Supporting Information

Brønsted Acid-Catalyzed Enantioselective Addition of 1,3-Diones to *in situ* Generated *N*-Acyl Ketimines

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Materials and Methods:

Unless otherwise stated, all reactions were performed in oven-dried glassware fitted with rubber septa under an inert atmosphere and were stirred with Teflon-coated magnetic stirring bars. Liquid reagents and solvents were transferred *via* syringe using standard Schlenk techniques. Tetrahydrofuran (THF), toluene, and diethyl ether (Et_2O) were distilled over sodium/benzophenone ketyl. Dichloromethane (CH_2Cl_2), and $CHCl_3$ were distilled over calcium hydride. All other solvents and reagents were used as received unless otherwise noted. Reaction temperatures above 23 °C refer to oil bath temperature. Thin-layer chromatography was performed using silica gel 60 F-254 pre-coated plates (0.25 mm) and visualized by UV irradiation. Silica gel of particle size 100-200 mesh was used for column chromatography. ^{1}H, ^{13}C, spectra were recorded using 400, 500, and 700 MHz spectrometers. Chemical shifts (δ) are reported in ppm relative to the residual solvent ($CDCl_3$) signal (δ = 7.26 ppm for ^{1}H NMR and δ = 77.0 ppm for ^{13}C NMR) and (DMSO-d_6) signal (δ = 2.50 ppm for ^{1}H NMR and δ = 39.9 ppm for ^{13}C NMR). Data for ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, and a number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sept (septet), m (multiplet), br (broad). High-Resolution Mass Spectrometry (HRMS) data were recorded on TOF-Q-II mass spectrometer. Optical rotations were measured on a commercial automatic polarimeter. The enantiomeric ratio was determined by chiral HPLC analysis with Daicel Chiralcel OD-H and Daicel Chiralpak IA, IC, ID, AD-H, AS-H columns.

General Procedure for the Synthesis of 3-hydroxyisoindolin-1-ones (2a-o):

3-Hydroxyisoindolin-1-ones (**2a-o**) were prepared according to the literature known procedure.[1,2]

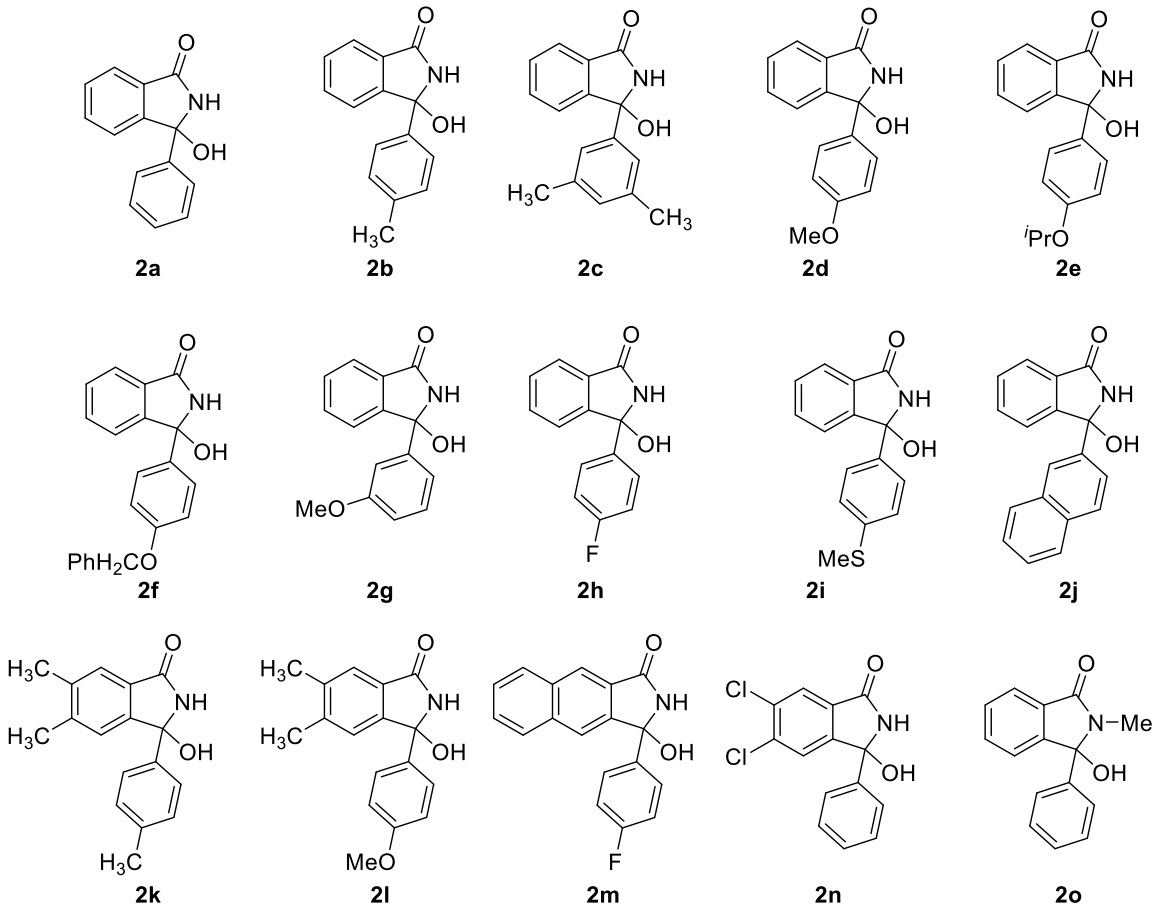
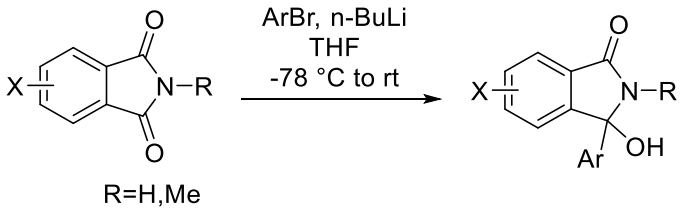


Figure 1. Structure of various substituted 3-hydroxyisoindolin-1-ones.

General Procedure for the Synthesis of 3-hydroxyisoindolin-1-ones (2a-n):[1,2]



A solution of aryl/alkyl bromide (4.0 equiv) in THF (15 mL) was taken in an oven-dried RB flask and cooled to –78 °C. The *n*-butyllithium solution (4.0 equiv, 1.6 M in hexane) was then slowly added at the same temperature and stirred for 30 min. A solution of phthalimide (1.0 equiv, 500 mg) in THF (15 mL) was added in one portion and stirred for another 15 min at –78 °C. The reaction mixture was then brought to room temperature and stirred for 4 h. Upon completion (monitored by TLC), the reaction mixture was quenched with saturated NH_4Cl

solution and acidified by 1N HCl to pH 5.0. The aqueous solution was extracted with ethyl acetate (thrice). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The pure product was obtained by washing the crude product with CH_2Cl_2/hexane (1:3, v/v) as a solvent.

General Procedure for the Synthesis of 1,3-dicarbonyl compounds (3a-j):

Dicarbonyl compounds **3a-h** were prepared according to the literature known procedure and **3i-j** is commercially available.[3]

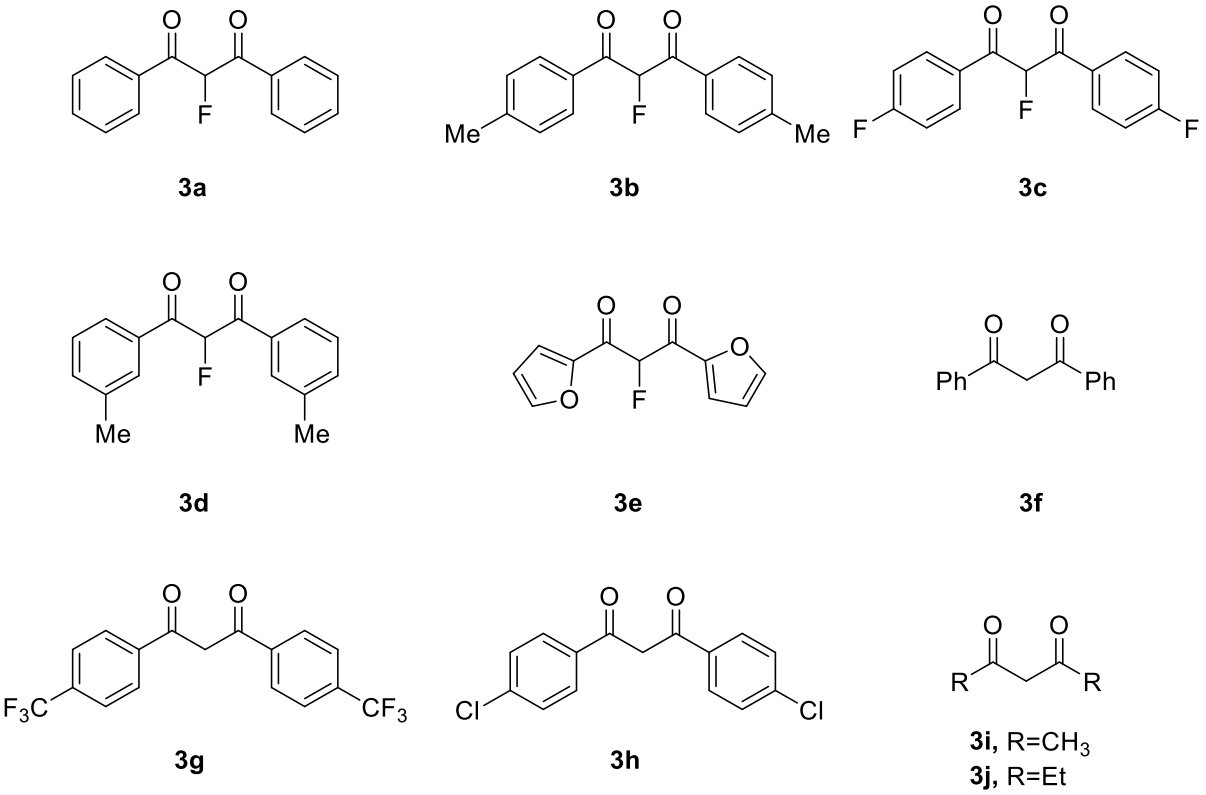
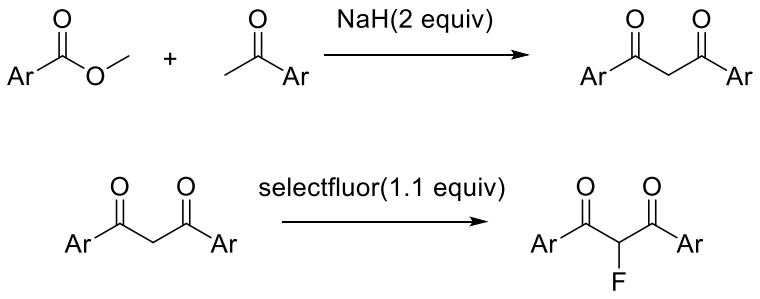


Figure 3.8. Structure of various dicarbonyl compounds

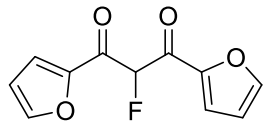
General Procedure for the Synthesis of dicarbonyl compounds (3a-h):



Step-I: To a solution of ketones (5 mmol,1 equiv) in THF (20 mL), sodium hydride (10 mmol) was added slowly at 0 °C. Then ester (5 mmol,1 equiv) was added dropwise to the solution at 0 °C. The mixture was stirred at ambient temperature for 4 h. Then the mixture was transferred to the ice-water (50 mL) and acidified by aqueous 3M HCl and extracted with EtOAc (50 mL x 3). The total organic layer was dried by sodium sulfate and evaporated under reduced pressure. The diketone product was purified by column chromatography.

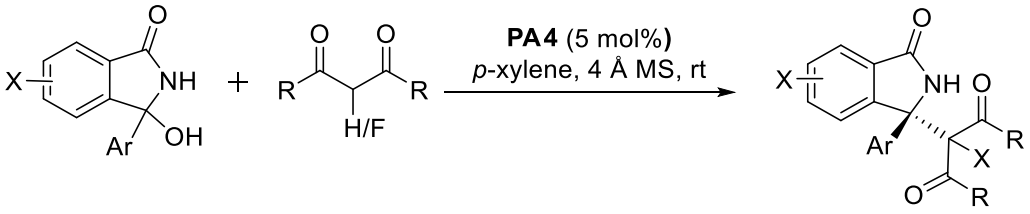
Step-II: The diketone (1 equiv, 5 mmol) and Selectfluor(1 equiv, 5 mmol) was added in CH_3CN (30 mL). Then the mixture was refluxed for 4 h for the full consumption of diketone monitoring by TLC. After consumption of diketone solvent was evaporated under reduced pressure, then extracted in DCM and wish with water and dried over Na_2SO_4. The product was purified by column column chromatography.

2-fluoro-1,3-di(furan-2-yl)propane-1,3-dione (3e): Pale yellow solid, 956 mg, 86% yield. R_f = 0.58 (40% EtOAc in hexanes) **MP**: 70-72 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 2H), 7.54 (s, 2H), 6.65 – 6.55 (m, 2H), 6.17 (d, *J* = 48.4 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 178.3 (d, *J* = 21.6 Hz), 149.2, 148.8, 122.7 (d, *J* = 5.9 Hz), 113.0, 94.3 (d, *J* = 198.5 Hz). **^{19}F NMR** (375 MHz, $CDCl_3$) δ -192.9. **HRMS** (ES+): Exact mass calcd for $C_{11}H_7FNO_4Na[M+Na]^+$: 245.0221 Found: 245.0222.



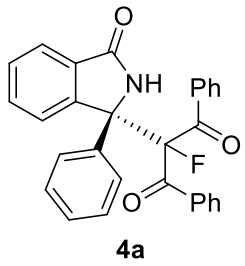
3e

General procedure for the enantioselective synthesis of 1,3-dione-based isoindolinones(4):



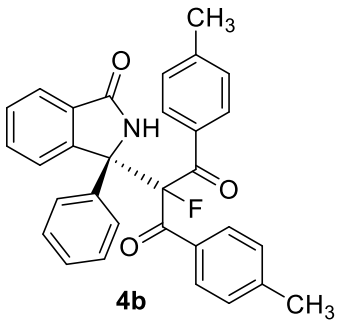
In a round-bottomed flask, 3-aryl-3-hydroxyisoindolinones **2** (0.2 mmol, 1 equiv), catalyst **PA4** (5 mol %), 1,3-dicarbonyls **3** (0.3 mmol, 1.5 equiv) and 50 mg 4Å MS were taken and anhydrous *p*-xylene (2.0 mL) was added to it. The mixture was stirred at room temperature (25 °C) for 24 h under a nitrogen atmosphere. After completion of the reaction (monitored by TLC), the residue was charged over a column packed with silica gel and purified by flash column chromatography using ethyl acetate and hexane as eluents to get the products **4**.

(*S*)-2-fluoro-2-(3-oxo-1-phenylisoindolin-1-yl)-1,3-diphenylpropane-1,3-dione(4a): Pale yellow solid, 88.09 mg, 98% yield. R_f = 0.37 (40% EtOAc in hexanes) **MP**: 178-180 °C. $[\alpha]_D^{22}$ = +373.43 ($CHCl_3$, c = 0.9633 for 93% ee). **HPLC** (Chiracel ODH , *n*-hexane/ *iso*-propanol = 90/10, 1.0 mL/min, 254 nm): t_R = 16.22 min (major), 13.84 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.72 (t, *J* = 7.4 Hz, 3H), 7.60 (dd, *J* = 8.0, 4.6 Hz, 4H), 7.55 (t, *J* = 7.6 Hz, 2H), 7.51 (s, 1H), 7.40 (dt, *J* = 16.3, 7.7 Hz, 4H), 7.30 – 7.27 (m, 2H), 7.24 (s, 2H), 7.19 (t, *J* = 7.7 Hz, 2H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 193.5 (d, *J* = 25.4 Hz), 191.2 (d, *J* = 23.4 Hz), 169.3, 146.4, 139.5 (d, *J* = 2.6 Hz), 135.2 (d, *J* = 3.9 Hz), 134.3 (d, *J* = 3.4 Hz), 134.1, 133.4, 132.3, 131.2, 129.7, 129.6 (d, *J* = 2.1 Hz), 129.6, 129.4, 129.0, 128.8, 128.2, 128.2, 126.2 (d, *J* = 3.5 Hz), 125.9 (d, *J* = 5.7 Hz), 124.1, 108.5, 107.2, 69.4 (d, *J* = 23.5 Hz). **^{19}F NMR** (375 MHz, $CDCl_3$) δ -151.5. **HRMS** (ES+): Exact mass calcd for $C_{29}H_{21}FNO_3[M+H]^+$: 450.1500 Found: 450.1525.



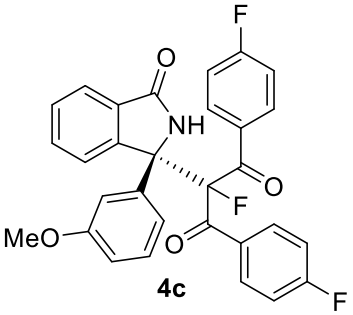
4a

***(S)*-2-fluoro-2-(3-oxo-1-phenylisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4b):**



4b

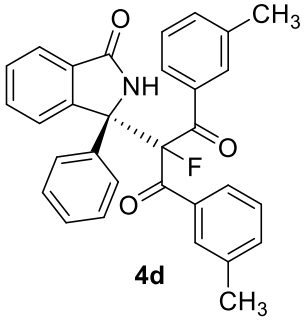
White solid, 90.73 mg, 95% yield. R_f = 0.510 (40% EtOAc in hexanes) **MP**: 60-62 °C. $[\alpha]_D^{22}$ = +307.196 ($CHCl_3$, c = 1.07 for 83% ee). **HPLC** (Chiracel ODH , *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 10.05 min (major), 8.73 min (minor). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.78 (d, *J* = 26.0 Hz, 2H), 7.69 – 7.57 (m, 5H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.24 (d, *J* = 15.3 Hz, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 2.35 (s, 3H), 2.28 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.7 (d, *J* = 25.0 Hz), 190.6 (d, *J* = 23.4 Hz), 169.6 (d, *J* = 3.2 Hz), 146.6, 145.3, 144.5, 139.5, 132.4 (d, *J* = 3.9 Hz), 132.3, 131.7 (d, *J* = 3.6 Hz), 131.2, 130.3, 129.9, 129.9, 129.8, 129.4, 129.3, 129.1, 128.9, 128.9, 128.1, 126.2, 126.0 (d, *J* = 5.Hz), 124.0, 108.4, 107.2, 69.6 (d, *J* = 23.7 Hz), 21.8, 21.7. **HRMS** (ES+): Exact mass calcd for $C_{31}H_{24}FNO_3K[M+K]^+$: 516.1372 Found: 516.1395.

(*S*)-2-fluoro-1,3-bis(4-fluorophenyl)-2-(1-(3-methoxyphenyl)-3-oxoisoindolin-1-yl)propane-1,3-dione(4c): 

4c

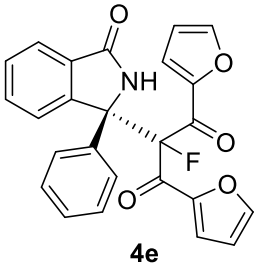
White solid, 91.75 mg, 89% yield. R_f = 0.44 (40% EtOAc in hexanes) **MP**: 100-102 °C. $[\alpha]_D^{22}$ = +171.62 ($CHCl_3$, c = 0.32 for 81% ee). **HPLC** (Chiralpak ASH , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 45.09 min (major), 17.67 min (minor). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 2H), 7.72 (d, *J* = 5.1 Hz, 1H), 7.65 (dd, *J* = 8.6, 5.3 Hz, 2H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.43 (s, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 5.7 Hz, 2H), 7.12 (s, 1H), 7.06 (t, *J* = 8.4 Hz, 2H), 6.85 (t, *J* = 8.4 Hz, 2H), 6.78 (dt, *J* = 6.3, 2.8 Hz, 1H), 3.69 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 191.5 (d, *J* = 25.1 Hz), 189.4 (d, *J* = 23.8 Hz), 169.2, 167.0, 166.4, 165.5, 165.0, 160.0, 146.2, 141.1 (d, *J* = 2.8 Hz), 132.8 – 132.6 (m), 132.5, 132.5 (d, *J* = 3.4 Hz), 132.4, 131.2 (d, *J* = 4.3 Hz), 130.5 (t, *J* = 3.3 Hz), 130.2, 129.6, 126.1, 124.2, 117.8 (d, *J* = 6.6 Hz), 116.2 (d, *J* = 22.1 Hz), 115.6 (d, *J* = 21.7 Hz), 113.3, 111.9 (d, *J* = 5.2 Hz), 108.7, 107.5, 69.3 (d, *J* = 23.3 Hz), 55.3. **HRMS** (ES+): Exact mass calcd for $C_{30}H_{20}F_3NO_4Na[M+Na]^+$: 538.1237 Found: 538.1230.

(*S*)-2-fluoro-2-(3-oxo-1-phenylisoindolin-1-yl)-1,3-di-m-tolylpropane-1,3-dione



(4d): White solid, 89.77 mg, 94% yield. R_f = 0.44 (40% EtOAc in hexanes) **MP**: 158-160 °C. $[\alpha]_D^{22}$ = -14.77. ($CHCl_3$, c = 0.44 for 80% ee). **HPLC** (Chiralcel ODH , *n*-hexane/ *iso*-propanol = 90/10, 1.0 mL/min, 254 nm): t_R = 16.52 min (major), 13.31 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 2.6 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.53 (d, *J* = 9.5 Hz, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.37 – 7.27 (m, 4H), 7.21 (dd, *J* = 17.4, 7.4 Hz, 4H), 7.08 (t, *J* = 7.7 Hz, 1H), 2.28 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.6 (d, *J* = 25.5 Hz), 191.4 (d, *J* = 23.6 Hz), 169.3, 146.5, 139.5, 138.6, 137.9, 135.1 (d, *J* = 3.7 Hz), 134.8, 134.3 (d, *J* = 3.7 Hz), 134.1, 132.1, 131.2, 130.1, 130.0 (d, *J* = 3.3 Hz), 129.2, 128.9, 128.5, 128.0 (d, *J* = 3.9 Hz), 126.7 (dd, *J* = 7.2, 5.4 Hz), 126.2, 125.9 (d, *J* = 5.5 Hz), 123.9, 108.8, 106.7, 69.4 (d, *J* = 23.7 Hz), 21.3, 21.2. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -150.9. **HRMS** (ES+): Exact mass calcd for $C_{31}H_{24}FNO_3Na[M+Na]^+$: 500.1632 Found: 500.1621.

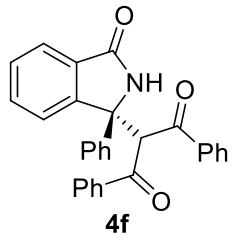
(*S*)-2-fluoro-1,3-di(furan-2-yl)-2-(3-oxo-1-phenylisoindolin-1-yl)propane-1,3-dione(4e):



4e

Pale yellow solid, 58.39 mg, 68% yield. $\boldsymbol{R_f}$ = 0.11 (40% EtOAc in hexanes) **MP**: 171-173 °C. $[\alpha]_D^{22}$ = +253 ($CHCl_3$, c = 2.03 for 26% ee). **HPLC** (Chiralpak ADH , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 49.08 min (major), 26.26 min (minor).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 5.1 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 4H), 7.58 (s, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.45 (s, 1H), 7.35 (t, *J* = 7.1 Hz, 2H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.23 (d, *J* = 6.9 Hz, 2H), 7.16 (t, *J* = 3.8 Hz, 1H), 6.48 (d, *J* = 2.8 Hz, 1H), 6.36 (d, *J* = 4.7 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 179.2 (d, *J* = 24.6 Hz), 176.9 (d, *J* = 25.7 Hz), 169.1, 149.5 (d, *J* = 4.1 Hz), 149.4 (d, *J* = 3.2 Hz), 148.8, 148.4, 146.0, 138.5 (d, *J* = 2.6 Hz), 132.3, 131.1, 129.5, 128.9, 128.3, 126.3 (d, *J* = 5.5 Hz), 125.9 (d, *J* = 3.6 Hz), 124.1, 122.8, 122.7 (d, *J* = 3.6 Hz), 122.6, 112.9 (d, *J* = 2.1 Hz), 112.5 (d, *J* = 2.2 Hz), 105.4, 103.3, 68.9 (d, *J* = 23.3 Hz). **^{19}F NMR** (375 MHz, $CDCl_3$) δ -157.7. **HRMS** (ES+): Exact mass calcd for $C_{25}H_{17}FNO_5[M+H]^+$: 430.1085 Found: 430.1114.

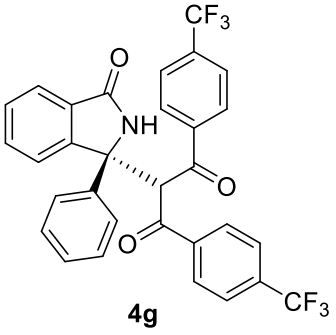
(*S*)-2-(3-oxo-1-phenylisoindolin-1-yl)-1,3-diphenylpropane-1,3-dione(4f): White solid,



4f

83.70 mg, 97% yield. $\boldsymbol{R_f}$ = 0.26 (40% EtOAc in hexanes) **MP**: 231-233 °C. $[\alpha]_D^{22}$ = +416.90 ($CHCl_3$, c = 0.33 for 93% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 15.15 min (major), 9.94 min (minor). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.60 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 2H), 7.99 (d, *J* = 7.7 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 3H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.47 (dq, *J* = 15.6, 7.5 Hz, 4H), 7.35 – 7.25 (m, 6H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ 194.3, 193.5, 168.4, 148.0, 142.5, 136.0 (d, *J* = 25.4 Hz), 133.9, 133.4, 131.6, 130.3, 129.0, 128.7, 128.6, 128.3, 128.2, 127.2, 124.8, 124.7, 122.5, 67.5, 60.3. **HRMS** (ES+): Exact mass calcd for $C_{29}H_{21}NO_3Na[M+Na]^+$: 454.1414 Found: 454.1411.

(*S*)-2-(3-oxo-1-phenylisoindolin-1-yl)-1,3-bis(4-(trifluoromethyl)phenyl)propane-1,3-

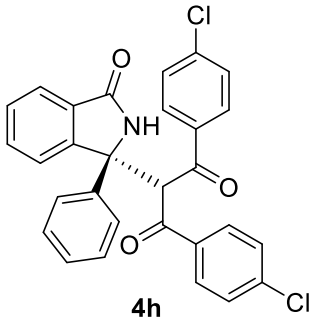


4g

dione(4g): White solid, 99.87 mg, 88% yield. $\boldsymbol{R_f}$ = 0.63 (40% EtOAc in hexanes) **MP**: 212-214 °C. $[\alpha]_D^{22}$ = +194.24 ($CHCl_3$, c = 0.33 for 43% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 16.42 min (major), 6.51 min (minor). **^{1}H NMR** (500 MHz, DMSO) δ 8.89 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 2H), 8.07 (d, *J* = 8.0 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 2H),

7.80 (t, *J* = 7.4 Hz, 3H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.57 (s, 1H), 7.29 (dt, *J* = 22.3, 7.9 Hz, 4H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ 194.4, 193.8, 168.4, 147.7, 142.2, 139.5, 139.3, 133.2, 132.2, 131.7, 130.4, 129.2, 129.0, 128.7, 128.4, 127.3, 126.2, 125.1, 124.8, 124.7, 122.6, 122.5, 67.4, 61.9. **^{19}F NMR** (375 MHz, DMSO-d_6) δ -61.8, -61.9. **HRMS** (ES+): Exact mass calcd for $C_{31}H_{20}F_6NO_3[M+H]^+$: 568.1342 Found: 568.1345.

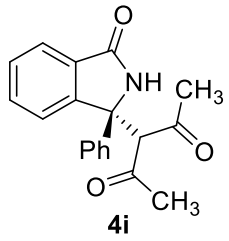
(*S*)-1,3-bis(4-chlorophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)propane-1,3-dione(4h):



4h

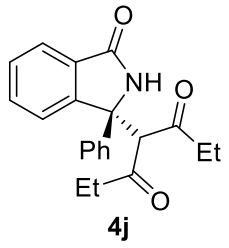
White solid, 91.06 mg, 91% yield. R_f = 0.40 (40% EtOAc in hexanes) **MP**: 216-218 °C. $[\alpha]_D^{22}$ = +79.11 ($CHCl_3$, c = 0.38 for 90% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 22.33 min (major), 7.98 min (minor). **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.71 (s, 1H), 7.99 (dd, *J* = 20.5, 8.3 Hz, 4H), 7.81 (t, *J* = 7.5 Hz, 3H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.42 (s, 1H), 7.34 (dt, *J* = 25.8, 8.1 Hz, 6H), 7.18 (dt, *J* = 15.2, 7.3 Hz, 2H). **^{13}C NMR** (175 MHz, DMSO-d_6) δ 193.2, 192.8, 168.4, 147.9, 142.3, 139.0, 138.5, 134.8, 134.6, 133.3, 132.4, 131.8, 130.6, 130.4, 130.1, 129.4, 129.3, 129.0, 128.7, 128.5, 128.3, 128.2, 127.3, 125.5, 124.8, 124.7, 122.7, 67.5, 60.8. **HRMS** (ES+): Exact mass calcd for $C_{29}H_{19}Cl_2NO_3Na[M+Na]^+$: 522.0634 Found: 522.0642.

(*S*)-3-(3-oxo-1-phenylisoindolin-1-yl)pentane-2,4-dionePale(4i): White solid, 59.01 mg, 96% yield. R_f = 0.2 (50% EtOAc in hexanes) **MP**: 70-72 °C. $[\alpha]_D^{22}$ = +306.30 ($CHCl_3$, c = 0.91 for 81% ee). **HPLC** (Chiralpak ODH , *n*-hexane/ *iso*-propanol = 80/20, 1.0 mL/min, 254 nm): t_R = 10.50 min (major), 13.12 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.75 (s, 1H), 7.57 – 7.52 (m, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.42 (ddd, *J* = 8.0, 5.7, 2.6 Hz, 1H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 5.29 (s, 1H), 2.15 (s, 3H), 1.81 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 202.6, 199.9, 169.7, 148.3, 140.9, 132.8, 130.3, 129.4, 129.2, 128.2, 125.9, 124.6, 124.3, 122.9, 71.8, 66.8, 32.0, 31.4. **HRMS** (ES+): Exact mass calcd for $C_{19}H_{18}NO_3[M+H]^+$: 308.1281 Found: 308.1252.



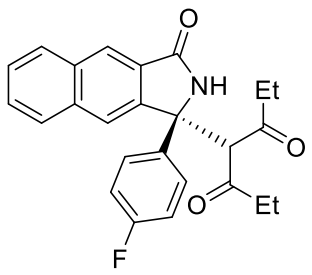
4i

(*S*)-4-(3-oxo-1-phenylisoindolin-1-yl)heptane-3,5-dionePale(4j): White solid, 38.90 mg, 58% yield. ***R_f*** = 0.16 (40% EtOAc in hexanes) **MP**: 238-240 °C. $[\alpha]_D^{22}$ = +373.320 ($CHCl_3$, c = 0.54 for 80% ee). **HPLC** (Chiralpak ADH , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 12.21 min (major), 15.70 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.73 (s, 1H), 7.52 (d, *J* = 4.1 Hz, 2H), 7.48 (d, *J* = 7.6 Hz, 2H), 7.42 (dt, *J* = 8.0, 4.1 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 5.23 (s, 1H), 2.48 – 2.33 (m, 2H), 2.29 – 2.18 (m, 1H), 1.98 – 1.87 (m, 1H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.68 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 205.1, 202.2, 169.6, 148.3, 141.0, 132.6, 130.5, 129.3, 129.1, 128.1, 124.6, 124.4, 122.8, 70.6, 70.6, 66.9, 38.3, 38.0, 7.7, 7.5. **HRMS** (ES+): Exact mass calcd for $C_{21}H_{21}NO_3Na[M+Na]^+$: 358.1414 Found: 358.1416.



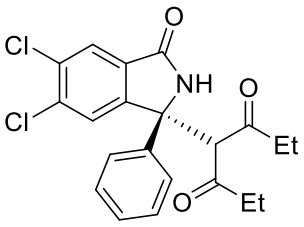
4j

(*S*)-4-(1-(4-fluorophenyl)-3-oxo-2,3-dihydro-1H-benzo[f]isoindol-1-yl)heptane-3,5-dione(4k):White solid, 79.07 mg, 98% yield. ***R_f*** = 0.22 (40% EtOAc in hexanes) **MP**: 88-90 °C. $[\alpha]_D^{22}$ = +228.32 ($CHCl_3$, c = 0.62 for 88% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 10.09 min (major), 9.14 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 35.2 Hz, 3H), 7.65 – 7.49 (m, 4H), 7.03 (t, *J* = 8.3 Hz, 2H), 5.28 (s, 1H), 2.43 (dd, *J* = 23.4, 7.3 Hz, 2H), 2.18 (d, *J* = 17.5 Hz, 1H), 1.93 (dd, *J* = 18.2, 8.0 Hz, 1H), 0.97 (t, *J* = 7.1 Hz, 3H), 0.63 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 205.3, 202.2, 169.3, 163.1, 161.7, 143.4, 137.8, 135.4, 133.2, 129.8, 128.4 (d, *J* = 4.6 Hz), 128.0, 127.3, 126.3 (d, *J* = 8.2 Hz), 125.5, 122.1, 116.3 (d, *J* = 21.6 Hz), 71.5, 66.4, 38.4, 38.0, 31.1, 7.8, 7.6. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -114.2. **HRMS** (ES+): Exact mass calcd for $C_{25}H_{23}FNO_3$ $[M+H]^+$: 404.1656 Found: 404.1679.



4k

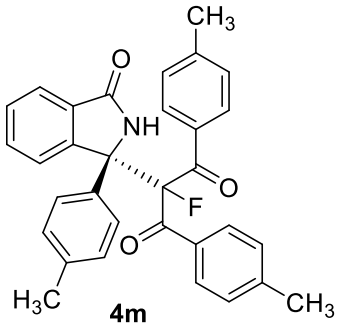
(*S*)-4-(5,6-dichloro-3-oxo-1-phenylisoindolin-1-yl)heptane-3,5-dione(4l): White solid, 64.68 mg, 80% yield. R_f = 0.43(40% EtOAc in hexanes) MP: 160-162 °C. $[\alpha]_D^{22}$ = +186.216 ($CHCl_3$, c = 0.37 for 95% ee). **HPLC** (Chiralpak ADH , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 7.70 min (major), 9.90 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (d, *J* = 4.4 Hz, 2H), 7.63 (s, 1H), 7.44 (d, *J* = 7.7 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 7.7 Hz, 1H), 5.18 (s, 1H), 2.47 (dq, *J* = 14.4, 7.2 Hz, 1H), 2.38 (ddd, *J* = 18.7, 9.6, 6.0 Hz, 2H), 2.06 (dq, *J* = 18.6, 7.1



4l

Hz, 1H), 0.93 (t, *J* = 7.2 Hz, 3H), 0.79 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 205.2, 201.8, 167.5, 147.6, 140.1, 137.1, 134.1, 130.4, 129.6, 128.6, 126.3, 126.3, 125.1, 125.1, 124.3, 70.2, 70.2, 66.6, 38.6, 38.0, 7.8, 7.5. **HRMS** (ES+): Exact mass calcd for $C_{21}H_{19}Cl_2NO_3Na[M+Na]^+$: 426.0634 Found: 426.0618.

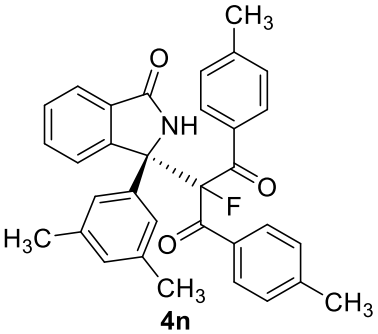
(*S*)-2-fluoro-2-(3-oxo-1-(p-tolyl)isoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4m):



4m

White solid, 89.46 mg, 91% yield. R_f = 0.63 (40% EtOAc in hexanes) **MP**: 98-100 °C. $[\alpha]_D^{22}$ = +272.390 ($CHCl_3$, c = 0.54 for 80% ee). **HPLC** (Chiralcel ODH , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 18.98 min (major), 15.47 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 6.7 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.47 (dq, *J* = 22.3, 7.8 Hz, 6H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 2.28 (d, *J* = 12.0 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.9 (d, *J* = 25.1 Hz), 190.6 (d, *J* = 23.4 Hz), 169.3, 146.9, 145.3, 144.4, 137.8, 136.6 (d, *J* = 2.6 Hz), 132.5 (d, *J* = 3.7 Hz), 132.2, 131.8 (d, *J* = 3.6 Hz), 131.3, 129.9 (dd, *J* = 6.5, 3.4 Hz), 129.6, 129.5, 129.2, 128.9, 126.1 (d, *J* = 3.4 Hz), 125.9 (d, *J* = 5.6 Hz), 124.0, 106.8, 69.3 (d, *J* = 23.8 Hz), 21.8, 21.7, 21.0. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -150.8. **HRMS** (ES+): Exact mass calcd for $C_{32}H_{26}FNO_3Na[M+Na]^+$: 514.1789 Found: 514.1751.

(*S*)-2-(1-(3,5-dimethylphenyl)-3-oxoisoindolin-1-yl)-2-fluoro-1,3-di-p-tolylpropane-1,3-dion(4n):

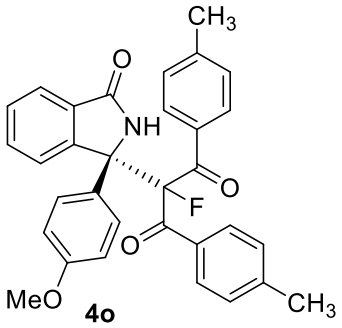


4n

White solid, 91 mg, 90% yield. R_f = 0.53 (40% EtOAc in hexanes) **MP**: 115-117 °C. $[\alpha]_D^{22}$ = +24.35 ($CHCl_3$, c = 1.33 for 88% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 14.96 min (major), 7.72 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.8, 2.6 Hz, 1H), 7.64 (dd, *J* = 8.3, 2.2 Hz, 2H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.40 (s, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 4H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.85 (s, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 2.20 (s, 6H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 193.2 (d, *J* = 25.3 Hz), 190.7 (d, *J* = 23.4 Hz), 169.4, 146.9, 145.1, 144.4, 139.5 (d, *J* = 2.8 Hz), 138.4, 132.6 (d, *J* = 3.8 Hz), 132.2, 132.0 (d, *J* = 3.5 Hz), 131.2, 129.9 (d, *J* = 7.3 Hz), 129.8, 129.8 (d, *J* = 5.5 Hz), 129.4, 129.2, 128.9, 126.2 (d, *J* = 3.3 Hz), 124.0, 123.6 (d, *J* = 5.3 Hz), 108.5,

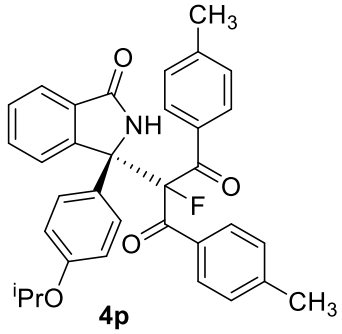
107.3, 69.4 (d, *J* = 23.5 Hz), 21.9, 21.7, 21.6. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -150.2. **HRMS** (ES+): Exact mass calcd for $C_{33}H_{28}FNO_3Na[M+Na]^+$: 528.1945 Found: 528.1919.

