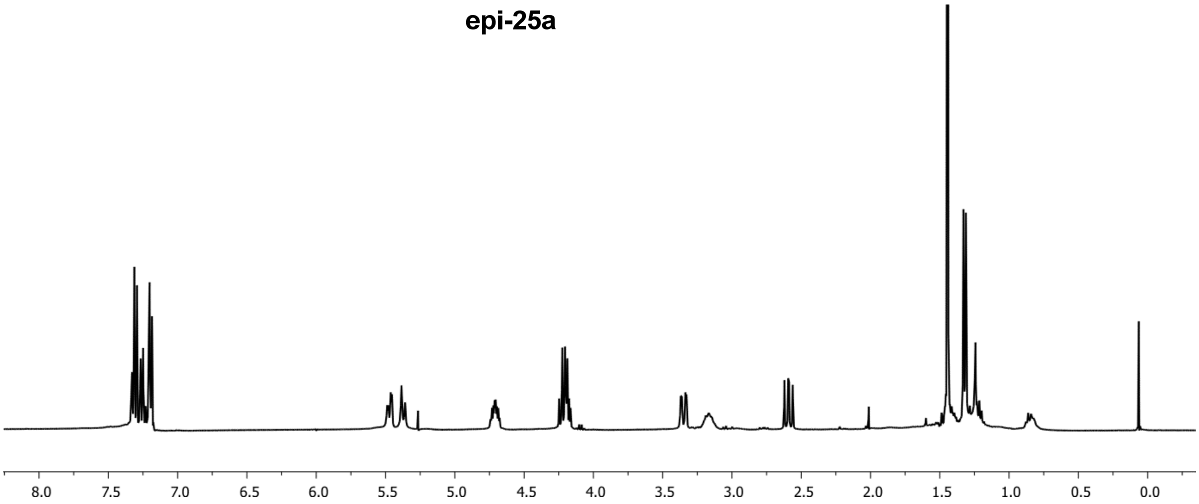


^{19}F NMR of compound **epi-25b** (470 MHz, CDCl$_3$, 298 K).

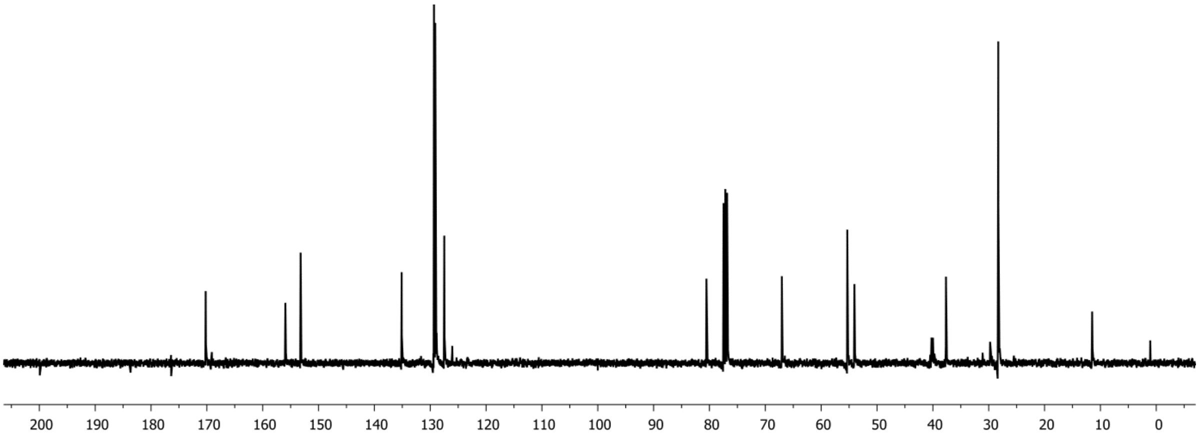
Compound epi-25a



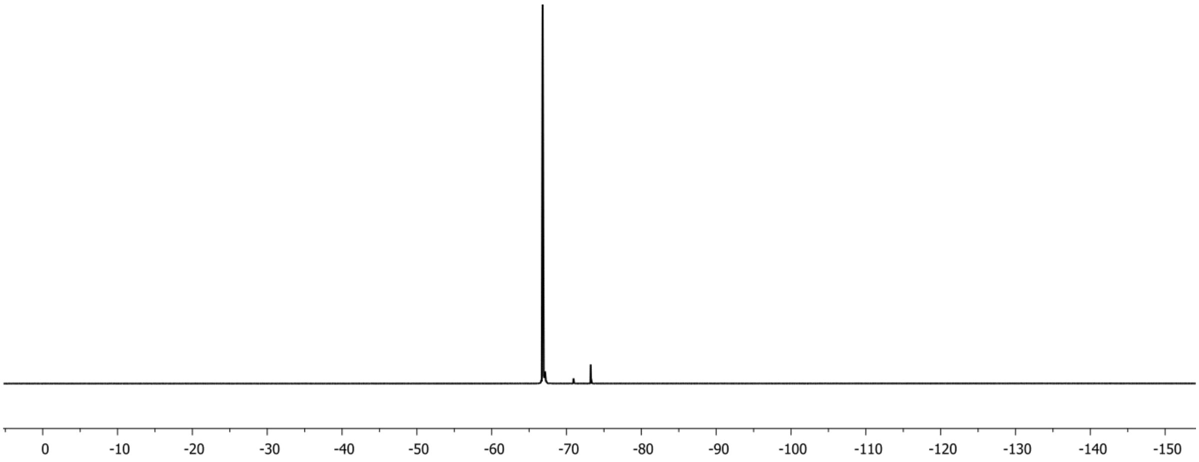
epi-25a



^{1}H NMR of compound **epi-25a** (500 MHz, CDCl$_3$, 298 K).

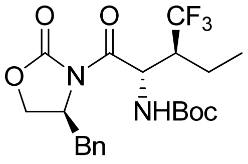


^{13}C NMR of compound **epi-25a** (125 MHz, CDCl$_3$, 298 K).

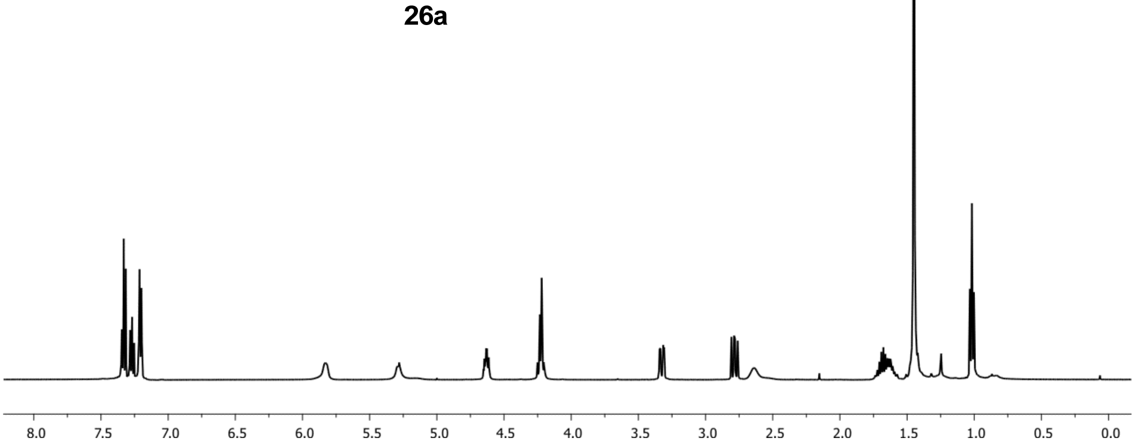


^{19}F NMR of compound **epi25a** (470 MHz, CDCl$_3$, 298 K).

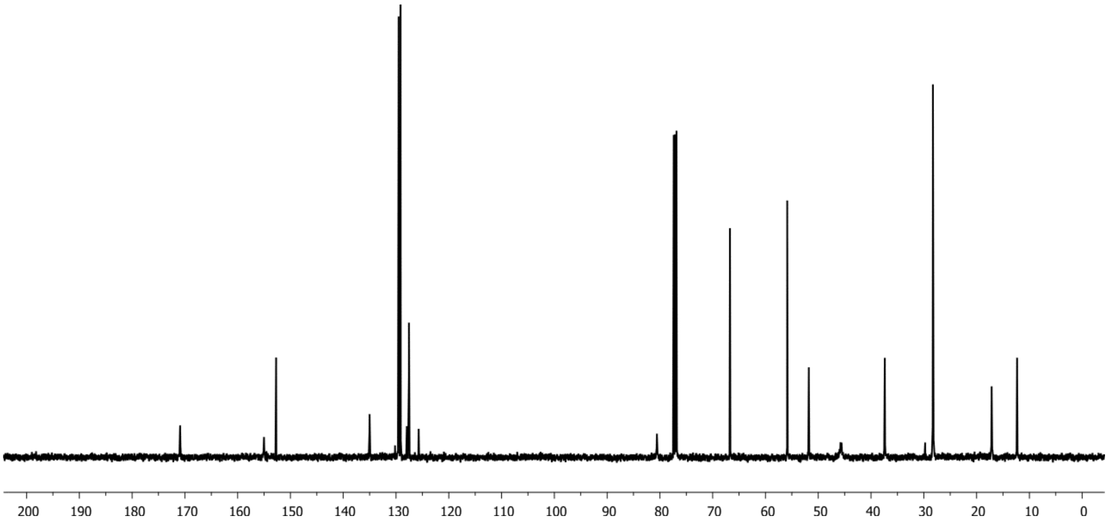
Compound 26a



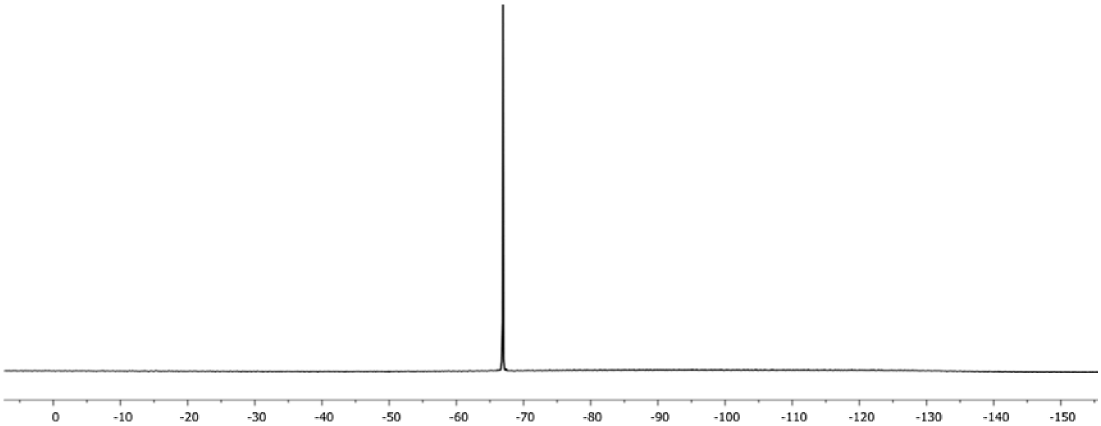
26a



^{1}H NMR of compound **26a** (500 MHz, $CDCl_3$, 298 K).

