Supplementary Materials

Asymmetric difluoroalkylation *via* Michael addition of *in situ* generated difluoroenol intermediate

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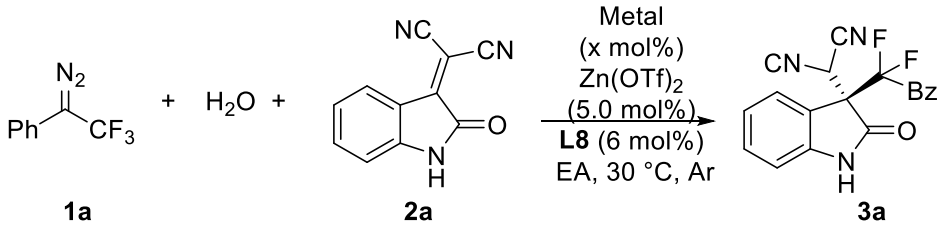
1. General Information

All reactions were performed in oven-dried glassware under atmosphere of argon. Solvents were purified and distilled by following the standard methods. Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). Flash column chromatography was performed using silica gel (300-400 mesh).The ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400 MHz and 500 MHz spectrometer; chemical shifts were reported in ppm with the solvent signal as reference, and coupling constants (*J*) were given in Hertz. The peak information was described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. The enantioselectivity was determined on HPLC using Chiralpak AD-H and IG-3 column. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI Source). All substrates whose syntheses were not described herein were either obtained from commercial suppliers or prepared using the referenced literature procedures.[1-4] Unless stated otherwise, all commercially available compounds (Energy Chemical, Bidepharmatech) were used as received.

2. Condition Optimization

Table S1: Optimization of metal catalysts.[a]



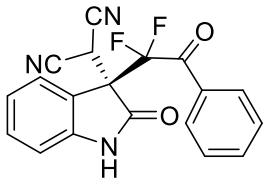
1a **2a** **3a**

Entry	Metal (x mol%)	Yield %[b] **3a**	*ee* %[c]
1	$Rh_2(OAc)_4$(2.0 mol%)	35	95
2	$Rh_2(esp)_2$ (1.0 mol%)	95	95
3	$Cu(MeCN)_4PF_6$ (5.0 mol%)	<5	-
4	FeTPPCl (5.0 mol%)	<5	-
5	CoTPP (5.0 mol%)	<5	-
6	$Pd(OAc)_2$(5.0 mol%)	<5	-

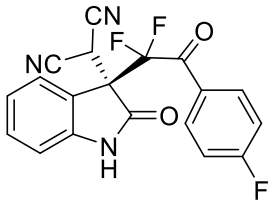
[a]The reaction was carried out on a 0.1 mmol scale: to the mixture of metal catalyst (x mol%), H_2O (2.7 μL, 0.15 mmol), $Zn(OTf)_2$ (1.9 mg, 5.0 mol%), and **L8** (5.2 mg, 6.0 mol%) in EA (0.5 mL), was added a solution of diazo compound **1a** (27.9 mg, 0.15 mmol) and **2a** (19.5 mg, 0.1 mmol) in EA (1.0 mL) *via* syringe in one pot under an argon atmosphere at 30 ℃, and the reaction mixture was stirred for additional 3 h under these conditions.

3. General Procedure for the Asymmetric Michael Addition Reaction

To a 10-mL oven-dried vial containing a magnetic stirring bar, $Rh_2(esp)_2$ (0.8 mg, 1.0 mol%,), H_2O (2.7 μL, 0.15 mmol), $Zn(OTf)_2$ (1.9 mg, 5.0 mol%) and **L8** (6.0 mol%) in Ethyl acetate (EA, 0.5 mL), wad added a solution of diazo compound **1** (0.15 mmol) in 0.5 mL EA and **2** (0.1 mmol) in 1.0 mL EA *via* syringe in one pot under an argon atmosphere at 30 ℃ after 15 min, and the reaction mixture was stirred for an additional 3 h under these conditions until consumption of the material (monitored by TLC). Then the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 4:1 to 2:1) to give the pure products **3** and **4** in good to high yields with excellent enantioselectivity.

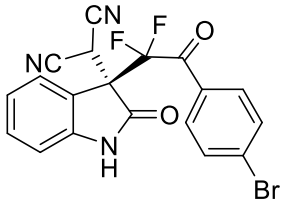


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (3a). Pale yellow solid. mp = 169 - 171 ℃, 33.3 mg, 95% yield. 95% *ee*. $[\alpha]_D^{20}$ = +7.1 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.78 (s, 1H), 8.02 – 7.97 (m, 2H), 7.70 – 7.61 (m, 2H), 7.50 – 7.44 (m, 2H), 7.46 – 7.39 (m, 1H), 7.18 – 7.11 (m, 1H), 7.07 – 7.01 (m, 1H), 4.95 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.5 (t, *J* = 36.0 Hz), 170.8 (d, *J* = 7.6 Hz), 142.0, 135.6, 132.1, 130.7, 130.5 (t, *J* = 3.3 Hz), 129.0, 125.9 (d, *J* = 3.3 Hz), 124.1, 120.9 (d, *J* = 3.7 Hz), 117.0 (dd, *J* = 272.1, 267.8 Hz), 111.6, 109.8, 109.0, 55.7 (t, *J* = 20.3 Hz), 27.1 (d, *J* = 5.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 309.3 Hz, 1F), -98.7 (d, *J* = 309.7 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{11}F_2N_3O_2Na$ $[M+Na]^+$: 374.0717, found 374.0711; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3, λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, t_{major} = 18.3 min, t_{minor} = 15.8 min.

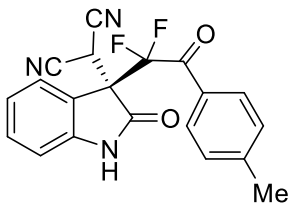


(*R*)-2-(3-(1,1-Difluoro-2-(4-fluorophenyl)-2-oxoethyl)-2-oxoindolin-3-yl)malononitrile (3b). Pale yellow solid. mp = 73 - 75 ℃, 33.2 mg, 90% yield. 96% *ee*. $[\alpha]_D^{20}$ = +9.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.62 (s, 1H), 8.09 – 8.01 (m, 2H), 7.70 – 7.64 (m, 1H), 7.48 – 7.39 (m, 1H), 7.21 – 7.10 (m, 3H), 7.08 – 7.01 (m, 1H), 4.93 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 184.2 (t, *J* = 30.8 Hz), 170.6 (d, *J* = 7.6 Hz), 168.5, 165.9, 142.0, 133.5, 132.2, 126.0 (d, *J* = 3.4 Hz), 124.2, 120.9 (d, *J* = 3.5 Hz), 117.0 (dd, *J* = 271.6, 267.8 Hz), 116.5 (d, *J* = 21.9

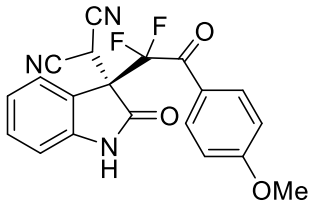
Hz), 111.7 (d, J = 7.9 Hz), 109.8, 108.9, 55.7 (t, J = 20.3 Hz), 27.1; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, J = 309.2 Hz, 1F), -98.6 (d, J = 309.2 Hz, 1F), -99.5 (s, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_3N_3O_2Na$ $[M+Na]^+$: 392.0623, found 392.0625; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3, λ = 254 nm, hexane : 2-propanol = 83:17, flow rate = 1.0 mL/min, t_{major} = 19.1 min, t_{minor} = 12.6 min.



(*R*)-2-(3-(2-(4-Bromophenyl)-1,1-difluoro-2-oxoethyl)-2-oxoindolin-3-yl)malononitrile (3c). Pale yellow solid. mp = 78 - 79 ℃, 36.1 mg, 84% yield. 92% *ee*. $[\alpha]_D^{20}$ = +10.2 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.70 (s, 1H), 7.95 – 7.79 (m, 2H), 7.69 – 7.63 (m, 1H), 7.64 – 7.59 (m, 2H), 7.47 – 7.40 (m, 1H), 7.19 – 7.12 (m, 1H), 7.06 – 7.01 (m, 1H), 4.93 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 184.9 (t, J = 30.9 Hz), 170.6 (d, J = 7.7 Hz), 141.9, 132.5, 132.2, 131.8 (t, J = 3.3 Hz), 131.5, 129.4, 126.0 (d, J = 3.4 Hz), 124.2, 120.7 (d, J = 3.6 Hz), 116.9 (dd, J = 271.6, 267.3 Hz), 111.6, 109.7, 108.9, 55.6 (t, J = 20.3 Hz), 27.1 (dd, J = 8.3, 2.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -97.3 (d, J = 309.3 Hz, 1F), -98.9 (d, J = 309.3 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}BrF_2N_3O_2Na$ $[M+Na]^+$: 451.9822, found 451.9820; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 52.5 min, t_{minor} = 28.2 min.

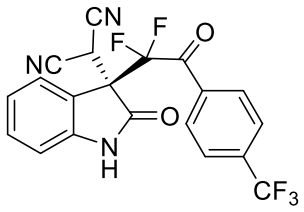


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-(p-tolyl)ethyl)-2-oxoindolin-3-yl)malononitrile (3d). Pale yellow foamy solid. mp = 63 - 66 ℃, 32.8 mg, 90% yield. 95% *ee*. $[\alpha]_D^{20}$ = +14.4 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.44 (s, 1H), 7.97 – 7.86 (m, 2H), 7.69 – 7.64 (m, 1H), 7.51 – 7.36 (m, 1H), 7.30 – 7.26 (m, 2H), 7.15 (m, 1H), 7.15 – 6.97 (m, 1H), 4.91 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.0 (t, *J* = 30.2 Hz), 170.6 (d, *J* = 7.8 Hz), 147.2, 141.9, 132.0, 130.7 (d, *J* = 3.2 Hz), 129.8, 128.1, 126.0 (d, *J* = 3.4 Hz), 124.0, 121.1 (d, *J* = 3.7 Hz), 117.8 (dd, *J* = 267.8, 268.0 Hz), 111.5, 109.8, 109.0, 55.6 (t, *J* = 20.3 Hz), 27.1 (d, *J* = 9.5 Hz), 22.1; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.6 (d, *J* = 309.2 Hz, 1F), -98.5 (d, *J* = 309.1 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_2Na$ $[M+Na]^+$: 388.0874, found 388.0874; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 25.2 min, t_{minor} = 31.8 min.

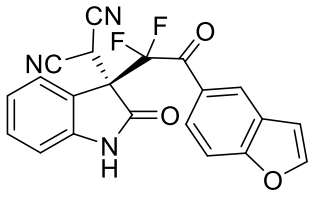


(*R*)-2-(3-(1,1-Difluoro-2-(4-methoxyphenyl)-2-oxoethyl)-2-oxoindolin-3-yl)malononitrile (3e). Pale yellow solid. mp = 70 - 72 ℃, 35.4 mg, 93% yield. 96% *ee*. $[\alpha]_D^{20}$ = +17.5 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.23 (s, 1H), 8.03 – 7.98 (m, 2H), 7.70 – 7.64 (m, 1H), 7.47 – 7.40 (m, 1H), 7.18 – 7.13 (m, 1H), 7.08 – 7.01 (m, 1H), 6.98 – 6.89 (m, 2H), 4.89 (s, 1H), 3.88 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 183.7 (t, *J* = 29.9 Hz), 170.6 (d, *J* = 7.9 Hz), 165.5, 141.9, 133.2 (d, *J* = 3.3 Hz), 132.0, 126.0 (d, *J* = 3.5 Hz), 124.0, 123.4, 121.2 (d, *J* = 3.7 Hz), 117.5 (dd, *J* = 272.4, 268.3 Hz), 114.4, 111.4, 109.9, 109.0, 55.8, 55.5 (t, *J* = 20.2 Hz), 27.1 (d, *J* = 9.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.1 (d, *J* = 307.6 Hz, 1F), -98.0 (d, *J* = 307.2 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_3Na$ $[M+Na]^+$: 404.0823, found 404.0825; HPLC conditions for

determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 75:25, flow rate = 1.0 mL/min, t_{major} = 29.9 min, t_{minor} = 43.5 min.

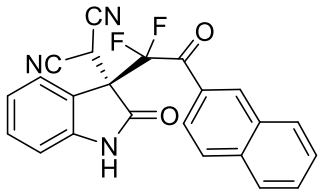


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-(4-(trifluoromethyl)phenyl)ethyl)-2-oxoindolin-3-yl)malononitrile (3f). Pale yellow solid. mp = 68 - 69 ℃, 37.3 mg, 89% yield. 95% *ee*. $[\alpha]_D^{20}$ = +12.1 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 9.04 (s, 1H), 8.12 – 8.05 (m, 2H), 7.76 – 7.65 (comp, 3H), 7.48 – 7.39 (m, 1H), 7.21 – 7.13 (m, 1H), 7.09 – 7.02 (m, 1H), 5.01 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 31.2 Hz), 170.8 (d, *J* = 6.9 Hz), 142.0, 136.4 (q, *J* = 33.0 Hz), 133.5, 132.3, 130.8, 126.0 (d, *J* = 3.7 Hz), 124.6, 124.2, 121.9, 120.6 (d, *J* = 3.3 Hz), 116.6 (dd, *J* = 271.1, 267.1 Hz), 111.8 (d, *J* = 5.3 Hz), 109.7, 108.8, 55.7 (t, *J* = 20.3 Hz), 27.0; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -63.6 (s, 3F), -97.9 (d, *J* = 309.6 Hz, 1F), -99.3 (d, *J* = 309.8 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{11}F_5N_3O_2$ $[M+H]^+$: 420.0771, found 420.0762; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 78:22, flow rate = 1.0 mL/min, t_{major} = 54.0 min, t_{minor} = 20.4 min.

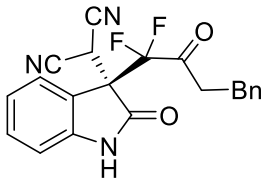


(*R*)-2-(3-(2-(Benzofuran-5-yl)-1,1-difluoro-2-oxoethyl)-2-oxoindolin-3-yl)malononitrile (3g). Pale yellow solid. mp = 73 -74 ℃, 35.6 mg, 91% yield. 95% *ee*. $[\alpha]_D^{20}$ = +4.4 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.67 (s, 1H), 8.36 (s, 1H), 8.00 – 7.92 (m, 1H), 7.72 – 7.65 (m, 2H), 7.57 – 7.50 (m, 1H), 7.45 – 7.37 (m, 1H), 7.18 – 7.10 (m, 1H), 7.07 – 7.01 (m, 1H), 6.85 (s, 1H), 4.97 (s, 1H); ^{13}C

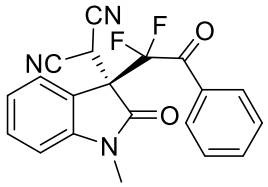
NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.0 (t, *J* = 30.9 Hz), 170.9 (d, *J* = 8.2 Hz), 158.6, 147.2, 142.0, 132.0, 128.0, 127.1, 125.9, 125.8, 125.5 (d, *J* = 4.3 Hz), 124.0, 121.1 (d, *J* = 3.8 Hz), 117.4 (dd, *J* = 271.9, 268.3 Hz), 112.3, 111.5, 109.9, 109.0, 107.6 (d, *J* = 2.5 Hz), 55.7 (t, *J* = 20.3 Hz), 27.1 (d, *J* = 8.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -95.6 (d, *J* = 307.9 Hz, 1F), -97.6 (d, *J* = 308.2 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{21}H_{11}F_2N_3O_3Na$ $[M+Na]^+$: 414.0666, found 414.0660; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 30.7 min, t_{minor} = 39.4 min.



(*R*)-2-(3-(1,1-Difluoro-2-(naphthalen-2-yl)-2-oxoethyl)-2-oxoindolin-3-yl)malononitrile (3h). Pale red solid. mp = 88 - 89 ℃, 36.1 mg, 90% yield. 95% *ee*. $[\alpha]_D^{20}$ = +19.2 (c = 0.5, MeOH); ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.67 - 8.58 (m, 2H), 7.99 – 7.88 (m, 2H), 7.88 – 7.81 (m, 2H), 7.73 – 7.61 (m, 2H), 7.61 – 7.53 (m, 1H), 7.46 – 7.37 (m, 1H), 7.19 – 7.10 (m, 1H), 7.08 – 7.01 (m, 1H), 4.98 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.5 (t, *J* = 30.2 Hz), 170.7 (d, *J* = 7.5 Hz), 142.1, 136.5, 133.7, 133.6, 132.2, 132.1, 130.4, 130.2, 129.0, 127.9, 127.5, 126.0 (d, *J* = 3.5 Hz), 124.5, 124.0, 121.1 (d, *J* = 3.6 Hz), 117.3 (dd, *J* = 272.2, 268.0 Hz), 111.6 (d, *J* = 7.3 Hz), 110.0, 109.1, 55.8 (t, *J* = 20.4 Hz), 27.2 (d, *J* = 6.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.0 (d, *J* = 307.9 Hz, 1F), -97.9 (d, *J* = 307.9 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{23}H_{13}F_2N_3O_2Na$ $[M+Na]^+$: 424.0874, found 424.0875; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 24.1 min, t_{minor} = 19.7 min.

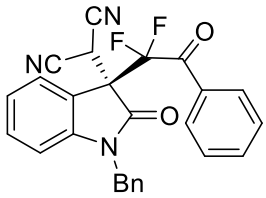


(*R*)-2-(3-(1,1-Difluoro-2-oxo-4-phenylbutyl)-2-oxoindolin-3-yl)malononitrile (3i). Yellow oil, 34.1 mg, 90% yield. 91% *ee*. $[\alpha]_D^{20}$ = +40.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.34 (s, 1H), 7.73 – 7.64 (m, 1H), 7.49 – 7.41 (m, 1H), 7.29 – 7.16 (comp, 4H), 7.10 – 7.04 (m, 2H), 7.01 – 6.94 (m, 1H), 4.89 (s, 1H), 3.08 – 2.95 (m, 1H), 2.94 – 2.75 (m, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 198.0 (dd, *J* = 33.6, 26.3 Hz), 169.9 (d, *J* = 5.5 Hz), 141.7, 139.5, 132.4, 128.7, 128.4, 126.6, 126.3, 124.5, 119.9 (d, *J* = 2.7 Hz), 113.7 (dd, *J* = 264.0, 245.9 Hz), 111.6, 109.7, 109.0, 55.5 (t, *J* = 22.4 Hz), 39.4, 28.3, 26.5 (d, *J* = 4.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -105.9 (d, *J* = 286.6 Hz, 1F), -107.9 (d, *J* = 285.6 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{21}H_{15}F_2N_3O_2Na$ $[M+Na]^+$: 402.1030, found 402.1025; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 87:13, flow rate = 1.0 mL/min, t_{major} = 16.6 min, t_{minor} = 12.3 min.

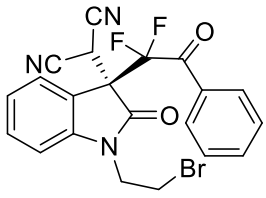


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-1-methyl-2-oxoindolin-3-yl)malononitrile (4a). Pale green solid. mp = 161 - 163 ℃, 32.8 mg, 90% yield. 99% *ee*. $[\alpha]_D^{20}$ = +8.6 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.03 – 7.95 (m, 2H), 7.73 – 7.68 (m, 1H), 7.68 – 7.61 (m, 1H), 7.56 – 7.49 (m, 1H), 7.50 – 7.43 (m, 2H), 7.22 – 7.15 (m, 1H), 7.07 – 7.02 (m, 1H), 4.92 (s, 1H), 3.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.6 Hz), 169.1 (d, *J* = 8.1 Hz), 144.9, 135.5, 132.1, 130.7, 130.4 (t, *J* = 3.3 Hz), 129.0, 125.7 (d, *J* = 3.4 Hz), 124.0, 120.4 (d, *J* = 3.9 Hz), 116.9 (dd, *J* = 267.4 Hz, *J* = 266.7, 267.4 Hz), 109.9, 109.8, 108.9, 55.2 (t,

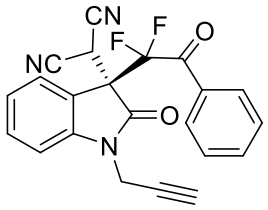
J = 20.2 Hz), 27.2, 27.1 (dd, *J* = 8.8, 2.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.8 (d, *J* = 309.3 Hz, 1F), -98.8 (d, *J* = 309.4 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_2Na$ $[M+Na]^+$: 388.0874, found 388.0863; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 70:30, flow rate = 1.0 mL/min, t_{major} = 20.6 min, t_{minor} = 51.9 min.



(*R*)-2-(1-benzyl-3-(1,1-Difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4b). Pale green solid. mp = 155 - 157 ℃, 39.7 mg, 90% yield. 99% *ee*. $[\alpha]_D^{20}$ = +15.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.05 – 7.97 (m, 2H), 7.74 – 7.68 (m, 1H), 7.70 – 7.61 (m, 1H), 7.52 – 7.44 (comp, 4H), 7.43 – 7.34 (comp, 3H), 7.36 – 7.28 (m, 1H), 7.19 – 7.11 (m, 1H), 6.93 – 6.77 (m, 1H), 5.02 (dd, *J* = 15.8, 15.9 Hz, 2H), 4.97 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm), 185.6 (t, *J* = 31.5 Hz), 169.5 (d, *J* = 7.7 Hz), 144.4, 135.5, 134.4, 132.0, 130.8, 130.5, 129.0, 128.9, 128.2, 127.7, 125.8 (d, *J* = 3.5 Hz), 124.1, 120.4 (d, *J* = 3.6 Hz), 117.0 (dd, *J* = 272.2, 268.3 Hz), 111.0 (d, *J* = 9.4 Hz), 110.0, 109.1, 55.4 (t, *J* = 20.4 Hz), 45.4, 27.1 (d, *J* = 10.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 308.5 Hz, 1F), -98.7 (d, *J* = 308.4 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{26}H_{17}F_2N_3O_2Na$ $[M+Na]^+$: 464.1187, found 464.1178; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 87:13, flow rate = 1.0 mL/min, t_{major} = 30.2 min, t_{minor} = 51.6 min.

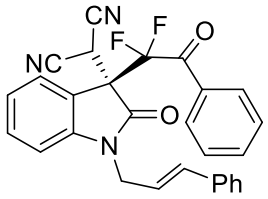


(*R*)-2-(1-(2-Bromoethyl)-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4c). Pale green solid. mp = 160 – 161 ℃, 43.4 mg, 95% yield. 99% *ee*. $[\alpha]_D^{20}$ = +10.4 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.04 – 7.94 (m, 2H), 7.74 – 7.68 (m, 1H), 7.70 – 7.62 (m, 1H), 7.58 – 7.49 (m, 1H), 7.52 – 7.44 (m, 2H), 7.24 – 7.15 (m, 1H), 7.17 – 7.10 (m, 1H), 4.88 (s, 1H), 4.24 (td, *J* = 7.5, 1.4 Hz, 2H), 3.62 (t, *J* = 7.6 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.2 (t, *J* = 30.6 Hz), 169.2 (d, *J* = 7.9 Hz), 143.7, 135.6, 132.2, 130.6 (d, *J* = 3.3 Hz), 130.5, 129.1, 126.1 (d, *J* = 3.6 Hz), 124.4 (d, *J* = 5.6 Hz), 120.3 (d, *J* = 3.7 Hz), 117.1 (dd, *J* = 272.7, 268.3 Hz), 110.0 (d, *J* = 7.7 Hz), 109.8, 108.9, 55.0 (t, *J* = 20.1 Hz), 42.7, 27.0 (d, *J* = 9.1 Hz), 25.9; ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.8 (d, *J* = 309.6 Hz, 1F), -98.6 (d, *J* = 309.5 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{21}H_{14}BrF_2N_3O_2Na$ $[M+Na]^+$: 480.0135, found 480.0137; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 70:30, flow rate = 1.0 mL/min, t_{major} = 17.9 min, t_{minor} = 49.7 min.

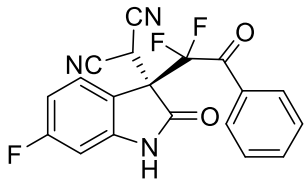


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-2-oxo-1-(prop-2-yn-1-yl)indolin-3-yl)malononitrile (4d). Pale green solid. mp = 157 - 159 ℃, 34.2 mg, 88% yield. 99% *ee*. $[\alpha]_D^{20}$ = +6.1 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.05 – 7.93 (m, 2H), 7.75 – 7.68 (m, 1H), 7.70 – 7.61 (m, 1H), 7.60 – 7.51 (m, 1H), 7.52 – 7.43 (m, 2H), 7.31 – 7.24 (m, 1H), 7.26 – 7.18 (m, 1H), 4.89 (s, 1H), 4.63 (dd, *J* = 2.6, 1.3 Hz, 2H), 2.37 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.1 (t, *J* = 30.5 Hz), 168.4 (d, *J* = 8.2 Hz), 143.1, 135.6, 132.1, 130.5, 130.4, 129.0, 125.8 (d, *J* = 3.7 Hz), 124.4, 120.3 (d, *J* = 3.9 Hz), 117.0 (dd, *J* = 268.0, 267.6 Hz), 110.8, 109.8, 108.6, 75.3, 73.6, 55.0 (t, *J* = 20.2 Hz), 30.3, 27.0 (dd, *J* = 8.8, 2.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 310.2 Hz, 1F), -98.6 (d, *J* = 310.5 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{22}H_{13}F_2N_3O_2Na$ $[M+Na]^+$: 412.0874, found

412.0872; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 65:35, flow rate = 1.0 mL/min, t_{major} = 27.1 min, t_{minor} = 63.9 min.

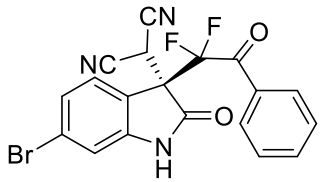


(*R*)-2-(1-Cinnamyl-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4e). Pale green solid. mp = 169 - 171 ℃, 42.1 mg, 90% yield. 99% *ee*. $[\alpha]_D^{20}$ = +10.8 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.10 – 7.99 (m, 2H), 7.76 – 7.70 (m, 1H), 7.69 – 7.61 (m, 1H), 7.52-7.43 (m, 3H), 7.43 – 7.37 (m, 2H), 7.37 – 7.28 (m, 2H), 7.30 – 7.23 (m, 1H), 7.22 – 7.14 (m, 1H), 7.14 – 7.06 (m, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.29 (dt, *J* = 15.9, 5.7 Hz, 1H), 4.95 (s, 1H), 4.68 – 4.59 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.5 Hz), 169.0 (d, *J* = 7.8 Hz), 144.2, 136.2, 135.5, 133.8, 132.1, 130.7 (d, *J* = 3.4 Hz), 130.4 (t, *J* = 3.2 Hz), 129.0, 128.7, 128.1, 126.7, 125.8 (d, *J* = 3.4 Hz), 124.0, 121.5, 120.4 (d, *J* = 3.7 Hz), 117.0 (dd, *J* = 272.5, 267.5 Hz), 110.8, 110.0, 109.1, 55.2 (t, *J* = 20.1 Hz), 43.1, 27.1 (dd, *J* = 8.8, 2.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.7 (d, *J* = 309.2 Hz, 1F), -98.7 (d, *J* = 309.1 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{28}H_{19}F_2N_3O_2Na$ $[M+Na]^+$: 490.1343, found 490.1339; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 70:30, flow rate = 1.0 mL/min, t_{major} = 23.9 min, t_{minor} = 86.2 min.

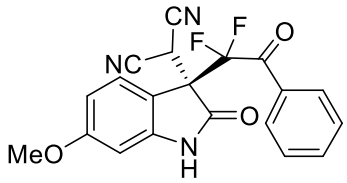


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-6-fluoro-2-oxoindolin-3-yl)malononitrile (4f). Pale yellow solid. mp = 156 - 158 ℃, 33.2 mg, 90% yield.

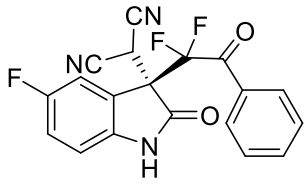
96% *ee*. $[\alpha]_D^{20}$ = +9.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.48 (s, 1H), 8.04 – 7.98 (m, 2H), 7.71 – 7.59 (m, 2H), 7.53 – 7.45 (m, 2H), 6.89 – 6.76 (m, 2H), 4.89 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.4 (t, *J* = 30.1 Hz), 170.8 (d, *J* = 8.0 Hz), 166.1, 164.1, 143.7 (d, *J* = 12.3 Hz), 135.8, 130.5 (t, *J* = 3.2 Hz), 129.1, 127.6 (d, *J* = 10.6 Hz), 117.0 (dd, *J* = 267.8, 267.6 Hz), 116.4 (t, *J* = 3.6 Hz), 110.8 (d, *J* = 22.9 Hz), 109.7, 108.9, 100.4 (d, *J* = 27.9 Hz), 55.3 (t, *J* = 20.3 Hz), 27.1 (d, *J* = 8.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.7 (d, *J* = 310.7 Hz, 1F), -98.6 (d, *J* = 310.8 Hz, 1F), -105.4 (s,1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_3N_3O_2Na$ $[M+Na]^+$: 392.0623, found 392.0621; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{major} = 36.8 min, t_{minor} = 52.4 min.



(*R*)-2-(6-Bromo-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4g). Pale yellow solid. mp = 189 - 191 ℃, 38.6 mg, 90% yield. 95% *ee*. $[\alpha]_D^{20}$ = +12.2 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 9.10 – 9.00 (m, 1H), 8.04 – 7.98 (m, 2H), 7.71 – 7.64 (m, 1H), 7.54 – 7.45 (comp, 3H), 7.32 – 7.25 (m, 1H), 7.22 (s, 1H), 4.95 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.3 Hz), 170.8 (d, *J* = 7.7 Hz), 143.2, 135.8, 130.6, 130.3, 129.1, 127.1, 127.0 (d, *J* = 3.3 Hz), 126.3, 119.8 (d, *J* = 3.9 Hz), 117.0 (dd, *J* = 272.0, 267.5 Hz), 115.2, 109.6, 108.8, 55.4 (t, *J* = 20.2 Hz), 26.8 (d, *J* = 9.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.7 (d, *J* = 310.5 Hz, 1F), -98.8 (d, *J* = 310.7 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}BrF_2N_3O_2Na$ $[M+Na]^+$: 451.9822, found 451.9823; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 13.6 min, t_{minor} = 23.7 min.

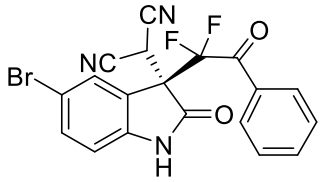


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-6-methoxy-2-oxoindolin-3-yl)malononitrile (4h). Pale yellow solid. mp = 121 - 123 ℃, 34.3 mg, 90% yield. 94% *ee*. $[\alpha]_D^{20}$ = +3.5 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.89 – 8.67 (m, 1H), 8.05 – 7.90 (m, 2H), 7.68 – 7.60 (m, 1H), 7.58 – 7.52 (m, 1H), 7.50 – 7.42 (m, 2H), 6.69 – 6.52 (m, 2H), 4.92 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.7 (t, *J* = 30.4 Hz), 171.4 (d, *J* = 7.3 Hz), 162.8, 143.4, 135.5, 130.7, 130.5 (d, *J* = 3.5 Hz), 129.0, 126.9 (d, *J* = 3.1 Hz), 117.0 (dd, *J* = 271.7, 267.6 Hz), 112.3 (d, *J* = 3.7 Hz), 110.0, 109.2, 108.9, 98.7, 55.7, 55.4 (d, *J* = 20.4 Hz), 27.2 (d, *J* = 8.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -97.2 (d, *J* = 308.2 Hz, 1F), -98.5 (d, *J* = 308.0 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_3Na$ $[M+Na]^+$: 404.0823, found 404.0822; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 20.5 min, t_{minor} = 15.3 min.

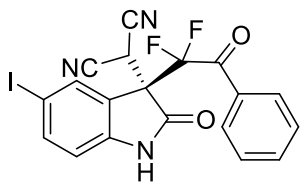


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-5-fluoro-2-oxoindolin-3-yl)malononitrile (4i). Pale yellow solid. mp = 156 - 158 ℃, 35.1 mg, 95% yield. 96% *ee*. $[\alpha]_D^{20}$ = +5.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.57 (s, 1H), 8.04 – 7.98 (m, 2H), 7.72 – 7.63 (m, 1H), 7.53 – 7.45 (m, 2H), 7.45 – 7.39 (m, 1H), 7.20 – 7.11 (m, 1H), 7.05 – 6.97 (m, 1H), 4.92 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.1 (t, *J* = 30.4 Hz), 170.7 (d, *J* = 8.0 Hz), 147.9, 144.1, 136.2, 130.6 (t, *J* = 3.1 Hz), 129.3, 128.8, 122.0 (d, *J* = 4.0 Hz), 121.8 (d, *J* = 4.1 Hz), 117.2 (dd, *J* = 274.7, 268.8 Hz), 111.7, 109.1, 108.6, 67.1, 55.3 (t, *J* = 20.5 Hz), 26.8 (d, *J* =

8.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.8 (d, *J* = 311.5 Hz, 1F), -98.8 (d, *J* = 311.4 Hz, 1F), -116.9 (s,1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_3N_3O_2Na$ $[M+Na]^+$: 392.0623, found 392.0618; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 15.2 min, t_{minor} = 18.6 min.

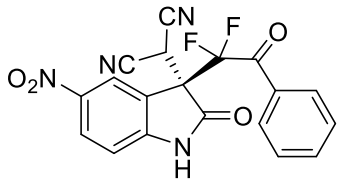


(*R*)-2-(5-Bromo-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4j). Pale yellow solid. mp = 188 - 189 ℃, 38.6 mg, 90% yield. 96% *ee*. $[\alpha]_D^{20}$ = +13.5 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.80 – 8.56 (m, 1H), 8.08 – 7.94 (m, 2H), 7.76 (s, 1H), 7.73 – 7.63 (m, 1H), 7.58 – 7.52 (m, 1H), 7.53 – 7.46 (m, 2H), 6.98 – 6.91 (m, 1H), 4.92 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.6 Hz), 170.2 (d, *J* = 7.5 Hz), 141.0, 135.9, 135.1, 130.6, 130.3 (t, *J* = 3.4 Hz), 129.2, 128.9 (d, *J* = 3.9 Hz), 122.9 (d, *J* = 3.7 Hz), 117.1 (dd, *J* = 273.3, 268.3 Hz), 116.6, 113.0 (d, *J* = 2.5 Hz), 109.4, 108.7, 55.6 (t, *J* = 20.3 Hz), 27.0 (d, *J* = 8.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.4 (d, *J* = 312.4 Hz, 1F), -98.6 (d, *J* = 312.3 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}BrF_2N_3O_2Na$ $[M+Na]^+$: 451.9822, found 451.9817; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 15.8 min, t_{minor} = 20.3 min.

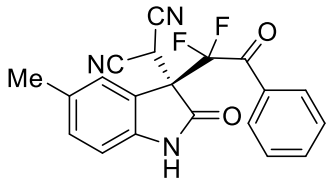


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-5-iodo-2-oxoindolin-3-yl)malononitrile (4k). Pale yellow solid. mp = 202 - 205 ℃, 43.4 mg, 91% yield.

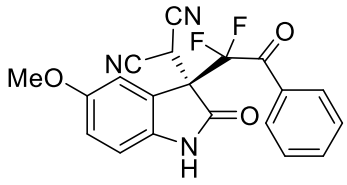
97% *ee*. $[\alpha]_D^{20}$ = +19.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.69 (s, 1H), 8.05 – 7.98 (m, 2H), 7.91 (s, 1H), 7.79 – 7.72 (m, 1H), 7.72 – 7.64 (m, 1H), 7.54 – 7.46 (m, 2H), 6.87 – 6.80 (m, 1H), 4.90 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.2 Hz), 170.1 (d, *J* = 7.8 Hz), 141.7, 141.1, 135.9, 134.3 (d, *J* = 4.1 Hz), 130.6 (t, *J* = 3.1 Hz), 130.3, 129.1, 123.2 (d, *J* = 3.7 Hz), 117.1 (dd, *J* = 273.3, 268.2 Hz), 113.5, 109.4, 108.7, 86.3, 55.4 (t, *J* = 20.3 Hz), 27.0 (d, *J* = 8.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.4 (d, *J* = 311.9 Hz, 1F), -98.6 (d, *J* = 311.7 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_2IN_3O_2Na$ $[M+Na]^+$: 499.9684, found 499.9681; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{major} = 31.9 min, t_{minor} = 26.4 min.



(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-5-nitro-2-oxoindolin-3-yl)malononitrile (4l). Pale yellow solid. mp = 189 - 191 ℃, 35.6 mg, 90% yield. 96% *ee*. $[\alpha]_D^{20}$ = +16.6 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.90 (s, 1H), 8.51 (s, 1H), 8.44 – 8.38 (m, 1H), 8.04 – 7.99 (m, 2H), 7.73 – 7.67 (m, 1H), 7.54 – 7.47 (m, 2H), 7.25 – 7.20 (m, 1H), 4.94 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.2 (t, *J* = 30.1 Hz), 170.3 (d, *J* = 8.0 Hz), 147.6, 144.3, 136.3, 130.7, 129.9, 129.3, 128.8, 122.0 (d, *J* = 4.0 Hz), 121.9, 117.2 (dd, *J* = 268.5, 269.4 Hz), 111.5, 109.0, 108.5, 55.3 (t, *J* = 20.5 Hz), 26.9 (d, *J* = 8.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.0 (d, *J* = 314.6 Hz, 1F), -98.4 (d, *J* = 314.7 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_2N_4O_4Na$ $[M+Na]^+$: 419.0568, found 419.0566; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 70:30, flow rate = 1.0 mL/min, t_{major} = 10.0 min, t_{minor} = 15.0 min.

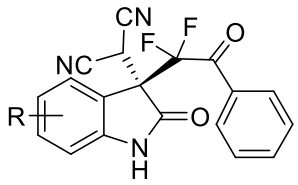


(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-5-methyl-2-oxoindolin-3-yl)malononitrile (4m). Pale yellow solid. mp = 178 - 180 ℃, 32.8 mg, 90% yield. 95% *ee*. $[\alpha]_D^{20}$ = +2.6 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 8.62 (s, 1H), 8.05 – 7.97 (m, 2H), 7.70 – 7.62 (m, 1H), 7.54 – 7.41 (m, 3H), 7.25 – 7.19 (m, 1H), 6.96 – 6.90 (m, 1H), 4.93 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.7 (t, *J* = 30.6 Hz), 170.7 (d, *J* = 7.6 Hz), 139.4, 135.5, 133.9, 132.5 (d, *J* = 5.4 Hz), 130.8 (t, *J* = 3.4 Hz), 130.5, 129.0, 126.5 (t, *J* = 3.1 Hz), 121.0 (d, *J* = 3.4 Hz), 117.0 (dd, *J* = 272.1, 267.7 Hz), 111.3 (d, *J* = 7.7 Hz), 109.9, 109.0, 55.7 (t, *J* = 20.1 Hz), 27.1, 21.3 (d, *J* = 8.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 309.7 Hz, 1F), -98.6 (d, *J* = 309.4 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_2Na$ $[M+Na]^+$: 388.0874, found 388.0874; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, t_{major} = 20.6 min, t_{minor} = 17.4 min.



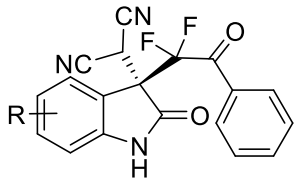
(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-5-methoxy-2-oxoindolin-3-yl)malononitrile (4n). Pale yellow solid. mp = 193 - 195 ℃, 34.7 mg, 91% yield. 96% *ee*. $[\alpha]_D^{20}$ = +4.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.39 (s, 1H), 8.14 – 7.92 (m, 2H), 7.70 – 7.61 (m, 1H), 7.52 – 7.36 (m, 2H), 7.26 (s, 1H), 6.98 – 6.92 (m, 2H), 4.92 (s, 1H), 3.78 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.6 (t, *J* = 30.6 Hz), 170.5 (d, *J* = 7.5 Hz), 156.6, 135.6, 135.0, 130.7 (d, *J* = 3.3 Hz), 130.5 (t, *J* = 3.2 Hz), 129.0, 122.0 (d, *J* = 3.6 Hz), 117.0 (dd, *J* = 267.8, 267.3 Hz), 116.9, 112.7 (d, *J* = 3.4 Hz), 112.1, 109.8, 109.0, 56.0 (d, *J* = 40.3 Hz), 56.0, 27.1 (dd,

J = 8.6, 2.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 309.7 Hz, 1F), -98.6 (d, *J* = 309.4 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{20}H_{13}F_2N_3O_3Na$ $[M+Na]^+$: 404.0823, found 404.0817; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H , λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, t_{major} = 44.8 min, t_{minor} = 41.2 min.



R = 4-F

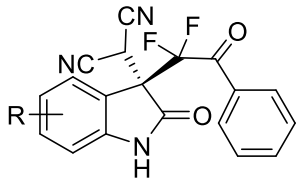
(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-4-fluoro-2-oxoindolin-3-yl)malononitrile (4o). Pale yellow solid. mp = 156 - 158 ℃, 34.7 mg, 94% yield. 95% *ee*. $[\alpha]_D^{20}$ = +7.7 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.75 (s, 1H), 8.02 – 7.96 (m, 2H), 7.69 – 7.61 (m, 1H), 7.51 – 7.43 (m, 2H), 7.45 – 7.35 (m, 1H), 6.89 – 6.80 (m, 2H), 5.01 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 186.0 (t, *J* = 30.1 Hz), 169.7 (d, *J* = 7.5 Hz), 160.6, 158.6, 144.0 (d, *J* = 7.0 Hz), 135.6, 134.3 (d, *J* = 9.1 Hz), 130.7, 130.5, 129.1, 116.7 (t, *J* = 271.7 Hz), 111.9 (d, *J* = 21.5 Hz), 109.3, 108.9, 107.7 (d, *J* = 3.4 Hz), 56.8 (d, *J* = 21.2 Hz), 26.0 (d, *J* = 6.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -94.3 (dd, *J* = 304.3, 52.9 Hz, 1F), -99.1 (dd, *J* = 304.0, 7.3 Hz, 1F), -108.3 (s, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{10}F_3N_3O_2Na$ $[M+Na]^+$: 392.0623, found 392.0621; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{major} = 32.3 min, t_{minor} =28.8 min.



R = 4-Br

(*R*)-2-(4-Bromo-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-

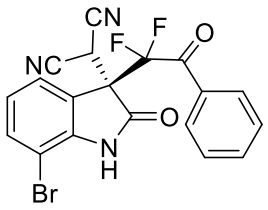
yl)malononitrile (4p). Pale yellow solid. mp = 190 - 192 ℃, 38.6 mg, 90% yield. 96% *ee*. $[\alpha]_D^{20}$ = +18.5 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 9.03 (s, 1H), 7.91 – 7.84 (m, 2H), 7.64 – 7.57 (m, 1H), 7.45 – 7.38 (m, 2H), 7.24 – 7.18 (m, 2H), 7.05 – 6.99 (m, 1H), 5.51 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 186.2 (t, *J* = 28.1 Hz), 168.8 (d, *J* = 7.1 Hz), 144.5, 135.4, 133.5, 131.3 (d, *J* = 2.8 Hz), 130.2 (t, *J* = 3.6 Hz), 129.0, 128.9, 120.1 (d, *J* = 4.6 Hz), 120.0, 116.5 (t, *J* = 273.8 Hz), 111.0, 109.2, 108.7, 57.1 (d, *J* = 20.9 Hz), 24.0 (d, *J* = 3.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -91.7 (d, *J* = 290.0 Hz, 1F), -96.9 (d, *J* = 289.5 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{11}BrF_2N_3O_2$ $[M+H]^+$: 430.0003, found 429.9994; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{major} = 33.9 min, t_{minor} =26.9 min.



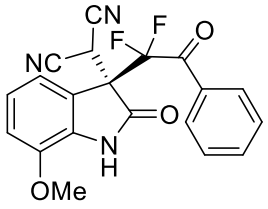
R = 4,7-Cl_2

(*R*)-2-(4,6-Dichloro-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4q). Pale yellow solid. mp = 210 - 213 ℃, 37.7 mg, 90% yield. 96% *ee*. $[\alpha]_D^{20}$ = +15.3 (c = 0.5, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) (δ, ppm) 9.06 (s, 1H), 8.01 – 7.79 (m, 2H), 7.68 – 7.61 (m, 1H), 7.49 – 7.43 (m, 2H), 7.10 – 7.05 (m, 1H), 7.02 – 6.97 (m, 1H), 5.28 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 186.0 (t, *J* = 29.3 Hz), 168.7 (d, *J* = 7.3 Hz), 144.9, 139.0, 135.7, 133.0, 130.9 (d, *J* = 3.0 Hz), 130.4, 129.1, 125.4 (d, *J* = 9.5 Hz), 117.2 (dd, *J* = 219.7, 320.4 Hz), 116.7, 111.0 (d, *J* = 10.7 Hz), 109.2, 108.5, 56.8 (t, *J* = 21.9 Hz), 24.6 (d, *J* = 12.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -91.9 (d, *J* = 297.5 Hz, 1F), -97.1 (d, *J* = 297.2 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_9Cl_2F_2N_3O_2Na$ $[M+Na]^+$: 441.9938, found 441.9935; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min,

t_{major} = 10.5 min, t_{minor} =8.8 min.

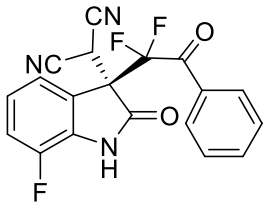


(*R*)-2-(7-Bromo-3-(1,1-difluoro-2-oxo-2-phenylethyl)-2-oxoindolin-3-yl)malononitrile (4r). Pale yellow solid. mp = 192 - 194 ℃, 39.5 mg, 92% yield. 94% *ee*. $[\alpha]_D^{20}$ = +18.3 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.18 (s, 1H), 8.05 – 7.97 (m, 2H), 7.72 – 7.63 (m, 1H), 7.65 – 7.55 (m, 2H), 7.53 – 7.45 (m, 2H), 7.11 – 7.02 (m, 1H), 4.91 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.4 (t, *J* = 30.1 Hz), 169.0 (d, *J* = 7.7 Hz), 141.5, 135.8, 134.9, 130.6, 130.5, 129.1, 125.2 (d, *J* = 8.0 Hz), 124.9 (d, *J* = 3.6 Hz), 122.0 (d, *J* = 3.8 Hz), 117.0 (dd, *J* = 268.2, 269.2 Hz), 109.5, 108.6, 104.3, 56.7 (t, *J* = 20.5 Hz), 27.0 (d, *J* = 8.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.8 (d, *J* = 310.9 Hz, 1F), -98.8 (d, *J* = 310.9 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{19}H_{11}BrF_2N_3O_2$ $[M+H]^+$: 430.0003, found 430.0004; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, t_{major} = 26.3 min, t_{minor} =17.7 min.



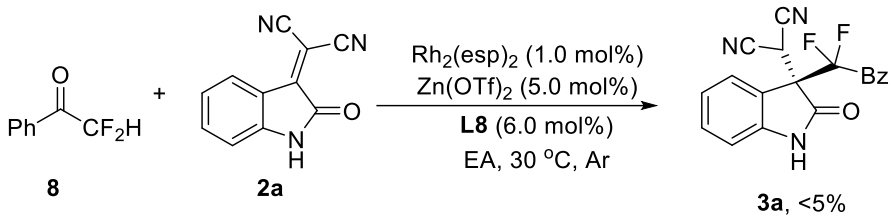
(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-7-methoxy-2-oxoindolin-3-yl)malononitrile (4s). Pale yellow solid. mp = 183 - 184 ℃, 36.2 mg, 95% yield. 96% *ee*. $[\alpha]_D^{20}$ = +3.7 (c = 0.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.10 (s, 1H), 8.04 – 7.95 (m, 2H), 7.69 – 7.61 (m, 1H), 7.52 – 7.42 (m, 2H), 7.31 – 7.23 (m, 1H), 7.16 – 7.08 (m, 1H), 7.05 – 6.97 (m, 1H), 4.92 (s, 1H), 3.90 (s, 3H); ^{13}C NMR

(126 MHz, $CDCl_3$) (δ, ppm) 185.6 (t, *J* = 30.6 Hz), 169.7 (d, *J* = 8.0 Hz), 144.5, 135.5, 131.0, 130.8, 130.5 (t, *J* = 3.2 Hz), 129.0, 124.7, 121.5 (d, *J* = 3.8 Hz), 117.7 (d, *J* = 3.5 Hz), 117.0 (dd, *J* = 267.6, 267.7 Hz), 114.2, 109.9, 108.9, 56.3 (t, *J* = 20.2 Hz), 55.9, 27.1 (dd, *J* = 8.7, 2.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.9 (d, *J* = 308.5 Hz, 1F), -98.99 (d, *J* = 309.0 Hz, 1F); HRMS (TOF MS ESI^+) calculated for $C_{20}H_{13}F_2N_3O_3Na$ $[M+Na]^+$: 404.0823, found 404.0819; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 36.5 min, t_{minor} =25.8 min.



(*R*)-2-(3-(1,1-Difluoro-2-oxo-2-phenylethyl)-7-fluoro-2-oxoindolin-3-yl)malononitrile (4t). Pale yellow solid. mp = 161 - 164 ℃, 33.2 mg, 90% yield. 95% *ee*. $[\alpha]_D^{20}$ = +5.8 (c = 0.5, MeOH); ^1H NMR (400 MHz, $CDCl_3$) (δ, ppm) 8.43 (s, 1H), 8.04 – 7.98 (m, 2H), 7.72 – 7.63 (m, 1H), 7.53 – 7.45 (comp, 3H), 7.30 – 7.20 (m, 1H), 7.19 – 7.09 (m, 1H), 4.92 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) (δ, ppm) 185.3 (t, *J* = 30.6 Hz), 169.6 (d, *J* = 7.8 Hz), 148.7, 146.2, 135.8, 130.5 (t, *J* = 3.2 Hz), 129.1, 124.9 (d, *J* = 6.2 Hz), 123.3 (t, *J* = 3.7 Hz), 121.7 (t, *J* = 3.7 Hz), 119.5, 119.3, 117.0 (dd, *J* = 273.2, 268.3 Hz), 109.6, 108.7, 56.0 (t, *J* = 20.4 Hz), 27.0 (dd, *J* = 9.1, 2.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -96.6 (d, *J* = 310.9 Hz, 1F), -98.9 (d, *J* = 311.2 Hz, 1F), -130.8 (s, 1F); HRMS (TOF MS ESI^+) calculated for $C_{19}H_{10}F_3N_3O_2Na$ $[M+Na]^+$: 392.0623, found 392.0625; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3 , λ = 254 nm, hexane : 2-propanol = 90:10, flow rate = 1.0 mL/min, t_{major} = 34.4 min, t_{minor} =31.2 min.

4. Control Experiment



To a 10-mL oven-dried vial containing a magnetic stirring bar, $Rh_2(esp)_2$ (0.8 mg, 1.0 mol%,), $Zn(OTf)_2$ (1.9 mg, 5.0 mol%) and **L8** (6.0 mol%) in Ethyl acetate (EA, 0.5 mL), wad added a solution of **8** (15.6 mg, 0.1 mmol) in 0.5 mL EA and **2a** (19.5 mg, 0.1 mmol) in 1.0 mL EA *via* syringe in one pot under an argon atmosphere at 30 ℃ after 15 min, and the reaction mixture was stirred for an additional 3 h under these conditions until consumption of the material (monitored by TLC). The resulting reaction mixture was concentrated under reduced pressure and the residue was directly subjected to proton NMR analysis with $CDCl_3$ as the solvent without any further purification. Most of the materials **8** and **2a** remained intact and no addition product **3a** was observed (Figure S1 below for details).

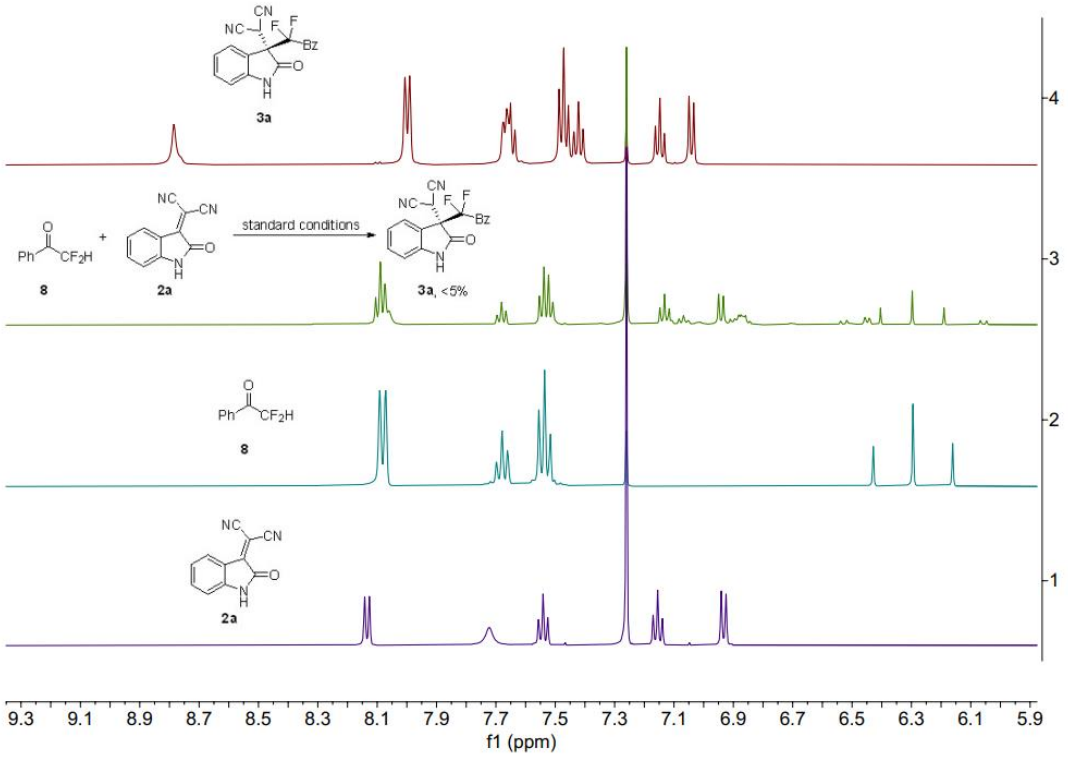
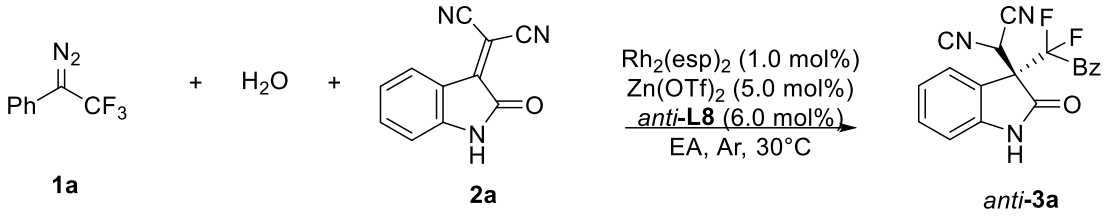
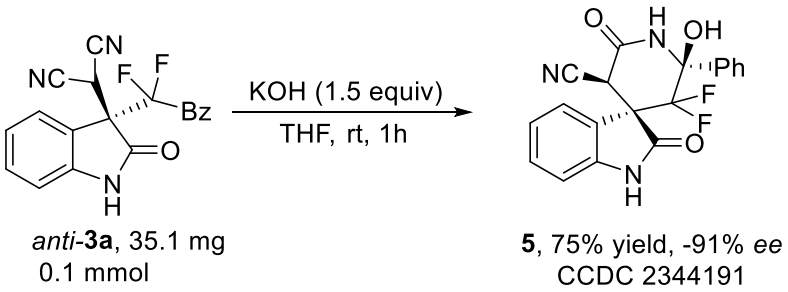


Figure S1. Proton NMR spectra of the crude reaction mixture of control experiment with **8** and **2a** under optimal conditions.