(*S*)-2-fluoro-2-(1-(4-methoxyphenyl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4o): White semisolid, 97.45 mg, 96% yield. R_f = 0.35 (40% EtOAc in hexanes). $[\alpha]_D^{22}$ = +279.264 ($CHCl_3$, c = 2.306 for 84% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 46.08 min (major), 18.17 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.65 (d, *J* = 6.3 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.52 (dd, *J* = 8.3, 4.5 Hz, 4H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.98 (d, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 3.71 (s, 3H), 2.34 (s, 3H), 2.28 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 192.8 (d, *J* = 25.1 Hz), 190.5 (d, *J* = 23.6 Hz), 169.3, 159.2, 146.9, 145.2, 144.4, 132.5 (d, *J* = 3.9 Hz), 132.2, 131.7 (d, *J* = 3.6 Hz), 131.3 (d, *J* = 2.6 Hz), 131.2, 129.8 (d, *J* = 7.3 Hz), 129.4, 129.1, 128.9, 127.4 (d, *J* = 5.8 Hz), 126.1, 123.9, 114.1 (d, *J* = 4.4 Hz), 108.7, 107.0, 69.2 (d, *J* = 24.0 Hz), 55.2 (d, *J* = 9.5 Hz), 21.8 (d, *J* = 5.5 Hz), 21.6 (d, *J* = 4.3 Hz). **HRMS** (ES+): Exact mass calcd for $C_{32}H_{26}FNO_4Na[M+Na]^+$: 530.1738 Found 530.1738.



4o

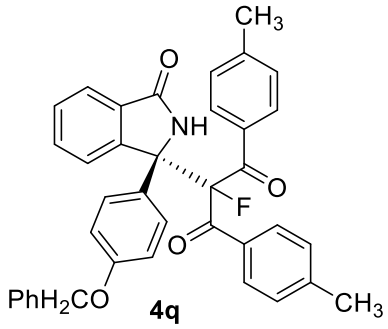
(*S*)-2-fluoro-2-(1-(4-isopropoxyphenyl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4p): White solid, 98.55 mg 92% yield. R_f = 0.70 (40% EtOAc in hexanes) **MP**: 146-148 °C. $[\alpha]_D^{22}$ = +6.11 ($CHCl_3$, c = 0.071 for 83% ee). **HPLC** (Chiralpak IC , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 27.52 min (major), 37.35 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 1H), 7.65 (dd, *J* = 8.3, 2.1 Hz, 2H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.53 – 7.46 (m, 4H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.75 (d, *J* = 9.0 Hz, 2H), 4.47 (p, *J* = 6.1 Hz, 1H), 2.36 (s, 3H), 2.29 (s, 3H), 1.28 (t, *J* = 6.4 Hz, 6H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.9 (d, *J* = 25.0 Hz), 190.6 (d, *J* = 23.5 Hz), 169.5, 157.6, 132.5 (d, *J* = 3.8 Hz), 132.2, 131.8 (d, *J* = 3.8 Hz), 131.2, 130.8 (d, *J* = 2.5 Hz), 130.3, 130.0 (d, *J* = 3.5 Hz), 129.9 (dd, *J* = 6.5, 3.3 Hz), 129.6, 129.4, 129.2, 128.9, 127.5 (d, *J* = 5.4 Hz), 126.1, 124.0, 115.7, 107.8 (d, *J* = 217.7 Hz), 69.8, 69.3 (d, *J* = 23.4 Hz), 22.1 (d, *J* = 7.1 Hz), 21.8 (d, *J* =



4p

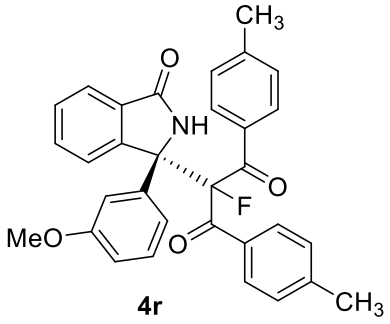
20.9 Hz). **HRMS** (ES+): Exact mass calcd for $C_{34}H_{31}FNO_4[M+H]^+$: 536.2232 Found: 536.2237.

(*S*)-2-(1-(4-benzylphenyl)-3-oxoisoindolin-1-yl)-2-fluoro-1,3-di-p-tolylpropane-1,3-dione(4q): White solid, 106.22 mg, 91% yield. R_f = 0.45 (40% EtOAc in hexanes) **MP**: 79-81 °C. $[\alpha]_D^{22}$ = +220.00 ($CHCl_3$, c = 0.266 for 81% ee). **HPLC** (Chiralpak IC , *n*-hexane/ *iso*-propanol = 50/50, 1.0 mL/min, 254 nm): t_R = 48.95 min (major), 41.59 min (minor) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.67 (s, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.54 – 7.50 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 6.5 Hz, 3H), 7.35 – 7.27 (m, 3H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.99 (s, 2H), 2.36 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.9 (d, *J* = 25.1 Hz), 190.6 (d, *J* = 23.2 Hz), 169.5, 158.5, 145.3, 144.4, 136.8, 132.6 (d, *J* = 3.7 Hz), 132.3, 131.8 (d, *J* = 3.3 Hz), 131.6, 131.3, 130.4, 129.9, 129.9 (d, *J* = 2.4 Hz), 129.5, 129.3 (d, *J* = 8.5 Hz), 129.0, 128.7, 128.2, 127.6, 127.5 (d, *J* = 5.8 Hz), 126.1 (d, *J* = 5.2 Hz), 124.1, 115.0, 108.4, 107.2, 70.1, 69.3 (d, *J* = 24.1 Hz), 21.9, 21.8. **HRMS** (ES+): Exact mass calcd for $C_{38}H_{31}FNO_4$ $[M+H]^+$: 584.2232 Found: 584.2200.

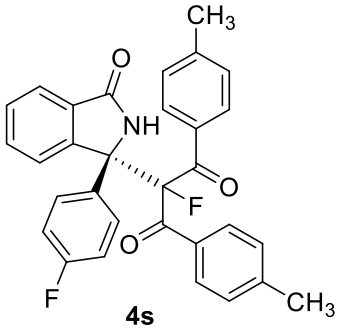


4q

(*S*)-2-fluoro-2-(1-(3-methoxyphenyl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4r) : White solid, 94.40 mg, 93% yield. R_f = 0.41 (40% EtOAc in hexanes). **MP**: 78-80 °C. $[\alpha]_D^{22}$ = +328.678 ($CHCl_3$, c = 1.89 for 89% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 30.43 min (major), 13.50 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 5.2 Hz, 1H), 7.65 (dd, *J* = 8.3, 2.2 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.47 – 7.42 (m, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.23 – 7.12 (m, 5H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 1H), 3.69 (s, 3H), 2.36 (s, 3H), 2.29 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.9 (d, *J* = 25.2 Hz), 190.6 (d, *J* = 23.6 Hz), 169.4, 159.9, 146.6, 145.3, 144.5, 141.4 (d, *J* = 2.6 Hz), 132.5 (d, *J* = 3.8 Hz), 132.3, 131.8 (d, *J* = 3.7 Hz), 131.2, 130.0 – 129.9 (m), 129.5, 129.3, 129.0, 126.2, 124.1, 118.1 (d, *J* = 6.7 Hz), 113.3, 112.0 (d, *J* = 5.4 Hz), 108.6, 107.4, 69.4 (d, *J* = 23.6 Hz), 55.3, 21.9, 21.7. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -150.2. **HRMS** (ES+): Exact mass calcd for $C_{32}H_{27}FNO_4$ $[M+H]^+$: 508.1919 Found: 508.1906.

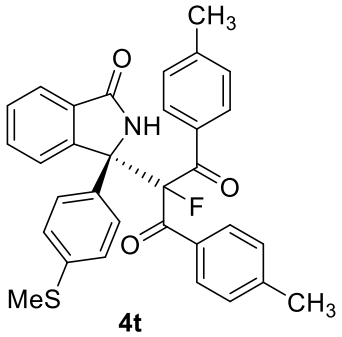


4r

(*S*)-2-fluoro-2-(1-(4-fluorophenyl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4s): 

4s

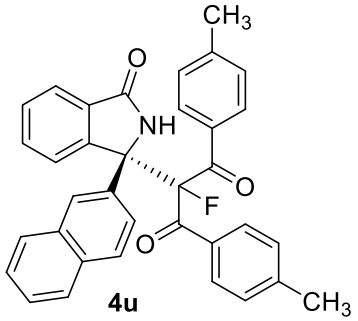
White solid, 93.16 mg, 94% yield. R_f = 0.44 (40% EtOAc in hexanes) **MP**: 110-112 °C. $[\alpha]_D^{22}$ = +78.33 ($CHCl_3$, c = 2.22 for 93% ee). **HPLC** (Chiralpak IC , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 40.36 min (major), 44.45 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.7 Hz, 1H), 7.65 (d, *J* = 6.2 Hz, 2H), 7.59 (t, *J* = 8.0 Hz, 3H), 7.51 (d, *J* = 8.1 Hz, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.95 (t, *J* = 8.5 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.7 (d, *J* = 25.2 Hz), 190.4 (d, *J* = 23.3 Hz), 169.2, 163.0, 161.6, 146.5, 145.6, 144.6, 135.5 (d, *J* = 3.1 Hz), 132.4 (d, *J* = 7.0 Hz), 131.5 (d, *J* = 3.3 Hz), 131.2, 129.9 (t, *J* = 6.4 Hz), 129.6, 129.4, 129.0, 128.0 (t, *J* = 7.1 Hz), 126.1, 124.2, 115.8 (d, *J* = 21.5 Hz), 108.4, 107.2, 69.1 (d, *J* = 23.8 Hz), 31.1, 21.9, 21.7. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -114.2, -150.7. **HRMS** (ES+): Exact mass calcd for $C_{31}H_{24}F_2NO_3[M+H]^+$: 496.1719 Found: 496.1707.

(*S*)-2-fluoro-2-(1-(4-(methylthio)phenyl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4t): 

4t

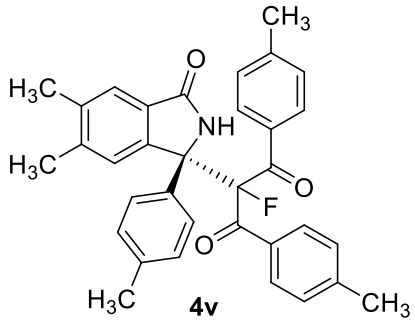
White solid, 89.02 mg, 85% yield. R_f = 0.39 (40% EtOAc in hexanes) MP: 126-128 °C. $[\alpha]_D^{22}$ = +127 ($CHCl_3$, c = 0.46 for 80 % ee). HPLC (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 41.14 min (major), 15.88 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.8, 2.6 Hz, 1H), 7.66 (dd, *J* = 8.4, 2.2 Hz, 2H), 7.57 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 5H), 7.47 – 7.41 (m, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 2.42 (s, 3H), 2.37 (s, 3H), 2.30 (s, 3H). **^{13}C NMR** (175 MHz, $CDCl_3$) δ 192.7 (d, *J* = 24.9 Hz), 190.5 (d, *J* = 23.4 Hz), 169.3, 146.6, 145.5, 144.5, 138.7, 136.2 (d, *J* = 2.9 Hz), 132.5 (d, *J* = 3.8 Hz), 132.3, 132.1, 131.7 (d, *J* = 3.8 Hz), 131.2, 129.9 (d, *J* = 6.4 Hz), 129.5, 129.0, 128.7, 126.5, 126.1, 124.1, 123.5, 119.6, 108.5, 107.2, 69.2 (d, *J* = 24.0 Hz), 21.9, 21.8, 15.5. **HRMS** (ES+): Exact mass calcd for $C_{32}H_{26}FNO_3SNa[M+Na]^+$: 546.1510 Found: 546.1500.

(*S*)-2-fluoro-2-(1-(naphthalen-2-yl)-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4u): White solid, 100.23 mg, 95% yield. R_f = 0.53 (40% EtOAc in hexanes) **MP**: 177-179 °C. $[\alpha]_D^{22}$ = +295.250 ($CHCl_3$, c = 1.17 for 84% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R =33.39 min (major), 15.72 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.79 – 7.69 (m, 4H), 7.66 (d, *J* = 8.5 Hz, 3H), 7.57 (dd, *J* = 19.3, 8.0 Hz, 4H), 7.43 (t, *J* = 7.7 Hz, 3H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H), 2.31 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 192.9 (d, *J* = 25.1 Hz), 190.6 (d, *J* = 23.5 Hz), 169.4, 146.8, 145.3, 144.5, 137.1 (d, *J* = 2.5 Hz), 133.3, 132.8, 132.6, 132.3, 131.8 (d, *J* = 3.5 Hz), 131.4, 130.0 (dd, *J* = 8.6, 6.4 Hz), 129.5, 129.4, 129.0, 128.8, 128.5, 127.5, 126.6 (d, *J* = 6.0 Hz), 126.3, 125.3 (d, *J* = 5.4 Hz), 124.2, 123.7 (d, *J* = 5.9 Hz), 69.7 (d, *J* = 23.7 Hz), 21.9, 21.8. **HRMS** (ES+): Exact mass calcd for $C_{35}H_{27}FNO_3[M+H]^+$: 528.1969 Found: 528.1962.



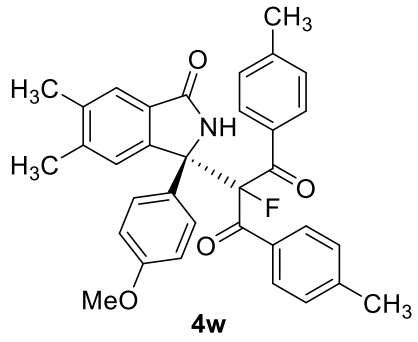
4u

(*S*)-2-(5,6-dimethyl-3-oxo-1-(p-tolyl)isoindolin-1-yl)-2-fluoro-1,3-di-p-tolylpropane-1,3-dione Pale(4v): White solid, 75.1 mg, 90% yield. R_f = 0.5 (40% EtOAc in hexanes) **MP**: 162-164 °C. $[\alpha]_D^{22}$ = +275.84 ($CHCl_3$, c = 1.78 for 84% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 31.26 min (major), 14.27 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 6.3 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 9.9 Hz, 2H), 7.30 (s, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 2.37 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 2.23 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.0 (d, *J* = 25.2 Hz), 190.9 (d, *J* = 23.0 Hz), 169.7, 145.2, 144.8, 144.1, 141.8, 138.2, 137.7, 136.7, 132.9 (d, *J* = 4.0 Hz), 131.8 (d, *J* = 3.5 Hz), 129.9 (d, *J* = 8.9 Hz), 129.5 (d, *J* = 9.5 Hz), 129.1, 128.6, 126.9, 126.0 (d, *J* = 5.6 Hz), 124.5, 108.6, 106.9, 69.0 (d, *J* = 24.2 Hz), 21.8, 21.7, 21.0, 20.6, 19.9. **^{19}F NMR** (375 MHz, $CDCl_3$) δ -150.9. **HRMS** (ES+): Exact mass calcd for $C_{34}H_{30}FNO_3Na[M+Na]^+$: 542.2102 Found: 542.2097.



4v

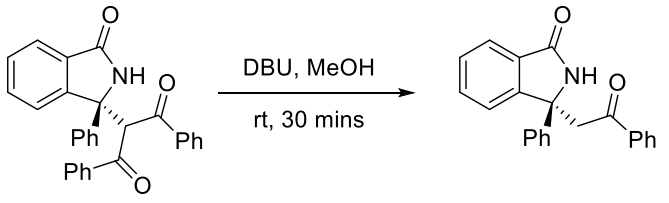
(*S*)-2-fluoro-2-(1-(4-methoxyphenyl)-5,6-dimethyl-3-oxoisoindolin-1-yl)-1,3-di-p-tolylpropane-1,3-dione(4w): White solid, 95.33 mg, 89% yield. R_f = 0.35 (40% EtOAc in hexanes) **MP**: 120-122 °C. $[\alpha]_D^{22}$ = +133.58 ($CHCl_3$, c = 0.81 for 63% ee). **HPLC** (Chiralpak IA , *n*-hexane/ *iso*-propanol = 60/40, 1.0 mL/min, 254 nm): t_R = 35.70 min (major), 16.18 min (minor). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 6.8 Hz, 2H), 7.50 (dd, *J* = 7.6, 4.5 Hz, 4H), 7.42 (d, *J* = 6.4 Hz, 2H), 7.31 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.81 – 6.76 (m, 2H), 3.74 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H), 2.23 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.0 (d, *J* = 25.4 Hz), 190.8 (d, *J* = 23.6 Hz), 169.7, 159.1, 145.2, 144.9, 144.1, 141.7, 138.2, 132.9 (d, *J* = 3.6 Hz), 131.9 (d, *J* = 3.7 Hz), 131.5, 129.8 (d, *J* = 8.3 Hz), 129.5, 129.1, 128.6, 127.6 (d, *J* = 5.8 Hz), 126.9, 124.5, 114.1, 108.6, 106.9, 68.9 (d, *J* = 24.0 Hz), 55.3 (d, *J* = 9.8 Hz), 21.8 (d, *J* = 6.0 Hz), 21.7 (d, *J* = 5.2 Hz), 20.6 (d, *J* = 3.6 Hz), 19.8. **HRMS** (ES+): Exact mass calcd for $C_{34}H_{31}FNO_3$ $[M+H]^+$: 536.2232 Found: 536.2234.



4w

General procedure for the synthesis of compound 5:

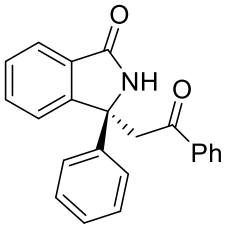
To a solution of compound **4f** (86.30 mg, 0.2 mmol, 1 equiv) in methanol DBU (30 µl, 0.2 mmol, 1 equiv) was added dropwise and the reaction mixture was stirred at rt. After the completion of the reaction (monitored by TLC), the solvent was evaporated in vacuo and the residue was dissolved in CH_2Cl_2(10 mL) and the organic layer was washed with water (2 X 10 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated on vacuo. Products **5** (64.17 mg, 98% yield) was isolated by flash column chromatography using ethyl acetate and hexane as eluents.



4f
93% ee

5
98% yield, 93% ee

(*S*)-3-(2-oxo-2-phenylethyl)-3-phenylisoindolin-1-one(5): White solid, 64.17 mg, 98% yield.



5

R_f = 0.30 (40% EtOAc in hexanes) **MP**: 118-120 °C. $[\alpha]_D^{22}$ = +274.2 (CH_2Cl_2, c = 1.00 for 93% ee) and $[\alpha]_D^{22}$ = +158.6 ($CHCl_3$, c = 0.25 for 93% ee). **HPLC** (Chiralpak ADH , *n*-hexane/ *iso*-propanol = 70/30, 1.0 mL/min, 254 nm): t_R = 18.14 min (major), 15.22 min (minor). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.8 Hz, 2H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.55 – 7.44 (m, 4H), 7.38 (dd, *J* = 19.7, 7.6 Hz, 3H), 7.29 (d, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 4.71 (d, *J* = 18.2 Hz, 1H), 3.26 (d, *J* = 18.1 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 197.1, 169.7, 151.6, 140.7, 136.4, 133.9, 132.5, 130.0, 129.0, 128.9, 128.6, 128.0, 127.6, 124.7, 124.5, 122.1, 64.52, 46.8. **HRMS** (ES+): Exact mass calcd for $C_{22}H_{18}NO_2[M+H]^+$: 328.1332 Found: 328.1336.

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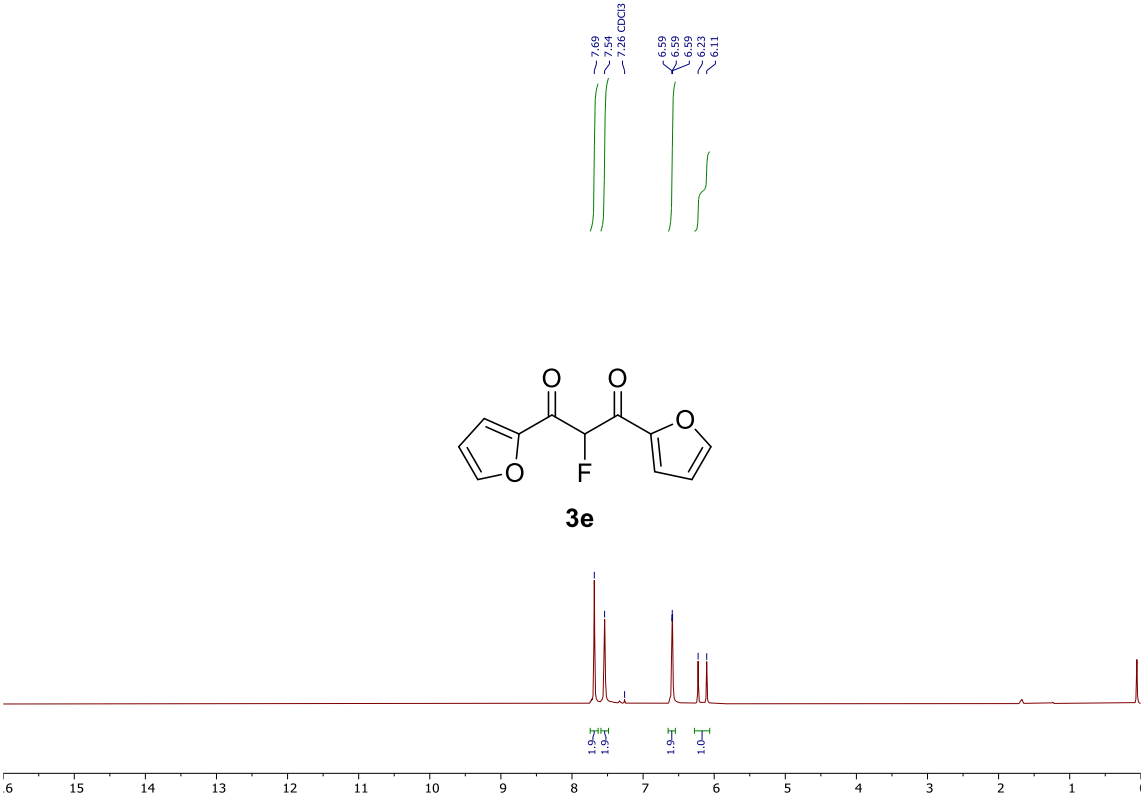
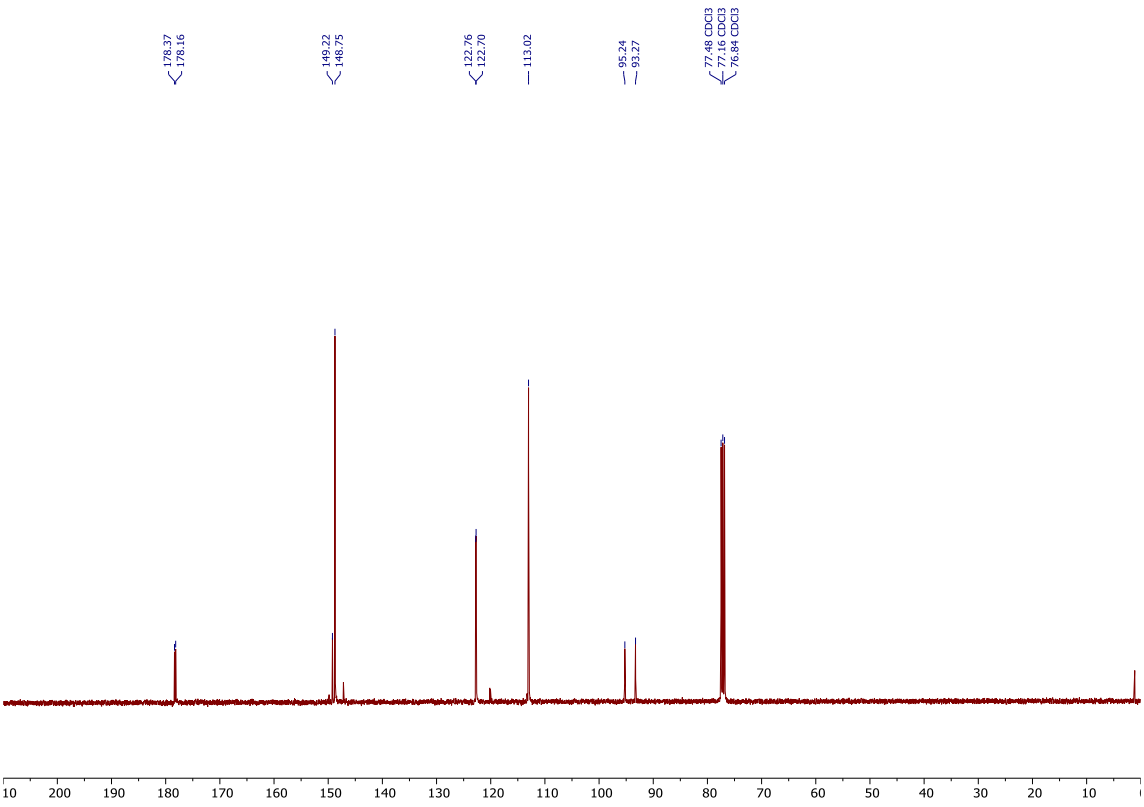
1. (a) T. Nishimura, A. Noishiki, Y. Ebe and T. Hayashi, *Angew. Chem., Int. Ed*. **2013**, *52*, 1777-1780. (b) J. Suc, I. Dokli and M. Gredičak, *Chem. Commun*. **2016**, *52*, 2071-2074. (c) Y.-P. Ruan, M.-D. Chen, M.-Z. He, X. Zhou and P.-Q. Huang, *Synth. Commun*. **2004**, *34*, 853-861. (d) N. Lu, L. Wang, L. Z. Zhanshan and W. Zhang, *Beilstein J. Org. Chem*. **2012**, *8*, 192-200. (e) Y. Du, T. K. Hyster, and T. Rovis, *Chem. Comm.* **2011**, *47*, 12074-76.
2. (a) J.-Q. Zhou, W.-J. Sheng, J.-H. Jia, Q. Ye, J.-R. Gao and Y.-X. Jia, *Tetrahedron Lett.* **2013,** *54*, 3082-3084. (b) M. Nagamoto, D. Yamauchia and T. Nishimura, *Chem. Commun.* **2016**, *52*, 5876-5879. (c) R. A. Unhale, N. Molleti, N. K. Ranaa, S. Dhanasekaran, S. Bhandary, V. K. Singh *Tetrahedron Lett.* **2017**, *58*, 145-151. (d) H.-z. Zhang, X.-l. Xu, H.-y. Chen, S. Ali, D. Wang, J.-w. Yu, Tao Xu, Fa-jun Nan *Acta Pharmacologica Sinica* **2015**, *36***,** 1137-1144, (e) A. Suneja, R. A. Unhale, and V. K. Singh *Org. Lett*., **2017**, *19*, 476-479. (f) Y. Zhang, Li He, and Lei Shi *Tetrahedron Lett.* **2018**, *59*, 1592–1595
3. (a) J. Qian, J. Zhang, H. Yang, L. Kanga and G. Jiang *Chem. Sci*., **2019**, *10*, 8812. (b) E. R. T. Robinson, C. Fallan, C, Simal, A. M. Z. Slawin and A. D. Smith *Chem. Sci*., **2013**, *4*, 2193–2200.

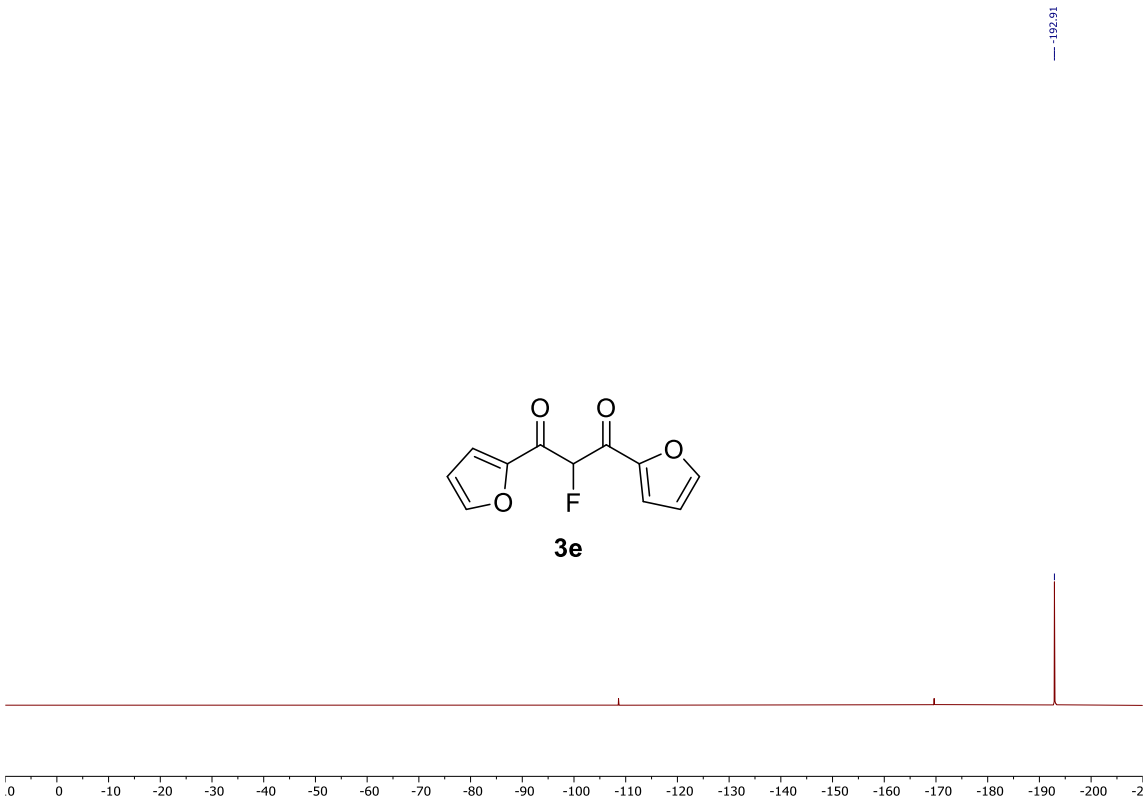
NMR Spectra of products:



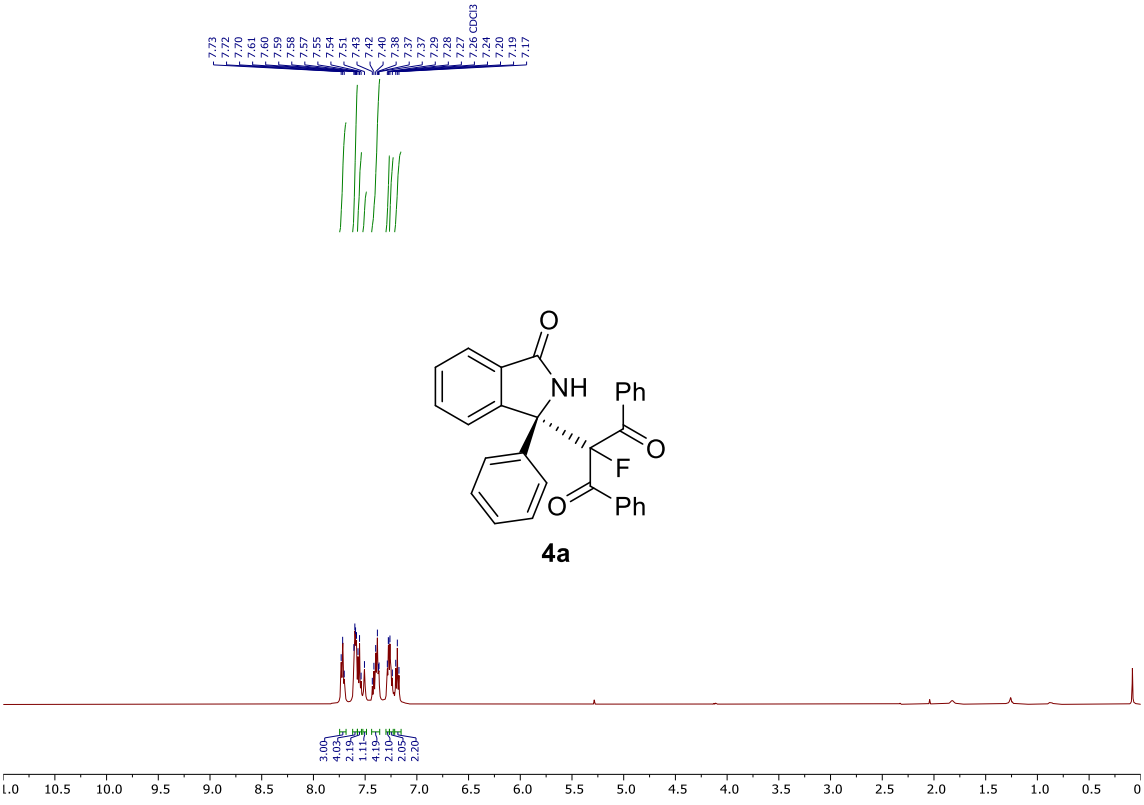
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3e**



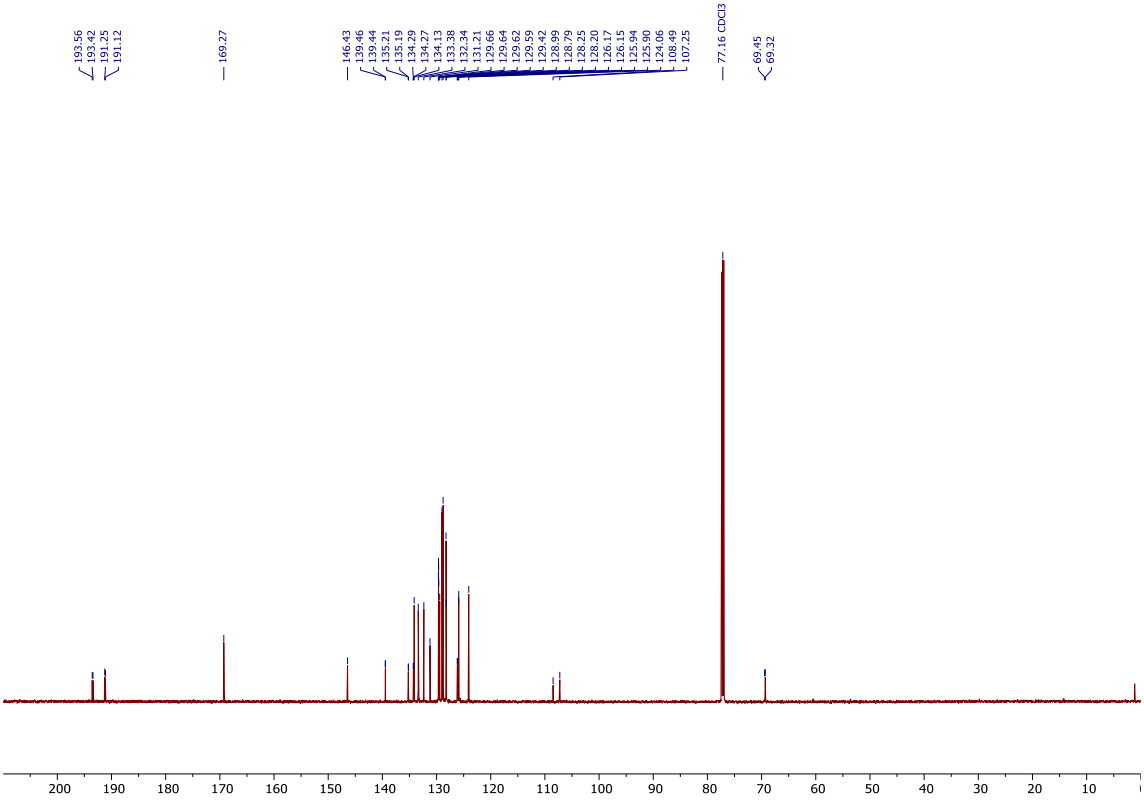
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3e**



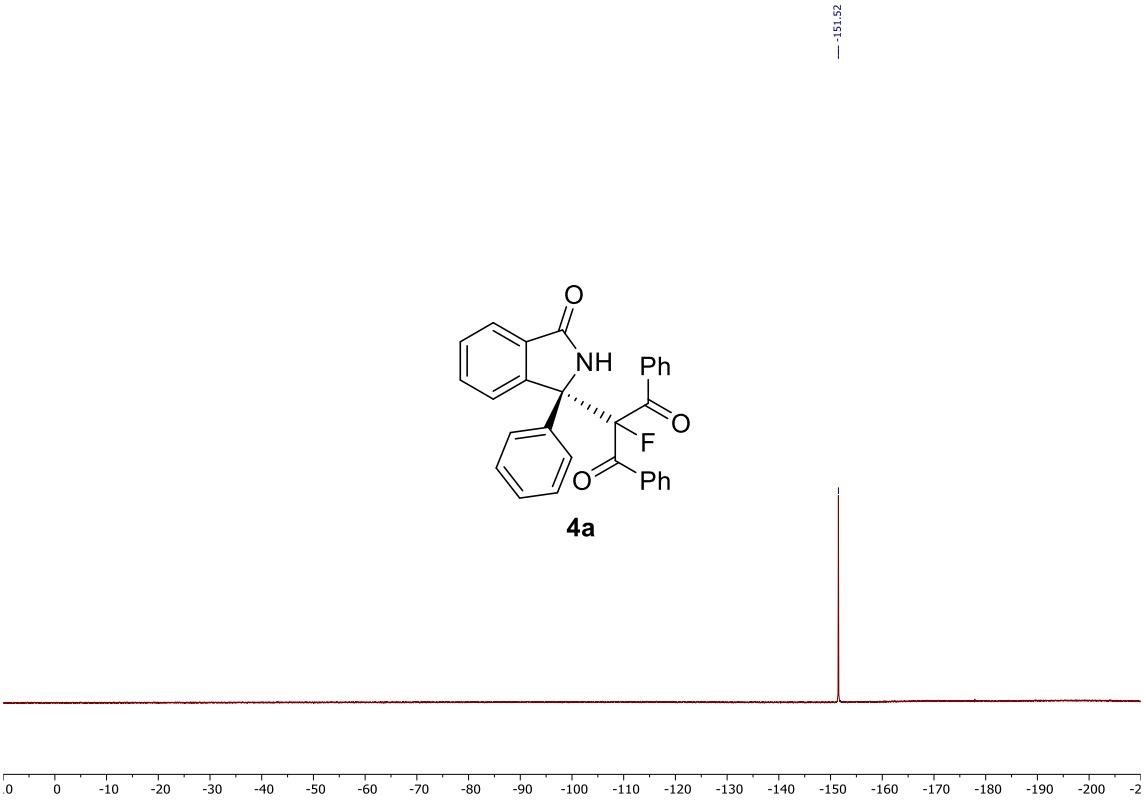
^{19}F NMR (375 MHz, $CDCl_3$) of compound **3e**



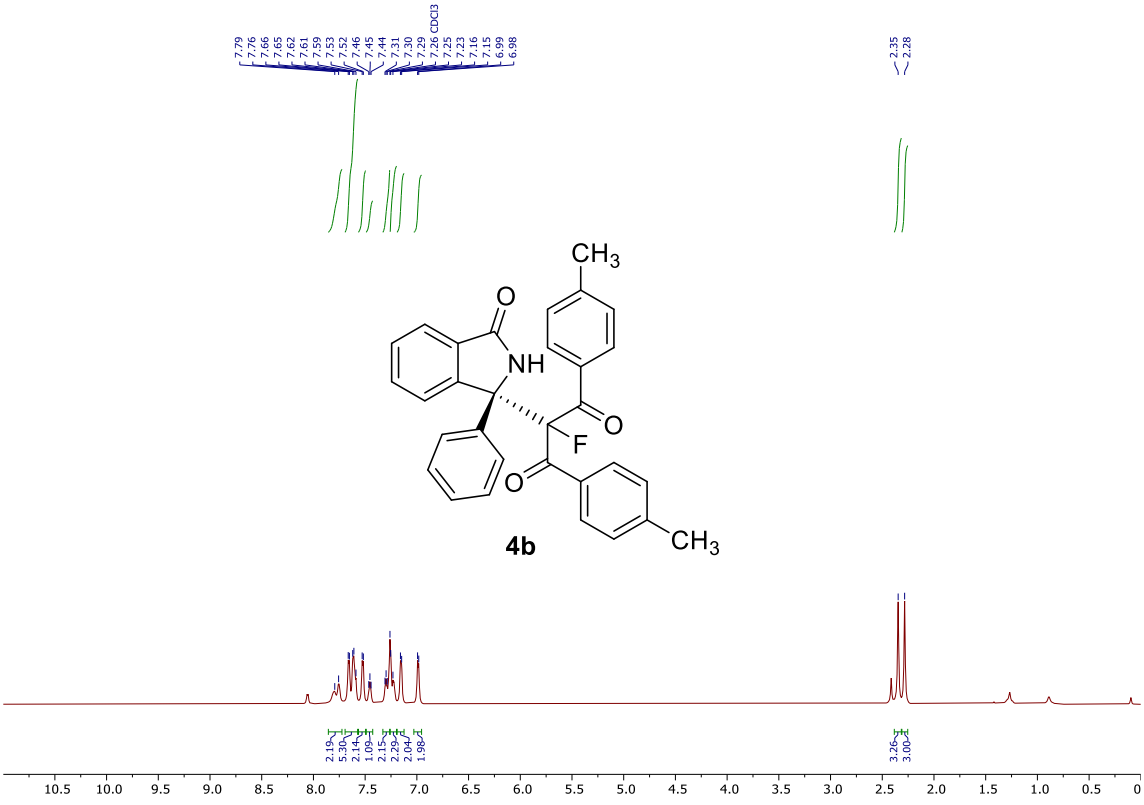
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4a**



