Organocatalytic Asymmetric Synthesis of α-Oxetanyl and α-Azetidinyl Tertiary Alkyl Fluorides and Chlorides

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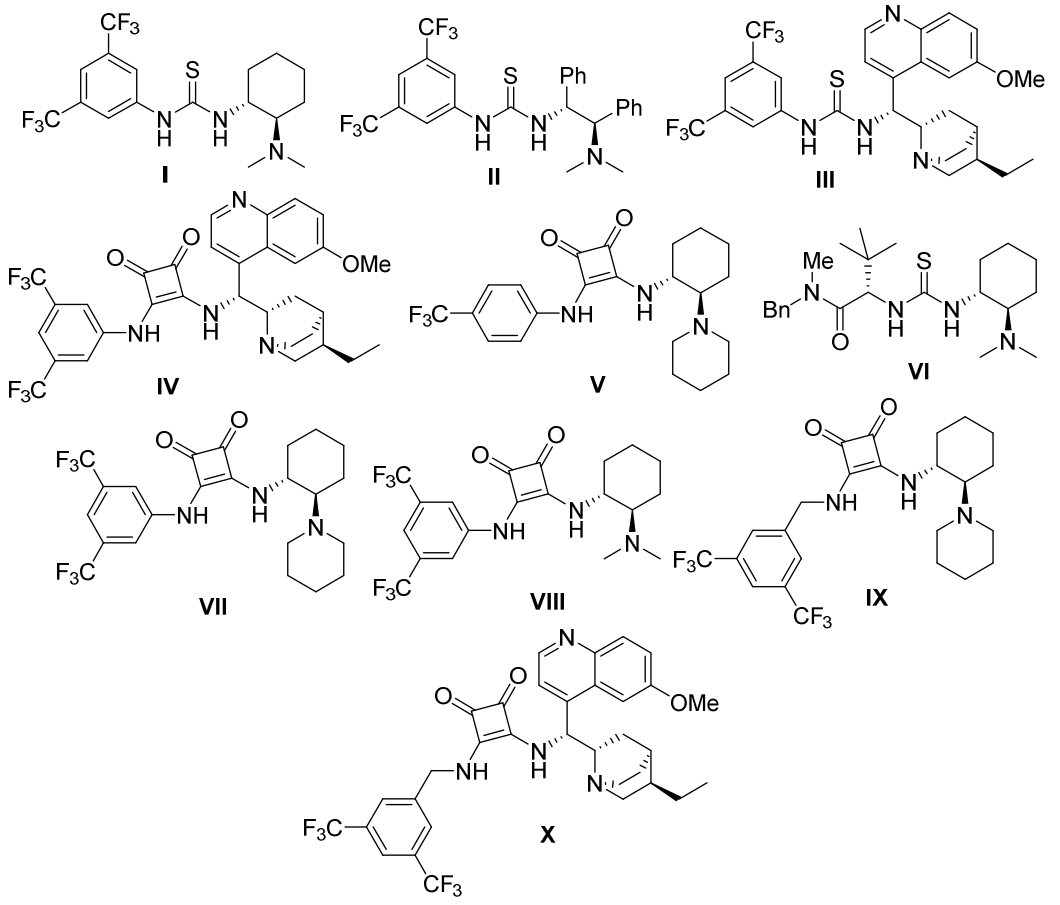
General Information

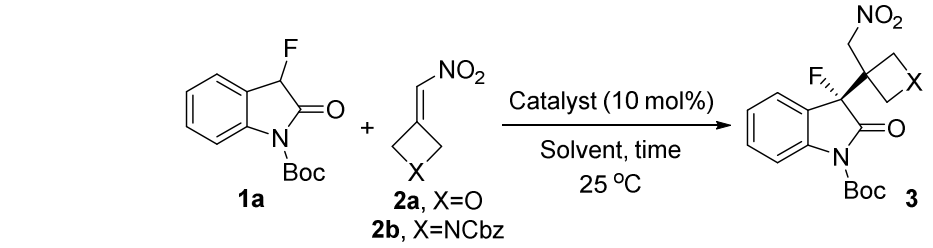
All commercially available reagents and solvents were used without further purification unless noted otherwise. Methyl *tert*-butyl ether and ethyl acetate were stored over 4Å molecular sieves prior to use. Reaction products were purified by column chromatography on silica gel (particle size 32-63 μm) unless stated otherwise. NMR spectra were obtained at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR), and 376 MHz (^{19}F NMR) in $CDCl_3$. Chemical shifts are reported in ppm relative to tetramethylsilane. *N*-Boc-3-chlorooxindole, [1] ethyl 2-fluoro-3-oxo-3-phenylpropanoate, [2] nitroalkene **2a**, **2c**, [3] and **2b**, [4] were synthesized following previously reported procedures. Catalysts **II**,[5] **IV**,[6] **VII**, **VIII**,[7] **IX**, **X**,[8] were prepared as described in the literature. Catalysts **I**, **III** and **V** are commercially available and were used without further purification.

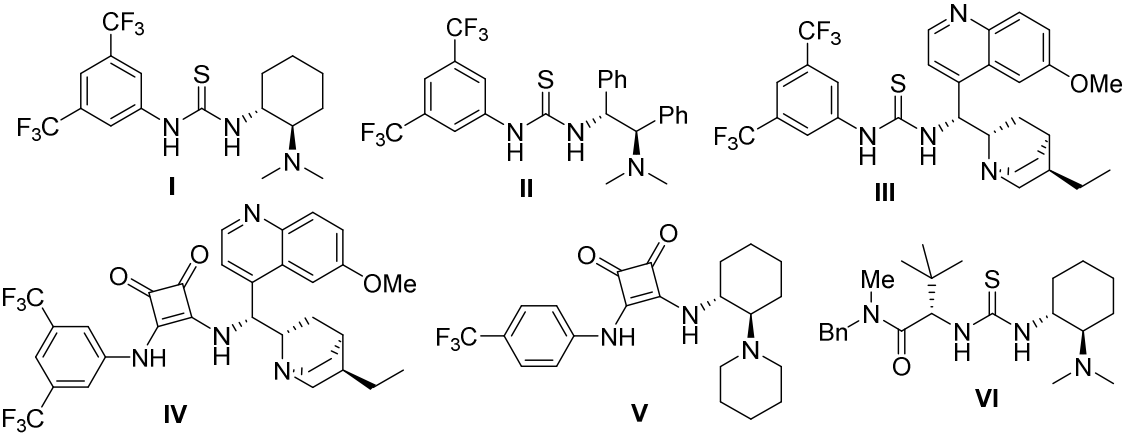
The reaction products were first prepared in racemic form to develop a chiral HPLC method for ee analysis. The isolated asymmetric reaction products were then analyzed accordingly.



1. Optimization Studies

Organocatalysis with *N*-Boc-3-fluorooxindole[a]

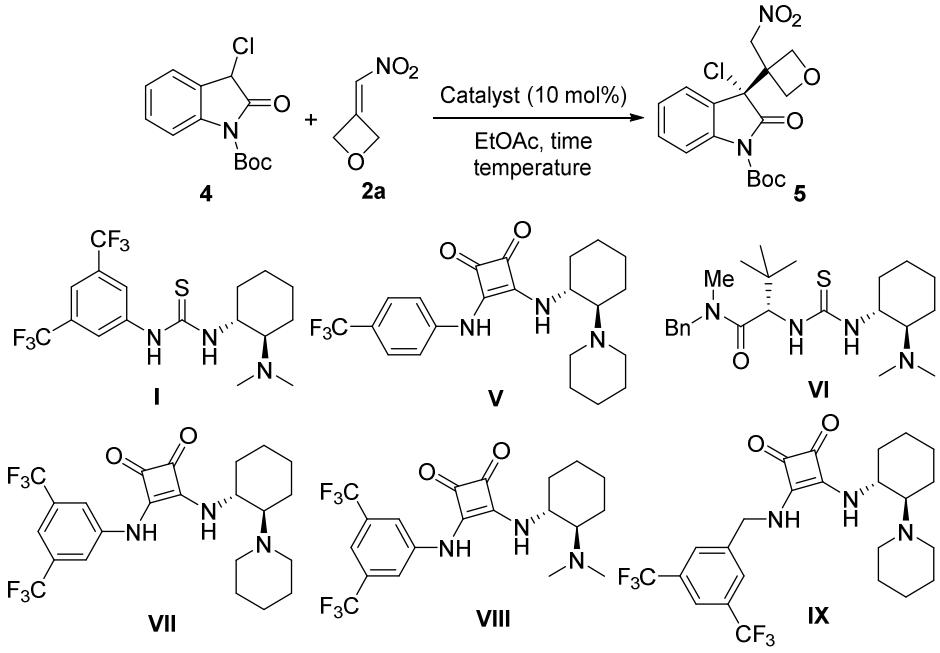




Entry	Catalyst	**2**	Time	Solvent	Conversion (%)[b]	ee (%)[c]
1	**I**	**2a**	18 h	MTBE	100	80
2	**II**	**2a**	18 h	MTBE	100	24
3	**III**	**2a**	18 h	MTBE	100	26
4	**IV**	**2a**	18 h	MTBE	100	65
5	**V**	**2a**	18 h	MTBE	73	91
6	**VI**	**2a**	7 h	MTBE	100	94
7	**VI**	**2b**	24 h	MTBE	64	93
8	**V**	**2b**	24 h	EtOAc	73	92
9[d]	**V**	**2b**	24 h	EtOAc	98	93

[a] Reaction conditions: Michael acceptor **2** (0.15 mmol), organocatalyst (10 mol%), **1a** (1.1 equiv.), solvent (0.45 mL) at 25 °C. [b] Determined by ^{1}H NMR. [c] Determined by chiral HPLC. [d] 1.4 equivalent of **1a** was used.

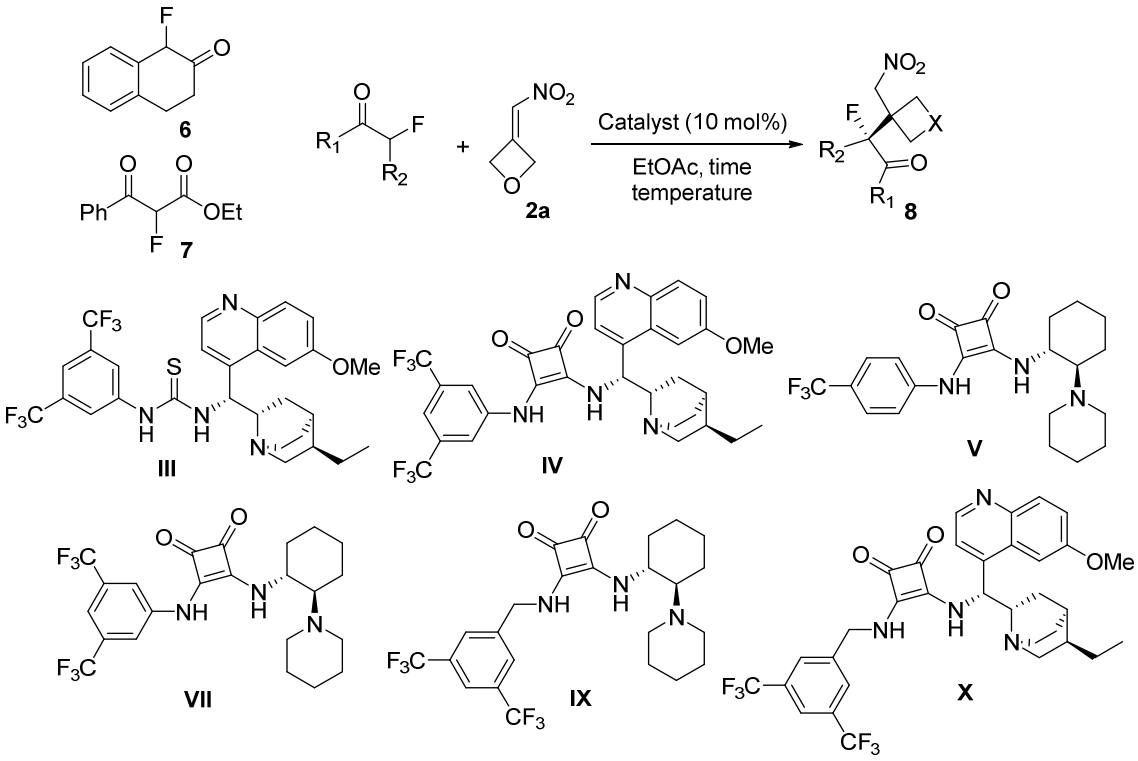
Organocatalysis with *N*-Boc-3-chlorooxindole[a]



Entry	Catalyst	Temperature	Time	Yield (%)[b]	ee (%)[c]
1	**I**	25 °C	18 h	81	53
2	**V**	25 °C	24 h	73	63
3	**VI**	25 °C	48 h	48	60
4	**V**	-10 °C	70 h	94	72
5	**VII**	-15 °C	48 h	52	63
6	**VIII**	-15 °C	48 h	45	63
7	**IX**	-15 °C	70 h	80	90

[a] Reaction conditions: Michael acceptor **2a** (0.15 mmol), organocatalyst (10 mol%), **4** (1.2 equiv.) in ethyl acetate (0.45 mL). [b] Isolated yield. [c] Determined by chiral HPLC.

Organocatalysis with other fluoroenolates[a]

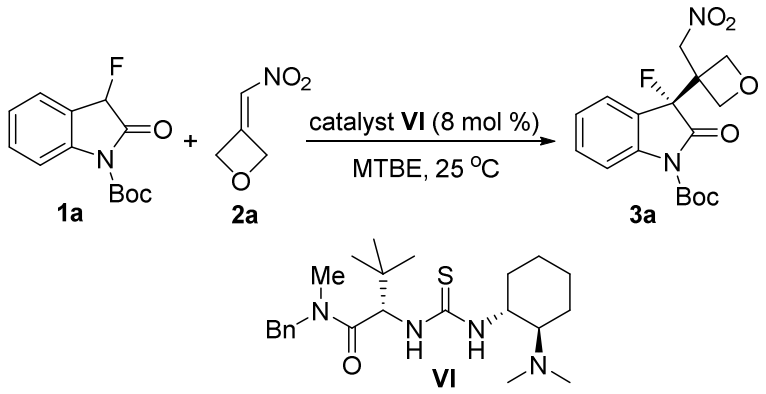


Entry	Nucleophile	Catalyst	Temperature	Time	Yield (%)[b]	ee (%)[c]
1	**6**	**V**	25 °C	48 h	63	82
2	**6**	**IX**	25 °C	48 h	58	83
3	**6**	**IX**	0 °C	110 h	84	87
4	**7**	**III**	25 °C	18 h	62	38
5	**7**	**IV**	-15 °C	70 h	28	-37
6	**7**	**V**	25 °C	18 h	24	-66
7	**7**	**VII**	25 °C	18 h	55	-22
8	**7**	**IX**	0 °C	70 h	98	78
9	**7**	**IX**	-15 °C	70 h	98	79
10	**7**	**X**	0 °C	65 h	58	60

[a] Reaction conditions: Michael acceptor **2a** (0.15 mmol), organocatalyst (10 mol%), nucleophile **6** or **7** (1.2 equiv.) in ethyl acetate (0.45 mL). [b] Isolated yield. [c] Determined by chiral HPLC. The "-"sign indicates a reversal of the sense of the asymmetric induction as seen by chiral HPLC.

Synthesis Procedures and Compound Characterization

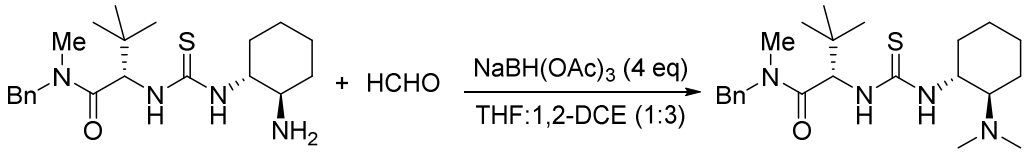
3.1. Representative example of the organocatalytic Michael addition (above 1 mmol scale)



First, *N*-Boc-3-fluorooxindole **1a** (773.9 mg, 3.08 mmol), nitroalkene **2a** (322.2 mg, 2.80 mmol) and catalyst **VI** (92.8 mg, 0.22 mmol) were placed into an oven-dried vial. Then, MTBE (1.25 mL) was added. The vial was then capped and stirred for 22 hours at room temperature. Upon completion, the solvent was evaporated by a gentle flow of nitrogen. The residue was purified by column chromatography (3.5:1 hexanes/ethyl acetate) to give **3a** (873 mg, 2.38 mmol) in 85% yield as a white solid. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 10.4 min, t_R(minor) = 11.5 min.

3.2. Synthesis of catalyst VI

Catalyst **VI** was synthesized following a literature procedure,[9] the last reductive methylation step was modified to improve the yield as described below.

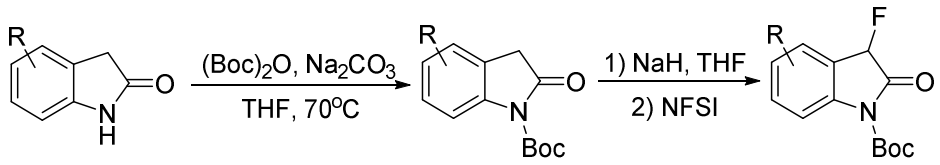


To a solution of (*S*)-2-(3-((1*R*,2*R*)-2-aminocyclohexyl)thioureido)-*N*-benzyl-*N*-3,3-trimethylbutanamide (396 mg, 1.01 mmol) in THF:1,2-dichloroethane (1:3, 40 mL) was added formaldehyde (37% aqueous solution, 185.5 mg, 2.32 mmol). The solution was stirred at room temperature for 15 minutes and then cooled to 0 °C. Sodium triacetoxyborohydride (856.3 mg, 4.04 mmol) was added in one portion. The reaction mixture was allowed to warm to room temperature and stirred for 18 hours. A saturated aqueous solution of sodium bicarbonate (10 mL) was added to quench the reaction. The mixture was poured onto brine (60 mL) and extracted with dichloromethane (15 mL, 3 times). The organic layers were

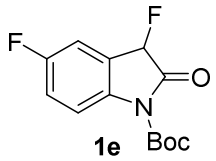
combined, dried over anhydrous Na_2SO_4, filtrated, and concentrated under reduced pressure. The residue was purified by flash chromatography using 4% – 12% MeOH/dichloromethane as mobile phase to give catalyst **VI** (356.9 mg, 0.85 mmol) in 84% yield as an off-white amorphous solid. This compound exists as a 4:1 mixture of rotamers. ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer) δ = 1.06 (s, 9H), 1.14 – 1.38 (m, 4H), 1.67 – 1.77 (m, 1H), 1.81 (d, *J* = 8.3 Hz, 1H), 1.84 – 1.91 (m, 1H), 2.28 (s, 6H), 2.37 – 2.56 (m, 2H), 3.17 (s, 3H), 3.44 – 3.68 (m, 1H), 4.39 (d, *J* = 14.6 Hz, 1H), 4.79 (d, *J* = 14.6 Hz, 1H), 5.55 (d, *J* = 9.2 Hz, 1H), 6.88 (br, 1H), 7.08 (br, 1H), 7.27 – 7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$, major rotamer) δ = 22.1, 24.7, 25.1, 27.0, 33.2, 36.2, 36.3, 40.2, 51.4, 54.5, 55.6, 60.6, 66.9, 127.5, 128.3, 128.7, 137.1, 172.4, 182.9. Anal. Calcd. for $C_{23}H_{38}N_4OS$: C, 65.99; H, 9.15; N, 13.38. Found: C, 65.87; H, 9.17; N, 13.36.

3.3. Synthesis of *N*-Boc-3-fluorooxindoles

N-Boc-3-fluorooxindoles **1a** – **1j** were prepared via a two-step synthesis from 2-oxindoles following a literature procedure.[10] Compounds **1e**, **1g**, **1h**, **1i** are new and fully characterized.



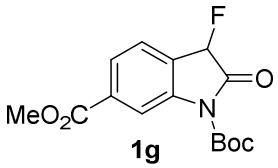
N-Boc-3,5-difluorooxindole (**1e**)



1e

Compound **1e** was synthesized from 5-fluoro-2-oxindole in 44% overall yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.63 (s, 9H), 5.69 (d, *J* = 50.8 Hz, 1H), 7.15 (ddd, *J* = 9.0, 8.3, 2.8 Hz, 1H), 7.22 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.89 (dd, *J* = 9.1, 4.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 84.8 (dd, $J_{C\text{-}F}$ = 191.0, 1.7 Hz), 85.4, 113.5 (dd, $J_{C\text{-}F}$ = 24.8, 1.1 Hz), 117.3 (dd, $J_{C\text{-}F}$ = 7.6, 1.5 Hz), 118.5 (dd, $J_{C\text{-}F}$ = 22.9, 3.2 Hz), 123.4 (dd, $J_{C\text{-}F}$ = 16.5, 8.3 Hz), 137.0 (dd, $J_{C\text{-}F}$ = 5.0, 2.8 Hz), 148.7, 160.1 (dd, $J_{C\text{-}F}$ = 245.7, 3.3 Hz), 168.5 (d, $J_{C\text{-}F}$ = 17.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -188.3 (d, *J* = 50.9 Hz, 1F), -116.6 (m, 1F). Anal. Calcd. for $C_{13}H_{13}F_2NO_3$: C, 57.99; H, 4.87; N, 5.20. Found: C, 57.88; H, 5.21; N, 5.60.

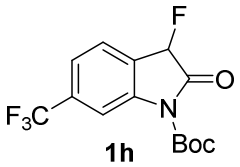
Methyl *N*-Boc-3-fluorooxindole-6-carboxylate (**1g**)



1g

Compound **1g** was synthesized from methyl 2-oxindole-6-carboxylate in 38% overall yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.66 (s, 9H), 3.95 (s, 3H), 5.75 (d, J = 50.5 Hz, 1H), 7.58 (dd, J = 7.8, 1.7 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 8.53 (d, J = 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 52.7, 84.7 (d, $J_{C\text{-}F}$ = 191.1 Hz), 85.7, 116.7 (d, $J_{C\text{-}F}$ = 1.3 Hz), 126.0, 126.1 (d, $J_{C\text{-}F}$ = 16.2 Hz), 126.6 (d, $J_{C\text{-}F}$ = 2.7 Hz), 133.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 141.1 (d, $J_{C\text{-}F}$ = 4.8 Hz), 148.4, 166.1 (d, $J_{C\text{-}F}$ = 1.3 Hz), 168.6 (d, $J_{C\text{-}F}$ = 17.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -189.8 (d, J = 50.5 Hz, 1F). Anal. Calcd. for $C_{15}H_{16}FNO_5$: C, 58.25; H, 5.21; N, 4.53. Found: C, 58.60; H, 5.48; N, 4.33.

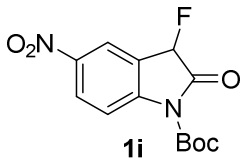
N-Boc-3-fluoro-6-trifluoromethyl-2-oxoindole (**1h**)



1h

Compound **1h** was synthesized from 6-trifluoromethyl-2-oxindole in 44% overall yield as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.65 (s, 9H), 5.76 (d, J = 50.6 Hz, 1H), 7.53 (dd, J = 8.2, 1.7 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 84.5 (d, $J_{C\text{-}F}$ = 191.5 Hz), 86.0, 113.2 (qd, $J_{C\text{-}F}$ = 3.9, 1.0 Hz), 122.2 (qd, $J_{C\text{-}F}$ = 3.7, 3.4 Hz), 124.9 (d, $J_{C\text{-}F}$ = 1.2 Hz), 125.3 (dq, $J_{C\text{-}F}$ = 16.3, 1.3 Hz), 126.4, 134.0 (qd, $J_{C\text{-}F}$ = 32.7, 3.1 Hz), 141.5 (d, $J_{C\text{-}F}$ = 4.8 Hz), 148.5, 168.2 (d, $J_{C\text{-}F}$ = 17.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -189.9 (d, J = 50.6 Hz, 1F), -63.0 (s, 3F). Anal. Calcd. for $C_{14}H_{13}F_4NO_3$: C, 52.67; H, 4.10; N, 4.39. Found: C, 52.48; H, 3.76; N, 4.54.

N-Boc-3-fluoro-5-nitro-2-oxoindole (**1i**)

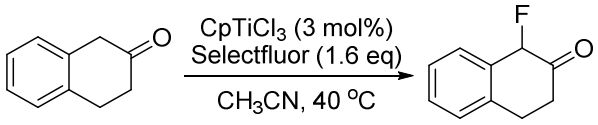


1i

Compound **1i** was synthesized from 5-nitro-2-oxindole in 34% overall yield as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.65 (s, 9H), 5.79 (d, J = 50.7 Hz, 1H), 8.11 (d, J = 8.6, 1.3 Hz, 1H), 8.34 – 8.41 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 84.0 (d, $J_{C\text{-}F}$ = 192.9 Hz), 86.6, 116.2 (d, $J_{C\text{-}F}$ = 1.2 Hz), 121.8, 122.8 (d, $J_{C\text{-}F}$ = 16.7 Hz), 127.9 (d, $J_{C\text{-}F}$ = 2.7 Hz),

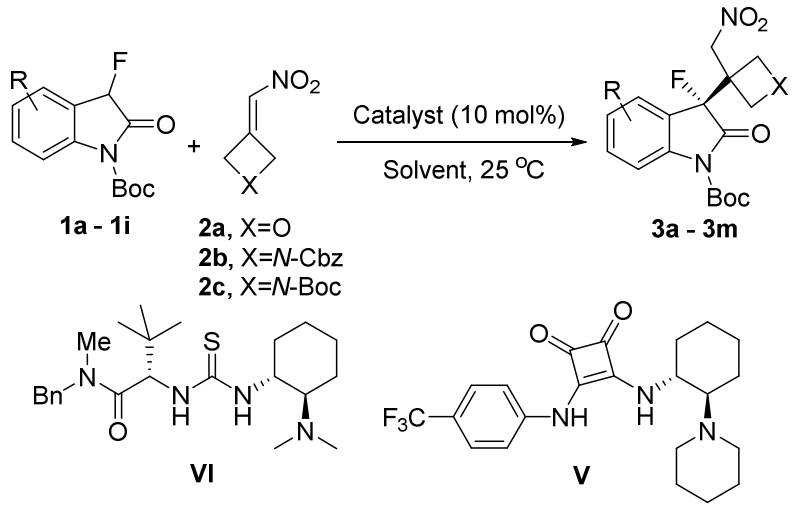
145.0 (d, $J_{C\text{-}F}$ = 3.0 Hz), 146.0 (d, $J_{C\text{-}F}$ = 4.3 Hz), 148.3, 167.8 (d, $J_{C\text{-}F}$ = 17.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -189.4 (d, *J* = 50.6 Hz, 1F). Anal. Calcd. for $C_{13}H_{13}FN_2O_5$: C, 52.71; H, 4.42; N, 9.46. Found: C, 53.04; H, 4.79; N, 9.25.

3.4. Synthesis of 1-fluoro-2-tetralone



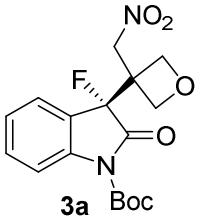
To a solution of β-tetralone (219.3 mg, 1.50 mmol) and selectfluor (850.2 mg, 2.40 mmol) in anhydrous acetonitrile (10 mL) was added cyclopentadienyltitanium(IV) trichloride (9.8 mg, 0.05 mmol). The reaction mixture was heated to 40 °C and stirred for 18 hours. Upon completion, the mixture was pour onto brine (40 mL) and extracted with ethyl acetate (8 mL, 3 times). The organic layers were combined, dried over anhydrous $MgSO_4$, filtrated, and concentrated under reduced pressure. The residue was purified by flash chromatography system using 1 – 8% ethyl acetate-hexanes to afford 1-fluoro-2-tetralone (135.6 mg, 0.83 mmol) in 55% yield as an amber oil. This compound slowly decomposes at room temperature and should be stored under -20 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.58 (m, 1H), 2.76 (m, 1H), 3.11 – 3.17 (m, 2H), 5.83 (d, *J* = 49.0 Hz, 1H), 7.25 (dd, *J* = 5.9, 2.4 Hz, 1H), 7.31 – 7.38 (m, 2H), 7.50 (dd, *J* = 6.2, 3.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.1, 34.6, 90.8 (d, *J* = 190.5 Hz), 125.1 (d, *J* = 8.0 Hz), 127.3, 127.4, 128.8 (d, *J* = 1.8 Hz), 132.4 (d, *J* = 18.4 Hz), 135.5 (d, *J* = 5.1 Hz), 203.7 (d, *J* = 13.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -197.4 (d, *J* = 49.0 Hz). Anal. Calcd. for $C_{10}H_9FO$: C, 73.16; H, 5.53; N, 0. Found: C, 73.36; H, 5.40; N, 0.14.

3.5. General procedure for the organocatalysis with *N*-Boc-3-fluorooxindoles



First, *N*-Boc-3-fluorooxindole **1** (0.165 mmol for nitroalkene **2a**, 0.210 mmol for nitroalkene **2b** or **2c**), nitroalkene (0.150 mmol) and organocatalyst (0.015 mmol, cat. **VI** for nitroalkene **2a**, cat. **V** for nitroalkene **2b** or **2c**) were placed into an oven-dried vial. Then, the solvent (0.45 mL, MTBE for nitroalkene **2a**, ethyl acetate for nitroalkene **2b** or **2c**) was added. The vial was then capped and stirred for 6 hours (nitroalkene **2a**) or 24 hours (nitroalkene **2b** or **2c**). Upon completion, the solvent was evaporated by a gentle flow of nitrogen and the residue was purified by column chromatography as described below. Racemic reaction products for HPLC analysis were obtained by applying racemic catalyst **I** in the above procedure.

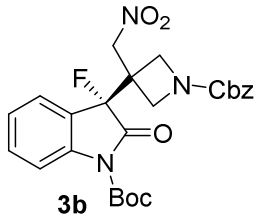
N-Boc-(*R*)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3a**)



Compound **3a** was obtained from *N*-Boc-3-fluorooxindole **1a** (41.5 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 49.7 mg (0.136 mmol, 90%) of a white solid. Mp 82.5-84.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ =1.63 (s, 9H), 4.63 (dd, *J* = 7.4, 3.0 Hz, 1H), 4.70 (s, 2H), 4.84 (dd, *J* = 6.7, 3.5 Hz, 1H), 5.31 (dd, *J* = 6.8, 1.7 Hz, 1H), 5.57 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.18 – 7.25 (m, 2H), 7.46 – 7.55 (m, 1H), 7.95 (dd, *J* = 8.3, 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.2 (d, $J_{C\text{-}F}$ = 30.0 Hz), 73.2 (d, $J_{C\text{-}F}$ = 4.6 Hz), 73.8 (d, $J_{C\text{-}F}$ = 4.2 Hz), 76.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 85.8, 90.5 (d, $J_{C\text{-}F}$ = 191.0 Hz), 116.4 (d, $J_{C\text{-}F}$ = 1.6 Hz), 121.0 (d, $J_{C\text{-}F}$ = 19.2 Hz), 124.9 (d, $J_{C\text{-}F}$ = 1.3 Hz), 125.5

(d, $J_{C\text{-}F}$ = 2.9 Hz), 133.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 141.3 (d, $J_{C\text{-}F}$ = 5.4 Hz), 148.3, 168.7 (d, $J_{C\text{-}F}$ = 21.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -150.6. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 9.1 min, t_R(minor) = 19.0 min. Anal. Calcd. for $C_{17}H_{19}FN_2O_6$: C, 55.74; H, 5.23; N, 7.65. Found: C, 55.65; H, 5.50; N, 7.57.

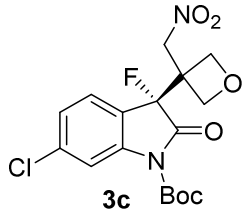
N-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3b**)



3b

Compound **3b** was obtained from *N*-Boc-3-fluorooxindole **1a** (52.8 mg, 0.210 mmol) and nitroalkene **2b** (37.3 mg, 0.150 mmol) using catalyst **V** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 69.0 mg (0.138 mmol, 93%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.63 (s, 9H), 4.08 (d, *J* = 9.7 Hz, 1H), 4.27 (d, *J* = 6.4 Hz, 1H), 4.46 – 4.61 (m, 2H), 4.64 (d, *J* = 9.0 Hz, 1H), 4.97 (d, *J* = 9.8 Hz, 1H), 5.12 (s, 2H), 7.21 (ddd, *J* = 7.6, 7.5, 1.4 Hz, 1H), 7.28 (dd, *J* = 7.8, 1.9 Hz, 1H), 7.31 – 7.41 (m, 5H), 7.51 (ddd, *J* = 7.9, 7.9 1.7 Hz, 1H), 7.95 (dd, *J* = 8.1, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 42.8 (d, $J_{C\text{-}F}$ = 30.2 Hz), 52.6, 52.8, 67.4, 76.5, 85.9, 90.5 (d, $J_{C\text{-}F}$ = 192.0 Hz), 116.5, 120.9 (d, $J_{C\text{-}F}$ = 19.0 Hz), 124.8, 125.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 128.2, 128.4, 128.7, 133.2 (d, $J_{C\text{-}F}$ = 3.2 Hz), 136.2, 141.3 (d, $J_{C\text{-}F}$ = 5.5 Hz), 148.3, 156.4, 168.5 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -152.8, -152.1. The ee was determined as 92% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 17.4 min, t_R(minor) =27.2 min. Anal. Calcd. for $C_{25}H_{26}FN_3O_7$: C, 60.12; H, 5.25; N, 8.41. Found: C, 59.91; H, 5.35; N, 8.66.

N-Boc-(*R*)-6-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3c**)

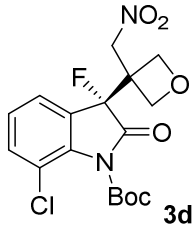


3c

Compound **3c** was obtained from *N*-Boc-3-fluoro-6-chloro-2-oxoindole **1c** (47.1 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 56.5 mg (0.141 mmol, 94%) of a white solid. Mp 130.8-131.7 °C. ^{1}H NMR (400 MHz,

$CDCl_3$) δ = 1.63 (s, 9H), 4.61 (dd, *J* = 7.4, 3.0 Hz, 1H), 4.74 (s, 2H), 4.82 (dd, *J* = 6.7, 3.5 Hz, 1H), 5.24 (dd, *J* = 6.8, 1.4 Hz, 1H), 5.53 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.15 (dd, *J* = 8.1, 2.2 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 8.04 (d, *J* = 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.0 (d, $J_{C\text{-}F}$ = 30.0 Hz), 73.1 (d, $J_{C\text{-}F}$ = 4.6 Hz), 73.8 (d, $J_{C\text{-}F}$ = 4.3 Hz), 76.7 (d, $J_{C\text{-}F}$ = 4.3 Hz), 86.4 (d, $J_{C\text{-}F}$ = 2.1 Hz), 90.2 (d, $J_{C\text{-}F}$ = 191.1 Hz), 117.3 (d, $J_{C\text{-}F}$ = 1.6 Hz), 119.3 (d, $J_{C\text{-}F}$ = 19.3 Hz), 125.7 (d, $J_{C\text{-}F}$ = 3.0 Hz), 125.8 (d, $J_{C\text{-}F}$ = 1.3 Hz), 139.3 (d, $J_{C\text{-}F}$ = 3.9 Hz), 142.3 (d, $J_{C\text{-}F}$ = 5.4 Hz), 148.1, 168.3 (d, $J_{C\text{-}F}$ = 22.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -149.8. The ee was determined as 90% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 9.5 min, t_R(minor) = 22.6 min. Anal. Calcd. for $C_{17}H_{18}ClFN_2O_6$: C, 50.95; H, 4.53; N, 6.99. Found: C, 50.93; H, 4.55; N, 6.86.

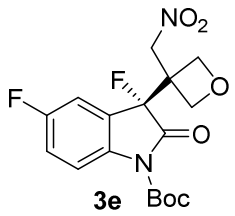
N-Boc-(*R*)-7-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3d**)



3d

Compound **3d** was obtained from *N*-Boc-3-fluoro-7-chloro-2-oxoindole **1d** (47.4 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 53.6 mg (0.134 mmol, 89%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.63 (s, 9H), 4.60 (dd, *J* = 7.5, 3.0 Hz, 1H), 4.68 (d, *J* = 13.1 Hz, 1H), 4.79 (d, *J* = 13.0 Hz, 1H), 4.87 (dd, *J* = 6.8, 3.5 Hz, 1H), 5.22 (dd, *J* = 6.5, 1.3 Hz, 1H), 5.50 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.15 – 7.21 (m, 2H), 7.49 (dd, *J* = 5.8, 3.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.8, 48.0 (d, $J_{C\text{-}F}$ = 29.4 Hz), 72.9 (d, $J_{C\text{-}F}$ = 4.8 Hz), 73.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 76.3 (d, $J_{C\text{-}F}$ = 4.4 Hz), 86.9, 91.1 (d, $J_{C\text{-}F}$ = 194.3 Hz), 120.4 (d, $J_{C\text{-}F}$ = 1.4 Hz), 123.6 (d, $J_{C\text{-}F}$ = 1.3 Hz), 124.3 (d, $J_{C\text{-}F}$ = 19.7 Hz), 126.3 (d, $J_{C\text{-}F}$ = 2.8 Hz), 134.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 138.4 (d, $J_{C\text{-}F}$ = 5.7 Hz), 146.6, 169.1 (d, $J_{C\text{-}F}$ = 22.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -153.6. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 10.9 min, t_R(minor) = 31.8 min. Anal. Calcd. for $C_{17}H_{18}ClFN_2O_6$: C, 50.95; H, 4.53; N, 6.99. Found: C, 50.87; H, 4.91; N, 6.83.

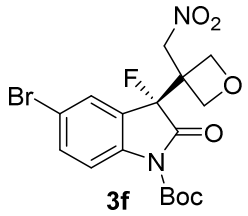
N-Boc-(*R*)-3,5-difluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3e**)



3e

Compound **3e** was obtained from *N*-Boc-3,5-difluorooxindole **1e** (44.4 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 52.4 mg (0.136 mmol, 91%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.63 (s, 9H), 4.62 (dd, *J* = 7.5, 3.1 Hz, 1H), 4.74 (s, 2H), 4.83 (dd, *J* = 6.7, 3.6 Hz, 1H), 5.24 (dd, *J* = 6.8, 1.4 Hz, 1H), 5.54 (dd, *J* = 7.5, 1.9 Hz, 1H), 6.95 (dd, *J* = 7.1, 2.6, 2.4 Hz, 1H), 7.22 (m, 1H), 7.97 (ddd, *J* = 9.1, 4.5, 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.0 (d, $J_{C\text{-}F}$ = 29.7 Hz), 73.0 (d, $J_{C\text{-}F}$ = 4.6 Hz), 73.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 76.6 (d, $J_{C\text{-}F}$ = 4.5 Hz), 86.1, 90.3 (dd, $J_{C\text{-}F}$ = 192.0, 1.6 Hz), 112.4 (d, $J_{C\text{-}F}$ = 25.0 Hz), 118.1 (dd, $J_{C\text{-}F}$ = 7.7, 1.5 Hz), 119.9 (dd, $J_{C\text{-}F}$ = 22.7, 3.2 Hz), 122.4 (dd, $J_{C\text{-}F}$ = 18.9, 7.8 Hz), 137.3 (dd, $J_{C\text{-}F}$ = 5.5, 2.8 Hz), 148.3, 160.0 (dd, $J_{C\text{-}F}$ = 247.4, 3.4 Hz), 168.3 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.4 (s, 1F), -115.2 (m, 1F). The ee was determined as 95% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 9.4 min, t_R(minor) = 38.4 min. Anal. Calcd. for $C_{17}H_{18}F_2N_2O_6$: C, 53.13; H, 4.72; N, 7.29. Found: C, 52.97; H, 5.08; N, 7.20.

N-Boc-(*R*)-5-bromo-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3f**)

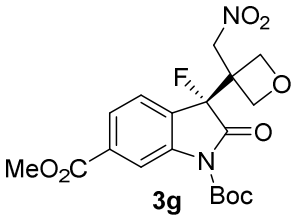


3f

Compound **3f** was obtained from *N*-Boc-3-fluoro-5-bromo-2-oxoindole **1f** (54.5 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 61.7 mg (0.139 mmol, 92%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.62 (s, 9H), 4.64 (dd, *J* = 7.5, 3.0 Hz, 1H), 4.71 (d, *J* = 12.9 Hz, 1H), 4.74 – 4.82 (m, 2H), 5.25 (dd, *J* = 6.7, 1.3 Hz, 1H), 5.54 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.32 (d, *J* = 2.1 Hz, 1H), 7.63 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.0 (d, $J_{C\text{-}F}$ = 29.8 Hz), 73.1 (d, $J_{C\text{-}F}$ = 4.8 Hz), 73.6 (d, $J_{C\text{-}F}$ = 4.2 Hz), 76.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 86.2, 90.2 (d, $J_{C\text{-}F}$ = 191.9 Hz), 118.1 (d, $J_{C\text{-}F}$ = 1.5 Hz), 118.4 (d, $J_{C\text{-}F}$ = 3.5 Hz), 122.9 (d, $J_{C\text{-}F}$ = 19.0 Hz), 127.8, 136.0 (d, $J_{C\text{-}F}$ = 3.2 Hz), 140.3 (d, $J_{C\text{-}F}$ = 5.3 Hz), 148.1, 167.9 (d, $J_{C\text{-}F}$

= 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.1. The ee was determined as 95% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 9.8 min, t_R(minor) = 33.7 min. Anal. Calcd. for $C_{17}H_{18}BrFN_2O_6$: C, 45.86; H, 4.08; N, 6.29. Found: C, 46.03; H, 4.07; N, 6.20.

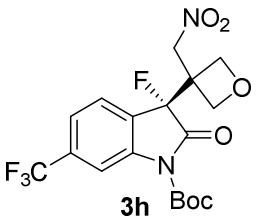
Methyl *N*-Boc-(*R*)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole-6-carboxylate (**3g**)



3g

Compound **3g** was obtained from methyl *N*-Boc-3-fluorooxindole-6-carboxylate **1g** (51.1 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 54.2 mg (0.128 mmol, 92%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.65 (s, 9H), 3.95 (s, 3H), 4.62 (dd, *J* = 7.5, 3.1 Hz, 1H), 4.74 (s, 2H), 4.84 (dd, *J* = 6.8, 3.6 Hz, 1H), 5.27 (dd, *J* = 6.8, 1.4 Hz, 1H), 5.56 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.31 (dd, *J* = 7.9, 2.2 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 8.59 (d, *J* = 1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.0 (d, $J_{C\text{-}F}$ = 29.6 Hz), 52.8, 73.1 (d, $J_{C\text{-}F}$ = 4.6 Hz), 73.8 (d, $J_{C\text{-}F}$ = 4.4 Hz), 76.6 (d, $J_{C\text{-}F}$ = 4.4 Hz), 86.4, 90.2 (d, $J_{C\text{-}F}$ = 191.5 Hz), 117.3 (d, $J_{C\text{-}F}$ = 1.4 Hz), 124.9 (d, $J_{C\text{-}F}$ = 1.3 Hz), 125.2 (d, $J_{C\text{-}F}$ = 18.6 Hz), 126.9 (d, $J_{C\text{-}F}$ = 2.8 Hz), 134.7 (d, $J_{C\text{-}F}$ = 3.1 Hz), 141.5 (d, $J_{C\text{-}F}$ = 5.3 Hz), 148.0, 165.7 (d, $J_{C\text{-}F}$ = 1.5 Hz), 168.3 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -152.0. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 14.7 min, t_R(minor) = 23.6 min. Anal. Calcd. for $C_{19}H_{21}FN_2O_8$: C, 53.77; H, 4.99; N, 6.60. Found: C, 54.34; H, 5.19; N, 6.42.

N-Boc-(*R*)-6-trifluoromethyl-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3h**)



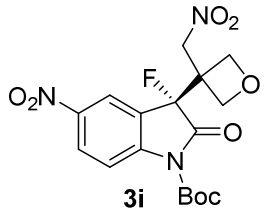
3h

Compound **3h** was obtained from *N*-Boc-3-fluoro-6-trifluoromethyl-2-oxoindole **1h** (52.7 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015

mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 63.4 mg (0.146 mmol, 97%) of a white amorphous solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.64 (s, 9H), 4.64 (dd, *J* = 7.5, 3.0 Hz, 1H), 4.77 (dd, *J* = 16.0, 13.4 Hz, 2H), 4.82 (dd, *J* = 6.9, 3.7 Hz, 1H), 5.23 (dd, *J* = 6.8, 1.8 Hz, 1H), 5.54 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.38 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 8.28 (d, *J* = 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.0 (d, $J_{C\text{-}F}$ = 29.5 Hz), 73.1 (d, $J_{C\text{-}F}$ = 4.8 Hz), 73.7 (d, $J_{C\text{-}F}$ = 4.7 Hz), 76.6 (d, $J_{C\text{-}F}$ = 4.3 Hz), 86.7, 90.1 (d, $J_{C\text{-}F}$ = 191.6 Hz), 113.8 (qd, $J_{C\text{-}F}$ = 3.8, 1.2 Hz), 122.4 (qd, $J_{C\text{-}F}$ = 3.9, 3.3 Hz), 123.2 (qd, $J_{C\text{-}F}$ = 255.2, 1.1 Hz) 125.4 (d, $J_{C\text{-}F}$ = 1.0 Hz), 125.6 (qd, $J_{C\text{-}F}$ = 178.1, 1.0 Hz), 135.1 (qd, $J_{C\text{-}F}$ = 33.0, 3.1 Hz), 141.9 (d, $J_{C\text{-}F}$ = 5.3 Hz), 148.0, 168.0 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -152.1 (s, 1F), -63.2 (s, 3F). The ee was determined as 96% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 7.2 min, t_R(minor) = 10.1 min. Anal. Calcd. for $C_{18}H_{18}F_4N_2O_6$: C, 49.78; H, 4.18; N, 6.45. Found: C, 49.83; H, 4.26; N, 6.37.

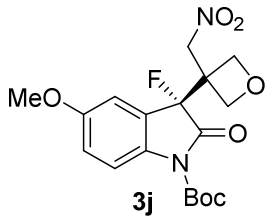
N-Boc-(*R*)-5-nitro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3i**)



3i

Compound **3i** was obtained from *N*-Boc-3-fluoro-5-nitro-2-oxoindole **1i** (48.9 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 53.1 mg (0.129 mmol, 86%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.64 (s, 9H), 4.63 (dd, *J* = 7.5, 3.1 Hz, 1H), 4.79 (d, *J* = 13.2 Hz, 1H), 4.83 – 4.89 (m, 2H), 5.26 (dd, *J* = 6.9, 1.4 Hz, 1H), 5.55 (dd, *J* = 7.5, 1.9 Hz, 1H), 8.09 (dd, *J* = 2.3, 2.3 Hz, 1H), 8.18 (dd, *J* = 9.1, 1.2 Hz, 1H), 8.43 (ddd, *J* = 9.1, 2.3, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 47.9 (d, $J_{C\text{-}F}$ = 29.6 Hz), 73.1 (d, $J_{C\text{-}F}$ = 4.8 Hz), 73.7 (d, $J_{C\text{-}F}$ = 4.6 Hz), 76.7 (d, $J_{C\text{-}F}$ = 4.3 Hz), 87.2, 89.8 (d, $J_{C\text{-}F}$ = 192.2 Hz), 116.8 (d, $J_{C\text{-}F}$ = 1.3 Hz), 120.6, 122.1 (d, $J_{C\text{-}F}$ = 19.3 Hz), 128.9 (d, $J_{C\text{-}F}$ = 2.7 Hz), 145.0 (d, $J_{C\text{-}F}$ = 3.0 Hz), 146.4 (d, $J_{C\text{-}F}$ = 4.8 Hz), 147.8, 167.8 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.3. The ee was determined as 93% using CHIRALPAK IA, hexanes/isopropanol 90:10, flow rate = 1mL/min condition. t_R(major) = 14.8 min, t_R(minor) = 17.4 min. Anal. Calcd. for $C_{17}H_{18}FN_3O_8$: C, 49.64; H, 4.41; N, 10.22. Found: C, 49.63; H, 4.48; N, 10.32.

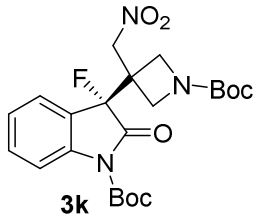
N-Boc-(*R*)-5-methoxy-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3j**)



3j

Compound **3j** was obtained from *N*-Boc-3-fluoro-5-methoxy-2-oxoindole **1j** (46.4 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **VI** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 55.3 mg (0.139 mmol, 93%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.63 (s, 9H), 3.81 (s, 3H), 4.63 (dd, *J* = 7.4, 3.0 Hz, 1H), 4.67 (d, *J* = 13.2 Hz, 1H), 4.71 (d, *J* = 13.3 Hz, 1H), 4.83 (dd, *J* = 6.7, 3.5 Hz, 1H), 5.31 (dd, *J* = 6.2, 1.1 Hz, 1H), 5.57 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.73 (dd, *J* = 2.2, 1.0 Hz, 1H), 7.01 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.87 (dd, *J* = 9.1, 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 48.2 (d, $J_{C\text{-}F}$ = 29.9 Hz), 56.0, 73.1 (d, $J_{C\text{-}F}$ = 4.7 Hz), 73.7 (d, $J_{C\text{-}F}$ = 4.0 Hz), 76.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 85.6, 90.6 (d, $J_{C\text{-}F}$ = 191.7 Hz), 111.2, 117.5, 117.5, 122.0 (d, $J_{C\text{-}F}$ = 18.7 Hz), 134.3 (d, $J_{C\text{-}F}$ = 5.4 Hz), 148.4, 157.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 168.7 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.3. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 12.0 min, t_R(minor) = 22.9 min. Anal. Calcd. for $C_{18}H_{21}FN_2O_7$: C, 54.54; H, 5.34; N, 7.07. Found: C, 54.06; H, 5.62; N, 6.80.