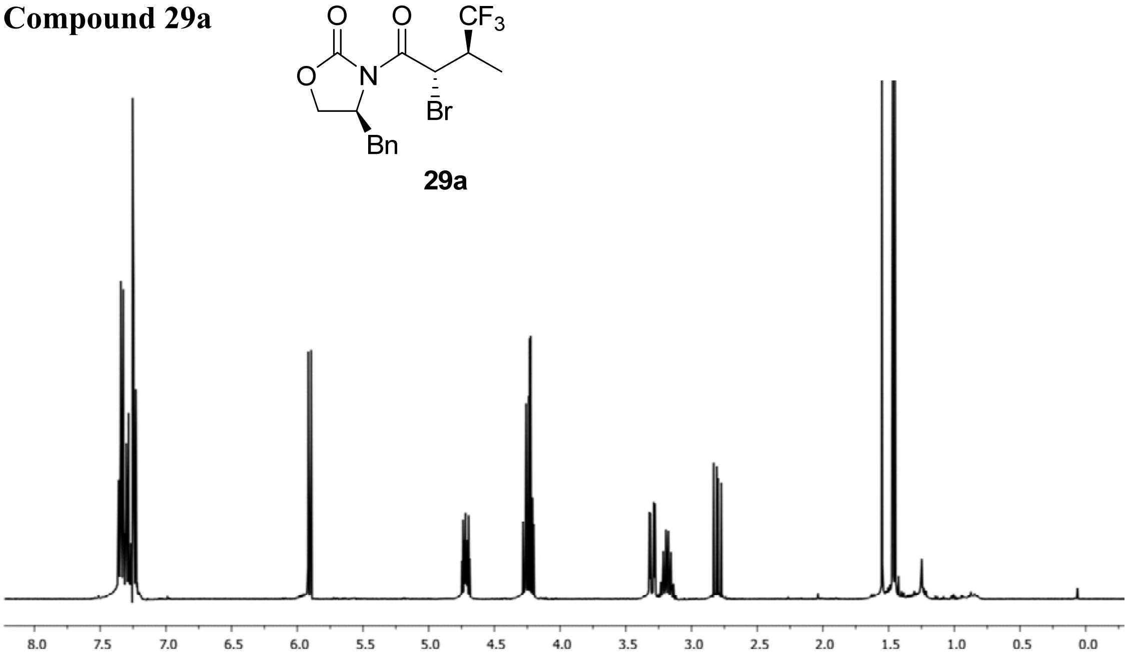


^{13}C NMR of compound **26a** (125 MHz, $CDCl_3$, 298 K).

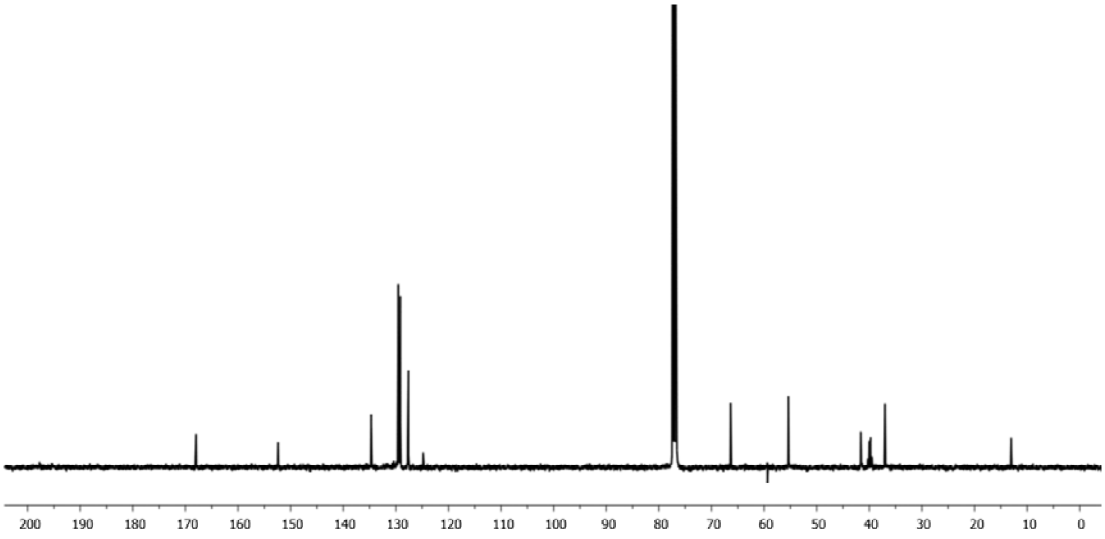


^{19}F NMR of compound **26a** (470 MHz, $CDCl_3$, 298 K).

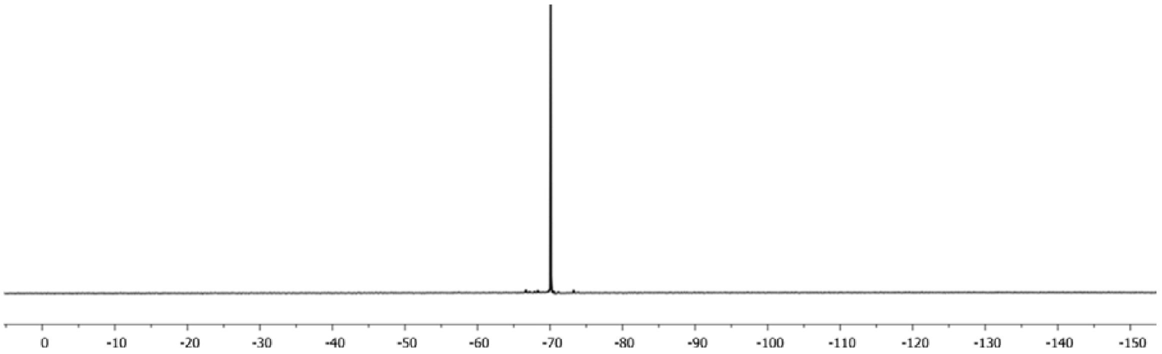
Compound 29a



^{1}H NMR of compound **29a** (500 MHz, CDCl$_3$, 298 K).

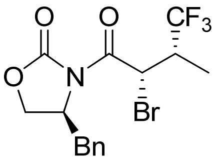


^{13}C NMR of compound **29a** (125 MHz, CDCl$_3$, 298 K).

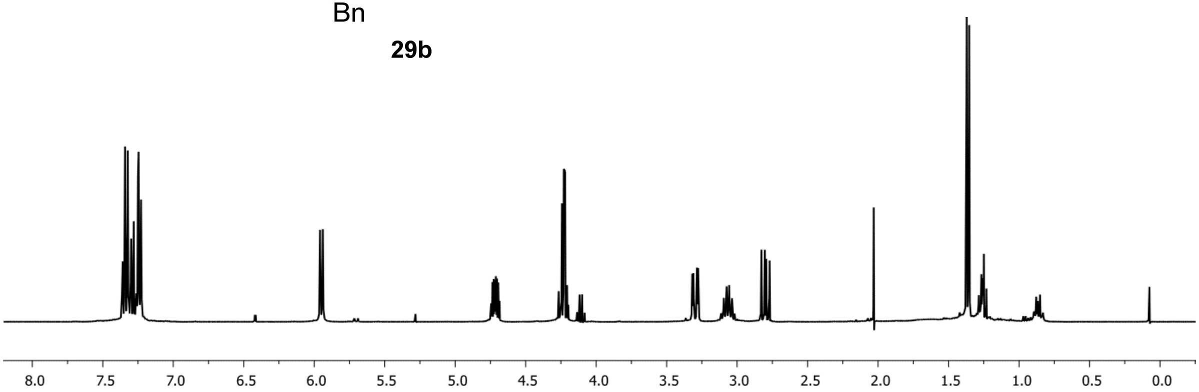


^{19}F NMR of compound **29a** (470 MHz, CDCl$_3$, 298 K).

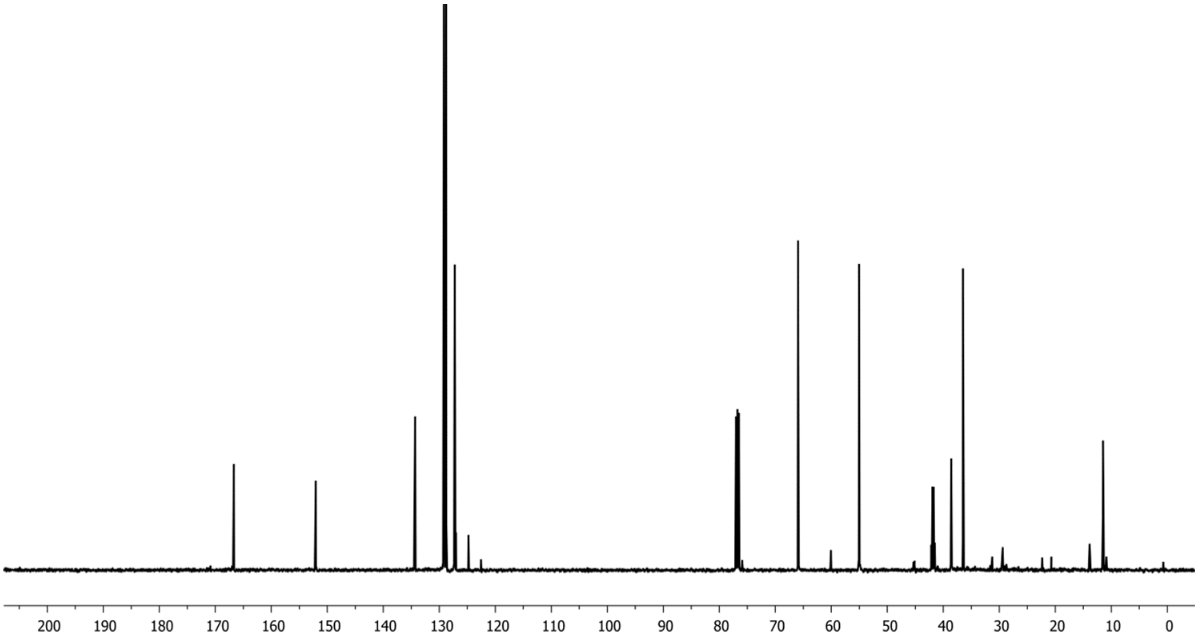
Compound 29b



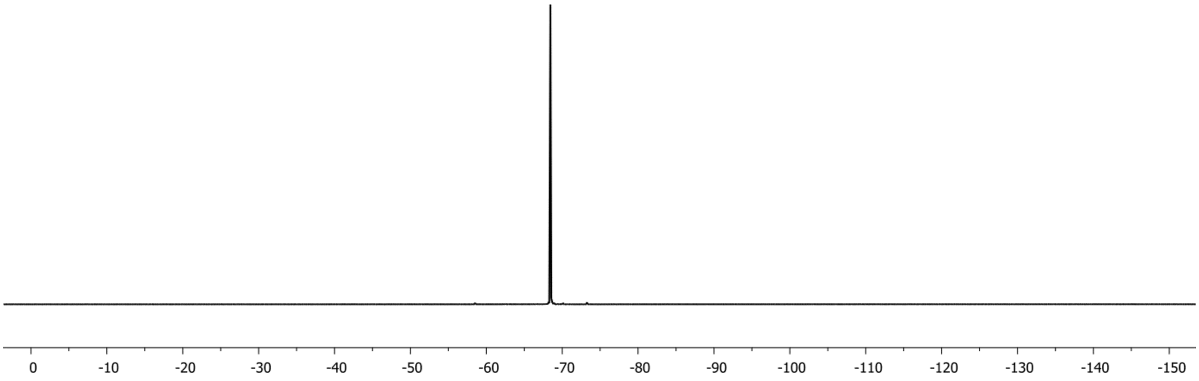
29b



^{1}H NMR of compound **29b** (500 MHz, $CDCl_3$, 298 K).

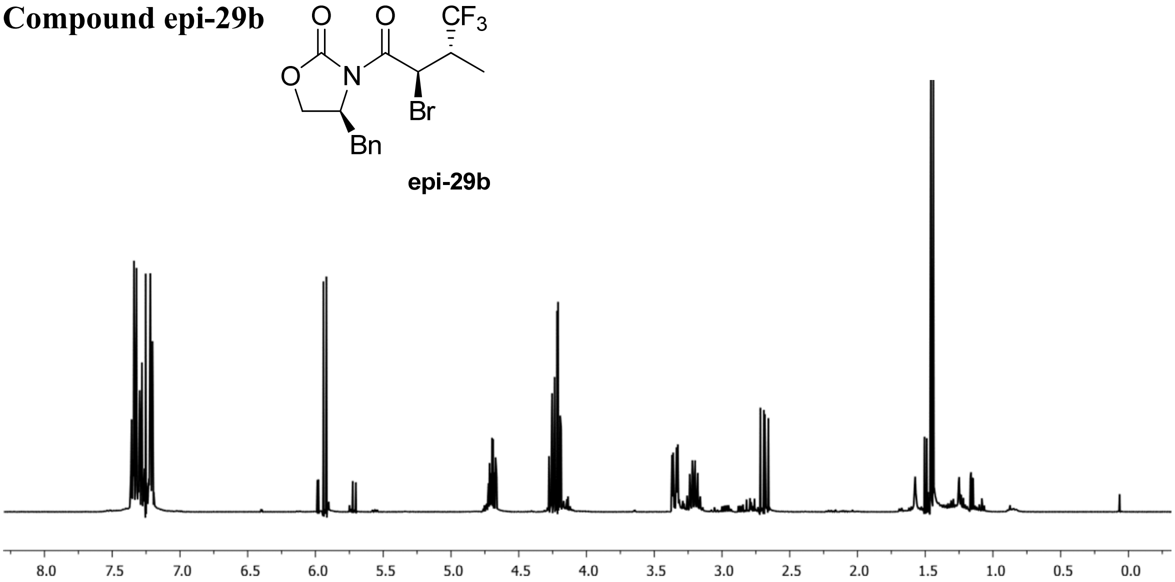


^{13}C NMR of compound **29b** (125 MHz, $CDCl_3$, 298 K).