5. General Procedure for Scale Up and Synthetic Applications

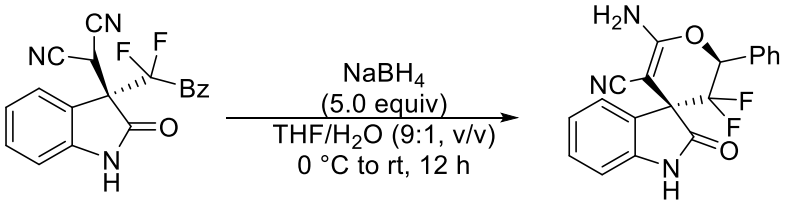


To a 100-mL oven-dried vial containing a magnetic stirring bar, $Rh_2(esp)_2$ (24.0 mg, 1.0 mol%,), H_2O (81.0 μL, 4.5 mmol), $Zn(OTf)_2$ (57.0 mg, 5.0 mol%) and *anti*-**L8** (6.0 mol%) in Ethyl acetate (EA, 15.0 mL), wad added a solution of diazo compound **1a** (837.0 mg, 4.5 mmol) in 5.0 mL EA and **2a** (585.0 mg, 3.0 mmol) in 15.0 mL EA *via* syringe in one pot under an argon atmosphere at 30 ℃ after 15 min, and the reaction mixture was stirred for an additional 3 h under these conditions until consumption of the material (monitored by TLC). Then the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 4:1 to 2:1) to give the 1.05 g pure products *anti*-**3**a in 95% yield with 93% *ee*. HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3, λ = 254 nm, hexane : 2-propanol = 85:15, flow rate = 1.0 mL/min, t_{major} = 15.7 min, t_{minor} = 18.2 min.



To a 10-mL oven-dried vial containing a magnetic stirring bar, *anti*-**3a** (35.1 mg, 0.1 mmol) in 1.0 mL THF, wad added a solution of KOH (8.4 mg, 0.15 mmol) in water *via* syringe in one pot under an argon atmosphere at room temperature, and the

reaction mixture was stirred for an additional 1 h under these conditions until consumption of the material (monitored by TLC). Then the reaction mixture was extracted with ethyl acetate (5.0 mL × 4), the combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum after filtration. The crude mixture was purified by silica gel column chromatography (using DCM as eluent) to give product **5** as white soild in 75% yield with 91% *ee*. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm) 10.93 (s, 1H), 10.20 (s, 1H), 9.92 (s, 1H), 7.83 – 7.63 (m, 2H), 7.58 – 7.43 (m, 3H), 7.37 – 7.29 (m, 1H), 7.17 – 7.10 (m, 1H), 7.08 – 7.00 (m, 1H), 6.98 – 6.92 (m, 1H), 3.18 (s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) (δ, ppm) 170.5 (d, J = 3.6 Hz), 168.8, 167.8, 142.7, 130.5, 130.4, 128.8, 128.5, 128.1, 126.6 (d, J = 3.6 Hz), 123.4 (d, J = 5.7 Hz), 122.2, 118.6 (dd, J = 268.0, 261.4 Hz), 110.8, 73.0 (t, J = 28.3 Hz), 60.2, 53.8 (t, J = 24.1 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -99.3 (d, J = 221.8 Hz, 1F), -108.2 (d, J = 221.4 Hz, 1F); HRMS (TOF MS ESI+) calculated for $C_{19}H_{14}F_2N_3O_3$ [M + H]$^+$: 370.1005, found 370.1007; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3, λ = 254 nm, hexane : propanol = 80:20, flow rate =1.0 mL/min, t_{major} = 17.4 min, t_{minor} = 25.3 min.

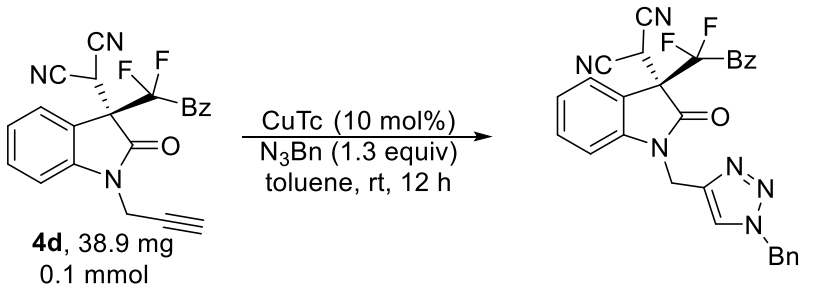


anti-**3a**, 35.1 mg
0.1 mmol

6, 80% yield, -91% *ee*

To a 10-mL oven-dried vial containing a magnetic stirring bar, *anti*-**3a** (35.1 mg, 0.1 mmol) in 2.0 mL mixture solvent of THF/H_2O (9/1, v/v), wad added $NaBH_4$ (18.9 mg, 5.0 mmol) at 0℃, and the reaction mixture was stirred for an additional 12 h under these conditions until consumption of the material (monitored by TLC). The reaction was quenched by adding 5.0 mL saturated NH4Cl (aq), which was kept stirring at room temperature till the generation of gas ceased. Then the reaction mixture was extracted with ethyl acetate (5.0 mL × 4), the combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under vacuum after filtration. The crude mixture

was purified by silica gel column chromatography (using DCM as eluent) to give product **6** as white soild in 80% yield with 91% *ee*. ^{1}H NMR (400 MHz, DMSO-d_6) (δ, ppm) 10.72 (s, 1H), 7.91 – 7.74 (m, 1H), 7.47 – 7.40 (m, 5H), 7.35 – 7.29 (m, 1H), 7.26 – 7.21 (m, 2H), 7.14 – 7.08 (m, 1H), 6.92 – 6.83 (m, 1H), 5.90 – 5.76 (m, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) (δ, ppm) 172.7, 164.5, 142.4, 130.3, 129.8, 129.7, 128.7, 128.3, 128.0, 127.9, 125.3, 122.3, 118.6 (d, *J* = 2.3 Hz), 115.5 (dd, *J* = 262.0, 248.5 Hz), 109.8, 75.5 (dd, *J* = 31.6, 22.5 Hz), 53.3 (d, *J* = 6.0 Hz); ^{19}F NMR (376 MHz, DMSO-d_6) δ -114.3 (d, *J* = 243.9 Hz, 1F), -120.9 (d, *J* = 244.0 Hz, 1F); HRMS (TOF MS ESI+) calculated for $C_{19}H_{14}F_2N_3O_2$ $[M + H]^+$: 354.1056, found 354.1058; HPLC conditions for determination of enantiomeric excess: Chiralpak IG-3, λ = 254 nm, hexane : propanol = 70:30, flow rate =1.0 mL/min, t_{major} = 7.8 min, t_{minor} = 12.7 min.



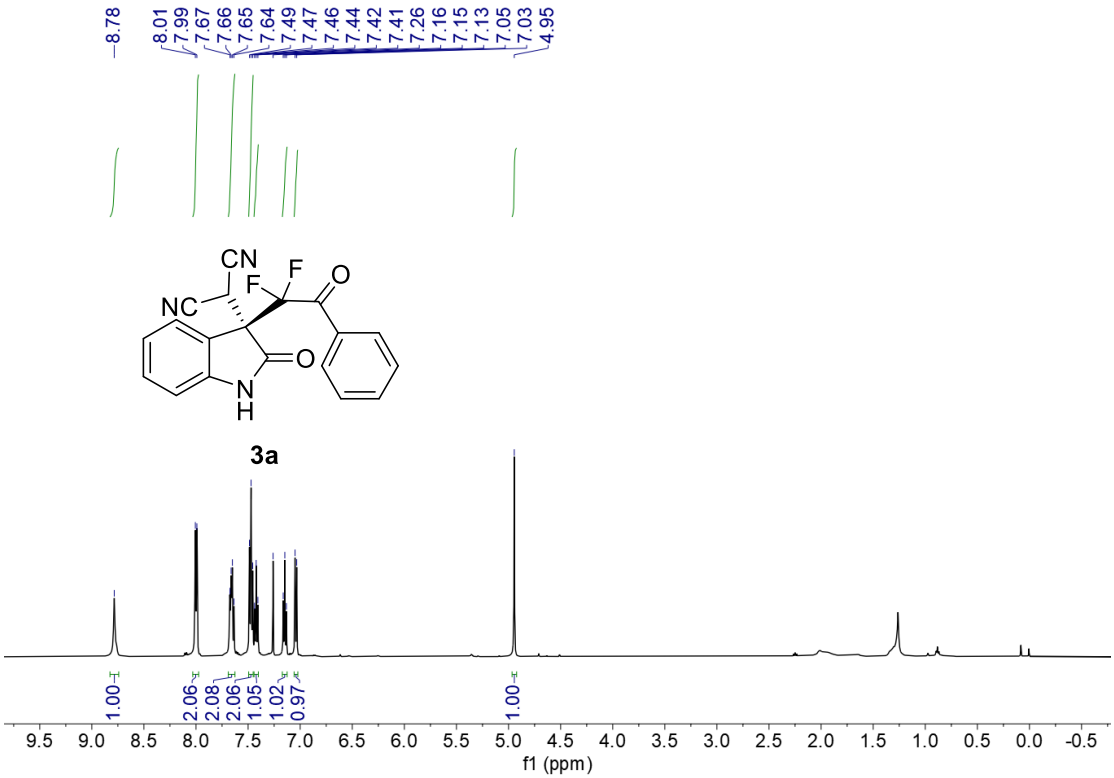
4d, 38.9 mg
0.1 mmol

7, 85% yield, -98% *ee*

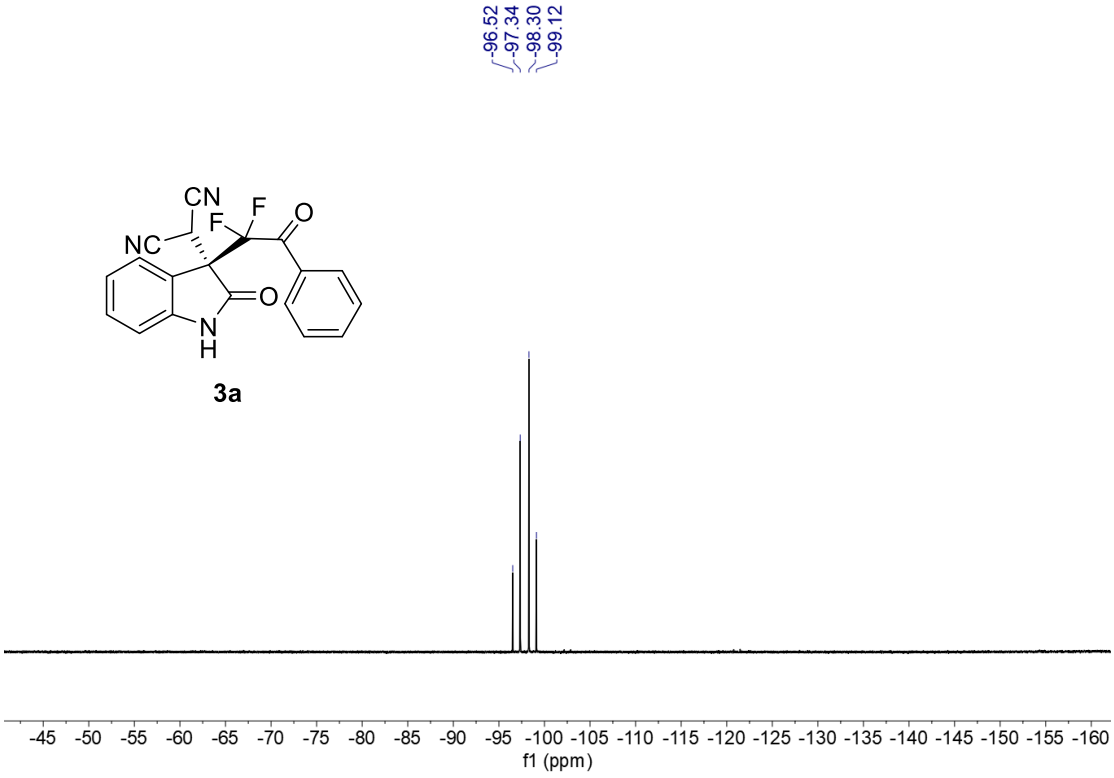
To a 10-mL oven-dried vial containing a magnetic stirring bar, CuTc (1.9 mg, 10 mol%), and **4d** (38.9 mg, 0.1 mmol) in toluene (0.5 mL), was added a solution of N_3Bn (17.3 mg, 0.13 mmol, 1.3 equiv.) in toluene (0.5 mL) dropwise at room temperature under a nitrogen atmosphere. After completion of the addition, the reaction mixture was stirred for additional 12 h under these conditions. When the reaction was completed (monitored by TLC), the solvent was removed under reduced pressure, yielding **7** in 85 % yields with 98% ee after separation by crystallization out in DCM. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm) 7.91 – 7.84 (m, 2H), 7.68 – 7.61 (m, 3H), 7.49 – 7.41 (m, 3H), 7.36 – 7.28 (m, 3H), 7.25 – 7.18 (m, 3H), 7.17 – 7.11 (m, 1H), 5.47 (q, *J* = 14.9 Hz, 2H), 5.15 (q, *J* = 15.8 Hz, 2H), 4.88 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) (δ, ppm) 185.4 (t, *J* = 30.7 Hz), 168.9 (d, *J* = 8.1 Hz), 143.5, 141.9,

135.6, 134.4, 132.3, 130.6, 130.4 (t, J = 3.3 Hz), 129.2, 129.0, 128.9, 128.3, 125.7 (d, J = 3.6 Hz), 124.2, 123.3, 120.0 (d, J = 3.5 Hz), 117.0 (dd, J = 272.9, 267.4 Hz), 111.2, 109.8, 109.0, 55.0 (d, J = 20.1 Hz), 54.5, 36.8, 27.0 (d, J = 8.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) (δ, ppm) -97.0 (d, J = 309.2 Hz, 1F), -98.6 (d, J = 309.2 Hz, 1F); HRMS (TOF MS ESI$^+$) calculated for $C_{29}H_{21}F_2N_6O_3$ $[M+H]^+$: 523.1696, found 523.1699; HPLC conditions for determination of enantiomeric excess: Chiralpak AD-H, λ = 254 nm, hexane : 2-propanol = 80:20, flow rate = 1.0 mL/min, t_{major} = 11.7 min, t_{minor} = 16.2 min.

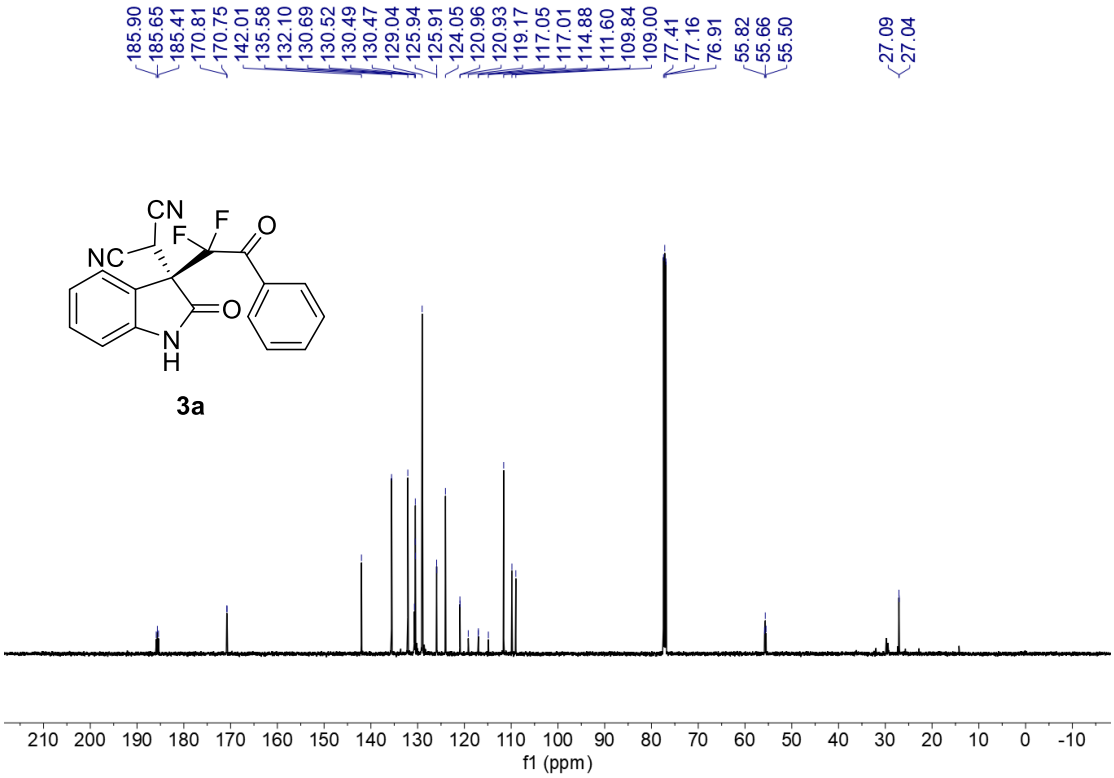
6. NMR Spectra of New Compounds 3-6



3a



3a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111.60
109.84
109.00
77.41
77.16
76.91
55.82
55.66
55.50
27.09
27.04
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O
N
H
3a
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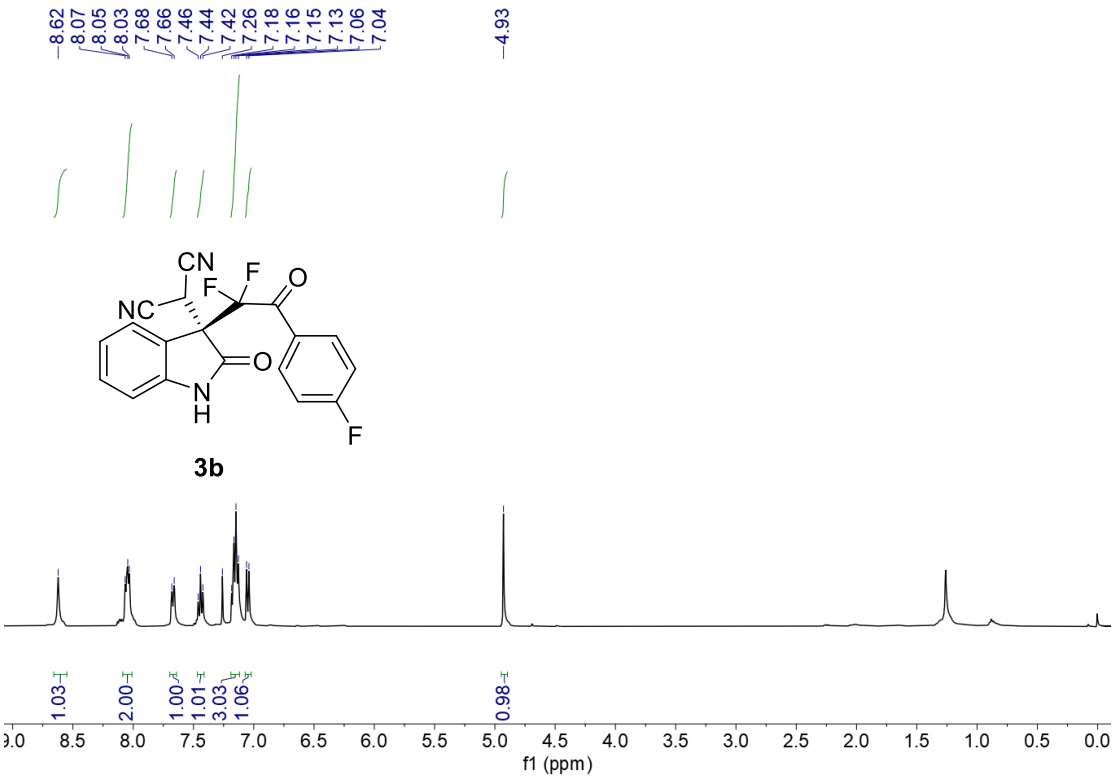
f1 (ppm)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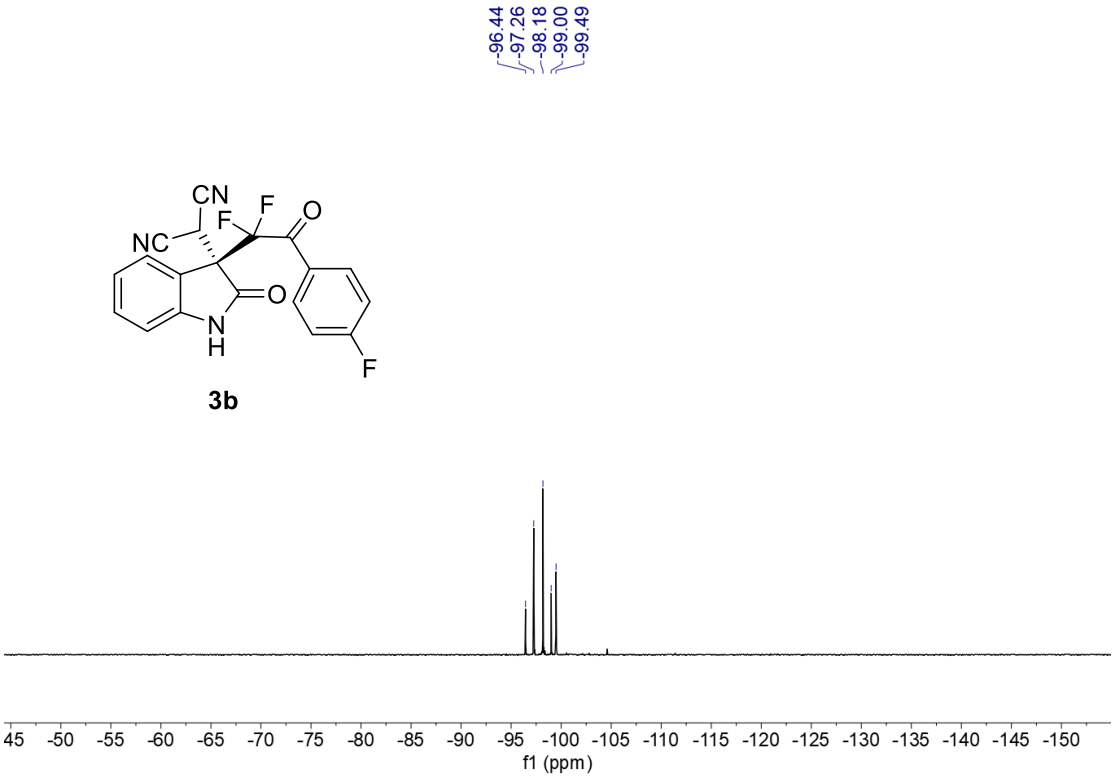
7.18
7.16
7.15
7.13
7.06
7.04
4.93
CN
F
F
O
NC
O
N
H
F
3b
1.03
2.00
1.00
1.01
3.03
1.06
0.98
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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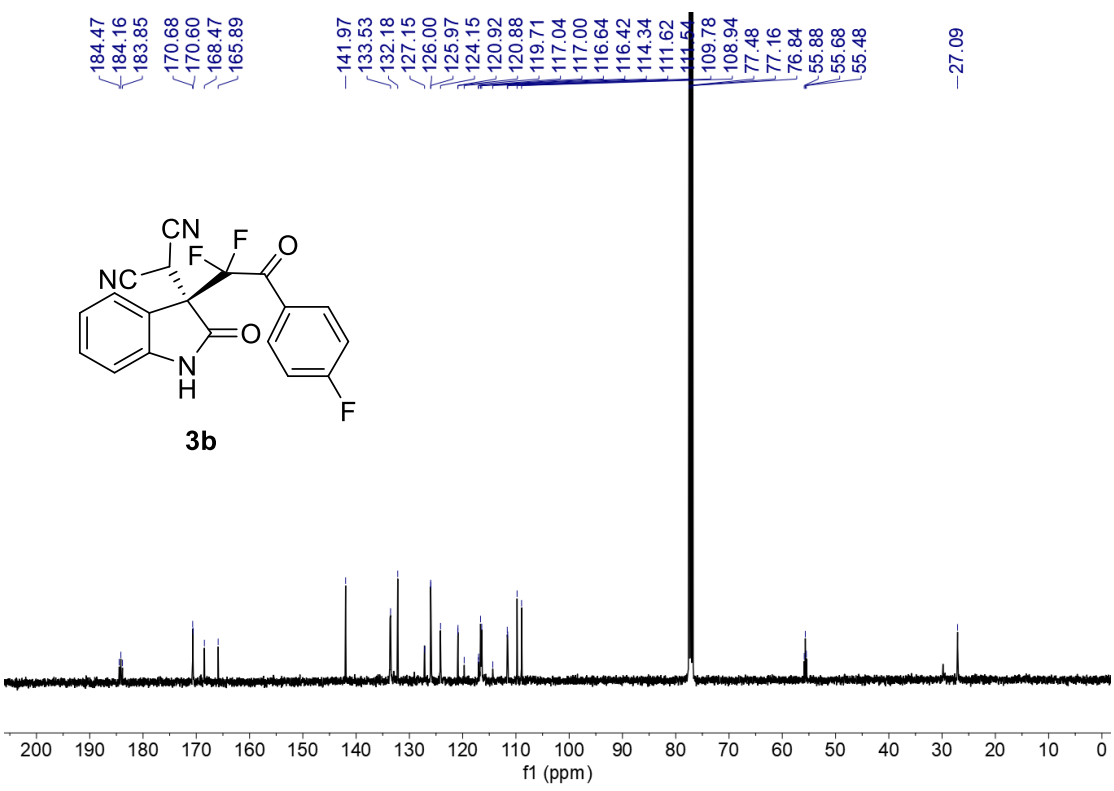
f1 (ppm)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132.18
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125.97
124.15
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120.88
119.71
117.04
117.00
116.64
116.42
114.34
111.62
111.54
109.78
108.94
77.48
77.16
76.84
55.88
55.68
55.48
27.09
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O
N
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F
3b
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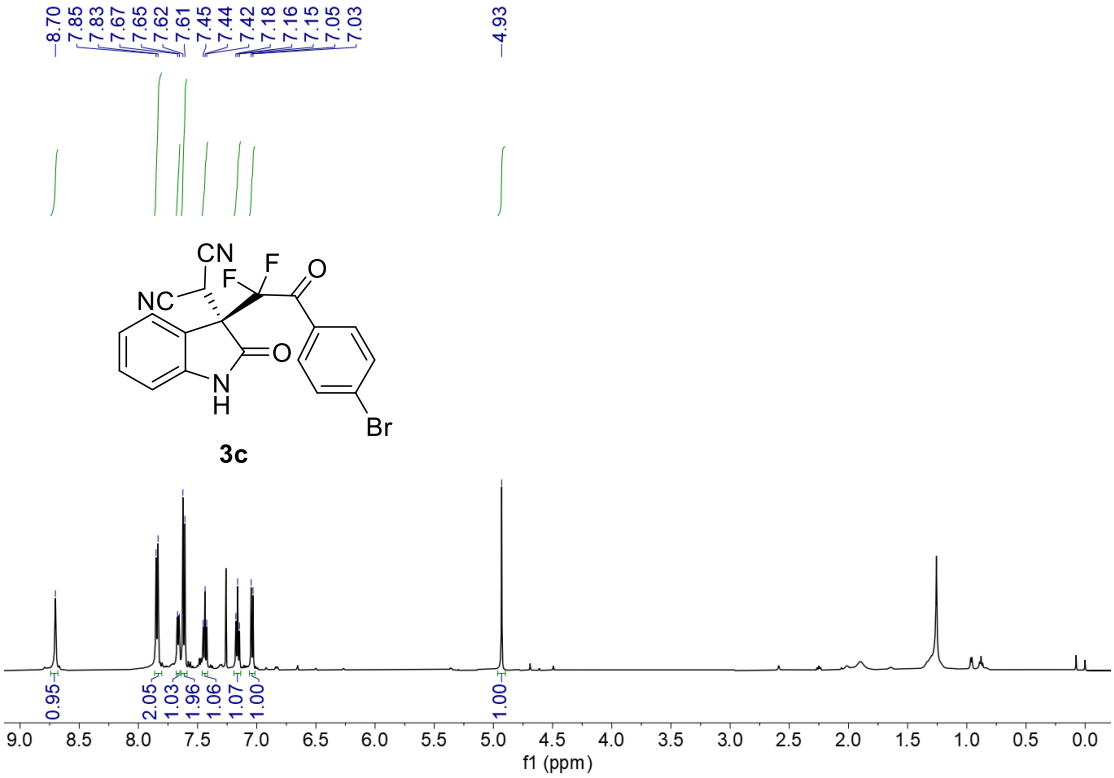
f1 (ppm)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7.05
7.03
4.93
CN
F
F
O
NC
O
N
H
Br
3c
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2.05
1.03
1.96
1.06
1.07
1.00
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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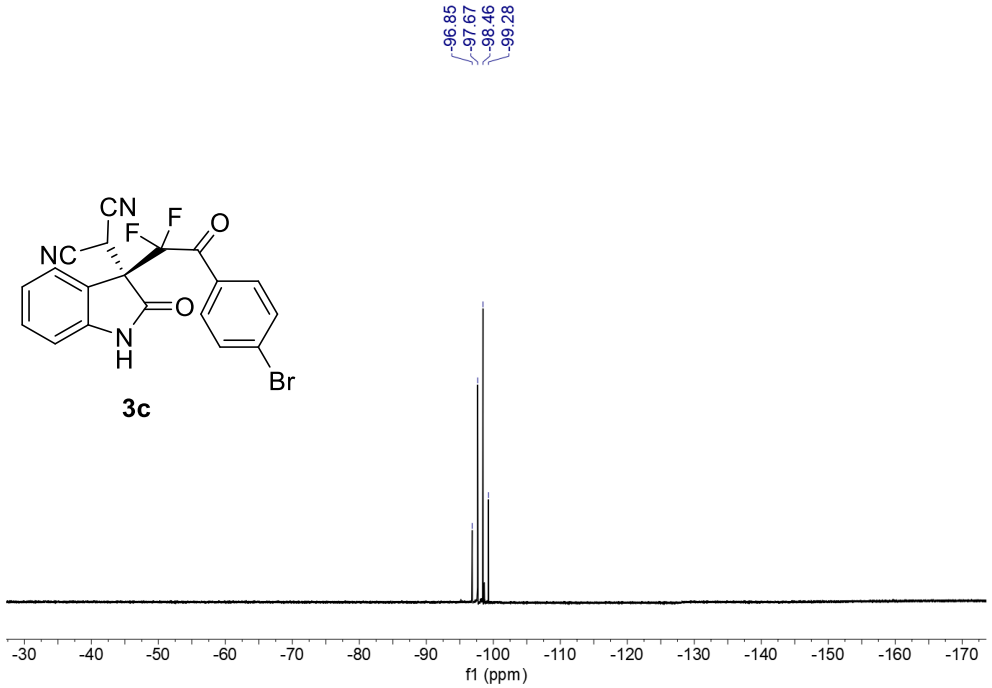
0.0
f1 (ppm)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-150
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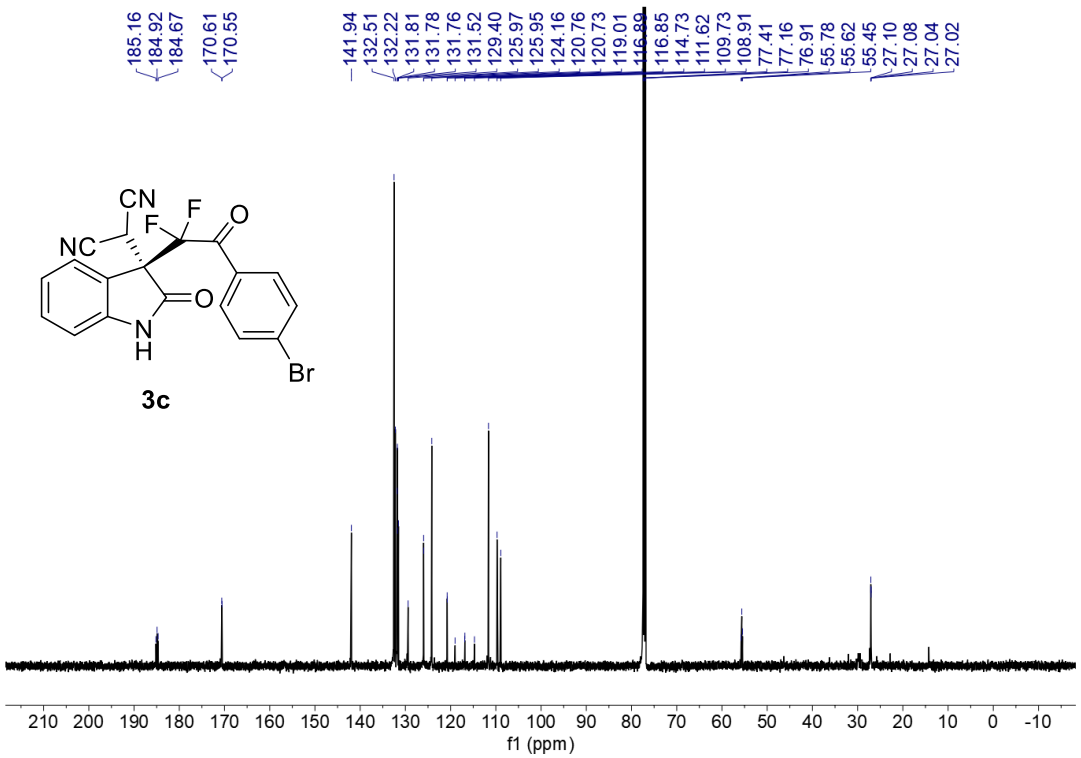
-170
f1 (ppm)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3c
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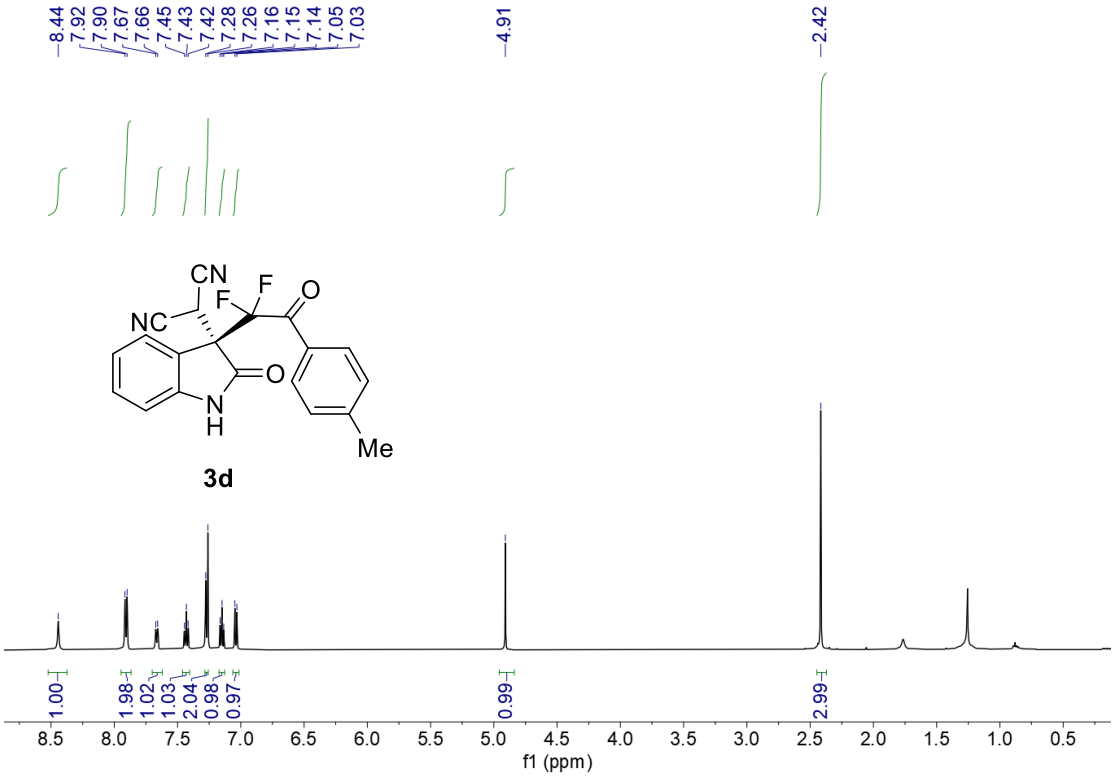
f1 (ppm)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N
H
Me
3d
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1.98
1.02
1.03
2.04
0.98
0.97
0.99
2.99
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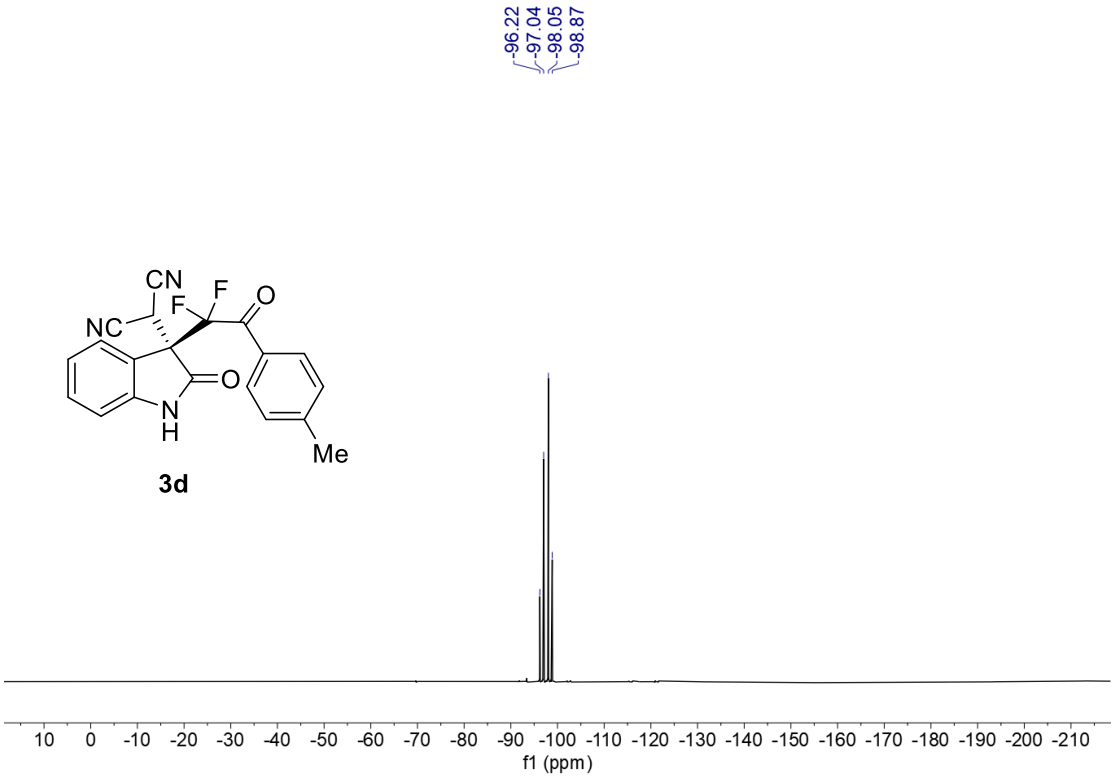
f1 (ppm)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3d
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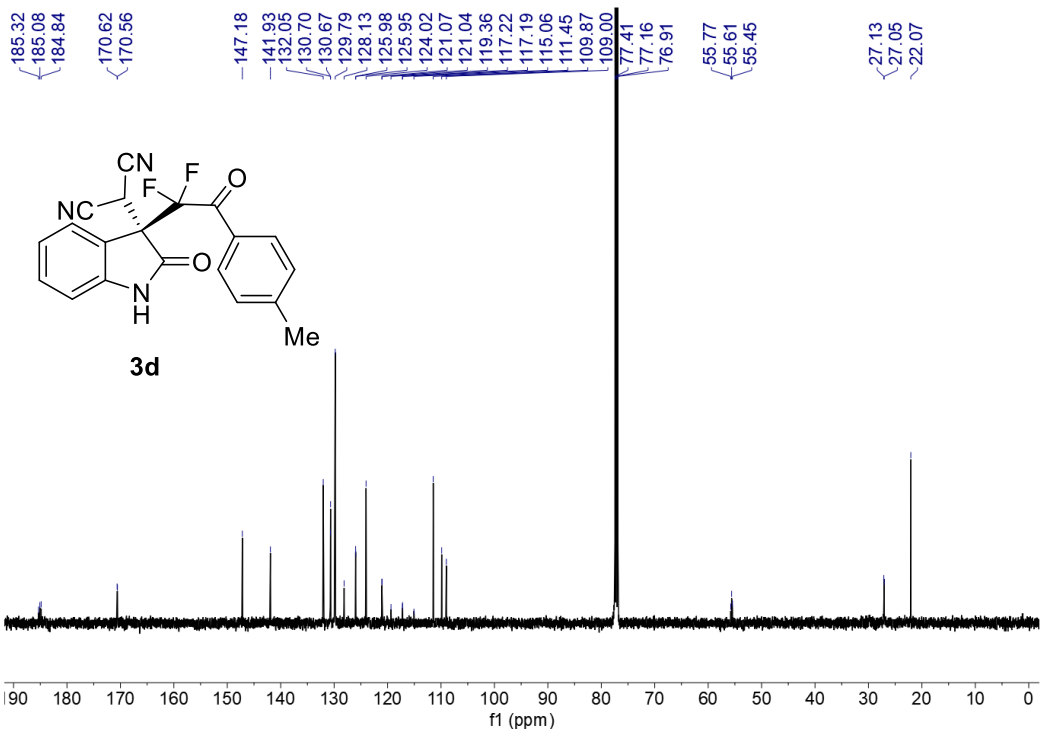
f1 (ppm)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27.05
22.07
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H
Me
3d
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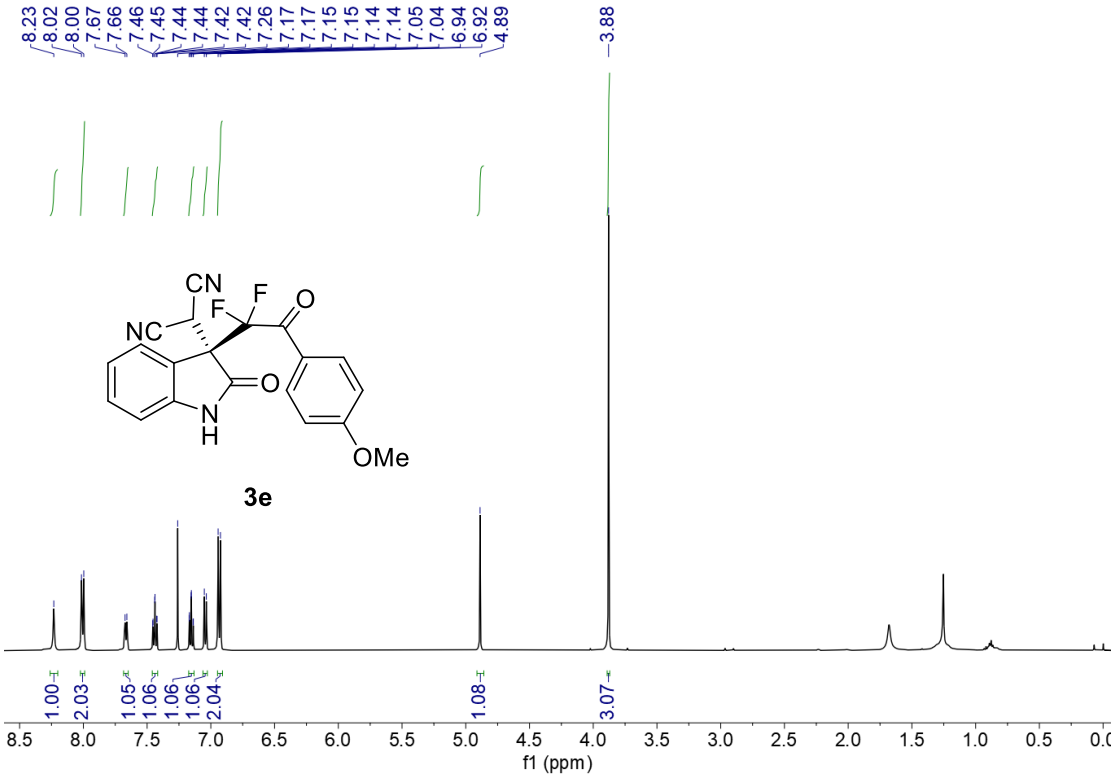
f1 (ppm)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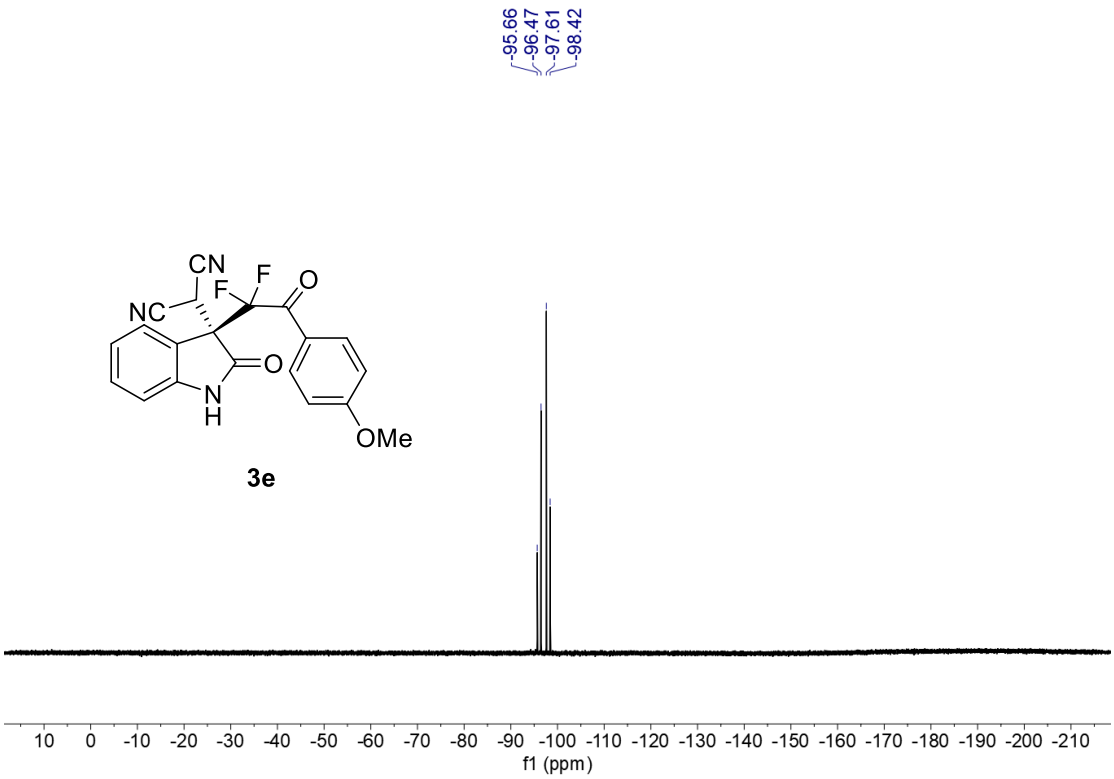
1.08
3.07
f1 (ppm)

3e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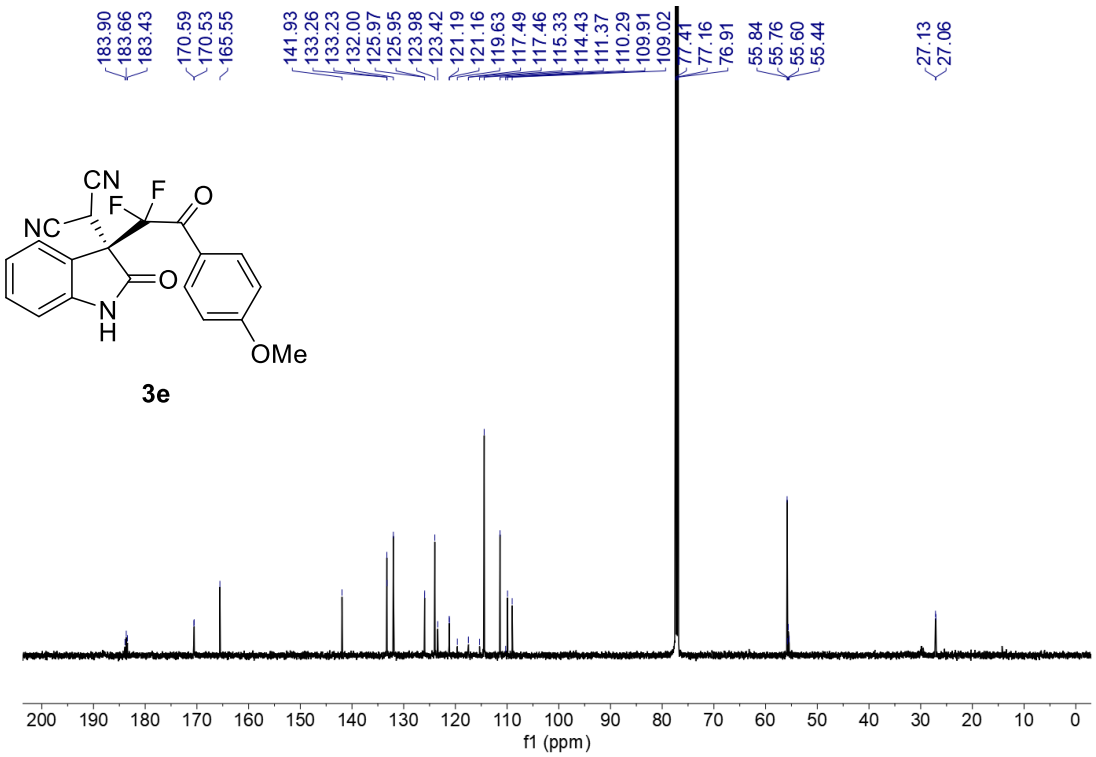
f1 (ppm)

3e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27.06
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N
H
OMe
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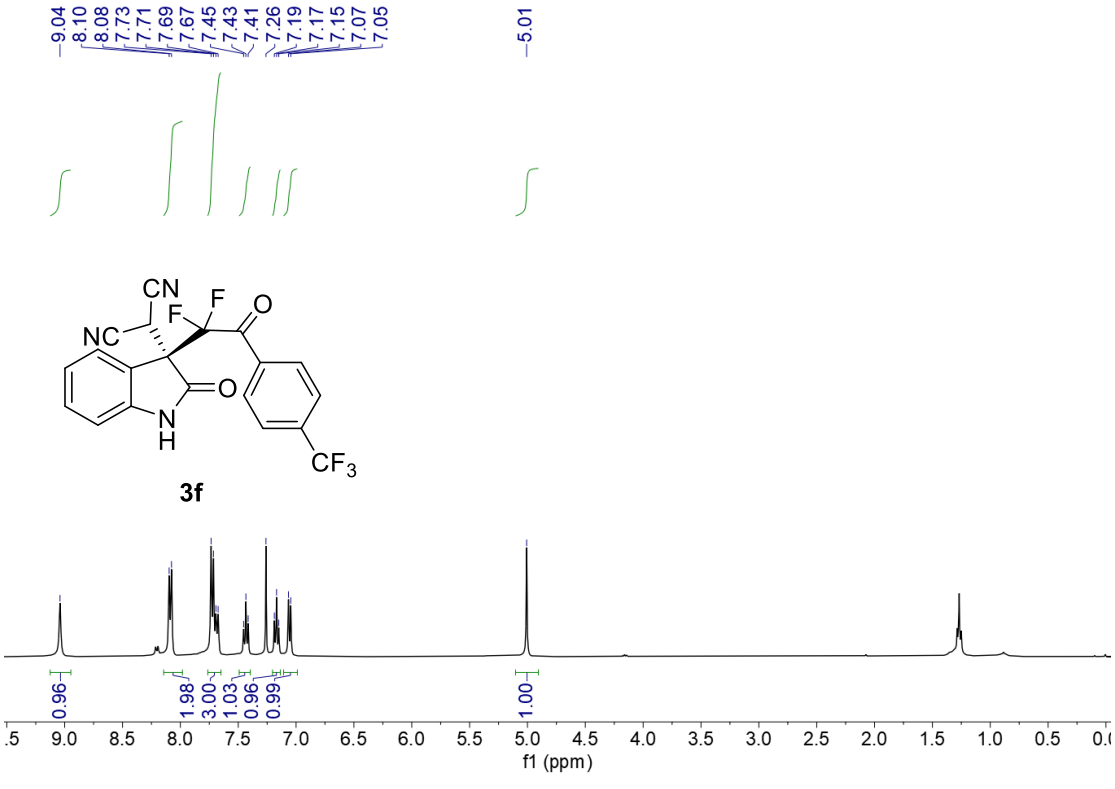
f1 (ppm)

3e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7.05
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N
H
CF3
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1.98
3.00
1.03
0.96
0.99
1.00
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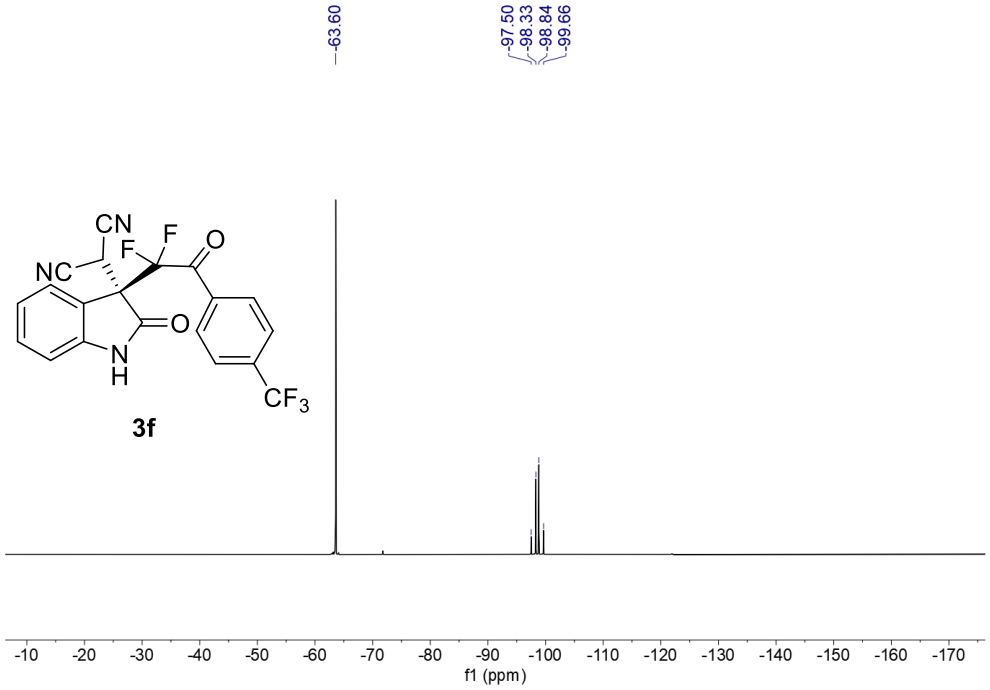
f1 (ppm)