N-Boc-(*S*)-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3k**)

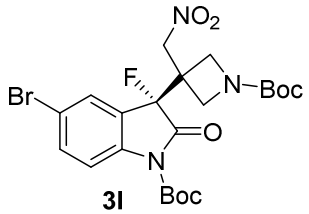


3k

Compound **3k** was obtained from *N*-Boc-3-fluorooxindole **1a** (52.8 mg, 0.210 mmol) and nitroalkene **2c** (32.2 mg, 0.150 mmol) using catalyst **V** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 67.8 mg (0.146 mmol, 97%) of a white solid, Mp 69.2-70.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.46 (s, 9H), 1.63 (s, 9H), 3.99 (d, *J* = 9.7 Hz, 1H), 4.15 (d, *J* = 14.1 Hz, 1H), 4.43 – 4.63 (m, 3H), 4.87 (d, *J* = 9.4 Hz, 1H), 7.23 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1H), 7.30 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.51 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1H), 7.96 (dd, *J* = 8.3, 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 28.4, 42.4 (d, $J_{C\text{-}F}$ = 30.3 Hz), 52.3, 52.7, 77.34 (d, $J_{C\text{-}F}$ = 5.3 Hz), 80.7, 85.8, 90.5 (d, $J_{C\text{-}F}$ = 191.2 Hz), 116.4 (d, $J_{C\text{-}F}$ = 1.5 Hz), 121.0 (d, $J_{C\text{-}F}$ = 19.0 Hz), 124.8, 125.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 133.1 (d, $J_{C\text{-}F}$ = 3.2 Hz), 141.3 (d, $J_{C\text{-}F}$ = 5.5 Hz), 148.3, 156.2, 168.6 (d, $J_{C\text{-}F}$ = 22.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.9, -152.8. The ee was determined as 93%

using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 6.9 min, t_R(minor) = 8.8 min. Anal. Calcd. for $C_{22}H_{28}FN_3O_7$: C, 56.77; H, 6.06; N, 9.03. Found: C, 56.44; H, 6.36; N, 9.04.

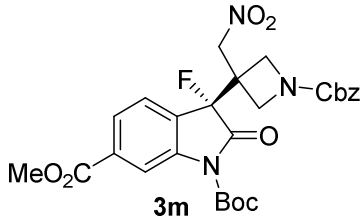
N-Boc-(*S*)-5-bromo-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3l**)



3l

Compound **3l** was obtained from *N*-Boc-3-fluoro-5-bromo-2-oxoindole **1f** (69.3 mg, 0.210 mmol) and nitroalkene **2c** (32.2 mg, 0.150 mmol) using catalyst **V** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (5:1 hexanes/ethyl acetate) gave 75.8 mg (0.139 mmol, 93%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.47 (s, 9H), 1.62 (s, 9H), 3.99 (d, *J* = 10.0 Hz, 1H), 4.12 (d, *J* = 9.0 Hz, 1H), 4.47 – 4.58 (m, 2H), 4.63 (d, *J* = 12.9 Hz, 1H), 4.83 (d, *J* = 9.6 Hz, 1H), 7.40 (d, *J* = 2.0 Hz, 1H), 7.64 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.88 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 28.5, 42.3 (d, $J_{C\text{-}F}$ = 30.1 Hz), 52.5, 52.6, 77.1, 80.9, 86.2, 90.2 (d, $J_{C\text{-}F}$ = 192.3 Hz), 118.1 (d, $J_{C\text{-}F}$ = 1.4 Hz), 118.4 (d, $J_{C\text{-}F}$ = 3.4 Hz), 123.0 (d, $J_{C\text{-}F}$ = 19.0 Hz), 127.8, 136.1 (d, $J_{C\text{-}F}$ = 3.1 Hz), 140.3 (d, $J_{C\text{-}F}$ = 5.4 Hz), 148.1, 156.1, 167.8 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -152.5, 152.6. The ee was determined as 92% using Phenomenex Amylose-1, hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 12.4 min, t_R(minor) = 14.8 min. Anal. Calcd. for $C_{22}H_{27}BrFN_3O_7$: C, 48.54; H, 5.00; N, 7.72. Found: C, 48.37; H, 5.18; N, 7.47.

Methyl *N*-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole-6-carboxylate (**3m**)

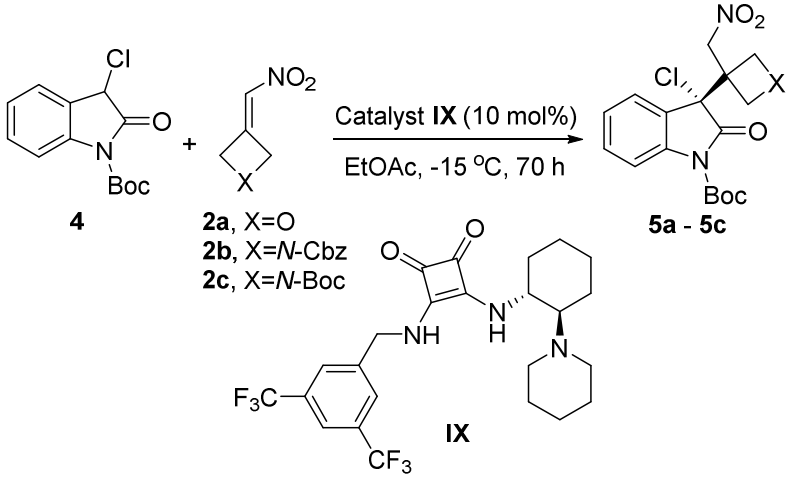


3m

Compound **3m** was obtained from methyl *N*-Boc-3-fluorooxindole-6-carboxylate **1g** (65.0 mg, 0.210 mmol) and nitroalkene **2b** (37.3 mg, 0.150 mmol) using catalyst **V** (6.3 mg, 0.015 mmol) by following the procedure described above. Chromatography (3.5:1 hexanes/ethyl acetate) gave 75.6 mg (0.136 mmol, 90%) of a white solid. Mp 71.2-72.5 °C. ^{1}H NMR (400

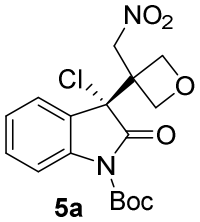
MHz, $CDCl_3$) δ = 1.65 (s, 9H), 3.95 (s, 3H), 4.07 (d, *J* = 8.4 Hz, 1H), 4.28 (d, *J* = 6.8 Hz, 1H), 4.48 – 4.66 (m, 3H), 4.96 (d, *J* = 9.3 Hz, 1H), 5.12 (s, 2H), 7.29 – 7.43 (m, 6H), 7.91 (d, *J* = 8.1 Hz, 1H), 8.59 (d, *J* = 1.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 42.7 (d, J_{C-F} = 29.8 Hz), 52.6, 52.9, 52.9, 67.5, 76.8, 86.4, 90.2 (d, J_{C-F} = 192.2 Hz), 117.4, 124.8, 125.0 (d, J_{C-F} = 18.7 Hz), 126.9 (d, J_{C-F} = 2.7 Hz), 128.3, 128.5, 128.7, 134.8 (d, J_{C-F} = 3.0 Hz), 136.1, 141.5 (d, J_{C-F} = 5.4 Hz), 147.9, 156.3, 165.7 (d, J_{C-F} = 1.7 Hz), 168.1 (d, J_{C-F} = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -153.9, -153.3. The ee was determined as 92% using CHIRALPAK IA, hexanes/isopropanol 90:10, flow rate = 1mL/min condition. t_R(major) = 21.0 min, t_R(minor) = 27.0 min. Anal. Calcd. for $C_{27}H_{28}FN_3O_9$: C, 58.17; H, 5.06; N, 7.54. Found: C, 58.24; H, 5.33; N, 7.39.

3.6. General procedure for the organocatalysis with *N*-Boc-3-chlorooxindole



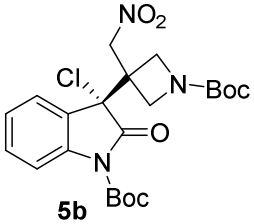
First, *N*-Boc-3-chlorooxindole **4** (48.2 mg, 0.180 mmol), nitroalkene **2** (0.150 mmol) and catalyst **IX** (7.3 mg, 0.015 mmol) were placed into an oven-dried vial. Then, ethyl acetate (0.45 mL) was added to the vial. The vial was then capped, and the solution was cooled to -15 °C and stirred for 70 hours. Upon completion, the solvent was evaporated by a gentle flow of nitrogen and the residue was purified by column chromatography as described below. Racemic reaction products for HPLC analysis were obtained by applying racemic mixture of catalyst **I** in the above procedure at room temperature.

N-Boc-(*R*)-3-chloro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**5a**)



Compound **5a** was obtained from *N*-Boc-3-chlorooxindole **4** (48.2 mg, 0.180 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) by following the procedure described above. Chromatography (6:1:1 hexanes/dichloromethane/ethyl acetate) gave 46.5 mg (0.121 mmol, 81%) of a pink amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ =1.64 (s, 9H), 4.64 – 4.70 (m, 2H), 4.72 (d, *J* = 12.5 Hz, 1H), 4.93 (d, *J* = 7.0 Hz, 1H), 5.34 (d, *J* = 7.0 Hz, 1H), 5.56 (d, *J* = 7.7 Hz, 1H), 7.17 – 7.25 (m, 2H), 7.45 (ddd, *J* = 8.6, 6.0, 3.0 Hz, 1H), 7.91 (dd, *J* = 8.3, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 48.8, 66.0, 74.1, 75.6, 76.9, 86.0, 116.2, 124.3, 124.8, 125.7, 132.0, 139.3, 148.3, 169.9. The ee was determined as 90% using Phenomenex Amylose-1, hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 12.5 min, t_R(minor) = 11.0 min. Anal. Calcd. for $C_{17}H_{19}ClN_2O_6$: C, 53.34; H, 5.00; N, 7.32. Found: C, 53.14; H, 5.16; N, 7.69.

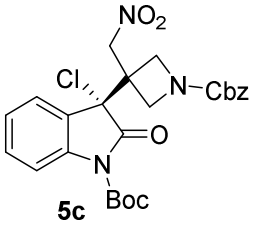
N-Boc-(*S*)-3-chloro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5b**)



5b

Compound **5b** was obtained from *N*-Boc-3-chlorooxindole **4** (48.2 mg, 0.180 mmol) and nitroalkene **2c** (32.1 mg, 0.150 mmol) by following the procedure described above. Chromatography (6:1:1 hexanes/dichloromethane/ethyl acetate) gave 64.9 mg (0.135 mmol, 90%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.45 (s, 9H), 1.64 (s, 9H), 4.04 (d, *J* = 10.4 Hz, 1H), 4.27 (d, *J* = 9.1 Hz, 1H), 4.47 – 4.68 (m, 3H), 4.85 (d, *J* = 8.9 Hz, 1H), 7.22 (ddd, *J* = 7.6, 7.6, 1.0 Hz, 1H), 7.28 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.45 (ddd, *J* = 8.2, 7.4, 1.5 Hz, 1H), 7.92 (dd, *J* = 8.3, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 28.4, 43.5, 53.5, 54.6, 66.0, 77.3, 80.7, 86.0, 116.2, 124.2, 124.8, 125.8, 132.0, 139.3, 148.4, 155.9, 169.7. The ee was determined as 97% using Phenomenex Amylose-1, hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 13.6 min, t_R(minor) = 19.1 min. Anal. Calcd. for $C_{22}H_{28}ClN_3O_7$: C, 54.83; H, 5.86; N, 8.72. Found: C, 54.72; H, 6.13; N, 8.49.

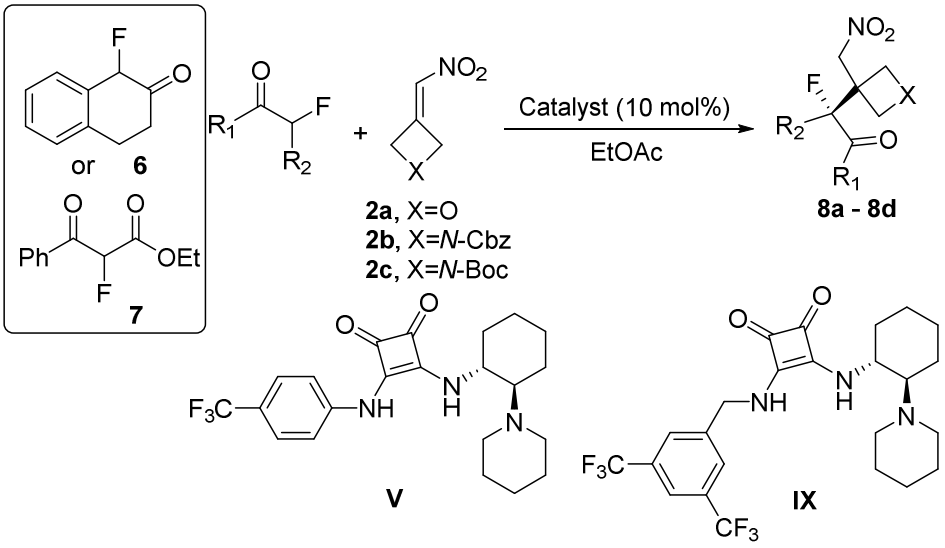
N-Boc-(*S*)-3-chloro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5c**)



5c

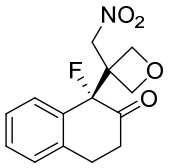
Compound **5c** was obtained from *N*-Boc-3-chlorooxindole **4** (48.2 mg, 0.180 mmol) and nitroalkene **2b** (37.2 mg, 0.150 mmol) by the procedure described above. Chromatography (6:1:1 hexanes/dichloromethane/ethyl acetate) gave 66.6 mg (0.129 mmol, 86%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.64 (s, 9H), 4.14 (d, *J* = 10.1 Hz, 1H), 4.38 (d, *J* = 9.6 Hz, 1H), 4.56 (s, 2H), 4.69 (d, *J* = 14.7 Hz, 1H), 4.94 (d, *J* = 12.1 Hz, 1H), 5.12 (d, *J* = 1.8 Hz, 2H), 7.19 (ddd, *J* = 7.6, 7.6, 1.0 Hz, 1H), 7.26 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.30 – 7.40 (m, 5H), 7.45 (ddd, *J* = 8.5, 7.5, 1.5 Hz, 1H), 7.92 (dd, *J* = 8.4, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 43.9, 53.7, 54.7, 65.9, 67.3, 77.1, 86.1, 116.2, 124.2, 124.6, 125.8, 128.2, 128.4, 128.7, 132.1, 136.3, 139.3, 148.3, 156.1, 169.7. The ee was determined as 96% using CHIRALCEL OD, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 13.9 min, t_R(minor) = 21.6 min. Anal. Calcd. for $C_{25}H_{26}ClN_3O_7$: C, 58.20; H, 5.08; N, 8.14. Found: C, 58.11; H, 5.29; N, 8.01.

3.7. General procedure for the organocatalysis with 1-fluoro-2-tetralone and ethyl 2-fluoro-3-oxo-3-phenylpropanoate



The organofluorine compound **6** or **7**, nitroalkene **2** (0.15 mmol) and organocatalyst (0.015 mmol, cat. **V** for 1-fluoro-2-tetralone, cat. **IX** for ethyl 2-fluoro-3-oxo-3-phenylpropanoate) were placed into an oven-dried vial and dissolved in ethyl acetate (0.45 mL). The vial was then capped, cooled to a specified temperature and stirred until completion. The solvent was then evaporated by a gentle flow of nitrogen and the residue was purified by column chromatography as described below. Racemic reaction products for HPLC analysis were obtained by applying racemic catalyst **I** in the above procedure at room temperature.

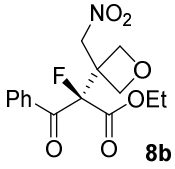
(*R*)-1-Fluoro-1-(3-(nitromethyl)oxetan-3-yl)-3,4-dihydronaphthalen-2(1H)-one (**8a**)



8a

Compound **8a** was obtained from 1-fluoro-2-tetralone **7** (31.9 mg, 0.195 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **V** (6.3 mg, 0.015 mmol) by following the procedure described above. The reaction was running at 0 °C for 110 hours. Chromatography (3.5:1 hexanes/ethyl acetate) gave 35.3 mg (0.126 mmol, 84%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.70 (d, *J* = 5.9 Hz, 1H), 2.72 (d, *J* = 5.9 Hz, 1H), 3.08 – 3.19 (m, 2H), 4.48 (dd, *J* = 7.4, 1.4 Hz, 1H), 4.54 (dd, *J* = 6.8, 3.1 Hz, 1H), 4.84 (d, *J* = 13.9 Hz, 1H), 4.94 (d, *J* = 6.8 Hz, 1H), 5.02 (d, *J* = 13.9 Hz, 1H), 5.16 (dd, *J* = 7.3, 1.2 Hz, 1H), 7.29 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.34 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.6, 1.5 Hz, 1H), 7.45 (ddd, *J* = 7.4, 7.4, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 27.8 , 35.8 , 49.2 (d, $J_{C\text{-}F}$ = 28.8 Hz), 73.9 (d, $J_{C\text{-}F}$ = 8.3 Hz), 74.0 (d, $J_{C\text{-}F}$ = 8.5 Hz), 76.7 (d, $J_{C\text{-}F}$ = 2.7 Hz), 92.9 (d, $J_{C\text{-}F}$ = 184.0 Hz), 127.2 (d, $J_{C\text{-}F}$ = 6.6 Hz), 127.9 , 129.2 , 130.5 (d, $J_{C\text{-}F}$ = 2.6 Hz), 131.8 (d, $J_{C\text{-}F}$ = 20.6 Hz), 138.2 (d, $J_{C\text{-}F}$ = 5.2 Hz), 204.3 (d, $J_{C\text{-}F}$ = 17.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -145.7. The ee was determined as 89% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 29.8 min, t_R(minor) = 23.3 min. Anal. Calcd. for $C_{14}H_{14}FNO_4$: C, 60.21; H, 5.05; N, 5.02. Found: C, 60.39; H, 4.79; N, 5.17.

Ethyl (*R*)-2-fluoro-2-(3-(nitromethyl)oxetan-3-yl)-3-oxo-3-phenylpropanoate (**8b**)

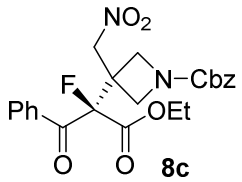


8b

Compound **8b** was obtained from ethyl 2-fluoro-3-oxo-3-phenylpropanoate **7** (34.7 mg, 0.165 mmol) and nitroalkene **2a** (17.3 mg, 0.150 mmol) using catalyst **IX** (7.6 mg, 0.015 mmol) by following the procedure described above. The reaction was running at -5 °C for 70 hours. Chromatography (5:1 hexanes/ethyl acetate) gave 47.8 mg (0.147mmol, 98%) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.16 (t, *J* = 7.1 Hz, 3H), 4.17 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.28 (dq, *J* = 10.8, 7.2 Hz, 1H), 4.73 (dd, *J* = 7.6, 2.0 Hz, 1H), 4.76 – 4.81 (m, 2H), 5.09 – 5.17 (m, 2H), 5.20 (d, *J* = 15.0 Hz, 1H), 7.49 (dd, *J* = 8.3, 7.5 Hz, 2H), 7.64 (dddd, *J* = 7.4, 7.4, 1.5, 1.5 Hz, 1H), 7.99 (dd, *J* = 8.6, 1.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.7, 47.2 (d, $J_{C\text{-}F}$ = 24.1 Hz), 63.7, 73.8 (d, $J_{C\text{-}F}$ = 8.0 Hz), 75.8 (d, $J_{C\text{-}F}$ = 2.7 Hz), 77.2, 96.6 (d,

$J_{C\text{-}F}$ = 202.5 Hz), 129.1, 129.7 (d, $J_{C\text{-}F}$ = 5.2 Hz), 133.1 (d, $J_{C\text{-}F}$ = 3.8 Hz), 134.9, 165.4 (d, $J_{C\text{-}F}$ = 25.5 Hz), 190.0 (d, $J_{C\text{-}F}$ = 24.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.6. The ee was determined as 78% using Phenomenex Amylose-1, hexanes/isopropanol 90:10, flow rate = 1mL/min condition. t_R(major) = 13.0 min, t_R(minor) = 15.1 min. Anal. Calcd. for $C_{15}H_{16}FNO_6$: C, 55.39; H, 4.96; N, 4.31. Found: C, 55.33; H, 5.34; N, 4.46.

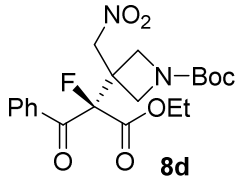
Ethyl (*R*)-2-fluoro-2-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8c**)



8c

Compound **8c** was obtained from ethyl 2-fluoro-3-oxo-3-phenylpropanoate **7** (34.7 mg, 0.165 mmol) and nitroalkene **2b** (37.2 mg, 0.150 mmol) using catalyst **IX** (7.6 mg, 0.015 mmol) by following the procedure described above. The reaction was running at -5 °C for 70 hours. Chromatography (5:1 hexanes/ethyl acetate) gave 63.9 mg (0.139mmol, 93%) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.13 (t, *J* = 7.1 Hz, 3H), 4.08 – 4.29 (m, 5H), 4.59 (d, *J* = 10.2 Hz, 1H), 4.96 (dd, *J* = 14.8, 1.7 Hz, 1H), 5.10 (s, 2H), 5.15 (d, *J* = 15.0 Hz, 1H), 7.28 – 7.39 (m, 5H), 7.48 (dd, *J* = 8.4, 7.3 Hz, 2H), 7.64 (dddd, *J* = 7.5, 7.5, 1.4, 1.4 Hz, 1H), 7.96 (dd, *J* = 8.7, 1.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.7, 41.9 (d, $J_{C\text{-}F}$ = 24.1 Hz), 53.2, 55.1, 63.8, 67.2, 76.6, 96.7 (d, $J_{C\text{-}F}$ = 202.9 Hz), 128.2, 128.3, 128.7, 129.1, 129.7 (d, $J_{C\text{-}F}$ = 5.3 Hz), 133.1 (d, $J_{C\text{-}F}$ = 3.7 Hz), 135.0, 136.3, 156.0, 165.1 (d, $J_{C\text{-}F}$ = 25.4 Hz), 189.9 (d, $J_{C\text{-}F}$ = 24.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.9, -161.7. The ee was determined as 77% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 22.8 min, t_R(minor) = 28.0 min. Anal. Calcd. for $C_{23}H_{23}FN_2O_7$: C, 60.26; H, 5.06; N, 6.11. Found: C, 59.96; H, 4.89; N, 5.72.

Ethyl (*R*)-2-fluoro-2-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8d**)



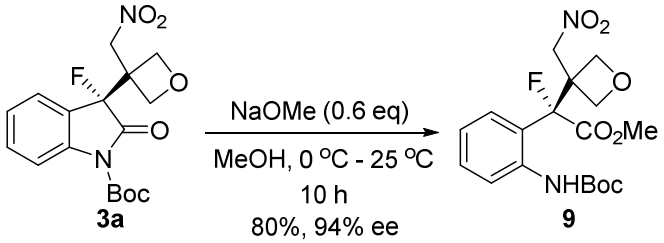
8d

Compound **8d** was obtained from ethyl 2-fluoro-3-oxo-3-phenylpropanoate **7** (34.7 mg, 0.165 mmol) and nitroalkene **2c** (32.1 mg, 0.150 mmol) using catalyst **IX** (7.6 mg, 0.015 mmol) by following the procedure described above. The reaction was running at -5 °C for 70 hours. Chromatography (5:1 hexanes/ethyl acetate) gave 58.6 mg (0.138mmol, 92%) of a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.16 (t, *J* = 7.1 Hz, 3H), 1.43 (s, 9H), 4.05 (d, *J* = 10.0 Hz, 1H), 4.10 (ddd, *J* = 10.1, 5.1, 2.8 Hz, 2H), 4.18 (dq, *J* = 10.9, 7.2 Hz, 1H), 4.27 (dq, *J* =

10.8, 7.2 Hz, 1H), 4.50 (d, *J* = 10.2 Hz, 1H), 4.95 (dd, *J* = 14.7, 1.7 Hz, 1H), 5.14 (d, *J* = 14.8 Hz, 1H), 7.48 (dd, *J* = 8.4, 7.3 Hz, 2H), 7.63 (dddd, *J* = 8.3, 8.3, 1.3, 1.3 Hz, 1H), 7.97 (dd, *J* = 7.4, 1.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.7, 28.4, 41.5 (d, $J_{C\text{-}F}$ = 24.1 Hz), 53.1, 54.9, 63.7, 77.3 (d, $J_{C\text{-}F}$ = 5.0 Hz), 80.5, 96.9 (d, $J_{C\text{-}F}$ = 202.5 Hz), 129.0, 129.7 (d, $J_{C\text{-}F}$ = 5.4 Hz), 133.3 (d, $J_{C\text{-}F}$ = 3.8 Hz), 134.9, 155.8, 165.2 (d, $J_{C\text{-}F}$ = 25.4 Hz), 190.1 (d, $J_{C\text{-}F}$ = 24.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.7. The ee was determined as 80% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 8.2 min, t_R(minor) = 12.1 min. Anal. Calcd. for $C_{20}H_{25}FN_2O_7$: C, 56.60; H, 5.94; N, 6.60. Found: C, 56.53; H, 6.00; N, 6.75.

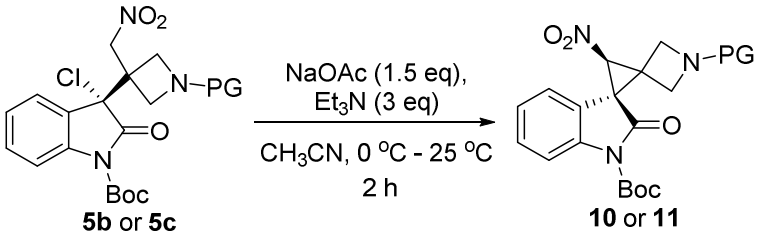
3.8. Selective Transformations

3.8.1. Oxindole ring methanolysis



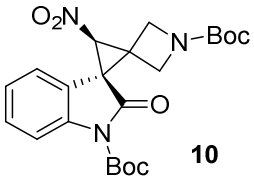
To a solution of compound **3a** (44.0 mg, 0.120 mmol) in anhydrous methanol (1.5 mL) was added sodium methoxide (3.9 mg, 0.072 mmol) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 10 hours. Upon completion, the reaction was quenched with aqueous NH_4Cl (0.5 mL) and extracted with Et_2O (4 mL, 3 times). The ether layers were combined, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The residue was purified by column chromatography (3:1:1 hexanes/dichloromethane/diethyl ether) to give compound **9** (38.1 mg, 0.096 mmol) in 80% yield as a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.52 (s, 9H), 3.86 (s, 3H), 4.74 – 4.86 (m, 4H), 4.98 (d, *J* = 7.6 Hz, 1H), 5.08 (d, *J* = 7.5 Hz, 1H), 6.95 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.00 (d, *J* = 7.0 Hz, 1H), 7.17 (ddd, *J* = 7.7, 7.7, 1.7 Hz 1H), 7.45 (ddd, *J* = 8.5, 7.1, 1.5 Hz, 1H), 7.82 (dd, *J* = 7.7, 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 48.1 (d, $J_{C\text{-}F}$ = 24.3 Hz), 53.7, 73.9 (d, $J_{C\text{-}F}$ = 6.9 Hz), 74.1 (d, $J_{C\text{-}F}$ = 7.4 Hz), 77.1 (d, $J_{C\text{-}F}$ = 3.8 Hz), 81.1, 97.9 (d, $J_{C\text{-}F}$ = 190.3 Hz), 124.5, 124.9 (d, $J_{C\text{-}F}$ = 19.9 Hz), 125.9 (d, $J_{C\text{-}F}$ = 9.1 Hz), 126.2, 130.9 (d, $J_{C\text{-}F}$ = 1.7 Hz), 136.9 (d, $J_{C\text{-}F}$ = 1.8 Hz), 152.8, 168.6 (d, $J_{C\text{-}F}$ = 25.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -154.0. The ee was determined as 94% using Phenomenex Amylose-1, hexanes/ethanol 90:10, flow rate = 1mL/min condition. t_R(major) = 10.4 min, t_R(minor) = 11.5 min. Anal. Calcd. for $C_{18}H_{23}FN_2O_7$: C, 54.27; H, 5.82; N, 7.03. Found: C, 53.95; H, 5.98; N, 7.06.

3.8.2. Stereoselective cyclopropanation



To a mixture of compound **5b** or **5c** (0.070 mmol) and sodium acetate (0.105 mmol, 1.5 eq) in anhydrous acetonitrile (0.7 mL) was added triethylamine (0.21 mmol, 3 eq) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 2 hours. Upon completion, the solvent was evaporated by a gentle flow of nitrogen and the residue was purified by column chromatography as described below.

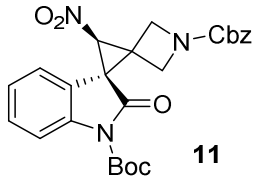
di-*tert*-Butyl (2'*S*,3'*S*)-3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**10**)



10

Compound **10** was obtained from **5b** (33.7 mg, 0.070 mmol) using sodium acetate (8.6 mg, 0.105 mmol) and triethylamine (29.3 μL, 0.21 mmol) by following the procedure described above. Chromatography (1:7 ethyl acetate/hexanes) gave 29.3 mg (0.066 mmol, 94%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.43 (s, 9H), 1.65 (s, 9H), 4.17 (d, *J* = 10.2 Hz, 1H), 4.32 (d, *J* = 10.2 Hz, 1H), 4.36 (d, *J* = 10.2 Hz, 1H), 4.69 (d, *J* = 10.1 Hz, 1H), 4.92 (s, 1H), 7.16 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.21 (ddd, *J* = 7.6, 7.4, 1.1 Hz, 1H), 7.43 (ddd, *J* = 8.3, 7.5, 1.5 Hz, 1H), 8.01 (dd, *J* = 8.3, 1.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 28.5, 35.2, 40.9, 50.7, 53.8, 70.9, 80.7, 85.7, 115.9, 119.4, 123.9, 125.0, 129.9, 141.3, 148.5, 155.7, 169.2. The ee was determined as 95% using CHIRALPAK IA, hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 6.2 min, t_R(minor) = 7.1 min. Anal. Calcd. for $C_{22}H_{27}N_3O_7$: C, 59.32; H, 6.11; N, 9.43. Found: C, 59.05; H, 6.35; N, 9.41.

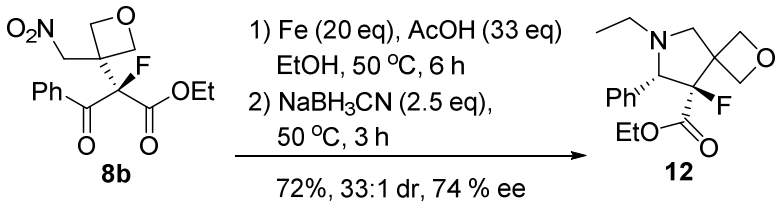
1-Benzyl 1"-(*tert*-butyl) (2'*S*,3'*S*)-3'-nitro-2"-oxodispiro[azetidine-3,1'-cyclopropane-2',3"-indoline]-1,1"-dicarboxylate (**11**)



11

Compound **11** was obtained from **5c** (34.6 mg, 0.067 mmol) using sodium acetate (8.2 mg, 0.100 mmol) and triethylamine (28.1 μL, 0.201 mmol) by following the procedure described above. Chromatography (1:5 ethyl acetate/hexanes) gave 29.0 mg (0.061 mmol, 90%) of a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.65 (s, 9H), 4.25 (d, *J* = 10.2 Hz, 1H), 4.41 (d, *J* = 10.3 Hz, 1H), 4.45 (d, *J* = 10.3 Hz, 1H), 4.79 (d, *J* = 10.2 Hz, 1H), 4.92 (s, 1H), 5.07 (d, *J* = 12.3 Hz, 1H), 5.11 (d, *J* = 12.2 Hz, 1H), 7.13 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.20 (ddd, *J* = 7.7, 7.7, 1.1 Hz, 1H), 7.29 – 7.38 (m, 5H), 7.43 (ddd, *J* = 8.3, 7.5, 1.4 Hz, 1H), 8.01 (dd, *J* = 8.3, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.2, 35.2, 40.8, 50.9, 54.0, 67.4, 70.7, 85.7, 115.9, 119.2, 123.8, 125.0, 128.3, 128.4, 128.7, 130.0, 136.2, 141.3, 148.5, 156.1, 169.1. The ee was determined as 95% using CHIRALPAK IA, hexanes/isopropanol 90:10, flow rate = 1mL/min condition. t_R(major) = 11.7 min, t_R(minor) = 18.1 min. Anal. Calcd. for $C_{25}H_{25}N_3O_7$: C, 62.62; H, 5.26; N, 8.76. Found: C, 62.54; H, 5.58; N, 8.73.

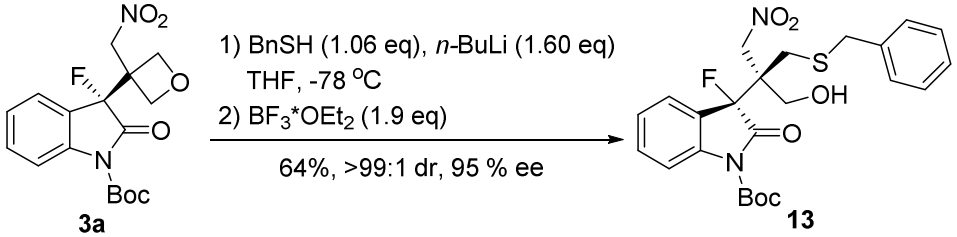
3.8.3. Reductive spiro pyrrolidine synthesis[11]



To a mixture of compound **8b** (31.8 mg, 0.098 mmol) and iron powder (110.0 mg, 1.97 mmol) in ethanol (2 mL) was added acetic acid (187 μL, 3.26 mmol). The reaction was heated to 50 °C and stirred for 6 hours. Upon complete consumption of **8b**, sodium cyanoborohydride (15.5 mg, 0.247 mmol) was added and the mixture was stirred at 50 °C for another 3 hours. Upon completion, the reaction was quenched with aqueous NH_4Cl (0.5 mL), extracted with Et_2O (4 mL, 3 times). The ether layers were combined, dried over Na_2SO_4, filtrated, and concentrated under reduced pressure. The residue was purified by chromatography (6:1 hexanes/ethyl acetate) to give compound **12** (21.8 mg, 0.071 mmol) in 72% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.94 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H), 2.25 (dq, *J* = 12.2, 6.9 Hz, 1H), 2.71 (dq, *J* = 12.2, 7.4 Hz, 1H), 3.00 (d, *J* = 9.2 Hz, 1H), 3.73 – 3.89 (m, 3H), 3.91 (d, *J* = 9.6 Hz, 1H), 4.47 (dd, *J* = 6.6, 2.5 Hz, 1H), 4.54 (dd, *J* = 6.8,

1.4 Hz, 1H), 4.91 (d, J = 6.7 Hz, 1H), 4.95 (d, J = 6.5 Hz, 1H), 7.26 – 7.31 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.9, 13.6, 47.6, 49.9 (d, $J_{C\text{-}F}$ = 20.9 Hz), 61.4, 62.5 (d, $J_{C\text{-}F}$ = 1.4 Hz), 75.7 (d, $J_{C\text{-}F}$ = 14.1 Hz), 77.2 (d, $J_{C\text{-}F}$ = 26.8 Hz), 79.4 (d, $J_{C\text{-}F}$ = 6.6 Hz), 102.4 (d, $J_{C\text{-}F}$ = 197.3 Hz), 128.0, 128.1, 128.1, 136.6 (d, $J_{C\text{-}F}$ = 4.5 Hz), 166.7 (d, $J_{C\text{-}F}$ = 28.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -157.2 (d, J = 29.6 Hz). The ee was determined as 74% using CHIRALCEL OD, hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 5.9 min, t_R(minor) = 6.5 min. Anal. Calcd. for $C_{17}H_{22}FNO_3$: C, 66.43; H, 7.21; N, 4.56. Found: C, 66.30; H, 7.30; N, 4.87.

3.8.4. Diastereoselective oxetane ring opening

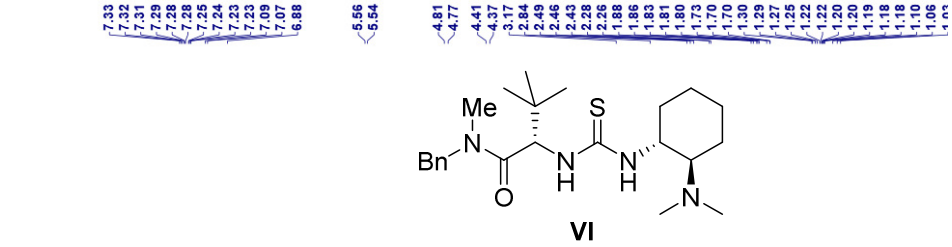


An oven-dried 25 mL 2-necked flask with rubber septum was charged with benzyl mercaptan (24.8 μL, 0.212 mmol) and anhydrous THF (0.8 mL) under nitrogen atmosphere. The solution was cooled to -78 °C and a 2.5 M solution of n-BuLi (128 μL, 0.352 mmol) was added. The mixture was stirred for 3 minutes before addition of $BF_3{\cdot}OEt_2$ (53.9 mg, 0.38 mmol). After another 10 minutes, a solution of compound **3a** (73.2 mg, 0.2 mmol) in anhydrous THF (0.4 mL) was added dropwise and the reaction was stirred at -78 °C for 90 minutes. The reaction was quenched by dropwise addition of 15% aqueous NH_4Cl (0.8 mL) at -78 °C. The cooling bath was removed to allow the flask to warm to room temperature. The reaction mixture was then extracted with Et_2O (4 mL, 3 times). The ether layers were combined, dried over Na_2SO_4, filtrated, and concentrated under reduced pressure. The residue was purified by chromatography (5:1 hexanes/ethyl acetate) to give compound **13** (62.4 mg, 0.127 mmol) in 64% yield as a white amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.58 (s, 9H), 2.06 (dd, J = 6.5, 5.0 Hz, 1H), 3.62 (d, J = 12.4 Hz, 1H), 3.80 (d, J = 12.4 Hz, 1H), 3.86 (ddd, J = 12.0, 6.6, 2.6 Hz, 1H), 4.00 (d, J = 12.5 Hz, 1H), 4.06 (d, J = 10.4 Hz, 1H), 4.12 (d, J = 10.4 Hz, 1H), 4.32 (dd, J = 12.0, 4.9 Hz, 1H), 4.63 (d, J = 12.4 Hz, 1H), 7.09 – 7.16 (m, 3H), 7.16 – 7.25 (m, 3H), 7.41 (ddd, J = 8.8, 7.5, 1.5 Hz, 1H), 7.46 (dd, J = 7.8, 1.6 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.4, 34.8 (d, $J_{C\text{-}F}$ = 5.4 Hz), 55.0 (d, $J_{C\text{-}F}$ = 26.6 Hz), 60.5 (d, $J_{C\text{-}F}$ = 12.2 Hz), 71.8, 75.3, 83.2, 108.9 (d, $J_{C\text{-}F}$ = 210.4 Hz), 115.7, 121.7 (d, $J_{C\text{-}F}$ = 24.0 Hz), 123.7 (d, $J_{C\text{-}F}$ = 2.6 Hz), 125.8, 127.3, 128.6, 129.1, 132.6 (d, $J_{C\text{-}F}$ = 2.7 Hz), 136.8, 143.1 (d, $J_{C\text{-}F}$ = 5.5 Hz), 150.6, 178.7 (d, $J_{C\text{-}F}$ = 21.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -151.2. The ee was determined as 95% using CHIRALPAK IB,

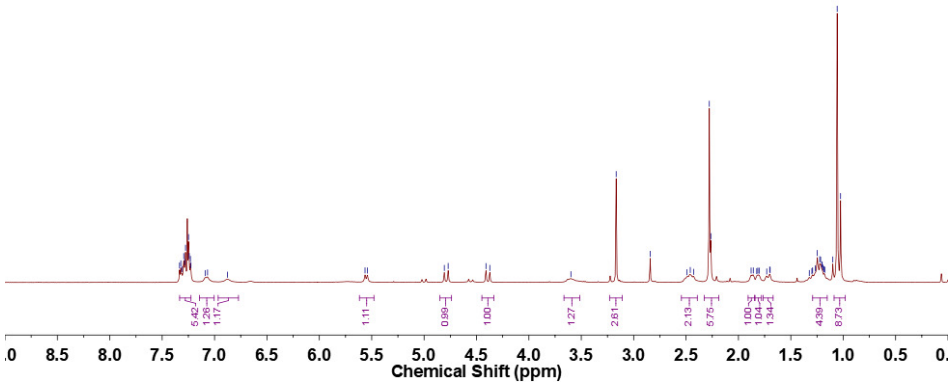
hexanes/isopropanol 95:5, flow rate = 1mL/min condition. t_R(major) = 19.6 min, t_R(minor) = 17.7 min. Anal. Calcd. for $C_{24}H_{27}FN_2O_6S$: C, 58.76; H, 5.55; N, 5.71. Found: C, 58.99; H, 5.78; N, 5.88.

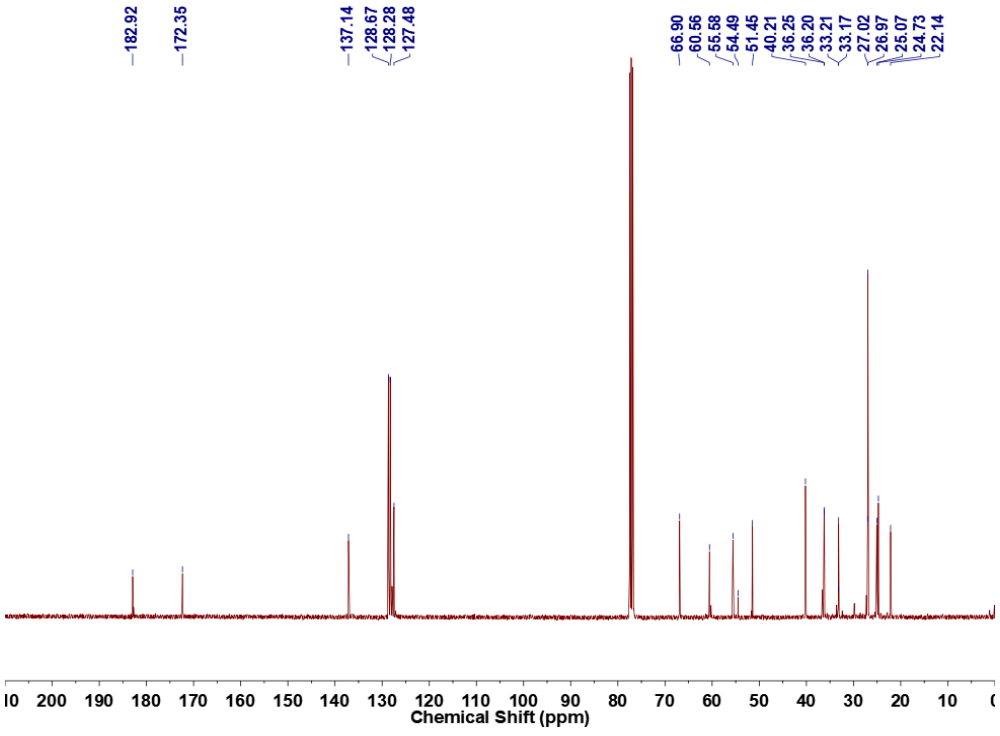
4. ^{1}H, ^{13}C, ^{19}F NMR Spectra

Catalyst **VI**

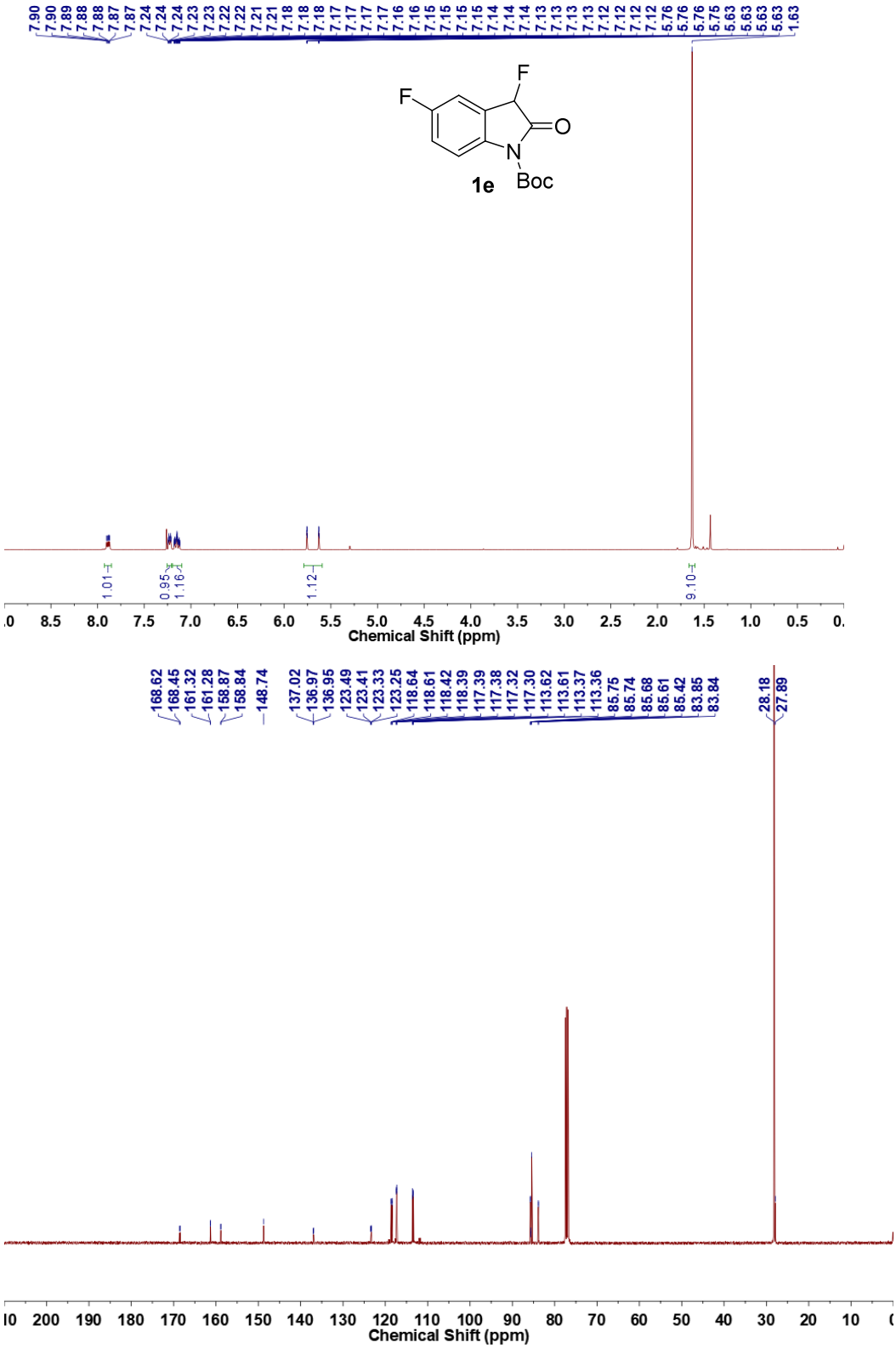


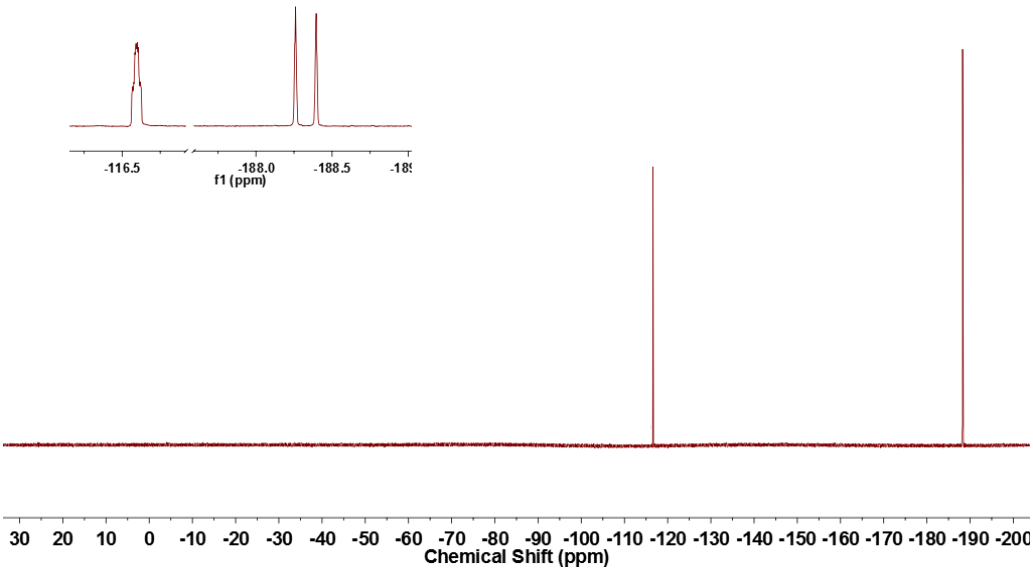
VI





N-Boc-3,5-difluorooxindole (**1e**)