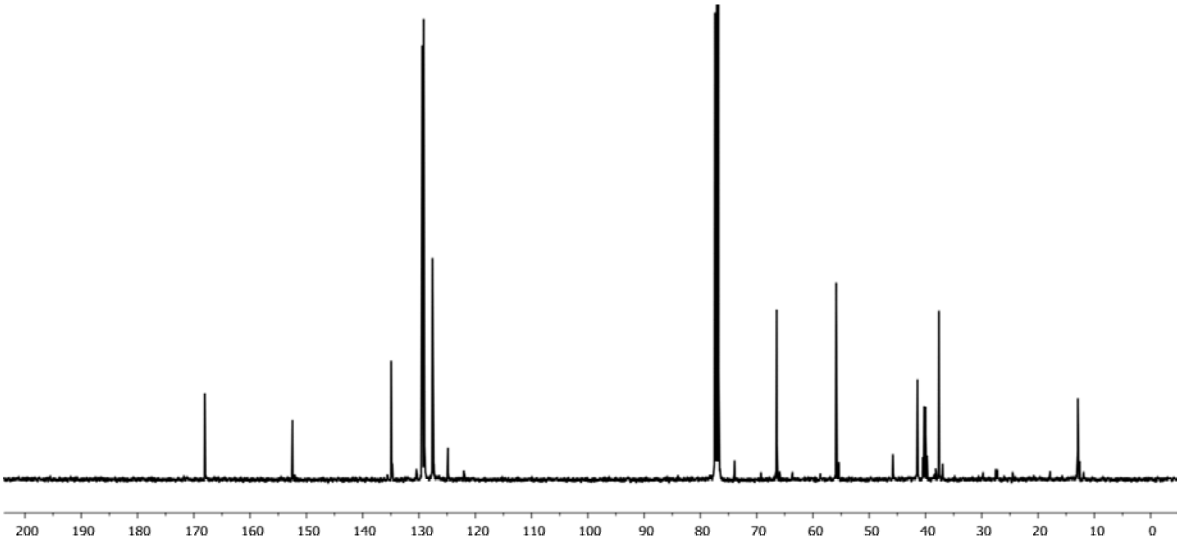
^{19}F NMR of compound **29b** (470 MHz, $CDCl_3$, 298 K).

Compound epi-29b

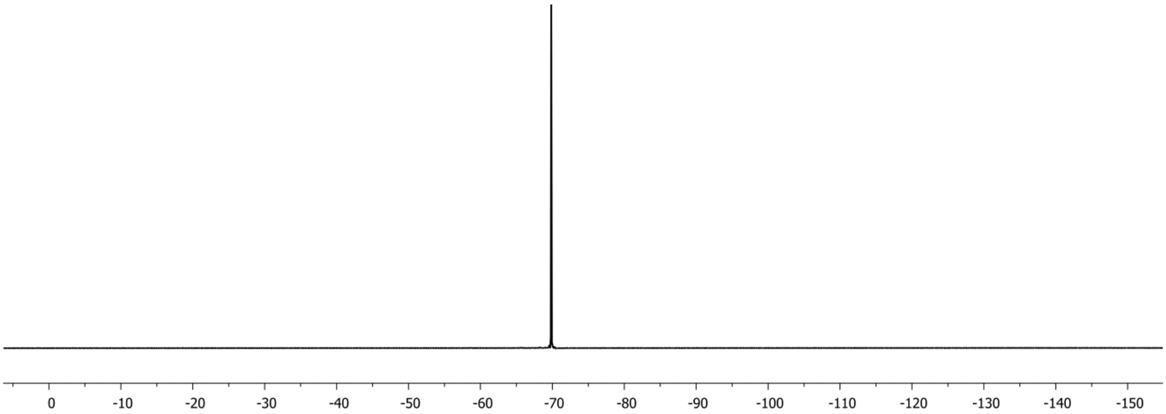


epi-29b

^{1}H NMR of compound **epi-29b** (500 MHz, $CDCl_3$, 298 K).

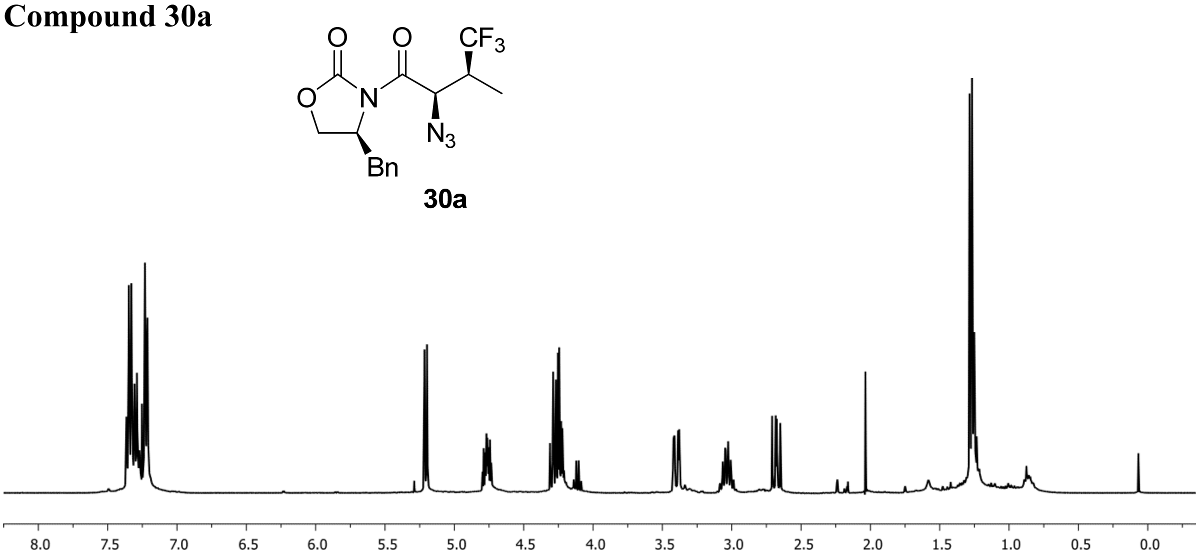


^{13}C NMR of compound **epi-29b** (125 MHz, $CDCl_3$, 298 K).



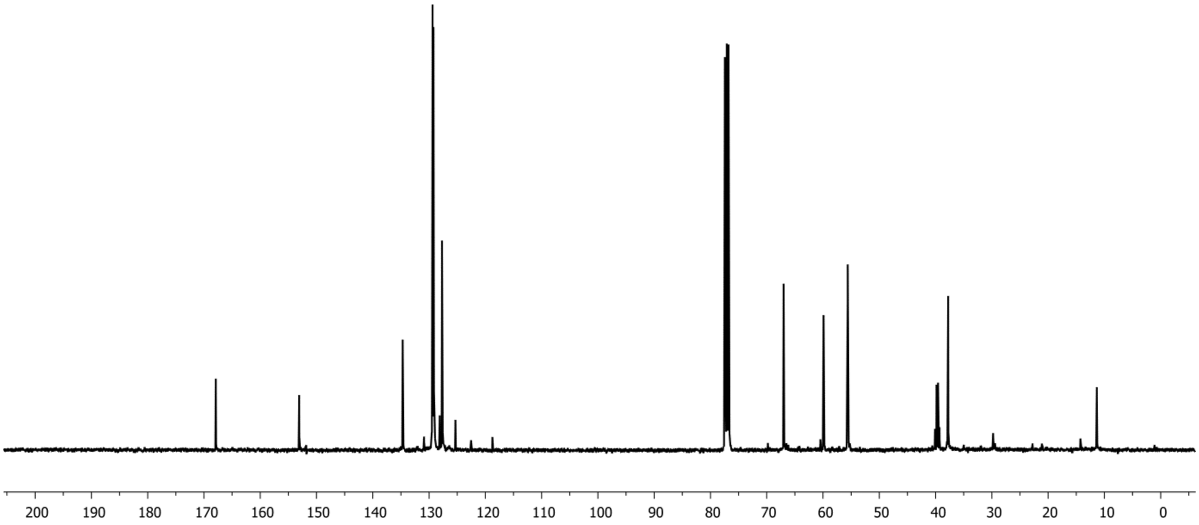
^{19}F NMR of compound **epi-29b** (470 MHz, $CDCl_3$, 298 K).

Compound 30a

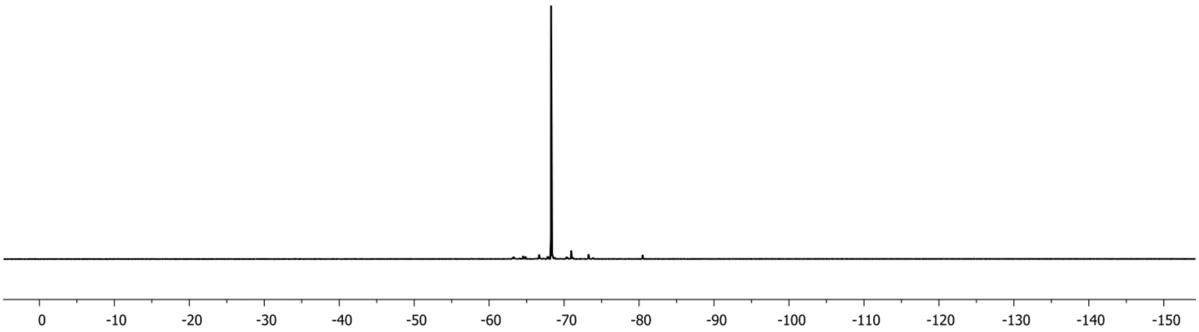


30a

^{1}H NMR of compound **30a** (500 MHz, $CDCl_3$, 298 K).

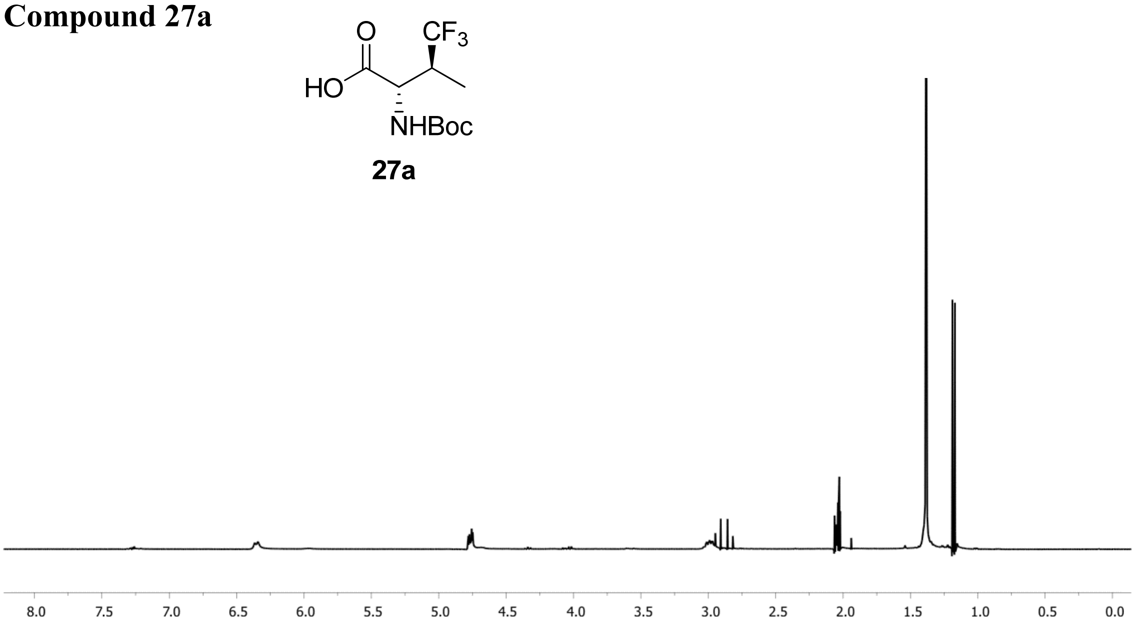


^{13}C NMR of compound **30a** (125 MHz, $CDCl_3$, 298 K).