3f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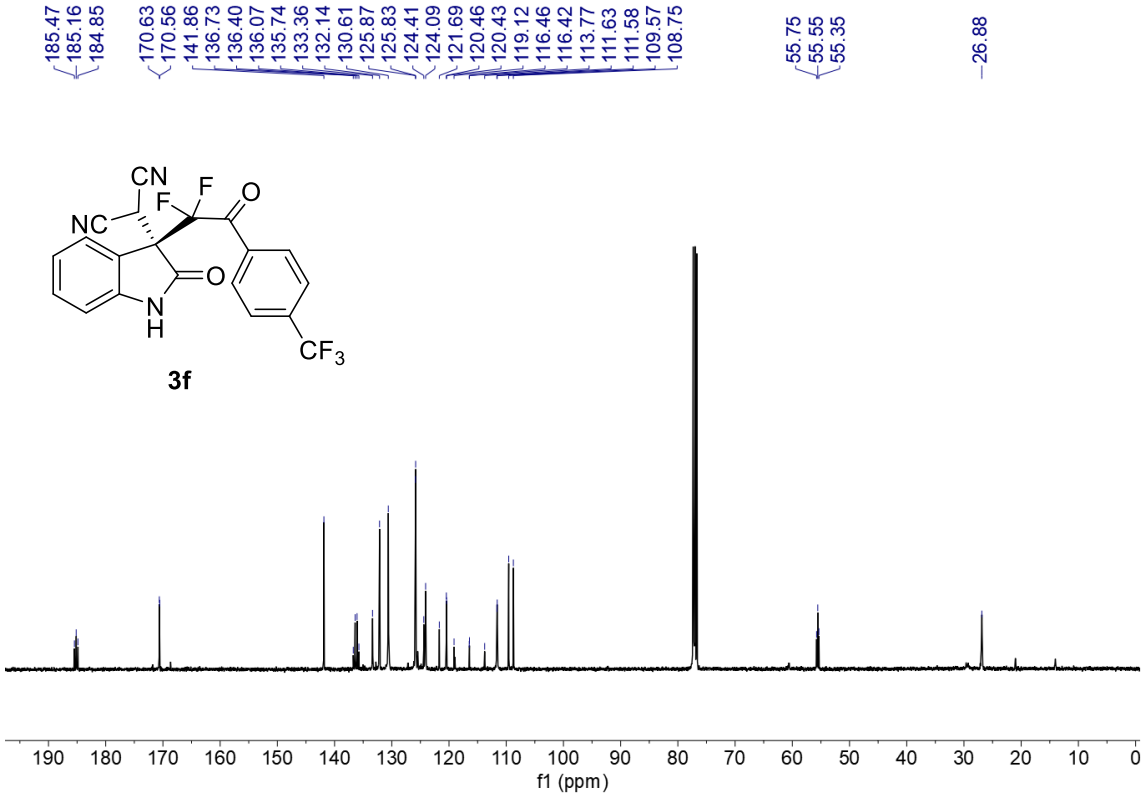
f1 (ppm)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111.58
109.57
108.75
55.75
55.55
55.35
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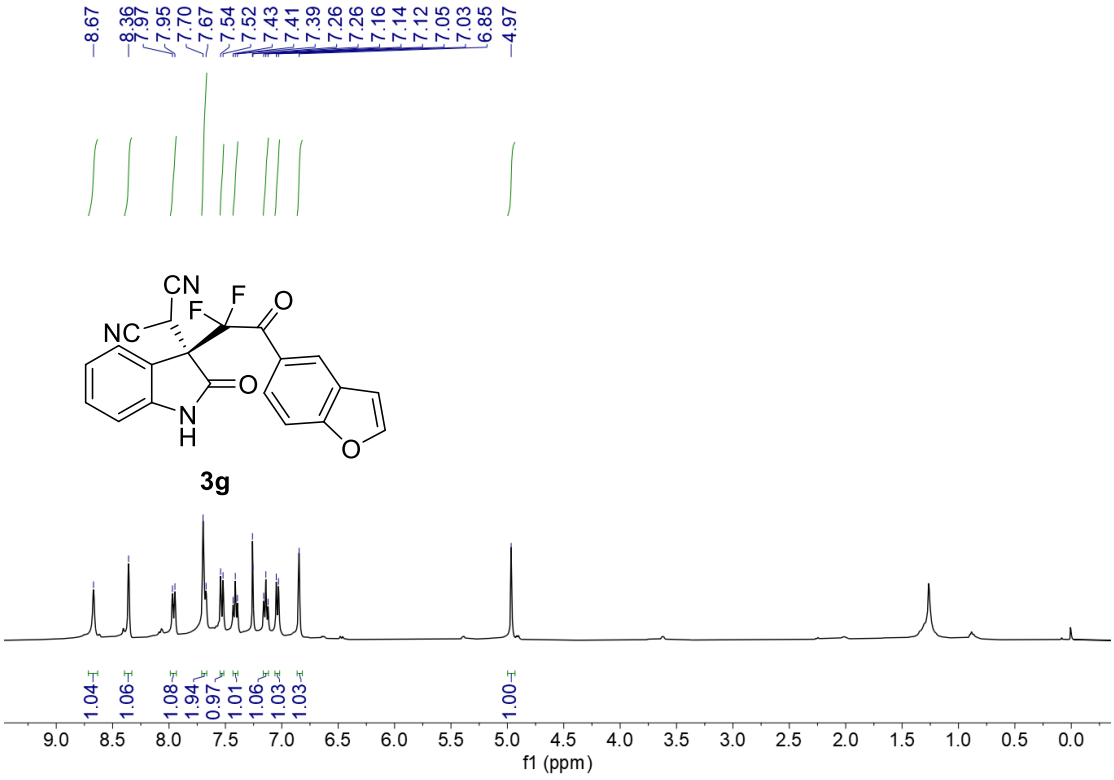
f1 (ppm)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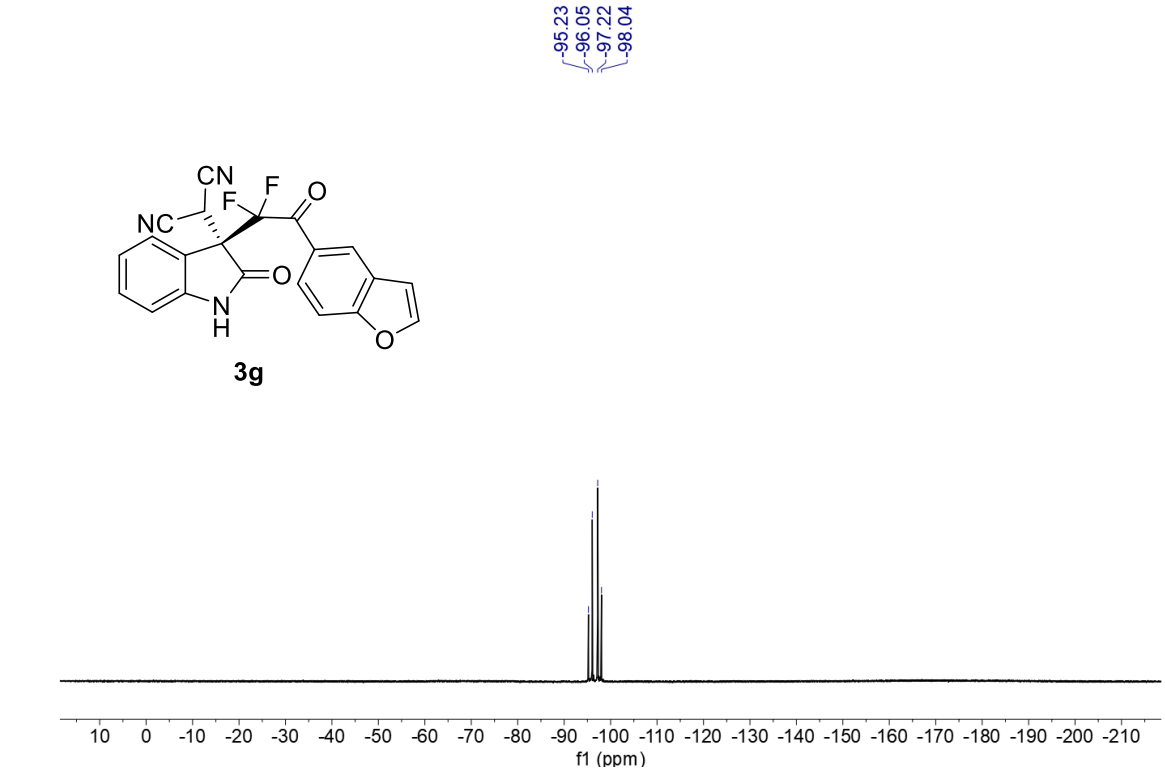
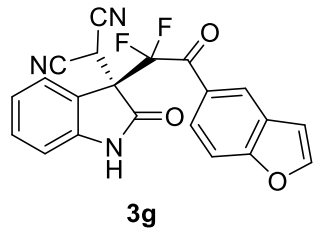
8.36
7.97
7.95
7.70
7.67
7.54
7.52
7.43
7.41
7.39
7.26
7.26
7.16
7.14
7.12
7.05
7.03
6.85
4.97
CN
F
F
O
NC
O
N
H
O
1.04
1.06
1.08
1.94
0.97
1.01
1.06
1.03
1.03
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3g


-95.23
-96.05
-97.22
-98.04
CN
F
F
O
NC
O
N
H
O
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

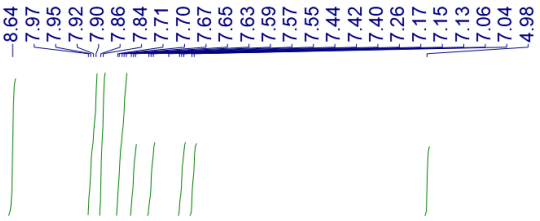
3g

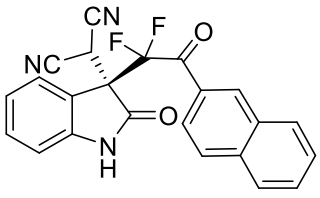

185.23
184.98
184.75
170.90
170.83
158.62
147.18
142.02
132.04
127.97
127.05
125.91
125.88
125.50
125.47
124.01
121.13
121.10
119.55
117.42
117.39
115.27
112.33
111.55
109.92
109.04
107.55
107.53
77.41
77.16
76.91
55.88
55.72
55.56
27.17
27.10


CN
F
F
O
NC
O
N
H
O

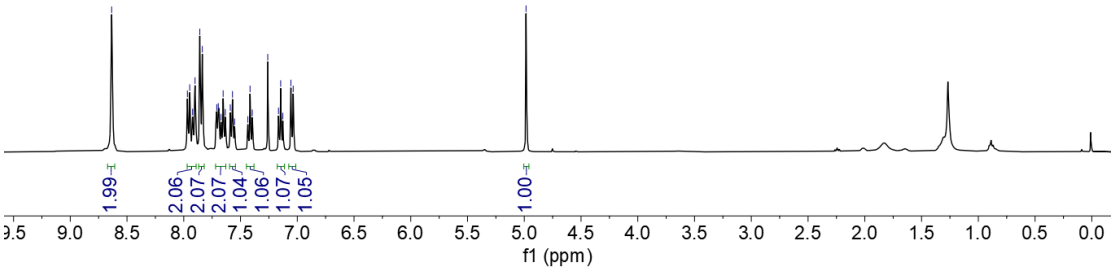
3g

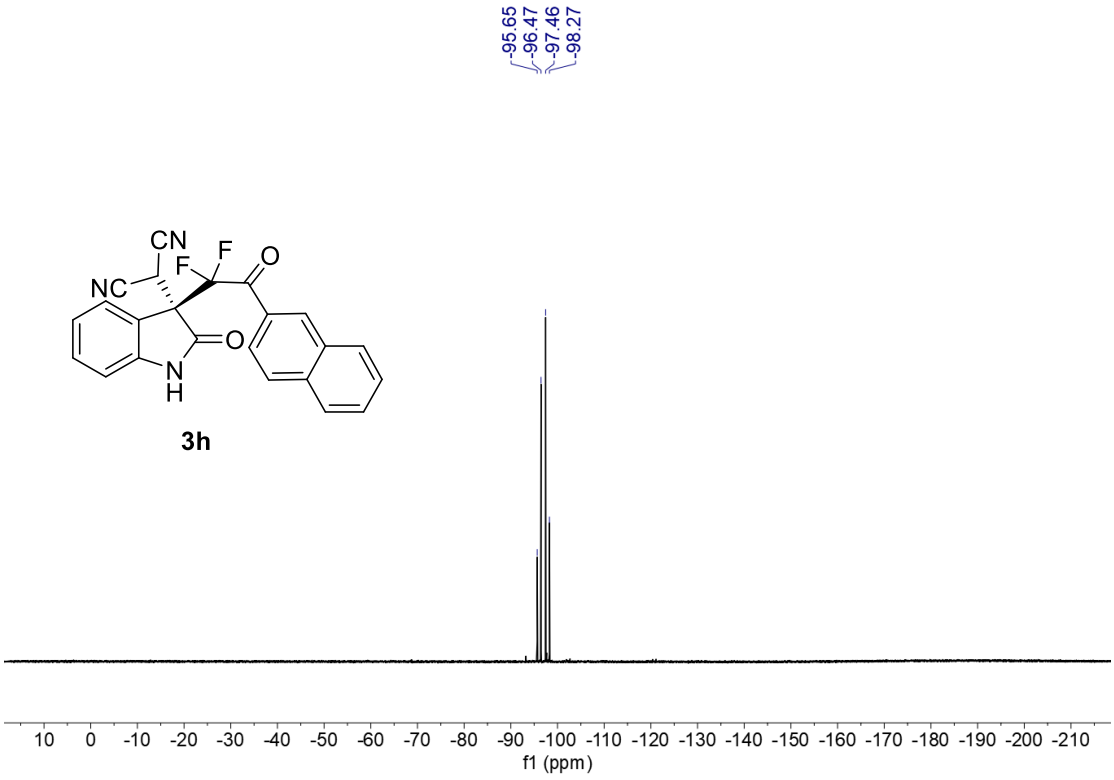
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

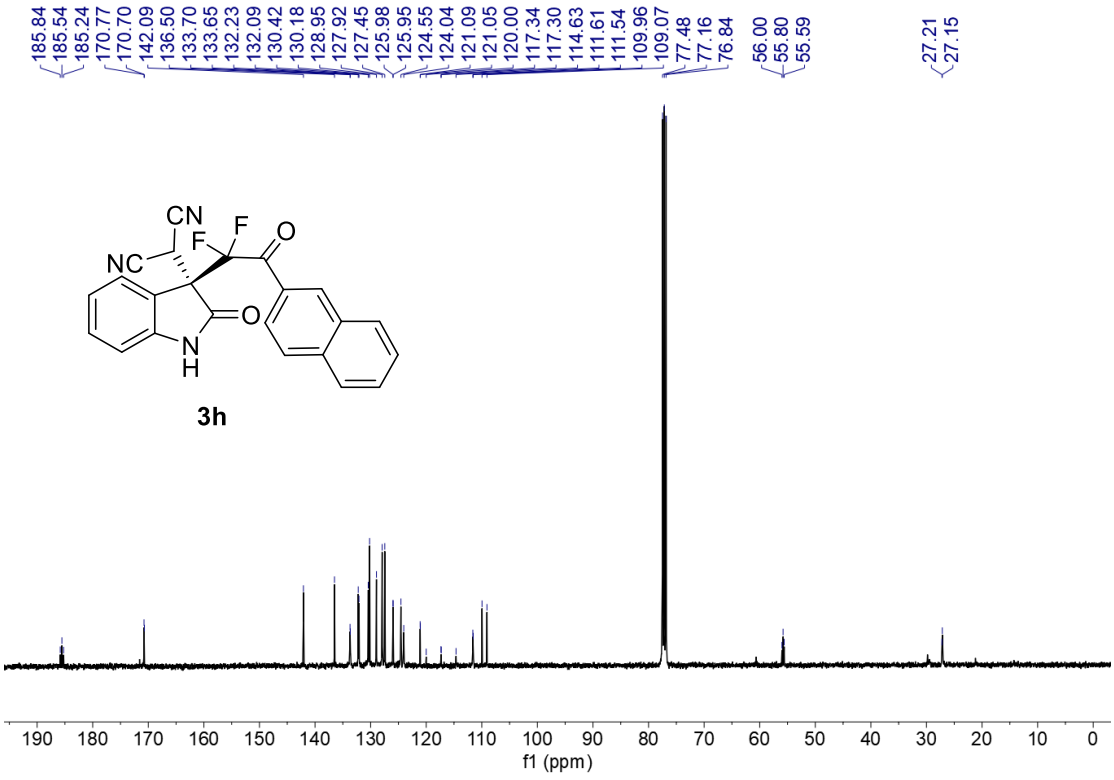

8.64
7.97
7.95
7.92
7.90
7.86
7.84
7.71
7.70
7.67
7.65
7.63
7.59
7.57
7.55
7.44
7.42
7.40
7.26
7.17
7.15
7.13
7.06
7.04
4.98

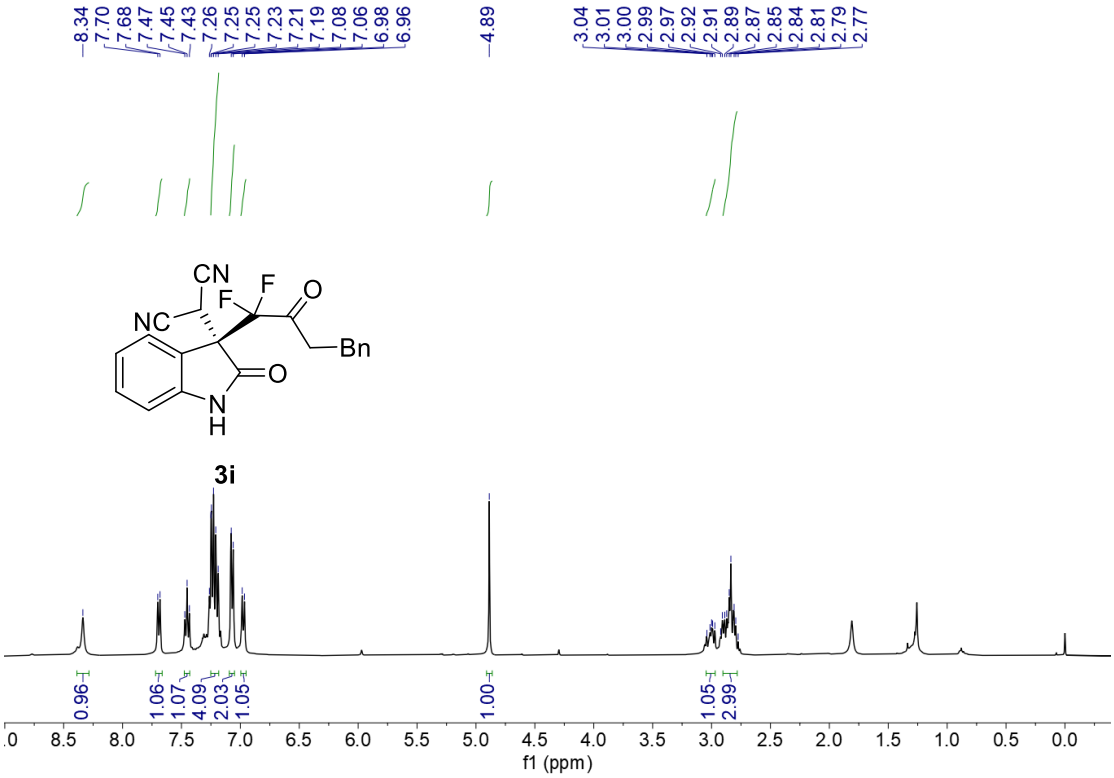

CN
F
F
O
NC
O
N
H

3h


1.99
2.06
2.07
2.07
1.04
1.06
1.07
1.05
1.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-95.65
-96.47
-97.46
-98.27
CN
F
F
O
NC
O
N
H
3h
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


185.84
185.54
185.24
170.77
170.70
142.09
136.50
133.70
133.65
132.23
132.09
130.42
130.18
128.95
127.92
127.45
125.98
125.95
124.55
124.04
121.09
121.05
120.00
117.34
117.30
114.63
111.61
111.54
109.96
109.07
77.48
77.16
76.84
56.00
55.80
55.59
27.21
27.15
CN
F
F
O
NC
O
N
H
3h
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.34
7.70
7.68
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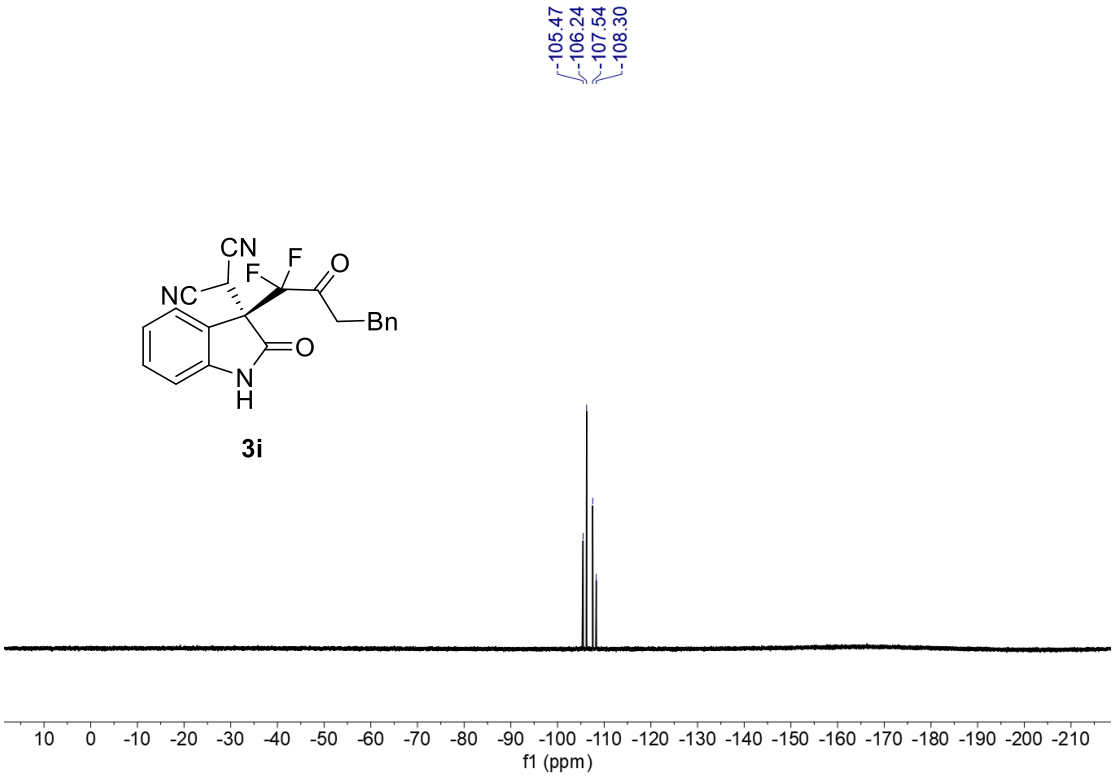
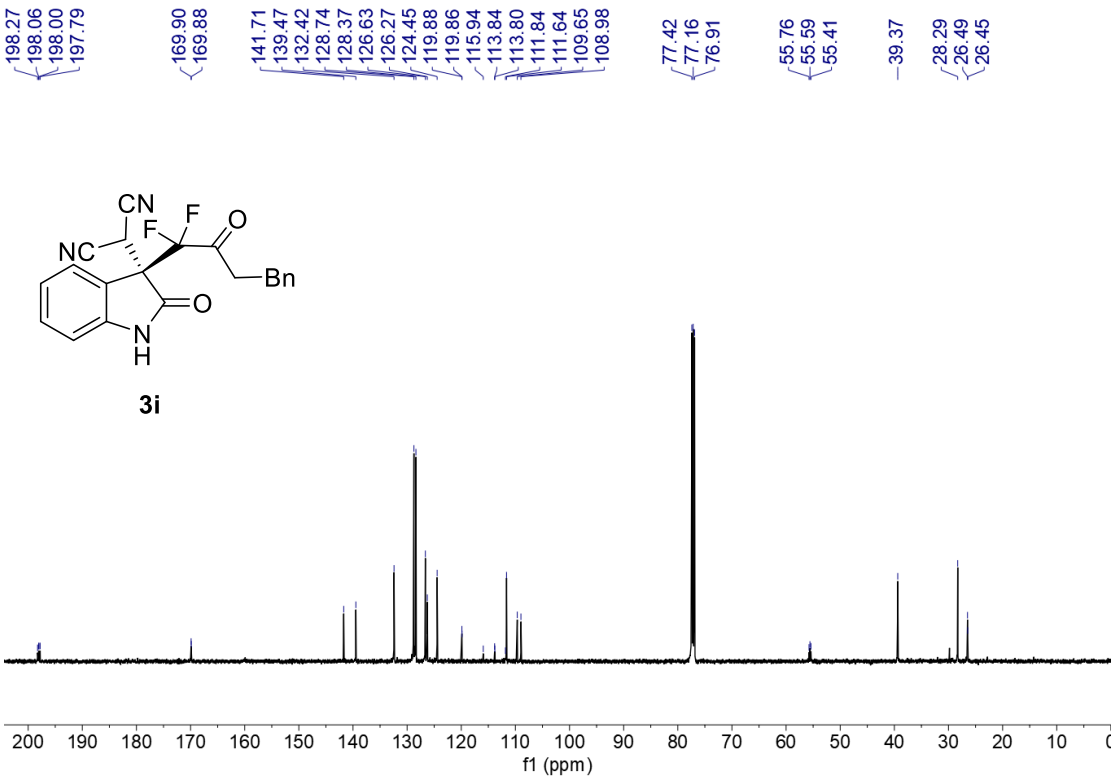
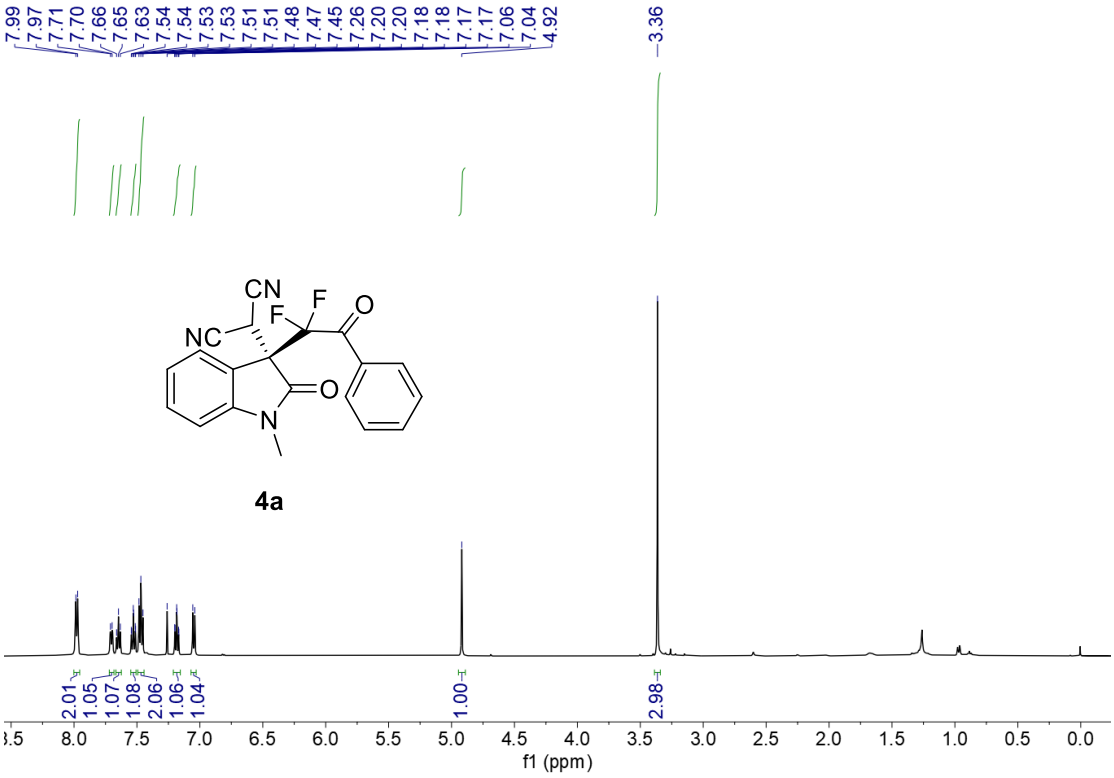
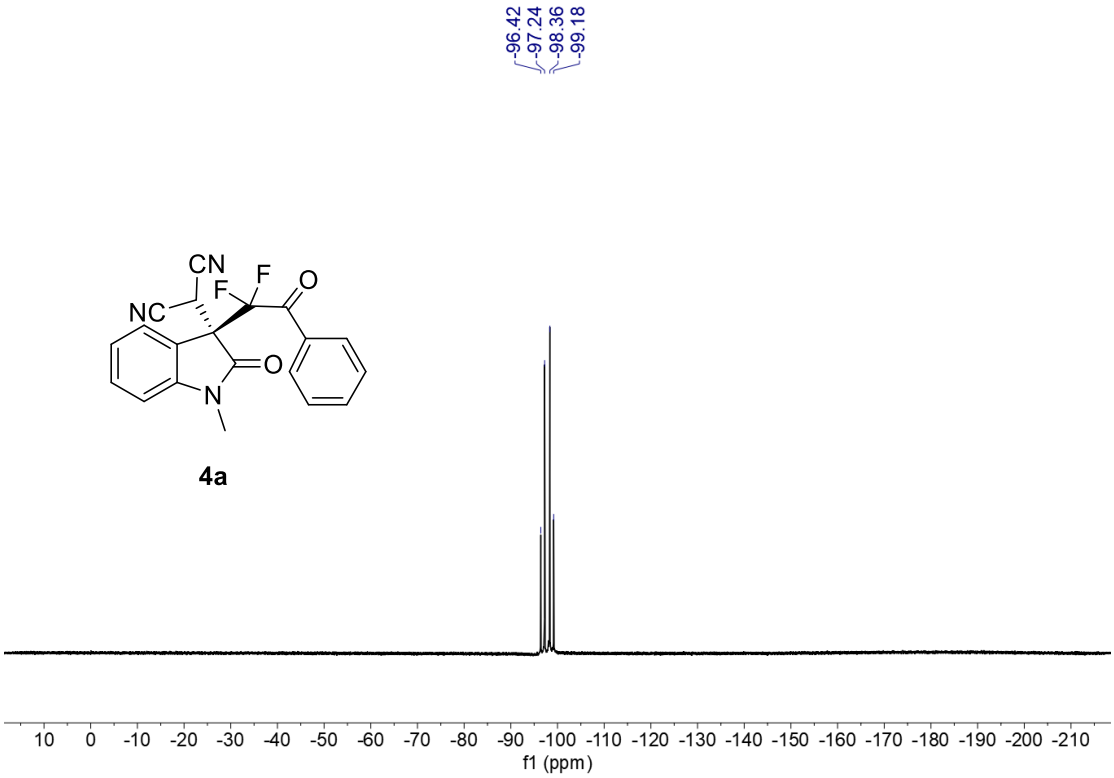
7.45
7.43
7.26
7.25
7.25
7.23
7.21
7.19
7.08
7.06
6.98
6.96
4.89
3.04
3.01
3.00
2.99
2.97
2.92
2.91
2.89
2.87
2.85
2.84
2.81
2.79
2.77
CN
F
F
O
NC
Bn
O
N
H
3i
0.96
1.06
1.07
4.09
2.03
1.05
1.00
1.05
2.99
f1 (ppm)

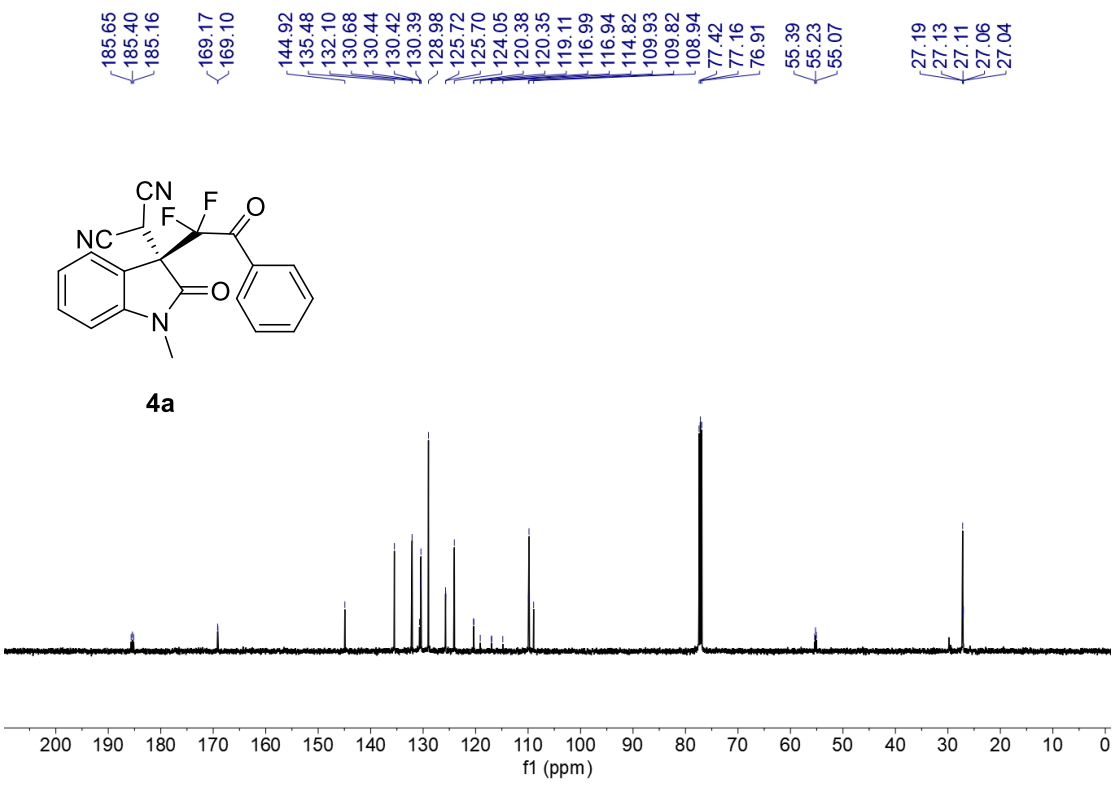

-105.47
-106.24
-107.54
-108.30
CN
F
F
O
NC
Bn
O
N
H
3i
f1 (ppm)


198.27
198.06
198.00
197.79
169.90
169.88
141.71
139.47
132.42
128.74
128.37
126.63
126.27
124.45
119.88
119.86
115.94
113.84
113.80
111.84
111.64
109.65
108.98
77.42
77.16
76.91
55.76
55.59
55.41
39.37
28.29
26.49
26.45
CN
F
F
O
NC
Bn
O
N
H
3i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

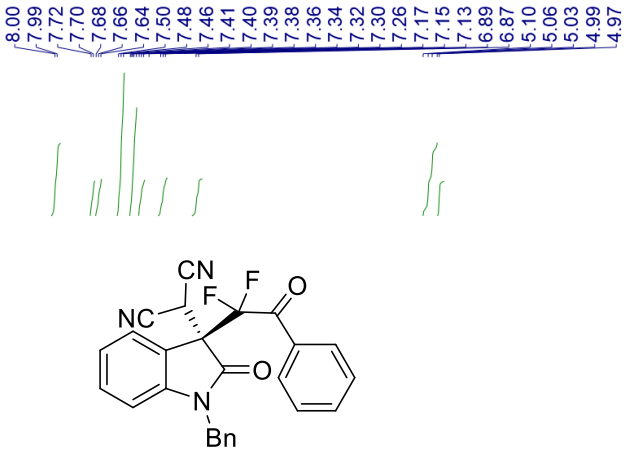

7.99
7.97
7.71
7.70
7.66
7.65
7.63
7.54
7.54
7.53
7.53
7.51
7.51
7.48
7.47
7.45
7.26
7.20
7.20
7.18
7.17
7.17
7.06
7.04
4.92
3.36
CN
F
F
O
NC
O
N
4a
2.01
1.05
1.07
1.08
2.06
1.06
1.04
1.00
2.98
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-96.42
-97.24
-98.36
-99.18
CN
F
F
O
NC
O
N
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

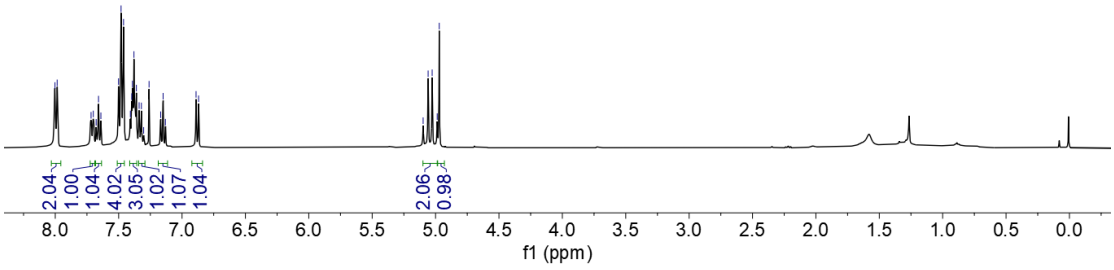
4a


185.65
185.40
185.16
169.17
169.10
144.92
135.48
132.10
130.68
130.44
130.42
130.39
128.98
125.72
125.70
124.05
120.38
120.35
119.11
116.99
116.94
114.82
109.93
109.82
108.94
77.42
77.16
76.91
55.39
55.23
55.07
27.19
27.13
27.11
27.06
27.04
CN
F
F
O
NC
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

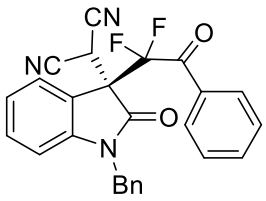
4a


8.00
7.99
7.72
7.70
7.68
7.66
7.64
7.50
7.48
7.46
7.41
7.40
7.39
7.38
7.36
7.34
7.32
7.30
7.26
7.17
7.15
7.13
6.89
6.87
5.10
5.06
5.03
4.99
4.97
CN
F
F
O
NC
O
N
Bn

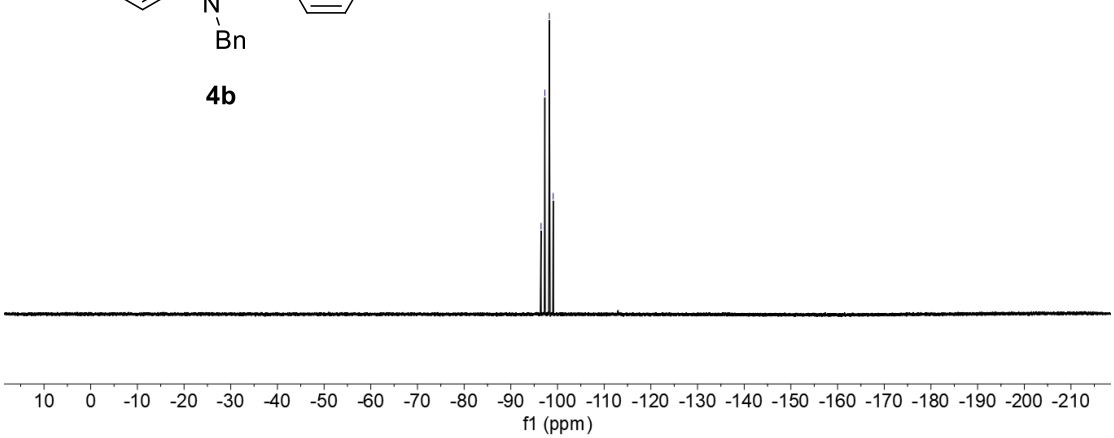
4b

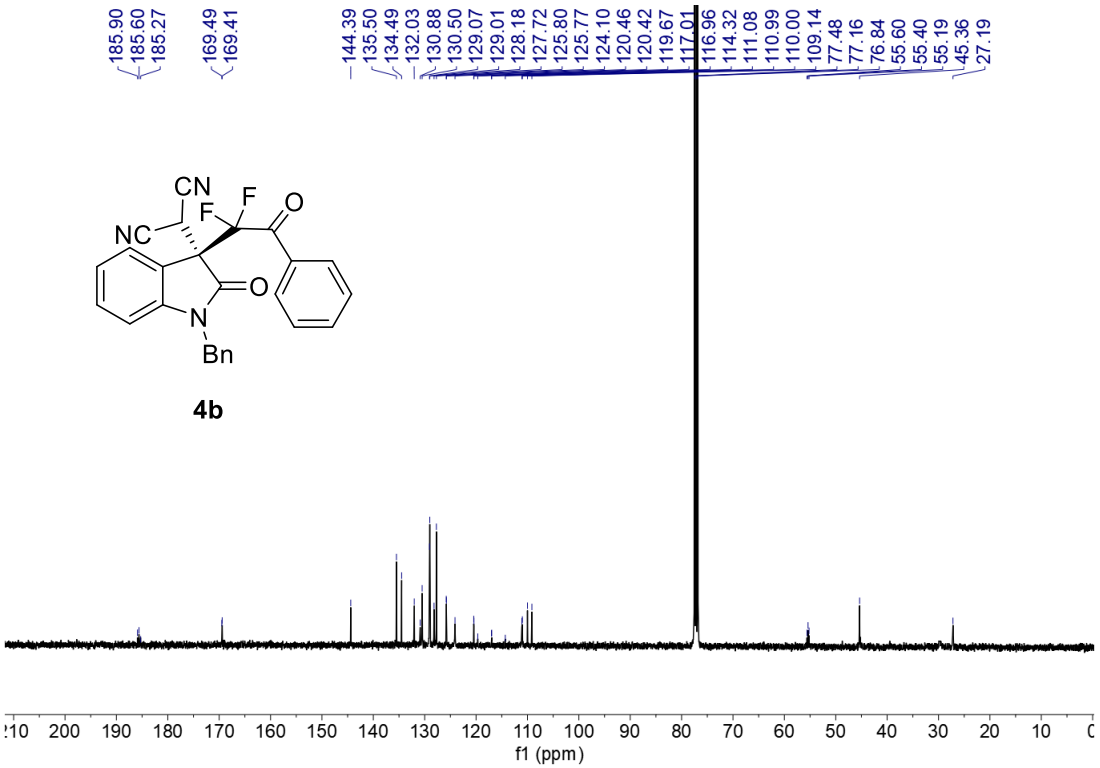

2.04
1.00
1.04
4.02
3.05
1.02
1.07
1.04
2.06
0.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-96.47
-97.29
-98.26
-99.08

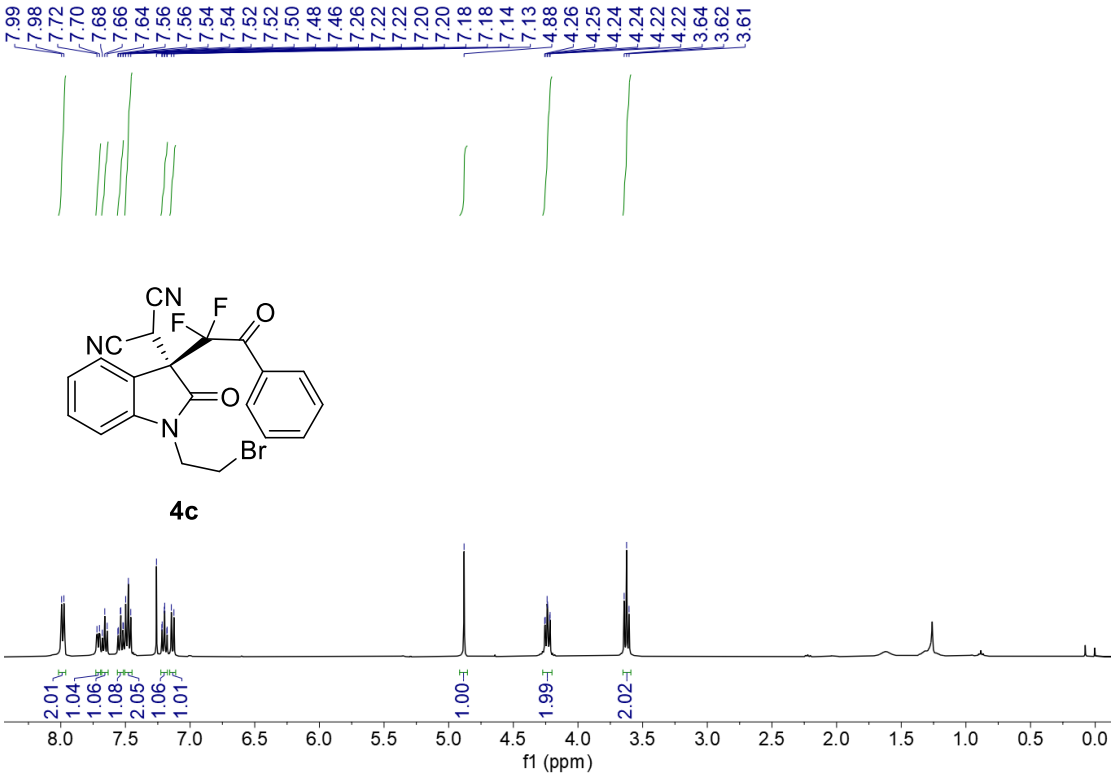

CN
F
F
O
NC
O
N
Bn

4b


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


185.90
185.60
185.27
169.49
169.41
144.39
135.50
134.49
132.03
130.88
130.50
129.07
129.01
128.18
127.72
125.80
125.77
124.10
120.46
120.42
119.67
117.01
116.96
114.32
111.08
110.99
110.00
109.14
77.48
77.16
76.84
55.60
55.40
55.19
45.36
27.19
CN
F
O
NC
O
N
Bn
f1 (ppm)

4b


7.99
7.98
7.72
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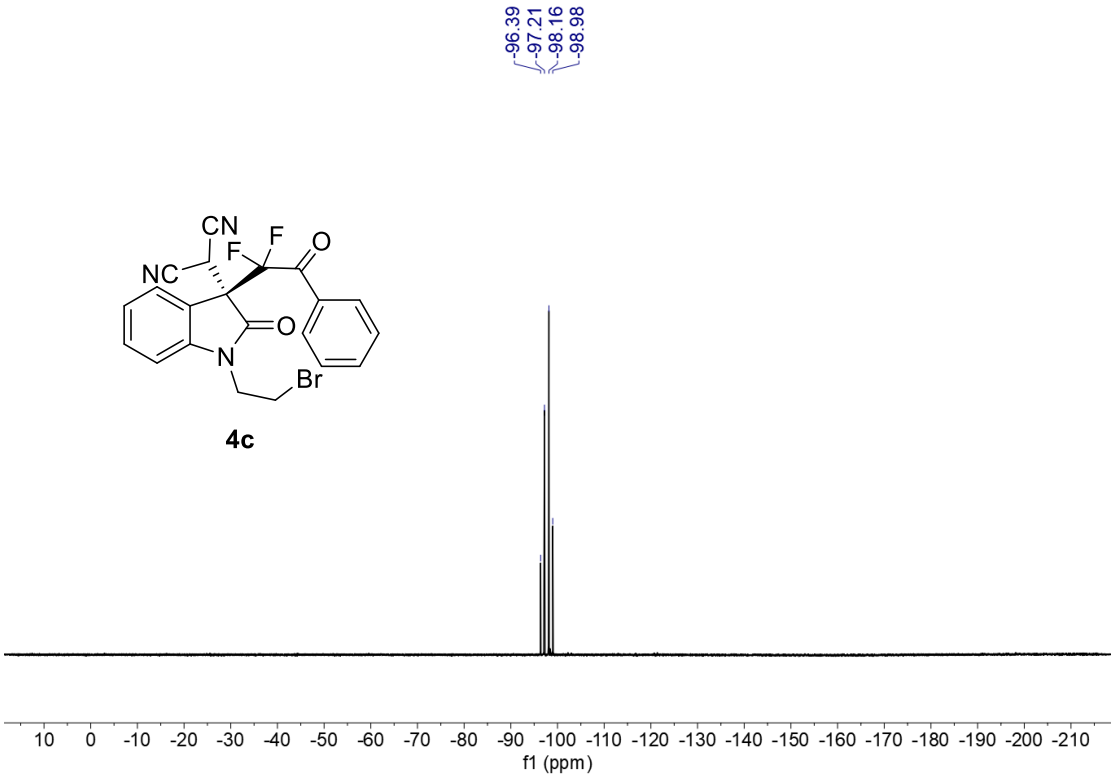
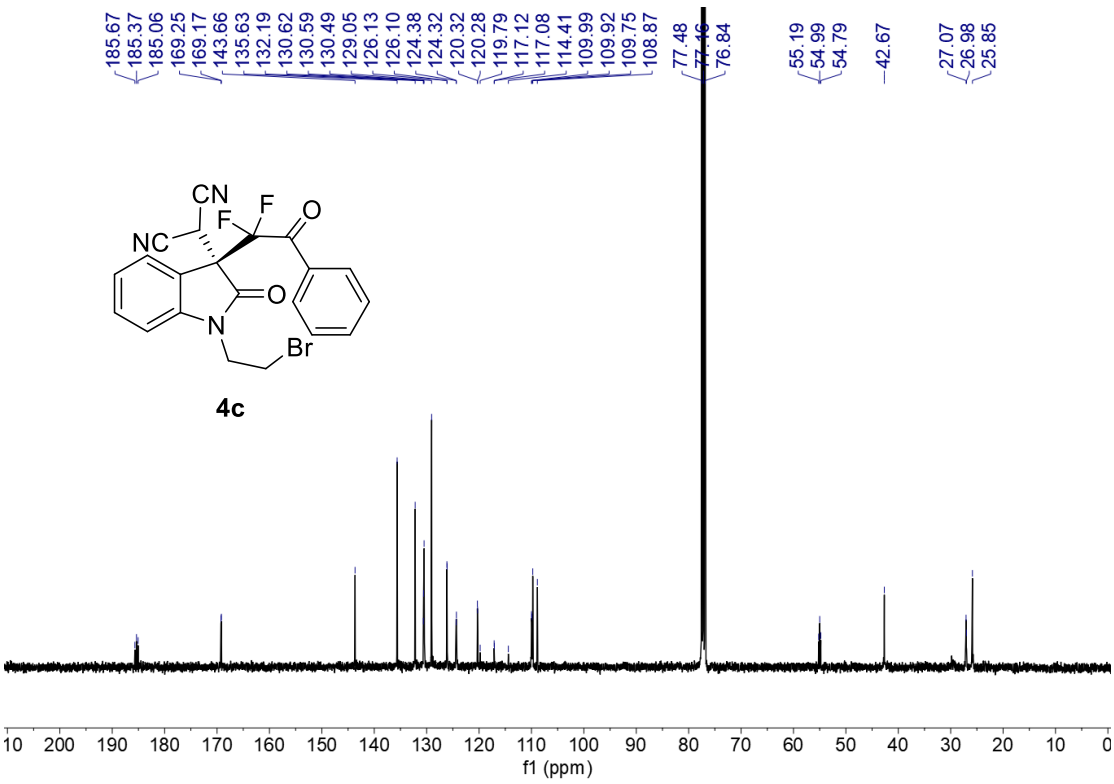
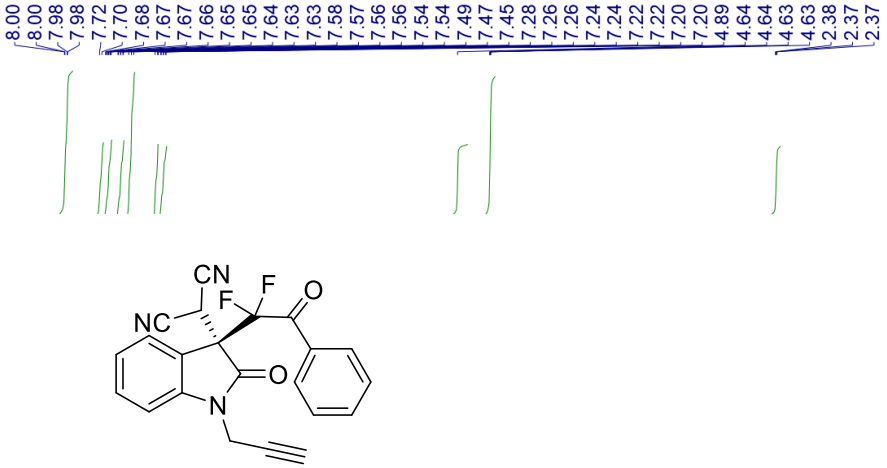
7.68
7.66
7.64
7.56
7.56
7.54
7.54
7.52
7.52
7.50
7.48
7.46
7.26
7.22
7.22
7.20
7.20
7.18
7.18
7.14
7.13
4.88
4.26
4.25
4.24
4.24
4.22
4.22
3.64
3.62
3.61
CN
F
O
NC
O
N
Br
2.01
1.04
1.06
1.08
2.05
1.06
1.01
1.00
1.99
2.02
f1 (ppm)

4c


-96.39
-97.21
-98.16
-98.98
CN
F
F
O
NC
O
N
Br
4c
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


185.67
185.37
185.06
169.25
169.17
143.66
135.63
132.19
130.62
130.59
130.49
129.05
126.13
126.10
124.38
124.32
120.32
120.28
119.79
117.12
117.08
114.41
109.99
109.92
109.75
108.87
77.48
77.16
76.84
55.19
54.99
54.79
42.67
27.07
26.98
25.85
CN
F
F
O
NC
O
N
Br
4c
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.00
8.00
7.98
7.98
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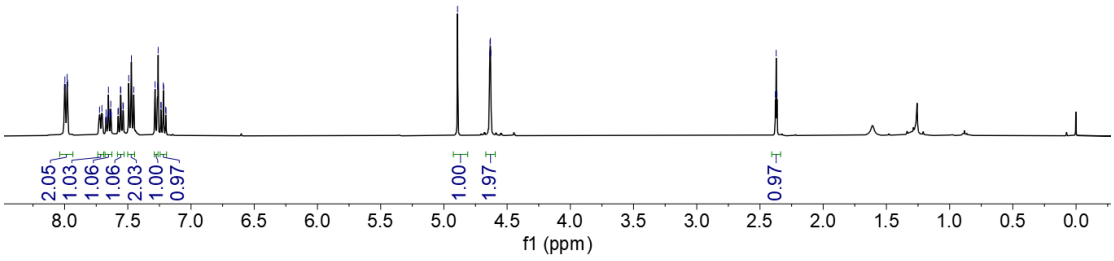
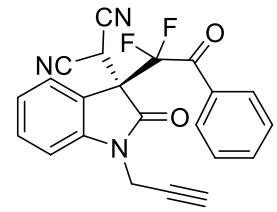
7.70
7.68
7.67
7.67
7.66
7.65
7.65
7.64
7.63
7.63
7.58
7.57
7.56
7.56
7.54
7.54
7.49
7.47
7.45
7.28
7.26
7.26
7.24
7.24
7.22
7.22
7.20
7.20
4.89
4.64
4.64
4.63
4.63
2.38
2.37
2.37

CN
F
O
NC
O
N

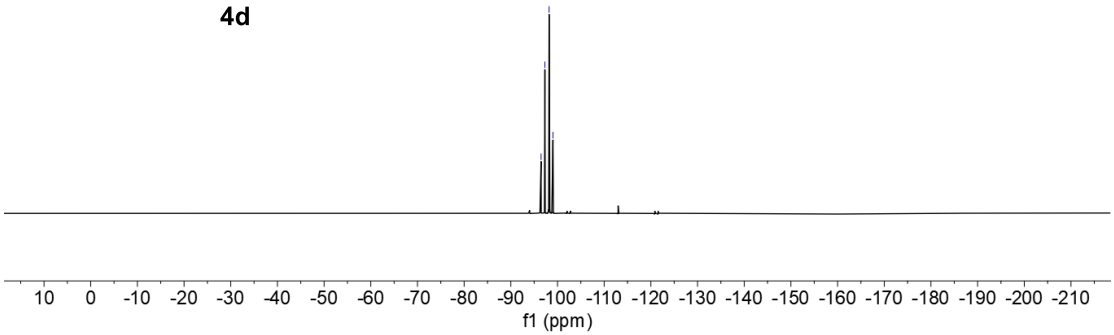
4d

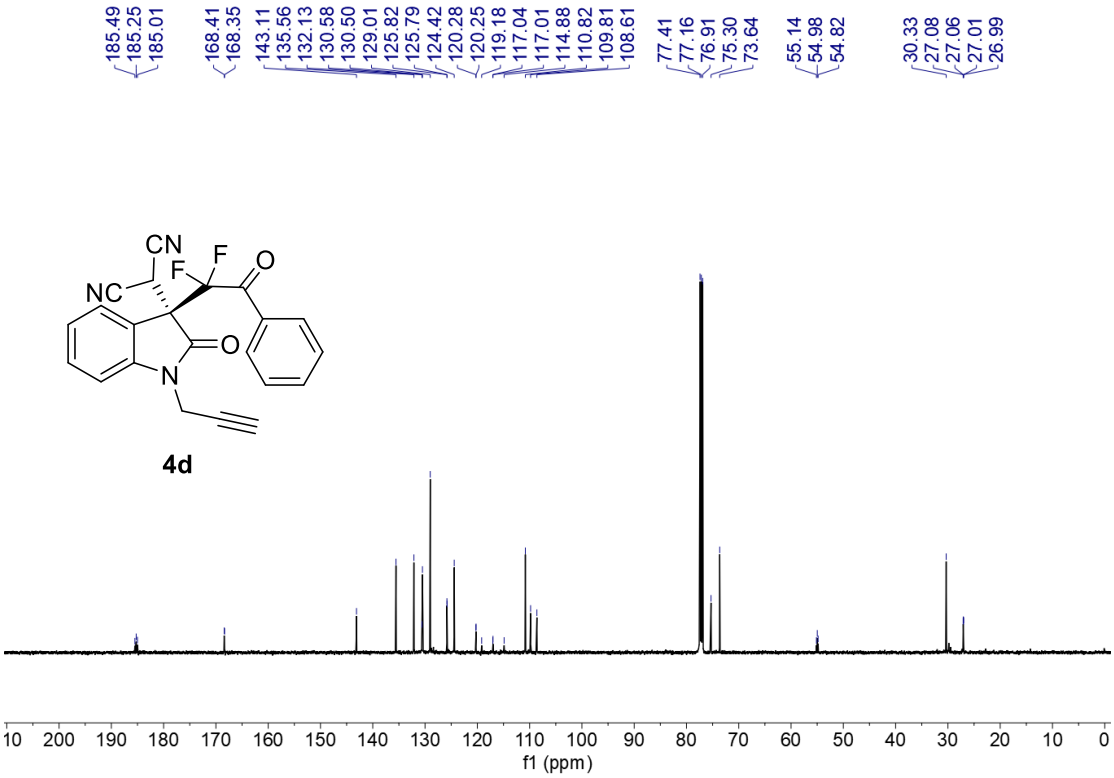

2.05
1.03
1.06
1.06
2.03
1.00
0.97
1.00
1.97
0.97
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

