Supporting Information

Catalytic Asymmetric Mannich Reaction of α-Fluoronitriles with Ketimines: Enantioselective and Diastereodivergent Construction of Vicinal Tetrasubstituted Stereocenters

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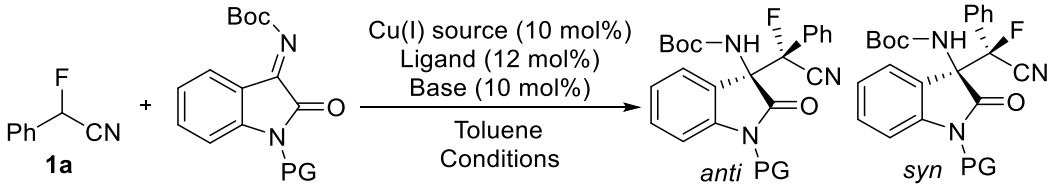
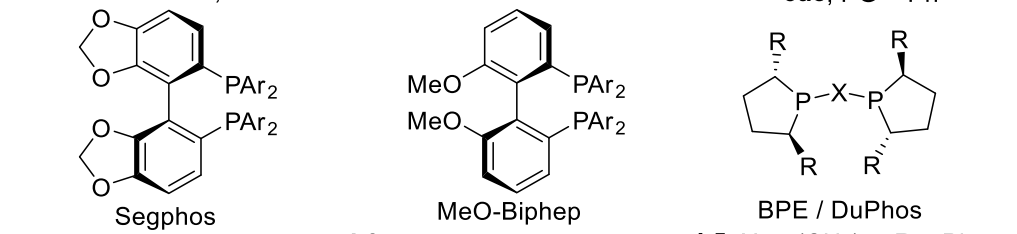
1. General Information

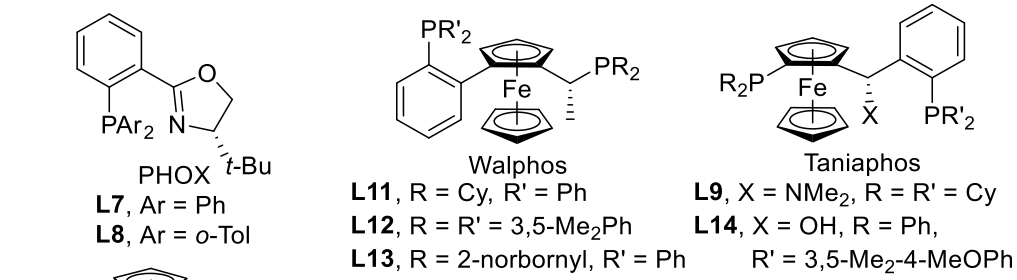
All commercially available reagents and solvents were used without further purification unless noted otherwise. The solvents were stored over 4Å molecular sieves prior to use. Reaction products were purified by column chromatography on silica gel (particle size 32-63 μm) unless stated otherwise. NMR 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. 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.

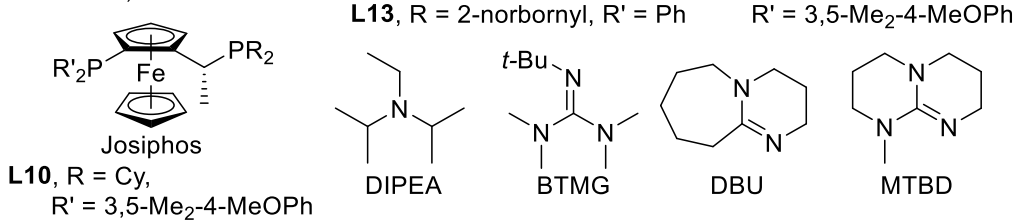
2. Optimization Studies

2.1 Screening of copper sources, ligands and bases







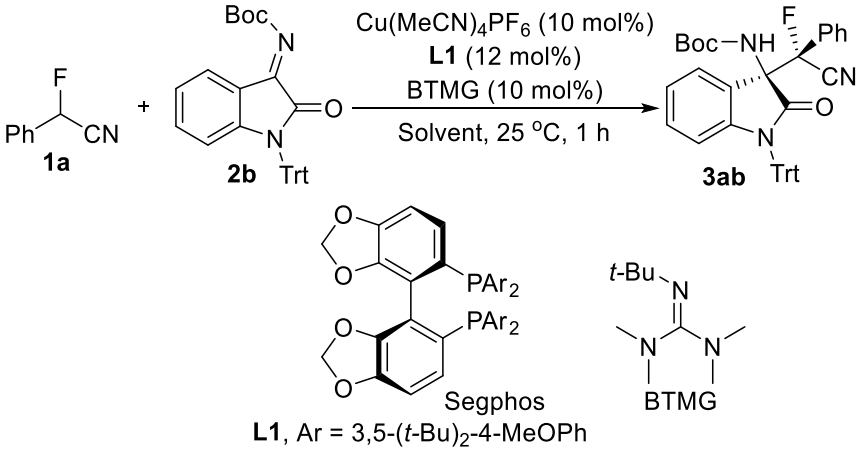


Entry	Cu(I) source	Ligand	2	Base, Conditions	Yield (%)	dr[a] (*anti*/*syn*)	*ee*[b] (%)
1	CuOAc	**L1**	**2a**	25 °C, 24 h	0	-	-
2	CuO^tBu	**L1**	**2a**	25 °C, 3 h	95	1.3:1	50
3	$Cu(PhMe)_{0.5}OTf$	**L1**	**2a**	DIPEA[c], 25 °C, 24 h	91	1.7:1	41
4	CuO^tBu	**L1**	**2b**	25 °C, 3 h	89	6.0:1	82
5	$Cu(PhMe)_{0.5}OTf$	**L1**	**2b**	DIPEA[c], 25 °C, 24 h	85	5.2:1	80
6	$Cu(PhMe)_{0.5}OTf$	**L2**	**2b**	DIPEA[c], 25 °C, 24 h	74	4.6:1	75
7	$Cu(PhMe)_{0.5}OTf$	**L1**	**2b**	BTMG, 25 °C, 1 h	98	5.8:1	83
8	$Cu(MeCN)_4PF_6$	**L1**	**2b**	BTMG, 25 °C, 1 h	98	6.7:1	83

9	$Cu(MeCN)_4PF_6$	**L1**	**2b**	DBU, 25 °C, 1 h	99	6.6:1	73
10	$Cu(MeCN)_4PF_6$	**L1**	**2b**	MTBD, 25 °C, 1 h	99	5.8:1	83
11	$Cu(MeCN)_4PF_6$	**L3**	**2b**	BTMG, 25 °C, 1 h	99	2.0:1	26
12	$Cu(MeCN)_4PF_6$	**L4**	**2b**	BTMG, 25 °C, 1 h	99	4.0:1	79
13	$Cu(MeCN)_4PF_6$	**L5**	**2b**	BTMG, 25 °C, 1 h	99	1.5:1	50
14	$Cu(MeCN)_4PF_6$	**L6**	**2b**	BTMG, 25 °C, 1 h	99	1.3:1	31
15	$Cu(MeCN)_4PF_6$	**L7**	**2b**	BTMG, 25 °C, 1 h	99	1.3:1	40
16	$Cu(MeCN)_4PF_6$	**L8**	**2b**	BTMG, 25 °C, 1 h	99	1.1:1	47
17	$Cu(MeCN)_4PF_6$	**L1**	**2b**	BTMG, -35 °C, 24 h	95	12.3:1	90
18[d]	$Cu(MeCN)_4PF_6$	**ent-L9**[e]	**2b**	BTMG, 25 °C, 1 h	97	1:1.6	3
19[d]	$Cu(MeCN)_4PF_6$	**ent-L9**[e]	**2a**	BTMG, 25 °C, 1 h	99	1:5.7	31
20[d]	$Cu(MeCN)_4PF_6$	**L10**	**2a**	BTMG, -35 °C, 24 h	75	1:2.5	4
21[d]	$Cu(MeCN)_4PF_6$	**L11**	**2a**	BTMG, -35 °C, 24 h	99	1:7.3	19
22[d]	$Cu(MeCN)_4PF_6$	**L12**	**2a**	BTMG, -35 °C, 24 h	99	1:5.6	60
23[d]	$Cu(MeCN)_4PF_6$	**ent-L13**[e]	**2a**	BTMG, -35 °C, 24 h	99	1:13.4	-70
24[d]	$Cu(MeCN)_4PF_6$	**ent-L13**[e]	**2c**	BTMG, -35 °C, 24 h	98	1:8.7	-75
25[d]	$Cu(MeCN)_4PF_6$	**L14**	**2a**	BTMG, -35 °C, 48 h	94	1:5.7	80
26[d]	$Cu(MeCN)_4PF_6$	**L14**	**2c**	BTMG, -35 °C, 72 h	94	1:3.0	98

Reaction condition: **1a** (0.055 mmol), **2** (0.050 mmol), Cu(I) source (0.005 mmol), ligand (0.006 mmol) and base in 0.3 mL toluene. [a] Determined by ^{19}F NMR analysis of the reaction mixture. [b] Determined by chiral HPLC analysis. The values correspond to the major diastereomer, the "-" sign indicates the reversion of the enantioselectivity. [c] The base loading was 80 mol%. [d] The loading of Cu(I) source, ligand, and base was reduced by half. [e] The enantiomer of the drawn ligand structure was used.

2.2 Screening of solvents



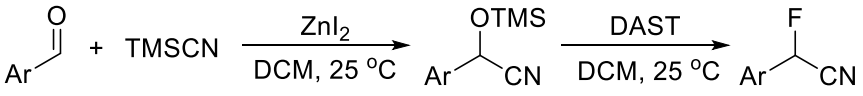
Entry	Solvent	Yield (%)	dr[a] (*anti*/*syn*)	*ee*[b] (%)
1	Toluene	99	6.7:1	83
2	Xylene	96	6.5:1	83
3	$PhCF_3$	99	5.6:1	80
4	MTBE	97	5.1:1	83
5	$CHCl_3$	20	5.8:1	n. d.

Reaction condition: **1a** (0.055 mmol), **2b** (0.050 mmol), $Cu(MeCN)_4PF_6$ (0.005 mmol), **L1** (0.006 mmol) and BTMG (0.005 mmol) in 0.3 mL solvent. [a]Determined by ^{19}F NMR analysis. [b]Determined by chiral HPLC analysis.

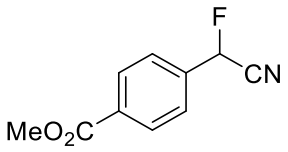
3. Synthetic Procedures and Compound Characterization

3.1 Synthesis of α-fluoro arylacetonitriles **1a**-**1l**

The α-fluoro arylacetonitriles were prepared *via* a two-step synthesis including cyanide addition and deoxyfluorination from aryl aldehydes using literature procedures.[1] Compounds **1f**-**1j**, and **1l** have not been reported previously.

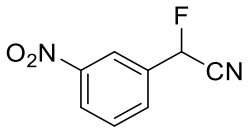


Methyl 4-(cyanofluoromethyl)benzoate (**1f**)



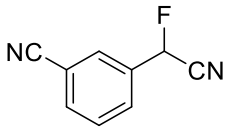
Compound **1f** was synthesized from methyl 4-formylbenzoate in 53% overall yield as a white solid, Mp 43.4-47.1 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.96 (s, 3H), 6.13 (d, *J* = 46.7 Hz, 1H), 7.63 (dd, *J* = 8.3, 1.7 Hz, 2H), 8.16 (dd, *J* = 8.3, 1.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 52.6, 79.7 (d, $J_{C\text{-}F}$ = 183.3 Hz), 114.9 (d, $J_{C\text{-}F}$ = 32.6 Hz), 127.3 (d, $J_{C\text{-}F}$ = 4.6 Hz), 130.6 (d, $J_{C\text{-}F}$ = 1.2 Hz), 132.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 135.7 (d, $J_{C\text{-}F}$ = 20.4 Hz), 166.0 (d, $J_{C\text{-}F}$ = 1.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -172.55 (d, *J* = 46.1 Hz). Anal. Calcd. for $C_{10}H_8FNO_2$: C, 62.18; H, 4.17; N, 7.25. Found: C, 62.14; H, 4.21; N, 7.28.

2-Fluoro-2-(3-nitrophenyl)acetonitrile (**1g**)



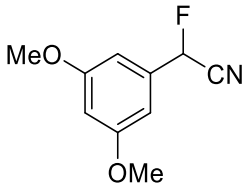
Compound **1g** was synthesized from 3-nitrobenzaldehyde in 42% overall yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.21 (d, *J* = 46.4 Hz, 1H), 7.74 (ddd, *J* = 7.5, 7.5, 0.7 Hz, 1H), 7.92 (dd, *J* = 7.8, 1.3 Hz, 1H), 8.39 (ddd, *J* = 8.3, 2.6, 1.2 Hz, 1H), 8.43 (dd, *J* = 1.9, 1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 79.0 (d, $J_{C\text{-}F}$ = 184.9 Hz), 114.4 (d, $J_{C\text{-}F}$ = 32.6 Hz), 122.5 (d, $J_{C\text{-}F}$ = 5.2 Hz), 126.1 (d, $J_{C\text{-}F}$ = 2.4 Hz), 130.9, 132.9 (d, $J_{C\text{-}F}$ = 4.3 Hz), 133.4 (d, $J_{C\text{-}F}$ = 21.5 Hz), 148.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -172.84 (d, *J* = 46.4 Hz). Anal. Calcd. for $C_8H_5FN_2O_2$: C, 53.34; H, 2.80; N, 15.55. Found: C, 53.32; H, 2.80; N, 15.53.

3-(Cyanofluoromethyl)benzonitrile (**1h**)



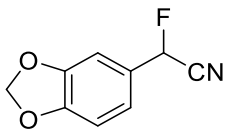
Compound **1h** was synthesized from 3-cyanobenzaldehyde in 47% overall yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.12 (d, *J* = 46.5 Hz, 1H), 7.67 (dd, *J* = 7.7, 7.7 Hz, 1H), 7.84 – 7.79 (m, 2H), 7.85 (d, *J* = 1.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 79.1 (d, J_{C-F} = 184.5 Hz), 114.1, 114.4 (d, J_{C-F} = 32.5 Hz), 117.5, 130.6 (d, J_{C-F} = 0.8 Hz), 130.8 (d, J_{C-F} = 4.8 Hz), 131.4 (d, J_{C-F} = 4.3 Hz), 133.1 (d, J_{C-F} = 21.4 Hz), 134.7 (d, J_{C-F} = 2.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -172.82 (d, *J* = 46.4 Hz). Anal. Calcd. for $C_9H_5FN_2$: C, 67.50; H, 3.15; N, 17.49. Found: C, 67.49; H, 3.16; N, 17.48.

2-(3,5-Dimethoxyphenyl)-2-fluoroacetonitrile (**1i**)



Compound **1i** was synthesized from 3,5-dimethoxybenzaldehyde in 58% overall yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.83 (s, 6H), 5.97 (d, *J* = 46.9 Hz, 1H), 6.56 (dd, *J* = 2.2, 2.1 Hz, 1H), 6.66 (ddd, *J* = 2.2, 2.1, 1.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.7, 80.2 (d, J_{C-F} = 182.6 Hz), 103.1 (d, J_{C-F} = 3.1 Hz), 105.3 (d, J_{C-F} = 4.7 Hz), 115.3 (d, J_{C-F} = 33.6 Hz), 133.4 (d, J_{C-F} = 20.6 Hz), 161.6 (d, J_{C-F} = 1.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -169.8 (dd, *J* = 46.8, 1.6 Hz). Anal. Calcd. for $C_{10}H_{10}FNO_2$: C, 61.53; H, 5.16; N, 7.18. Found: C, 61.57; H, 5.14; N, 7.20.

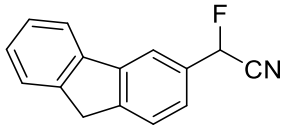
2-(Benzo[d][1,3]dioxol-5-yl)-2-fluoroacetonitrile (**1j**)



Compound **1j** was synthesized from benzo[d][1,3]dioxole-5-carbaldehyde in 71% overall yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.92 (d, *J* = 47.4 Hz, 1H), 6.05 (s, 2H), 6.87 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.00 – 7.07 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 80.1 (d, J_{C-F} = 181.4

Hz), 102.1, 108.1 (d, $J_{C\text{-}F}$ = 3.1 Hz), 108.9 (d, $J_{C\text{-}F}$ = 2.3 Hz), 115.4 (d, $J_{C\text{-}F}$ = 35.1 Hz), 122.8 (d, $J_{C\text{-}F}$ = 5.1 Hz), 125.2 (d, $J_{C\text{-}F}$ = 21.2 Hz), 148.7 (d, $J_{C\text{-}F}$ = 2.1 Hz), 150.3 (d, $J_{C\text{-}F}$ = 3.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.49 (d, J = 47.5 Hz). Anal. Calcd. for $C_9H_6FNO_2$: C, 60.34; H, 3.38; N, 7.82. Found: C, 60.33; H, 3.36; N, 7.80.

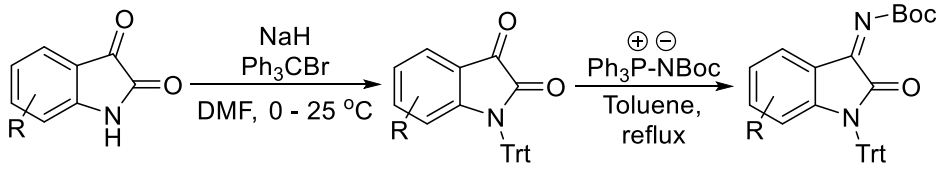
2-(9H-Fluoren-3-yl)-2-fluoroacetonitrile (**1l**)



Compound **1m** was synthesized from 9H-fluorene-3-carbaldehyde in 69% overall yield as a white solid, Mp 86.2-88.8 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.97 (s, 2H), 6.11 (d, J = 47.3 Hz, 1H), 7.38 (dd, J = 7.4, 1.5 Hz, 1H), 7.43 (d, J = 7.2 Hz, 1H), 7.56 (dd, J = 7.8, 3.3 Hz, 1H), 7.59 (dd, J = 6.9, 1.3 Hz, 1H), 7.75 (s, 1H), 7.84 (d, J = 6.9 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 37.0, 80.6 (d, $J_{C\text{-}F}$ = 181.3 Hz), 115.6 (d, $J_{C\text{-}F}$ = 34.6 Hz), 120.6 (d, $J_{C\text{-}F}$ = 2.2 Hz), 120.7, 124.6 (d, $J_{C\text{-}F}$ = 4.1 Hz), 125.4, 126.9 (d, $J_{C\text{-}F}$ = 4.3 Hz), 127.2, 128.1, 129.6 (d, $J_{C\text{-}F}$ = 20.4 Hz), 140.4 (d, $J_{C\text{-}F}$ = 1.9 Hz), 143.9 (d, $J_{C\text{-}F}$ = 0.6 Hz), 144.4 (d, $J_{C\text{-}F}$ = 2.0 Hz), 145.0 (d, $J_{C\text{-}F}$ = 3.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -163.51 (d, J = 47.4 Hz). Anal. Calcd. for $C_{15}H_{10}FN$: C, 80.70; H, 4.52; N, 6.27. Found: C, 80.70; H, 4.54; N, 6.23.

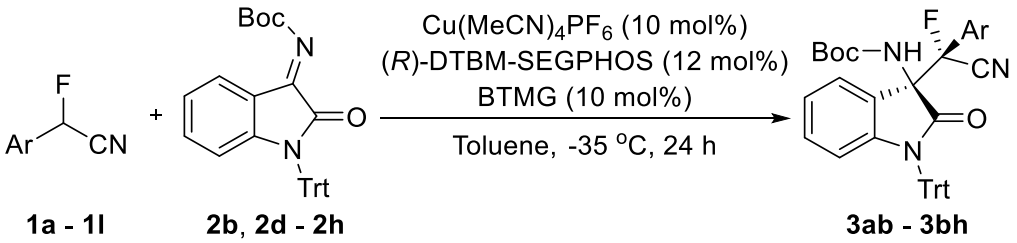
3.2 Synthesis of ketimines

Ketimines **2a**-**2h** were prepared following a literature procedure.[2]



3.3 Procedures for the addition of α-fluoro arylacetonitriles **1** to ketimines **2**

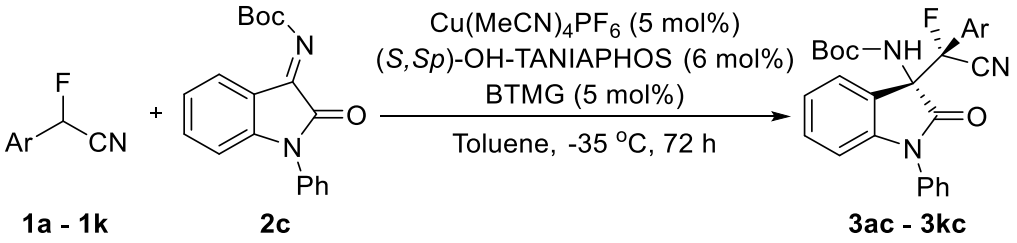
Procedure A: Synthesis of the *anti*-diastereomer



1a - 1l **2b**, **2d - 2h** **3ab - 3bh**

A mixture of $Cu(CH_3CN)_4PF_6$ (1.9 mg, 0.005 mmol) and (*R*)-DTBM-SEGPHOS, **L1** (7.1 mg, 0.006 mmol) was dissolved in anhydrous toluene (0.15 mL) under nitrogen at room temperature and stirred for 30 minutes. Ketimine **2** (0.05 mmol) and α-fluoroarylacetonitrile **1** (0.055 mmol) were placed in a jacketed flask under nitrogen. The copper(I) complex solution was then transferred into this jacketed flask using another 0.2 mL of anhydrous toluene. The reaction mixture was cooled to -35 °C, gently stirred, and a solution of 2-*tert*-butyl-1,1,3,3-tetramethylguanidine, BTMG (10.0 µL, 0.5 *M* in dry toluene) was added. Upon completion of the reaction (24 hours), the solvent was removed under reduced pressure and the crude residue was purified by column chromatography as described below.

Procedure B: Synthesis of the *syn*-diastereomer



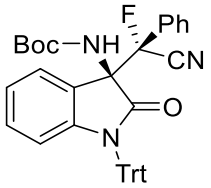
1a - 1k **2c** **3ac - 3kc**

A mixture of $Cu(CH_3CN)_4PF_6$ (1.9 mg, 0.005 mmol) and (*S,Sp*)-OH-TANIAPHOS, **L14** (4.8 mg, 0.006 mmol) was dissolved in anhydrous THF (0.15 mL) under nitrogen at room temperature and stirred for 30 minutes. Ketimine **2c** (32.2 mg, 0.10 mmol) and α-fluoro arylacetonitrile **1** (0.11 mmol) were placed in a jacketed flask under nitrogen. The copper(I) complex solution was then transferred into this jacketed flask using another 0.2 mL of anhydrous toluene. The reaction mixture was cooled to -35 °C, gently stirred, followed by addition of a solution of 2-*tert*-butyl-1,1,3,3-tetramethylguanidine, BTMG (10.0 µL, 0.5 *M* in dry toluene). Upon completion of the reaction (72 hours), the solvent was removed under reduced pressure and the crude residue was purified by column chromatography as described below.

Gram scale synthesis of α-fluoro β-aminonitrile *anti*-**3ab**

First, $Cu(CH_3CN)_4PF_6$ (28.0 mg, 0.075 mmol), (*R*)-DTBM-SEGPHOS, **L1** (106.2 mg, 0.090 mmol), ketimine **2b** (733.0 mg, 1.50 mmol), and α-fluoro benzylnitrile **1a** (218.9 mg, 1.65 mmol) were dissolved using anhydrous toluene (4.5 mL) in a jacketed flask under nitrogen. Then, the reaction mixture was cooled to -35 °C and stirred for an hour followed by addition of BTMG (12.8 mg, 0.075 mmol). The reaction mixture was stirred at -35 °C for 48 hours. Upon completion, the solvent was removed under reduced pressure and the crude residue was purified by column chromatography to give **3ab** (937.7 mg) in 98% yield as a yellow crystalline solid. Mp 119.8-122.2 °C. The dr was determined as 12.7:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 90% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(major) = 10.2 min, t_R(minor) = 13.4 min.

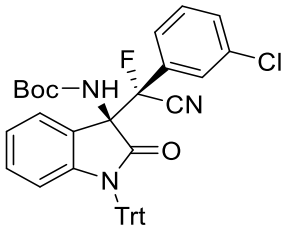
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ab**)



Compound **3ab** was obtained from α-fluoro benzylnitrile **1a** (7.4 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 29.7 mg (95%) of a yellow crystalline solid. Mp 119.8-122.2 °C. The dr was determined as 12.7:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 90% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 10.1 min, t_R(major) = 12.7 min. ^1H NMR (400 MHz, $CDCl_3$) δ = 1.34 (s, 9H), 5.88 (d, *J* = 2.6 Hz, 1H), 6.10 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.85 – 6.97 (m, 7H), 7.02 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.09 – 7.17 (m, 9H), 7.22 (dd, *J* = 8.1, 1.1 Hz, 2H), 7.42 (dd, *J* = 7.8, 7.5Hz, 2H), 7.55 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.72 (dd, *J* = 7.6, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.2 (d, $J_{C\text{-}F}$ = 21.5 Hz), 75.8, 81.0, 93.4 (d, $J_{C\text{-}F}$ = 201.1 Hz), 115.2 (d, $J_{C\text{-}F}$ = 31.8 Hz), 116.6, 122.5, 122.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 124.3, 126.8, 127.0, 127.2, 128.5 (d, $J_{C\text{-}$

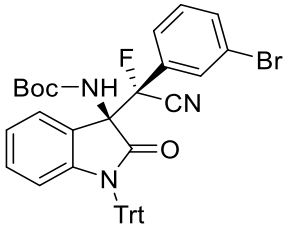
$_F$ = 1.5 Hz), 129.8, 129.9, 130.3 (d, J_{C-F} = 22.9 Hz), 131.1, 141.0, 144.5, 153.8, 173.1 (d, J_{C-F} = 1.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.0 (s, major diastereomer), -150.6 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{40}H_{34}FN_3NaO_3$ 646.2476, found 646.2479.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3bb**)



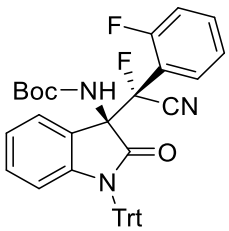
Compound **3bb** was obtained from 2-(3-chlorophenyl)-2-fluoroacetonitrile **1b** (9.3 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 31.9 mg (97%) of a yellow amorphous solid. The dr was determined as 36.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 97% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 8.1 min, t_R(major) = 9.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 5.85 (d, *J* = 2.4 Hz, 1H), 6.16 (d, *J* = 8.2 Hz, 1H), 6.92 (dd, *J* = 7.7, 7.5 Hz, 1H), 6.94 – 6.98 (m, 6H), 7.01 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.05 (dd, *J* = 7.8, 7.4 Hz, 1H), 7.12 – 7.19 (m, 9H), 7.29 (dd, *J* = 2.1, 2.0 Hz, 1H), 7.34 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.53 (ddd, *J* = 8.1, 2.1, 1.0 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.0 (d, J_{C-F} = 21.2 Hz), 75.9, 81.1, 92.7 (d, J_{C-F} = 202.7 Hz), 114.8 (d, J_{C-F} = 31.9 Hz), 116.8, 122.2 (d, J_{C-F} = 3.1 Hz), 122.7, 124.4, 125.2 (d, J_{C-F} = 7.3 Hz), 126.9 (d, J_{C-F} = 9.5 Hz), 127.1, 127.3, 129.3, 129.6, 129.7, 131.4, 132.2 (d, J_{C-F} = 22.9 Hz) 135.1, 140.9, 144.4, 153.8, 172.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.0 (s, major diastereomer), -150.6 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{40}H_{33}ClFN_3NaO_3$ 680.2087, found 680.2088.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-bromophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3cb**)



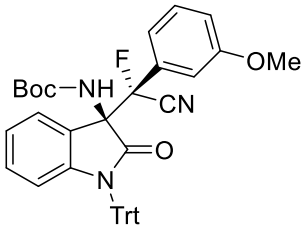
Compound **3cb** was obtained from 2-(3-bromophenyl)-2-fluoroacetonitrile **1c** (11.8 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 34.6 mg (98%) of a yellow amorphous solid. The dr was determined as 39.5:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 97% using Phenomenex Amylose-2, hexanes/ethanol 95:5 flow rate = 1 mL/min condition. t_R(minor) = 12.6 min, t_R(major) = 14.4 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ =1.36 (s, 9H), 5.85 (d, *J* = 2.4 Hz, 1H), 6.16 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.89 – 6.98 (m, 7H), 7.02 – 7.08 (m, 2H), 7.12 – 7.20 (m, 9H), 7.27 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.43 (dd, *J* = 2.0, 1.9 Hz, 1H), 7.69 (ddd, *J* = 8.1, 2.0, 1.0 Hz, 1H), 7.74 (dd, *J* = 7.5, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.1 (d, J_{C-F} = 21.4 Hz), 75.9, 81.1, 92.7 (d, J_{C-F} = 203.0 Hz), 114.8 (d, J_{C-F} = 31.9 Hz), 116.8, 122.2 (d, J_{C-F} = 3.2 Hz), 122.7, 123.0 (d, J_{C-F} = 1.6 Hz), 124.3, 125.6 (d, J_{C-F} = 7.3 Hz), 127.1, 127.4, 129.4, 129.6, 129.7, 129.8, 132.4 (d, J_{C-F} = 23.0 Hz), 134.3, 140.9, 144.3, 153.8, 172.8 (d, J_{C-F} = 1.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.2 (s, major diastereomer), -150.4 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{40}H_{33}BrFN_3NaO_3$ 724.1582, found 724.1585.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-fluorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3db**)



Compound **3db** was obtained from 2-(2-fluorophenyl)-2-fluoroacetonitrile **1d** (8.4 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 30.2 mg (94%) of a yellow amorphous solid. The dr was determined as 9.4:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 93% using Phenomenex Amylose-2, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(minor) = 16.3 min, t_R(major) = 18.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.32 (s, 9H), 5.85 (d, *J* = 2.3 Hz 1H), 6.20 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.86 – 6.98 (m, 2H), 7.13 – 7.19 (m, 15H), 7.23 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.29 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.37 (dd, *J* = 8.7, 7.6 Hz, 1H), 7.44 (m, 1H), 7.53 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.6 (d, $J_{C\text{-}F}$ = 24.0 Hz), 69.4, 75.8, 81.0, 92.3 (d, $J_{C\text{-}F}$ = 202.9 Hz), 113.6 (d, $J_{C\text{-}F}$ = 30.6 Hz), 116.3, 116.8 (d, $J_{C\text{-}F}$ = 23.0 Hz), 121.9, 122.3, 124.4 (dd, $J_{C\text{-}F}$ = 3.7, 1.4 Hz), 125.5, 127.0, 127.3, 127.9, 129.2 (d, $J_{C\text{-}F}$ = 15.4 Hz), 129.8, 129.9, 133.2 (d, $J_{C\text{-}F}$ = 8.4 Hz), 141.6 (d, $J_{C\text{-}F}$ = 68.2 Hz), 142.0, 144.4, 153.6, 158.9 (dd, $J_{C\text{-}F}$ = 253.5, 4.4 Hz), 172.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -156.2 (d, *J* = 7.7 Hz, major diastereomer), -154.5 (d, *J* = 12.3 Hz, minor diastereomer), -107.2 (m, major and minor diastereomers). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{40}H_{33}F_2N_3NaO_3$ 664.2382, found 664.2384.

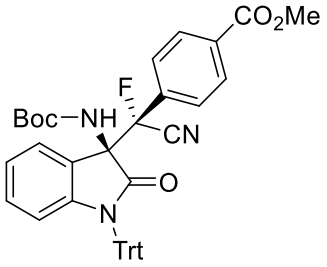
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3eb**)



Compound **3eb** was obtained from 2-(3-methoxyphenyl)-2-fluoroacetonitrile **1e** (9.1 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 31.5 mg (96%) of a yellow amorphous solid. The dr was determined as 24.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 91% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 10.7 min, t_R(major) = 11.7 min. ^{1}H NMR (400

MHz, $CDCl_3$) δ = 1.34 (s, 9H), 3.61 (s, 3H), 5.88 (d, *J* = 2.7 Hz, 1H), 6.13 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.65 (dd, *J* = 2.1, 2.0 Hz, 1H), 6.82 (ddd, *J* = 7.9, 1.9, 1.0 Hz, 1H), 6.90 (dd, *J* = 8.0, 7.9 Hz, 1H), 6.97 – 6.92 (m, 6H), 7.03 (dd, *J* = 8.2, 7.9 Hz, 1H), 7.07 (ddd, *J* = 8.3, 2.5, 0.9 Hz, 1H), 7.10 – 7.17 (m, 9H), 7.33 (dd, *J* = 8.3, 7.8 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.4, 66.2 (d, J_{C-F} = 21.4 Hz), 75.8, 81.0, 93.1 (d, J_{C-F} = 202.0 Hz), 112.1 (d, J_{C-F} = 8.5 Hz), 115.2 (d, J_{C-F} = 32.0 Hz), 116.7, 117.3, 118.8 (d, J_{C-F} = 8.7 Hz), 122.5, 122.8 (d, J_{C-F} = 3.2 Hz), 124.2, 127.0, 127.2, 129.1, 129.5 (d, J_{C-F} = 1.1 Hz), 129.8, 131.4 (d, J_{C-F} = 22.9 Hz), 141.0, 144.6, 153.8, 159.5, 173.1 (d, J_{C-F} = 1.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.1 (s, major diastereomer), -149.0 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{36}FN_3NaO_4$ 676.2582, found 676.2584.

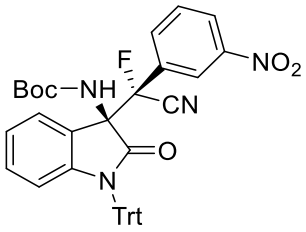
Methyl 4-((*S*)-((*R*)-3-((*tert*-butoxycarbonyl)amino)-2-oxo-1-tritylindolin-3-yl)(cyano)fluoromethyl)benzoate (**3fb**)



Compound **3fb** was obtained from methyl 4-(cyanofluoromethyl)benzoate **1f** (10.6 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (6.5:1 hexanes/ethyl acetate) gave 33.6 mg (99%) of a yellow amorphous solid. The dr was determined as 9.1:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 91% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 17.0 min, t_R(major) = 20.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 3.97 (s, 3H), 5.86 (d, *J* = 2.4 Hz, 1H), 6.11 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.87 – 6.97 (m, 7H), 7.05 (ddd, *J* = 7.8, 7.6, 1.0 Hz, 1H), 7.08 – 7.17 (m, 9H), 7.26 (dd, *J* = 8.6, 0.9 Hz, 2H), 7.74 (dd, *J* = 7.7, 1.5 Hz, 1H), 8.03 (dd, *J* = 8.6, 0.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.3, 52.7, 66.1 (d, J_{C-F} = 21.2 Hz), 76.1, 81.3, 93.2 (d, J_{C-F} = 202.3 Hz), 115.0 (d, J_{C-F} = 32.0 Hz), 116.9, 122.4 (d, J_{C-F} = 2.9 Hz), 122.8, 124.6, 127.2, 127.4, 129.5, 129.7 (d, J_{C-F} = 1.5 Hz),

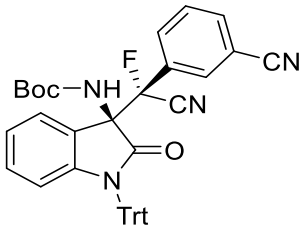
129.9, 133.0, 134.8 (d, $J_{C\text{-}F}$ = 23.0 Hz), 141.1, 144.6, 153.9, 166.0, 172.8 (d, $J_{C\text{-}F}$ = 1.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.2 (s, major diastereomer), -151.7 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{42}H_{36}FN_3NaO_5$ 704.2531, found 704.2534.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-nitrophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3gb**)



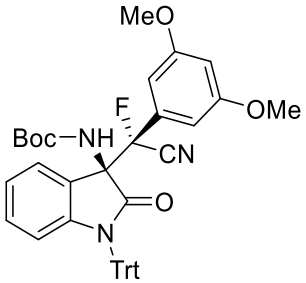
Compound **3gb** was obtained from 2-(3-nitrophenyl)-2-fluoroacetonitrile **1g** (9.9 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (5:1 hexanes/ethyl acetate) gave 32.1 mg (96%) of a yellow amorphous solid. The dr was determined as 8.5:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 94% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 11.0 min, t_R(major) = 14.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.38 (s, 9H), 5.83 (d, *J* = 2.0 Hz, 1H), 6.16 (d, *J* = 8.2, 0.9 Hz, 1H), 6.91 – 6.99 (m, 7H), 7.08 (dd, *J* = 7.6, 7.5 Hz, 1H), 7.11 – 7.19 (m, 9H), 7.40 (dd, *J* = 7.5, 2.3 Hz, 1H), 7.54 (dd, *J* = 8.1, 7.9 Hz, 1H), 7.78 (dd, *J* = 7.6, 1.4 Hz, 1H), 8.10 (dd, *J* = 2.0, 1.9 Hz, 1H), 8.36 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 65.8 (d, $J_{C\text{-}F}$ = 21.5 Hz), 75.9, 81.4, 92.4 (d, $J_{C\text{-}F}$ = 203.5 Hz), 114.4 (d, $J_{C\text{-}F}$ = 31.7 Hz), 116.8, 121.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 122.0 (d, $J_{C\text{-}F}$ = 9.5 Hz), 122.6 (d, $J_{C\text{-}F}$ = 29.3 Hz), 122.9, 124.7, 125.9, 127.1, 127.4, 129.5, 129.6 (d, $J_{C\text{-}F}$ = 6.2 Hz), 132.3, 132.6 (d, $J_{C\text{-}F}$ = 7.0 Hz) 140.8, 144.2, 147.9, 153.7, 172.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.7 (s, major diastereomer), -150.7 (s, minor diastereomer). Anal. Calcd. for $C_{40}H_{33}FN_4O_5$: C, 71.84; H, 4.97; N, 8.38. Found: C, 71.83; H, 5.21; N, 8.33.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-cyanophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3hb**)



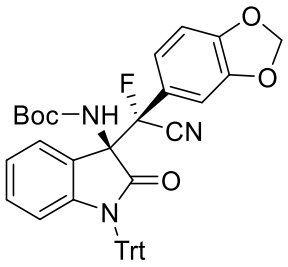
Compound **3hb** was obtained from 2-(3-cyanophenyl)-2-fluoroacetonitrile **1h** (8.8 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (6:1 hexanes/ethyl acetate) gave 31.4 mg (97%) of a yellow amorphous solid. The dr was determined as 9.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 95% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 11.6 min, t_R(major) = 16.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37 (s, 9H), 5.81 (d, *J* = 2.2 Hz, 1H), 6.18 (dd, *J* = 8.2, 0.8 Hz, 1H), 6.92 – 7.02 (m, 7H), 7.08 (dd, *J* = 7.8, 7.6 Hz, 1H), 7.12 – 7.22 (m, 9H), 7.36 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.48 – 7.55 (m, 2H), 7.75 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.80 (ddd, *J* = 7.8, 2.1, 1.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 65.8 (d, $J_{C\text{-}F}$ = 21.5 Hz), 75.9, 81.4, 92.5 (d, $J_{C\text{-}F}$ = 202.8 Hz), 114.5 (d, $J_{C\text{-}F}$ = 31.9 Hz), 114.6, 116.9, 117.2, 121.8 (d, $J_{C\text{-}F}$ = 2.8 Hz), 122.9, 124.8, 127.2, 127.5, 129.3 (d, $J_{C\text{-}F}$ = 1.2 Hz), 129.6, 129.7, 130.4 (d, $J_{C\text{-}F}$ = 9.3 Hz), 131.0 (d, $J_{C\text{-}F}$ = 7.3 Hz), 132.1 (d, $J_{C\text{-}F}$ = 23.4 Hz), 134.5, 140.8, 144.4, 153.7, 172.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.8 (s, major diastereomer), -151.8 (s, minor diastereomer). Anal. Calcd. for $C_{41}H_{33}FN_4O_3$: C, 75.91; H, 5.13; N, 8.64. Found: C, 75.63; H, 5.35; N, 8.73.

tert-Butyl ((*R*)-3-((*S*)-cyano(3,5-dimethoxyphenyl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ib**)



Compound **3ib** was obtained from 2-(3,5-dimethoxyphenyl)-2-fluoroacetonitrile **1i** (10.7 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 28.5 mg (83%) of a yellow amorphous solid. The dr was determined as >50:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 91% using Phenomenex Amylose-2, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(major) = 15.9 min, t_R(minor) = 19.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.33 (s, 9H), 3.60 (s, 6H), 5.89 (d, *J* = 2.9 Hz, 1H), 6.17 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.28 (bs, 2H), 6.59 (dd, *J* = 2.2, 2.2 Hz, 1H), 6.93 (ddd, *J* = 8.0, 7.7, 1.5 Hz, 1H), 6.95 – 7.00 (m, 6H), 7.04 (ddd, *J* = 7.6, 7.5, 1.0 Hz, 1H), 7.09 – 7.20 (m, 9H), 7.76 (dd, *J* = 7.6, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.5, 66.1 (d, $J_{C\text{-}F}$ = 21.0 Hz), 75.7, 81.0, 92.9 (d, $J_{C\text{-}F}$ = 202.7 Hz), 103.5, 104.6 (d, $J_{C\text{-}F}$ = 9.1 Hz), 115.1 (d, $J_{C\text{-}F}$ = 32.1 Hz), 116.7, 122.4, 123.1 (d, $J_{C\text{-}F}$ = 3.2 Hz), 124.1, 127.0, 127.3, 129.0, 129.7, 131.9 (d, $J_{C\text{-}F}$ = 22.9 Hz), 141.0, 144.7, 153.9, 160.7, 173.1 (d, $J_{C\text{-}F}$ = 1.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -161.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{42}H_{38}FN_3NaO_5$ 706.2688, found 706.2690.

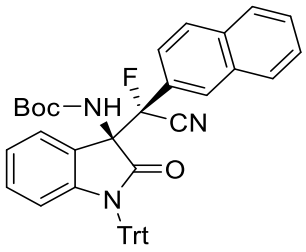
tert-Butyl ((*R*)-3-((*S*)-benzo[d][1,3]dioxol-5-yl(cyano)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3jb**)



Compound **3jb** was obtained from 2-(benzo[d][1,3]dioxol-5-yl)-2-fluoroacetonitrile **1j** (9.9 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A except for stirring the reaction mixture at -5 ^{o}C. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 26.8 mg (81%) of a yellow amorphous solid. The dr was determined as 45.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 86% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 12.0 min, t_R(major) = 13.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 5.79 (d,

J = 1.4 Hz, 1H), 5.86 (d, *J* = 2.6 Hz, 1H), 6.04 (d, *J* = 1.4 Hz, 1H), 6.12 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.55 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.84 (d, *J* = 2.0 Hz, 1H), 6.89 (dd, *J* = 7.9, 7.8 Hz, 1H), 6.97 – 7.05 (m, 7H), 7.15 – 7.21 (m, 9H), 7.71 (dd, *J* = 7.6, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.4 (d, $J_{C\text{-}F}$ = 21.8 Hz), 75.9, 81.0, 93.4 (d, $J_{C\text{-}F}$ = 201.3 Hz), 102.0, 107.5 (d, $J_{C\text{-}F}$ = 10.5 Hz), 107.9, 115.2 (d, $J_{C\text{-}F}$ = 31.4 Hz), 116.6, 121.6 (d, $J_{C\text{-}F}$ = 6.5 Hz), 122.5, 122.7 (d, $J_{C\text{-}F}$ = 2.9 Hz), 124.1, 127.1, 127.3, 127.9, 129.1, 129.9, 141.1, 144.6, 148.2 (d, $J_{C\text{-}F}$ = 1.5 Hz), 150.0 (d, $J_{C\text{-}F}$ = 1.2 Hz), 153.9, 173.1 (d, $J_{C\text{-}F}$ = 1.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -157.8 (s, major diastereomer), -148.5 (s, minor diastereomer). Anal. Calcd. for $C_{41}H_{34}FN_3O_5$: C, 73.75; H, 5.13; N, 6.29. Found: C, 73.99; H, 5.25; N, 6.43.

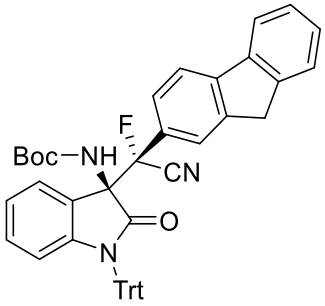
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-naphthyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3kb**)



Compound **3kb** was obtained from 2-(2-naphthyl)-2-fluoroacetonitrile **1k** (10.2 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (6.5:1 hexanes/ethyl acetate) gave 33.2 mg (99%) of a white amorphous solid. The dr was determined as 33.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 93% using CHIRALPAK IA, hexanes/isopropanol/ethanol 96:2.5:1.5, flow rate = 1 mL/min condition. t_R(major) = 10.4 min, t_R(minor) = 17.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 5.96 (d, *J* = 2.5 Hz, 1H), 6.02 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.75 – 6.84 (m, 6H), 6.86 – 6.95 (m, 7H), 7.01 – 7.09 (m, 4H), 7.21 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.63 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.73 (d, *J* = 1.4 Hz, 1H), 7.77 – 7.84 (m, 2H), 7.86 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.93 (dd, *J* = 8.2, 1.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 66.4 (d, $J_{C\text{-}F}$ = 21.4 Hz), 75.7, 81.0, 93.6 (d, $J_{C\text{-}F}$ = 201.9 Hz), 115.3 (d, $J_{C\text{-}F}$ = 31.8 Hz), 116.6, 122.6, 122.7 (d, $J_{C\text{-}F}$ = 3.2 Hz), 123.1 (d, $J_{C\text{-}F}$ = 7.6 Hz), 124.3, 126.8, 127.0, 127.1, 127.4 (d, $J_{C\text{-}F}$ = 22.6 Hz), 127.5, 128.0, 128.3, 128.4 (d, $J_{C\text{-}F}$ = 1.4 Hz), 129.1, 129.6, 129.8, 132.4 (d, $J_{C\text{-}}$

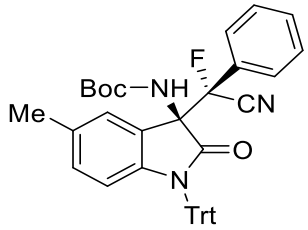
$_F$ = 1.1 Hz), 134.2, 140.8, 144.4, 153.9, 173.1 (d, J_{C-F} = 1.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.8 (s, major diastereomer), -149.1 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{44}H_{36}FN_3NaO_3$ 696.2633, found 696.2633.

tert-Butyl ((*R*)-3-((*S*)-cyano(9H-fluoren-2-yl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3lb**)



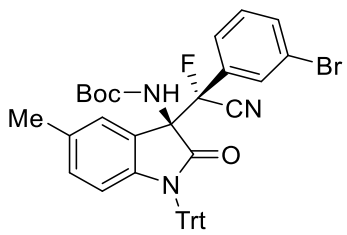
Compound **3lb** was obtained from 2-(9H-fluoren-2-yl)-2-fluoroacetonitrile **1l** (12.3 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 34.4 mg (97%) of a white crystalline solid. Mp 152.5-154.8 °C. The dr was determined as 12.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 88% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(major) = 18.2 min, t_R(minor) = 25.4 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37 (s, 9H), 3.77 (d, *J* = 22.2 Hz, 1H), 3.87 (d, *J* = 22.0 Hz, 1H), 5.93 (d, *J* = 2.3 Hz, 1H), 6.08 (dd, *J* = 8.2, 0.9 Hz, 1H), 6.88 (dd, *J* = 8.0, 1.4 Hz, 1H), 6.90 – 6.95 (m, 6H), 6.95 – 7.03 (m, 9H), 7.05 (ddd, *J* = 7.8, 7.7, 1.0 Hz, 1H), 7.15 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.39 (ddd, *J* = 7.4, 7.4, 1.2 Hz, 1H), 7.42 – 7.48 (m, 2H), 7.55 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.73 – 7.79 (m, 2H), 7.84 (dd, *J* = 7.6, 1.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.3, 36.9, 66.7 (d, J_{C-F} = 21.8 Hz), 76.0, 81.1, 94.1 (d, J_{C-F} = 201.5 Hz), 115.6 (d, J_{C-F} = 31.5 Hz), 116.7, 119.7, 120.7, 122.6, 123.1 (d, J_{C-F} = 3.2 Hz), 123.4, 123.5 (d, J_{C-F} = 8.6 Hz), 124.4, 125.4, 126.0 (d, J_{C-F} = 7.3 Hz), 127.0, 127.3, 127.4, 128.1, 129.1, 129.8, 130.0, 140.5, 141.2, 143.5 (d, J_{C-F} = 1.2 Hz), 144.6, 144.8 (d, J_{C-F} = 0.8 Hz), 154.0, 173.3 (d, J_{C-F} = 1.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.3 (s, major diastereomer), -148.9 (s, minor diastereomer). Anal. Calcd. for $C_{47}H_{38}FN_3O_3$: C, 79.30; H, 5.38; N, 5.90. Found: C, 78.93; H, 5.66; N, 5.94.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ad**)



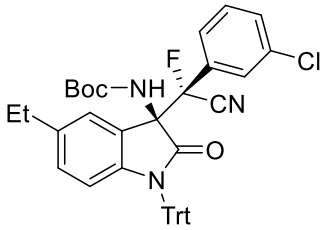
Compound **3ad** was obtained from 2-(phenyl)-2-fluoroacetonitrile **1a** (7.4 mg, 0.055 mmol) and *tert*-butyl (5-methyl-2-oxo-1-tritylindolin-3-ylidene)carbamate **2d** (25.1 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 29.4 mg (92%) of a yellow amorphous solid. The dr was determined as 9.8:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 84% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 10.1 min, t_R(major) = 12.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35 (s, 9H), 2.29 (s, 3H), 5.86 (d, *J* = 2.7 Hz, 1H), 6.00 (d, *J* = 8.3 Hz, 1H), 6.70 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.87 – 7.00 (m, 6H), 7.08 – 7.18 (m, 9H), 7.21 – 7.25 (m, 2H), 7.40 – 7.46 (m, 2H), 7.52 (d, *J* = 2.2 Hz, 1H), 7.55 (dd, *J* = 7.8, 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.1, 28.1, 66.3 (d, $J_{C\text{-}F}$ = 21.6 Hz), 75.7, 80.9, 93.4 (d, $J_{C\text{-}F}$ = 201.1 Hz), 115.3 (d, $J_{C\text{-}F}$ = 31.7 Hz), 116.3, 122.5 (d, $J_{C\text{-}F}$ = 2.9 Hz), 124.9, 126.8, 126.9, 127.2, 128.5, 129.8, 129.9 (d, $J_{C\text{-}F}$ = 5.5 Hz), 130.3 (d, $J_{C\text{-}F}$ = 22.6 Hz), 131.1, 132.0, 141.1, 141.9, 153.9, 173.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.8 (s, major diastereomer), -150.5 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{36}FN_3NaO_3$ 637.2735, found 637.2686.

tert-Butyl ((*R*)-3-((*S*)-(3-bromophenyl)(cyano)fluoromethyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3cd**)



Compound **3cd** was obtained from 2-(3-bromophenyl)-2-fluoroacetonitrile **1c** (11.8 mg, 0.055 mmol) and *tert*-butyl (5-methyl-2-oxo-1-tritylindolin-3-ylidene)carbamate **2d** (25.1 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 33.4 mg (93%) of a yellow amorphous solid. The dr was determined as 31.5:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 96% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 10.9 min, t_R(major) = 15.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 2.30 (s, 3H), 5.81 (d, *J* = 2.4 Hz, 1H), 6.05 (d, *J* = 8.3 Hz, 1H), 6.73 (ddd, *J* = 8.4, 1.8, 0.8 Hz, 1H), 6.90 – 7.00 (m, 6H), 7.05 (dd, *J* = 7.9, 2.1 Hz, 1H), 7.14 – 7.18 (m, 9H), 7.29 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.44 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.52 (dd, *J* = 1.9, 0.9 Hz, 1H), 7.69 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.1, 28.2, 66.2 (d, $J_{C\text{-}F}$ = 21.4 Hz), 75.9, 81.1, 92.7 (d, $J_{C\text{-}F}$ = 202.5 Hz), 114.8 (d, $J_{C\text{-}F}$ = 31.9 Hz), 116.6, 122.2 (d, $J_{C\text{-}F}$ = 3.1 Hz), 123.0 (d, $J_{C\text{-}F}$ = 1.7 Hz), 124.9, 125.7 (d, $J_{C\text{-}F}$ = 7.2 Hz), 127.0, 127.3, 129.7, 129.8 (d, $J_{C\text{-}F}$ = 2.1 Hz), 129.9, 130.1, 132.3, 132.5 (d, $J_{C\text{-}F}$ = 23.0 Hz), 134.3, 141.1, 141.9, 153.9, 172.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.9 (s, major diastereomer), -150.4 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{35}BrFN_3NaO_3$ 738.1738, found 738.1741.

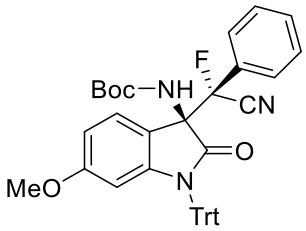
tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-ethyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3be**)



Compound **3be** was obtained from 2-(3-chlorophenyl)-2-fluoroacetonitrile **1b** (9.3 mg, 0.055 mmol) and *tert*-butyl (5-ethyl-2-oxo-1-tritylindolin-3-ylidene)carbamate **2e** (25.8 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 29.7 mg (87%) of a yellow amorphous solid. The dr was determined as 34.1:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 89% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 8.1 min, t_R(major) = 10.3 min. ^{1}H NMR (400

MHz, $CDCl_3$) δ = 1.23 (t, *J* = 7.6 Hz, 3H), 1.34 (s, 9H), 2.68 – 2.51 (m, 2H), 5.82 (d, *J* = 2.5 Hz, 1H), 6.07 (d, *J* = 8.4 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.91 – 6.99 (m, 6H), 7.01 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.12 – 7.19 (m, 9H), 7.24 (dd, *J* = 2.0, 2.0 Hz, 1H), 7.34 (dd, *J* = 8.0, 7.9 Hz, 1H), 7.52 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.55 (d, *J* = 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 15.4, 28.1, 28.3, 66.1 (d, J_{C-F} = 21.2 Hz), 75.8, 81.1, 92.8 (d, J_{C-F} = 202.5 Hz), 114.9 (d, J_{C-F} = 31.8 Hz), 116.6, 122.2 (d, J_{C-F} = 2.8 Hz), 123.8, 125.1 (d, J_{C-F} = 7.6 Hz), 127.0, 127.1, 127.3, 128.7, 129.6 (d, J_{C-F} = 1.2 Hz), 129.7, 131.3, 132.3 (d, J_{C-F} = 23.0 Hz), 135.0 (d, J_{C-F} = 1.7 Hz), 138.7, 141.1, 142.0, 153.8, 172.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.9 (s, major diastereomer), -150.6 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{42}H_{37}ClFN_3NaO_3$ 708.2400, found 708.2402.

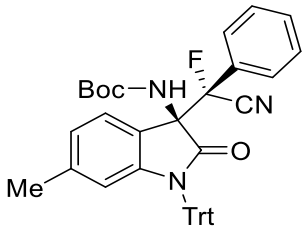
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3af**)



Compound **3af** was obtained from 2-(phenyl)-2-fluoroacetonitrile **1a** (7.4 mg, 0.055 mmol) and *tert*-butyl (6-methoxy-2-oxo-1-tritylindolin-3-ylidene)carbamate **2f** (25.9 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 30.7 mg (95%) of a yellow amorphous solid. The dr was determined as 20.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 93% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 11.4 min, t_R(major) = 14.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 3.43 (s, 3H), 5.69 (d, *J* = 2.3 Hz, 1H), 5.86 (d, *J* = 2.7 Hz, 1H), 6.53 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.89 – 6.97 (m, 6H), 7.09 – 7.19 (m, 9H), 7.24 (dd, *J* = 7.4, 1.5 Hz, 2H), 7.44 (dd, *J* = 7.8, 7.8 Hz, 2H), 7.56 (dd, *J* = 7.5, 7.4 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.0, 65.9 (d, J_{C-F} = 21.5 Hz), 75.8, 80.9, 93.4 (d, J_{C-F} = 201.8 Hz), 104.5, 107.3, 114.2 (d, J_{C-F} = 3.4 Hz), 115.3 (d, J_{C-F} = 32.0 Hz), 125.0, 126.9, 127.0, 127.2, 128.5 (d, J_{C-F} = 1.4 Hz), 129.8, 130.4 (d, J_{C-F} = 22.9 Hz), 131.1, 140.9, 145.7, 153.9, 160.0, 173.5

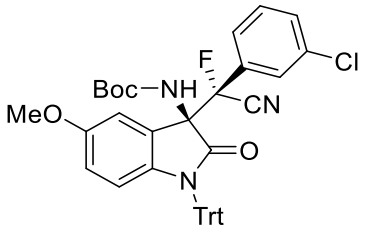
(d, $J_{C\text{-}F}$ = 1.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.5 (s, major diastereomer), -150.8 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{36}FN_3NaO_4$ 676.2582, found 676.2584.

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ag**)



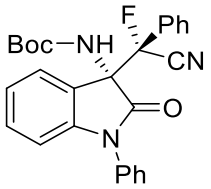
Compound **3ag** was obtained from 2-(phenyl)-2-fluoroacetonitrile **1a** (7.4 mg, 0.055 mmol) and *tert*-butyl (6-methyl-2-oxo-1-tritylindolin-3-ylidene)carbamate **2g** (25.1 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 29.8 mg (94%) of a yellow amorphous solid. The dr was determined as 15.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 92% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 10.7 min, t_R(major) = 12.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35 (s, 9H), 1.98 (s, 3H), 5.85 (d, *J* = 2.6 Hz, 1H), 5.88 (s, 1H), 6.82 (dd, *J* = 8.3, 7.8 Hz, 1H), 6.89 – 6.97 (m, 6H), 7.09 – 7.17 (m, 9H), 7.20 – 7.24 (m, 2H), 7.39 – 7.45 (m, 2H), 7.59 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 22.2, 28.1, 66.1 (d, $J_{C\text{-}F}$ = 21.5 Hz), 75.7, 80.9, 93.5 (d, $J_{C\text{-}F}$ = 201.5 Hz), 115.3 (d, $J_{C\text{-}F}$ = 31.7 Hz), 117.6, 119.5 (d, $J_{C\text{-}F}$ = 3.3 Hz), 123.4, 124.1, 126.9, 127.2, 128.4 (d, $J_{C\text{-}F}$ = 1.2 Hz), 129.3, 129.8, 130.4 (d, $J_{C\text{-}F}$ = 22.9 Hz), 131.1, 139.2, 141.1, 144.4, 153.9, 173.3 (d, $J_{C\text{-}F}$ = 1.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.5 (s, major diastereomer), -150.8 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{36}FN_3NaO_3$ 660.2633, found 660.2633.

tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3bh)**



Compound **3bh** was obtained from 2-(3-chlorophenyl)-2-fluoroacetonitrile **1b** (9.3 mg, 0.055 mmol) and *tert*-butyl (5-methoxy-2-oxo-1-tritylindolin-3-ylidene)carbamate **2h** (25.9 mg, 0.050 mmol) by following procedure A. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 31.5 mg (92%) of a yellow amorphous solid. The dr was determined as 24.4:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 85% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 9.4 min, t_R(major) = 11.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37 (s, 9H), 3.75 (s, 3H), 5.83 (d, *J* = 2.6 Hz, 1H), 6.07 (d, *J* = 8.9 Hz, 1H), 6.47 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.92 – 6.98 (m, 6H), 7.04 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.12 – 7.20 (m, 9H), 7.31 (d, *J* = 2.7 Hz, 1H), 7.33 – 7.39 (m, 2H), 7.54 (dd, *J* = 8.1, 2.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.5, 66.3 (d, $J_{C\text{-}F}$ = 21.3 Hz), 75.8, 81.2, 92.7 (d, $J_{C\text{-}F}$ = 202.6 Hz), 110.4, 114.7, 114.8 (d, $J_{C\text{-}F}$ = 31.9 Hz), 117.4, 123.4 (d, $J_{C\text{-}F}$ = 3.2 Hz), 125.2 (d, $J_{C\text{-}F}$ = 7.1 Hz), 126.9 (d, $J_{C\text{-}F}$ = 9.8 Hz), 127.1, 127.3, 129.6, 129.7, 131.4, 132.2 (d, $J_{C\text{-}F}$ = 23.1 Hz), 135.2 (d, $J_{C\text{-}F}$ = 1.6 Hz), 137.4, 141.0, 153.8, 155.3, 172.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.8 (s, major diastereomer), -150.7 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{41}H_{35}ClFN_3NaO_4$ 710.2192, found 710.2196.

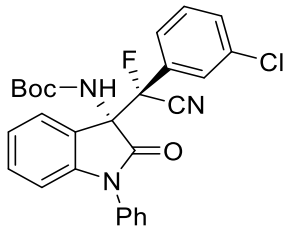
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(phenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ac**)



Compound **3ac** was obtained from α-fluoro benzylnitrile **1a** (14.8 mg, 0.11 mmol) and *tert*-butyl (2-oxo-1-phenylindolin-3-ylidene)carbamate **2c** (32.2 mg, 0.10 mmol) by following procedure B. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 42.1 mg (92%) of a yellow amorphous solid. The dr was determined as 1:3.0 using ^{19}F NMR. The ee of the major diastereomer

was determined as 98% using CHIRALPAK IA, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(minor) = 9.4 min, t_R(major) = 11.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (s, 9H), 6.00 (s, 1H), 6.41 (d, *J* = 7.8 Hz, 1H), 6.85 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.09 – 7.14 (m, 2H), 7.14 – 7.23 (m, 3H), 7.31 – 7.41 (m, 5H), 7.55 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 67.7 (d, J_{C-F} = 22.5 Hz), 81.6, 93.8 (d, J_{C-F} = 194.3 Hz), 109.3, 111.3, 114.1 (d, J_{C-F} = 30.9 Hz), 123.2, 125.5 (d, J_{C-F} = 2.5 Hz), 126.1, 126.5 (d, J_{C-F} = 5.9 Hz), 127.9, 128.2, 129.4, 130.6 (d, J_{C-F} = 23.5 Hz), 130.5, 130.7, 133.5, 144.1, 153.4, 169.2 (d, J_{C-F} = 7.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -156.7 (s, major diastereomer), -162.1 (s, minor diastereomer). Anal. Calcd. for $C_{27}H_{24}FN_3O_3$: C, 70.88; H, 5.29; N, 9.18. Found: C, 70.49; H, 5.66; N, 8.93.