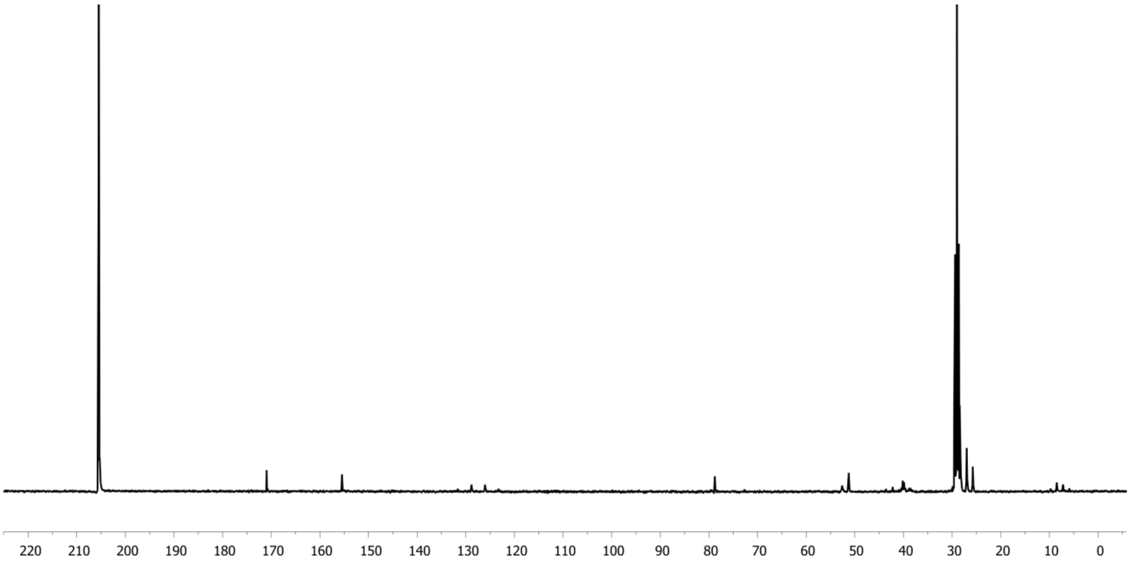


^{19}F NMR of compound **30a** (470 MHz, $CDCl_3$, 298 K).

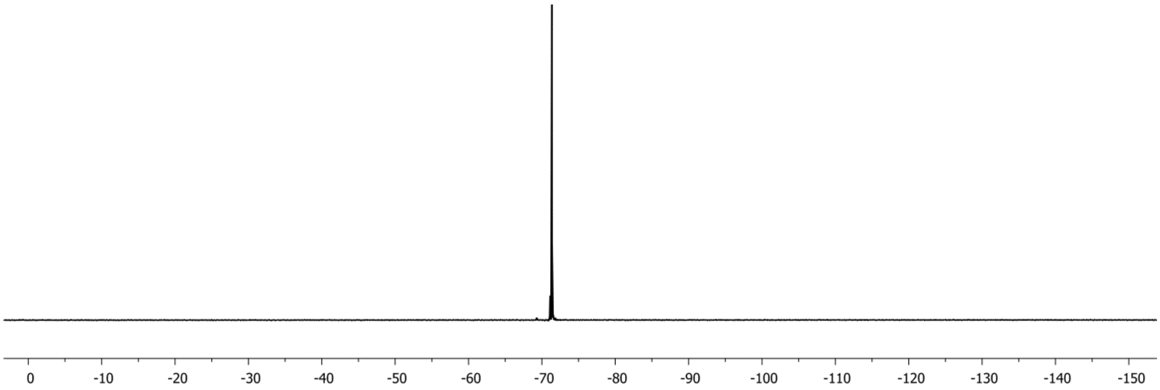
Compound 27a



^{1}H NMR of compound **27a** (500 MHz, C_3D_6O, 298 K).

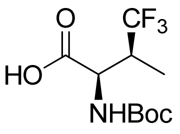


^{13}C NMR of compound **27a** (125 MHz, C_3D_6O, 298 K).

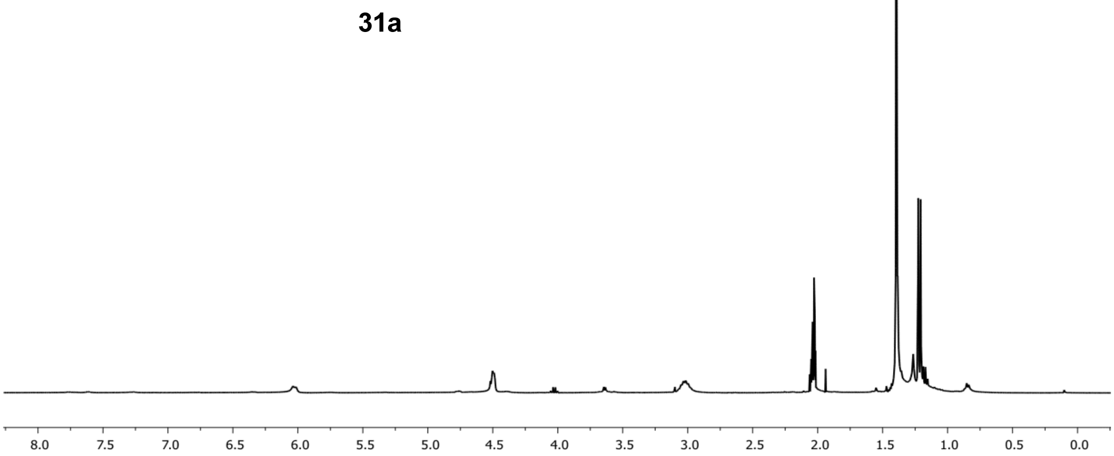


^{19}F NMR of compound **27a** (470 MHz, $CDCl_3$, 298 K).

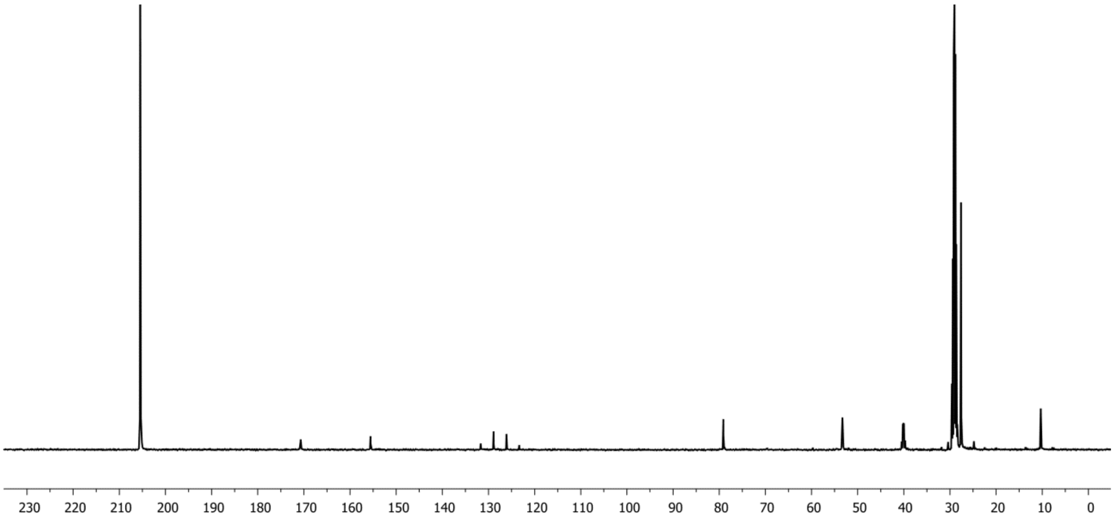
Compound 31a



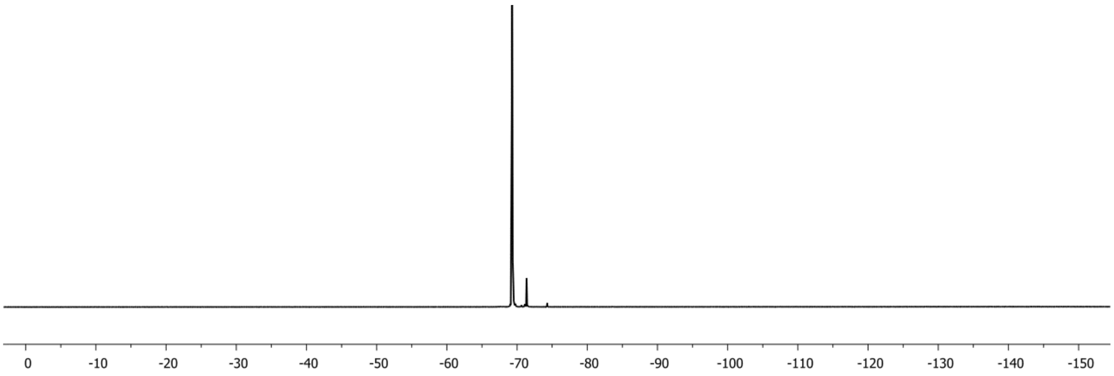
31a



^{1}H NMR of compound **31a** (500 MHz, C_3D_6O, 298 K).

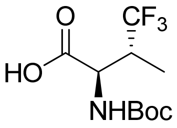


^{13}C NMR of compound **31a** (125 MHz, C_3D_6O, 298 K).

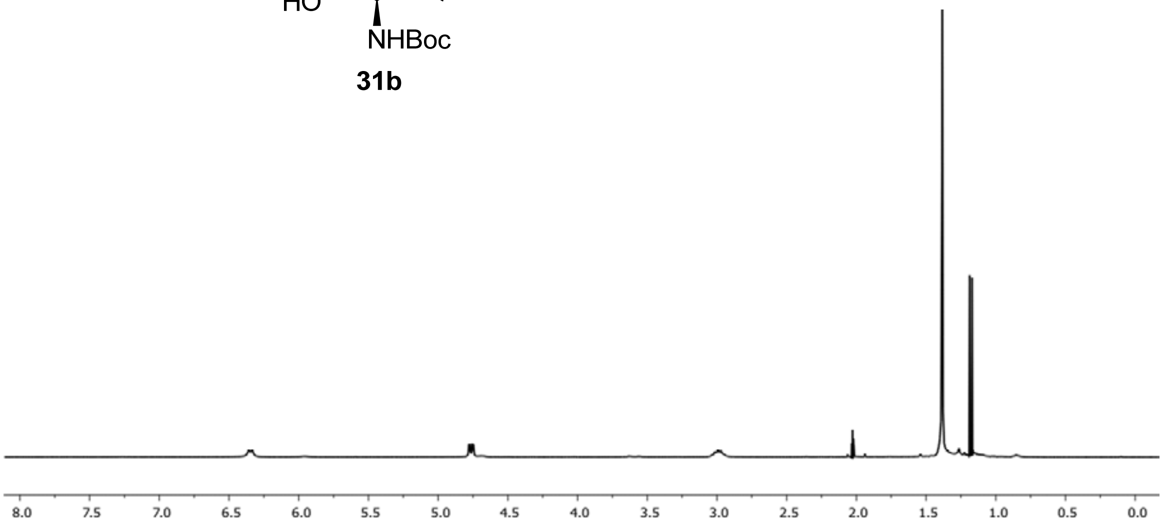


^{19}F NMR of compound **31a** (470 MHz, C_3D_6O, 298 K).