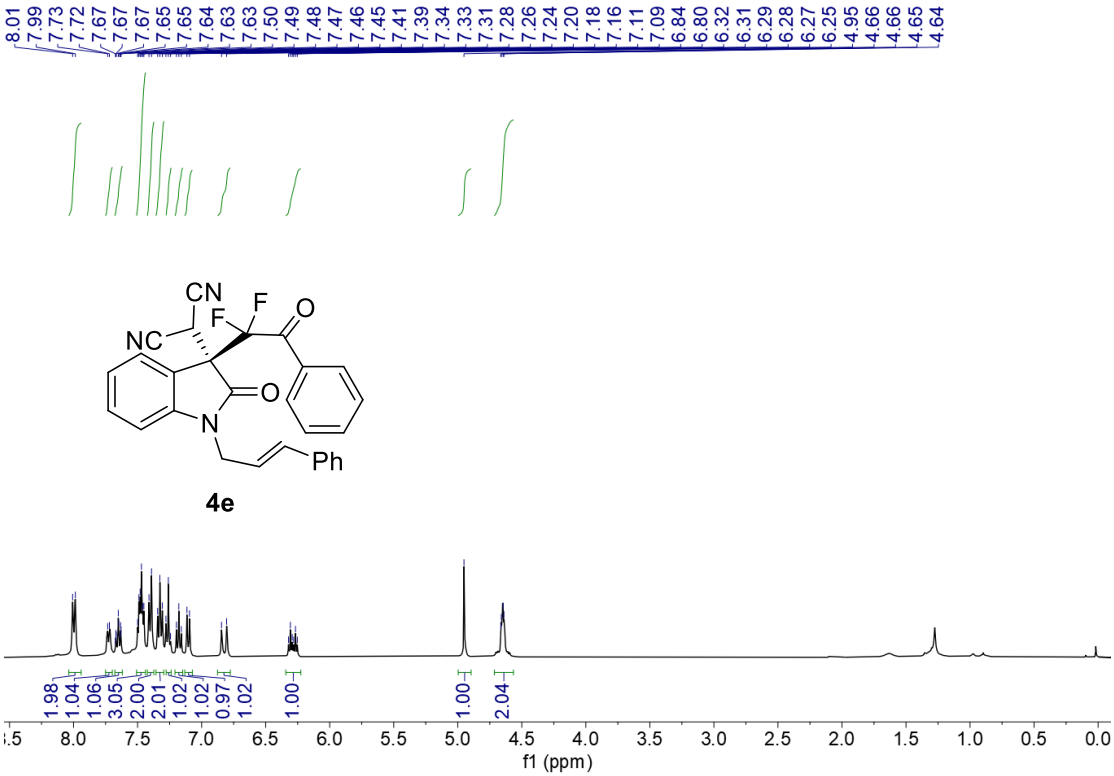

-96.48
-97.30
-98.20
-99.03

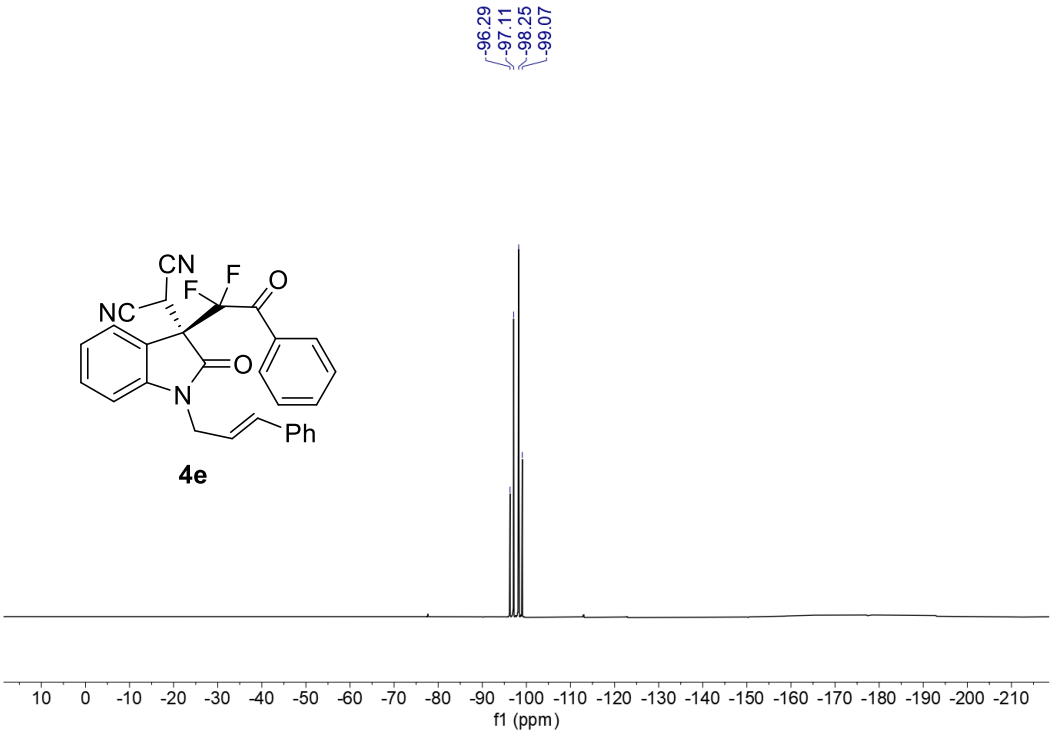

CN
F
O
NC
O
N

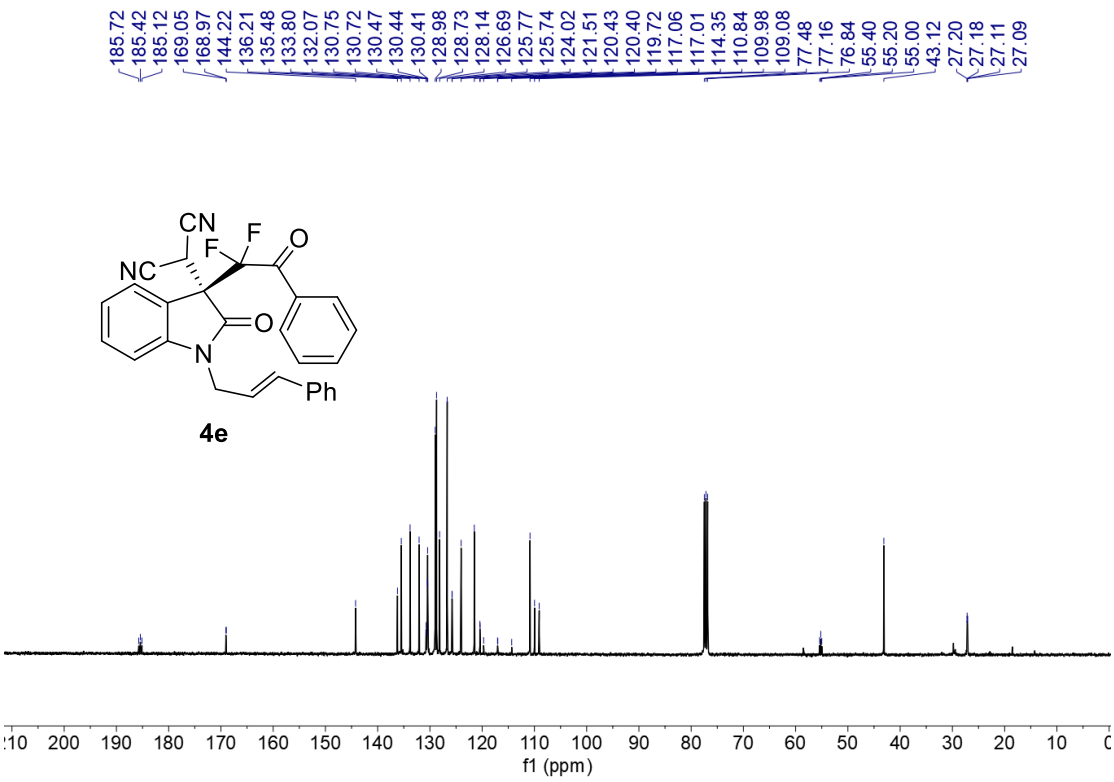
4d


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


185.49
185.25
185.01
168.41
168.35
143.11
135.56
132.13
130.58
130.50
129.01
125.82
125.79
124.42
120.28
120.25
119.18
117.04
117.01
114.88
110.82
109.81
108.61
77.41
77.16
76.91
75.30
73.64
55.14
54.98
54.82
30.33
27.08
27.06
27.01
26.99
CN
F
F
O
NC
O
N
4d
f1 (ppm)


8.01
7.99
7.73
7.72
7.67
7.67
7.67
7.65
7.65
7.64
7.63
7.63
7.50
7.49
7.48
7.47
7.46
7.45
7.41
7.39
7.34
7.33
7.31
7.28
7.26
7.24
7.20
7.18
7.16
7.11
7.09
6.84
6.80
6.32
6.31
6.29
6.28
6.27
6.25
4.95
4.66
4.66
4.65
4.64
CN
F
F
O
NC
O
N
Ph
4e
1.98
1.04
1.06
3.05
2.00
2.01
1.02
1.02
0.97
1.02
1.00
1.00
2.04
f1 (ppm)


-96.29
-97.11
-98.25
-99.07
CN
F
F
O
NC
O
N
Ph
4e
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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185.12
169.05
168.97
144.22
136.21
135.48
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132.07
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130.47
130.44
130.41
128.98
128.73
128.14
126.69
125.77
125.74
124.02
121.51
120.43
120.40
119.72
117.06
117.01
114.35
110.84
109.98
109.08
77.48
77.16
76.84
55.40
55.20
55.00
43.12
27.20
27.18
27.11
27.09
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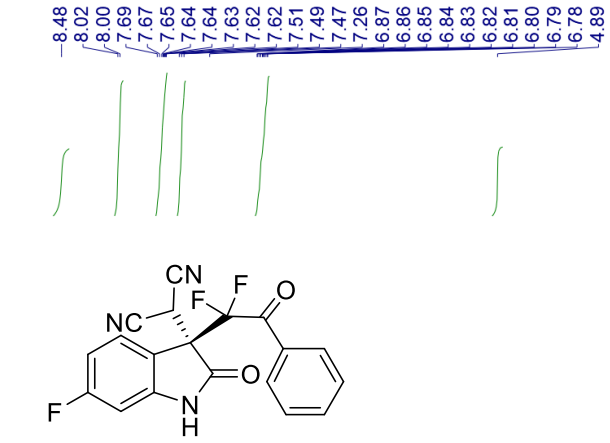
F
F
O
NC
O
N
Ph
4e
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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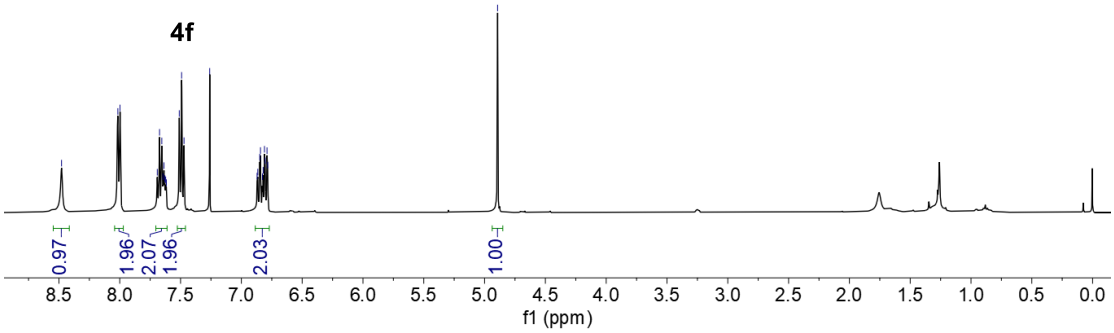
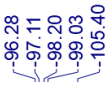
8.00
7.69
7.67
7.65
7.64
7.64
7.63
7.62
7.62
7.51
7.49
7.47
7.26
6.87
6.86
6.85
6.84
6.83
6.82
6.81
6.80
6.79
6.78
4.89
CN
F
F
O
NC
O
N
H
F

4f


0.97
1.96
2.07
1.96
2.03
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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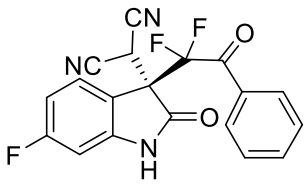
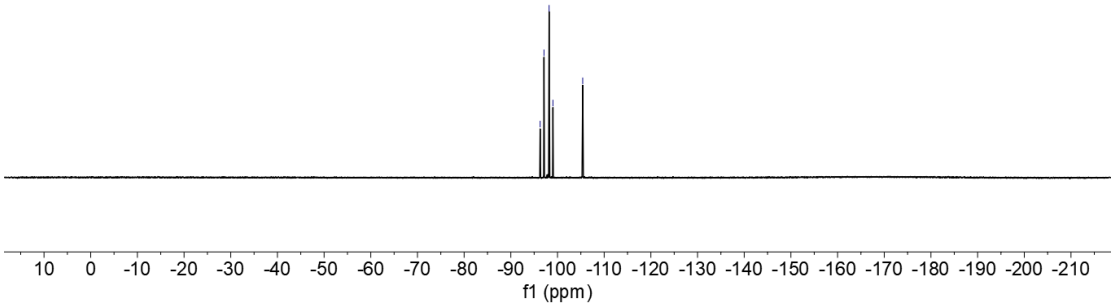
-97.11
-98.20
-99.03
-105.40


CN
F
F
O
NC
O
N
H
F

4f


10
0
-10
-20
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-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
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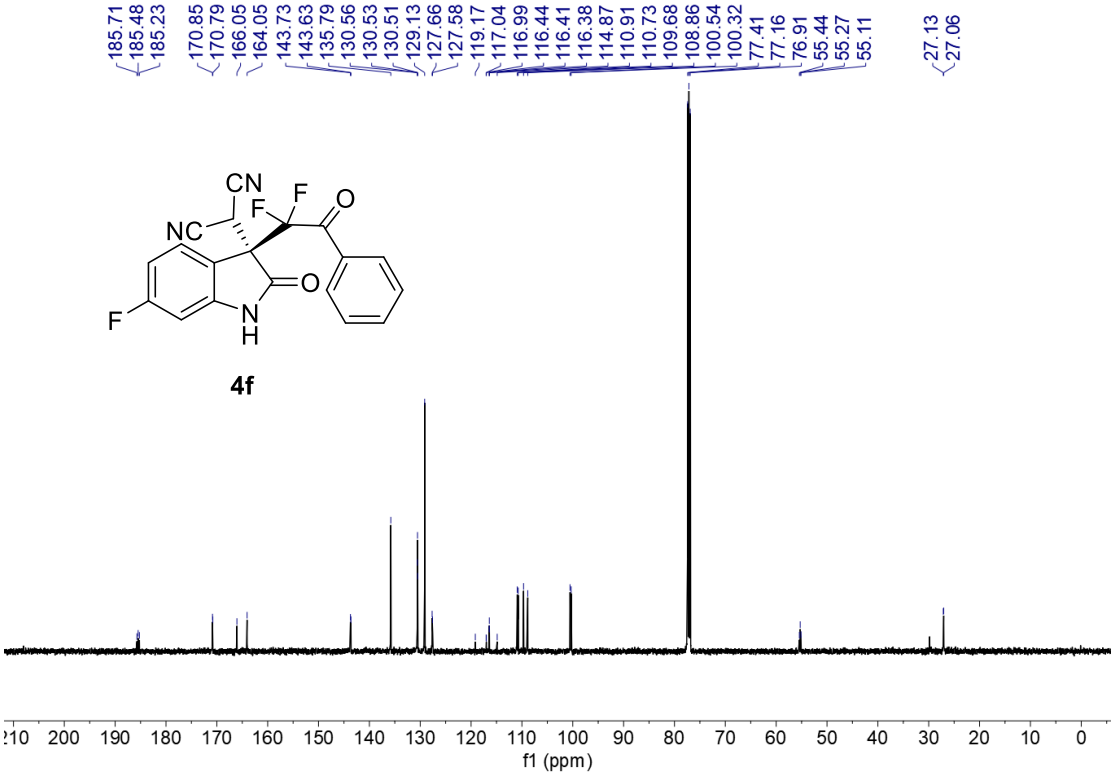
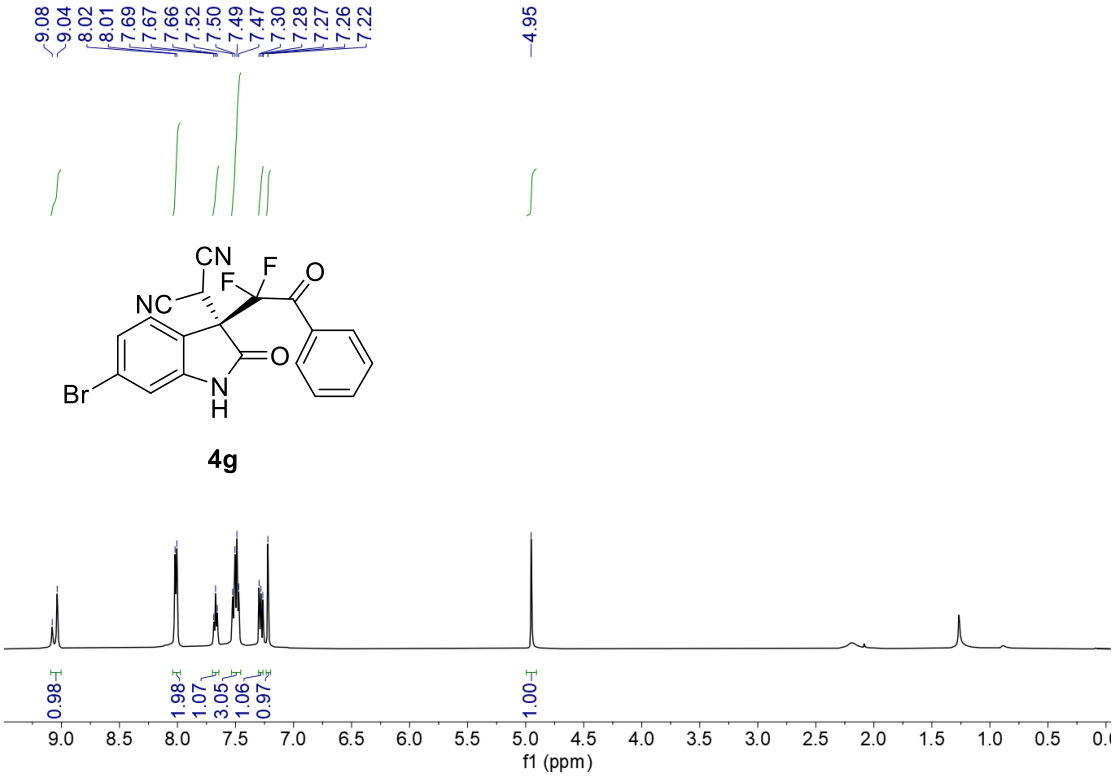
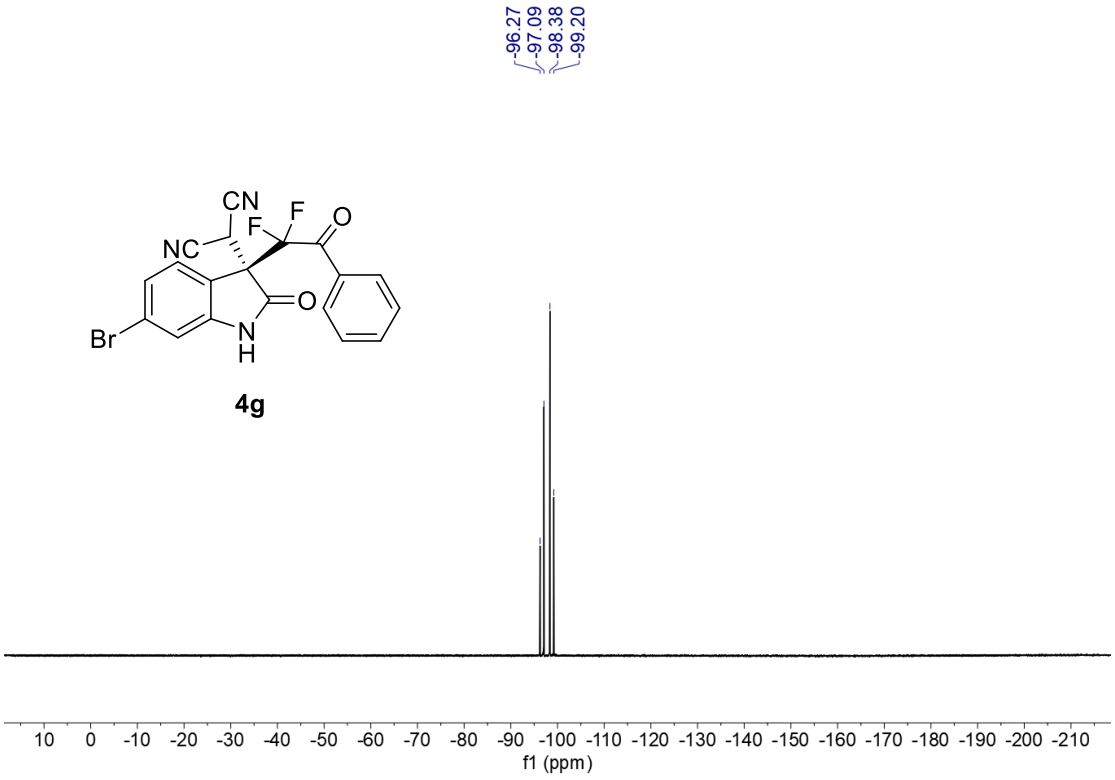
-160
-170
-180
-190
-200
-210
f1 (ppm)

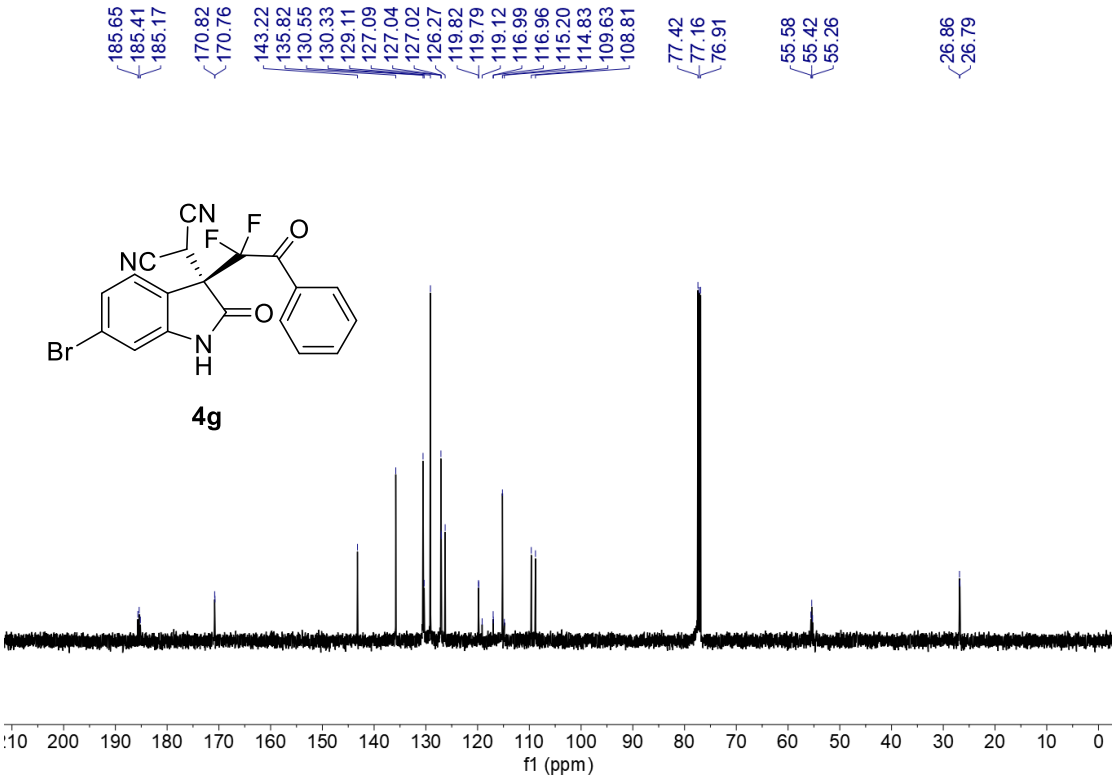

185.71
185.48
185.23
170.85
170.79
166.05
164.05
143.73
143.63
135.79
130.56
130.53
130.51
129.13
127.66
127.58
119.17
117.04
116.99
116.44
116.41
116.38
114.87
110.91
110.73
109.68
108.86
100.54
100.32
77.41
77.16
76.91
55.44
55.27
55.11
27.13
27.06
CN
F
F
O
NC
O
N
H
F
f1 (ppm)

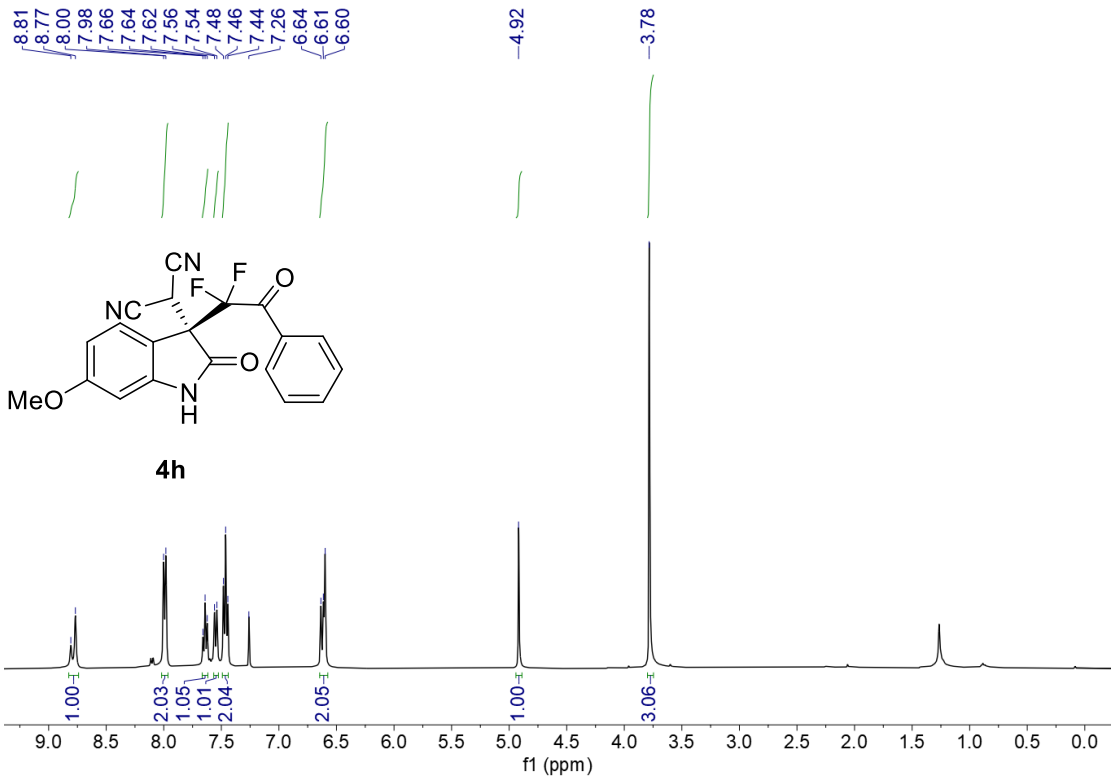
4f


9.08
9.04
8.02
8.01
7.69
7.67
7.66
7.52
7.50
7.49
7.47
7.30
7.28
7.27
7.26
7.22
4.95
CN
F
F
O
NC
O
N
H
Br
0.98
1.98
1.07
3.05
1.06
0.97
1.00
f1 (ppm)

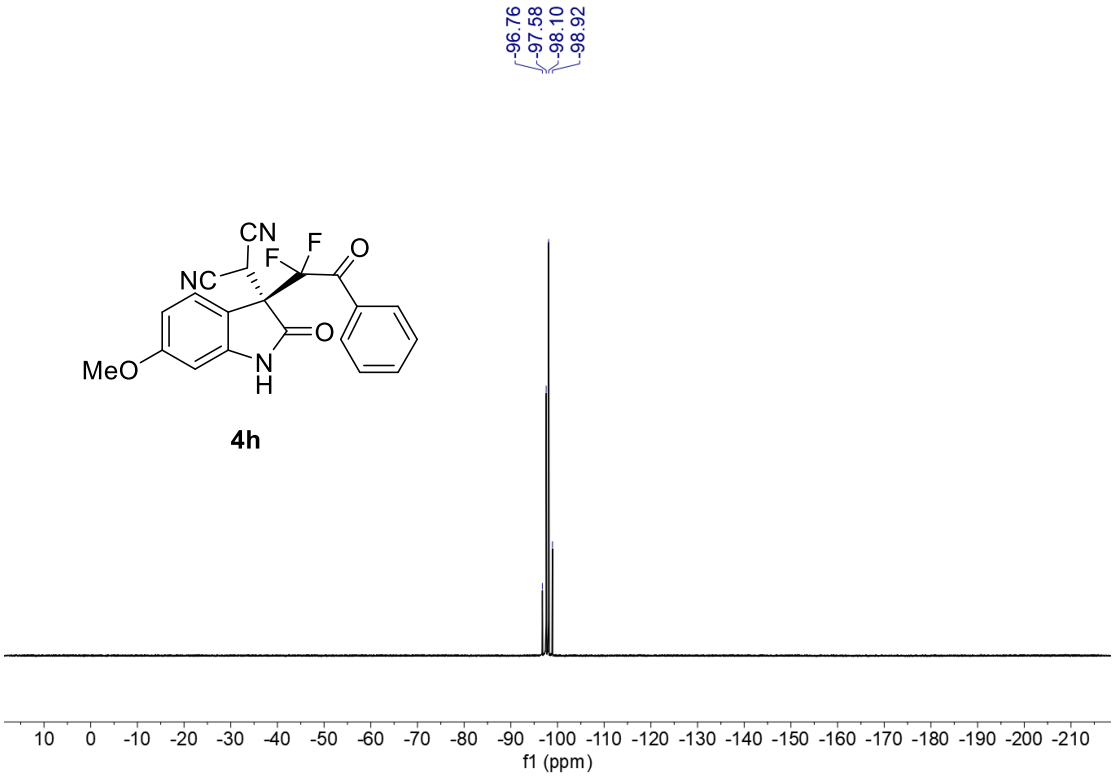
4g


-96.27
-97.09
-98.38
-99.20
CN
F
F
O
NC
O
Br
N
H
4g
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

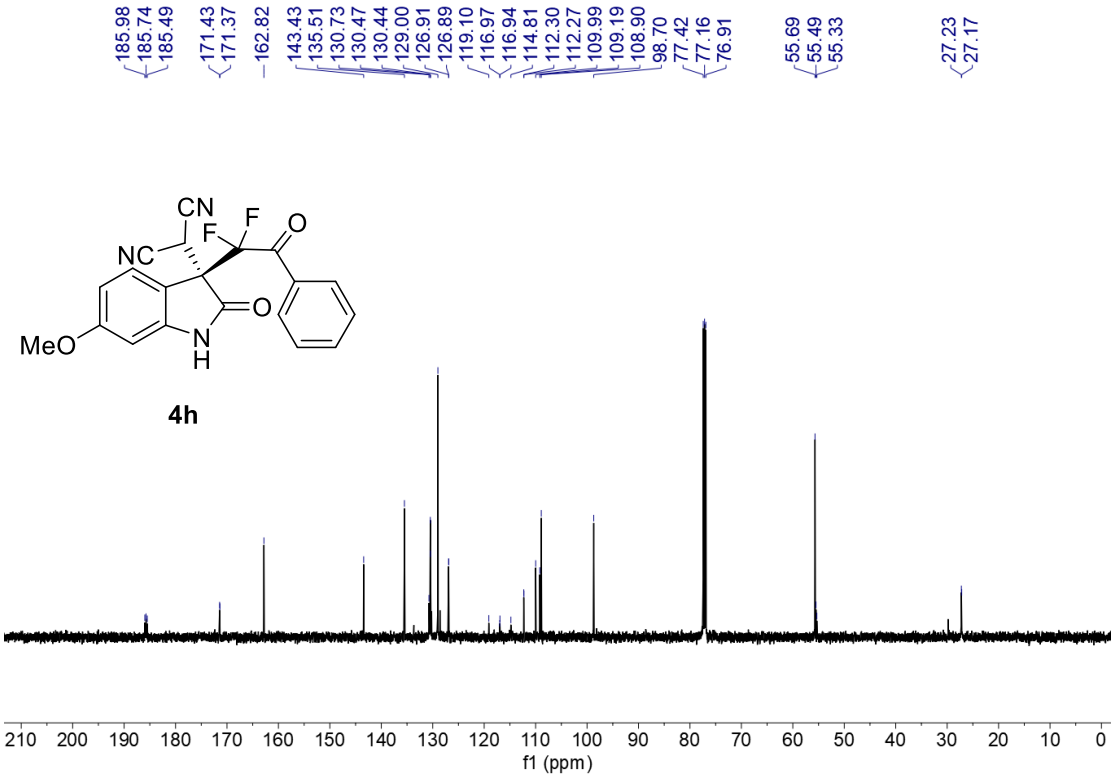

185.65
185.41
185.17
170.82
170.76
143.22
135.82
130.55
130.33
129.11
127.09
127.04
127.02
126.27
119.82
119.79
119.12
116.99
116.96
115.20
114.83
109.63
108.81
77.42
77.16
76.91
55.58
55.42
55.26
26.86
26.79
CN
F
F
O
NC
O
Br
N
H
4g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.81
8.77
8.00
7.98
7.66
7.64
7.62
7.56
7.54
7.48
7.46
7.44
7.26
6.64
6.61
6.60
4.92
3.78
CN
F
F
O
NC
O
MeO
N
H
1.00
2.03
1.05
1.01
2.04
2.05
1.00
3.06
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

4h


-96.76
-97.58
-98.10
-98.92
CN
F
F
O
NC
O
MeO
N
H
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

4h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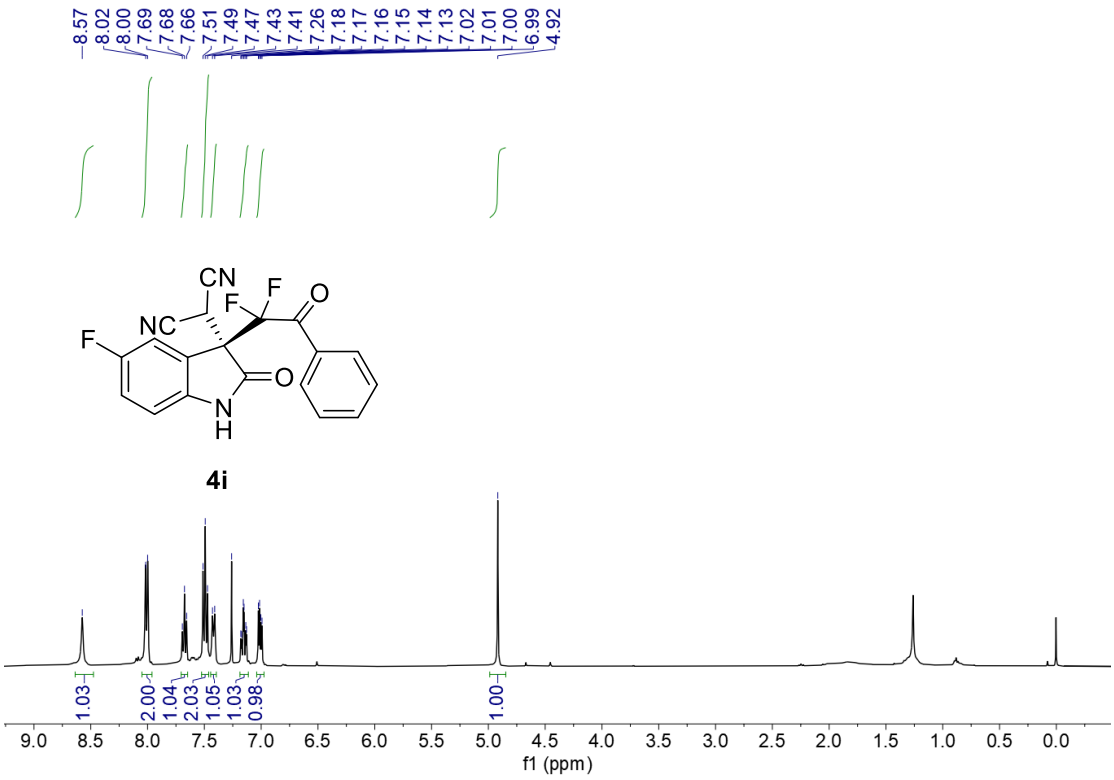
185.74
185.49
171.43
171.37
162.82
143.43
135.51
130.73
130.47
130.44
129.00
126.91
126.89
119.10
116.97
116.94
114.81
112.30
112.27
109.99
109.19
108.90
98.70
77.42
77.16
76.91
55.69
55.49
55.33
27.23
27.17
CN
F
F
O
NC
O
N
H
MeO
4h
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.02
8.00
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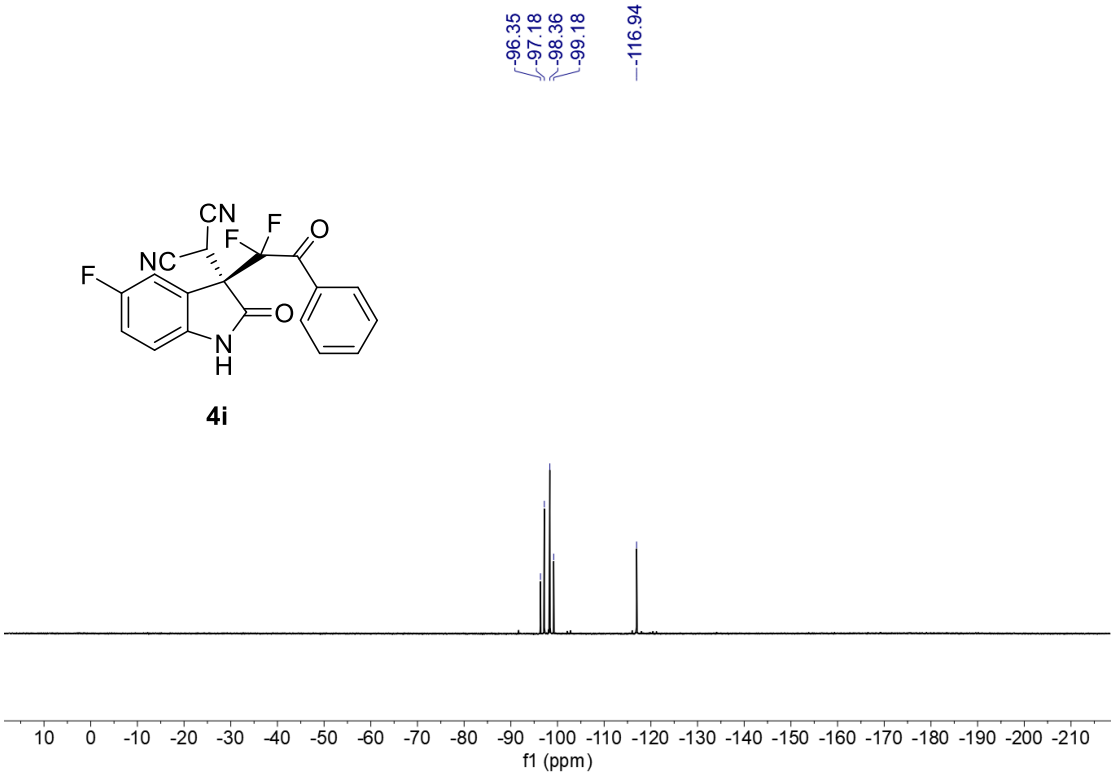
7.66
7.51
7.49
7.47
7.43
7.41
7.26
7.18
7.17
7.16
7.15
7.14
7.13
7.02
7.01
7.00
6.99
4.92
CN
F
F
O
NC
O
N
H
4i
1.03
2.00
1.04
2.03
1.05
1.03
0.98
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-96.35
-97.18
-98.36
-99.18
-116.94
CN
F
F
O
NC
F
O
N
H
4i
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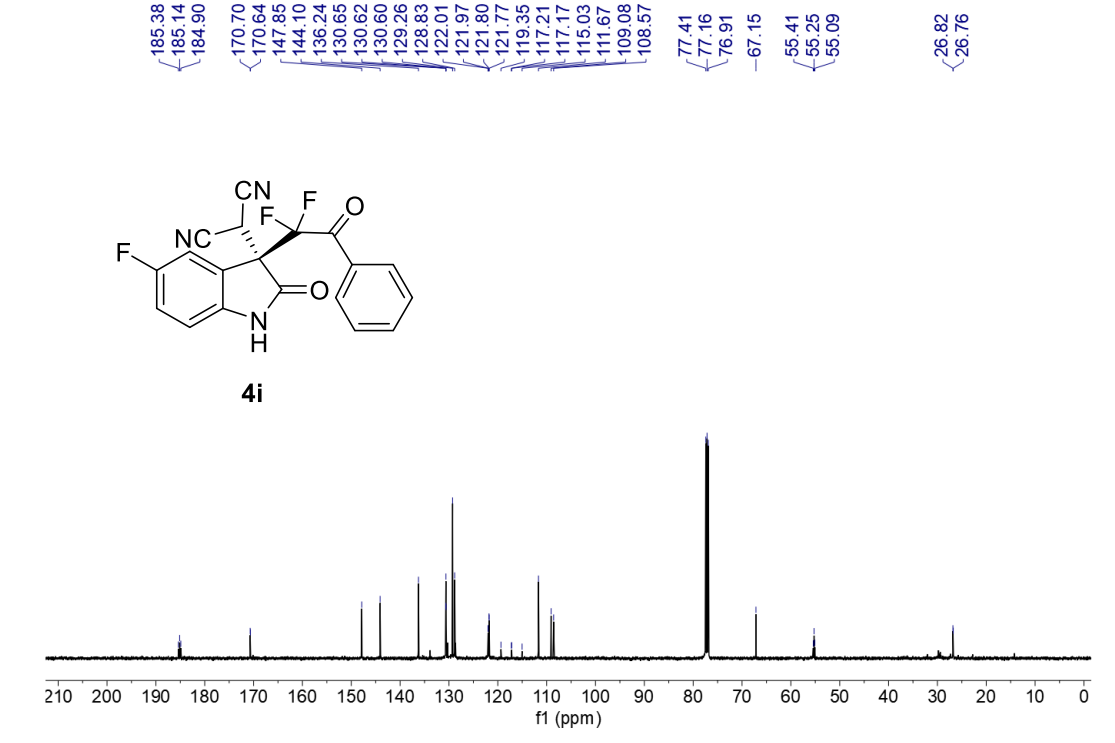
f1 (ppm)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184.90
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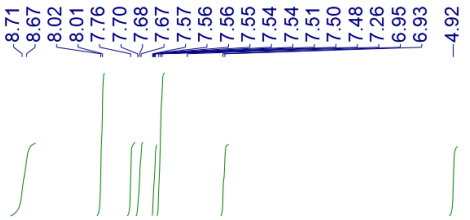
170.64
147.85
144.10
136.24
130.65
130.62
130.60
129.26
128.83
122.01
121.97
121.80
121.77
119.35
117.21
117.17
115.03
111.67
109.08
108.57
77.41
77.16
76.91
67.15
55.41
55.25
55.09
26.82
26.76
CN
F
F
O
NC
F
O
N
H
4i
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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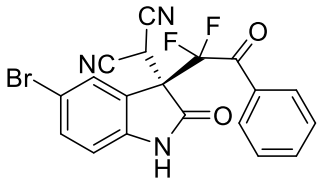
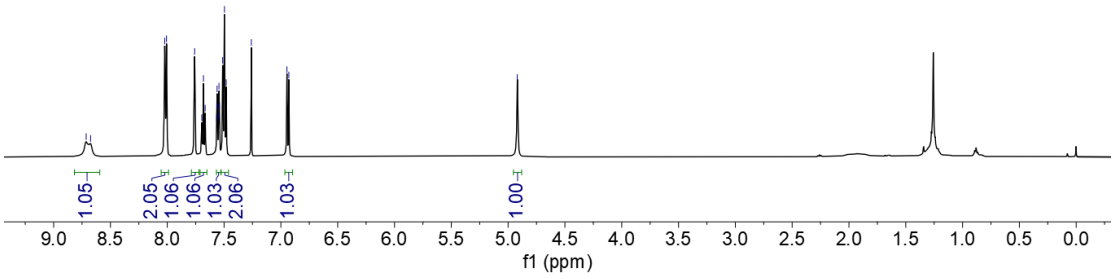
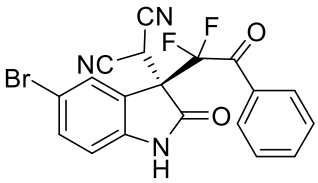
8.67
8.02
8.01
7.76
7.70
7.68
7.67
7.57
7.56
7.56
7.55
7.54
7.54
7.51
7.50
7.48
7.26
6.95
6.93
4.92


CN
F
F
O
NC
Br
O
N
H

4j

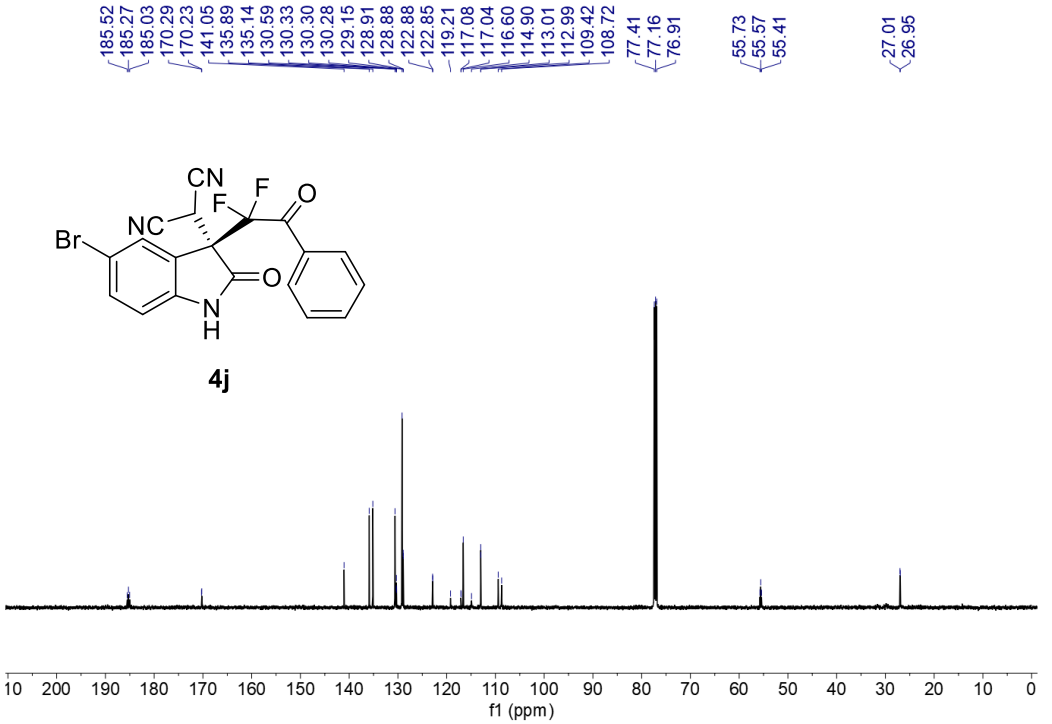

1.05
2.05
1.06
1.06
1.03
2.06
1.03
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-95.98
-96.81
-98.18
-99.01


CN
F
F
O
NC
Br
O
N
H

4j

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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185.03
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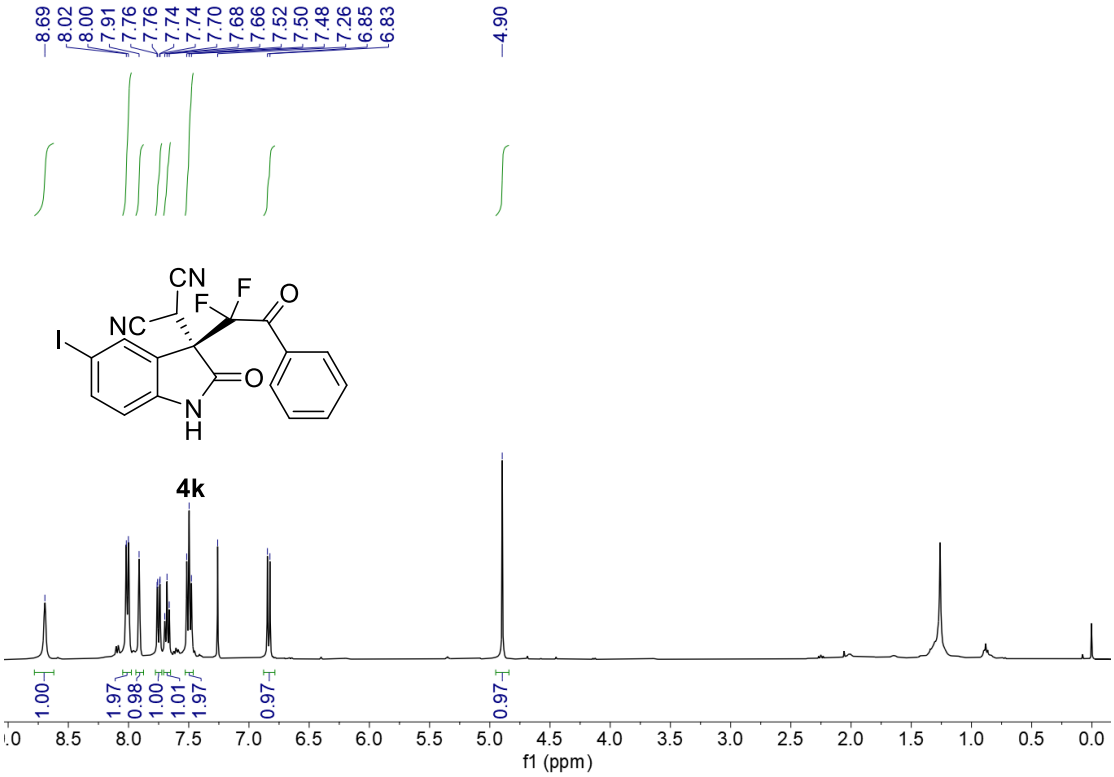
170.23
141.05
135.89
135.14
130.59
130.33
130.30
130.28
129.15
128.91
128.88
122.88
122.85
119.21
117.08
117.04
116.60
114.90
113.01
112.99
109.42
108.72
77.41
77.16
76.91
55.73
55.57
55.41
27.01
26.95
CN
F
F
O
NC
Br
O
N
H
4j
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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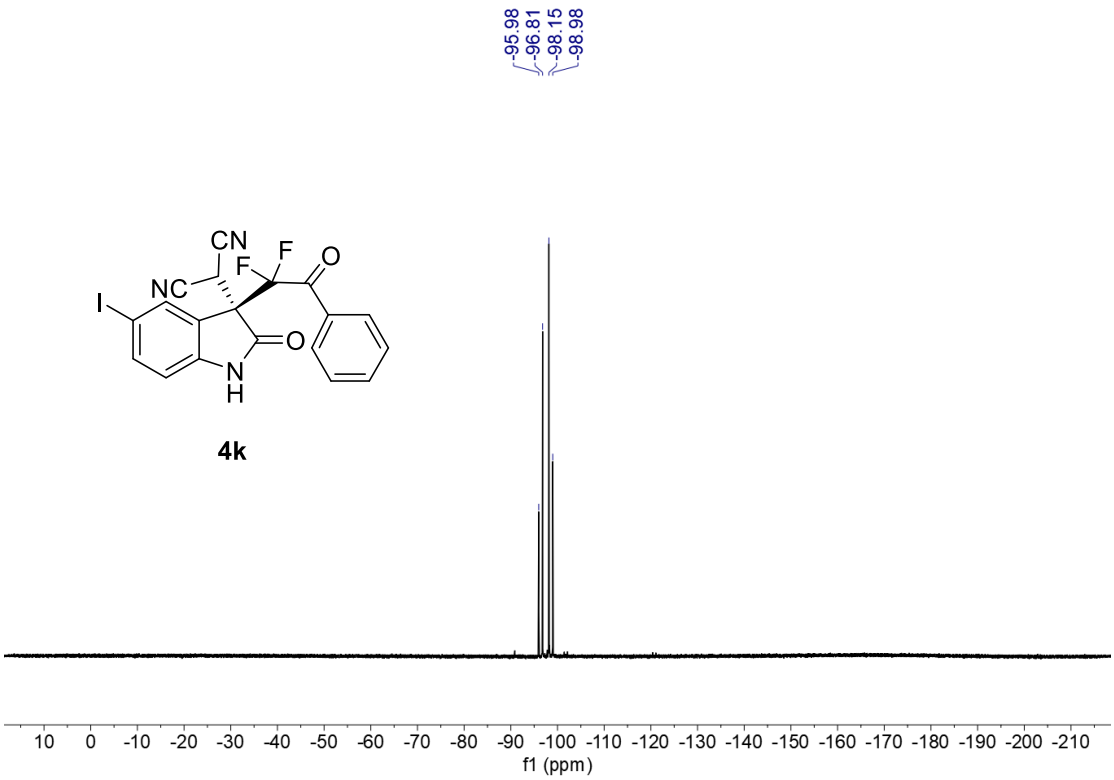
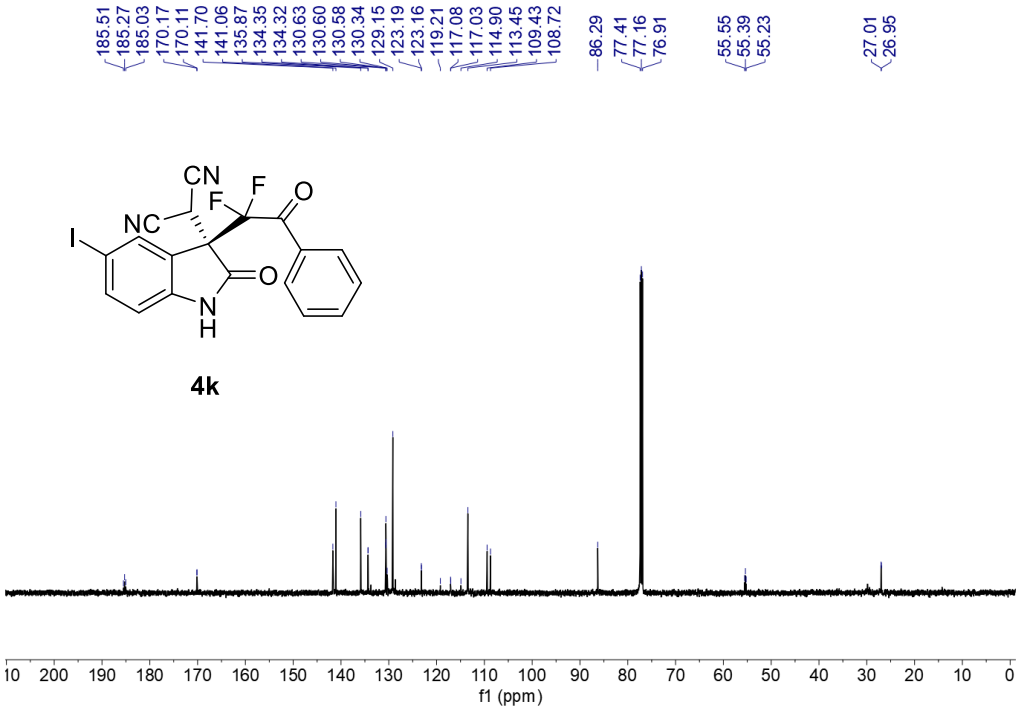
7.76
7.74
7.74
7.70
7.68
7.66
7.52
7.50
7.48
7.26
6.85
6.83
4.90
CN
F
F
O
NC
I
O
N
H
4k
1.00
1.97
0.98
1.00
1.01
1.97
0.97
0.97
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-95.98
-96.81
-98.15
-98.98
CN
F
F
O
NC
I
O
N
H
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