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-188.0
-188.5
f1 (ppm)
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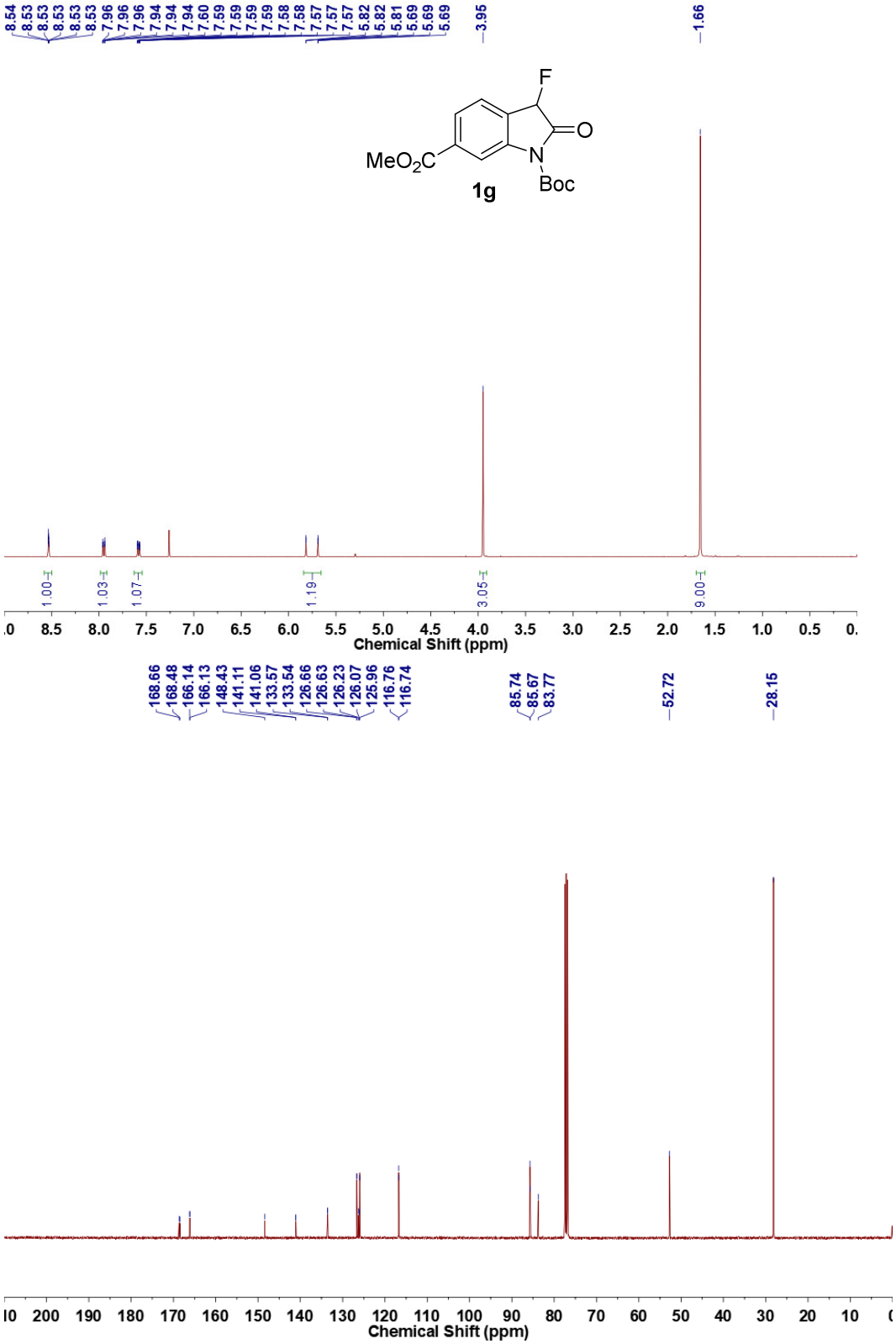
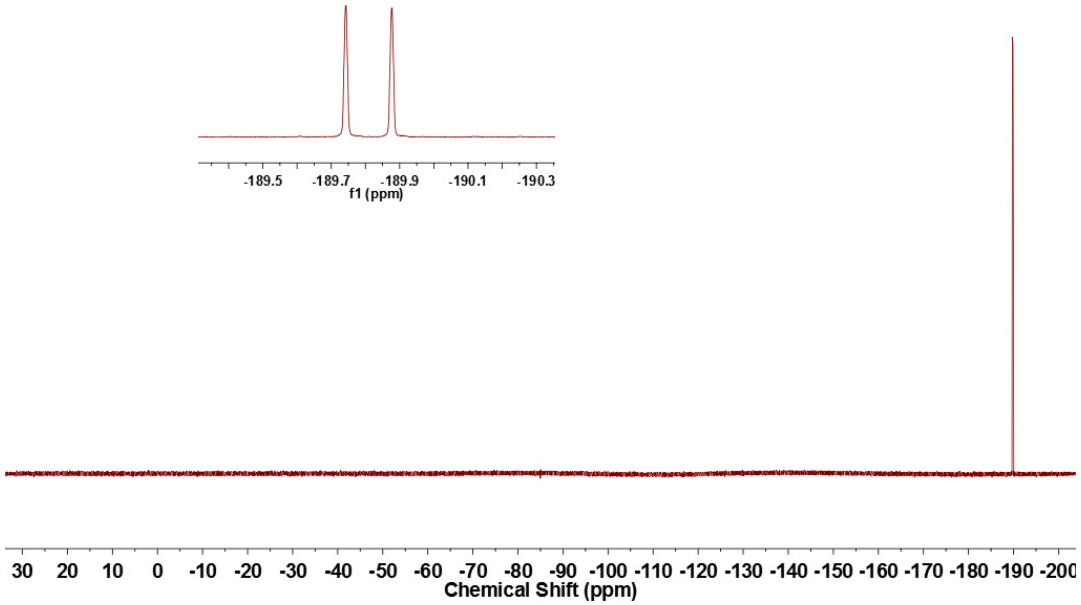
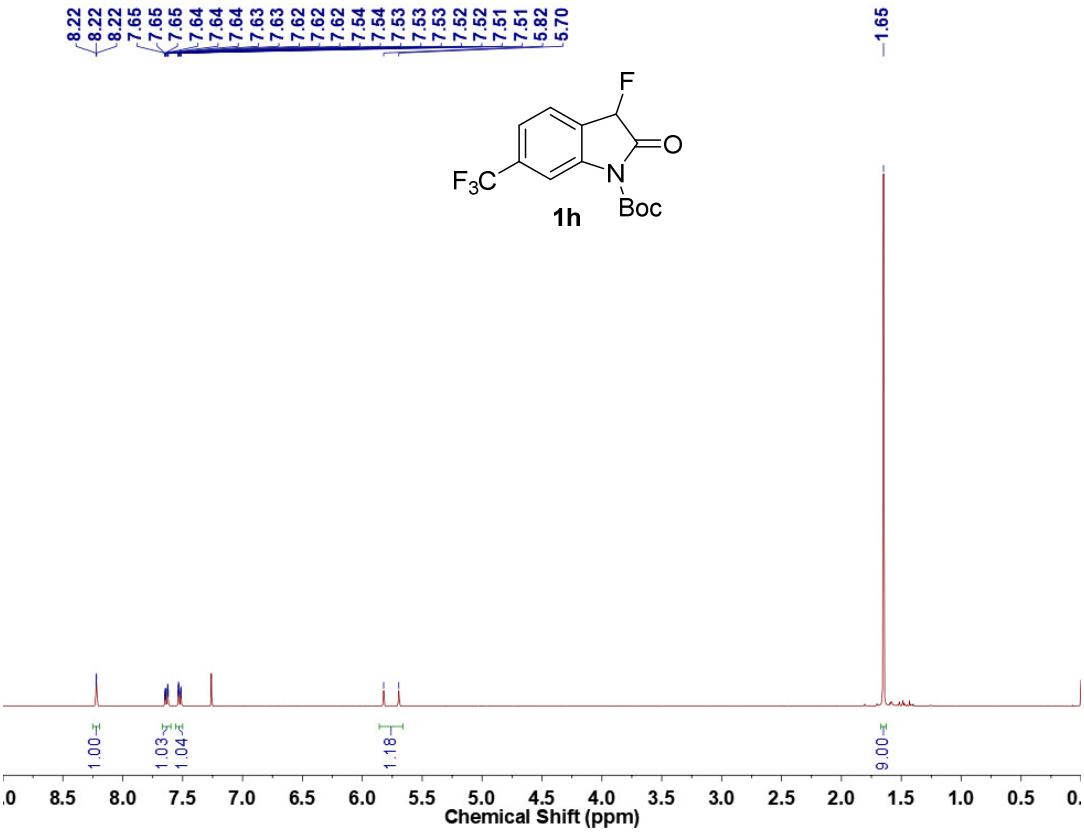
Chemical Shift (ppm)

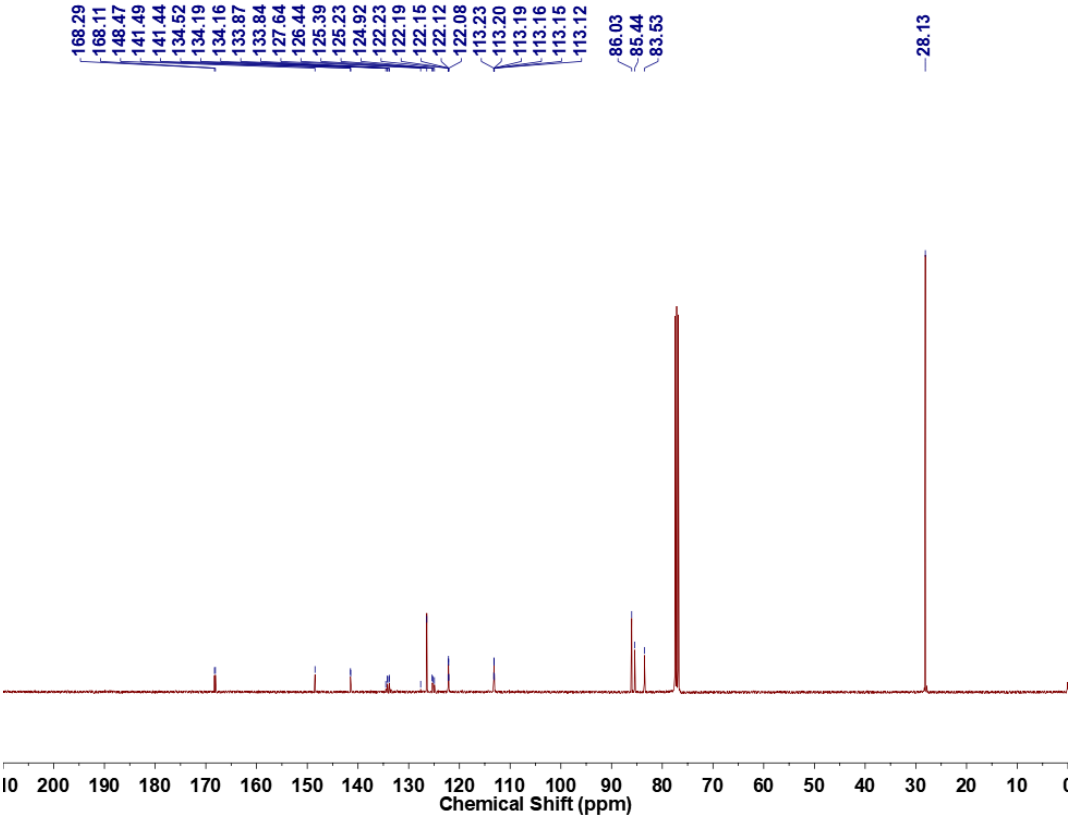
Methyl *N*-Boc-3-fluorooxindole-6-carboxylate (**1g**)

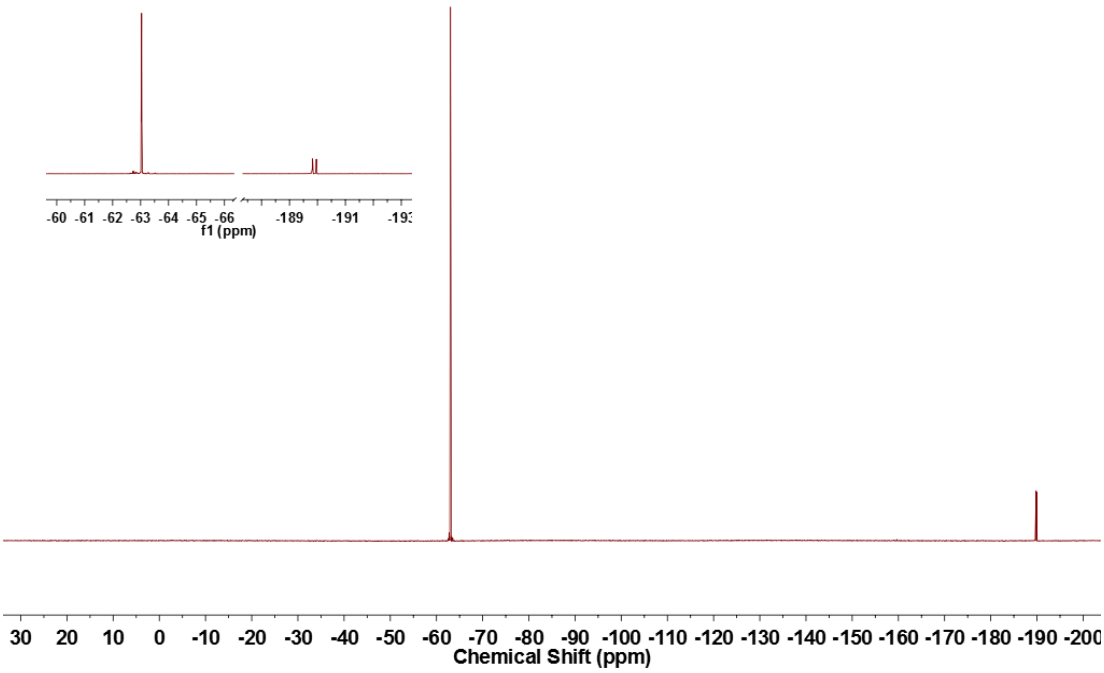



-189.5
-189.7
-189.9
-190.1
-190.3
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

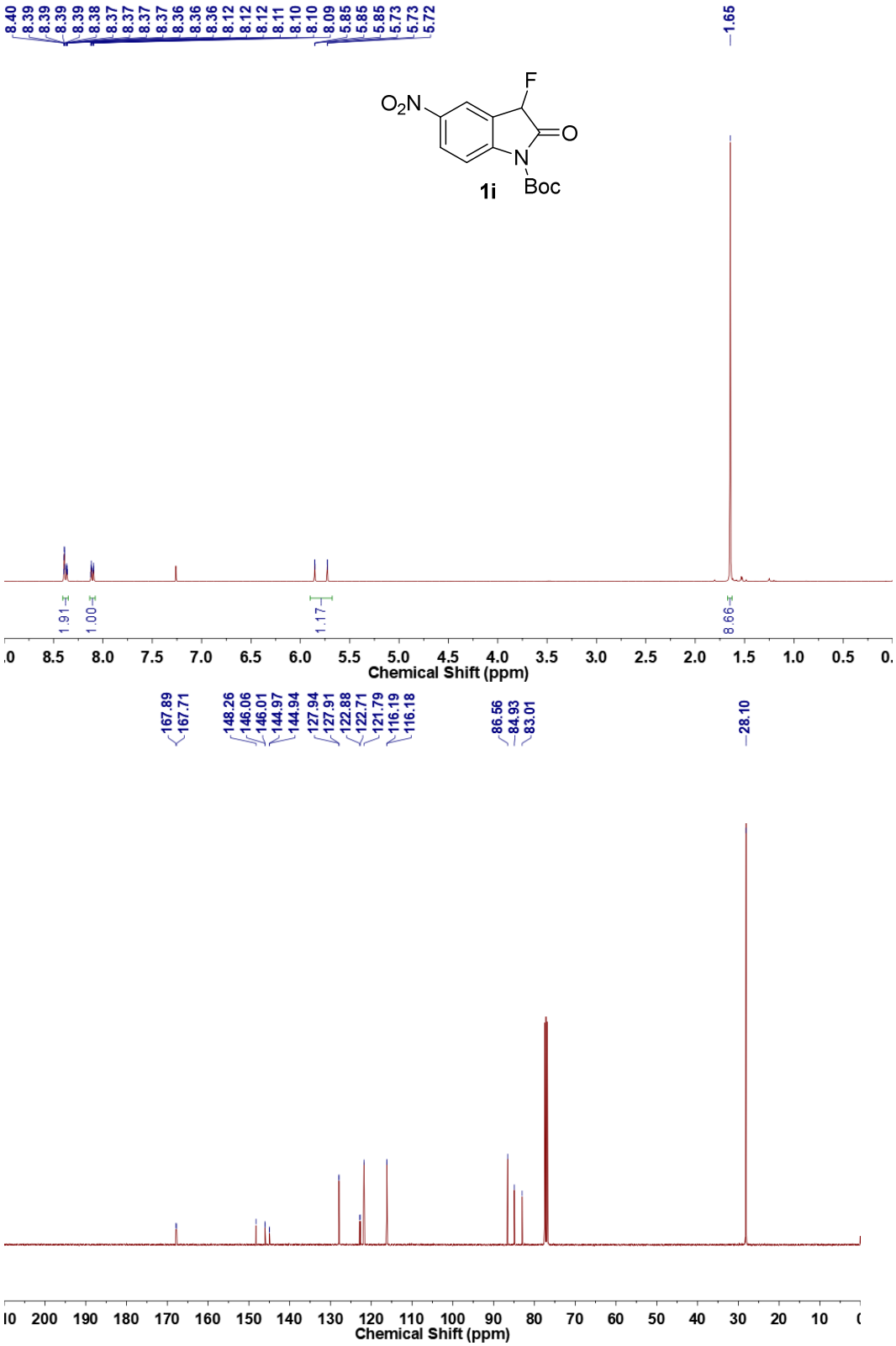
N-Boc-3-fluoro-6-trifluoromethyl-2-oxoindole (**1h**)

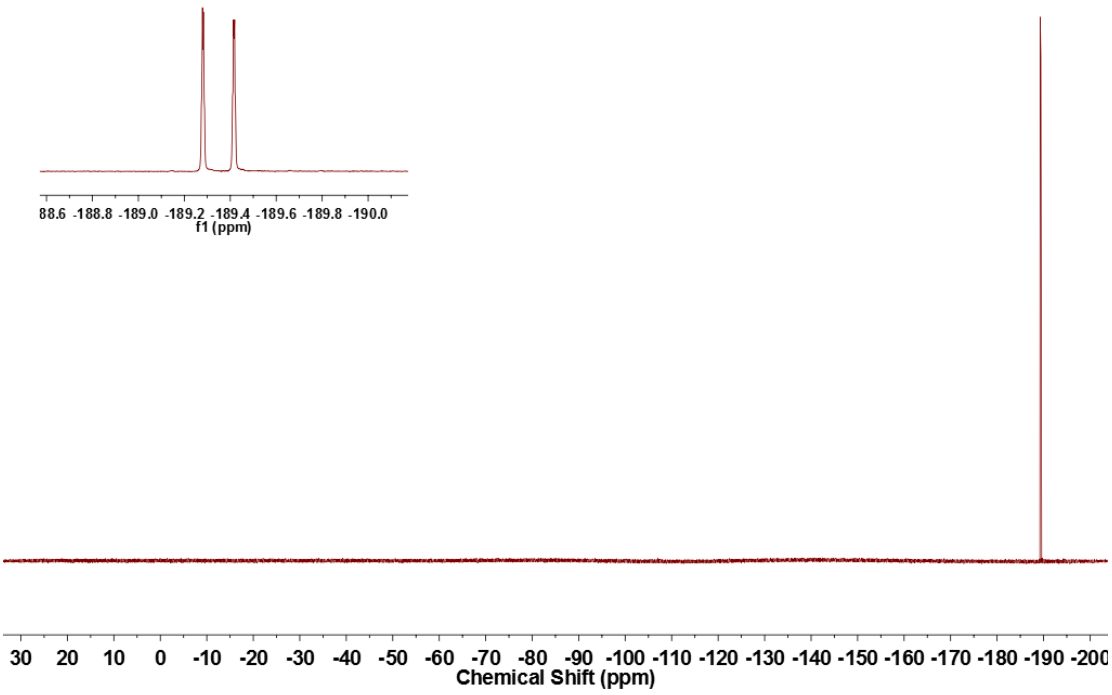




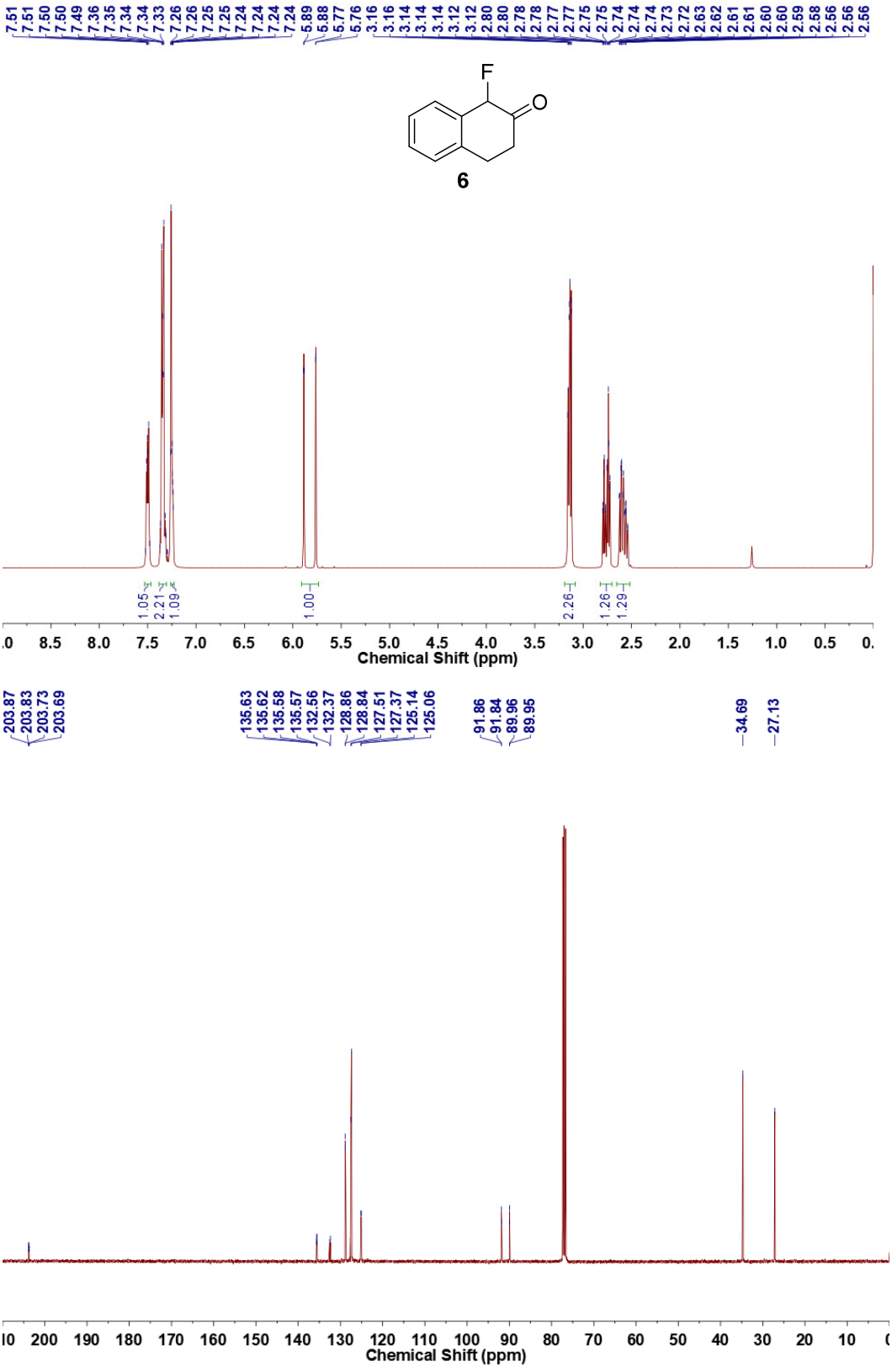

-60 -61 -62 -63 -64 -65 -66
f1 (ppm)
-189 -191 -193
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

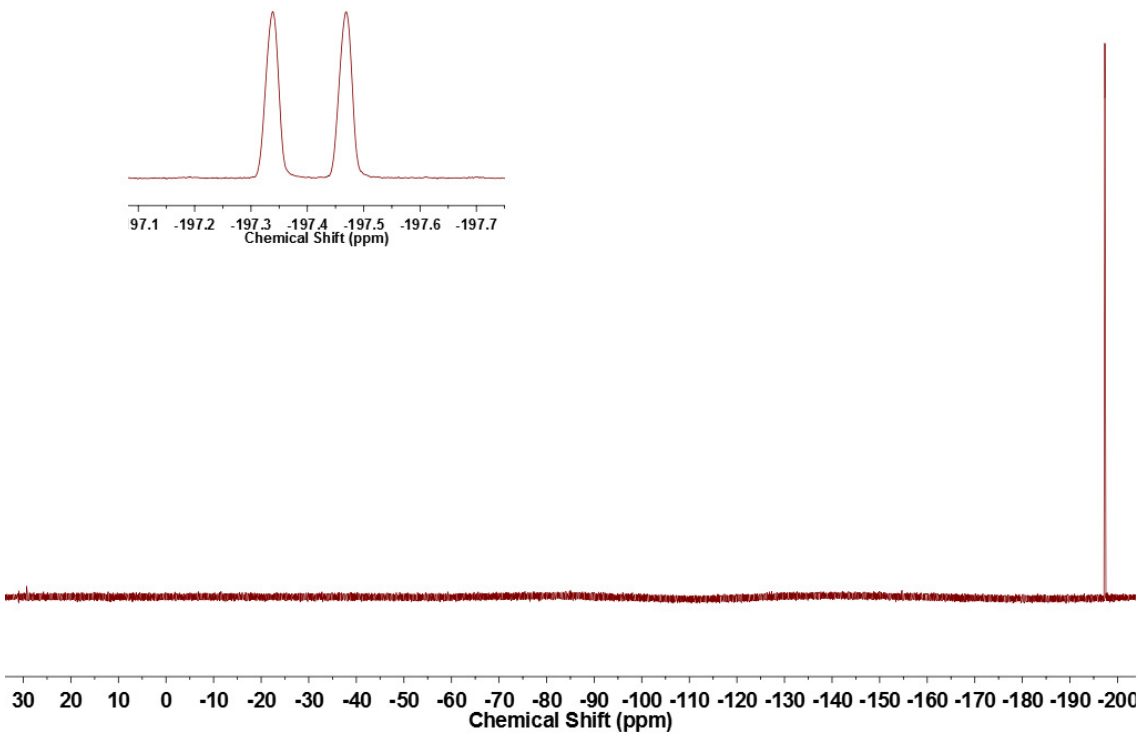
N-Boc-3-fluoro-5-nitro-2-oxoindole (**1i**)



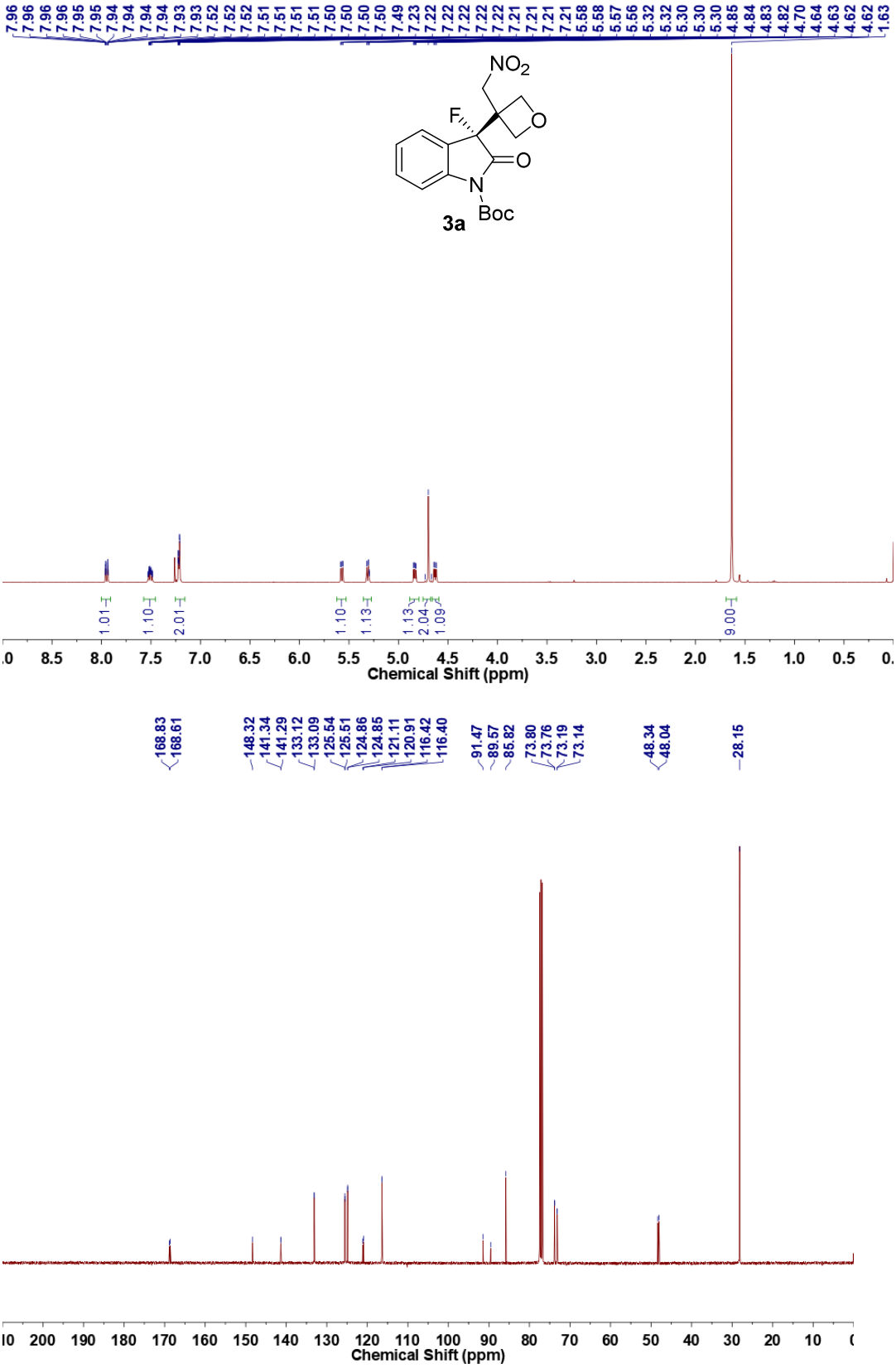

88.6 -188.8 -189.0 -189.2 -189.4 -189.6 -189.8 -190.0
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

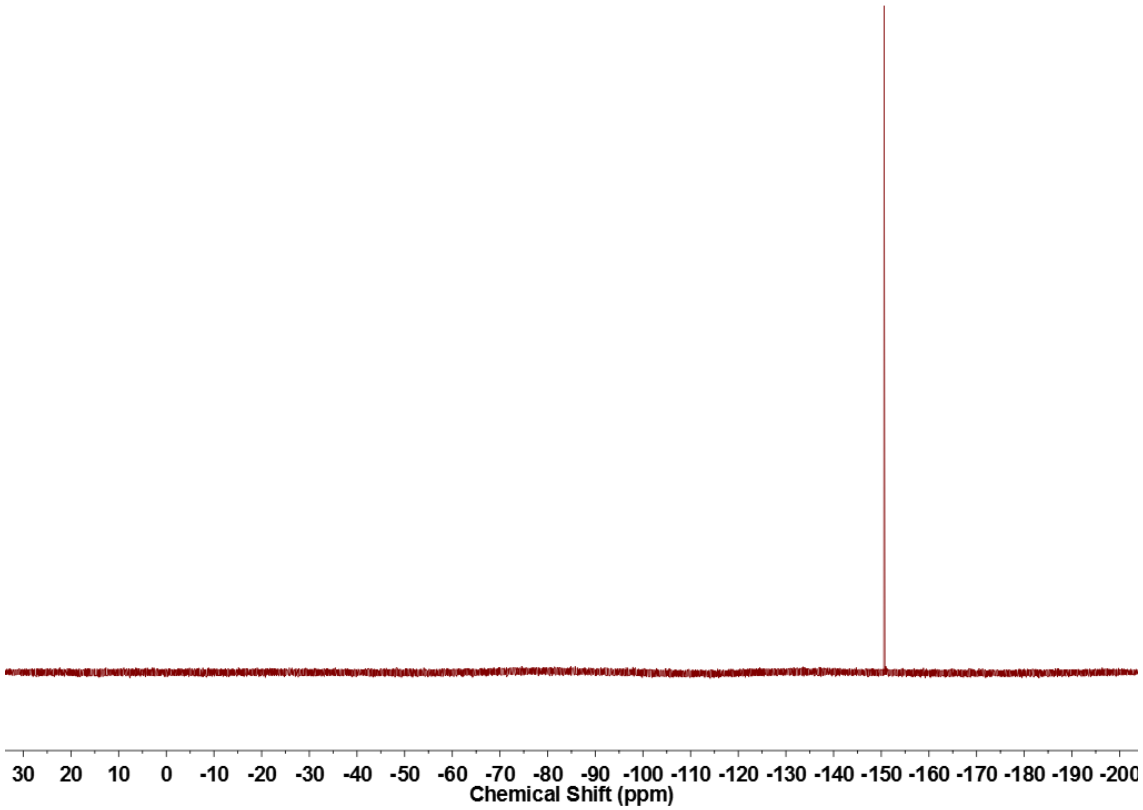
1-Fluoro-2-tetralone (**6**)



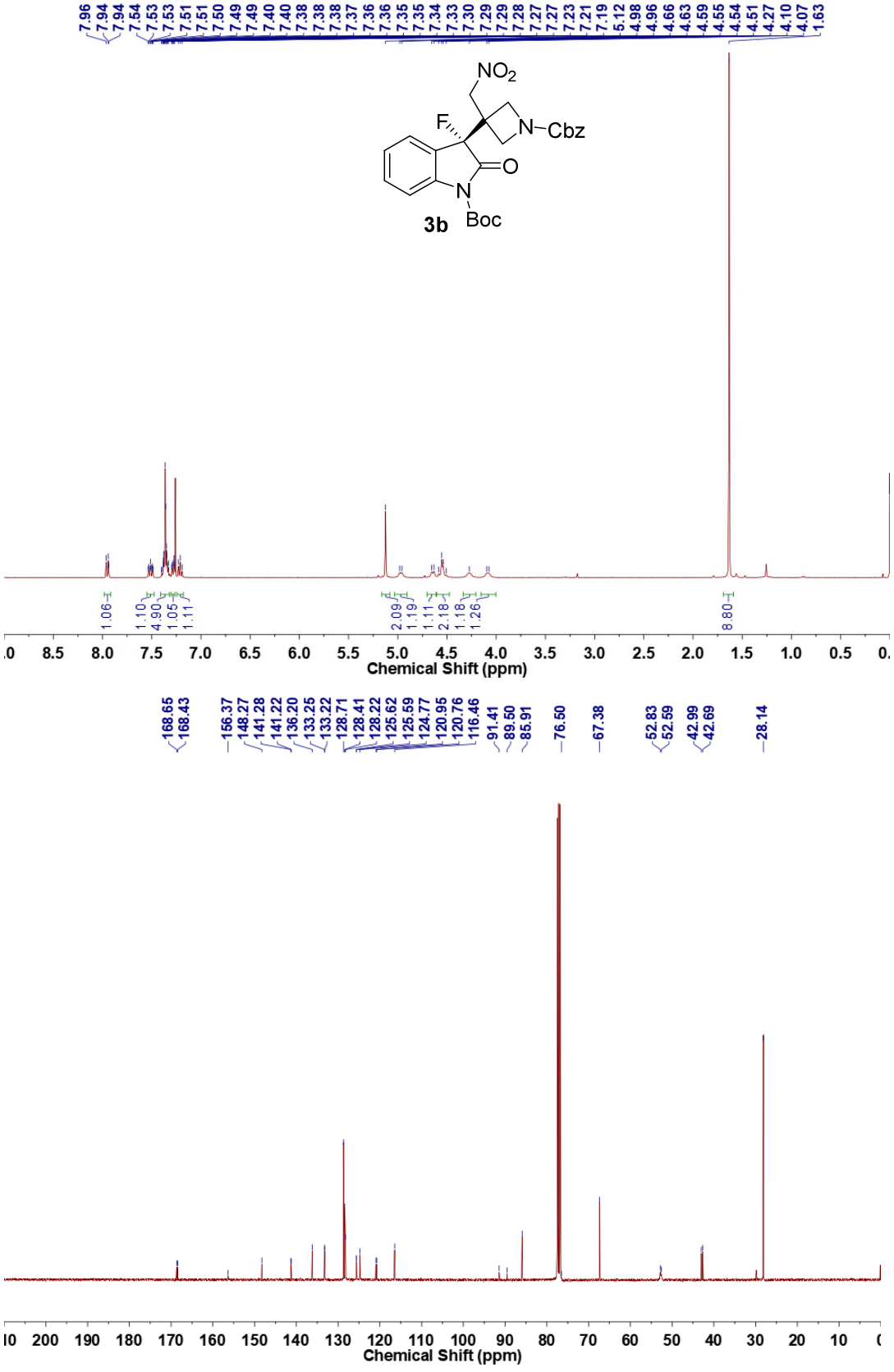

97.1 -197.2 -197.3 -197.4 -197.5 -197.6 -197.7
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

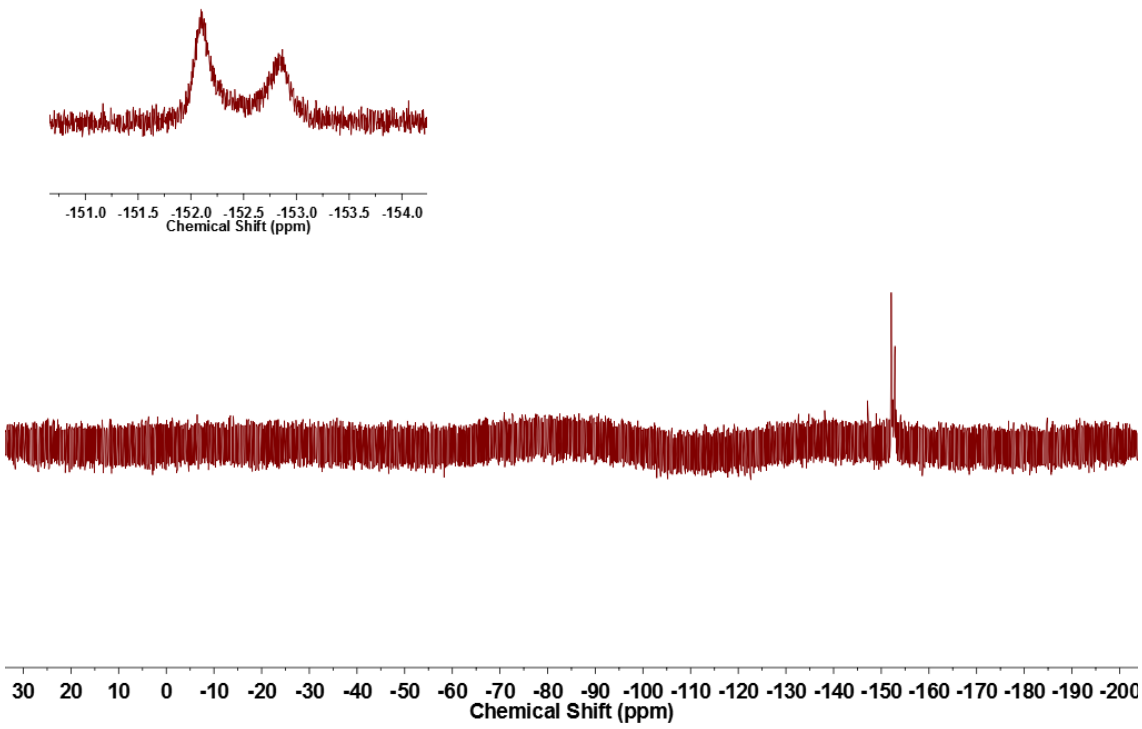
N-Boc-(*R*)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3a**)



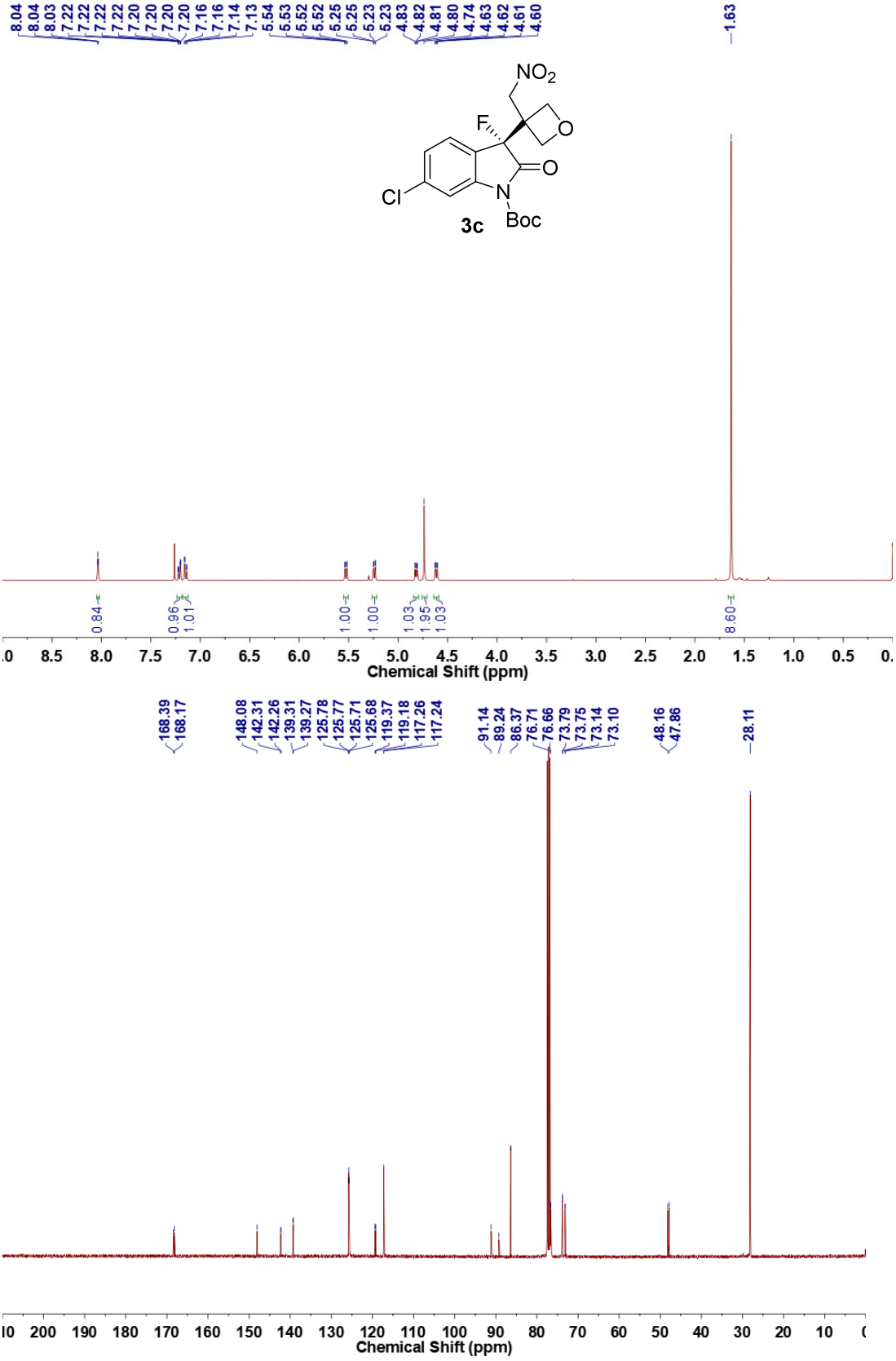

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

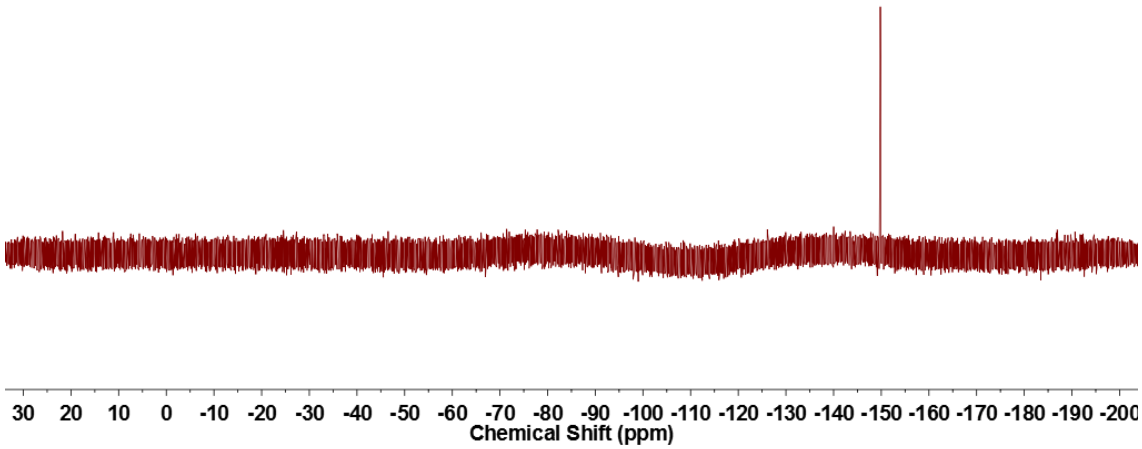
N-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3b**)



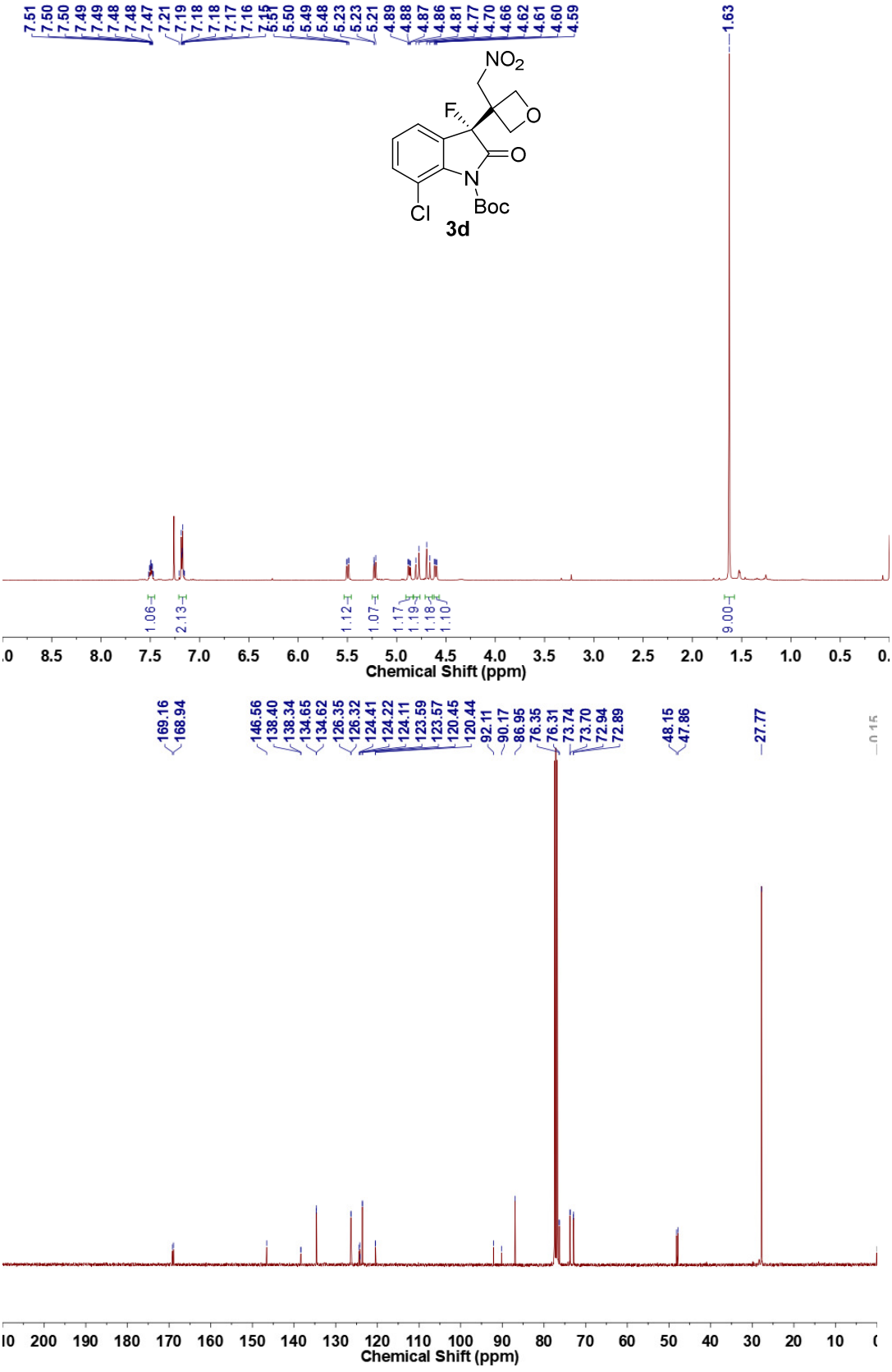

-151.0 -151.5 -152.0 -152.5 -153.0 -153.5 -154.0
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

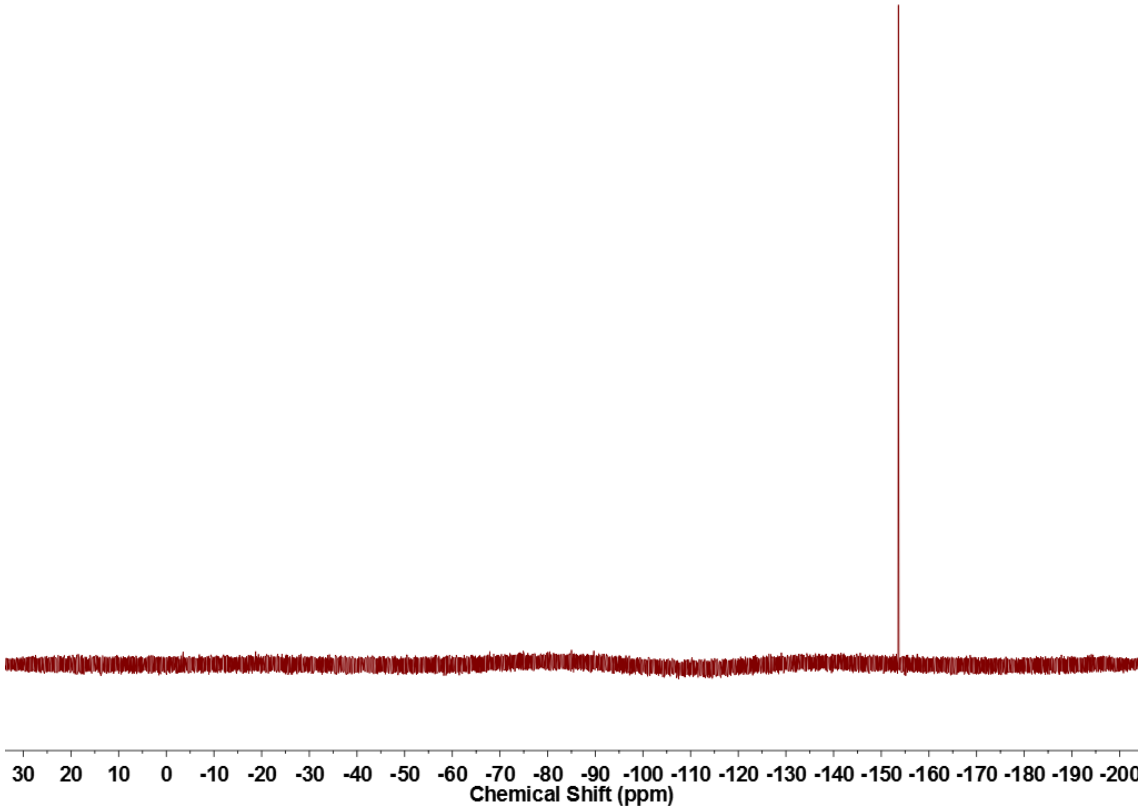
N-Boc-(*R*)-6-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3c**)