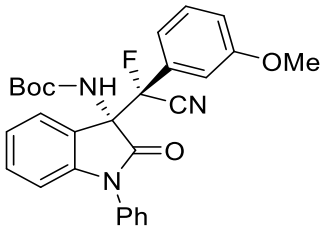
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3bc**)



Compound **3bc** was obtained from 2-(3-chlorophenyl)-2-fluoroacetonitrile **1b** (18.6 mg, 0.11 mmol) and (2-oxo-1-phenylindolin-3-ylidene)carbamate **2c** (32.2 mg, 0.10 mmol) by following procedure B. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 49.0 mg (99%) of a yellow crystalline solid. Mp 177.9-180.2 ºC. The dr was determined as 1:5.9 using ^{19}F NMR. The ee of the major diastereomer was determined as 82% using CHIRALPAK IA, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(minor) = 8.6 min, t_R(major) = 10.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (s, 9H), 6.01 (s, 1H), 6.46 (d, *J* = 7.5 Hz, 1H), 6.93 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.04 (dd, *J* = 2.0, 2.0 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.16 (d, *J* = 6.5 Hz, 1H), 7.21 (dd, *J* = 7.7, 7.6 Hz, 1H), 7.31 – 7.37 (m, 2H), 7.41 (dd, *J* = 8.2, 6.6 Hz, 2H), 7.54 (dd, *J* = 7.4, 1.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.3, 67.6 (d, J_{C-F} = 22.5 Hz), 81.6, 81.9, 93.2 (d, J_{C-F} = 195.1 Hz), 109.6, 113.7 (d, J_{C-F} = 30.8 Hz), 123.1, 123.6, 125.0 (d, J_{C-F} = 5.9 Hz), 125.6 (d, J_{C-F} = 2.4 Hz), 126.2, 126.7 (d, J_{C-F} = 6.5 Hz), 128.5, 129.3, 129.6, 130.8, 130.9 (d, J_{C-F} = 0.9 Hz), 131.6 (d, J_{C-F} = 22.8 Hz), 133.5, 134.3, 144.1, 153.5, 169.2 (d, J_{C-F} = 7.8

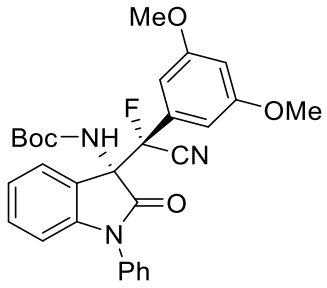
Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -157.1 (s, major diastereomer), -162.1 (s, minor diastereomer). Anal. Calcd. for $C_{27}H_{23}ClFN_3O_3$: C, 65.92; H, 4.71; N, 8.54. Found: C, 66.22; H, 5.09; N, 8.19.

tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ec**)



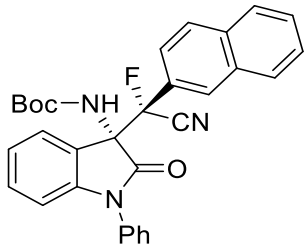
Compound **3ec** was obtained from 2-(3-methoxyphenyl)-2-fluoroacetonitrile **1e** (18.2 mg, 0.11 mmol) and *tert*-butyl (2-oxo-1-phenylindolin-3-ylidene)carbamate **2c** (32.2 mg, 0.10 mmol) by following procedure B. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 43.5 mg (87%) of a yellow amorphous solid. The dr was determined as 1:3.0 using ^{19}F NMR. The ee of the major diastereomer was determined as 96% using Phenomenex Amylose-2, hexanes/ethanol 80:20, flow rate = 1 mL/min condition. t_R(minor) = 12.5 min, t_R(major) = 13.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.33 (m, 9H), 3.46 (s, 3H), 6.01 (s, 1H), 6.43 – 6.50 (m, 2H), 6.78 (d, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.91 – 6.85 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 1H), 7.15 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.20 (dd, *J* = 7.7, 7.5 Hz, 1H), 7.34 (dd, *J* = 7.2, 5.7 Hz, 1H), 7.39 (dd, *J* = 7.4, 6.4 Hz, 2H), 7.54 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.2, 67.7 (d, $J_{C\text{-}F}$ = 22.6 Hz), 81.6, 93.6 (d, $J_{C\text{-}F}$ = 194.7 Hz), 109.4, 110.5 (d, $J_{C\text{-}F}$ = 6.5 Hz), 114.0 (d, $J_{C\text{-}F}$ = 31.0 Hz), 117.7, 119.1 (d, $J_{C\text{-}F}$ = 5.7 Hz), 123.1, 124.7, 125.4 (d, $J_{C\text{-}F}$ = 2.5 Hz), 126.1, 128.2, 129.0, 129.4, 130.4, 130.7 (d, $J_{C\text{-}F}$ = 22.2 Hz), 133.5, 144.2, 153.4, 158.9, 169.2 (d, $J_{C\text{-}F}$ = 7.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -156.3 (s, major diastereomer), -161.6 (s, minor diastereomer). Anal. Calcd. for $C_{28}H_{26}FN_3O_4$: C, 68.98; H, 5.38; N, 8.62. Found: C, 68.79; H, 5.78; N, 8.22.

tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3,5-dimethoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ic**)



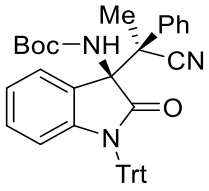
Compound **3ic** was obtained from 2-(3,5-dimethoxyphenyl)-2-fluoroacetonitrile **1i** (21.4 mg, 0.10 mmol) and *tert*-butyl (2-oxo-1-phenylindolin-3-ylidene)carbamate **2c** (32.2 mg, 0.10 mmol) by following procedure B. Chromatography purification (7.5:1 hexanes/ethyl acetate) gave 43.5 mg (84%) of an off-white crystalline solid. Mp 187.2-189.4 ^{o}C. The dr was determined as 1:5.3 using ^{19}F NMR. The ee of the major diastereomer was determined as 90% using CHIRALPAK IA, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(minor) = 10.8 min, t_R(major) = 14.5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (s, 9H), 3.48 (s, 6H), 5.97 (s, 1H), 6.20 (d, *J* = 2.2 Hz, 2H), 6.41 (dd, *J* = 2.3, 2.3 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 2H), 7.14 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.20 (dd, *J* = 7.7, 7.2 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.40 (dd, *J* = 7.5, 7.4 Hz, 2H), 7.52 (dd, *J* = 7.4, 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 55.4, 67.7 (d, $J_{C\text{-}F}$ = 22.6 Hz), 81.6, 93.5 (d, $J_{C\text{-}F}$ = 195.1 Hz), 103.7, 104.2 (d, $J_{C\text{-}F}$ = 6.3 Hz), 109.5, 114.0 (d, $J_{C\text{-}F}$ = 30.9 Hz), 123.1, 124.6, 125.3 (d, $J_{C\text{-}F}$ = 2.3 Hz), 126.0, 128.2, 129.3, 130.4, 131.3 (d, $J_{C\text{-}F}$ = 22.5 Hz), 133.5, 144.2, 153.4, 160.1, 169.2 (d, $J_{C\text{-}F}$ = 7.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -156.4 (s, major diastereomer), -161.3 (s, minor diastereomer). Anal. Calcd. for $C_{29}H_{28}FN_3O_5$: C, 67.30; H, 5.45; N, 8.12. Found: C, 67.34; H, 5.60; N, 7.89.

tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(2-naphthyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3kc**)



Compound **3kc** was obtained from 2-(2-naphthyl)-2-fluoroacetonitrile **1k** (20.4 mg, 0.11 mmol) and *tert*-butyl (2-oxo-1-phenylindolin-3-ylidene)carbamate **2c** (32.2 mg, 0.10 mmol) by following procedure B. Chromatography purification (7:1 hexanes/ethyl acetate) gave 46.7 mg (92%) of a white amorphous solid. The dr was determined as 1:6.7 using ^{19}F NMR. The ee of the major diastereomer was determined as 88% using CHIRALPAK IA, hexanes/ethanol 95:5, flow rate = 1 mL/min condition. t_R(minor) = 11.4 min, t_R(major) = 15.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35 (s, 9H), 6.05 (s, 1H), 6.27 (dd, *J* = 6.5, 2.2 Hz, 1H), 6.57 (d, *J* = 6.7 Hz, 2H), 7.09 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.12 – 7.17 (m, 2H), 7.17 – 7.24 (m, 3H), 7.47 (dd, *J* = 8.2, 6.9 Hz, 1H), 7.55 (dd, *J* = 8.2, 6.9 Hz, 1H), 7.60 (dd, *J* = 7.5, 3.1 Hz, 2H), 7.65 (m, 2H), 7.78 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 67.8 (d, $J_{C\text{-}F}$ = 22.8 Hz), 81.6, 94.0 (d, $J_{C\text{-}F}$ = 194.3 Hz), 109.4, 114.2 (d, $J_{C\text{-}F}$ = 30.9 Hz), 122.5 (d, $J_{C\text{-}F}$ = 5.8 Hz), 123.2, 123.4 (d, $J_{C\text{-}F}$ = 3.6 Hz), 124.9, 125.5 (d, $J_{C\text{-}F}$ = 2.3 Hz), 126.0, 126.6, 126.8, 126.9, 127.1 (d, $J_{C\text{-}F}$ = 6.0 Hz), 127.5, 127.8, 128.1, 128.6, 129.2, 130.4, 131.9, 133.3, 133.7, 144.1, 153.4, 169.3 (d, $J_{C\text{-}F}$ = 7.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -156.2 (s, major diastereomer), -161.6 (s, minor diastereomer). Anal. Calcd. for $C_{31}H_{26}FN_3O_3$: C, 73.36; H, 5.16; N, 8.28. Found: C, 72.98; H, 5.48; N, 7.91.

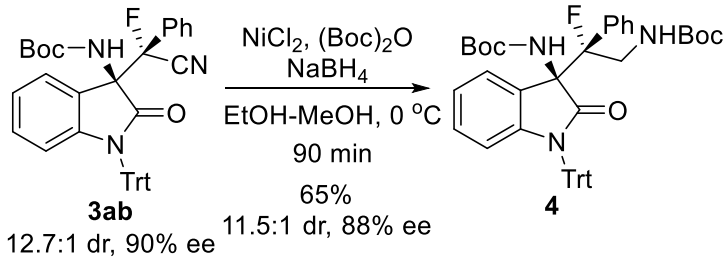
tert-Butyl ((*S*)-3-((*R*)-1-cyano-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**9**)



Compound **9** was obtained from α-methylphenylacetonitrile **8** (10.2 mg, 0.055 mmol) and *tert*-butyl (2-oxo-1-tritylindolin-3-ylidene)carbamate **2b** (24.4 mg, 0.050 mmol) by following procedure A. Chromatographic purification (6.5:1 hexanes/ethyl acetate) gave 30.4 mg (98%) of a pale yellow crystalline solid. Mp 114.5-117.4 °C. The dr was determined as >19:1 using ^{1}H NMR. The ee of the major diastereomer was determined as 85% using CHIRALPAK IA, hexanes/ethanol 98:2, flow rate = 1 mL/min condition. t_R(major) = 6.2 min, t_R(minor) = 8.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (s, 9H), 1.99 (s, 3H), 5.47 (s, 1H), 6.07 (d, *J* = 8.1 Hz, 1H), 6.83 (ddd, *J* = 7.9, 7.8, 1.4 Hz, 1H), 6.95 (ddd, *J* = 7.7, 7.6, 1.0 Hz, 1H), 7.01 – 7.09 (m, 6H), 7.10 – 7.19 (m, 9H), 7.22 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.31 (dd, *J* = 7.7, 7.6 Hz, 2H), 7.42 (dd, *J* = 7.3, 7.4 Hz, 1H),

7.57 (d, J = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 19.9, 28.3, 48.2, 64.2, 75.8, 80.7, 116.2, 121.7, 122.1, 124.4, 126.5, 127.0, 127.3, 128.3, 128.5, 129.0, 129.4, 130.1, 134.2, 141.4, 144.2, 153.4, 174.4. Anal. Calcd. for $C_{41}H_{37}N_3O_3$: C, 79.46; H, 6.02; N, 6.78. Found: C, 79.30; H, 6.28; N, 6.54.

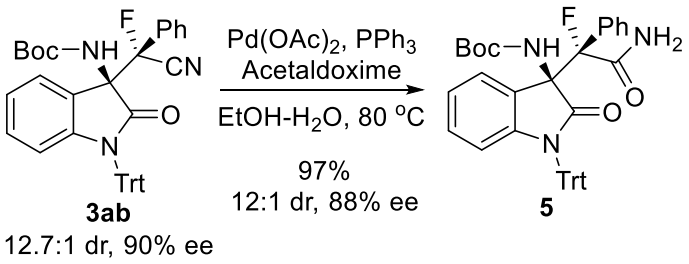
3.4 Reduction of an α-fluoro β-aminonitrile to an β-fluoro α,γ-diamine



A solution of compound **3ab** (62.3 mg, 0.10 mmol), $NiCl_2$ (13.0 mg, 0.10 mmol), $(Boc)_2O$ (43.7 mg, 0.20 mg) in methanol (2.0 mL) was stirred at 0 °C. Then, $NaBH_4$ (45.4 mg, 1.20 mmol) in ethanol (2.0 mL) was added in two portions (1.0 mL each). The reaction was stirred at 0 °C for 90 minutes and quenched with a saturated solution of NH_4Cl (1.0 mL). The reaction mixture was poured onto brine (15 mL) and extracted with EtOAc (4 mL, 3 times). The ethyl acetate layers were combined, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The residue was purified by flash chromatography (80:14:6 hexanes/EtOAc/CH_2Cl_2) to give compound **4** (47.5 mg, 0.065 mmol) in 65% yield as a white amorphous solid. The dr was determined as 11.5:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 88% using CHIRALPAK IA, hexanes/isopropanol 95:5, flow rate = 1 mL/min condition. t_R(major) = 10.3 min, t_R(minor) = 15.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.26 (s, 9H), 1.28 (s, 9H), 4.22 (m, 1H), 4.35 (m, 1H), 4.43 (bs, 1H), 5.73 (d, J = 3.2 Hz, 1H), 6.17 (d, J = 8.2 Hz, 1H), 6.87 (dd, J = 8.1, 7.7 Hz, 1H), 6.94 (dd, J = 7.5, 6.9 Hz, 1H), 7.03 – 6.97 (m, 6H), 7.15 – 7.07 (m, 11H), 7.32 (d, J = 7.2 Hz, 1H), 7.32 – 7.44 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.3, 28.4, 44.2 (d, $J_{C\text{-}F}$ = 19.3 Hz), 67.0 (d, $J_{C\text{-}F}$ = 20.7 Hz), 75.5, 79.8, 80.4, 100.5 (d, $J_{C\text{-}F}$ = 192.0 Hz), 116.4, 122.2, 124.4, 125.5 (d, $J_{C\text{-}F}$ = 3.9 Hz), 126.8, 127.3, 127.6, 128.2 (d, $J_{C\text{-}F}$ = 10.3 Hz), 129.4, 129.8, 130.0, 134.5 (d, $J_{C\text{-}F}$ = 22.3 Hz), 141.6, 144.7, 154.5, 155.8, 176.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -174.7 (m, minor diastereomer),

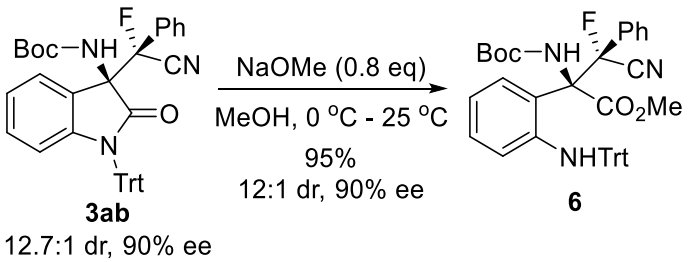
-173.2 (m, major diastereomer). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{45}H_{47}FN_3O_5$ 728.3500, found 728.3496.

3.5 Partial nitrile hydrolysis



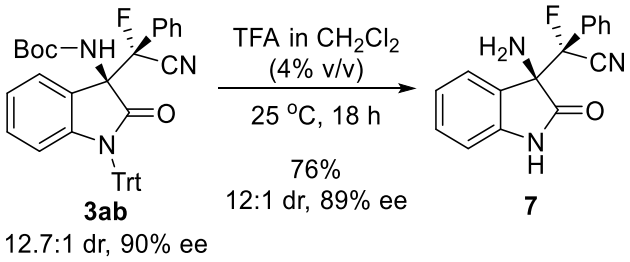
A mixture of compound **3ab** (62.3 mg, 0.10 mmol), acetaldoxime (29.2 mg, 0.40 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), PPh_3 (7.9 mg, 0.030 mmol) in ethanol-water (1.2 mL, 8:1) was heated to 80 °C and stirred for 18 hours. Upon completion, the reaction mixture was poured onto aqueous NH_4Cl solution (15 mL) and extracted with EtOAc (4 mL, 3 times). The ethyl acetate layers were combined, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The residue was purified by column chromatography (5:1 hexanes/EtOAc) to give compound **5** (62.0 mg, 0.097 mmol) in 97% yield as an off-white crystalline solid. Mp 176.3-179.7 °C. The dr was determined as 12.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 88% using Phenomenex Amylose-2, hexanes/ethanol 93:7, flow rate = 1 mL/min condition. t_R(major) = 12.9 min, t_R(minor) = 21.6 min. ^1H NMR (400 MHz, $CDCl_3$) δ = 1.27 (s, 9H), 5.52 (d, *J* = 7.1 Hz, 1H), 5.97 (dd, J = 7.6, 1.5 Hz, 1H), 6.10 (bs, 1H), 6.25 (d, *J* = 8.2 Hz, 1H), 6.57 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.84 (ddd, *J* = 7.9, 7.9, 1.4 Hz, 1H), 7.14 – 7.24 (m, 9H), 7.35 (dd, *J* = 7.7, 6.8 Hz, 2H), 7.41 (dd, *J* = 7.7, 7.3 Hz, 1H), 7.46 – 7.52 (m, 2H), 7.51 – 7.56 (m, 6H), 7.69 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 67.1 (d, J_{C-F} = 31.9 Hz), 75.0, 80.1, 95.1 (d, J_{C-F} = 194.4 Hz), 115.1, 120.9, 125.1 (d, J_{C-F} = 4.9 Hz), 126.44 (d, J_{C-F} = 12.1 Hz), 126.7, 127.3, 127.4, 127.7 (d, J_{C-F} = 2.5 Hz), 127.9, 129.3, 129.5, 133.0 (d, J_{C-F} = 21.4 Hz), 142.0, 144.7, 154.8, 171.3 (d, J_{C-F} = 21.4 Hz), 175.1 (d, J_{C-F} = 1.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -165.9 (s, major diastereomer), -160.2 (s, minor diastereomer). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd. for $C_{40}H_{36}FN_3NaO_4$ 664.2582, found 664.2583.

3.6 Oxindole lactam ring opening



To a solution of compound **3ab** (62.3 mg, 0.10 mmol) in anhydrous methanol (2.0 mL) was added sodium methoxide (4.3 mg, 0.08 mmol) at 0 °C. The reaction was stirred for 18 hours and allowed to warm to room temperature. Upon completion, the reaction mixture was poured onto aqueous NH_4Cl solution (15 mL) and extracted with EtOAc (4 mL, 3 times). The ethyl acetate layers were combined, dried over $MgSO_4$, filtrated, and concentrated under reduced pressure. The residue was purified by column chromatography (5:1 hexanes/EtOAc) to give compound **6** (66.1 mg, 0.10 mmol) in 95% yield as an off-white crystalline solid. Mp 137.6-140.3 °C. The dr was determined as 12.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 91% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(minor) = 7.9 min, t_R(major) = 9.0 min. ^1H NMR (400 MHz, $CDCl_3$) δ = 1.14 (s, 9H), 3.95 (s, 3H), 6.23 – 6.49 (m, 2H), 6.65 (dd, *J* = 6.1, 6.1 Hz, 1H), 6.86 (ddd, *J* = 7.9, 7.8, 1.4 Hz, 1H), 7.14 – 7.18 (m, 3H), 7.19 (s, 1H), 7.20 – 7.25 (m, 6H), 7.30 – 7.48 (m, 9H), 7.52 (dd, *J* = 6.2, 6.1, 2H), 8.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 28.1, 54.7, 67.2 (d, $J_{C\text{-}F}$ = 31.0 Hz), 75.0, 80.4, 95.6 (d, $J_{C\text{-}F}$ = 176.3 Hz), 115.2 (d, $J_{C\text{-}F}$ = 34.5 Hz), 115.5, 121.0, 125.3, 125.8, 126.7 (d, $J_{C\text{-}F}$ = 11.6 Hz), 126.8, 127.4, 127.6, 128.0 (d, $J_{C\text{-}F}$ = 8.8 Hz), 129.6, 130.0, 134.0 (d, $J_{C\text{-}F}$ = 21.9 Hz), 142.1, 144.9, 154.3, 166.4 (d, $J_{C\text{-}F}$ = 31.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ = -153.0 (s, minor diastereomer), -158.5 (s, major diastereomer). HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd. for $C_{41}H_{39}FN_3O_4$ 656.2919, found 656.2921.

3.7 Deprotection of **3ab**

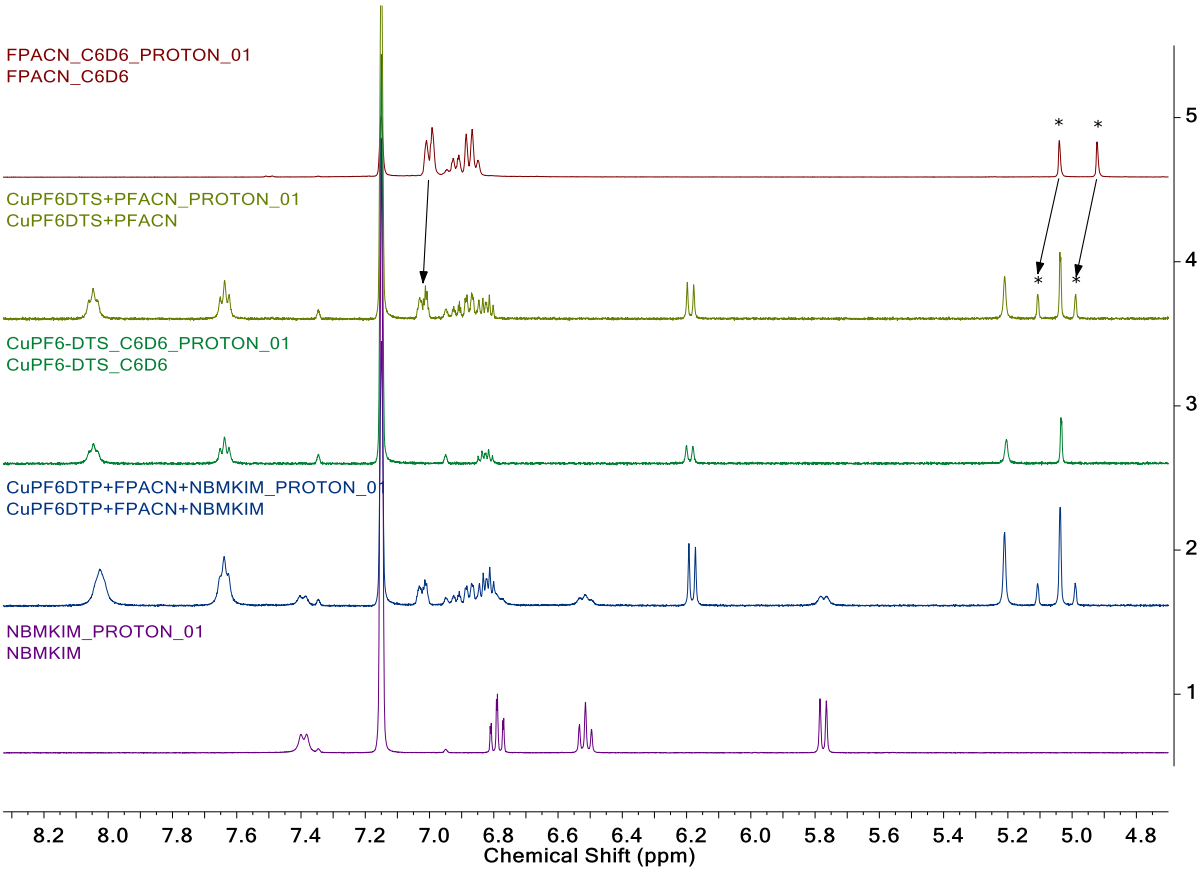


To a solution of **3ab** (65.7 mg, 0.10 mmol) in dichloromethane (5 mL) was added trifluoroacetic acid (200 µL). The reaction mixture was stirred at room temperature for 18 hours, poured onto a saturated solution of sodium bicarbonate (30 mL) and extracted with dichloromethane (5 mL, 3 times). The organic layers were combined, dried over Na_2SO_4, filtrated, and concentrated under reduced pressure. The residue was purified by column chromatography (4.5:3.5:2 hexanes/EtOAc/dichloromethane) to give compound **7** (22.6 mg, 0.08 mmol) in 76% yield as a pale yellow crystalline solid. Mp 174.6-176.8 °C. The dr was determined as 12.0:1 using ^{19}F NMR. The ee of the major diastereomer was determined as 89% using Phenomenex Amylose-2, hexanes/ethanol 90:10, flow rate = 1 mL/min condition. t_R(major) = 14.5 min, t_R(minor) = 17.8 min. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.32 (bs, 2H), 6.69 (d, *J* = 7.8 Hz, 1H), 7.07 (ddd, *J* = 7.6, 7.5, 1.0 Hz, 1H), 7.18 – 7.24 (m, 3H), 7.26 (m, 1H), 7.30 (ddd, *J* = 7.8, 7.7, 1.3 Hz, 1H), 7.36 (ddd, *J* = 6.9, 6.9, 1.5 Hz, 2H), 7.52 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 65.9 (d, $J_{C\text{-}F}$ = 25.0 Hz), 94.8 (d, $J_{C\text{-}F}$ = 197.5 Hz), 110.1, 115.7 (d, $J_{C\text{-}F}$ = 31.5 Hz), 123.0, 125.0 (d, $J_{C\text{-}F}$ = 3.1 Hz), 126.0 (d, $J_{C\text{-}F}$ = 7.4 Hz), 126.1, 127.9, 130.2 (d, $J_{C\text{-}F}$ = 0.9 Hz), 131.0, 140.8, 176.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -160.3 (s, minor diastereomer), -164.1(s, major diastereomer). Anal. Calcd. for $C_{16}H_{12}FN_3O$: C, 68.32; H, 4.30; N, 14.94. Found: C, 68.50; H, 4.68; N, 14.69.

4. Mechanistic Studies

^{1}H NMR analysis of the binding of 1a to Cu(I)-DTBM-Segphos complex.

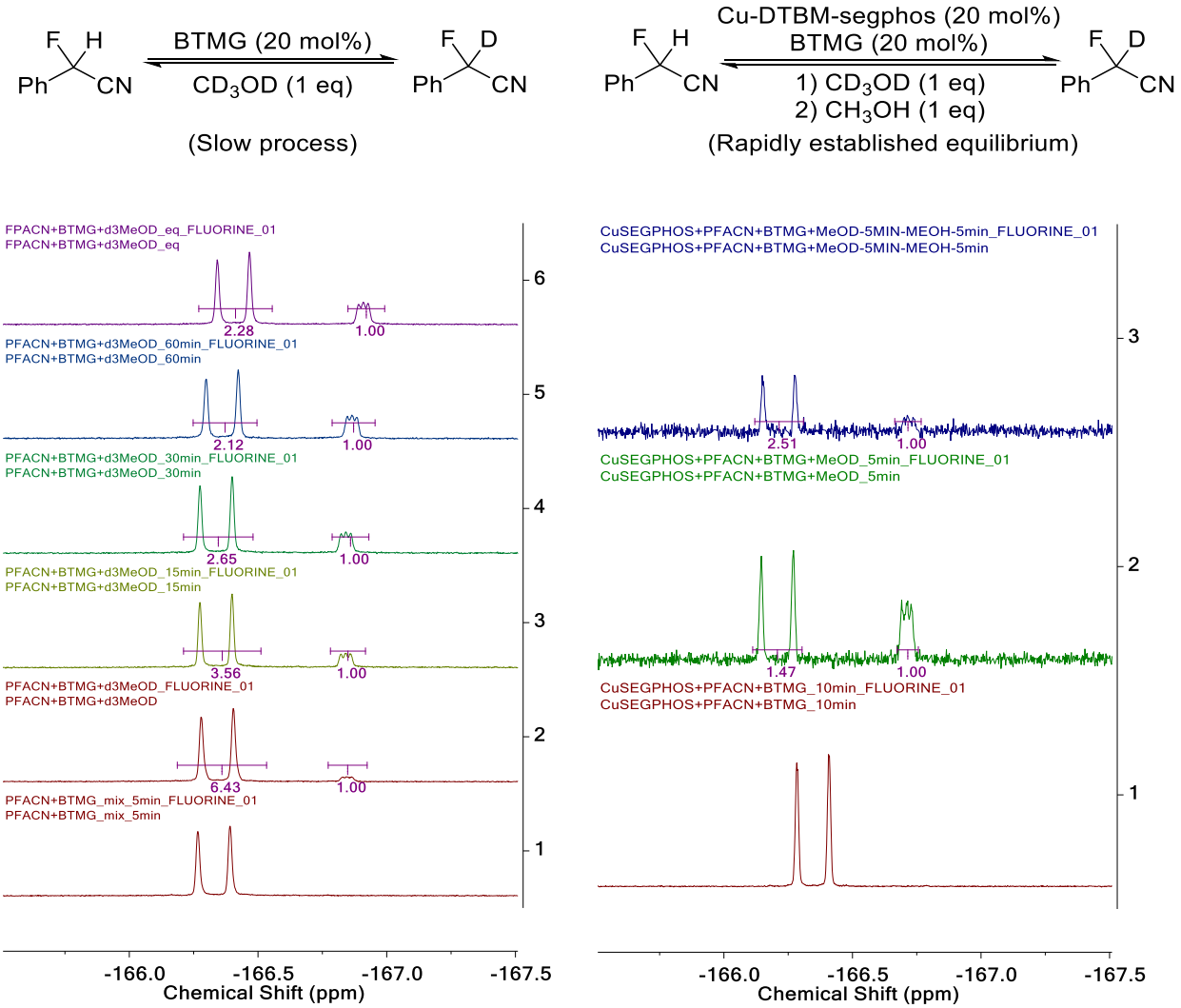
Addition of one equivalent of α-fluorobenzylnitrile **1a** into a benzene-d_6 solution of Cu(I)-biphosphine complex prepared *in situ* from $Cu(MeCN)_4PF_6$ and (*R*)-DTBM-Segphos (1:1) led to the downfield shifting of the α-fluorobenzylnitrile α-proton, indicating the coordination of **1a** to the Cu(I) complex. Mixing of **1a**, the *N*-methyl isatin derived ketimine **2d**, and Cu(I)-DTBM-Segphos complex (1:1:1) in benzene-d_6 gave the same extent of downfield shifting for the **1a** α-proton, while changes of the ketimine signals were negligible. This suggests that the **1a** preferably binds to the Cu(I)-DTBM-Segphos complex in the presence of the ketimine.



All ^{1}H NMR spectra were obtained in benzene-d_6. From bottom to top: Stack 1: *N*-methyl isatin derived ketimine **2d**. Stack 2: α-fluorobenzylnitrile **1a** + Cu(I)-DTBM-Segphos complex + *N*-methyl isatin derived ketimine **2d** (1:1:1). Stack 3: Cu(I)-DTBM-Segphos complex. Stack 4: α-fluorobenzylnitrile **1a** and Cu(I)-DTBM-Segphos complex (1:1). Stack 5: α-fluorobenzylnitrile **1a**.

^{19}F NMR analysis of the cooperative Cu(I)complex/base catalyzed H/D exchange of α-fluorobenzylnitrile 1a.

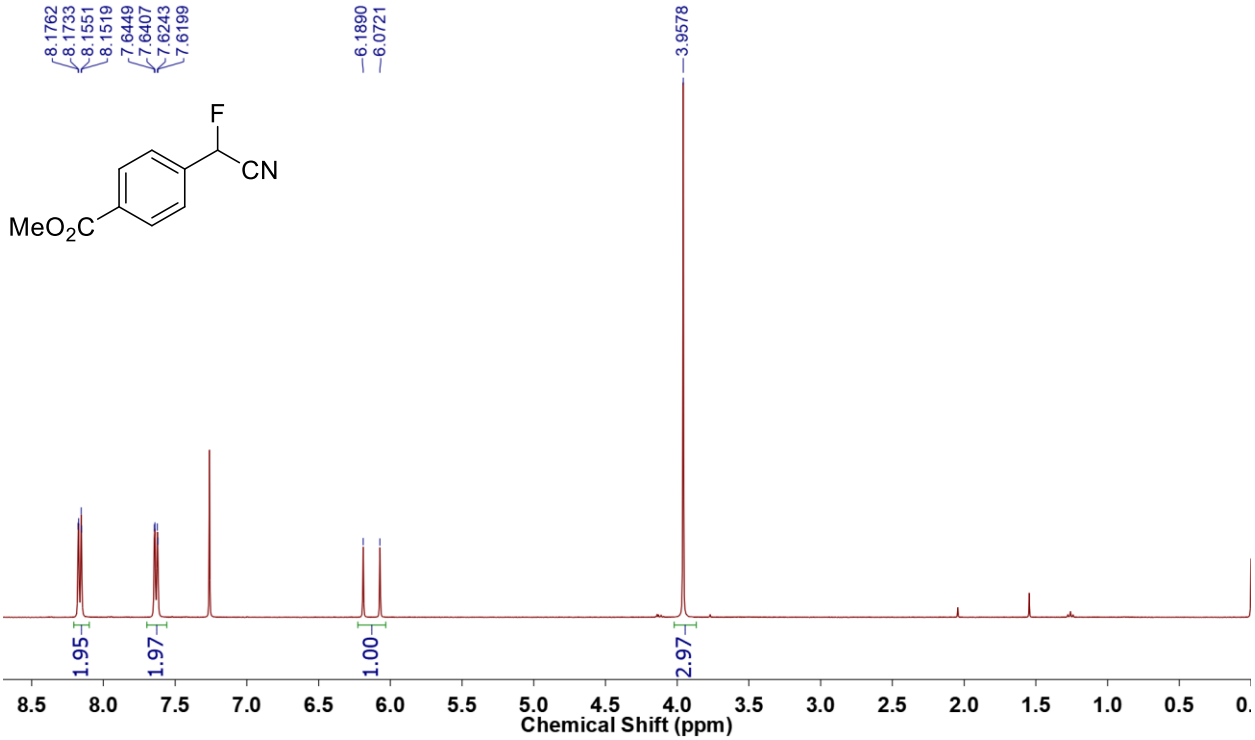
In the presence of 20 mol% of BTMG, the H/D exchange of the α-proton in α-fluorobenzylnitrile **1a** in the presence of one equivalent of methanol-d_4 was slow. The ratio of the deuterated vs. protonated **1a** species increased from 1:6 to 1:2 after 60 minutes and stagnated at 1:2 after 18 hours. When 20 mol% of Cu(I)-DTBM-Segphos complex and BTMG were used to facilitate the H/D exchange between **1a** and methanol-d_4, the integration ratio of the deuterated vs. protonated **1a** species reached a 1:1.5 ratio within 5 minutes. Adding another equivalent of CH_3OH into this mixture decreased the integration ratio of the deuterated vs. protonated **1a** species to 1:2.5 within 5 minutes.

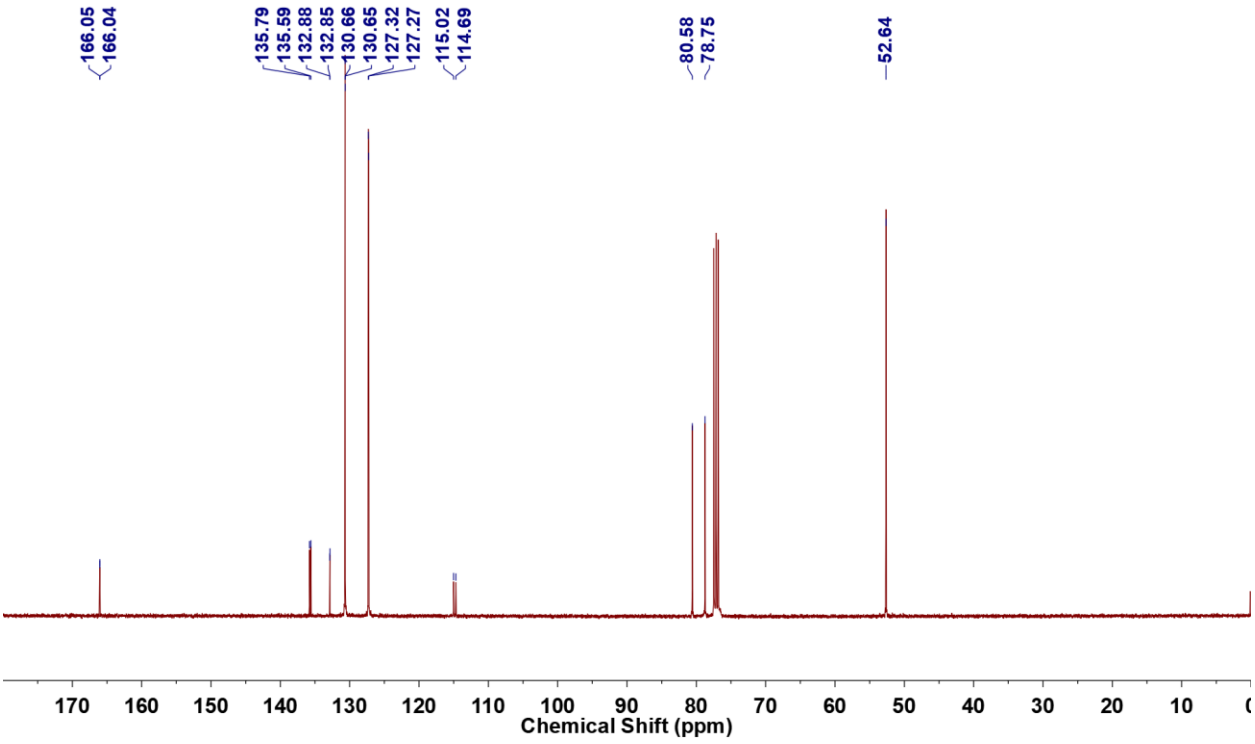


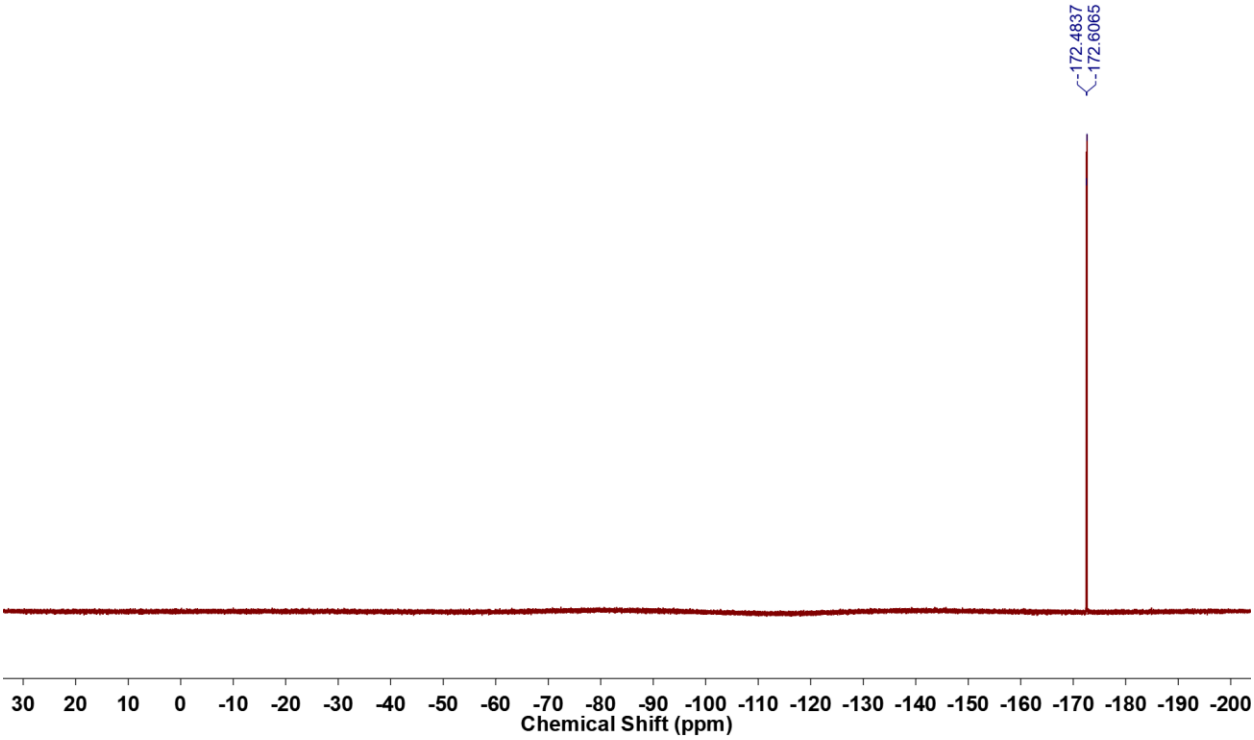
All ^{19}F NMR spectra were obtained in benzene-d_6. Left: H/D exchange in the presence of 20 mol% BTMG. From bottom to top: Stack 1: α-fluorobenzylnitrile **1a**. Stack 2: α-fluorobenzylnitrile **1a** + CD_3OD after 5 minutes (H:D = 6.43:1). Stack 3: α-fluorobenzylnitrile **1a** + CD_3OD after 15 minutes (H:D = 3.58:1). Stack 4: α-fluorobenzylnitrile **1a** + CD_3OD after 30 minutes (H:D = 2.65:1). Stack 5: α-fluorobenzylnitrile **1a** + CD_3OD after 60 minutes (H:D = 2.12:1). Stack 6: α-fluorobenzylnitrile **1a** + CD_3OD after 18 hours (H:D = 2.26:1). Right: H/D exchange in the presence of 20 mol% BTMG and Cu(I)-DTBM-Segphos complex. From bottom to top: Stack 1: α-fluorobenzylnitrile **1a**. Stack 2: 5 minutes after addition of 1 eq of CD_3OD (H:D = 1.47:1). Stack 3: 5 minutes after addition of 1 eq of CH_3OH into the reaction mixture of Stack 2 (H:D = 2.51:1).

5. ^{1}H, ^{13}C, ^{19}F NMR Spectra

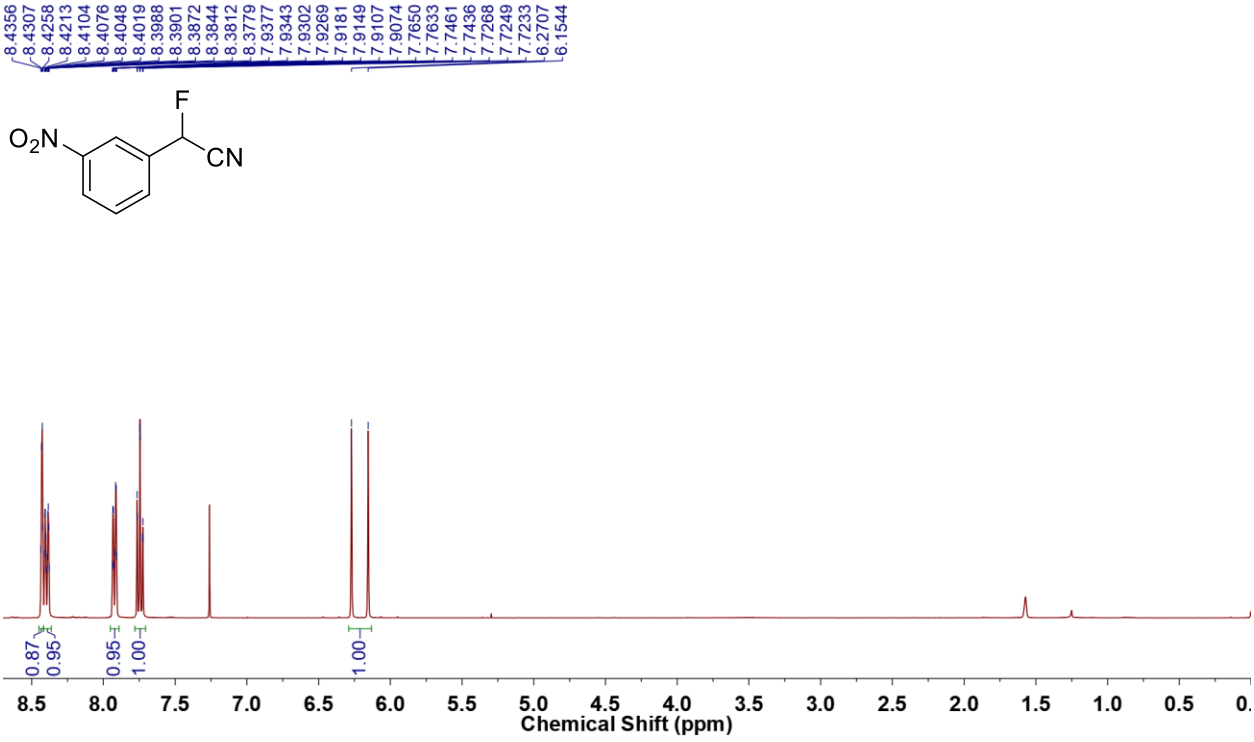
Methyl 4-(cyanofluoromethyl)benzoate (**1f**)

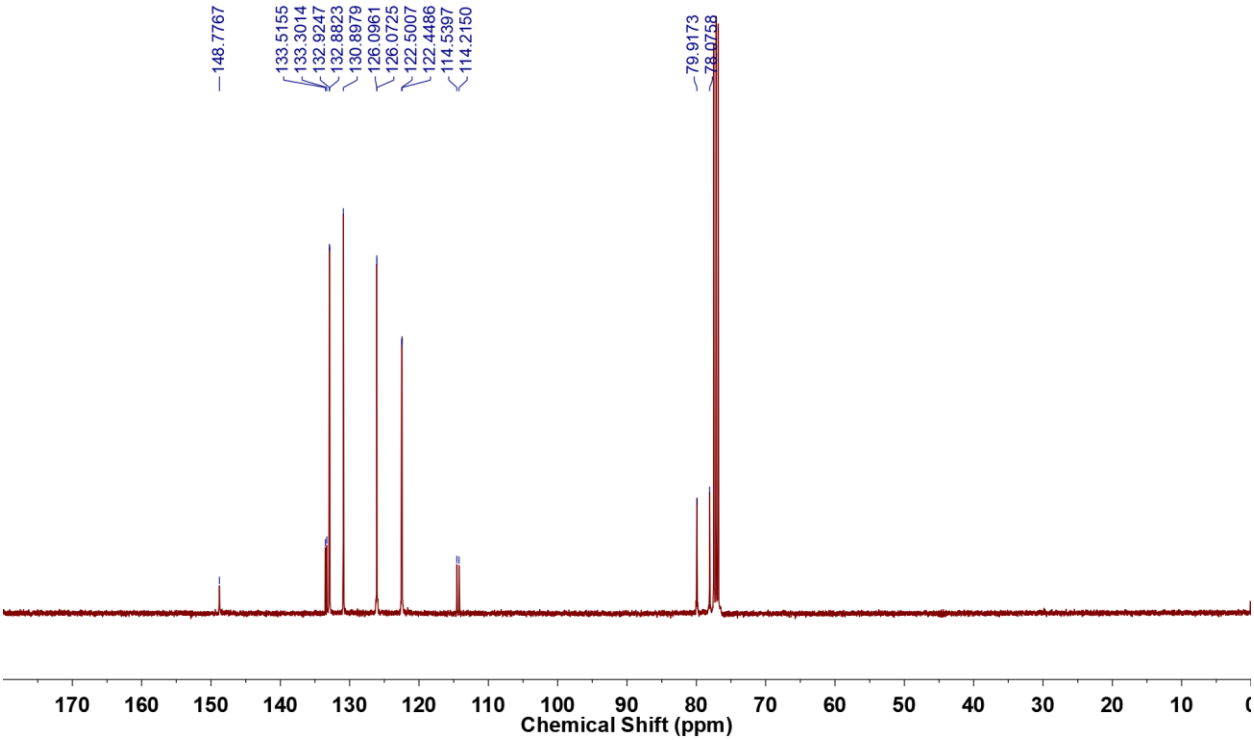






2-Fluoro-2-(3-nitrophenyl)acetonitrile (**1g**)




148.7767
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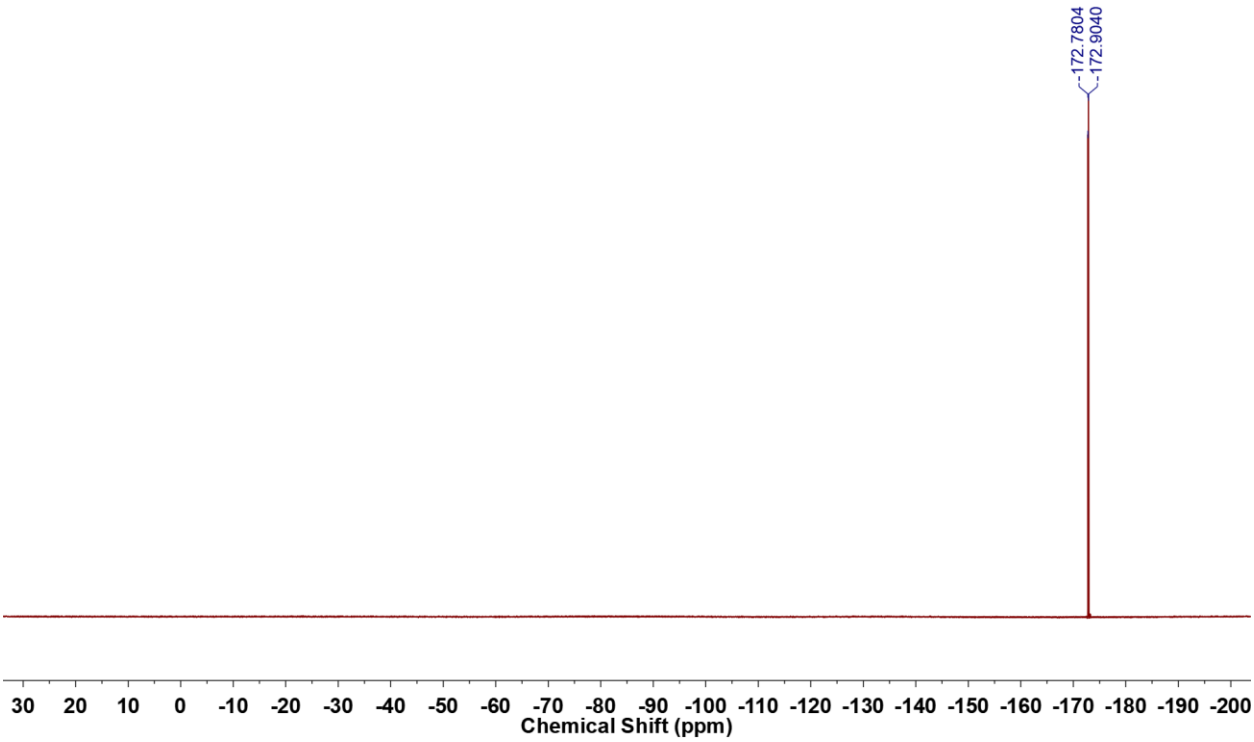
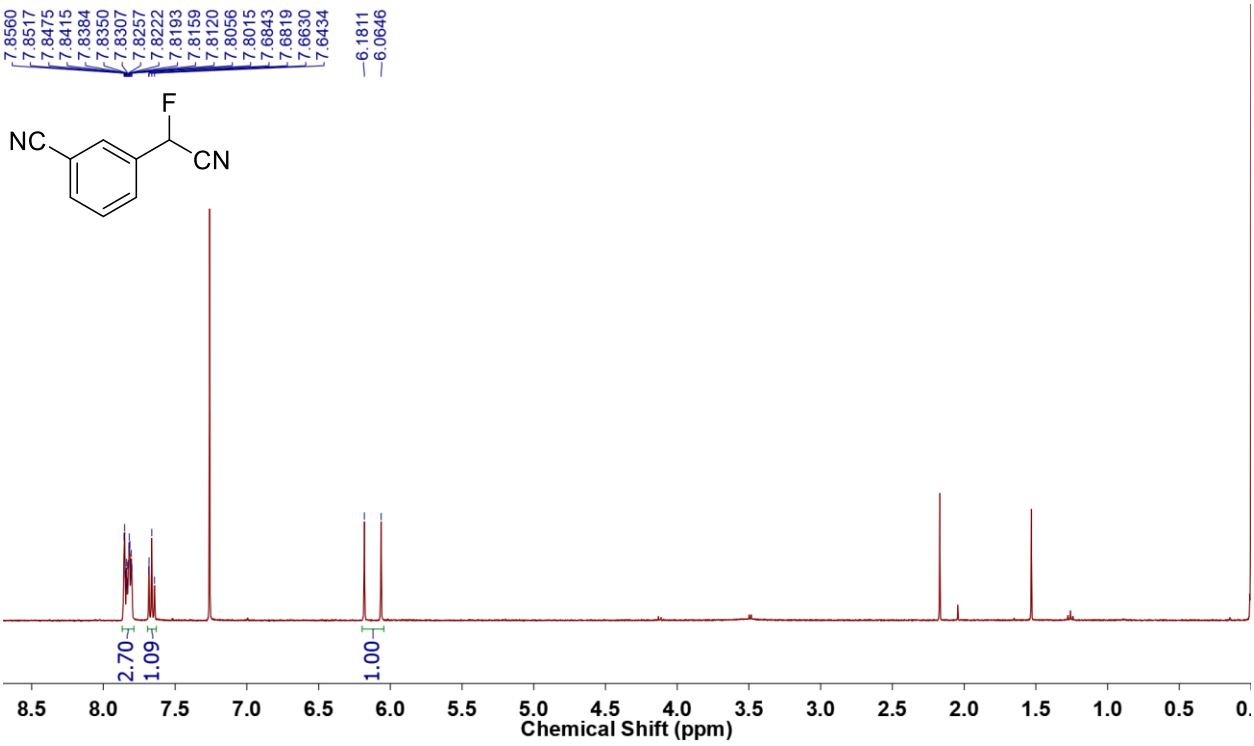
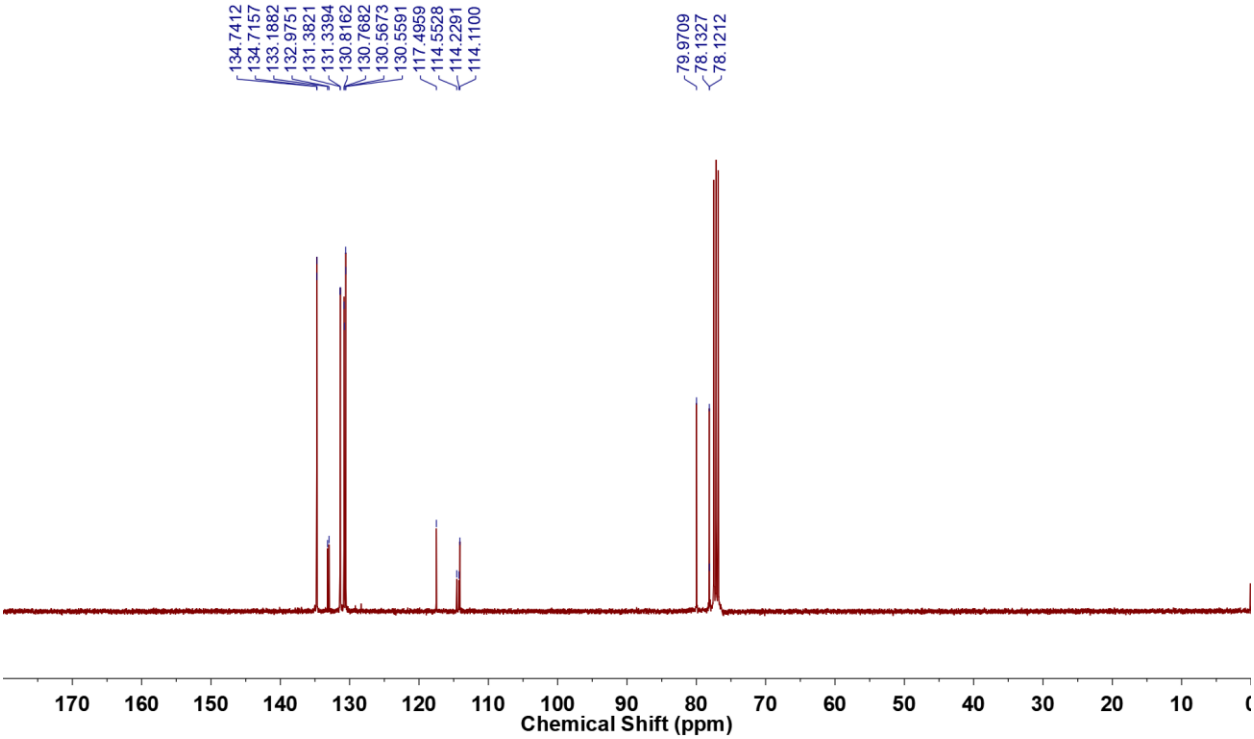
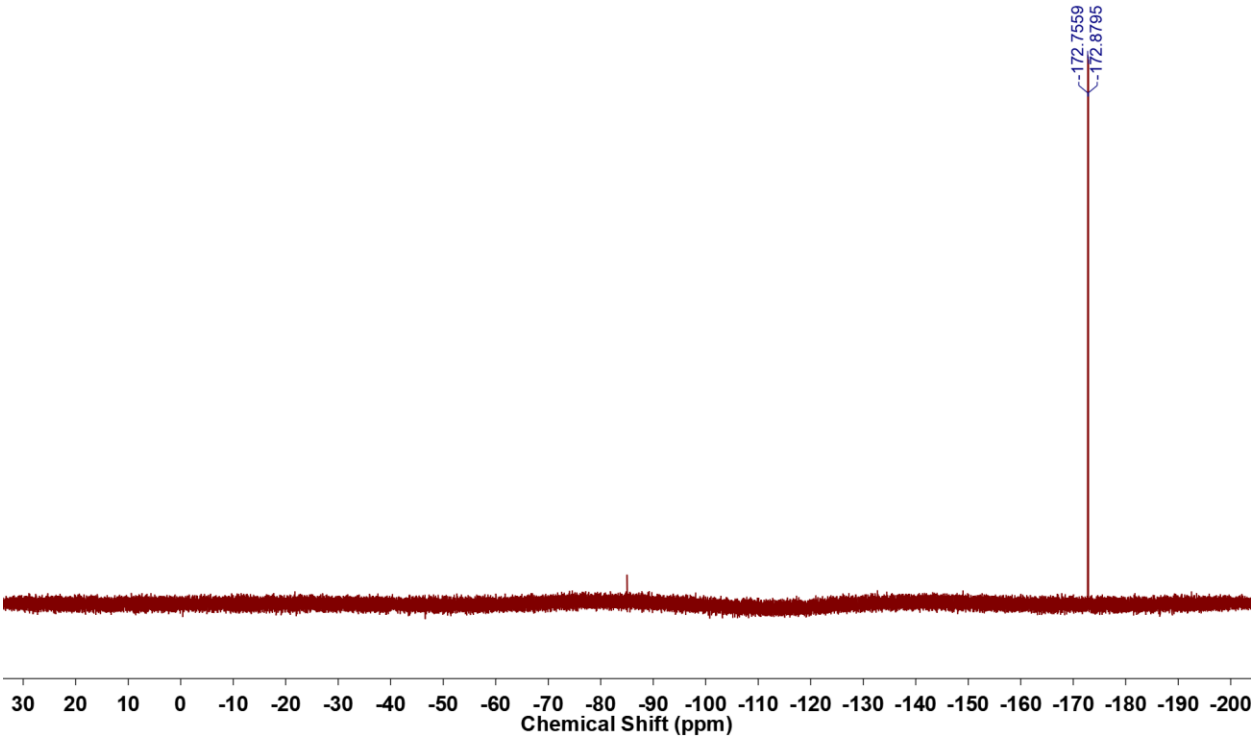
133.3014
132.9247
132.8823
130.8979
126.0961
126.0725
122.5007
122.4486
114.5397
114.2150
79.9173
78.0758
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-172.7804
-172.9040
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)

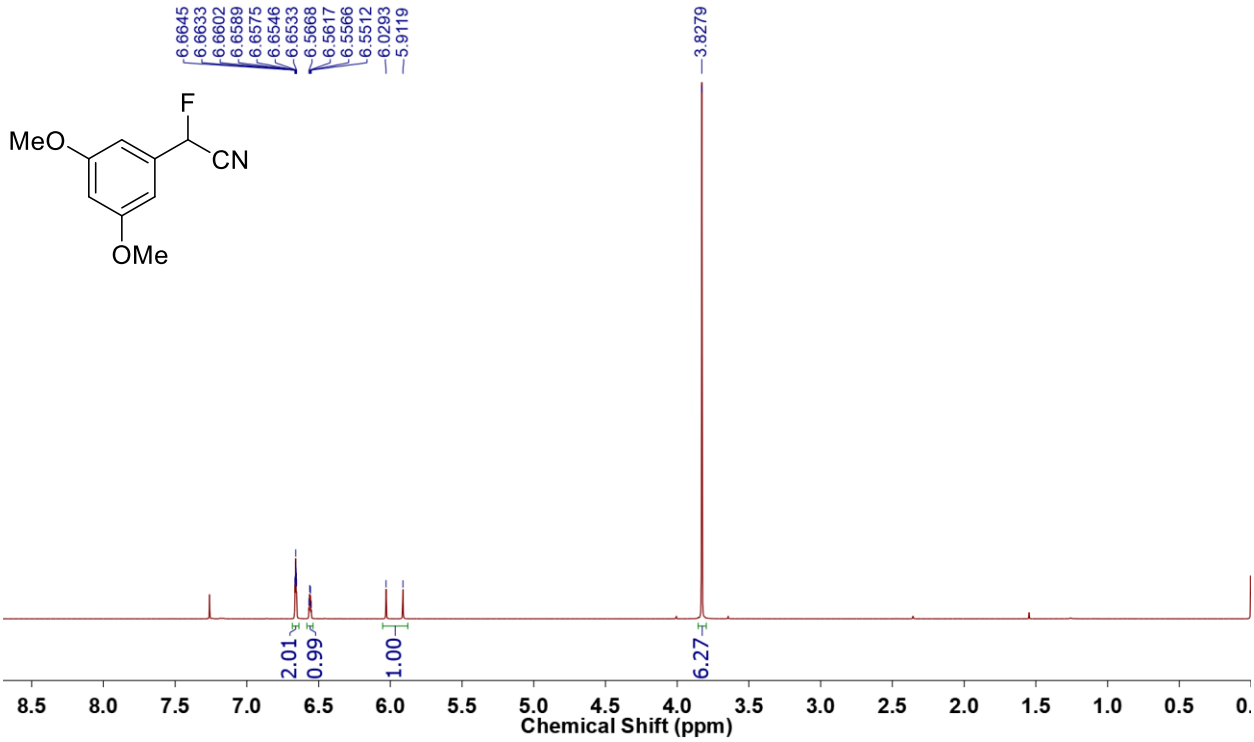
3-(Cyanofluoromethyl)benzonitrile (**1h**)