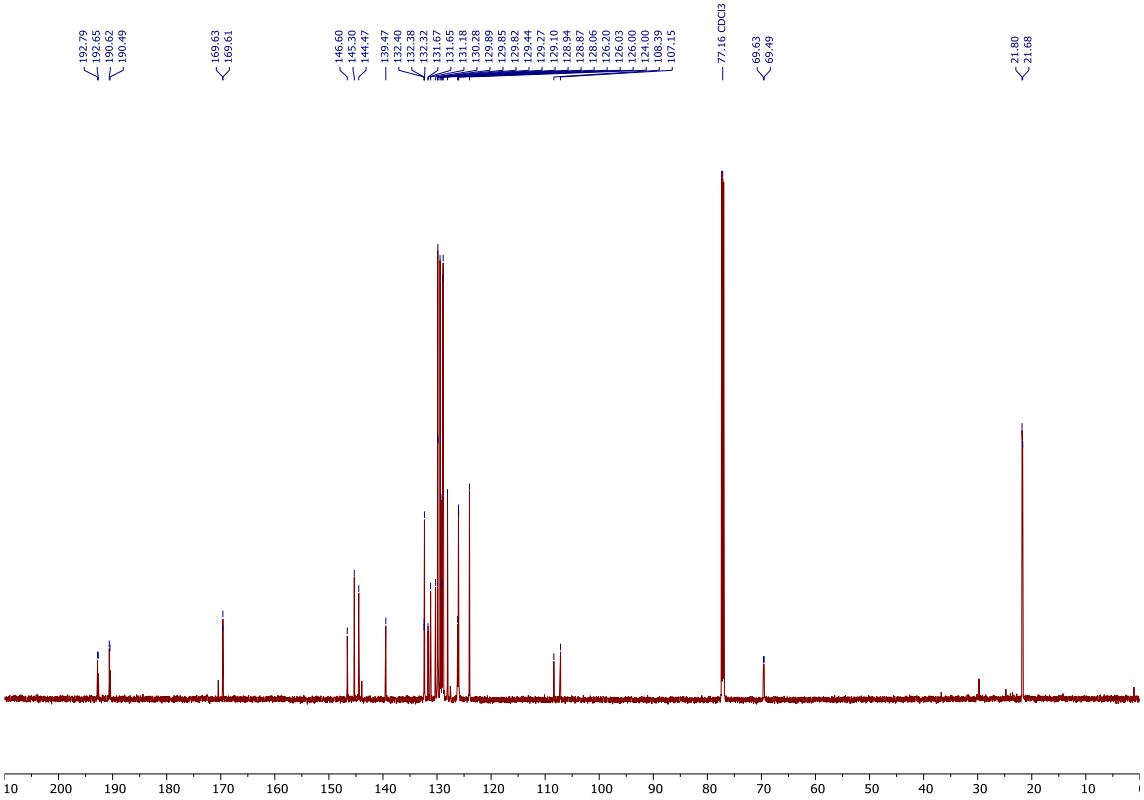
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4a**



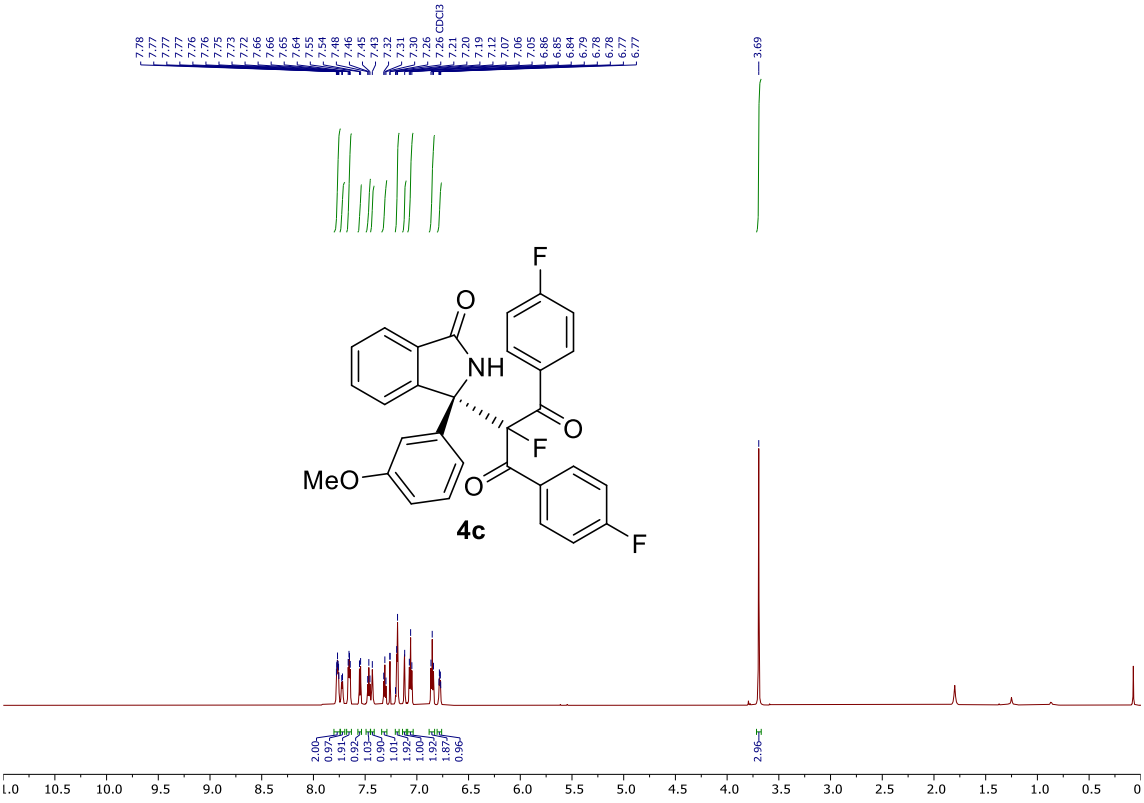
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4a**



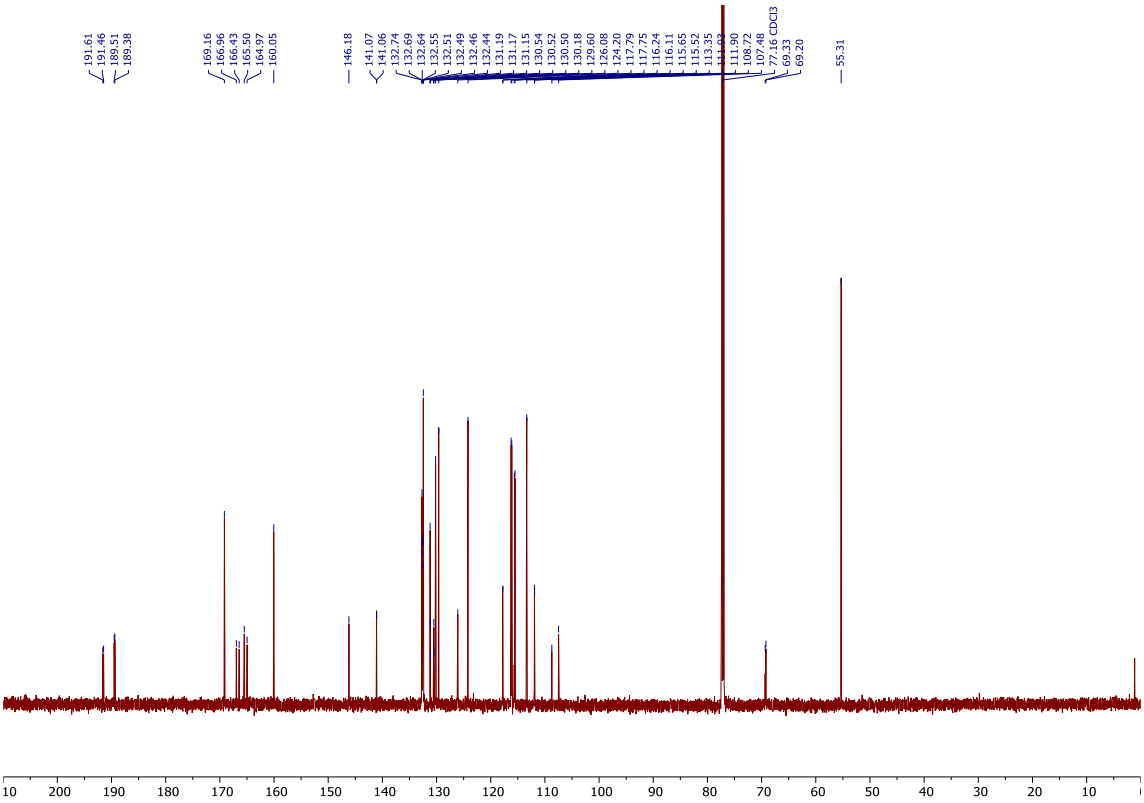
^{1}H NMR (700 MHz, $CDCl_3$) of compound **4b**



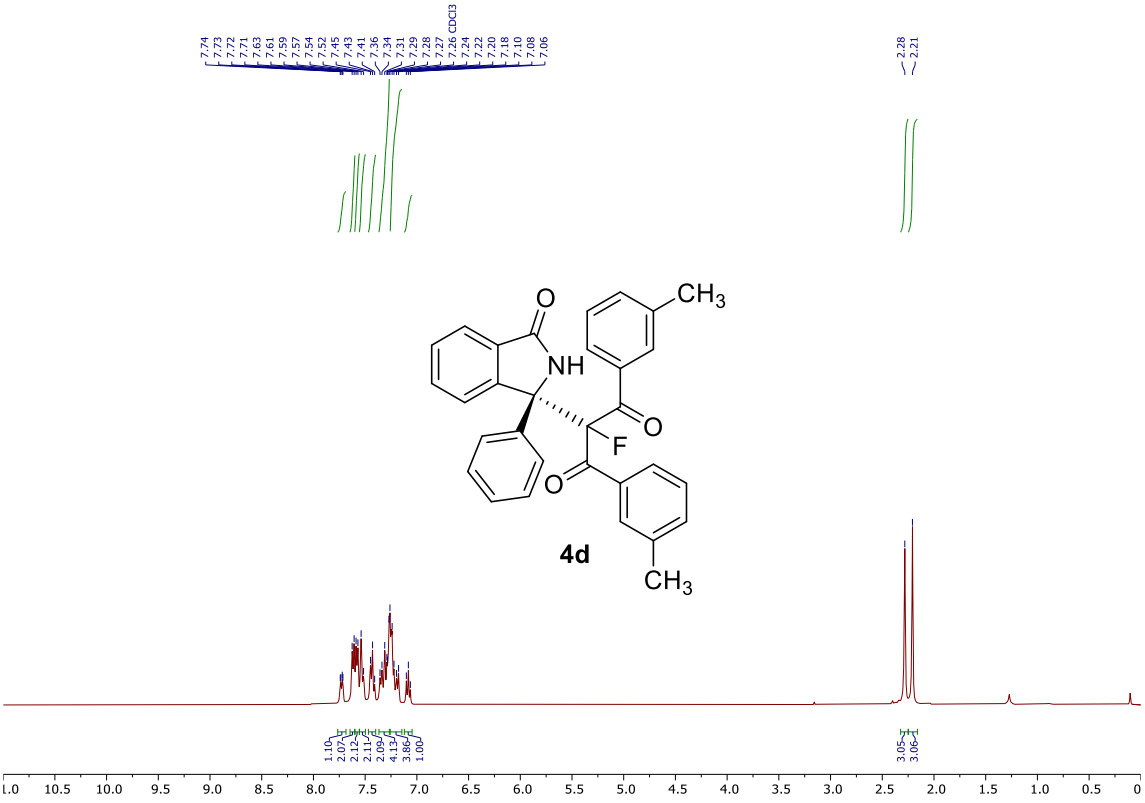
^{13}CNMR (175 MHz, $CDCl_3$) of compound **4b**



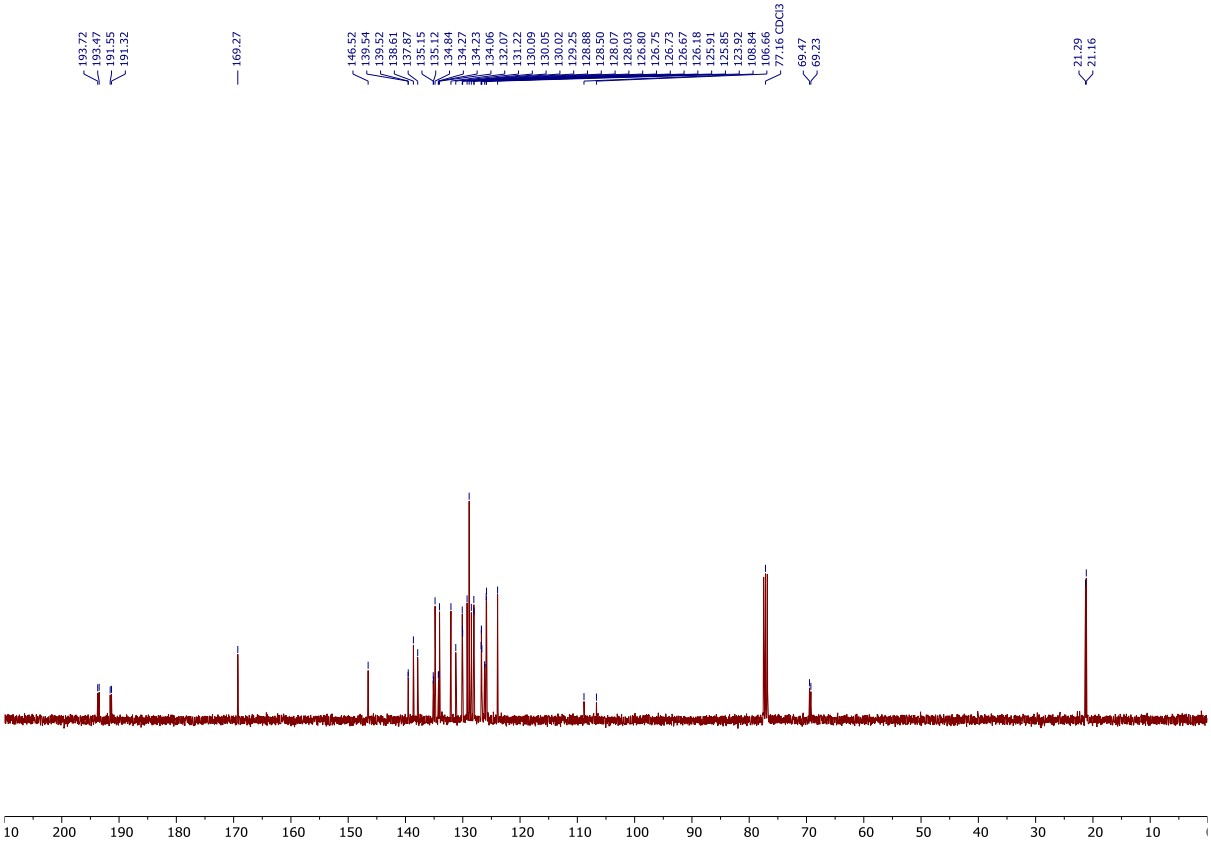
^{1}H NMR (700 MHz, $CDCl_3$) of compound **4c**



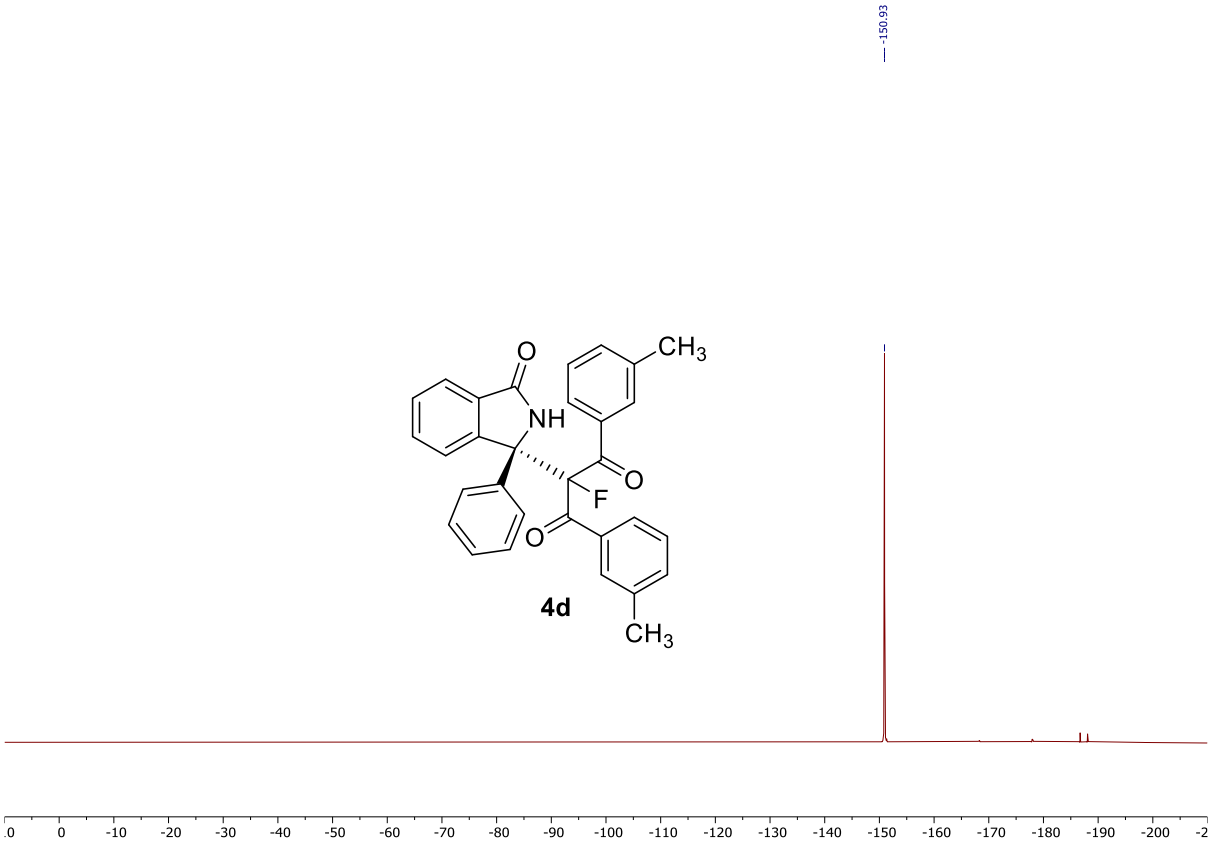
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4c**



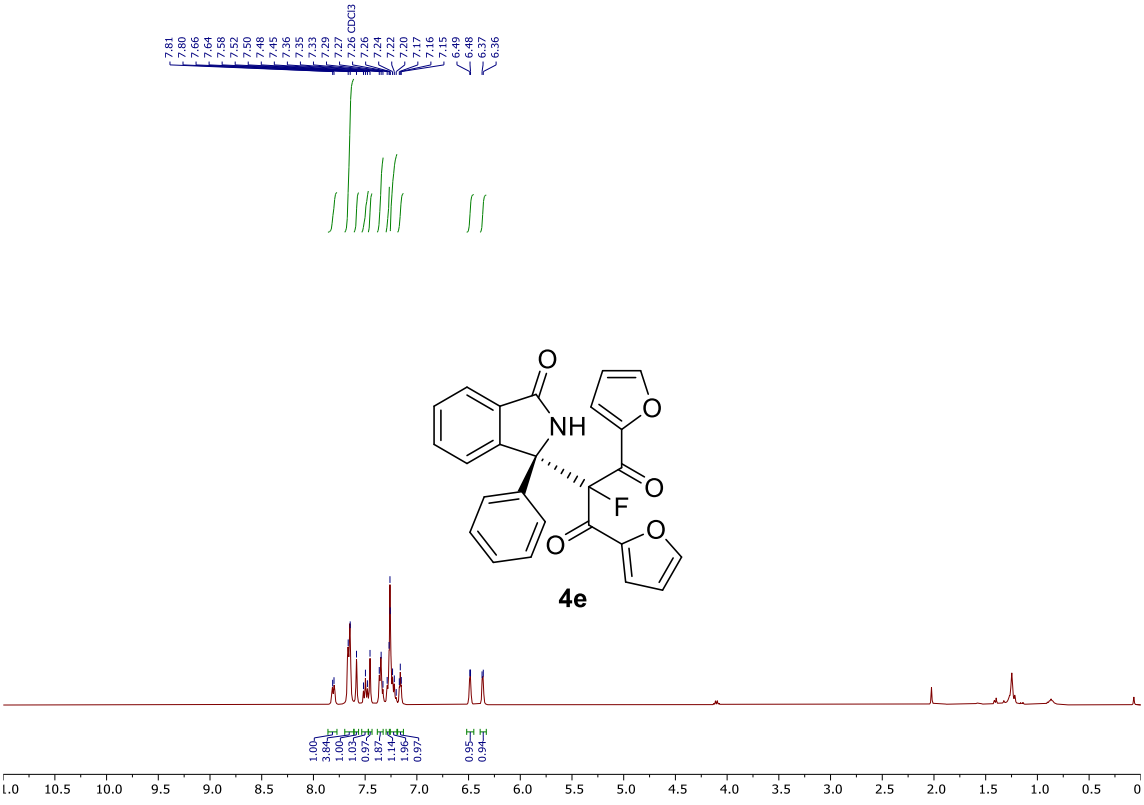
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4d**



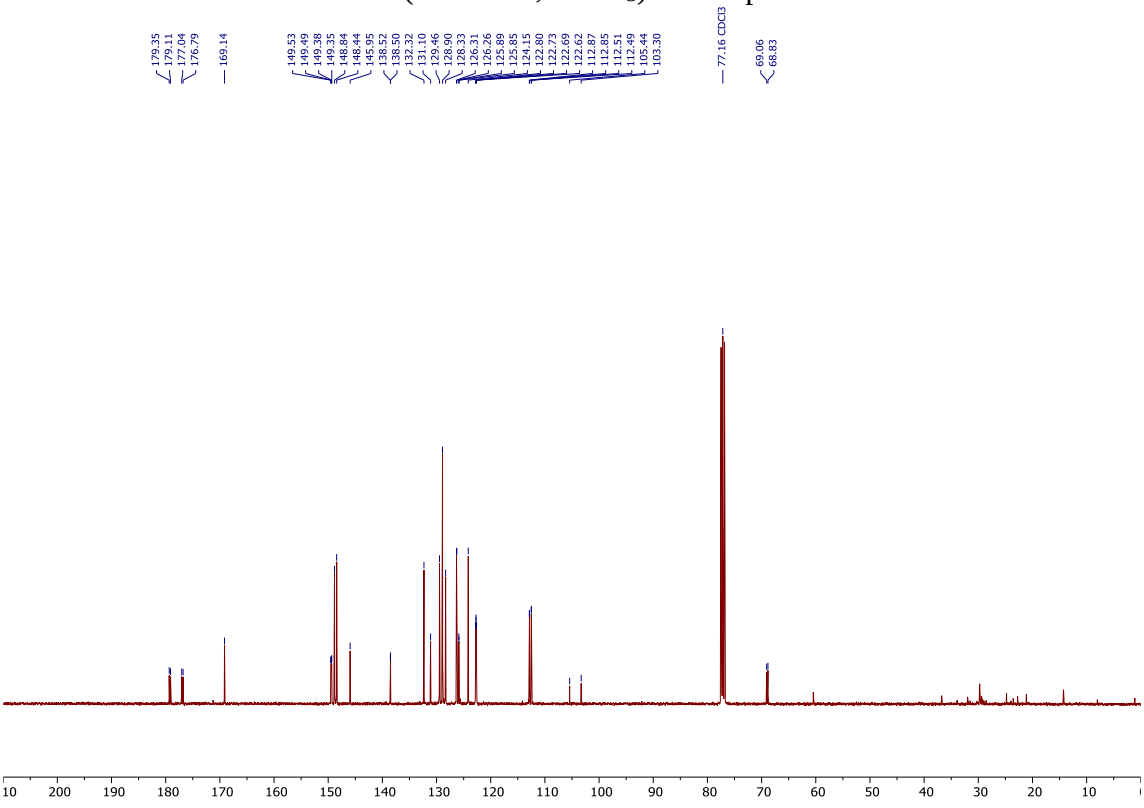
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4d**



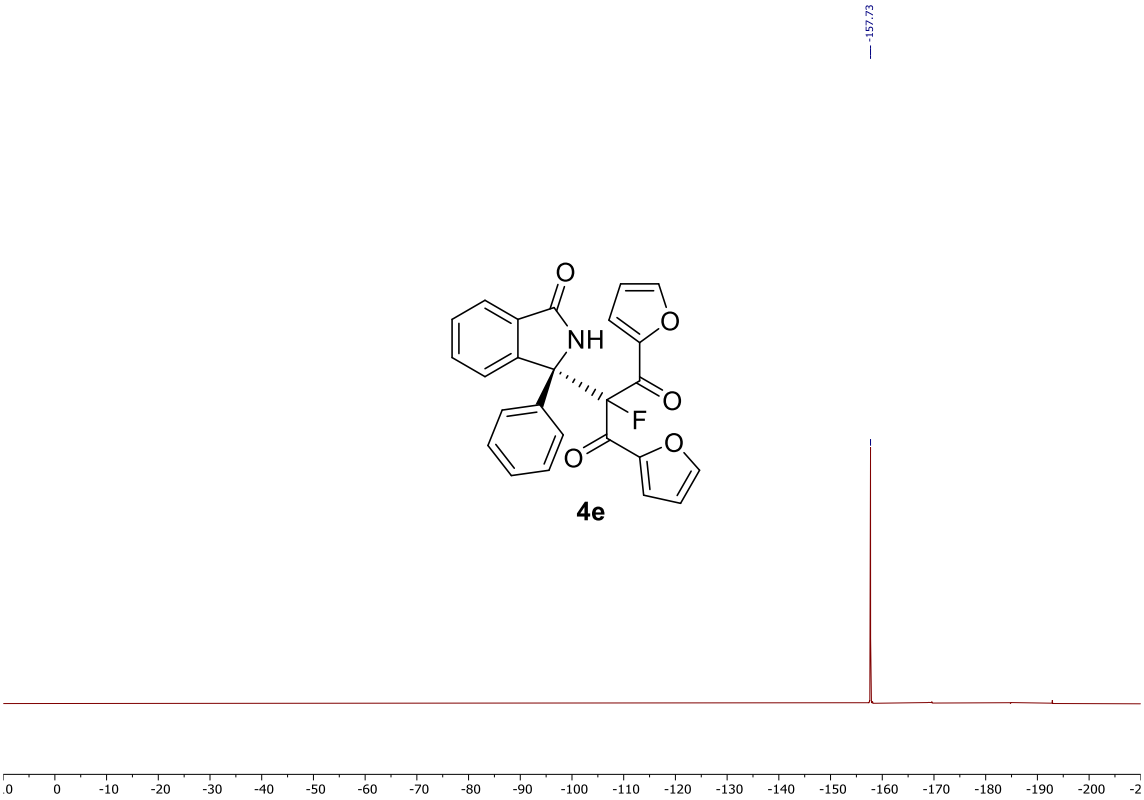
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4d**



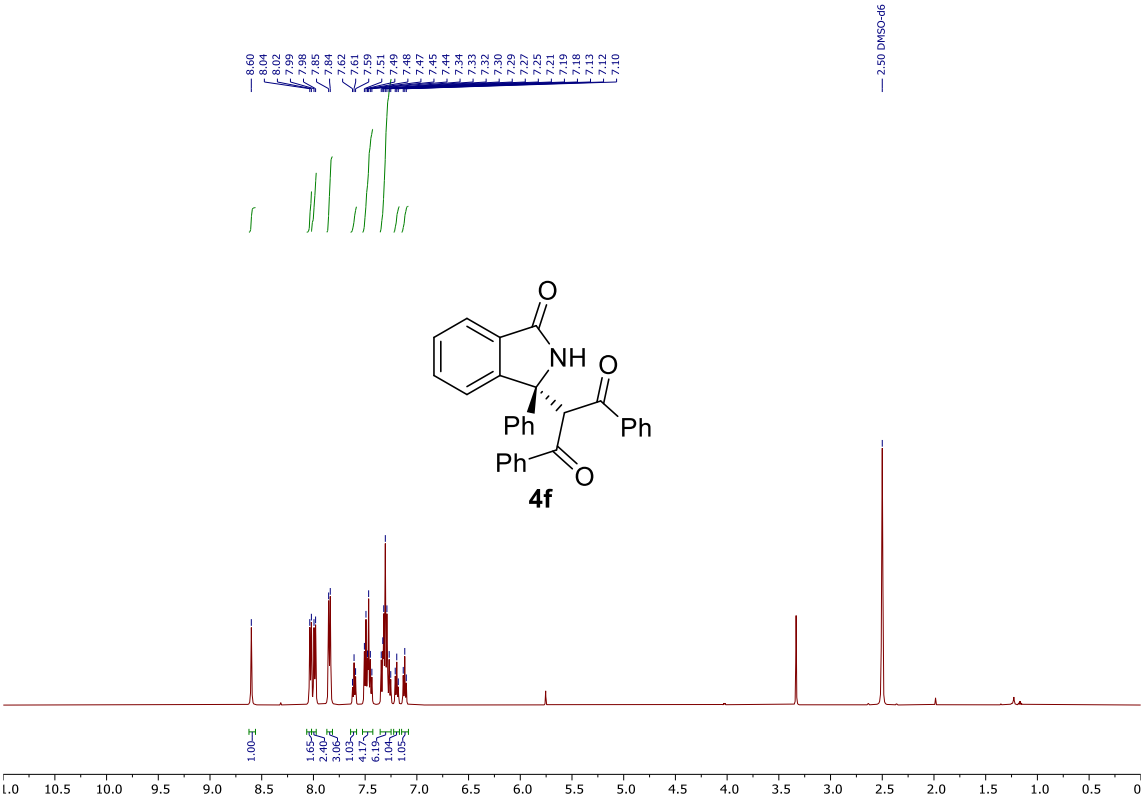
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4e**



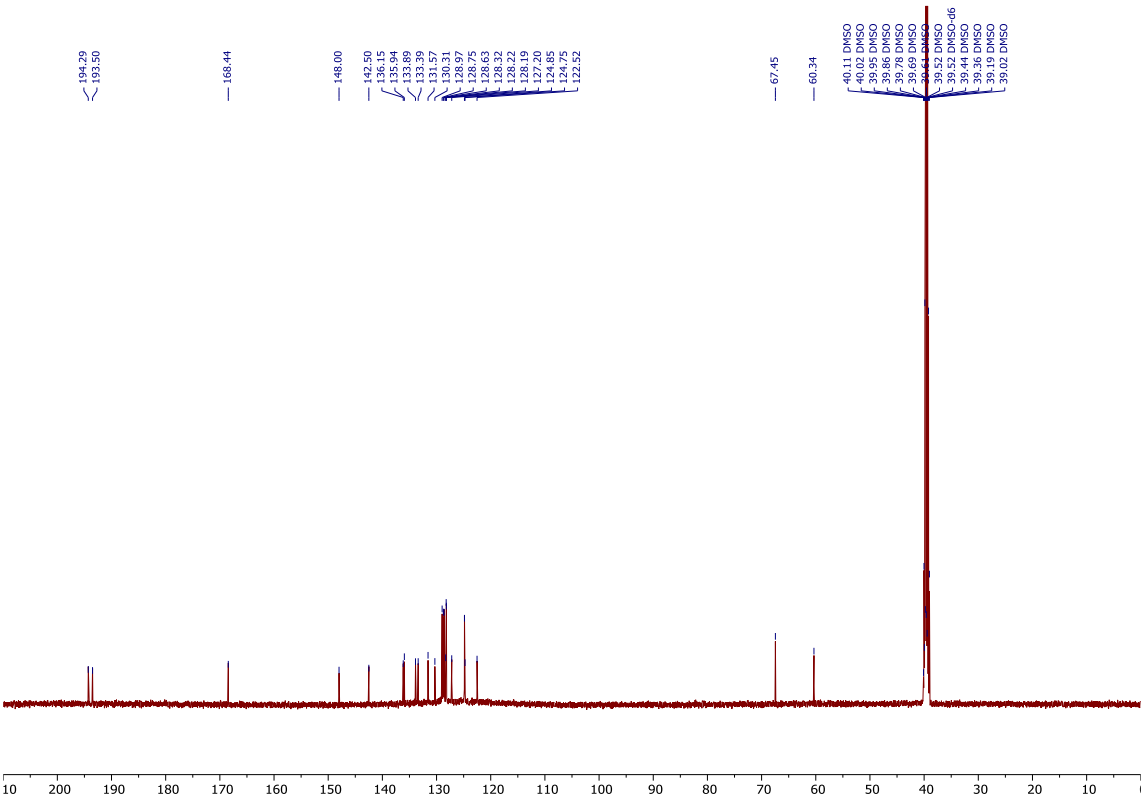
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4e**



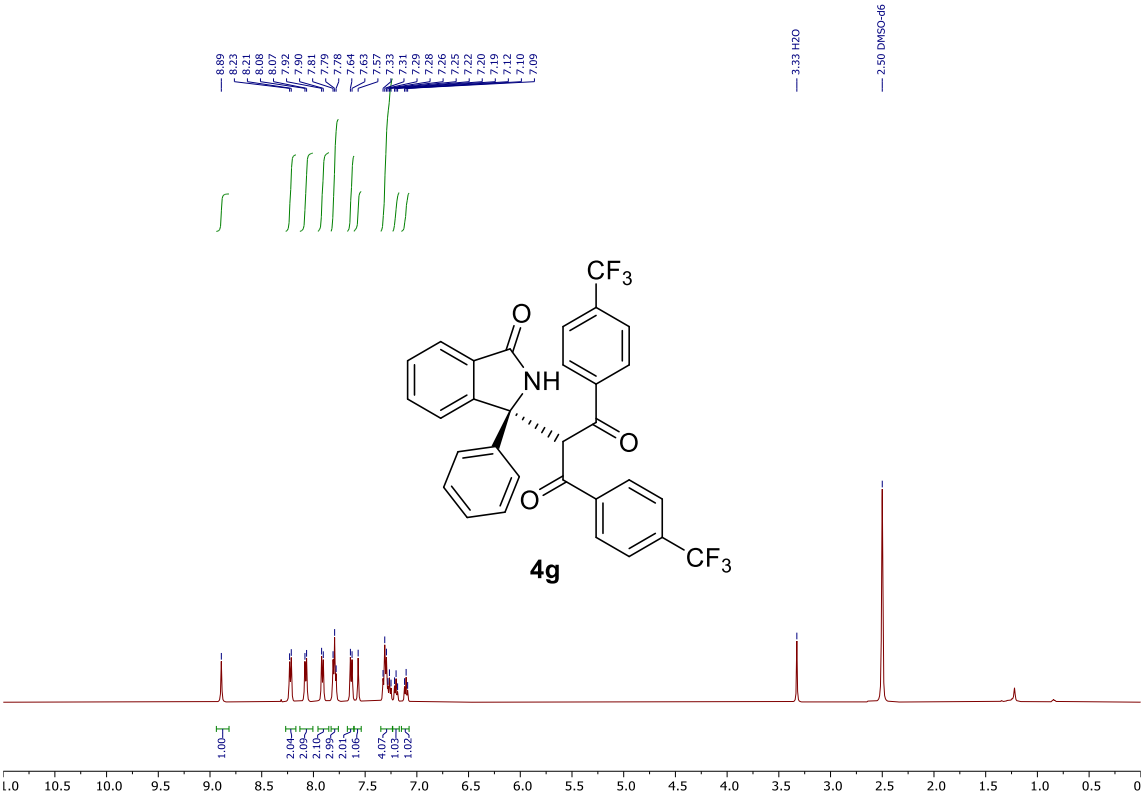
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4e**



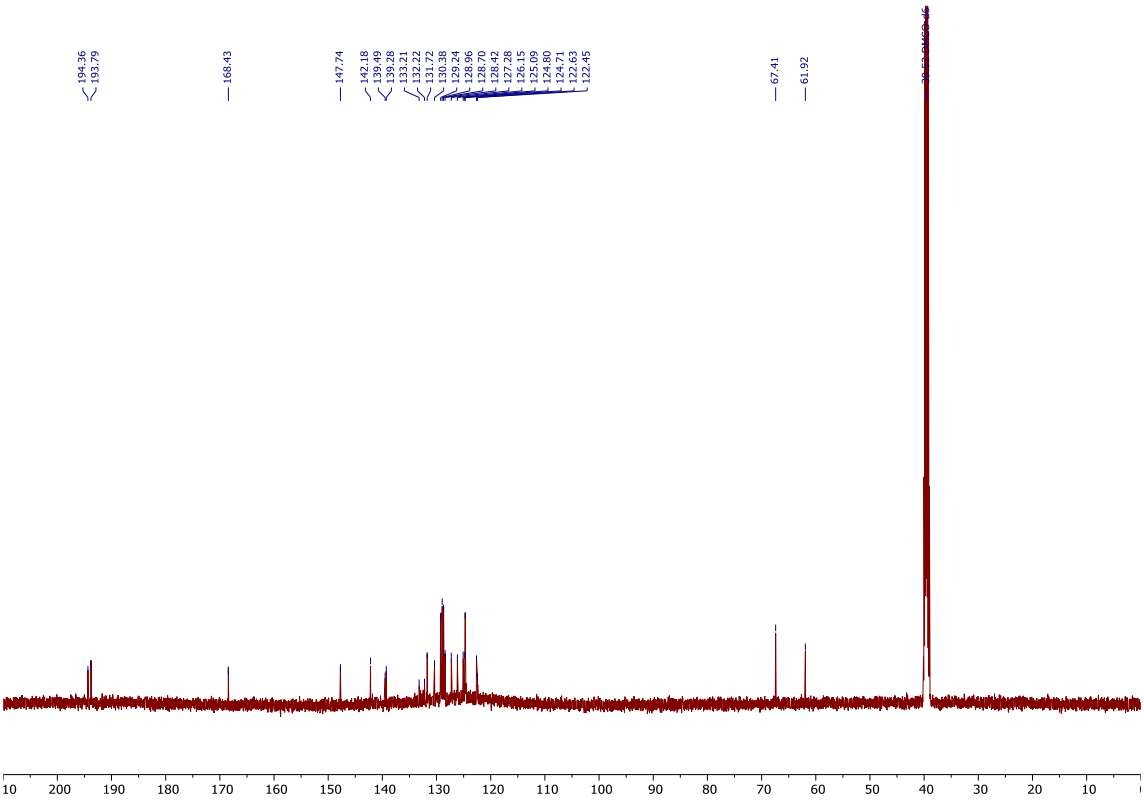
^{1}H NMR (500 MHz, DMSO-d$_6$) of compound **4f**