4k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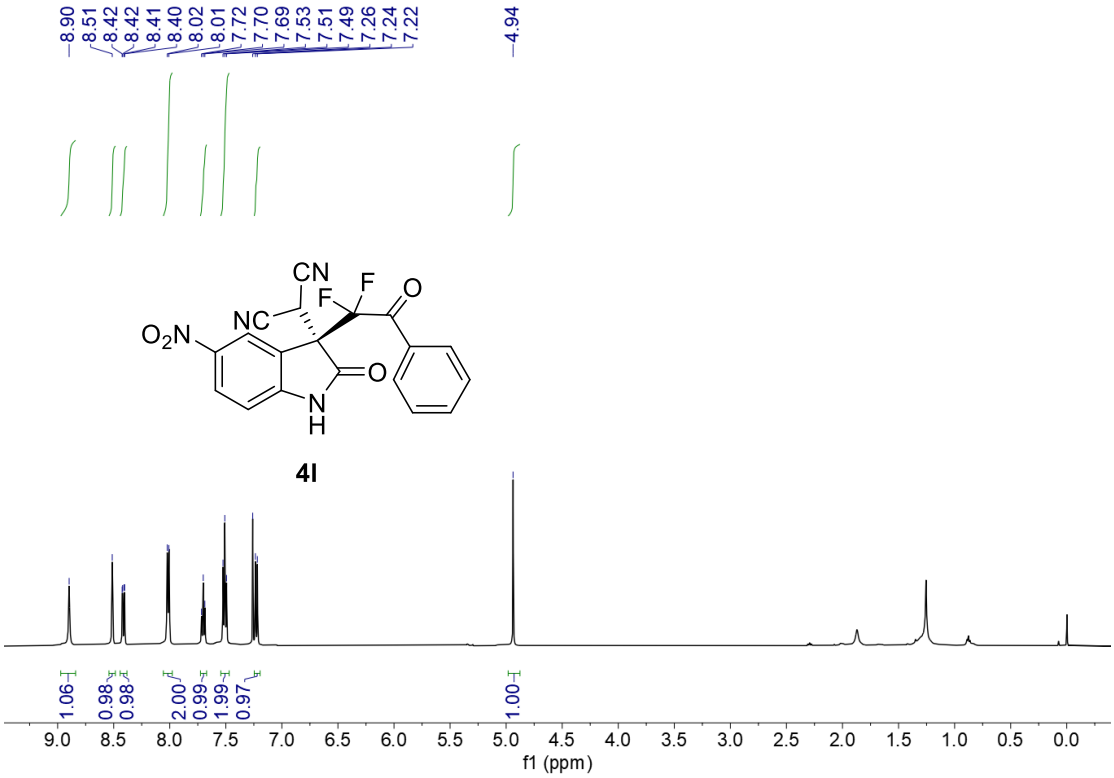
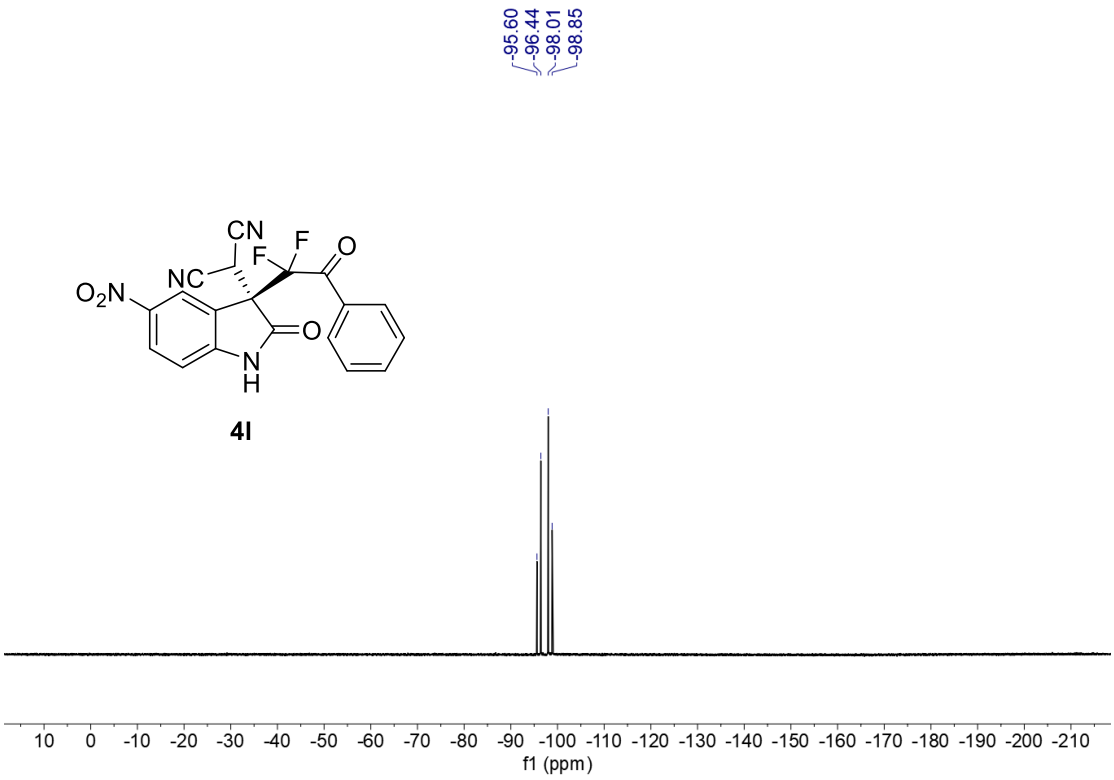
170.17
170.11
141.70
141.06
135.87
134.35
134.32
130.63
130.60
130.58
130.34
129.15
123.19
123.16
119.21
117.08
117.03
114.90
113.45
109.43
108.72
86.29
77.41
77.16
76.91
55.55
55.39
55.23
27.01
26.95
CN
F
F
O
NC
I
O
N
H
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

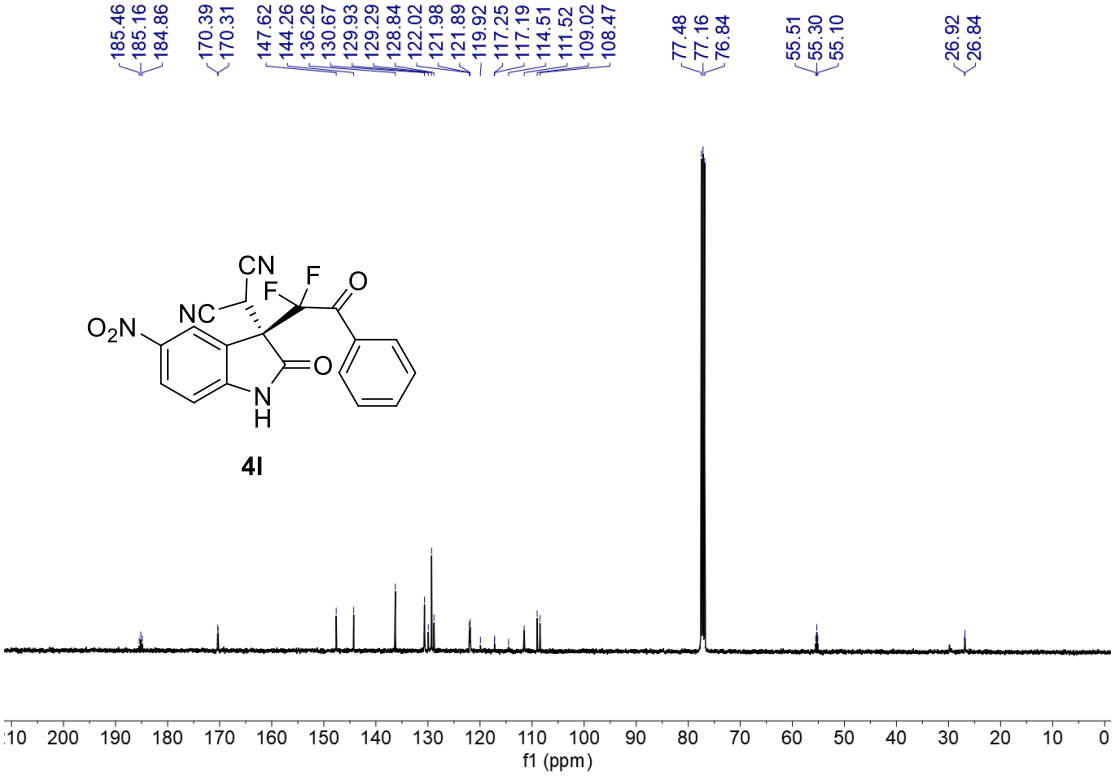
4k

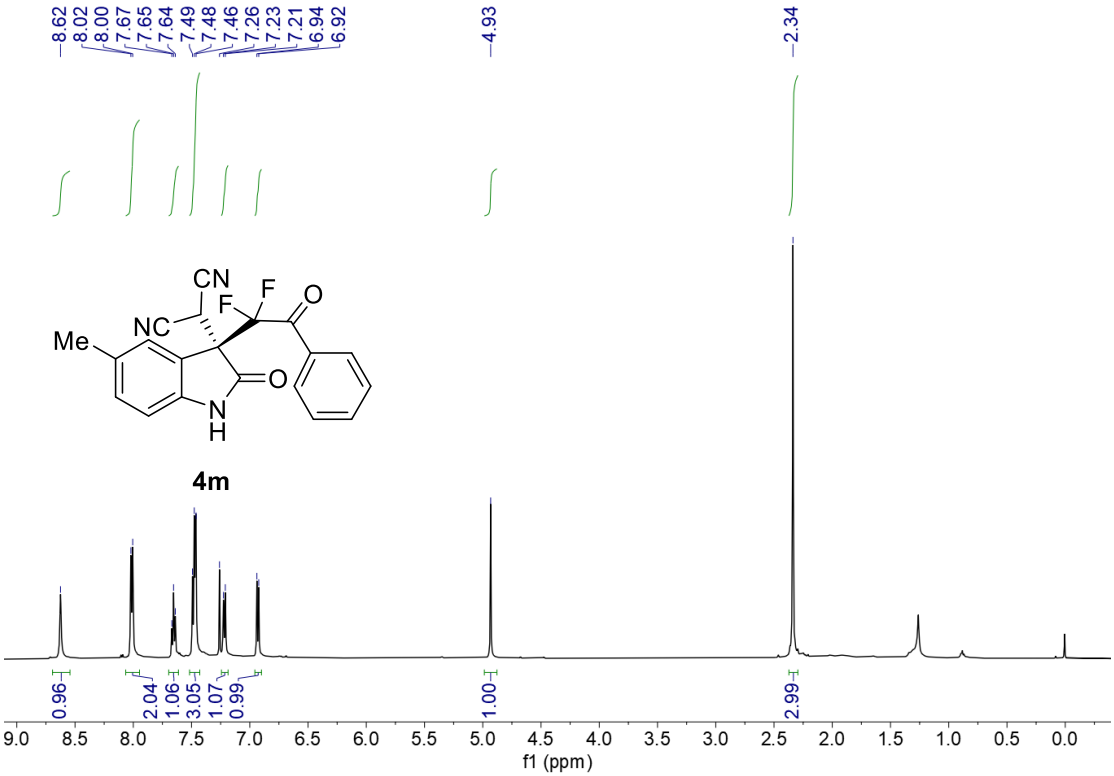

8.90
8.51
8.42
8.42
8.41
8.40
8.02
8.01
7.72
7.70
7.69
7.53
7.51
7.49
7.26
7.24
7.22
4.94
CN
F
F
O
NC
O2N
O
N
H
1.06
0.98
0.98
2.00
0.99
1.99
0.97
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

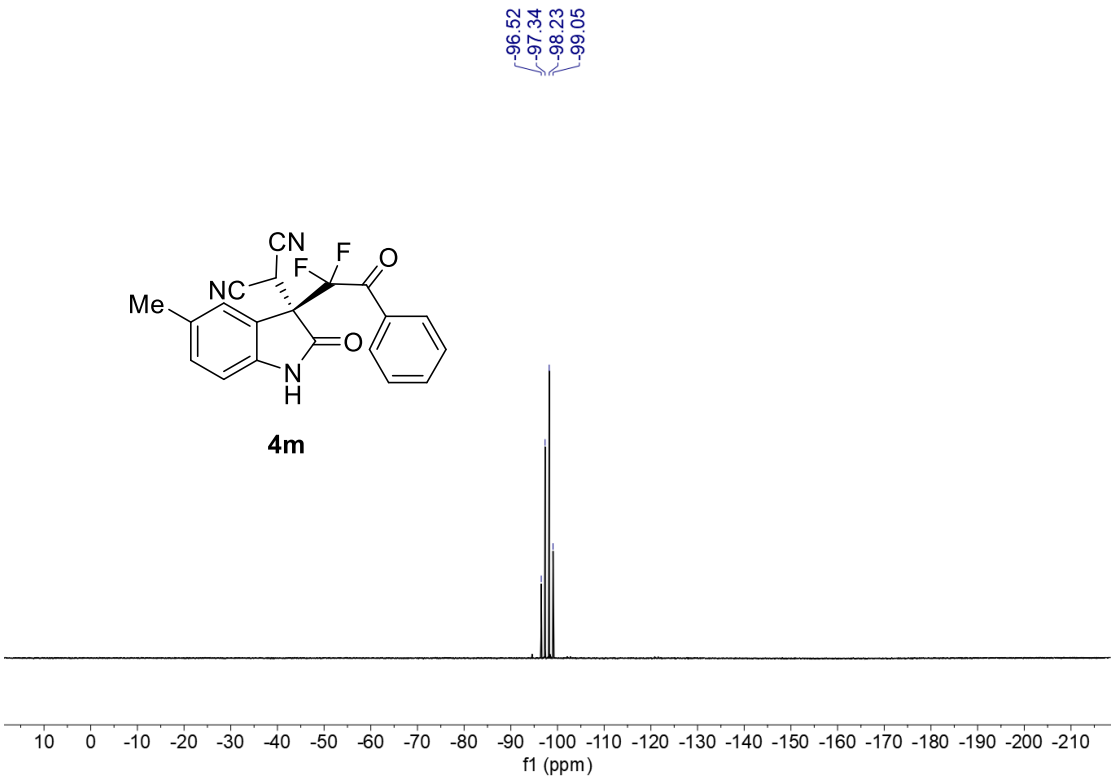
4l

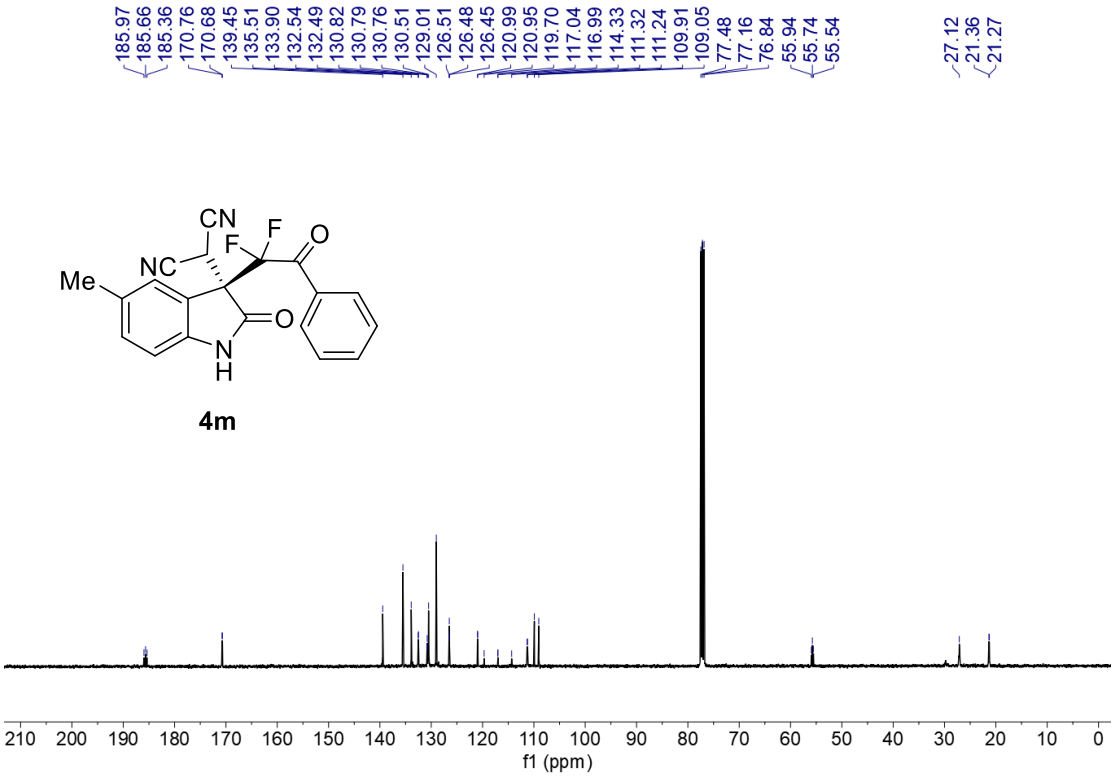

-95.60
-96.44
-98.01
-98.85
CN
F
F
O
NC
O2N
O
N
H
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

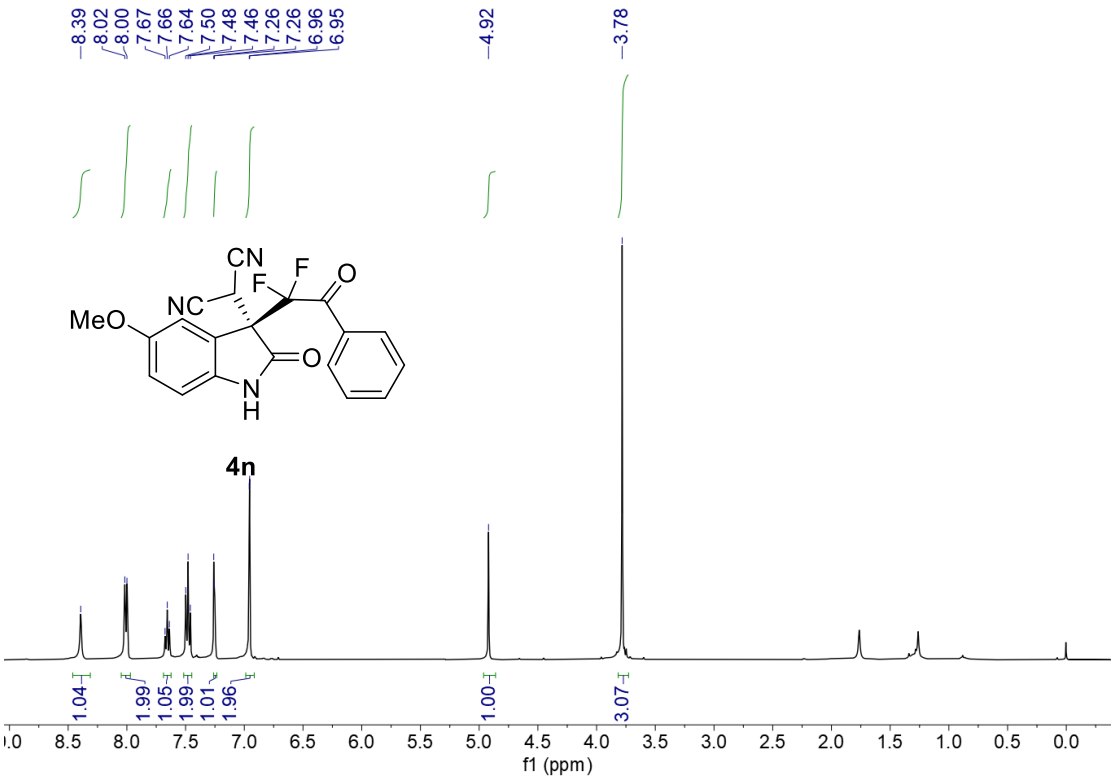
4l

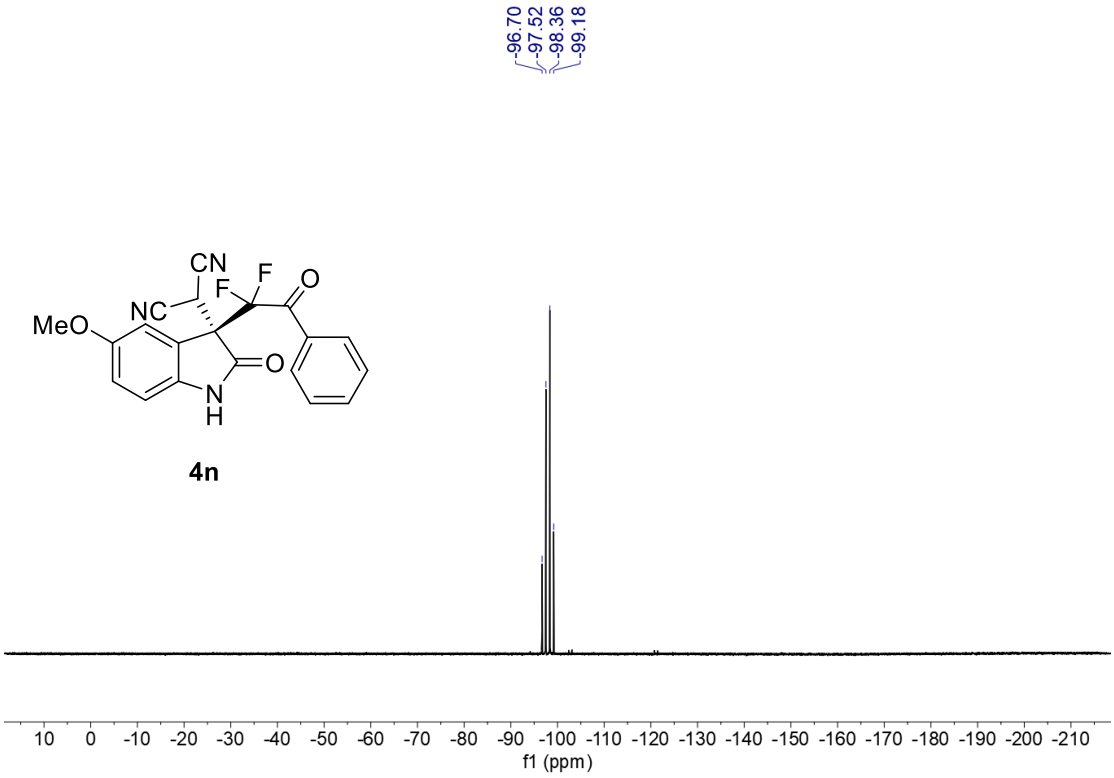

185.46
185.16
184.86
170.39
170.31
147.62
144.26
136.26
130.67
129.93
129.29
128.84
122.02
121.98
121.89
119.92
117.25
117.19
114.51
111.52
109.02
108.47
77.48
77.16
76.84
55.51
55.30
55.10
26.92
26.84
CN
F
F
O
NC
O2N
O
N
H
4l
f1 (ppm)

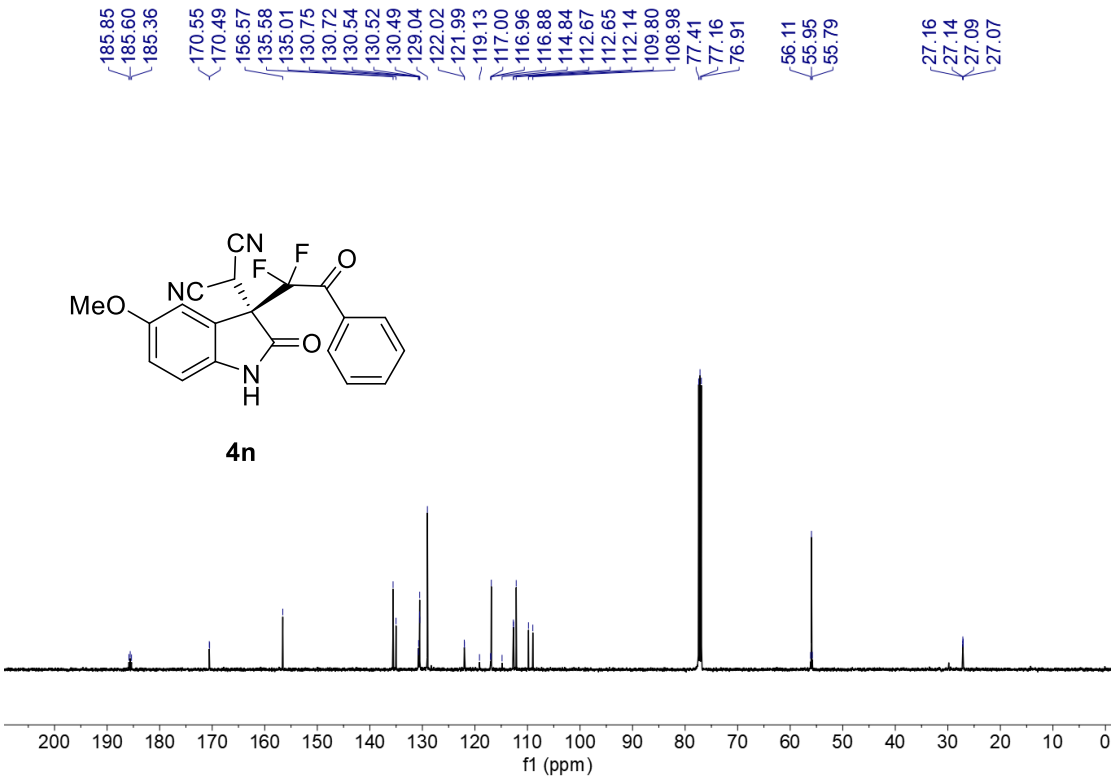

8.62
8.02
8.00
7.67
7.65
7.64
7.49
7.48
7.46
7.26
7.23
7.21
6.94
6.92
4.93
2.34
CN
F
F
O
NC
Me
O
N
H
4m
0.96
2.04
1.06
3.05
1.07
0.99
1.00
2.99
f1 (ppm)

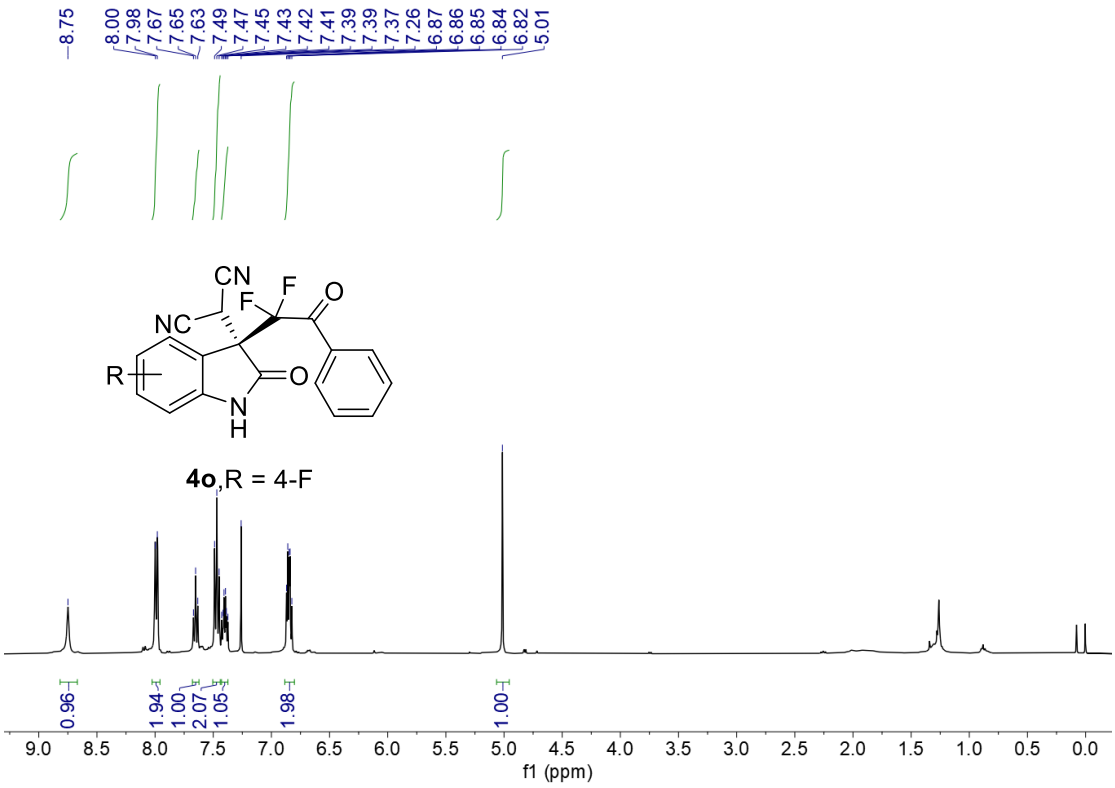

-96.52
-97.34
-98.23
-99.05
CN
F
F
O
NC
Me
O
N
H
4m
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

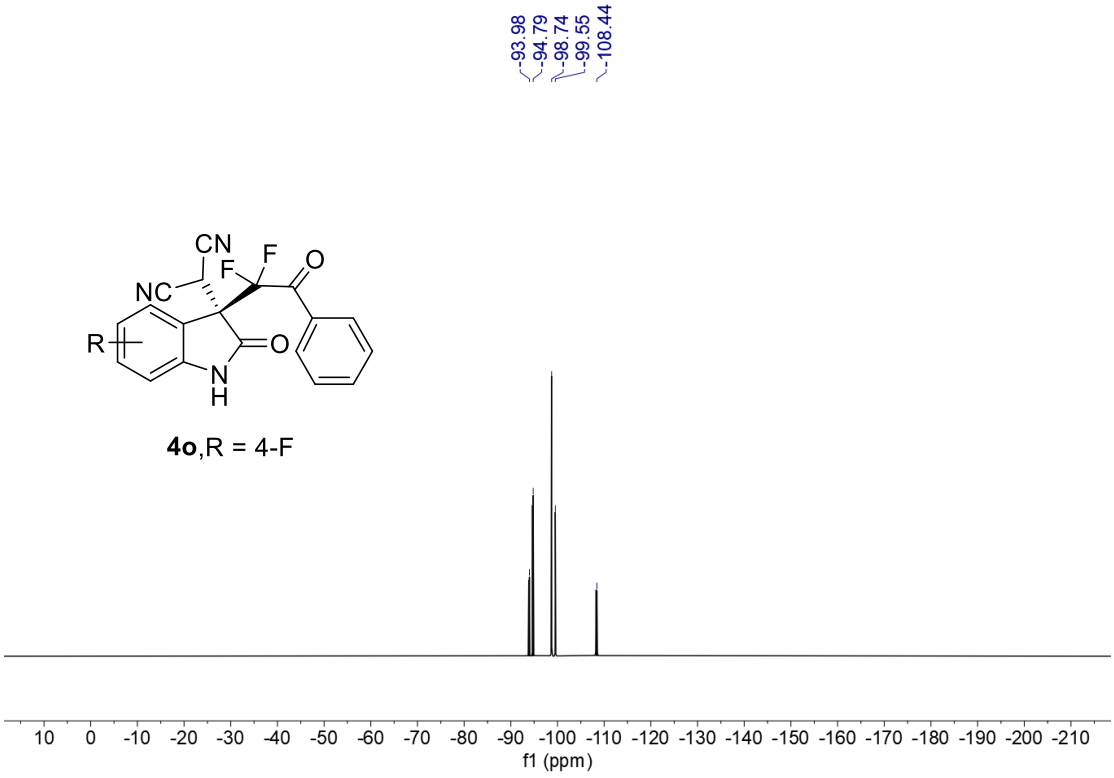

185.97
185.66
185.36
170.76
170.68
139.45
135.51
133.90
132.54
132.49
130.82
130.79
130.76
130.51
129.01
126.51
126.48
126.45
120.99
120.95
119.70
117.04
116.99
114.33
111.32
111.24
109.91
109.05
77.48
77.16
76.84
55.94
55.74
55.54
27.12
21.36
21.27
CN
F
F
O
NC
Me
O
N
H
4m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

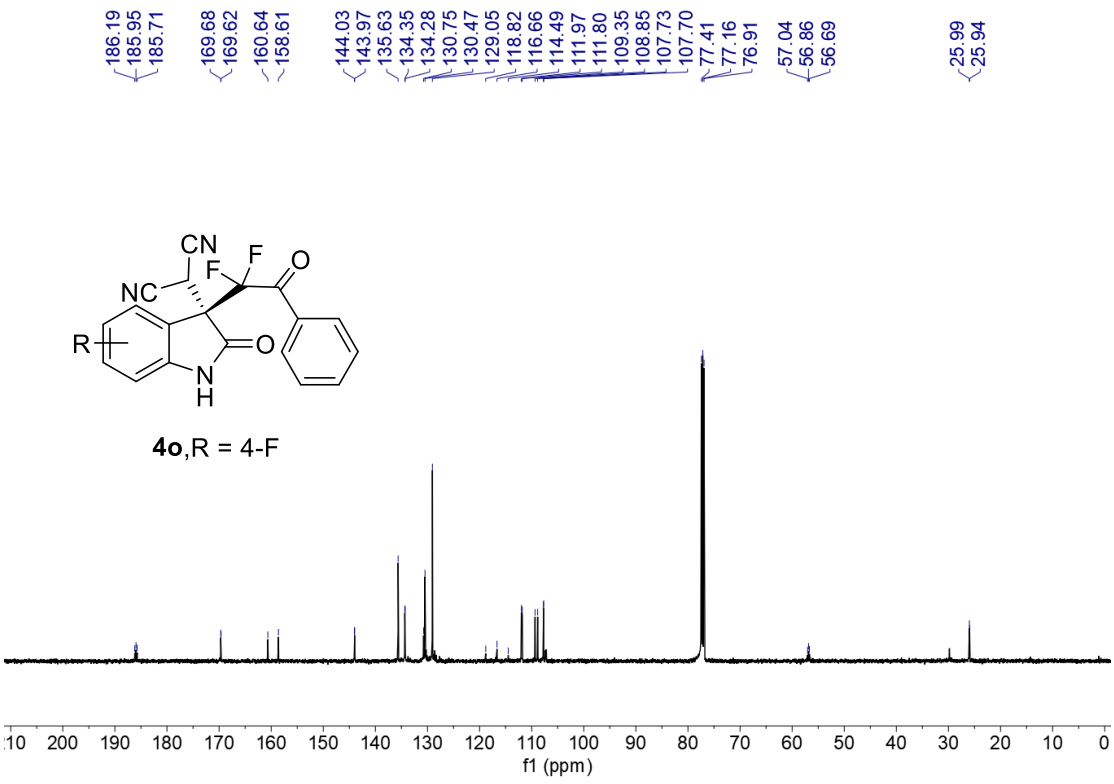

8.39
8.02
8.00
7.67
7.66
7.64
7.50
7.48
7.46
7.26
7.26
6.96
6.95
4.92
3.78
CN
F
F
O
NC
MeO
O
N
H
4n
1.04
1.99
1.05
1.99
1.01
1.96
1.00
3.07
f1 (ppm)

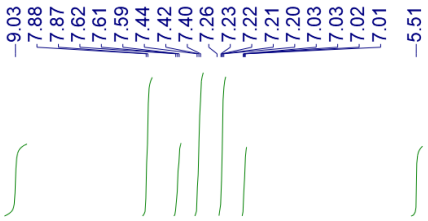

-96.70
-97.52
-98.36
-99.18
CN
F
F
O
NC
MeO
O
N
H
4n
f1 (ppm)

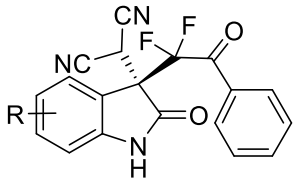

185.85
185.60
185.36
170.55
170.49
156.57
135.58
135.01
130.75
130.72
130.54
130.52
130.49
129.04
122.02
121.99
119.13
117.00
116.96
116.88
114.84
112.67
112.65
112.14
109.80
108.98
77.41
77.16
76.91
56.11
55.95
55.79
27.16
27.14
27.09
27.07
CN
F
F
O
NC
MeO
O
N
H
4n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.75
8.00
7.98
7.67
7.65
7.63
7.49
7.47
7.45
7.43
7.42
7.41
7.39
7.39
7.37
7.26
6.87
6.86
6.85
6.84
6.82
5.01
CN
F
F
O
NC
R
O
N
H
4o,R = 4-F
0.96
1.94
1.00
2.07
1.05
1.98
1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

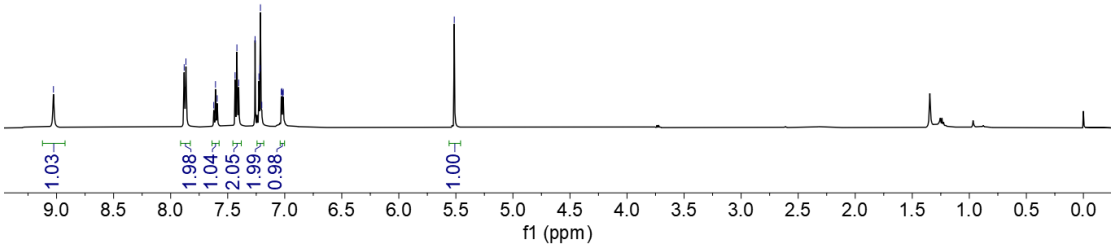

-93.98
-94.79
-98.74
-99.55
-108.44
CN
F
F
O
NC
R
O
N
H
4o,R = 4-F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

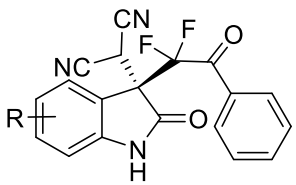

186.19
185.95
185.71
169.68
169.62
160.64
158.61
144.03
143.97
135.63
134.35
134.28
130.75
130.47
129.05
118.82
116.66
114.49
111.97
111.80
109.35
108.85
107.73
107.70
77.41
77.16
76.91
57.04
56.86
56.69
25.99
25.94
CN
F
F
O
NC
R
O
N
H
4o,R = 4-F
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



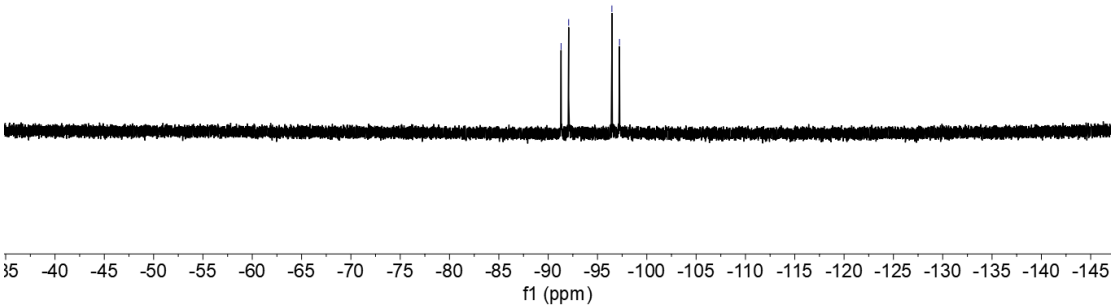


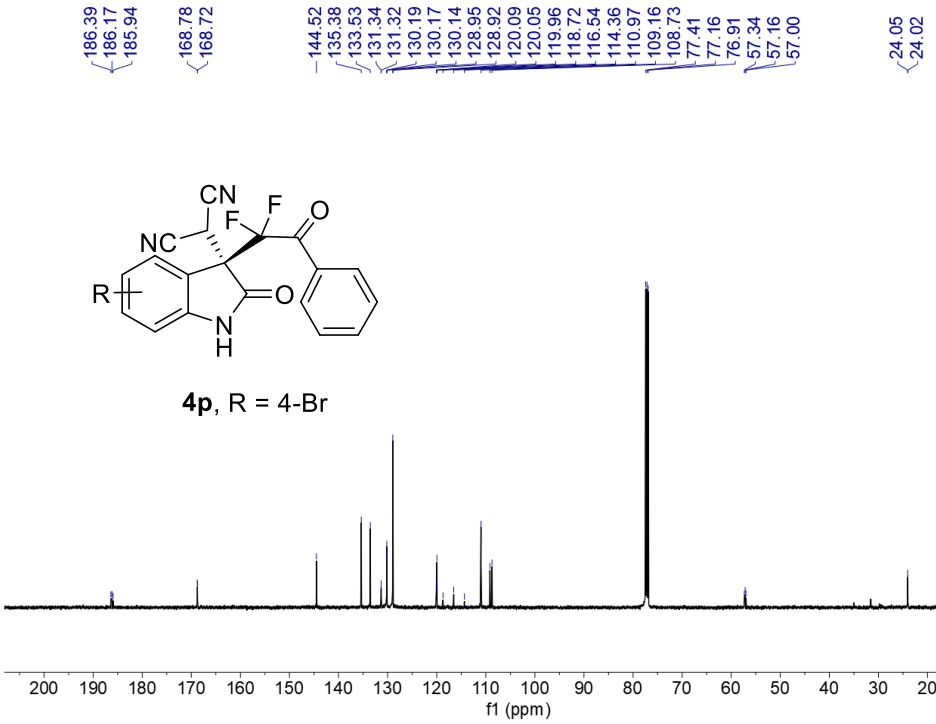
4p, R = 4-Br



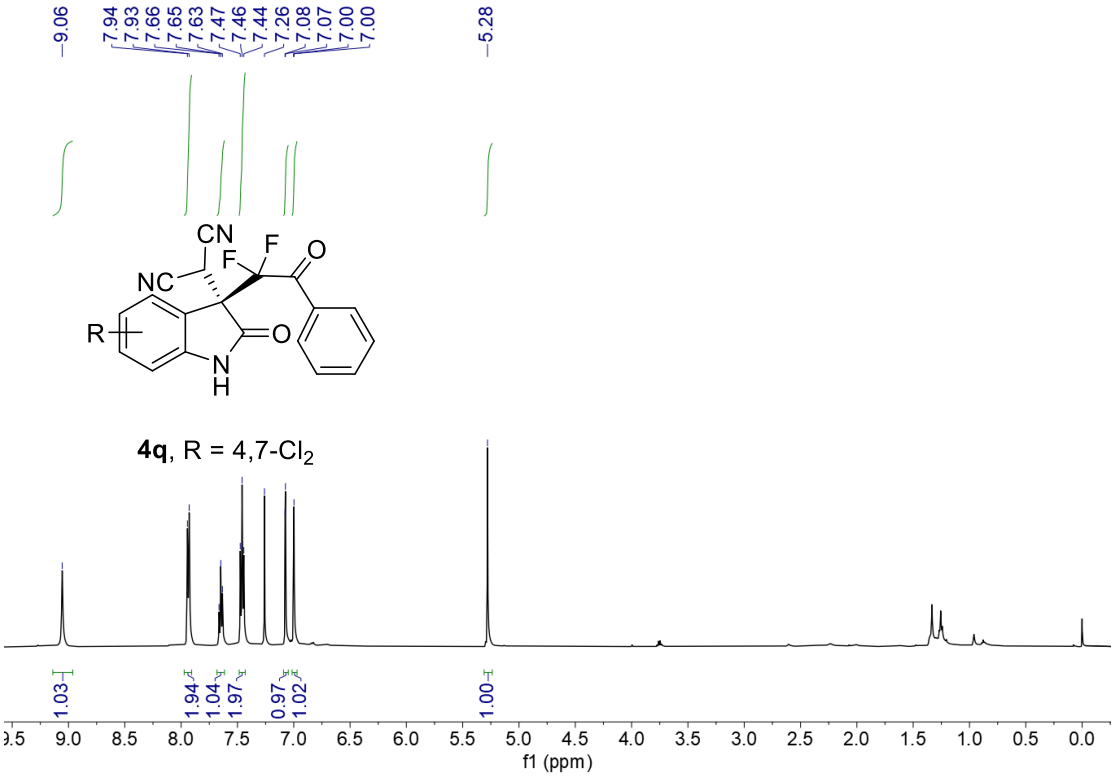


4p, R = 4-Br

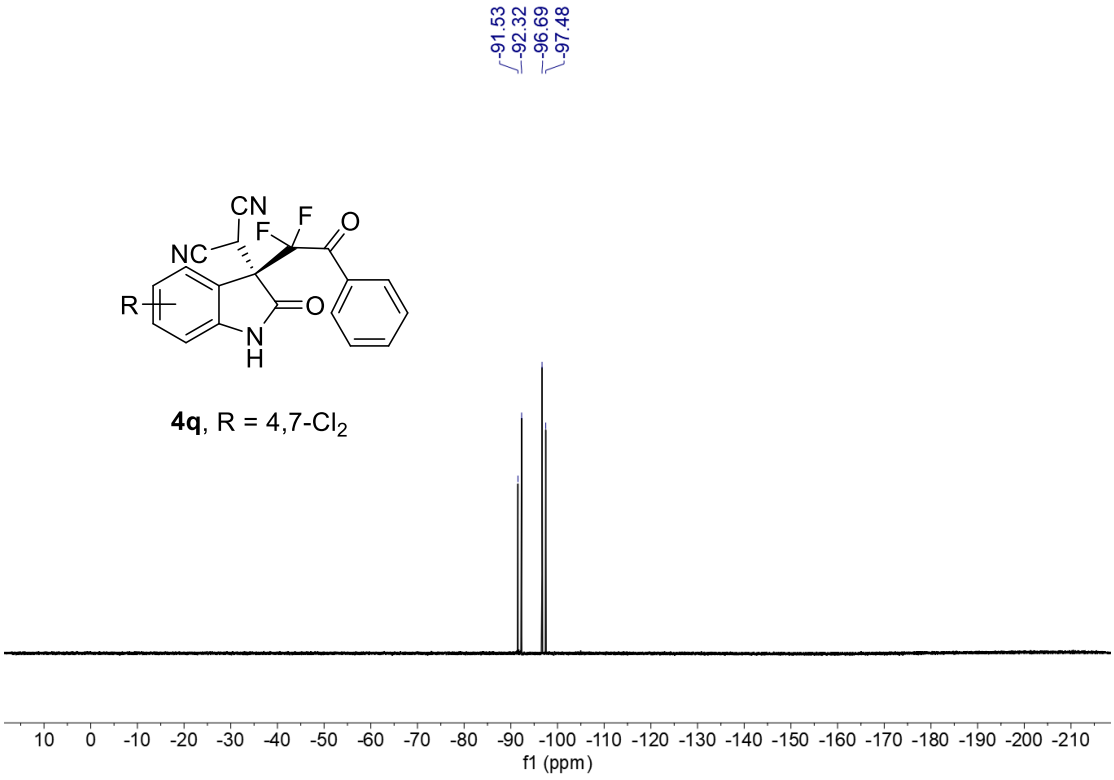




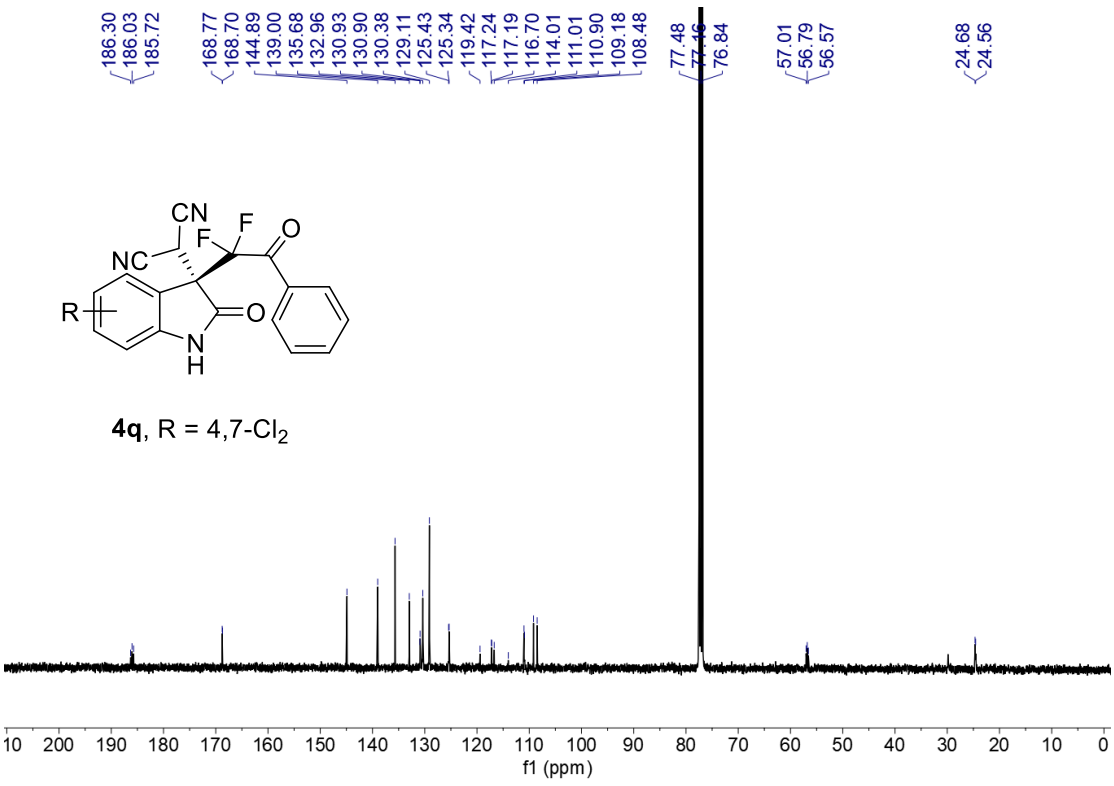
4p, R = 4-Br



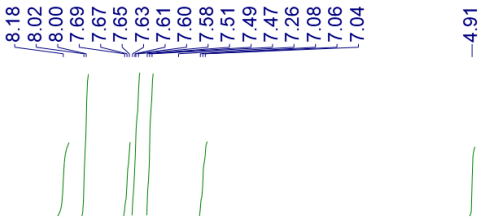
4q, R = 4,7-Cl_2

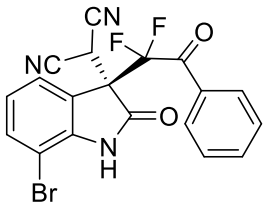


4q, R = 4,7-Cl_2

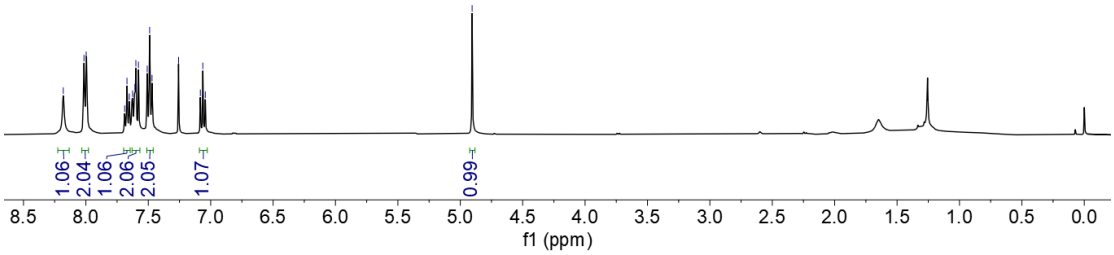


4q, R = 4,7-Cl_2

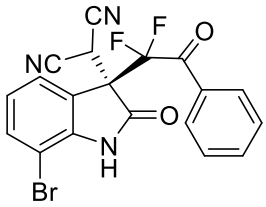

8.18
8.02
8.00
7.69
7.67
7.65
7.63
7.61
7.60
7.58
7.51
7.49
7.47
7.26
7.08
7.06
7.04
4.91


CN
F
F
O
NC
O
N
H
Br

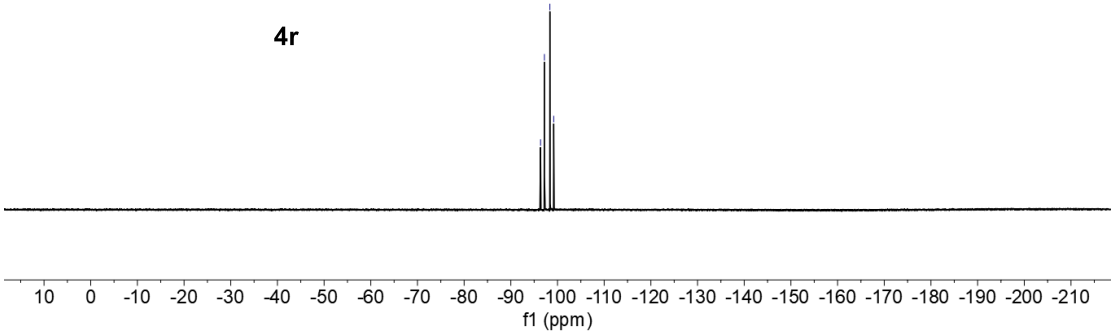
4r

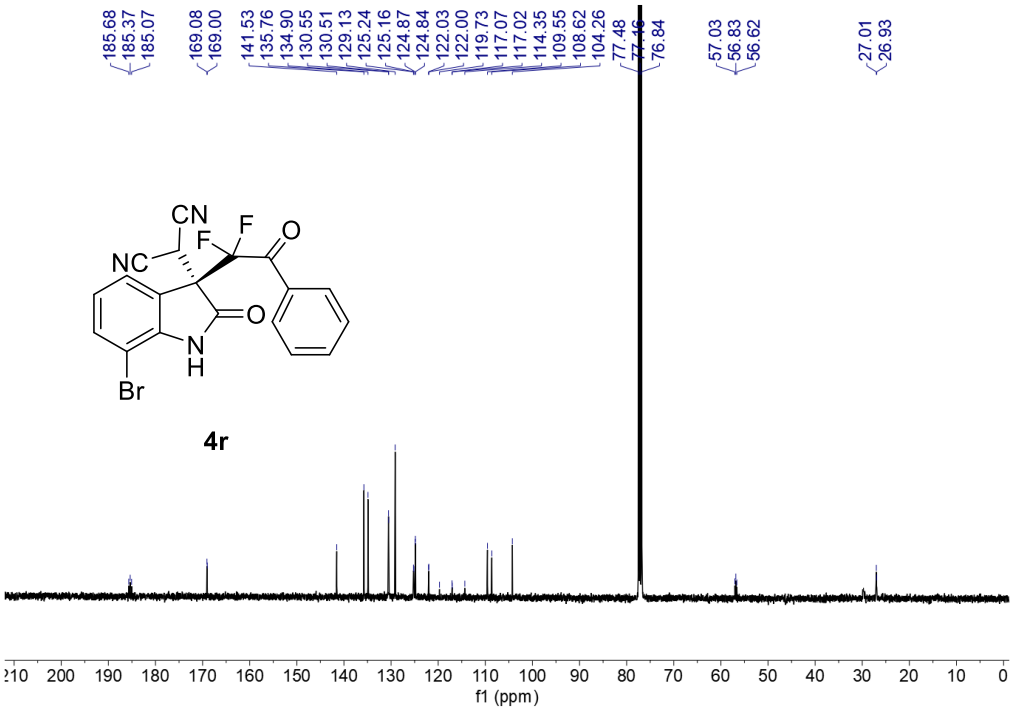

1.06
2.04
1.06
2.06
2.05
1.07
0.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