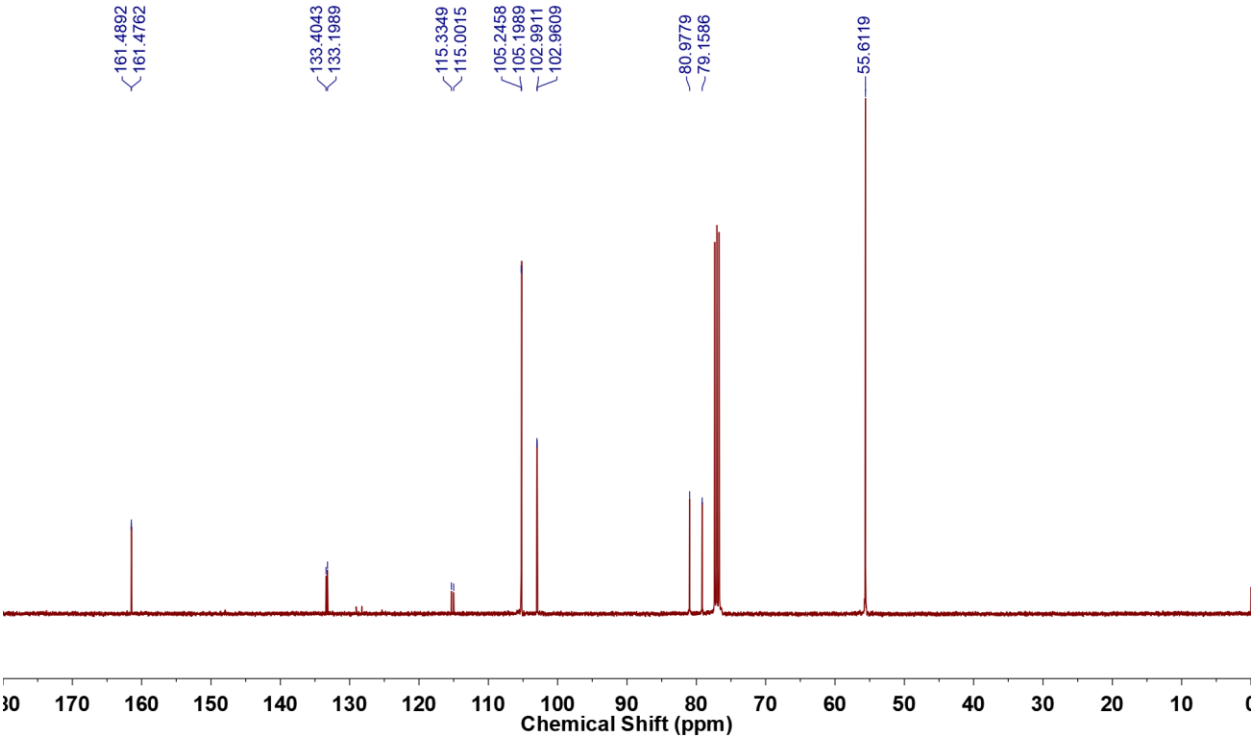


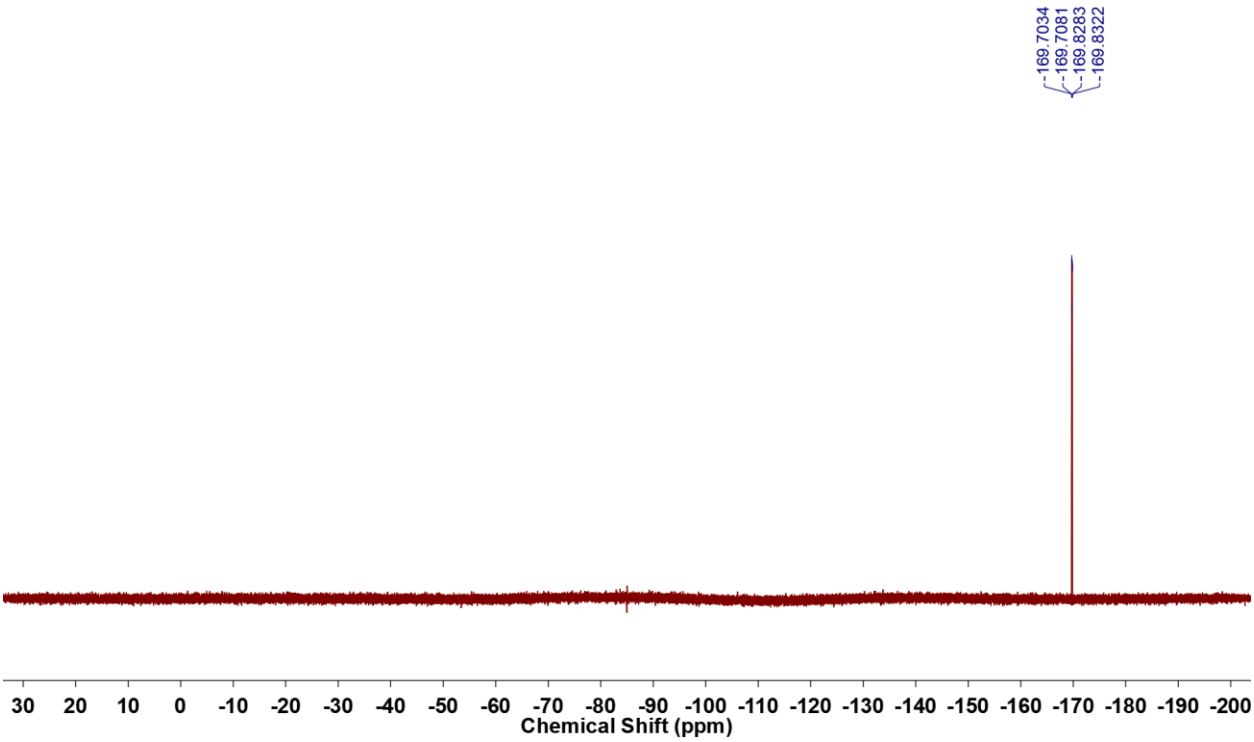




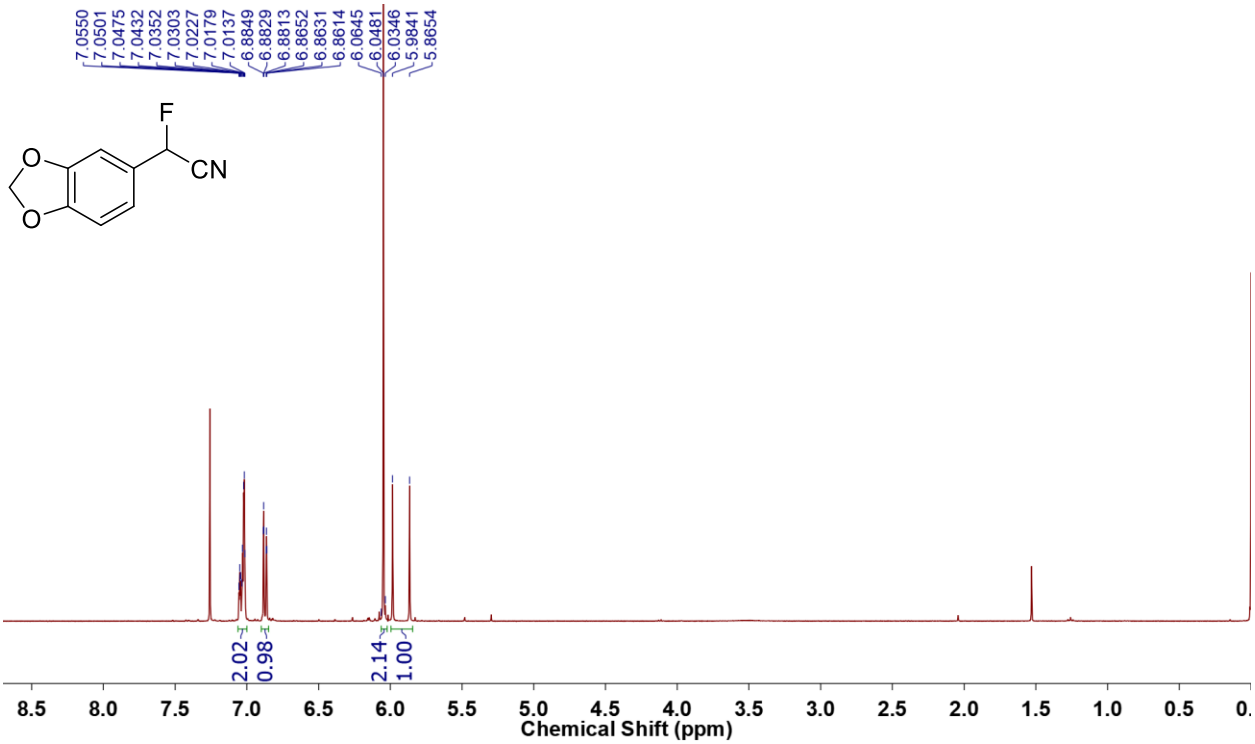
2-(3,5-Dimethoxyphenyl)-2-fluoroacetonitrile (**1i**)

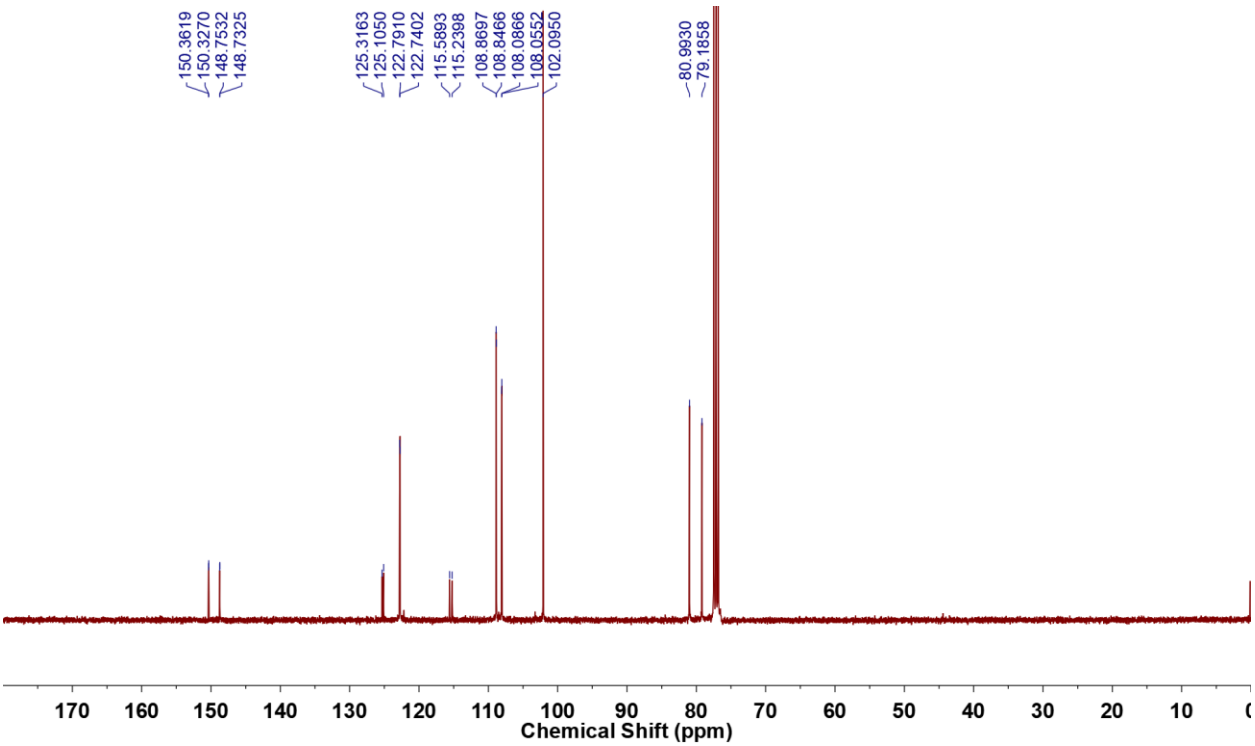


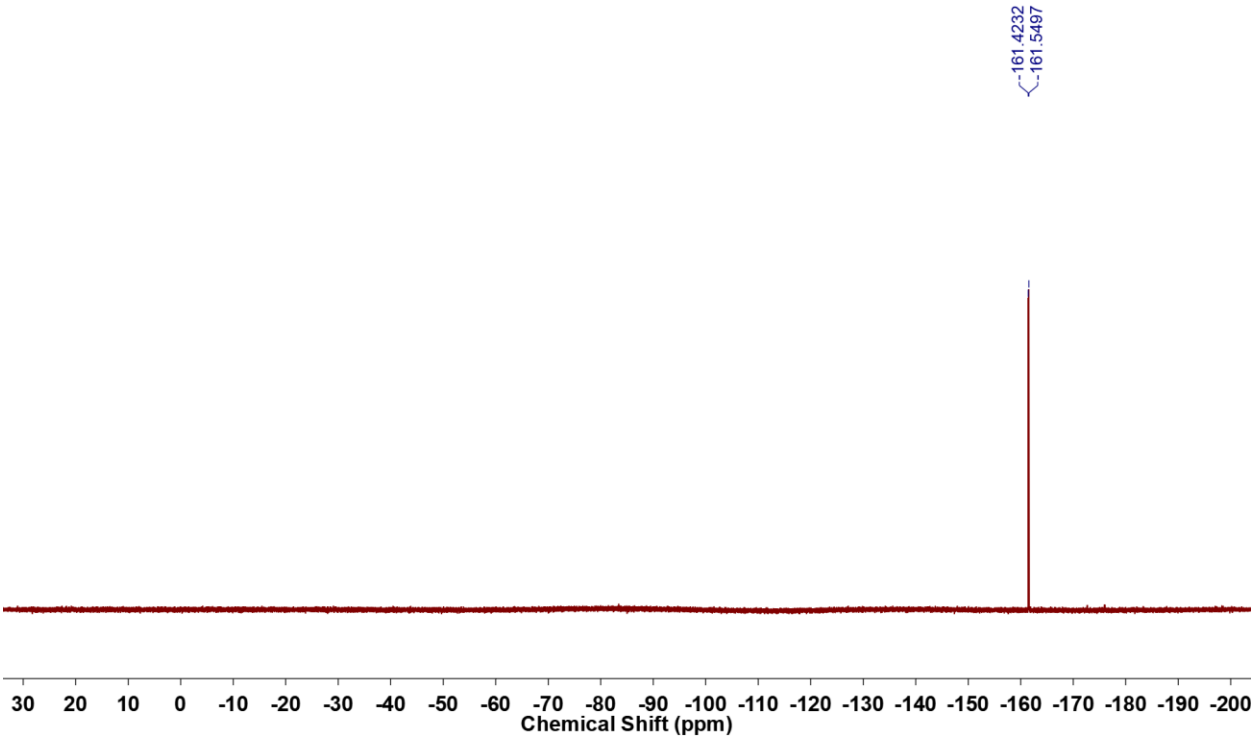

161.4892
161.4762
133.4043
133.1989
115.3349
115.0015
105.2458
105.1989
102.9911
102.9609
80.9779
79.1586
55.6119
Chemical Shift (ppm)


169.7034
169.7081
169.8283
169.8322
Chemical Shift (ppm)

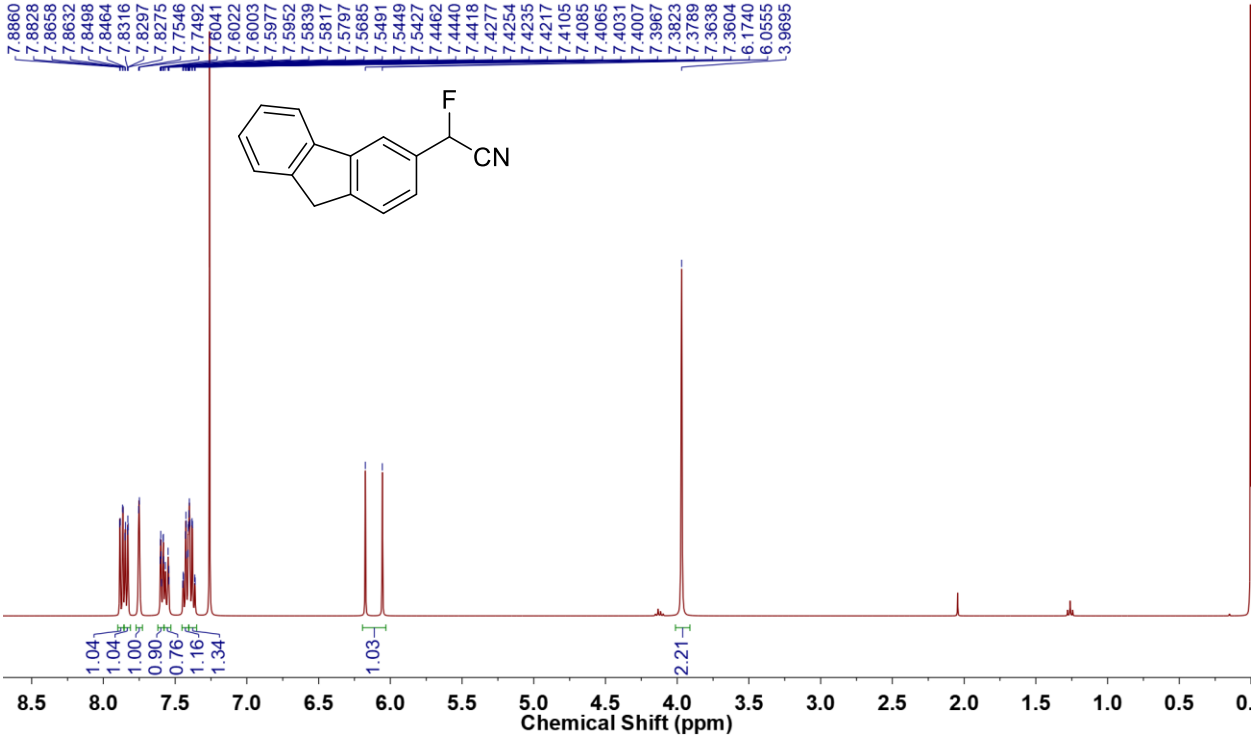
2-(Benzo[d][1,3]dioxol-5-yl)-2-fluoroacetonitrile (**1j**)

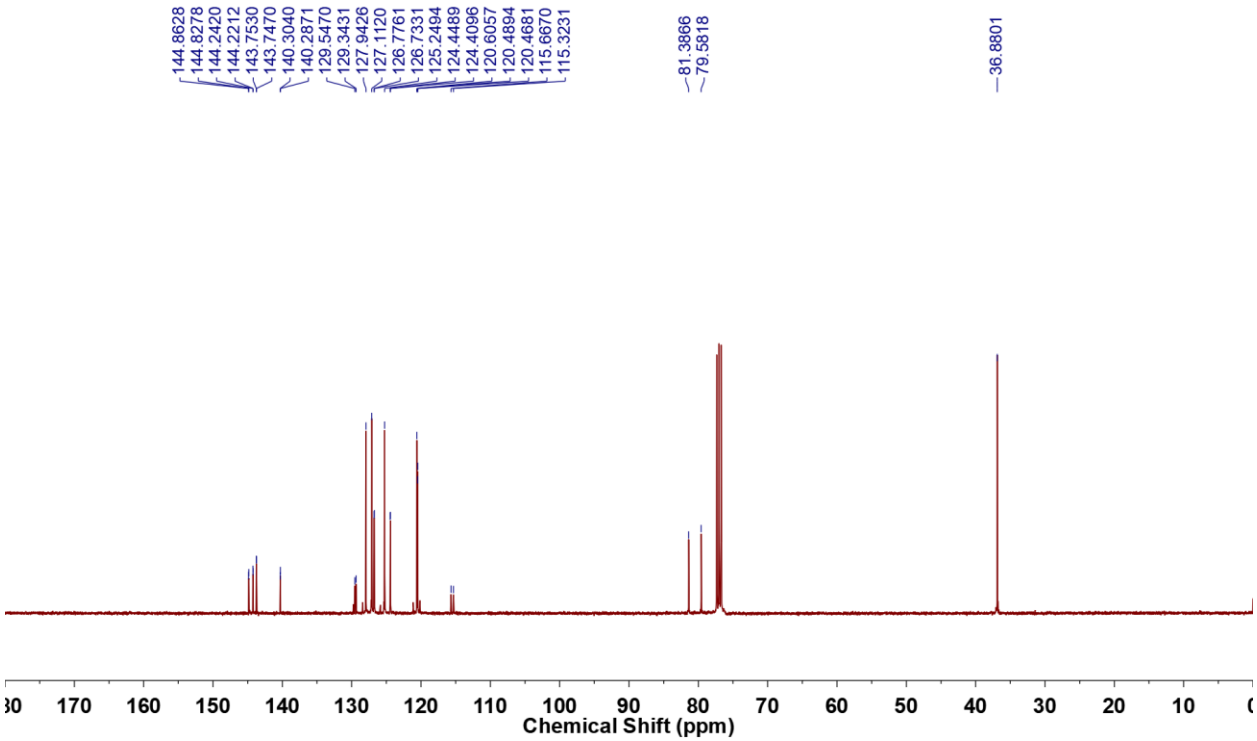






2-(9H-Fluoren-3-yl)-2-fluoroacetonitrile (**1l**)




144.8628
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144.2420
144.2212
143.7530
143.7470
140.3040
140.2871
129.5470
129.3431
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127.1120
126.7761
126.7331
125.2494
124.4489
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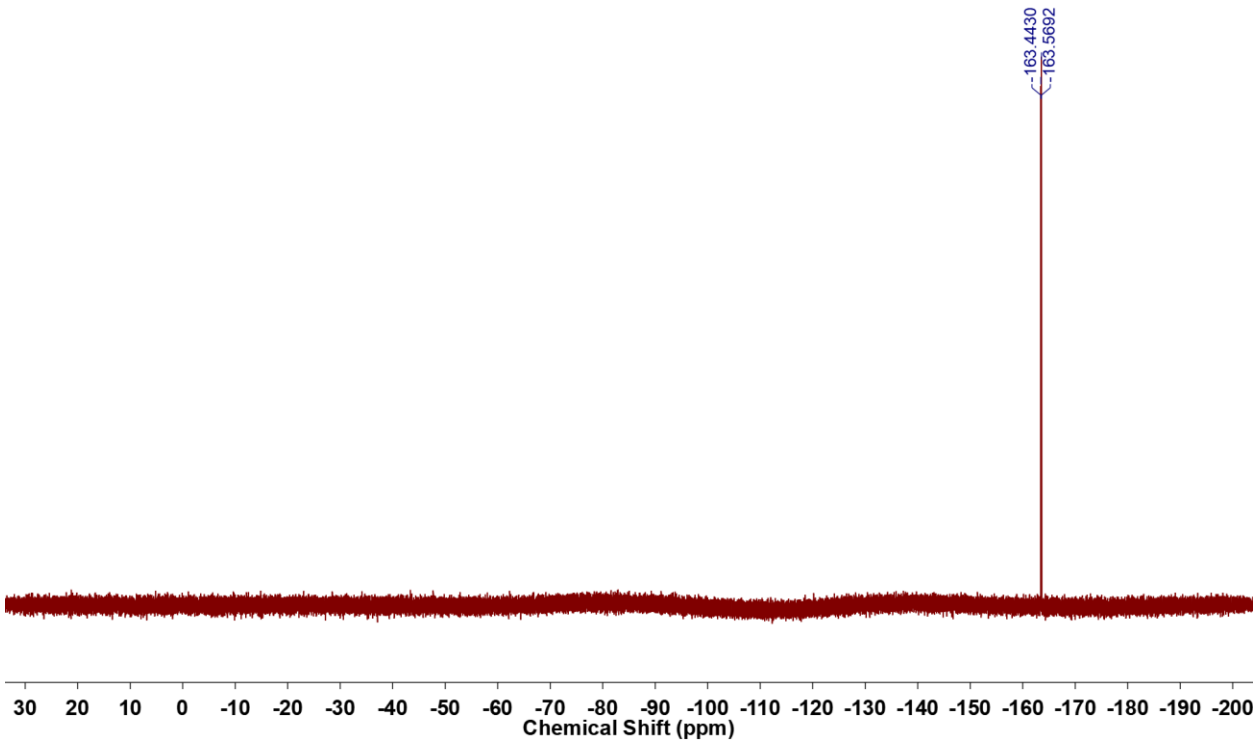
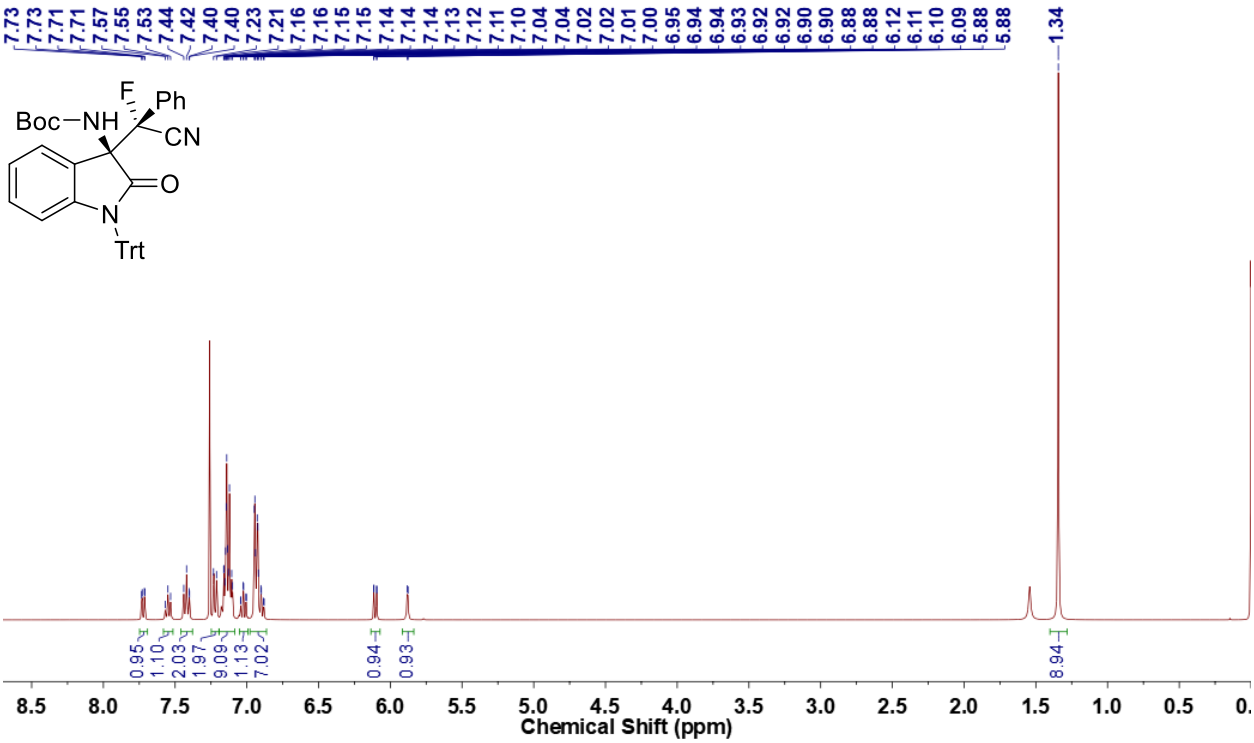
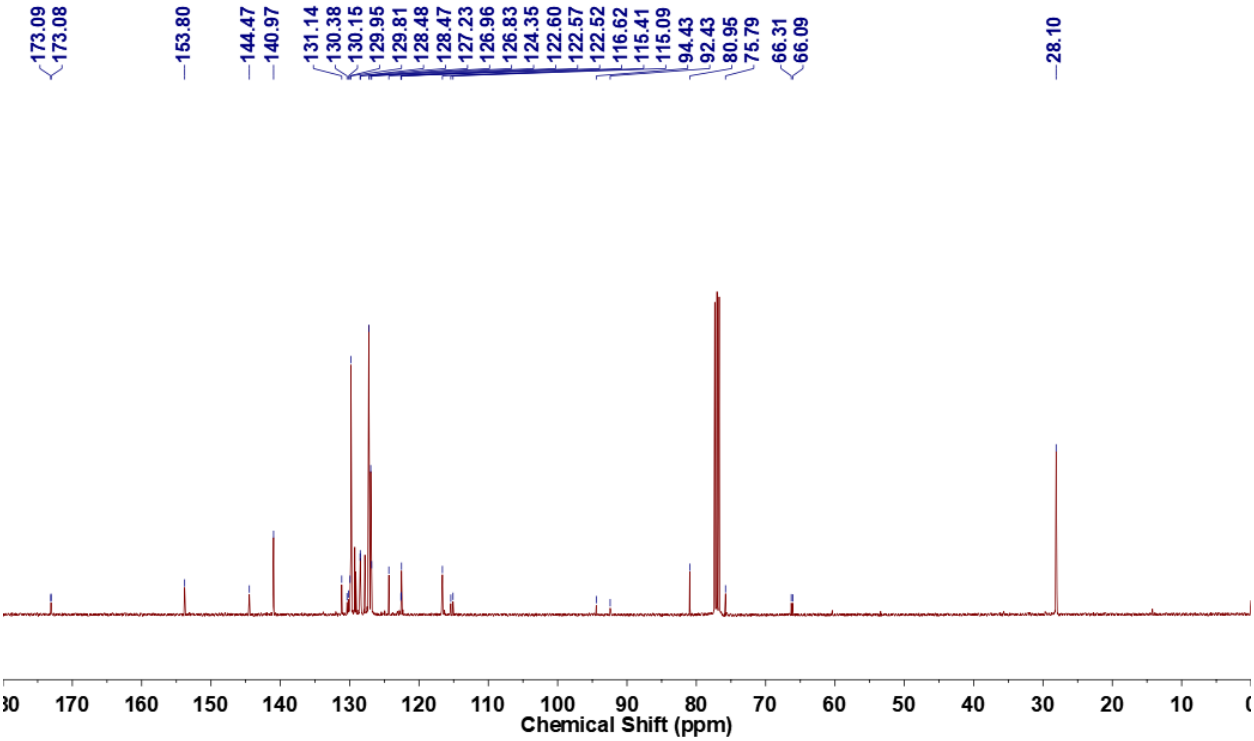
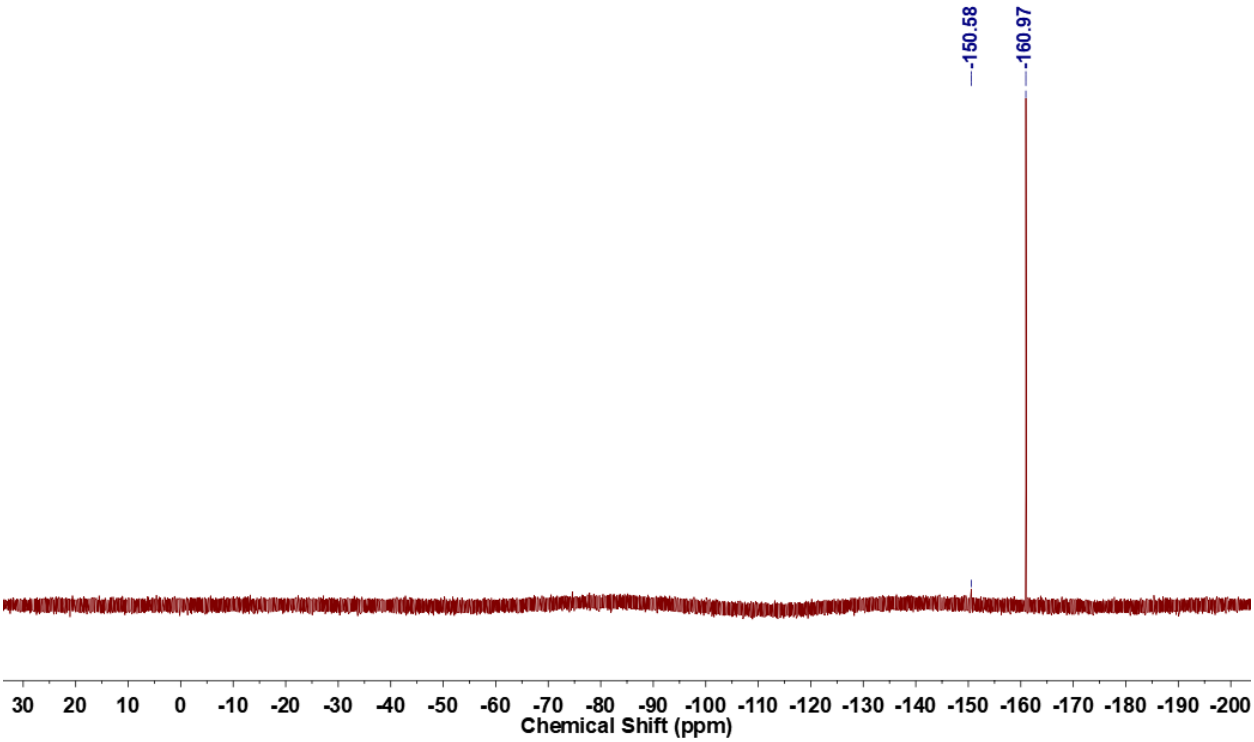
120.4681
115.6670
115.3231
81.3866
79.5818
36.8801
Chemical Shift (ppm)


-163.4430
-163.5692
Chemical Shift (ppm)

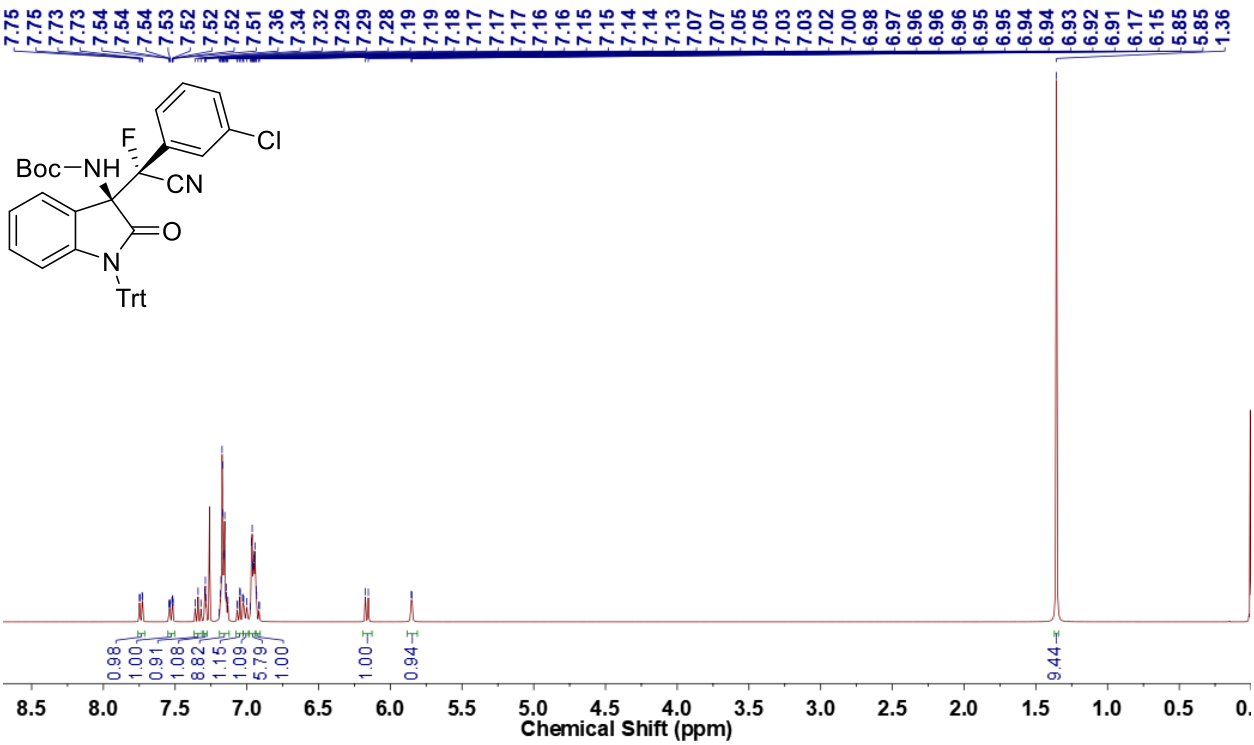
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ab**)

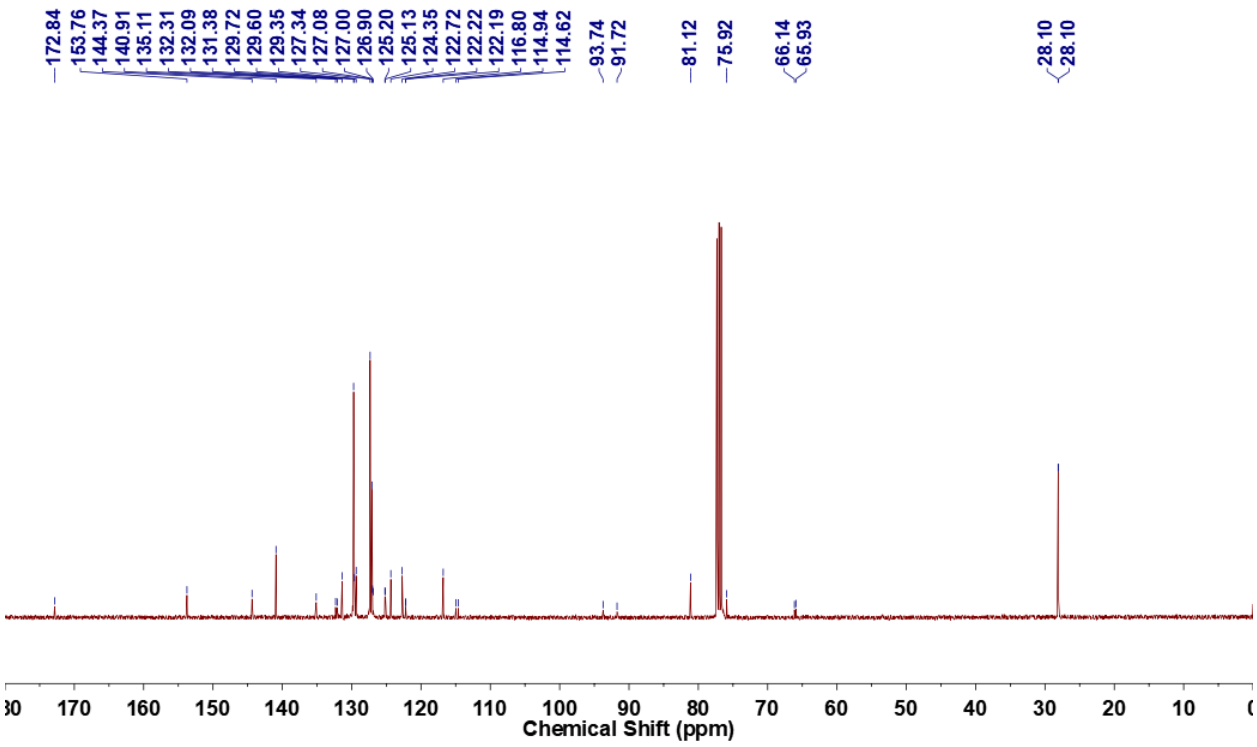


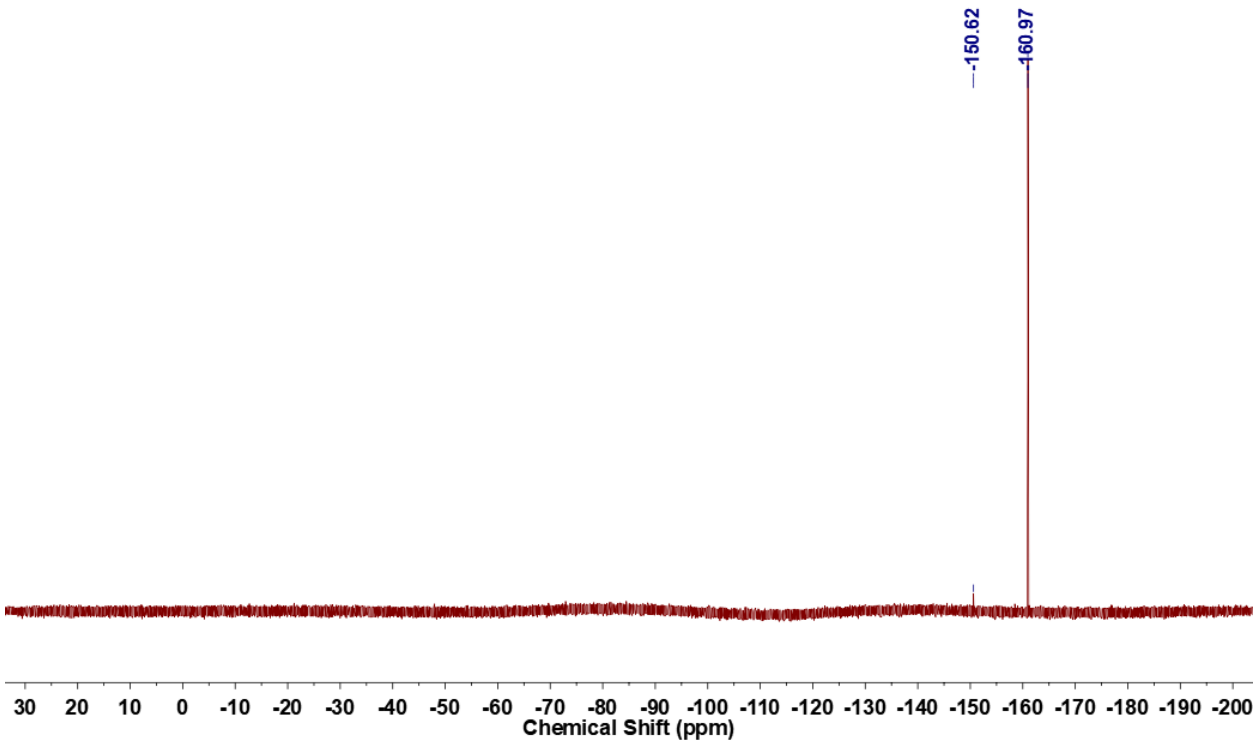




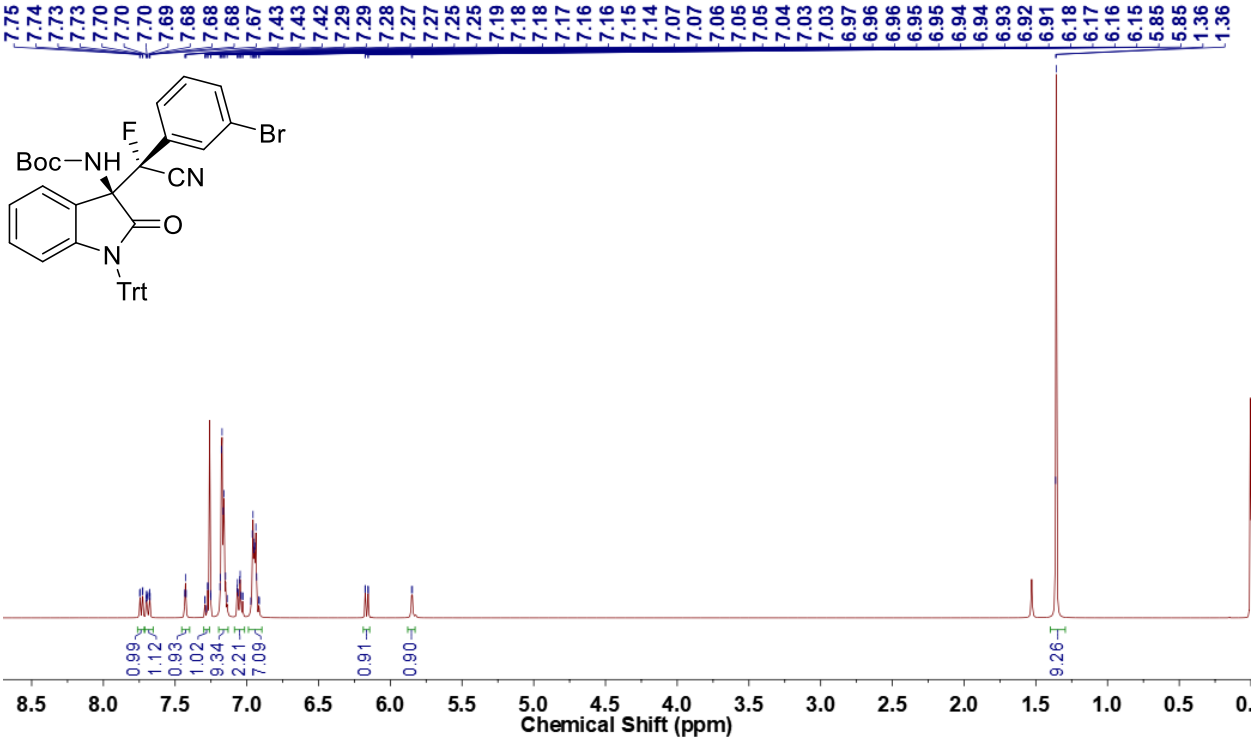
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3bb**)

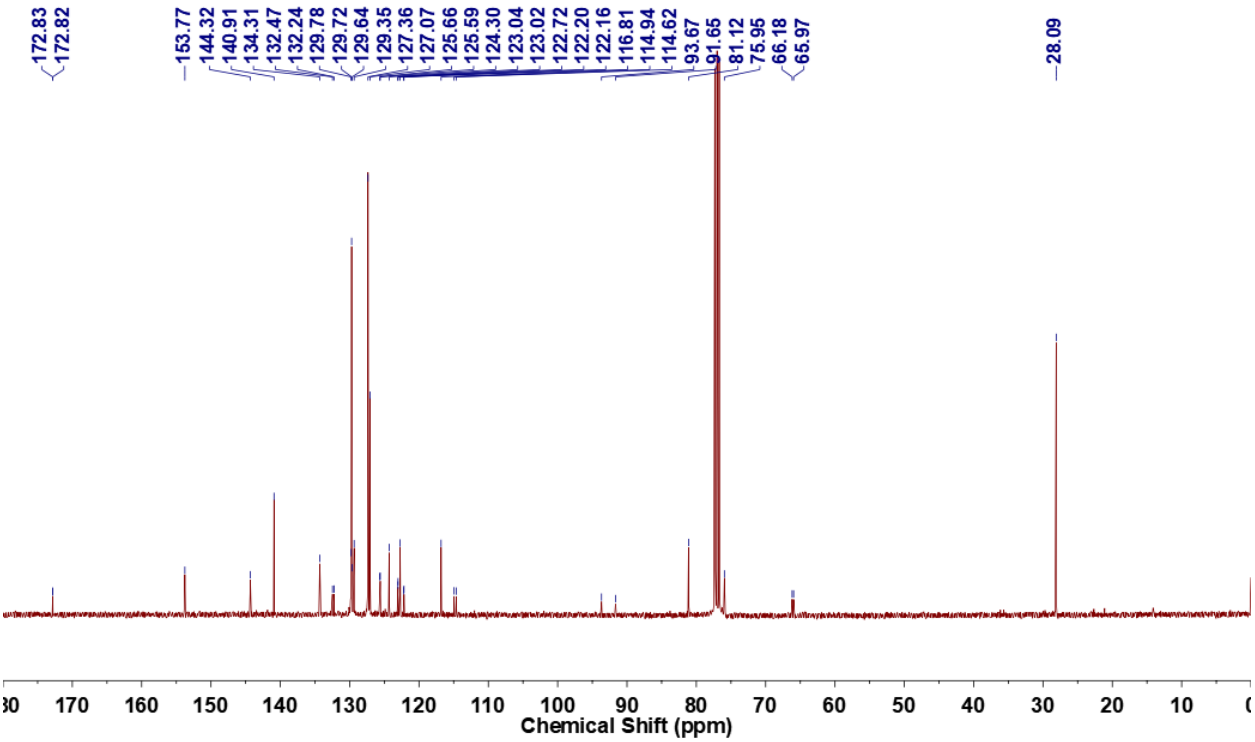


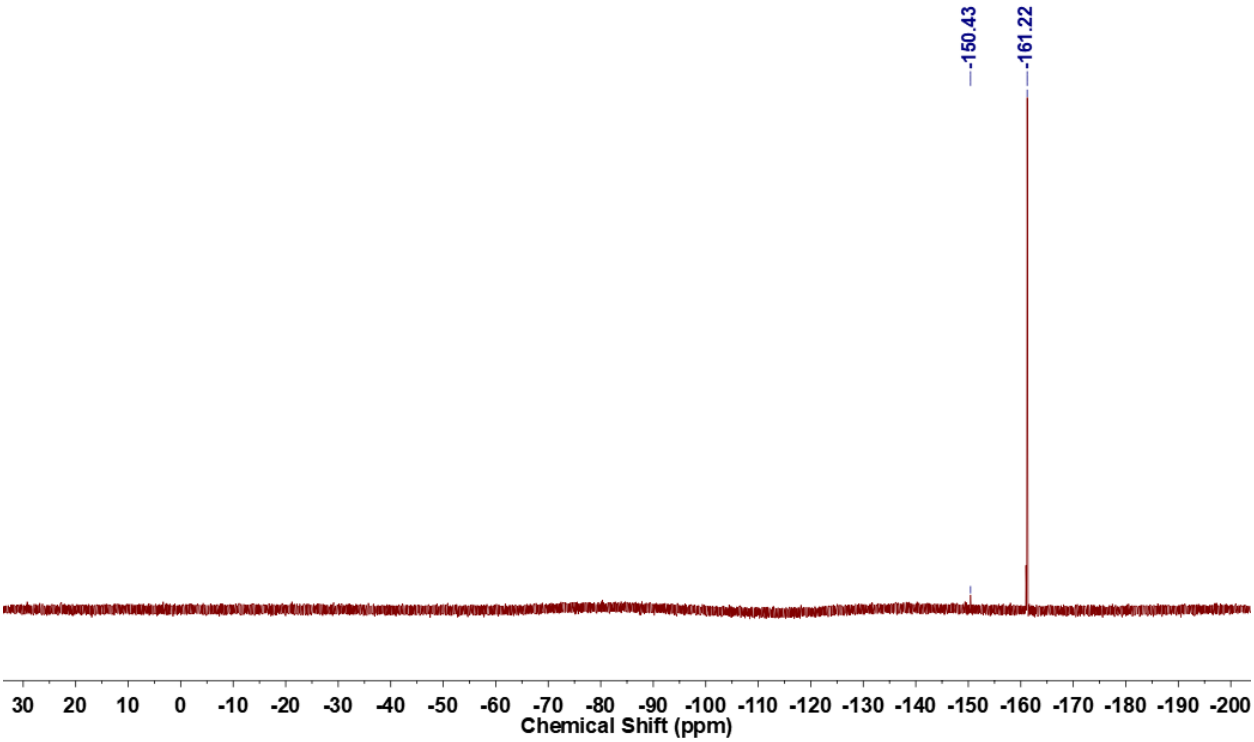

172.84
153.76
144.37
140.91
135.11
132.31
132.09
131.38
129.72
129.60
129.35
127.34
127.08
127.00
126.90
125.20
125.13
124.35
122.72
122.22
122.19
116.80
114.94
114.62
93.74
91.72
81.12
75.92
66.14
65.93
28.10
28.10
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-150.62
-160.97
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)

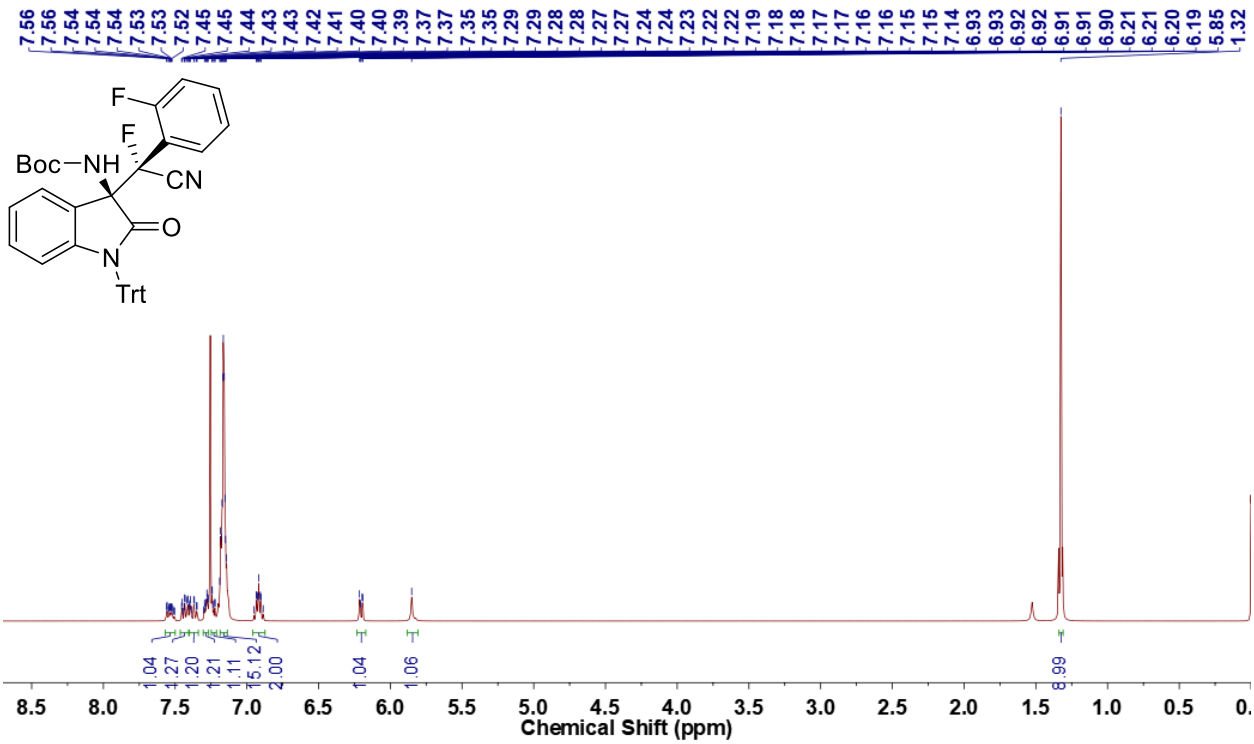
tert-Butyl ((*R*)-3-((S)-cyanofluoro(3-bromophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3cb**)

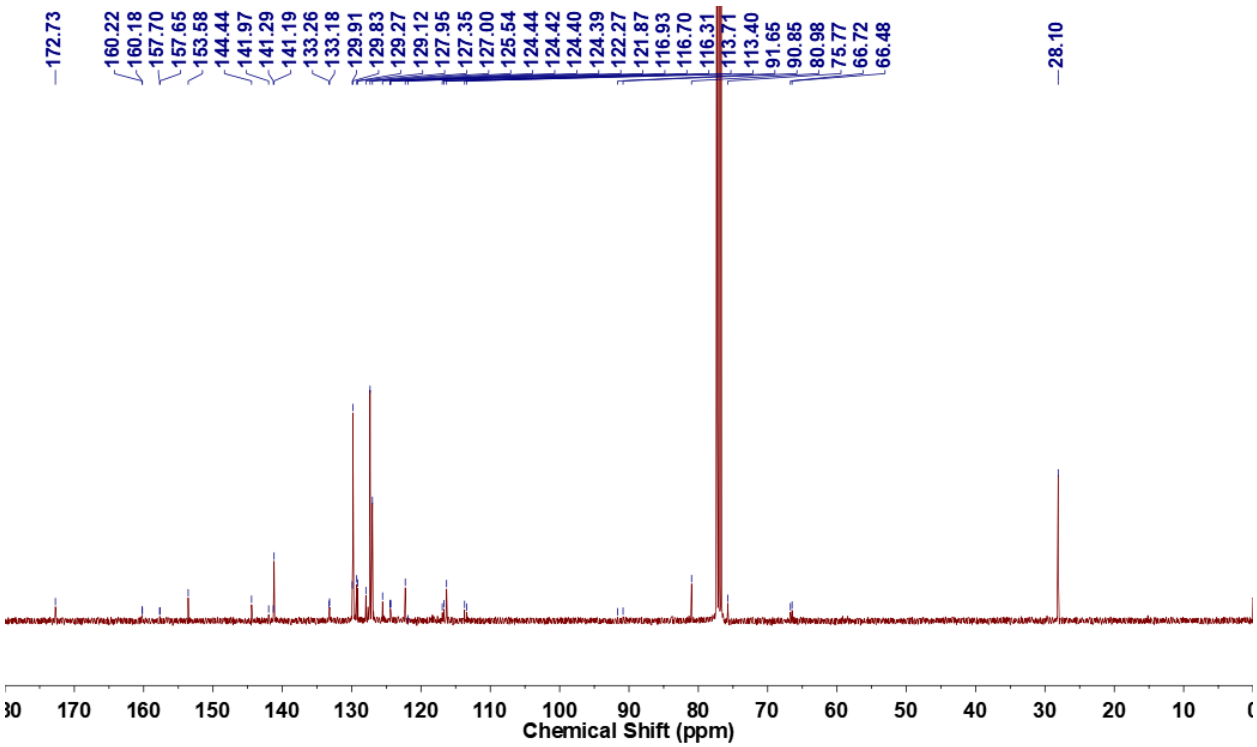


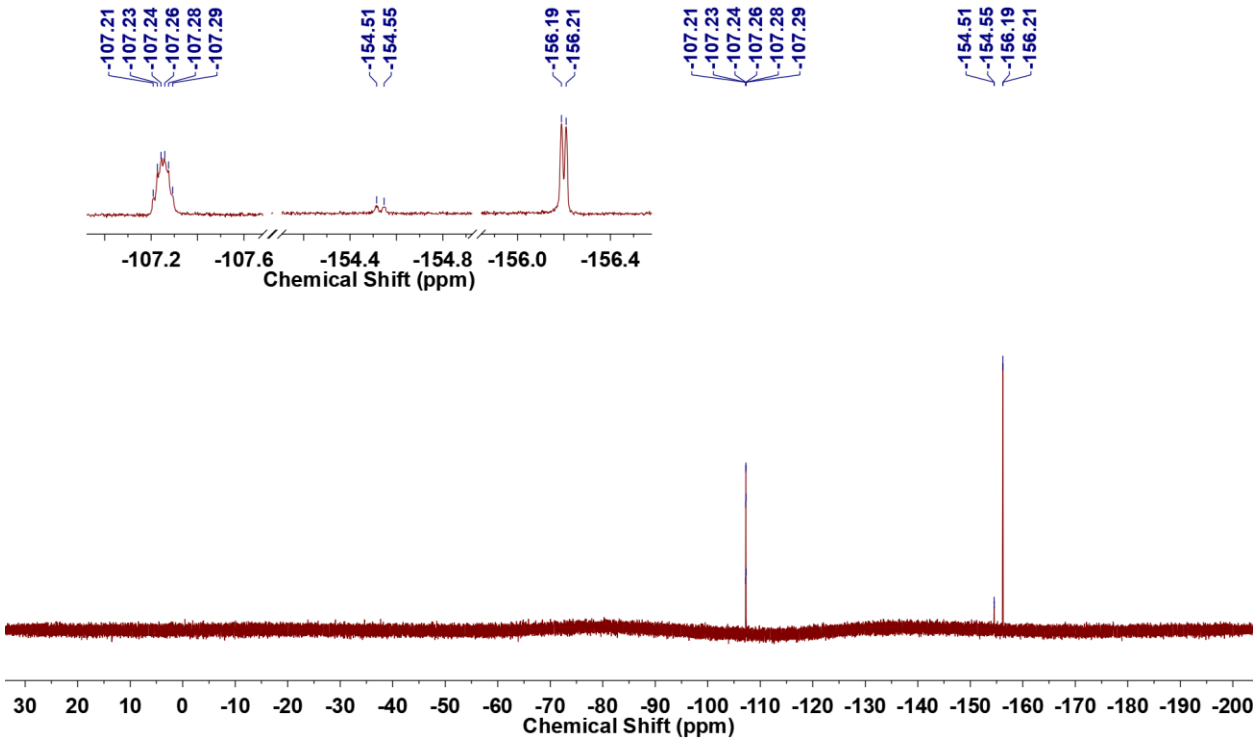




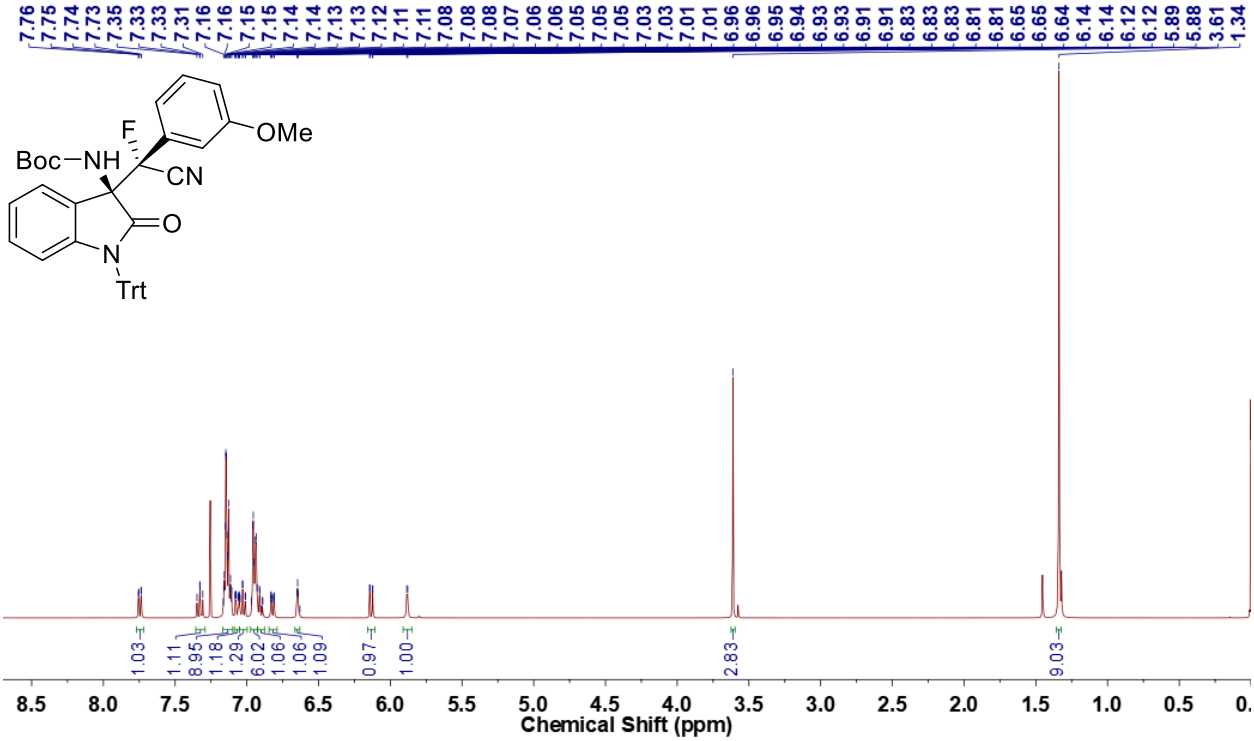
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-fluorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3db**)