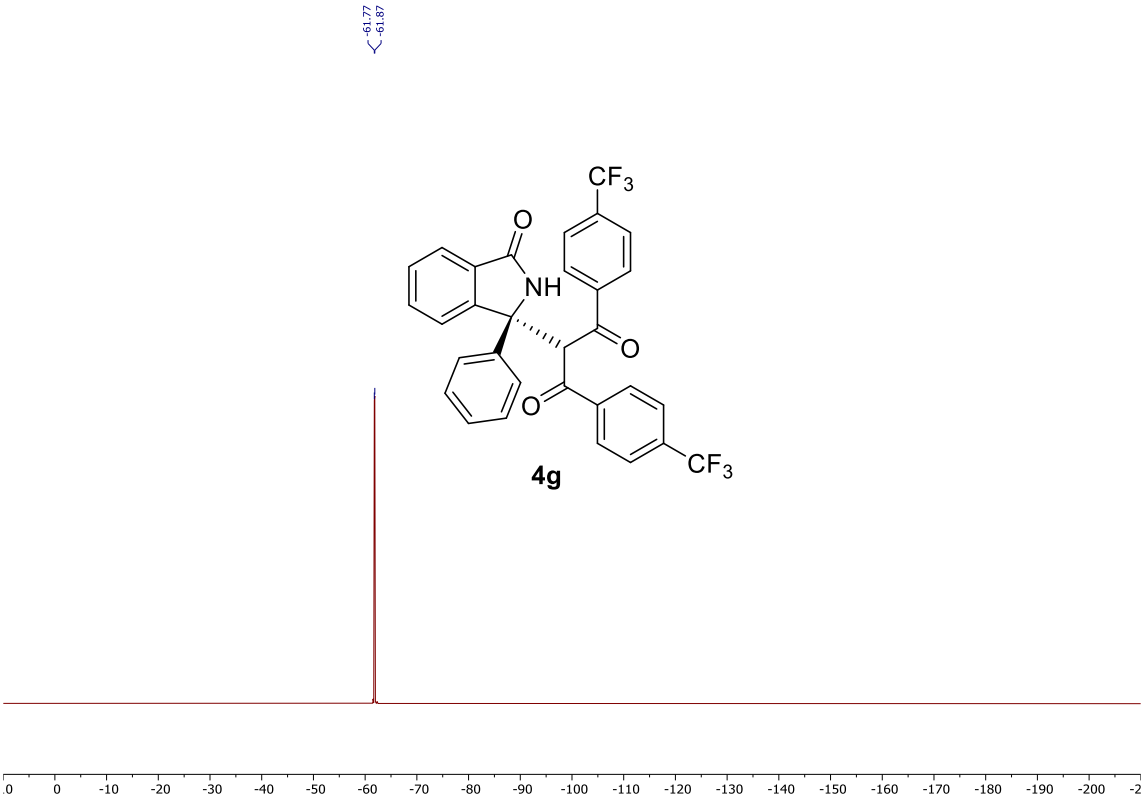
^{13}C NMR (125 MHz, DMSO-d$_6$) of compound **4f**



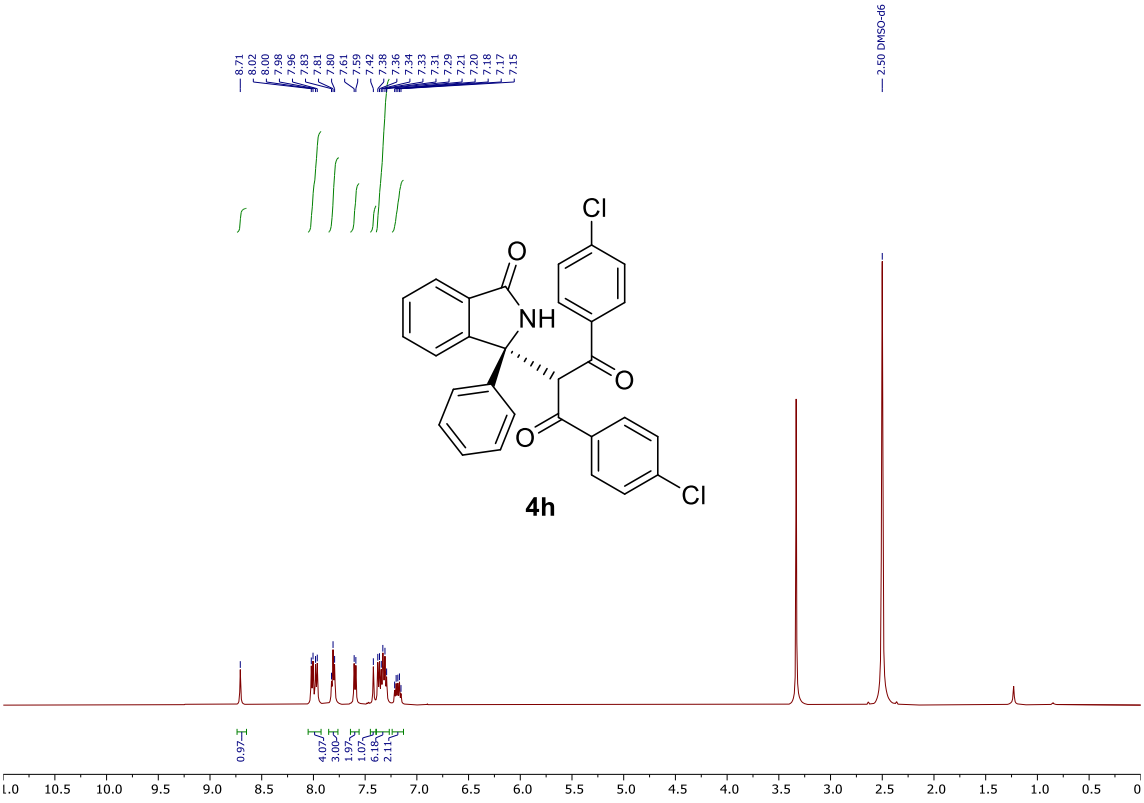
^{1}H NMR (500 MHz, DMSO-d$_6$) of compound **4g**



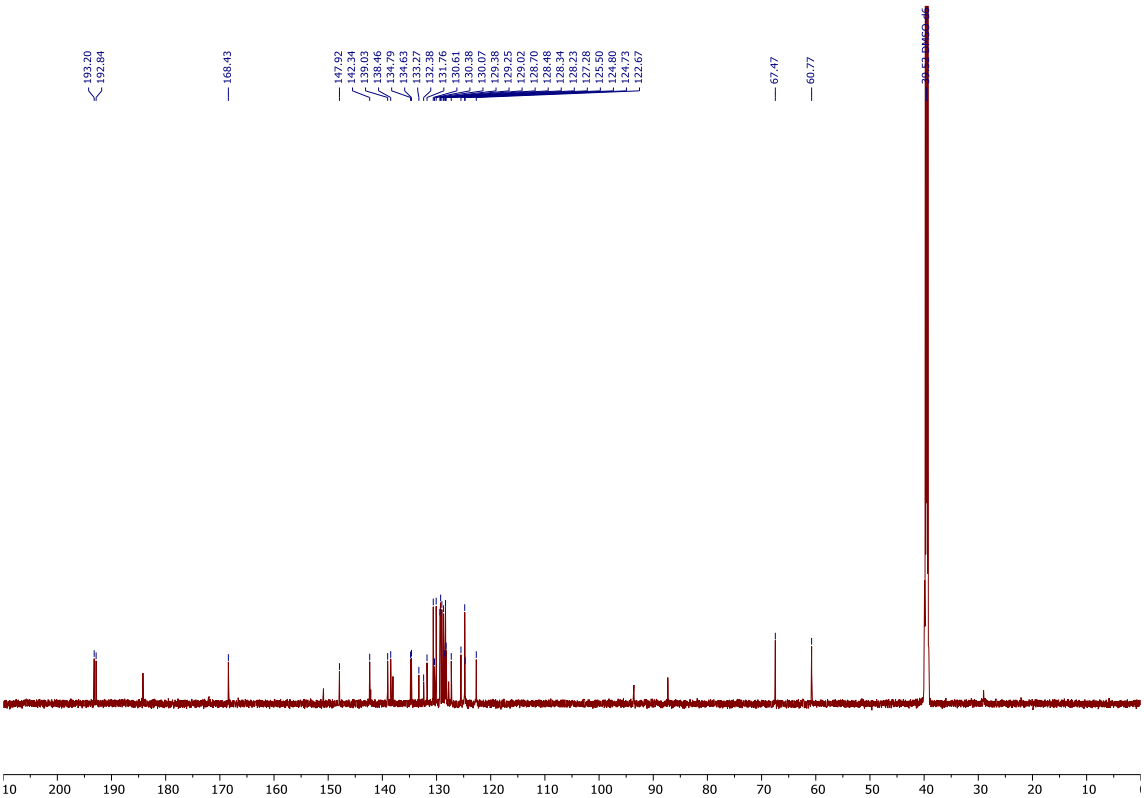
^{13}C NMR (125 MHz, DMSO-d$_6$) of compound **4g**



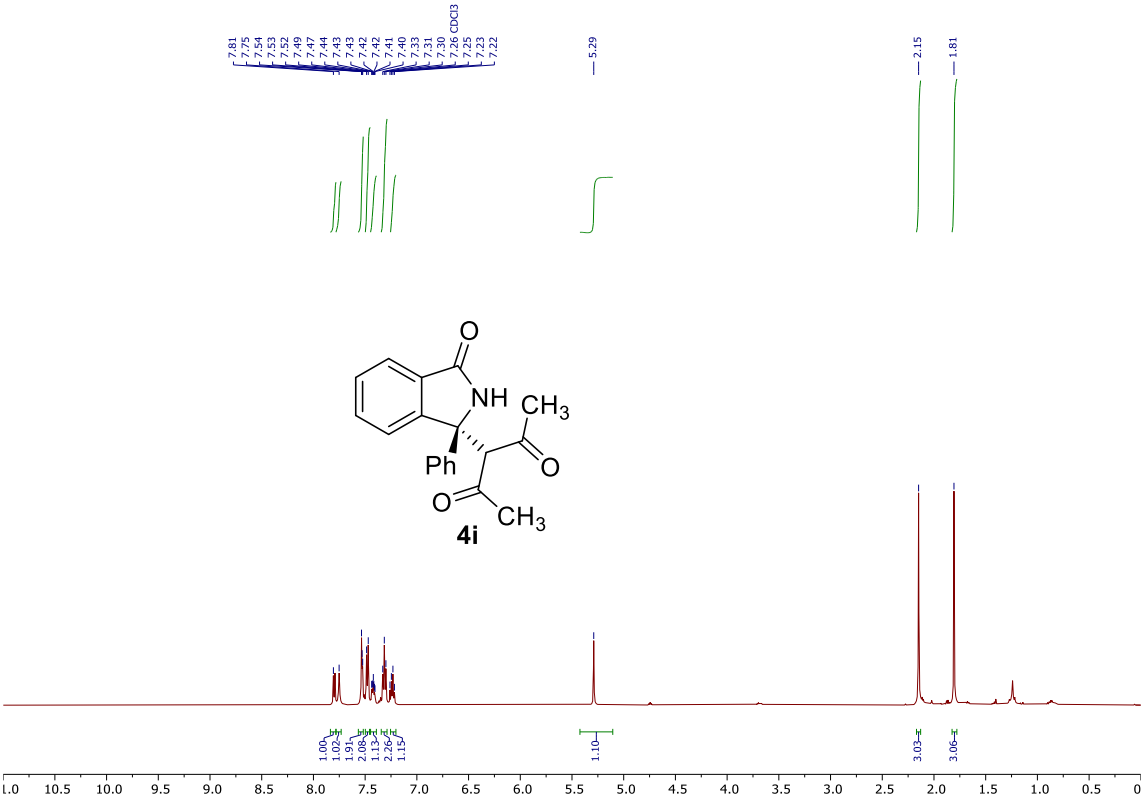
^{19}F NMR (375 MHz, DMSO-d_6) of compound **4g**



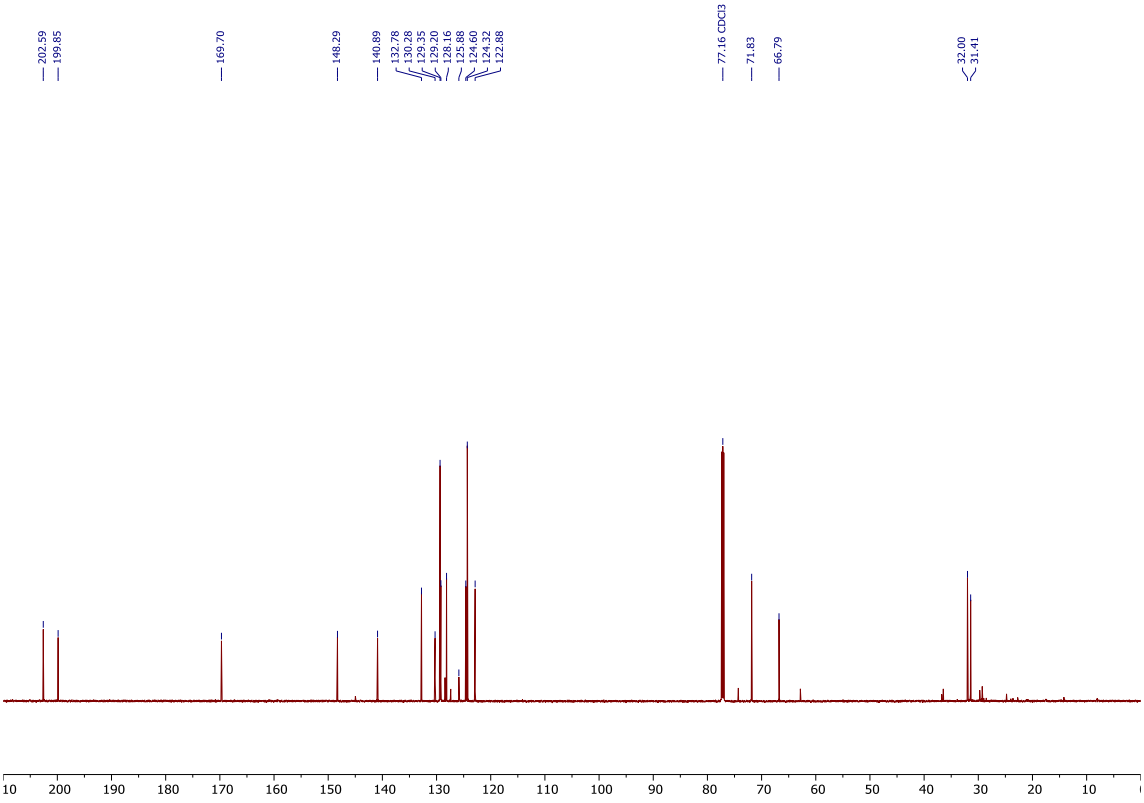
^{1}H NMR (500 MHz, DMSO-d_6) of compound **4h**



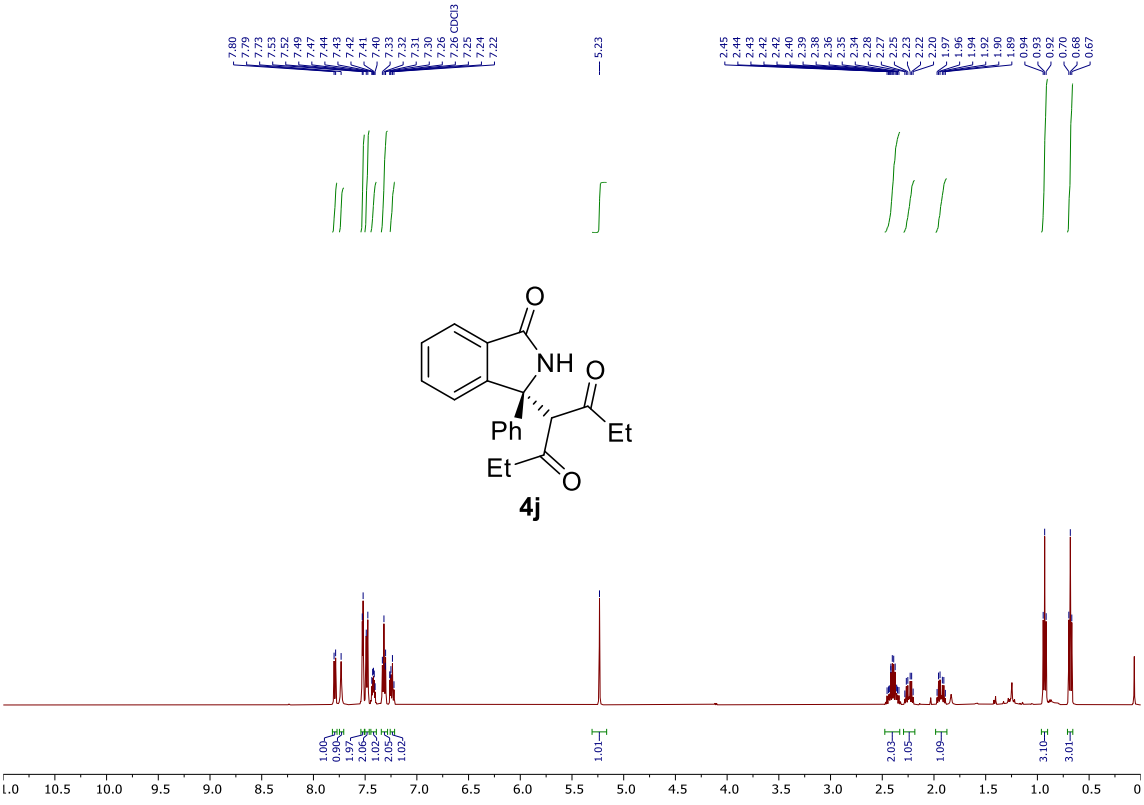
^{13}C NMR (175 MHz, DMSO-d_6) of compound **4h**



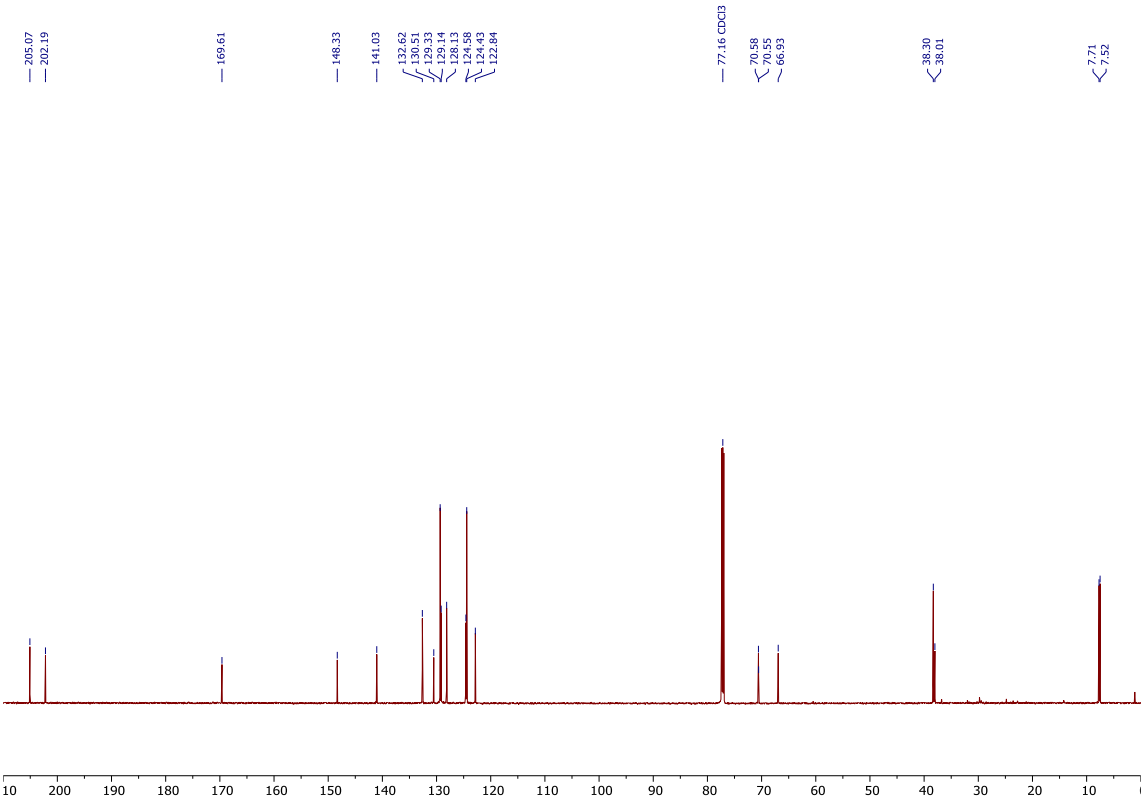
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4i**



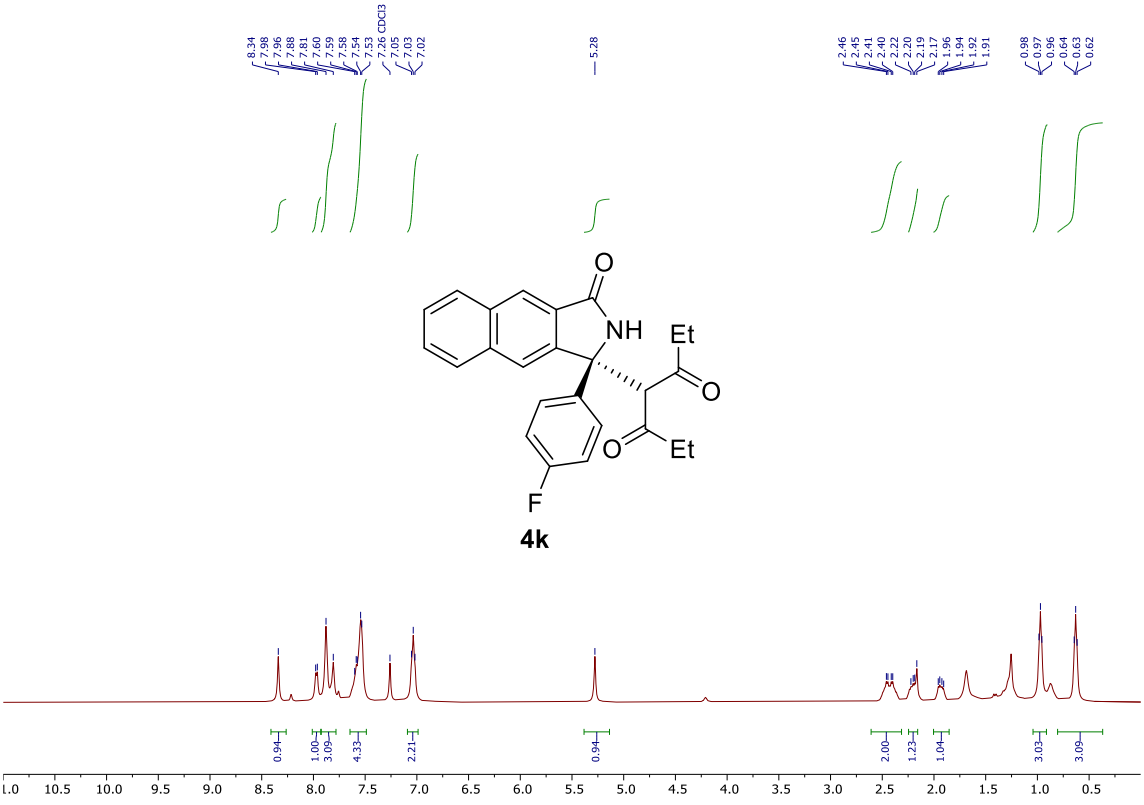
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4i**



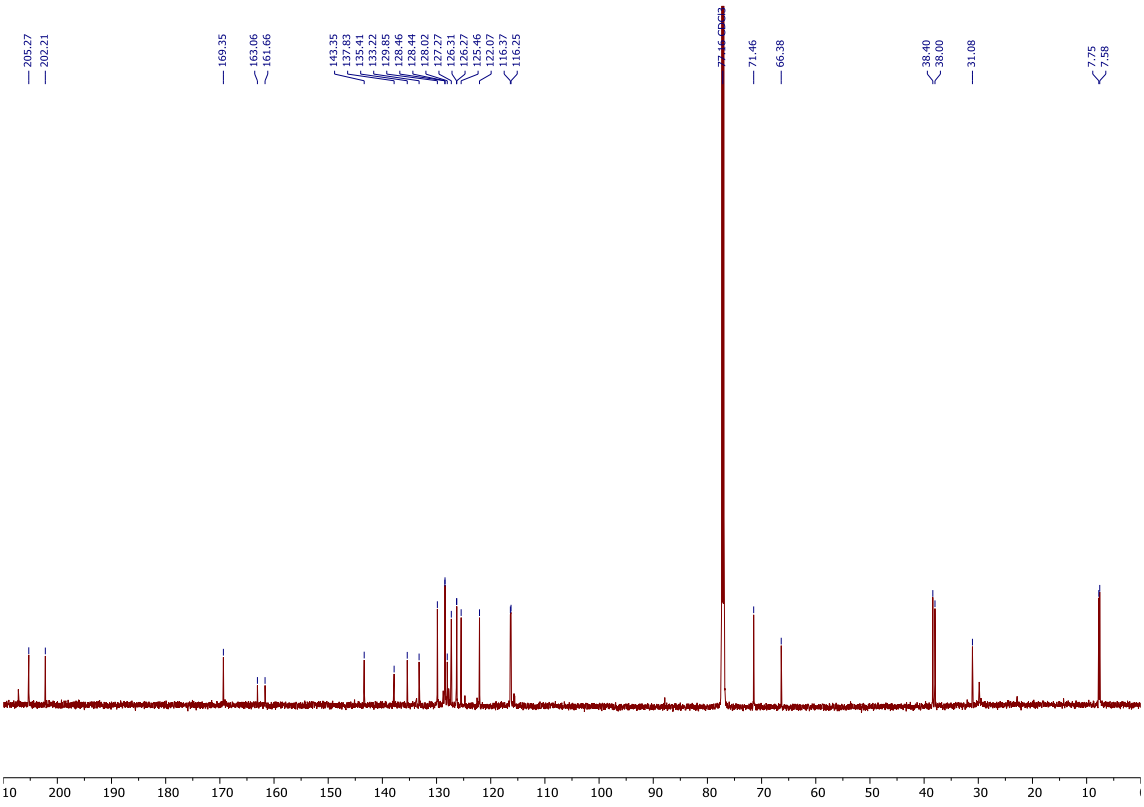
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4j**



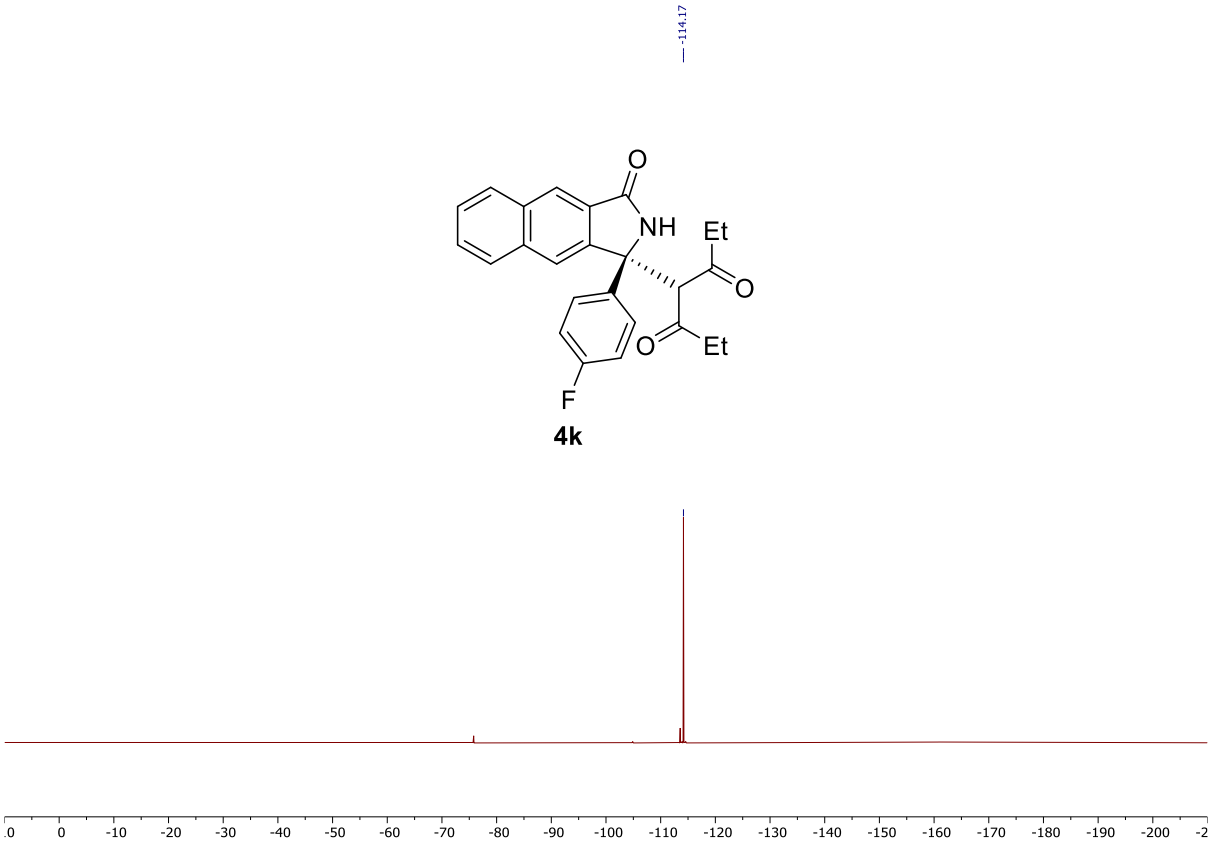
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4j**



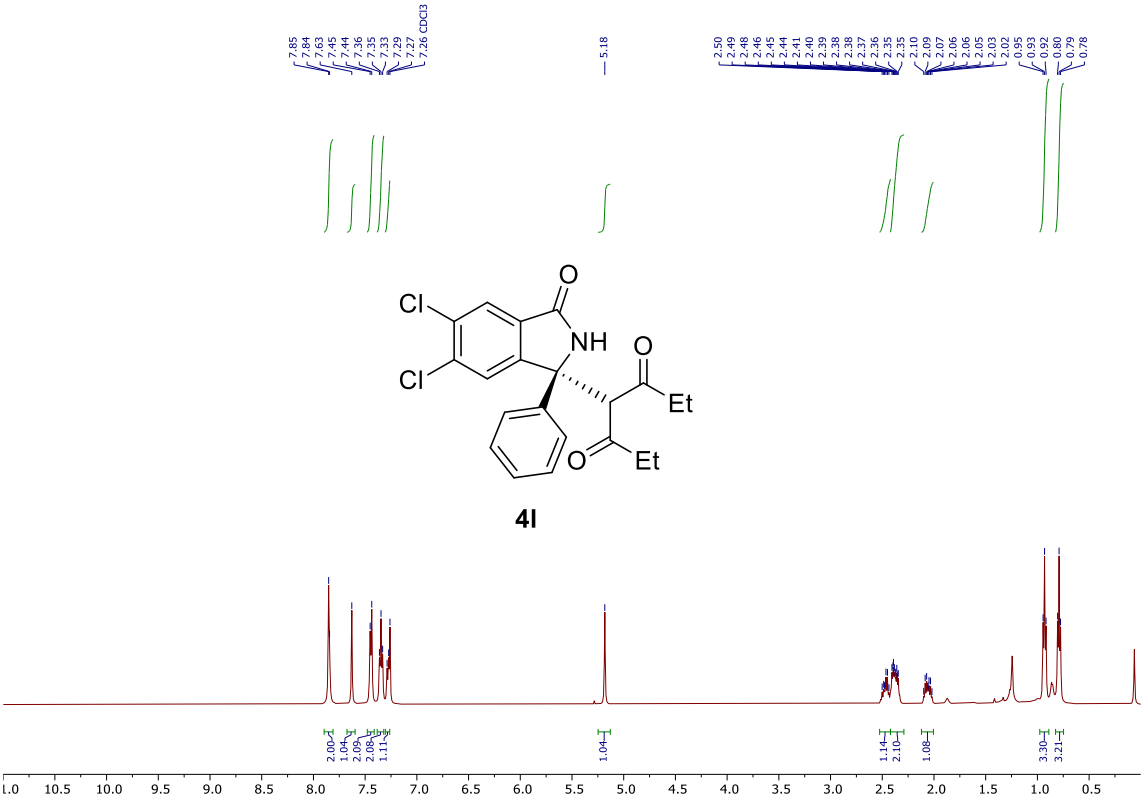
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4k**



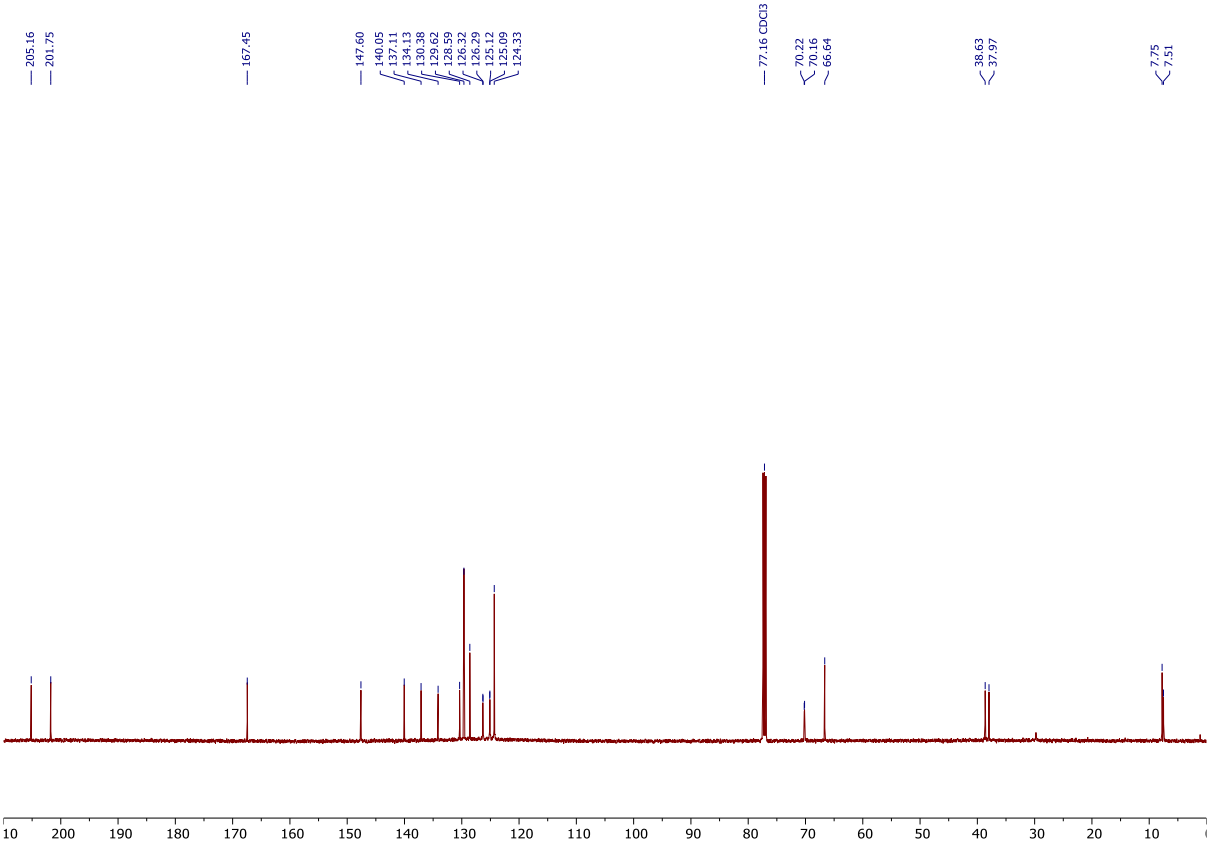
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4k**



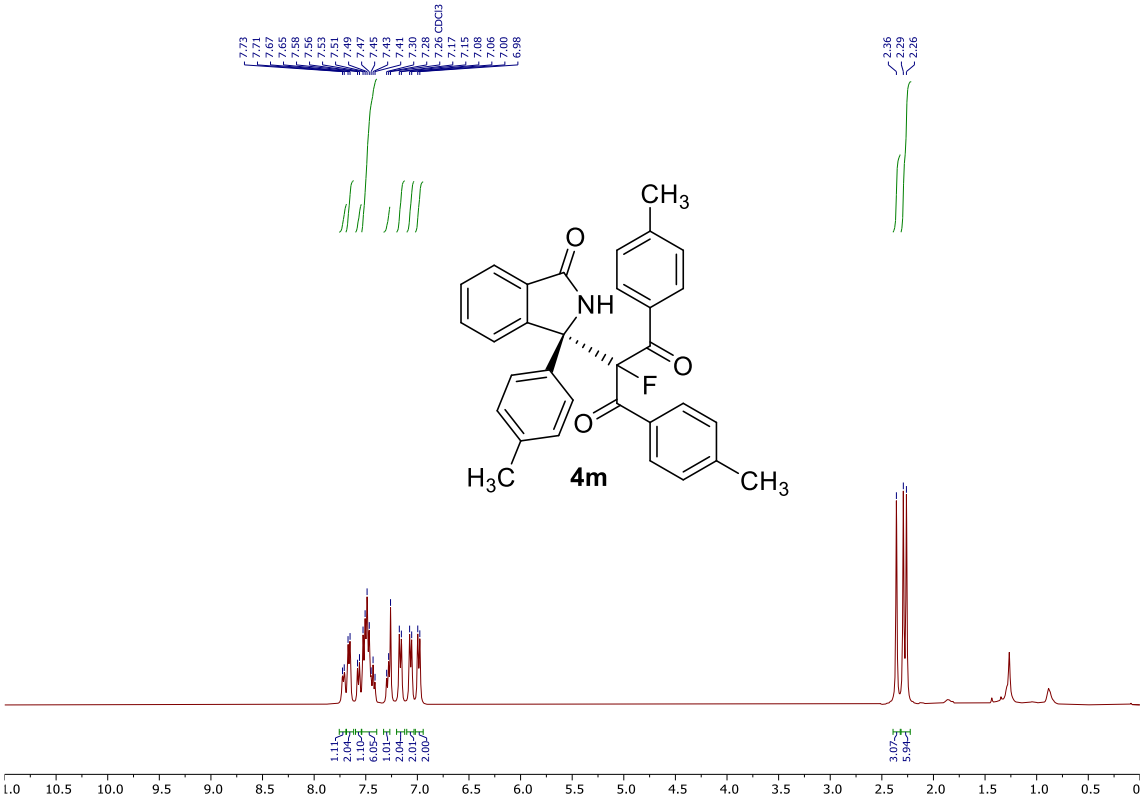
^{19}F NMR (175 MHz, $CDCl_3$) of compound **4k**



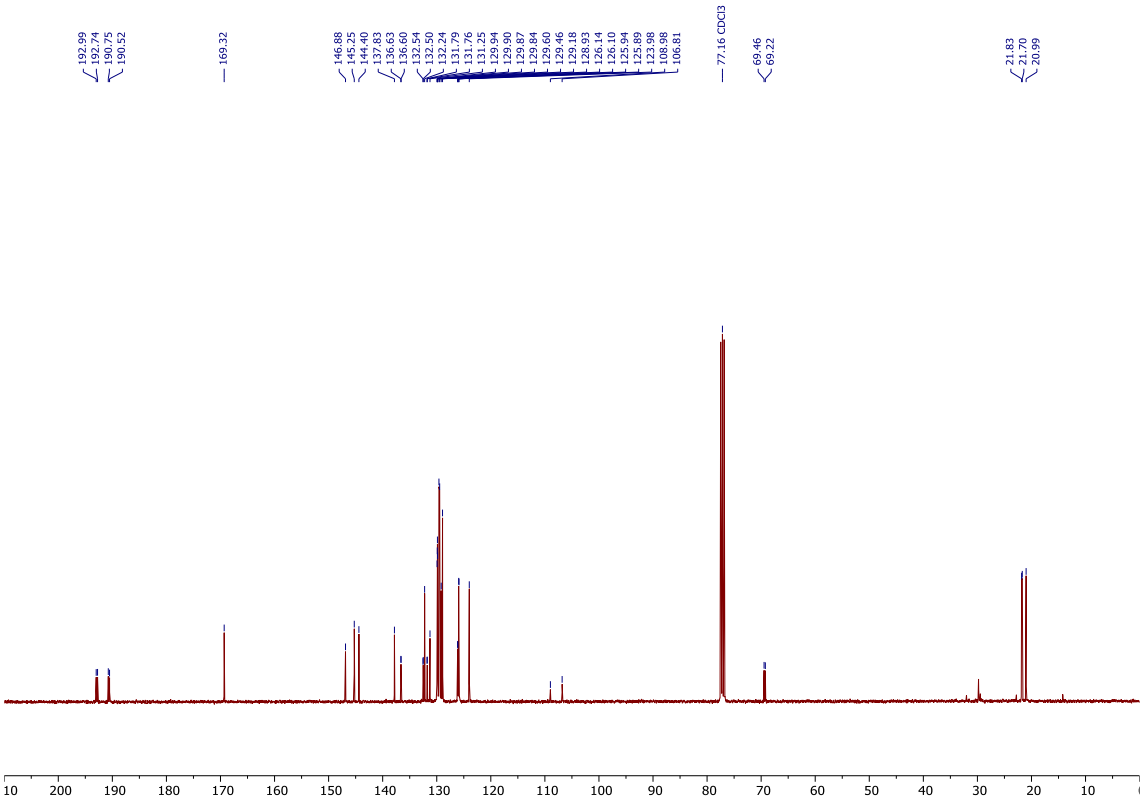
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4l**