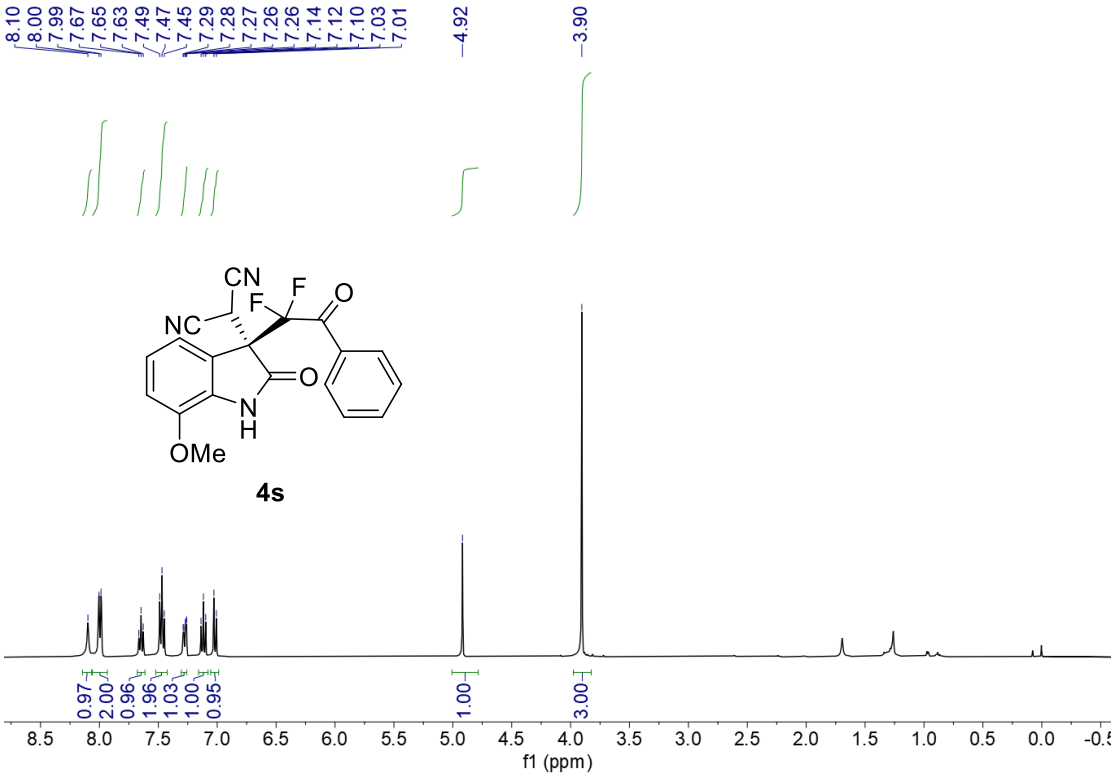

-96.37
-97.20
-98.37
-99.19

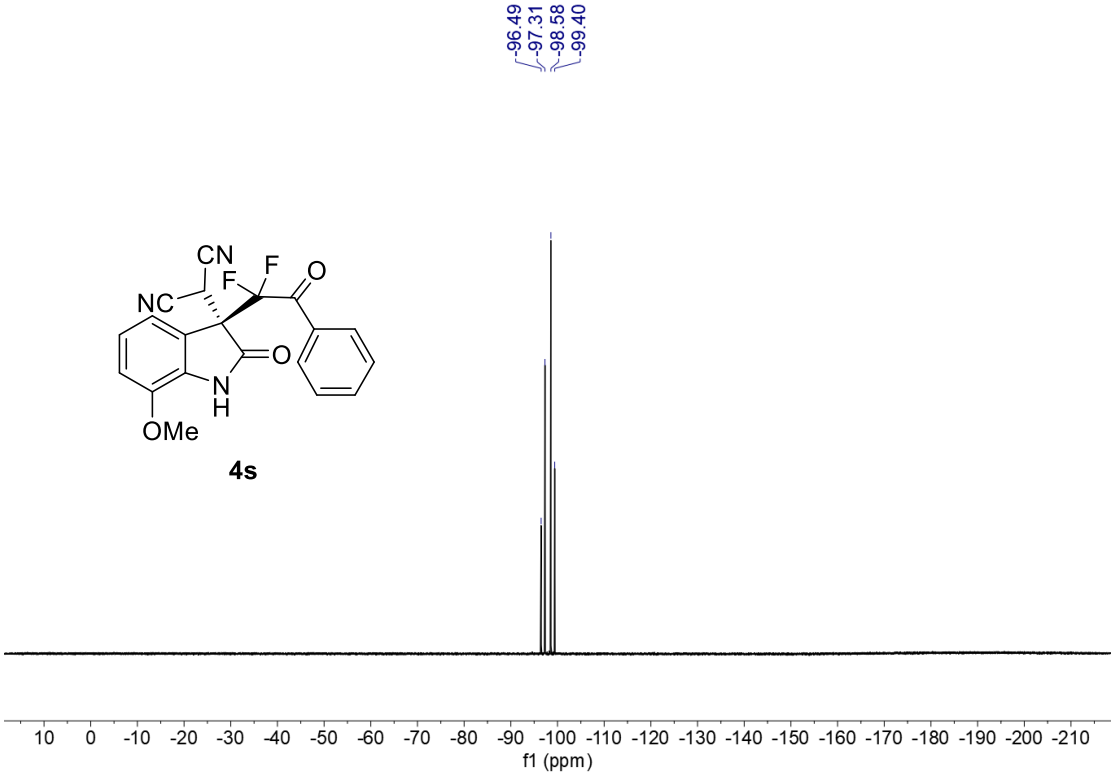

CN
F
F
O
NC
O
N
H
Br

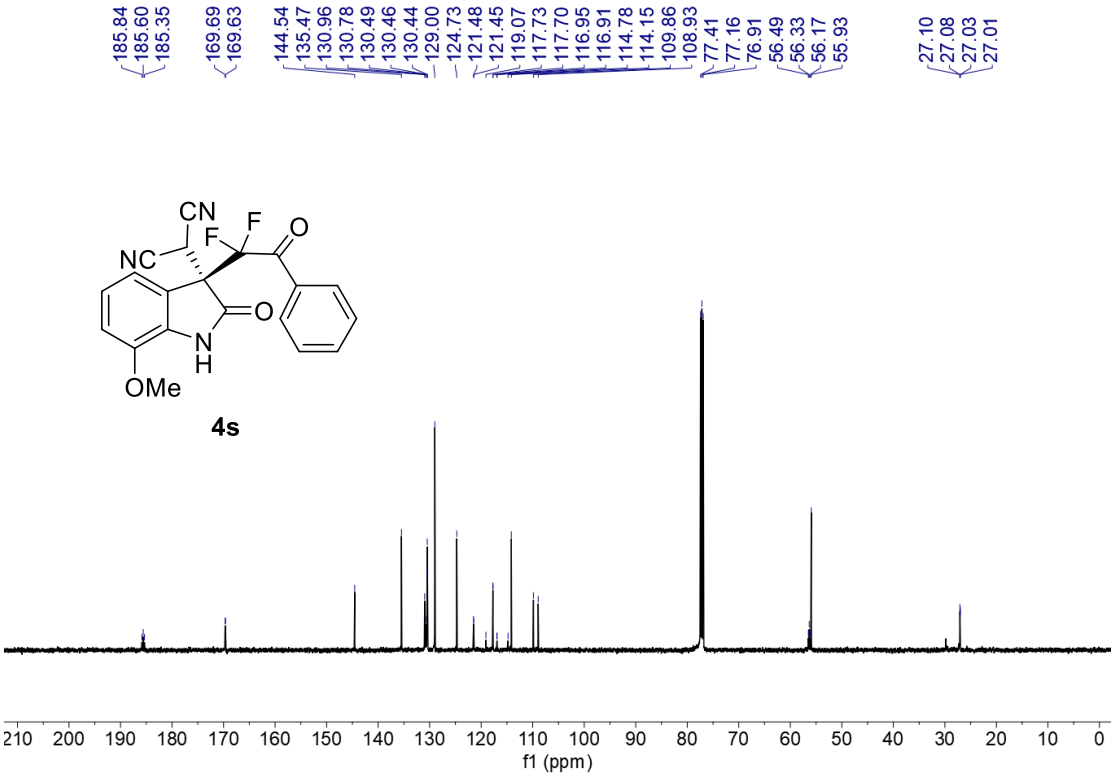
4r

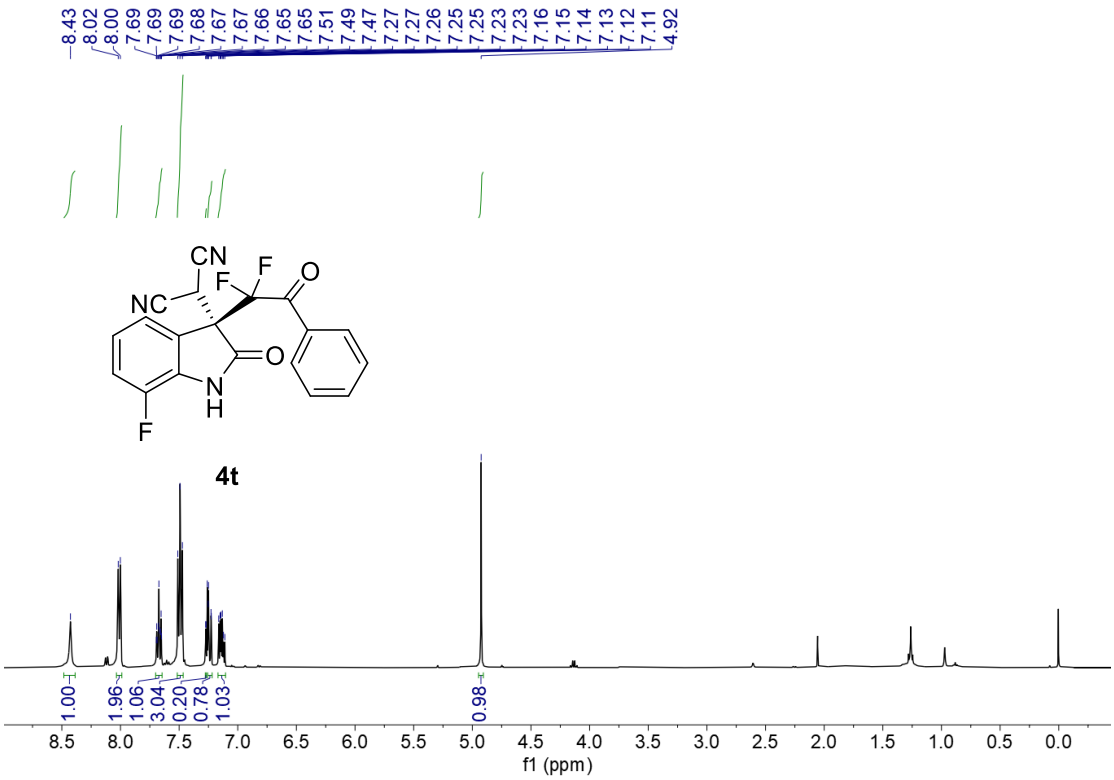

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


185.68
185.37
185.07
169.08
169.00
141.53
135.76
134.90
130.55
130.51
129.13
125.24
125.16
124.87
124.84
122.03
122.00
119.73
117.07
117.02
114.35
109.55
108.62
104.26
77.48
77.16
76.84
57.03
56.83
56.62
27.01
26.93
CN
F
F
O
NC
O
N
H
Br
4r
f1 (ppm)


8.10
8.00
7.99
7.67
7.65
7.63
7.49
7.47
7.45
7.29
7.28
7.27
7.26
7.26
7.14
7.12
7.10
7.03
7.01
4.92
3.90
CN
F
F
O
NC
O
N
H
OMe
4s
0.97
2.00
0.96
1.96
1.03
1.00
0.95
1.00
3.00
f1 (ppm)


-96.49
-97.31
-98.58
-99.40
CN
F
F
O
NC
O
N
H
OMe
4s
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


185.84
185.60
185.35
169.69
169.63
144.54
135.47
130.96
130.78
130.49
130.46
130.44
129.00
124.73
121.48
121.45
119.07
117.73
117.70
116.95
116.91
114.78
114.15
109.86
108.93
77.41
77.16
76.91
56.49
56.33
56.17
55.93
27.10
27.08
27.03
27.01
CN
F
F
O
NC
O
N
H
OMe
4s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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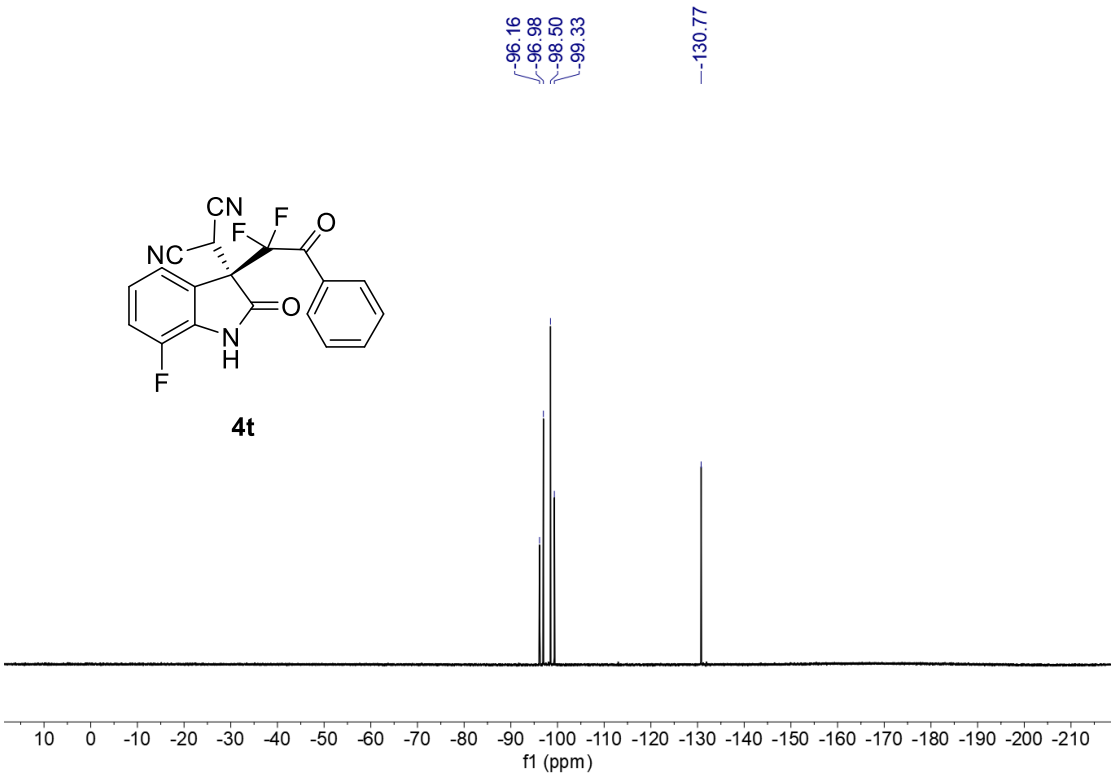
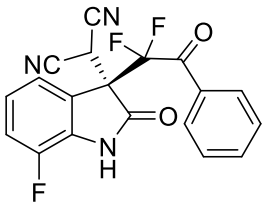
8.02
8.00
7.69
7.69
7.69
7.68
7.67
7.67
7.66
7.65
7.65
7.51
7.49
7.47
7.27
7.27
7.26
7.25
7.25
7.23
7.23
7.16
7.15
7.14
7.13
7.12
7.11
4.92
CN
F
O
NC
O
N
H
F
4t
1.00
1.96
1.06
3.04
0.20
0.78
1.03
0.98
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

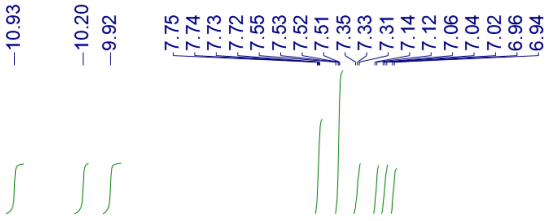

-96.16
-96.98
-98.50
-99.33
-130.77
CN
F
O
NC
O
N
H
F
4t
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

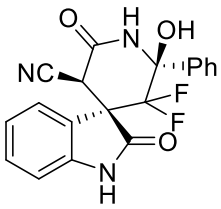

185.65
185.34
185.04
169.65
169.57
148.68
146.23
135.77
130.57
130.54
130.50
129.12
124.93
124.87
123.37
123.33
123.30
121.75
121.71
121.67
119.70
119.47
119.30
117.04
116.99
114.32
109.57
108.65
77.48
77.16
76.84
56.13
55.92
55.72
27.10
27.07
27.01
26.98


CN
F
F
O
NC
O
N
H
F

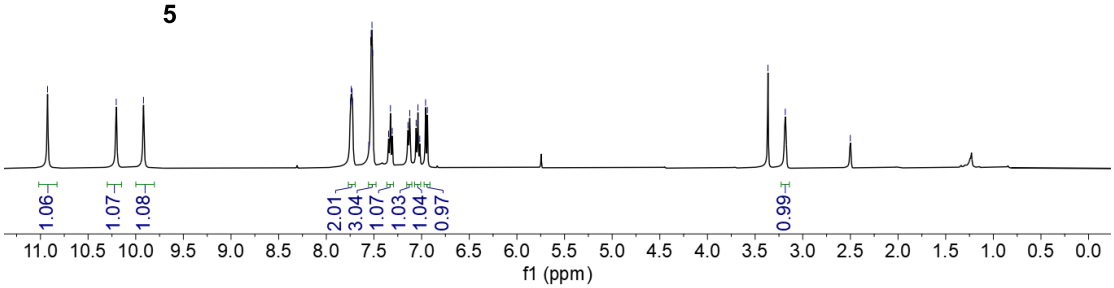
4t

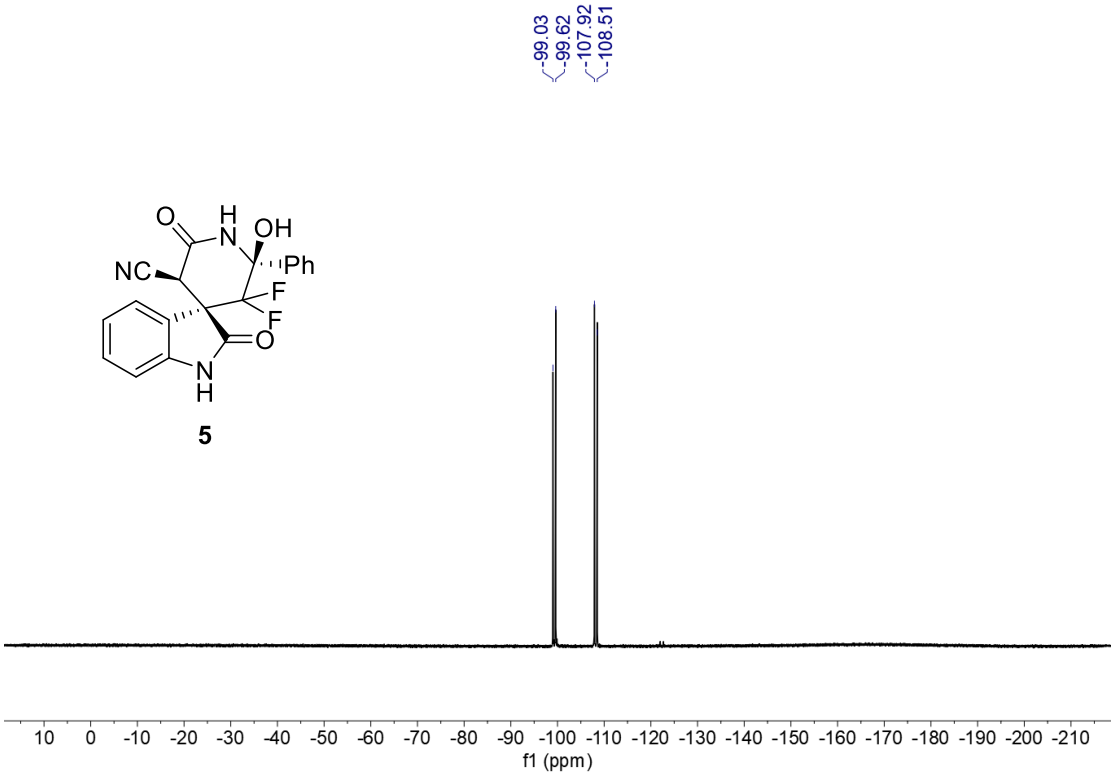
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.93
10.20
9.92
7.75
7.74
7.73
7.72
7.55
7.53
7.52
7.51
7.35
7.33
7.31
7.14
7.12
7.06
7.04
7.02
6.96
6.94
3.36
3.18
2.50


O
H
N
OH
NC
Ph
F
F
O
N
H

5


1.06
1.07
1.08
2.01
3.04
1.07
1.03
1.04
0.97
0.99
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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-99.62
-107.92
-108.51
O
H
N
OH
NC
Ph
F
F
O
N
H
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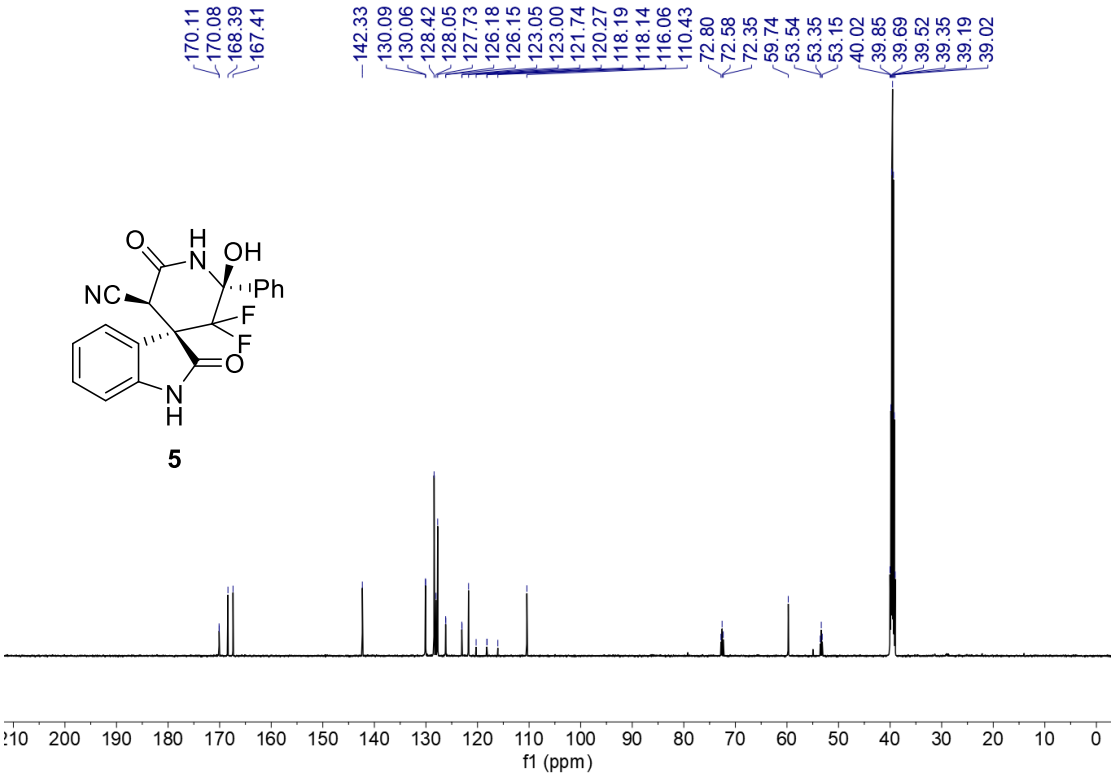
f1 (ppm)

5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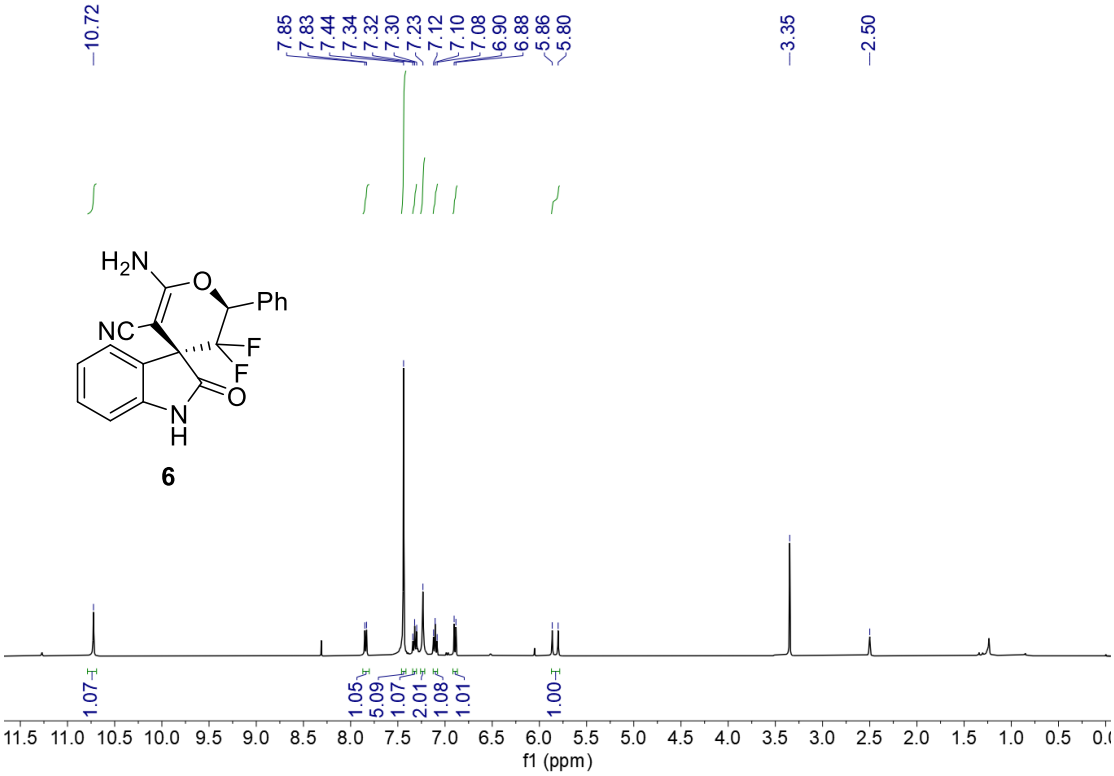
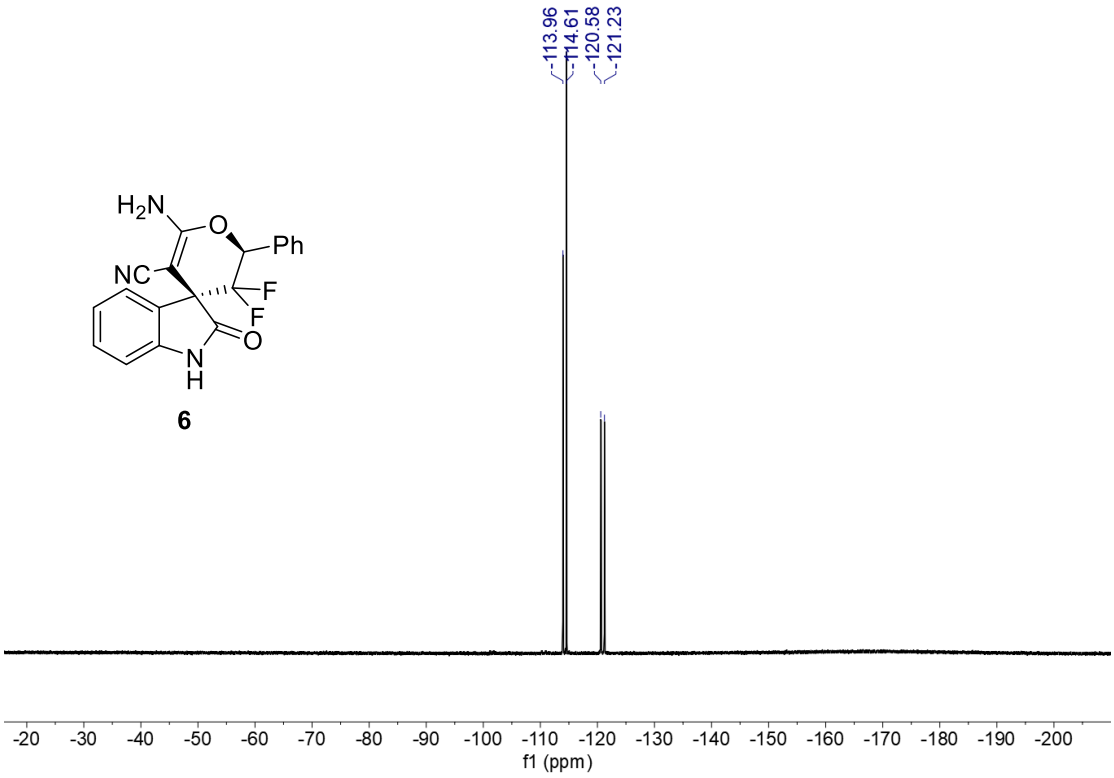
168.39
167.41
142.33
130.09
130.06
128.42
128.05
127.73
126.18
126.15
123.05
123.00
121.74
120.27
118.19
118.14
116.06
110.43
72.80
72.58
72.35
59.74
53.54
53.35
53.15
40.02
39.85
39.69
39.52
39.35
39.19
39.02
O
H
N
OH
NC
Ph
F
F
O
N
H
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

5


10.72
7.85
7.83
7.44
7.34
7.32
7.30
7.23
7.12
7.10
7.08
6.90
6.88
5.86
5.80
3.35
2.50
1.07
1.05
5.09
1.07
2.01
1.08
1.01
1.00
f1 (ppm)

H2N
O
Ph
NC
F
F
O
N
H

6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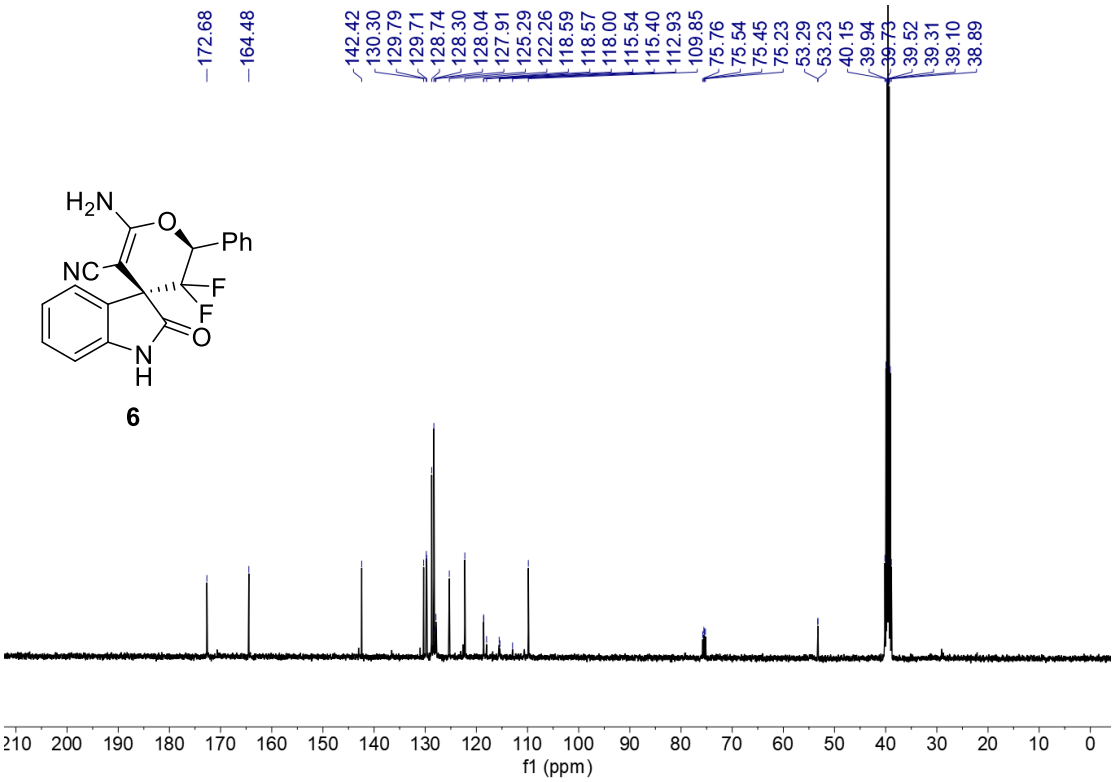
-121.23
f1 (ppm)

H2N
O
Ph
NC
F
F
O
N
H

6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129.71
128.74
128.30
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127.91
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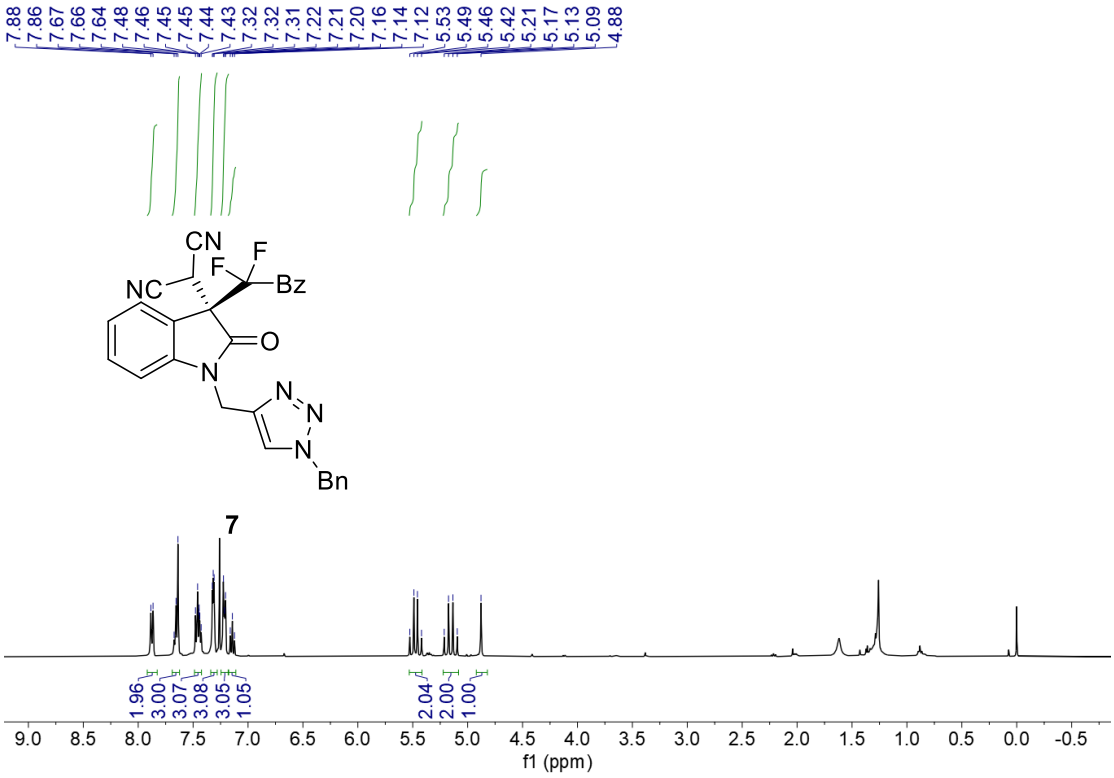
122.26
118.59
118.57
118.00
115.54
115.40
112.93
109.85
75.76
75.54
75.45
75.23
53.29
53.23
40.15
39.94
39.73
39.52
39.31
39.10
38.89
H2N
O
Ph
NC
F
F
O
N
H
6
f1 (ppm)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7.86
7.67
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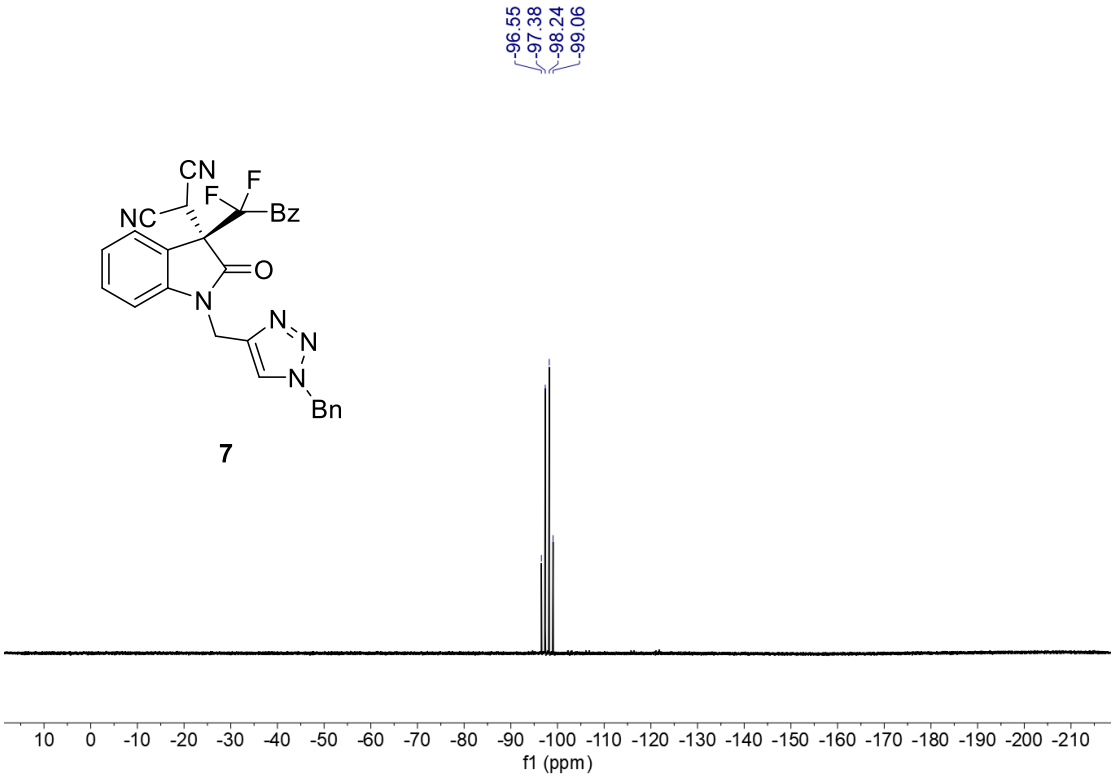
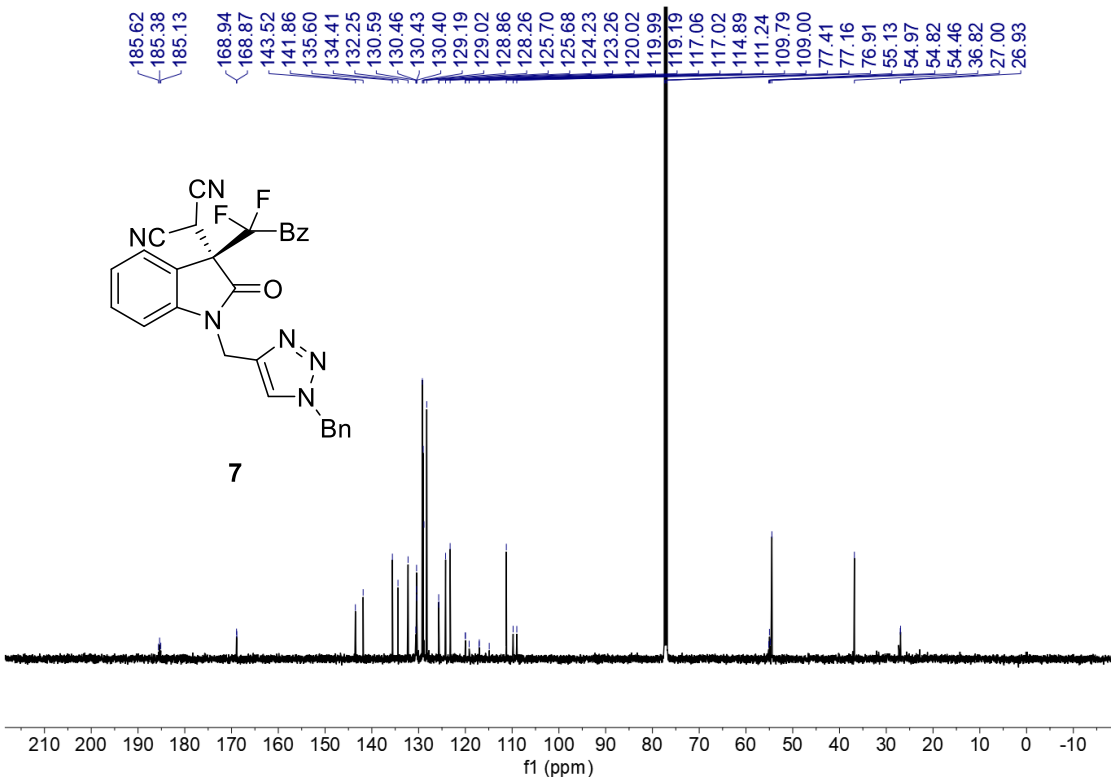
7.48
7.46
7.45
7.45
7.44
7.43
7.32
7.32
7.31
7.22
7.21
7.20
7.16
7.14
7.12
5.53
5.49
5.46
5.42
5.21
5.17
5.13
5.09
4.88
CN
F
F
Bz
NC
O
N
N
N
N
Bn
7
1.96
3.00
3.07
3.08
3.05
1.05
2.04
2.00
1.00
f1 (ppm)


-96.55
-97.38
-98.24
-99.06
CN
F
F
Bz
NC
O
N
N
N
N
Bn
7
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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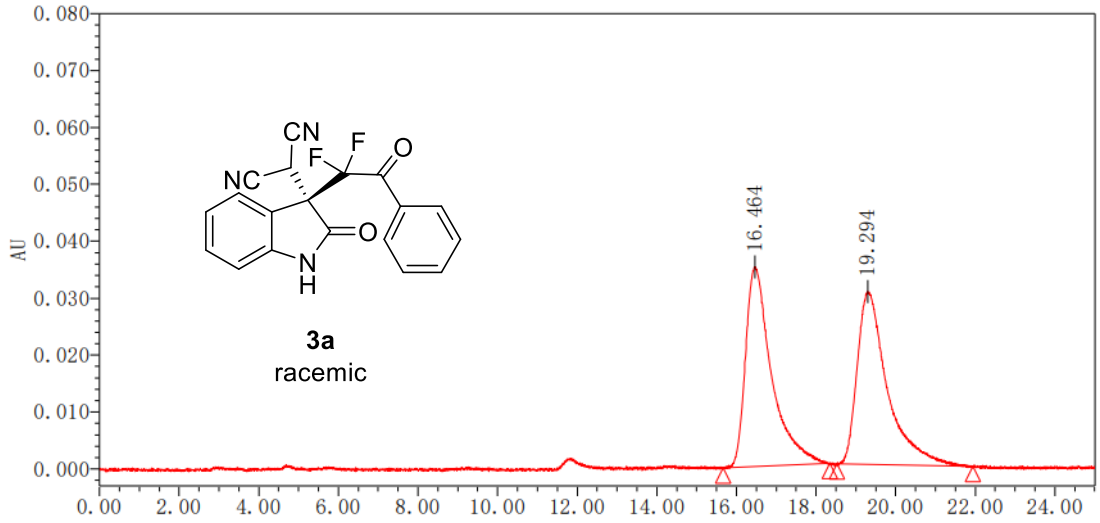
168.87
143.52
141.86
135.60
134.41
132.25
130.59
130.46
130.43
130.40
129.19
129.02
128.86
128.26
125.70
125.68
124.23
123.26
120.02
119.99
119.19
117.06
117.02
114.89
111.24
109.79
109.00
77.41
77.16
76.91
55.13
54.97
54.82
54.46
36.82
27.00
26.93
CN
F
F
Bz
NC
O
N
N
N
N
Bn
7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

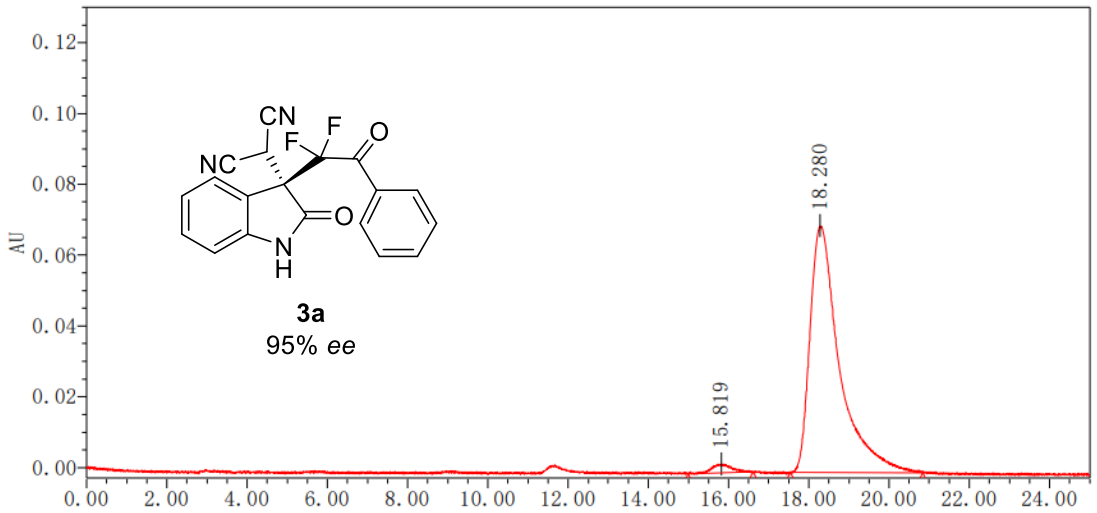
7. HPLC Analyses Figures of Compounds 3-6

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 85:15

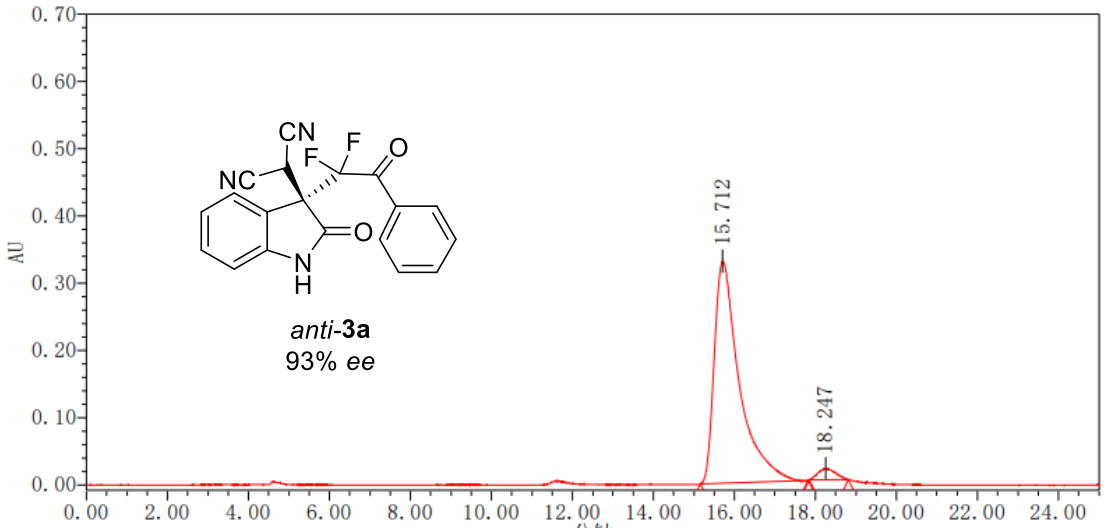
flow rate = 1.0 mL/min



Entry	RT min	Height mV	Area mV.sec	% Area %
1	16.464	35029	1591738	49.99
2	19.294	30312	1592458	50.01



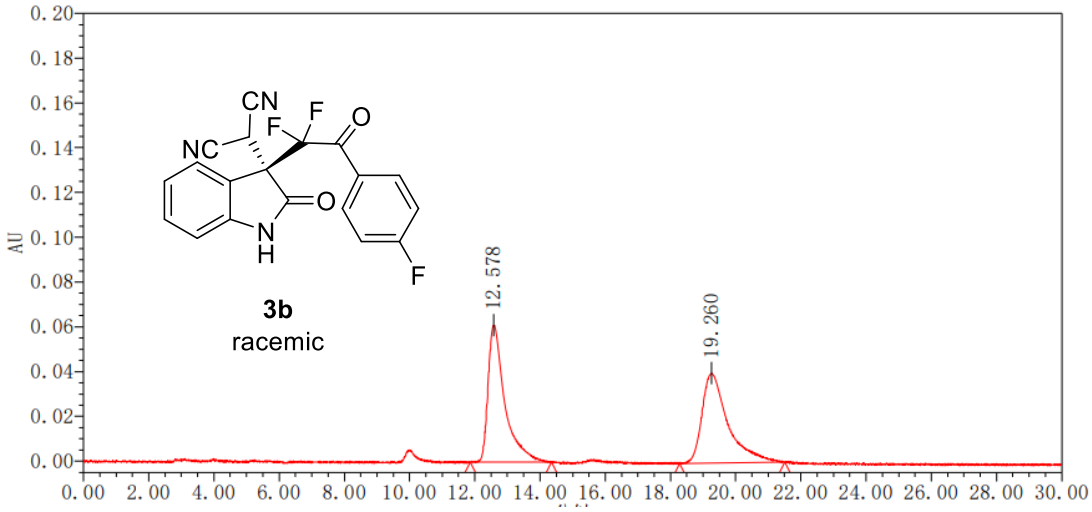
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.819	2407	80515	2.23
2	18.280	69647	3537074	97.77



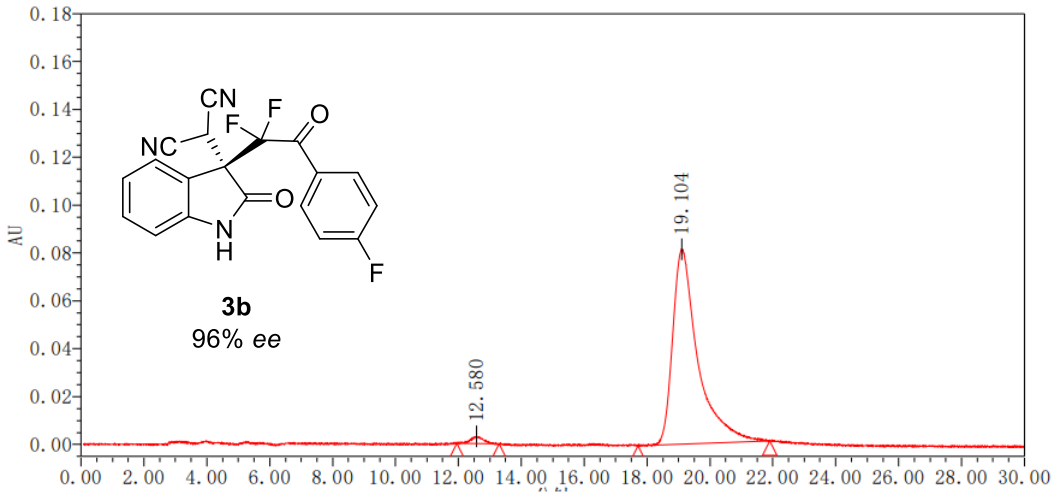
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.712	330115	14218255	96.59
2	18.247	16318	501727	3.41

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 83:17

flow rate = 1.0 mL/min



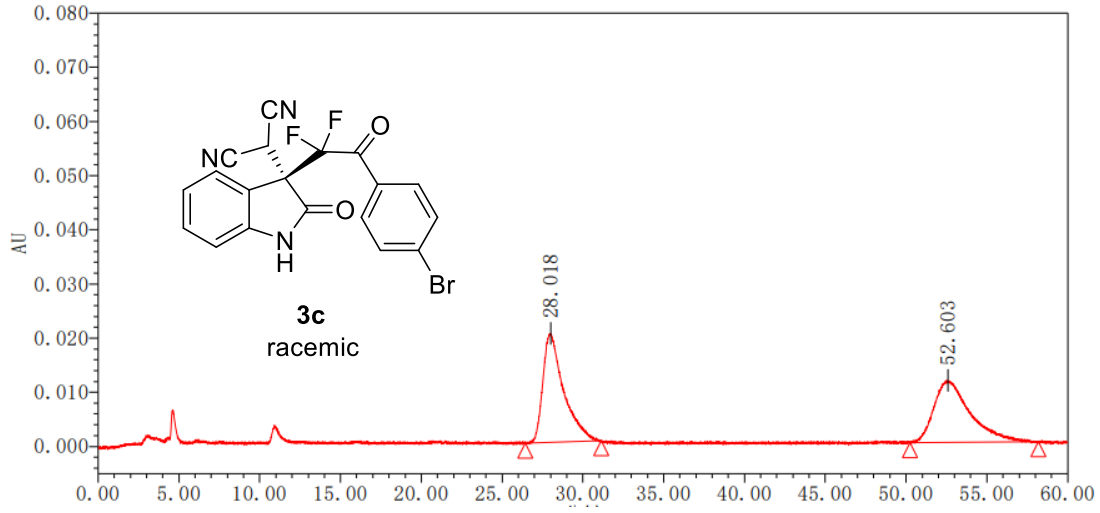
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.578	61106	2173851	49.68
2	19.260	40121	2202211	50.32



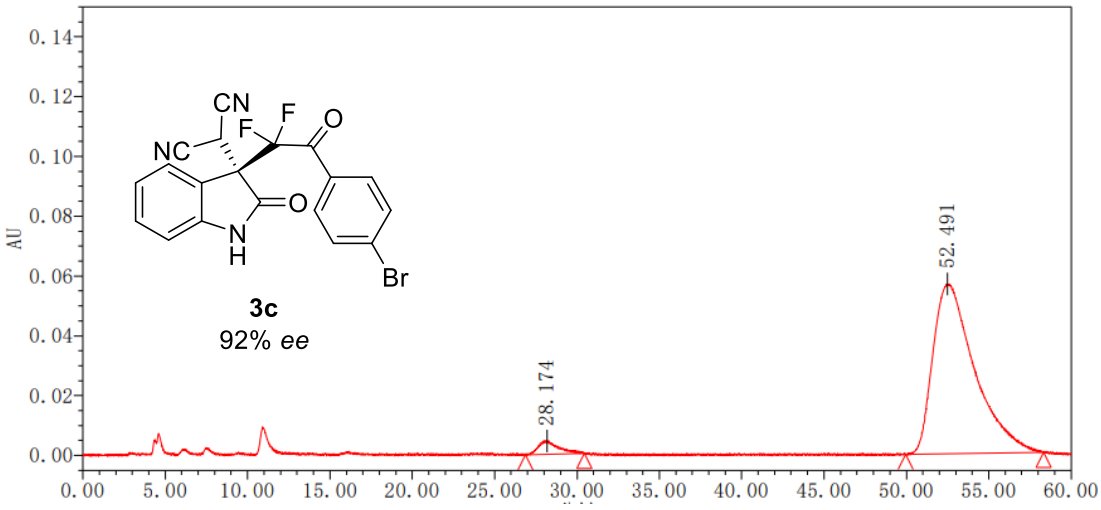
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.580	2959	86091	1.86
2	19.104	81365	4532567	98.14