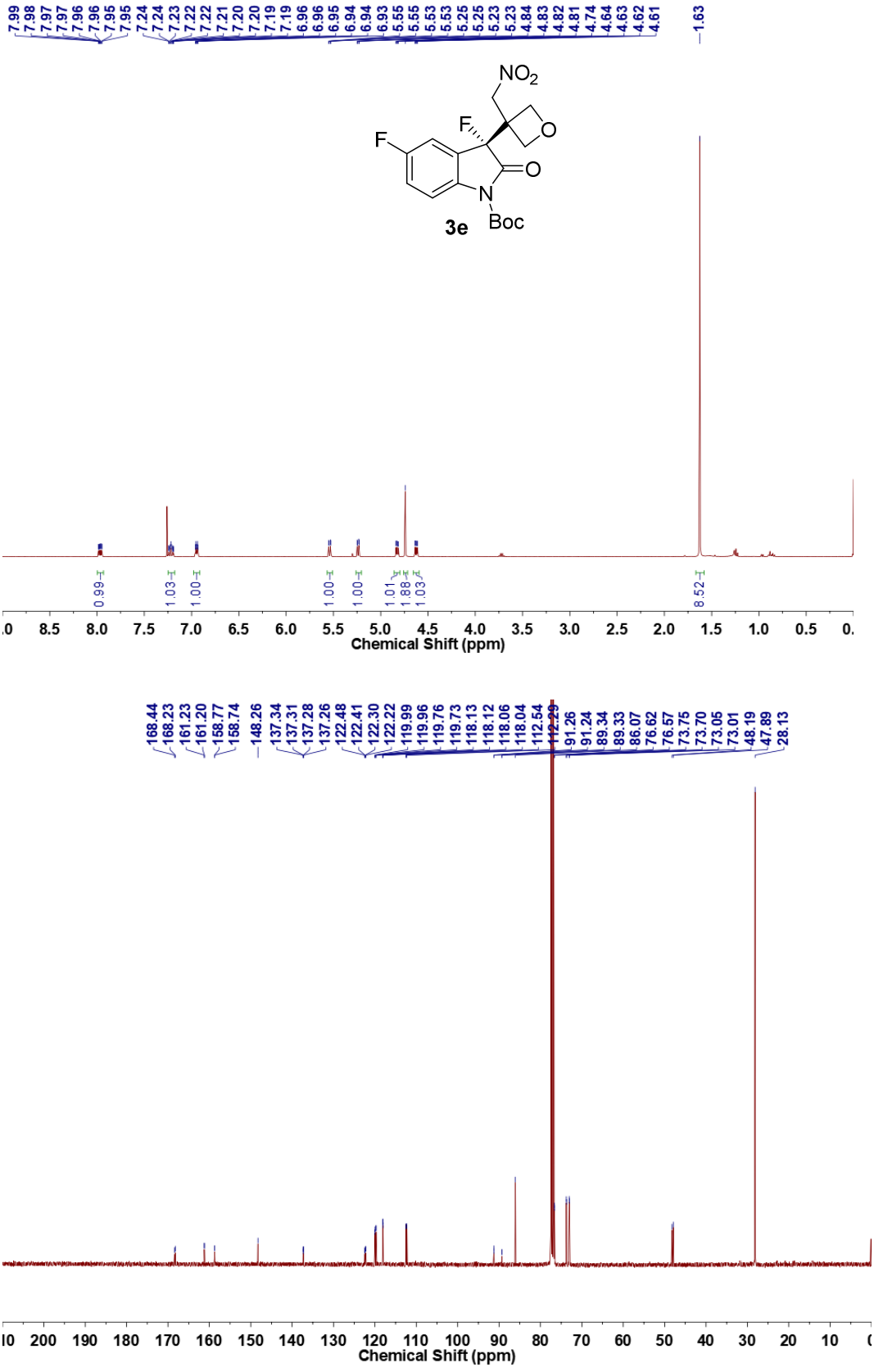

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

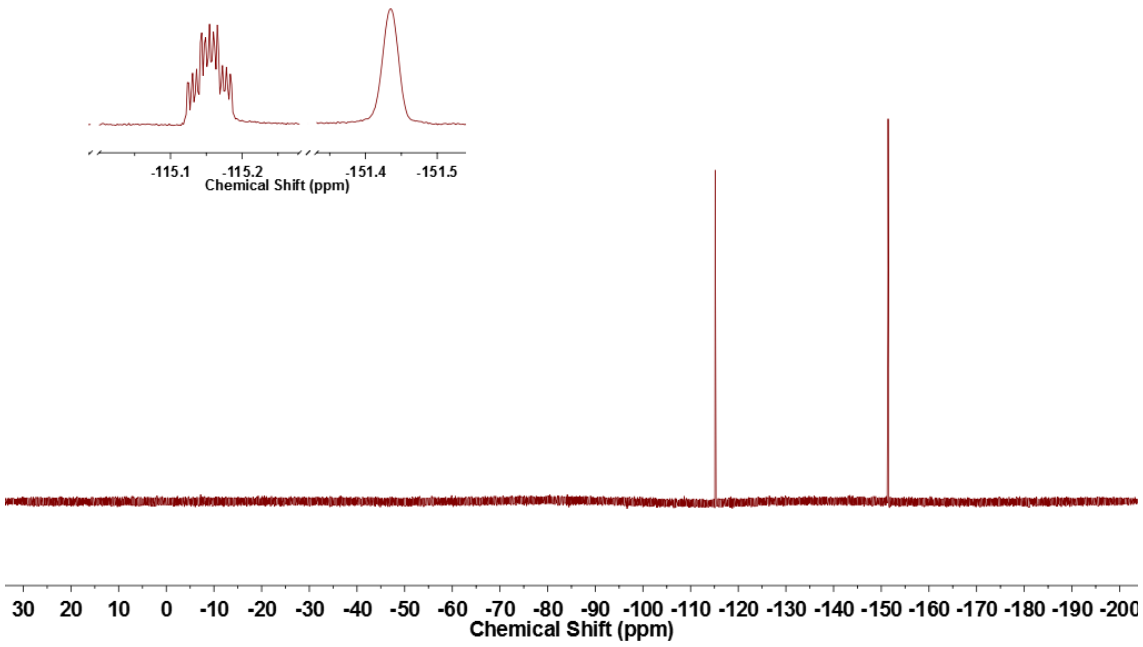
N-Boc-(*R*)-7-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3d**)



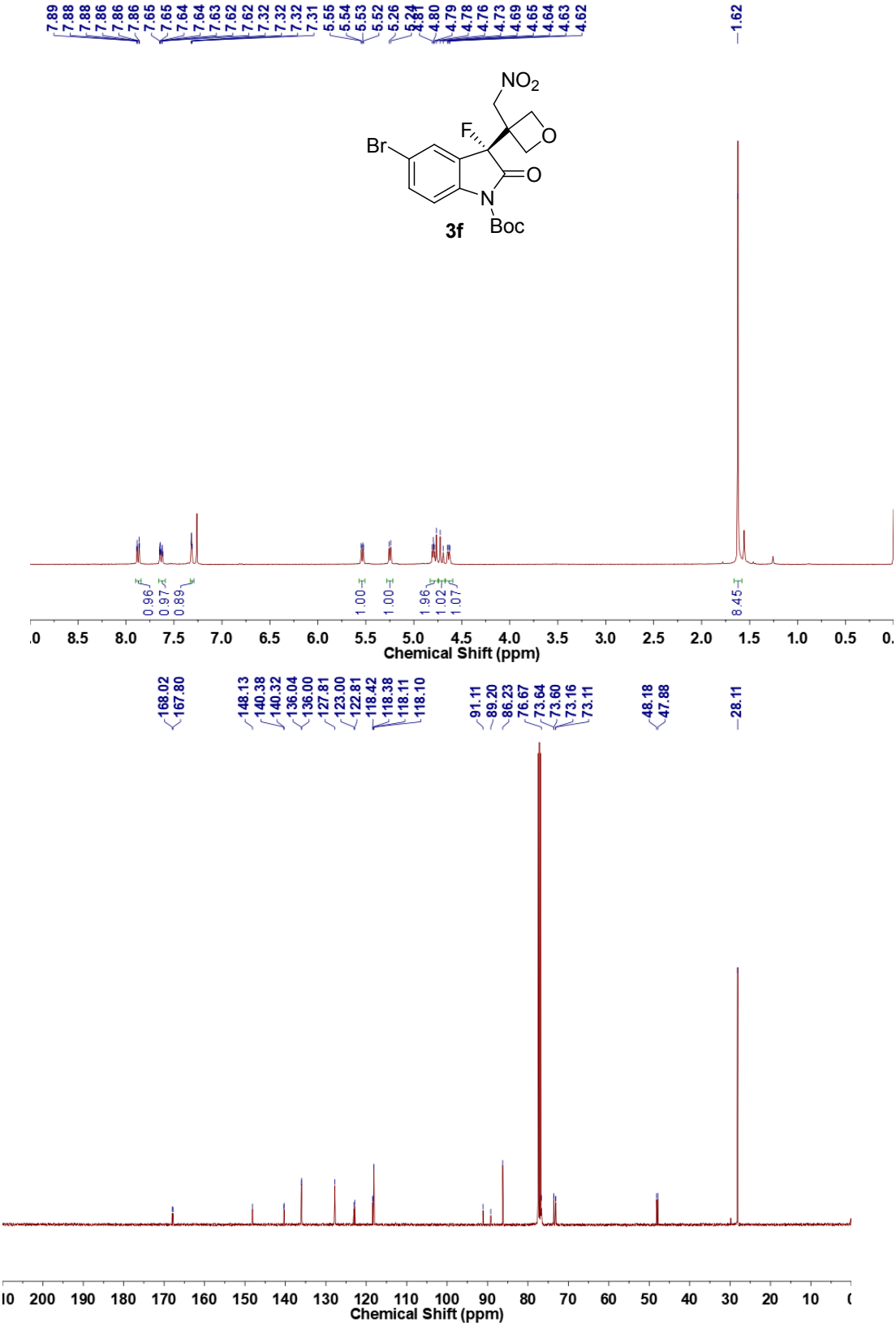

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

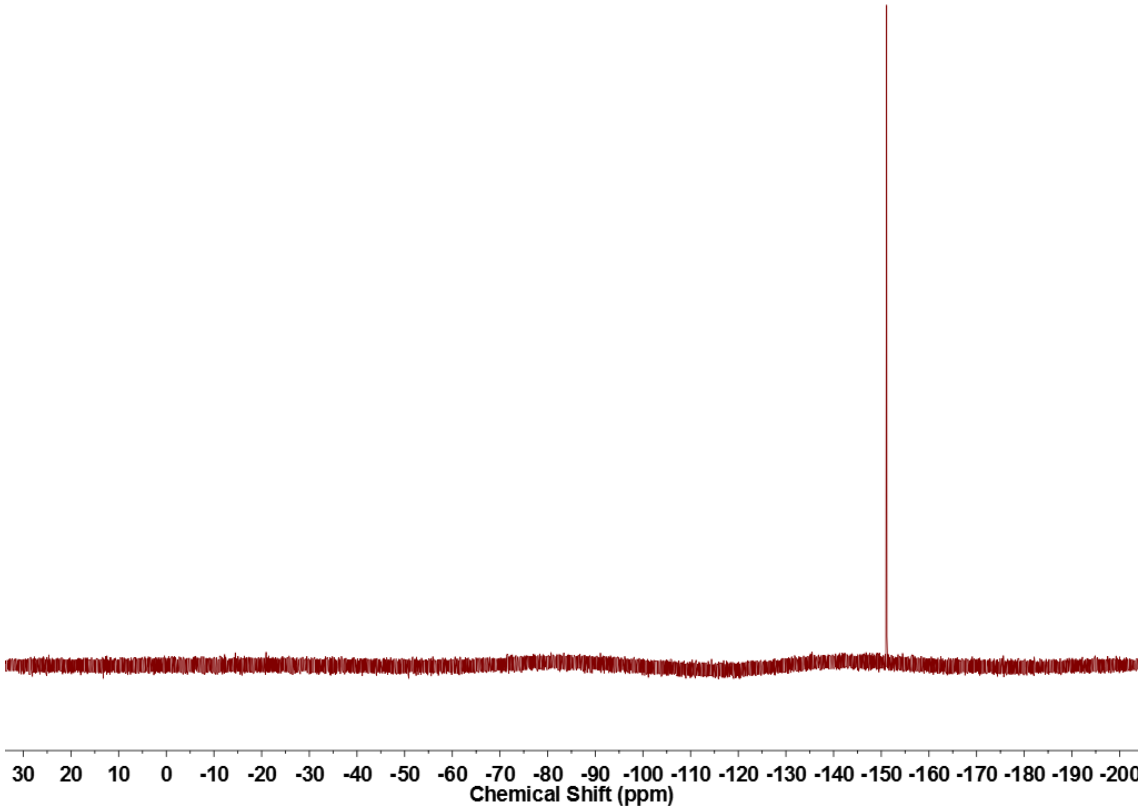
N-Boc-(*R*)-3,5-difluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3e**)



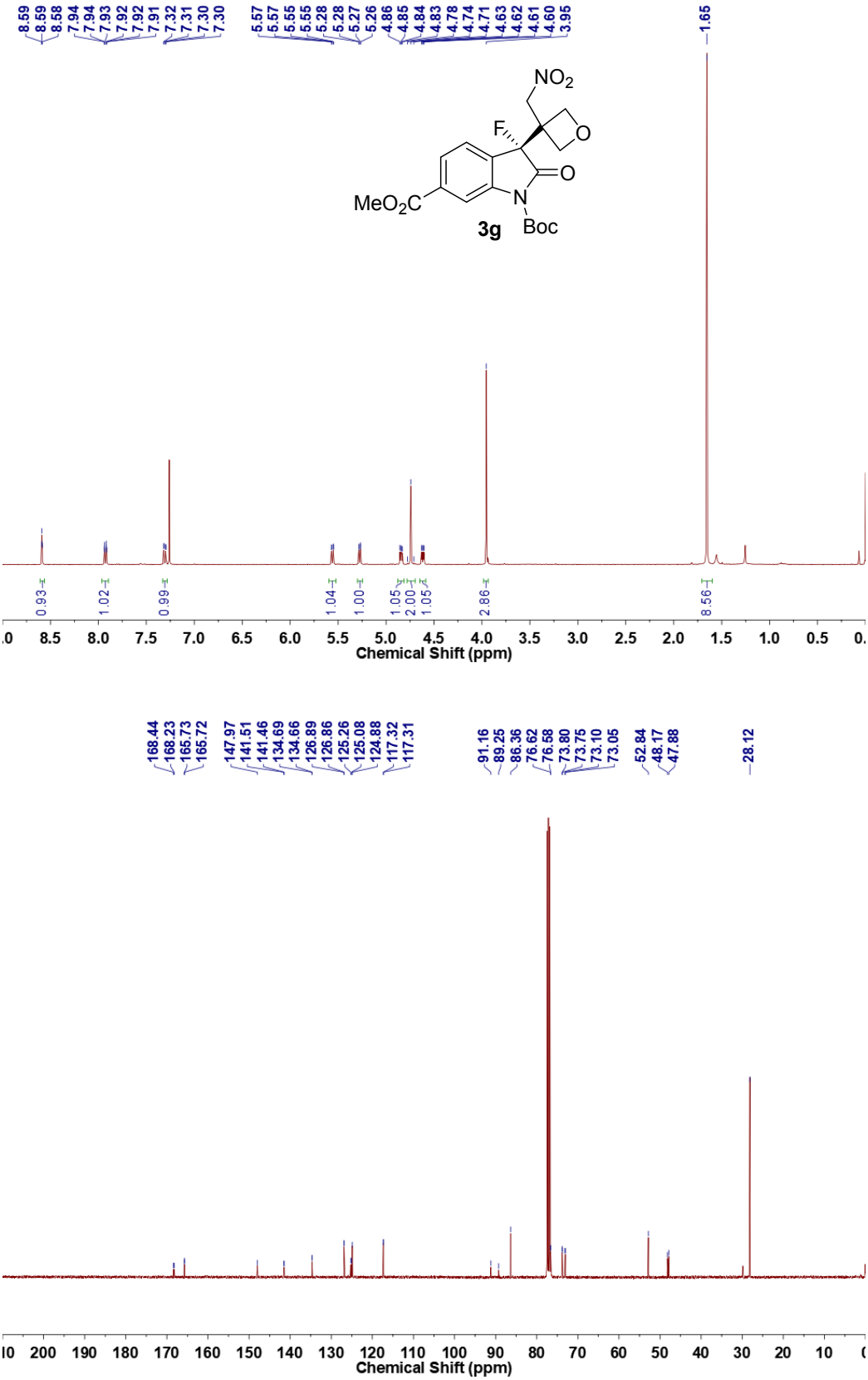

-115.1
-115.2
-151.4
-151.5
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

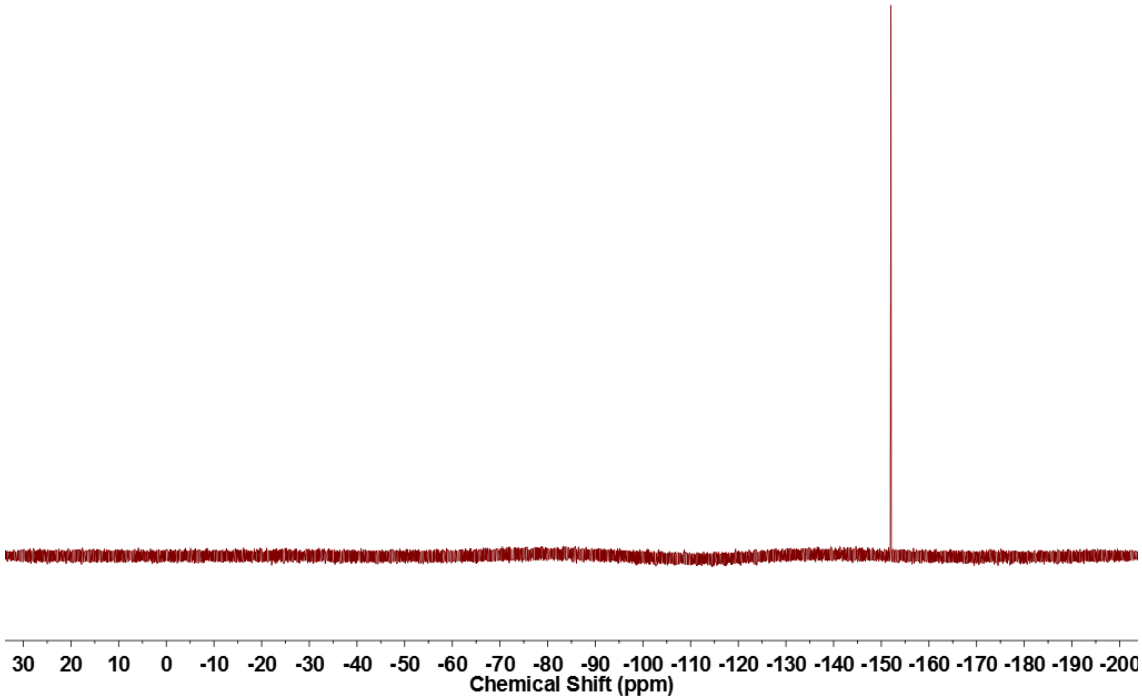
N-Boc-(*R*)-5-bromo-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3f**)



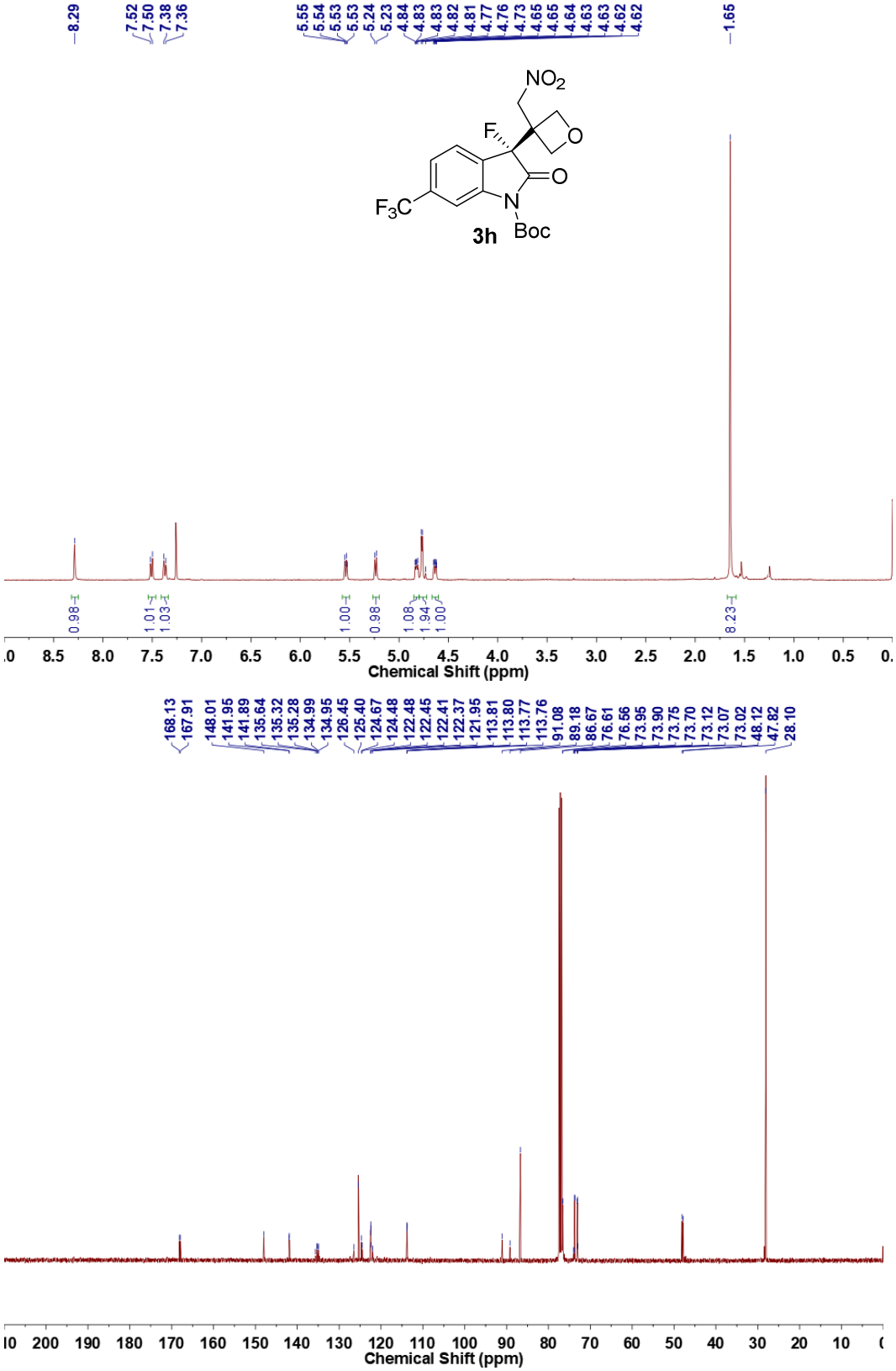

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

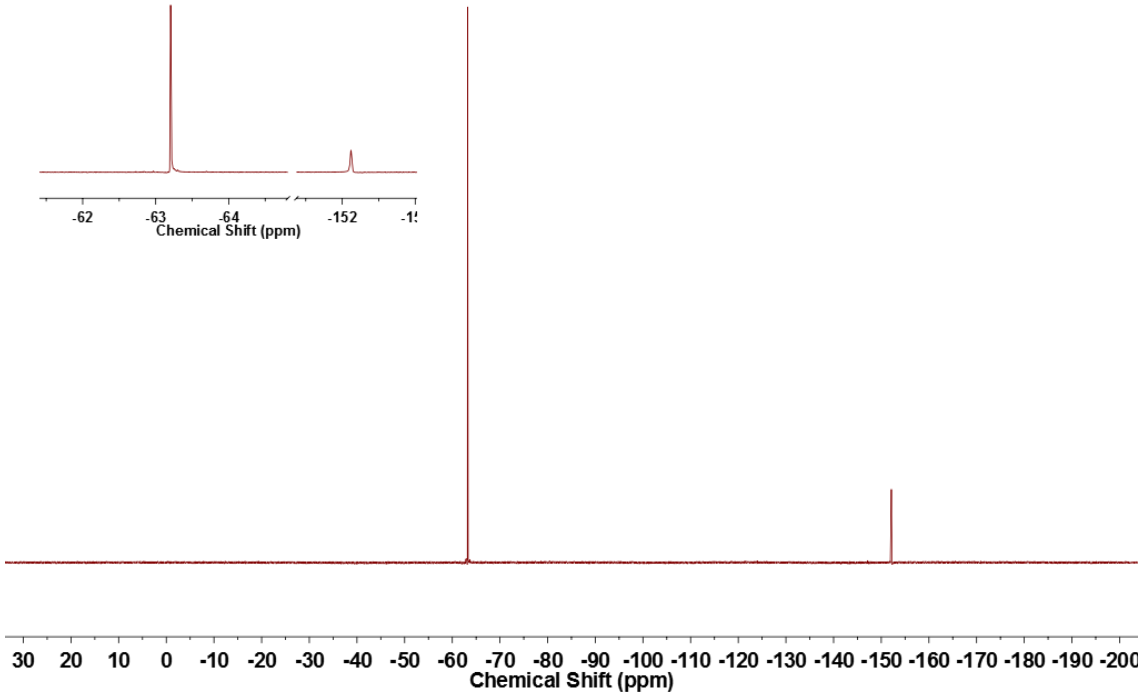
Methyl *N*-Boc-(R)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole-6-carboxylate (**3g**)



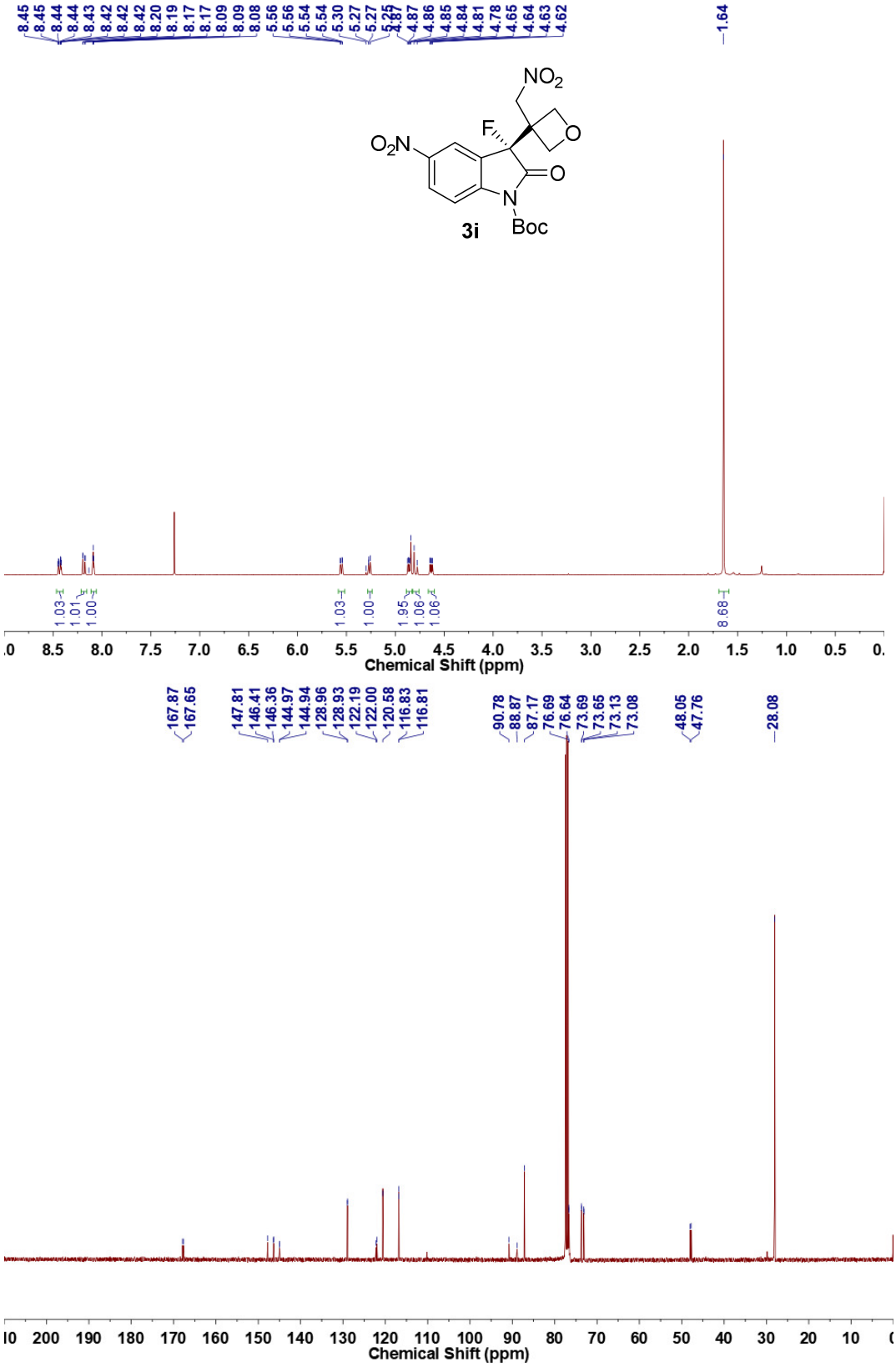

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

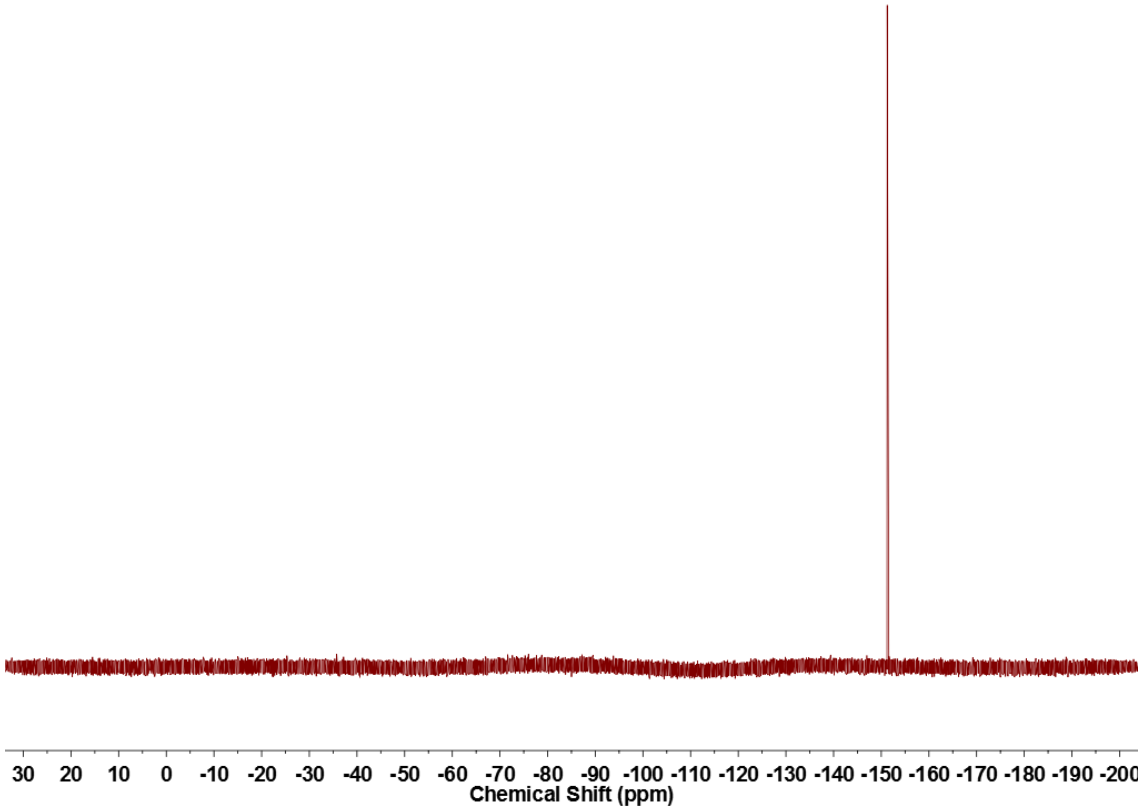
N-Boc-(*R*)-6-trifluoromethyl-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3h**)



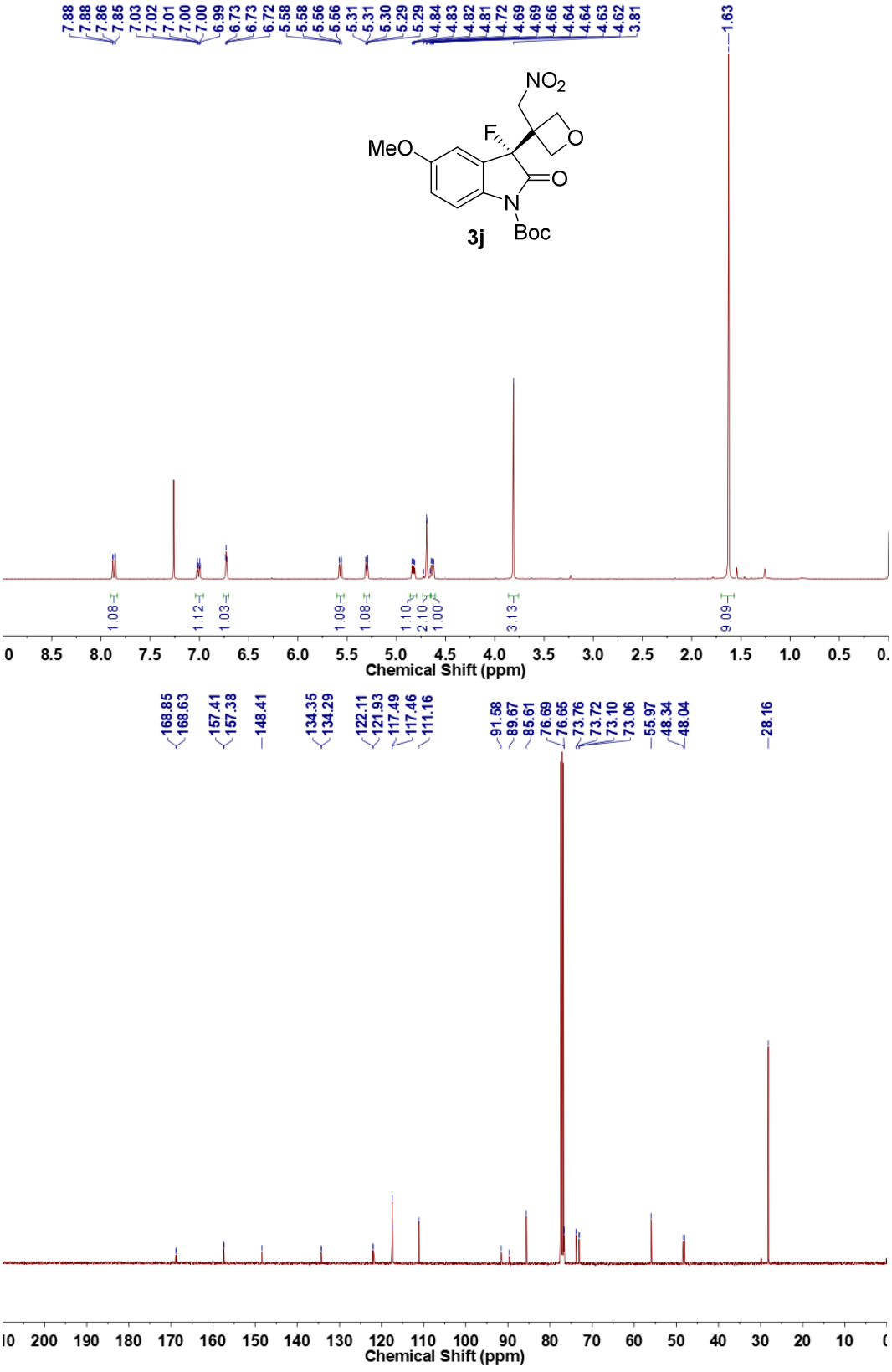

-62
-63
-64
-152
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

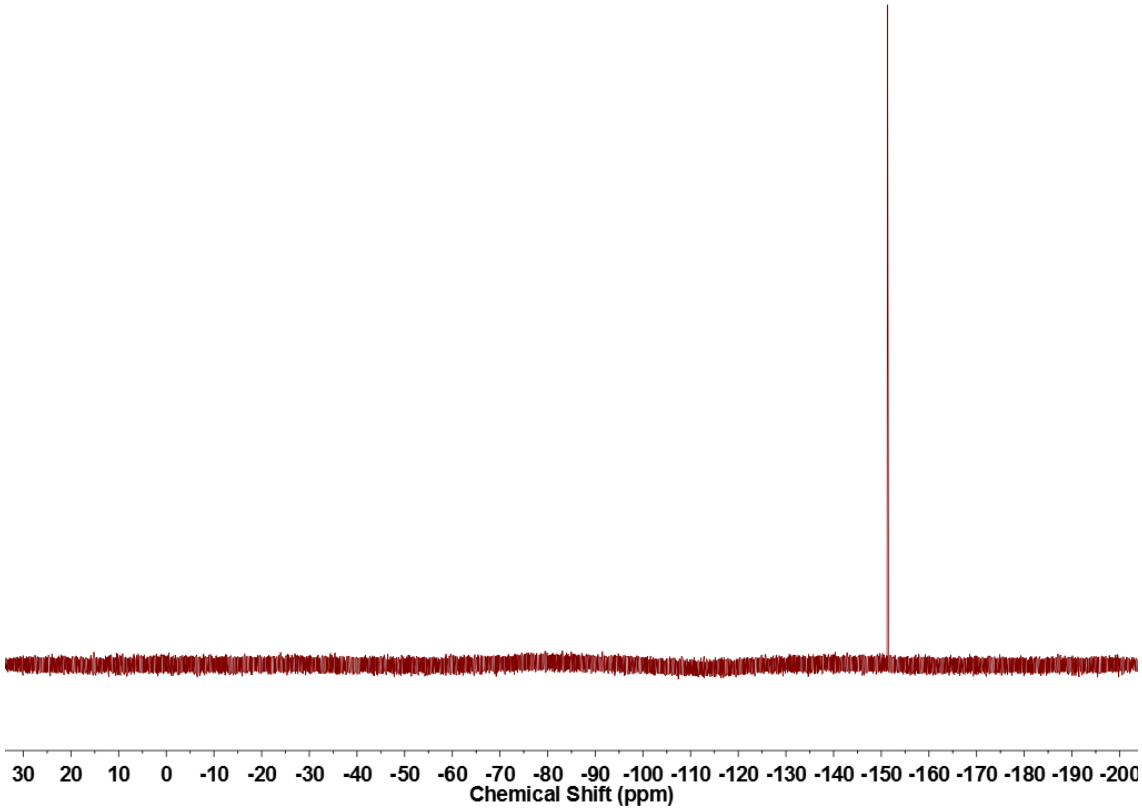
N-Boc-(*R*)-5-nitro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3i**)



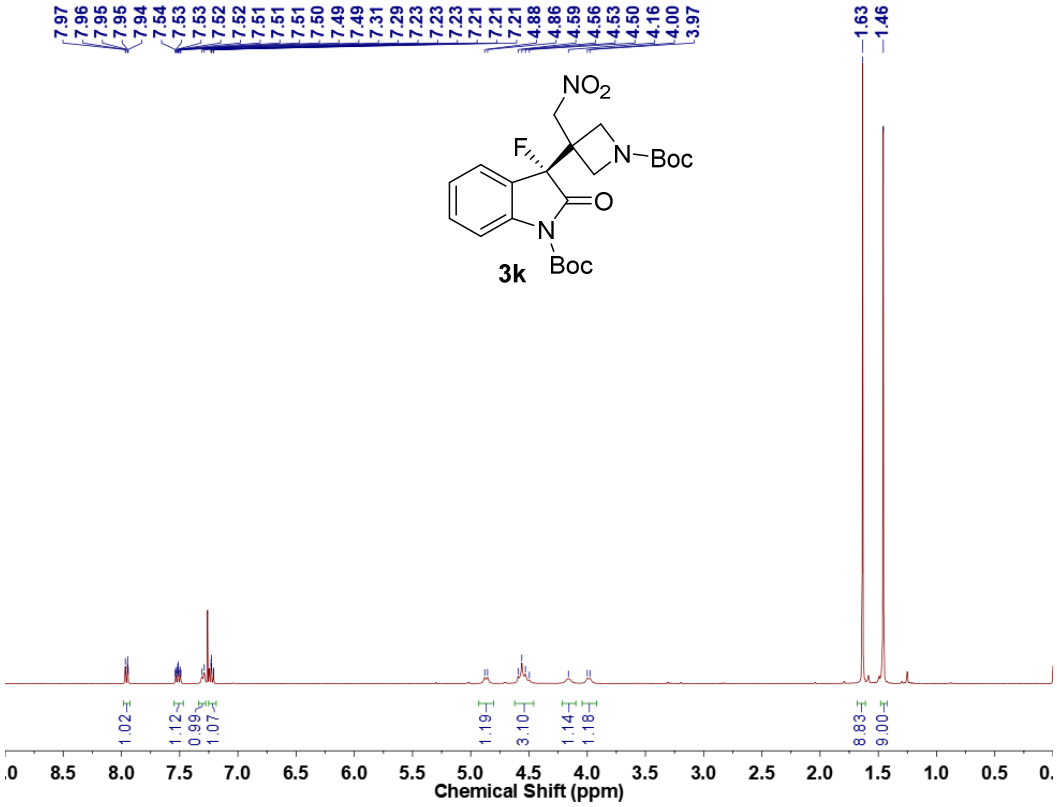

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

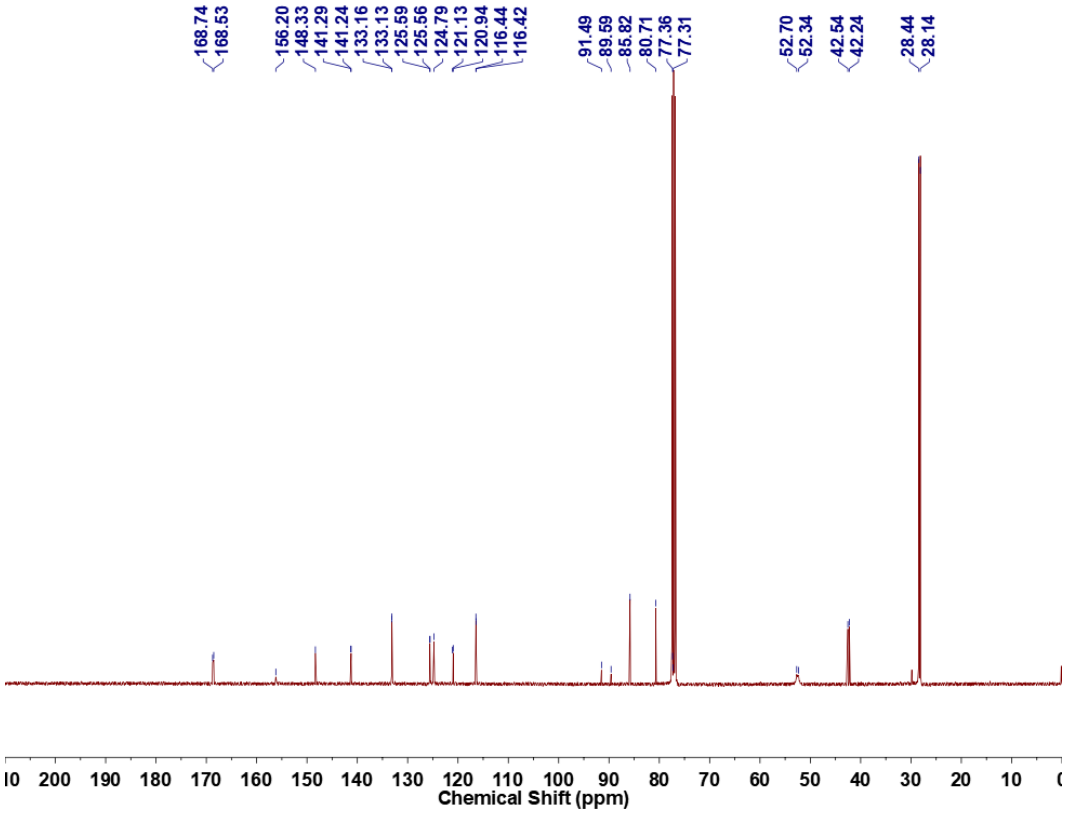
N-Boc-(*R*)-5-methoxy-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3j**)

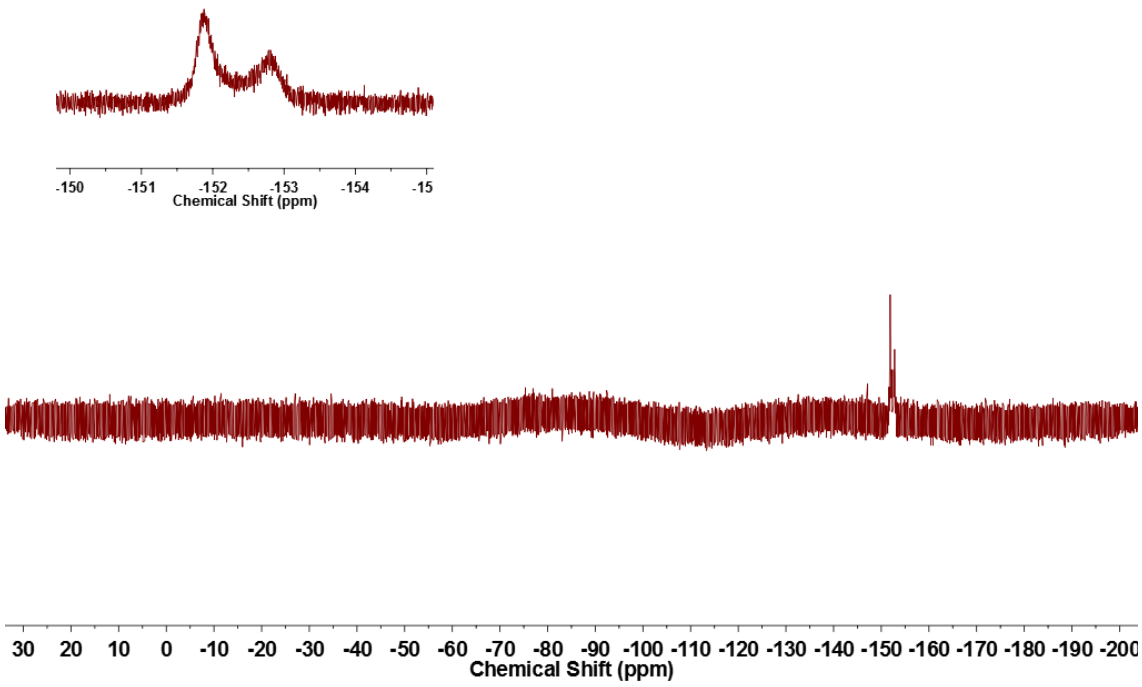



30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

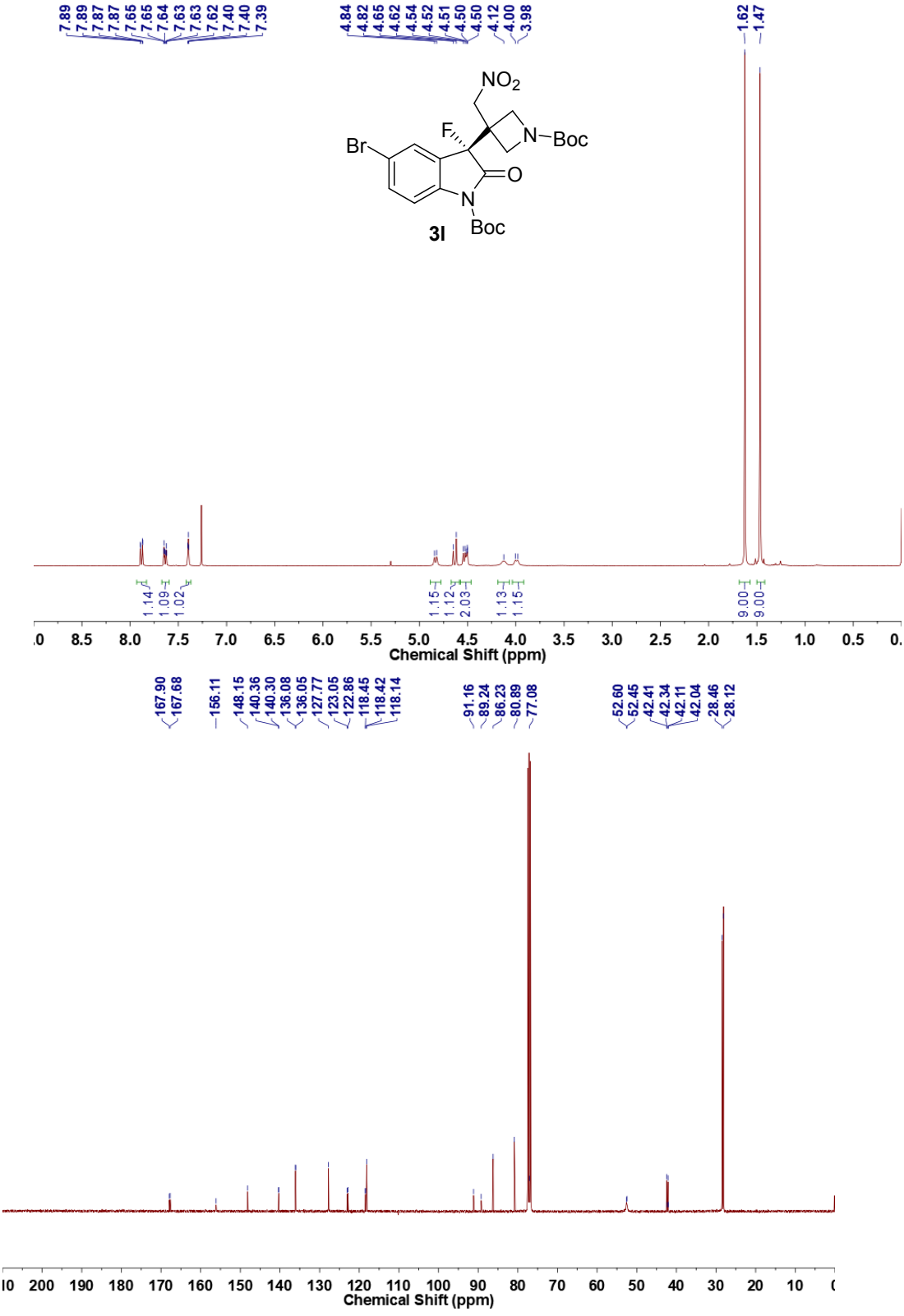
N-Boc-(*S*)-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3k**)