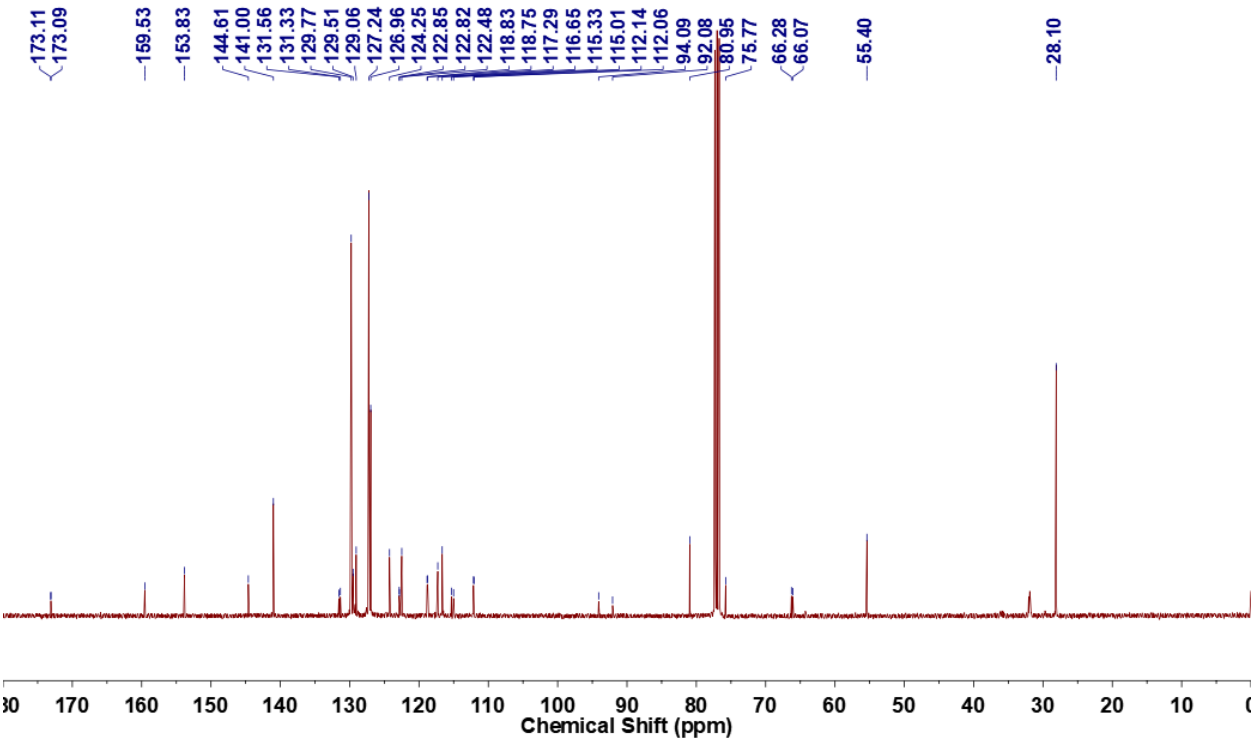


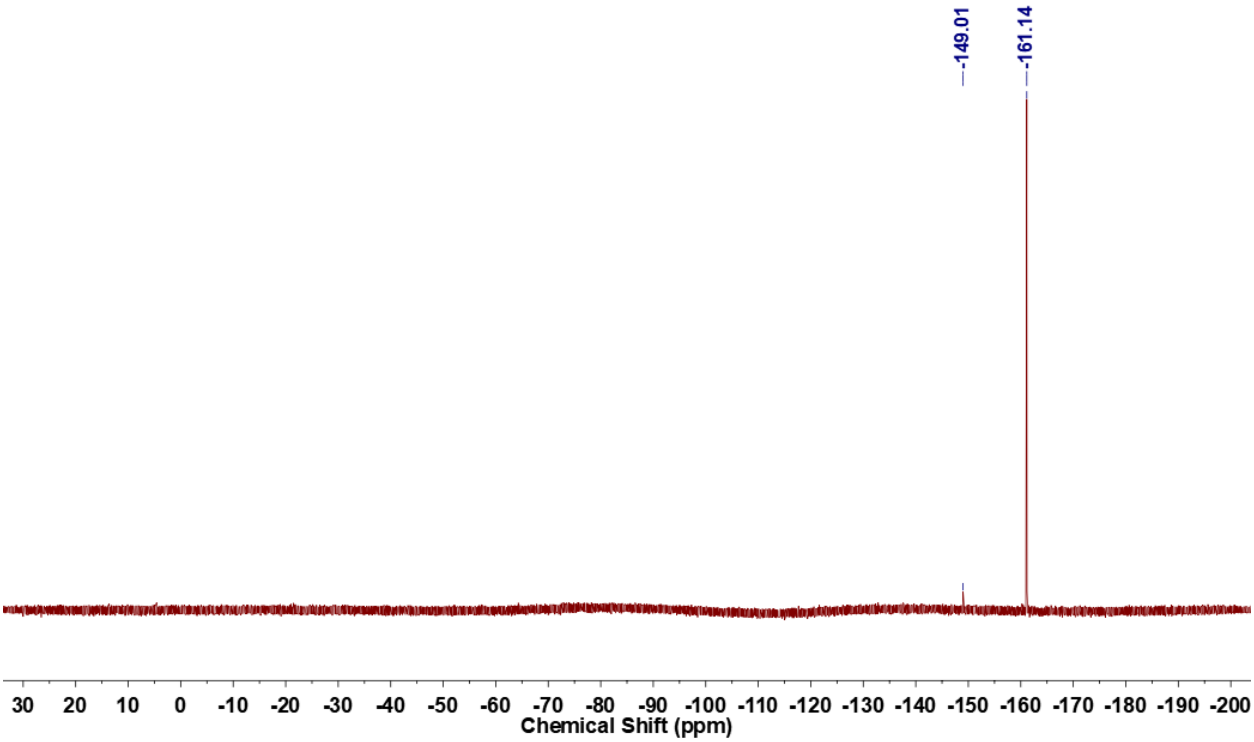

172.73
160.22
160.18
157.70
157.65
153.58
144.44
141.97
141.29
141.19
133.26
133.18
129.91
129.83
129.27
129.12
127.95
127.35
127.00
125.54
124.44
124.42
124.40
124.39
122.27
121.87
116.93
116.70
116.31
113.71
113.40
91.65
90.85
80.98
75.77
66.72
66.48
28.10
Chemical Shift (ppm)


-107.21
-107.23
-107.24
-107.26
-107.28
-107.29
-154.51
-154.55
-156.19
-156.21
Chemical Shift (ppm)

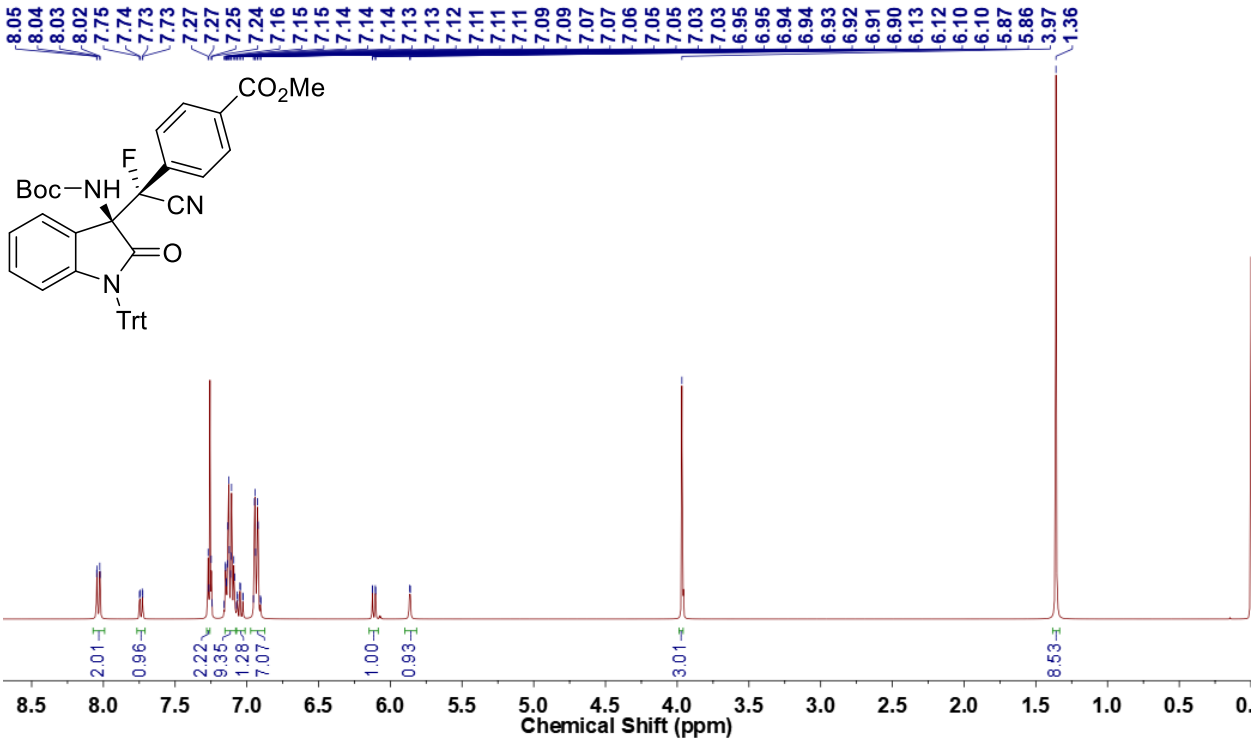
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3eb**)

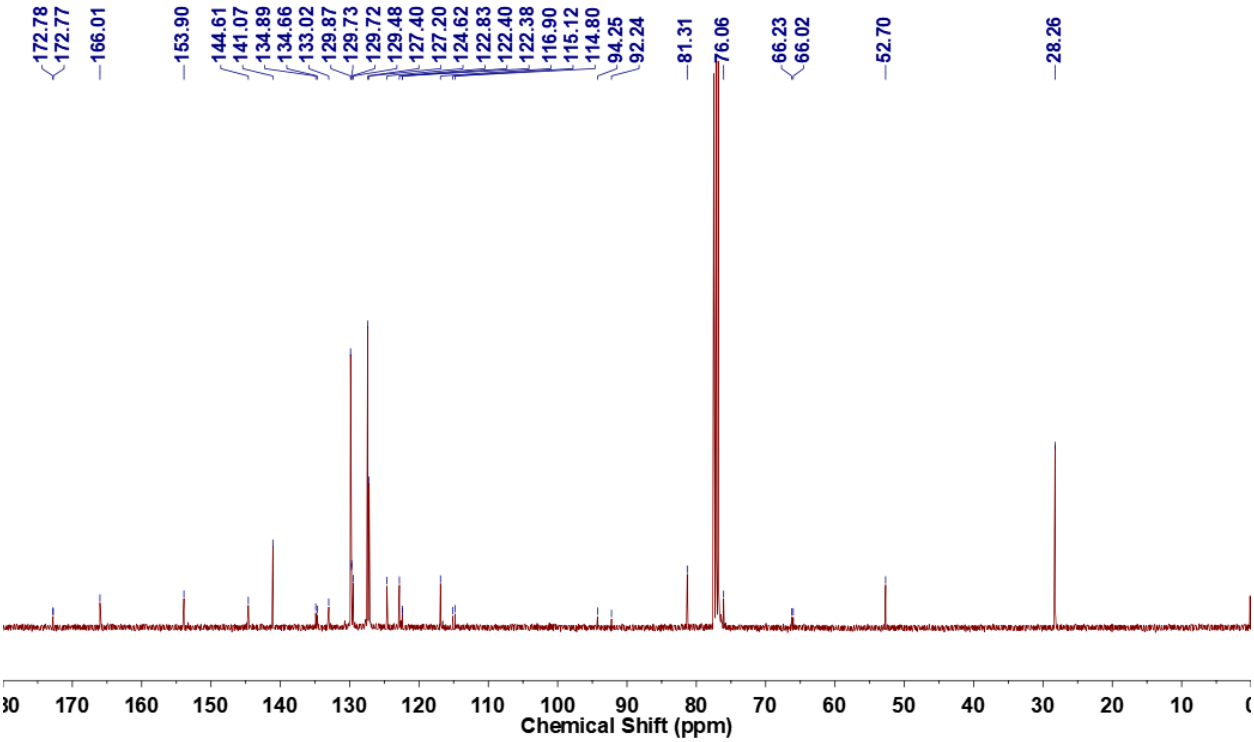


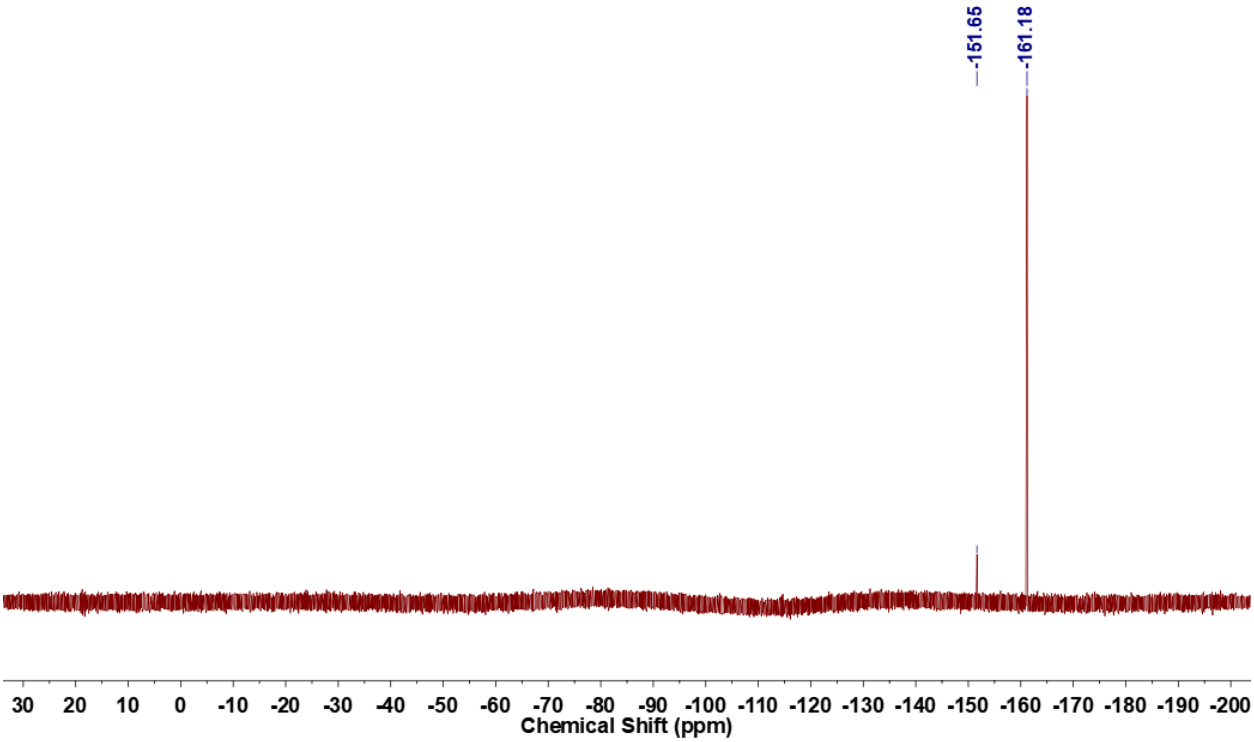




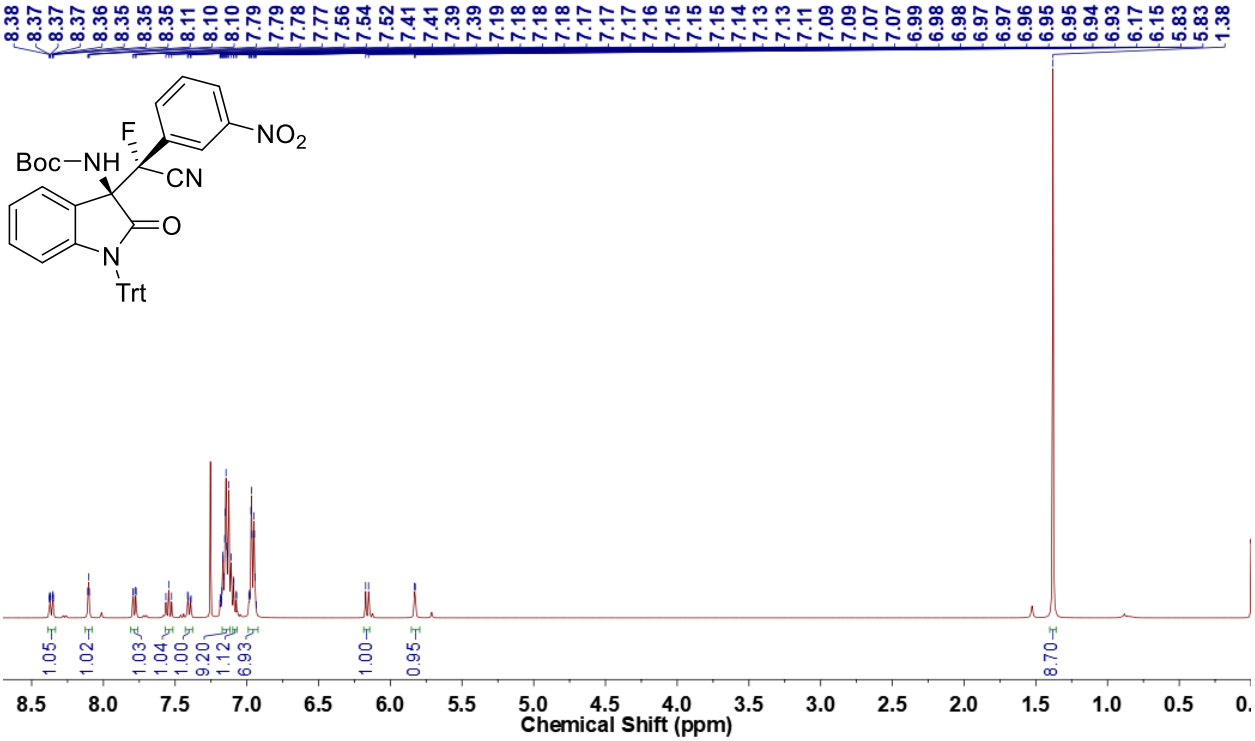
Methyl 4-((*S*)-((*R*)-3-((*tert*-butoxycarbonyl)amino)-2-oxo-1-tritylindolin-3-yl)(cyano)fluoromethyl)benzoate (**3fb**)

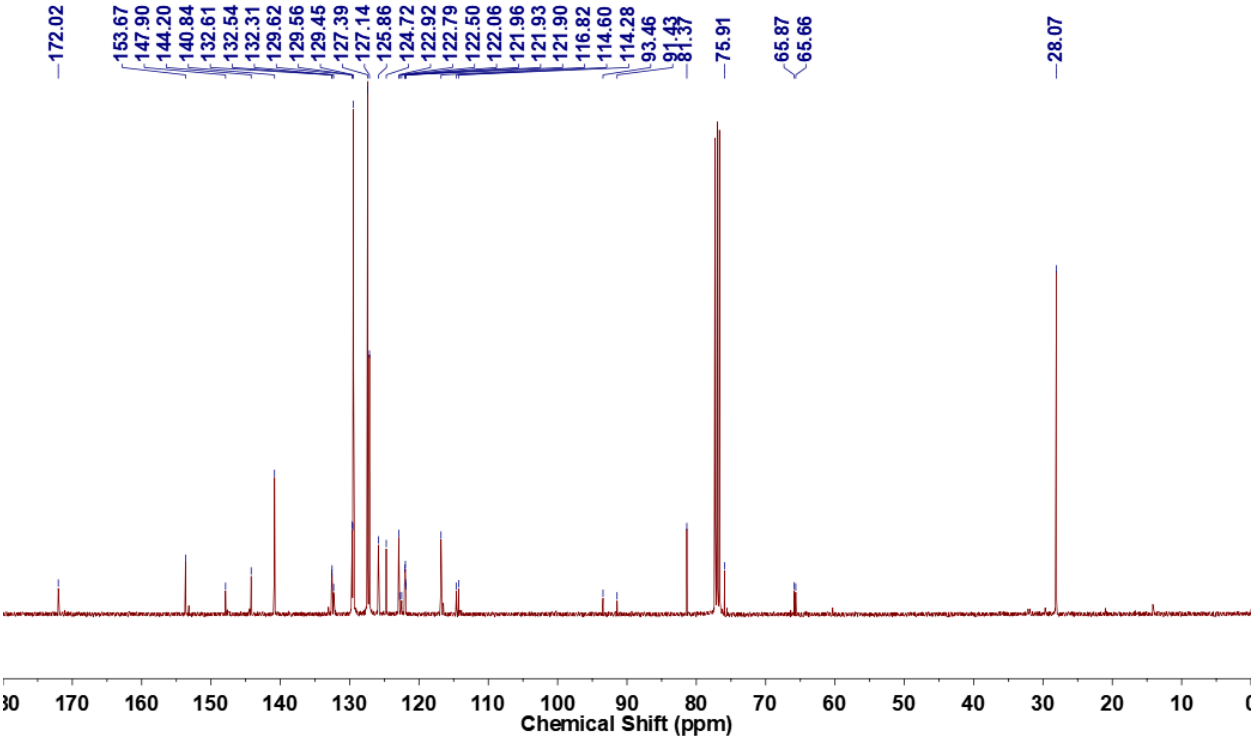


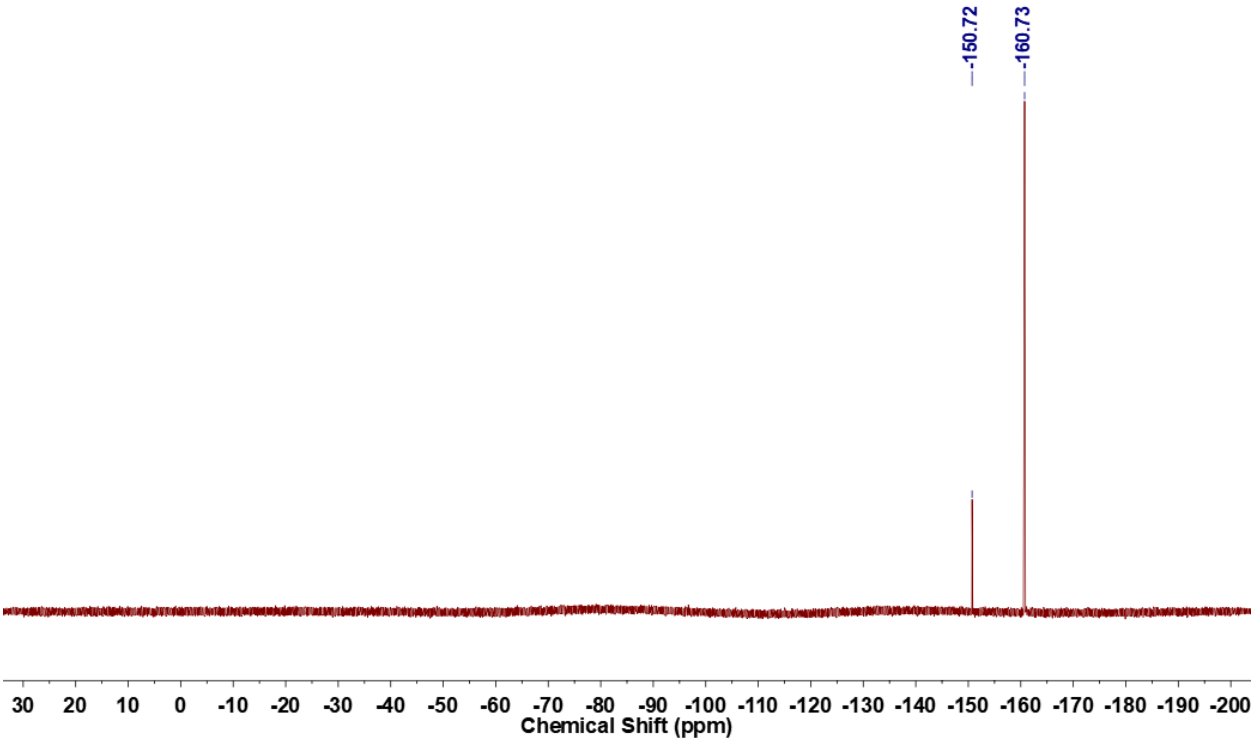

172.78
172.77
166.01
153.90
144.61
141.07
134.89
134.66
133.02
129.87
129.73
129.72
129.48
127.40
127.20
124.62
122.83
122.40
122.38
116.90
115.12
114.80
94.25
92.24
81.31
76.06
66.23
66.02
52.70
28.26
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-151.65
-161.18
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)

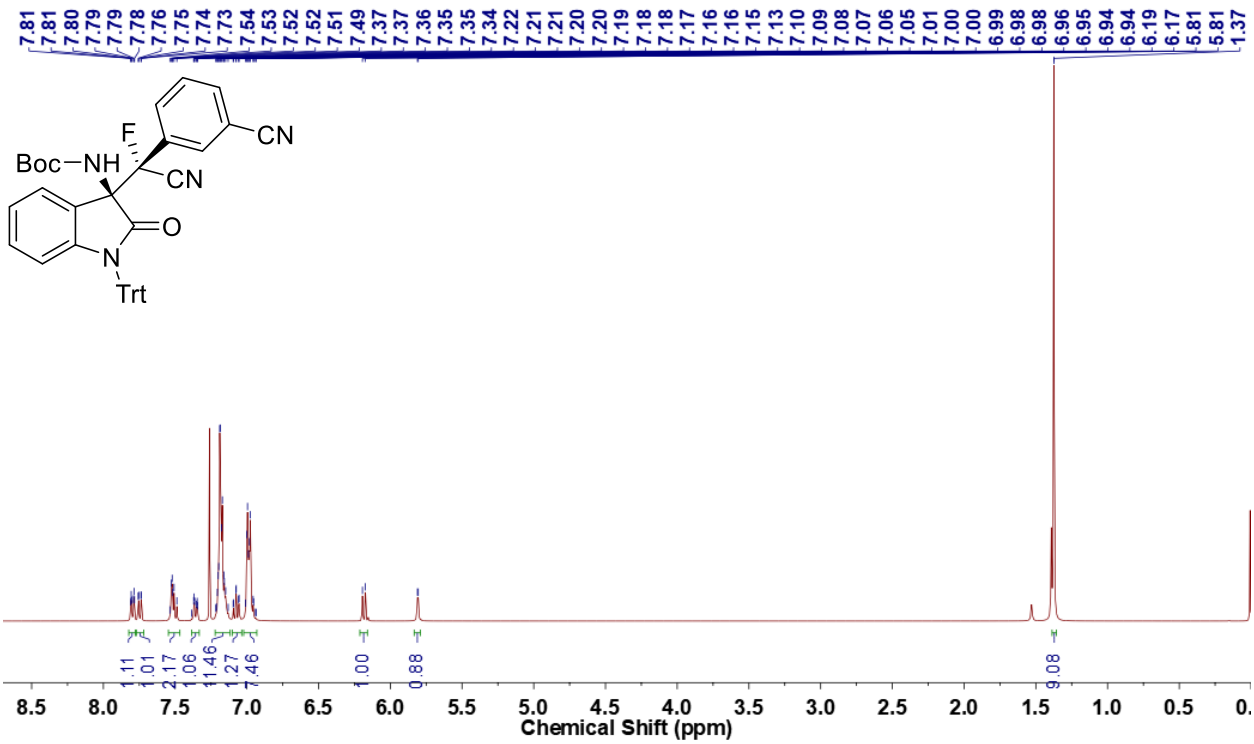
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-nitrophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3gb**)

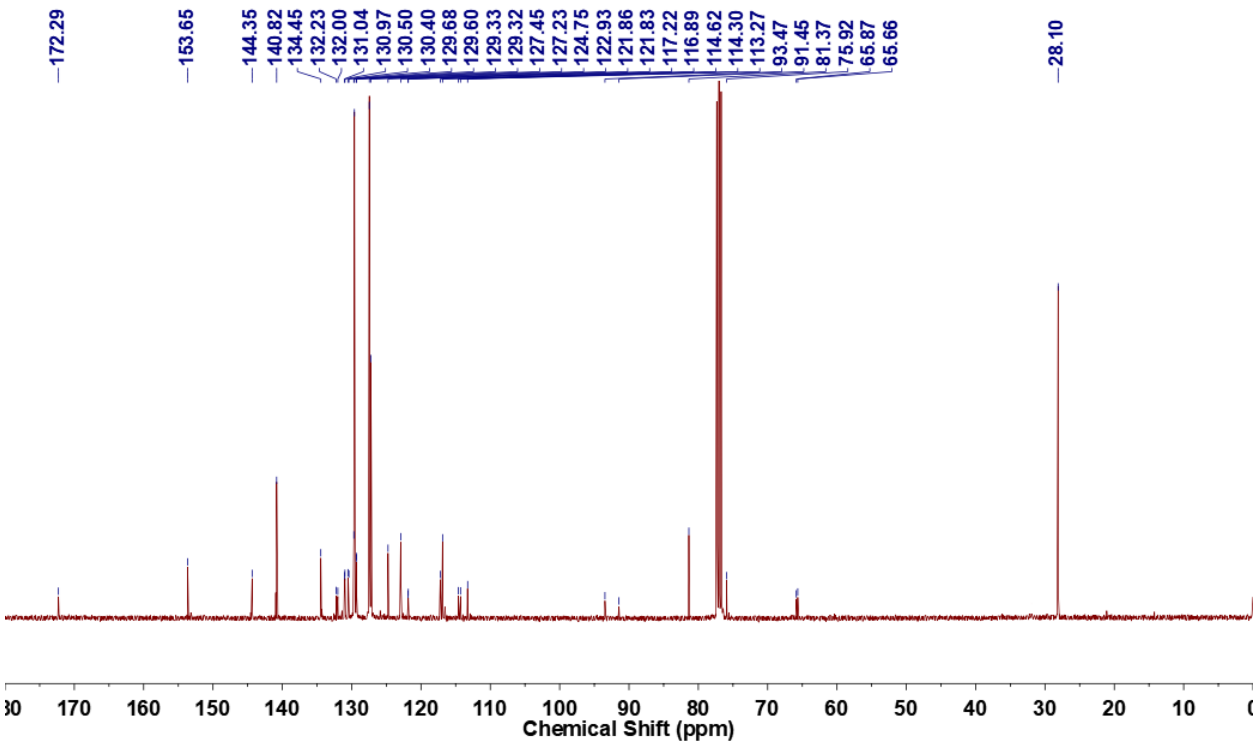


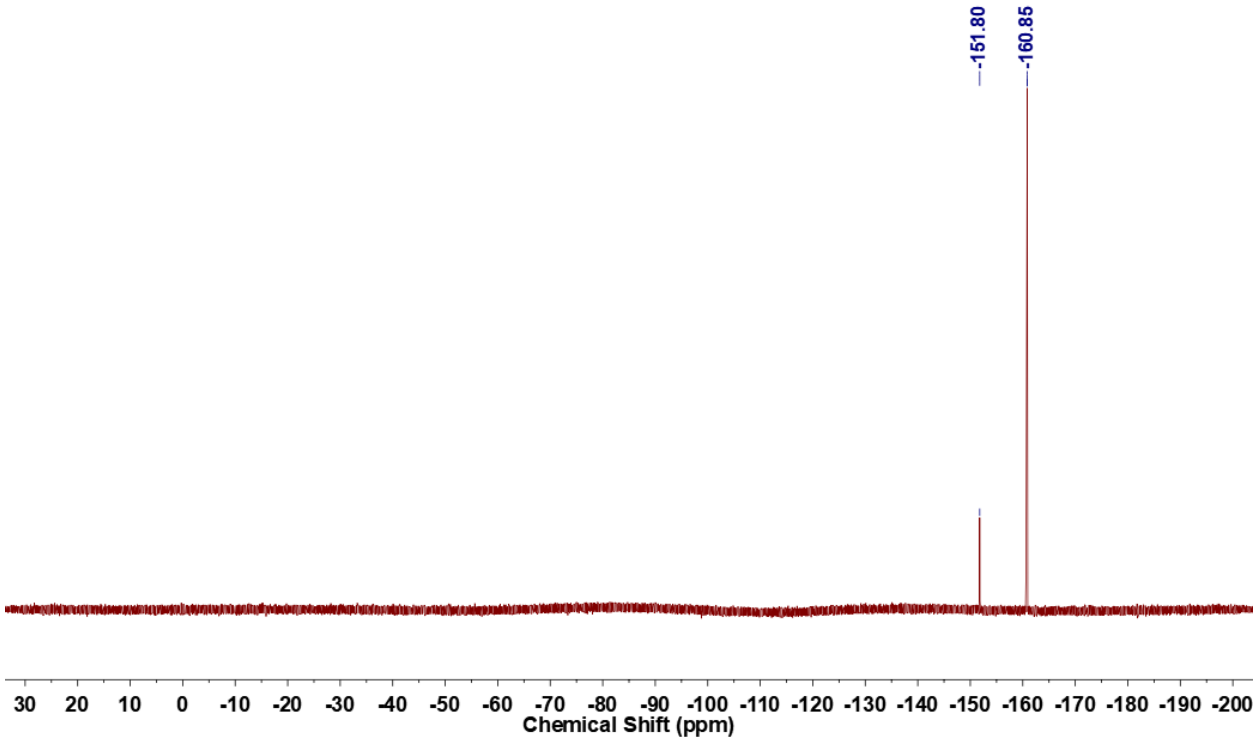




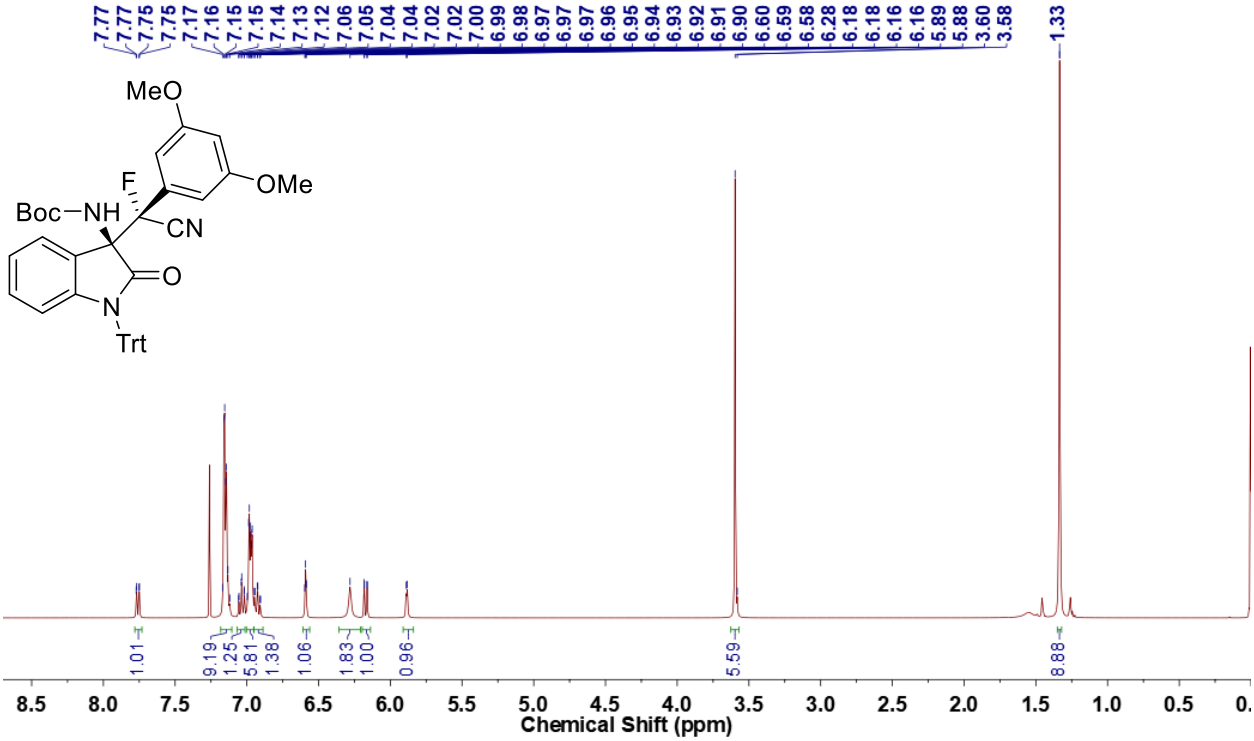
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-cyanophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3hb**)

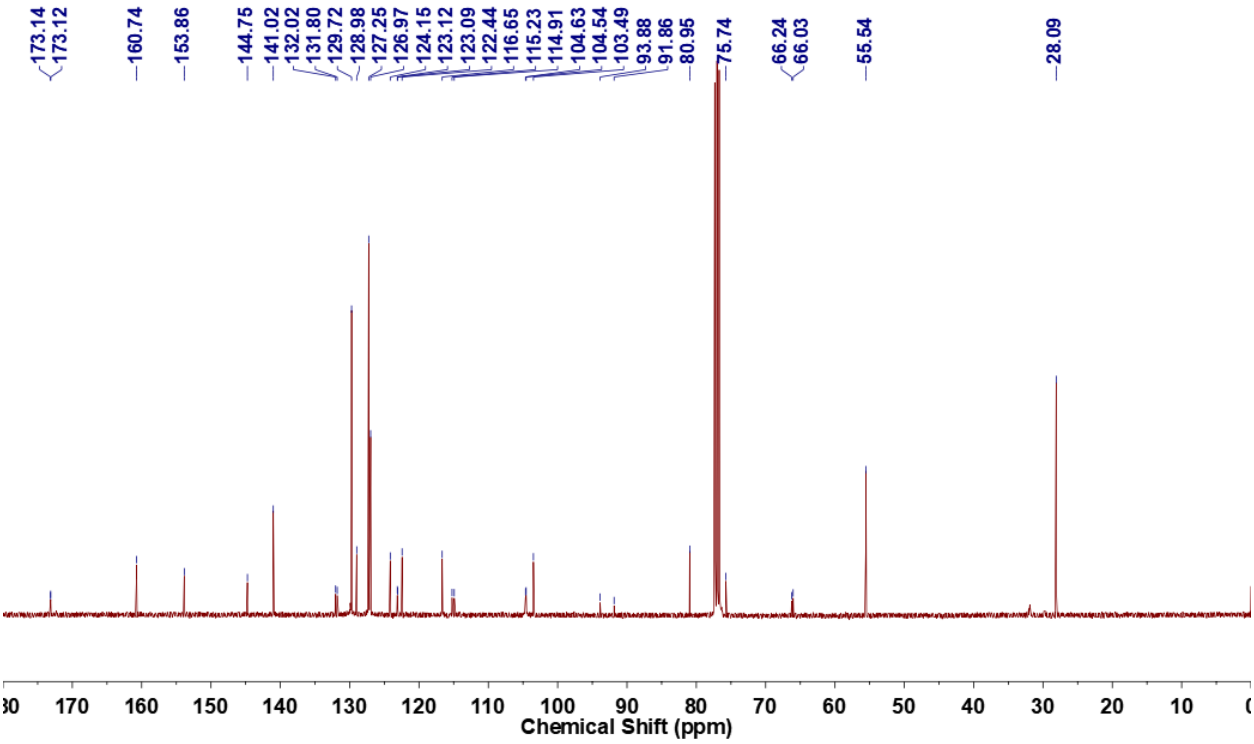


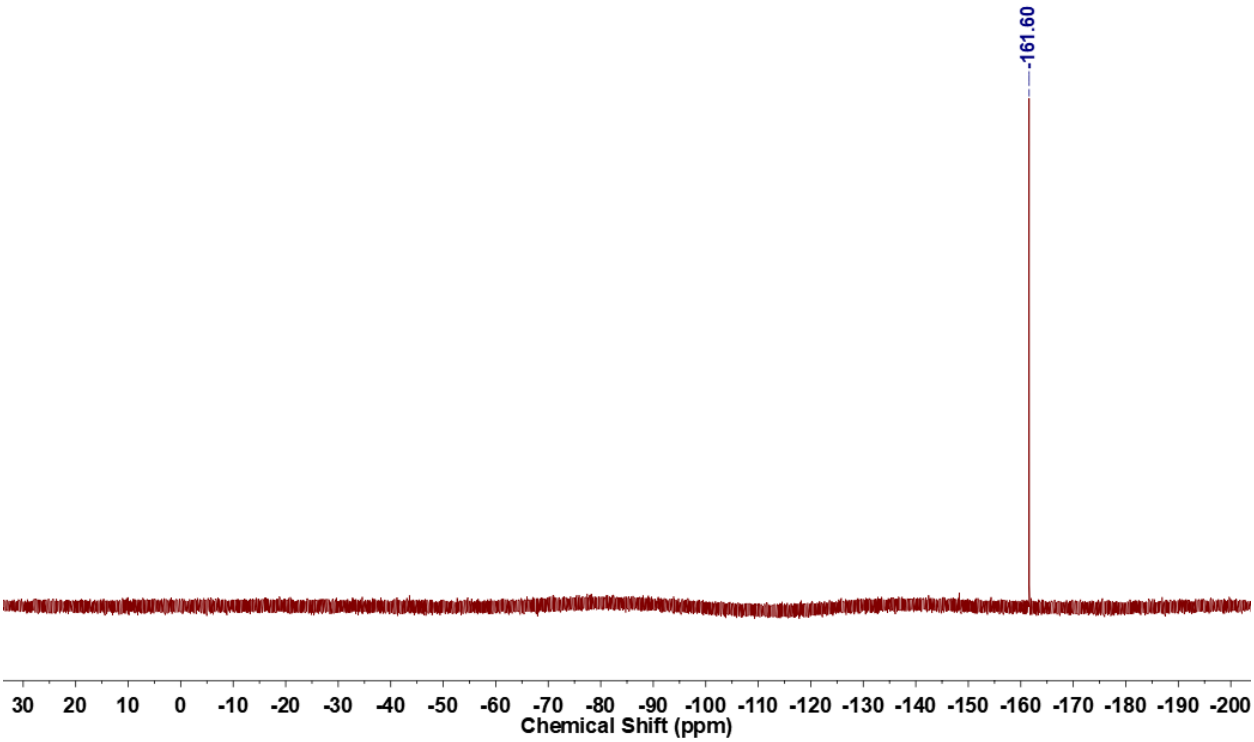

172.29
153.65
144.35
140.82
134.45
132.23
132.00
131.04
130.97
130.50
130.40
129.68
129.60
129.33
129.32
127.45
127.23
124.75
122.93
121.86
121.83
117.22
116.89
114.62
114.30
113.27
93.47
91.45
81.37
75.92
65.87
65.66
28.10
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-151.80
-160.85
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)

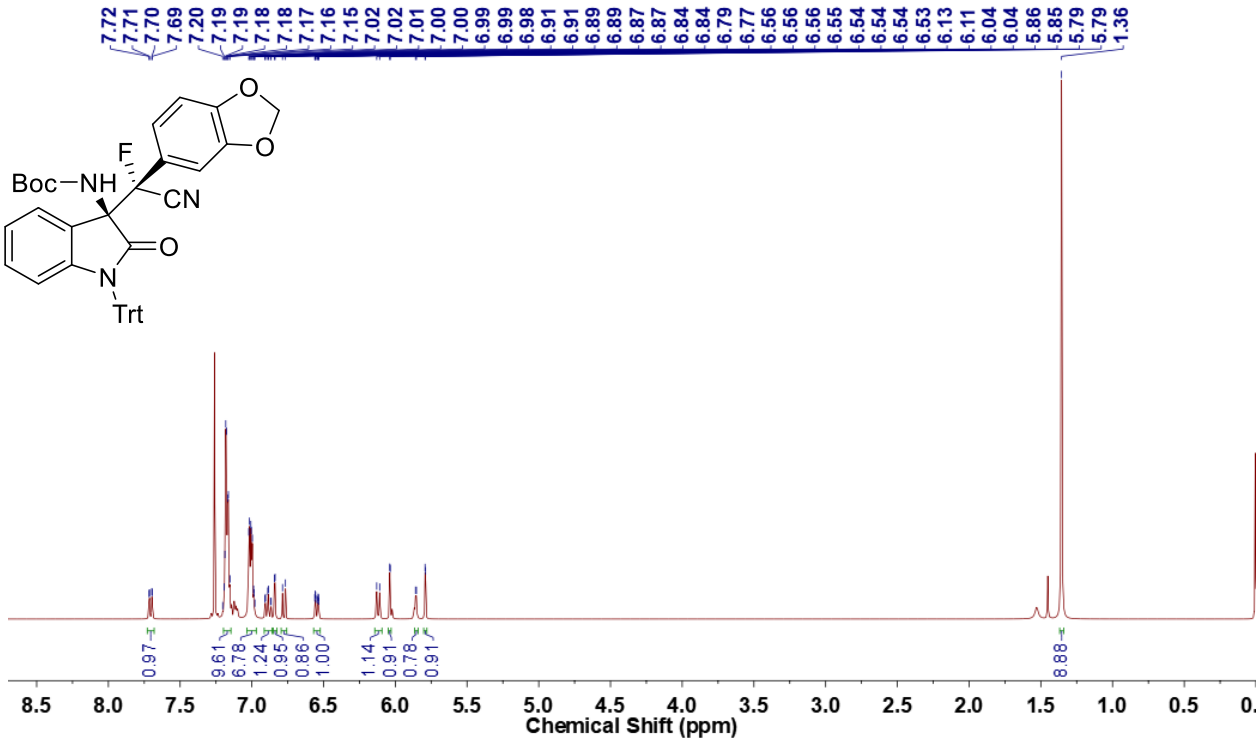
tert-Butyl ((*R*)-3-((*S*)-cyano(3,5-dimethoxyphenyl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ib**)

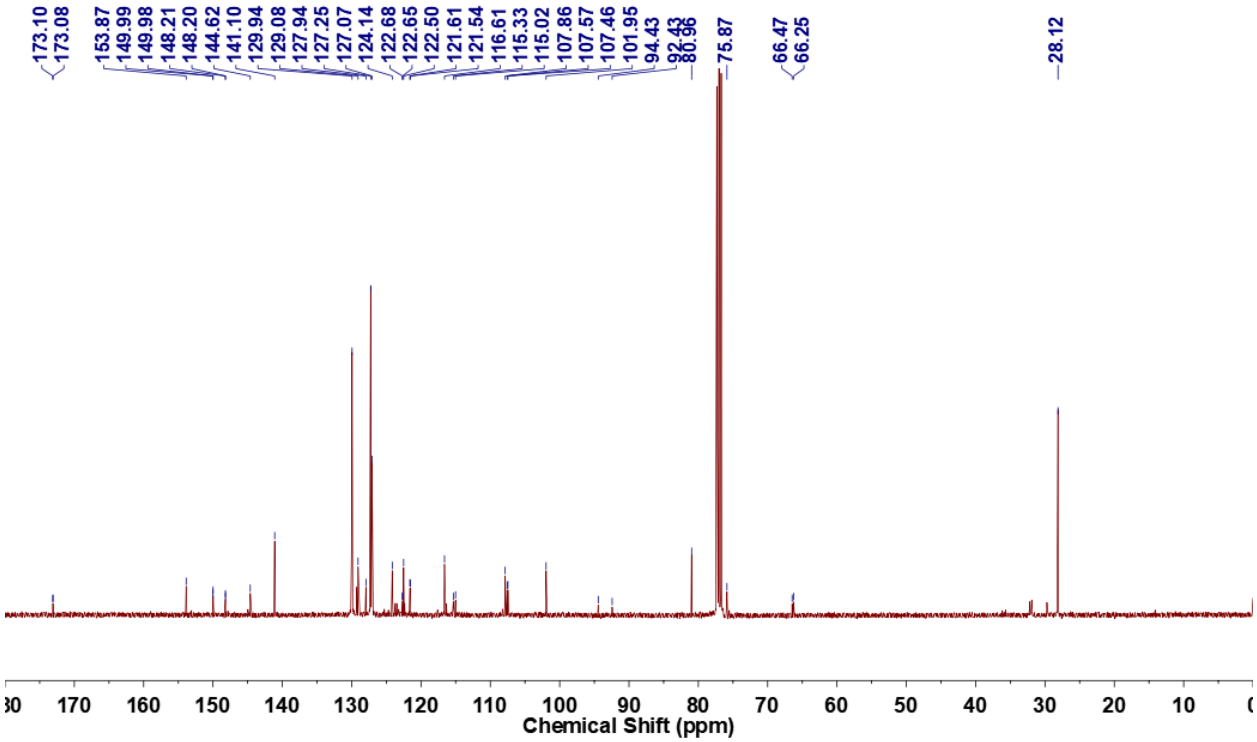


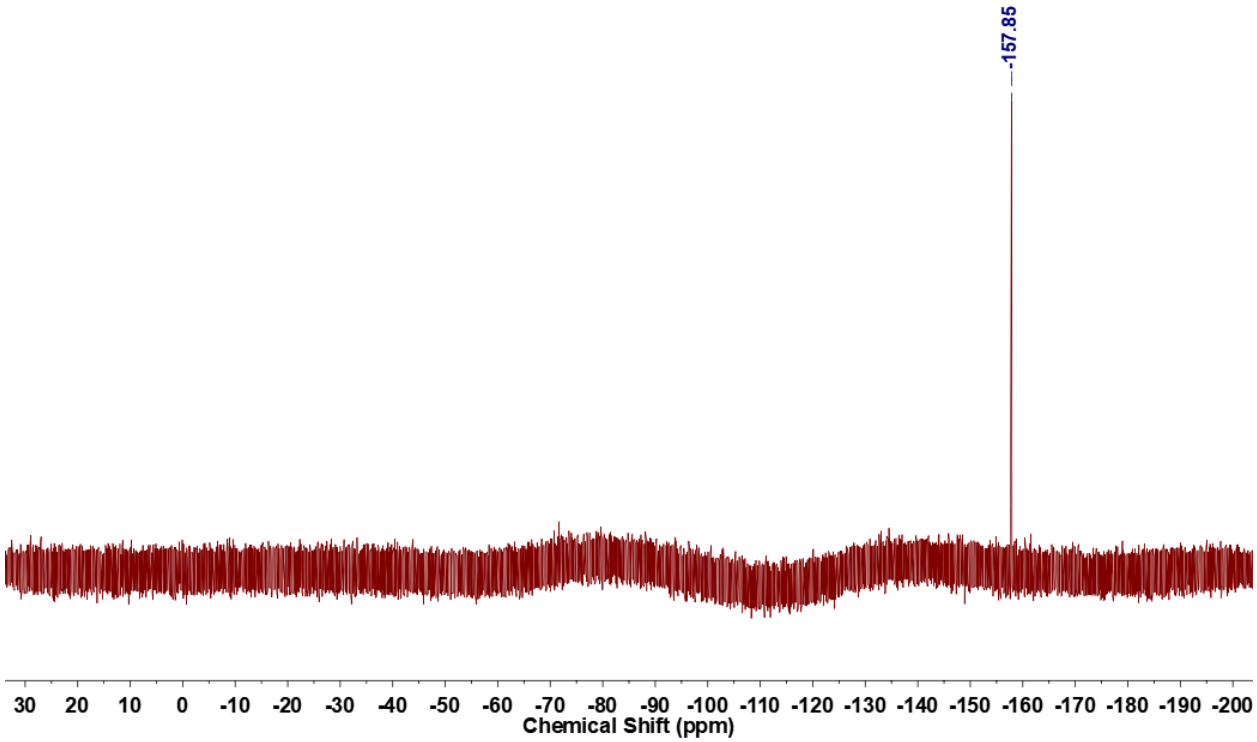




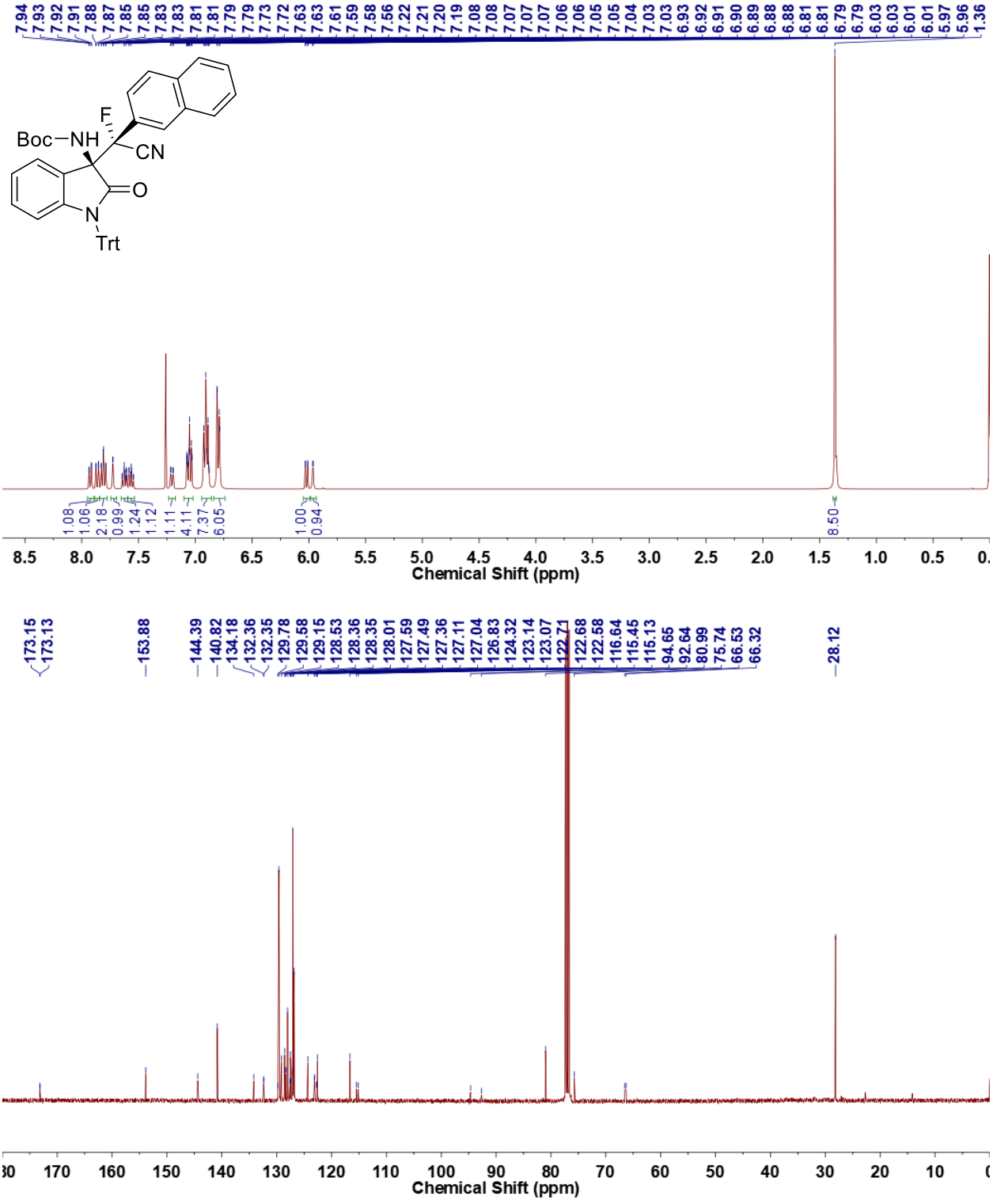
tert-Butyl ((*R*)-3-((*S*)-benzo[d][1,3]dioxol-5-yl(cyano)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3jb**)

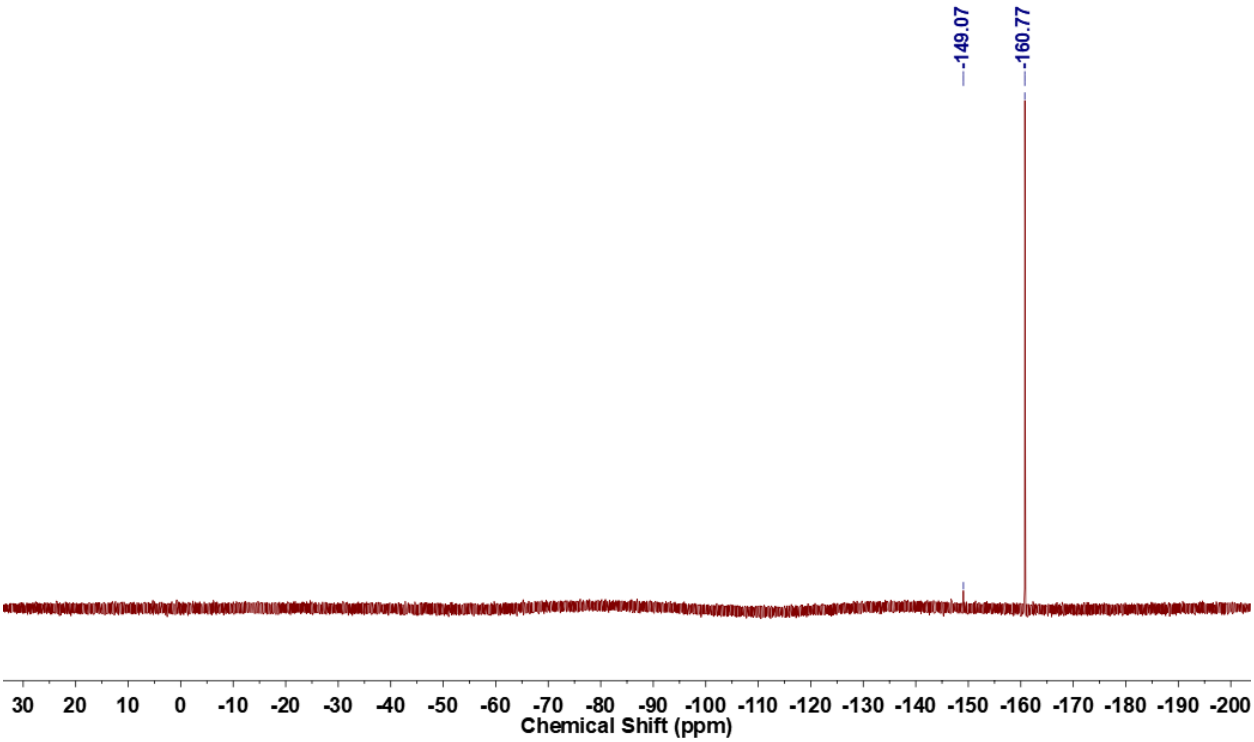



173.10
173.08
153.87
149.99
149.98
148.21
148.20
144.62
141.10
129.94
129.08
127.94
127.25
127.07
124.14
122.68
122.65
122.50
121.61
121.54
116.61
115.33
115.02
107.86
107.57
107.46
101.95
94.43
92.43
80.96
75.87
66.47
66.25
28.12
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)

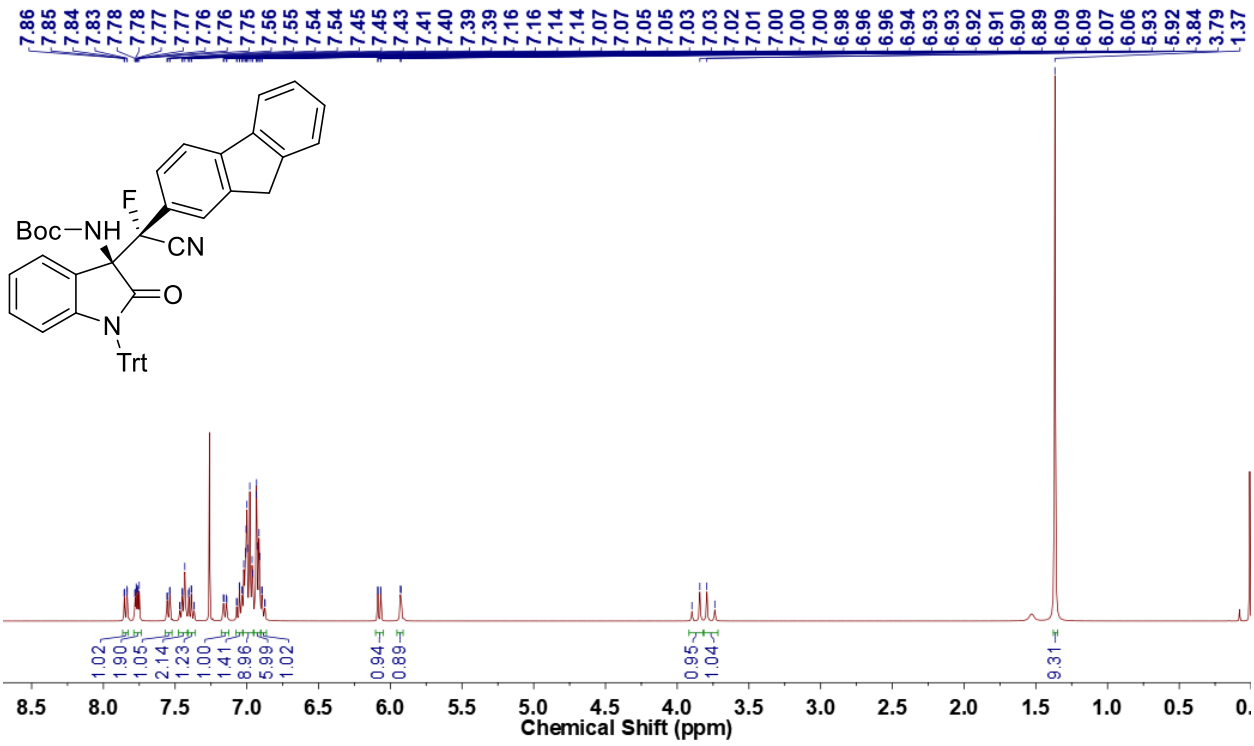

-157.85
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

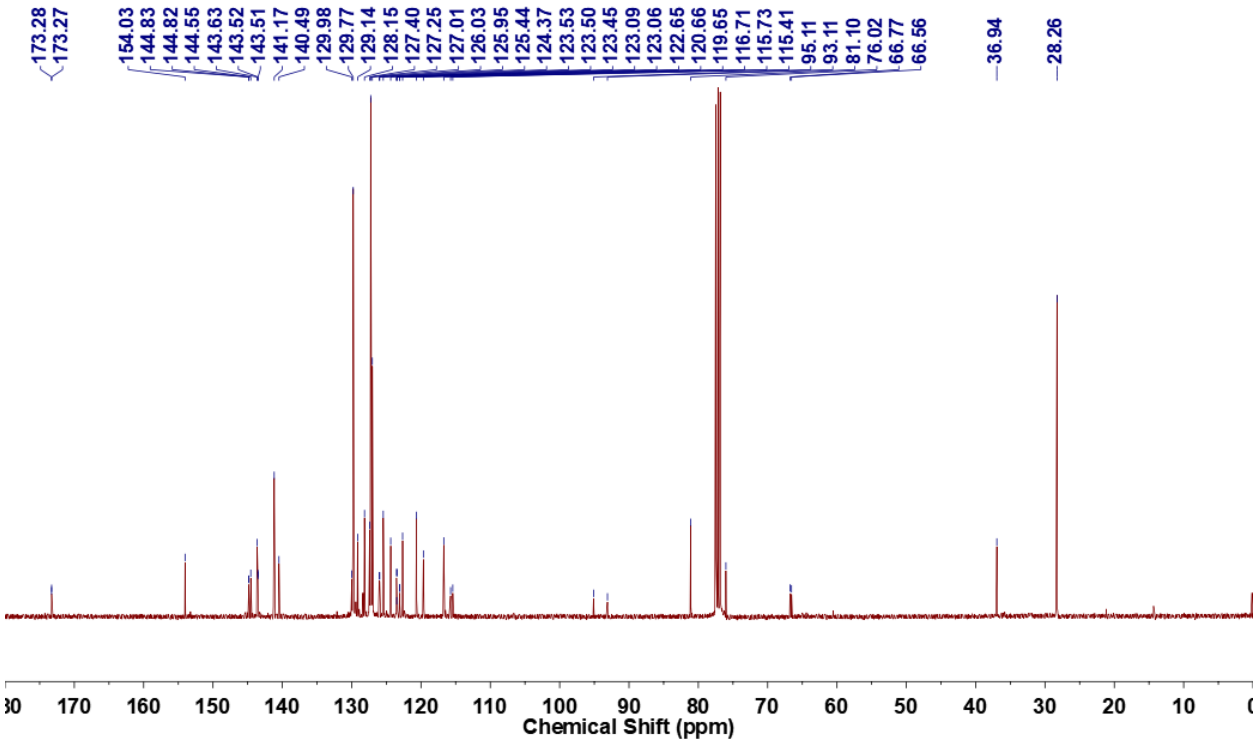
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-naphthyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3kb**)