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



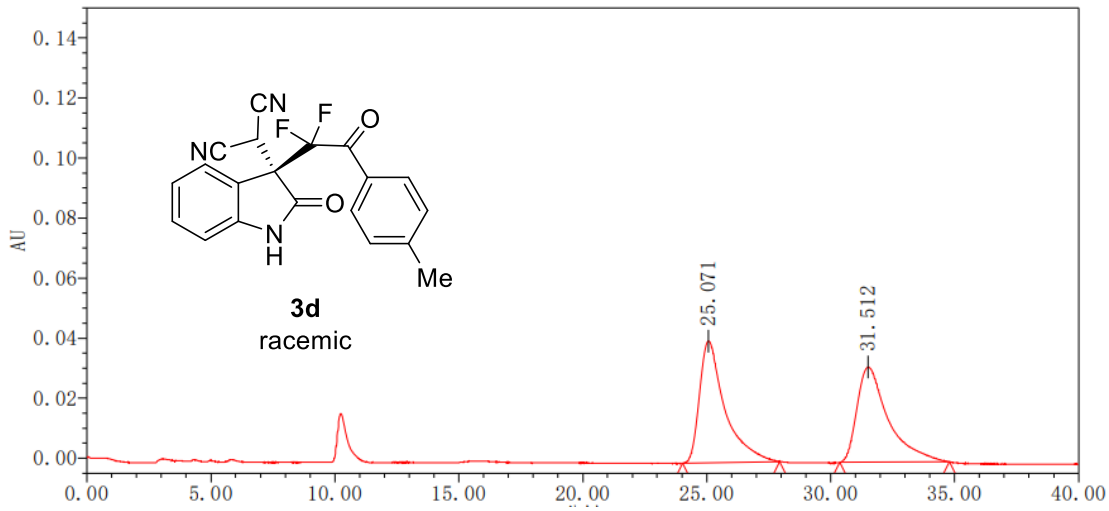
Entry	RT min	Height mV	Area mV.sec	% Area %
1	28.018	20055	1792135	50.49
2	52.603	11420	1757506	49.51



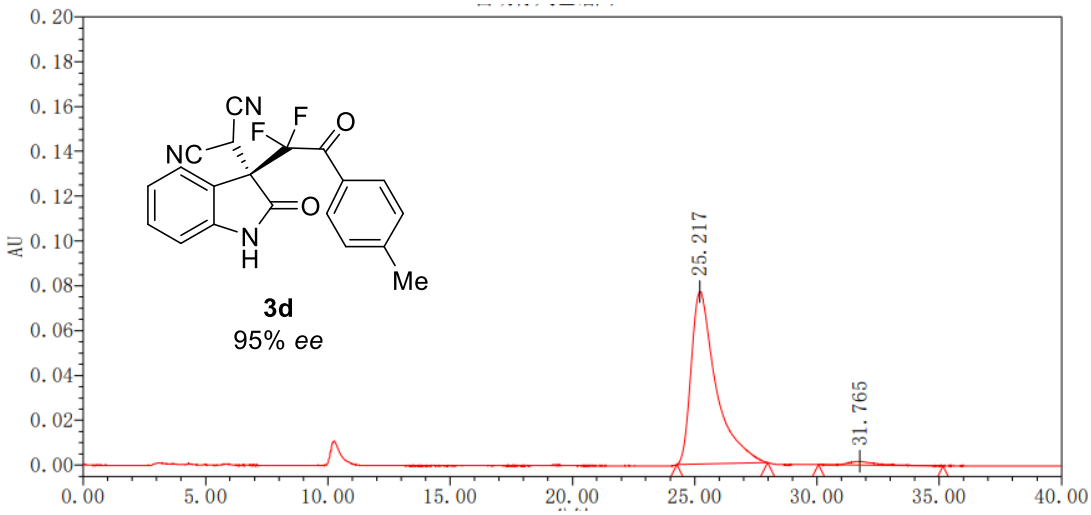
Entry	RT min	Height mV	Area mV.sec	% Area %
1	28.174	4380	373068	3.60
2	52.491	56795	9985564	96.40

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



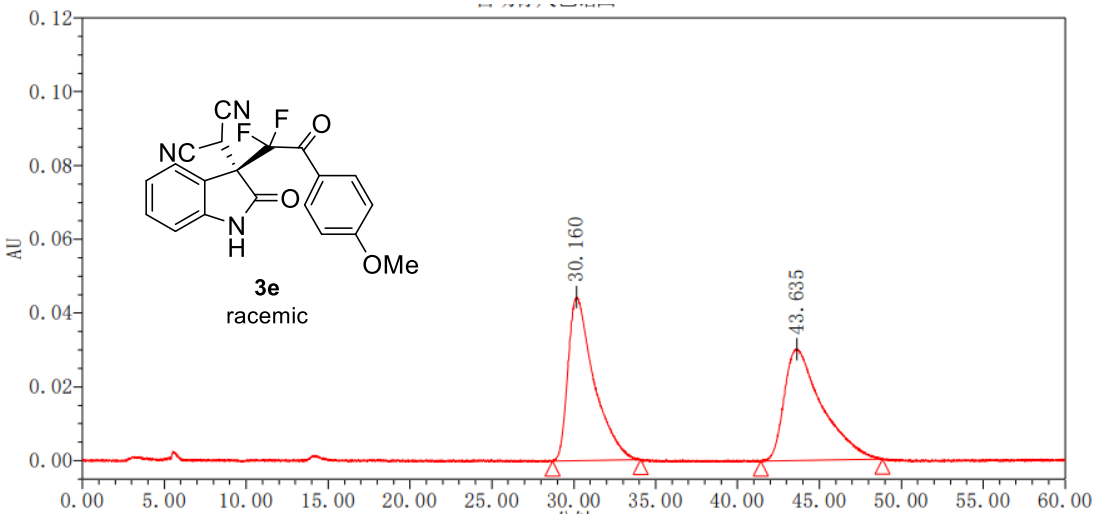
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.071	40534	2876282	50.90
2	31.512	31714	2774801	49.10



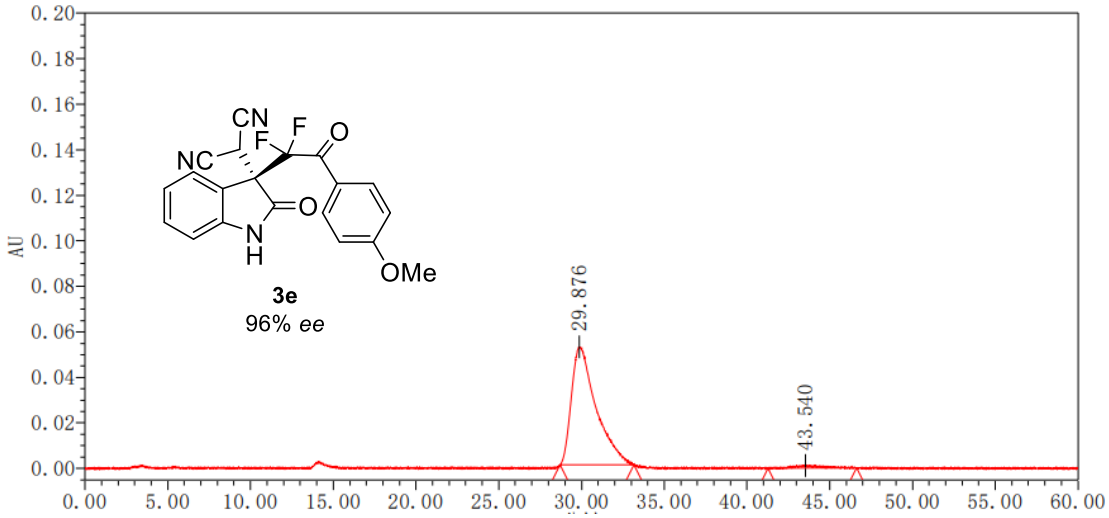
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.217	77127	5449420	97.81
2	31.765	1584	122007	2.19

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 75:25

flow rate = 1.0 mL/min



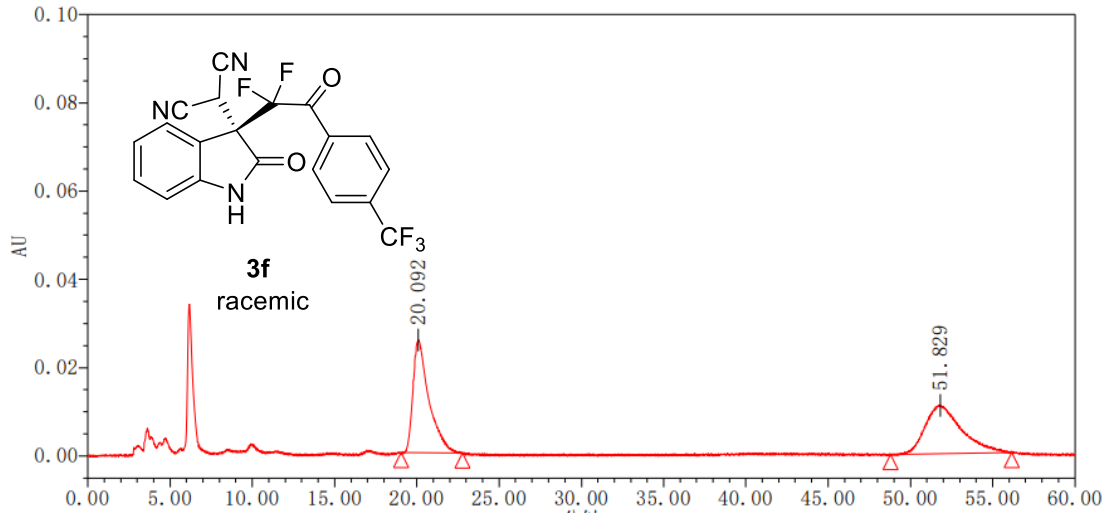
Entry	RT min	Height mV	Area mV.sec	% Area %
1	30.160	44310	4892306	50.32
2	43.635	30179	4830046	49.68



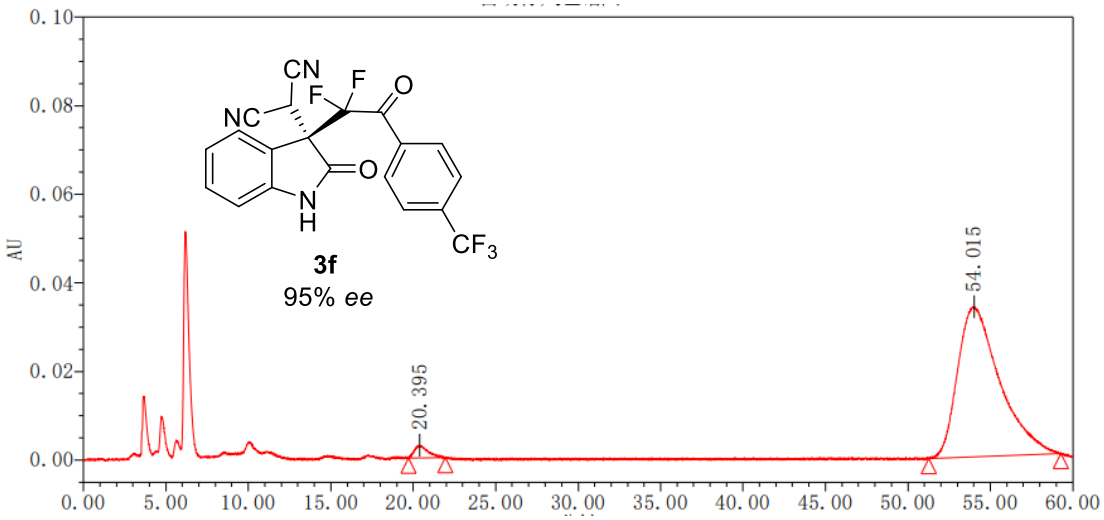
Entry	RT min	Height mV	Area mV.sec	% Area %
1	29.876	51792	5363294	98.01
2	43.540	1045	108763	1.99

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 78:22

flow rate = 1.0 mL/min



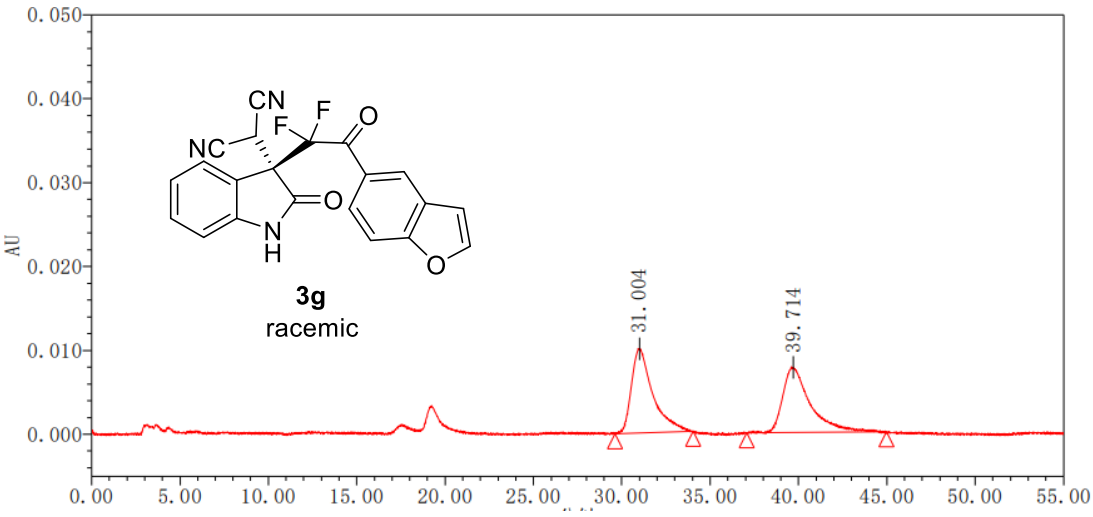
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.092	25577	1735714	50.78
2	51.829	10885	1682169	49.22



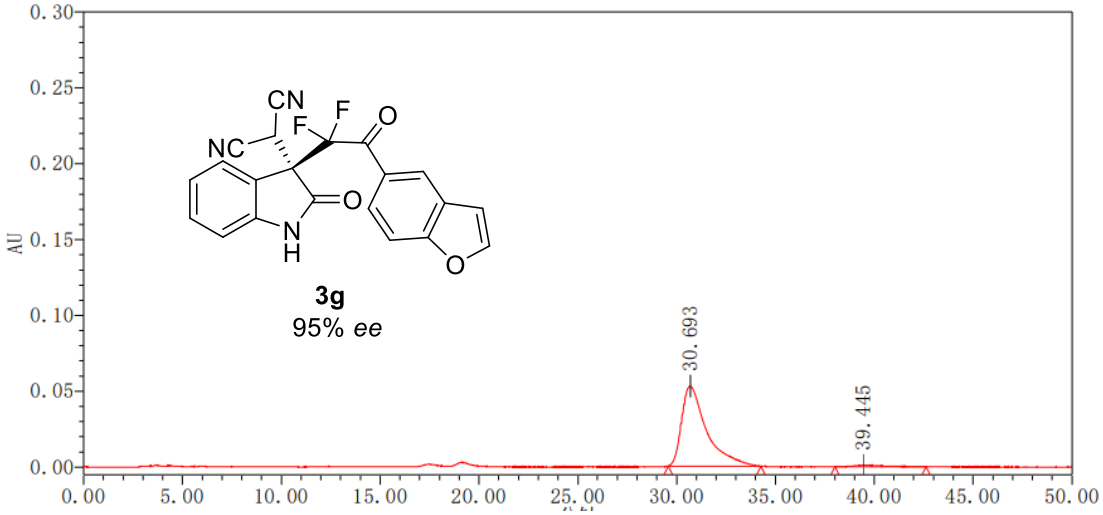
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.395	2810	155333	2.52
2	54.015	33838	6003845	97.48

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



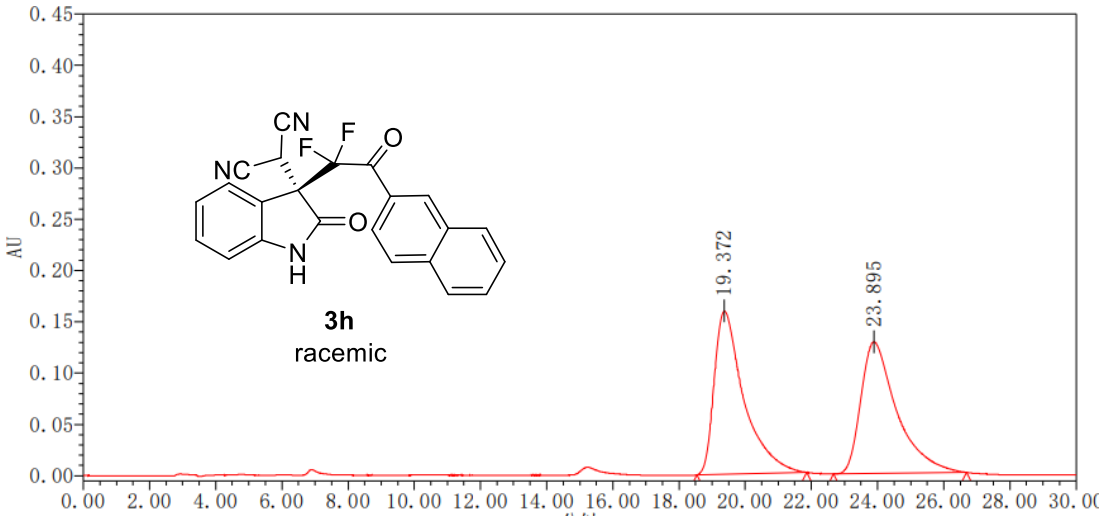
Entry	RT min	Height mV	Area mV.sec	% Area %
1	31.004	10046	844798	49.96
2	39.714	7767	846218	50.04



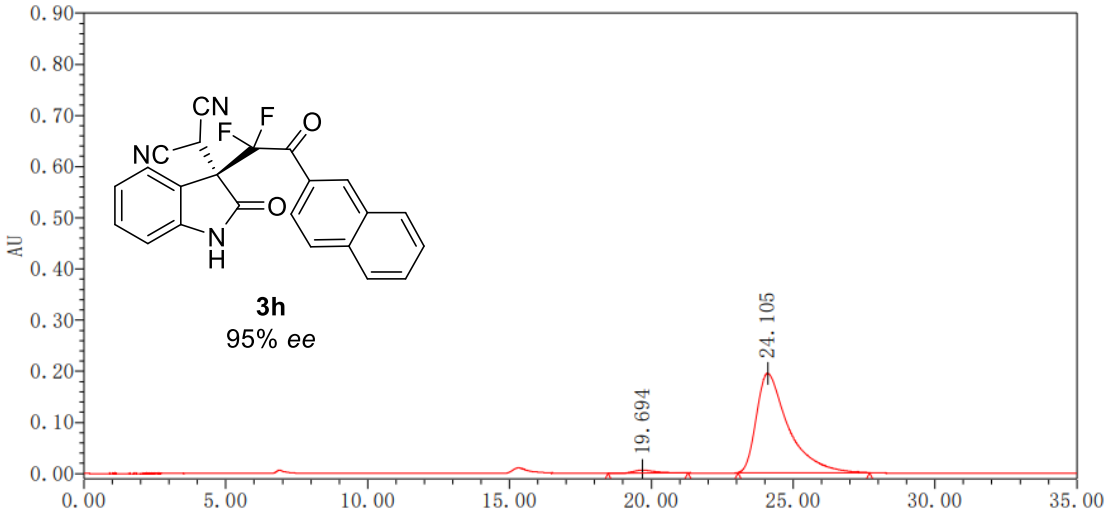
Entry	RT min	Height mV	Area mV.sec	% Area %
1	30.693	52679	4621376	97.50
2	39.445	1092	118264	2.50

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



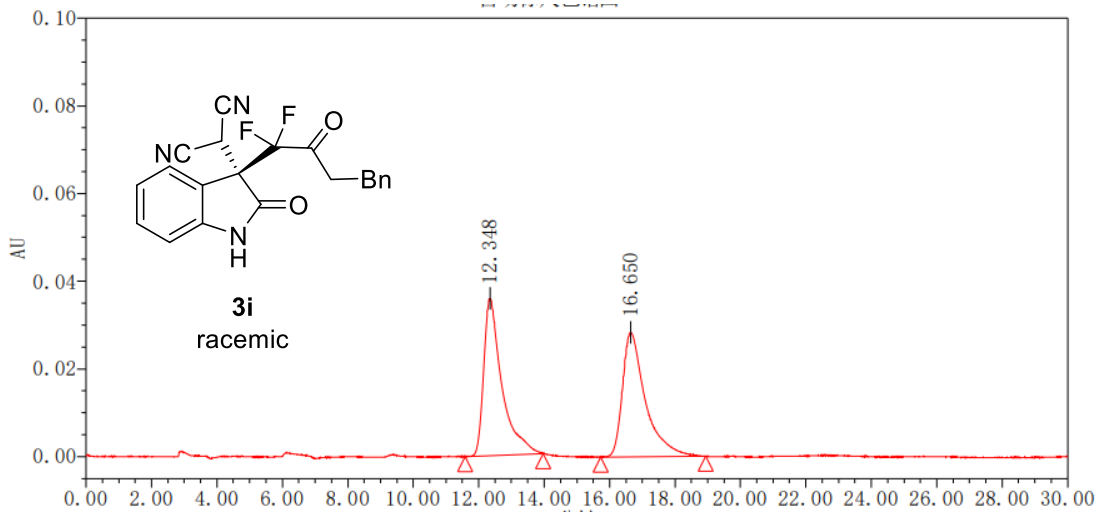
Entry	RT min	Height mV	Area mV.sec	% Area %
1	19.372	159110	9874406	50.47
2	23.895	128427	9691539	49.53



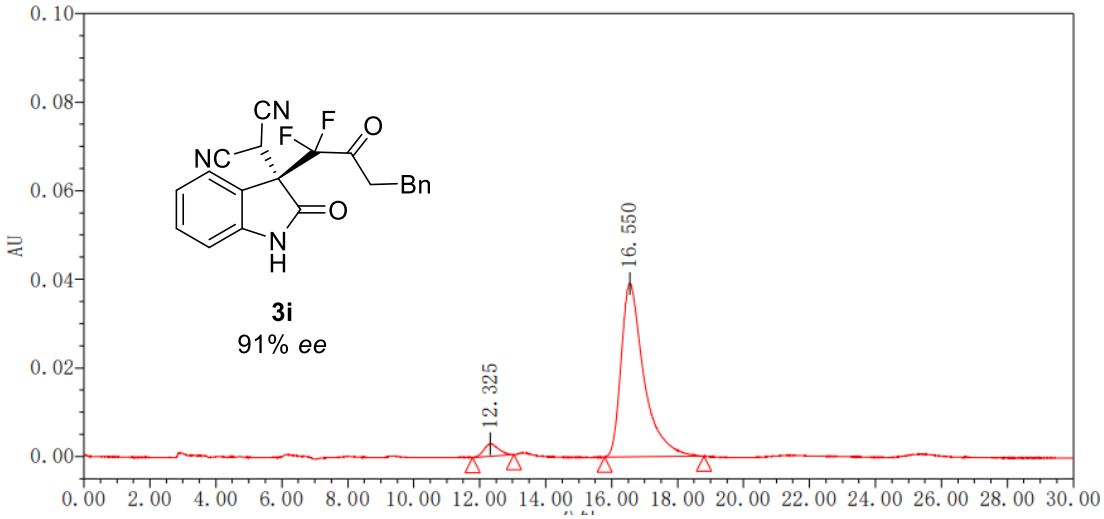
Entry	RT min	Height mV	Area mV.sec	% Area %
1	19.694	5871	333258	2.15
2	24.105	193973	15161412	97.85

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 87:13

flow rate = 1.0 mL/min



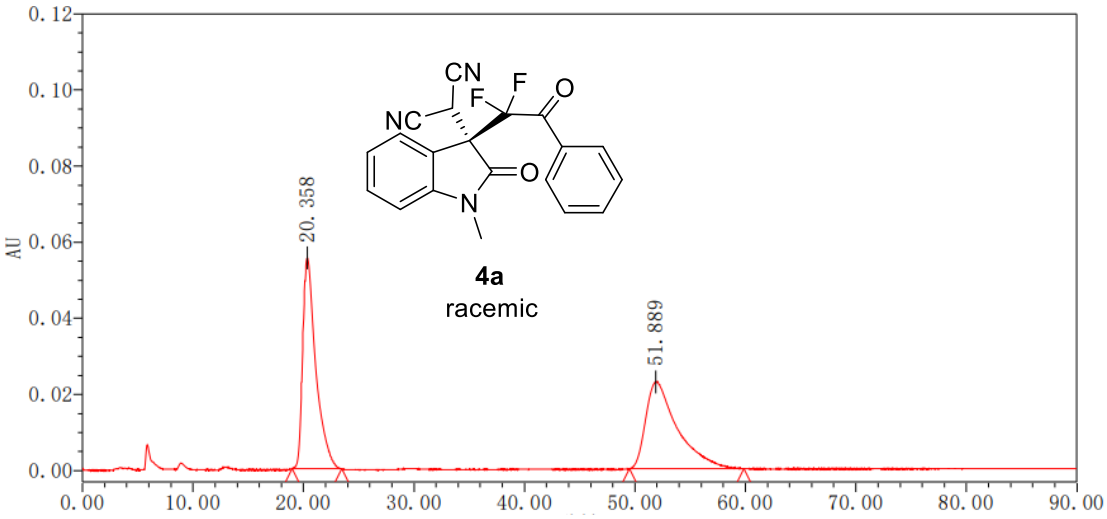
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.348	35843	1388219	50.13
2	16.650	28390	1381288	49.87



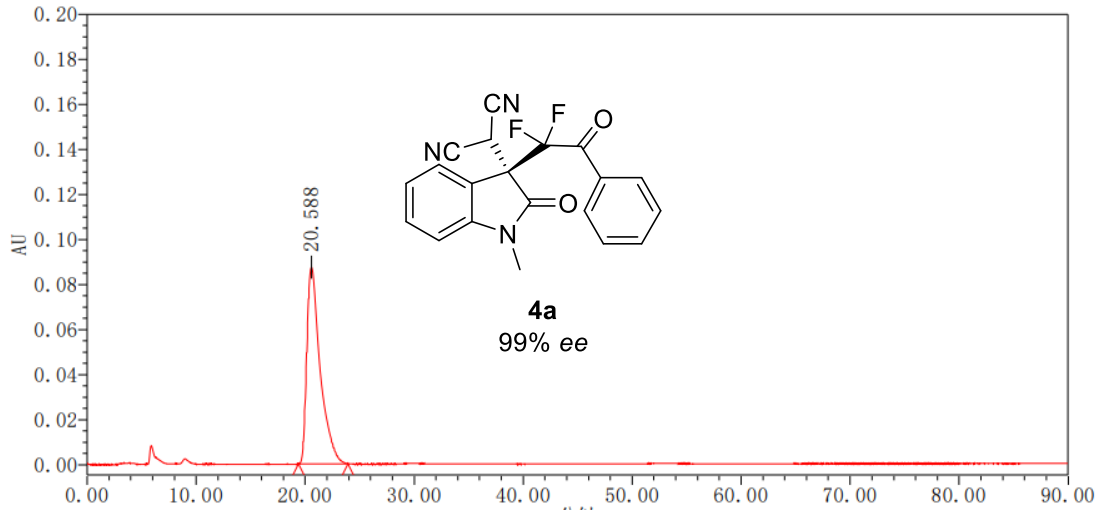
Entry	RT min	Height mV	Area mV.sec	% Area %
1	12.325	2812	87029	4.42
2	16.550	39123	1880166	95.58

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 70:30

flow rate = 1.0 mL/min



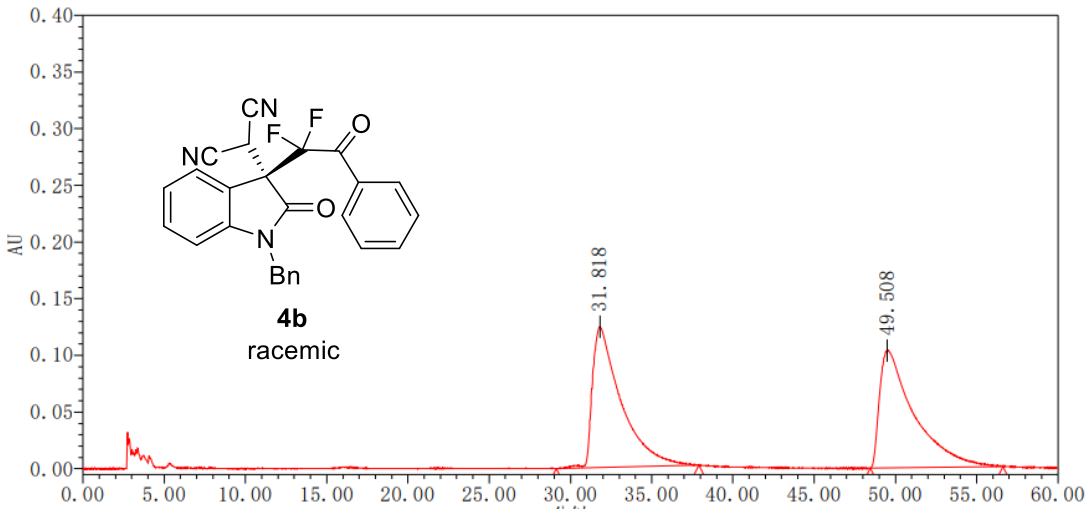
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.358	55397	4607284	50.36
2	51.889	22874	4541561	49.64



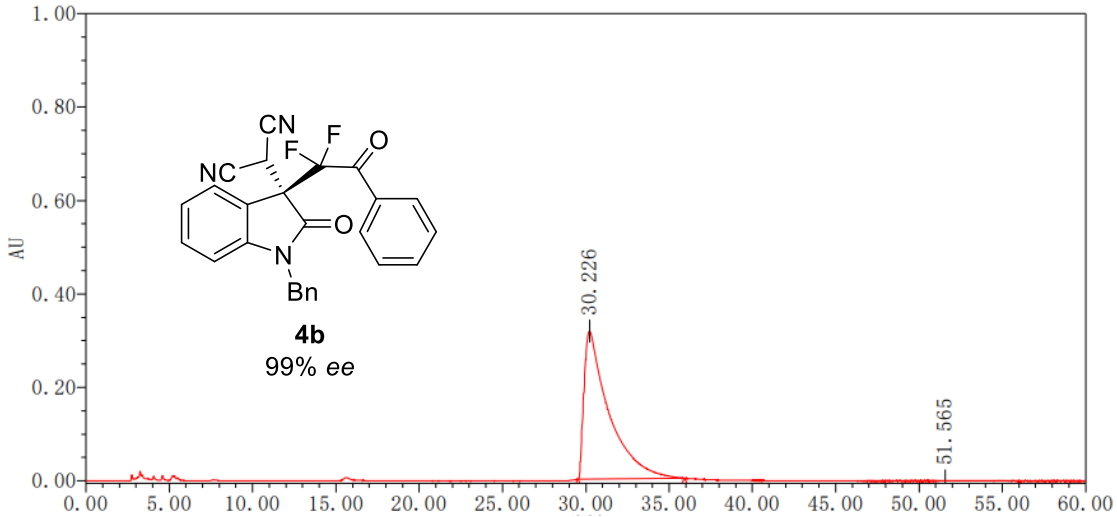
Entry	RT min	Height mV	Area mV.sec	% Area %
1	20.588	87451	7455951	100

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 87:13

flow rate = 1.0 mL/min



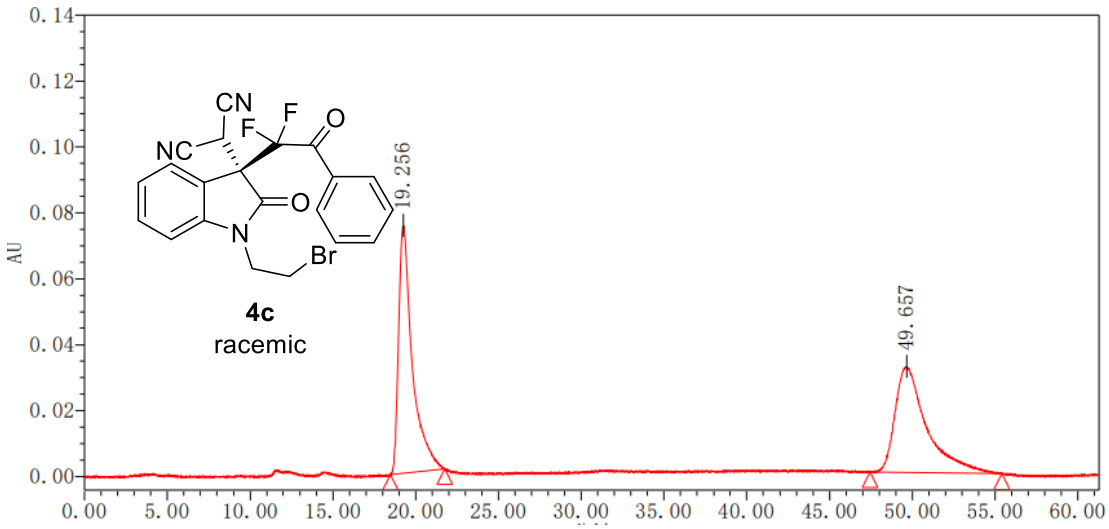
Entry	RT min	Height mV	Area mV.sec	% Area %
1	31.818	124211	15242440	50.03
2	49.508	103653	15226670	49.97



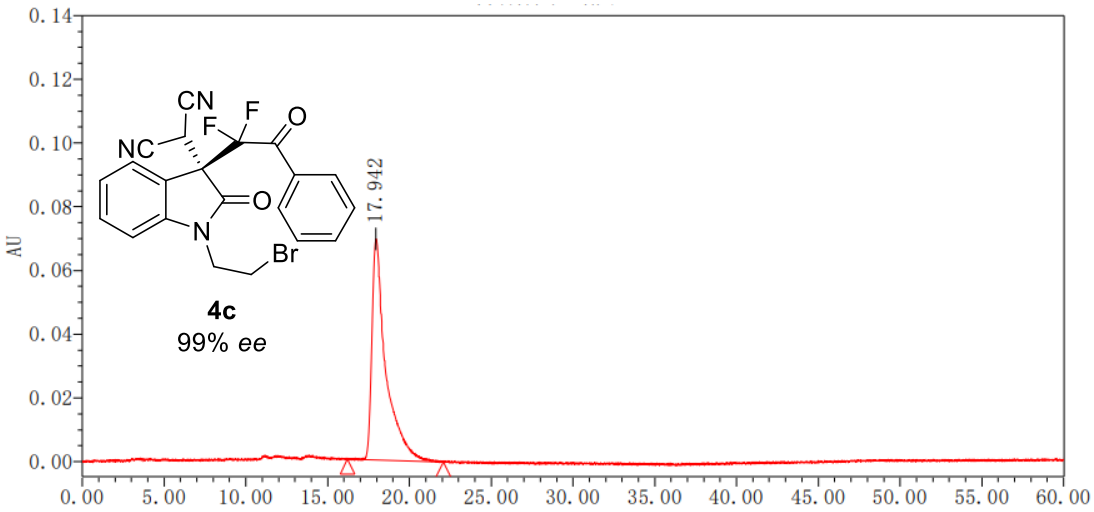
Entry	RT min	Height mV	Area mV.sec	% Area %
1	30.226	316944	32843260	99.82
2	51.565	467	60760	0.18

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 70:30

flow rate = 1.0 mL/min



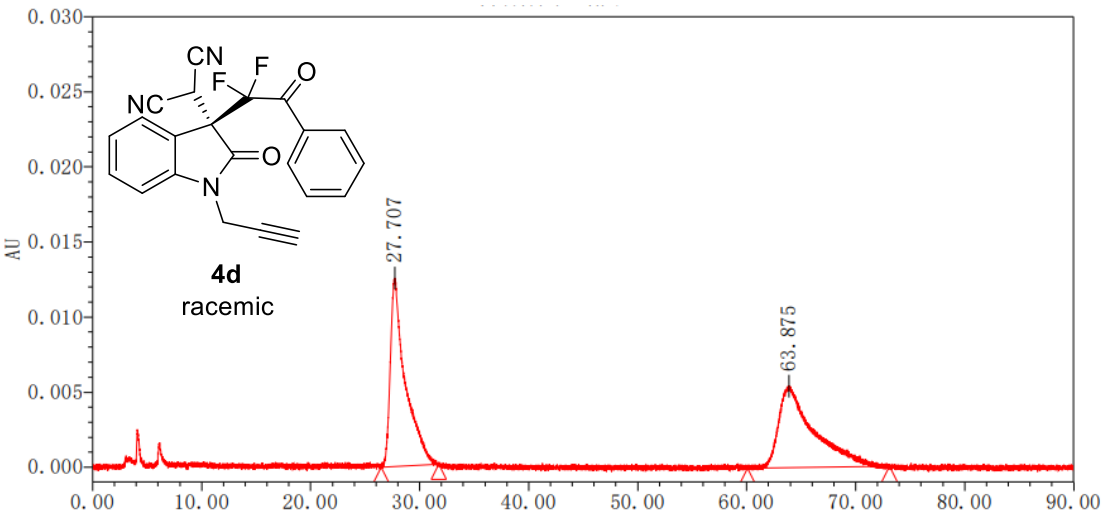
Entry	RT min	Height mV	Area mV.sec	% Area %
1	19.256	75175	4281462	50.06
2	49.657	32147	4271038	49.94



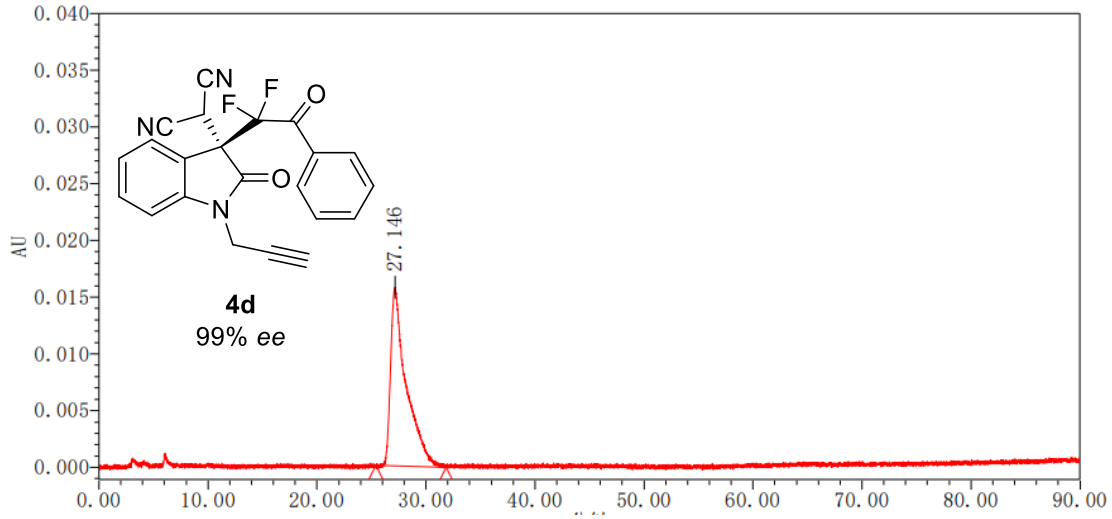
Entry	RT min	Height mV	Area mV.sec	% Area %
1	17.942	69398	4123621	100

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 65:35

flow rate = 1.0 mL/min



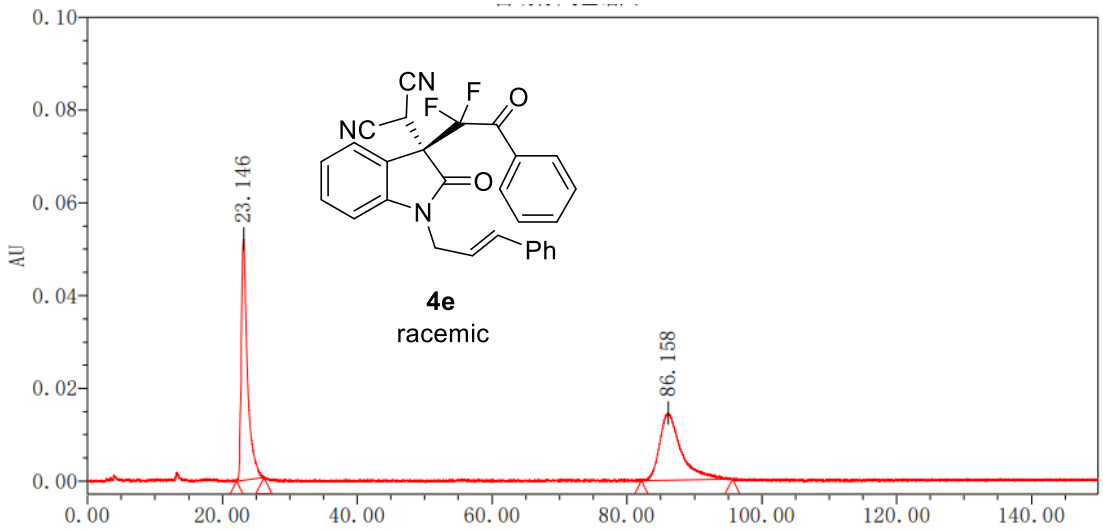
Entry	RT min	Height mV	Area mV.sec	% Area %
1	27.707	12550	1206705	50.04
2	63.875	5418	1204696	49.96



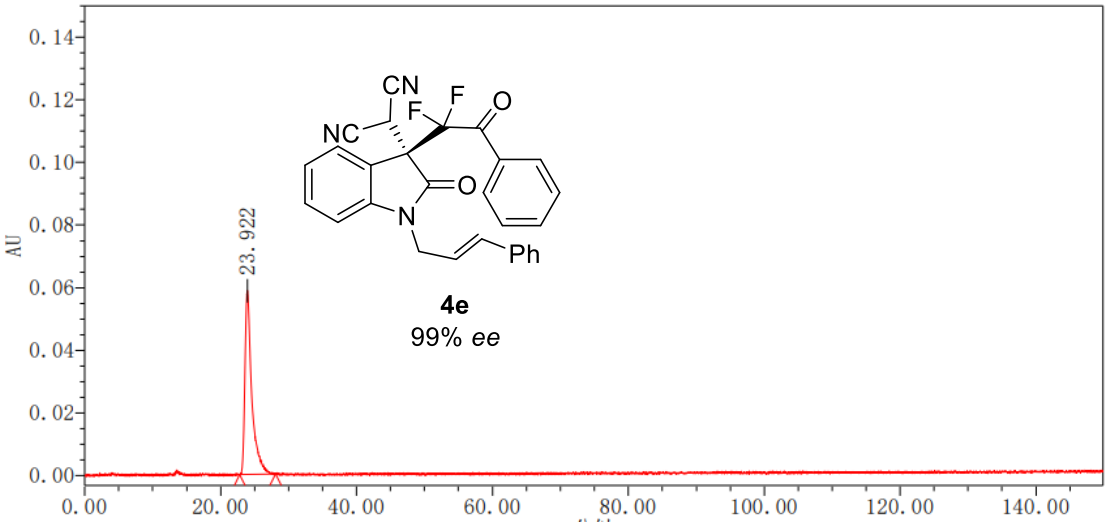
Entry	RT min	Height mV	Area mV.sec	% Area %
1	27.146	15752	1568886	100

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 70:30

flow rate = 1.0 mL/min



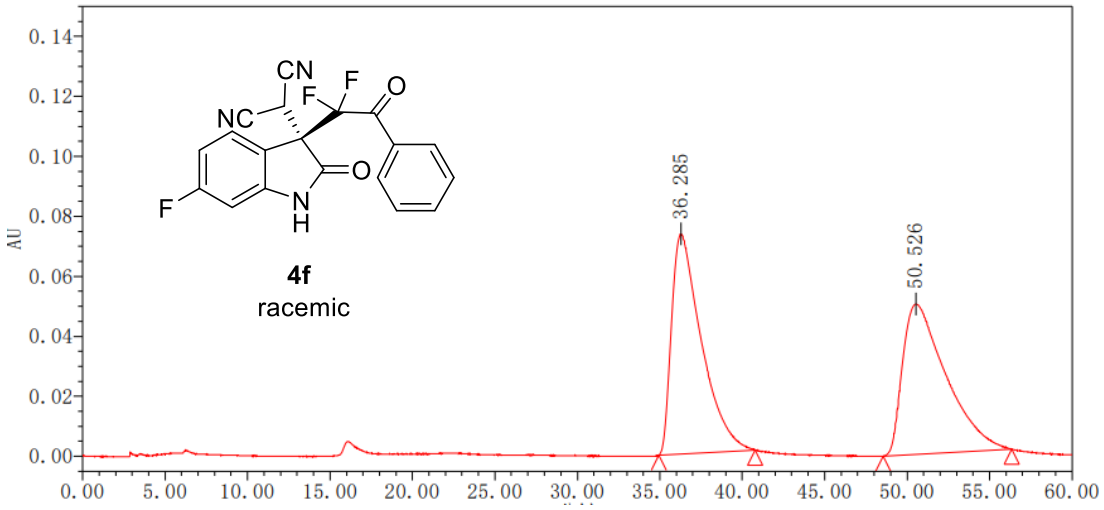
Entry	RT min	Height mV	Area mV.sec	% Area %
1	23.146	51971	3280345	50.41
2	63.875	5418	3227588	49.59



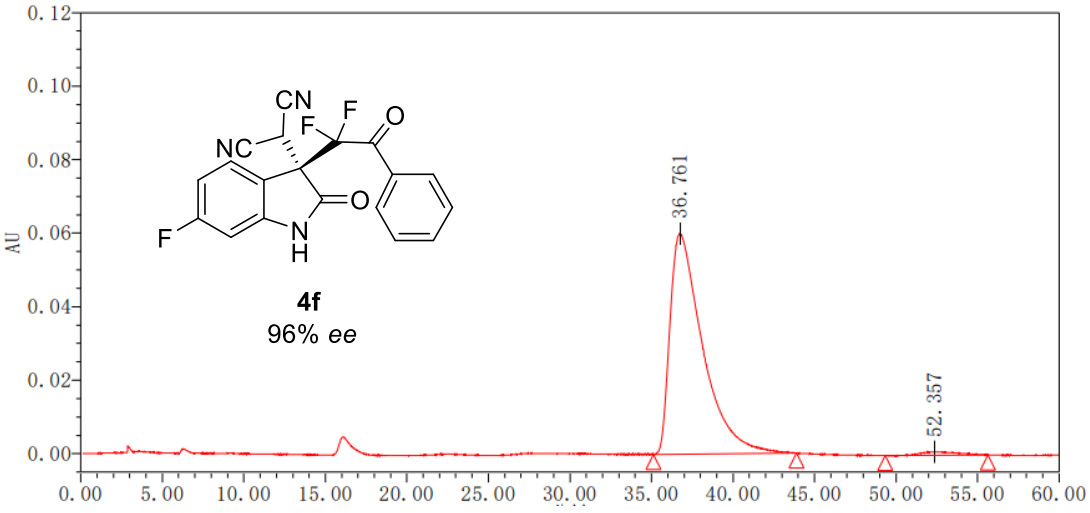
Entry	RT min	Height mV	Area mV.sec	% Area %
1	23.922	58733	4059131	100

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



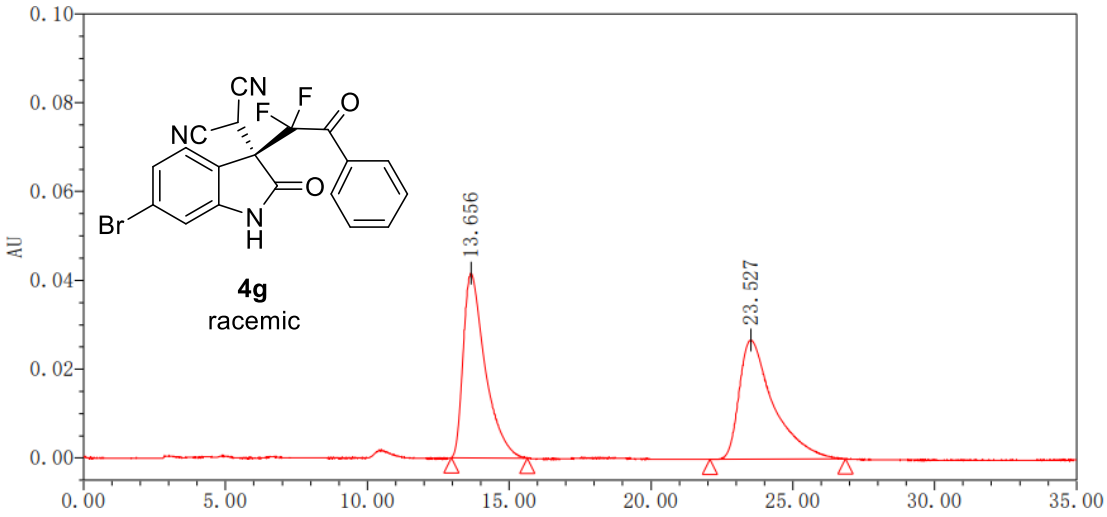
Entry	RT min	Height mV	Area mV.sec	% Area %
1	36.285	73382	9251359	50.29
2	49.508	103653	9144926	49.71



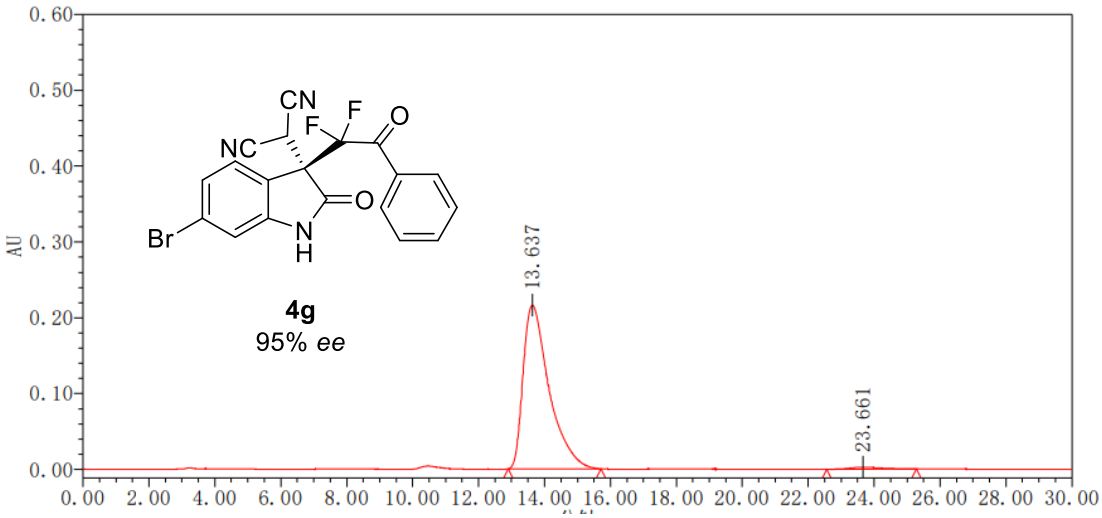
Entry	RT min	Height mV	Area mV.sec	% Area %
1	36.761	60008	8360467	98.31
2	52.357	912	143775	1.69

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



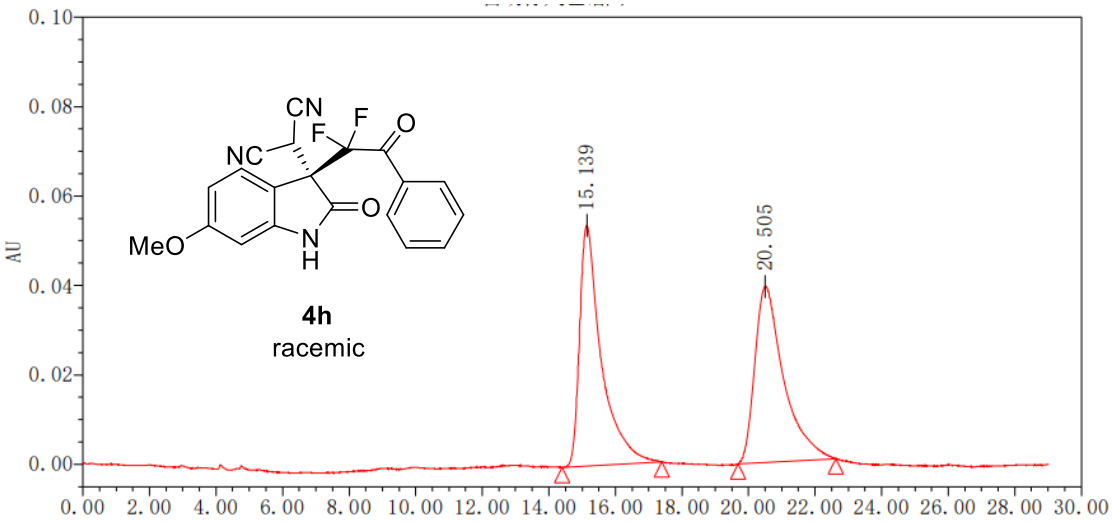
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.656	41526	2235226	49.94
2	23.527	26808	2240755	50.06



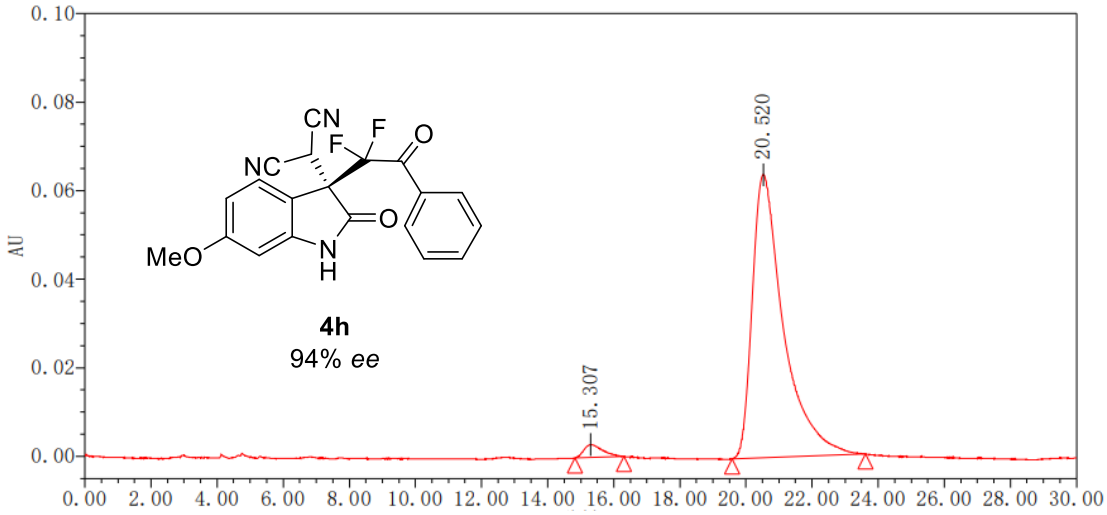
Entry	RT min	Height mV	Area mV.sec	% Area %
1	13.637	215874	11800067	98.64
2	23.661	2439	162117	1.36

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



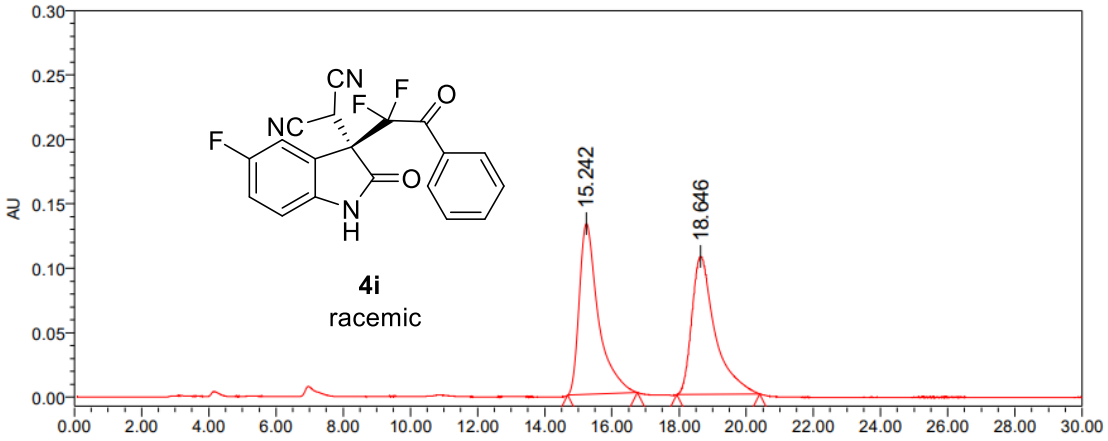
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.139	53795	2439434	50.78
2	20.505	39323	2364902	49.22