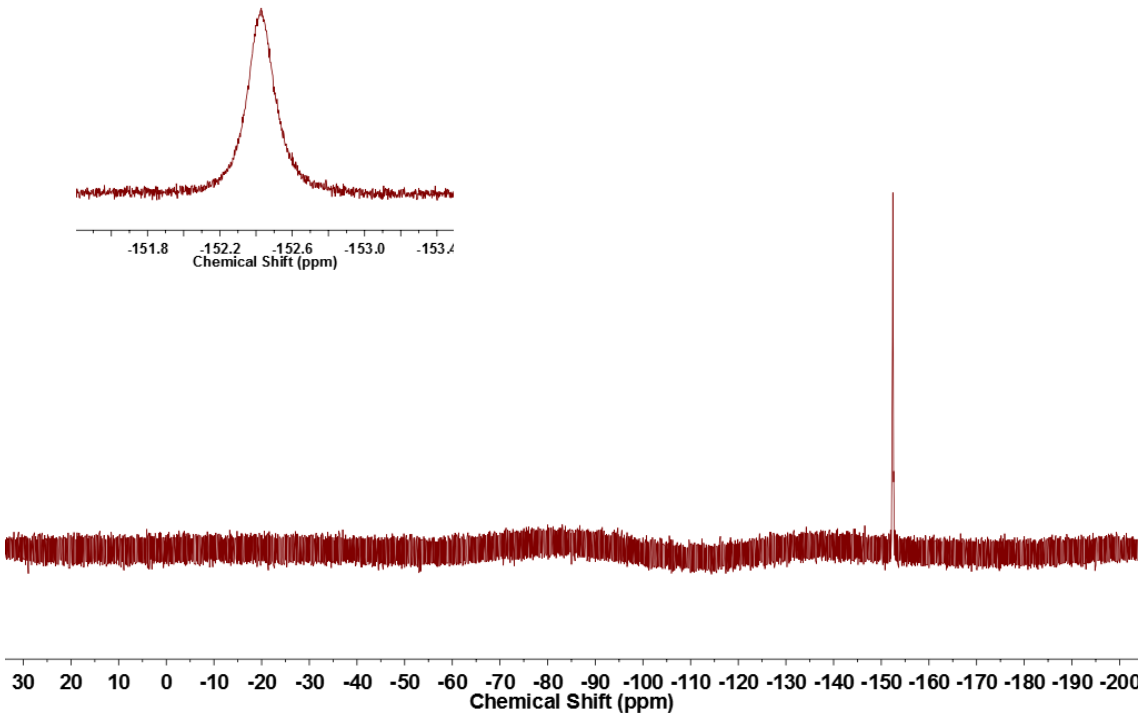




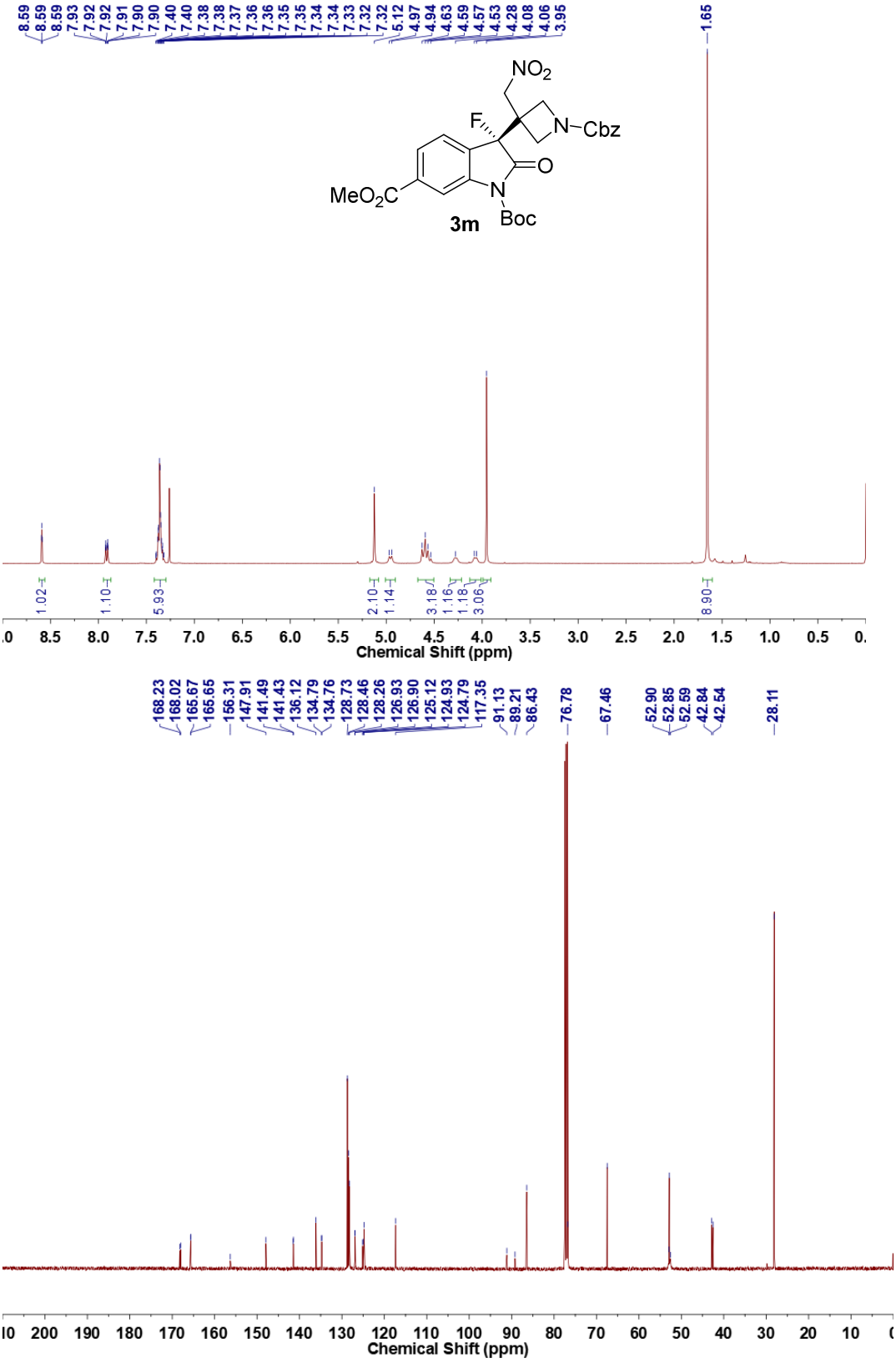

-150
-151
-152
-153
-154
-15
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

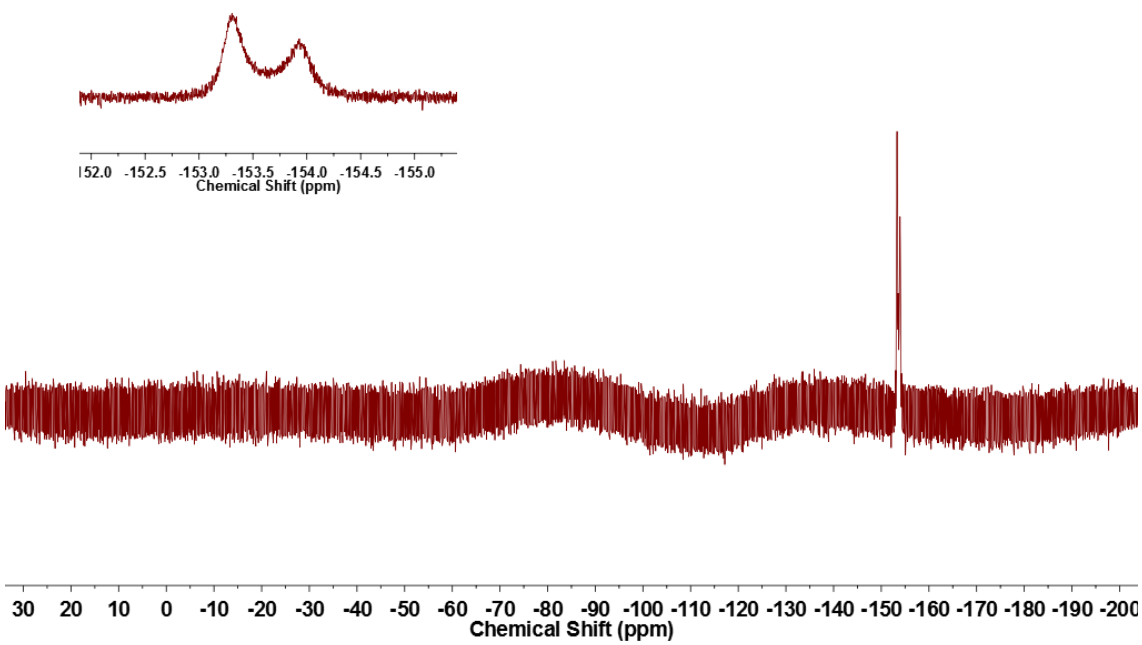
N-Boc-(*S*)-5-bromo-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3l**)



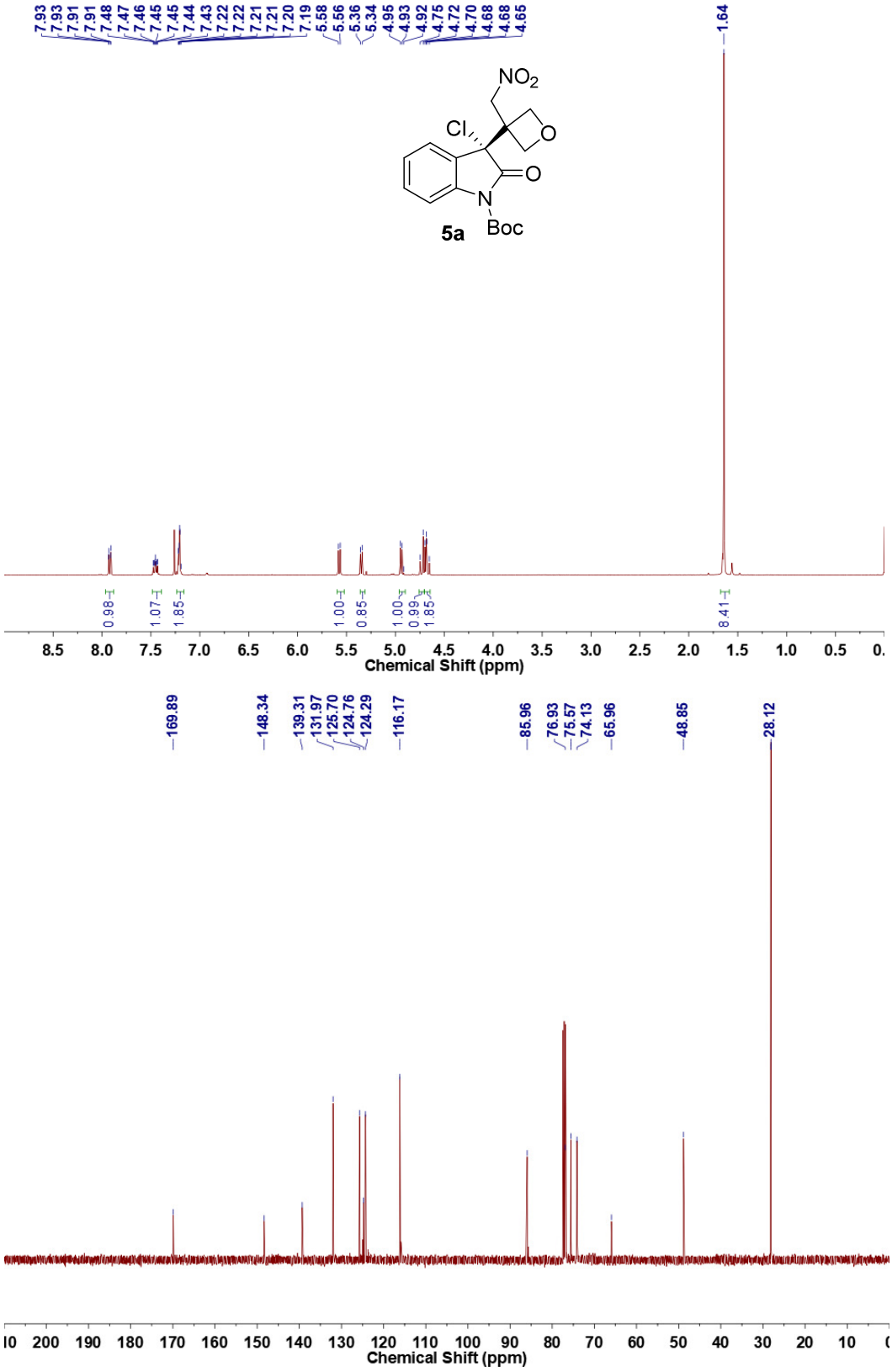

-151.8
-152.2
-152.6
-153.0
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

Methyl *N*-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole-6-carboxylate (**3m**)

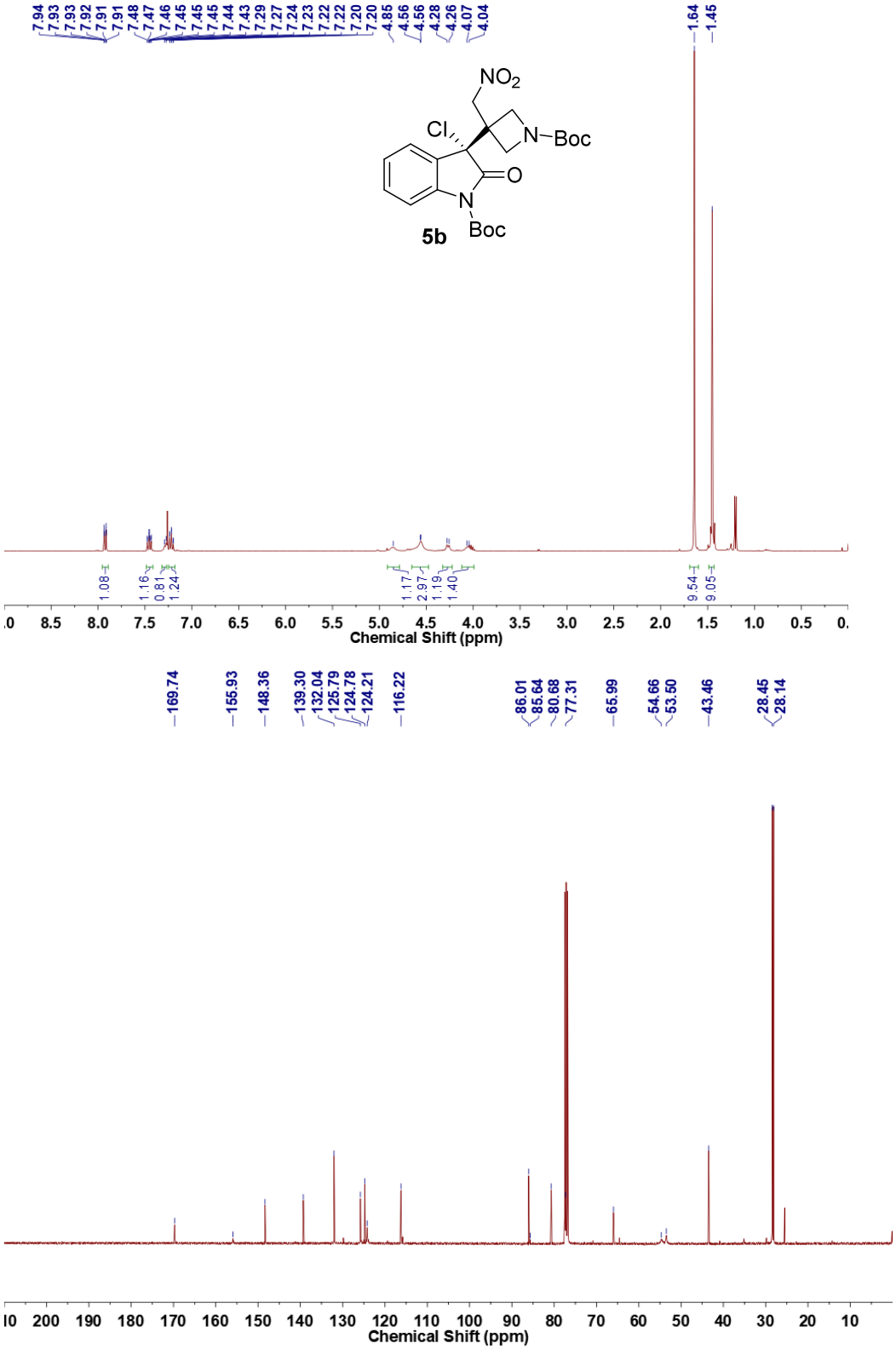



152.0 -152.5 -153.0 -153.5 -154.0 -154.5 -155.0
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

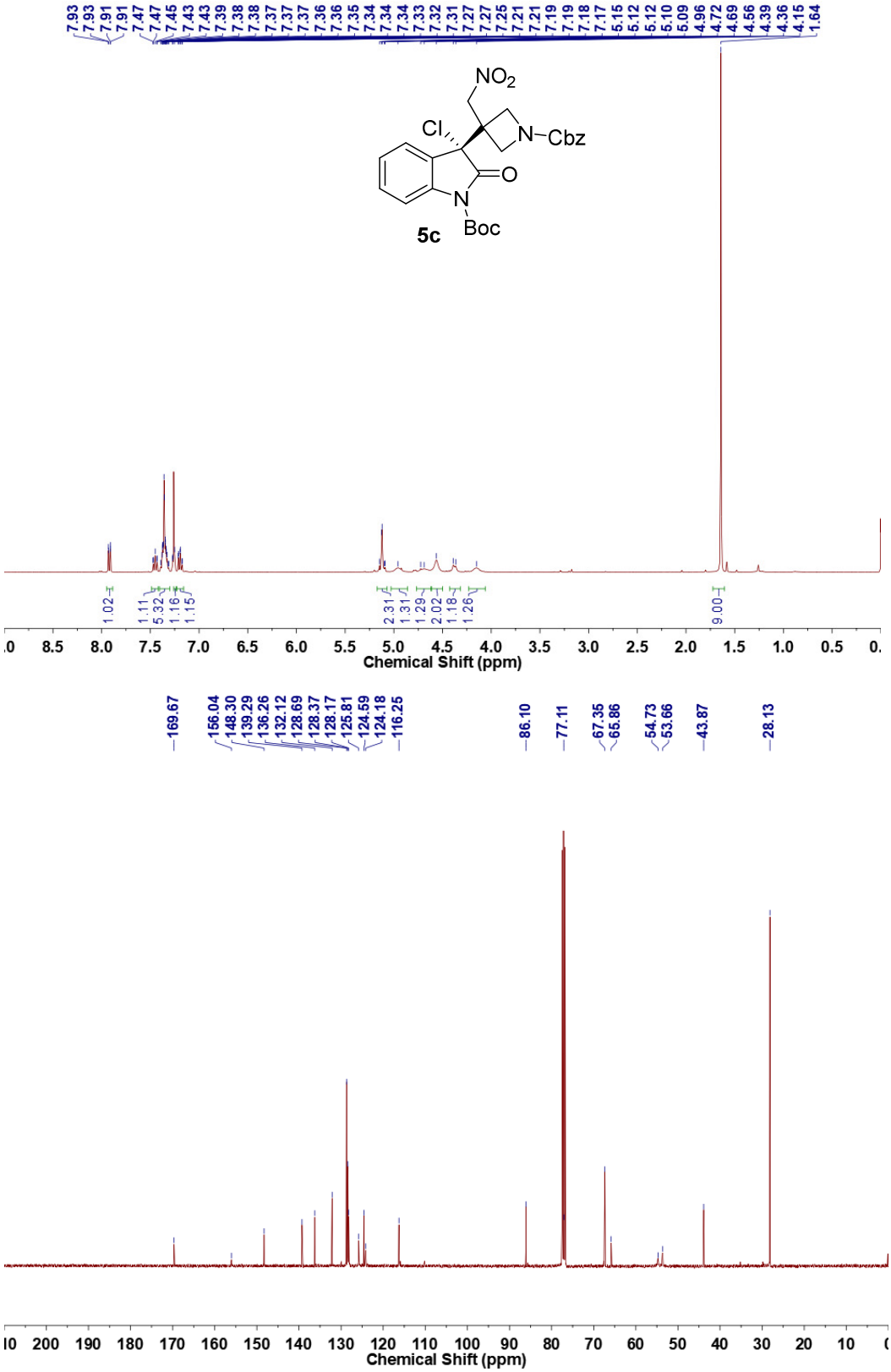
N-Boc-(*R*)-3-chloro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**5a**)



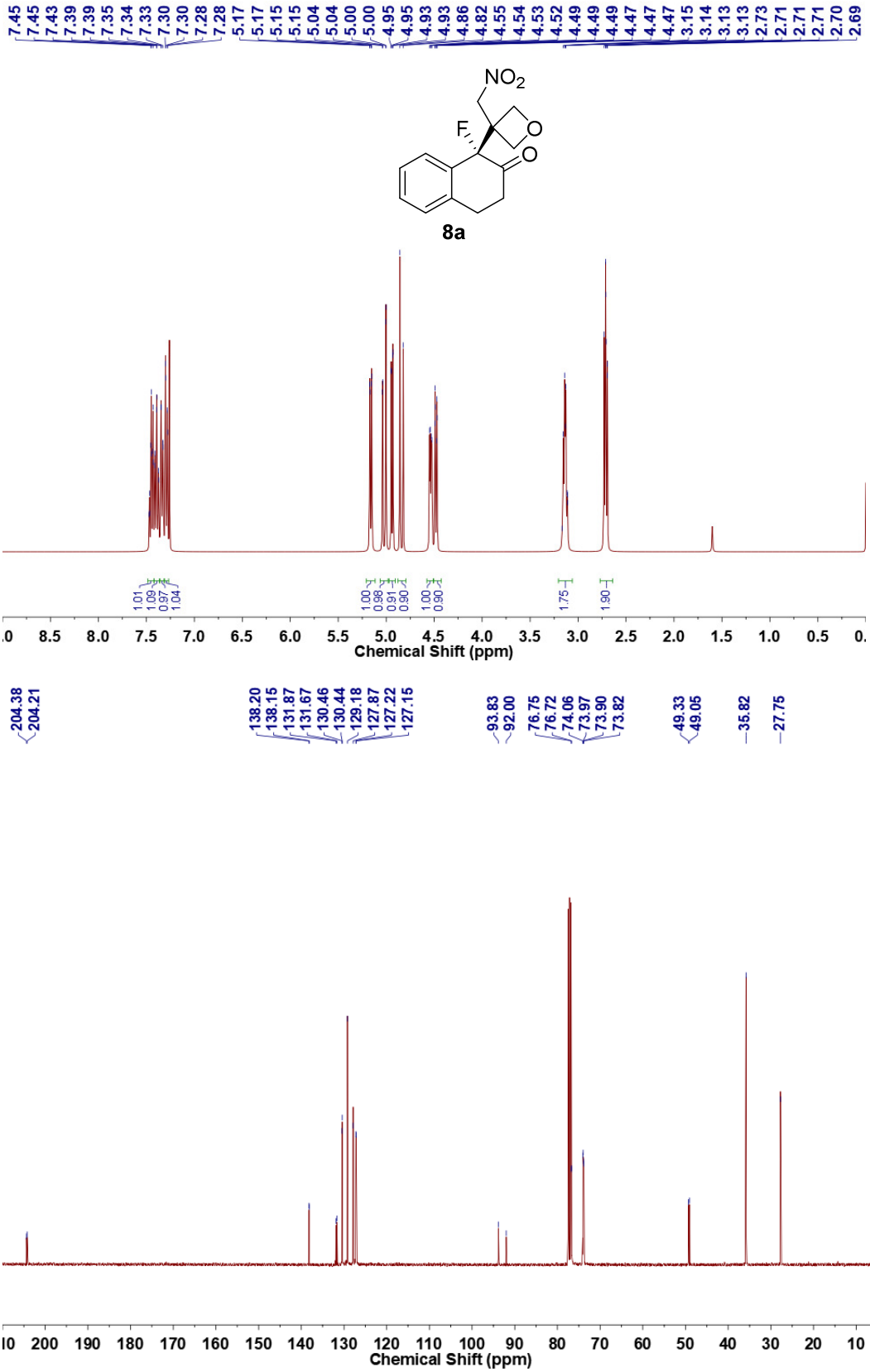
N-Boc-(*S*)-3-chloro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5b**)

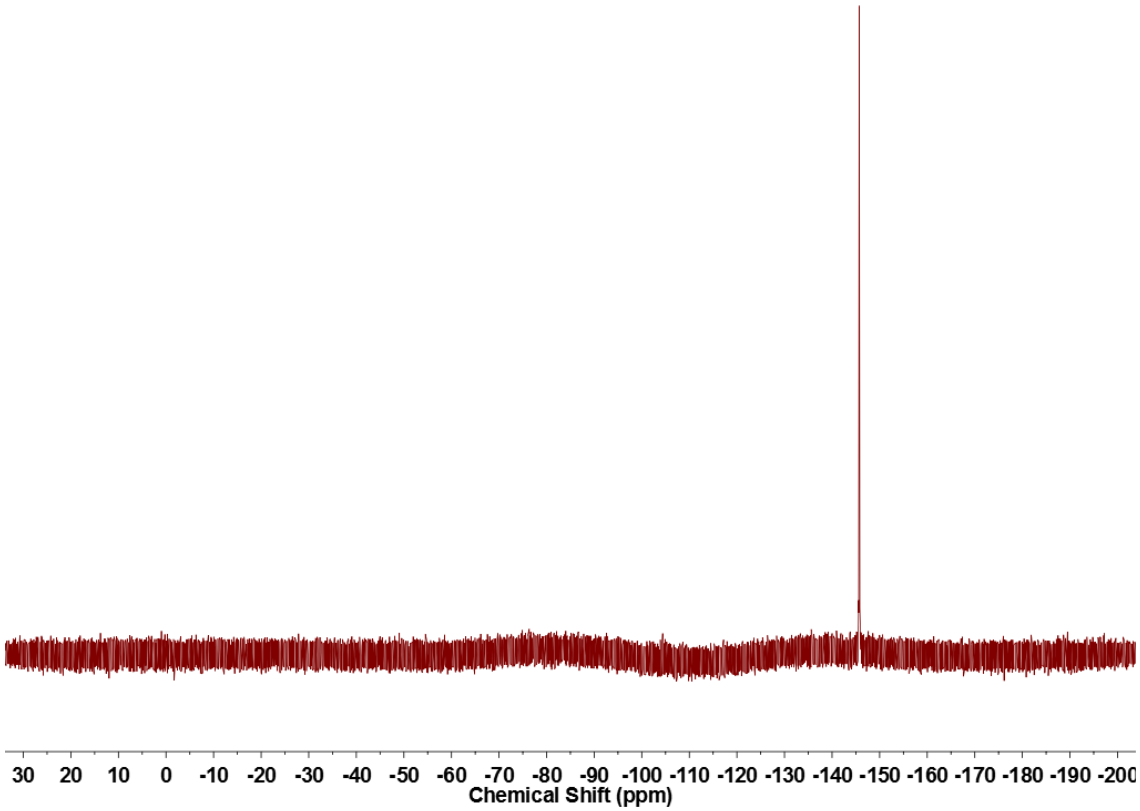


N-Boc-(*S*)-3-chloro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5c**)

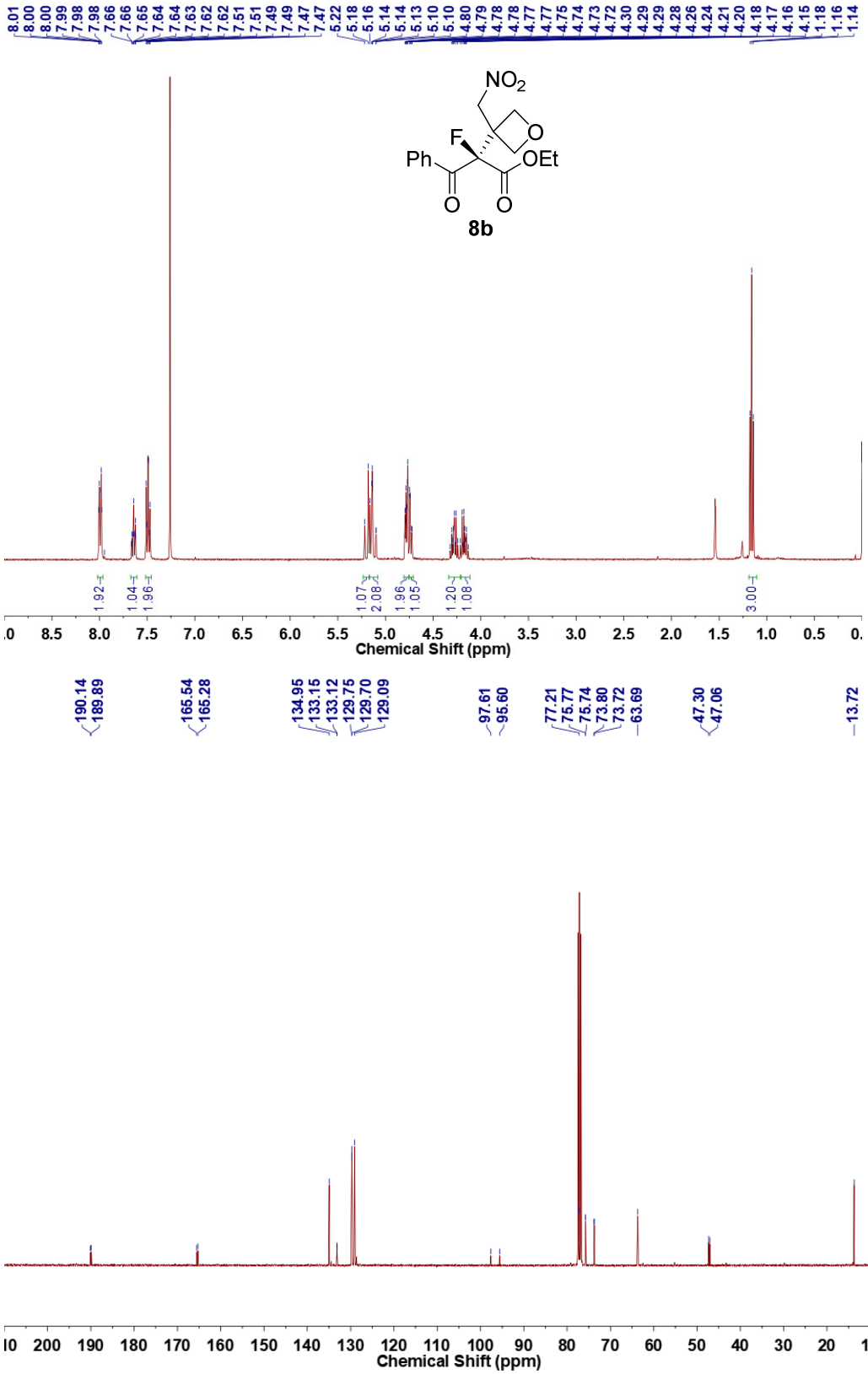


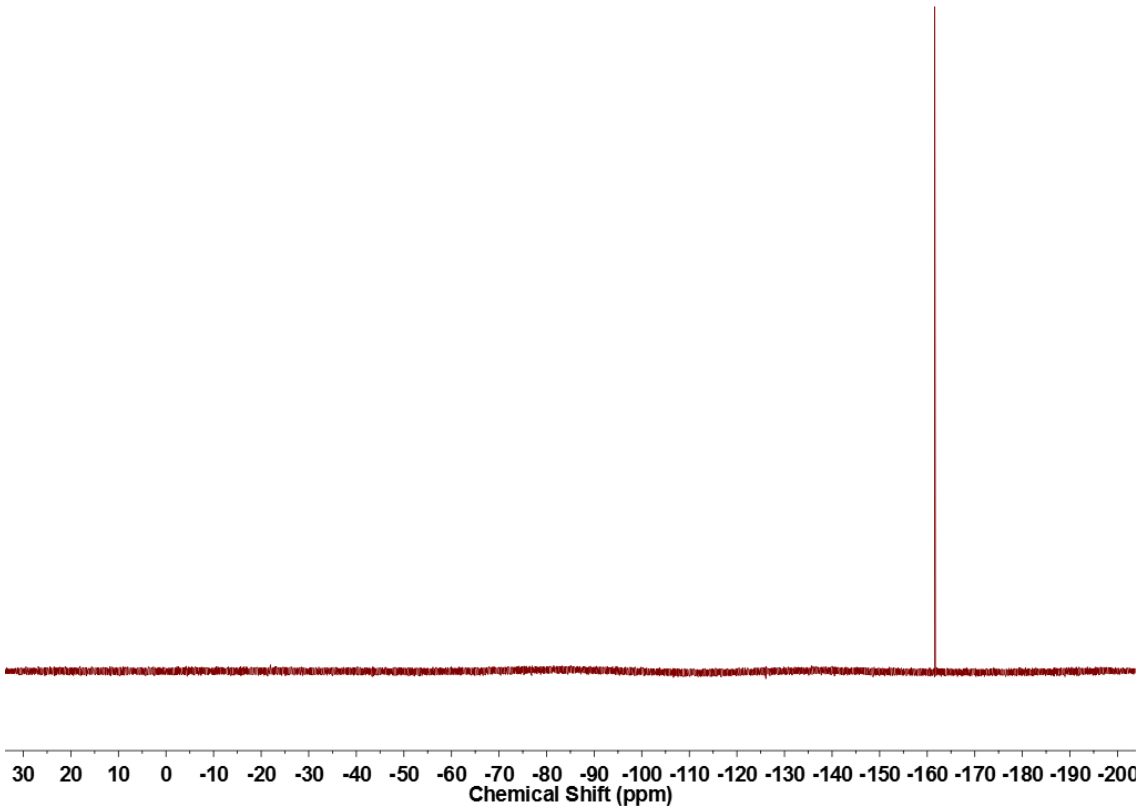
(*R*)-1-Fluoro-1-(3-(nitromethyl)oxetan-3-yl)-3,4-dihydronaphthalen-2(1H)-one (**8a**)



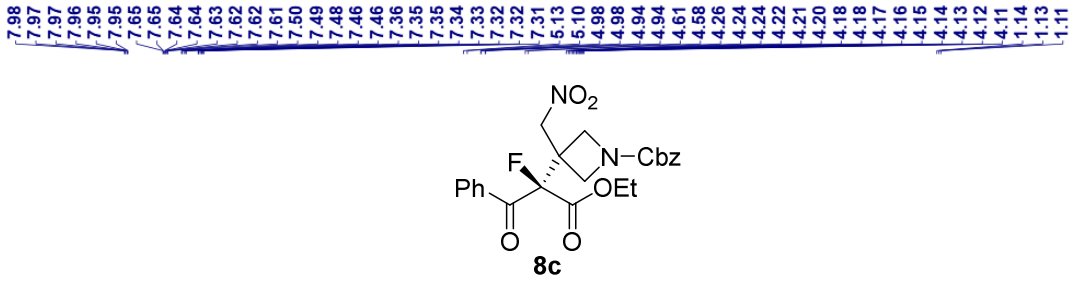

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

Ethyl (*R*)-2-fluoro-2-(3-(nitromethyl)oxetan-3-yl)-3-oxo-3-phenylpropanoate (**8b**)

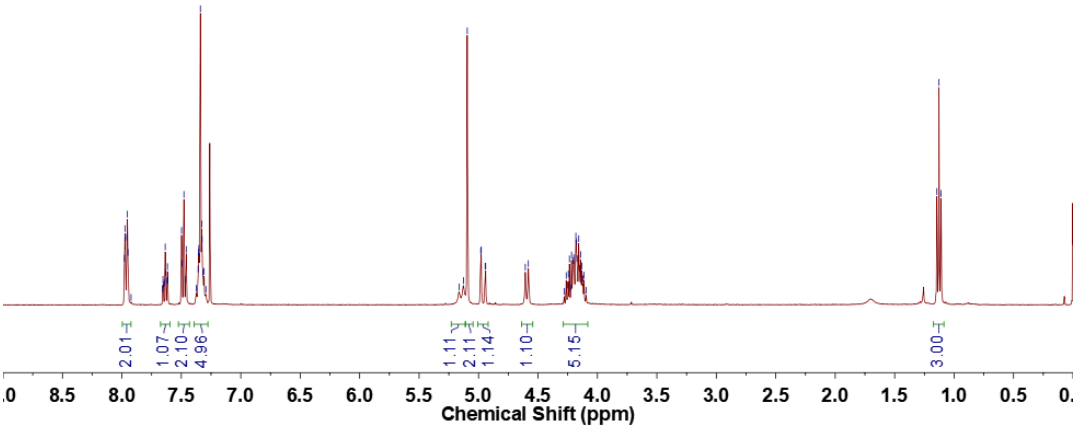


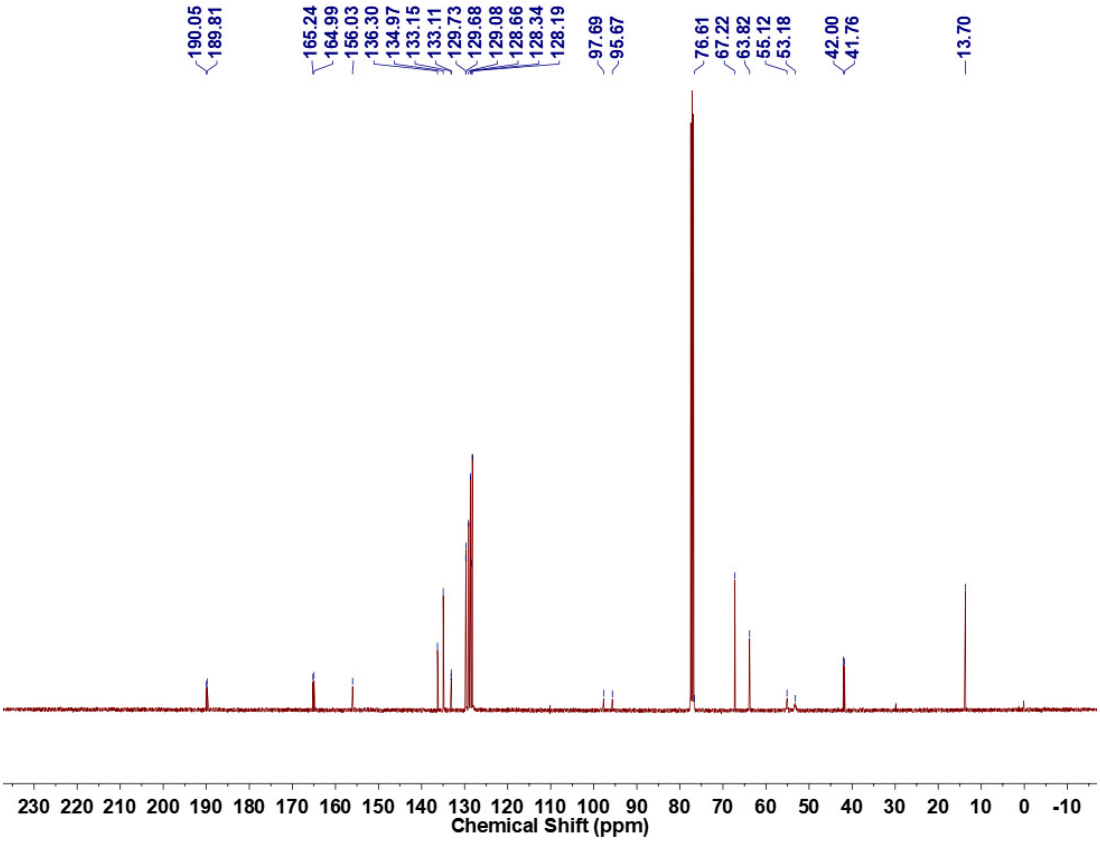

30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

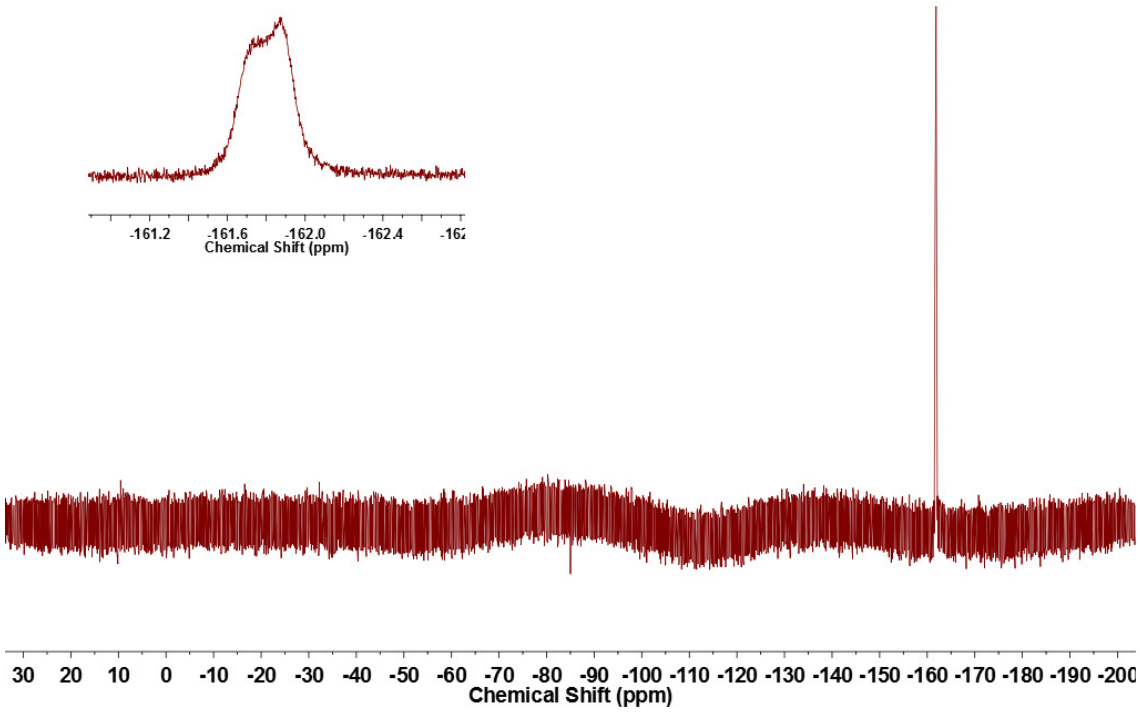
Ethyl (*R*)-2-fluoro-2-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8c**)



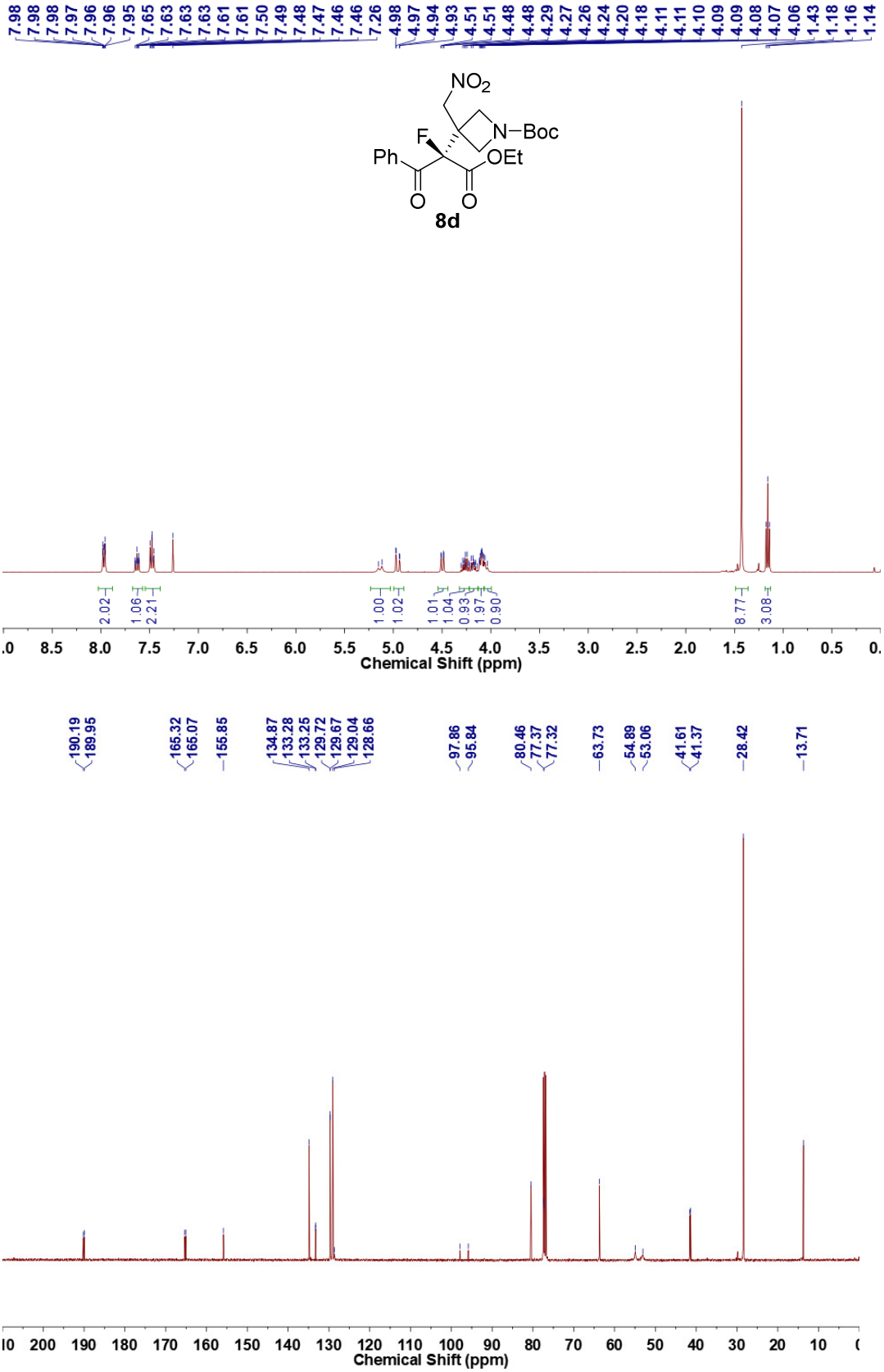
8c

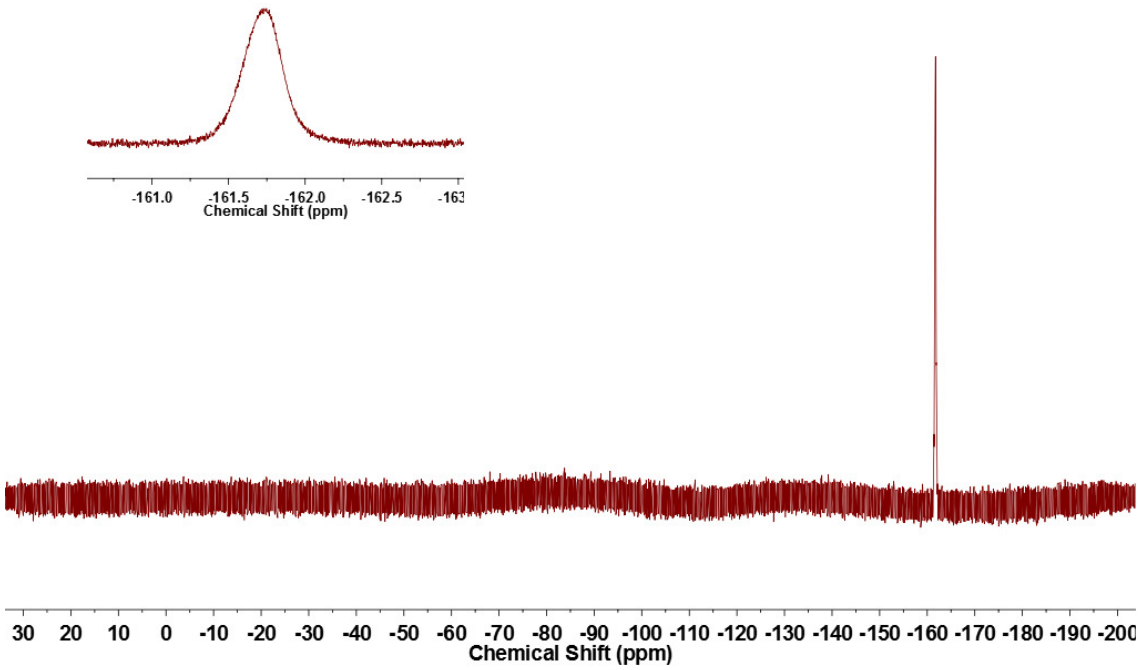




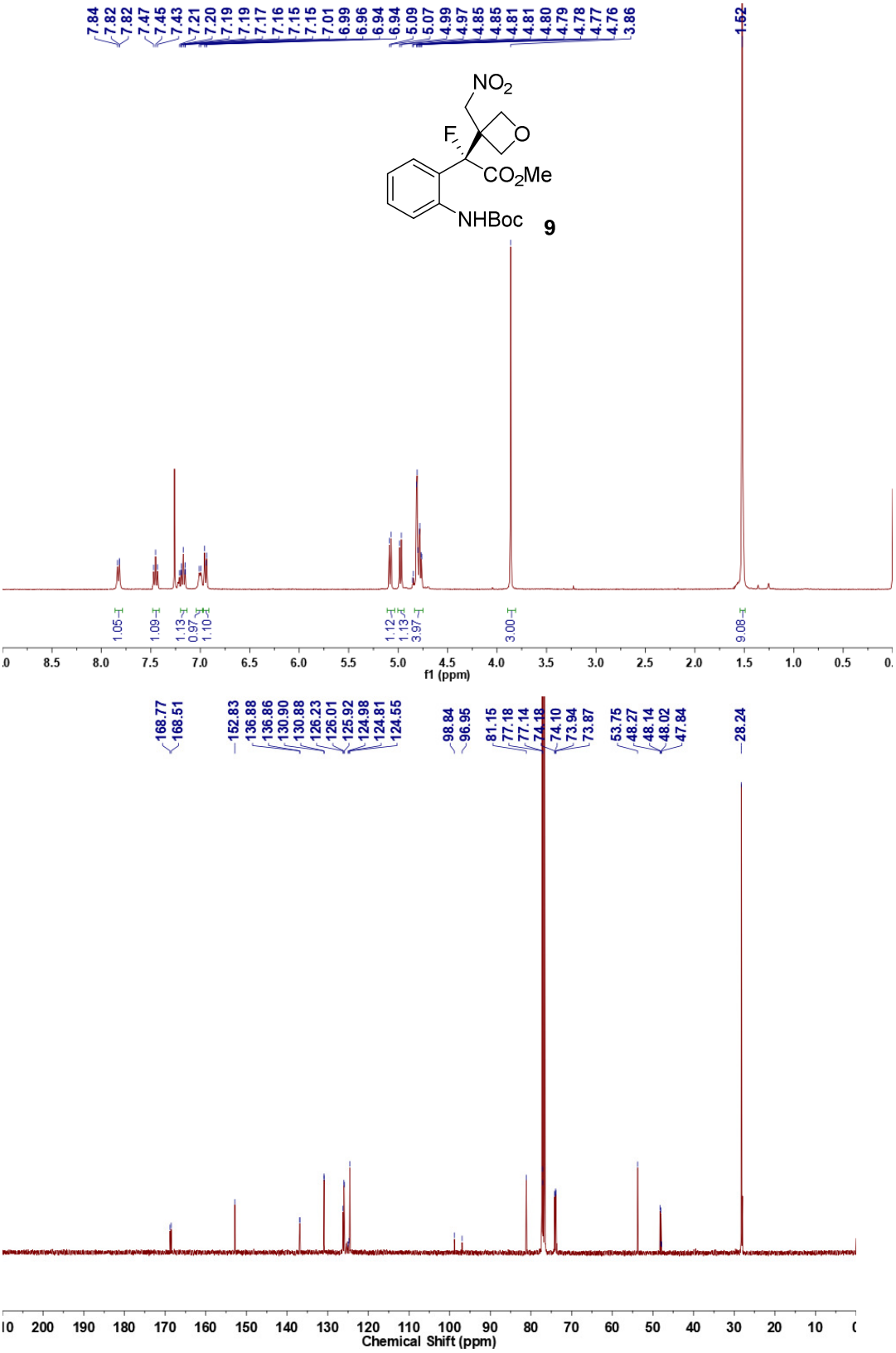

-161.2
-161.6
-162.0
-162.4
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