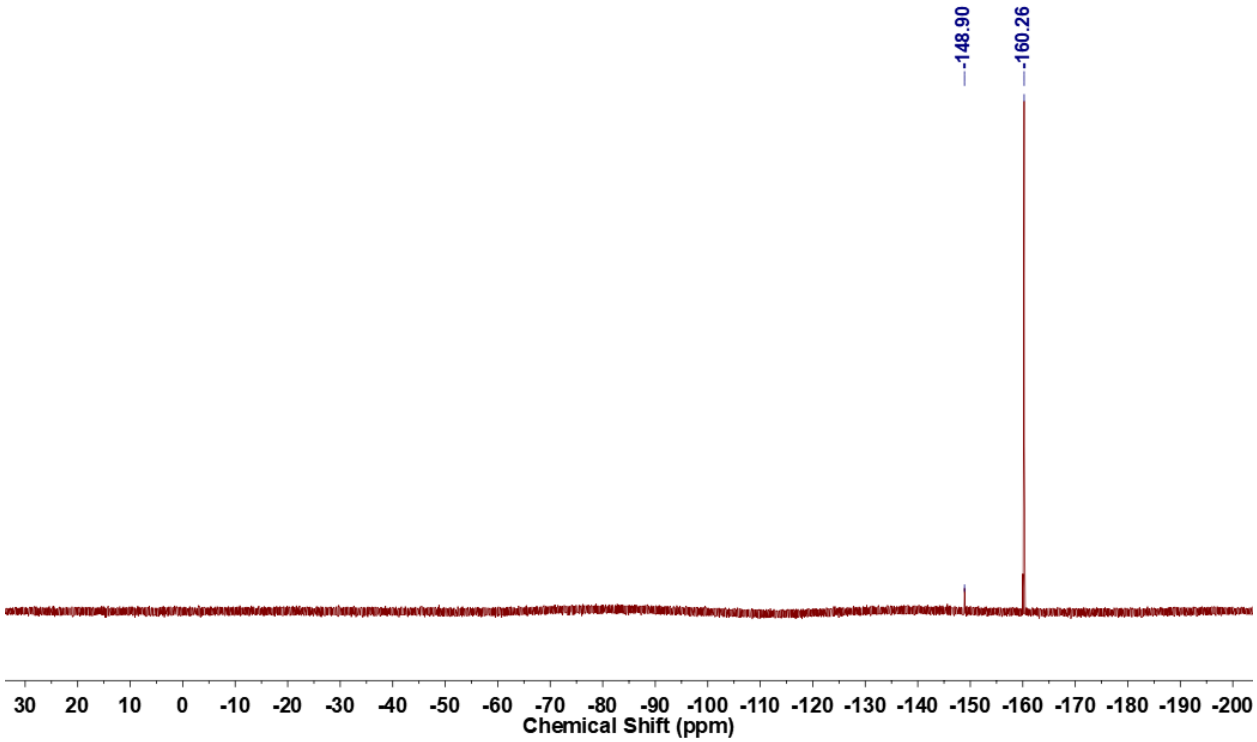




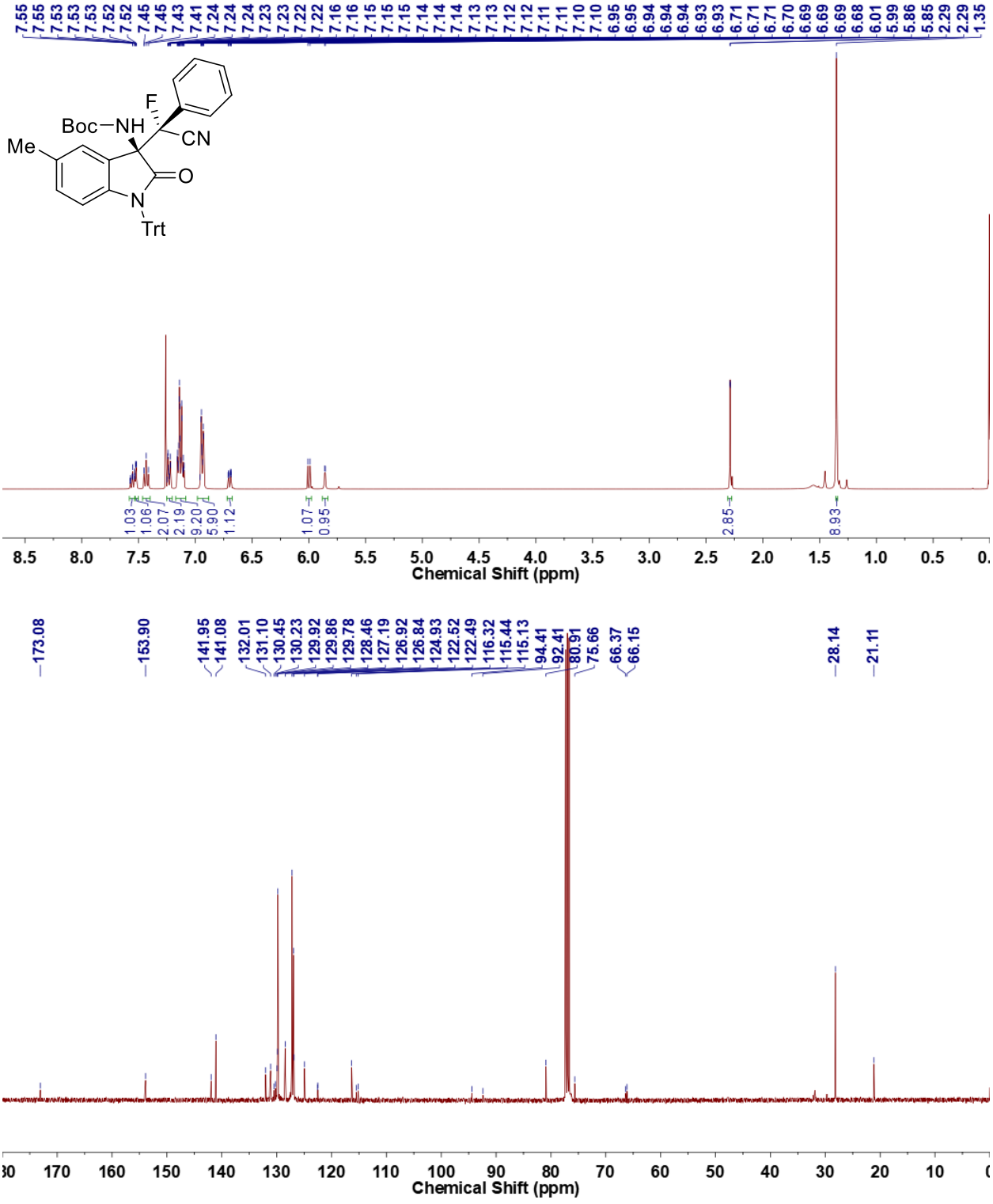
tert-Butyl ((*R*)-3-((*S*)-cyano(9H-fluoren-2-yl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3lb**)

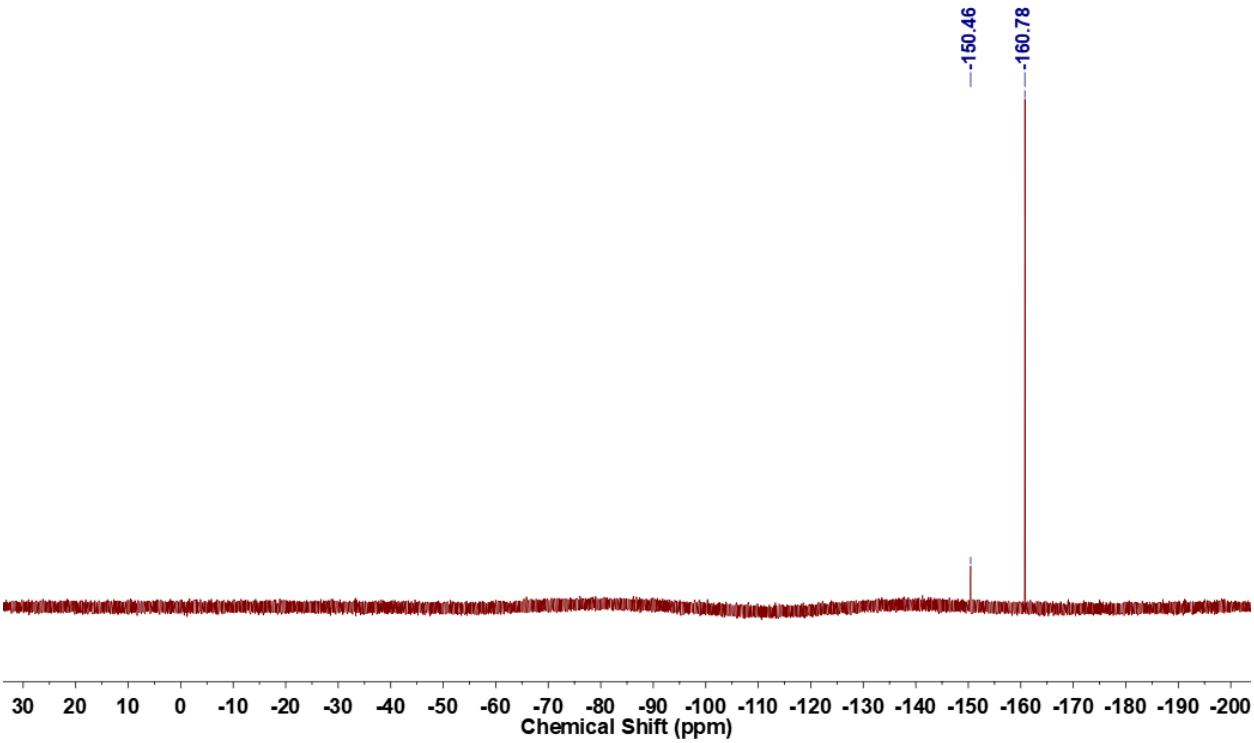



173.28
173.27
154.03
144.83
144.82
144.55
143.63
143.52
143.51
141.17
140.49
129.98
129.77
129.14
128.15
127.40
127.25
127.01
126.03
125.95
125.44
124.37
123.53
123.50
123.45
123.09
123.06
122.65
120.66
119.65
116.71
115.73
115.41
95.11
93.11
81.10
76.02
66.77
66.56
36.94
28.26
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)

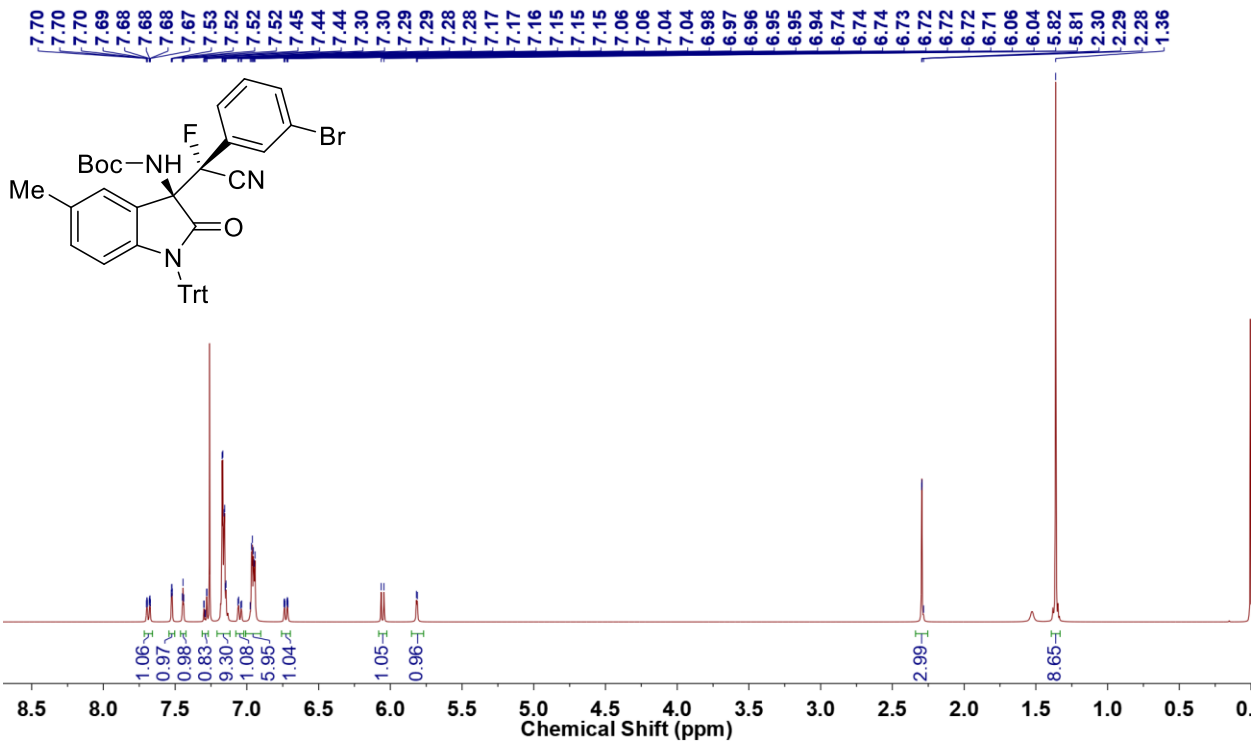

-148.90
-160.26
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

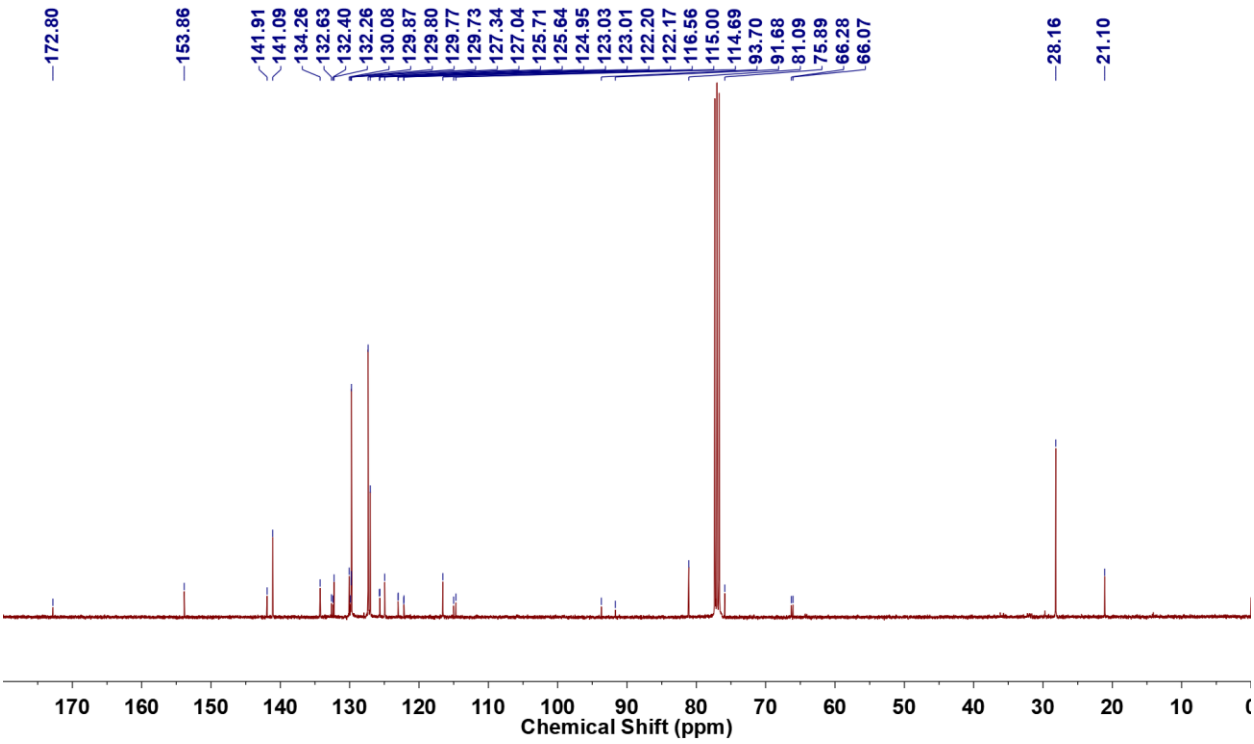
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ad**)

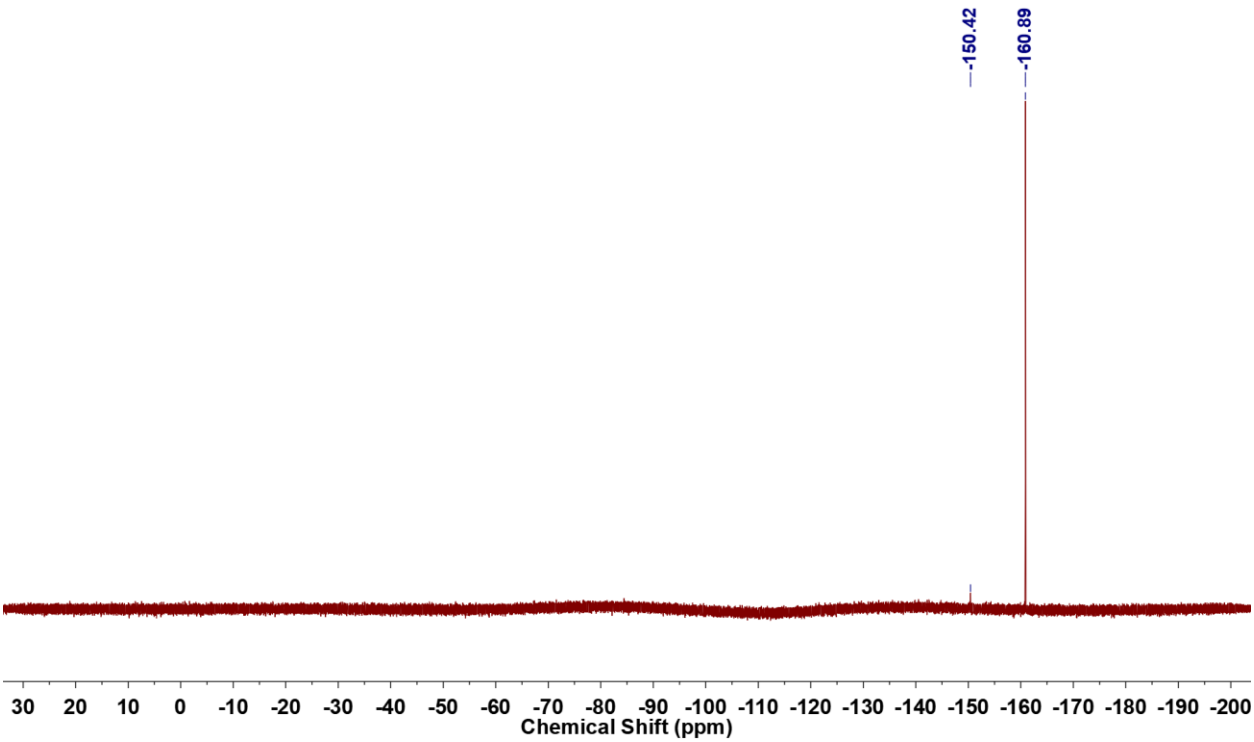




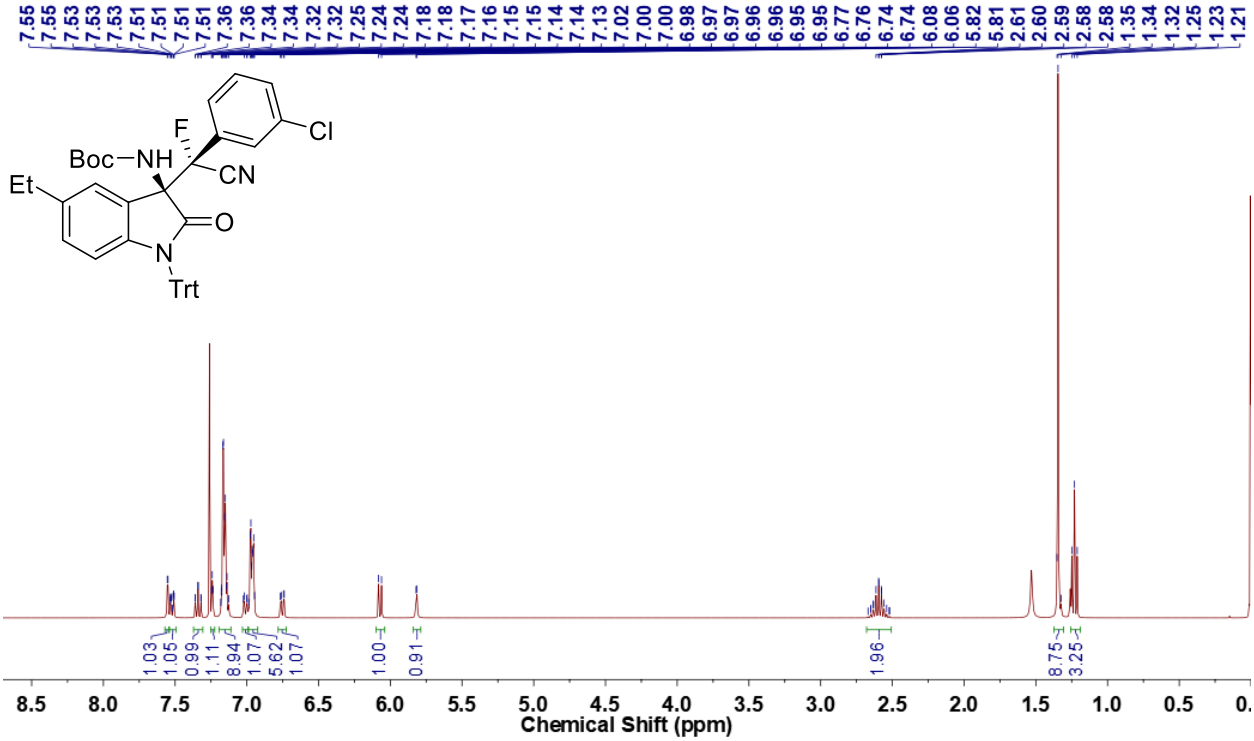
tert-Butyl ((*R*)-3-((*S*)-(3-bromophenyl)(cyano)fluoromethyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3cd**)

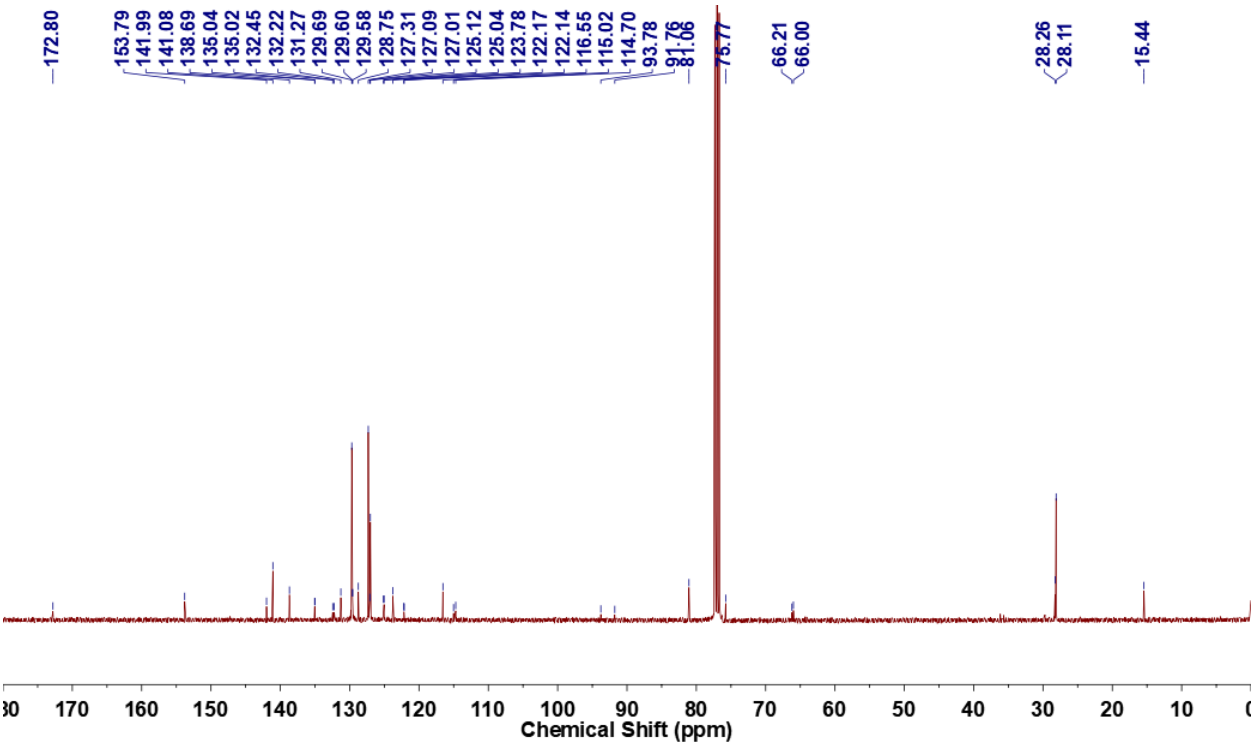


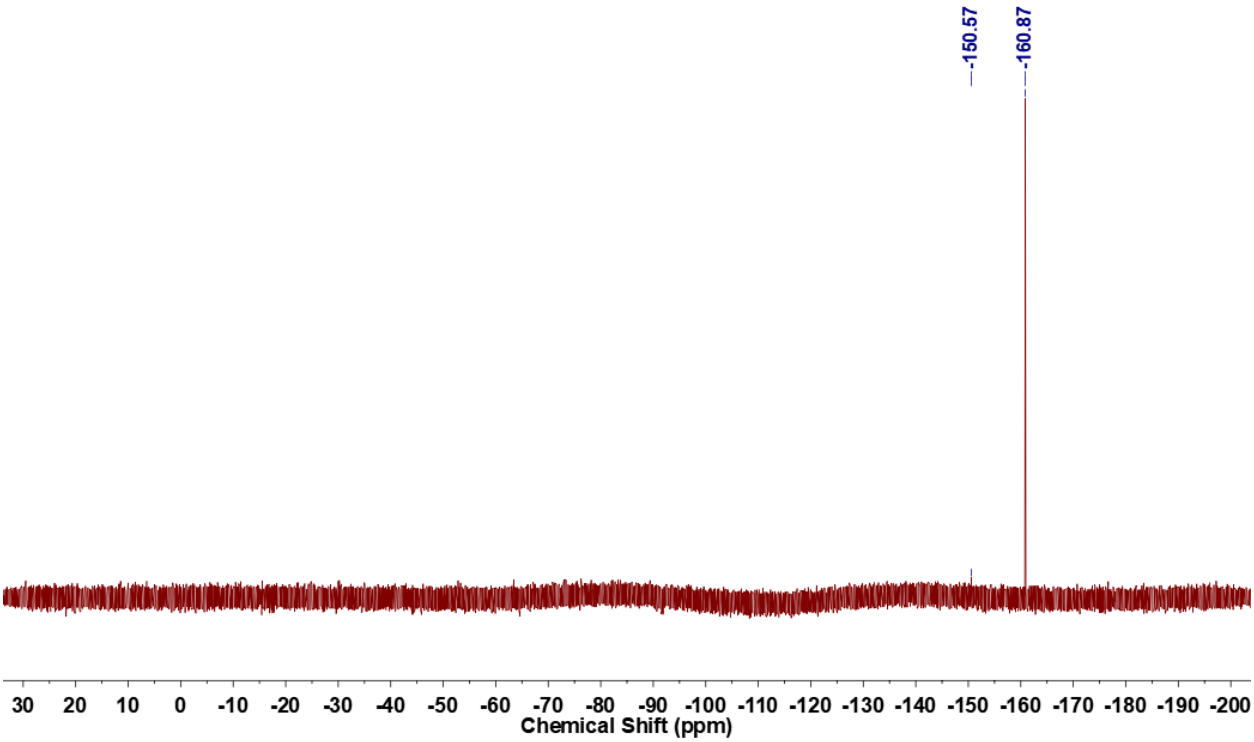

172.80
153.86
141.91
141.09
134.26
132.63
132.40
132.26
130.08
129.87
129.80
129.77
129.73
127.34
127.04
125.71
125.64
124.95
123.03
123.01
122.20
122.17
116.56
115.00
114.69
93.70
91.68
81.09
75.89
66.28
66.07
28.16
21.10
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-150.42
-160.89
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)

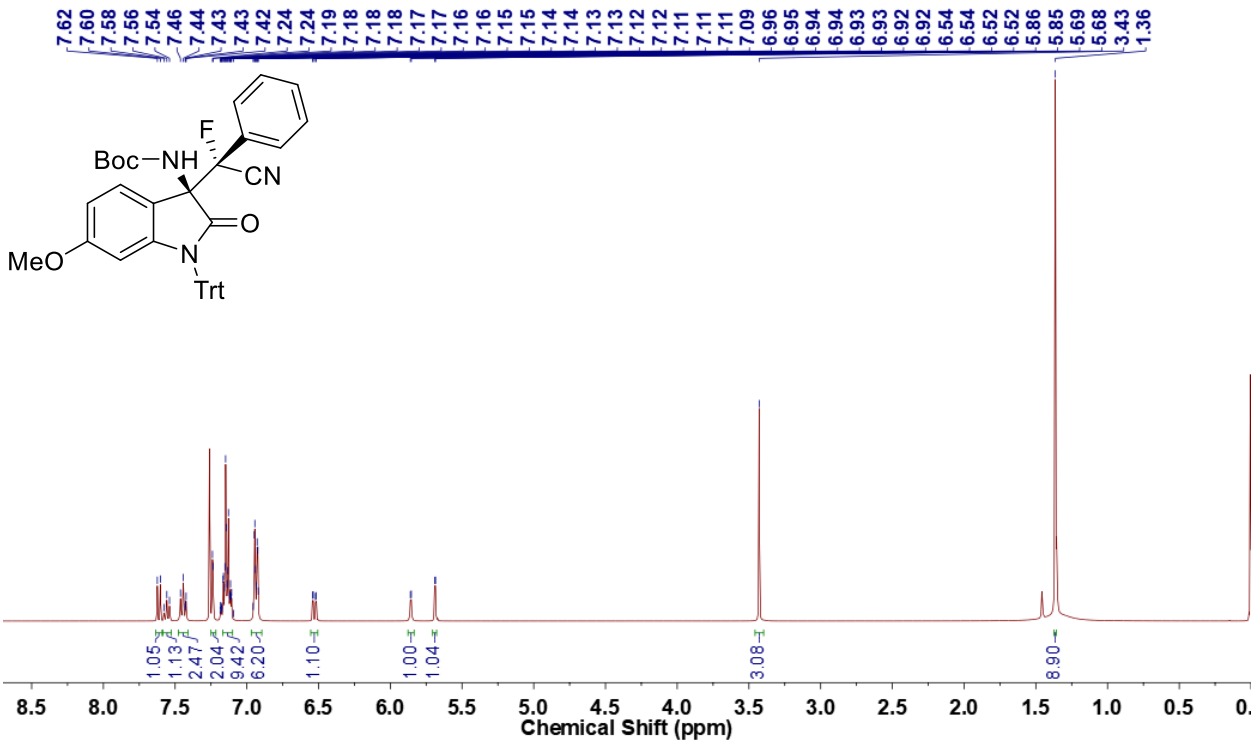
tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-ethyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3be**)

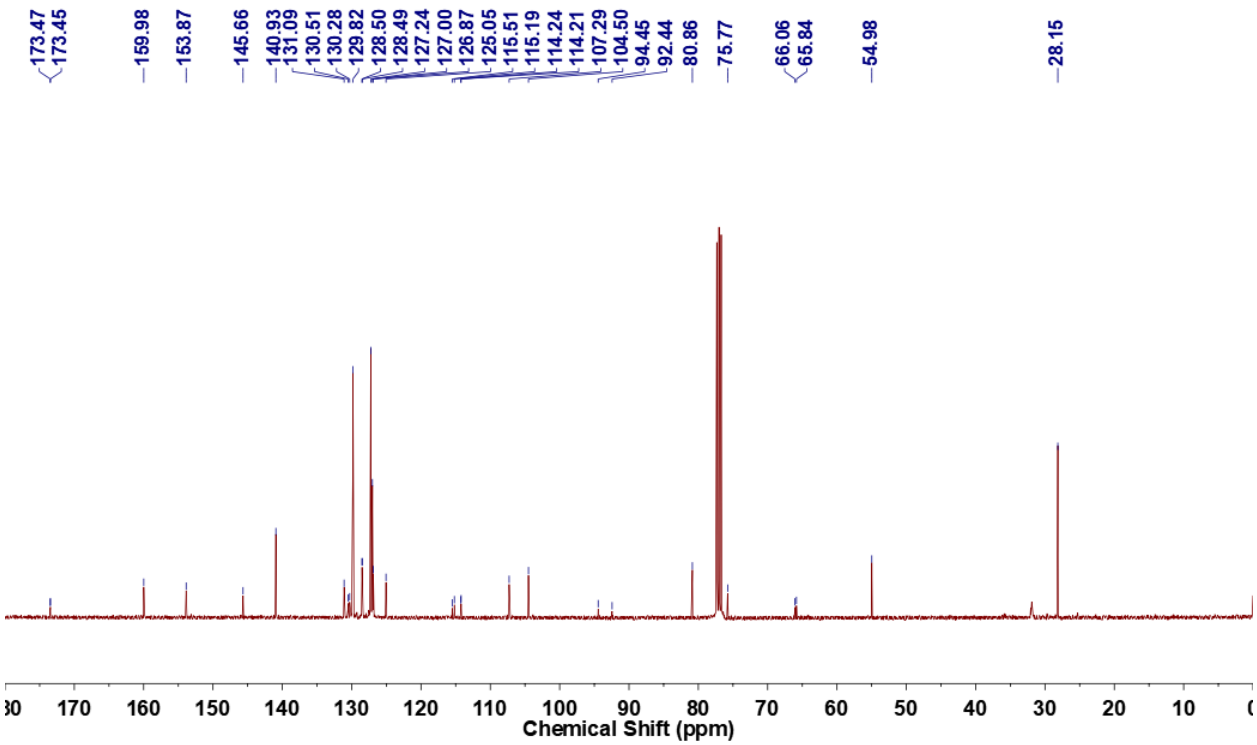


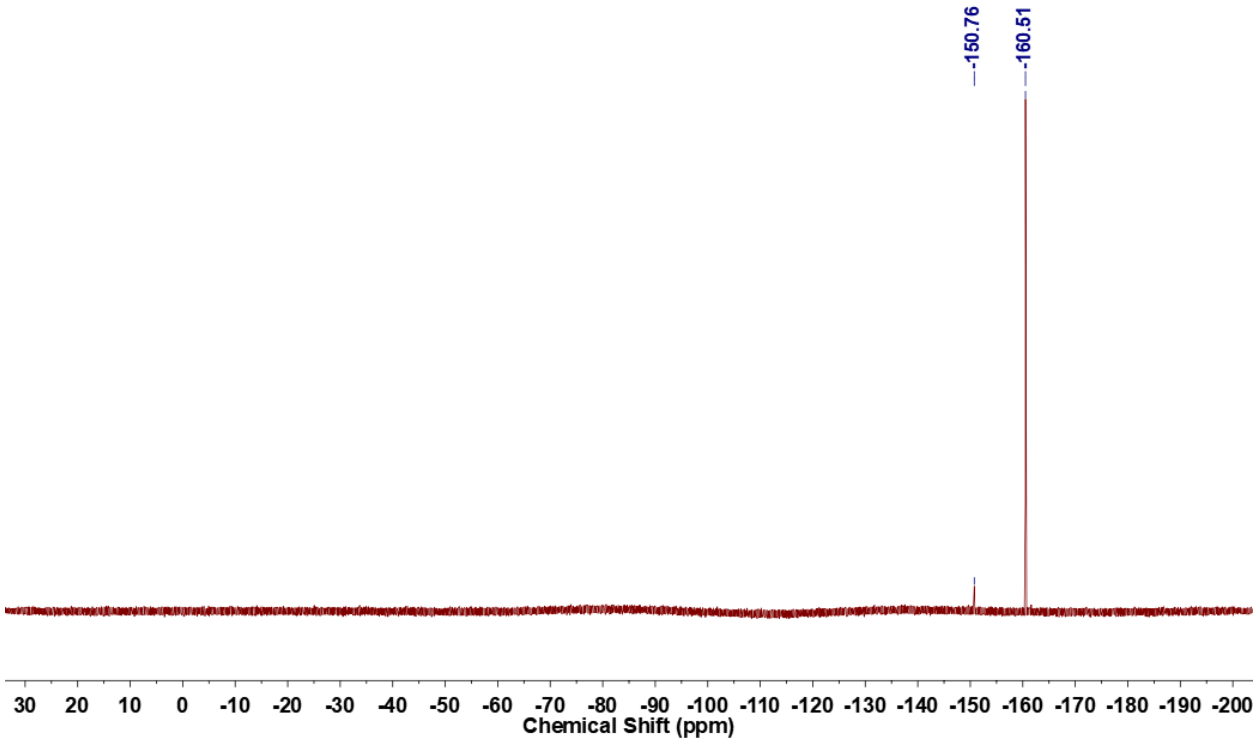




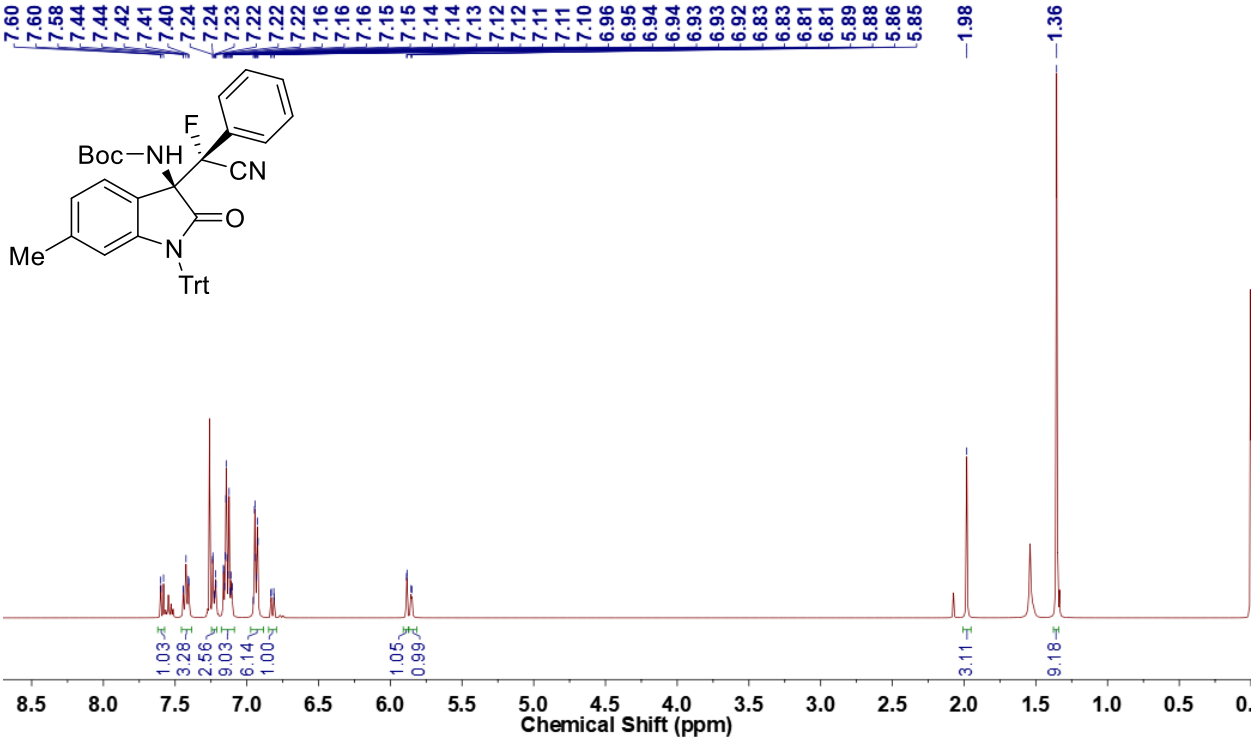
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3af**)

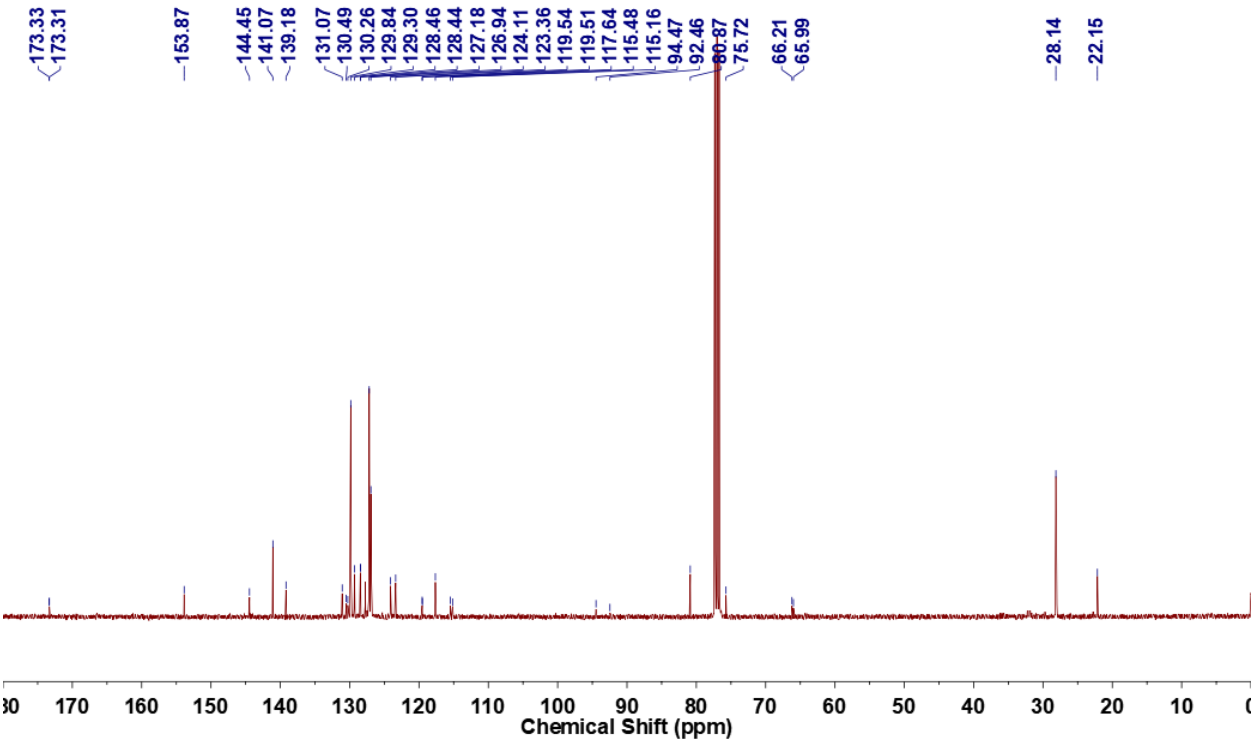


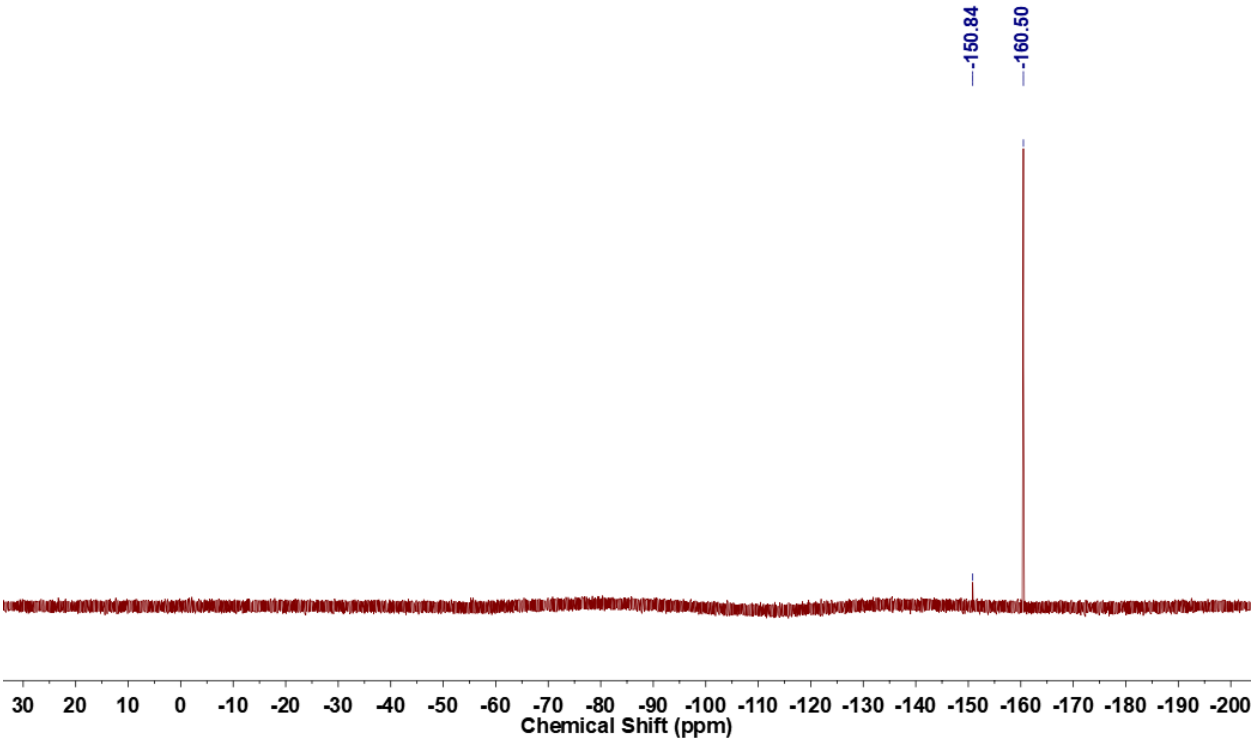

173.47
173.45
159.98
153.87
145.66
140.93
131.09
130.51
130.28
129.82
128.50
128.49
127.24
127.00
126.87
125.05
115.51
115.19
114.24
114.21
107.29
104.50
94.45
92.44
80.86
75.77
66.06
65.84
54.98
28.15
Chemical Shift (ppm)


-150.76
-160.51
Chemical Shift (ppm)

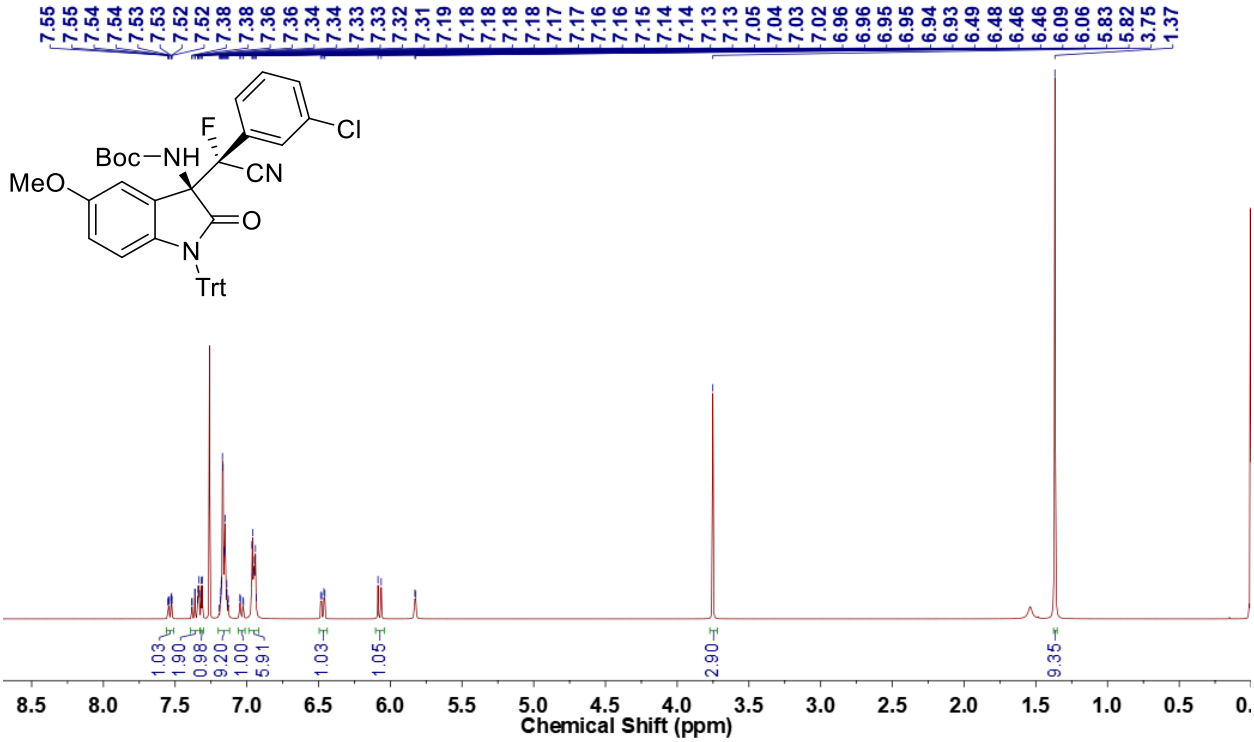
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ag**)

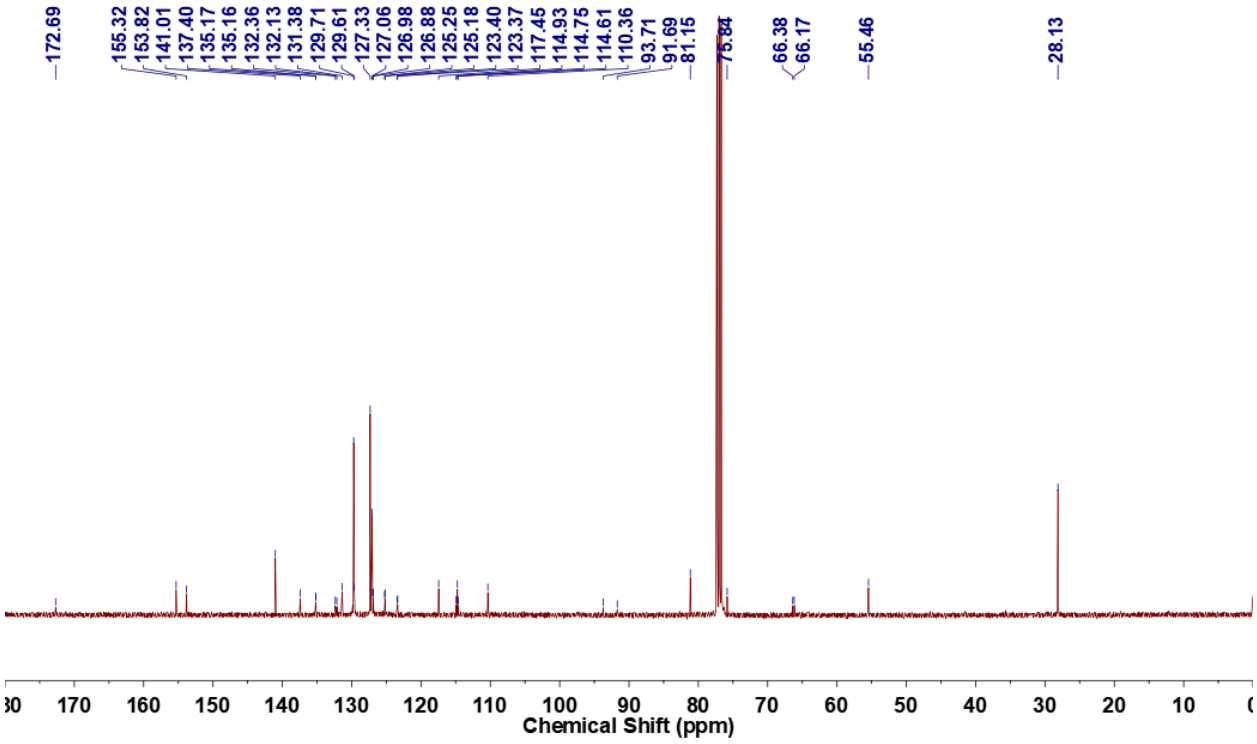


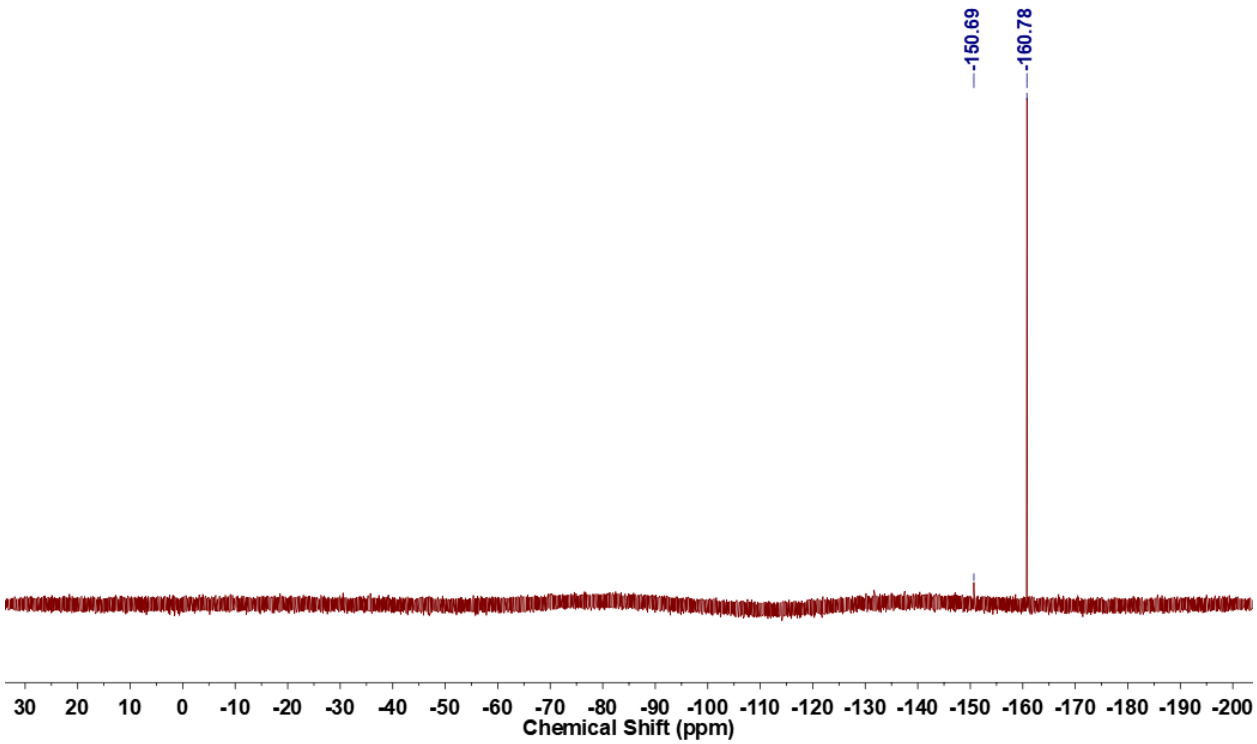




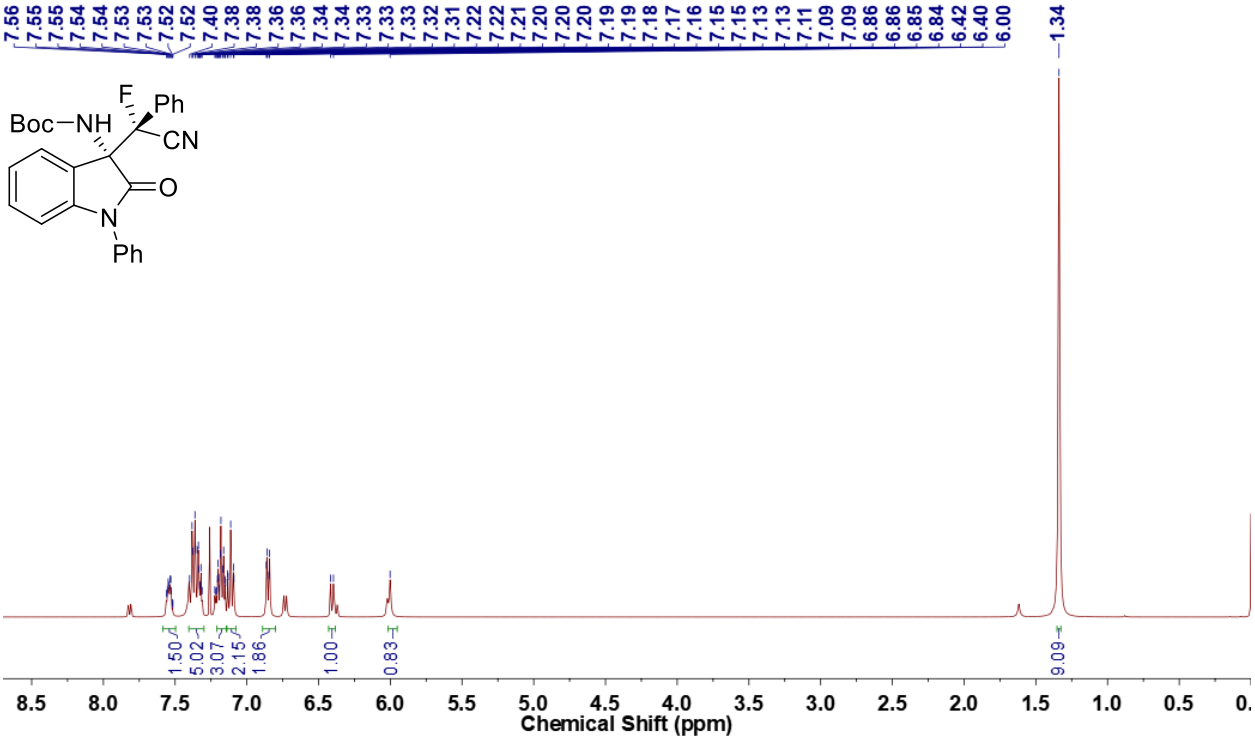
tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3bh)**

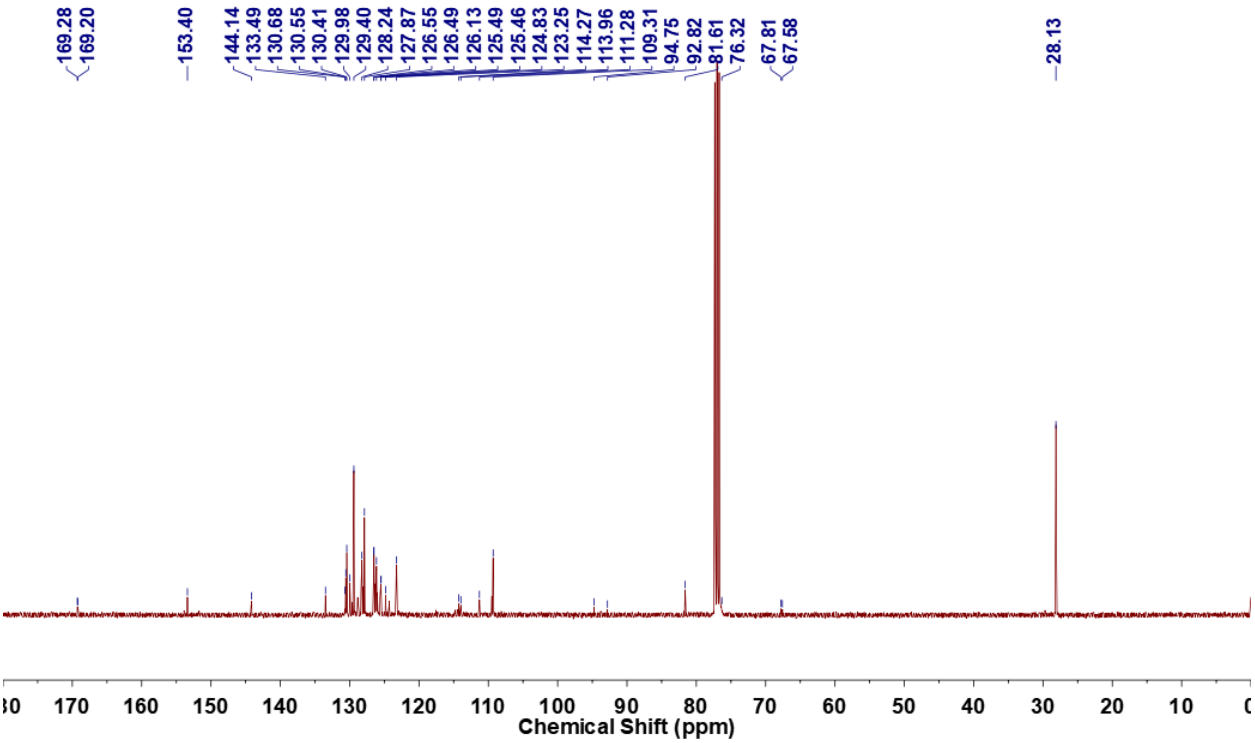


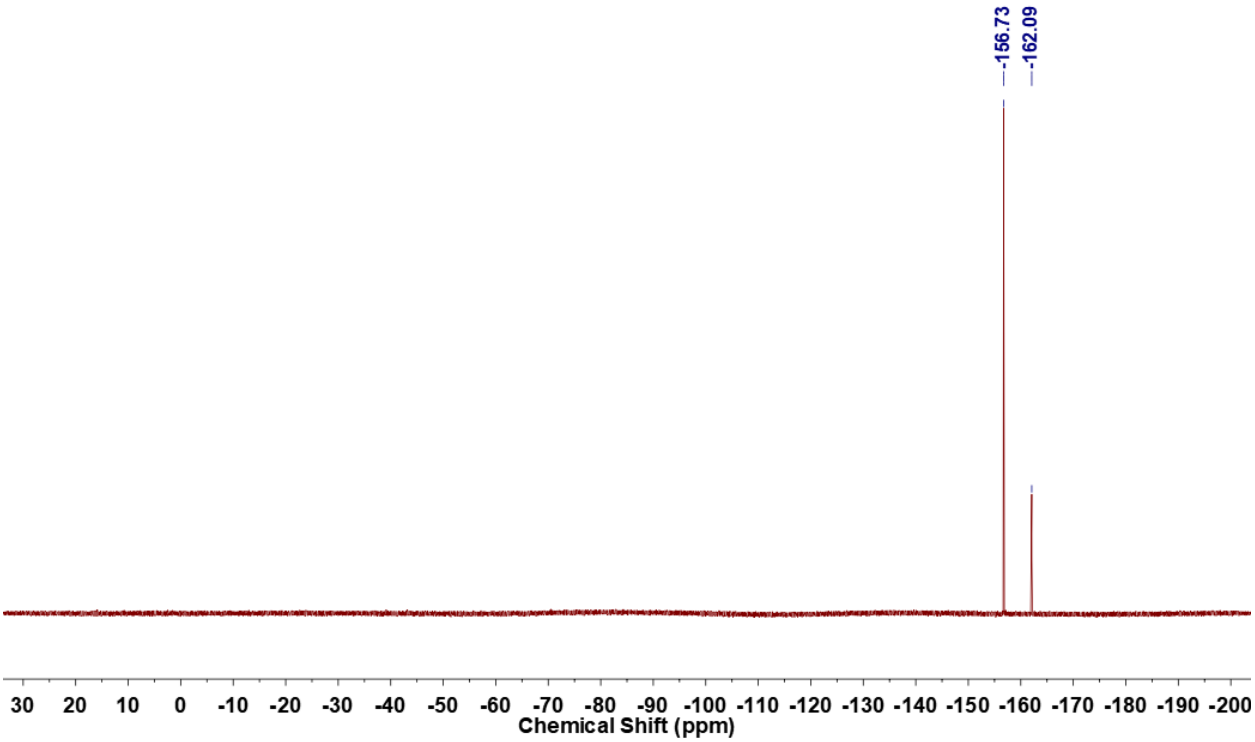

172.69
155.32
153.82
141.01
137.40
135.17
135.16
132.36
132.13
131.38
129.71
129.61
127.33
127.06
126.98
126.88
125.25
125.18
123.40
123.37
117.45
114.93
114.75
114.61
110.36
93.71
91.69
81.15
75.84
66.38
66.17
55.46
28.13
Chemical Shift (ppm)