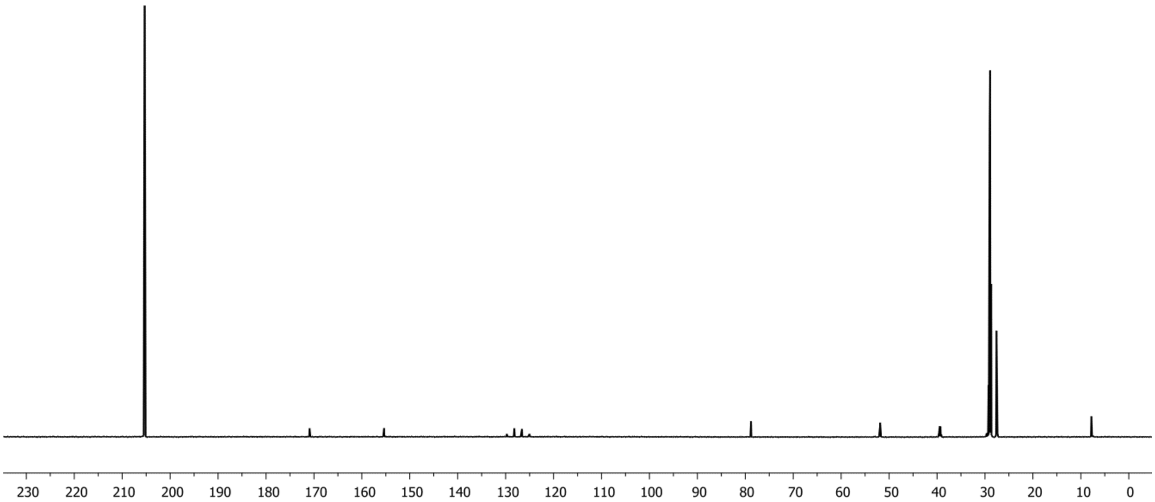
Compound 31b



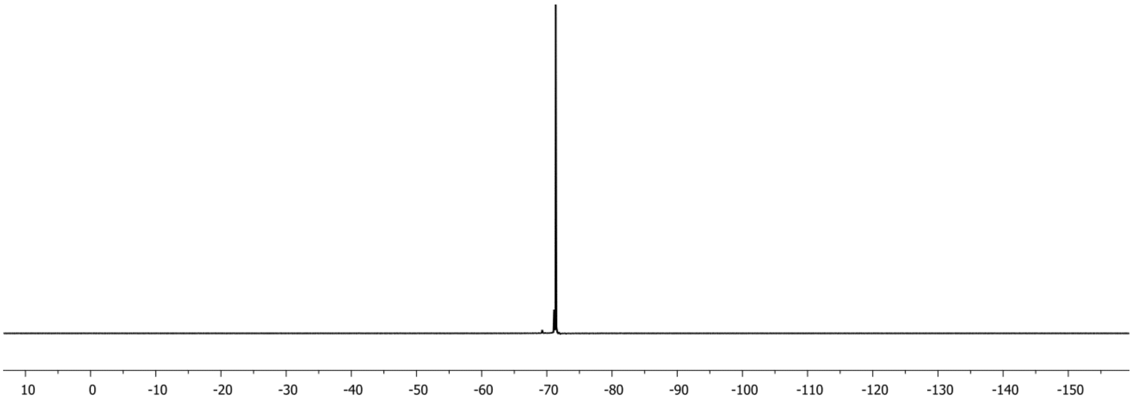
31b



^{1}H NMR of compound **31b** (500 MHz, C_3D_6O, 298 K).

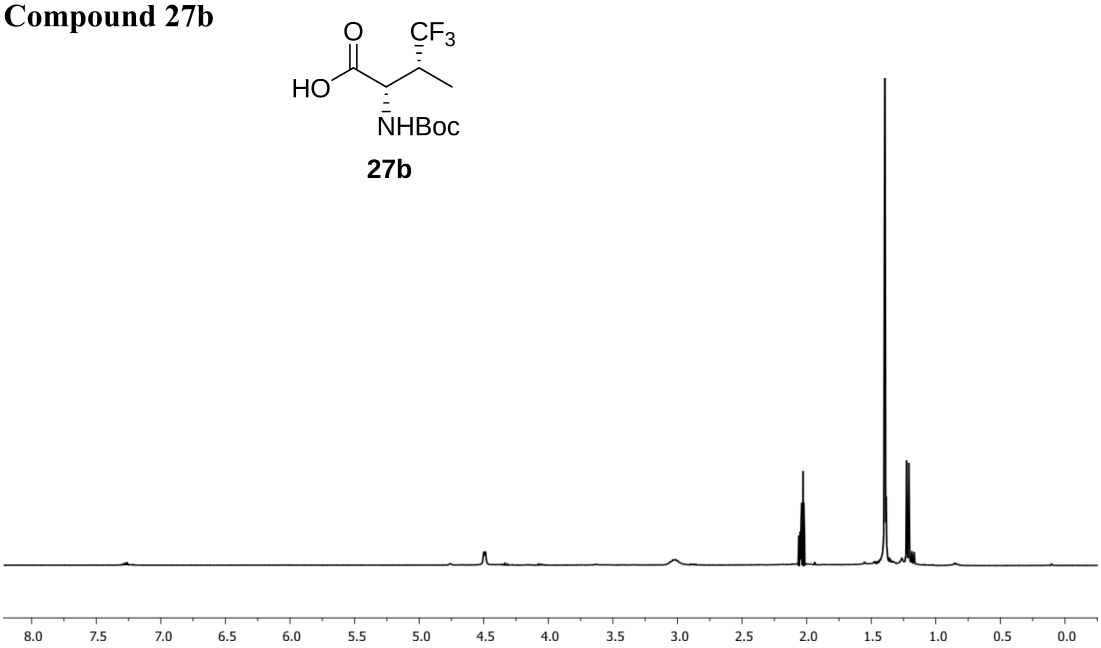


^{13}C NMR of compound **31b** (125 MHz, C_3D_6O, 298 K).



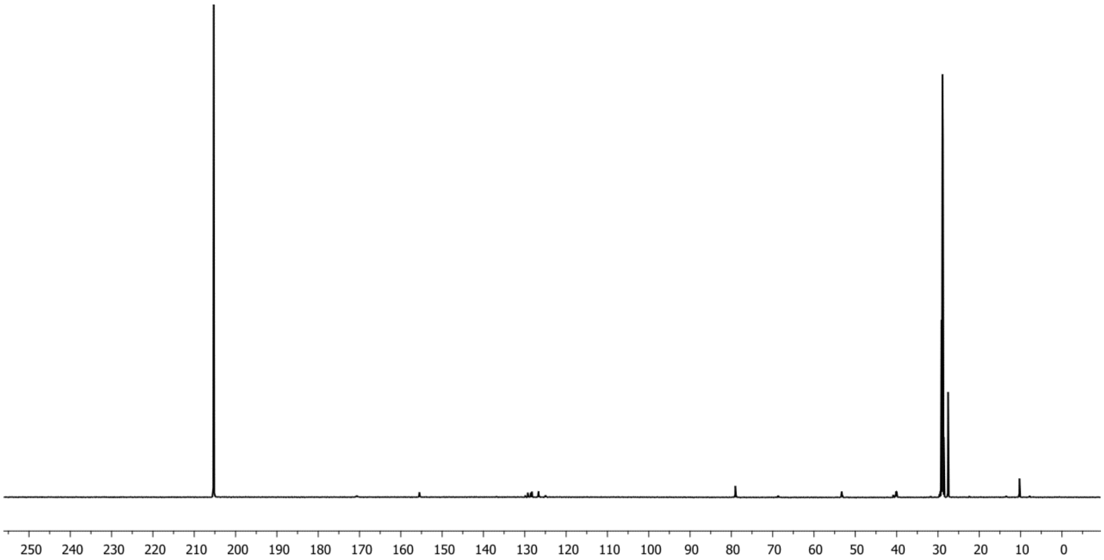
^{19}F NMR of compound **31b** (470 MHz, C_3D_6O, 298 K).

Compound 27b

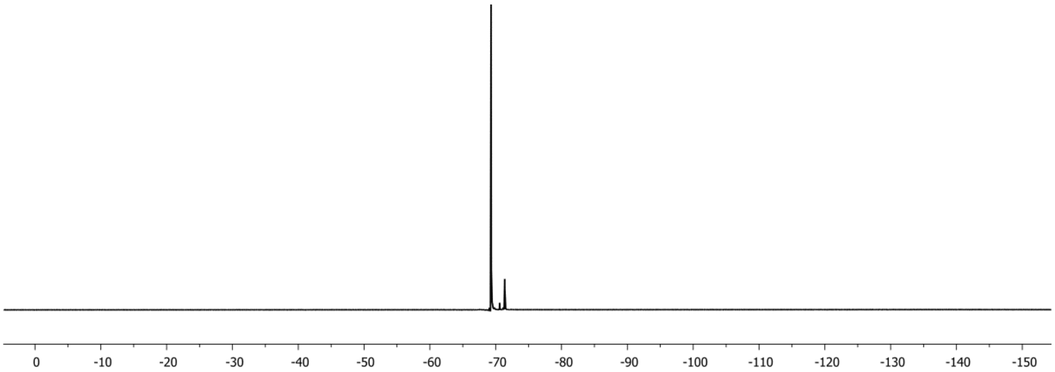


27b

^{1}H NMR of compound **27b** (500 MHz, C_3D_6O, 298 K).

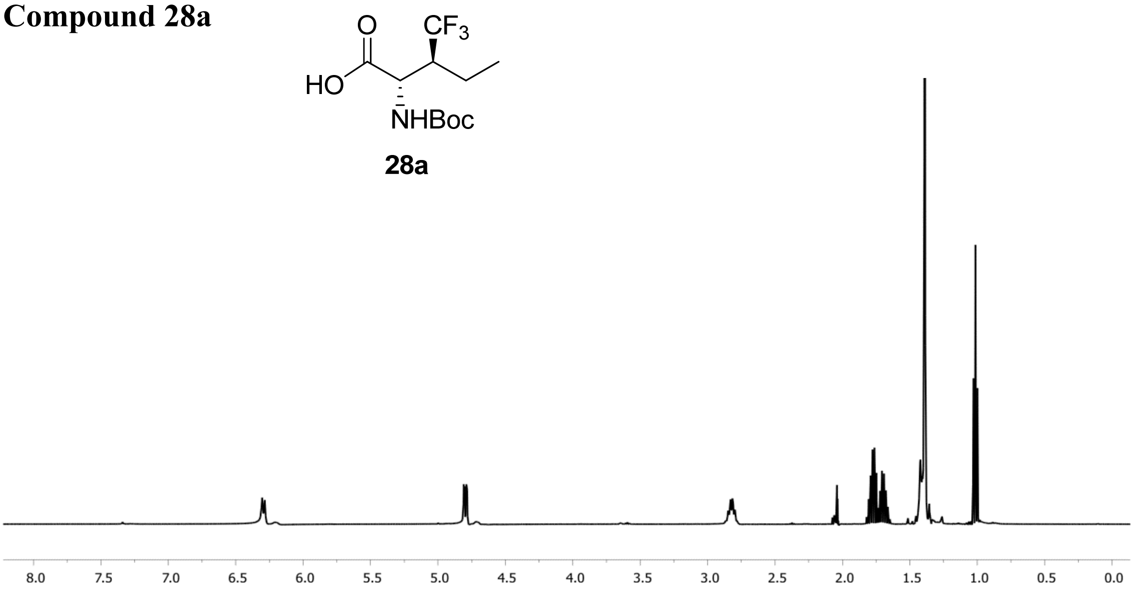


^{13}C NMR of compound **27b** (125 MHz, C_3D_6O, 298 K).