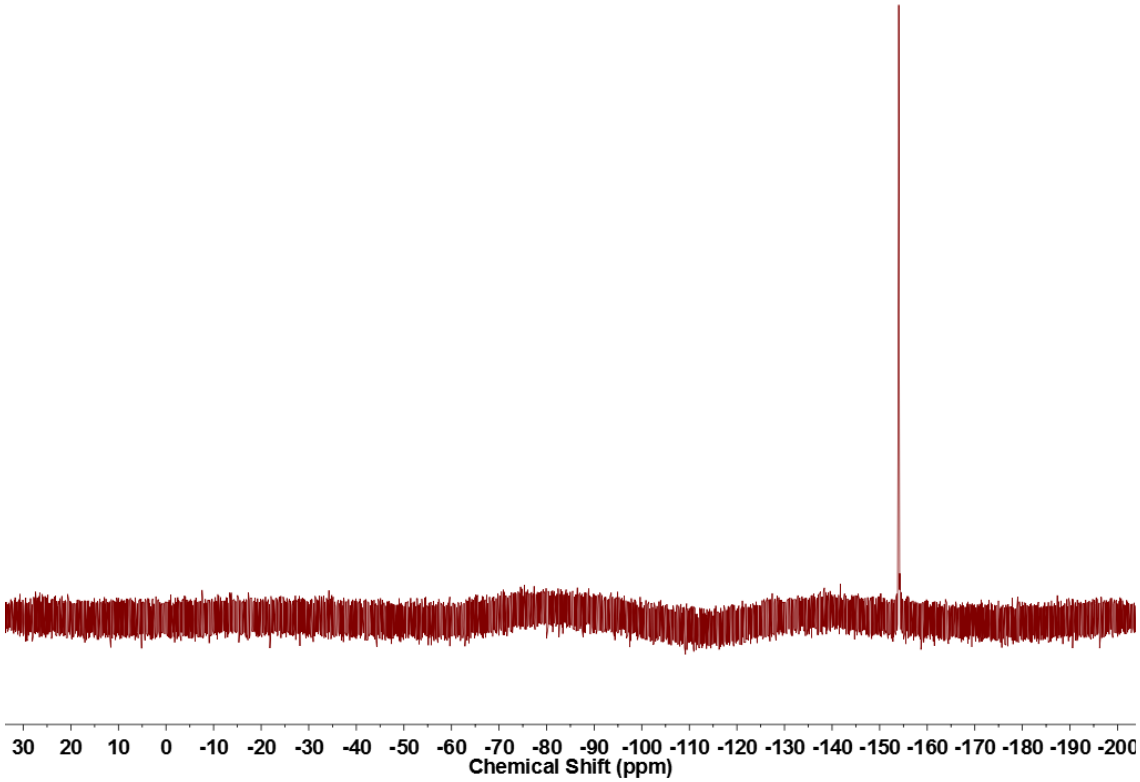
Ethyl (*R*)-2-fluoro-2-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8d**)



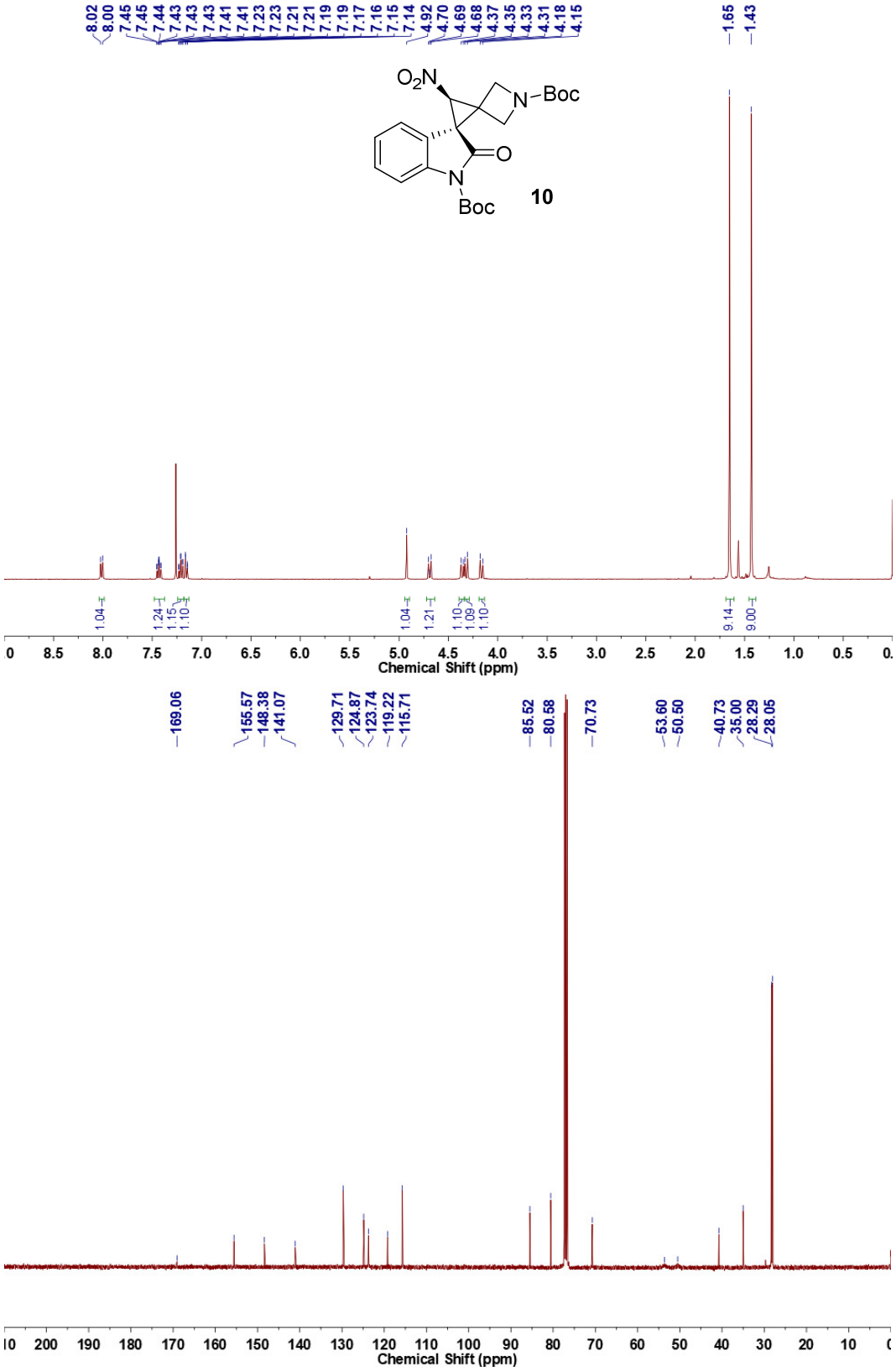

-161.0
-161.5
-162.0
-162.5
Chemical Shift (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

Methyl (R)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-fluoro-2-(3 (nitromethyl)oxetan-3-yl)acetate (**9**)

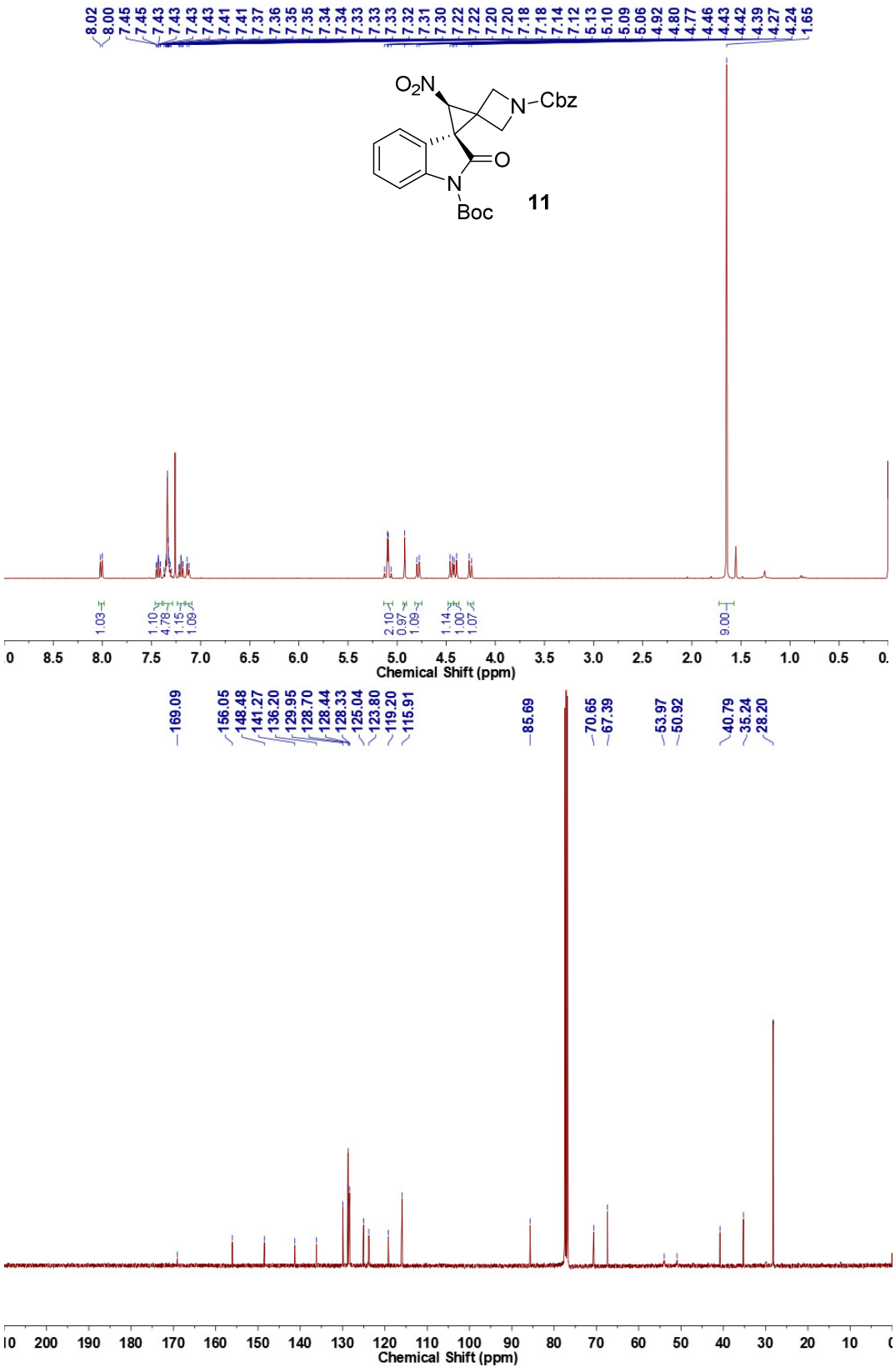



30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

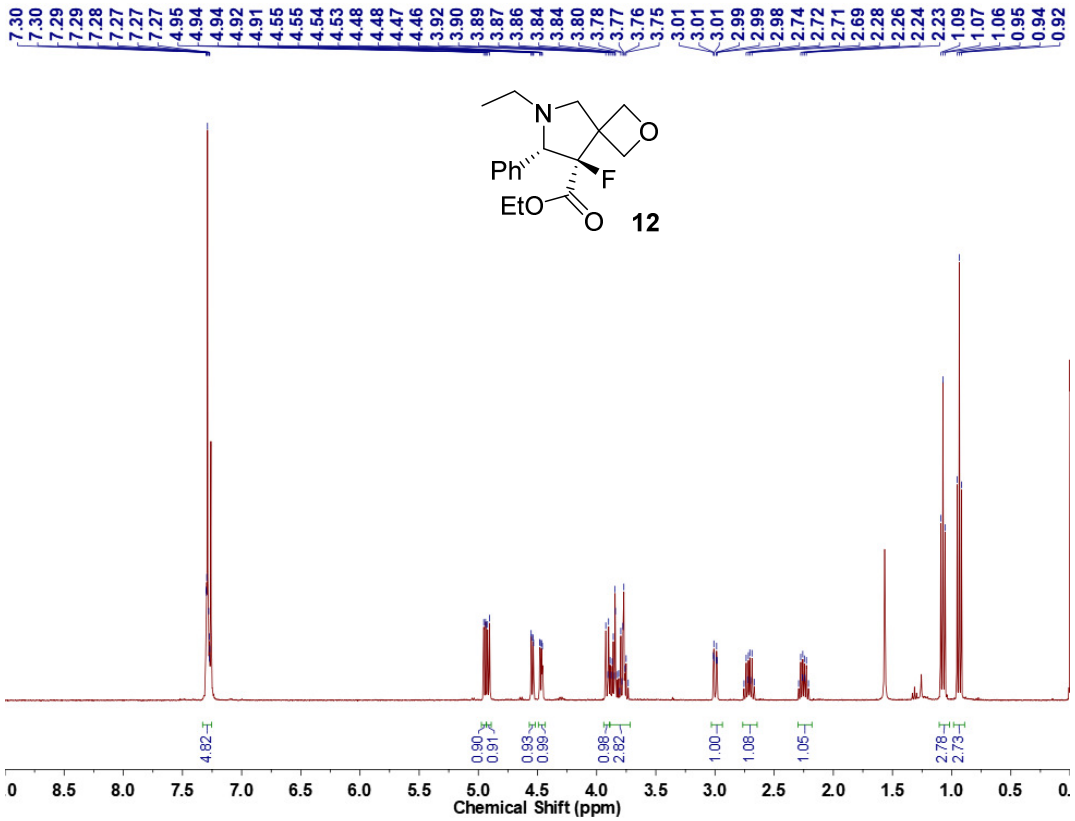
Di-*tert*-butyl (2'*S*,3'*S*)-3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**10**)

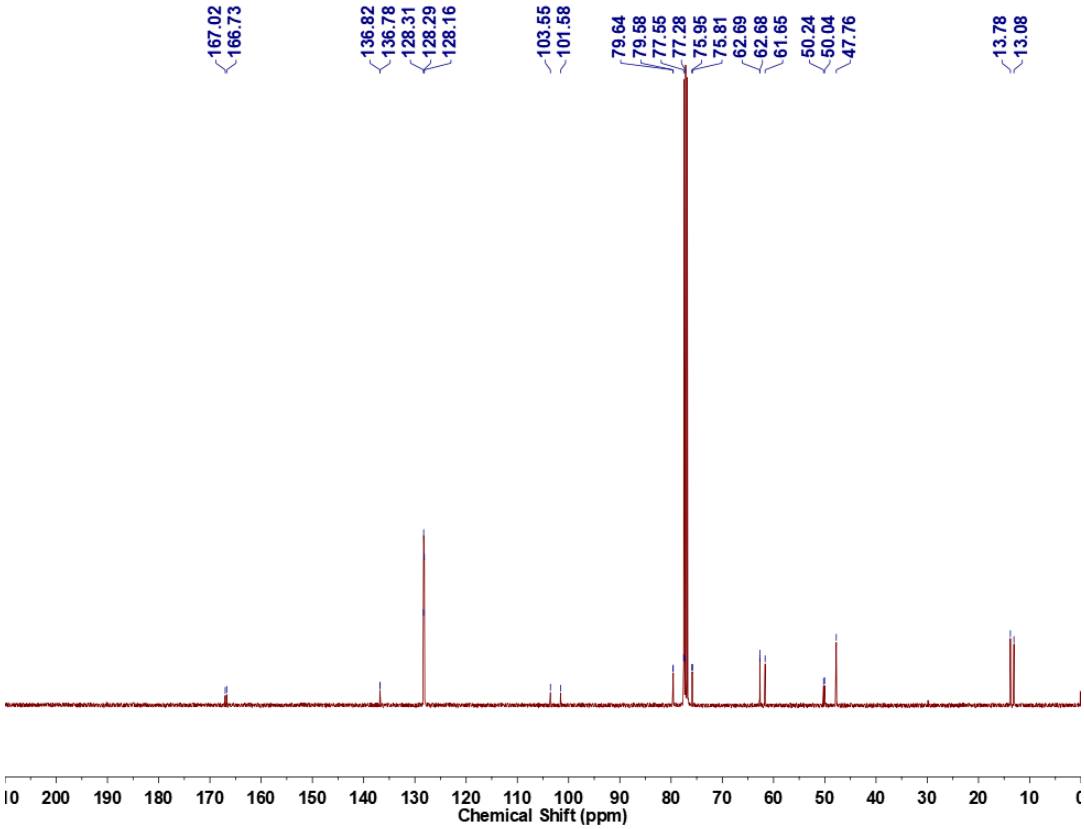


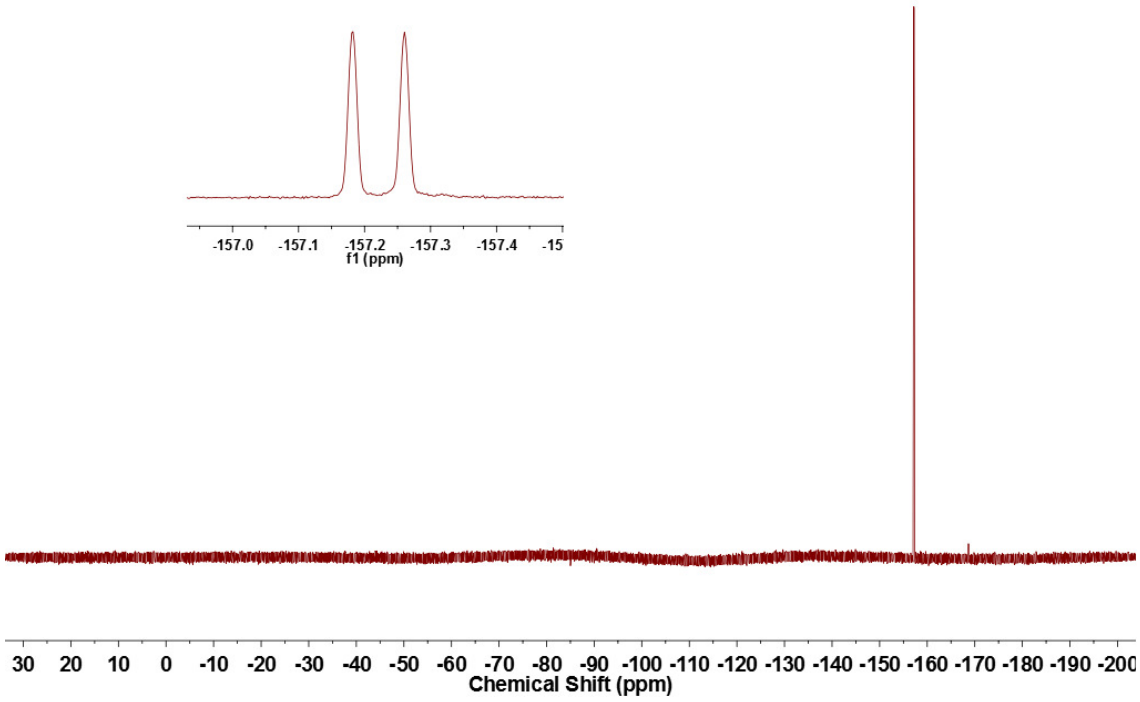
1-Benzyl 1''-(*tert*-butyl) (2'*S*,3'*S*)-3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**11**)



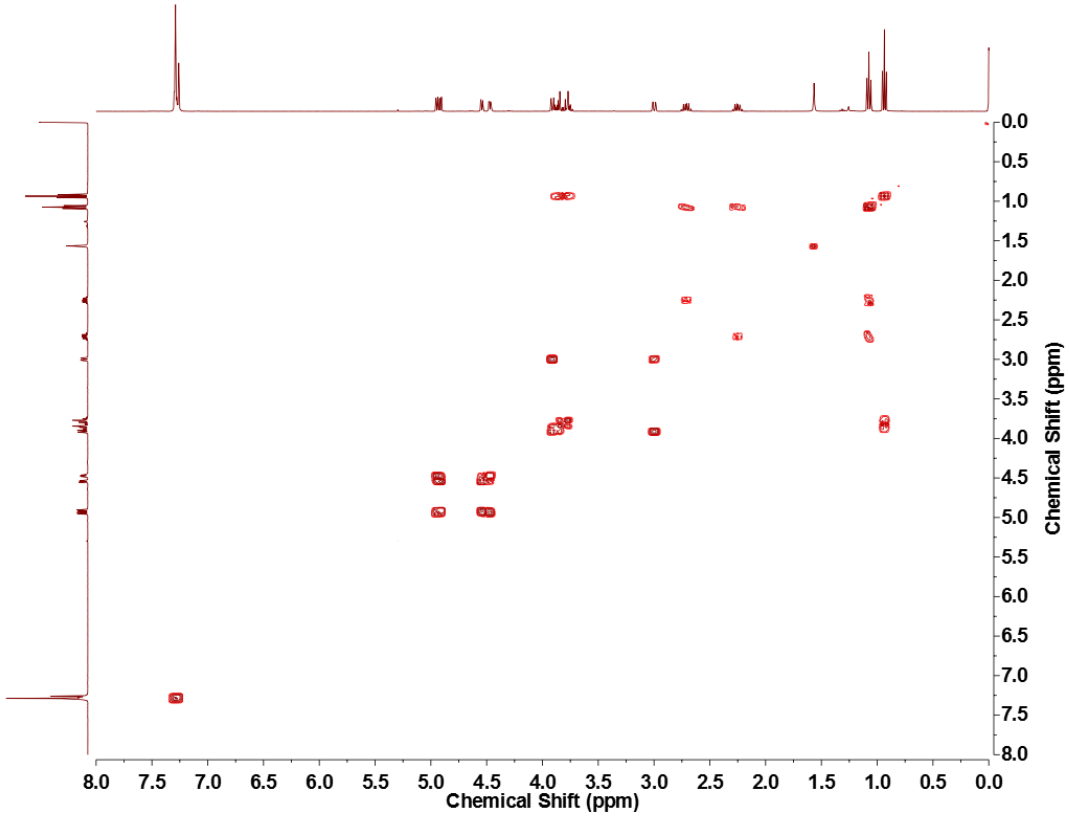
Ethyl (7*S*,8*R*)-6-ethyl-8-fluoro-7-phenyl-2-oxa-6-azaspiro[3.4]octane-8-carboxylate (**12**)



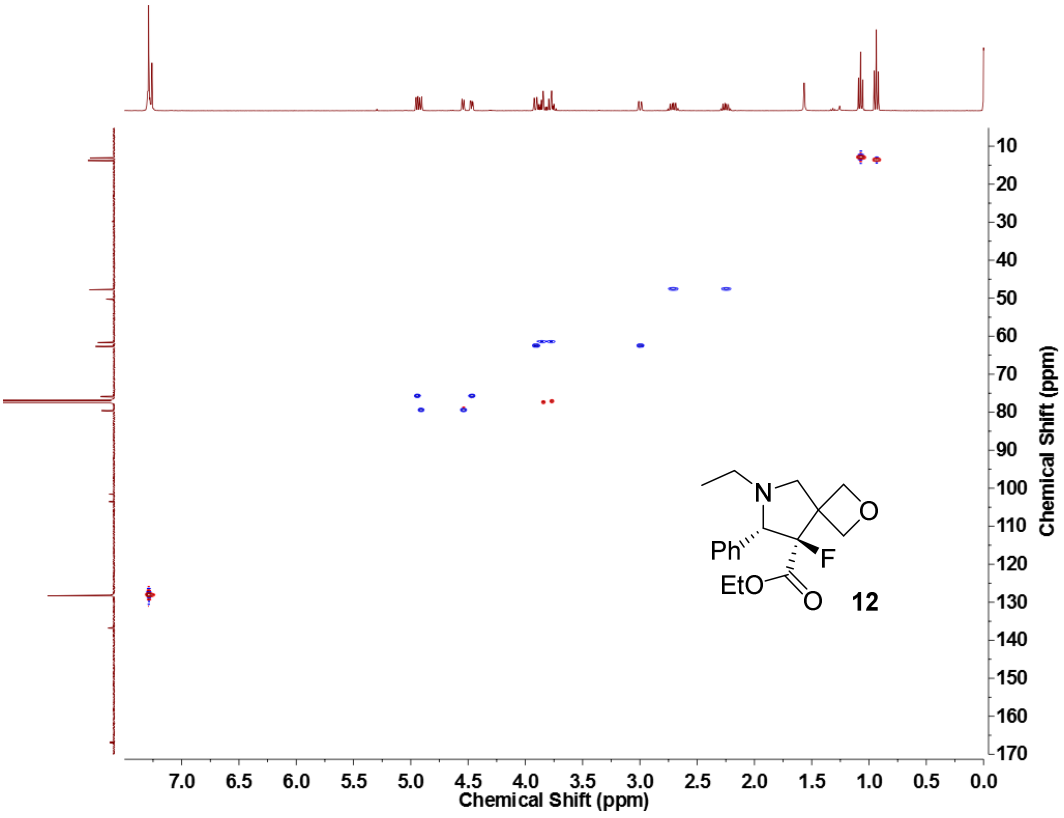



-157.0
-157.1
-157.2
-157.3
-157.4
-15
f1 (ppm)
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

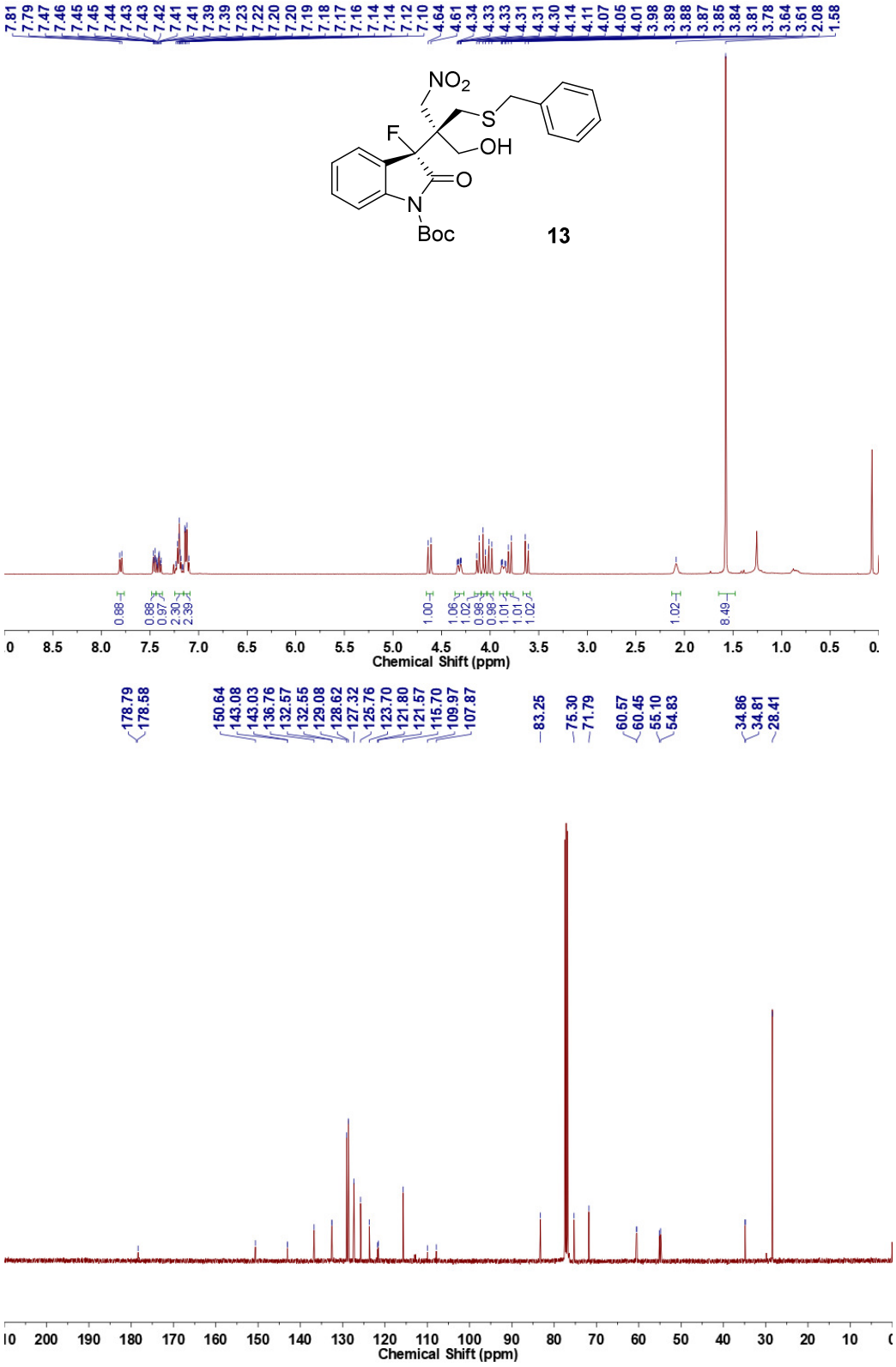
COSY spectrum of compound **12**

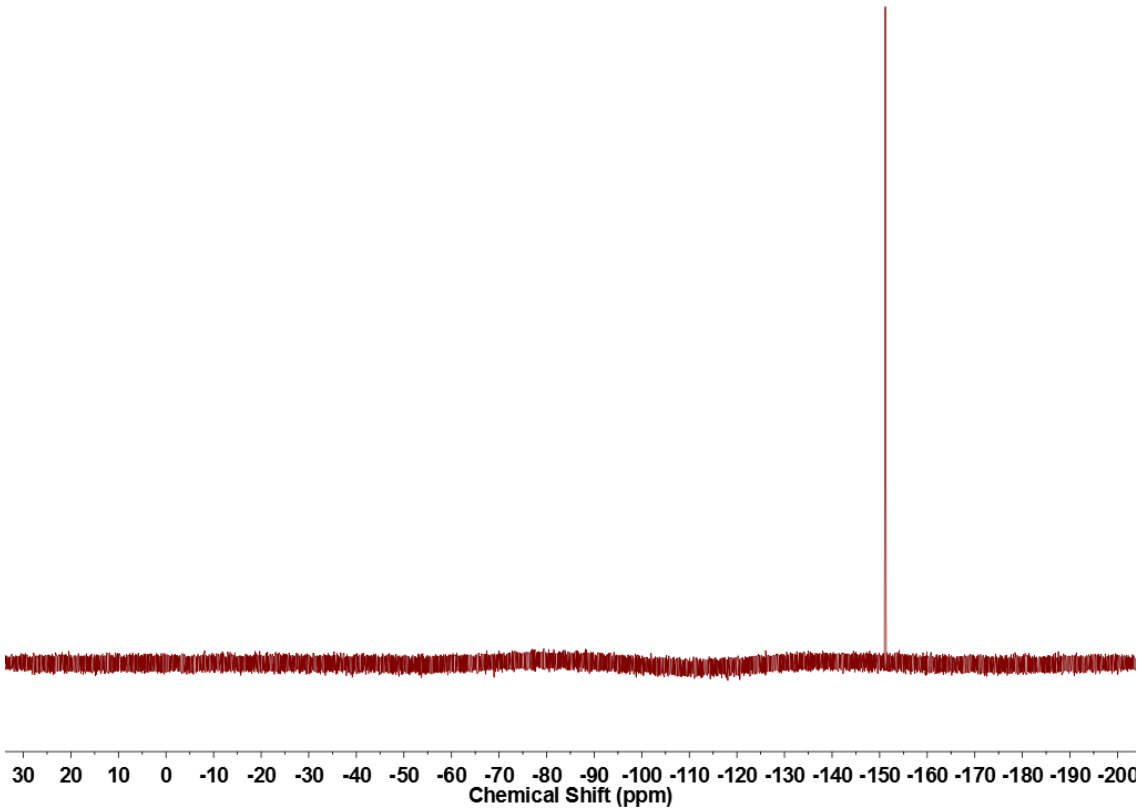


HSQC spectrum of compound **12**



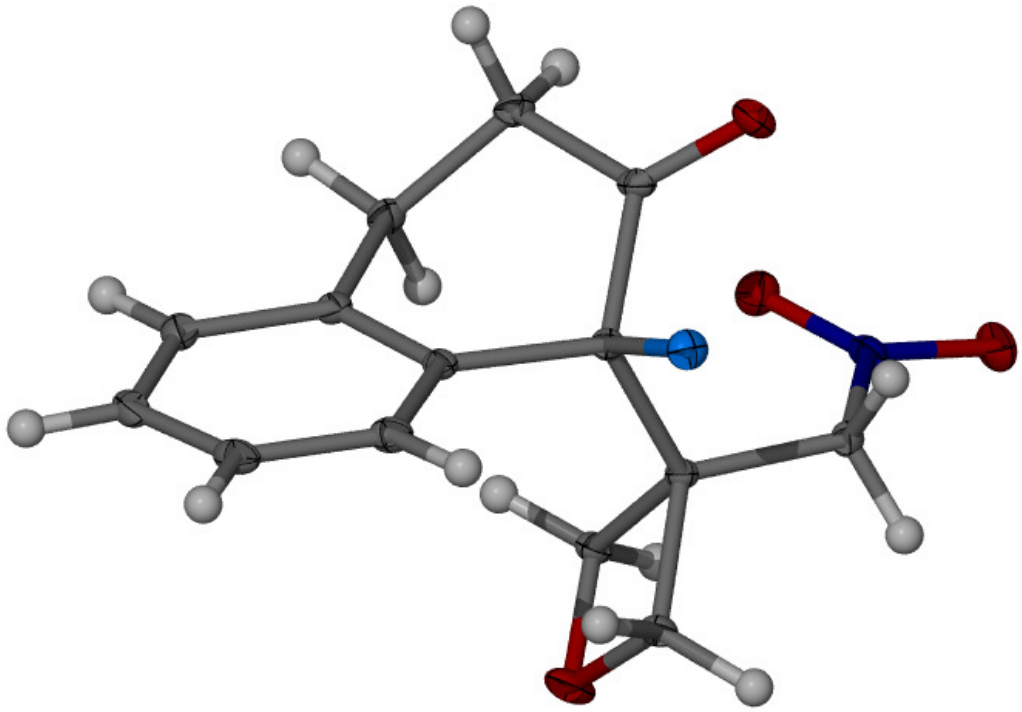
tert-Butyl (R)-3-((S)-1-(benzylthio)-3-hydroxy-2-(nitromethyl)propan-2-yl)-3-fluoro-2-oxoindole-1-carboxylate (**13**)




30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

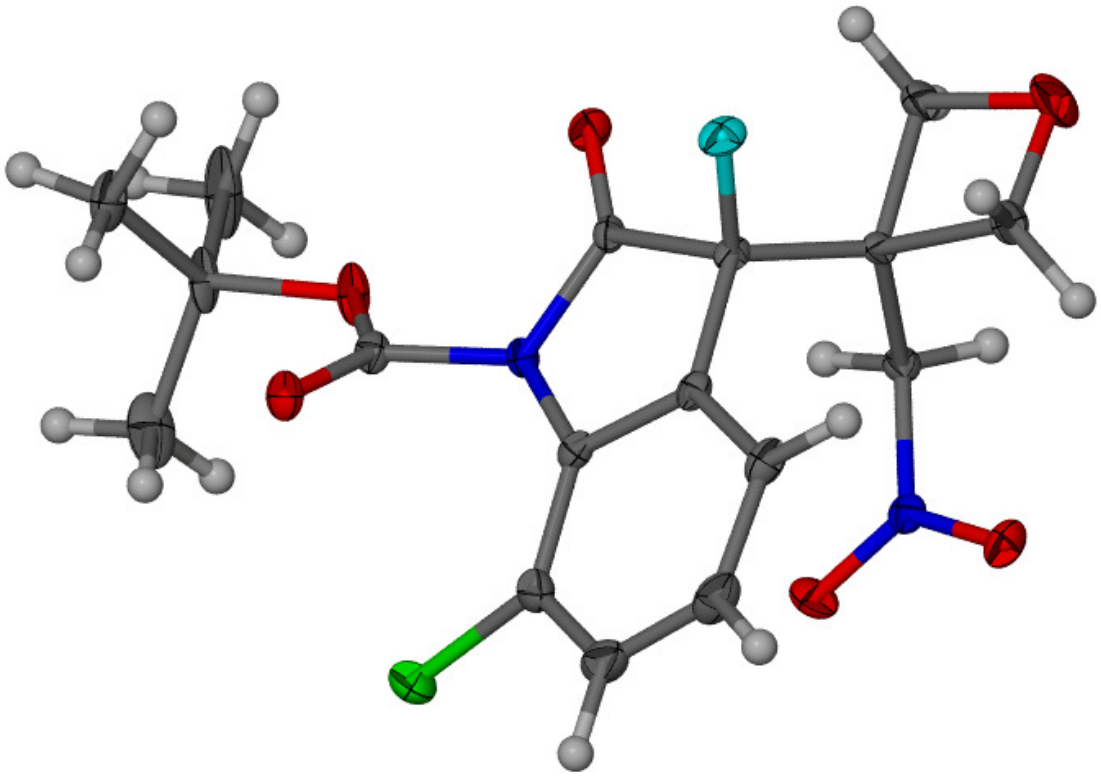
5. Crystallographic Data

(*R*)-1-Fluoro-1-(3-(nitromethyl)oxetan-3-yl)-3,4-dihydronaphthalen-2(1H)-one (**8a**)



A single crystal was obtained by slow evaporation of a solution of **8a** in CH_2Cl_2. Single crystal X-ray analysis was performed at 100 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and corrected using the Apex 3 program. The structures were solved by direct methods and refined with full-matrix least-square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameter. Crystal data: $C_{14}H_{14}FNO_4$, M = 279.26, colorless block, 0.43 x 0.77 x 0.92 mm^3, monoclinic, space group $P2_1$, a = 8.4753(5), b = 7.4483(4), c = 9.7720(6) Å, V = 601.09(6) $Å^3$, Z = 2. Absolute structure parameter = 0.087(680) (Flack, H. D. *Acta Cryst*. **1983**, *A39*, 876-881).

N-Boc-(*R*)-7-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3d**)

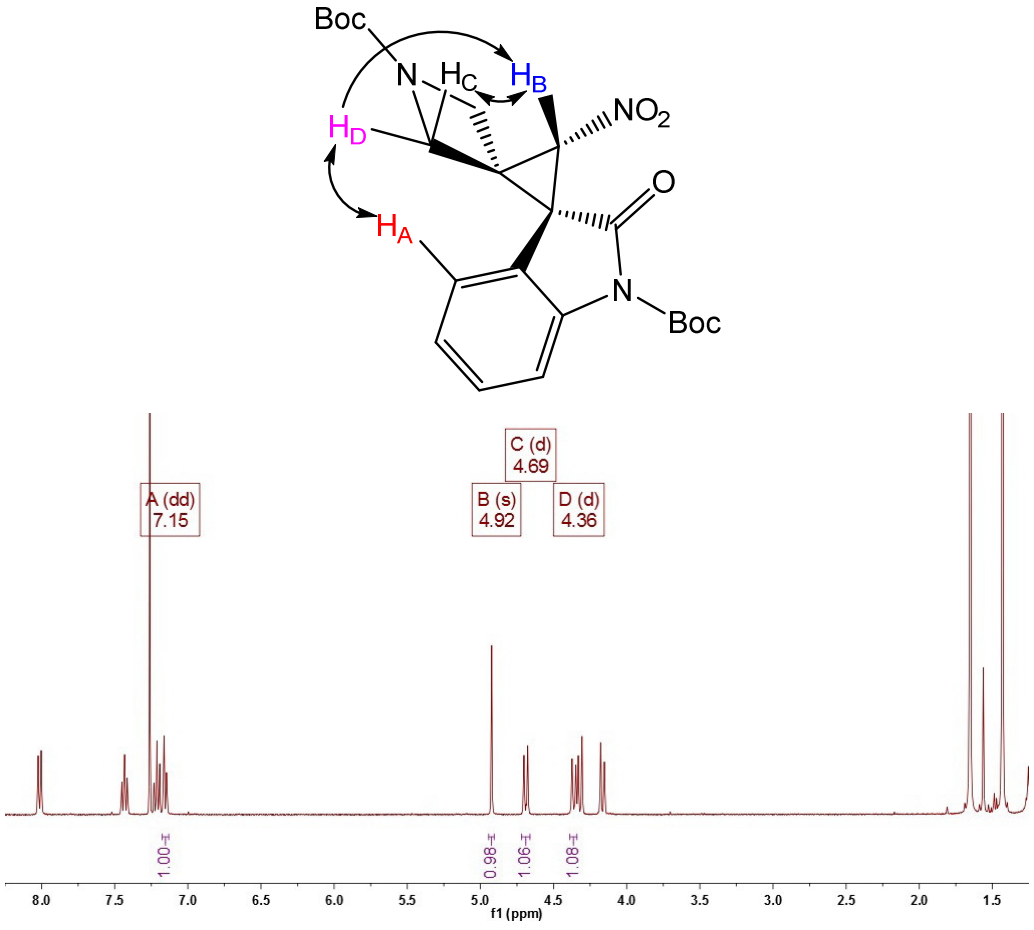


A single crystal was obtained by recrystallization of **3d** from ethanol. Single crystal X-ray analysis was performed at 273 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and corrected using the Apex 3 program. The structures were solved by direct methods and refined with full-matrix least-square analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameter. Crystal data: $C_{17}H_{18}ClFN_2O_6$, M = 400.78, colorless block, 0.55 x 0.72 x 0.94 mm^3, orthorhombic, space group $P2_12_1$, a = 7.7160(15), b = 10.0892(19), c = 23.357(5) Å, V = 1818.3(6) Å^3, Z = 4. Absolute structure parameter = 0.116(73) (Flack, H. D. *Acta Cryst*. **1983**, *A39*, 876-881).

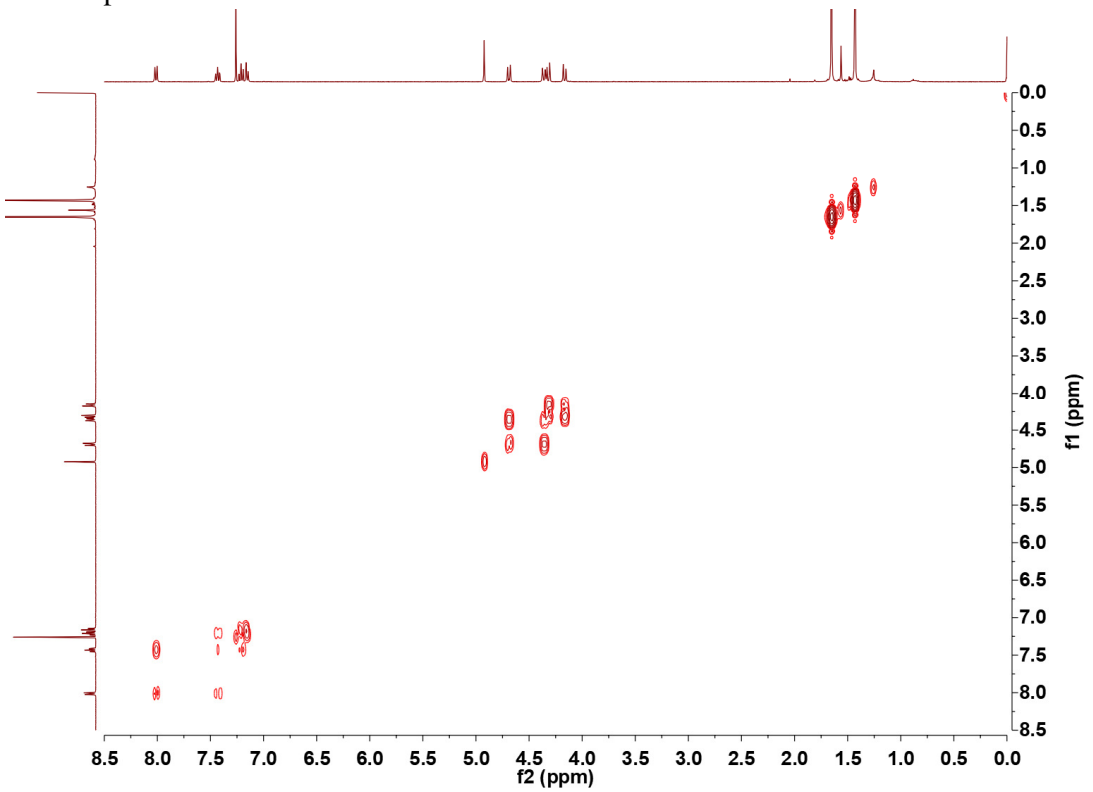
6. Determination of the Relative Configuration of Compounds 10 and 13

A) Di-*tert*-butyl (2'*S*,3'*S*)-3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**10**)

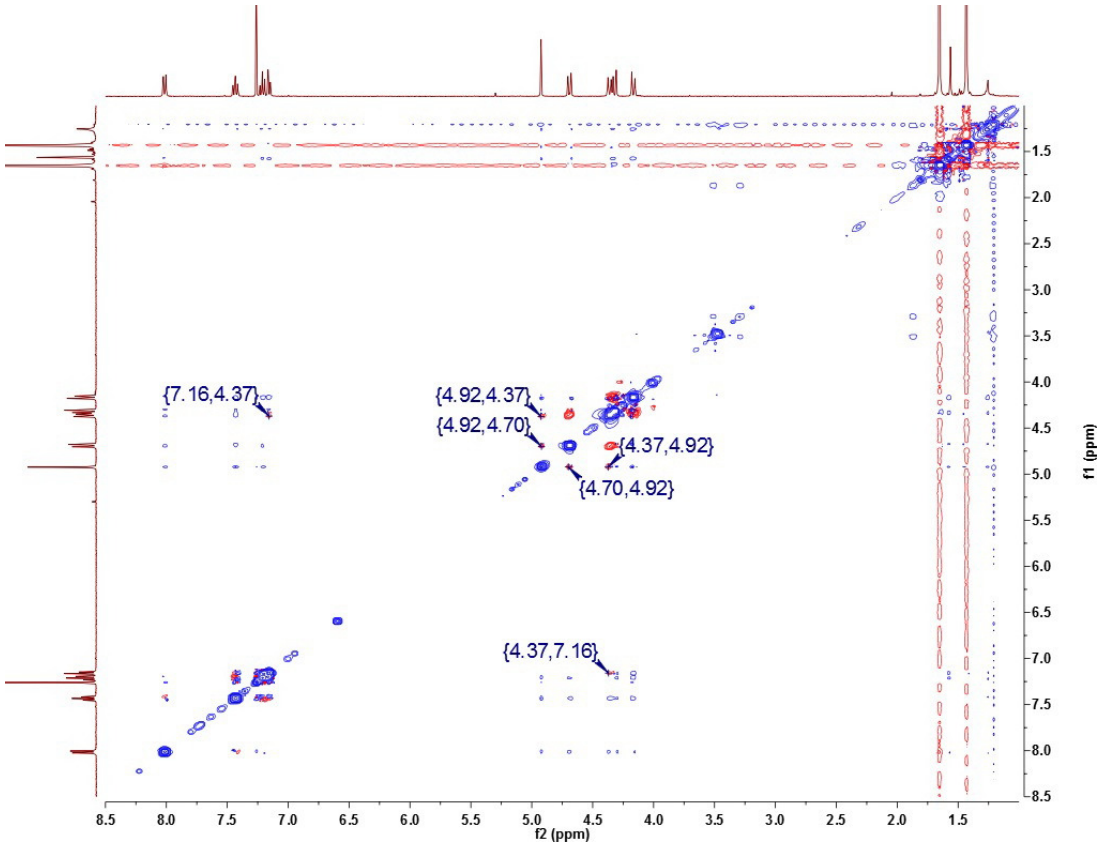
The ^{1}H NMR signals of H_A, H_B, H_C and H_D in compound **10** were first assigned based on chemical shift and COSY analysis. The ^{1}H^{1}H NOESY experiment showed that the tertiary proton H_B located at the cyclopropane ring has NOE's with the methylene protons H_C and H_D on one side of azetidine ring. The methylene proton H_D showed NOE with H_A at C4 in the oxindole ring. In agreement with these results, the *syn* relative configuration of the cyclopropane ring is shown below.