-150.69
-160.78
Chemical Shift (ppm)

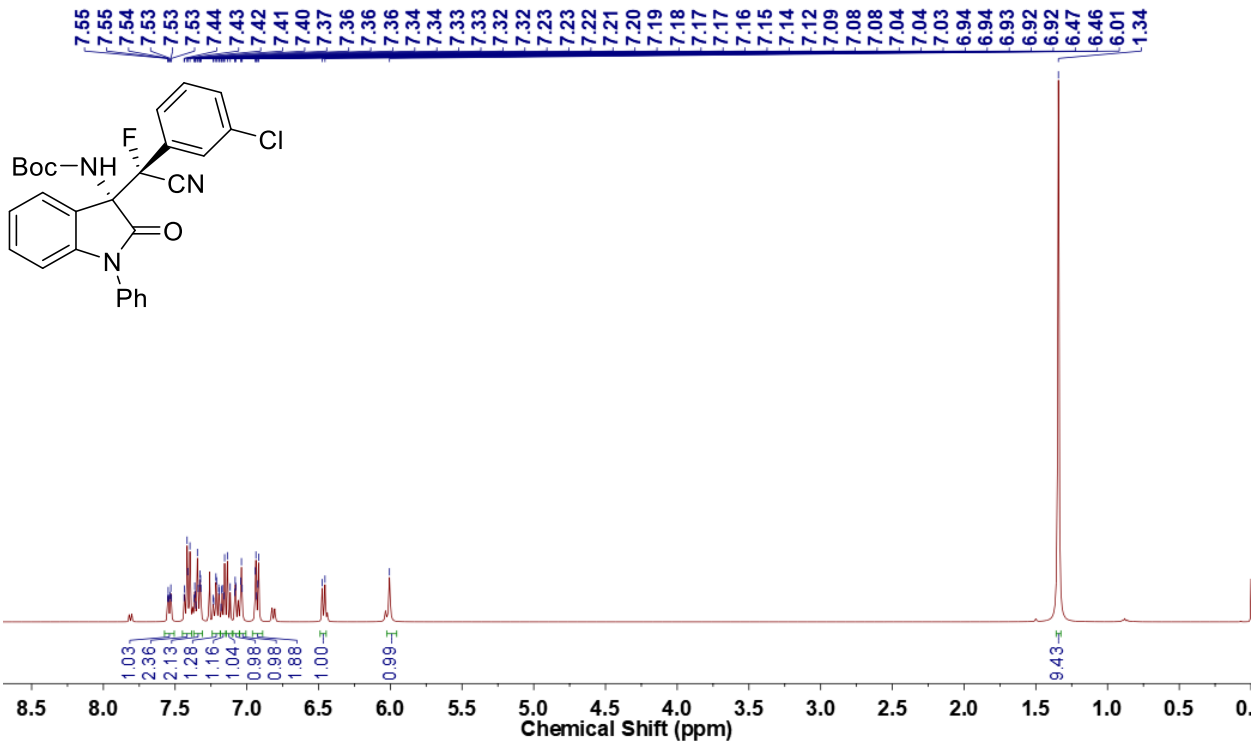
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(phenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ac**)

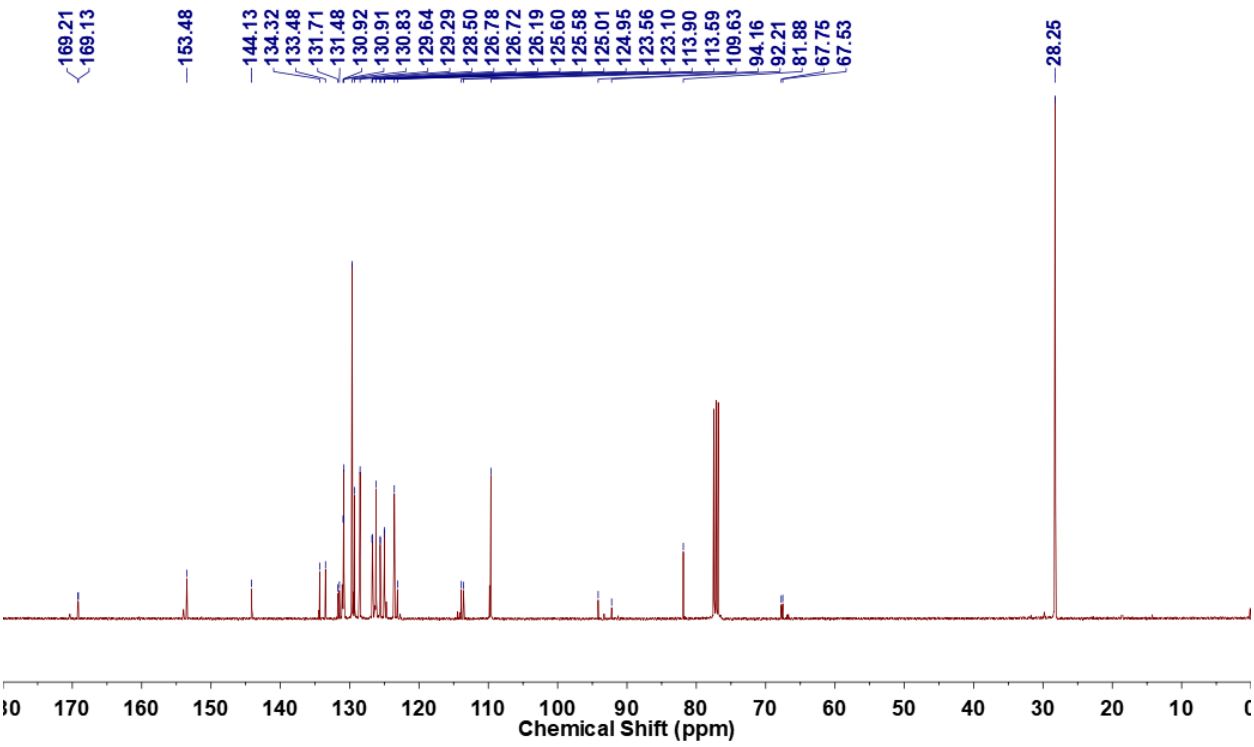


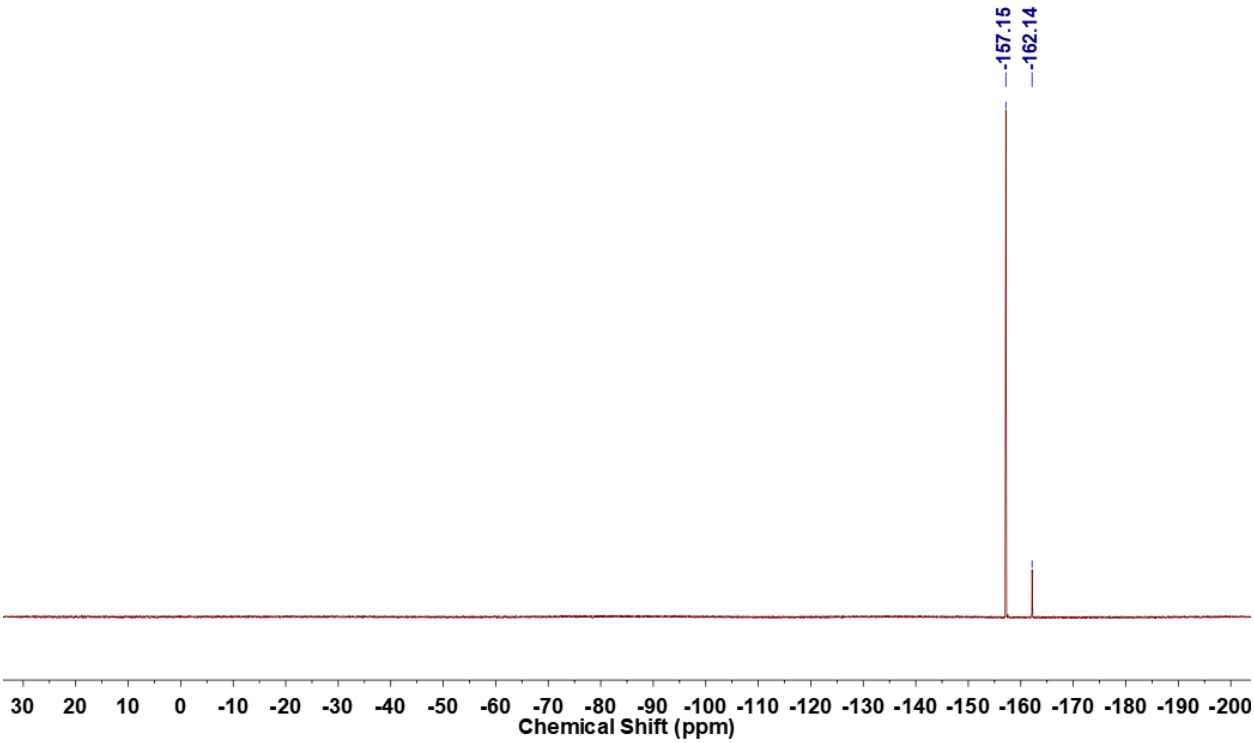




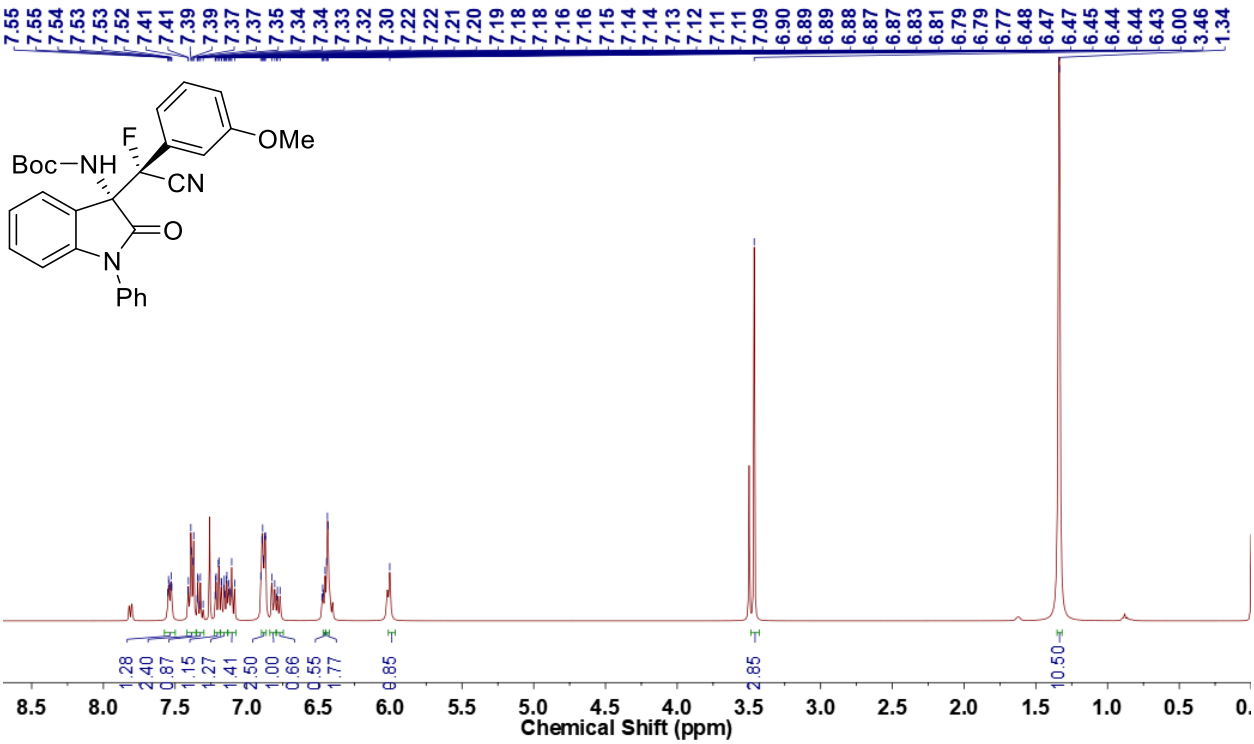
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3bc**)

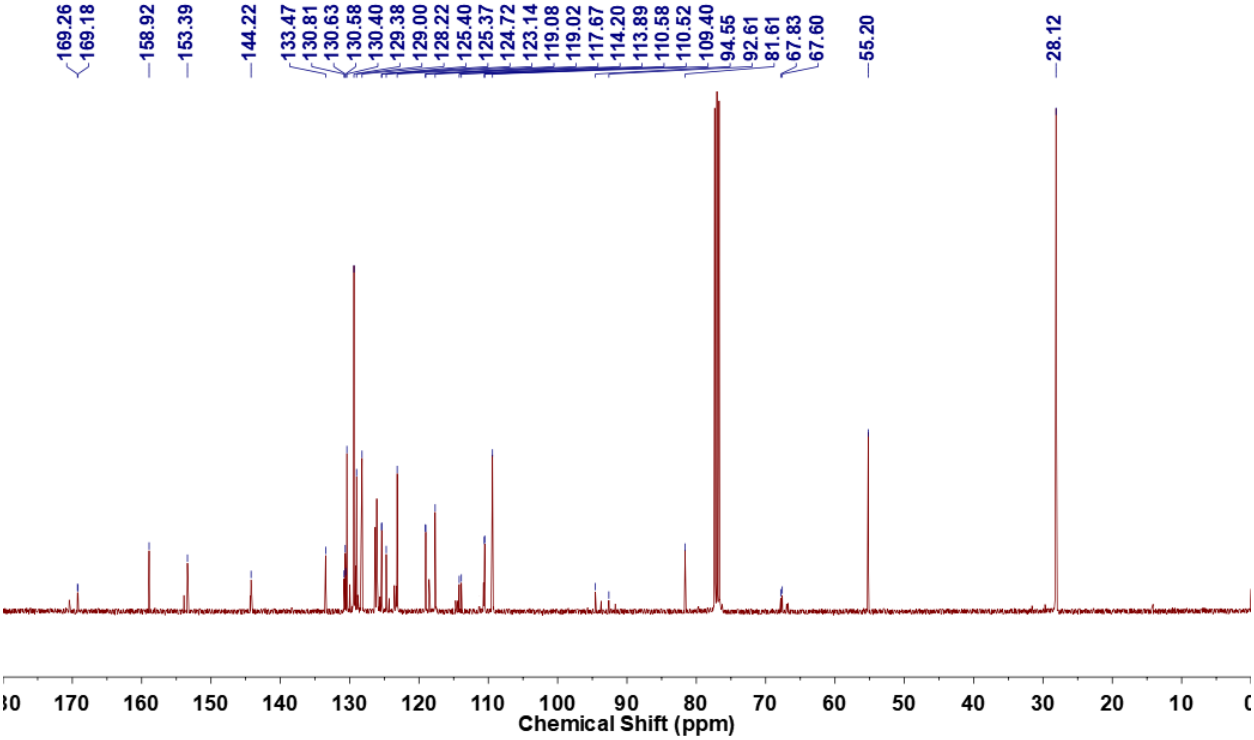


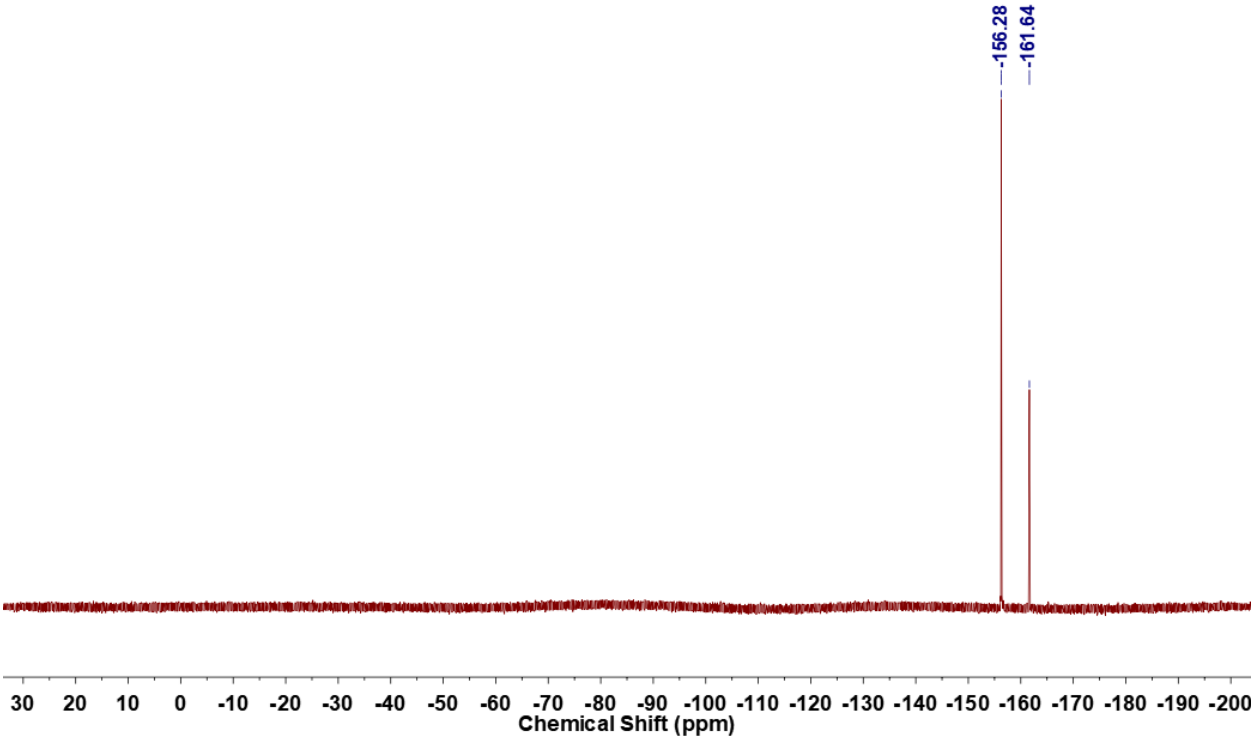

169.21
169.13
153.48
144.13
134.32
133.48
131.71
131.48
130.92
130.91
130.83
129.64
129.29
128.50
126.78
126.72
126.19
125.60
125.58
125.01
124.95
123.56
123.10
113.90
113.59
109.63
94.16
92.21
81.88
67.75
67.53
28.25
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-157.15
-162.14
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)

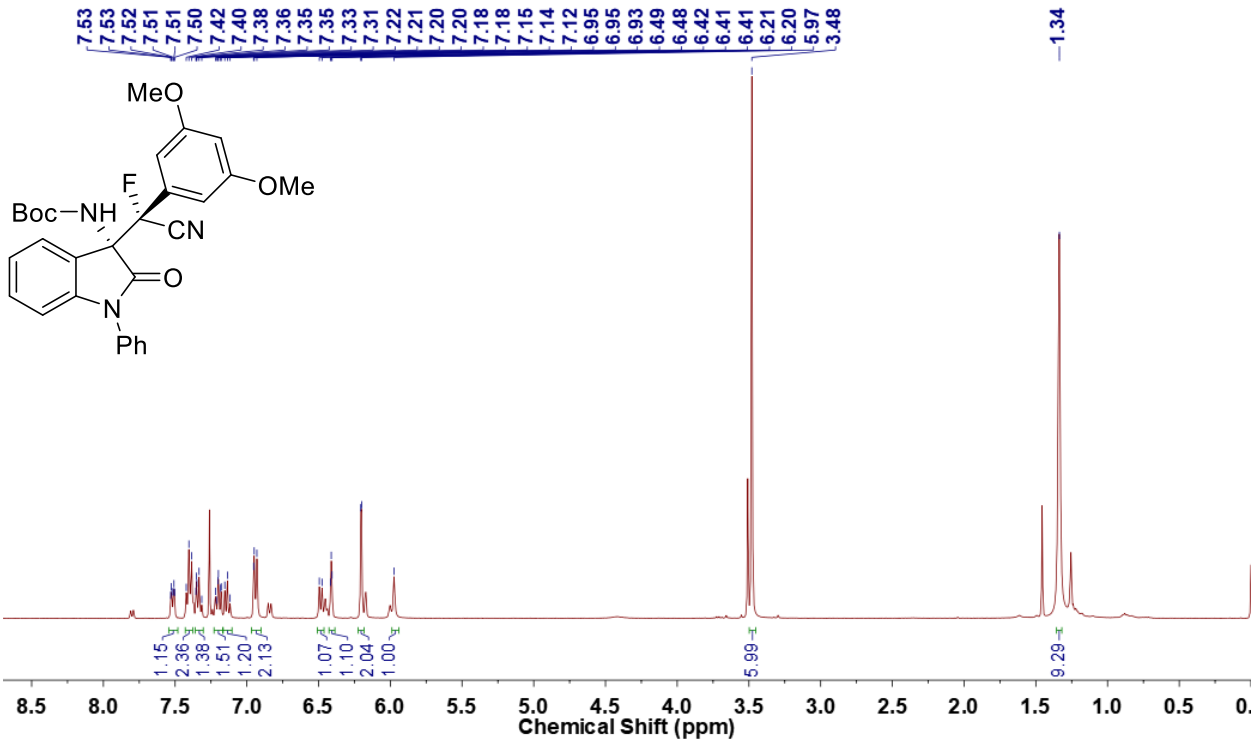
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ec**)

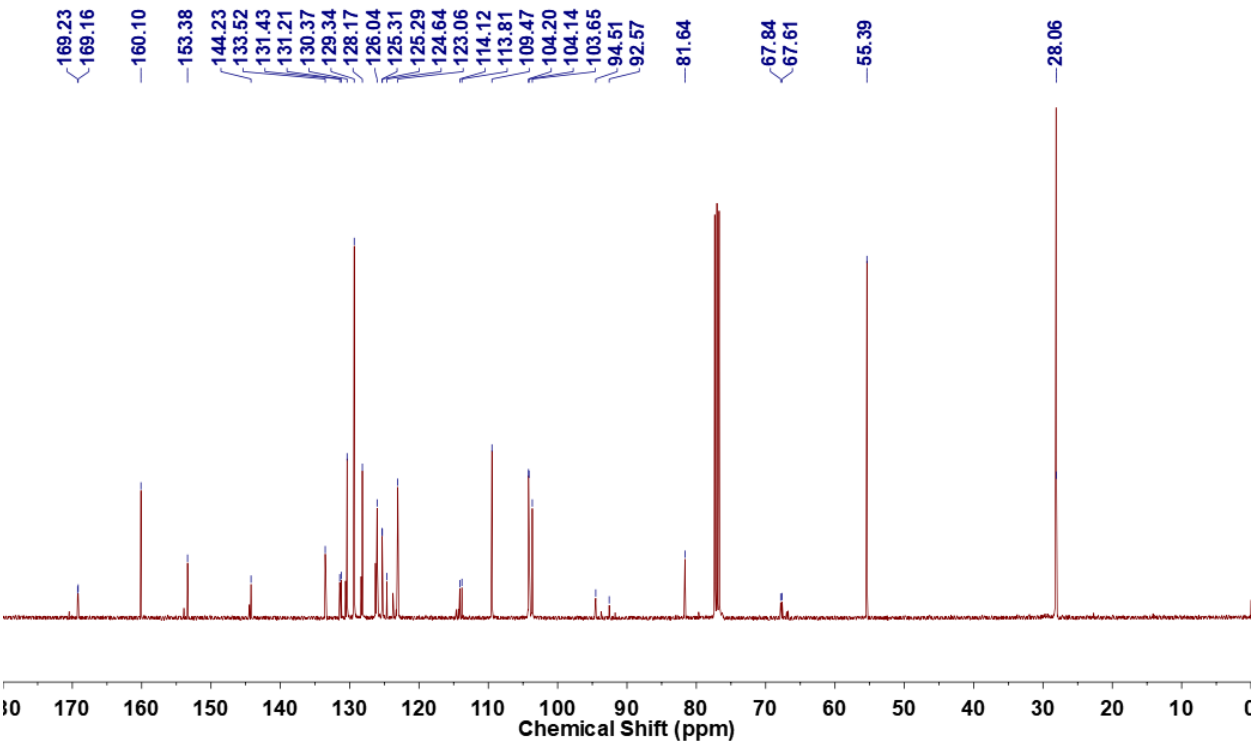


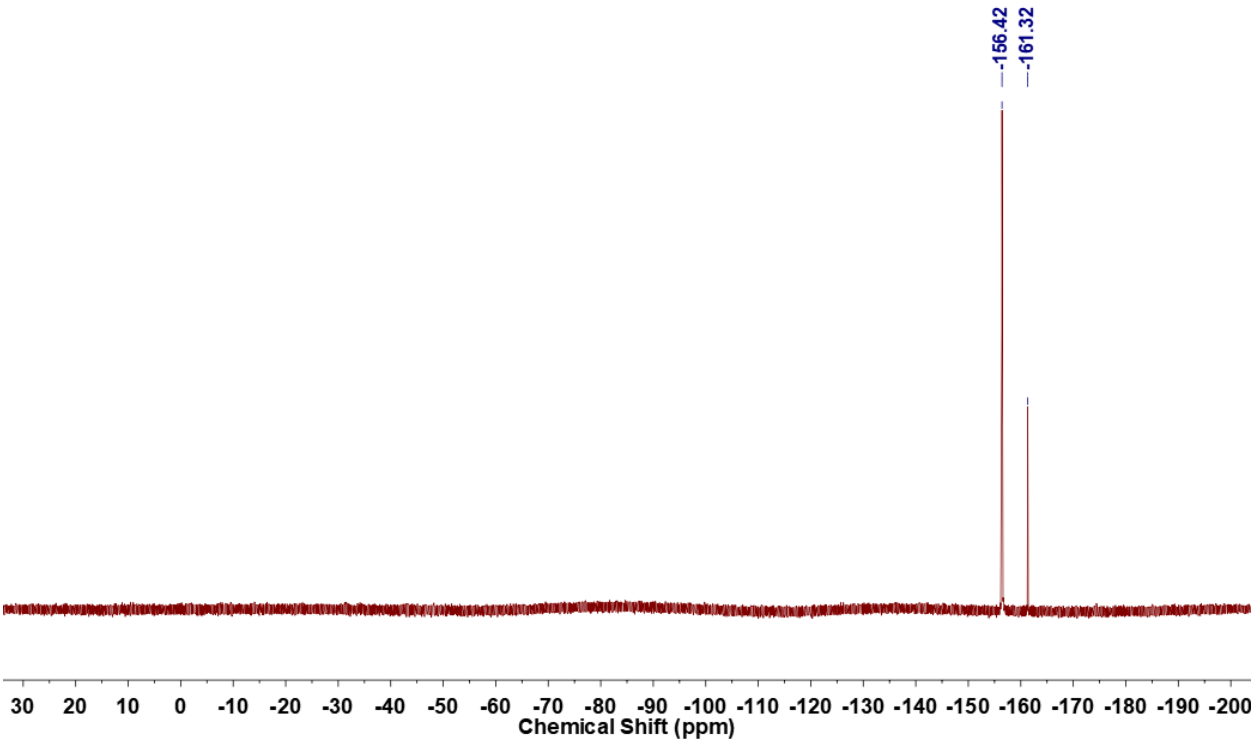




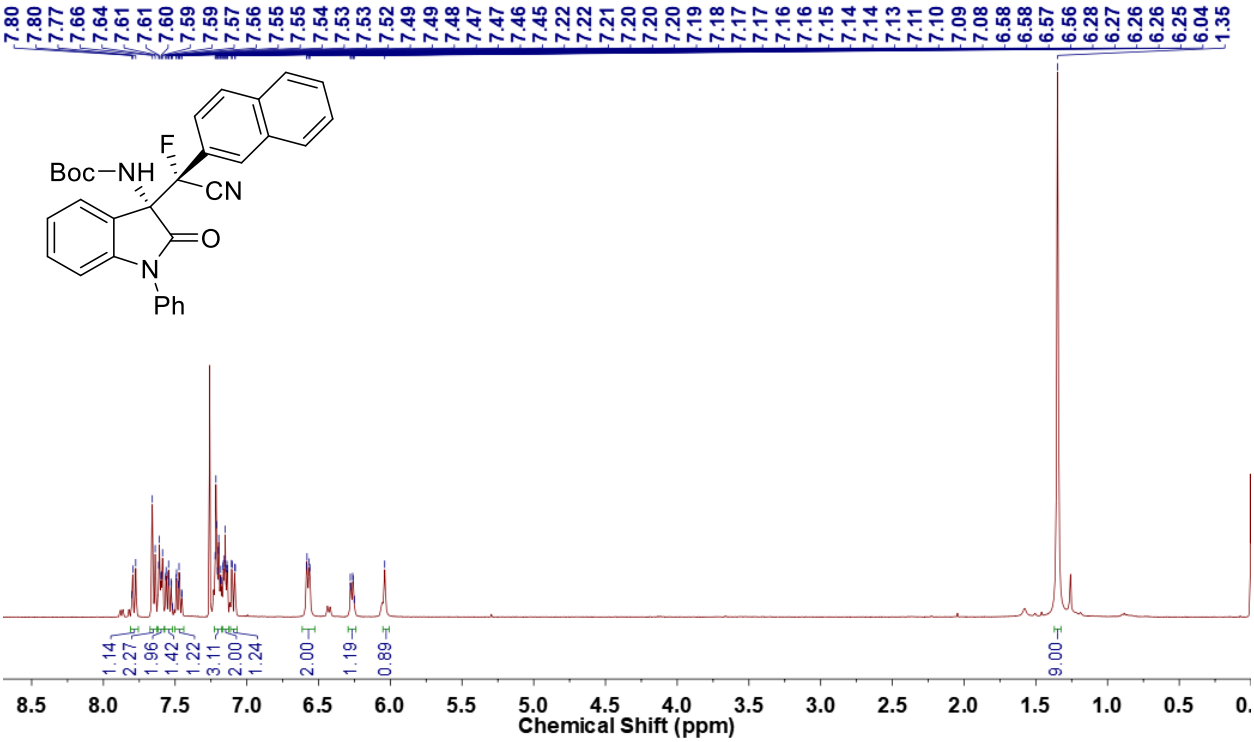
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3,5-dimethoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ic**)

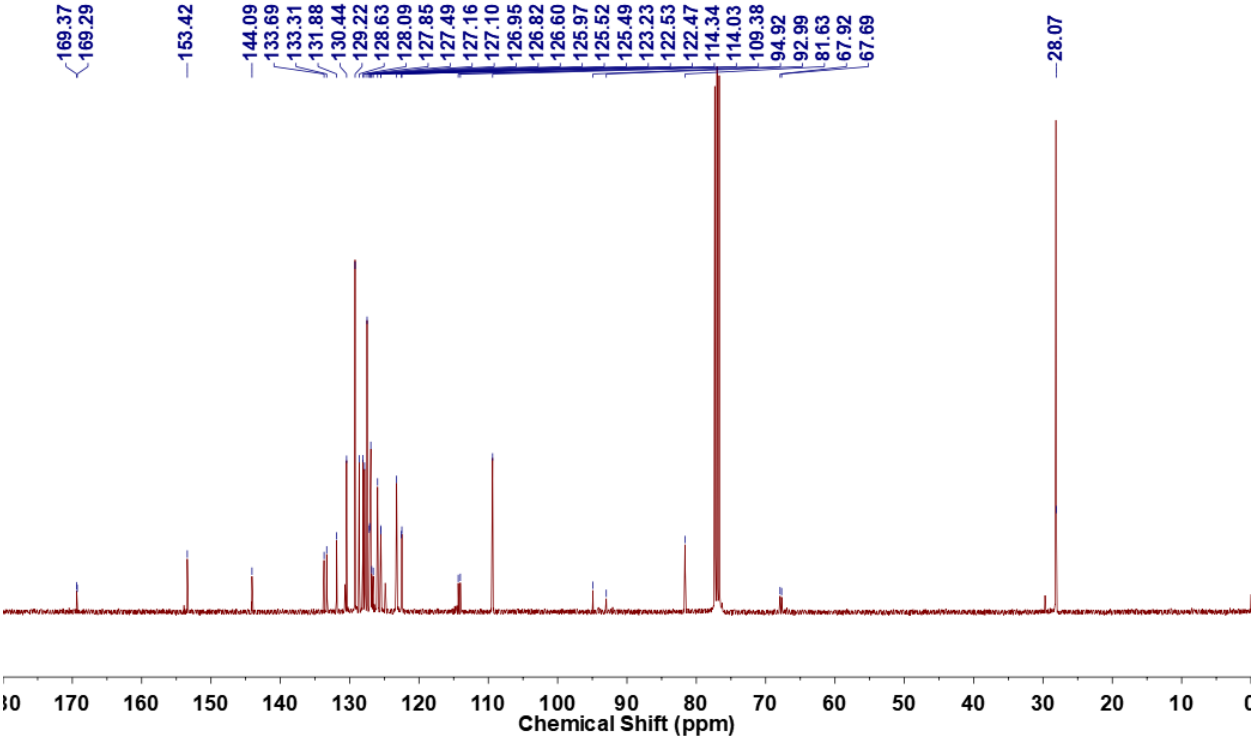


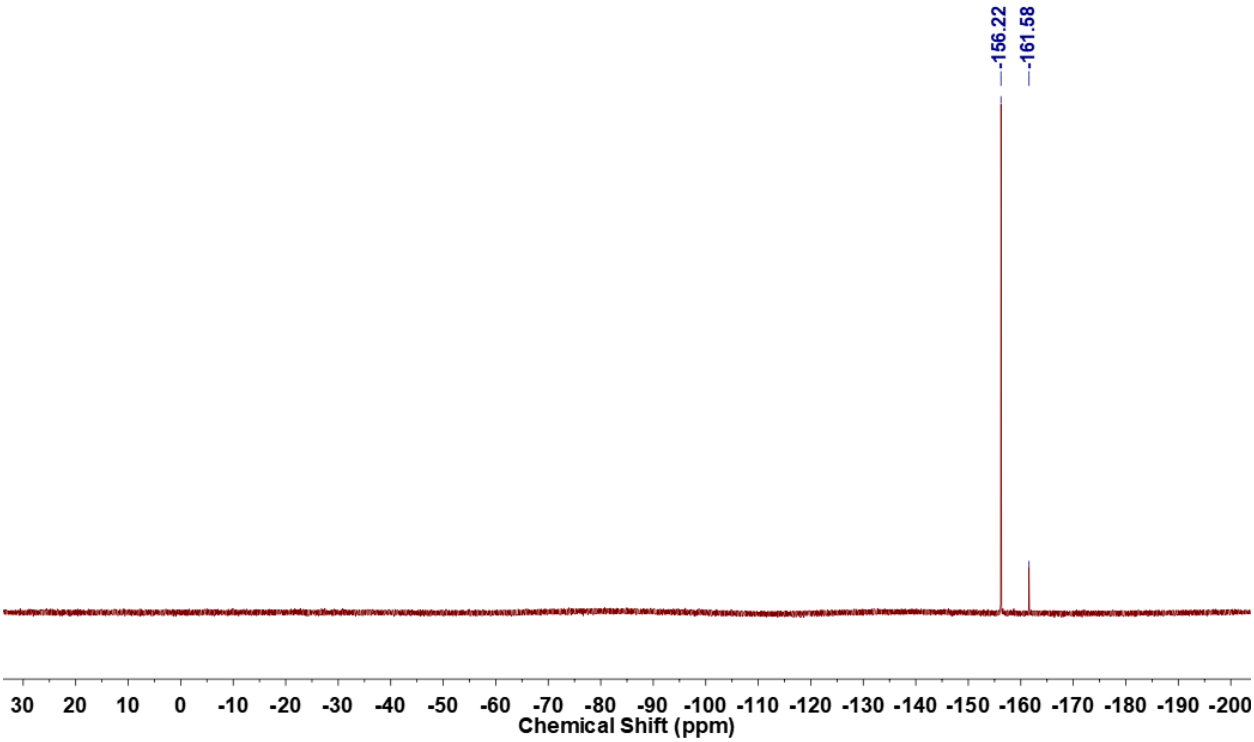

169.23
169.16
160.10
153.38
144.23
133.52
131.43
131.21
130.37
129.34
128.17
126.04
125.31
125.29
124.64
123.06
114.12
113.81
109.47
104.20
104.14
103.65
94.51
92.57
81.64
67.84
67.61
55.39
28.06
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-156.42
-161.32
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)

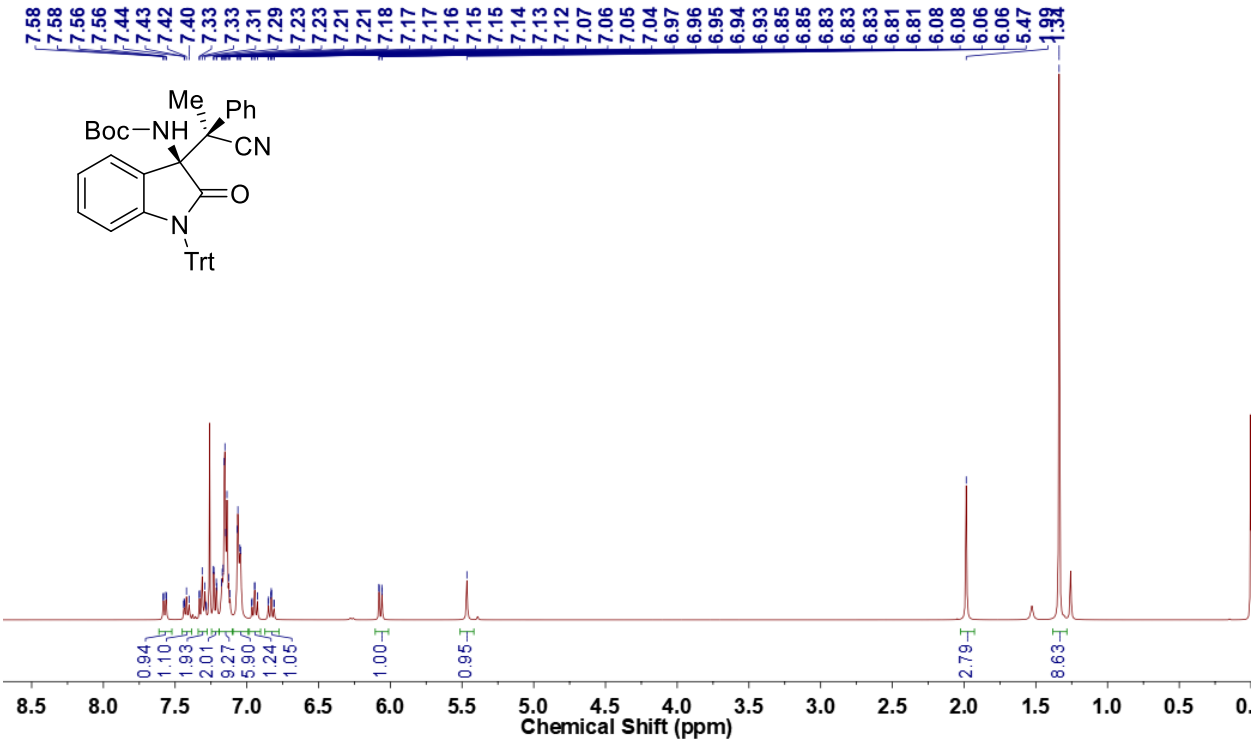
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(2-naphthyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3kc**)

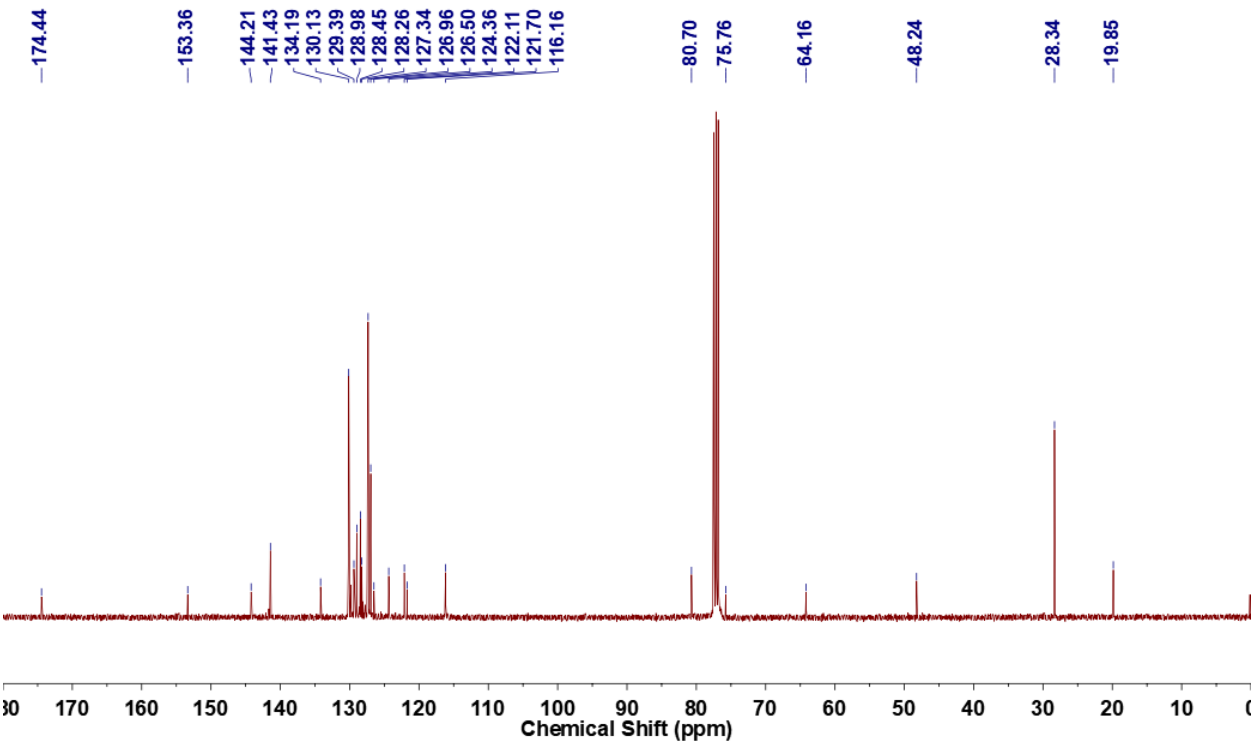




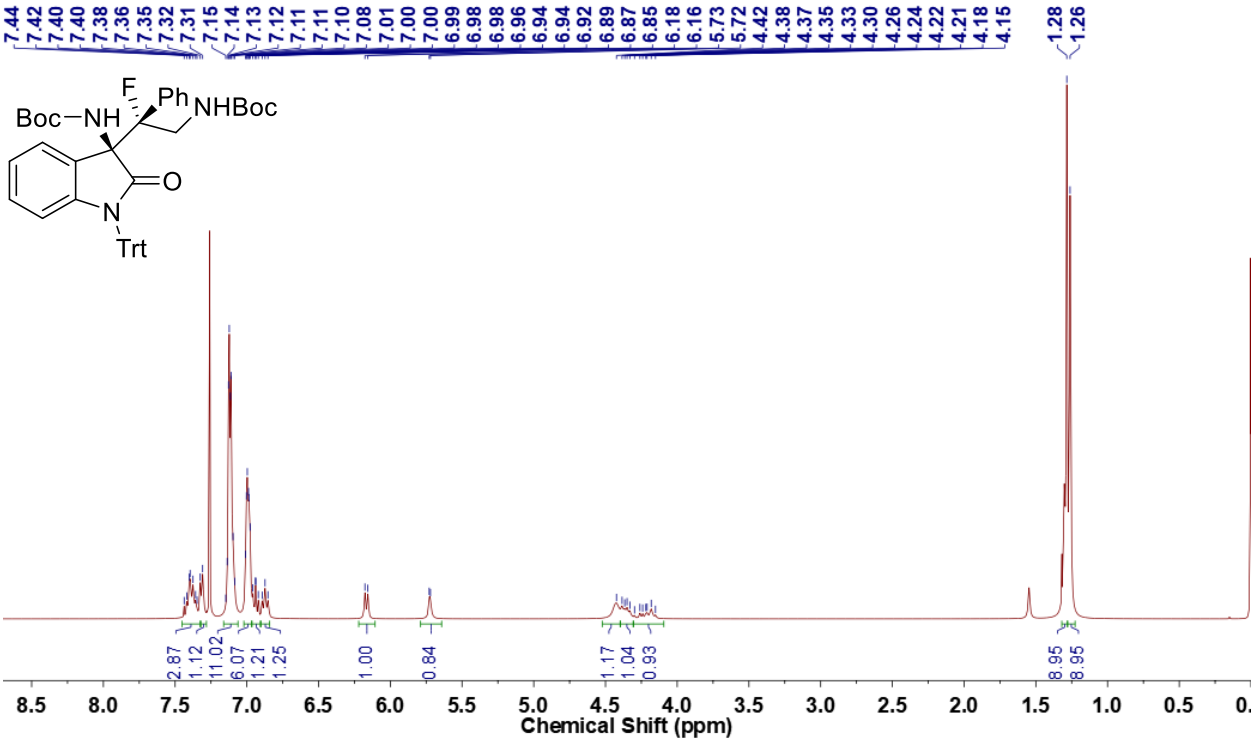


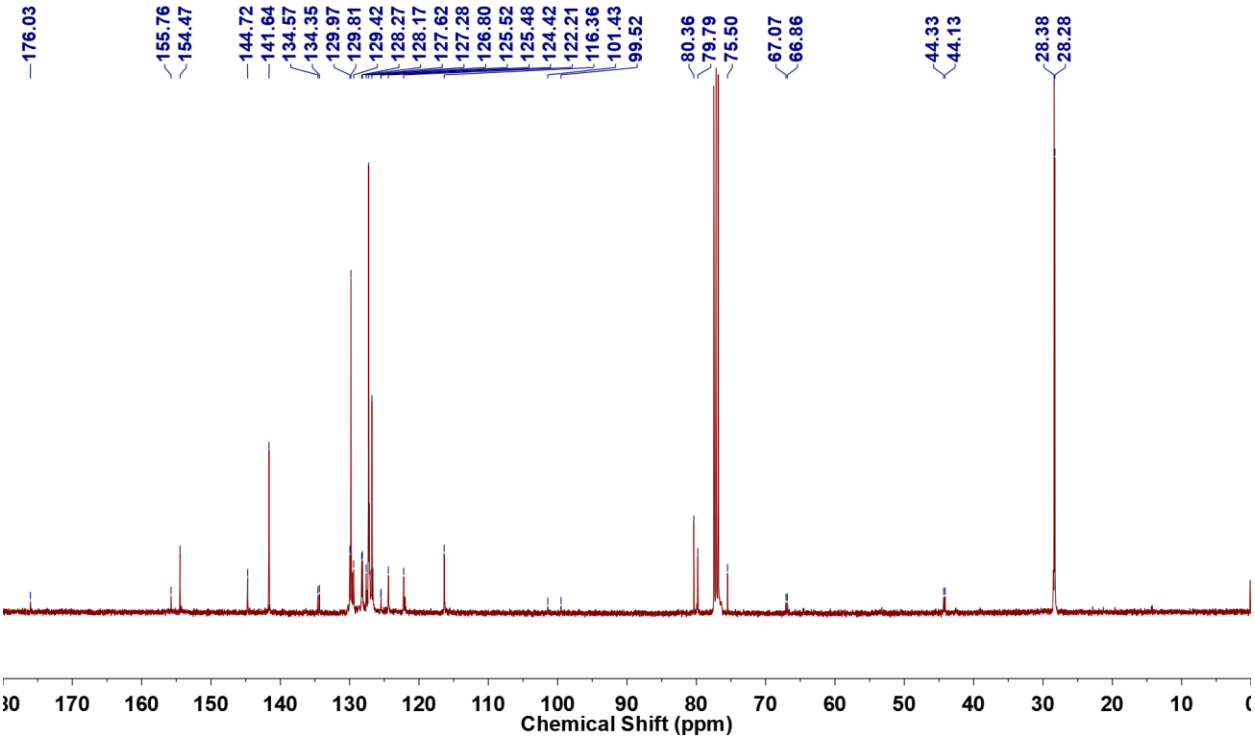
tert-Butyl ((*S*)-3-((*R*)-1-cyano-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**9**)

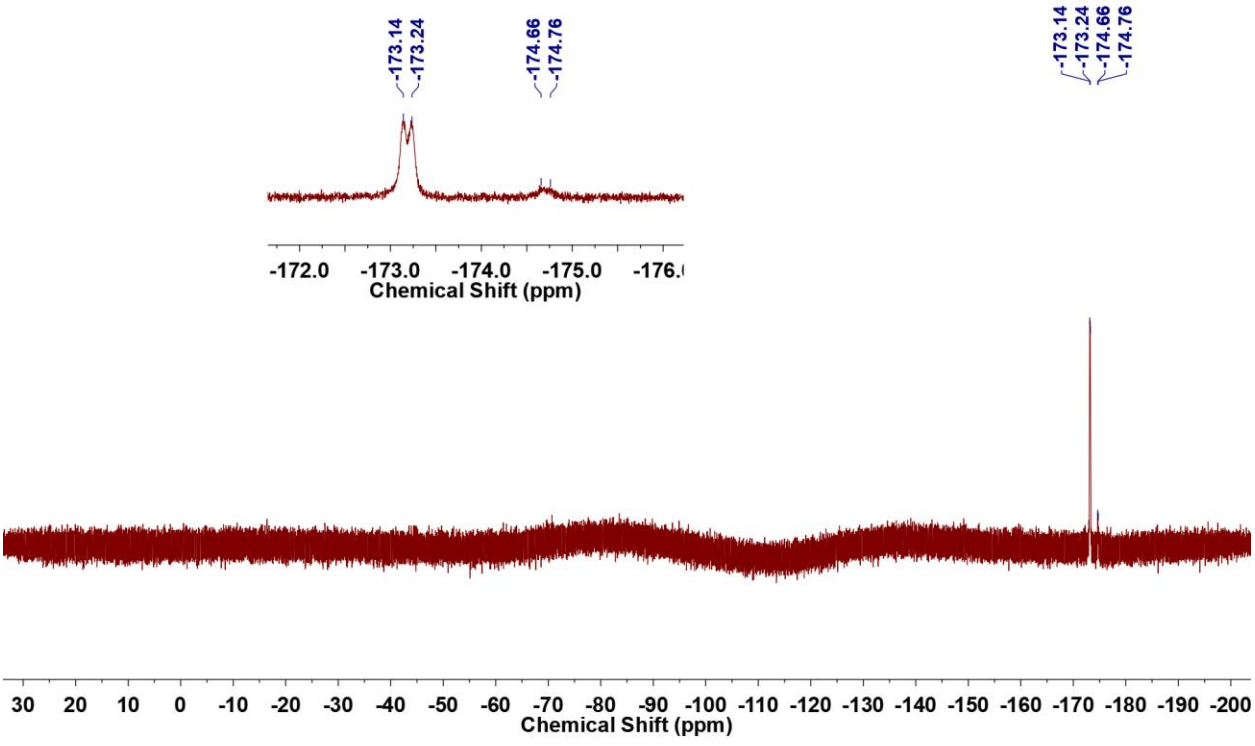




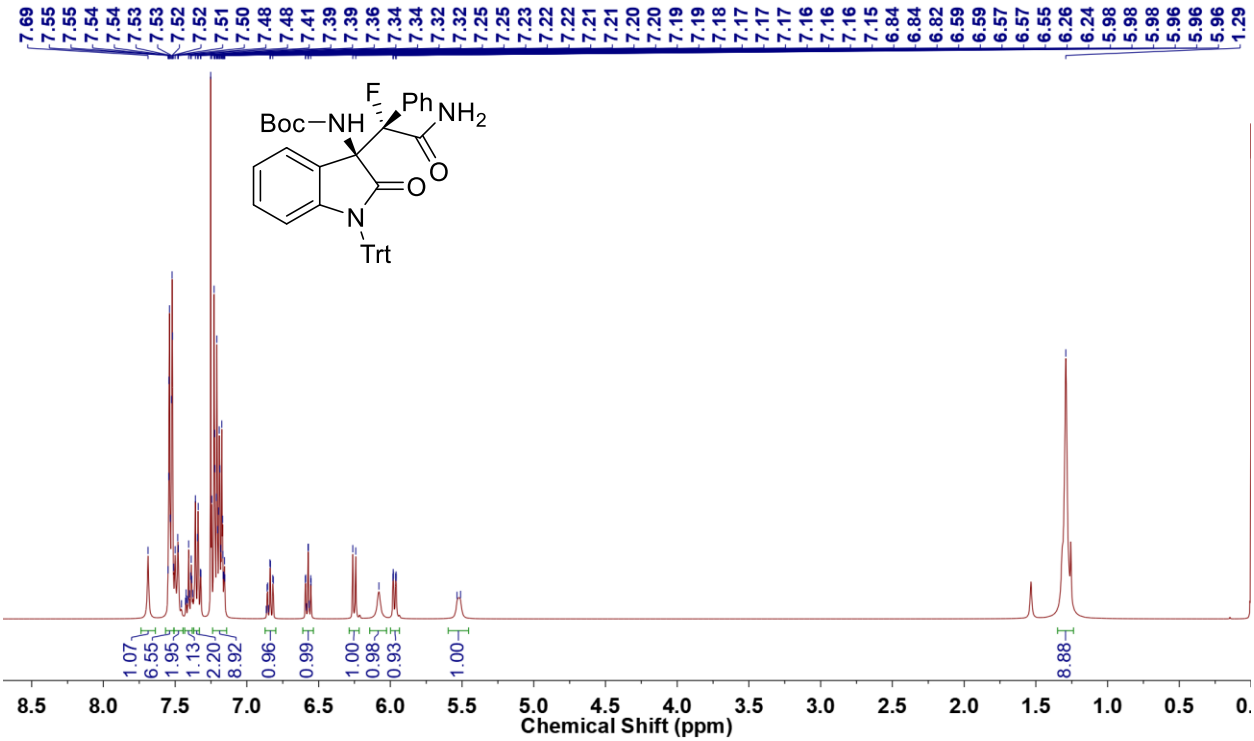
tert-Butyl ((*R*)-3-((*R*)-2-((tert-butoxycarbonyl)amino)-1-fluoro-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**4**)

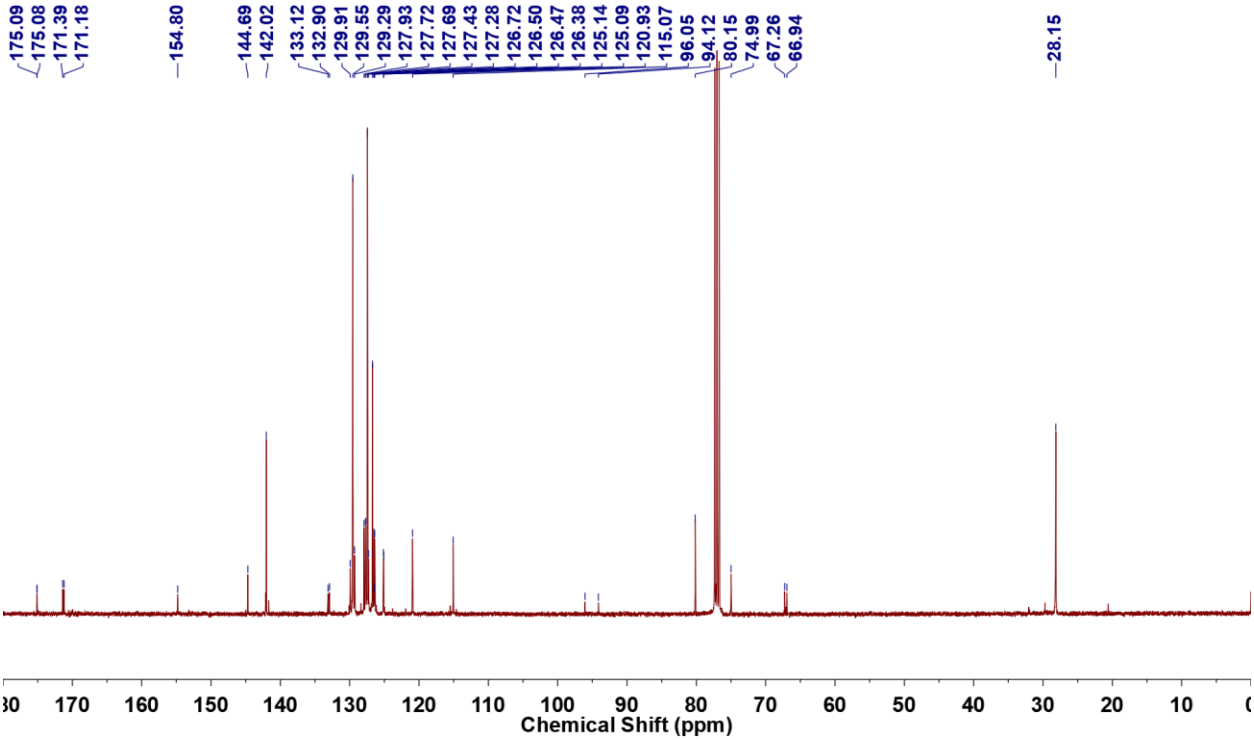


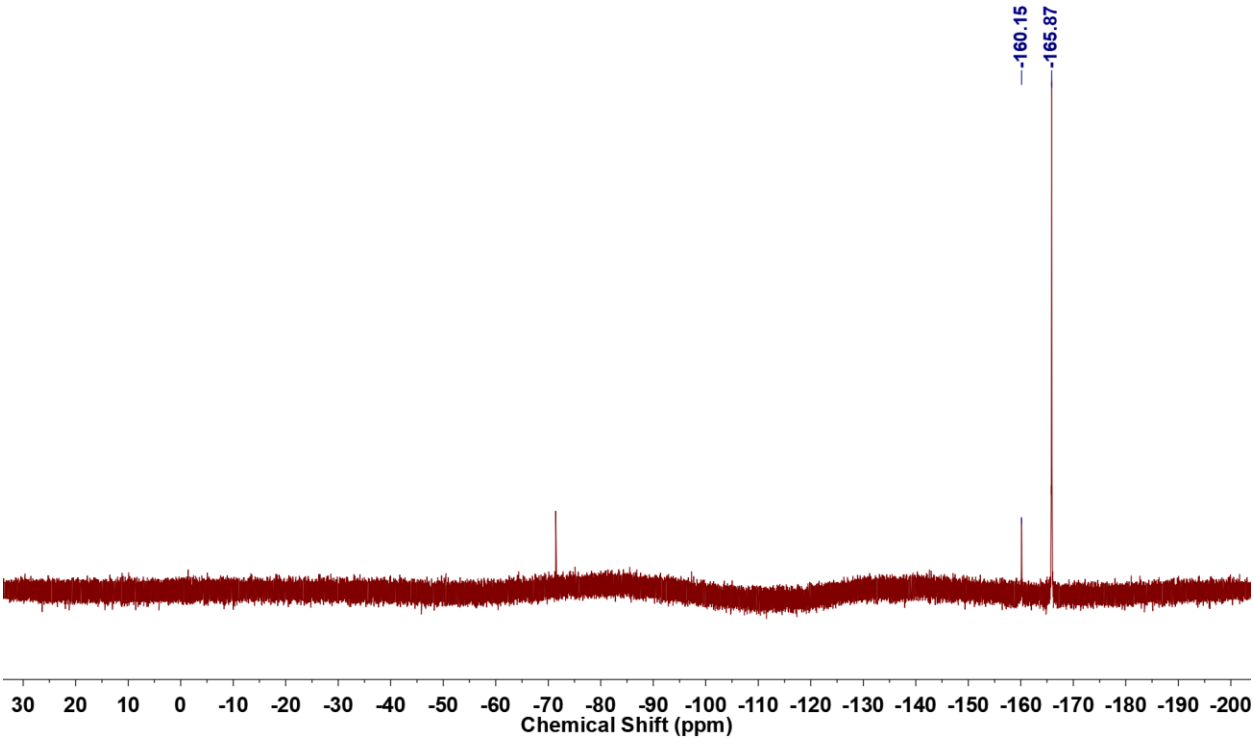

176.03
155.76
154.47
144.72
141.64
134.57
134.35
129.97
129.81
129.42
128.27
128.17
127.62
127.28
126.80
125.52
125.48
124.42
122.21
116.36
101.43
99.52
80.36
79.79
75.50
67.07
66.86
44.33
44.13
28.38
28.28
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
Chemical Shift (ppm)


-173.14
-173.24
-174.66
-174.76
-172.0 -173.0 -174.0 -175.0
Chemical Shift (ppm)
-173.14
-173.24
-174.66
-174.76
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)