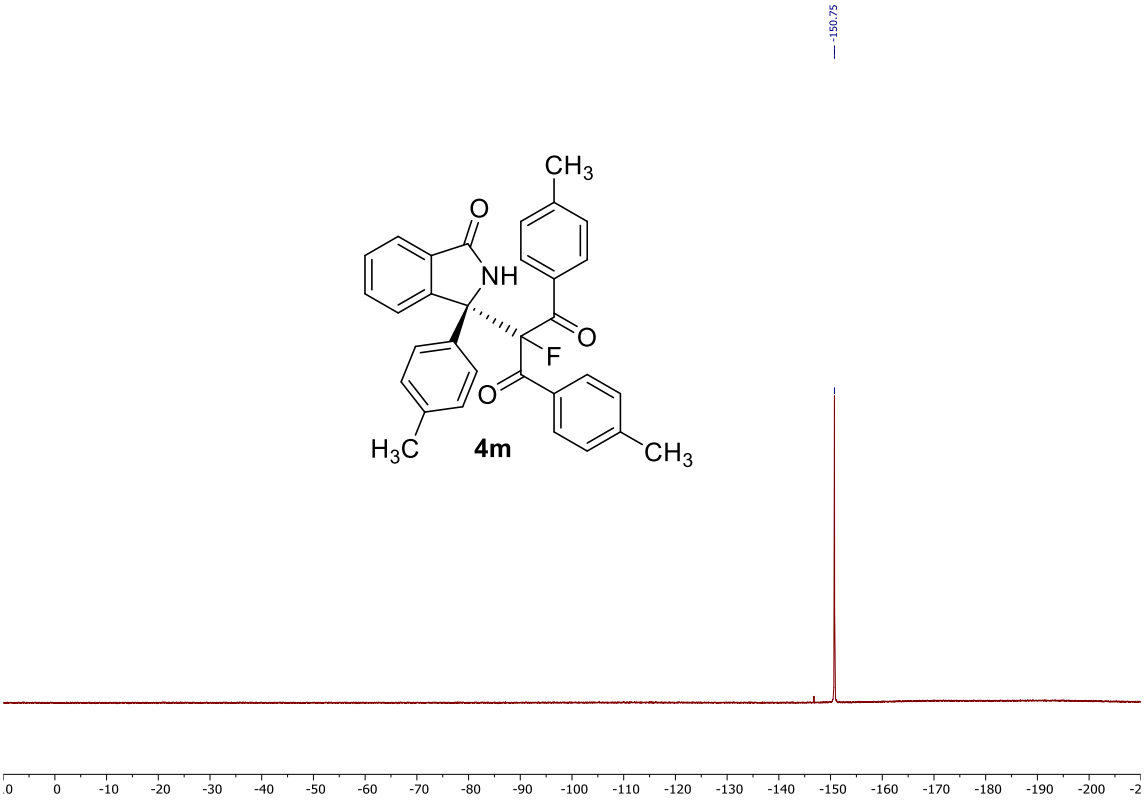
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4l**



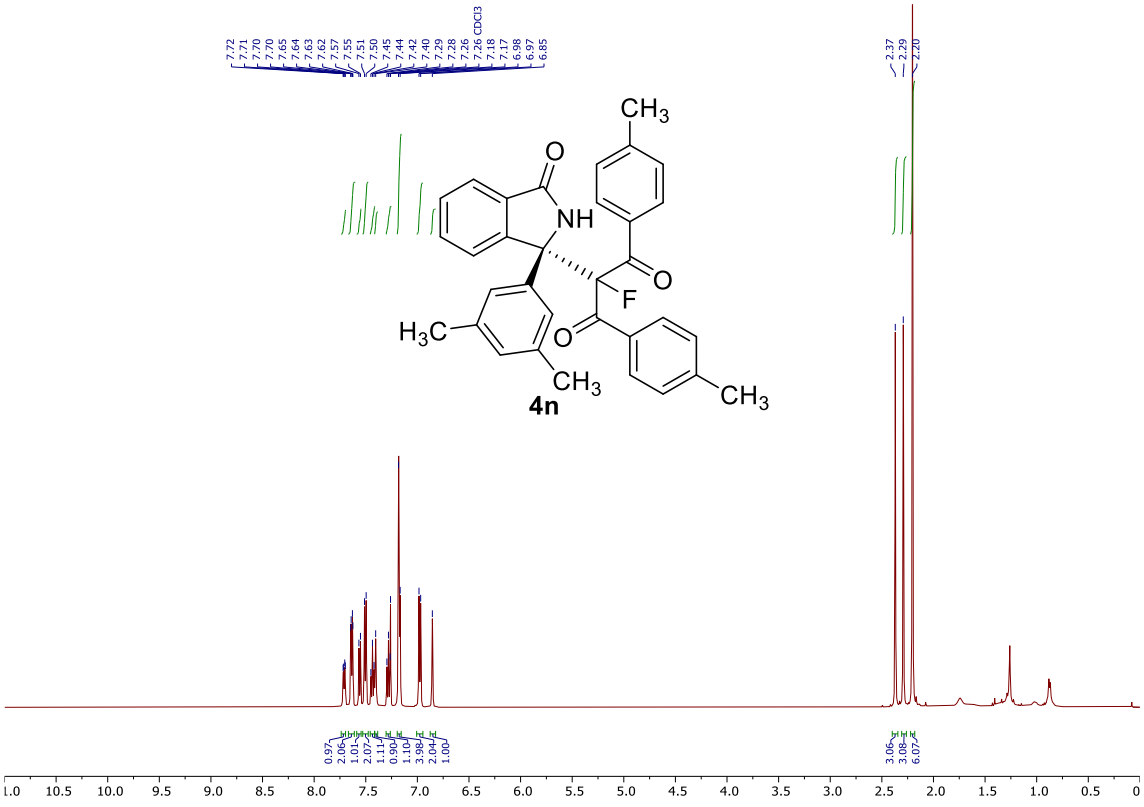
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4m**



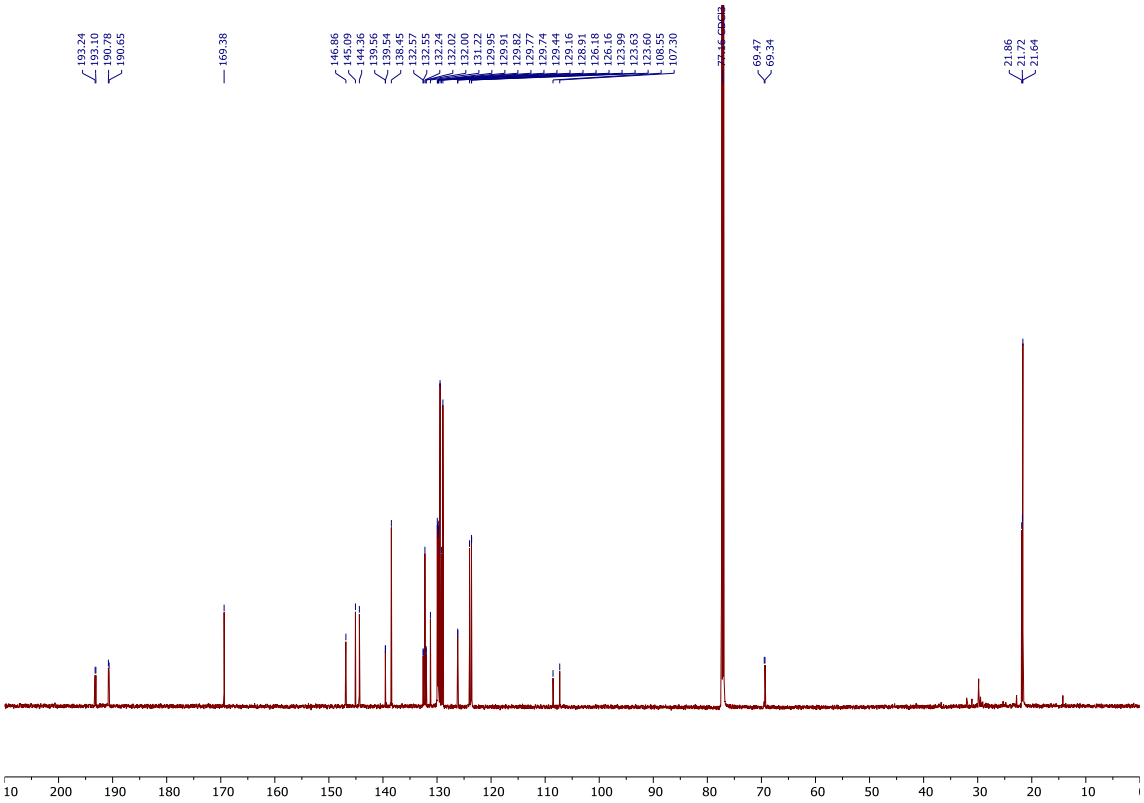
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4m**



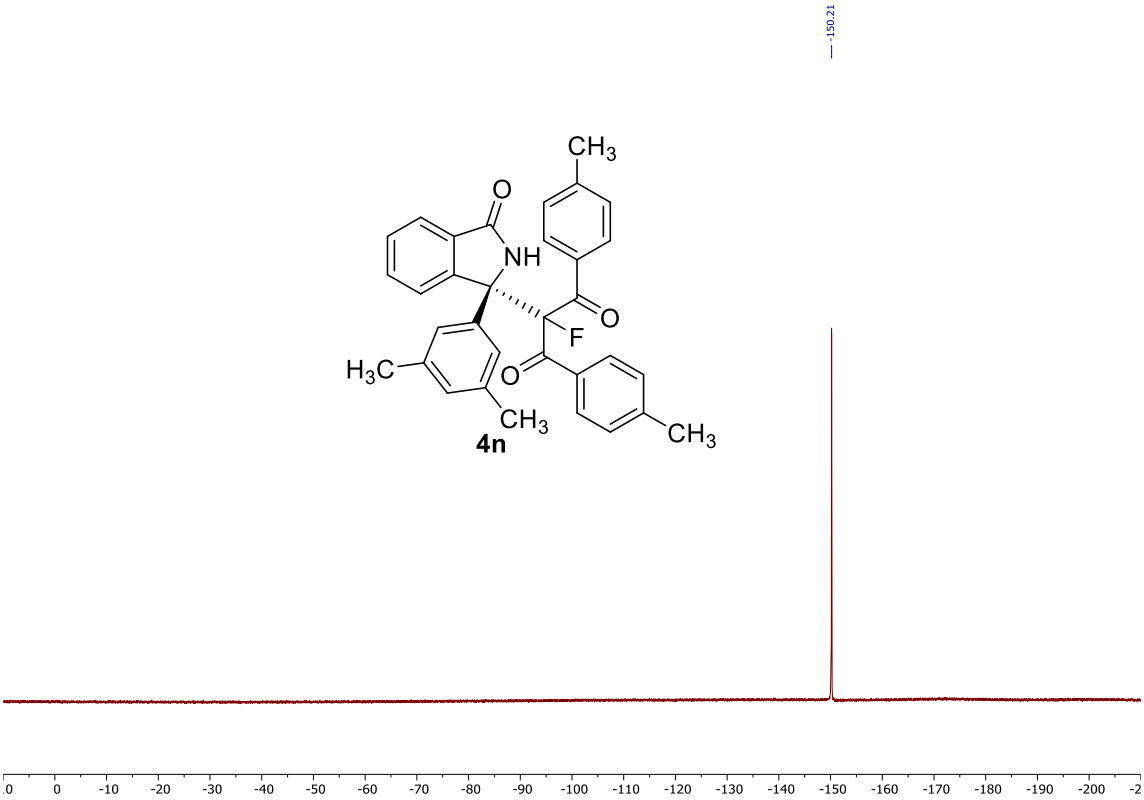
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4m**



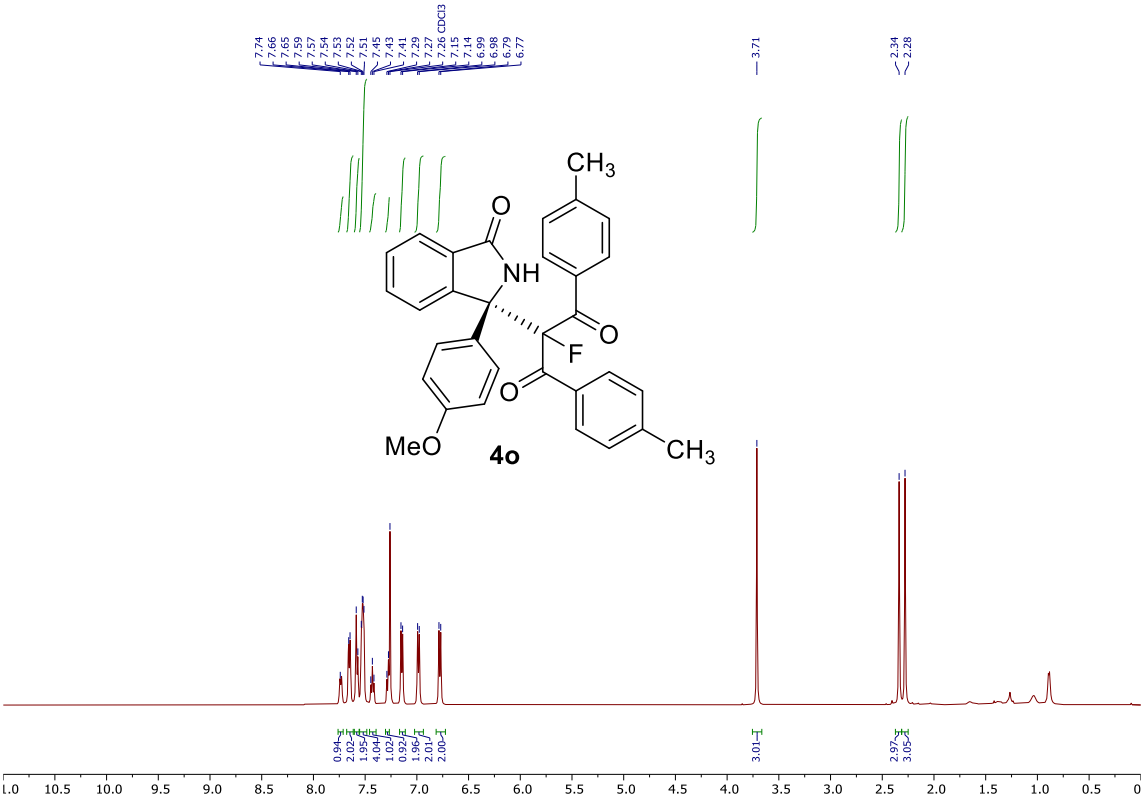
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4n**



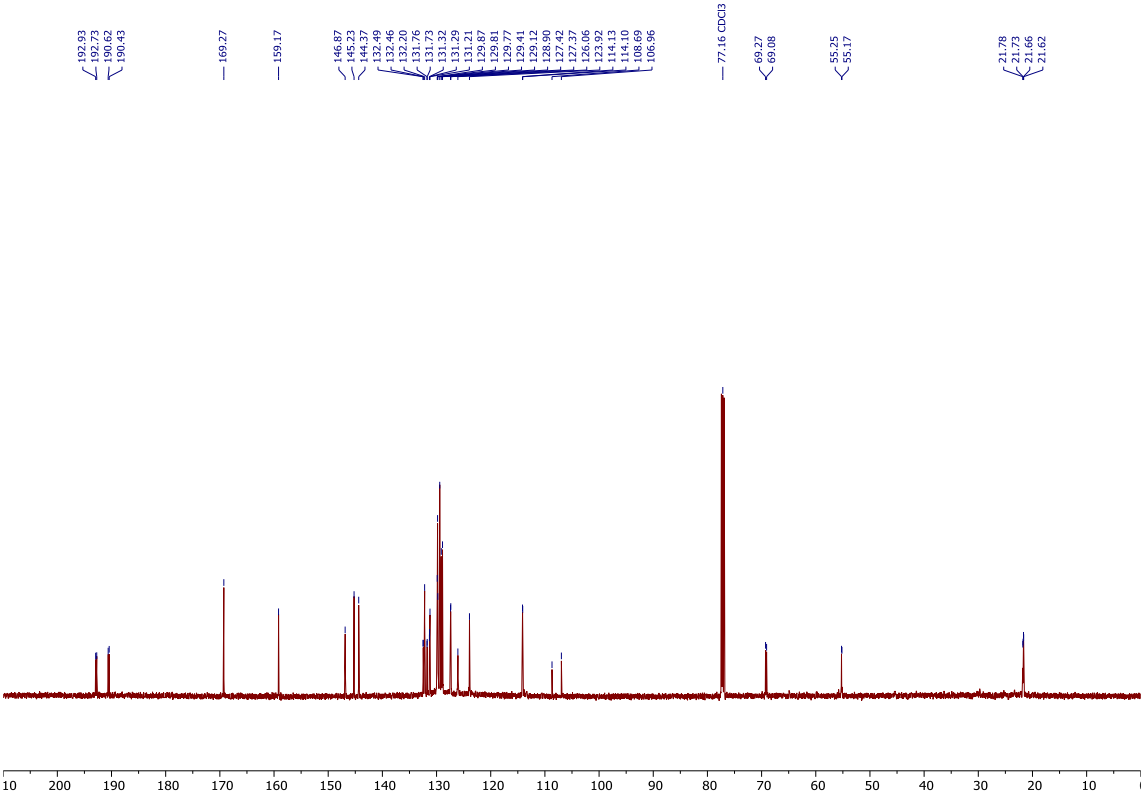
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4n**



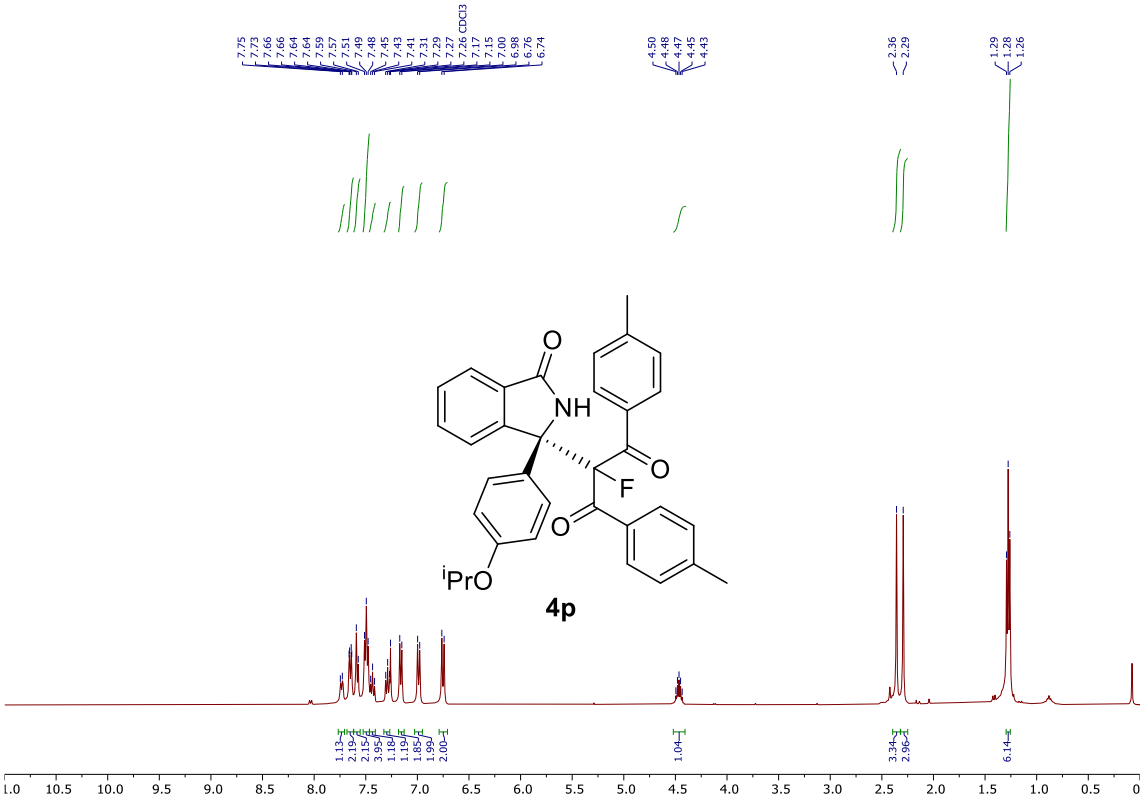
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4n**



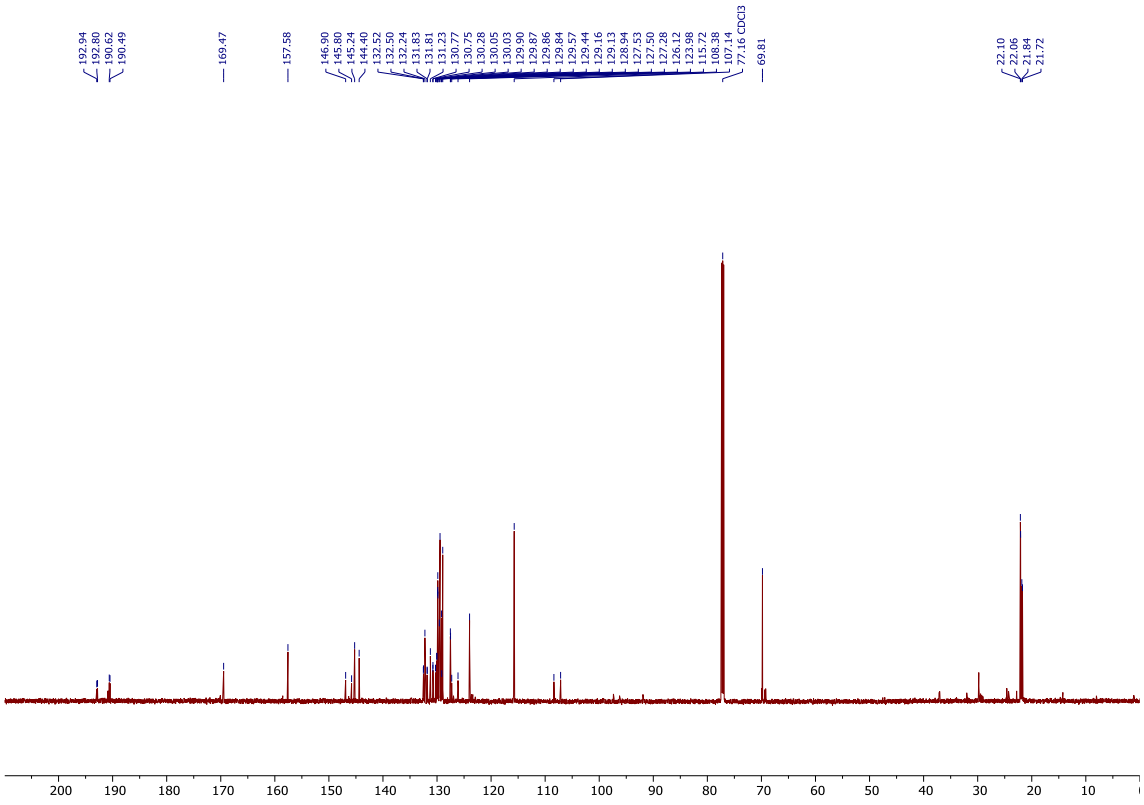
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4o**



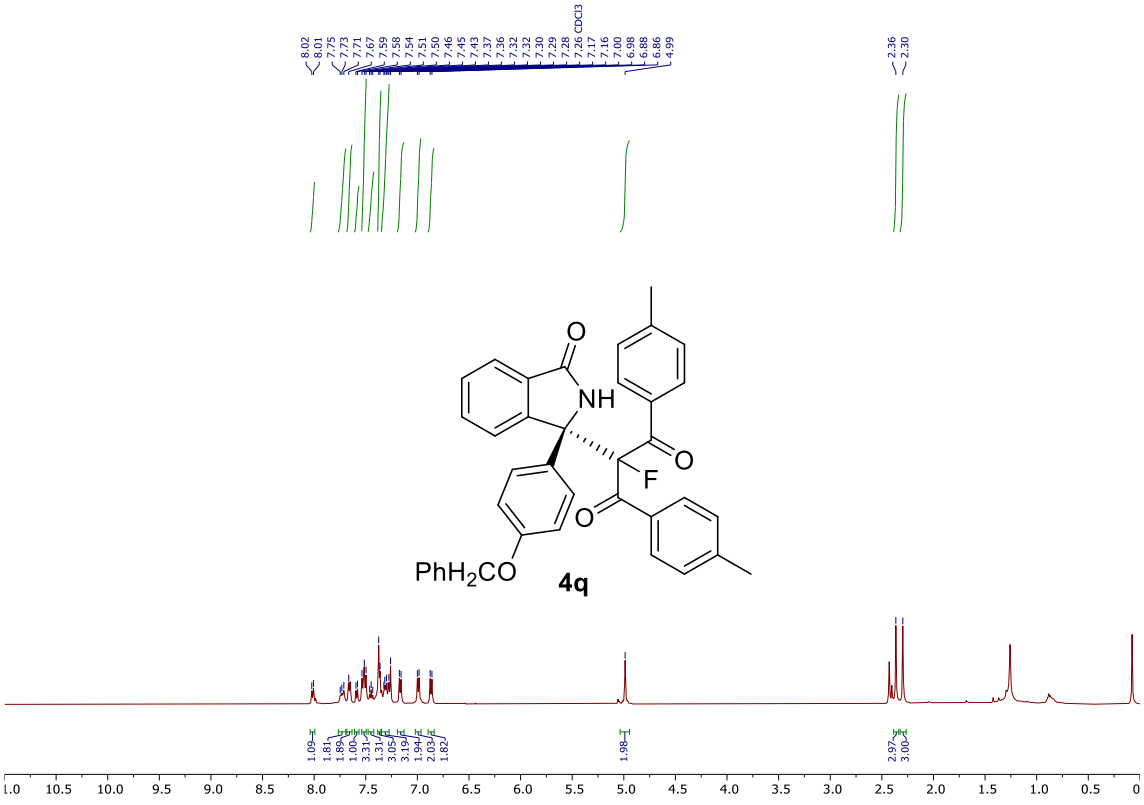
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4o**



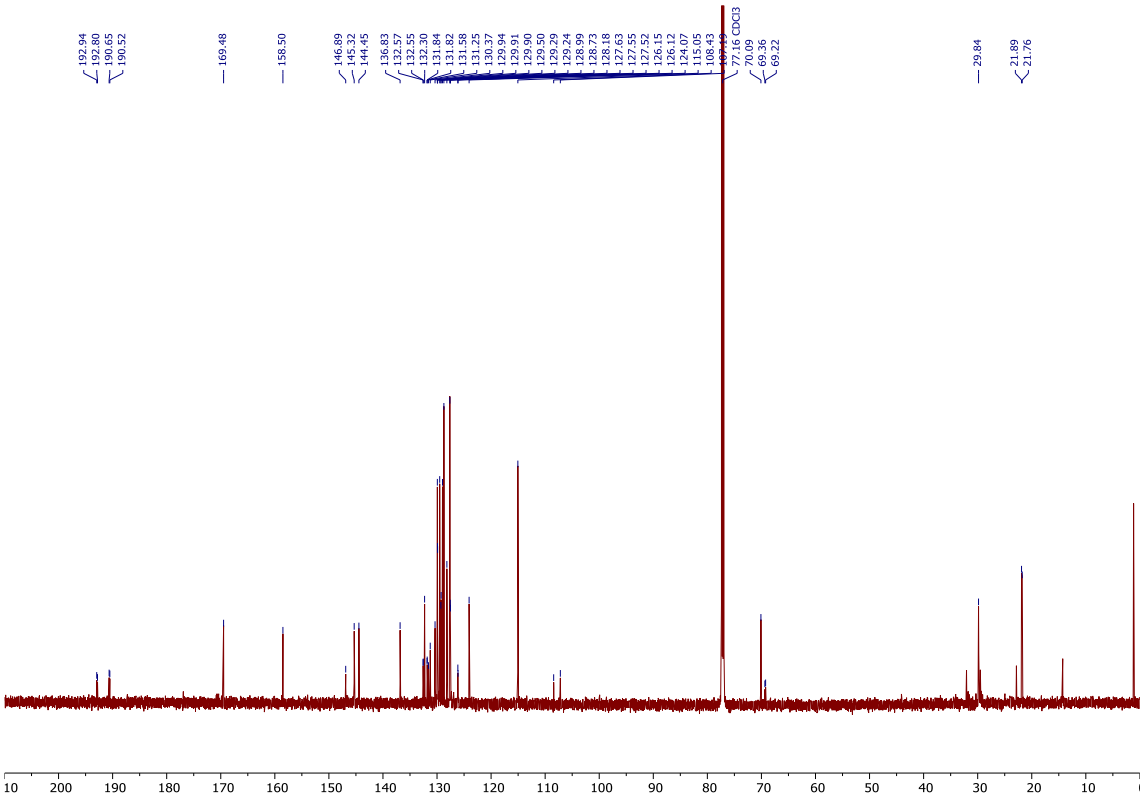
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4p**



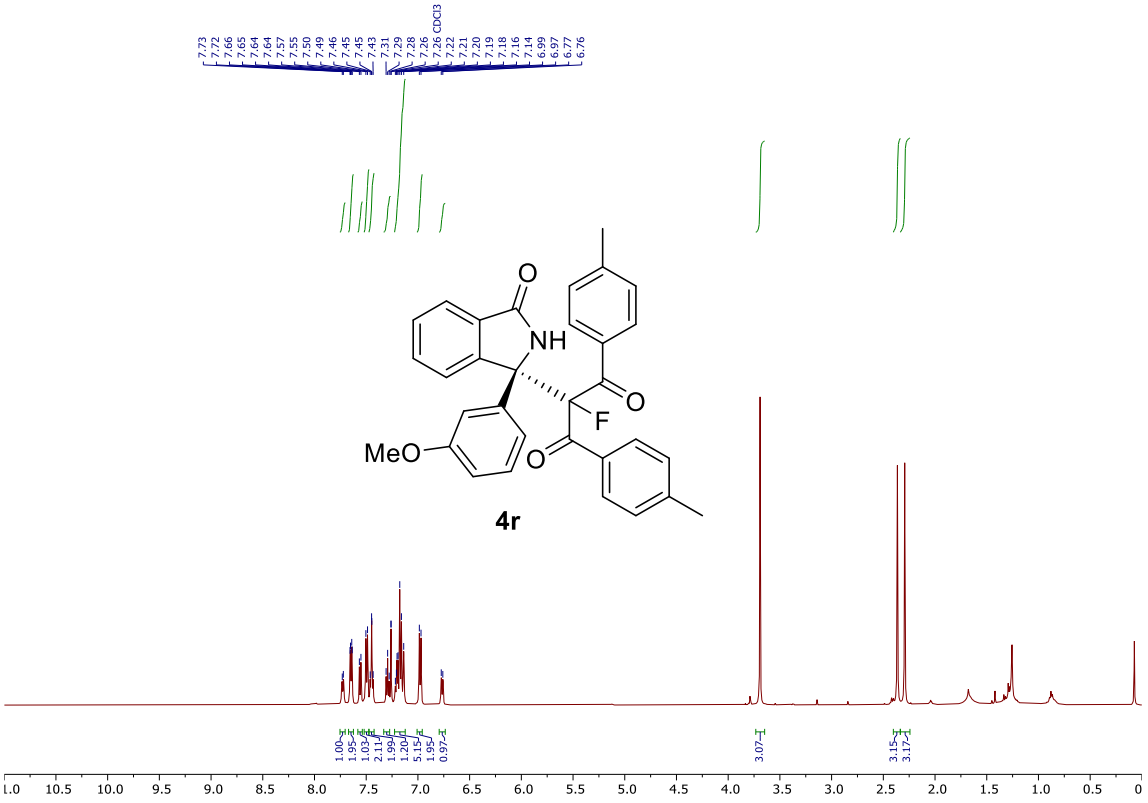
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4p**



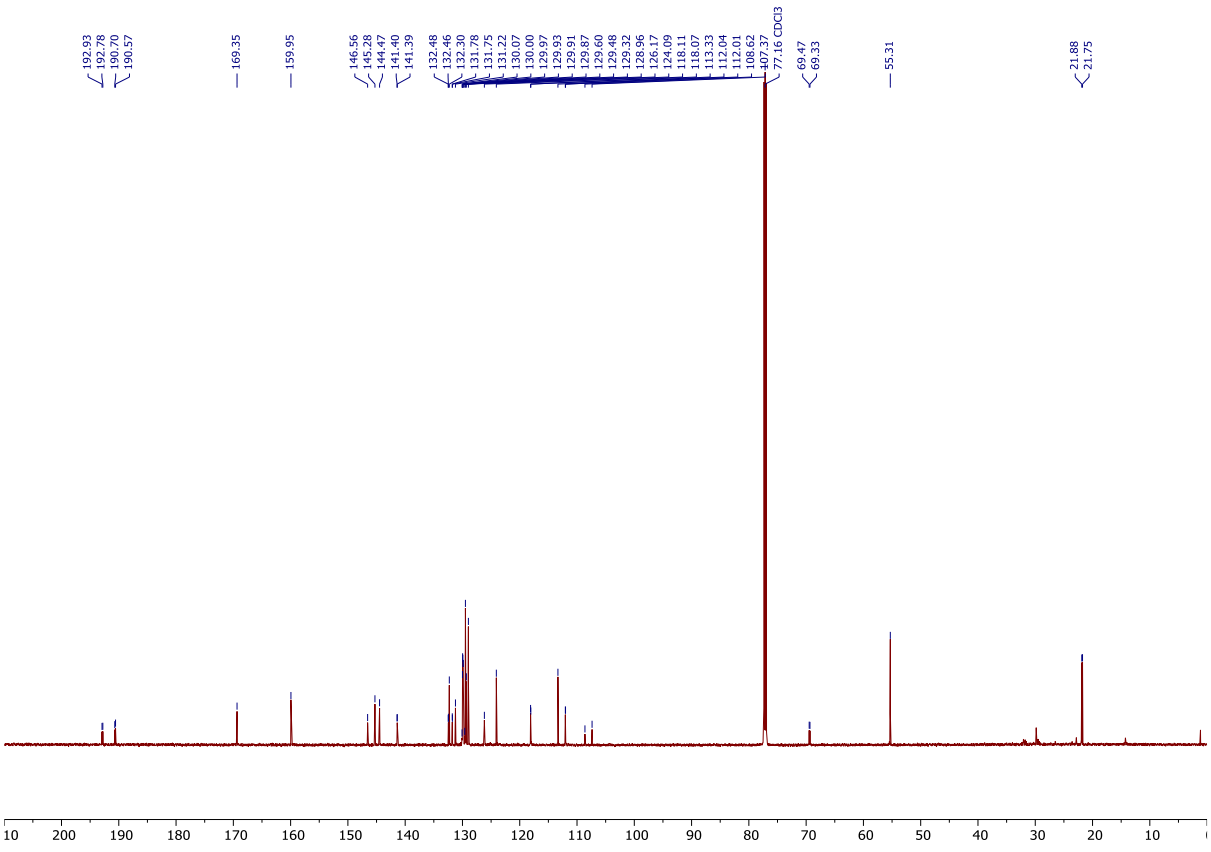
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4q**



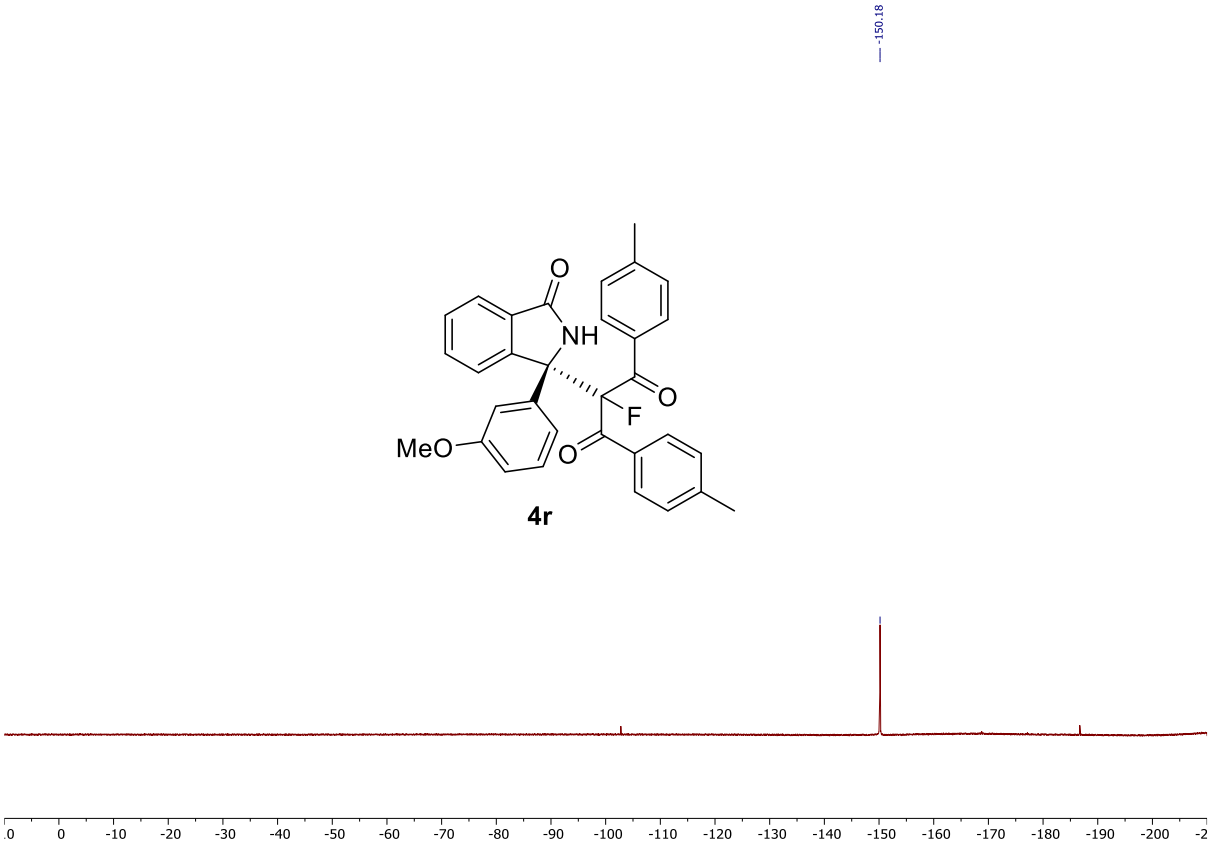
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4q**