COSY spectrum of **10**

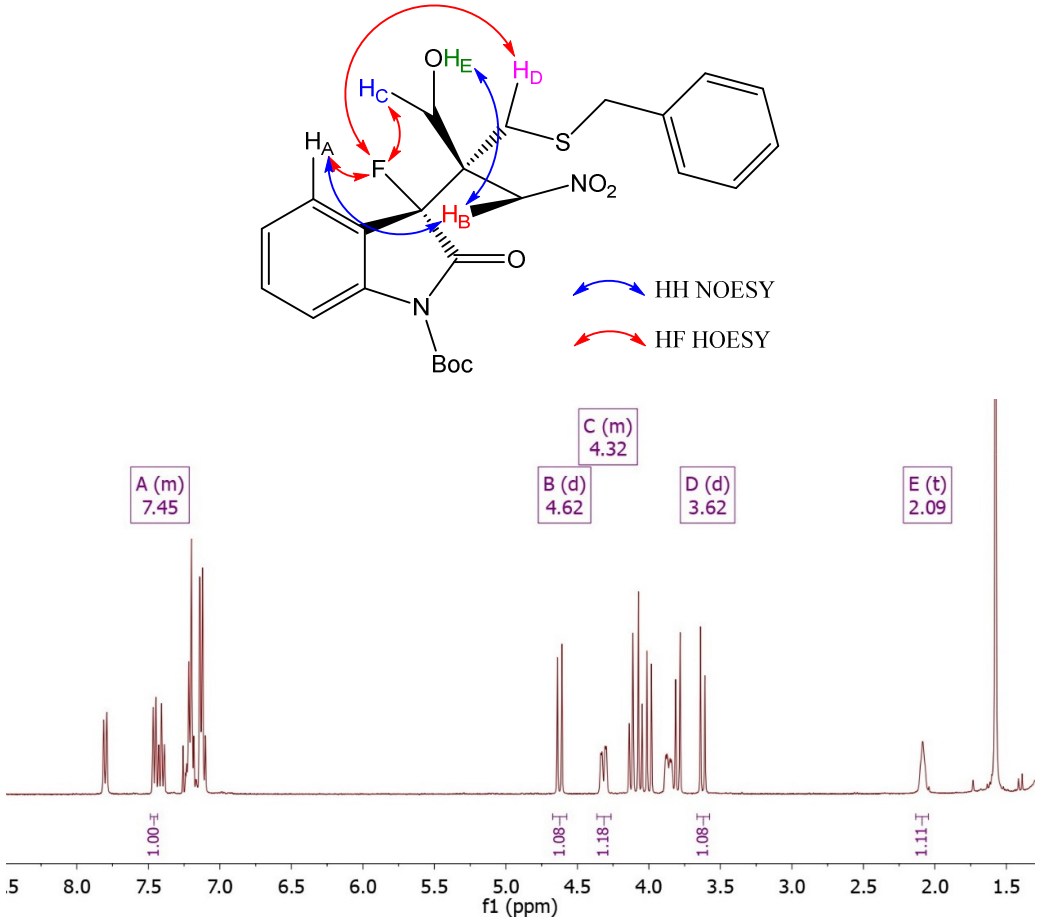


$^{1}H^{1}H$ NOESY spectrum of **10**

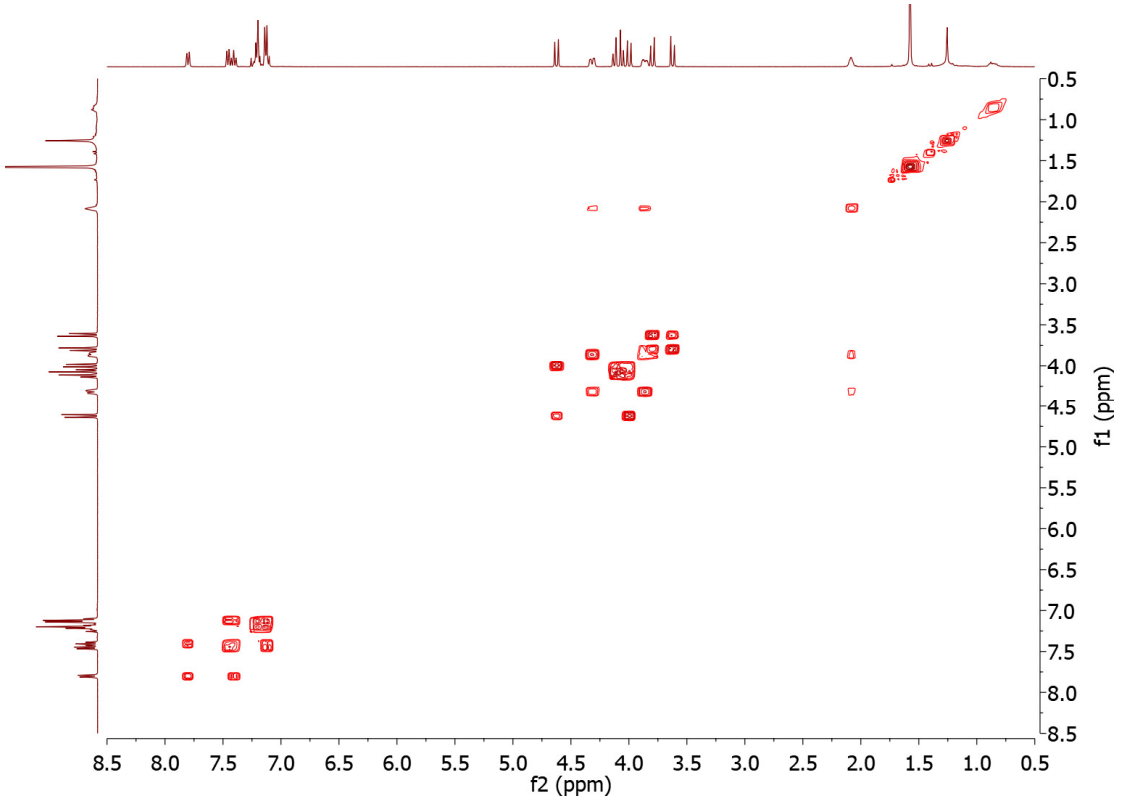


B) *tert*-Butyl (R)-3-((S)-1-(benzylthio)-3-hydroxy-2-(nitromethyl)propan-2-yl)-3-fluoro-2-oxoindole-1-carboxylate (**13**)

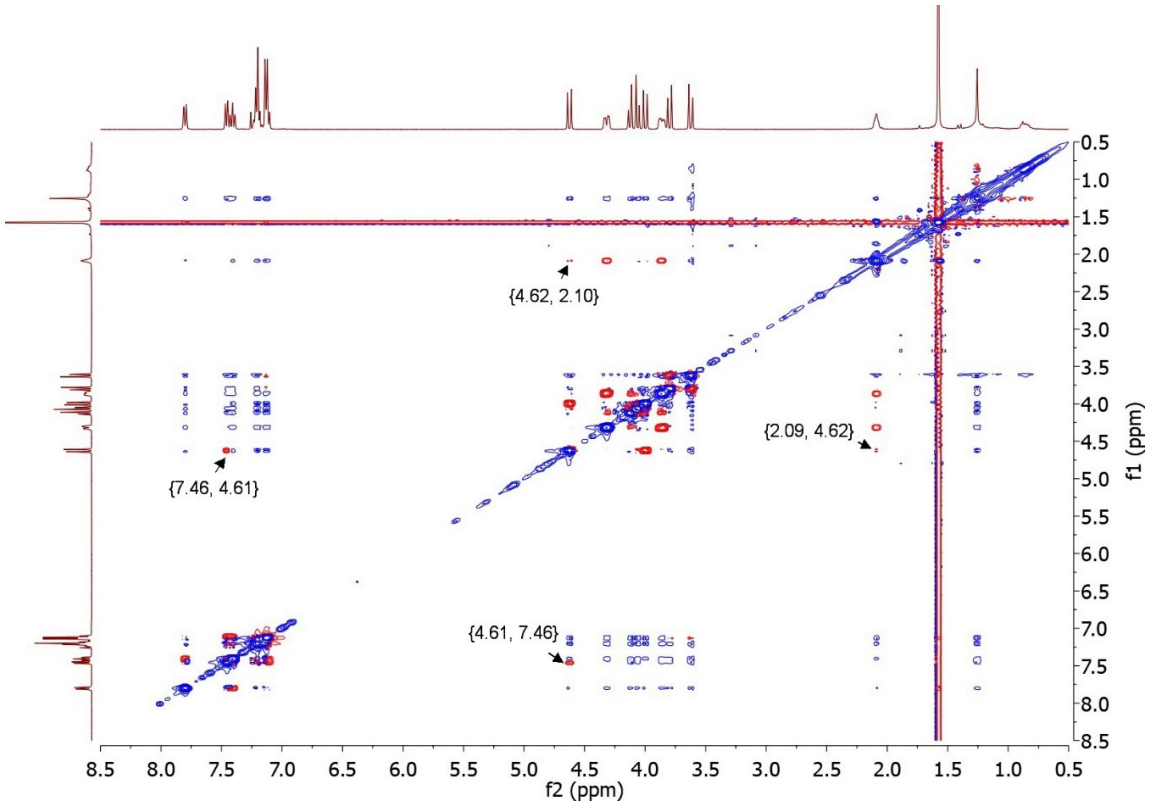
The ^{1}H NMR signals of H_A, H_B, H_C, H_D and H_E in compound **13** were first assigned based on COSY analysis. $^{1}H^{1}H$ NOESY and $^{1}H^{19}F$ HOESY experiments were used to determine the nuclei with close contact. The methylene proton H_B on the CH_2NO_2 group showed NOE's with the aromatic proton H_A at C4 in the oxindole ring and the hydroxyl proton H_E in the CH_2OH group. The fluorine nuclei (F) showed heteronuclear NOE's with the aromatic proton H_A at C4 in the oxindole ring, the methylene proton H_C in the CH_2OH group and the methylene proton H_D in the thioether group. In agreement with these results, the relative stereochemistry is shown below.



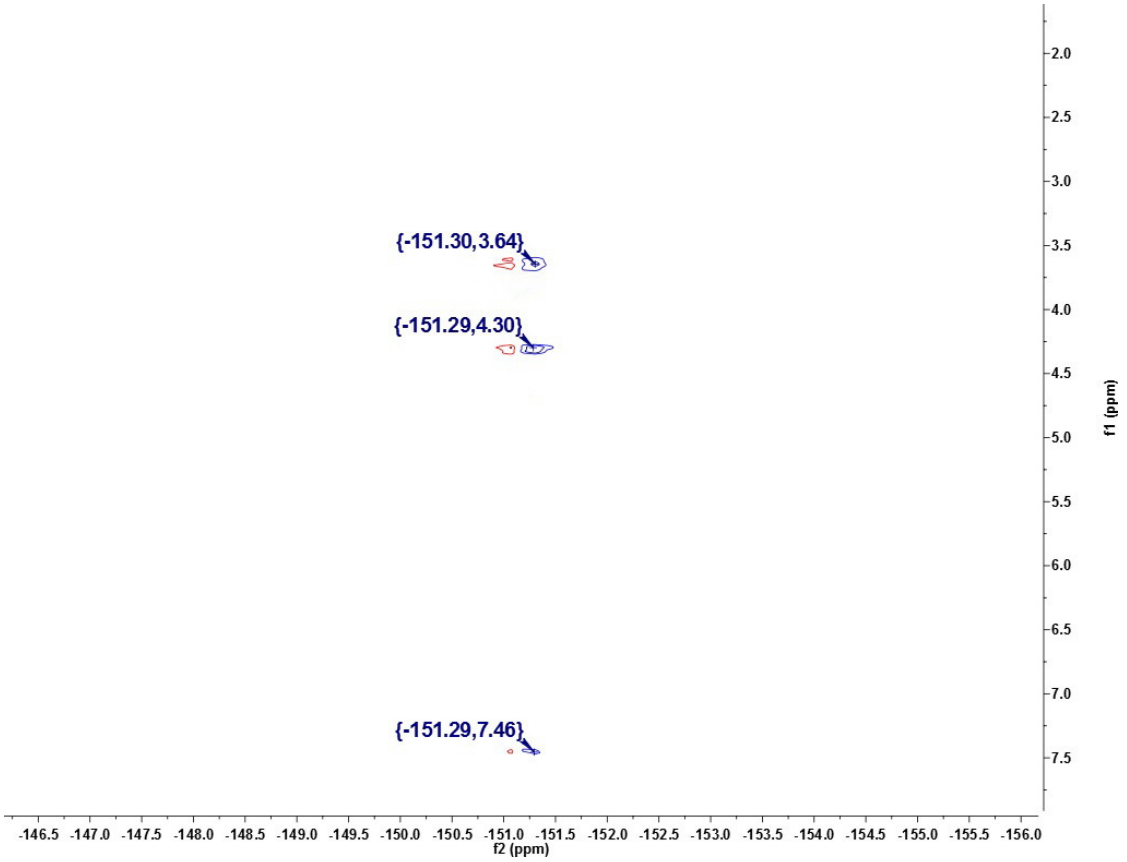
COSY spectrum of **13**



$^{1}H^{1}H$ NOESY spectrum of **13**

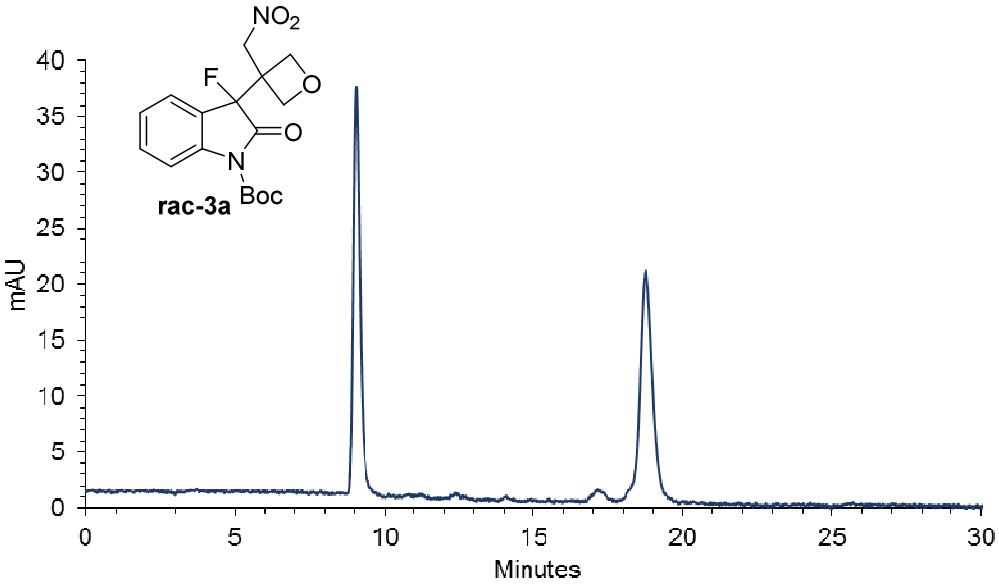


$^{1}H^{19}F$ HOESY spectrum of **13**



7. HPLC Chromatograms

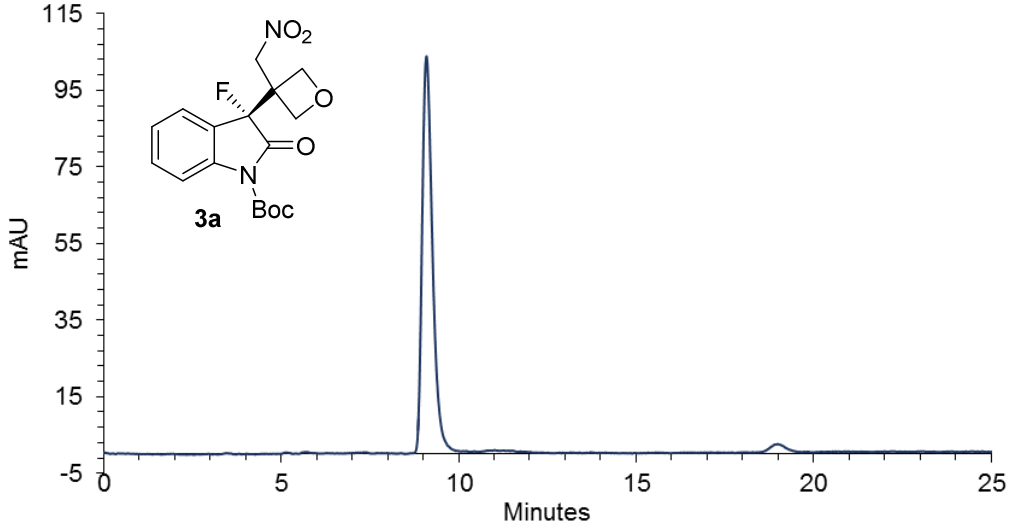
N-Boc-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3a**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.064	8346.76953	50.4613
18.763	8194.16406	49.5387

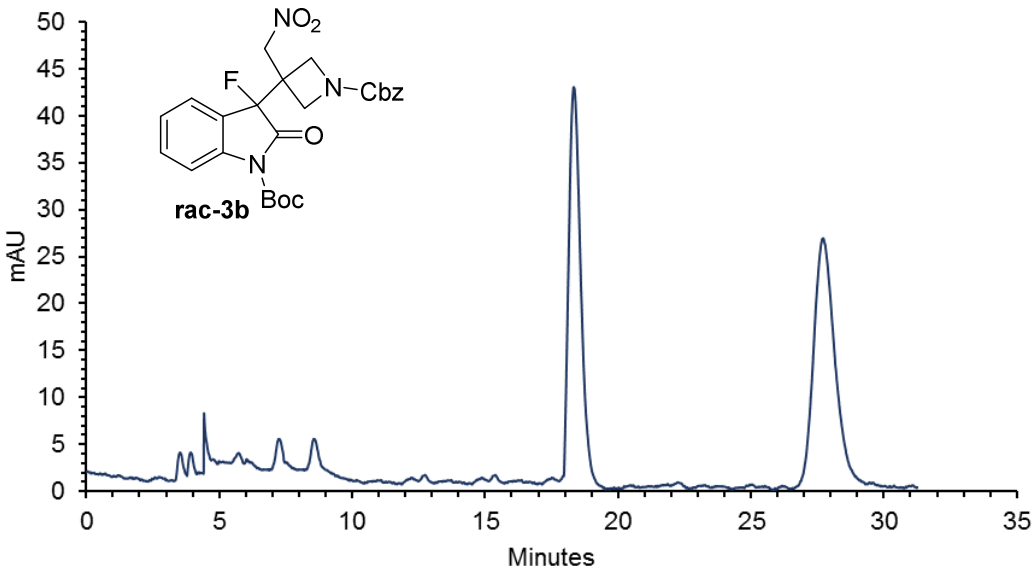
N-Boc-(*R*)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3a**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.092	3.20732E+04	97.5408
18.975	808.61774	2.4592

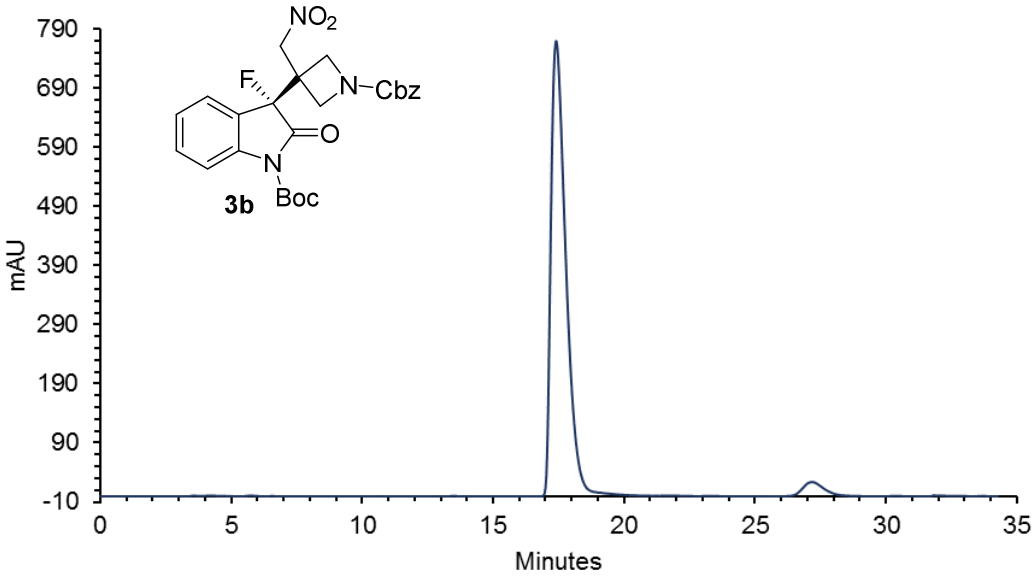
N-Boc-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**rac-3b**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
18.343	2247.52417	48.1238
27.721	2422.77332	51.8762

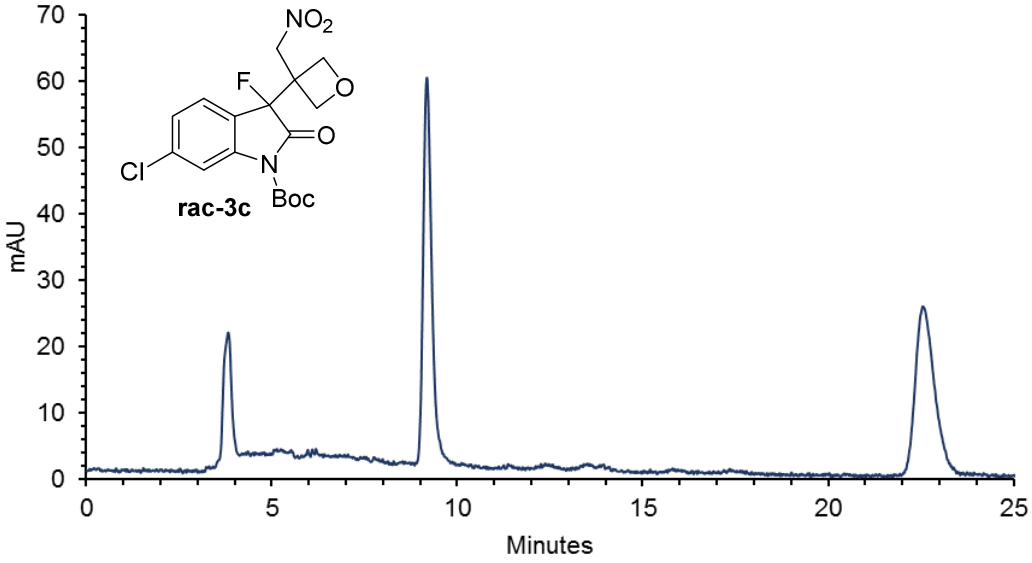
N-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3b**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
17.393	4884.85010	95.9192
27.120	207.82164	4.0808

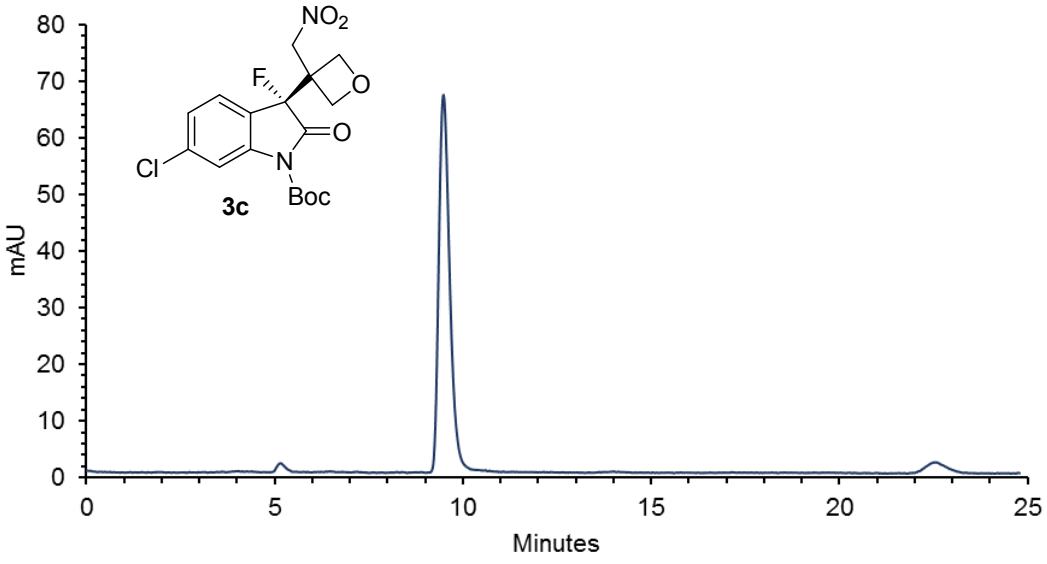
N-Boc-6-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3c**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.194	946.37256	50.2104
22.564	938.44312	49.7896

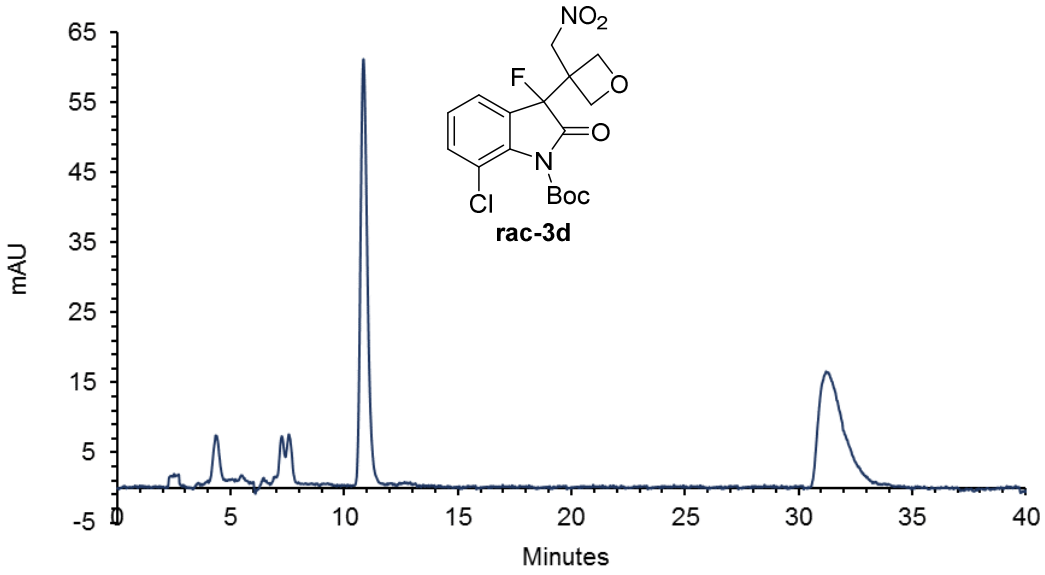
N-Boc-(*R*)-6-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3c**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.49	1325.73474	95.9136
22.572	56.48281	4.0864

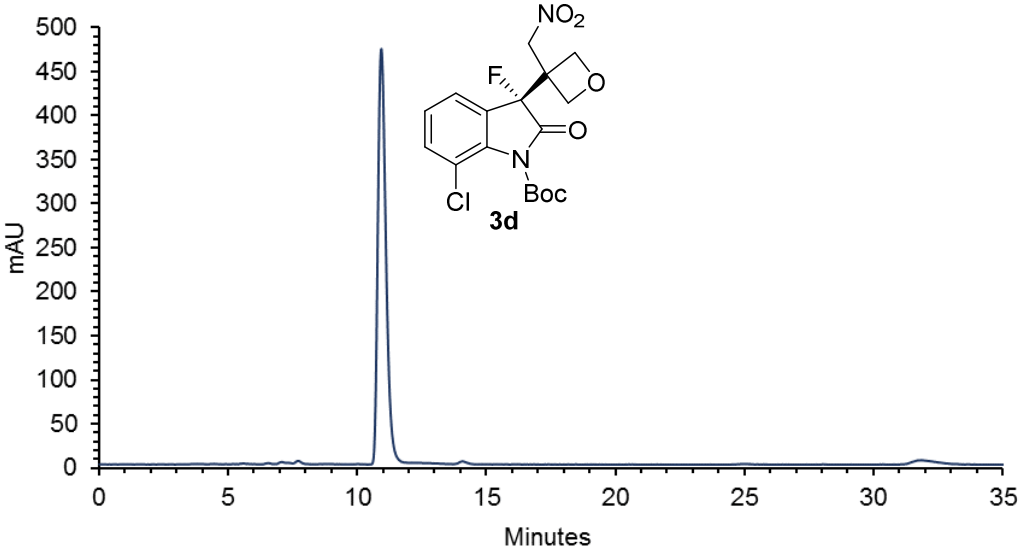
N-Boc-7-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3d**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
10.850	1276.97595	51.4685
31.226	1204.10742	48.5315

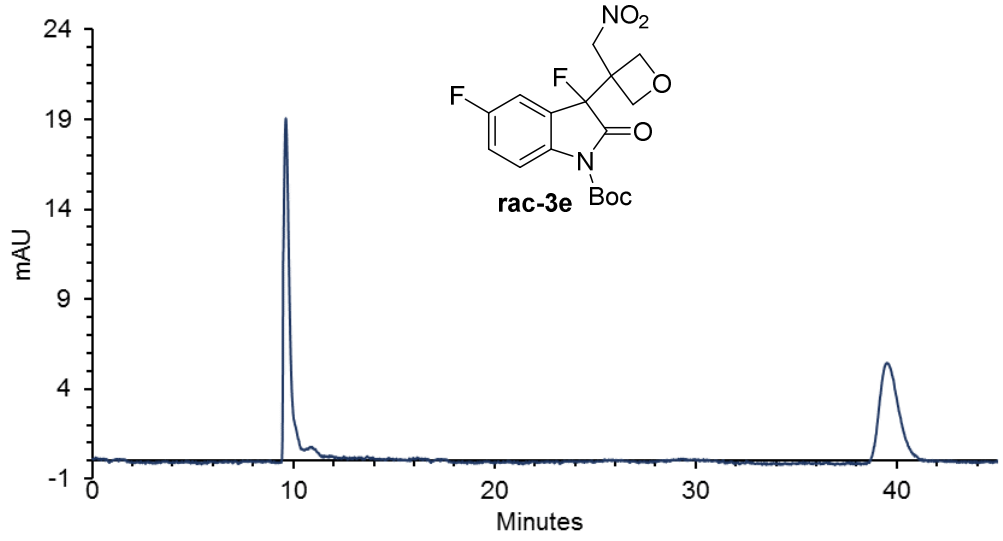
N-Boc-(*R*)-7-chloro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3d**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
10.930	1.02346E+04	97.4664
31.866	266.04330	2.5336

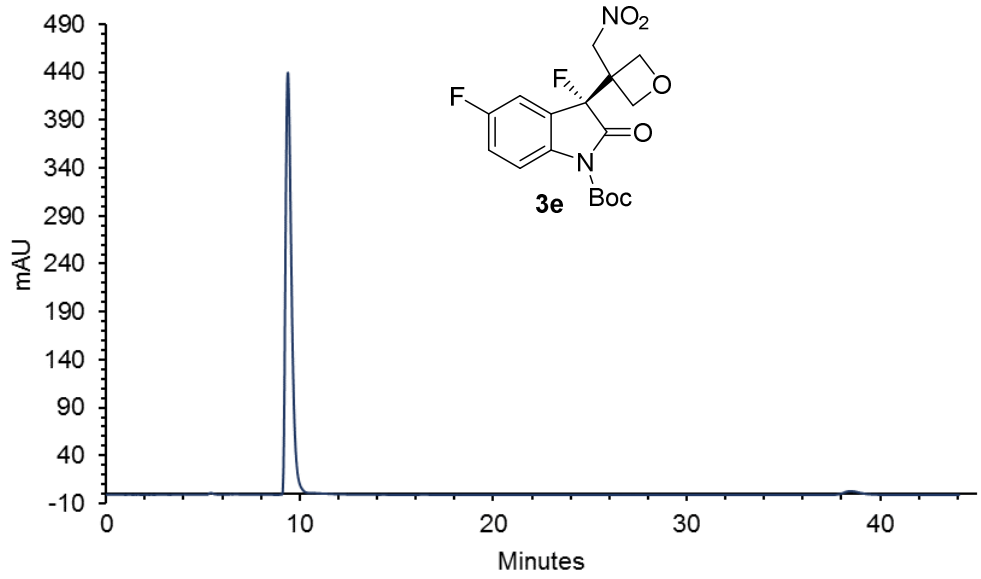
N-Boc-3,5-difluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3e**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.615	376.40601	52.9430
39.525	334.55905	47.0570

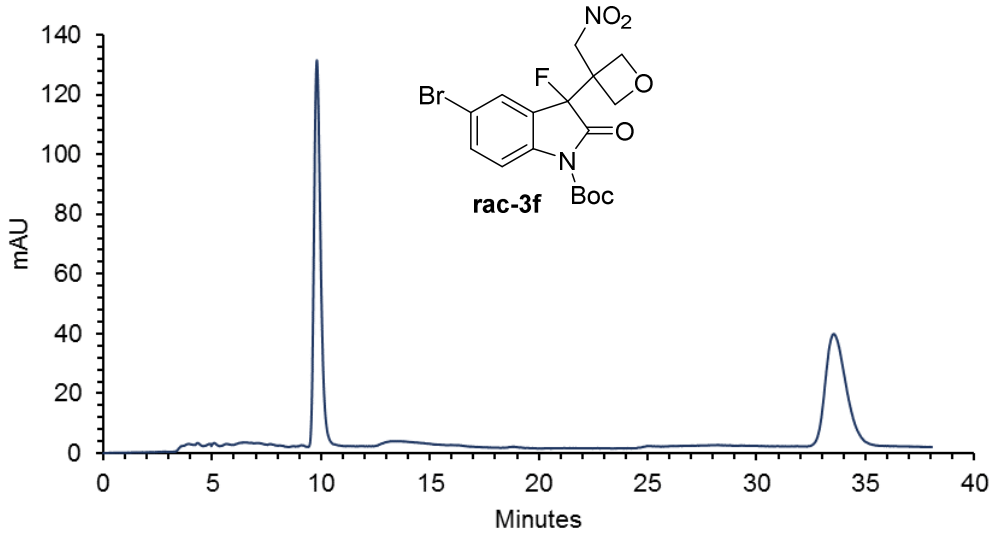
N-Boc-(*R*)-3,5-difluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3e**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.394	9468.01465	97.9407
38.383	199.07681	2.0593

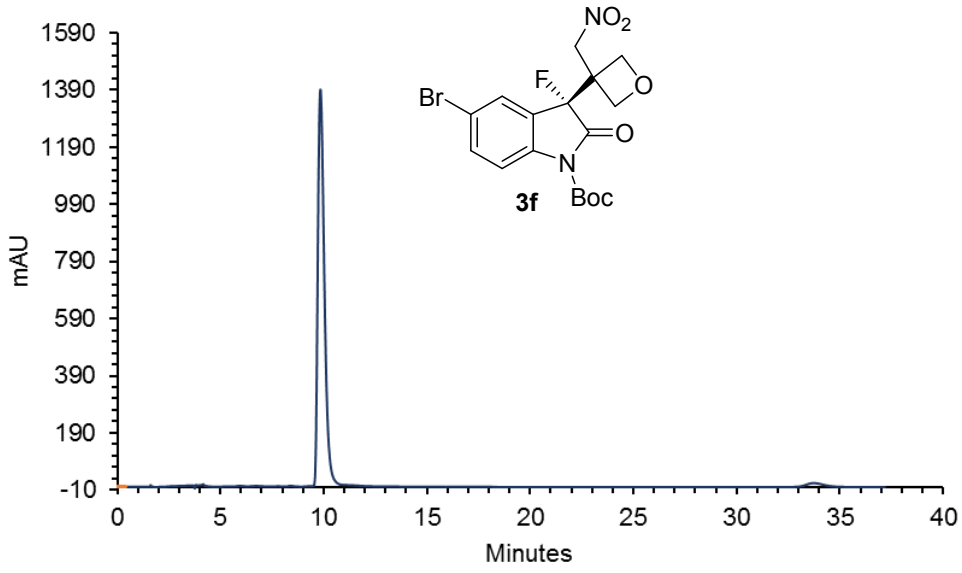
N-Boc-5-bromo-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3f**)



Signal 3: DAD1 C, Sig=243,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.801	2680.43262	52.3143
33.535	2443.27734	47.6857

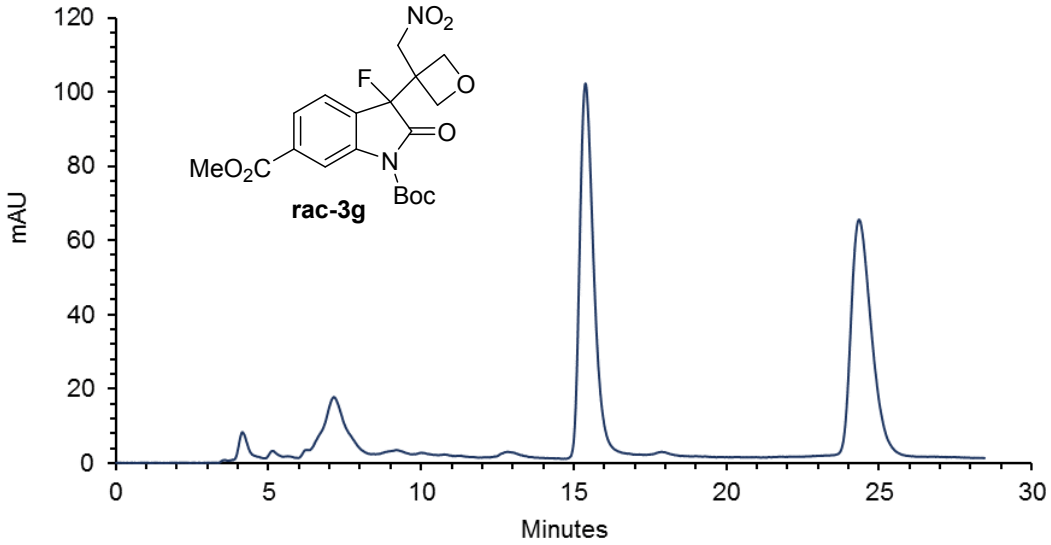
N-Boc-(*R*)-5-bromo-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3f**)



Signal 3: DAD1 C, Sig=243,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
9.820	3.05083E+04	97.5068
33.724	780.09155	2.4932

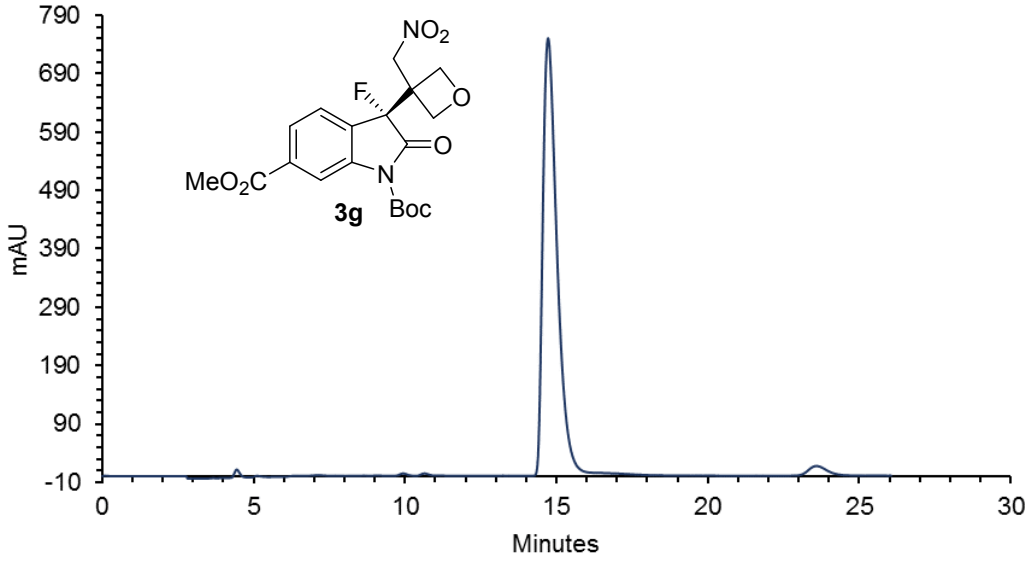
Methyl *N*-Boc-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole-6-carboxylate (**rac-3g**)



Signal 3: DAD1 C, Sig=243,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
15.387	3154.85596	51.9750
24.353	2915.09644	48.0250

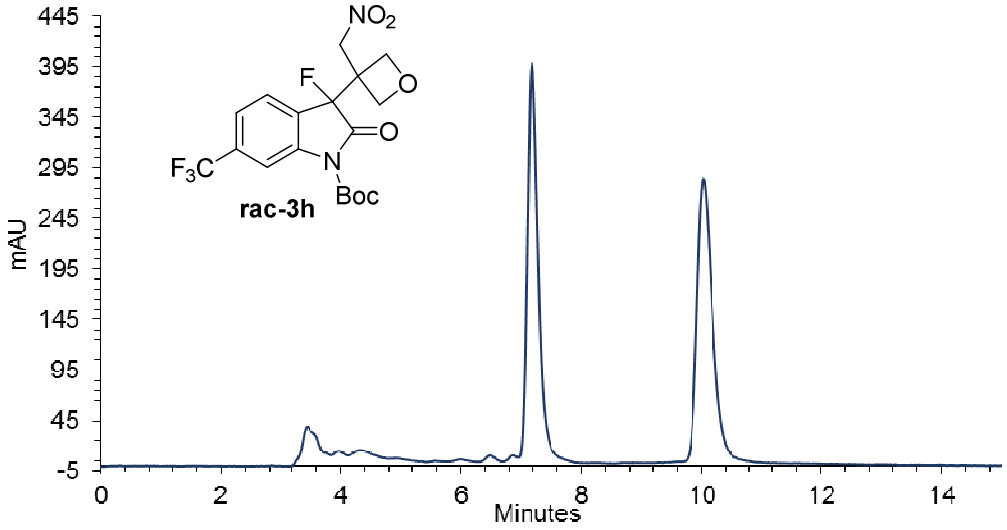
Methyl *N*-Boc-(R)-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole-6-carboxylate (**3g**)



Signal 3: DAD1 C, Sig=243,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
14.72	2.47417E+04	97.2327
23.581	704.15558	2.7673

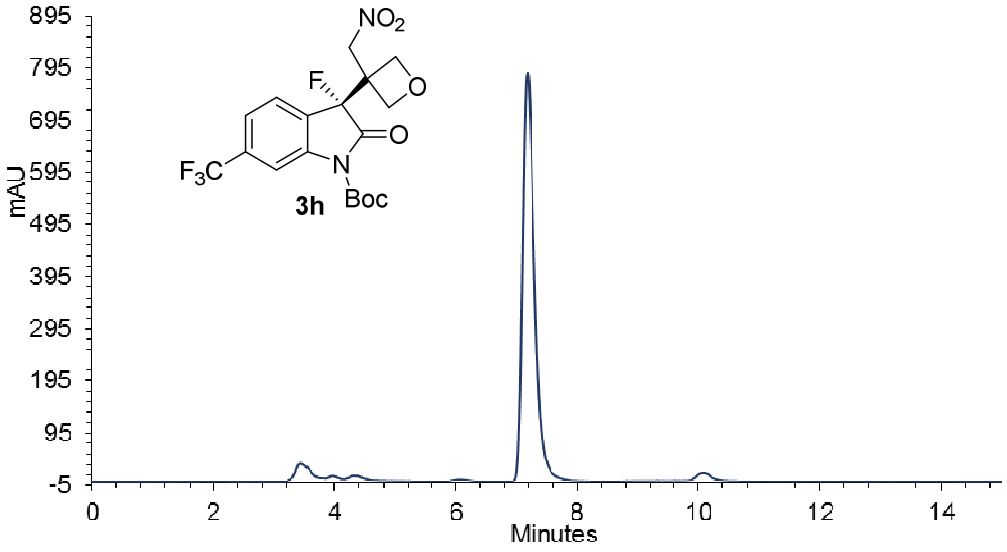
N-Boc-6-trifluoromethyl-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3h**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
7.179	5113.88818	49.6032
10.037	5195.71289	50.3968

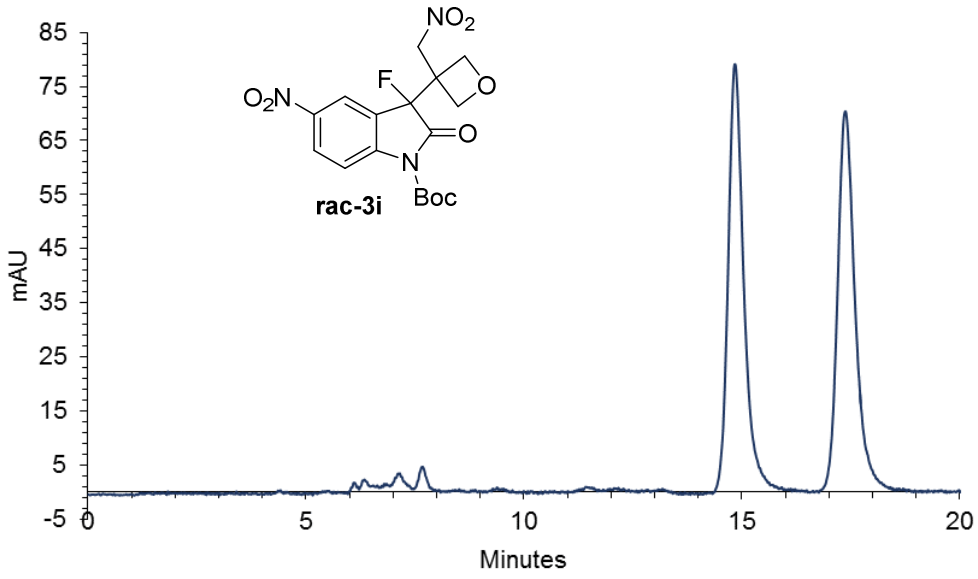
N-Boc-(*R*)-6-trifluoromethyl-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3h**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
7.178	1.06681E+04	97.9678
10.088	221.29810	2.0322

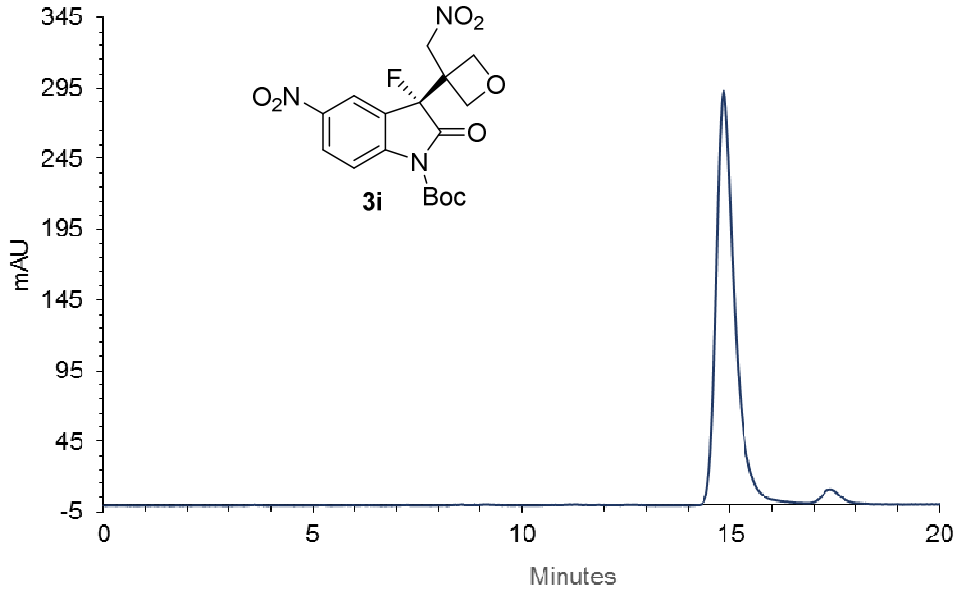
N-Boc-5-nitro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3i**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
13.791	1938.41724	49.6021
16.325	1969.51978	50.3979

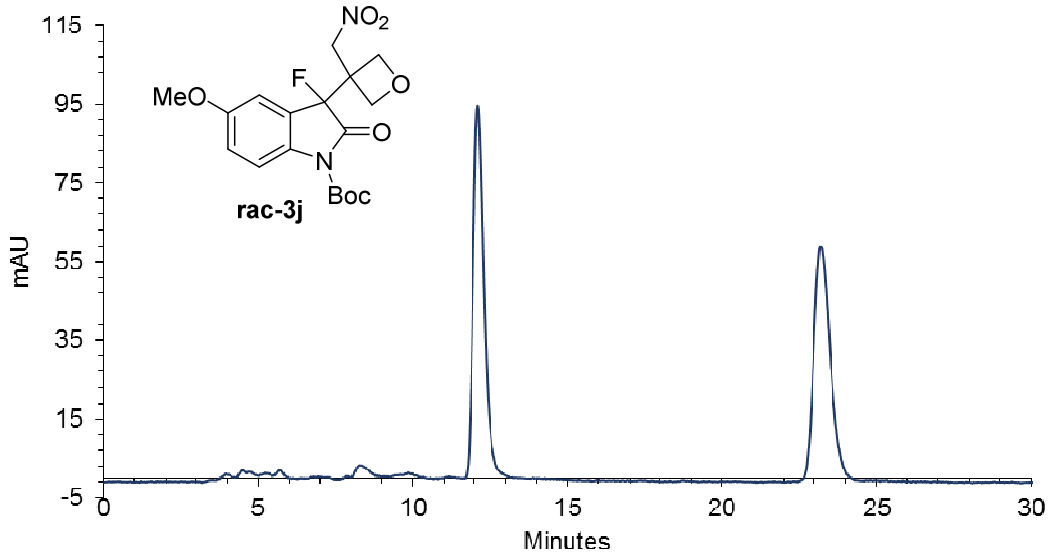
N-Boc-(*R*)-5-nitro-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3i**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
14.837	8915.25488	96.7233
17.383	302.02209	3.2767

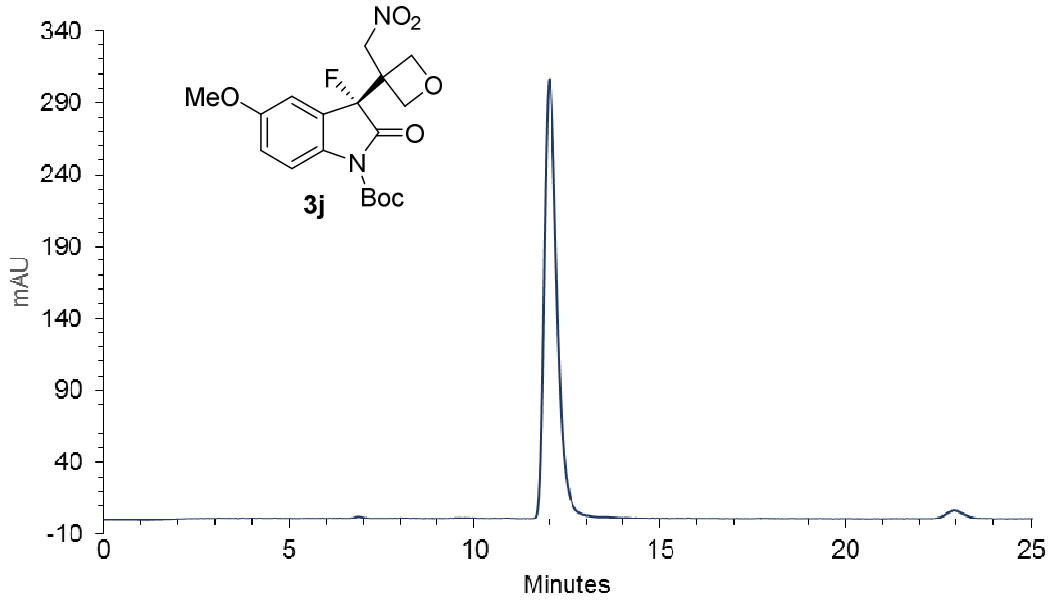
N-Boc-5-methoxy-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-3j**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.096	2285.90900	50.7470
23.191	2218.61300	49.2530

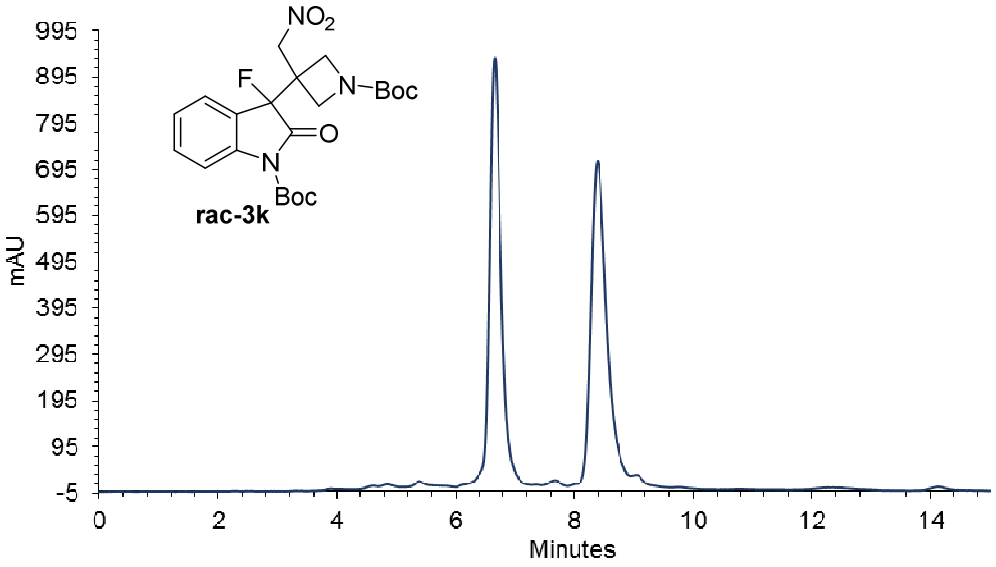
N-Boc-(*R*)-5-methoxy-3-fluoro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**3j**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.020	7362.36500	97.2591
22.916	207.48350	2.7409