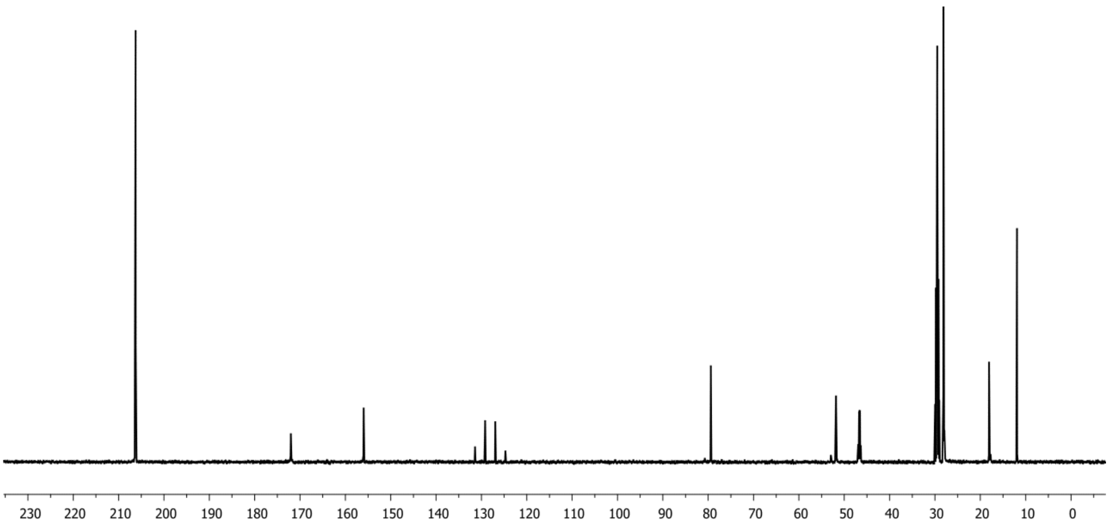
^{19}F NMR of compound **27b** (470 MHz, C_3D_6O, 298 K).

Compound 28a

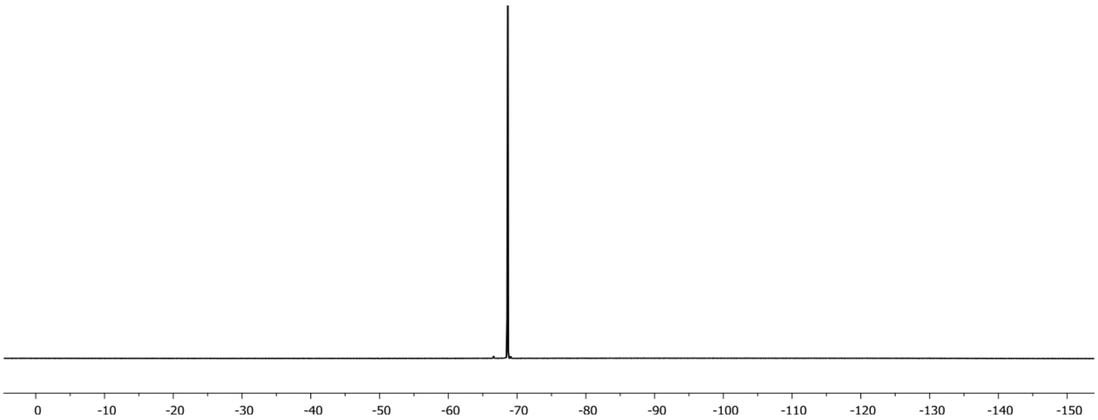


28a

^{1}H NMR of compound **28a** (500 MHz, C_3D_6O, 298 K).

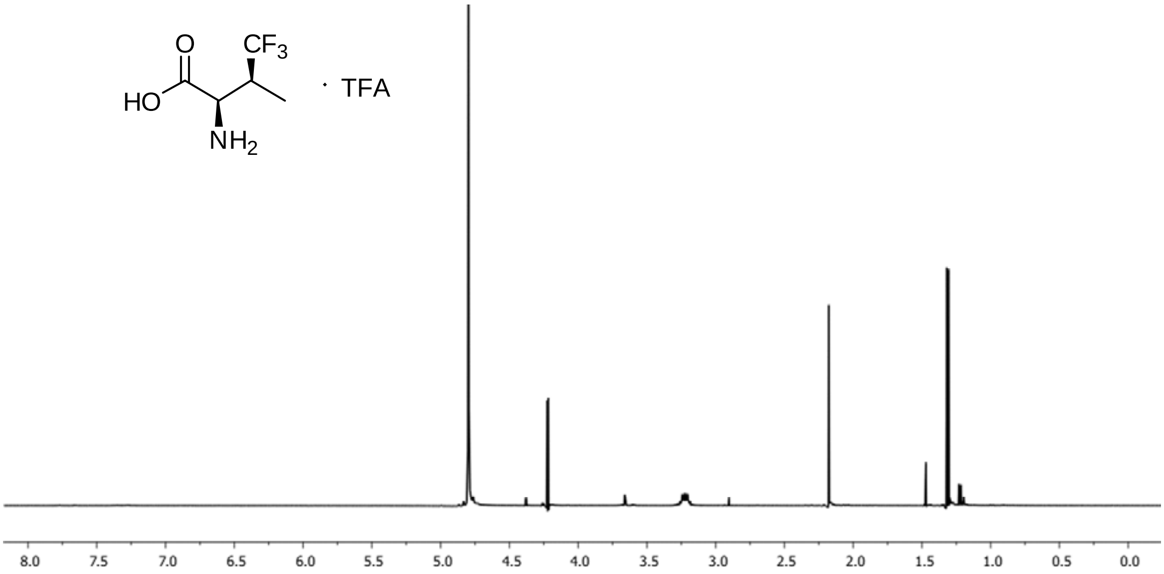


^{13}C NMR of compound **28a** (125 MHz, C_3D_6O, 298 K).

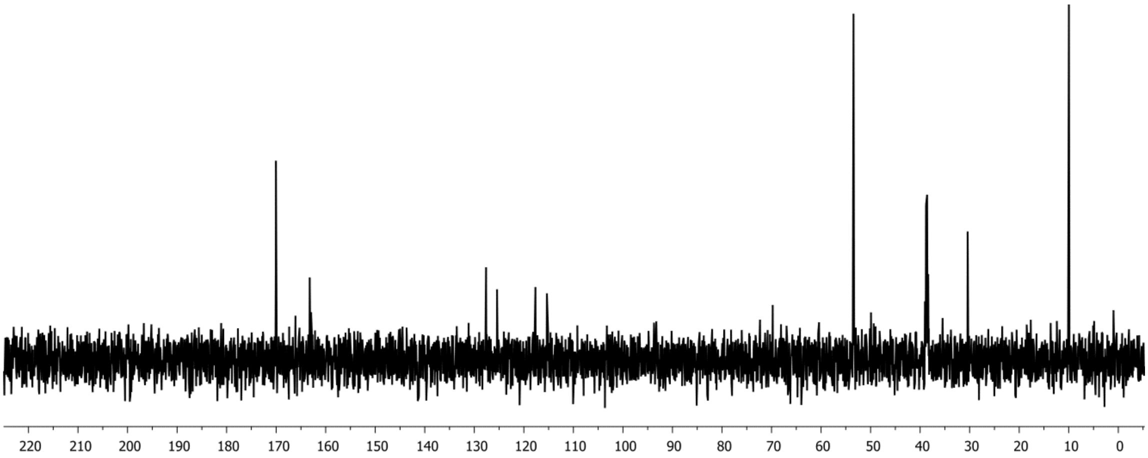


^{19}F NMR of compound **28a** (470 MHz, C_3D_6O, 298 K).

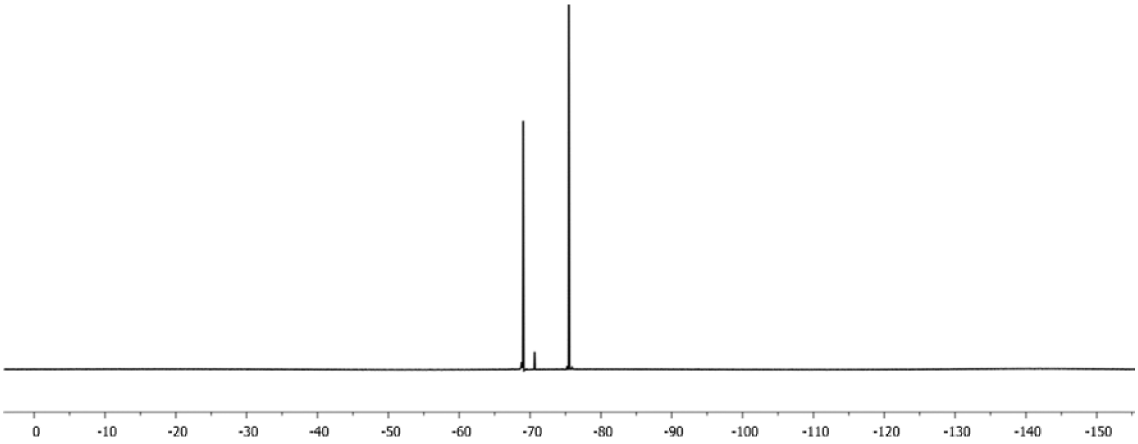
(2*R*,3*S*)-2-amino-4,4,4-trifluoro-3-methylbutanoic acid



^{1}H NMR (500 MHz, D_2O, 298 K).

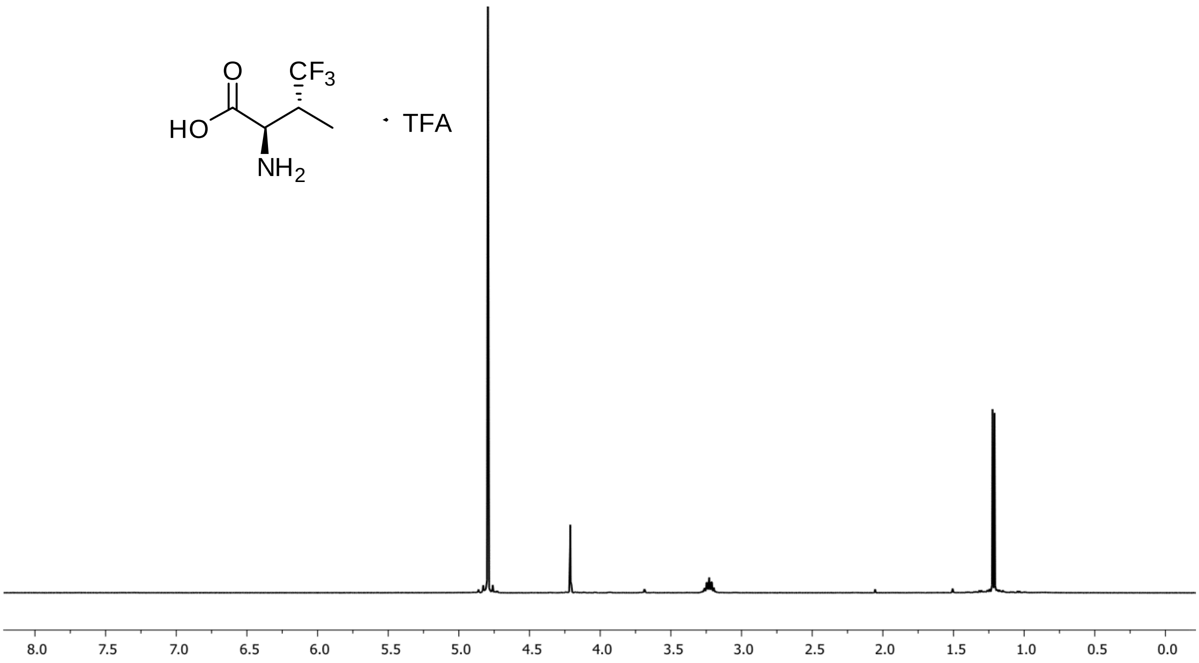


^{13}C NMR (125 MHz, D_2O, 298 K).