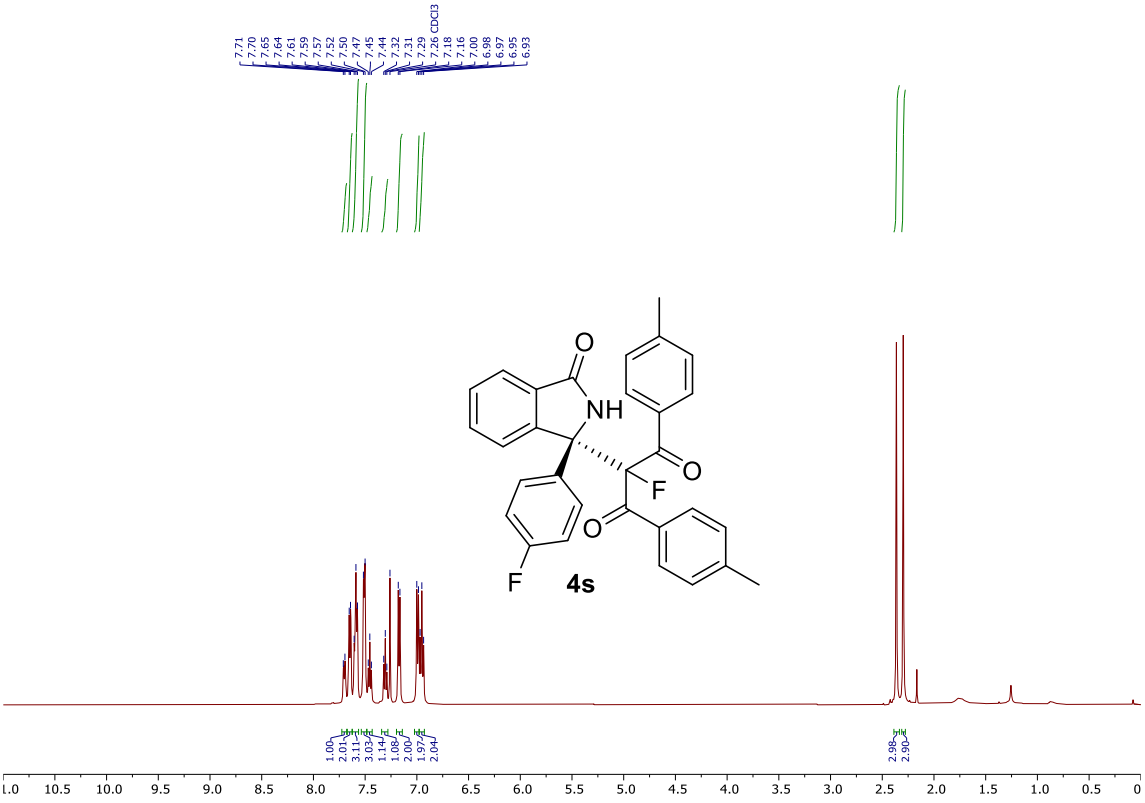
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4r**



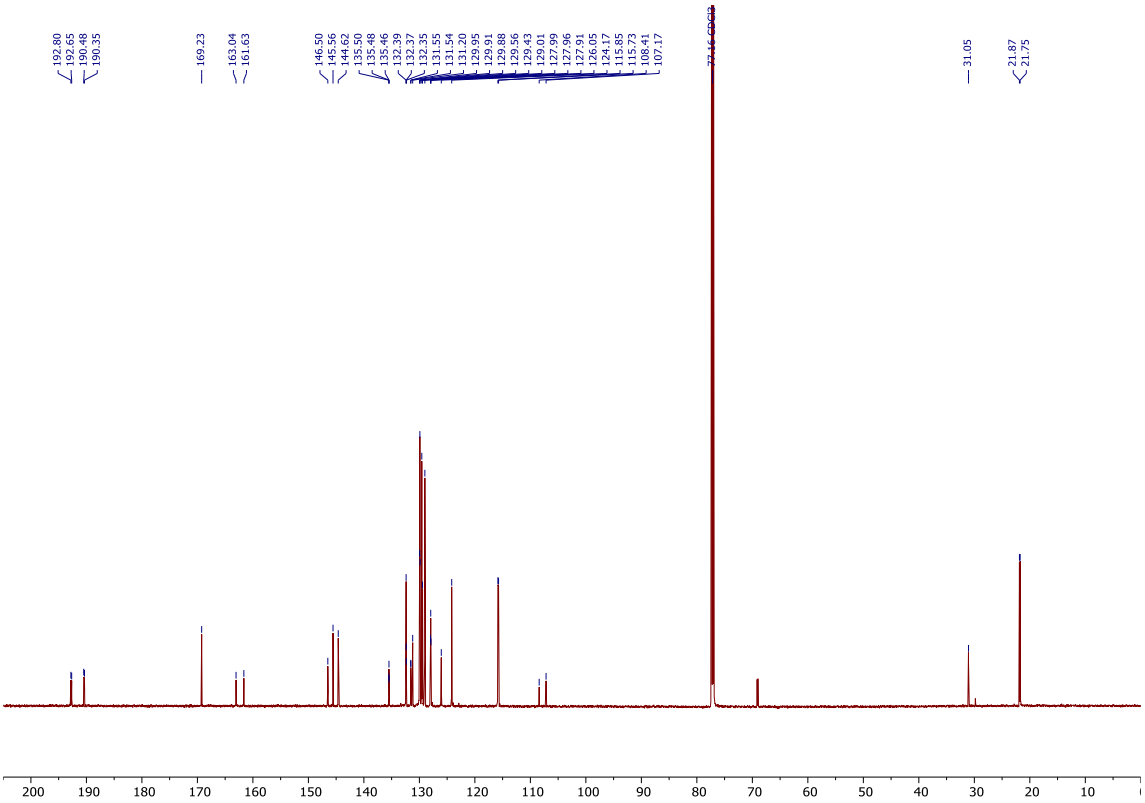
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4r**



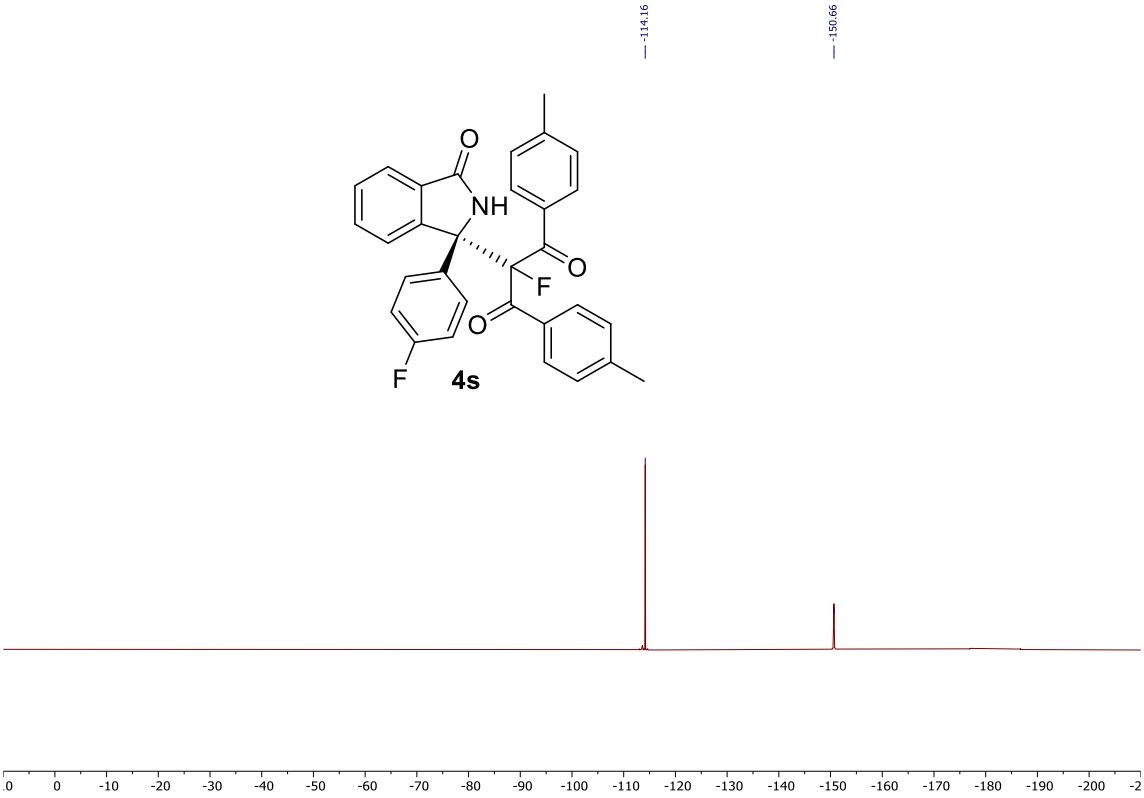
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4r**



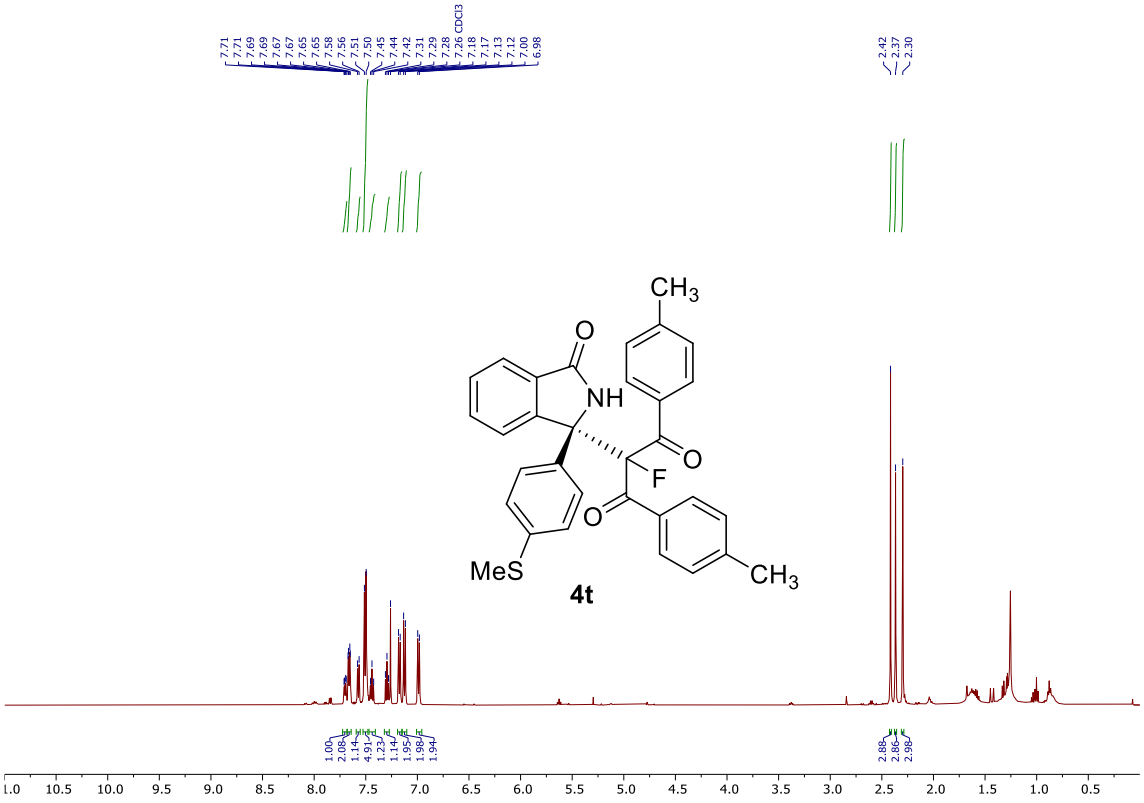
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4s**



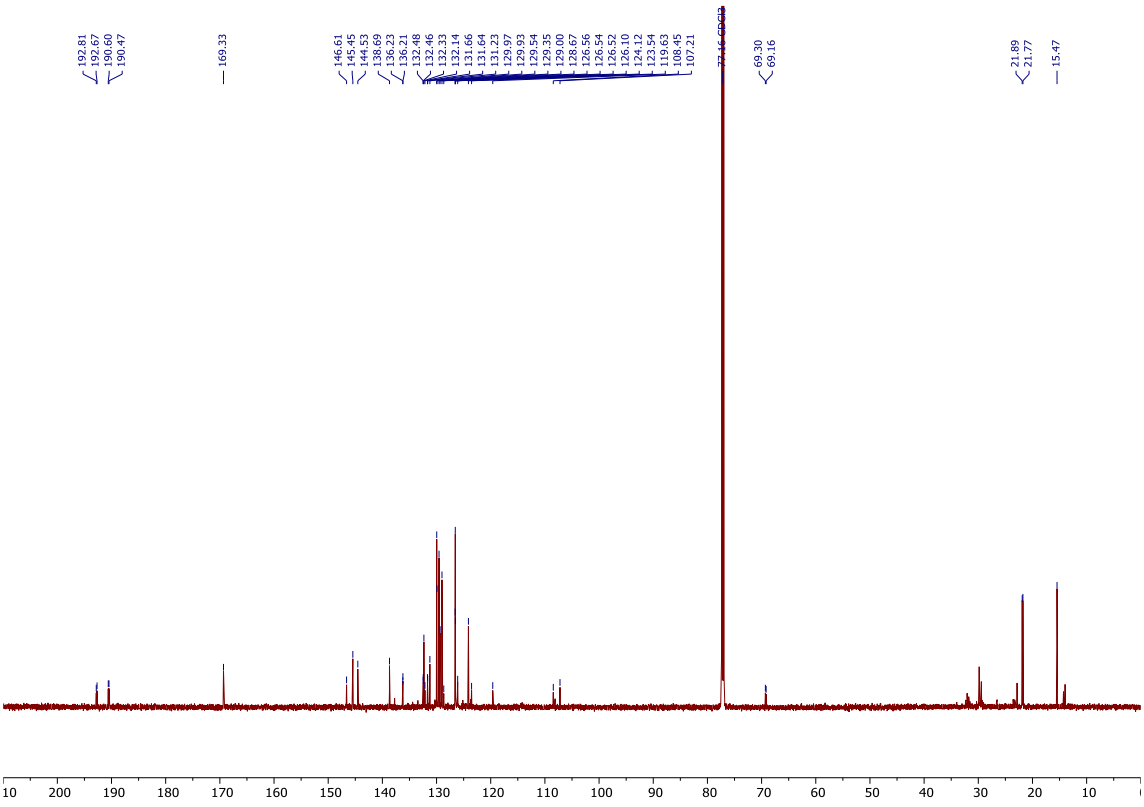
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4s**



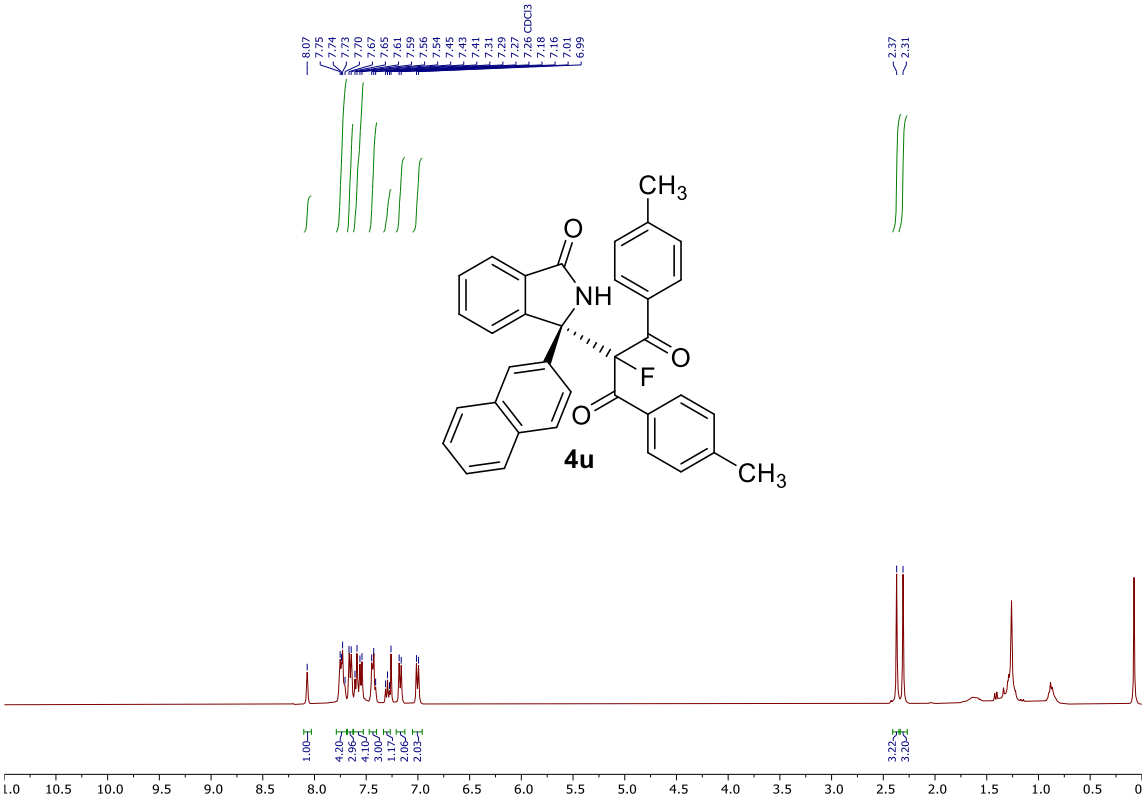
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4s**



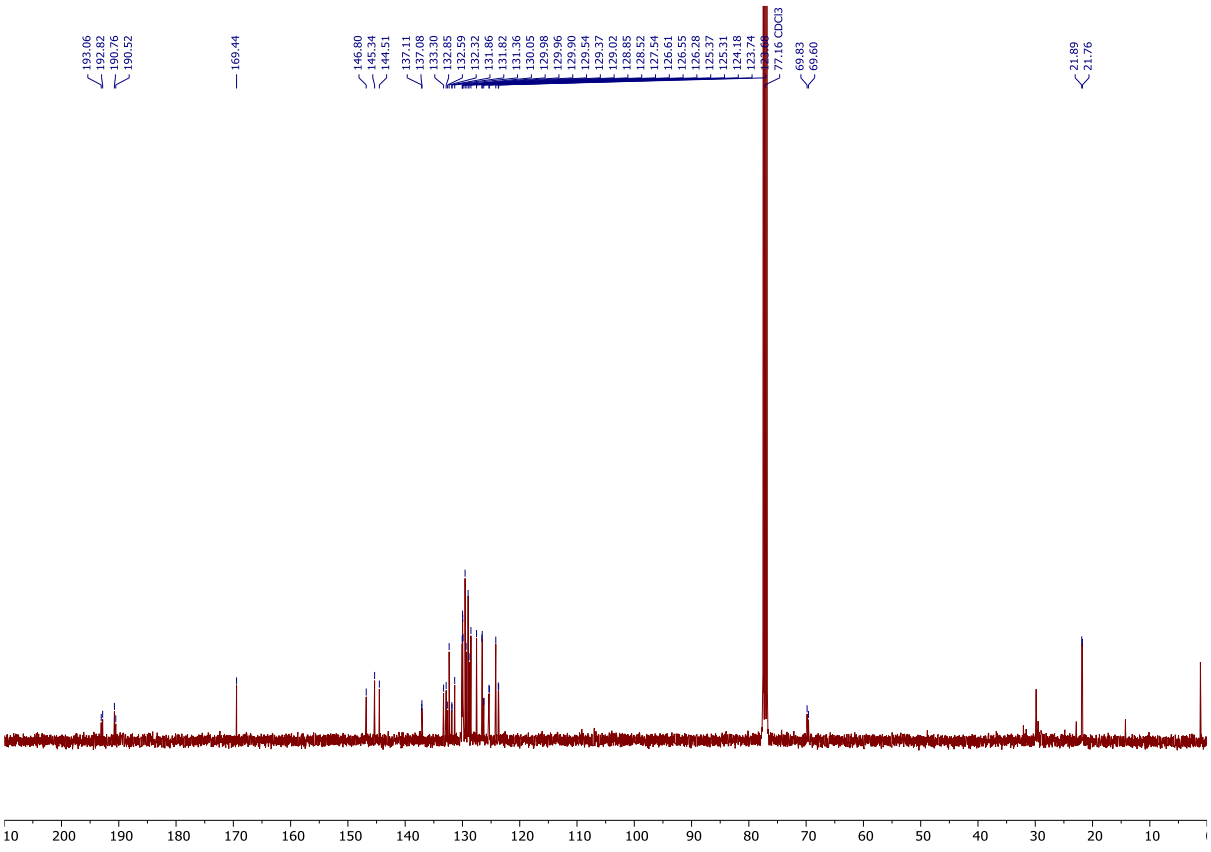
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4t**



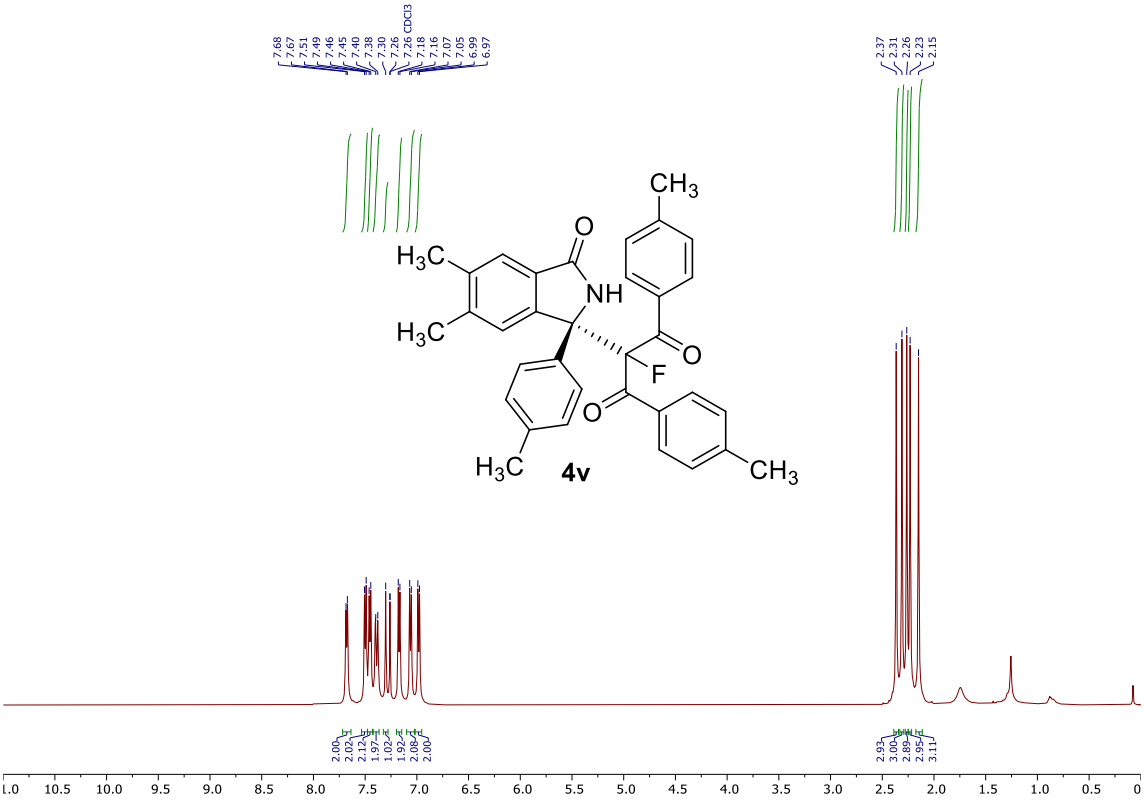
^{13}C NMR (175 MHz, $CDCl_3$) of compound **4t**



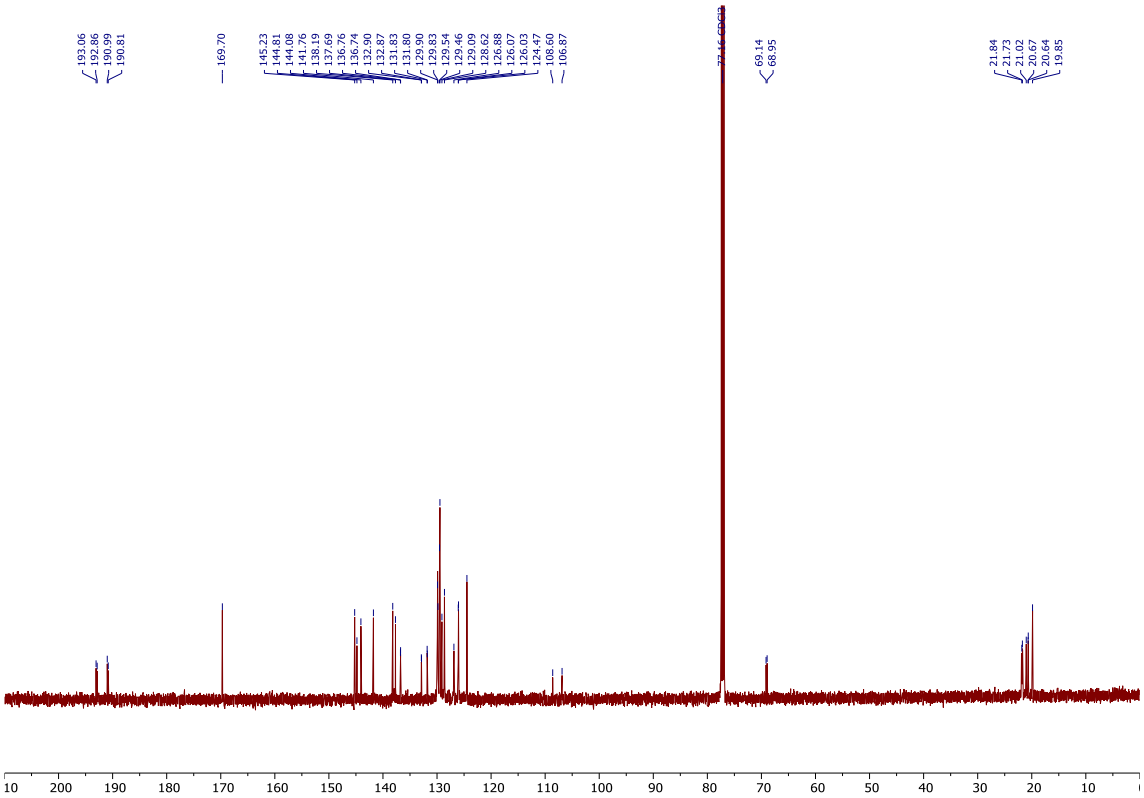
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4u**



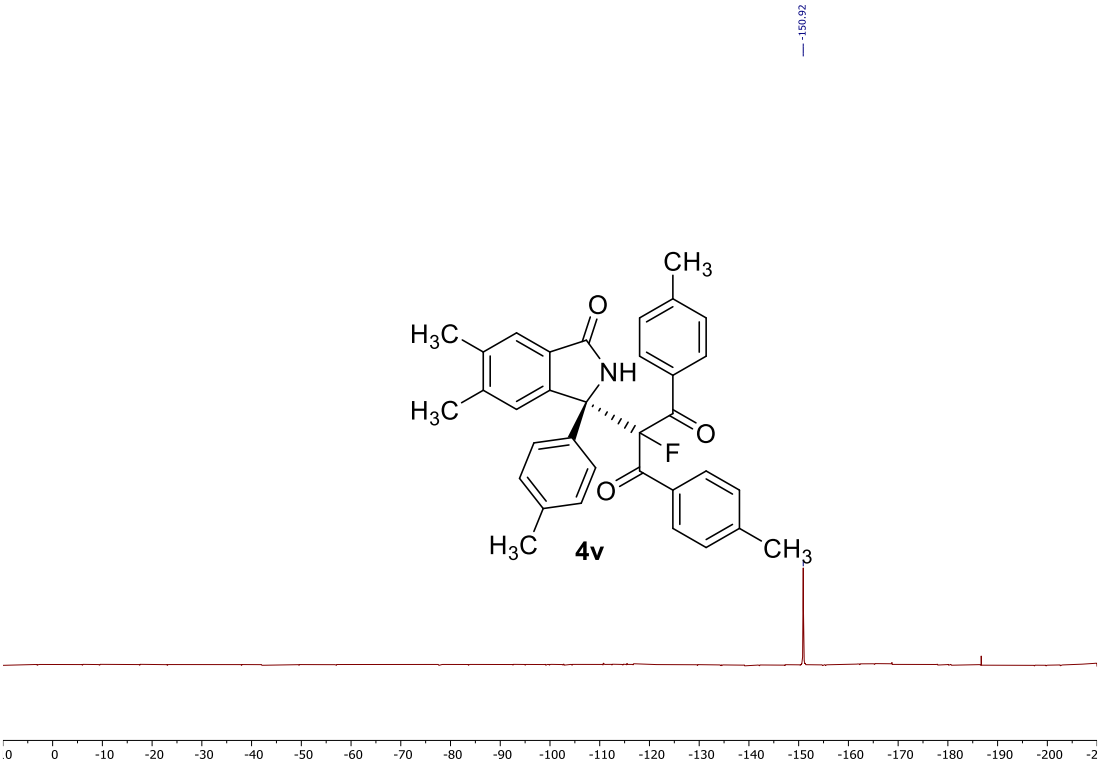
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4u**



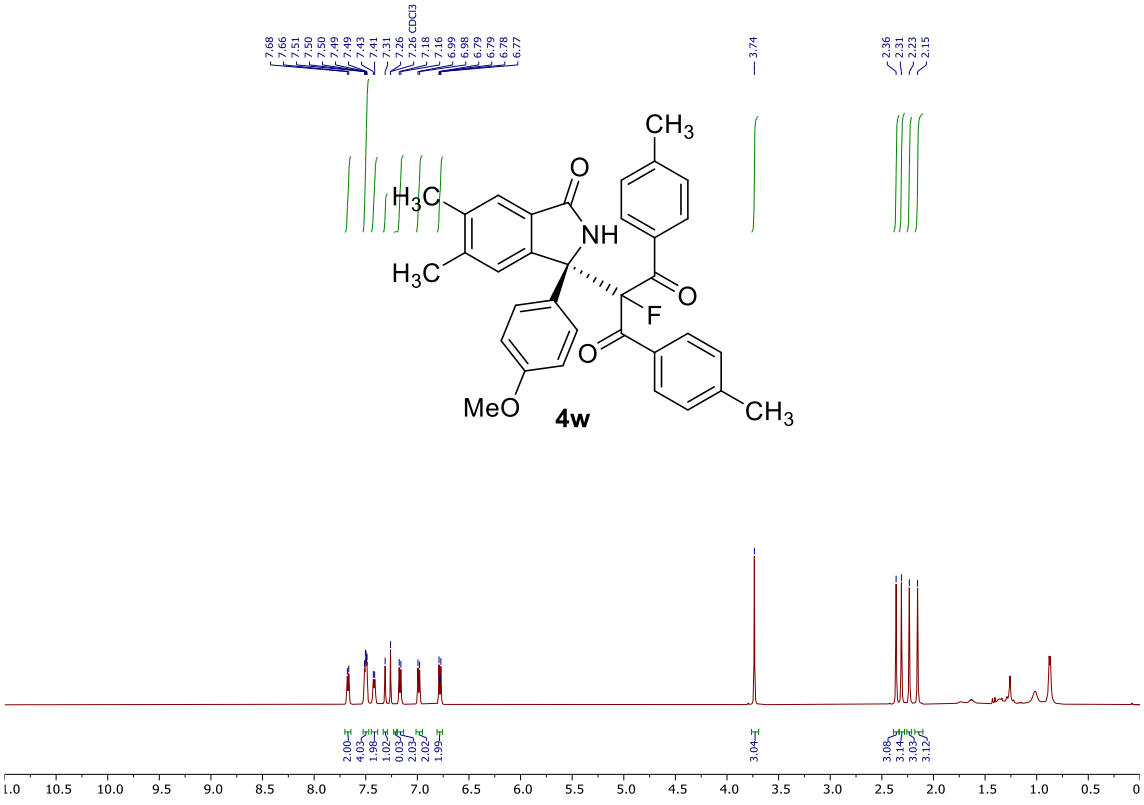
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4v**



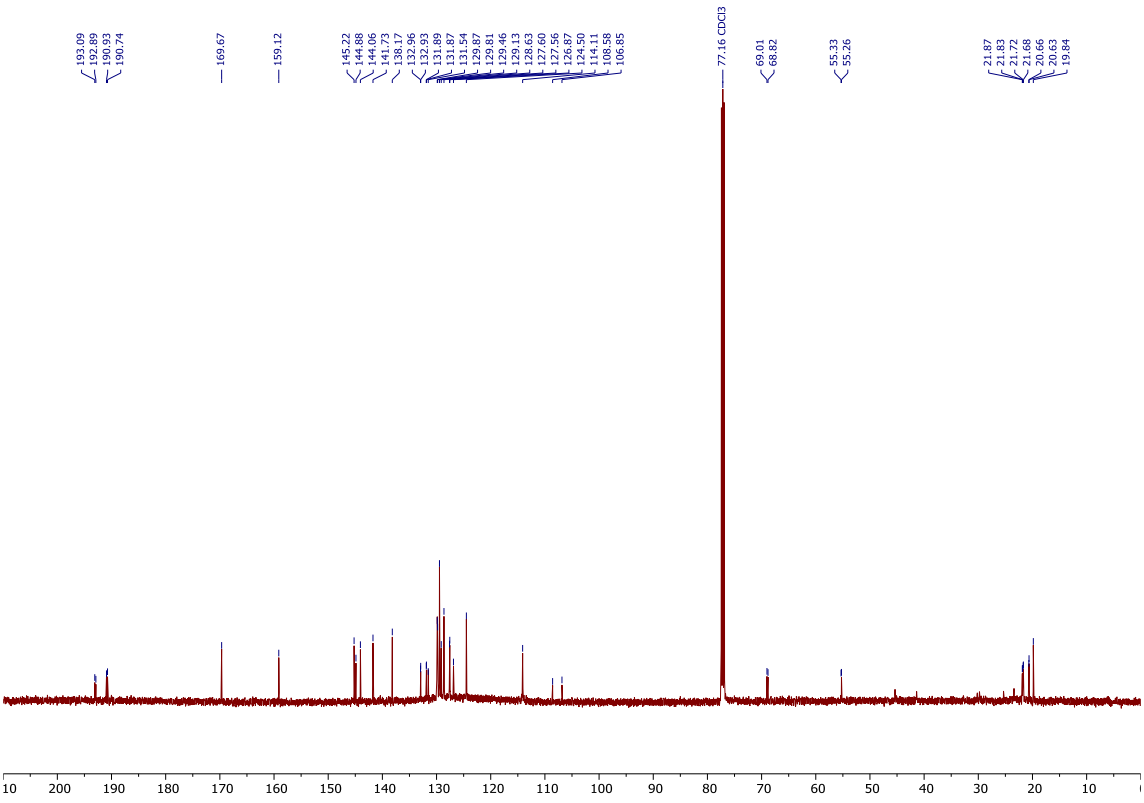
^{13}C NMR (125 MHz, $CDCl_3$) of compound **4v**



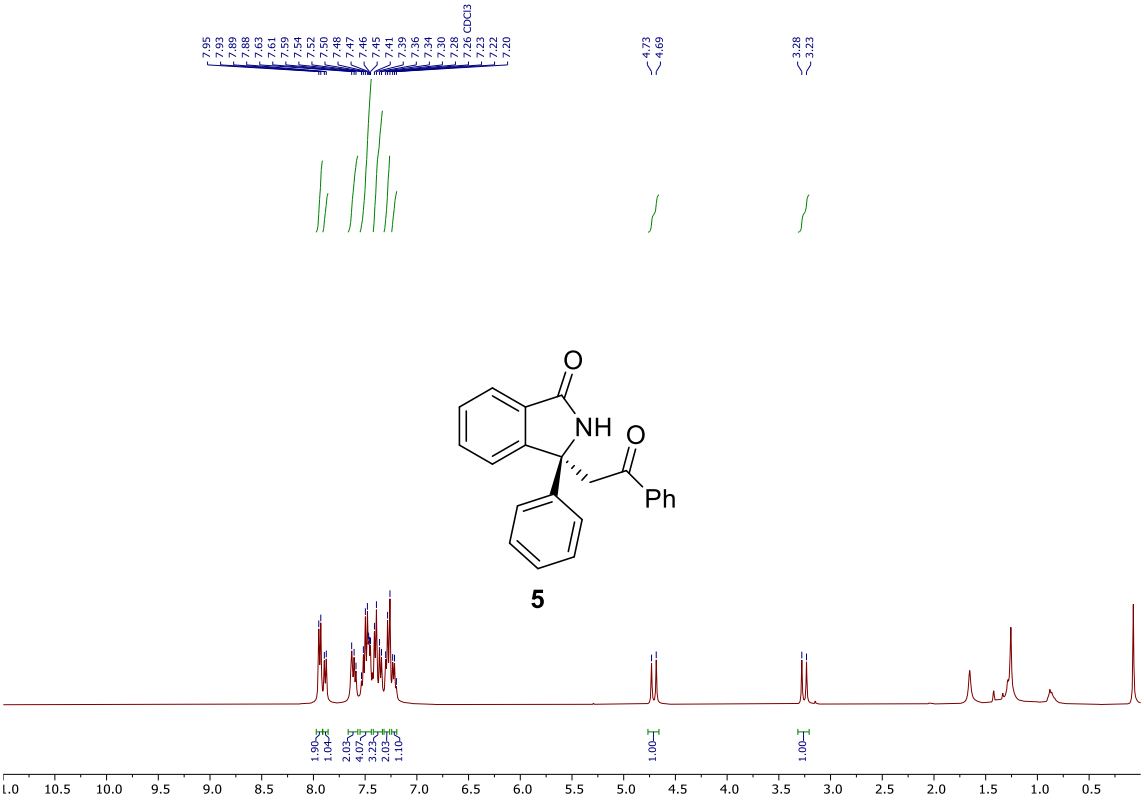
^{19}F NMR (375 MHz, $CDCl_3$) of compound **4v**



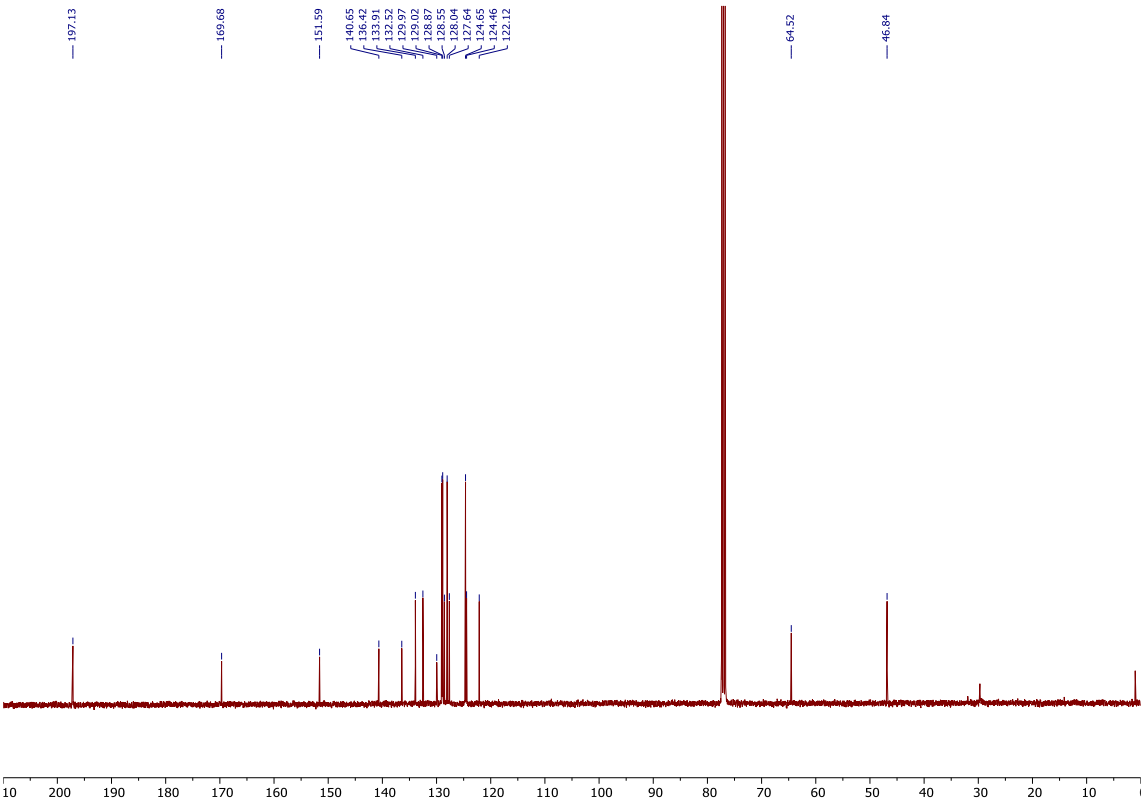
^{1}H NMR (500 MHz, $CDCl_3$) of compound **4w**