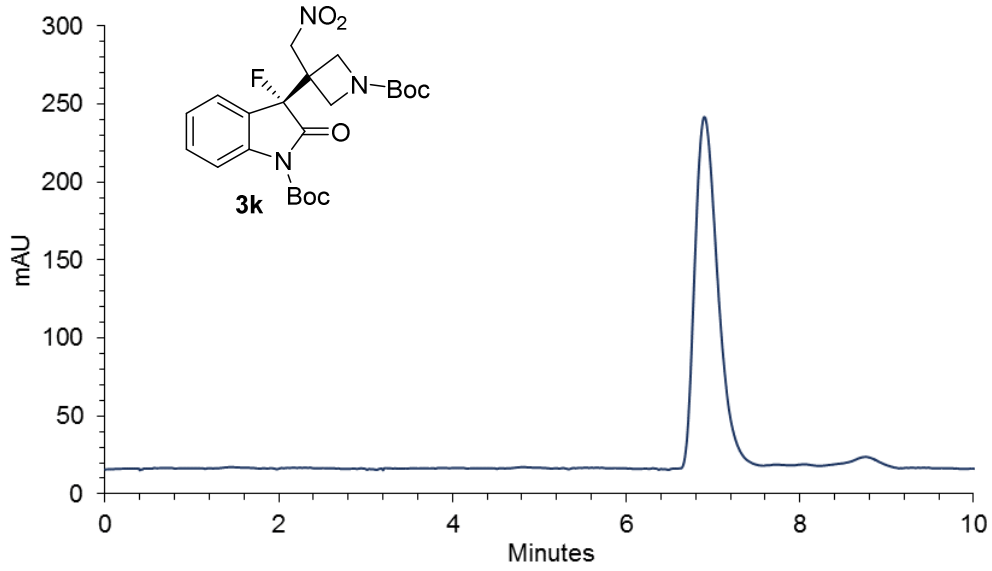
N-Boc-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**rac-3k**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.655	2351.03723	50.5242
8.392	2302.24927	49.4758

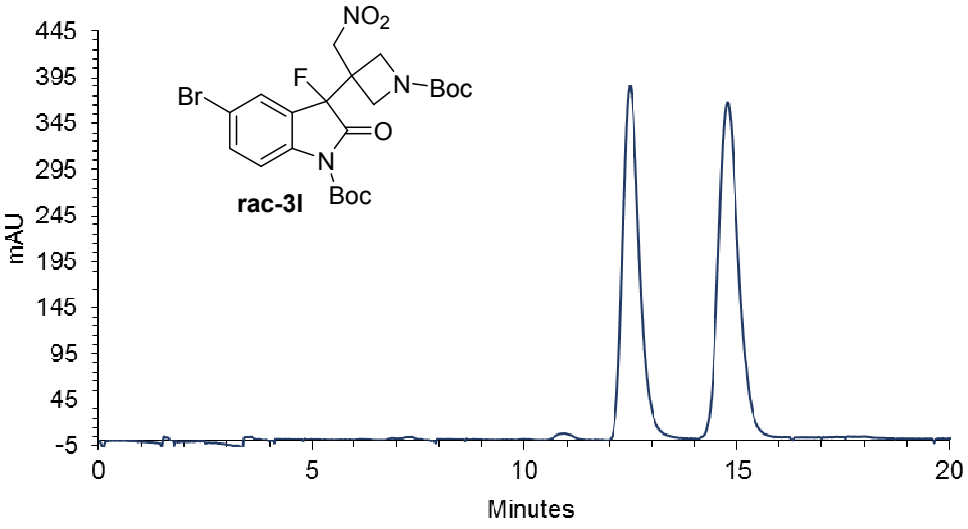
N-Boc-(*S*)-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3k**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.899	4222.46387	96.8449
8.760	137.56226	3.1551

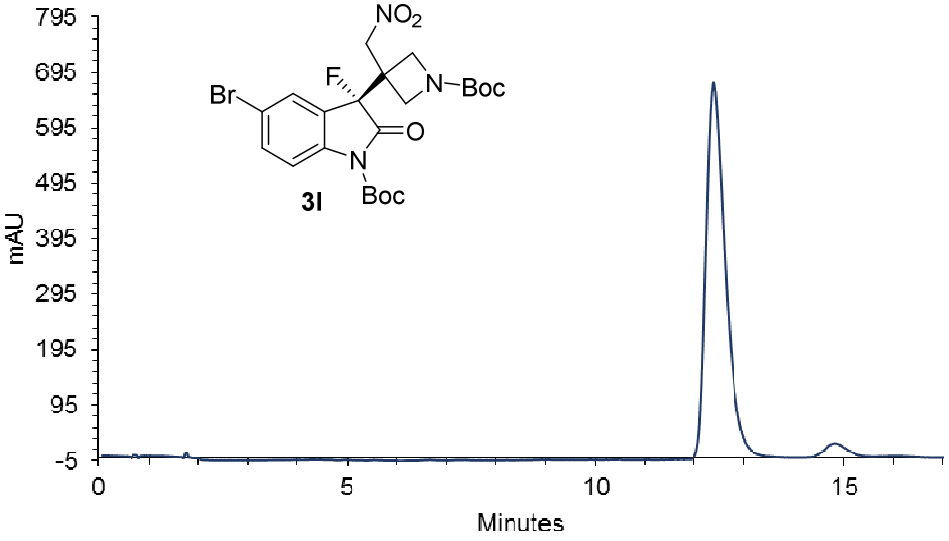
N-Boc-5-bromo-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**rac-3l**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.484	2595.81055	45.8368
14.781	3067.34888	54.1632

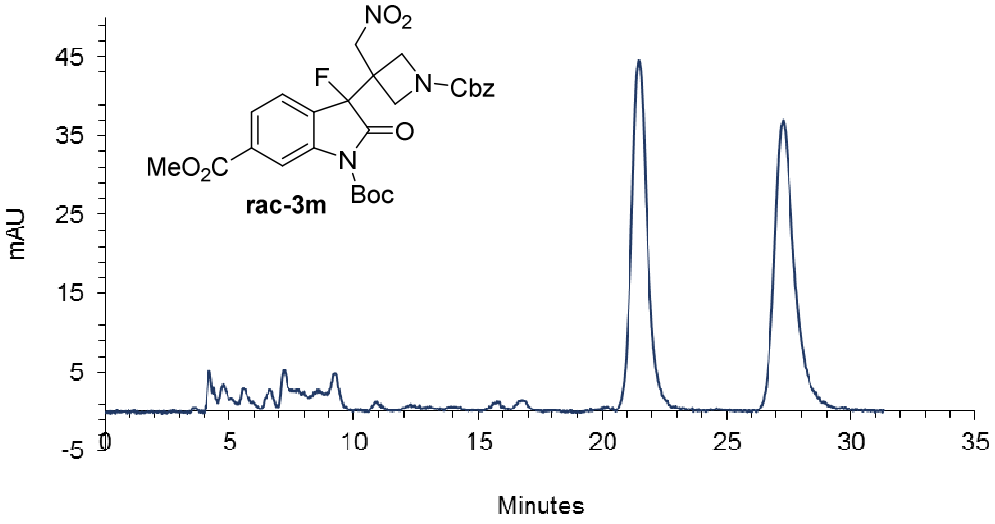
N-Boc-(*S*)-5-bromo-3-fluoro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**3l**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.383	679.41742	96.0164
14.826	25.16455	3.9836

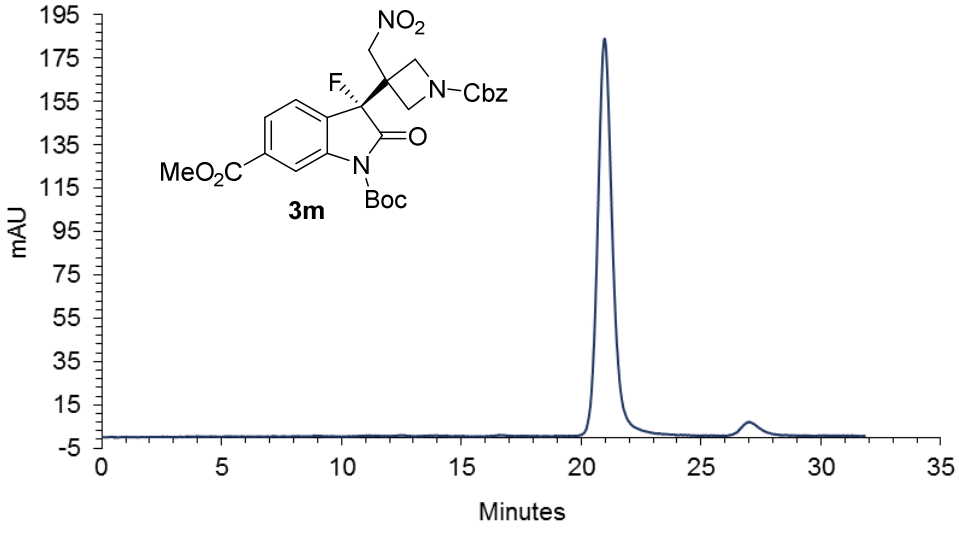
Methyl *N*-Boc-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole-6-carboxylate (**rac-3m**)



Signal 4: DAD1 D, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
21.469	1920.67400	48.4998
27.269	2039.49500	51.5002

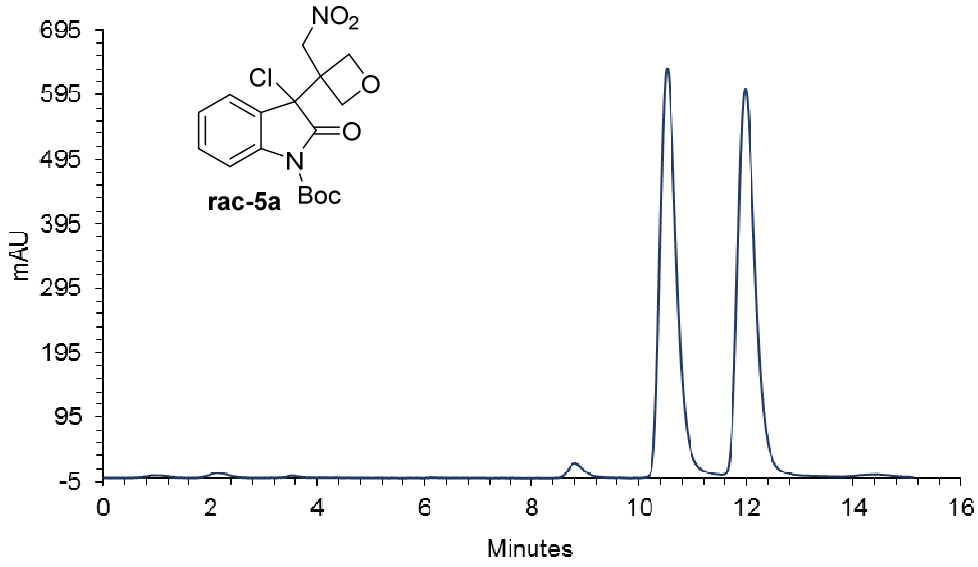
Methyl *N*-Boc-(*S*)-3-fluoro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole-6-carboxylate (**3m**)



Signal 4: DAD1 D, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
20.973	7737.50200	96.2193
27.011	304.03010	3.7807

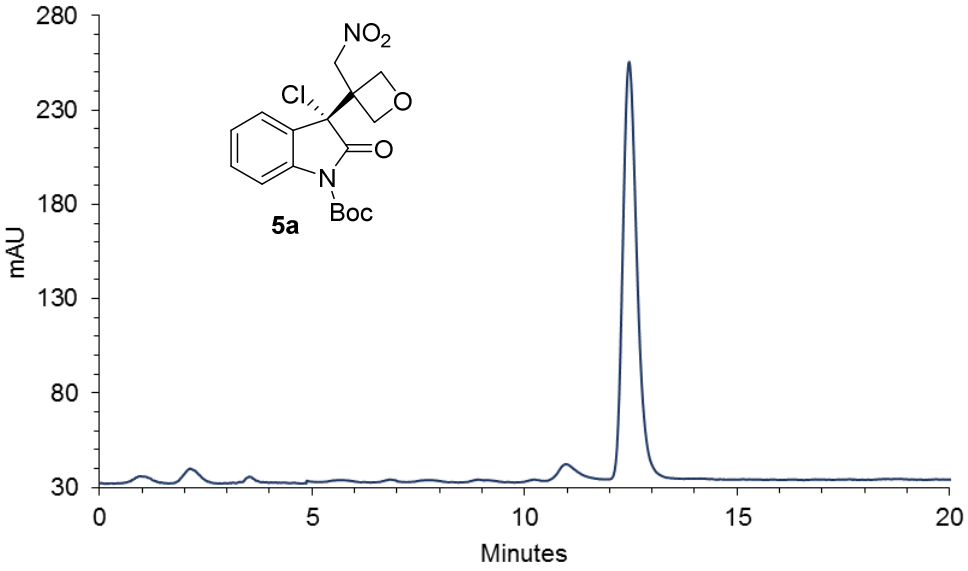
N-Boc-3-chloro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**rac-5a**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
10.520	1.38931E+04	49.8218
11.979	1.39925E+04	50.1782

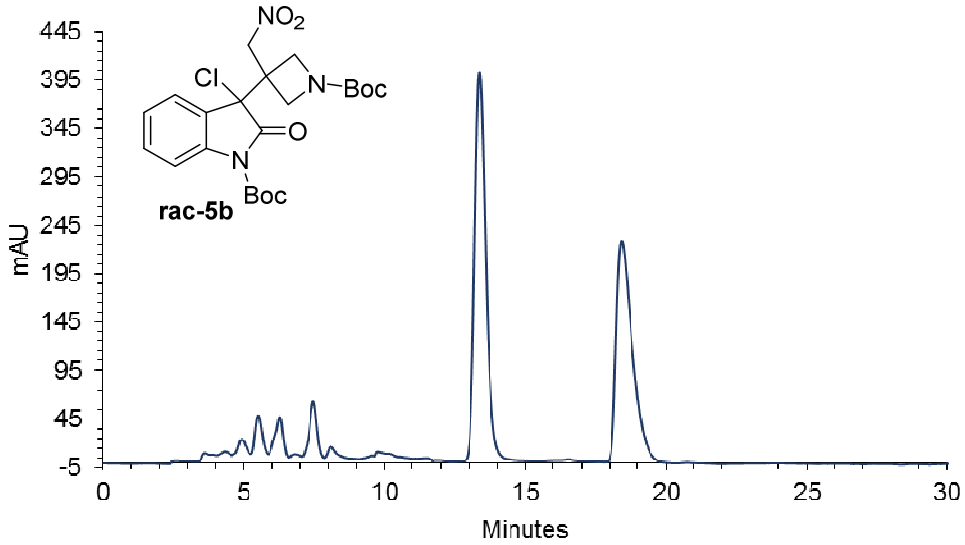
N-Boc-(*R*)-3-chloro-3-(3-(nitromethyl)oxetan-3-yl)-2-oxoindole (**5a**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
10.979	188.52080	3.5688
12.459	5093.91309	96.4312

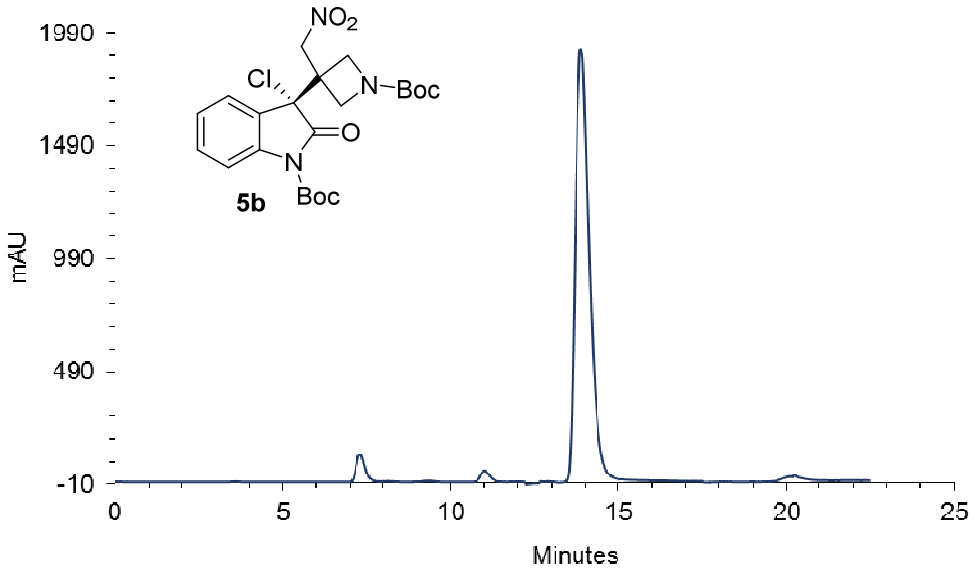
N-Boc-3-chloro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**rac-5b**)



Signal 3: DAD1 C, Sig=225,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
13.380	1.10441E+04	52.0818
18.439	1.01612E+04	47.9182

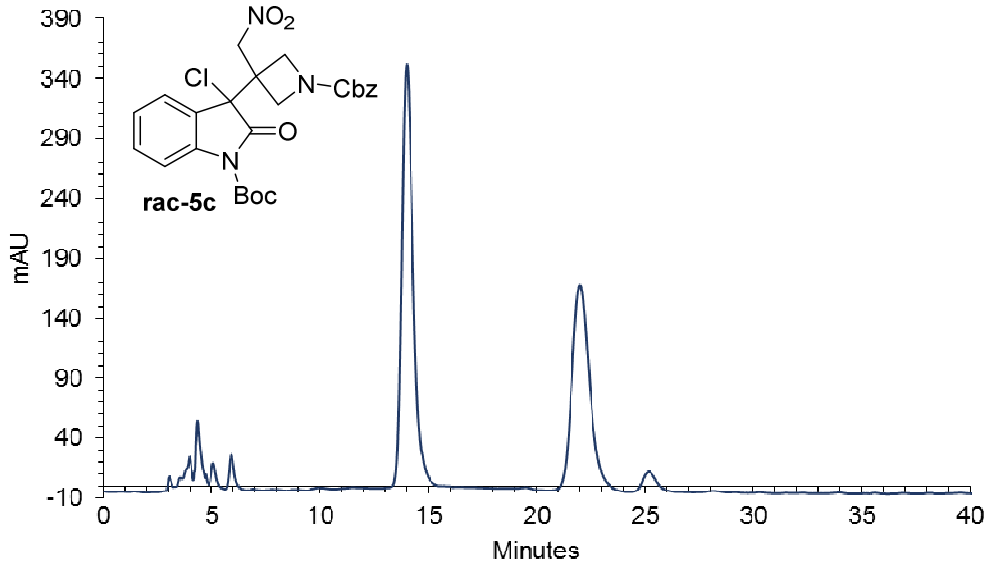
N-Boc-(*S*)-3-chloro-3-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5b**)



Signal 3: DAD1 C, Sig=225,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
13.875	5.61593E+04	98.7131
20.223	732.11316	1.2869

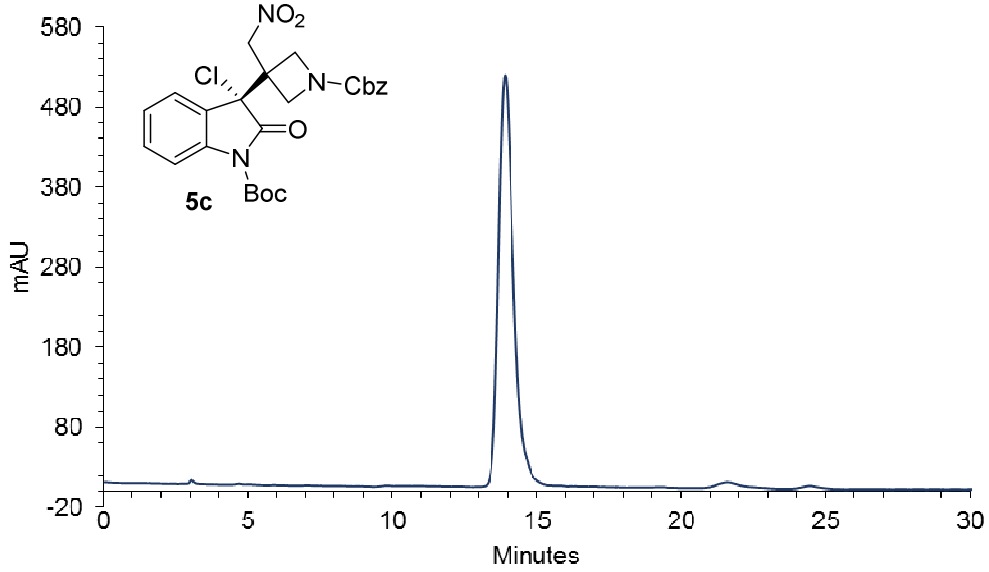
N-Boc-3-chloro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**rac-5c**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
13.973	8333.23535	50.1671
21.979	8277.70459	49.8329

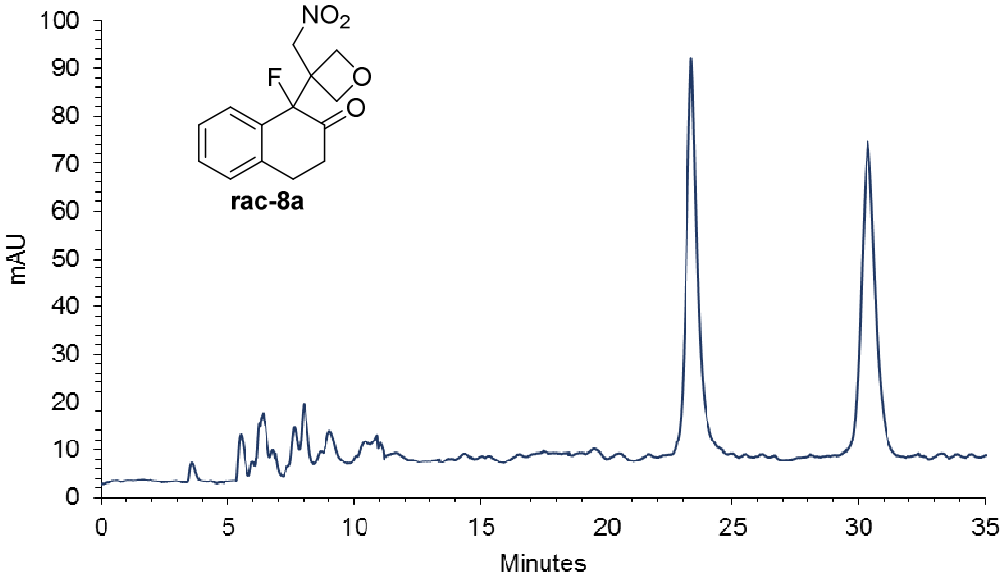
N-Boc-(*S*)-3-chloro-3-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-2-oxoindole (**5c**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
13.893	1.10842E+04	98.4420
21.595	175.42534	1.5580

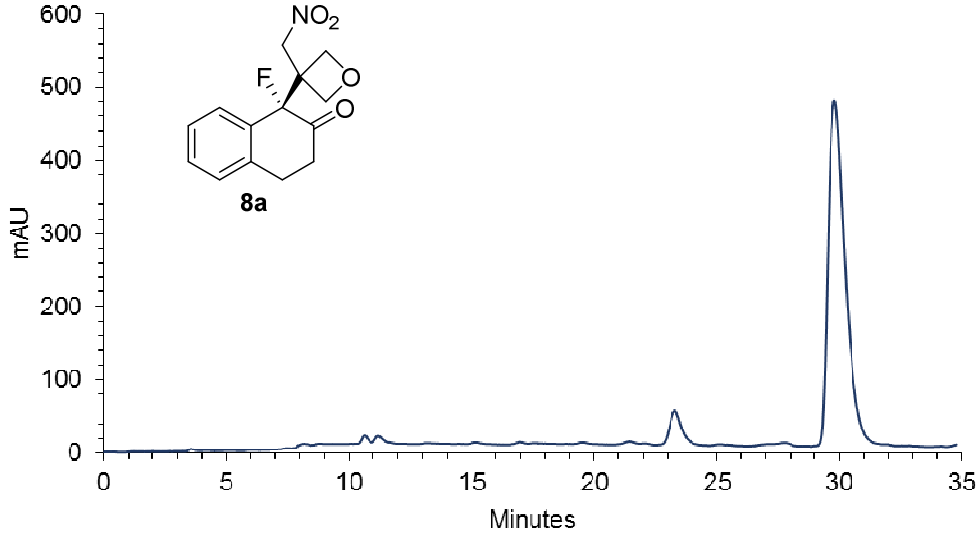
1-Fluoro-1-(3-(nitromethyl)oxetan-3-yl)-3,4-dihydronaphthalen-2(1H)-one (**rac-8a**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
23.223	1273.43945	47.8612
30.346	1387.25184	52.1388

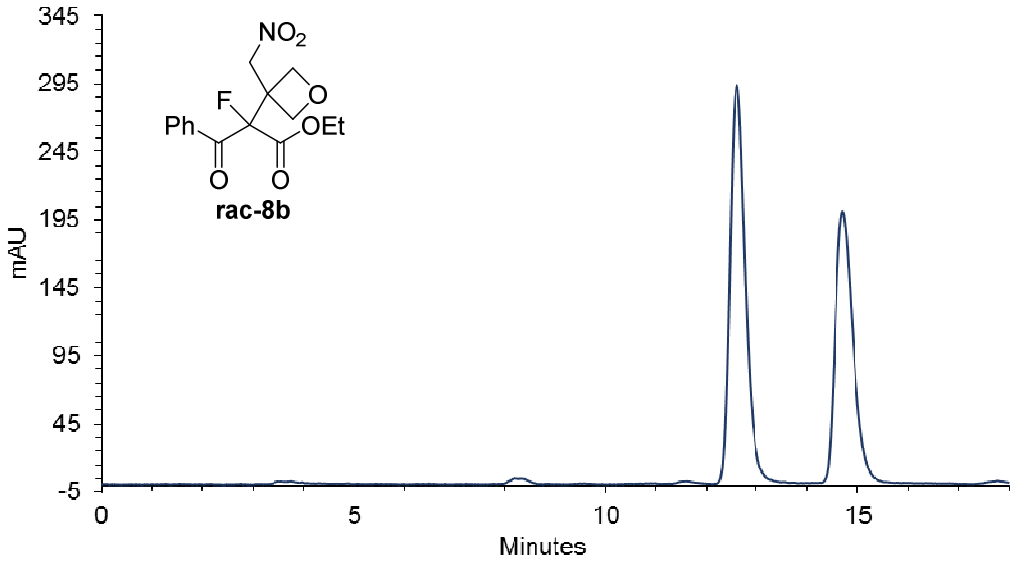
(*R*)-1-Fluoro-1-(3-(nitromethyl)oxetan-3-yl)-3,4-dihydronaphthalen-2(1H)-one (**8a**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
23.294	1335.05505	5.6591
29.798	2.22563E+04	94.3409

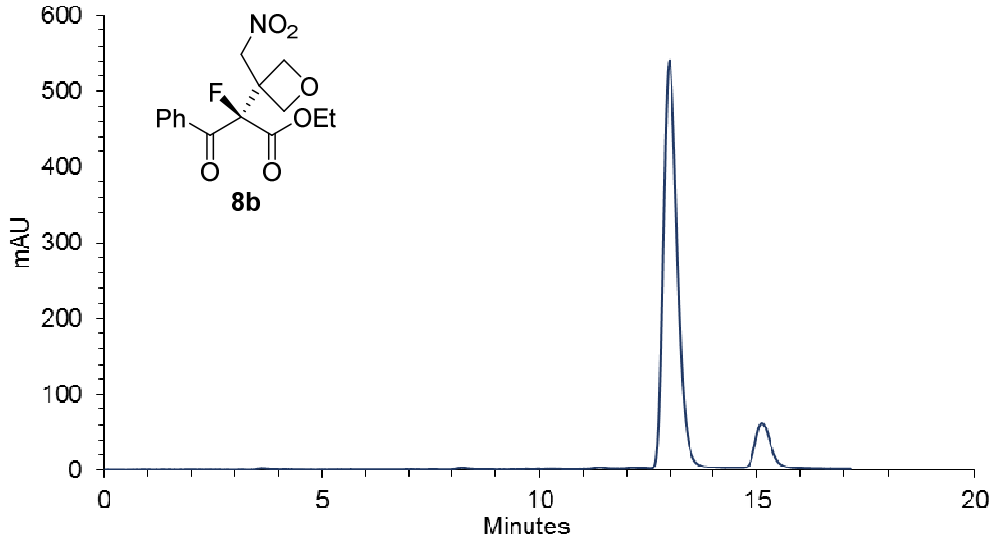
Ethyl 2-fluoro-2-(3-(nitromethyl)oxetan-3-yl)-3-oxo-3-phenylpropanoate (**rac-8b**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.600	6279.61768	50.8086
14.702	6079.75244	49.1914

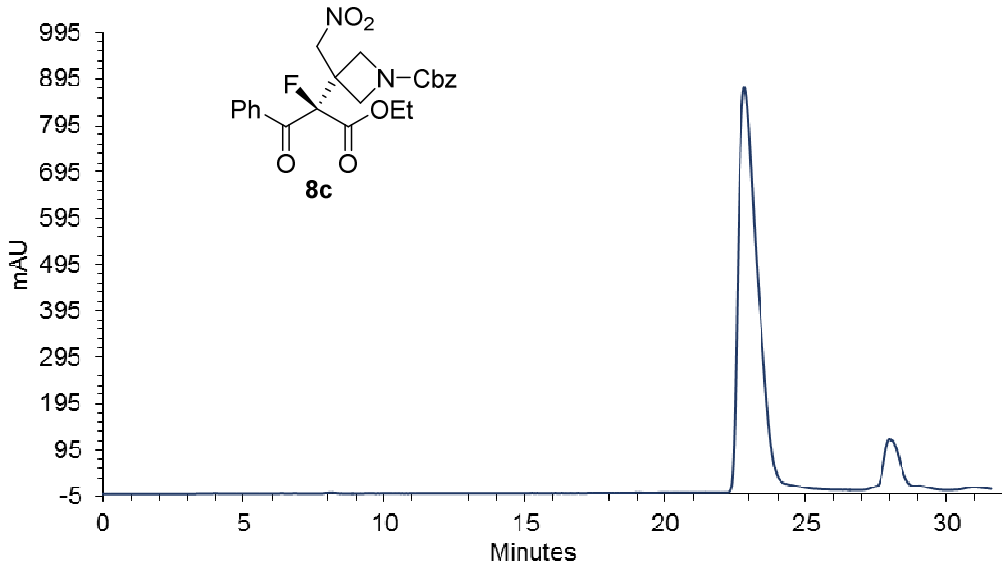
Ethyl (*R*)-2-fluoro-2-(3-(nitromethyl)oxetan-3-yl)-3-oxo-3-phenylpropanoate (**8b**)



Signal 2: DAD1 B, Sig=230,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
12.986	1.20336E+04	89.2595
15.113	1447.99487	10.7405

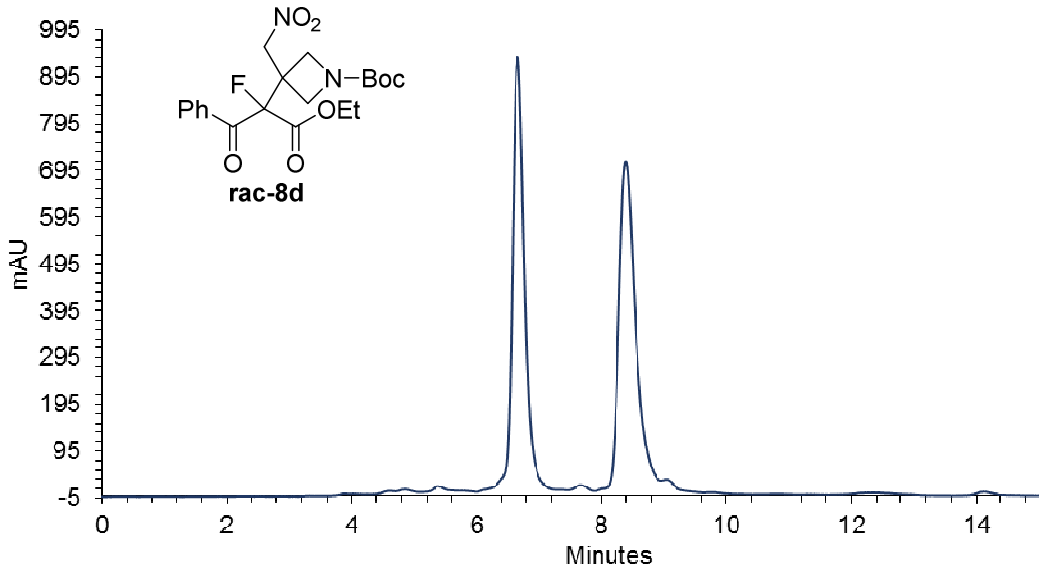
Ethyl (*R*)-2-fluoro-2-(*N*-Cbz-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8c**)



Signal 3: DAD1 C, Sig=243,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
22.822	4.17577E+04	87.9253
28.035	6486.72754	12.0747

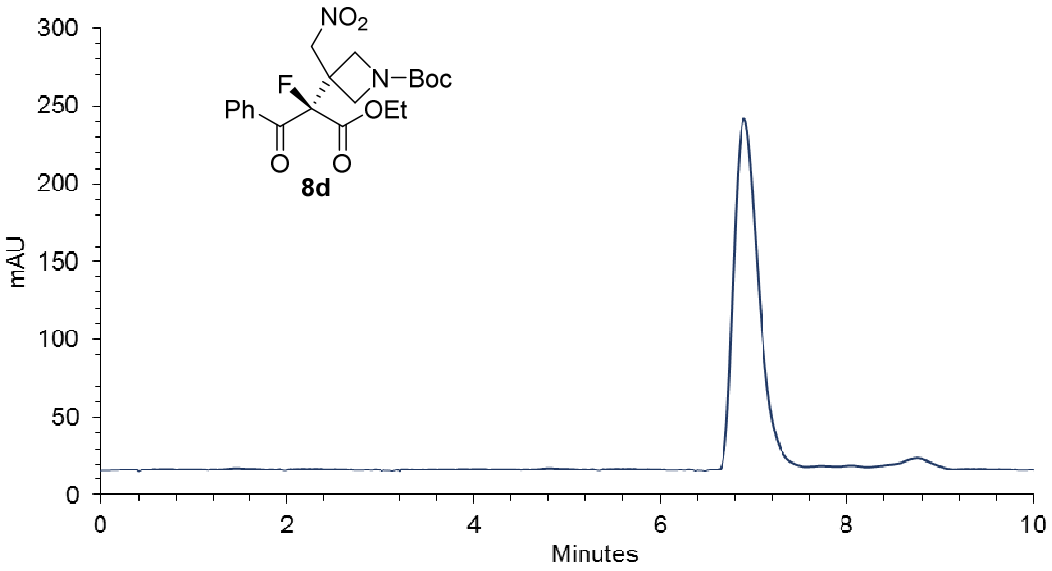
Ethyl 2-fluoro-2-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**rac-8d**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.746	1.10441E+04	54.6594
8.425	9161.16602	45.3406

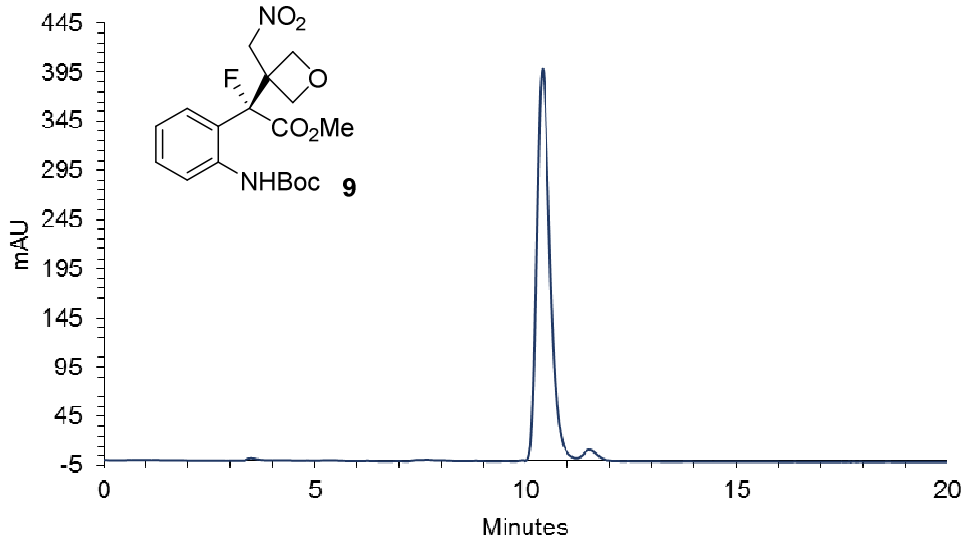
Ethyl (*R*)-2-fluoro-2-(*N*-Boc-3-(nitromethyl)azetidin-3-yl)-3-oxo-3-phenylpropanoate (**8d**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.852	2.03128E+04	89.9897
8.789	2259.54761	10.0103

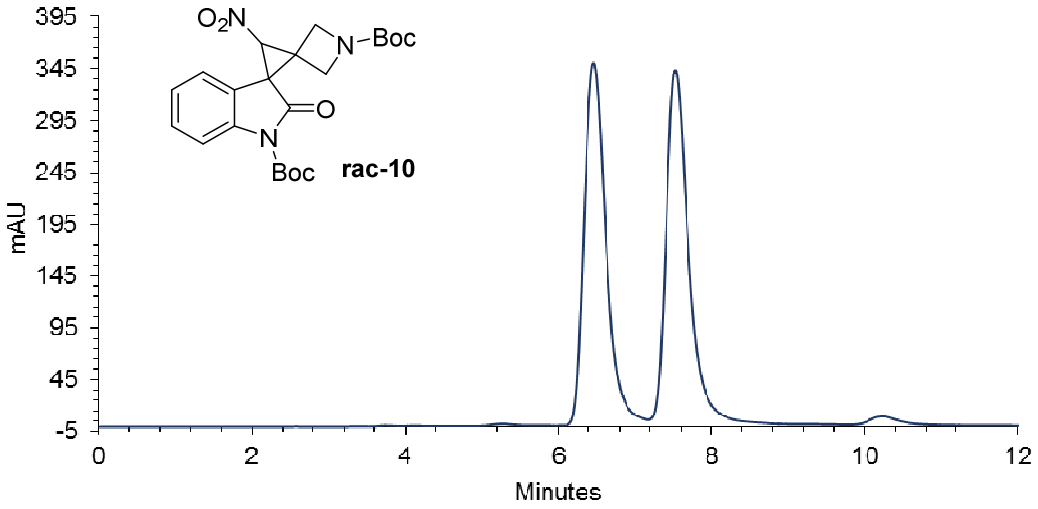
Methyl (R)-2-(2-((*tert*-butoxycarbonyl)amino)phenyl)-2-fluoro-2-(3 (nitromethyl)oxetan-3-yl)acetate (**9**)



Signal 4: DAD1 D, Sig=221,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
10.409	7706.35889	97.0787
11.528	231.90334	2.9213

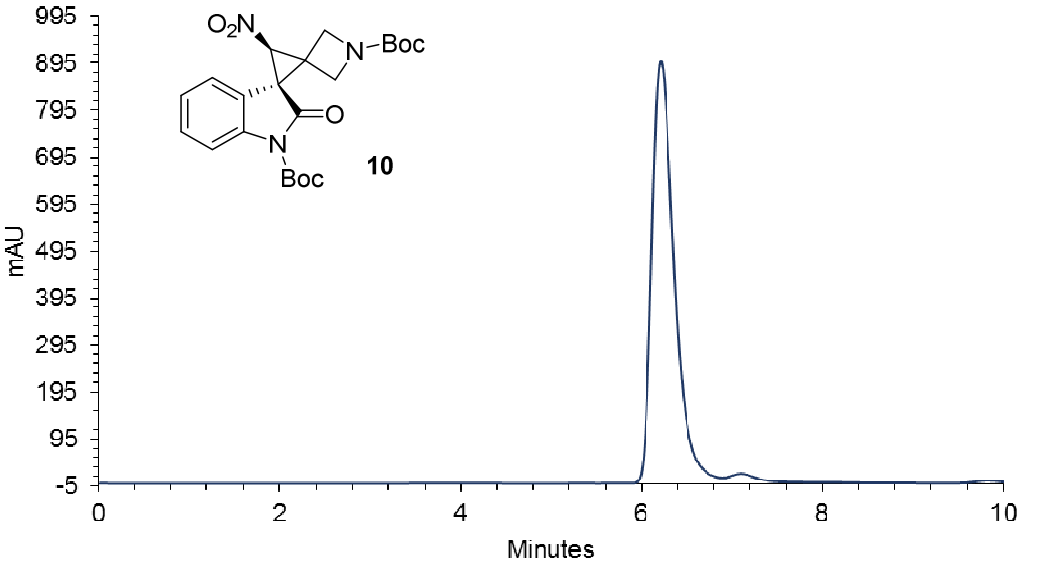
Di-*tert*-butyl 3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**rac-10**)



Signal 4: DAD1 D, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.462	6953.29102	49.8104
7.530	7006.23682	50.1896

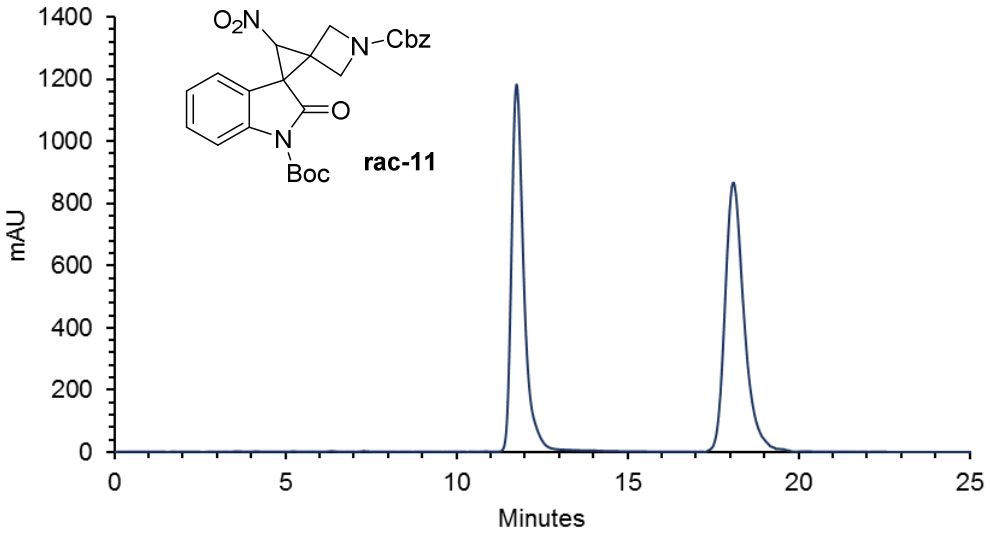
Di-*tert*-butyl (2'*S*,3'*S*)-3'-nitro-2''-oxodispiro[azetidine-3,1'-cyclopropane-2',3''-indoline]-1,1''-dicarboxylate (**10**)



Signal 4: DAD1 D, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
6.218	1.54833E+04	97.4536
7.103	404.56036	2.5464

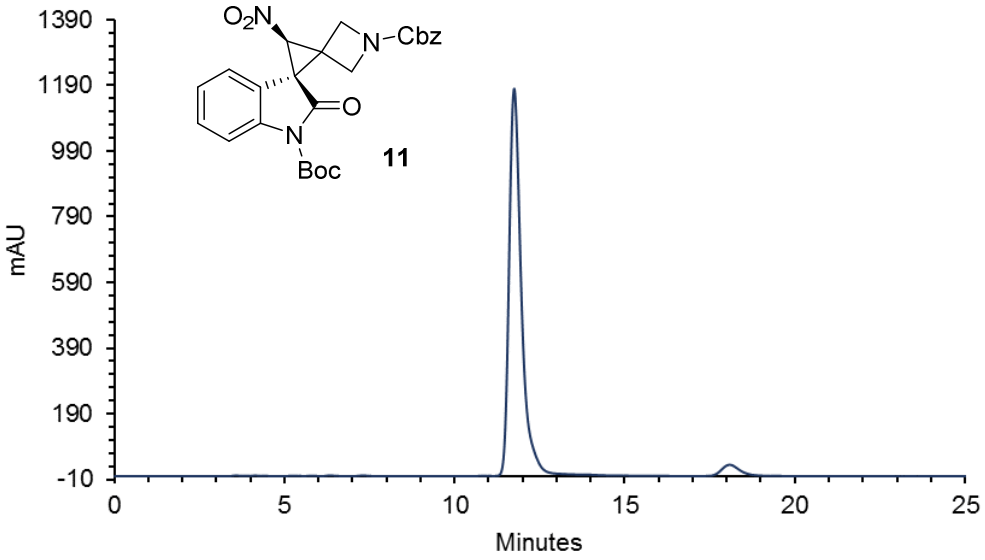
1-Benzyl 1"-(*tert*-butyl)-3'-nitro-2"-oxodispiro[azetidine-3,1'-cyclopropane-2',3"-indoline]-1,1"-dicarboxylate (**rac-11**)



Signal 1: DAD1 A, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
11.753	8224.5926	50.3007
18.122	8126.2694	49.6993

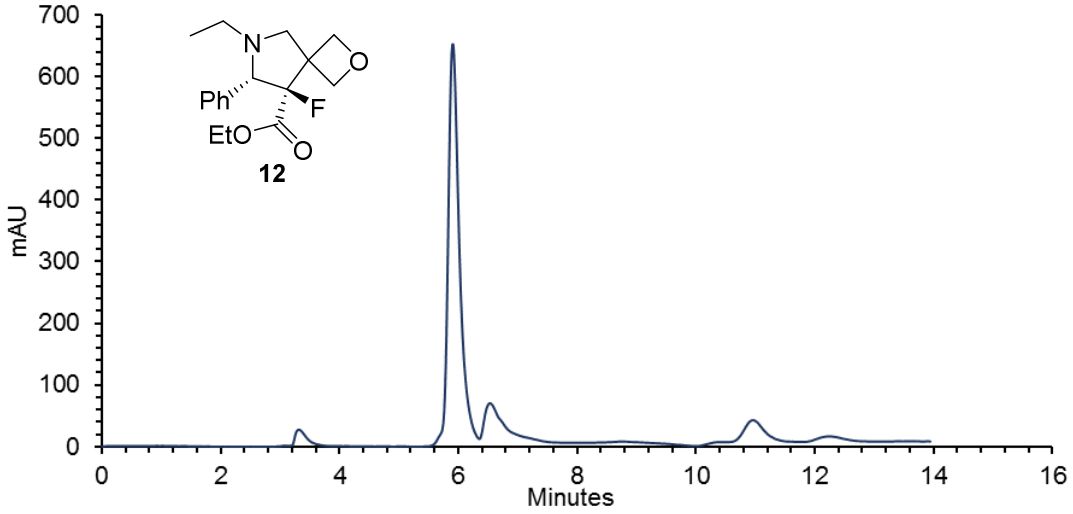
1-Benzyl 1"-(*tert*-butyl)-(2'*S*,3'*S*)-3'-nitro-2"-oxodispiro[azetidine-3,1'-cyclopropane-2',3"-indoline]-1,1"-dicarboxylate (**11**)



Signal 1: DAD1 A, Sig=245,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
11.744	1.20180e4	97.3481
18.081	327.38605	2.6519

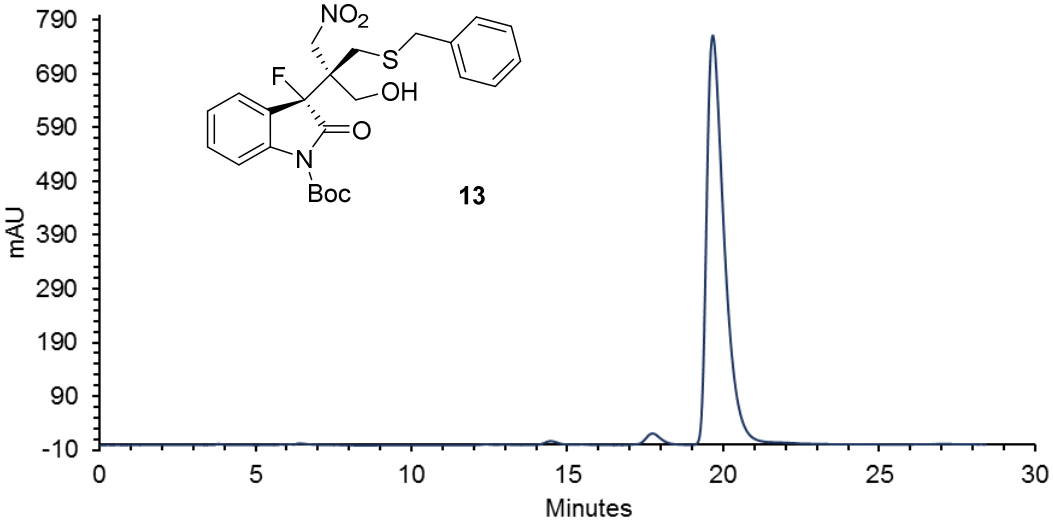
Ethyl (7S,8R)-6-ethyl-8-fluoro-7-phenyl-2-oxa-6-azaspiro[3.4]octane-8-carboxylate (**12**)



Signal 5: DAD1 E, Sig=235,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
5.910	6201.01025	86.9386
6.537	931.61804	13.0614

tert-Butyl (R)-3-((S)-1-(benzylthio)-3-hydroxy-2-(nitromethyl)propan-2-yl)-3-fluoro-2-oxoindole-1-carboxylate (**13**)



Signal 1: DAD1 A, Sig=254,4 Ref=550,100

Ret. Time [min]	Area [mAU*s]	Area %
17.725	209.65608	2.2745
19.649	9008.13867	97.7255

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