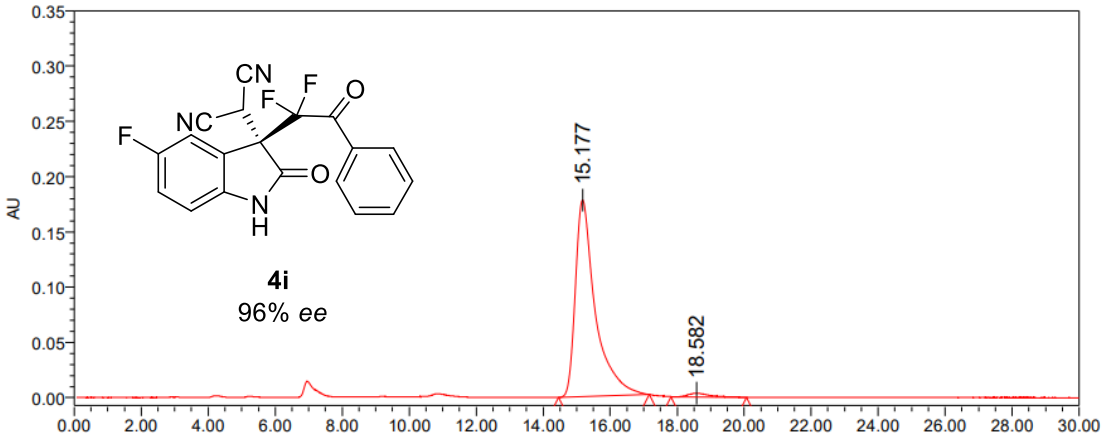
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.307	2934	116006	2.69
2	20.520	63924	4189752	97.31

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



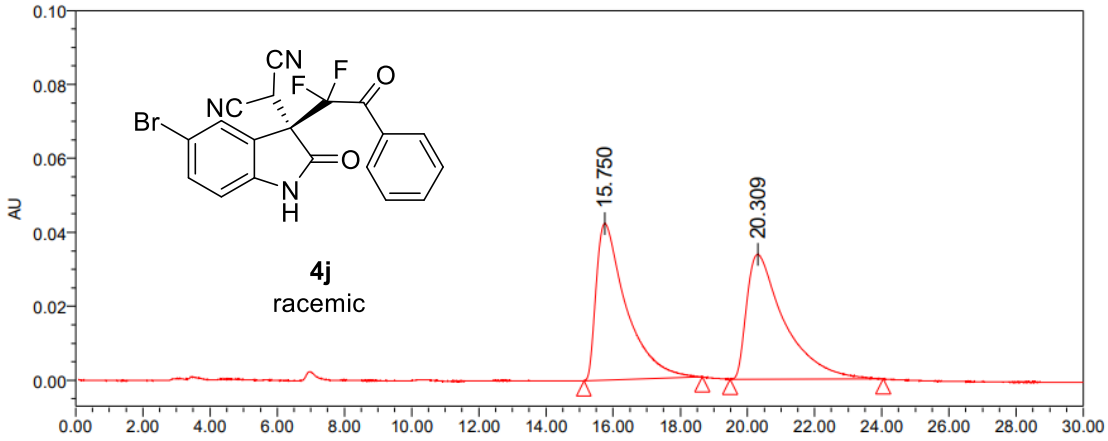
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.242	132632	5227234	50.29
2	18.646	107191	5166616	49.71



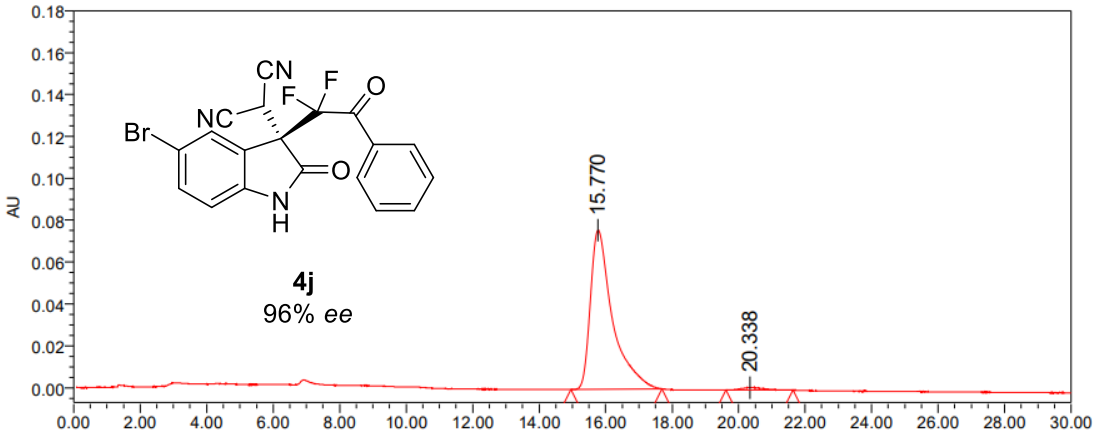
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.177	177905	7340732	98.10
2	18.582	3308	142174	1.90

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



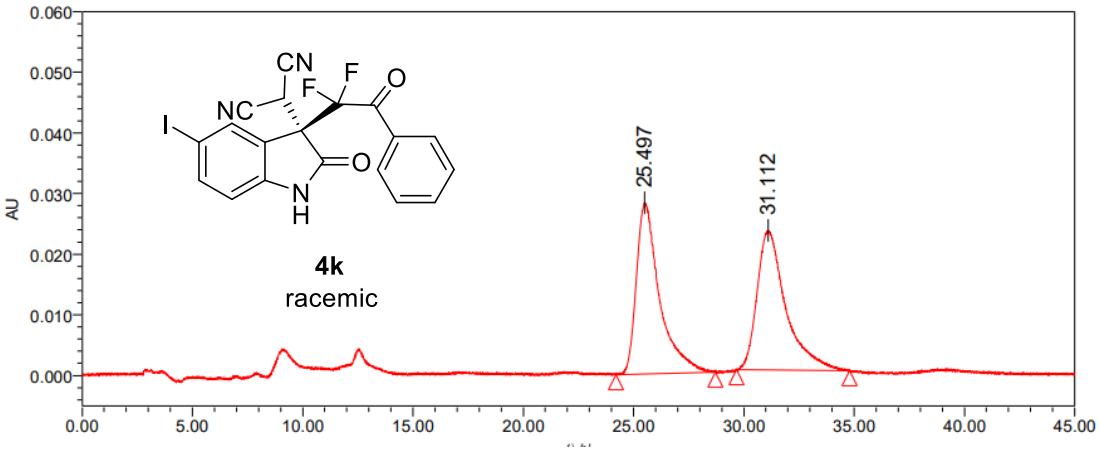
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.750	42330	2626976	49.97
2	20.309	33778	2630050	50.03



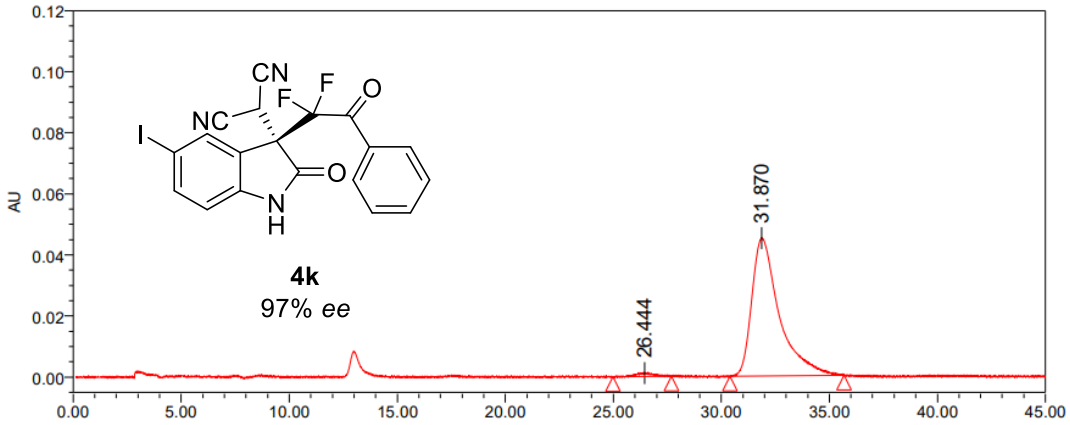
Entry	RT min	Height mV	Area mV.sec	% Area %
1	15.770	75975	3497690	98.27
2	20.338	1286	61618	1.73

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



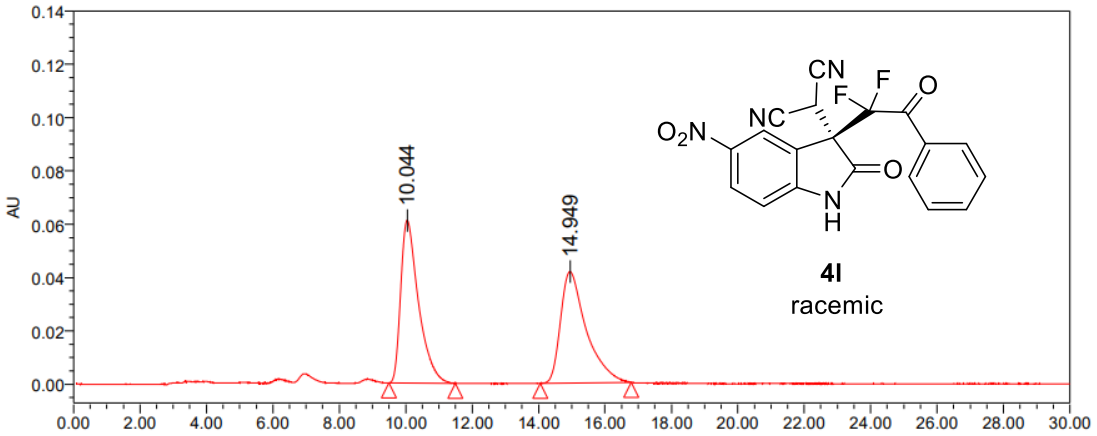
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.497	28213	2065639	49.79
2	31.112	23046	2083111	50.21



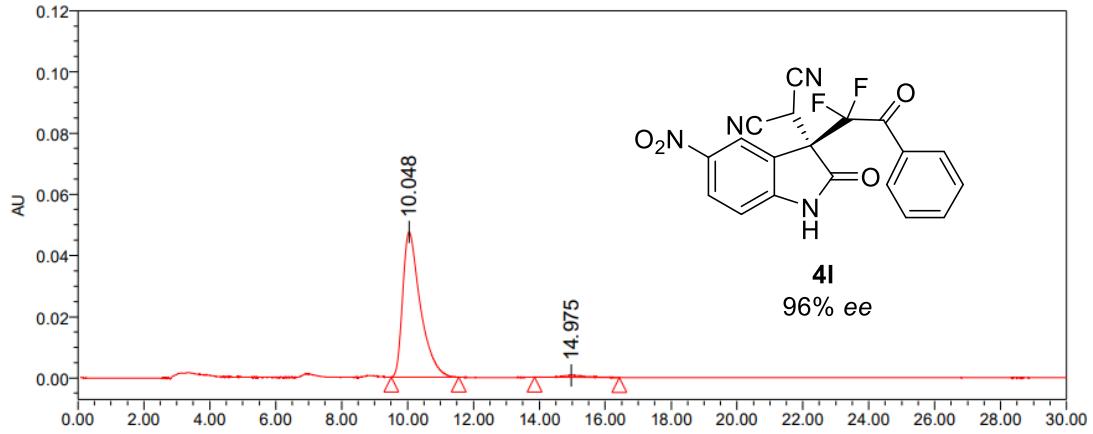
Entry	RT min	Height mV	Area mV.sec	% Area %
1	26.444	1074	59709	1.48
2	31.870	45127	3980371	98.52

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 70:30

flow rate = 1.0 mL/min



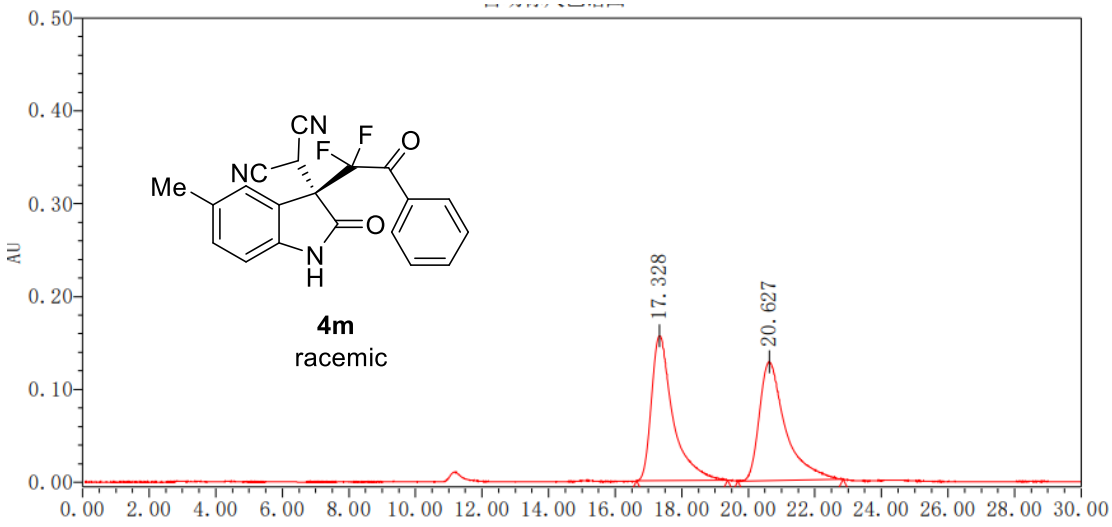
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.044	61050	2264348	50.28
2	14.949	41761	2238692	49.72



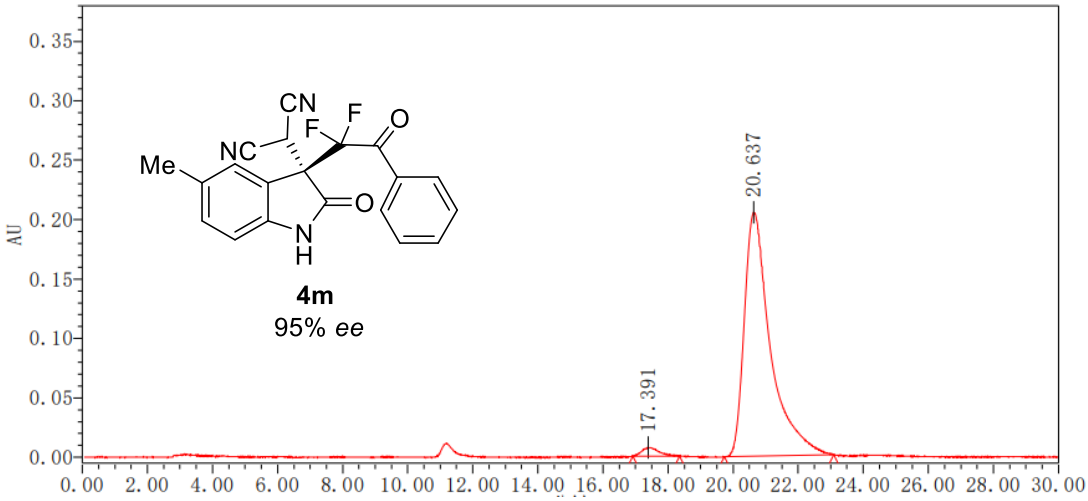
Entry	RT min	Height mV	Area mV.sec	% Area %
1	10.048	47345	1756495	98.21
2	14.975	652	32017	1.79

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



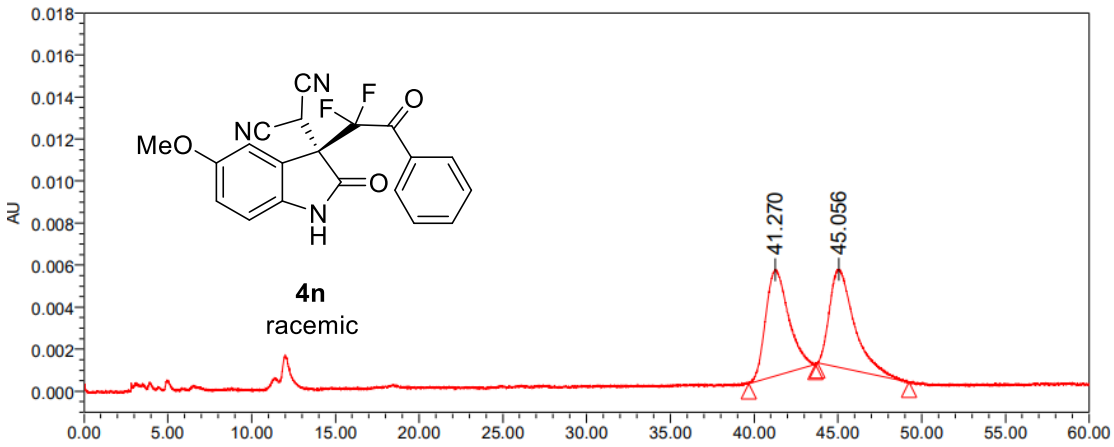
Entry	RT min	Height mV	Area mV.sec	% Area %
1	17.328	156352	7000187	50.23
2	20.627	127606	6936803	49.77



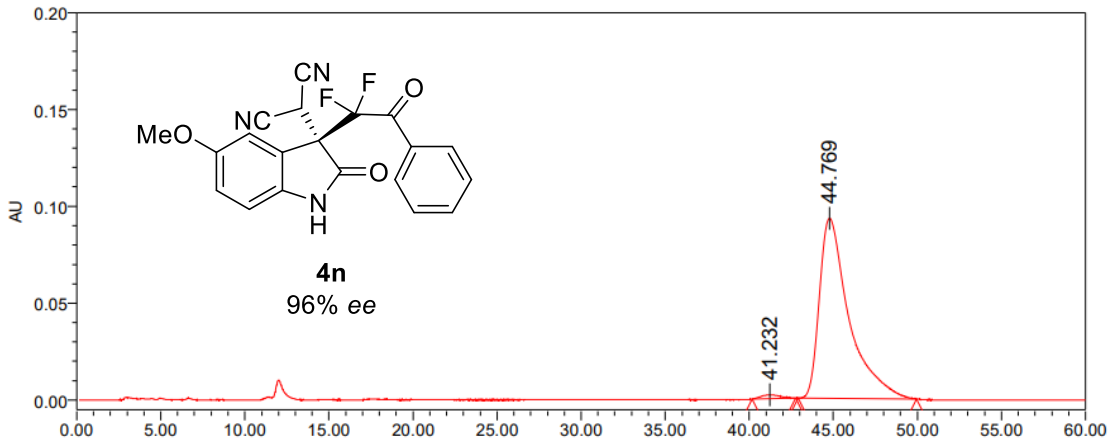
Entry	RT min	Height mV	Area mV.sec	% Area %
1	17.391	7245	267827	2.29
2	20.637	205262	11416605	97.71

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



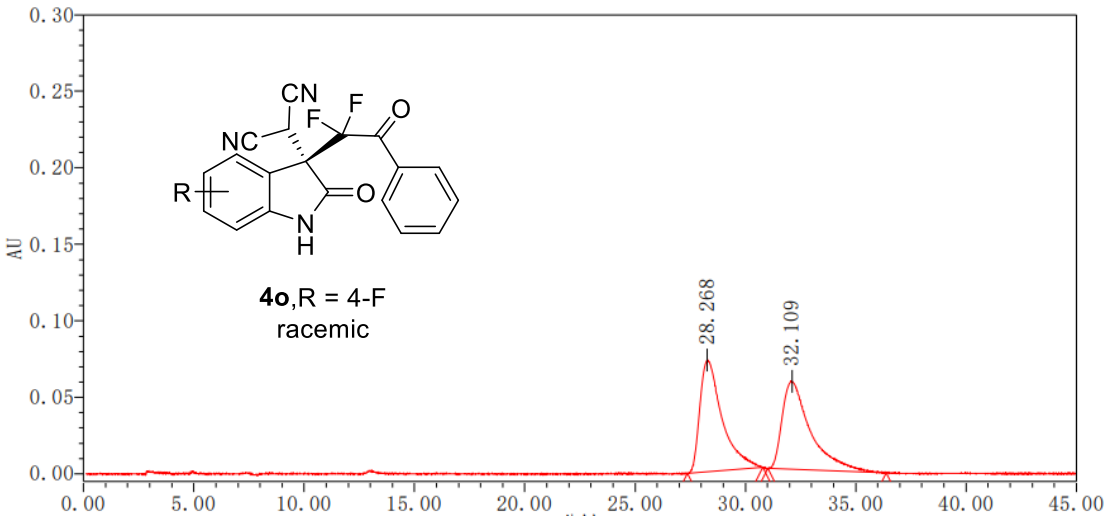
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	41.270	5050	477983	49.84
2	45.056	4658	481146	50.16



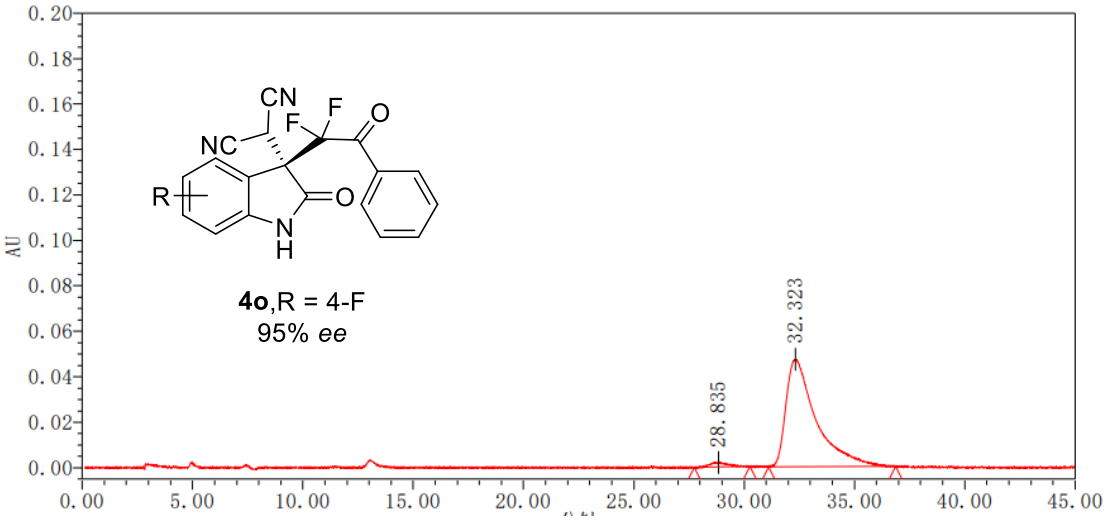
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	41.232	2017	159417	1.38
2	44.769	92994	11379363	98.62

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



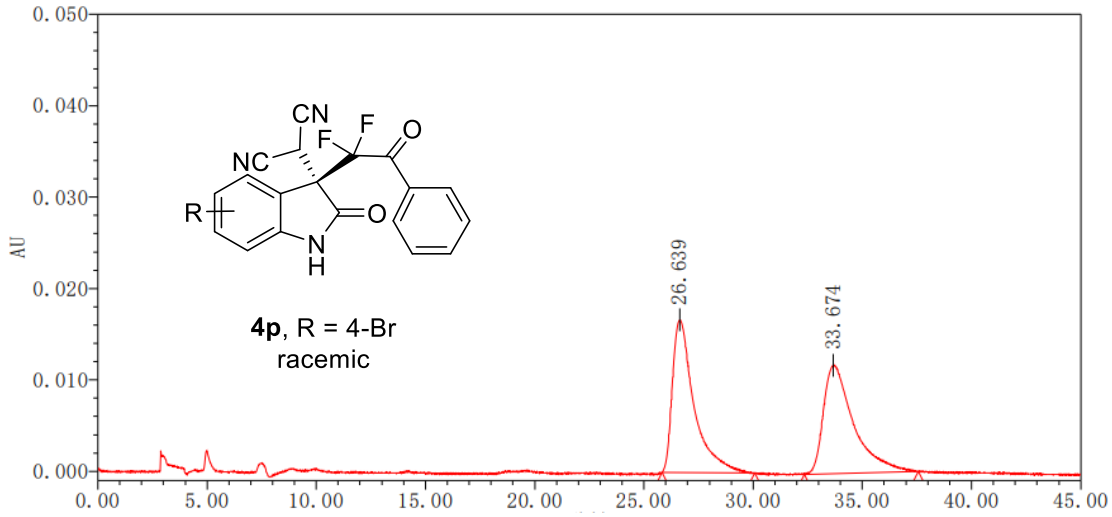
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	28.268	72916	5109807	50.11
2	32.109	57371	5087894	49.89



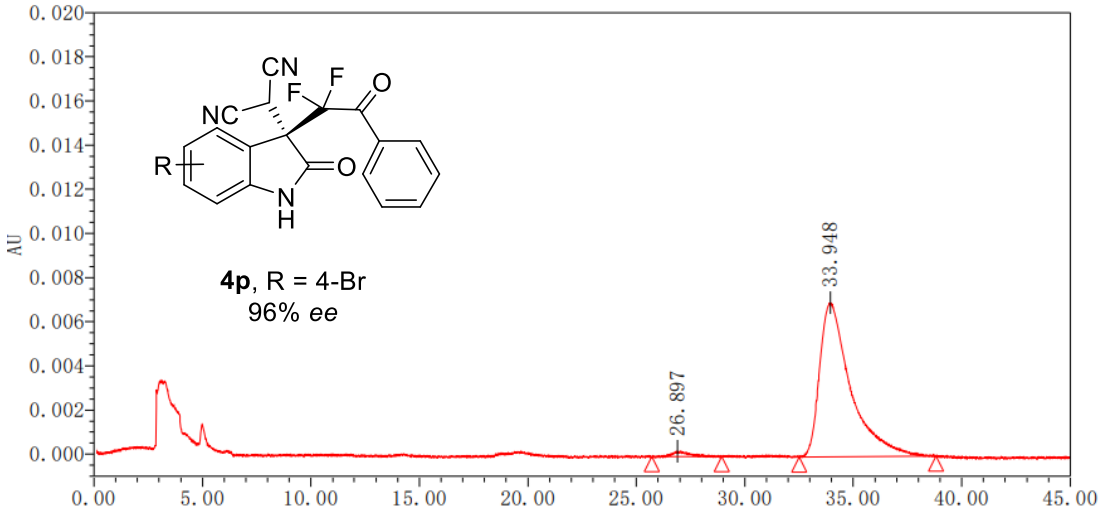
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	28.835	2004	110556	2.41
2	32.323	47381	4479993	97.59

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



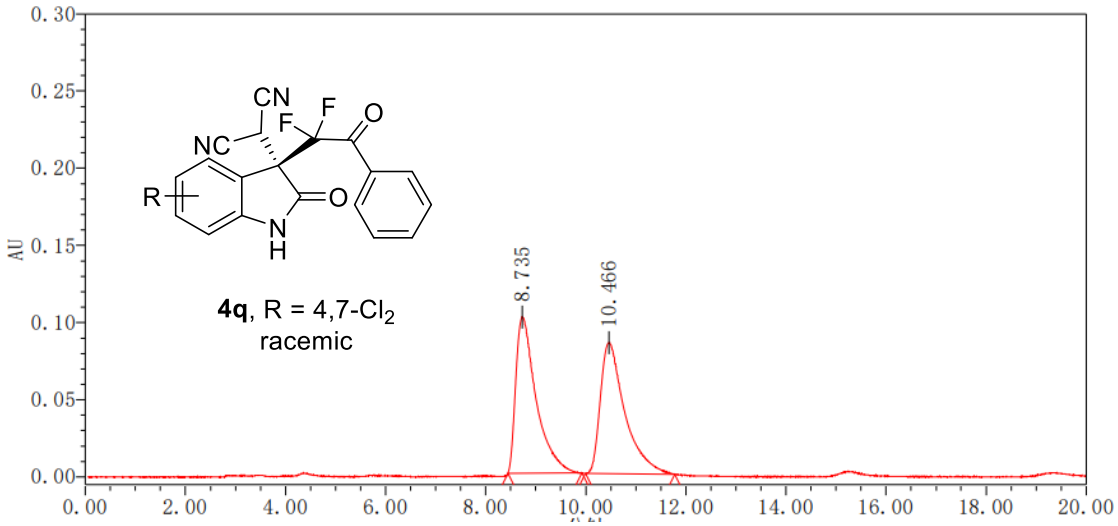
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	26.639	16689	1149732	50.24
2	33.674	11855	1138838	49.76



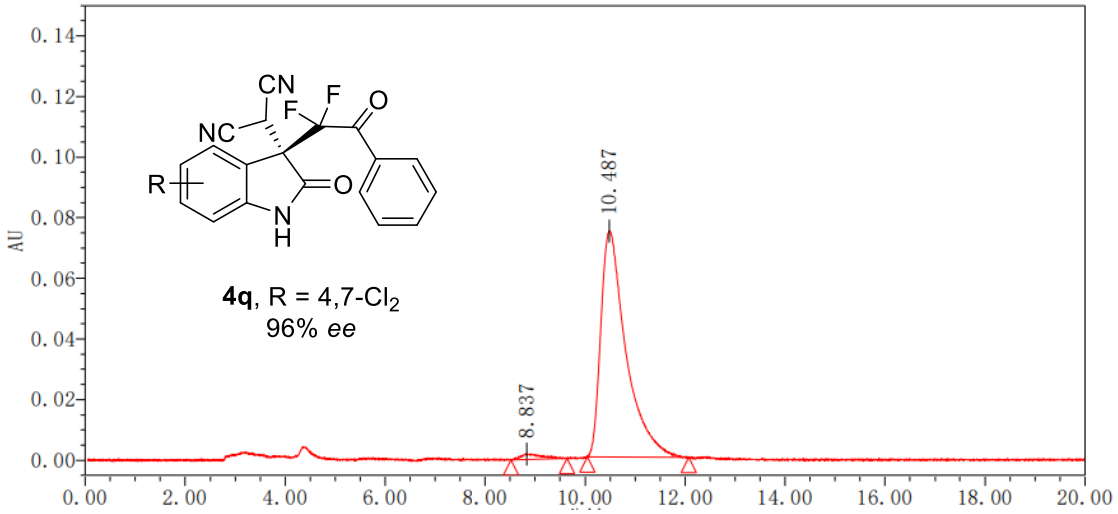
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	26.897	249	12691	1.83
2	33.948	6978	693293	98.17

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



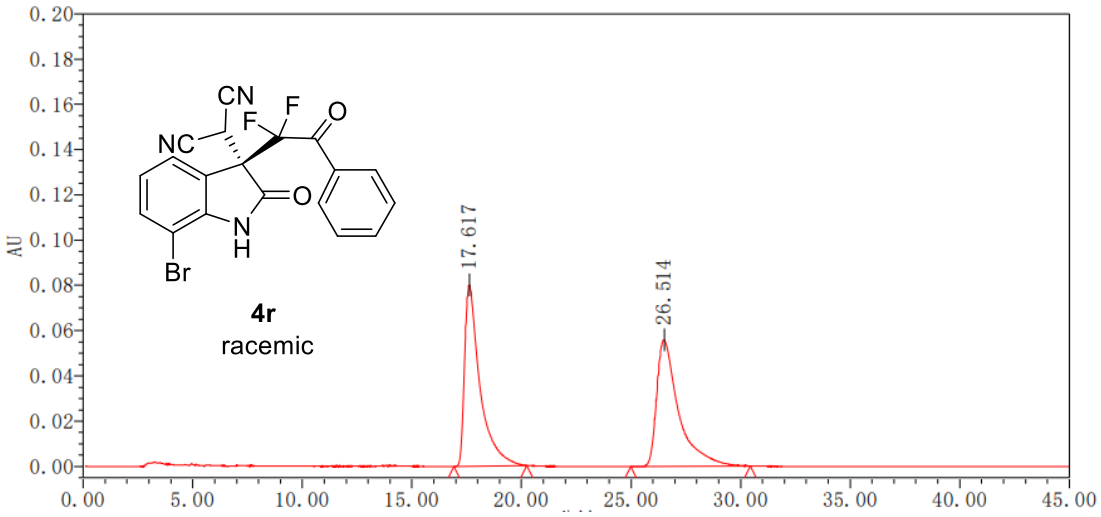
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	8.735	101318	2865741	49.85
2	10.466	84986	2883083	50.15



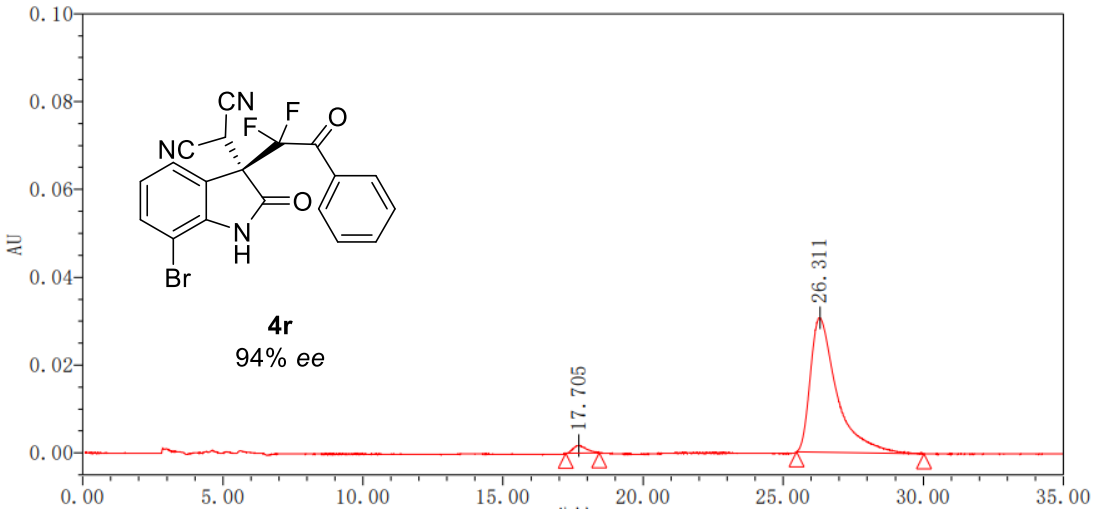
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	8.837	1788	51980	1.95
2	10.487	74660	2609658	98.05

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 85:15

flow rate = 1.0 mL/min



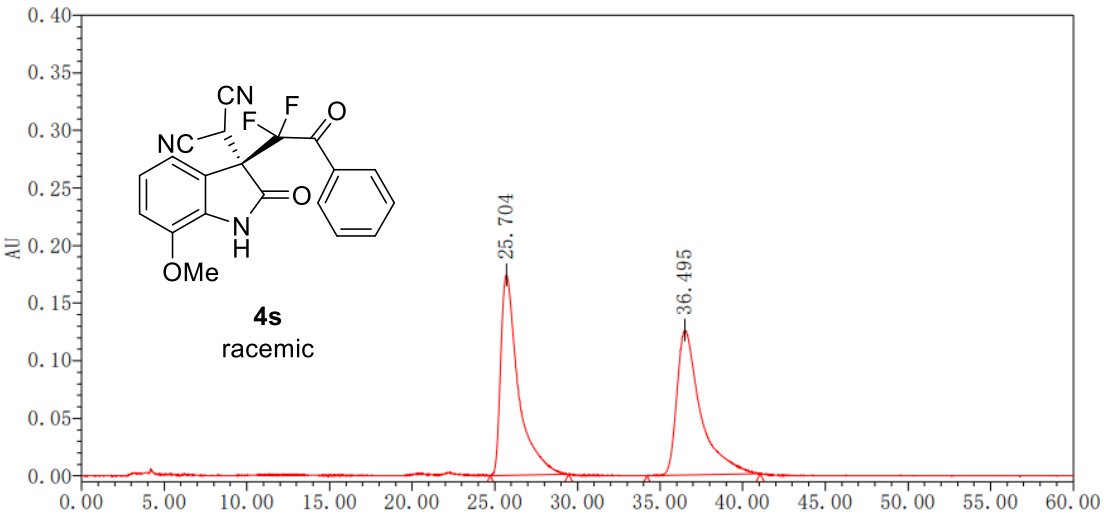
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	17.617	80090	3942273	50.28
2	26.514	55934	3897778	49.72



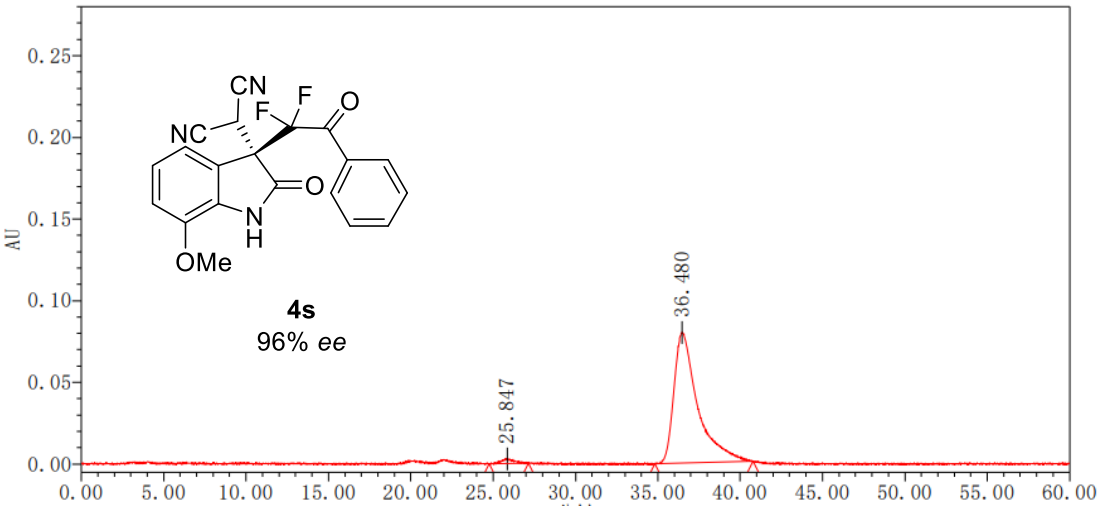
Entry	RT min	Height Mv	Area Mv.sec	% Area %
1	17.705	1747	58573	2.81
2	26.311	30636	2025936	97.19

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



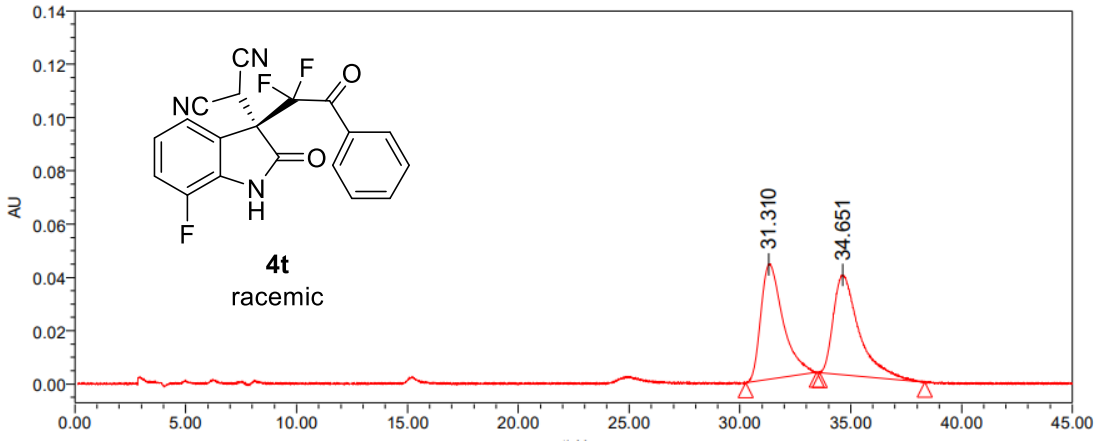
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.704	174028	12793759	50.33
2	36.495	125758	12626148	49.67



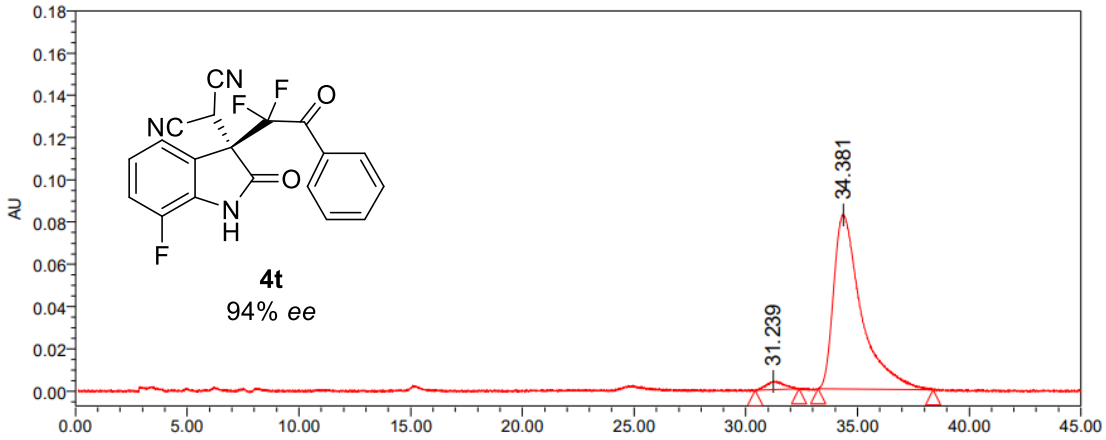
Entry	RT min	Height mV	Area mV.sec	% Area %
1	25.847	2638	140669	1.72
2	36.480	80056	8049494	98.28

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 90:10

flow rate = 1.0 mL/min



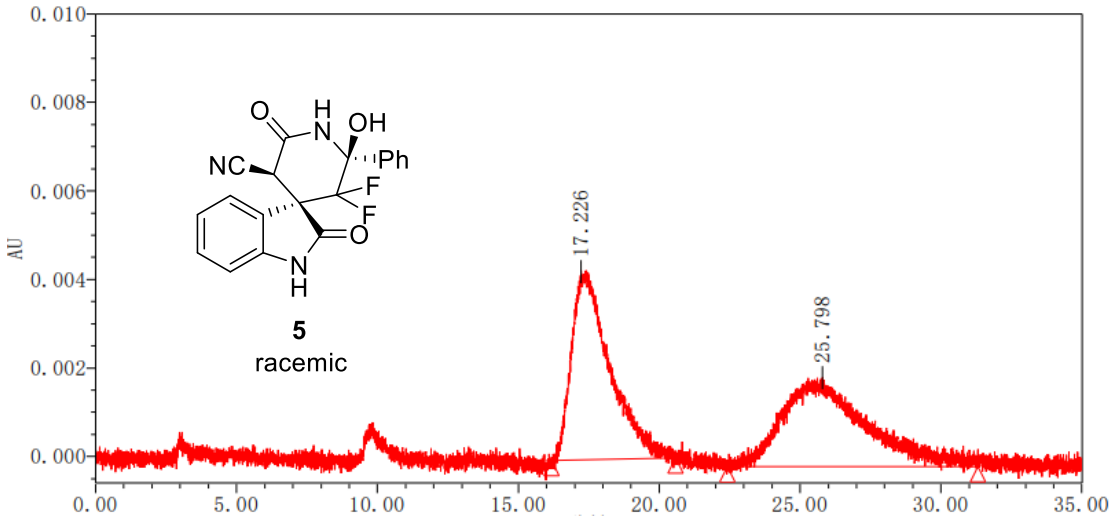
Entry	RT min	Height mV	Area mV.sec	% Area %
1	31.310	43290	3019182	50.04
2	34.651	37411	3014373	49.96



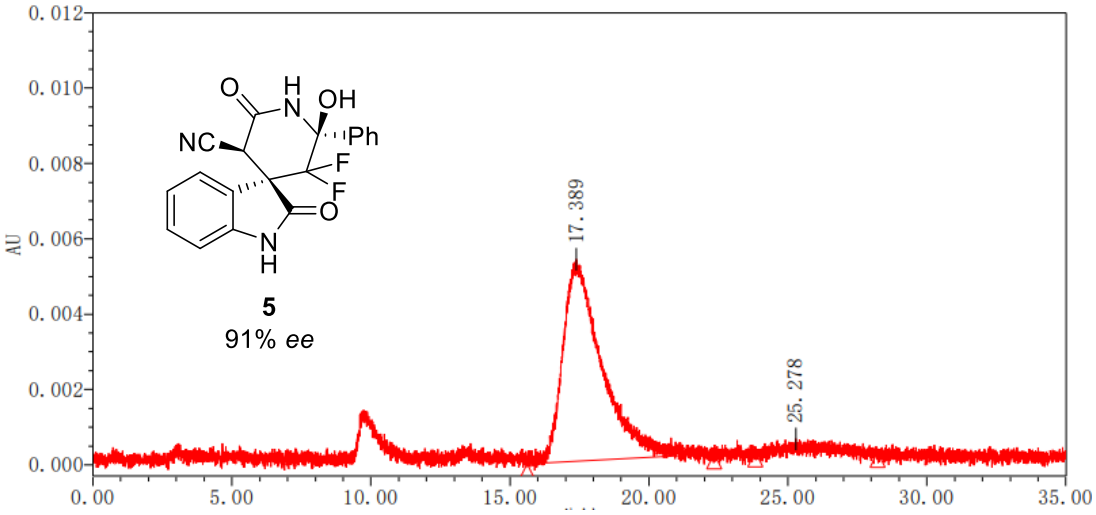
Entry	RT min	Height mV	Area mV.sec	% Area %
1	31.239	3866	217991	2.98
2	34.381	82255	7093829	97.02

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min



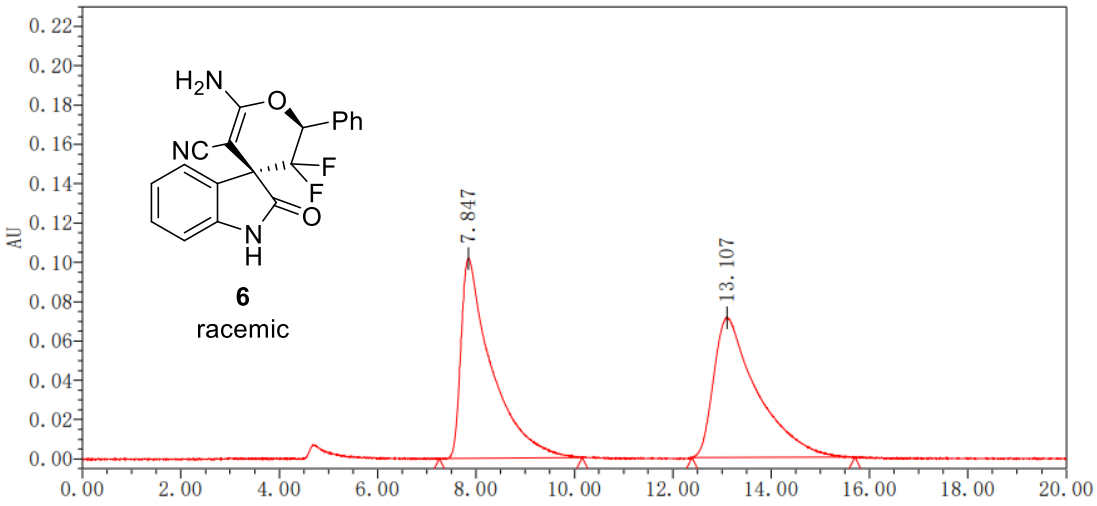
Entry	RT min	Height mV	Area mV.sec	% Area %
1	17.226	4279	402521	49.96
2	25.798	1999	403092	50.04



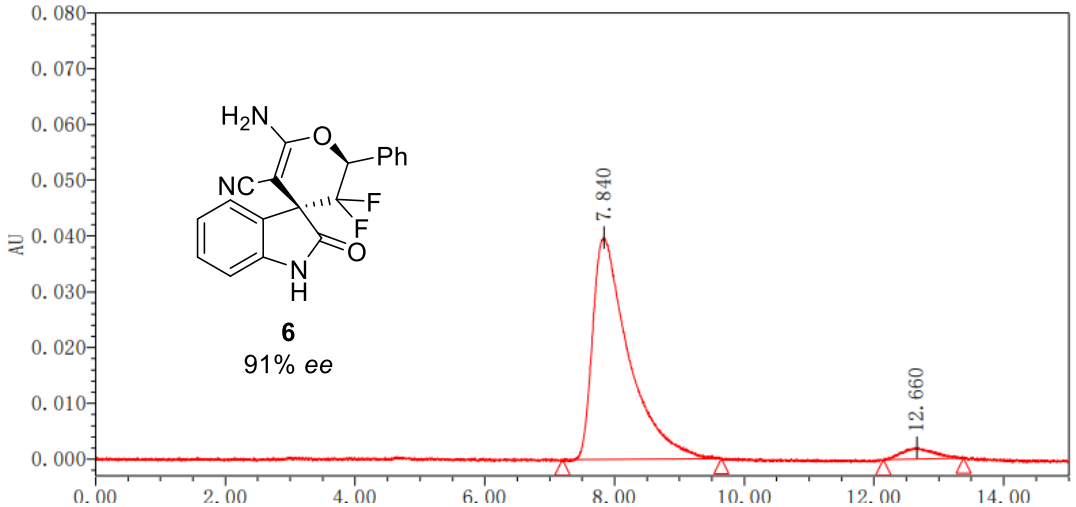
Entry	RT min	Height mV	Area mV.sec	% Area %
1	17.389	5370	528526	95.63
2	25.278	341	24135	4.37

Condition: Daicel Chiralpak IG-3 , λ = 254 nm, hexane/2-propanol = 70:30

flow rate = 1.0 mL/min



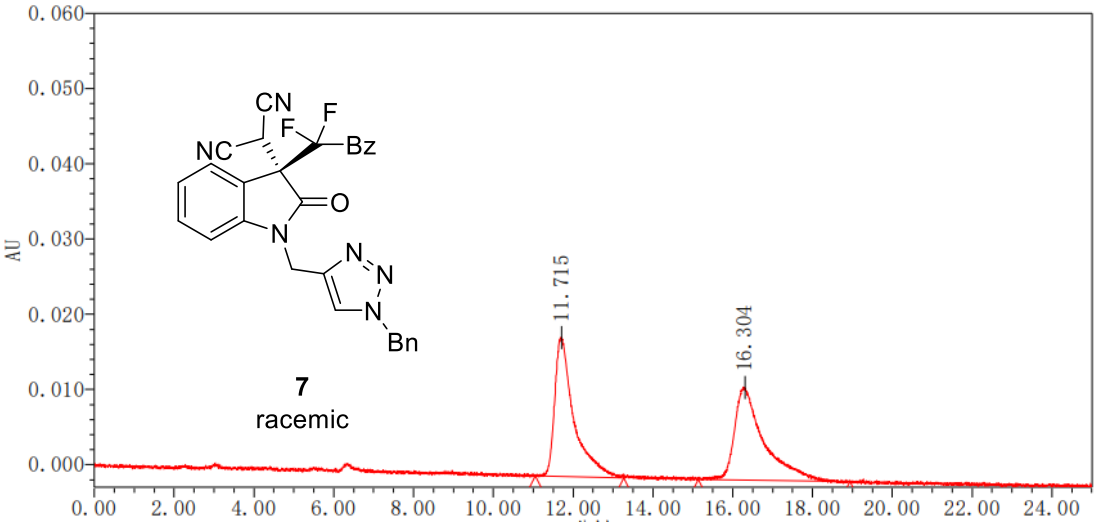
Entry	RT min	Height mV	Area mV.sec	% Area %
1	7.847	101727	4413163	50.27
2	13.107	71259	4365280	49.73



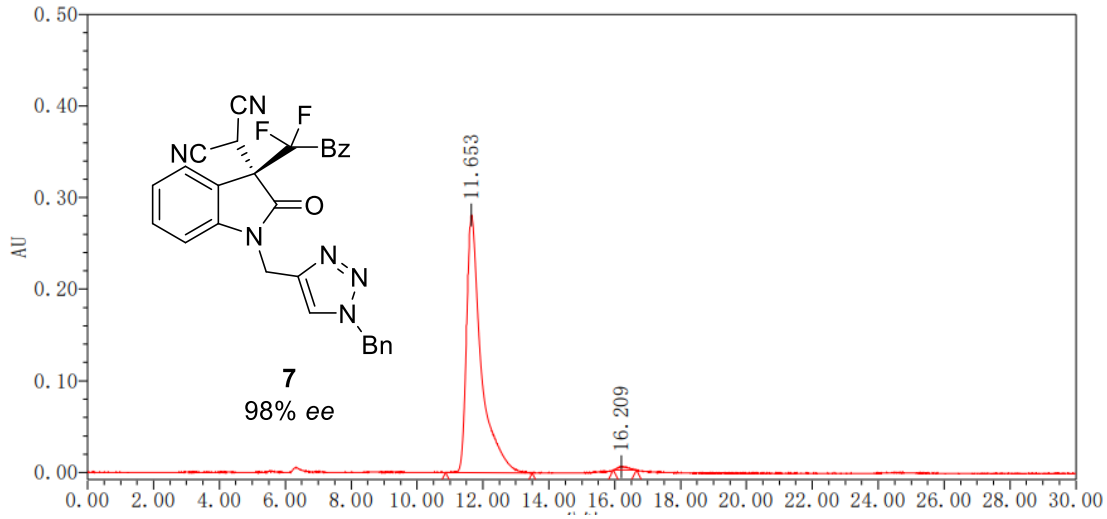
Entry	RT min	Height mV	Area mV.sec	% Area %
1	7.840	39780	1539161	95.73
2	12.660	2057	68653	4.27

Condition: Daicel Chiralpak AD-H , λ = 254 nm, hexane/2-propanol = 80:20

flow rate = 1.0 mL/min

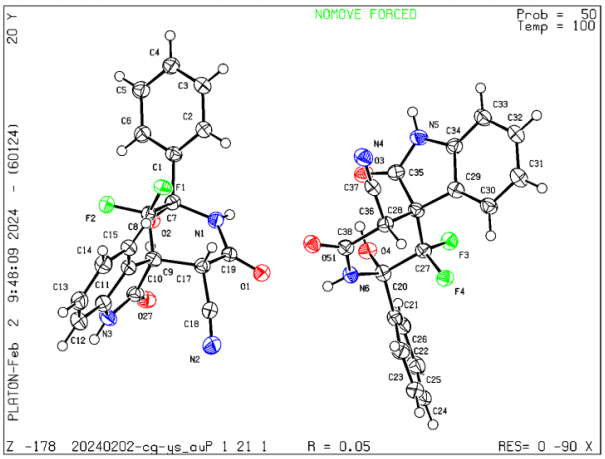


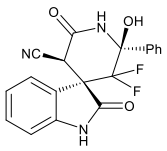
Entry	RT min	Height mV	Area mV.sec	% Area %
1	11,715	18521	620498	49.79
2	16.304	12334	625837	50.21



Entry	RT min	Height mV	Area mV.sec	% Area %
1	11.653	281041	8769299	99.03
2	16.209	3771	85930	0.97

8. Single-Crystal X-ray Diffraction of 5





5
CCDC 2344191

Datablock: 20240202-cg-ys_auto

Bond precision: C-C = 0.0055 A Wavelength=1.54184

Cell: a=14.9260(4) b=6.5272(2) c=17.0520(4)
alpha=90 beta=90.776(2) gamma=90
Temperature: 100 K

	Calculated	Reported
Volume	1661.14(8)	1661.14(8)
Space group	P 21	P 1 21 1
Hall group	P 2yb	P 2yb
Moiety formula	C19 H13 F2 N3 O3	2(C19 H13 F2 N3 O3)
Sum formula	C19 H13 F2 N3 O3	C38 H26 F4 N6 O6
Mr	369.32	738.65
Dx,g cm-3	1.477	1.477
Z	4	2
Mu (mm-1)	0.998	0.998
F000	760.0	760.0
F000'	762.78	
h,k,lmax	18,8,21	18,7,21
Nref	6934[3784]	6494
Tmin,Tmax	0.965,0.980	0.240,1.000
Tmin'	0.779	

Correction method= # Reported T Limits: Tmin=0.240 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.72/0.94 Theta(max)= 76.031

R(reflections)= 0.0472(5678) wR2(reflections)= 0.1386(6494)

S = 1.094 Npar= 497

9. References

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