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

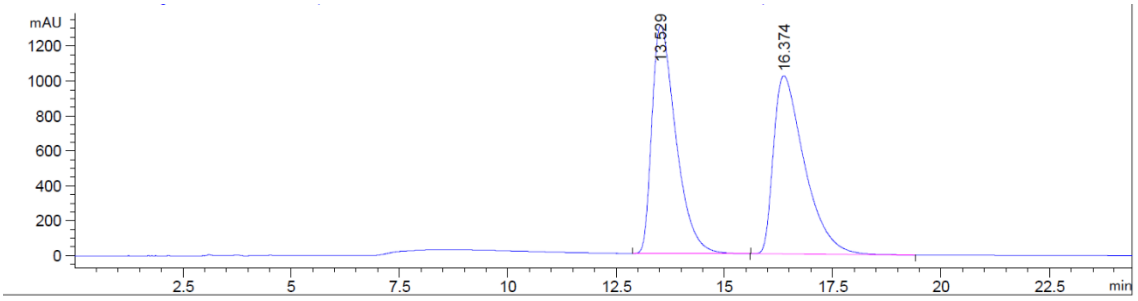


^{1}H NMR (400 MHz, $CDCl_3$) of compound **5**



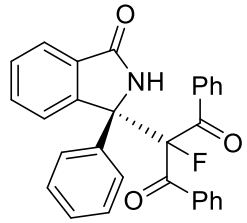
^{13}C NMR (100 MHz, $CDCl_3$) of compound **5**

HPLC Traces

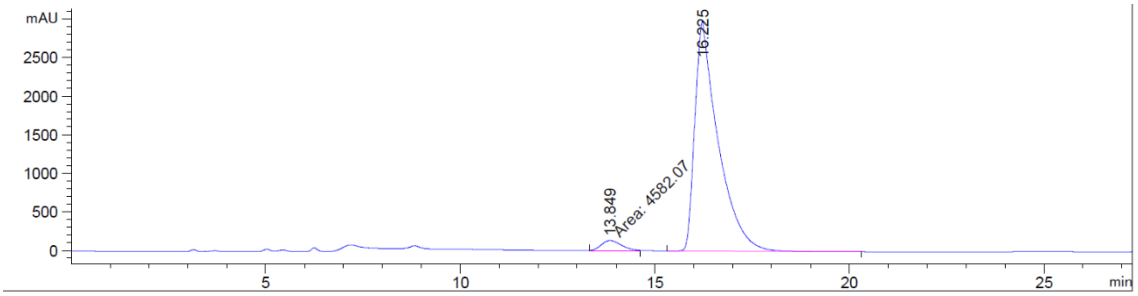


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.529	BB	0.5808	5.03016e4	1307.54114	49.7563
2	16.374	BB	0.7247	5.07944e4	1020.49634	50.2437
Totals :				1.01096e5	2328.03748	

HPLC chromatogram of **4a** racemic

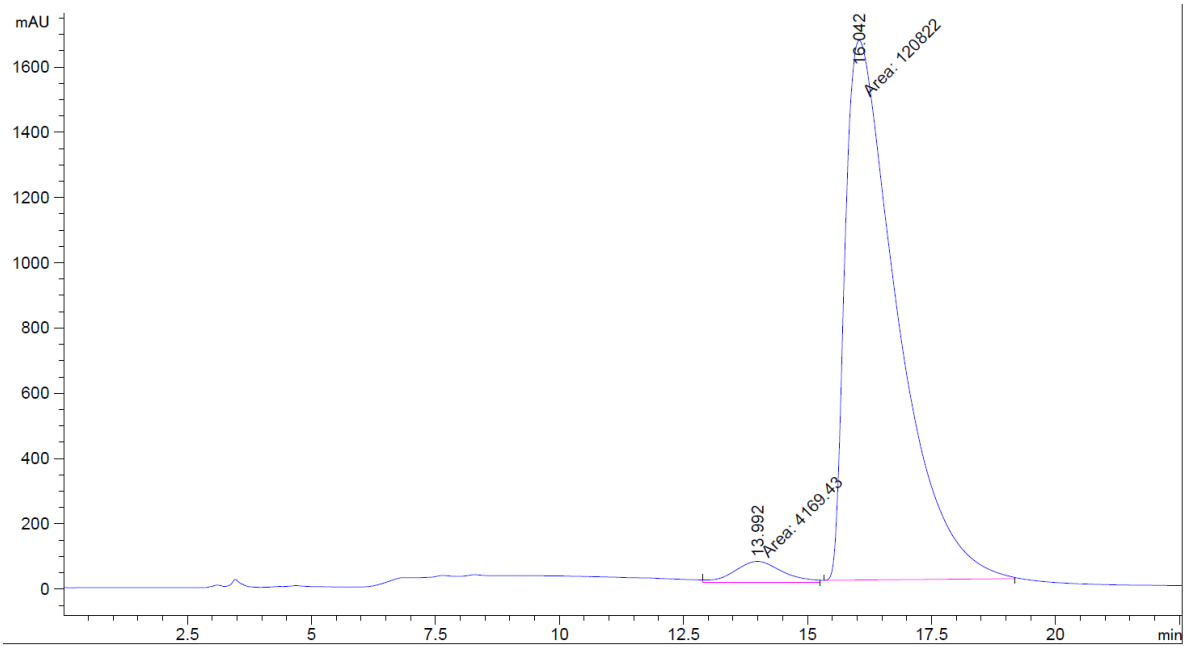


4a



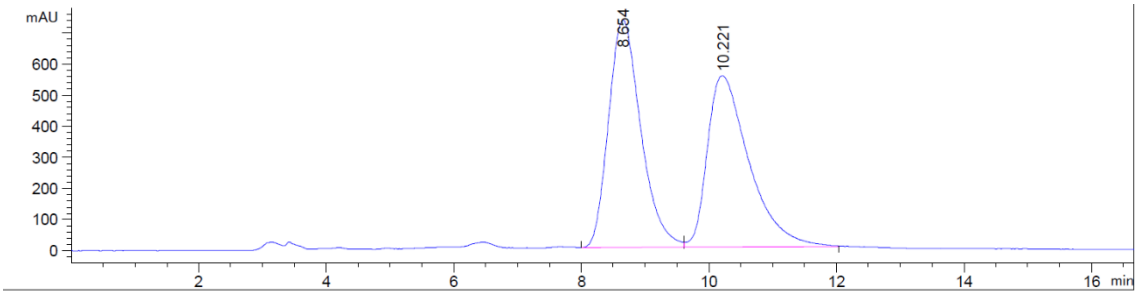
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.849	MM	0.5838	4582.06689	130.81880	3.5736
2	16.225	BB	0.4988	1.23639e5	2987.67822	96.4264
Totals :				1.28221e5	3118.49702	

HPLC chromatogram of **4a** chiral



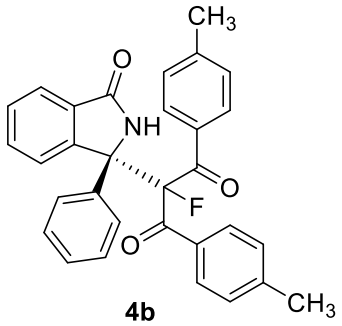
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.992	MM	1.1003	4169.43359	63.15630	3.3358
2	16.042	MM	1.2179	1.20822e5	1653.46533	96.6642
Totals :				1.24991e5	1716.62163	

HPLC chromatogram of **4a** chiral (gram scale reaction)

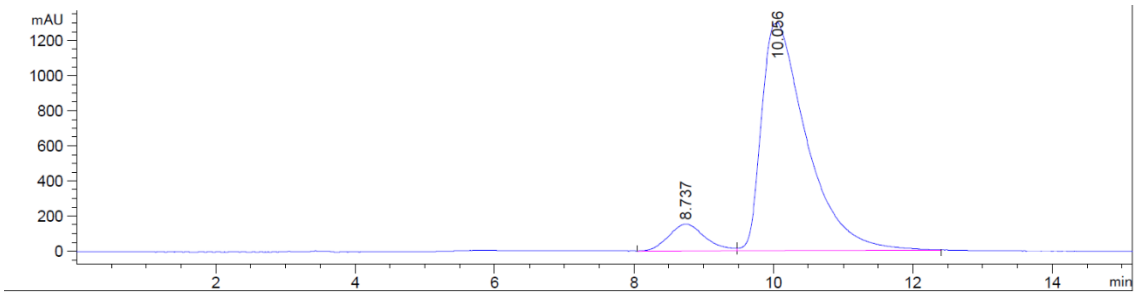


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.654	BV	0.4942	2.57262e4	731.67773	50.6823
2	10.221	VV	0.6149	2.50336e4	550.15796	49.3177
Totals :				5.07598e4	1281.83569	

HPLC chromatogram of **4b** racemic

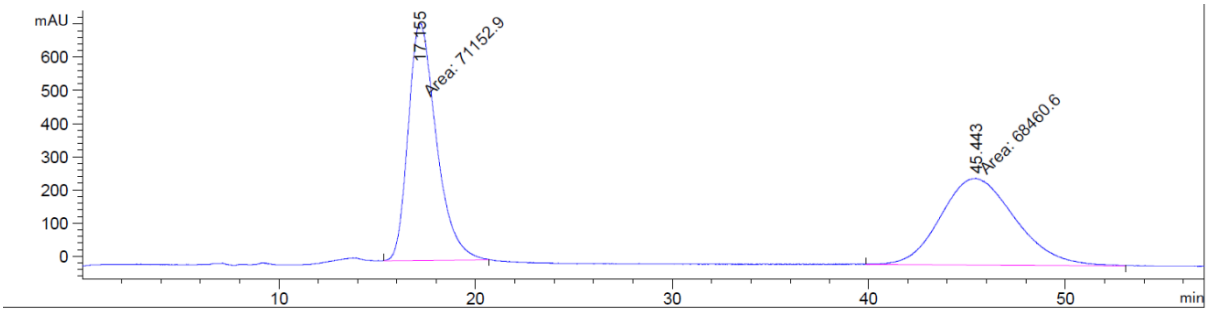


4b



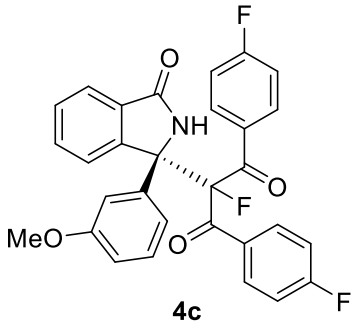
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.737	BV	0.4662	5517.20166	153.19827	8.6307
2	10.056	VV	0.5376	5.84081e4	1301.32202	91.3693
Totals :				6.39253e4	1454.52029	

HPLC chromatogram of **4b** chiral

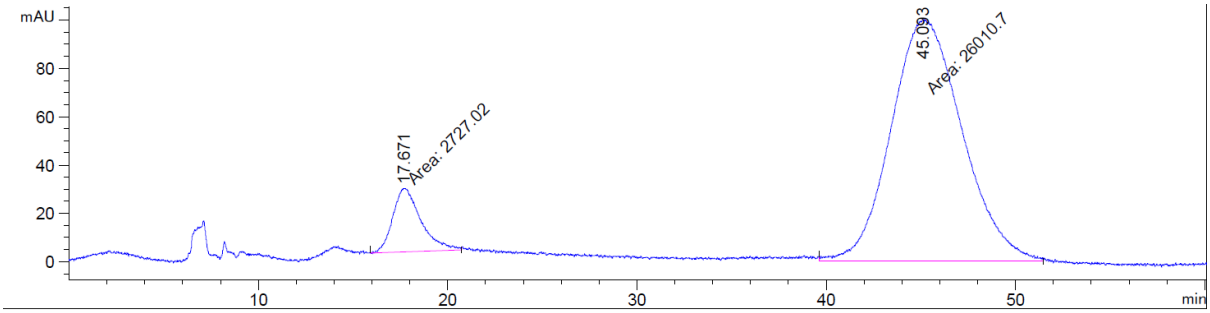


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.155	MM	1.6594	7.11529e4	714.62378	50.9642
2	45.443	MM	4.3744	6.84606e4	260.84015	49.0358
Totals :				1.39613e5	975.46393	

HPLC chromatogram of **4c** racemic

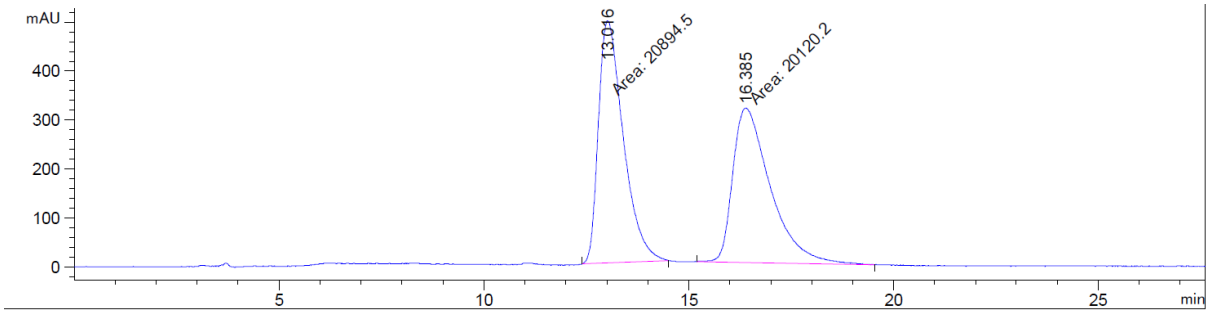


4c



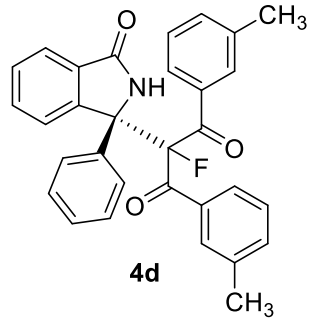
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.671	MM	1.7249	2727.02490	26.34985	9.4893
2	45.093	MM	4.3384	2.60107e4	99.92543	90.5107
Totals :				2.87378e4	126.27528	

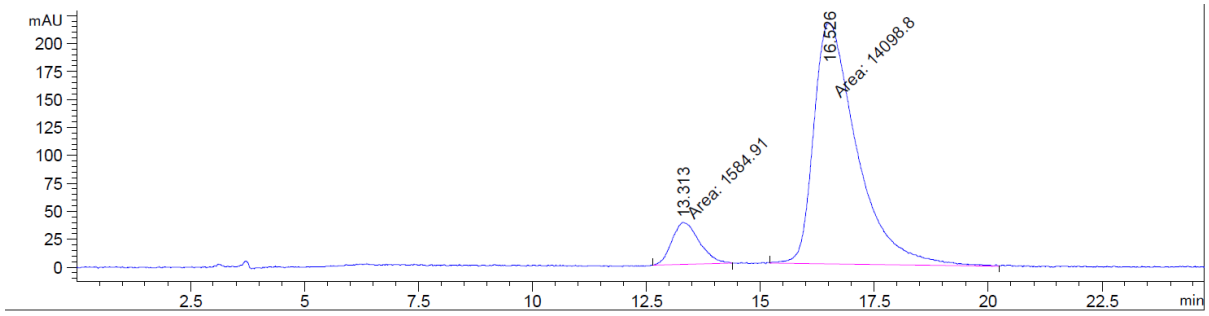
HPLC chromatogram of **4c** chiral



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.016	MM	0.7050	2.08945e4	493.96524	50.9439
2	16.385	MM	1.0649	2.01202e4	314.91339	49.0561
Totals :				4.10147e4	808.87863	

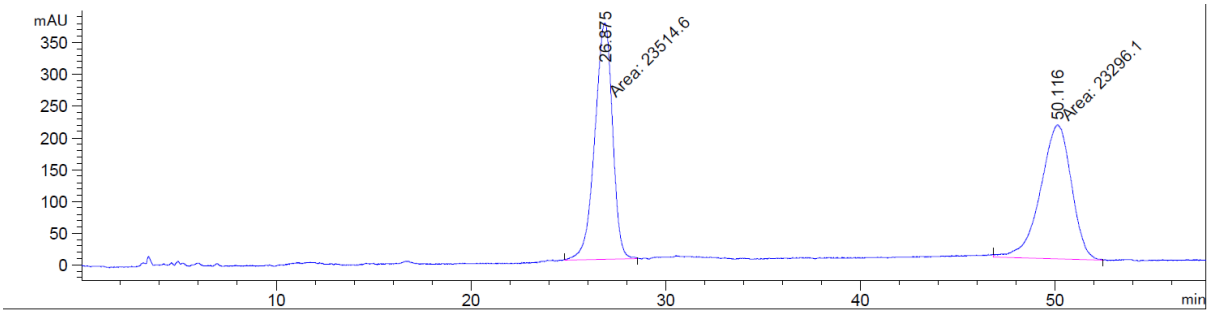
HPLC chromatogram of **4d** racemic





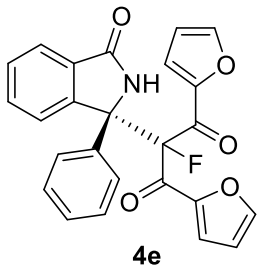
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.313	MM	0.6992	1584.90576	37.78160	10.1054
2	16.526	MM	1.0952	1.40988e4	214.55579	89.8946
Totals :				1.56838e4	252.33739	

HPLC chromatogram of **4d** chiral

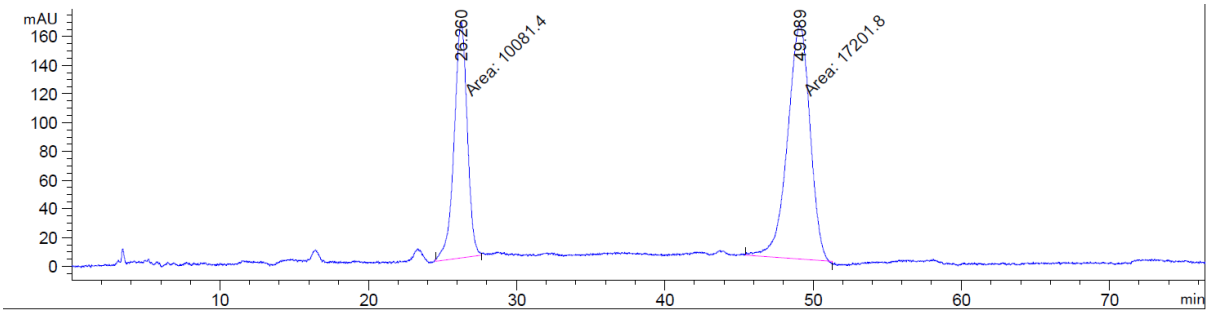


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.875	MM	1.0558	2.35146e4	371.19095	50.2334
2	50.116	MM	1.8381	2.32961e4	211.23781	49.7666
Totals :				4.68107e4	582.42876	

HPLC chromatogram of **4e** racemic

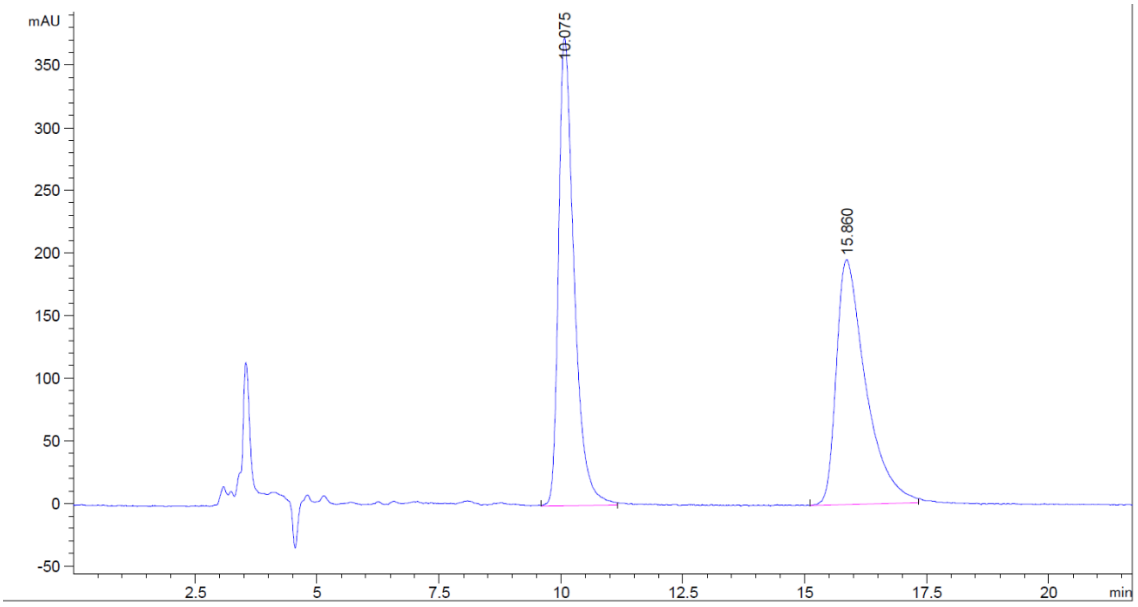


4e



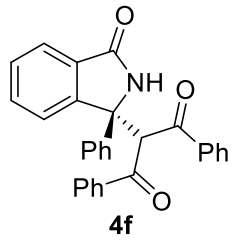
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.260	MM	1.0219	1.00814e4	164.42439	36.9511
2	49.089	MM	1.7633	1.72018e4	162.58900	63.0489
Totals :				2.72832e4	327.01340	

HPLC chromatogram of **4e** chiral

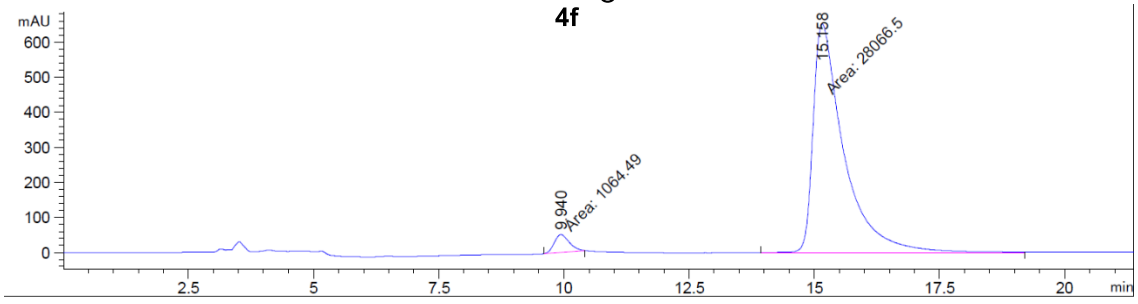


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.075	BV	0.3367	8285.81348	373.62039	50.1725
2	15.860	BV	0.5864	8228.83691	195.75299	49.8275
Totals :				1.65147e4	569.37338	

HPLC chromatogram of **4f** racemic

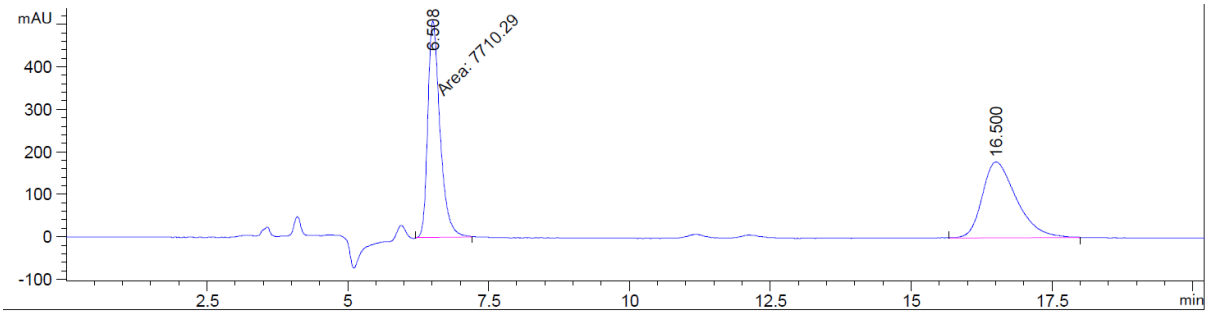


4f



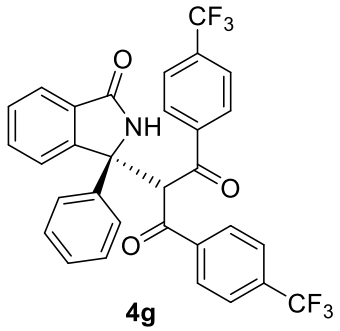
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.940	MM	0.3491	1064.48901	50.82296	3.6541
2	15.158	MM	0.7167	2.80665e4	652.70996	96.3459
Totals :				2.91310e4	703.53292	

HPLC chromatogram of **4f** chiral

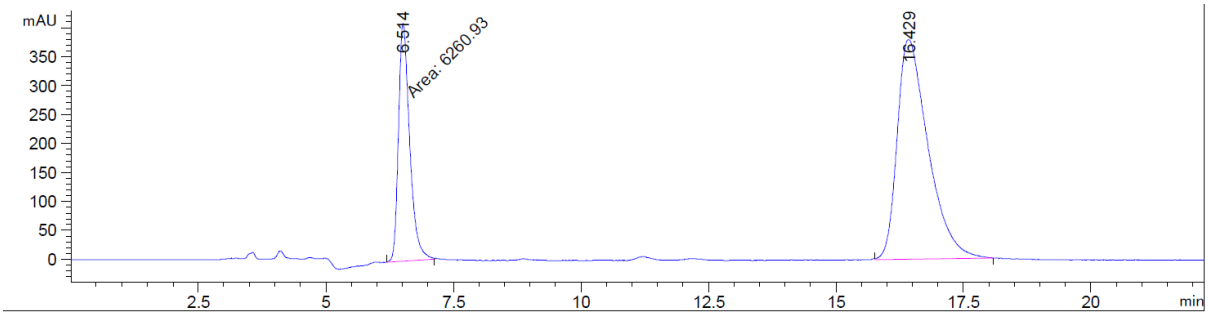


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.508	MM	0.2516	7710.28857	510.77701	50.5626
2	16.500	VV	0.5842	7538.71191	178.70856	49.4374
Totals :				1.52490e4	689.48557	

HPLC chromatogram of **4g** racemic

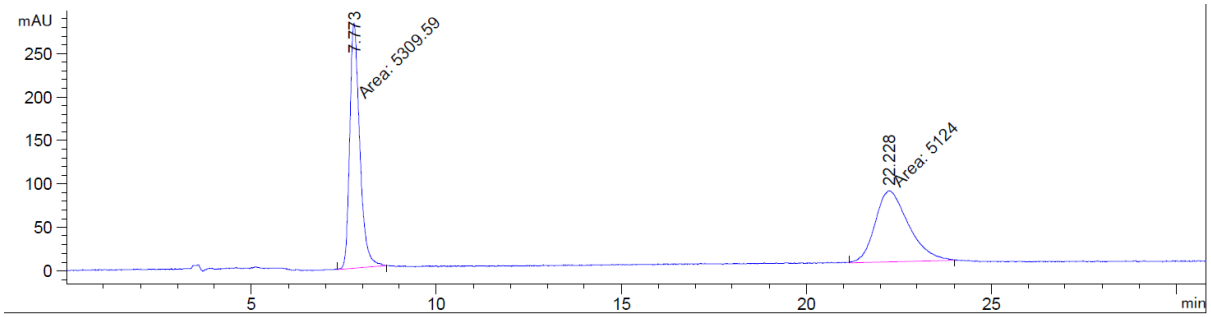


4g



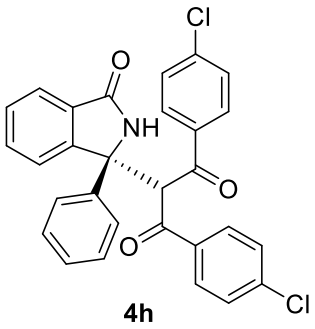
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.514	MM	0.2541	6260.92627	410.67273	28.1016
2	16.429	VV	0.6092	1.60187e4	378.91846	71.8984
Totals :				2.22796e4	789.59119	

HPLC chromatogram of **4g** chiral

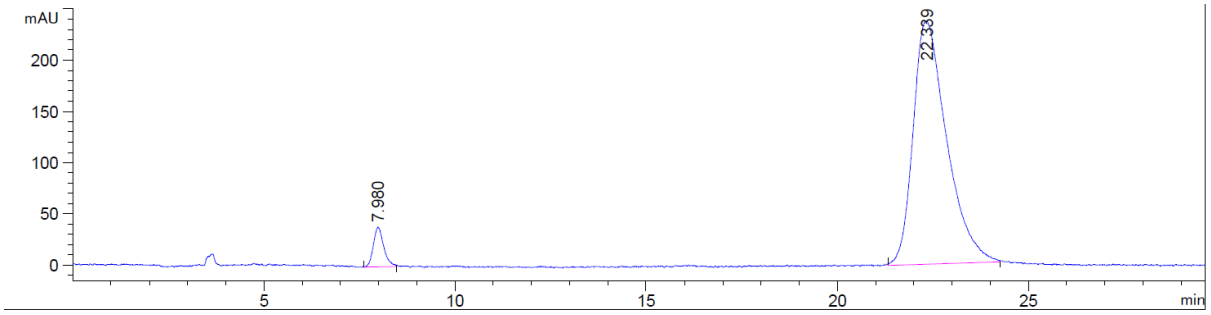


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.773	MM	0.3143	5309.59033	281.51450	50.8894
2	22.228	MM	1.0424	5124.00098	81.92521	49.1106
Totals :				1.04336e4	363.43970	

HPLC chromatogram of **4h** racemic

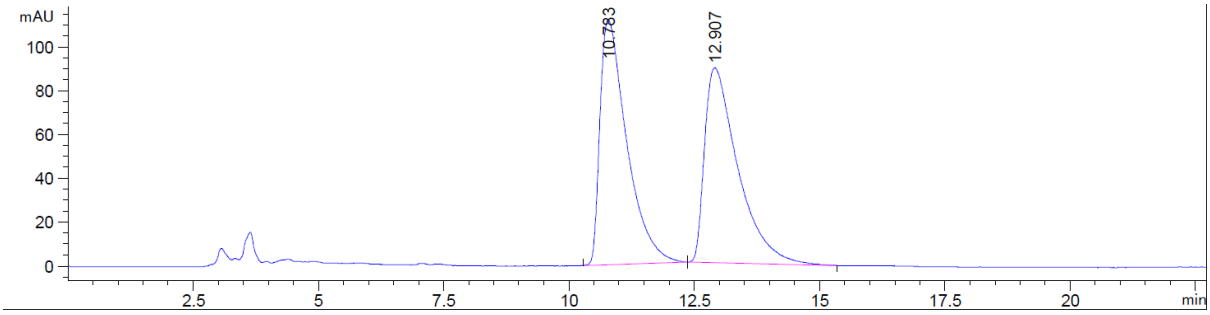


4h



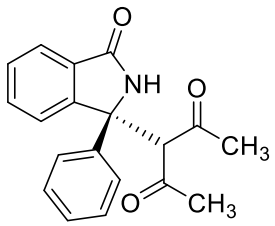
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.980	BV	0.2647	728.90668	38.53090	4.7825
2	22.339	VV	0.7269	1.45123e4	237.50404	95.2175
Totals :				1.52412e4	276.03494	

HPLC chromatogram of **4h** chiral

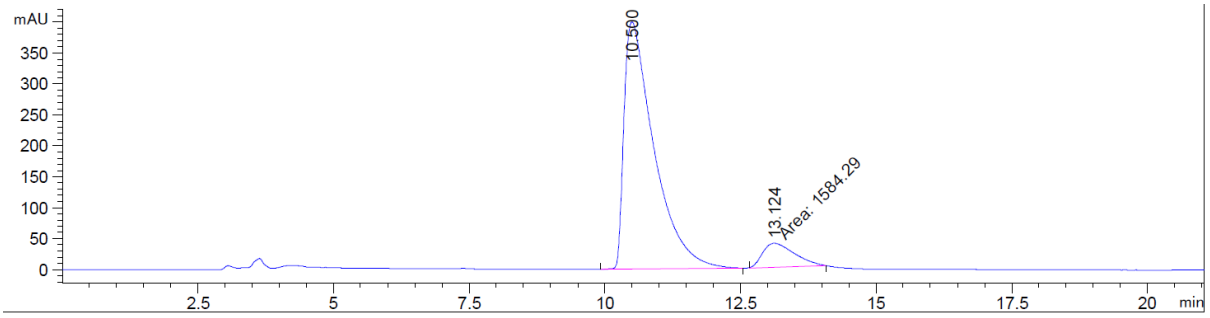


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.783	BB	0.5403	4144.24902	111.85332	50.1904
2	12.907	BB	0.6697	4112.81152	88.91048	49.8096
Totals :				8257.06055	200.76380	

HPLC chromatogram of **4i** racemic

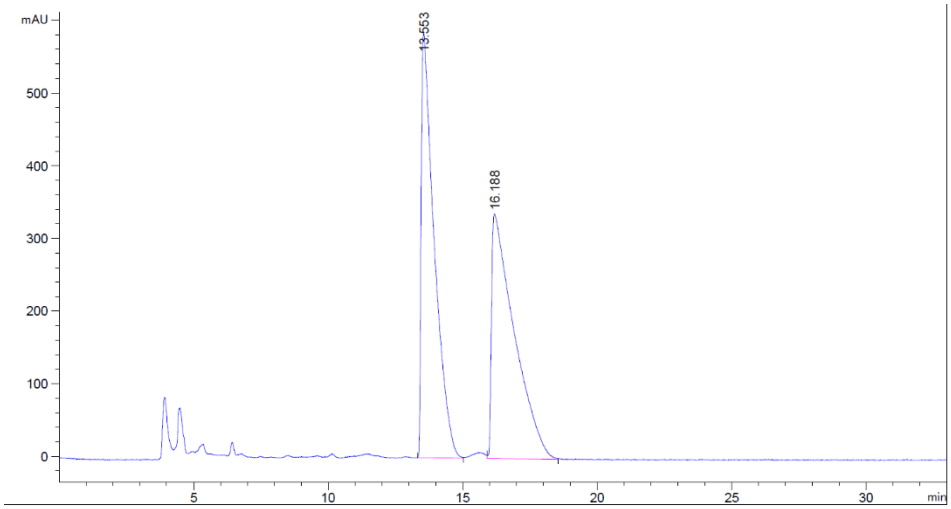


4i



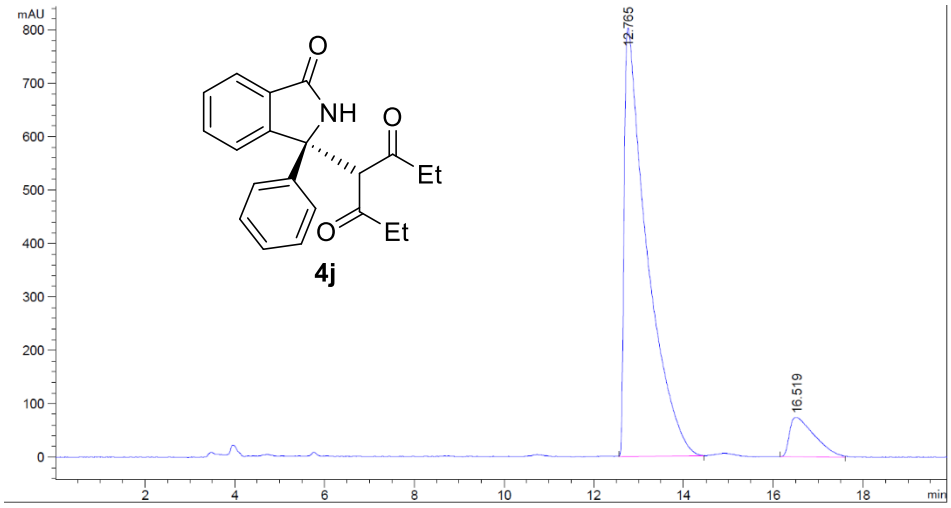
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.500	BB	0.5585	1.53397e4	399.05505	90.6388
2	13.124	MM	0.6817	1584.28918	38.73573	9.3612
Totals :				1.69240e4	437.79078	

HPLC chromatogram of **4i** chiral



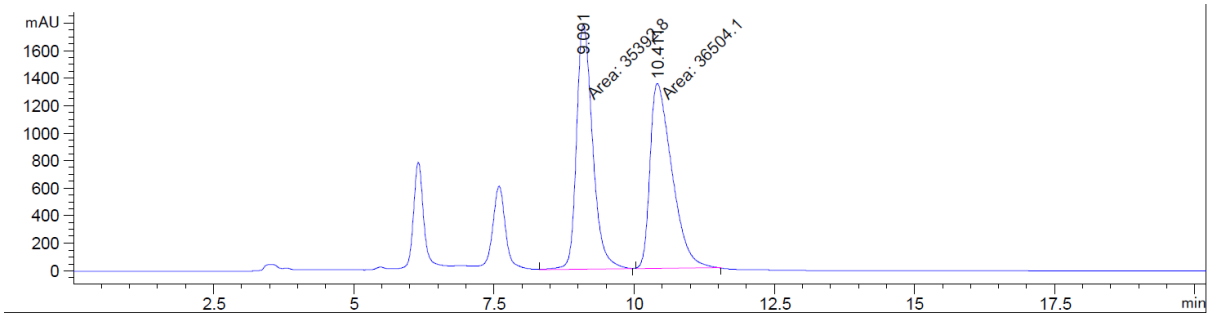
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.553	BV	0.4444	1.96312e4	583.66406	50.0132
2	16.188	VV	0.7324	1.96208e4	336.42612	49.9868
Totals :				3.92519e4	920.09018	

HPLC chromatogram of **4j** racemic



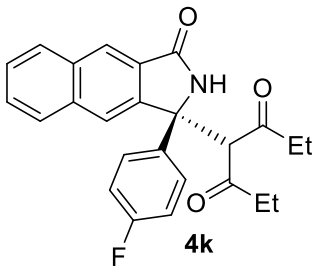
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.765	VB	0.4652	2.81190e4	801.77197	90.7718
2	16.519	BV	0.5135	2858.66724	73.86597	9.2282
Totals :				3.09777e4	875.63794	

HPLC chromatogram of **4j** chiral

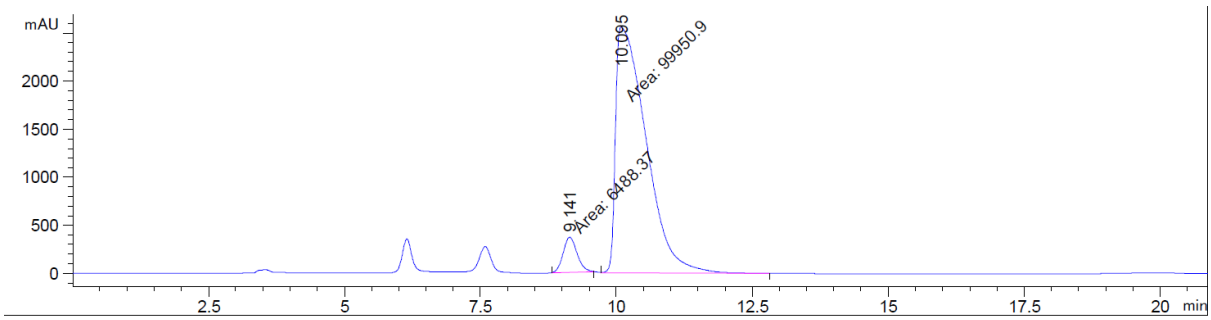


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.091	MM	0.3327	3.53928e4	1773.14648	49.2271
2	10.411	MM	0.4530	3.65041e4	1343.10046	50.7729
Totals :				7.18969e4	3116.24695	

HPLC chromatogram of **4k** racemic

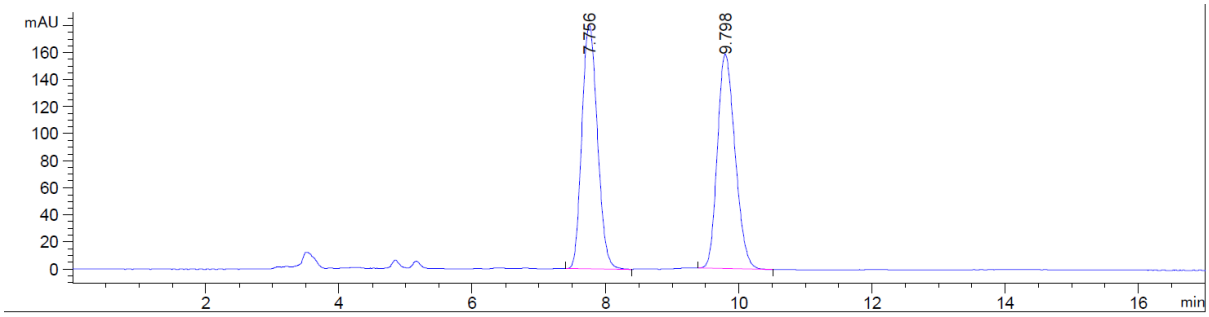


4k



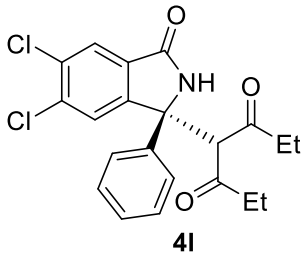
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.141	MM	0.2967	6488.36523	364.47546	6.0958
2	10.095	MM	0.6515	9.99509e4	2556.80298	93.9042
Totals :				1.06439e5	2921.27844	