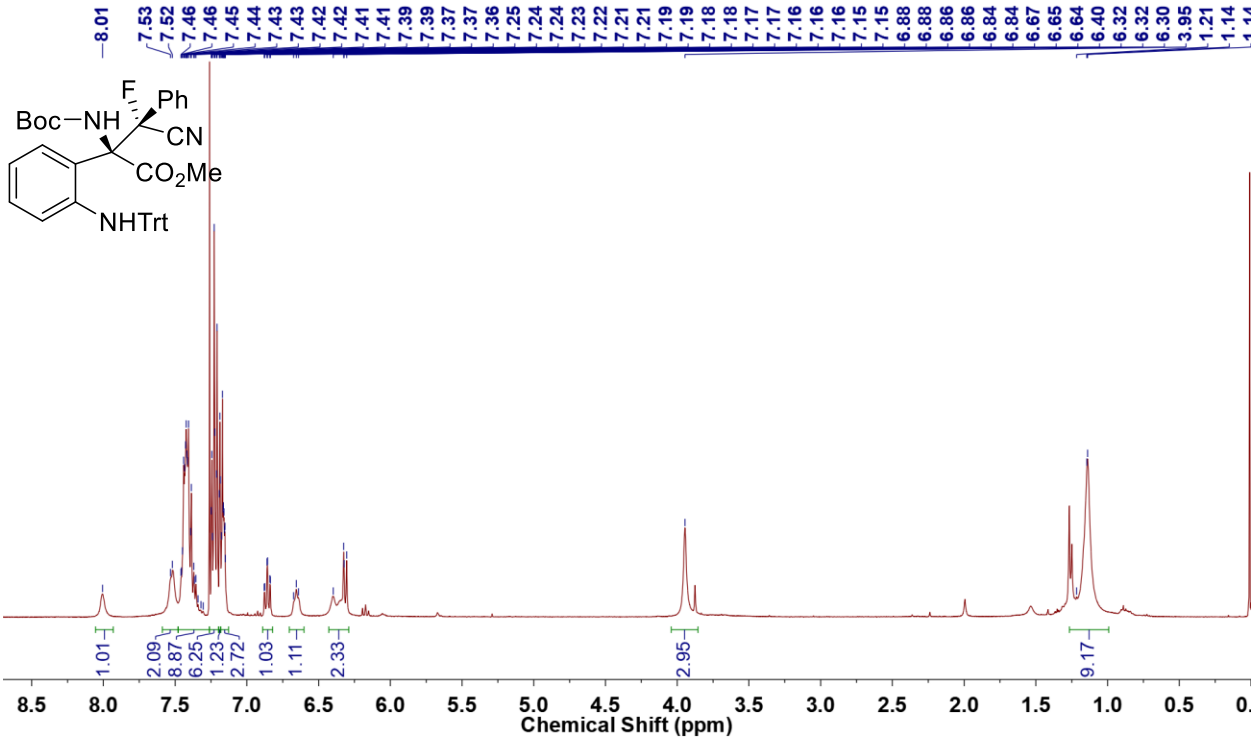
tert-Butyl ((*R*)-3-((*S*)-2-amino-1-fluoro-2-oxo-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**5**)

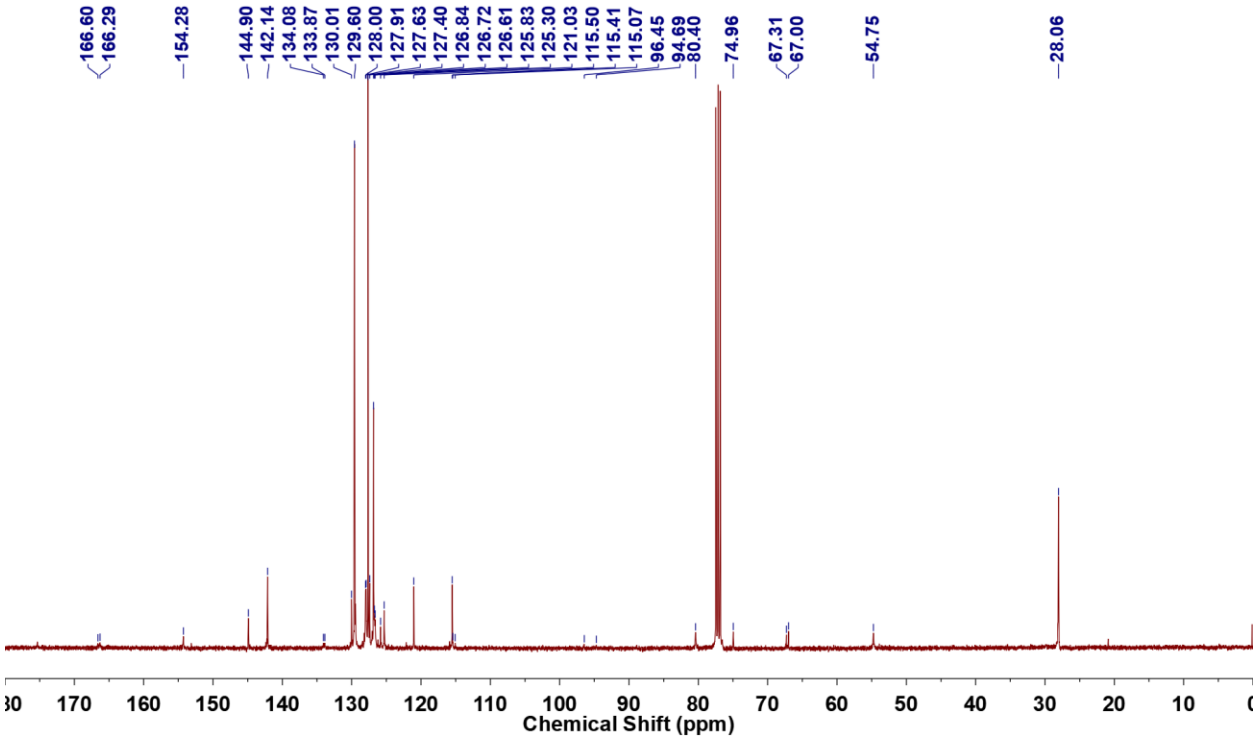


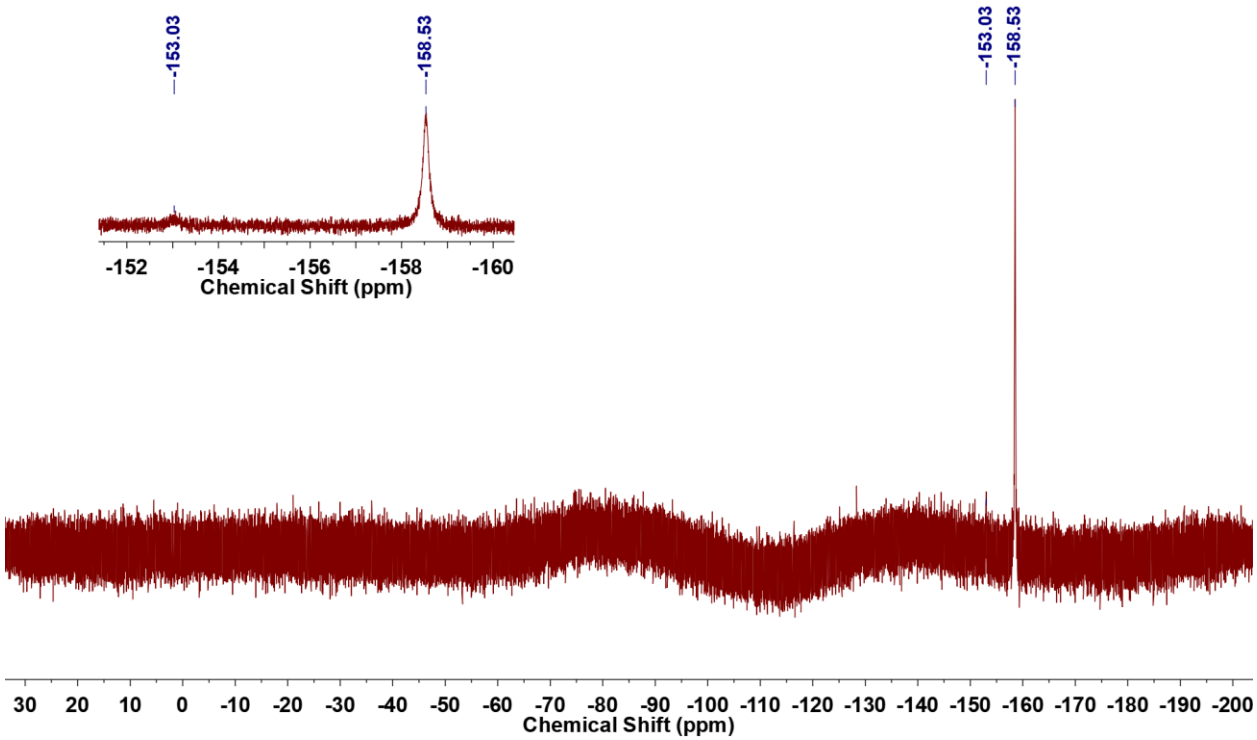




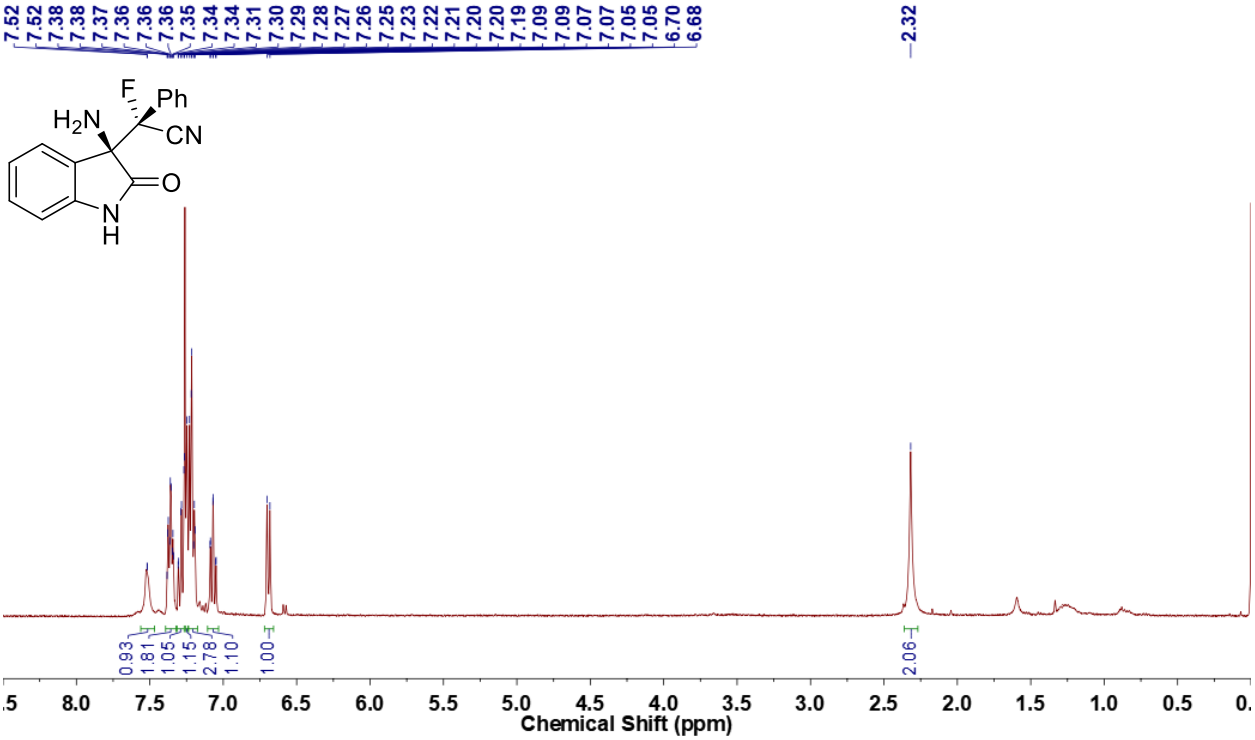
Methyl (2*R*,3*S*)-2-((*tert*-butoxycarbonyl)amino)-3-cyano-3-fluoro-3-phenyl-2-(2-(tritylamino)-phenyl)propanoate (**6**)

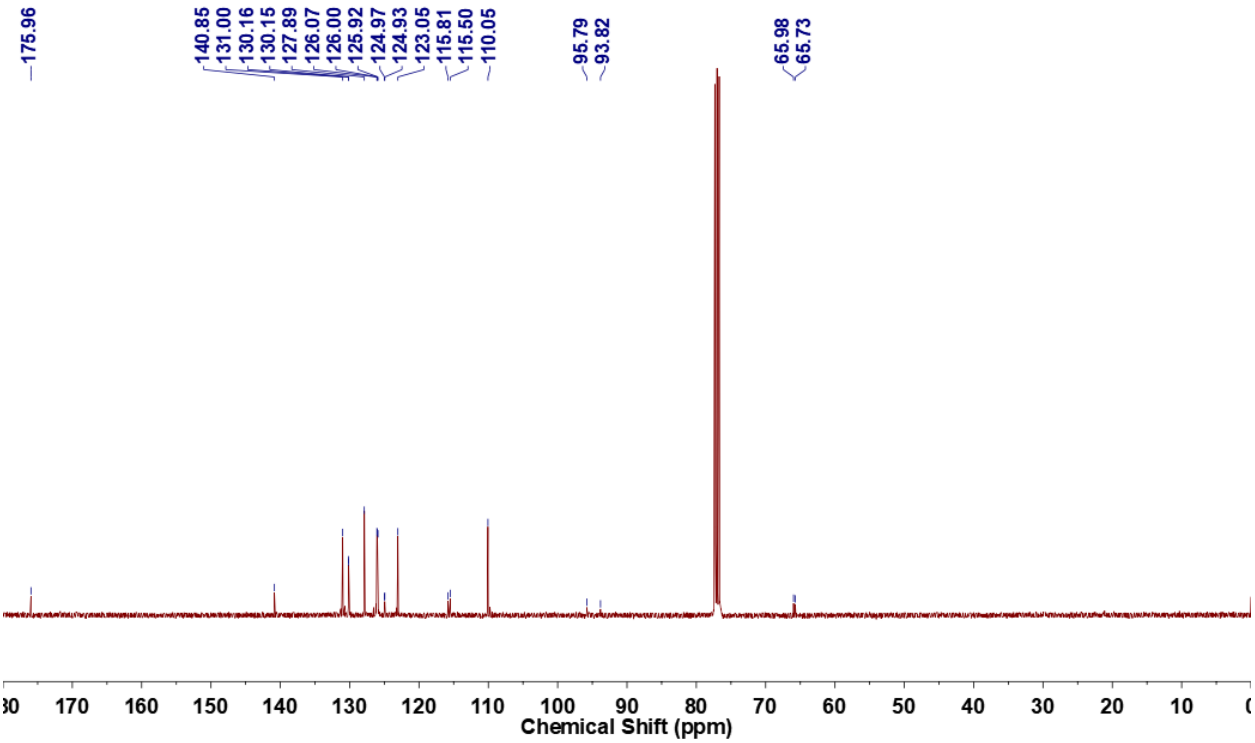


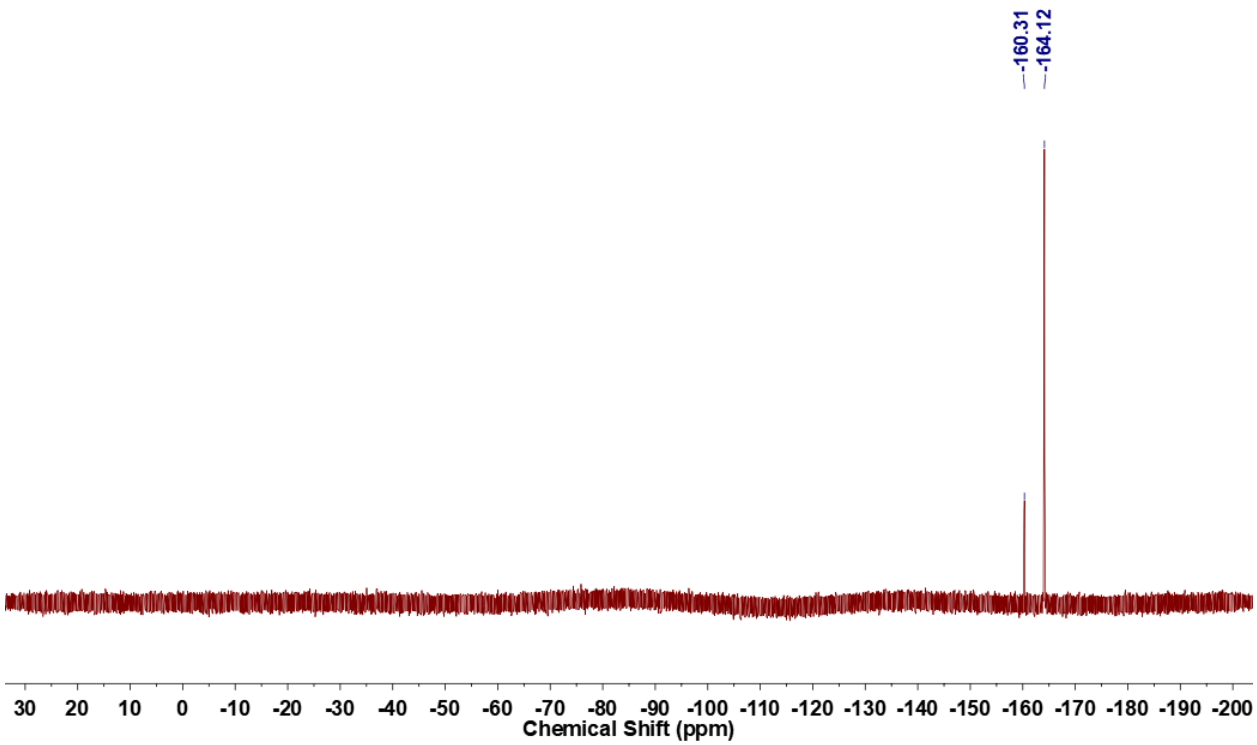

166.60
166.29
154.28
144.90
142.14
134.08
133.87
130.01
129.60
128.00
127.91
127.63
127.40
126.84
126.72
126.61
125.83
125.30
121.03
115.50
115.41
115.07
96.45
94.69
80.40
74.96
67.31
67.00
54.75
28.06
Chemical Shift (ppm)


-153.03
-158.53
-152
-154
-156
-158
-160
Chemical Shift (ppm)
-153.03
-158.53
Chemical Shift (ppm)

(*S*)-2-((*R*)-3-amino-2-oxoindolin-3-yl)-2-fluoro-2-phenylacetonitrile (**7**)

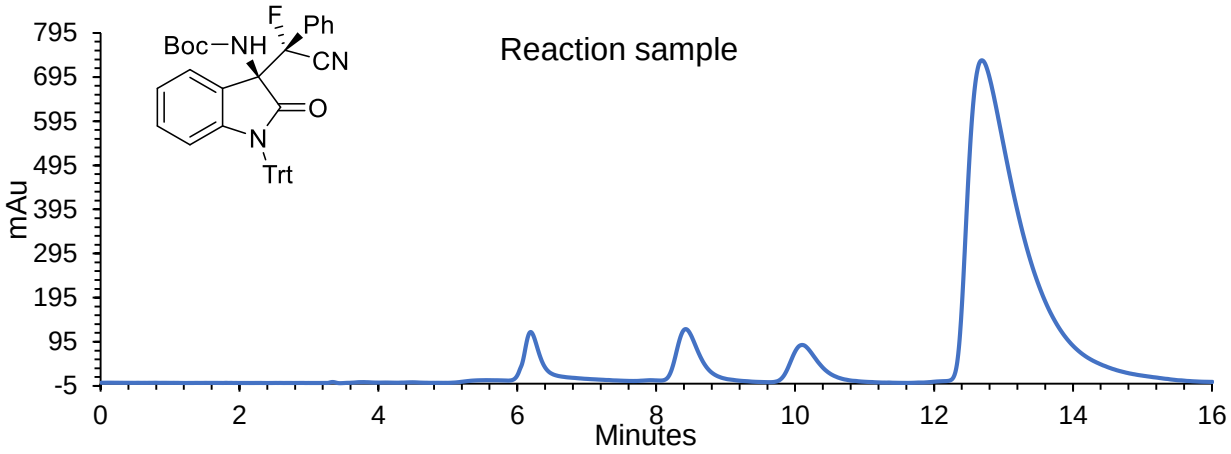





-160.31
-164.12
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
Chemical Shift (ppm)

6. HPLC Chromatograms

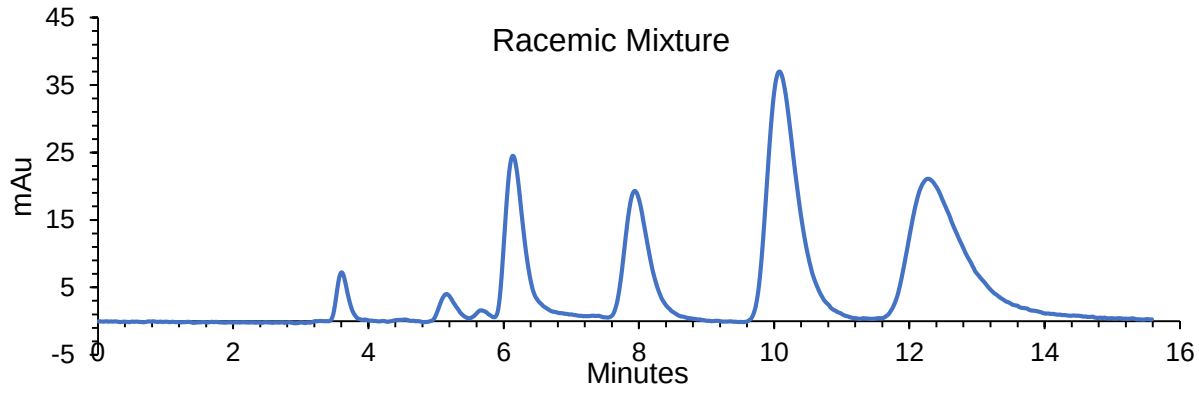
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ab**)



Signal 4: DAD1 D, Sig=232,4 Ref=550,100

Ret. Time [min]	Area %
10.101	5.1346
12.688	94.8654

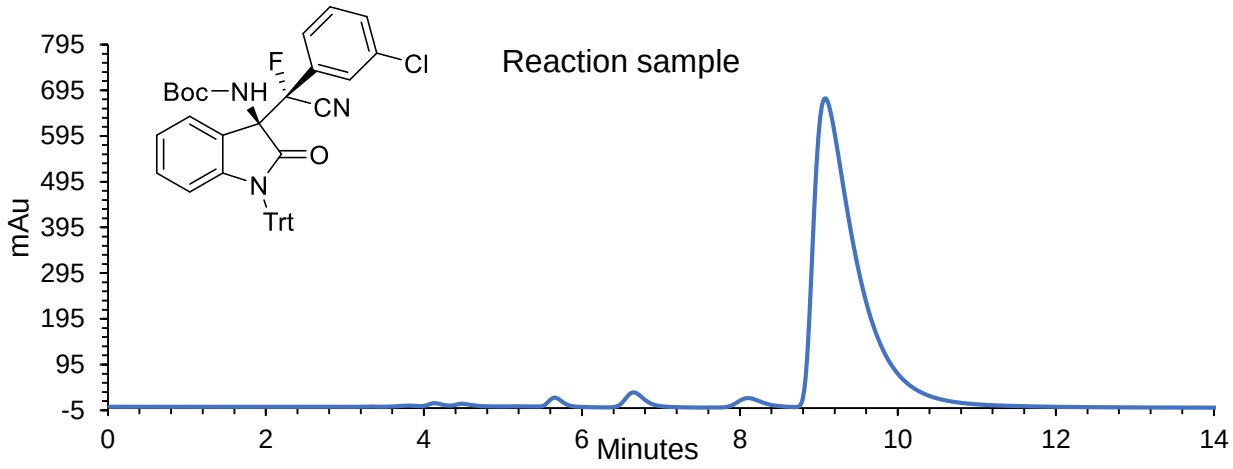
dr = 12.7:1, major ee = 90%



Signal 4: DAD1 D, Sig=232,4 Ref=550,100

Ret. Time [min]	Area %
6.182	14.5638
7.989	14.8100
10.102	36.4560
12.280	34.1703

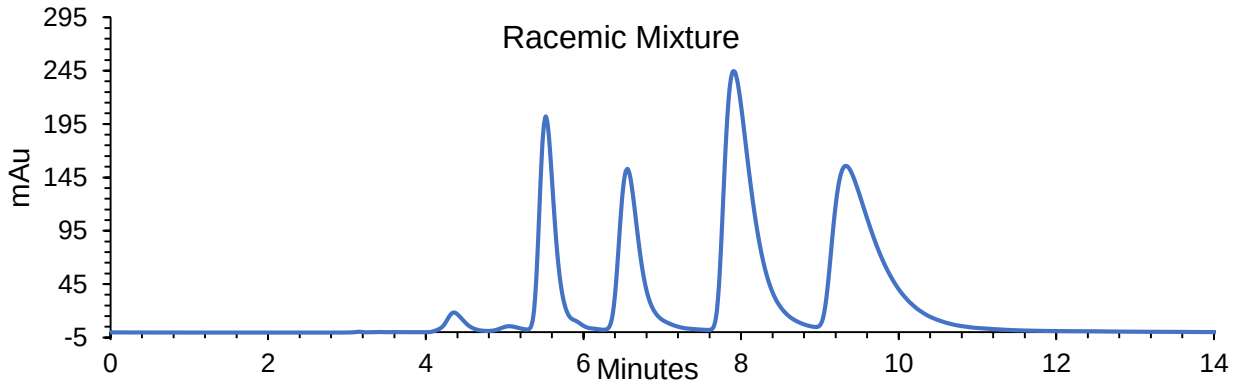
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3bb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.155	1.7213
9.115	98.2787

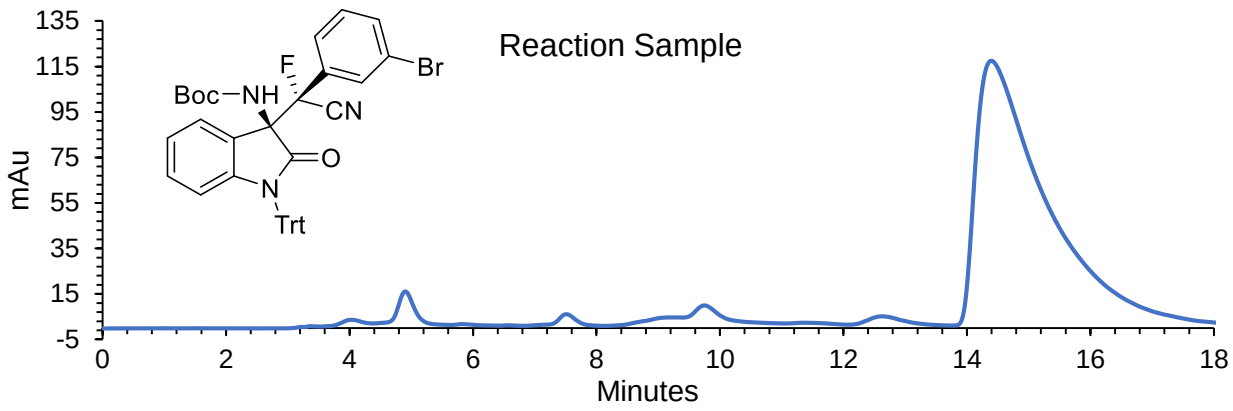
dr = 36.0:1, major ee = 97%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
5.522	16.1457
6.556	16.2053
7.907	33.7320
9.331	33.9171

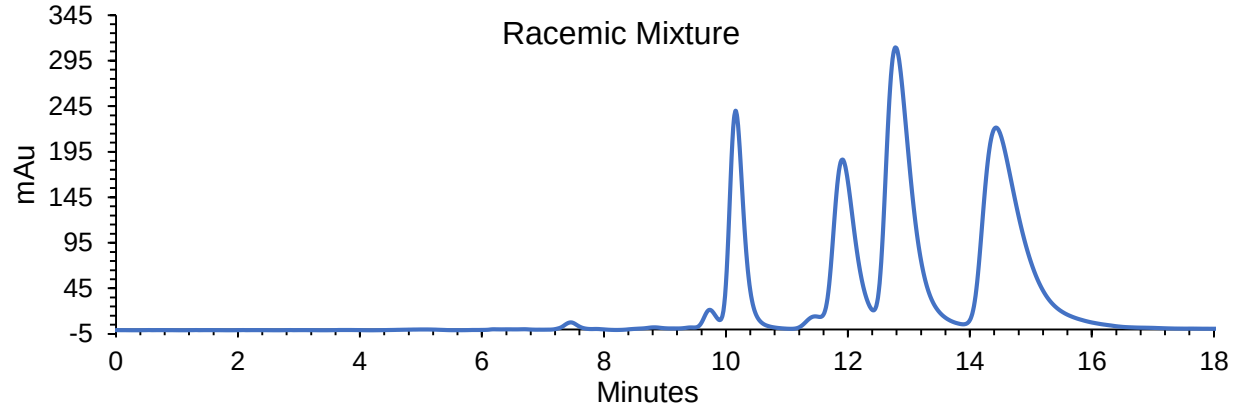
tert-Butyl ((*R*)-3-((S)-cyanofluoro(3-bromophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3cb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
12.641	1.6586
14.393	98.3414

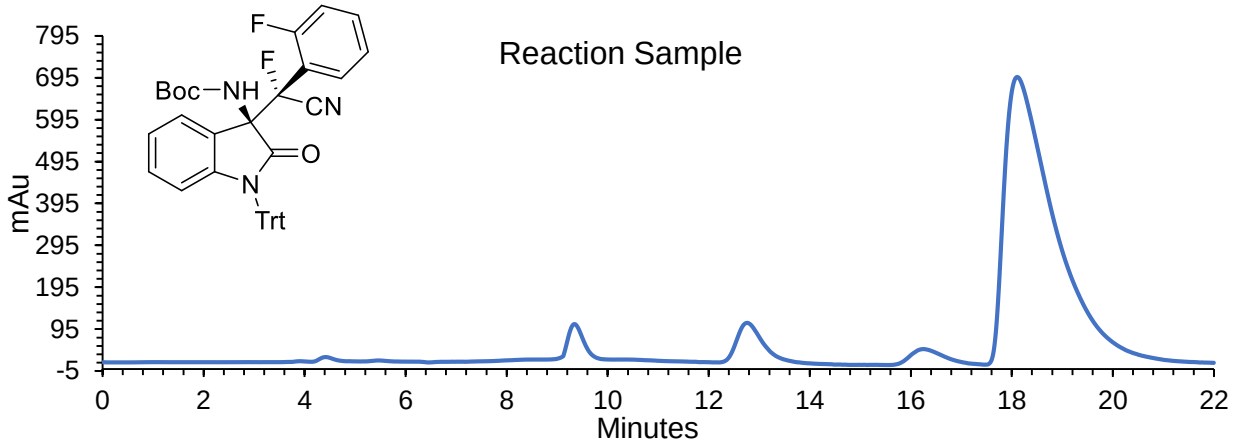
dr = 39.5:1, major ee = 97%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
5.522	16.1457
6.556	16.2053
7.907	33.7320
9.331	33.9171

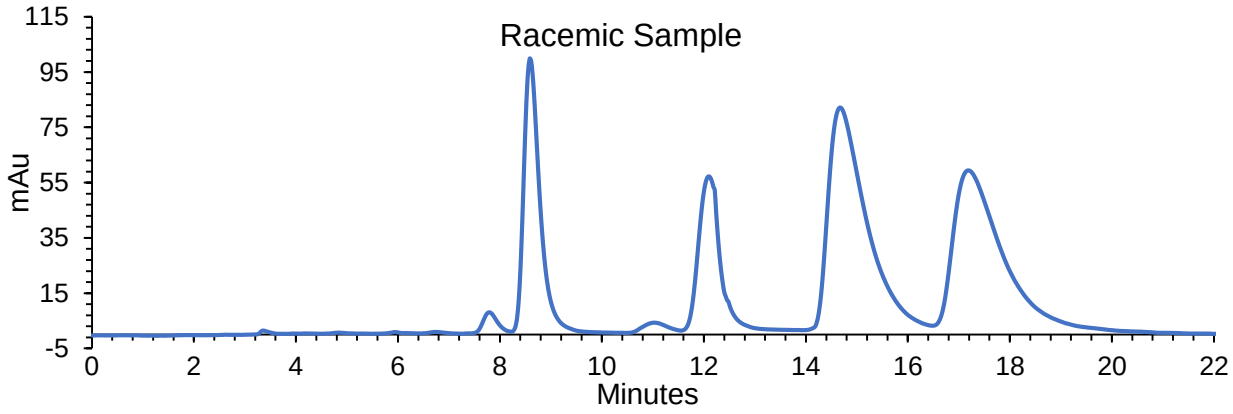
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-fluorophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3db**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
16.265	3.5224
18.228	96.4776

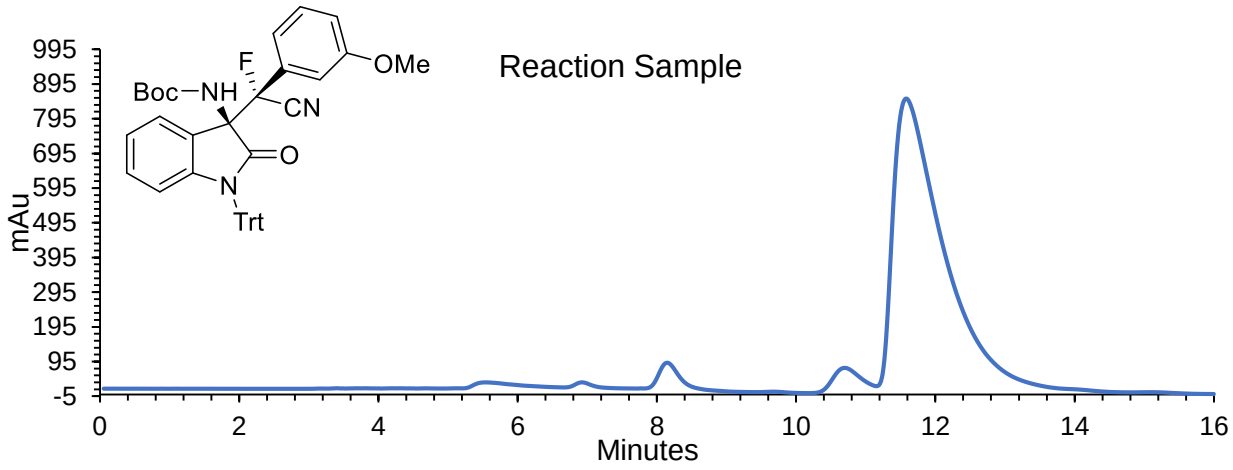
dr = 9.4:1, major ee = 93%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.596	18.1803
12.098	16.8515
14.674	32.6184
17.187	32.3498

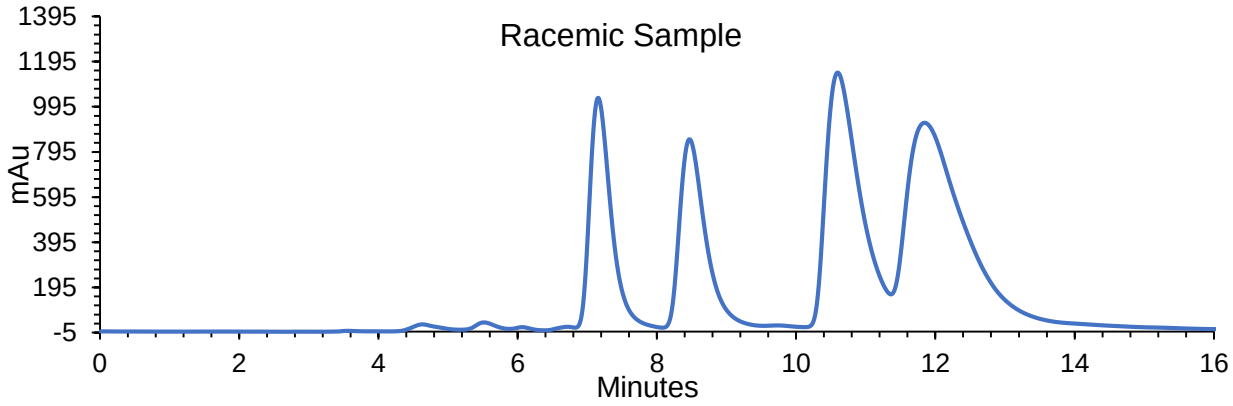
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3eb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.701	4.5910
11.673	95.4090

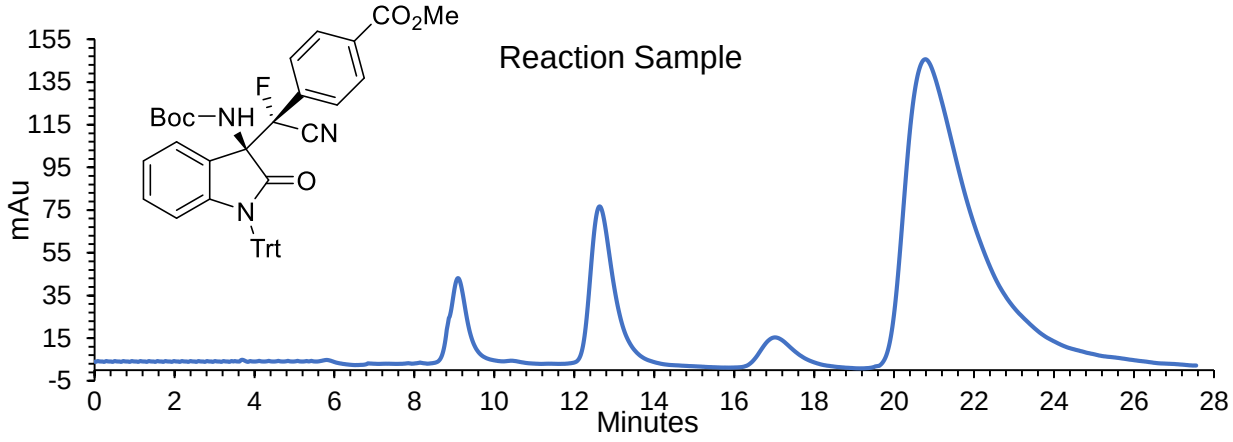
dr = 24.0:1, major ee = 91%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.156	16.3114
8.468	16.3783
10.597	31.4988
11.951	35.8115

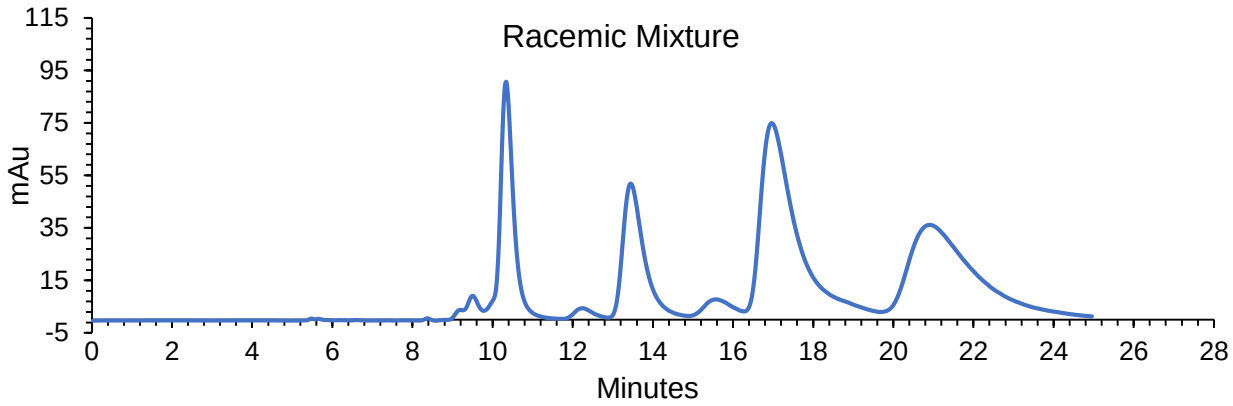
Methyl 4-((*S*)-((*R*)-3-((*tert*-butoxycarbonyl)amino)-2-oxo-1-tritylindolin-3-yl)(cyano)fluoromethyl)benzoate (**3fb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
17.057	4.5427
20.815	95.4573

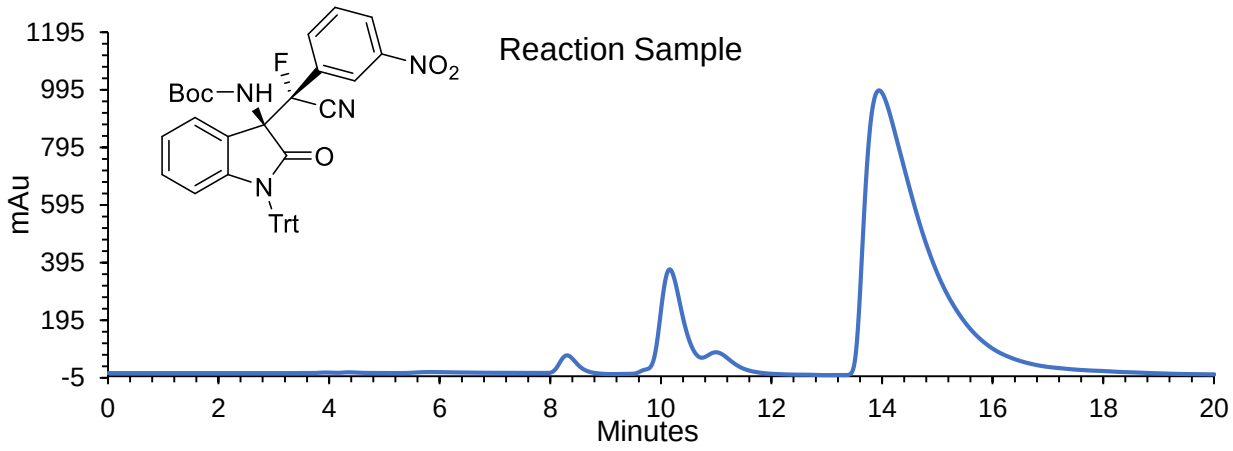
dr = 9.1:1, major ee = 91%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.042	16.5155
11.155	14.5521
14.673	36.7462
18.615	32.1862

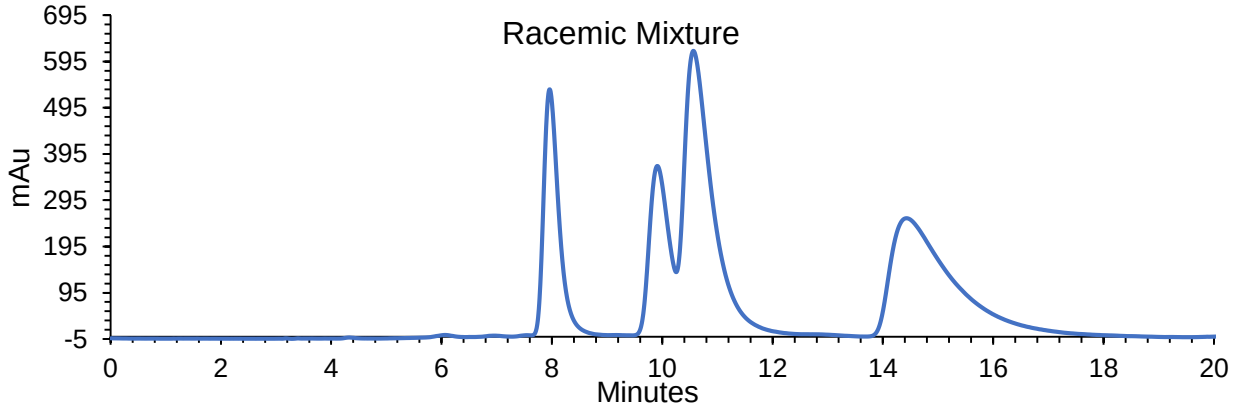
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-nitrophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3gb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.025	3.1150
14.017	96.8850

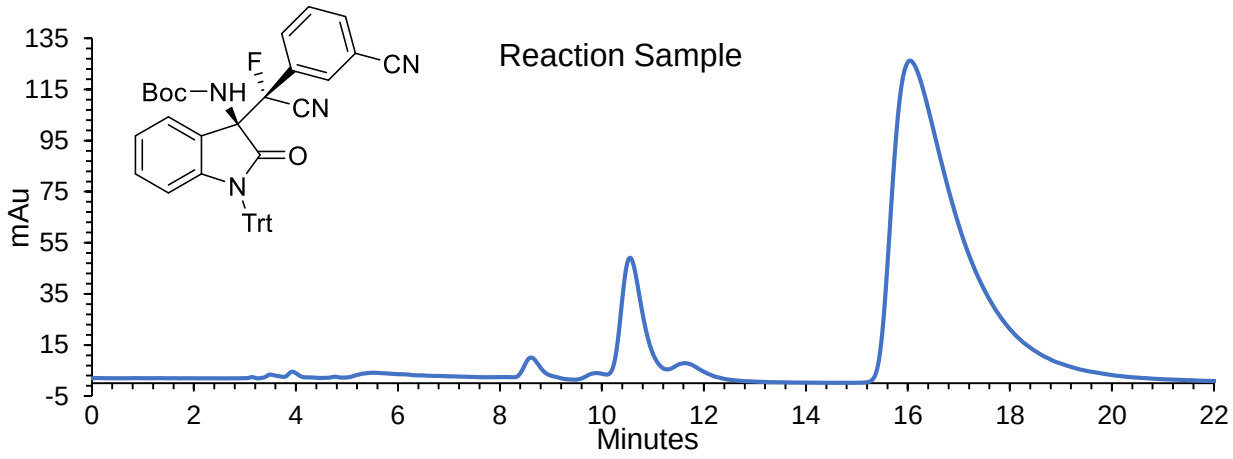
dr = 8.5:1, major ee = 94%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.960	17.2714
9.912	14.6366
10.566	35.4541
14.428	32.6379

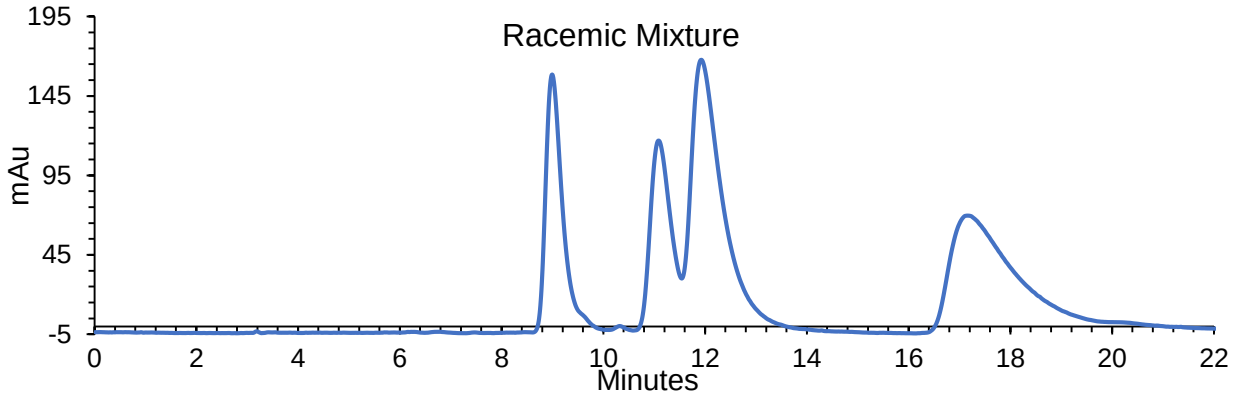
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(3-cyanophenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3hb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.586	2.6551
16.117	97.3449

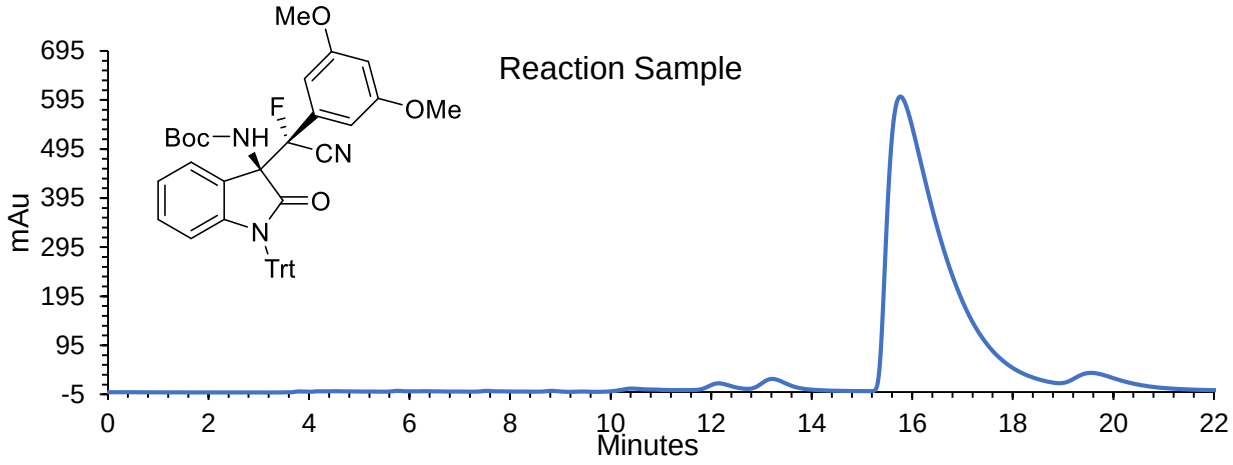
dr = 9.0:1, major ee = 95%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.995	17.4883
11.088	15.7295
11.926	33.5708
17.163	33.2114

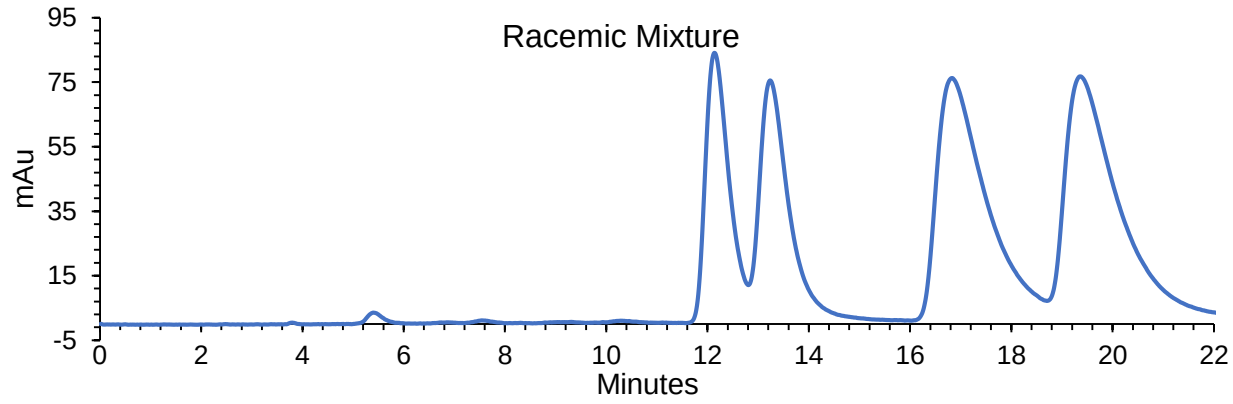
tert-Butyl ((*R*)-3-((*S*)-cyano(3,5-dimethoxyphenyl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3ib**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
15.945	95.6199
19.588	4.3801

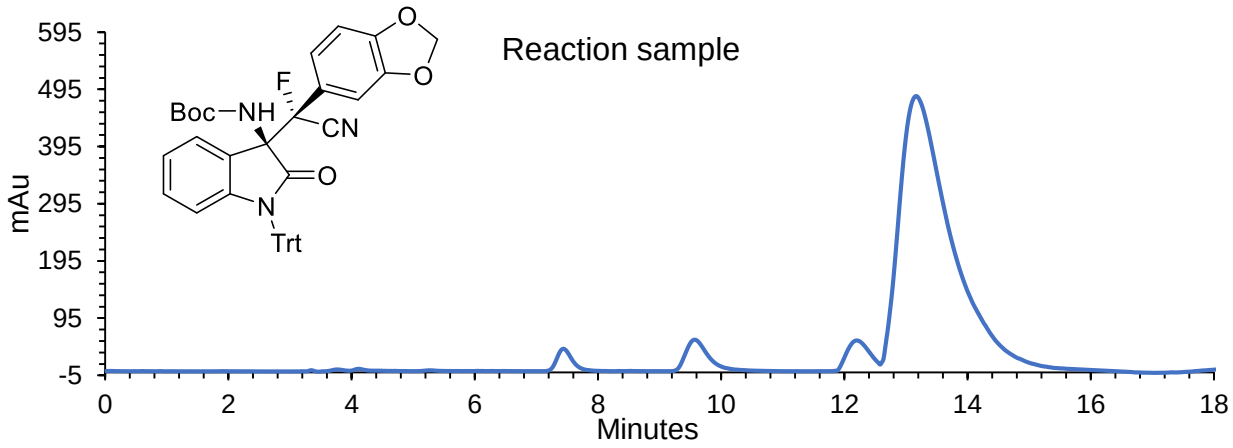
dr > 50:1, major ee = 91%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
12.139	17.1359
13.239	18.5697
16.832	31.6607
19.364	32.6337

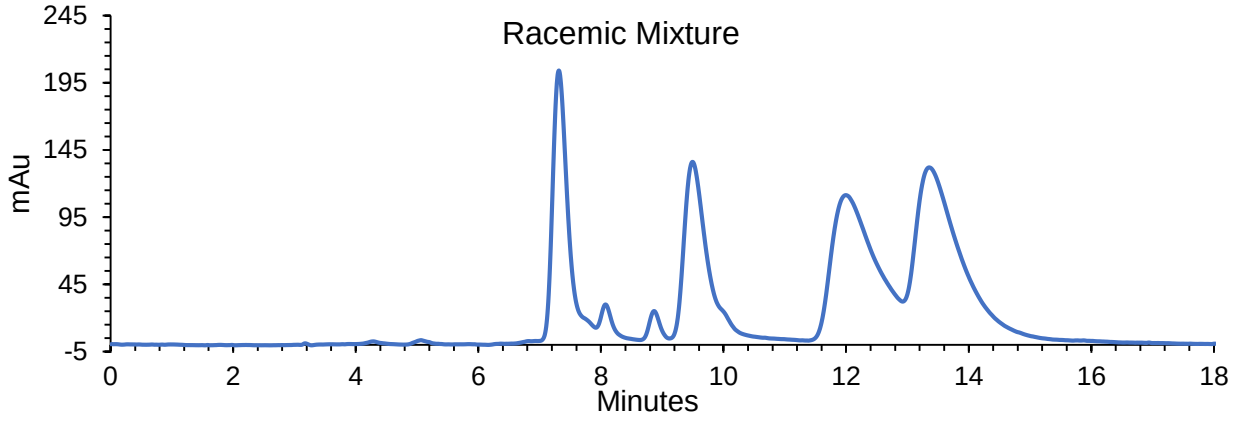
tert-Butyl ((*R*)-3-((*S*)-benzo[d][1,3]dioxol-5-yl(cyano)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3jb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
12.047	7.1268
13.195	92.8731

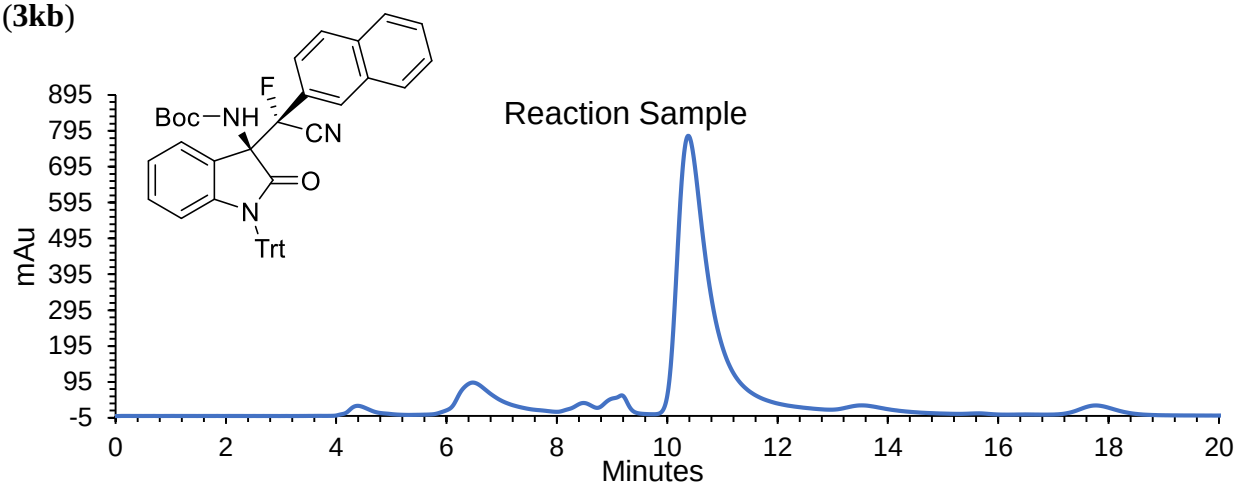
dr = 45.0:1, major ee = 86%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.315	18.3953
9.496	18.8296
12.062	31.3979
13.422	31.7771

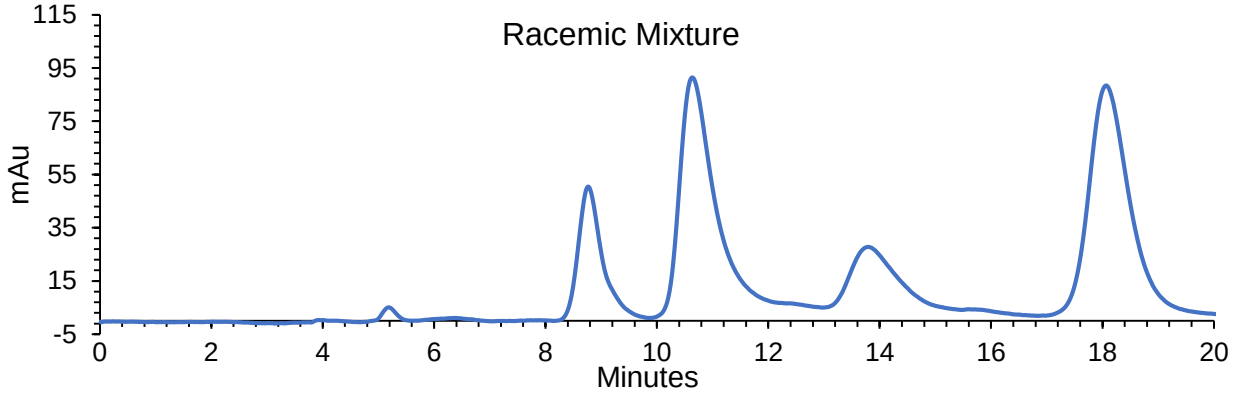
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(2-naphthyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3kb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.380	96.5062
17.774	3.4938

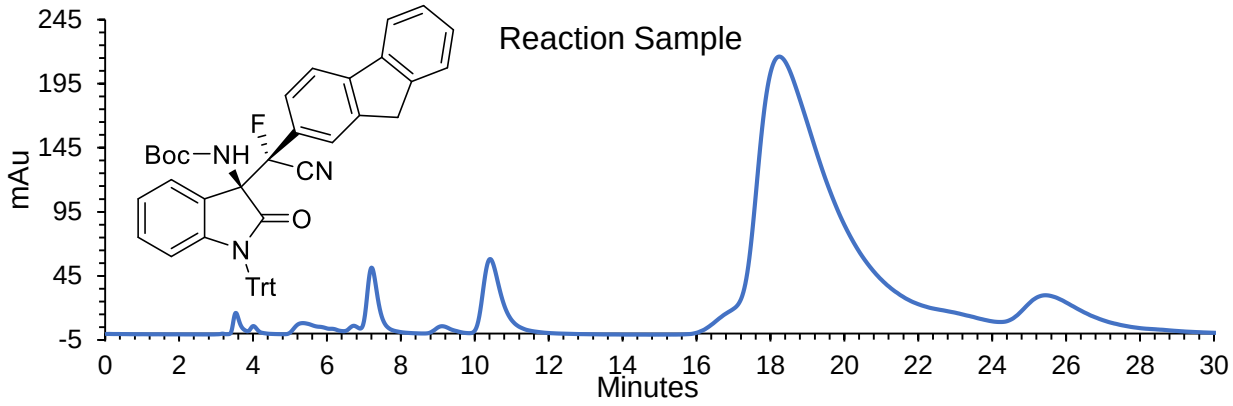
dr = 33.0:1, major ee = 93%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.769	12.0778
10.639	37.2049
13.878	13.8520
18.066	36.8653

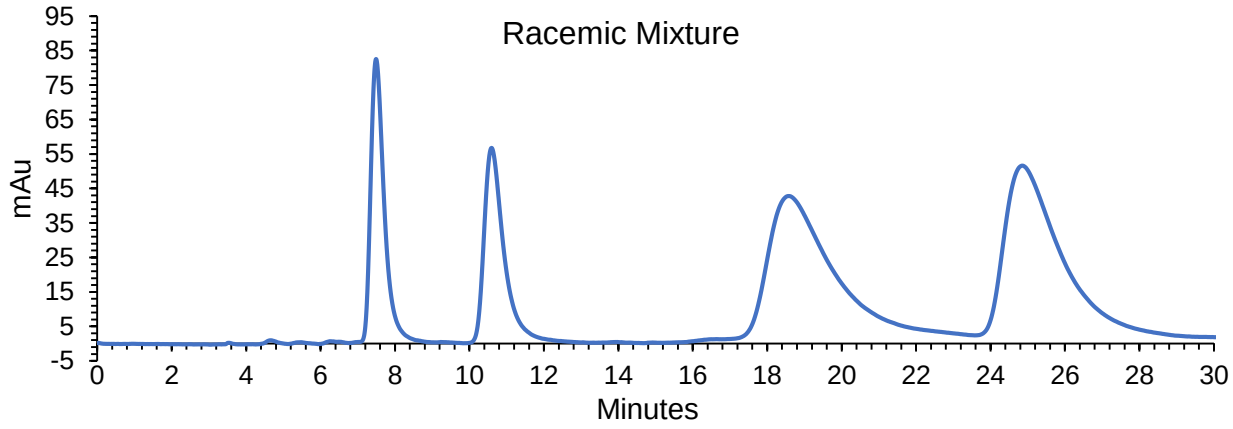
tert-Butyl ((*R*)-3-((*S*)-cyano(9H-fluoren-2-yl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**3lb**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
18.238	94.2969
25.440	5.7031

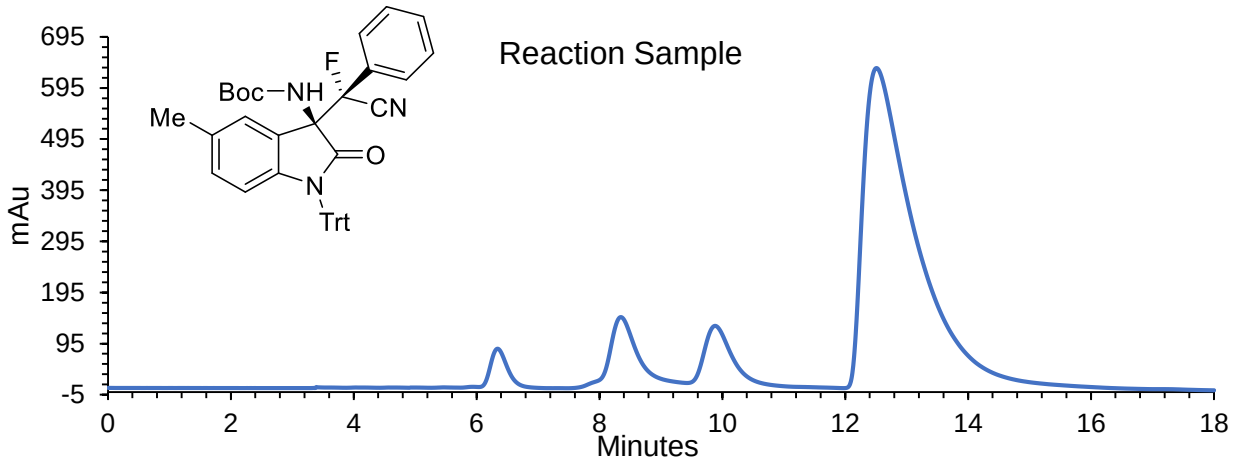
dr = 12.0:1, major ee = 88%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.488	14.4763
10.591	14.1141
18.571	34.7723
24.851	36.6373