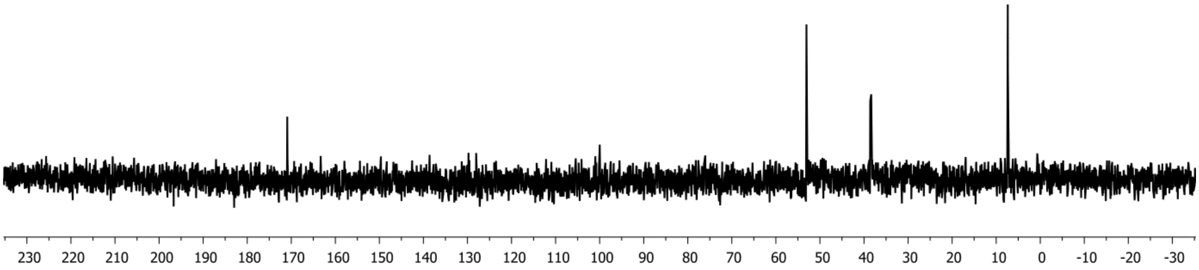


^{19}F NMR (470 MHz, D_2O, 298 K).

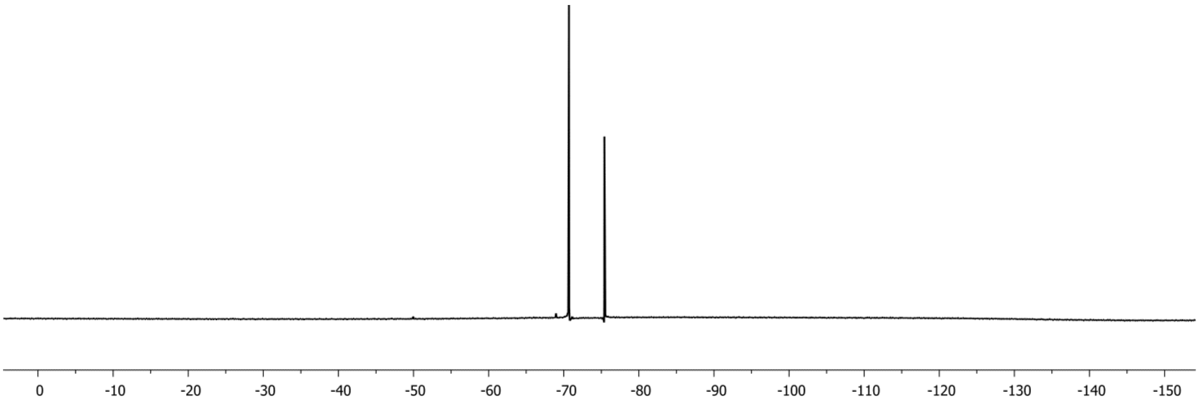
(2*R*,3*R*)-2-amino-4,4,4-trifluoro-3-methylbutanoic acid



^{1}H NMR (500 MHz, D_2O, 298 K).

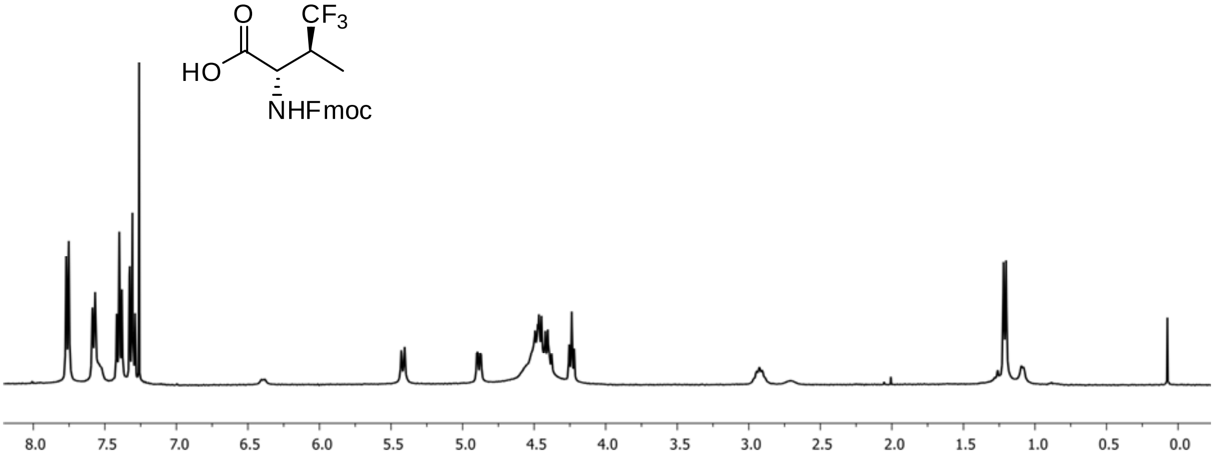


^{13}C NMR (125 MHz, D_2O, 298 K).

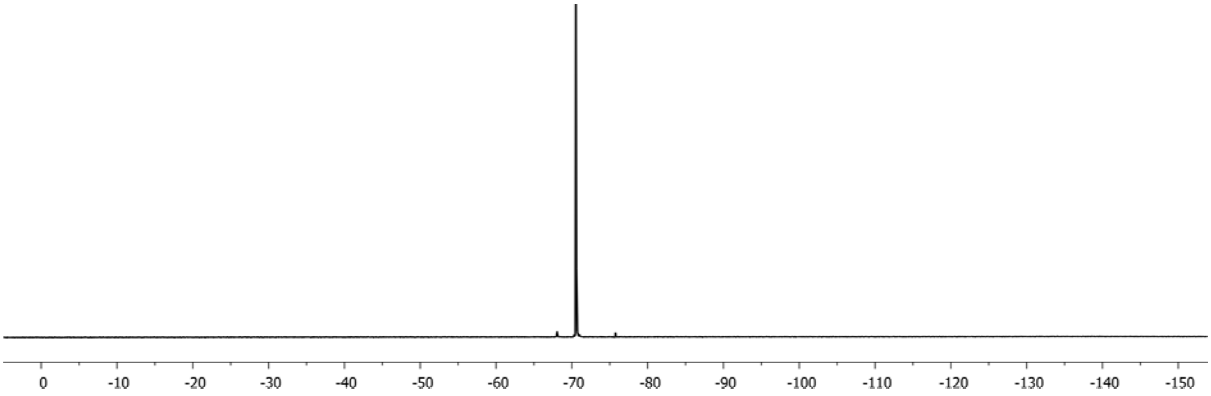


^{19}F NMR (470 MHz, D_2O, 298 K).

(2*S*,3*S*)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4,4,4-tri-fluoro-3-methylbutanoic acid

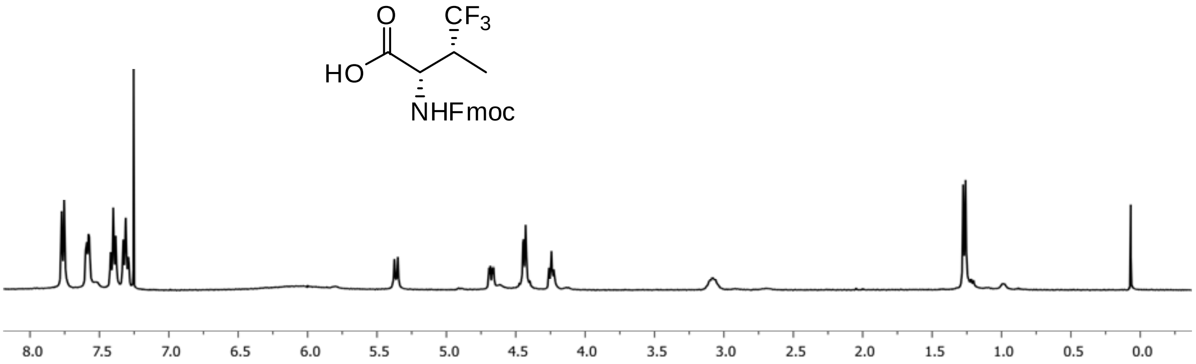


^{1}H NMR (400 MHz, $CDCl_3$, 298 K).

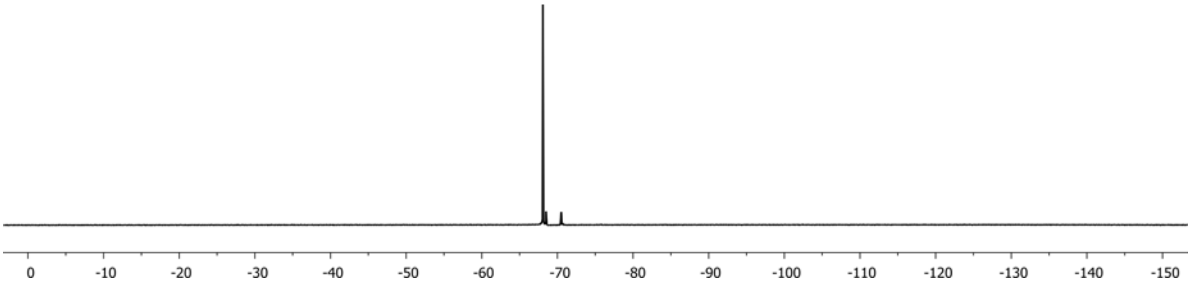


^{19}F NMR (470 MHz, $CDCl_3$, 298 K).

(2*S*,3*R*)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4,4,4-tri-fluoro-3-methylbutanoic acid

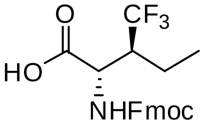


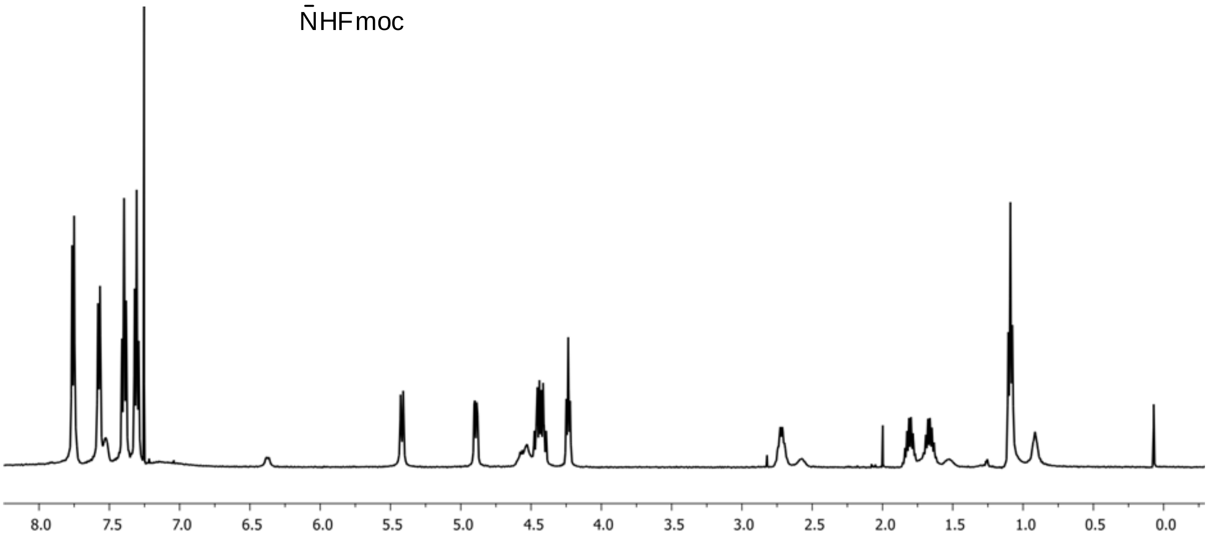
^{1}H NMR (400 MHz, CDCl$_3$, 298 K).