HPLC chromatogram of **4k** chiral

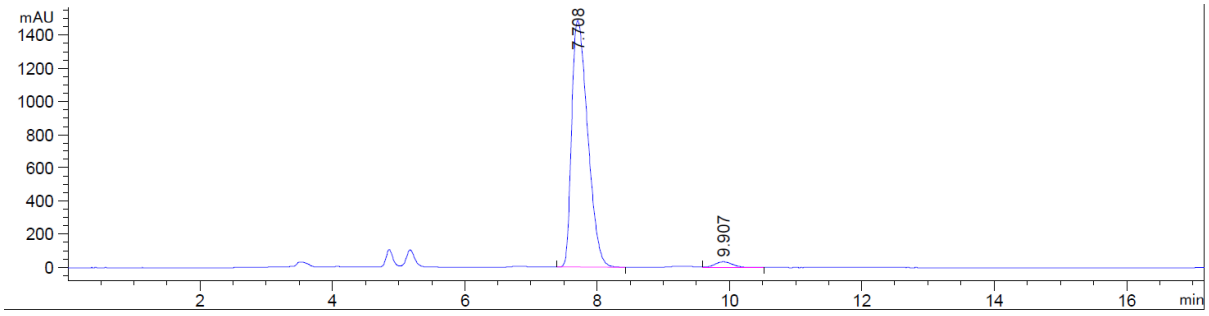


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.756	BB	0.2573	2925.06079	180.27457	49.9932
2	9.798	BB	0.2894	2925.85303	158.48206	50.0068
Totals :				5850.91382	338.75662	

HPLC chromatogram of **4l** racemic

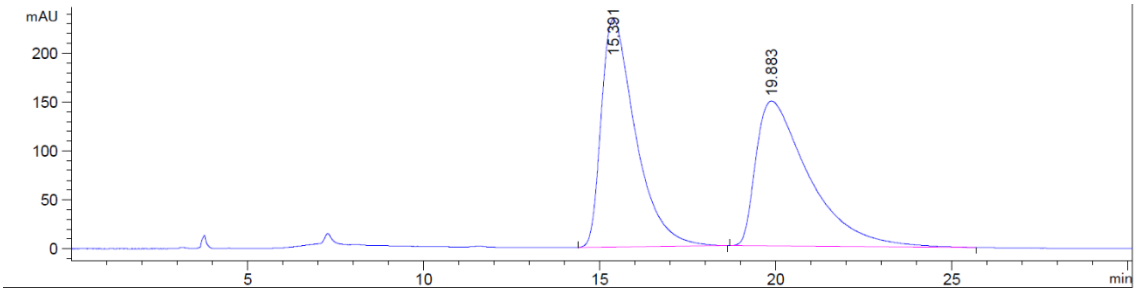


4l



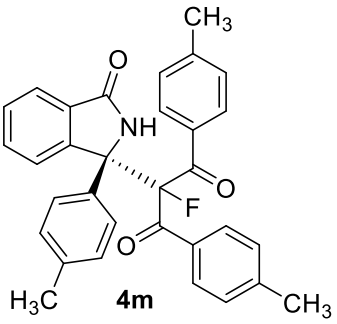
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.708	BB	0.2657	2.49094e4	1485.07678	97.4656
2	9.907	VB	0.2970	647.70886	34.19622	2.5344
Totals :				2.55571e4	1519.27300	

HPLC chromatogram of **4l** chiral

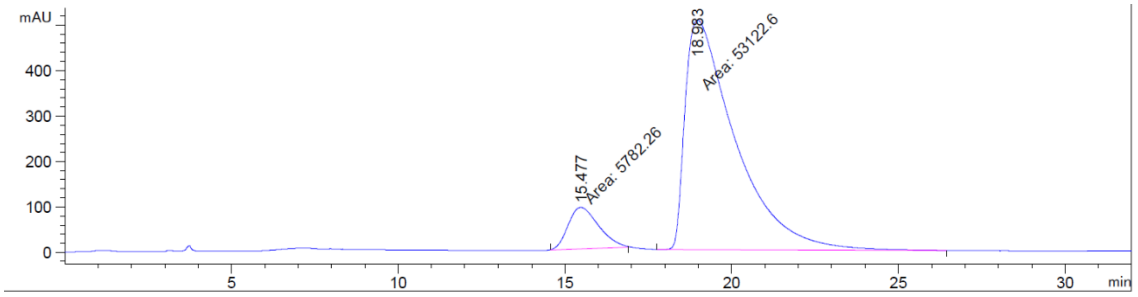


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.391	BB	0.9798	1.57462e4	233.18463	50.2902
2	19.883	BB	1.4334	1.55645e4	148.18640	49.7098
Totals :				3.13108e4	381.37103	

HPLC chromatogram of **4m** racemic

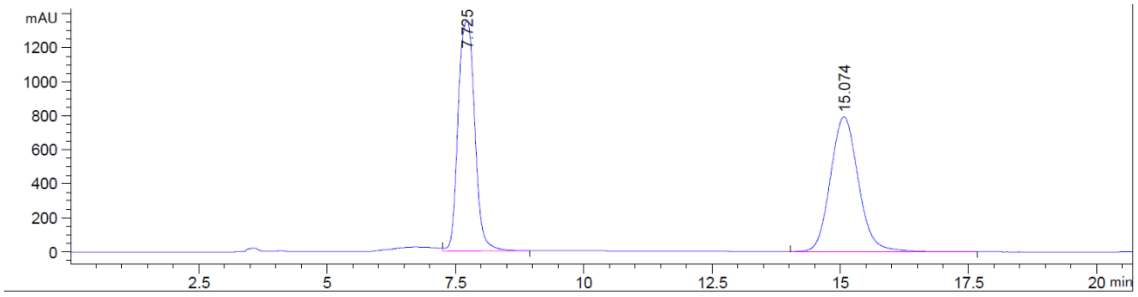


4m



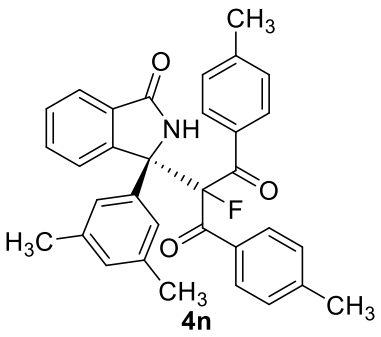
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.477	MM	1.0557	5782.25732	91.28695	9.8163
2	18.983	MM	1.7505	5.31226e4	505.78296	90.1837
Totals :				5.89049e4	597.06991	

HPLC chromatogram of **4m** chiral

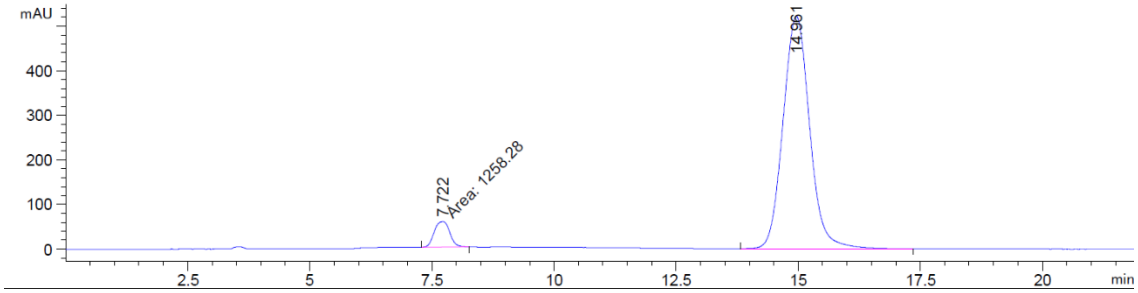


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.725	VB	0.3625	3.04498e4	1353.35486	50.3875
2	15.074	BB	0.5856	2.99814e4	792.02185	49.6125
Totals :				6.04312e4	2145.37671	

HPLC chromatogram of **4n** racemic

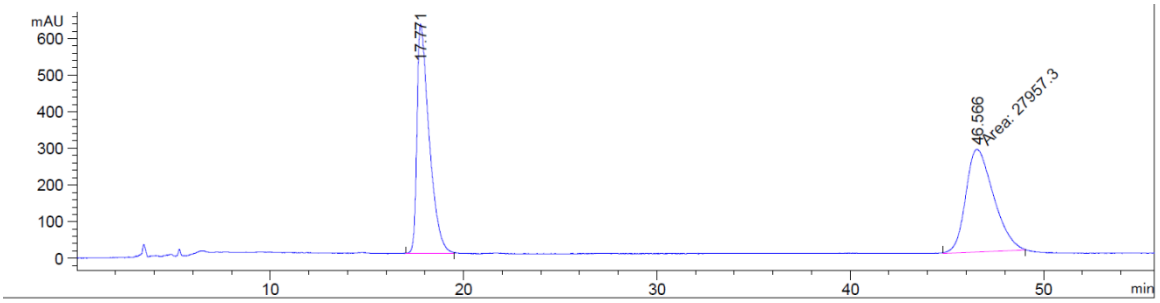


4n



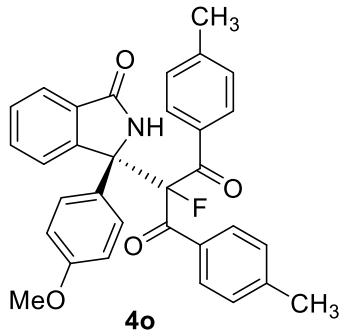
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.722	MM	0.3660	1258.27820	57.30379	5.9907
2	14.961	BB	0.5899	1.97455e4	521.29187	94.0093
Totals :				2.10038e4	578.59566	

HPLC chromatogram of **4n** chiral

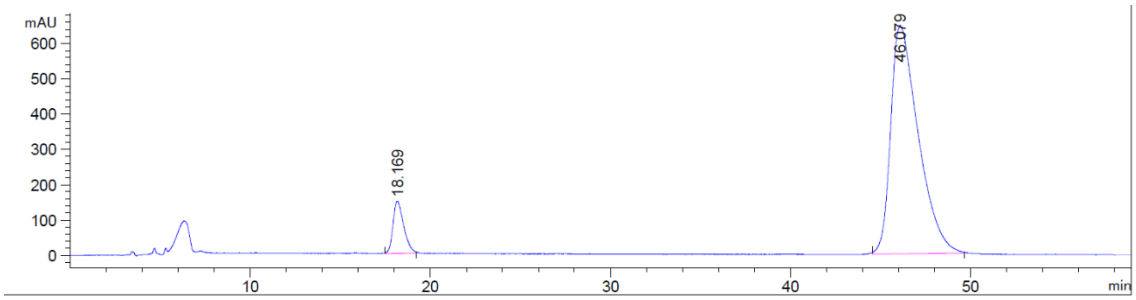


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.771	VV	0.5907	2.74118e4	626.25201	49.5074
2	46.566	MM	1.6656	2.79573e4	279.74890	50.4926
Totals :				5.53691e4	906.00092	

HPLC chromatogram of **4o** racemic

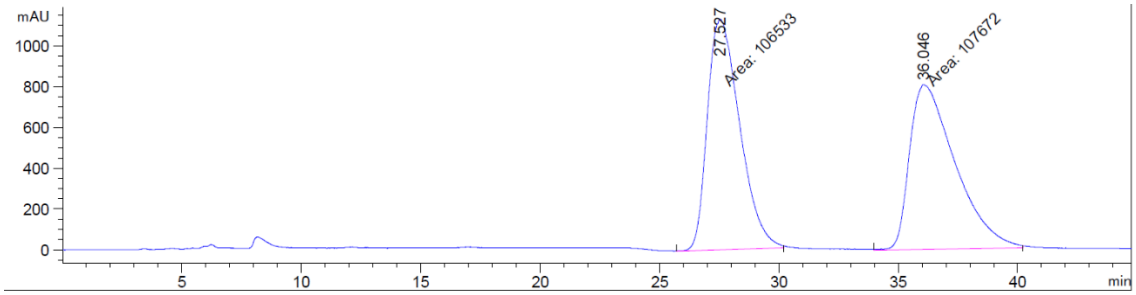


4o



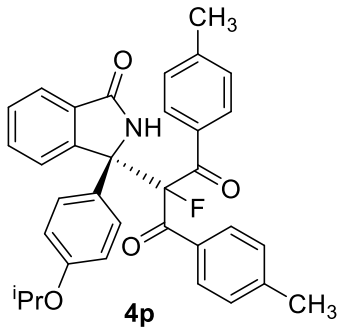
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.169	VV	0.5439	6120.37598	148.16852	8.1625
2	46.079	VV	1.2495	6.88612e4	648.13336	91.8375
Totals :				7.49816e4	796.30188	

HPLC chromatogram of **4o** chiral

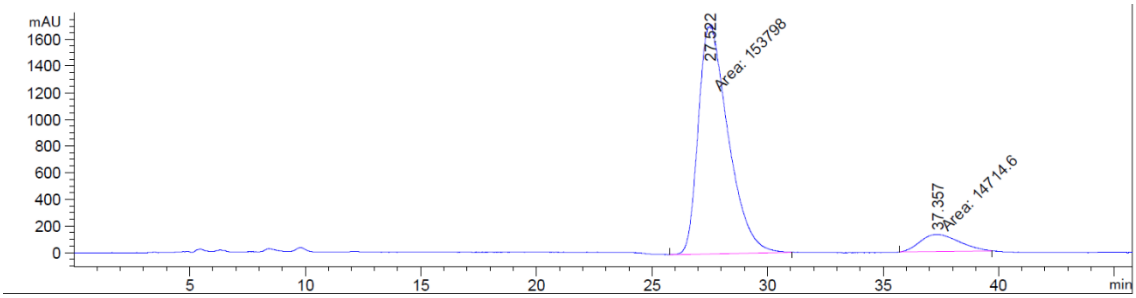


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.527	MM	1.5691	1.06533e5	1131.54724	49.7342
2	36.046	MM	2.2181	1.07672e5	809.04773	50.2658
Totals :				2.14205e5	1940.59497	

HPLC chromatogram of **4p** racemic

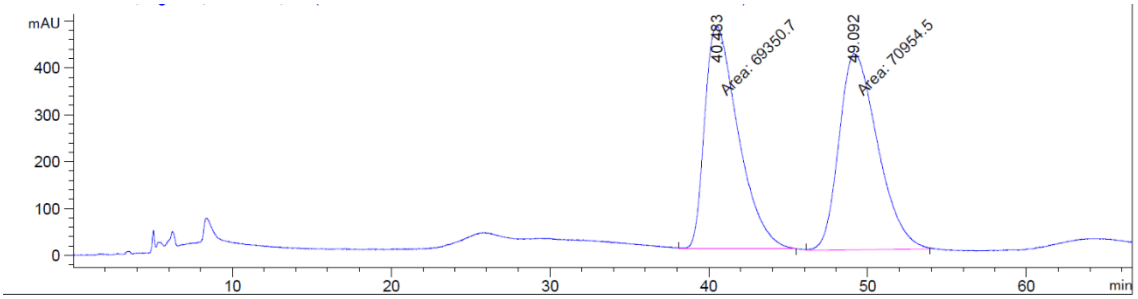


4p



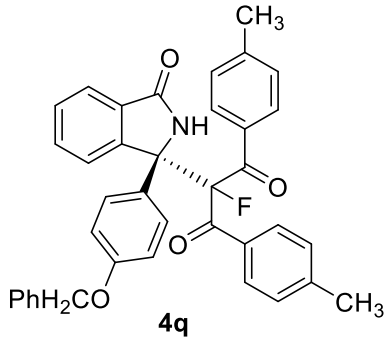
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.522	MM	1.4899	1.53798e5	1720.42603	91.2680
2	37.357	MM	1.9281	1.47146e4	127.19748	8.7320
Totals :				1.68513e5	1847.62350	

HPLC chromatogram of **4p** chiral

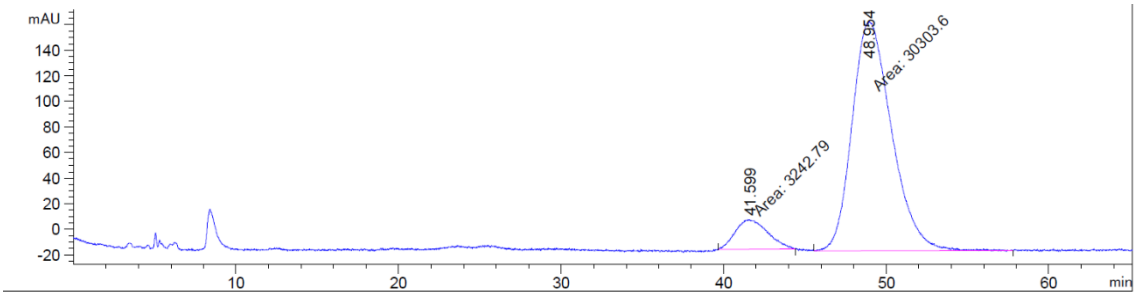


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.483	MM	2.4312	6.93507e4	475.42886	49.4284
2	49.092	MM	2.8184	7.09545e4	419.59790	50.5716
Totals :				1.40305e5	895.02676	

HPLC chromatogram of **4q** racemic

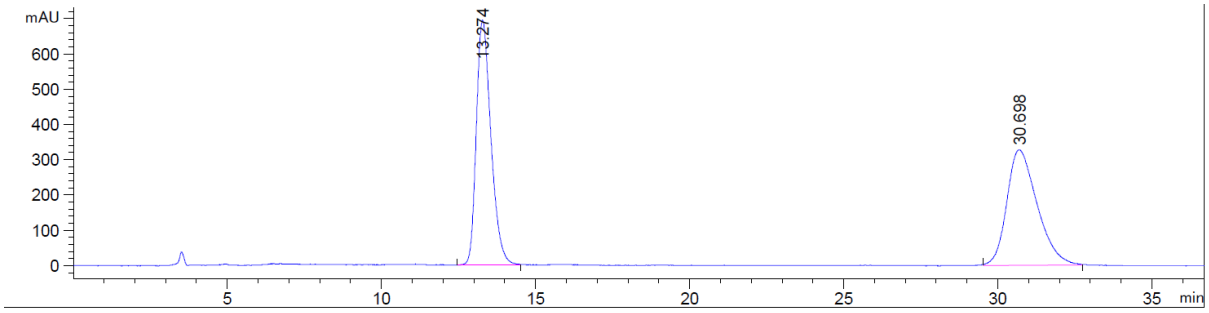


4q



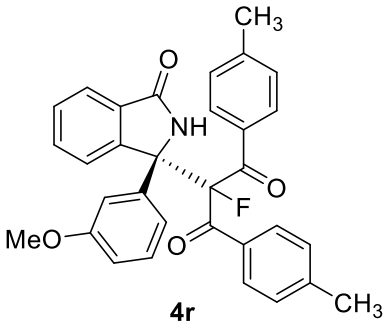
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.599	MM	2.3223	3242.78638	23.27246	9.6666
2	48.954	MM	2.8159	3.03036e4	179.36209	90.3334
Totals :				3.35464e4	202.63455	

HPLC chromatogram of **4q** chiral

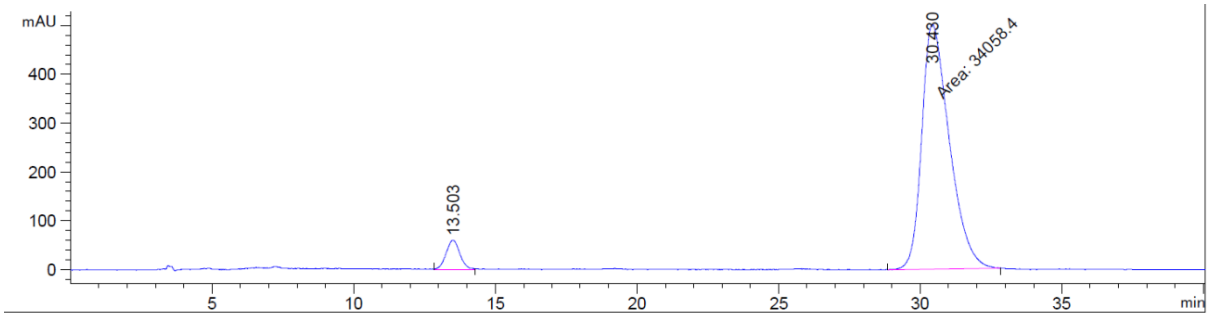


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.274	VV	0.4347	2.29092e4	694.72046	50.5597
2	30.698	VV	0.8191	2.24020e4	327.87146	49.4403
Totals :				4.53112e4	1022.59192	

HPLC chromatogram of **4r** racemic

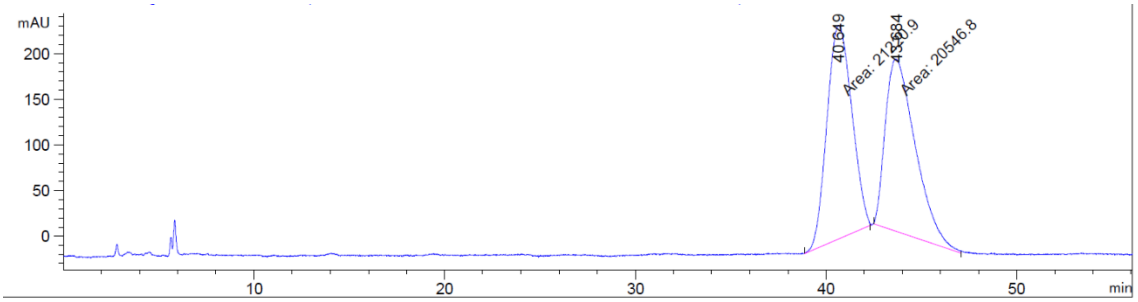


4r



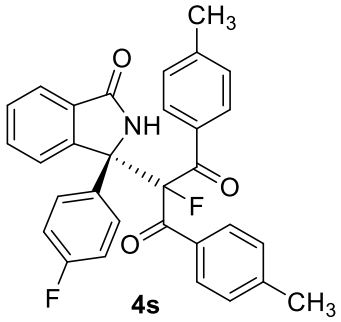
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.503	BV	0.4415	1981.13367	59.64598	5.4971
2	30.430	MM	1.1296	3.40584e4	502.52390	94.5029
Totals :				3.60396e4	562.16988	

HPLC chromatogram of **4r** chiral

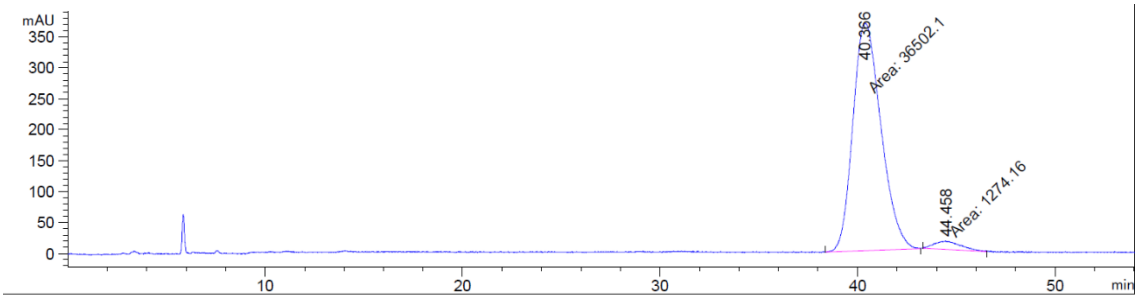


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.649	MM	1.5111	2.12209e4	234.06209	50.8069
2	43.684	MM	1.8155	2.05468e4	188.62613	49.1931
Totals :				4.17678e4	422.68822	

HPLC chromatogram of **4s** racemic

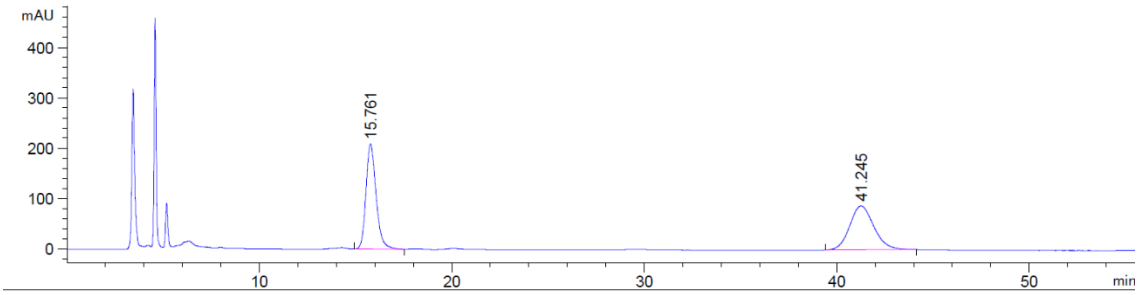


4s



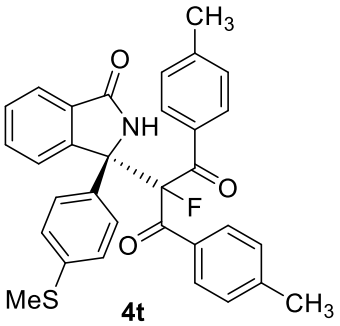
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.366	MM	1.6523	3.65021e4	368.20032	96.6271
2	44.458	MM	1.5492	1274.15930	13.70734	3.3729
Totals :				3.77763e4	381.90766	

HPLC chromatogram of **4s** chiral

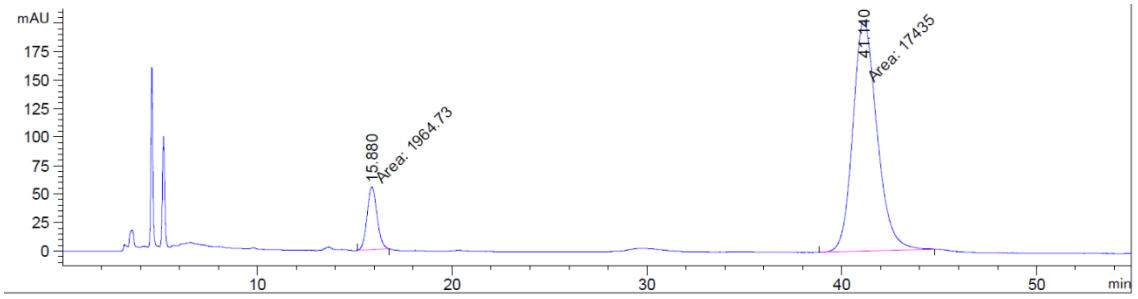


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.761	BB	0.5607	7623.18359	208.42767	50.0501
2	41.245	BB	1.0671	7607.91797	87.09919	49.9499
Totals :				1.52311e4	295.52686	

HPLC chromatogram of **4t** racemic

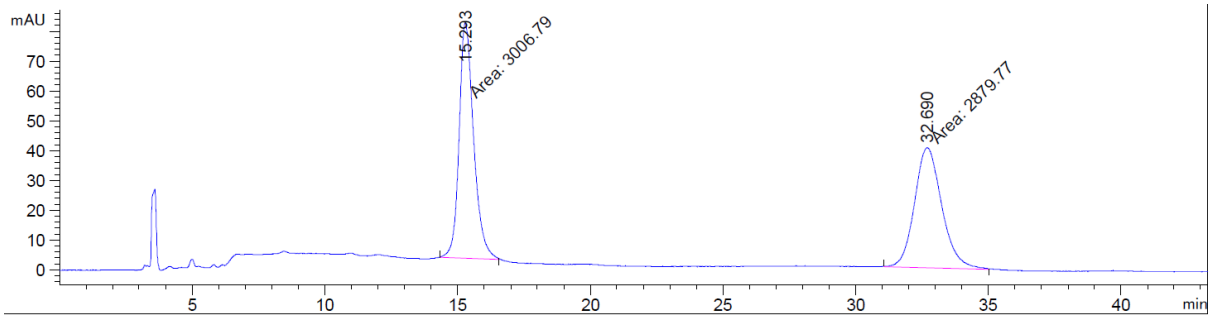


4t



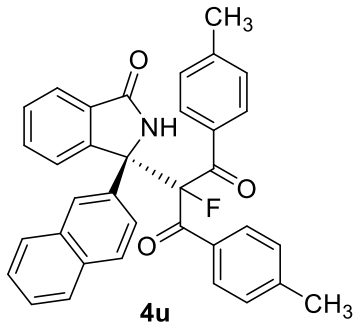
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.880	MM	0.5928	1964.72681	55.24300	10.1276
2	41.140	MM	1.4366	1.74350e4	202.26727	89.8724
Totals :				1.93997e4	257.51027	

HPLC chromatogram of **4t** chiral

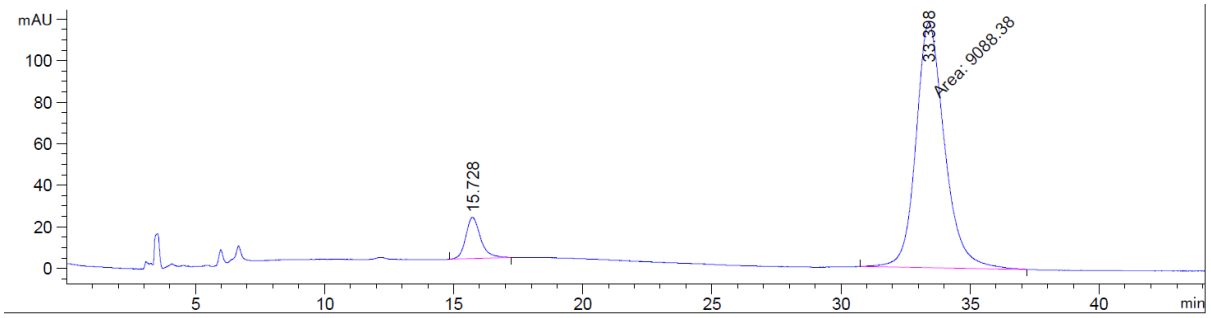


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.293	MM	0.6345	3006.79419	78.98090	51.0789
2	32.690	MM	1.1919	2879.77148	40.26720	48.9211
Totals :				5886.56567	119.24809	

HPLC chromatogram of **4u** racemic

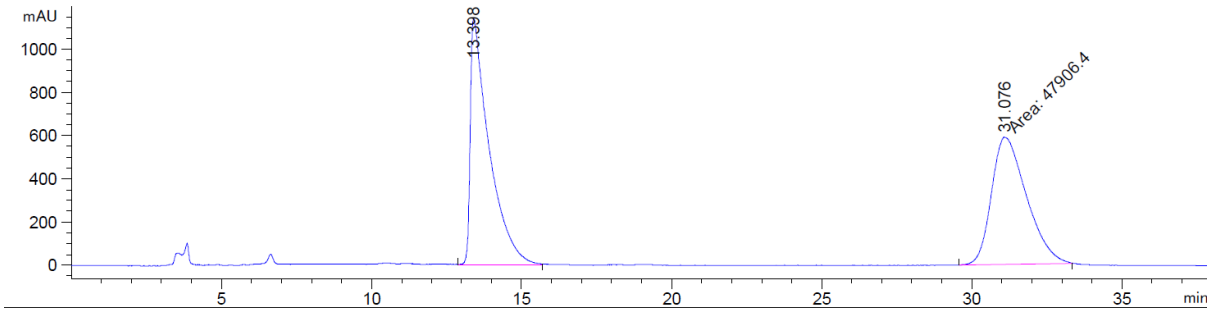


4u



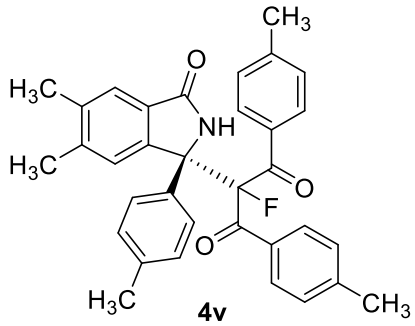
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.728	BB	0.5442	790.10626	19.77421	7.9983
2	33.398	MM	1.2861	9088.38184	117.77646	92.0017
Totals :				9878.48810	137.55067	

HPLC chromatogram of **4u** chiral

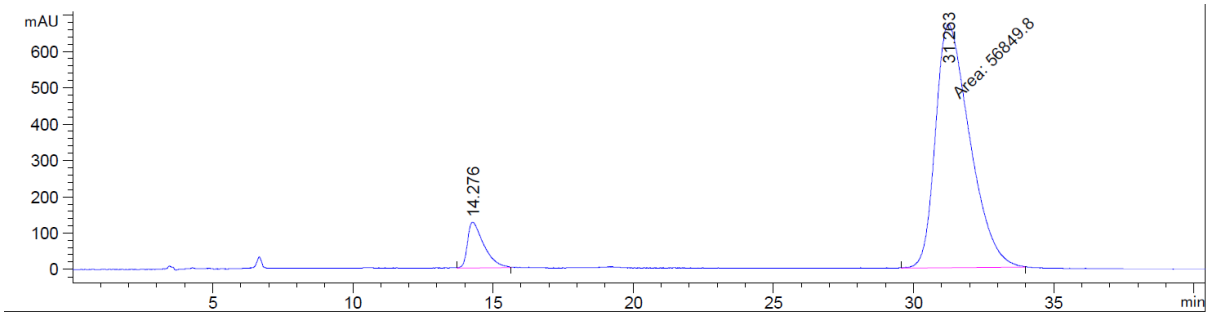


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.398	BV	0.5409	4.93449e4	1135.61365	50.7396
2	31.076	MM	1.3546	4.79064e4	589.40857	49.2604
Totals :				9.72513e4	1725.02222	

HPLC chromatogram of **4v** racemic

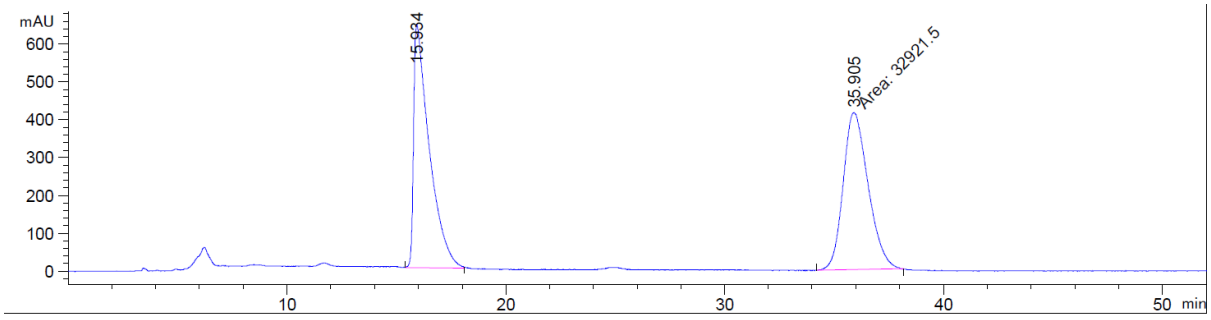


4v



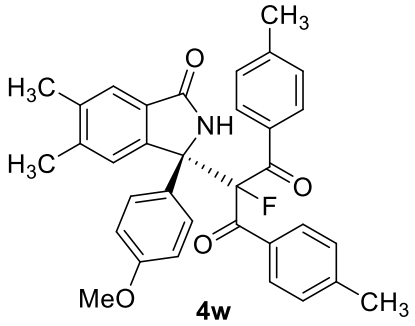
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.276	VV	0.5356	5050.03760	125.46751	8.1584
2	31.263	MM	1.4139	5.68498e4	670.10645	91.8416
Totals :				6.18998e4	795.57396	

HPLC chromatogram of **4v** chiral

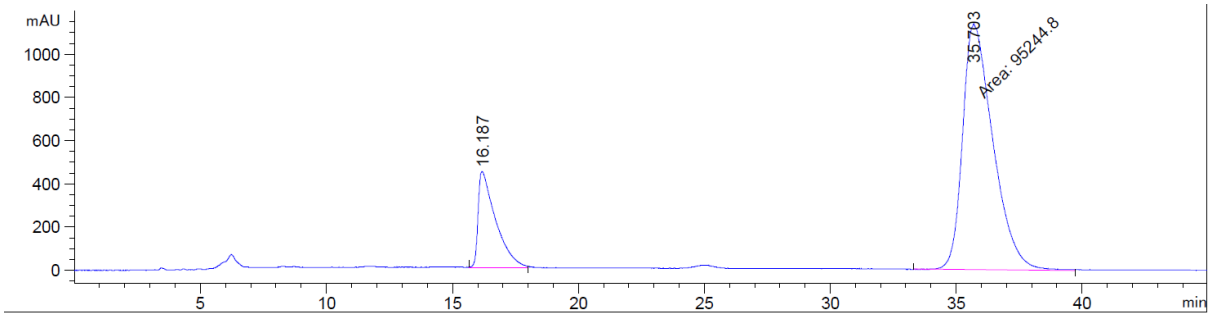


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.934	BV	0.6371	3.19340e4	643.34369	49.2387
2	35.905	MM	1.3211	3.29215e4	415.34058	50.7613
Totals :				6.48555e4	1058.68427	

HPLC chromatogram of **4w** racemic

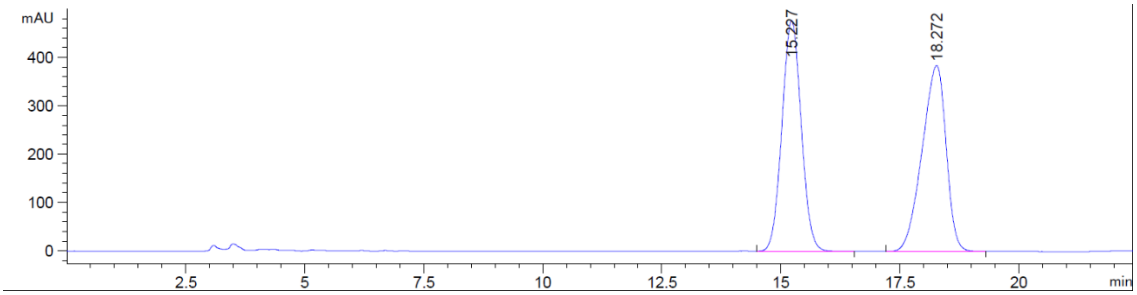


4w



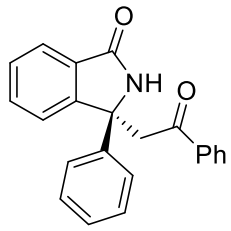
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.187	VV	0.6244	2.12817e4	443.05759	18.2634
2	35.703	MM	1.3935	9.52448e4	1139.16931	81.7366
Totals :				1.16526e5	1582.22690	

HPLC chromatogram of **4w** chiral

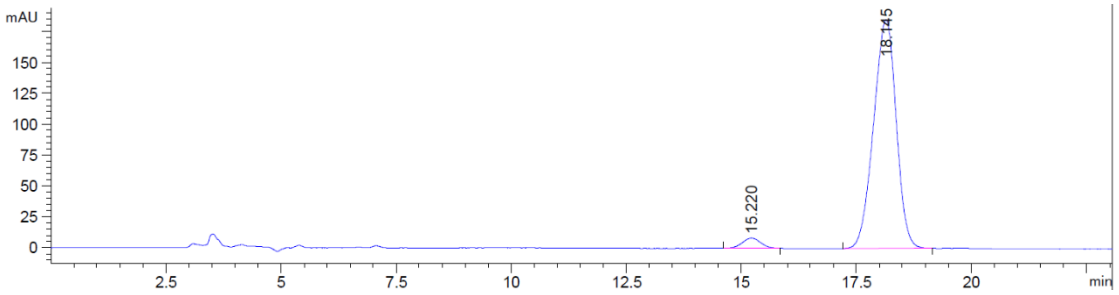


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.227	BB	0.4384	1.33906e4	475.75555	49.8250
2	18.272	BB	0.5382	1.34846e4	383.49411	50.1750
Totals :				2.68752e4	859.24966	

HPLC chromatogram of **5** racemic



5



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.220	BB	0.3542	227.80238	8.24848	3.4746
2	18.145	BB	0.5393	6328.32520	184.91411	96.5254
Totals :				6556.12758	193.16259	

HPLC chromatogram of **5** chiral