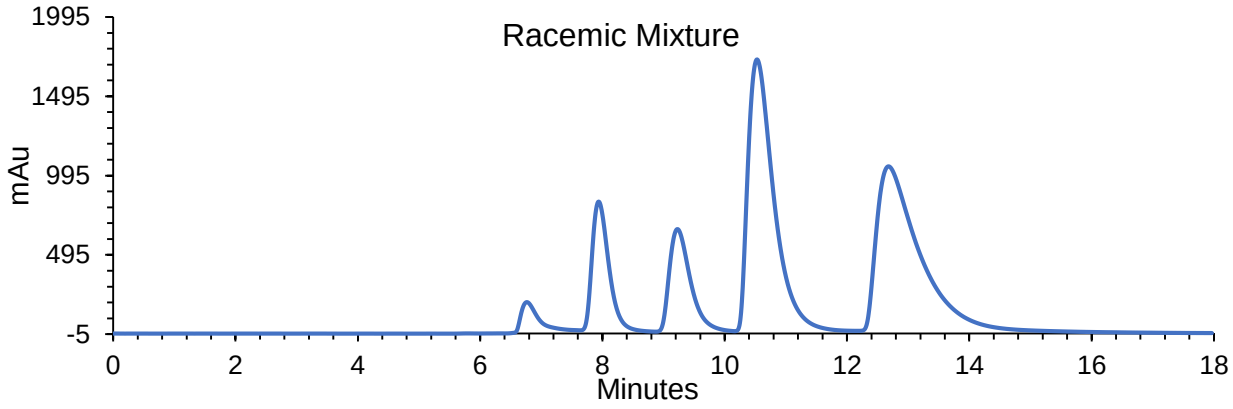
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ad**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.110	8.1233
12.657	91.8767

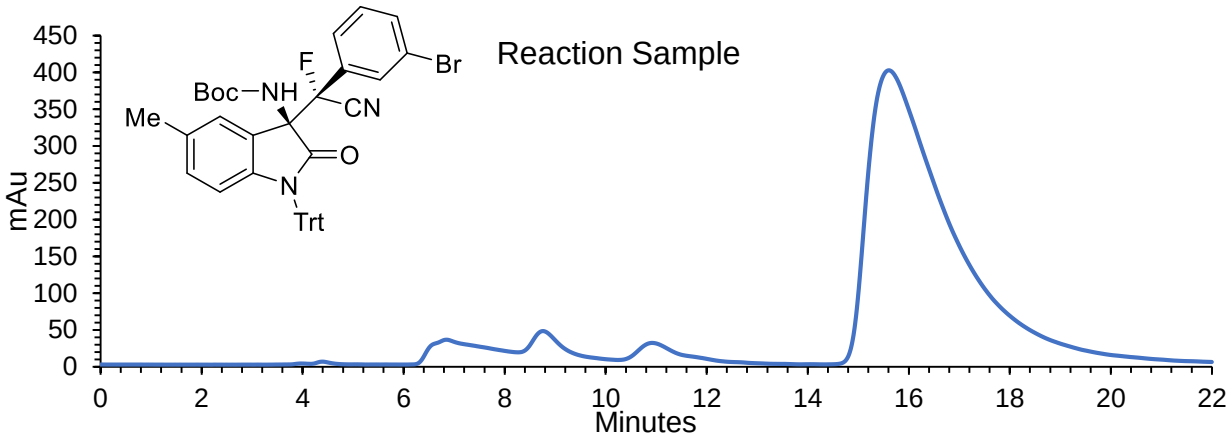
dr = 9.8:1, major ee = 84%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
6.338	12.2721
8.487	11.7683
10.304	38.2352
12.810	37.7244

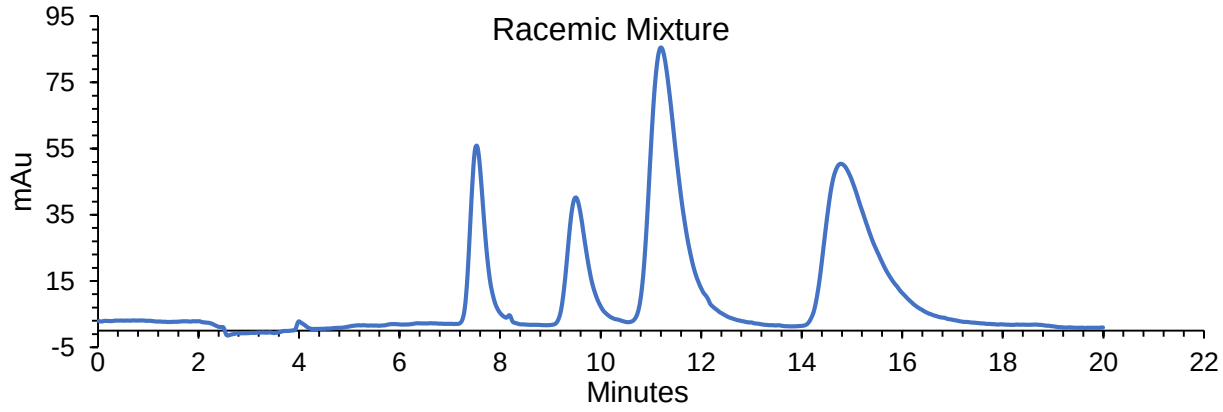
tert-Butyl ((*R*)-3-((*S*)-(3-bromophenyl)(cyano)fluoromethyl)-5-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3cd**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.907	1.9519
15.607	98.0481

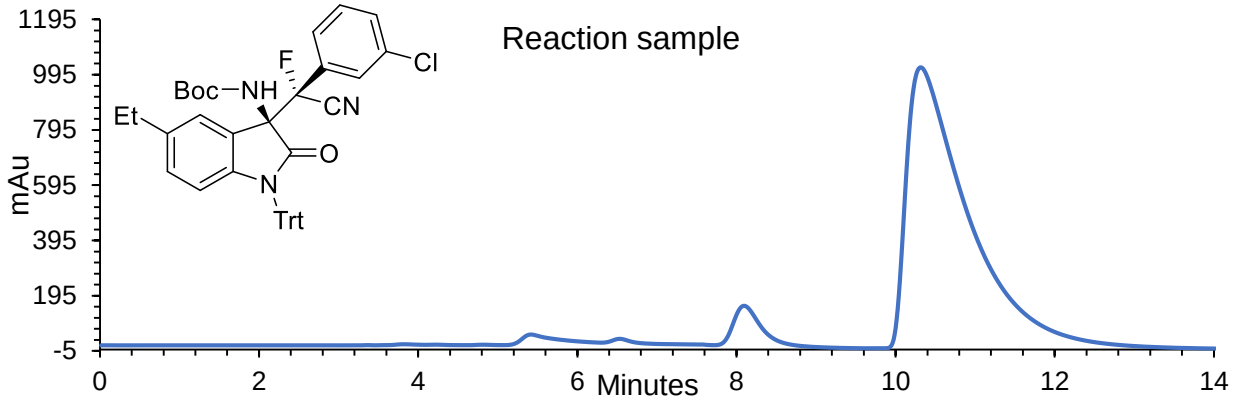
dr = 31.5:1, major ee = 96%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.529	12.1279
9.502	12.2120
11.200	39.2398
14.778	36.4203

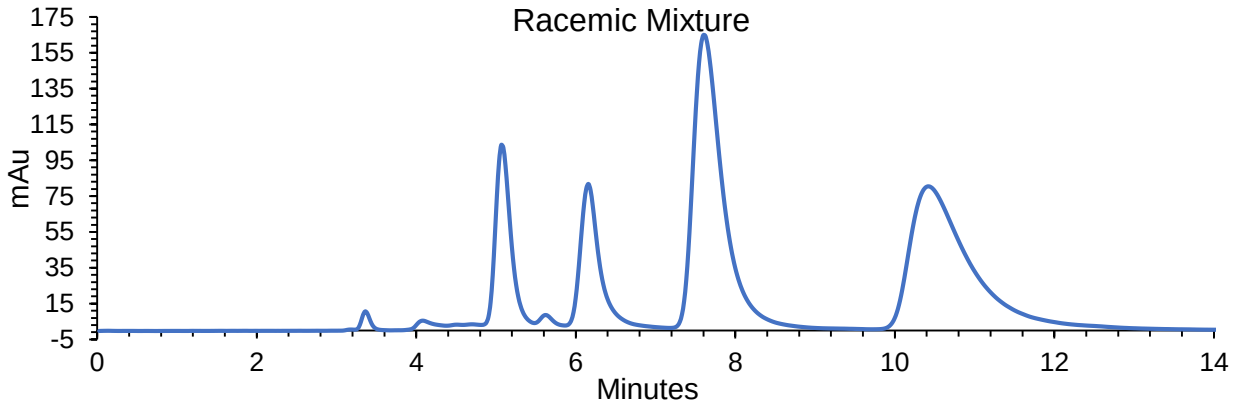
tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-ethyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3be**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.096	5.4445
10.316	94.5555

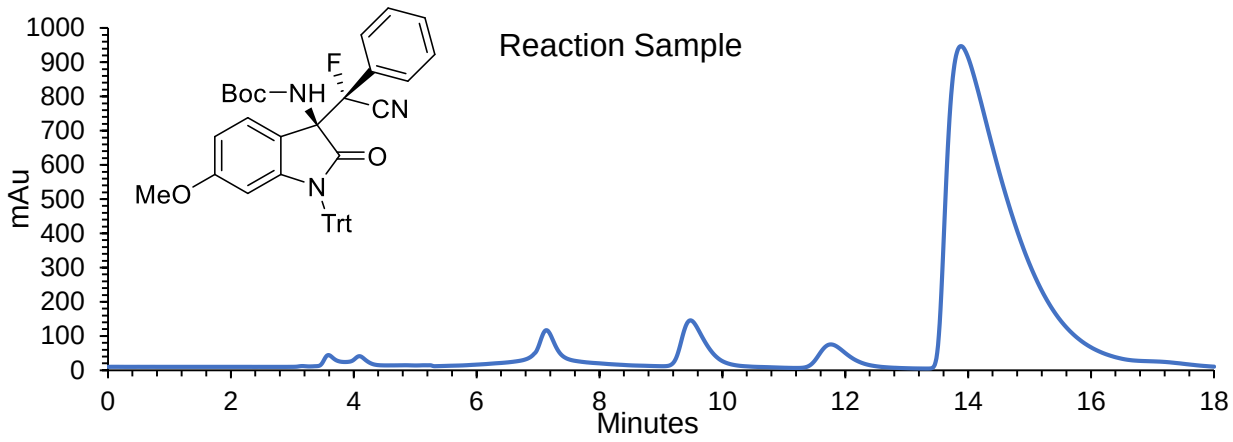
dr = 34.1:1, major ee = 89%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
5.075	12.1505
6.157	12.0943
7.610	38.3502
10.422	37.4050

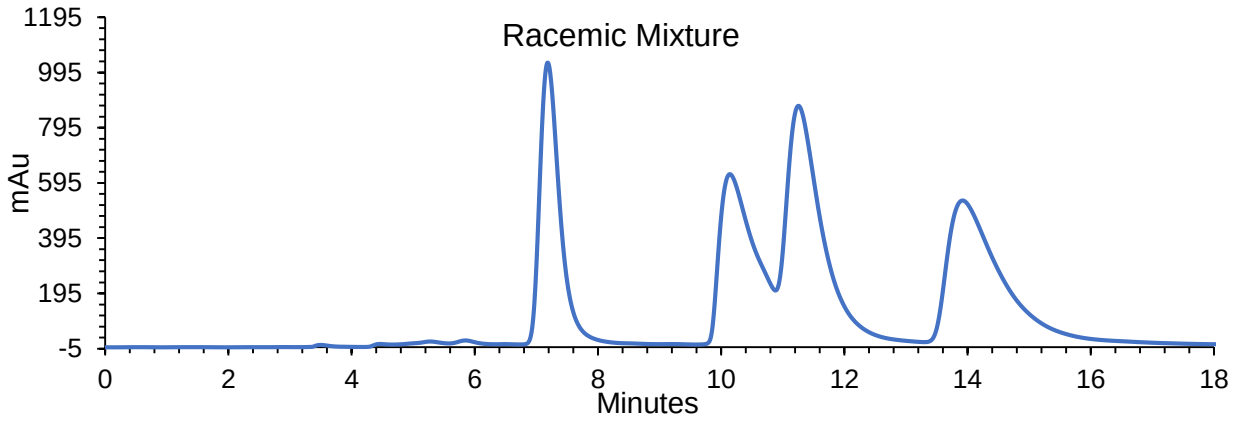
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3af**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.498	3.3118
14.031	96.6882

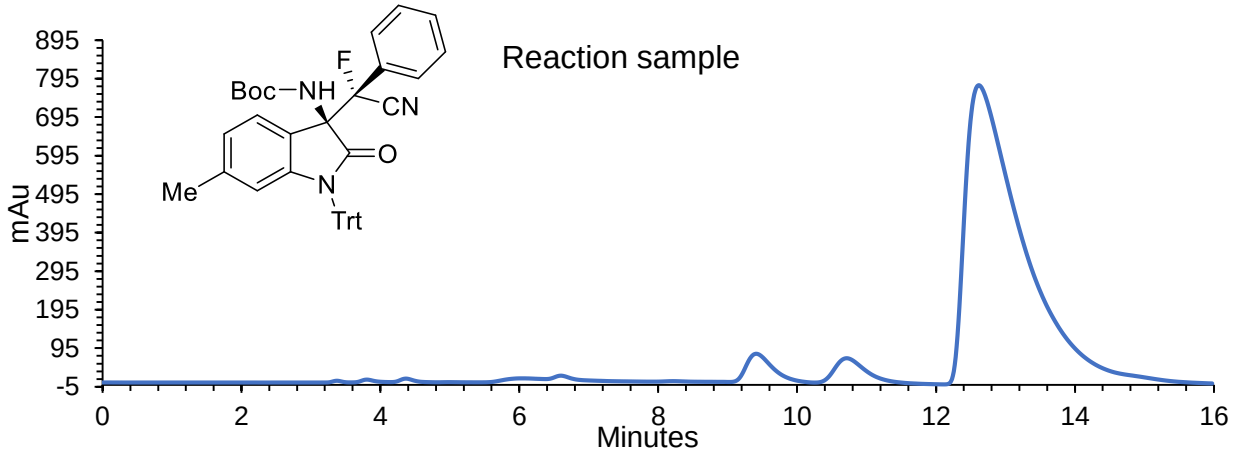
dr = 20.0:1, major ee = 93%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.185	20.3286
10.143	21.0017
11.257	30.8672
13.921	27.8026

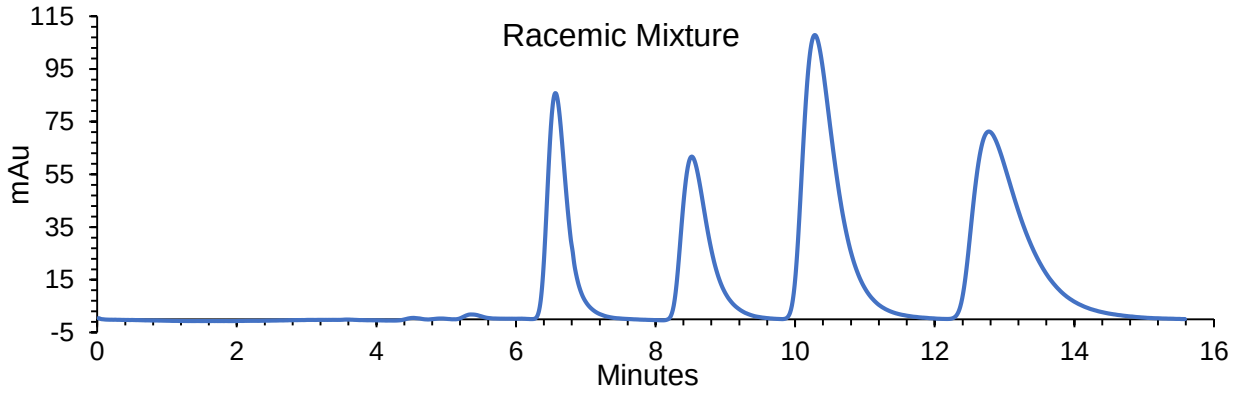
tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-6-methyl-2-oxo-1-tritylindolin-3-yl)carbamate (**3ag**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.710	4.1180
12.615	95.8820

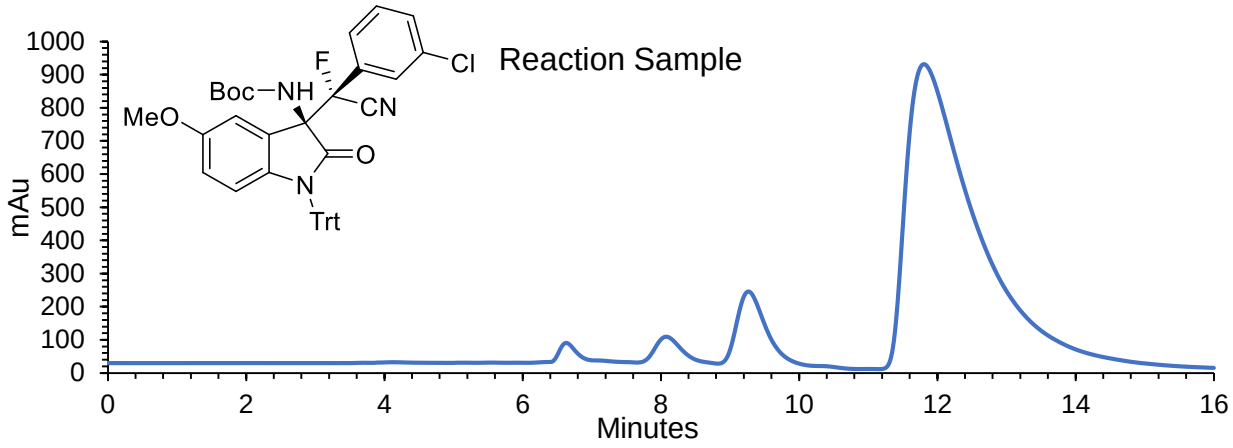
dr = 15.0:1, major ee = 92%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
6.566	16.1542
8.519	16.0271
10.283	34.4789
12.776	33.3398

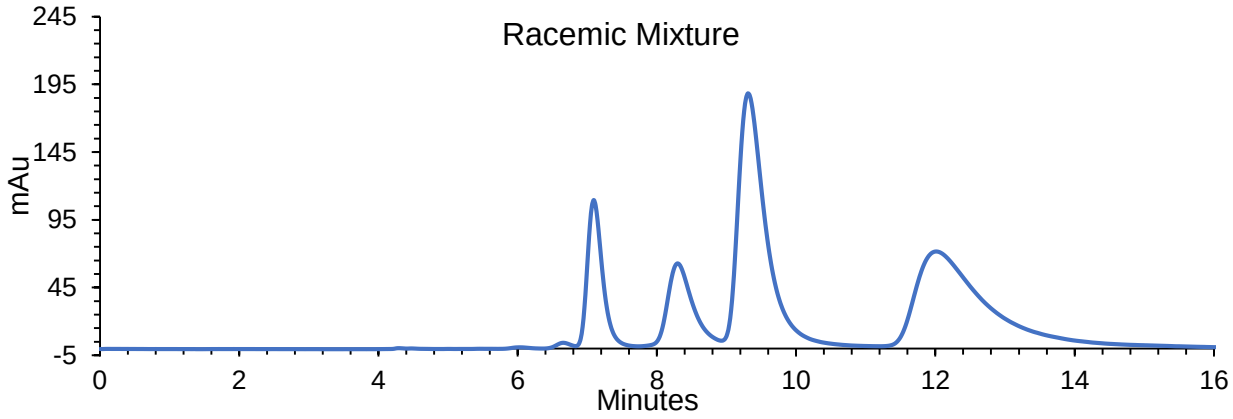
tert-Butyl ((*R*)-3-((*S*)-(3-chlorophenyl)(cyano)fluoromethyl)-5-methoxy-2-oxo-1-tritylindolin-3-yl)carbamate (**3bh)**



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
9.441	7.4428
11.948	92.5572

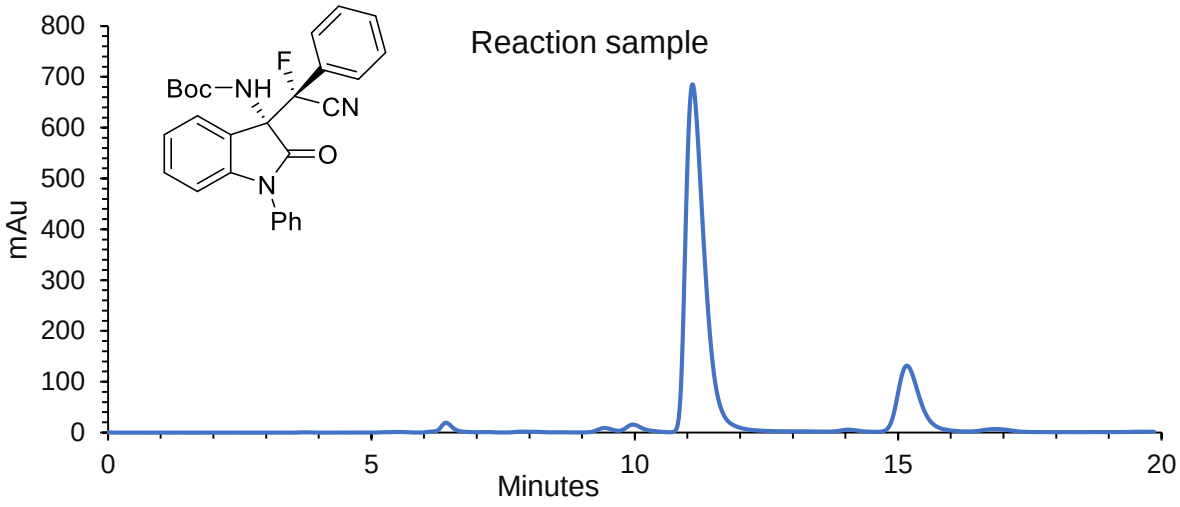
dr = 24.4:1, major ee = 85%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
7.058	12.4289
8.216	12.4276
9.304	38.6803
12.017	36.4632

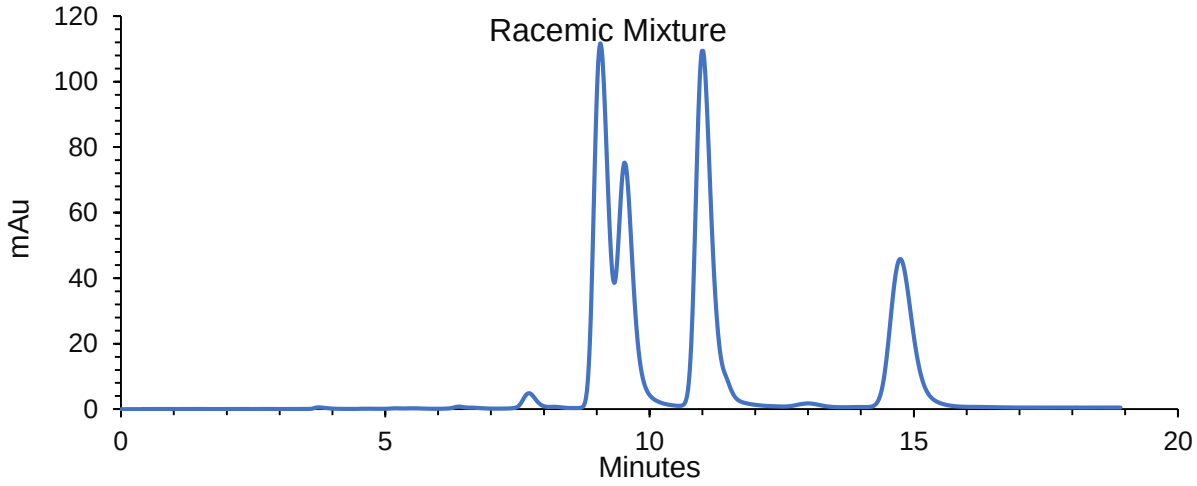
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(phenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ac**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
9.419	1.2693
11.093	98.7307

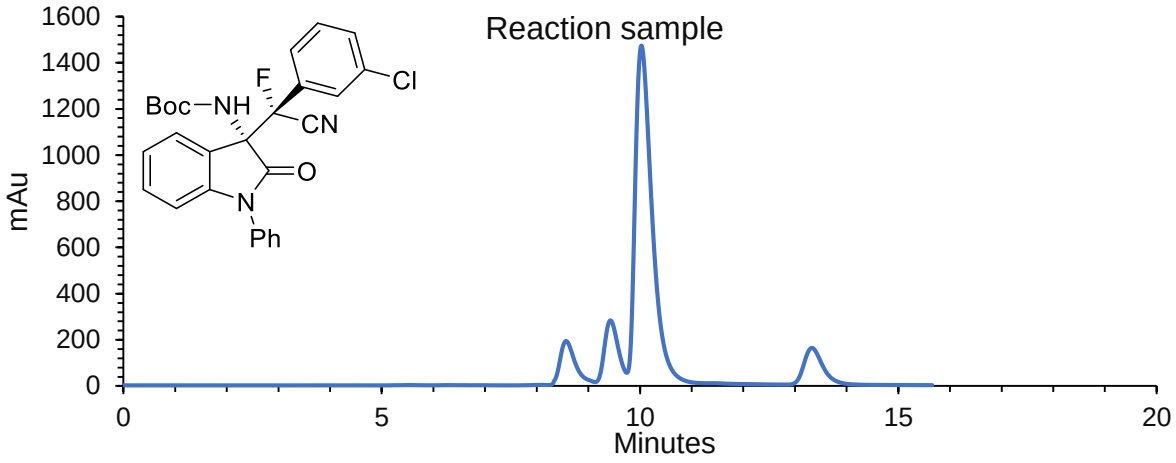
dr = 1:3.0, major ee = 97%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
9.071	28.5179
9.530	21.2529
11.003	31.7566
14.744	18.4727

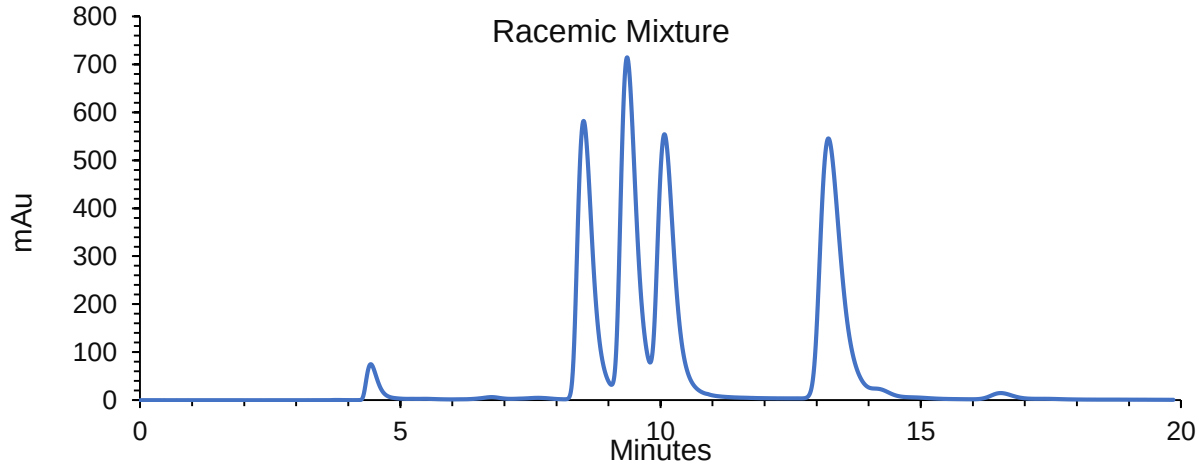
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-phenylindolin-3-yl) carbamate (**3bc**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.570	8.4763
10.029	91.5237

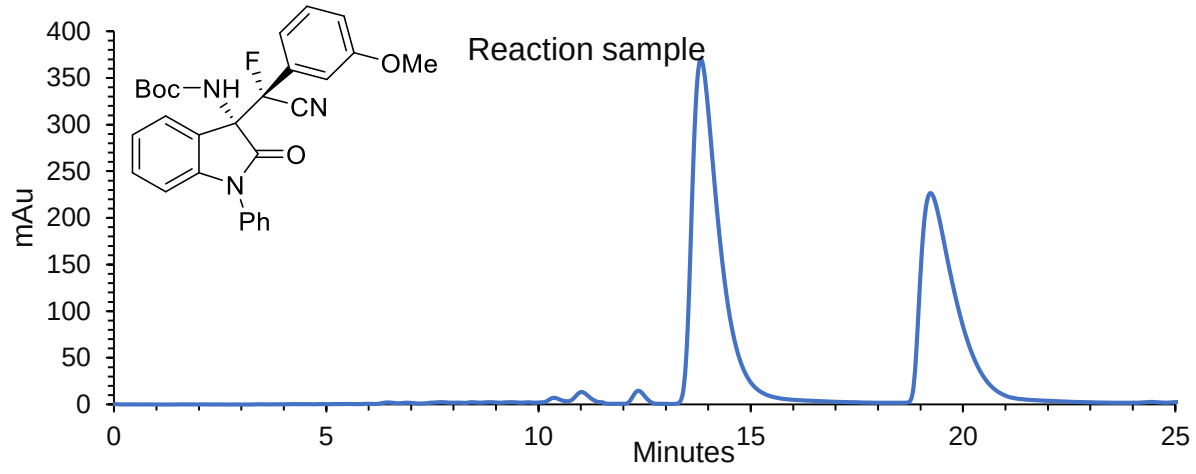
dr = 1:5.9, major ee = 83%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
8.522	21.3029
9.357	28.0775
10.075	23.0336
13.225	27.5861

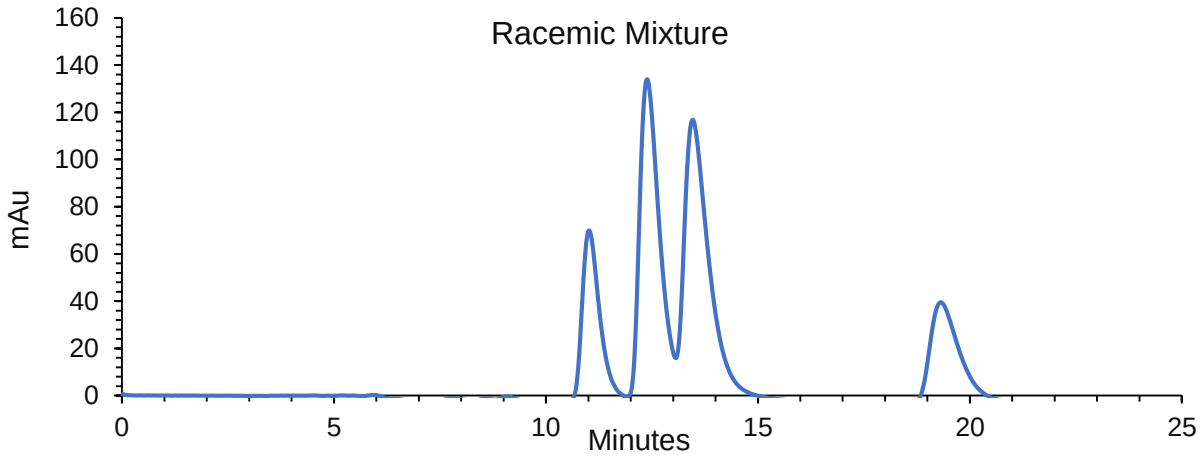
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3-methoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl) carbamate (**3ec**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
12.474	1.9638
13.827	98.0362

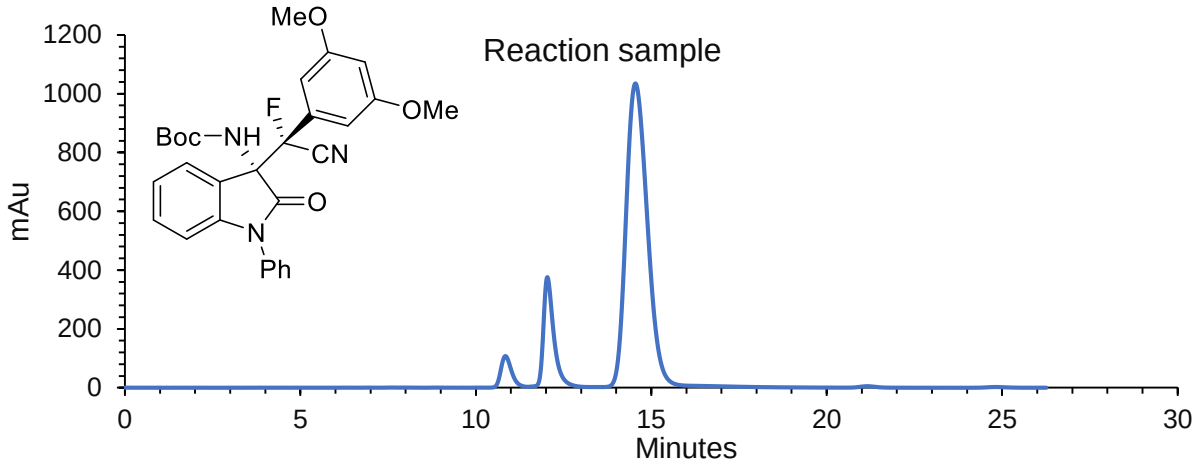
dr = 1:2.8, major ee = 96%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.018	15.7267
12.387	33.2605
13.462	35.9257
19.313	15.0871

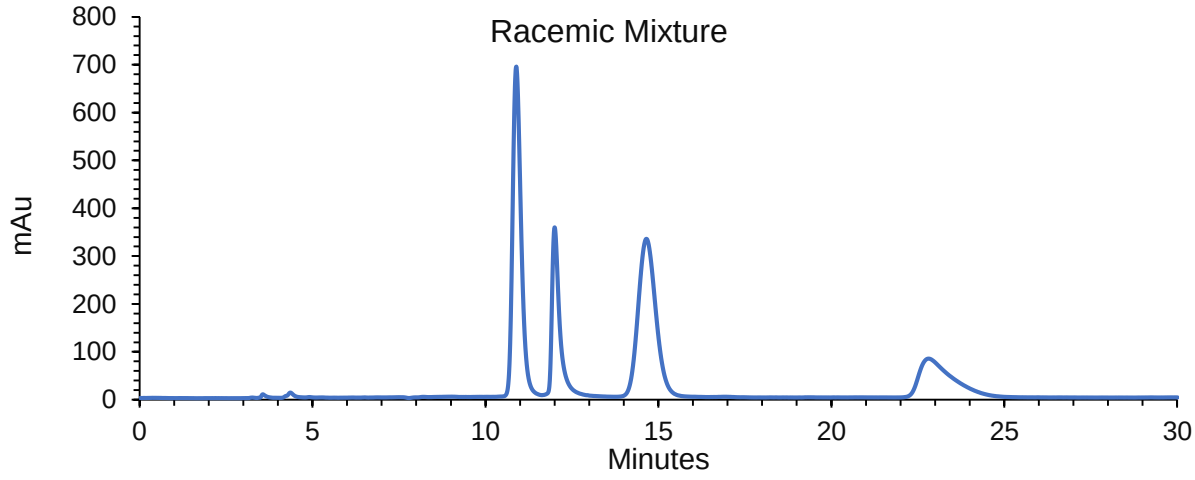
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(3,5-dimethoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ic**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.848	5.0399
14.552	94.9601

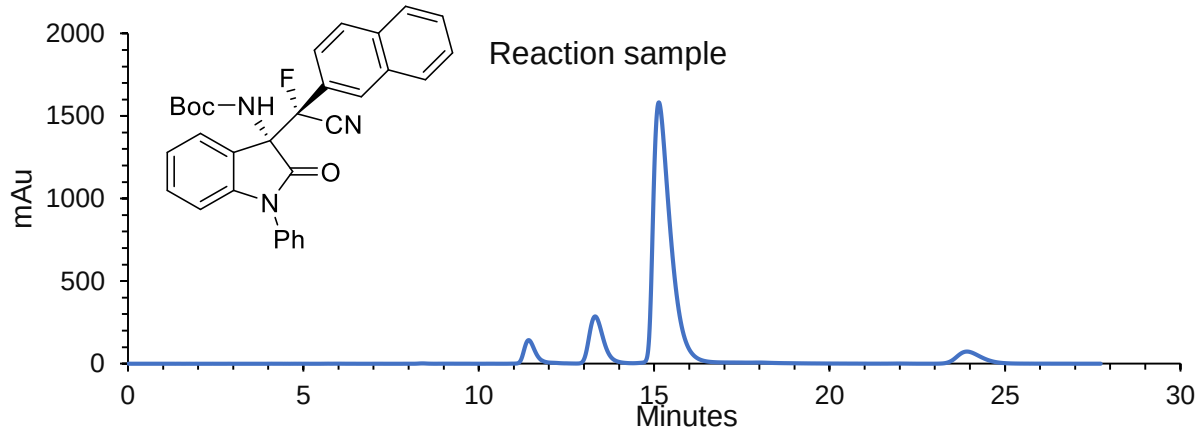
dr = 1:5.3, major ee = 90%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
10.886	34.4593
11.998	15.4849
14.651	32.6387
22.811	17.4171

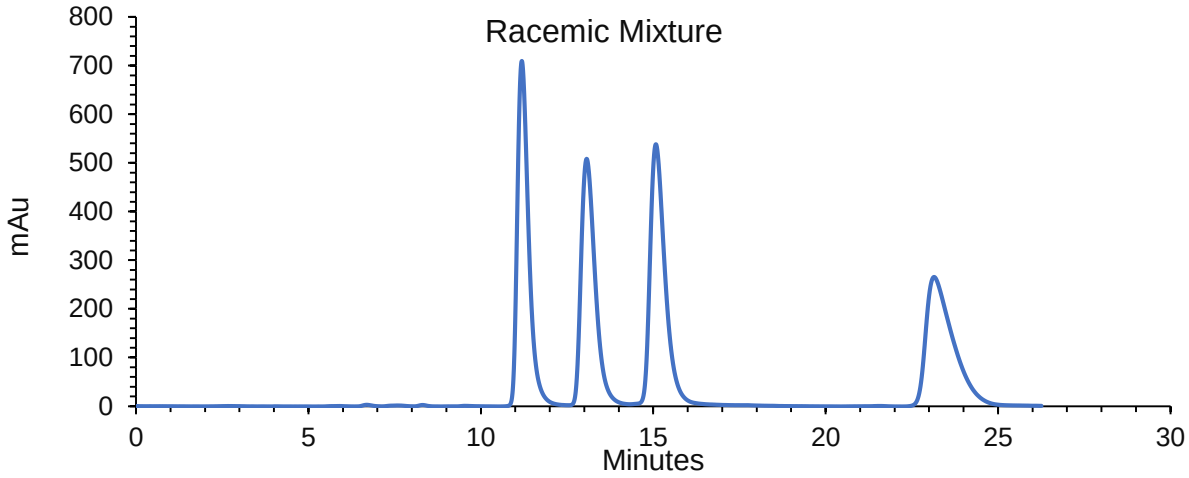
tert-Butyl ((*S*)-3-((*S*)-(cyanofluoro(2-naphthyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3kc**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.422	5.9705
15.133	94.0295

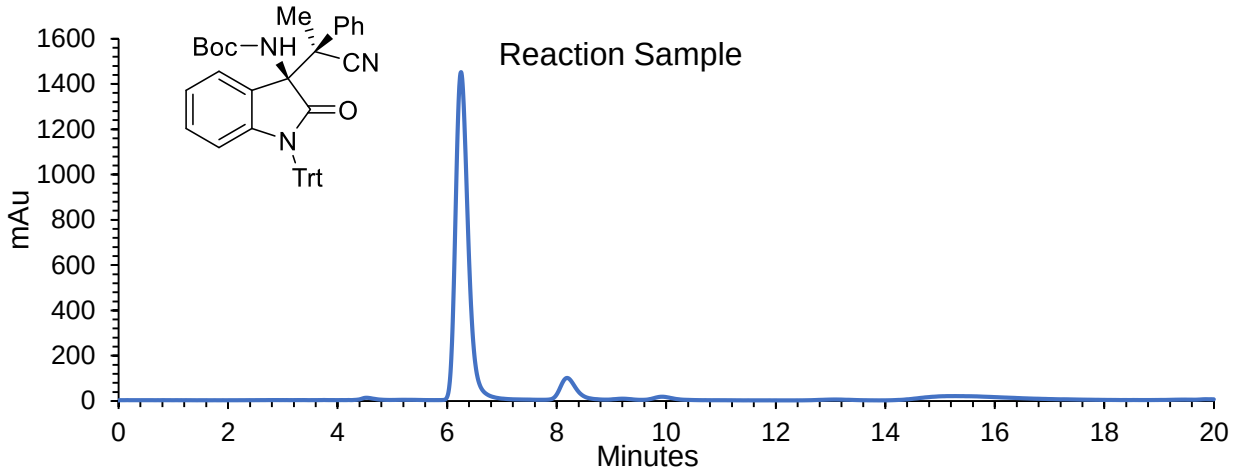
dr = 1:6.7, major ee = 88%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
11.186	26.4770
13.067	23.6692
15.074	26.6387
23.142	23.4824

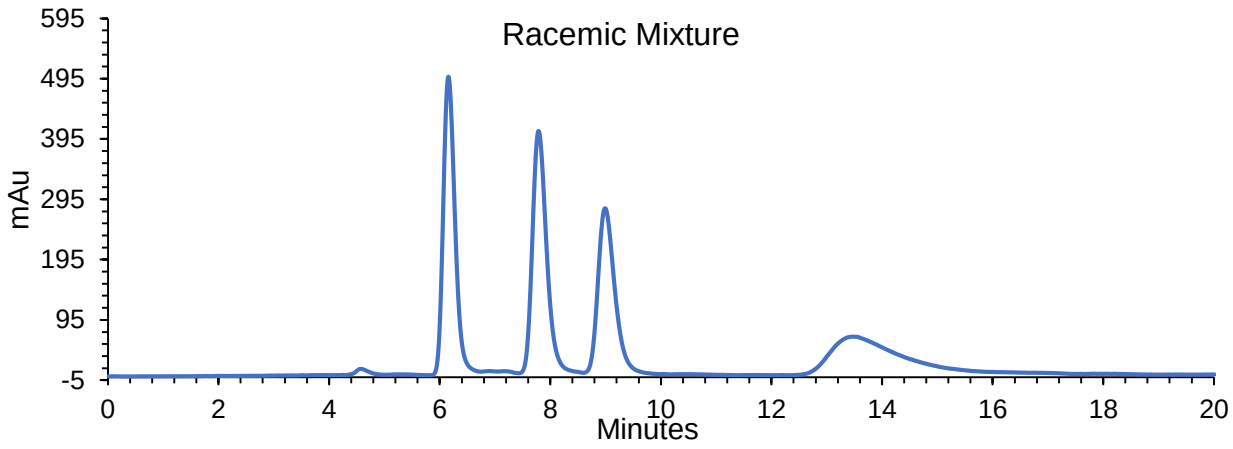
tert-Butyl ((*S*)-3-((*R*)-1-cyano-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**9**)



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
6.254	92.6403
8.187	7.3597

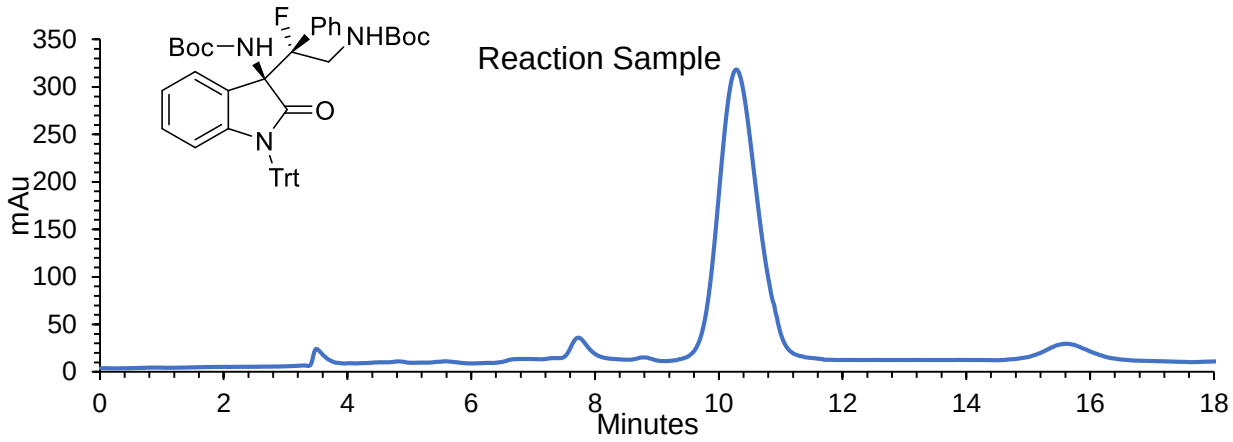
dr = >19:1, major ee = 85%



Signal 4: DAD1 D, Sig=254,2 Ref=550,100

Ret. Time [min]	Area %
6.157	33.4102
7.784	32.6024
8.997	16.5718
13.464	17.4156

tert-Butyl ((*R*)-3-((*R*)-2-((tert-butoxycarbonyl)amino)-1-fluoro-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**4**)

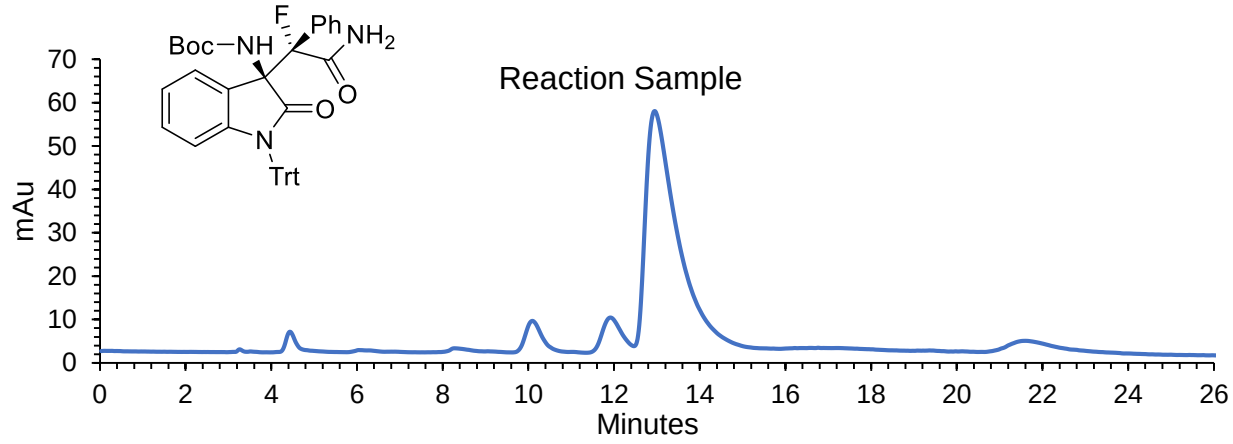


Signal 4: DAD1 D, Sig=245,2 Ref=550,100

Ret. Time [min]	Area %
10.282	94.2216
15.615	5.7784

dr = 11.5:1, major ee = 88%

tert-Butyl ((*R*)-3-((*S*)-2-amino-1-fluoro-2-oxo-1-phenylethyl)-2-oxo-1-tritylindolin-3-yl)carbamate (**5**)

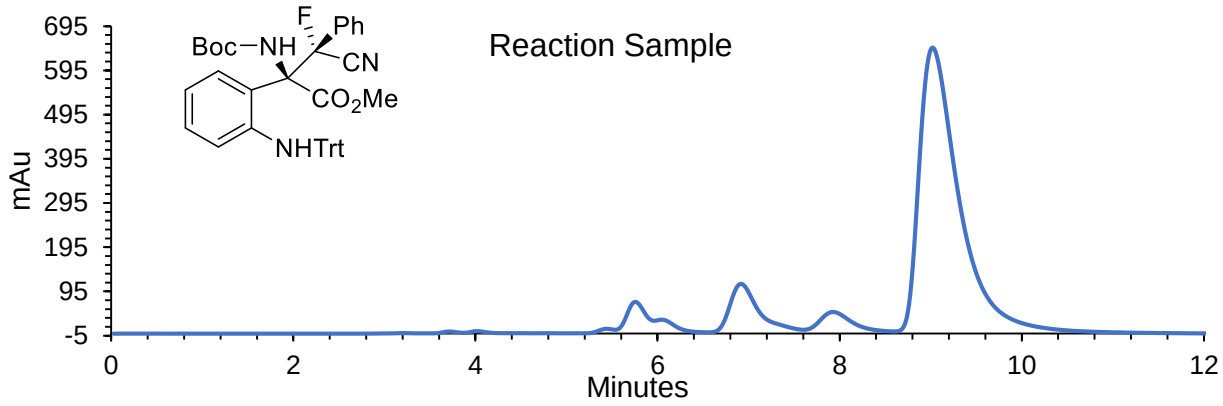


Signal 4: DAD1 D, Sig=245,2 Ref=550,100

Ret. Time [min]	Area %
12.948	93.8947
21.601	6.1053

dr = 12.0:1, major ee = 88%

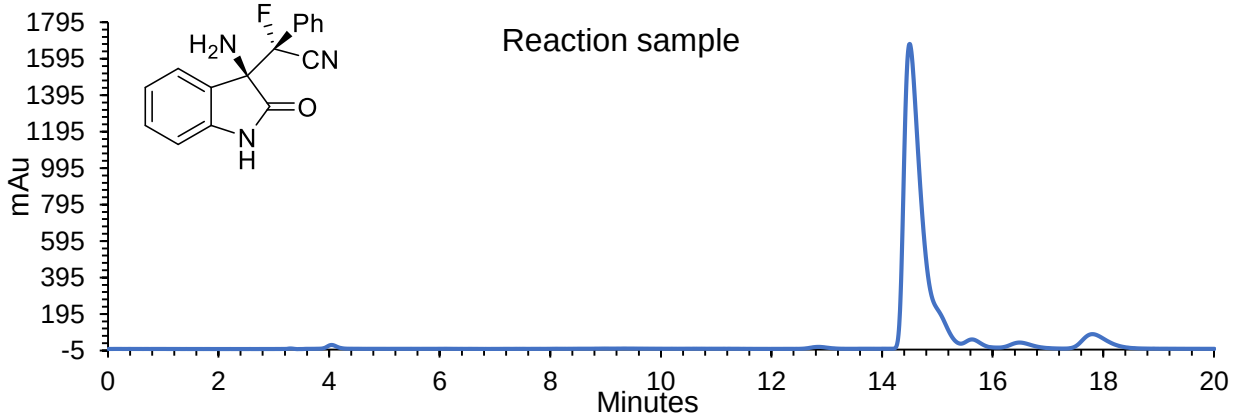
Methyl (2*R*,3*S*)-2-((*tert*-butoxycarbonyl)amino)-3-cyano-3-fluoro-3-phenyl-2-(2-(tritylamino)-phenyl)propanoate (**6**)




```
Signal 4: DAD1 D, Sig=245,2 Ref=550,100

  Ret. Time [min]          Area %

       7.930               4.2144

       9.023              95.7856
```

dr = 12.0:1, major ee = 91%

(*S*)-2-((*R*)-3-amino-2-oxoindolin-3-yl)-2-fluoro-2-phenylacetonitrile (**7**)

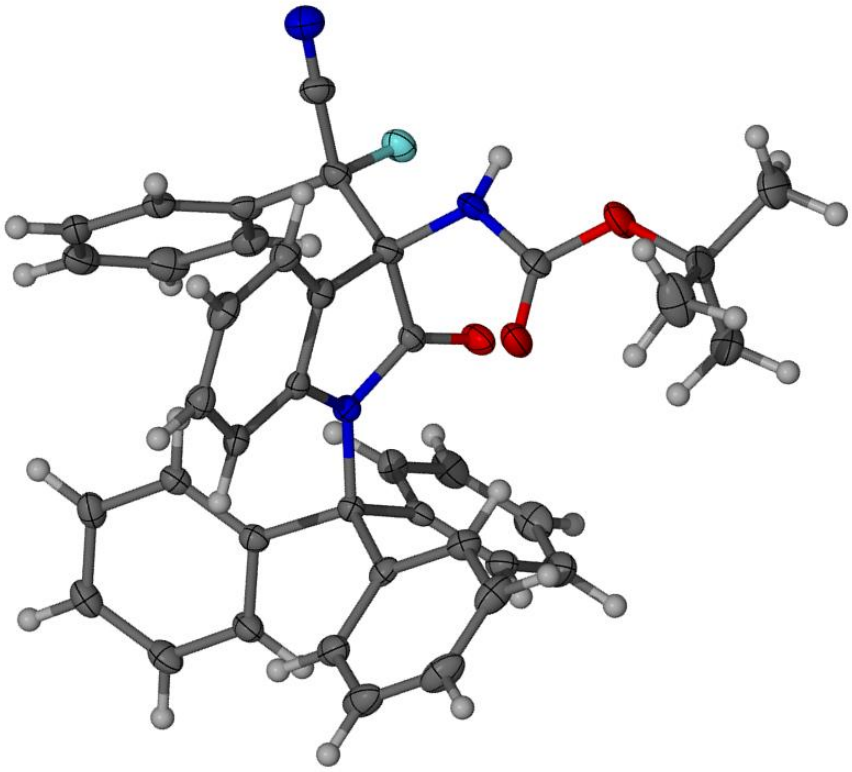



```
Signal 4: DAD1 D, Sig=254,2 Ref=550,100

  Ret. Time [min]          Area %

      14.505              94.3396

      17.798               5.6604
```

dr = 12.0:1, major ee = 89%

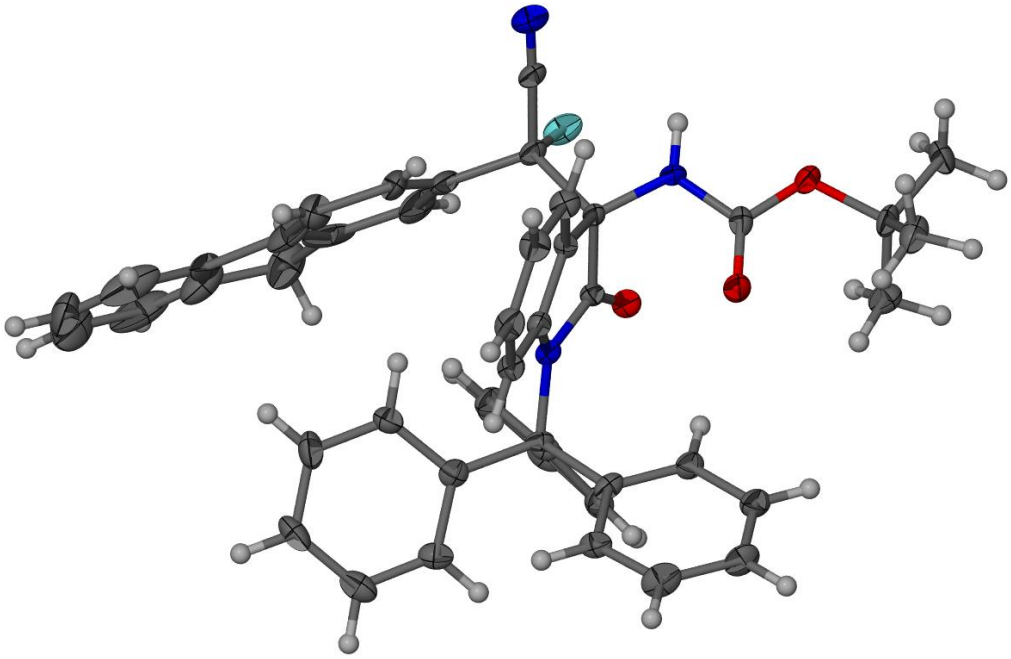
7. Crystallographic Data

tert-Butyl ((*R*)-3-((*S*)-cyanofluoro(phenyl)methyl)-2-oxo-1-tritylindolin-3-yl)carbamate **3ab**



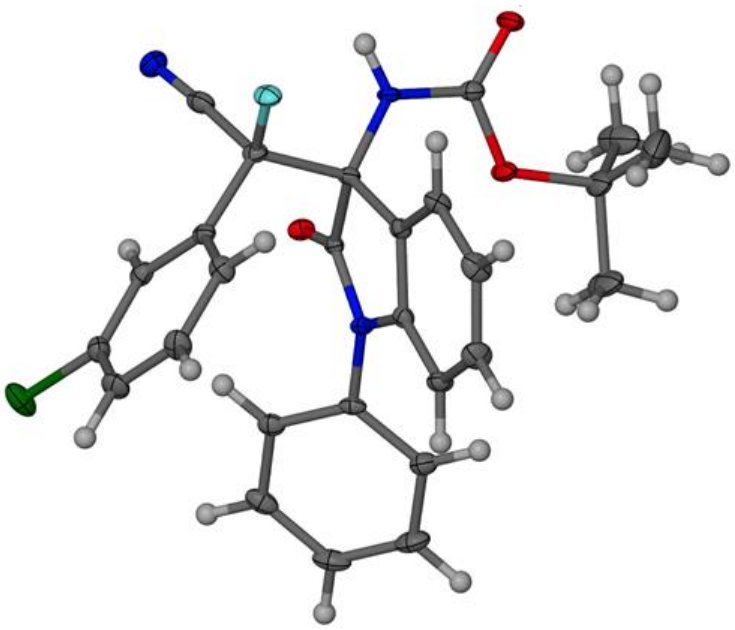
A single crystal was obtained by slow evaporation of a solution of **3ab** in ethanol. Single crystal X-ray analysis was performed at 100 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and corrected using the APEX 3 program. 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: $C_{40}H_{34}FN_3O_3$, C_2H_6O, M = 669.77, colorless prism, 0.282 x 0.213 x 0.089 mm^3, monoclinic, space group $P2_1$, a = 9.9121(4), b = 39.1264(17), c = 9.9531(5) Å, V = 3525.4(3) Å^3, Z = 4. Absolute structure parameter = -0.01(5).[3]

tert-Butyl ((*R*)-3-((*S*)-cyano(9H-fluoren-2-yl)fluoromethyl)-2-oxo-1-tritylindolin-3-yl)carbamate **3lb**



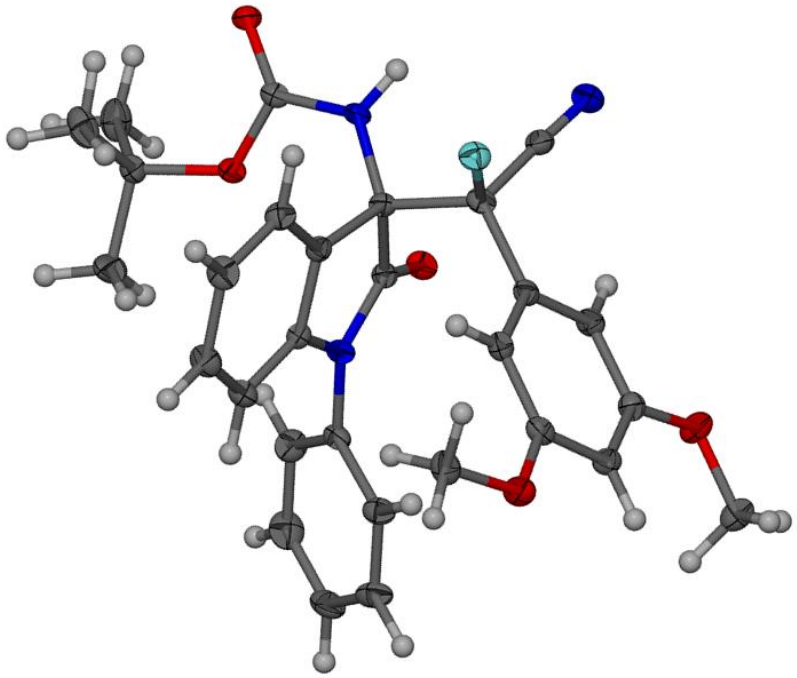
A single crystal was obtained by slow evaporation of a solution of **3lb** in hexanes/ethyl ether/dichloromethane (2:2:1). Single crystal X-ray analysis was performed at 100 K using a Siemens platform diffractometer with graphite monochromated Mo-Kα radiation (λ = 0.71073 Å). Data were integrated and 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: $C_{47}H_{38}FN_3O_3$, CH_2Cl_2, M = 796.73, colorless prism, 0.444 x 0.408 x 0.153 mm^3, orthorhombic, space group $P2_12_12_1$, a = 9.0002(7), b = 20.7380(17), c = 21.1515(17) Å, V = 3947.9(5) Å^3, Z = 4. Absolute structure parameter = 0.04(3).[3]

syn-tert-Butyl (3-(cyanofluoro(3-chlorophenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3bc**)



A single crystal was obtained by slow evaporation of a solution of **3bc** in hexanes/ethanol/chloroform (3:1:1). 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: $C_{27}H_{23}ClFN_3O_3$, M = 491.93, colorless prism, 0.35 x 0.12 x 0.04 mm^3, monoclinic, space group $P2_1/c$ a = 15.1949(7), b = 8.5818(4), c = 20.7071(10) Å, V = 2515.5(2) Å^3, Z = 4.

tert-Butyl ((*S*)-3-((*S*)-cyanofluoro(3,5-dimethoxyphenyl)methyl)-2-oxo-1-phenylindolin-3-yl)carbamate (**3ic**)



A single crystal was obtained by layering of a solution of **3ic** with hexanes / ethanol / chloroform (3:1:1). 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: $C_{29}H_{28}FN_3O_5$, M = 517.54, colorless plate, 0.41 x 0.27 x 0.08 mm^3, monoclinic, space group $P2_1$, a = 8.9884(5), b = 20.0594(11), c = 14.4200(8) , V = 2600.0(2) Å^3, Z = 4. Absolute structure parameter = 0.058(151).[4]

8. References

1 a) LeTourneau, M. E.; McCarthy, J. R., A Novel Synthesis of α-Fluoroacetonitriles. Application to A Convenient Preparation of 2-Fluoro-2-phenethylamines. *Tetrahedron Lett.* **1984**, *46*, 5227-5230. b) Venkatachalam, T. K.; Uckun, F. M., Synthesis of β-Fluorophenethyl Halopyridyl Thiourea Compounds as Non-nucleoside Inhibitors of HIV-1 Reverse Transcriptase. *Synth. Commun.* **2004**, *13*, 2463-2472.

2 Nakamura, S.; Hyodo, K.; Nakamura, M.; Nakane, D.; Masuda, H., Catalytic Enantioselective Allylation of Ketimines by Using Palladium Pincer Complexes with Chiral Bis(imidazoline)s. *Chem. Eur. J.* **2013**, *19*, 7304-7309.

3 Flack, H. D., On Enantiomorph-polarity Estimation. *Acta Cryst.* **1983**, *A39*, 876-881.

4 Parsons, S.; Flack, H. D.; Wagner, T., Use of Intensity Quotients and Differences in Absolute Structure Refinement. *Acta Cryst*. **2013**, *B69*, 249-259.