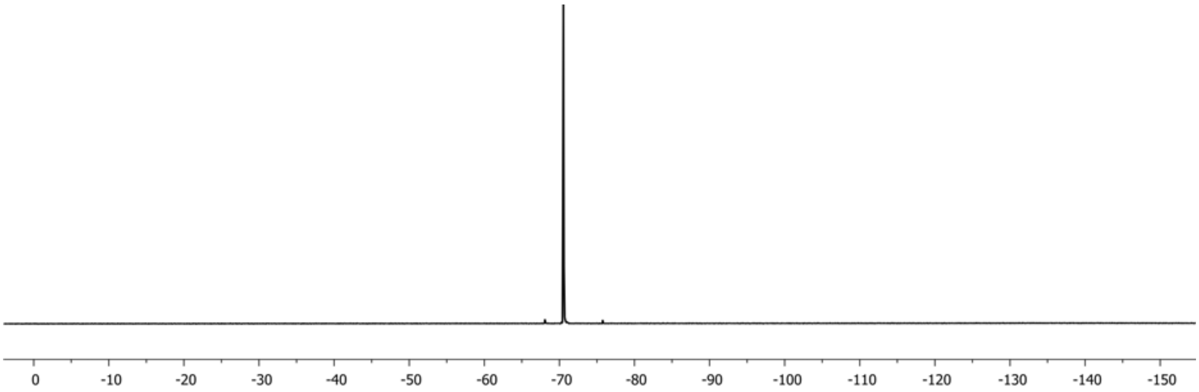
^{19}F NMR (470 MHz, CDCl$_3$, 298 K).

(2*R*,3*R*)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-4,4,4-trifluor-3-methylbutanoic acid





^{1}H NMR (400 MHz, CDCl$_3$, 298 K).



^{19}F NMR (470 MHz, CDCl$_3$, 298 K).

X-Ray Crystal Structure Analysis

X-ray single crystal diffraction of compounds 2a, 26a, was performed on a Bruker AXS Smart CCD. X-ray single crystal diffraction of compound 25a was performed on an Agilent SuperNova, Dual, Cu at zero, Atlas (We thank Dr. Alexandra Griffin, Agilent Technologies, UK for the data collection). X-ray crystallographic details are given in Table 1. The structures were solved by direct methods, using SHELXS-97[1] and refined with the least squares method (SHELXL-97[1]) using WINGX[2]. Molecular Graphics: ORTEP-3 for Windows[3].

Table 1. Crystallographic Data of 2a, 25a and 26a

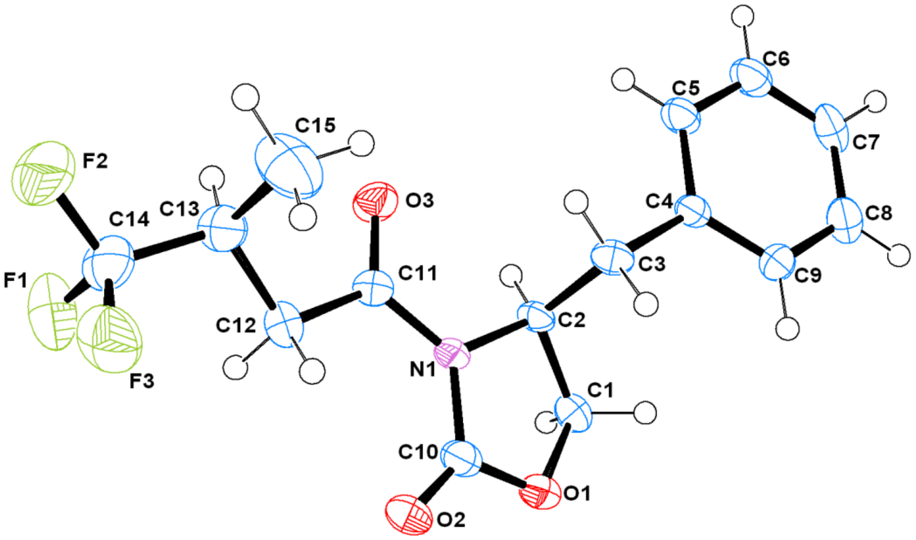
Compound reference	**2a**	**25a**	**26a**
Chemical formula	$C_{15}H_{16}F_3NO_3$	$C_{20}H_{25}F_3N_2O_5$	$C_{21}H_{27}F_3N_2O_5$
Formula Mass	315.29	430.42	444.45
Crystal system	Orthorhombic	Orthorhombic	Orthorhombic
a/Å	5.409(2)	6.34460(10)	6.3032(14)
b/Å	11.831(5)	16.7461(2)	17.505(4)
c/Å	22.811(10)	19.6159(2)	19.677(4)
α/°	90.00	90.00	90.00
β/°	90.00	90.00	90.00
γ/°	90.00	90.00	90.00
Unit cell volume/Å^3	1459.7(11)	2084.14(5)	2171.1(8)
Temperature/K	133(2)	100(2)	133(2)
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
No. of formula units per unit cell, Z	4	4	4
Radiation type	MoKα	CuKα	MoKα
No. of reflections measured	10619	11926	35355
No. of independent reflections	1531	4175	6616
R_{int}	0.0627	0.0250	0.0254
Final R_1 values ($I > 2\sigma(I)$)	0.0472	0.0295	0.0346
Final $wR(F^2)$ values (all data)	0.1266	0.0758	0.0886
Goodness of fit on F^2	1.121	1.059	1.063
Flack parameter	2(2)	-0.02(9)	-0.1(4)
CCDC number	887851	887849	887850

The CCDC numbers given in Table 1 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

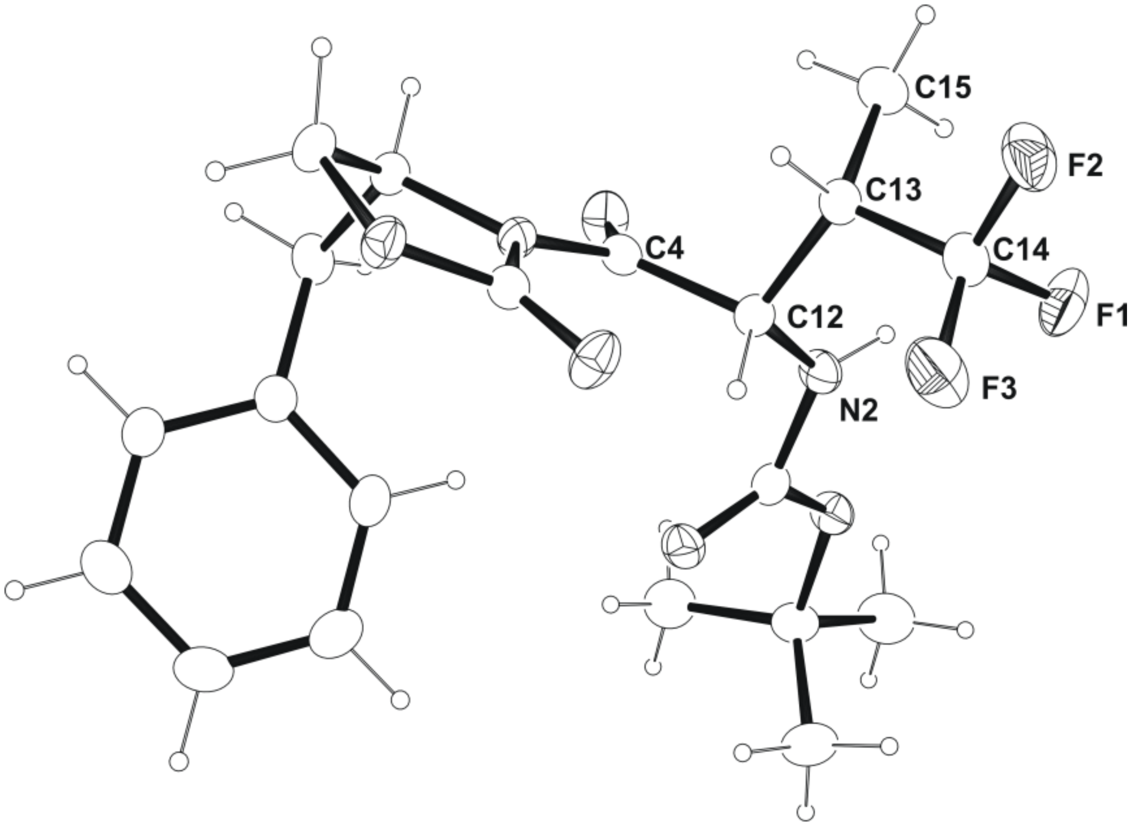
[1] *SHELX-97* (release 97-2): G. M. Sheldrick, *Acta Cryst A*, 2008, **A64**, 112-122.

[2] WINGX, L.J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837.

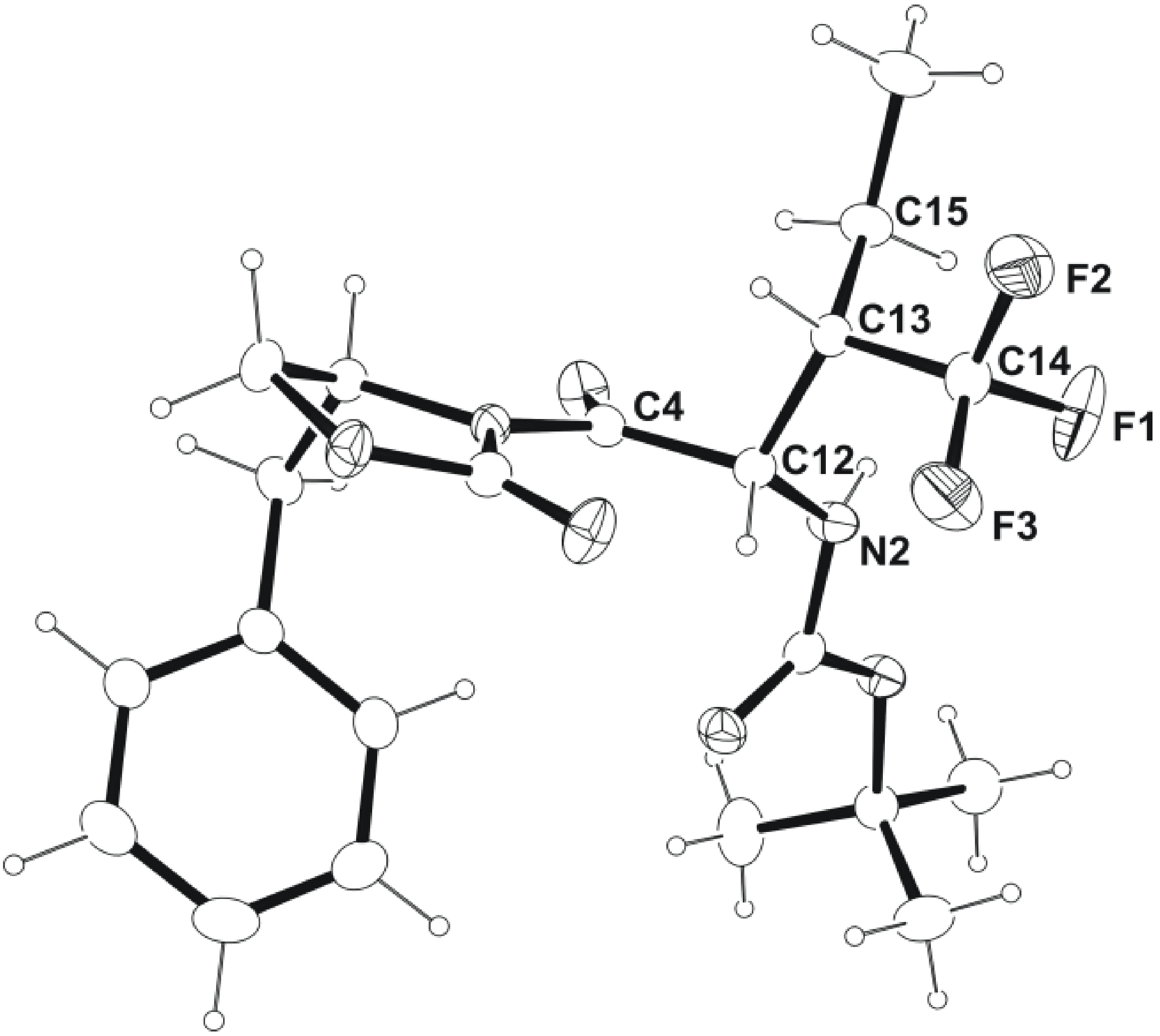
[3] ORTEP-3 for Windows: L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.



Molecular structure ORTEP[3] of compound **2a**



Molecular structure ORTEP[3] of compound **25a**



Molecular structure ORTEP[3] of compound **26a**